

Supplementary table 1. Clinical, personal and family history of carriers and affected patients.

ID	Clinical and personal history	Relative(s) included in the present study	Additional family history, marriage and childbearing history
C1	Negative	C3 (brother), C8 (mother)	Maternal cousins affected by LHON
C2	Negative	C4 (brother), C7 (mother), P1 (maternal first cousin)	Two maternal uncles affected by LHON
C3	<ul style="list-style-type: none"> – Migraine without aura – Current smoker (40 cigarettes per day) 	C1 (brother), C8 (mother)	Maternal cousins affected by LHON
C4	Negative	C2 (brother), C7 (mother), P1 (maternal first cousin)	Two maternal uncles affected by LHON
C5	Negative	None	Mother affected by LHON
C6	Negative	P6 (brother)	Maternal uncle affected by LHON
C7	<ul style="list-style-type: none"> – Migraine without aura – Arterial hypertension in treatment with Olmesartan and Amlodipine – Former smoker 	C2 (son), C4 (son), P1 (nephew)	Two brothers affected by LHON
C8	<ul style="list-style-type: none"> – Migraine with aura – Psoriasis under treatment with topical steroid – Dizziness under treatment with Betaistine – Vasovagal syncope – Magnesium supplementation 	C1 (son), C3 (son)	Nephews affected by LHON
C9	<ul style="list-style-type: none"> – Migraine with aura – Arterial hypertension under treatment with Telmisartan – Vitamin B supplementation 	P5 (son)	Negative
C10	Negative	None	One son affected by LHON and one asymptomatic son
P1	<ul style="list-style-type: none"> – Current intake of Idebenone 900 mg/day – No relevant medical history except for sleep 	C2 (maternal first cousin), C4 (maternal first cousin), C7 (aunt)	Two maternal uncles affected by LHON

	parasomnia (somnambulism)		
P2	<ul style="list-style-type: none"> – Current intake of Idebenone 900 mg/day – No relevant medical history 	None	Negative
P5	<ul style="list-style-type: none"> – Current intake of Idebenone 900 mg/day, multivitamin supplementation – No relevant medical history except for allergic rhinitis in therapy with antihistaminic drug 	C9 (mother)	Negative
P4	<ul style="list-style-type: none"> – Current intake of Idebenone 900 mg/day – No relevant medical history 	None	Negative
P8	<ul style="list-style-type: none"> – Current intake of Idebenone 900 mg/day – Current smoker 	None	Negative
P3	<ul style="list-style-type: none"> – Current intake of Idebenone 900 mg/day – Mood disorder (depression) in the last 6 years in therapy with Valproic acid, Venlafaxine, Olanzapine and Delorazepam – Migraine without aura 	None	Negative
P7	<ul style="list-style-type: none"> – Current intake of Idebenone 900 mg/day, vitamin B supplementation – Current smoker 	None	Negative
P6	<ul style="list-style-type: none"> – Current intake of Idebenone 900 mg/day – Viral meningitis at 17 years – Former smoker 	C6 (sister)	Maternal uncle affected by LHON