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Supplementary information to:

Original article:

EXPLORING MITO-NUCLEAR GENETIC FACTORS IN LEBER'S HEREDITARY OPTIC NEUROPATHY: INSIGHTS FROM COMPREHENSIVE PROFILING OF UNIQUE CASES

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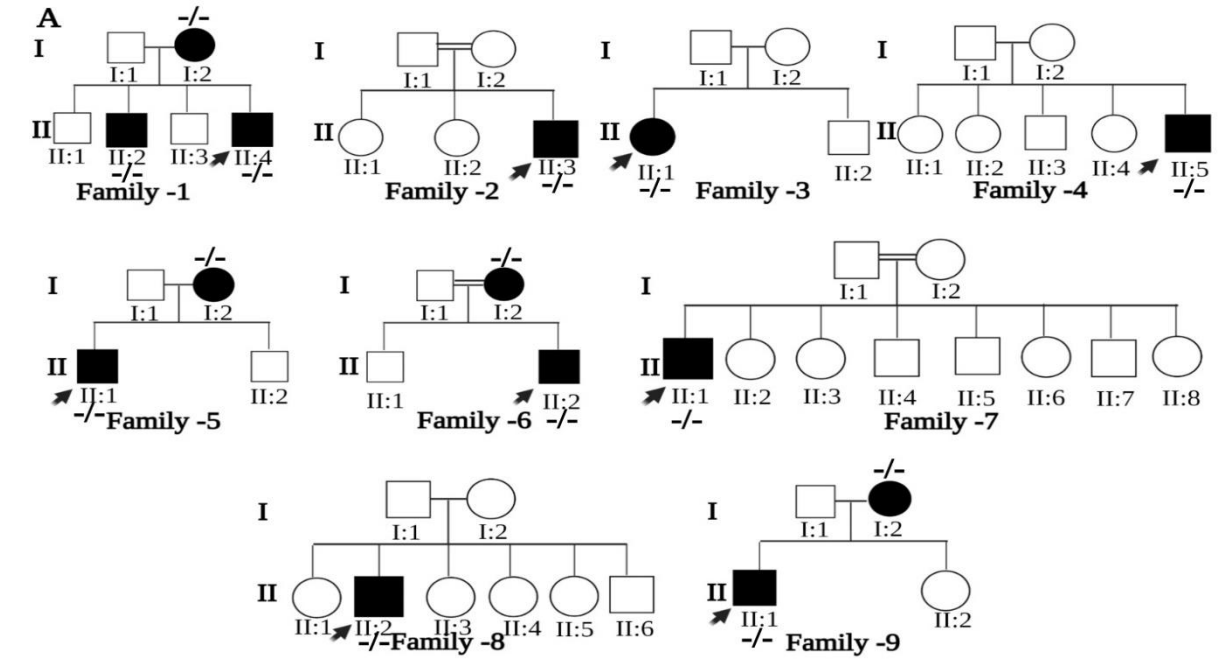

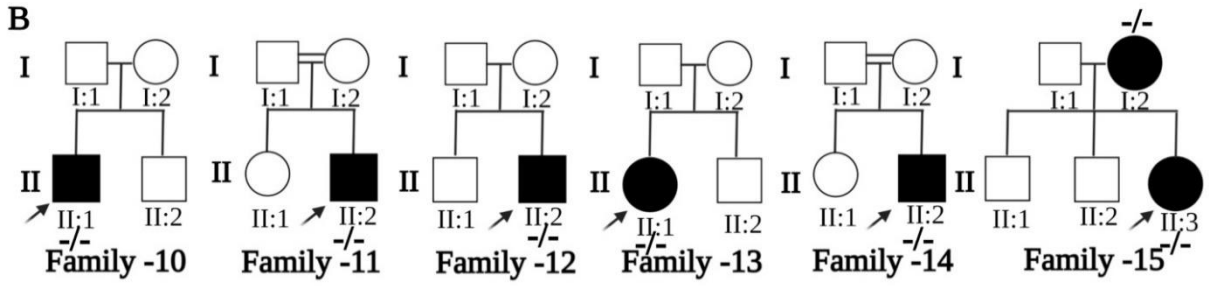

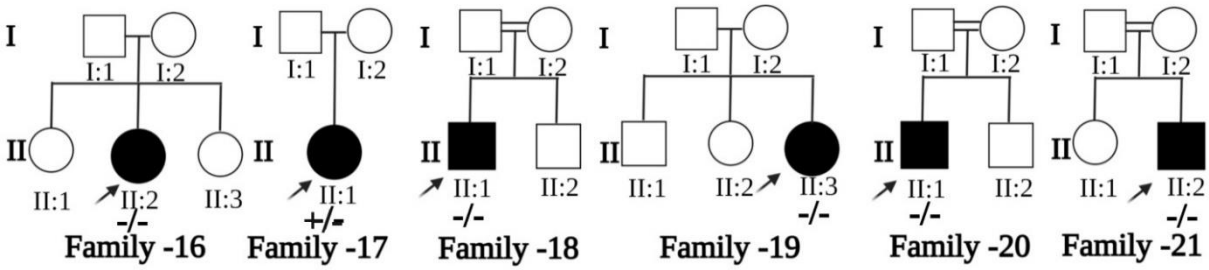

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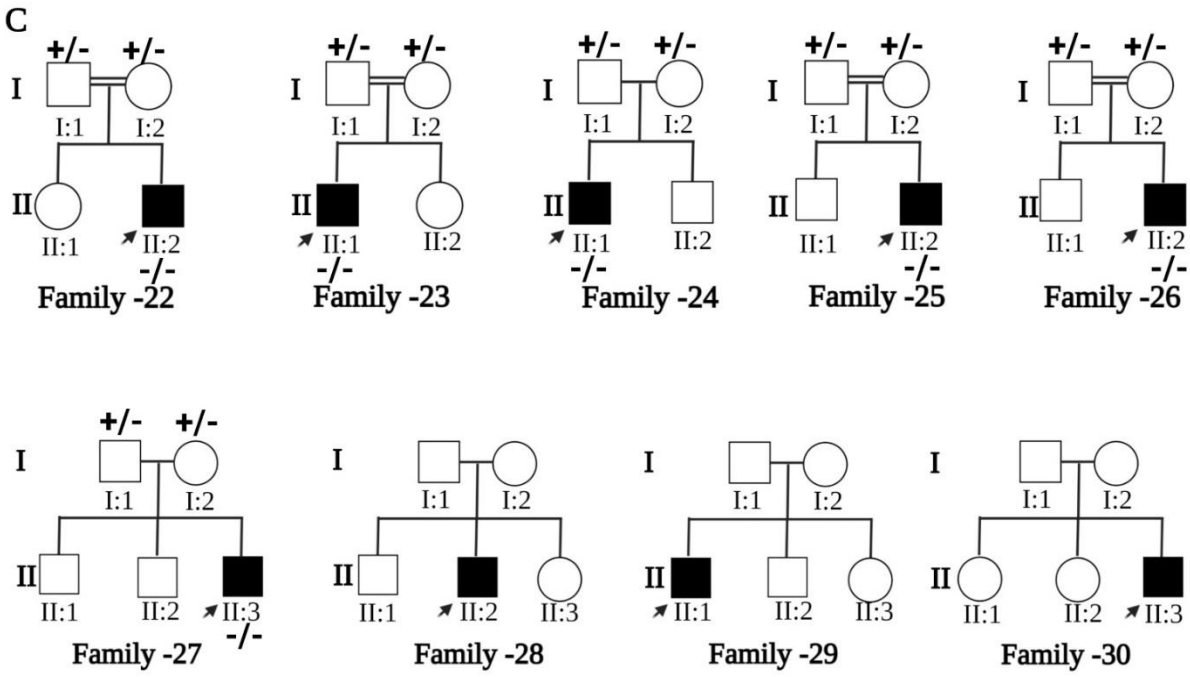

Supplementary Figure 1: Pedigree of thirty unrelated probands involved in this study. Solid symbols with an arrow represent proband. Consanguinity is represented by a double line. The genotype is denoted by (–/–) for homozygous variant carriers, (+/–) for heterozygous variant carriers. **A**- Group I; **B**- Group II and **C**- Group III

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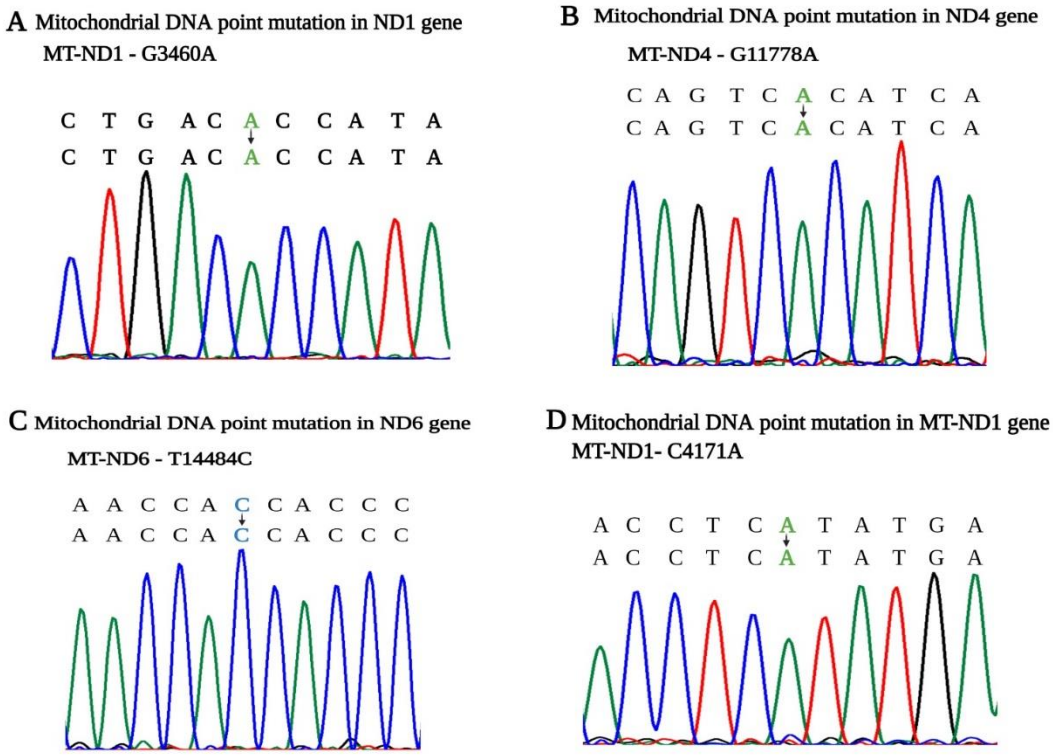
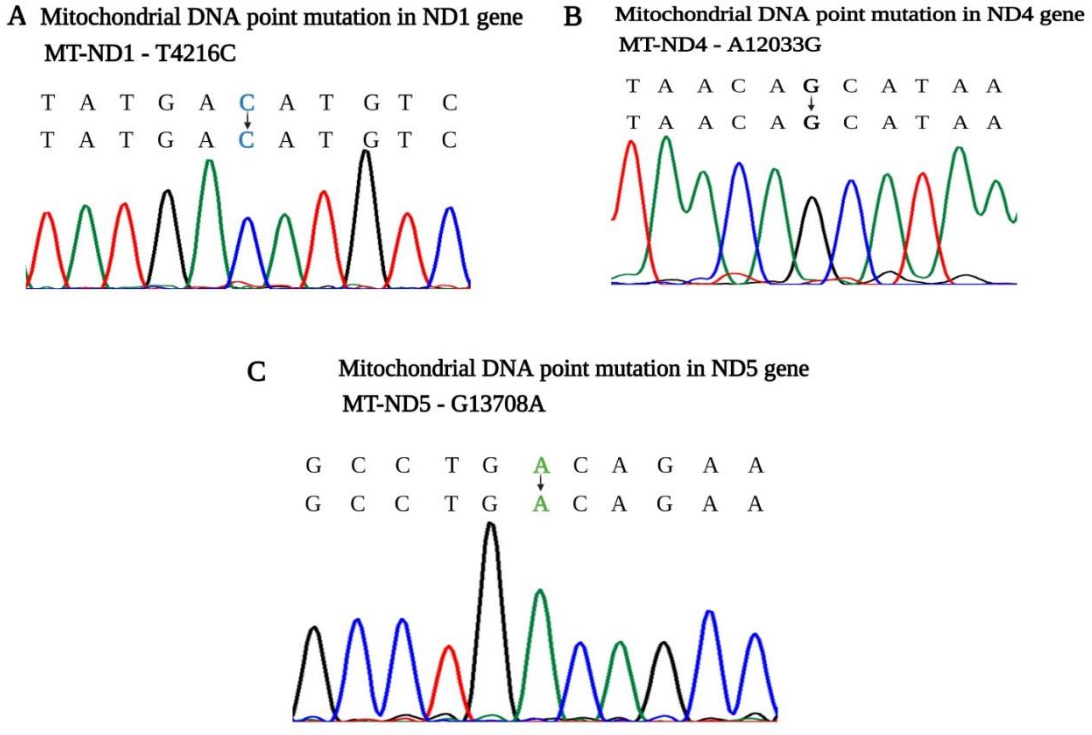


Supplementary Figure 2: Representative chromatogram of the probands in group I harboring primary mitochondrial DNA mutations (MT-ND1, MT-ND4 and MT-ND6 genes)



Supplementary Figure 2a: Sequencing chromatogram of the probands in group I harboring a co-occurrence secondary mitochondrial DNA mutations (MT-ND1, MT-ND4 and MT-ND5 genes)

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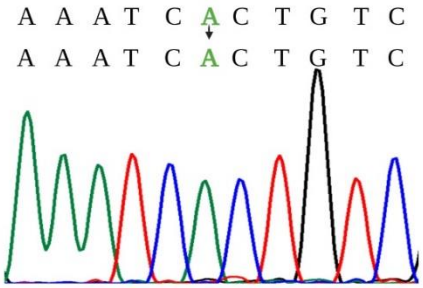
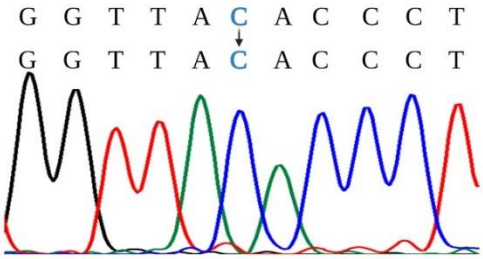
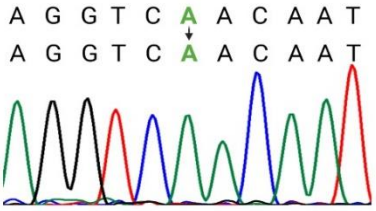
A Mitochondrial DNA point mutation in ATP6 gene
MT-ATP6 - G9139A



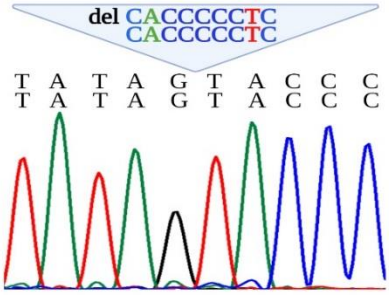
B Mitochondrial DNA point mutation in MT-TM gene
MT-TM - T4454C



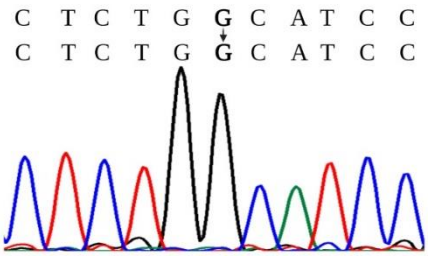
C Mitochondrial DNA point mutation in MT-CO2 gene
MT-CO2- G7859A



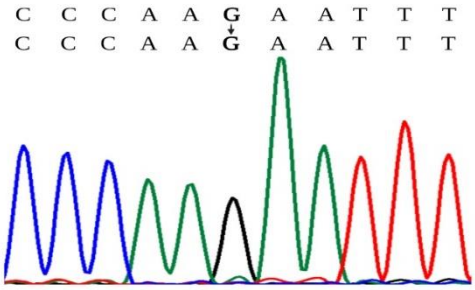
D Mitochondrial DNA deletion mutation in MT-NC7
MT-NC7 - (del CACCCCCTC)



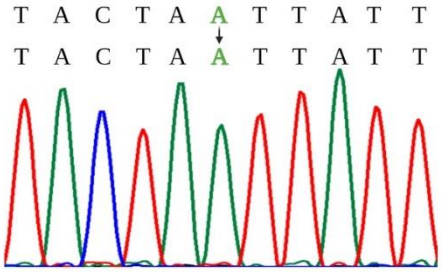
E Mitochondrial DNA point mutation in ND2 gene
MT-ND2 - A4842G



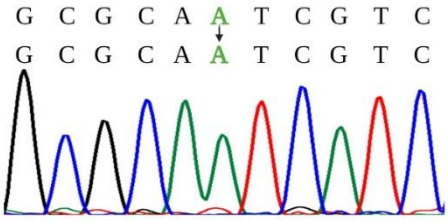
F Mitochondrial DNA point mutation in TL2 gene
MT-TL2 - A12308G

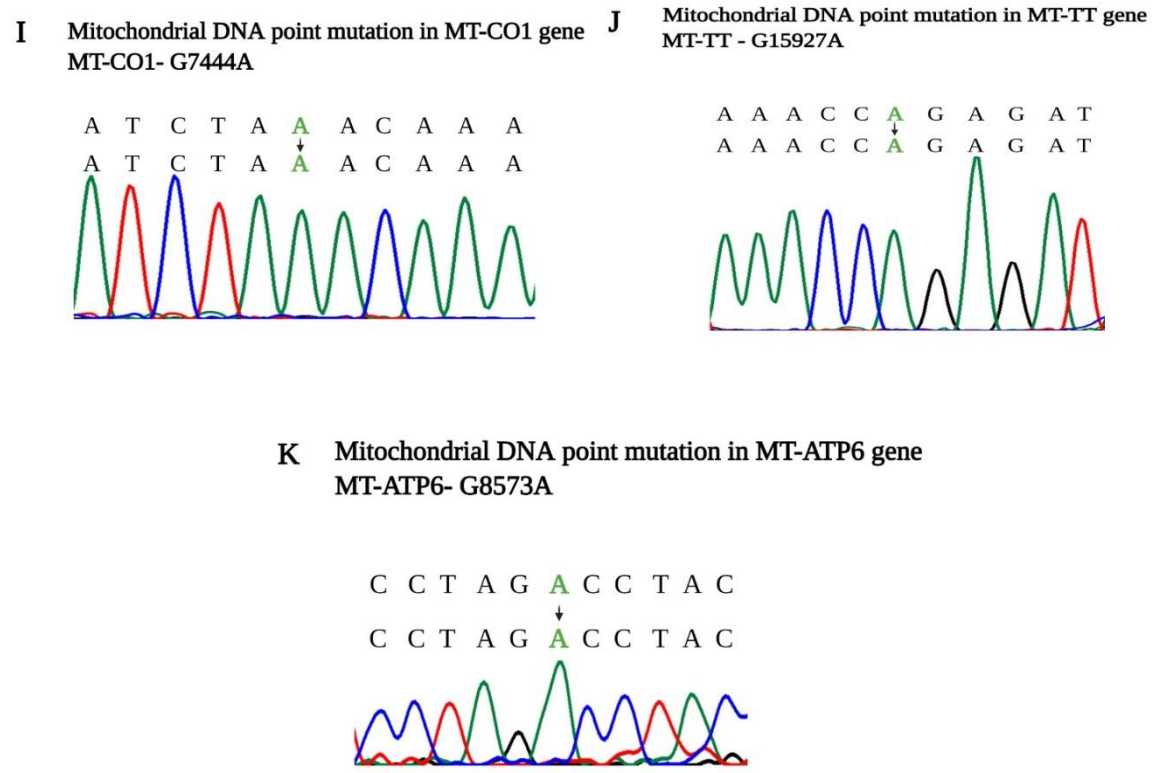


G Mitochondrial DNA point mutation in ATP6 gene
MT-ATP6 - G8950A



H Mitochondrial DNA point mutation in ND4 gene
MT-ND4 - G11696A





Supplementary Figure 3: Sequencing chromatogram from **A-K** represents the probands from group II harboring secondary mitochondrial DNA mutations.

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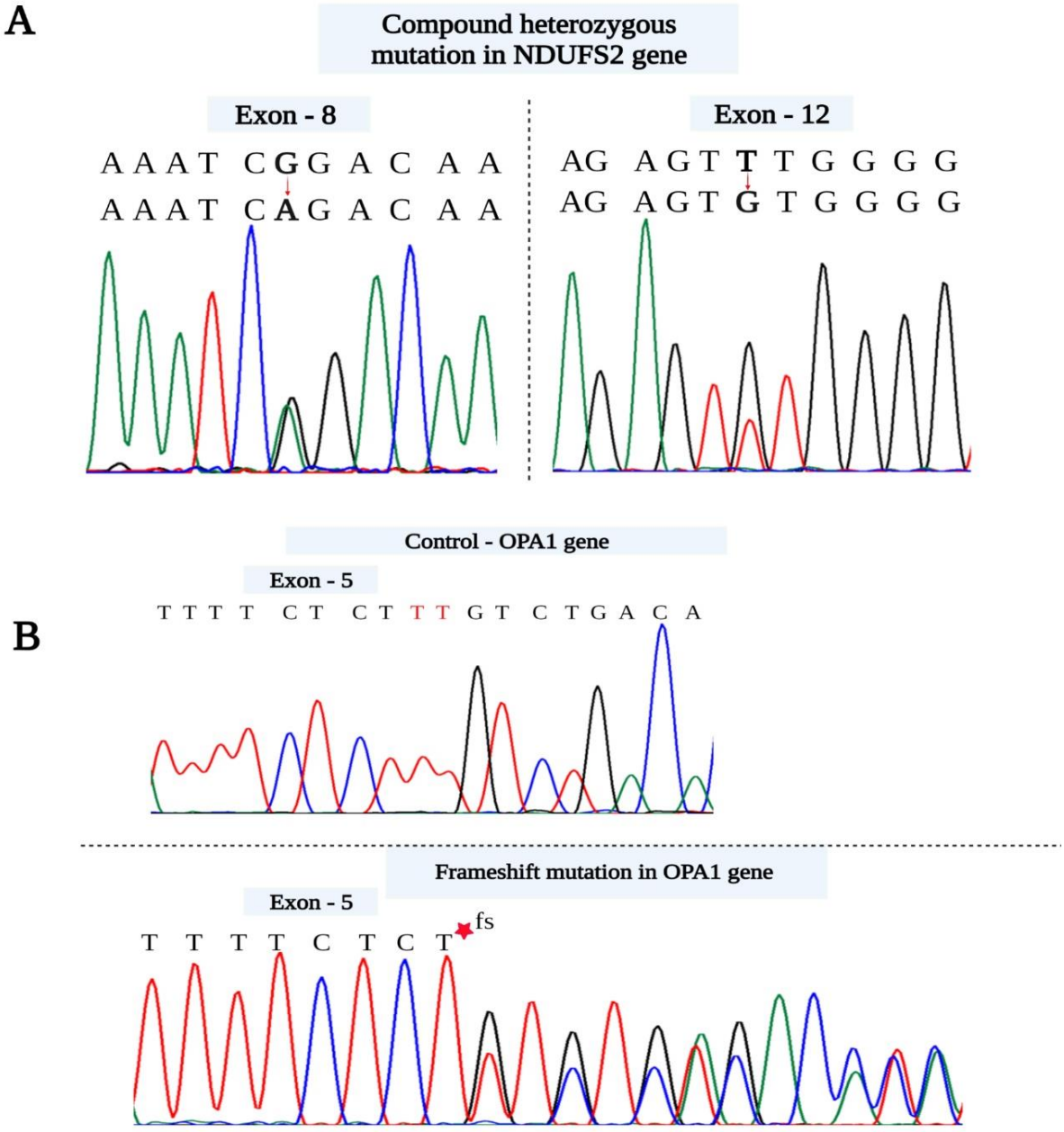

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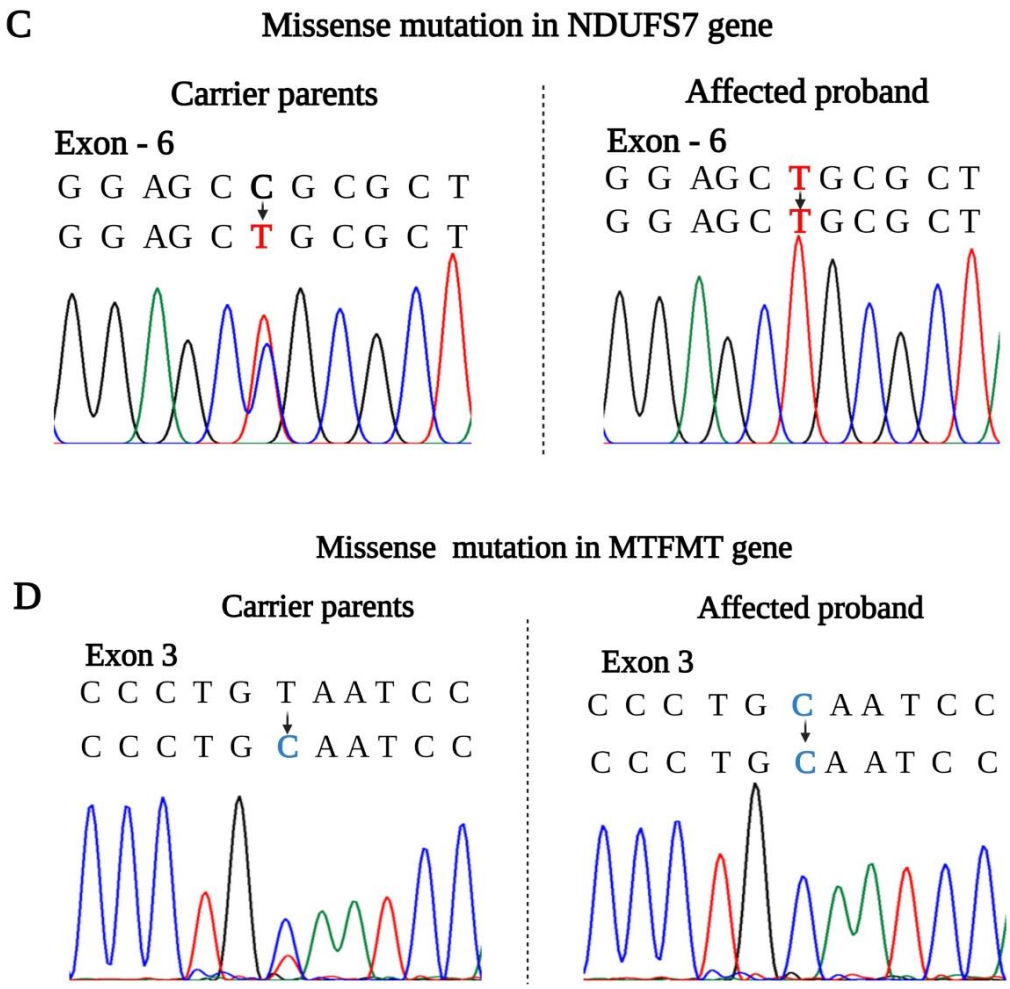

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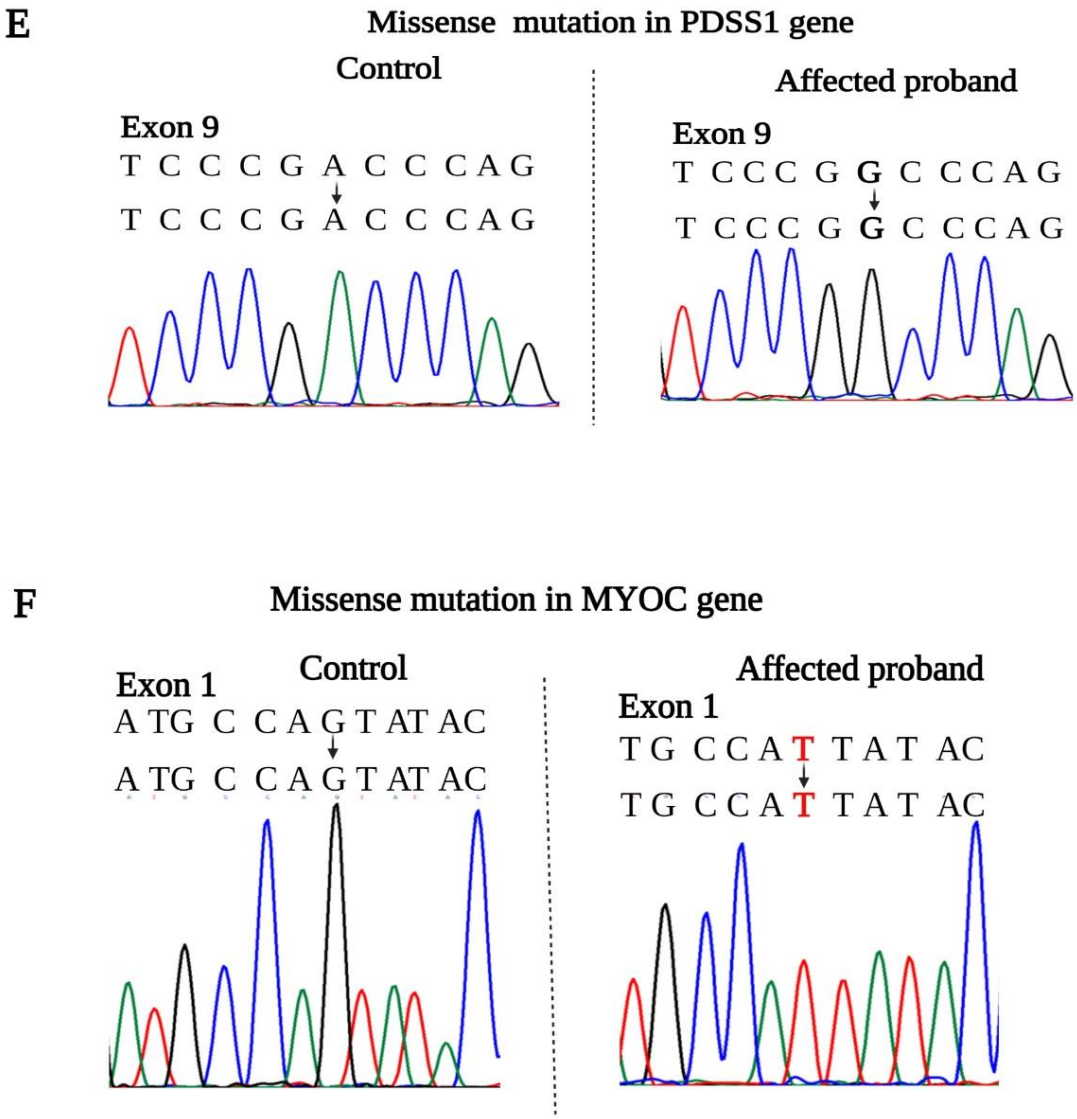

Supplementary Figure 4: Sequencing chromatogram from **A-F** represents the probands from group II harboring nuclear DNA mutations (NDUFS2, OPA1, NDUFS7, MTFMT, PDSS1 and MYOC gene)

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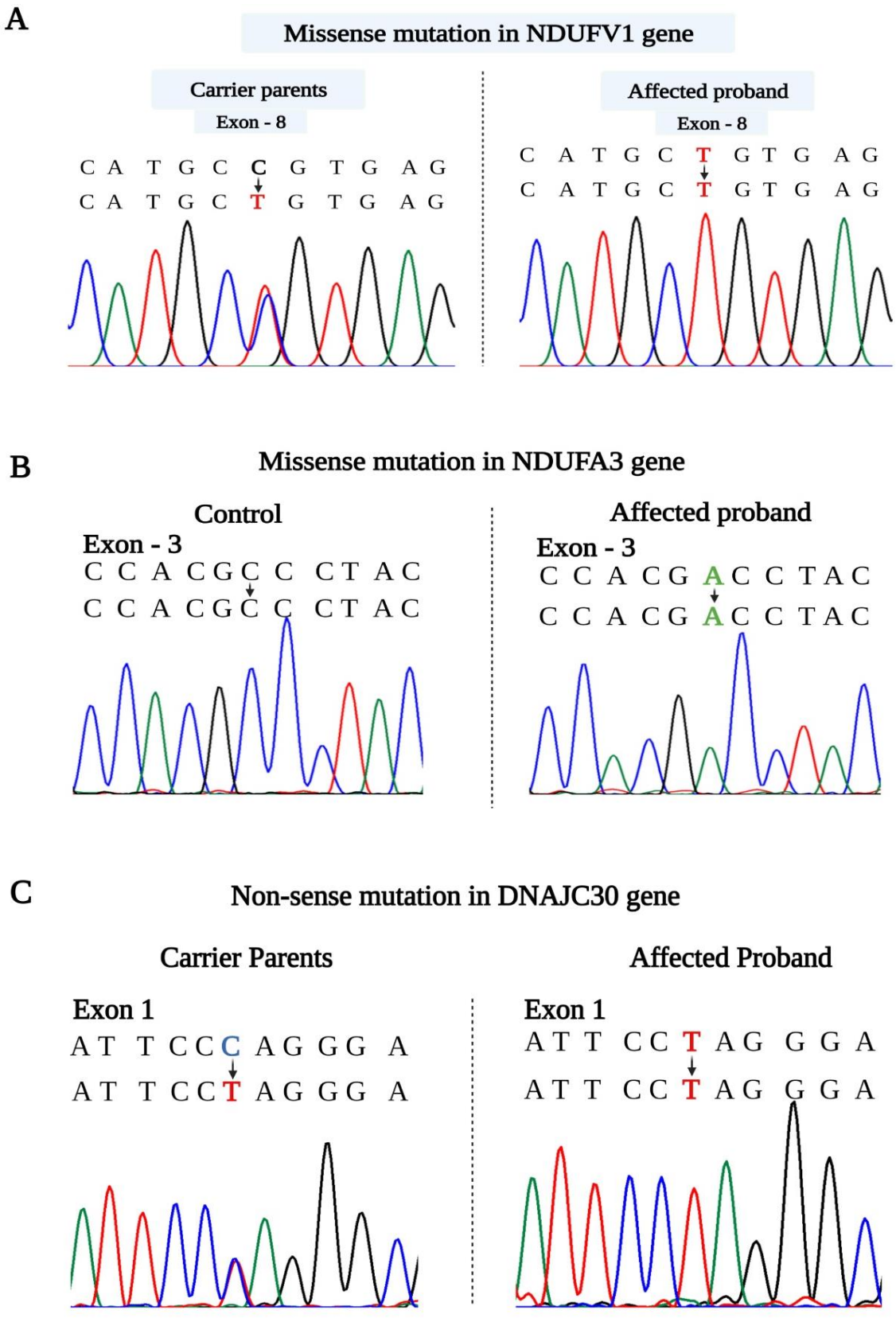

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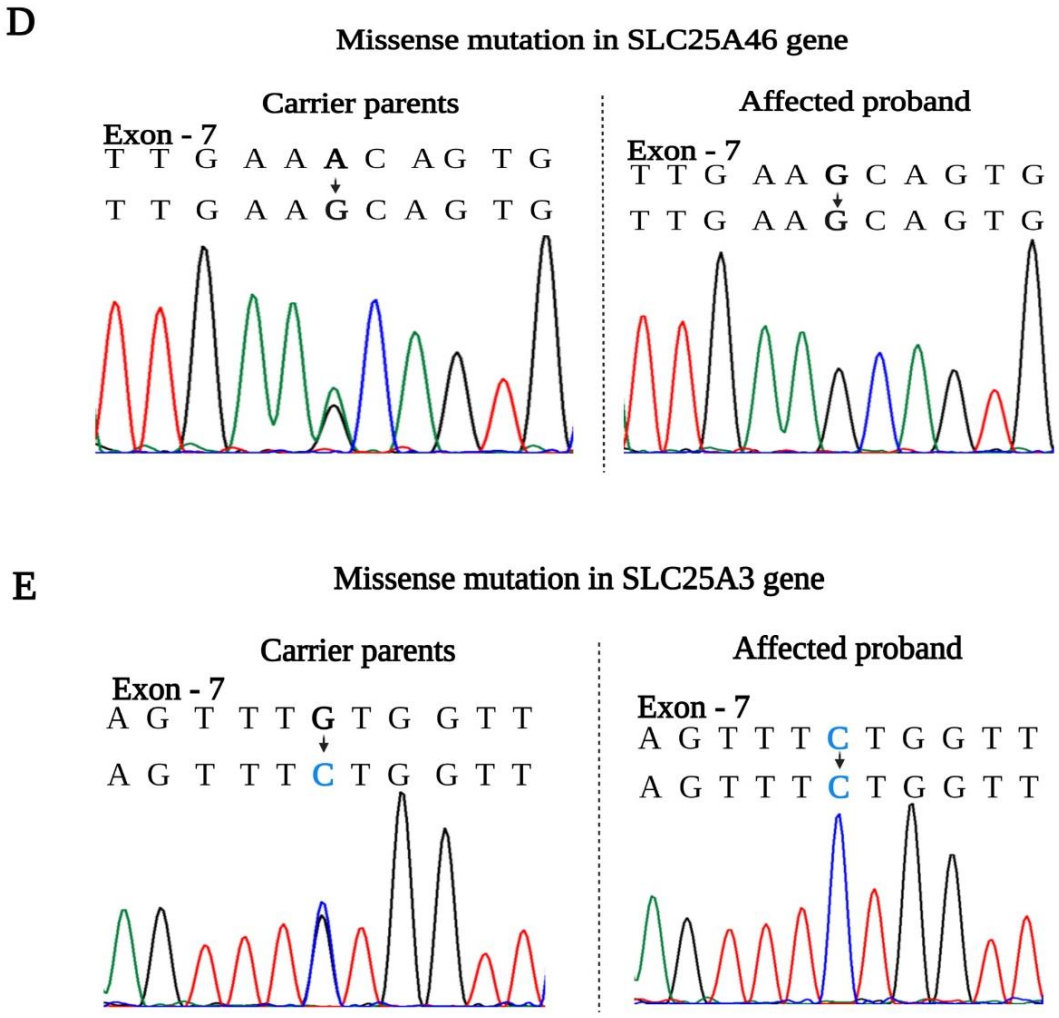

Supplementary Figure 5: Sequencing chromatogram from **A-E** represents the probands from group III harboring nuclear DNA mutations (NDUFV1, NDUFA3, DNAJC30, SLC25A46 and SLC25A3 gene

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Supplementary Table 1: Illustrates the key component of the sample group, family history and male to female ratio

Group	Probands	Total (Familial/ Sporadic)	Male (Familial/ Sporadic)	Female (Familial/ Sporadic)	Ratio (Male: Female)
	Total screened (n=30)	30 (5/25)	24 (4/20)	6 (1/5)	4:01
Group I (1)	LHON primary mutation (n=9)	9 (4/5)	8 (4/4)	1 (-/1)	8:01
Group II (2)	Secondary mitochondrial DNA mutation (n=12)	12 (1/11)	7 (-/7)	5 (1/4)	1.4:1
	*Secondary mitochondrial DNA mutation alone (n=6)	6(1/5)	4 (-/4)	2 (1/1)	2:01
	#Secondary mitochondrial DNA mutation + Nuclear gene mutation (n=6)	6 (-/6)	3 (-/3)	3 (-/3)	1:01
Group III (no mtDNA mutation)	Nuclear gene mutation (n=6)	6 (-/6)	6 (-/6)	0 (-/-)	NA
	No mutation (n=3)	3 (-/3)	3 (-/3)	0 (-/-)	NA

* indicates patients harbor only secondary mtDNA mutation
# indicates patients harbor both secondary mtDNA mutation and nuclear gene mutation