**Table S2: Detailed list of pathogenic, likely or possibly pathogenic variants**

| Patient | Gender, Age | Gene | Pathogenic variants | Variant type | Familial segregation | Familial data | ExAC/ gnomAD | SIFT/ Polyphen 2 | MPA score | CADD | Splice AI | ACMG Class | Clinical features | CK | Muscle biopsy |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| I15 | M, 4y | *ACTA1* NM_001100 .3 | c.493G>C p.(Val165Leu) | Missense | *De novo* variant | Sporadic | Absent | S : - P : D (0.93) | 7.7 | 4,127 | AG: 0 (-3) AL: 0 (38) DG: 0 (-8) DL: 0 (1) | 5 | Severe neonatal hypotonia with respiratory failure | x2 | Non-specific myopathic changes |
| I2 | M, <1y | *ACTA1* | c.449C>T p.(Thr150Ile) | Missense | Parents not tested | Sporadic | Absent | S : - P : B (0.38) | 9 | 3,368 | AG: 0 (31) AL: 0 (48) DG: 0 (-5) DL: 0 (48) | 4 | Severe neonatal hypotonia with arthrogryposis | Nl | Non-specific myopathic changes |
| I100 | M, <1y | *ACTA1* | c.1057A>G p.(Thr353Ala) | Missense | Parents not tested | Sporadic | Absent | S : - P : D (0.91) | 9 | 3,93 | AG: 0 (36) AL: 0 (-12) DG: 0 (5) DL: 0 (37) | 4 | Severe neonatal hypotonia with respiratory failure | Nl | Non-specific myopathic changes |
| I135 | M, <1y | *ACTA1* | c.553C>T p.(Arg185Cys) | Missense | *De novo* variant | Sporadic | Absent | S : - P : D (0.99) | 10 | 4,574 | AG: 0 (-44) AL: 0 (-27) DG: 0 (2) DL: 0 (-35) | 5 | Severe neonatal hypotonia | x2 | Non-specific myopathic changes |
| I192 | M, 20y | *ACTA1* | c.889G>A p.(Ala297Thr) | Missense | *De novo* variant | Sporadic | Absent | S : - P : B (0.07) | 6.6 | 2,541 | AG: 0 (9) AL: 0 (40) DG: 0 (10) DL: 0 (5) | 5 | Asymptomatic CK elevation | x20 | Non-specific myopathic changes |
| I32 | F, 40y | *ANO5* NM_213599 .2 | c.1622_1623insA p.(Met543AsnFs*) | Frameshift indel | Mother was heterozygous | AR (one affected sister) | 4.37e-05/ 3.68e-05 | | 10 | 5,605 | AG: 0 (7) AL: 0 (-17) DG: 0 (6) DL: 0.25 (7) | 5 | Exercise intolerance | x20 | Dystrophic pattern |
| | | | c.1991T>C p.(Phe664ser) | Missense | Father not tested | | Absent | S : T (0.1) P : D (0.97) | 6 | 3,034 | AG: 0 (-4) AL: 0 (-2) DG: 0 (38) DL: 0 (-39) | 3 | | | |
| I53 | M, 51y | *ANO5* | c.656A>G (homozygous) p.(Tyr219Cys) | Missense | Not tested | Sporadic. Familial consanguinity | 8.309e-06/ 7.09e-06 | S : D (0.02) P : D (0.99) | 9 | 4,013 | AG: 0 (-7) AL: 0 (13) DG: 0.01 (45) DL: 0 (-7) | 4 | LGMD | x20 | Dystrophic pattern. Normal IHC |
| I303 | F, 30y | *CACNA1S* NM_000069 .2 | c.5104C>T p.(Arg1702*) | Nonsense | Father was heterozygous | Affected deceased brother | 9.309e-05/ 8.492e-05 | | 10 | 6,754 | AG: 0 (-23) AL: 0 (40) DG: 0 (2) DL: 0.02 (-30) | 5 | Neonatal hypotonia | Nl | Non-specific myopathic changes |
| | | | c.2970G>A p.(Trp990*) | Nonsense | Mother was heterozygous | | Absent | | 10 | 9,326 | AG: 0 (-9) AL: 0 (41) DG: 0.79 (4) DL: 0 (0) | 5 | | | |
| I164 | M,20y | *CACNA1S* | c.2447T>G p.(Leu816Arg) | Missense | Present in his pauci-symptomatic father | AD | Absent | S : D (0.0) P : D (0.99) | 10 | 3,232 | AG: 0 (50) AL: 0 (8) DG: 0 (-40) DL: 0 (-43) | 4 | Neonatal hypotonia | Nl | Non-specific myopathic changes |
| I43 | F, 36y | *CAPN3* NM_000070 .2 | c.1250C>T p.(Thr417Met) | Missense | Parents not tested | Sporadic | 4.95e-05/ 4,95e-05 | S : D (0.017) P : D (0.99) | 9 | 4,084 | AG: 0 (17) AL: 0 (-19) DG: 0 (40) DL: 0 (42) | 4 | LGMD | x20 | Dystrophic pattern. Normal IHC |
| | | | c.1536+3A>G | Splicing | | | Absent | | 10 | 2,852 | AG: 0.04 (-14) AL: 0 (-3) DG: 0 (-15) DL: 0.27 (-3) | 4 | | | |

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|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| I219 | M, 23 y | *CAPN3* | c.1469G>A (homozygous) p.(Arg490Gln) | Missense | Not tested | Sporadic | 5.95e-05/ 6,725e-05 | S : D (0.01) P : D (1) | 8 | 4,12 | AG: 0 (2) AL: 0 (-32) DG: 0 (-44) DL: 0 (19) | 4 | LGMD | x10 | Dystrophic pattern. Normal IHC |
| I144, I148 | F,9y M, 40y | *COL6A1* NM_001848 .2 | c.299_428+152delinsGA CAGGA | CNV | Affected brother and father were heterozygous | AD | Absent | S: D (0) P: D (0.99) | 10 | NA | NA | 5 | CM with early joint contractures | x2 | Non-specific myopathic changes |
| I269 | F, 36y | *COL6A1* | c.806G>A p.(Gly269Glu) | Missense | *De novo* variant | Sporadic | Absent | S : D (0) P : D (0.99) | 10 | 4,685 | AG: 0.55 (3) AL: 0 (9) DG: 0 (3) DL: 0 (8) | 4 | CM with contractures and respiratory failure | UNK | Dystrophic pattern |
| I65 | M, 10y | *COL6A1* | c.739-1G>A | Splicing | Present in affected father | AD | Absent | | 10 | 5,196 | AG: 0.48 (22) AL: 1 (1) DG: 0 (-50) DL: 0 (21) | 5 | CM with contractures | Nl | Not done |
| I93 | M, 10y | *COL6A2* NM_001849 .3 | c.403G>A p.(Asp135Asn) | Missense | Present in mother | Sporadic | Absent/ 4e-06 | S : D (0) P : D (0.98) | 10 | 4,049 | AG: 0 (30) AL: 0 (-33) DG: 0 (3) DL: 0 (22) | 4 | LGMD with contractures | x5 | Dystrophic pattern |
| | | | c.2905G>A p.(Val969Met) | Missense | Present in father | | 1.702e-05/ 2e-06 | S : D (0.007) P : D (0.983) | 9 | 3,592 | AG: 0 (29) AL: 0 (-3) DG: 0 (2) DL: 0 (-1) | 4 | | | |
| I429 | M, 20y | *COL6A3* NM_004369 .3 | c.6170A>G p.(Glu2057Gly) | Missense | Not tested | Sporadic | Absent | S : T (0.082) P : D (0.974) | 8 | 2,928 | AG: 0 (36) AL: 0 (13) DG: 0 (-44) DL: 0 (-40) | 4 | LGMD | x3 | Not done |
| I542 | M, 4y | *COL6A3* | c.6230G>T p.(Gly2077Val) | Missense | *De novo* variant | Sporadic | Absent | S : D (0) P : D (1) | 10 | 4,371 | AG: 0 (-18) AL: 0 (49) DG: 0 (19) DL: 0 (1) | 4 | CM | Nl | Non-specific myopathic changes |
| I58 | F, 35y | *COL6A3* | c.5035G>T p.(Gly1679Trp) | Missense | Present in affected mother, uncle and cousin | AD | Absent | S : D (0) P : D (1) | 10 | 4,116 | AG: 0 (-12) AL: 0 (-48) DG: 0 (2) DL: 0 (4) | 4 | LGMD with retractions | | Non-specific myopathic changes |
| I287 | F, 16y | *DMD* NM_004006 .2 | del <45-51> (heterozygous) | CNV : Deletion | Present in mother | Sporadic | | | | NA | NA | 5 | Asymptomatic elevation of CK | x10 | Not done |
| I56 | F, 45Y | *DMD* | c.2665C>T p.(Arg889*) | Nonsense | Mother was heterozygous | X-linked The mother had high CK | Absent | | 10 | 6,71 | AG: 0 (49) AL: 0.01 (42) DG: 0 (42) DL: 0 (4) | 5 | LGMD | x10 | Dystrophic pattern. IHC studies not done |
| I12 | F, 61 y | *DYSF* NM_003494 .3 | c.1168G>A p.(Asp390Asn) | Missense | Affected brother carrying the same variants. Parents not tested | AR | Absent/ 7.981e-06 | S : D (0) P : D (0.9) | 8 | 3,87 | AG: 0 (-16) AL: 0 (-50) DG: 0.08 (-16) DL: 0 (33) | 4 | LGMD | x10 | Dystrophic pattern. IHC: Absence of dysferlin staining |
| | | | c.5302C>T p.(Arg1768Trp) | Missense | | | 10.62e-06/ 8.283e-06 | S : D (0) P : D (1) | 9 | 4,429 | AG: 0 (14) AL: 0 (-30) DG: 0 (42) DL: 0 (38) | 4 | | | |
| I16 | M, 68y | *DYSF* | c.755C>T p.(Thr252Met) | Missense | Parents not tested | AR (one affected sister) | Absent/ 11.93e-06 | S : D (0) P : D (1) | 10 | 3,583 | AG: 0 (-28) AL: 0 (-15) DG: 0 (37) DL: 0 (40) | 4 | LGMD | x2 | Dystrophic pattern. IHC of dysferlin on muscle biopsy not done |
| | | | c.3118C>T p.(Arg1040Trp) | Missense | | | Absent | S : D (0) P : D (0.99) | 10 | 4,146 | AG: 0 (-10) AL: 0 (-48) DG: 0 (-20) DL: 0 (8) | 4 | | | |
| I111 | F, 4y | *FLNC* NM_001458 .4 | c.4927+2T>A | Splicing | *De novo* variant | Sporadic | Absent | | 10 | 5,384 | AG: 0 (2) AL: 0 (-18) DG: 0.03 (2) DL: 0.99 (-2) | 4 | CM with restrictive cardiomyopathy | Nl | Non-specific myopathic changes |

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|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| I298 | M, 38y | *FLNC* | c.3557C>T p.(Ala1186Val) | Missense | *De novo* variant | Sporadic | Absent | S : D (0.001) P : D (0.8) | 9 | 3,452 | AG: 0 (41) AL: 0 (-12) DG: 0.01 (-50) DL: 0 (46) | 4 | Myopathy with contractures and early onset cardiomyopathy | UNK | Cytoplasmic bodies |
| I202 | M, <1y | *FKRP* NM_024301.4 | c.1364C>A (homozygous) p.(Ala455Asp) | Missense | Mother and father were heterozygous | Sporadic (Consanguinity) | Absent | S : D (0.005) P : D (0.898) | 8 | 4,068 | AG: 0 (17) AL: 0 (47) DG: 0 (16) DL: 0 (2) | 4 | CMD with cerebellar atrophy | x50 | Not done |
| I218 | M, 50y | *FKRP* | c.826C>A (homozygous) p.(Leu276Ile) | Missense | Not tested | Sporadic | 0,003961/0.001104 | S : T (0.065) P : B (0.3) | 5 | 2,015 | AG: 0 (4) AL: 0 (16) DG: 0 (2) DL: 0 (-9) | 4 | Severe LGMD | UNK | Dystrophic pattern. IHC not done |
| I354 | F, <1y | *FKRP* | c.1384C>T (homozygous) p.(Pro462Ser) | Missense | Mother and father were heterozygous | Sporadic Familial consanguinity | 1.448e-05/9.037e-06 | S : D (0) P : D (0.996) | 10 | 3,891 | AG: 0 (27) AL: 0 (-3) DG: 0 (-2) DL: 0 (-4) | 4 | CMD | x30 | Dystrophic pattern. Absence of α-dystroglycan staining |
| I24 | M, 40y | *GMPPB* NM_013334.3 | c.902C>G p.(Ser301Cys) | Missense | Mother not tested | Sporadic | Absent | S : D (0) P : B (0.152) | 7 | 2,304 | AG: 0 (32) AL: 0 (-5) DG: 0 (-37) DL: 0 (-41) | 4 | LGMD | x10 | Dystrophic pattern |
| | | | c.1069G>A p.(Val357Ile) | Missense | Present in father | | 7.438e-05/6.017e-05 | S: D (0) P: D (1) | 8 | 3,857 | AG: 0 (-38) AL: 0.01 (36) DG: 0.01 (9) DL: 0 (-38) | 4 | | | |
| I252 | F, <1y | *LAMA2* NM_000426.3 | c.1884+1_1884+6del (homozygous) | Frameshift indel | Not tested | Sporadic | Absent | | 10 | NA | NA | 5 | Severe neonatal hypotonia | x20 | Not done |
| I29 | M, 17y | *LAMA2* | c.752T>C (homozygous) p.(Leu251Pro) | Missense | Parents was heterozygous | Sporadic | Absent | S : D (0) P : D (0.998) | 10 | 4,006 | AG: 0 (-13) AL: 0 (33) DG: 0 (49) DL: 0 (-34) | 4 | CMD, intellectual deficiency and epilepsy | x50 | Dystrophic pattern. Absence of α-dystroglycan staining |
| I30 | M, 28y | *LAMA2* | c.2461A>C p.(Thr821Pro) | Missense | Mother was heterozygous | Sporadic | Absent | S : D (0.002) P : D (0.998) | 10 | 3,853 | AG: 0 (-10) AL: 0 (-18) DG: 0 (-4) DL: 0 (-19) | 4 | LGMD | x10 | Dystrophic pattern. Normal IHC |
| | | | c.3976C>T p.(Arg1326*) | Nonsense | Father was heterozygous | | Absent | | 10 | 7,952 | AG: 0 (-10) AL: 0 (-47) DG: 0 (-47) DL: 0 (15) | 5 | | | |
| I20 | F, 2y | *LMNA* NM_170707.3 | c.1357C>T p.(Arg453Trp) | Missense | *De novo* variant | Sporadic | Absent | S : D (0) P : D (0.993) | 9 | 4,613 | AG: 0 (40) AL: 0 (-46) DG: 0 (-25) DL: 0 (23) | 5 | CMD | x10 | Dystrophic pattern |
| I207 | M, <1y | *MTM1* NM_000252.2 | c.290G>A p.(Gly97Glu) | Missense | Mother was heterozygous | Sporadic | Absent | S : D (0.001) P : D (0.999) | 10 | 3,897 | AG: 0 (-14) AL: 0 (16) DG: 0 (47) DL: 0 (-28) | 4 | Severe neonatal hypotonia with Respiratory failure | Nl | Not done |
| I7 | M, <1y | *MTM1* | c.519C>G p.(Tyr173*) | Nonsense | Not tested | Sporadic | Absent | | 10 | 5,834 | AG: 0 (1) AL: 0 (-49) DG: 0.01 (5) DL: 0 (9) | 5 | Severe neonatal hypotonia with respiratory failure | Nl | Centronuclear myopathy |
| I40 | F, 48y | *MTM1* | c.1261-10A>G (ivs11) | Splicing | Sister affected | X-Linked | Absent | | 10 | 3,022 | AG: 0.93 (1) AL: 0.86 (10) DG: 0 (1) DL: 0 (17) | 4 | LGMD | x2 | Non-specific myogenic changes |

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|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| I195 | F, 56y | *MYH7* NM_000257.2 | c.5791-1G>T | Splicing | Present in mother | Sporadic (the clinical examination of the mother was not available) | Absent | | 10 | 5,392 | AG: 0.22 (29)<br>AL: 0.95 (-1)<br>DG: 0 (-13)<br>DL: 0 (-9) | 4 | Early onset cardiomyopathy and LGMD of adult onset | UNK | Minicores |
| I208 | M, 4y | *MYH7* | c.5000T>C p.(Leu1667Pro) | Missense | *De novo* variant | Sporadic | Absent | S : D (0)<br>P : D (0.94) | 10 | 4,225 | AG: 0 (18)<br>AL: 0 (-47)<br>DG: 0 (-1)<br>DL: 0 (-4) | 4 | CM | Nl | Minicores |
| I36, I37 | M, 40y | *MYH7* | c.4795A>C p.(Thr1599Pro) | Missense | Present in affected daughter | AD | Absent | S : D (0.001)<br>P : P (0653) | 10 | 3,461 | AG: 0 (-16)<br>AL: 0 (0)<br>DG: 0 (19)<br>DL: 0 (-44) | 4 | Distal myopathy | x5 | Non-specific myogenic pattern<br>IHC study: normal |
| I62 | F, 50y | *MYOT* NM_006790 | c.179C>G p.(Ser60Cys) | Missense | Present in affected brother | Affected brother | Absent | S : D (0.004)<br>P : D (0.894) | 5 | 3,687 | AG: 0 (-49)<br>AL: 0 (47)<br>DG: 0 (-1)<br>DL: 0 (-40) | 4 | Distal myopathy | x2 | Non-specific myogenic pattern<br>IHC study: normal |
| I353 | M, 19y | *NEB* NM_001271208.1 | c.2835+5G>A | Splicing | Present in mother | Sporadic | Absent | | 10 | 3,159 | AG: 0 (-19)<br>AL: 0 (25)<br>DG: 0 (26)<br>DL: 0.83 (5) | 4 | CM | Nl | Rods |
| | | | c.15178delC p.(His5060Thrfs*11) | Frameshift | Father not tested | | Absent | | 10 | NA | AG: 0.02 (-24)<br>AL: 0 (39)<br>DG: 0.05 (45)<br>DL: 0 (39) | 5 | | | |
| I76, I77 | M, 54y F, 50y | *NEB* | c.21928T>C p.(Ser7310Pro) | Missense | Father not tested | AR (one affected sister) | Absent | S : T (0.114)<br>P : P (0.653) | 3 | 3,876 | AG: 0 (-43)<br>AL: 0 (12)<br>DG: 0.01 (-43)<br>DL: 0 (-17) | 4 | Distal myopathy | Nl | Non-specific myopathic changes |
| | | | c.8860del p.(Ala2954Profs*8) | Frameshift | Mother was heterozygous | | Absent | | 10 | NA | AG: 0 (-29)<br>AL: 0 (28)<br>DG: 0 (-6)<br>DL: 0.04 (-29) | 5 | | | |
| I173 | F, 16y | *NEB* | c.5039G>A p.(Tyr1680Cys) | Missense | Father was heterozygous | Sporadic | Absent | S : D (0)<br>P : D (0.999) | 7 | 4,135 | AG: 0.02 (-30)<br>AL: 0 (7)<br>DG: 0 (-21)<br>DL: 0 (3) | 3 | CM | Nl | Rods |
| | | | c.17541dupA p.(Tyr5848Ilefs*15) | Frameshift | Mother was Heterozygous | | Absent | | 10 | 6,815 | AG: 0 (5)<br>AL: 0 (23)<br>DG: 0 (0)<br>DL: 0 (1) | 5 | | | |
| I112 | M, 60y | *NEB* | c.21790G>C p.(Asp7264His) | Missense | Parents not tested | Sporadic | 0.001906/0.001829 | S : D (0.001)<br>P : D (0.897) | 6 | 4,263 | AG: 0 (-22)<br>AL: 0 (-1)<br>DG: 0 (-38)<br>DL: 0 (-50) | 4 | Distal myopathy | Nl | Non-specific myopathic changes |
| | | | c.194C>T p.(Pro65Leu) | Missense | | | 14.12e-05/11.77e-05 | S : D (0)<br>P : B (0.32) | 4 | 2,865 | AG: 0 (1)<br>AL: 0 (42)<br>DG: 0 (1)<br>DL: 0 (-16) | 3 | | | |
| I1 | M, <1y | *NEB* | c.6075+5G>A | Splicing | Present in father | Sporadic | Absent | | 10 | 4,228 | AG: 0 (-34)<br>AL: 0 (-6)<br>DG: 0.92 (-46)<br>DL: 0.96 (5) | 4 | Severe neonatal hypotonia and distal arthrogryposis. | Nl | Rods |
| | | | c.13661_13666delinsAp. (Ser4554Asnfs*10) | Frameshift | Present in mother | | Absent | | 10 | NA | NA | 5 | | | |
| I67 | F, 1y | *NEB* | c.23998dupG p.(Glu8000Glyfs*11) | Frameshift | Father was heterozygous | Sporadic | Absent | | 10 | NA | AG: 0 (44)<br>AL: 0 (-41)<br>DG: 0 (-26)<br>DL: 0.16 (-35) | 4 | Severe neonatal hypotonia with | Nl | Non-specific myopathic changes |

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|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | c.518delA p.(Lys173Serfs*55) | Frameshift | Mother was heterozygous | | Absent | | 10 | NA | AG: 0.02 (-2) AL: 0 (46) DG: 0 (-2) DL: 0 (11) | 5 | respiratory failure. | | |
| I604 | M, 7Y | *NEB* | c.8889+1G>A | Splicing | Father was heterozygous | Sporadic | Absent | | 10 | 5,898 | AG: 0 (0) AL: 0 (35) DG: 0 (-25) DL: 0.99 (1) | 4 | Severe neonatal hypotonia with respiratory failure and arthrogryposis | x2 | Rods |
| | | | c.8038C>T p.(Arg2680*) | Nonsense | Mother was heterozygous | | Absent | | 10 | 7,495 | AG: 0 (-39) AL: 0 (15) DG: 0 (-33) DL: 0 (-13) | 5 | | | |
| I14 | F, 75y | *PABPN1* NM_004643 .3 | c.30_32dup p.(Ala11dup) | Trinucleotid repeat expansion | Not tested | Sporadic | | | | 2,144 | NA | 4 | LGMD with axial weakness | Nl | Myofibrillar aspect with rimmed vacuoles |
| I5 | M, <1y | *RYR1* NM_000540 .2 | c.11186T>C p.(Met3729Thr) | Missense | Parents not tested | Sporadic | Absent | S : D (0.021) P : D (0.946) | 9 | 3,832 | AG: 0 (-44) AL: 0 (8) DG: 0 (7) DL: 0 (-24) | 4 | Distal arthrogryposis. Neonatal death | Nl | Cores |
| | | | c.11122A>C p.(Thr3708Pro) | Missense | | | Absent | S : T (0.157) P : P (0.876) | 7 | 4 | AG: 0 (19) AL: 0 (-35) DG: 0 (-23) DL: 0 (19) | 4 | | | |
| I42 | F, 11y | *RYR1* | c.38T>C p.(Leu13Pro) | Missense | Mother was heterozygous | Sporadic | Absent | S : D (0.023) P : D (1) | 9 | 4,104 | AG: 0 (7) AL: 0 (-24) DG: 0 (-11) DL: 0 (7) | 4 | CM | Nl | Non-specific myopathic changes |
| | | | c.7628C>T p.(Thr2543Ile) | Missense | Mother was heterozygous | | Absent/ 3.190 e-05 | S : T (0.09) P : P (0.506) | 6 | 2,996 | AG: 0.06 (-2) AL: 0 (-8) DG: 0 (-2) DL: 0 (1) | 3 | | | |
| | | | c.13690C>T p.(Arg4564Trp) | Missense | Father was heterozygous | | 4.118e-05/ 3.579e-05 | S : D (0) P : D (0.997) | 9 | 4,097 | AG: 0 (-24) AL: 0 (-30) DG: 0 (-2) DL: 0 (46) | 3 | | | |
| I220 | M, 3y | *RYR1* | c.14762T>C p.(Phe4921Ser) | Missense | *De novo* variant | Sporadic | Absent | S : D (0) P : D (0.994) | 9 | 4,335 | AG: 0 (-5) AL: 0 (-20) DG: 0 (-43) DL: 0 (-20) | 5 | CM | Nl | Non-specific myopathic changes |
| I175 | F,10y | *RYR1* | c.12727G>A p.(Glu4243Lys) | Missense | *De novo* variant | Sporadic | Absent | S : D (0.02) P : D (1) | 9 | 4,183 | AG: 0 (3) AL: 0 (9) DG: 0 (8) DL: 0 (-28) | 4 | CM | Nl | Non-specific myopathic changes |
| I176 | M, <1y | *RYR1* | c.5926C>T p.(Arg1976Cys) | Missense | Present in mother | Sporadic | Absent | S : D (0) P : D (1) | 8 | 3,999 | AG: 0 (22) AL: 0 (-6) DG: 0 (-2) DL: 0 (2) | 4 | Severe neonatal hypotonia | Nl | Non-specific myopathic changes |
| | | | c.10649G>C p.(Arg3550Pro) | Missense | Present in father | | Absent | S : D (0) P : D (1) | 8 | 3,809 | AG: 0 (-22) AL: 0 (19) DG: 0.03 (37) DL: 0 (-5) | 4 | | | |
| I155 | F, 51y | *RYR1* | c.6697T>C p.(Cys2233Arg) | Missense | Parents not tested | AD (affected son) | Absent | S : D (0.001) P : D (0.996) | 9 | 0,025 | AG: 0 (1) AL: 0 (-37) DG: 0 (14) DL: 0 (-23) | 5 | CM | Nl | Nl |
| I519 | F, 26y | *RYR1* | c.10348-6C>G | Splicing | Father not tested | Sporadic | 2.475e-05/ 3.182e-05 | | 10 | 0,45 | AG: 0 (-41) AL: 0.47 (6) DG: 0 (35) DL: 0 (15) | 5 | CM | Nl | Non-specific myopathic changes |
| | | | c.14172+4A>G | Splicing | Present in mother | | 8.245e-06/ 7.958e-06 | | 10 | 2,34 | AG: 0 (50) AL: 0 (-46) DG: 0.01 (-20) DL: 0.08 (-4) | 4 | | | |

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|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| I526 | M, 8y | *RYR1* | c.1205T>C p.(Met402Thr) | Missense | Mother was heterozygous | Sporadic | 8.245e-06/ 3.97e-06 | S : D (0.003) P : P (0.73) | 8 | 2,684 | AG: 0 (1) AL: 0 (10) DG: 0 (-4) DL: 0 (39) | 5 | CM | Nl | Minicores |
| | | | c.10496dupG p.(Arg3499fs) | Frameshift delins | Father not tested | | Absent/ 4.06e-06 | | 10 | 5,692 | AG: 0 (23) AL: 0 (-22) DG: 0 (9) DL: 0 (-22) | 5 | | | |
| I152 | M, 35 y | *RYR1* | c.6617C>T (homozygous) p.(Thr2206Met) | Missense | Parents not tested | Affected sister | 3.305e-05/ 2.123e-05 | S : D (0) P : D (0.998) | 9 | 3,864 | AG: 0 (-1) AL: 0 (-48) DG: 0 (35) DL: 0 (10) | 4 | LGMD | x20 | Non-specific myopathic changes |
| I46 | M, 60 y | *RYR1* | c.4711A>G p.(Ile1571Val) | Missense | Parents not tested | Sporadic | 0.001339/8. 548e-04 | S : T (0.729) P : D (0.978) | 6 | 1,318 | AG: 0 (-3) AL: 0 (16) DG: 0 (30) DL: 0 (10) | 4 | Proximal and distal weakness | UNK | Myofibrillar aspects |
| | | | c.10097G>A p.(Arg3366His) | Missense | | | 9.272e-04/ 8.605e-04 | S : D (0.006) P : D (0.997) | 7 | 2,753 | AG: 0.01 (5) AL: 0 (17) DG: 0 (7) DL: 0 (-5) | 4 | | | |
| | | | c.11798A>G p.(Tyr3933Cys) | Missense | | | 9.233e-04/ 8,487e-04 | S : D (0) P : D (0.997) | 9 | 4,166 | AG: 0 (-50) AL: 0 (-8) DG: 0 (14) DL: 0 (3) | 4 | | | |
| | | | c.7028-10G>A | Splicing | | | Absent/ 1,864e-05 | | 10 | 2,885 | AG: 1 (2) AL: 0.97 (10) DG: 0 (41) DL: 0 (9) | 5 | | | |
| I28 | F, 14y | *SGCA* NM_000023 .2 | c.850C>T (homozygous) p.(Arg284Cys) | Missense | Mother and father were heterozygous | AR Consanguinity (Affected sister) | 1.237e-04/ 1.485e-04 | S : D (0) P : D (0.995) | 9 | 4,412 | AG: 0 (-13) AL: 0 (-9) DG: 0 (0) DL: 0 (11) | | Exercise intolerance | x40 | Dystrophic pattern. Normal IHC |
| I31 | M, 15y | *SGCG* NM_000231 .2 | c.800_801del (homozygous) p.(Cys267Serfs*51) | Frameshift | Parents were heterozygous | Sporadic | Absent | | 10 | 4,452 | AG: 0 (-22) AL: 0 (13) DG: 0 (41) DL: 0 (0) | 5 | LGMD | x50 | Dystrophic pattern. Absence of γ-sarcoglycan staining |
| I427 | M, 20y | *STIM1* NM_003156 .3 | c.910C>T p.(Arg304Trp*) | Nonsense | Not tested | Sporadic | Absent | S : D (0.001) P : D (0.998) | 8 | 3,912 | AG: 0 (15) AL: 0 (-24) DG: 0 (-2) DL: 0 (6) | 5 | Features of Stormorken syndrome: myalgia, headaches, myosis | x30 | Tubular aggregates |
| I26 | M, 14y | *TTN* NM_001267 550.1 | c.51437-4_51444del | Frameshift delins | Not feasible (adopted child) | Sporadic | Absent | | 10 | NA | NA | 4 | CM | Nl | Centronuclear myopathy |
| | | | c.26503A>T p.(Lys8835*) | Nonsense | | | Absent | | 10 | 9,482 | AG: 0 (32) AL: 0.02 (20) DG: 0 (20) DL: 0 (-48) | 5 | | | |
| I398 | F, 10y | *TTN* | c.56648-1G>A | Splicing | Mother was heterozygous | Sporadic | 9.008e-06/ 5.321e-06 | | 10 | 5,739 | AG: 0.11 (-19) AL: 0.99 (-1) DG: 0 (-13) DL: 0 (-38) | 4 | CM with arthrogryposis and rigid spine | Nl | Cores |
| | | | c.40011delA p.(Lys13337fs) | Frameshift | Father was heterozygous | | Absent | | 10 | NA | AG: 0 (37) AL: 0 (38) DG: 0.1 (-46) DL: 0 (9) | 5 | | | |

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|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| I47 | F, 44y | *TTN* | c.65575+2T>G | Splicing | Mother was heterozygous, father not tested | Sporadic | Absent | | 10 | 5,014 | AG: 0 (7)<br>AL: 0 (22)<br>DG: 0.02 (-30)<br>DL: 1 (2) | 5 | CM | Nl | Excessive internal nuclei. |
| | | | c.68029A>G<br>p.(Thr22677Ala) | Missense<br>Predicted to affect splicing | Absent in mother, father not tested | | Absent | S: D (0.012)<br>P: P (0.622) | 4.4 | 2,467 | AG: 0 (-16)<br>AL: 0 (-18)<br>DG: 0 (-40)<br>DL: 0 (38) | 4 | | | |
| 142, I162 | F, 40y | *TTN* | c.1662+15_3101-3del | CNV | Affected mother was heterozygous | AD | Absent | | | NA | NA | 5 | Distal Myopathy | x2 | Minicores |
| I420 | M, 56y | *TTN* | c.35713+1del | Splicing | Not tested | Affected brother and sister | 5.58 e-05 | | 10 | 5,074 | AG: 0 (-24)<br>AL: 0 (22)<br>DG: 0.08 (2)<br>DL: 0.98 (1) | 4 | LGMD with cardiomyopathy | x5 | Myofibrillar features |
| | | | c.7120C>T<br>p.(Gln2374*) | Nonsense | | | Absent | | 10 | 7,175 | AG: 0 (-3)<br>AL: 0 (38)<br>DG: 0 (22)<br>DL: 0 (18) | 5 | | | |
| I74, I73 | F, 4y | *TTN* | c.106531G>C;<br>p.(Ala35511Pro) | Missense (predicted to affect splicing) | Present in father | AR (one affected sister) | Absent | UNK | 10 | 5,054 | AG: 0 (0)<br>AL: 0 (50)<br>DG: 0 (-4)<br>DL: 0.62 (0) | 5 | CM | Nl | Centronuclear myopathy |
| | | | c.105036C>A<br>p.(Tyr35012*) | Nonsense | Present in mother | | Absent | | 10 | 15,61 | AG: 0 (-25)<br>AL: 0 (9)<br>DG: 0 (-25)<br>DL: 0 (-6) | 5 | | | |
| I401 | F, 1y | *TNNT1*<br>NM_003283.5 | c.192+244_388-1191del (del<8-9>) (homozygous) | In Frame CNV deletion | Father and mother heterozygous | Sporadic | Absent | | 10 | NA | NA | 4 | Severe neonatal hypotonia | Nl | Rods |
| I72 | F, 11y | *TNNT1* | c.200A>G<br>p.(His67Arg) | Missense | *De novo* variant | Sporadic | Absent | S : D (0.002)<br>P : B (0.22) | 7 | 3,721 | AG: 0.01 (42)<br>AL: 0 (7)<br>DG: 0 (-49)<br>DL: 0 (-2) | 4 | Neonatal hypotonia | Nl | Excessive internal nuclei. Absence of rods |
| I60 | M, 50y | *TRIP4* | del <8-9> (homozygous) | In Frame CNV deletion | Absent in two sister and one brother | Sporadic Consanguinity | Absent | | | NA | NA | 4 | Congenital myopathy with late onset cardiomyopathy | Nl | Rods |

AD: Autosomal Dominant; AR: Autosomal Recessive; CM: Congenital myopathy; LGMD: Limb girdle muscular dystrophy; CK: Creatin Kinase; Unknown: UNK; ND: Not done; NA : Not Applicable; IHC: Immunohistochemical; S: SIFT; P: POLYPHEN2; CNV: Copy number variation; D: Deleterious; P: Pathogenic; B: Benign; T: Tolerated; Splice AI – AG: Acceptor Gain AL: Acceptor Loss DG: Donor Gain DL: Donor Loss (distance in bp)