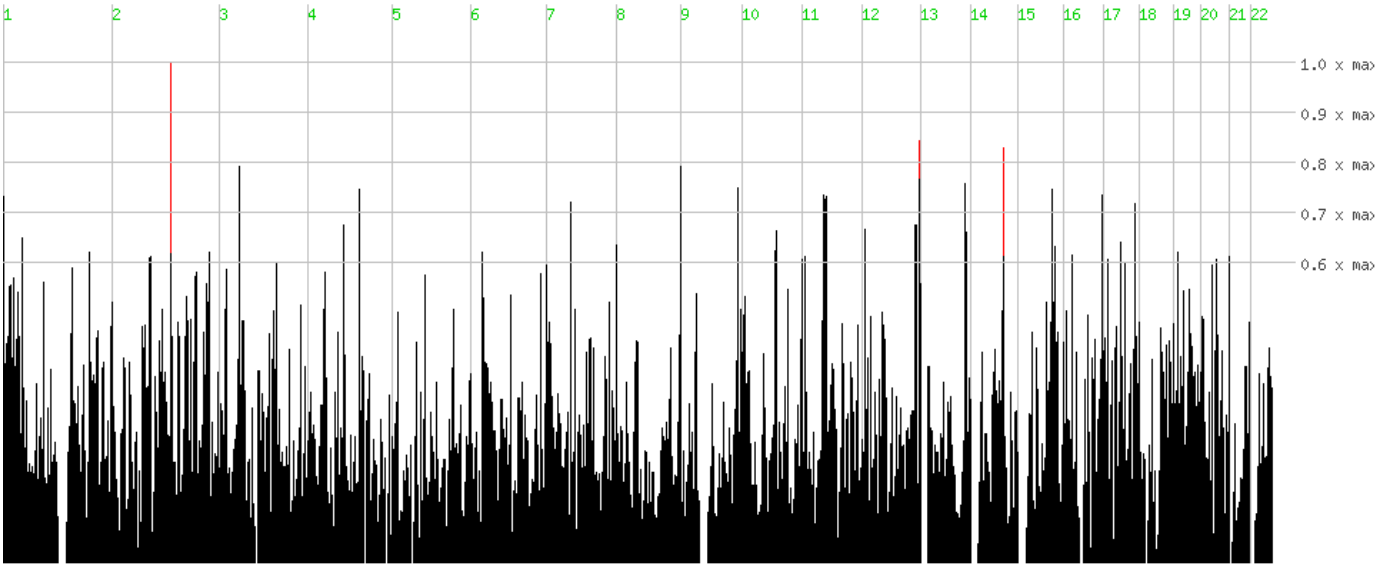
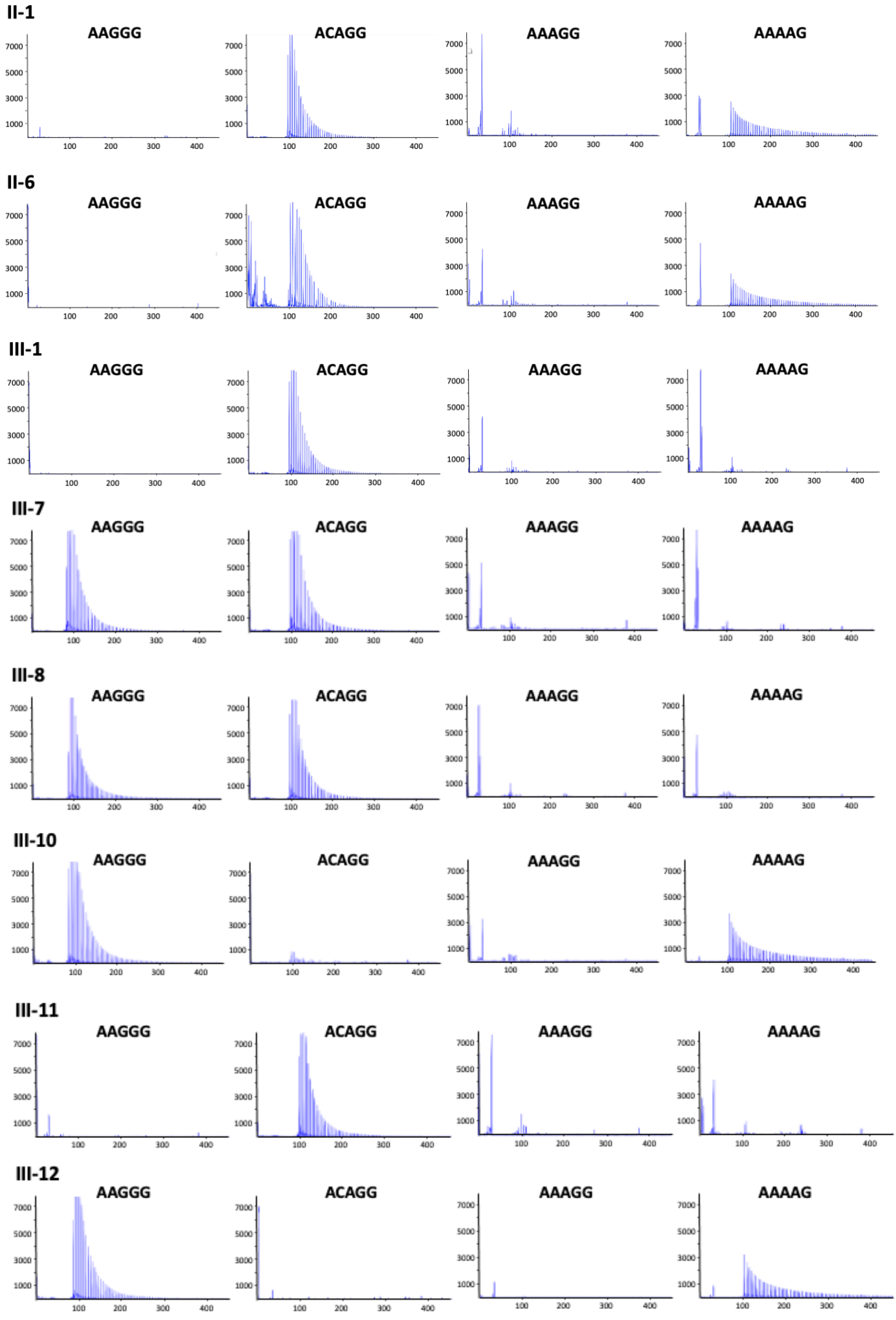
eFigure 1. Homozygosity mapping performed using WES data

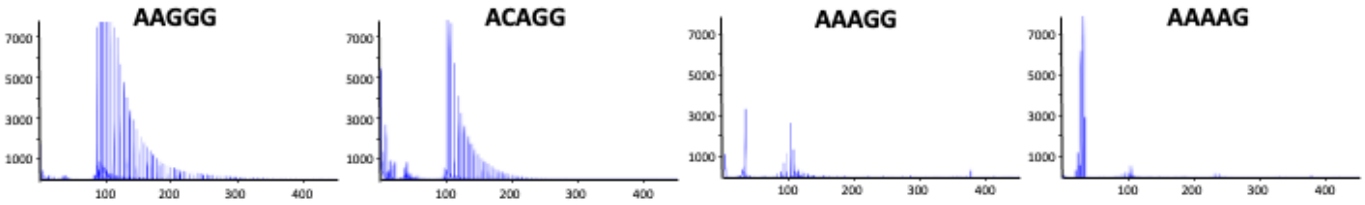


Results of homozygosity mapping using WES data from III-7, III-8, III-9, III-10, III-11, III-12 and IV-9. Homozygous regions shared by affected individual were found in chr2: 131483929-131733828, chr12: 132621405-132701489, chr14: 73245595-74493665, but chr4: 39348425-39348483, a repeat site of *RFC1*-related disorder, was not included.

eFigure 2. RP-PCR results.



IV-10



eTable 1. Information on haplotypes for each genotype of our family and previous reports.

Marker ID	Position (hg 38)	Ref	Alt	Our family			Cortes et al.[9]	Scriba et al.
				$(AAGGG)_{exp}$	$(ACAGG)_{exp}$	$(AAAAG)_{exp}$	$(AAGGG)_{exp}$	$(ACAGG)_{exp}$
rs3733275	chr4:39121077	C	T	1	1	1	1	1
rs2044917	chr4:39147871	G	A	2	1	1	2	2
rs2711991	chr4:39149733	G	A	1	2	2	1	2
rs2062229	chr4:39285146	G	T	2	2	2	2	2
rs2066790	chr4:39317086	A	G	1	1	2	1	1
rs11096992	chr4:39327482	G	A	2	2	2	2	2
rs17584703	chr4:39363236	T	C	2	2	1	2	2
rs6844176	chr4:39364970	T	C	1	1	1	1	1
rs6823497	chr4:39384201	A	C	1	2	1	1	1
rs13135439	chr4:39403531	T	G	1	1	1	1	2
rs11940694	chr4:39413373	A	G	1	1	1	1	2
rs7674434	chr4:39417789	T	G	1	1	1	2	1

The core haplotype as reported by Cortes et al. is highlighted green. The shared haplotype in $(AAGGG)_{exp}$ and $(ACAGG)_{exp}$ alleles between our family and previous families are highlighted gold and light blue, respectively. The genotypes are expressed as 1 for the reference allele and 2 for the minor allele.

eTable 2. Haplotype information between core haplotypes.

						Patient ID		
Marker ID	**Position (hg38)**	**Reference allele frequency**	**Minor allele frequency**	**Ref**	**Alt**	**III-9**	**III-11**	**III-12**
						$(AAGGG)_{exp}$ /$(ACAGG)_{exp}$	$(ACAGG)_{exp}$ /$(ACAGG)_{exp}$	$(AAGGG)_{exp}$ /$(AAAAG)_{exp}$
rs2066790	chr4:39317086	0.71885	0.28115	A	G	1/1	1/1	1/2
rs11096991	Chr4:39319011	0.720647	0.279353	T	C	1/1	1/1	1/2
rs17334999	chr4:39319613	0.976238	0.023762	G	A	1/1	1/1	1/2
rs947301858	chr4:39323277	0.999976	0.000024	C	T	1/2	2/2	1/1
rs11096992	chr4:39327482	0.575479	0.424521	G	A	2/2	2/2	2/2
rs3821988	chr4:39335075	0.728235	0.271765	T	G	1/1	1/1	1/2
rs3796517	chr4:39335333	0.728235	0.271765	A	G	1/1	1/1	1/2
rs13133909	chr4:39337140	0.898363	0.101637	C	T	2/2	2/2	1/2
rs12650831	chr4:39344537	0.897364	0.102636	G	A	2/2	2/2	1/2
rs12642089	chr4:39351032	0.899361	0.100639	C	T	2/2	2/2	1/2
rs13142220	chr4:39353881	0.96246	0.03754	G	A	1/2	1/1	1/2
rs368936934	chr4:39355460	0.999745	0.000255	A	G	1/2	2/2	1/1
rs11730570	chr4:39356201	0.730831	0.269169	C	T	1/1	1/1	1/2
rs113299742	chr4:39357916	0.858427	0.141573	G	A	2/2	2/2	1/2
rs4975009	chr4:39359931	0.720447	0.279553	T	C	1/1	1/1	1/2
rs71606156	chr4:39360243	0.865615	0.134385	G	A	2/2	2/2	1/2
rs4974938	chr4:39360357	0.547923	0.452077	G	T	2/2	2/2	2/2
rs71606157	chr4:39360603	0.867212	0.132788	C	T	2/2	2/2	1/2
rs1905361	chr4:39361321	0.825479	0.174521	G	A	2/2	2/2	1/2
rs180927344	chr4:39361583	0.998003	0.001997	T	C	1/2	1/1	1/2
rs16995255	chr4:39363068	0.719649	0.280351	C	G	1/1	1/1	1/2
rs17584703	chr4:39363236	0.824281	0.175719	T	C	2/2	2/2	1/2
rs75817445	chr4:39363531	0.865016	0.134984	T	C	2/2	2/2	1/2
rs6844176	chr4:39364970	0.582069	0.417931	T	C	1/1	1/1	1/1

In 97 SNVs other than the core haplotype highlighted in green, the haplotypes of 93 SNVs were same between the $(AAGGG)_{exp}$ and $(ACAGG)_{exp}$ alleles. All four SNVs that were different haplotypes in $(AAGGG)_{exp}$ and $(ACAGG)_{exp}$, highlighted in orange, had very low allele frequencies. The genotypes are expressed as 1 for the reference allele and 2 for the minor allele. The frequency of SNVs was referred to the 1000 Genomes Phase 3 dataset.

eTable 3. Haplotype information in our family.

Marker ID	**II-1**	**II-6**	**III-1**	**III-7**	**III-8**	**III-9**	**III-10**	**III-11**	**III-12**	**IV-9**	**IV-10**	$(AAGGG)_{exp}$	$(ACAGG)_{exp}$	$(AAAAG)_{exp}$
	M2/W	M2/W	M2/M2	M1/M2	M1/M2	M1/M2	M1/W	M2/M2	M1/W	M2/M2	M1/M2	M1	M2	W
rs2066790	1/2	1/2	1/1	1/1	1/1	1/1	1/2	1/1	1/2	1/1	1/1	1	1	2
rs947301858	1/2	1/2	2/2	1/2	1/2	1/2	1/1	2/2	1/1	2/2	1/2	1	2	1
rs11096992	2/2	2/2	2/2	2/2	2/2	2/2	2/2	2/2	2/2	2/2	2/2	2	2	2
rs13142220	1/1	1/1	1/1	1/2	1/2	1/2	1/2	1/1	1/2	1/1	1/2	2	1	1
rs368936934	1/2	1/2	2/2	1/2	1/2	1/2	1/1	2/2	1/1	2/2	1/2	1	2	1
rs180927344	1/1	1/1	1/1	1/2	1/2	1/2	1/2	1/1	1/2	1/1	1/2	2	1	1
rs17584703	1/2	1/2	1/2	2/2	2/2	2/2	1/2	2/2	1/2	2/2	2/2	2	2	1
rs6844176	1/1	1/1	1/1	1/1	1/1	1/1	1/1	1/1	1/1	1/1	1/1	1	1	1

Haplotype information of SNVs forming the core haplotype and four informative SNVs between core haplotype in our family. The core haplotype were highlighted in green and the four informative SNVs were highlighted in orange. The genotypes are expressed as 1 for the reference allele and 2 for the minor allele. M1, M2, and W in the second row represent the genotypes of the repeats, with M1 representing $(AAGGG)_{exp}$, M2 representing $(ACAGG)_{exp}$, and M3 representing $(AAAAG)_{exp}$. The haplotype of each of the M1, M2, and W are shown in the three columns on the right.

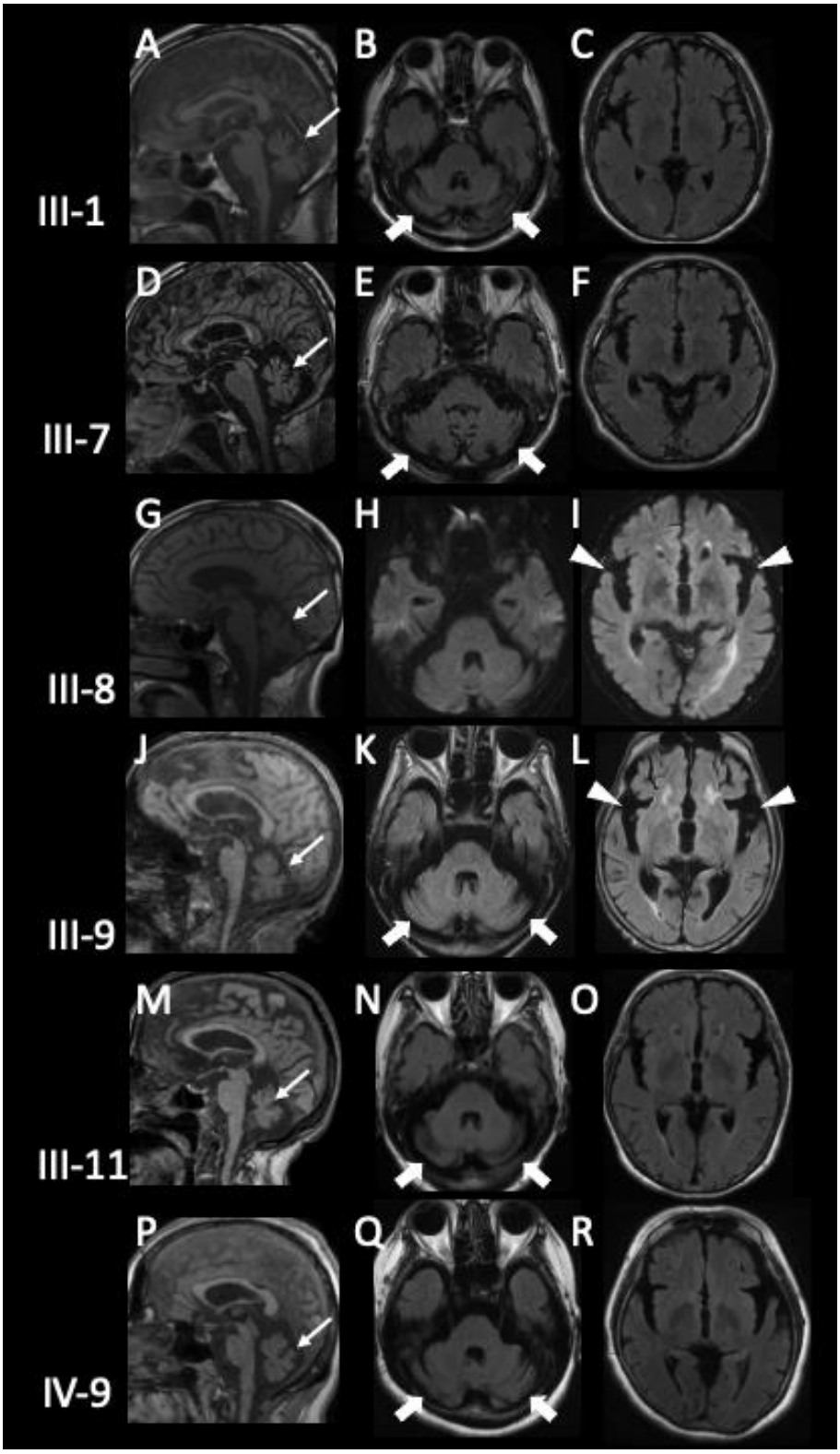
eTable 4. Summary of genetic, clinical and laboratory findings.

Patient	II-10	III-1	III-7	III-8	III-9	III-11	IV-9	IV-10
Genotype	N.A.	$(ACAGG)_{exp}$/ $(ACAGG)_{exp}$	$(AAGGG)_{exp}$/ $(ACAGG)_{exp}$	$(AAGGG)_{exp}$/ $(ACAGG)_{exp}$	$(AAGGG)_{exp}$/ $(ACAGG)_{exp}$	$(ACAGG)_{exp}$/ $(ACAGG)_{exp}$	$(ACAGG)_{exp}$/ $(ACAGG)_{exp}$	$(AAGGG)_{exp}$/ $(ACAGG)_{exp}$
Repeat number	N.A.	2000, 800	2100, 800	2000, 600	2000, 600	1900, 800	1900, 1900	1900, 700
Age at onset of ataxia	66	59	59	59	58	59	44	−
Age at last evaluation	70	69	71	79	77	75	57	52
Gender	Male	Male	Male	Male	Female	Female	Female	Female
Symptom								
Cough	N.A.	−	+	+	+	+	−	+
Sensory symptom	N.A.	+	+	N.A.	+	+	+	+
Dysarthria	N.A.	+	+	+	+	+	+	−
Vomiting attack	N.A.	−	+	−	+	−	+	−
Ataxic gait	+	+	+	+	+	+	+	−
Limb ataxia	N.A.	+	+	+	+	+	+	−
Nystagmus	N.A.	+	+	+	+	+	+	−
Muscle atrophy	N.A.	+	−	+	+	+	+	−
Muscle weakness	N.A.	+	−	+	+	+	+	−
Fasciculation	N.A.	+	−	−	−	−	−	−
Tendon reflexes	N.A.	Reduced	Reduced	Reduced	Reduced	Reduced	Brisk	Normal
Babinski refrex	N.A.	−	+	−	−	−	−	−
Autonomic Dysfunction	N.A.	OH	UR	Co	Co	−	−	−
Head tremor	N.A.	−	+	+	+	+	+	−
Resting tremor	N.A.	−	+	−	−	+	+	−
Bradykinesia	N.A.	−	+	−	−	+	+	−
Rigidity	N.A.	−	−	−	−	+	+	−
Cognitive impairment	N.A.	−	−	+	+	+ (revealed by cognitive function tests)	+ (revealed by cognitive function tests)	−
Other symptoms	N.A.	Central sleep apnea	−	−	−	−	Vocal dystonia, striatal foot	−
Investigation								
Schellong test	N.A.	+	N.A.	−	N.A.	N.A.	−	N.A.
MMSE	N.A.	N.A.	N.A.	N.A.	24/30(68y.o.)	28/30(75y.o.)	29/30(56y.o.)	N.A.
FAB	N.A.	N.A.	N.A.	N.A.	10/18(68y.o.)	10/18(75y.o.)	14/18(56y.o.)	N.A.
OSIT-J	N.A.	N.A.	N.A.	N.A.	N.A.	5/12(75y.o.)	9/12(57y.o.)	N.A.
NCS	N.A.							
Small or absent SNAPs	N.A.	+	+	+	+	N.A.	+	+
Small CMAPs	N.A.	+	−	−	+	N.A.	+	−

Neurological change in EMG	N.A.	+	N.A.	N.A.	N.A.	N.A.	+	N.A.
Brain MRI								
Cerebellar atrophy	N.A.	+	+	+	+	+	+	−
Cerebral atrophy	N.A.	−	−	+	+	−	+	−
DaT scan	N.A.	N.A.	N.A.	N.A.	Normal	N.A.	Decline	N.A.
SPECT (Decrease)	N.A.	N.A.	N.A.	N.A.	Frontal lobe, perisylvian fissure	N.A.	Part of the frontal lobe, cerebellum	N.A.
18F-FDG-PET (Decreased glucose metabolism)	N.A.	N.A.	N.A.	N.A.	Frontal lobe, perisylvian fissure	Cerebellum	N.A.	N.A.
MIBG myocardial scintigraphy	N.A.	N.A.	N.A.	N.A.	N.A.	N.A.	−	N.A.
Vestibular function tests								
Caloric test	N.A.	N.A.	N.A.	No bilateral horizontal nystagmus response	N.A.	N.A.	Normal	N.A.
Optokinetic response	N.A.	N.A.	N.A.	Reduced	N.A.	N.A.	N.A.	N.A.
Head impulse test	N.A.	N.A.	N.A.	N.A.	N.A.	Bilateral compensatory eye movements	N.A.	N.A.
Complications	N.A.	Hypothyroidism	DM	RA	DM	DM	−	DM

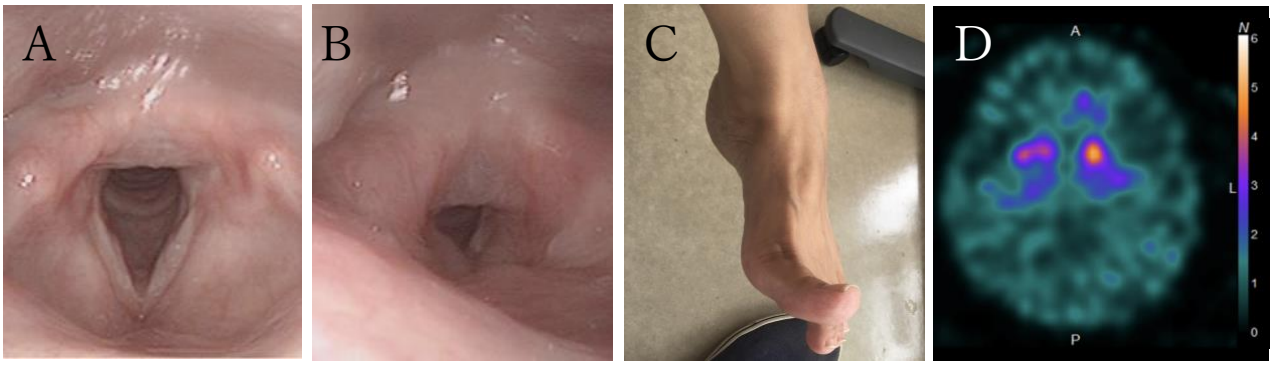
N.A.: not available, OH: orthostatic hypotension, UR: urinary retention, Co: constipation, MMSE: Mini Mental State Examination, FAB: frontal assessment battery, OSIT-J: Odor Stick Identification Test for Japanese, NCS: nerve conduction study, OKR: optokinetic response, DM: diabetes mellitus, RA: rheumatoid arthritis.

eFigure 3. MRI images of patients.



The sagittal views are T1WI images, and the other axial views are FLAIR images. The age at the time of MRI imaging was 69 years for III-1, 72 years for III-7, 70 years for III-8, 77 years for III-9, 75 years for III-11, and 57 years for IV-9. IV-10 is not shown because there was no cerebellar or cerebral atrophy. The axial view shows atrophy of the cerebellar vermis (arrows in A, D, G, J, M, P). In the cerebellar axial view, atrophy of the cerebellar hemispheres was observed (large arrows in B, E, K, N, Q). Enlargement of the sylvian fissure was observed in III-8, and III-9 (arrow head in I, L).

eFigure 4. Images of vocal cord dystonia, striatal foot, and DAT scan.



(A, B) Images of the laryngoscope at rest (A) and during vocalization (B). Impaired vocal cord adduction was observed during vocalization. (C) Photo of the foot of IV-9 at the age of 57. It shows a so-called "striatal foot" with extension of her first toe, flexion of the other toes, equinovarus foot positioning. (D) DaTscan at age 56 of IV-9 showed clear decrease of tracer accumulation in the bilateral basal ganglia.

eDetailed medical history of representative cases III-9 and IV-9

Patient III-9

The patient III-9 was the third woman of six siblings, whose father II-10 had been ataxic since his late 60s and was diagnosed as spinocerebellar degeneration. She became aware of dysarthria and numbness in the lower limbs at the age of 58. Gradually, she began to fall repeatedly. Severe dizziness and vomiting continuing for about 3 days occurred about once a year, so she often needed hospitalization. She visited our neurology department at the age of 62. Physical examination revealed impaired smooth pursuit eye movement, gaze nystagmus, ataxic dysarthria, ataxia of the limbs and trunk, muscle atrophy and weakness of the distal limbs, weakness of the tendon reflex and hypoesthesia in distal limbs. Brain MRI at this time showed atrophy of the cerebellum. Nerve conduction study (NCS) showed axonal sensorimotor neuropathy. Brain MRI performed at the age of 66 showed the enlargement of the Sylvian fissure in addition to the cerebellar atrophy. 18F-fluorodeoxyglucose-positron emission tomography (18F-FDG PET) revealed reduced uptake of tracer in the cerebellum, frontal lobe, and around the sylvian fissure (Figure 5). Cognitive function tests performed at the age of 68 showed Mini-Mental State Examination (MMSE) 24/30 and Frontal Assessment Battery (FAB) 10/18. She presented no-no type head tremor in a sitting or standing position at the age of 70. She became bedridden at the age of 72. N-isopropyl-123I-ρ-iodoamphetamine (IMP) SPECT at the age of 77 showed decreased blood flow in the cerebellum, frontal lobe, and around the sylvian fissure (Figure 4A). Dopamine Transporter Scan (DaTscan) performed at the age of 77 showed no decrease of tracer accumulation in the basal ganglia. At the age of 77, she had disorientation, irritability, and poor comprehension. She became central venous nutrition due to dysphagia at the age of 77 and died of weakness at the age of 79.

Patient IV-9

IV-9 is the daughter of III-1 and III-9, and her parents were cousins. She had a chronic cough even before she became aware of her ataxia. At the age of 44, she became aware of wobbling while walking and gradually worsened. Like her mother, she was occasionally hospitalized due to severe dizziness and vomiting. She had dysarthria at the age of 47. She visited our department at this time, examination revealed ataxia and dysarthria. She had numbness in both legs at the age of 49 and dysphasia at the age of 52. At the age of 52, she visited for hoarseness and laryngoscopy revealed impaired vocal cord adduction during vocalization (eFigure 5A, B in the Supplemental Material). Hoarseness improved in a few days, and the abnormal findings of the laryngoscopy also improved. Examination at the age of 56 revealed no-no type head tremor in a sitting or standing position and pill-rolling-like resting tremor in both upper limbs, mild rigidity and bradykinesia. Brain MRI showed atrophy of the cerebellum and mild atrophy of cerebral gray matter (Figure 3C, eFigure 4 in the Supplemental Material). The Odor Stick Identification Test for the Japanese showed normal olfactory function (9/13). The Noise Pareidolia was positive (5/40). Iodine- 123-metaiodobenzylguanidine (123I-MIBG) scintigraphy didn’t showed apparent damage of the myocardial sympathetic nerve (H/M ratio: early 2.53, delay 2.07). DaTscan showed clear decrease of tracer accumulation in the bilateral basal ganglia (eFigure 5C in the Supplemental Material). NCS showed axonal sensorimotor neuropathy and electromyography showed chronic neurogenic changes in the upper limbs. A bilateral caloric stimulation test was normal. She didn't have any cognitive impairments that would have greatly troubled her in her daily life, but sometimes she felt she could not put her words together properly, and the topic often shifted to irrelevant things. Cognitive function tests performed at the age of 56 showed

MMSE 28/30 and FAB 14/18. At the age of 57, she needed a walker. At the age of 57, she presented bilateral striatal foot, in which her bilateral first toes were extended, the other toes were flexed, and her feet were in equinovarus positioning. (eFigure 5D in the Supplemental Material).