

Hematologically Important Mutations: Red Cell Pyruvate Kinase

(1st update)

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Pyruvate kinase (PK) deficiency is known to be the most common cause of chronic nonspherocytic hemolytic anemia (CNSHA). Two PK genes are present in mammals, *PKLR* and *PKM*, but only the former codes for the isoenzyme normally expressed in the red cell (R-type).

A total of 82 mutations in the *PKLR* gene associated with CNSHA are here reported in Table 1, whereas Table 2 provides the polymorphic sites identified in the gene. Mutations and polymorphisms are designated using the cDNA sequence of the R-type isoenzyme and genomic DNA sequence of the *PKLR* gene, with the A of the initiation ATG being assigned num-

ber +1. The GenBank accession numbers are D10326 D90465 for the cDNA and U47654 for the genomic DNA. The numbering system in the tables varies from that of GenBank and in order to designate the initiated A as +1 it is necessary to subtract 39 from the GenBank sequences.

Additional information can be found in the published reviews (1,2) and a continuously updated review can be found on the World Wide Web in OMIM at:

<http://www3.ncbi.nlm.nih.gov:80/htbinpost/Omim/dispim?266200>

Table 1. Mutations Reported in *PKLR* Gene

Variant Name ^a	cDNA Nucleotide Substitution	Genomic Nucleotide Substitution	Amino Acid Substitution	Exon	Reference
*	IVS2(-1) g → a	1105a	Splice Site	IVS2	(3)
“Essen”	183 16bp 184 ins	1188 16bp 1189 ins	Frameshift	3	(4)
*	227–231 TGGAC del	1232–1236 del	Frameshift	3	(5)
*	238 T → C	1243C	80 Ser → Pro	3	(6)
*	IVS3(-2) a → c	2467c	Splice Site	IVS3	(5)
*	307 C del	2492 del	Frameshift	4	(7)
*	320 T → C	2505C	107 Met → Thr	4	(8)
“Val de Marne”	343 G → C	2528C	115 la → Pro	4	(9)
“Beaujon”	359 C → T	2544T	120 Ser → Phe	4	(9)

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Table 1. (Continued)

Variant Name ^a	cDNA Nucleotide Substitution	Genomic Nucleotide Substitution	Amino Acid Substitution	Exon	Reference
*	391–393 ATC del	2672–2674 del	131 Ile del	5	(10)
*					(8)
*	401 T → A	2682A	134 Val → Asp	5	(10)
Beppu	434 C del	2715 del	Frameshift	5	(11)
*	464 T → C	2745C	155 Leu → Pro	5	(10)
Linz	487 C → T	2768T	163 Arg → Cys	5	(12)
Sassari	514 G → C	2928C	172 Glu → Gln	6	(5)
*	603 G → A	3017A	201 Trp → End	6	(8)
*	628–629 GT del	3042–3043 del	Frameshift	6	(13)
*	663 GAC 664 ins	3077 GAC 3078 ins	221 Asp 222 ins	6	(11)
*	721 G → T	3497T	241 Glu → End	7	(10)
“Bukarest”					(14)
*					(7)
*					(8)
*					(15)
*					(9)
*	787 G → A	3563A	263 Gly → Arg	7	(13)
“Torre Annunziata”	787 G → T	3563T	263 Gly → Trp	7	(16)
*	808 C → T	3584T	270 Arg → End	7	(7)
*	823 G → C	3599C	275 Gly → Arg	7	(8)
*	823 G → A	3599A	275 Gly → Arg	7	(5)
*	841 G → A	3617A	281 Asp → Asn	7	(11)
*	859 T → G	3635G	287 Phe → Val	7	(11)
“Dordrecht”	929 T → A	3705A	310 Ile → Asn	7	(17)
Hong Kong	941 T → C	3717C	314 Ile → Thr	7	(18)
Kowloon	IVS7(+1) g → t	3742t	Splice Site	IVS7	(19)
*	991 G → A	3863A	331 Asp → Asn	8	(4)
*	993 C → A	3865A	331 Asp → Glu	8	(7)
“Parma”					(16)
*	994 G → A	3866A	332 Gly → Ser	8	(3)
*					(20)
*					(21)
*					(13)
*	1006 G → T	3878T	336 Ala → Ser	8	(3)

Table 1. (Continued)

Variant Name ^a	cDNA Nucleotide Substitution	Genomic Nucleotide Substitution	Amino Acid Substitution	Exon	Reference
*	1010 G → C	3882C	337 Arg → Pro	8	(22)
*	1010 G → A	3882A	337 Arg → Gln	8	(13)
*	1022 G → C	3894C	341 Gly → Ala	8	(7)
*	1024 A → T	3896T	342 Ile → Phe	8	(21)
*	1055 C → A	3927A	352 Ala → Asp	8	(4)
*	1060–1062 AAG del	3932–3934 del	354 Lys del	8	(3)
*					(13)
*	1075 C → T	3947T	359 Arg → Cys	8	(11)
*	1076 G → A	3948A	359 Arg → His	8	(10)
*	1081 A → G	3953G	361 Asn → Asp	8	(3)
*					(13)
*	1089 G1090 ins	3961 G 3962 ins	Frameshift	8	(7)
Tjaereborg	1091 G → A	3963A	364 Gly → Asp	8	(23)
“Osaka”	1102 G → T	3974T	368 Val → Phe	8	(24)
*	1127 G → T	4643T	376 Ser → Ile	9	(13)
Tokio Beirut Nagasaki Mosul	1151 C → T	4667T	384 Thr → Met	9	(25)
					(12)
					(26)
					(14)
“Mantova”	1168 G → A	4684A	390 Asp → Asn	9	(15)
*	1174 G → A	4690A	392 Ala → Thr	9	(3)
*	1178 A → G	4694G	393 Asn → Ser	9	(7)
“Paris”					(9)
*	1179 T → A	4695A	393 Asn → lys	9	(7)
Mondor	1195 G del	4711 del	Frameshift	9	(27)
*	1203 AGC 1204 ins	4719 AGC 4720 ins	401 Cys 402 ins	9	(3)
Fukushima Maebashi Sendai	1261 C → A	4777A	421 Gln → Lys	9	(26)
					(26)
					(18)
*	1269 G → A	4785A	Splice Site	9	(11)
“Torre Annunziata”	1269 G → C	4785C	Splice Site	9	(20)
Naniwa *	1276 C → T	4886T	426 Arg → Trp	10	(11)
					(8)
Sapporo	1277 G → A	4887A	426 Arg → Gln	10	(28)

Table 1. (Continued)

Variant Name ^a	cDNA Nucleotide Substitution	Genomic Nucleotide Substitution	Amino Acid Substitution	Exon	Reference
*	1281G → T	4891T	427 Glu → Asp	10	(13)
*	1373 G → A	4983A	458 Gly → Asp	10	(7)
*	1376 C → T	4986T	459 Ala → Val	10	(8)
*	1378 G → A	4988A	460 Val → Met	10	(7)
*					(8)
Hadano	1403 C → T	5013T	468 Ala → Val	10	(18)
Amish Shinshu	1436 G → A	5046A	479 Arg → His and Splice Site	10	(29) (18)
Gypsy	1437–1618 del	5768–6905 del	Frameshift	11	(7)
*	1454 C → T	6303T	485 Ser → Phe	11	(13)
*	1456 C → T	6305T	486 Arg → Trp	11	(10)
*					(30)
*					(7)
“Soresina” Milano					(15)
“Parma” *					(15) (13)
*	1468 C → T	6317T	490 Arg → Trp	11	(11)
*					(6)
“Tama” “Gifu”					(31) (31)
*	1483 G → A	6332A	495 Ala → Thr	11	(4)
*	1484 C → T	6333T	495 Ala → Val	11	(10)
*					(7)
*					(8)
“Rouen”	1488 Cdel	6337 del	Frameshift	11	(9)
*	1492 C → T	6341T	498 Arg → Cys	11	(32)
*	1493 G → A	6342A	498 Arg → His	11	(7)
*					(3)
*	1501 C → T	6350T	501 Gln → End	11	(8)
*	1523 T → G	6372G	508 Leu → End	11	(30)
*	1529 G → A	6378A	510 Arg → Gln	11	(10)
*					(3)
“Hamburg”					(14)
“Koln”					(14)
Aprica					(20)
*					(30)
*	(7)				

Table 1. (Continued)

Variant Name ^a	cDNA Nucleotide Substitution	Genomic Nucleotide Substitution	Amino Acid Substitution	Exon	Reference
*					(8)
*					(9)
*					(23)
*					(13)
“Soresina”	1552 C → A	6401A	518 Arg → Ser	11	(5)
*	1574 G 1575 ins	6423 G 6424 ins	Frameshift	11	(8)
*	1594 C → T	6443T	532 Arg → Trp	11	(3)
“Bukarest”					(14)
*					(15)
*	1654 G → A	7568A	552 Val → Met	12	(8)
*	1675 C → G	7589G	559 Arg → Gly	12	(8)
*	1698 C → A	7612A	566 Asn → Lys	12	(11)

^a The variants reported in quotes have been found heterozygous for the corresponding mutation.

* The variant has no name.

Table 2. Polymorphisms Reported in the PKLR Gene

Polymorphis Site cDNA Number	Polymorphic Site Genomic Number	Exon	Reference
IVS5(+51)c/t	2838 C/T	IVS5	(33)
			(15)
			(34)
T _{10/19} ^a	5972–5981 (T ₁₀)	IVS11	(35)
Microsatellite ATT	7181–7222 (14 ATT)	IVS12	(36)
1705 A/C	7619 A/C	Exon 12	(26)
1738 C/T	7652 C/T	Exon 12	(15)
			(17)
1992 C/T	7906 C/T	Exon 12	(35)

^a T-stretch occurring in the two forms (T)₁₀ and (T)₁₉.

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