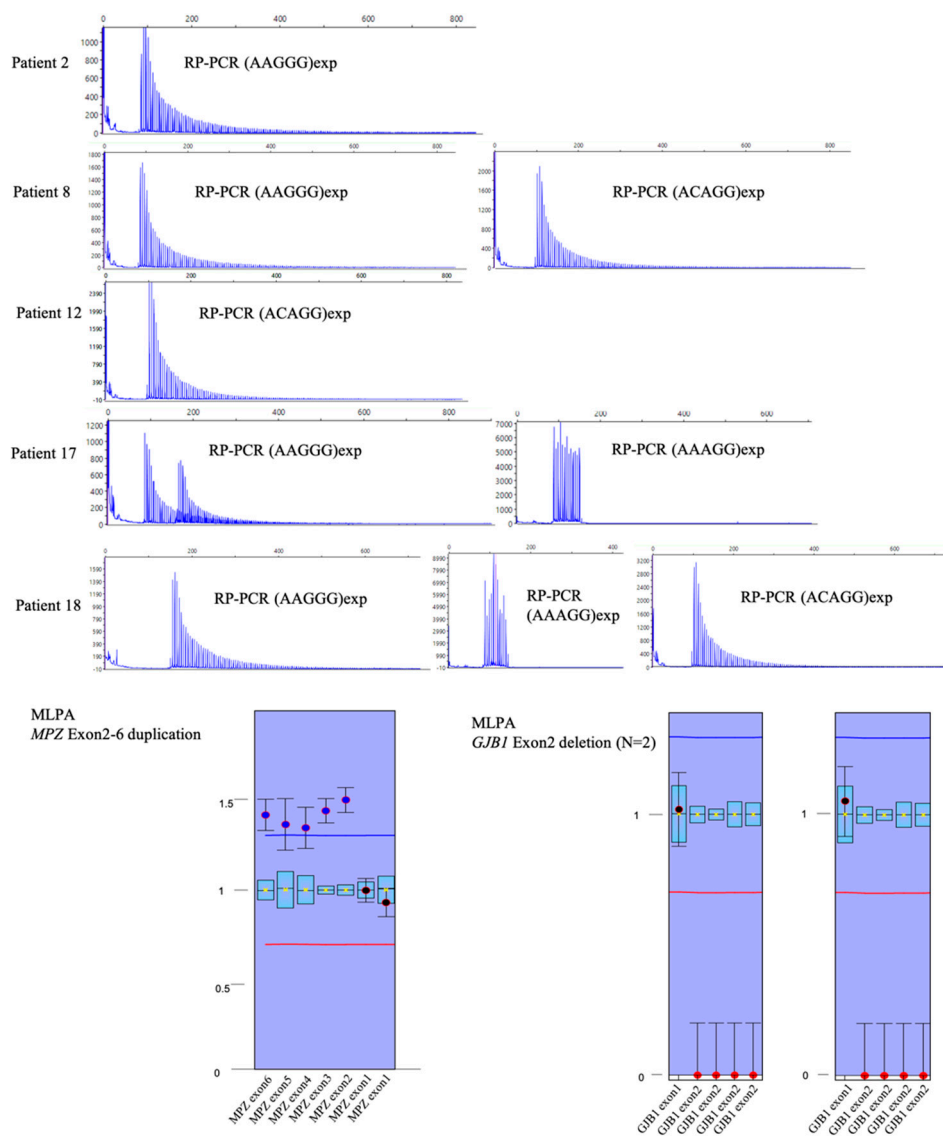


## Supporting information

**Figure S1.** RP-PCR of each repeat expansion genotypes in *RFC1* and MLPA of *MPZ* and *GJB1*.

Multi-type bi-allelic *RFC1* repeat expansions, including [(AAGGG)exp/(AAGGG)exp] (patient 2), [(AAGGG)exp/(ACAGG)exp] (patient 8), [(ACAGG)exp/(ACAGG)exp] (patient 12), [(AAGGG)exp/(AAAGG)<sub>13</sub>(AAGGG)exp] (patient 17), and [(ACAGG)exp/(AAAGG)<sub>12</sub>(AAGGG)exp] (patient 18). MLPA analysis reveals a duplication of *MPZ* exon 2–6 (1 case) and a deletion of *GJB1* exon 2 (2 cases).



**Table S1.** Targeted IPN-related gene panels for DNA microarray and NGS.

Targeted 28 genes of Microarray Chip sequencing 2007-2012	<i>AARS1</i>	<i>APTX</i>	<i>DNM2</i>	<i>EGR2</i>	<i>GAN1</i>	<i>GARS</i>	<i>GDAP1</i>	<i>GJB1</i>
	<i>HSPB1</i>	<i>HSPB8</i>	<i>LITAF</i>	<i>LMNA</i>	<i>LMNA</i>	<i>MFN2</i>	<i>MPZ</i>	<i>MTMR2</i>
	<i>NDRG1</i>	<i>NEFL</i>	<i>PMP22</i>	<i>PRX</i>	<i>RAB7</i>	<i>SBF2</i>	<i>SETX</i>	<i>SH3TC2</i>
	<i>SLC12A6</i>	<i>SOX10</i>	<i>TDP1</i>	<i>YARS1</i>				
Targeted panel using Miseq (60 genes) 2012-2014	<i>AARS1</i>	<i>APTX</i>	<i>ARHGEF10</i>	<i>DHH</i>	<i>DNM2</i>	<i>EGR2</i>	<i>FGD4</i>	<i>FIG4</i>
	<i>GAN</i>	<i>GARS</i>	<i>GDAP1</i>	<i>GJB1</i>	<i>HARS</i>	<i>HK1</i>	<i>HOXD10</i>	<i>HSPB1</i>
	<i>HSPB8</i>	<i>KARS</i>	<i>LITAF</i>	<i>LMNA</i>	<i>MARS</i>	<i>MED25</i>	<i>MFN2</i>	<i>MPZ</i>
	<i>MTMR2</i>	<i>NDRG1</i>	<i>NEFL</i>	<i>PMP22</i>	<i>PRPS1</i>	<i>PRX</i>	<i>RAB7A</i>	<i>SBF2</i>
	<i>SETX</i>	<i>SH3TC2</i>	<i>SLC12A6</i>	<i>SOX10</i>	<i>TDP1</i>	<i>TRPV4</i>	<i>TTR</i>	<i>YARS</i>
	20 candidate gene							
Targeted panel using Ion Proton (72 genes) 2014-2021	<i>AARS</i>	<i>APTX</i>	<i>ARHGEF10</i>	<i>BSCL2</i>	<i>COA7</i>	<i>DCAF8</i>	<i>DCTN1</i>	<i>DHH</i>
	<i>DHTKD1</i>	<i>DNM2</i>	<i>DYNC1H1</i>	<i>EGR2</i>	<i>FBLN5</i>	<i>FBXO38</i>	<i>FGD4</i>	<i>FIG4</i>
	<i>GALC</i>	<i>GAN</i>	<i>GARS</i>	<i>GDAP1</i>	<i>GJB1</i>	<i>GJB3</i>	<i>GNB4</i>	<i>HARS</i>
	<i>HK1</i>	<i>HOXD10</i>	<i>HSPB1</i>	<i>HSPB3</i>	<i>HSPB8</i>	<i>IGHMBP2</i>	<i>INF2</i>	<i>KARS</i>
	<i>KIF1A</i>	<i>LITAF</i>	<i>LMNA</i>	<i>LRSAM1</i>	<i>MARS</i>	<i>MED25</i>	<i>MFN2</i>	<i>MME</i>
	<i>MPZ</i>	<i>MTMR2</i>	<i>NDRG1</i>	<i>NEFL</i>	<i>PDK3</i>	<i>PLEKHG5</i>	<i>PMP22</i>	<i>PRPS1</i>
	<i>PRX</i>	<i>RAB7A</i>	<i>REEP1</i>	<i>SACS</i>	<i>SBF1</i>	<i>SBF2</i>	<i>SETX</i>	<i>SH3TC2</i>
	<i>SLC12A6</i>	<i>SLC5A7</i>	<i>SOX10</i>	<i>SURF1</i>	<i>TDP1</i>	<i>TFG</i>	<i>TRIM2</i>	<i>TRPV4</i>
	<i>TTR</i>	<i>YARS</i>	6 candidate gene					
Targeted panel using Ion Proton (103 genes) 2022-	<i>AARS1</i>	<i>ABHD12</i>	<i>AIFM1</i>	<i>APTX</i>	<i>ARHGEF10</i>	<i>ATL1</i>	<i>ATL3</i>	<i>ATP1A1</i>
	<i>BAG3</i>	<i>BICD2</i>	<i>BSCL2</i>	<i>COA3</i>	<i>COA7</i>	<i>COX6A1</i>	<i>DCTN1</i>	<i>DHTKD1</i>
	<i>DNAJB2</i>	<i>DNM2</i>	<i>DNMT1</i>	<i>DRP2</i>	<i>DYNC1H1</i>	<i>EGR2</i>	<i>FBLN5</i>	<i>FGD4</i>
	<i>FIG4</i>	<i>FUS</i>	<i>GALC</i>	<i>GAN</i>	<i>GARS1</i>	<i>GDAP1</i>	<i>GJB1</i>	<i>GJB3</i>
	<i>GNB4</i>	<i>GNE</i>	<i>HARS1</i>	<i>HINT1</i>	<i>HOXD10</i>	<i>HSPB1</i>	<i>HSPB3</i>	<i>HSPB8</i>
	<i>IGHMBP2</i>	<i>INF2</i>	<i>KARS1</i>	<i>KIF1A</i>	<i>LAMA2</i>	<i>LITAF</i>	<i>LMNA</i>	<i>LRSAM1</i>
	<i>MARS1</i>	<i>MCM3AP</i>	<i>MFN2</i>	<i>MME</i>	<i>MORC2</i>	<i>MPV17</i>	<i>MPZ</i>	<i>MTMR2</i>
	<i>NAGLU</i>	<i>NDRG1</i>	<i>NEFH</i>	<i>NEFL</i>	<i>NTRK1</i>	<i>PDK3</i>	<i>PDXK</i>	<i>PLEKHG5</i>
	<i>PMP2</i>	<i>PMP22</i>	<i>PNKP</i>	<i>POLG</i>	<i>POLR3B</i>	<i>PRDM12</i>	<i>PRPS1</i>	<i>PRX</i>
	<i>RAB7A</i>	<i>REEP1</i>	<i>SACS</i>	<i>SBF1</i>	<i>SBF2</i>	<i>SCN11A</i>	<i>SCN9A</i>	<i>SCO2</i>
	<i>SETX</i>	<i>SH3TC2</i>	<i>SIGMAR1</i>	<i>SLC12A6</i>	<i>SLC25A46</i>	<i>SLC52A3</i>	<i>SLC5A7</i>	<i>SOD1</i>
	<i>SORD</i>	<i>SPG11</i>	<i>SPTLC1</i>	<i>SPTLC2</i>	<i>SURF1</i>	<i>TDP1</i>	<i>TFG</i>	<i>TRPV4</i>
	<i>TTR</i>	<i>VCP</i>	<i>WARS1</i>	<i>WNK1</i>	<i>YARS1</i>	2 candidate gene		

**Table S2.** Primers of flanking and repeat-primed PCR for *RFC1* repeat expansion analyses

Protocol	Primer (5'-3')
Flanking PCR	Forward: TCAAGTGATACTCCAGCTACACCGTTGC Reverse: CAGCATTGTGGGAGACAGGCCAATCACT
Repeat-primed PCR	<b>AAGGG (pathogenic)</b> Forward: [6FAM]TCAAGTGATACTCCAGCTACACCGT Anchor: CAGGAAACAGCTATGACC Reverse: CAGGAAACAGCTATGACCGGGAAGGGAAGGGAAGGGAA
	<b>ACAGG (pathogenic)</b> Forward: [6FAM]TCAAGTGATACTCCAGCTACACCGT Anchor: CAGGAAACAGCTATGACC Reverse: CAGGAAACAGCTATGACCACAGGACAGGACAGGACAGG
	<b>AAAAG (benign)</b> Forward: [6FAM]TCAAGTGATACTCCAGCTACACCGT Anchor: CAGGAAACAGCTATGACC Reverse1: CAGGAAACAGCTATGACCAACAGAGCAAGACTCTGTTTCAAAAAAG AAAAGAAAAGAAAAGAAAA Reverse2: CAGGAAACAGCTATGACCAACAGAGCAAGACTCTGTTTCAAAAAAGA AAAGAAAAGAAAAGAAAA Reverse3: CAGGAAACAGCTATGACCAACAGAGCAAGACTCTGTTTCAAAAAGAA AAGAAAAGAAAAGAAAA
	<b>AAAGG (benign)</b> Forward: [6FAM]TCAAGTGATACTCCAGCTACACCGT Anchor: CAGGAAACAGCTATGACC Reverse: CAGGAAACAGCTATGACCGGAAAGGAAAGGAAAGGAAA

**Table S3.** Clinical and electrophysiological information of 18 cases with *RFC1* repeat expansion

Patient	Pt 1	Pt 2	Pt 3	Pt 4	Pt 5	Pt 6	Pt 7	Pt 8	Pt 9	Pt 10	Pt 11	Pt 12	Pt 13	Pt 14	Pt 15	Pt 16	Pt 17	Pt 18
<i>RFC1</i> repeat	(AAGGG) <sub>exp</sub>					(AAGGG) <sub>exp</sub>					(ACAGG) <sub>exp</sub>					(AAGGG) <sub>exp</sub>		
	(AAGGG) <sub>exp</sub>					(AAGGG) <sub>exp</sub>					(ACAGG) <sub>exp</sub>					(AAGGG) <sub>exp</sub>		
Onset age	33	40	49	50	0	1	72	53	64	10	44	65	60	72	71	76	25	50
Exam age	37	43	53	70	1	40	78	70	76	16	45	74	72	74	75	80	45	65
Sex	M	M	M	M	M	M	M	M	M	M	M	M	M	F	M	F	M	F
Genotype	S	S	NA	S	S	S	S	S	R	S	S	S/R	S	S	S	S	S	S
Muscle weakness	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Upper limb MMT (proximal)	5	5	3-4	5	NA	NA	4	5	5	4	5	5	5	5	5	5	5	5
Upper limb MMT (distal)	5	5	4-5	4	NA	NA	1	4	4	3	4	5	4	5	3	5	4	4
Lower limb MMT (proximal)	5	5	3-4	5	NA	3	4	5	5	4	5	5	4	4	5	5	5	5
Lower limb MMT (distal)	3	4	4-5	5	NA	4	0-1	4	4	3	5	4	4	4	4	5	4	5
Muscle atrophy	+	+	NA	+	—	NA	+	—	NA	+	—	+	+	+	+	+	+	+
DTR	Decrease	Decrease	NA	Absent	Decrease	Decrease	Absent	Absent	Decrease	Hyper	Decrease	Absent	Absent	Absent	Absent	Absent	Normal	Absent
Sensory disturbance	+	+	+	+	NA	+	+	+	+	+	+	+	+	+	+	+	+	+
Cerebellar ataxia	—	—	+	—	NA	NA	—	+	—	—	—	+	—	—	+	—	—	+
Cerebellar atrophy	—	—	Mild atrophy	NA	NA	NA	—	—	NA	NA	NA	+	—	NA	+	NA	—	—
Vestibular dysfunction	—	—	NA	—	NA	NA	—	+	—	—	—	NA	—	—	NA	NA	NA	+
Chronic cough	—	NA	NA	NA	NA	NA	—	+	NA	—	—	NA	+	+	NA	NA	NA	NA
Pyramidal sign	—	—	NA	—	—	—	—	—	—	+	—	—	—	—	—	—	—	—
Parkinsonism	—	NA	+	—	—	NA	—	—	—	—	—	—	—	—	—	—	—	—
Cognitive impairment	—	NA	NA	—	NA	NA	—	—	NA	ADHD	—	NA	—	—	—	—	—	—
Involuntary movement	—	NA	NA	—	NA	NA	—	—	NA	—	—	—	—	Tremor	—	—	—	—
Autonomic dysfunction	—	NA	NB, OH, ED	—	NA	NA	—	Constipation	Constipation	—	—	—	—	—	—	OH, NB	hypohidrosis	—
								Hypohidrosis	Pollakiuria	—	—	—	—	—	—	—	—	—
Muscle cramp	+	NA	NA	NA	NA	NA	—	+	NA	—	—	Fasciculation	—	+	NA	NA	NA	—
Creatine Kinase (IU/L)	450	NA	400-2200	NA	NA	339-700	322	—	NA	27	—	91	385	125	531	NA	386	85
Other symptom	—	—	—	—	—	—	—	Epilepsy	Diplopia	Neurofibromatosis	—	—	—	—	—	—	—	—
Median MNCV (m/s)	57.1/57.9	59.2/56.5	NA	55.4	37.4	56	46	49	48	46.8	57	53.3	43.7	56.4	57.5	Normal	50.6	56.5
Median CMAP (mV)	9.94/10.5	14.7/16.4	NA	5.3	7.4	11.7	0.3	8.6	4.52	NA	9.5	5.5	8.7	3.4	4.13	Normal	6.16	8.48
Median SCV (m/s)	30.2	54.5/58.8	NA	NE	46.4	NA	NE	NE	31	NA	39.8	NE	NE	NE	NE	Decrease	48	58.0
Median SNAP (μV)	64	21.4/28.7	NA	NE	5.1	NA	NE	NE	2	NA	12.8	NE	NE	NE	NE	Decrease	0.4	2.6
Tibial MNCV (m/s)	43.8/42.3	47.9/43.6	NA	41.4	45.5	43	39.5	34	38	38.6	47.9	38.0	35.8	42.1	31.1	Decrease	40.2	43.8
Tibial CMAP (mV)	10.2/6.95	20.1/6.9	NA	2.4	1	7	0.2	1.5	5.8	NA	8.6	1.2	4.1	9.5	0.49	Decrease	3.2	6.15
Sural SCV (m/s)	58.8/52.9	47.8/49.2	NA	NE	43.1	NA	NE	NE	NE	NA	NE	NE	NE	NE	NE	NE	NE	NE
Sural SNAP (μV)	7.6/9.3	12.9/9.4	NA	NE	11	NA	NE	NE	NE	NA	NE	NE	NE	NE	NE	NE	NE	NE

M: male; F: female; S: sporadic; R: autosomal recessive; R/S: sporadic or autosomal recessive;

MMT: manual muscle test; NA: not available; DTR: deep tendon reflex; ADHD: attention-deficit

hyperactivity disorder; NB: neurogenic bladder; OH: orthostatic hypotension; ED: erectile

dysfunction; CK: creatine kinase (U/L); MNCV: motor nerve conduction velocity; CMAP:

compound motor action potential; SCV: sensory nerve conduction velocity; SNAP: sensory nerve

action potential; NE: not evoked. Normal range: median CMAP > 3.1 mV; median MCV > 49.6 m/s;

median SNAP > 7.0 μV; median SCV > 47.2 m/s; tibial CMAP > 4.4mV; tibial MCV > 41.7 m/s;

sural SNAP > 5.0 μV; sural SCV > 40.8 m/s; CK (male) 59–248 IU/mL and (female) 41–153 IU/mL.