

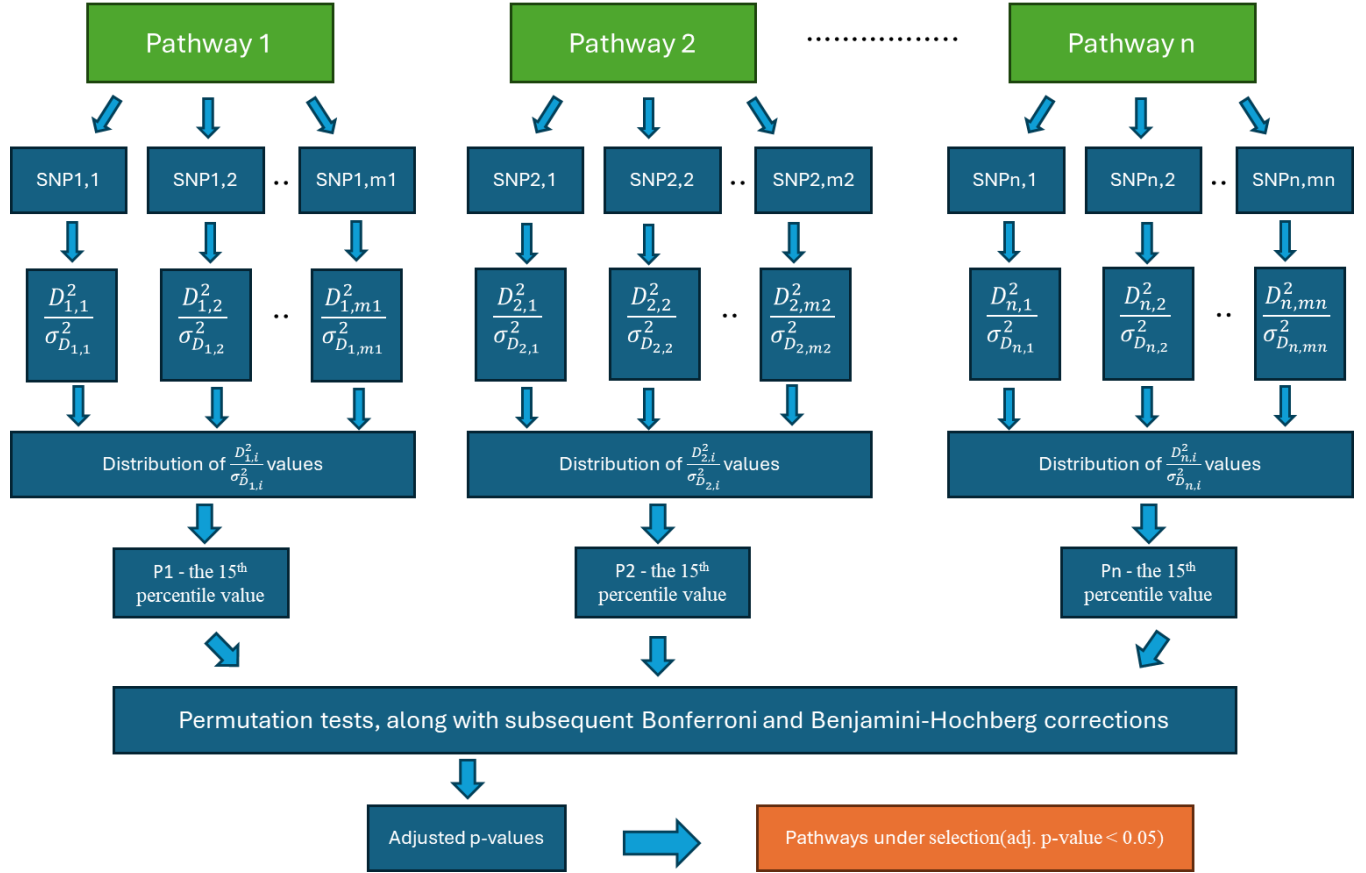
SUPPLEMENTARY MATERIAL

Europeans and Americans of European origin show differences between their biological pathways related to the major histocompatibility complex

Andrey Vaulin, Evgeny Karpulevich, Artem Kasianov, Irina Morozova

Supplementary figures

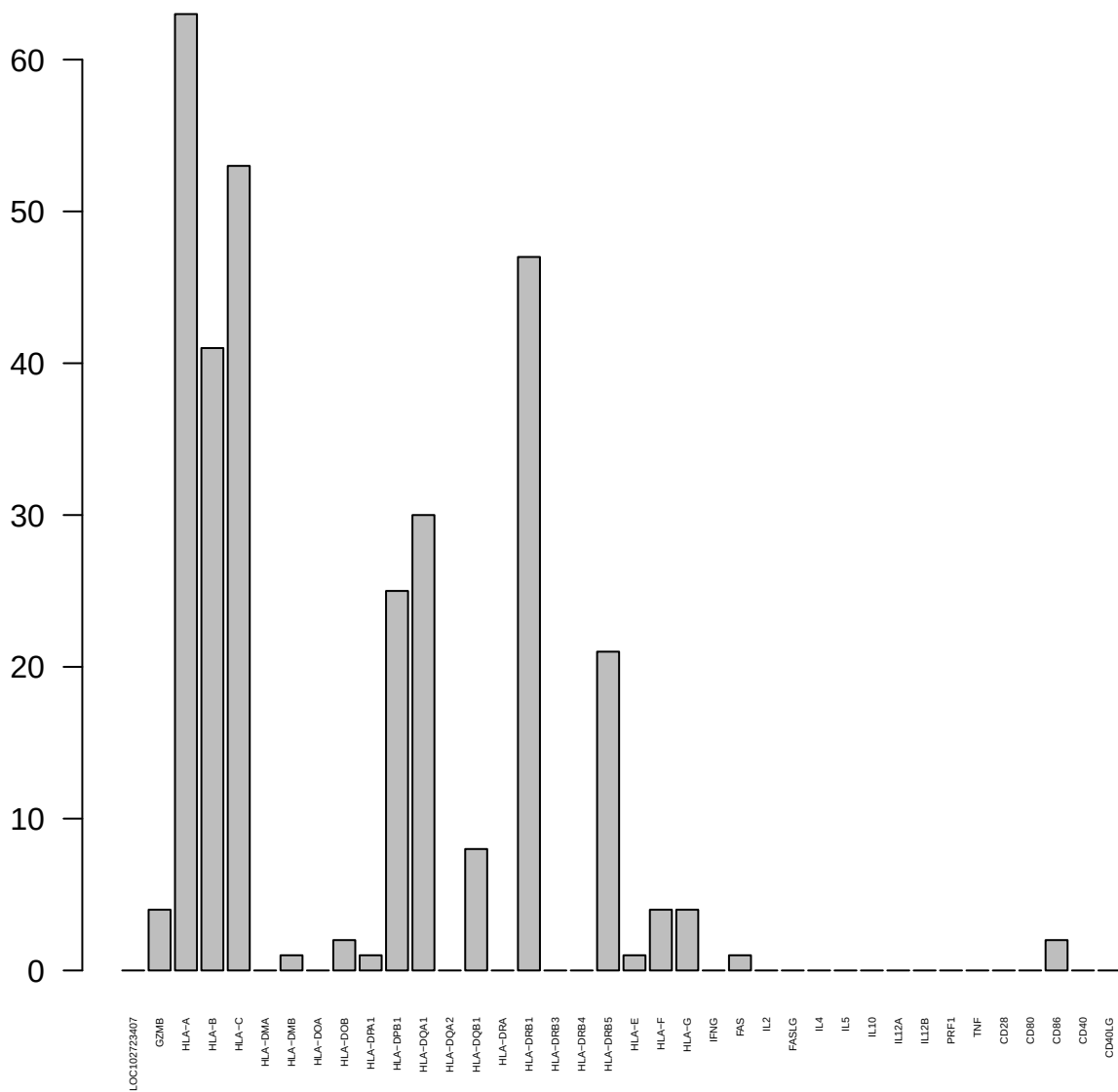
Supplementary figure 1. Scheme of analysis of selective pressure.



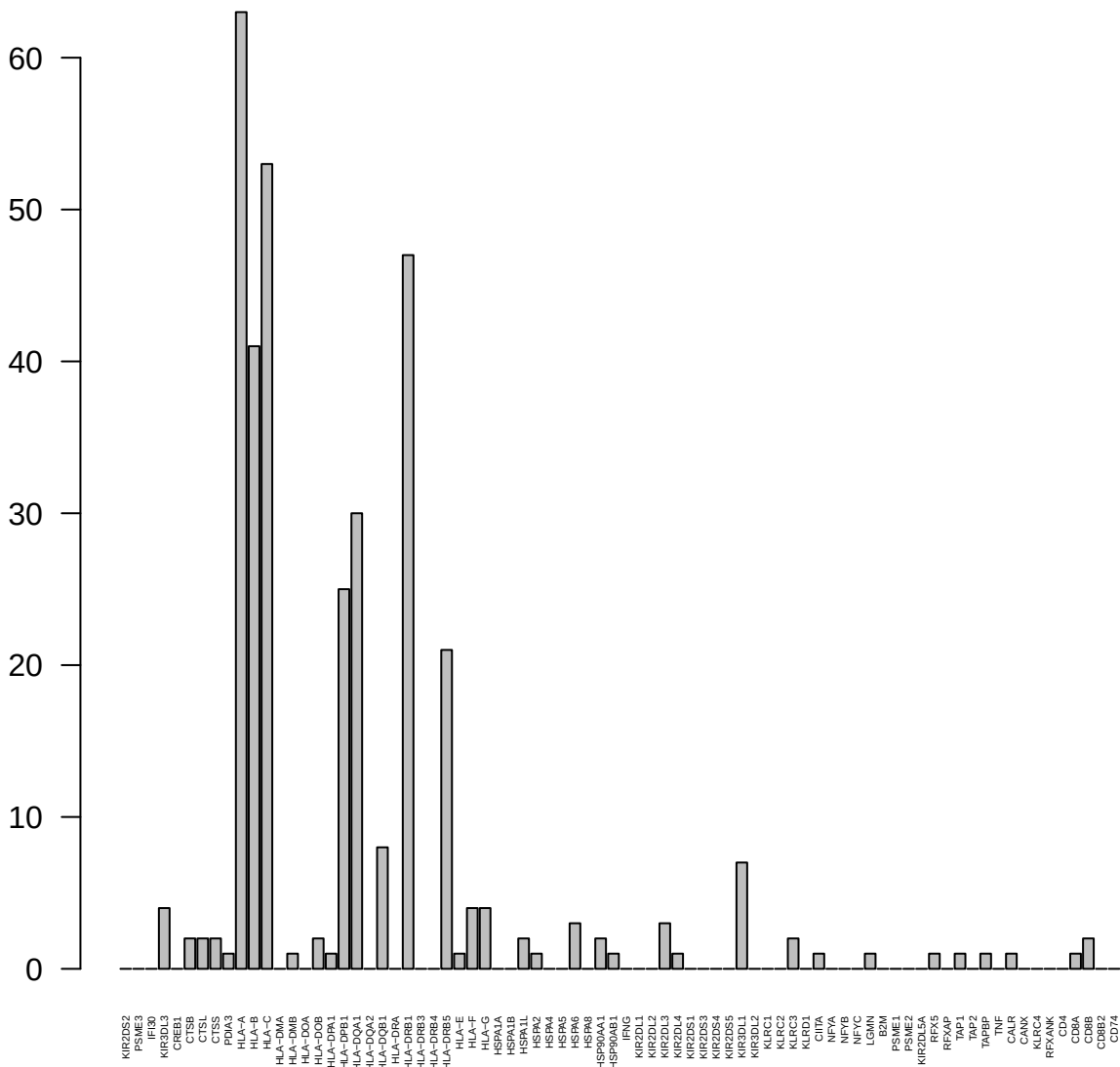
$D_{i,j} = p_1^{i,j} - p_2^{i,j}$ represents the allele frequency difference at $SNP_{i,j}$ between population 1 and population 2, and $\sigma_{D_{i,j}}^2$ is the variance.

Supplementary figure 2. The SNP distributions in the genes of analysed pathways

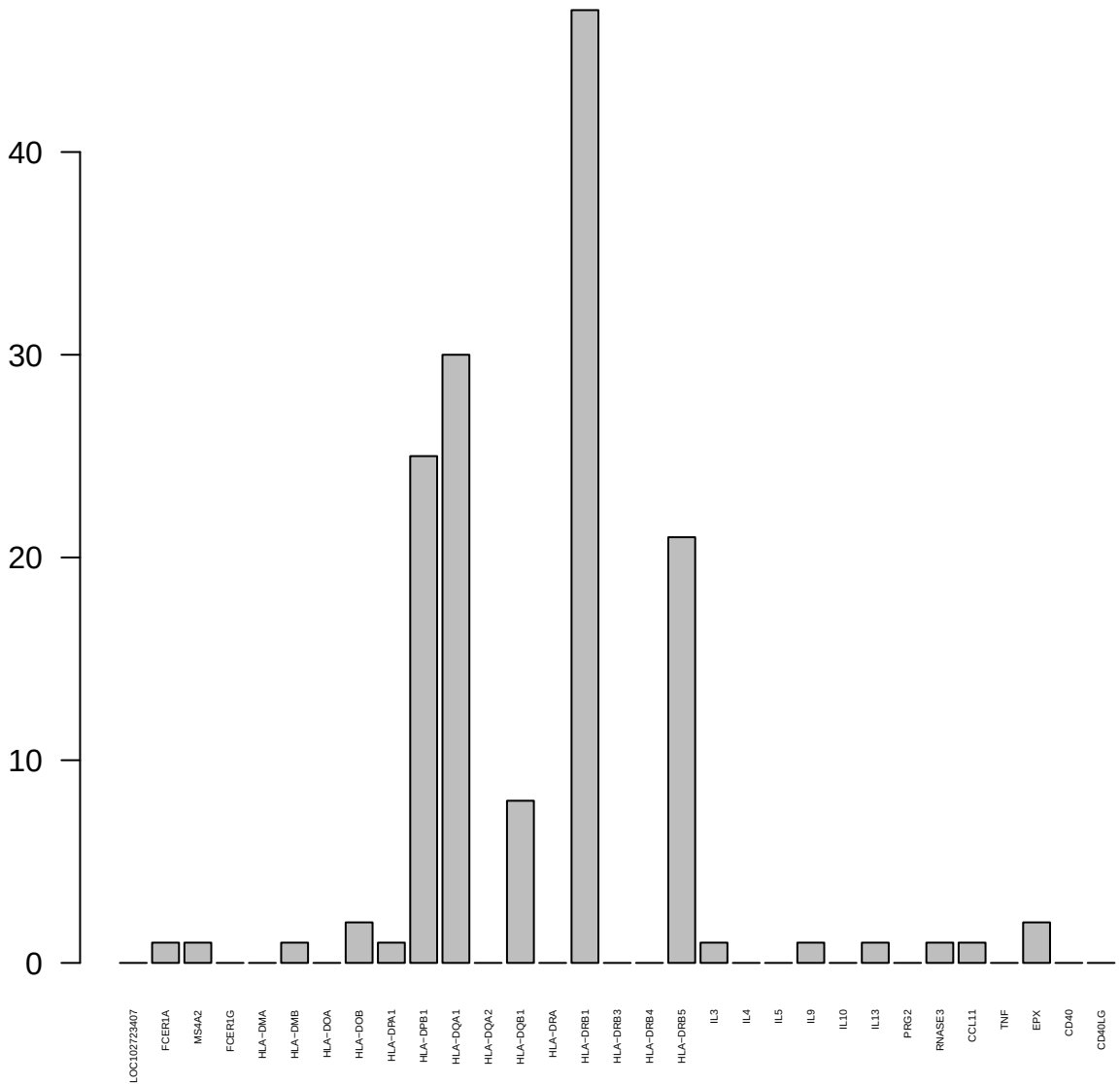
Allograft rejection



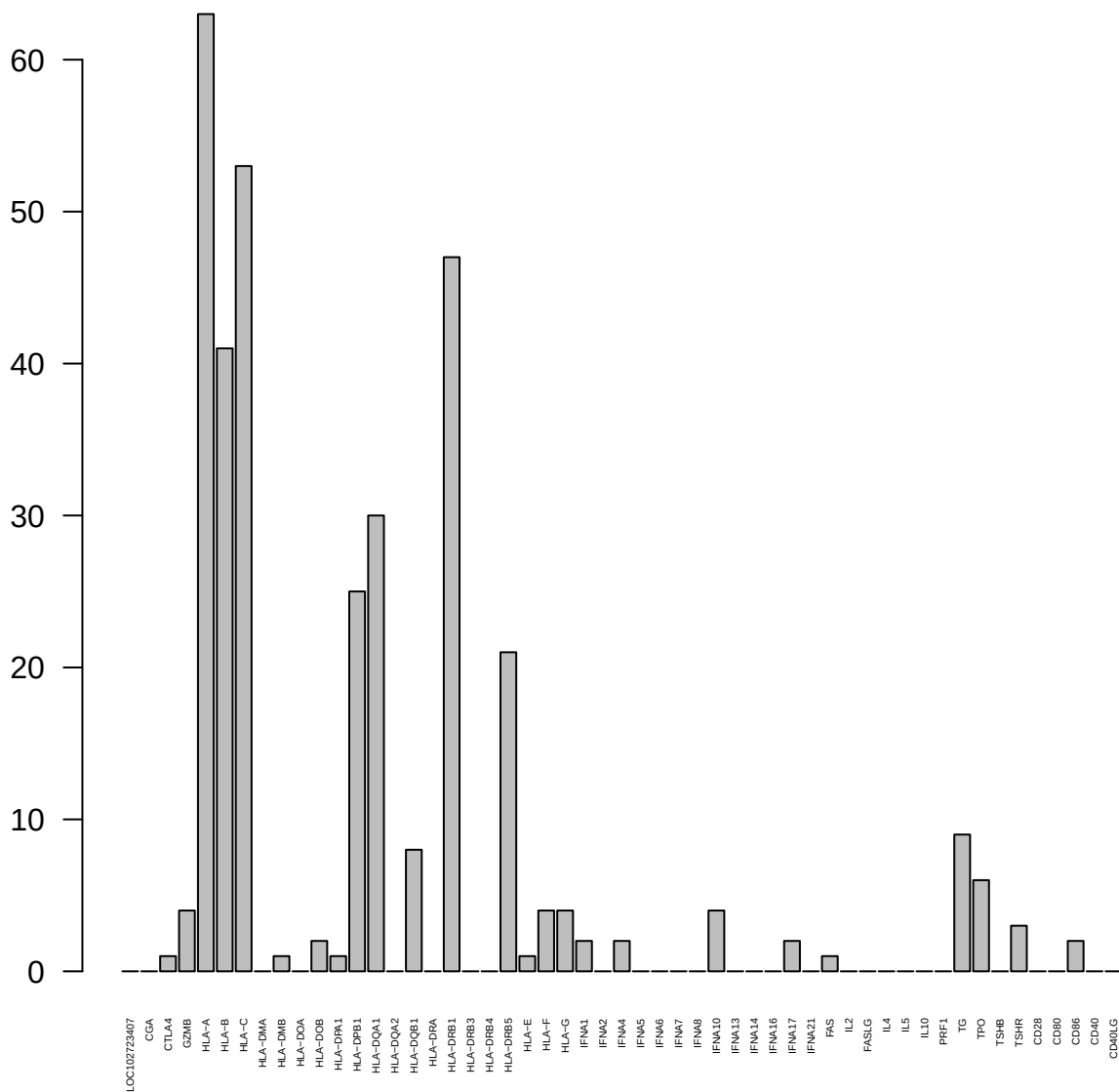
Antigen processing and presentation



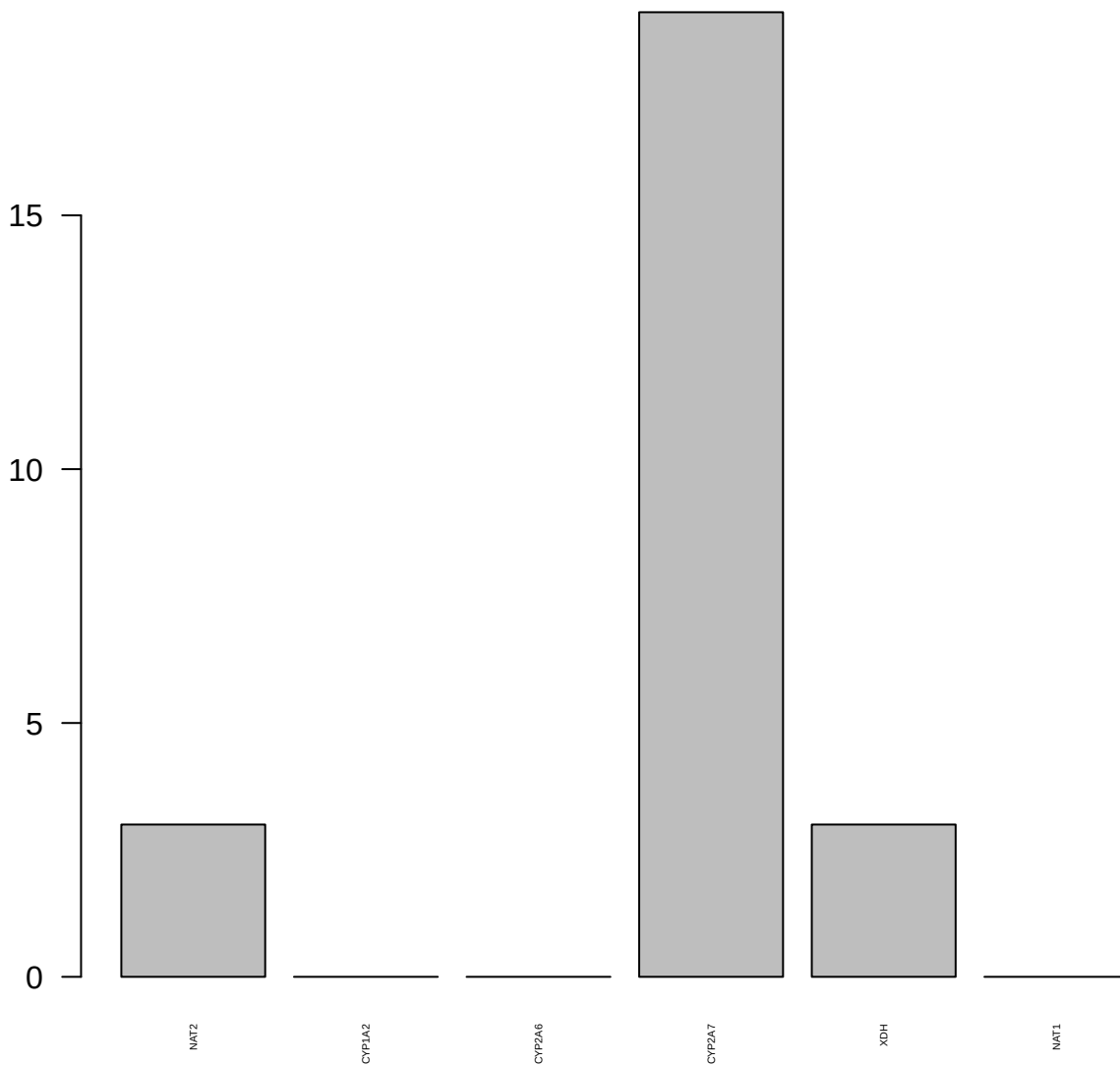
Asthma



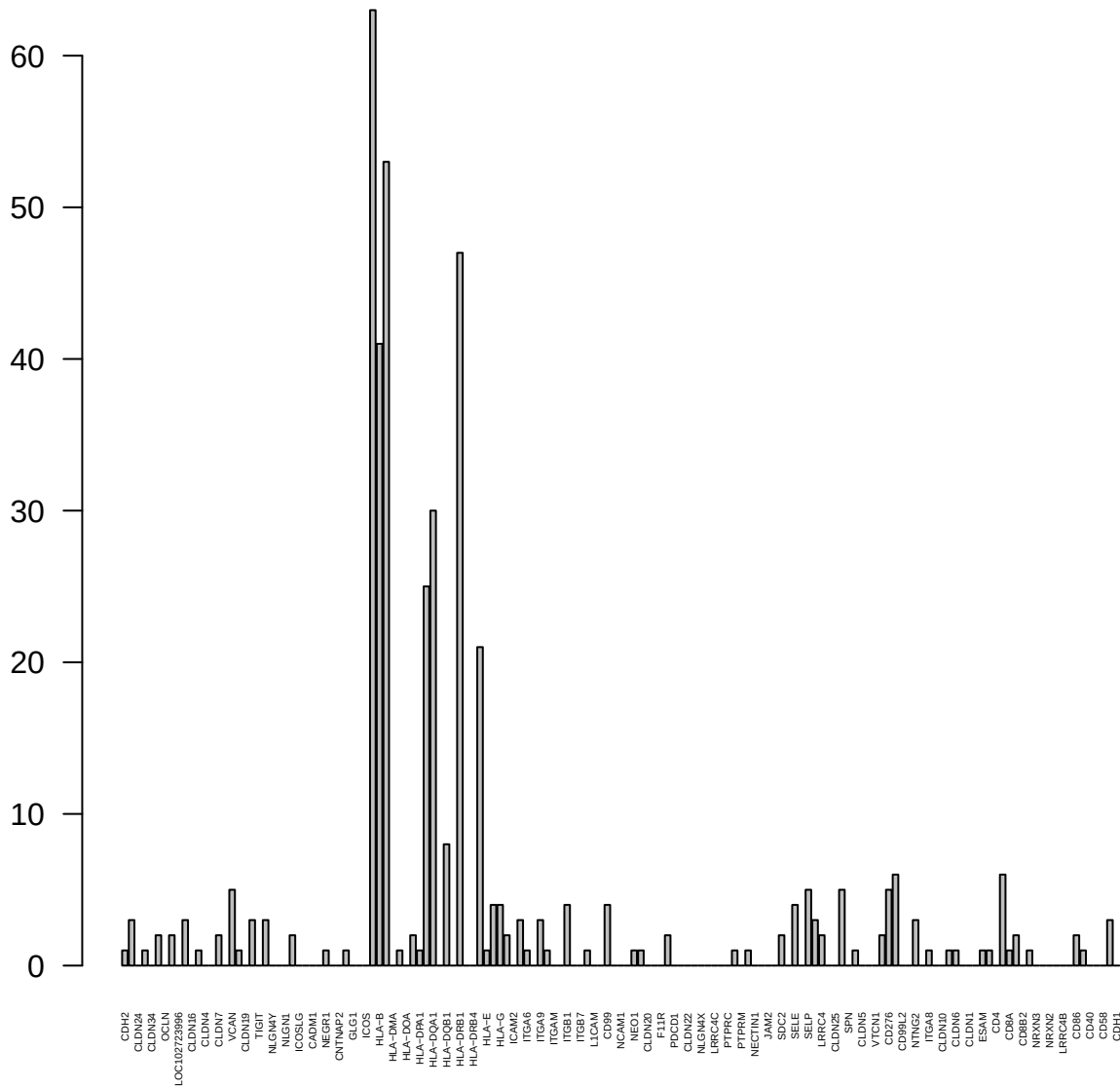
Autoimmune thyroid disease



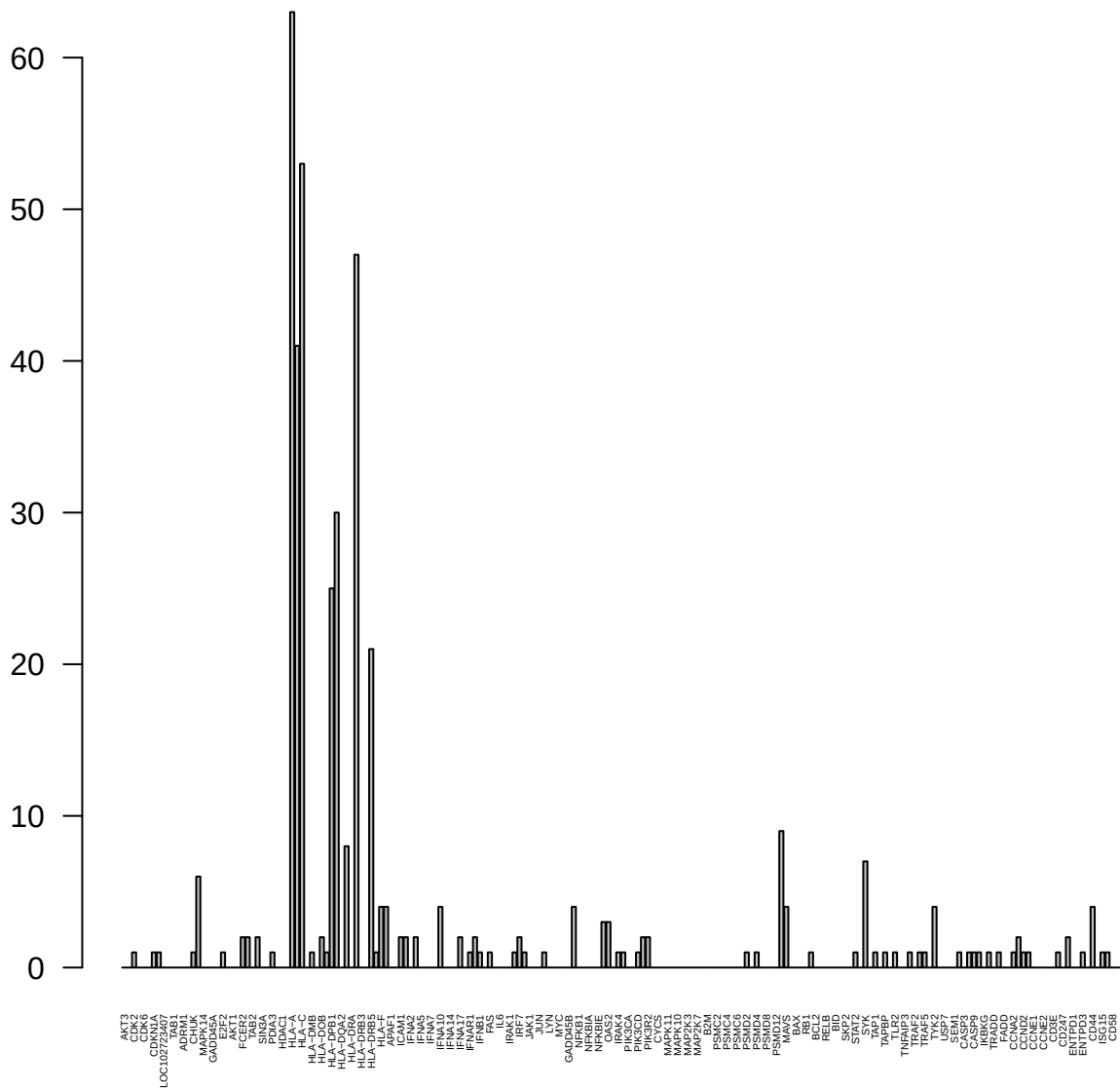
Caffeine metabolism



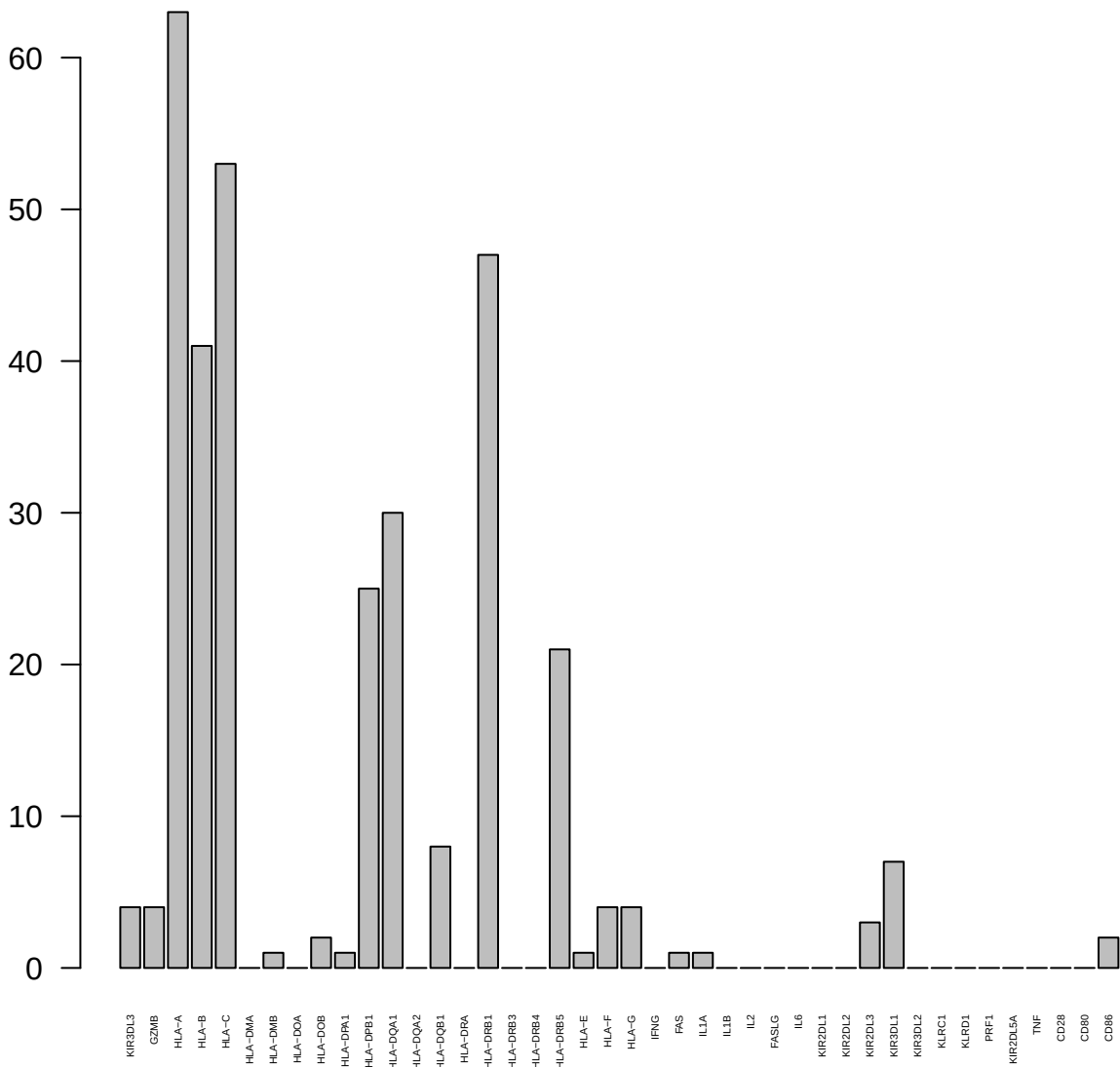
Cell adhesion molecules



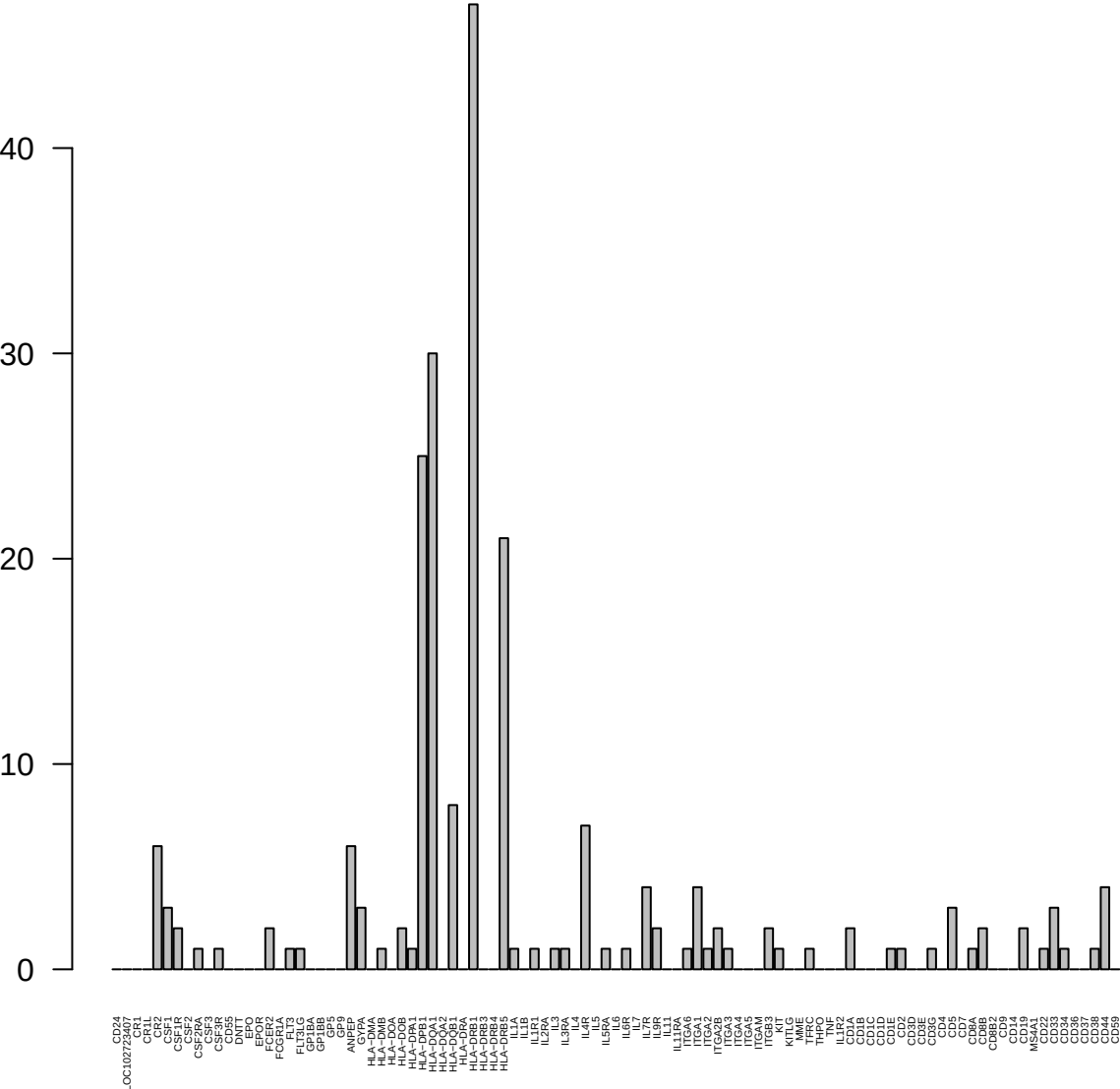
Epstein-Barr virus infection



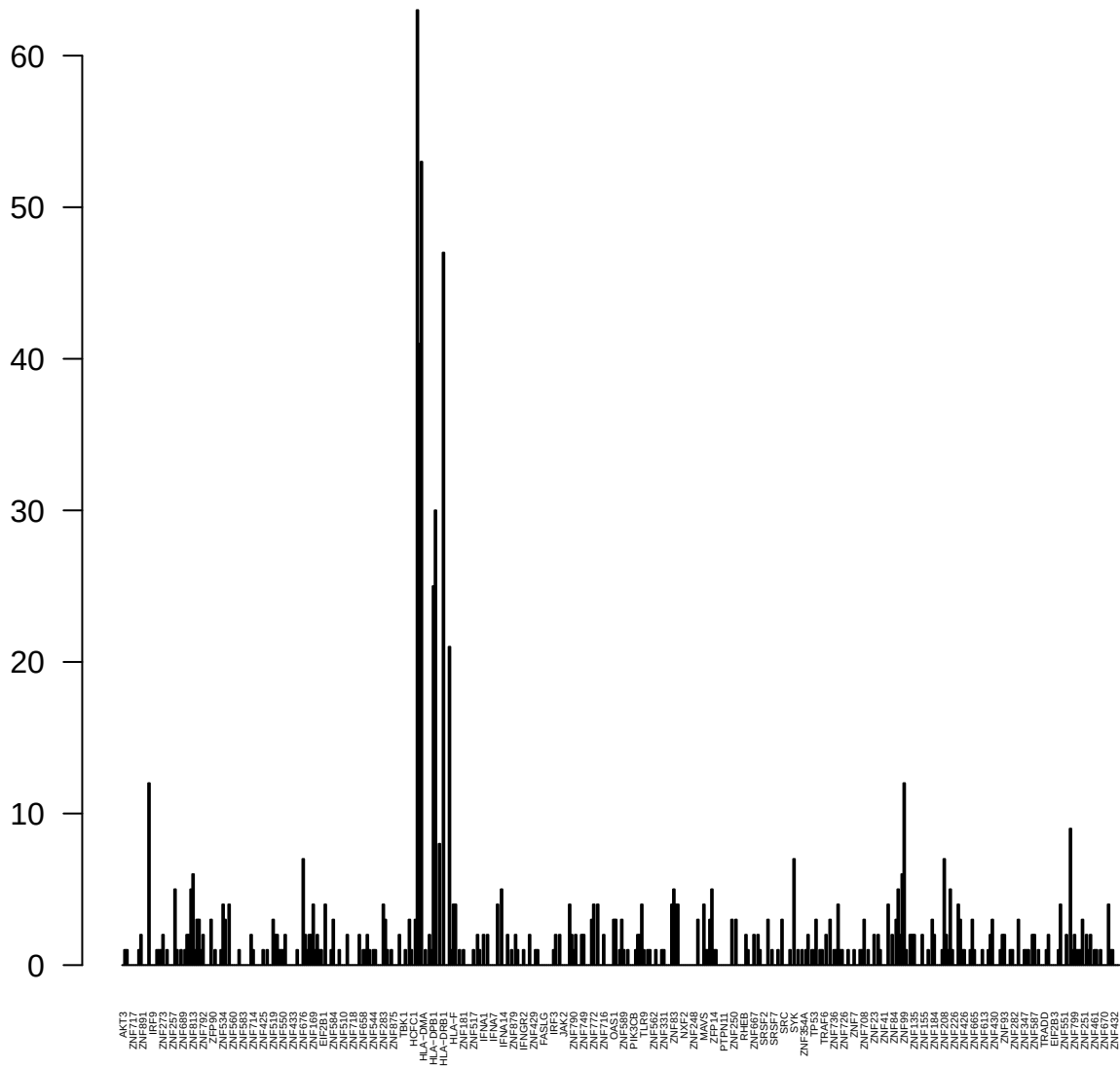
Graft-versus-host disease



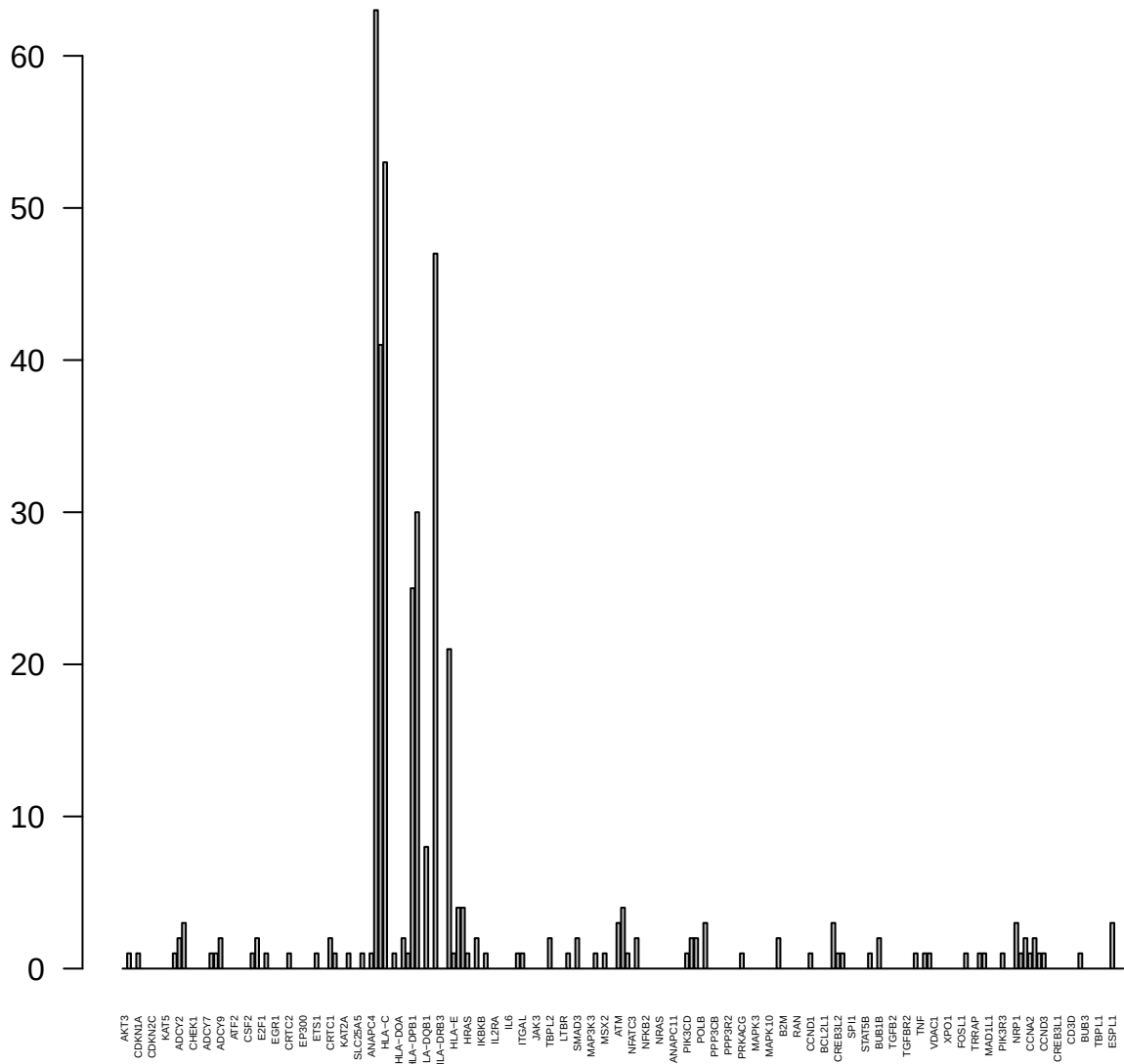
Hematopoietic cell lineage



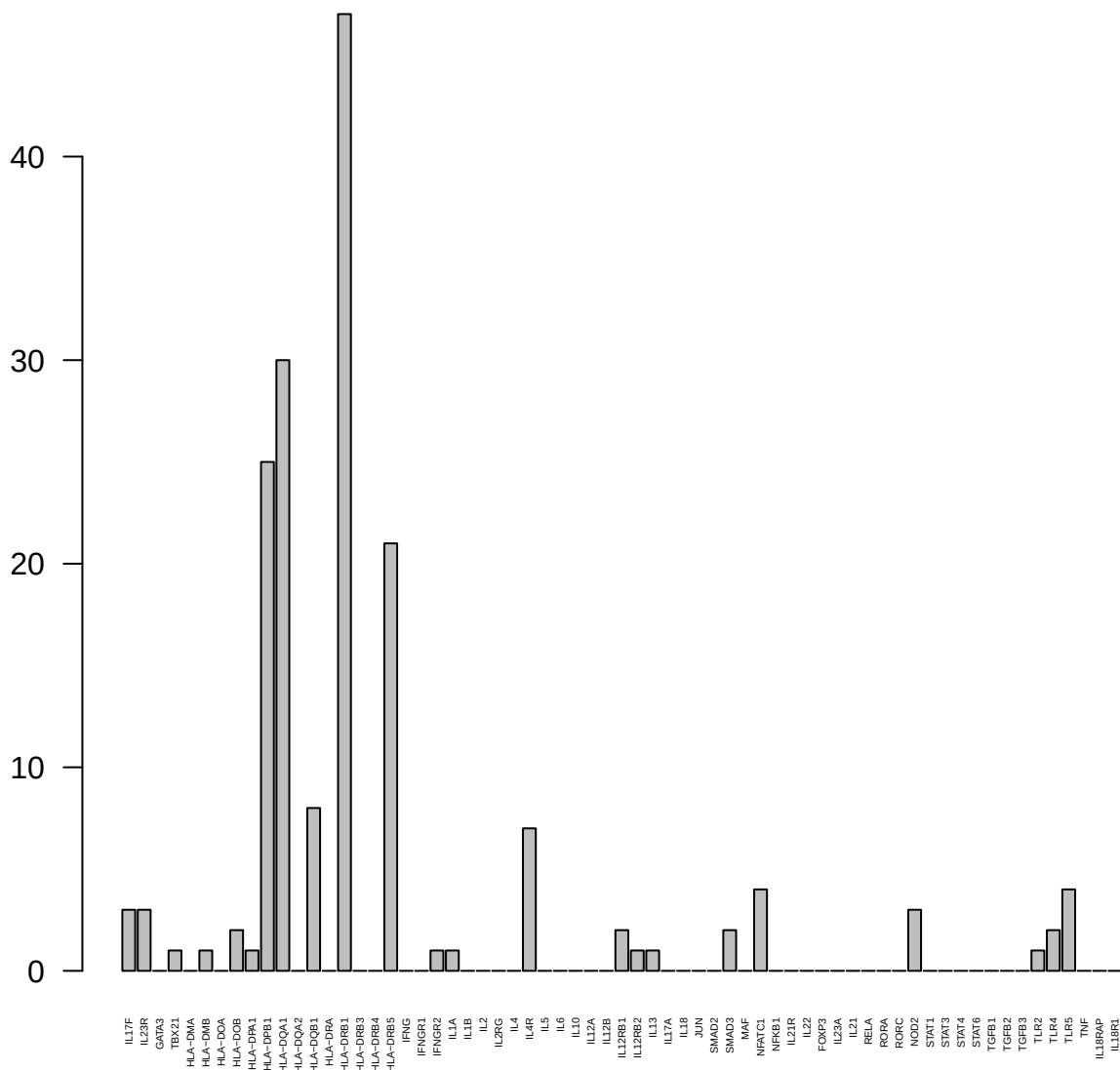
Herpes simplex virus 1 infection



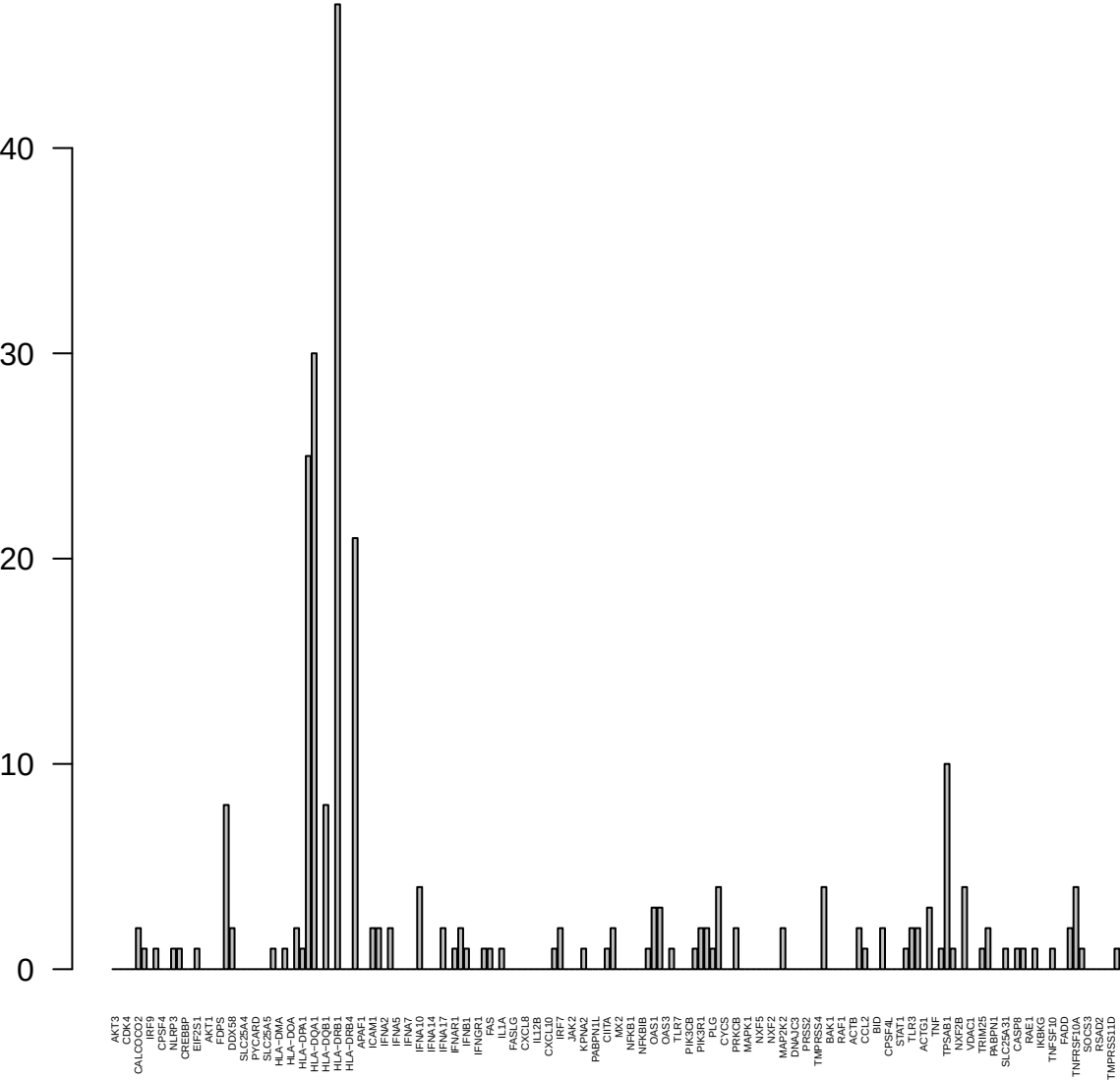
Human T-cell leukemia virus 1 infection



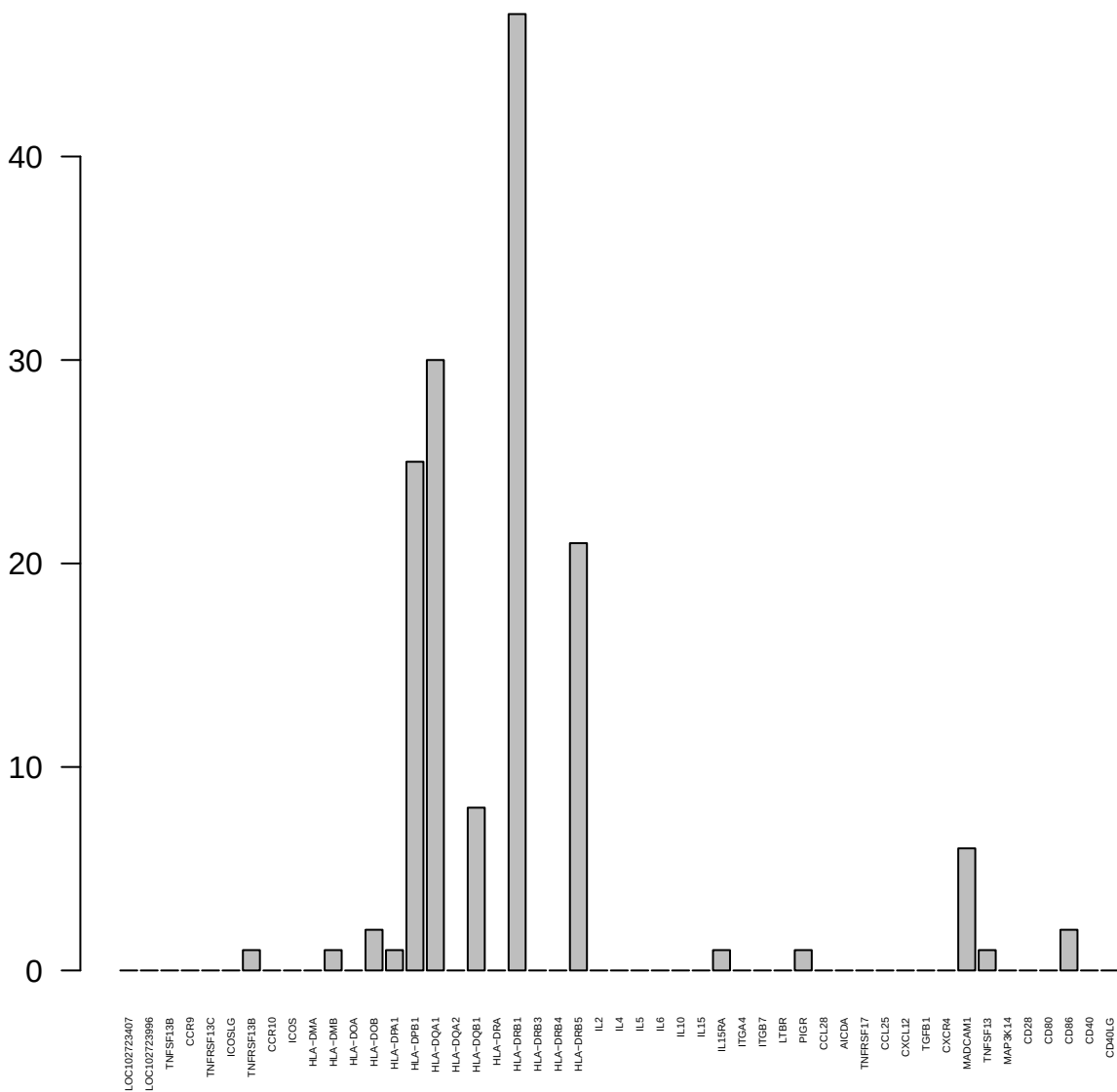
Inflammatory bowel disease



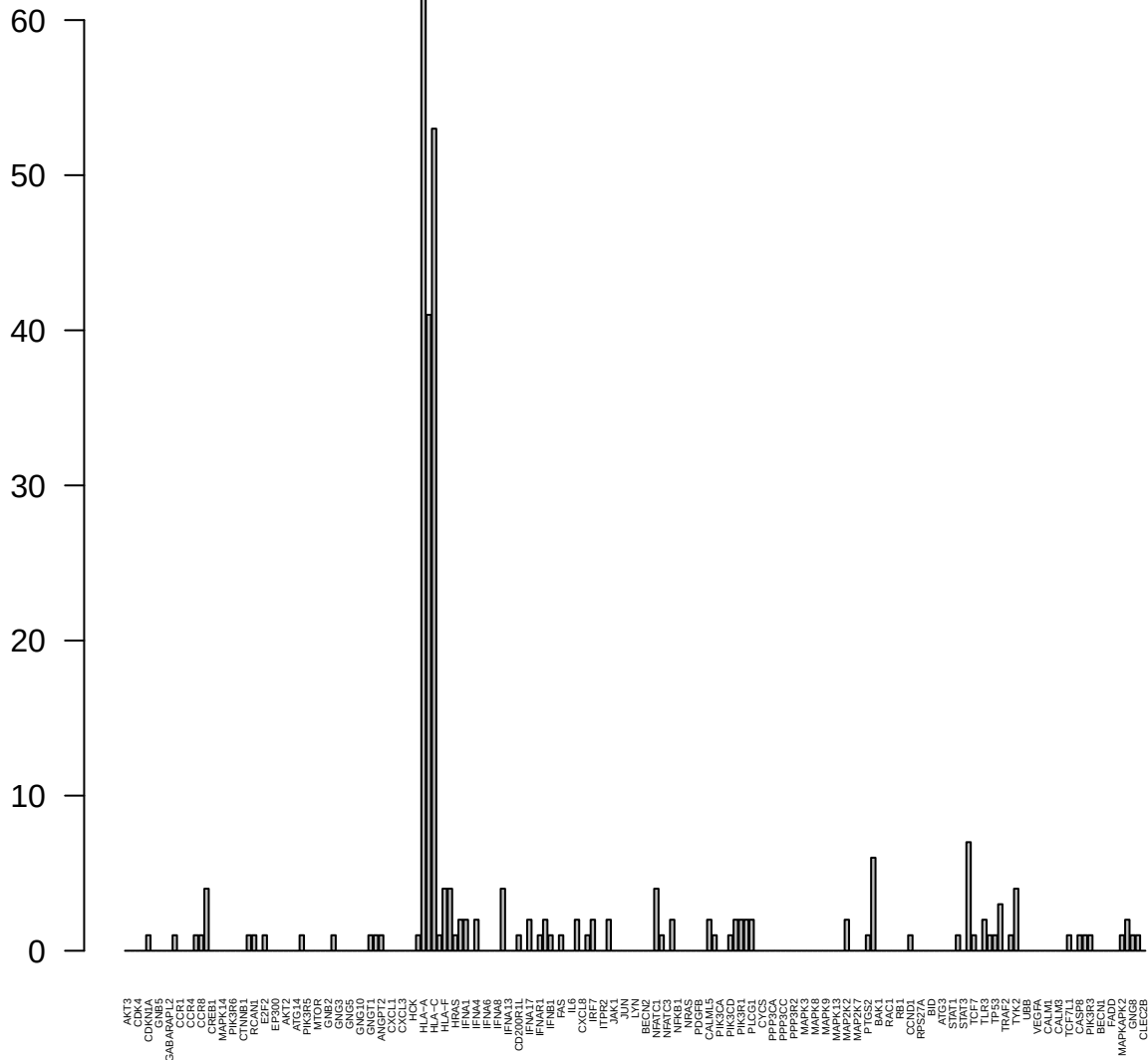
Influenza A



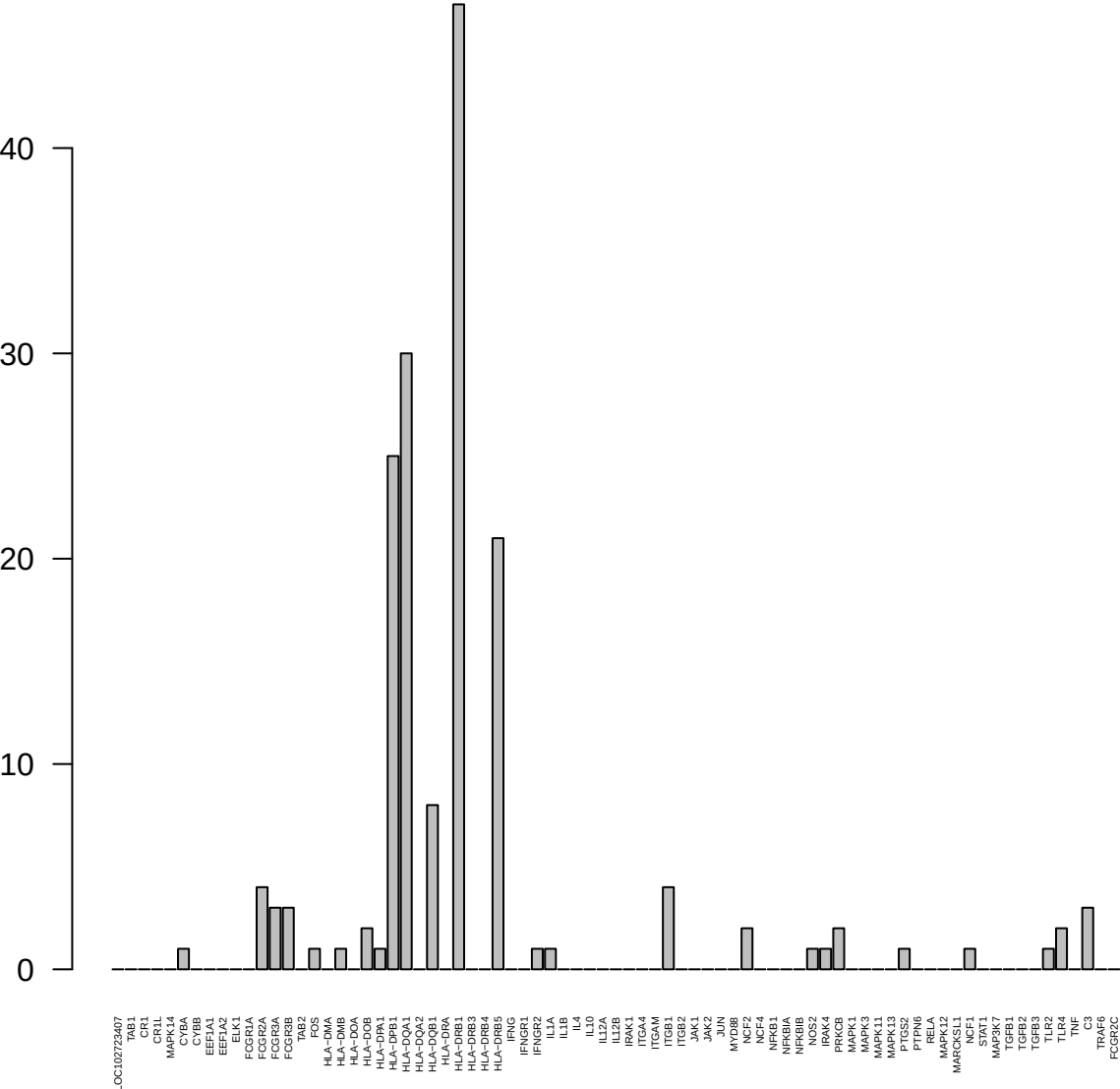
Intestinal immune network for IgA production



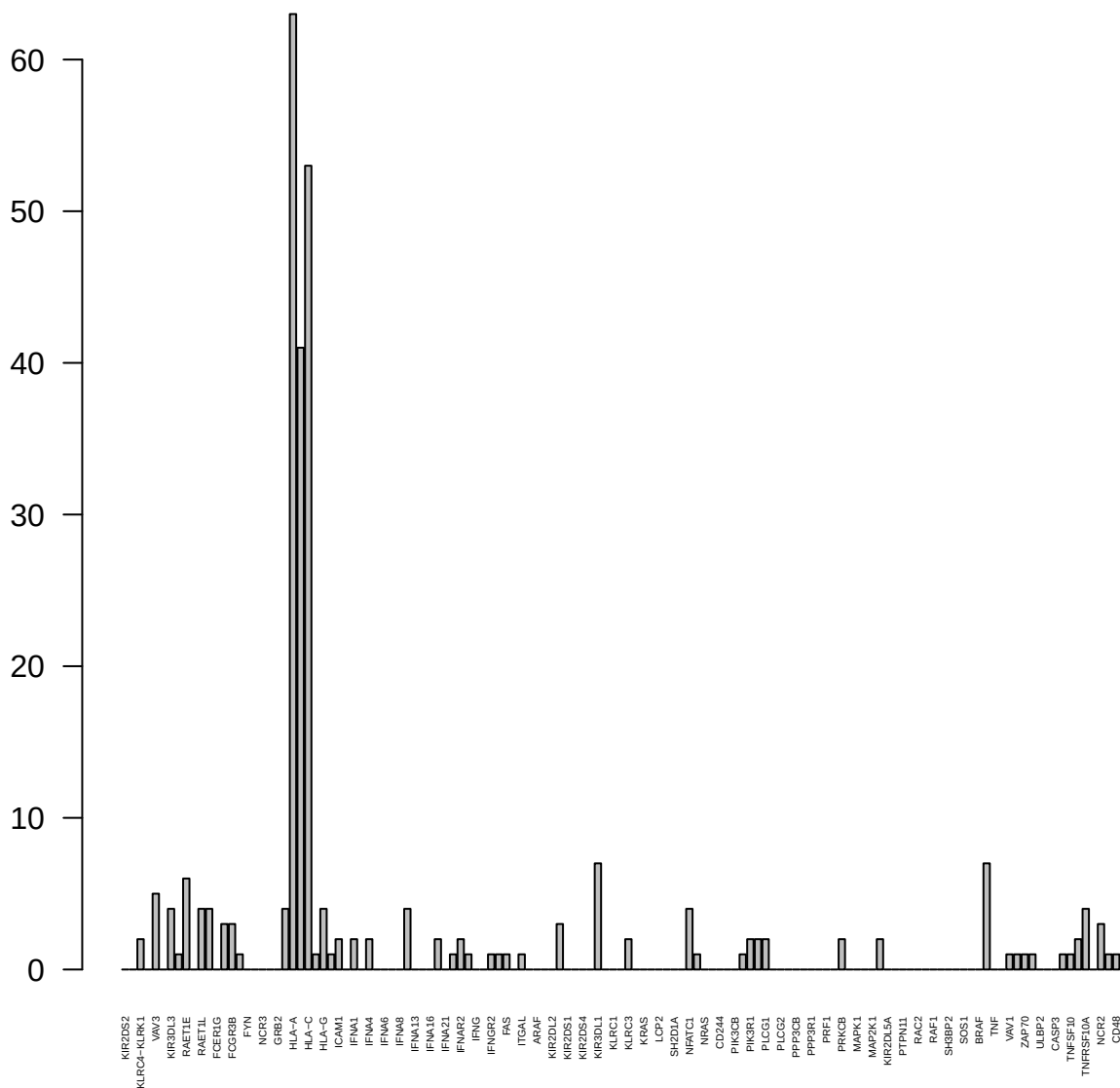
Kaposi sarcoma-associated herpesvirus infection



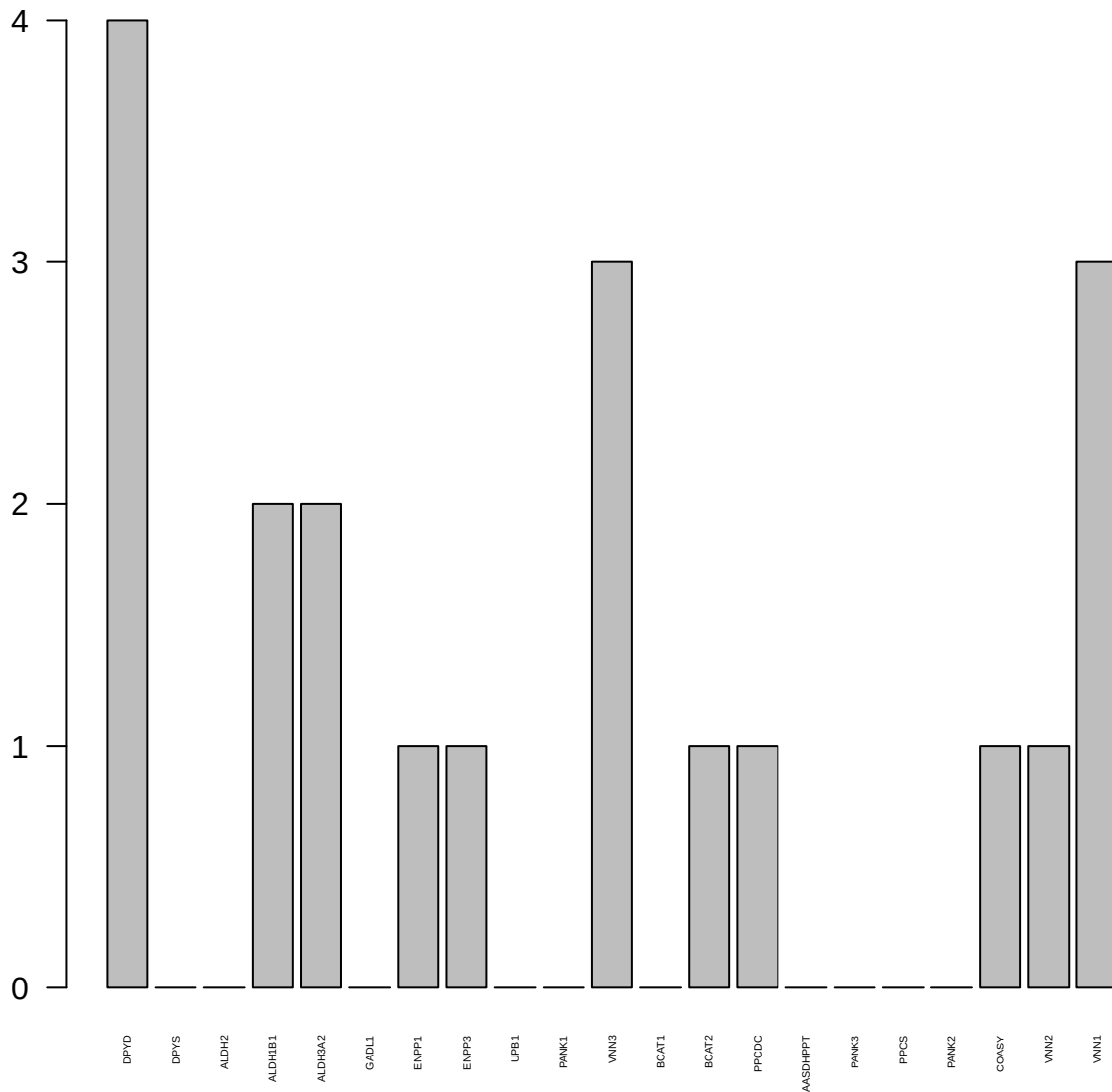
Leishmaniasis



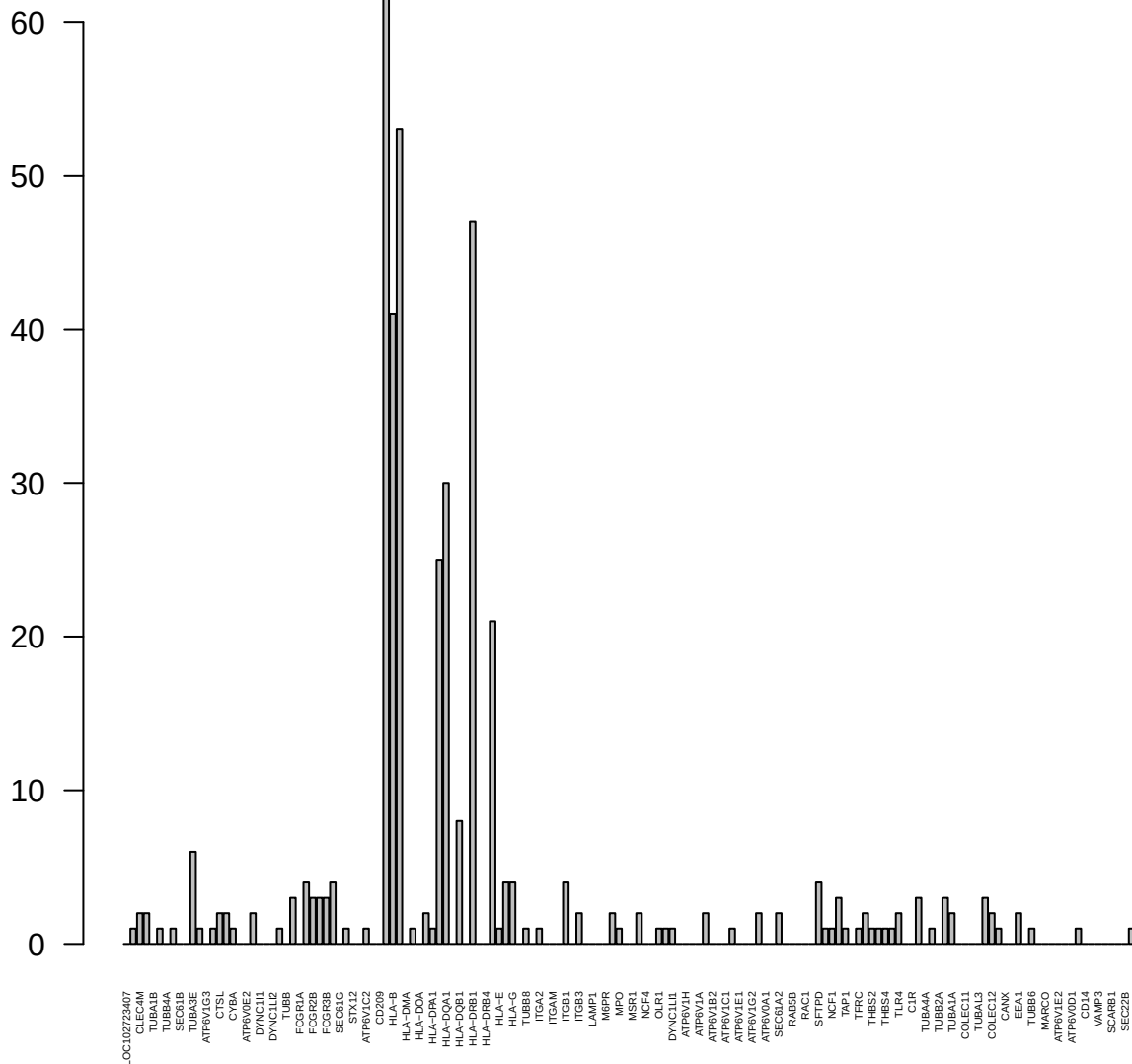
Natural killer cell mediated cytotoxicity



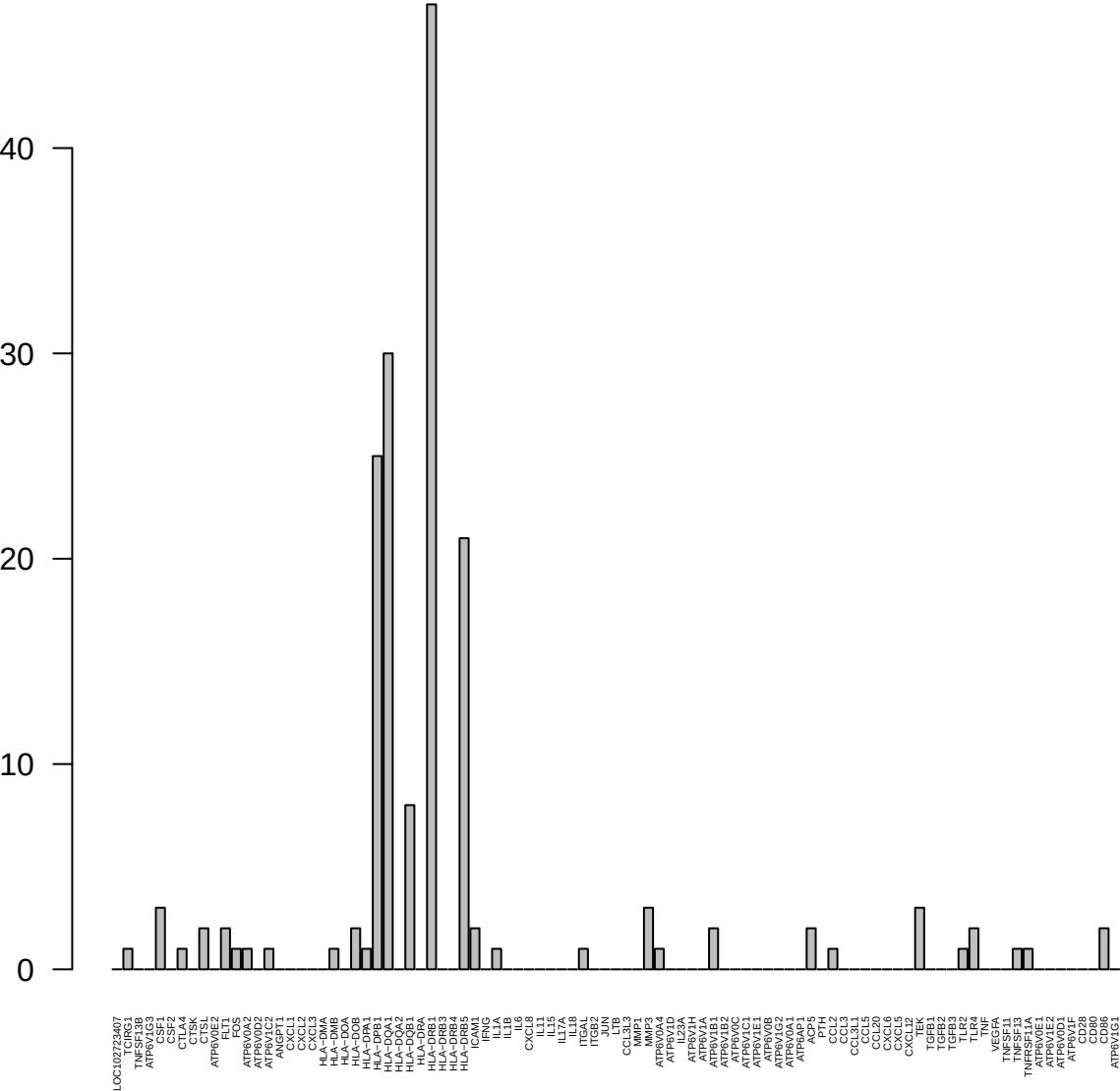
Pantothenate and CoA biosynthesis



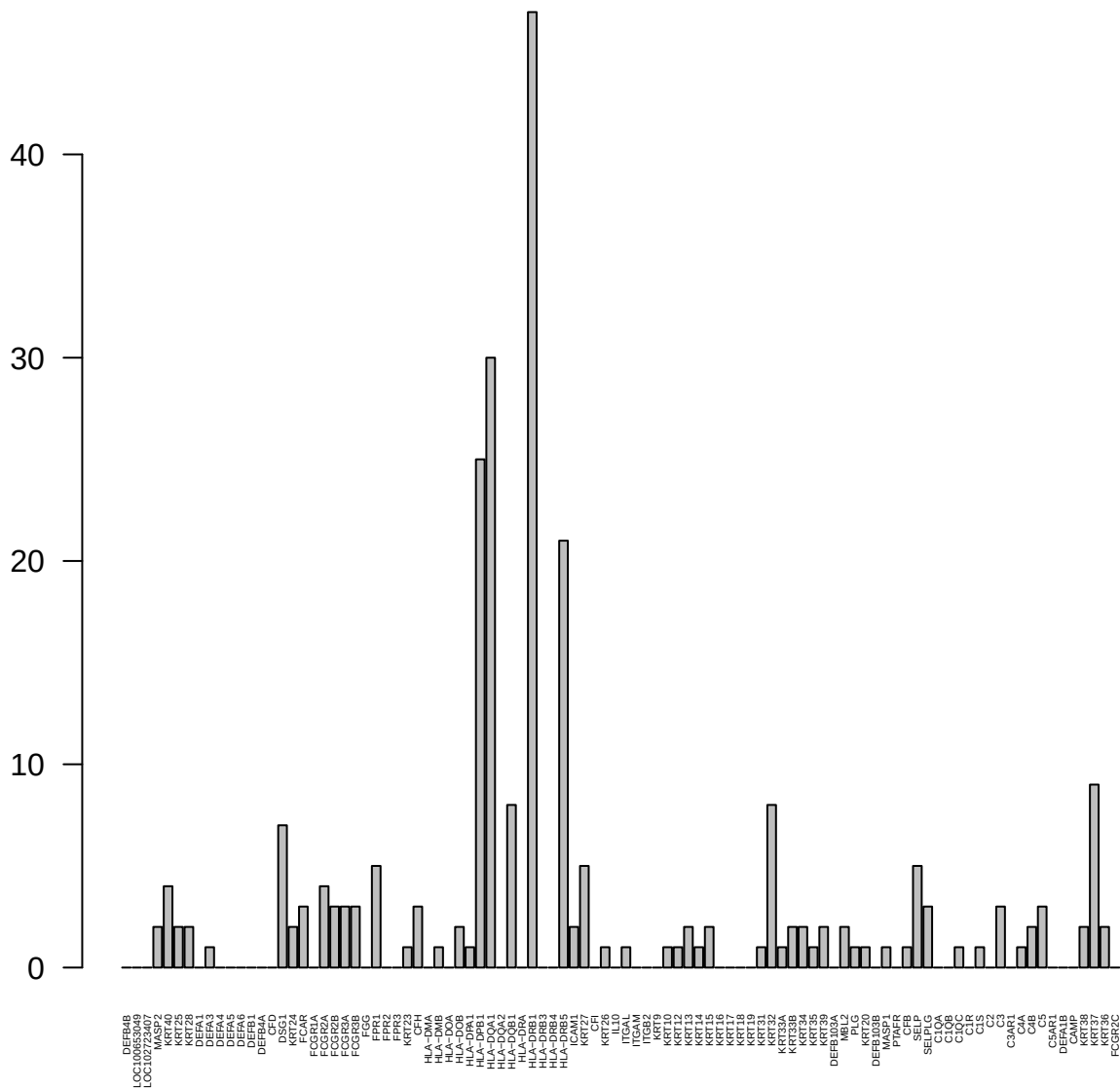
Phagosome



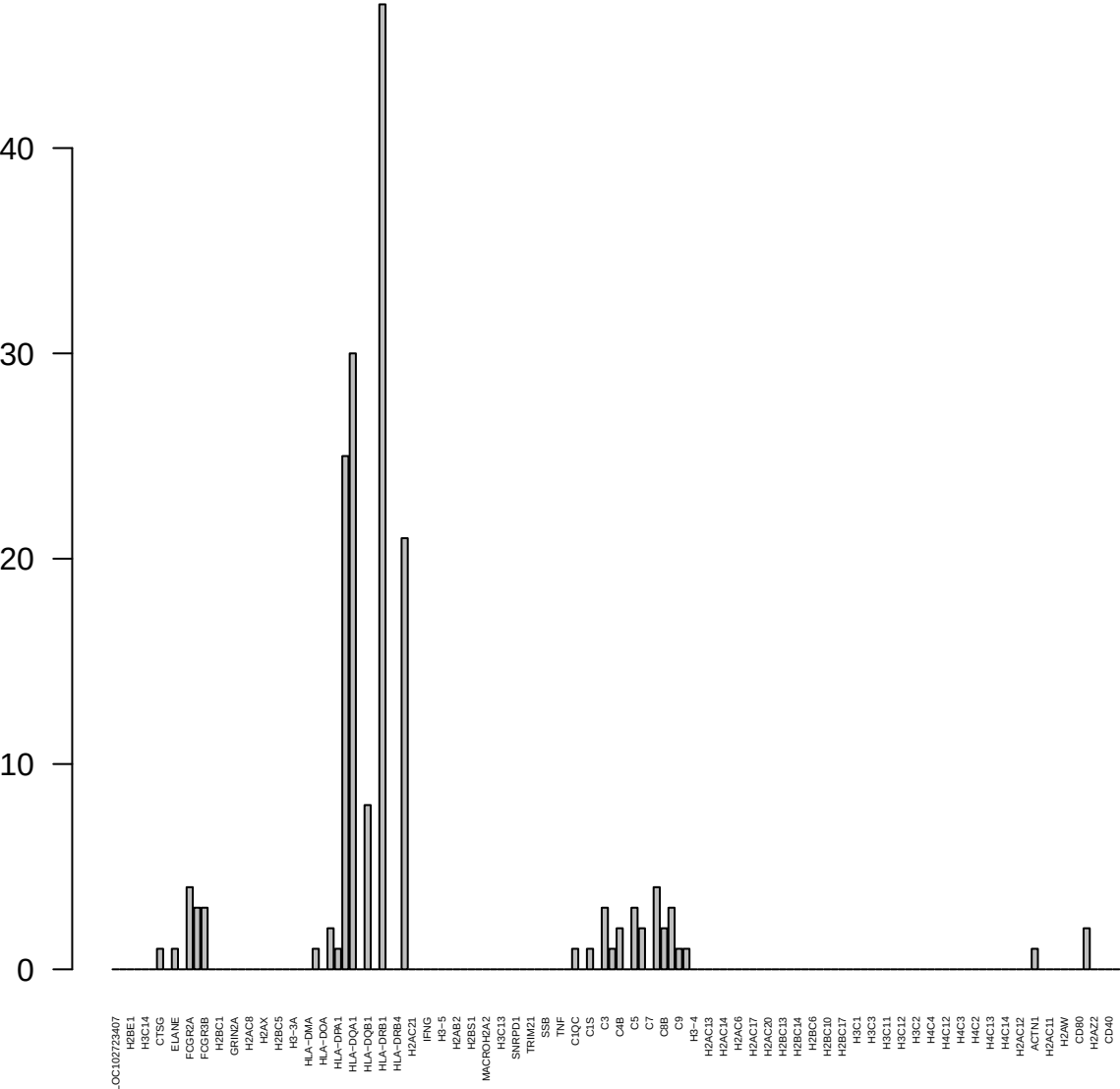
Rheumatoid arthritis



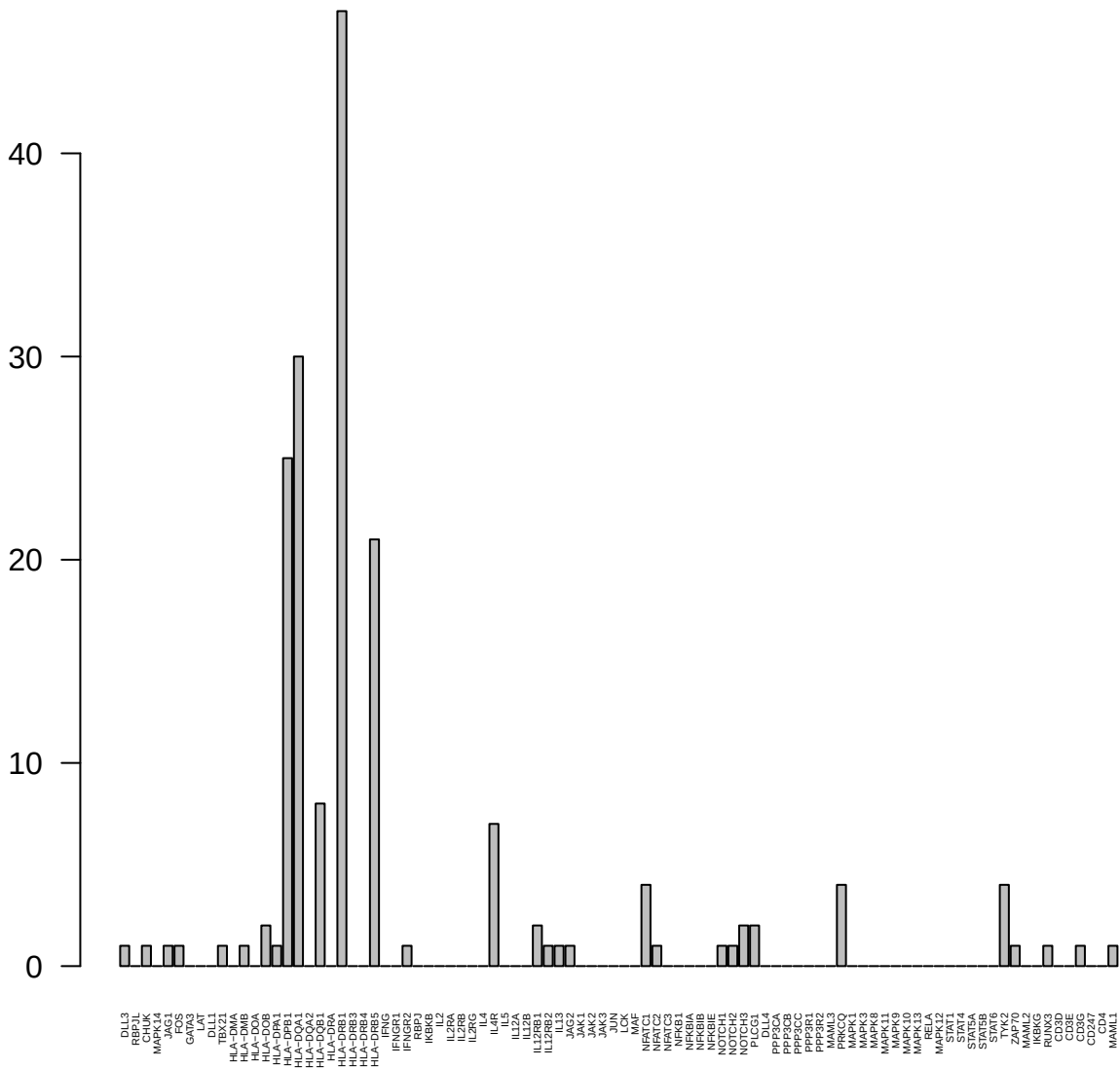
Staphylococcus aureus infection



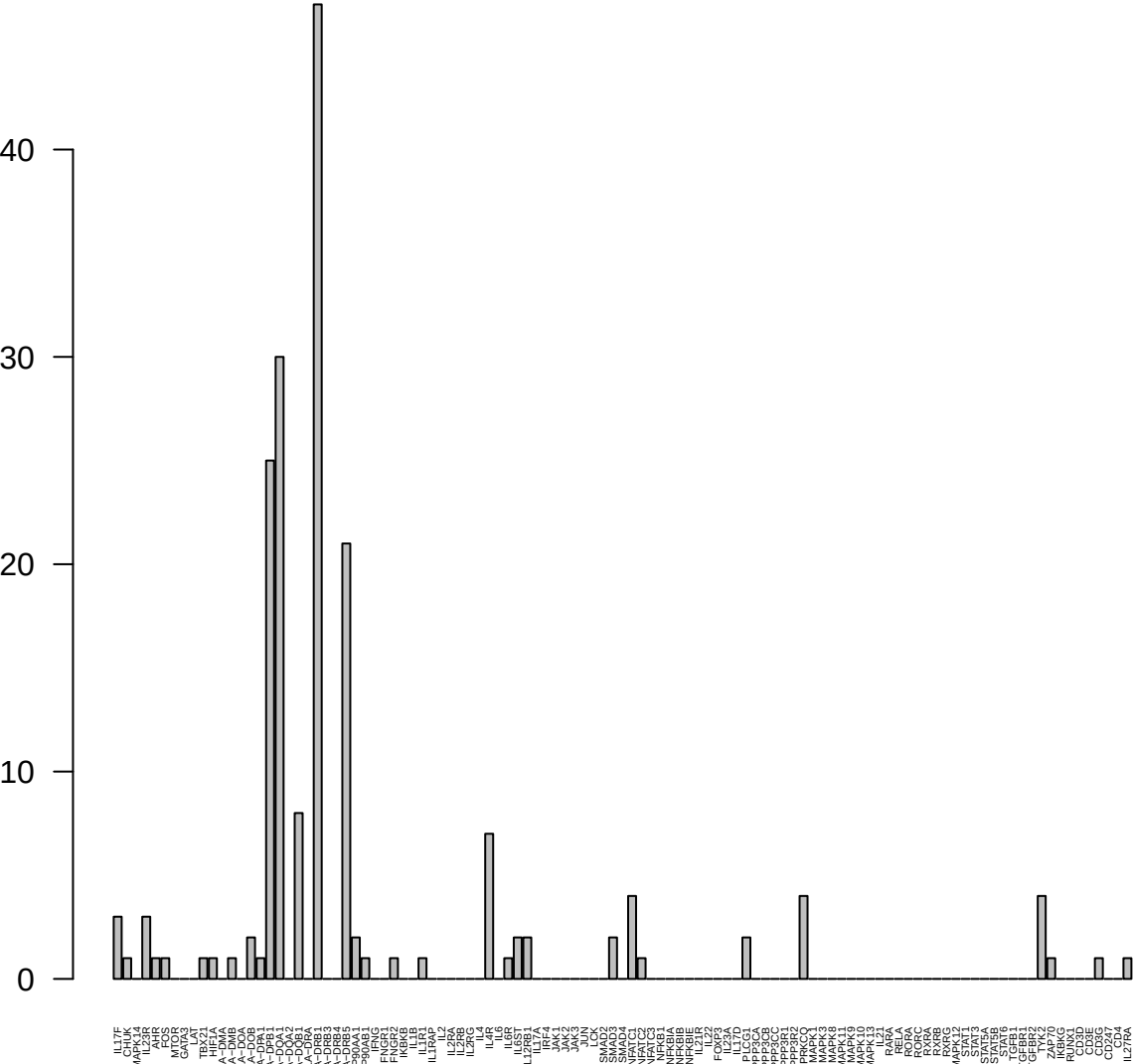
Systemic lupus erythematosus



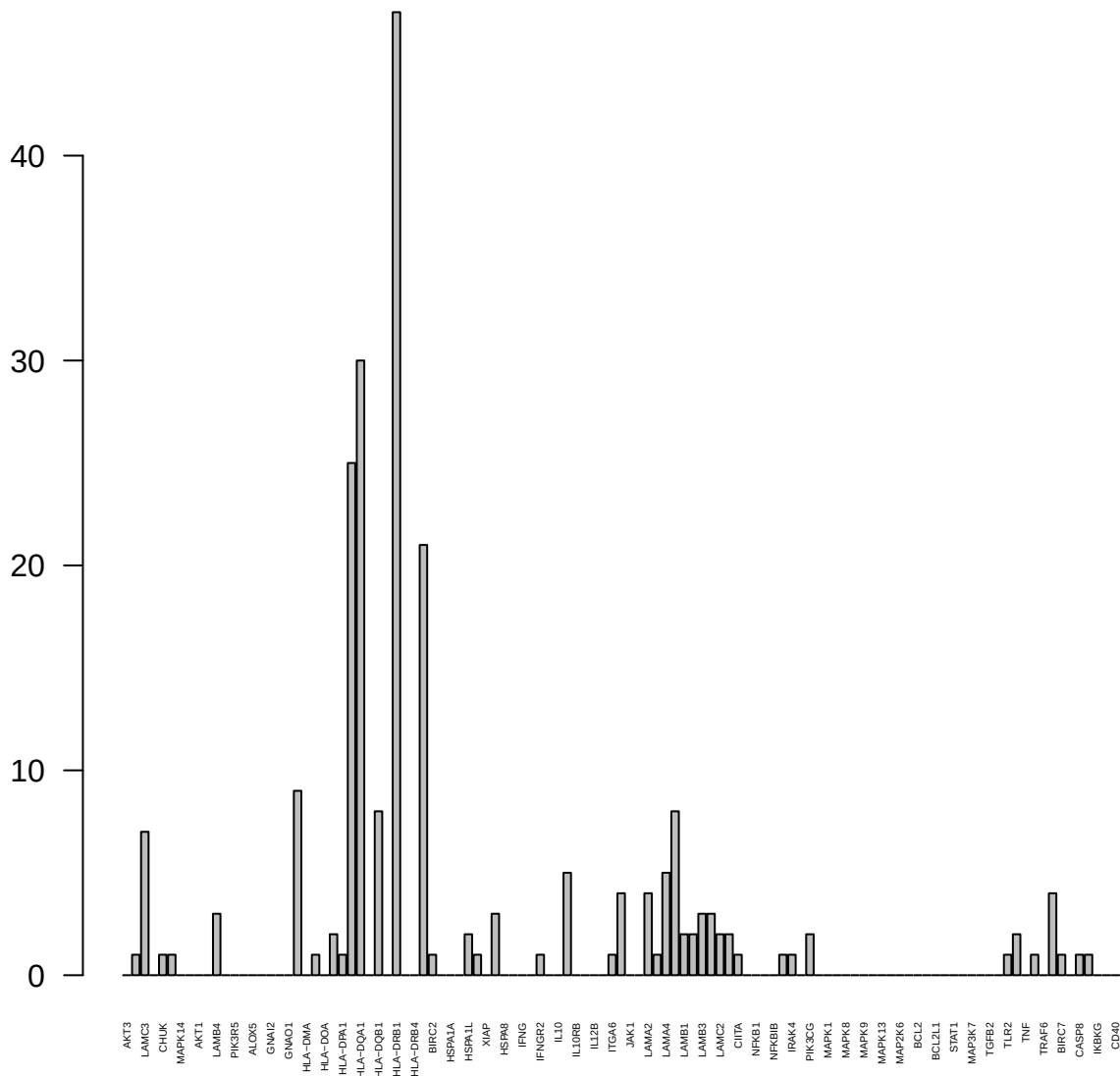
Th1 and Th2 cell differentiation



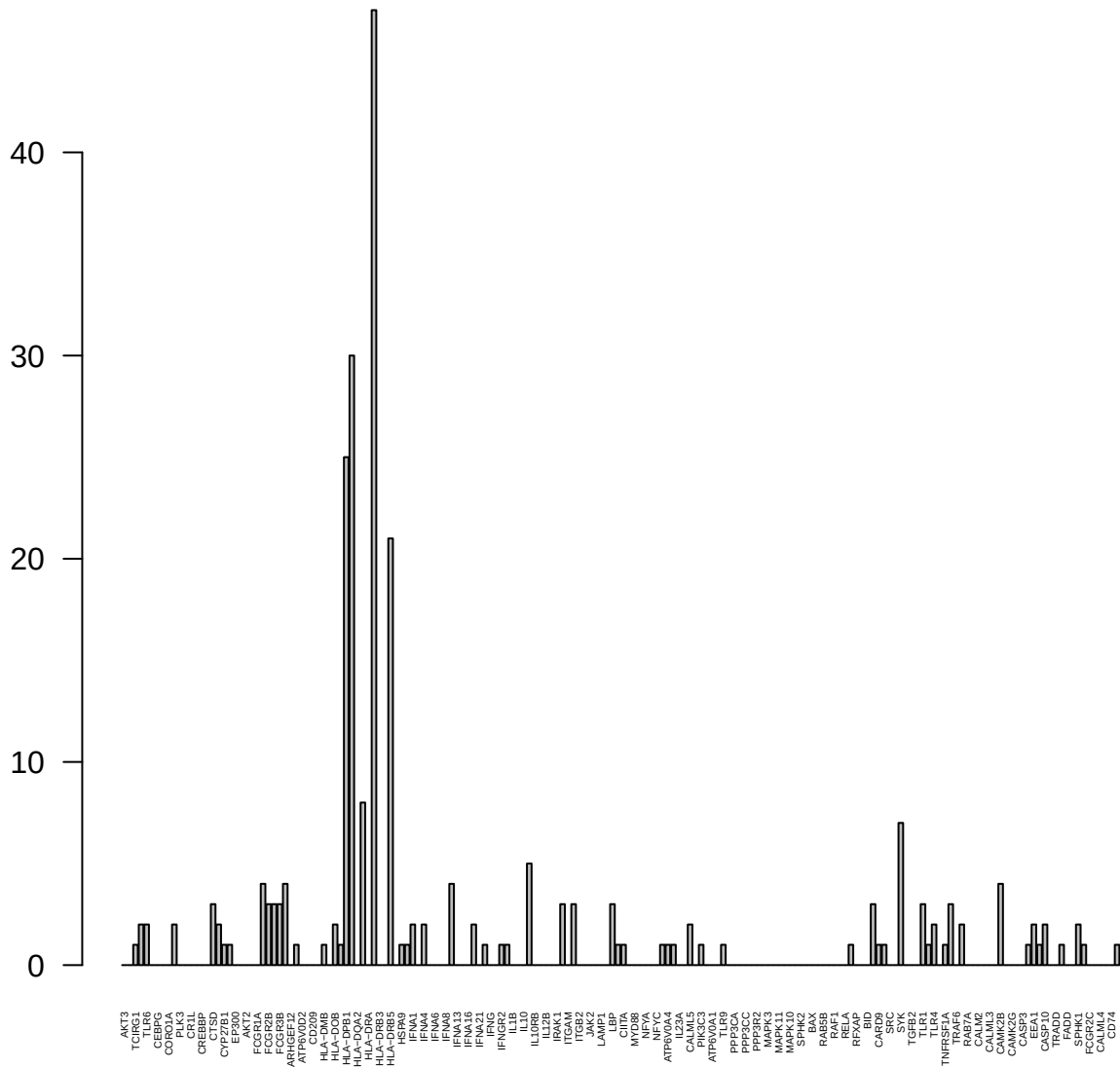
Th17 cell differentiation



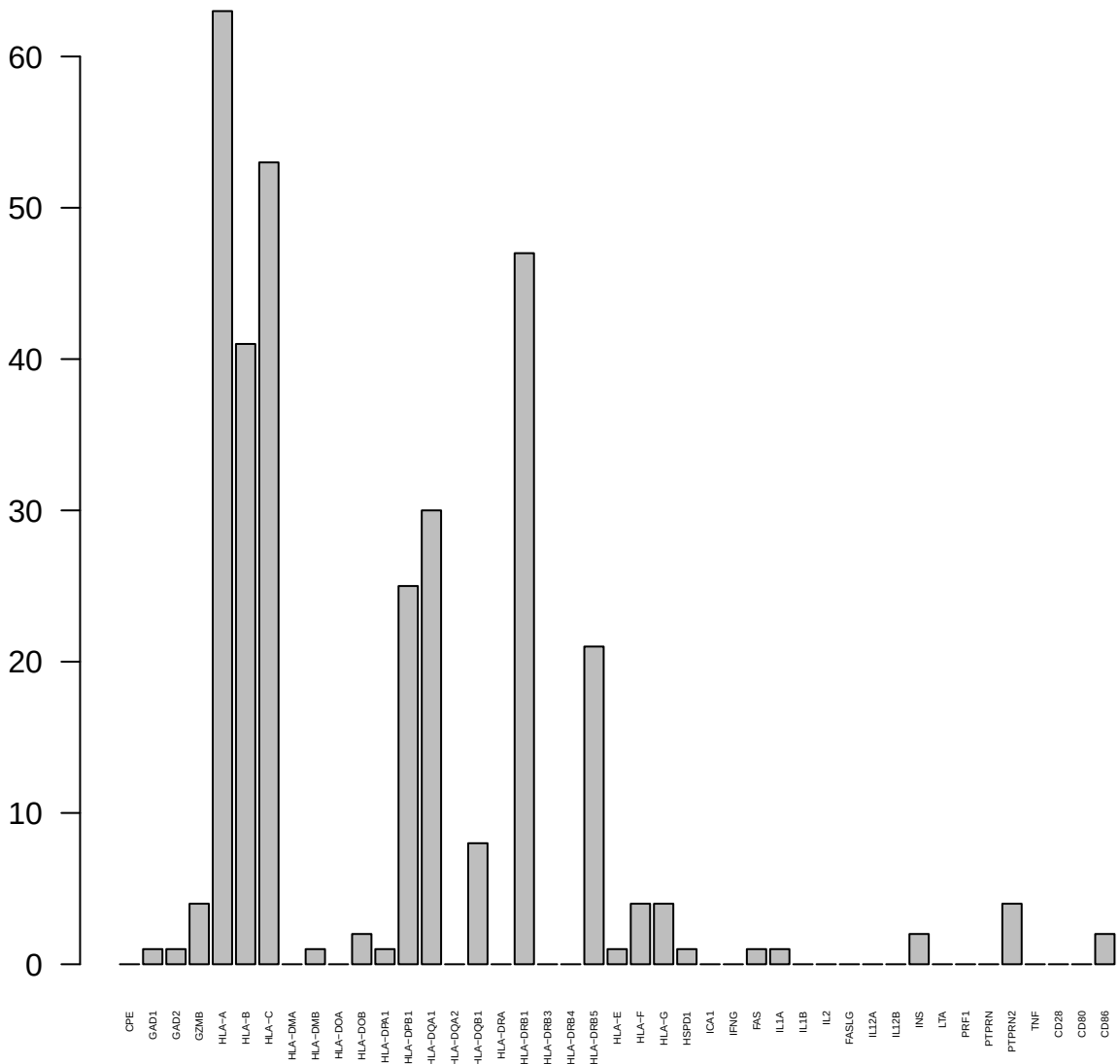
Toxoplasmosis



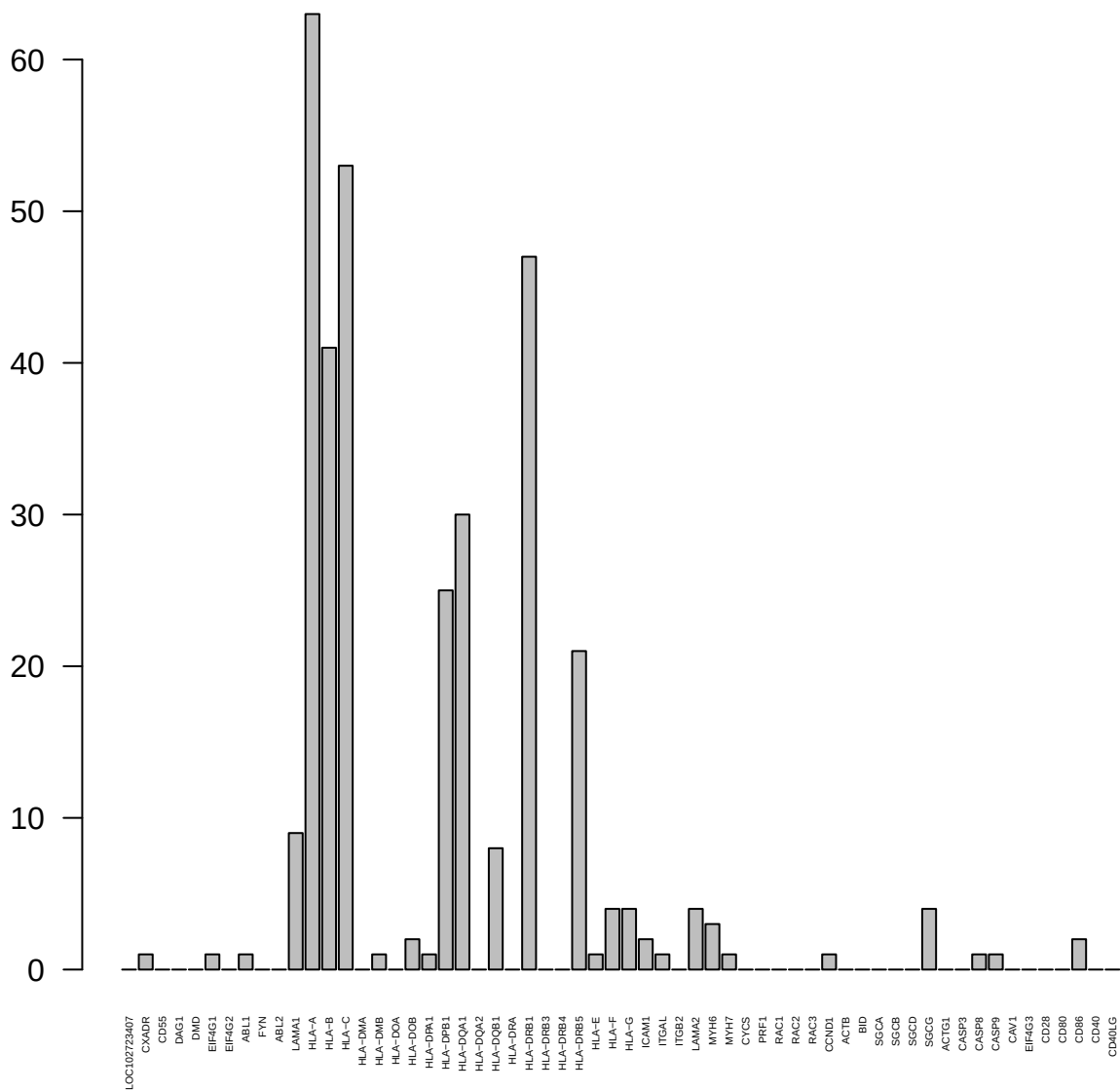
Tuberculosis



Type I diabetes mellitus



Viral myocarditis



Supplementary tables

Supplementary table 1. Analysis of non-synonymous SNPs in biological pathways in the European and American groups.

Pathway name	Pathway ID	<i>p</i> -value	Statistic for population differentiation	Number of SNPs	Number of genes	Bonferroni adjusted <i>p</i> -value	Benjamini-Hochberg test
Caffeine metabolism	hsa00232	0	1.36220554	25	3	0	True
Hematopoietic cell lineage	hsa04640	0	0.180106628	216	48	0	True
Rheumatoid arthritis	hsa05323	4.00E-06	0.205856906	170	30	0.001372	True
Intestinal immune network for IgA production	hsa04672	8.00E-06	0.201808902	147	14	0.002744	True
Tuberculosis	hsa05152	8.00E-06	0.160507233	245	63	0.002744	True
Staphylococcus aureus infection	hsa05150	1.20E-05	0.163118448	251	55	0.004116	True
Systemic lupus erythematosus	hsa05322	1.20E-05	0.201830158	174	27	0.004116	True
Asthma	hsa05310	4.00E-05	0.201617596	144	16	0.01372	True
Type I diabetes mellitus	hsa04940	6.40E-05	0.129627443	318	23	0.021952	True
Leishmaniasis	hsa05140	8.00E-05	0.173907824	167	25	0.02744	True
Th17 cell differentiation	hsa04659	0.000114	0.160673899	183	32	0.03923174	True
Allograft rejection	hsa05330	0.000115	0.129263145	308	17	0.03943073	True
Th1 and Th2 cell differentiation	hsa04658	0.00012	0.163642565	176	31	0.04103244	True
Graft-versus-host disease	hsa05332	0.000124	0.127692181	323	21	0.04240893	True
Autoimmune thyroid disease	hsa05320	0.000129	0.12560372	337	25	0.04419807	True
Inflammatory bowel disease	hsa05321	0.00025	0.161052628	171	23	0.08579204	True
Epstein-Barr virus infection	hsa05169	0.000312	0.107253818	413	75	0.10696288	True
Human T-cell leukemia virus 1 infection	hsa05166	0.000556	0.107253818	390	74	0.19070388	True
Antigen processing and presentation	hsa04612	0.000818	0.108072171	343	36	0.28041203	True
Phagosome	hsa04145	0.001071	0.102113	408	72	0.36725342	True
Cell adhesion molecules	hsa04514	0.001125	0.100046331	416	65	0.38573999	True
Viral myocarditis	hsa05416	0.001238	0.107253818	333	28	0.42477832	True
Herpes simplex virus 1 infection	hsa05168	0.001478	0.085851619	793	248	0.50697647	True
Influenza A	hsa05164	0.001515	0.11908972	250	67	0.51969697	True
Pantothenate and CoA biosynthesis	hsa00770	0.002089	0.591686676	20	11	0.71649398	True
Kaposi sarcoma-associated herpesvirus infection	hsa05167	0.002929	0.10739021	268	66	1.00480431	True
Natural killer cell mediated cytotoxicity	hsa04650	0.002956	0.109026916	272	52	1.01383306	True
Toxoplasmosis	hsa05145	0.002966	0.120146627	223	43	1.01732115	True

Human immunodeficiency virus 1 infection	hsa05170	0.008093	0.09744027	251	59	2.77597928	False
Primary bile acid biosynthesis	hsa00120	0.009058	0.457630534	17	7	3.10688406	False
Cellular senescence	hsa04218	0.011927	0.101342722	234	52	4.09112595	False
Protein export	hsa03060	0.012101	1.451158335	5	4	4.15053243	False
Thermogenesis	hsa04714	0.014069	0.140355894	90	56	4.82554868	False
Transcriptional misregulation in cancer	hsa05202	0.019026	0.142244511	78	50	6.52587519	False
Neutrophil extracellular trap formation	hsa04613	0.020816	0.129880262	99	43	7.13988343	False
Lipid and atherosclerosis	hsa05417	0.024108	0.103841549	175	79	8.26904532	False
Measles	hsa05162	0.028703	0.131757226	89	54	9.84500574	False
Biosynthesis of amino acids	hsa01230	0.030941	0.195662745	41	29	10.6126238	False
Fluid shear stress and atherosclerosis	hsa05418	0.031847	0.12956105	82	56	10.9235669	False
Toll-like receptor signaling pathway	hsa04620	0.03453	0.148815278	59	34	11.8439227	False
One carbon pool by folate	hsa00670	0.035311	0.29542903	21	10	12.1115819	False
JAK-STAT signaling pathway	hsa04630	0.035817	0.119820638	100	56	12.2851003	False
Sphingolipid metabolism	hsa00600	0.03937	0.253264925	25	16	13.503937	False
Human cytomegalovirus infection	hsa05163	0.040783	0.086758808	278	69	13.9885808	False
Ferroptosis	hsa04216	0.041118	0.353613799	15	12	14.1036184	False
Osteoclast differentiation	hsa04380	0.048924	0.09852119	149	46	16.7808219	False
Glycosphingolipid biosynthesis - globo and isoglobo series	hsa00603	0.049213	0.617050761	8	4	16.8799213	False
Antifolate resistance	hsa01523	0.051282	0.280003992	21	13	17.5897436	False
Phenylalanine metabolism	hsa00360	0.054878	0.323409159	14	8	18.8231707	False
B cell receptor signaling pathway	hsa04662	0.059211	0.093145445	116	32	20.3092105	False
C-type lectin receptor signaling pathway	hsa04625	0.059603	0.154359869	44	28	20.4437086	False
mRNA surveillance pathway	hsa03015	0.064286	0.116911764	51	27	22.05	False
Arginine biosynthesis	hsa00220	0.065693	0.325887156	12	9	22.5328467	False
Oocyte meiosis	hsa04114	0.066667	0.125793365	60	35	22.8666667	False
Sphingolipid signaling pathway	hsa04071	0.083333	0.123429819	64	38	28.5833333	False
Non-homologous end-joining	hsa03450	0.086538	0.526045337	8	4	29.6826923	False
cGMP-PKG signaling pathway	hsa04022	0.09	0.099207042	91	54	30.87	False
Thiamine metabolism	hsa00730	0.091837	0.316938915	13	7	31.5	False
Basal transcription factors	hsa03022	0.101124	0.289163158	16	11	34.6853933	False
Phosphatidylinositol signaling system	hsa04070	0.102273	0.117812996	56	38	35.0795455	False
Fc gamma R-mediated phagocytosis	hsa04666	0.103448	0.094647972	78	33	35.4827586	False

Peroxisome	hsa04146	0.105882	0.13056987	64	35	36.3176471	False
Chronic myeloid leukemia	hsa05220	0.105882	0.17202045	23	16	36.3176471	False
Taste transduction	hsa04742	0.108434	0.0887456	85	43	37.1927711	False
Adherens junction	hsa04520	0.109756	0.143933467	41	22	37.6463415	False
Progesterone-mediated oocyte maturation	hsa04914	0.111111	0.131560564	46	30	38.1111111	False
Glutathione metabolism	hsa00480	0.115385	0.129031306	33	18	39.5769231	False
Inositol phosphate metabolism	hsa00562	0.116883	0.120383239	42	29	40.0909091	False
Diabetic cardiomyopathy	hsa05415	0.118421	0.093903268	82	54	40.6184211	False
Adrenergic signaling in cardiomyocytes	hsa04261	0.12	0.111884872	68	38	41.16	False
NF-kappa B signaling pathway	hsa04064	0.121622	0.094615974	68	37	41.7162162	False
Hepatitis B	hsa05161	0.121622	0.092280331	97	51	41.7162162	False
Retrograde endocannabinoid signaling	hsa04723	0.123288	0.112662097	55	34	42.2876712	False
Estrogen signaling pathway	hsa04915	0.123288	0.085574783	116	61	42.2876712	False
Circadian entrainment	hsa04713	0.125	0.092461835	47	26	42.875	False
Platelet activation	hsa04611	0.138462	0.081201425	98	40	47.4923077	False
Protein digestion and absorption	hsa04974	0.142857	0.092958782	106	47	49	False
Vibrio cholerae infection	hsa05110	0.142857	0.158147449	22	13	49	False
DNA replication	hsa03030	0.145161	0.188808478	12	8	49.7903226	False
Glycosphingolipid biosynthesis - lacto and neolacto series	hsa00601	0.147541	0.147375667	24	13	50.6065574	False
Olfactory transduction	hsa04740	0.147541	0.068262272	900	285	50.6065574	False
2-Oxocarboxylic acid metabolism	hsa01210	0.15	0.22094741	8	5	51.45	False
Renin secretion	hsa04924	0.155172	0.108108481	44	23	53.2241379	False
Mismatch repair	hsa03430	0.163636	0.126190478	22	9	56.1272727	False
Bacterial invasion of epithelial cells	hsa05100	0.163636	0.137125893	26	15	56.1272727	False
Coronavirus disease - COVID-19	hsa05171	0.176471	0.075595795	158	75	60.5294118	False
RNA degradation	hsa03018	0.18	0.10121412	47	25	61.74	False
Regulation of lipolysis in adipocytes	hsa04923	0.18	0.106107676	34	21	61.74	False
Steroid biosynthesis	hsa00100	0.1875	0.171766214	14	8	64.3125	False
Renin-angiotensin system	hsa04614	0.1875	0.088478167	25	11	64.3125	False
Riboflavin metabolism	hsa00740	0.191489	0.276113552	8	5	65.6808511	False
Gastric acid secretion	hsa04971	0.209302	0.088175691	44	27	71.7906977	False
Necroptosis	hsa04217	0.214286	0.082493786	90	47	73.5	False
Fc epsilon RI signaling pathway	hsa04664	0.214286	0.096885762	48	19	73.5	False

Insulin secretion	hsa04911	0.214286	0.091166029	53	26	73.5	False
African trypanosomiasis	hsa05143	0.219512	0.140535082	25	12	75.2926829	False
Tyrosine metabolism	hsa00350	0.225	0.104600961	36	17	77.175	False
Pancreatic secretion	hsa04972	0.230769	0.089299321	55	32	79.1538462	False
D-Glutamine and D-glutamate metabolism	hsa00471	0.236842	1.656159854	1	1	81.2368421	False
mTOR signaling pathway	hsa04150	0.236842	0.078367017	66	42	81.2368421	False
Viral carcinogenesis	hsa05203	0.236842	0.071024787	243	60	81.2368421	False
ABC transporters	hsa02010	0.243243	0.072838724	81	28	83.4324324	False
Cytokine-cytokine receptor interaction	hsa04060	0.243243	0.074946997	182	110	83.4324324	False
Salivary secretion	hsa04970	0.243243	0.073626343	53	31	83.4324324	False
beta-Alanine metabolism	hsa00410	0.25	0.09472303	36	18	85.75	False
Arachidonic acid metabolism	hsa00590	0.25	0.090214864	71	24	85.75	False
Prion disease	hsa05020	0.25	0.06949002	135	78	85.75	False
SNARE interactions in vesicular transport	hsa04130	0.257143	0.194894571	8	6	88.2	False
Neurotrophin signaling pathway	hsa04722	0.257143	0.080481909	43	31	88.2	False
Inflammatory mediator regulation of TRP channels	hsa04750	0.264706	0.084543638	88	39	90.7941176	False
Non-alcoholic fatty liver disease	hsa04932	0.264706	0.07762436	55	39	90.7941176	False
Taurine and hypotaurine metabolism	hsa00430	0.272727	0.184201368	9	5	93.5454545	False
Longevity regulating pathway	hsa04211	0.272727	0.096336699	49	34	93.5454545	False
Long-term potentiation	hsa04720	0.272727	0.099063826	30	18	93.5454545	False
Fatty acid biosynthesis	hsa00061	0.28125	0.136071073	17	8	96.46875	False
Phosphonate and phosphinate metabolism	hsa00440	0.28125	0.990814056	1	1	96.46875	False
Relaxin signaling pathway	hsa04926	0.28125	0.084759213	49	34	96.46875	False
Renal cell carcinoma	hsa05211	0.28125	0.152214319	19	14	96.46875	False
Aminoacyl-tRNA biosynthesis	hsa00970	0.290323	0.113776808	21	13	99.5806452	False
Platinum drug resistance	hsa01524	0.290323	0.086862936	55	31	99.5806452	False
Autophagy - other	hsa04136	0.290323	0.144436038	17	10	99.5806452	False
Rap1 signaling pathway	hsa04015	0.3	0.069249109	124	68	102.9	False
Calcium signaling pathway	hsa04020	0.3	0.06206996	152	83	102.9	False
Hepatitis C	hsa05160	0.3	0.080535577	89	52	102.9	False
Acute myeloid leukemia	hsa05221	0.3	0.084893	36	22	102.9	False
Ribosome biogenesis in eukaryotes	hsa03008	0.310345	0.070764137	62	27	106.448276	False
RNA polymerase	hsa03020	0.321429	0.110468012	11	9	110.25	False

Oxytocin signaling pathway	hsa04921	0.321429	0.069038989	110	52	110.25	False
Small cell lung cancer	hsa05222	0.321429	0.079178445	86	41	110.25	False
Fatty acid elongation	hsa00062	0.333333	0.174260322	13	11	114.333333	False
Biosynthesis of unsaturated fatty acids	hsa01040	0.333333	0.100024993	21	12	114.333333	False
Glutamatergic synapse	hsa04724	0.333333	0.07270102	71	36	114.333333	False
Maturity onset diabetes of the young	hsa04950	0.333333	0.12687186	13	8	114.333333	False
Pathogenic Escherichia coli infection	hsa05130	0.333333	0.071022883	98	53	114.333333	False
Spliceosome	hsa03040	0.346154	0.080223489	45	29	118.730769	False
Viral protein interaction with cytokine and cytokine receptor	hsa04061	0.346154	0.077997086	59	33	118.730769	False
GABAergic synapse	hsa04727	0.346154	0.065961364	46	26	118.730769	False
Aldosterone-regulated sodium reabsorption	hsa04960	0.346154	0.155132433	20	13	118.730769	False
Hepatocellular carcinoma	hsa05225	0.346154	0.067430867	69	45	118.730769	False
Pyrimidine metabolism	hsa00240	0.36	0.072460695	36	22	123.48	False
Arginine and proline metabolism	hsa00330	0.36	0.093181032	39	22	123.48	False
Mannose type O-glycan biosynthesis	hsa00515	0.36	0.1494534	13	9	123.48	False
NOD-like receptor signaling pathway	hsa04621	0.36	0.068323712	153	71	123.48	False
Dopaminergic synapse	hsa04728	0.36	0.081411358	45	28	123.48	False
Insulin signaling pathway	hsa04910	0.36	0.073551439	77	42	123.48	False
Gap junction	hsa04540	0.375	0.072177048	51	28	128.625	False
Aldosterone synthesis and secretion	hsa04925	0.375	0.089148914	63	32	128.625	False
Endocrine and other factor-regulated calcium reabsorption	hsa04961	0.375	0.094982035	28	18	128.625	False
Spinocerebellar ataxia	hsa05017	0.375	0.062613746	78	47	128.625	False
Nitrogen metabolism	hsa00910	0.391304	0.121078101	14	6	134.217391	False
MAPK signaling pathway	hsa04010	0.391304	0.063088644	154	84	134.217391	False
Ras signaling pathway	hsa04014	0.391304	0.060944793	124	70	134.217391	False
RIG-I-like receptor signaling pathway	hsa04622	0.391304	0.101593575	39	22	134.217391	False
RNA transport	hsa03013	0.409091	0.074654025	95	44	140.318182	False
TNF signaling pathway	hsa04668	0.409091	0.076851007	55	36	140.318182	False
Chagas disease	hsa05142	0.409091	0.083369383	41	30	140.318182	False
Amoebiasis	hsa05146	0.409091	0.060590151	102	44	140.318182	False
Citrate cycle (TCA cycle)	hsa00020	0.428571	0.05207362	22	9	147	False
TGF-beta signaling pathway	hsa04350	0.428571	0.096207444	32	24	147	False
Cytosolic DNA-sensing pathway	hsa04623	0.428571	0.061326469	34	20	147	False

Circadian rhythm	hsa04710	0.428571	0.096124973	17	9	147	False
Thyroid hormone synthesis	hsa04918	0.428571	0.062987044	63	25	147	False
Type II diabetes mellitus	hsa04930	0.428571	0.070160509	30	19	147	False
AGE-RAGE signaling pathway in diabetic complications	hsa04933	0.428571	0.087752701	49	31	147	False
Nicotine addiction	hsa05033	0.428571	0.10499847	17	9	147	False
Endometrial cancer	hsa05213	0.428571	0.068644738	33	22	147	False
Purine metabolism	hsa00230	0.45	0.053722362	86	55	154.35	False
ErbB signaling pathway	hsa04012	0.45	0.06885383	40	22	154.35	False
Lysosome	hsa04142	0.45	0.0642956	104	59	154.35	False
Complement and coagulation cascades	hsa04610	0.45	0.066041049	115	50	154.35	False
Epithelial cell signaling in Helicobacter pylori infection	hsa05120	0.45	0.068071263	22	12	154.35	False
Melanoma	hsa05218	0.45	0.065508354	28	19	154.35	False
Histidine metabolism	hsa00340	0.473684	0.046465798	24	12	162.473684	False
Phenylalanine, tyrosine and tryptophan biosynthesis	hsa00400	0.473684	0.208660621	5	3	162.473684	False
Folate biosynthesis	hsa00790	0.473684	0.075471236	25	12	162.473684	False
Fatty acid metabolism	hsa01212	0.473684	0.06481648	43	29	162.473684	False
HIF-1 signaling pathway	hsa04066	0.473684	0.064195631	74	42	162.473684	False
Vascular smooth muscle contraction	hsa04270	0.473684	0.07467856	90	41	162.473684	False
Long-term depression	hsa04730	0.473684	0.062987846	38	16	162.473684	False
Carbohydrate digestion and absorption	hsa04973	0.473684	0.065273814	38	20	162.473684	False
Chemical carcinogenesis	hsa05204	0.473684	0.077363775	108	43	162.473684	False
Colorectal cancer	hsa05210	0.473684	0.066553815	43	28	162.473684	False
Glycosaminoglycan degradation	hsa00531	0.5	0.07564926	22	12	171.5	False
Vitamin B6 metabolism	hsa00750	0.5	0.273155399	5	4	171.5	False
VEGF signaling pathway	hsa04370	0.5	0.07299016	42	20	171.5	False
Apelin signaling pathway	hsa04371	0.5	0.056515605	68	44	171.5	False
Leukocyte transendothelial migration	hsa04670	0.5	0.064717177	60	34	171.5	False
Cortisol synthesis and secretion	hsa04927	0.5	0.057920809	39	20	171.5	False
Glioma	hsa05214	0.5	0.075329528	36	20	171.5	False
Prostate cancer	hsa05215	0.5	0.070876915	55	34	171.5	False
PD-L1 expression and PD-1 checkpoint pathway in cancer	hsa05235	0.5	0.051944131	47	26	171.5	False
Other glycan degradation	hsa00511	0.529412	0.05383796	23	8	181.588235	False
Linoleic acid metabolism	hsa00591	0.529412	0.039528236	33	10	181.588235	False

Endocrine resistance	hsa01522	0.529412	0.065496754	48	31	181.588235	False
Ribosome	hsa03010	0.529412	0.044018927	25	20	181.588235	False
Autophagy - animal	hsa04140	0.529412	0.061500931	69	40	181.588235	False
Serotonergic synapse	hsa04726	0.529412	0.068951031	80	35	181.588235	False
Insulin resistance	hsa04931	0.529412	0.056861466	69	41	181.588235	False
Huntington disease	hsa05016	0.529412	0.050824534	166	89	181.588235	False
Human papillomavirus infection	hsa05165	0.529412	0.047903174	447	138	181.588235	False
Pancreatic cancer	hsa05212	0.529412	0.07012509	35	19	181.588235	False
D-Arginine and D-ornithine metabolism	hsa00472	0.5625	0.231743234	1	1	192.9375	False
Other types of O-glycan biosynthesis	hsa00514	0.5625	0.058472865	29	18	192.9375	False
Neomycin, kanamycin and gentamicin biosynthesis	hsa00524	0.5625	0.083536137	8	4	192.9375	False
EGFR tyrosine kinase inhibitor resistance	hsa01521	0.5625	0.052055697	37	23	192.9375	False
AMPK signaling pathway	hsa04152	0.5625	0.069989898	88	50	192.9375	False
Synaptic vesicle cycle	hsa04721	0.5625	0.063865379	26	17	192.9375	False
Adipocytokine signaling pathway	hsa04920	0.5625	0.063191191	44	21	192.9375	False
Cushing syndrome	hsa04934	0.5625	0.039858343	75	44	192.9375	False
Glycolysis / Gluconeogenesis	hsa00010	0.6	0.038079441	60	31	205.8	False
Oxidative phosphorylation	hsa00190	0.6	0.063552056	35	25	205.8	False
Valine, leucine and isoleucine biosynthesis	hsa00290	0.6	0.940785833	1	1	205.8	False
Amino sugar and nucleotide sugar metabolism	hsa00520	0.6	0.039675914	38	19	205.8	False
Glycosaminoglycan biosynthesis - keratan sulfate	hsa00533	0.6	0.125326032	6	5	205.8	False
Fanconi anemia pathway	hsa03460	0.6	0.053678474	80	29	205.8	False
FoxO signaling pathway	hsa04068	0.6	0.061572942	73	41	205.8	False
Neuroactive ligand-receptor interaction	hsa04080	0.6	0.049810333	171	107	205.8	False
Longevity regulating pathway - multiple species	hsa04213	0.6	0.070757296	35	23	205.8	False
Alzheimer disease	hsa05010	0.6	0.055583476	174	105	205.8	False
Morphine addiction	hsa05032	0.6	0.062071597	39	27	205.8	False
Yersinia infection	hsa05135	0.6	0.056779857	64	36	205.8	False
Pathways in cancer	hsa05200	0.6	0.053512697	339	192	205.8	False
Non-small cell lung cancer	hsa05223	0.6	0.061075075	38	24	205.8	False
Fatty acid degradation	hsa00071	0.642857	0.032706325	40	25	220.5	False
p53 signaling pathway	hsa04115	0.642857	0.036740549	35	24	220.5	False
Vasopressin-regulated water reabsorption	hsa04962	0.642857	0.069976594	17	11	220.5	False

Carbon metabolism	hsa01200	0.692308	0.043222986	80	50	237.461538	False
Chemokine signaling pathway	hsa04062	0.692308	0.052089358	79	48	237.461538	False
Phospholipase D signaling pathway	hsa04072	0.692308	0.067295738	111	53	237.461538	False
T cell receptor signaling pathway	hsa04660	0.692308	0.055253904	45	26	237.461538	False
Amphetamine addiction	hsa05031	0.692308	0.058845347	32	17	237.461538	False
Legionellosis	hsa05134	0.692308	0.045974243	23	12	237.461538	False
Bladder cancer	hsa05219	0.692308	0.068435646	26	15	237.461538	False
Gastric cancer	hsa05226	0.692308	0.041339343	65	43	237.461538	False
Galactose metabolism	hsa00052	0.75	0.036648918	39	20	257.25	False
Mucin type O-glycan biosynthesis	hsa00512	0.75	0.0436471	19	12	257.25	False
PPAR signaling pathway	hsa03320	0.75	0.03020285	54	35	257.25	False
cAMP signaling pathway	hsa04024	0.75	0.052382663	137	70	257.25	False
Sulfur relay system	hsa04122	0.75	0.043010168	10	1	257.25	False
Cardiac muscle contraction	hsa04260	0.75	0.062611204	29	18	257.25	False
Hippo signaling pathway - multiple species	hsa04392	0.75	0.033958799	24	11	257.25	False
IL-17 signaling pathway	hsa04657	0.75	0.074030648	33	22	257.25	False
Collecting duct acid secretion	hsa04966	0.75	0.049720138	19	9	257.25	False
Pathways of neurodegeneration - multiple diseases	hsa05022	0.75	0.034327887	259	134	257.25	False
Alcoholism	hsa05034	0.75	0.029618822	36	22	257.25	False
Salmonella infection	hsa05132	0.75	0.037640369	116	68	257.25	False
Central carbon metabolism in cancer	hsa05230	0.75	0.050666988	51	33	257.25	False
Ubiquinone and other terpenoid-quinone biosynthesis	hsa00130	0.818182	0.034274713	9	8	280.636364	False
Starch and sucrose metabolism	hsa00500	0.818182	0.033961882	36	19	280.636364	False
Various types of N-glycan biosynthesis	hsa00513	0.818182	0.024605255	21	13	280.636364	False
Ether lipid metabolism	hsa00565	0.818182	0.03180018	43	16	280.636364	False
Pyruvate metabolism	hsa00620	0.818182	0.022099952	45	22	280.636364	False
Drug metabolism - other enzymes	hsa00983	0.818182	0.024390344	97	40	280.636364	False
Proteasome	hsa03050	0.818182	0.030624871	24	14	280.636364	False
Base excision repair	hsa03410	0.818182	0.03476227	42	13	280.636364	False
Mitophagy - animal	hsa04137	0.818182	0.02170801	25	16	280.636364	False
Tight junction	hsa04530	0.818182	0.039259676	88	46	280.636364	False
Signaling pathways regulating pluripotency of stem cells	hsa04550	0.818182	0.03485189	67	45	280.636364	False
Ovarian steroidogenesis	hsa04913	0.818182	0.038654051	48	21	280.636364	False

Glucagon signaling pathway	hsa04922	0.818182	0.040676055	63	35	280.636364	False
Parathyroid hormone synthesis, secretion and action	hsa04928	0.818182	0.028681114	75	35	280.636364	False
GnRH secretion	hsa04929	0.818182	0.054785796	37	21	280.636364	False
Parkinson disease	hsa05012	0.818182	0.044798392	109	59	280.636364	False
Shigellosis	hsa05131	0.818182	0.057007266	99	57	280.636364	False
Proteoglycans in cancer	hsa05205	0.818182	0.045464898	129	65	280.636364	False
Choline metabolism in cancer	hsa05231	0.818182	0.033940428	75	36	280.636364	False
Pentose phosphate pathway	hsa00030	0.9	0.02196557	23	16	308.7	False
Synthesis and degradation of ketone bodies	hsa00072	0.9	0.009815344	8	6	308.7	False
Cysteine and methionine metabolism	hsa00270	0.9	0.020063647	31	19	308.7	False
Valine, leucine and isoleucine degradation	hsa00280	0.9	0.01742794	41	26	308.7	False
Tryptophan metabolism	hsa00380	0.9	0.012973882	33	20	308.7	False
alpha-Linolenic acid metabolism	hsa00592	0.9	0.032024191	30	10	308.7	False
Glycosphingolipid biosynthesis - ganglio series	hsa00604	0.9	0.059424647	7	5	308.7	False
Propanoate metabolism	hsa00640	0.9	0.035091158	34	19	308.7	False
Nicotinate and nicotinamide metabolism	hsa00760	0.9	0.016457501	27	17	308.7	False
Lipoic acid metabolism	hsa00785	0.9	0.027991234	1	1	308.7	False
Metabolism of xenobiotics by cytochrome P450	hsa00980	0.9	0.043847821	108	40	308.7	False
Drug metabolism - cytochrome P450	hsa00982	0.9	0.035854467	99	36	308.7	False
Nucleotide excision repair	hsa03420	0.9	0.038198487	25	15	308.7	False
Cell cycle	hsa04110	0.9	0.017359387	51	35	308.7	False
Protein processing in endoplasmic reticulum	hsa04141	0.9	0.038304841	99	53	308.7	False
PI3K-Akt signaling pathway	hsa04151	0.9	0.040330304	333	154	308.7	False
Apoptosis	hsa04210	0.9	0.039708959	102	49	308.7	False
Apoptosis - multiple species	hsa04215	0.9	0.035350235	10	8	308.7	False
Notch signaling pathway	hsa04330	0.9	0.010403556	28	18	308.7	False
Cholinergic synapse	hsa04725	0.9	0.02676574	67	36	308.7	False
Regulation of actin cytoskeleton	hsa04810	0.9	0.025670674	128	70	308.7	False
GnRH signaling pathway	hsa04912	0.9	0.030137218	79	31	308.7	False
Thyroid hormone signaling pathway	hsa04919	0.9	0.013152913	59	40	308.7	False
Growth hormone synthesis, secretion and action	hsa04935	0.9	0.022028045	52	28	308.7	False
Fat digestion and absorption	hsa04975	0.9	0.015683639	40	18	308.7	False
Cholesterol metabolism	hsa04979	0.9	0.023112408	70	29	308.7	False

Cocaine addiction	hsa05030	0.9	0.033511441	18	9	308.7	False
Pertussis	hsa05133	0.9	0.014075183	42	24	308.7	False
Malaria	hsa05144	0.9	0.044342766	39	22	308.7	False
Thyroid cancer	hsa05216	0.9	0.013071865	15	12	308.7	False
Primary immunodeficiency	hsa05340	0.9	0.010187918	21	13	308.7	False
Arrhythmogenic right ventricular cardiomyopathy	hsa05412	0.9	0.03711698	73	32	308.7	False
Pentose and glucuronate interconversions	hsa00040	1	0.007360912	54	23	343	False
Fructose and mannose metabolism	hsa00051	1	0.012872808	24	14	343	False
Ascorbate and aldarate metabolism	hsa00053	1	0.002838359	44	21	343	False
Steroid hormone biosynthesis	hsa00140	1	0.005488717	53	26	343	False
Alanine, aspartate and glutamate metabolism	hsa00250	1	0.009474799	33	17	343	False
Glycine, serine and threonine metabolism	hsa00260	1	0.016469191	24	17	343	False
Lysine degradation	hsa00310	1	0.023333807	50	29	343	False
Selenocompound metabolism	hsa00450	1	0.009117427	14	8	343	False
N-Glycan biosynthesis	hsa00510	1	0.023035668	23	18	343	False
Glycosaminoglycan biosynthesis - chondroitin sulfate / dermatan	hsa00532	1	0.00636141	13	7	343	False
Glycosaminoglycan biosynthesis - heparan sulfate / heparin	hsa00534	1	0.002968249	6	5	343	False
Glycerolipid metabolism	hsa00561	1	0.001678582	32	24	343	False
Glycosylphosphatidylinositol (GPI)-anchor biosynthesis	hsa00563	1	0.006063496	28	12	343	False
Glycerophospholipid metabolism	hsa00564	1	0.017282353	65	35	343	False
Glyoxylate and dicarboxylate metabolism	hsa00630	1	0.025331426	16	13	343	False
Butanoate metabolism	hsa00650	1	0.017198726	32	20	343	False
Retinol metabolism	hsa00830	1	0.010567497	87	33	343	False
Porphyrin and chlorophyll metabolism	hsa00860	1	0.006523936	52	25	343	False
Terpenoid backbone biosynthesis	hsa00900	1	0.005393034	14	9	343	False
Sulfur metabolism	hsa00920	1	0.001619477	1	1	343	False
Metabolic pathways	hsa01100	1	0.040530533	1051	590	343	False
Biosynthesis of cofactors	hsa01240	1	0.015820946	111	65	343	False
Homologous recombination	hsa03440	1	0.014624833	36	17	343	False
Ubiquitin mediated proteolysis	hsa04120	1	0.01310138	52	30	343	False
Endocytosis	hsa04144	1	0.029161217	291	85	343	False
Wnt signaling pathway	hsa04310	1	0.029560374	85	49	343	False
Hedgehog signaling pathway	hsa04340	1	0.010253202	46	23	343	False

Axon guidance	hsa04360	1	0.034146483	113	62	343	False
Hippo signaling pathway	hsa04390	1	0.008001676	62	46	343	False
Focal adhesion	hsa04510	1	0.026357067	218	87	343	False
ECM-receptor interaction	hsa04512	1	0.034527911	179	55	343	False
Phototransduction	hsa04744	1	0.00448716	10	7	343	False
Melanogenesis	hsa04916	1	0.028599945	41	27	343	False
Prolactin signaling pathway	hsa04917	1	0.011937957	22	17	343	False
Proximal tubule bicarbonate reclamation	hsa04964	1	0.055868254	15	7	343	False
Bile secretion	hsa04976	1	0.01623169	96	48	343	False
Vitamin digestion and absorption	hsa04977	1	0.0208268	39	10	343	False
Mineral absorption	hsa04978	1	0.025396425	36	20	343	False
Amyotrophic lateral sclerosis	hsa05014	1	0.038782719	210	105	343	False
MicroRNAs in cancer	hsa05206	1	0.015815322	113	63	343	False
Basal cell carcinoma	hsa05217	1	0.010994625	27	22	343	False
Breast cancer	hsa05224	1	0.010869731	78	46	343	False
Hypertrophic cardiomyopathy	hsa05410	1	0.013720733	83	32	343	False
Dilated cardiomyopathy	hsa05414	1	0.009501237	86	34	343	False
Biotin metabolism	hsa00780	1	0	0	0	343	False

Supplementary table 2. Analysis of synonymous SNPs in biological pathways in the European and American groups.

Pathway name	Pathway ID	<i>p</i> -value	Statistic for population differentiation	Number of SNPs	Number of genes	Bonferroni adjusted <i>p</i> -value	Benjamini-Hochberg test
Glycolysis / Gluconeogenesis	hsa00010	0.692308	0.036710893	67	31	235.384615	False
Citrate cycle (TCA cycle)	hsa00020	1	0.0058879	24	10	340	False
Pentose phosphate pathway	hsa00030	0.130435	0.14360179	31	12	44.3478261	False
Pentose and glucuronate interconversions	hsa00040	1	0.007500408	41	22	340	False
Fructose and mannose metabolism	hsa00051	0.9	0.030933938	35	15	306	False
Galactose metabolism	hsa00052	0.346154	0.060039837	50	17	117.692308	False
Ascorbate and aldarate metabolism	hsa00053	1	0.005569898	37	20	340	False
Fatty acid biosynthesis	hsa00061	0.6	0.056461033	28	10	204	False
Fatty acid elongation	hsa00062	0.6	0.066517564	10	9	204	False
Fatty acid degradation	hsa00071	0.9	0.061964116	32	21	306	False
Synthesis and degradation of ketone bodies	hsa00072	1	0.008493684	7	5	340	False
Steroid biosynthesis	hsa00100	0.529412	0.070384005	25	12	180	False
Primary bile acid biosynthesis	hsa00120	0.031486	0.421475692	11	6	10.7052897	False
Ubiquinone and other terpenoid-quinone biosynthesis	hsa00130	0.75	0.057941499	7	5	255	False
Steroid hormone biosynthesis	hsa00140	1	0.02460373	57	31	340	False
Oxidative phosphorylation	hsa00190	0.9	0.015848618	45	23	306	False
Arginine biosynthesis	hsa00220	0.105882	0.22385046	16	10	36	False
Purine metabolism	hsa00230	0.136364	0.082801519	117	64	46.3636364	False
Caffeine metabolism	hsa00232	0.084112	0.190371722	18	5	28.5981308	False
Pyrimidine metabolism	hsa00240	0.214286	0.088787879	41	28	72.8571429	False
Alanine, aspartate and glutamate metabolism	hsa00250	0.75	0.016848655	34	17	255	False
Glycine, serine and threonine metabolism	hsa00260	0.264706	0.080367128	30	18	90	False
Cysteine and methionine metabolism	hsa00270	0.529412	0.041574962	37	22	180	False
Valine, leucine and isoleucine degradation	hsa00280	0.9	0.022035881	32	21	306	False
Valine, leucine and isoleucine biosynthesis	hsa00290	0.126761	3.132213111	1	1	43.0985916	False
Lysine degradation	hsa00310	0.9	0.037009837	59	29	306	False
Arginine and proline metabolism	hsa00330	0.692308	0.04586238	41	23	235.384615	False
Histidine metabolism	hsa00340	0.257143	0.119036272	18	12	87.4285714	False
Tyrosine metabolism	hsa00350	0.391304	0.068428207	25	15	133.043478	False

Phenylalanine metabolism	hsa00360	0.209302	0.194515226	12	7	71.1627907	False
Tryptophan metabolism	hsa00380	1	0.031479877	22	17	340	False
Phenylalanine, tyrosine and tryptophan biosynthesis	hsa00400	0.15	0.191746173	8	4	51	False
beta-Alanine metabolism	hsa00410	0.089109	0.152418522	25	15	30.2970297	False
Taurine and hypotaurine metabolism	hsa00430	0.176471	0.335356594	6	5	60	False
Phosphonate and phosphinate metabolism	hsa00440	0.692308	0.11025989	3	2	235.384615	False
Selenocompound metabolism	hsa00450	0.6	0.060528733	12	5	204	False
D-Glutamine and D-glutamate metabolism	hsa00471	0.195652	1.966602209	1	1	66.5217391	False
D-Arginine and D-ornithine metabolism	hsa00472	0.75	0.231743234	1	1	255	False
Glutathione metabolism	hsa00480	0.12	0.13219059	26	15	40.8	False
Starch and sucrose metabolism	hsa00500	0.36	0.061840753	40	19	122.4	False
N-Glycan biosynthesis	hsa00510	0.818182	0.020715714	43	22	278.181818	False
Other glycan degradation	hsa00511	0.409091	0.144399509	9	7	139.090909	False
Mucin type O-glycan biosynthesis	hsa00512	0.111111	0.128964027	28	17	37.7777778	False
Various types of N-glycan biosynthesis	hsa00513	0.9	0.01364725	32	18	306	False
Other types of O-glycan biosynthesis	hsa00514	0.132353	0.137905793	40	26	45	False
Mannose type O-glycan biosynthesis	hsa00515	0.034388	0.235206229	22	13	11.6918845	False
Amino sugar and nucleotide sugar metabolism	hsa00520	0.692308	0.052757991	33	19	235.384615	False
Neomycin, kanamycin and gentamicin biosynthesis	hsa00524	0.333333	0.09037704	9	4	113.333333	False
Glycosaminoglycan degradation	hsa00531	0.5625	0.122091191	10	6	191.25	False
Glycosaminoglycan biosynthesis chondroitin sulfate / dermatan s	hsa00532	0.5625	0.065637828	20	10	191.25	False
Glycosaminoglycan biosynthesis keratan sulfate	hsa00533	0.9	0.063009295	10	8	306	False
Glycosaminoglycan biosynthesis heparan sulfate / heparin	hsa00534	0.157895	0.139283598	27	14	53.6842105	False
Glycerolipid metabolism	hsa00561	0.9	0.017145977	38	25	306	False
Inositol phosphate metabolism	hsa00562	0.692308	0.042533746	71	37	235.384615	False
Glycosylphosphatidylinositol (GPI)-anchor biosynthesis	hsa00563	0.818182	0.041325131	17	11	278.181818	False
Glycerophospholipid metabolism	hsa00564	0.692308	0.039901134	70	45	235.384615	False
Ether lipid metabolism	hsa00565	0.9	0.017106092	34	19	306	False
Arachidonic acid metabolism	hsa00590	0.084906	0.117138226	59	31	28.8679245	False
Linoleic acid metabolism	hsa00591	0.321429	0.084516534	29	17	109.285714	False
alpha-Linolenic acid metabolism	hsa00592	1	0.054416755	20	11	340	False
Sphingolipid metabolism	hsa00600	0.28125	0.081719255	31	21	95.625	False
Glycosphingolipid biosynthesis lacto and neolacto series	hsa00601	0.079646	0.159881474	26	14	27.079646	False

Glycosphingolipid biosynthesis globo and isoglobo series	hsa00603	0.005425	0.709352446	11	5	1.84461806	False
Glycosphingolipid biosynthesis ganglio series	hsa00604	0.010495	1.840941569	4	3	3.56842989	False
Pyruvate metabolism	hsa00620	0.9	0.036034714	50	23	306	False
Glyoxylate and dicarboxylate metabolism	hsa00630	0.9	0.027776404	27	19	306	False
Propanoate metabolism	hsa00640	0.818182	0.036034714	37	17	278.181818	False
Butanoate metabolism	hsa00650	1	0.009399607	26	15	340	False
One carbon pool by folate	hsa00670	0.082569	0.316594396	13	8	28.0733945	False
Thiamine metabolism	hsa00730	0.75	0.029044422	11	7	255	False
Riboflavin metabolism	hsa00740	0.051724	0.731210404	6	5	17.5862069	False
Vitamin B6 metabolism	hsa00750	0.818182	0.080636715	4	3	278.181818	False
Nicotinate and nicotinamide metabolism	hsa00760	0.152542	0.159109141	26	18	51.8644068	False
Pantothenate and CoA biosynthesis	hsa00770	0.046729	0.435968873	11	8	15.8878505	False
Biotin metabolism	hsa00780	0.391304	0.348442738	3	2	133.043478	False
Lipoic acid metabolism	hsa00785	0.9	0.034571947	6	3	306	False
Folate biosynthesis	hsa00790	0.6	0.037722852	20	10	204	False
Retinol metabolism	hsa00830	0.9	0.02460373	64	37	306	False
Porphyrin and chlorophyll metabolism	hsa00860	1	0.02460373	43	23	340	False
Terpenoid backbone biosynthesis	hsa00900	1	0.007706144	12	8	340	False
Nitrogen metabolism	hsa00910	0.078261	0.318624011	12	9	26.6086957	False
Sulfur metabolism	hsa00920	0.9	0.023708186	5	2	306	False
Aminoacyl-tRNA biosynthesis	hsa00970	0.818182	0.010793577	21	12	278.181818	False
Metabolism of xenobiotics by cytochrome P450	hsa00980	0.321429	0.070611108	72	40	109.285714	False
Drug metabolism cytochrome P450	hsa00982	0.160714	0.08711399	68	38	54.6428571	False
Drug metabolism other enzymes	hsa00983	0.9	0.043101147	76	39	306	False
Biosynthesis of unsaturated fatty acids	hsa01040	1	0.016067408	8	6	340	False
Metabolic pathways	hsa01100	0.818182	0.049284182	1149	631	278.181818	False
Carbon metabolism	hsa01200	0.9	0.038093132	99	48	306	False
2-Oxocarboxylic acid metabolism	hsa01210	0.5625	0.13121737	9	7	191.25	False
Fatty acid metabolism	hsa01212	0.5	0.051225558	42	23	170	False
Biosynthesis of amino acids	hsa01230	0.090909	0.097067198	56	29	30.9090909	False
Biosynthesis of cofactors	hsa01240	0.9	0.021868196	101	61	306	False
EGFR tyrosine kinase inhibitor resistance	hsa01521	0.9	0.0270725	63	35	306	False
Endocrine resistance	hsa01522	0.9	0.024131255	88	39	306	False

Antifolate resistance	hsa01523	0.272727	0.091494938	25	10	92.7272727	False
Platinum drug resistance	hsa01524	0.176471	0.096216776	39	21	60	False
ABC transporters	hsa02010	0.409091	0.059543325	82	28	139.090909	False
Ribosome biogenesis in eukaryotes	hsa03008	0.45	0.05944553	68	31	153	False
Ribosome	hsa03010	1	0.011562091	34	25	340	False
RNA transport	hsa03013	0.75	0.039544494	103	55	255	False
mRNA surveillance pathway	hsa03015	0.5	0.058191134	60	37	170	False
RNA degradation	hsa03018	0.28125	0.076376077	53	27	95.625	False
RNA polymerase	hsa03020	1	0.022003728	31	12	340	False
Basal transcription factors	hsa03022	0.310345	0.107546348	23	13	105.517241	False
DNA replication	hsa03030	0.115385	0.126293281	23	14	39.2307692	False
Spliceosome	hsa03040	1	0.019738416	81	48	340	False
Proteasome	hsa03050	0.5	0.07165822	27	17	170	False
Protein export	hsa03060	1	0.033539905	10	6	340	False
PPAR signaling pathway	hsa03320	0.818182	0.035941237	68	37	278.181818	False
Base excision repair	hsa03410	0.157895	0.140751475	30	11	53.6842105	False
Nucleotide excision repair	hsa03420	0.214286	0.100912193	29	20	72.8571429	False
Mismatch repair	hsa03430	0.5	0.073254185	17	12	170	False
Homologous recombination	hsa03440	1	0.023126146	35	19	340	False
Non-homologous end-joining	hsa03450	0.140625	0.303940595	7	6	47.8125	False
Fanconi anemia pathway	hsa03460	0.123288	0.089201955	65	29	41.9178082	False
MAPK signaling pathway	hsa04010	0.6	0.049941155	216	119	204	False
ErbB signaling pathway	hsa04012	0.75	0.026227324	61	33	255	False
Ras signaling pathway	hsa04014	1	0.037316791	178	92	340	False
Rap1 signaling pathway	hsa04015	0.409091	0.065757333	224	106	139.090909	False
Calcium signaling pathway	hsa04020	0.391304	0.061463221	248	113	133.043478	False
cGMP-PKG signaling pathway	hsa04022	0.214286	0.073626343	181	76	72.8571429	False
cAMP signaling pathway	hsa04024	0.002649	0.109525934	224	109	0.90070997	False
Cytokine-cytokine receptor interaction	hsa04060	0.1875	0.069832972	146	100	63.75	False
Viral protein interaction with cytokine and cytokine receptor	hsa04061	0.642857	0.041643663	39	28	218.571429	False
Chemokine signaling pathway	hsa04062	0.9	0.037565844	128	65	306	False
NF-kappa B signaling pathway	hsa04064	0.104651	0.097539418	67	39	35.5813954	False
HIF-1 signaling pathway	hsa04066	0.642857	0.041087189	115	48	218.571429	False

FoxO signaling pathway	hsa04068	0.692308	0.050136826	84	45	235.384615	False
Phosphatidylinositol signaling system	hsa04070	0.9	0.040099884	99	51	306	False
Sphingolipid signaling pathway	hsa04071	0.473684	0.049375432	74	47	161.052632	False
Phospholipase D signaling pathway	hsa04072	1	0.0270725	172	76	340	False
Neuroactive ligand-receptor interaction	hsa04080	0.692308	0.041513984	278	152	235.384615	False
Cell cycle	hsa04110	0.692308	0.043080464	59	37	235.384615	False
Oocyte meiosis	hsa04114	0.391304	0.063613106	75	40	133.043478	False
p53 signaling pathway	hsa04115	1	0.005537886	37	20	340	False
Ubiquitin mediated proteolysis	hsa04120	1	0.014308227	92	48	340	False
Sulfur relay system	hsa04122	0.642857	0.234559939	3	1	218.571429	False
SNARE interactions in vesicular transport	hsa04130	0.173077	0.179247438	12	9	58.8461539	False
Autophagy other	hsa04136	0.75	0.047791238	22	10	255	False
Mitophagy animal	hsa04137	0.9	0.027481342	40	26	306	False
Autophagy animal	hsa04140	1	0.006920465	79	45	340	False
Protein processing in endoplasmic reticulum	hsa04141	0.391304	0.065632605	113	64	133.043478	False
Lysosome	hsa04142	0.321429	0.072320856	77	51	109.285714	False
Endocytosis	hsa04144	0.272727	0.060221901	253	106	92.7272727	False
Phagosome	hsa04145	0.089109	0.074634506	292	70	30.2970297	False
Peroxisome	hsa04146	0.230769	0.090760141	57	38	78.4615385	False
mTOR signaling pathway	hsa04150	0.818182	0.02929627	117	60	278.181818	False
PI3K-Akt signaling pathway	hsa04151	1	0.031875767	430	155	340	False
AMPK signaling pathway	hsa04152	1	0.01834821	120	53	340	False
Apoptosis	hsa04210	0.057692	0.116854938	106	56	19.6153846	False
Longevity regulating pathway	hsa04211	1	0.011530927	88	39	340	False
Longevity regulating pathway multiple species	hsa04213	0.473684	0.062392728	67	30	161.052632	False
Apoptosis multiple species	hsa04215	0.134328	0.197988286	15	8	45.6716418	False
Ferroptosis	hsa04216	0.310345	0.080985715	30	19	105.517241	False
Necroptosis	hsa04217	0.529412	0.055919826	85	53	180	False
Cellular senescence	hsa04218	1	0.027519506	169	58	340	False
Cardiac muscle contraction	hsa04260	0.428571	0.047949263	67	31	145.714286	False
Adrenergic signaling in cardiomyocytes	hsa04261	0.310345	0.058805113	139	65	105.517241	False
Vascular smooth muscle contraction	hsa04270	0.45	0.056644043	121	58	153	False
Wnt signaling pathway	hsa04310	0.818182	0.035025151	109	55	278.181818	False

Notch signaling pathway	hsa04330	1	0.012139013	62	28	340	False
Hedgehog signaling pathway	hsa04340	1	0.016837258	71	25	340	False
TGF-beta signaling pathway	hsa04350	0.257143	0.096251243	38	22	87.4285714	False
Axon guidance	hsa04360	0.346154	0.054600882	196	82	117.692308	False
VEGF signaling pathway	hsa04370	1	0.015020302	36	23	340	False
Apelin signaling pathway	hsa04371	0.75	0.051135599	143	55	255	False
Osteoclast differentiation	hsa04380	0.692308	0.052375798	110	53	235.384615	False
Hippo signaling pathway	hsa04390	0.5625	0.053379204	99	54	191.25	False
Hippo signaling pathway multiple species	hsa04392	0.5625	0.045321806	36	12	191.25	False
Focal adhesion	hsa04510	0.9	0.039754715	321	103	306	False
ECM-receptor interaction	hsa04512	1	0.036311228	244	58	340	False
Cell adhesion molecules	hsa04514	0.333333	0.067102132	301	72	113.333333	False
Adherens junction	hsa04520	0.310345	0.084748357	70	28	105.517241	False
Tight junction	hsa04530	0.9	0.016697585	117	55	306	False
Gap junction	hsa04540	0.333333	0.080050009	108	43	113.333333	False
Signaling pathways regulating pluripotency of stem cells	hsa04550	0.219512	0.072172134	91	49	74.6341463	False
Complement and coagulation cascades	hsa04610	0.473684	0.05736134	115	47	161.052632	False
Platelet activation	hsa04611	1	0.031277015	148	57	340	False
Antigen processing and presentation	hsa04612	0.272727	0.063052277	198	37	92.7272727	False
Neutrophil extracellular trap formation	hsa04613	0.9	0.032022701	100	43	306	False
Renin-angiotensin system	hsa04614	0.346154	0.059640232	25	14	117.692308	False
Toll-like receptor signaling pathway	hsa04620	0.054217	0.126430411	59	41	18.4337349	False
NOD-like receptor signaling pathway	hsa04621	0.391304	0.056221458	132	62	133.043478	False
RIG-I-like receptor signaling pathway	hsa04622	0.75	0.040676211	21	16	255	False
Cytosolic DNA-sensing pathway	hsa04623	0.692308	0.039978253	39	27	235.384615	False
C-type lectin receptor signaling pathway	hsa04625	0.6	0.048561892	69	38	204	False
JAK-STAT signaling pathway	hsa04630	0.098901	0.09251591	85	48	33.6263736	False
Hematopoietic cell lineage	hsa04640	0.050916	0.088584296	141	45	17.311609	False
Natural killer cell mediated cytotoxicity	hsa04650	0.375	0.057536097	168	53	127.5	False
IL-17 signaling pathway	hsa04657	0.05	0.13837357	46	31	17	False
Th1 and Th2 cell differentiation	hsa04658	0.007022	0.123837043	131	42	2.38764045	False
Th17 cell differentiation	hsa04659	0.002806	0.135462275	134	46	0.95409137	False
T cell receptor signaling pathway	hsa04660	0.6	0.043123962	59	38	204	False

B cell receptor signaling pathway	hsa04662	0.45	0.052624538	92	40	153	False
Fc epsilon RI signaling pathway	hsa04664	1	0.03285177	43	23	340	False
Fc gamma R-mediated phagocytosis	hsa04666	0.45	0.057175892	76	42	153	False
TNF signaling pathway	hsa04668	0.818182	0.055947482	67	46	278.181818	False
Leukocyte transendothelial migration	hsa04670	1	0.023601256	74	40	340	False
Intestinal immune network for IgA production	hsa04672	0.015684	0.136530447	86	17	5.33249686	False
Circadian rhythm	hsa04710	0.45	0.093309847	21	11	153	False
Circadian entrainment	hsa04713	0.036873	0.113340672	120	44	12.5368732	False
Thermogenesis	hsa04714	1	0.0270725	130	63	340	False
Long-term potentiation	hsa04720	0.243243	0.077169452	57	28	82.7027027	False
Synaptic vesicle cycle	hsa04721	0.346154	0.07219459	49	28	117.692308	False
Neurotrophin signaling pathway	hsa04722	0.9	0.029009912	60	38	306	False
Retrograde endocannabinoid signaling	hsa04723	0.195652	0.077024601	107	54	66.5217391	False
Glutamatergic synapse	hsa04724	0.230769	0.065760247	130	53	78.4615385	False
Cholinergic synapse	hsa04725	0.9	0.037396719	121	52	306	False
Serotonergic synapse	hsa04726	0.07563	0.095319532	96	48	25.7142857	False
GABAergic synapse	hsa04727	0.529412	0.056445144	84	42	180	False
Dopaminergic synapse	hsa04728	0.080357	0.112455389	80	46	27.3214286	False
Long-term depression	hsa04730	0.5	0.053426362	77	30	170	False
Olfactory transduction	hsa04740	0.040917	0.073862325	414	215	13.9116203	False
Taste transduction	hsa04742	0.5	0.053055956	89	46	170	False
Phototransduction	hsa04744	0.264706	0.160828629	11	9	90	False
Inflammatory mediator regulation of TRP channels	hsa04750	0.333333	0.071997547	118	54	113.333333	False
Regulation of actin cytoskeleton	hsa04810	1	0.029921577	191	99	340	False
Insulin signaling pathway	hsa04910	0.9	0.0270725	127	56	306	False
Insulin secretion	hsa04911	0.473684	0.061989131	92	40	161.052632	False
GnRH signaling pathway	hsa04912	0.5	0.055338785	112	44	170	False
Ovarian steroidogenesis	hsa04913	0.333333	0.066727733	68	30	113.333333	False
Progesterone-mediated oocyte maturation	hsa04914	0.3	0.067055191	66	33	102	False
Estrogen signaling pathway	hsa04915	0.5	0.059645275	152	75	170	False
Melanogenesis	hsa04916	0.321429	0.072203658	67	36	109.285714	False
Prolactin signaling pathway	hsa04917	0.818182	0.024054539	44	29	278.181818	False
Thyroid hormone synthesis	hsa04918	0.219512	0.074899249	85	33	74.6341463	False

Thyroid hormone signaling pathway	hsa04919	1	0.020282124	134	56	340	False
Adipocytokine signaling pathway	hsa04920	0.473684	0.034307566	66	30	161.052632	False
Oxytocin signaling pathway	hsa04921	0.6	0.04751891	179	74	204	False
Glucagon signaling pathway	hsa04922	0.9	0.037523129	92	39	306	False
Regulation of lipolysis in adipocytes	hsa04923	0.048733	0.136487718	55	26	16.5692008	False
Renin secretion	hsa04924	0.059603	0.114509853	70	32	20.2649007	False
Aldosterone synthesis and secretion	hsa04925	0.36	0.066031536	120	51	122.4	False
Relaxin signaling pathway	hsa04926	0.310345	0.064630096	99	50	105.517241	False
Cortisol synthesis and secretion	hsa04927	0.121622	0.090909845	73	29	41.3513514	False
Parathyroid hormone synthesis, secretion and action	hsa04928	0.321429	0.069359367	111	47	109.285714	False
GnRH secretion	hsa04929	0.085714	0.110288936	79	32	29.1428571	False
Type II diabetes mellitus	hsa04930	1	0.0270725	52	23	340	False
Insulin resistance	hsa04931	0.75	0.040557137	104	44	255	False
Non-alcoholic fatty liver disease	hsa04932	1	0.01432104	70	43	340	False
AGE-RAGE signaling pathway in diabetic complications	hsa04933	0.45	0.056626198	74	35	153	False
Cushing syndrome	hsa04934	0.086538	0.081598551	132	61	29.4230769	False
Growth hormone synthesis, secretion and action	hsa04935	0.75	0.044012451	97	47	255	False
Type I diabetes mellitus	hsa04940	0.000762	0.133566243	173	25	0.2590121	False
Maturity onset diabetes of the young	hsa04950	1	0.022525078	20	11	340	False
Aldosterone-regulated sodium reabsorption	hsa04960	0.692308	0.049296797	38	18	235.384615	False
Endocrine and other factor-regulated calcium reabsorption	hsa04961	0.529412	0.048667709	68	30	180	False
Vasopressin-regulated water reabsorption	hsa04962	0.020542	0.22485458	32	15	6.98438784	False
Proximal tubule bicarbonate reclamation	hsa04964	0.6	0.048604801	21	9	204	False
Collecting duct acid secretion	hsa04966	0.264706	0.093615222	25	10	90	False
Salivary secretion	hsa04970	0.28125	0.073534293	92	43	95.625	False
Gastric acid secretion	hsa04971	0.019157	0.138017095	80	39	6.51340996	False
Pancreatic secretion	hsa04972	0.054545	0.092025256	125	55	18.5454546	False
Carbohydrate digestion and absorption	hsa04973	0.333333	0.060392579	52	25	113.333333	False
Protein digestion and absorption	hsa04974	0.023607	0.103788342	160	59	8.02644004	False
Fat digestion and absorption	hsa04975	1	0.01697683	37	19	340	False
Bile secretion	hsa04976	0.75	0.041475478	110	52	255	False
Vitamin digestion and absorption	hsa04977	1	0.017855386	29	10	340	False
Mineral absorption	hsa04978	0.191489	0.109058105	54	25	65.106383	False

Cholesterol metabolism	hsa04979	0.642857	0.052576914	63	21	218.571429	False
Alzheimer disease	hsa05010	0.428571	0.052957954	248	120	145.714286	False
Parkinson disease	hsa05012	0.375	0.061442384	131	65	127.5	False
Amyotrophic lateral sclerosis	hsa05014	1	0.037202433	275	120	340	False
Huntington disease	hsa05016	0.642857	0.045456339	214	94	218.571429	False
Spinocerebellar ataxia	hsa05017	0.18	0.06348219	158	68	61.2	False
Prion disease	hsa05020	0.125	0.07374782	192	80	42.5	False
Pathways of neurodegeneration multiple diseases	hsa05022	1	0.036816458	381	163	340	False
Cocaine addiction	hsa05030	0.078947	0.133377993	37	18	26.8421053	False
Amphetamine addiction	hsa05031	0.214286	0.086534171	59	32	72.8571429	False
Morphine addiction	hsa05032	0.142857	0.075604797	83	46	48.5714286	False
Nicotine addiction	hsa05033	0.243243	0.095118629	50	21	82.7027027	False
Alcoholism	hsa05034	0.209302	0.106936214	63	36	71.1627907	False
Bacterial invasion of epithelial cells	hsa05100	0.818182	0.037459336	55	30	278.181818	False
Vibrio cholerae infection	hsa05110	0.529412	0.04640218	35	16	180	False
Epithelial cell signaling in Helicobacter pylori infection	hsa05120	0.5	0.069070624	35	19	170	False
Pathogenic Escherichia coli infection	hsa05130	1	0.030833132	147	73	340	False
Shigellosis	hsa05131	0.321429	0.056099446	173	85	109.285714	False
Salmonella infection	hsa05132	0.024085	0.096812904	183	94	8.18882466	False
Pertussis	hsa05133	0.818182	0.043722059	65	33	278.181818	False
Legionellosis	hsa05134	0.310345	0.082302054	43	24	105.517241	False
Yersinia infection	hsa05135	0.75	0.041096912	102	54	255	False
Leishmaniasis	hsa05140	0.013305	0.119495704	118	28	4.52368281	False
Chagas disease	hsa05142	0.064286	0.114171431	70	43	21.8571429	False
African trypanosomiasis	hsa05143	0.692308	0.06328131	28	13	235.384615	False
Malaria	hsa05144	0.642857	0.054907727	44	20	218.571429	False
Toxoplasmosis	hsa05145	0.75	0.050652583	215	53	255	False
Amoebiasis	hsa05146	0.5	0.049668069	147	48	170	False
Staphylococcus aureus infection	hsa05150	0.006356	0.117222607	163	53	2.1612001	False
Tuberculosis	hsa05152	0.002041	0.119495704	178	67	0.69399086	False
Hepatitis C	hsa05160	0.818182	0.033498501	84	55	278.181818	False
Hepatitis B	hsa05161	0.9	0.039142771	104	60	306	False
Measles	hsa05162	0.004096	0.187286106	72	51	1.39275766	False

Human cytomegalovirus infection	hsa05163	0.3	0.062961042	231	83	102	False
Influenza A	hsa05164	0.642857	0.039847739	180	66	218.571429	False
Human papillomavirus infection	hsa05165	1	0.039426249	465	147	340	False
Human T-cell leukemia virus 1 infection	hsa05166	0.032175	0.081924219	278	87	10.9395109	False
Kaposi sarcoma-associated herpesvirus infection	hsa05167	0.692308	0.043595886	203	65	235.384615	False
Herpes simplex virus 1 infection	hsa05168	0.529412	0.05212677	569	235	180	False
Epstein-Barr virus infection	hsa05169	0.039872	0.082130336	245	77	13.5566188	False
Human immunodeficiency virus 1 infection	hsa05170	0.157895	0.076106347	186	71	53.6842105	False
Coronavirus disease COVID-19	hsa05171	0.5	0.04203102	164	84	170	False
Pathways in cancer	hsa05200	1	0.040112102	444	205	340	False
Transcriptional misregulation in cancer	hsa05202	1	0.018835146	94	56	340	False
Viral carcinogenesis	hsa05203	0.818182	0.044913582	171	62	278.181818	False
Chemical carcinogenesis	hsa05204	0.05	0.109354989	81	44	17	False
Proteoglycans in cancer	hsa05205	0.818182	0.034760333	195	75	278.181818	False
MicroRNAs in cancer	hsa05206	1	0.020282124	144	62	340	False
Colorectal cancer	hsa05210	1	0.055260519	57	30	340	False
Renal cell carcinoma	hsa05211	0.75	0.045082793	29	21	255	False
Pancreatic cancer	hsa05212	0.9	0.030948836	42	22	306	False
Endometrial cancer	hsa05213	0.529412	0.05945795	38	20	180	False
Glioma	hsa05214	0.818182	0.028462357	56	31	278.181818	False
Prostate cancer	hsa05215	0.9	0.019496926	72	38	306	False
Thyroid cancer	hsa05216	1	0.008984974	23	14	340	False
Basal cell carcinoma	hsa05217	0.6	0.060436117	42	22	204	False
Melanoma	hsa05218	0.6	0.041543881	39	23	204	False
Bladder cancer	hsa05219	0.5	0.053422434	28	13	170	False
Chronic myeloid leukemia	hsa05220	0.818182	0.017391006	31	23	278.181818	False
Acute myeloid leukemia	hsa05221	1	0.00633826	31	20	340	False
Small cell lung cancer	hsa05222	1	0.038636911	133	41	340	False
Non-small cell lung cancer	hsa05223	0.75	0.036372013	51	25	255	False
Breast cancer	hsa05224	1	0.023249354	113	53	340	False
Hepatocellular carcinoma	hsa05225	0.5625	0.05032074	102	50	191.25	False
Gastric cancer	hsa05226	1	0.0270725	86	45	340	False
Central carbon metabolism in cancer	hsa05230	0.818182	0.032009008	83	38	278.181818	False

Choline metabolism in cancer	hsa05231	1	0.010257894	101	55	340	False
PD-L1 expression and PD-1 checkpoint pathway in cancer	hsa05235	0.36	0.063319958	66	37	122.4	False
Asthma	hsa05310	0.01506	0.145041161	78	11	5.12048193	False
Autoimmune thyroid disease	hsa05320	0.011241	0.105835346	177	26	3.82194245	False
Inflammatory bowel disease	hsa05321	0.005704	0.145557088	105	28	1.93931097	False
Systemic lupus erythematosus	hsa05322	0.016611	0.114420246	120	27	5.64784053	False
Rheumatoid arthritis	hsa05323	0.001082	0.151876436	121	36	0.36796537	False
Allograft rejection	hsa05330	0.004371	0.120644911	162	19	1.48627382	False
Graft-versus-host disease	hsa05332	0.007723	0.108217067	171	22	2.62588817	False
Primary immunodeficiency	hsa05340	0.818182	0.035677905	31	18	278.181818	False
Hypertrophic cardiomyopathy	hsa05410	1	0.028513873	134	47	340	False
Arrhythmogenic right ventricular cardiomyopathy	hsa05412	1	0.020282124	112	43	340	False
Dilated cardiomyopathy	hsa05414	0.692308	0.040271151	146	52	235.384615	False
Diabetic cardiomyopathy	hsa05415	0.642857	0.033259605	122	61	218.571429	False
Viral myocarditis	hsa05416	0.058824	0.082491662	209	32	20	False
Lipid and atherosclerosis	hsa05417	0.391304	0.067231287	164	90	133.043478	False
Fluid shear stress and atherosclerosis	hsa05418	0.095745	0.094910733	95	55	32.5531915	False

Note. Number of SNPs and Number of genes represent the numbers of non-synonymous (Supplementary table 1) and synonymous (Supplementary table 2) SNPs and the number of genes where these SNPs were found.