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| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Gene;**  **HGNC ID** | **Phenotype** | | **Coding variant HGVS; chr:pos:ref:alt** | **Non-coding region variant** | | | | | |
| **Normalised specific disease** | **Abstracted selected HPO terms** | **Details**  **HGVS; chr:pos:ref:alt** | **gnomAD FAF** | **GEL AF** | **SpliceAI** | **PhyloP** | **CADD** |
| *GAA*;  HGNC:4065 | Limb girdle muscular dystrophy | Abnormality of the calf musculature; muscular dystrophy; respiratory insufficiency; Abnormality of the eye; progressive muscle weakness | NC\_000017.11:g.80118288G>A; ENST00000302262.8:c.2577G>A; p.(Trp859Ter); chr17:80118288:G:A  Nonsense | NC\_000017.11:g.80101399C>G;  NG\_029761.1:g.69768C>G; chr17:80101399:C:G  Core Promoter | 2.75x10-3 | 3.17x10-3 | NA | -0.19 | 5.88 |
| *NPHP3*;  HGNC:7907 | Proteinuric renal disease | Abnormal renal corpuscle morphology; abnormal liver morphology; abnormal urine metabolite level | NC\_000003.12:g.132691199G>A; ENST00000337331.10:c.2563C>T;  p.(Gln855Ter); chr3:132691199:G:A  Nonsense | NC\_000003.12:g.132684549C>T; ENST00000337331.10:c.3570+5G>A; chr3:132684549:C:T  Intronic | 5.14x10-6 | 8.95x10-5 | 0.04 | 6.15 | 21.0 |
| *ALMS1*;  HGNC:428 | Cone dysfunction syndrome | Abnormal visual electrophysiology; Abnormal eye physiology; Abnormal retinal morphology; Abnormality of vision | NC\_000002.12:g.73572649del;  ENST00000613296.6:c.10772del;  p.(Thr3591LysfsTer6) ;  chr2:73572648:AC:A  Frameshift | NC\_000002.12:g.73573562G>A; ENST00000613296.6:c.11547+138G>A;  chr2:73573562:G:A  Intronic | 1.72x10-3 | 1.73x10-3 | 0.01 | 3.84 | 20.2 |
| *LAMA2*;  HGNC:6482 | Congenital myopathy | Abnormal skeletal muscle morphology; muscle weakness; abnormal muscle physiology; abnormal joint physiology | NC\_000006.12:g.129316089C>T;  ENST00000421865.3:c.3976C>T;  p.(Arg1326Ter); chr6:129316089:C:T  Nonsense | NC\_000006.12:g.129475370dup; ENST00000421865.3:c.7440-20dup; chr6:129475360:G:GT  Intronic | 4.71x10-4 | 5.88x10-4 | 0.10 | NA | 8.48 |
| *IGHMBP2*;  HGNC:5542 | Charcot-Marie-Tooth disease | Peripheral axonal degeneration | NC\_000011.10:g.68936909del;  ENST00000255078.8:c.2429del;  p.(Pro810LeufsTer21); chr11:68936904:GC:G  Frameshift | NC\_000011.10:g.68929807G>A; ENST00000255078.8:c.1235+450G>A;  chr11:68929807:G:A  Intronic | 9.51x10-5 | 1.66x10-4 | 0.12 | -1.91 | 0.21 |
| *PKHD1;*  HGNC:9016 | Cystic kidney disease | Abnormality of urine homeostasis; abnormality of urethra; abnormality of the kidney; abnormal renal morphology | NC\_000006.12:g.52028249G>A;  ENST00000371117.8:c.3467C>T;  p.(Ser1156Leu); chr6:52028249:G:A Missense | NC\_000006.12:g.51882440T>C;  ENST00000371117.8:c.7350+653A>G; chr6:51882440:T:C Intronic | 0.00 | 7.68x10-5 | 0.95 | -0.30 | 8.22 |
| *PAH;*  HGNC:8582 | Undiagnosed metabolic disorders | Abnormality of metabolism/ homeostasis; tremor; abnormality of bone mineral density | NC\_000012.12:g.102844359G>C;  ENST00000553106.6:c.1042C>G;  p.(Leu348Val); chr12:102844359:G:C Missense | NC\_000012.12:g.102843790C>T;  ENST00000553106.6:c.1066-11G>A;  chr12:102843790:C:T Intronic | 3.74x10-4 | 3.84x10-4 | 0.98 | 0.88 | 23.5 |

Table 1: Candidate coding/non-coding variant pairs. Shown are variant details, selected annotations, and phenotypic data relating to the proband. All chromosome coordinates related to GRCh38. HPO: Human Phenotype Ontology; AF: Allele Frequency; FAF: gnomAD v3.0 filtering AF.