

GO-terms enriched in heatmap gene clusters for mouse and *Eimeria falciformis*

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1 Objective

bla bla bla

2 Results for *E. falciformis*

Cluster 1, BP, Ef. Overrepresented GO biological process terms among parasite genes which are highly abundant on day 7 p.i.. Compared to cluster 2, which also have a high abundance on day 7, these genes cluster more closely with genes in cluster 4, which are highly expressed in oocysts. In total the cluster contains 201 genes of which 96 have GO annotations, and 105 do not.

The eight first GO terms in this list are supported by the same three genes. Unintuitively, seven of these eight terms are associated with wound healing and coagulation. However, orthologs in ToxoDB ((((((a blastx (NCBI) of the sequences)))))) pointed to other *Eimeria* spp. and *Toxoplasma gondii* proteins annotated as PAN domain containing proteins. The PAN domain is found in plasminogen /hepatocyte growth factor family and in coagulation factor XI family, explaining the GO blood coagulation terms. Of interest here, the same domain has also been reported to be common in nematodes such as *Caenorhabditis elegans*, however the function is not understood. (Thordai99)

Alignments to *Eimeria* spp. and *Hammondia hammondi*, contain the annotation micronemal protein MIC4 (NCBI...), a microneme protein, reported by, e.g., the Tomley group (Brown01). Later publications on *T. gondii* (Marchant12) also associate these domains and proteins with micronemes and therefore invasion. In our case, this is a peculiar result, since the enrichment appears on day 7 p.i.. A possible role at this timepoint is suggested by work on the fungi *Sclerotinia sclerotiorum* where Yu et al. reported an important role for PAN domain proteins in cell wall integrity (Yu12). This role for MIC proteins has to our knowledge not been investigated in apicomplexan parasites. The other two GO terms in the cluster of day seven upregulated genes are DNA replication and DNA replication initiation, which most likely reflects late stage schizogony or gamete formation.

GO.ID	Term	Annotated	Significant	Expected	p.value	adj.p
GO:0007596	blood coagulation	5	3	0.18	0.00	0.01
GO:0007599	hemostasis	5	3	0.18	0.00	0.01
GO:0009611	response to wounding	5	3	0.18	0.00	0.01
GO:0042060	wound healing	5	3	0.18	0.00	0.01
GO:0050817	coagulation	5	3	0.18	0.00	0.01
GO:0050878	regulation of body fluid levels	5	3	0.18	0.00	0.01
GO:0032501	multicellular organismal process	6	3	0.22	0.00	0.01
GO:0044707	single-multicellular organism process	6	3	0.22	0.00	0.01
GO:0006260	DNA replication	34	6	1.26	0.00	0.01
GO:0006270	DNA replication initiation	3	2	0.11	0.00	0.04

Cluster 2, BP, Ef. Overrepresented GO biological process terms among parasite genes which are highly abundant on day 7 p.i.. Compared to cluster 1, which is also upregulated on day 7 p.i., these genes cluster more closely with cluster 6, which contains genes highly abundant in sporozoites. In total the cluster contains 271 genes of which 107 have GO annotations, and 164 do not.

The term 'single-organism process' is enriched contains the largest number of genes in this cluster (38). All genes contributing to other GO terms in this list, except those terms indicating motility (top 3), are contained in the 38 single-organism genes. Among the GO terms themselves, annotations such as purine/nucleoside/nucleotide metabolic process dominate this list, but these genes are also found among the genes for the 'single organism' terms. A closer look at these 38 genes reveals 12 genes annotated as either dynein, kinesin or tubulin chains/proteins, indicating activity related to parasite motility. Also potentially linked to motility is the occurrence of growth arrest specific protein 8, Gas8, which in the mouse has been reported to be highly expressed in the testes and important for mouse sperm function (Yeh02). Other genes among the 38 indicate carbon fixation (glycolysis/gluconeogenesis) or different conversions of nucleoside phosphates. In addition, a Ras family protein, RNA polymerase II transcription initiation factor and Sec23 and Sec24 were among orthologs identified in *E. falciformis* cluster 2. In the list of enriched GO molecular functions 'microtubule motor activity' points towards parasite movement. Also, under the term 'protein binding', dynein and kinesin genes which are different from the dynein and kinesin genes in the biological process list, appear. Orthologs to genes which contribute to the enrichment of other GO terms in this list also indicate motility with annotations including 'flagellar' or 'intraflagellar'. In addition, there are two 'EF-hand domain containing proteins' annotations and also direct naming of such proteins: caltractin and centrin-1, as well as troponin. Caltractin and centrin-1 are associated with the centrosome and

structure and function of microtubuli, in mammals, and troponin which is linked to muscle function (UniProt). Cluster 1, MF, Ef. Overrepresented GO molecular function terms among parasite genes which are highly abundant on day 7 p.i.. Compared to cluster 2, which also have a high abundance on day 7, these genes cluster more closely with genes in cluster 4, which are highly expressed in oocysts. Four GO molecular functions are enriched in cluster 1 (adj. p-value = 0.14), supported by ten different genes, i.e., there is overlap in the genes. Carbon metabolism genes are represented by 6-phosphogluconate dehydrogenase and glycogen phosphorylase family protein 1. UDP-glucose 4-epimerase and amiloride-sensitive amine oxidase are reported as upregulated in gametocytes in *E. tenella* by RNA-seq (Walker15) and suggested by those authors to play a role in cyst wall synthesis.

Cluster 2, MF, Ef. Overrepresented GO molecular function terms among parasite genes which are highly abundant on day 7 p.i.. Compared to cluster 1, which is also upregulated on day 7 p.i., these genes cluster more closely with cluster 6, which contains genes highly abundant in sporozoites.

Cluster 3, BP, Ef. Overrepresented GO biological process terms among parasite genes which have a low abundance in sporulated oocysts and sporozoites. In mouse stages, i.e., day 3, 5, and 7 samples there is a tendency to upregulation among these genes. In total the cluster contains 204 genes of which 121 have GO annotations, and 83 do not.

Cluster 3, MF, Ef. Overrepresented GO molecular function terms among parasite genes which have a low abundance in sporulated oocysts and sporozoites. In mouse stages, i.e., day 3, 5, and 7 samples there is a tendency to upregulation among these genes.

Cluster 4, BP, Ef. Overrepresented GO biological process terms among parasite genes which are highly abundant in sporulated oocysts. These genes cluster most closely with cluster 1, in which genes are highly abundant on day 7 p.i.. In cluster 4, genes have below average abundance in all day 3 and 5 samples. In total the cluster contains 316 genes of which 157 have GO annotations, and 159 do not.

Cluster 4, MF, Ef. Overrepresented GO molecular function terms among parasite genes which are highly abundant in sporulated oocysts. These genes cluster most closely with cluster 1, in which genes are highly abundant on day 7 p.i.. In cluster 4, genes have below average abundance in all day 3 and 5 samples.

Cluster 5, BP, Ef. Overrepresented GO biological process terms among parasite genes which have low abundance in sporulated oocysts, sporozoites and on day 7 p.i.. These genes seem to increase in abundance upon infection and decrease late in infection, i.e., on day 7. In total the cluster contains 183 genes of which 83 have GO annotations, and 100 do not.

Cluster 5, MF, Ef. Overrepresented GO molecular function terms among parasite genes which have low abundance in sporulated oocysts, sporozoites and on day 7 p.i.. These genes seem to increase in abundance upon infection and decrease late in infection, i.e., on day 7.

Cluster 6, BP, Ef. Overrepresented GO biological process terms among parasite genes which are highly abundant in sporozoites but mainly downregulated in sporulated oocysts, apart from a few genes in the cluster. This cluster seems to distinguish sporozoites from sporulated oocysts and have an average mRNA abundance in all other samples. In total the cluster contains 180 genes of which 70 have GO annotations, and 110 do not.

Cluster 6, MF, Ef. Overrepresented GO molecular function terms among parasite genes which are highly abundant in sporozoites but mainly downregulated in sporulated oocysts, apart from a few genes in the cluster. This cluster seems to distinguish sporozoites from sporulated oocysts and have an average mRNA abundance in all other samples.

Cluster 7, BP, Ef. Overrepresented GO biological process terms among parasite genes which have low abundance in sporulated oocysts. In sporozoites and early in infection, i.e., day 3 and 5 p.i., some of these genes are highly

abundant. On day 7 p.i. these mRNAs have a below average abundance. In total the cluster contains 263 genes of which 131 have GO annotations, and 132 do not.

Cluster 7, MF, Ef. Overrepresented GO molecular function terms among parasite genes which have low abundance in sporulated oocysts. In sporozoites and early in infection, i.e., day 3 and 5 p.i., some of these genes are highly abundant. On day 7 p.i. these mRNAs have a below average abundance.

GO.ID	Term	Annotated	Significant	Expected	p.value	adj.p
GO:0006928	movement of cell or subcellular componen...	40	13	1.43	0.00	0.00
GO:0007018	microtubule-based movement	38	12	1.36	0.00	0.00
GO:0007017	microtubule-based process	48	13	1.71	0.00	0.00
GO:0044763	single-organism cellular process	518	34	18.50	0.00	0.00
GO:0044699	single-organism process	670	38	23.93	0.00	0.00
GO:0006165	nucleoside diphosphate phosphorylation	17	5	0.61	0.00	0.00
GO:0046939	nucleotide phosphorylation	18	5	0.64	0.00	0.00
GO:0009132	nucleoside diphosphate metabolic process	19	5	0.68	0.00	0.00
GO:0005975	carbohydrate metabolic process	67	9	2.39	0.00	0.00
GO:0009144	purine nucleoside triphosphate metabolic...	32	6	1.14	0.00	0.01
GO:0009199	ribonucleoside triphosphate metabolic pr...	32	6	1.14	0.00	0.01
GO:0009205	purine ribonucleoside triphosphate metab...	32	6	1.14	0.00	0.01
GO:0009141	nucleoside triphosphate metabolic proces...	33	6	1.18	0.00	0.01
GO:0006096	glycolytic process	14	4	0.50	0.00	0.01
GO:0006757	ATP generation from ADP	14	4	0.50	0.00	0.01
GO:0009135	purine nucleoside diphosphate metabolic ...	14	4	0.50	0.00	0.01
GO:0009179	purine ribonucleoside diphosphate metabo...	14	4	0.50	0.00	0.01
GO:0009185	ribonucleoside diphosphate metabolic pro...	14	4	0.50	0.00	0.01
GO:0016052	carbohydrate catabolic process	14	4	0.50	0.00	0.01
GO:0044724	single-organism carbohydrate catabolic p...	14	4	0.50	0.00	0.01
GO:0046031	ADP metabolic process	14	4	0.50	0.00	0.01
GO:0006006	glucose metabolic process	7	3	0.25	0.00	0.01
GO:0006090	pyruvate metabolic process	15	4	0.54	0.00	0.01
GO:0009150	purine ribonucleotide metabolic process	37	6	1.32	0.00	0.01
GO:0042278	purine nucleoside metabolic process	37	6	1.32	0.00	0.01
GO:0046128	purine ribonucleoside metabolic process	37	6	1.32	0.00	0.01
GO:0006163	purine nucleotide metabolic process	38	6	1.36	0.00	0.01
GO:0009259	ribonucleotide metabolic process	38	6	1.36	0.00	0.01
GO:0044723	single-organism carbohydrate metabolic p...	39	6	1.39	0.00	0.01
GO:0009119	ribonucleoside metabolic process	40	6	1.43	0.00	0.01
GO:0072521	purine-containing compound metabolic pro...	40	6	1.43	0.00	0.01
GO:0046034	ATP metabolic process	29	5	1.04	0.00	0.01
GO:0019693	ribose phosphate metabolic process	42	6	1.50	0.00	0.01
GO:0019318	hexose metabolic process	9	3	0.32	0.00	0.01
GO:0009117	nucleotide metabolic process	57	7	2.04	0.00	0.01
GO:0016310	phosphorylation	163	13	5.82	0.00	0.01
GO:0006094	gluconeogenesis	3	2	0.11	0.00	0.01
GO:0019319	hexose biosynthetic process	3	2	0.11	0.00	0.01
GO:0046364	monosaccharide biosynthetic process	3	2	0.11	0.00	0.01
GO:0005996	monosaccharide metabolic process	10	3	0.36	0.00	0.01
GO:0006753	nucleoside phosphate metabolic process	60	7	2.14	0.00	0.01
GO:0019362	pyridine nucleotide metabolic process	20	4	0.71	0.00	0.01
GO:0046496	nicotinamide nucleotide metabolic proces...	20	4	0.71	0.00	0.01
GO:0072524	pyridine-containing compound metabolic p...	20	4	0.71	0.00	0.01
GO:0009116	nucleoside metabolic process	46	6	1.64	0.00	0.01
GO:1901657	glycosyl compound metabolic process	46	6	1.64	0.00	0.01
GO:1901135	carbohydrate derivative metabolic proces...	78	8	2.79	0.01	0.01
GO:0006733	oxidoreduction coenzyme metabolic proces...	21	4	0.75	0.01	0.01
GO:0009126	purine nucleoside monophosphate metaboli...	34	5	1.21	0.01	0.01
GO:0009167	purine ribonucleoside monophosphate meta...	34	5	1.21	0.01	0.01
GO:0009161	ribonucleoside monophosphate metabolic p...	35	5	1.25	0.01	0.01
GO:0016051	carbohydrate biosynthetic process	12	3	0.43	0.01	0.01
GO:0044712	single-organism catabolic process	23	4	0.82	0.01	0.01
GO:0009123	nucleoside monophosphate metabolic proce...	36	5	1.29	0.01	0.01

GO.ID	Term	Annotated	Significant	Expected	p.value	adj.p
GO:0048037	cofactor binding	79	8	2.80	0.01	0.14
GO:0031177	phosphopantetheine binding	4	2	0.14	0.01	0.14
GO:0072341	modified amino acid binding	4	2	0.14	0.01	0.14
GO:0050662	coenzyme binding	52	6	1.84	0.01	0.14

GO.ID	Term	Annotated	Significant	Expected	p.value	adj.p
GO:0003777	microtubule motor activity	32	12	1.26	0.00	0.00
GO:0003774	motor activity	43	12	1.69	0.00	0.00
GO:0008603	cAMP-dependent protein kinase regulator ...	7	4	0.28	0.00	0.00
GO:0005509	calcium ion binding	72	11	2.84	0.00	0.00
GO:0019207	kinase regulator activity	13	4	0.51	0.00	0.02
GO:0019887	protein kinase regulator activity	13	4	0.51	0.00	0.02
GO:0004347	glucose-6-phosphate isomerase activity	2	2	0.08	0.00	0.02
GO:0005515	protein binding	616	37	24.26	0.00	0.03
GO:0008061	chitin binding	4	2	0.16	0.01	0.10

GO.ID	Term	Annotated	Significant	Expected	p.value	adj.p
GO:0044281	small molecule metabolic process	183	31	10.19	0.00	0.00
GO:1901564	organonitrogen compound metabolic proces...	294	40	16.37	0.00	0.00
GO:1901566	organonitrogen compound biosynthetic pro...	240	33	13.37	0.00	0.00
GO:0006082	organic acid metabolic process	109	21	6.07	0.00	0.00
GO:0019752	carboxylic acid metabolic process	109	21	6.07	0.00	0.00
GO:0043436	oxoacid metabolic process	109	21	6.07	0.00	0.00
GO:0044249	cellular biosynthetic process	426	46	23.72	0.00	0.00
GO:0009058	biosynthetic process	446	47	24.84	0.00	0.00
GO:0044710	single-organism metabolic process	379	42	21.11	0.00	0.00
GO:1901576	organic substance biosynthetic process	428	45	23.84	0.00	0.00
GO:0044711	single-organism biosynthetic process	103	18	5.74	0.00	0.00
GO:0009126	purine nucleoside monophosphate metaboli...	34	10	1.89	0.00	0.00
GO:0009167	purine ribonucleoside monophosphate meta...	34	10	1.89	0.00	0.00
GO:0032787	monocarboxylic acid metabolic process	28	9	1.56	0.00	0.00
GO:0009161	ribonucleoside monophosphate metabolic p...	35	10	1.95	0.00	0.00
GO:0006753	nucleoside phosphate metabolic process	60	13	3.34	0.00	0.00
GO:0009123	nucleoside monophosphate metabolic proce...	36	10	2.00	0.00	0.00
GO:0009150	purine ribonucleotide metabolic process	37	10	2.06	0.00	0.00
GO:0044271	cellular nitrogen compound biosynthetic ...	339	36	18.88	0.00	0.00
GO:0055086	nucleobase-containing small molecule met...	72	14	4.01	0.00	0.00
GO:0006163	purine nucleotide metabolic process	38	10	2.12	0.00	0.00
GO:0009259	ribonucleotide metabolic process	38	10	2.12	0.00	0.00
GO:0009144	purine nucleoside triphosphate metabolic...	32	9	1.78	0.00	0.00
GO:0009199	ribonucleoside triphosphate metabolic pr...	32	9	1.78	0.00	0.00
GO:0009205	purine ribonucleoside triphosphate metab...	32	9	1.78	0.00	0.00
GO:0009119	ribonucleoside metabolic process	40	10	2.23	0.00	0.00
GO:0072521	purine-containing compound metabolic pro...	40	10	2.23	0.00	0.00
GO:0009117	nucleotide metabolic process	57	12	3.17	0.00	0.00
GO:0009132	nucleoside diphosphate metabolic process	19	7	1.06	0.00	0.00
GO:0009141	nucleoside triphosphate metabolic proces...	33	9	1.84	0.00	0.00
GO:0006807	nitrogen compound metabolic process	591	51	32.91	0.00	0.00
GO:0019693	ribose phosphate metabolic process	42	10	2.34	0.00	0.00
GO:0008152	metabolic process	1280	85	71.28	0.00	0.00
GO:0046034	ATP metabolic process	29	8	1.62	0.00	0.00
GO:0042278	purine nucleoside metabolic process	37	9	2.06	0.00	0.00
GO:0046128	purine ribonucleoside metabolic process	37	9	2.06	0.00	0.00
GO:0009116	nucleoside metabolic process	46	10	2.56	0.00	0.00
GO:1901657	glycosyl compound metabolic process	46	10	2.56	0.00	0.00
GO:0072330	monocarboxylic acid biosynthetic process	11	5	0.61	0.00	0.00
GO:0034641	cellular nitrogen compound metabolic pro...	563	48	31.35	0.00	0.00
GO:0006165	nucleoside diphosphate phosphorylation	17	6	0.95	0.00	0.00
GO:0019637	organophosphate metabolic process	88	14	4.90	0.00	0.00
GO:1901293	nucleoside phosphate biosynthetic proces...	32	8	1.78	0.00	0.00
GO:0046939	nucleotide phosphorylation	18	6	1.00	0.00	0.00
GO:0043604	amide biosynthetic process	185	22	10.30	0.00	0.00
GO:0006412	translation	175	21	9.75	0.00	0.00
GO:0043603	cellular amide metabolic process	189	22	10.53	0.00	0.00
GO:0043043	peptide biosynthetic process	177	21	9.86	0.00	0.00
GO:0006091	generation of precursor metabolites and ...	27	7	1.50	0.00	0.00
GO:0006633	fatty acid biosynthetic process	8	4	0.45	0.00	0.00
GO:0006518	peptide metabolic process	181	21	10.08	0.00	0.00
GO:0016053	organic acid biosynthetic process	28	7	1.56	0.00	0.00
GO:0046394	carboxylic acid biosynthetic process	28	7	1.56	0.00	0.00
GO:0006096	glycolytic process	14	5	0.78	0.00	0.00
GO:0006757	ATP generation from ADP	14	5	0.78	0.00	0.00
GO:0009135	purine nucleoside diphosphate metabolic ...	14	5	0.78	0.00	0.00
GO:0009179	purine ribonucleoside diphosphate metabo...	14	5	0.78	0.00	0.00
GO:0009185	ribonucleoside diphosphate metabolic pfo...	14	5	0.78	0.00	0.00
GO:0016052	carbohydrate catabolic process	14	5	0.78	0.00	0.00
GO:0044724	single-organism carbohydrate catabolic p...	14	5	0.78	0.00	0.00
GO:0046031	ADP metabolic process	14	5	0.78	0.00	0.00

GO.ID	Term	Annotated	Significant	Expected	p.value	adj.p
GO:0004312	fatty acid synthase activity	2	2	0.09	0.00	0.07
GO:0051920	peroxiredoxin activity	2	2	0.09	0.00	0.07
GO:0003824	catalytic activity	1318	74	58.58	0.00	0.07
GO:0016746	transferase activity, transferring acyl ...	46	7	2.04	0.00	0.08
GO:0019205	nucleobase-containing compound kinase ac...	8	3	0.36	0.00	0.08
GO:0016615	malate dehydrogenase activity	3	2	0.13	0.01	0.09
GO:0003746	translation elongation factor activity	10	3	0.44	0.01	0.09
GO:0008135	translation factor activity, RNA binding	30	5	1.33	0.01	0.09

GO.ID	Term	Annotated	Significant	Expected	p.value	adj.p
GO:0030154	cell differentiation	3	3	0.17	0.00	0.02
GO:0032502	developmental process	4	3	0.23	0.00	0.02
GO:0044767	single-organism developmental process	4	3	0.23	0.00	0.02
GO:0048869	cellular developmental process	4	3	0.23	0.00	0.02
GO:0009062	fatty acid catabolic process	2	2	0.12	0.00	0.04
GO:0016042	lipid catabolic process	2	2	0.12	0.00	0.04
GO:0044242	cellular lipid catabolic process	2	2	0.12	0.00	0.04
GO:0072329	monocarboxylic acid catabolic process	2	2	0.12	0.00	0.04
GO:0006563	L-serine metabolic process	3	2	0.17	0.01	0.10

GO.ID	Term	Annotated	Significant	Expected	p.value	adj.p
GO:0004871	signal transducer activity	7	4	0.39	0.00	0.03
GO:0005057	receptor signaling protein activity	4	3	0.22	0.00	0.03
GO:0060089	molecular transducer activity	9	4	0.50	0.00	0.03
GO:0048037	cofactor binding	79	12	4.37	0.00	0.03
GO:0005496	steroid binding	2	2	0.11	0.00	0.04
GO:0032934	sterol binding	2	2	0.11	0.00	0.04
GO:0043178	alcohol binding	2	2	0.11	0.00	0.04
GO:0008233	peptidase activity	113	14	6.26	0.00	0.04
GO:0016614	oxidoreductase activity, acting on CH-OH...	21	5	1.16	0.00	0.05
GO:0070011	peptidase activity, acting on L-amino ac...	107	13	5.92	0.01	0.05
GO:0004252	serine-type endopeptidase activity	22	5	1.22	0.01	0.05
GO:0030170	pyridoxal phosphate binding	22	5	1.22	0.01	0.05
GO:0004702	receptor signaling protein serine/threon...	3	2	0.17	0.01	0.06
GO:0004707	MAP kinase activity	3	2	0.17	0.01	0.06
GO:0005102	receptor binding	3	2	0.17	0.01	0.06

GO.ID	Term	Annotated	Significant	Expected	p.value	adj.p
GO:0009126	purine nucleoside monophosphate metaboli...	34	7	0.99	0.00	0.00
GO:0009167	purine ribonucleoside monophosphate meta...	34	7	0.99	0.00	0.00
GO:0009161	ribonucleoside monophosphate metabolic p...	35	7	1.02	0.00	0.00
GO:0009123	nucleoside monophosphate metabolic proce...	36	7	1.05	0.00	0.00
GO:0009150	purine ribonucleotide metabolic process	37	7	1.08	0.00	0.00
GO:0042278	purine nucleoside metabolic process	37	7	1.08	0.00	0.00
GO:0046128	purine ribonucleoside metabolic process	37	7	1.08	0.00	0.00
GO:0006163	purine nucleotide metabolic process	38	7	1.10	0.00	0.00
GO:0009259	ribonucleotide metabolic process	38	7	1.10	0.00	0.00
GO:0009119	ribonucleoside metabolic process	40	7	1.16	0.00	0.00
GO:0072521	purine-containing compound metabolic pro...	40	7	1.16	0.00	0.00
GO:0046034	ATP metabolic process	29	6	0.84	0.00	0.00
GO:0019693	ribose phosphate metabolic process	42	7	1.22	0.00	0.00
GO:0009144	purine nucleoside triphosphate metabolic...	32	6	0.93	0.00	0.00
GO:0009199	ribonucleoside triphosphate metabolic pr...	32	6	0.93	0.00	0.00
GO:0009205	purine ribonucleoside triphosphate metab...	32	6	0.93	0.00	0.00
GO:0009116	nucleoside metabolic process	46	7	1.34	0.00	0.00
GO:1901657	glycosyl compound metabolic process	46	7	1.34	0.00	0.00
GO:0009141	nucleoside triphosphate metabolic proces...	33	6	0.96	0.00	0.00
GO:0055086	nucleobase-containing small molecule met...	72	8	2.09	0.00	0.00
GO:0006091	generation of precursor metabolites and ...	27	5	0.78	0.00	0.00
GO:0009117	nucleotide metabolic process	57	7	1.66	0.00	0.00
GO:0006753	nucleoside phosphate metabolic process	60	7	1.74	0.00	0.01
GO:1901135	carbohydrate derivative metabolic proces...	78	7	2.27	0.01	0.02
GO:0006793	phosphorus metabolic process	242	14	7.03	0.01	0.02
GO:0006796	phosphate-containing compound metabolic ...	242	14	7.03	0.01	0.02
GO:0006096	glycolytic process	14	3	0.41	0.01	0.02
GO:0006757	ATP generation from ADP	14	3	0.41	0.01	0.02
GO:0009135	purine nucleoside diphosphate metabolic ...	14	3	0.41	0.01	0.02
GO:0009179	purine ribonucleoside diphosphate metabo...	14	3	0.41	0.01	0.02
GO:0009185	ribonucleoside diphosphate metabolic pro...	14	3	0.41	0.01	0.02
GO:0016052	carbohydrate catabolic process	14	3	0.41	0.01	0.02
GO:0044724	single-organism carbohydrate catabolic p...	14	3	0.41	0.01	0.02
GO:0046031	ADP metabolic process	14	3	0.41	0.01	0.02
GO:0006090	pyruvate metabolic process	15	3	0.44	0.01	0.02
GO:0055085	transmembrane transport	84	7	2.44	0.01	0.03

GO.ID	Term	Annotated	Significant	Expected	p.value	adj.p
GO:0030145	manganese ion binding	4	2	0.12	0.01	0.12

GO.ID	Term	Annotated	Significant	Expected	p.value	adj.p
GO:0007154	cell communication	63	8	1.68	0.00	0.02
GO:0007165	signal transduction	58	7	1.54	0.00	0.02
GO:0023052	signaling	58	7	1.54	0.00	0.02
GO:0044700	single organism signaling	58	7	1.54	0.00	0.02
GO:0007186	G-protein coupled receptor signaling pat...	3	2	0.08	0.00	0.03
GO:0007205	protein kinase C-activating G-protein co...	3	2	0.08	0.00	0.03
GO:0051716	cellular response to stimulus	99	8	2.64	0.00	0.05
GO:0009405	pathogenesis	5	2	0.13	0.01	0.07
GO:0051704	multi-organism process	5	2	0.13	0.01	0.07

GO.ID	Term	Annotated	Significant	Expected	p.value	adj.p
GO:0004143	diacylglycerol kinase activity	3	2	0.07	0.00	0.17
GO:0005543	phospholipid binding	13	3	0.32	0.00	0.17
GO:0008289	lipid binding	16	3	0.39	0.01	0.19
GO:0003951	NAD+ kinase activity	6	2	0.15	0.01	0.19

GO.ID	Term	Annotated	Significant	Expected	p.value	adj.p
GO:0034660	ncRNA metabolic process	79	13	3.11	0.00	0.00
GO:0006399	tRNA metabolic process	62	10	2.44	0.00	0.00
GO:0006418	tRNA aminoacylation for protein translat...	40	7	1.57	0.00	0.02
GO:0043038	amino acid activation	42	7	1.65	0.00	0.02
GO:0043039	tRNA aminoacylation	42	7	1.65	0.00	0.02
GO:0016070	RNA metabolic process	239	19	9.40	0.00	0.02
GO:0046488	phosphatidylinositol metabolic process	15	4	0.59	0.00	0.03
GO:0006650	glycerophospholipid metabolic process	17	4	0.67	0.00	0.04
GO:0046486	glycerolipid metabolic process	17	4	0.67	0.00	0.04
GO:0090304	nucleic acid metabolic process	325	22	12.79	0.00	0.04
GO:0006139	nucleobase-containing compound metabolic...	406	25	15.97	0.01	0.07

GO.ID	Term	Annotated	Significant	Expected	p.value	adj.p
GO:0052689	carboxylic ester hydrolase activity	12	5	0.56	0.00	0.01
GO:0016307	phosphatidylinositol phosphate kinase ac...	4	3	0.19	0.00	0.02
GO:0004725	protein tyrosine phosphatase activity	6	3	0.28	0.00	0.05
GO:0004812	aminoacyl-tRNA ligase activity	41	7	1.92	0.00	0.05
GO:0016875	ligase activity, forming carbon-oxygen b...	42	7	1.96	0.00	0.05
GO:0016876	ligase activity, forming aminoacyl-tRNA ...	42	7	1.96	0.00	0.05
GO:0008026	ATP-dependent helicase activity	60	8	2.81	0.01	0.08
GO:0070035	purine NTP-dependent helicase activity	60	8	2.81	0.01	0.08

3 Results for mouse

Cluster 1, BP, Mm. Overrepresented GO biological process terms among mouse genes which have low abundance pre infection and become more abundant in most day 3 and 5 samples from immunocompetent mice, but less in immune deficient Rag1-/- mice. The upregulation trend is most clear in three first infection day 5 samples, which also form a separate sample cluster. On day 7, most of these genes are not differentially abundant, or below average, i.e., they seem to peak on day 5 p.i.. In total the cluster contains 273 genes of which 244 have GO annotations, and 29 do not.

Cluster 1, MF, Mm. Overrepresented GO molecular function terms among mouse genes which have low abundance pre infection and become more abundant in most day 3 and 5 samples from immunocompetent mice, but less in immune deficient Rag1-/- mice. The upregulation trend is most clear in three first infection day 5 samples, which also form a separate sample cluster. On day 7, most of these genes are not differentially abundant, or below average, i.e., they seem to peak on day 5 p.i..

Cluster 2, BP, Mm. Overrepresented GO biological process terms among mouse genes which are downregulated on day 7 p.i. and upregulated pre infection, i.e., these genes become more and more downregulated during infection. In total the cluster contains 198 genes of which 183 have GO annotations, and 15 do not.

Cluster 2, MF, Mm. Overrepresented GO molecular function terms among mouse genes which are downregulated on day 7 p.i. and upregulated pre infection, i.e., these genes become more and more downregulated during infection.

Cluster 3, BP, Mm. Overrepresented GO biological process terms among mouse genes which are upregulated pre infection and downregulated on day 7 p.i., except in one NMRI second infection sample, possibly indicating no or poor infection in this sample. As in cluster 2, these mRNAs are most highly abundant before infection and become less abundant over the course of infection. In total the cluster contains 465 genes of which 440 have GO annotations, and 25 do not

Cluster 3, MF, Mm. Overrepresented GO molecular function terms among mouse genes which are upregulated pre infection and downregulated on day 7 p.i., except in one NMRI second infection sample, possibly indicating no or poor infection in this sample. As in cluster 2, these mRNAs are most highly abundant before infection and become less abundant over the course of infection.

Cluster 4, BP, Mm. Overrepresented GO biological process terms among mouse genes which are highly abundant on day 7 p.i.. There is overall no clear difference between pre infection and days 3 or 5 among these genes. A slight tendency to higher abundance in second infection samples can be seen among these genes. In total the cluster contains 377 genes of which 360 have GO annotations, and 17 do not

Cluster 4, MF, Mm. Overrepresented GO molecular function terms among mouse genes which are highly abundant on day 7 p.i.. There is overall no clear difference between pre infection and days 3 or 5 among these genes. A slight tendency to higher abundance in second infection samples can be seen among these genes.

GO.ID	Term	Annotated	Significant	Expected	p.value	adj.p
GO:0045087	innate immune response	362	51	7.18	0.00	0.00
GO:0006955	immune response	713	65	14.14	0.00	0.00
GO:0002376	immune system process	1406	85	27.88	0.00	0.00
GO:0006952	defense response	755	61	14.97	0.00	0.00
GO:0098542	defense response to other organism	295	38	5.85	0.00	0.00
GO:0043207	response to external biotic stimulus	464	45	9.20	0.00	0.00
GO:0051707	response to other organism	464	45	9.20	0.00	0.00
GO:0009607	response to biotic stimulus	488	45	9.68	0.00	0.00
GO:0034097	response to cytokine	360	38	7.14	0.00	0.00
GO:0034341	response to interferon-gamma	47	16	0.93	0.00	0.00
GO:0002252	immune effector process	461	39	9.14	0.00	0.00
GO:0009615	response to virus	220	27	4.36	0.00	0.00
GO:0051607	defense response to virus	192	25	3.81	0.00	0.00
GO:0071345	cellular response to cytokine stimulus	292	29	5.79	0.00	0.00
GO:0035456	response to interferon-beta	35	12	0.69	0.00	0.00
GO:0002682	regulation of immune system process	774	47	15.35	0.00	0.00
GO:0045088	regulation of innate immune response	152	20	3.01	0.00	0.00
GO:0071346	cellular response to interferon-gamma	34	11	0.67	0.00	0.00
GO:0035458	cellular response to interferon-beta	29	10	0.58	0.00	0.00
GO:0051704	multi-organism process	1006	51	19.95	0.00	0.00
GO:0050776	regulation of immune response	385	29	7.63	0.00	0.00
GO:0031347	regulation of defense response	367	28	7.28	0.00	0.00
GO:0034340	response to type I interferon	26	9	0.52	0.00	0.00
GO:0006950	response to stress	2191	81	43.44	0.00	0.00
GO:0042832	defense response to protozoan	21	8	0.42	0.00	0.00
GO:0009617	response to bacterium	253	22	5.02	0.00	0.00
GO:0001562	response to protozoan	23	8	0.46	0.00	0.00
GO:0002683	negative regulation of immune system pro...	261	22	5.18	0.00	0.00
GO:0019882	antigen processing and presentation	72	12	1.43	0.00	0.00
GO:0019884	antigen processing and presentation of e...	25	8	0.50	0.00	0.00
GO:0010033	response to organic substance	1390	58	27.56	0.00	0.00
GO:0009605	response to external stimulus	1176	52	23.32	0.00	0.00
GO:0043900	regulation of multi-organism process	281	22	5.57	0.00	0.00
GO:0044403	symbiosis, encompassing mutualism throug...	234	20	4.64	0.00	0.00
GO:0044419	interspecies interaction between organis...	234	20	4.64	0.00	0.00
GO:0060337	type I interferon signaling pathway	22	7	0.44	0.00	0.00
GO:0071357	cellular response to type I interferon	22	7	0.44	0.00	0.00
GO:0042742	defense response to bacterium	105	13	2.08	0.00	0.00
GO:0044764	multi-organism cellular process	212	18	4.20	0.00	0.00
GO:0035455	response to interferon-alpha	15	6	0.30	0.00	0.00
GO:0001816	cytokine production	397	25	7.87	0.00	0.00
GO:0043903	regulation of symbiosis, encompassing mu...	139	14	2.76	0.00	0.00
GO:0002237	response to molecule of bacterial origin	162	15	3.21	0.00	0.00
GO:0050792	regulation of viral process	122	13	2.42	0.00	0.00
GO:0048525	negative regulation of viral process	69	10	1.37	0.00	0.00
GO:0045089	positive regulation of innate immune res...	127	13	2.52	0.00	0.00
GO:0051250	negative regulation of lymphocyte activa...	90	11	1.78	0.00	0.00
GO:0002684	positive regulation of immune system pro...	494	27	9.79	0.00	0.00
GO:0002478	antigen processing and presentation of e...	20	6	0.40	0.00	0.00
GO:0045824	negative regulation of innate immune res...	31	7	0.61	0.00	0.00
GO:0050778	positive regulation of immune response	298	20	5.91	0.00	0.00
GO:0032606	type I interferon production	45	8	0.89	0.00	0.00
GO:0080134	regulation of response to stress	830	37	16.46	0.00	0.00
GO:0031349	positive regulation of defense response	180	15	3.57	0.00	0.00
GO:0045071	negative regulation of viral genome repl...	33	7	0.65	0.00	0.00
GO:0048002	antigen processing and presentation of p...	47	8	0.93	0.00	0.00
GO:0002695	negative regulation of leukocyte activat...	100	11	1.98	0.00	0.00
GO:0001817	regulation of cytokine production	12	344	6.82	0.00	0.00
GO:0019221	cytokine-mediated signaling pathway	188	15	3.73	0.00	0.00
GO:0032607	interferon-alpha production	14	5	0.28	0.00	0.00
GO:1903901	negative regulation of viral life cycle	66	9	1.31	0.00	0.00

GO.ID	Term	Annotated	Significant	Expected	p.value	adj.p
GO:0016763	transferase activity, transferring pento...	38	7	0.77	0.00	0.00
GO:0003950	NAD+ ADP-ribosyltransferase activity	17	5	0.34	0.00	0.00
GO:0003725	double-stranded RNA binding	57	8	1.15	0.00	0.00
GO:0097367	carbohydrate derivative binding	1554	53	31.39	0.00	0.00
GO:0001730	2'-5'-oligoadenylate synthetase activity	5	3	0.10	0.00	0.00
GO:0004298	threonine-type endopeptidase activity	18	4	0.36	0.00	0.00
GO:0070003	threonine-type peptidase activity	18	4	0.36	0.00	0.00
GO:0003692	left-handed Z-DNA binding	2	2	0.04	0.00	0.00
GO:0003726	double-stranded RNA adenosine deaminase ...	2	2	0.04	0.00	0.00
GO:0004833	tryptophan 2,3-dioxygenase activity	2	2	0.04	0.00	0.00
GO:0033754	indoleamine 2,3-dioxygenase activity	2	2	0.04	0.00	0.00
GO:0046980	tapasin binding	2	2	0.04	0.00	0.00
GO:0003823	antigen binding	58	6	1.17	0.00	0.01
GO:0023029	MHC class Ib protein binding	3	2	0.06	0.00	0.01
GO:0046978	TAP1 binding	3	2	0.06	0.00	0.01
GO:0046979	TAP2 binding	3	2	0.06	0.00	0.01
GO:0043168	anion binding	1880	56	37.97	0.00	0.01
GO:0003924	GTPase activity	170	10	3.43	0.00	0.01
GO:0030151	molybdenum ion binding	4	2	0.08	0.00	0.01
GO:0043167	ion binding	3732	96	75.38	0.00	0.01
GO:0023026	MHC class II protein complex binding	15	3	0.30	0.00	0.01
GO:0061133	endopeptidase activator activity	5	2	0.10	0.00	0.02
GO:0023023	MHC protein complex binding	17	3	0.34	0.00	0.02
GO:0005539	glycosaminoglycan binding	78	6	1.58	0.00	0.02
GO:0016701	oxidoreductase activity, acting on singl...	18	3	0.36	0.01	0.02
GO:0016702	oxidoreductase activity, acting on singl...	18	3	0.36	0.01	0.02
GO:0042287	MHC protein binding	18	3	0.36	0.01	0.02
GO:0016814	hydrolase activity, acting on carbon-nit...	19	3	0.38	0.01	0.02
GO:0017076	purine nucleotide binding	1372	41	27.71	0.01	0.02
GO:0032553	ribonucleotide binding	1375	41	27.77	0.01	0.02
GO:0035639	purine ribonucleoside triphosphate bindi...	1342	40	27.11	0.01	0.02
GO:0032550	purine ribonucleoside binding	1348	40	27.23	0.01	0.02
GO:0001883	purine nucleoside binding	1350	40	27.27	0.01	0.02
GO:0032549	ribonucleoside binding	1351	40	27.29	0.01	0.02
GO:0001882	nucleoside binding	1358	40	27.43	0.01	0.02
GO:0019239	deaminase activity	22	3	0.44	0.01	0.02
GO:0032555	purine ribonucleotide binding	1364	40	27.55	0.01	0.02

GO.ID	Term	Annotated	Significant	Expected	p.value	adj.p
GO:0055114	oxidation-reduction process	650	28	9.76	0.00	0.00
GO:0044281	small molecule metabolic process	1261	42	18.94	0.00	0.00
GO:0006629	lipid metabolic process	796	29	11.95	0.00	0.00
GO:0044710	single-organism metabolic process	3313	76	49.76	0.00	0.00
GO:0006805	xenobiotic metabolic process	42	6	0.63	0.00	0.00
GO:0071466	cellular response to xenobiotic stimulus	46	6	0.69	0.00	0.00
GO:0009410	response to xenobiotic stimulus	51	6	0.77	0.00	0.00
GO:0006140	regulation of nucleotide metabolic proce...	103	8	1.55	0.00	0.00
GO:1901387	positive regulation of voltage-gated cal...	2	2	0.03	0.00	0.00
GO:0009117	nucleotide metabolic process	400	16	6.01	0.00	0.00
GO:0017144	drug metabolic process	23	4	0.35	0.00	0.00
GO:0019369	arachidonic acid metabolic process	24	4	0.36	0.00	0.00
GO:0006753	nucleoside phosphate metabolic process	408	16	6.13	0.00	0.00
GO:0008202	steroid metabolic process	169	9	2.54	0.00	0.01
GO:0055086	nucleobase-containing small molecule met...	443	16	6.65	0.00	0.01
GO:0015701	bicarbonate transport	14	3	0.21	0.00	0.01
GO:0042738	exogenous drug catabolic process	14	3	0.21	0.00	0.01
GO:0006631	fatty acid metabolic process	243	11	3.65	0.00	0.01
GO:0051289	protein homotetramerization	53	5	0.80	0.00	0.01
GO:0009992	cellular water homeostasis	4	2	0.06	0.00	0.01
GO:0032782	bile acid secretion	4	2	0.06	0.00	0.01
GO:0042737	drug catabolic process	15	3	0.23	0.00	0.01
GO:0006690	icosanoid metabolic process	55	5	0.83	0.00	0.01
GO:1901568	fatty acid derivative metabolic process	55	5	0.83	0.00	0.01
GO:0015850	organic hydroxy compound transport	116	7	1.74	0.00	0.01
GO:0043583	ear development	116	7	1.74	0.00	0.01
GO:0051262	protein tetramerization	87	6	1.31	0.00	0.01
GO:0055085	transmembrane transport	563	18	8.46	0.00	0.01
GO:0045989	positive regulation of striated muscle c...	5	2	0.08	0.00	0.01
GO:0042445	hormone metabolic process	89	6	1.34	0.00	0.01
GO:0051186	cofactor metabolic process	265	11	3.98	0.00	0.01
GO:0030104	water homeostasis	18	3	0.27	0.00	0.01
GO:0071333	cellular response to glucose stimulus	62	5	0.93	0.00	0.01
GO:0019637	organophosphate metabolic process	668	20	10.03	0.00	0.01
GO:0046903	secretion	625	19	9.39	0.00	0.01
GO:0071326	cellular response to monosaccharide stim...	64	5	0.96	0.00	0.01
GO:0071331	cellular response to hexose stimulus	64	5	0.96	0.00	0.01
GO:0019373	epoxygenase P450 pathway	6	2	0.09	0.00	0.01
GO:0019532	oxalate transport	6	2	0.09	0.00	0.01
GO:0048505	regulation of timing of cell differentia...	6	2	0.09	0.00	0.01
GO:0071322	cellular response to carbohydrate stimul...	68	5	1.02	0.00	0.01
GO:1900542	regulation of purine nucleotide metaboli...	98	6	1.47	0.00	0.01
GO:0050433	regulation of catecholamine secretion	21	3	0.32	0.00	0.01
GO:0015711	organic anion transport	207	9	3.11	0.00	0.01
GO:0016042	lipid catabolic process	172	8	2.58	0.00	0.01
GO:0003214	cardiac left ventricle morphogenesis	7	2	0.11	0.00	0.01
GO:0006833	water transport	7	2	0.11	0.00	0.01
GO:0032099	negative regulation of appetite	7	2	0.11	0.00	0.01
GO:1902358	sulfate transmembrane transport	7	2	0.11	0.00	0.01
GO:0001678	cellular glucose homeostasis	72	5	1.08	0.00	0.01
GO:0032787	monocarboxylic acid metabolic process	377	13	5.66	0.00	0.01
GO:0007200	phospholipase C-activating G-protein cou...	23	3	0.35	0.00	0.01
GO:0050432	catecholamine secretion	23	3	0.35	0.00	0.01
GO:0001676	long-chain fatty acid metabolic process	47	4	0.71	0.01	0.01
GO:0032105	negative regulation of response to extra...	24	3	0.36	0.01	0.01
GO:0032108	negative regulation of response to nutri...	24	3	0.36	0.01	0.01
GO:0055082	cellular chemical homeostasis	342	12	5.14	0.01	0.01
GO:0032612	interleukin-1 production	14 48	4	0.72	0.01	0.01
GO:0006820	anion transport	302	11	4.54	0.01	0.01
GO:0032096	negative regulation of response to food	8	2	0.12	0.01	0.01
GO:0033604	negative regulation of catecholamine sec...	8	2	0.12	0.01	0.01

GO.ID	Term	Annotated	Significant	Expected	p.value	adj.p
GO:0016491	oxidoreductase activity	523	25	7.99	0.00	0.00
GO:0016614	oxidoreductase activity, acting on CH-OH...	110	11	1.68	0.00	0.00
GO:0016616	oxidoreductase activity, acting on the C...	92	10	1.41	0.00	0.00
GO:0004090	carbonyl reductase (NADPH) activity	4	3	0.06	0.00	0.00
GO:0004769	steroid delta-isomerase activity	2	2	0.03	0.00	0.00
GO:0008390	testosterone 16-alpha-hydroxylase activi...	2	2	0.03	0.00	0.00
GO:0033695	oxidoreductase activity, acting on CH or...	2	2	0.03	0.00	0.00
GO:0034875	caffeine oxidase activity	2	2	0.03	0.00	0.00
GO:0004089	carbonate dehydratase activity	10	3	0.15	0.00	0.00
GO:0015106	bicarbonate transmembrane transporter ac...	11	3	0.17	0.00	0.01
GO:0015168	glycerol transmembrane transporter activ...	3	2	0.05	0.00	0.01
GO:0015254	glycerol channel activity	3	2	0.05	0.00	0.01
GO:0008392	arachidonic acid epoxygenase activity	12	3	0.18	0.00	0.01
GO:0008391	arachidonic acid monooxygenase activity	13	3	0.20	0.00	0.01
GO:0016712	oxidoreductase activity, acting on paire...	14	3	0.21	0.00	0.01
GO:0022838	substrate-specific channel activity	139	8	2.12	0.00	0.01
GO:0015166	polyol transmembrane transporter activit...	4	2	0.06	0.00	0.01
GO:0015250	water channel activity	4	2	0.06	0.00	0.01
GO:0016229	steroid dehydrogenase activity	33	4	0.50	0.00	0.01
GO:0052689	carboxylic ester hydrolase activity	111	7	1.70	0.00	0.01
GO:0008395	steroid hydroxylase activity	16	3	0.24	0.00	0.01
GO:0015301	anion:anion antiporter activity	16	3	0.24	0.00	0.01
GO:0020037	heme binding	57	5	0.87	0.00	0.01
GO:0016298	lipase activity	84	6	1.28	0.00	0.01
GO:0015267	channel activity	146	8	2.23	0.00	0.01
GO:0022803	passive transmembrane transporter activi...	146	8	2.23	0.00	0.01
GO:0003824	catalytic activity	4065	81	62.10	0.00	0.01
GO:0022857	transmembrane transporter activity	468	16	7.15	0.00	0.01
GO:0003854	3-beta-hydroxy-delta5-steroid dehydrogen...	5	2	0.08	0.00	0.01
GO:0005372	water transmembrane transporter activity	5	2	0.08	0.00	0.01
GO:0019825	oxygen binding	18	3	0.27	0.00	0.01
GO:0008237	metallopeptidase activity	90	6	1.37	0.00	0.01
GO:0050662	coenzyme binding	157	8	2.40	0.00	0.01
GO:0046906	tetrapyrrole binding	64	5	0.98	0.00	0.01
GO:0022892	substrate-specific transporter activity	531	17	8.11	0.00	0.01
GO:0019531	oxalate transmembrane transporter activi...	6	2	0.09	0.00	0.01
GO:0072341	modified amino acid binding	41	4	0.63	0.00	0.01
GO:0010296	prenylcysteine methylesterase activity	21	3	0.32	0.00	0.01
GO:0018731	1-oxa-2-oxocycloheptane lactonase activi...	21	3	0.32	0.00	0.01
GO:0018732	sulfolactone hydrolase activity	21	3	0.32	0.00	0.01
GO:0018734	butyrolactone hydrolase activity	21	3	0.32	0.00	0.01
GO:0034892	endosulfan lactone lactonase activity	21	3	0.32	0.00	0.01
GO:0035460	L-ascorbate 6-phosphate lactonase activi...	21	3	0.32	0.00	0.01
GO:0043905	Ser-tRNA(Thr) hydrolase activity	21	3	0.32	0.00	0.01
GO:0043906	Ala-tRNA(Pro) hydrolase activity	21	3	0.32	0.00	0.01
GO:0043907	Cys-tRNA(Pro) hydrolase activity	21	3	0.32	0.00	0.01
GO:0043908	Ser(Gly)-tRNA(Ala) hydrolase activity	21	3	0.32	0.00	0.01
GO:0047376	all-trans-retinyl-palmitate hydrolase, a...	21	3	0.32	0.00	0.01
GO:0050253	retinyl-palmitate esterase activity	21	3	0.32	0.00	0.01
GO:0052767	mannosyl-oligosaccharide 1,6-alpha-manno...	21	3	0.32	0.00	0.01
GO:0052768	mannosyl-oligosaccharide 1,3-alpha-manno...	21	3	0.32	0.00	0.01
GO:0080030	methyl indole-3-acetate esterase activit...	21	3	0.32	0.00	0.01
GO:0080031	methyl salicylate esterase activity	21	3	0.32	0.00	0.01
GO:0080032	methyl jasmonate esterase activity	21	3	0.32	0.00	0.01
GO:0018733	3,4-dihydrocoumarin hydrolase activity	22	3	0.34	0.00	0.01
GO:0051723	protein methylesterase activity	22	3	0.34	0.00	0.01
GO:0008271	secondary active sulfate transmembrane t...	7	2	0.11	0.00	0.01
GO:0015665	alcohol transmembrane transporter acti...	7	2	0.11	0.00	0.01
GO:0016725	oxidoreductase activity, acting on CH or...	7	2	0.11	0.00	0.01
GO:0048037	cofactor binding	208	9	3.18	0.00	0.01
GO:0004222	metalloendopeptidase activity	46	4	0.70	0.01	0.01

GO.ID	Term	Annotated	Significant	Expected	p.value	adj.p	
GO:0006805	xenobiotic metabolic process	42	18	1.51	0.00	0.00	
GO:0006082	organic acid metabolic process	661	68	23.81	0.00	0.00	
GO:0044281	small molecule metabolic process	1261	101	45.43	0.00	0.00	
GO:0032787	monocarboxylic acid metabolic process	377	49	13.58	0.00	0.00	
GO:0071466	cellular response to xenobiotic stimulus	46	18	1.66	0.00	0.00	
GO:0009813	flavonoid biosynthetic process	13	11	0.47	0.00	0.00	
GO:0052696	flavonoid glucuronidation	13	11	0.47	0.00	0.00	
GO:0043436	oxoacid metabolic process	652	66	23.49	0.00	0.00	
GO:0019752	carboxylic acid metabolic process	612	63	22.05	0.00	0.00	
GO:0009812	flavonoid metabolic process	14	11	0.50	0.00	0.00	
GO:0052695	cellular glucuronidation	14	11	0.50	0.00	0.00	
GO:0009410	response to xenobiotic stimulus	51	18	1.84	0.00	0.00	
GO:0006063	uronic acid metabolic process	15	11	0.54	0.00	0.00	
GO:0019585	glucuronate metabolic process	15	11	0.54	0.00	0.00	
GO:0052697	xenobiotic glucuronidation	8	8	0.29	0.00	0.00	
GO:0006629	lipid metabolic process	796	66	28.68	0.00	0.00	
GO:0009719	response to endogenous stimulus	729	60	26.26	0.00	0.00	
GO:0071495	cellular response to endogenous stimulus	561	50	20.21	0.00	0.00	
GO:0009725	response to hormone	385	37	13.87	0.00	0.00	
GO:0006631	fatty acid metabolic process	243	28	8.75	0.00	0.00	
GO:0044255	cellular lipid metabolic process	604	49	21.76	0.00	0.00	
GO:0055114	oxidation-reduction process	650	50	23.42	0.00	0.00	
GO:0042445	hormone metabolic process	89	15	3.21	0.00	0.00	
GO:0032870	cellular response to hormone stimulus	278	28	10.02	0.00	0.00	
GO:0044710	single-organism metabolic process	3313	163	119.36	0.00	0.00	
GO:0034754	cellular hormone metabolic process	43	10	1.55	0.00	0.00	
GO:0005996	monosaccharide metabolic process	177	20	6.38	0.00	0.00	
GO:0042178	xenobiotic catabolic process	9	5	0.32	0.00	0.00	
GO:0042537	benzene-containing compound metabolic pr...	15	6	0.54	0.00	0.00	
GO:0006790	sulfur compound metabolic process	200	21	7.21	0.00	0.00	
GO:0019395	fatty acid oxidation	66	11	2.38	0.00	0.00	
GO:0034440	lipid oxidation	67	11	2.41	0.00	0.00	
GO:0044699	single-organism process	7965	325	286.96	0.00	0.00	
GO:0042221	response to chemical	1868	99	67.30	0.00	0.00	
GO:1901615	organic hydroxy compound metabolic proce...	299	26	10.77	0.00	0.00	
GO:0010817	regulation of hormone levels	267	24	9.62	0.00	0.00	
GO:0016042	lipid catabolic process	172	18	6.20	0.00	0.00	
GO:0006811	ion transport	785	50	28.28	0.00	0.00	
GO:0022600	digestive system process	51	9	1.84	0.00	0.00	
GO:0044242	cellular lipid catabolic process	117	14	4.22	0.00	0.00	
GO:0042738	exogenous drug catabolic process	14	5	0.50	0.00	0.00	
GO:0051386	regulation of neurotrophin TRK receptor ...	8	4	0.29	0.00	0.00	
GO:0044344	cellular response to fibroblast growth f...	42	8	1.51	0.00	0.00	
GO:0008202	steroid metabolic process	169	17	6.09	0.00	0.00	
GO:0017144	drug metabolic process	23	6	0.83	0.00	0.00	
GO:0042737	drug catabolic process	15	5	0.54	0.00	0.00	
GO:0005975	carbohydrate metabolic process	481	34	17.33	0.00	0.00	
GO:0072329	monocarboxylic acid catabolic process	68	10	2.45	0.00	0.00	
GO:0071774	response to fibroblast growth factor	44	8	1.59	0.00	0.00	
GO:0007586	digestion	56	9	2.02	0.00	0.00	
GO:0072001	renal system development	141	15	5.08	0.00	0.00	
GO:0044539	long-chain fatty acid import	4	3	0.14	0.00	0.00	
GO:0051387	negative regulation of neurotrophin TRK ...	4	3	0.14	0.00	0.00	
GO:0042493	response to drug	158	16	5.69	0.00	0.00	
GO:0006672	ceramide metabolic process	58	9	2.09	0.00	0.00	
GO:0008543	fibroblast growth factor receptor signal...	35	7	1.26	0.00	0.00	
GO:0044723	single-organism carbohydrate metabolic p...	435	31	15.67	0.00	0.00	
GO:0007267	cell-cell signaling	16	456	32	16.43	0.00	0.00
GO:0070887	cellular response to chemical stimulus	1330	72	47.92	0.00	0.00	
GO:0001822	kidney development	131	14	4.72	0.00	0.00	
GO:0006040	amino sugar metabolic process	26	6	0.94	0.00	0.00	

GO.ID	Term	Annotated	Significant	Expected	p.value	adj.p
GO:0015020	glucuronosyltransferase activity	55	16	2.00	0.00	0.00
GO:0008194	UDP-glycosyltransferase activity	106	18	3.85	0.00	0.00
GO:0016878	acid-thiol ligase activity	15	7	0.54	0.00	0.00
GO:0048037	cofactor binding	208	23	7.56	0.00	0.00
GO:0042803	protein homodimerization activity	538	42	19.54	0.00	0.00
GO:0046983	protein dimerization activity	797	55	28.95	0.00	0.00
GO:0003857	3-hydroxyacyl-CoA dehydrogenase activity	8	5	0.29	0.00	0.00
GO:0016758	transferase activity, transferring hexos...	142	18	5.16	0.00	0.00
GO:0016877	ligase activity, forming carbon-sulfur b...	28	8	1.02	0.00	0.00
GO:0015645	fatty acid ligase activity	14	6	0.51	0.00	0.00
GO:0004364	glutathione transferase activity	24	7	0.87	0.00	0.00
GO:0016757	transferase activity, transferring glyco...	208	21	7.56	0.00	0.00
GO:0016405	CoA-ligase activity	11	5	0.40	0.00	0.00
GO:0016421	CoA carboxylase activity	6	4	0.22	0.00	0.00
GO:0016616	oxidoreductase activity, acting on the C...	92	13	3.34	0.00	0.00
GO:0051287	NAD binding	46	9	1.67	0.00	0.00
GO:0016491	oxidoreductase activity	523	38	19.00	0.00	0.00
GO:0003824	catalytic activity	4065	187	147.66	0.00	0.00
GO:0016614	oxidoreductase activity, acting on CH-OH...	110	14	4.00	0.00	0.00
GO:0016885	ligase activity, forming carbon-carbon b...	7	4	0.25	0.00	0.00
GO:0031406	carboxylic acid binding	128	15	4.65	0.00	0.00
GO:0043177	organic acid binding	129	15	4.69	0.00	0.00
GO:0016712	oxidoreductase activity, acting on paire...	14	5	0.51	0.00	0.00
GO:0033293	monocarboxylic acid binding	41	8	1.49	0.00	0.00
GO:0070330	aromatase activity	8	4	0.29	0.00	0.00
GO:0005496	steroid binding	53	9	1.93	0.00	0.00
GO:0038023	signaling receptor activity	361	28	13.11	0.00	0.00
GO:0022838	substrate-specific channel activity	139	15	5.05	0.00	0.00
GO:0050662	coenzyme binding	157	16	5.70	0.00	0.00
GO:0004467	long-chain fatty acid-CoA ligase activit...	9	4	0.33	0.00	0.00
GO:0004774	succinate-CoA ligase activity	9	4	0.33	0.00	0.00
GO:0015267	channel activity	146	15	5.30	0.00	0.00
GO:0022803	passive transmembrane transporter activi...	146	15	5.30	0.00	0.00
GO:0016831	carboxy-lyase activity	26	6	0.94	0.00	0.00
GO:0016830	carbon-carbon lyase activity	37	7	1.34	0.00	0.00
GO:0008144	drug binding	76	10	2.76	0.00	0.00
GO:0004872	receptor activity	448	31	16.27	0.00	0.00
GO:0042802	identical protein binding	915	53	33.24	0.00	0.00
GO:0004075	biotin carboxylase activity	5	3	0.18	0.00	0.00
GO:0005007	fibroblast growth factor-activated recep...	5	3	0.18	0.00	0.00
GO:0004888	transmembrane signaling receptor activit...	294	23	10.68	0.00	0.00
GO:0022836	gated channel activity	97	11	3.52	0.00	0.00
GO:1901681	sulfur compound binding	129	13	4.69	0.00	0.00
GO:0001972	retinoic acid binding	6	3	0.22	0.00	0.00
GO:0022857	transmembrane transporter activity	468	31	17.00	0.00	0.00
GO:0005216	ion channel activity	135	13	4.90	0.00	0.00
GO:0004553	hydrolase activity, hydrolyzing O-glycos...	119	12	4.32	0.00	0.00
GO:0001517	N-acetylglucosamine 6-O-sulfotransferase...	14	4	0.51	0.00	0.00
GO:0004027	alcohol sulfotransferase activity	14	4	0.51	0.00	0.00
GO:0004394	heparan sulfate 2-O-sulfotransferase act...	14	4	0.51	0.00	0.00
GO:0016232	HNK-1 sulfotransferase activity	14	4	0.51	0.00	0.00
GO:0017095	heparan sulfate 6-O-sulfotransferase act...	14	4	0.51	0.00	0.00
GO:0018721	trans-9R,10R-dihydrodiolphenanthrene sul...	14	4	0.51	0.00	0.00
GO:0018722	1-phenanthrol sulfotransferase activity	14	4	0.51	0.00	0.00
GO:0018723	3-phenanthrol sulfotransferase activity	14	4	0.51	0.00	0.00
GO:0018724	4-phenanthrol sulfotransferase activity	14	4	0.51	0.00	0.00
GO:0018725	trans-3,4-dihydrodiolphenanthrene sulfot...	14	4	0.51	0.00	0.00
GO:0018726	9-phenanthrol sulfotransferase activity 17	14	4	0.51	0.00	0.00
GO:0018727	2-phenanthrol sulfotransferase activity	14	4	0.51	0.00	0.00
GO:0019111	phenanthrol sulfotransferase activity	14	4	0.51	0.00	0.00
GO:0034483	heparan sulfate sulfotransferase activit...	14	4	0.51	0.00	0.00

GO.ID	Term	Annotated	Significant	Expected	p.value	adj.p	
GO:0002376	immune system process	1406	126	41.64	0.00	0.00	
GO:0006955	immune response	713	85	21.12	0.00	0.00	
GO:0050896	response to stimulus	4441	229	131.52	0.00	0.00	
GO:0006954	inflammatory response	327	53	9.68	0.00	0.00	
GO:0044700	single organism signaling	2975	176	88.11	0.00	0.00	
GO:0006952	defense response	755	80	22.36	0.00	0.00	
GO:0023052	signaling	2981	176	88.28	0.00	0.00	
GO:0007165	signal transduction	2773	167	82.12	0.00	0.00	
GO:0001775	cell activation	589	69	17.44	0.00	0.00	
GO:0007154	cell communication	3137	178	92.90	0.00	0.00	
GO:0022610	biological adhesion	800	79	23.69	0.00	0.00	
GO:0002684	positive regulation of immune system pro...	494	61	14.63	0.00	0.00	
GO:0007155	cell adhesion	791	78	23.43	0.00	0.00	
GO:0002682	regulation of immune system process	774	76	22.92	0.00	0.00	
GO:0001816	cytokine production	397	53	11.76	0.00	0.00	
GO:0065007	biological regulation	6468	274	191.55	0.00	0.00	
GO:0048518	positive regulation of biological proces...	3404	182	100.81	0.00	0.00	
GO:0045321	leukocyte activation	515	60	15.25	0.00	0.00	
GO:0040011	locomotion	903	79	26.74	0.00	0.00	
GO:0098602	single organism cell adhesion	516	58	15.28	0.00	0.00	
GO:0051239	regulation of multicellular organismal p...	1538	108	45.55	0.00	0.00	
GO:0007159	leukocyte cell-cell adhesion	332	46	9.83	0.00	0.00	
GO:0016337	single organismal cell-cell adhesion	474	55	14.04	0.00	0.00	
GO:0051716	cellular response to stimulus	3741	189	110.79	0.00	0.00	
GO:0098609	cell-cell adhesion	507	56	15.01	0.00	0.00	
GO:0044707	single-multicellular organism process	3409	176	100.96	0.00	0.00	
GO:0050789	regulation of biological process	6161	259	182.46	0.00	0.00	
GO:0048870	cell motility	784	70	23.22	0.00	0.00	
GO:0051674	localization of cell	784	70	23.22	0.00	0.00	
GO:0032501	multicellular organismal process	3487	177	103.27	0.00	0.00	
GO:0050794	regulation of cellular process	5853	249	173.34	0.00	0.00	
GO:0016477	cell migration	740	67	21.92	0.00	0.00	
GO:0001817	regulation of cytokine production	344	44	10.19	0.00	0.00	
GO:0034109	homotypic cell-cell adhesion	361	45	10.69	0.00	0.00	
GO:0048583	regulation of response to stimulus	2109	126	62.46	0.00	0.00	
GO:0048584	positive regulation of response to stimu...	1130	85	33.47	0.00	0.00	
GO:0050865	regulation of cell activation	319	42	9.45	0.00	0.00	
GO:0048522	positive regulation of cellular process	3048	160	90.27	0.00	0.00	
GO:0046649	lymphocyte activation	435	49	12.88	0.00	0.00	
GO:0035556	intracellular signal transduction	1570	103	46.50	0.00	0.00	
GO:0002694	regulation of leukocyte activation	301	40	8.91	0.00	0.00	
GO:0070486	leukocyte aggregation	314	40	9.30	0.00	0.00	
GO:1902531	regulation of intracellular signal trans...	991	76	29.35	0.00	0.00	
GO:0050900	leukocyte migration	164	29	4.86	0.00	0.00	
GO:0009605	response to external stimulus	1176	83	34.83	0.00	0.00	
GO:0030155	regulation of cell adhesion	414	45	12.26	0.00	0.00	
GO:0051249	regulation of lymphocyte activation	259	35	7.67	0.00	0.00	
GO:0006928	movement of cell or subcellular componen...	992	74	29.38	0.00	0.00	
GO:0001819	positive regulation of cytokine producti...	232	33	6.87	0.00	0.00	
GO:0006950	response to stress	2191	123	64.89	0.00	0.00	
GO:0060326	cell chemotaxis	145	26	4.29	0.00	0.00	
GO:0050793	regulation of developmental process	1367	89	40.48	0.00	0.00	
GO:0023051	regulation of signaling	1746	104	51.71	0.00	0.00	
GO:0044763	single-organism cellular process	7155	274	211.90	0.00	0.00	
GO:0006935	chemotaxis	270	34	8.00	0.00	0.00	
GO:0008219	cell death	1372	88	40.63	0.00	0.00	
GO:0042330	taxis	271	34	8.03	0.00	0.00	
GO:0065008	regulation of biological quality	18	1978	112	58.58	0.00	0.00
GO:0016265	death	1376	88	40.75	0.00	0.00	
GO:0070887	cellular response to chemical stimulus	1330	86	39.39	0.00	0.00	
GO:0042110	T cell activation	305	36	9.03	0.00	0.00	
GO:0050822	T cell activation	305	36	9.03	0.00	0.00	

GO.ID	Term	Annotated	Significant	Expected	p.value	adj.p
GO:0005515	protein binding	5370	227	156.32	0.00	0.00
GO:0060089	molecular transducer activity	621	52	18.08	0.00	0.00
GO:0005125	cytokine activity	79	17	2.30	0.00	0.00
GO:0004871	signal transducer activity	534	45	15.54	0.00	0.00
GO:0004872	receptor activity	448	40	13.04	0.00	0.00
GO:0005102	receptor binding	851	58	24.77	0.00	0.00
GO:0038023	signaling receptor activity	361	33	10.51	0.00	0.00
GO:0004896	cytokine receptor activity	56	12	1.63	0.00	0.00
GO:0004888	transmembrane signaling receptor activit...	294	27	8.56	0.00	0.00
GO:0005126	cytokine receptor binding	144	18	4.19	0.00	0.00
GO:0003823	antigen binding	58	11	1.69	0.00	0.00
GO:0016493	C-C chemokine receptor activity	6	4	0.17	0.00	0.00
GO:0008009	chemokine activity	19	6	0.55	0.00	0.00
GO:0042379	chemokine receptor binding	28	7	0.82	0.00	0.00
GO:0001637	G-protein coupled chemoattractant recept...	12	5	0.35	0.00	0.00
GO:0004950	chemokine receptor activity	12	5	0.35	0.00	0.00
GO:0005085	guanyl-nucleotide exchange factor activi...	155	15	4.51	0.00	0.00
GO:0005509	calcium ion binding	273	21	7.95	0.00	0.00
GO:0001948	glycoprotein binding	74	10	2.15	0.00	0.00
GO:0098772	molecular function regulator	792	43	23.05	0.00	0.00
GO:0008528	G-protein coupled peptide receptor activ...	25	6	0.73	0.00	0.00
GO:0042605	peptide antigen binding	25	6	0.73	0.00	0.00
GO:0001653	peptide receptor activity	26	6	0.76	0.00	0.00
GO:0005488	binding	8136	268	236.84	0.00	0.00
GO:0048365	Rac GTPase binding	38	7	1.11	0.00	0.00
GO:0050839	cell adhesion molecule binding	112	12	3.26	0.00	0.00
GO:0019956	chemokine binding	10	4	0.29	0.00	0.00
GO:0004930	G-protein coupled receptor activity	103	11	3.00	0.00	0.00
GO:0004908	interleukin-1 receptor activity	5	3	0.15	0.00	0.00
GO:0019957	C-C chemokine binding	5	3	0.15	0.00	0.00
GO:1990782	protein tyrosine kinase binding	44	7	1.28	0.00	0.00
GO:0046983	protein dimerization activity	797	41	23.20	0.00	0.00
GO:0019899	enzyme binding	1457	64	42.41	0.00	0.00
GO:0019900	kinase binding	537	30	15.63	0.00	0.00
GO:0005544	calcium-dependent phospholipid binding	25	5	0.73	0.00	0.00
GO:0005088	Ras guanyl-nucleotide exchange factor ac...	101	10	2.94	0.00	0.00
GO:0005415	nucleoside:sodium symporter activity	2	2	0.06	0.00	0.00
GO:0035717	chemokine (C-C motif) ligand 7 binding	2	2	0.06	0.00	0.00
GO:0071791	chemokine (C-C motif) ligand 5 binding	2	2	0.06	0.00	0.00
GO:0042277	peptide binding	145	12	4.22	0.00	0.00
GO:0030971	receptor tyrosine kinase binding	42	6	1.22	0.00	0.00
GO:0001664	G-protein coupled receptor binding	134	11	3.90	0.00	0.00
GO:0019901	protein kinase binding	485	26	14.12	0.00	0.00
GO:0044877	macromolecular complex binding	1139	50	33.16	0.00	0.00
GO:0005178	integrin binding	63	7	1.83	0.00	0.00
GO:0032403	protein complex binding	757	36	22.04	0.00	0.00
GO:0005543	phospholipid binding	248	16	7.22	0.00	0.00
GO:0004859	phospholipase inhibitor activity	3	2	0.09	0.00	0.00
GO:0019834	phospholipase A2 inhibitor activity	3	2	0.09	0.00	0.00
GO:0031726	CCR1 chemokine receptor binding	3	2	0.09	0.00	0.00
GO:0034988	Fc-gamma receptor I complex binding	3	2	0.09	0.00	0.00
GO:0035662	Toll-like receptor 4 binding	3	2	0.09	0.00	0.00
GO:0033218	amide binding	164	12	4.77	0.00	0.01
GO:0016209	antioxidant activity	50	6	1.46	0.00	0.01
GO:0008289	lipid binding	425	23	12.37	0.00	0.01
GO:0005149	interleukin-1 receptor binding	11	3	0.32	0.00	0.01
GO:0048020	CCR chemokine receptor binding	11	3	0.32	0.00	0.01
GO:0003779	actin binding	19	263	7.66	0.00	0.01
GO:0046977	TAP binding	12	3	0.35	0.00	0.01
GO:0016175	superoxide-generating NADPH oxidase acti...	4	2	0.12	0.00	0.01
GO:0050786	RAGE receptor binding	4	2	0.12	0.00	0.01

4 Conclusions

Mouse

Parasite