

Supplementary Table S1. 1,189 putative SAVs derived from HGMD employed in this study.

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NM_000022.2:c.424C>T,NP_000013.2:p.R142X
NM_000026.2:c.618C>A,NP_000017.1:p.A206A
NM_000027.3:c.677G>A,NP_000018.2:p.G226D
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NM_000033.3:c.1224G>A,NP_000024.2:p.E408E
NM_000033.3:c.900G>A,NP_000024.2:p.E300E
NM_000035.3:c.324G>A,NP_000026.2:p.K108K
NM_000037.3:c.5005G>T,NP_000028.3:p.E1669X
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NM_000038.5:c.1548G>C,NP_000029.2:p.K516N
NM_000038.5:c.1548G>T,NP_000029.2:p.K516N
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NM_033084.3:c.376A>G,NP_149075.2:p.S126G
NM_033084.3:c.782A>T,NP_149075.2:p.K261M
NM_033163.3:c.216G>A,NP_149353.1:p.T72T
NM_033305.2:c.7806G>A,NP_150648.2:p.P2602P
NM_033305.2:c.8035G>A,NP_150648.2:p.A2679T
NM_033305.2:c.9474G>A,NP_150648.2:p.R3158R
NM_033453.2:c.94C>A,NP_258412.1:p.P32T
NM_033496.2:c.278G>A,NP_277031.1:p.R93Q
NM_052845.3:c.290G>A,NP_443077.1:p.G97E
NM_052845.3:c.584G>A,NP_443077.1:p.R195H
NM_058172.5:c.1179G>A,NP_477520.2:p.E393E

NM_080877.2:c.756G>A,NP_543153.1:p.Q252Q
NM_080877.2:c.846G>A,NP_543153.1:p.P282P
NM_080916.1:c.591G>A,NP_550438.1:p.Q197Q
NM_130799.2:c.654G>T,NP_570711.1:p.R218R
NM_133433.3:c.3574G>A,NP_597677.2:p.E1192K
NM_133433.3:c.4321G>T,NP_597677.2:p.V1441L
NM_133433.3:c.5427G>T,NP_597677.2:p.R1809S
NM_138694.3:c.2593G>T,NP_619639.3:p.V865F
NM_138694.3:c.657C>T,NP_619639.3:p.G219G
NM_139241.2:c.893T>G,NP_640334.2:p.M298R
NM_139242.3:c.626C>T,NP_640335.2:p.S209L
NM_144605.3:c.474G>A,NP_653206.2:p.V158V
NM_144997.5:c.1300G>A,NP_659434.2:p.E434K
NM_144997.5:c.1300G>C,NP_659434.2:p.E434Q
NM_144997.5:c.1300G>T,NP_659434.2:p.E434X
NM_152701.3:c.11112T>G,NP_689914.2:p.S3704R
NM_153609.2:c.1868G>C,NP_705837.1:p.S623T
NM_153638.2:c.1355A>G,NP_705902.2:p.D452G
NM_153694.4:c.657T>C,NP_710161.1:p.T219T
NM_153704.5:c.2241G>A,NP_714915.3:p.Q747Q
NM_153704.5:c.2439G>A,NP_714915.3:p.A813A
NM_170707.2:c.1821G>A,NP_733821.1:p.V607V
NM_170707.2:c.1868C>G,NP_733821.1:p.T623S
NM_172250.2:c.733G>A,NP_758454.1:p.G245S
NM_173076.2:c.5690G>C,NP_775099.2:p.R1897T
NM_173076.2:c.7436G>A,NP_775099.2:p.R2479K
NM_173660.4:c.414C>T,NP_775931.3:p.L138L

NM_173660.4:c.48C>T,NP_775931.3:p.G16G
NM_176824.2:c.340A>G,NP_789794.1:p.M114V
NM_177438.2:c.2457C>G,NP_803187.1:p.Y819X
NM_177924.3:c.412G>T,NP_808592.2:p.E138X
NM_181714.3:c.955G>A,NP_859065.2:p.A319T
NM_194277.2:c.252G>A,NP_919253.1:p.V84V
NM_194456.1:c.1579G>A,NP_919438.1:p.A527T
NM_194456.1:c.1943C>T,NP_919438.1:p.A648V
NM_194456.1:c.413T>C,NP_919438.1:p.I138T
NM_194456.1:c.712C>T,NP_919438.1:p.L238F
NM_194456.1:c.729G>A,NP_919438.1:p.R243R
NM_198056.2:c.1890G>A,NP_932173.1:p.T630T
NM_198056.2:c.4299G>A,NP_932173.1:p.G1433G
NM_198056.2:c.4719C>T,NP_932173.1:p.G1573G
NM_198309.2:c.459G>A,NP_938051.1:p.T153T
NM_198578.3:c.3342A>G,NP_940980.3:p.L1114L
NM_198843.2:c.501G>T,NP_942140.2:p.G167G
NM_198843.2:c.718G>A,NP_942140.2:p.A240T
NM_199242.2:c.1847A>G,NP_954712.1:p.E616G
NM_203447.3:c.1418A>G,NP_982272.2:p.K473R
NM_206933.2:c.2052A>G,NP_996816.2:p.Q684Q
NM_206933.2:c.2993G>A,NP_996816.2:p.R998K
NM_206933.2:c.4251G>T,NP_996816.2:p.Q1417H
NM_206933.2:c.5776G>A,NP_996816.2:p.E1926K
NM_206933.2:c.949C>A,NP_996816.2:p.R317R
NM_207122.1:c.1174G>A,NP_997005.1:p.A392T
NM_207346.2:c.1251A>G,NP_997229.2:p.P417P

NM_207346.2:c.285G>C,NP_997229.2:p.A95A
NM_207352.3:c.327G>A,NP_997235.3:p.E109E
NM_207517.2:c.4979C>T,NP_997400.2:p.T1660I
NM_213599.2:c.1295C>G,NP_998764.1:p.A432G

Supplementary Table S2. Unseen test set of 352 variants (238 SAVs and 114 SNVs) employed in this study.

HGVS	Class
NM_000132.3:c.6046C>T,NP_000123.1:p.R2016W	SAV
NM_000194.2:c.602A>T,NP_000185.1:p.D201V	SAV
NM_000194.2:c.597C>T,NP_000185.1:p.F199F	SAV
NM_000194.2:c.590A>T,NP_000185.1:p.E197V	SAV
NM_000194.2:c.580G>T,NP_000185.1:p.D194Y	SAV
NM_000194.2:c.551C>T,NP_000185.1:p.P184L	SAV
NM_000194.2:c.544G>A,NP_000185.1:p.E182K	SAV
NM_000194.2:c.539G>T,NP_000185.1:p.G180V	SAV
NM_000194.2:c.538G>A,NP_000185.1:p.G180R	SAV
NM_000194.2:c.482C>A,NP_000185.1:p.A161E	SAV
NM_000194.2:c.143G>A,NP_000185.1:p.R48H	SAV
NM_000194.2:c.119G>T,NP_000185.1:p.G40V	SAV
NM_000533.3:c.409C>T,NP_000524.3:p.R137W	SAV
NM_000533.3:c.409C>G,NP_000524.3:p.R137G	SAV
NM_000052.5:c.3904G>A,NP_000043.3:p.G1302R	SAV
NM_004493.2:c.574C>A,NP_004484.1:p.R192R	SAV
NM_005765.2:c.321C>T,NP_005756.2:p.D107D	SAV
NM_004006.2:c.5434T>A,NP_003997.1:p.F1812I	SAV
NM_004006.2:c.5435T>A,NP_003997.1:p.F1812Y	SAV
NM_004006.2:c.5436C>T,NP_003997.1:p.F1812F	SAV
NM_004006.2:c.5436C>G,NP_003997.1:p.F1812L	SAV
NM_004006.2:c.5436C>A,NP_003997.1:p.F1812L	SAV
NM_004006.2:c.5437A>T,NP_003997.1:p.N1813Y	SAV
NM_000284.3:c.592G>A,NP_000275.1:p.A198T	SAV
NM_000284.3:c.555A>G,NP_000275.1:p.G185G	SAV
NM_000284.3:c.523G>A,NP_000275.1:p.A175T	SAV
NM_000284.3:c.498C>T,NP_000275.1:p.I166I	SAV
NM_000284.3:c.483C>T,NP_000275.1:p.Y161Y	SAV
NM_001250.4:c.408A>T,NP_001241.1:p.T136T	SAV
NM_000022.2:c.643G>A,NP_000013.2:p.A215T	SAV
NM_000527.4:c.1773C>T,NP_000518.1:p.N591N	SAV
NM_000515.3:c.175G>C,NP_000506.2:p.E59Q	SAV
NM_000515.3:c.176A>G,NP_000506.2:p.E59G	SAV
NM_000515.3:c.177A>C,NP_000506.2:p.E59D	SAV
NM_000515.3:c.177A>G,NP_000506.2:p.E59E	SAV
NM_000515.3:c.194A>T,NP_000506.2:p.E65V	SAV
NM_000515.3:c.195A>T,NP_000506.2:p.E65D	SAV
NM_000515.3:c.198G>T,NP_000506.2:p.Q66H	SAV

NM_000515.3:c.200A>G,NP_000506.2:p.K67R	SAV
NM_007294.3:c.5080G>A,NP_009225.1:p.E1694K	SAV
NM_000267.3:c.6792C>T,NP_000258.1:p.Y2264Y	SAV
NM_000267.3:c.946C>A,NP_000258.1:p.L316M	SAV
NM_000267.3:c.945G>A,NP_000258.1:p.Q315Q	SAV
NM_000267.3:c.557A>T,NP_000258.1:p.D186V	SAV
NM_000080.3:c.532T>G,NP_000071.1:p.F178V	SAV
NM_000303.2:c.415G>A,NP_000294.1:p.E139K	SAV
NM_000137.2:c.696C>T,NP_000128.1:p.N232N	SAV
NM_000138.4:c.6354C>T,NP_000129.3:p.I2118I	SAV
NM_002225.3:c.214G>A,NP_002216.2:p.D72N	SAV
NM_002225.3:c.158G>T,NP_002216.2:p.R53L	SAV
NM_002225.3:c.157C>T,NP_002216.2:p.R53C	SAV
NM_001077351.1:c.408G>A,NP_001070819.1:p.R136R	SAV
NM_000321.2:c.1345G>A,NP_000312.2:p.G449R	SAV
NM_000059.3:c.8165C>G,NP_000050.2:p.T2722R	SAV
NM_000059.3:c.620C>T,NP_000050.2:p.T207I	SAV
NM_000059.3:c.617C>G,NP_000050.2:p.S206C	SAV
NM_000059.3:c.599C>A,NP_000050.2:p.T200K	SAV
NM_000059.3:c.599C>T,NP_000050.2:p.T200I	SAV
NM_000059.3:c.587G>T,NP_000050.2:p.S196I	SAV
NM_000059.3:c.587G>A,NP_000050.2:p.S196N	SAV
NM_000059.3:c.581G>A,NP_000050.2:p.W194X	SAV
NM_000059.3:c.572A>T,NP_000050.2:p.D191V	SAV
NM_000059.3:c.559G>A,NP_000050.2:p.E187K	SAV
NM_000059.3:c.521G>A,NP_000050.2:p.R174H	SAV
NM_000190.3:c.66C>G,NP_000181.2:p.R22R	SAV
NM_000051.3:c.6154G>A,NP_000042.3:p.E2052K	SAV
NM_001609.3:c.1165A>G,NP_001600.1:p.M389V	SAV
NM_022494.1:c.618C>T,NP_071939.1:p.T206T	SAV
NM_020975.4:c.1941C>T,NP_066124.1:p.I647I	SAV
NM_000492.3:c.1731C>T,NP_000483.3:p.Y577Y	SAV
NM_000492.3:c.1728A>T,NP_000483.3:p.G576G	SAV
NM_000492.3:c.1728A>G,NP_000483.3:p.G576G	SAV
NM_000492.3:c.1719T>C,NP_000483.3:p.S573S	SAV
NM_000492.3:c.1704G>A,NP_000483.3:p.L568L	SAV
NM_000492.3:c.1698T>A,NP_000483.3:p.A566A	SAV
NM_000492.3:c.1694A>G,NP_000483.3:p.D565G	SAV
NM_000038.5:c.1869G>T,NP_000029.2:p.R623R	SAV
NM_000521.3:c.1481A>G,NP_000512.1:p.D494G	SAV
NM_000344.3:c.840C>T,NP_000335.1:p.F280F	SAV
NM_017411.3:c.885A>C,NP_059107.1:p.X295Y	SAV
NM_017411.3:c.885A>T,NP_059107.1:p.X295Y	SAV

NM_017411.3:c.883T>G,NP_059107.1:p.X295E	SAV
NM_017411.3:c.880A>C,NP_059107.1:p.N294H	SAV
NM_017411.3:c.879A>C,NP_059107.1:p.L293F	SAV
NM_017411.3:c.879A>G,NP_059107.1:p.L293L	SAV
NM_001008388.4:c.109G>C,NP_001008389.1:p.E37Q	SAV
NM_001184.3:c.1995A>G,NP_001175.2:p.E665E	SAV
NM_000249.3:c.1976G>T,NP_000240.1:p.R659L	SAV
NM_000249.3:c.1976G>C,NP_000240.1:p.R659P	SAV
NM_000249.3:c.216T>C,NP_000240.1:p.D72D	SAV
NM_000249.3:c.214G>T,NP_000240.1:p.D72Y	SAV
NM_000249.3:c.214G>C,NP_000240.1:p.D72H	SAV
NM_001875.4:c.2265C>A,NP_001866.2:p.S755S	SAV
NM_000233.3:c.892G>A,NP_000224.2:p.E298K	SAV
NM_002838.4:c.177C>G,NP_002829.3:p.P59P	SAV
NM_000016.4:c.362C>T,NP_000007.1:p.T121I	SAV
NM_005910.5:c.888T>C,NP_005901.2:p.N296N	SAV
NM_005910.5:c.852T>C,NP_005901.2:p.L284L	SAV
NM_005910.5:c.837T>G,NP_005901.2:p.N279K	SAV
NM_000492.3:c.1722T>A,NP_000483.3:p.P574P	SAV
NM_000492.3:c.1719T>G,NP_000483.3:p.S573S	SAV
NM_000492.3:c.1716C>T,NP_000483.3:p.D572D	SAV
NM_000492.3:c.1713A>G,NP_000483.3:p.L571L	SAV
NM_000492.3:c.1357T>A,NP_000483.3:p.L453M	SAV
NM_000492.3:c.1357T>C,NP_000483.3:p.L453L	SAV
NM_000492.3:c.1356G>T,NP_000483.3:p.Q452H	SAV
NM_000492.3:c.1356G>C,NP_000483.3:p.Q452H	SAV
NM_000492.3:c.1355A>C,NP_000483.3:p.Q452P	SAV
NM_000492.3:c.1355A>T,NP_000483.3:p.Q452L	SAV
NM_000492.3:c.1355A>G,NP_000483.3:p.Q452R	SAV
NM_000492.3:c.1354C>A,NP_000483.3:p.Q452K	SAV
NM_000492.3:c.1354C>G,NP_000483.3:p.Q452E	SAV
NM_000492.3:c.1227T>G,NP_000483.3:p.F409L	SAV
NM_000344.3:c.881A>C,NP_000335.1:p.N294T	SAV
NM_000344.3:c.871C>T,NP_000335.1:p.H291Y	SAV
NM_000344.3:c.854A>T,NP_000335.1:p.K285I	SAV
NM_000132.3:c.1569G>T,NP_000123.1:p.L523L	SAV
NM_000116.3:c.525G>A,NP_000107.1:p.V175V	SAV
NM_001456.3:c.5423C>T,NP_001447.2:p.A1808V	SAV
NM_000202.5:c.395C>G,NP_000193.1:p.S132W	SAV
NM_000202.5:c.1122C>T,NP_000193.1:p.G374G	SAV
NM_000074.2:c.256G>T,NP_000065.1:p.E86X	SAV
NM_000194.2:c.209G>T,NP_000185.1:p.G70V	SAV
NM_000061.2:c.119A>G,NP_000052.1:p.Y40C	SAV

NM_000061.2:c.942A>G,NP_000052.1:p.K314K	SAV
NM_004006.2:c.5985T>G,NP_003997.1:p.Y1995X	SAV
NM_000453.2:c.1593C>G,NP_000444.1:p.Y531X	SAV
NM_000215.3:c.1767C>T,NP_000206.2:p.G589G	SAV
NM_006397.2:c.75C>T,NP_006388.2:p.R25R	SAV
NM_006397.2:c.69G>A,NP_006388.2:p.V23V	SAV
NM_000527.4:c.1216C>A,NP_000518.1:p.R406R	SAV
NM_001972.2:c.558C>A,NP_001963.1:p.V186V	SAV
NM_000088.3:c.3790A>G,NP_000079.2:p.M1264V	SAV
NM_000212.2:c.1815C>T,NP_000203.2:p.G605G	SAV
NM_007294.3:c.190T>G,NP_009225.1:p.C64G	SAV
NM_000267.3:c.3831C>T,NP_000258.1:p.G1277G	SAV
NM_000267.3:c.3278T>A,NP_000258.1:p.V1093E	SAV
NM_000267.3:c.2764G>A,NP_000258.1:p.G922S	SAV
NM_000267.3:c.2709G>A,NP_000258.1:p.V903V	SAV
NM_000267.3:c.1466A>G,NP_000258.1:p.Y489C	SAV
NM_000267.3:c.989C>T,NP_000258.1:p.A330V	SAV
NM_004360.3:c.1901C>T,NP_004351.1:p.A634V	SAV
NM_000196.3:c.771C>G,NP_000187.3:p.V257V	SAV
NM_000517.4:c.69C>T,NP_000508.1:p.G23G	SAV
NM_000520.4:c.972T>A,NP_000511.2:p.V324V	SAV
NM_000119.2:c.1747G>T,NP_000110.2:p.E583X	SAV
NM_000431.2:c.75C>T,NP_000422.1:p.G25G	SAV
NM_001017535.1:c.702C>G,NP_001017535.1:p.V234V	SAV
NM_000051.3:c.7865C>T,NP_000042.3:p.A2622V	SAV
NM_000019.3:c.380C>T,NP_000010.1:p.A127V	SAV
NM_006019.3:c.671G>A,NP_006010.2:p.W224X	SAV
NM_000518.4:c.75T>A,NP_000509.1:p.G25G	SAV
NM_000518.4:c.79G>A,NP_000509.1:p.E27K	SAV
NM_000314.4:c.334C>G,NP_000305.3:p.L112V	SAV
NM_194456.1:c.410A>G,NP_919438.1:p.D137G	SAV
NM_194456.1:c.601C>G,NP_919438.1:p.Q201E	SAV
NM_000181.3:c.1617C>T,NP_000172.2:p.S539S	SAV
NM_005514.6:c.360G>C,NP_005505.2:p.Q120H	SAV
NM_022132.4:c.1309A>G,NP_071415.1:p.I437V	SAV
NM_000163.4:c.723C>T,NP_000154.1:p.G241G	SAV
NM_000163.4:c.594A>G,NP_000154.1:p.E198E	SAV
NM_005141.4:c.605T>A,NP_005132.2:p.L202Q	SAV
NM_000297.3:c.2614C>T,NP_000288.1:p.R872X	SAV
NM_005787.5:c.165C>T,NP_005778.1:p.G55G	SAV
NM_001184.3:c.2022A>G,NP_001175.2:p.G674G	SAV
NM_000094.3:c.4965C>T,NP_000085.1:p.G1655G	SAV
NM_000060.2:c.100G>A,NP_000051.1:p.G34S	SAV

NM_000784.3:c.435G>T,NP_000775.1:p.G145G	SAV
NM_003126.2:c.1086A>G,NP_003117.2:p.R362R	SAV
NM_001257374.1:c.1488C>T,NP_001244303.1:p.G496G	SAV
NM_001257374.1:c.1486G>A,NP_001244303.1:p.G496S	SAV
NM_001005741.2:c.750A>G,NP_001005741.1:p.R250R	SAV
NM_033380.2:c.2677G>A,NP_203699.1:p.G893S	SAV
NM_033380.2:c.384G>A,NP_203699.1:p.K128K	SAV
NM_014008.3:c.49A>G,NP_054727.1:p.T17A	SAV
NM_000397.3:c.1152G>C,NP_000388.2:p.K384N	SAV
NM_003560.2:c.1077G>A,NP_003551.2:p.S359S	SAV
NM_006031.5:c.5993A>C,NP_006022.3:p.Q1998P	SAV
NM_022095.3:c.3332G>A,NP_071378.1:p.R1111H	SAV
NM_000214.2:c.886G>A,NP_000205.1:p.D296N	SAV
NM_144577.3:c.742G>A,NP_653178.3:p.A248T	SAV
NM_000528.3:c.2355G>A,NP_000519.2:p.T785T	SAV
NM_001083962.1:c.655G>A,NP_001077431.1:p.D219N	SAV
NM_020964.2:c.1007A>G,NP_066015.2:p.Q336R	SAV
NM_015295.2:c.4566G>A,NP_056110.2:p.T1522T	SAV
NM_001257970.1:c.349G>A,NP_001244899.1:p.G117S	SAV
NM_000342.3:c.1626G>A,NP_000333.1:p.K542K	SAV
NM_007294.3:c.4675G>A,NP_009225.1:p.E1559K	SAV
NM_007294.3:c.5074G>C,NP_009225.1:p.D1692H	SAV
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