Diego Blood Group System

Number of antigens 22

Low prevalence	Di[a], Wr[a], Wd[a], Rb[a], WARR, ELO, Wu, Bp[a], Mo[a], Hg[a], Vg[a], Sw[a], BOW, NFLD, Jn[a], KREP, Tr[a], Fr[a], SW1
High prevalence	Di[b], Wr[b], DISK

Terminology

ISBT symbol (number)	DI (010)
CD number	CD233
History	Named after the producer of the first anti-Di[a], discovered during the investigation of a case of HDFN in a Venezuelan family. Diego was described in 1955 by Layrisse et al; it had been mentioned briefly by Levine et al. in 1954.

Expression

Tissues	Intercalated cells of the distal and collecting tubules of the kidney An isoform of band 3 is expressed in the distal nephron of the kidney

Gene

Chromosome	17q21.31
Name	*DI* (*SLC4A1*, *AE1*, *EPB3*)
Organization	20 exons distributed over 20 kbp of gDNA
Product	Band 3 (Anion Exchanger 1; Anion Transport Protein)

The Blood Group Antigen (3/e). DOI: http://dx.doi.org/10.1016/B978-0-12-415849-8.00012-0

Database accession numbers

GenBank	NM_000342 (mRNA); M27819 (mRNA)
Entrez Gene ID	6521

Molecular bases of Diego phenotypes[1]

Reference allele *DI*02* or *DI*B* (Accession number NM_000342) encodes Di^b (DI2), DI4, DI22. Nucleotide differences, and amino acids affected, are given.

Allele encodes	Allele name	Exon	Nucleotide	Restriction enzyme	Amino acid	Ethnicity (prevalence)
Di(a+b–) or DI:1,–2	*DI*01 or DI*A*	19	2561C>T	*Msp*I–	Pro854Leu	South Americans, Native Americans, Japanese, Chinese, Poles (Many)
Wr(a+b–) or DI:3,–4	*DI*02.03*	16	1972G>A		Glu658Lys	(Many)
Wd(a+) or DI:5	*DI*02.05*	14	1669G>A	*Msl*I+	Val557Met	Hutterites, Namibians (Rare)
Rb(a+) or DI:6	*DI*02.06*	14	1643C>T	*Eco*NI+	Pro548Leu	Caucasians (Rare)
WARR+ or DI:7	*DI*02.07*	14	1654C>T	*Bbs*I –	Thr552Ile	Native Americans (Rare)
ELO+ or DI:8	*DI*02.08*	12	1294C>T	*Msp*I –	Arg432Trp	Caucasians (Rare)
Wu+, DISK– or DI:9,–22	*DI*02.09*	14	1694G>C	*Apa*I –	Gly565Ala	Scandinavians, Dutch, Blacks, Irish (Several)
Bp(a+) or DI:10	*DI*02.10*	14	1707C>A	*Tth*2 –	Asn569Lys	English, Italians (Rare)
Mo(a+) or DI:11	*DI*02.11*	16	1967G>A	*Msm*I+	Arg656His	Belgians, Norwegians (Rare)
Hg(a+) or DI:12	*DI*02.12*	16	1966C>T	*Cac*8I+	Arg656Cys	Welsh, Australians (Rare)

(*Continued*)

(Continued)

Allele encodes	Allele name	Exon	Nucleotide	Restriction enzyme	Amino acid	Ethnicity (prevalence)
Vg(a+) or DI:13	*DI*02.13*	14	1663T>C	*Dra*III+	Tyr555His	Australians (Rare)
Sw(a+) or DI:14	*DI*02.14*	16	1937G>A		Arg646Gln	Caucasians (Rare)
BOW+ or DI:15	*DI*02.15*	14	1681C>T	*Ban*I – *Bst*EIII+	Pro561Ser	Caucasians (Rare)
NFLD+ or DI:16	*DI*02.16*	12; 14	1287A>T 1681C>G		Glu429Asp Pro561Ala	French Canadians, Japanese (Few)
Jn(a+) or DI:17	*DI*02.17*	14	1696C>T		Pro566Ser	Poles, Slovaks (Rare)
KREP+ or DI:18	*DI*02.18*	14	1696C>G		Pro566Ala	Poles (Rare)
Tr(a+) or DI:19	*DI*02.19*	14	1653G>C	*Bbs*I –	Lys551Asn	English (Rare)
Fr(a+) or DI:20	*DI*02.20*	13	1438G>A	*Bsa*I – *BsmA*I –	Glu480Lys	Mennonites (Several)
SW1 or DI:21	*DI*02.21*	16	1936C>T		Arg646Trp	Caucasians (Rare)

Molecular basis for silencing of *DI*

The nucleotide difference from *DI*02* reference allele (Accession number NM_000342), and the amino acid affected, are given.

Allele name	Exon	Nucleotide	Restriction enzyme	Amino acid	Ethnicity (prevalence)
*DI*02N.01*	13	1462G>A	*Nla*III+	Val488Met[1]	Portuguese (Rare)

Amino acid sequence

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MEELQDDYED  MMEENLEQEE  YEDPDIPESQ  MEEPAAHDTE  ATATDYHTTS   50
HPGTHKVYVE  LQELVMDEKN  QELRWMEAAR  WVQLEENLGE  NGAWGRPHLS  100
HLTFWSLLEL  RRVFTKGTVL  LDLQETSLAG  VANQLLDRFI  FEDQIRPQDR  150
EELLRALLLK  HSHAGELEAL  GGVKPAVLTR  SGDPSQPLLP  QHSSLETQLF  200
CEQGDGGTEG  HSPSGILEKI  PPDSEATLVL  VGRADFLEQP  VLGFVRLQEA  250
AELEAVELPV  PIRFLFVLLG  PEAPHIDYTQ  LGRAAATLMS  ERVFRIDAYM  300
AQSRGELLHS  LEGFLDCSLV  LPPTDAPSEQ  ALLSLVPVQR  ELLRRRYQSS  350
PAKPDSSFYK  GLDLNGGPDD  PLQQTGQLFG  GLVRDIRRRY  PYYLSDITDA  400
FSPQVLAAVI  FIYFAALSPA  ITFGGLLGEK  TRNQMGVSEL  LISTAVQGIL  450
FALLGAQPLL  VVGFSGPLLV  FEEAFFSFCE  TNGLEYIVGR  VWIGFWLILL  500
VVLVVAFEGS  FLVRFISRYT  QEIFSFLISL  IFIYETFSKL  IKIFQDHPLQ  550
KTYNYNVLMV  PKPQGPLPNT  ALLSLVLMAG  TFFFAMMLRK  FKNSSYFPGK  600
LRRVIGDFGV  PISILIMVLV  DFFIQDTYTQ  KLSVPDGFKV  SNSSARGWVI  650
HPLGLRSEFP  IWMMFASALP  ALLVFILIFL  ESQITTLIVS  KPERKMVKGS  700
GFHLDLLLVV  GMGGVAALFG  MPWLSATTVR  SVTHANALTV  MGKASTPGAA  750
AQIQEVKEQR  ISGLLVAVLV  GLSILMEPIL  SRIPLAVLFG  IFLYMGVTSL  800
SGIQLFDRIL  LLFKPPKYHP  DVPYVKRVKT  WRMHLFTGIQ  IICLAVLWVV  850
KSTPASLALP  FVLILTVPLR  RVLLPLIFRN  VELQCLDADD  AKATFDEEEG  900
RDEYDEVAMP  V                                            911
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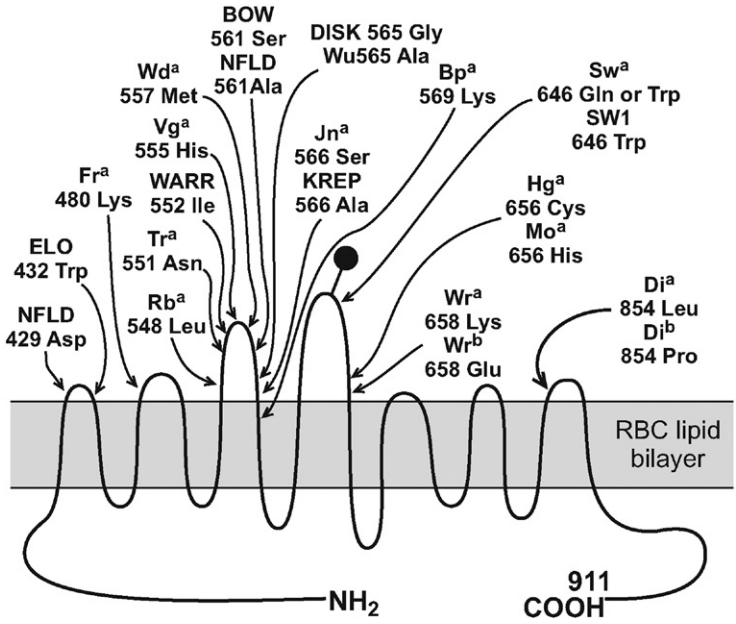
Carrier molecule[2,3]

A multipass glycoprotein.

Band 3 on intact RBCs is cleaved by α-chymotrypsin at residues 553 and 555 in the third extracellular loop.



M_r (SDS-PAGE)	95,000–105,000
CHO: N-glycan	One (Asn642) in the 4th extracellular loop (carries more than half the ABH antigens on the RBC)
Copies per RBC	1,000,000

Function

Band 3 makes up 20% of the RBC membrane proteins; it has two functionally independent domains and numerous roles.
N-terminus cytoplasmic domain (residues 1–359):
Anchored to the membrane skeleton via ankyrin and protein 4.2, and contributes to maintaining the structural integrity of the RBC; interacts with several glycolytic enzymes, hemoglobin, catalase, and hemichromes (the oxidation products of denatured hemoglobin).
C-terminus membrane domain (residues 360–911):
Anion exchange (HCO_3^- and Cl^-) across the RBC membrane; contributes to the stability of the lipid bilayer through interaction with adjacent phospholipid molecules.
Band 3 may be involved in the removal of senescent or defective RBCs from the circulation and sequestration of RBCs infected with *Plasmodium falciparum*.

Disease association[2]

A severely hydropic baby, who lacked band 3 and protein 4.2, had to be resuscitated and kept alive by transfusions.
Products of variant alleles of band 3 have been implicated in the pathogenesis of South East Asian ovalocytosis, congenital acanthocytosis, hereditary spherocytosis, and distal renal tubular acidosis.
Band 3 has a role in the attachment of malarial parasites to the surface of RBCs, and in the adhesion of parasitized cells to the vascular epithelium.

Phenotypes (% occurrence)

Phenotype	Caucasians	Blacks	Asians	South American Indians
Di(a+b–)	<0.01	<0.01	<0.01	<0.1
Di(a–b+)	>99.9	>99.9	90	64
Di(a+b+)	<0.1	<0.1	10	36
Null: Di(a–b–) in one, transfusion-dependent case				
Unusual: Weak Di(b+)				

Comments

Band 3 and glycophorin A (GPA) interact during biosynthesis and within the RBC membrane: GPA appears to be a chaperone to aid the correct folding and efficient transport of band 3 to the RBC membrane. Lack of GPA in the RBC membrane results in failure to express Wr^b (**DI4**) antigen. An altered form of band 3 present in South East Asian ovalocytes is due to a deletion of amino acid residues 400 to 408[4].

References

[1] Zelinski, T., 1998. Erythrocyte band 3 antigens and the Diego blood group system. Transfus Med Rev 12, 36–45.

[2] Bruce, L.J., Tanner, M.J., 1999. Erythroid band 3 variants and disease. Baillieres Best Pract Res Clin Haematol 12, 637–654.

[3] Schofield, A.E., et al., 1994. The structure of the human red blood cell anion exchanger (EPB3, AE1, band 3) gene. Blood 84, 2000–2012.

[4] Tanner, M.J., 1993. Molecular and cellular biology of the erythrocyte anion exchanger (AE1). Semin Hematol 30, 34–57.

Di^a Antigen

Terminology

ISBT symbol (number)	DI1 (010001 or 10.1)
Obsolete name	Diego
History	Named after Mrs. Diego, producer of the first example of anti-Di^a; reported in detail in 1955; identified as a result of HDFN.

Occurrence

Most populations	0.01%
South American Indians	From 2% in Caracas Indians to 54% in Kainganges Indians
Japanese	12%
Chippewa Indians (Canada)	11%
Chinese	5%
Hispanics	1%
Poles	0.47%

Antithetical antigen

Di^b (**DI2**)

Expression

Cord RBCs	Expressed

Molecular basis associated with Di^a antigen[1]

Amino acid	Leu854
Nucleotide	T at bp 2561 in exon19

Di^a is predominantly associated with band 3 Memphis variant II, which has a mutation of Lys56 to Glu in the cytoplasmic domain. RBCs with the band 3 Memphis variant II bind stilbene disulfonate (H_2DIDS) more readily than do RBCs with Memphis variant I or common type band 3. Di^a with Lys56 has been found in Amazonian Indians[2], but is not associated with antigen expression.

Effect of enzymes and chemicals on Di^a antigen on intact RBCs

Ficin/Papain	Resistant
Trypsin	Resistant
α-Chymotrypsin	Resistant
DTT 200 mM	Resistant
Acid	Resistant

In vitro characteristics of alloanti-Di^a

Immunoglobulin class	IgG (often IgG1 and IgG3)
Optimal technique	IAT
Complement binding	Some

Clinical significance of alloanti-Di^a

Transfusion Reaction	None to severe/delayed
HDFN	Mild to severe

Comments

In contrast to many of the Diego system antibodies, anti-Di^a is usually found as a single specificity; only occasionally does it occur in sera containing multiple antibodies to low-prevalence antigens. Examples of agglutinating anti-Di^a and naturally-occurring anti-Di^a exist, but are rare.

References

[1] Bruce, L.J., et al., 1994. Band 3 Memphis variant II. Altered stilbene disulfonate binding and the Diego (Di^a) blood group antigen are associated with the human erythrocyte band 3 mutation Pro^{854}-- > Leu. J Biol Chem 269, 16155–16158.

[2] Baleotti Jr., W., et al., 2003. A novel *DI *A* allele without the Band 3-Memphis mutation in Amazonian Indians. Vox Sang 84, 326–330.

Di^b Antigen

Terminology

ISBT symbol (number)	DI2 (010002; 10.2)
Obsolete name	Luebano
History	Anti-Di^b identified in 1967; detected an antigen of high prevalence that is antithetical to Di^a.

Occurrence

Most populations	100%
Native Americans	99%

Antithetical antigen

Di^a (**DI1**)

Expression

Cord RBCs	Expressed
Altered	Weak on South East Asian ovalocytes, and on the Di(a–b+) and Di(a+b+) RBCs of some Hispanic-Americans

Molecular basis associated with Di^b antigen[1]

Amino acid	Pro854
Nucleotide	C at bp 2561 in exon 19

Effect of enzymes and chemicals on Di^b antigen on intact RBCs

Ficin/Papain	Resistant
Trypsin	Resistant
α-Chymotrypsin	Resistant
DTT 200 mM	Resistant
Acid	Resistant

In vitro characteristics of alloanti-Di^b

Immunoglobulin class	IgG
Optimal technique	IAT
Complement binding	No

Clinical significance of alloanti-Di^b

Transfusion reaction	None to moderate/delayed
HDFN	Mild

Autoanti-Di^b

Yes

Comments

Anti-Di^b demonstrates dosage, reacting more strongly with Di(a–b+) than with Di(a+b+) RBCs.
Siblings of patients with anti-Di^b should be tested for compatibility, and the patient urged to donate blood for cryogenic storage when his/her clinical state permits.

Reference

[1] Bruce, L.J., et al., 1994. Band 3 Memphis variant II. Altered stilbene disulfonate binding and the Diego (Di^a) blood group antigen are associated with the human erythrocyte band 3 mutation Pro^{854}--> Leu. J Biol Chem 269, 16155–16158.

Wr^a Antigen

Terminology

ISBT symbol (number)	DI3 (010003 or 10.3)
Obsolete names	Wright; 700001; 211001
History	Identified in 1953 as the cause of HDFN in the Wright family; assigned to the Diego blood group system in 1995.

Occurrence

All populations	<0.01%

Antithetical antigen

Wr^b (**DI4**)

Expression

Cord RBCs	Expressed

Molecular basis associated with Wr^a antigen[1]

Amino acid	Lys658
Nucleotide	A at bp 1972 in exon 16

Effect of enzymes and chemicals on Wr^a antigen on intact RBCs

Ficin/Papain	Resistant
Trypsin	Resistant
α-Chymotrypsin	Resistant
DTT 200 mM	Resistant
Acid	Resistant

In vitro characteristics of alloanti-Wr^a

Immunoglobulin class	IgM; IgG
Optimal technique	RT; IAT

Clinical significance of alloanti-Wr^a

Transfusion reaction	None to severe/immediate or delayed/hemolytic
HDFN	Mild to severe

Comments

Alloanti-Wr^a is often an apparent naturally-occurring antibody and is found in the serum of 1% to 2% of blood donors. It is frequently found in multispecific sera and is a common specificity in patients with AIHA.

Reference

[1] Bruce, L.J., et al., 1995. Changes in the blood group Wright antigens are associated with a mutation at amino acid 658 in human erythrocyte band 3: a site of interaction between band 3 and glycophorin A under certain conditions. Blood 85, 541–547.

Wr^b Antigen

Terminology

ISBT symbol (number)	DI4 (010004 or 10.4)
Obsolete names	Fritz; MF; 901010; 900024; 211002
History	Anti-Wr^b identified in 1971; detected an antigen of high prevalence antithetical to Wr^a; assigned to Diego blood group system in 1995.

Occurrence

All populations	100%

Antithetical antigen

Wr^a (**DI3**)

Expression

Cord RBCs	Expressed
Altered	On ENEP– (HAG+), ENAV– (MARS+)[1], and ENEV– RBCs[2]

Molecular basis associated with Wr^b antigen[3]

Amino acid	Glu658
Nucleotide	G at bp 1972 in exon 16

For expression, Wr^b antigen requires the presence of amino acid residues 78 (previously 59) to 95 (previously 76) of GPA[4].

Effect of enzymes and chemicals on Wr^b antigen on intact RBCs

Ficin/Papain	Resistant (one example); sensitive (one example)[5]
Trypsin	Resistant
α-Chymotrypsin	Resistant
DTT 200 mM	Resistant
Acid	Resistant

In vitro characteristics of alloanti-Wr^b

Immunoglobulin class	IgM plus IgG
Optimal technique	IAT

Clinical significance of alloanti-Wr^b

Transfusion reaction	Not known because only three individuals with Wr(a+b–) RBCs and alloanti-Wr^b have been described, but chemiluminescence assay suggests that anti-Wr^b may cause accelerated destruction of transfused incompatible RBCs[1]
HDFN	Positive DAT but not clinical HDFN

Autoanti-Wr^b

Yes; fairly common specificity in patients with AIHA. Some autoanti-Wr^b appear to be benign while others are not: in two cases autoanti-Wr^b, reactive at 37°C, resulted in fatal intravascular hemolysis.

Comments

Alloanti-Wr^b can be a component in the plasma of immunized En(a–) people. RBCs that lack GPA, i.e., with the En(a–) or M^kM^k phenotype, type as Wr(a–b–). Some hybrid glycophorin molecules, e.g., En^a.UK, GP.Mur, GP.Hop, GP.Hil, GP.Bun, GP.HF, GP.JL, GP.SAT, GP.TK or GP.Dantu do not express Wr^b. All these hybrids have glutamic acid at residue 658 of band 3, but lack the required amino acids from GPA[6]. GP.HAG [Gln82 (previously 63) Lys of GPA], GP.MARS [Ala84 (previously 65) Pro of GPA], and GP.ENEV [Val81 (previously 62) Gly of GPA] have an altered expression of Wr^b.

References

[1] Poole, J., 2000. Red cell antigens on band 3 and glycophorin A. Blood Rev 14, 31–43.

[2] Velliquette, R.W., et al., 2010. Novel single nucleotide change in *GYP*A* in a person who made an alloantibody to a new high prevalence MNS antigen called ENEV. Transfusion 50, 856–860.

[3] Bruce, L.J., et al., 1995. Changes in the blood group Wright antigens are associated with a mutation at amino acid 658 in human erythrocyte band 3: a site of interaction between band 3 and glycophorin A under certain conditions. Blood 85, 541–547.

[4] Reid, M.E., 1999. Contribution of MNS to the study of glycophorin A and glycophorin B. Immunohematology 15, 5–9.
[5] Storry, J.R., et al., 2001. A new Wr(a−b−) proband with anti-Wr^{b} recognizing a ficin sensitive antigen [abstract]. Transfusion 41 (Suppl.), 23S.
[6] Huang, C.-H., et al., 1996. Human red blood cell Wright antigens: a genetic and evolutionary perspective on glycophorin A-band 3 interaction. Blood 87, 3942–3947.

Wd^{a} Antigen

Terminology

ISBT symbol (number)	DI5 (010005 or 10.5)
Obsolete names	Waldner; 700030
History	Reported in 1983; first described in the Waldner family; identified when RBCs were being typed with a serum known to contain anti-Fr^{a}; assigned to Diego blood group system in 1996.

Occurrence

Found only in two Schmiedeleut Hutterite families, one family in Holland with probable Hutterite connections, and two Namibian sisters.

Expression

Cord RBCs	Expressed

Molecular basis associated with Wd^{a} antigen[1,2]

Amino acid	Met557
Nucleotide	A at bp 1669 in exon 14
Wd(a–) (wild type)	Val557 and G at bp 1669

Effect of enzymes and chemicals on Wd^{a} antigen on intact RBCs

Ficin/Papain	Resistant
Trypsin	Resistant
α-Chymotrypsin	Sensitive
DTT 200 mM	Resistant
Acid	Resistant

In vitro characteristics of alloanti-Wd^{a}

Immunoglobulin class	IgM; IgG (at least one IgG example reported)
Optimal technique	RT; IAT

Clinical significance of alloanti-Wd^a

Anti-Wd^a was not made by any of six Wd(a–) women, who between them gave birth to 30 Wd(a+) children[3]. In the same study, anti-Wd^a was found in the serum of 1 of 358 pregnant women. No other data are available.

Comments

Anti-Wd^a is a common specificity in multispecific sera.

References

[1] Bruce, L.J., et al., 1996. The low-incidence blood group antigen, Wd^a, is associated with the substitution Val_{557}--> Met in human erythrocyte band 3 (AE1). Vox Sang 71, 118–120.

[2] Jarolim, P., et al., 1997. Blood group antigens Rb^a, Tr^a, and Wd^a are located in the third ectoplasmic loop of erythroid band 3. Transfusion 37, 607–615.

[3] Lewis, M., Kaita, H., 1981. A "new" low incidence "Hutterite" blood group antigen Waldner (Wd^a). Am J Hum Genet 33, 418–420.

Rb^a Antigen

Terminology

ISBT symbol (number)	DI6 (010006 or 10.6)
Obsolete names	Redelberger; 700027
History	Reported in 1978; found on the RBCs of Mr. Redelberger, a donor and donor recruiter; assigned to Diego blood group system in 1996.

Occurrence

Found in three families.

Expression

Cord RBCs	Expressed

Molecular basis associated with Rb^a antigen[1]

Amino acid	Leu548
Nucleotide	T at bp 1643 in exon 14
Rb(a–) (wild type)	Pro548 and C at bp 1643

Effect of enzymes and chemicals on Rb^a antigen on intact RBCs

Ficin/Papain	Variable
Trypsin	Resistant
α-Chymotrypsin	Variable
Pronase	Variable

In vitro characteristics of alloanti-Rb^a

Immunoglobulin class	IgM (predominantly); IgG from the original report
Optimal technique	RT, IAT

Clinical significance of alloanti-Rb^a

Five Rb(a–) women, who gave birth to Rb(a+) children, did not make anti-Rb^a. No other data are available.

Comments

Common specificity in multispecific sera.

Reference

[1] Jarolim, P., et al., 1997. Blood group antigens Rb^a, Tr^a, and Wd^a are located in the third ectoplasmic loop of erythroid band 3. Transfusion 37, 607–615.

WARR Antigen

Terminology

ISBT symbol (number)	DI7 (010007 or 10.7)
Obsolete names	Warrior; 700055
History	Identified in 1991 as a result of HDFN in the Warrior family; assigned to Diego blood group system in 1996.

Occurrence

Found in two kindred, both with Native American heritage. The eldest WARR+ member in the Warrior kindred was of Absentee Shawnee ancestry[1].

Expression

Cord RBCs	Expressed

Molecular basis associated with WARR antigen[2]

Amino acid	Ile552
Nucleotide	T at bp 1654 in exon 14
WARR– (wild type)	Thr552 and C at bp 1654

Effect of enzymes and chemicals on WARR antigen on intact RBCs

Ficin/Papain	Resistant
Trypsin	Resistant

α-Chymotrypsin	Sensitive
Pronase	Sensitive
DTT 200 mM	Resistant

In vitro characteristics of alloanti-WARR

Immunoglobulin class	IgG
Optimal technique	IAT

Clinical significance of alloanti-WARR

Transfusion reaction	No data are available
HDFN	Mild

Comments

It is a common specificity in multispecific sera and immune anti-WARR exists.

References

[1] Coghlan, G., et al., 1995. A "new" low-incidence red cell antigen, WARR: unique to native Americans? Vox Sang 68, 187–190.

[2] Jarolim, P., et al., 1997. A Thr_{552}--> Ile substitution in erythroid band 3 gives rise to the warrior blood group antigen. Transfusion 37, 398–405.

ELO Antigen

Terminology

ISBT symbol (number)	DI8 (010008 or 10.8)
Obsolete name	700051
History	Antigen recognized in 1979; reported in detail in 1993; named after the first name of the original proband; assigned to Diego blood group system in 1998.

Occurrence

All populations	<0.01%

Expression

Cord RBCs	Expressed

Molecular basis associated with ELO antigen[1]

Amino acid	Trp432
Nucleotide	T at bp 1294 in exon 12
ELO– (wild type)	Arg432 and C at bp 1294

Effect of enzymes and chemicals on ELO antigen on intact RBCs

Ficin/Papain	Resistant
Trypsin	Resistant
α-Chymotrypsin	Variable
Pronase	Variable
DTT 200 mM	Resistant

In vitro characteristics of alloanti-ELO

Immunoglobulin class	IgG
Optimal technique	IAT

Clinical significance of alloanti-ELO

Transfusion reaction	No data are available
HDFN	Mild to severe

Comments

Several examples of immune monospecific anti-ELO exist and it is often found in multispecific sera.

Reference

[1] Zelinski, T., 1998. Erythrocyte band 3 antigens and the Diego blood group system. Transfus Med Rev 12, 36–45.

Wu Antigen

Terminology

ISBT symbol (number)	DI9 (010009 or 10.9)
Obsolete names	Wulfsberg (700013); Hov (700038); Haakestad
History	Identified in 1967; named after the original Wu+ donor; assigned to Diego blood group system in 1998.

Occurrence

Less than 0.01% (Dutch, Danish, and Norwegian ancestry; also in one Irish and one Black proband).

Antithetical antigen

DISK (**DI22**)

Expression

Cord RBCs	Expressed

Molecular basis associated with Wu antigen[1]

Amino acid	Ala565
Nucleotide	C at bp 1694 in exon 14

Effect of enzymes and chemicals on Wu antigen on intact RBCs

Ficin/Papain	Resistant
Trypsin	Resistant
α-Chymotrypsin	Sensitive
Pronase	Sensitive
DTT 200 mM	Resistant

In vitro characteristics of alloanti-Wu

Immunoglobulin class	IgM; IgG (few)
Optimal technique	RT; IAT

Clinical significance of alloanti-Wu

No data are available.

Comments

Anti-Wu is often found in multispecific sera and may be naturally-occurring. Several members in one family of Dutch descent are likely to be homozygous for *Wu*, and an Irish woman homozygous for *Wu* (*DI*02.09* allele) was reported. The serological relationship with NFLD and BOW[2] cannot (yet) be explained by the molecular knowledge.

References

[1] Zelinski, T., 1998. Erythrocyte band 3 antigens and the Diego blood group system. Transfus Med Rev 12, 36–45.

[2] Kaita, H., et al., 1992. A serologic relationship among the NFLD, BOW, and Wu red cell antigens. Transfusion 32, 845–847.

Bp^{a} Antigen

Terminology

ISBT symbol (number)	DI10 (010010 or 10.10)
Obsolete names	Bishop; 700010
History	Antigen discovered in 1964 on the RBCs of Mr. Bishop; assigned to Diego blood group system in 1998.

Occurrence

There are two probands (English and Italian).

Expression

Cord RBCs	Presumed expressed

Molecular basis associated with Bp^a antigen[1]

Amino acid	Lys569
Nucleotide	A at bp 1707 in exon 14
Bp(a–) (wild type)	Asn569 and C at bp 1707

Effect of enzymes and chemicals on Bp^a antigen on intact RBCs[2]

Ficin/Papain	Sensitive
Trypsin	Sensitive
α-Chymotrypsin	Sensitive
Pronase	Sensitive
DTT 200 mM	Presumed resistant

In vitro characteristics of alloanti-Bp^a

Immunoglobulin class	IgM
Optimal technique	RT

Clinical significance of alloanti-Bp^a

Transfusion reaction	No data are available
HDFN	No

Comments

Alloanti-Bp^a is often found in sera containing multiple naturally-occurring antibodies (including anti-Wr^a), and in sera from patients with AIHA. The band 3 amino acid substitution associated with expression of Bp^a antigen is likely to be located within the RBC lipid bilayer; thus, the enzyme sensitivity of Bp^a is somewhat surprising and may indicate the interaction with another enzyme sensitive component in the formation of the Bp^a epitope.

References

[1] Zelinski, T., 1998. Erythrocyte band 3 antigens and the Diego blood group system. Transfus Med Rev 12, 36–45.

[2] Jarolim, P., et al., 1998. Characterization of seven low incidence blood group antigens carried by erythrocyte band 3 protein. Blood 92, 4836–4843.

Mo^a Antigen

Terminology

ISBT symbol (number)	DI11 (010011 or 10.11)
Obsolete names	Moen; 700022

History	Antigen found in 1972 when random donors were screened for Jn^a; assigned to Diego blood group system in 1998.

Occurrence

Three probands have been reported: one from Norway and two from Belgium.

Antithetical antigen

Hg^a (**DI12**)

Expression

Cord RBCs	Presumed expressed

Molecular basis associated with Mo^a antigen[1]

Amino acid	His656
Nucleotide	A at bp 1967 in exon 16
Mo(a–) (wild type)	Arg656 and G at bp 1967

Effect of enzymes and chemicals on Mo^a antigen on intact RBCs

Ficin/Papain	Resistant
Trypsin	Resistant
α-Chymotrypsin	Resistant
Pronase	Resistant
DTT 200 mM	Resistant

In vitro characteristics of alloanti-Mo^a

Immunoglobulin class	IgM; IgG
Optimal technique	RT; IAT

Clinical significance of alloanti-Mo^a

No data are available because the antigen is rare.

Comments

Anti-Mo^a may be naturally-occurring, and is found in multispecific sera.

Reference

[1] Zelinski, T., 1998. Erythrocyte band 3 antigens and the Diego blood group system. Transfus Med Rev 12, 36–45.

Hg^a Antigen

Terminology

ISBT symbol (number)	DI12 (010012 or 10.12)
Obsolete names	Hughes; 700034; Tarplee; Tarp
History	The Hg^a antigen was described in 1983. Its name was derived from the maiden name (Hughes) of the original Hg(a+) panel donor identified during routine antibody screening tests. Hg^a joined the Diego blood group system in 1998.

Occurrence

Reported in three Welsh families and an Australian donor from New South Wales.

Antithetical antigen

Mo^a (**DI11**)

Expression

Cord RBCs	Expressed

Molecular basis associated with Hg^a antigen[1]

Amino acid	Cys656
Nucleotide	T at bp 1966 in exon 16
Hg(a–) (wild type)	Arg656 and C at bp 1966

Effect of enzymes and chemicals on Hg^a antigen on intact RBCs[2]

Ficin/Papain	Resistant
Trypsin	Resistant
α-Chymotrypsin	Resistant
Pronase	Resistant
DTT 200 mM	Presumed resistant

In vitro characteristics of alloanti-Hg^a

Immunoglobulin class	IgM; IgG
Optimal technique	RT; IAT

Clinical significance of alloanti-Hg^a

No data are available because the antigen is rare.

Comments

Anti-Hg^a is found in multispecific sera; anti-Hg^a as a single specificity has not been reported.

References

[1] Zelinski, T., 1998. Erythrocyte band 3 antigens and the Diego blood group system. Transfus Med Rev 12, 36–45.

[2] Jarolim, P., et al., 1998. Characterization of seven low incidence blood group antigens carried by erythrocyte band 3 protein. Blood 92, 4836–4843.

Vg^a Antigen

Terminology

ISBT symbol (number)	DI13 (010013 or 10.13)
Obsolete names	VanVugt; 700029
History	Antigen reported in 1981; found while screening Australian donors with anti-Wu; named after the first antigen positive donor Miss Van Vugt; assigned to Diego blood group system in 1998.

Occurrence

Only one family reported.

Expression

Cord RBCs	Presumed expressed

Molecular basis associated with Vg^a antigen[1]

Amino acid	His555
Nucleotide	C at bp 1663 in exon 14
Vg(a–) (wild type)	Tyr555 and T at bp 1663

Effect of enzymes and chemicals on Vg^a antigen on intact RBCs[2]

Ficin/Papain	Resistant
Trypsin	Resistant
α-Chymotrypsin	Sensitive
Pronase	Sensitive
DTT 200 mM	Presumed resistant

In vitro characteristics of alloanti-Vg^a

Immunoglobulin class	IgM and rarely IgG
Optimal technique	RT (IAT)

Clinical significance of alloanti-Vg^a

No data are available.

Comments

Anti-Vg^a is a relatively common antibody (11 examples of anti-Vg^a were found among 1669 donor sera), and is found in multispecific sera that frequently also contain anti-Wr^a.

References

[1] Zelinski, T., 1998. Erythrocyte band 3 antigens and the Diego blood group system. Transfus Med Rev 12, 36–45.

[2] Jarolim, P., et al., 1998. Characterization of seven low incidence blood group antigens carried by erythrocyte band 3 protein. Blood 92, 4836–4843.

Sw^a Antigen

Terminology

ISBT symbol (number)	DI14 (010014 or 10.14)
Obsolete names	Swann; 700004
History	Antigen identified in 1959, when serum from an AIHA patient was cross-matched against RBCs from donor Donald Swann; assigned to Diego blood group system in 1998.

Occurrence

All populations	<0.01%

Expression

Cord RBCs	Presumed expressed

Molecular basis associated with Sw^a antigen[1]

Amino acid	Gln or Trp646
Nucleotide	T at bp 1936 or A at bp 1937 in exon 16
Sw(a–) (wild type)	Arg646 and C at bp 1936 or G at bp 1937

Effect of enzymes and chemicals on Sw^a antigen on intact RBCs

Ficin/Papain	Resistant
Trypsin	Resistant
α-Chymotrypsin	Resistant
DTT 200 mM	Presumed resistant

In vitro characteristics of alloanti-Sw^a

Immunoglobulin class	IgM; IgG
Optimal technique	RT (IAT)

Clinical significance of alloanti-Sw^a

No data are available because the antigen is rare.

Comments[2,3]

Anti-Sw^a is often found in AIHA and in multispecific sera. Anti-Sw^a and anti-Fr^a, when present in the same serum, show cross-reactivity and cannot be separated by absorption.
Anti-Sw^a also react with SW1+ (see **DI21**) RBCs: RBCs may be Sw(a+), SW1– (Gln646, the more common type) or Sw(a+) SW1+ (Trp646). Sw(a–), SW1+ RBCs have not been found.

References

[1] Zelinski, T., et al., 2000. Distinctive Swann blood group genotypes: molecular investigations. Vox Sang 79, 215–218.
[2] Contreras, M., et al., 1987. Swa: a subdivision. Vox Sang 52, 115–119.
[3] Lewis, M., et al., 1988. The Swann phenotype 700:4,-41: genetic studies. Vox Sang 54, 184–187.

BOW Antigen

Terminology

ISBT symbol (number)	DI15 (010015 or 10.15)
Obsolete names	Bowyer; 700046
History	Antigen reported in 1988; identified on the RBCs of a donor (Bowyer) during an incompatible cross-match; assigned to Diego blood group system in 1998.

Occurrence

Only a few probands have been reported.

Antithetical antigen

NFLD (**DI16**) (at amino acid 561, see Comments).

Expression

Cord RBCs	Presumed expressed

Molecular basis associated with BOW antigen[1]

Amino acid	Ser561
Nucleotide	T at bp 1681 in exon 14
BOW–, NFLD– (wild type)	Pro561 and C at bp 1681

Effect of enzymes and chemicals on BOW antigen on intact RBCs

Ficin/Papain	Resistant
Trypsin	Resistant
α-Chymotrypsin	Sensitive
Pronase	Sensitive
DTT 200 mM	Resistant

In vitro characteristics of alloanti-BOW

Immunoglobulin class	IgG; some IgM
Optimal technique	IAT; RT

Clinical significance of alloanti-BOW

No data are available because the antigen is rare.

Comments

Several examples of immune monospecific anti-BOW exist and it is often found in multispecific sera. Molecular analysis showed that both BOW and NFLD are associated with a substitution at amino acid residue 561: serine is present when BOW is expressed and alanine is present when NFLD is expressed. Thus, BOW and NFLD can be considered antithetical, even though NFLD has a second mutation of Glu429Asp.

The serological relationship to Wu[2] cannot be explained by the molecular knowledge, although the critical residue (565Ala) for Wu is relatively close to residue 561 of band 3.

References

[1] McManus, K., et al., 2000. Amino acid substitutions in human erythroid protein band 3 account for the low-incidence antigens NFLD and BOW. Transfusion 40, 325–329.

[2] Kaita, H., et al., 1992. A serologic relationship among the NFLD, BOW, and Wu red cell antigens. Transfusion 32, 845–847.

NFLD Antigen

Terminology

ISBT symbol (number)	DI16 (010016 or 10.16)
Obsolete names	Newfoundland; 700037
History	Antigen reported in 1984; was found on the RBCs of a French Canadian in Newfoundland; assigned to Diego system in 1998.

Occurrence

Only a few probands (two French Canadian and two Japanese families) have been reported.

Antithetical antigen

BOW (**DI15**) (at amino acid 561, see Comments).

Expression

Cord RBCs	Presumed expressed

Molecular basis associated with NFLD antigen[1]

Amino acid	Asp429 and Ala561
Nucleotide	T at bp 1287 in exon 12 and G at bp 1681 in exon 14

NFLD–, BOW– (wild type) Glu429 with A at bp 1287, and Pro561 with C at bp 1681

Effect of enzymes and chemicals on NFLD antigen on intact RBCs

Ficin/Papain	Resistant
Trypsin	Resistant
α-Chymotrypsin	Sensitive
Pronase	Sensitive
DTT 200 mM	Resistant
Acid	Presumed resistant

In vitro characteristics of alloanti-NFLD

Immunoglobulin class	IgM and IgG
Optimal technique	RT (with albumin); IAT

Clinical significance of alloanti-NFLD

A Japanese NFLD– woman gave birth to three NFLD+ children without making anti-NFLD. No other data are available.

Comments

Anti-NFLD is found in multispecific sera. Molecular analysis showed that both NFLD and BOW are associated with a substitution at amino acid residue 561: alanine is present when NFLD is expressed and serine is present when BOW is expressed. Thus, NFLD and BOW can be considered antithetical at this residue. However, NFLD has a second mutation of Glu429Asp. The epitope defining NFLD may be created through an association and/or interaction between the first (residue 429) and third (residue 561) extracellular loops of band 3.
The serological relationship to Wu[2] cannot be explained by the molecular knowledge although the critical residue (565Ala) for expression of Wu is relatively close to residue 561 of band 3.

References

[1] McManus, K., et al., 2000. Amino acid substitutions in human erythroid protein band 3 account for the low-incidence antigens NFLD and BOW. Transfusion 40, 325–329.
[2] Kaita, H., et al., 1992. A serologic relationship among the NFLD, BOW, and Wu red cell antigens. Transfusion 32, 845–847.

Jn^a Antigen

Terminology

ISBT symbol (number)	DI17 (010017 or 10.17)
Obsolete names	Nunhart; JN; 700014
History	Antigen described in 1967; identified on the RBCs of Mr. J.N. during a study of the incidence of Wr^a in the Prague population; assigned to Diego blood group system in 1998.

Occurrence

Two probands (one of Polish, the other of Slovakian descent)[1].

Antithetical antigen

KREP (**DI18**)

Expression

Cord RBCs	Presumed expressed

Molecular basis associated with Jn^a antigen[1]

Amino acid	Ser566
Nucleotide	T at bp 1696 in exon 14
Jn(a–) (wild type)	Pro566 and C at bp 1696

Effect of enzymes and chemicals on Jn^a antigen on intact RBCs

Ficin/Papain	Resistant
Trypsin	Resistant
α-Chymotrypsin	Sensitive
DTT 200 mM	Resistant

In vitro characteristics of alloanti-Jn^a

Immunoglobulin class	IgM (no data regarding presence of an IgG component)
Optimal technique	RT

Clinical significance of alloanti-Jn^a

No data are available because the antigen is rare.

Comments

Anti-Jn^a is found in multispecific sera that also contain anti-KREP. The majority are naturally-occurring.

Reference

[1] Poole, J., 1999. The Diego blood group system – an update. Immunohematology 15, 135–143.

KREP Antigen

Terminology

ISBT symbol (number)	DI18 (010018 or 10.18)
Obsolete name	IK
History	Found in 1997 during investigation of the second Jn(a+) proband; named after the antigen-positive donor; assigned to Diego blood group system in 1998.

Occurrence

One Polish proband (IK)[1].

Antithetical antigen

Jn^a (**DI17**)

Expression

Cord RBCs	Presumed expressed

Molecular basis associated with KREP antigen[1]

Amino acid	Ala566
Nucleotide	G at bp 1696 in exon 14
KREP– (wild type)	Pro566 and C at bp 1696

Effect of enzymes and chemicals on KREP antigen on intact RBCs

Ficin/Papain	Resistant
Trypsin	Resistant
α-Chymotrypsin	Sensitive
DTT 200 mM	Resistant

In vitro characteristics of alloanti-KREP

Immunoglobulin class	IgM (no data regarding presence of an IgG component)
Optimal technique	RT

Clinical significance of alloanti-KREP

No data are available, but unlikely because anti-KREP have been naturally-occurring.

Comments

Anti-KREP is naturally-occurring and is present in multispecific sera. Among 13 sera tested, 12 contained anti-Jn^a and anti-KREP, and only one serum contained anti-KREP without anti-Jn^a.

Reference

[1] Poole, J., 1999. The Diego blood group system – an update. Immunohematology 15, 135–143.

Tr^a Antigen

Terminology

ISBT symbol (number)	DI19 (010019 or 10.19)
Obsolete names	Traversu; Lanthois; 700008
History	Antigen found in the 1960s during random testing of English blood donors with a multispecific serum, that also contained anti-Wr^a; named after the first positive donor, Traversu.

Occurrence

Only found in two English probands.

Expression

Cord RBCs	Presumed expressed

Molecular basis associated with Tr^a antigen[1]

Amino acid	Asn551
Nucleotide	G at bp 1653 in exon 14
Tr(a–) (wild type)	Lys551 and C at bp 1653

Effect of enzymes and chemicals on Tr^a antigen on intact RBCs

Ficin/Papain	Resistant
Trypsin	Resistant
α-Chymotrypsin	Sensitive
DTT 200 mM	Presumed resistant

In vitro characteristics of alloanti-Tr^a

Immunoglobulin class	IgM and IgG
Optimal technique	RT; IAT

Clinical significance of alloanti-Tr^a

No data are available because the antigen is rare.

Comments

Anti-Tr^a was found as a separable specificity in 12 of 18 plasma samples that contained anti-Wr^a.
Anti-Tr^a is found in multispecific sera and in plasma from patients with AIHA.

Reference

[1] Jarolim, P., et al., 1997. Blood group antigens Rb^a, Tr^a, and Wd^a are located in the third ectoplasmic loop of erythroid band 3. Transfusion 37, 607–615.

Fr^a Antigen

Terminology

ISBT symbol (number)	DI20 (010020 or 10.20)
Obsolete names	Froese; 700026
History	Reported in 1978; named after the family (Froese) in which it was first recognized; assigned to Diego blood group system in 2000.

Occurrence

The reported Fr(a+) probands originate from three Mennonite kindred in Manitoba, Canada.

Expression

Cord RBCs	Expressed

Molecular basis associated with Fr^a antigen[1]

Amino acid	Lys480
Nucleotide	A at bp 1438 in exon 13
Fr(a–) (wild type)	Glu480 and G at bp 1438

Effect of enzymes and chemicals on Fr^a antigen on intact RBCs

Ficin/Papain	Resistant
Trypsin	Presumed resistant
α-Chymotrypsin	Presumed resistant
DTT 200 mM	Presumed resistant

In vitro characteristics of alloanti-Fr^a

Immunoglobulin class	IgG; IgM (few)
Optimal technique	IAT; RT

Clinical significance of alloanti-Fr^a

Transfusion reaction	No data are available
HDFN	Positive DAT, but no clinical HDFN

Comments

Several examples of immune monospecific anti-Fr^a exist, and it is often found in multispecific sera. Anti-Fr^a and anti-Sw^a, when present in the same serum show cross-reactivity and cannot be separated by absorption[2].

References

[1] McManus, K., et al., 2000. An amino acid substitution in the putative second extracellular loop of RBC band 3 accounts for the Froese blood group polymorphism. Transfusion 40, 1246–1249.

[2] Contreras, M., et al., 1987. Swa: a subdivision. Vox Sang 52, 115–119.

SW1 Antigen

Terminology

ISBT symbol (number)	DI21 (010021 or 10.21)
Obsolete name	700041
History	SW1 was documented in 1987; revealed by heterogeneity among sera containing anti-Sw^a; assigned to Diego blood group system in 2000.

Occurrence

Most populations	<0.01%

Expression

Cord RBCs	Presumed expressed

Molecular basis associated with SW1 antigen[1]

Amino acid	Trp646
Nucleotide	T at bp 1936 in exon 16
SW1–, Sw(a+)	Gln646 and A at bp 1936
SW1–, Sw(a–) (wild type)	Arg646 and C at bp 1936

Effect of enzymes and chemicals on SW1 antigen on intact RBCs

Ficin/Papain	Resistant
Trypsin	Resistant
α-Chymotrypsin	Resistant
DTT 200 mM	Presumed resistant

In vitro characteristics of alloanti-SW1

Immunoglobulin class	IgM; IgG
Optimal technique	RT; IAT

Clinical significance of alloanti-SW1

No data are available because the antigen is rare.

Comments

Examples of anti-SW1 exist that do not react with Sw(a+) RBCs, but all anti-Sw^a react with SW1+ RBCs[1]. See Sw^a (**DI14**) for more details.

Reference

[1] Zelinski, T., et al., 2000. Distinctive Swann blood group genotypes: molecular investigations. Vox Sang 79, 215–218.

DISK Antigen

Terminology

ISBT symbol (number)	DI22 (010022 or 10.22)
History	Named in 2010 when an antibody to a high prevalence ficin-resistant, α-chymotrypsin-sensitive antigen was found in an untransfused Irish female and shown to be antithetical to Wu.

Occurrence

One Irish DISK– proband has been reported, and members of the Dutch family suspected to express a double dose of Wu antigen are also anticipated to be DISK–

Antithetical antigen

Wu (**DI9**)

Expression

Cord RBCs	Expressed

Molecular basis associated with DISK antigen[1]

Amino acid	Gly565
Nucleotide	G at bp 1694 in exon 14

Effect of enzymes and chemicals on DISK antigen on intact RBCs

Ficin/Papain	Resistant
Trypsin	Resistant
α-Chymotrypsin	Sensitive
DTT 200 mM	Presumed resistant

In vitro characteristics of alloanti-DISK

Immunoglobulin class	IgM; IgG
Optimal technique	RT; 37C; IAT

Clinical significance of alloanti-DISK

No data. However, serological characteristics of the only anti-DISK suggest a highly clinically significant antibody.

Comment

RBCs from the proband's brother reacted more weakly with anti-DISK, suggesting that the antibody exhibits dosage.
Siblings of patients with anti-DISK should be tested for compatibility, and the patient urged to donate blood for cryogenic storage when his/her clinical state permits.

Reference

[1] Poole, J., et al., 2010. Novel high incidence antigen in the Diego blood group system (DISK) and clinical significance of anti-DISK. Vox Sang 99 (Suppl. 1), 54–55.