

International Society of Blood Transfusion Committee on Terminology for Red Cell Surface Antigens: Cape Town report

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Introduction

The Committee met in Cape Town during the 2006 International Society of Blood Transfusion (ISBT) Congress (see Appendix 1 for Committee members). Some changes to the classification documented in Blood Group Terminology 2004 [1] were agreed and are described below. The full updated classification can be found on the Blood Group Terminology

website at <http://www.blood.co.uk/ibgrl>. New antigens were added to the MNS, Kell, Scianna, Cromer, Indian, Knops, and JMh systems (Table 1). In line with convention, amino acid positions are numbered with the translation-initiating methionine as 1, although the more traditional numbering for glycophorin A, with number 1 representing the first amino acid of the mature protein, is also provided.

MNS system

Three new antigens were added to the MNS system: two of high incidence and one of low incidence. MNS44 is defined by an antibody produced by an individual with MNS:–44 red cells, which also express MNS32 (DANE) [2]. The rare MNS:–44

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Table 1 New blood group antigens

Number	Symbol	Incidence	Molecular basis	Reference
MNS44	ENDA	High	<i>GYP(A-B-A)</i>	[2]
MNS45	ENEV	High	<i>GYP A 242T>G V81G (V62G)</i>	[4]
MNS46	MNTD	Low	<i>GYP A 107C>G T36R (T17R)</i>	[5]
KEL29	KALT	High	1988G>A R623K	[6]
KEL30	KTIM	High	1033G>A D305N	[6]
KEL31	KYO	Low	875G>A R292Q	[7]
SC6	SCER	High	242G>A R81Q	[9]
SC7	SCAN	High	103G>A G35S	[9]
CROM14	CROV	High	466G>A E156K	[11]
CROM15	CRAM	High	740A>G Q247R	[12]
IN3	INFI	High	255C>G H85Q	[13]
IN4	INJA	High	488C>A T163R	[13]
KN9	KCAM	Variable	4870A>G I161V	[14]
JMH2	JMHK	High	619C>T R207W	[15]
JMH3	JMHL	High	620G>A R207Q	[15]
JMH4	JMHG	High	1379G>A R460H	[15]
JMH5	JMHM	High	1381C>T R461C	[15]

phenotype results from heterozygosity for M^k and for a novel *GYP(A-B-A)* hybrid gene, which is identical to that encoding GP.Dane apart from lacking the substitution predicted to convert I65 (I46 when amino acid 1 is the first residue of the mature protein) of glycophorin A (GPA) to N64 (N45) in GP.Dane [2,3].

MNS45, defined by an antibody from a patient with the rare MNS:–45 phenotype, results from homozygosity for a single nucleotide polymorphism (SNP) encoding V81G (V62G) in GPA [4].

Expression of the rare MNS46 antigen results from heterozygosity for an SNP in *GYP A* encoding a T36R (T17R) substitution in GPA [5]. Anti-MNS46 was found in 0.02% of Japanese blood donors [5].

Kell system

Two antigens of high incidence and one of low incidence were added to the Kell system. KEL29 and KEL30 are defined by antibodies produced by individuals with the rare KEL:–29 and KEL:–30 phenotypes, which resulted from homozygosity for SNPs in *KEL* encoding R623K and D305N, respectively [6]. KEL31 expression results from heterozygosity for a *KEL* SNP encoding R292G [7]. The only example of anti-KEL31 was found in a Japanese blood donor [7].

Scianna system

SC5 (STAR), described in the 2004 report [1], has now been published in full [8]. The two new antigens of the Scianna system, SC6 and SC7, are of high incidence. SC:–6 and SC:–7

phenotypes result from SNPs in *ERMAP*, encoding R81Q and G35S substitutions in *ERMAP*, respectively [9]. Anti-SC6 and -SC7 were previously reported as antibodies to high incidence antigens that were absent from SC:–1,–2,–3 red cells [10].

Cromer system

Two new antigens of high incidence were added: CROM14 and CROM15. CROM:–14 arose from homozygosity for an SNP in *CD55* encoding E156K in the second complement control protein (CCP) domain of CD55 and CROM:–15 from homozygosity for an SNP encoding Q247R in the fourth CCP domain of CD55 [11,12]. Antibodies to both antigens were present in the sera of the *propositi*, whose red cells lacked the corresponding antigens.

Indian system

Two new antigens of the Indian system, IN3 and IN4, are of high incidence. IN:–3 and IN:–4 phenotypes result from homozygosity for SNPs in *CD44* encoding H85Q and T163R in CD44, respectively [13]. Anti-IN3 and -IN4 have been produced by three and two individuals, respectively, whose red cells lack the corresponding antigen.

Knops system

KN9 was identified by several antibodies, originally identified incorrectly as anti-KN3 (McC^a). KN9, which has an incidence of about 98% in Caucasians and 20% in West Africans, results from an SNP in exon 29 of *CR1* encoding I1615 in place of V1615 in CD35 [14].

JMH system

Four new antigens were added to the JMH system, each defined by alloantibodies to high incidence antigens that do not react with JMH:–1 red cells. Absence of these antigens is associated with homozygosity for SNPs in the *SEMA7A* gene encoding amino acid substitutions in the semaphorin domain of Sema7A (Table 1) [15]. JMH1 retains its original meaning as representing the antigen recognized by antibodies made by individuals apparently lacking the JMH protein, Sema7A.

Gene terminology

A few changes were made affecting recommended terminology for blood group genes. The commonly used symbols *FY*A*, *FY*B*, *JK*A*, etc. are acceptable alternatives to *FY*1*, *FY*2*, *JK*1*, etc. In the Rh system, the recommended DCE terminology for alleles of *RHCE* is *RHCE*ce*, *RHCE*Ce*, *RHCE*CE*, etc., and for variants of *RHD* is *RHD*DVI*, *RHD*DFR*, etc.

Additional information on blood group genes and proteins

The Human Genome Organization (HUGO) Gene Nomenclature Committee (HGNC) (<http://www.gene.ucl.ac.uk/nomenclature/index.html>) approves names and symbols for human genes. These symbols are based, where possible, on the functions of the products of the genes and are listed in Table 1 of the 2004 report [1], although three changes have subsequently been made: *FY* to *DARC*; *DO* to *ART4*; and *DAF* to *CD55*. The HGNC symbol (e.g. *DARC*) should be used in all circumstances except when referring to serologically defined alleles or molecularly defined alleles that represent a serologically defined antigen (e.g. *FY*1* or *FY*A*, but not *DARC*1* or *DARC*A*).

The Dombrock glycoprotein, ADP-ribosyltransferase 4 (*ART4*), is CD297 (<http://mpr.nci.nih.gov/PROW>).

Future considerations

A new collection containing antigens on GPA that are determined primarily by glycosylation of the protein will be established. These will include Hu, M₁, Tm, Sj, and Can. Other matters to be discussed are blood group allele terminology and common or consensus alleles for each blood group gene.

References

- Daniels GL, Fletcher A, Garratty G, Henry S, Jørgensen J, Judd WJ, Levene C, Lomas-Francis C, Moulds JJ, Moulds JM, Moulds M, Overbeeke M, Reid ME, Rouger P, Scott M, Sistonen P, Smart E, Tani Y, Wendel S, Zelinski T: Blood group terminology 2004. From the ISBT Committee on Terminology for red cell surface antigens. *Vox Sang* 2004; **87**:304–316
- Velliquette R, Palacajornsuk P, Hue-Roye K, Lingren S, Ilstrup S, Reid ME, Lomas-Francis C: Novel GYP(A-B-A) hybrid gene in a DANE+ person who made an antibody to a high prevalence MNS antigen. *Transfusion* 2005; **45**:5A (Abstract)
- Huang C-H, Skov F, Daniels G, Tippett P, Blumenfeld OO: Molecular analysis of human glycophorin MiiX gene shows a silent segment transfer and untemplated mutation resulting from gene conversion via sequence repeats. *J Biol Chem* 1992; **80**:2379–2387
- Lomas-Francis C, Hu Z, Hue-Roye K, Velliquette RW, Reid ME, Allen JL, Mribella D: Novel single nucleotide change in GYP A in a person who made an alloantibody to a new high prevalence MNS antigen called ENEV. *Transfusion* 2006; **46**:25A (Abstract)
- Uchikawa M, Tsuneyama H, Ogasawara K, Suzuki Y, Yabe R, Enomoto T, Satake M, Nakajima K: Molecular basis for a novel low frequency antigen in the MNS blood group system, Td. *Vox Sang* 2006; **91** (Suppl 3):133 (Abstract)
- Lee S, Debnath AK, Wu X, Scofield T, George T, Kakaiya R, Yogore MG, III, Sausais L, Yacob M, Lomas-Francis C, Reid ME: Molecular basis of two novel high prevalence antigens in the Kell blood group system, KALT and KTIM. *Transfusion* 2006; **46**:1323–1327
- Uchikawa M, Onodera T, Ogasawara K, Tsuneyama H, Toyoda C, Yabe R, Enomoto T, Satake M, Nakajima K: Molecular basis for a novel low-frequency antigen in the Kell blood group system, KYO. *Vox Sang* 2006; **91** (Suppl. 3):136 (Abstract)
- Hue-Roye K, Chaudhuri A, Velliquette RW, Fetics S, Thomas R, Balk M, Wagner FF, Flegel WA, Reid ME: STAR: a novel high-prevalence antigen in the Scianna blood group system. *Transfusion* 2005; **45**:245–247
- Flegel WA, Chen Q, Reid ME, Martin J, Orsini LA, Poole J, Moulds MK, Wagner FF: SCER and SCAN: two novel high-prevalence antigens in the Scianna blood group system. *Transfusion* 2005; **45**:1940–1944
- Devine P, Dawson FE, Motschman TL, Skradski KJ, Orsini L, Moulds JJ, Taswell HF: Serologic evidence that Scianna null (Sc:–1,–2) red cells lack multiple high-frequency antigens. *Transfusion* 1988; **28**:346–349
- Ivankovik Z, Gobulic Cepulic B, Hue-Roye K, Alcantara C, Lomas-Francis C, Reid ME, Poole J, Lublin D. CROV: a new high prevalence Cromer blood group antigen. *Transfusion* 2005; **45**:122A (Abstract)
- Hue-Roye K, Lomas-Francis C, Velliquette RW, Reid ME, Poole J, Mason R, Belaygorod L, Lublin DM. CRAM: a new high prevalence Cromer blood group antigen and disappearance of the corresponding alloantibody during pregnancy. *Transfusion* 2006; **46**:25A
- Poole J, Tilley L, Warke N, Banks J, Ahrens N, Armstrong D, Williams M, Daniels G: Molecular basis of two novel high incidence antigens on CD44 (Indian blood group system). *Trans Med* 2005; **15** (Suppl. 1):30 (Abstract)
- Moulds JM, Pierce S, Peck KB, Tulley ML, Doumbo O, Moulds JJ: KAM: a new allele in the Knops blood group system. *Transfusion* 2005; **45**:27A (Abstract)
- Seltsam A, Strigens S, Levene C, Yahalom V, Moulds M, Moulds JJ, Hustinx H, Weisbach V, Figueroa D, Bade-Doeding C, DeLuca DS, Blasczyk R: The molecular diversity of SEMA7A that carries the JMH blood group antigens. *Transfusion* 2007; **47**:133–146.

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