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## Accepted Manuscript

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

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**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These tables list both published and a number of unpublished mutations in genes associated with early onset defects in mitochondrial DNA (mtDNA) maintenance including C10orf2, SUCLG1, SUCLA2, TYMP, RRM2B, MPV17, DGUOK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.

Keywords mtDNA, mtDNA depletion, C10orf2, SUCLG1, SUCLA2, TYMP, RRM2B, MPV17, DGUOK,TK2.

Table 1: Reference sequences used

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

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

Gene	Mutation	Protein	Ref or Contributor (if unpublished)
<i>C10orf2</i>	c.952G>A	p.A318T	[1]
<i>C10orf2</i>	c.1287C>T	reduced mRNA level	[2]
<i>C10orf2</i>	c.1370C>T	p.T457I	[3]
<i>C10orf2</i>	c.1523A>G	p.Y508C	[2]
Ref Seq	<b>NM_021830.3</b>		

Table 3: Mutations in the genes for the  $\alpha$  subunit *SUCLG1* and ATP dependent  $\beta$  subunit *SUCLA2* of Succinyl CoA ligase associated with mtDNA depletion syndrome

Gene	Mutation	Protein	Ref or Contributor (if unpublished)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

Table 4: Mutations in the Thymidine phosphorylase gene, *TYMP*, associated with myoneurogastrointestinal encephalomyopathy, MNGIE

Gene	Mutation	Protein	Ref or Contributor (if unpublished)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



<i>TYMP</i>	c.1327_1346del	p.D443PfsX62	[23]
<i>TYMP</i>	c.1393G>A	p.A465T	[12] [24]
<i>TYMP</i>	c.1410dupC	p.S471LfsX41	[18]
<i>TYMP</i>	c.1412C>T	p.S471L	[18]
<i>TYMP</i>	c.1412C>A	p.S471X	[25]
<i>TYMP</i>	c.1431dupT	p.L478SfsX34	Monica Arenas Hernandez & Jo Poulton
Ref Seq	<b>NM_001113755.1</b>		

Table 5: Mutations in the gene for the p53 dependent  $\beta$  subunit of ribonucleotide reductase, *RRM2B*, associated with mtDNA depletion syndrome

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

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

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

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

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

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

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

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