Table S1: Description of CVI cohort

Person	In manuscript	Age at examination in years (+ months when under 4 years)	Gender	Gestational age (weeks)	Intellectual disability/ developmental delay	NGS (platform)
CVI1	Individual 1	12	M	42	+	+ (Illumina Hiseq 2000)
CVI2		3+8	M	42	+	+ (Illumina Hiseq 2000)
CVI3		1+7	M	At term	+	+ (Illumina Hiseq 2000)
CVI4		21	M	40	+	+ (Illumina Hiseq 2000)
CVI5		12	M	37	+	+ (Illumina Hiseq 2000)
CVI6		11	F	42	+	+ (Illumina Hiseq 2000)
CVI7		8	M	40	+	+ (Illumina Hiseq 2000)
CVI8		7	M	38	+	+ (Illumina Hiseq 2000)
CVI9		7	F	41	+	+ (Illumina Hiseq 2000)
CVI10		7	M	38	+	+ (Illumina Hiseq 2000)
CVI11	Individual 2	4	F	41	+	+ (SOLiD 5500XL)
CVI12		4	F	40	+	+ (SOLiD 5500XL)
CVI13		9	M	40	+	
CVI14	Individual 3	18	F	At term	+	
CVI15	Individual 4	24	F	36	+	
CVI16		3+7	M	37	+	
CVI17		3+4	M	35	+	
CVI18		2+10	M	41	+	
CVI19		2+1	F	40	+	
CVI20		1+6	M	37	+	
CVI21		38	F	At term	+	
CVI22		36	M	42	+	
CVI23		33	F	At term	-	
CVI24		33	M	41	+	
CVI25		30	F	40	+	
CVI26		29	M	At term	+	
CVI27		28	M	At term	+	
CVI28		28	F	At term	+	
CVI29		26	F	At term	+	
CVI30		26	M	39	+	
CVI31		23	F	39	+	
CVI32		22	F	42	+	
CVI33		20	F	40	+	
CVI34		18	M	At term	+	
CVI35		17	M	40	+	
CVI36		17	M	At term	-	
CVI37		15	F	40	+	
CVI38		15	M	42	+	
CVI39		2	F	38	+	
CVI40		14	M	32	-	
CVI41		13	M	40	-	
CVI42		13	F	At term	+	
CVI43		13	F	40	+	
CVI44		12	M	42	+	
CVI45		10	M	39	+	
CVI46		9	M	40	+	
CVI47		7	M	41	+	
CVI48		7	F	40	+	
CVI49		7	M	38	+	
CVI50		6	M	41	+	
CVI51		6	M	37	+	
CVI52		6	M	37	+	
CVI53		6	F	At term	+	
CVI54		5	M	At term	+	
CVI55		5	M	39	+	
CVI56		4	F	36	+	

Table S2: Pathogenicity prediction of the identified mutations in *NR2F1*

	Individual 1	Individual 2	Individual 3	Individual 6
Coding DNA change	c.344G>C	c.339C>A	c.755T>C	c.335G>A
Protein change	p.Arg115Pro	p.Ser113Arg	p.Leu252Pro	p.Arg112Lys
PhyloP	5.05	1.90	4.56	5.05
Conservation down to	C. elegans	C. elegans	C. elegans	C. elegans
Pholyphen2 (score)	Probably damaging (1.00)	Probably damaging (1.00)	Probably damaging (0.99)	Probably damaging (0.995)
Sift (score)	Deleterious (0.00)	Deleterious (0.00)	Deleterious (0.00)	Deleterious (0.00)
Mutation Taster (Score)	Disease causing (0.99)	Disease causing (0.99)	Disease causing (0.99)	Disease causing (0.99)
MutPred	0.888	0.848	0.939	0.947
EVS frequency	0	0	0	0
dbSNP frequency	0	0	0	0

Table S3: Additional phenotype of the individuals in which a *NR2F1* defect was identified

	Individual 1	Individual 2	Individual 3	Individual 4	Individual 5	Individual 6
Gender	M	F	F	F	F	F
Birth weight (grams)	3510 (p7)	3855 (p70)	3780 (p70)	2500 (p50)	4150 (p86)	2800 (p12)
Gestational age (weeks)	42	41	AT	36	41	40
Age at investigations (years)	12	2+4	18	24	4	35
Height (cm)	159 (p84)	87 (p16)	185 (p99)	170 (p50)	107 (p55)	158 (p21)
Dysmorphisms	Protruding ears, long nostrils, prominent alea nasi, flattened thorax, long fingers and toes.	Epicanthal folds, upturned nose point, broad mouth, full lips, simple protruding ears with upturned ear lobes, tapering fingers and fetal fingers pads, curly slow growing hair.	Upslanting palpebral fissures, small nasal ridge, retrognathia, high palate, long fingers and toes.	Tapering fingers, extra flexion crease dig IV right, II-III syndactyly toes.	Broad high nasal bridge, prominent antihelix of the ear, clinodactyly dig V.	Right helix incompletely folded. Prominent Darwin's tubercle on right ear. Pointed chin. Synophrys (familial).
Hearing	-	-	-	-	-	-
Other abnormalities		Hypotonia.	Hypotonia.	Neonatal feeding problems.	Neonatal feeding problems.	Mild slowing in rapid alternating movements. Mild spasticity.
Refraction error	OD S+7.25=C-2.25x164" OS S+6.75=C-1.75x30"	OD S+3 OS S+3	OD S+0.25=C-0.50x4" OS S-0.25=C-0.75x11"	OD S 0=C-1.00x111" OS S-0.71=C-0.25x50"	OD S+1.75 OS S+1.75	OD S-2.00=C+4.00x180" OS S-2.00=C+4.00x180"
Correction of refraction	+	-	-	+	-	-
Visual acuity OD	0.06	ND	0.08	0.08	ND	0.1
Visual acuity OS	0.03	ND	0.1	0.2	ND	0.1
Visual acuity ODS	0.125	20/260 (0.08)	0.16	0.25	0.2	0.1
Method (distance)	LH (3 m)	TAC (55 cm)	Landolt C 2.6' (5 m)	Landolt C 2.6' (5 m)	TAC (55 cm)	Snellen
Strabismus	+	+	+	+	+	+
Oculomotor disturbance	-	-	+	-	+	-
Nystagmus	Latent.	-	Latent.	Latent.	Latent.	-
Visual field defects	+	+	+	-	+	ND
Slit lamp examination	Iris transillumination.	-	-	Deep anterior chamber, mild lens opacity.	Slight iris transillumination	Bilateral keratoconus.
Optic disc	Small and large excavation.	Pale.	Pale and large excavation.	Partial pale.	OD small and pale. OS pale and large excavation.	Pale.
Macula	Not recognizable.	Normal.	Normal.	Normal.	Normal.	Inner retinal atrophy with muted umbo and foveal light reflexes.
VEP (age)	Flash: late response; pattern onset: late response; pattern reversal: normal respons (8 years).	Flash: long latency times (10 months).	Flash:normal; pattern reversal: long latency (8 years).	ND	ND	ND
ERG (age)	Normal (8 years).	ND	Normal (8 years).	Normal (11 years).	ND	ND
Other ocular features	Crowding, fluctuating visual performance, excentric fixation.			Crowding.		Keratitis sicca managed with punctal plugs OU.

ND = not done.

Supplemental Table S4: Optic nerve abnormality cohort

Person	Variant identified	Gender	Age (years)	Disease
ONA1	c.909G>C; p.Gln303His	M	68	OPA
ONA2		V	68	OPA
ONA3		M	60	OPA
ONA4		V	39	OPA
ONA5		M	48	OPA
ONA6		M	46	OPA
ONA7		M	41	OPA
ONA7		M	74	LHON
ONA8		M	69	LHON
ONA9		M	64	LHON
ONA10		V	63	LHON
ONA11		M	63	LHON
ONA12		M	58	LHON
ONA13		M	57	LHON
ONA14		V	56	LHON
ONA15		V	56	LHON
ONA16		M	53	LHON
ONA17		M	52	LHON
ONA18		M	52	LHON
ONA19		V	51	LHON
ONA20		M	51	LHON
ONA21		V	47	LHON
ONA22		M	45	LHON
ONA23		M	44	LHON
ONA24		V	38	LHON
ONA25		M	34	LHON
ONA26		M	33	LHON
ONA27		V	25	LHON
ONA28		M	25	LHON
ONA29		V	21	LHON
ONA30		M	13	LHON
ONA31		M	13	LHON
ONA32		V	9	LHON
ONA33		M	50	LHON
ONA34		M	3	Opticopathy and developmental delay
ONA35		V	33	Optic nerve abnormaliy
ONA36		V	30	OPA and deafness

OPA = optic atrophy, LHON = Leber hereditary optic neuropathy.