Table S1. Count of all observed SNVs in the COSMIC database.

		TO			
		A	**C**	**G**	**T**
FROM	**A**	0	94,513	2,006,240	1,121,852
	C	1,965,512	0	990,818	3,788,310
	G	3,788,966	989,193	0	2,017,502
	T	1,124,289	2,007,011	951,101	0

Table S2. Counts of SNVs in G4 regions from the COSMIC database.

		TO			
		A	**C**	**G**	**T**
FROM	**A**	0	601	7,191	768
	C	2,529	0	2,937	8,094
	G	21,349	4,450	0	10,791
	T	742	1,608	8,861	0

Table S3. Changes in putative G4 from the COSMIC database across both strands before and after mutation. (0: absence of pG4; +: presence of pG4 in forward strand; -: presence of pG4 in reverse strand)

G4 with reference allele	G4 with alternate allele	SNV locations	%	G4hunter score (reference)	Sd (reference)	G4hunter score (alternate)	Sd (alternate)
-	-	13,793	36.77	-1.222	0.387	-1.219	0.4
-	0	3,581	9.55	-1.026	0.351	-0.901	0.345
-	+	6	0.02	0.175	0.37	0.279	0.36
0	-	1,354	3.61	-1.082	0.356	-1.196	0.359
0	+	1,374	3.66	1.085	0.368	1.201	0.371
+	0	3,655	9.74	0.993	0.359	0.871	0.355
+	+	13,753	36.66	1.222	0.376	1.219	0.391

Table S4. Count and proportion of variants in experimentally validated G4 regions for different functional regions. Note that annotation regions may overlap, resulting in a single SNV assigned to multiple annotations.

	COSMIC		CLINVAR	
Annotation	**Count**	**Frequency**	**Count**	**Frequency**
CDS	7,495	32.49	1,031	61.41
5' UTR	1,254	5,44	198	11.79
3' UTR	2,197	9.52	210	12.51
EXON	12,498	34.16	1,552	65.26
INTRON	17,264	47.19	804	33.81
PROMOTER	1,288	3,52	20	0.84
ENHANCER	155	0.42	--	--
CpG ISLAND	164	0.45	--	--
GENCODE lncRNA	1,492	6.47	--	--
INTERGENIC	5,441	23.586	--	--

Table S5. Significant GO:BP enrichments for all COSMIC and CLINVAR G4 mutations.

GO ID	GO Description	Universe	COSMIC and CLINVAR	Adjusted P-value
GO:0007399	nervous system development	1648	1087	3.01E-48
GO:0048856	anatomical structure development	4152	2427	6.54E-48
GO:0032502	developmental process	4584	2644	1.02E-46
GO:0048731	system development	2976	1790	1.56E-42
GO:0007275	multicellular organism development	3266	1938	2.46E-41
GO:0009653	anatomical structure morphogenesis	1871	1181	1.16E-38
GO:0048699	generation of neurons	969	670	1.07E-37
GO:0000902	cell morphogenesis	718	520	4.07E-37
GO:0030154	cell differentiation	2860	1706	5.88E-37
GO:0048869	cellular developmental process	2879	1715	1.04E-36
GO:0022008	neurogenesis	1096	736	6.89E-35
GO:0030182	neuron differentiation	923	636	7.71E-35
GO:0048468	cell development	1355	877	4.69E-33
GO:0032501	multicellular organismal process	5319	2948	8.54E-33
GO:0048858	cell projection morphogenesis	459	352	1.36E-32
GO:0048666	neuron development	729	516	2.16E-32
GO:0032989	cellular component morphogenesis	549	407	3.74E-32
GO:0030030	cell projection organization	1164	766	7.19E-32
GO:0120039	plasma membrane bounded cell projection morphogenesis	455	348	9.12E-32
GO:0031175	neuron projection development	656	471	9.40E-32
GO:0120036	plasma membrane bounded cell projection organization	1144	754	1.22E-31
GO:0032990	cell part morphogenesis	469	355	8.10E-31
GO:0048812	neuron projection morphogenesis	441	337	1.53E-30
GO:0000904	cell morphogenesis involved in differentiation	495	367	1.01E-28
GO:0023051	regulation of signaling	2733	1601	2.82E-28
GO:0010646	regulation of cell communication	2727	1596	7.06E-28
GO:0051128	regulation of cellular component organization	1929	1170	3.23E-27
GO:0061564	axon development	323	256	5.08E-27
GO:0030029	actin filament-based process	717	495	1.15E-26
GO:0050793	regulation of developmental process	1810	1101	5.46E-26
GO:0048667	cell morphogenesis involved in neuron differentiation	381	291	6.02E-26
GO:0007409	axonogenesis	298	237	3.00E-25
GO:0023052	signaling	5190	2837	8.54E-25
GO:0007154	cell communication	5221	2844	1.92E-23
GO:0016043	cellular component organization	5370	2912	1.84E-22
GO:0051239	regulation of multicellular organismal process	2117	1248	3.72E-22
GO:0048513	animal organ development	2176	1277	1.06E-21
GO:0030036	actin cytoskeleton organization	637	435	1.52E-21
GO:0035556	intracellular signal transduction	2168	1267	1.65E-20
GO:0007155	cell adhesion	1216	754	1.02E-19
GO:0009966	regulation of signal transduction	2464	1416	2.43E-19
GO:0007010	cytoskeleton organization	1309	799	2.62E-18
GO:0031344	regulation of cell projection organization	467	326	7.18E-18
GO:0050804	modulation of chemical synaptic transmission	252	195	8.78E-18
GO:0120035	regulation of plasma membrane bounded cell projection organization	453	317	1.42E-17
GO:0071840	cellular component organization or biogenesis	5539	2962	1.45E-17
GO:0099177	regulation of trans-synaptic signaling	253	195	1.99E-17
GO:0048522	positive regulation of cellular process	4704	2544	2.87E-17
GO:0099536	synaptic signaling	522	356	5.07E-17
GO:0048523	negative regulation of cellular process	3896	2135	6.91E-17
GO:0034330	cell junction organization	518	353	8.99E-17
GO:0010975	regulation of neuron projection development	288	215	1.91E-16
GO:0022603	regulation of anatomical structure morphogenesis	700	456	2.19E-16
GO:0045595	regulation of cell differentiation	1129	693	2.71E-16
GO:0007417	central nervous system development	584	389	4.80E-16
GO:0050794	regulation of cellular process	9523	4886	6.17E-16
GO:0048518	positive regulation of biological process	5294	2827	8.88E-16
GO:0099537	trans-synaptic signaling	501	340	1.25E-15
GO:0098916	anterograde trans-synaptic signaling	495	336	1.93E-15
GO:0007268	chemical synaptic transmission	495	336	1.93E-15
GO:0007165	signal transduction	4776	2566	2.30E-15
GO:0009987	cellular process	14783	7306	2.42E-15
GO:0048583	regulation of response to stimulus	3327	1835	3.42E-15
GO:0097485	neuron projection guidance	169	137	5.04E-15
GO:0007411	axon guidance	169	137	5.04E-15

Table S5 (continued).

GO ID	GO Description	Universe	COSMIC and CLINVAR	Adjusted P-value
GO:0065007	biological regulation	10721	5447	5.19E-15
GO:0048519	negative regulation of biological process	4381	2365	6.60E-15
GO:0065008	regulation of biological quality	2937	1634	6.88E-15
GO:0032879	regulation of localization	1615	947	7.50E-15
GO:0051716	cellular response to stimulus	5982	3159	9.70E-15
GO:0050789	regulation of biological process	10085	5143	1.21E-14
GO:0007267	cell-cell signaling	1269	761	1.63E-14
GO:0051094	positive regulation of developmental process	967	595	6.68E-14
GO:0051179	localization	4343	2335	1.81E-13
GO:0050770	regulation of axonogenesis	100	88	2.65E-13
GO:0051049	regulation of transport	1327	786	3.15E-13
GO:0048870	cell motility	1362	804	4.26E-13
GO:0007167	enzyme-linked receptor protein signaling pathway	795	497	5.75E-13
GO:0009887	animal organ morphogenesis	582	378	7.07E-13
GO:0050808	synapse organization	275	198	3.52E-12
GO:0051960	regulation of nervous system development	257	187	3.93E-12
GO:0016477	cell migration	1210	717	7.09E-12
GO:0009888	tissue development	1239	732	8.83E-12
GO:0003012	muscle system process	305	215	8.94E-12
GO:0055085	transmembrane transport	1060	635	1.60E-11
GO:0051130	positive regulation of cellular component organization	844	518	1.69E-11
GO:0006810	transport	3620	1956	1.92E-11
GO:0065009	regulation of molecular function	2121	1192	2.01E-11
GO:0040011	locomotion	1075	641	4.38E-11
GO:0098660	inorganic ion transmembrane transport	622	394	5.04E-11
GO:0042391	regulation of membrane potential	319	221	7.21E-11
GO:0051234	establishment of localization	3775	2029	7.97E-11
GO:0007015	actin filament organization	395	265	8.57E-11
GO:0045944	positive regulation of transcription by RNA polymerase II	952	573	1.11E-10
GO:0007420	brain development	384	258	1.44E-10
GO:0098655	cation transmembrane transport	656	411	1.57E-10
GO:0023057	negative regulation of signaling	1067	634	1.61E-10
GO:0061061	muscle structure development	407	271	1.72E-10
GO:0007169	transmembrane receptor protein tyrosine kinase signaling pathway	511	330	1.77E-10
GO:0034220	ion transmembrane transport	816	498	2.25E-10
GO:0016310	phosphorylation	1444	833	2.28E-10
GO:1902531	regulation of intracellular signal transduction	1429	825	2.39E-10
GO:0007264	small GTPase mediated signal transduction	389	260	2.86E-10
GO:0010648	negative regulation of cell communication	1060	629	2.89E-10
GO:0050767	regulation of neurogenesis	208	153	3.26E-10
GO:0060322	head development	402	267	4.05E-10
GO:0040012	regulation of locomotion	842	511	4.05E-10
GO:0006936	muscle contraction	260	184	4.79E-10
GO:0022604	regulation of cell morphogenesis	240	172	4.91E-10
GO:0098662	inorganic cation transmembrane transport	572	362	6.98E-10
GO:0097435	supramolecular fiber organization	710	438	7.39E-10
GO:0006811	ion transport	1187	694	9.42E-10
GO:0030001	metal ion transport	678	420	9.61E-10
GO:0048167	regulation of synaptic plasticity	122	98	1.02E-09
GO:2000026	regulation of multicellular organismal development	981	584	1.04E-09
GO:0045597	positive regulation of cell differentiation	624	390	1.13E-09
GO:2000145	regulation of cell motility	818	496	1.14E-09
GO:0030334	regulation of cell migration	767	468	1.35E-09
GO:0048585	negative regulation of response to stimulus	1287	745	2.06E-09
GO:0072359	circulatory system development	729	446	2.71E-09
GO:1903508	positive regulation of nucleic acid-templated transcription	1297	749	3.44E-09
GO:0045893	positive regulation of DNA-templated transcription	1297	749	3.44E-09
GO:0051173	positive regulation of nitrogen compound metabolic process	2565	1404	3.55E-09
GO:0051962	positive regulation of nervous system development	147	113	3.93E-09
GO:0031346	positive regulation of cell projection organization	247	174	3.98E-09
GO:0006812	cation transport	886	530	4.38E-09
GO:0009968	negative regulation of signal transduction	1009	595	6.51E-09
GO:0032970	regulation of actin filament-based process	330	222	6.52E-09

Table S5 (continued).

GO ID	GO Description	Universe	COSMIC and CLINVAR	Adjusted P-value
GO:0006468	protein phosphorylation	1268	732	6.97E-09
GO:0071805	potassium ion transmembrane transport	185	136	7.67E-09
GO:1902680	positive regulation of RNA biosynthetic process	1303	750	8.22E-09
GO:0031325	positive regulation of cellular metabolic process	2522	1378	1.21E-08
GO:0044087	regulation of cellular component biogenesis	774	467	1.61E-08
GO:0044057	regulation of system process	392	256	1.94E-08
GO:0060560	developmental growth involved in morphogenesis	135	104	2.36E-08
GO:0048588	developmental cell growth	129	100	3.06E-08
GO:0032535	regulation of cellular component size	256	177	3.24E-08
GO:0060284	regulation of cell development	315	211	4.14E-08
GO:0051056	regulation of small GTPase mediated signal transduction	238	166	4.61E-08
GO:0098609	cell-cell adhesion	743	448	5.00E-08
GO:0031589	cell-substrate adhesion	290	196	6.49E-08
GO:0001667	ameboidal-type cell migration	333	220	1.12E-07
GO:0099587	inorganic ion import across plasma membrane	112	88	1.40E-07
GO:0098659	inorganic cation import across plasma membrane	112	88	1.40E-07
GO:0009893	positive regulation of metabolic process	3177	1700	1.57E-07
GO:0051254	positive regulation of RNA metabolic process	1433	810	1.66E-07
GO:0051240	positive regulation of multicellular organismal process	1137	655	1.76E-07
GO:0050769	positive regulation of neurogenesis	119	92	2.53E-07
GO:0010604	positive regulation of macromolecule metabolic process	2889	1553	2.57E-07
GO:0044093	positive regulation of molecular function	1305	742	2.64E-07
GO:0031324	negative regulation of cellular metabolic process	1858	1028	2.90E-07
GO:0060627	regulation of vesicle-mediated transport	417	266	2.97E-07
GO:0045935	positive regulation of nucleobase-containing compound metabolic process	1620	905	3.26E-07
GO:0006793	phosphorus metabolic process	2354	1281	3.36E-07
GO:0051641	cellular localization	2721	1467	3.45E-07
GO:0035725	sodium ion transmembrane transport	129	98	3.60E-07
GO:0006813	potassium ion transport	200	141	4.40E-07
GO:0033043	regulation of organelle organization	1015	588	5.17E-07
GO:1990138	neuron projection extension	112	87	5.18E-07
GO:0048638	regulation of developmental growth	167	121	5.36E-07
GO:0006796	phosphate-containing compound metabolic process	2336	1270	5.65E-07
GO:0042221	response to chemical	2943	1577	5.88E-07
GO:0001508	action potential	117	90	6.38E-07
GO:0034329	cell junction assembly	341	222	6.89E-07
GO:0023056	positive regulation of signaling	1380	778	7.95E-07
GO:0032956	regulation of actin cytoskeleton organization	296	196	9.18E-07
GO:0030516	regulation of axon extension	61	53	9.20E-07
GO:1905114	cell surface receptor signaling pathway involved in cell-cell signaling	388	248	9.30E-07
GO:0003015	heart process	193	136	9.57E-07
GO:0048646	anatomical structure formation involved in morphogenesis	751	446	1.03E-06
GO:0016049	cell growth	358	231	1.03E-06
GO:0010647	positive regulation of cell communication	1374	774	1.07E-06
GO:0006996	organelle organization	3147	1677	1.11E-06
GO:0061387	regulation of extent of cell growth	67	57	1.13E-06
GO:0051093	negative regulation of developmental process	619	374	1.58E-06
GO:0007507	heart development	338	219	1.67E-06
GO:0048589	developmental growth	273	182	1.68E-06
GO:0003013	circulatory system process	443	277	2.44E-06
GO:0042127	regulation of cell population proliferation	1218	690	2.85E-06
GO:0071495	cellular response to endogenous stimulus	974	562	2.94E-06
GO:0007265	Ras protein signal transduction	278	184	3.20E-06
GO:0060047	heart contraction	187	131	3.55E-06
GO:0009719	response to endogenous stimulus	1076	615	3.74E-06
GO:0060828	regulation of canonical Wnt signaling pathway	211	145	3.96E-06
GO:0051493	regulation of cytoskeleton organization	450	280	4.00E-06
GO:0090066	regulation of anatomical structure size	328	212	4.16E-06
GO:0031327	negative regulation of cellular biosynthetic process	1292	727	4.83E-06
GO:0045892	negative regulation of DNA-templated transcription	1051	601	5.22E-06
GO:0003008	system process	1358	761	5.26E-06
GO:0006814	sodium ion transport	166	118	5.64E-06

Table S5 (continued).

GO ID	GO Description	Universe	COSMIC and CLINVAR	Adjusted P-value
GO:0010557	positive regulation of macromolecule biosynthetic process	1492	830	5.80E-06
GO:0009891	positive regulation of biosynthetic process	1593	882	5.89E-06
GO:0086001	cardiac muscle cell action potential	73	60	6.04E-06
GO:0051172	negative regulation of nitrogen compound metabolic process	1927	1053	6.26E-06
GO:1903507	negative regulation of nucleic acid-templated transcription	1056	603	6.56E-06
GO:0009890	negative regulation of biosynthetic process	1315	738	6.62E-06
GO:1902679	negative regulation of RNA biosynthetic process	1057	603	7.97E-06
GO:0098657	import into cell	216	147	8.46E-06
GO:0048675	axon extension	81	65	8.67E-06
GO:0050772	positive regulation of axonogenesis	47	42	9.25E-06
GO:0060537	muscle tissue development	218	148	9.60E-06
GO:0050807	regulation of synapse organization	124	92	9.86E-06
GO:0008283	cell population proliferation	1383	772	9.86E-06
GO:0001558	regulation of cell growth	320	206	1.11E-05
GO:0031328	positive regulation of cellular biosynthetic process	1568	867	1.13E-05
GO:0009790	embryo development	505	308	1.26E-05
GO:0007166	cell surface receptor signaling pathway	2271	1225	1.38E-05
GO:0035637	multicellular organismal signaling	128	94	1.60E-05
GO:0010631	epithelial cell migration	261	172	1.68E-05
GO:0060070	canonical Wnt signaling pathway	254	168	1.68E-05
GO:0010632	regulation of epithelial cell migration	204	139	1.92E-05
GO:0045596	negative regulation of cell differentiation	439	271	2.07E-05
GO:0050896	response to stimulus	7117	3620	2.09E-05
GO:0030111	regulation of Wnt signaling pathway	274	179	2.22E-05
GO:0010558	negative regulation of macromolecule biosynthetic process	1251	701	2.32E-05
GO:0098739	import across plasma membrane	172	120	2.36E-05
GO:0034762	regulation of transmembrane transport	385	241	2.39E-05
GO:0040007	growth	515	312	2.61E-05
GO:0071310	cellular response to organic substance	1734	949	2.81E-05
GO:0050803	regulation of synapse structure or activity	129	94	3.02E-05
GO:0000165	MAPK cascade	599	357	3.11E-05
GO:0014706	striated muscle tissue development	144	103	3.19E-05
GO:0035295	tube development	616	366	3.29E-05
GO:0090132	epithelium migration	263	172	3.75E-05
GO:0050806	positive regulation of synaptic transmission	89	69	3.90E-05
GO:0009892	negative regulation of metabolic process	2418	1295	4.08E-05
GO:0010033	response to organic substance	2106	1137	4.17E-05
GO:0046777	protein autophosphorylation	199	135	4.63E-05
GO:0048738	cardiac muscle tissue development	138	99	4.67E-05
GO:0001505	regulation of neurotransmitter levels	143	102	4.68E-05
GO:0061337	cardiac conduction	91	70	5.39E-05
GO:0016358	dendrite development	155	109	5.39E-05
GO:0090257	regulation of muscle system process	157	110	6.38E-05
GO:0034765	regulation of ion transmembrane transport	325	206	6.51E-05
GO:0051253	negative regulation of RNA metabolic process	1157	649	6.64E-05
GO:0006941	striated muscle contraction	142	101	6.81E-05
GO:0008361	regulation of cell size	119	87	7.72E-05
GO:0030155	regulation of cell adhesion	614	363	7.77E-05
GO:0035239	tube morphogenesis	547	327	7.90E-05
GO:0090130	tissue migration	267	173	8.81E-05
GO:0036211	protein modification process	2994	1581	9.04E-05
GO:0099003	vesicle-mediated transport in synapse	121	88	9.62E-05
GO:0050905	neuromuscular process	73	58	1.07E-04
GO:0030048	actin filament-based movement	113	83	1.10E-04
GO:0042692	muscle cell differentiation	243	159	1.16E-04
GO:0022607	cellular component assembly	2547	1355	1.30E-04
GO:0030900	forebrain development	155	108	1.31E-04
GO:0060078	regulation of postsynaptic membrane potential	61	50	1.38E-04
GO:0007517	muscle organ development	179	122	1.38E-04
GO:0009967	positive regulation of signal transduction	1255	697	1.57E-04
GO:0048639	positive regulation of developmental growth	83	64	1.74E-04
GO:0048729	tissue morphogenesis	348	217	1.83E-04
GO:0070887	cellular response to chemical stimulus	2288	1223	1.83E-04
GO:0043269	regulation of ion transport	458	277	1.97E-04

Table S5 (continued).

GO ID	GO Description	Universe	COSMIC and CLINVAR	Adjusted P-value
GO:0043269	regulation of ion transport	458	277	1.97E-04
GO:0035249	synaptic transmission, glutamatergic	66	53	2.05E-04
GO:0099504	synaptic vesicle cycle	114	83	2.07E-04
GO:0040008	regulation of growth	416	254	2.14E-04
GO:0051129	negative regulation of cellular component organization	566	335	2.15E-04
GO:0021537	telencephalon development	101	75	2.19E-04
GO:0098900	regulation of action potential	48	41	2.21E-04
GO:0045934	negative regulation of nucleobase-containing compound metabolic process	1273	705	2.32E-04
GO:0099565	chemical synaptic transmission, postsynaptic	51	43	2.34E-04
GO:0051241	negative regulation of multicellular organismal process	755	435	2.53E-04
GO:0010720	positive regulation of cell development	177	120	2.71E-04
GO:0140352	export from cell	627	367	2.74E-04
GO:1902532	negative regulation of intracellular signal transduction	436	264	3.33E-04
GO:0032409	regulation of transporter activity	244	158	3.37E-04
GO:0010605	negative regulation of macromolecule metabolic process	2244	1198	3.49E-04
GO:0008016	regulation of heart contraction	164	112	3.83E-04
GO:1904062	regulation of cation transmembrane transport	291	184	4.13E-04
GO:0070727	cellular macromolecule localization	1880	1013	4.24E-04
GO:0010594	regulation of endothelial cell migration	154	106	4.36E-04
GO:0043542	endothelial cell migration	194	129	5.00E-04
GO:0048598	embryonic morphogenesis	308	193	5.37E-04
GO:0008104	protein localization	1874	1009	5.38E-04
GO:0044089	positive regulation of cellular component biogenesis	416	252	5.87E-04
GO:0050790	regulation of catalytic activity	1498	817	6.20E-04
GO:0198738	cell-cell signaling by wnt	343	212	6.32E-04
GO:0040017	positive regulation of locomotion	472	282	6.67E-04
GO:0060048	cardiac muscle contraction	111	80	6.71E-04
GO:0008154	actin polymerization or depolymerization	155	106	7.08E-04
GO:1903522	regulation of blood circulation	188	125	7.51E-04
GO:0030335	positive regulation of cell migration	443	266	7.90E-04
GO:0051247	positive regulation of protein metabolic process	1264	696	8.30E-04
GO:0021953	central nervous system neuron differentiation	74	57	8.76E-04
GO:0030100	regulation of endocytosis	159	108	9.23E-04
GO:0016055	Wnt signaling pathway	339	209	9.76E-04
GO:0006836	neurotransmitter transport	137	95	1.04E-03
GO:0016192	vesicle-mediated transport	1326	727	1.05E-03
GO:2000147	positive regulation of cell motility	463	276	1.13E-03
GO:0010243	response to organonitrogen compound	613	356	1.16E-03
GO:0007163	establishment or maintenance of cell polarity	177	118	1.25E-03
GO:0030178	negative regulation of Wnt signaling pathway	146	100	1.30E-03
GO:0099173	postsynapse organization	99	72	1.41E-03
GO:0006937	regulation of muscle contraction	119	84	1.42E-03
GO:0007229	integrin-mediated signaling pathway	104	75	1.44E-03
GO:0070252	actin-mediated cell contraction	86	64	1.50E-03
GO:0008360	regulation of cell shape	116	82	1.72E-03
GO:0008015	blood circulation	363	221	1.74E-03
GO:0060429	epithelium development	689	395	1.79E-03
GO:0043087	regulation of GTPase activity	301	187	1.79E-03
GO:0032412	regulation of ion transmembrane transporter activity	222	143	1.84E-03
GO:0018193	peptidyl-amino acid modification	1035	575	1.97E-03
GO:0055001	muscle cell development	118	83	2.04E-03
GO:0070848	response to growth factor	516	303	2.08E-03
GO:0043085	positive regulation of catalytic activity	960	536	2.08E-03
GO:0031623	receptor internalization	98	71	2.09E-03
GO:0051050	positive regulation of transport	709	405	2.15E-03
GO:0010977	negative regulation of neuron projection development	85	63	2.27E-03
GO:0031345	negative regulation of cell projection organization	125	87	2.31E-03
GO:1901699	cellular response to nitrogen compound	468	277	2.40E-03
GO:0086065	cell communication involved in cardiac conduction	58	46	2.49E-03
GO:0031532	actin cytoskeleton reorganization	105	75	2.56E-03
GO:0051146	striated muscle cell differentiation	170	113	2.56E-03
GO:0051649	establishment of localization in cell	1698	913	2.68E-03
GO:0046903	secretion	638	367	2.72E-03

Table S5 (continued).

GO ID	GO Description	Universe	COSMIC and CLINVAR	Adjusted P-value
GO:0046578	regulation of Ras protein signal transduction	139	95	2.74E-03
GO:0031399	regulation of protein modification process	1259	689	2.83E-03
GO:0071417	cellular response to organonitrogen compound	413	247	2.92E-03
GO:0048813	dendrite morphogenesis	97	70	3.06E-03
GO:0060291	long-term synaptic potentiation	49	40	3.09E-03
GO:0071526	semaphorin-plexin signaling pathway	40	34	3.13E-03
GO:0050771	negative regulation of axonogenesis	43	36	3.22E-03
GO:0022898	regulation of transmembrane transporter activity	229	146	3.28E-03
GO:0032940	secretion by cell	571	331	3.39E-03
GO:0051174	regulation of phosphorus metabolic process	1126	620	3.43E-03
GO:0042325	regulation of phosphorylation	1004	557	3.54E-03
GO:0098901	regulation of cardiac muscle cell action potential	30	27	3.62E-03
GO:0040013	negative regulation of locomotion	278	173	3.69E-03
GO:0007416	synapse assembly	126	87	3.77E-03
GO:0019220	regulation of phosphate metabolic process	1125	619	3.93E-03
GO:0043408	regulation of MAPK cascade	534	311	3.94E-03
GO:0045229	external encapsulating structure organization	237	150	4.35E-03
GO:0051966	regulation of synaptic transmission, glutamatergic	51	41	4.76E-03
GO:0006898	receptor-mediated endocytosis	214	137	4.77E-03
GO:0086003	cardiac muscle cell contraction	62	48	5.00E-03
GO:0098703	calcium ion import across plasma membrane	36	31	5.04E-03
GO:0086002	cardiac muscle cell action potential involved in contraction	48	39	5.09E-03
GO:0033036	macromolecule localization	2245	1186	5.15E-03
GO:0001944	vasculature development	492	288	5.17E-03
GO:0050890	cognition	156	104	5.19E-03
GO:0030198	extracellular matrix organization	234	148	5.31E-03
GO:0060079	excitatory postsynaptic potential	45	37	5.32E-03
GO:1901888	regulation of cell junction assembly	144	97	5.54E-03
GO:0050678	regulation of epithelial cell proliferation	236	149	5.67E-03
GO:1902903	regulation of supramolecular fiber organization	311	190	6.64E-03
GO:0043062	extracellular structure organization	235	148	7.38E-03
GO:0002009	morphogenesis of an epithelium	275	170	7.74E-03
GO:0042592	homeostatic process	1249	680	7.85E-03
GO:0043412	macromolecule modification	3198	1659	8.65E-03
GO:0086091	regulation of heart rate by cardiac conduction	41	34	9.11E-03
GO:0110053	regulation of actin filament organization	216	137	9.48E-03
GO:0031400	negative regulation of protein modification process	409	242	1.05E-02
GO:0001568	blood vessel development	469	274	1.06E-02
GO:0090090	negative regulation of canonical Wnt signaling pathway	118	81	1.13E-02
GO:0048592	eye morphogenesis	81	59	1.14E-02
GO:0051246	regulation of protein metabolic process	2072	1095	1.17E-02
GO:0007423	sensory organ development	271	167	1.19E-02
GO:2001257	regulation of cation channel activity	153	101	1.31E-02
GO:0070588	calcium ion transmembrane transport	235	147	1.31E-02
GO:0007611	learning or memory	115	79	1.37E-02
GO:0048863	stem cell differentiation	155	102	1.44E-02
GO:0031401	positive regulation of protein modification process	814	454	1.44E-02
GO:0060341	regulation of cellular localization	766	429	1.48E-02
GO:0021954	central nervous system neuron development	40	33	1.51E-02
GO:0071363	cellular response to growth factor stimulus	499	289	1.51E-02
GO:1901379	regulation of potassium ion transmembrane transport	70	52	1.53E-02
GO:0030041	actin filament polymerization	129	87	1.53E-02
GO:0048514	blood vessel morphogenesis	439	257	1.60E-02
GO:0050773	regulation of dendrite development	62	47	1.62E-02
GO:0009792	embryo development ending in birth or egg hatching	198	126	1.68E-02
GO:0051961	negative regulation of nervous system development	85	61	1.69E-02
GO:0090596	sensory organ morphogenesis	119	81	1.79E-02
GO:0001501	skeletal system development	289	176	1.82E-02
GO:0120031	plasma membrane bounded cell projection assembly	483	280	1.85E-02
GO:0006816	calcium ion transport	313	189	1.85E-02
GO:0010634	positive regulation of epithelial cell migration	133	89	1.92E-02
GO:0031098	stress-activated protein kinase signaling cascade	202	128	1.93E-02
GO:0009628	response to abiotic stimulus	712	400	1.97E-02
GO:1990573	potassium ion import across plasma membrane	48	38	1.99E-02

Table S5 (continued).

GO ID	GO Description	Universe	COSMIC and CLINVAR	Adjusted P-value
GO:0150104	transport across blood-brain barrier	87	62	2.03E-02
GO:0010232	vascular transport	87	62	2.03E-02
GO:0007160	cell-matrix adhesion	195	124	2.04E-02
GO:0032880	regulation of protein localization	672	379	2.06E-02
GO:0043254	regulation of protein-containing complex assembly	332	199	2.11E-02
GO:0051258	protein polymerization	233	145	2.14E-02
GO:0000122	negative regulation of transcription by RNA polymerase II	751	420	2.14E-02
GO:0007612	learning	53	41	2.48E-02
GO:0045664	regulation of neuron differentiation	96	67	2.77E-02
GO:0010959	regulation of metal ion transport	298	180	2.80E-02
GO:0030010	establishment of cell polarity	108	74	2.86E-02
GO:0007269	neurotransmitter secretion	91	64	2.87E-02
GO:0099643	signal release from synapse	91	64	2.87E-02
GO:0051963	regulation of synapse assembly	58	44	2.89E-02
GO:0016079	synaptic vesicle exocytosis	58	44	2.89E-02
GO:0150063	visual system development	207	130	3.03E-02
GO:0051403	stress-activated MAPK cascade	198	125	3.03E-02
GO:0061572	actin filament bundle organization	136	90	3.22E-02
GO:0048762	mesenchymal cell differentiation	191	121	3.23E-02
GO:0007215	glutamate receptor signaling pathway	44	35	3.51E-02
GO:0086009	membrane repolarization	44	35	3.51E-02
GO:0048880	sensory system development	213	133	3.64E-02
GO:0032878	regulation of establishment or maintenance of cell polarity	26	23	3.65E-02
GO:0001654	eye development	204	128	3.68E-02
GO:0048640	negative regulation of developmental growth	60	45	3.78E-02
GO:0030031	cell projection assembly	498	286	3.80E-02
GO:0043549	regulation of kinase activity	599	339	3.81E-02
GO:0050881	musculoskeletal movement	41	33	3.82E-02
GO:0050879	multicellular organismal movement	41	33	3.82E-02
GO:1990778	protein localization to cell periphery	279	169	3.89E-02
GO:0051017	actin filament bundle assembly	133	88	3.94E-02
GO:0086005	ventricular cardiac muscle cell action potential	29	25	4.10E-02
GO:0050919	negative chemotaxis	35	29	4.26E-02
GO:0030517	negative regulation of axon extension	32	27	4.29E-02
GO:0048878	chemical homeostasis	769	427	4.30E-02
GO:0042327	positive regulation of phosphorylation	663	372	4.31E-02
GO:0050768	negative regulation of neurogenesis	80	57	4.32E-02
GO:0031323	regulation of cellular metabolic process	4966	2520	4.38E-02
GO:0043009	chordate embryonic development	183	116	4.45E-02
GO:0010721	negative regulation of cell development	109	74	4.53E-02
GO:0045785	positive regulation of cell adhesion	369	217	4.75E-02
GO:0006887	exocytosis	267	162	4.91E-02
GO:0045216	cell-cell junction organization	169	108	4.96E-02
GO:0001764	neuron migration	87	61	4.98E-02

Table S6. Significant GO:BP enrichments for all COSMIC G4 mutations.

GO ID	GO Description	Universe	COSMIC	Adjusted
GO:0007399	nervous system development	1648	1074	3.73E-48
GO:0048856	anatomical structure development	4152	2391	3.71E-47
GO:0032502	developmental process	4584	2606	2.53E-46
GO:0048731	system development	2976	1762	2.21E-41
GO:0007275	multicellular organism development	3266	1908	2.56E-40
GO:0048699	generation of neurons	969	663	7.68E-38
GO:0009653	anatomical structure morphogenesis	1871	1162	2.2E-37
GO:0000902	cell morphogenesis	718	515	2.79E-37
GO:0030154	cell differentiation	2860	1682	1.33E-36
GO:0048869	cellular developmental process	2879	1691	2.15E-36
GO:0022008	neurogenesis	1096	728	4.84E-35
GO:0030182	neuron differentiation	923	629	7.45E-35
GO:0048858	cell projection morphogenesis	459	349	9.15E-33
GO:0032989	cellular component morphogenesis	549	404	1.13E-32
GO:0048468	cell development	1355	865	1.38E-32
GO:0032501	multicellular organismal process	5319	2904	1.87E-32
GO:0030030	cell projection organization	1164	758	3.34E-32
GO:0048666	neuron development	729	510	3.54E-32
GO:0120039	plasma membrane bounded cell projection morphogenesis	455	345	6.29E-32
GO:0120036	plasma membrane bounded cell projection organization	1144	746	6.38E-32
GO:0031175	neuron projection development	656	466	1.03E-31
GO:0032990	cell part morphogenesis	469	352	4.87E-31
GO:0048812	neuron projection morphogenesis	441	334	1.2E-30
GO:0023051	regulation of signaling	2733	1582	7.93E-29
GO:0010646	regulation of cell communication	2727	1578	1.24E-28
GO:0000904	cell morphogenesis involved in differentiation	495	363	1.5E-28
GO:0051128	regulation of cellular component organization	1929	1154	5.21E-27
GO:0061564	axon development	323	253	1.39E-26
GO:0030029	actin filament-based process	717	489	1.87E-26
GO:0048667	cell morphogenesis involved in neuron differentiation	381	288	8.11E-26
GO:0007409	axonogenesis	298	235	2.6E-25
GO:0050793	regulation of developmental process	1810	1084	2.62E-25
GO:0023052	signaling	5190	2793	2.45E-24
GO:0007154	cell communication	5221	2801	3.47E-23
GO:0016043	cellular component organization	5370	2874	3.66E-23
GO:0030036	actin cytoskeleton organization	637	432	3E-22
GO:0051239	regulation of multicellular organismal process	2117	1227	3.02E-21
GO:0048513	animal organ development	2176	1257	4.1E-21
GO:0007155	cell adhesion	1216	749	6.57E-21
GO:0035556	intracellular signal transduction	2168	1250	1.57E-20
GO:0009966	regulation of signal transduction	2464	1398	1.28E-19
GO:0007010	cytoskeleton organization	1309	791	7.32E-19
GO:0050804	modulation of chemical synaptic transmission	252	194	3.06E-18
GO:0071840	cellular component organization or biogenesis	5539	2923	3.12E-18
GO:0099177	regulation of trans-synaptic signaling	253	194	6.91E-18
GO:0048522	positive regulation of cellular process	4704	2510	9.93E-18
GO:0031344	regulation of cell projection organization	467	322	1.09E-17
GO:0099536	synaptic signaling	522	353	2.18E-17
GO:0120035	regulation of plasma membrane bounded cell projection organization	453	313	2.39E-17
GO:0034330	cell junction organization	518	349	9.31E-17
GO:0048523	negative regulation of cellular process	3896	2101	2.01E-16
GO:0048518	positive regulation of biological process	5294	2788	3.67E-16
GO:0050794	regulation of cellular process	9523	4812	4.06E-16
GO:0045595	regulation of cell differentiation	1129	683	5.21E-16
GO:0010975	regulation of neuron projection development	288	212	5.22E-16
GO:0099537	trans-synaptic signaling	501	337	6.23E-16
GO:0098916	anterograde trans-synaptic signaling	495	333	9.95E-16
GO:0007268	chemical synaptic transmission	495	333	9.95E-16
GO:0048583	regulation of response to stimulus	3327	1812	1.08E-15
GO:0007417	central nervous system development	584	383	1.53E-15
GO:0065007	biological regulation	10721	5366	1.62E-15
GO:0009987	cellular process	14783	7189	2.34E-15
GO:0022603	regulation of anatomical structure morphogenesis	700	447	2.71E-15
GO:0007165	signal transduction	4776	2527	3.25E-15
GO:0007267	cell-cell signaling	1269	754	3.55E-15
GO:0097485	neuron projection guidance	169	136	3.85E-15

Table S6 (continued).

GO ID	GO Description	Universe	COSMIC	Adjusted
GO:0007411	axon guidance	169	136	3.85E-15
GO:0051716	cellular response to stimulus	5982	3114	4.88E-15
GO:0050789	regulation of biological process	10085	5066	5.3E-15
GO:0032879	regulation of localization	1615	935	5.33E-15
GO:0065008	regulation of biological quality	2937	1610	8.9E-15
GO:0048519	negative regulation of biological process	4381	2326	2.42E-14
GO:0050770	regulation of axonogenesis	100	88	7.4E-14
GO:0051094	positive regulation of developmental process	967	587	8.44E-14
GO:0051049	regulation of transport	1327	777	1.58E-13
GO:0051179	localization	4343	2298	3.85E-13
GO:0050808	synapse organization	275	197	1.2E-12
GO:0051960	regulation of nervous system development	257	186	1.51E-12
GO:0048870	cell motility	1362	790	1.94E-12
GO:0007167	enzyme-linked receptor protein signaling pathway	795	487	5.4E-12
GO:0065009	regulation of molecular function	2121	1178	7.37E-12
GO:0009887	animal organ morphogenesis	582	370	7.74E-12
GO:0098660	inorganic ion transmembrane transport	622	392	8.1E-12
GO:0007015	actin filament organization	395	264	1.69E-11
GO:0003012	muscle system process	305	212	1.71E-11
GO:0051130	positive regulation of cellular component organization	844	511	2.1E-11
GO:0040011	locomotion	1075	634	2.15E-11
GO:0016477	cell migration	1210	705	2.25E-11
GO:0098655	cation transmembrane transport	656	408	4.28E-11
GO:0006810	transport	3620	1924	5E-11
GO:0055085	transmembrane transport	1060	624	5.85E-11
GO:0009888	tissue development	1239	718	6.11E-11
GO:0061061	muscle structure development	407	269	7.1E-11
GO:0016310	phosphorylation	1444	824	8.45E-11
GO:0034220	ion transmembrane transport	816	493	1.05E-10
GO:0042391	regulation of membrane potential	319	218	1.17E-10
GO:0098662	inorganic cation transmembrane transport	572	360	1.47E-10
GO:0050767	regulation of neurogenesis	208	152	1.8E-10
GO:1902531	regulation of intracellular signal transduction	1429	814	2.13E-10
GO:0045944	positive regulation of transcription by RNA polymerase II	952	564	2.35E-10
GO:0051234	establishment of localization	3775	1995	2.45E-10
GO:0007420	brain development	384	254	3.26E-10
GO:0030001	metal ion transport	678	416	4.56E-10
GO:0040012	regulation of locomotion	842	504	4.98E-10
GO:0097435	supramolecular fiber organization	710	433	5.41E-10
GO:0007264	small GTPase mediated signal transduction	389	256	6.15E-10
GO:0007169	transmembrane receptor protein tyrosine kinase signaling pathway	511	324	6.85E-10
GO:0060322	head development	402	263	7.88E-10
GO:0023057	negative regulation of signaling	1067	622	8.51E-10
GO:0010648	negative regulation of cell communication	1060	618	9.87E-10
GO:0051962	positive regulation of nervous system development	147	113	1.03E-09
GO:0045597	positive regulation of cell differentiation	624	385	1.21E-09
GO:0006811	ion transport	1187	684	1.24E-09
GO:0048167	regulation of synaptic plasticity	122	97	1.24E-09
GO:0006936	muscle contraction	260	181	1.25E-09
GO:0051173	positive regulation of nitrogen compound metabolic process	2565	1387	1.3E-09
GO:0030334	regulation of cell migration	767	462	1.33E-09
GO:0006468	protein phosphorylation	1268	726	1.34E-09
GO:2000145	regulation of cell motility	818	489	1.52E-09
GO:0022604	regulation of cell morphogenesis	240	169	1.56E-09
GO:0071805	potassium ion transmembrane transport	185	136	1.7E-09
GO:2000026	regulation of multicellular organismal development	981	575	1.88E-09
GO:0006812	cation transport	886	524	2.72E-09
GO:1903508	positive regulation of nucleic acid-templated transcription	1297	739	3.11E-09
GO:0045893	positive regulation of DNA-templated transcription	1297	739	3.11E-09
GO:0031346	positive regulation of cell projection organization	247	172	4.48E-09
GO:0048585	negative regulation of response to stimulus	1287	732	6.54E-09
GO:0031325	positive regulation of cellular metabolic process	2522	1360	6.74E-09
GO:0060560	developmental growth involved in morphogenesis	135	104	6.79E-09
GO:1902680	positive regulation of RNA biosynthetic process	1303	740	7.32E-09
GO:0048588	developmental cell growth	129	100	9.07E-09
GO:0032970	regulation of actin filament-based process	330	219	9.35E-09

Table S6 (continued).

GO ID	GO Description	Universe	COSMIC	Adjusted
GO:0009968	negative regulation of signal transduction	1009	586	1.04E-08
GO:0098609	cell-cell adhesion	743	445	1.17E-08
GO:0032535	regulation of cellular component size	256	176	1.4E-08
GO:0044087	regulation of cellular component biogenesis	774	461	1.54E-08
GO:0044057	regulation of system process	392	253	1.88E-08
GO:0051056	regulation of small GTPase mediated signal transduction	238	165	2.2E-08
GO:0098659	inorganic cation import across plasma membrane	112	88	4.74E-08
GO:0099587	inorganic ion import across plasma membrane	112	88	4.74E-08
GO:0031589	cell-substrate adhesion	290	194	5.36E-08
GO:0060284	regulation of cell development	315	208	6.43E-08
GO:0072359	circulatory system development	729	434	7.08E-08
GO:0050769	positive regulation of neurogenesis	119	92	8.43E-08
GO:0006813	potassium ion transport	200	141	1.05E-07
GO:0031324	negative regulation of cellular metabolic process	1858	1016	1.24E-07
GO:0060627	regulation of vesicle-mediated transport	417	264	1.34E-07
GO:0051254	positive regulation of RNA metabolic process	1433	799	1.48E-07
GO:0044093	positive regulation of molecular function	1305	733	1.63E-07
GO:0051240	positive regulation of multicellular organismal process	1137	646	1.77E-07
GO:1990138	neuron projection extension	112	87	1.81E-07
GO:0009893	positive regulation of metabolic process	3177	1674	1.93E-07
GO:0010604	positive regulation of macromolecule metabolic process	2889	1531	2.03E-07
GO:1905114	cell surface receptor signaling pathway involved in cell-cell signaling	388	247	2.48E-07
GO:0045935	positive regulation of nucleobase-containing compound metabolic process	1620	893	2.49E-07
GO:0042221	response to chemical	2943	1557	2.51E-07
GO:0035725	sodium ion transmembrane transport	129	97	3.85E-07
GO:0023056	positive regulation of signaling	1380	769	4.04E-07
GO:0030516	regulation of axon extension	61	53	4.35E-07
GO:0034329	cell junction assembly	341	220	4.37E-07
GO:0006793	phosphorus metabolic process	2354	1261	4.9E-07
GO:0051641	cellular localization	2721	1444	5.04E-07
GO:0033043	regulation of organelle organization	1015	580	5.1E-07
GO:0061387	regulation of extent of cell growth	67	57	5.2E-07
GO:0010647	positive regulation of cell communication	1374	765	5.58E-07
GO:0016049	cell growth	358	229	6.06E-07
GO:0032956	regulation of actin cytoskeleton organization	296	194	7.37E-07
GO:0006796	phosphate-containing compound metabolic process	2336	1250	8.5E-07
GO:0060828	regulation of canonical Wnt signaling pathway	211	145	9.9E-07
GO:0045892	negative regulation of DNA-templated transcription	1051	597	1E-06
GO:0051093	negative regulation of developmental process	619	370	1.02E-06
GO:0048638	regulation of developmental growth	167	119	1.13E-06
GO:0006996	organelle organization	3147	1652	1.13E-06
GO:0001667	ameboidal-type cell migration	333	214	1.26E-06
GO:0048589	developmental growth	273	180	1.54E-06
GO:1903507	negative regulation of nucleic acid-templated transcription	1056	598	1.85E-06
GO:0031327	negative regulation of cellular biosynthetic process	1292	719	2.24E-06
GO:1902679	negative regulation of RNA biosynthetic process	1057	598	2.26E-06
GO:0042127	regulation of cell population proliferation	1218	681	2.26E-06
GO:0051172	negative regulation of nitrogen compound metabolic process	1927	1041	2.45E-06
GO:0090066	regulation of anatomical structure size	328	210	2.86E-06
GO:0009890	negative regulation of biosynthetic process	1315	730	2.92E-06
GO:0051493	regulation of cytoskeleton organization	450	277	2.94E-06
GO:0003015	heart process	193	133	3.77E-06
GO:0048675	axon extension	81	65	3.8E-06
GO:0060070	canonical Wnt signaling pathway	254	168	3.9E-06
GO:0071495	cellular response to endogenous stimulus	974	553	4.87E-06
GO:0050772	positive regulation of axonogenesis	47	42	5.03E-06
GO:0003013	circulatory system process	443	272	5.81E-06
GO:0001508	action potential	117	87	8.02E-06
GO:0001558	regulation of cell growth	320	204	8.08E-06
GO:0010557	positive regulation of macromolecule biosynthetic process	1492	817	8.38E-06
GO:0010558	negative regulation of macromolecule biosynthetic process	1251	694	8.82E-06
GO:0009891	positive regulation of biosynthetic process	1593	868	8.93E-06
GO:0009719	response to endogenous stimulus	1076	604	9.26E-06
GO:0030111	regulation of Wnt signaling pathway	274	178	1E-05
GO:0050807	regulation of synapse organization	124	91	1.07E-05
GO:0050896	response to stimulus	7117	3567	1.15E-05

Table S6 (continued).

GO ID	GO Description	Universe	COSMIC	Adjusted
GO:0007265	Ras protein signal transduction	278	180	1.19E-05
GO:0036211	protein modification process	2994	1566	1.32E-05
GO:0007166	cell surface receptor signaling pathway	2271	1207	1.39E-05
GO:0060047	heart contraction	187	128	1.41E-05
GO:0007507	heart development	338	213	1.5E-05
GO:0045596	negative regulation of cell differentiation	439	268	1.62E-05
GO:0051253	negative regulation of RNA metabolic process	1157	644	1.66E-05
GO:0031328	positive regulation of cellular biosynthetic process	1568	853	1.82E-05
GO:0008283	cell population proliferation	1383	759	1.9E-05
GO:0003008	system process	1358	746	2.09E-05
GO:0000165	MAPK cascade	599	353	2.24E-05
GO:0048646	anatomical structure formation involved in morphogenesis	751	433	2.29E-05
GO:0071310	cellular response to organic substance	1734	936	2.3E-05
GO:0034762	regulation of transmembrane transport	385	238	2.38E-05
GO:0098657	import into cell	216	144	2.44E-05
GO:0040007	growth	515	308	2.56E-05
GO:0006814	sodium ion transport	166	115	2.78E-05
GO:0008361	regulation of cell size	119	87	3.03E-05
GO:0050803	regulation of synapse structure or activity	129	93	3.1E-05
GO:0030155	regulation of cell adhesion	614	360	3.42E-05
GO:0009790	embryo development	505	302	3.52E-05
GO:0098739	import across plasma membrane	172	118	4.28E-05
GO:0001505	regulation of neurotransmitter levels	143	101	4.33E-05
GO:0010033	response to organic substance	2106	1120	4.51E-05
GO:0034765	regulation of ion transmembrane transport	325	204	4.69E-05
GO:0009892	negative regulation of metabolic process	2418	1275	4.96E-05
GO:0090257	regulation of muscle system process	157	109	5.34E-05
GO:0060537	muscle tissue development	218	144	5.78E-05
GO:0050806	positive regulation of synaptic transmission	89	68	5.99E-05
GO:0046777	protein autophosphorylation	199	133	6.67E-05
GO:0060078	regulation of postsynaptic membrane potential	61	50	7.28E-05
GO:0009967	positive regulation of signal transduction	1255	689	8.73E-05
GO:0045934	negative regulation of nucleobase-containing compound metabolic process	1273	698	9.18E-05
GO:0022607	cellular component assembly	2547	1336	0.000101
GO:0007517	muscle organ development	179	121	0.000103
GO:0099003	vesicle-mediated transport in synapse	121	87	0.000106
GO:0035249	synaptic transmission, glutamatergic	66	53	0.000106
GO:0070887	cellular response to chemical stimulus	2288	1207	0.000112
GO:0016358	dendrite development	155	107	0.000112
GO:0030900	forebrain development	155	107	0.000112
GO:0035637	multicellular organismal signaling	128	91	0.000126
GO:0042692	muscle cell differentiation	243	157	0.000127
GO:0010632	regulation of epithelial cell migration	204	135	0.000129
GO:0010631	epithelial cell migration	261	167	0.000131
GO:0035295	tube development	616	358	0.000132
GO:0099565	chemical synaptic transmission, postsynaptic	51	43	0.000132
GO:0070727	cellular macromolecule localization	1880	1002	0.000162
GO:0140352	export from cell	627	363	0.000185
GO:0050905	neuromuscular process	73	57	0.000203
GO:0086001	cardiac muscle cell action potential	73	57	0.000203
GO:0010720	positive regulation of cell development	177	119	0.000204
GO:0008104	protein localization	1874	998	0.000208
GO:0050790	regulation of catalytic activity	1498	809	0.000218
GO:0099504	synaptic vesicle cycle	114	82	0.000241
GO:0043269	regulation of ion transport	458	273	0.000241
GO:0198738	cell-cell signaling by wnt	343	211	0.000251
GO:0051247	positive regulation of protein metabolic process	1264	690	0.00026
GO:0061337	cardiac conduction	91	68	0.00026
GO:0090132	epithelium migration	263	167	0.000269
GO:0035239	tube morphogenesis	547	320	0.00027
GO:0048639	positive regulation of developmental growth	83	63	0.000281
GO:0021537	telencephalon development	101	74	0.000288
GO:0040008	regulation of growth	416	250	0.000312
GO:1904062	regulation of cation transmembrane transport	291	182	0.000353
GO:0032409	regulation of transporter activity	244	156	0.000361
GO:0010605	negative regulation of macromolecule metabolic process	2244	1180	0.000368

Table S6 (continued).

GO ID	GO Description	Universe	COSMIC	Adjusted
GO:0048729	tissue morphogenesis	348	213	0.000371
GO:0006941	striated muscle contraction	142	98	0.000389
GO:0016055	Wnt signaling pathway	339	208	0.000396
GO:1902532	negative regulation of intracellular signal transduction	436	260	0.000441
GO:0014706	striated muscle tissue development	144	99	0.000447
GO:0040017	positive regulation of locomotion	472	279	0.000478
GO:0044089	positive regulation of cellular component biogenesis	416	249	0.000511
GO:0031399	regulation of protein modification process	1259	685	0.000532
GO:0090130	tissue migration	267	168	0.000573
GO:0008154	actin polymerization or depolymerization	155	105	0.000608
GO:0030335	positive regulation of cell migration	443	263	0.000628
GO:0051129	negative regulation of cellular component organization	566	328	0.000642
GO:0098900	regulation of action potential	48	40	0.000679
GO:0016192	vesicle-mediated transport	1326	718	0.000692
GO:0048738	cardiac muscle tissue development	138	95	0.000696
GO:0018193	peptidyl-amino acid modification	1035	570	0.000741
GO:0030100	regulation of endocytosis	159	107	0.000773
GO:0042325	regulation of phosphorylation	1004	554	0.000779
GO:0051174	regulation of phosphorus metabolic process	1126	616	0.000825
GO:0051050	positive regulation of transport	709	402	0.000828
GO:2000147	positive regulation of cell motility	463	273	0.000841
GO:0043085	positive regulation of catalytic activity	960	531	0.000914
GO:0030048	actin filament-based movement	113	80	0.00094
GO:0019220	regulation of phosphate metabolic process	1125	615	0.000956
GO:0031623	receptor internalization	98	71	0.000992
GO:0006836	neurotransmitter transport	137	94	0.000993
GO:0031345	negative regulation of cell projection organization	125	87	0.000996
GO:0010977	negative regulation of neuron projection development	85	63	0.001143
GO:0032412	regulation of ion transmembrane transporter activity	222	142	0.001145
GO:0030178	negative regulation of Wnt signaling pathway	146	99	0.001179
GO:0031532	actin cytoskeleton reorganization	105	75	0.001196
GO:0010243	response to organonitrogen compound	613	351	0.001236
GO:0048598	embryonic morphogenesis	308	189	0.001311
GO:0008016	regulation of heart contraction	164	109	0.0015
GO:0006937	regulation of muscle contraction	119	83	0.001537
GO:0051241	negative regulation of multicellular organismal process	755	424	0.001593
GO:0007416	synapse assembly	126	87	0.00167
GO:0007229	integrin-mediated signaling pathway	104	74	0.001771
GO:0099173	postsynapse organization	99	71	0.001812
GO:0046903	secretion	638	363	0.001834
GO:0007163	establishment or maintenance of cell polarity	177	116	0.001975
GO:0071526	semaphorin-plexin signaling pathway	40	34	0.001997
GO:0050771	negative regulation of axonogenesis	43	36	0.00202
GO:0022898	regulation of transmembrane transporter activity	229	145	0.002021
GO:0055001	muscle cell development	118	82	0.002235
GO:1903522	regulation of blood circulation	188	122	0.002262
GO:0043412	macromolecule modification	3198	1641	0.002376
GO:0043408	regulation of MAPK cascade	534	308	0.002429
GO:0043087	regulation of GTPase activity	301	184	0.002542
GO:0031401	positive regulation of protein modification process	814	453	0.002569
GO:0046578	regulation of Ras protein signal transduction	139	94	0.002601
GO:1901699	cellular response to nitrogen compound	468	273	0.002746
GO:0032940	secretion by cell	571	327	0.002793
GO:0051966	regulation of synaptic transmission, glutamatergic	51	41	0.002884
GO:0008015	blood circulation	363	217	0.003065
GO:0051246	regulation of protein metabolic process	2072	1085	0.0031
GO:0098703	calcium ion import across plasma membrane	36	31	0.003323
GO:0060079	excitatory postsynaptic potential	45	37	0.003335
GO:0048813	dendrite morphogenesis	97	69	0.003994
GO:0010594	regulation of endothelial cell migration	154	102	0.004056
GO:0071417	cellular response to organonitrogen compound	413	243	0.004126
GO:0051146	striated muscle cell differentiation	170	111	0.004196
GO:0070588	calcium ion transmembrane transport	235	147	0.004516
GO:0070848	response to growth factor	516	297	0.004593
GO:0008360	regulation of cell shape	116	80	0.004638
GO:0021953	central nervous system neuron differentiation	74	55	0.004743

Table S6 (continued).

GO ID	GO Description	Universe	COSMIC	Adjusted
GO:0045229	external encapsulating structure organization	237	148	0.004792
GO:0051649	establishment of localization in cell	1698	897	0.004864
GO:0060048	cardiac muscle contraction	111	77	0.004996
GO:1901888	regulation of cell junction assembly	144	96	0.005129
GO:0090090	negative regulation of canonical Wnt signaling pathway	118	81	0.005334
GO:0033036	macromolecule localization	2245	1168	0.005414
GO:0006816	calcium ion transport	313	189	0.005544
GO:0060341	regulation of cellular localization	766	426	0.005581
GO:0043542	endothelial cell migration	194	124	0.005618
GO:0040013	negative regulation of locomotion	278	170	0.00585
GO:0006898	receptor-mediated endocytosis	214	135	0.005907
GO:0030198	extracellular matrix organization	234	146	0.005907
GO:0031400	negative regulation of protein modification process	409	240	0.006128
GO:0110053	regulation of actin filament organization	216	136	0.006298
GO:0060429	epithelium development	689	386	0.006326
GO:0030041	actin filament polymerization	129	87	0.007112
GO:0031098	stress-activated protein kinase signaling cascade	202	128	0.007442
GO:0060291	long-term synaptic potentiation	49	39	0.007819
GO:0043062	extracellular structure organization	235	146	0.008136
GO:1901379	regulation of potassium ion transmembrane transport	70	52	0.00878
GO:1902903	regulation of supramolecular fiber organization	311	187	0.008847
GO:0032880	regulation of protein localization	672	376	0.009649
GO:0043549	regulation of kinase activity	599	338	0.010664
GO:2001257	regulation of cation channel activity	153	100	0.011535
GO:0000122	negative regulation of transcription by RNA polymerase II	751	416	0.011781
GO:0002009	morphogenesis of an epithelium	275	167	0.012154
GO:0051403	stress-activated MAPK cascade	198	125	0.012154
GO:1990573	potassium ion import across plasma membrane	48	38	0.012766
GO:0120031	plasma membrane bounded cell projection assembly	483	277	0.013638
GO:0051258	protein polymerization	233	144	0.01366
GO:0045664	regulation of neuron differentiation	96	67	0.014735
GO:0007160	cell-matrix adhesion	195	123	0.015007
GO:0061572	actin filament bundle organization	136	90	0.015215
GO:0042327	positive regulation of phosphorylation	663	370	0.015238
GO:0007612	learning	53	41	0.015592
GO:0070252	actin-mediated cell contraction	86	61	0.016224
GO:0051338	regulation of transferase activity	718	398	0.016558
GO:0098901	regulation of cardiac muscle cell action potential	30	26	0.016851
GO:0051963	regulation of synapse assembly	58	44	0.017849
GO:0086065	cell communication involved in cardiac conduction	58	44	0.017849
GO:0051017	actin filament bundle assembly	133	88	0.018951
GO:0050678	regulation of epithelial cell proliferation	236	145	0.019404
GO:1990778	protein localization to cell periphery	279	168	0.021945
GO:0042592	homeostatic process	1249	666	0.022003
GO:0009792	embryo development ending in birth or egg hatching	198	124	0.022257
GO:0071363	cellular response to growth factor stimulus	499	284	0.022775
GO:0007215	glutamate receptor signaling pathway	44	35	0.023272
GO:0048640	negative regulation of developmental growth	60	45	0.023304
GO:0051961	negative regulation of nervous system development	85	60	0.023796
GO:0010959	regulation of metal ion transport	298	178	0.023909
GO:0097553	calcium ion transmembrane import into cytosol	146	95	0.024141
GO:0048762	mesenchymal cell differentiation	191	120	0.024283
GO:0048863	stem cell differentiation	155	100	0.02487
GO:0050879	multicellular organismal movement	41	33	0.025765
GO:0086091	regulation of heart rate by cardiac conduction	41	33	0.025765
GO:0050881	musculoskeletal movement	41	33	0.025765
GO:0032878	regulation of establishment or maintenance of cell polarity	26	23	0.026744
GO:0030031	cell projection assembly	498	283	0.027121
GO:0010232	vascular transport	87	61	0.027857
GO:0150104	transport across blood-brain barrier	87	61	0.027857
GO:0050919	negative chemotaxis	35	29	0.029641
GO:0050773	regulation of dendrite development	62	46	0.029645
GO:0030517	negative regulation of axon extension	32	27	0.030265
GO:0042982	amyloid precursor protein metabolic process	67	49	0.030628
GO:0007423	sensory organ development	271	163	0.030834
GO:0045785	positive regulation of cell adhesion	369	215	0.032573

Table S6 (continued).

GO ID	GO Description	Universe	COSMIC	Adjusted
GO:0009611	response to wounding	392	227	0.034051
GO:0050890	cognition	156	100	0.035799
GO:0001932	regulation of protein phosphorylation	882	479	0.035846
GO:0031323	regulation of cellular metabolic process	4966	2482	0.036928
GO:0051899	membrane depolarization	64	47	0.037241
GO:0001944	vasculature development	492	279	0.037414
GO:0002090	regulation of receptor internalization	43	34	0.037523
GO:0099643	signal release from synapse	91	63	0.037593
GO:0007269	neurotransmitter secretion	91	63	0.037593
GO:0010634	positive regulation of epithelial cell migration	133	87	0.038739
GO:0043254	regulation of protein-containing complex assembly	332	195	0.039459
GO:0045773	positive regulation of axon extension	22	20	0.039621
GO:0018108	peptidyl-tyrosine phosphorylation	246	149	0.040743
GO:0090596	sensory organ morphogenesis	119	79	0.040966
GO:0021954	central nervous system neuron development	40	32	0.042039
GO:2000249	regulation of actin cytoskeleton reorganization	40	32	0.042039
GO:0001933	negative regulation of protein phosphorylation	261	157	0.042119
GO:0018212	peptidyl-tyrosine modification	248	150	0.042279
GO:0010562	positive regulation of phosphorus metabolic process	722	397	0.042279
GO:0045937	positive regulation of phosphate metabolic process	722	397	0.042279
GO:0051668	localization within membrane	570	319	0.042433
GO:0048592	eye morphogenesis	81	57	0.042492
GO:0033554	cellular response to stress	1640	858	0.043396
GO:0045055	regulated exocytosis	162	103	0.044095
GO:1901021	positive regulation of calcium ion transmembrane transporter activity	37	30	0.046133
GO:0051347	positive regulation of transferase activity	447	255	0.046166
GO:0044092	negative regulation of molecular function	758	415	0.046963
GO:0006935	chemotaxis	480	272	0.049239
GO:0042330	taxis	480	272	0.049239

Table S7. Significant GO:BP enrichments for all CLINVAR G4 mutations.

GO ID	GO Description	Universe	CLINVAR	Adjusted P-value
GO:0006941	striated muscle contraction	142	32	1.1E-11
GO:0060048	cardiac muscle contraction	111	27	2.1E-10
GO:0050905	neuromuscular process	73	22	4.5E-10
GO:0035637	multicellular organismal signaling	128	28	1.1E-09
GO:0001508	action potential	117	26	5.2E-09
GO:0030048	actin filament-based movement	113	25	1.5E-08
GO:0070252	actin-mediated cell contraction	86	20	7.0E-07
GO:0061337	cardiac conduction	91	20	1.9E-06
GO:0086001	cardiac muscle cell action potential	73	18	2.0E-06
GO:0006937	regulation of muscle contraction	119	22	7.3E-06
GO:0086003	cardiac muscle cell contraction	62	15	5.8E-05
GO:0051899	membrane depolarization	64	15	8.9E-05
GO:1903115	regulation of actin filament-based movement	32	11	9.0E-05
GO:0060415	muscle tissue morphogenesis	47	13	9.1E-05
GO:0048644	muscle organ morphogenesis	47	13	9.1E-05
GO:0002027	regulation of heart rate	84	17	1.1E-04
GO:0098900	regulation of action potential	48	13	1.2E-04
GO:0086002	cardiac muscle cell action potential involved in contraction	48	13	1.2E-04
GO:0050954	sensory perception of mechanical stimulus	106	18	5.7E-04
GO:0086065	cell communication involved in cardiac conduction	58	13	1.0E-03
GO:0006942	regulation of striated muscle contraction	78	15	1.1E-03
GO:0007605	sensory perception of sound	100	17	1.1E-03
GO:0086091	regulation of heart rate by cardiac conduction	41	11	1.2E-03
GO:0050881	musculoskeletal movement	41	11	1.2E-03
GO:0050879	multicellular organismal movement	41	11	1.2E-03
GO:0019226	transmission of nerve impulse	42	11	1.5E-03
GO:0055008	cardiac muscle tissue morphogenesis	42	11	1.5E-03
GO:0048738	cardiac muscle tissue development	138	20	1.5E-03
GO:0055001	muscle cell development	118	18	2.5E-03
GO:0003009	skeletal muscle contraction	36	10	2.5E-03
GO:0014706	striated muscle tissue development	144	20	2.8E-03
GO:0086005	ventricular cardiac muscle cell action potential	29	9	3.1E-03
GO:0050885	neuromuscular process controlling balance	16	7	3.4E-03
GO:0098901	regulation of cardiac muscle cell action potential	30	9	4.2E-03
GO:0003229	ventricular cardiac muscle tissue development	39	10	5.3E-03
GO:0048592	eye morphogenesis	81	14	8.1E-03
GO:0055010	ventricular cardiac muscle tissue morphogenesis	33	9	9.3E-03
GO:0055117	regulation of cardiac muscle contraction	61	12	9.8E-03
GO:0086019	cell-cell signaling involved in cardiac conduction	34	9	1.2E-02
GO:0008306	associative learning	19	7	1.2E-02
GO:0086010	membrane depolarization during action potential	35	9	1.5E-02
GO:0050953	sensory perception of light stimulus	138	18	1.9E-02
GO:0086004	regulation of cardiac muscle cell contraction	28	8	2.0E-02
GO:0043589	skin morphogenesis	5	4	2.6E-02
GO:0002028	regulation of sodium ion transport	68	12	2.7E-02
GO:0048661	positive regulation of smooth muscle cell proliferation	49	10	3.6E-02
GO:0048483	autonomic nervous system development	31	8	4.1E-02
GO:0060348	bone development	108	15	4.5E-02

Table S8. Significant GO:BP enrichments for COSMIC and CLINVAR G4 mutations leading to the loss of a G4.

GO ID	GO Description	Universe	COSMIC and CLINVAR	Adjusted P-value
GO:0032502	developmental process	4584	1138	3.23E-24
GO:0048856	anatomical structure development	4152	1043	2.82E-23
GO:0007399	nervous system development	1648	488	1.15E-22
GO:0009653	anatomical structure morphogenesis	1871	539	2.18E-22
GO:0048731	system development	2976	784	9.30E-22
GO:0007275	multicellular organism development	3266	842	1.00E-20
GO:0032501	multicellular organismal process	5319	1270	1.40E-20
GO:0030154	cell differentiation	2860	742	3.10E-18
GO:0048699	generation of neurons	969	309	3.31E-18
GO:0048869	cellular developmental process	2879	745	5.24E-18
GO:0016043	cellular component organization	5370	1259	6.78E-17
GO:0022008	neurogenesis	1096	335	1.06E-16
GO:0030182	neuron differentiation	923	292	1.76E-16
GO:0071840	cellular component organization or biogenesis	5539	1277	2.38E-14
GO:0023051	regulation of signaling	2733	694	3.06E-14
GO:0010646	regulation of cell communication	2727	692	4.16E-14
GO:0048666	neuron development	729	236	4.22E-14
GO:0000904	cell morphogenesis involved in differentiation	495	175	7.97E-14
GO:0048468	cell development	1355	385	9.16E-14
GO:0048513	animal organ development	2176	567	3.84E-13
GO:0023052	signaling	5190	1196	9.50E-13
GO:0032989	cellular component morphogenesis	549	186	1.02E-12
GO:0007154	cell communication	5221	1200	2.02E-12
GO:0031175	neuron projection development	656	212	2.53E-12
GO:0048667	cell morphogenesis involved in neuron differentiation	381	140	3.85E-12
GO:0034330	cell junction organization	518	176	4.81E-12
GO:0000902	cell morphogenesis	718	226	6.91E-12
GO:0048812	neuron projection morphogenesis	441	155	9.70E-12
GO:0007010	cytoskeleton organization	1309	365	1.42E-11
GO:0009966	regulation of signal transduction	2464	621	1.59E-11
GO:0009887	animal organ morphogenesis	582	190	2.87E-11
GO:0007155	cell adhesion	1216	342	3.26E-11
GO:0120036	plasma membrane bounded cell projection organization	1144	325	3.84E-11
GO:0120039	plasma membrane bounded cell projection morphogenesis	455	157	3.85E-11
GO:0048858	cell projection morphogenesis	459	157	8.90E-11
GO:0030030	cell projection organization	1164	328	9.33E-11
GO:0032990	cell part morphogenesis	469	159	1.42E-10
GO:0030029	actin filament-based process	717	219	5.92E-10
GO:0061564	axon development	323	118	1.06E-09
GO:0007409	axonogenesis	298	111	1.25E-09
GO:0050808	synapse organization	275	104	2.31E-09
GO:0050793	regulation of developmental process	1810	465	4.44E-09
GO:0051128	regulation of cellular component organization	1929	490	6.77E-09
GO:0007165	signal transduction	4776	1078	4.27E-08
GO:0016477	cell migration	1210	325	7.79E-08
GO:0048870	cell motility	1362	359	8.30E-08
GO:0098609	cell-cell adhesion	743	217	8.39E-08
GO:0051716	cellular response to stimulus	5982	1316	9.92E-08
GO:0035556	intracellular signal transduction	2168	534	1.26E-07
GO:0048583	regulation of response to stimulus	3327	777	1.74E-07
GO:0051239	regulation of multicellular organismal process	2117	522	1.84E-07
GO:0099537	trans-synaptic signaling	501	157	2.02E-07
GO:0099536	synaptic signaling	522	162	2.28E-07
GO:0009888	tissue development	1239	329	2.43E-07
GO:0098916	anterograde trans-synaptic signaling	495	155	2.81E-07
GO:0007268	chemical synaptic transmission	495	155	2.81E-07
GO:0065007	biological regulation	10721	2221	3.01E-07
GO:0072359	circulatory system development	729	211	3.69E-07
GO:0065008	regulation of biological quality	2937	692	5.65E-07
GO:0050794	regulation of cellular process	9523	1993	7.40E-07
GO:0007267	cell-cell signaling	1269	333	7.84E-07
GO:0003008	system process	1358	351	1.64E-06
GO:0007417	central nervous system development	584	173	2.68E-06
GO:0009987	cellular process	14783	2936	4.03E-06

Table S8 (continued).

GO ID	GO Description	Universe	COSMIC and CLINVAR	Adjusted P-value
GO:0040011	locomotion	1075	285	5.65E-06
GO:0050789	regulation of biological process	10085	2089	8.77E-06
GO:1905114	cell surface receptor signaling pathway involved in cell-cell signaling	388	123	1.03E-05
GO:0030036	actin cytoskeleton organization	637	183	1.15E-05
GO:0050804	modulation of chemical synaptic transmission	252	88	1.18E-05
GO:0030048	actin filament-based movement	113	49	1.44E-05
GO:0099177	regulation of trans-synaptic signaling	253	88	1.46E-05
GO:0006812	cation transport	886	240	1.55E-05
GO:0030001	metal ion transport	678	192	1.58E-05
GO:0010975	regulation of neuron projection development	288	97	1.61E-05
GO:0060047	heart contraction	187	70	1.80E-05
GO:0006811	ion transport	1187	307	1.99E-05
GO:0048518	positive regulation of biological process	5294	1158	2.05E-05
GO:0034329	cell junction assembly	341	110	2.35E-05
GO:0032879	regulation of localization	1615	400	2.54E-05
GO:0044057	regulation of system process	392	122	3.78E-05
GO:0007411	axon guidance	169	64	4.59E-05
GO:0097485	neuron projection guidance	169	64	4.59E-05
GO:0051179	localization	4343	964	4.59E-05
GO:0048522	positive regulation of cellular process	4704	1036	5.30E-05
GO:0007507	heart development	338	108	5.46E-05
GO:0006936	muscle contraction	260	88	6.00E-05
GO:0055085	transmembrane transport	1060	276	6.09E-05
GO:0034220	ion transmembrane transport	816	221	6.22E-05
GO:0042391	regulation of membrane potential	319	103	6.34E-05
GO:0048523	negative regulation of cellular process	3896	872	6.65E-05
GO:0003015	heart process	193	70	7.53E-05
GO:0007166	cell surface receptor signaling pathway	2271	536	8.29E-05
GO:0003012	muscle system process	305	99	8.73E-05
GO:1902531	regulation of intracellular signal transduction	1429	356	9.28E-05
GO:0061061	muscle structure development	407	124	1.07E-04
GO:0040012	regulation of locomotion	842	225	1.46E-04
GO:0098655	cation transmembrane transport	656	182	1.81E-04
GO:0048646	anatomical structure formation involved in morphogenesis	751	203	2.65E-04
GO:0048519	negative regulation of biological process	4381	964	2.73E-04
GO:0048729	tissue morphogenesis	348	108	2.78E-04
GO:0007416	synapse assembly	126	50	2.85E-04
GO:0022603	regulation of anatomical structure morphogenesis	700	191	3.10E-04
GO:0051960	regulation of nervous system development	257	85	3.10E-04
GO:0030334	regulation of cell migration	767	206	3.51E-04
GO:0050905	neuromuscular process	73	34	3.51E-04
GO:0031589	cell-substrate adhesion	290	93	3.99E-04
GO:0050896	response to stimulus	7117	1503	4.02E-04
GO:0031344	regulation of cell projection organization	467	136	4.37E-04
GO:0003013	circulatory system process	443	130	5.12E-04
GO:0065009	regulation of molecular function	2121	498	5.42E-04
GO:0006810	transport	3620	807	5.65E-04
GO:0120035	regulation of plasma membrane bounded cell projection organization	453	132	6.34E-04
GO:0008015	blood circulation	363	110	7.79E-04
GO:0030111	regulation of Wnt signaling pathway	274	88	7.79E-04
GO:0007420	brain development	384	115	8.24E-04
GO:0051130	positive regulation of cellular component organization	844	221	9.67E-04
GO:2000145	regulation of cell motility	818	215	1.04E-03
GO:0006996	organelle organization	3147	708	1.04E-03
GO:0070252	actin-mediated cell contraction	86	37	1.15E-03
GO:0051056	regulation of small GTPase mediated signal transduction	238	78	1.44E-03
GO:0050877	nervous system process	755	200	1.46E-03
GO:0051234	establishment of localization	3775	834	1.55E-03
GO:0060048	cardiac muscle contraction	111	44	1.57E-03
GO:0051094	positive regulation of developmental process	967	247	1.64E-03
GO:0098662	inorganic cation transmembrane transport	572	158	1.65E-03
GO:0051963	regulation of synapse assembly	58	28	1.69E-03
GO:0060322	head development	402	118	1.74E-03
GO:0001667	ameboidal-type cell migration	333	101	2.14E-03

Table S8 (continued).

GO ID	GO Description	Universe	COSMIC and CLINVAR	Adjusted P-value
GO:0048638	regulation of developmental growth	167	59	2.18E-03
GO:0007167	enzyme-linked receptor protein signaling pathway	795	208	2.19E-03
GO:0008016	regulation of heart contraction	164	58	2.57E-03
GO:0051049	regulation of transport	1327	324	2.69E-03
GO:0006941	striated muscle contraction	142	52	2.76E-03
GO:0045595	regulation of cell differentiation	1129	281	2.82E-03
GO:0097435	supramolecular fiber organization	710	188	3.17E-03
GO:0035637	multicellular organismal signaling	128	48	3.20E-03
GO:0098660	inorganic ion transmembrane transport	622	168	3.22E-03
GO:0001505	regulation of neurotransmitter levels	143	52	3.47E-03
GO:0048598	embryonic morphogenesis	308	94	3.66E-03
GO:0010647	positive regulation of cell communication	1374	333	3.80E-03
GO:0006816	calcium ion transport	313	95	4.16E-03
GO:0009967	positive regulation of signal transduction	1255	307	4.32E-03
GO:0099565	chemical synaptic transmission, postsynaptic	51	25	4.41E-03
GO:0009719	response to endogenous stimulus	1076	268	4.62E-03
GO:0099587	inorganic ion import across plasma membrane	112	43	5.31E-03
GO:0098659	inorganic cation import across plasma membrane	112	43	5.31E-03
GO:0009790	embryo development	505	140	5.37E-03
GO:0098742	cell-cell adhesion via plasma-membrane adhesion molecules	195	65	5.93E-03
GO:0007169	transmembrane receptor protein tyrosine kinase signaling pathway	511	141	6.44E-03
GO:0023057	negative regulation of signaling	1067	265	6.57E-03
GO:1903522	regulation of blood circulation	188	63	6.84E-03
GO:0050807	regulation of synapse organization	124	46	7.05E-03
GO:0001508	action potential	117	44	7.54E-03
GO:0023056	positive regulation of signaling	1380	332	7.60E-03
GO:0051962	positive regulation of nervous system development	147	52	8.38E-03
GO:0198738	cell-cell signaling by wnt	343	101	8.47E-03
GO:0010631	epithelial cell migration	261	81	8.86E-03
GO:0043269	regulation of ion transport	458	128	9.01E-03
GO:0016358	dendrite development	155	54	9.18E-03
GO:0050803	regulation of synapse structure or activity	129	47	9.61E-03
GO:1903115	regulation of actin filament-based movement	32	18	9.75E-03
GO:1901888	regulation of cell junction assembly	144	51	9.80E-03
GO:0040008	regulation of growth	416	118	9.86E-03
GO:0007612	learning	53	25	1.00E-02
GO:0022607	cellular component assembly	2547	575	1.03E-02
GO:0010648	negative regulation of cell communication	1060	262	1.06E-02
GO:0042221	response to chemical	2943	656	1.07E-02
GO:0086001	cardiac muscle cell action potential	73	31	1.16E-02
GO:0071495	cellular response to endogenous stimulus	974	243	1.17E-02
GO:0090130	tissue migration	267	82	1.17E-02
GO:0090132	epithelium migration	263	81	1.19E-02
GO:0090596	sensory organ morphogenesis	119	44	1.21E-02
GO:0048738	cardiac muscle tissue development	138	49	1.34E-02
GO:0007269	neurotransmitter secretion	91	36	1.45E-02
GO:0099643	signal release from synapse	91	36	1.45E-02
GO:0016055	Wnt signaling pathway	339	99	1.47E-02
GO:0040007	growth	515	140	1.52E-02
GO:0048589	developmental growth	273	83	1.55E-02
GO:0098703	calcium ion import across plasma membrane	36	19	1.76E-02
GO:0099003	vesicle-mediated transport in synapse	121	44	1.91E-02
GO:0014706	striated muscle tissue development	144	50	2.13E-02
GO:0016310	phosphorylation	1444	342	2.13E-02
GO:0007517	muscle organ development	179	59	2.24E-02
GO:0034762	regulation of transmembrane transport	385	109	2.30E-02
GO:0006836	neurotransmitter transport	137	48	2.39E-02
GO:0044087	regulation of cellular component biogenesis	774	197	2.41E-02
GO:0086003	cardiac muscle cell contraction	62	27	2.50E-02
GO:0007611	learning or memory	115	42	2.61E-02
GO:0009968	negative regulation of signal transduction	1009	248	2.74E-02
GO:0090257	regulation of muscle system process	157	53	2.86E-02
GO:0035249	synaptic transmission, glutamatergic	66	28	3.09E-02
GO:0060560	developmental growth involved in morphogenesis	135	47	3.44E-02

Table S8 (continued).

GO ID	GO Description	Universe	COSMIC and CLINVAR	Adjusted P-value
GO:0002009	morphogenesis of an epithelium	275	82	3.61E-02
GO:0007264	small GTPase mediated signal transduction	389	109	3.61E-02
GO:0002027	regulation of heart rate	84	33	3.80E-02
GO:0043542	endothelial cell migration	194	62	3.82E-02
GO:0051668	localization within membrane	570	150	4.30E-02
GO:0086091	regulation of heart rate by cardiac conduction	41	20	4.31E-02
GO:0060828	regulation of canonical Wnt signaling pathway	211	66	4.44E-02
GO:0051965	positive regulation of synapse assembly	35	18	4.46E-02
GO:0048588	developmental cell growth	129	45	4.73E-02
GO:0099504	synaptic vesicle cycle	114	41	4.75E-02
GO:0042127	regulation of cell population proliferation	1218	291	4.82E-02
GO:0050890	cognition	156	52	4.83E-02
GO:0007158	neuron cell-cell adhesion	16	11	4.94E-02

Table S9. Significant GO:BP enrichments for COSMIC G4 mutations leading to the loss of a G4.

GO ID	GO Description	Universe	COSMIC	Adjusted P-value
GO:0009653	anatomical structure morphogenesis	1871	381	1.50E-10
GO:0016043	cellular component organization	5370	931	4.07E-10
GO:0032502	developmental process	4584	804	5.37E-09
GO:0071840	cellular component organization or biogenesis	5539	945	1.77E-08
GO:0048856	anatomical structure development	4152	734	1.85E-08
GO:0048699	generation of neurons	969	216	1.86E-08
GO:0007399	nervous system development	1648	333	2.19E-08
GO:0030182	neuron differentiation	923	204	1.65E-07
GO:0032501	multicellular organismal process	5319	904	2.10E-07
GO:0048731	system development	2976	543	2.40E-07
GO:0022008	Neurogenesis	1096	233	3.56E-07
GO:0007275	multicellular organism development	3266	587	4.31E-07
GO:0048666	neuron development	729	167	5.80E-07
GO:0030154	cell differentiation	2860	521	8.72E-07
GO:0048869	cellular developmental process	2879	523	1.24E-06
GO:0048468	cell development	1355	273	2.92E-06
GO:0010646	regulation of cell communication	2727	493	9.55E-06
GO:0023051	regulation of signaling	2733	492	1.83E-05
GO:0034330	cell junction organization	518	122	2.98E-05
GO:0031175	neuron projection development	656	147	3.28E-05
GO:0009966	regulation of signal transduction	2464	447	4.09E-05
GO:0048513	animal organ development	2176	401	4.17E-05
GO:0051128	regulation of cellular component organization	1929	360	6.48E-05
GO:0000904	cell morphogenesis involved in differentiation	495	116	9.06E-05
GO:0007010	cytoskeleton organization	1309	256	0.000164105
GO:0023052	Signaling	5190	860	0.000200273
GO:0007154	cell communication	5221	863	0.000302145
GO:0007155	cell adhesion	1216	239	0.000305302
GO:0050808	synapse organization	275	72	0.000421197
GO:0009887	animal organ morphogenesis	582	129	0.000483951
GO:0032989	cellular component morphogenesis	549	123	0.000504882
GO:0048667	cell morphogenesis involved in neuron differentiation	381	91	0.001066523
GO:0061564	axon development	323	80	0.001103984
GO:0065007	biological regulation	10721	1650	0.001653583
GO:0048812	neuron projection morphogenesis	441	101	0.002100476
GO:0120036	plasma membrane bounded cell projection organization	1144	222	0.002358738
GO:0048583	regulation of response to stimulus	3327	568	0.002363352
GO:0007409	Axonogenesis	298	74	0.002622931
GO:0003008	system process	1358	257	0.002627434
GO:0030030	cell projection organization	1164	225	0.002676372
GO:0035556	intracellular signal transduction	2168	387	0.002733973
GO:0032879	regulation of localization	1615	298	0.003442374
GO:0051239	regulation of multicellular organismal process	2117	378	0.003636668
GO:0000902	cell morphogenesis	718	149	0.003637049
GO:0007165	signal transduction	4776	786	0.003677398
GO:0098609	cell-cell adhesion	743	153	0.004206573
GO:0120039	plasma membrane bounded cell projection morphogenesis	455	102	0.00520267
GO:0006811	ion transport	1187	227	0.005379723
GO:0051179	Localization	4343	718	0.007233245
GO:0044057	regulation of system process	392	90	0.007238929
GO:0051716	cellular response to stimulus	5982	962	0.007709961
GO:0048858	cell projection morphogenesis	459	102	0.007839606
GO:0065008	regulation of biological quality	2937	503	0.00859953
GO:0097485	neuron projection guidance	169	47	0.009226901
GO:0007411	axon guidance	169	47	0.009226901
GO:0009888	tissue development	1239	234	0.009565902
GO:0050794	regulation of cellular process	9523	1473	0.010601198
GO:0006812	cation transport	886	175	0.011607738
GO:0032990	cell part morphogenesis	469	103	0.012164938
GO:0055085	transmembrane transport	1060	203	0.017138186
GO:0048598	embryonic morphogenesis	308	73	0.018555392
GO:0007417	central nervous system development	584	122	0.022813937
GO:0009790	embryo development	505	108	0.02527435
GO:0031589	cell-substrate adhesion	290	69	0.028200129

Table S9 (continued).

GO ID	GO Description	Universe Count	COSMIC Count	Adjusted P-value
GO:0040011	Locomotion	1075	204	0.029753799
GO:0050793	regulation of developmental process	1810	322	0.033576014
GO:0050905	neuromuscular process	73	25	0.036424405
GO:0048523	negative regulation of cellular process	3896	643	0.039903379
GO:0010975	regulation of neuron projection development	288	68	0.042350124
GO:0052697	xenobiotic glucuronidation	11	8	0.042820644
GO:0016477	cell migration	1210	225	0.043542025
GO:0003013	circulatory system process	443	96	0.043990329
GO:0048646	anatomical structure formation involved in morphogenesis	751	149	0.045881349
GO:0003012	muscle system process	305	71	0.046497064
GO:0048519	negative regulation of biological process	4381	715	0.049876587

Table S10. Significant GO:BP enrichments for CLINVAR G4 mutations leading to the loss of a G4.

GO ID	GO Description	Universe	CLINVAR	Adjusted P-value
GO:0006936	muscle contraction	260	21	1.07E-06
GO:0003012	muscle system process	305	22	1.86E-06
GO:0060048	cardiac muscle contraction	111	14	5.31E-06
GO:0006941	striated muscle contraction	142	15	9.47E-06
GO:0060047	heart contraction	187	16	3.82E-05
GO:0003015	heart process	193	16	4.82E-05
GO:0086003	cardiac muscle cell contraction	62	10	6.95E-05
GO:0086002	cardiac muscle cell action potential involved in contraction	48	9	9.09E-05
GO:0070252	actin-mediated cell contraction	86	11	1.12E-04
GO:0030048	actin filament-based movement	113	12	1.84E-04
GO:0086001	cardiac muscle cell action potential	73	10	2.19E-04
GO:0008016	regulation of heart contraction	164	13	8.37E-04
GO:0001508	action potential	117	11	1.31E-03
GO:0035637	multicellular organismal signaling	128	11	2.48E-03
GO:0008015	blood circulation	363	18	2.56E-03
GO:0003013	circulatory system process	443	20	2.56E-03
GO:1903522	regulation of blood circulation	188	13	2.64E-03
GO:0060348	bone development	108	10	3.32E-03
GO:0086005	ventricular cardiac muscle cell action potential	29	6	4.45E-03
GO:0061337	cardiac conduction	91	9	5.54E-03
GO:0044057	regulation of system process	392	17	1.65E-02
GO:0002027	regulation of heart rate	84	8	2.02E-02
GO:0001501	skeletal system development	289	14	2.76E-02
GO:0030279	negative regulation of ossification	26	5	2.93E-02
GO:0060537	muscle tissue development	218	12	3.16E-02

Table S11: Significant GO:BP enrichments for COSMIC and CLINVAR G4 mutations leading to the gain of a G4.

GO ID	GO Description	Universe	COSMIC And CLINVAR	Adjusted P-value
GO:0048856	anatomical structure development	4152	588	5.78E-18
GO:0032502	developmental process	4584	634	2.01E-17
GO:0048731	system development	2976	448	5.64E-17
GO:0007275	multicellular organism development	3266	480	1.76E-16
GO:0007399	nervous system development	1648	279	1.92E-15
GO:0009653	anatomical structure morphogenesis	1871	303	2.95E-14
GO:0048869	cellular developmental process	2879	419	7.27E-13
GO:0030154	cell differentiation	2860	416	1.07E-12
GO:0007155	cell adhesion	1216	209	2.10E-11
GO:0032501	multicellular organismal process	5319	684	2.28E-11
GO:0030029	actin filament-based process	717	138	2.88E-10
GO:1903508	positive regulation of nucleic acid-templated transcription	1297	215	3.71E-10
GO:0045893	positive regulation of DNA-templated transcription	1297	215	3.71E-10
GO:1902680	positive regulation of RNA biosynthetic process	1303	215	5.95E-10
GO:0045944	positive regulation of transcription by RNA polymerase II	952	167	2.58E-09
GO:0010646	regulation of cell communication	2727	384	3.03E-09
GO:0000902	cell morphogenesis	718	135	3.17E-09
GO:0023051	regulation of signaling	2733	384	4.14E-09
GO:0050793	regulation of developmental process	1810	274	5.89E-09
GO:0032989	cellular component morphogenesis	549	110	7.78E-09
GO:0051254	positive regulation of RNA metabolic process	1433	227	7.96E-09
GO:0030036	actin cytoskeleton organization	637	121	2.50E-08
GO:0048858	cell projection morphogenesis	459	95	3.88E-08
GO:0032990	cell part morphogenesis	469	96	5.73E-08
GO:0045935	positive regulation of nucleobase-containing compound metabolic process	1620	245	1.21E-07
GO:0010557	positive regulation of macromolecule biosynthetic process	1492	229	1.43E-07
GO:0048522	positive regulation of cellular process	4704	594	2.02E-07
GO:0031328	positive regulation of cellular biosynthetic process	1568	237	2.77E-07
GO:0048812	neuron projection morphogenesis	441	90	2.81E-07
GO:0007267	cell-cell signaling	1269	200	2.89E-07
GO:0120039	plasma membrane bounded cell projection morphogenesis	455	92	2.89E-07
GO:0048513	animal organ development	2176	309	3.69E-07
GO:0009891	positive regulation of biosynthetic process	1593	239	4.60E-07
GO:0009887	animal organ morphogenesis	582	109	6.23E-07
GO:0023052	signaling	5190	642	8.45E-07
GO:0048699	generation of neurons	969	160	8.71E-07
GO:0000904	cell morphogenesis involved in differentiation	495	96	1.14E-06
GO:0048468	cell development	1355	208	1.18E-06
GO:0007154	cell communication	5221	644	1.30E-06
GO:0030182	neuron differentiation	923	153	1.64E-06
GO:0022008	neurogenesis	1096	175	1.72E-06
GO:0030030	cell projection organization	1164	183	2.34E-06
GO:0120036	plasma membrane bounded cell projection organization	1144	180	3.05E-06
GO:0007010	cytoskeleton organization	1309	199	6.53E-06
GO:0099536	synaptic signaling	522	96	1.86E-05
GO:0048667	cell morphogenesis involved in neuron differentiation	381	76	2.12E-05
GO:0048518	positive regulation of biological process	5294	642	2.88E-05
GO:0031175	neuron projection development	656	113	3.77E-05
GO:0050804	modulation of chemical synaptic transmission	252	56	4.32E-05
GO:0099177	regulation of trans-synaptic signaling	253	56	4.97E-05
GO:0009966	regulation of signal transduction	2464	330	5.42E-05
GO:0022603	regulation of anatomical structure morphogenesis	700	118	6.09E-05
GO:0051173	positive regulation of nitrogen compound metabolic process	2565	341	6.44E-05
GO:0051239	regulation of multicellular organismal process	2117	289	8.50E-05
GO:0016043	cellular component organization	5370	646	9.41E-05
GO:0048666	neuron development	729	121	9.62E-05
GO:0031325	positive regulation of cellular metabolic process	2522	335	9.64E-05
GO:0099537	trans-synaptic signaling	501	90	1.58E-04
GO:0048589	developmental growth	273	57	2.93E-04
GO:0048523	negative regulation of cellular process	3896	484	2.94E-04
GO:0048870	cell motility	1362	197	3.32E-04
GO:0007268	chemical synaptic transmission	495	88	3.49E-04
GO:0098916	anterograde trans-synaptic signaling	495	88	3.49E-04

Table S11 (continued).

GO ID	GO Description	Universe	COSMIC And CLINVAR	Adjusted P-value
GO:0009987	cellular process	14783	1556	6.39E-04
GO:0034330	cell junction organization	518	90	7.04E-04
GO:0009888	tissue development	1239	180	8.89E-04
GO:0035556	intracellular signal transduction	2168	288	1.05E-03
GO:0007417	central nervous system development	584	98	1.09E-03
GO:0010604	positive regulation of macromolecule metabolic process	2889	369	1.09E-03
GO:0045595	regulation of cell differentiation	1129	166	1.22E-03
GO:0051128	regulation of cellular component organization	1929	260	1.31E-03
GO:0099587	inorganic ion import across plasma membrane	112	30	1.40E-03
GO:0098659	inorganic cation import across plasma membrane	112	30	1.40E-03
GO:0060322	head development	402	73	1.69E-03
GO:0071840	cellular component organization or biogenesis	5539	653	1.79E-03
GO:0048519	negative regulation of biological process	4381	529	2.36E-03
GO:0007409	axonogenesis	298	58	2.40E-03
GO:0009893	positive regulation of metabolic process	3177	398	2.59E-03
GO:0016477	cell migration	1210	174	2.61E-03
GO:0051716	cellular response to stimulus	5982	697	3.27E-03
GO:0060560	developmental growth involved in morphogenesis	135	33	3.51E-03
GO:0007420	brain development	384	69	4.70E-03
GO:0048729	tissue morphogenesis	348	64	4.93E-03
GO:0007165	signal transduction	4776	568	5.32E-03
GO:0061564	axon development	323	60	7.13E-03
GO:0014074	response to purine-containing compound	75	22	7.97E-03
GO:0048670	regulation of collateral sprouting	9	7	8.28E-03
GO:0048588	developmental cell growth	129	31	9.81E-03
GO:1990138	neuron projection extension	112	28	1.23E-02
GO:0050794	regulation of cellular process	9523	1052	1.23E-02
GO:0007167	enzyme-linked receptor protein signaling pathway	795	120	1.26E-02
GO:0098657	import into cell	216	44	1.26E-02
GO:0009719	response to endogenous stimulus	1076	154	1.31E-02
GO:0032970	regulation of actin filament-based process	330	60	1.36E-02
GO:0031344	regulation of cell projection organization	467	78	1.63E-02
GO:0071495	cellular response to endogenous stimulus	974	141	1.80E-02
GO:0120035	regulation of plasma membrane bounded cell projection organization	453	76	1.80E-02
GO:0098739	import across plasma membrane	172	37	1.85E-02
GO:0034329	cell junction assembly	341	61	1.88E-02
GO:0051094	positive regulation of developmental process	967	140	1.91E-02
GO:0048583	regulation of response to stimulus	3327	407	1.94E-02
GO:0007156	homophilic cell adhesion via plasma membrane adhesion molecules	63	19	2.15E-02
GO:0007015	actin filament organization	395	68	2.20E-02
GO:0032535	regulation of cellular component size	256	49	2.21E-02
GO:0048638	regulation of developmental growth	167	36	2.28E-02
GO:0007169	transmembrane receptor protein tyrosine kinase signaling pathway	511	83	2.39E-02
GO:0098742	cell-cell adhesion via plasma-membrane adhesion molecules	195	40	2.62E-02
GO:0051093	negative regulation of developmental process	619	96	3.43E-02
GO:0050789	regulation of biological process	10085	1103	3.55E-02
GO:0010243	response to organonitrogen compound	613	95	3.86E-02
GO:0098609	cell-cell adhesion	743	111	4.07E-02
GO:0048639	positive regulation of developmental growth	83	22	4.10E-02
GO:1905114	cell surface receptor signaling pathway involved in cell-cell signaling	388	66	4.13E-02
GO:0051172	negative regulation of nitrogen compound metabolic process	1927	249	4.44E-02
GO:0072359	circulatory system development	729	109	4.60E-02

Table S12. Significant GO:BP enrichments for COSMIC G4 mutations leading to the gain of a G4.

GO ID	GO Description	Universe	COSMIC	Adjusted P-value
GO:1903508	positive regulation of nucleic acid-templated transcription	1297	121	2.51E-05
GO:0045893	positive regulation of DNA-templated transcription	1297	121	2.51E-05
GO:1902680	positive regulation of RNA biosynthetic process	1303	121	3.28E-05
GO:0051254	positive regulation of RNA metabolic process	1433	129	6.57E-05
GO:0007155	cell adhesion	1216	111	0.00034137
GO:0045944	positive regulation of transcription by RNA polymerase II	952	92	0.00035644
GO:0045935	positive regulation of nucleobase-containing compound metabolic process	1620	137	0.00095303
GO:0046907	intracellular transport	1373	118	0.00307086
GO:0010557	positive regulation of macromolecule biosynthetic process	1492	126	0.00321361
GO:0031328	positive regulation of cellular biosynthetic process	1568	130	0.00562818
GO:0048856	anatomical structure development	4152	292	0.00721462
GO:0048522	positive regulation of cellular process	4704	325	0.00728079
GO:0009891	positive regulation of biosynthetic process	1593	130	0.01262319
GO:0010604	positive regulation of macromolecule metabolic process	2889	213	0.01326194
GO:0007275	multicellular organism development	3266	236	0.01514072
GO:0048731	system development	2976	218	0.01552671
GO:0051649	establishment of localization in cell	1698	136	0.01953263
GO:0009653	anatomical structure morphogenesis	1871	147	0.02240799
GO:0051173	positive regulation of nitrogen compound metabolic process	2565	191	0.02564038
GO:0032502	developmental process	4584	314	0.02643181
GO:0030036	actin cytoskeleton organization	637	62	0.03246111
GO:0051641	cellular localization	2721	200	0.03443678

Table S13. Significant GO:BP enrichments for CLINVAR G4 mutations leading to the gain of a G4.

GO ID	GO Description	Universe	CLINVAR	Adjusted P-value
GO:0001508	action potential	117	6	4.30E-02
GO:0086001	cardiac muscle cell action potential	73	5	4.96E-02

Table S14. Significant GO:CC enrichments for COSMIC and CLINVAR G4 mutations.

GO ID	GO Description	Universe	COSMIC and CLINVAR	Adjusted P-value
GO:0030054	cell junction	1385	893	2.16E-34
GO:0071944	cell periphery	5199	2884	2.79E-34
GO:0042995	cell projection	1567	979	3.89E-30
GO:0005886	plasma membrane	4762	2634	7.87E-29
GO:0120025	plasma membrane bounded cell projection	1540	959	1.11E-28
GO:0098590	plasma membrane region	794	529	4.09E-24
GO:0043005	neuron projection	839	553	1.42E-23
GO:0045202	synapse	652	445	2.85E-23
GO:0016020	membrane	7611	3986	9.36E-21
GO:0098797	plasma membrane protein complex	540	364	2.72E-17
GO:0030424	axon	339	243	4.48E-16
GO:0031226	intrinsic component of plasma membrane	1632	951	2.93E-15
GO:0005887	integral component of plasma membrane	1560	913	2.97E-15
GO:0015629	actin cytoskeleton	441	300	7.75E-15
GO:0036477	somatodendritic compartment	444	300	3.31E-14
GO:0005856	cytoskeleton	1812	1033	5.15E-13
GO:0031252	cell leading edge	289	206	5.23E-13
GO:0097060	synaptic membrane	160	126	9.52E-13
GO:0070161	anchoring junction	707	442	2.07E-12
GO:0043235	receptor complex	395	266	3.53E-12
GO:0098794	postsynapse	293	204	3.32E-11
GO:0005911	cell-cell junction	369	247	8.94E-11
GO:0097447	dendritic tree	341	230	1.79E-10
GO:0030425	dendrite	338	228	2.23E-10
GO:0005737	cytoplasm	10633	5335	1.52E-09
GO:0005912	adherens junction	144	110	1.96E-09
GO:0043228	non-membrane-bounded organelle	4394	2308	4.06E-09
GO:0043232	intracellular non-membrane-bounded organelle	4393	2307	4.57E-09
GO:0031224	intrinsic component of membrane	2600	1406	1.40E-08
GO:0005938	cell cortex	209	147	2.90E-08
GO:0099572	postsynaptic specialization	163	119	4.37E-08
GO:0005829	cytosol	5137	2662	6.95E-08
GO:0099081	supramolecular polymer	659	396	1.20E-07
GO:0098793	presynapse	241	164	1.37E-07
GO:0016021	integral component of membrane	2485	1339	1.60E-07
GO:0014069	postsynaptic density	151	110	2.64E-07
GO:0045211	postsynaptic membrane	106	82	3.26E-07
GO:0098984	neuron to neuron synapse	163	117	3.38E-07
GO:0099512	supramolecular fiber	650	389	3.45E-07
GO:0031982	vesicle	3535	1861	4.51E-07
GO:0042383	sarcolemma	77	63	5.11E-07
GO:0098978	glutamatergic synapse	82	66	7.67E-07
GO:0012505	endomembrane system	3988	2083	8.67E-07
GO:0032279	asymmetric synapse	158	113	9.15E-07
GO:0043025	neuronal cell body	209	143	1.00E-06
GO:0098588	bounding membrane of organelle	1644	905	1.02E-06
GO:0031253	cell projection membrane	215	146	1.50E-06
GO:0097708	intracellular vesicle	1967	1068	1.67E-06
GO:0031410	cytoplasmic vesicle	1966	1067	1.92E-06
GO:0043226	organelle	12740	6294	1.95E-06
GO:0019898	extrinsic component of membrane	282	184	1.95E-06
GO:0034702	ion channel complex	247	164	2.08E-06
GO:0044297	cell body	237	158	2.57E-06
GO:0034703	cation channel complex	218	147	2.71E-06
GO:0150034	distal axon	144	103	4.39E-06
GO:0005884	actin filament	105	79	5.83E-06
GO:0012506	vesicle membrane	881	504	8.55E-06
GO:0042734	presynaptic membrane	53	45	1.25E-05
GO:0030027	lamellipodium	135	96	2.09E-05
GO:0045177	apical part of cell	267	172	2.18E-05
GO:0005622	intracellular anatomical structure	13666	6714	2.42E-05
GO:0030659	cytoplasmic vesicle membrane	868	494	2.79E-05
GO:0019897	extrinsic component of plasma membrane	156	108	3.06E-05
GO:0099080	supramolecular complex	978	549	6.16E-05

Table S14 (continued).

GO ID	GO Description	Universe	COSMIC and CLINVAR	Adjusted P-value
GO:0009925	basal plasma membrane	177	119	8.22E-05
GO:0045178	basal part of cell	184	123	8.39E-05
GO:0042641	actomyosin	64	51	8.50E-05
GO:0031256	leading edge membrane	111	80	1.00E-04
GO:0098802	plasma membrane signaling receptor complex	176	118	1.14E-04
GO:0030863	cortical cytoskeleton	82	62	1.36E-04
GO:0044304	main axon	39	34	1.57E-04
GO:0048786	presynaptic active zone	39	34	1.57E-04
GO:0099634	postsynaptic specialization membrane	45	38	1.83E-04
GO:0016323	basolateral plasma membrane	158	107	1.85E-04
GO:0008328	ionotropic glutamate receptor complex	32	29	1.85E-04
GO:0098839	postsynaptic density membrane	35	31	2.38E-04
GO:0030055	cell-substrate junction	395	238	2.60E-04
GO:0030426	growth cone	88	65	2.96E-04
GO:0030427	site of polarized growth	93	68	3.11E-04
GO:0099513	polymeric cytoskeletal fiber	482	284	3.57E-04
GO:0005901	caveola	61	48	3.61E-04
GO:0005925	focal adhesion	387	233	3.62E-04
GO:0098796	membrane protein complex	1115	614	3.62E-04
GO:0016324	apical plasma membrane	234	149	4.01E-04
GO:0097517	contractile actin filament bundle	58	46	4.01E-04
GO:0001725	stress fiber	58	46	4.01E-04
GO:0000785	chromatin	1214	663	5.89E-04
GO:0098858	actin-based cell projection	133	91	6.17E-04
GO:0005604	basement membrane	65	50	7.08E-04
GO:0009898	cytoplasmic side of plasma membrane	160	106	9.53E-04
GO:0032432	actin filament bundle	64	49	1.11E-03
GO:0043292	contractile fiber	173	113	1.26E-03
GO:0005794	Golgi apparatus	1365	737	1.26E-03
GO:0045121	membrane raft	209	133	1.45E-03
GO:0005768	endosome	810	452	1.57E-03
GO:0030016	myofibril	165	108	1.74E-03
GO:0098862	cluster of actin-based cell projections	96	68	1.83E-03
GO:0098857	membrane microdomain	210	133	2.05E-03
GO:0044309	neuron spine	90	64	2.72E-03
GO:0044853	plasma membrane raft	87	62	3.30E-03
GO:0070382	exocytic vesicle	151	99	3.62E-03
GO:0043197	dendritic spine	89	63	3.94E-03
GO:0030017	sarcomere	146	96	4.06E-03
GO:0043229	intracellular organelle	11898	5852	4.14E-03
GO:0034705	potassium channel complex	91	64	4.68E-03
GO:0044291	cell-cell contact zone	50	39	4.80E-03
GO:0048471	perinuclear region of cytoplasm	440	255	5.80E-03
GO:0032589	neuron projection membrane	38	31	7.16E-03
GO:0031674	I band	97	67	7.44E-03
GO:0016342	catenin complex	32	27	7.57E-03
GO:0005769	early endosome	295	177	7.71E-03
GO:0030864	cortical actin cytoskeleton	62	46	8.23E-03
GO:0001726	ruffle	118	79	8.51E-03
GO:1902495	transmembrane transporter complex	331	196	8.99E-03
GO:0098878	neurotransmitter receptor complex	37	30	1.18E-02
GO:0030018	Z disc	86	60	1.19E-02
GO:0032420	stereocilium	31	26	1.29E-02
GO:0008021	synaptic vesicle	128	84	1.42E-02
GO:0031234	extrinsic component of cytoplasmic side of plasma membrane	95	65	1.48E-02
GO:0015630	microtubule cytoskeleton	1159	622	1.58E-02
GO:0030315	T-tubule	36	29	1.92E-02
GO:0016010	dystrophin-associated glycoprotein complex	17	16	2.25E-02
GO:0032281	AMPA glutamate receptor complex	20	18	3.07E-02
GO:0031941	filamentous actin	29	24	3.62E-02
GO:0005815	microtubule organizing center	724	397	3.66E-02
GO:0043194	axon initial segment	12	12	4.29E-02
GO:0008076	voltage-gated potassium channel complex	82	56	4.75E-02
GO:0034399	nuclear periphery	96	64	5.00E-02

Table S15. Significant GO:CC enrichments for COSMIC G4 mutations.

GO ID	GO Description	Universe	COSMIC	Adjusted P-value
GO:0071944	cell periphery	5199	2843	5.77E-34
GO:0030054	cell junction	1385	879	3.22E-33
GO:0042995	cell projection	1567	967	4.83E-30
GO:0005886	plasma membrane	4762	2598	7.93E-29
GO:0120025	plasma membrane bounded cell projection	1540	947	1.55E-28
GO:0045202	synapse	652	440	3.61E-23
GO:0098590	plasma membrane region	794	520	5.03E-23
GO:0043005	neuron projection	839	545	5.77E-23
GO:0016020	membrane	7611	3925	2.66E-20
GO:0030424	axon	339	242	1.07E-16
GO:0098797	plasma membrane protein complex	540	358	1.46E-16
GO:0005887	integral component of plasma membrane	1560	900	5.34E-15
GO:0015629	actin cytoskeleton	441	297	6.5E-15
GO:0031226	intrinsic component of plasma membrane	1632	936	9.92E-15
GO:0036477	somatodendritic compartment	444	296	6.2E-14
GO:0097060	synaptic membrane	160	126	2.17E-13
GO:0031252	cell leading edge	289	204	4.97E-13
GO:0005856	cytoskeleton	1812	1018	8.96E-13
GO:0070161	anchoring junction	707	436	3.3E-12
GO:0098794	postsynapse	293	202	3.02E-11
GO:0043235	receptor complex	395	259	8.91E-11
GO:0097447	dendritic tree	341	227	2.74E-10
GO:0030425	dendrite	338	225	3.47E-10
GO:0005911	cell-cell junction	369	242	5.32E-10
GO:0005912	adherens junction	144	110	5.79E-10
GO:0043228	non-membrane-bounded organelle	4394	2279	1.51E-09
GO:0043232	intracellular non-membrane-bounded organelle	4393	2278	1.7E-09
GO:0005737	cytoplasm	10633	5250	4.16E-09
GO:0099572	postsynaptic specialization	163	119	1.28E-08
GO:0005938	cell cortex	209	146	1.83E-08
GO:0031224	intrinsic component of membrane	2600	1385	2.07E-08
GO:0014069	postsynaptic density	151	110	8.66E-08
GO:0016021	integral component of membrane	2485	1322	1.01E-07
GO:0045211	postsynaptic membrane	106	82	1.31E-07
GO:0005829	cytosol	5137	2619	1.67E-07
GO:0098793	presynapse	241	162	1.7E-07
GO:0098984	neuron to neuron synapse	163	116	2.92E-07
GO:0099081	supramolecular polymer	659	389	3.35E-07
GO:0098978	glutamatergic synapse	82	66	3.5E-07
GO:0019898	extrinsic component of membrane	282	184	4.45E-07
GO:0034702	ion channel complex	247	164	5.27E-07
GO:0034703	cation channel complex	218	147	7.57E-07
GO:0032279	asymmetric synapse	158	112	8.12E-07
GO:0099512	supramolecular fiber	650	382	9.7E-07
GO:0042383	sarcolemma	77	62	1.08E-06
GO:0043025	neuronal cell body	209	141	1.5E-06
GO:0043226	organelle	12740	6199	1.51E-06
GO:0012505	endomembrane system	3988	2050	1.58E-06
GO:0031253	cell projection membrane	215	144	2.15E-06
GO:0005884	actin filament	105	79	2.5E-06
GO:0098588	bounding membrane of organelle	1644	889	3E-06
GO:0044297	cell body	237	156	3.16E-06
GO:0031982	vesicle	3535	1825	3.48E-06
GO:0097708	intracellular vesicle	1967	1050	3.97E-06
GO:0150034	distal axon	144	102	4.31E-06
GO:0031410	cytoplasmic vesicle	1966	1049	4.54E-06
GO:0042734	presynaptic membrane	53	45	7.12E-06
GO:0012506	vesicle membrane	881	497	9.91E-06
GO:0019897	extrinsic component of plasma membrane	156	108	1.15E-05
GO:0030027	lamellipodium	135	95	2.2E-05
GO:0005622	intracellular anatomical structure	13666	6611	2.35E-05
GO:0030659	cytoplasmic vesicle membrane	868	487	3.36E-05
GO:0042641	actomyosin	64	51	4.76E-05
GO:0099080	supramolecular complex	978	542	5.51E-05
GO:0030863	cortical cytoskeleton	82	62	7.1E-05

Table S15 (continued).

GO ID	GO Description	Universe	COSMIC	Adjusted P-value
GO:0048786	presynaptic active zone	39	34	0.000103
GO:0044304	main axon	39	34	0.000103
GO:0099634	postsynaptic specialization membrane	45	38	0.000116
GO:0031256	leading edge membrane	111	79	0.000126
GO:0008328	ionotropic glutamate receptor complex	32	29	0.000128
GO:0045177	apical part of cell	267	167	0.000152
GO:0030426	growth cone	88	65	0.000155
GO:0030427	site of polarized growth	93	68	0.000159
GO:0098839	postsynaptic density membrane	35	31	0.000161
GO:0001725	stress fiber	58	46	0.000242
GO:0097517	contractile actin filament bundle	58	46	0.000242
GO:0030055	cell-substrate junction	395	235	0.000271
GO:0045178	basal part of cell	184	120	0.000291
GO:0009925	basal plasma membrane	177	116	0.000304
GO:0098796	membrane protein complex	1115	606	0.000328
GO:0005925	focal adhesion	387	230	0.000389
GO:0009898	cytoplasmic side of plasma membrane	160	106	0.000405
GO:0005604	basement membrane	65	50	0.000416
GO:0098802	plasma membrane signaling receptor complex	176	115	0.000416
GO:0098858	actin-based cell projection	133	90	0.000646
GO:0099513	polymeric cytoskeletal fiber	482	279	0.000661
GO:0032432	actin filament bundle	64	49	0.000663
GO:0000785	chromatin	1214	653	0.000752
GO:0016323	basolateral plasma membrane	158	104	0.000776
GO:0005901	caveola	61	47	0.000777
GO:0016324	apical plasma membrane	234	146	0.000888
GO:0043292	contractile fiber	173	112	0.001057
GO:0005768	endosome	810	447	0.001123
GO:0030016	myofibril	165	107	0.001521
GO:0070382	exocytic vesicle	151	99	0.001679
GO:0098862	cluster of actin-based cell projections	96	67	0.002472
GO:0034705	potassium channel complex	91	64	0.002626
GO:0043229	intracellular organelle	11898	5765	0.002825
GO:1902495	transmembrane transporter complex	331	196	0.002936
GO:0045121	membrane raft	209	130	0.003563
GO:0030017	sarcomere	146	95	0.003962
GO:0005769	early endosome	295	176	0.004405
GO:0001726	ruffle	118	79	0.004484
GO:0044853	plasma membrane raft	87	61	0.004808
GO:0098857	membrane microdomain	210	130	0.00492
GO:0032589	neuron projection membrane	38	31	0.005071
GO:0030864	cortical actin cytoskeleton	62	46	0.005237
GO:0016342	catenin complex	32	27	0.005544
GO:0005794	Golgi apparatus	1365	720	0.006418
GO:0008021	synaptic vesicle	128	84	0.007447
GO:0098878	neurotransmitter receptor complex	37	30	0.008507
GO:0031234	extrinsic component of cytoplasmic side of plasma membrane	95	65	0.008596
GO:0044309	neuron spine	90	62	0.009397
GO:0031674	I band	97	66	0.009766
GO:0048471	perinuclear region of cytoplasm	440	250	0.011477
GO:0043197	dendritic spine	89	61	0.013481
GO:0030315	T-tubule	36	29	0.014156
GO:0030018	Z disc	86	59	0.016795
GO:0032281	AMPA glutamate receptor complex	20	18	0.02496
GO:0015630	microtubule cytoskeleton	1159	611	0.027121
GO:1990351	transporter complex	356	204	0.02757
GO:0031941	filamentous actin	29	24	0.027799
GO:0008076	voltage-gated potassium channel complex	82	56	0.029877
GO:0044291	cell-cell contact zone	50	37	0.033809
GO:0043194	axon initial segment	12	12	0.036977
GO:0016363	nuclear matrix	79	54	0.037414
GO:0099240	intrinsic component of synaptic membrane	34	27	0.037971
GO:0032420	stereocilium	31	25	0.042583
GO:0005815	microtubule organizing center	724	391	0.043147

Table S16. Significant GO:CC enrichments for CLINVAR G4 mutations.

GO ID	GO Description	Universe	CLINVAR	Adjusted P-value
GO:0030017	sarcomere	146	26	9.1E-08
GO:0031674	I band	97	16	5.6E-04
GO:0042383	sarcolemma	77	14	7.7E-04
GO:0036379	myofilament	25	8	1.6E-03
GO:0030315	T-tubule	36	9	3.3E-03
GO:0005865	striated muscle thin filament	21	7	4.4E-03
GO:0014704	intercalated disc	32	8	9.8E-03
GO:0030018	Z disc	86	13	1.1E-02
GO:0043202	lysosomal lumen	87	13	1.2E-02
GO:0033268	node of Ranvier	12	5	2.1E-02
GO:0043194	axon initial segment	12	5	2.1E-02
GO:1990584	cardiac Troponin complex	3	3	2.2E-02
GO:0044291	cell-cell contact zone	50	9	4.0E-02
GO:0005861	troponin complex	8	4	4.8E-02

Table S17. Significant KEGG enrichments for COSMIC and CLINVAR G4 mutations.

KEGG ID	KEGG Description	Universe	COSMIC and CLINVAR	Adjusted P-value
KEGG:04360	Axon guidance	181	137	9.52E-13
KEGG:04921	Oxytocin signaling pathway	154	120	1.19E-12
KEGG:05412	Arrhythmogenic right ventricular cardiomyopathy	77	68	1.05E-11
KEGG:04010	MAPK signaling pathway	294	201	2.43E-11
KEGG:04724	Glutamatergic synapse	114	92	4.31E-11
KEGG:04015	Rap1 signaling pathway	210	151	5.83E-11
KEGG:05200	Pathways in cancer	529	330	1.01E-10
KEGG:04510	Focal adhesion	200	143	5.00E-10
KEGG:04929	GnRH secretion	64	57	5.44E-10
KEGG:04728	Dopaminergic synapse	132	100	4.36E-09
KEGG:04261	Adrenergic signaling in cardiomyocytes	150	111	4.46E-09
KEGG:04072	Phospholipase D signaling pathway	147	109	5.47E-09
KEGG:04014	Ras signaling pathway	234	159	1.91E-08
KEGG:01522	Endocrine resistance	95	75	4.97E-08
KEGG:04725	Cholinergic synapse	113	86	7.34E-08
KEGG:04020	Calcium signaling pathway	239	160	9.32E-08
KEGG:04912	GnRH signaling pathway	93	73	1.37E-07
KEGG:05414	Dilated cardiomyopathy	95	74	1.96E-07
KEGG:04713	Circadian entrainment	97	75	2.75E-07
KEGG:04720	Long-term potentiation	67	55	9.00E-07
KEGG:05215	Prostate cancer	97	74	9.96E-07
KEGG:04934	Cushing syndrome	153	107	1.96E-06
KEGG:04750	Inflammatory mediator regulation of TRP channels	98	74	2.12E-06
KEGG:05410	Hypertrophic cardiomyopathy	90	69	2.26E-06
KEGG:04810	Regulation of actin cytoskeleton	216	143	2.26E-06
KEGG:04012	ErbB signaling pathway	84	65	3.13E-06
KEGG:04925	Aldosterone synthesis and secretion	98	73	6.95E-06
KEGG:04151	PI3K-Akt signaling pathway	353	216	1.11E-05
KEGG:04722	Neurotrophin signaling pathway	119	85	1.35E-05
KEGG:04911	Insulin secretion	86	65	1.49E-05
KEGG:04022	cGMP-PKG signaling pathway	166	112	1.84E-05
KEGG:05213	Endometrial cancer	58	47	2.40E-05
KEGG:04370	VEGF signaling pathway	59	47	6.10E-05
KEGG:04730	Long-term depression	59	47	6.10E-05
KEGG:04660	T cell receptor signaling pathway	103	74	6.17E-05
KEGG:05214	Glioma	75	57	6.46E-05
KEGG:04927	Cortisol synthesis and secretion	64	50	7.72E-05
KEGG:04070	Phosphatidylinositol signaling system	97	70	9.54E-05
KEGG:04919	Thyroid hormone signaling pathway	121	84	1.09E-04
KEGG:04662	B cell receptor signaling pathway	79	59	1.11E-04
KEGG:01521	EGFR tyrosine kinase inhibitor resistance	79	59	1.11E-04
KEGG:05165	Human papillomavirus infection	331	200	1.17E-04
KEGG:04928	Parathyroid hormone synthesis, secretion and action	106	75	1.33E-04
KEGG:05166	Human T-cell leukemia virus 1 infection	219	139	1.37E-04
KEGG:04330	Notch signaling pathway	59	46	2.38E-04
KEGG:05224	Breast cancer	147	98	2.42E-04
KEGG:05031	Amphetamine addiction	69	52	3.10E-04
KEGG:04727	GABAergic synapse	89	64	3.38E-04
KEGG:04380	Osteoclast differentiation	125	85	3.47E-04
KEGG:04390	Hippo signaling pathway	157	103	3.97E-04
KEGG:05225	Hepatocellular carcinoma	166	108	4.11E-04
KEGG:05205	Proteoglycans in cancer	205	129	6.14E-04
KEGG:05222	Small cell lung cancer	92	65	7.28E-04
KEGG:04935	Growth hormone synthesis, secretion and action	120	81	8.95E-04
KEGG:04658	Th1 and Th2 cell differentiation	89	63	9.14E-04
KEGG:04666	Fc gamma R-mediated phagocytosis	96	67	1.01E-03
KEGG:04611	Platelet activation	124	83	1.13E-03
KEGG:04971	Gastric acid secretion	76	55	1.22E-03
KEGG:05220	Chronic myeloid leukemia	76	55	1.22E-03
KEGG:04512	ECM-receptor interaction	88	62	1.36E-03
KEGG:05032	Morphine addiction	90	63	1.60E-03
KEGG:04310	Wnt signaling pathway	170	108	1.92E-03
KEGG:04926	Relaxin signaling pathway	129	85	2.15E-03
KEGG:04371	Apelin signaling pathway	138	90	2.24E-03

Table S17 (continued).

KEGG ID	KEGG Description	Universe	COSMIC and CLINVAR	Adjusted P-value
KEGG:05235	PD-L1 expression and PD-1 checkpoint pathway in cancer	89	62	2.34E-03
KEGG:05231	Choline metabolism in cancer	98	67	2.83E-03
KEGG:04910	Insulin signaling pathway	137	89	3.06E-03
KEGG:04922	Glucagon signaling pathway	107	72	3.22E-03
KEGG:04144	Endocytosis	251	151	3.24E-03
KEGG:05226	Gastric cancer	148	95	3.33E-03
KEGG:04659	Th17 cell differentiation	105	70	6.43E-03
KEGG:05210	Colorectal cancer	86	59	7.15E-03
KEGG:04540	Gap junction	88	60	8.16E-03
KEGG:05135	Yersinia infection	136	87	8.37E-03
KEGG:04520	Adherens junction	71	50	9.16E-03
KEGG:04930	Type II diabetes mellitus	46	35	9.21E-03
KEGG:00562	Inositol phosphate metabolism	73	51	1.07E-02
KEGG:04931	Insulin resistance	108	71	1.10E-02
KEGG:04916	Melanogenesis	101	67	1.14E-02
KEGG:04024	cAMP signaling pathway	220	132	1.16E-02
KEGG:04917	Prolactin signaling pathway	70	49	1.35E-02
KEGG:05230	Central carbon metabolism in cancer	70	49	1.35E-02
KEGG:04960	Aldosterone-regulated sodium reabsorption	37	29	1.51E-02
KEGG:05223	Non-small cell lung cancer	72	50	1.56E-02
KEGG:05218	Melanoma	72	50	1.56E-02
KEGG:05163	Human cytomegalovirus infection	223	133	1.57E-02
KEGG:04664	Fc epsilon RI signaling pathway	67	47	1.68E-02
KEGG:04625	C-type lectin receptor signaling pathway	104	68	1.90E-02
KEGG:04721	Synaptic vesicle cycle	78	53	2.32E-02
KEGG:04071	Sphingolipid signaling pathway	119	76	2.41E-02
KEGG:04152	AMPK signaling pathway	121	77	2.59E-02
KEGG:04726	Serotonergic synapse	112	72	2.62E-02
KEGG:05219	Bladder cancer	41	31	2.74E-02
KEGG:04270	Vascular smooth muscle contraction	134	84	2.83E-02
KEGG:04933	AGE-RAGE signaling pathway in diabetic complications	100	65	3.26E-02
KEGG:05221	Acute myeloid leukemia	67	46	4.10E-02

Table S18. Significant KEGG enrichments for COSMIC G4 mutations.

GO ID	GO Description	Universe	COSMIC	Adjusted P-value
KEGG:04611	Platelet activation	124	81	0.002339
KEGG:05226	Gastric cancer	148	94	0.002757
KEGG:04144	Endocytosis	251	149	0.002928
KEGG:05166	Human T-cell leukemia virus 1 infection	219	132	0.003096
KEGG:04926	Relaxin signaling pathway	129	83	0.00414
KEGG:04024	cAMP signaling pathway	220	132	0.004174
KEGG:04935	Growth hormone synthesis, secretion and action	120	78	0.004212
KEGG:04520	Adherens junction	71	50	0.005182
KEGG:04930	Type II diabetes mellitus	46	35	0.005861
KEGG:00562	Inositol phosphate metabolism	73	51	0.006052
KEGG:04666	Fc gamma R-mediated phagocytosis	96	64	0.006737
KEGG:04658	Th1 and Th2 cell differentiation	89	60	0.007009
KEGG:05231	Choline metabolism in cancer	98	65	0.007447
KEGG:04960	Aldosterone-regulated sodium reabsorption	37	29	0.010324
KEGG:04910	Insulin signaling pathway	137	86	0.010713
KEGG:04916	Melanogenesis	101	66	0.012641
KEGG:04721	Synaptic vesicle cycle	78	53	0.013364
KEGG:05135	Yersinia infection	136	85	0.014406
KEGG:05235	PD-L1 expression and PD-1 checkpoint pathway in cancer	89	59	0.015883
KEGG:04922	Glucagon signaling pathway	107	69	0.015977
KEGG:05230	Central carbon metabolism in cancer	70	48	0.019532
KEGG:05210	Colorectal cancer	86	57	0.020522
KEGG:05218	Melanoma	72	49	0.022161
KEGG:04931	Insulin resistance	108	69	0.023655
KEGG:04152	AMPK signaling pathway	121	76	0.025197
KEGG:04270	Vascular smooth muscle contraction	134	83	0.025742
KEGG:05163	Human cytomegalovirus infection	223	130	0.026284
KEGG:05220	Chronic myeloid leukemia	76	51	0.027645
KEGG:04659	Th17 cell differentiation	105	67	0.030128
KEGG:04625	C-type lectin receptor signaling pathway	104	66	0.041098
KEGG:05030	Cocaine addiction	49	35	0.043077
KEGG:04071	Sphingolipid signaling pathway	119	74	0.045066
KEGG:04917	Prolactin signaling pathway	70	47	0.04558
KEGG:04540	Gap junction	88	57	0.047383

Table S19. Significant KEGG enrichments for CLINVAR G4 mutations.

KEGG ID	KEGG Description	Universe	CLINVAR	Adjusted P-value
KEGG:05414	Dilated cardiomyopathy	95	21	6.7E-07
KEGG:05410	Hypertrophic cardiomyopathy	90	20	1.4E-06
KEGG:05412	Arrhythmogenic right ventricular cardiomyopathy	77	18	3.4E-06
KEGG:04261	Adrenergic signaling in cardiomyocytes	150	23	1.0E-04
KEGG:04512	ECM-receptor interaction	88	16	5.1E-04
KEGG:04260	Cardiac muscle contraction	87	15	1.8E-03
KEGG:05221	Acute myeloid leukemia	67	12	7.9E-03
KEGG:05230	Central carbon metabolism in cancer	70	12	1.2E-02
KEGG:04919	Thyroid hormone signaling pathway	121	16	2.0E-02
KEGG:05220	Chronic myeloid leukemia	76	12	2.4E-02
KEGG:04912	GnRH signaling pathway	93	13	4.1E-02

Table S20. Significant KEGG enrichments for COSMIC and CLINVAR G4 mutations leading to a G4 loss.

KEGG ID	KEGG Description	Universe	COSMIC and CLINVAR	Adjusted P-value
KEGG:05412	Arrhythmogenic right ventricular cardiomyopathy	77	44	4.37E-11
KEGG:05414	Dilated cardiomyopathy	95	50	7.37E-11
KEGG:05410	Hypertrophic cardiomyopathy	90	48	1.15E-10
KEGG:04261	Adrenergic signaling in cardiomyocytes	150	61	1.83E-07
KEGG:04921	Oxytocin signaling pathway	154	60	1.62E-06
KEGG:04010	MAPK signaling pathway	294	95	7.23E-06
KEGG:04015	Rap1 signaling pathway	210	73	1.11E-05
KEGG:04510	Focal adhesion	200	70	1.52E-05
KEGG:04020	Calcium signaling pathway	239	80	1.63E-05
KEGG:04725	Cholinergic synapse	113	44	1.41E-04
KEGG:04151	PI3K-Akt signaling pathway	353	104	2.35E-04
KEGG:04514	Cell adhesion molecules	153	53	6.96E-04
KEGG:05200	Pathways in cancer	529	142	9.19E-04
KEGG:04022	cGMP-PKG signaling pathway	166	56	9.35E-04
KEGG:04024	cAMP signaling pathway	220	69	1.41E-03
KEGG:04512	ECM-receptor interaction	88	34	2.64E-03
KEGG:04810	Regulation of actin cytoskeleton	216	67	2.74E-03
KEGG:04925	Aldosterone synthesis and secretion	98	36	5.22E-03
KEGG:04360	Axon guidance	181	57	6.73E-03
KEGG:04929	GnRH secretion	64	26	8.78E-03
KEGG:04713	Circadian entrainment	97	35	9.76E-03
KEGG:04911	Insulin secretion	86	32	1.00E-02
KEGG:04662	B cell receptor signaling pathway	79	30	1.07E-02
KEGG:04934	Cushing syndrome	153	49	1.34E-02
KEGG:04724	Glutamatergic synapse	114	39	1.42E-02
KEGG:05165	Human papillomavirus infection	331	91	1.55E-02
KEGG:04014	Ras signaling pathway	234	68	1.95E-02
KEGG:04728	Dopaminergic synapse	132	43	2.21E-02
KEGG:05032	Morphine addiction	90	32	2.49E-02
KEGG:04390	Hippo signaling pathway	157	49	2.56E-02
KEGG:05224	Breast cancer	147	46	3.61E-02
KEGG:04730	Long-term depression	59	23	4.14E-02
KEGG:04727	GABAergic synapse	89	31	4.49E-02

Table S21. Significant KEGG enrichments for COSMIC G4 mutations leading to a G4 loss.

KEGG ID	KEGG Description	Universe	COSMIC	Adjusted P-value
KEGG:05410	Hypertrophic cardiomyopathy	90	37	9.29E-08
KEGG:05414	Dilated cardiomyopathy	95	38	1.37E-07
KEGG:05412	Arrhythmogenic right ventricular cardiomyopathy	77	32	9.49E-07
KEGG:04261	Adrenergic signaling in cardiomyocytes	150	43	5.39E-04
KEGG:04020	Calcium signaling pathway	239	59	1.65E-03
KEGG:04921	Oxytocin signaling pathway	154	42	2.51E-03
KEGG:04360	Axon guidance	181	45	1.33E-02
KEGG:04022	cGMP-PKG signaling pathway	166	42	1.47E-02
KEGG:04015	Rap1 signaling pathway	210	50	1.76E-02
KEGG:04510	Focal adhesion	200	48	1.92E-02
KEGG:04024	cAMP signaling pathway	220	51	2.94E-02
KEGG:04151	PI3K-Akt signaling pathway	353	74	3.78E-02

Table S22. Significant KEGG enrichments for CLINVAR G4 mutations leading to a G4 loss.

KEGG ID	KEGG Description	Universe	CLINVAR	Adjusted P-value
KEGG:05410	Hypertrophic cardiomyopathy	90	10	5.17E-04
KEGG:05414	Dilated cardiomyopathy	95	10	7.44E-04
KEGG:05412	Arrhythmogenic right ventricular cardiomyopathy	77	9	9.61E-04
KEGG:04261	Adrenergic signaling in cardiomyocytes	150	9	4.67E-02
KEGG:05221	Acute myeloid leukemia	67	6	5.00E-02

Table S23: Significant GO:CC enrichments for COSMIC and CLINVAR G4 mutations leading to a G4 gain.

KEGG ID	KEGG Description	Universe	COSMIC and CLINVAR	Adjusted P-value
KEGG:04929	GnRH secretion	64	22	1.99E-05
KEGG:05200	Pathways in cancer	529	89	5.62E-05
KEGG:04724	Glutamatergic synapse	114	30	8.27E-05
KEGG:04725	Cholinergic synapse	113	28	6.58E-04
KEGG:04919	Thyroid hormone signaling pathway	121	29	8.96E-04
KEGG:04015	Rap1 signaling pathway	210	42	1.20E-03
KEGG:04261	Adrenergic signaling in cardiomyocytes	150	33	1.45E-03
KEGG:05202	Transcriptional misregulation in cancer	192	39	1.70E-03
KEGG:04713	Circadian entrainment	97	24	3.03E-03
KEGG:04930	Type II diabetes mellitus	46	15	3.49E-03
KEGG:05210	Colorectal cancer	86	22	3.76E-03
KEGG:04010	MAPK signaling pathway	294	52	3.76E-03
KEGG:04928	Parathyroid hormone synthesis, secretion and action	106	25	4.76E-03
KEGG:04072	Phospholipase D signaling pathway	147	31	5.89E-03
KEGG:04730	Long-term depression	59	17	5.93E-03
KEGG:04921	Oxytocin signaling pathway	154	32	6.02E-03
KEGG:05218	Melanoma	72	19	7.97E-03
KEGG:04728	Dopaminergic synapse	132	28	1.16E-02
KEGG:04934	Cushing syndrome	153	31	1.22E-02
KEGG:04512	ECM-receptor interaction	88	21	1.52E-02
KEGG:05213	Endometrial cancer	58	16	1.62E-02
KEGG:04961	Endocrine and other factor-regulated calcium reabsorption	53	15	1.89E-02
KEGG:04510	Focal adhesion	200	37	1.91E-02
KEGG:04974	Protein digestion and absorption	103	23	2.09E-02
KEGG:04810	Regulation of actin cytoskeleton	216	39	2.15E-02
KEGG:05030	Cocaine addiction	49	14	2.72E-02
KEGG:04720	Long-term potentiation	67	17	2.91E-02
KEGG:04911	Insulin secretion	86	20	3.02E-02
KEGG:04151	PI3K-Akt signaling pathway	353	56	3.34E-02
KEGG:05165	Human papillomavirus infection	331	53	3.80E-02
KEGG:04540	Gap junction	88	20	4.06E-02

Table S24. Significant KEGG enrichments for COSMIC G4 mutations leading to a G4 gain.

KEGG ID	KEGG Description	Universe	COSMIC	Adjusted P-value
KEGG:05218	Melanoma	72	13	1.45E-02
KEGG:04072	Phospholipase D signaling pathway	147	20	1.59E-02
KEGG:05030	Cocaine addiction	49	10	2.90E-02

Table S25. Significant INTERPRO enrichments for COSMIC and CLINVAR G4 mutations.

INTERPRO ID	COSMIC and CLINVAR	UNIVERSE	FDR
IPR011993:Pleckstrin homology-like domain	150	446	1.41E-10
IPR001849:Pleckstrin homology domain	95	277	1.4E-06
IPR011009:Protein kinase-like domain	158	547	4.88E-06
IPR000719:Protein kinase, catalytic domain	146	502	9.19E-06
IPR013098:Immunoglobulin I-set	52	140	0.000295
IPR008271:Serine/threonine-protein kinase, active site	96	316	0.000295
IPR017441:Protein kinase, ATP binding site	113	390	0.000331
IPR017970:Homeobox, conserved site	65	193	0.000418
IPR001781:Zinc finger, LIM-type	32	75	0.001657
IPR001452:Src homology-3 domain	72	230	0.001677
IPR002219:Protein kinase C-like, phorbol ester/diacylglycerol binding	29	67	0.003026
IPR003598:Immunoglobulin subtype 2	76	254	0.004198
IPR013164:Cadherin, N-terminal	28	65	0.004198
IPR008936:Rho GTPase activation protein	35	95	0.013732
IPR015425:Actin-binding FH2	11	15	0.013732
IPR000008:C2 calcium-dependent membrane targeting	48	148	0.018196
IPR020479:Homeodomain, metazoa	34	93	0.018196
IPR013088:Zinc finger, NHR/GATA-type	24	57	0.021614
IPR001025:Bromo adjacent homology (BAH) domain	9	11	0.025203
IPR000536:Nuclear hormone receptor, ligand-binding, core	21	48	0.031914
IPR009057:Homeodomain-like	95	360	0.04254
IPR001478:PDZ domain	50	163	0.04254
IPR001628:Zinc finger, nuclear hormone receptor-type	20	46	0.045727

Table S26. Significant INTERPRO enrichments for COSMIC G4 mutations.

INTERPRO ID	COSMIC	Universe	FDR
IPR011993:Pleckstrin homology-like domain	147	446	1.30E-10
IPR001849:Pleckstrin homology domain	93	277	1.46E-06
IPR011009:Protein kinase-like domain	153	547	1.13E-05
IPR000719:Protein kinase, catalytic domain	141	502	2.55E-05
IPR013098:Immunoglobulin I-set	50	140	7.98E-04
IPR017441:Protein kinase, ATP binding site	109	390	7.98E-04
IPR017970:Homeobox, conserved site	63	193	7.98E-04
IPR008271:Serine/threonine-protein kinase, active site	91	316	1.39E-03
IPR002219:Protein kinase C-like, phorbol ester/diacylglycerol binding	29	67	1.98E-03
IPR001781:Zinc finger, LIM-type	31	75	2.42E-03
IPR013164:Cadherin, N-terminal	28	65	2.72E-03
IPR001452:Src homology-3 domain	69	230	3.73E-03
IPR008936:Rho GTPase activation protein	35	95	7.92E-03
IPR015425:Actin-binding FH2	11	15	1.09E-02
IPR020479:Homeodomain, metazoa	34	93	1.09E-02
IPR003598:Immunoglobulin subtype 2	72	254	1.39E-02
IPR000008:C2 calcium-dependent membrane targeting	47	148	1.68E-02
IPR001025:Bromo adjacent homology (BAH) domain	9	11	2.07E-02
IPR001478:PDZ domain	50	163	2.28E-02
IPR013088:Zinc finger, NHR/GATA-type	23	57	3.61E-02
IPR009057:Homeodomain-like	93	360	3.71E-02
IPR015919:Cadherin-like	39	121	4.08E-02
IPR002126:Cadherin	38	118	4.83E-02

Table S27. Significant INTERPRO enrichments for CLINVAR G4 mutations.

INTERPRO ID	CLINVAR	UNIVERSE	FDR
IPR000595:Cyclic nucleotide-binding domain	7	36	0.009358
IPR018490:Cyclic nucleotide-binding-like	7	39	0.009358

Table S28: Top 50 significant transcription factor enrichments for COSMIC and CLINVAR G4.

Transcription Factor ID	Transcription Factor Description	Universe	COSMIC and CLINVAR	FDR
TF:M09636_1	Factor: MAZ; motif: GGGMGGGGSSGGGGGGGGGGG; match class: 1	14379	7641	6.97E-262
TF:M09973_1	Factor: CPBP; motif: GNNRGGGHGGGGNNGGGRN; match class: 1	6788	4243	1.01E-254
TF:M09826_1	Factor: BTEB3; motif: CCNNSCCNSCCCCKCCCCC; match class: 1	7694	4675	1.41E-249
TF:M07289_1	Factor: GKLF; motif: NNNRGGNGNGGSN; match class: 1	10800	6111	2.57E-248
TF:M07039_1	Factor: ETF; motif: CCCCGCCCCYN; match class: 1	13890	7403	5.24E-241
TF:M09973	Factor: CPBP; motif: GNNRGGGHGGGGNNGGGRN	11087	6214	2.70E-238
TF:M09984	Factor: MAZ; motif: GGGGGAGGGGGNGRGRRRGNRG	9762	5614	4.46E-236
TF:M12351_1	Factor: TIEG1; motif: NCCCNSNCCCCGCCCCC; match class: 1	8412	4966	9.71E-228
TF:M09723	Factor: BTEB1; motif: GGGGGCGGGGCNGSGGGNGS	10228	5801	4.64E-226
TF:M09826	Factor: BTEB3; motif: CCNNSCCNSCCCCKCCCCC	11731	6462	1.50E-224
TF:M09984_1	Factor: MAZ; motif: GGGGGAGGGGGNGRGRRRGNRG; match class: 1	5696	3615	3.02E-220
TF:M10026	Factor: PATZ; motif: GGGGNGGGGGMKGGRRNGGNRN	8607	5037	2.42E-219
TF:M07040_1	Factor: GKLF; motif: NNRRGRRNGNSNNN; match class: 1	8337	4909	3.67E-219
TF:M00986_1	Factor: Churchill; motif: CGGGNN; match class: 1	10609	5947	4.14E-216
TF:M09723_1	Factor: BTEB1; motif: GGGGGCGGGGCNGSGGGNGS; match class: 1	6131	3819	2.47E-213
TF:M12160_1	Factor: KLF15; motif: RCCMCRCCCMCN; match class: 1	8212	4823	1.49E-208
TF:M10432_1	Factor: MAZ; motif: GGGMGGGGS; match class: 1	4484	2948	2.74E-203
TF:M12351	Factor: TIEG1; motif: NCCCNSNCCCCGCCCCC	12580	6766	2.59E-200
TF:M10432	Factor: MAZ; motif: GGGMGGGGS	9496	5399	2.34E-199
TF:M00933	Factor: Sp1; motif: CCCCGCCCCN	9913	5589	4.40E-199
TF:M10529	Factor: Sp1; motif: RGGGMGGRGSNGGGG	7039	4230	1.45E-197
TF:M04953	Factor: Sp1; motif: GGNDGGRGGCGGGG	8852	5093	1.56E-196
TF:M02089_1	Factor: E2F-3; motif: GGCGGGN; match class: 1	9606	5440	8.00E-196
TF:M10112	Factor: Miz-1; motif: NNRGGWGGGGGAGGGGMRR	8878	5103	9.30E-196
TF:M12160	Factor: KLF15; motif: RCCMCRCCCMCN	12959	6914	1.26E-195
TF:M09636	Factor: MAZ; motif: GGGMGGGGSSGGGGGGGGGGG	16533	8315	1.88E-194
TF:M10026_1	Factor: PATZ; motif: GGGGNGGGGGMKGGRRNGGNRN; match class: 1	5053	3219	9.11E-192
TF:M01104_1	Factor: MOVO-B; motif: GNGGGGG; match class: 1	5798	3599	1.13E-191
TF:M00932_1	Factor: Sp1; motif: NNGGGGCGGGGNN; match class: 1	6212	3805	5.40E-191
TF:M07395_1	Factor: Sp1; motif: NGGGGCGGGGN; match class: 1	6529	3956	1.81E-188
TF:M00931	Factor: Sp1; motif: GGGGCGGGGC	10524	5832	8.08E-187
TF:M00933_1	Factor: Sp1; motif: CCCCGCCCCN; match class: 1	5316	3340	7.30E-186
TF:M09834	Factor: ZNF148; motif: NNNNNNCCNNCCCCTCCCCCACCCN	7099	4227	3.40E-185
TF:M00932	Factor: Sp1; motif: NNGGGGCGGGGNN	10669	5892	5.01E-185
TF:M01303	Factor: SP1; motif: GGGGYGGGGNS	8089	4697	5.64E-183
TF:M03876_1	Factor: Kaiso; motif: GCMGGGRGCRGS; match class: 1	9311	5267	3.63E-182
TF:M07436	Factor: WT1; motif: NNGGGNGGGSGN	6637	3990	4.64E-181
TF:M07226	Factor: SP1; motif: NCCCCKCCCCC	8460	4865	2.87E-180
TF:M07397	Factor: ZBP89; motif: CCCCKCCCCCNN	7289	4306	2.95E-180
TF:M07289	Factor: GKLF; motif: NNNRGGNGNGGSN	14918	7675	3.00E-180
TF:M00196	Factor: Sp1; motif: NGGGGGCGGGGYN	10479	5792	1.13E-179

Table S28 (continued).

Transcription Factor ID	Transcription Factor Description	Universe	COSMIC and CLINVAR	FDR
TF:M10071	Factor: Sp1; motif: NGGGGGCGGGGCCNGGGGGGGG	8705	4978	1.41E-179
TF:M00931_1	Factor: Sp1; motif: GGGGCGGGGC; match class: 1	6075	3707	2.15E-179
TF:M11529_1	Factor: E2F-2; motif: GCGCGCGCNCS; match class: 1	14789	7621	5.14E-179
TF:M07395	Factor: Sp1; motif: NGGGGCGGGGN	10901	5975	1.19E-177
TF:M00196_1	Factor: Sp1; motif: NGGGGGCGGGGYN; match class: 1	6084	3703	4.14E-176
TF:M09970	Factor: KLF3; motif: NNNNNNGGGCGGGGCNNGN	7907	4589	3.12E-175
TF:M07039	Factor: ETF; motif: CCCCGCCCCYN	16656	8320	3.08E-174
TF:M01104	Factor: MOVO-B; motif: GNGGGGG	10486	5777	3.21E-173
TF:M12703_1	Factor: ZNF383; motif: SSNGGGMGGNGSNGGS; match class: 1	4453	2863	3.94E-173

Table S29. Count and percentage of effect of SNV calculated by thermodynamic MFE and ED changes in the G quadruplex sequence.

Change in Stability by SNV	Change in multiconfirm by SNV	Frequency	Percentage
Further stabilized	less diversity	6,417	17.105
no change	less diversity	3,835	10.222
Destabilized	less diversity	5,383	14.349
Further stabilized	no change	34	0.091
no change	no change	5,378	14.335
Destabilized	no change	39	0.104
Further stabilized	more diversity	3,984	10.619
no change	more diversity	2,849	7.594
Destabilized	more diversity	9,597	25.581

Table S30. Effect of transition mutation G→A in chr10:122,143,482 on potential binding for multiple transcription factors. All effects are strong.

Motif Position	Gene Symbol	Transcription factor binding match	Reference P-value	Alternate P-value	Allele Difference	Allele Effect Size
-3|6	NHLH1	tgtgtgggcAggtgggttg	0.0018	2.86E-05	2.1672	0.1850
-8|2	FOXO3	atgtgtgggcAggtgggttgg	0.0033	0.0001	2.3166	0.1431
-3|6	TAL1	tgtgtgggcAggtgggttg	0.0045	0.0001	2.3166	0.1814
-12|7	TP53	gtccattccatgtgtgggcAggtgggttgggtggggtga	0.0031	0.0001	2.3166	0.1149
-4|7	HES5	catgtgtgggcAggtgggttggg	0.0040	0.0001	2.2697	0.1547
-4|7	HES7	catgtgtgggcAggtgggttggg	0.0041	0.0002	2.2817	0.14880
1|8	USF2	gtgtgggcAggtgggtt	0.0026	0.0002	1.8992	0.1282
-11|3	EGR3	ttccatgtgtgggcGggtgggttgggtgg	3.47E-06	0.0002	-1.8709	-0.1170
-12|2	EGR3	ttccatgtgtgggcGggtgggttgggtgg	5.21E-06	0.0002	-1.8638	-0.1082
-11|2	EGR1	tccatgtgtgggcGggtgggttgggtg	6.63E-06	0.0002	-1.8447	-0.1058
-9|1	EGR2	atgtgtgggcGggtgggttgg	5.96E-06	0.0002	-1.4785	-0.1112
-11|2	EGR1	tccatgtgtgggcGggtgggttgggtg	4.59E-06	0.0003	-1.6940	-0.1215
-11|3	EGR2	ttccatgtgtgggcGggtgggttgggtgg	5.46E-06	0.0003	-1.7277	-0.1245
-12|3	EGR1	attccatgtgtgggcGggtgggttgggtggg	1.35E-05	0.0004	-1.9116	-0.1130
-8|1	EGR1	tgtgtgggcGggtgggttg	1.62E-05	0.0006	-1.9401	-0.1347
-6|3	ZNF740	tgtgtgggcGggtgggttg	4.86E-05	0.0011	-1.6642	-0.1248
-6|3	SP1	tgtgtgggcGggtgggttg	0.0001	0.0017	-1.0496	-0.1072
-6|4	KLF16	atgtgtgggcGggtgggttgg	0.0001	0.0021894	-1.5426264	-0.12738754
-7|9	SP4	cattccatgtgtgggcGggtgggttgggtgggg	0.0002	0.0023592	-1.76102043	-0.10166014
-6|4	SP1	atgtgtgggcGggtgggttgg	0.0002	0.00291348	-1.15354231	-0.11339262
-3|6	SP1	tgtgtgggcGggtgggttg	0.0002	0.00323868	-1.21127823	-0.11785306
-6|3	ZNF740	tgtgtgggcGggtgggttg	0.0002	0.00376701	-1.71699463	-0.13807642
-9|2	ZBTB7A	catgtgtgggcGggtgggttggg	0.0004	0.0038684	-1.3008656	-0.11661897
-11|5	SP4	cattccatgtgtgggcGggtgggttgggtgggg	0.0002	0.0047031	-1.86702905	-0.14590419
-6|4	SP3	atgtgtgggcGggtgggttgg	0.0003	0.00499582	-1.29081923	-0.13319603