

## Supplementary Online Content

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This supplementary material has been provided by the authors to give readers additional information about their work.

## **eMethods.** Supplemental Methods

### **Whole exome sequencing**

*Discovery cohort.* All members of each family were sequenced at the same center (44 samples/15 families at the Center for Inherited Disease Research [CIDR], and 53 samples/18 families at the HudsonAlpha Institute for Biotechnology). One family with 4 members was sequenced at both centers (eMethods). The Agilent SureSelect 50Mb Human All Exon Kit (CIDR) and Nimblegen 44.1Mb SeqCap EZ Exome Capture version 2.0 (HudsonAlpha) were used for capture, and the Illumina HiSeq 2000 system was used for 100bp paired-end sequencing.

Samples were aligned to the human genome (build hg19) using Burrows Wheeler Aligner<sup>1</sup>. The Genome Analysis Toolkit (GATK)<sup>2</sup> was used for local realignment, base quality score recalibration, and multi-sample variant calling (Unified Genotyper) for the samples sequenced at CIDR and HudsonAlpha separately. GATK Variant Quality Score Recalibration<sup>3</sup> and recommended GATK training sets were used to create a high-quality set of variant calls.

ANNOVAR<sup>4</sup> was used to annotate high quality variants for predictions of variant location and function (using the RefSeq and UCSC databases). Custom scripts annotated variants for their allelic frequency in 1000 Genomes European American populations (2012, <http://www.1000genomes.org>)<sup>5</sup>, Exome Sequencing Project (ESP) European American populations (5400 release, <http://evs.gs.washington.edu/EVS/>)<sup>6</sup>, and dbSNP 137 (<http://www.ncbi.nlm.nih.gov/SNP/>)<sup>7</sup>. Allele frequencies were obtained from an internal frequency database of 283 unrelated samples without a known neurological phenotype sequenced at CIDR. SIFT<sup>8</sup>, Polyphen2<sup>9</sup>, MutPred<sup>10</sup>, and Gerp<sup>11</sup> were used to predict mutation deleteriousness and degree of locus conservation. Custom scripts annotated genes within relevant Gene Ontology (GO) (<http://www.geneontology.org>) categories,<sup>12</sup> and genes were determined to be brain-expressed based on significant expression above background.

*Replication cohort.* WES was performed at the Baylor College of Medicine (BCM) Human Genome Sequencing Center (HGSC) through the Baylor-Hopkins Center for Mendelian

Genomics initiative. Preparation and sequencing of genomic DNA was performed as previously described.<sup>13</sup> The BCM HGSC Core-developed library (VCRome 2.1)<sup>14</sup> was used for capture (covered all genes nominated from the discovery analysis at a depth of >50X), and the Illumina HiSeq 2000 system was used for sequencing. Sequencing data were processed through the HGSC-developed Mercury pipeline using the Atlas2 variant calling method<sup>15,16</sup> and annotated using the Cassandra annotation pipeline<sup>17</sup> based on ANNOVAR.

### **Gene Ontology and brain expression**

Custom scripts annotated genes that fell within Gene Ontology (GO) (<http://www.geneontology.org>)<sup>12</sup> categories of interest (GO:0042417 dopamine metabolic process, GO:0050780 dopamine receptor binding, GO:0007270 neuron-neuron synaptic transmission, GO:0050804 regulation of synaptic transmission, GO:0007212 dopamine receptor signaling pathway, GO:0004952 dopamine receptor activity, GO:0006511 ubiquitin-dependent protein catabolic process, GO:0006979 response to oxidative stress, GO:0016567 protein ubiquitination, GO:0031396 regulation of protein ubiquitination). Genes were determined to be brain-expressed based on significant expression above the background, as computed and normalized across Allen Brain Institute samples, following Allen Human Brain Atlas protocols (<http://www.brain-map.org>, downloaded 05/17/2012).

### **Family sequenced at both sequencing centers used in the discovery analysis**

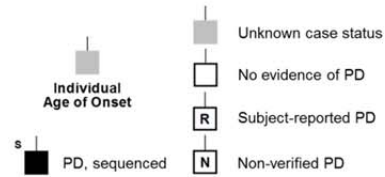
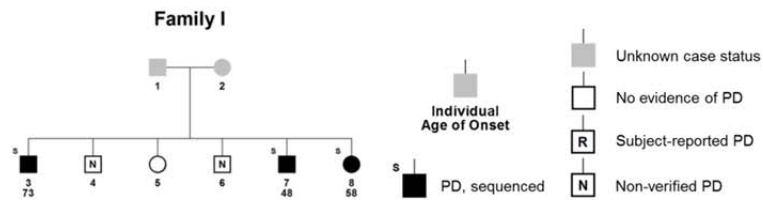
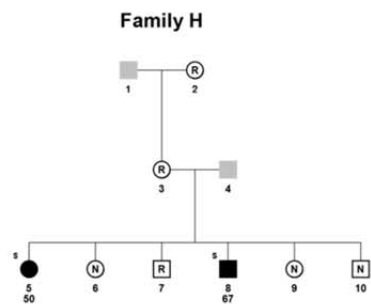
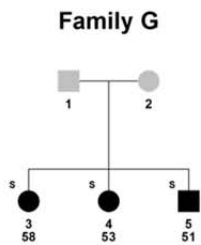
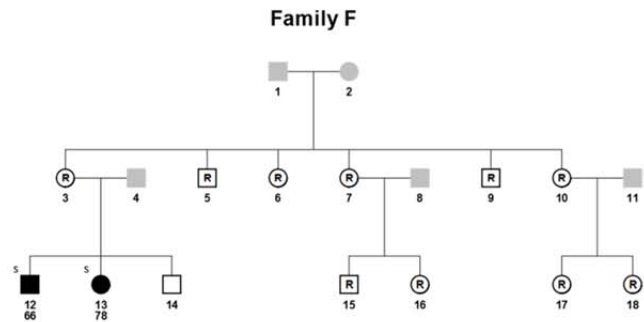
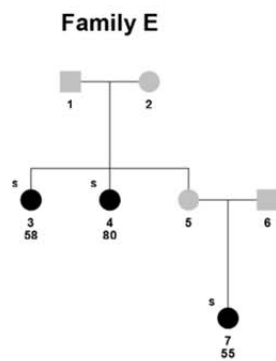
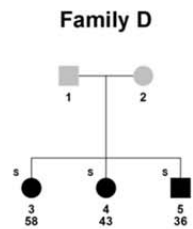
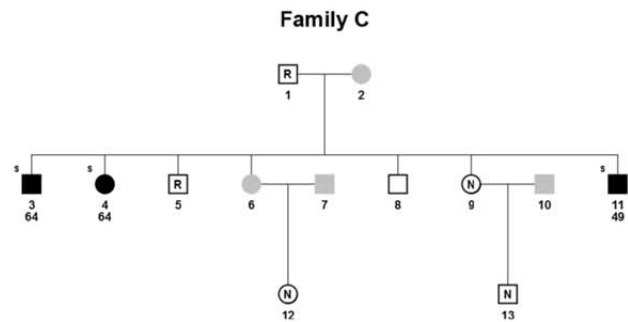
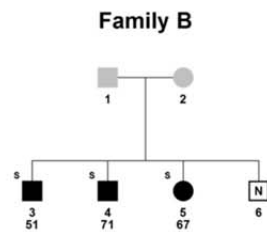
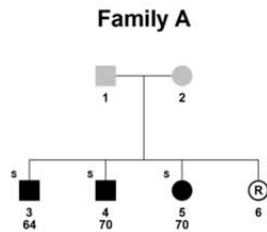
For the one family sequenced at both centers, summary sequencing statistics were compared to assess quality. Because two different captures were used, statistics were calculated only for those loci targeted by both capture kits. The intersection of variants found at both sequencing centers (32,280) and those sets of single nucleotide variants (SNVs) found only at one center (3,061 for the Center for Inherited Disease Research [CIDR]; 640 for HudsonAlpha) were examined. For SNVs found at the intersection, the genotype concordance rate was 99.0%, transition/transversion ratio was 3.0, and 99.0% were found in dbSNP137. Of those SNVs only identified at CIDR, the transition/transversion ratio was 2.4, and 98.3% were found in dbSNP137. For those SNVs found only at HudsonAlpha, the transition/transversion ratio was 1.8, and 86.1% were identified in dbSNP137.

### **Sequencing statistics**

For the discovery cohort, each sample sequenced at CIDR achieved a mean coverage of 98X for targeted bases, with an average of 93% of targeted bases covered at least 8X. The transition/transversion ratio was 3.3, and 94.4% of variants were found in dbSNP137. The sequencing data achieved 99.6% concordance with OmniExpress GWAS array genotype calls performed on the same individuals. Each sample sequenced at HudsonAlpha achieved a mean coverage of 57X for targeted bases, with an average of 93% of targeted bases covered at least 8X. The average transition/transversion ratio per sample was 3.2, and 91.5% of variants were found in dbSNP137.

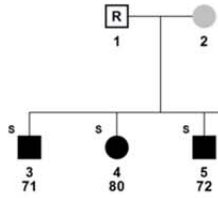
For the replication cohort, samples achieved an average of 94% of the targeted exome bases covered to a depth of 20X or greater. Sequencing yields averaged 9.9 Gb per sample. All three genes nominated from the discovery analysis were covered to a depth of 50X or greater.

**eFigure 1.** Pedigrees of Discovery Cohort Families A-I. Some subject genders have been changed to preserve pedigree confidentiality.

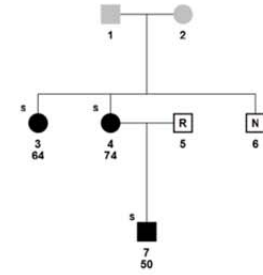


**eFigure 2.** Pedigrees of Discovery Cohort Families J-Q. Some subject genders have been changed to preserve pedigree confidentiality.

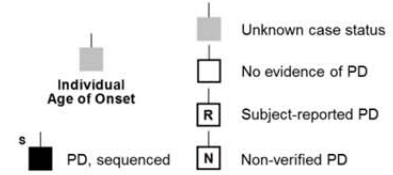
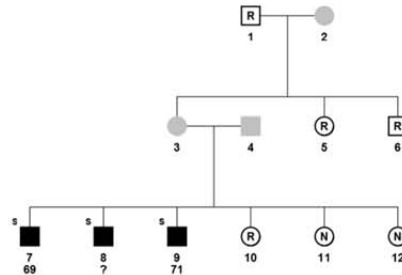
Family J



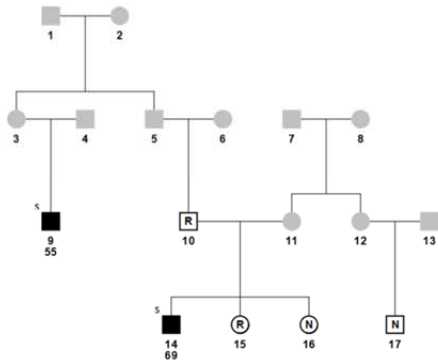
Family K



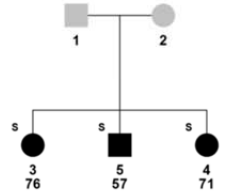
Family L



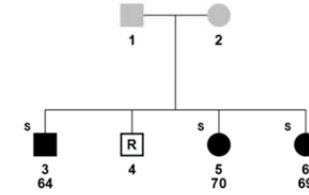
Family M



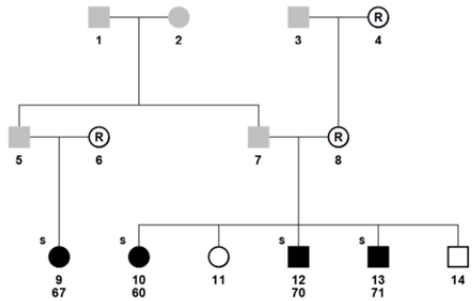
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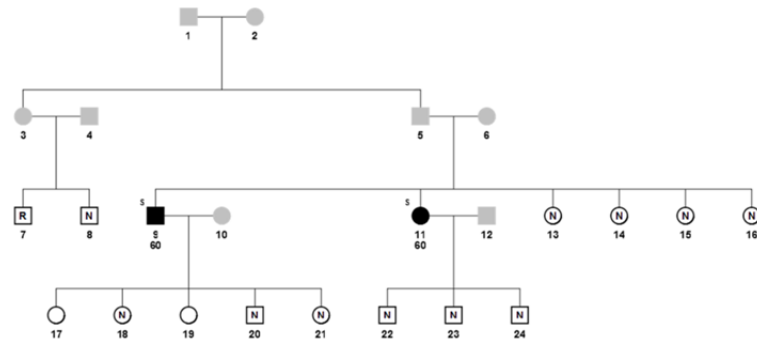
Family O



Family P

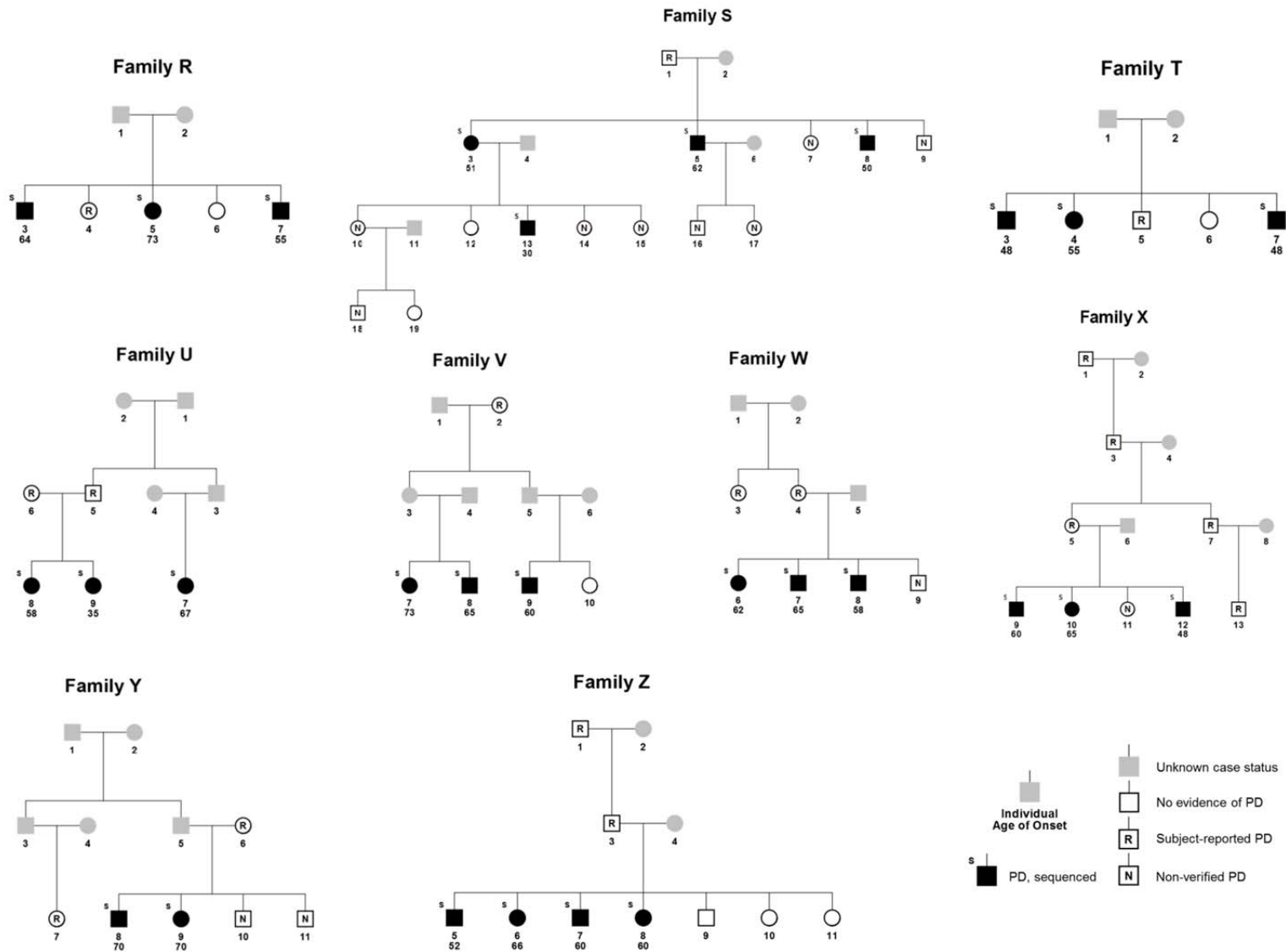


Family Q



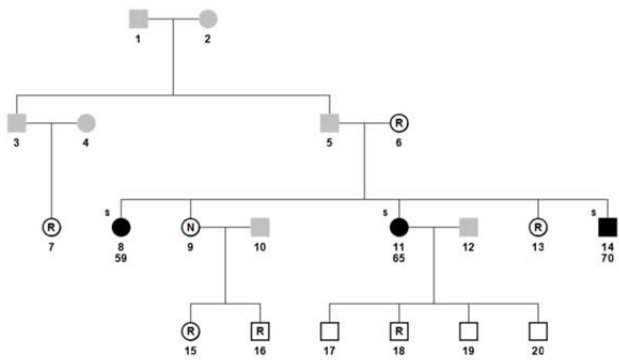


**eFigure 3.** Pedigrees of Discovery Cohort Families R-Z. Some subject genders have been changed to preserve pedigree confidentiality.

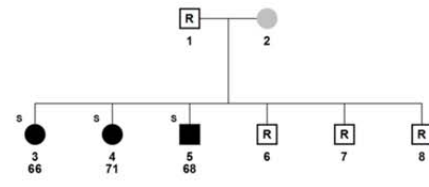


**eFigure 4.** Pedigrees of Discovery Cohort Families AA-AF. Some subject genders have been changed to preserve pedigree confidentiality.

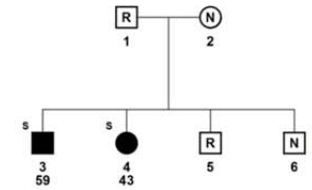
Family AA



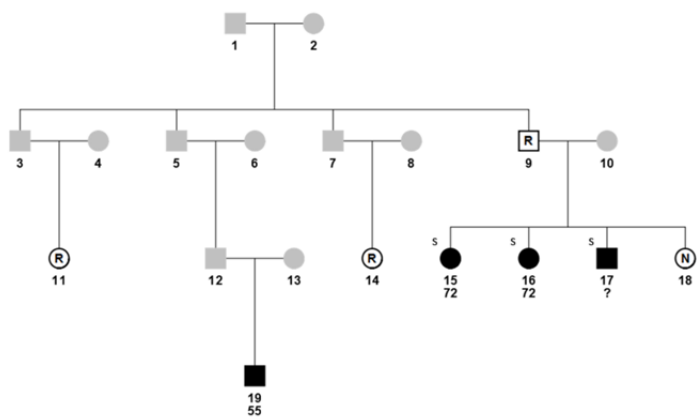
Family AB



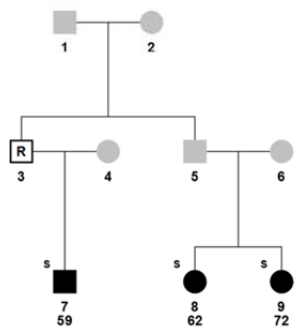
Family AC



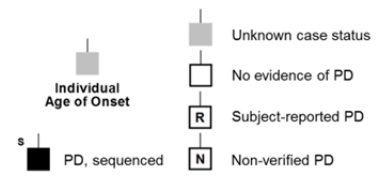
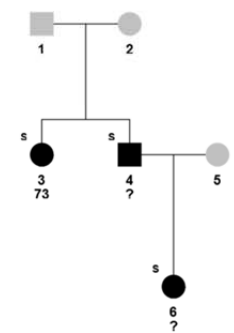
Family AD



Family AE



Family AF



**eTable 1.** Single-Nucleotide Variants Identified in the Filtered Genes With GO Annotation

Gene	Chr	Position	Ref	Alt	Exonic Prediction	Amino Acid Change	Families
UBE4B	1	10239594	C	T	nonsynonymous	NM_006048:c.C3434T:p.T1145M	AA,
KIF1B	1	10363664	G	T	nonsynonymous	NM_183416:c.G2421T:p.M807I	AD,
KIF1B	1	10363944	G	A	nonsynonymous	NM_183416:c.G2701A:p.E901K	AA,
KIF1B	1	10364260	A	G	nonsynonymous	NM_183416:c.A3017G:p.E1006G	Q,
PINK1	1	20964534	C	T	nonsynonymous	NM_032409:c.C587T:p.P196L	K,
PINK1	1	20971158	A	T	nonsynonymous	NM_032409:c.A952T:p.M318L	A,
USP48	1	22030884	T	C	nonsynonymous	NM_032236:c.A2386G:p.I796V	J,
NCDN	1	36025965	A	T	nonsynonymous	NM_001014841:c.A162T:p.K54N	I,
KCNC4	1	110765766	G	A	nonsynonymous	NM_001039574:c.G859A:p.V287I	N,
KCNJ10	1	160012270	C	T	nonsynonymous	NM_002241:c.G53A:p.R18Q	J,
DCAF8	1	160210035	G	A	nonsynonymous	NM_015726:c.C175T:p.R59C	A,
PPOX	1	161138933	C	G	nonsynonymous	NM_000309:c.C767G:p.P256R	X,
RC3H1	1	173952711	A	G	nonsynonymous	NM_172071:c.T437C:p.V146A	L,
TNR	1	175372714	T	G	nonsynonymous	NM_003285:c.A538C:p.N180H	P,
TNR	1	175375355	T	C	nonsynonymous	NM_003285:c.A496G:p.T166A	S,
TNR	1	175375388	A	T	nonsynonymous	NM_003285:c.T463A:p.C155S	AD,
PTPRC	1	198668761	G	C	nonsynonymous	NM_002838:c.G361C:p.D121H	Y,
PTPRC	1	198691595	T	A	nonsynonymous	NM_080921:c.T1221A:p.H407Q	Y,
TRIM17	1	228598822	A	G	nonsynonymous	NM_001024940:c.T581C:p.L194P	X,
TRIM17	1	228602563	G	C	nonsynonymous	NM_001024940:c.C211G:p.Q71E	X,
USP34	2	61415378	T	G	nonsynonymous	NM_014709:c.A10500C:p.L3500F	W,
TACR1	2	75278553	C	T	nonsynonymous	NM_001058:c.G757A:p.V253M	K,
USP39	2	85843539	G	C	nonsynonymous	NM_006590:c.G221C:p.R74P	AB,
RNF103	2	86831051	C	A	nonsynonymous	NM_005667:c.G1973T:p.C658F	I,
DNAJC10	2	183594621	G	C	nonsynonymous	NM_018981:c.G680C:p.S227T	AB,

ERBB4	2	212570096	T	C	nonsynonymous	NM_001042599:c.A1145G:p.E382G	R,
RNF25	2	219529924	T	G	nonsynonymous	NM_022453:c.A620C:p.Y207S	AB,
SERPINE2	2	224866427	A	G	nonsynonymous	NM_001136528:c.T191C:p.M64T	P,O,
OXTR	3	8809162	C	T	nonsynonymous	NM_000916:c.G712A:p.A238T	AC,
ATG7	3	11389483	C	T	nonsynonymous	NM_001144912:c.C1141T:p.R381W	I,
USP19	3	49146480	G	A	nonsynonymous	NM_006677:c.C3868T:p.R1290W	Z,
USP19	3	49152707	G	A	nonsynonymous	NM_006677:c.C1667T:p.A556V	Z,
USP4	3	49321424	T	C	nonsynonymous	NM_199443:c.A2395G:p.I799V	W,
PXK	3	58410621	G	C	nonsynonymous	NM_017771:c.G1671C:p.Q557H	Z,
PSMD6	3	64008067	T	C	nonsynonymous	NM_014814:c.A278G:p.K93R	AA,
ATG3	3	112262938	G	A	nonsynonymous	NM_022488:c.C359T:p.T120M	B,
TNK2	3	195594494	C	T	nonsynonymous	NM_005781:c.G2630A:p.R877H	C,B,AF ,A,
FGFR3	4	1803438	G	A	nonsynonymous	NM_000142:c.G707A:p.S236N	A,
FGFR3	4	1808659	G	A	nonsynonymous	NM_022965:c.G1936A:p.D646N	I,
HTT	4	3101073	G	C	nonsynonymous	NM_002111:c.G420C:p.E140D	A,
HTT	4	3189510	T	C	nonsynonymous	NM_002111:c.T5122C:p.C1708R	R,
WFS1	4	6303849	A	T	nonsynonymous	NM_001145853:c.A2327T:p.E776V	P,Z,
WFS1	4	6303974	C	T	nonsynonymous	NM_001145853:c.C2452T:p.R818C	Z,
HERC5	4	89380540	A	G	nonsynonymous	NM_016323:c.A308G:p.D103G	R,
USP38	4	144106616	C	G	nonsynonymous	NM_032557:c.C13G:p.L5V	Z,
ANAPC10	4	145916716	G	C	nonsynonymous	NM_014885:c.C367G:p.P123A	AB,
LIFR	5	38489213	T	C	nonsynonymous	NM_001127671:c.A2302G:p.R768G	J,
FBXO4	5	41934110	T	C	nonsynonymous	NM_012176:c.T709C:p.Y237H	AD,
SNCAIP	5	121786667	G	C	nonsynonymous	NM_005460:c.G2125C:p.E709Q	J,
FBXL21	5	135272512	C	T	nonsynonymous	NM_012159:c.C229T:p.H77Y	B,
FBXL21	5	135277065	G	A	nonsynonymous	NM_012159:c.G1010A:p.C337Y	W,
RNF130	5	179407158	T	C	nonsynonymous	NM_018434:c.A736G:p.T246A	X,

TBC1D7	6	13316909	G	T	nonsynonymous	NM_001143966:c.C332A:p.A111D	C,
DTNBP1	6	15524661	C	T	nonsynonymous	NM_183040:c.G907A:p.A303T	AB,
DTNBP1	6	15524679	G	A	nonsynonymous	NM_183040:c.C889T:p.H297Y	W,
PSMB9	6	32823948	G	A	nonsynonymous	NM_002800:c.G94A:p.V32I	AD,I,
CUL9	6	43172498	G	T	nonsynonymous	NM_015089:c.G4352T:p.S1451I	O,
CUL9	6	43191017	G	A	nonsynonymous	NM_015089:c.G7166A:p.R2389Q	P,
GRIK2	6	102337644	G	C	nonsynonymous	NM_001166247:c.G1654C:p.V552L	K,
HACE1	6	105232954	C	T	nonsynonymous	NM_020771:c.G1315A:p.A439T	K,
GRM1	6	146720826	G	A	nonsynonymous	NM_000838:c.G2651A:p.G884E	Q,AF,
PSMB1	6	170858128	T	C	nonsynonymous	NM_002793:c.A187G:p.I63V	X,
RNF216	7	5765020	C	A	nonsynonymous	NM_207111:c.G1439T:p.S480I	Z,
USP42	7	6189373	C	T	nonsynonymous	NM_032172:c.C1546T:p.H516Y	AA,
USP42	7	6189906	T	G	nonsynonymous	NM_032172:c.T2079G:p.F693L	AA,
USP42	7	6194213	G	A	nonsynonymous	NM_032172:c.G3028A:p.E1010K	I,
CAMK2B	7	44259684	C	T	nonsynonymous	NM_172084:c.G1327A:p.A443T	AA,
FBXO24	7	100192117	G	A	nonsynonymous	NM_001163499:c.G869A:p.R290H	X,
TRIM56	7	100731638	C	T	nonsynonymous	NM_030961:c.C1045T:p.L349F	AA,AD,
NUB1	7	151042447	G	T	nonsynonymous	NM_016118:c.G12T:p.K4N	K,
ADRA1A	8	26722027	A	C	nonsynonymous	NM_000680:c.T460G:p.S154A	Y,H,X,
VCPIP1	8	67547341	C	T	nonsynonymous	NM_025054:c.G3064A:p.V1022I	I,
UBE2W	8	74722861	T	C	nonsynonymous	NM_018299:c.A214G:p.M72V	O,
DCAF13	8	104427354	C	T	nonsynonymous	NM_015420:c.C136T:p.H46Y	A,
TRIB1	8	126448541	G	A	nonsynonymous	NM_025195:c.G947A:p.R316H	P,
KLHL9	9	21333719	C	T	nonsynonymous	NM_018847:c.G1140A:p.M380I	AB,
TOPORS	9	32542278	T	C	nonsynonymous	NM_001195622:c.A2050G:p.N684D	U,I,

VCP	9	35068298	T	C	nonsynonymous	NM_007126:c.A79G:p.I27V	B,
FBXO10	9	37541219	C	T	nonsynonymous	NM_012166:c.G547A:p.V183I	J,
DCAF10	9	37801039	C	A	nonsynonymous	NM_024345:c.C176A:p.A59D	AA,
KIAA0368	9	114192904	T	G	nonsynonymous	NM_001080398:c.A1387C:p.I463L	AD,
USP20	9	132636945	G	A	nonsynonymous	NM_001008563:c.G1831A:p.D611N	X,
ANAPC2	9	140069828	C	T	nonsynonymous	NM_013366:c.G2117A:p.R706H	P,
CHAT	10	50824106	C	T	nonsynonymous	NM_001142933:c.C8T:p.P3L	AA,G,
CHAT	10	50863188	G	A	nonsynonymous	NM_001142929:c.G1328A:p.R443Q	L,
USP54	10	75258901	C	G	nonsynonymous	NM_152586:c.G4541C:p.G1514A	AD,
USP54	10	75276693	G	A	nonsynonymous	NM_152586:c.C3491T:p.S1164F	B,
USP54	10	75279642	C	T	nonsynonymous	NM_152586:c.G2591A:p.R864H	AD,
FGFR2	10	123325158	G	A	nonsynonymous	NM_001144913:c.C170T:p.S57L	AB,
ARRB1	11	74985208	G	A	nonsynonymous	NM_004041:c.C824T:p.T275I	J,
USP35	11	77921132	C	T	nonsynonymous	NM_020798:c.C2231T:p.A744V	R,
GRM5	11	88242079	G	C	nonsynonymous	NM_000842:c.C3224G:p.T1075R	AA,
GRIA4	11	105842721	A	T	nonsynonymous	NM_000829:c.A2375T:p.K792I	O,
LRRK2	12	40707778	G	A	nonsynonymous	NM_198578:c.G4541A:p.R1514Q	R,AE,
PAN2	12	56716948	A	C	nonsynonymous	NM_001127460:c.T2403G:p.I801M	AF,A,
LRP1	12	57577915	C	T	nonsynonymous	NM_002332:c.C5977T:p.R1993W	Z,
HSP90B1	12	104332224	C	T	nonsynonymous	NM_003299:c.C962T:p.P321L	W,
USP30	12	109519188	C	T	nonsynonymous	NM_032663:c.C770T:p.A257V	R,
NOS1	12	117768159	T	G	nonsynonymous	NM_000620:c.A716C:p.Q239P	AB,
LMO7	13	76395444	A	G	nonsynonymous	NM_015842:c.A1640G:p.E547G	P,
LMO7	13	76427253	T	G	nonsynonymous	NM_015842:c.T3691G:p.S1231A	Q,
CUL4A	13	113882307	T	C	nonsynonymous	NM_001008895:c.T386C:p.V129A	N,
TEP1	14	20859870	G	A	nonsynonymous	NM_007110:c.C1985T:p.A662V	R,
HECTD	14	31641277	G	A	nonsynonymous	NM_015382:c.C1208T:p.A403V	A,



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JKAMP	14	59970780	A	G	nonsynonymous	NM_001098625:c.A908G:p.N303S	AD,
KIAA03 17	14	75136678	T	C	nonsynonymous	NM_001039479:c.A1760G:p.Q587R	X,
UBE3A	15	25616729	C	T	nonsynonymous	NM_130838:c.G532A:p.A178T	W,
HERC2	15	28502335	T	C	nonsynonymous	NM_004667:c.A2389G:p.M797V	B,
UBR1	15	43262758	C	T	nonsynonymous	NM_174916:c.G4417A:p.A1473T	X,
RNF111	15	59387091	G	C	nonsynonymous	NM_017610:c.G2953C:p.E985Q	O,
FBXO22	15	76205566	C	T	nonsynonymous	NM_012170:c.C302T:p.T101I	Z,
AXIN1	16	338189	C	T	nonsynonymous	NM_181050:c.G2414A:p.R805Q	J,
GRIN2A	16	9858173	G	T	nonsynonymous	NM_001134407:c.C3228A:p.N1076K	P,
SHISA9	16	13329217	C	T	nonsynonymous	NM_001145204:c.C1226T:p.P409L	W,
PLK1	16	23700676	T	A	nonsynonymous	NM_005030:c.T1388A:p.L463H	N,
GNAO1	16	56309967	G	A	nonsynonymous	NM_020988:c.G286A:p.G96S	Z,
CDH1	16	68855966	G	A	nonsynonymous	NM_004360:c.G1774A:p.A592T	L,W,
USP43	17	9603565	C	T	nonsynonymous	NM_153210:c.C1534T:p.R512C	B,
USP43	17	9631730	C	T	nonsynonymous	NM_153210:c.C2795T:p.P932L	AD,
RNF135	17	29326155	G	T	nonsynonymous	NM_032322:c.G1245T:p.W415C	AD,
GFAP	17	42982167	A	G	nonsynonymous	uc002ihp.l:exon1:c.A970G:p.I324V,	J,
CRHR1	17	43893886	C	T	nonsynonymous	NM_001145146:c.C179T:p.A60V	A,
SMURF 2	17	62602755	A	G	nonsynonymous	NM_022739:c.T56C:p.L19P	AD,
RGS9	17	63156654	A	G	nonsynonymous	NM_001081955:c.A313G:p.T105A	N,
RGS9	17	63156655	C	G	nonsynonymous	NM_001081955:c.C314G:p.T105R	N,
RGS9	17	63221214	G	A	nonsynonymous	NM_001081955:c.G1493A:p.R498H	AD,
UNC13 D	17	73826167	G	A	nonsynonymous	NM_199242:c.C2896T:p.R966W	Z,
SPHK1	17	74381682	C	T	nonsynonymous	NM_182965:c.C215T:p.T72I	O,
USP36	17	76802280	G	C	nonsynonymous	NM_025090:c.C2174G:p.S725C	AA,
USP36	17	76832433	C	G	nonsynonymous	NM_025090:c.G13C:p.D5H	P,

STRA13	17	79977215	G	A	nonsynonymous	NM_144998:c.C131T:p.A44V	AA,
NETO1	18	70417409	C	T	nonsynonymous	NM_001201465:c.G1429A:p.V477I	R,
UNC13A	19	17749893	G	A	nonsynonymous	NM_001080421:c.C3080T:p.P1027L	A,
PIK3R2	19	18280042	A	C	nonsynonymous	NM_005027:c.A2125C:p.T709P	I,
PVR	19	45153113	G	C	nonsynonymous	NM_001135768:c.G460C:p.V154L	AD,
CBLC	19	45295664	A	G	nonsynonymous	NM_001130852:c.A892G:p.M298V	C,L,
CBLC	19	45296767	G	A	nonsynonymous	NM_001130852:c.G1036A:p.E346K	R,
TRIB3	20	371958	G	A	nonsynonymous	NM_021158:c.G319A:p.V107M	AB,
TRIB3	20	372097	G	A	nonsynonymous	NM_021158:c.G458A:p.R153H	AC,
UBOX5	20	3102335	T	C	nonsynonymous	NM_014948:c.A950G:p.Q317R	X,
MYLK2	20	30408306	C	G	nonsynonymous	NM_033118:c.C430G:p.P144A	J,
AURKA	20	54945309	T	C	nonsynonymous	NM_003600:c.A1117G:p.M373V	I,
GNAS	20	57429447	C	T	nonsynonymous	NM_001077490:c.C940T:p.R314W	AC,
USP25	21	17220006	C	T	nonsynonymous	uc011aby.1:exon19:c.C2362T:p.P788S	Z,
USP25	21	17222109	C	T	nonsynonymous	uc011aby.1:exon20:c.C2465T:p.P822L,uc002yjj.1:exon19:c.C2351T:p.P784L	B,AD,
TTC3	21	38538018	T	C	nonsynonymous	NM_001001894:c.T3502C:p.C1168R	Z,
TTC3	21	38568259	C	T	nonsynonymous	NM_001001894:c.C5501T:p.A1834V	Z,
IRAK1	X	153278550	G	A	nonsynonymous	NM_001025243:c.C1637T:p.T546M	AB,I,
USP9Y	Y	14898465	C	T	nonsynonymous	NM_004654:c.C3293T:p.A1098V	P,J,
PAXIP1	7	154767989	T	C	nonsynonymous	NM_007349:exon6:c.A491G:p.D164G	C,
DCAF4	14	73421186	C	T	nonsynonymous	NM_181341:exon9:c.C820T:p.L274F,NM_001163509:exon11:c.C937T:p.L313F,NM_181340:exon10:c.C700T:p.L234F,NM_015604:exon11:c.C1000T:p.L334F	L,
CUL7	6	43006016	G	T	nonsynonymous	NM_014780:exon25:c.C4762A:p.L1588I,NM_001168370:exon25:c.C5014A:p.L1672I	F,
BCAN	1	156622525	C	A	nonsynonymous	NM_021948:exon8:c.C1783A:p.L595I,NM_198427:exon8:c.C1783A:p.L595I	Y,
C12orf5	12	112681251	C	T	nonsynonymous	NM_001109662:exon31:c.G4348A:p.V1450	U,

1						M	
HACE1	6	105233073	T	C	nonsynonymous	NM_020771:exon12:c.A1196G:p.D399G	C,
HSPA5	9	127999166	T	C	nonsynonymous	NM_005347:exon8:c.A1670G:p.E557G	N,
GNAS	20	57478823	G	A	nonsynonymous	NM_080426:exon4:c.G367A:p.V123M,NM_001077489:exon4:c.G364A:p.V122M,NM_080425:exon5:c.G2338A:p.V780M,NM_000516:exon5:c.G409A:p.V137M,NM_001077488:exon5:c.G412A:p.V138M	U,
CTR9	11	10795596	A	G	nonsynonymous	NM_014633:exon22:c.A2765G:p.N922S	D,
UBR3	2	170897489	C	T	nonsynonymous	NM_172070:exon32:c.C4654T:p.R1552C	Q,
AXIN1	16	348076	C	T	nonsynonymous	NM_003502:exon6:c.G1430A:p.R477H,NM_181050:exon6:c.G1430A:p.R477H	G,
N4BP1	16	48577065	C	T	nonsynonymous	NM_153029:exon7:c.G2441A:p.R814Q	AF,
TRIM56	7	100732376	G	A	nonsynonymous	NM_030961:exon3:c.G1783A:p.A595T	T,
TOPORS	9	32550953	G	A	nonsynonymous	NM_005802:exon2:c.C17T:p.P6L	AE,
BUB1B	15	40512901	A	C	nonsynonymous	NM_001211:exon23:c.A3094C:p.N1032H	S,
CLU	8	27472251	G	T	nonsynonymous	NM_001831:exon1:c.C48A:p.S16R	S,
DAXX	6	33286928	G	A	nonsynonymous	NM_001141970:exon7:c.C2045T:p.P682L,NM_001350:exon7:c.C2009T:p.P670L,NM_001141969:exon7:c.C2009T:p.P670L	T,
PDE1B	12	54969851	C	T	nonsynonymous	NM_000924:exon13:c.C1343T:p.A448V,NM_001165975:exon12:c.C1283T:p.A428V	E,
FBXW2	9	123540764	T	C	nonsynonymous	NM_012164:exon4:c.A550G:p.I184V	Y,
TRIM25	17	54981668	T	C	nonsynonymous	NM_005082:exon3:c.A875G:p.K292R	AC,
FBXL6	8	145580028	A	G	nonsynonymous	NM_024555:exon7:c.T1139C:p.L380P,NM_012162:exon7:c.T1157C:p.L386P	N,
WNT10B	12	49360194	A	G	nonsynonymous	NM_003394:exon5:c.T854C:p.I285T	D,
RNF20	9	104313033	G	A	nonsynonymous	NM_019592:exon10:c.G1238A:p.R413K	S,
FBXO24	7	100187366	C	T	nonsynonymous	NM_012172:exon1:c.C103T:p.R35W	N,

APC2	19	1455153	T	C	nonsynonymous	NM_005883:exon5:c.T419C:p.F140S	E,
PCGF1	2	74733329	C	T	nonsynonymous	NM_032673:exon4:c.G403A:p.V135I	V,
FLNA	X	153595185	C	T	nonsynonymous	NM_001456:exon6:c.G902A:p.R301Q,NM_01110556:exon6:c.G902A:p.R301Q	H,
APC2	19	1461980	G	A	nonsynonymous	NM_005883:exon14:c.G1657A:p.V553M	E,
FBXO25	8	413124	C	T	nonsynonymous	NM_012173:exon8:c.C760T:p.R254W,NM_183421:exon9:c.C961T:p.R321W,NM_183420:exon9:c.C961T:p.R321W	C,
TOPORS	9	32550896	G	C	nonsynonymous	NM_005802:exon2:c.C74G:p.S25W	Y,
DCAF6	1	167962499	G	T	nonsynonymous	NM_001198957:exon6:c.G631T:p.A211S,NM_001198956:exon7:c.G724T:p.A242S,NM_001017977:exon7:c.G724T:p.A242S,NM_018442:exon7:c.G724T:p.A242S	H,
DNAJB2	2	220148163	C	T	nonsynonymous	NM_001039550:exon8:c.C571T:p.R191W,NM_006736:exon8:c.C571T:p.R191W	V,
CAMK2B	7	44298500	C	A	nonsynonymous	NM_172078:exon4:c.G246T:p.E82D,NM_172080:exon4:c.G246T:p.E82D,NM_172079:exon4:c.G246T:p.E82D,NM_001220:exon4:c.G246T:p.E82D,NM_172083:exon4:c.G246T:p.E82D,NM_172081:exon4:c.G246T:p.E82D,NM_172082:exon4:c.G246T:p.E82D,NM_172084:exon4:c.G246T:p.E82D	D,
PSMD13	11	249005	A	G	nonsynonymous	NM_002817:exon9:c.A722G:p.N241S,NM_175932:exon7:c.A728G:p.N243S	E,
FBXW11	5	171337591	T	C	nonsynonymous	NM_033645:exon2:c.A256G:p.I86V,NM_033644:exon3:c.A319G:p.I107V,NM_012300:exon3:c.A358G:p.I120V	AF,
PAXIP1	7	154760785	G	A	nonsynonymous	NM_007349:exon7:c.C1126T:p.H376Y	E,
USP53	4	120169906	A	T	nonsynonymous	NM_019050:exon6:c.A241T:p.I81L	C,V,
UNC13B	9	35398605	G	A	nonsynonymous	NM_006377:exon31:c.G3640A:p.V1214I	C,

FBXO24	7	100187349	T	A	nonsynonymous	NM_012172:exon1:c.T86A:p.V29D	E,
ANAPC7	12	110820715	C	T	nonsynonymous	NM_001137664:exon7:c.G970A:p.V324I,NM_016238:exon7:c.G970A:p.V324I	D,
LMO7	13	76430740	C	G	stopgain	NM_015842:exon26:c.C4061G:p.S1354X	AF,
CUL2	10	35322199	C	T	nonsynonymous	NM_001198777:exon11:c.G1005A:p.M335I,NM_001198778:exon11:c.G1062A:p.M354I,:NM_003591:exon11:c.G1005A:p.M335I,NM_001198779:exon11:c.G1044A:p.M348I	F,
TAF1	X	70597546	C	G	nonsynonymous	NM_138923:exon6:c.C805G:p.L269V,NM_004606:exon6:c.C868G:p.L290V	F,
RNF111	15	59368402	A	G	nonsynonymous	NM_017610:exon7:c.A1936G:p.M646V	U,
TEP1	14	20848556	G	A	nonsynonymous	NM_007110:exon34:c.C4841T:p.A1614V	AE,
RAB27A	15	55497811	C	T	nonsynonymous	NM_004580:exon6:c.G560A:p.R187Q,NM_183234:exon7:c.G560A:p.R187Q,NM_183235:exon7:c.G560A:p.R187Q,NM_183236:exon7:c.G560A:p.R187Q	T,
N4BP1	16	48595895	G	T	nonsynonymous	NM_153029:exon2:c.C659A:p.A220D	V,
PSEN1	14	73673178	A	G	nonsynonymous	NM_000021:exon9:c.A953G:p.E318G,NM_007318:exon9:c.A941G:p.E314G	L,
UBE2C	20	44441403	C	G	nonsynonymous	NM_007019:exon1:c.C69G:p.S23R,NM_181800:exon1:c.C69G:p.S23R,NM_181803:exon1:c.C69G:p.S23R,NM_181799:exon1:c.C69G:p.S23R	T,
DBN1	5	176887438	C	G	nonsynonymous	NM_080881:exon11:c.G956C:p.R319P,NM_004395:exon10:c.G950C:p.R317P	E,
EDEM3	1	184702008	G	A	nonsynonymous	NM_025191:exon6:c.C575T:p.P192L	AC,
TNK2	3	195595212	C	T	nonsynonymous	NM_005781:exon12:c.G1912A:p.V638M,NM_001010938:exon13:c.G2146A:p.V716M	AE,
FBXO5	6	153296753	C	A	nonsynonymous	NM_012177:exon2:c.G107T:p.C36F	D,
RNF168	3	196198714	C	G	nonsynonymous	NM_152617:exon6:c.G1692C:p.Q564H	E,
FBXL12	19	9922084	C	T	nonsynonymous	NM_017703:exon3:c.G469A:p.V157M	N,
TNKS	8	9437705	A	T	nonsynonymous	NM_003747:exon2:c.A710T:p.Q237L	N,

ZRANB1	10	126631562	A	C	nonsynonymous	NM_017580:exon1:c.A500C:p.K167T	E,
SLC9A3R1	17	72759575	G	A	nonsynonymous	NM_004252:exon3:c.G673A:p.E225K	L,
BCL10	1	85742023	C	A	nonsynonymous	NM_003921:exon1:c.G13T:p.A5S	D,
CHAT	10	50822376	C	G	nonsynonymous	NM_020549:exon1:c.C141G:p.D47E	T,
RAB27A	15	55522666	G	A	nonsynonymous	NM_004580:exon3:c.C172T:p.P58S,NM_183234:exon4:c.C172T:p.P58S,NM_183235:exon4:c.C172T:p.P58S,NM_183236:exon4:c.C172T:p.P58S	C,
VGF	7	100806582	G	A	nonsynonymous	NM_003378:exon2:c.C1543T:p.P515S	S,
TRPC4AP	20	33609007	G	A	nonsynonymous	NM_199368:exon9:c.C1180T:p.R394C,NM_015638:exon9:c.C1204T:p.R402C	AF,
TRIP12	2	230678650	G	A	nonsynonymous	NM_004238:exon12:c.C1778T:p.T593M	G,
SLC24A2	9	19619662	C	A	nonsynonymous	NM_020344:exon4:c.G998T:p.S333I,NM_001193288:exon4:c.G998T:p.S333I	C,
MYLK2	20	30407387	G	A	nonsynonymous	NM_033118:exon2:c.G4A:p.A2T	E,
RFWD3	16	74670306	T	C	nonsynonymous	NM_018124:exon8:c.A1364G:p.Y455C	F,
ATG3	3	112253090	C	A	nonsynonymous	uc003dzc.2:exon11:c.G889T:p.V297L	S,
PARK2	6	162206852	G	A	nonsynonymous	NM_004562:exon7:c.C823T:p.R275W,NM_013988:exon4:c.C376T:p.R126W,NM_013987:exon6:c.C739T:p.R247W	F,
PVRL2	19	45385488	G	A	nonsynonymous	NM_001042724:exon6:c.G1063A:p.A355T	AF,
GNA12	7	2771123	T	C	nonsynonymous	NM_007353:exon4:c.A838G:p.I280V	Y,
ANAPC5	12	121756084	G	A	nonsynonymous	NM_001137559:exon15:c.C1553T:p.A518V,NM_016237:exon15:c.C1889T:p.A630V	V,AE,
AMFR	16	56441903	C	T	nonsynonymous	NM_001144:exon4:c.G639A:p.M213I	Y,
PSMF1	20	1145081	G	A	nonsynonymous	NM_006814:exon6:c.G725A:p.R242H,NM_178578:exon7:c.G725A:p.R242H	L,
TOPORS	9	32541880	G	C	nonsynonymous	NM_001195622:exon2:c.C2448G:p.H816Q,NM_005802:exon3:c.C2643G:p.H881Q	AC,

PIK3R1	5	67586574	G	T	nonsynonymous	NM_181504:exon1:c.G18T:p.W6C	L,
RNF103	2	86831751	G	C	nonsynonymous	NM_001198951:exon5:c.C1261G:p.L421V,NM_005667:exon4:c.C1273G:p.L425V	G,
TNR	1	175355171	T	C	nonsynonymous	NM_003285:exon8:c.A1774G:p.T592A	C,
CYLD	16	50783988	G	A	nonsynonymous	NM_015247:exon4:c.G379A:p.V127M,NM_001042355:exon3:c.G379A:p.V127M,NM_01042412:exon3:c.G379A:p.V127M	H,

Chr=chromosome; Ref=reference allele; Alt=alternate allele

**eTable 2.** Primer Sequences for Sanger Sequencing Verification of Identified Variants of Interest

<b>Gene</b>	<b>Chromosome</b>	<b>Position</b>	<b>Reference Allele</b>	<b>Alternate Allele</b>	<b>Forward Primer</b>	<b>Reverse Primer</b>
<i>TNK2</i>	3	195594092	G	A	CCTGGAGGAAGAGGAAGGTC	TGTCGTCAAACCTCTGCACCT
<i>TNK2</i>	3	195594494	C	T	TCTGTGGCAGCCGAGCAG	CAAGCTCACCTGGGAAGACC
<i>TNK2</i>	3	195595212	C	T	CCTGGAAGATCTCTGCGGTC	GAGGTCACGCTCATCGACTT
<i>TNK2</i>	3	195605390	A	G	AGAGCCAGAGTGAGCAGGAG	CAAGATCCAGATGGTGAGCA
<i>TNR</i>	1	175355171	T	C	GCGCTGCTTTTCCTGTATGC	CCCTCGAGCCAAAGTCGATT
<i>TNR</i>	1	175355213	G	A	TGACACACCTTGCCTCATTC	CGAGCCAAAGTCGATTTTCAT
<i>TNR</i>	1	175372714	T	G	AGCTGCAGTCTGTTGGGC	ACCAAACCTACGTTGAGCTTCA
<i>TNR</i>	1	175375355	T	C	CGGCAGCTACAGACTAGGAC	TACATGGGCCAGACCTCAGA
<i>TNR</i>	1	175375388	A	T	CGGCAGCTACAGACTAGGAC	TACATGGGCCAGACCTCAGA



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