Names for MNS (ISBT 002) Blood Group Alleles

General description: The MNS blood group system consists of 48 antigens carried on glycophorin A (GPA), glycophorin B (GPB) or on hybrids of these glycophorins. These proteins are single pass type I membrane glycoproteins that are heavily O-glycosylated. GPA carries an N-glycan. GPA consists of 131 amino acids, GPB of 72 amino acids and both have a leader sequence of 19 amino acids that is cleaved from the membrane bound protein. The hybrid proteins vary in length based on their composition but also have a 19 amino acid leader sequence. GPA is encoded by *GYPA*, GPB by *GYPB*. A third gene in this family, *GYPE*, normally does not encode detectable protein at the red cell surface but the gene has been shown to be involved in some gene rearrangements that encode cell-surface borne hybrid proteins. As described above, the proteins are encoded by *GYPA* or *GYPB*, or *MNS* if analysis is to predict a blood group antigen.

Gene name:	*GYPA*	*GYPB*	*GYPE*
Number of exons:	7	5 plus 1 pseudoexon	4 plus 2 pseudoexons
Initiation codon:	Exon 2	Exon 2	Exon 2
Stop codon:	Exon 7	Exon 6‡	Exon 6‡
Entrez GeneID:	2993	2994	2996
LRG sequence:	NG_007470.3 (genomic) NM_002099.5 (transcript)	NG_007483.2 (genomic) NM_002100.5 (transcript)	NG_009173.1 (genomic) NM_002102.3 (transcript)

‡ Exon numbering accounts for the presence of pseudoexons in *GYPB* and *GYPE*. Thus, *GYPB* pseudoexon 3 corresponds to the *GYPA* exon 3 sequence. This *GYPB* pseudoexon is involved in many gene rearrangements encoding hybrid glycophorins in this blood group system. Similarly, *GYPE* pseudoexons 3 and 4 correspond to *GYPA* exon 3 and 4 sequences. These *GYPE* pseudoexons are involved in gene rearrangements encoding hybrids.

Reference allele (*GYPA*): *GYPA*01*
Acceptable: *GYPA*M* or *M* if inferred by hemagglutination

Reference allele (*GYPB*): *GYPB*04*
Acceptable: *GYPB*s* or *s* if inferred by hemagglutination

Table 1. MNS alleles with single nucleotide polymorphisms that generate blood group antigens.
A. *GYPA*: Reference allele *MNS*01* encodes M, En^{a}, ENKT, ENEP, ENEH, ENAV, ENDA, ENEV.
Note: In most cases, the nucleotide changes also can occur on an N allele; these nucleotide changes are not given.

Phenotype	**Allele name**	**Nucleotide change**	**Exon**	**Predicted amino acid change**	**Comments**
MNS:1 or M+	*GYPA*01* or *GYPA*M*				
MNS:2 or N+	*GYPA*02* or *GYPA*N*	c.59C>T; c.71G>A; c.72T>G	2	p.Ser20Leu; p.Gly24Glu	
MNS:1,-2,8† or M^{c}+	*GYPA*08* or *GYP*Mc*	c.71G>A; c.72T>G	2	p.Gly24Glu	
MNS:7,9,–40 or Vw+	*GYPA*09* or *GYPA*Vw*	c.140C>T	3	p.Thr47Met	
MNS:−1,−2,11,32 or M^{g}+DANE+	*GYPA*11* or *GYPA*Mg*	c.68C>A	2	p.Thr23Asn	
MNS:12 or Vr+	*GYPA*12* or *GYPA*Vr*	c.197C>A	3	p.Ser66Tyr	
MNS:14 or Mt(a+)	*GYPA*14* or *GYPA*Mta*	c.230C>T	3	p.Thr77Ile	
MNS:16 or Ri(a+)	*GYPA*16* or *GYPA*Ria*	c.226G>A	3	p.Glu76Lys	
MNS:18 or Ny(a+)	*GYPA*18* or *GYP*Nya*	c.138T>A	3	p.Asp46Glu	
MNS:7,19,–40 or Hut+	*GYPA*19* or *GYPA*Hut*	c.140C>A	3	p.Thr47Lys	
MNS:31 or Or+	*GYPA*31* or *GYPA*Or*	c.148C>T	3	p.Arg50Trp	
MNS:37 or ERIK+	*GYPA*37* or *GYPA*ERIK*	c.232G>A	4	p.Gly78Arg	See also *GYP*EBH* in hybrid table
MNS:38 or Os(a+)	*GYPA*38* or *GYPA*Osa*	c.217C>T	3	p.Pro73Ser	
MNS:–39,41 or HAG+	*GYPA*41* or *GYPA*HAG*	c.250G>C	4	p.Ala84Pro	

Phenotype	Allele name	Nucleotide change	Exon	Predicted amino acid change	Comments
MNS:–42,43 or MARS+	*GYPA*43* or *GYPA*MARS*	c.244C>A	4	p.Gln82Lys	
MNS:–45 or ENEV–	*GYPA*–45*	c.242T>G	4	p.Val81Gly	
MNS:46 or MNTD+	*GYPA*46* or *GYPA*MNTD*	c.107C>G	3	p.Thr36Arg	
MNS:47 or SARA+	*GYPA*47* or *GYPA*SARA*	c.240G>T	4	p.Arg80Ser	

† Most anti-M but only few anti-N react with M^c+ RBCs

Table 1. MNS alleles with single nucleotide polymorphisms that generate blood group antigens.
B. *GYPB*: Reference allele *GYPB*04* encodes 'N', s. Expression of the U antigen involves GPB and another protein, probably RhAG.

Phenotype	Allele name	Nucleotide change	Exon	Predicted amino acid change	Comments
MNS:4 or s+	*GYPB*04* or *GYPB*s*				
MNS:3 or S+	*GYPB*03 or GYPB*S*	c.143C>T	4	p.Thr48Met	
MNS:4,6 or s+, He+	*GYPB*06.01*	c.59T>G; c.60A>G; c.67A>T; c.71A>G; c.72G>T	2	p.Leu20Trp; p.Thr23Ser; p.Glu24Gly	
MNS:3,6 or S+, He+	*GYPB*06.02*	c.59T>G; c.60A>G; c.67A>T; c.71A>G; c.72G>T; c.143C>T	2 4	p.Leu20Trp; p.Thr23Ser; p.Glu24Gly; p.Thr48Met	
MNS:21or M^{v}+	*GYPB*21 or GYPB*Mv*	c.65C>G	2	p.Thr22Ser	
MNS:23 or s^{D}+	*GYPB*23* or *GYPB*sD*	c.173C>G	4	p.Pro58Arg	
MNS:24 or Mit+	*GYPB*24 or GYPB*Mit*	c.161G>A	4	p.Arg54His	
MNS:–3,w5 or S–U+^{w}	*GYPB*03N.01* *or GYPB*NY*	c.143C>T; c.208G>T; c.230C>T; c.251C>G	4 5	p.Thr48Met; p.Val70Leu; p.Thr77Met; p.Thr84Ser; Alternative splicing	

Phenotype	Allele name	Nucleotide change	Exon	Predicted amino acid change	Comments
MNS:–3,w5 or S–U+^{w}	*GYPB*03N.02* or *GYP*He(NY)*	c.59T>G; c.60A>G; c.67A>T; c.71A>G; c.72G>T; c.143C>T; c.208G>T; c.230C>T; c.251C>G	2 4 5	p.Leu20Trp; p.Thr23Ser; p.Glu24Gly; p.Thr48Met; p.Val70Leu; p.Thr77Met; p.Thr84Ser; Alternative splicing	
MNS:–3,w5 or S–U+^{w}	*GYPB*03N.03* or *GYPB*P2*	143C>T; c.270+5G>T	4 Intron 5	p.Thr48Met; Alternative splicing	
MNS:–3,w5 or S–U+^{w}	*GYPB*03N.04* or *GYP*He(P2)*	c.59T>G; c.60A>G; c.67A>T; c.71A>G; c.72G>T; c.143C>T; c.270+5G>T	2 4 Intron 5	p.Leu20Trp; p.Thr23Ser; p.Glu24Gly; p.Thr48Met; Alternative splicing	
MNS:–4,w5	*GYPB*04N.01*	c.270+5G>A	Intron 5		

Table 2. MNS alleles created by gene rearrangement events within the *GYP* gene family
A: parent allele *GYPA.*

Phenotype	Allele name	Nucleotide change	Predicted amino acid change	Comments
GYP(A-A) hybrid series				
MNS:15 or St(a+)	*GYP*101.01* or *GYP*Zan*	*GYPA*: del exon 3	GPA: p.Asp46_Thr77del	*GYP(A1-2-BΨ3-A4-7)*
MNS:15 or St(a+)	*GYP*101.02* or *GYP*EBH*	*GYPA*: c.232G>A; *GYPA*: del exon 3	GPA: p.Asp46_Thr77del	Nucleotide change at 232 destabilises normal splicing. St^a is encoded by a *GYPA* transcript that lacks exon 3. Full-length transcript encodes ERIK (MNS37; see table 1).
MNS:15 or St(a+)	*GYP*101.03* or *GYP*Mar*	*GYPA* del exon 3	GPA: p.Asp46_Thr77del	*GYP(A1-2-EΨ3-A4-7)*
MNS:6,15 or He+,St(a+)	*GYP*101.04* or *GYP*Cal*	*GYPA*: c.58G>T; *GYPA*: c.67A>T; *GYPA*: del exon 3	GPA: p.Gly20Trp; GPA: p.Thr23Ser; GPA: p.Asp46_Thr77del	*GYP(A1-2-BΨ3-A4-7)*
GYP(A-B) series				
MNS:−3,4,20,34 or S−s+, Hil+, MINY+	*GYP*201.01* or *GYP*Hil*	*GYP(A1-232–B233-312)*	GP(A1-77-B78-104)	
MNS:3,−4,32,33 or S+s−, TSEN+, MINY+	*GYP*202.01* or *GYP*JL*	*GYP(A1-232–B233-312)*; c.239C>T	GP(A1-77-B78-104); p.Thr80Met	
MNS:−1,2,−3,−4,−5,36 or M−N+S−s−U−, SAT+	*GYP*203.01* or *GYP*SAT*	*GYP(A1-271–B272-369)*; c.59C>T; c.71G>A; c.72T>G	GYPA(1-90-B91-123); p.Ser20Leu; p.Gly24Glu	breakpoint in intron 4 not defined Previously *GYP*TK*

Phenotype	Allele name	Nucleotide change	Predicted amino acid change	Comments
GYP(A-B-A) series				
	*GYP*Vw*			Numbers have not been assigned to these alleles in this series and they are included in table 1. It has been proposed that they are derived from hybrid genes but the crossover points have not been determined experimentally.
	*GYP*Hut*			
	*GYP*Mc*			
	*GYP*Mg*			
MNS:10,32 or Mur+, DANE+	*GYP*301.01* or *GYP*Dane*	*GYP(A1-159–BΨ160-177–A178-450);* c.191T>A	GP(A1-52-B53-58-A59-149); p.Ile46Asn	Also expresses Mur antigen Not known if the allele encodes ENDA as person homozygous for *GYP*301.01* has not been found.
MNS:10,32,–44 or Mur+, DANE+, ENDA–	*GYP*301.02* or *GYP*Dane*	*GYP(A1-159–BΨ160-177–A178-450)*	GP(A1-52-B53-58-A59-149)	Also expresses Mur antigen; does not express ENDA.
MNS:26,27 or Hop+,Nob+	*GYP*302.01* or *GYP*Joh*	*GYP(A1-202–BΨ203–A204-450)*	GPA(1-67)-B(68)-GPA(69-150); p.Arg68Thr	Gene conversion in exon 3 replaces *GYPA* nucleotide 203 with the corresponding nucleotide from *GYPBΨ3*. This is the minimum but the breakpoint is not defined.
MNS:–26,27,−29 or Hop–,Nob+, ENKT−	*GYP*302.02* or *GYP*Nob*	*GYP(A1-202–BΨ203-212–A213-450)*; c.203G>C; c.212A>C	GPA(1-67)-B(68-72)-GPA(73-150); p.Arg68Thr; p.Tyr71Ser	Gene conversion in exon 3 replaces *GYPA* nucleotides (203-212) with corresponding nucleotides from *GYPBΨ3*. This is the minimum but the breakpoint is not defined.

Phenotype	Allele name	Nucleotide change	Predicted amino acid change	Comments
MNS:20, –34 or Hil+, MINY–	*GYP*303* or *GYP*KI*	*GYP(A1-238–B239-242–A243-450)*; c.239G>C; c.242T>G	GPA(1-79)-B(80-81)-GPA(82-150); p.Arg80Thr; p.Val81Gly	Gene conversion in exon 4 replaces *GYPA* nucleotides (239-242) with corresponding nucleotides from *GYPB*. This is the minimum but the breakpoint is not defined.

Table 2. *MNS* alleles created by gene rearrangement events within the *GYP* gene family:
B: parent allele *GYPB*

Phenotype	Allele name	Nucleotide change	Predicted amino acid change	Comments
GYP(B-A) hybrid series				
MNS:15 or St(a+)	*GYP*401* or *GYP*Sch*	*GYP(B1-136-A137-354)*	GPB(1-46)-A(47-118)	Reciprocal product is *GYP.Hil*
MNS:–3,4,25 or S−s+,Dantu+	*GYP*402* or *GYP*Dantu*	*GYP(B1-175-A176-354)*	GPB(1-58)-A(59-118)	Reciprocal product is *GYP.Tk*
GYP(B-A-B) hybrid series				
MNS:–3,4,7,10,20,34,35 S–s+, Mi(a+), Mur+, Hil+, MINY+, MUT+	*GYP*501* *GYP*Mur*	*GYP(B1-136-Bψ137-204-A205-229-B230-366)*	GP(B1-69-A70-77-B78-122) †GPB^{s} ins 46-77 DKHKRDTYPAHTANEVSEI SVRTVYPPEEET	Novel sequence derived from composite exon; *GYPB* 5' pseudoexon 3 + *GYPA* 3' exon 3
MNS:3,–4,7,10,26,33,34,35 S+s–, Mi(a+), Mur+, Hop+, TSEN+, MINY+, MUT+	*GYP*502* *GYP*Hop*	*GYP(B1-136-Bψ137-204-A205-229-B230-366)*; c.236C>G	GP(B1-69-A70-77-B78-122) †GPB^{S} ins 46-77 DKHKRDTYPAHTANEVSEI SVRTVYPPEEET; p.Thr80Met	Novel sequence derived from composite exon; *GYPB* 5' pseudoexon 3 + *GYPA* 3' exon 3
MNS:–3,4,7,10,20,2634,35 S–s+, Mi(a+), Mur+, Hil+, MINY+, MUT+,	*GYP*503* *GYP*Bun*	*GYP(B1-136-Bψ137-210-A211-229-B230-366)*	GP(B1-71-A72-77-B78-122) †GPB^{s} ins 46-77 DKHKRDTYPAHTANEVSEI SVRTVYPPEEET	Novel sequence derived from composite exon; *GYPB* 5' pseudoexon 3 + *GYPA* 3' exon 3

Phenotype	Allele name	Nucleotide change	Predicted amino acid change	Comments
MNS:–3,4,7, 20,34,35 or S–s+, Mi(a+), Hil+, MINY+, MUT+	*GYP*504 GYP*HF*	*GYP(B1-136-Bψ137-159-A160-232-B233-369)*	GP(B1-53-A54-78-B79-123) †GPB^{s} ins 46-77 DKHKRDTYAATPRAHEVSE ISVRTVYPPEEET	Novel sequence derived from composite exon; *GYPB* 5' pseudoexon 3 + *GYPA* 3' exon 3
MNS:–3,–4,–5,6 or S–s–U–He+	*GYP*505 GYP*He(GL)*	*GYP(B1-12-A13-78-B79-168)*	GP(B1-4-A5-26-B27-59)	
MNS:–3,4,10,20,34,35,48 or s+ Mur+ MUT+, MINY+, Hil+, Kipp+	*GYP*506 GYP*KIP*		GPB(1-26)-GPψB(27-54)-GPA(55-57)-B^{s}(58-103)	

†The insertion interrupts the JENU antigen on GPB

Phenotype	Allele name	Nucleotide change	Predicted amino acid change	Comments
GYP deletion hybrids				
MNS:–1,–2−28 or M–N– En(a–)	*GYPA*01N*	Del *GYPA* exons 2-7; *GYPB* exon 1	GPA absent	
MNS:–3,–4,–5 or S–s–U–	*GYPB*01N*	Del *GYPB* exons 2-5; *GYPE* exon 1	GPB absent	
MNS:–1,–2,–3,–4,–5 or M^kM^kM–N–S–s–U−	*GYP*01N*	Del *GYPA* exons 2-7; *GYPB* exons 1-5	GPA and GPB absent	