Supplementary Table 1

ID	Sex	Phenotype summary	FH	CK IU/L	Neuro-physiology	Muscle biopsy	Gene	Pathogenic/ likely pathogenic variant	Variant Previously reported
Childhood onset									
4	M	Limb girdle weakness.	Con	3408	N/A	General dystrophic features	DES	c.[1289-2A>G];[(1289-2A>G)] p.[?];[?]	Yes
20	F	Severe limb-girdle weakness since birth with contractures at the knees and elbows.	AR Con	N/A	N/A	Myopathic with rimmed vacuoles	TTN	c.[106332_106333insCT]; [(106332_106333insCT)] p.[(Gly35445fs)];[(Gly35445fs)]	No
21	M	Myopathy with multiple contractures. Keloid scars. Mitral and aortic valve replacement.	AD	302	Myopathic	Mitochondrial hyperplasia^	FLNA	c.4726G>A p.(Gly1576Arg)	Yes
33	M	Distal weakness.	AD	N/A	N/A	General myopathic features	MYH7	c.4424G>C p.(Arg1475Pro)	No
35	F	Delayed motor milestones, mild weakness of NF and LL. Mild contracture of elbow	No	69	Myopathic	Myopathic changes with core-like lesions	DOK7	c.[1120_1121insGCCT(;) 1330_1331insCTGG] p.[(Ser374fs(;)Ser444fs)]	Yes Yes
36	M	Mild weakness in distal UL and proximal LL. NF weakness. Elbows and wrists contractures.	No	N/A	Myopathic	N/A	COL6A1	c.877G>A p.(Gly293Arg)	Yes
39*	F	Progressive weakness from childhood. Contractures.	No	1474	N/A	General dystrophic features	STIM1	c.262A>G p.(Ser88Gly)	Yes

		Permanent PM. Thrombocytopenia.							
40	M	Scapulo-peroneal muscular weakness, congenital hip dislocation.	No	279	Mixed	Tubular aggregate	BICD2	c.629A>C p.(His210Pro)	No
52	M	Mild proximal and neck flexion weakness, mild elbow contracture.	No	121	Myopathic	Myopathic with lobulated and COX negative fibres	COL6A3	c.6220G>A p.(Gly2074Ser)	No
55	F	Proximal weakness, cardiomyopathy.	AR	76	N/A	Minicores^	TTN	c.[61913_61914del (;) c.68329+1G>A] p.[(Tyr20638fs (;) ?)]	No No
58	M	Prevalent distal weakness.	AD	413	Myopathic	Myopathic with nemaline bodies	TPM3	c.8A>G p.(Glu3Gly)	No
59	M	Distal weakness and cardiomyopathy.	No	800	Mixed	Myopathic with core-like lesions	MYH7	c.5390T>C p.(Leu1797Pro)	No
67	F	Neck and limb weakness, contractures of shoulder, elbows, finger flexors and ankles.	No	82	Myopathic	Myopathic with lobulated and COX negative fibres	COL6A1	c.1056+1G>A p.?	Yes
68	M	Proximal>distal weakness. Episode of respiratory crisis.	No	50	Myopathic	Myopathic with core-like lesion^	SEPN1	c.[943G>A];[(943G>A)] p.[(Gly315Ser)];[(Gly315Ser)]	Yes
71	M	NF weakness, contracture of neck and paraspinal muscles and minimal at elbow, respiratory failure, scoliosis.	No	451	Myopathic	N/A	SEPN1	c.[1379C>T];[(1379C>T)] p.[(Ser460Phe)];[(Ser460Phe)]	No

Juvenile/adult onset									
3	F	Proximal weakness (LL>UL).	AR Con	745	Myopathic	General dystrophic features	GMPPB	c.[458C>T];[(458C>T)] p.[(Thr153Ile)];[(Thr153Ile)]	Yes
9°	F	Distal>proximal weakness.	No	404	Chronic neurogenic changes	Myopathic with vacuoles	HSPB1	c.[418C>G];[418C>G] p.[(Arg140Gly)];[(Arg140Gly)]	Yes
10	M	Proximal weakness (LL>UL).	AD	N/A	Myopathic	Myopathic with rimmed vacuoles	DNAJB6	c.279C>G p.(Phe93Leu)	Yes
12	F	Proximal weakness in UL and LL.	No	250	Myopathic	Tubular aggregate	ORAI1	c.298G>A p.(Gly100Ser)	Yes
16	F	Distal LL weakness.	No	563	Myopathic	Myopathic with rimmed vacuoles	TTN	c.[107800G>T(;)30186T>G] p.[(Gly35934*(;)Tyr10062*)]	No No
25	M	Distal weakness, dysphonia.	AD	192	Myopathic	N/A	DNAJB6	c.298T>G p.(Phe100Val)	Yes
32	M	Prevalent distal weakness (UL>LL), cardiomyopathy.	AD	80	Myopathic	Myopathic with nemaline bodies	ACTA1	c.971C>G p.(Pro324Arg)	No
56	F	Scapulo-peroneal myopathy, subtle contracture of the elbows, knees and ankles.	AD	506	Myopathic	Myopathic with rimmed vacuoles and protein aggregation	FHL1	c.310T>A p.(Cys104Ser)	Yes
72	F	Distal>proximal weakness in LL.	No	681	Myopathic	Myopathic with rimmed vacuoles	TTN^{-}	c.[107840T>A (;)63793G>A] p.[(Ile35947Asn(;)Asp21265Asn)]	Yes No
79	F	Minimal facial weakness, proximal weakness.	No	155	N/A	General myopathic features	DOK7	c.[1120_1121insGCCT]; [(1120_1121insGCCT)] p.[(Ser374fs)];[(Ser374fs)]	Yes

81	F	Muscle fatigue and aching, mild proximal weakness. Hyposplenism.	No	657	N/A	Tubular aggregate (1st biopsy) Myopathic with inflammation (2nd biopsy)	STIM1	c.241G>A p.(Gly81Ser)	No
100	F	Distal> proximal LL weakness.	No	206	Mixed	General myopathic features	GNE	c.[2179G>A(;)1853T>C] p.[(Val727Met(;)Ile618Thr)]	Yes Yes
Late onset									
23	F	Proximal LL weakness.	AR	500	Mixed	General dystrophic features	ANO5	c.[2498T>A(;)185dupA] p.[(Met833Lys(;)Gln62fs)]	Yes No
24	M	Distal lower limb weakness.	No	392	Myopathic	N/A	MYOT	c.179C>G p.(Ser60Cys)	Yes
30	M	Distal lower limb weakness.	No	243	Myopathic	Normal/minimal change	GNE	c.[1225G>T(;)922C>T] p.[(Asp409Tyr(;)Arg308Cys)]	Yes Yes
62	M	Distal LL>UL weakness.	No	538	Mixed	Neurogenic	MFN2	c.311G>A p.(Arg104Gln)	No
73	M	Distal>proximal weakness.	AD	209	Myopathic	Myopathic with rimmed vacuoles	VCP	c.475C>T p.(Arg159Cys)	Yes

CK: creatine kinase (normal range in our laboratory: 26-140 in female, 38-204 in male); Con: consanguinity; FH: family history; LL: lower limbs, NF: Neck flexor, PM: pacemaker, UL: upper limbs. ^ Original report/slides not retrievable; *Case reported in Harris *et al* 2017 [1]; °Case reported in Bugiardini *et al* 2017 [2]; ~ 63793G>A variant in *TTN* is reported in the table because it can contribute to the phenotype caused by 107840T>A likely pathogenic variant as reported in Evila et al.[3]

RefSeq transcripts: *ACTA1* (NM_001100), *ANO5* (NM_213599), *BICD2* (NM_001003800), *COL6A1* (NM_001848), *COL6A3* (NM_004369), *DES* (NM_001927), *DNAJB6* (NM_058246), *DOK7* (NM_173660), *FHL1* (NM_001159702), *GMPPB* (NM_013334), *GNE* (NM_001128227), *HSPB1* (NM_001540), *MFN2* (NM_014874), *MYH7* (NM_000257), *MYOT* (NM_006790), *TTN* (NM_001267550), *FLNA* (NM_001110556), *ITGA7* (NM_002206), *ORAI1* (NM_032790), *SEPN1* (NM_020451.2), *STIM1* (NM_003156), *TPM3* (NM_152263), *VCP* (NM_007126).

References

[1] Harris E, Burki U, Marini-Bettolo C, Neri M, Scotton C, Hudson J, et al. Complex phenotypes associated with STIM1 mutations in both coiled coil and EF-hand domains. Neuromuscul Disord 2017;27:861–72. doi:10.1016/j.nmd.2017.05.002.

[2] Bugiardini E, Rossor AM, Lynch DS, Swash M, Pittman AM, Blake JC, et al. Homozygous mutation in HSPB1 causing distal vacuolar myopathy and motor neuropathy. Neurol Genet 2017;3. doi:10.1212/NXG.0000000000000168.

[3] Evila A, Palmio J, Vihola A, Savarese M, Tasca G, Penttila S, et al. Targeted Next-Generation Sequencing Reveals Novel TTN Mutations Causing Recessive Distal Titinopathy. Mol Neurobiol 2016. doi:10.1007/s12035-016-0242-3.