

Supplemental Table 1: GSA results for all analyzed pathways.

KEGG pathway ID	KEGG pathway name	N genes	N SNPs	Gene-set association p-value			
				GM _{0.1}	PC-GM _{0.1}	GM ₁	PC-GM ₁
	Synthesis and degradation of						
72	ketone bodies	9	128	0.051	0.003	0.086	0.0009
3320	PPAR signaling pathway	69	1377	0.042	0.004	0.1	0.034
4260	Cardiac muscle contraction	80	2667	0.186	0.011	0.174	0.025
4520	Adherens junction	77	4063	0.154	0.012	0.132	0.014
3410	Base excision repair	35	487	0.06	0.015	0.015	0.007
5414	Dilated cardiomyopathy	92	5405	0.71	0.019	0.764	0.199
910	Nitrogen metabolism	23	359	0.016	0.02	0.031	0.011
	Hypertrophic cardiomyopathy						
5410	(HCM)	89	5006	0.591	0.02	0.641	0.265
511	Other glycan degradation	16	193	0.077	0.023	0.225	0.091
4320	Dorso-ventral axis formation	25	987	0.016	0.025	0.022	0.055
650	Butanoate metabolism	34	560	0.438	0.035	0.659	0.167
	Neuroactive ligand-receptor						
4080	interaction	302	8682	0.008	0.073	0.008	0.022
4740	Olfactory transduction	389	3513	0.344	0.073	0.332	0.188
3060	Protein export	9	114	0.288	0.081	0.214	0.264
4340	Hedgehog signaling pathway	56	1302	0.261	0.085	0.23	0.05
3420	Nucleotide excision repair	44	727	0.101	0.088	0.107	0.055
100	Steroid biosynthesis	17	253	0.023	0.09	0.02	0.034
3440	Homologous recombination	28	653	0.203	0.092	0.194	0.117
4514	Cell adhesion molecules (CAMs)	134	6142	0.068	0.096	0.097	0.054
620	Pyruvate metabolism	40	833	0.402	0.102	0.545	0.199
5110	Vibrio cholerae infection	56	1428	0.75	0.103	0.794	0.2
680	Methane metabolism	6	139	0.334	0.108	0.695	0.134
4110	Cell cycle	128	2154	0.01	0.11	0.035	0.072
310	Lysine degradation	44	835	0.231	0.116	0.227	0.345
4810	Regulation of actin cytoskeleton	216	6849	0.265	0.129	0.058	0.021
920	Sulfur metabolism	13	621	0.775	0.129	0.805	0.142
	Glycosphingolipid biosynthesis -						
601	lacto and neolacto series	26	527	0.017	0.133	0.006	0.04
	SNARE interactions in vesicular						
4130	transport	38	762	0.379	0.134	0.446	0.244
	Amino sugar and nucleotide sugar						
520	metabolism	44	942	0.045	0.137	0.089	0.446
240	Pyrimidine metabolism	98	2047	0.253	0.141	0.21	0.028
5020	Prion diseases	35	939	0.182	0.148	0.457	0.127
	Glycosphingolipid biosynthesis -						
603	globo series	14	334	0.037	0.159	0.03	0.112
3430	Mismatch repair	23	459	0.107	0.16	0.281	0.284
4530	Tight junction	134	6157	0.512	0.165	0.398	0.308
3010	Ribosome	88	546	0.347	0.178	0.47	0.22
5220	Chronic myeloid leukemia	75	1949	0.312	0.179	0.171	0.073
5212	Pancreatic cancer	72	1857	0.534	0.203	0.288	0.105
4660	T cell receptor signaling pathway	108	2989	0.291	0.208	0.181	0.146
4020	Calcium signaling pathway	178	8062	0.254	0.211	0.118	0.138

4512	ECM-receptor interaction	84	3716	0.656	0.213	0.677	0.285
514	O-Mannosyl glycan biosynthesis Epithelial cell signaling in	3	62	0.221	0.214	0.108	0.15
5120	Helicobacter pylori infection	68	1538	0.524	0.216	0.463	0.207
533	Keratan sulfate biosynthesis	16	377	0.169	0.217	0.137	0.137
3018	RNA degradation	59	907	0.474	0.228	0.517	0.366
4940	Type I diabetes mellitus	44	1175	0.068	0.229	0.094	0.347
3020	RNA polymerase	29	390	0.274	0.232	0.208	0.116
360	Phenylalanine metabolism	22	337	0.004	0.235	0.069	0.34
140	Steroid hormone biosynthesis Progesterone-mediated oocyte	55	1925	0.878	0.239	0.73	0.614
4914	maturation Fatty acid elongation in	86	2679	0.493	0.244	0.39	0.133
62	mitochondria Alanine aspartate and glutamate	8	122	0.301	0.25	0.321	0.387
250	metabolism	31	629	0.5	0.256	0.873	0.605
330	Arginine and proline metabolism	54	709	0.356	0.257	0.244	0.384
565	Ether lipid metabolism	36	709	0.373	0.262	0.213	0.135
790	Folate biosynthesis	11	154	0.608	0.268	0.42	0.282
564	Glycerophospholipid metabolism	69	1645	0.406	0.27	0.53	0.245
561	Glycerolipid metabolism	45	1387	0.385	0.273	0.54	0.485
3050	Proteasome	48	592	0.178	0.278	0.134	0.318
4350	TGF-beta signaling pathway Complement and coagulation	87	1754	0.576	0.291	0.683	0.373
4610	ascades Cysteine and methionine	69	1390	0.704	0.291	0.721	0.55
270	metabolism Fc gamma R-mediated	34	595	0.536	0.295	0.193	0.143
4666	phagocytosis	97	3294	0.061	0.32	0.054	0.108
4930	Type II diabetes mellitus	47	1935	0.294	0.321	0.463	0.517
4144	Endocytosis	187	5235	0.26	0.327	0.041	0.109
590	Arachidonic acid metabolism	58	1153	0.33	0.329	0.168	0.444
532	Chondroitin sulfate biosynthesis	22	1208	0.863	0.341	0.86	0.258
640	Propanoate metabolism Biosynthesis of unsaturated fatty	33	902	0.819	0.341	0.767	0.441
1040	acids	22	476	0.643	0.352	0.65	0.24
4620	Toll-like receptor signaling pathway Valine leucine and isoleucine	101	1524	0.275	0.353	0.312	0.263
280	degradation Porphyrin and chlorophyll	44	994	0.504	0.362	0.391	0.313
860	metabolism	41	1476	0.57	0.363	0.681	0.605
4210	Apoptosis	88	1820	0.033	0.372	0.056	0.243
300	Lysine biosynthesis	4	75	0.443	0.372	0.291	0.308
380	Tryptophan metabolism Metabolism of xenobiotics by	40	837	0.024	0.378	0.091	0.487
980	cytochrome P450	70	2005	0.876	0.384	0.753	0.687
5210	Colorectal cancer	85	2645	0.594	0.389	0.325	0.421
5322	Systemic lupus erythematosus Cytokine-cytokine receptor	140	1860	0.158	0.394	0.164	0.226
4060	interaction	278	4254	0.166	0.395	0.093	0.346
3022	Basal transcription factors	38	583	0.694	0.395	0.836	0.916

5014 Amyotrophic lateral sclerosis (ALS)	53	1671	0.109	0.398	0.039	0.142
Leukocyte transendothelial						
4670 migration	118	3811	0.452	0.405	0.398	0.075
Vascular smooth muscle						
4270 contraction	125	5555	0.965	0.405	0.895	0.513
562 Inositol phosphate metabolism	54	2147	0.99	0.405	0.968	0.795
5213 Endometrial cancer	52	2505	0.476	0.41	0.395	0.348
Phosphatidylinositol signaling						
4070 system	76	3675	0.987	0.415	0.985	0.868
52 Galactose metabolism	26	603	0.058	0.421	0.07	0.465
534 Heparan sulfate biosynthesis	26	1103	0.818	0.424	0.636	0.269
770 Pantothenate and CoA biosynthesis	15	816	0.401	0.426	0.491	0.24
10 Glycolysis / Gluconeogenesis	62	1030	0.622	0.446	0.334	0.378
51 Fructose and mannose metabolism	34	866	0.103	0.46	0.063	0.367
340 Histidine metabolism	29	541	0.012	0.461	0.077	0.425
2010 ABC transporters	44	2362	0.504	0.472	0.506	0.612
Maturity onset diabetes of the						
4950 young	25	359	0.959	0.473	0.927	0.858
5219 Bladder cancer	42	894	0.809	0.49	0.386	0.319
5416 Viral myocarditis	73	2768	0.725	0.49	0.773	0.783
Arrhythmogenic right ventricular						
5412 cardiomyopathy (ARVC)	76	6053	0.776	0.492	0.777	0.796
5221 Acute myeloid leukemia	60	1509	0.225	0.493	0.178	0.39
5340 Primary immunodeficiency	35	502	0.096	0.507	0.087	0.444
4662 B cell receptor signaling pathway	75	2192	0.293	0.509	0.174	0.286
3040 Spliceosome	128	1396	0.842	0.514	0.782	0.556
4330 Notch signaling pathway	47	1160	0.743	0.514	0.856	0.623
970 Aminoacyl-tRNA biosynthesis	41	944	0.519	0.515	0.696	0.473
4360 Axon guidance	129	6537	0.544	0.517	0.382	0.261
785 Lipoic acid metabolism	3	24	0.641	0.52	0.73	0.489
450 Selenoamino acid metabolism	26	393	0.863	0.528	0.888	0.852
4720 Long-term potentiation	70	4033	0.166	0.533	0.08	0.315
4142 Lysosome	117	1973	0.608	0.534	0.584	0.336
RIG-I-like receptor signaling						
4622 pathway	71	842	0.935	0.535	0.845	0.458
5217 Basal cell carcinoma	55	1104	0.679	0.541	0.621	0.515
900 Terpenoid backbone biosynthesis	15	223	0.603	0.549	0.506	0.57
Natural killer cell mediated						
4650 cytotoxicity	141	2804	0.345	0.561	0.232	0.308
4114 Oocyte meiosis	114	3244	0.555	0.564	0.332	0.238
NOD-like receptor signaling						
4621 pathway	62	907	0.986	0.568	0.942	0.804
5222 Small cell lung cancer	84	3549	0.56	0.571	0.393	0.553
4920 Adipocytokine signaling pathway	67	1642	0.244	0.579	0.145	0.401
230 Purine metabolism	157	5506	0.427	0.59	0.387	0.235
Nicotinate and nicotinamide						
760 metabolism	24	528	0.387	0.594	0.427	0.448
4012 ErbB signaling pathway	87	3884	0.265	0.596	0.048	0.367

Glycosphingolipid biosynthesis -						
604 ganglio series	20	725	0.759	0.597	0.753	0.789
4510 Focal adhesion	201	7682	0.66	0.598	0.469	0.565
4115 p53 signaling pathway	69	1129	0.072	0.605	0.232	0.385
5330 Allograft rejection	38	665	0.279	0.609	0.21	0.528
5332 Graft-versus-host disease	42	643	0.305	0.61	0.259	0.605
5016 Huntington's disease	185	3669	0.396	0.613	0.617	0.69
4010 MAPK signaling pathway	273	8509	0.302	0.616	0.029	0.188
4120 Ubiquitin mediated proteolysis	138	3396	0.821	0.621	0.553	0.383
5310 Asthma	30	500	0.205	0.621	0.131	0.48
4640 Hematopoietic cell lineage	88	1588	0.684	0.621	0.44	0.545
5012 Parkinson's disease	133	1804	0.767	0.648	0.562	0.732
Valine leucine and isoleucine						
290 biosynthesis	11	269	0.419	0.654	0.438	0.536
903 Limonene and pinene degradation	14	157	0.596	0.659	0.439	0.64
4623 Cytosolic DNA-sensing pathway	56	533	0.759	0.662	0.634	0.413
3030 DNA replication	36	567	0.363	0.665	0.448	0.634
Glyoxylate and dicarboxylate						
630 metabolism	16	398	0.261	0.666	0.355	0.564
Aldosterone-regulated sodium						
4960 reabsorption	42	1147	0.711	0.673	0.687	0.567
5216 Thyroid cancer	29	841	0.895	0.679	0.833	0.535
592 alpha-Linolenic acid metabolism	19	284	0.686	0.682	0.264	0.463
Antigen processing and						
4612 presentation	89	1010	0.187	0.688	0.063	0.478
30 Pentose phosphate pathway	27	447	0.667	0.692	0.683	0.739
5218 Melanoma	71	2219	0.308	0.696	0.137	0.452
3450 Non-homologous end-joining	14	262	0.857	0.699	0.907	0.664
4630 Jak-STAT signaling pathway	155	2570	0.144	0.704	0.059	0.243
5215 Prostate cancer	89	2496	0.659	0.712	0.387	0.533
480 Glutathione metabolism	50	569	0.798	0.712	0.713	0.601
Pentose and glucuronate						
40 interconversions	28	1337	0.82	0.715	0.777	0.688
Drug metabolism - cytochrome						
982 P450	72	2239	0.712	0.716	0.739	0.802
4310 Wnt signaling pathway	151	4179	0.776	0.732	0.46	0.305
53 Ascorbate and aldarate metabolism						
4912 GnRH signaling pathway	101	3859	0.868	0.745	0.611	0.585
740 Riboflavin metabolism	16	342	0.17	0.745	0.358	0.866
4150 mTOR signaling pathway	52	1409	0.331	0.758	0.227	0.655
500 Starch and sucrose metabolism	52	1940	0.697	0.758	0.579	0.718
780 Biotin metabolism	2	99	0.839	0.766	0.786	0.767
190 Oxidative phosphorylation	135	1358	0.555	0.774	0.327	0.479
4140 Regulation of autophagy	35	368	0.451	0.774	0.673	0.713
1100 Metabolic pathways	1104	24490	0.836	0.774	0.781	0.796
4664 Fc epsilon RI signaling pathway	79	2494	0.495	0.775	0.348	0.528
410 beta-Alanine metabolism	22	919	0.852	0.777	0.896	0.908
5200 Pathways in cancer	330	10613	0.853	0.781	0.596	0.745
20 Citrate cycle (TCA cycle)	32	550	0.215	0.782	0.063	0.408
Glycosylphosphatidylinositol(GPI)-						
563 anchor biosynthesis	25	403	0.391	0.782	0.49	0.804

5320 Autoimmune thyroid disease	53	975	0.522	0.785	0.399	0.701
5214 Glioma	65	2015	0.282	0.789	0.132	0.57
5010 Alzheimer's disease	169	4346	0.534	0.789	0.442	0.765
4370 VEGF signaling pathway	76	1800	0.552	0.799	0.214	0.373
4730 Long-term depression	70	3992	0.791	0.802	0.666	0.517
D-Arginine and D-ornithine						
472 metabolism	1	14	0.8	0.803	0.767	0.803
600 Sphingolipid metabolism	40	718	0.896	0.808	0.77	0.552
5211 Renal cell carcinoma	70	1810	0.346	0.811	0.135	0.646
Intestinal immune network for IgA						
4672 production	48	824	0.371	0.814	0.317	0.788
510 N-Glycan biosynthesis	46	1135	0.997	0.815	1	0.951
Pathogenic Escherichia coli						
5130 infection	59	1020	0.562	0.824	0.631	0.555
5223 Non-small cell lung cancer	54	2469	0.555	0.827	0.277	0.731
61 Fatty acid biosynthesis	6	212	0.992	0.841	0.995	0.968
4614 Renin-angiotensin system	17	309	0.849	0.843	0.772	0.736
71 Fatty acid metabolism	42	721	0.89	0.85	0.769	0.99
591 Linoleic acid metabolism	29	494	0.77	0.862	0.408	0.746
983 Drug metabolism - other enzymes	51	2245	0.959	0.87	0.938	0.888
4742 Taste transduction	52	1518	0.512	0.879	0.772	0.945
4146 Peroxisome	78	1266	0.429	0.896	0.618	0.755
Glycine serine and threonine						
260 metabolism	31	497	0.887	0.896	0.941	0.98
350 Tyrosine metabolism	46	910	0.267	0.913	0.534	0.97
830 Retinol metabolism	64	1893	0.963	0.914	0.83	0.946
120 Primary bile acid biosynthesis	16	438	0.953	0.917	0.821	0.945
531 Glycosaminoglycan degradation	21	595	0.232	0.925	0.312	0.935
4540 Gap junction	90	4042	0.928	0.933	0.839	0.796
4710 Circadian rhythm - mammal	13	273	0.896	0.94	0.835	0.941
750 Vitamin B6 metabolism	6	156	0.802	0.945	0.795	0.901
4062 Chemokine signaling pathway	190	5233	0.627	0.946	0.292	0.667
4722 Neurotrophin signaling pathway	126	3668	0.534	0.947	0.145	0.632
670 One carbon pool by folate	17	521	0.836	0.956	0.677	0.914
D-Glutamine and D-glutamate						
471 metabolism	4	43	0.979	0.957	0.925	0.923
460 Cyanoamino acid metabolism	7	79	0.872	0.957	0.829	0.953
730 Thiamine metabolism	8	284	0.639	0.958	0.846	0.961
4910 Insulin signaling pathway	137	3427	0.601	0.959	0.434	0.872
Ubiquinone and other terpenoid-						
130 quinone biosynthesis	7	75	0.986	0.96	0.977	0.979
4916 Melanogenesis	102	2979	0.954	0.97	0.861	0.86
232 Caffeine metabolism	7	175	0.937	0.974	0.948	0.962
Taurine and hypotaurine						
430 metabolism	10	123	0.971	0.975	0.95	0.97
512 O-Glycan biosynthesis	30	1450	0.852	0.987	0.926	0.973
Phenylalanine tyrosine and						
400 tryptophan biosynthesis	5	100	0.994	0.991	0.956	0.985