

Supplemental Table S2. KEGG pathway enrichment analysis

Pathway	P value	P athway ID	Genes
Complement and coagulation cascades	4.84E-07	ko04610	F10;F2;Kng1;Tfpi;A2m;Fga;Proc;Masp1;Fgg;Serpina1a;Serpina1b
ECM-receptor interaction	2.89E-05	ko04512	Itga5;Itga2;Col6a3;Col1a2;Gp9;Col6a1;Vtn;Spp1;Col6a2
Protein digestion and absorption	3.23E-05	ko04974	Col6a3;Col1a2;Fxyd2;Pga5;Col6a1;Col15a1;Slc7a9;Col9a2;Col6a2
Malaria	0.00059139	ko05144	Il1b;Tlr4;Hba-a2;Gypa;Cd40;Tgfb1
Focal adhesion	0.001955538	ko04510	Itga5;Itga2;Col6a3;Col1a2;Mylk3;Col6a1;Vtn;Rac2;Spp1;Pak6;Col6a2
Fat digestion and absorption	0.00212801	ko04975	Apoa1;Apoa4;Pla2g12b;Apob;Pla2g10
Vitamin digestion and absorption	0.002299541	ko04977	Apoa1;Apoa4;Apob;Cubn
Adherens junction	0.004544279	ko04520	Tcf7l2;Wasf1;Pvrl1;Tcf7l1;Rac2;Ptpfrf
African trypanosomiasis	0.01013418	ko05143	Il1b;Hba-a2;Apoa1;Apol6
Alcoholism	0.01085911	ko05034	Creb3l3;Grin2d;Hist1h2be;Gnb2;Maob;Hist1h2bq;Hist2h2aa1;Hist1h2al;Hist1h3d
Vascular smooth muscle contraction	0.0126069	ko04270	Ramp3;Myh14;Mylk3;Pla2g12b;Pla2g10;Gucy1b2;Myl6b
Toxoplasmosis	0.01377428	ko05145	Hspa1b;Tlr4;Hspa1a;Pla2g12b;Cd40;Pla2g10;Tgfb1
Cocaine addiction	0.01658364	ko05030	Creb3l3;Grin2d;Dlga4;Maob
Mineral absorption	0.02356049	ko04978	Trf;Fxyd2;Slc34a2;Slc39a4

Basal cell carcinoma	0.02356049 ko05217	Tcf7l2;Tcf7l1;Fzd7;Wnt4
Steroid hormone biosynthesis	0.02356049 ko00140	Ugt1a7c;Hsd3b6;Akr1c18;Sult1e1
Fructose and mannose metabolism	0.02493874 ko00051	Sord;Hkdc1;Aldob
Thyroid cancer	0.02493874 ko05216	Tcf7l2;Tcf7l1;Ncoa4
Glutamatergic synapse	0.03251517 ko04724	Cacna1a;Grin2d;Dlg4;Gnb2;Pla2g12b;Pla2g10
Hematopoietic cell lineage	0.03383215 ko04640	Itga5;Il1b;Itga2;Gp9;Gypa
Long-term depression	0.03397513 ko04730	Cacna1a;Pla2g12b;Pla2g10;Gucy1b2
Legionellosis	0.03397513 ko05134	Hspa1b;Il1b;Tlr4;Hspa1a
Glycolysis / Gluconeogenesis	0.04004045 ko00010	Aldh1b1;Hkdc1;Aldob;Eno2
Nicotine addiction	0.04061471 ko05033	Cacna1a;Grin2d;Gabrd
Systemic lupus erythematosus	0.04062022 ko05322	Hist1h2be;Cd40;Hist1h2bq;Hist2h2aa1;Hist1h2al;Hist1h3d
Colorectal cancer	0.04219037 ko05210	Tcf7l2;Tcf7l1;Tgfb1;Rac2
Fc gamma R-mediated phagocytosis	0.04378753 ko04666	Wasf1;Inpp1;Pla2g12b;Pla2g10;Rac2
Axon guidance	0.04667541 ko04360	Efnb1;Ntn1;Sema4b;Sema4a;Rac2;Pak6
Melanogenesis	0.04935856 ko04916	Tcf7l2;Creb3l3;Tcf7l1;Fzd7;Wnt4
Prion diseases	0.05666535 ko05020	Hspa1b;Il1b;Hspa1a
Ascorbate and aldarate metabolism	0.05806675 ko00053	Ugt1a7c;Aldh1b1
Starch and sucrose metabolism	0.06380825 ko00500	Enpp1;Ugt1a7c;Hkdc1
Histidine metabolism	0.06398496 ko00340	Aldh1b1;Maob
Arrhythmogenic right ventricular cardiomyopathy (ARVC)	0.07003433 ko05412	Itga5;Itga2;Tcf7l2;Tcf7l1
alpha-Linolenic acid metabolism	0.07009597 ko00592	Pla2g12b;Pla2g10
Hedgehog signaling	0.0713449 ko04340	Lrp2;Wnt4;Csnk1g2

pathway			
Cell adhesion molecules (CAMs)	0.07626341	ko04514	Pvrl1;Cldn23;Cldn20;Cd40;Ptprf;Jam2
Glycosaminoglycan biosynthesis - heparan sulfate / heparin	0.07638856	ko00534	Extl3;Hs6st1
Regulation of actin cytoskeleton	0.07649903	ko04810	Itga5;Itga2;Wasf1;F2;Myh14;Mylk3;Rac2;Pak6
Allograft rejection	0.07926091	ko05330	Gzmb;Prf1;Cd40
PPAR signaling pathway	0.0820168	ko03320	Apoc3;Apoa1;Acadl;Apoa2
Graft-versus-host disease	0.08754097	ko05332	Il1b;Gzmb;Prf1
Rheumatoid arthritis	0.09162289	ko05323	Il1b;Tlr4;Atp6v0d2;Tgfb1
Arachidonic acid metabolism	0.09493943	ko00590	Pla2g12b;Pla2g10;Ptgds;Ephx2
Viral myocarditis	0.09493943	ko05416	Myh14;Prf1;Cd40;Rac2
Neomycin, kanamycin and gentamicin biosynthesis	0.1048253	ko00524	Hkdc1
Type I diabetes mellitus	0.1051285	ko04940	Il1b;Gzmb;Prf1
GABAergic synapse	0.1052224	ko04727	Cacna1a;Gnb2;Slc6a12;Gabbrd
Pentose and glucuronate interconversions	0.1102099	ko00040	Ugt1a7c;Aldh1b1
Salmonella infection	0.1123477	ko05132	Il1b;Tlr4;Wasf1;Myh14
Cytosolic DNA-sensing pathway	0.1239728	ko04623	Il1b;Ifi202b;Zbp1
Ether lipid metabolism	0.1246595	ko00565	Pla2g12b;Pla2g10
MAPK signaling pathway	0.1283392	ko04010	Hspa1b;Il1b;Cacna1a;Hspa1a;Pla2g12b;Pla2g10;Tgfb1;Rac2
Inositol phosphate metabolism	0.1288639	ko00562	Itpka;Inpp1l1;Itpkb
Cytokine-cytokine receptor interaction	0.1306298	ko04060	Il1b;Ccr1l1;Cd40;Tnfrsf11b;Tgfb1;Tnfrsf12;Ccr1;Tnfrsf18
Hypertrophic cardiomyopathy (HCM)	0.1349454	ko05410	Itga5;Itga2;Myh14;Tgfb1

Leishmaniasis	0.1388467	ko05140	Il1b;Tlr4;Tgfb1
Dilated cardiomyopathy (DCM)	0.1428612	ko05414	Itga5;Itga2;Myh14;Tgfb1
Drug metabolism - cytochrome P450	0.1428612	ko00982	Fmo2;Ugt1a7c;Maob;Gstm2
Autoimmune thyroid disease	0.1439339	ko05320	Gzmb;Prf1;Cd40
Measles	0.1463162	ko05162	Hspa1b;Il1b;Tlr4;Hspa1a;Cblc
Pathways in cancer	0.1478849	ko05200	Itga2;Tcf7l2;Tcf7l1;Fzd7;Cblc;Wnt4;Ncoa4;Tgfb1;Gstm2;Rac2
Amphetamine addiction	0.1490819	ko05031	Creb3l3;Grin2d;Maob
Toll-like receptor signaling pathway	0.1509559	ko04620	Il1b;Tlr4;Cd40;Spp1
Tight junction	0.1531841	ko04530	Cldn23;Myh14;Cldn20;Llg12;Jam2
VEGF signaling pathway	0.1542887	ko04370	Pla2g12b;Pla2g10;Rac2
Bacterial invasion of epithelial cells	0.1595519	ko05100	Itga5;Wasf1;Cblc
Prostate cancer	0.1762343	ko05215	Tcf7l2;Creb3l3;Tcf7l1;Gstm2
Amoebiasis	0.1805817	ko05146	Il1b;Tlr4;Col1a2;Tgfb1
Sulfur metabolism	0.180744	ko00920	Sult1e1
Pertussis	0.1811253	ko05133	Itga5;Il1b;Tlr4
Serotonergic synapse	0.1819334	ko04726	Cacna1a;Gnb2;Maob;Pla2g12b;Pla2g10
Wnt signaling pathway	0.1819334	ko04310	Tcf7l2;Tcf7l1;Fzd7;Wnt4;Rac2
Fc epsilon RI signaling pathway	0.1866379	ko04664	Pla2g12b;Pla2g10;Rac2
Morphine addiction	0.1866379	ko05032	Cacna1a;Gnb2;Gabrd
Intestinal immune network for IgA production	0.1940208	ko04672	Cd40;Tgfb1
Collecting duct acid secretion	0.1940208	ko04966	Atp6v0d2;Slc4a1
Riboflavin metabolism	0.1986992	ko00740	Enpp1

Other types of O-glycan biosynthesis	0.2020259	ko00514	Ugt1a7c;St6gal1
Basal transcription factors	0.210068	ko03022	Taf7l;Gtf2i
Pancreatic secretion	0.2119524	ko04972	Fxyd2;Pla2g12b;Pla2g10;Rab27b
Tryptophan metabolism	0.2262421	ko00380	Aldh1b1;Maob
Type II diabetes mellitus	0.2262421	ko04930	Cacna1a;Hkdc1
Phosphatidylinositol signaling system	0.2263226	ko04070	Itpka;Inpp1l;Itpkb
Linoleic acid metabolism	0.2343638	ko00591	Pla2g12b;Pla2g10
Leukocyte transendothelial migration	0.23523	ko04670	Cldn23;Cldn20;Rac2;Jam2
Ribosome	0.2496813	ko03010	Rpsa;Rpl26;Rps2
Glycosphingolipid biosynthesis - ganglio series	0.2502463	ko00604	St8sia5
Fatty acid degradation	0.2506525	ko00071	Aldh1b1;Acadl
Phagosome	0.2569167	ko04145	Itga5;Tlr4;Itga2;Atp6v0d2;Clec7a
Influenza A	0.2569167	ko05164	Hspa1b;Il1b;Tlr4;Hspa1a;Furin
Glycosaminoglycan biosynthesis - keratan sulfate	0.2666836	ko00533	B3gnt7
Dopaminergic synapse	0.2687598	ko04728	Cacna1a;Creb3l3;Gnb2;Maob
Carbohydrate digestion and absorption	0.2751325	ko04973	Hkdc1;Fxyd2
Insulin signaling pathway	0.2833895	ko04910	Hkdc1;Inpp1l;Cblc;Ptpfr
Endocytosis	0.2897222	ko04144	Hspa1b;Hspa1a;Rab11fip3;Cblc;Tgfb1;Izumo1r
Tuberculosis	0.2905166	ko05152	Il1b;Tlr4;Atp6v0d2;Clec7a;Tgfb1
Calcium signaling pathway	0.2947742	ko04020	Cacna1a;Grin2d;Itpka;Mylk3;Itpkb
Pantothenate and CoA biosynthesis	0.298489	ko00770	Enpp1
Retrograde	0.3033068	ko04723	Cacna1a;Gnb2;Gabrd

endocannabinoid
signaling

Endometrial cancer	0.3076937	ko05213	Tcf7l2;Tcf7l1
Arginine and proline metabolism	0.3238774	ko00330	Aldh1b1;Maob
Renin-angiotensin system	0.3289199	ko04614	Cma1
Acute myeloid leukemia	0.3399637	ko05221	Tcf7l2;Tcf7l1
Phenylalanine metabolism	0.3436385	ko00360	Maob
NF-kappa B signaling pathway	0.3453999	ko04064	Il1b;Tlr4;Cd40
Chagas disease (American trypanosomiasis)	0.3574053	ko05142	Il1b;Tlr4;Tgfb1
Pathogenic Escherichia coli infection	0.3574053	ko05130	Tlr4;Cldn23;Cldn20
Asthma	0.3580355	ko05310	Cd40
Maturity onset diabetes of the young	0.3580355	ko04950	Hnf4a
Synaptic vesicle cycle	0.3796144	ko04721	Cacna1a;Atp6v0d2
Cholinergic synapse	0.3813172	ko04725	Cacna1a;Creb3l3;Gnb2
Glycosylphosphatidylinos itol (GPI)-anchor biosynthesis	0.3858924	ko00563	Pigz
Shigellosis	0.3952004	ko05131	Itga5;Wasf1
Alzheimer's disease	0.4025841	ko05010	Il1b;Grin2d;ApoE;Snca
Renal cell carcinoma	0.4106058	ko05211	Tgfb1;Pak6
Pancreatic cancer	0.4106058	ko05212	Tgfb1;Rac2
Chronic myeloid leukemia	0.4182365	ko05220	Cblc;Tgfb1
Mucin type O-glycan biosynthesis	0.4254358	ko00512	Galnt10
Protein export	0.4254358	ko03060	Srp9
Epithelial cell signaling in Helicobacter pylori infection	0.4408221	ko05120	Atp6v0d2;Jam2
Protein processing in endoplasmic reticulum	0.4419287	ko04141	Hspa1b;Cryaa;Ubqln2;Hs pa1a
Staphylococcus aureus infection	0.4482438	ko05150	Masp1;Fgg

Pentose phosphate pathway	0.4624418	ko00030	Aldob
Salivary secretion	0.4629197	ko04970	Fxyd2;Gucy1b2
Osteoclast differentiation	0.468675	ko04380	Il1b;Tnfrsf11b;Tgfb1
Antigen processing and presentation	0.4701717	ko04612	Hspa1b;Hspa1a
Propanoate metabolism	0.4742416	ko00640	Aldh1b1
beta-Alanine metabolism	0.4742416	ko00410	Aldh1b1
B cell receptor signaling pathway	0.477365	ko04662	Inpp11;Rac2
Spliceosome	0.4799319	ko03040	Hspa1b;Hspa1a;Sf3a2
Retinol metabolism	0.4844987	ko00830	Ugt1a7c;Bco1
Proximal tubule bicarbonate reclamation	0.4857834	ko04964	Fxyd2
Nicotinate and nicotinamide metabolism	0.4857834	ko00760	Enpp1
Chemokine signaling pathway	0.4899637	ko04062	Ccr111;Gnb2;Rac2;Ccr1
Natural killer cell mediated cytotoxicity	0.4910765	ko04650	Gzmb;Prf1;Rac2
Galactose metabolism	0.4970727	ko00052	Hkdc1
Neuroactive ligand-receptor interaction	0.4990109	ko04080	Grin2d;F2;Adcyap1r1;P2ry1;Gzma;Gabrd
Peroxisome	0.5055344	ko04146	Crat;Ephx2
Lysosome	0.5075713	ko04142	Atp6v0d2;Ctsm;Ctsh
ErbB signaling pathway	0.512422	ko04012	Cblc;Pak6
Cardiac muscle contraction	0.5192464	ko04260	Fxyd2;Myh14
Glycine, serine and threonine metabolism	0.5294805	ko00260	Maob
Porphyrin and chlorophyll metabolism	0.5294805	ko00860	Ugt1a7c
Glycerophospholipid metabolism	0.5327036	ko00564	Pla2g12b;Pla2g10
Tyrosine metabolism	0.5398139	ko00350	Maob
Primary immunodeficiency	0.5398139	ko05340	Cd40

Aldosterone-regulated sodium reabsorption	0.5499212	ko04960	Fxyd2
mRNA surveillance pathway	0.5524037	ko03015	Casc3;Upf1
Pyruvate metabolism	0.5694771	ko00620	Aldh1b1
GnRH signaling pathway	0.5777502	ko04912	Pla2g12b;Pla2g10
Metabolism of xenobiotics by cytochrome P450	0.5839211	ko00980	Ugt1a7c;Gstm2
Vasopressin-regulated water reabsorption	0.5881864	ko04962	Creb3l3
Aminoacyl-tRNA biosynthesis	0.5881864	ko00970	Lars2
Transcriptional misregulation in cancer	0.6097234	ko05202	Gzmb;Zeb2;Cd40;Hist1h3d
Metabolic pathways	0.6158857	ko01100	Sord;Enpp1;St8sia5;Ugt1a7c;Extl3;Aldh1b1;Bco1;Hkdc1;Itpka;Aldob;Galnt10;Maob;Pla2g12b;Itpkb;Acadl;Pla2g10;Ptgds;Gda;Hsd3b6;Atp6v0d2;Ephx2;Eno2;St6gal1
Amino sugar and nucleotide sugar metabolism	0.6232094	ko00520	Hkdc1
Bile secretion	0.6308927	ko04976	Ugt1a7c;Fxyd2
Lysine degradation	0.6314912	ko00310	Aldh1b1
Purine metabolism	0.6375425	ko00230	Enpp1;Gda;Gucy1b2
T cell receptor signaling pathway	0.6474136	ko04660	Cblc;Pak6
Notch signaling pathway	0.6552642	ko04330	Jag2
Glutathione metabolism	0.6552642	ko00480	Gstm2
Vibrio cholerae infection	0.6552642	ko05110	Atp6v0d2
N-Glycan biosynthesis	0.6628439	ko00510	St6gal1
Valine, leucine and isoleucine degradation	0.6846013	ko00280	Aldh1b1
Glycerolipid metabolism	0.6846013	ko00561	Aldh1b1
Drug metabolism - other	0.6846013	ko00983	Ugt1a7c

enzymes

Amyotrophic lateral sclerosis (ALS)	0.6915383	ko05014	Grin2d
Endocrine and other factor-regulated calcium reabsorption	0.6983233	ko04961	Fxyd2
NOD-like receptor signaling pathway	0.7114504	ko04621	Il1b
Long-term potentiation	0.7418317	ko04720	Grin2d
Herpes simplex infection	0.7519819	ko05168	Il1b;Pvrl1;Gtf2i
Hepatitis C	0.7630491	ko05160	Cldn23;Cldn20
Taste transduction	0.7741109	ko04742	Cacna1a
TGF-beta signaling pathway	0.7887092	ko04350	Tgfb1
RNA degradation	0.7979154	ko03018	Eno2
HTLV-I infection	0.801519	ko05166	Fzd7;Wnt4;Cd40;Tgfb1
Epstein-Barr virus infection	0.8044369	ko05169	Hspa1b;Hspa1a;Cd40
Gap junction	0.8109806	ko04540	Gucy1b2
Apoptosis	0.8192197	ko04210	Il1b
Gastric acid secretion	0.827101	ko04971	Mylk3
Small cell lung cancer	0.8309123	ko05222	Itga2
RNA transport	0.8416951	ko03013	Casc3;Upf1
Huntington's disease	0.8941062	ko05016	Creb3l3;Dlg4
Parkinson's disease	0.898787	ko05012	Snca
Oxidative phosphorylation	0.9053471	ko00190	Atp6v0d2
Cell cycle	0.9094834	ko04110	Tgfb1
Ubiquitin mediated proteolysis	0.942125	ko04120	Cblc
Jak-STAT signaling pathway	0.9505198	ko04630	Cblc
