Supp. Materials and Methods

Patients

Patient selection was based on the clinical presentation and/or histological findings suggesting centronuclear myopathy: muscle weakness with or without facial weakness, and a muscle biopsy showing a large proportion of atrophic fibers with centralized nuclei. Venous blood was collected from CNM patients and unaffected relatives after obtaining informed consent.

Molecular studies

Genomic DNA was prepared from peripheral blood, lymphoblasts or fibroblasts by routine procedures. Mutation analysis was performed by PCR (primer sequences available on request) and Sanger sequencing of the coding sequence and adjacent exon-intron boundaries of *DNM2* as described previously (Bitoun, et al., 2005). Identified sequence variants were confirmed by an independent PCR and sequencing of amplicons. Where possible, further family members were analyzed for segregation of the variant. Mutations were numbered according to GenBank NM_001005360.2 and P50570.2. Nucleotide numbering reflects cDNA numbering with +1 corresponding to the A of the ATG translation initiation codon.

Total RNA from patients and control cell lines was extracted with TRIzol reagent followed by RNase-free DNase treatment (Invitrogen, Carlsbad, CA). cDNA synthesis was performed using SuperScript II Reverse Transcriptase (Invitrogen) and oligo(dT) priming (Promega, Madison, WI).

Routine histochemical techniques were carried out on quadriceps or deltoid muscle biopsies from patients. Transverse sections (10 µm) were stained with hematoxylin-eosin, NADH-TR, Gomori trichrome, Periodic acid-Schiff and ATPase and assessed for centralized nuclei, fiber morphology, fiber type distribution, radial arrangements of sarcoplasmic strands and fatty infiltrations.

Sequence alignment and structural model

Protein sequence alignement was performed with ClustalW program using the following sequences: human dynamin 2, human DNM1, human DNM3, Danio rerio dynamin 2 ortholog (Dnm2l), Drosophila melanogaster dynamin (Shi), and Caenorhabditis elegans dynamin (dyn-1).

The coding mutations found in patients with CNM or CMT were displayed on the structural model of nucleotide-free human dynamin 1 (Faelber, et al., 2011) (PDB: 3SNH) using the PyMOL program.

Supp. References

Bitoun M, Maugenre S, Jeannet PY, Lacene E, Ferrer X, Laforet P, Martin JJ, Laporte J, Lochmuller H, Beggs AH and others. 2005. Mutations in dynamin 2 cause dominant centronuclear myopathy. Nat Genet 37(11):1207-9.

Faelber K, Posor Y, Gao S, Held M, Roske Y, Schulze D, Haucke V, Noe F, Daumke O. 2011. Crystal structure of nucleotide-free dynamin. Nature 477(7366):556-60.

SUPP. TABLE S1. *DNM2* mutations in Centronuclear Myopathy and Charcot-Marie-Tooth Peripheral Neuropathy

CENTRONUCLEAR MYOPATHY								
Family	**Exon**	**Nucleotide change (1)**	**Predicted alteration**	**CpG**	**Protein domain (2)**	**Segregation (3)**	**Number of patients (4)**	**Reference**
ABJ51	8	c.1102G>C	p.Glu368Gln	Yes	Middle	Dominant	5	Echaniz-Laguna et al., 2007
AIP45	8	c.1102G>C	p.Glu368Gln	Yes	Middle	Sporadic	1	This study
9346	8	c.1102G>A	p.Glu368Lys	Yes	Middle	Sporadic (de novo)	1	Bitoun et al., 2005
DNM77	8	c.1102G>A	p.Glu368Lys	Yes	Middle	Sporadic (de novo)	1	Tosch et al., 2006
patient 3	8	c.1102G>A	p.Glu368Lys	Yes	Middle	Sporadic	1	Jeub et al., 2008
patient 4	8	c.1102G>A	p.Glu368Lys	Yes	Middle	Sporadic	1	Susman et al., 2010
patient 5	8	c.1102G>A	p.Glu368Lys	Yes	Middle	Sporadic	1	Susman et al., 2010
family 4	8	c.1102G>A	p.Glu368Lys	Yes	Middle	Siblings (de novo)	2	Hanisch et al., 2011
AHE18	8	c.1102G>A	p.Glu368Lys	Yes	Middle	Sporadic (de novo)	1	This study
AKO67	8	c.1102G>A	p.Glu368Lys	Yes	Middle	Sporadic (de novo)	1	This study
ALY11	8	c.1102G>A	p.Glu368Lys	Yes	Middle	Sporadic	1	This study
BOS183	8	c.1102G>A	p.Glu368Lys	Yes	Middle	Sporadic	1	This study
BOS593	8	c.1102G>A	p.Glu368Lys	Yes	Middle	Sporadic (de novo)	1	This study
BOS839	8	c.1102G>A	p.Glu368Lys	Yes	Middle	Sporadic (de novo)	1	This study
BOS848	8	c.1102G>A	p.Glu368Lys	Yes	Middle	Dominant	2	This study
BOS905	8	c.1102G>A	p.Glu368Lys	Yes	Middle	Sporadic (de novo)	1	This study
BOS1132	8	c.1102G>A	p.Glu368Lys	Yes	Middle	Sporadic	1	This study
CHI1	8	c.1102G>A	p.Glu368Lys	Yes	Middle	Sporadic	1	This study
CHI2	8	c.1102G>A	p.Glu368Lys	Yes	Middle	Sporadic	1	This study
CHI9	8	c.1102G>A	p.Glu368Lys	Yes	Middle	Sporadic	1	This study
DNM118	8	c.1102G>A	p.Glu368Lys	Yes	Middle	Sporadic	1	This study
11451	8	c.1106G>A	p.Arg369Gln	Yes	Middle	Dominant	14	Bitoun et al., 2005
patient 2	8	c.1106G>A	p.Arg369Gln	Yes	Middle	Sporadic	1	Jeub et al., 2008
EH62	8	c.1106G>A	p.Arg369Gln	Yes	Middle	Sporadic (de novo)	1	This study
EH64	8	c.1106G>A	p.Arg369Gln	Yes	Middle	Sporadic	1	This study
14815	8	c.1105C>T	p.Arg369Trp	Yes	Middle	Dominant	3	Bitoun et al., 2005
722	8	c.1105C>T	p.Arg369Trp	Yes	Middle	Sporadic	1	Bitoun et al., 2005
961	8	c.1105C>T	p.Arg369Trp	Yes	Middle	Dominant	5	Bitoun et al., 2005
only patient	8	c.1105C>T	p.Arg369Trp	Yes	Middle	Sporadic	1	Liewluk et al., 2010
ABZ97	8	c.1105C>T	p.Arg369Trp	Yes	Middle	Dominant	2	This study

CENTRONUCLEAR MYOPATHY								
Family	**Exon**	**Nucleotide change (1)**	**Predicted alteration**	**CpG**	**Protein domain (2)**	**Segregation (3)**	**Number of patients (4)**	**Reference**
AHE2	8	c.1105C>T	p.Arg369Trp	Yes	Middle	Dominant (consanguinity loop)	5	This study
ALM82	8	c.1105C>T	p.Arg369Trp	Yes	Middle	Dominant	2	This study
BOS898	8	c.1105C>T	p.Arg369Trp	Yes	Middle	Dominant	1 (5)	This study
BOS929	8	c.1105C>T	p.Arg369Trp	Yes	Middle	Dominant	2 (5)	This study
DNM174	8	c.1105C>T	p.Arg369Trp	Yes	Middle	Sporadic	1	This study
3012	11	c.1393C>T	p.Arg465Trp	Yes	Middle	Dominant	9	Bitoun et al., 2005
E/393	11	c.1393C>T	p.Arg465Trp	Yes	Middle	Dominant	2 (5)	Bitoun et al., 2005
E/703	11	c.1393C>T	p.Arg465Trp	Yes	Middle	Dominant	4	Bitoun et al., 2005
E/CNM3	11	c.1393C>T	p.Arg465Trp	Yes	Middle	Dominant	4	Bitoun et al., 2005
IBB/CNM1	11	c.1393C>T	p.Arg465Trp	Yes	Middle	Dominant	4	Bitoun et al., 2005
IBB/CNM2	11	c.1393C>T	p.Arg465Trp	Yes	Middle	Dominant	3	Bitoun et al., 2005
only family	11	c.1393C>T	p.Arg465Trp	Yes	Middle	Dominant	2	Schessl et al., 2007
patient 1	11	c.1393C>T	p.Arg465Trp	Yes	Middle	Sporadic	1	Jeub et al., 2008
CENTRONUCLEAR MYOPATHY								
Family	**Exon**	**Nucleotide change (1)**	**Predicted alteration**	**CpG**	**Protein domain (2)**	**Segregation (3)**	**Number of patients (4)**	**Reference**
only family	11	c.1393C>T	p.Arg465Trp	Yes	Middle	Dominant	5	Zanoteli et al., 2009
family 1	11	c.1393C>T	p.Arg465Trp	Yes	Middle	Dominant	5	Susman et al., 2010
patient 1	11	c.1393C>T	p.Arg465Trp	Yes	Middle	Sporadic	1	Hanisch et al., 2011
patient 2	11	c.1393C>T	p.Arg465Trp	Yes	Middle	Sporadic (de novo)	1	Hanisch et al., 2011
patient 3	11	c.1393C>T	p.Arg465Trp	Yes	Middle	Sporadic	1	Hanisch et al., 2011
ALY5	11	c.1393C>T	p.Arg465Trp	Yes	Middle	Sporadic	1	This study
ADT93	11	c.1393C>T	p.Arg465Trp	Yes	Middle	Dominant	3	This study
AEB17	11	c.1393C>T	p.Arg465Trp	Yes	Middle	Sporadic	1	This study
AFW12	11	c.1393C>T	p.Arg465Trp	Yes	Middle	Sporadic	1	This study
BOS601	11	c.1393C>T	p.Arg465Trp	Yes	Middle	Dominant	1 (5)	This study
BOS835	11	c.1393C>T	p.Arg465Trp	Yes	Middle	Dominant	1 (5)	This study
BOS893	11	c.1393C>T	p.Arg465Trp	Yes	Middle	Unknown	1	This study

CENTRONUCLEAR MYOPATHY								
Family	**Exon**	**Nucleotide change (1)**	**Predicted alteration**	**CpG**	**Protein domain (2)**	**Segregation (3)**	**Number of patients (4)**	**Reference**
BOS928	11	c.1393C>T	p.Arg465Trp	Yes	Middle	Dominant	1 (5)	This study
BOS930	11	c.1393C>T	p.Arg465Trp	Yes	Middle	Dominant	1 (5)	This study
BOS1059	11	c.1393C>T	p.Arg465Trp	Yes	Middle	Dominant	1 (5)	This study
BOS1061	11	c.1393C>T	p.Arg465Trp	Yes	Middle	Sporadic	1	This study
CHI5	11	c.1393C>T	p.Arg465Trp	Yes	Middle	Sporadic	1	This study
CHI7	11	c.1393C>T	p.Arg465Trp	Yes	Middle	Sporadic	1	This study
FM71	11	c.1393C>T	p.Arg465Trp	Yes	Middle	Dominant	2	This study
AML18	14	c.1564C>T	p.Arg522Cys	Yes	PH	Sporadic	1	This study
family 2	14	c.1565G>A	p.Arg522His	Yes	PH	Dominant	4	Susman et al., 2010
family 3	14	c.1565G>A	p.Arg522His	Yes	PH	Dominant	2	Susman et al., 2010
ABZ99	14	c.1565G>A	p.Arg522His	Yes	PH	Sporadic	1	This study
AEK95	14	c.1565G>A	p.Arg522His	Yes	PH	Sporadic	1	This study
AFT16	14	c.1565G>A	p.Arg522His	Yes	PH	Sporadic	1	This study
AIL9	14	c.1565G>A	p.Arg522His	Yes	PH	Dominant	3	This study
ALY14	14	c.1565G>A	p.Arg522His	Yes	PH	Sporadic	1	This study
BOS909	14	c.1565G>A	p.Arg522His	Yes	PH	Dominant	1 (5)	This study
BOS1145	14	c.1565G>A	p.Arg522His	Yes	PH	Sporadic	1	This study
CHI8	14	c.1565G>A	p.Arg522His	Yes	PH	Sporadic	1	This study
CHI10	14	c.1565G>A	p.Arg522His	Yes	PH	Sporadic	1	This study
DNM62	14	c.1565G>A	p.Arg522His	Yes	PH	Dominant	2	This study
CHI4	14	c.1567A>G	p.Arg523Gly	No	PH	Sporadic	1	This study
only patient	15	c.1678G>A	p.Glu560Lys	No	PH	Dominant	5	Bitoun et al., 2009b
EH58	15	c.1678G>A	p.Glu560Lys	No	PH	Sporadic (consanguinity loop; de novo)	1	This study
ADA38	16	c.1853C>A	p.Ala618Asp	No	PH	Dominant	2	Melberg et al., 2010
patient 1	16	c.1852G>A	p.Ala618Thr	Yes	PH	Sporadic	1	Bitoun et al., 2007
patient 7	16	c.1852G>A	p.Ala618Thr	Yes	PH	Sporadic	1	Susman et al., 2010
ALY9	16	c.1852G>A	p.Ala618Thr	Yes	PH	Sporadic	1	This study
patient 2	16	c.1856C>T	p.Ser619Leu	Yes	PH	Sporadic	1	Bitoun et al., 2007
patient 3	16	c.1856C>T	p.Ser619Leu	Yes	PH	Sporadic	1	Bitoun et al., 2007
patient 8	16	c.1856C>T	p.Ser619Leu	Yes	PH	Sporadic	1	Susman et al., 2010

CENTRONUCLEAR MYOPATHY								
Family	**Exon**	**Nucleotide change (1)**	**Predicted alteration**	**CpG**	**Protein domain (2)**	**Segregation (3)**	**Number of patients (4)**	**Reference**
ACA46	**16**	**c.1856C>T**	**p.Ser619Leu**	**Yes**	**PH**	**Sporadic (consanguinity loop; de novo)**	**1**	**This study**
CENTRONUCLEAR MYOPATHY								
Family	**Exon**	**Nucleotide change (1)**	**Predicted alteration**	**CpG**	**Protein domain (2)**	**Segregation (3)**	**Number of patients (4)**	**Reference**
ADT88	**16**	**c.1856C>T**	**p.Ser619Leu**	**Yes**	**PH**	**Sporadic**	**1**	**This study**
ADU43	**16**	**c.1856C>T**	**p.Ser619Leu**	**Yes**	**PH**	**Sporadic (de novo)**	**1**	**This study**
AG078	**16**	**c.1856C>T**	**p.Ser619Leu**	**Yes**	**PH**	**Sporadic (de novo)**	**1**	**This study**
AGY84	**16**	**c.1856C>T**	**p.Ser619Leu**	**Yes**	**PH**	**Sporadic (de novo)**	**1**	**This study**
BOS746	**16**	**c.1856C>T**	**p.Ser619Leu**	**Yes**	**PH**	**Sporadic**	**1**	**This study**
CHI3	**16**	**c.1856C>T**	**p.Ser619Leu**	**Yes**	**PH**	**Sporadic**	**1**	**This study**
CHI6	**16**	**c.1856C>T**	**p.Ser619Leu**	**Yes**	**PH**	**Sporadic**	**1**	**This study**
patient 4	**16**	**c.1856C>G**	**p.Ser619Trp**	**Yes**	**PH**	**Sporadic**	**1**	**Bitoun et al., 2007**
only patient	**16**	**c.1862T>C**	**p.Leu621Pro**	**No**	**PH**	**Sporadic**	**1**	**Jungbluth et al., 2010**
patient 5	**16**	**c.1873_1875delGTC**	**p.Val625del**	**/**	**PH-GED**	**Sporadic**	**1**	**Bitoun et al., 2007**
patient 6	**16**	**c.1880C>A**	**p.Pro627His**	**No**	**PH-GED**	**Sporadic**	**1**	**Susman et al., 2010**
BOS1021	**16**	**c.1880C>G**	**p.Pro627Arg**	**Yes**	**PH-GED**	**Dominant**	**2**	**This study**
ADM1	**16**	**c.1885_1893+8del17(AAGGACCAGgtgaggag)**	**donor splice deletion**	**/**	**PH-GED**	**Dominant**	**7**	**This study**
only family	**17**	**c.1948G>A**	**p.Glu650Lys**	**No**	**GED**	**Dominant**	**5**	**Bitoun et al., 2009a**

CHARCOT-MARIE-TOOTH NEUROPATHY								
Family	**Exon**	**Nucleotide change**	**Predicted alteration**	**CpG**	**Protein domain**	**Segregation**	**Number of patients**	**Reference**
only family	8	c.1072G>A	p.Gly358Arg	Yes	Middle	Dominant	3	Gallardo et al., 2008
family A	14	c.1609G>T	p.Gly537Cys	Yes	PH	Dominant	4	Fabrizi et al., 2007
DUK1118	14	c.1664_1671+1delATGAGGAGg	p.Asp555_Glu557del;Lys554fs	/	PH	Dominant	13	Zuchner et al.,2005
only patient	15	c.1675-1677del	p.Lys559del	/	PH	Sporadic (de novo)	1	Bitoun et al., 2008
CMT310	15	c.1684A>G	p.Lys562Glu	No	PH	Dominant	17	Zuchner et al., 2005
CMT48	15	c.1684_1686delAAG	p.Lys562del	/	PH	Dominant	?	Zuchner et al., 2005
family B	15	c.1709T>A	p.Leu570His	No	PH	Dominant	3	Fabrizi et al., 2007

All patients are heterozygous for the nucleotide change

(1) Mutations were numbered according to GenBank NM_001005360.2 and P50570.2. Nucleotide numbering reflects cDNA numbering with +1 corresponding to the A of the ATG translation initiation codon

(2) PH: Pleckstrin Homology; GED: GTPase Effector domain

(3) segregation : for sporadic cases, we indicate a de novo mutation when confirmed by sequencing the parents

(4) for families ABJ51 and ADM1, 2 patients and 1 patient were respectively confirmed at the molecular level. In all other families, all patients were confirmed at the molecular level.

(5) Other family members have been clinically diagnosed, but not molecularly.

SUPP. TABLE S2. Clinical Data from Affected Individuals with Centronuclear Myopathy and *DNM2* Mutations

Patient	Sex	Mutation	Onset	Pregnancy / birth	Development	Age at last exam	Independent walking	Central nuclei	Fiber hypotrophy
AIP45	F	**E368Q**	Neonatal	Hypotonia	Speech and motor development delayed	14	Maximum 20 min, No running, difficultly climbing stairs, frequent falls	Yes	Yes
AHE18	F	**E368K**	Childhood	Normal	Motor development delayed	6		Yes	Yes
AKO67	F	**E368K**	Childhood	Normal	Motor development delayed	8		Yes	Yes
ALY11	F	**E368K**		Reduced fetal movements	Normal	20		Yes	Yes
BOS183-1	F	**E368K**	Neonatal	Hypotonia, respiratory insufficiency	Motor development delayed	Deceased age 30.5	Difficultly	Yes (50-80%)	Yes
BOS848-1	F	**E368K**	Childhood (12)	Hypotonia	Normal	34	Cannot run, difficultly climbing stairs	Yes (22%)	Yes
BOS848-2 (son)	M	**E368K**	Neonatal	Mild hypotonia	Motor development delayed	4	Can run, difficultly climbing stairs		
BOS593-1	F	**E368K**	Childhood (7)	Hypotonia		36	Cannot run, difficultly climbing stairs	Yes	
BOS839-1	M	**E368K**	Neonatal	Hypotonia	Speech and motor development delayed	16	Difficultly	Yes	
BOS905-1	F	**E368K**	Childhood	Normal	Normal	11	Can run slowly and climb stairs, occasional falls	Yes (24%)	Yes
BOS1132-1	F	**E368K**	Neonatal	Reduced fetal movements; hypotonia, respiratory insufficiency	Motor development delayed	30	Difficultly climbing stairs, cannot run, wheelchair for long distances	Yes (80%)	Yes
CHI1	M	**E368K**	Neonatal	Normal	Normal	22	Wheelchair-bound at age 12	Yes	
CHI2	F	**E368K**	Childhood	Normal	Motor development delayed	28	No	Yes	Yes
CHI9	M	**E368K**	Neonatal	Reduced fetal movements	Motor development delayed	9.5		Yes	
DNM118	M	**E368K**	Neonatal	Polyhydramnios, reduced fetal movements, neonatal hypoxia	Motor development delayed	25		Yes (90%)	Yes
EH62	F	**R369Q**	Childhood (5)	Normal	Normal	33	Cannot run, difficultly climbing stairs	Yes	Yes
EH64	F	**R369Q**	Adulthood (24)		Normal	38	No		Yes
AHE2	F	**R369W**	Adulthood (40)				Mild waddling gait	Yes	Yes

Patient	Sex	Mutation	Onset	Pregnancy / birth	Development	Age at last exam	Independent walking	Central nuclei	Fiber hypotrophy
AHE3 (brother)	M	**R369W**	Adulthood (49)						
AHE4 (daughter)	F	**R369W**	Adolescence (13)				Mild waddling gait	Yes	Yes
AHE5 (son)	M	**R369W**	Adolescence (17)				Difficultly	Yes	Yes
BOS898-1	F	**R369W**	Adolescence		Normal	60	Difficultly, needs cane/walker	Yes (39%)	Yes
ALM82	F	**R369W**	childhood			33		Yes	Yes
AMR39 (daughter)	F	**R369W**	childhood (4)		Normal	8	Yes		
BOS929-1	F	**R369W**	Childhood			58	Difficultly climbing stairs, cannot run, wheelchair for long distances	Yes (21%)	Yes
BOS929-6 (cousin)	M	**R369W**	Adulthood (mid 50s)			67	Needs cane, wheelchair for long distances	Yes (>95%)	Yes
ABZ97	M	**R369W**	Adulthood (48)	Normal	Normal	56	No	Yes	Yes
AGJ49 (son)	M	**R369W**	Adolescence (15)	Normal	Normal	27			
DNM174	M	**R369W**	Adulthood (30)		Normal	42	No	Yes (90%)	Yes

Patient	Sex	Mutation	Onset	Pregnancy / birth	Development	Age at last exam	Independent walking	Central nuclei	Fiber hypotrophy
ADT93a	F	**R465W**	Childhood	Hypotonia	Normal	36	Difficultly	Yes	Yes
ADT93b (mother)	F	**R465W**	Childhood	Asphyxia		64	Difficultly	Yes	
ADT93c (uncle)	M	**R465W**	Childhood			60	Difficultly		
AEB17	M	**R465W**	Childhood	Normal	Normal	26			
AFW12	F	**R465W**	Adulthood (56)			66	Difficultly climbing stairs and running	Yes (85%)	Yes
ALY5	M	**R465W**	neonatal	Reduced fetal movements	Normal	26	Maximum 200 m	Yes	Yes
BOS601-1	M	**R465W**	Childhood			56	Walks with cane	Yes (43%)	Yes
BOS835-1	M	**R465W**	Childhood (2)		Motor development delayed	59	Mostly wheelchair-bound	Yes (>90%)	Yes
BOS893-1	F	**R465W**	Adolescence	Normal	Normal	33	Difficultly climbing stairs, cannot run	Yes (88%)	Yes
BOS928-1	F	**R465W**	Childhood (11)		Normal	17	Foot drop, can run	Yes (47%)	Yes
BOS930-1	F	**R465W**	Childhood (7)	Normal	Normal	25	Cannot run or climb stairs	Yes (62%)	Yes
BOS1059-1	M	**R465W**	Childhood (<4)	Normal	Speech development delayed	27	Difficultly climbing stairs, cannot run, fatigues with long walking distances	Yes (> 50%)	Yes
BOS1061-1	F	**R465W**	Childhood (10)	Normal	Normal	36.5	Mild waddling gait with footdrop; cannot climb stairs or run; wheelchair for longer distances	Yes (> 50%)	

Patient	Sex	Mutation	Onset	Pregnancy / birth	Development	Age at last exam	Independent walking	Central nuclei	Fiber hypotrophy
CHI5	F	**R465W**					No	Yes	Yes
CHI7	F	**R465W**	Adolescence	Normal	Normal	45	No	Yes	Yes
FM71	F	**R465W**							
AML18	F	**R522C**	Adulthood (40-50)	Normal		71	Steppage gait	Yes	Yes
ABZ99	M	**R522H**	Adulthood (44)	Normal	Normal				
AEK95	F	**R522H**	Adulthood (50)			65		Yes (>50%)	Yes
AFT16	M	**R522H**	Childhood			37	Cannot run	Yes (>50%)	Yes
AIL9	F	**R522H**	Adulthood	Normal	Normal	42	Yes	Yes	Yes
AKZ27	M	**R522H**				52			
ALP71	F	**R522H**	Childhood (8)			50			
ALY14	M	**R522H**		Normal	Normal	51		Yes	Yes
BOS909-1	F	**R522H**	Adulthood (50s)			59	Ataxic and waddling gait, foot drop	Yes (>50%)	Yes
BOS1145-1	F	**R522H**	Adolescence			51	Cannot climb stairs or run, wheelchair for long distances	Yes (70%)	Yes
CHI8	F	**R522H**	Adulthood			29			
CHI10	F	**R522H**	Adulthood (50s)		Normal	55	Difficultly	Yes	
DNM62	M	**R522H**	Childhood (7)		Normal	55	No	Yes	
DNM63 (son)	M	**R522H**	Adulthood (19)			26		Yes	
CHI4	M	**R523G**		Normal	Normal	47		Yes	
EH58	F	**E560K**	Childhood (2)				Needs support, unable to climb stairs	Yes (>95%)	
ALY9	M	**A618T**	Neonatal	Normal	Motor development delayed	19		Yes	
ACA46	M	**S619L**	Neonatal	Reduced fetal movements, APGAR 3/6, hypotonia	Motor development delayed, tube feeding	Deceased < 1	No	Yes	
ADT88	M	**S619L**	Neonatal	APGAR 3/5	Speech and motor development delayed	9	No		
ADU43	M	**S619L**	Neonatal	Polyhydramnios, APGAR: 6/8	Speech and motor development delayed	5	Difficlulty climbing stairs, cannot run	Yes	No
AGO78	M	**S619L**	Neonatal	APGAR 2/9, hypotonia	Motor development delayed	6	No	Yes	
AGY84	M	**S619L**	Neonatal	APGAR 2/5, hypotonia	Motor development delayed	3 months		Yes (30%)	Yes

BOS746-1	M	**S619L**	Neonatal	APGAR 7/8, hypotonia	Motor development delayed	8	No	Yes (18%)	Yes
CHI3	M	**S619L**	Neonatal	APGAR 6/6, severe hypotonia	Motor development delayed	12	No	Yes	Yes
CHI6	M	**S619L**	Neonatal	Polyhydramnios, small fetal size, no movements, weak cry	Motor development delayed	4	Difficultly	Yes (>90%)	No
BOS1021-1 (daughter)	F	**P627R**	Childhood (7)	Normal	Normal	39	Waddling gait with foot drop, difficultly climbing stairs, cannot run	Yes	Yes
BOS1021-2 (mother)	F	**P627R**	Childhood (3)		Normal	70	Waddling steppage gait, difficulty climbing stairs, cannot run, wheelchair for long distances	Yes (>90%)	
ADM1a	M	**Exon 16 donor splice deletion**	Adulthood (42)			50		Yes (65%)	Yes
ADM1b (daughter)	F	**Exon 16 donor splice deletion**	Adolescence (15)			22		Yes (33%)	Yes
ADM1c (sister)	F	**Exon 16 donor splice deletion**	Adulthood (20)			55		Yes (48%)	Yes
ADM1d (cousin)	F	**Exon 16 donor splice deletion**	Childhood (10)			46		Yes (37%)	Yes

Members of the same family are highlighted in grey

Patient	Mutation	Fiber hypertrophy	Type I fiber predominance	Radial arrangements	Central accumulations of glycogen, mitochondria	CPK	Ventilation	Muscle weakness	Facial weakness	Ptosis
AIP45	**E368Q**					Normal	Normal	Diffuse	Yes	Yes
AHE18	**E368K**	Yes		No	No		Normal			Yes
AKO67	**E368K**	Yes			No	Normal	Normal	Proximal and axial	Yes	Yes
ALY11	**E368K**		Yes			Normal	VC 56%	Diffuse	Yes	Yes
BOS183-1	**E368K**	Yes	No	Yes	Yes	Normal	Sleep apnea	Diffuse	Yes	Yes
BOS848-1	**E368K**	Yes		Yes	Only mitochondria		Normal	Diffuse	Yes	Yes
BOS848-2 (son)	**E368K**						Normal	Diffuse		
BOS593-1	**E368K**								Yes	Yes
BOS839-1	**E368K**						Normal	Diffuse	Yes	
BOS905-1	**E368K**	Yes	No	No	Yes	Normal	Normal	Hips and ankles	Yes	Yes
BOS1132-1	**E368K**	Yes	Yes (75%)		Mitochondria		Abnormal	Diffuse		Yes
CHI1	**E368K**						Abnormal		Yes	Yes

Patient	Mutation	Fiber hypertrophy	Type I fiber predominance	Radial arrangements	Central accumulations of glycogen, mitochondria	CPK	Ventilation	Muscle weakness	Facial weakness	Ptosis
CHI2	**E368K**	No	Yes	Yes	No	Normal	Normal	Diffuse	Yes	Yes
CHI9	**E368K**						Normal		Yes	
DNM118	**E368K**		Yes			Normal	VC 30%	Diffuse	Yes	Yes
EH62	**R369Q**		Yes			Normal	Normal	Diffuse, prevalent axial and distal	Yes	No
EH64	**R369Q**			Yes			Normal	Proximal		No
AHE2	**R369W**	Yes	Yes	Yes	No	Normal		Proximal	Yes	
AHE3 (brother)	**R369W**									
AHE4 (daughter)	**R369W**	Yes	Yes	Yes	No	Normal		Proximal	Yes	No
AHE5 (son)	**R369W**	Yes	Yes	Yes	No			Distal	Yes	No
BOS898-1	**R369W**	Yes	No	Yes	Mitochondria		Sleep apnea	Diffuse	No	
ALM82	**R369W**	Yes	Yes			Normal	Normal	Proximal		No
AMR39 (daughter)	**R369W**							Proximal in upper limbs, diffuse in lower limbs		Yes
BOS929-1	**R369W**	Yes	No		Yes			Diffuse	Yes	Yes
BOS929-6 (cousin)	**R369W**		No				Abnormal	Diffuse		
ABZ97	**R369W**		Yes	Yes	Only glycogen	Slightly elevated	Normal	Diffuse	Yes	Yes
AGJ49 (son)	**R369W**						Normal	Distal	No	No
DNM174	**R369W**		Yes		Yes	Normal		Proximal	Yes	Yes
ADT93a	**R465W**		Yes			Slightly elevated	Normal	Diffuse		No
ADT93b (mother)	**R465W**		Yes	Yes		Normal	Normal	Diffuse	Yes	Yes
ADT93c (uncle)	**R465W**					Normal	Normal	Diffuse	Yes	No
AEB17	**R465W**					Normal	Normal	Distal		Yes
AFW12	**R465W**			Yes	Only glycogen	Slightly elevated		Proximal	Yes	Yes
ALY5	**R465W**		Yes			Slightly elevated	VC 74%	Diffuse	Yes	Yes

Patient	Mutation	Fiber hypertrophy	Type I fiber predominance	Radial arrangements	Central accumulations of glycogen, mitochondria	CPK	Ventilation	Muscle weakness	Facial weakness	Ptosis
BOS601-1	**R465W**	Yes	No	Yes	Mitochondria		Normal	Distal > Proximal		
BOS835-1	**R465W**	Yes		Yes		Normal	Normal	Diffuse		
BOS893-1	**R465W**	Yes					Normal	Distal	No	No
BOS928-1	**R465W**	Yes	No	Yes	Yes		Normal	Diffuse	No	No
BOS930-1	**R465W**	Yes			Yes	Normal	Normal	Diffuse		
BOS1059-1	**R465W**		Yes			Normal	Asthma	Diffuse	Yes	Yes
BOS1061-1	**R465W**		Yes				Abnormal	Diffuse	Yes	

Patient	Mutation	Fiber hypertrophy	Type I fiber predominance	Radial arrangements	Central accumulations of glycogen, mitochondria	CPK	Ventilation	Muscle weakness	Facial weakness	Ptosis
CHI5	**R465W**		Yes		No	Slightly elevated				
CHI7	**R465W**	No	Yes		Yes		Normal		Yes	No
FM71	**R465W**									
AML18	**R522C**	No	Yes			Normal	Normal	Distal	Yes	Yes
ABZ99	**R522H**					Normal		Diffuse		No
AEK95	**R522H**							Proximal amd axial		
AFT16	**R522H**		Yes	Yes			Normal	Proximal	Yes	Yes
AIL9	**R522H**	Yes	Yes	Yes		Slightly elevated	Normal	Distal	No	No
AKZ27	**R522H**						Normal			No
ALP71	**R522H**					Normal				Yes
ALY14	**R522H**					Normal	VC 88%	Diffuse	Yes	Yes
BOS909-1	**R522H**					Normal	Normal	Diffuse	Yes	
BOS1145-1	**R522H**	Yes	Yes				Normal	Diffuse	Yes	Yes
CHI8	**R522H**							Mild in hip flexors, tibialis anterior and hand muscles	Yes	
CHI10	**R522H**									
DNM62	**R522H**		Yes		Yes	Normal	Normal	Proximal	No	No
DNM63 (son)	**R522H**		Yes		Yes	Slightly elevated		Diffuse	Yes	No
CHI4	**R523G**						Normal		Yes	No
EH58	**E560K**		No				VC 22%	Diffuse		Yes
ALY9	**A618T**					Normal	Abnormal	Proximal	Yes	Yes
ACA46	**S619L**		No	Yes	No	Normal	Abnormal	Diffuse	Yes	No
ADT88	**S619L**						Abnormal		Yes	
ADU43	**S619L**	No	No	No	No	Normal	Abnormal	Proximal and axial	Yes	Yes
AGO78	**S619L**					Normal	Normal	Diffuse	Yes	Yes
AGY84	**S619L**						Abnormal	Diffuse		Yes
BOS746-1	**S619L**	No	No		Mitochondria		Abnormal	Diffuse		
CHI3	**S619L**	No	Yes	No	No		Abnormal	Diffuse	Yes	Yes
CHI6	**S619L**	No	Yes	Yes	No	Normal	Normal	Proximal	Yes	Yes
BOS1021-1 (daughter)	**P627R**					Slightly elevated	VC 67%	Diffuse	Yes	No
BOS1021-2 (mother)	**P627R**					Normal	VC 60%	Diffuse	Yes	No
ADM1a	**Exon 16 donor splice deletion**		Yes	Yes		Normal		Distal	Yes	No
ADM1b (daughter)	**Exon 16 donor splice deletion**		Yes	Yes		Slightly elevated	Normal	Diffuse		Yes
ADM1c (sister)	**Exon 16 donor splice deletion**		Yes	Yes		Normal	VC 85%	Distal		No
ADM1d (cousin)	**Exon 16 donor splice deletion**		Yes	Yes		Normal	VC 75 %	Diffuse		Yes

Patient	Mutation	Ophthalmoplegia /paresis	Contractures	Cardiac involvement	Mental impairment	EMG	Deep tendon reflexes	Hyperlordosis
AIP45	**E368Q**	Yes	Yes	VSD	No	Myopathic	Absent	No
AHE18	**E368K**		Yes		No		Weak	Yes
AKO67	**E368K**	No	Yes	No	No		Weak/absent	Yes
ALY11	**E368K**	Yes	Yes	No	No		Weak/absent	No
BOS183-1	**E368K**	Yes	No	Left atrial enlargement	No	Myopathic, neuropathic	Absent	No
BOS848-1	**E368K**	No	Yes	No	No		Absent	
BOS848-2 (son)	**E368K**	Yes	No	Heart murmur at birth	No		Weak	Yes
BOS593-1	**E368K**						Weak/absent	
BOS839-1	**E368K**	Yes	No	Supraventricular tachycardia and mitral valve prolapse	No		Weak/absent	
BOS905-1	**E368K**	Yes	No	No	No	Fibrillations, myotonic discharges	Weak/absent	Yes
BOS1132-1	**E368K**	No		leaky tricuspid valve and possible PDA	No			
CHI1	**E368K**	Yes		Dilated right ventricle	Moderate		Weak	
CHI2	**E368K**	Yes	No	No	No		Absent	Yes
CHI9	**E368K**	No	No				Weak	No
DNM118	**E368K**	Yes		No		Myotonic discharges	Absent	Yes
EH62	**R369Q**	No	No		No	Myopathic		
EH64	**R369Q**	No	No	No	No	Spontaneous activity in hand muscles	Weak/absent	
AHE2	**R369W**			No			Absent	
AHE3 (brother)	**R369W**							
AHE4 (daughter)	**R369W**	No		No	No		Absent	
AHE5 (son)	**R369W**	No		No			Weak	
BOS898-1	**R369W**	No	No	No	No	Myopathic	Weak	Yes
ALM82	**R369W**	No	No	No	No			
AMR39 (daughter)	**R369W**		No	No		Myopathic	Weak in knees, absent in ankles	
BOS929-1	**R369W**	No	No		No	Myopathic	Weak/absent	Yes
BOS929-6 (cousin)	**R369W**			No	No			
ABZ97	**R369W**	No	No	No	No	Myopathic, neuropathic	Absent	
AGJ49 (son)	**R369W**	No		No	Yes			
DNM174	**R369W**	Yes	No	No	No	Myopathic	Weak	Yes
ADT93a	**R465W**	No		No	No	Myopathic	Weak/absent	
ADT93b (mother)	**R465W**	No		No	No	Myopathic	Absent	
ADT93c (uncle)	**R465W**	No			No	Myopathic	Absent	
AEB17	**R465W**	Yes	No	No	No		Absent	
AFW12	**R465W**	Yes				Myopathic	Absent	Yes

Patient	Mutation	Ophthalmoplegia /paresis	Contractures	Cardiac involvement	Mental impairment	EMG	Deep tendon reflexes	Hyperlordosis
ALY5	**R465W**	Yes	No	No	slight reading disability		Absent	No
Patient	**Mutation**	**Ophthalmoplegia /paresis**	**Contractures**	**Cardiac involvement**	**Mental impairment**	**EMG**	**Deep tendon reflexes**	**Hyperlordosis**
BOS601-1	**R465W**			Bicuspid aortic valve	No		Weak	
BOS835-1	**R465W**		No	No	No			No
BOS893-1	**R465W**	No	No	No	No		Weak/absent	No
BOS928-1	**R465W**	No	Yes		Dyslexia	Myopathic, neuropathic, myotonic discharges	Weak/absent	
BOS930-1	**R465W**			No	No	Myopathic	Weak/absent	
BOS1059-1	**R465W**	No	No	No	No	Myopathic	Weak/absent	Mild
BOS1061-1	**R465W**	Yes		Premature ventricular contraction	No	Myopathic	Weak	
CHI5	**R465W**							
CHI7	**R465W**	No		No	No		Weak	Yes
FM71	**R465W**							
AML18	**R522C**	Yes	No	No	No	Myopathic	Weak	Camptocormia
ABZ99	**R522H**	No	No	No	No	Myopathic, neuropathic	Weak	
AEK95	**R522H**							
AFT16	**R522H**	No	No		No	Myopathic, neuropathic	Normal	Yes
AIL9	**R522H**	No	No	No	No		Absent	
AKZ27	**R522H**	No	Yes		No		Absent	
ALP71	**R522H**	Yes	Yes	Conduction trouble, syncope			Absent	
ALY14	**R522H**	Yes	No	No	No		Weak/absent	No
BOS909-1	**R522H**			No	No	Myopathic	Weak/absent	
BOS1145-1	**R522H**	Yes		No	No		Absent	Yes
CHI8	**R522H**	No	No		No		Weak/absent	No
CHI10	**R522H**				No	Myopathic		
DNM62	**R522H**	No	Yes	No	No		Weak	
DNM63 (son)	**R522H**	No			No			
CHI4	**R523G**	No	No	No	No		Weak	No
EH58	**E560K**	Yes						
ALY9	**A618T**	Yes	Yes	No	No			
ACA46	**S619L**	No	No	No		Neuropathic	Absent	
ADT88	**S619L**	Yes	Yes	Sinusal tachycardia	No		Weak	
ADU43	**S619L**	Yes	No		No		Absent	
AGO78	**S619L**	Yes	Yes		No		Weak	
AGY84	**S619L**		Yes			Myopathic	Weak	
BOS746-1	**S619L**	No		No				
CHI3	**S619L**	Yes	Yes	No	No		Absent	Yes
CHI6	**S619L**	Yes	No	No	No		Weak	Yes
BOS1021-1 (daughter)	**P627R**	No	No	No	No		Absent	
BOS1021-2 (mother)	**P627R**	No	Yes	No	No	Myopathic	Weak/Absent	

Patient	Mutation	Ophthalmoplegia /paresis	Contractures	Cardiac involvement	Mental impairment	EMG	Deep tendon reflexes	Hyperlordosis
ADM1a	**Exon 16 donor splice deletion**	Yes		No	No	Myopathic	Weak	
ADM1b (daughter)	**Exon 16 donor splice deletion**	No		No	No	Myopathic	Weak	
ADM1c (sister)	**Exon 16 donor splice deletion**	No		No	No	Myopathic	Weak	
ADM1d (cousin)	**Exon 16 donor splice deletion**	No		No		Myopathic	Weak	