Genomics Research Centre Diagnostics Clinic Genotyping Analysis Report

05 July, 2016

**Patient:** DG1051

**RUNID:** XXXX

**Analysis Performed:** Alignment against hg19 -> annotation pipeline (dbSNP, SnpSIFT, VEP, UCSC gene symbols) -> variant filtering

|  |
| --- |
| Parameters |
| ##fileformat=VCFv4.1 |
| ##fileDate=20160102 |
| ##fileUTCtime=2016-01-02T02:30:30 |
| ##source=tvc 5.0-7 (517ac65) - Torrent Variant Caller |
| ##parametersName=AmpliSeq Exome Panel - Proton - Germ Line - Low Stringency |
| ##parametersDetails=ampliseqexome\_germline\_low\_stringency\_p1, TS version: 4.4 |
| ##tmapVersion=5.0.7 (517ac65) (201509092132) |
| ##reference=/results/referenceLibrary/tmap-f3/hg19/hg19.fasta |
| ##SnpSiftVersion=SnpSift 4.2 (build 2015-12-05), by Pablo Cingolani |
| ##VEP=v82 cache=/home/gringer/.vep/homo\_sapiens\_merged/82\_GRCh37 db=. sift=sift5.2.2 gencode=GENCODE 19 regbuild=13 ESP=20141103 ClinVar=201507 polyphen=2.2.2 genebuild=2011-04 assembly=GRCh37.p13 dbSNP=144 COSMIC=71 HGMD-PUBLIC=20152 |

**Date Analysis Performed:** 05 July, 2016

## Quality Metrics

Something from Proton/Torrent? {...now have text files from the server in ../coverage\_stats...}

* CoverageAnalysisReport
* SampleName: DG1051
* ReferenceGenome: hg19
* TargetRegions: AmpliSeqExome.20141113.designed
* Alignments: IonXpress\_021\_R\_2016\_01\_01\_13\_47\_40\_user\_BBDefault-15-ExomePanel\_Hi-Q\_Cassie\_Run\_2A\_31.12.15\_Auto\_user\_BBDefault-15-ExomePanel\_Hi-Q\_Cassie\_Run\_2A\_31.12.15\_54
* Numberofmappedreads: 30504053
* Percentreadsontarget: 90.32%
* Numberofamplicons: 293903
* Totalassignedampliconreads: 27549758
* Percentassignedampliconreads: 90.32%
* Averagereadsperamplicon: 93.74
* Uniformityofampliconcoverage: 92.93%
* Ampliconswithatleast1read: 99.48%
* Ampliconswithatleast20reads: 92.24%
* Ampliconswithatleast100reads: 36.70%
* Ampliconswithatleast500reads: 0.12%
* Ampliconswithnostrandbias: 92.27%
* Ampliconsreadingend-to-end: 40.49%
* Totalalignedbasereads: 5388024284
* Totalbasereadsontarget: 4907730621
* Basesintargetregions: 57742646
* Percentbasereadsontarget: 91.09%
* Averagebasecoveragedepth: 84.99
* Uniformityofbasecoverage: 92.29%
* Targetbasecoverageat1x: 99.29%
* Targetbasecoverageat20x: 90.33%
* Targetbasecoverageat100x: 31.30%
* Targetbasecoverageat500x: 0.08%
* Targetbaseswithnostrandbias: 82.45%
* Percentend-to-endreads: 59.73%

### Depth of coverage

total variants = 37226  
max coverage = 854 reads  
min coverage = 5 reads  
mean coverage = 94 reads  
median coverage = 77 reads

A total of **6.2%** of all variants have < 20x coverage.

*Note*: these statistics come from the DP data contained within the VCF file.

### VEP summary statistics

#### General Statistics

* Variants processed 37227
* Variants remaining after filtering 37227
* Novel / existing variants 754 (2.0%) / 36473 (98.0%)
* Overlapped genes 31829
* Overlapped transcripts 143186
* Overlapped regulatory features 6812

#### Variant Statistics

* sequence\_alteration 76
* substitution 301
* insertion 564
* deletion 654
* SNV 35632

#### Consequences (most severe)

* splice\_acceptor\_variant 58
* stop\_gained 78
* frameshift\_variant 190
* stop\_lost 43
* start\_lost 34
* inframe\_insertion 58
* inframe\_deletion 80
* protein\_altering\_variant 2
* missense\_variant 9246
* splice\_region\_variant 1564
* synonymous\_variant 9672
* stop\_retained\_variant 12
* coding\_sequence\_variant 2
* mature\_miRNA\_variant 1
* 5\_prime\_UTR\_variant 1234
* 3\_prime\_UTR\_variant 1675
* non\_coding\_transcript\_exon\_variant 1529
* intron\_variant 11563
* upstream\_gene\_variant 101
* downstream\_gene\_variant 34

#### Coding consequences

* stop\_gained 316
* frameshift\_variant 912
* stop\_lost 115
* inframe\_insertion 402
* inframe\_deletion 508
* missense\_variant 53100
* synonymous\_variant 65576
* coding\_sequence\_variant 70

#### SIFT summary

* deleterious - low confidence 1199
* tolerated - low confidence 4205
* deleterious 6232
* tolerated 29115

#### Polyphen summary

* unknown 1700
* possibly damaging 3251
* probably damaging 3313
* benign 35172

## Tier 0 Annotations - Diagnostic Panel Genes

This tier contains variants identified within the current diagnostic panel genes.

There are **35** variants present within the diagnostic panel genes.

### Tier 0.1 – Top Most Damaging Mutations/Variants

There are 0 most damaging mutations in this tier.

**Note:** *MutationTaster prediction*: **A** (disease causing automatic), **D** (disease causing), **N** (polymorphism) or **P** (polymorphism automatic). *SIFT prediction*: smaller than 0.05 is predicted as **D**(amaging), otherwise it is predicted as **T**(olerated). *Polyphen2 prediction*: **D** (probably damaging [0.957,1]), **P** (possibly damaging [0.453,0.956]) and **B** (benign [0,0.452]). Multiple predictions separated by ";".

### Tier 0.2 – Mutations

There are **0** variants that are amino acid changing and don't have an rs number.

### Tier 0.3 – Variants

There are **0** variants that are not amino acid changing and have no associated rs number.  
There are **0** variants that are amino acid changing, have a rs number and MAF < 1%.  
There are **1** variants that are not amino acid changing, have a rs number and MAF < 1%.

Not amino acid changing and has no rs#; amino acid changing, has rs#, but MAF <1%; not amino acid changing, have a rs number and MAF < 1%.

|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| location | genotype | ref | alt | dbSNP | gene | transcript | coding | AAchange | MutationTaster | SIFT | Polyphen2 | coverage | ref\_freq | alt\_freq |
| chr19:15289613 | T/T | A | T | rs11670823 | *NOTCH3* | ENST00000600841 | . | . | . | . | . | 48 A(0) T(48) | 0.48 | 0 |

### Tier 0.4 – Rare SNPs

There are **7** variants classified as rare SNPs.

Any variant with rs number and MAF >1% <10%

|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| location | genotype | ref | alt | dbSNP | gene | transcript | coding | AAchange | MutationTaster | SIFT | Polyphen2 | coverage | ref\_freq | alt\_freq |
| chr1:160093648 | G/A | G | A | rs41265763 | *ATP1A2* | ENST00000478587 | . | . | . | . | . | 109 G(63) A(46) | 0.91 | 0.086 |
| chr1:160097315 | C/A | C | A | rs2295623 | *ATP1A2* | XM\_005245210.1 | . | . | . | . | . | 89 C(50) A(39) | 0.92 | 0.081 |
| chr2:166930214 | A/A | T | A | rs566839 | *SCN1A;.* | NM\_006920.4 | . | . | . | . | . | 65 T(0) A(65) | 0.015 | 0.99 |
| chr10:118957027 | A/G | A | G | rs67346047 | *KCNK18* | ENST00000452430 | c.28N>G | p.Arg10Gly | P | T | B | 94 A(45) G(47) | 0.91 | 0.089 |
| chr19:13355900 | G/G | T | G | rs16039 | *CACNA1A* | NM\_023035.2 | . | . | . | . | . | 24 T(0) G(23) | 0.012 | 0.99 |
| chr19:13418707 | C/T | C | T | rs16015 | *CACNA1A* | NM\_001127221.1 | . | . | . | . | . | 69 C(39) T(26) | 0.9 | 0.099 |
| chr19:15281459 | C/G | C | G | rs56277836 | *NOTCH3* | ENST00000597756 | . | . | . | . | . | 40 C(14) G(26) | 0.95 | 0.05 |

## Tier 1 Annotations – Disease Specific Genes

There are a total of **100** variants in this tier.

{FHM, Ataxia, etc. For epilepsy and others, perhaps tiers could have specific names as there may be more tiers than the “standard” arrangement and some may be more likely to check for a specific patient }

### Tier 1.1 – Top Most Damaging Mutations/Variants

Any of the following:

* Amino acid changing variant
  + no rs#
  + has rs#, but MAF <1%
* No AA change
  + no rs#

{All sorted by the number of predictors showing “Damaging” or the equivalent}

Top Most Damaging Mutations/Variants

|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| location | genotype | ref | alt | dbSNP | gene | transcript | coding | AAchange | MutationTaster | SIFT | Polyphen2 | coverage | ref\_freq | alt\_freq |
| chr1:201016296 | G/A | G | A | rs3850625 | *CACNA1S* | ENST00000362061 | c.4558N>T | p.Arg1520Cys | P | D | P | 184 G(110) A(73) | 0.92 | 0.084 |
| chr6:16306751 | G/A | G | A | rs16885 | *ATXN1* | NM\_001128164.1 | c.2257N>T | p.Pro753Ser | P | D | B | 235 G(108) A(123) | 0.88 | 0.12 |
| chr19:35524824 | T/C | T | C | rs55742440 | *SCN1B* | ENST00000262631 | c.629N>C | p.Leu210Pro | P | D | B | 237 T(113) C(124) | 0.62 | 0.38 |

**Note:** *MutationTaster prediction*: **A** (disease causing automatic), **D** (disease causing), **N** (polymorphism) or **P** (polymorphism automatic). *SIFT prediction*: smaller than 0.05 is predicted as **D**(amaging), otherwise it is predicted as **T**(olerated). *Polyphen2 prediction*: **D** (probably damaging [0.957,1]), **P** (possibly damaging [0.453,0.956]) and **B** (benign [0,0.452]). Multiple predictions separated by ";".

### Tier 1.2 – Mutations

There are **0** variants that are amino acid changing and don't have an rs number.

### Tier 1.3 – Variants

There are **0** variants that are not amino acid changing and have no associated rs number.  
There are **5** variants that are amino acid changing, have a rs number and MAF < 1%.  
There are **17** variants that are not amino acid changing, have a rs number and MAF < 1%.

Not amino acid changing and has no rs#; amino acid changing, has rs#, but MAF <1%; not amino acid changing, have a rs number and MAF < 1%.

|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| location | genotype | ref | alt | dbSNP | gene | transcript | coding | AAchange | MutationTaster | SIFT | Polyphen2 | coverage | ref\_freq | alt\_freq |
| chr2:165987772 | G/G | T | G | rs62174900 | *SCN2A;SCN3A* | ENST00000360093 | c.2400N>C | . | . | . | . | 32 T(1) G(31) | 0.82 | 0 |
| chr2:167144995 | T/C | T | C | rs13402180 | *LOC101929680;BC051759* | ENST00000409672 | c.1266N>G | . | . | . | . | 70 T(36) C(33) | 0.65 | 0 |
| chr2:167163043 | T/C | T | C | rs9646771 | *SCN9A* | NM\_002977.3 | c.447N>G | . | . | . | . | 37 T(16) C(21) | 0.36 | 0 |
| chr3:38739574 | C/C | T | C | rs6599241 | *SCN10A* | ENST00000449082 | c.5137N>G | p.Met1713Val | P | T | B | 232 T(0) C(232) | 0 | 1 |
| chr5:36686404 | G/A | G | A | rs2229894 | *SLC1A3* | NM\_001166695.1 | . | . | . | . | . | 142 G(77) A(65) | 0 | 0 |
| chr6:16327615 | A/G | A | G | rs179990 | *ATXN1* | NM\_000332.3 | c.927N>C | . | . | . | . | 154 A(71) G(82) | 0.22 | 0.0012 |
| chr6:80631539 | A/A | T | A | rs700483 | *ELOVL4* | ENST00000369816 | . | . | . | . | . | 56 T(0) A(56) | 0 | 1 |
| chr12:2791132 | G/G | A | G | rs10774053 | *CACNA1C-AS1;CACNA1C* | ENST00000501371 | c.5461N>G | p.Met1821Val | P | T | B | 91 A(0) G(91) | 0.23 | 0 |
| chr12:2791205 | G/G | A | G | rs10774054 | *CACNA1C-AS1;CACNA1C* | NM\_000719.6 | c.5534N>G | p.Lys1845Arg | P | T | B | 89 A(3) G(86) | 0 | 1 |
| chr13:52524560 | C/T | C | T | rs9526811 | *ATP7B* | XM\_005266425.1 | . | . | . | . | . | 91 C(44) T(47) | 0.69 | 0 |
| chr13:52544805 | C/G | C | G | rs1801244 | *ATP7B* | ENST00000344297 | c.1366N>C | p.Val456Leu | P | T | B | 55 C(33) G(21) | 0.62 | 0 |
| chr16:28905547 | C/T | C | T | rs41292388 | *NPIPB8;NPIPL1* | NM\_173201.3 | c.1167N>T | . | . | . | . | 75 C(32) T(41) | 1 | 0.0014 |
| chr16:29825126 | C/C | T | C | rs11150573 | *LOC100289283;PRRT2* | ENST00000562594 | c.751N>C | . | . | . | . | 150 T(0) C(150) | 0.0082 | 0.99 |
| chr17:42273151 | G/A | G | A | rs199654550 | *ATXN7L3* | ENST00000319511 | . | . | . | . | . | 95 G(56) A(39) | 1 | 2e-04 |
| chr17:62049235 | G/G | A | G | rs9892013 | *SCN4A* | ENST00000578147 | . | . | . | . | . | 26 A(0) G(26) | 0.0052 | 0.99 |
| chrX:49061742 | C/T | C | T | rs33910054 | *CACNA1F* | NM\_001256789.1 | c.5789N>A | p.Arg1930His | P | T | B | 163 C(80) T(82) | 0 | 0 |
| chrX:49069366 | C/T | C | T | rs2071316 | *CACNA1F* | ENST00000486943 | . | . | . | . | . | 207 C(105) T(101) | 0 | 0 |
| chrX:49071964 | A/G | A | G | rs2075866 | *CACNA1F* | NM\_001256789.1 | c.3114N>C | . | . | . | . | 279 A(136) G(142) | 0 | 0 |
| chrX:49077072 | G/A | G | A | rs5906756 | *CACNA1F* | NM\_001256789.1 | . | . | . | . | . | 53 G(29) A(22) | 0 | 0 |
| chrX:49081291 | G/A | G | A | rs2235127 | *CACNA1F* | ENST00000376265 | c.1647N>T | . | . | . | . | 54 G(19) A(33) | 0 | 0 |
| chrX:49087487 | G/A | G | A | rs5905724 | *CACNA1F* | ENST00000376265 | . | . | . | . | . | 114 G(57) A(55) | 0 | 0 |
| chrX:49093528 | T/C | T | C | rs2294016 | *CCDC22* | ENST00000323022 | . | . | . | . | . | 54 T(19) C(34) | 0 | 0 |

### Tier 1.4 – Rare SNPs

There are **14** variants classified as rare SNPs.

Any variant with rs number and MAF >1% <10%

|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| location | genotype | ref | alt | dbSNP | gene | transcript | coding | AAchange | MutationTaster | SIFT | Polyphen2 | coverage | ref\_freq | alt\_freq |
| chr1:201012597 | G/A | G | A | rs41267497 | *CACNA1S* | ENST00000367338 | c.4860N>T | . | . | . | . | 65 G(36) A(29) | 0.95 | 0.046 |
| chr1:201016296 | G/A | G | A | rs3850625 | *CACNA1S* | ENST00000362061 | c.4558N>T | p.Arg1520Cys | P | D | P | 184 G(110) A(73) | 0.92 | 0.084 |
| chr3:10442779 | C/T | C | T | rs26797 | *ATP2B2* | XM\_005265179.1 | . | . | . | . | . | 108 C(50) T(58) | 0.91 | 0.093 |
| chr3:38622467 | C/C | T | C | rs7430407 | *SCN5A* | NM\_000335.4 | c.3183N>G | . | . | . | . | 107 T(1) C(106) | 0.077 | 0.92 |
| chr3:38739845 | G/G | A | G | rs6599242 | *SCN10A* | ENST00000449082 | c.4866N>C | . | . | . | . | 126 A(0) G(125) | 0.075 | 0.92 |
| chr3:63981635 | C/T | C | T | rs3733125 | *ATXN7* | ENST00000487717 | c.2137N>T | . | . | . | . | 62 C(31) T(31) | 0.91 | 0.09 |
| chr4:72433759 | T/T | C | T | rs1453453 | *SLC4A4* | XM\_005265703.1 | . | . | . | . | . | 41 C(0) T(40) | 0.088 | 0.91 |
| chr7:105250905 | A/A | G | A | rs940370 | *ATXN7L1* | XM\_005250220.1 | . | . | . | . | . | 114 G(0) A(114) | 0.029 | 0.97 |
| chr11:66472274 | C/C | T | C | rs4930388 | *SPTBN2* | ENST00000529997 | c.2473N>G | p.Ser825Gly | P | T | B | 495 T(0) C(495) | 0.012 | 0.99 |
| chr12:2706720 | C/C | G | C | rs215983 | *CACNA1C* | XM\_005253767.1 | . | . | . | . | . | 31 G(0) C(31) | 0.049 | 0.95 |
| chr17:42272586 | G/A | G | A | rs11652516 | *ATXN7L3* | ENST00000538716 | . | . | . | . | . | 88 G(36) A(50) | 0.96 | 0.036 |
| chr17:62041068 | C/C | T | C | rs6504191 | *SCN4A* | ENST00000581514 | c.1570N>G | p.Ser524Gly | P | T | B | 96 T(0) C(96) | 0.056 | 0.94 |
| chr18:12337688 | C/C | G | C | rs78550590 | *AFG3L2* | ENST00000586691 | . | . | . | . | . | 77 G(0) C(76) | 0.93 | 0.072 |
| chr19:42489516 | C/C | A | C | rs2217342 | *ATP1A3* | NM\_152296.4 | c.705N>G | . | . | . | . | 116 A(0) C(116) | 0.098 | 0.9 |

## Tier 2 Annotations – Pathway Specific Genes

There are a total of **2982** variants in this tier.

{CNS, Muscle, Cardiac, etc. Drawn from KEGG or similar database?}

### Tier 2.1 – Top Most Damaging Mutations/Variants

Any of the following:

* Amino acid changing variant
  + no rs#
  + has rs#, but MAF <1%
* No AA change
  + no rs#

{All sorted by the number of predictors showing “Damaging” or the equivalent}

Top Most Damaging Mutations/Variants

|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| location | genotype | ref | alt | dbSNP | gene | transcript | coding | AAchange | MutationTaster | SIFT | Polyphen2 | coverage | ref\_freq | alt\_freq |
| chr2:219540139 | T/C | T | C | . | *STK36* | ENST00000473034 | c.215N>C | p.Met72Thr | D | D | D | 9 T(6) C(3) | 0 | 0 |
| chr3:52550165 | G/T | G | T | . | *STAB1* | XM\_005264974.1 | c.4055N>T | p.Gly1352Val | D | D | D | 5 G(2) T(3) | 0 | 0 |
| chr9:140811767 | C/T | C | T | . | *CACNA1B* | ENST00000371372 | c.850N>T | p.Arg284Trp | D | D | D | 31 C(22) T(8) | 0 | 0 |
| chr12:110771929 | G/A | G | A | . | *ATP2A2* | XR\_243009.1 | c.1319N>A | p.Arg440His | D | D | D | 44 G(20) A(24) | 0 | 0 |

### Tier 2.2 – Mutations

There are **26** variants that are amino acid changing without associated rs numbers.

Amino acid changing variant, no rs#

|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| location | genotype | ref | alt | dbSNP | gene | transcript | coding | AAchange | MutationTaster | SIFT | Polyphen2 | coverage | ref\_freq | alt\_freq |
| chr12:110771929 | G/A | G | A | . | *ATP2A2* | XR\_243009.1 | c.1319N>A | p.Arg440His | D | D | D | 44 G(20) A(24) | 0 | 0 |
| chr2:219540139 | T/C | T | C | . | *STK36* | ENST00000473034 | c.215N>C | p.Met72Thr | D | D | D | 9 T(6) C(3) | 0 | 0 |
| chr3:52550165 | G/T | G | T | . | *STAB1* | XM\_005264974.1 | c.4055N>T | p.Gly1352Val | D | D | D | 5 G(2) T(3) | 0 | 0 |
| chr9:140811767 | C/T | C | T | . | *CACNA1B* | ENST00000371372 | c.850N>T | p.Arg284Trp | D | D | D | 31 C(22) T(8) | 0 | 0 |
| chr1:218520044 | A/T | A | T | . | *TGFB2* | XR\_247038.1 | . | p.Met1? | D | D | P | 91 A(68) T(22) | 0 | 0 |
| chr11:102824914 | T/C | T | C | . | *MMP13* | ENST00000340273 | c.608N>G | p.Asp203Gly | D | D | P | 8 T(5) C(3) | 0 | 0 |
| chr15:25958907 | A/C | A | C | . | *ATP10A* | ENST00000356865 | c.2258N>G | p.Ile753Ser | D | D | P | 5 A(2) C(3) | 0 | 0 |
| chr9:136216844 | 1/2 | GCC | CCG,GC,GGC | . | *RPL7A* | ENST00000468019 | . | p.Ala145Pro | D | D | B | 38 GCC(8) CCG,GC,GGC(7,12,9) | 0 | 0 |
| chr9:33796766 | C/T | C | T | . | *PRSS3* | NM\_002771.3 | c.145N>T | p.Gln49Ter | A | . | . | 128 C(100) T(26) | 0 | 0 |
| chr9:130941340 | C/G | C | G | . | *CIZ1* | XM\_005251890.1 | c.843N>C | p.Gln281His | N | D | P | 7 C(2) G(5) | 0 | 0 |
| chr12:132335725 | C/G | C | G | . | *MMP17* | ENST00000535271 | c.338N>G | p.Ala113Gly | N | D | B | 48 C(21) G(27) | 0 | 0 |
| chr6:33281641 | C/G | C | G | . | *TAPBP* | XM\_005248860.1 | c.38N>C | p.Gly13Ala | N | D | B | 15 C(3) G(10) | 0 | 0 |
| chr7:39379457 | A/G | A | G | . | *POU6F2* | ENST00000517348 | c.728N>G | p.Gln243Arg | N | D | B | 13 A(6) G(6) | 0 | 0 |
| chr9:33796762 | C/G | C | G | . | *PRSS3* | NM\_001197097.2 | c.333N>G | p.Ser111Arg | N | D | B | 127 C(98) G(25) | 0 | 0 |
| chr3:129695641 | A/G | A | G | . | *TRH* | ENST00000302649 | c.299N>G | p.Glu100Gly | N | T | P | 62 A(46) G(14) | 0 | 0 |
| chr15:65157457 | G/C | G | C | . | *PLEKHO2* | NM\_025201.4 | c.693N>C | p.Glu231Asp | N | T | B | 36 G(27) C(9) | 0 | 0 |
| chr15:65157459 | C/G | C | G | . | *PLEKHO2* | ENST00000437723 | c.845N>G | p.Ala282Gly | N | T | B | 31 C(22) G(9) | 0 | 0 |
| chrX:1531648 | C/T | C | T | . | *ASMTL-AS1* | ENST00000602357 | c.1622N>A | p.Arg541Lys | N | T | B | 25 C(9) T(15) | 0 | 0 |
| chr11:2909504 | T/G | T | G | . | *SLC22A18AS* | ENST00000471157 | c.668N>C | p.Asn223Thr | N | . | B | 71 T(54) G(17) | 0 | 0 |
| chr12:93196421 | TG/TG | T | TG | . | *EEA1* | ENST00000322349 | . | p.Lys810ThrfsTer8 | . | . | . | 44 T(37) TG(7) | 0 | 0 |
| chr14:23306047 | CT/CT | C | CT | . | *MMP14* | ENST00000557221 | . | p.Pro8SerfsTer57 | . | . | . | 120 C(94) CT(20) | 0 | 0 |
| chr17:19319361 | C/G | C | G | . | *RNF112* | ENST00000437646 | c.1769N>G | p.Ala590Gly | . | . | . | 13 C(5) G(5) | 0 | 0 |
| chr19:38806514 | CG/C | CG | C | . | *YIF1B* | XM\_005259384.1 | . | p.Arg15GlyfsTer45 | . | . | . | 31 CG(12) C(17) | 0 | 0 |
| chr21:44838332 | C/C | CG | C | . | *SIK1* | ENST00000478426 | . | p.Ala518ArgfsTer62 | . | . | . | 94 CG(14) C(51) | 0 | 0 |
| chr3:49395675 | C,CCG/C,CCG | CCGCCG | C,CCG | . | *GPX1* | ENST00000419349 | . | p.Ala11GlyfsTer137 | . | . | . | 6 CCGCCG(1) C,CCG(2,2) | 0 | 0 |
| chrX:1522163 | 0/2 | CAG | C,CG | . | *ASMTL-AS1* | ENST00000443929 | . | p.Ter606Lys | . | . | . | 28 CAG(11) C,CG(7,10) | 0 | 0 |

### Tier 2.3 – Variants

There are **21** variants that are not amino acid changing and have no associated rs number.  
There are **166** variants that are amino acid changing, have a rs number and MAF < 1%.  
There are **427** variants that are not amino acid changing, have a rs number and MAF < 1%.

Not amino acid changing and has no rs#; amino acid changing, has rs#, but MAF <1%; not amino acid changing, have a rs number and MAF < 1% (first 50 variants ranked by 'most damaging').

|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| location | genotype | ref | alt | dbSNP | gene | transcript | coding | AAchange | MutationTaster | SIFT | Polyphen2 | coverage | ref\_freq | alt\_freq |
| chr1:155175089 | C/T | C | T | rs72704117 | *THBS3* | ENST00000447623 | c.305N>A | p.Arg102Gln | D | D | D | 88 C(44) T(42) | 0.99 | 0.0056 |
| chr1:230927671 | G/A | G | A | rs140529301 | *CAPN9* | ENST00000354537 | c.1719N>A | p.Met573Ile | D | D | D | 101 G(52) A(49) | 1 | 0.001 |
| chr10:81921766 | C/T | C | T | rs34414015 | *ANXA11* | ENST00000447489 | c.1006N>A | p.Glu336Lys | D | D | D | 72 C(34) T(38) | 1 | 0.0018 |
| chr11:67809268 | C/T | C | T | rs36027301 | *TCIRG1* | ENST00000532635 | c.124N>T | p.Arg42Trp | D | D | D | 101 C(40) T(59) | 0.98 | 0 |
| chr12:69233096 | C/T | C | T | rs78419579 | *MDM2* | ENST00000356290 | c.358N>T | p.Leu120Phe | D | D | D | 88 C(42) T(35) | 1 | 0 |
| chr12:85674230 | G/T | G | T | rs115596276 | *ALX1* | XM\_005269165.1 | c.191N>T | p.Arg64Leu | D | D | D | 22 G(10) T(12) | 1 | 0.0016 |
| chr17:21319121 | C/T | C | T | rs1714864 | *KCNJ12* | XM\_005256625.1 | c.467N>T | p.Pro156Leu | D | D | D | 431 C(233) T(197) | 0 | 0 |
| chr17:21319786 | G/A | G | A | rs78547883 | *KCNJ12* | ENST00000331718 | c.1132N>A | p.Glu378Lys | D | D | D | 206 G(152) A(53) | 0 | 0 |
| chr17:21319943 | A/G | A | G | rs5021699 | *KCNJ12* | XM\_005256625.1 | c.1289N>G | p.Glu430Gly | D | D | D | 294 A(214) G(78) | 0 | 0 |
| chr17:41215926 | C/G | C | G | rs80356860 | *BRCA1* | ENST00000309486 | c.5180N>C | p.Gly1727Ala | D | D | D | 36 C(25) G(11) | 1 | 2e-04 |
| chr17:48604679 | G/C | G | C | rs61754788 | *MYCBPAP* | ENST00000437498 | c.2330N>C | p.Arg777Thr | D | D | D | 119 G(62) C(57) | 0.99 | 0.0082 |
| chr9:33796758 | T/A | T | A | rs796833541 | *PRSS3* | XM\_005251519.1 | c.137N>A | p.Ile46Asn | D | D | D | 126 T(98) A(25) | 0 | 0 |
| chr14:69994973 | C/T | C | T | rs376567575 | *PLEKHD1* | ENST00000322564 | c.1358N>T | p.Pro453Leu | D | D | P | 232 C(116) T(115) | 0 | 0 |
| chr17:21318698 | C/T | C | T | rs1657738 | *KCNJ12* | XM\_005256625.1 | c.44N>T | p.Ser15Leu | D | D | P | 161 C(115) T(46) | 0 | 0 |
| chr1:165667795 | T/G | T | G | rs201507277 | *ALDH9A1* | NM\_000696.3 | . | p.Met1? | D | D | B | 31 T(16) G(14) | 1 | 0 |
| chr17:21318782 | G/A | G | A | rs78117732 | *KCNJ12* | ENST00000331718 | c.128N>A | p.Arg43His | D | D | B | 132 G(80) A(52) | 0 | 0 |
| chr17:21319230 | G/C | G | C | rs1657742 | *KCNJ12* | ENST00000583088 | c.576N>C | p.Gln192His | D | D | B | 144 G(81) C(63) | 0 | 0 |
| chr16:67976320 | A/T | A | T | rs4986970 | *LCAT* | ENST00000573846 | c.161N>A | p.Ser55Thr | D | T | D | 58 A(29) T(28) | 0.99 | 0.0084 |
| chr3:46939587 | C/T | C | T | rs121434601 | *PTH1R* | XM\_005265343.1 | c.448N>T | p.Arg150Cys | D | T | D | 111 C(59) T(52) | 1 | 4e-04 |
| chr15:34159941 | T/G | T | G | rs61729119 | *AVEN* | XM\_005254588.1 | c.728N>C | p.Glu243Ala | D | T | P | 75 T(33) G(42) | 0.99 | 0 |
| chr3:52282458 | C/G | C | G | rs116696868 | *PPM1M* | ENST00000296487 | c.648N>G | p.His216Gln | D | T | P | 37 C(18) G(19) | 1 | 0.0032 |
| chr10:47087501 | C/T | C | T | rs3824733 | *NPY4R* | NM\_001278794.1 | c.718N>T | p.Arg240Cys | D | T | B | 224 C(166) T(58) | 0 | 0 |
| chr11:124749145 | G/A | G | A | rs148372884 | *ROBO3* | ENST00000397801 | c.3527N>A | p.Arg1176His | D | T | B | 22 G(5) A(16) | 1 | 0.0032 |
| chr17:21318821 | A/C | A | C | rs1714865 | *KCNJ12* | XM\_005256625.1 | c.167N>C | p.Glu56Ala | D | T | B | 509 A(342) C(166) | 0 | 0 |
| chr17:21318867 | G/A | G | A | rs73979893 | *KCNJ12* | XM\_005256625.1 | c.213N>A | p.Met71Ile | D | T | B | 417 G(275) A(138) | 0 | 0 |
| chr7:81588641 | G/C | G | C | rs748929082 | *CACNA2D1* | XM\_005250570.1 | c.3094N>G | p.Gln1032Glu | D | T | B | 37 G(20) C(17) | 0 | 0 |
| chr9:73477830 | T/C | T | C | rs140494112 | *TRPM3* | XM\_005252221.1 | c.456N>G | . | D | T | . | 42 T(26) C(16) | 0 | 0 |
| chr13:45912819 | C/T | C | T | rs147579094 | *TPT1* | ENST00000610057 | c.130N>A | . | D | . | . | 116 C(62) T(50) | 1 | 2e-04 |
| chr9:33796801 | G/A | G | A | rs143707562 | *PRSS3* | ENST00000429677 | . | . | D | . | . | 118 G(92) A(26) | 1 | 2e-04 |
| chr7:107312690 | G/T | G | T | rs111033199 | *SLC26A4* | XM\_005250425.1 | c.412N>T | p.Val138Phe | A | D | D | 28 G(13) T(15) | 0 | 0 |
| chr1:111060752 | C/T | C | T | rs34970857 | *KCNA10* | NM\_005549.2 | c.658N>A | p.Val220Met | N | D | P | 144 C(76) T(68) | 0.93 | 0 |
| chr17:41245027 | G/A | G | A | rs1800709 | *BRCA1* | ENST00000473961 | c.2380N>T | p.Arg794Trp | N | D | P | 109 G(52) A(57) | 1 | 0.0022 |
| chr5:38904082 | T/C | T | C | rs35117676 | *OSMR* | XM\_005248387.1 | c.1090N>C | p.Tyr364His | N | D | P | 40 T(24) C(16) | 1 | 0.0036 |
| chr7:50514904 | C/T | C | T | rs62445870 | *FIGNL1* | ENST00000436590 | c.82N>A | p.Gly28Arg | N | D | P | 67 C(26) T(40) | 0.99 | 0.0076 |
| chr17:41244429 | C/T | C | T | rs4986852 | *BRCA1* | ENST00000484087 | c.3119N>A | p.Ser1040Asn | N | T | D | 66 C(33) T(33) | 0.99 | 0.0098 |
| chr5:38921864 | G/A | G | A | rs144394280 | *OSMR* | XM\_005248387.1 | c.1736N>A | p.Gly579Asp | N | T | D | 25 G(11) A(14) | 0.99 | 0.006 |
| chr11:63072184 | C/T | C | T | rs72926329 | *SLC22A10* | ENST00000544661 | c.1421N>T | p.Thr474Met | N | T | B | 59 C(31) T(28) | 0.98 | 0 |
| chr17:21319860 | 0/2 | C | A,T | rs2917720 | *KCNJ12* | XM\_005256625.1 | c.1206N>A | p.Asp402Glu | N | T | B | 468 C(171) A,T(148,148) | 0 | 0 |
| chr17:74387455 | C/T | C | T | rs34070229 | *UBE2O* | ENST00000590379 | c.3451N>A | p.Ala1151Thr | N | T | B | 45 C(21) T(24) | 1 | 0.0042 |
| chr2:220439634 | G/A | G | A | rs149916845 | *INHA* | XM\_005246422.1 | c.487N>A | p.Val163Met | N | T | B | 88 G(49) A(38) | 0 | 0 |
| chr3:151045976 | T/C | T | C | rs61736003 | *P2RY13;MED12L* | ENST00000273432 | c.868N>G | p.Arg290Gly | N | T | B | 30 T(14) C(16) | 0.99 | 0.0094 |
| chr4:1843324 | C/T | C | T | rs116753949 | *LETM1* | ENST00000512669 | c.344N>A | p.Arg115His | N | T | B | 50 C(24) T(26) | 0.98 | 0 |
| chr5:1065514 | A/G | A | G | rs56350427 | *SLC12A7* | ENST00000583759 | c.2321N>C | p.Met774Thr | N | T | B | 50 A(29) G(21) | 0.99 | 0.0052 |
| chr5:76331449 | G/A | G | A | rs34203073 | *AGGF1* | ENST00000503538 | c.397N>A | p.Glu133Lys | N | T | B | 95 G(44) A(48) | 0.99 | 0.0078 |
| chr7:39504235 | A/C | A | C | rs149617494 | *POU6F2* | NM\_001166018.1 | c.1918N>C | p.Thr640Pro | N | T | B | 111 A(56) C(54) | 1 | 8e-04 |
| chr9:33796799 | A/T | A | T | rs200709040 | *PRSS3* | NM\_001197097.2 | c.199N>T | p.Thr67Ser | N | T | B | 121 A(95) T(26) | 0 | 0 |
| chrX:139587212 | C/T | C | T | rs112180170 | *SOX3* | NM\_005634.2 | c.14N>A | p.Arg5Gln | N | T | B | 32 C(19) T(13) | 0 | 0 |
| chr10:18828635 | T/G | T | G | rs58225473 | *CACNB2* | ENST00000377329 | c.1686N>G | p.Asp562Glu | P | D | D | 97 T(52) G(45) | 0.9 | 0 |
| chr11:62886800 | C/C | G | C | rs4963245 | *SLC22A24* | ENST00000498718 | c.514N>G | p.Arg172Gly | P | D | D | 70 G(0) C(70) | 0.84 | 0 |
| chr12:121600253 | T/C | T | C | rs208294 | *P2RX7* | ENST00000535928 | c.193N>C | p.Tyr65His | P | D | D | 71 T(30) C(41) | 0.47 | 0 |

### Tier 2.4 – Rare SNPs

There are **408** variants classified as rare SNPs.

Any variant with rs number and MAF >1% <10% (top 50 variants)

|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| location | genotype | ref | alt | dbSNP | gene | transcript | coding | AAchange | MutationTaster | SIFT | Polyphen2 | coverage | ref\_freq | alt\_freq |
| chr16:57935470 | C/T | C | T | rs79889567 | *CNGB1* | XM\_005255797.1 | c.2854N>A | p.Val952Met | D | D | D | 62 C(34) T(28) | 0.98 | 0.019 |
| chr17:48761053 | G/A | G | A | rs11568591 | *ABCC3* | ENST00000504586 | c.3890N>A | p.Arg1297His | D | D | D | 58 G(34) A(24) | 0.98 | 0.02 |
| chr5:96228072 | C/T | C | T | rs75263594 | *ERAP2* | ENST00000513084 | c.1040N>T | p.Thr347Met | D | D | D | 34 C(15) T(19) | 0.99 | 0.011 |
| chr6:73904557 | C/T | C | T | rs61743058 | *KCNQ5* | ENST00000402622 | c.1751N>T | p.Pro584Leu | D | D | B | 173 C(82) T(89) | 0.98 | 0.017 |
| chr9:136319589 | G/A | G | A | rs28503257 | *ADAMTS13* | ENST00000536611 | c.3097N>A | p.Ala1033Thr | D | T | D | 223 G(100) A(122) | 0.98 | 0.016 |
| chr17:3844345 | G/A | G | A | rs9895012 | *ATP2A3* | ENST00000576957 | c.2020N>T | p.Arg674Cys | D | T | B | 99 G(51) A(48) | 0.99 | 0.013 |
| chr18:44057673 | C/T | C | T | rs74316327 | *LOXHD1* | ENST00000300591 | c.1301N>A | p.Arg434His | D | T | B | 158 C(70) T(88) | 0.97 | 0.027 |
| chr1:41300690 | G/A | G | A | rs55964611 | *KCNQ4* | ENST00000506017 | c.1503N>A | . | D | . | . | 78 G(40) A(38) | 0.99 | 0.012 |
| chr19:1808275 | G/A | G | A | rs61739534 | *ATP8B3* | NM\_001178002.2 | c.303N>T | . | D | . | . | 20 G(9) A(11) | 0.98 | 0.018 |
| chr8:143994266 | A/G | A | G | rs61757294 | *CYP11B2* | ENST00000323110 | c.1157N>C | p.Val386Ala | A | T | B | 99 A(79) G(20) | 0.95 | 0.053 |
| chr17:40932955 | C/A | C | A | rs61754326 | *WNK4* | ENST00000253794 | c.239N>A | p.Ala80Asp | N | D | B | 25 C(12) A(13) | 0.98 | 0.022 |
| chr5:140636 | G/A | G | A | rs12523402 | *PLEKHG4B* | ENST00000512035 | c.214N>A | p.Ala72Thr | N | D | B | 75 G(46) A(29) | 0.97 | 0.033 |
| chr11:2436464 | C/T | C | T | rs34551253 | *TRPM5* | ENST00000533881 | c.1366N>A | p.Ala456Thr | N | T | B | 64 C(33) T(31) | 0.99 | 0.011 |
| chr19:39025366 | C/G | C | G | rs4802584 | *RYR1* | ENST00000599547 | c.11266N>G | p.Gln3756Glu | N | T | B | 129 C(70) G(59) | 0.96 | 0.035 |
| chr2:141242918 | T/C | T | C | rs34488772 | *LRP1B* | NM\_018557.2 | c.9419N>G | p.Gln3140Arg | N | T | B | 52 T(27) C(25) | 0.96 | 0.039 |
| chr4:138442527 | T/C | T | C | rs151070417 | *PCDH18* | ENST00000507846 | c.3064N>G | p.Thr1022Ala | N | T | B | 144 T(73) C(69) | 0.99 | 0.011 |
| chr6:46047640 | T/C | T | C | rs723580 | *CLIC5* | NM\_001114086.1 | c.340N>G | p.Thr114Ala | N | T | B | 59 T(33) C(26) | 0.96 | 0.036 |
| chr6:131520691 | A/G | A | G | rs34324046 | *AKAP7* | XM\_005267228.1 | c.680N>G | p.Lys227Arg | N | T | B | 17 A(11) G(6) | 0.99 | 0.013 |
| chr11:35222681 | C/T | C | T | rs35356320 | *CD44* | ENST00000526553 | c.846N>T | . | N | . | . | 37 C(19) T(18) | 0.97 | 0.027 |
| chr1:160654758 | G/G | C | G | rs2295615 | *CD48* | ENST00000598917 | c.304N>C | p.Glu102Gln | P | D | D | 89 C(0) G(89) | 0.92 | 0.077 |
| chr10:123970722 | T/A | T | A | rs2295876 | *TACC2* | ENST00000360561 | c.1016N>A | p.Leu339His | P | D | D | 102 T(46) A(56) | 0.91 | 0.089 |
| chr11:89017961 | A/A | G | A | rs1126809 | *TYR* | NM\_000372.4 | c.1205G>A | p.Arg402Gln | P | D | D | 78 G(0) A(77) | 0.92 | 0.081 |
| chr12:21028208 | C/C | G | C | rs60140950 | *SLCO1B3* | ENST00000544370 | c.767N>C | p.Gly256Ala | P | D | D | 39 G(0) C(38) | 0.93 | 0.066 |
| chr12:21200089 | G/G | A | G | rs11045681 | *SLCO1B7;.* | ENST00000553473 | c.932N>G | p.Tyr311Cys | P | D | D | 97 A(0) G(97) | 0.92 | 0.076 |
| chr12:21207389 | C/C | T | C | rs11045699 | *SLCO1B7;.* | ENST00000554957 | c.1360N>C | p.Phe454Leu | P | D | D | 18 T(1) C(17) | 0.93 | 0.071 |
| chr17:56438301 | G/A | G | A | rs2680701 | *RNF43* | ENST00000407977 | c.692N>T | p.Pro231Leu | P | D | D | 42 G(20) A(22) | 0.92 | 0.082 |
| chr18:44104437 | T/C | T | C | rs12606417 | *LOXHD1* | ENST00000300591 | c.1535N>G | p.Glu512Gly | P | D | D | 35 T(15) C(20) | 0.94 | 0.062 |
| chr4:47538044 | G/A | G | A | rs35012290 | *ATP10D* | XM\_005248120.1 | c.1009N>A | p.Ala337Thr | P | D | D | 61 G(30) A(31) | 0.95 | 0.054 |
| chr6:110760008 | A/G | A | G | rs12210538 | *SLC22A16* | XM\_005267183.1 | c.716N>C | p.Met239Thr | P | D | D | 129 A(68) G(59) | 0.91 | 0.091 |
| chr9:6328947 | C/C | T | C | rs3847262 | *TPD52L3* | ENST00000344545 | c.352N>C | p.Phe118Leu | P | D | D | 233 T(3) C(230) | 0.077 | 0.92 |
| chr1:16375510 | G/A | G | A | rs11588392 | *CLCNKB;.* | NM\_000085.4 | c.44N>A | p.Gly15Glu | P | D | B | 251 G(137) A(114) | 0.91 | 0.094 |
| chr11:20648364 | G/C | G | C | rs3740870 | *SLC6A5* | XM\_005253225.1 | c.1371N>C | p.Lys457Asn | P | D | B | 92 G(39) C(53) | 0.91 | 0.09 |
| chr11:130275749 | T/C | T | C | rs11222085 | *ADAMTS8* | XM\_003846367.2 | c.2374N>G | p.Thr792Ala | P | D | B | 64 T(28) C(35) | 0.92 | 0.084 |
| chr12:21487544 | A/G | A | G | rs10841795 | *SLCO1A2* | ENST00000452078 | c.38N>C | p.Ile13Thr | P | D | B | 32 A(10) G(22) | 0.95 | 0.052 |
| chr17:43912159 | G/C | G | C | rs16940681 | *CRHR1* | ENST00000339069 | c.838N>C | p.Glu280Gln | P | D | B | 18 G(10) C(8) | 0.91 | 0.086 |
| chr7:50514577 | C/T | C | T | rs10235371 | *FIGNL1* | XM\_005271782.1 | c.76N>A | p.Val26Met | P | D | B | 105 C(62) T(43) | 0.94 | 0.063 |
| chr15:31453147 | G/A | G | A | rs75638145 | *TRPM1* | ENST00000542188 | c.16N>T | p.Arg6Trp | P | D | . | 243 G(127) A(115) | 0.94 | 0.064 |
| chr9:141016262 | G/G | T | G | rs2278973 | *CACNA1B* | ENST00000371355 | c.6644N>G | p.Leu2215Arg | P | D | . | 127 T(0) G(127) | 0.089 | 0 |
| chr12:49951377 | C/T | C | T | rs59261129 | *KCNH3* | NM\_012284.1 | c.2659N>T | p.Arg887Cys | P | T | D | 124 C(63) T(60) | 0.93 | 0.073 |
| chr16:57949224 | G/T | G | T | rs10459809 | *CNGB1* | ENST00000564448 | c.2233N>A | p.Leu745Ile | P | T | P | 11 G(4) T(7) | 0.91 | 0.092 |
| chr17:6441376 | G/A | G | A | rs28493751 | *PITPNM3* | NM\_031220.3 | c.49N>T | p.Pro17Ser | P | T | P | 92 G(49) A(43) | 0.95 | 0.053 |
| chr17:78449948 | C/T | C | T | rs144443274 | *NPTX1* | ENST00000535681 | c.299N>A | p.Gly100Asp | P | T | P | 117 C(62) T(55) | 0.92 | 0.078 |
| chr19:44470189 | A/A | T | A | rs454301 | *ZNF155;ZNF221* | ENST00000591168 | c.535N>A | p.Phe179Ile | P | T | P | 64 T(0) A(64) | 0.056 | 0.94 |
| chr1:13940864 | G/G | C | G | rs2486188 | *PDPN* | ENST00000510906 | c.314N>G | p.Ala105Gly | P | T | B | 48 C(0) G(48) | 0.019 | 0.98 |
| chr1:16344466 | C/T | C | T | rs3738640 | *HSPB7* | ENST00000375692 | c.257N>A | p.Arg86His | P | T | B | 79 C(27) T(51) | 0.91 | 0.09 |
| chr1:16386447 | C/C | G | C | rs11576236 | *FAM131C* | XM\_005245733.1 | c.368N>G | p.Pro123Arg | P | T | B | 161 G(0) C(161) | 0.084 | 0.92 |
| chr1:40363054 | C/C | G | C | rs3134614 | *MYCL;MYCL1* | ENST00000397332 | c.644N>G | p.Thr215Ser | P | T | B | 122 G(0) C(120) | 0.064 | 0.94 |
| chr1:41296828 | T/G | T | G | rs34287852 | *KCNQ4* | NM\_172163.2 | c.1365N>G | p.His455Gln | P | T | B | 99 T(46) G(52) | 0.91 | 0.094 |
| chr1:115576023 | G/G | A | G | rs10776792 | *TSHB* | ENST00000369517 | c.40N>G | p.Thr14Ala | P | T | B | 136 A(1) G(135) | 0.016 | 0.98 |
| chr1:153431406 | G/G | C | G | rs3014837 | *S100A7* | ENST00000368722 | c.84N>C | p.Glu28Asp | P | T | B | 35 C(0) G(35) | 0.017 | 0.98 |

## Tier 3 Annotations – All Other Genes

There are a total of **34111** variants in this tier.

{Anything not included in the previous sets. I would suggest perhaps moving the Rare SNPs for this tier down to Tier 4, as there will be too many to work with. That may also need to be done for the Epilepsy or other panels where there’s more than 30 or so targeted genes in a tier}.

### Tier 3.1 – Top Most Damaging Mutations/Variants

Any of the following:

* Amino acid changing variant
  + no rs#
  + has rs#, but MAF <1%
* No AA change
  + no rs#

{All sorted by the number of predictors showing “Damaging” or the equivalent}

Top most damaging variants.

|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| location | genotype | ref | alt | dbSNP | gene | transcript | coding | AAchange | MutationTaster | SIFT | Polyphen2 | coverage | ref\_freq | alt\_freq |
| chr1:17313568 | C/T | C | T | . | *ATP13A2* | XM\_005245812.1 | c.3041N>A | p.Gly1014Asp | D | D | D | 14 C(7) T(6) | 0 | 0 |
| chr1:36564606 | C/G | C | G | . | *COL8A2* | XM\_005270479.1 | c.481N>C | p.Gly161Arg | D | D | D | 35 C(24) G(8) | 0 | 0 |
| chr1:156914957 | C/G | C | G | . | *ARHGEF11* | XM\_005245629.1 | c.2725N>C | p.Ala909Pro | D | D | D | 59 C(33) G(26) | 0 | 0 |
| chr1:186052079 | A/T | A | T | . | *HMCN1* | ENST00000367492 | c.8870N>T | p.Asn2957Ile | D | D | D | 21 A(14) T(6) | 0 | 0 |
| chr2:210837971 | C/A | C | A | . | *UNC80* | XM\_005246476.1 | c.8351N>A | p.Ser2784Tyr | D | D | D | 110 C(39) A(70) | 0 | 0 |
| chr4:727510 | A/C | A | C | . | *PCGF3* | ENST00000400151 | c.41N>C | p.His14Pro | D | D | D | 225 A(113) C(112) | 0 | 0 |
| chr4:177190166 | T/C | T | C | . | *ASB5* | NM\_080874.3 | c.94N>G | p.Lys32Glu | D | D | D | 18 T(9) C(2) | 0 | 0 |
| chr5:43388530 | A/C | A | C | . | *CCL28* | ENST00000489442 | c.113N>G | p.Ile38Ser | D | D | D | 135 A(75) C(60) | 0 | 0 |
| chr6:46111360 | G/T | G | T | . | *ENPP4* | NM\_014936.4 | c.1345N>T | p.Asp449Tyr | D | D | D | 43 G(17) T(25) | 0 | 0 |
| chr6:110107601 | A/G | A | G | . | *FIG4* | ENST00000230124 | c.1214N>G | p.Glu405Gly | D | D | D | 12 A(8) G(4) | 0 | 0 |
| chr7:87092127 | A/C | A | C | . | *ABCB4* | NM\_018849.2 | c.233N>G | p.Phe78Cys | D | D | D | 62 A(29) C(33) | 0 | 0 |
| chr8:665976 | A/C | A | C | . | *ERICH1* | NM\_207332.1 | c.54N>G | p.Phe18Leu | D | D | D | 13 A(8) C(5) | 0 | 0 |
| chr9:5805182 | C/T | C | T | . | *ERMP1* | XM\_005251587.1 | c.1759N>A | p.Gly587Arg | D | D | D | 61 C(30) T(31) | 0 | 0 |
| chr10:54041962 | 1/2 | CTTTT | CTT,CTTTG | . | *PRKG1* | XM\_005269972.1 | . | p.Phe438LeufsTer18 | D | D | D | 51 CTTTT(19) CTT,CTTTG(14,6) | 0 | 0 |
| chr12:104388200 | T/A | T | A | . | *GLT8D2* | XM\_005269171.1 | c.680N>T | p.Asn227Ile | D | D | D | 143 T(105) A(34) | 0 | 0 |
| chr16:21139072 | G/A | G | A | . | *DNAH3* | ENST00000261383 | c.1144N>T | p.Pro382Ser | D | D | D | 79 G(59) A(18) | 0 | 0 |
| chr16:74760153 | T/G | T | G | . | *FA2H* | ENST00000219368 | c.583N>C | p.Asn195His | D | D | D | 21 T(16) G(4) | 0 | 0 |
| chr17:27910559 | C/T | C | T | . | *GIT1* | ENST00000579937 | c.164N>A | p.Arg55His | D | D | D | 82 C(38) T(42) | 0 | 0 |
| chr18:43446816 | G/A | G | A | . | *EPG5* | ENST00000592272 | c.345N>T | p.Leu116Phe | D | D | D | 58 G(26) A(32) | 0 | 0 |
| chr19:8550921 | G/G | A | G | . | *HNRNPM* | ENST00000598999 | c.1249N>G | p.Met417Val | D | D | D | 5 A(1) G(3) | 0 | 0 |
| chr19:40719994 | A/C | A | C | . | *MAP3K10* | NM\_152479.5 | c.2408N>C | p.Lys803Thr | D | D | D | 6 A(3) C(3) | 0 | 0 |
| chr20:3063815 | A/C | A | C | . | *AVP* | ENST00000380293 | c.130N>G | p.Cys44Gly | D | D | D | 45 A(29) C(10) | 0 | 0 |
| chrX:153176426 | A/C | A | C | . | *ARHGAP4* | ENST00000434679 | c.1631N>G | p.Val544Gly | D | D | D | 9 A(0) C(8) | 0 | 0 |

### Tier 3.2 – Mutations

There are **185** variants that are amino acid changing without associated rs numbers.

Amino acid changing variant, no rs# (first 50 'most damaging' variants)

|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| location | genotype | ref | alt | dbSNP | gene | transcript | coding | AAchange | MutationTaster | SIFT | Polyphen2 | coverage | ref\_freq | alt\_freq |
| chr1:17313568 | C/T | C | T | . | *ATP13A2* | XM\_005245812.1 | c.3041N>A | p.Gly1014Asp | D | D | D | 14 C(7) T(6) | 0 | 0 |
| chr1:36564606 | C/G | C | G | . | *COL8A2* | XM\_005270479.1 | c.481N>C | p.Gly161Arg | D | D | D | 35 C(24) G(8) | 0 | 0 |
| chr1:156914957 | C/G | C | G | . | *ARHGEF11* | XM\_005245629.1 | c.2725N>C | p.Ala909Pro | D | D | D | 59 C(33) G(26) | 0 | 0 |
| chr1:186052079 | A/T | A | T | . | *HMCN1* | ENST00000367492 | c.8870N>T | p.Asn2957Ile | D | D | D | 21 A(14) T(6) | 0 | 0 |
| chr10:54041962 | 1/2 | CTTTT | CTT,CTTTG | . | *PRKG1* | XM\_005269972.1 | . | p.Phe438LeufsTer18 | D | D | D | 51 CTTTT(19) CTT,CTTTG(14,6) | 0 | 0 |
| chr12:104388200 | T/A | T | A | . | *GLT8D2* | XM\_005269171.1 | c.680N>T | p.Asn227Ile | D | D | D | 143 T(105) A(34) | 0 | 0 |
| chr16:21139072 | G/A | G | A | . | *DNAH3* | ENST00000261383 | c.1144N>T | p.Pro382Ser | D | D | D | 79 G(59) A(18) | 0 | 0 |
| chr16:74760153 | T/G | T | G | . | *FA2H* | ENST00000219368 | c.583N>C | p.Asn195His | D | D | D | 21 T(16) G(4) | 0 | 0 |
| chr17:27910559 | C/T | C | T | . | *GIT1* | ENST00000579937 | c.164N>A | p.Arg55His | D | D | D | 82 C(38) T(42) | 0 | 0 |
| chr18:43446816 | G/A | G | A | . | *EPG5* | ENST00000592272 | c.345N>T | p.Leu116Phe | D | D | D | 58 G(26) A(32) | 0 | 0 |
| chr19:8550921 | G/G | A | G | . | *HNRNPM* | ENST00000598999 | c.1249N>G | p.Met417Val | D | D | D | 5 A(1) G(3) | 0 | 0 |
| chr19:40719994 | A/C | A | C | . | *MAP3K10* | NM\_152479.5 | c.2408N>C | p.Lys803Thr | D | D | D | 6 A(3) C(3) | 0 | 0 |
| chr2:210837971 | C/A | C | A | . | *UNC80* | XM\_005246476.1 | c.8351N>A | p.Ser2784Tyr | D | D | D | 110 C(39) A(70) | 0 | 0 |
| chr20:3063815 | A/C | A | C | . | *AVP* | ENST00000380293 | c.130N>G | p.Cys44Gly | D | D | D | 45 A(29) C(10) | 0 | 0 |
| chr4:727510 | A/C | A | C | . | *PCGF3* | ENST00000400151 | c.41N>C | p.His14Pro | D | D | D | 225 A(113) C(112) | 0 | 0 |
| chr4:177190166 | T/C | T | C | . | *ASB5* | NM\_080874.3 | c.94N>G | p.Lys32Glu | D | D | D | 18 T(9) C(2) | 0 | 0 |
| chr5:43388530 | A/C | A | C | . | *CCL28* | ENST00000489442 | c.113N>G | p.Ile38Ser | D | D | D | 135 A(75) C(60) | 0 | 0 |
| chr6:46111360 | G/T | G | T | . | *ENPP4* | NM\_014936.4 | c.1345N>T | p.Asp449Tyr | D | D | D | 43 G(17) T(25) | 0 | 0 |
| chr6:110107601 | A/G | A | G | . | *FIG4* | ENST00000230124 | c.1214N>G | p.Glu405Gly | D | D | D | 12 A(8) G(4) | 0 | 0 |
| chr7:87092127 | A/C | A | C | . | *ABCB4* | NM\_018849.2 | c.233N>G | p.Phe78Cys | D | D | D | 62 A(29) C(33) | 0 | 0 |
| chr8:665976 | A/C | A | C | . | *ERICH1* | NM\_207332.1 | c.54N>G | p.Phe18Leu | D | D | D | 13 A(8) C(5) | 0 | 0 |
| chr9:5805182 | C/T | C | T | . | *ERMP1* | XM\_005251587.1 | c.1759N>A | p.Gly587Arg | D | D | D | 61 C(30) T(31) | 0 | 0 |
| chrX:153176426 | A/C | A | C | . | *ARHGAP4* | ENST00000434679 | c.1631N>G | p.Val544Gly | D | D | D | 9 A(0) C(8) | 0 | 0 |
| chr1:27101415 | G/A | G | A | . | *ARID1A* | ENST00000532781 | c.3548N>A | p.Arg1183Lys | D | D | P | 17 G(11) A(6) | 0 | 0 |
| chr11:118353200 | C/A | C | A | . | *KMT2A* | ENST00000531904 | c.326N>A | p.Pro109Gln | D | D | P | 140 C(104) A(26) | 0 | 0 |
| chr2:86304982 | C/G | C | G | . | *POLR1A* | ENST00000424089 | c.1380N>C | p.Met460Ile | D | D | P | 8 C(4) G(4) | 0 | 0 |
| chr20:43571762 | C/G | C | G | . | *TOMM34* | XR\_244131.1 | c.918N>C | p.Gln306His | D | D | P | 30 C(15) G(15) | 0 | 0 |
| chr3:4345181 | C/G | C | G | . | *SETMAR* | ENST00000448413 | c.127N>G | p.Pro43Ala | D | D | P | 47 C(33) G(14) | 0 | 0 |
| chr6:160210450 | G/C | G | C | . | *TCP1* | ENST00000543532 | c.51N>G | p.Ile17Met | D | D | P | 107 G(52) C(54) | 0 | 0 |
| chr1:35859302 | C/T | C | T | . | *ZMYM4* | ENST00000470175 | c.2882N>T | p.Ser961Phe | D | D | B | 19 C(14) T(5) | 0 | 0 |
| chr16:72829255 | T/G | T | G | . | *ZFHX3* | ENST00000397992 | c.7323N>C | p.Gln2441His | D | D | B | 134 T(71) G(63) | 0 | 0 |
| chr6:11104741 | C/G | C | G | . | *SMIM13* | NM\_207582.2 | c.803N>C | p.Gly268Ala | D | D | B | 13 C(5) G(8) | 0 | 0 |
| chr1:153005001 | G/C | G | C | . | *SPRR1B* | ENST00000392661 | c.180N>C | p.Lys60Asn | D | T | D | 19 G(10) C(9) | 0 | 0 |
| chr12:96674652 | A/G | A | G | . | *CDK17* | NM\_001170464.2 | c.1468N>C | p.Phe490Leu | D | T | D | 19 A(6) G(13) | 0 | 0 |
| chr15:86278346 | G/C | G | C | . | *AKAP13* | XM\_005254856.1 | c.7496N>C | p.Gly2499Ala | D | T | D | 112 G(63) C(49) | 0 | 0 |
| chr17:44109623 | G,GG/G,GG | GC | G,GG | . | *KANSL1* | ENST00000576870 | c.2687N>C | p.Gly896AlafsTer54 | D | T | D | 48 GC(8) G,GG(30,8) | 0 | 0 |
| chr17:48192954 | A/G | A | G | . | *SAMD14* | NM\_174920.3 | c.796N>C | p.Phe266Leu | D | T | D | 22 A(14) G(8) | 0 | 0 |
| chr20:21686540 | G/C | G | C | . | *PAX1* | ENST00000485038 | c.190N>C | p.Gly64Arg | D | T | D | 90 G(52) C(38) | 0 | 0 |
| chr14:95942057 | C/G | C | G | . | *SYNE3* | ENST00000334258 | c.102N>C | p.Gln34His | D | T | P | 31 C(19) G(9) | 0 | 0 |
| chr17:77809016 | G/C | G | C | . | *CBX4* | ENST00000269397 | c.425N>G | p.Pro142Arg | D | T | P | 17 G(11) C(6) | 0 | 0 |
| chr19:7928346 | C/T | C | T | . | *EVI5L* | ENST00000601984 | c.310N>T | p.Pro104Ser | D | T | P | 135 C(98) T(37) | 0 | 0 |
| chr4:140812084 | C/T | C | T | . | *MAML3* | NM\_018717.4 | c.506N>A | p.Arg169Gln | D | T | P | 78 C(41) T(37) | 0 | 0 |
| chr7:43484261 | C/A | C | A | . | *HECW1* | XM\_005249664.1 | c.1490N>A | p.Ala497Asp | D | T | P | 8 C(5) A(3) | 0 | 0 |
| chr1:6157383 | C/A | C | A | . | *KCNAB2* | XM\_005263511.1 | c.980N>A | p.Ala327Glu | D | T | B | 92 C(31) A(60) | 0 | 0 |
| chr1:27736386 | G/A | G | A | . | *WASF2* | NM\_001201404.1 | c.1139N>T | p.Pro380Leu | D | T | B | 13 G(7) A(5) | 0 | 0 |
| chr10:126686557 | C/T | C | T | . | *CTBP2* | ENST00000334808 | c.541N>A | p.Glu181Lys | D | T | B | 126 C(98) T(28) | 0 | 0 |
| chr19:1154247 | C/G | C | G | . | *SBNO2* | ENST00000587024 | c.29N>C | p.Arg10Thr | D | T | B | 29 C(18) G(7) | 0 | 0 |
| chr19:40902581 | A/G | A | G | . | *PRX* | NM\_181882.2 | c.1600N>C | p.Ser534Pro | D | T | B | 5 A(2) G(3) | 0 | 0 |
| chr2:43452524 | T/C | T | C | . | *ZFP36L2* | NM\_006887.4 | c.419N>G | p.Gln140Arg | D | T | B | 9 T(6) C(3) | 0 | 0 |
| chr3:172365834 | C/G | C | G | . | *NCEH1* | NM\_001146278.1 | c.209N>C | p.Gly70Ala | D | T | B | 64 C(47) G(17) | 0 | 0 |

### Tier 3.3 – Variants

{Not amino acid changing and has no rs#; amino acid changing, has rs#, but MAF <1%}

There are **211** variants that are not amino acid changing and have no associated rs number.  
There are **2311** variants that are amino acid changing, have a rs number and MAF < 1%.  
There are **4372** variants that are not amino acid changing, have a rs number and MAF < 1%.

Not amino acid changing and has no rs#; amino acid changing, has rs#, but MAF <1%; not amino acid changing, have a rs number and MAF < 1% (first 50 variants ranked by 'most damaging').

|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| location | genotype | ref | alt | dbSNP | gene | transcript | coding | AAchange | MutationTaster | SIFT | Polyphen2 | coverage | ref\_freq | alt\_freq |
| chr1:1390852 | C/T | C | T | rs200476672 | *ATAD3C* | XM\_005244736.1 | c.391N>T | p.Arg131Trp | D | D | D | 137 C(49) T(88) | 1 | 0 |
| chr1:17690083 | C/T | C | T | rs142092052 | *PADI4* | ENST00000467001 | c.1825N>T | p.Arg609Cys | D | D | D | 87 C(43) T(44) | 1 | 0.0022 |
| chr1:28271918 | G/C | G | C | rs143396392 | *SMPDL3B* | ENST00000466793 | c.237N>C | p.Lys79Asn | D | D | D | 344 G(159) C(185) | 1 | 2e-04 |
| chr1:35227162 | C/T | C | T | rs9426009 | *GJB4* | ENST00000542839 | c.307N>T | p.Arg103Cys | D | D | D | 105 C(43) T(62) | 0.99 | 0.0096 |
| chr1:66102159 | G/A | G | A | rs776269726 | *LEPR* | XM\_005270950.1 | c.2959N>A | p.Ala987Thr | D | D | D | 75 G(38) A(37) | 0 | 0 |
| chr1:144864162 | C/T | C | T | rs145067181 | *PDE4DIP;LOC100288142* | XR\_246991.1 | c.6341N>A | p.Arg2114His | D | D | D | 307 C(234) T(73) | 1 | 0 |
| chr1:144866643 | G/A | G | A | rs1620560 | *PDE4DIP;LOC100288142* | ENST00000494734 | c.6007N>T | p.Arg2003Cys | D | D | D | 323 G(157) A(166) | 0 | 0 |
| chr1:144871738 | C/A | C | A | rs1698605 | *PDE4DIP;LOC100288142* | ENST00000369354 | c.5224N>T | p.Ala1742Ser | D | D | D | 250 C(184) A(65) | 0 | 0 |
| chr1:144880832 | T/C | T | C | rs12568796 | *PDE4DIP;LOC100288142* | ENST00000369356 | c.3628N>G | p.Lys1210Glu | D | D | D | 226 T(170) C(55) | 0 | 0 |
| chr1:144882823 | C/T | C | T | rs1698647 | *PDE4DIP;LOC100288142* | XR\_247000.1 | c.3607N>A | p.Ala1203Thr | D | D | D | 57 C(35) T(22) | 0 | 0 |
| chr1:144916748 | C/G | C | G | rs1747930 | *PDE4DIP;LOC100288142* | ENST00000533963 | c.1607N>C | p.Ser536Thr | D | D | D | 14 C(10) G(4) | 0 | 0 |
| chr1:144918957 | T/A | T | A | rs1061308 | *PDE4DIP;LOC100288142* | XR\_247000.1 | c.1640N>T | p.Glu547Val | D | D | D | 266 T(127) A(138) | 0 | 0 |
| chr1:144931330 | C/T | C | T | rs2762745 | *PDE4DIP;LOC100288142* | XR\_246997.1 | c.379N>A | p.Ala127Thr | D | D | D | 478 C(242) T(236) | 0 | 0 |
| chr1:144994658 | C/A | C | A | rs1664022 | *PDE4DIP;LOC100288142* | ENST00000528129 | c.74N>T | p.Arg25Leu | D | D | D | 499 C(232) A(267) | 0 | 0 |
| chr1:145281408 | C/T | C | T | rs3927729 | *NOTCH2NL;LOC100288142* | ENST00000468030 | c.383N>T | p.Pro128Leu | D | D | D | 605 C(490) T(115) | 0 | 0 |
| chr1:145281633 | C/A | C | A | rs28576333 | *NOTCH2NL;LOC100288142* | ENST00000369340 | c.563N>A | p.Pro188His | D | D | D | 848 C(615) A(232) | 0 | 0 |
| chr1:150530548 | C/G | C | G | rs56228576 | *ADAMTSL4* | ENST00000369038 | c.2305N>G | p.Leu769Val | D | D | D | 96 C(52) G(43) | 0.99 | 0 |
| chr1:156616814 | C/G | C | G | rs115373136 | *BCAN* | ENST00000479949 | c.313N>G | p.Arg105Gly | D | D | D | 276 C(126) G(149) | 0.99 | 0.0056 |
| chr1:162367103 | G/T | G | T | rs34001279 | *SH2D1B* | ENST00000359567 | c.366N>A | p.Asn122Lys | D | D | D | 40 G(24) T(16) | 0.89 | 0 |
| chr1:171753009 | C/T | C | T | rs150575910 | *METTL13* | ENST00000361735 | c.25N>T | p.Arg9Trp | D | D | D | 107 C(46) T(61) | 1 | 2e-04 |
| chr1:182555758 | G/A | G | A | rs114166108 | *RNASEL* | ENST00000444138 | c.184N>T | p.Pro62Ser | D | D | D | 178 G(98) A(79) | 1 | 2e-04 |
| chr1:212957827 | T/C | T | C | rs34978978 | *NSL1* | ENST00000366975 | c.322N>G | p.Ile108Val | D | D | D | 58 T(31) C(27) | 1 | 0.0018 |
| chr1:223934845 | C/T | C | T | rs140704789 | *CAPN2* | ENST00000480581 | c.473N>T | p.Ser158Phe | D | D | D | 11 C(7) T(4) | 1 | 4e-04 |
| chr1:230492801 | C/T | C | T | rs41315609 | *PGBD5* | ENST00000391860 | c.391N>A | p.Ala131Thr | D | D | D | 121 C(54) T(67) | 0.99 | 0.007 |
| chr1:233512244 | C/T | C | T | rs745749354 | *KIAA1804* | NM\_032435.2 | c.233N>T | p.Pro78Leu | D | D | D | 57 C(27) T(30) | 0 | 0 |
| chr10:7759650 | G/A | G | A | rs138977046 | *ITIH2* | ENST00000473227 | c.454N>A | p.Val152Met | D | D | D | 278 G(157) A(119) | 1 | 8e-04 |
| chr10:24816911 | A/G | A | G | rs138435732 | *KIAA1217* | XM\_005252504.1 | c.2921N>G | p.Tyr974Cys | D | D | D | 112 A(49) G(62) | 0 | 0 |
| chr10:24909344 | G/C | G | C | rs751405078 | *ARHGAP21* | ENST00000396432 | c.1480N>G | p.Arg494Gly | D | D | D | 54 G(26) C(26) | 0 | 0 |
| chr10:46999922 | G/T | G | T | rs4926046 | *GPRIN2* | ENST00000374314 | c.1042N>T | p.Val348Leu | D | D | D | 160 G(125) T(35) | 0 | 0 |
| chr10:70987024 | G/A | G | A | rs145939161 | *HKDC1* | XR\_246124.1 | c.125N>A | p.Arg42Gln | D | D | D | 88 G(51) A(36) | 0.99 | 0.0062 |
| chr10:126686593 | G/A | G | A | rs78860838 | *CTBP2* | XM\_005269561.1 | c.709N>T | p.Arg237Cys | D | D | D | 127 G(98) A(28) | 0 | 0 |
| chr11:193865 | T/G | T | G | rs2686894 | *SCGB1C1* | ENST00000525282 | c.209N>G | p.Ile70Arg | D | D | D | 110 T(60) G(50) | 0.51 | 0 |
| chr11:8118860 | C/T | C | T | rs565455543 | *TUB* | ENST00000305253 | c.791N>T | p.Pro264Leu | D | D | D | 31 C(19) T(12) | 1 | 0 |
| chr11:48347067 | C/T | C | T | rs73464001 | *OR4C3* | NM\_001004702.1 | c.575N>T | p.Pro192Leu | D | D | D | 107 C(62) T(45) | 0 | 0 |
| chr11:56468198 | A/G | A | G | rs4990194 | *OR9G1;OR8U8* | NM\_001005213.1 | c.335N>G | p.Tyr112Cys | D | D | D | 324 A(159) G(162) | 0.99 | 0.0056 |
| chr11:64083320 | T/C | T | C | rs201072913 | *ESRRA* | ENST00000406310 | c.1154N>C | p.Leu385Pro | D | D | D | 519 T(426) C(90) | 0 | 0 |
| chr11:64083328 | C/T | C | T | rs79204587 | *ESRRA* | XM\_005273817.1 | c.1162N>T | p.Leu388Phe | D | D | D | 517 C(426) T(88) | 0 | 0 |
| chr11:64083331 | C/T | C | T | rs80310817 | *ESRRA* | ENST00000539854 | c.1165N>T | p.Arg389Cys | D | D | D | 517 C(428) T(89) | 0 | 0 |
| chr11:114453389 | C/A | C | A | rs192956484 | *NXPE4* | ENST00000536916 | c.451N>T | p.Ala151Ser | D | D | D | 111 C(41) A(69) | 1 | 4e-04 |
| chr11:118107852 | C/T | C | T | rs142071163 | *MPZL3* | ENST00000278949 | c.364N>A | p.Asp122Asn | D | D | D | 159 C(76) T(83) | 0 | 0 |
| chr12:27840420 | C/T | C | T | rs138624973 | *PPFIBP1* | ENST00000540503 | c.1909N>T | p.Arg637Trp | D | D | D | 55 C(27) T(28) | 1 | 0.0028 |
| chr12:30878976 | G/C | G | C | rs73079976 | *CAPRIN2* | NM\_001002259.1 | c.1829N>G | p.Pro610Arg | D | D | D | 30 G(11) C(19) | 0.99 | 0 |
| chr12:52695897 | G/A | G | A | rs57242951 | *KRT86* | ENST00000552441 | c.197N>A | p.Arg66His | D | D | D | 60 G(23) A(36) | 1 | 0.0034 |
| chr12:62979252 | A/C | A | C | rs61753654 | *MON2* | ENST00000393632 | c.4881N>C | p.Glu1627Asp | D | D | D | 22 A(12) C(10) | 1 | 0.0018 |
| chr12:71158453 | G/A | G | A | rs144705265 | *PTPRR* | NM\_002849.3 | c.127N>T | p.Arg43Cys | D | D | D | 26 G(17) A(9) | 1 | 0.0014 |
| chr12:95528593 | G/A | G | A | rs117456480 | *FGD6* | NM\_018351.3 | c.3004N>T | p.Arg1002Cys | D | D | D | 60 G(35) A(25) | 1 | 0.002 |
| chr12:108686549 | A/G | A | G | rs192034694 | *CMKLR1* | ENST00000552995 | c.191N>C | p.Ile64Thr | D | D | D | 133 A(75) G(57) | 1 | 0.0022 |
| chr12:123262080 | C/T | C | T | rs150571965 | *CCDC62* | ENST00000341952 | c.79N>T | p.Arg27Trp | D | D | D | 191 C(97) T(94) | 0.99 | 0.0056 |
| chr13:23909622 | G/T | G | T | rs140551762 | *SACS* | ENST00000423156 | c.7952N>A | p.Pro2651Gln | D | D | D | 77 G(36) T(41) | 1 | 0 |
| chr14:52493997 | G/A | G | A | rs144461334 | *NID2* | NM\_007361.3 | c.2596N>T | p.Arg866Trp | D | D | D | 65 G(36) A(28) | 1 | 4e-04 |

## Tier 4 Annotations – Polymorphisms

{Polymorphisms for all Tiers}.

### Tier 4.1 – Polymorphisms for Tier 1 Genes

There are **79** variants with rs numbers and ref MAF > 10%

### Tier 4.2 – Polymorphisms for Tier 2 Genes

There are **2456** variants with rs numbers and ref MAF > 10%

### Tier 4.3 – Polymorphisms for Tier 3 Genes

There are **28050** variants with rs numbers and ref MAF > 10%

# Appendix

### Complete Tier 0 variant table

All variants for Tier 0 (diagnostic panel genes)

|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| location | genotype | ref | alt | dbSNP | gene | transcript | coding | AAchange | MutationTaster | SIFT | Polyphen2 | coverage | ref\_freq | alt\_freq |
| chr1:160093648 | G/A | G | A | rs41265763 | *ATP1A2* | ENST00000478587 | . | . | . | . | . | 109 G(63) A(46) | 0.91 | 0.086 |
| chr1:160097315 | C/A | C | A | rs2295623 | *ATP1A2* | XM\_005245210.1 | . | . | . | . | . | 89 C(50) A(39) | 0.92 | 0.081 |
| chr1:160097666 | G/A | G | A | rs6695366 | *ATP1A2* | ENST00000392233 | . | . | . | . | . | 177 G(94) A(83) | 0.18 | 0.82 |
| chr2:166892788 | T/T | C | T | rs2298771 | *LOC102724058;SCN1A* | NM\_001202435.1 | c.3115N>A | p.Ala1039Thr | P | T | B | 18 C(0) T(18) | 0.21 | 0.79 |
| chr2:166893081 | A/A | G | A | rs7601520 | *LOC102724058;SCN1A* | ENST00000595647 | . | . | . | . | . | 18 G(0) A(18) | 0.21 | 0.79 |
| chr2:166897864 | G/G | A | G | rs6432860 | *SCN1A* | ENST00000423058 | c.2259N>C | . | . | . | . | 122 A(0) G(116) | 0.21 | 0.79 |
| chr2:166900606 | C/C | A | C | rs6753355 | *SCN1A* | NM\_006920.4 | . | . | . | . | . | 38 A(0) C(38) | 0.21 | 0.79 |
| chr2:166903228 | T/T | C | T | rs6432861 | *SCN1A* | ENST00000595647 | . | . | . | . | . | 71 C(0) T(71) | 0.5 | 0.5 |
| chr2:166903445 | C/C | T | C | rs7580482 | *SCN1A* | NM\_006920.4 | c.1212N>G | . | . | . | . | 52 T(0) C(52) | 0.29 | 0.71 |
| chr2:166905375 | G/G | A | G | rs1542484 | *SCN1A* | ENST00000409050 | . | . | . | . | . | 122 A(0) G(122) | 0.5 | 0.5 |
| chr2:166905480 | A/A | G | A | rs994399 | *SCN1A* | ENST00000303395 | . | . | . | . | . | 133 G(1) A(132) | 0.29 | 0.71 |
| chr2:166930214 | A/A | T | A | rs566839 | *SCN1A;.* | NM\_006920.4 | . | . | . | . | . | 65 T(0) A(65) | 0.015 | 0.99 |
| chr10:118957027 | A/G | A | G | rs67346047 | *KCNK18* | ENST00000452430 | c.28N>G | p.Arg10Gly | P | T | B | 94 A(45) G(47) | 0.91 | 0.089 |
| chr19:13317980 | G/T | G | T | rs7254351 | *CACNA1A* | NM\_000068.3 | . | . | . | . | . | 59 G(28) T(28) | 0.49 | 0.51 |
| chr19:13355900 | G/G | T | G | rs16039 | *CACNA1A* | NM\_023035.2 | . | . | . | . | . | 24 T(0) G(23) | 0.012 | 0.99 |
| chr19:13411482 | A/A | G | A | rs16018 | *CACNA1A* | NM\_001127222.1 | . | . | . | . | . | 106 G(1) A(104) | 0.26 | 0.74 |
| chr19:13418707 | C/T | C | T | rs16015 | *CACNA1A* | NM\_001127221.1 | . | . | . | . | . | 69 C(39) T(26) | 0.9 | 0.099 |
| chr19:13445144 | T/T | C | T | rs2306348 | *CACNA1A* | XM\_005260066.1 | . | . | . | . | . | 133 C(0) T(133) | 0.35 | 0.65 |
| chr19:13445208 | T/T | C | T | rs2248069 | *CACNA1A* | NM\_000068.3 | c.1182N>A | . | . | . | . | 139 C(2) T(136) | 0.36 | 0.64 |
| chr19:15271771 | A/A | G | A | rs1044009 | *NOTCH3* | ENST00000595514 | c.6512N>T | p.Ala2171Val | P | T | B | 70 G(0) A(70) | 0.37 | 0.63 |
| chr19:15276143 | T/T | C | T | rs2074618 | *NOTCH3* | ENST00000597756 | . | . | . | . | . | 76 C(0) T(76) | 0.13 | 0.87 |
| chr19:15276919 | A/A | G | A | rs2074619 | *NOTCH3* | ENST00000263388 | . | . | . | . | . | 116 G(2) A(114) | 0.13 | 0.87 |
| chr19:15276923 | T/T | C | T | rs10416777 | *NOTCH3* | ENST00000263388 | . | . | . | . | . | 114 C(0) T(114) | 0.13 | 0.87 |
| chr19:15278057 | G/G | A | G | rs1548555 | *NOTCH3* | ENST00000597756 | . | . | . | . | . | 42 A(0) G(42) | 0.13 | 0.87 |
| chr19:15281386 | A/A | C | A | rs2074620 | *NOTCH3* | ENST00000595514 | . | . | . | . | . | 23 C(0) A(23) | 0.46 | 0.54 |
| chr19:15281459 | C/G | C | G | rs56277836 | *NOTCH3* | ENST00000597756 | . | . | . | . | . | 40 C(14) G(26) | 0.95 | 0.05 |
| chr19:15285052 | C/C | T | C | rs1044006 | *NOTCH3* | ENST00000263388 | c.4407N>G | . | . | . | . | 165 T(0) C(165) | 0.13 | 0.87 |
| chr19:15289613 | T/T | A | T | rs11670823 | *NOTCH3* | ENST00000600841 | . | . | . | . | . | 48 A(0) T(48) | 0.48 | 0 |
| chr19:15290125 | A/A | G | A | rs56061231 | *NOTCH3* | ENST00000595045 | . | . | . | . | . | 57 G(2) A(53) | 0.48 | 0.52 |
| chr19:15292271 | T/T | C | T | rs11669950 | *NOTCH3* | ENST00000600841 | . | . | . | . | . | 96 C(0) T(96) | 0.47 | 0.53 |
| chr19:15292366 | T/T | C | T | rs11669982 | *NOTCH3* | ENST00000595045 | . | . | . | . | . | 111 C(1) T(110) | 0.26 | 0.74 |
| chr19:15292437 | C/C | T | C | rs1043997 | *NOTCH3* | ENST00000601011 | c.2742N>G | . | . | . | . | 101 T(0) C(100) | 0.26 | 0.74 |
| chr19:15295134 | A/A | G | A | rs1043996 | *NOTCH3* | ENST00000595045 | c.2538N>T | . | . | . | . | 22 G(0) A(22) | 0.48 | 0.52 |
| chr19:15300069 | C/C | T | C | rs10423702 | *NOTCH3* | ENST00000263388 | . | . | . | . | . | 311 T(1) C(309) | 0.15 | 0.85 |
| chr19:15302844 | C/C | T | C | rs1043994 | *NOTCH3* | NM\_000435.2 | c.606N>G | . | . | . | . | 25 T(0) C(25) | 0.14 | 0.86 |

### MutationAssessor HTML links

These variants are all **MutationTaster\_pred=D [damaging]** and **MutationAssessor\_pred=H [high]**.

MutationAssessor links for the Top Most Damaging Mutations/Variants

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| LOCATION | REF | ALT | RSNO | GENESYM | DP\_coverage | URL |
| 1:36564606 | C | G | . | COL8A2 | 35 | <http://mutationassessor.org/r3/?cm=var&var=hg19,1,36564606,C,G&fts=all> |
| 11:8118860 | C | T | rs565455543 | TUB | 31 | <http://mutationassessor.org/r3/?cm=var&var=hg19,11,8118860,C,T&fts=all> |
| 11:64083320 | T | C | rs201072913 | ESRRA | 519 | <http://mutationassessor.org/r3/?cm=var&var=hg19,11,64083320,T,C&fts=all> |
| 11:64083331 | C | T | rs80310817 | ESRRA | 517 | <http://mutationassessor.org/r3/?cm=var&var=hg19,11,64083331,C,T&fts=all> |
| 11:67809268 | C | T | rs36027301 | TCIRG1 | 101 | <http://mutationassessor.org/r3/?cm=var&var=hg19,11,67809268,C,T&fts=all> |
| 16:16173232 | G | T | rs45511401 | ABCC1 | 161 | <http://mutationassessor.org/r3/?cm=var&var=hg19,16,16173232,G,T&fts=all> |
| 17:36935737 | C | T | rs111394547 | PIP4K2B | 27 | <http://mutationassessor.org/r3/?cm=var&var=hg19,17,36935737,C,T&fts=all> |
| 17:45669359 | T | G | rs200616431 | NPEPPS | 311 | <http://mutationassessor.org/r3/?cm=var&var=hg19,17,45669359,T,G&fts=all> |
| 2:160994197 | C | T | rs55841905 | ITGB6 | 179 | <http://mutationassessor.org/r3/?cm=var&var=hg19,2,160994197,C,T&fts=all> |
| 5:140222738 | T | A | rs62622825 | PCDHA1;. | 155 | <http://mutationassessor.org/r3/?cm=var&var=hg19,5,140222738,T,A&fts=all> |
| 6:32012987 | A | G | rs62402693 | TNXA;TNXB | 103 | <http://mutationassessor.org/r3/?cm=var&var=hg19,6,32012987,A,G&fts=all> |
| 6:38905957 | C | T | rs61757218 | DNAH8 | 82 | <http://mutationassessor.org/r3/?cm=var&var=hg19,6,38905957,C,T&fts=all> |
| 6:46135884 | C | G | rs34109856 | ENPP5 | 112 | <http://mutationassessor.org/r3/?cm=var&var=hg19,6,46135884,C,G&fts=all> |
| 6:46682233 | G | A | rs370831021 | PLA2G7 | 61 | <http://mutationassessor.org/r3/?cm=var&var=hg19,6,46682233,G,A&fts=all> |
| 7:87092127 | A | C | . | ABCB4 | 62 | <http://mutationassessor.org/r3/?cm=var&var=hg19,7,87092127,A,C&fts=all> |
| 9:33796758 | T | A | rs796833541 | PRSS3 | 126 | <http://mutationassessor.org/r3/?cm=var&var=hg19,9,33796758,T,A&fts=all> |
| X:153176426 | A | C | . | ARHGAP4 | 9 | <http://mutationassessor.org/r3/?cm=var&var=hg19,X,153176426,A,C&fts=all> |