Supplementary Online Content

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This supplementary material has been provided by the authors to give readers additional information about their work.

eTable1. Primers used for PCR Amplification and Sequencing of CoQ_{10} Biosynthetic Genes (Primers 5'➔3').

Gene-Exon	Forward	Reverse	PCR condition
FDPS-Exon 1/2	AATTGTCCCCAAGCACATT	GCCACACAGGTACAGAGCAA	A
FDPS-Exon 3	TGGGAGAGAGCAAGGAGAAA	TGGCCGTAGCACACTAGAGA	A
FDPS-Exon 4/5	TGAGCTGTGACTGCACCACT	ACCCTTCCTCGCTTTCTTTC	A
FDPS-Exon 6/7	GCCTTAAGTTTTGGGGCTTT	GTTTTTCACCAGGGGTAGCA	A
FDPS-Exon 8/9	AGGTTGGACCATCAGTCAGG	CCACATGCACACACACAGAG	A
FDPS-Exon 10	GGCTTTGGAGATGTTCTGGA	CACCCACCTAGAGGGTTTGA	A
MVD-Exon 1	ACCTACGTCAGCAACCCATC	AGTTTCCCCGTCTGTCGAG	B
MVD-Exon 2	ACAGGTTGTGCGGTGAGAGA	CGCTAGGCCATCTCATCCTA	C
MVD-Exon 3	TGGTTGCTCCACAAGGTG	ACAGAGGCAGAAGCACTTTC	A
MVD-Exon 4	TCCCGGGTAAGAAACTCTCC	GGTGAGGGGATGCTCTTTTA	A
MVD-Exon 5	GAAGCCCTGTCATCTGGAAA	CAACCACGCTTCTGTTCCTT	A
MVD-Exon 6	GCTGGGATCTGGAAGTTGC	ATCTCTGCATTTGGCTCCTG	D
MVD-Exon 7	AGGAGCCAAATGCAGAGATG	AGGGTGGAGCTTTCAGACAC	D
MVD-Exon 8	GCCTAGACTGAGCTCTTGGAGA	TCAGGTGCCTCCGTCTCTT	A
MVD-Exon 9	AAAAGAAACCTGTCCCCACA	ATGAATGGACAAAGGCGTTC	C
MVD-Exon 10	TGGATTTCTATCCCCAGGTG	GCACTTGGTGGTTTCCTGAG	A
PSAP-Exon 1	CTTCCTCACTCCTCCCCATA	CCAGAGAAAGCCAGCGAAC	E
PSAP-Exon 2	TGTCCCATACAGCTTGGTGA	CTGAGCCTCCATCTCCTCTG	E
PSAP-Exon 3	AGGGTGGAGAACCAGGATGT	TCAGGCCTACACCATTCCTC	E
PSAP-Exon 4	TGTCTGCTTTTGCCTGATTG	GCTGTGCCAAAGGAGCTATT	E
PSAP-Exon 5	TTCTTTCCATCCCACCAGAG	GCCCCAGTTTAAGAACCACA	E
PSAP-Exon 6	CTAATGCTGCAGCCCTGAGT	TTGTCTGAACGCCCTACTCC	E
PSAP-Exon 7	TATTAAAGCTGGCCCAGAGC	GGTCGATTTAGCCCAATTCA	E
PSAP-Exon 8	AGAGGGAGGTAGCCTTGACC	CAGGGAACCGAAAGAAACAA	E
PSAP-Exon 9	TGGTCTCTGTGTCCCCTTTC	CTACAAAGCAGGGCAATGGT	E
PSAP-Exon 10	ACCATTGCCCTGCTTTGTAG	CCAGCCTTGGCATACTTCAT	E
PSAP-Exon 11	ACCCAGTGGGCTGGGAAT	GCTGGCTCCCTACCTTCTTG	E
PSAP-Exon 12	TCAGCAACCCTGATGTTCTG	AAAGCAGGGTGGAGAGTTGA	E
PSAP-Exon 13	GATCCTGTCCTGGGTCTTCA	CAGAGCTCTCTCCTCCT	E
ADCK1-Exon 2	GGTAGAGCTGGGATTTGAACTT	CATAGCAGGCATGTCTATCTGC	E
ADCK1-Exon 3	GCAAGGTTTGGGCAGAGTAG	GGCAGCTGCTTCAGGATTTA	E
ADCK1-Exon 4	CACCAAGGGAAAAGGTGTGT	TTTTCTGAAGCATCCCAACC	E
ADCK1-Exon 5	GCGGGACTCTGTCTCAACAC	CACTCCACTCACCAGCTTGA	E
ADCK1-Exon 6	TGGAATTCAGAGGAGGGATG	TTGCAAATTGCCTTCAAGTG	E
ADCK1-Exon 7	GAGTAGCCAGCCTCCCTCTT	GCTGGCCTAAATGACCTGAA	E
ADCK1-Exon 8	AACAATCACTCCCACCACAAC	AAGGGTCCTTTCCAGCTACC	E
ADCK1-Exon 9	AAACAGATGTCGTGGGAAGG	TACTTGGAAGGGGTCCACAG	E
ADCK1-Exon 10	TCCTAGCAGTGCCAAGACAG	AGACTGGTGGGGAAAGGTG	E
ADCK1-Exon 11	CTCCCGATTGGGTAGTGGTA	ACCTCGCTGAGGTGTGACTT	E
ADCK4-Exon 1	CTCCACCCCTGTGACTAAAC	CATGTCAGATAGCCCCGTA	F
ADCK4-Exon 2/4	ATTTAGTGGGTGGGAATGAG	TGCCCTTTCTAATTGAGGTC	F
ADCK4-Exon 5	AAAAAGAGTTGGGAGACAAGC	TTTAGGCCTGTTCAAAGCA	F
ADCK4-Exon 6/7	TCAGACTCCTGTGTTCATCC	ACTCTGGTGATTCCCATTTT	F
ADCK4-Exon 8/9	AAGGGAGCTCTCTCTGAGC	CTCCTGCTTTCTCTCTCTGG	F
ADCK4-Exon 10	GGCCTAGAGTAGGAGCTGTG	AAGCTCACAGAGGACAAAGG	G
ADCK4-Exon 11/12	ATGGAGGACTTCTGAGAGCA	CTGAATCCCACTTGGAAAAG	F

A: Touchdown PCR cycles were 2 min at 94°C; 10 cycles of 1 min at 94°C, 1 min at 67°C-57°C (-1°C per cycle), and 1 min at 72°C; 20 cycles of 1 min at 94°C, 1 min at 57°C, and 1 min at 72°C; and a final cycle of 5 min at 72°C.

Gene-Exon	Forward	Reverse	PCR condition
ADCK4-Exon 13	ATGGGGAGGGAGACAGAT	TTAAGTGCTTGGTGTGTGCT	G
ADCK4-Exon 14	GATGAGAATGGAGGTGGGTA	AGACAAGCCCCTCCTAGAGT	G
ADCK4-Exon 15	GCTCTGGAAGGAGTGGAAG	CCTGGCTTAGTTTTCGGATA	H
ADCK5-Exon 2	TTAGAGTTAGGCTGCCTCAGA	GTTGTGGGTACAGGAGAAGG	A
ADCK5-Exon 3	ACAGGAGTGAGACGTGGTG	CAGCTGTAAAATCCTCAGCA	A
ADCK5-Exon 4/5	GGTGAGGCTAGACCATGAGG	CTGGAAGGACAGGTGCTCAG	A
ADCK5-Exon 6/7	AGGTGAGTGTGCGCTCAG	TCCTACCAGCTCTGCCTACG	A
ADCK5-Exon 8/9	GAGCAAACACGTAGGCAGA	GGCCTTGATGAGCTTTTCT	A
ADCK5-Exon 10/13	GGCAGTGCATGACGTGAG	GACAGCCCTGCACACACC	A
ADCK5-Exon 14/15	CCGCTACTTCCTTATGGCTA	TGCAGATCCTGGACGACT	A

B: 1 Touchdown PCR cycles were 2 min at 94°C; 10 cycles of 1 min at 94°C, 1 min at 60°C-50°C (-1°C per cycle), and 1 min at 72°C; 20 cycles of 1 min at 94°C, 1 min at 50°C, and 1 min at 72°C; and a final cycle of 5 min at 72°C.

C: PCR cycles were 2 min at 94°C; 35 cycles of 30 s at 94°C, 30 s at 60°C, and 30 s at 72°C; and 5 min at 72°C.

D: Touchdown PCR cycles were 2 min at 94°C; 10 cycles of 30s at 94°C, 30 s at 65°C-55°C (-1°C per cycle), and 30 s at 72°C; 20 cycles of 30s at 94°C, 30 s at 55°C, and 30 s at 72°C; and a final cycle of 5 min at 72°C.

E: PCR cycles were 2 min at 94°C; 35 cycles of 30 s at 94°C, 30 s at 59°C, and 30 s at 72°C; and 5 min at 72°C.

F: PCR cycles were 2 min at 94°C; 35 cycles of 1 min at 94°C, 1 min at 57°C, and 1 min at 72°C; and 5 min at 72°C.

G: 10, 13, 14 Touchdown PCR cycles were 2 min at 94°C; 10 cycles of 30s at 94°C, 30 s at 65°C-55°C (-1°C per cycle), and 1 min at 72°C; 20 cycles of 30s at 94°C, 30 s at 55°C, and 1 min at 72°C; and a final cycle of 5 min at 72°C.

H: PCR cycles were 2 min at 94°C; 35 cycles of 30 sec at 94°C, 30 sec at 57°C, and 1 min at 72°C; and 5 min at 72°C.

PDSS1, PDSS2, COQ2, COQ3, COQ4, COQ5, COQ6, COQ7, ADCK3, COQ9, COQ10, ADCK2, APTX, ETFDH, POLG1

genes were sequenced as previously described.[1-5]

P#	P1	P2	P3	P4
Age(y)/sex	3/F	3/F	early childhood/F	13/M
Consanguinity	-	-	-	NA
Geographic origin	NA	NA	Brazil	Italy
Clinical features	MW, S, EI, MDD, CA, RM	MW, EI, MDD, RM	MW, CA, S, EI, PEO, Pt, RM	MW, S, RM
Muscle morphology	M	M	M	M
Muscle RCE Activities	↓ I+III, II+III	NA	↓ I+III, II+III	↓ I+III, II+III
Lactate	↑	↑	NA	↑
Serum CK (U/l)	2-20 fold elevation	2-20 fold elevation	<1000	1000-5000
Muscle CoQ10	3.7%	5.4%	4.7 µg/g	39%
Fibroblasts CoQ10	N	NA	NA	NA
Reference	6	6	7	8

eTable 2. Encephalomyopathy patients. **P#**: patient number; **Age**: age at onset; **NA**: data not available; **MW**: muscle weakness **S**: seizures; **EI**: exercise intolerance; **MDD:** motor-developmental delay/mental retardation; ; **CA**: cerebellar ataxia; **RM**: recurrent myoglobinuria; **PEO**: progressive external ophthalmoplegia; **Pt**: ptosis; ; **M**: mitochondrial changes (ragged-red fibers, COX negative fibers ± lipid accumulation); **N**: normal; **RCE**: respiratory chain enzyme; **UP**: unpublished.

P#	Age, y/sex	Consanguinity	Geographic origin	Clinical features	Muscle morphology	Muscle RCE Activities	Lactate	Serum CK, U/L	Muscle CoQ_{10} (µg/g)	Fibroblasts CoQ_{10}	Mutation	Reference
P5	15/M	NA	Italy	MW, RM	M	↓ I+III, II+III	↑	> 5000	35%	N	NA	8
P6	11/M	-	NA	MW, EI, F, C	M	↓ I, I+III and II+III	↑	< 1000	9.11 (19.81±2.61)	NA	NA	9
P7	6/M	NA	Hungary	MW, EI,	M	↓ I, II +III, IV	↑	1000-5000	1.7nmol/UCS (2.7-7.0)	NA	NA	10
P8	32/F	NA	Germany	MW, EI, IDDM, HTN	M	↓ I, II +III, IV	↑	1000-5000	0.6nmol/UCS (2.7-7.0)	NA	**ETFDH** p.P456L+K590E	10, 11
P9	29/M	+	Turkey	MW, F, MP	M	↓ I, II +III, IV	↑ after excercise	1000-5000	0.8 nmol/UCS (2.7-7.0)	NA	**ETFDH** Homozygous p.L377P	10, 11
P10	12/M	+	Middle East	EI, C, F	M	↓ I, II +III, IV	N	1000-5000	0.8 nmol/UCS (2.7-7.0)	NA	**ETFDH** Homozygous p.L377P	11
P11	14/F	+	Middle East	MW, F, EI	NA	NA		1000-5000	NA	NA	**ETFDH** Homozygous p.L377P	11
P12	12/F	+	Turkey	MW, EI, MP	M	↓ I, II +III, IV	NA	1000-5000	1.28 nmol/UCS (2.7-7.0)	NA	**ETFDH** Homozygous p.L377P	11
P13	NA/F	+	Turkey	MW, MP	NA	NA	NA	NA	NA	NA	**ETFDH** Homozygous p.L377P	11
P14	12/F	+	Turkey	MW, MP	M	↓ I, II +III, IV	NA	< 1000	0.87 nmol/UCS (2.7-7.0)	NA	**ETFDH** Homozygous p.P483L	11
P15	26/M	NA	Italy	MW, EI, RM	P	N	N	< 1000	12.2	NA	NA	UP
P16	10/F	NA	Italy	RM	NA	N	N	> 5000	13.9	NA	NA	UP
P17	26/M	NA	Italy	EI, RM	P	NA	N	1000-5000	12	NA	NA	UP
P18	NA/M	NA	Italy	RM	N	NA	N	NA	16	NA	NA	UP

eTable 3. Isolated myopathy patients. **P#**: patient number; **Age**: age at onset; **NA**: data not available; **MW:** muscle weakness; **RM**: recurrent myoglobinuria; **IDDM**: insulin dependent diabetes mellitus; **HTN**: hypertension; **F**: fatigue; **EI**: exercise intolerance; **C**: cramps; **MP**: myalgia; **M**: mitochondrial changes (ragged-red fibers, COX negative fibers ± lipid accumulation); **N**: normal; **P**: pathologic; **RCE**: respiratory chain enzyme; **UP**: unpublished. *,° siblings

	Age, sex	Consanguinity	Geographic origin	Clinical features	Renal dysfunction	Muscle morphology	Muscle RCE Activities	Lactate	Muscle CoQ_{10} (µg/g)	Fibroblasts CoQ_{10}	Mutation	Reference
P19	3mo/M	NA	France	OA, R, Ca, SND, CA, Dys, HC,	Nephrotic syndrome	N	N	NA	NA	↓	NA	[17]
P20	6mo/F	NA	France	MDD, CA, UMN, SND, B	Nephrotic syndrome (FSGS)	NA	NA	NA	NA	↓	NA	[17]
P21	1y/F	NA	France	SND, CA	Nephrotic syndrome (FSGS)	NA	N	NA	NA	↓	NA	[17]
P22	birth/M	-	Pakistan	MDD, MW, S, UMN, Ne, HC	Tubular dysfunction	M	↓ II+III	↑	37 (140-580)	↓	***COQ9*** homozygous p.R244X	[18,19]
P23	5d/M	+	Azerbaijan	H, PI, LS	-	M	↓ I, I+III and II+III (liver)	↑	NA	NA	NA	[20]
P24	12mo/M	+	North Africa	MDD, MW, CA, S UMN, OA, R, My	Nephrotic syndrome (FSGS)	N	↓ I, I+III and II+III	N	12	↓	***COQ2*** homozygous p.Y297C	[12-15]
P25	3mo/M	-	Germany	MDD, MW, S, LS	Nephrotic syndrome	M	↓ II+III	↑	4.6	↓	***PDSS2*** P.Q322X+S382L	[2]
P26	1y/M	+	Morocco	SND, LR, Ob, V, MDD, Ne, MC	-	M	↓ II+III (fibroblasts)	↑	NA	↓	***PDSS1*** homozygous p.D308E	[1]
P27	2y/F	+	Morocco	SND, V, Ob, MC, OA, Ne, MDD, LR	-	NA	NA	↑	NA	↓	***PDSS1*** homozygous p.D308E	[1]
P28	Birth/F	-	France	H, S, IDDM,	Nephrotic syndrome	NA	↓ I, I+III and II+III (liver)	↑	NA	↓	***COQ2*** homozygous p.N401fsX4	[1]

	Age, sex	Consanguinity	Geographic origin	Clinical features	Renal dysfunction	Muscle morphology	Muscle RCE Activities	Lactate	Muscle CoQ_{10} (µg/g)	Fibroblasts CoQ_{10}	Mutation	Reference
												15
P29	Birth /M	-	France	IDDM, H	Acute kidney failure	NA	NA	NA	NA	NA	(brother of P28; parents heterozygous for the mutations)	1
P30	Birth /M	+	Italy	S	Acute kidney failure (crescentic GN)	P	↓ II+III	↑	0.8	N	***COQ2*** homozygous p.S146N	14
P31	1.2y/ NA	+	Lebanon	SND, CA	SRNS (FSGS)	NA	NA	NA	NA	NA	***COQ6*** homozygous p.G255R	16
P32	0.3y/ NA	+	Turkey	S	SRNS (DMS)	NA	NA	NA	NA	NA	***COQ6*** homozygous p.G255R	16
P33	2.5y/ NA	+	Turkey	S	SRNS (FSGS)	NA	NA	NA	NA	NA	***COQ6*** homozygous p.A353D	16
P34	4y/F	+	Brazil	CA, UMN	Proteinuria	NA	NA	NA	17.2	NA	NA	UP
P35	Birth /F	NA	Romania	MDD, MW, LS, H, HC	-	N	N	↑	45.6 (76-177)	↓	NA	UP

eTable 4. Infantile Multisystemic patients. **P#**: patient number; **Age**: age at onset; **NA**: data not available; **MDD:** motor-developmental delay/mental retardation; **MW:** muscle weakness**; CA:** cerebellar ataxia**; S:** seizures**; Dys:** dystonia; **UMN:** upper motor neuron signs; **OA:** optic atrophy; **R:** retinopathy; **B:** blindness; **My:** myoclonus; **LS**: Leigh syndrome; **Ne:** neuropathy**; HC:** hypertrophic cardiomyopathy; **V:** valvulopathy**; H**: hepatopathy; **PI**: pancreatic insufficiency; **Ca:** cataract; **SND:** sensorineural hearing loss; **LR:** livedo reticularis; **O:** obesity; **MC**: macrocephaly; **SRNS:** steroid-resistant nephrotic syndrome; **FSGS:** focal segmental glomerulosclerosis; **GN**: glomerulonephritis; **DMS**: diffuse mesangial sclerosis; **M**: mitochondrial changes (ragged-red fibers, COX negative fibers ± lipid accumulation); **N**: normal; **P**: pathologic; **RCE**: respiratory chain enzyme; **UP**: unpublished.

P#	Age, y/sex	Consanguinity	Geographic origin	Clinical features	Muscle morphology	Muscle RCE Activities	Lactate	Muscle CoQ_{10} (µg/g)	Fibroblasts CoQ_{10}	Mutation	Reference
P36	9/F	+	North Africa	nephrotic syndrome (FSGS)	NA	↓ I+III, II+III in fibroblasts	N	NA	18 (nv 105±14)	***COQ2*** homozygous p.Y297C	12-15
P37	18/M	-	Eastern Europe	SRNS (collapsing GN)	M	↓ II+III in muscle	↑	12	20.9	***COQ2*** p.R197H+ N228S	14
P38	6.4/NA	+	Lebanon	SRNS (FSGS), congenital SND	NA	NA	NA	NA	NA	***COQ6*** homozygous p.G255R	16
P39	0.3/NA	+	Lebanon	SRNS, congenital SND	NA	NA	NA	NA	NA	***COQ6*** homozygous p.G255R	16
P40	<1y/NA	+	Lebanon	SRNS (FSGS), congenital SNS	NA	NA	NA	NA	NA	NA	16
P41	0.3/F	+	Turkey	SRNS, SND, facial dysmorphism	NA	NA	NA	NA	NA	***COQ6*** homozygous p.G255R	16
P42	0.2/M	+	Turkey	Nephrolithiasis, SND	NA	NA	NA	NA	NA	***COQ6*** homozygous p.G255R	16
P43	6/NA	+	Turkey	SRNS (FSGS), SND	NA	NA	NA	NA	NA	***COQ6*** homozygous p.A353D	16
P44	2.5/NA	+	Turkey	SRNS (FSGS), SND	NA	NA	NA	NA	NA	***COQ6*** homozygous p. A353D	16

P45	3/NA	-	Turkey	SRNS (FSGS), SND	NA	NA	NA	NA	NA	***COQ6*** heterozygous p. W447X	16
P46	3/NA	-	Turkey	SRNS (FSGS), SND	NA	NA	NA	NA	NA	***COQ6*** p.Q461fsX478	16

eTable 5. Isolated nephropathy patients (+/- sensorineural hearing loss). **P#**: patient number; **Age**: age at onset; **NA**: data not available; **GN**: glomerulonephritis; **SRNS:** Steroid-resistant nephrotic syndrome **FSGS**: focal segmental glomerulosclerosis; **SNR:** sensorineural hearing loss; **M**: mitochondrial changes (ragged-red fibers, COX negative fibers ± lipid accumulation); **N**: normal; **P**: pathologic; **RCE**: respiratory chain enzyme; **UP**: unpublished

P#	Age/sex	Consanguinity	Geographic origin	Clinical features	Muscle morph-ology	Muscle RCE Activities	Cerebellar atrophy (MRI)	Lactic acid	Muscle CoQ_{10} (µg/g)	Fibroblasts CoQ_{10}	Mutation	Reference
P47	2/M	-	NA	MW, CA, S, Pt, R	M	↓ I+III, II+III	+	↑	16%	NA	NA	[21]
P48	1y/M	-	US	CA, MDD, MW, S, Ne, My, DW	M	↓ I+III, II+III	+	↑	8.9	N	NA	[22]
P49	first months/F	NA	US	CA, MDD, MW, S, UMN, CCA	P	↓ I+III	+	N	6.6	N	NA	[22]
P50	16y/F	-	South Asia	CA, MW, UMN	P	↓ I+III, II+III	+	NA	7.4	N	NA	[22]
P51	2y/M	NA	US	CA, MW, MDD, Ne, HCol, HA	N	NA	+	N	7.1	N	**APTX** homozygous p.W279X	[22,23]
P52	4y/F	NA	US	CA, MW, S, Ne, PEO, HCol	N	NA	+	N	7.1	N	**APTX** homozygous p.W279X	[22,23]
P53	4y/M	NA	US	CA, MW, Ne, Dys	NA	↓ I, III, IV	+	N	8.2	N	**APTX** homozygous p.W279X	[22,23]
P54	6mo/M	NA	US	CA, MDD, MW, Ne, Dys, OMA	P	NA	+	N	NA	NA	**APTX** p.W279X+?	[23]
P55	2mo/F	-	Italy	CA, MDD, S	N	↓ I+III, II+III	+	NA	12.8	NA	NA	[24]
P56	birth/F	-	Italy	CA, MDD, MW	N	NA	+	NA	9.9	NA	NA	[24]

P#	Age/sex	Consanguinity	Geographic origin	Clinical features	Muscle morph-ology	Muscle RCE Activities	Cerebellar atrophy (MRI)	Lactic acid	Muscle CoQ_{10} (µg/g)	Fibroblasts CoQ_{10}	Mutation	Reference
P57	6y/F	-	Italy	CA, S	N	↓ I+III, II+III	+	NA	2.9	NA	NA	[24]
P58	9y/M	-	South Eastern Europe	CA, My	N	NA	+	NA	5.9	↓	NA	[24]
P59	10mo/M	-	US	CA, MDD, Ne, OMA	N	N	+	NA	12.1	NA	NA	[24]
P60	2y/F	-	South Asia	CA, MDD, MW, S, UMN	N	N	+	↑	11	NA	NA	[24]
P61	2mo/M	-	US	CA, MDD, S	P	N	+	NA	8.2	NA	NA	[24]
P62	5y/M	-	US	CA, UMN, Gy,De	P	↓ I+III, II+III	+	N	12.6	↓	**ADCK3** p.Y514C+ T584del	[24,25]
P63	3y/F	-	Italy	CA, MDD, UMN	P	N	+	NA	9.2	NA	NA	[24]
P64	birth/F	-	NA	CA, MDD, MW, PEO	N	↓ I+III, II+III	+	NA	12.2	NA	NA	[24]
P65	9y/M	-	US	CA	N	N	+	NA	2.9	NA	NA	[24]
P66	2y/F	-	Italy	CA, MW, UMN	P	N	+	NA	8.7	NA	NA	[24]
P67	8y/F	-	Italy	CA, MW, UMN	P	NA	+	NA	14.8	NA	NA	[24]
P68	39y/M	-	Italy	CA, Ne, HG, D, EI	P	N	+	N	15.8	NA	NA	[26]
P69	30y/M	-	Italy	CA, MW, Ne, HG, EI	P	N	+	N	13.5	NA	NA	[26]
P70	3y/F	-	NA	EI, S, MW, CA	M	↓ I+III, II+III	+	↑	<1 µg/g (19-30)	N	**ADCK3** p.G272D+ c.1812_1813insG	[27,28]

P#	Age/sex	Consanguinity	Geographic origin	Clinical features	Muscle morph-ology	Muscle RCE Activities	Cerebellar atrophy (MRI)	Lactic acid	Muscle CoQ_{10} (µg/g)	Fibroblasts CoQ_{10}	Mutation	Reference
P71	15mo/F	-	NA	CA	N (mitochondrial accumulation at electron microscopy)	↓ I+III, II+III	+	N	56 mU/U (157-488)	↓	NA	[29]
P72	7y/NA	NA	NA	CA, OMA, Dys, Ch, MDD, Ne, HA	N	N	+	NA	11.3 nmol/g (16.9-36.3)	NA	***APTX*** homozygous p.W279X	[30]
P73	4y/NA	NA	NA	CA, Ch, Ne, OMA, ,Dys, MDD, HCol, HA	P	N	+	NA	13.3 nmol/g (16.9-36.3)	NA	***APTX*** homozygous p.W279X	[30]
P74	5y/NA	NA	NA	CA, Ch, Ne, OMA, MDD, HCol, HA	P	N	+	NA	12.8 nmol/g (16.9-36.3)	NA	***APTX*** homozygous p.W279X	[30]
P75	15y/NA	NA	NA	CA, Ne, MDD, HA	P	N	+	NA	16.3 nmol/g (16.9-36.3)	NA	***APTX*** p.W279X+D267G	[30]
P76	18y/NA	NA	NA	CA, Ne, Dys, Ch, MDD, HCol, HA	P	N	+	NA	17.6 nmol/g (16.9-36.3)	NA	***APTX*** p.W279X+D267G	[30]
P77	2y/M	NA	NA	CA, Ch, OMA, Dys, MDD, Ne, HCol, HA	NA	NA	+	NA	16.8 nmol/g (16.9-36.3)	NA	***APTX*** homozygous p.A198V	[30]
P78	18m/M	-	Reunion Island	CA, S, MDD	M	↓ II+III	+	↑	2.6 pmol/mg8(19-30)	N	***ADCK3*** homozygous p.E551K	[28]
P79	18m/F	-	France	CA, S, Pt, MDD	NA	N	+	NA	9.4 pmol/g (19-30)	NA	***ADCK3*** p.R213W+G272V	[28]
P80	NA/F	-	France	CA, S	NA	NA	+	NA	NA	NA	***ADCK3***	[28]

P#	Age/sex	Consanguinity	Geographic origin	Clinical features	Muscle morph-ology	Muscle RCE Activities	Cerebellar atrophy (MRI)	Lactic acid	Muscle CoQ_{10} (µg/g)	Fibroblasts CoQ_{10}	Mutation	Reference
											p.R213W+G272V	
P81	6y/F	+	Lebanon	CA, MDD, OMA, Ch, Ne, HCol,	N	N	+	N	61.8 µg/g (76-177)	NA	***APTX*** homozygous p.A198V	[31]
P82	4y/M	NA	Algeria	CA, MDD, Ne	NA	↓ I+III, II+III.	+	N	NA	↓	***ADCK3*** p.Q167LfsX36	[25]
P83	3y/F	NA	Algeria	CA, MDD, SND	NA	NA	NA	N	NA*	NA*	***ADCK3*** p.K314_Q360del +G549S	[25]
P84	7y/M	NA	Algeria	CA, EI	NA	↓ I+III	+	↑	NA	N	***ADCK3*** p.D420WfsX40+I 467AfsX22	[25]
P85	11y/M	NA	Algeria	CA	NA	NA	+	NA	NA	NA	***ADCK3*** p.D420WfsX40+I 467AfsX22	[25]
P86	4y/M	NA	Algeria	Ca, EI, MDD	NA	NA	+	↑	NA	NA	***ADCK3*** p.D420WfsX40+I 467AfsX22	[25]
P87	8y/F	NA	Algeria	CA, EI, MDD	NA	NA	+	↑	NA	NA	***ADCK3*** p.D420WfsX40+I 467AfsX22	[25]
P88	3y/M	+	Netherlands	CA, MDD, De, My, EI, Dys	NA	NA	+	NA	NA	NA	***ADCK3*** homozygous p.R348X	[32]
P89	9y/M	+	Netherlands	CA, EI, MDD	NA	NA	+	NA	NA	NA	***ADCK3*** homozygous p.R348X	[32]
P90	3y/M	+	Netherlands	CA, MDD, S	NA	NA	+	NA	NA	NA	***ADCK3*** homozygous p.R348X	[32]

P#	Age/sex	Consanguinity	Geographic origin	Clinical features	Muscle morph-ology	Muscle RCE Activities	Cerebellar atrophy (MRI)	Lactic acid	Muscle CoQ_{10} (μg/g)	Fibroblast s CoQ_{10}	Mutation	Reference
P91	2y/F	-	NA	CA, UMN, EI, Dys,	N	NA	+	NA	NA	NA	***ADCK3*** p.R348X+L379X	32
P92	Infancy/ M	-	NA	CA, F	N	↓ II+III	+	NA	NA	NA	***ADCK3*** p.R348X+L379X	32
P93	<6y/F	NA	NA	CA	NA	↓ I+III, II+III	NA	NA	1.31-2.6 nmol/citrat e synthase (2.7-8.5)	↓	NA	33
P94	<8y/F	NA	NA	CA	NA	↓ I+III, II+III	NA	NA	1.31-2.6 nmol/citrat e synthase (2.7-8.5)	↓	***ADCK3*** p.L609V+?	33
P95	<12y/F	NA	NA	CA	NA	↓ I+III, II+III	NA	NA	1.31-2.6 nmol/citrat e synthase (2.7-8.5)	↓	NA	33
P96	<8y/F	NA	NA	CA, S, MDD	NA	↓ I+III, II+III	NA	NA	1.31-2.6 nmol/citrat e synthase (2.7-8.5)	↓	NA	33
P97	<12y/F	NA	NA	CA	NA	↓ I+III, II+III	NA	NA	1.31-2.6 nmol/citrat e synthase (2.7-8.5)	↓	NA	33
P98	<13y/M	NA	NA	CA	NA	↓ I+III, II+III	NA	NA	1.31-2.6 nmol/citrat e synthase (2.7-8.5)	↓	NA	33
P99	<38y/M	NA	NA	CA	NA	↓ I+III, II+III	NA	NA	1.31-2.6 nmol/citrat e synthase (2.7-8.5)	↓	NA	33
P100	6y/F	NA	Italy	CA, MW	NA	NA	+	NA	59 pg/mg (89-194)	N	***APTX*** homozygous p.W279X	34

P#	Age/sex	Consanguinity	Geographic origin	Clinical features	Muscle morph-ology	Muscle RCE Activities	Cerebellar atrophy (MRI)	Lactic acid	Muscle CoQ_{10} (µg/g)	Fibroblasts CoQ_{10}	Mutation	Reference
P101	6y/F	+	Italy	CA, S, MDD	N	↓ II+III	+	N	2.9 µg/g (20-79)	NA	***ADCK3*** homozygous p.R348X	[35]
P102	Birth/NA	NA	NA	CA	NA	NA	+	N	10.2 µg/g (20-79)	NA	NA	[35]
P103	<10y/NA	NA	NA	CA	NA	↓ II+III	+	N	14.38 µg/g (20-79)	NA	NA	[35]
P104	<10y/NA	NA	NA	CA	NA	N	+	N	15.1 µg/g (20-79)	NA	NA	[35]
P105	Birth/NA	NA	NA	CA	NA	NA	+	N	17.25 µg/g (20-79)	NA	NA	[35]
P106	<10y/NA	NA	NA	CA	NA	NA	+	N	10 µg/g (20-79)	NA	NA	[35]
P107	Birth/NA	NA	NA	CA	NA	N	+	N	15 µg/g (20-79)	NA	NA	[35]
P108	Birth/NA	NA	NA	CA	NA	NA	+	N	14.2 µg/g (20-79)	NA	NA	[35]
P109	Birth/NA	NA	NA	CA	NA	NA	+	N	9.24 µg/g (20-79)	NA	NA	[35]
P110	15y/F	-	England	CA, Dys, MW, S,	M	NA	+	NA	N	NA	***ADCK3*** p.R271C+A304T	[36]
P111	27y/F	-	German	CA, S, Mi, My, MW	M	↓ I, IV	+	NA	51.1 U/g (160-1200)	NA	***ADCK3*** homozygous p. A304V	[36]
P112	16mo/F	-	Norway	CA, S, MW, MDD	N	NA	+	NA	NA	NA	***ADCK3*** homozygous p. R299W	[36]
P113	18mo/F	-	Kosovo	CA, MDD, MW, UMN, S	M	↓ I, II+III, IV	+	NA	150.9 U/g (160-1200)	NA	***ADCK3*** p. Y429C+?	[36]
P114	13y/NA	NA	NA	CA, S, Dys, MDD	NA	NA	+	NA	↓	NA	NA	[36]

P#	Age/sex	Consanguinity	Geographic origin	Clinical features	Muscle morph-ology	Muscle RCE Activities	Cerebellar atrophy (MRI)	Lactic acid	Muscle CoQ_{10} (μg/g)	Fibroblast s CoQ_{10}	Mutation	Reference
P115	30y/NA	NA	NA	CA, Dys	NA	NA	+	NA	↓	NA	NA	[36]
P116	32y/NA	NA	NA	CA, Ne	NA	NA	+	NA	↓	NA	NA	[36]
P117	2y/NA	NA	NA	CA, OMA, Dys, OA	NA	NA	-	NA	↓	NA	NA	[36]
P118	1y/M	-	US	CA, MDD, Ne, PEO, Pt	N	N	+	NA	11.5	N	NA	UP
P119	3y/F	-	Brazil	CA, MDD, S	M	NA	-	↑	NA	N	NA	UP
P120	childhood/M	+	Brazil	CA, UMN, Ne, R, D,	NA	NA	NA	N	5	NA	NA	UP
P121	childhood/F	NA	US	CA, Mi, My, HB	NA	NA	-	N	NA	↓	NA	UP
P122	4y/F	NA	US	CA, UMN, PEO	NA	NA	+	NA	NA	↓	NA	UP
P123	childhood/F	NA	NA	CA, PEO, Dy, Hy	N	NA	-	↑in CSF	15	↓	NA	UP
P124	NA/M	NA	US	CA	NA	NA	-	NA	NA	↓	NA	UP
P125	2y/F	-	US	CA, MDD, S, HG	N	N	+	NA	11	↓	NA	UP
P126	NA/F	-	US	CA	NA	NA	NA	NA	NA	NA	NA	UP
P127	NA/M	-	US	CA	NA	NA	NA	NA	NA	NA	NA	UP
P128	childhood/F	-	US	CA	NA	NA	NA	NA	2.9	↓	NA	UP
P129	8y/F	NA	Brazil	CA	M	NA	+	NA	17.62	NA	NA	UP
P130	birth/F	NA	Brazil	CA, MDD, CH	M	NA	+	NA	10.78	NA	NA	UP

P#	Age/sex	Consanguinity	Geographic origin	Clinical features	Muscle morph-ology	Muscle RCE Activities	Cerebellar atrophy (MRI)	Lactic acid	Muscle CoQ_{10} (μg/g)	Fibroblasts CoQ_{10}	Mutation	Reference
P131	6mo/M	NA	Brazil	CA, MDD, UMN, PEO, Pt, Dy	NA	N	+	NA	17.7	NA	NA	UP
P132	16y/F	-	US	CA, Ne, OA	M	N	-	NA	18.7	NA	NA	UP
P133	28y/M	NA	Germany	CA, MW, EI	M	↓ I+III, IV	NA	NA	105.5 (v.n. 160-1200)	NA	NA	UP
P134	62y/M	NA	Italy	CA, MW, L	M	NA	NA	NA	11.2	NA	NA	UP
P135	12y/F	NA	US	CA, HT, IDDM	NA	N	-	NA	14.2	NA	NA	UP
P136	6y/M	+	Italy	CA, MW, MDD, Ne	P	NA	+	NA	11	NA	NA	UP
P137	NA/NA	NA	Brazil	CA	NA	NA	NA	NA	11.2	NA	NA	UP
P138	8mo/M	NA	Brazil	CA, MDD, S, MW, EI	M	N	+	↑	3.4	NA	NA	UP
P139	22y/M	NA	NA	CA, Ne, Dy,MD	NA	NA	+	NA	NA	↓	NA	UP
P140	NA/M	NA	NA	CA	NA	N	+	NA	15.7	NA	NA	UP

eTable 6. Cerebellar ataxia patients. **P#**: patient number; **Age**: age at onset/diagnosis; **NA**: data not available; **CA**: cerebellar ataxia; **MDD**: motor-developmental delay/mental retardation, **MW**: muscle weakness; **S**: seizures; **Ne**: neuropathy; **My**: myoclonus; **DW**: Dandy-Walker syndrome; **UMN**: upper motor neuron signs; **CCA**: agenesis of corpus callosum; **Dys**: dystonia; **Ch**: chorea; **OMA**: oculomotor apraxia; **HA**: hypoalbuminemia; **HCol**: Hypercholesterolemia; **De**: depression; **SND:** sensorineural hearing loss; **Gy**: gynecomastia; **PEO:** progressive external ophthalmoplegia; **Pt**: ptosis; **D**: deafness; **EI**: excercise intolerance; **HG**: hypogonadism; **R**: retinopathy; **Mi**: migraine; **HB**: hyperactive behavior; **Dy**: dysphagia; **Hy**: hypoglicemia; **CH**: congenital hypotonia; **OA**: optic atrophy; **L**: lipomas; **HT**: hypothyroidism; **IDDM**: insulin dependent diabetes mellitus; **MD**: memory deficit; **M**: mitochondrial changes (ragged-red fibers, COX negative fibers ± lipid accumulation); **N**: normal; **P**: pathologic; **RCE**: respiratory chain enzyme; **UP**: unpublished. *: CoQ_{10} level was low in lymphoblasts.

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