Supplemental Table S4: Summary of mitochondrial DNA variants of importance identified in cohort.

Gene	Variant position	Amino acid change	Mutpred score	ACMG classification*	GenBank frequency, variant allele frequency	Patient, ethnicity, sex	Clinical profile	Biochemical profile	Reference
MT-ND2	m.5186A>T	p. Trp239Cys	0.549	VUS	0.0653%, 100%	S097, NA, F	FTT, DD, CNS	CI	None to date
MT-TA	m.5628T>C	Ala	Yarham score: 13	Likely benign	0.15692%, 100%	S059, A, M	DD, CNS, Eye, D, M, GIT	CI, CIII, CIV, CII+CIII	Gamba et al (2012)[45]
MT-TC	m.5814T>C	Cys	Yarham score: 14	VUS	0.33345%, 100%	S058, A, M	FTT, Mac, DD, DR, Dys, BE, CNS, M, E, L, S	CI, CIII, CIV	Santorelli et al (1997)[46]
MT-CO3	m.9355A>G	p.Asn50Ser	0.591	VUS	0.06%, 100%	S043, A, F	DD, DR, CNS, Eye, M	CIII, CIV	None to date
MT-ND4	m.11087T>C	p.Phe110Leu	0.788	VUS	0.24%, 100%	S028, A, M	M, GIT, R, E, S	CI, CII+CIII	Gaspar et al (2015)[47]
MT-ND5	m.13802C>T	p.Thr489Met	0.6	VUS	0.07192%, 100%	S019, NA, F	DD, Dys, CNS, Eye, D, M	CI, CII+CIII	Bayona-Bafaluy et al (2011)[48]
MT-ND6	m.14405A>G	p.Val90Ala	0.597	VUS	0.055%, 100%	S112, A, M	DD, CNS, Eye, M	CI, CII, CIV	None to date
MT-ND6	m.14502T>C	p.Ile58Val	0.385	Likely benign	0.39%, 82%	S126, NA, M	FTT, GIT	CI	Zhao et al (2009)[49]
MT-CYB	m.14790A>G	p.Asn15Ser	0.704	VUS	0.02288%, 100%	S028, A, M	M, GIT, R, E, S	CI, CII+CIII	Cavadas et al (2015)[50]
MT-CYB	m.15257G>A	p.Asp171Asn	0.785	VUS	1.30%, 100%	S038NA, F	DD, M, GIT, E	CI, CIII	Brown et al (1992)[37]
MT-CYB	m.15272A>G	p.Thr176Ala	0.562	VUS	0.00654%,	S037, NA, F	DD, DR, CNS,	CIII	Van der Walt et al

		100%	D, PNS, M, Skin	(2012)[8]

**Variant classification using ACMG criteria, including phenotypic evaluation.*

A: African, NA: Non-African; Mac: Macrocephaly; FTT: Failure to thrive; DD: Developmental delay; DR: Developmental regression; CNS: Central nervous system involvement; Eye: Eye involvement; D: Sens. Deafness; M: Muscle involvement; GIT: Gastro-intestinal involvement; R: Renal involvement; C: Cardiac involvement; E: Endocrine abnormalities; L: Liver involvement; S: Skeletal involvement; Skin: Skin involvement; VUS: variant of uncertain significance.