**Supplementary Materials**

Supplementary Table 1. Summary of molecular diagnosis

|  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Patient | Gene | Transcript ID | Mutation | Zygosity | Segregation analysis | MAF | Taiwan biobank | SIFT | Polyphen-2 | ACMG classification | ClinVar |
| Patients with definite or probable diagnosis based on a positive whole-exome sequencing result | | | | | | | | | | | | |
| Myopathy-definite diagnosis | | | | | | | | | | | | |
| 1 | GNE | NM\_001128227.3 | c.[1618C > T];[829C > T]  p.[His540Tyr];[Arg277Trp] | Het/Het | **AR/AR** | 0.001/0.0001 | 0.00100/NA | Deleterious/Benign | Damaging/Probably damaging | LP/P | LP/P |
| 2 | ETFDH | NM\_0044534 | c.[250G > A];[250G > A]  p.[Ala84Thr];[Ala84Thr] | Hom | Not checked | 0.0045 | 0.00450 | Deleterious | Damaging | P | P |
| 3 | ETFDH | NM\_004453.3 | c.[250G > A]; [250G > A] p.[Ala84Thr]; [Ala84Thr] | Hom | Not checked | 0.00396 | 0.00396 | Deleterious | Damaging | P | P |
| 4 | TCAP | NM\_003673.3  Exon1 | c.23\_24insCGAGGTGT  p.Glu12\_ArgfsTer20 | Hom | Not checked | 0.001 | NA | - | - | P | P |
| 5 | TCAP | NM\_003673.4 | c.26\_33dup  p.Glu12\_Argfs\*20 | Hom | Not checked | 0.0025 | 0.00250 | - | - | P | P |
| 6 | DMD | NA | g.(?- 31929601)\_(32035615-?)del  Exon 45-47 deletion | Het | Not checked | NA | NA | - | - | P | - |
| 7 | GNE | NM\_001128227 | c.[1399C > T];[815T > G]  p.[Gln467X];[Ile272Ser] | Het/Het | **AR/AR** | 5.798e-05/0.00033 | NA/0.00033 | -/Tolerated | -/Benign | P/LP | LP/Conflicting interpretations of pathogenicity |
| 8 | CLCN1 | NM\_000083.3 | c.[178C>T]; [1444G>A]  p. [Gln60Ter];[Gly482Arg] | Het/Het | **AR/AR** | NA/0.0001 | NA/NA | -/Deleterious | -/Damaging | P/LP | -/P |
| Myopathy-probable diagnosis | | | | | | | | | | | |
| 9 | CAPN3 | NM\_000070.3 | c.[1621C > T];[1621 = ]  p.[Arg541Trp];[Arg541 = ] | Het | Not checked | 0.001 | 0.001 | Deleterious | Damaging | LP | Conflicting  interpretations of  pathogenicity |
| 10 | TTN | NM\_000070.3 | c.[95136T>G];[95136=]  p.[Cys31712Trp];[Cys31712= | Het | Not checked | 0.001 | 0.001 | Deleterious | Damaging | LP | Conflicting  interpretations of  pathogenicity |
| 11 | DYSF | NM\_003494 | c.[1277G > T];[1667T > C]  p.[Gly426Val];[Leu556Pro] | Het/Het | Not checked | -/0.00066 | -/0.00066 | Deleterious/Deleterious | Damaging/Benign | P/LP | -/LP |
| 12 | SCN4A | NM\_000334 | c.[2297T > C];[2297T = ] p.[Met766Thr];[Met766 = ] | Het | Not checked | 0.00066 | 0.00066 | Deleterious | Damaging | LP | - |
| 13 | FHL1 | NM\_001449.4 | c.[394T > C];[394 = ] p.[Cys132Arg];[Cys132 = ] | Het | Not checked | NA | NA | Deleterious | Damaging | LP | - |
| Neuropathy-definite diagnosis | | | | | | | | | | | | |
| 14 | PMP22 | NA | g.(?-15230907)\_(15569020\_?)del  Total deletion of PMP22 gene | Het | Not checked | NA | NA | - | - | P | - |
| Neuropathy-probable diagnosis | | | | | | | | | | | |
| 15 | FBXO38 | NM\_030793.4 | c.[1389G > A];[1389G = ]  p.[Met463Ile];[Met463 = ] | Het | Not checked | NA | NA | Deleterious | Damaging | LP | - |
| 16 | POLG | NM\_002693.3 | c.[3535T > C];[3535T = ] p.[Phe1179Leu];[Phe1179 = ] | Het | Not checked | NA | NA | Deleterious | Damaging | LP | - |
| 17 | OPA1 | NM\_130831 | c.2600-2601del  p.Val867Glufs\* | Het | Not checked | NA | NA | - | - | P | - |
| Patients with definite or probable diagnosis based on an inconclusive whole-exome sequencing result but supporting clinical data | | | | | | | | | | | | |
| Myopathy-definite diagnosis | | | | | | | | | | | | |
| 18 | DES | NM\_001927 | c.1189\_1206del  p.397\_402del | Het | Not checked | NA | NA | - | - | VUS | - |
| 19 | DMD | NA | g.(?\_32287478)\_(32699344-?)dup  Exon 8~43 duplication | Het | Not checked | NA | NA | - | - | VUS | - |
| 20 | TK2 | NM\_004614 | c.[367C > G];[157-2A > C]  p.[R123G];[splice site] | Het/Het | **AR/AR** | 0.0068/NA | 0.00450/NA | Tolerated | Possibly damaging | VUS/LP | -/- |
| Myopathy-probable diagnosis | | | | | | | | | | | | |
| 21 | SLCO2A1 | NM\_005630 | c.[T1069C];[ G1106A]  p.[Tyr357His];[Gly369Asp] | Het/Het | Not checked | 0.0002/0.002 | 0.00033/0.00033 | Deleterious/Deleterious | deleterious/deleterious | VUS/LP | -/- |
| 22 | TTN | NM\_133378 | c.[1800+1G > A];[1800+1 = ] | Het | Not checked | 0.00231 | 0.00231 | - | - | VUS | Conflicting  interpretations of  pathogenicity |
| 23 | POLG | NM\_002693 | c.[2653A > C];[ 924G > C]  p.[Thr885Pro];[Gln308His] | Het/Het | Not checked | 0.0006/NA | NA/NA | Tolerated/Deleterious | Benign/Damaging | VUS/LP | -/- |
| Neuropathy-probable diagnosis | | | | | | | | | | | | |
| 24 | NEFH | NM\_021076 | c.[G559T];[G559 = ]  p.[Asp187Tyr];[Asp187 = ] | Het | Not checked | NA | NA | - | - | VUS | - |
| 25 | NEFH | NM\_021076 | c.2230\_2247del  p.744\_749del | Het | Not checked | 0.5614 | 0.5614 | - | - | VUS | - |
| 26 | SCO2 | NM\_005138.3 | c.[544C > T];[ 358C > T]  p.[Gln182Ter];[Arg120Trp] | Het/Het | Not checked | 0.0001/0.004 | NA/0.00400 | -/ Deleterious | -/Probably damaging | P/VUS | -/VUS |
| Patients who were diagnosed with further work-up | | | | | | | | | | | | |
| Myopathy-definite diagnosis | | | | | | | | | | | | |
| 27 | Not found | - | - | - | - | - | - | - | - | - | - |
| 28 | MT-TL1 | - | m.3243A > G | Heteroplasmy level: 33.41% | Not checked | NA | NA | - | - | P | P |
| Neuropathy-definite diagnosis | | | | | | | | | | | | |
| 29 | ATXN3 | - | CAG repeat numbers:  28/63\* (Pathogenic≧52) | Het | Not checked | NA | NA | - | - | P | - |
| Neuropathy-probable diagnosis | | | | | | | | | | | | |
| 30 | Not found | - | - | - | - | - | - | - | - | - | - |
| Patients without diagnosis by whole-exome sequencing and in further work-up | | | | | | | | | | | | |
| Myopathy | | | | | | | | | | | | |
| 31 | Not found | - | - | - | - | - | - | - | - | - | - |
| 32 | Not found | - | - | - | - | - | - | - | - | - | - |
| 33 | ACAD9 | NM\_014049.5 | c.[797G > A];[797G = ]  p.[Arg266Gln];[Arg266 = ] | Het | Not checked | 0.000061 | NA | Deleterious | Probably damaging | LP | P |
| 34 | Not found | - | - | - | - | - | - | - | - | - | - |
| 35 | Not found | - | - | - | - | - | - | - | - | - | - |
| 36 | Not found | - | - | - | - | - | - | - | - | - | - |
| 37 | ANO5 | NM\_213599.2 | c.191dupA  p.Asn64LysfsTer15 | Het | Not checked | 0.0022 | NA | - | - | P | P/LP |
|  | FKRP | NM\_024301.4 | c.[826C > A]; [826 = ]  p.[Leu276Ile]; [Leu276 = ] | Het |  | 0.0168 | NA | Tolerated | Benign | P | P |
| Neuropathy | | | | | | | | | | | | |
| 38 | POLG | NM\_002693.2 | c.[2890C > T],[2890C = ]  p.[Arg964Cys]; [Arg964 = ] | Het | Not checked | 0.0123 | 0.01055 | Deleterious | Damaging | P | Conflicting  interpretations of  pathogenicity |
| 39 | SPTLC1 | NM\_006415  .3 | c.[766C > T];[766C = ]  p.[Pro256Ser];[Pro256 = ] | Het | not cosegregation | NA | NA | Deleterious | Damaging | VUS | - |
| 40 | HARS | NM\_002109 | c.1255\_1256delinsCT p.Lys419Leu | Het | not cosegregation | - | - | - | - | VUS | - |
| 41 | Not found | - | - | - | - | - | - | - | - | - | - |

Het: heterozygote, Hom: homozygote; P: pathogenic; LP: likely pathogenic; VUS: variant of uncertain significance; AD: autosomal dominant; AR: autosomal recessive; XL: X-linked