The 901 Series of High-Incidence Antigens

901 Series of High-Incidence Antigens

Antigens in this series occur in more than 90% of people; as the responsible genes are not known, they cannot be placed in a Blood Group System, and do not meet the criteria for being placed in a Collection.

Originally, high-incidence antigens were in the 900 series. At the 1988 meeting of the ISBT Working Party on Terminology[1], many of the 900 series antigens were transferred to Blood Group Systems or the newly-established Blood Group Collections, thereby generating many obsolete 900 numbers. Consequently, the 900 Series was replaced by the 901 Series.

Number	Symbol	Name
901003 or 901.3	At[a]	August
901008 or 901.8	Emm	
901009 or 901.9	AnWj	Anton
901012 or 901.12	Sd[a]	Sid
901014 or 901.14	PEL	
901016 or 901.16	MAM	

Obsolete: 901001 Vel, 901002 Lan, 901004 Jo[a], 901005 Jr[a], 901006 Ok[a], 901007 JMH, 901010 Wr[b], 901011 MER2, 901013 Duclos, and 901015 ABTI.

Reference

[1] Lewis, M., et al., 1990. Blood group terminology 1990. ISBT working party on terminology for red cell surface antigens. Vox Sang 58, 152–169.

The Blood Group Antigen (3/e). DOI: http://dx.doi.oxg/10.1016/B978-0-12-415849-8.00044-2

At^a Antigen

Terminology

ISBT symbol (number)	At^a (901003 or 901.3)
Obsolete names	El; Elridge; 900006
History	Reported in 1967; named after the first antigen-negative proband (Mrs Augustine) to make anti-At^a.

Occurrence

Most populations	100%
Blacks	>99%

Expression

Cord RBCs	Expressed

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

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

In vitro characteristics of alloanti-At^a

Immunoglobulin class	IgG
Optimal technique	IAT

Clinical significance of alloanti-At^a

Transfusion reaction	No to severe[1,2,3]
HDFN	Most At(a+) babies born to At(a–) mothers were not affected; only one mild case

Comments

Many At(a–) probands originate from the Caribbean or Southern USA.
In three patients, the anti-At^a was concomitant with autoimmune disease[2].

References

[1] Cash, K.L., et al., 1999. Severe delayed hemolytic transfusion reaction secondary to anti-At(a). Transfusion 39, 834–837.

[2] Ramsey, G., et al., 1995. Clinical significance of anti-At^a. Vox Sang 69, 135–137.

[3] Sweeney, J.D., et al., 1995. At(a−) phenotype: Description of a family and reduced survival of At(a+) red cells in the proposita with anti-At^a. Transfusion 35, 63–67.

Emm Antigen

Terminology

ISBT symbol (number)	Emm (901008 or 901.8)
Obsolete names	Emma; 900028
History	Reported in 1987, and named after the first antigen-negative proband to make anti-Emm.

Occurrence

Six probands with the Emm– phenotype have been found: three Americans, a French Madagascan, a Pakistani, and a French Canadian.

Expression

Cord RBCs	Expressed

Effect of enzymes and chemicals on Emm antigen on intact RBCs

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

In vitro characteristics of alloanti-Emm

Immunoglobulin class	IgG more common than IgM (4 of 5)
Optimal technique	IAT; 4°C (the original anti-Emm)
Complement binding	Some (2 of 5)

Clinical significance of alloanti-Emm

No data are available. Six of the seven examples of anti-Emm were in non-transfused males[1].

Comments

Emm is carried on a GPI-linked protein in the RBC membrane[2], thus, absent from PNHIII RBCs.

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References

[1] Daniels, G.L., et al., 1987. Emm. A red cell antigen of very high frequency. Transfusion 27, 319–321.

[2] Telen, M.J., et al., 1990. Evidence that several high-frequency human blood group antigens reside on phosphatidylinositol-linked erythrocyte membrane proteins. Blood 75, 1404–1407.

AnWj Antigen

Terminology

ISBT symbol (number)	AnWj (901009 or 901.9)
Obsolete names	Wj; 005015; Lu15
History	Reported in 1982 as an alloantibody to an antigen called Anton, and in 1983 as an autoantibody to an antigen called Wj. In 1985, it was shown that both antibodies detected the same antigen, and the name AnWj was applied.

Occurrence

Genetic form of AnWj-negative found in two Israeli women and one Arab-Israeli family.

Expression

Cord RBCs	Not expressed
Altered	Weak on dominant Lu(a–b–) RBCs Expression varies from person to person

Molecular basis associated with AnWj antigen

Carried on CD44 proteoglycan[1,2]. The AnWj epitope is likely to reside in the glycosylated region encoded by exons 5 and 15. If this is true, all information regarding CD44 (Indian blood group system, [**IN**]) would apply.

Effect of enzymes and chemicals on AnWj antigen on intact RBCs

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

In vitro characteristics of alloanti-AnWj

Immunoglobulin class	IgG
Optimal technique	IAT
Complement binding	Rare

Clinical significance of alloanti-AnWj

Transfusion reaction	Severe in one case[3]
HDFN	No

Autoanti-AnWj

Yes, may appear to be an alloantibody because of transient suppression of AnWj antigen. Such patients frequently tolerate transfusion of AnWj+ RBCs.

Comments

Only two examples of alloanti-AnWj (both in Israeli women) have been described. The AnWj– phenotype is usually the result of transient (often long-term) suppression of AnWj.
AnWj antigen is the receptor for *Haemophilus influenzae*[4].

References

[1] Telen, M.J., et al., 1993. The ANWJ blood group antigen/hemophilus influenzae receptor resides on a high-molecular-weight protein expressed by CD44 transfectants [abstract]. Clin Res 41, 161A.
[2] Udani, M., et al., 1995. Erythroid progenitors express a CD44 variant with reduced hyaluronic acid binding ability and reduced expression of the epitope associated with *Hemophilus influenzae* hemagglutination [abstract]. Blood 86 (Suppl. 1), 472a.
[3] de Man, A.J., et al., 1992. An example of anti-AnWj causing haemolytic transfusion reaction. Vox Sang 63 238–238.
[4] van Alphen, L., et al., 1986. The Anton blood group antigen is the erythrocyte receptor for *Haemophilis influenzae*. FEMS Microbiol Lett 37, 69–71.

Sd^a Antigen

Terminology

ISBT symbol (number)	Sd^a (901012 or 901.12)
Other names	Sid
History	Reported in 1967 after many years of investigation. Named for Sidney Smith, head of the maintenance department at the Lister Institute in London which housed the laboratory of Race and Sanger. For many years, his RBCs were frequently used as a Sd(a++) control.

Occurrence

All populations	91% of RBC samples express Sd^a; however, 96% of urine samples have Sd^a substance; 4% of people are truly Sd(a–)

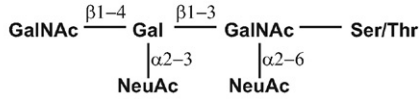
Expression

Soluble form	Urine (Tamm-Horsfall glycoprotein)
Newborns	Not expressed on RBCs; expressed in saliva, urine, and meconium

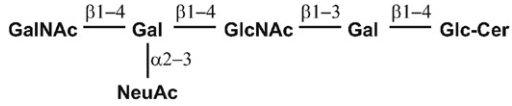
Adult RBCs	Strength of expression varies greatly; the strongest expression is on Cad phenotype RBCs
Altered	Marked reduction of Sd^a expression occurs in pregnancy
Other tissues	Stomach, colon, kidney, lymph nodes

Molecular basis associated with antigen[1]

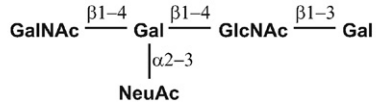
Sd^a-active Pentasaccharide from GPA



Sd^a-active ganglioside



Sd^a-active Tamm-Horsfall glycoprotein



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

Ficin/Papain	Resistant (enhanced)
Trypsin	Resistant (enhanced)
α-Chymotrypsin	Resistant (enhanced)
Sialidase	Usually resistant
DTT 200 mM	Resistant
Acid	Resistant

In vitro characteristics of alloanti-Sd^a

Immunoglobulin class	IgM more common than IgG
Optimal technique	RT; IAT
Neutralization	Urine (guinea pig and human)
Complement binding	Yes, some

Clinical significance of alloanti-Sd^a

Transfusion reaction	Two cases reported associated with transfusion of Sd(a++) RBCs
HDFN	No

Comments

Agglutinates are typically small and refractile in a sea of free RBCs. Anti-Rx (formerly anti-Sd^x) can be confused with anti-Sd^a because of similar type of agglutination[2] .

Tamm-Horsfall protein in urine binds specifically to type 1[3] fimbriated *E. coli*, thereby preventing adherence of pathogenic *E. coli* to urothelial receptors.

Hemagglutination inhibition tests with urine are the most reliable way of determining Sd^a status.

Urine inhibition tests (particularly using guinea pig urine) are useful for the identification of anti-Sd^a.

In 2003, two groups[4,5] independently reported the characterization of a genetic locus (*B4GALNT2*, also known as *GALGT2*) located at 17q21.32 that appeared to encode a glycosyltransferase with the enzyme activity (β4GalNAcT) required for synthesis of Sd^a-active epitopes by addition of GalNAc in a β1,4 linkage to relevant precursor structures (Gal substituted with an α-2,3-NeuNAc). However, there is still no published evidence that mutations in this gene give rise to the Sd(a+^{weak}) and/or Sd(a–) phenotypes. It is also unclear if the acceptor profile of this enzyme is compatible with its identity as the Sd^a histo-blood group synthetase. Notably, two transcript forms code for a short and a long form of the enzyme by using different exon 1 sequences (exon 1S or 1L, respectively), but the same exons 2–11. It is tempting to speculate that these two forms, which are driven by two different promoters, may be differentially expressed in erythroid and other tissues in a way similar to the transcript forms of the *GCNT2* locus responsible for I antigen expression. In summary, however, more work is needed before the Sd^a antigen can be promoted to a blood group system.

References

[1] Watkins, W.M., 1995. Sd^a and Cad antigens. In: Cartron, J.-P., Rouger, P. (Eds.), Molecular Basis of Human Blood Group Antigens. Plenum Press, New York, NY, pp. 51–375.

[2] Issitt, P.D., 1991. The antigens Sd^a and Cad. In: Moulds, J.M., Woods, L.L. (Eds.), *Blood groups*: *P*, *I*, *Sd^a and Pr*. American Association of Blood Banks, Arlington, VA, pp. 53–71.

[3] Pak, J., et al., 2001. Tamm-Horsfall protein binds to type 1 fimbriated *Escherichia coli* and prevents *E. coli* from binding to uroplakin Ia and Ib receptors. J Biol Chem 276, 9924–9930.

[4] Lo, P.L., et al., 2003. Molecular cloning of the human beta1,4 N-acetylgalactosaminyltransferase responsible for the biosynthesis of the Sd^a histo-blood group antigen: the sequence predicts a very long cytoplasmic domain. *J Biochem* (Tokyo) 134, 675–682.

[5] Montiel, M.D., et al., 2003. Molecular cloning, gene organization and expression of the human UDP-GalNAc:Neu5Acα2-3Galβ-R β1,4-*N*-acetylgalactosaminyltransferase responsible for the biosynthesis of the blood group Sd^a/Cad antigen: evidence for an unusual extended cytoplasmic domain. Biochem J 373, 369–379.

PEL Antigen

Terminology

ISBT symbol (number)	PEL (901014 or 901.14)
Obsolete name	Pelletier
History	Identified in 1980, and reported in 1996 when the antigen was named after the first antigen-negative proband who made anti-PEL.

Occurrence

PEL– phenotype has been found in two French Canadian families.

Expression

Cord RBCs	Expressed
Altered	Weak expression (shown by absorption studies) in two French Canadian families[1]

Effect of enzymes and chemicals on PEL antigen on intact RBCs

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

In vitro characteristics of alloanti-PEL

Immunoglobulin class	Presumed IgG
Optimal technique	IAT

Clinical significance of alloanti-PEL

Transfusion reaction	Reduced survival of ^{51}Cr-labelled RBCs
HDFN	No

Comments

An antibody (provisionally named anti-MTP) with similar specificity to anti-PEL was made by the probands from the two French Canadian families with suppressed PEL expression[1].

Reference

[1] Daniels, G.L., et al., 1996. PEL, a "new" high-frequency red cell surface antigen. Vox Sang 70, 31–33.

MAM Antigen

Terminology

ISBT symbol (number)	MAM (901016 or 901.16)
History	Reported in 1993; assigned to the 901 Series in 1999; name is derived from the initials of the first antigen-negative proband to make anti-MAM[1].

Occurrence

Four MAM– probands have been reported: one with Irish and Cherokee descent; two Arabs; and a Jordanian.

Expression

Cord RBCs	Expressed
Other blood cells	Lymphocytes, granulocytes, monocytes, and probably on platelets

Molecular basis associated with MAM antigen[2]

M_r assessment based on SDS-PAGE revealed a diffuse banding pattern of approximately 23,000–80,000, but with a discrete band also at 18,000. Possibly on N-glycosylated proteins[3].

Effect of enzymes and chemicals on MAM antigen on intact RBCs

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

In vitro characteristics of alloanti-MAM

Immunoglobulin class	IgG
Optimal technique	IAT

Clinical significance of alloanti-MAM

Transfusion reaction	Monocyte monolayer assay suggests anti-MAM is potentially clinically significant
HDFN	No to severe

Comments

Anti-MAM may also cause neonatal thrombocytopenia; however, two MAM+ babies born to two different women with anti-MAM had no thrombocytopenia or anemia[4].

References

[1] Anderson, G., et al., 1993. An antibody to a high frequency antigen found on red cells, platelets, lymphocytes, and monocytes [abstract]. Transfusion 33 (Suppl.), 23S.

[2] Montgomery Jr., W.M., et al., 2000. MAM: a "new" high-incidence antigen found on multiple cell lines. Transfusion 40, 1132–1139.

[3] Li, W., Denomme, G.A., 2002. MAM is an N-glycan linked carbohydrate antigen expressed on all blood cells [abstract]. Transfusion 42 (Suppl.), 10S.

[4] Denomme, G.A., et al., 2000. First example of maternal-fetal incompatibility due to anti-MAM with an absence of thrombocytopenia [abstract]. Transfusion 40 (Suppl.), 28S.