ABO Blood Group System

Number of antigens 4

Polymorphic A, B, A,B, and A1

Terminology

ISBT symbol (number) ABO (001)

History In 1900, Landsteiner mixed sera and RBCs from his colleagues and observed agglutination. On the basis of the agglutination pattern, he named the first two blood groups A and B, using the first letters of the alphabet. RBCs not agglutinated by either sera were first called C, but became known as "ohne A" and "ohne B" (*ohne* is German for "without"), and finally O. In 1907, Jansky proposed using Roman numerals I, II, III, IV for O, A, B, and AB respectively, and in 1910, Moss proposed using I, II, III, and IV for AB, A, B, and O, respectively. These numerical terminologies were used respectively in Europe and America until 1927 when Landsteiner suggested, in order to avoid confusion, to use throughout the world the symbols A, B, O, and AB. When the ISBT nomenclature was first described in 1982, there were five ABO antigens, but ABO5 is now obsolete after the H antigen was removed to form the H system in 1990.

Expression

Soluble form Saliva and all body fluids except CSF (in secretors)

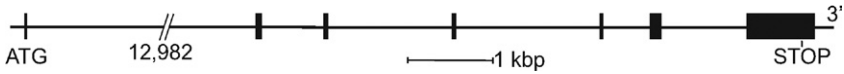
Other blood cells Lymphocytes, but also other leucocytes express A/B antigens, most prominently in secretors (antigens adsorbed from plasma), platelets (very strongly in ~5% of individuals)

The Blood Group Antigen (3/e). DOI: http://dx.doi.oxg/10.1016/B978-0-12-415849-8.00003-X

Tissues	On most epithelial cells (particularly glandular epithelia), and on endothelial cells. Broad tissue distribution (often termed "histo-blood group" antigens)

Gene[1,2]

Chromosome	9q34.1–q34.2
Name	*ABO*
Organization	7 exons distributed over 19.5 kbp of gDNA
Product	3-α-*N*-acetylgalactosaminyltransferase for A 3-α-galactosyltransferase for B



Database accession numbers

GenBank	NG_006669.1 (gDNA reference used by the NCBI website, http://www.ncbi.nlm.nih.gov/sites/varvu?gene=28); AF134412–AF134416 (represent different *A*, *B* and *O*-mRNA)
Entrez Gene ID	28

Amino acid sequence

Residues differing between the highly homologous A and B transferases are shown in bold; the two residues most important for donor sugar specificity are underlined.

A transferase (encoded by *ABO*A1.01*, based on AF134412)^

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MAEVLRTLAG  KPKCHALRPM  ILFLIMLVLV  LFGYGVLSPR  SLMPGSLERG   50
FCMAVREPDH  LQRVSLPRMV  YPQPKVLTPC  RKDVLVVTPW  LAPIVWEGTF  100
NIDILNEQFR  LQNTTIGLTV  FAIKKYVAFL  KLFLETAEKH  FMVGHRVHYY  150
VFTDQPAAVP  RVTLGTGRQL  SVLEVRAYKR  WQDVSMRRME  MISDFCERRF  200
LSEVDYLVCV  DVDMEFRDHV  GVEILTPLFG  TLHPGFYGSS  REAFTYERRP  250
QSQAYIPKDE  GDFYYLGGFF  GGSVQEVQRL  TRACHQAMMV  DQANGIEAVW  300
HDESHLNKYL  LRHKPTKVLS  PEYLWDQQLL  GWPAVLRKLR  FTAVPKNHQA  350
VRNP                                                       354
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^B transferase (encoded by *ABO*B.01*, based on AF134414) has G, S, M, and A instead of R, G, L, and G at the four positions that differ between A and B, in bold above.

Carrier molecule description[3]

A and B antigens are not the primary gene products.
Antigens are defined by immunodominant terminal sugars (α3GalNAc for A; α3Gal for B) attached to one of several different types of acceptor molecules (see below), which are oligosaccharide chains carried on either glycoproteins (~90%) or glycosphingolipids (~10%). On glycoproteins, ABO antigens are expressed mainly on N-glycans containing polylactosaminyl units predominantly on band 3 (DI), the glucose transporter, RhAG, and CHIP-1 (CO). Some precursor types (3 and 4) may only be expressed on glycolipids and not on glycoproteins. The precursor of A and B antigens is the H antigen (H1).

Peripheral core	Structure^	Predominantly found in
Type 1	Galβ(1–3)GlcNAcβ(1–3)-R	Secretions, plasma, endodermal tissues (small amounts adsorbed onto RBCs)
Type 2	Galβ(1–4)GlcNAcβ(1–3)-R	Ecto- and mesodermal tissues (main structure on RBCs)
Type 3	Galβ(1–3)GalNAcα(1–3)-R	O-linked mucin type, repetitive A (also on RBCs)
Type 4	Galβ(1–3)GalNAcβ(1–3)-R	Glycolipids in kidney (also on RBCs)

^Shown without the H-specific Fuc α2-linked to Gal.
R = Inner core structure or linkage (towards protein or lipid anchor).

Molecular basis associated with the various ABO phenotypes[4–6]

Close to 200 alleles at the *ABO* locus have been described (see dbRBC), and a selection of them is listed below. Some are associated with the common A_1, A_2, and B phenotypes, but most convey weak (A subgroups and B subgroups) or null (group O) phenotypes. Some alleles encode glycosyltransferases that have the ability to synthesize both A and B antigens and give rise to the cisAB or B(A) phenotypes. Even the normal A and B glycosyltransferases may be able to synthesize trace amounts of the "wrong" antigen (respectively, B and A), but the *cisAB* and *B*(*A*) alleles make more than normal amounts of the "wrong" antigen, to a degree that it may be detected serologically by routine reagents.
The *ABO* allele nomenclature listed here is under consideration by the ISBT, and must be considered provisional. Since various terminologies have been in use for several years[4], previously used allele names are given in parallel with the provisional ISBT allele names. The new allele names follow the ISBT naming format (see www.isbt-web.org) and nucleotide differences from the reference allele, *ABO*A1.01* (AF134412), and amino acids affected are given for all alleles

except the *B* and B^{weak} alleles for which *ABO*B.01* (AF134414) is used as reference. Alleles that differ from consensus or other alleles only by silent mutations are not listed here due to space restrictions. For more alleles, finally approved names, and details including the original reference for each allele, see dbRBC and the ISBT website.

Molecular bases associated with the A_1 and A_2 phenotypes

Phenotype	Provisional ISBT allele name	dbRBC allele name	Other allele names§	Exon	Nucleotide	Amino acid change	Ethnicity (prevalence)
A_1	*ABO*A1.01*	*A101*	*A^1, A^1–1, A(Pro)*	–	–	–	All (Common)
A_1	*ABO*A1.02*	*A102*	*$A1^v$, A^1–2, A(Leu)*	7	467C>T	Pro156Leu	Mainly Asians (Common)
A_2	*ABO*A2.01*	*A201*	*A^2, A^2–1*	7 7	467C>T 1061delC	Pro156Leu 354fs^	Non-Asians (Common)
A_2	*ABO*A2.02*	*A202*	*A106*	7	1054C>T	Arg352Trp	Japanese (Few)
A_2	*ABO*A2.03*	*A203*	*A107*	7	1054C>G	Arg352Gly	Japanese (Few)
A_2	*ABO*A2.04#*	*A204*	*R101*	6 7 7 7 7 7	297A>G 526C>G 657C>T 703G>A 771C>T 829G>A	– Arg176Gly – Gly235Ser – Val277Met	Japanese (Rare)
A_2	*ABO*A2.05*	*A205*	*A111*	7 7	467C>T 1009G>A	Pro156Leu Arg337Gly	Japanese (Few)
A_2	*ABO*A2.06*	*A206*	*A^1–A^2, $A^{2(467C)}$*	7	1061delC	354fs^	All (Rare)
A_2	*ABO*A2.07*	*A207*	–	7	539G>C	Arg180Pro	Taiwanese (Rare)
A_2	*ABO*A2.08*	*A208*	–	7 7	467C>T 539G>C	Pro156Leu Arg180Pro	Chinese (Rare)
A_2	*ABO*A2.09*	*A209*	*Avar, A207*	7 7 7	467C>T 527G>A 1061delC	Pro156Leu Arg176His 354fs^	Taiwanese, Kuwaitis (Rare)
A_2	*ABO*A2.10*	*A210*	–	6 7	268T>C 467C>T	Trp90Arg Pro156Leu	Chinese (Rare)

(*Continued*)

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Phenotype	Provisional ISBT allele name	dbRBC allele name	Other allele names[§]	Exon	Nucleotide	Amino acid change	Ethnicity (prevalence)
A_2	*ABO*A2.11*	*A211*	–	6 7	266C>T 467C>T	Pro89Leu Pro156Leu	Chinese (Rare)
A_2	*ABO*A2.12*	*A212*	–	4 7 7	190G>A 527G>A 1061delC	Val64Ile Arg176His 354fs^	American (Rare)
A_2	*ABO*A2.13*	*A213*	–	7 7	467C>T 742C>T	Pro156Leu Arg248Cys	Chinese (Rare)
A_2	*ABO*A2.16*	*A216*	*A2.16.01.1*	3 4 4 7 7	106G>T 188G>A 189C>T 467C>T 1061delC	Val36Phe Arg63His – Pro156Leu 354fs^	Austrian (Rare)
A_2	*ABO*A2.17*	*A217*	–	7 7	407C>T 467C>T	Thr136Met Pro156Leu	Chinese (Rare)
A_2	*ABO*A2.18*	*A218*	–	7 7	467C>T 722G>A	Pro156Leu Arg241Gln	Chinese (Rare)
A_2	*ABO*A2.19*	*A219*	–	7 7	467C>T 778G>A	Pro156Leu Glu260Lys	Chinese (Rare)
A_2	*ABO*A2.20*	*A220*	–	7 7	467C>T 829G>A	Pro156Leu Val277Met	Chinese (Rare)

[§]For instance, those introduced by the authors of the original publications.
^A frame-shift extends the glycosyltransferase by 21 amino acids.
[#]May be a hybrid between a *B* and an *O* allele.

Comments

The *A103–A107* alleles in dbRBC do not give rise to an altered amino acid sequence compared to other alleles, and so are not included here. *A108* and *A109* are listed as unpublished, and had no phenotype registered in dbRBC. *A214* and *A215* represent the same coding sequence as *ABO*A2.01*, but have been registered under other names due to intron polymorphisms. Also, their phenotypes are not given in dbRBC. Some alleles listed above are unpublished, but have been submitted to GenBank/dbRBC.

It is also notable that many of the alleles registered as associated with the rare A_2 phenotype in Asia (e.g., *A2.08*, *A2.13*, *A2.17*, *A2.18*, and *A2.20*) cause amino acid substitutions that have been associated with weaker A subgroups in other studies. In the case of *A2.18* and *A2.19*, the phenotype was given as A, not A_2.

Molecular bases associated with weak A subgroup phenotypes (most of them are rare)

Phenotype	Provisional ISBT allele name	dbRBC allele name	Other allele names[§]	Exon	Nucleotide	Amino acid change	Ethnicity
A_3	*ABO*A3.01*	*A301*	*A3, A^3–1*	7	871G>A	Asp291Asn	French, American
A_3	*ABO*A3.02*	*A302*	*A_3*	7 7	829G>A 1061delC	Val277Met 354fs^	Brazilian
A_3	*ABO*A3.03*	*A303*	*A^3*	7	838C>T	Leu280Phe	Taiwanese
A_3	*ABO*A3.04*	*A304*	*A^3, $A^{2(539G>A)}$*	7	539G>A[#]	Arg180His	Swedish
A_3	*ABO*A3.05*	*A305*	–	7	820G>A	Val274Met	Taiwanese
A_3	*ABO*A3.06*	*A306*	–	7 7	467C>T 820G>A	Pro156Leu Val274Met	Taiwanese
A_3	*ABO*A3.07*	*A307*	–	7 7	467C>T 745C>T	Pro156Leu Arg249Trp	Taiwanese
A_{weak}	*ABO*AW.01*	*Aw01*	*A^w–1*	7	407C>T[#]	Thr136Met	English
A_{weak}	*ABO*AW.02*	*Aw02*	*A^w–2*	6	350G>C[#]	Gly117Ala	Caucasian
A_{weak}	*ABO*AW.03*	*Aw03*	*A^w–3*	4	203G>C[#]	Arg68Thr	Scandinavian
A_{weak}	*ABO*AW.04*	*Aw04*	*A^w–4*	7	721C>T	Arg241Trp	German
A_{weak}	*ABO*AW.05*	*Aw05*	*A^w–5*	7	965A>G	Glu322Gly	Finnish
A_{weak}	*ABO*AW.06*	*Aw06*	–	7	502C>G	Arg168Gly	Caucasian
A_{weak}	*ABO*AW.07*	*Aw07*	–	7	592C>T[#]	Arg198Trp	German
A_{weak}	*ABO*AW.08*	*Aw08*	*O^2–4*	5 6 7 7 7	220C>T 297A>G 488C>T 526C>G 802G>A	Pro74Ser – Thr163Met Arg176Gly Gly268Arg	Caucasian
A_{weak}	*ABO*AW.09*	*Aw09*	*O^{1v}–A^2 hybrid*	2 3 4 5	46G>A[#] 106G>T 188G>A 220C>T	Ala16Thr Val36Phe Arg63His Pro74Ser	African
A_{weak}	*ABO*AW.10*	*Aw10*	*Avar*	7	784G>A	Asp262Asn	Korean
A_{weak}	*ABO*AW.11*	*Aw11*	–	7 7	523G>A 721C>T	Val175Met Arg241Trp	German
A_{weak}	*ABO*AW.12*	*Aw12*	–	7 7	467C>T 556A>G	Pro156Leu Met186Val	Chinese

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Phenotype	Provisional ISBT allele name	dbRBC allele name	Other allele names[§]	Exon	Nucleotide	Amino acid change	Ethnicity
A_{weak}	*ABO*AW.13*	*Aw13*	–	1	2T>C	Start codon disrupted	Caucasian
A_{weak}	*ABO*AW.14*	*Aw14*	–	7 7	467C>T 699C>A	Pro156Leu His233Gln	Korean
A_{weak}	*ABO*AW.15*	*Aw15*	–	6–7	IVS6:+4a>t	Altered splicing	Turkish
A_{weak}	*ABO*AW.16*	*Aw16*	–	1	1A>G[♯]	Start codon disrupted	Swiss
A_{weak}	*ABO*AW.17*	*Aw17*	–	5	236C>T[♯]	Pro79Leu	Caucasian
A_{weak}	*ABO*AW.18*	*Aw18*	–	6	347T>C[♯]	Ile116Thr	Swedish
A_{weak}	*ABO*AW.19*	*Aw19*	–	7	434A>G[♯]	His145Arg	Swiss
A_{weak}	*ABO*AW.20*	*Aw20*	–	7	607G>A[♯]	Glu203Lys	Canadian
A_{weak}	*ABO*AW.21*	*Aw21*	–	7	607G>C[♯]	Glu203Gln	Portuguese
A_{weak}	*ABO*AW.22*	*Aw22*	–	7	634G>A[♯]	Val212Met	Swiss
A_{weak}	*ABO*AW.23*	*Aw23*	–	7	722G>A[♯]	Arg241Gln	French
A_{weak}	*ABO*AW.24*	*Aw24*	–	7	742C>T[♯]	Arg248Cys	American
A_{weak}	*ABO*AW.25*	*Aw25*	–	7	829G>A[♯]	Val277Met	African
A_{weak}	*ABO*AW.26*	*Aw26*	O^1–A^2 hybrid	7	527G>A[♯]	Arg176His	Turkish
A_{weak}	*ABO*AW.27*	*Aw27*	–	7 7	527G>A 1061delC	Arg176His 354fs^	Syrian
A_{weak}	*ABO*AW.28*	*Aw28*	–	1–2	IVS2:+2t>c	Altered splicing	German
A_{weak}	*ABO*AW.29*	*Aw29*	–	6	311T>A	Ile104Asn	Caucasian
A_x/A_{weak}	*ABO*AW.30.01*	*Ax01*	A^x, A^x–1, *A108*	7	646T>A	Phe216Ile	Caucasian
A_x/A_{weak}	*ABO*AW.30.02*	*Ax04*	–	7 7	646T>A 681G>A	Phe216Ile –	Japanese
A_x/A_{weak}	*ABO*AW.31.01*	*Ax02*	A^x–3	6 7 7 7 7	297A>G 646T>A 681G>A 771C>T 829G>A	– Phe216Ile – – Val277Met	Swedish
A_x/A_{weak}	*ABO*AW.31.02*	*Ax03*	A^x–2	7 7 7 7	646T>A 681G>A 771C>T 829G>A	Phe216Ile – – Val277Met	Swedish[‡]

(*Continued*)

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Phenotype	Provisional ISBT allele name	dbRBC allele name	Other allele names[§]	Exon	Nucleotide	Amino acid change	Ethnicity
A_x/A_{weak}	*ABO*AW.31.03*	*Ax05*	*A^x–4*	7 7 7 7	646T>A 681G>A 771C>T 829G>A	Phe216Ile – – Val277Met	Polish[†]
A_x/A_{weak}	*ABO*AW.31.04*	*Ax06*	*A^x–5*	7 7 7 7	646T>A 681G>A 771C>T 829G>A	Phe216Ile – – Val277Met	American[‡]
A_x/A_{weak}	*ABO*AW.31.05*	*Ax08*	–	7 7 7 7	646T>A 681G>A 771C>T 829G>A	Phe216Ile – – Val277Met	German[†]
A_x/A_{weak}	*ABO*AW.32*	*Ax07*	*A^x–6*	7	996G>A	Trp332Stop	New Zealand
A_x/A_{weak}	*ABO*AW.33*	*Ax09*	*A^x–4*	7 7	467C>T 543G>T	Pro156Leu Trp181Cys	Chinese
A_x/A_{weak}	*ABO*AW.34*	*Ax10*	–	7 7 7	467C>T 829G>A 1009A>G	Pro156Leu Val277Met Arg337Gly	Chinese
A_x/A_{weak}	*ABO*AW.35*	*Ax11*	–	7 7	467C>T 860C>T	Pro156Leu Ala287Val	Taiwanese
A_x/A_{weak}	*ABO*AW.36*	*Ax12*	–	7	607G>A	Glu203Lys	Chinese
A_x/A_{weak}	*ABO*AW.37*	*Ax13*	–	7	940A>G	Lys314Glu	Chinese
A_x/A_{weak}	*ABO*AW.38*	*Ax14*	–	7	426G>C	Met142Ile	Chinese
A_x/A_{weak}	*ABO*AW.39*	*Ax15*	–	7	385T>C	Phe129Leu	Chinese
A_x/A_{weak}	*ABO*AW.40*	*Ax16*	–	7	499G>T	Gly167Cys	Chinese
A_x/A_{weak}	*ABO*AW.41*	*Ax17*	–	6	370A>G	Lys124Glu	Chinese
A_x/A_{weak}	*ABO*AW.42*	*Ax18*	–	7 7	467C>T 905A>G	Pro156Leu Asp302Gly	Chinese
A_x/A_{weak}	*ABO*AW.43*	*Ax19*	–	7 7	467C>T 721C>T	Pro156Leu Arg241Trp	Chinese
A_{finn}/A_{weak}	*ABO*AW.44*	–	*A^{finn}*	6–7	IVS6:+4a>g	Altered splicing	Finns

(*Continued*)

(Continued)

Phenotype	Provisional ISBT allele name	dbRBC allele name	Other allele names[§]	Exon	Nucleotide	Amino acid change	Ethnicity
A_{bantu}/A_{weak}	*ABO*AW.45*	*Abantu 01*	A^{bantu}, O^{1bantu}–A^{2}	4–5	IVS4:+1delG[#]	Altered splicing	Bantu
A_m	*ABO*AM.01*	*Am.01*	*A112*	7	467C>T 761C>T	Pro156Leu Ala254Val	Japanese
A_m	*ABO*AM.02*	*Am.02*	–	7	664G>A	Val222Met	Taiwanese
A_{el}	*ABO*AEL.01*	*Ael01*	A^{el}–*1, A109*	7	804insG	269fs[¤]	Caucasians
A_{el}	*ABO*AEL.02*	*Ael02*	*A110*	7 7 7	467C>T 646T>A 681G>A	Pro156Leu Phe216Ile –	Japanese
A_{el}	*ABO*AEL.03*	*Ael03*	*Aelvar*	7	804delG	269fs288Stop	African
A_{el}	*ABO*AEL.04*	*Ael04*		6–7	IVS6:+5g>a	Altered splicing	Taiwanese
A_{el}	*ABO*AEL.05*	*Ael05*		7 7	467C>T 767T>C	Pro156Leu Ile256Thr	Chinese
A_{el}	*ABO*AEL.06*	*Ael06*		7 7	425T>C 467C>T	Met142Thr Pro156Leu	Chinese
A_{el}	*ABO*AEL.07*	*Ael07*	A^{1v}–O^{1v} hybrid	7 7 7 7	467C>T 681G>A 771C>T 829G>A	Pro156Leu – – Val277Met	Taiwanese
A_{el}	*ABO*AEL.08*	*Ael08*		7 7	467C>T 804insG	Pro156Leu 269fs[¤]	Chinese

[§]For instance, those introduced by the authors of the original publications.
[^]A frame-shift extends the glycosyltransferase by 21 amino acids.
[#]This allele also carries the two *ABO*A2.01*-related SNPs 467C > T and 1061delC which result in Pro156Leu and 354fs and extension of the protein by 21 amino acids.
[¤]This frame-shifting mutation theoretically extends the protein by 37 amino acids.
[†]These alleles differ in their intron 6 sequence, and are probable hybrid alleles with different crossing-over points between common *ABO* alleles.

Molecular bases associated with B phenotype^

(The seven B-associated polymorphisms are only shown for the first allele but are present in the others.)

Phenotype	Provisional ISBT allele name	dbRBC allele name	Other allele names§	Exon	Nucleotide	Amino acid change	Ethnicity
B	*ABO*B.01*	*B101*	*B*	6 7 7 7 7 7 7	297A>G 526C>G 657C>T 703G>A 796C>A 803G>C 930G>A	– Arg176Gly – Gly235Ser Leu266Met Gly268Ala –	All (Common)
B	*ABO*B.02*	*B108*	*Bvar*	7	892G>T	Ala298Ser	Taiwanese (Rare)
B	*ABO*B.03*	*B112*	–	7	559C>T	Arg187Cy	Chinese (Rare)

§For instance, by the authors of the original publication.

^Other variants of *B* alleles exist, but the ones listed in dbRBC are either based on: (1) lack of one of the silent *A* vs. *B* SNPs (e.g., *B102* has 930G, *B103* has 657C); (2) silent mutations (*B109* has 498C > T); (3) intron SNPs (e.g., *B107*, *B113*, *B114*, *B116*); (4) a sequence identical to a proven B_{weak} (*B110*); (5) unpublished (*B113–B116*).

Molecular bases associated with weak B subgroup phenotypes (all rare)

Differences compared to *ABO*B.01* are given.

Phenotype	Provisional ISBT allele name	dbRBC allele name	Other allele names§	Exon	Nucleotide	Amino acid change	Ethnicity
B_3	*ABO*B3.01*	*B301*	*B*^{3}	7	1054C>T	Arg352Trp	Japanese
B_3	*ABO*B3.02*	*B302*	–	7	646T>A	Phe216Ile	Japanese
B_3	*ABO*B3.03*	*B303*	–	3–4	IVS3:+5g>a	Altered splicing	Asians
B_3	*ABO*B3.04*	*B304*	–	6	247G>T	Asp83Tyr	Taiwanese
B_3	*ABO*B3.05*	*B305*	–	7	425T>C	Met142Thr	Chinese
B_3	*ABO*B3.06*	*B306*	*Bvar*	7	547G>A	Asp183Asn	Koreans
B_3	*ABO*B3.07*	*B307*	–	7	410T>C	Ala137Val	Chinese

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Phenotype	Provisional ISBT allele name	dbRBC allele name	Other allele names[§]	Exon	Nucleotide	Amino acid change	Ethnicity
B_3	*ABO*B3.08*	*B308*	–	7	938A>C	His313Pro	Koreans
B_x/B_{weak}	*ABO*BW.01*	*Bx01*	*B^w–1*	7	871G>A	Asp291Asn	Japanese
B_{weak}	*ABO*BW.02*	*Bw02*	*B^w–2*	7	873G>C	Asp291Glu	French
B_{weak}	*ABO*BW.03*	*Bw03*	*B^w–3*	7	721C>T	Arg241Trp	Swedish
B_{weak}	*ABO*BW.04*	*Bw04*	*B^w–4*	7	548A>G	Asp183Gly	Swedish
B_{weak}	*ABO*BW.05*	*Bw05*	*B^w–5*	7	539G>A	Arg180His	American
B_{weak}	*ABO*BW.06*	*Bw06*	*B^w–6*	7	1036A>G	Lys346Glu	Finnish
B_{weak}	*ABO*BW.07*	*Bw07*	*B^w–7*	7	1055G>A	Arg352Gln	Indian, American
B_{weak}	*ABO*BW.08*	*Bw08*	*B^w–8*	7	863T>G	Met288Arg	Turkish
B_{weak}	*ABO*BW.09*	*Bw09*	*Bw08*	7	1037A>T	Lys346Glu	German
B_{weak}	*ABO*BW.10*	*Bw10*	–	7	556A>G	Met186Val	Brazilian
B_{weak}	*ABO*BW.11*	*Bw11*	*B^w–11*	7	695T>C	Leu232Pro	Chinese, Thai
B_{weak}	*ABO*BW.12*	*Bw12*	–	6	278C>T	Leu93Pro	Chinese
B_{weak}	*ABO*BW.14*	*Bw14*	*B^w–14*	7	523G>A	Val175Met	Caucasian, Chinese[^]
B_{weak}	*ABO*BW.15*	*Bw15*	*B^w–15*	7	565A>G	Met189Val	Turkish
B_{weak}	*ABO*BW.16*	*Bw16*	*B^w–16*	7	575T>C	Ile192Thr	Hindustani
B_{weak}	*ABO*BW.17*	*Bw17*	*B^w–17*	7	784G>A	Asp262Asn	Indian
B_{weak}	*ABO*BW.18*	*Bw18*	*B^w–18*	7	802G>A	Ala268Thr	French
B_{weak}	*ABO*BW.19*	*Bw19*	*B^w–19*	7 7	646T>A 681G>A	Phe216Ile –	Chinese
B_{weak}[#]	*ABO*BW.20*	*Bw20*	–	7	816insG	272fs392Stop	German
B_{weak}	*ABO*BW.21*	*Bw21*	–	7	688G>C	Gly230Arg	Turkish
B_{weak}	*ABO*BW.22*	*Bw22*	–	7	503G>T	Arg168Leu	Chinese
B_{weak}	*ABO*BW.23*	*Bw23*	–	7	743G>C	Arg248Pro	Chinese
B_{weak}	*ABO*BW.24*	*Bw24*	–	7	558G>T	Met186Ile	Chinese
B_{weak}	*ABO*BW.25*	*Bw25*	–	3 7	103G>A 619C>G	Gly35Arg Leu207Val	German
B_{weak}	*ABO*BW.26*	*Bw26*	*O^2–B* hybrid[¤]	2	53G>T	Arg18Leu	Swiss
B_{weak}	*ABO*BW.27*	*Bx02*	*Bel06*	7	905A>G	Asp302Gly	Chinese
B_{weak}	*ABO*BW.28*	*Bx03*	–	7	541T>C	Trp181Arg	Chinese

(*Continued*)

(Continued)

Phenotype	Provisional ISBT allele name	dbRBC allele name	Other allele names[§]	Exon	Nucleotide	Amino acid change	Ethnicity
B_{weak}	*ABO*BW.29*	*Bx04*	–	7	588C>G	Cys196Trp	Chinese
B_{weak}	*ABO*BW.30*	*Bx05*	–	7	976G>T	Asp326Tyr	Chinese
B_{weak}	*ABO*BW.31*	*Bx06*	–	7	900G>C	Trp300Cys	Chinese
B_{weak}	*ABO*BW.32*	*Bx07*	–	7	808T>A	Phe270Ile	Chinese
B_{weak}	*ABO*BW.33*	*Bx08*	–	7	550G>A	Val184Met	Chinese
B_{weak}	*ABO*BW.34*	*Bx09*	–	7	889G>A	Glu297Lys	Chinese
B_{el}	*ABO*BEL.01*	*Bel01*	*B105*	7	641T>G	Met214Arg	Japanese
B_{el}	*ABO*BEL.02*	*Bel02*	*B106*	7	669G>T	Glu223Asp	Japanese
B_{el}	*ABO*BEL.03*	*Bel03*	–	7	502C>T	Arg168Trp	Taiwanese
B_{el}	*ABO*BEL.04*	*Bel04*	–	7	[†]	[†]	Brazilian Japanese
B_{el}	*ABO*BEL.05*	*Bel05*	–	7	952G>A	Val318Met	Chinese

[§]For instance, by the authors of the original publication.
[^]Apparently normal B phenotype in two Chinese donors.
[#]According to the original publication, adsorption/elution was negative so allele designation questionable.
[¤]A hybrid between an *O* allele (exons 1–4) and *B* (exons 5–7).
[†]467C > T;646T > A;681G > A;771C > T;796C > A ;803G > C;829G > A, resulting in Pro156Leu;Phe216Ile; Met266Leu;Gly268Ala;Met277Val, i.e., an unusual combination of allelic markers from *ABO*A1.02, *B.01* and a common *O* allele. Possibly a hybrid allele.

Molecular bases associated with cisAB and B(A) phenotypes (all rare except *ABO*cisAB.01*, which is infrequent in Asians)

Differences compared to *ABO*A1.01* are given.

Phenotype	Provisional ISBT allele name	dbRBC allele name	Other allele names	Exon	Nucleotide	Amino acid change	Ethnicity
cisAB	*ABO*cisAB.01*	*cis–AB01*	*cisAB–1*	7 7	467C>T 803G>C	Pro156Leu Gly268Ala	Asian
cisAB	*ABO*cisAB.02*	*cis–AB02*	*cisAB–2*	7 7 7 7	526C>G 657C>T 703G>A 803G>C	Arg176Gly – Gly235Ser Gly268Ala	Australian

(*Continued*)

(Continued)

Phenotype	Provisional ISBT allele name	dbRBC allele name	Other allele names	Exon	Nucleotide	Amino acid change	Ethnicity
cisAB	*ABO*cisAB.03*	*cis–AB03*	*cis AB. tlse(*)01, cisAB–3*	6 7 7 7 7 7 7 7	297A>G 526C>G 657C>T 700C>T 703G>A 796C>A 803G>C 930G>A	– Arg176Gly – Pro234Ser Gly235Ser Leu266Met Gly268Ala –	French
cisAB	*ABO*cisAB.04*	*cis–AB04*	*cisAB–4*	7 7	467C>T 796C>A	Pro156Leu Leu266Met	Chinese
cisAB	*ABO*cisAB.05*	*cis–AB05*	*cisAB–5*	6 7 7 7 7 7	297A>G 526C>G 657C>T 703G>A 796C>A 930G>A	– Arg176Gly – Gly235Ser Leu266Met –	Chinese^
cisAB	*ABO*cisAB.06*	*cis–AB06*	–	6 7 7 7 7 7	297A>G 657C>T 703G>A 796C>A 803G>C 930G>A	– – Gly235Ser Leu266Met Gly268Ala –	Chinese
B(A)	*ABO*BA.01*	*B(A)01*	*B(A)–1*	6 7 7 7 7	297A>G 526C>G 796C>A 803G>C 930G>A	– Arg176Gly Leu266Met Gly268Ala –	
B(A)	*ABO*BA.02*	*B(A)02*	*B(A)–2*	6 7 7 7 7 7 7 7	297A>G 526C>G 657C>T 700C>G 703G>A 796C>A 803G>C 930G>A	– Arg176Gly – Pro234Ala Gly235Ser Leu266Met Gly268Ala –	Taiwanese
B(A)	*ABO*BA.03*	*B(A)03*	*B(A)–3*	6 7 7 7 7 7	297A>G 526C>G 657C>T 796C>A 803G>C 930G>A	– Arg176Gly – Leu266Met Gly268Ala –	Caucasian
B(A)	*ABO*BA.04*	*B(A)04*	*B(A)–4*	6 7 7 7 7	297A>G 526C>G 640A>G 657C>T 703G>A	– Arg176Gly Met214Val – Gly235Ser	Chinese

(*Continued*)

(Continued)

Phenotype	Provisional ISBT allele name	dbRBC allele name	Other allele names	Exon	Nucleotide	Amino acid change	Ethnicity
				7 7 7	796C>A 803G>C 930G>A	Leu266Met Gly268Ala –	
B(A)	*ABO*BA.05*	*B(A)05*	*B(A)–5*	6 7 7 7 7 7 7 7	297A>G 526C>G 641T>C 657C>T 703G>A 796C>A 803G>C 930G>A	– Arg176Gly Met214Thr – Gly235Ser Leu266Met Gly268Ala –	Chinese
B(A)	*ABO*BA.06*	*B(A)06*	*B(A)–6*, *B(A)^{v}*	6 7 7 7 7 7	297A>G 526C>G 657C>T 703G>A 796C>A 930G>A	– Arg176Gly – Gly235Ser Leu266Met –	Chinese

^This allele may be identical to *ABO*BA.06*. The polymorphisms and amino acids reported for both alleles are the same according to dbRBC, and the *cis-AB05* entry has been accepted in dbRBC without publication or GenBank submission so difficult to compare.

Molecular bases associated with O (null) phenotype^

Differences compared to *ABO*A1.01* are given, and the genetic alteration inducing the null phenotype is noted in bold (if known).

Phenotype	Provisional ISBT allele name	dbRBC allele name	Other allele names§	Exon	Nucleotide	Amino acid change	Ethnicity
O	*ABO*O.01.01*	*O01*	*O^{1}*	6	**261delG**	88fs118Stop	All (Common)
O	*ABO*O.01.02*	*O02*	*O^{1v}*	3 4 4 5 6 6 7 7 7 7	106G>T 188G>A 189C>T 220C>T **261delG** 297A>G 646T>A 681G>A 771C>T 829G>A	Val36Phe Arg63His – Pro74Ser 88fs118Stop – – – – –	All (Common)

(*Continued*)

(Continued)

Phenotype	Provisional ISBT allele name	dbRBC allele name	Other allele names[§]	Exon	Nucleotide	Amino acid change	Ethnicity
O?	*ABO*O.02.01*	*O03*	*O²–1*	2 5 6 7 7	53G>T 220C>T 297A>G 526C>G **802G>A**	Arg18Leu Pro74Ser – Arg176Gly Gly268Arg	All but Asians (Many)
O?	*ABO*O.02.02*	*O48*	*O²–2*	2 5 6 7 7 7 7	53G>T 220C>T 297A>G 526C>G 649C>T 689G>A **802G>A**	Arg18Leu Pro74Ser – Arg176Gly Arg217Cys Gly229Asp Gly268Arg	Israeli (Rare)
O?	*ABO*O.02.03*	*O49*	*O²–3*	2 5 6 7 7 7	53G>T 220C>T 297A>G 526C>G 689G>A **802G>A**	Arg18Leu Pro74Ser – Arg176Gly Gly229Asp Gly268Arg	Caucasians (Many)
O?	*ABO*O.02.04*	*O50*	*O²–4*	2 5 6 7 7 7	53G>T 220C>T 297A>G 488C>T 526C>G **802G>A**	Arg18Leu Pro74Ser – Thr163Met Arg176Gly Gly268Arg	Caucasians (Several)
O?	*ABO*O.03*	*O08*	*O³*	7 7 7	467C>T **804insG** **1061delC**	Pro156Leu 269fs[♯] 354fs[♯]	Caucasians (Rare)
O?	*ABO*O.04*	*O51*	*O⁴, O41*	2	**87_88insG**	29fs56Stop	Caucasians (Rare)
O?	*ABO*O.05*	*O52*	*O⁵*	6	**322C>T**	Gln108Stop	Caucasians (Rare)
O?	*ABO*O.06*	*O53*	*O⁶*	7	**542G>A**	Trp181Stop	Caucasians (Rare)
O	*ABO*O.07*	*O14*	*O301*	7 7	467C>T **893C>T**	Pro156Leu Ala298Val	Japanese (Rare)
O	*ABO*O.08*	*O15*	*O302*	7	**927C>A**	Tyr309Stop	Japanese (Rare)
O?	*ABO*O.09.01*	*O19*	*R102*	7 7 7 7	646T>A 681G>A 771C>T 829G>A	Phe216Ile – – Val277Met	Japanese[¤] (Rare)

(*Continued*)

(Continued)

Phenotype	Provisional ISBT allele name	dbRBC allele name	Other allele names[§]	Exon	Nucleotide	Amino acid change	Ethnicity
O?	*ABO*O.09.02*	*O20*	*R103*	6 7 7 7 7	297A>G 646T>A 681G>A 771C>T 829G>A	– Phe216Ile – – Val277Met	Japanese[¤] (Rare)
O?	*ABO*O10*	*O72*	–	2	**67insG**	23fs	

[§]For instance, by the authors of the original publication.
[#]These two frame-shifts neutralize each other and the protein product has normal size (354 amino acids).
[¤]These hybrid alleles involve exon 7 of *ABO*O.01.02*, and are similar or identical to so-called A^x hybrids (*ABO*AW.31.01* to *ABO*AW.31.05*). The allele *in trans* may determine the resulting phenotype.

[^]Multiple variants of these alleles exist with numerous silent SNPs, but >95% of all *O* alleles depend on 261delG for their inactivation. The major alleles inactivated by principally different mechanisms are listed.

Comments

Hybrid *ABO* alleles are not uncommon. Null alleles including exon 6 from one of the common *O* alleles containing 261delG but with exon 7 elements from A^2 or *B* may interfere with *ABO* genotyping and cause risk for erroneous reporting of A^2 and *B* alleles, respectively. Since the products of these *O* alleles are truncated in the same way as *ABO*O.01.01* and *ABO*O.01.02*, they have not been included in the above table, as is also the case for other allelic variants featuring 261delG. If only position 261 has been tested to determine *O* allele status, *ABO*O.01* can be used for reporting.

Most of the *O* alleles lacking 261delG have been involved in serological ABO typing discrepancies. Despite the presence of premature stop codons in various exons, the phenotype produced varies from group O to weak expression of A antigen, but weakening of anti-A and anti-A1 is often observed. It can therefore be debated if they should be classified as *O* alleles or not. The mechanisms behind these phenomena have not yet been clarified.

Function

The A and B glycosyltransferase use, respectively, UDP-GalNAc and UDP-Gal as their donor substrates, and the various forms of H precursor structures as their acceptor substrates. There have been many speculative arguments as to the general function of ABO structures but it is clear that human "knock-outs," i.e., individuals with the null phenotype (group O), are not seriously affected. Instead, this phenotype is actually beneficial in many situations, perhaps best exemplified by its protective role in decreasing rosetting in severe malaria[7]. In an evolutionary perspective, glycan diversity (including ABO differences) is thought to have been

a key survival factor, serving as a primitive immune system via the herd immunity concept[8]. Accordingly, it was important that members of a certain population had different carbohydrate epitopes serving as involuntary receptors for pathogen lectins, and also different naturally-occurring antibodies neutralizing pathogens with ABO-mimicking sugar coats on their surfaces. Only in this way would the population be likely to survive over time despite lethal pandemics. In addition to this fundamental function, other potential functions of ABO antigens have been proposed, including roles in embryogenesis, cell–cell interaction in carcinogenesis[9], and modulation of sialic acid recognition[10].

Disease association[5,7,11]

Expression of A and B antigens may be weakened in normal states such as during pregnancy, at young or old age, as well as due to disease. Weakening or even disappearance of A and B antigens can be the result of chromosome 9 translocations, development of (pre-) malignant hematological disease such as leukemia (especially in the acute and chronic myelogenous types) and myelodysplastic syndrome, and any disease inducing stress hematopoiesis, e.g., thalassemia and Diamond-Blackfan anemia. Stress hematopoiesis induces reduced branching of carbohydrate chains, and thus fewer A, B, H, and I antigens. Changes in sugar chains are often observed during carcinogenesis, and therefore altered ABH antigens can be considered tumor markers. Loss of A and B antigens have been described in various solid tumors. The acquired B antigen is a consequence of microbial infection in which the terminal GalNAc of the A antigen is deacetylated by bacterial enzymes, and thereby is made more similar to Gal. ABO phenotypes are associated with susceptibility to numerous diseases including cancer, thrombosis, and bleeding. There is also a strong correlation between susceptibility to certain infections and ABO status, most prominently severe forms of *Plasmodium falciparum* malaria.

Phenotypes (% occurrence)

	Caucasians^	Blacks^	Asian^	Mexican
A_1	33	19	27	22
A_2	10	8	rare	6
B	9	20	25	13
O	44	49	43	55
A_1B	3	3	5	4
A_2B	1	1	rare	rare
Null	O is the amorph; O_h (the Bombay phenotype) depends on the *FUT1/FUT2* loci, see H system [**018**]			
Unusual	Many subgroups of A and B (see phenotype tables in major text books)			

^Major variation occurs between ethnic subgroups within these main populations.

Comments

Aberrant ABO results created by modern medical practices (in addition to the mixed-field reactions seen after transfusion of ABO-non-identical RBCs) include: ABO-non-identical stem cell transplantation; ABO-incompatible solid organ transplantation; *in vitro* fertilization; artificial insemination; surrogate motherhood.
There is a vast literature on clinical, serological, microbiological, biochemical, enzymatic, structural, and molecular genetic aspects of the ABO system. The reader is recommended to search the databases for the numerous reviews written on various aspects of these different ABO-related topics.

References

[1] Yamamoto, F., et al., 1990. Cloning and characterization of DNA complementary to human UDP-GalNAc: Fuca1—>2Gala1—>3GalNAc transferase (histo-blood group A transferase) mRNA. J Biol Chem 265, 1146–1151.

[2] Yamamoto, F., et al., 1990. Molecular genetic basis of the histo-blood group ABO system. Nature 345, 229–235.

[3] Clausen, H., Hakomori, S., 1989. ABH and related histo-blood group antigens; immunochemical differences in carrier isotypes and their distribution. Vox Sang 56, 1–20.

[4] Chester, M.A., Olsson, M.L., 2001. The ABO blood group gene: a locus of considerable genetic diversity. Transfus Med Rev 15, 177–200.

[5] Storry, J.R., Olsson, M.L., 2009. The ABO blood group system revisited: a review and update. Immunohematology 25, 48–59.

[6] Yamamoto, F., 2004. Review: ABO blood group system – ABH oligosaccharide antigens, anti-A and anti-B, A and B glycosyltransferases and ABO genes. Immunohematology 20, 3–22.

[7] Cserti, C.M., Dzik, W.H., 2007. The ABO blood group system and *Plasmodium falciparum* malaria. Blood 110, 2250–2258.

[8] Gagneux, P., Varki, A., 1999. Evolutionary considerations in relating oligosaccharide diversity to biological function. Glycobiology 9, 747–755.

[9] Ichikawa, D., et al., 1997. Histo-blood group A/B versus H status of human carcinoma cells as correlated with haptotactic cell motility: approach with A and B gene transfection. Cancer Res 57, 3092–3096.

[10] Cohen, M., et al., 2009. ABO blood group glycans modulate sialic acid recognition on erythrocytes. Blood 114, 3668–3676.

[11] Anstee, D.J., 2010. The relationship between blood groups and disease. Blood 115, 4635–4643.

A Antigen

Terminology

ISBT symbol (number)	ABO1 (001001 or 1.1)
Other names and history	See System page

Occurrence

Caucasians	43%
Blacks	27%

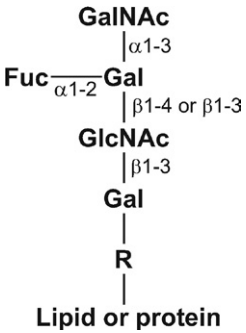
Asians	28%
Mexicans	28%
South American Indians	0%

These numbers do not include group AB, which would increase the numbers (all except South American Indians) by approximately 4%.

Expression

Cord RBCs	Weak
Altered	Weak in A subgroup and other variants; some diseases

Molecular basis associated with A antigen



See ABO Blood Group System page for genetic basis of A subgroups.

Effect of enzymes and chemicals on A 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-A

Immunoglobulin class	IgM; IgG
Optimal technique	RT or below; IAT for IgG component^
Neutralization	Saliva from A secretors
Complement binding	Yes; some hemolytic

^May be particularly relevant when testing or titrating the sera of platelet donors, pregnant women, and patients waiting for or having undergone ABO-incompatible organ transplantation or following ABO-non-identical stem cell transplantation complicated by pure red cell aplasia due to anti-A.

Clinical significance of alloanti-A

Transfusion reaction	None to severe; immediate/delayed; intravascular/extravascular
HDFN	No to moderate (rarely severe)

Autoanti-A

Rare

Comments

Serum from group A individuals contains naturally-occurring anti-B (see B antigen section).

B Antigen

Terminology

ISBT symbol (number)	ABO2 (001002 or 1.2)
Other names and history	See System page

Occurrence

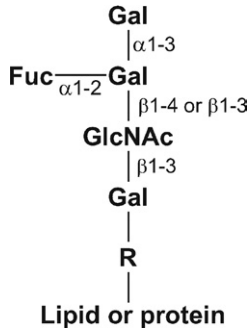
Caucasians	9%
Blacks	20%
Asians	27%
Mexicans	13%
South American Indians	0%

These numbers do not include group AB, which would increase the numbers (all except South American Indians) by approximately 4%.

Expression

Cord RBCs	Weak
Altered	Weak in B subgroup and other variants; some diseases

Molecular basis associated with B antigen



See ABO system page for genetic basis of B subgroups.

Effect of enzymes and chemicals on B 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-B

Immunoglobulin class	IgM; IgG
Optimal technique	RT or below; IAT for IgG component^
Neutralization	Saliva from B secretors
Complement binding	Yes; some hemolytic

^May be particularly relevant when testing or titrating the sera of platelet donors, pregnant women, and patients waiting for or having undergone ABO-incompatible organ transplantation or following ABO-non-identical stem cell transplantation complicated by pure red cell aplasia due to anti-B.

Clinical significance of alloanti-B

Transfusion reaction	No to severe; immediate/delayed; intravascular/extravascular
HDFN	No to moderate (rarely severe)

Autoanti-B

Rare

Comments

Serum from group B individuals contains naturally-occurring anti-A and anti-A1 (see A and A1 antigen sections).

A,B Antigen

Terminology

ISBT symbol (number)	ABO3 (001003 or 1.3)
History	Discussed since the 1950s and many hypotheses about the molecular background of this antigen have been presented. At one point referred to as the C antigen of the ABO system. Acknowledged by the ISBT in the first workshop report in 1982.

Occurrence

Found in all individuals expressing A and/or B antigens (e.g., 56% of Caucasians according to the phenotype table in the ABO system section above).

Expression

Cord RBCs	Weak
Altered	Weakened when A and B antigens are weak

Molecular basis associated with A,B antigen[1]

Once the molecular differences between A and B antigens were revealed, it was hypothesized that the structures common to the oligosaccharide terminals ending with α3GalNAc and α3Gal, respectively, would make up the epitope recognized by anti-A,B. The only difference between A and B antigens is situated at carbon position 2 of the terminal residue, i.e., A has a NHAc group, whereas B has an OH group. The A,B epitope was shown to depend on the surface common to the terminal sugars in A and B. Monoclonal anti-A,B and polyclonal anti-A,B from group O sera react with this epitope.

Effect of enzymes and chemicals on A,B 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-A,B

Immunoglobulin class	IgM; IgG
Optimal technique	RT or below; IAT for IgG component^
Neutralization	Saliva from A, B or AB secretors
Complement binding	Rare

^May be particularly relevant when testing or titrating the sera of platelet donors, pregnant women, and patients waiting for or having undergone ABO-incompatible organ transplantation or following ABO-non-identical stem cell transplantation complicated by pure red cell aplasia due to anti-A and anti-B.

Clinical significance of anti-A,B

Transfusion reaction	None to mild/delayed
HDFN	No to severe^

^No data to differentiate anti-A or anti-B from anti-A,B as the implicated antibody specificity in affected fetuses/infants to group O mothers in whom ABO-related HDFN is more common. However, group O individuals (who are the only anti-A,B makers) produce more IgG antibodies against ABO antigens compared to A and B individuals. Anti-A,B crosses the placenta more frequently than do anti-A and anti-B.

Autoantibody

Rare

Comments

Anti-A,B is an antibody specificity selectively found in the plasma of group O individuals and that cannot be separated into anti-A and anti-B.
Polyclonal anti-A,B from group O individuals reacts strongly with A_x subgroup RBCs, while anti-A may not react or react only weakly.

Reference

[1] Korchagina, E.Y., et al., 2005. Design of the blood group AB glycotope. Glycoconj J 22, 127–133.

A1 Antigen

Terminology

ISBT symbol (number)	ABO4 (001004 or 1.4)
History	The two major A subgroups, A_1 and A_2, were discovered already in 1911 by von Dungern and Hirszfeld, but remained unnamed until 1930 when the blood group A phenotype was subdivided by the presence or absence of (what later became known as) A1 antigen, recognized by antibodies in the serum of some individuals with the A_2 phenotype

Occurrence

Caucasians	34% (approximately 80% of group A)
Blacks	19%
Asians	27%

These numbers do not include group AB.

Expression

Cord RBCs	Weak
Altered	A_{int} (a subgroup with phenotype characteristics in between A_1 and A_2)

Acquired B syndrome (almost exclusively found in A1-positive individuals following modification of the terminal GalNAc of the A antigen on their RBCs by a bacterial deacetylase during infection to cause crossreactivity with some anti-B reagents).

Molecular basis associated with A1 antigen[1–6]

Even if the difference between the A1-positive A_1 phenotype and the A1-negative A_2 phenotype can easily be demonstrated by simple hemagglutination assays using lectin reagents diluted correctly (e.g., *Dolichos biflorus* positive with A_1 RBCs and negative with A_2, whilst *Ulex europaeus* is negative with A_1 and positive with A_2), the molecular identity of the A1 antigen is still under debate. It is unequivocal that a quantitative difference exists so that A_1 RBCs possess approximately 4–5 times more A antigen than A_2 RBCs. In addition, the common A^2 allele has distinct features (mainly the 1061delC polymorphism) compared to A^1 alleles, and encodes a glycosyltransferase that is qualitatively different (e.g., regarding its pH optimum, enzymic activity, and molecular size) from the A_1 transferase.

A_1 RBCs have higher amounts of A type 3 glycolipid (the repetitive A epitope) and A type 4 (globo-A). A_2 RBCs may have A type 3 at levels that are difficult to detect serologically on whole RBCs compared to A_1, and may lack A type 4.

Effect of enzymes and chemicals on A1 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-A1

Immunoglobulin class	IgM more common than IgG
Optimal technique	RT or below
Neutralization	Saliva from A (A_1) secretors
Complement binding	Rare

Clinical significance of alloanti-A1

Transfusion reaction	None to mild/delayed
HDFN	No

Autoantibody

Rare

Comments

Anti-A1 is found in serum from 1–2% of A_2 and 25% of A_2B individuals, and is a component of anti-A from group O and B people.

References

[1] Clausen, H., et al., 1984. Blood group A glycolipid (Ax) with globo-series structure which is specific for blood group A1 erythrocytes: one of the chemical bases for A1 and A2 distinction. Biochem Biophys Res Commun 124, 523–529.

[2] Clausen, H., et al., 1985. Repetitive A epitope (type 3 chain A) defined by blood group A1-specific monoclonal antibody TH-1: chemical basis of qualitative A1 and A2 distinction. Proc Natl Acad Sci USA 82, 1199–1203.

[3] Clausen, H., et al., 1986. Novel blood group H glycolipid antigens exclusively expressed in blood group A and AB erythrocytes (type 3 chain H). II. Differential conversion of different H substrates by A1 and A2 enzymes, and type 3 chain H expression in relation to secretor status. J Biol Chem 261, 1388–1392.

[4] Schachter, H., et al., 1973. Qualitative differences in the N-acetyl-D-galactosaminyltransferases produced by human A1 and A2 genes. Proc Natl Acad Sci USA 70, 220–224.

[5] Svensson, L., et al., 2009. Blood group A(1) and A(2) revisited: an immunochemical analysis. Vox Sang 96, 56–61.

[6] Yamamoto, F., et al., 1992. Human histo-blood group A2 transferase coded by A2 allele, one of the A subtypes, is characterized by a single base deletion in the coding sequence, which results in an additional domain at the carboxyl terminal. Biochem Biophys Res Commun 187, 366–374.