

Hematologically Important Mutations: Red Cell Pyruvate Kinase

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Pyruvate kinase (PK) deficiency is known to be the most common cause of chronic nonspherocytic hemolytic anemia. 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). To date 59 different mutations have been reported including missense, nonsense and splice site mutations, deletions and insertions. Mutations are designated

using the R-type cDNA sequence, with the A of the initiation ATG being assigned number 1. Amino acids are numbered from the first methionine of the deduced R-type enzyme. The twelve exons of the *PKLR* gene are numbered from 1 to 12. The cDNA sequences for the L/R-type are reported in GenBank with accession number J03640 and D90465. More information can be found in the published reviews (1,2).

Mutations reported in the *PKLR* gene

Variant Name ^a	cDNA Nucleotide Substitution	Amino Acid Substitution	Exon	Reference
*	IVS2(-1) g→a	Splice Site	IVS2	(3)
*	238 T→C	80 Ser→Pro	3	(4)
*	307 C→del	Frameshift	4	(5)
*	320 T→C	107 Met→Thr	4	(6)
*	391-392-393 ATC→del	131 Ile→del	5	(7)
*	401 T→A	134 Val→Asp	5	(7)
Beppu	434C→del	Frameshift	5	(8)
*	464 T→C	155 Leu→Pro	5	(7)
Linz	487 C→T	163 Arg→Cys	5	(9)
*	603 G→A	201 Trp→End	6	(6)

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Variant Name ^a	cDNA Nucleotide Substitution	Amino Acid Substitution	Exon	Reference
*	663 C→CGAC	221 Asp→AspAsp	6	(8)
* "Bukarest" *	721G→T	241 Glu→End	7	(7) (10) (11)
*	808 C→T	270 Arg→End	7	(5)
*	823 G→C	275 Gly→Arg	7	(6)
*	841 G→A	281 Asp→Asn	7	(8)
*	859 T→G	287 Phe→Val	7	(8)
Hong Kong	941 T→C	314 Ile→Thr	7	(12)
Kowloon	IVS7(+1) g→t	Splice Site	IVS7	(13)
*	993 C→A	331 Asp→Glu	8	(5)
* *	994 G→A	332 Gly→Ser	8	(3) (14)
*	1006 G→T	336 Ala→Ser	8	(3)
*	1010 G→C	337 Arg→Pro	8	(15)
*	1022 G→C	341 Gly→Ala	8	(5)
*	1060-1061-1062 AAG→del	354 Lys→del	8	(3)
*	1075 C→T	359 Arg→Cys	8	(8)
*	1076 G→A	359 Arg→His	8	(7)
*	1081 A→G	361 Asn→Asp	8	(3)
*	1089 G→GG	Frameshift	8	(5)
"Osaka"	1102 G→T	368 Val→Phe	8	(16)
Tokyo Beirut Nagasaki Mosul	1151 C→T	384 Thr→Met	9	(17) (9) (18) (10)
"Mantova"	1168 G→A	390 Asp→Asn	9	(11)
*	1174 G→A	392 Ala→Thr	9	(3)
*	1178 A→G	393 Asn→Ser	9	(5)
*	1179 T→A	393 Asn→Lys	9	(5)
*	1203 C→CAGC	401 Cys→CysSer	9	(3)

Variant Name ^a	cDNA Nucleotide Substitution	Amino Acid Substitution	Exon	Reference
Fukushima Maebashi Sendai	1261 C→A	421 Gln→Lys	9	(18) (18) (12)
*	1269 G→A	Splice Site	9	(8)
*	1269 G→C	Splice Site	9	(14)
*	1276 C→T	426 Arg→Trp	10	(8)
Sapporo	1277 G→A	426 Arg→Gln	10	(19)
*	1373 G→A	458 Gly→Asp	10	(5)
*	1376 C→T	459 Ala→Val	10	(6)
*	1378 G→A	460 Val→Met	10	(5)
Hadano	1403 C→T	468 Ala→Val	10	(12)
Amish Shinshu	1436 G→A	479 Arg→His/Splice Site	10	(20) (12)
Gypsy	1437-1618 (182 nt del)	ex 11 del/Frameshift	11	(5)
* * "Soresina" Milano "Parma"	1456 C→T	486 Arg→Trp	11	(7) (21) (11) (11) (11)
* * "Tama" "Gifu"	1468 C→T	490 Arg→Trp	11	(8) (4) (22) (22)
*	1484 C→T	495 Ala→Val	11	(7)
* *	1493 G→A	498 Arg→His	11	(5) (3)
*	1501 C→T	501 Gln→End	11	(6)
*	1523 T→G	508 Leu→End	11	(21)
* * "Hamburg" "Koln" * * *	1529 G→A	510 Arg→Gln	11	(7) (3) (10) (10) (14) (21) (6)
"Soresina"	1552 C→A	518 Arg→Ser	11	(23)
*	1574 G→GG	Frameshift	11	(6)

Variant Name ^a	cDNA Nucleotide Substitution	Amino Acid Substitution	Exon	Reference
* "Bukarest" *	1594 C→T	532 Arg→Trp	11	(3) (10) (11)
*	1654 G→A	552 Val→Met	12	(6)
*	1675 C→G	559 Arg→Gly	12	(6)
*	1698 C→A	566 Asn→Lys	12	(8)

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

* No name has been assigned.

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