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Hematologically Important Mutations: Glucose-6-Phosphate Dehydrogenase

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A total of 122 mutations or combination of mutations of the X-linked gene for glucose-6-phosphate dehydrogenase, associated with 177 variants thought at one time to be distinct, are now known to us. Previous tabulations, providing somewhat more detailed information about these mutations (1,2) and comprehensive reviews of the deficiency (2,3) may be found in the cited sources and in OMIM on the World Wide Web (http://www.ncbi.nlm.nih.gov/htbin-post/Omim/dispmim?305900).

The cDNA numbers shown in the table are based on the Genbank sequence with the accession number X03674 and the genomic numbers on the sequence with accession number X55448. In each case the A of the ATG start codon is numbered +1. Note that this numbering is different from that used in the GenBank files. It is necessary to subtract 470 from the GenBank cDNA sequence and 3350 from the GenBank genomic sequence to standardize these sequences to begin at the start codon. Variants added since the previous tabulation (4) and corrections are shown in bold.

Table. G6PD variants that have been characterized at the DNA level

Variant Name*	cDNA Nucleotide Substitution	Genomic Nucleotide Substitution	Amino Acid Substitution	Class**	References
"Lages"	**40 G→A**	**40A**	**14 Gly→Arg**	**2 or 3**	**(5)**
Gaohe Gaozhou	95 A→G	95G	32 His→Arg	3 3	(6)

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Variant Name*	cDNA Nucleotide Substitution	Genomic Nucleotide Substitution	Amino Acid Substitution	Class**	References
"Honiara"	99 A→G 1360 C→T	99G 13763T	33 Ile→Met **454 Arg→Cys**	1	(7)
"Sunderland"	105-107 del	105-107 del	**35 or 36 Ile del**	1	(8)
"Gidra"	**110 T→C**	**110C**	**37 Met→Thr**	NA	**(9)**
Orissa	131 C→G	9988G	44 Ala→Gly	3	(10)
Aures	143 T→C	10000C	48 Ile→Thr	2	(11)
"Kozukata"	159 G→C	10111C	53 Trp→Cys	1	(12)
"Kamogawa"	169 C→T	10121T	57 Arg→Trp	2	(12)
Metaponto	172 G→A	10124A	58 Asp→Asn	3	(13)
Musashino	**185 C→T**	**10137T**	**62 Pro→Phe**	**3**	**(14)**
A- Distrito Federal "Matera" Castilla Alabama Betica Tepic Ferrara Laghouat Kabyle	 202 G→A 376 A→G	 10154A 10877G	 68 Val→Met 126 Asn→Asp	3 3 3 3 3 2 3 2 3 3	(15) (16) (13) (16) (17) (18) (16) (19) (20) (20)
Namouru	208 T→C	10160C	70 Tyr→His	2	(21)
Murcia	209 A→G	10161G	70 Tyr→Cys	1	(22)
Swansea	224 T→C	10176C	75 Leu→Pro	1	(23)
Ube Konan	241 C→T	10193T	81 Arg→Cys	3 3	(24)
Lagosanto	242 G→A	10194A	81 Arg→His	3	(25)
Urayasu	281-283 del	10782-10784	**95 Lys del**	2	(26)

Variant Name*	cDNA Nucleotide Substitution	Genomic Nucleotide Substitution	Amino Acid Substitution	Class**	References
"Vancouver "	317 C→G 544 C→T 592 C→T	10818G	106 Ser→Cys 182 Arg→Trp 198 Arg→Cys	1	(27)
"Hammersmith"	**323 T→A**	**10824A**	**108 Val→Glu**	**3**	**(28)**
São Borja	337 G→A	10838A	113 Asp→Asn	4	(29)
A	376 A→G	10877G	126 Asn→Asp	4	(30)
Vanua Lava	383 T→C	10884C	128 Leu→Pro	2	(21)
Quing Yan	392 G→T	10893T	131 Gly→Val	3	(31)
"Cairo"	404 A→C	10905C	135 Asn→Thr	2	(32)
"Valladolid"	**406 C→T**	**10907T**	**136 Arg→Cys**	**2**	**(33)**
Ilesha	466 G→A	10967A	156 Glu→Lys	3	(13)
Mahidol	487 G→A	11658A	163 Gly→Ser	3	(34)
Plymouth	488 G→A	11659A	163 Gly→Asp	1	(23)
Taipei	493 A→G	11664G	165 Asn→Asp	2	**(35)**
Naone	497 G→A	11668A	166 Arg→His	2	(21)
"Volendam"	514 C→T	11684T	172 Pro→Ser	1	(36)
"Nankang"	517 T→C	11687C	173 Phe→Leu	2	**(37)**
"Miaoli"	**519 C→G**	**11689G**	**173 Phe→Leu**	**NA**	**(38)**
Shinshu	527 A→G	11698G	176 Asp→Gly	1	(39)
"Chikugo"	535 A→T	11706T	179 Ser→Cys	1	(40)
Malaga	542 A→T	11713T	181 Asp→Val	3	(41)

Variant Name*	cDNA Nucleotide Substitution	Genomic Nucleotide Substitution	Amino Acid Substitution	Class**	References
Santamaria	542 A→T 376 A→G	11713T 10877G	181 Asp→Val 126 Asn→Asp	2	(42)
Tsukui	561-563 del	11732-11734 del	188 or 189 Ser del	1	(26)
Mediterranean Dallas Birmingham Sassari Cagliari Panama	563 C→T	11734T	188 Ser→Phe	2 2 1 2 2 1	(13) (43) (43) (44) (44) (17)
Coimbra "Shunde"	592 C→T	11763T	198 Arg→Cys	2	(45) (46)
"Santiago"	593 G→C	11764C	198 Arg→Pro	1	(47)
Sibari	634 A→G	11805G	212 Met→Val	3	(48)
Minnesota Marion Gastonia "LeJeune"	637 G→T	11808T	213 Val→Leu	1 1 1 1	(49) (49) (49) (50)
Harilaou	648 T→G	11996G	216 Phe→Leu	1	(51)
Radlowo	**679 C→T**	**12027T**	**227 Arg→Try**	NA	(52)
"Mexico City"	680 G→A	12028A	227 Arg→Gln	3	(47)
A-	680 G→T 376 A→G	12028**T** 10877G	227 Arg→Leu 126 Asn→Asp	3	(15)
"North Dallas"	**683-685 del**	**12031-12033 del**	**229 Asn del**	**1**	**(53)**
Asahikawa	695 G→A	12043A	232 Cys→Tyr	2	**(14)**
Durham	713 A→G	12061G	238 Lys→ Arg	1	(54)
"Stonybrook"	724-729 GGCACT del	12072-12077	242-243 Gly&Thr del	1	(55)

Variant Name*	cDNA Nucleotide Substitution	Genomic Nucleotide Substitution	Amino Acid Substitution	Class**	References
Wayne	769 **C→G**	12117**G**	257 Arg→Gly	1	(50)
"Cleveland" Corum	820 G→A	12533A	274 Glu→Lys	1 1	(55)(56,57)
Wexham	833 C→T	12546T	278 Ser→Phe	1	(23)
"Chinese-1"	835 A→T	12548T	279 Thr→Ser	2	(58)
Seattle Lodi Modena Ferrara II Athens-like **Mexico**	844 G→C	12557C	282 Asp→His	3 3 3 3 2 or 3 3	(44) (59) **(60)** (61) (62) **(63,64)**
"Papua"	**849 C→A**	**12562A**	**283 Asp→Glu**	**NA**	**(9)**
"Osaka"	853 C→T	12566T	285 Arg→Cys	2	(12)
Montalbano	854 G→A	12567A	285 Arg→His	3	(65)
Viangchan Jammu	871 G→A	13031A	291 Val→Met	3 2	(50)
West Virginia	910 G→T	13070T	303 Val→Phe	1	(55)
"Seoul"	916 G→A	13076A	306 Gly→Ser	2	(40)
"Omiya"	**921G→C**	**13081C**	**307Gln→His**	**1**	**(66)**
"Ludhiana"	**929 G→A**	**13089A**	**310 Gly→Glu**	**2**	**(67)**
Kalyan Kerala	949 G→A	13109A	317 Glu→Lys	3 3	(68)
A- Betica Selma Guantanamo	968 T→C 376 A→G	13128C 10877G	323 Leu→Pro 126 Asn→Asp	3 2 3 3	(15) (18) (18) (69)
"Nara"	953-976 del	13113-13136 del	319-326 del	1	(70)

Variant Name*	cDNA Nucleotide Substitution	Genomic Nucleotide Substitution	Amino Acid Substitution	Class**	References
"Manhattan"	**962 G→A**	**13142A**	**321 Gly→Glu**	**1**	**(71)**
"Farroupilha"	**977C→A**	**13137A**	**326Pro→His**	**2 or 3**	**(5)**
Chatham	1003 G→A	13163A	335 Ala→Thr	3	(13)
"Fushan"	1004 C→A	13164A	335 Ala→Asp	2	(55)
"Chinese-5"	1024 C→T	13184T	342 Leu→Phe	3	(31)
"Mira d'Aire"	**1048 G→C**	**13208C**	**350 Asp→His**	**4**	**(72)**
Partenope	1052 G→T	13351T	351 Gly→Val	2	**(73)**
"Ierapetra"	1057 C→T	13356T	353 Pro→Ser	2	(47)
"Iwatsuki"	**1081G→A**	**13380A**	**361Ala→Thr**	**1**	**(66)**
"Serres"	**1082 C→T**	**13381T**	**361 Ala→Val**	**1**	**(74)**
Loma Linda	1089 C→A	13388A	363 Asn→Lys	1	(49)
Calvo Mackenna	1138 A→G	13437G	380 Ile→Val	1	(75)
Riley	1139 T→C	13438C	380 Ile→Thr	1	(75)
"Olomouc"	1141 T→C	13440C	381 Phe→Leu	2	(55)
Tomah	1153 T→C	13452C	385 Cys→Arg	1	**(76)**
"Lynwood"	**1154 G→T**	**13453T**	**385 Cys→Phe**	**1**	**(71)**
"Girona"	**1155 C→G**	**13454G**	**385 Cys→Trp**	**1**	**(33)**
Iowa Walter Reed Iowa City Springfield	1156 A→G	13455G	386 Lys→Glu	1 1 1 1	(76)
Guadalajara	1159 C→T	13458T	387 Arg→Cys	1	(47)

Variant Name*	cDNA Nucleotide Substitution	Genomic Nucleotide Substitution	Amino Acid Substitution	Class**	References
"Mt. Sinai"	1159 C→T 376 A→G	13458T 10877G	387 Arg→Cys 126 Asn→Asp	1	(77)
Beverly Hills Genova Worcester **Yamaguchi** **Iwate** **Niigata**	1160 G→A	13459A	387 Arg→His	1 1 1 2 1 1	(76) (78) (17) **(14)** **(14)** **(14)**
"Hartford"	**1162 A→G**	**13461G**	**388 Asn→Asp**	**1**	**(71)**
"Praha"	1166 A→G	13465G	389 Glu→Gly	1	(55)
Wisconsin	1177 C→G	13476G	393 Arg→Gly	1	(75)
Nashville Anaheim "Calgary" Portici	1178 G→A	13477A	393 Arg→His	1 1 1 1	(49) (49) (17) (79)
Alhambra	1180 G→C	13479C	394 Val→Leu	1	(47)
Bari	1187 C→T	13486T	396 Pro→Leu	1	(80)
Puerto Limon	1192 G→A	13491A	398 Glu→Lys	1	(42)
"Anadia"	1193 A→G	13492G	398 Glu→Gly	2	(81)
Clinic	1215 G→A	13514A	405 Met→Ile	1	**(22)**
"Abeno"	**1220 A→C**	**13519C**	**407 Lys→Thr**	**2**	**(9)**
Riverside	1228 G→T	13527T	410 Gly→Cys	1	(76)
"Kawasaki"	**1229 G→C**	**13528C**	**410 Gly→Ala**	**1**	**(9)**
"Shinagawa"	1229 G→A	**13528A**	410 Gly→Asp	1	(39,47)
Tokyo **Fukushima**	1246 G→A	13545A	416 Glu→Lys	1 2	(23) (82) **(14)**

Variant Name*	cDNA Nucleotide Substitution	Genomic Nucleotide Substitution	Amino Acid Substitution	Class**	References
"Georgia"	1284 C→A	13560A	428 Tyr→End	1	(55)
"Vansdorf"	3' intron 10 splice site del	13689-13690 del	N/A	1	(55)
Pawnee	1316 G→C	13719C	439 Arg→Pro	2	(47)
Telti Kobe	1318 C→T	13721T	440 Leu→Phe	1 1	(23) (83)
Santiago de Cuba **Morioka**	1339 G→A	13742A	447 Gly→Arg	1 1	(13) **(14)**
S. Antioco	1342 A→G	13745G	448 Ser→Gly	2	**(73)**
Cassano	1347 G→C	13750C	449 Gln→His	2	(48)
"Harima"	**1358 T→A**	**13761A**	**453 Val→Glu**	**1**	**(66)**
Union Maewo **"Chinese-2"**	1360 C→T	13763T	454 Arg→Cys	2 2 2	(58,84) (48,85) **(58,86)**
Andalus	1361 G→A	13764A	454 Arg→His	2	(87)
Cosenza	1376 G→C	13884C	459 Arg→Pro	2	(48)
Canton Taiwan-Hakka Gifu-like Agrigento-like	1376 G→T	13884T	459 Arg→Leu	3 2 2 3	(88) (89) **(89)** **(89)**
"Bangkok Noi"	**1376 G→T** **1502 G→T**	**13884T** **14107G**	**459 Arg→Leu** **501 Phe→Cys**	**1**	**(90)**
Kamiube	1387 C→T	13895T	463 Arg→Cys	3	**(14)**

Variant Name*	cDNA Nucleotide Substitution	Genomic Nucleotide Substitution	Amino Acid Substitution	Class**	References
Kaiping Anant Dhon Petrich Sapporo Wosera	1388 G→A	13896A	463 Arg→His	2 3 2 2 1 NA	(89) (89) (89) **(91)** **(92)** **(91)**
Neapolis	**1400 C→G**	**13908G**	**467 Pro→Arg**	**3**	**(93)**
"Fukaya"	1462 G→A	14067A	488 Gly→Ser	1	(40)
"Campinas"	1463 G→T	14068T	488 Gly→Val	1	(94)
"Arakawa"	**1466 C→T**	**14071T**	**489 Pro→Leu**	**1**	**(9)**

*There is considerable variability in the extent to which the variants listed in this table have been characterized. Therefore quotation marks have been placed around all variants that have not yet been published as well as around those for which not all of the following parameters are available. (I) Residual activity in RBC; (ii) electrophoretic mobility in one of the standard buffer systems; (iii) Km G6P and/or activity on substrate analogues; (iv) stability *in vitro* and/or *in vivo* for class 1 variants, and some of them have a bearing on clinical manifestations. All the published variants for which these parameters are available are listed without quotation marks.

**The class of each variant is given according to Yoshida et al. (95): Class 1: Severe enzyme deficiency with chronic non-spherocytic hemolytic anemia; Class 2: Severe enzyme deficiency (<10% of normal); Class 3: Moderate to mild enzyme deficiency (10-60% of normal); Class 4: Very mild or no enzyme deficiency (60-100% of normal); NA: not available.

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