

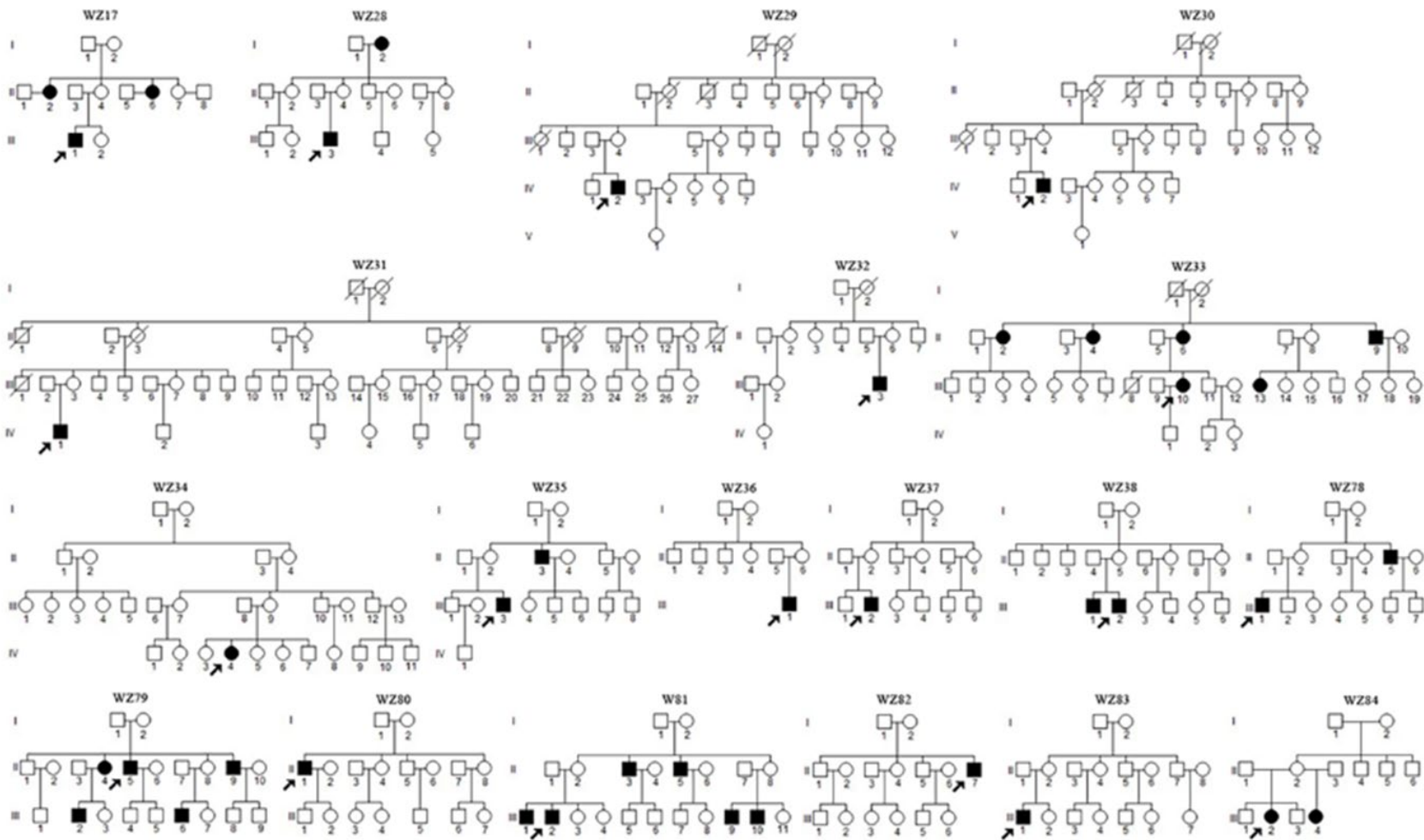
*Supplementary data*

**Leber's hereditary optic neuropathy was manifested by ND1 3460G>A mutation-induced alterations in mitochondrial function, apoptosis and mitophagy**

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**Supplemental Figure S1, S2**

**Supplemental Table S1, S2, S3 and S4**



**Figure S 1.** Nineteen Han Chinese pedigrees with Leber's hereditary optic neuropathy. Vision impairment individuals are indicated by filled symbols. Arrow denotes the probands.



Table S1. Summary of clinical data for 19 probands carrying m.3460G>A mutation.

Subject	Gender	Age of test (years)	Age-of-onset (years)	Visual acuity (right)	Visual acuity (left)	level of vision impairment
WZ17-III-1	M	14	14	0.05	0.02	Severe
WZ28-III-3	M	16	16	0.02	0.03	Severe
WZ29-IV-2	M	23	22	0.1	0.1	Mild
WZ30-IV-2	M	18	18	0.02	0.03	Severe
WZ31-IV-1	M	27	25	0.1	0.1	Mild
WZ32-III-3	M	20	20	0.08	0.03	Moderate
WZ33-IV-9	F	38	15	0.03	0.05	Severe
WZ34-IV-4	F	19	19	0.01	FC/30cm	Profound
WZ35-III-3	M	33	23	0.02	0.02	Severe
WZ36-III-1	M	26	26	0.06	0.05	Moderate
WZ37-III-2	M	14	14	0.1	0.04	Mild
WZ38-III-2	M	19	19	FC/20cm	0.04	Profound
WZ78-III-1	M	25	25	0.08	0.08	Moderate
WZ79-II-5	F	21	17	0.06	0.1	Moderate
WZ80-II-1	M	24	19	0.03	0.02	Severe
WZ81-III-2	M	22	20	0.01	0.01	Profound
WZ82-II-7	M	40	20	0.08	0.06	Moderate
WZ83-III-1	M	5	5	FC/1m	FC/1.5m	Profound
WZ84-III-2	M	7	5	0.06	0.08	Moderate

The degree of visual impairment was defined according to the visual acuity as follows:  
normal >0.3, mild =0.3-0.1; moderate<0.1-0.05; severe<0.05-0.02; and profound <0.02.  
M, Male; F, Female; CF, counting fingers;

**Table S2. Summary of clinical and molecular data for 19 Chinese families carrying the m.3460G>A mutation.**

Pedigree	Number of matrilineal relatives	Penetrance	Average age-at-onset	Ratio Affected male/affected female	mtDNA haplogroup
WZ17	7	42.9	14	1/2	M7b2
WZ28	9	22.2	16	1/1	D5
WZ29	24	4.2	22	1/0	B5b
WZ30	28	10.7	18	1/0	R9
WZ31	36	2.8	25	1/0	F1
WZ32	9	11.1	20	1/0	C4a1
WZ33	21	28.6	28.7	1/5	A
WZ34	14	7.1	19	0/1	M7b1
WZ35	6	33.3	23	2/0	M12
WZ36	7	14.3	26	1/0	M7c1
WZ37	8	12.5	14	1/0	H2
WZ38	13	15.4	20	2/0	F1a1
WZ78	9	22.2	28.5	2/0	D5b1
WZ79	10	50	16	4/1	M8a2
WZ80	9	11.1	19	1/0	D4b1
WZ81	12	50	19.8	6/0	B5b2
WZ82	7	14.3	20	1/0	B5a
WZ83	9	11.1	5	1/0	D4
WZ84	9	22.2	6	0/2	F2a3

Table S3. Summary of rRNA variants and missense variants in polypeptide genes in 19 Chinese probands.

Gene	Position	Replacement	WZ17	WZ28	WZ29	WZ30	WZ31	WZ32	WZ33	WZ34	WZ35	WZ36	WZ37	WZ38	WZ78	WZ79	WZ80	WZ81	WZ82	WZ83	WZ84	Amino Acid Change	Conservation index (%) <sup>§</sup>	No. of 485 Controls	Previously Reported <sup>#</sup>	
Phe 12S rRNA	593	T-C																			C	31.25	1	Yes		
	663	A-G									G												78.57	20	Yes	
	669	T-C													C								70.59	0	Yes	
	681	T-C			C																		85.71	7	No	
	709	G-A			A	A					A												71.43	67	Yes	
	750	A-G	G	G	G	G	G	G	G	G	G	G	G	G	G	G	G	G	G	A	A		100.00	1	Yes	
	961	C-CC			CC																		14.29	1	Yes	
	1005	T-C																				C	35.71	15	Yes	
	1048	C-T			T										T								64.29	8	Yes	
	1107	T-C			C										C							C	85.71	20	Yes	
	1438	A-G			G	G	G	G	G	G	G	G	G	G	G	G	G	G	G	G	G	G	100.00	339	Yes	
	1598	G-A			A																	A	50.00	15	Yes	
	16S rRNA	1715	A-T									T												71.43	3	Yes
		1719	G-A												A									7.14	5	Yes
		1736	A-G									G												57.14	0	Yes
		1824	T-C																				C	21.43	18	Yes
2143		A-G																	G				17.65	0	No	
2389		C-T									T												76.47	4	Yes	
2706		A-G	G	G	G	G	G	G	G	G	G	G	G	G	G	G	G	G	G	G	G		57.14	343	Yes	
2835		C-T																				T	57.14	9	Yes	
3010		G-A																				A	50.00	60	Yes	
3172		C-CC									CC												35.71	0	Yes	
3290		T-C																				C	43.75	2	Yes	
Leu(UUR) ND1		3460	G-A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A52T	94.12	0	Yes
		4048	G-A	A																			D248N	7.14	13	Yes
Ile Gln		4216	T-C																				Y304H	50.00	5	Yes
		4316	A-G									G												94.12	0	Yes
ND2		4336	T-C			C																		70.59	0	Yes
	4824	A-G									G											T114A	100.00	21	Yes	
CO1 CO2 ATP8 ATP6	4924	G-A			A																	S152N	17.65	0	Yes	
	5178	C-A			A																	L237M	57.14	77	Yes	
	5301	A-G			G																	I278V	42.86	20	Yes	
	5442	T-C																				C	35.71	15	Yes	
	5460	G-A									A											A331T	7.14	11	Yes	
	6253	T-C			C																	C	M117T	57.14	7	Yes
	7853	G-A									A											V90I	28.57	17	Yes	
	8414	C-T																				L17F	71.43	57	Yes	
	8584	G-A			A						A											A20T	50.00	58	Yes	
	8618	T-C																				A	A20T	50.00	58	Yes
CO3 ND3 ND4L ND4	8618	T-C																				I31T	58.82	1	Yes	
	8684	C-T																				T53I	64.29	14	Yes	
	8701	A-G	G	G		G		G	G	G	G	G	G	G	G	G	G	G	G	G	G	T59A	64.29	160	Yes	
	8794	C-T																				H90Y	71.43	23	Yes	
	8860	A-G	G	G	G	G	G	G	G	T	G	G	G	G	G	G	G	G	G	G	G	T112A	78.57	334	Yes	
	9010	G-A																				A162T	100.00	0	Yes	
	9300	G-A																				A32T	47.06	0	Yes	
	9490	C-T																				A95V	76.47	0	Yes	
	10345	T-C			C																	I96T	50.00	0	Yes	
	10398	A-G	G	G	G	G	G	G	G	G	G	G	G	G	G	G	G	G	G	G	G	T114A	35.71	193	Yes	
Ser <sup>(AGY)</sup> ND5	10609	T-C																				M47T	64.29	29	Yes	
	11204	T-C																				F149L	100.00	1	Yes	
	11969	G-A									A											A404T	92.86	9	Yes	
	12030	A-G																				N424S	47.06	0	Yes	
	12223	A-G																				G	94.12	0	Yes	
	12338	T-C																				C	M1T	100.00	16	Yes
	12358	A-G																				T8A	57.14	6	Yes	
	12361	A-G			G																	T9A	35.71	15	Yes	
	12406	G-A									A											V24I	64.29	31	Yes	
	12811	T-C			C																	Y159H	71.43	11	Yes	
Glu Cytb	12906	C-A																				I190M	7.14	2	Yes	
	12940	G-A									A											A202T	7.14	2	Yes	
	13135	G-A									A											A267T	28.57	9	Yes	
	13637	A-G									G											Q434R	52.94	0	Yes	
	13780	A-G																				A458T	29.41	0	Yes	
	13928	G-C																				C	S531T	14.29	47	Yes
	14318	T-C									C											N119S	50.00	12	Yes	
	14502	T-C																				I58V	71.43	5	Yes	
	14693	A-G																					100.00	6	Yes	
	14727	T-C																					M1V	94.12	0	Yes
Thr	14766	C-T																				T7S	50.00	339	Yes	
	14831	G-A																				A29T	29.41	0	Yes	
	15071	T-C																				Y109H	28.71	0	Yes	
	15204	T-C																					I153T	78.57	3	Yes
	15218	A-G																				T158A	85.71	2	Yes	
	15326	A-G	G	G	G	G	G	G	G	G	G	G	G	G	G	G	G	G	G	G	G	T194A	64.29	333	Yes	
	15651	C-T																				A302V	70.59	0	Yes	
	15662	A-G																				G	I306V	21.43	14	Yes
	15851	A-G																				G	I369V	14.29	14	Yes
	15924	A-G			G																		81.25	4	Yes	
15927	G-A																					A	68.75	14	Yes	

<sup>§</sup>Conservation of amino acid for polypeptides or nucleotide for RNAs in 17 vertebrates: Bos Taurus, Cebus albifrons, Gorilla gorilla, Homo sapiens, Hylobates lar, Lemur catta, Macaca mulatta, Macaca sylvanus, Mus musculus, Nycticebus coucang, Pan paniscus, Pongo pygmaeus, Pongo abelii, Papio hamadryas, Tarsius bancanus, and Xenopus laevis.

<sup>#</sup>See the online mitochondrial genome database <http://www.mitomap.org> and <http://www.genpat.uu.se/mtDB>.

Table S4. Haplogroup distribution of mtDNA from 19 Han Chinese LHON families carrying m.3460G>A mutation and from 485 Chinese control subjects.

Group	Microgroup M							Macrogroup N							
	M8	M9	M7	M11	M12	D	G	N9	N10	A	B	R9	F	H2	U
Frequency of mtDNA haplogroup (%)															
Control (n=485)	11.1	2.3	6.8	0.6	0.0	23.1	3.5	7.8	0.2	5.8	18.8	3.1	15.9	0.6	0.4
LHON Pedigree (n=19)	10.5	0.0	15.8	0.0	5.3	21.1	0.0	0.0	0.0	5.3	15.8	5.3	15.8	5.3	0.0
Ratio (affected males/females)	5:1	-	2:3	-	2:0	5:1	-	-	-	1:5	7:0	1:2	3:2	1:0	-
Average penetrance (%)	30.6	-	21.4	-	33.3	16.7	-	-	-	28.6	22.8	10.7	13.5	12.5	-
Average age-of-onset (years)	18	-	19.7	-	23	17.1	-	-	-	28.7	20.6	18	17	14	-