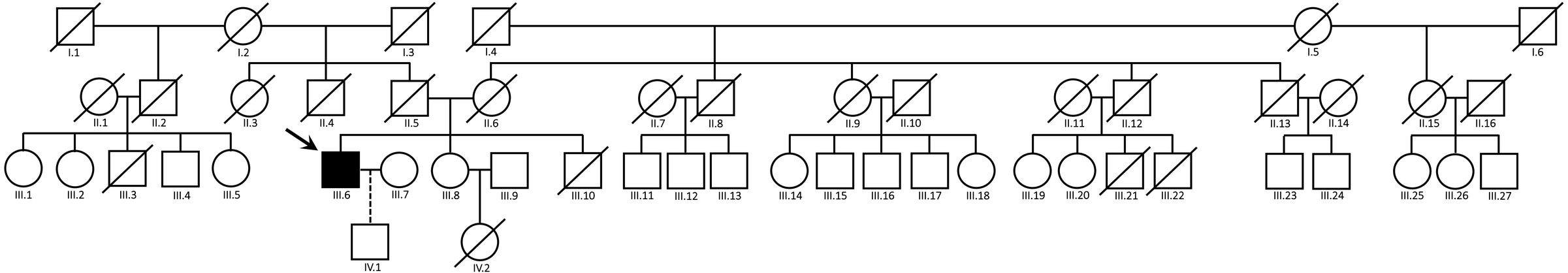
Supplementary Table 1 – List of p.S85C *MATR3*-associated VCPDM patients reported so far.

Ethnic background	N° of families (patients)	AAOO (years)	Symptoms at onset	Shoulder weakness	Dysphagia	Vocal cord dysfunction	Respiratory impairment	↓ or altered sensation	NCS	EMG	Muscle biopsy	Predominant distribution of lesions in skeletal MRI	CPK	Ref
North American	1 (37)	35 – 57	Voice change, distal weakness	+	++	++	+	-	N / LCV	Myo > Neu	Vacuoles (R), central nuclei, atrophy, end-stage myopathy	NA	N – 8x	[1; 2]
Bulgarian	1 (19)	36 – 54	Distal weakness	+	+	+	-	-	NA	NA	End-stage myopathy, vacuoles (A)	NA	2x – 4x	[2]
German	6 (15)	30 – 55	Distal weakness, myalgias, walking difficulties, speech disturbances, stiffness	-/+	-/++	-/++	++	-	NR	PSW/F: PS, BB FDI, TA, VL HFD: PS, BB, FDI, TA	NR	PS, BF, ST, SM, GA, SO, TP, PE, TA	N – 8x	[3]
Asian	1 (3)	44 – 68	Walking difficulties, dysphagia	+	++	+	++	+	Neu	Myo = Neu	Vacuoles (R, A), internal nuclei	GL, QU, PS	N – 2x	[4]
American	1 (6)	31 – 48	Distal weakness	++	+	+	++	-	NA	Myo	Vacuoles (R)	SO, GA	N – 2x	[5]
French	1 (3)	40s	Bilateral foot drop	+	-	+	+	-	N	Myo	Fiber size variability, internal nuclei, vacuoles (R, not-R, A)	PS, TR, TEN, TA, foot	NA	[6]
Italian	1 (1)	39	Bilateral foot drop	-	-	+	-	-	NA	Myo – Neu	Fiber size variability, internal nuclei, nuclear clumps, vacuoles (R), endomysial fibrosis	GL, AD, BF, TA, GA, SO	2x	[7]
Italian	1 (1)	40	Myalgias at thighs	++	+	+	+	++	Neu	Neu	Fiber size variability,	GA, ST, SM, BF, QU, TA, AD	2x	*Cur*

	vacuoles (not-R), central nuclei

AAOO: age at onset; N°: number; ↓: reduced; NCS: nerve conduction studies; EMG: electromyography; MRI: muscle resonance imaging; CPK: creatine phosphokinase; Ref: reference; N: normal; LCV; low conduction velocities; Myo: myopathy; Neu: neuropathy; R: rimmed; A: autophagic; NA: not available; NR: Individual patient data not retrievable; PSW: positive sharp waves; F: fibrillation potentials; HFD: high frequency discharges; TA: tibialis anterior; TB: tibialis posterior; PS: paraspinal muscles; PE: peroneus; ST: semitendinosus; SM: semimembranosus; GA: gastrocnemius; BF: biceps femoris; QU: quadriceps; VL: vastus lateralis; AD: adductors; SO: soleus; GL: gluteus; TEN: tenar eminence; TR: triceps; BB: biceps brachii; FDI: first dorsalis interosseus; Cur: current.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I.2
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I.4
I.5
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II.1
II.2
II.3
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II.7
II.8
II.9
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II.11
II.12
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II.14
II.15
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III.1
III.2
III.3
III.4
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III.16
III.17
III.18
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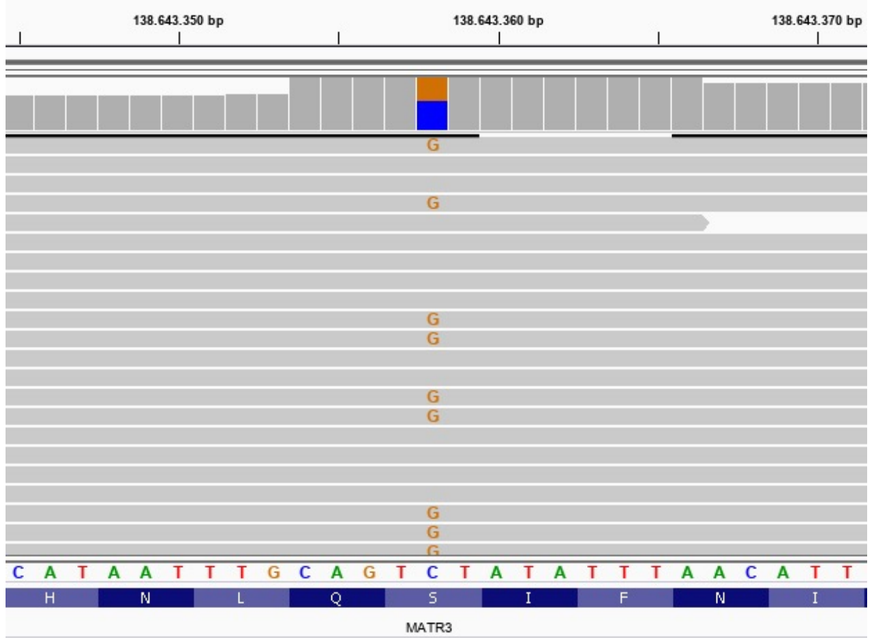
III.20
III.21
III.22
III.23
III.24
III.25
III.26
III.27
IV.1
IV.2

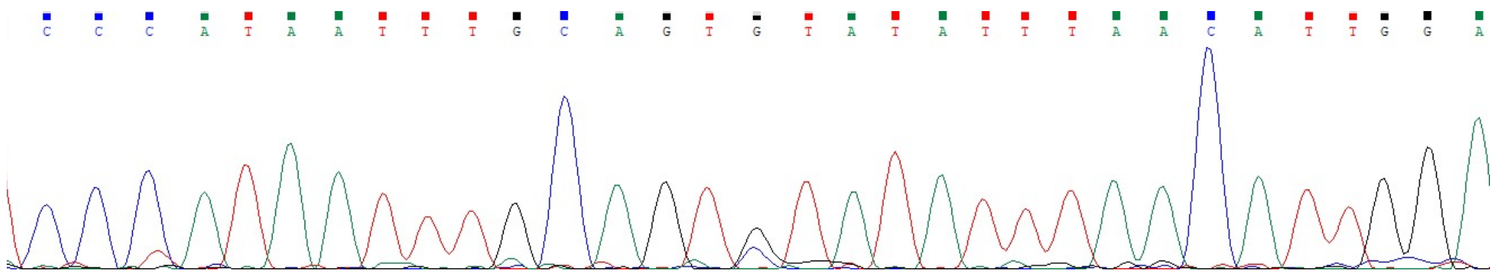
a



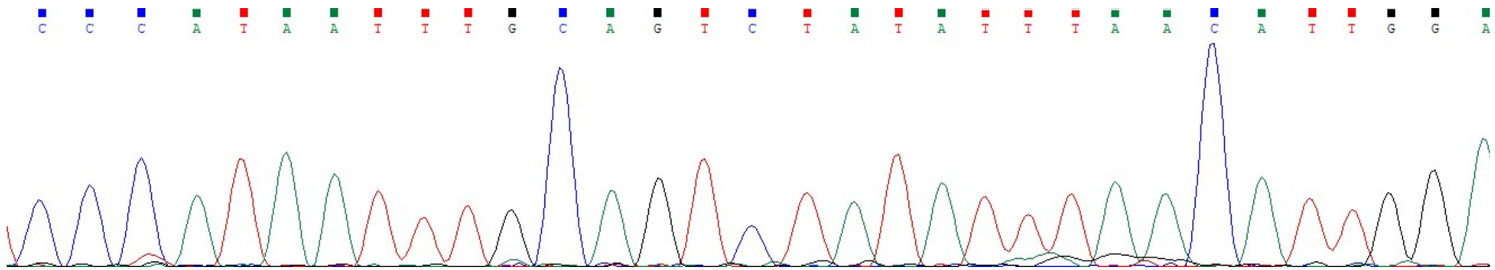
c.254C>G

p.S85C

b



c



Supplementary Table 2 – List of genes included in our Next Generation Sequencing panel.

Chromosome	Gene
12	*AAAS*
20	*AARS*
1	*AGL*
2	*ALS2*
14	*ANG*
11	*ANO5*
10	*ANXA11*
8	*ARHGEF10*
8	*ASAH1*
12	*ATXN2*
10	*BAG3*
9	*BICD2*
11	*BSCL2*
3	*CAV3*
22	*CHCHD10*
3	*CHMP2B*
15	*CHRNA3*
12	*COX6A1*
11	*CRYAB*
12	*DAO*
2	*DCTN1*
2	*DES*
10	*DHTKD1*
7	*DNAJB6*
17	*DNAJC7*
19	*DNM2*
19	*DNMT1*
X	*DRP2*
14	*DYNC1H1*
2	*DYSF*
X	*EMD*
10	*EGR2*
2	*ERBB4*
10	*ERLIN1*
9	*EXOSC3*
5	*FBXO38*
12	*FGD4*
X	*FHL1*
6	*FIG4*

7	*FLNC*
16	*FUS*
17	*GAA*
6	*GARS*
8	*GDAP1*
3	*GBE1*
9	*GNE*
X	*GJB1*
9	*GLE1*
3	*GLT8D1*
3	*GNB4*
15	*HEXA*
5	*HEXB*
5	*HINT1*
12	*HNRNPA1*
7	*HSPB1*
5	*HSPB3*
12	*HSPB8*
11	*IGHMBP2*
14	*INF2*
11	*KARS*
12	*KIF5A*
10	*LDB3*
16	*LITAF*
2	*LIMS2*
1	*LMNA*
9	*LRSAM1*
12	*MARS1*
5	*MATR3*
1	*MFN2*
1	*MPZ*
11	*MTMR2*
14	*MYH7*
5	*MYOT*
8	*NDRG1*
22	*NEFH*
4	*NEK1*
8	*NEFL*
10	*OPTN*
12	*ORAI1*
17	*PFN1*
1	*PLEKHG5*

17	*PMP22*
X	*PRPS1*
19	*PRX*
11	*PYGM*
3	*RAB7A*
2	*REEP1*
11	*SBF2*
22	*SCO2*
9	*SETX*
5	*SH3TC2*
9	*SIGMAR1*
2	*SLC5A7*
8	*SLC52A2*
20	*SLC52A3*
X	*SMPX*
5	*SMN1*
21	*SOD1*
15	*SPG11*
9	*SPTLC1*
5	*SQSTM1*
11	*STIM1*
9	*SURF1*
1	*SYT2*
17	*TAF15*
1	*TARDBP*
12	*TBK1*
17	*TCAP*
3	*TFG*
2	*TIA1*
16	*TK2*
12	*TRPV4*
18	*TTR*
2	*TUBA4A*
19	*TUBB4A*
X	*UBA1*
X	*UBQLN2*
19	*UNC13A*
20	*VAPB*
8	*VCP*
14	*VRK1*
4	*YARS*

Supplement

eTable 1 – List of p.S85C *MATR3*-associated VCPDM patients reported so far.

eTable 2 – List of genes included in our Next Generation Sequencing panel.

eFigure 1 – Family's pedigree. Circles indicate females, squares indicate males; the black symbol indicates the proband affected by VCPDM; diagonal lines indicate deceased individuals; the arrow indicates the index patient; the dotted line indicates an adoptive child. Age and cause of death of individuals: II.2 – 74 years, car accident; II.3 – 72 years, ischemic stroke; II.4 – 21 years, during war; II.5 (father) – 65 years, ischemic stroke; II.6 (mother) – 33 years, childbirth; III.3 – 60 years, myocardial infarction; II.8 – 75 years, cardiovascular causes; II.9 – 80 years, cardiovascular causes; II.12 – 70 years old, sepsis; II.13 – 80 years, unknown; II.15 – 60 years, unknown; III.10 – childbirth; III.21 – 38 years, ischemic stroke; III.22 – 50 years, hepatocarcinoma; IV.2 – 24 years, car accident.

eFigure 2 – Genetic and bioinformatic analysis. a) IGV screenshot displaying the heterozygous chr5:138643358C/G substitution in the proband. b) Electropherogram of the heterozygous c.254C>G, p.S85C *MATR3* mutation in the proband. c) Electropherogram of the wild-type nucleotide at position 254 of *MATR3* NM_199189 transcript in proband's sister.