Globoside Blood Group System

Number of antigens 1

High prevalence	P

Terminology

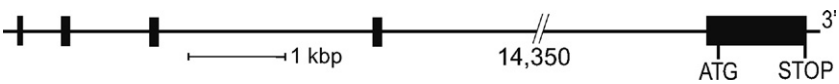
ISBT symbol (number)	GLOB (028)
History	The P antigen was promoted to Globoside (GLOB) Collection and in 2002, when the molecular basis of globoside deficiency was defined, P became a blood group system (GLOB).

Expression

Other blood cells	Erythroid precursor cells, lymphocytes, monocytes
Tissues	Endothelium, placenta (trophoblasts and interstitial cells), fibroblasts, fetal liver, fetal heart, kidney, prostate, peripheral nerves

Gene

Chromosome	3q26.1
Name	*GLOB* (*B3GALNT1*); the previously widely used *B3GALT3* should not be used
Organization	At least five exons (multiple transcripts exist so exact number is still unclear), distributed over ~19 kbp
Product	UDP-*N*-acetylgalactosamine: globotriaosylceramide 3-β-*N*-acetylgalactosaminyltransferase (Gb_4Cer/globoside synthase EC2.4.1.79; β3GalNAcT1; P synthase)[1]



The Blood Group Antigen (3/e). DOI: http://dx.doi.org/10.1016/B978-0-12-415849-8.00030-2

Database accession numbers

GenBank	NM_033169 (mRNA); AB050855 (gene)
Entrez Gene ID	8706

Molecular bases of the P^k (P–, GLOB:–1) phenotype due to changes in *B3GALNT1*[1]

Nucleotide differences from the reference allele, *GLOB*01* (*B3GALNT1*01*; Accession number AB050855), and amino acids affected, are given. This reference allele encodes a 3-β-*N*-acetylgalactosaminyltransferase, which adds *N*-acetylgalactosamine to the lactosylceramide (P^k antigen) to form globoside (P antigen). The null phenotype caused by these alleles can be either P1+ or P1–, i.e., the RBCs have P_1^k or P_2^k phenotype.

Allele name	Exon	Nucleotide	Amino acid	Ethnicity (prevalence)
*GLOB*01N.01*	5	202C>T	Arg67Stop	Finnish (Few)
*GLOB*01N.02*	5	292_293insA	Arg97fs102Stop	Italian (Rare)
*GLOB*01N.03*	5	433C>T	Arg145Stop	North American (Rare)
*GLOB*01N.04*	5	537_538insA	Asp180fs182Stop	Arabian (Few)
*GLOB*01N.05*	5	648A>C	Arg216Ser	Canadian (Rare)
*GLOB*01N.06*	5	797A>C	Glu266Ala	French (Rare)
*GLOB*01N.07*	5	811G>A	Gly271Arg	European (Few)
*GLOB*01N.08*	5	959G>A	Trp320Stop	Swiss (Rare)
*GLOB*01N.09*	5	203delG	Arg68fs84Stop	Maghreb (Rare)
*GLOB*01N.10*	5 5	376G>A 598delT	Asp126Asn Ser200fs209Stop	French (Rare)
*GLOB*01N.11*	5	456T>G	Tyr152Stop	Saudi Arabian (Rare)
*GLOB*01N.12*	5	449A>G	Asp150Gly	Turkish (Rare)

Molecular basis of p (PP1P^k–) phenotype due to changes in *A4GALT*

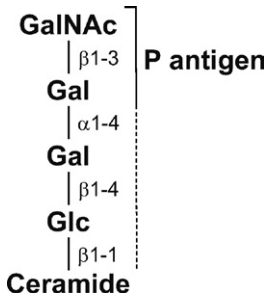
See P1PK blood group system.

Amino acid sequence of 3-β-*N*-acetylgalactosaminyltransferase

```
MASALWTVLP  SRMSLRSLKW  SLLLLSLLSF  FVMWYLSLPH  YNVIERVNWM    50
YFYEYEPIYR  QDFHFTLREH  SNCSHQNPFL  VILVTSHPSD  VKARQAIRVT   100
WGEKKSWWGY  EVLTFFLLGQ  EAEKEDKMLA  LSLEDEHLLY  GDIIRQDFLD   150
TYNNLTLKTI  MAFRWVTEFC  PNAKYVMKTD  TDVFINTGNL  VKYLLNLNHS   200
EKFFTGYPLI  DNYSYRGFYQ  KTHISYQEYP  FKVFPPYCSG  LGYIMSRDLV   250
PRIYEMMGHV  KPIKFEDVYV  GICLNLLKVN  IHIPEDTNLF  FLYRIHLDVC   300
QLRRVIAAHG  FSSKEIITFW  QVMLRNTTCH  Y                       331
```

Carrier molecule

The P antigen is not a primary gene product; it is located on glycolipids.



For a diagram of the biosynthetic pathway, see P1PK system.

Copies per RBC ~15,000,000

Function

The enzyme transfers GalNAc to the terminal Gal of the P^k antigen to synthesize the P antigen.

Disease association[2]

P is a receptor for Parvovirus B19 and some P-fimbriated *E. coli.*
Anti-P is associated with paroxysmal cold hemoglobinuria (PCH).
Cytotoxic IgM and IgG3 antibodies directed against P and/or P^k antigens are associated with a higher than normal rate of spontaneous abortion in women with the rare p [Tj(a–)], P_1^k, and P_2^k phenotypes.

Phenotypes

Phenotype	Occurrence	RBC Antigens	Antibody
P_1	80%^	P, P1, P^k	None
P_2	20%^	P, P^k	Anti-P1
P_1^k	Rare	P1, P^k	Anti-P
P_2^k	Rare	P^k	Anti-P (and anti-P1)
p	Rare	None	Anti-PP1P^k (formerly anti-Tj^a)

Null: P_1^k and P_2^k phenotypes (p phenotype also lacks P but depends on nucleotide changes in *A4GALT*, see P1PK system, **003**).
^= in Caucasians; for other population groups, see P1PK system, **003**.

References

[1] Hellberg, A., et al., 2002. Molecular basis of the Globside-deficient P^k blood group phenotype. Identification of four inactivating mutations in the UDP-N-acetylgalactosamine: globotriaosylceramide 3-beta-N-acetylgalactosaminyltransferase gene. J Biol Chem 277, 29455–29459.
[2] Moulds, J.M., et al., 1996. Human blood groups: incidental receptors for viruses and bacteria. Transfusion 36, 362–374.

P Antigen

Terminology

ISBT symbol (number)	GLOB1 (028001 or 28.1)
Obsolete names	Globoside; Gb_4Cer; Gb4; 003002; 209001
History	Anti-P was recognized in 1955 as a component in sera of people with the p phenotype, and in 1959 as the specificity made by people with the P^k phenotype. This resulted in renaming the original anti-P as anti-P_1 (now called anti-P1; see P1PK system, **003**).

Occurrence

All populations	>99.9%

Antigen-negative RBCs have mainly been found in Scandinavians, Israelis, Amish, Finns and Arabs.

Expression

Cord RBCs	Expressed

Molecular basis associated with P antigen

For molecular basis of P-negative phenotypes, see System pages.

Effect of enzymes and chemicals on P antigen on intact RBCs

Ficin/Papain	Resistant (markedly enhanced)
Trypsin	Resistant (markedly enhanced)
α-Chymotrypsin	Resistant (markedly enhanced)
DTT 200 mM	Resistant
Acid	Resistant

In vitro characteristics of alloanti-P

Immunoglobulin class	IgM and IgG
Optimal technique	RT; 37°C; IAT
Complement binding	Yes; some hemolytic

Clinical significance of alloanti-P

Transfusion reaction	No to severe (rare) because anti-P is rare (cross-match would be incompatible)
HDFN	No to mild (in P^k mothers with anti-P)
Spontaneous abortions	Cytotoxic IgM and IgG3 antibodies directed against P and/or P^k antigens are associated with a higher than normal rate of spontaneous abortion in women with the rare p [Tj(a–)], P_1^k, and P_2^k phenotypes.

Autoanti-P

Yes, as a biphasic autohemolysin in PCH, detected by the Donath-Landsteiner test. May occur after viral illness, particularly in children.

Comments

Anti-P is compatible with P_1^k and P_2^k phenotype RBCs. Some anti-P react weakly with untreated p phenotype RBCs, while many anti-P react positively when tested against papain-treated p RBCs. This is due to the PX2 antigen (see GLOB Collection).

Experts recommend that if transfusion is necessary and P^k phenotype RBCs are not available, p RBCs can be tried as the clinical significance of anti-PX2 is unknown. If p units cannot be obtained, the recommendation is to transfuse with P-positive washed RBCs (to remove complement) that is infused through an approved blood warmer.

Siblings of patients with anti-P should be tested for compatibility, and the patient urged to donate blood for cryogenic storage when his/her clinical state permits.