Names for GLOB (ISBT 028) Blood Group Alleles

Intro

General description

The GLOB system was established in 2002 when the P antigen (globoside) was moved from the 209 collection. P is the most common neutral glycosphingolipid in the red cell membrane, belongs to the globoseries and has the following structure: GalNAcβ3Galα4Galβ4Glcβ1 ceramide, also known as globoside (Gb4Cer). The *B3GALT3* gene was first reported in 1998 by Amado *et al* . (1) to be a member of the β1,3-galactosyl-transferase gene family and its product given the name β3Gal-T3. It was later shown by Okajima *et al* . (2) to possess UDP-*N* -acetyl-galactosamine:globotriaosyl-ceramide 3-β-*N* -acetylgalactosaminyl-transferase or globoside synthase activity and the gene name changed to *B3GALNT1* and its product renamed β3GalNAc-T1. This enzyme is responsible for the final step in the synthesis of the P antigen, the transfer of GalNAc to the terminal Gal of the P^k antigen. The final proof of this was the identification in 2002 by Hellberg *et al* . (3) of critical mutations in the *B3GALNT1* gene as the genetic basis of P_1^k and P_2^k, the rare globoside-deficient null phenotypes of the GLOB system. Westman *et al* . (4) showed in 2015 that the same glycosyltransferase is responsible for PX2 antigen synthesis. In addition, 2019 Hagman-Ricci *et al.* (5) reported that the B antigen can be elongated by β3GalNAc-T1 to form the ExtB antigen. Thus, the system now comprises three antigens.

Gene name:	*GLOB* (*B3GALNT1*)
Number of exons:	5
Initiation codon:	Within exon 5
Stop codon:	Within exon 5
Entrez Gene ID:	26879
LRG:	LRG_820
LRG sequence:	NG_007854.1 (genomic) NM_033169.3 (transcript)
Reference allele:	*GLOB*01 (B3GALNT1*01)* Acceptable: *P* if inferred by haemagglutination
Reference allele *GLOB*01* encodes:	GLOB1 (P),GLOB4 (PX2) and if group B/AB also GLOB5 (ExtB).
Antithetical antigens:	-

Phenotype	Allele name	Nucleotide change	Exon Intron	Predicted amino acid change	(Reference No.) PMID	Accession number	rs number
GLOB:1 (P+)	*GLOB*01*						
GLOB:1 (P+)	*GLOB*01.02*	c.376G>A	5	p.Asp126Asn			rs2231257
Null Phenotypes (The null phenotype caused by these alleles can either be P1+ or P1–, i.e. P1k or P2k)							
GLOB:–1 (P–)	*GLOB*01N.01*	c.202C>T	5	p.Arg68Ter	PMID:12023287	AF494103	rs200235398
GLOB:–1 (P–)	*GLOB*01N.02*	c.292dup	5	p.Arg98LysfsTer6	PMID:15142124	AY505344	n.a.
GLOB:–1 (P–)	*GLOB*01N.03*	c.433C>T	5	p.Arg145Ter	PMID:15142124	AY505345	rs755471824
GLOB:–1 (P–)	*GLOB*01N.04*	c.537dup	5	p.Asp180ArgfsTer3	PMID:12023287	AF494104	rs751995528
GLOB:–1 (P–)	*GLOB*01N.05*	c.648A>C	5	p.Arg216Ser	PMID:15142124	AY505346	n.a.
GLOB:–1 (P–)	*GLOB*01N.06*	c.797A>C	5	p.Glu266Ala	PMID:12023287	AF494106	rs28937582
GLOB:–1 (P–)	*GLOB*01N.07*	c.811G>A	5	p.Gly271Arg	PMID:12023287	AF494105	rs104893683
GLOB:–1 (P–)	*GLOB*01N.08*	c.959G>A	5	p.Trp320Ter	PMID:15142124	AY505347	rs1458558563
GLOB:–1 (P–)	*GLOB*01N.09*	c.203del	5	p.Arg68Glnfster17	PMID: 23927681	FR871173	n.a.
GLOB:–1 (P–)	*GLOB*01N.10*	c.376G>A c.598del	5 5	p.Asp126Asn p.Ser200GlnfsTer10	PMID: 23927681	FR871175	rs2231257 n.a.
GLOB:–1 (P–)	*GLOB*01N.11*	c.456T>G	5	p.Tyr152Ter	PMID: 23927681	FR871176	n.a.
GLOB:–1 (P–)	*GLOB*01N.12*	c.449A>G	5	p.Asp150Gly	PMID: 23927681	FR871174	n.a.
GLOB:–1 (P–)	*GLOB*01N.13*	c.420T>G	5	p.Tyr140Ter	PMID: 29873420	MG459010	n.a.

References

PMID 9582303 Amado M, Almeida R, Carneiro F et al. A family of human beta3-galactosyltransferases. Characterization of four members of a UDP-galactose:beta-N-acetyl-glucosamine/beta-N-acetyl-galactosamine beta-1,3-galactosyltransferase family. J Biol Chem 1998;273:12770-8.

PMID 10993897 Okajima T, Nakamura Y, Uchikawa M et al. Expression cloning of human globoside synthase cDNAs. Identification of beta3Gal-T3 as UDP-N-acetylgalactosamine:globotriaosylceramide beta1,3-N-acetylgalactosaminyltransferase. J Biol Chem 2000;275:40498-503

PMID 12023287 Hellberg A, Poole J, Olsson ML. Molecular basis of the globoside-deficient P(k) blood group phenotype. Identification of four inactivating mutations in the UDP-Nacetylgalactosamine: globotriaosylceramide 3-beta-Nacetylgalactosaminyltransferase gene. J Biol Chem 2002; 277:29455-9.

PMID 26055721 Westman JS, Benktander J, Storry JR, et al. Identification of the molecular and genetic basis of PX2, a glycosphingolipid blood group antigen lacking on globoside-deficient erythrocytes. J Biol Chem 2015;290:18505–18

Abstract (1) J Ricci Hagman, A Barone, JS Westman JR Storry, C Jin, AK Hult, S Teneberg, ML Olsson β1,3GalNAc-T1-dependent extension of the human blood group B antigen gives rise to a novel glycolipid structure on erythrocytes Vox Sanguinis 2019;114(S1)4C-S20-06 (Abstract)

PMID 15142124 Hellberg A, Ringressi A, Yahalom V, Safwenberg J, Reid ME, Olsson ML. Genetic heterogeneity at the glycosyltransferase loci underlying the GLOB blood group system and collection. Br J Haematol 2004;125: 528-36.

PMID 23927681 Westman JS, Hellberg A, Peyrard T, Hustinx H, Thuresson B, Olsson ML. P1 /P2 genotyping of known and novel null alleles in the P1PK and GLOB histo-blood group systems. Transfusion. 2013 Nov;53(11 Suppl 2):2928-39

PMID 29873420 Ricci Hagman J, Hult AK, Westman JS, Hosseini-Maaf B, Jongruamklang P, Saipin S, Bejrachandra S, Olsson ML. Multiple miscarriages in two sisters of Thai origin with the rare P k phenotype caused by a novel nonsense mutation at the B3GALNT1 locus
Transfus Med. 2019 Jun;29:202-208. doi: 10.1111/tme.12544. Epub 2018 Jun 6.

Track of changes

			from	to
1	**Version**		**v4.0_8th April 2019**	**v5.0 30-JUN-2022**
2	Author	created	Jill Story, April 2019	Åsa Hellberg, February 2021
3	Review	reviewed	C.Hyland, April 2019	Martin L Olsson, May 2022
4	General	Document created	Word version	First version. Spread-sheets "Intro", "Allele Table", "References", and "Versioning" created.
5	Intro	Intro added		General description, gene name, number of exons, initiation codon, stop codon, Entrez Gene Id and Reference allele information added.
6	Allele Table	Table created		Table columns "Phenotype", "Allele name", "Nucleotide change", "Exon", "Predicted amino acid change", "(Reference No.) PMID", "Accession number" and "rs-number" created and content to table columns added.
7	Allele Table	added		*GLOB*01*
8	Allele Table	added		*GLOB*01.02*
9	Allele Table	added		*GLOB*01N.01-GLOB*01N.13*
10	References	added		References
11	Allele	changed	*GLOB* 02*	*GLOB*01.02*
12	Allele	changed	*GLOB* 02N.01*	*GLOB*01N.10*

1	**Version**		**v4.0_8th April 2019**	**v5.0 30-JUN-2022**
13	Allele	changed		**Additional information regarding *GLOB*01N.10*:** Bioinformatic analysis of the *B3GALNT1* locus revealed it to be highly conserved, although an allele with the c.376G>A mutation was found in 5.2 percent of the population worldwide. This allele, shown to be associated with normal expression of P, was named *GLOB*02* . Subsequently, the c.598delT mutation linked to c.376G>A was therefore renamed *GLOB*02N.01* (and *GLOB*01N.10* was retired). **However, in this version, due to an alteration of the principle for this nomenclature, the name is changed back to *GLOB*01N.10*.**
14	**End Version**		**v4.0_8th April 2019**	**v5.0 30-JUN-2022**

Track of changes

			from	to
1	**Version**		**v3.0_22nd June 2016**	**v4.0_8th April 2019**
2	Author	created	Jill Story, June 2016	Jill Story, April 2019
3	Review	reviewed	n.a.	C.Hyland, April 2019
4	General	Document created	Word version	Word version
5	Intro	Intro changed		LRG sequence 819
6	Intro	Intro changed		NG_007469.3 (genomic)
7	**End Version**			