

Supplementary Table 1: Significant Pathways of the RA associated genes from RADB database

description_RA	adjustedPValue_RA	pValue_RA
immune system process	1.63E-71	4.41E-75
immune response	6.05E-64	3.28E-67
regulation of immune system process	1.67E-48	1.36E-51
regulation of response to stimulus	4.55E-48	4.93E-51
regulation of cytokine production	1.89E-40	2.56E-43
regulation of immune response	1.01E-39	1.85E-42
defense response	1.01E-39	1.91E-42
positive regulation of immune system process	1.33E-39	2.88E-42
response to stimulus	1.28E-35	3.12E-38
positive regulation of biological process	1.11E-34	3.26E-37
regulation of defense response	1.11E-34	3.3E-37
response to stress	2E-33	6.51E-36
regulation of multicellular organismal process	1.56E-31	5.48E-34
positive regulation of cellular process	1.46E-29	5.56E-32
positive regulation of response to stimulus	3.91E-29	1.59E-31
regulation of immune effector process	5.67E-29	2.6E-31
regulation of leukocyte activation	5.67E-29	2.61E-31
regulation of cell activation	1.08E-28	5.27E-31
regulation of lymphocyte activation	2.16E-28	1.11E-30
inflammatory response	3.44E-28	1.87E-30

regulation of T cell activation	1.23E-27	7.03E-30
multi-organism process	4.65E-27	2.78E-29
response to chemical stimulus	2.47E-26	1.54E-28
regulation of response to stress	3.96E-26	2.57E-28
response to wounding	6.53E-26	4.43E-28
cell activation	7.01E-26	4.94E-28
regulation of T cell proliferation	6.28E-25	4.6E-27
regulation of lymphocyte proliferation	7.11E-25	5.4E-27
regulation of mononuclear cell proliferation	1.03E-24	8.1E-27
regulation of leukocyte proliferation	1.48E-24	1.21E-26
response to molecule of bacterial origin	1.56E-24	1.31E-26
regulation of interleukin-6 production	3.89E-24	3.37E-26
positive regulation of cytokine production	2.73E-23	2.44E-25
regulation of adaptive immune response based on somatic recombination of immune receptors built from immunoglobulin superfamily domains	3.07E-23	2.83E-25
innate immune response	3.44E-23	3.26E-25
negative regulation of biological process	4.24E-23	4.14E-25
regulation of adaptive immune response	5.37E-23	5.39E-25
response to other organism	7.01E-23	7.23E-25
signaling	8.07E-23	8.53E-25
regulation of response to external stimulus	9.03E-23	9.8E-25
regulation of cytokine biosynthetic process	9.03E-23	1E-24
response to biotic stimulus	1.45E-22	1.65E-24
positive regulation of multicellular organismal process	3.29E-22	3.84E-24
regulation of apoptosis	4.15E-22	4.95E-24
leukocyte activation	4.98E-22	6.08E-24
regulation of programmed cell death	7.54E-22	9.41E-24
negative regulation of immune system process	1.18E-21	1.5E-23

regulation of cell proliferation	1.18E-21	1.54E-23
regulation of cell death	1.23E-21	1.64E-23
response to bacterium	2.64E-21	3.58E-23
response to organic substance	5.8E-21	8.03E-23
antigen processing and presentation	6.24E-21	8.8E-23
positive regulation of lymphocyte activation	8.1E-21	1.16E-22
regulation of inflammatory response	1.2E-20	1.75E-22
positive regulation of defense response	1.52E-20	2.26E-22
positive regulation of leukocyte activation	1.6E-20	2.43E-22
regulation of localization	2.6E-20	4.02E-22
positive regulation of immune response	2.66E-20	4.18E-22
positive regulation of cell activation	6.33E-20	1.01E-21
biological regulation	1.66E-19	2.7E-21
response to lipopolysaccharide	1.92E-19	3.17E-21
I-kappaB kinase/NF-kappaB cascade	3.16E-19	5.32E-21
regulation of biological process	3.3E-19	5.64E-21
positive regulation of cell communication	3.55E-19	6.16E-21
positive regulation of T cell activation	4.07E-19	7.18E-21
regulation of leukocyte mediated immunity	1.64E-18	2.93E-20
regulation of protein transport	2.09E-18	3.8E-20
negative regulation of response to stimulus	2.47E-18	4.59E-20
regulation of innate immune response	2.47E-18	4.62E-20
positive regulation of metabolic process	2.74E-18	5.2E-20
positive regulation of signal transduction	2.94E-18	5.66E-20
regulation of transport	3.38E-18	6.6E-20
positive regulation of signaling process	5.89E-18	1.17E-19
positive regulation of signaling pathway	6.48E-18	1.3E-19
regulation of lymphocyte mediated immunity	9.98E-18	2.03E-19
regulation of establishment of protein localization	1.09E-17	2.24E-19

positive regulation of cytokine biosynthetic process	1.61E-17	3.36E-19
signaling pathway	1.63E-17	3.44E-19
signal transduction	3.5E-17	7.49E-19
regulation of signaling pathway	4.17E-17	9.04E-19
regulation of developmental process	4.56E-17	1E-18
regulation of signal transduction	4.74E-17	1.05E-18
positive regulation of cellular metabolic process	4.83E-17	1.09E-18
regulation of protein localization	5.08E-17	1.16E-18
negative regulation of cellular process	5.86E-17	1.35E-18
regulation of cell communication	6.18E-17	1.44E-18
regulation of signaling process	6.42E-17	1.52E-18
regulation of cellular process	6.86E-17	1.64E-18
positive regulation of protein transport	7.62E-17	1.85E-18
lymphocyte activation	7.62E-17	1.86E-18
positive regulation of macromolecule metabolic process	1.12E-16	2.77E-18
positive regulation of innate immune response	1.19E-16	2.97E-18
positive regulation of lymphocyte proliferation	1.92E-16	4.84E-18
positive regulation of transport	2.7E-16	6.89E-18
positive regulation of mononuclear cell proliferation	2.76E-16	7.12E-18
positive regulation of leukocyte proliferation	3.99E-16	1.04E-17
regulation of production of molecular mediator of immune response	6.63E-16	1.74E-17
signal transmission	9.67E-16	2.59E-17
signaling process	9.67E-16	2.59E-17
response to external stimulus	1.6E-15	4.33E-17
adaptive immune response based on somatic recombination of immune receptors built from immunoglobulin superfamily domains	1.6E-15	4.38E-17
positive regulation of T cell proliferation	1.86E-15	5.15E-17

adaptive immune response	2.21E-15	6.17E-17
positive regulation of intracellular protein kinase cascade	3.21E-15	9.05E-17
positive regulation of interleukin-6 production	3.6E-15	1.03E-16
regulation of protein secretion	4.2E-15	1.21E-16
regulation of intracellular protein kinase cascade	5.31E-15	1.54E-16
positive regulation of molecular function	5.34E-15	1.56E-16
negative regulation of apoptosis	1.18E-14	3.49E-16
positive regulation of cell proliferation	1.48E-14	4.42E-16
regulation of transcription factor activity	1.53E-14	4.64E-16
regulation of transcription regulator activity	1.53E-14	4.64E-16
intracellular protein kinase cascade	1.63E-14	5.03E-16
signal transmission via phosphorylation event	1.63E-14	5.03E-16
positive regulation of protein secretion	1.85E-14	5.79E-16
negative regulation of programmed cell death	1.85E-14	5.81E-16
T cell activation	3.64E-14	1.16E-15
negative regulation of defense response	3.9E-14	1.25E-15
negative regulation of cell death	3.98E-14	1.29E-15
interspecies interaction between organisms	3.98E-14	1.3E-15
positive regulation of transcription factor activity	5.62E-14	1.86E-15
positive regulation of transcription regulator activity	5.62E-14	1.86E-15
regulation of biological quality	6.06E-14	2.02E-15
regulation of interleukin-12 production	6.63E-14	2.24E-15
regulation of interferon-gamma production	6.63E-14	2.25E-15
negative regulation of cytokine production	9.31E-14	3.18E-15
positive regulation of cellular biosynthetic process	1.07E-13	3.67E-15
immune response-regulating signaling pathway	1.54E-13	5.36E-15
mononuclear cell proliferation	1.93E-13	6.75E-15
positive regulation of response to external stimulus	2.05E-13	7.24E-15
regulation of binding	2.06E-13	7.32E-15

positive regulation of biosynthetic process	2.11E-13	7.56E-15
leukocyte migration	2.92E-13	1.06E-14
negative regulation of cell activation	2.92E-13	1.06E-14
leukocyte proliferation	2.99E-13	1.09E-14
regulation of chemokine production	3.23E-13	1.19E-14
positive regulation of NF-kappaB transcription factor activity	3.94E-13	1.46E-14
regulation of cellular localization	4.41E-13	1.65E-14
negative regulation of leukocyte activation	5.56E-13	2.1E-14
regulation of DNA binding	5.84E-13	2.22E-14
positive regulation of DNA binding	8.53E-13	3.26E-14
response to endogenous stimulus	8.81E-13	3.39E-14
response to steroid hormone stimulus	9.41E-13	3.65E-14
anti-apoptosis	1.07E-12	4.16E-14
negative regulation of multicellular organismal process	1.2E-12	4.7E-14
innate immune response-activating signal transduction	1.2E-12	4.74E-14
negative regulation of cell proliferation	1.27E-12	5.07E-14
negative regulation of lymphocyte activation	1.41E-12	5.64E-14
immune effector process	1.93E-12	7.81E-14
activation of innate immune response	2.65E-12	1.08E-13
positive regulation of binding	2.86E-12	1.17E-13
interaction with host	3.66E-12	1.51E-13
response to hypoxia	7.89E-12	3.28E-13
antigen processing and presentation of peptide or polysaccharide antigen via MHC class II	1E-11	4.2E-13
pattern recognition receptor signaling pathway	1E-11	4.2E-13
regulation of I-kappaB kinase/NF-kappaB cascade	1.05E-11	4.44E-13
negative regulation of T cell activation	1.28E-11	5.45E-13
activation of immune response	1.54E-11	6.59E-13
regulation of molecular function	1.71E-11	7.36E-13

regulation of cell differentiation	1.77E-11	7.66E-13
regulation of immunoglobulin production	2.09E-11	9.12E-13
regulation of B cell activation	2.1E-11	9.21E-13
negative regulation of immune effector process	2.2E-11	9.71E-13
cytokine production	2.69E-11	1.2E-12
regulation of smooth muscle cell proliferation	2.69E-11	1.2E-12
lymphocyte proliferation	2.88E-11	1.3E-12
response to oxygen levels	2.98E-11	1.35E-12
positive regulation of chemokine production	3.13E-11	1.43E-12
regulation of locomotion	3.21E-11	1.47E-12
cell surface receptor linked signaling pathway	3.24E-11	1.5E-12
response to drug	3.24E-11	1.5E-12
cytokine-mediated signaling pathway	3.33E-11	1.56E-12
negative regulation of leukocyte proliferation	3.63E-11	1.72E-12
negative regulation of lymphocyte proliferation	3.63E-11	1.72E-12
negative regulation of mononuclear cell proliferation	3.63E-11	1.72E-12
initiation of signal transduction	4.2E-11	2.03E-12
signal initiation by diffusible mediator	4.2E-11	2.03E-12
signal initiation by protein/peptide mediator	4.2E-11	2.03E-12
locomotion	4.4E-11	2.14E-12
response to hormone stimulus	4.73E-11	2.31E-12
negative regulation of T cell proliferation	6.28E-11	3.08E-12
immune response-activating signal transduction	6.93E-11	3.42E-12
cellular response to stimulus	7.62E-11	3.78E-12
regulation of protein metabolic process	7.74E-11	3.86E-12
positive regulation of macromolecule biosynthetic process	7.97E-11	4E-12
regulation of interleukin-8 production	8.51E-11	4.29E-12
positive regulation of nitrogen compound metabolic process	8.87E-11	4.5E-12
regulation of leukocyte migration	8.89E-11	4.53E-12

symbiosis, encompassing mutualism through parasitism	9.09E-11	4.66E-12
positive regulation of developmental process	9.4E-11	4.84E-12
response to cytokine stimulus	1.19E-10	6.15E-12
regulation of tumor necrosis factor production	1.37E-10	7.14E-12
regulation of secretion	1.48E-10	7.74E-12
immune system development	2.09E-10	1.1E-11
negative regulation of transport	2.61E-10	1.38E-11
regulation of protein amino acid phosphorylation	2.72E-10	1.45E-11
regulation of cytokine secretion	3.15E-10	1.68E-11
positive regulation of gene expression	3.71E-10	1.99E-11
intracellular signaling pathway	3.71E-10	2E-11
microglial cell activation involved in immune response	3.9E-10	2.11E-11
regulation of protein modification process	4.47E-10	2.44E-11
regulation of interleukin-2 production	4.52E-10	2.48E-11
positive regulation of interleukin-12 production	4.85E-10	2.67E-11
regulation of NF-kappaB import into nucleus	5.06E-10	2.8E-11
positive regulation of catalytic activity	5.98E-10	3.33E-11
positive regulation of apoptosis	6.53E-10	3.65E-11
regulation of interleukin-2 biosynthetic process	7.02E-10	3.94E-11
positive regulation of programmed cell death	8.03E-10	4.53E-11
antigen processing and presentation of peptide antigen	8.58E-10	4.86E-11
positive regulation of phosphorylation	8.62E-10	4.91E-11
hemopoietic or lymphoid organ development	8.87E-10	5.08E-11
defense response to bacterium	8.97E-10	5.16E-11
cell activation involved in immune response	9.39E-10	5.45E-11
leukocyte activation involved in immune response	9.39E-10	5.45E-11
positive regulation of cell death	1.03E-09	6.01E-11
positive regulation of protein amino acid phosphorylation	1.04E-09	6.08E-11
negative regulation of response to external stimulus	1.04E-09	6.1E-11

positive regulation of protein modification process	1.15E-09	6.8E-11
positive regulation of phosphate metabolic process	1.3E-09	7.77E-11
positive regulation of phosphorus metabolic process	1.3E-09	7.77E-11
positive regulation of secretion	1.3E-09	7.77E-11
regulation of transcription factor import into nucleus	1.3E-09	7.86E-11
toll-like receptor signaling pathway	1.3E-09	7.87E-11
hemopoiesis	1.38E-09	8.4E-11
I-kappaB phosphorylation	1.56E-09	9.53E-11
cellular response to biotic stimulus	1.68E-09	1.03E-10
regulation of phosphorylation	2.28E-09	1.4E-10
regulation of B cell mediated immunity	2.29E-09	1.42E-10
regulation of immunoglobulin mediated immune response	2.29E-09	1.42E-10
leukocyte chemotaxis	2.53E-09	1.58E-10
response to defenses of other organism involved in symbiotic interaction	2.61E-09	1.65E-10
response to host	2.61E-09	1.65E-10
response to host defenses	2.61E-09	1.65E-10
leukocyte differentiation	2.89E-09	1.84E-10
negative regulation of developmental process	2.97E-09	1.89E-10
positive regulation of I-kappaB kinase/NF-kappaB cascade	3.07E-09	1.96E-10
intracellular signal transduction	3.33E-09	2.15E-10
positive regulation of cytokine secretion	3.33E-09	2.16E-10
regulation of cell killing	3.33E-09	2.16E-10
positive regulation of immune effector process	3.38E-09	2.2E-10
homeostatic process	4.26E-09	2.78E-10
regulation of cell migration	5.29E-09	3.47E-10
cell migration	6.11E-09	4.03E-10
positive regulation of nucleobase, nucleoside, nucleotide and nucleic acid metabolic process	6.23E-09	4.12E-10

positive regulation of B cell activation	6.59E-09	4.38E-10
regulation of cellular protein metabolic process	7.75E-09	5.17E-10
regulation of metabolic process	7.93E-09	5.33E-10
response to glucocorticoid stimulus	7.93E-09	5.33E-10
regulation of multi-organism process	8.35E-09	5.64E-10
regulation of protein import into nucleus	8.91E-09	6.08E-10
regulation of phosphate metabolic process	8.91E-09	6.09E-10
regulation of phosphorus metabolic process	8.91E-09	6.09E-10
regulation of angiogenesis	9.67E-09	6.99E-10
macrophage activation	9.67E-09	7.05E-10
modulation by organism of defense response of other organism involved in symbiotic interaction	9.67E-09	7.13E-10
modulation by organism of immune response of other organism involved in symbiotic interaction	9.67E-09	7.13E-10
modulation by organism of innate immunity in other organism involved in symbiotic interaction	9.67E-09	7.13E-10
modulation by symbiont of host defense response	9.67E-09	7.13E-10
modulation by symbiont of host immune response	9.67E-09	7.13E-10
modulation by symbiont of host innate immunity	9.67E-09	7.13E-10
pathogen-associated molecular pattern dependent induction by organism of innate immunity of other organism involved in symbiotic interaction	9.67E-09	7.13E-10
pathogen-associated molecular pattern dependent induction by symbiont of host innate immunity	9.67E-09	7.13E-10
pathogen-associated molecular pattern dependent modulation by organism of innate immunity in other organism involved in symbiotic interaction	9.67E-09	7.13E-10
pathogen-associated molecular pattern dependent modulation by symbiont of host innate immunity	9.67E-09	7.13E-10

positive regulation by organism of defense response of other organism involved in symbiotic interaction	9.67E-09	7.13E-10
positive regulation by organism of immune response of other organism involved in symbiotic interaction	9.67E-09	7.13E-10
positive regulation by organism of innate immunity in other organism involved in symbiotic interaction	9.67E-09	7.13E-10
positive regulation by symbiont of host defense response	9.67E-09	7.13E-10
positive regulation by symbiont of host immune response	9.67E-09	7.13E-10
positive regulation by symbiont of host innate immunity	9.67E-09	7.13E-10
response to host immune response	9.67E-09	7.13E-10
response to immune response of other organism involved in symbiotic interaction	9.67E-09	7.13E-10
regulation of interferon-alpha production	9.76E-09	7.22E-10
regulation of leukocyte mediated cytotoxicity	9.83E-09	7.3E-10
cell chemotaxis	1.02E-08	7.58E-10
positive regulation of locomotion	1.05E-08	7.82E-10
regulation of nitric oxide biosynthetic process	1.05E-08	7.85E-10
regulation of peptidyl-tyrosine phosphorylation	1.14E-08	8.57E-10
positive regulation of cellular protein metabolic process	1.16E-08	8.81E-10
positive regulation of protein metabolic process	1.17E-08	8.85E-10
cellular response to chemical stimulus	1.48E-08	1.13E-09
negative regulation of inflammatory response	1.52E-08	1.16E-09
positive regulation of adaptive immune response based on somatic recombination of immune receptors built from immunoglobulin superfamily domains	1.54E-08	1.18E-09
positive regulation of nitric oxide biosynthetic process	1.54E-08	1.18E-09
positive regulation of peptidyl-tyrosine phosphorylation	1.56E-08	1.21E-09
regulation of intracellular protein transport	1.65E-08	1.28E-09
positive regulation of kinase activity	1.67E-08	1.3E-09
chemotaxis	1.73E-08	1.35E-09

taxis	1.73E-08	1.35E-09
regulation of macromolecule metabolic process	1.77E-08	1.39E-09
regulation of behavior	1.89E-08	1.49E-09
cell motility	1.96E-08	1.56E-09
localization of cell	1.96E-08	1.56E-09
regulation of interleukin-6 biosynthetic process	2.01E-08	1.6E-09
positive regulation of inflammatory response	2.09E-08	1.67E-09
response to corticosteroid stimulus	2.17E-08	1.74E-09
positive regulation of adaptive immune response	2.33E-08	1.87E-09
aging	0.000000028	2.27E-09
regulation of nucleocytoplasmic transport	2.81E-08	2.28E-09
cellular response to molecule of bacterial origin	2.84E-08	2.31E-09
macrophage activation involved in immune response	2.85E-08	2.35E-09
microglial cell activation	2.85E-08	2.35E-09
positive regulation of interleukin-8 production	2.85E-08	2.35E-09
positive regulation of protein kinase activity	3.07E-08	2.53E-09
leukocyte mediated immunity	3.32E-08	2.75E-09
lymphocyte differentiation	0.000000035	2.9E-09
positive regulation of transferase activity	3.55E-08	2.96E-09
positive regulation of cellular component organization	3.65E-08	3.05E-09
regulation of cellular component movement	3.98E-08	3.34E-09
positive regulation of transcription	4.67E-08	3.92E-09
negative regulation of immune response	0.000000052	4.39E-09
regulation of gene-specific transcription	6.32E-08	5.35E-09
response to abiotic stimulus	6.55E-08	5.56E-09
positive regulation of smooth muscle cell proliferation	7.65E-08	6.52E-09
positive regulation of transcription from RNA polymerase II promoter	7.81E-08	6.67E-09
humoral immune response	8.67E-08	7.43E-09

positive regulation of RNA metabolic process	8.76E-08	7.53E-09
positive regulation of cell migration	0.000000102	8.75E-09
response to peptide hormone stimulus	0.000000114	9.87E-09
regulation of cellular metabolic process	0.000000122	1.06E-08
cellular component movement	0.000000135	1.17E-08
regulation of T cell mediated immunity	0.000000137	0.000000012
positive regulation of leukocyte migration	0.000000156	1.37E-08
B cell proliferation	0.000000167	1.47E-08
regulation of isotype switching	0.000000167	1.47E-08
myeloid leukocyte activation	0.000000178	1.57E-08
positive regulation of transcription, DNA-dependent	0.000000187	1.66E-08
regulation of homeostatic process	0.000000188	1.67E-08
positive regulation of isotype switching	0.000000213	0.000000019
regulation of B cell proliferation	0.000000216	1.94E-08
regulation of cytokine production involved in immune response	0.000000234	0.000000021
positive regulation of isotype switching to IgG isotypes	0.000000266	0.000000024
regulation of interferon-alpha biosynthetic process	0.000000266	0.000000024
regulation of chemotaxis	0.000000283	2.56E-08
response to insulin stimulus	0.000000299	2.72E-08
positive regulation of cellular component movement	0.0000003	2.73E-08
regulation of intracellular transport	0.000000313	2.86E-08
T cell differentiation	0.000000324	2.97E-08
multicellular organismal homeostasis	0.000000331	3.04E-08
positive regulation of interferon-gamma production	0.000000333	0.000000031
positive regulation of interleukin-2 biosynthetic process	0.000000333	0.000000031
positive regulation of NF-kappaB import into nucleus	0.000000333	0.000000031
positive regulation of tumor necrosis factor production	0.000000333	0.000000031
B cell activation	0.000000375	0.000000035

regulation of type I interferon production	0.000000377	3.53E-08
regulation of catalytic activity	0.000000377	3.54E-08
lymphocyte mediated immunity	0.000000386	3.64E-08
negative regulation of NF-kappaB transcription factor activity	0.000000386	3.66E-08
response to gamma radiation	0.000000386	3.66E-08
system development	0.000000416	3.94E-08
negative regulation of cell differentiation	0.000000416	3.96E-08
response to virus	0.000000517	4.94E-08
response to estrogen stimulus	0.000000521	4.98E-08
positive regulation of JAK-STAT cascade	0.000000555	5.34E-08
regulation of DNA recombination	0.000000555	5.34E-08
modification by symbiont of host morphology or physiology	0.00000057	5.54E-08
positive regulation of DNA recombination	0.00000057	5.54E-08
regulation of immunoglobulin secretion	0.00000057	5.54E-08
regulation of toll-like receptor signaling pathway	0.00000057	5.54E-08
detection of biotic stimulus	0.000000587	5.73E-08
organ development	0.000000613	0.00000006
regulation of JAK-STAT cascade	0.000000696	6.85E-08
regulation of response to biotic stimulus	0.000000696	6.85E-08
positive regulation of leukocyte mediated immunity	0.000000774	7.66E-08
positive regulation of lymphocyte mediated immunity	0.000000774	7.66E-08
regulation of lymphocyte differentiation	0.000000793	7.87E-08
positive regulation of behavior	0.00000105	0.000000105
anatomical structure homeostasis	0.00000119	0.000000119
regulation of T cell differentiation	0.00000132	0.000000132
negative regulation of interleukin-6 production	0.00000134	0.000000135
T-helper 1 type immune response	0.00000134	0.000000135
defense response to virus	0.00000137	0.000000138

positive regulation of interleukin-6 biosynthetic process	0.00000139	0.00000014
homeostasis of number of cells	0.0000014	0.000000142
regulation of lipid transport	0.00000155	0.000000158
positive regulation of MAPKKK cascade	0.00000156	0.000000159
regulation of alpha-beta T cell activation	0.00000202	0.000000206
behavior	0.00000207	0.000000213
locomotory behavior	0.00000209	0.000000215
response to temperature stimulus	0.0000021	0.000000216
positive regulation of chemotaxis	0.00000255	0.000000264
regulation of system process	0.0000026	0.000000269
defense response to Gram-negative bacterium	0.00000277	0.00000029
negative regulation of alpha-beta T cell activation	0.00000277	0.00000029
regulation of chemokine biosynthetic process	0.00000277	0.00000029
response to peptidoglycan	0.00000277	0.00000029
tissue homeostasis	0.00000296	0.000000311
antigen processing and presentation of peptide antigen via MHC class I	0.000003	0.000000316
positive regulation of interleukin-1 production	0.000003	0.000000316
regulation of myeloid cell differentiation	0.000003	0.000000317
positive regulation of angiogenesis	0.00000402	0.000000428
positive regulation of intracellular protein transport	0.00000402	0.000000428
positive regulation of B cell proliferation	0.00000404	0.000000431
oxygen and reactive oxygen species metabolic process	0.00000416	0.000000444
cell death	0.00000424	0.000000454
tissue remodeling	0.00000439	0.000000476
chronic inflammatory response	0.00000439	0.000000479
positive regulation of interferon-beta biosynthetic process	0.00000439	0.000000479
positive regulation of interleukin-12 biosynthetic process	0.00000439	0.000000479
positive regulation of MHC class II biosynthetic process	0.00000439	0.000000479

regulation of calcidiol 1-monooxygenase activity	0.00000439	0.000000479
regulation of interferon-beta biosynthetic process	0.00000439	0.000000479
regulation of isotype switching to IgG isotypes	0.00000439	0.000000479
apoptosis	0.00000441	0.000000483
negative regulation of myeloid cell differentiation	0.00000451	0.000000496
positive regulation of transcription factor import into nucleus	0.00000458	0.000000505
positive regulation of organelle organization	0.00000467	0.000000515
regulation of primary metabolic process	0.00000473	0.000000524
response to ionizing radiation	0.00000476	0.000000528
death	0.000005	0.000000555
anatomical structure development	0.00000506	0.000000564
negative regulation of ion transport	0.00000541	0.000000606
regulation of interleukin-1 production	0.00000541	0.000000606
immune response-regulating cell surface receptor signaling pathway	0.00000601	0.000000674
positive regulation of gene-specific transcription	0.00000666	0.000000749
programmed cell death	0.0000067	0.000000756
positive regulation of cell differentiation	0.00000694	0.000000785
positive regulation of MAP kinase activity	0.00000694	0.000000787
positive regulation of interferon-alpha biosynthetic process	0.00000706	0.000000805
regulation of interleukin-17 production	0.00000706	0.000000805
smooth muscle adaptation	0.00000706	0.000000805
multicellular organismal catabolic process	0.00000728	0.000000839
positive regulation of intracellular transport	0.00000728	0.000000839
positive regulation of stress-activated protein kinase signaling cascade	0.00000728	0.000000839
regulation of acute inflammatory response	0.00000728	0.000000839
negative regulation of transcription factor activity	0.0000073	0.000000845
negative regulation of transcription regulator activity	0.0000073	0.000000845

cell proliferation	0.00000854	0.000000991
multicellular organismal development	0.00000855	0.000000994
negative regulation of macrophage derived foam cell differentiation	0.00000867	0.00000102
negative regulation of smooth muscle cell proliferation	0.00000867	0.00000102
positive regulation of interleukin-1 secretion	0.00000867	0.00000102
regulation of activated T cell proliferation	0.00000867	0.00000102
regulation of interferon-gamma biosynthetic process	0.00000867	0.00000102
respiratory burst	0.00000867	0.00000102
regulation of leukocyte chemotaxis	0.00000965	0.00000114
regulation of viral reproduction	0.00000965	0.00000114
myeloid cell activation involved in immune response	0.0000098	0.00000117
regulation of phagocytosis	0.0000098	0.00000117
response to nutrient levels	0.0000101	0.00000121
detection of molecule of bacterial origin	0.0000103	0.00000125
hydrogen peroxide biosynthetic process	0.0000103	0.00000125
negative regulation of leukocyte mediated immunity	0.0000103	0.00000125
negative regulation of lymphocyte mediated immunity	0.0000103	0.00000125
positive regulation of chemokine biosynthetic process	0.0000103	0.00000125
regulation of interleukin-12 biosynthetic process	0.0000103	0.00000125
regulation of transcription from RNA polymerase II promoter	0.0000104	0.00000126
regulation of transferase activity	0.0000106	0.00000128
response to extracellular stimulus	0.000012	0.00000146
regulation of MAPKKK cascade	0.0000137	0.00000167
developmental process	0.0000138	0.0000017
negative regulation of cytokine biosynthetic process	0.0000138	0.0000017
positive regulation of JNK cascade	0.0000138	0.0000017
regulation of kinase activity	0.0000138	0.0000017

cellular defense response	0.0000139	0.00000172
negative regulation of lipid storage	0.0000141	0.00000174
regulation of interleukin-1 secretion	0.0000141	0.00000174
positive regulation of nucleocytoplasmic transport	0.0000164	0.00000204
regulation of tyrosine phosphorylation of STAT protein	0.0000164	0.00000204
regulation of cell adhesion	0.0000179	0.00000223
blood circulation	0.0000179	0.00000224
circulatory system process	0.0000179	0.00000224
positive regulation of lipid metabolic process	0.0000183	0.0000023
response to radiation	0.0000183	0.0000023
regulation of protein kinase activity	0.0000189	0.00000238
wound healing	0.000019	0.0000024
modification of morphology or physiology of other organism involved in symbiotic interaction	0.0000192	0.00000244
positive regulation of cell killing	0.0000192	0.00000244
T cell proliferation	0.0000192	0.00000244
positive regulation of response to biotic stimulus	0.0000215	0.00000273
regulation of vascular endothelial growth factor production	0.0000221	0.00000283
regulation of viral genome replication	0.0000221	0.00000283
negative regulation of molecular function	0.0000242	0.00000311
regulation of MAP kinase activity	0.0000251	0.00000322
negative regulation of DNA binding	0.0000256	0.0000033
negative regulation of binding	0.0000261	0.00000336
positive regulation of protein import into nucleus	0.0000263	0.00000341
positive regulation of tyrosine phosphorylation of STAT protein	0.0000263	0.00000341
leukocyte homeostasis	0.0000268	0.00000348
di-, tri-valent inorganic cation homeostasis	0.0000269	0.0000035
metal ion homeostasis	0.0000291	0.00000379

regulation of gene-specific transcription from RNA polymerase II promoter	0.0000295	0.00000386
interleukin-1-mediated signaling pathway	0.0000298	0.00000393
MyD88-dependent toll-like receptor signaling pathway	0.0000298	0.00000393
negative regulation of receptor biosynthetic process	0.0000298	0.00000393
organ or tissue specific immune response	0.0000298	0.00000393
response to lipoprotein stimulus	0.0000298	0.00000393
multicellular organismal macromolecule metabolic process	0.0000338	0.00000448
calcium ion homeostasis	0.0000375	0.00000498
negative regulation of multi-organism process	0.00004	0.00000533
positive regulation of activated T cell proliferation	0.00004	0.00000533
regulation of MHC class II biosynthetic process	0.00004	0.00000533
negative regulation of protein metabolic process	0.0000473	0.00000632
regulation of blood pressure	0.0000479	0.00000641
cellular response to lipopolysaccharide	0.0000495	0.00000665
regulation of interferon-beta production	0.0000495	0.00000665
cellular metal ion homeostasis	0.00005	0.00000674
negative regulation of secretion	0.0000517	0.00000698
regulation of macrophage derived foam cell differentiation	0.0000626	0.00000846
regulation of myeloid leukocyte differentiation	0.0000672	0.00000911
positive regulation of interferon-gamma biosynthetic process	0.0000701	0.00000954
positive regulation of T cell mediated immunity	0.0000701	0.00000954
natural killer cell activation	0.000071	0.00000973
neutrophil chemotaxis	0.000071	0.00000973
positive regulation of leukocyte mediated cytotoxicity	0.000071	0.00000973
regulation of biosynthetic process	0.0000758	0.0000104
cellular calcium ion homeostasis	0.0000807	0.0000111
defense response to Gram-positive bacterium	0.0000807	0.0000111
regulation of lipid storage	0.0000807	0.0000111

regulation of growth	0.0000861	0.0000119
regulation of macromolecule biosynthetic process	0.0000861	0.0000119
viral reproductive process	0.0000894	0.0000124
response to nutrient	0.0000897	0.0000125
negative regulation of protein transport	0.0000934	0.000013
acute inflammatory response	0.0000977	0.0000136
lymphocyte activation involved in immune response	0.0000985	0.0000139
membrane protein proteolysis	0.0000985	0.0000139
negative regulation of transcription factor import into nucleus	0.0000985	0.0000139
positive regulation of lipid transport	0.0000985	0.0000139
regulation of anatomical structure morphogenesis	0.0000992	0.000014
positive regulation of T cell differentiation	0.000102	0.0000145
immunoglobulin mediated immune response	0.000109	0.0000155
positive regulation of interleukin-1 beta secretion	0.000112	0.0000159
positive regulation of stress-activated MAPK cascade	0.000112	0.0000159
positive regulation of survival gene product expression	0.000112	0.0000159
response to estradiol stimulus	0.000117	0.0000167
multicellular organismal metabolic process	0.000119	0.0000169
B cell mediated immunity	0.000128	0.0000183
negative regulation of macromolecule metabolic process	0.00013	0.0000186
regulation of cellular biosynthetic process	0.00013	0.0000186
response to heat	0.000134	0.0000192
cellular developmental process	0.000138	0.00002
negative regulation of cell communication	0.000139	0.00002
regeneration	0.000158	0.0000229
collagen metabolic process	0.000163	0.0000236
cell differentiation	0.000165	0.0000239
phagocytosis	0.000173	0.0000252

activation of NF-kappaB-inducing kinase activity	0.000173	0.0000253
multicellular organismal process	0.000173	0.0000253
regulation of interleukin-1 beta secretion	0.000173	0.0000253
negative regulation of growth	0.000174	0.0000255
chemical homeostasis	0.000176	0.0000259
negative regulation of innate immune response	0.000176	0.0000262
negative regulation of interferon-gamma production	0.000176	0.0000262
negative regulation of viral reproduction	0.000176	0.0000262
positive regulation of T-helper cell differentiation	0.000176	0.0000262
positive regulation of toll-like receptor signaling pathway	0.000176	0.0000262
regulation of smooth muscle cell apoptosis	0.000176	0.0000262
regulation of T cell mediated cytotoxicity	0.000176	0.0000262
collagen catabolic process	0.000176	0.0000263
negative regulation of protein import into nucleus	0.000176	0.0000263
virus-host interaction	0.000176	0.0000263
cellular response to bacterial lipopeptide	0.000176	0.000027
cellular response to bacterial lipoprotein	0.000176	0.000027
cytokine production involved in immune response	0.000176	0.000027
detection of bacterial lipopeptide	0.000176	0.000027
detection of bacterial lipoprotein	0.000176	0.000027
negative regulation of toll-like receptor signaling pathway	0.000176	0.000027
positive regulation of calcidiol 1-monooxygenase activity	0.000176	0.000027
positive regulation of interleukin-17 production	0.000176	0.000027
regulation of cell-cell adhesion involved in gastrulation	0.000176	0.000027
regulation of heterotypic cell-cell adhesion	0.000176	0.000027
response to bacterial lipopeptide	0.000176	0.000027
response to bacterial lipoprotein	0.000176	0.000027
induction of apoptosis	0.000193	0.0000295
positive regulation of lymphocyte differentiation	0.000194	0.0000297

elevation of cytosolic calcium ion concentration	0.000202	0.0000311
induction of programmed cell death	0.000202	0.0000311
viral reproduction	0.000215	0.0000332
blood vessel remodeling	0.000228	0.0000353
negative regulation of myeloid leukocyte differentiation	0.000228	0.0000353
positive regulation of cell cycle process	0.000232	0.0000359
regulation of cellular component organization	0.000235	0.0000365
regulation of stress-activated protein kinase signaling cascade	0.000236	0.0000367
cytokine biosynthetic process	0.000245	0.0000384
cytoplasmic sequestering of transcription factor	0.000245	0.0000384
positive regulation of interleukin-1 beta production	0.000245	0.0000384
cell-cell signaling	0.000258	0.0000404
negative regulation of signaling pathway	0.000283	0.0000445
positive regulation of ERK1 and ERK2 cascade	0.000291	0.0000458
positive regulation of leukocyte chemotaxis	0.000294	0.0000465
regulation of cholesterol transport	0.000294	0.0000465
regulation of interleukin-1 beta production	0.000294	0.0000465
regulation of sterol transport	0.000294	0.0000465
positive regulation of gene-specific transcription from RNA polymerase II promoter	0.000312	0.0000495
cellular di-, tri-valent inorganic cation homeostasis	0.000319	0.0000506
positive regulation of immune response to tumor cell	0.000319	0.0000512
positive regulation of response to tumor cell	0.000319	0.0000512
regulation of immune response to tumor cell	0.000319	0.0000512
regulation of response to tumor cell	0.000319	0.0000512
regulation of symbiosis, encompassing mutualism through parasitism	0.000319	0.0000512
regulation of T-helper 1 type immune response	0.000319	0.0000512

regulation of ossification	0.000319	0.0000513
cation homeostasis	0.000323	0.000052
cell communication	0.000329	0.000053
rhythmic process	0.000333	0.0000539
cytokine metabolic process	0.000345	0.0000561
negative regulation of lymphocyte differentiation	0.000345	0.0000561
negative regulation of tumor necrosis factor production	0.000345	0.0000561
positive regulation of type I interferon production	0.000345	0.0000561
negative regulation of metabolic process	0.000347	0.0000566
negative regulation of nucleocytoplasmic transport	0.00037	0.0000605
response to progesterone stimulus	0.00037	0.0000605
JAK-STAT cascade	0.000418	0.0000685
regulation of JNK cascade	0.000425	0.0000698
cytosolic calcium ion homeostasis	0.000466	0.0000766
lymphocyte homeostasis	0.000471	0.0000776
regulation of osteoclast differentiation	0.000471	0.0000776
cellular catabolic process	0.000476	0.0000785
negative regulation of fat cell differentiation	0.00048	0.0000796
positive regulation of phagocytosis	0.00048	0.0000796
regulation of stress-activated MAPK cascade	0.00048	0.0000796
regulation of ion transport	0.00048	0.0000798
cellular process	0.000487	0.0000811
negative regulation of NF-kappaB import into nucleus	0.000535	0.00009
positive regulation of CD4-positive, alpha beta T cell differentiation	0.000535	0.00009
positive regulation of fever	0.000535	0.00009
regulation of cholesterol efflux	0.000535	0.00009
regulation of fever	0.000535	0.00009
regulation of interleukin-8 biosynthetic process	0.000535	0.00009

anatomical structure morphogenesis	0.000541	0.000091
hydrogen peroxide metabolic process	0.000581	0.0000983
positive regulation of synaptic transmission	0.000581	0.0000983
regulation of RNA stability	0.000581	0.0000983
ion homeostasis	0.000596	0.000101
positive regulation of hydrolase activity	0.0006	0.000102
endocrine hormone secretion	0.000603	0.000105
innate immune response activating cell surface receptor signaling pathway	0.000603	0.000105
negative regulation of alpha-beta T cell proliferation	0.000603	0.000105
negative regulation of collagen biosynthetic process	0.000603	0.000105
negative regulation of cytokine production involved in immune response	0.000603	0.000105
negative regulation of humoral immune response	0.000603	0.000105
negative regulation of leukocyte mediated cytotoxicity	0.000603	0.000105
negative regulation of production of molecular mediator of immune response	0.000603	0.000105
positive regulation of muscle cell apoptosis	0.000603	0.000105
positive regulation of nitric-oxide synthase biosynthetic process	0.000603	0.000105
positive regulation of smooth muscle cell apoptosis	0.000603	0.000105
receptor biosynthetic process	0.000603	0.000105
regulation of interleukin-18 production	0.000603	0.000105
regulation of killing of cells of another organism	0.000603	0.000105
regulation of macrophage cytokine production	0.000603	0.000105
regulation of vitamin D biosynthetic process	0.000603	0.000105
regulation of vitamin metabolic process	0.000603	0.000105
response to L-ascorbic acid	0.000603	0.000105
T-helper 2 type immune response	0.000603	0.000105

negative regulation of calcium ion transport	0.000627	0.00011
positive regulation of acute inflammatory response	0.000627	0.00011
regulation of gene expression	0.000635	0.000112
positive regulation of endocytosis	0.000676	0.000119
leukocyte cell-cell adhesion	0.000698	0.000123
production of molecular mediator of immune response	0.000698	0.000123
response to toxin	0.000749	0.000132
ovulation cycle	0.000769	0.000136
response to oxidative stress	0.000788	0.00014
cellular ion homeostasis	0.0008	0.000142
lymph node development	0.000812	0.000146
macrophage chemotaxis	0.000812	0.000146
negative regulation of adaptive immune response	0.000812	0.000146
negative regulation of adaptive immune response based on somatic recombination of immune receptors built from immunoglobulin superfamily domains	0.000812	0.000146
negative regulation of cytokine secretion	0.000812	0.000146
negative regulation of I-kappaB kinase/NF-kappaB cascade	0.000812	0.000146
positive regulation of heat generation	0.000812	0.000146
regulation of heat generation	0.000812	0.000146
regulation of muscle cell apoptosis	0.000812	0.000146
regulation of receptor biosynthetic process	0.000812	0.000146
cytoplasmic sequestering of protein	0.000818	0.000149
ovulation	0.000818	0.000149
positive regulation of alpha-beta T cell differentiation	0.000818	0.000149
regulation of natural killer cell mediated cytotoxicity	0.000818	0.000149
regulation of natural killer cell mediated immunity	0.000818	0.000149
negative regulation of intracellular protein transport	0.000837	0.000153
regulation of cell-cell adhesion	0.000837	0.000153

regulation of fat cell differentiation	0.000837	0.000153
response to interleukin-1	0.000837	0.000153
response to organic cyclic substance	0.000878	0.000161
regulation of endopeptidase activity	0.000928	0.00017
cellular chemical homeostasis	0.000993	0.000182
protein amino acid phosphorylation	0.000994	0.000183
female sex differentiation	0.00101	0.000186
apoptotic mitochondrial changes	0.00102	0.000188
positive regulation of transmission of nerve impulse	0.00102	0.000188
regulation of monooxygenase activity	0.00102	0.000188
positive regulation of caspase activity	0.00102	0.000189
positive regulation of peptidase activity	0.00102	0.000189
immune response-activating cell surface receptor signaling pathway	0.00105	0.000196
regulation of ERK1 and ERK2 cascade	0.00105	0.000196
cellular cation homeostasis	0.00115	0.000215
cellular extravasation	0.00119	0.000225
lymphocyte costimulation	0.00119	0.000225
muscle adaptation	0.00119	0.000225
regulation of alpha-beta T cell proliferation	0.00119	0.000225
regulation of mitochondrial membrane potential	0.00119	0.000225
regulation of T-helper cell differentiation	0.00119	0.000225
regulation of tumor necrosis factor biosynthetic process	0.00119	0.000225
response to exogenous dsRNA	0.00119	0.000225
response to fluid shear stress	0.00119	0.000225
T cell costimulation	0.00119	0.000225
negative regulation of intracellular transport	0.00121	0.000229
positive regulation of cell cycle	0.00125	0.000236
regulation of nitrogen compound metabolic process	0.00125	0.000238

response to vitamin	0.00128	0.000243
regulation of multicellular organismal metabolic process	0.00132	0.000256
regulation of smooth muscle cell migration	0.00132	0.000256
regulation of survival gene product expression	0.00132	0.000256
germinal center formation	0.00132	0.000258
negative regulation of cell killing	0.00132	0.000258
negative regulation of collagen metabolic process	0.00132	0.000258
negative regulation of growth of symbiont in host	0.00132	0.000258
negative regulation of interleukin-8 production	0.00132	0.000258
negative regulation of multicellular organismal metabolic process	0.00132	0.000258
negative regulation of T cell mediated immunity	0.00132	0.000258
positive regulation of immunoglobulin secretion	0.00132	0.000258
purine deoxyribonucleotide catabolic process	0.00132	0.000258
regulation of germinal center formation	0.00132	0.000258
regulation of growth of symbiont in host	0.00132	0.000258
regulation of histone deacetylation	0.00132	0.000258
regulation of nitric-oxide synthase biosynthetic process	0.00132	0.000258
response to lipoteichoic acid	0.00132	0.000258
T cell mediated immunity	0.00132	0.000258
regulation of peptidase activity	0.00136	0.000265
placenta development	0.00141	0.000275
positive regulation of neurological system process	0.00141	0.000277
protein import into nucleus, translocation	0.00141	0.000277
negative regulation of locomotion	0.00149	0.000293
regulation of endocytosis	0.00149	0.000293
activation of protein kinase activity	0.00155	0.000306
B cell differentiation	0.00157	0.000309
response to inorganic substance	0.0016	0.000316

2'-deoxyribonucleotide metabolic process	0.00165	0.000328
initiation of viral infection	0.00165	0.000328
positive regulation of alpha-beta T cell activation	0.00165	0.000328
release of cytochrome c from mitochondria	0.00165	0.000328
detection of bacterium	0.00165	0.000329
negative regulation of T cell differentiation	0.00165	0.000329
regulation of humoral immune response	0.00165	0.000329
cellular response to organic substance	0.00167	0.000333
transmembrane receptor protein tyrosine kinase signaling pathway	0.00171	0.000341
negative regulation of cellular protein metabolic process	0.00171	0.000342
activation of caspase activity	0.0018	0.000361
cell cycle arrest	0.002	0.0004
negative regulation of cellular metabolic process	0.00204	0.000411
regulation of cytokine-mediated signaling pathway	0.00205	0.000413
regulation of vasodilation	0.00205	0.000413
regulation of hydrolase activity	0.00212	0.000427
regulation of caspase activity	0.00215	0.000433
post-translational protein modification	0.00224	0.000452
positive regulation of histone modification	0.00228	0.000464
positive regulation of interferon-beta production	0.00228	0.000464
positive regulation vascular endothelial growth factor production	0.00228	0.000464
regulation of CD4-positive, alpha beta T cell differentiation	0.00228	0.000464
regulation of interleukin-10 production	0.00228	0.000464
detection of chemical stimulus	0.0023	0.000469
response to organic nitrogen	0.00238	0.000487
cytoplasmic sequestering of NF-kappaB	0.00242	0.000504
leukocyte tethering or rolling	0.00242	0.000504

lymphocyte chemotaxis	0.00242	0.000504
modulation of growth of symbiont involved in interaction with host	0.00242	0.000504
negative regulation of growth of symbiont involved in interaction with host	0.00242	0.000504
negative regulation of interleukin-12 production	0.00242	0.000504
negative regulation of protein maturation by peptide bond cleavage	0.00242	0.000504
negative regulation of viral genome replication	0.00242	0.000504
positive regulation of natural killer cell mediated cytotoxicity directed against tumor cell target	0.00242	0.000504
positive regulation of natural killer cell mediated immune response to tumor cell	0.00242	0.000504
positive regulation of steroid biosynthetic process	0.00242	0.000504
regulation of natural killer cell mediated cytotoxicity directed against tumor cell target	0.00242	0.000504
regulation of natural killer cell mediated immune response to tumor cell	0.00242	0.000504
regulation of protein amino acid deacetylation	0.00242	0.000504
regulation of T-helper 1 cell differentiation	0.00242	0.000504
regulation of T-helper 2 cell differentiation	0.00242	0.000504
positive regulation of lipid biosynthetic process	0.00246	0.000515
positive regulation of protein kinase B signaling cascade	0.00246	0.000515
regulation of alpha-beta T cell differentiation	0.00246	0.000515
development of primary female sexual characteristics	0.00256	0.000536
regulation of DNA metabolic process	0.00261	0.000547
response to lipid	0.00262	0.000552
regulation of neurological system process	0.00267	0.000561
regulation of nucleobase, nucleoside, nucleotide and nucleic acid metabolic process	0.0027	0.000569

regulation of cellular response to stress	0.00278	0.000587
positive regulation of homeostatic process	0.00288	0.000609
regulation of anatomical structure size	0.00292	0.000618
positive regulation of DNA metabolic process	0.00296	0.000633
deoxyribonucleotide catabolic process	0.00296	0.000634
membrane protein ectodomain proteolysis	0.00296	0.000634
negative regulation of B cell activation	0.00296	0.000634
positive regulation of peptidyl-serine phosphorylation	0.00296	0.000634
positive regulation of production of molecular mediator of immune response	0.00296	0.000634
positive regulation of vasodilation	0.00296	0.000634
regulation of membrane protein ectodomain proteolysis	0.00296	0.000634
superoxide anion generation	0.00296	0.000634
T cell activation involved in immune response	0.00296	0.000634
positive regulation of mitosis	0.00296	0.000635
positive regulation of nuclear division	0.00296	0.000635
organ regeneration	0.003	0.000645
regulation of mRNA stability	0.0036	0.000775
detection of stimulus	0.00367	0.000791
response to protein stimulus	0.00367	0.000791
positive regulation of natural killer cell mediated cytotoxicity	0.0039	0.000844
positive regulation of natural killer cell mediated immunity	0.0039	0.000844
cellular macromolecule catabolic process	0.00394	0.000857
monocyte chemotaxis	0.00394	0.000863
negative regulation of leukocyte migration	0.00394	0.000863
positive regulation of interleukin-8 biosynthetic process	0.00394	0.000863
positive regulation of synaptic transmission, glutamatergic	0.00394	0.000863
positive regulation of tolerance induction	0.00394	0.000863
regulation of B cell apoptosis	0.00394	0.000863

regulation of tolerance induction	0.00394	0.000863
response to caffeine	0.00394	0.000863
acute-phase response	0.00397	0.000869
negative regulation of protein modification process	0.00398	0.000875
negative regulation of cell cycle	0.00398	0.000878
cell surface pattern recognition receptor signaling pathway	0.00398	0.000902
cellular response to diacylated bacterial lipopeptide	0.00398	0.000902
cellular response to triacylated bacterial lipopeptide	0.00398	0.000902
chemokine production	0.00398	0.000902
chronic inflammatory response to antigenic stimulus	0.00398	0.000902
cytosol to ER transport	0.00398	0.000902
detection of diacylated bacterial lipopeptide	0.00398	0.000902
detection of fungus	0.00398	0.000902
detection of triacylated bacterial lipopeptide	0.00398	0.000902
dibenzo-p-dioxin metabolic process	0.00398	0.000902
hepatic immune response	0.00398	0.000902
interferon-gamma biosynthetic process	0.00398	0.000902
negative regulation of complement activation, lectin pathway	0.00398	0.000902
negative regulation of T cell mediated cytotoxicity	0.00398	0.000902
positive regulation of heterotypic cell-cell adhesion	0.00398	0.000902
positive regulation of interleukin-18 production	0.00398	0.000902
positive regulation of vitamin D biosynthetic process	0.00398	0.000902
positive regulation of vitamin metabolic process	0.00398	0.000902
regulation of complement activation, lectin pathway	0.00398	0.000902
regulation of interleukin-23 production	0.00398	0.000902
regulatory T cell differentiation	0.00398	0.000902
response to diacylated bacterial lipopeptide	0.00398	0.000902
response to triacylated bacterial lipopeptide	0.00398	0.000902
RNA destabilization	0.00398	0.000902

smooth muscle hyperplasia	0.00398	0.000902
base-excision repair	0.00411	0.000936
endocrine process	0.00411	0.000936
immunoglobulin production	0.00411	0.000936
response to fungus	0.00411	0.000936
superoxide metabolic process	0.00411	0.000936
negative regulation of intracellular protein kinase cascade	0.00432	0.000986
regulation of cell cycle	0.00442	0.00101
negative regulation of macromolecule biosynthetic process	0.00446	0.00102
cellular response to stress	0.00457	0.00105
positive regulation of cell adhesion	0.00457	0.00105
regulation of vesicle-mediated transport	0.00457	0.00105
negative regulation of cell growth	0.00461	0.00106
maintenance of location	0.00475	0.00109
response to reactive oxygen species	0.00475	0.00109
negative regulation of protein secretion	0.00476	0.0011
regulation of collagen biosynthetic process	0.00476	0.0011
response to interferon-gamma	0.00476	0.0011
deoxyribonucleotide metabolic process	0.00484	0.00112
response to acid	0.00484	0.00112
nucleoside monophosphate biosynthetic process	0.00495	0.00115
positive regulation of cell division	0.00495	0.00115
viral infectious cycle	0.00495	0.00115
cellular response to hormone stimulus	0.00498	0.00116
regulation of transcription	0.00528	0.00123
activation of plasma proteins involved in acute inflammatory response	0.00562	0.00131
protein polyubiquitination	0.00562	0.00131
macromolecule catabolic process	0.00563	0.00132

base-excision repair, AP site formation	0.00573	0.00135
embryonic placenta morphogenesis	0.00573	0.00135
positive regulation of cholesterol efflux	0.00573	0.00135
positive regulation of interleukin-10 production	0.00573	0.00135
regulation of gastrulation	0.00573	0.00135
response to UV-B	0.00573	0.00135
female gonad development	0.00589	0.00139
maternal placenta development	0.00592	0.0014
regulation of collagen metabolic process	0.00592	0.0014
regulation of metal ion transport	0.00592	0.0014
response to vitamin D	0.00592	0.0014
rhythmic behavior	0.00592	0.0014
vasodilation	0.00592	0.0014
ovulation cycle process	0.0064	0.00152
DNA catabolic process	0.00642	0.00153
organ morphogenesis	0.00669	0.00159
hemostasis	0.00685	0.00163
regulation of neuron apoptosis	0.00685	0.00164
detection of external stimulus	0.00694	0.00166
heterocycle catabolic process	0.00694	0.00166
tube development	0.00694	0.00166
negative regulation of cell size	0.00729	0.00175
cofactor transport	0.00733	0.00176
positive regulation of calcium-mediated signaling	0.00733	0.00176
T cell homeostasis	0.00733	0.00176
cellular response to endogenous stimulus	0.00746	0.0018
protein oligomerization	0.00758	0.00183
regulation of RNA metabolic process	0.00771	0.00186
maintenance of protein location in cell	0.00774	0.00187

cellular homeostasis	0.00776	0.00188
regulation of cell growth	0.00786	0.0019
regulation of oxidoreductase activity	0.00788	0.00191
response to ethanol	0.00809	0.00197
B cell homeostasis	0.00809	0.00198
negative regulation of fibroblast proliferation	0.00809	0.00198
positive regulation of cholesterol transport	0.00809	0.00198
positive regulation of sterol transport	0.00809	0.00198
purine deoxyribonucleotide metabolic process	0.00809	0.00198
regulation of interleukin-4 production	0.00809	0.00198
regulation of mitochondrial membrane permeability	0.00809	0.00198
gland development	0.00864	0.00211
negative regulation of biosynthetic process	0.0087	0.00213
negative regulation of angiogenesis	0.0087	0.00214
regulation of calcium ion transport	0.00873	0.00214
alpha-beta T cell activation	0.00883	0.00218
calcium ion transport into cytosol	0.00883	0.00218
macromolecule modification	0.00883	0.00218
regulation of synaptic transmission, glutamatergic	0.00883	0.00218
myeloid cell differentiation	0.00894	0.00221
regulation of lipid metabolic process	0.00908	0.00225
activation of MAPK activity	0.00939	0.00233
regulation of mitotic cell cycle	0.00939	0.00233
ovarian follicle development	0.0097	0.00241
response to amine stimulus	0.0097	0.00241
protein maturation	0.00979	0.00243
positive regulation of endothelial cell proliferation	0.00991	0.00247
regulation of protein kinase B signaling cascade	0.00991	0.00247
response to UV	0.01	0.0025

gland morphogenesis	0.0101	0.00252
brain segmentation	0.0102	0.00265
cellular response to lipoteichoic acid	0.0102	0.00265
central nervous system segmentation	0.0102	0.00265
depurination	0.0102	0.00265
innate immune response in mucosa	0.0102	0.00265
interferon-gamma production	0.0102	0.00265
interleukin-6-mediated signaling pathway	0.0102	0.00265
maternal process involved in parturition	0.0102	0.00265
mucosal immune response	0.0102	0.00265
multicellular organismal macromolecule catabolic process	0.0102	0.00265
multicellular organismal protein catabolic process	0.0102	0.00265
myeloid cell apoptosis	0.0102	0.00265
natural killer cell activation involved in immune response	0.0102	0.00265
negative regulation of calcidiol 1-monooxygenase activity	0.0102	0.00265
negative regulation of complement activation	0.0102	0.00265
negative regulation of low-density lipoprotein receptor biosynthetic process	0.0102	0.00265
negative regulation of phagocytosis	0.0102	0.00265
neutrophil apoptosis	0.0102	0.00265
neutrophil homeostasis	0.0102	0.00265
peptide antigen transport	0.0102	0.00265
positive regulation of germinal center formation	0.0102	0.00265
positive regulation of killing of cells of another organism	0.0102	0.00265
positive regulation of macrophage cytokine production	0.0102	0.00265
positive regulation of multi-organism process	0.0102	0.00265
positive regulation of T cell differentiation in the thymus	0.0102	0.00265
positive regulation of T-helper 2 cell differentiation	0.0102	0.00265
protein digestion	0.0102	0.00265

regulation of regulatory T cell differentiation	0.0102	0.00265
response to low-density lipoprotein stimulus	0.0102	0.00265
response to molecule of fungal origin	0.0102	0.00265
response to ozone	0.0102	0.00265
sequestering of triglyceride	0.0102	0.00265
T cell proliferation involved in immune response	0.0102	0.00265
tolerance induction	0.0102	0.00265
bone remodeling	0.0102	0.00266
heterophilic cell-cell adhesion	0.0102	0.00266
regulation of organic acid transport	0.0102	0.00266
regulation of peptidyl-serine phosphorylation	0.0102	0.00266
response to amino acid stimulus	0.0102	0.00266
response to tumor necrosis factor	0.0102	0.00266
regulation of endothelial cell proliferation	0.0103	0.00269
phosphate metabolic process	0.0104	0.00272
phosphorus metabolic process	0.0104	0.00272
regulation of organelle organization	0.0104	0.00272
entry into cell of other organism involved in symbiotic interaction	0.0104	0.00276
entry into host	0.0104	0.00276
entry into host cell	0.0104	0.00276
entry into other organism involved in symbiotic interaction	0.0104	0.00276
entry of virus into host cell	0.0104	0.00276
lipopolysaccharide-mediated signaling pathway	0.0104	0.00276
methionine biosynthetic process	0.0104	0.00276
movement in environment of other organism involved in symbiotic interaction	0.0104	0.00276
movement in host environment	0.0104	0.00276

positive regulation of cytokine production involved in immune response	0.0104	0.00276
positive regulation of membrane protein ectodomain proteolysis	0.0104	0.00276
positive regulation of tyrosine phosphorylation of Stat5 protein	0.0104	0.00276
regulation of endocrine process	0.0104	0.00276
regulation of protein maturation by peptide bond cleavage	0.0104	0.00276
regulation of protein processing	0.0104	0.00276
regulation of T-helper 2 type immune response	0.0104	0.00276
response to hyperoxia	0.0104	0.00276
response to purine	0.0104	0.00276
positive regulation of anti-apoptosis	0.0106	0.00284
endocytosis	0.0111	0.00297
membrane invagination	0.0111	0.00297
protein complex assembly	0.0111	0.00297
protein complex biogenesis	0.0111	0.00297
regulation of cell cycle process	0.0112	0.003
tube morphogenesis	0.0114	0.00307
morphogenesis of a branching epithelium	0.0117	0.00313
cellular response to unfolded protein	0.0118	0.00321
cytosolic calcium ion transport	0.0118	0.00321
endoplasmic reticulum unfolded protein response	0.0118	0.00321
negative regulation of blood pressure	0.0118	0.00321
negative regulation of homeostatic process	0.0118	0.00321
positive regulation of positive chemotaxis	0.0118	0.00321
regulation of calcium-mediated signaling	0.0118	0.00321
regulation of defense response to virus	0.0118	0.00321
regulation of insulin receptor signaling pathway	0.0118	0.00321

regulation of transcription, DNA-dependent	0.0119	0.00323
response to endoplasmic reticulum stress	0.012	0.00325
response to hydrogen peroxide	0.012	0.00327
regulation of cell division	0.0123	0.00334
negative regulation of signal transduction	0.0129	0.00353
maintenance of location in cell	0.0131	0.00357
protein modification process	0.0134	0.00365
membrane protein intracellular domain proteolysis	0.0135	0.00372
negative regulation of behavior	0.0135	0.00372
negative regulation of cytokine-mediated signaling pathway	0.0135	0.00372
positive regulation of organic acid transport	0.0135	0.00372
regulation of cell adhesion mediated by integrin	0.0135	0.00372
regulation of T cell differentiation in the thymus	0.0135	0.00372
blood coagulation	0.0139	0.00382
coagulation	0.0139	0.00382
morphogenesis of an epithelium	0.0139	0.00383
regulation of blood vessel endothelial cell migration	0.0139	0.00383
regulation of histone modification	0.0139	0.00383
regulation of positive chemotaxis	0.0139	0.00383
negative regulation of cell migration	0.014	0.00388
negative regulation of signaling process	0.0143	0.00397
regulation of transforming growth factor beta receptor signaling pathway	0.0147	0.00409
vascular process in circulatory system	0.0147	0.00409
enzyme linked receptor protein signaling pathway	0.0148	0.0041
ER-nucleus signaling pathway	0.0151	0.00419
response to osmotic stress	0.0151	0.00419
female gamete generation	0.0152	0.00422
negative regulation of catalytic activity	0.0154	0.0043

protein processing	0.0156	0.00434
nucleobase metabolic process	0.0162	0.00453
positive regulation of fatty acid metabolic process	0.0162	0.00453
maintenance of protein location	0.0164	0.00458
mammary gland development	0.0164	0.00459
phosphorylation	0.0164	0.00459
regulation of body fluid levels	0.0164	0.00461
induction of positive chemotaxis	0.0172	0.00485
negative regulation of osteoclast differentiation	0.0172	0.00485
neutrophil mediated immunity	0.0172	0.00485
nucleobase biosynthetic process	0.0172	0.00485
regulation of myeloid cell apoptosis	0.0172	0.00485
regulation of tyrosine phosphorylation of Stat5 protein	0.0172	0.00485
organic ether metabolic process	0.0175	0.00495
astrocyte activation	0.0178	0.0052
branch elongation involved in mammary gland duct branching	0.0178	0.0052
defense response to protozoan	0.0178	0.0052
heat generation	0.0178	0.0052
intracellular protein transport in other organism involved in symbiotic interaction	0.0178	0.0052
intracellular transport of viral proteins in host cell	0.0178	0.0052
multicellular organismal protein metabolic process	0.0178	0.0052
negative regulation of calcium ion transport into cytosol	0.0178	0.0052
negative regulation of cytokine secretion involved in immune response	0.0178	0.0052
negative regulation of defense response to virus	0.0178	0.0052
negative regulation of interleukin-2 biosynthetic process	0.0178	0.0052
negative regulation of interleukin-4 production	0.0178	0.0052

negative regulation of macrophage differentiation	0.0178	0.0052
negative regulation of sequestering of triglyceride	0.0178	0.0052
negative regulation of tumor necrosis factor biosynthetic process	0.0178	0.0052
nucleotide-binding oligomerization domain containing 2 signaling pathway	0.0178	0.0052
nucleotide-binding oligomerization domain containing signaling pathway	0.0178	0.0052
positive regulation of histone acetylation	0.0178	0.0052
positive regulation of histone deacetylation	0.0178	0.0052
positive regulation of interferon-alpha production	0.0178	0.0052
positive regulation of myeloid leukocyte cytokine production involved in immune response	0.0178	0.0052
positive regulation of skeletal muscle tissue development	0.0178	0.0052
positive regulation of T-helper 1 cell differentiation	0.0178	0.0052
pyrimidine nucleoside monophosphate biosynthetic process	0.0178	0.0052
pyrimidine nucleoside monophosphate metabolic process	0.0178	0.0052
regulation of cell-cell adhesion mediated by integrin	0.0178	0.0052
regulation of granulocyte macrophage colony-stimulating factor biosynthetic process	0.0178	0.0052
regulation of granulocyte macrophage colony-stimulating factor production	0.0178	0.0052
regulation of low-density lipoprotein receptor biosynthetic process	0.0178	0.0052
regulation of protein heterodimerization activity	0.0178	0.0052
regulation of viral protein levels in host cell	0.0178	0.0052
response to muramyl dipeptide	0.0178	0.0052
rhombomere 5 development	0.0178	0.0052
symbiont intracellular protein transport in host	0.0178	0.0052
toll-like receptor 4 signaling pathway	0.0178	0.0052

uterus development	0.0178	0.0052
vagina development	0.0178	0.0052
myeloid leukocyte differentiation	0.0181	0.00531
positive regulation of JUN kinase activity	0.0181	0.00531
ribonucleoside monophosphate biosynthetic process	0.0181	0.00531
sulfur amino acid metabolic process	0.0181	0.00531
regulation of synaptic transmission	0.0189	0.00555
negative regulation of cellular biosynthetic process	0.0197	0.00579
negative regulation of cellular component movement	0.0197	0.00579
lipid localization	0.0201	0.00593
circadian sleep/wake cycle	0.0207	0.00616
mammary gland alveolus development	0.0207	0.00616
methionine metabolic process	0.0207	0.00616
negative regulation of sequestering of calcium ion	0.0207	0.00616
positive regulation of actin filament polymerization	0.0207	0.00616
positive regulation of blood vessel endothelial cell migration	0.0207	0.00616
regulation of lymphocyte apoptosis	0.0207	0.00616
regulation of potassium ion transport	0.0207	0.00616
regulation of sequestering of calcium ion	0.0207	0.00616
release of sequestered calcium ion into cytosol	0.0207	0.00616
regulation of lipid biosynthetic process	0.0218	0.0065
blood vessel development	0.0218	0.00651
regulation of membrane potential	0.0218	0.00651
complement activation	0.0222	0.00663
regulation of anti-apoptosis	0.0222	0.00663
reproductive process	0.0232	0.00695
ribonucleoside monophosphate metabolic process	0.0238	0.00712
cellular response to insulin stimulus	0.0241	0.00723
reproduction	0.0245	0.00736

regulation of blood vessel size	0.0245	0.00737
regulation of tube size	0.0245	0.00737
bone resorption	0.0253	0.00767
decidualization	0.0253	0.00767
labyrinthine layer morphogenesis	0.0253	0.00767
positive regulation of cell-cell adhesion	0.0253	0.00767
regulation of antigen receptor-mediated signaling pathway	0.0253	0.00767
regulation of mast cell activation	0.0253	0.00767
regulation of response to extracellular stimulus	0.0253	0.00767
regulation of response to nutrient levels	0.0253	0.00767
regulation of sensory perception	0.0253	0.00767
regulation of sensory perception of pain	0.0253	0.00767
regulation of sodium ion transport	0.0253	0.00767
catabolic process	0.0254	0.00771
cellular response to protein stimulus	0.0268	0.00817
positive regulation of ossification	0.0268	0.00817
regulation of chromosome organization	0.0268	0.00817
regulation of JUN kinase activity	0.0268	0.00817
regulation of systemic arterial blood pressure mediated by a chemical signal	0.0268	0.00817
response to dsRNA	0.0268	0.00817
nucleoside monophosphate metabolic process	0.027	0.00837
antigen processing and presentation of exogenous peptide antigen via MHC class II	0.027	0.00849
antigen processing and presentation of peptide antigen via MHC class II	0.027	0.00849
B cell lineage commitment	0.027	0.00849
CD8-positive, alpha-beta T cell differentiation	0.027	0.00849
cellular response to corticosteroid stimulus	0.027	0.00849

cellular response to glucocorticoid stimulus	0.027	0.00849
fat-soluble vitamin biosynthetic process	0.027	0.00849
interleukin-2 production	0.027	0.00849
membrane to membrane docking	0.027	0.00849
negative regulation of B cell apoptosis	0.027	0.00849
negative regulation of CD4-positive, alpha beta T cell differentiation	0.027	0.00849
negative regulation of interleukin-6 biosynthetic process	0.027	0.00849
negative regulation of neuroblast proliferation	0.027	0.00849
negative regulation of potassium ion transport	0.027	0.00849
negative regulation of systemic arterial blood pressure	0.027	0.00849
negative regulation of T-helper cell differentiation	0.027	0.00849
positive regulation of antigen receptor-mediated signaling pathway	0.027	0.00849
positive regulation of branching involved in ureteric bud morphogenesis	0.027	0.00849
positive regulation of cyclin-dependent protein kinase activity involved in G1/S	0.027	0.00849
positive regulation of protein amino acid deacetylation	0.027	0.00849
positive regulation of T cell mediated cytotoxicity	0.027	0.00849
purine nucleoside catabolic process	0.027	0.00849
purine ribonucleoside catabolic process	0.027	0.00849
regulation of branching involved in ureteric bud morphogenesis	0.027	0.00849
regulation of complement activation	0.027	0.00849
regulation of cyclin-dependent protein kinase activity involved by G1/S	0.027	0.00849
regulation of cytokine secretion involved in immune response	0.027	0.00849

regulation of humoral immune response mediated by circulating immunoglobulin	0.027	0.00849
regulation of macrophage chemotaxis	0.027	0.00849
regulation of T cell cytokine production	0.027	0.00849
response to protozoan	0.027	0.00849
response to yeast	0.027	0.00849
T cell lineage commitment	0.027	0.00849
wound healing involved in inflammatory response	0.027	0.00849
vasculature development	0.0271	0.00855
cell adhesion	0.0281	0.00887
response to carbohydrate stimulus	0.0282	0.00892
regulation of fibroblast proliferation	0.0286	0.00902
biological adhesion	0.0286	0.00904
carboxylic acid transport	0.0292	0.00924
regulation of transmission of nerve impulse	0.0292	0.00924
fatty acid transport	0.0293	0.00931
positive regulation of oxidoreductase activity	0.0293	0.00931
regulation of morphogenesis of a branching structure	0.0293	0.00931
regulation of steroid biosynthetic process	0.0293	0.00931
response to cold	0.0293	0.00931
alpha-beta T cell differentiation	0.0293	0.00938
branching involved in mammary gland duct morphogenesis	0.0293	0.00938
circadian behavior	0.0293	0.00938
complement activation, alternative pathway	0.0293	0.00938
homeostasis of number of cells within a tissue	0.0293	0.00938
positive regulation of monooxygenase activity	0.0293	0.00938
purine base metabolic process	0.0293	0.00938
regulation of glutamate secretion	0.0293	0.00938
organic acid transport	0.0303	0.0097

complement activation, classical pathway	0.0329	0.0105
MAPKKK cascade	0.033	0.0106
urogenital system development	0.0332	0.0107
morphogenesis of a branching structure	0.0335	0.0108
peptide transport	0.0338	0.0109
protein maturation by peptide bond cleavage	0.0338	0.0109
tissue development	0.0345	0.0111
aspartate family amino acid biosynthetic process	0.0348	0.0113
female pregnancy	0.0349	0.0113
folic acid and derivative metabolic process	0.0348	0.0113
hemopoietic progenitor cell differentiation	0.0348	0.0113
positive regulation of steroid metabolic process	0.0348	0.0113
response to fatty acid	0.0348	0.0113
sulfur amino acid biosynthetic process	0.0348	0.0113
T cell selection	0.0348	0.0113
regulation of heart contraction	0.0357	0.0116
cellular aromatic compound metabolic process	0.0359	0.0117
cellular membrane organization	0.036	0.0117
regulation of cellular component size	0.0362	0.0118
skeletal system development	0.0361	0.0118
mammary gland morphogenesis	0.0363	0.0119
platelet activation	0.0363	0.0119
positive regulation of cytoskeleton organization	0.0365	0.0119
regulation of calcium ion transport into cytosol	0.0363	0.0119
telomere maintenance	0.0363	0.0119
membrane organization	0.0367	0.012
cellular response to peptide hormone stimulus	0.0375	0.0123
antigen processing and presentation of endogenous peptide antigen	0.0375	0.0125

antigen processing and presentation of endogenous peptide antigen via MHC class I	0.0375	0.0125
antigen processing and presentation of exogenous peptide antigen	0.0375	0.0125
benzene and derivative metabolic process	0.0375	0.0125
branching involved in embryonic placenta morphogenesis	0.0375	0.0125
inflammatory response to antigenic stimulus	0.0375	0.0125
myeloid cell homeostasis	0.0375	0.0125
negative regulation of alpha-beta T cell differentiation	0.0375	0.0125
negative regulation of cholesterol storage	0.0375	0.0125
negative regulation of granulocyte differentiation	0.0375	0.0125
negative regulation of interleukin-2 production	0.0375	0.0125
opsonization	0.0375	0.0125
positive regulation of muscle organ development	0.0375	0.0125
positive regulation of response to extracellular stimulus	0.0375	0.0125
positive regulation of response to nutrient levels	0.0375	0.0125
positive regulation of striated muscle tissue development	0.0375	0.0125
positive regulation of tumor necrosis factor biosynthetic process	0.0375	0.0125
protein metabolic process	0.0376	0.0125
ribonucleoside catabolic process	0.0375	0.0125
virion attachment to host cell surface receptor	0.0375	0.0125
monocarboxylic acid transport	0.0391	0.013
proteolysis involved in cellular protein catabolic process	0.0393	0.0131
regulation of hormone secretion	0.0393	0.0131
humoral immune response mediated by circulating immunoglobulin	0.0398	0.0133
negative regulation of hormone secretion	0.0398	0.0133
telomere organization	0.0398	0.0133

negative regulation of insulin receptor signaling pathway	0.0398	0.0134
negative regulation of ossification	0.0398	0.0134
positive regulation of Rho GTPase activity	0.0398	0.0134
positive regulation of viral reproduction	0.0398	0.0134
purine nucleoside monophosphate biosynthetic process	0.0398	0.0134
purine ribonucleoside monophosphate biosynthetic process	0.0398	0.0134
regulation of tyrosine phosphorylation of Stat3 protein	0.0398	0.0134
heterocycle metabolic process	0.0402	0.0135
negative regulation of gene-specific transcription	0.0414	0.0139
negative regulation of cell adhesion	0.0419	0.0142
regulation of proteolysis	0.0419	0.0142
response to hexose stimulus	0.0419	0.0142
response to monosaccharide stimulus	0.0419	0.0142
response to unfolded protein	0.0419	0.0142
cellular protein catabolic process	0.0422	0.0143
protein catabolic process	0.0422	0.0143
cellular nitrogen compound catabolic process	0.0447	0.0152
regulation of cell size	0.045	0.0153
mRNA stabilization	0.0462	0.0157
RNA stabilization	0.0462	0.0157
blood vessel morphogenesis	0.0464	0.0158
DNA damage response, signal transduction resulting in induction of apoptosis	0.0485	0.0165
regulation of bone mineralization	0.0485	0.0165
macromolecule metabolic process	0.0485	0.0166
response to DNA damage stimulus	0.049	0.0167
sex differentiation	0.0491	0.0168
reproductive developmental process	0.0493	0.0169
antigen processing and presentation of exogenous antigen	0.0493	0.0171

betaine transport	0.0493	0.0171
carnitine transport	0.0493	0.0171
cellular response to steroid hormone stimulus	0.0493	0.0171
epithelial structure maintenance	0.0493	0.0171
hemoglobin metabolic process	0.0493	0.0171
low-density lipoprotein particle clearance	0.0493	0.0171
maintenance of gastrointestinal epithelium	0.0493	0.0171
negative regulation of B cell proliferation	0.0493	0.0171
negative regulation of glucose transport	0.0493	0.0171
negative regulation of response to biotic stimulus	0.0493	0.0171
negative regulation of smooth muscle cell migration	0.0493	0.0171
positive regulation of glutamate secretion	0.0493	0.0171
positive regulation of osteoclast differentiation	0.0493	0.0171
regulation of amino acid transport	0.0493	0.0171
rhombomere development	0.0493	0.0171
toxin metabolic process	0.0493	0.0171
vitamin D metabolic process	0.0493	0.0171
negative regulation of transcription, DNA-dependent	0.0494	0.0172
response to metal ion	0.0497	0.0173
gliogenesis	0.0499	0.0174
cellular amino acid biosynthetic process	0.0521	0.0181
myeloid leukocyte mediated immunity	0.0523	0.0183
purine nucleoside monophosphate metabolic process	0.0523	0.0183
purine ribonucleoside monophosphate metabolic process	0.0523	0.0183
regulation of glucose transport	0.0523	0.0183
positive regulation of catabolic process	0.0528	0.0185
branching morphogenesis of a tube	0.053	0.0186
DNA repair	0.0554	0.0195
induction of apoptosis by intracellular signals	0.0557	0.0196

regulation of nervous system development	0.0567	0.0199
negative regulation of RNA metabolic process	0.0576	0.0203
regulation of transmembrane receptor protein serine/threonine kinase signaling pathway	0.0588	0.0207
proteolysis	0.0592	0.0209
positive regulation of myeloid leukocyte differentiation	0.0594	0.021
temperature homeostasis	0.0594	0.021
mammary gland epithelium development	0.0619	0.0222
nucleobase, nucleoside and nucleotide metabolic process	0.0619	0.0223
antigen processing and presentation of endogenous antigen	0.0619	0.0224
astrocyte development	0.0619	0.0224
nucleoside catabolic process	0.0619	0.0224
regulation of granulocyte differentiation	0.0619	0.0224
regulation of histone acetylation	0.0619	0.0224
regulation of kidney development	0.0619	0.0224
circadian rhythm	0.0625	0.0227
nucleobase, nucleoside and nucleotide catabolic process	0.0625	0.0227
nucleobase, nucleoside, nucleotide and nucleic acid catabolic process	0.0625	0.0227
positive regulation of cellular catabolic process	0.0625	0.0227
regulation of catabolic process	0.0634	0.023
growth	0.0647	0.0235
protein import into nucleus	0.065	0.0237
regulation of protein catabolic process	0.065	0.0237
positive regulation of protein polymerization	0.0655	0.024
positive regulation of myeloid cell differentiation	0.0661	0.0243
receptor metabolic process	0.0661	0.0243
regulation of biomineral formation	0.0661	0.0243
regulation of neurogenesis	0.0661	0.0243

response to alkaloid	0.0662	0.0244
lipid transport	0.0665	0.0245
negative regulation of transcription	0.0685	0.0255
cellular component organization	0.0685	0.0259
embryonic placenta development	0.0685	0.0261
epithelium development	0.0685	0.0264
regulation of amine transport	0.0685	0.0266
regulation of systemic arterial blood pressure	0.0685	0.0266
mammary gland duct morphogenesis	0.0685	0.0272
organic cation transport	0.0685	0.0272
cellular amino acid and derivative metabolic process	0.0685	0.0277
negative regulation of lymphocyte apoptosis	0.0685	0.0282
nuclear import	0.0685	0.0282
regulation of sequestering of triglyceride	0.0685	0.0282
neurogenesis	0.0685	0.0286
macromolecular complex subunit organization	0.0685	0.0297
response to light stimulus	0.0685	0.0299
in utero embryonic development	0.0691	0.0303
aspartate family amino acid metabolic process	0.0694	0.0306
posttranscriptional regulation of gene expression	0.0694	0.0306
vitamin transport	0.0694	0.0306
hormone secretion	0.0711	0.0314
glial cell differentiation	0.072	0.0318
regulation of mitosis	0.072	0.0318
regulation of nuclear division	0.072	0.0318
development of primary sexual characteristics	0.0728	0.0323
regulation of cellular catabolic process	0.0731	0.0324
secretion	0.0755	0.0335
DNA modification	0.0765	0.034

macromolecular complex assembly	0.0765	0.034
positive regulation of Ras GTPase activity	0.0767	0.0342
axis elongation	0.0768	0.0346
branch elongation of an epithelium	0.0768	0.0346
parturition	0.0768	0.0346
regulation of macrophage differentiation	0.0768	0.0346
multicellular organism reproduction	0.0789	0.0356
reproductive process in a multicellular organism	0.0789	0.0356
generation of neurons	0.079	0.0357
regulation of endothelial cell migration	0.0809	0.0367
positive regulation of endothelial cell migration	0.0836	0.038
tissue morphogenesis	0.0851	0.0387
cellular nitrogen compound biosynthetic process	0.0851	0.0388
gonad development	0.0862	0.0393
regulation of cell development	0.0862	0.0393
astrocyte differentiation	0.0899	0.0414
negative regulation of monooxygenase activity	0.0899	0.0414
quaternary ammonium group transport	0.0899	0.0414
regulation of hormone levels	0.0901	0.0416
purine nucleotide catabolic process	0.0909	0.042
regulation of skeletal muscle tissue development	0.0909	0.042
hormone transport	0.0915	0.0425
positive regulation of protein catabolic process	0.0915	0.0425
regulation of steroid metabolic process	0.0915	0.0425
mitochondrion organization	0.0947	0.0441
nucleoside phosphate metabolic process	0.0965	0.045
nucleotide metabolic process	0.0965	0.045
nucleotide catabolic process	0.0975	0.0456
primary metabolic process	0.1	0.047

positive regulation of cyclin-dependent protein kinase activity	0.103	0.0488
regulation of cholesterol storage	0.103	0.0488
steroid metabolic process	0.106	0.0499

Supplementary Table 2: Significant Pathways (From KEGG database) of the genes with exonic SNPs

GO ID	GO Term	Ontology Source	Term P Value	% Associated Genes	Associated Genes Found
GO:0005321	Inflammatory bowel disease (IBD)	KEGG_01.03.2017	0.00	55.38	[FOXP3, HLA-DMA, HLA-DMB, HLA-DOA, HLA-DPB1, HLA-DQA1, HLA-DQA2, HLA-DQB1, HLA-DRA, HLA-DRB1, HLA-DRB4, IFNG, IL10, IL12A, IL12B, IL12RB1, IL13, IL17A, IL17F, IL18, IL1A, IL1B, IL2, IL23R, IL4, IL4R, IL6, NFKB1, NOD2, STAT4, TBX21, TGFB1, TLR2, TLR4, TLR5, TNF]
GO:0005140	Leishmaniasis	KEGG_01.03.2017	0.00	50.68	[CYBA, FCGR2A, FCGR3A, FCGR3B, HLA-DMA, HLA-DMB, HLA-DOA, HLA-DPB1, HLA-DQA1, HLA-DQA2, HLA-DQB1, HLA-DRA, HLA-DRB1, HLA-DRB4, IFNG, IL10, IL12A, IL12B, IL1A, IL1B, IL4, IRAK1, IRAK4, ITGAM, MYD88, NCF2, NCF4, NFKB1, NFKBIA, NFKBIB, NOS2, PTGS2, TGFB1, TLR2, TLR4, TNF, TRAF6]
GO:0004940	Type I diabetes mellitus	KEGG_01.03.2017	0.00	65.12	[CD28, CD80, CD86, HLA-A, HLA-B, HLA-DMA, HLA-DMB, HLA-DOA, HLA-DPB1, HLA-DQA1, HLA-DQA2, HLA-DQB1, HLA-DRA, HLA-DRB1, HLA-DRB4, HLA-E, HLA-F, HLA-G, HSPD1, ICA1, IFNG, IL12A, IL12B, IL1A, IL1B, IL2, LTA, TNF]
GO:0004659	Th17 cell differentiation	KEGG_01.03.2017	0.00	37.38	[AHR, CD247, CD3G, CD4, CHUK, FOXP3, HLA-DMA, HLA-DMB, HLA-DOA, HLA-DPB1, HLA-DQA1, HLA-DQA2, HLA-DQB1, HLA-DRA, HLA-DRB1, HLA-DRB4, IFNG, IKBKB, IL12RB1, IL17A, IL17F, IL1B, IL1R1, IL2, IL23R, IL2RB, IL4, IL4R, IL6, IL6R, NFKB1, NFKBIA, NFKBIB, NFKBIE, PPP3R2, PRKCQ, RUNX1, TBX21, TGFB1, TYK2]
GO:0005330	Allograft rejection	KEGG_01.03.2017	0.00	68.42	[CD28, CD40, CD80, CD86, HLA-A, HLA-B, HLA-DMA, HLA-DMB, HLA-DOA, HLA-DPB1, HLA-DQA1, HLA-DQA2, HLA-DQB1, HLA-DRA, HLA-DRB1, HLA-DRB4, HLA-E, HLA-F, HLA-G, IFNG, IL10, IL12A, IL12B, IL2, IL4, TNF]

GO:0005152	Tuberculosis	KEGG_01.03.2017	0.00	27.37	[BCL2, CD14, CD209, CIITA, CLEC4E, CLEC7A, CYP27B1, FCGR2A, FCGR2B, FCGR3A, FCGR3B, HLA-DMA, HLA-DMB, HLA-DOA, HLA-DPB1, HLA-DQA1, HLA-DQA2, HLA-DQB1, HLA-DRA, HLA-DRB1, HLA-DRB4, HSPD1, IFNB1, IFNG, IL10, IL12A, IL12B, IL18, IL1A, IL1B, IL6, IRAK1, IRAK4, ITGAM, MYD88, NFKB1, NOD2, NOS2, PPP3R2, TGFB1, TIRAP, TLR1, TLR2, TLR4, TLR6, TLR9, TNF, TNFRSF1A, TRAF6]
GO:0005152	Tuberculosis	KEGG_01.03.2017	0.00	27.37	[BCL2, CD14, CD209, CIITA, CLEC4E, CLEC7A, CYP27B1, FCGR2A, FCGR2B, FCGR3A, FCGR3B, HLA-DMA, HLA-DMB, HLA-DOA, HLA-DPB1, HLA-DQA1, HLA-DQA2, HLA-DQB1, HLA-DRA, HLA-DRB1, HLA-DRB4, HSPD1, IFNB1, IFNG, IL10, IL12A, IL12B, IL18, IL1A, IL1B, IL6, IRAK1, IRAK4, ITGAM, MYD88, NFKB1, NOD2, NOS2, PPP3R2, TGFB1, TIRAP, TLR1, TLR2, TLR4, TLR6, TLR9, TNF, TNFRSF1A, TRAF6]
GO:0005168	Herpes simplex infection	KEGG_01.03.2017	0.00	25.95	[C5, CCL2, CCL5, CHUK, HLA-A, HLA-B, HLA-DMA, HLA-DMB, HLA-DOA, HLA-DPB1, HLA-DQA1, HLA-DQA2, HLA-DQB1, HLA-DRA, HLA-DRB1, HLA-DRB4, HLA-E, HLA-F, HLA-G, IFIH1, IFNB1, IFNG, IKBKB, IKBKE, IL12A, IL12B, IL15, IL1B, IL6, LTA, MYD88, NFKB1, NFKBIA, NFKBIB, SOCS3, TAP1, TAP2, TLR2, TLR3, TLR9, TNF, TNFRSF14, TNFRSF1A, TP53, TRAF1, TRAF5, TRAF6, TYK2]
GO:0005332	Graft-versus-host disease	KEGG_01.03.2017	0.00	60.98	[CD28, CD80, CD86, HLA-A, HLA-B, HLA-DMA, HLA-DMB, HLA-DOA, HLA-DPB1, HLA-DQA1, HLA-DQA2, HLA-DQB1, HLA-DRA, HLA-DRB1, HLA-DRB4, HLA-E, HLA-F, HLA-G, IFNG, IL1A, IL1B, IL2, IL6, KLRC1, TNF]
GO:0005323	Rheumatoid arthritis	KEGG_01.03.2017	0.00	37.78	[ATP6V1G2, CCL2, CCL5, CD28, CD80, CD86, CTLA4, CXCL8, HLA-DMA, HLA-DMB, HLA-DOA, HLA-DPB1, HLA-DQA1, HLA-DQA2, HLA-DQB1, HLA-DRA, HLA-DRB1, HLA-DRB4, ICAM1, IFNG, IL15, IL17A, IL18, IL1A, IL1B, IL6, MMP1, MMP3, TGFB1, TLR2, TLR4, TNF, TNFSF13B, VEGFA]
GO:0004658	Th1 and Th2 cell differentiation	KEGG_01.03.2017	0.00	36.96	[CD247, CD3G, CD4, CHUK, HLA-DMA, HLA-DMB, HLA-DOA, HLA-DPB1, HLA-DQA1, HLA-DQA2, HLA-DQB1, HLA-DRA, HLA-DRB1, HLA-DRB4, IFNG, IKBKB, IL12A, IL12B, IL12RB1, IL13, IL2, IL2RB, IL4, IL4R, NFKB1, NFKBIA, NFKBIB, NFKBIE, PPP3R2, PRKCO, RBPJ, STAT4, TBX21, TYK2]

GO:0005145	Toxoplasmosis	KEGG_01.03.2017	0.00	31.86	[BCL2, CCR5, CD40, CHUK, CIITA, HLA-DMA, HLA-DMB, HLA-DOA, HLA-DPB1, HLA-DQA1, HLA-DQA2, HLA-DQB1, HLA-DRA, HLA-DRB1, HLA-DRB4, HSPA1L, IFNG, IKBKB, IL10, IL12A, IL12B, IRAK1, IRAK4, MYD88, NFKB1, NFKBIA, NFKBIB, NOS2, SOCS1, TGFB1, TLR2, TLR4, TNF, TNFRSF1A, TRAF6, TYK2]
GO:0005164	Influenza A	KEGG_01.03.2017	0.00	24.86	[AGFG1, CCL2, CCL5, CIITA, CXCL8, DDX39B, HLA-DMA, HLA-DMB, HLA-DOA, HLA-DPB1, HLA-DQA1, HLA-DQA2, HLA-DQB1, HLA-DRA, HLA-DRB1, HLA-DRB4, HSPA1L, ICAM1, IFIH1, IFNB1, IFNG, IKBKB, IKBKE, IL12A, IL12B, IL18, IL1A, IL1B, IL6, IRAK4, MYD88, NFKB1, NFKBIA, NFKBIB, NLRP3, SOCS3, TLR3, TLR4, TLR7, TNF, TNFRSF10A, TNFRSF1A, TYK2]
GO:0004060	Cytokine-cytokine receptor interaction	KEGG_01.03.2017	0.00	19.26	[AMH, CCL2, CCL21, CCL24, CCL26, CCL5, CCR2, CCR5, CCR6, CD40, CX3CR1, CXCL8, EGFR, GDF5, IFNB1, IFNG, IFNK, IL10, IL12A, IL12B, IL12RB1, IL13, IL15, IL17A, IL17F, IL18, IL1A, IL1B, IL1R1, IL2, IL23R, IL26, IL2RB, IL3, IL4, IL4R, IL6, IL6R, IL7R, INHBA, LTA, PRL, TGFB1, TNF, TNFRSF10A, TNFRSF14, TNFRSF1A, TNFRSF1B, TNFRSF6B, TNFSF13B, TNFSF4, VEGFA]
GO:0005142	Chagas disease (American trypanosomiasis)	KEGG_01.03.2017	0.00	31.37	[ACE, CCL2, CCL5, CD247, CD3G, CHUK, CXCL8, IFNB1, IFNG, IKBKB, IL10, IL12A, IL12B, IL1B, IL2, IL6, IRAK1, IRAK4, MYD88, NFKB1, NFKBIA, NOS2, PLCB1, SERPINE1, TGFB1, TLR2, TLR4, TLR6, TLR9, TNF, TNFRSF1A, TRAF6]
GO:0004064	NF-kappa B signaling pathway	KEGG_01.03.2017	0.00	32.63	[BCL2, CCL21, CD14, CD40, CHUK, CXCL8, ICAM1, IKBKB, IL1B, IL1R1, IRAK1, IRAK4, LTA, MAP3K14, MYD88, NFKB1, NFKB2, NFKBIA, PARP1, PRKCQ, PTGS2, TIRAP, TLR4, TNF, TNFAIP3, TNFRSF1A, TNFSF13B, TRAF1, TRAF5, TRAF6, VCAM1]
GO:0005162	Measles	KEGG_01.03.2017	0.00	26.87	[CD209, CD28, CD3G, CDK6, CHUK, FCGR2B, HSPA1L, IFIH1, IFNB1, IFNG, IKBKE, IL12A, IL12B, IL13, IL1A, IL1B, IL2, IL2RB, IL4, IL6, IRAK1, IRAK4, MYD88, NFKB1, NFKBIA, NFKBIB, PRKCQ, TLR2, TLR4, TLR7, TLR9, TNFAIP3, TNFRSF10A, TP53, TRAF6, TYK2]
GO:0004620	Toll-like receptor signaling pathway	KEGG_01.03.2017	0.00	30.77	[CCL5, CD14, CD40, CD80, CD86, CHUK, CXCL8, IFNB1, IKBKB, IKBKE, IL12A, IL12B, IL1B, IL6, IRAK1, IRAK4, IRF5, MYD88, NFKB1, NFKBIA, TIRAP, TLR1, TLR2, TLR3, TLR4, TLR5, TLR6, TLR7, TLR8, TLR9, TNF, TRAF6]

GO:0004620	Toll-like receptor signaling pathway	KEGG_01.03.2017	0.00	30.77	[CCL5, CD14, CD40, CD80, CD86, CHUK, CXCL8, IFNB1, IKKBK, IKBKE, IL12A, IL12B, IL1B, IL6, IRAK1, IRAK4, IRF5, MYD88, NFKB1, NFKBIA, TIRAP, TLR1, TLR2, TLR3, TLR4, TLR5, TLR6, TLR7, TLR8, TLR9, TNF, TRAF6]
GO:0005320	Autoimmune thyroid disease	KEGG_01.03.2017	0.00	43.40	[CD28, CD40, CD80, CD86, CTLA4, HLA-A, HLA-B, HLA-DMA, HLA-DMB, HLA-DOA, HLA-DPB1, HLA-DQA1, HLA-DQA2, HLA-DQB1, HLA-DRA, HLA-DRB1, HLA-DRB4, HLA-E, HLA-F, HLA-G, IL10, IL2, IL4]
GO:0004145	Phagosome	KEGG_01.03.2017	0.00	24.03	[ATP6V1G2, CD14, CD209, CLEC7A, CYBA, CYBB, FCAR, FCGR2A, FCGR2B, FCGR3A, FCGR3B, HLA-A, HLA-B, HLA-DMA, HLA-DMB, HLA-DOA, HLA-DPB1, HLA-DQA1, HLA-DQA2, HLA-DQB1, HLA-DRA, HLA-DRB1, HLA-DRB4, HLA-E, HLA-F, HLA-G, ITGAM, ITGAV, MBL2, NCF2, NCF4, SFTPD, TAP1, TAP2, TLR2, TLR4, TLR6]
GO:0004672	Intestinal immune network for IgA production	KEGG_01.03.2017	0.00	44.90	[CD28, CD40, CD80, CD86, HLA-DMA, HLA-DMB, HLA-DOA, HLA-DPB1, HLA-DQA1, HLA-DQA2, HLA-DQB1, HLA-DRA, HLA-DRB1, HLA-DRB4, IL10, IL15, IL2, IL4, IL6, MAP3K14, TGFB1, TNFSF13B]
GO:0005150	Staphylococcus aureus infection	KEGG_01.03.2017	0.00	39.29	[C2, C5, CFH, FCAR, FCGR2A, FCGR2B, FCGR3A, FCGR3B, HLA-DMA, HLA-DMB, HLA-DOA, HLA-DPB1, HLA-DQA1, HLA-DQA2, HLA-DQB1, HLA-DRA, HLA-DRB1, HLA-DRB4, ICAM1, IL10, ITGAM, MBL2]
GO:0004612	Antigen processing and presentation	KEGG_01.03.2017	0.00	32.47	[CD4, CD8A, CIITA, HLA-A, HLA-B, HLA-DMA, HLA-DMB, HLA-DOA, HLA-DPB1, HLA-DQA1, HLA-DQA2, HLA-DQB1, HLA-DRA, HLA-DRB1, HLA-DRB4, HLA-E, HLA-F, HLA-G, HSPA1L, IFNG, KLRC1, KLRC2, TAP1, TAP2, TNF]
GO:0004514	Cell adhesion molecules (CAMs)	KEGG_01.03.2017	0.00	22.76	[CD226, CD274, CD28, CD4, CD40, CD58, CD80, CD86, CD8A, CTLA4, HLA-A, HLA-B, HLA-DMA, HLA-DMB, HLA-DOA, HLA-DPB1, HLA-DQA1, HLA-DQA2, HLA-DQB1, HLA-DRA, HLA-DRB1, HLA-DRB4, HLA-E, HLA-F, HLA-G, ICAM1, ITGAM, ITGAV, PDCD1, PDCD1LG2, PTPRC, SELE, VCAM1]
GO:0005133	Pertussis	KEGG_01.03.2017	0.00	31.58	[C2, C5, CASP7, CD14, CXCL8, IL10, IL12A, IL12B, IL1A, IL1B, IL6, IRAK1, IRAK4, IRF1, ITGAM, MYD88, NFKB1, NLRP3, NOS2, SERPING1, TIRAP, TLR4, TNF, TRAF6]

GO:0005418	Fluid shear stress and atherosclerosis	KEGG_01.03.2017	0.00	22.54	[BCL2, CCL2, CHUK, CYBA, CYBB, DUSP1, GPC1, GSTM1, GSTP1, GSTT1, HMOX1, ICAM1, IFNG, IKBKB, IL1A, IL1B, IL1R1, ITGAV, MMP2, MMP9, NCF2, NFKB1, NOS3, PLAT, RAC2, SELE, SUMO4, TNF, TNFRSF1A, TP53, VCAM1, VEGFA]
GO:0005416	Viral myocarditis	KEGG_01.03.2017	0.00	35.59	[CD28, CD40, CD80, CD86, HLA-A, HLA-B, HLA-DMA, HLA-DMB, HLA-DOA, HLA-DPB1, HLA-DQA1, HLA-DQA2, HLA-DQB1, HLA-DRA, HLA-DRB1, HLA-DRB4, HLA-E, HLA-F, HLA-G, ICAM1, RAC2]
GO:0005310	Asthma	KEGG_01.03.2017	0.00	51.61	[CD40, HLA-DMA, HLA-DMB, HLA-DOA, HLA-DPB1, HLA-DQA1, HLA-DQA2, HLA-DQB1, HLA-DRA, HLA-DRB1, HLA-DRB4, IL10, IL13, IL3, IL4, TNF]
GO:0004640	Hematopoietic cell lineage	KEGG_01.03.2017	0.00	26.80	[CD14, CD24, CD3G, CD4, CD8A, HLA-DMA, HLA-DMB, HLA-DOA, HLA-DPB1, HLA-DQA1, HLA-DQA2, HLA-DQB1, HLA-DRA, HLA-DRB1, HLA-DRB4, IL1A, IL1B, IL1R1, IL3, IL4, IL4R, IL6, IL6R, IL7R, ITGAM, TNF]
GO:0005144	Malaria	KEGG_01.03.2017	0.00	38.78	[CCL2, CD40, CXCL8, ICAM1, IFNG, IL10, IL12A, IL18, IL1B, IL6, KLRK1, MYD88, SELE, TGFB1, TLR2, TLR4, TLR9, TNF, VCAM1]
GO:0004668	TNF signaling pathway	KEGG_01.03.2017	0.00	25.00	[CASP7, CCL2, CCL5, CHUK, ICAM1, IKBKB, IL15, IL1B, IL6, ITCH, LTA, MAP3K14, MMP3, MMP9, NFKB1, NFKBIA, NOD2, PTGS2, SELE, SOCS3, TNF, TNFAIP3, TNFRSF1A, TNFRSF1B, TRAF1, TRAF5, VCAM1]
GO:0004380	Osteoclast differentiation	KEGG_01.03.2017	0.00	22.31	[CHUK, CYBA, CYBB, FCGR2A, FCGR2B, FCGR3A, FCGR3B, IFNB1, IFNG, IKBKB, IL1A, IL1B, IL1R1, LCP2, MAP3K14, NCF2, NCF4, NFKB1, NFKB2, NFKBIA, PPARG, PPP3R2, SOCS1, SOCS3, TGFB1, TNF, TNFRSF1A, TRAF6, TYK2]
GO:0005166	HTLV-I infection	KEGG_01.03.2017	0.00	16.02	[ANAPC4, CD3G, CD40, CHUK, EGR2, HLA-A, HLA-B, HLA-DMA, HLA-DMB, HLA-DOA, HLA-DPB1, HLA-DQA1, HLA-DQA2, HLA-DQB1, HLA-DRA, HLA-DRB1, HLA-DRB4, HLA-E, HLA-F, HLA-G, ICAM1, IKBKB, IL15, IL1R1, IL2, IL2RB, IL6, LTA, MAP3K1, MAP3K14, NFKB1, NFKB2, NFKBIA, PPP3R2, PTTG1, TGFB1, TNF, TNFRSF1A, TP53, VCAM1, ZFP36]
GO:0005134	Legionellosis	KEGG_01.03.2017	0.00	34.55	[CASP7, CD14, CXCL8, HSPA1L, HSPD1, IL12A, IL12B, IL18, IL1B, IL6, ITGAM, MYD88, NFKB1, NFKB2, NFKBIA, TLR2, TLR4, TLR5, TNF]

GO:0005169	Epstein-Barr virus infection	KEGG_01.03.2017	0.00	17.33	[BCL2, CD40, CD58, CHUK, HLA-A, HLA-B, HLA-DPB1, HLA-DQA1, HLA-DQA2, HLA-DQB1, HLA-DRA, HLA-DRB1, HLA-DRB4, HLA-E, HLA-F, HLA-G, HSPA1L, ICAM1, IFNG, IKBKB, IL10, IRAK1, MAP3K14, NFKB1, NFKB2, NFKBIA, NFKBIB, NFKBIE, RBPJ, TNFAIP3, TP53, TRAF1, TRAF5, TRAF6, TYK2]
GO:0004657	IL-17 signaling pathway	KEGG_01.03.2017	0.00	24.73	[CCL2, CHUK, CXCL8, IFNG, IKBKB, IKBKE, IL13, IL17A, IL17F, IL1B, IL4, IL6, MMP1, MMP13, MMP3, MMP9, NFKB1, NFKBIA, PTGS2, TNF, TNFAIP3, TRAF5, TRAF6]
GO:0004621	NOD-like receptor signaling pathway	KEGG_01.03.2017	0.00	18.24	[ATG5, BCL2, CARD8, CCL2, CCL5, CHUK, CXCL8, CYBA, CYBB, IFNB1, IKBKB, IKBKE, IL18, IL1B, IL6, IRAK4, MYD88, NFKB1, NFKBIA, NFKBIB, NLRP3, NOD2, P2RX7, PLCB1, TANK, TLR4, TNF, TNFAIP3, TRAF5, TRAF6, TYK2]
GO:0004660	T cell receptor signaling pathway	KEGG_01.03.2017	0.00	22.33	[CD247, CD28, CD3G, CD4, CD8A, CHUK, CTLA4, IFNG, IKBKB, IL10, IL2, IL4, LCP2, MAP3K14, NFKB1, NFKBIA, NFKBIB, NFKBIE, PDCD1, PPP3R2, PRKCQ, PTPRC, TNF]
GO:0005143	African trypanosomiasis	KEGG_01.03.2017	0.00	40.00	[ICAM1, IFNG, IL10, IL12A, IL12B, IL18, IL1B, IL6, MYD88, PLCB1, SELE, TLR9, TNF, VCAM1]
GO:0004622	RIG-I-like receptor signaling pathway	KEGG_01.03.2017	0.00	24.29	[ATG5, CHUK, CXCL8, IFIH1, IFNB1, IFNK, IKBKB, IKBKE, IL12A, IL12B, MAP3K1, NFKB1, NFKBIA, NFKBIB, TANK, TNF, TRAF6]
GO:0004933	AGE-RAGE signaling pathway in diabetic complications	KEGG_01.03.2017	0.00	20.20	[AGER, BCL2, CCL2, CXCL8, CYBB, F3, ICAM1, IL1A, IL1B, IL6, MMP2, NFKB1, NOS3, PLCB1, SELE, SERPINE1, TGFB1, TNF, VCAM1, VEGFA]
GO:0004630	Jak-STAT signaling pathway	KEGG_01.03.2017	0.00	16.03	[BCL2, IFNB1, IFNG, IFNK, IL10, IL12A, IL12B, IL12RB1, IL13, IL15, IL2, IL23R, IL2RB, IL3, IL4, IL4R, IL6, IL6R, IL7R, PRL, PTPN2, SOCS1, SOCS3, STAT4, TYK2]
GO:0005161	Hepatitis B	KEGG_01.03.2017	0.00	15.97	[BCL2, CDK6, CHUK, CXCL8, EGR2, IFIH1, IFNB1, IKBKB, IKBKE, IL6, MAP3K1, MMP9, MYD88, NFKB1, NFKBIA, STAT4, TGFB1, TIRAP, TLR2, TLR3, TLR4, TNF, TP53]
GO:0005322	Systemic lupus erythematosus	KEGG_01.03.2017	0.00	16.54	[C2, C5, CD28, CD40, CD80, CD86, FCGR2A, FCGR3A, FCGR3B, HLA-DMA, HLA-DMB, HLA-DOA, HLA-DPB1, HLA-DQA1, HLA-DQA2, HLA-DQB1, HLA-DRA, HLA-DRB1, HLA-DRB4, IFNG, IL10, TNF]

GO:0004650	Natural killer cell mediated cytotoxicity	KEGG_01.03.2017	0.00	15.79	[CD244, CD247, FCGR3A, FCGR3B, HLA-A, HLA-B, HLA-E, HLA-G, ICAM1, IFNB1, IFNG, KLRC1, KLRC2, KLRK1, LCP2, MICA, MICB, PPP3R2, RAC2, TNF, TNFRSF10A]
GO:0005146	Amoebiasis	KEGG_01.03.2017	0.00	17.71	[CD14, CXCL8, IFNG, IL10, IL12A, IL12B, IL1B, IL1R1, IL6, ITGAM, NFKB1, NOS2, PLCB1, TGFB1, TLR2, TLR4, TNF]
GO:0004920	Adipocytokine signaling pathway	KEGG_01.03.2017	0.00	20.29	[ACSL6, ADIPOQ, CHUK, IKBKB, NFKB1, NFKBIA, NFKBIB, NFKBIE, PPARA, PRKCQ, SOCS3, TNF, TNFRSF1A, TNFRSF1B]
GO:0005340	Primary immunodeficiency	KEGG_01.03.2017	0.00	27.03	[ADA, AIRE, CD4, CD40, CD8A, CIITA, IL7R, PTPRC, TAP1, TAP2]
GO:0000670	One carbon pool by folate	KEGG_01.03.2017	0.00	35.00	[ATIC, DHFR, MTHFD1, MTHFR, MTR, SHMT1, TYMS]
GO:0005222	Small cell lung cancer	KEGG_01.03.2017	0.00	16.67	[BCL2, CDK6, CHUK, FHIT, IKBKB, ITGAV, NFKB1, NFKBIA, NOS2, PTGS2, TP53, TRAF1, TRAF5, TRAF6]
GO:0004610	Complement and coagulation cascades	KEGG_01.03.2017	0.00	16.46	[A2M, BDKRB1, C2, C5, CFH, F3, FGB, ITGAM, MBL2, PLAT, PLAUR, SERPINE1, SERPING1]
GO:0005160	Hepatitis C	KEGG_01.03.2017	0.00	12.98	[CHUK, CXCL8, EGFR, IFNB1, IKBKB, IKBKE, IRF1, NFKB1, NFKBIA, PPARA, SOCS3, TLR3, TNF, TNFRSF1A, TP53, TRAF6, TYK2]
GO:0005132	Salmonella infection	KEGG_01.03.2017	0.00	15.12	[CD14, CXCL8, FLNB, IFNG, IL18, IL1A, IL1B, IL6, MYD88, NFKB1, NOS2, TLR4, TLR5]
GO:0004623	Cytosolic DNA-sensing pathway	KEGG_01.03.2017	0.00	17.19	[CCL5, CHUK, IFNB1, IKBKB, IKBKE, IL18, IL1B, IL6, NFKB1, NFKBIA, NFKBIB]
GO:0005202	Transcriptional misregulation in cancer	KEGG_01.03.2017	0.00	11.11	[CD14, CD40, CD86, CXCL8, ETV7, EYA1, FLI1, IL2RB, IL3, IL6, ITGAM, MMP3, MMP9, NFKB1, PLAT, PPARG, REL, RUNX1, TP53, TRAF1]
GO:0004210	Apoptosis	KEGG_01.03.2017	0.00	11.59	[BAK1, BCL2, CASP7, CHUK, ERN1, IKBKB, IL3, MAP3K14, NFKB1, NFKBIA, PARP1, TNF, TNFRSF10A, TNFRSF1A, TP53, TRAF1]
GO:0004066	HIF-1 signaling pathway	KEGG_01.03.2017	0.00	12.87	[BCL2, CYBB, EGFR, HMOX1, IFNG, IL6, IL6R, NFKB1, NOS2, NOS3, SERPINE1, TLR4, VEGFA]

GO:0005200	Pathways in cancer	KEGG_01.03.2017	0.00	8.35	[BCL2, BDKRB1, CDK6, CHUK, CTNNA2, CXCL8, DCC, EGFR, FH, GNB3, GSTP1, IKBKB, IL6, ITGAV, MMP1, MMP2, MMP9, NFKB1, NFKB2, NFKBIA, NOS2, PLCB1, PPARG, PTGER4, PTGS2, RAC2, RUNX1, TGFB1, TP53, TRAF1, TRAF5, TRAF6, VEGFA]
GO:0005120	Epithelial cell signaling in Helicobacter pylori infection	KEGG_01.03.2017	0.00	14.71	[ADAM17, ATP6V1G2, CCL5, CHUK, CXCL8, EGFR, IKBKB, MAP3K14, NFKB1, NFKBIA]
GO:0004932	Non-alcoholic fatty liver disease (NAFLD)	KEGG_01.03.2017	0.00	10.74	[ADIPOQ, CASP7, CXCL8, ERN1, IKBKB, IL1A, IL1B, IL6, IL6R, ITCH, NFKB1, PPARG, SOCS3, TGFB1, TNF, TNFRSF1A]
GO:0004062	Chemokine signaling pathway	KEGG_01.03.2017	0.00	9.89	[CCL2, CCL21, CCL24, CCL26, CCL5, CCR2, CCR5, CCR6, CHUK, CX3CR1, CXCL8, GNB3, IKBKB, NFKB1, NFKBIA, NFKBIB, PLCB1, RAC2]
GO:0005219	Bladder cancer	KEGG_01.03.2017	0.00	17.07	[CXCL8, EGFR, MMP1, MMP2, MMP9, TP53, VEGFA]
GO:0005212	Pancreatic cancer	KEGG_01.03.2017	0.00	14.06	[CDK6, CHUK, EGFR, IKBKB, NFKB1, RAC2, TGFB1, TP53, VEGFA]
GO:0004722	Neurotrophin signaling pathway	KEGG_01.03.2017	0.00	10.92	[BCL2, IKBKB, IRAK1, IRAK3, IRAK4, MAP3K1, NFKB1, NFKBIA, NFKBIB, NFKBIE, SH2B3, TP53, TRAF6]
GO:0004010	MAPK signaling pathway	KEGG_01.03.2017	0.00	8.63	[CACNA1C, CD14, CHUK, DUSP1, EGFR, FLNB, HSPA1L, IKBKB, IL1A, IL1B, IL1R1, MAP3K1, MAP3K14, NFKB1, NFKB2, PPP3R2, RAC2, TGFB1, TNF, TNFRSF1A, TP53, TRAF6]
GO:0004662	B cell receptor signaling pathway	KEGG_01.03.2017	0.00	12.68	[CHUK, FCGR2B, IKBKB, NFKB1, NFKBIA, NFKBIB, NFKBIE, PPP3R2, RAC2]
GO:0005203	Viral carcinogenesis	KEGG_01.03.2017	0.01	8.96	[BAK1, CCR5, CDK6, EGR2, GTF2H4, HLA-A, HLA-B, HLA-E, HLA-F, HLA-G, NFKB1, NFKB2, NFKBIA, RBPJ, REL, TP53, TRAF1, TRAF5]
GO:0005014	Amyotrophic lateral sclerosis (ALS)	KEGG_01.03.2017	0.01	13.73	[BCL2, CAT, PPP3R2, TNF, TNFRSF1A, TNFRSF1B, TP53]
GO:0005131	Shigellosis	KEGG_01.03.2017	0.01	12.31	[ATG5, CHUK, CXCL8, IKBKB, NFKB1, NFKBIA, NFKBIB, NOD2]

GO:0004917	Prolactin signaling pathway	KEGG_01.03.2017	0.01	11.43	[CYP17A1, ESR1, ESR2, IRF1, NFKB1, PRL, SOCS1, SOCS3]
GO:0005220	Chronic myeloid leukemia	KEGG_01.03.2017	0.01	11.27	[CDK6, CHUK, IKBKB, NFKB1, NFKBIA, RUNX1, TGFB1, TP53]
GO:0005205	Proteoglycans in cancer	KEGG_01.03.2017	0.01	8.37	[EGFR, ERBB3, ESR1, FLNB, GPC1, IGF2, IL12B, ITGAV, MMP2, MMP9, PLAUR, TGFB1, TLR2, TLR4, TNF, TP53, VEGFA]
GO:0003410	Base excision repair	KEGG_01.03.2017	0.02	15.15	[MBD4, MPG, OGG1, PARP1, XRCC1]
GO:0004151	PI3K-Akt signaling pathway	KEGG_01.03.2017	0.02	7.31	[BCL2, CDK6, CHUK, COL9A1, EFNA1, EGFR, GNB3, IFNB1, IKBKB, IL2, IL2RB, IL3, IL4, IL4R, IL6, IL6R, IL7R, ITGAV, NFKB1, NOS3, PRL, TLR2, TLR4, TP53, VEGFA]
GO:0004930	Type II diabetes mellitus	KEGG_01.03.2017	0.02	13.04	[ADIPOQ, CACNA1C, IKBKB, SOCS1, SOCS3, TNF]
GO:0004670	Leukocyte transendothelial migration	KEGG_01.03.2017	0.02	9.65	[CTNNA2, CYBA, CYBB, ICAM1, ITGAM, MMP2, MMP9, NCF2, NCF4, RAC2, VCAM1]
GO:0005020	Prion diseases	KEGG_01.03.2017	0.02	14.29	[C5, CCL5, IL1A, IL1B, IL6]
GO:0004931	Insulin resistance	KEGG_01.03.2017	0.03	9.35	[IKKB, IL6, NFKB1, NFKBIA, NOS3, PPARA, PRKCQ, SOCS3, TNF, TNFRSF1A]
GO:0003050	Proteasome	KEGG_01.03.2017	0.05	11.36	[IFNG, PSMB1, PSMB2, PSMB8, PSMB9]

Supplementary Table 3: Functional Impact of exonic SNPs based on Literature mining approach

dbSNP ID	Gene	AA change	Bioinfo. Prediction	Literature Prediction	Functional Impact	Reference
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rs11593766	CASP7_HUMAN	D4E	Delete rious	1. the G allele of rs11593766 were associated with reduced risk Endometrial Cancer (Chinese Population) rs11593766, is located in exon 2 and causes a Glu to Asp change at the N-terminal end of the protein.		http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2764360/
				2. associated with a significantly increased risk of lung cancer		http://www.ncbi.nlm.nih.gov/pubmed/19058873?dopt=Abstract
rs2070600	RAGE_HUMAN	G82S	Delete rious	1. rs2070600 has functional significance: for example, it promotes higher ligand affinity and the production of proinflammatory proteins upon activation.		http://www.nature.com/gene/journal/v3/n3/full/6363861a.html
				2. In healthy adult mice and humans, AGER is highly expressed in the lungs and absence of it contributes to the pathogenesis of idiopathic pulmonary fibrosis.		Chavakis et al (2003), J M Englert et al (2007), M A Queisser et al (2008).
				3. Increased risk of RA		http://www.nature.com/gene/journal/v3/n3/full/6363861a.html
rs2372536	PUR9_HUMAN	T116S	Neutra l	Earlier studies have described an association between individuals possessing the GG genotype of a common c.347C>G; p.T112S polymorphism (rs2372536) and a decreased response to methotrexate in the treatment of rheumatoid arthritis.		http://www.ncbi.nlm.nih.gov/pubmed/15457444?dopt=Abstract&holding=npg
rs4673	CY24A_HUMAN	Y72H	Delete rious	Lesser rate of Event free survival was observed in Leukemia Patients (DLBCL treated) in the Population of Helsinki, Europe		http://www.nature.com/leu/journal/v23/n6/full/leu2008398a.html

				meta-analysis indicates that the NAD(P)H oxidase P22 phox gene 242 T allele might be associated with an increased T2DM risk in Chinese Population		http://www.ncbi.nlm.nih.gov/pubmed/24156725?dopt=Abstract
rs4684677						
rs2071554	DOB_HUMAN	R18Q	Deleterious	a missense variation in the first exon of <i>HLA-DOB</i> (major histocompatibility complex class II, DO beta), was associated with increased risk of death in all patients of lung cancer		http://europepmc.org/articles/pmc4141040
rs2075800	HS71L_HUMAN	E602K	Deleterious	SNP rs2075800 changes a negatively charged amino acid (Glu) to a positively charged amino acid (Lys). This charge shift may influence the 3D structure of HSP70 protein and altered protein folding.		https://www.karger.com/Article/Pdf/341815
rs2397084	IL17F_HUMAN	E126G	Deleterious	RA patients with the IL17F polymorphism (E126G) has longer disease duration than the patients with the wild type alleles		http://onlinelibrary.wiley.com/doi/10.1111/j.1365-3083.2010.02411.x/pdf

rs17561	IL1A_HUMAN	A114S	Delete rious	rs17561 is one of only 8 SNPs leading to a predicted intolerable amino acid change, that it is by far the most widely studied cytokine SNP, and that minor alleles here have been "strongly" associated with risk of numerous diseases involving an inflammatory response such as allergic rhinitis, atopy, nasal polyposis, malaria, gingival hyperinflammatory response, systemic sclerosis , severity of periodontitis , antibody responses to periodontal microbiota and, more recently, ankylosing spondylitis (http://cancerres.aacrjournals.org/content/72/5/1064.full.pdf)	Interestingly, the A114S variant coded by IL1A:rs17561 falls in the recognition domain for Calpain-mediated cleavage that removes the precursor peptide to yield the active IL1A protein. Importantly, Calpain processes the S114 variant 100-fold more effectively than the A114 IL1A protein, which may suggest that patients harboring the S114 IL1A protein could produce higher levels of active IL1A and subsequently modulate the inflammatory response.	http://onlinelibrary.wiley.com/doi/10.1002.mc.22275/supinfo
rs1805010	IL4RA_HUMAN	I75V	Delete rious	These data suggested that the ile50 variant significantly upregulates receptor response to IL4, with resultant increased activation of STAT6, and hence increased cell proliferation and increased IgE production.	To investigate the functional aspects of the ile50 and val50 variants of IL4R, Mitsuyasu et al. (1998) transfected complete cDNAs for these variants into mouse and human B-lymphocyte lines. In response to human IL4, the ile50-transfected mouse cells showed almost 3 times greater cell growth and approximately 3 times greater induction of luciferase activity (expression under the control of the IgE promoter) compared with val50-transfected cells (15.5- vs 5.4-fold increase, respectively). CD23 expression decrease?? jerome robert	Mitsuyasu, H., Izuhara, K., Mao, X.-Q., Gao, P.-S., Arinobu, Y., Enomoto, T., Kawai, M., Sasaki, S., Dake, Y., Hamasaki, N., Shirakawa, T., Hopkin, J. M. Ile50val variant of IL4R-alpha upregulates IgE synthesis and associates with atopic asthma. (Letter) Nature Genet. 19: 119-120, 1998. [PubMed: 9620765]

rs4644	LEG3_HUMAN	P64H	Deleterious	The protein with His64 is cleaved by MMP-2 and MMP-9, but the form of the protein with Pro64 is resistant to cleavage. The rs4644 polymorphism (Pro64His mutation) is also related to breast cancer development. Genotype analyses have indicated that the His64 genotype is associated with an increased incidence of breast cancer.	Functional germline mutation in the galectin-3 gene at position (rs4644) substituting proline with histidine (P64H), which results in susceptibility to matrix metalloproteinase cleavage and acquisition of resistance to drug-induced apoptosis.	http://atlasgeneticsoncology.org/Genes/LGALS3ID44396ch14q22.html http://onlinelibrary.wiley.com/doi/10.1002/cnrcr.26078/pdf
rs1800450	MBL2_HUMAN	G54D	Deleterious		The change occurs in the fifth collagen repeat of the protein, which the authors predicted may disrupt the collagen helix sufficiently to hinder MBL assembly and secretion by hepatocytes. Study of 16 members of the 3 families showed autosomal dominant co-inheritance of the G54D mutation and low serum MBP concentrations . (http://www.ncbi.nlm.nih.gov/pubmed/1675710) The G54D change showed a reduced capacity to activate complement through the MPB-initiated classical pathway . The authors suggested that both homozygous and heterozygous individuals would have reduced serum levels of the protein. (http://www.ncbi.nlm.nih.gov/pubmed/1304173)	MBP deficiency may confer a life-long risk of infection.

rs1800451	MBL2_HUMAN	G57E	Delete rious		Like the G54D (154545.0001) mutation, the substitution of a carboxylic acid for an axial glycine in the translated protein would be expected to disrupt the secondary structure of the collagenous triple helix of the MBL subunits. The serum MBP values in Gambians heterozygous for the mutation were significantly lower (614372) than values in wildtype individuals. (http://www.ncbi.nlm.nih.gov/pubmed/1675710)	
rs5030737	MBL2_HUMAN	R52C	Delete rious		this variant could explain cases of MBL2 deficiency (614372) not determined by the other variants. MBL is a soluble molecule that can activate the lectin pathway of the complement system; deficiency may thus lead to defects in the complement system	https://www.ncbi.nlm.nih.gov/pubmed/8206524

rs1801133	MTHR_HUMAN	A222V	Deleterious	<p>The alteration created a HinfI site that was used to screen 114 unselected French Canadian chromosomes; the allele frequency of the substitution was 0.38. The mutation in the heterozygous or homozygous state correlated with reduced enzyme activity and increased thermolability in lymphocyte extracts; in vitro expression of the mutagenized cDNA containing the mutation confirmed its effect on thermolability of MTHFR.</p> <p>(https://www.ncbi.nlm.nih.gov/pubmed/7647779)</p>	<p>Individuals homozygous for the mutation had significantly elevated plasma homocysteine levels. Thus, the 677C-T mutation may represent an important genetic risk factor in vascular disease.</p> <p>Both the 677C-T and 1298A-C SNPs in the MTHFR gene decrease the activity of the enzyme, leading to hyperhomocysteinemia (603174), particularly in folate-deficient states.</p>	
rs5743708	TLR2_HUMAN	R753Q	Deleterious	<p>an increased risk of TB in carriers of a nonsynonymous 2258G-A SNP in the TLR2 gene, which causes an arg753-to-gln (R753Q) substitution. The risk of developing TB was 6.0-fold and 1.6-fold higher in AA homozygotes and GA heterozygotes, respectively.</p> <p>(http://erj.ersjournals.com/content/23/2/219.long)</p>	<p>Schroder et al. (2005) found that monocytes and lymphocytes from healthy subjects produced more TNF (191160) and IFNG (147570), respectively, in response to high concentrations of Borrelia lysate than did healthy subjects heterozygous for the R753Q SNP.(https://www.ncbi.nlm.nih.gov/pubmed/16081826)</p> <p>TLR2 with R753Q was compromised in its ability to activate</p>	

					NFKB(https://www.ncbi.nlm.nih.gov/pubmed/22992740)	
rs3775291	TLR3_HUMAN	L412F	Deleterious			
rs4986790	TLR4_HUMAN	D299G		Arbour et al. (2000) showed that 2 common cosegregating missense mutations (asp299 to gly and thr399 to ile, 603030.0002) that affect the extracellular domain of the TLR4 receptor are associated with blunted response to inhaled lipopolysaccharide in humans. (Endotoxin hyporesponsiveness) (https://www.ncbi.nlm.nih.gov/pubmed/10835634)	Apetoh et al. (2007) found that the D299G SNP reduces the interaction between TLR4 and HMGB1 (163905) and abolishes the capacity of monocyte-derived dendritic cells to crosspresent dying melanoma cells to Mart1 (605513)-specific HLA-A2 (see 142800)-restricted cytotoxic T lymphocytes, a biologic property that depends on HMGB1 in wildtype monocyte-derived dendritic cells. (https://www.ncbi.nlm.nih.gov/pubmed/17704786)	
rs11209026	IL23R_HUMAN	R381Q	Deleterious	(R381Q) substitution (rs11209026), that confers strong protection against Crohn disease (https://www.ncbi.nlm.nih.gov/pubmed/17068223) a significant association with protection from UC (https://www.ncbi.nlm.nih.gov/pubmed	the arg381 residue is highly conserved among higher vertebrates and is located within the binding domain for JAK2 kinase, which is the first mediator of the IL23R signaling cascade (https://www.ncbi.nlm.nih.gov/pubmed/17587057)	

				/17786191) Capon et al. (2007) reported a significant association between the R381Q variant and protection against psoriasis (https://www.ncbi.nlm.nih.gov/pubmed/17587057)		
rs1061170	CFAH_HUMAN	Y402H	Benign	Haines et al. (2005) independently determined that the 1277T-C transition in exon 9 of the CFH gene, resulting in the Y402H variant, increased the risk of ARMD with odds ratios between 2.45 and 5.57. They stated that the Y402H variant likely explains approximately 43% of ARMD (Age related macular degeneration). (https://www.ncbi.nlm.nih.gov/pubmed/15761120)	Clark et al. (2006) reported that the Y402H variant (Y384H in the mature protein) is adjacent to a heparin-binding site in complement control protein module-7 (CCP7) of CFH. They found that the variants differentially recognized heparin (https://www.ncbi.nlm.nih.gov/pubmed/16787919)	Adopting a structural approach, Herbert et al. (2007) characterized interaction of the Y402H site with chemically defined glycosaminoglycans (GAGs). They found that residue 402 occupies a critical position on a face of CCP7 that recognizes GAGs, suggesting that variation at this site would modulate the ability to distinguish between GAGs according to type and density of sulfation
					Johnson et al. (2006) genotyped 28 postmortem donor eyes for the Y402H variant and found that there was no difference in ocular CFH-labeling patterns between genotypes. However, H/H eyes had significantly higher levels of the CFH-binding CRP in the choroidal stroma, with no differences in CFH transcription levels or evidence for local ocular CRP transcription. Johnson et al. (2006) suggested that increased levels of CRP in the choroid may reflect a state of chronic inflammation resulting from attenuated CFH complement-inhibitory activity in H/H individuals, and the authors also	Weismann et al. (2011) demonstrated that the CFH polymorphism H402 markedly reduces the ability of CFH to bind malondialdehyde (MDA), a common lipid peroxidation product that accumulates in many pathophysiologic processes including ARMD Lauer et al. (2011) showed that the Y402H polymorphism affected surface recruitment of CFH by monomeric CRP (123260) to specific patches on necrotic RPE cells. Reduced monomeric CRP binding of the CFH H402 variant resulted in complement activation, generation of antiinflammatory mediators, inflammation, and pathology.

					noted that there may be alterations in the CRP-binding site in CFH, which lies within the domain containing the Y402H polymorphism (https://www.ncbi.nlm.nih.gov/pubmed/17079491)	
rs231775	CTLA4_HUMAN	T17A	Benign	A allele of the CTLA4 position 49 polymorphism conferred an HLA-independent predisposition to celiac disease. (https://www.ncbi.nlm.nih.gov/pubmed/10189842)		
rs4684677	GHRL_HUMAN	Q90L	Deleterious	Hinney et al. (2002) identified a novel variant in the ghrelin gene, an A-to-T transversion that led to a nonconservative amino acid change from gln to leu at codon 90 (Q90L; rs4684677). The frequency of the leu90 allele was significantly higher in the extremely obese (601665) children and adolescents than in the normal-weight students.		
rs1801275	IL4RA_HUMAN	Q576R	Benign	Khurana Hershey et al. (1997) described a polymorphism of the IL4A gene that occurred with increased frequency in patients with allergic inflammatory disorders. The variant allele consisted of an A-to-G transition at nucleotide 1902, causing a change from glutamine to arginine at codon 576 (Q576R) in the cytoplasmic	The R576 allele was associated with higher levels of expression of CD23 (151445) by interleukin-4 than was the wildtype allele. This enhanced signaling was associated with a change in the binding specificity of the adjacent tyrosine	

				domain of the interleukin-4 receptor alpha protein.	residue at position 575 to signal-transducing molecules.	
					Functional studies suggested that the S503P and Q576R polymorphisms independently reduce STAT6 (601512) binding and STAT6 phosphorylation, leading to reduced total IgE levels.(https://www.ncbi.nlm.nih.gov/pubmed/10233717)	
rs1805010	IL4RA_HUMAN	I75V	Deleterious			
rs2228145	IL6RA_HUMAN	D358A	Benign	In a study using admixture mapping to locate regions of the genome associated with acute-phase inflammatory markers and soluble receptors, Reich et al. (2007) identified a missense SNP, rs8192284, that was significantly associated with circulating levels of IL6SR (614689). This SNP, an A-to-C transversion that results in an asp358-to-ala (D358A) amino acid substitution(https://www.ncbi.nlm.nih.gov/pubmed/17357077)		
				Galicia et al. (2004), who had identified the association of rs8192284 with IL6SR in Japanese, noted that this SNP occurs at the proteolytic cleavage site of IL6R and that consequently, variability could affect the level of the circulating soluble receptor.		

				(https://www.ncbi.nlm.nih.gov/pubmed/15306846)		
rs1127354	ITPA_HUMAN	P32T	Benign	In patients with ITPase deficiency (613850), Sumi et al. (2002) found a 94C-A transversion in exon 2 of the ITPA gene that resulted in a pro32-to-thr (P32T) substitution.	All 6 individuals who were homozygous for the 94C-A mutation had completely deficient erythrocyte ITPase activity, accompanied by the abnormal accumulation of ITP and red blood cells. (https://www.ncbi.nlm.nih.gov/pubmed/12384777) Human fibroblasts with the P32T variant showed an almost 10-fold decrease in immunoreactive ITPA. Stepchenkova et al. (2009) proposed that the P32T variant exerts its effect in certain human tissues by cumulative effects of destabilization of transcripts, protein stability, and availability. (https://www.ncbi.nlm.nih.gov/pubmed/19631656)	https://www.ncbi.nlm.nih.gov/pubmed/12384777
rs237025	SUMO4_HUMAN	M55V	Benign	Bohren et al. (2004) and Guo et al. (2004) identified an A-to-G transition in the SUMO4 gene resulting in a met55 to val amino acid change (M55V), at an evolutionarily conserved residue of the crucial CUE domain. Both groups demonstrated association of the polymorphism with susceptibility to type I diabetes	Guo et al. (2004) observed that the M55V substitution resulted in 5.5 times greater NF-kappa-B transcriptional activity and in approximately 2 times greater expression of IL12B (161561), an NF-kappa-B-dependent gene. Wang et al. (2005) suggested that heterogeneity might be responsible for the differences of results. They emphasized the importance of functional evidence providing support for the role of susceptibility genes in disease	

					pathogenesis and pointed to the evidence Guo et al. (2004) provided for a reduced sumoylation function of the 55V variant, which showed increased frequency in individuals with type I diabetes. Wang et al. (2005) suggested that this variant increases susceptibility for type I diabetes by reducing levels of protective heat-shock proteins, which may have antiapoptotic effects and a protective role in autoimmune-mediated beta-cell death during the development of type I diabetes.	
rs2230500	KPCL_HUMAN	V374I	Benign	Kubo et al. (2007) demonstrated association between cerebral infarction (601367) and a nonsynonymous SNP in exon 9 of the PRKCH gene, a 1425G-A transition that causes a val374-to-ile amino acid substitution (rs2230500).		
rs2476601	PTN22_HUMAN	R620W	Benign	Bottini et al. (2004) found that an 1858C-T transition in the PTPN8 gene resulting in an arg620-to-trp (R620W) amino acid substitution was associated with insulin-dependent diabetes mellitus (IDDM; 222100). Begovich et al. (2004) found that the minor allele (T) was associated with susceptibility to rheumatoid arthritis (RA; 180300).	association of this SNP with type I diabetes and rheumatoid arthritis, the data provided compelling evidence that PTPN22 plays a fundamental role in regulating the immune system and the development of autoimmunity.	
				They found that T cells with the at-risk allele produced less interleukin-2 (IL2; 147680) upon T-cell antigen receptor (TCR) stimulation, and that the encoded phosphatase had higher	Rieck et al. (2007) concluded that the PTPN22 1858T variant is associated with a dampened response of both the T- and B-cell antigen receptors, and that the	http://www.omim.org/entry/600716?search=PTPN22&highlight=ptpn22#26

				catalytic activity and was a more potent negative regulator of T lymphocyte activation. Vang et al. (2005) concluded that the autoimmune-predisposing allele, 1858T, is a gain-of-function mutant.	620W isoform has enhanced inhibitory function in lymphocytes	
rs17235409	NRAM1_HUMAN	D543N	Benign	Stienstra et al. (2006) studied 182 patients with Buruli ulcer disease (610446) and 191 healthy subjects in Ghana and found that a G-to-A SNP in exon 15 of the SLC11A1 gene, resulting in an asp543-to-asn (D543N) substitution, was significantly associated with susceptibility to disease		https://www.ncbi.nlm.nih.gov/pubmed/16395392
rs1050152	S22A4_HUMAN	L503F	Benign	Functional studies in fibroblasts revealed that the less-common 503F variant has less affinity for carnitine (2.7-fold lower uptake) and other endogenous substances but greater affinity for tetraethyl ammonium (3.7-fold greater uptake) and various	In transfected HEK293 fibroblasts, Taubert et al. (2005) analyzed transport of the physiologic substrate of OCTN1, L-ergothioneine (ET), and found that the 503F variant was associated with a 3-fold higher substrate	

				<p>xenobiotics than the wildtype 503L variant.</p>	<p>affinity and 2-fold lower maximum transport velocity, resulting in a 50% higher initial transport capacity at low ET levels. The authors suggested that carriers of the 503F allele accumulate higher ET concentrations in OCTN1-expressing cells compared with carriers of the wildtype 503L allele.</p> <p>(https://www.ncbi.nlm.nih.gov/pubmed/16162962)</p> <p>Cox et al. (2007) noted that the proline variant has been associated with higher circulating levels of acid-activatable TGF-beta and increased rates of TGF-beta secretion in in vitro transfection experiments.</p>	
rs4986790	TLR4_HUMAN	D299G	Benign	<p>Arbour et al. (2000) showed that 2 common cosegregating missense mutations (asp299 to gly and thr399 to ile, 603030.0002) that affect the extracellular domain of the TLR4 receptor are associated with blunted response to inhaled lipopolysaccharide in humans.</p>		
rs10516487	BANK1_HUMAN	R61H	Benign	<p>Kozyrev et al. (2008) identified an association between systemic lupus erythematosus (SLE; 152700) and a nonsynonymous substitution, rs10516487, in the BANK1 gene. This SNP consists of a G-to-A transition that results in substitution of his for arg at codon 61, with the G allele conferring risk.</p>		

rs1799864	CCR2_HUMAN	V64I	Benign	Smith et al. (1997) demonstrated that the rarer 64I allele of a val64-to-ile polymorphism of CCR2 confers relative resistance to infection by HIV-1 (609423) Mummidì et al. (1998) found that the CCR2-64I allele was associated with a delay in disease progression in African Americans but not in Caucasians.		

Supplementary Table 4: Significant Pathways of GSE15573 (PBMCs from RA patients) dataset and GSE35455 (PBMCs from Methotrexate treated RA patients) dataset

GSE15573	Common Pathways	GSE35455 MTX
RA PBMCs		RA Treated with Methotrexate
Spliceosome	Alzheimer disease	Calcium signaling pathway

Diabetic cardiomyopathy	Amyotrophic lateral sclerosis	Phagosome
Parkinson disease	Base excision repair	Focal adhesion
Huntington disease	Diabetic cardiomyopathy	Pathways of neurodegeneration
Amyotrophic lateral sclerosis	Fluid shear stress and atherosclerosis	Parkinson disease
Shigellosis	Human T-cell leukemia virus 1 infection	Lysosome
Th1 and Th2 cell differentiation	Huntington disease	Non-alcoholic fatty liver disease
SNARE interactions in vesicular transport	Neurotrophin signaling pathway	Epstein-Barr virus infection
Alzheimer disease	Parkinson disease	Human papillomavirus infection
Neurotrophin signaling pathway	Pathways of neurodegeneration	Amyotrophic lateral sclerosis
Th17 cell differentiation	Phagosome	Th1 and Th2 cell differentiation
Prion disease	Prion disease	Glycosphingolipid biosynthesis
Oxidative phosphorylation	Th1 and Th2 cell differentiation	Viral myocarditis
Histidine metabolism	Th17 cell differentiation	Bladder cancer
Glycerolipid metabolism	Tuberculosis	Proteoglycans in cancer
Human T-cell leukemia virus 1 infection	Vibrio cholerae infection	Alzheimer disease
Mismatch repair		Protein export
Fluid shear stress and atherosclerosis		Lipid and atherosclerosis
Glycolysis / Gluconeogenesis		Notch signaling pathway
Pyruvate metabolism		Arrhythmogenic right ventricular cardiomyopathy
Collecting duct acid secretion		Pathways in cancer
Phototransduction		ECM-receptor interaction
Tuberculosis		Non-homologous end-joining
Phagosome		Proteasome
mRNA surveillance pathway		Thyroid hormone signaling pathway
Arginine and proline metabolism		Prion disease
Cysteine and methionine metabolism		PI3K-Akt signaling pathway
N-Glycan biosynthesis		Diabetic cardiomyopathy

Vibrio cholerae infection		Protein processing in endoplasmic reticulum
Oxytocin signaling pathway		Thyroid cancer
Cellular senescence		Small cell lung cancer
Citrate cycle (TCA cycle)		Tuberculosis
RNA transport		MAPK signaling pathway
Pertussis		Hypertrophic cardiomyopathy
Pathways of neurodegeneration		Parathyroid hormone synthesis, secretion and action
Circadian rhythm		Huntington disease
Synaptic vesicle cycle		Non-small cell lung cancer
Base excision repair		Neurotrophin signaling pathway
Human cytomegalovirus infection		Pathogenic Escherichia coli infection
cGMP-PKG signaling pathway		Vibrio cholerae infection
		Dilated cardiomyopathy
		Platelet activation
		Insulin signaling pathway
		Rheumatoid arthritis
		Epithelial cell signaling in Helicobacter pylori infection
		Neuroactive ligand-receptor interaction
		Antigen processing and presentation
		Peroxisome
		Leukocyte transendothelial migration
		Aldosterone synthesis and secretion
		Amino sugar and nucleotide sugar metabolism
		Adherens junction
		Fluid shear stress and atherosclerosis

		NOD-like receptor signaling pathway
		cAMP signaling pathway
		Adipocytokine signaling pathway
		Regulation of actin cytoskeleton
		Other glycan degradation
		Rap1 signaling pathway
		Endometrial cancer
		Human T-cell leukemia virus 1 infection
		Cell adhesion molecules
		Glycine, serine and threonine metabolism
		Hematopoietic cell lineage
		Acute myeloid leukemia
		Base excision repair
		Fructose and mannose metabolism
		Transcriptional misregulation in cancer
		Apelin signaling pathway
		Pancreatic cancer
		Breast cancer
		Circadian entrainment
		Steroid biosynthesis
		Ubiquitin mediated proteolysis
		Galactose metabolism
		Chemokine signaling pathway
		Th17 cell differentiation
		Ras signaling pathway
		Staphylococcus aureus infection
		Estrogen signaling pathway
		Nitrogen metabolism

		Cardiac muscle contraction
		Toxoplasmosis
		Cushing syndrome
		AGE-RAGE signaling pathway in diabetic complications

Supplementary Table 5: Significant Pathways of GSE15573 (PBMCs from RA patients) dataset and GSE35455 (PBMCs from Tocilizumab treated RA patients) dataset

GSE15573	Common Pathways	GSE35455 TCMB
RA PBMCs		RA treated with Tocilizumab
Spliceosome	Alzheimer disease	Calcium signaling pathway

Diabetic cardiomyopathy	Amyotrophic lateral sclerosis	Non-alcoholic fatty liver disease
Parkinson disease	Base excision repair	Epstein-Barr virus infection
Huntington disease	Diabetic cardiomyopathy	Pathways of neurodegeneration
Amyotrophic lateral sclerosis	Fluid shear stress and atherosclerosis	Pathways in cancer
Shigellosis	Human T-cell leukemia virus 1 infection	Phagosome
Th1 and Th2 cell differentiation	Human cytomegalovirus infection	Parkinson disease
SNARE interactions in vesicular transport	Huntington disease	Huntington disease
Alzheimer disease	Neurotrophin signaling pathway	Amyotrophic lateral sclerosis
Neurotrophin signaling pathway	Oxidative phosphorylation	Cell adhesion molecules
Th17 cell differentiation	Oxytocin signaling pathway	Th1 and Th2 cell differentiation
Prion disease	Parkinson disease	PI3K-Akt signaling pathway
Oxidative phosphorylation	Pathways of neurodegeneration	Arrhythmogenic right ventricular cardiomyopathy
Histidine metabolism	Phagosome	Focal adhesion
Glycerolipid metabolism	Prion disease	Hypertrophic cardiomyopathy
Human T-cell leukemia virus 1 infection	Shigellosis	Proteoglycans in cancer
Mismatch repair	Synaptic vesicle cycle	Viral myocarditis
Fluid shear stress and atherosclerosis	Th1 and Th2 cell differentiation	Pathogenic Escherichia coli infection
Glycolysis / Gluconeogenesis	Th17 cell differentiation	Protein export
Pyruvate metabolism	Tuberculosis	Prion disease
Collecting duct acid secretion	Vibrio cholerae infection	Protein processing in endoplasmic reticulum
Phototransduction		Neuroactive ligand-receptor interaction
Tuberculosis		MAPK signaling pathway
Phagosome		Human papillomavirus infection
mRNA surveillance pathway		Lysosome
Arginine and proline metabolism		Vibrio cholerae infection
Cysteine and methionine metabolism		Aldosterone synthesis and secretion
N-Glycan biosynthesis		Apelin signaling pathway

Vibrio cholerae infection		Epithelial cell signaling in Helicobacter pylori infection
Oxytocin signaling pathway		Glycosphingolipid biosynthesis
Cellular senescence		Lipid and atherosclerosis
Citrate cycle (TCA cycle)		Th17 cell differentiation
RNA transport		Tuberculosis
Pertussis		Thyroid hormone signaling pathway
Pathways of neurodegeneration		C-type lectin receptor signaling pathway
Circadian rhythm		Proteasome
Synaptic vesicle cycle		Ras signaling pathway
Base excision repair		ECM-receptor interaction
Human cytomegalovirus infection		Adipocytokine signaling pathway
cGMP-PKG signaling pathway		cAMP signaling pathway
		Diabetic cardiomyopathy
		Non-homologous end-joining
		Fluid shear stress and atherosclerosis
		Base excision repair
		Fructose and mannose metabolism
		Neurotrophin signaling pathway
		AMPK signaling pathway
		Dilated cardiomyopathy
		Rheumatoid arthritis
		Thyroid cancer
		Mineral absorption
		Insulin signaling pathway
		NOD-like receptor signaling pathway
		Antigen processing and presentation
		Small cell lung cancer
		Mitophagy

		Peroxisome
		Leukocyte transendothelial migration
		Notch signaling pathway
		Pancreatic cancer
		Alzheimer disease
		Rap1 signaling pathway
		Oxidative phosphorylation
		Endocrine and other factor-regulated calcium reabsorption
		Hepatitis C
		Bladder cancer
		Terpenoid backbone biosynthesis
		Transcriptional misregulation in cancer
		Primary immunodeficiency
		Melanoma
		Prostate cancer
		Estrogen signaling pathway
		TNF signaling pathway
		Cardiac muscle contraction
		Hedgehog signaling pathway
		Renin-angiotensin system
		Platelet activation
		RIG-I-like receptor signaling pathway
		Type II diabetes mellitus
		Oxytocin signaling pathway
		Tight junction
		Human T-cell leukemia virus 1 infection
		Ubiquitin mediated proteolysis
		Synaptic vesicle cycle

		Glutathione metabolism
		Pentose phosphate pathway
		Retrograde endocannabinoid signaling
		GnRH signaling pathway
		Thermogenesis
		Human cytomegalovirus infection
		Non-small cell lung cancer
		Toxoplasmosis
		Inflammatory bowel disease
		Influenza A
		Endometrial cancer
		Apoptosis
		IL-17 signaling pathway
		FoxO signaling pathway
		Shigellosis
		Hepatitis B
		Parathyroid hormone synthesis, secretion and action
		ABC transporters
		Leishmaniasis

Supplementary Table 6: Significant Pathways of GSE97779 (Synovial macrophages from RA patients) dataset and GSE35455 (PBMCs from Methotrexate treated RA patients) dataset

GSE97779	Common Pathways	GSE35455 MTX
RA Synovial Macrophages		RA Treated with Methotrexate

Osteoclast differentiation	AGE-RAGE signaling pathway in diabetic complications	Calcium signaling pathway
PD-L1 expression and PD-1 checkpoint pathway in cancer	Acute myeloid leukemia	Phagosome
Herpes simplex virus 1 infection	Apelin signaling pathway	Focal adhesion
B cell receptor signaling pathway	Bladder cancer	Pathways of neurodegeneration
Lysosome	Chemokine signaling pathway	Parkinson disease
Renal cell carcinoma	Endometrial cancer	Lysosome
Epstein-Barr virus infection	Epithelial cell signaling in Helicobacter pylori infection	Non-alcoholic fatty liver disease
Pathways in cancer	Epstein-Barr virus infection	Epstein-Barr virus infection
Hepatitis B	Fluid shear stress and atherosclerosis	Human papillomavirus infection
Acute myeloid leukemia	Focal adhesion	Amyotrophic lateral sclerosis
Human T-cell leukemia virus 1 infection	Fructose and mannose metabolism	Th1 and Th2 cell differentiation
Neurotrophin signaling pathway	Hematopoietic cell lineage	Glycosphingolipid biosynthesis
Autophagy	Human T-cell leukemia virus 1 infection	Viral myocarditis
C-type lectin receptor signaling pathway	Human papillomavirus infection	Bladder cancer
AGE-RAGE signaling pathway in diabetic complications	Insulin signaling pathway	Proteoglycans in cancer
Human immunodeficiency virus 1 infection	Leukocyte transendothelial migration	Alzheimer disease
Ubiquitin mediated proteolysis	Lipid and atherosclerosis	Protein export
T cell receptor signaling pathway	Lysosome	Lipid and atherosclerosis
Prolactin signaling pathway	MAPK signaling pathway	Notch signaling pathway
Sphingolipid signaling pathway	NOD-like receptor signaling pathway	Arrhythmogenic right ventricular cardiomyopathy
Salmonella infection	Neurotrophin signaling pathway	Pathways in cancer
Leishmaniasis	Non-alcoholic fatty liver disease	ECM-receptor interaction
FoxO signaling pathway	Non-small cell lung cancer	Non-homologous end-joining

Chronic myeloid leukemia	PI3K-Akt signaling pathway	Proteasome
Apoptosis	Pancreatic cancer	Thyroid hormone signaling pathway
TNF signaling pathway	Pathogenic Escherichia coli infection	Prion disease
ErbB signaling pathway	Pathways in cancer	PI3K-Akt signaling pathway
Tuberculosis	Peroxisome	Diabetic cardiomyopathy
VEGF signaling pathway	Phagosome	Protein processing in endoplasmic reticulum
Non-small cell lung cancer	Protein processing in endoplasmic reticulum	Thyroid cancer
Proteoglycans in cancer	Proteoglycans in cancer	Small cell lung cancer
Fc gamma R-mediated phagocytosis	Ras signaling pathway	Tuberculosis
Prostate cancer	Small cell lung cancer	MAPK signaling pathway
Human cytomegalovirus infection	Th1 and Th2 cell differentiation	Hypertrophic cardiomyopathy
MAPK signaling pathway	Th17 cell differentiation	Parathyroid hormone synthesis, secretion and action
Th17 cell differentiation	Thyroid cancer	Huntington disease
Transcriptional misregulation in cancer	Thyroid hormone signaling pathway	Non-small cell lung cancer
Phagosome	Toxoplasmosis	Neurotrophin signaling pathway
Kaposi sarcoma-associated herpesvirus infection	Transcriptional misregulation in cancer	Pathogenic Escherichia coli infection
Pancreatic cancer	Tuberculosis	Vibrio cholerae infection
Measles	Ubiquitin mediated proteolysis	Dilated cardiomyopathy
Longevity regulating pathway	Vibrio cholerae infection	Platelet activation
HIF-1 signaling pathway	secretion and action	Insulin signaling pathway
Th1 and Th2 cell differentiation		Rheumatoid arthritis
AMPK signaling pathway		Epithelial cell signaling in Helicobacter pylori infection
Cellular senescence		Neuroactive ligand-receptor interaction
mTOR signaling pathway		Antigen processing and presentation

Central carbon metabolism in cancer		Peroxisome
Colorectal cancer		Leukocyte transendothelial migration
Focal adhesion		Aldosterone synthesis and secretion
Glioma		Amino sugar and nucleotide sugar metabolism
Insulin resistance		Adherens junction
Lipid and atherosclerosis		Fluid shear stress and atherosclerosis
Protein processing in endoplasmic reticulum		NOD-like receptor signaling pathway
Viral carcinogenesis		cAMP signaling pathway
NF-kappa B signaling pathway		Adipocytokine signaling pathway
Hepatitis C		Regulation of actin cytoskeleton
Fatty acid degradation		Other glycan degradation
Pathogenic Escherichia coli infection		Rap1 signaling pathway
Lysine degradation		Endometrial cancer
Bladder cancer		Human T-cell leukemia virus 1 infection
Peroxisome		Cell adhesion molecules
Small cell lung cancer		Glycine, serine and threonine metabolism
Influenza A		Hematopoietic cell lineage
Amoebiasis		Acute myeloid leukemia
Hepatocellular carcinoma		Base excision repair
Toxoplasmosis		Fructose and mannose metabolism
Yersinia infection		Transcriptional misregulation in cancer
Hematopoietic cell lineage		Apelin signaling pathway
p53 signaling pathway		Pancreatic cancer
N-Glycan biosynthesis		Breast cancer
Thyroid hormone signaling pathway		Circadian entrainment
Legionellosis		Steroid biosynthesis

Valine, leucine and isoleucine degradation		Ubiquitin mediated proteolysis
Glycosaminoglycan biosynthesis		Galactose metabolism
Insulin signaling pathway		Chemokine signaling pathway
Melanoma		Th17 cell differentiation
Endometrial cancer		Ras signaling pathway
Toll-like receptor signaling pathway		Staphylococcus aureus infection
Leukocyte transendothelial migration		Estrogen signaling pathway
Fluid shear stress and atherosclerosis		Nitrogen metabolism
Human papillomavirus infection		Cardiac muscle contraction
Apelin signaling pathway		Toxoplasmosis
Non-alcoholic fatty liver disease		Cushing syndrome
Various types of N-glycan biosynthesis		AGE-RAGE signaling pathway in diabetic complications
PI3K-Akt signaling pathway		
Chemokine signaling pathway		
Growth hormone synthesis, secretion and action		
Relaxin signaling pathway		
JAK-STAT signaling pathway		
Chagas disease		
Fc epsilon RI signaling pathway		
Sphingolipid metabolism		
Ras signaling pathway		
Pyruvate metabolism		
Circadian rhythm		
Long-term potentiation		
Ferroptosis		

Epithelial cell signaling in Helicobacter pylori infection		
NOD-like receptor signaling pathway		
Shigellosis		
Phospholipase D signaling pathway		
Axon guidance		
Thyroid cancer		
Natural killer cell mediated cytotoxicity		
Glycosaminoglycan degradation		
Nicotinate and nicotinamide metabolism		
Fructose and mannose metabolism		
Bacterial invasion of epithelial cells		
Vibrio cholerae infection		

Supplementary Table 7: Significant Pathways of GSE97779 (Synovial macrophages from RA patients) dataset and GSE35455 (PBMCs from Tocilizumab treated RA patients) dataset

GSE97779	Common Pathways	GSE35455 TCMB
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RA Synovial Macrophages		RA treated with Tocilizumab
Osteoclast differentiation	AMPK signaling pathway	Calcium signaling pathway
PD-L1 expression and PD-1 checkpoint pathway in cancer	Apelin signaling pathway	Non-alcoholic fatty liver disease
Herpes simplex virus 1 infection	Apoptosis	Epstein-Barr virus infection
B cell receptor signaling pathway	Bladder cancer	Pathways of neurodegeneration
Lysosome	C-type lectin receptor signaling pathway	Pathways in cancer
Renal cell carcinoma	Endometrial cancer	Phagosome
Epstein-Barr virus infection	Epithelial cell signaling in Helicobacter pylori infection	Parkinson disease
Pathways in cancer	Epstein-Barr virus infection	Huntington disease
Hepatitis B	Fluid shear stress and atherosclerosis	Amyotrophic lateral sclerosis
Acute myeloid leukemia	Focal adhesion	Cell adhesion molecules
Human T-cell leukemia virus 1 infection	FoxO signaling pathway	Th1 and Th2 cell differentiation
Neurotrophin signaling pathway	Fructose and mannose metabolism	PI3K-Akt signaling pathway
Autophagy	Hepatitis B	Arrhythmogenic right ventricular cardiomyopathy
C-type lectin receptor signaling pathway	Hepatitis C	Focal adhesion
AGE-RAGE signaling pathway in diabetic complications	Human T-cell leukemia virus 1 infection	Hypertrophic cardiomyopathy
Human immunodeficiency virus 1 infection	Human cytomegalovirus infection	Proteoglycans in cancer
Ubiquitin mediated proteolysis	Human papillomavirus infection	Viral myocarditis
T cell receptor signaling pathway	Influenza A	Pathogenic Escherichia coli infection
Prolactin signaling pathway	Insulin signaling pathway	Protein export
Sphingolipid signaling pathway	Leishmaniasis	Prion disease
Salmonella infection	Leukocyte transendothelial migration	Protein processing in endoplasmic reticulum

Leishmaniasis	Lipid and atherosclerosis	Neuroactive ligand-receptor interaction
FoxO signaling pathway	Lysosome	MAPK signaling pathway
Chronic myeloid leukemia	MAPK signaling pathway	Human papillomavirus infection
Apoptosis	Melanoma	Lysosome
TNF signaling pathway	NOD-like receptor signaling pathway	Vibrio cholerae infection
ErbB signaling pathway	Neurotrophin signaling pathway	Aldosterone synthesis and secretion
Tuberculosis	Non-alcoholic fatty liver disease	Apelin signaling pathway
VEGF signaling pathway	Non-small cell lung cancer	Epithelial cell signaling in Helicobacter pylori infection
Non-small cell lung cancer	PI3K-Akt signaling pathway	Glycosphingolipid biosynthesis
Proteoglycans in cancer	Pancreatic cancer	Lipid and atherosclerosis
Fc gamma R-mediated phagocytosis	Pathogenic Escherichia coli infection	Th17 cell differentiation
Prostate cancer	Pathways in cancer	Tuberculosis
Human cytomegalovirus infection	Peroxisome	Thyroid hormone signaling pathway
MAPK signaling pathway	Phagosome	C-type lectin receptor signaling pathway
Th17 cell differentiation	Prostate cancer	Proteasome
Transcriptional misregulation in cancer	Protein processing in endoplasmic reticulum	Ras signaling pathway
Phagosome	Proteoglycans in cancer	ECM-receptor interaction
Kaposi sarcoma-associated herpesvirus infection	Ras signaling pathway	Adipocytokine signaling pathway
Pancreatic cancer	Shigellosis	cAMP signaling pathway
Measles	Small cell lung cancer	Diabetic cardiomyopathy
Longevity regulating pathway	TNF signaling pathway	Non-homologous end-joining
HIF-1 signaling pathway	Th1 and Th2 cell differentiation	Fluid shear stress and atherosclerosis
Th1 and Th2 cell differentiation	Th17 cell differentiation	Base excision repair
AMPK signaling pathway	Thyroid cancer	Fructose and mannose metabolism
Cellular senescence	Thyroid hormone signaling pathway	Neurotrophin signaling pathway

mTOR signaling pathway	Toxoplasmosis	AMPK signaling pathway
Central carbon metabolism in cancer	Transcriptional misregulation in cancer	Dilated cardiomyopathy
Colorectal cancer	Tuberculosis	Rheumatoid arthritis
Focal adhesion	Ubiquitin mediated proteolysis	Thyroid cancer
Glioma	Vibrio cholerae infection	Mineral absorption
Insulin resistance	secretion and action	Insulin signaling pathway
Lipid and atherosclerosis		NOD-like receptor signaling pathway
Protein processing in endoplasmic reticulum		Antigen processing and presentation
Viral carcinogenesis		Small cell lung cancer
NF-kappa B signaling pathway		Mitophagy
Hepatitis C		Peroxisome
Fatty acid degradation		Leukocyte transendothelial migration
Pathogenic Escherichia coli infection		Notch signaling pathway
Lysine degradation		Pancreatic cancer
Bladder cancer		Alzheimer disease
Peroxisome		Rap1 signaling pathway
Small cell lung cancer		Oxidative phosphorylation
Influenza A		Endocrine and other factor-regulated calcium reabsorption
Amoebiasis		Hepatitis C
Hepatocellular carcinoma		Bladder cancer
Toxoplasmosis		Terpenoid backbone biosynthesis
Yersinia infection		Transcriptional misregulation in cancer
Hematopoietic cell lineage		Primary immunodeficiency
p53 signaling pathway		Melanoma
N-Glycan biosynthesis		Prostate cancer
Thyroid hormone signaling pathway		Estrogen signaling pathway
Legionellosis		TNF signaling pathway

Valine, leucine and isoleucine degradation		Cardiac muscle contraction
Glycosaminoglycan biosynthesis		Hedgehog signaling pathway
Insulin signaling pathway		Renin-angiotensin system
Melanoma		Platelet activation
Endometrial cancer		RIG-I-like receptor signaling pathway
Toll-like receptor signaling pathway		Type II diabetes mellitus
Leukocyte transendothelial migration		Oxytocin signaling pathway
Fluid shear stress and atherosclerosis		Tight junction
Human papillomavirus infection		Human T-cell leukemia virus 1 infection
Apelin signaling pathway		Ubiquitin mediated proteolysis
Non-alcoholic fatty liver disease		Synaptic vesicle cycle
Various types of N-glycan biosynthesis		Glutathione metabolism
PI3K-Akt signaling pathway		Pentose phosphate pathway
Chemokine signaling pathway		Retrograde endocannabinoid signaling
Growth hormone synthesis, secretion and action		GnRH signaling pathway
Relaxin signaling pathway		Thermogenesis
JAK-STAT signaling pathway		Human cytomegalovirus infection
Chagas disease		Non-small cell lung cancer
Fc epsilon RI signaling pathway		Toxoplasmosis
Sphingolipid metabolism		Inflammatory bowel disease
Ras signaling pathway		Influenza A
Pyruvate metabolism		Endometrial cancer
Circadian rhythm		Apoptosis
Long-term potentiation		IL-17 signaling pathway
Ferroptosis		FoxO signaling pathway
Epithelial cell signaling in Helicobacter pylori infection		Shigellosis

NOD-like receptor signaling pathway		Hepatitis B
Shigellosis		Parathyroid hormone synthesis, secretion and action
Phospholipase D signaling pathway		ABC transporters
Axon guidance		Leishmaniasis
Thyroid cancer		
Natural killer cell mediated cytotoxicity		
Glycosaminoglycan degradation		
Nicotinate and nicotinamide metabolism		
Fructose and mannose metabolism		
Bacterial invasion of epithelial cells		
Vibrio cholerae infection		

Supplementary Table 8: Significant Pathways of GSE10500 (Synovial macrophages from RA patients) dataset and GSE35455 (PBMCs from Methotrexate treated RA patients) dataset

GSE10500	Common Pathways	GSE35455 MTX
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RA Synovial Macrophages		RA Treated with Methotrexate
Osteoclast differentiation	Acute myeloid leukemia	Calcium signaling pathway
Transcriptional misregulation in cancer	Antigen processing and presentation	Phagosome
Apoptosis	Breast cancer	Focal adhesion
Human T-cell leukemia virus 1 infection	Diabetic cardiomyopathy	Pathways of neurodegeneration
Glioma	Epstein-Barr virus infection	Parkinson disease
Epstein-Barr virus infection	Hematopoietic cell lineage	Lysosome
Complement and coagulation cascades	Human T-cell leukemia virus 1 infection	Non-alcoholic fatty liver disease
Small cell lung cancer	Human papillomavirus infection	Epstein-Barr virus infection
Cellular senescence	Leukocyte transendothelial migration	Human papillomavirus infection
Hepatitis C	Lipid and atherosclerosis	Amyotrophic lateral sclerosis
Hematopoietic cell lineage	Neurotrophin signaling pathway	Th1 and Th2 cell differentiation
MicroRNAs in cancer	Non-small cell lung cancer	Glycosphingolipid biosynthesis
JAK-STAT signaling pathway	Pancreatic cancer	Viral myocarditis
Chagas disease	Pathogenic Escherichia coli infection	Bladder cancer
NF-kappa B signaling pathway	Pathways in cancer	Proteoglycans in cancer
T cell receptor signaling pathway	Rap1 signaling pathway	Alzheimer disease
Salmonella infection	Small cell lung cancer	Protein export
Human papillomavirus infection	Transcriptional misregulation in cancer	Lipid and atherosclerosis
Leukocyte transendothelial migration		Notch signaling pathway
Pathways in cancer		Arrhythmogenic right ventricular cardiomyopathy
Pathogenic Escherichia coli infection		Pathways in cancer
Acute myeloid leukemia		ECM-receptor interaction
Viral carcinogenesis		Non-homologous end-joining
Prolactin signaling pathway		Proteasome
Melanoma		Thyroid hormone signaling pathway
Non-small cell lung cancer		Prion disease

Human immunodeficiency virus 1 infection		PI3K-Akt signaling pathway
Cytokine-cytokine receptor interaction		Diabetic cardiomyopathy
Measles		Protein processing in endoplasmic reticulum
Lipid and atherosclerosis		Thyroid cancer
Chronic myeloid leukemia		Small cell lung cancer
Pancreatic cancer		Tuberculosis
Antigen processing and presentation		MAPK signaling pathway
Breast cancer		Hypertrophic cardiomyopathy
PD-L1 expression and PD-1 checkpoint pathway in cancer		Parathyroid hormone synthesis, secretion and action
IL-17 signaling pathway		Huntington disease
Hepatocellular carcinoma		Non-small cell lung cancer
Prostate cancer		Neurotrophin signaling pathway
Viral protein interaction with cytokine and cytokine receptor		Pathogenic Escherichia coli infection
Amoebiasis		Vibrio cholerae infection
Longevity regulating pathway		Dilated cardiomyopathy
Toll-like receptor signaling pathway		Platelet activation
HIF-1 signaling pathway		Insulin signaling pathway
Type II diabetes mellitus		Rheumatoid arthritis
TNF signaling pathway		Epithelial cell signaling in Helicobacter pylori infection
Kaposi sarcoma-associated herpesvirus infection		Neuroactive ligand-receptor interaction
Neurotrophin signaling pathway		Antigen processing and presentation
Diabetic cardiomyopathy		Peroxisome
Cell cycle		Leukocyte transendothelial migration

Rap1 signaling pathway		Aldosterone synthesis and secretion
		Amino sugar and nucleotide sugar metabolism
		Adherens junction
		Fluid shear stress and atherosclerosis
		NOD-like receptor signaling pathway
		cAMP signaling pathway
		Adipocytokine signaling pathway
		Regulation of actin cytoskeleton
		Other glycan degradation
		Rap1 signaling pathway
		Endometrial cancer
		Human T-cell leukemia virus 1 infection
		Cell adhesion molecules
		Glycine, serine and threonine metabolism
		Hematopoietic cell lineage
		Acute myeloid leukemia
		Base excision repair
		Fructose and mannose metabolism
		Transcriptional misregulation in cancer
		Apelin signaling pathway
		Pancreatic cancer
		Breast cancer
		Circadian entrainment
		Steroid biosynthesis
		Ubiquitin mediated proteolysis
		Galactose metabolism
		Chemokine signaling pathway
		Th17 cell differentiation

		Ras signaling pathway
		Staphylococcus aureus infection
		Estrogen signaling pathway
		Nitrogen metabolism
		Cardiac muscle contraction
		Toxoplasmosis
		Cushing syndrome
		AGE-RAGE signaling pathway in diabetic complications

Supplementary Table 9: Significant Pathways of GSE10500 (Synovial macrophages from RA patients) dataset and GSE35455 (PBMCs from Tocilizumab treated RA patients) dataset

GSE10500	Common Pathways	GSE35455 TCMB
RA Synovial Macrophages		RA treated with Tocilizumab

Osteoclast differentiation	Antigen processing and presentation	Calcium signaling pathway
Transcriptional misregulation in cancer	Apoptosis	Non-alcoholic fatty liver disease
Apoptosis	Diabetic cardiomyopathy	Epstein-Barr virus infection
Human T-cell leukemia virus 1 infection	Epstein-Barr virus infection	Pathways of neurodegeneration
Glioma	Hepatitis C	Pathways in cancer
Epstein-Barr virus infection	Human T-cell leukemia virus 1 infection	Phagosome
Complement and coagulation cascades	Human papillomavirus infection	Parkinson disease
Small cell lung cancer	IL-17 signaling pathway	Huntington disease
Cellular senescence	Leukocyte transendothelial migration	Amyotrophic lateral sclerosis
Hepatitis C	Lipid and atherosclerosis	Cell adhesion molecules
Hematopoietic cell lineage	Melanoma	Th1 and Th2 cell differentiation
MicroRNAs in cancer	Neurotrophin signaling pathway	PI3K-Akt signaling pathway
JAK-STAT signaling pathway	Non-small cell lung cancer	Arrhythmogenic right ventricular cardiomyopathy
Chagas disease	Pancreatic cancer	Focal adhesion
NF-kappa B signaling pathway	Pathogenic Escherichia coli infection	Hypertrophic cardiomyopathy
T cell receptor signaling pathway	Pathways in cancer	Proteoglycans in cancer
Salmonella infection	Prostate cancer	Viral myocarditis
Human papillomavirus infection	Rap1 signaling pathway	Pathogenic Escherichia coli infection
Leukocyte transendothelial migration	Small cell lung cancer	Protein export
Pathways in cancer	TNF signaling pathway	Prion disease
Pathogenic Escherichia coli infection	Transcriptional misregulation in cancer	Protein processing in endoplasmic reticulum
Acute myeloid leukemia	Type II diabetes mellitus	Neuroactive ligand-receptor interaction

Viral carcinogenesis		MAPK signaling pathway
Prolactin signaling pathway		Human papillomavirus infection
Melanoma		Lysosome
Non-small cell lung cancer		Vibrio cholerae infection
Human immunodeficiency virus 1 infection		Aldosterone synthesis and secretion
Cytokine-cytokine receptor interaction		Apelin signaling pathway
Measles		Epithelial cell signaling in Helicobacter pylori infection
Lipid and atherosclerosis		Glycosphingolipid biosynthesis
Chronic myeloid leukemia		Lipid and atherosclerosis
Pancreatic cancer		Th17 cell differentiation
Antigen processing and presentation		Tuberculosis
Breast cancer		Thyroid hormone signaling pathway
PD-L1 expression and PD-1 checkpoint pathway in cancer		C-type lectin receptor signaling pathway
IL-17 signaling pathway		Proteasome
Hepatocellular carcinoma		Ras signaling pathway
Prostate cancer		ECM-receptor interaction
Viral protein interaction with cytokine and cytokine receptor		Adipocytokine signaling pathway
Amoebiasis		cAMP signaling pathway
Longevity regulating pathway		Diabetic cardiomyopathy
Toll-like receptor signaling pathway		Non-homologous end-joining
HIF-1 signaling pathway		Fluid shear stress and atherosclerosis
Type II diabetes mellitus		Base excision repair
TNF signaling pathway		Fructose and mannose metabolism

Kaposi sarcoma-associated herpesvirus infection		Neurotrophin signaling pathway
Neurotrophin signaling pathway		AMPK signaling pathway
Diabetic cardiomyopathy		Dilated cardiomyopathy
Cell cycle		Rheumatoid arthritis
Rap1 signaling pathway		Thyroid cancer
		Mineral absorption
		Insulin signaling pathway
		NOD-like receptor signaling pathway
		Antigen processing and presentation
		Small cell lung cancer
		Mitophagy
		Peroxisome
		Leukocyte transendothelial migration
		Notch signaling pathway
		Pancreatic cancer
		Alzheimer disease
		Rap1 signaling pathway
		Oxidative phosphorylation
		Endocrine and other factor-regulated calcium reabsorption
		Hepatitis C
		Bladder cancer
		Terpenoid backbone biosynthesis
		Transcriptional misregulation in cancer
		Primary immunodeficiency
		Melanoma
		Prostate cancer

		Estrogen signaling pathway
		TNF signaling pathway
		Cardiac muscle contraction
		Hedgehog signaling pathway
		Renin-angiotensin system
		Platelet activation
		RIG-I-like receptor signaling pathway
		Type II diabetes mellitus
		Oxytocin signaling pathway
		Tight junction
		Human T-cell leukemia virus 1 infection
		Ubiquitin mediated proteolysis
		Synaptic vesicle cycle
		Glutathione metabolism
		Pentose phosphate pathway
		Retrograde endocannabinoid signaling
		GnRH signaling pathway
		Thermogenesis
		Human cytomegalovirus infection
		Non-small cell lung cancer
		Toxoplasmosis
		Inflammatory bowel disease
		Influenza A
		Endometrial cancer
		Apoptosis
		IL-17 signaling pathway
		FoxO signaling pathway

		Shigellosis
		Hepatitis B
		Parathyroid hormone synthesis, secretion and action
		ABC transporters
		Leishmaniasis

Supplementary Table 10: Significant Pathways of GSE77298 (Synovial biopsies of from RA patients) dataset and GSE35455 (PBMCs from Methotrexate treated RA patients) dataset

GSE77298	Common Pathways	GSE35455 MTX
RA Synovial Biopsy		RA Treated with Methotrexate

Adrenergic signaling in cardiomyocytes	AGE-RAGE signaling pathway in diabetic complications	Calcium signaling pathway
Lysosome	Adherens junction	Phagosome
Viral myocarditis	Adipocytokine signaling pathway	Focal adhesion
Dilated cardiomyopathy	Antigen processing and presentation	Pathways of neurodegeneration
Tuberculosis	Apelin signaling pathway	Parkinson disease
Rheumatoid arthritis	Arrhythmogenic right ventricular cardiomyopathy	Lysosome
Natural killer cell mediated cytotoxicity	Bladder cancer	Non-alcoholic fatty liver disease
Hypertrophic cardiomyopathy	Calcium signaling pathway	Epstein-Barr virus infection
Epstein-Barr virus infection	Cardiac muscle contraction	Human papillomavirus infection
Calcium signaling pathway	Cell adhesion molecules	Amyotrophic lateral sclerosis
Arrhythmogenic right ventricular cardiomyopathy	Chemokine signaling pathway	Th1 and Th2 cell differentiation
Leishmaniasis	Circadian entrainment	Glycosphingolipid biosynthesis
Protein processing in endoplasmic reticulum	Diabetic cardiomyopathy	Viral myocarditis
NF-kappa B signaling pathway	Dilated cardiomyopathy	Bladder cancer
Graft-versus-host disease	ECM-receptor interaction	Proteoglycans in cancer
Phagosome	Epithelial cell signaling in Helicobacter pylori infection	Alzheimer disease
Pathogenic Escherichia coli infection	Epstein-Barr virus infection	Protein export
ECM-receptor interaction	Focal adhesion	Lipid and atherosclerosis
Antigen processing and presentation	Glycine	Notch signaling pathway
Human cytomegalovirus infection	Human T-cell leukemia virus 1 infection	Arrhythmogenic right ventricular cardiomyopathy
Proteoglycans in cancer	Human papillomavirus infection	Pathways in cancer
Human immunodeficiency virus 1 infection	Hypertrophic cardiomyopathy	ECM-receptor interaction

Chemokine signaling pathway	Insulin signaling pathway	Non-homologous end-joining
Cell adhesion molecules	Leukocyte transendothelial migration	Proteasome
Yersinia infection	Lipid and atherosclerosis	Thyroid hormone signaling pathway
IL-17 signaling pathway	Lysosome	Prion disease
Regulation of actin cytoskeleton	NOD-like receptor signaling pathway	PI3K-Akt signaling pathway
Endocrine and other factor-regulated calcium reabsorption	Neurotrophin signaling pathway	Diabetic cardiomyopathy
Lipid and atherosclerosis	PI3K-Akt signaling pathway	Protein processing in endoplasmic reticulum
Relaxin signaling pathway	Pathogenic Escherichia coli infection	Thyroid cancer
Focal adhesion	Pathways in cancer	Small cell lung cancer
Glycolysis / Gluconeogenesis	Phagosome	Tuberculosis
Amoebiasis	Platelet activation	MAPK signaling pathway
Fc gamma R-mediated phagocytosis	Protein processing in endoplasmic reticulum	Hypertrophic cardiomyopathy
Allograft rejection	Proteoglycans in cancer	Parathyroid hormone synthesis, secretion and action
Kaposi sarcoma-associated herpesvirus infection	Regulation of actin cytoskeleton	Huntington disease
Glucagon signaling pathway	Rheumatoid arthritis	Non-small cell lung cancer
AGE-RAGE signaling pathway in diabetic complications	Staphylococcus aureus infection	Neurotrophin signaling pathway
Leukocyte transendothelial migration	Th1 and Th2 cell differentiation	Pathogenic Escherichia coli infection
Human papillomavirus infection	Th17 cell differentiation	Vibrio cholerae infection
B cell receptor signaling pathway	Thyroid hormone signaling pathway	Dilated cardiomyopathy
Sphingolipid signaling pathway	Toxoplasmosis	Platelet activation
Autoimmune thyroid disease	Transcriptional misregulation in cancer	Insulin signaling pathway
NOD-like receptor signaling pathway	Tuberculosis	Rheumatoid arthritis

Axon guidance	Vibrio cholerae infection	Epithelial cell signaling in Helicobacter pylori infection
Endocytosis	Viral myocarditis	Neuroactive ligand-receptor interaction
Pertussis	secretion and action	Antigen processing and presentation
GnRH signaling pathway	serine and threonine metabolism	Peroxisome
Growth hormone synthesis, secretion and action		Leukocyte transendothelial migration
cGMP-PKG signaling pathway		Aldosterone synthesis and secretion
N-Glycan biosynthesis		Amino sugar and nucleotide sugar metabolism
Vibrio cholerae infection		Adherens junction
Human T-cell leukemia virus 1 infection		Fluid shear stress and atherosclerosis
Glycine, serine and threonine metabolism		NOD-like receptor signaling pathway
Thyroid hormone signaling pathway		cAMP signaling pathway
Intestinal immune network for IgA production		Adipocytokine signaling pathway
Epithelial cell signaling in Helicobacter pylori infection		Regulation of actin cytoskeleton
Th17 cell differentiation		Other glycan degradation
Oxytocin signaling pathway		Rap1 signaling pathway
Cardiac muscle contraction		Endometrial cancer
p53 signaling pathway		Human T-cell leukemia virus 1 infection
Salmonella infection		Cell adhesion molecules
Adherens junction		Glycine, serine and threonine metabolism
Bacterial invasion of epithelial cells		Hematopoietic cell lineage
Cellular senescence		Acute myeloid leukemia
Toxoplasmosis		Base excision repair

Various types of N-glycan biosynthesis		Fructose and mannose metabolism
PI3K-Akt signaling pathway		Transcriptional misregulation in cancer
Phenylalanine metabolism		Apelin signaling pathway
Dopaminergic synapse		Pancreatic cancer
Fc epsilon RI signaling pathway		Breast cancer
Type I diabetes mellitus		Circadian entrainment
Influenza A		Steroid biosynthesis
TNF signaling pathway		Ubiquitin mediated proteolysis
Adipocytokine signaling pathway		Galactose metabolism
Insulin signaling pathway		Chemokine signaling pathway
Transcriptional misregulation in cancer		Th17 cell differentiation
Tyrosine metabolism		Ras signaling pathway
Tight junction		Staphylococcus aureus infection
Gap junction		Estrogen signaling pathway
Inflammatory bowel disease		Nitrogen metabolism
Apelin signaling pathway		Cardiac muscle contraction
PD-L1 expression and PD-1 checkpoint pathway in cancer		Toxoplasmosis
Staphylococcus aureus infection		Cushing syndrome
Serotonergic synapse		AGE-RAGE signaling pathway in diabetic complications
Mineral absorption		
Diabetic cardiomyopathy		
Thyroid hormone synthesis		
Chagas disease		
Pancreatic secretion		
Pathways in cancer		
Bladder cancer		
Ferroptosis		

Osteoclast differentiation		
Pentose phosphate pathway		
Circadian entrainment		
Cholesterol metabolism		
Neurotrophin signaling pathway		
VEGF signaling pathway		
Th1 and Th2 cell differentiation		
Apoptosis		
Renin-angiotensin system		
Platelet activation		
Protein digestion and absorption		

Supplementary Table 11: Significant Pathways of GSE77298 (Synovial biopsies of RA patients) dataset and GSE35455 (PBMCs from Tocilizumab treated RA patients) dataset

GSE77298	Common Pathways	GSE35455 TCMB
RA Synovial Biopsy		RA treated with Tocilizumab
Adrenergic signaling in cardiomyocytes	Adipocytokine signaling pathway	Calcium signaling pathway
Lysosome	Antigen processing and presentation	Non-alcoholic fatty liver disease
Viral myocarditis	Apelin signaling pathway	Epstein-Barr virus infection
Dilated cardiomyopathy	Apoptosis	Pathways of neurodegeneration
Tuberculosis	Arrhythmogenic right ventricular cardiomyopathy	Pathways in cancer
Rheumatoid arthritis	Bladder cancer	Phagosome
Natural killer cell mediated cytotoxicity	Calcium signaling pathway	Parkinson disease
Hypertrophic cardiomyopathy	Cardiac muscle contraction	Huntington disease
Epstein-Barr virus infection	Cell adhesion molecules	Amyotrophic lateral sclerosis
Calcium signaling pathway	Diabetic cardiomyopathy	Cell adhesion molecules
Arrhythmogenic right ventricular cardiomyopathy	Dilated cardiomyopathy	Th1 and Th2 cell differentiation
Leishmaniasis	ECM-receptor interaction	PI3K-Akt signaling pathway
Protein processing in endoplasmic reticulum	Endocrine and other factor-regulated calcium reabsorption	Arrhythmogenic right ventricular cardiomyopathy
NF-kappa B signaling pathway	Epithelial cell signaling in Helicobacter pylori infection	Focal adhesion
Graft-versus-host disease	Epstein-Barr virus infection	Hypertrophic cardiomyopathy
Phagosome	Focal adhesion	Proteoglycans in cancer
Pathogenic Escherichia coli infection	GnRH signaling pathway	Viral myocarditis
ECM-receptor interaction	Human T-cell leukemia virus 1 infection	Pathogenic Escherichia coli infection
Antigen processing and presentation	Human cytomegalovirus infection	Protein export
Human cytomegalovirus infection	Human papillomavirus infection	Prion disease
Proteoglycans in cancer	Hypertrophic cardiomyopathy	Protein processing in endoplasmic reticulum
Human immunodeficiency virus 1 infection	IL-17 signaling pathway	Neuroactive ligand-receptor interaction
Chemokine signaling pathway	Inflammatory bowel disease	MAPK signaling pathway

Cell adhesion molecules	Influenza A	Human papillomavirus infection
Yersinia infection	Insulin signaling pathway	Lysosome
IL-17 signaling pathway	Leishmaniasis	Vibrio cholerae infection
Regulation of actin cytoskeleton	Leukocyte transendothelial migration	Aldosterone synthesis and secretion
Endocrine and other factor-regulated calcium reabsorption	Lipid and atherosclerosis	Apelin signaling pathway
Lipid and atherosclerosis	Lysosome	Epithelial cell signaling in Helicobacter pylori infection
Relaxin signaling pathway	Mineral absorption	Glycosphingolipid biosynthesis
Focal adhesion	NOD-like receptor signaling pathway	Lipid and atherosclerosis
Glycolysis / Gluconeogenesis	Neurotrophin signaling pathway	Th17 cell differentiation
Amoebiasis	Oxytocin signaling pathway	Tuberculosis
Fc gamma R-mediated phagocytosis	PI3K-Akt signaling pathway	Thyroid hormone signaling pathway
Allograft rejection	Pathogenic Escherichia coli infection	C-type lectin receptor signaling pathway
Kaposi sarcoma-associated herpesvirus infection	Pathways in cancer	Proteasome
Glucagon signaling pathway	Pentose phosphate pathway	Ras signaling pathway
AGE-RAGE signaling pathway in diabetic complications	Phagosome	ECM-receptor interaction
Leukocyte transendothelial migration	Platelet activation	Adipocytokine signaling pathway
Human papillomavirus infection	Protein processing in endoplasmic reticulum	cAMP signaling pathway
B cell receptor signaling pathway	Proteoglycans in cancer	Diabetic cardiomyopathy
Sphingolipid signaling pathway	Renin-angiotensin system	Non-homologous end-joining
Autoimmune thyroid disease	Rheumatoid arthritis	Fluid shear stress and atherosclerosis
NOD-like receptor signaling pathway	TNF signaling pathway	Base excision repair
Axon guidance	Th1 and Th2 cell differentiation	Fructose and mannose metabolism
Endocytosis	Th17 cell differentiation	Neurotrophin signaling pathway
Pertussis	Thyroid hormone signaling pathway	AMPK signaling pathway
GnRH signaling pathway	Tight junction	Dilated cardiomyopathy

Growth hormone synthesis, secretion and action	Toxoplasmosis	Rheumatoid arthritis
cGMP-PKG signaling pathway	Transcriptional misregulation in cancer	Thyroid cancer
N-Glycan biosynthesis	Tuberculosis	Mineral absorption
Vibrio cholerae infection	Vibrio cholerae infection	Insulin signaling pathway
Human T-cell leukemia virus 1 infection	Viral myocarditis	NOD-like receptor signaling pathway
Glycine, serine and threonine metabolism	secretion and action	Antigen processing and presentation
Thyroid hormone signaling pathway		Small cell lung cancer
Intestinal immune network for IgA production		Mitophagy
Epithelial cell signaling in Helicobacter pylori infection		Peroxisome
Th17 cell differentiation		Leukocyte transendothelial migration
Oxytocin signaling pathway		Notch signaling pathway
Cardiac muscle contraction		Pancreatic cancer
p53 signaling pathway		Alzheimer disease
Salmonella infection		Rap1 signaling pathway
Adherens junction		Oxidative phosphorylation
Bacterial invasion of epithelial cells		Endocrine and other factor-regulated calcium reabsorption
Cellular senescence		Hepatitis C
Toxoplasmosis		Bladder cancer
Various types of N-glycan biosynthesis		Terpenoid backbone biosynthesis
PI3K-Akt signaling pathway		Transcriptional misregulation in cancer
Phenylalanine metabolism		Primary immunodeficiency
Dopaminergic synapse		Melanoma
Fc epsilon RI signaling pathway		Prostate cancer
Type I diabetes mellitus		Estrogen signaling pathway
Influenza A		TNF signaling pathway
TNF signaling pathway		Cardiac muscle contraction

Adipocytokine signaling pathway		Hedgehog signaling pathway
Insulin signaling pathway		Renin-angiotensin system
Transcriptional misregulation in cancer		Platelet activation
Tyrosine metabolism		RIG-I-like receptor signaling pathway
Tight junction		Type II diabetes mellitus
Gap junction		Oxytocin signaling pathway
Inflammatory bowel disease		Tight junction
Apelin signaling pathway		Human T-cell leukemia virus 1 infection
PD-L1 expression and PD-1 checkpoint pathway in cancer		Ubiquitin mediated proteolysis
Staphylococcus aureus infection		Synaptic vesicle cycle
Serotonergic synapse		Glutathione metabolism
Mineral absorption		Pentose phosphate pathway
Diabetic cardiomyopathy		Retrograde endocannabinoid signaling
Thyroid hormone synthesis		GnRH signaling pathway
Chagas disease		Thermogenesis
Pancreatic secretion		Human cytomegalovirus infection
Pathways in cancer		Non-small cell lung cancer
Bladder cancer		Toxoplasmosis
Ferroptosis		Inflammatory bowel disease
Osteoclast differentiation		Influenza A
Pentose phosphate pathway		Endometrial cancer
Circadian entrainment		Apoptosis
Cholesterol metabolism		IL-17 signaling pathway
Neurotrophin signaling pathway		FoxO signaling pathway
VEGF signaling pathway		Shigellosis
Th1 and Th2 cell differentiation		Hepatitis B
Apoptosis		Parathyroid hormone synthesis, secretion and action

Renin-angiotensin system		ABC transporters
Platelet activation		Leishmaniasis
Protein digestion and absorption		