

Title: Ornithine Transcarbamylase Deficiency *GeneReview* Table 8

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Note: The following information is provided by the authors listed above and has not been reviewed by *GeneReviews* staff.

Table 8. Notable OTC Pathogenic Variants

Reference Sequence	DNA Nucleotide Change	Predicted Protein Change	Comment [Reference]
NM_000531.6 NP_000522.3	c.1A>T	p.Met1Leu	Loss of translation initiation [Yamaguchi et al 2006]
	c.77G>A	p.Arg26Gln	May affect splicing of intron 1 & OTC import into mitochondria [Grompe et al 1989]
	c.77G>C	p.Arg26Pro	May affect splicing of intron 1 & OTC import into mitochondria [Kim et al 2006]
	c.134T>C	p.Leu45Pro	Replacement w/Pro may disrupt secondary structure and folding of OTC protein [Grompe et al 1989].
	c.140A>T	p.Asn47Ile	Predicted disruption of protein-protein interactions [Tuchman et al 1997, Haskins et al 2020]
	c.154G>A	p.Glu52Lys	Predicted disruption of protein-protein interactions [McCullough et al 2000, Haskins et al 2020]
	c.155A>G	p.Glu52Gly	Predicted disruption of protein-protein interactions [Yamaguchi et al 2006, Haskins et al 2020]
	c.158T>G	p.Ile53Ser	Replacement of hydrophobic Ile w/hydrophilic Ser may disrupt OTC protein folding [Yamaguchi et al 2006].
	c.170T>A	p.Leu57Gln	Replacement of hydrophobic Leu w/hydrophilic Gln may disrupt OTC protein folding [Yamaguchi et al 2006].
	c.196A>G	p.Arg66Gly	Kido et al [2021]
	c.227T>C	p.Leu76Ser	Genet et al [2000]
	c.236G>A	p.Gly79Glu	Tuchman et al [1992]
	c.248G>A	p.Gly83Asp	Replacement of Gly w/bulky Asp may disrupt OTC protein folding [Bartholomew & McClellan 1998].
	c.275G>A	p.Arg92Gln	Carbamyl phosphate binding site [Grompe et al 1991]

c.275G>T	p.Arg92Leu	Carbamyl phosphate binding site [Yamaguchi et al 2006]
c.275G>C	p.Arg92Pro	Carbamyl phosphate binding site [Yamaguchi et al 2006]
c.304G>C	p.Ala102Pro	Replacement w/Pro may disrupt secondary structure & folding of OTC protein [Storkanova et al 2013].
c.305C>A	p.Ala102Glu	Tuchman et al [1997]
c.374C>T	p.Thr125Met	Predicted disruption of protein-protein interactions [Gilbert-Dussardier et al 1996, Haskins et al 2020]
c.377A>G	p.Asp126Gly	Matsuura et al [1994]
c.418G>C	p.Ala140Pro	Replacement w/Pro may disrupt secondary structure & folding of OTC protein [Yamaguchi et al 2006].
c.422G>A	p.Arg141Gln	Carbamyl phosphate binding site [Maddalena et al 1988]
c.443T>C	p.Leu148Ser	Replacement of hydrophobic Leu w/hydrophilic Ser may disrupt OTC protein folding [Yamaguchi et al 2006].
c.464C>A	p.Ala155Glu	Replacement of small, hydrophobic Ala residue w/bulky, charged Glu may disrupt OTC protein folding [Yamaguchi et al 2006].
c.479T>A	p.Ile160Asn	Replacement of hydrophobic Ile w/hydrophilic Asn may disrupt OTC protein folding [Yamaguchi et al 2006].
c.479T>C	p.Ile160Thr	Replacement of hydrophobic Ile w/hydrophilic Thr may disrupt OTC protein folding [Yamaguchi et al 2006].
c.481A>G	p.Asn161Asp	Genet et al [2000]
c.482A>G	p.Asn161Ser	Tuchman & Plante [1995]
c.484G>A	p.Gly162Arg	Replacement of Gly w/bulky, charged Arg may disrupt OTC protein folding [Feldmann et al 1992].
c.485G>A	p.Gly162Glu	Replacement of Gly w/bulky, charged Glu may disrupt OTC protein folding [Yamaguchi et al 2006].
c.490T>C	p.Ser164Pro	Yamaguchi et al [2006]
c.505C>T	p.Pro169Ser	Kido et al [2021]
c.506C>T	p.Pro169Leu	Genet et al [2000]
c.516C>G	p.Ile172Met	Matsuura et al [1994]
c.526T>C	p.Tyr176His	Tuchman et al [2002]
c.533C>T	p.Thr178Met	Oppliger Leibundgut et al [1995]

c.536T>C	p.Leu179Pro	Replacement w/Pro may disrupt secondary structure & folding of OTC protein [Yamaguchi et al 2006].
c.539_540AG>CC	p.Gln180Pro	Replacement w/Pro may disrupt secondary structure & folding of OTC protein [Hubler et al 2001].
c.542A>G	p.Glu181Gly	May affect splicing of intron 5 [Tuchman et al 1998]
c.545A>T	p.His182Leu	Tuchman et al [1994a]
c.548A>G	p.Tyr183Cys	Reish et al [1993]
c.562G>C	p.Gly188Arg	Gilbert-Dussardier et al [1996]
c.572T>G	p.Leu191Arg	Replacement of hydrophobic Leu w/charged Arg may disrupt OTC protein folding [Yamaguchi et al 2006].
c.576C>G	p.Ser192Arg	Replacement of Ser w/bulky, charged Arg may disrupt OTC protein folding [Matsuura et al 1993].
c.583G>A	p.Gly195Arg	Replacement of Gly w/bulky, charged Arg may disrupt OTC protein folding [Tuchman et al 1994b].
c.586G>T	p.Asp196Tyr	Tuchman et al [1998]
c.587A>T	p.Asp196Val	Matsuura et al [1993]
c.593A>T	p.Asn198Ile	Yamaguchi et al [2006]
c.596A>G	p.Asn199Ser	Ornithine binding site [Tuchman et al 2002]
c.602T>C	p.Leu201Pro	Replacement w/Pro may disrupt secondary structure & folding of OTC protein [Shimadzu et al 1998].
c.613A>G	p.Met205Val	Genet et al [2000]
c.614T>C	p.Met205Thr	Kim et al [2006]
c.617T>G	p.Met206Arg	Bowling et al [1999]
c.620G>A	p.Ser207Asn	Yamaguchi et al [2006]
c.621C>A	p.Ser207Arg	Shimadzu et al [1998]
c.626C>T	p.Ala209Val	Garcia-Perez et al [1995]
c.640C>T	p.His214Tyr	Yoo et al [1996]
c.646C>G	p.Gln216Glu	Grompe et al [1989]
c.659C>T	p.Pro220Leu	Yamaguchi et al [2006]
c.663G>C	p.Lys221Asn	Yamaguchi et al [2006]
c.674C>G	p.Pro225Arg	Garcia-Perez et al [1997]
c.674C>T	p.Pro225Leu	Hentzen et al [1991]
c.698C>T	p.Ala233Val	Yamaguchi et al [2006]

	c.716A>T	p.Glu239Val	Yamaguchi et al [2006]
	c.740C>A	p.Thr247Lys	Tuchman & Plante [1995]
	c.746A>G	p.Asp249Gly	Kim et al [2006]
	c.757G>A	p.Ala253Thr	Yamaguchi et al [2006]
	c.757G>C	p.Ala253Pro	Replacement w/Pro may disrupt secondary structure & folding of OTC protein [Yamaguchi et al 2006].
	c.806G>A	p.Gly269Glu	Ornithine binding site [Zimmer et al 1995]
	c.842T>C	p.Phe281Ser	Kim et al [2006]
	c.860C>T	p.Thr287Ile	Lu et al [2020]
	c.867G>C	p.Lys289Asp	Predicted disruption of protein-protein interactions [Caldovic et al 2015, Haskins et al 2020]
	c.867G>T	p.Lys289Asn	Predicted disruption of protein-protein interactions [Tuchman et al 2002, Haskins et al 2020]
	c.893G>C	p.Trp298Ser	Ensenauer et al [2005]
	c.904C>T	p.His302Tyr	Catalytic site [Oppliger Leibundgut et al 1995]
	c.905A>G	p.His302Arg	Catalytic site [Genet et al 2000]
	c.907T>C	p.Cys303Arg	Catalytic site [Calvas et al 1998]
	c.907T>G	p.Cys303Gly	Catalytic site [Tuchman et al 2002]
	c.914C>G	p.Pro305Arg	Catalytic site [Yamaguchi et al 2006]
	c.932T>A	p.Val311Glu	Replacement of hydrophobic Val w/charged Glu may disrupt OTC protein folding [Caldovic et al 2015].
	c.959G>T	p.Arg320Leu	Predicted disruption of protein-protein interactions [Grompe et al 1989, Haskins et al 2020]
	c.994T>A	p.Trp332Arg	Rapp et al [2001]
	c.995G>C	p.Trp332Ser	Wang et al [2014]
	c.1005G>A	p.Met335Ile	Tuchman et al [2002]
	c.1015G>C	p.Val339Leu	Tuchman et al [1997]
	c.1016T>G	p.Val339Gly	Wang et al [2014]
	c.1028C>G	p.Thr343Arg	Caldovic et al [2015]
	c.1039C>T	p.Pro347Ser	Caldovic et al [2015]
NM_000531.6	c.540+265G>A	--	Deep intronic variant. Creates a novel acceptor splice site allowing use of a cryptic donor splice site in intron 5 and insertion of 135 bp between exons 5 and 6 of the <i>OTC</i> mRNA [Engel et al 2008, Kumar et al 2021]

	c.867+1126A>G	--	Deep intronic variant. Creates a novel donor splice site allowing use of two cryptic acceptor splice sites in intron 8 and insertion of either 22 or 117 bp between exons 8 and 9 of the <i>OTC</i> mRNA [Engel et al 2008]
	c.1005+1091C>G	--	Deep intronic variant. Creates a novel donor splice site allowing use of two cryptic acceptor splice sites in intron 9 and insertion of either 181 or 184 bp between exons 9 and 10 of the <i>OTC</i> mRNA [Engel et al 2008]

Variants listed in the table have been provided by the authors. GeneReviews staff have not independently verified the classification of variants.

GeneReviews follows the standard naming conventions of the Human Genome Variation Society (varnomen.hgvs.org). See [Quick Reference](#) for an explanation of nomenclature.

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