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Review

Collated mutations in mitochondrial DNA (mtDNA) depletion syndrome (excluding the mitochondrial gamma polymerase, POLG1)

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ABSTRACT

These tables list both published and a number of unpublished mutations in genes associated with early onset defects in mitochondrial DNA (mtDNA) maintenance including C10orf2, SUCLG1, SUCLA2, TYMP, RRM2B, MPV17, DGUOK and TK2. The list should not be taken as evidence that any particular mutation is pathogenic. We have included genes known to cause mtDNA depletion, excluding POLG1, because of the existing database (http://tools.niehs.nih.gov/polg/). We have also excluded mutations in *C10orf2* associated with dominant adult onset disorders.

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Table 1
Reference sequences used.

Gene	Ref Seq
C10orf2	NM_021830.3
SUCLG1	NM_003849.2
SUCLA2	NM_003850.2
TYMP	NM_001113755.1
RRM2B	NM_015713.3
MPV17	NM_002437.4
DGUOK	NM_080916.1
TK2	NM_004614.3

Table 2
Mutations in the Twinkle helicase gene, *C10orf2*, associated with mtDNA depletion syndrome.

Gene	Mutation	Protein	Reference or contributor (if unpublished)
C10orf2	c.952G>A	p.A318T	[1]
C10orf2	c.1287C>T	Reduced mRNA level	[2]
C10orf2	c.1370C>T	p.T457I	[3]
C10orf2	c.1523A>G	p.Y508C	[2]
Ref Seq	NM_021830.3		

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Table 3
Mutations in the genes for the α subunit *SUCLG1* and ATP dependent β subunit *SUCLA2* of succinyl CoA ligase associated with mtDNA depletion syndrome.

Gene	Mutation	Protein	Reference or contributor (if unpublished)
SUCLG1	c.152_153delAT	p.Y51CfsX2	[4]
SUCLA2	c.352G>A	p.G118R	[5]
SUCLA2	c.[454T>A; 456C>A]	p.C152R	Rita Horvath and Birgit Czermin
SUCLA2	c.534+1G>A	Splice mutation	[6]
SUCLA2	c.789_802+29delinsATAAA	Splice mutation	[7]
SUCLA2	c.850C>T	p.R284C	[5]
SUCLG1 Ref Seq	NM_003849.2		
SUCLA2 Ref Seq	NM_003850.2		

Table 4
Mutations in the thymidine phosphorylase gene, *TYMP*, associated with myoneurogastrointestinal encephalomyopathy, MNGIE.

Gene	Mutation	Protein	Reference or contributor (if unpublished)
TYMP	c.51_52delCT	p.F18LfsX105	[8]
TYMP	c.99dupC	p.K34QfsX90	[9]
TYMP	c.128A>C	p.K43T	[10]
TYMP	c.131G>A	p.R44Q	[11]
TYMP	c.162C>G	p.I54M	[12]
TYMP	c.215-1G>C	Splice mutation	[13]
TYMP	c.228G>A	p.M76I	[14]
TYMP	c.261G>T	p.E87D	[15]
TYMP	c.275C>A	p.T92N	[16]
TYMP	c.340G>A	p.D114N	[15]
TYMP	c.398T>C	p.L133P	[17]
TYMP	c.433G>A	p.G145R	[18]
TYMP	c.457G>A	p.G153S	[18]
TYMP	c.467A>G	p.D156G	[10]
TYMP	c.478T>C	p.S160P	[18]
TYMP	c.516+2T>C	Splice mutation	[18]
TYMP	c.518T>G	p.M173R	[8]
TYMP	c.530T>C	p.L177P	[8]
TYMP	c.605G>C	p.R202T	[19]
TYMP	c.605G>A	p.R202K	Rita Horvath and Birgit Czermin
TYMP	c.622G>A	p.V208M	[19]
TYMP	c.665A>G	p.K222R	[18]
TYMP	c.707T>C	p.F236S	[20]
TYMP	c.760A>C	p.T254P	[10]
TYMP	c.784delC	p.L262X	[15]
TYMP	c.847C>G	p.H283D	[14]
TYMP	c.854T>C	p.L285P	[19]
TYMP	c.856G>A	p.E286K	[15]
TYMP	c.865G>A	p.E289K	[8]
TYMP	c.866A>C	p.E289A	[18]
TYMP	c.928+1G>A	Splice mutation	[15]
TYMP	c.929-6_929-3delCCGC	Splice mutation	[18,8]
TYMP	c.931G>C	p.G311R	[19]
TYMP	c.938T>C	p.L313P	[10]
TYMP	c.994_1011dup	p.A332_G337dup	[21]
TYMP	c.1088delG	p.G363EfsX151	Monica Arenas Hernandez
TYMP	c.1112T>C	p.L371P	[12]
TYMP	c.1160-1G>C	Splice mutation	[18]
TYMP	c.1160-1G>A	Splice mutation	[8]
TYMP	c.1160G>A	p.G387D	[15]
TYMP	c.1193_1198del	p.A398_L399del	[18]
TYMP	c.1211dupT	p.G405RfsX107	[10]
TYMP	c.1282G>A	p.G428S	[10]
TYMP	c.1299T>A	Splice mutation	[12]
TYMP	c.1300+1G>A	Splice mutation	[22]
TYMP	c.1301-1G>A	Splice mutation	[18]
TYMP	c.1327_1346del	p.D443PfsX62	[23]
TYMP	c.1393G>A	p.A465T	[12,24]
TYMP	c.1410dupC	p.S471LfsX41	[18]
TYMP	c.1412C>T	p.S471L	[18]
TYMP	c.1412C>A	p.S471X	[25]
TYMP	c.1431dupT	p.L478SfsX34	Monica Arenas Hernandez and Jo Poulton
Ref Seq	NM_001113755.1		

Table 5
Mutations in the gene for the p53 dependent β subunit of ribonucleotide reductase, *RRM2B*, associated with mtDNA depletion syndrome.

Gene	Mutation	Protein	Reference or contributor (if unpublished)
RRM2B	c.190T>C	p.W64R	[26]
RRM2B	c.253_255delGAG	p.E85del	[26]
RRM2B	c.322-2A>G	Splice mutation	[26]
RRM2B	c.580G>A	p.E194K	[26]
RRM2B	c.581A>G	p.E194G	[26]
RRM2B	c.584delG	p.G195EfsX14	[27]
RRM2B	c.671T>G	p.I224S	[27]
RRM2B	c.846G>C	p.M282I	[27]
RRM2B	c.850C>T	p.Q284X	[26]
RRM2B	c.920delA	p.N307IfsX11	[27]
RRM2B	c.949T>G	p.L317V	[27]
Ref Seq	NM_015713.3		

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Table 6
Mutations in the *MPV17* gene associated with mtDNA depletion syndrome.

Gene	Mutation	Protein	Reference or contributor (if unpublished)
MPV17	c.70G>T	p.G24W	[28]
MPV17	c.70+5G>A	Splice mutation	[29]
MPV17	c.116_140del	p.E39GfsX6	[30]
MPV17	c.148C>T	p.R50W	[31,30]
MPV17	c.149G>A	p.R50Q	[30]
MPV17	c.186+1G>T	Splice mutation	Massimo Zeviani
MPV17	c.206G>A	p.W69X	[31]
MPV17	c.234_242del	p.G79_T81del	[31]
MPV17	c.263_265delAGA	p.K88del	[31]
MPV17	c.284delG	p.G95AfsX7	Massimo Zeviani
MPV17	c.359G>A	p.W120X	[28]
MPV17	c.462-903_*420+177delinsC	Exon 8 deletion	[28]
MPV17	c.498C>A	p.N166K	[30]
Ref Seq	NM_002437.4		

Table 7
Mutations in the deoxyguanosine kinase gene, *DGUOK*, associated with mtDNA depletion syndrome.

Gene	Mutation	Protein	Reference or contributor (if unpublished)
DGUOK	c.1A>G	p.M1V	[32]
DGUOK	c.2T>C	p.M1T	[32,33,34,34]
DGUOK	c.3G>A	p.M1I	[32,33]
DGUOK	c.4G>T	p.A2S	[35]
DGUOK	c.20_23delTTCT	p.F7X	Claude Jardel and Anne Lombès
DGUOK	c.81delC	p.S28PfsX28	[32]
DGUOK	c.130G>A	p.E44K	[36]
DGUOK	c.137A>G	p.N46S	[32,35]
DGUOK	c.142+1G>A	Splice mutation	[32,35]
DGUOK	c.151A>C	p.K51Q	[32]
DGUOK	c.155C>T	p.S52F	[32,33]
DGUOK	c.195G>A	p.W65X	[32]
DGUOK	c.235C>T	p.Q79X	[32,37]
DGUOK	c.255delA	p.A86PfsX13	[38,32]
DGUOK	c.256-2A>C	Splice mutation	[32]
DGUOK	c.313C>T	p.R105X	[32,39]
DGUOK	c.318G>A	p.W106X	[32,37]
DGUOK	c.319T>C	p.S107P	[32]
DGUOK	c.352C>T	p.R118C	[32]
DGUOK	c.424_425delAG	p.R142VfsX5	[32]
DGUOK	c.425G>A	p.R142K	[32,40]
DGUOK	c.444-11C>G	Splice mutation	[32]
DGUOK	c.487_490dupGACA	p.I164RfsX53	[32]
DGUOK	c.493G>A	p.E165K	Claude Jardel and Anne Lombès
DGUOK	c.494A>T	p.E165V	[32,34]
DGUOK	c.509A>G	p.Q170R	[32,33]
DGUOK	c.533G>A	p.W178X	[32]
DGUOK	c.572A>G	p.Y191C	[32]
DGUOK	c.591G>A	Splice mutation	[32,35]
DGUOK	c.592-8T>G	Splice mutation	[36]
DGUOK	c.592-4_592-3delTT	Splice mutation	[32]
DGUOK	c.605_606delGA	p.R202TfsX13	[32,41]
DGUOK	c.609_610delGT	p.Y204PfsX11	[40]
DGUOK	c.632A>G	p.E211G	[34]
DGUOK	c.677A>G	p.H226R	[32]
DGUOK	c.677dupA	p.H226QfsX15	Jo Poulton and Carl Fratter
DGUOK	c.679G>A	p.E227K	[40]
DGUOK	c.707+3_707+6delAAGT	Splice mutation	Claude Jardel and Anne Lombès, Rita Horvath and Birgit Czermin
DGUOK	c.737C>G	p.P246R	[42]
DGUOK	c.749T>C	p.L250S	[32,41]
DGUOK	c.763G>T	p.D255Y	[32,43]
DGUOK	c.763_766dupGATT	p.F256X	[32,40]
DGUOK	c.797T>G	p.L266R	[32,35,34]
Ref Seq	NM_080916.1		

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Table 8
Mutations in the mitochondrial thymidine kinase gene, *TK2*, associated with mtDNA depletion syndrome.

Gene	Mutation	Protein	Reference or contributor (if unpublished)
TK2	c.134dupT	p.W46VfsX40	Claude Jardel and Anne Lombès
TK2	c.259C>T	p.Q87X	[44]
TK2	c.268dupG	p.E90GfsX102	[45]
TK2	c.282+2T>C	Splice mutation	Rita Horvath and Birgit Czermin
TK2	c.285C>G	p.I95M	[46]
TK2	c.299A>G	p.N100S	[44]
TK2	c.317C>T	p.T106M	[47]
TK2	c.324C>G	p.C108W	[48]
TK2	c.394C>T	p.R132C	Claude Jardel and Anne Lombès
TK2	c.404A>G	p.N135S	[49]
TK2	c.449C>T	p.T150M	[46,41,50]
TK2	c.460T>A	p.Y154N	[36]
TK2	c.486_487delinsAA	p.H163N	[51,46]
TK2	c.499C>T	p.Q167X	[49]
TK2	c.514C>T	p.R172W	[52]
TK2	c.515G>A	p.R172Q	[36]
TK2	c.542C>T	p.A181V	[48]
TK2	c.673C>G	p.R225G	[45,53]
TK2	c.673C>T	p.R225W	[47,52]
TK2	c.701G>A	p.R234K	[41]
TK2	c.730_732delAAG	p.K244del	[53]
TK2	c.761T>A	p.I254N	[51]
TK2	c.770T>C	p.L257P	[48]
TK2	c.886C>T	p.R296X	[45]
Ref Seq	NM_004614.3		

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