

Point missense & nonsense mutations found in the AGT gene (AGXT) in PH1

Nucleotide changes				Amino acid changes			Segregating amino acid at position 11	Allelic frequency	Molecular phenotype	Reference first reporting mutation
Exon No.	Base no.	Normal base	Mutant base	Residue No.	Normal residue	Mutant residue				
1	2	T	C	1	Met	Thr				Yuen et al, <i>J.Inher.Metab.Dis.</i> 26 (Suppl 2) 196 (2003)
1	121	G	A	41	Gly	Arg	Pro/Leu		Intraperoxisomal aggregation & accelerated degradation	Danpure et al, <i>Am.J.Hum.Genet.</i> 53, 417-432 (1993)
1	122	G	T	41	Gly	Val	Pro			Pirulli et al, <i>Hum.Genet.</i> 104, 523-525 (1999)
2	198	C	G	66	Tyr	Ter	Pro			Purdue et al, <i>Hum.Genet.</i> 87, 394-396 (1991)
2	244	G	A	82	Gly	Arg	Leu			Van Woerden et al, <i>Kid.Int.</i> 66, 746-752 (2004)
2	245	G	A	82	Gly	Glu	Pro		Inhibition of cofactor binding & loss of catalytic activity	Purdue et al, <i>Genomics</i> 13, 215-218 (1992)
2	322	T	C	108	Trp	Arg	Leu	11% (Italy)		von Schnakenburg et al, <i>J.Nephrol.</i> 11, 15-17 (1998)
2	331	C	T	111	Arg	Ter	Pro			Coulter-Mackie et al, <i>Mol.Genet.Metab.</i> 82, 64-68 (2004)
2	336	C	A	112	Ala	Asp	Pro			Coulter-Mackie et al, <i>Mol.Genet.Metab.</i> 78, 44-50 (2003)
2	346	G	A	116	Gly	Arg	Pro			Pirulli et al, <i>Hum.Genet.</i> 104, 523-525 (1999)
4	454	T	A	152	Phe	Ile	Leu	1-7%		Danpure et al, <i>Am.J.Hum.Genet.</i> 53, 417-432 (1993)
4	466	G	A	156	Gly	Arg	Pro	11% (Italy)		Pirulli et al, <i>Hum.Genet.</i> 104, 523-525 (1999). Rinat et al, <i>J.Am.Soc.Nephrol.</i> 10, 2352-2358 (1999)
4	508	G	A	170	Gly	Arg	Leu	15-35% (Europe & N. America)	Peroxisome-to-mitochondrion mistargeting	Purdue et al, <i>J.Cell Biol.</i> 111, 2341-2351 (1990)
4	518	G	A	173	Cys	Tyr	Pro			von Schnakenburg et al, <i>J.Nephrol.</i> 11, 15-17 (1998)
5	547	G	A	183	Asp	Asn	Pro			Basmaison et al, <i>Hum.Mutat.</i> online #327 (2000)
5	560	C	T	187	Ser	Phe	Pro			Minatogawa et al, <i>Hum.Mol.Genet.</i> 1, 643-644 (1992)
5	568	G	A	190	Gly	Arg	Pro	3%		von Schnakenburg et al, <i>J.Nephrol.</i> 11, 15-17 (1998)
5	584	T	G	195	Met	Arg				Frishberg et al. <i>Am.J.Nephrol.</i> 25, 269-275 (2005)
6	613	T	C	205	Ser	Pro	Pro		Accelerated degradation	Nishiyama et al, <i>Biochem.Biophys.Res. Commun.</i> 176, 1093-1099 (1991)
6	653	C	T	218	Ser	Leu	Pro			Coulter-Mackie et al, <i>Mol.Genet.Metab.</i> 86, 172-178 (2005)
7	697	C	T	233	Arg	Cys	Leu			von Schnakenburg et al, <i>J.Med.Genet.</i> 34, 489-492 (1997)
7	698	G	A	233	Arg	His				von Schnakenburg et al, <i>J.Med.Genet.</i> 34, 489-492 (1997)
7	727	G	C	243	Asp	His				Frishberg et al. <i>Am.J.Nephrol.</i> 25, 269-275 (2005)
7	731	T	C	244	Ile	Thr	Leu	6-9% (much greater in parts of Spain)	Accelerated degradation & possible aggregation	von Schnakenburg et al, <i>J.Med.Genet.</i> 34, 489-492 (1997)
7	738	G	A	246	Trp	Ter	Pro			von Schnakenburg et al, <i>J.Med.Genet.</i> 34, 489-492 (1997)
7	753	G	A	251	Trp	Ter	Pro			Coulter-Mackie et al, <i>Mol.Genet.Metab.</i> 82, 64-68 (2004)
8	837	T	G	279	Ile	Met				Frishberg et al. <i>Am.J.</i>

**Other mutations (insertions, deletions, splice-site variations)
found in the AGT gene (AGXT) in PH1**

Location of mutation in AGXT gene	Nucleotide change	What happens	Consequence for AGT polypeptide	Reference first reporting mutation
Exon 1	33-34insC	insertion	frameshift	Pirulli et al, <i>Hum.Genet.</i> 104, 523-525 (1999)
E1	33delC	deletion	frameshift	Pirulli et al, <i>Hum.Genet.</i> 104, 523-525 (1999)
E2	227-228insTCACACT	insertion	frameshift	Basmaison et al, <i>Hum. Mutat. Online</i> #327 (2000)
E2	285-286insGAG	insertion	insertion of extra Glu between Glu95-Pro96	Pirulli et al, <i>Hum.Genet.</i> 104, 523-525 (1999)
I4	IVS4-1G→A	replacement	splice site mutation	Basmaison et al, <i>Hum. Mutat. Online</i> #327 (2000)
E5	570delG	deletion	frameshift	Coulter-Mackie et al, <i>Mol.Genet.Metab.</i> 82, 64-68 (2004)
E6/I6	679-(IVS6+2)delAAGT	deletion	frameshift	Coulter-Mackie et al, <i>Mol.Genet.Metab.</i> 74, 314-321 (2001)
E7	744delC	deletion	frameshift	Coulter-Mackie et al, <i>Mol.Genet.Metab.</i> 82, 64-68 (2004)
I7	IVS7-1G→C	replacement	splice site mutation	Coulter-Mackie et al, <i>Mol.Genet.Metab.</i> 82, 64-68 (2004)
E8	797-802delCATCAins ACAATCTAG	complex replacement (deletion + insertion)	frameshift	von Schnakenburg et al, <i>Nephron.</i> 778, 485-488 (1998)
E8	824-825insAG	insertion	frameshift	Yuen et al, <i>J.Inher.Metab.Dis.</i> 26 (Suppl 2) 196 (2003)
I8	IVS8+1G→T	replacement	splice site mutation	Coulter-Mackie et al, <i>Mol.Genet.Metab.</i> 82, 64-68 (2004)
I8	IVS8-3C→G	replacement	splice site mutation	Basmaison et al, <i>Hum. Mutat. Online</i> #327 (2000)
I8	IVS8-1G→A	replacement	splice site mutation	Basmaison et al, <i>Hum. Mutat. Online</i> #327 (2000)
E9	886-888delGCG	deletion	deletion of Ala296	von Schnakenburg et al, <i>J.Nephrol.</i> 11, 15-17 (1998)
E10	976delG	deletion	frameshift	Pirulli et al, <i>Hum.Genet.</i> 104, 523-525 (1999)
E10	983-988delCTGGCT	deletion	replacement of Ala328-Tyr330 by Asp	Coulter-Mackie et al, <i>Mol.Genet.Metab.</i> 82, 64-68 (2004)
E11	1125-1126delCG	deleted	frameshift	Coulter-Mackie et al, <i>Mol.Genet.Metab.</i> 74, 314-321 (2001)
5'-UTR-I5		macro (5kb) deletion		Coulter-Mackie et al, <i>Mol.Genet.Metab.</i> 74, 314-321 (2001)
5'-UTR-I7		macro (7kb) deletion		Nogueira et al, <i>Hum. Mutat. Online</i> #311 (2000)

Unless otherwise indicated, much of the information in this table has been taken from Coulter-Mackie & Rumsby, *Mol. Genet. Metab.* 83, 38-46 (2004)

Normal polymorphisms in the AGT gene (AGXT)

Nucleotide changes				Amino acid changes			Allelic frequency	Molecular phenotype	Reference first reporting polymorphism
Location	Base No.	Original base	New base	Residue No.	Original residue	New residue			
Exon 1	32	C	T	11	Pro	Leu	20%	5% of AGT rerouted from peroxisomes to mitochondria	Purdue et al, <i>J.Cell Biol.</i> 111, 2341-2351 (1990)
Exon 2	264	C	T	88	Ala	Ala		None (silent)	Purdue et al, <i>J.Cell Biol.</i> 111, 2341-2351 (1990)
Exon 6	654	G	A	218	Ser	Ser		None (silent)	Purdue et al, <i>Genomics</i> 10, 34-42 (1991)
Exon 10	976	G	A	326	Val	Ile		Unknown	Coulter-Mackie et al, <i>Mol.Genet.Metab.</i> 78, 44-50 (2003)
Exon 10	1020	A	G	340	Ile	Met	20%	Little or none	Purdue et al, <i>J.Cell Biol.</i> 111, 2341-2351 (1990)
3'-UTR	1220	C	A	---	---	---		Unknown	von Schnakenburg et al, <i>J.Med.Genet.</i> 34, 489-492 (1997)
Intron 1	74bp duplication						20%	None known	Purdue et al, <i>Hum.Genet.</i> 87, 394-396 (1991)
Intron 4	VNTR							None known	Danpure et al, <i>Hum.Genet.</i> 94, 55-64 (1994)