Supplemental Table S5: Summary of nuclear DNA variants of interest identified in the cohort.

Gene	Variant position (allele call)	Amino acid change	RefSNP ID	ACMG classification*	ExAC frequency	Patient, race, sex	Clinical profile	Biochemical profile	Reference
ACADVL‡	194C>T (+/+)	p.Pro65Leu	rs28934585§	Likely benign	0.1135 (African)	S027, A, M	DD, CNS, Eye, PNS, M, L	CIII, CIV, CII+CIII	Watanabe et al (2000)[51]
COX4I2†	c.412G>A (+/-)	p.Glu138Lys	rs119455950§	VUS	0.006936 (African)	S094, A, F	DD, CNS	CI	Shteyer et al (2009)[52]
DARS2†	c.1013G>A (+/-)	p.Gly338Glu	rs141298312	VUS	0.0065 (Caucasian)	S024, NA, M	DR, BE, CNS, PNS, M	CI	-
GLUD2‡	c.1492T>G (+/+)	p.Ser498Ala	rs9697983§	Likely benign	0.04979 (African)	S002, A, F	Mac, DD, M	CIII, CII+CIII	Plaitakis et al (2010)[53]
NDUFA9†	c.224G>T (+/-)	p.Arg75Leu	rs35263902	VUS	0 (African)	S049, A, M	BE, CNS, PNS	CIII	-
POLG†	c.3287G>A (+/-)	p.Arg1096His	rs368435864	VUS	0.00009623 (African)	S094, A, F	DD, CNS	CI	-
SDHA†	c.1523C>T (+/-)	p.Thr508Ile	rs151266052§	VUS	0.00821 (African)	S007, A, M	DD, Eye, M	CII, CIII CII+CIII	Alston et al (2012)[54]
						S004, A, F	FTT, DD, Dys, Eye, M	CIII	
SDHB†	c.32G>A (+/-)	p.Arg11His	rs111430410§	VUS	0.005455 (African)	S015, A, M	Mac, DD, Eye, M, E	CI, CII, CIII, CIV, CII+CIII	Martins et al (2013)[55]
						S034, A, F	DD, CNS, Eye, E	CIII	
SDHD†	c.34G>A (+/-)	p.Gly12Ser	rs34677591‡§	VUS	0.01018 (Caucasian)	S050, NA, F	DD, M, GIT, C	CIII, CIV	Ni et al (2008)[56]

							S028, A, M	M, GIT, R, E, S	CI	
TRMU†	c.28G>T (+/+)	p.Ala10Ser	rs11090865§	VUS	0.3933 (African)		S059, A, M	DD, CNS, Eye, D, M, GIT	CI, CIII, CIV, CII+CIII	Meng et al (2017)[57]
							S109, A, F	FTT, DD, CNS, Eye, D, R, E	CI, CIII	

*Variant classification using ACMG criteria, including phenotypic evaluation.

† Variants identified using panel NGS.

‡Variants identified using WES.

§Previously reported pathogenic.

+/+: Homozygous; +/-: Heterozygous; A: African; NA: Non-African; M: Male; F: Female; VUS: variant of uncertain significance; FTT: Failure to thrive; Mac: Macrocephaly; DD: Developmental delay; Dys: Dysmorphism; BE: Behaviour and emotional; CNS: Central nervous system involvement; Eye: Eye involvement; D: Deafness; PNS: Peripheral nervous system – neuropathy; M: Muscle involvement, S; Skin: Skin involvement; GIT: Gastrointestinal involvement, C: Cardiac involvement; R: Renal involvement; E: Endocrine; L: Liver involvement; S: Skeletal involvement.