

**Table 1. Mutations of the *PAX3* gene characterized in Waardenburg syndrome.**

Exon	cDNA*	ARN/protein	In original paper	Inheritance	Phenotype	Remarks	Origin	Reference
Intron 1	c.86-2A>G	splice defect	86-2 A→G	familial	WS1			[Attaie et al., 1997]
	c.86-2A>T	splice defect	86→2A→T	?	WS1			[Soejima et al., 1997]
Exon 2	c.101dupG	p.Gln35ProfsX79	FS113TER	familial	WS1			[Morell et al., 1993]
	<b>c.115A&gt;T</b>	<b>p.Asn39Tyr</b>		<b>familial</b>	<b>WS1</b>			<b>This paper</b>
	c.133T>C	p.Phe45Leu	F45L	familial	WS1		America (indian) / UK / Ireland	[Tassabehji et al., 1994]
	c.139A>C	p.Asn47His	c.352A>C; Asn→His at 47	familial	WS3			[Hoth et al., 1993]
	c.141C>G	p.Asn47Lys		familial	CDHS			[Asher et al., 1996]
	c.142G>C	p.Gly48Arg	Gly48→Arg	familial	WS1			[Pandya et al., 1996]
	c.142_145dupGGCA	p.Pro50GlnfsX65	Ins146+4 (R49fsX160)	?	WS1		Turkey	[Wollnik et al., 2003]
	c.149C>T	p.Pro50Leu	Pro(CCG) to Leu(CTG) in exon 2	familial	WS1		Brazil	[Baldwin et al., 1992]
	c.167G>T	p.Arg56Leu	c.380G>T; Arg→Leu at 56	familial	WS1			[Hoth et al., 1993]
	<b>c.167G&gt;A</b>	<b>p.Arg56His</b>		<b>de novo</b>	<b>WS1</b>			<b>This paper</b>
	c.169delC	p.His57ThrfsX53	1bp del of (C)169	familial	WS1		France	[Pandya et al., 1996]
	c.175A>T	p.Ile59Phe	A to T, Ile to Phe at 59	familial	WS1			[Soejima et al., 1997]
	c.178G>A	p.Val60Met	V60M	?	WS1			[Baldwin et al., 1995]
	c.178G>A	p.Val60Met	G178A (V60M)	?	WS1		Turkey	[Wollnik et al., 2003]
	c.184A>G	p.Met62Val	M62V	familial	WS1			[Hol et al., 1998]
	c.185_202del18	p.Met62_Ile67del	loss of amino acids 29 to 34 of the paired domain	familial	WS1			[Tassabehji et al., 1992]
	c.191_207del17	p.His64LeufsX44	nt 191del(17)	?	WS1			[Tassabehji et al., 1995]
	<b>c.202C&gt;G</b>	<b>p.Arg68Gly</b>		<b>familial</b>	<b>WS1</b>			<b>This paper</b>
	c.218C>T	p.Ser73Leu	S73L	familial	WS1		Iran	[Sotirova et al., 2000]
	c.223C>T	p.Gln75X	Gln75→Term	familial	WS1		Italy	[Pandya et al., 1996]
c.?	p.Val78Met	V78M	?	WS1			[Tassabehji et al., 1995]	
<b>c.241G&gt;C</b>	<b>p.Gly81Arg</b>		<b>familial</b>	<b>WS1</b>			<b>This paper</b>	
c.242G>C	p.Gly81Ala	Gly to Ala in exon 2	familial	WS1	Initially reported as WS2		[Tassabehji et al., 1993]	
c.251C>T	p.Ser84Phe	S84F	familial	WS1 in heterozygotes WS3 in homozygotes	Consanguineous family	Palestin	[Zlotogora et al., 1995]	
c.253A>G	p.Lys85Glu	K85E	familial	WS1			[Baldwin et al., 1995]	
<b>c.260delT</b>	<b>p.Leu87ArgfsX23</b>		<b>?</b>	<b>WS1</b>			<b>This paper</b>	
c.266_279del14	p.Tyr90LeufsX19	14 bp deletion in the paired domain	familial	WS1		Indonesia	[Morell et al., 1992]	
c.268T>C	p.Tyr90His	T268C (Y90H)	familial	WS1 in heterozygotes WS3 in homozygotes	Consanguineous family	Turkey	[Wollnik et al., 2003]	
c.288delA	p.Arg97ValfsX13	Single base deletion in exon 2	familial	WS1			[Tassabehji et al., 1993]	
c.291dupT	p.Pro98SerfsX16	Insertion (T) in position 292	familial	WS1			[Wildhardt et al., 1996]	
c.?	p.Gly99Ser	G99S	?	WS3 (compound heterozygote)	p.[Gly99Ser]+[Arg270Cys]		[Bottani et al., 1999]	

	c.296G>A	p.Gly99Asp	G99D	familial	WS1		[Tassabehji et al., 1994]
	c.297_321+3del28	splice defect		familial	WS1		[Baldwin et al., 1994]
Exon 3	c.358delG	p.Glu120AsnfsX32	nt 358del(G)	?	WS1		[Tassabehji et al., 1995]
	c.365_369delAAAGA	p.Lys122ArgfsX21	nt 364del(5)	?	WS		[Tassabehji et al., 1995]
	c.385_397del13	p.Phe129SerfsX19	384del(13)	familial	WS3		[Tekin et al., 2001]
	c.434_449del16	p.Arg145GlnfsX2	434del16	?	WS3		[Read and Newton, 1997]
	<b>c.446delC</b>	<b>p.Pro149ArgfsX3</b>		<b>sporadic</b>	<b>WS1</b>		<b>This paper</b>
Intron 3	c.451+1G>T	splice defect		familial	WS1		[Tassabehji et al., 1994]
	c.451+1G>A	splice defect	G to A at exon3-intron 3 boundary	familial	WS	South Africa	[Butt et al., 1994]
	c.452-2A>G	splice defect		familial	WS1		[Tassabehji et al., 1994]
Exon 4	c.558_559delCA	p.His186GlnfsX17	CA deletion in exon 4	familial	WS1		[Tassabehji et al., 1993]
	c.?	p.Arg195X	R195X	?	WS1		[Read and Newton, 1997]
	c.586G>A	p.Ala196Thr or splice defect	A196T	sporadic	WS1	Asia	[Tassabehji et al., 1995]
	c.586G>A	p.Ala196Thr or splice defect	G586A (A196T)	familial	WS1	Turkey	[Wollnik et al., 2003]
Exon 5	c.598C>T	p.Gln200X	Q200X	familial	WS1	+ spina bifida in 2 patients	[Baldwin et al., 1995]
	c.598_602delCAATC	p.Gln200ArgfsX2	5bp deletion in exon 5	familial	WS1	+ spina bifida in 2 patients	[Hol et al., 1995]
	c.602C>A	p.Ser201X	S201X	familial	WS1		[Baldwin et al., 1995]
	c.626_627delCT	p.Ser209X	S209X	de novo	WS1		China [Yang et al., 2007]
	c.628G>T	p.Glu210X	Glu210→Term	familial	WS1	Same number of CA repeats in the 5' of the gene	[Pandya et al., 1996]
	c.628G>T	p.Glu210X	Glu210→Term	familial	WS1		Ireland? [Pandya et al., 1996]
	c.667C>T	p.Arg223X	Arg223 to stop	familial	WS1		[Baldwin et al., 1994]
	c.667C>T	p.Arg223X	Arg223→Term	familial	WS1		Ireland / UK / Italy / America (indian) / Germany [Pandya et al., 1996]
	c.667C>T	p.Arg223X	R223X	sporadic	WS1		China [Yang et al., 2007]
	<b>c.667C&gt;T</b>	<b>p.Arg223X</b>		<b>de novo</b>	<b>WS1</b>		<b>This paper</b>
	<b>c.667C&gt;T</b>	<b>p.Arg223X</b>		<b>familial</b>	<b>WS1</b>		<b>This paper</b>
	c.?	p.Arg223Gln	R223Q	familial	WS1		[DeStefano et al., 1998]
	c.701T>C	p.Leu234Pro	701T>C	familial	WS1		China [Qin et al., 2006]
	c.703G>T	p.Glu235X	E235X	familial	WS1		[Baldwin et al., 1995]
	<b>c.712_714delTTTins CATTACCCTG</b>	<b>p.Phe238HisfsX10</b>		<b>de novo</b>	<b>WS1</b>		<b>This paper</b>
	c.713T>C	p.Phe238Ser	F238S	?	WS1		[Baldwin et al., 1995]
	c.728A>C	p.Tyr243Ser		?	WS1	+ unilateral macular degeneration	[Kozawa et al., 2009]
	c.?	p.Glu251X	E251X	?	WS1		[Tassabehji et al., 1995]
	c.?	p.Gln254X	Q254X	?	WS1		[Tassabehji et al., 1995]
Intron 5	c.792+1G>A	splice defect	IVS5+1G>A	familial	WS1		Turkey [Wollnik et al., 2003]
Exon 6	c.793G>T	p.Val265Phe or splice defect	Valine to Phenylalanine at 265	familial	WS1		[Lalwani et al., 1995]

	c.?	p.Trp266X	W266X	?	WS1		[Read and Newton, 1997]
	c.?	p.Trp266Cys	W266C	?	WS1		[Tassabehji et al., 1995]
	c.799T>A	p.Phe267Ile	801T→A	?	WS1		[Nakamura et al., 2009]
	c.?	p.Asn269Leu	N269L	-	-	Found at the heterozygous state in a WS3 related	[Read and Newton, 1997]
	c.?	p.Arg270Cys	R270C	?	WS1		[Tassabehji et al., 1995]
	c.808C>T	p.Arg270Cys	Arg270→Cys	familial	WS1	Germany	[Pandya et al., 1996]
	c.?	p.Arg270Cys	R270C	?	WS3 (compound heterozygote)	p.[Gly99Ser]+[Arg270Cys]	[Bottani et al., 1999]
	c.?	p.Arg270Leu	R270L	?	WS1		[Read and Newton, 1997]
	c.811C>G	p.Arg271Gly	Arg 271 [GCC]→Gly 271 [GGC]	familial	WS1		[Lalwani et al., 1995]
	c.?	p.Arg271Cys	R271C	?	WS1		[Tassabehji et al., 1995]
	c.811C>T	p.Arg271Cys	C to T at 811, Arg to Cys at 271	?	WS1		[Wildhardt et al., 1996]
	c.811C>T	p.Arg271Cys	810C→T	familial	WS1		[Morell et al., 1997]
	<b>c.811C&gt;T</b>	<b>p.Arg271Cys</b>		<b>familial</b>	<b>WS1</b>		<b>This paper</b>
	c.?	p.Arg271His	R271H	?	WS1		[Tassabehji et al., 1995]
	c.[812G>A;818G>A]	p.[Arg271His;Arg273Lys]	Arg271→His; Arg273→Lys	familial	WS1	2 variations on the same allele; the effect of an isolated p.Arg273Lys is unknown	Germany / Holland [Pandya et al., 1996]
	c.?	p.Trp274X	W274X	?	WS1		[Tassabehji et al., 1995]
	c.821G>A	p.Trp274X	820G→A	familial	WS1		[Morell et al., 1997]
	c.844C>T	p.Gln282X	Q282X	familial	WS1	+ spina bifida in one patient	[Hol et al., 1998]
	<b>c.873dupC</b>	<b>p.Gly292ArgfsX118</b>		<b>familial</b>	<b>WS1</b>		<b>This paper</b>
	c.879dupG	p.Phe294ValfsX116	874ins1	familial	WS1	Possibly germ-line mosaicism	[Baldwin et al., 1995], [Morell et al., 1997]
	c.879dupG	p.Phe294ValfsX116	nt 874ins(G)	?	WS		[Tassabehji et al., 1995]
	c.879dupG	p.Phe294ValfsX116	nt 874ins(G)	?	WS1		[Tassabehji et al., 1995]
	<b>c.879delG</b>	<b>p.Phe294SerfsX87</b>		<b>familial</b>	<b>WS1</b>		<b>This paper</b>
	c.?	p.Tyr305X	Y305X	?	WS1		[Read and Newton, 1997]
	c.916delC	p.Gln306SerfsX75	nt 916del(C)	?	WS1 or WS3		[Tassabehji et al., 1995]
	<b>c.936C&gt;A</b>	<b>p.Tyr312X</b>		<b>?</b>	<b>WS1</b>		<b>This paper</b>
	c.937C>T	p.Gln313X	Q313X	familial	WS1		[Baldwin et al., 1995]
	c.954delA	p.Gln319LysfsX62	954del1	familial	WS1	+ spina bifida in 1 patient	[Baldwin et al., 1995]
Intron 6	<b>c.958+28A&gt;T</b>	<b>splice defect</b>		<b>?</b>	<b>WS1</b>	<b>In silico analysis predicts creation of a new donor splice site</b>	<b>This paper</b>
Exon 7	<b>c.965C&gt;A</b>	<b>p.Ser322X</b>		<b>familial</b>	<b>WS1</b>	<b>Likely germline mosaicism</b>	<b>This paper</b>
	c.1173G>C	p.Gln391His or splice defect	Q391H	familial	WS1	+ septo-optic dysplasia in the propositus	[Carey et al., 1998]
Exon 8	c.1185_1186insTGA	p.Leu396X	1185ins3	familial	WS1		Brazil [Baldwin et al., 1995]
	<b>c.1271delC</b>	<b>p.Thr424ArgfsX10</b>		<b>familial</b>	<b>WS1</b>		<b>Guadeloupe</b> <b>This paper</b>

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Non synonymous polymorphisms as reported in literature and in dbSNP (when confirmed in at least one control population):

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Exon 6	c.944C>A	p.Thr315Lys	T315K	rs2234675 in dbSNP frequency 0.00 - 0.08	[Tassabehji et al., 1995]
Exon 7	c.1121C>T	p.Ser374Leu		rs45607236 in dbSNP frequency 0.00 - 0.03	

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\*cDNA nucleotide numbering with +1 as the A of the initiation codon in the reference sequence NM\_181457.2. CDHS = craniofacial-deafness-hand syndrome.