

Hematologically Important Mutations: Molecular Abnormalities of Glucose Phosphate Isomerase Deficiency

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The primary structure of glucose phosphate isomerase (GPI) was found to be identical with neuroleukin by comparison of the cDNA sequences (GenBank Accession No. K03515) (1, 2). The cDNA sequence encodes 558 amino acid residues. The enzyme consists of two identical subunits with the molecular weight of approximately 63,000. In humans, GPI gene locus has been determined to be located on chromosome 19 (3), and the gene spans over 40 kilobases

including 18 exons and 17 introns (4-6).

GPI deficiency is the fourth most common hereditary enzyme defect of red cells. So far, more than 40 unrelated families have been reported (7). Among 15 patients which have been analysed, 16 missense mutations, 1 nonsense mutation and 1 splicing mutation due to a four nucleotide deletion at the junction of exon/intron 16 have been identified (table) (8-11).

Table: Molecular Abnormalities of Glucose Phosphate Isomerase (GPI) Deficiency

Variant Name	Genotype	cDNA Nucleotide Substitution	Deduced Amino Acid Substitution	Mutation on Other Allele	Reference
GPI Matsumoto	Homozygote	14 C → T	5 Thr → Ile	14 C → T	8
*	Homozygote	247 C → T	83 Arg → Trp	247 C → T	9
*	Homozygote	301 G → A	101 Val → Met	301 G → A	10
GPI Iwate	Homozygote	671 C → T	224 Thr → Met	671 C → T	8
GPI Narita, Morcone	Homozygote	1028 A → G	343 Gln → Arg	1028 A → G	8,10
*	Homozygote	1574 T → C	524 Ile → Thr	1574 T → C	11
GPI Fukuoka	Homozygote	1615 G → A	539 Asp → Asn	1615 G → A	8

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Variant Name	Genotype	cDNA Nucleotide Substitution	Deduced Amino Acid Substitution	Mutation on Other Allele	Reference
*	Heterozygote	286 C→T	nonsense mutation	584 C→T	10
*	Heterozygote	475 G→A	158 Gly→Ser	1040 G→A	11
*	Heterozygote	584 C→T	195 Thr→Ile	286 C→T exon/IVS-16 del	10
*	Heterozygote	818 G→A	273 Arg→His	1039 C→T	9
*	Heterozygote	833 C→T	278 Ser→Leu	1459 C→T	9
*	Heterozygote	1039 C→T	347 Arg→Cys	818 G→A	9
*	Heterozygote	1040 G→A	347 Arg→His	475 G→A	11
GPI 'Kinki'	Heterozygote	1124 C→G	375 Thr→Arg	1615 G→A	8
*	Heterozygote	exon/IVS-16 del	splicing mutation	584 C→T	10
*	Heterozygote	1459 C→T	487 Leu→Phe	833 C→T	9
*	Heterozygote	1483 G→A	495 Glu→Lys	671 C→T	9

*No name assigned.

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