

Table SI. Pathways identified from the mutated genes/proteins analyzed using the ConsensusPathDB database.

Pathway name	Number of genes size	Number of candidate genes (%)	P-value	Q-value	Pathway source
Receptor-type tyrosine-protein phosphatases	20	6 (30.0)	0.0000422	0.0165	Reactome
The retinoid cycle in cones (daylight vision)	7	4 (57.1)	0.0000453	0.0165	Reactome
The activation of arylsulfatases	14	5 (38.5)	0.0000493	0.0165	Reactome
Protein-protein interactions at synapses	88	11 (12.5)	0.0002160	0.0539	Reactome
mRNA surveillance pathway-Homo sapiens (human)	91	11 (12.1)	0.0002910	0.0539	KEGG
γ carboxylation, hypusine formation and arylsulfatase activation	40	7 (17.9)	0.0003310	0.0539	Reactome
Nucleotide Metabolism	19	5 (26.3)	0.0003750	0.0539	Wikipathways
RNA transport-Homo sapiens (human)	171	15 (8.8)	0.0008690	0.0990	KEGG
Neuronal System	368	25 (6.8)	0.0009780	0.0990	Reactome
Rho GTPase cycle	144	13 (9.3)	0.0011200	0.0990	Reactome
Biogenic amines are oxidatively deaminated to aldehydes by MAOA and MAOB	2	2 (100.0)	0.0011900	0.0990	Reactome
Rett syndrome causing genes	48	7 (14.6)	0.0012100	0.0990	Wikipathways
Ectoderm differentiation	142	13 (9.2)	0.0012800	0.0990	Wikipathways
Recycling pathway of L1	29	5 (17.9)	0.0024500	0.17600	Reactome
Sodium/proton exchangers	9	3 (33.3)	0.0029500	0.1760	Reactome
Death receptor signalling	141	12 (8.7)	0.0029800	0.1760	Reactome
Pentose phosphate pathway-Homo sapiens (human)	30	5 (16.7)	0.0033600	0.1760	KEGG
Regulation of CDC42 activity	30	5 (16.7)	0.0033600	0.1760	PID
5-Phosphoribose 1-diphosphate biosynthesis	3	2 (66.7)	0.0034900	0.1760	Reactome
PRPP biosynthesis	3	2 (66.7)	0.0034900	0.1760	HumanCyc
NRAGE signals death through JNK	61	7 (11.9)	0.0040600	0.1800	Reactome
Putrescine degradation III	10	3 (30.0)	0.0041000	0.1800	HumanCyc
Opsins	10	3 (30.0)	0.0041000	0.1800	Reactome
Cell death signaling via NRAGE, NRIF and NADE	78	8 (10.5)	0.0046100	0.1930	Reactome
p75 NTR receptor-mediated signaling	99	9 (9.4)	0.0059000	0.2370	Reactome
Mitochondrial ABC transporters	4	2 (50.0)	0.0068300	0.2370	Reactome
Amine oxidase reactions	4	2 (50.0)	0.0068300	0.2370	Reactome
Ion influx/efflux at host-pathogen interface	4	2 (50.0)	0.0068300	0.2370	Reactome
Wax biosynthesis	4	2 (50.0)	0.0068300	0.2370	Reactome
P2Y receptors	12	3 (25.0)	0.0071400	0.2400	Reactome
Signaling by Rho GTPases	435	25 (5.8)	0.0078400	0.2550	Reactome
Miscellaneous transport and binding events	24	4 (16.7)	0.0086300	0.2680	Reactome
GABA A receptor activation	13	3 (23.1)	0.0090500	0.2680	Reactome
TRAF6 mediated IRF7 activation in TLR7/8 or 9 signaling	13	3 (23.1)	0.0090500	0.2680	Reactome
Ion channel transport	179	13 (7.3)	0.0093000	0.2680	Reactome
Celecoxib pathway, pharmacodynamics	58	4 (6.9)	0.0002350	0.0351	PharmGKB
Sympathetic nerve pathway (pre- and post-ganglionic junction)	12	2 (16.7)	0.0017200	0.0626	PharmGKB
Presynaptic depolarization and calcium channel opening	13	2 (15.4)	0.0020300	0.0626	Reactome
GPCR dopamine D1-like receptor	50	3 (6.0)	0.0022500	0.0626	INOH
Vitamin B12 metabolism	51	3 (5.9)	0.0023900	0.0626	Wikipathways
Chromatin modifying enzymes	272	6 (2.2)	0.0029400	0.0626	Reactome
Chromatin organization	272	6 (2.2)	0.0029400	0.0626	Reactome
HH-Ncore	20	2 (10.0)	0.0048300	0.0799	Signalink
Canonical Wnt signaling pathway	20	2 (10.0)	0.0048300	0.0799	PID
Termination of O-glycan biosynthesis	26	2 (7.7)	0.0080900	0.1150	Reactome
Phase 2-plateau phase	28	2 (7.1)	0.0093400	0.1150	Reactome
Selenium micronutrient network	83	3 (3.6)	0.0093500	0.1150	Wikipathways

PID, Pathway Interaction Database; HumanCyc, Encyclopedia of Human Genes and Metabolism; PharmGKB, Pharmacogenomics Knowledge Base; INOH, Integrating Network Objects with Hierarchies.

Table SII. Therapeutic candidate drugs predicted using the mutated genes.

Gene	FDA approved drug candidates (Score >10)
c-KIT	Imatinib (98) Sunitinib (46) Dasatinib (45) Sorafenib (35) Nilotinib (27) Regorafenib (19) Ponatinib (11)
AR	Nilutamide (17) Flutamide (16) Bicalutamide (15) Fluoxymesterone (12) Methyltestosterone (10) Oxandrolone (10)
AVPR2	Conivaptan (17) Vasopressin (11)
MAOB	Pargyline (16)
CLCN2	Lubiprostone (14)
HTR2C	Olanzapine (13) Mirtazapine (11)
POLA1	Clofarabine (13)
BTK	Ibrutinib (13)
GSR	Carmustine (12)
CYSLTR1	Zafirlukast (12)
TLR7	Imiquimod (12)
APOB	Atorvastatin (10)
ARAF	Sorafenib (10)
BCHE, L3RA, ASMT, STS, GPR143, ELK1, SLC38A5, EBP, GATA1, HDAC6, KCND1, SYP, CACNA1F, FOXP3, TSPYL2, ALAS2, SLC7A3, IL2RG, HDAC8, ATRX, COX7B, ATP7A, LPAR4, SYTL4, TSC22D3, PSMD10, COL4A6, COL4A5, GUCY2F, TRPC5, AGTR2, NDUFA1, GRIA3, XIAP, STAG2, AIFM1, GPR119, HPRT1, CD40LG, F9, IDS, CNGA2, GABRE, GABRA3, GABRQ, MAGEA1, G6PD, MECP2, NR0B1, DMD, OTC, BCOR, MAOA, NDUFB11, TNK2, LRP2, GJB5, CACNA1E, DCP1B, KDM6B, HTT, MUC2, CACNA1D, ARID1A, PI4K2A, KCNQ3, CACNA2D1, IFNG	Not applicable

FDA, food and drug administration.