

# Hematologically Important Mutations: Triosephosphate Isomerase

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The glycolytic enzyme triosephosphate isomerase (E 5.3.1.1) is coded in humans by a single gene, TPI1, located at 12p13. Thirteen mutations have now been described, an increase from the five listed in a prior tabulation (1), published less than 6 months ago.

The clinical syndrome of triosephosphate deficiency is inherited as an autosomal recessive disorder, characterized by hemolytic anemia and neuromuscular disease. Descriptions of the clinical manifestations can be found in the original publications on the disorder (2,3) and in the cited references. A continuously updated review can be found on the World Wide Web in OMIM at:

<http://www3.ncbi.nlm.nih.gov/htbin-post/Omim/dispim?190450>.

In accordance with recent recommendations for the use of systematic names in the nomenclature for mutations (4), both the cDNA and genomic DNA numbers presented here begin

with +1, which designates the A in the ATG initiation codon. Nucleotide numbers 5' to the initiation A are designated with negative numbers, with -1 for the base immediately preceding the +1 A.

The numbering of the mutations listed here is based on the sequences contributed to GenBank by Lynne E. Maquat and her colleagues. The GenBank accession numbers are M10036 (revised August 7, 1995) for the cDNA sequence and X69723 (revised March 22, 1995) for the genomic sequence. It is important to note that the numbering system in the table varies from the GenBank numbering in order to designate the initiation A as +1. In the case of the cDNA sequence, 367 has been subtracted from the GenBank sequence number, and in the case of the genomic DNA sequence, 633 has been subtracted. For nucleotide numbers 5' to the initiation A, 368 has been subtracted for the cDNA sequence and 634 for the genomic sequence.

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## TPI Mutations

Variant Name	cDNA Nucleotide Substitution	Genomic Nucleotide Substitution	Amino Acid Substitution	Reference	Observed Genotypes (Genomic Nucleotide)	Reference
-5/-8	--	(-45A,-43G)*	Not applicable	(5)	(-45A,-43G)/2A (-45A,-43G)***/1591C	(6) (14)
--	2 T→A	2A	1 Met→Lys	(6)	(-45A,-43G)/2A	(6)
--	86-87 del	86-87 del	29 Leu→frameshift	(6)	86-87 del/1591C	(6)
41	125 G→A	1290A	42 Cys→Tyr	(7)	1290A/1591C	(7)
72 C <sub>2013</sub>	218 G→C	1383C	73 Gly→Ala	(5)	**	(5)
104	315 G→C	1591C	105 Glu→Asp	(8)	(-45A,-43G)***/1591C 1290A/1591C 1591C/1591C 1591C/2158G 1591C/2487T	(14) (7) (8) (7) (11)
122 Manchester	367 G→A	1717A	123 Gly→Arg	(9)	**	(9)
--	436 G→T	1786T	146 Glu→Stop	(10)	1786T/2768C	(10)
154 A <sub>2740</sub>	463 G→A	2110A	155 Val→Met	(5)	**	(5)
170	511 A→G	2158G	171 Ile→Val	(7)	1591C/2158G	(7)
189	568 C→T	2487T	190 Arg→Stop	(11)	1591C/2487T	(11)
231	694 G→A	2741A	232 Val→Met	(12)	2741A/2741A	(12)
240	721 T→C	2768C	241 Phe→Leu	(13)	1786T/2768C	(10)

\*Both substitutions, -45 G→A and -43 A→G, occur together in affected subjects. Additionally, some of the subjects have a third substitution, -61 T→G. In addition, Watanabe et al. (5) have noted what they consider to be an error in GenBank genomic sequence X69723, which lacks an additional C between positions -44 and -45. The trivial designation "-5/-8" refers to numbering in reference to the transcription initiation site at -38 and takes the additional C into account.

\*\*Heterozygotes only; other allele is normal.

\*\*\* -61T→G also present.

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