

Table S5 Functional enrichment of genes with large-effect mutation variants.

Mutation Type	Category	Term	Count	P-value
SNP	KEGG_PATHWAY	hsa00590:Arachidonic acid metabolism	18	2.47E-07
	KEGG_PATHWAY	hsa04512:ECM-receptor interaction	14	7.58E-03
	KEGG_PATHWAY	hsa04510:Focal adhesion	25	1.13E-02
	KEGG_PATHWAY	hsa00591:Linoleic acid metabolism	7	1.41E-02
	GOTERM_MF_2	GO:0043167~ion binding	359	1.08E-05
	GOTERM_CC_2	GO:0044425~membrane part	512	3.67E-05
	GOTERM_MF_2	GO:0046906~tetrapyrrole binding	23	8.38E-05
	GOTERM_CC_2	GO:0031012~extracellular matrix	43	1.85E-04
	GOTERM_CC_2	GO:0009986~cell surface	43	2.24E-04
	GOTERM_CC_2	GO:0016020~membrane	552	2.34E-04
	GOTERM_MF_2	GO:0019825~oxygen binding	11	6.19E-04
	GOTERM_BP_2	GO:0007155~cell adhesion	73	6.38E-04
	GOTERM_BP_2	GO:0045058~T cell selection	7	1.45E-03
	GOTERM_BP_2	GO:0009605~response to external stimulus	86	4.35E-03
	GOTERM_CC_2	GO:0044420~extracellular matrix part	17	5.89E-03
	GOTERM_CC_2	GO:0000267~cell fraction	96	6.38E-03
	GOTERM_BP_2	GO:0016044~membrane organization	40	1.12E-02
	GOTERM_MF_2	GO:0001871~pattern binding	20	1.13E-02
	GOTERM_BP_2	GO:0006949~syncytium formation	5	1.37E-02
	GOTERM_MF_2	GO:0030246~carbohydrate binding	37	1.54E-02
GOTERM_MF_2	GO:0005201~extracellular matrix structural constituent	13	1.63E-02	
GOTERM_MF_2	GO:0043176~amine binding	15	2.12E-02	
Indel	KEGG_PATHWAY	hsa05200:Pathways in cancer	64	4.18E-04
	KEGG_PATHWAY	hsa00562:Inositol phosphate metabolism	16	2.39E-03
	KEGG_PATHWAY	hsa04020:Calcium signaling pathway	37	2.39E-03

KEGG_PATHWAY	hsa04070:Phosphatidylinositol signaling system	19	4.56E-03
KEGG_PATHWAY	hsa05220:Chronic myeloid leukemia	18	1.20E-02
KEGG_PATHWAY	hsa04510:Focal adhesion	38	1.26E-02
KEGG_PATHWAY	hsa04810:Regulation of actin cytoskeleton	40	1.34E-02
KEGG_PATHWAY	hsa05222:Small cell lung cancer	19	1.75E-02
KEGG_PATHWAY	hsa05414:Dilated cardiomyopathy	20	2.17E-02
GOTERM_MF_2	GO:0005515~protein binding	1224	4.35E-14
GOTERM_MF_2	GO:0060589~nucleoside-triphosphatase regulator activity	107	2.90E-12
GOTERM_MF_2	GO:0008047~enzyme activator activity	80	9.90E-08
GOTERM_MF_2	GO:0001882~nucleoside binding	279	3.21E-07
GOTERM_BP_2	GO:0051234~establishment of localization	412	2.38E-05
GOTERM_MF_2	GO:0043167~ion binding	634	2.98E-05
GOTERM_BP_2	GO:0048856~anatomical structure development	392	4.16E-05
GOTERM_BP_2	GO:0006810~transport	405	5.38E-05
GOTERM_BP_2	GO:0007275~multicellular organismal development	436	8.66E-05
GOTERM_BP_2	GO:0006996~organelle organization	218	1.66E-04
GOTERM_BP_2	GO:0009653~anatomical structure morphogenesis	198	1.98E-04
GOTERM_MF_2	GO:0000166~nucleotide binding	349	2.13E-04
GOTERM_MF_2	GO:0003712~transcription cofactor activity	72	3.15E-04
GOTERM_BP_2	GO:0048518~positive regulation of biological process	313	5.27E-04
GOTERM_MF_2	GO:0016564~transcription repressor activity	63	6.91E-04
GOTERM_BP_2	GO:0055085~transmembrane transport	101	9.20E-04
GOTERM_BP_2	GO:0048869~cellular developmental process	264	1.16E-03
GOTERM_BP_2	GO:0065009~regulation of molecular function	159	1.27E-03
GOTERM_BP_2	GO:0048646~anatomical structure formation involved in morphogenesis	67	1.30E-03
GOTERM_BP_2	GO:0048522~positive regulation of cellular process	283	1.42E-03
GOTERM_CC_2	GO:0043234~protein complex	392	1.86E-03

	GOTERM_MF_2	GO:0016740~transferase activity	268	3.37E-03
	GOTERM_BP_2	GO:0050793~regulation of developmental process	113	3.39E-03
	GOTERM_CC_2	GO:0042995~cell projection	118	4.01E-03
	GOTERM_BP_2	GO:0007155~cell adhesion	116	4.37E-03
	GOTERM_MF_2	GO:0022857~transmembrane transporter activity	146	5.48E-03
	GOTERM_BP_2	GO:0007049~cell cycle	126	5.92E-03
	GOTERM_MF_2	GO:0022892~substrate-specific transporter activity	154	6.54E-03
	GOTERM_BP_2	GO:0048519~negative regulation of biological process	271	6.60E-03
	GOTERM_BP_2	GO:0051128~regulation of cellular component organization	79	7.21E-03
	GOTERM_CC_2	GO:0016020~membrane	1018	7.34E-03
	GOTERM_CC_2	GO:0000267~cell fraction	172	7.92E-03
	GOTERM_BP_2	GO:0016044~membrane organization	67	8.76E-03
	GOTERM_CC_2	GO:0044420~extracellular matrix part	26	1.02E-02
	GOTERM_BP_2	GO:0009790~embryonic development	94	1.07E-02
	GOTERM_CC_2	GO:0043233~organelle lumen	275	1.08E-02
	GOTERM_BP_2	GO:0007017~microtubule-based process	47	1.13E-02
	GOTERM_MF_2	GO:0016563~transcription activator activity	71	1.17E-02
	GOTERM_BP_2	GO:0048523~negative regulation of cellular process	247	1.23E-02
	GOTERM_BP_2	GO:0070271~protein complex biogenesis	84	1.39E-02
	GOTERM_BP_2	GO:0050794~regulation of cellular process	933	1.43E-02
	GOTERM_BP_2	GO:0009893~positive regulation of metabolic process	143	1.57E-02
	GOTERM_BP_2	GO:0050789~regulation of biological process	969	1.68E-02
	GOTERM_CC_2	GO:0009986~cell surface	61	1.96E-02
	GOTERM_BP_2	GO:0051301~cell division	52	2.01E-02
	GOTERM_BP_2	GO:0009892~negative regulation of metabolic process	122	2.05E-02
	GOTERM_BP_2	GO:0009056~catabolic process	188	2.20E-02
Insertion	KEGG_PATHWAY	hsa00240:Pyrimidine metabolism	9	1.19E-02
	KEGG_PATHWAY	hsa02010:ABC transporters	6	1.35E-02

	KEGG_PATHWAY	hsa04144:Endocytosis	13	1.65E-02
	GOTERM_BP_2	GO:0006996~organelle organization	77	3.17E-06
	GOTERM_CC_2	GO:0043228~non-membrane-bounded organelle	123	1.57E-04
	GOTERM_BP_2	GO:0030029~actin filament-based process	21	2.03E-04
	GOTERM_MF_2	GO:0001882~nucleoside binding	81	3.56E-04
	GOTERM_CC_2	GO:0005622~intracellular	415	4.16E-04
	GOTERM_MF_2	GO:0060589~nucleoside-triphosphatase regulator activity	29	4.50E-04
	GOTERM_BP_2	GO:0007017~microtubule-based process	20	9.95E-04
	GOTERM_CC_2	GO:0044424~intracellular part	400	1.21E-03
	GOTERM_MF_2	GO:0016874~ligase activity	26	1.94E-03
	GOTERM_MF_2	GO:0016787~hydrolase activity	103	2.08E-03
	GOTERM_MF_2	GO:0000166~nucleotide binding	101	2.56E-03
	GOTERM_CC_2	GO:0045178~basal part of cell	6	3.38E-03
	GOTERM_CC_2	GO:0044446~intracellular organelle part	175	3.81E-03
	GOTERM_CC_2	GO:0044422~organelle part	175	4.97E-03
	GOTERM_BP_2	GO:0022402~cell cycle process	32	5.48E-03
	GOTERM_CC_2	GO:0043234~protein complex	113	5.79E-03
	GOTERM_MF_2	GO:0005515~protein binding	307	6.54E-03
	GOTERM_CC_2	GO:0000267~cell fraction	53	1.02E-02
	GOTERM_CC_2	GO:0043233~organelle lumen	80	1.90E-02
	GOTERM_BP_2	GO:0043170~macromolecule metabolic process	216	1.99E-02
	GOTERM_BP_2	GO:0007049~cell cycle	38	2.16E-02
	GOTERM_BP_2	GO:0051128~regulation of cellular component organization	25	2.27E-02
	GOTERM_CC_2	GO:0043229~intracellular organelle	334	2.36E-02
Deletion	KEGG_PATHWAY	hsa04144:Endocytosis	19	5.25E-03
	KEGG_PATHWAY	hsa00970:Aminoacyl-tRNA biosynthesis	7	1.62E-02
	GOTERM_MF_2	GO:0060589~nucleoside-triphosphatase regulator activity	46	1.03E-06
	GOTERM_MF_2	GO:0001882~nucleoside binding	122	4.75E-06

	GOTERM_BP_2	GO:0006996~organelle organization	101	2.94E-05
	GOTERM_CC_2	GO:0043228~non-membrane-bounded organelle	175	3.09E-05
	GOTERM_CC_2	GO:0042995~cell projection	59	1.29E-04
	GOTERM_MF_2	GO:0000166~nucleotide binding	151	1.50E-04
	GOTERM_CC_2	GO:0005622~intracellular	599	2.99E-04
	GOTERM_MF_2	GO:0005515~protein binding	458	5.11E-04
	GOTERM_BP_2	GO:0030029~actin filament-based process	26	5.12E-04
	GOTERM_CC_2	GO:0044422~organelle part	255	9.24E-04
	GOTERM_CC_2	GO:0000267~cell fraction	79	9.39E-04
	GOTERM_BP_2	GO:0007017~microtubule-based process	26	1.04E-03
	GOTERM_CC_2	GO:0044446~intracellular organelle part	252	1.43E-03
	GOTERM_BP_2	GO:0022402~cell cycle process	46	1.59E-03
	GOTERM_BP_2	GO:0030030~cell projection organization	33	1.94E-03
	GOTERM_CC_2	GO:0044424~intracellular part	573	3.04E-03
	GOTERM_MF_2	GO:0008047~enzyme activator activity	29	6.52E-03
	GOTERM_CC_2	GO:0043234~protein complex	158	7.05E-03
	GOTERM_MF_2	GO:0016874~ligase activity	32	8.84E-03
	GOTERM_MF_2	GO:0016740~transferase activity	111	9.33E-03
	GOTERM_MF_2	GO:0016787~hydrolase activity	140	1.00E-02
	GOTERM_CC_2	GO:0044463~cell projection part	21	1.55E-02
	GOTERM_BP_2	GO:0051128~regulation of cellular component organization	35	1.56E-02
	GOTERM_CC_2	GO:0045178~basal part of cell	6	1.63E-02
	GOTERM_CC_2	GO:0043233~organelle lumen	112	1.97E-02
	GOTERM_BP_2	GO:0051641~cellular localization	62	2.03E-02
CNV	GOTERM_CC_2	GO:0044456~synapse part	9	1.53E-03
	GOTERM_CC_2	GO:0008021~synaptic vesicle	4	2.96E-02
	GOTERM_CC_2	GO:0045211~postsynaptic membrane	5	3.19E-02