Kell Blood Group System

Number of antigens 34

Polymorphic	K
Low prevalence	Kp^a, Js^a, Ul^a, K17, Kp^c, K23, K24, VLAN, VONG, KYO
High prevalence	k, Kp^b, Ku, Js^b, K11, K12, K13, K14, K16, K18, K19, Km, K22, TOU, RAZ, KALT, KTIM, KUCI, KANT, KASH, KELP, KETI, KHUL

Terminology

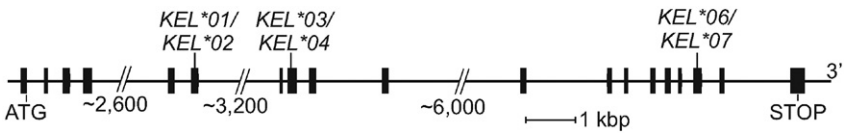
ISBT symbol (number)	KEL (006)
CD number	CD238
History	Named in 1946 after the first antibody producer (Mrs. Kelleher) of anti-K that caused HDFN.

Expression

Other blood cells	Appears early in erythropoiesis, but may also be expressed on myeloid progenitors and possibly on megakaryocytes
Tissues	Primarily in bone marrow, fetal liver, testes; lesser amounts in other tissues including various parts of the brain, lymphoid organs, heart, and skeletal muscle.

Gene

Chromosome	7q34
Name	*KEL*
Organization	19 exons distributed over 21.5 kbp of gDNA
Product	Kell glycoprotein



The Blood Group Antigen (3/e). DOI: http://dx.doi.org/10.1016/B978-0-12-415849-8.00008-9

Database accession numbers

GenBank	M64934 (mRNA); AH008123 (gene) NM_000420 (mRNA)
Entrez Gene ID	3792

Molecular basis of Kell phenotypes

The reference allele, *KEL*02* (Accession number M64934) encodes k (KEL2) KEL4, KEL5, KEL7, KEL11, KEL12, KEL13, KEL14, KEL18, KEL19, KEL20, KEL22, KEL26, KEL27, KEL29, KEL30, KEL32, KEL33, KEL35, KEL36. Nucleotide differences from this reference allele, and the amino acids affected, are given.

Allele encodes	Allele name	Exon	Nucleotide†	Restriction enzyme	Amino acid	Ethnicity (prevalence)
K+k– or KEL:1,–2	*KEL*01.01*	6	578C>T	*Bsm*I+	Thr193Met	Caucasians (9%), Blacks (2%), Iranian Jews (12%)
K+^{W} or KEL:1weak	*KEL*01.02*	6	577A>T	*Bsm*I as ref. allele	Thr193Ser	(Rare)
K+^{W}, Kp(a+) or KEL:1weak,3	*KEL*01.03*	6,8	578C>T 841C>T		Thr193Met Arg281Trp	(Rare)[1]
Kp(a+b–c–) or KEL:3,–4,–21	*KEL*02.03*	8	841C>T	*Nla*III+	Arg281Trp	Caucasians (2%)
Js(a+b–) or KEL:6,–7	*KEL*02.06*	17	1790T>C	*Mnl*I–	Leu597Pro	Blacks (20%)
Ul(a+) or KEL:10	*KEL*02.10*	13	1481A>T	*Acc*I+	Glu494Val	Finns > Japanese (Several)
K12– or KEL:–12	*KEL*02.–12*	15	1643A>G	*Nla*III–	His548Arg	Caucasians (Rare)
K14– or KEL:–14,–24	*KEL*02.–14.1*	6	538C>T		Arg180Cys	Japanese (Rare)
K14– or KEL:–14	*KEL*02.–14.2*	6	539G>A		Arg180His	Japanese (Rare)
Wk(a+) K11– or KEL:–11,17	*KEL*02.17*	8	905T>C	*Hae*III+	Val302Ala	(Several)
K18– or KEL:–18	*KEL*02.–18.1*	4	388C>T	*Taq*II+	Arg130Trp	(Rare)
K18– or KEL:–18	*KEL*02.–18.2*	4	389G>A	*Eco*57+	Arg130Gln	(Rare)
K19– or KEL:–19	*KEL*02.–19*	13	1475G>A		Arg492Gln	(Rare)
Kp(c+) or KEL:–3,–4,21	*KEL*02.21*	8	842G>A	*Pvu*II+	Arg281Gln	Japanese > Caucasians (Rare)
K22– or KEL:–22	*KEL*02.–22*	9	965C>T	*Tsp*45I+	Ala322Val	Iranian Jews (Rare)
K23+ or KEL:23	*KEL*02.23*	10	1145A>G	*Bcn*I+	Gln382Arg	(Rare)
K24+ or KEL:–14,24	*KEL*02.24*	6	539G>C	*Hae*III+	Arg180Pro	French Cajuns (Rare)

(*Continued*)

(Continued)

Allele encodes	Allele name	Exon	Nucleotide†	Restriction enzyme	Amino acid	Ethnicity (prevalence)
VLAN+ VONG– or KEL:25,–28	*KEL*02.25*	8	743G>A	*Psp*GI+^	Arg248Gln	(Rare)
TOU– or KEL:–26	*KEL*02.–26*	11	1217G>A		Arg406Gln	Native American, Hispanic (Rare)
RAZ– or KEL:–27	*KEL*02.–27*	8	745G>A	*Eco*RI+^	Glu249Lys	(Rare)
VLAN– VONG+ or KEL:–25,28	*KEL*02.28*	8	742C>T		Arg248Trp	Chinese (Rare)
KALT– or KEL:–29	*KEL*02.–29*	17	1868G>A	*Tfi*I–^	Arg623Lys	(Rare)
KTIM– or KEL:–30	*KEL*02.–30*	8	913G>A	*Taq*I–	Asp305Asn	(Rare)
KYO+ or KEL:31	*KEL*02.31*	8	875G>A		Arg292Gln	Japanese (Rare)
KUCI– or KEL:–32	*KEL*02.–32*	11	1271C>T	*FnuH*I–	Ala424Val	American Indian (Rare)
KANT– or KEL:–33	*KEL*02.–33*	11	1283G>T		Arg428Leu	European (Rare)
KASH– or KEL:–34	*KEL*02. –34*	8	758A>G		Tyr253Cys	(Rare)
KELP– or KEL:–35	*KEL*02.–35*	8 18	780G>T 2024G>A	*Gsa*I– *Taq*I–	Leu260Phe Arg675Gln	(Rare)
KETI– or KEL:–36	*KEL*02.–36*^^	12	1391C>T	*Bsm*AI–	Thr464Ile	European (Few)
KHUL– or KEL:–37	*KEL*02.–37*	8	877C>T		Arg293Trp	Asian (Rare)

†Nucleotide #1 is the first nucleotide of the translation/initiation codon, which is 120 bp downstream from that given in early reports.
^Nucleotide change(s) introduced into primer(s).
^^Has been also found on an allele with the 905 T>C change associated with K11–K17+.

Molecular bases for silencing of *KEL*

Homozygosity or compound heterozygosity leads to the K_0 ($Kell_{null}$) phenotype. Nucleotide differences from *KEL*02* reference allele (Accession number M64934), and the amino acids affected, are given.

Allele name	Exon/ intron	Nucleotide†	Restriction enzyme	Amino acid	Ethnicity (prevalence)
*KEL*01N.01*	15	1678C>G		Pro560Ala	(Rare)
*KEL*02N.01*	Intron 3	IVS3+1 g>c	*Dde*I+	Alternative splicing	Taiwanese (Rare)
*KEL*02N.02*	4 17	382C>T on a 1790T>C background		Arg128Stop Leu597Pro	Blacks (Rare)
*KEL*02N.03*	4	246T>A		Cys82Stop	Yugoslavians (Rare)
*KEL*02N.04*	9	1042C>T	*Tsp*45I –	Gln348Stop	Portuguese, Caucasians (Rare)
*KEL*02N.05*	18	2027G>A	*Alu*I–	Ser676Asn	Israeli (Rare)
*KEL*02N.06*	Intron 3	IVS3+1 g>a	*Nla*III+	Alternative splicing	Reunion Islands (Few)
*KEL*020N.7*	6	574C>T		Arg192Stop	(Rare)
*KEL*02N.08*	Intron 5	IVS5–2a>g		Alternative splicing	Japanese (Rare)
*KEL*02N.09*	12	1377G>A		Trp459Stop	Japanese (Rare)
*KEL*02N.10*	13	1420C>T		Gln474Stop	Swedish (Rare)
*KEL*02N.11*	8	903delG		fs, Stop	Swedish (Rare)
*KEL*02N.12*	Intron 8	IVS8+1 g>a		Alternative splicing	(Rare)
*KEL*02N.13*	Intron 8	IVS8+1 g>t		Alternative splicing	(Rare)
*KEL*02N.14*	9	948G>A		Trp316Stop	(Rare)
*KEL*02N.15*	11	1216C>T		Arg406Stop	(Rare)
*KEL*02N.16*	13	1477C>T		Gln493Stop	(Rare)

(*Continued*)

(Continued)

Allele name	Exon/ intron	Nucleotide†	Restriction enzyme	Amino acid	Ethnicity (prevalence)
*KEL*02N.17*	14	1546C>T		Arg516Stop	(Rare)
*KEL*02N.18*	Obsolete				
*KEL*02N.19*	18	2023C>T		Arg675Stop	(Rare)
*KEL*02N.20*	15	1596G>A		Trp532Stop	(Rare)
*KEL*02N.21*	18	1947C>G		Tyr649Stop	(Rare)
*KEL*02N.22*	Intron 7	IVS7–1 g>c		Alternative splicing	(Rare)
*KEL*02N.23*	3	185insT		Glu239Stop	Chinese (Rare)

†Nucleotide #1 is the first nucleotide of the translation/initiation codon, which is 120 bp downstream from that given in early reports.

Molecular bases of weak Kell antigens

Homozygosity or compound heterozygosity leads to the $Kell_{mod}$ phenotype. Nucleotide differences from the *KEL*02* reference allele (Accession number M64934), and amino acids affected, are given. K_{mod} is an umbrella term used to describe various phenotypes with very weak expression of Kell antigens and increased expression of Kx antigen. Classification of a mod phenotype may depend on the reagents and techniques used.

Allele name	Exon	Nucleotide†	Restriction enzyme	Amino acid	Ethnicity (prevalence)	Other
*KEL*01M.01*	6	578C>G		Thr193Arg	Taiwanese (Rare)	KEL:1 weak
*KEL*02M.01*	10	1088G>A	*Hae*III+	Ser363Asn	Caucasian (Rare)	
*KEL*02M.02*	18	2030A>G		Tyr677Cys	Caucasian	
*KEL*02M.03*	9	986T>C		Leu329Pro	Caucasian (Rare)	KEL:–13
*KEL*02M.04*	19	2107G>A		Gly703Arg	Caucasian (Rare)	

(*Continued*)

(Continued)

Allele name	Exon	Nucleotide†	Restriction enzyme	Amino acid	Ethnicity (prevalence)	Other
*KEL*02M.05*	16	1719C>T		Gly573Gly	(Rare)	
*KEL*02M.06*	4 11	306C>A 1298C>T		Asp102Glu Pro433Leu	(Rare)	
*KEL*02M.07*	16	1763A>G		Tyr588Cys	(Rare)	
*KEL*02M.08*	13	1490A>T		Asp497Val	(Rare)	
*KEL*02M.09*	16	1757T>G		Ile586Ser	(Rare)	
*KEL*02M.10*	8	787G>A		Gly263Arg	(Rare)	
*KEL*02M.11*	11	1268C>T		Ala423Val	Caucasian (Rare)	KEL:2 weak. KEL:7 weak.

†Nucleotide #1 is the first nucleotide of the translation/initiation codon, which is 120 bp downstream from that given in early reports.

Amino acid sequence[2]

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MEGGDQSEEE  PRERSQAGGM  GTLWSQESTP  EERLPVEGSR  PWAVARRVLT   50
AILILGLLLC  FSVLLFYNFQ  NCGPRPCETS  VCLDLRDHYL  ASGNTSVAPC  100
TDFFSFACGR  AKETNNSFQE  LATKNKNRLR  RILEVQNSWH  PGSGEEKAFQ  150
FYNSCMDTLA  IEAAGTGPLR  QVIEELGGWR  ISGKWTSLNF  NRTLRLLMSQ  200
YGHFPFFRAY  LGPHPASPHT  PVIQIDQPEF  DVPLKQDQEQ  KIYAQIFREY  250
LTYLNQLGTL  LGGDPSKVQE  HSSLSISITS  RLFQFLRPLE  QRRAQGKLFQ  300
MVTIDQLKEM  APAIDWLSCL  QATFTPMSLS  PSQSLVVHDV  EYLKNMSQLV  350
EEMLLKQRDF  LQSHMILGLV  VTLSPALDSQ  FQEARRKLSQ  KLRELTEQPP  400
MPARPRWMKC  VEETGTFFEP  TLAALFVREA  FGPSTRSAAM  KLFTAIRDAL  450
ITRLRNLPWM  NEETQNMAQD  KVAQLQVEMG  ASEWALKPEL  ARQEYNDIQL  500
GSSFLQSVLS  CVRSLRARIV  QSFLQPHPQH  RWKVSPWDVN  AYYSVSDHVV  550
VFPAGLLQPP  FFHPGYPRAV  NFGAAGSIMA  HELLHIFYQL  LLPGGCLACD  600
NHALQEAHLC  LKRHYAAFPL  PSRTSFNDSL  TFLENAADVG  GLAIALQAYS  650
KRLLRHHGET  VLPSLDLSPQ  QIFFRSYAQV  MCRKPSPQDS  HDTHSPPHLR  700
VHGPLSSTPA  FARYFRCARG  ALLNPSSRCQ  LW                      732
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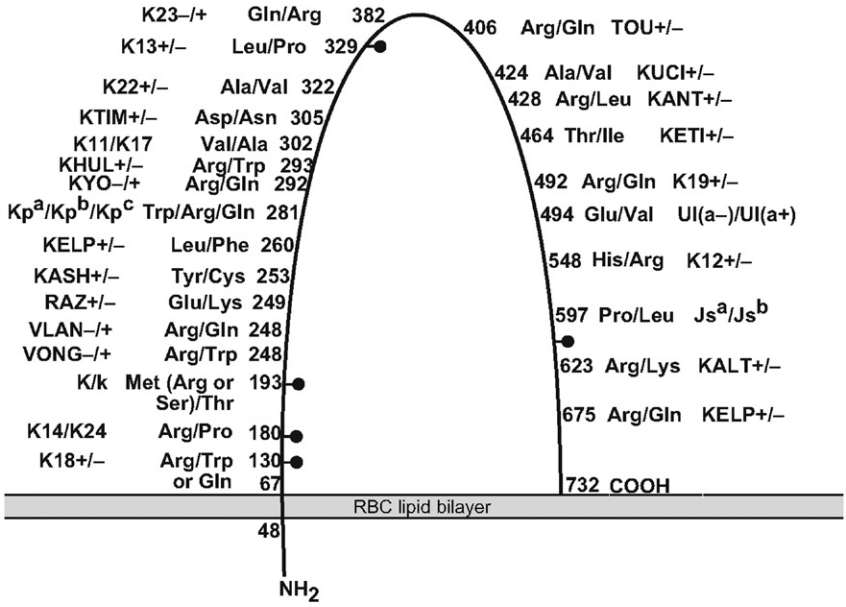
Carrier molecule

Single-pass RBC membrane glycoprotein (type II) that is highly folded via disulfide bonds. In the RBC membrane Kell glycoprotein is covalently linked at Cys72 to the Cys347 of the XK protein.



M_r (SDS-PAGE)	93,000; 79,000–80,000 after N-glycanase treatment
CHO: N-glycan	5 sites
Cysteine residues	16 (1 of which is in the membrane)
Copies per RBC	3,500–18,000[3]

Function

Kell glycoprotein is an endothelin-3-converting enzyme, preferentially cleaving big endothelin-3, creating bioactive endothelin-3, which is a potent vasoconstrictor. Kell glycoprotein is a member of the Neprilysin (M13) sub-family of zinc endopeptidases and, in common with all of them, shares a pentameric sequence, HEXXH, which is central to zinc binding and catalytic activity[2].

Disease association

In one study, 1 in 250 patients with AIHA had autoantibodies directed to Kell system antigens. Transiently depressed Kell system antigens have been associated with the presence of autoantibodies mimicking alloantibodies in AIHA, and with microbial infection. The Kell protein was reduced in one case of ITP[4]. Kell antigens are weak on RBCs from McLeod CGD (X-linked type) males. Antibodies to antigens in the Kell blood group system have caused HDFN, due both to immune destruction of RBCs and, more

significantly, suppression of erythropoiesis[5]. This can result in severe anemia, which may be prolonged and without overt signs of hemolysis.

Phenotypes (% occurrence)

Phenotype	Caucasians	Blacks
K–k+	91	98
K+k–	0.2	Rare
K+k+	8.8	2
Kp(a+b–)	Rare	0
Kp(a–b+)	97.7	100
Kp(a+b+)	2.3	Rare
Js(a+b–)	0	1
Js(a–b+)	100	80
Js(a+b+)	Rare	19
Null: K_0; very rare, but a little less rare in Finland, Japan, and Reunion Islands		
Unusual: K_{mod}, McLeod (see Kx blood group system [**XK, 019**]) and table below showing comparison of Kell phenotypes), Kp(a+b–), Leach and Gerbich types of Ge-negative		

Comparison of Kell phenotypes[6]

Phenotype	Expression of antigen		Possible antibody in serum	RBC morphology
	Kell system	Kx		
Inherited Kell system phenotypes				
Common	Normal	Weak	Alloantibody	Discocytes
Kp(a+b–)	Slight/moderate reduction	Slight increase	Anti-Kp^b	Discocytes
K_{mod}	Marked reduction^	Moderate increase	Anti-Ku-like (not mutually compatible)	Discocytes
K_0 heterozygote	Normal	Moderate increase	None	Discocytes

(*Continued*)

(Continued)

Phenotype	Expression of antigen		Possible antibody in serum	RBC morphology
	Kell system	Kx		
K_0	None†	Marked increase††	Anti-Ku	Discocytes
Inherited Kx system phenotypes				
McLeod CGD	Marked reduction	None	Anti-KL (anti-Kx+ anti-Km)	Acanthocytes
McLeod non-CGD	Marked reduction	None	Anti-Km (anti-Kx in one case)	Acanthocytes
McLeod carriers‡	Normal to marked reduction	Not known	None	Discocytes and acanthocytes
Other				
Gerbich and Leach phenotypes	Slight decrease	Normal/ weak	Not Kell-related	Discocytes and elliptocytes in Leach phenotype
AIHA (Kell-related)	Normal to marked reduction	Slight increase (when Kell reduced)	"Kell-related" antibodies or non-specific	Discocytes or spherocytes (due to the hemolytic anemia)
Thiol-treated RBCs	Not detectable	Slight increase	Not applicable	Not known

^Will adsorb and elute antibody to inherited antigens in Kell system.
†Do not adsorb and elute.
††Xk protein is decreased; antigen may be more accessible.
‡The proportion of normal to McLeod phenotype RBCs varies in different carrier females. Only affected males present with 100% of RBCs having the McLeod phenotype.

Comparison of features of McLeod phenotype with normal and K_0 RBCs

Features	Normal Kell phenotype	K_0	McLeod non-CGD	McLeod CGD
Kell system antigens	++++	0	Weak	Weak
Kx antigen	+	++	0	0
Km antigen	++	0	0	0
Antibodies made	To lacking Kell antigens	Anti-Ku	Anti-Km (anti-Kx in one case)	Anti-Kx+ −Km
Creatine kinase level	Normal	Normal	Elevated	Normal or elevated
Blood for transfusion	Normal antigen-negative phenotype	K_0	McLeod or K_0	McLeod
Gene defect	Not applicable	Changes in *KEL*	Changes in *XK*	Deletion of *XK* and *CGD*^
Morphology	Discocytes	Discocytes	Acanthocytes	Acanthocytes
Pathology	None	None	Muscular and neurological defects	Muscular and neurological defects with CGD

^=The official name for the CDG gene is now *CBB*.

Comments

It is incorrect to refer to the K and k antigens as, respectively, K1 and K2; in the numerical terminology they should be referred to as KEL1 and KEL2. However, some Kell antigens were assigned a traditional numerical name, e.g., K11 and K14, and thus can be referred to as either K11 or KEL11, and K14 or KEL14.

Historically, no Kell system haplotype had more than one low-prevalence antigen. Recently, a novel *KEL*1,3* allele was reported that encoded K and Kp^a on the same molecule[1].

The Kp^a antigen *in cis* weakens the expression of Kell antigens (*cis*-modifying effect)[1,7]. K_{mod} is an umbrella term used to describe various phenotypes with very weak expression of Kell antigens and increased expression of Kx.

Kell antigens are sensitive to treatment by a mixture of α-chymotrypsin and trypsin or to sequential treatment of antigen-positive RBCs with these enzymes.

Antibodies produced by K_{mod} individuals are not necessarily mutually compatible.

References

[1] Körmöczi, G.F., et al., 2009. A novel KEL*1,3 allele with weak Kell antigen expression confirming the cis-modifier effect of KEL3. Transfusion 49, 733–739.

[2] Lee, S., 2007. The value of DNA analysis for antigens of the Kell and Kx blood group systems. Transfusion 47 (Suppl.), 32S–39S.

[3] Parsons, S.F., et al., 1993. Monoclonal antibodies against Kell glycoprotein: serology, immunochemistry and quantification of antigen sites. Transf Med 3, 137–142.

[4] Williamson, L.M., et al., 1994. Transient loss of proteins carrying Kell and Lutheran red cell antigens during constructive relapses of autoimmune thrombocytopenia. Br J Haematol 87, 805–812.

[5] Vaughan, J.I., et al., 1998. Inhibition of erythroid progenitor cells by anti-Kell antibodies in fetal alloimmune anemia. N Engl J Med 338, 798–803.

[6] Øyen, R., et al., 1997. Review: conditions causing weak expression of Kell system antigens. Immunohematology 13, 75–79.

[7] Yazdanbakhsh, K., et al., 1999. Identification of a defect in the intracellular trafficking of a Kell blood group variant. Blood 94, 310–318.

K Antigen

Terminology

ISBT symbol (number)	KEL1 (006001 or 6.1)
Obsolete names	Kell; K1
History	Named after first antibody producer (Mrs. Kelleher) of anti-K, which caused HDFN; reported in 1946.

Occurrence

Caucasians	9%
Blacks	2%
Asians	Rare
Iranian Jews	12%
Arabs	As high as 25%

Antithetical antigen

k (**KEL2**)

Expression

Cord RBCs	Expressed
Altered	See table showing Comparison of Kell Phenotypes on System pages Weak with Arg193 or Ser193

Molecular basis associated with K antigen[1,2,3]

Amino acid	Met193
Nucleotide	T at bp 578 (previously reported as 698) in exon 6
Weak expression of K	578C>G (Thr193Arg) and 577A>T (Thr193Ser)

All three changes disrupt the N-glycosylation motif, so Asn191 is not glycosylated.

Effect of enzymes and chemicals on K antigen on intact RBCs

Ficin/Papain	Resistant
Trypsin	Resistant
α-Chymotrypsin	Resistant*
DTT 200 mM/50 mM	Sensitive/sensitive (thus sensitive to WARM™ and ZZAP)
Acid	Sensitive (thus sensitive to EGA)

*May be weakened or sensitive if the enzyme preparation is contaminated with trypsin.

In vitro characteristics of alloanti-K

Immunoglobulin class	IgG more common than IgM
Optimal technique	IAT, sometimes RT; may not react well by LISS procedures
Complement binding	Rare

Clinical significance of alloanti-K

Transfusion reaction	Mild to severe/delayed/hemolytic
HDFN	Mild to severe (rare); often with anemia, which is sometimes delayed

Comments

Some bacteria elicit production of IgM anti-K. Expression of K can be acquired as a result of bacterial activity *in vivo* and *in vitro*.

References

[1] Lee, S., et al., 1995. Molecular basis of the Kell (K1) phenotype. Blood 85, 912–916.

[2] Poole, J., et al., 2006. A KEL gene encoding serine at position 193 of the Kell glycoprotein results in expression of KEL1 antigen. Transfusion 46, 1879–1885.

[3] Uchikawa, M., et al., 2000. Molecular basis of unusual Kmod phenotype with K+^{w}k−[abstract]. Vox Sang 78 (Suppl. 1), 0011.

k Antigen

Terminology

ISBT symbol (number)	KEL2 (006002 or 6.2)
Obsolete names	Cellano; K2
History	Identified in 1949 when an antibody was shown to recognize the antithetical antigen to K. Cellano, the original name, was derived by rearranging the proband's last name (Nocella).

Occurrence

Caucasians	99.8%
Blacks	100%

Antithetical antigen

K (**KEL1**)

Expression

Cord RBCs	Expressed
Altered	See table showing Comparison of Kell Phenotypes on System pages Weakened in rare genetic variants; weak expression with concomitant 423Val[1]

Molecular basis associated with k antigen[2]

Amino acid	Thr193
Nucleotide	C at bp 578 (previously reported as 698) in exon 6

Effect of enzymes and chemicals on k antigen on intact RBCs

Ficin/Papain	Resistant
Trypsin	Resistant
α-Chymotrypsin	Resistant (see K [**KEL1**])
DTT 200 mM/50 mM	Sensitive/sensitive (thus sensitive to WARM™ and ZZAP)
Acid	Sensitive (thus sensitive to EGA)

In vitro characteristics of alloanti-k

Immunoglobulin class	IgG more common than IgM
Optimal technique	IAT

Clinical significance of alloanti-k

Transfusion reaction	Mild to moderate/delayed
HDFN	Mild to severe (rare)

Comments

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

References

[1] Lee, S., 1997. Molecular basis of Kell blood group phenotypes. Vox Sang 73, 1–11.
[2] Lee, S., et al., 1995. Molecular basis of the Kell (K1) phenotype. Blood 85, 912–916.

Kp^a Antigen

Terminology

ISBT symbol (number)	KEL3 (006003 or 6.3)
Obsolete names	Penny; K3
History	Identified in 1957; the antigen, which was shown to be related to the Kell System, took its name from "K" for "Kell" and "p" for the first letter of the antibody producer's name (Penny).

Occurrence

Caucasians	2%
Blacks	<0.01%

Antithetical antigens

Kp^b (**KEL4**), Kp^c (**KEL21**)

Expression

Cord RBCs	Expressed
Altered	See table showing Comparison of Kell Phenotypes on System pages

Molecular basis associated with Kp^a antigen[1]

Amino acid	Trp281
Nucleotide	T at bp 841 in exon 8 (previously reported as 961)

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

Ficin/Papain	Resistant
Trypsin	Resistant
α-Chymotrypsin	Resistant (see K [**KEL1**])
DTT 200 mM/50 mM	Sensitive/sensitive (thus sensitive to WARM™ and ZZAP)
Acid	Sensitive (thus sensitive to EGA)

In vitro characteristics of alloanti-Kp^a

Immunoglobulin class	IgG
Optimal technique	IAT

Clinical significance of alloanti-Kp^a

Transfusion reaction	Mild to moderate/delayed
HDFN	Mild to severe

Comments

In the presence of Kp^a, other inherited Kell system antigens are suppressed (*cis*-modifier effect) to varying degrees.
Until recently, in people with K+Kp(a+) RBCs, *K* was always *in trans* to *Kp^a*. However, Körmöczi et al. reported a novel *KEL*1,3* allele that encoded K and Kp^a on the same molecule[2].
Anti-Kp^a is often found with anti-K.

References

[1] Lee, S., et al., 1996. Point mutations characterize *KEL10*, the *KEL3*, *KEL4*, and *KEL21* alleles, and the *KEL17* and *KEL11* alleles. Transfusion 36, 490–494.
[2] Körmöczi, G.F., et al., 2009. A novel *KEL*1,3* allele with weak Kell antigen expression confirming the cis-modifier effect of KEL3. Transfusion 49, 733–739.

Kp^b Antigen

Terminology

ISBT symbol (number)	KEL4 (006004 or 6.4)
Obsolete names	Rautenberg; K4
History	Identified in 1958 and recognized to be antithetical to Kp^a.

Occurrence

All populations	100%

Antithetical antigens

Kp^a (**KEL3**); Kp^c (**KEL21**)

Expression

Cord RBCs	Expressed
Altered	Weak on RBCs from some patients with AIHA

See table showing Comparison of Kell phenotypes on System pages.

Molecular basis associated with Kp^b antigen[1]

Amino acid	Arg281
Nucleotide	C at bp 841 (previously reported as 961), G at bp 842 (previously reported as 962) in exon 8

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

Ficin/Papain	Resistant
Trypsin	Resistant
α-Chymotrypsin	Resistant (see K [**KEL1**])
DTT 200 mM/50 mM	Sensitive/sensitive (thus sensitive to WARM™ and ZZAP)
Acid	Sensitive (thus sensitive to EGA)

In vitro characteristics of alloanti-Kp^b

Immunoglobulin class	IgG, rarely IgM
Optimal technique	IAT

Clinical significance of alloanti-Kp^b

Transfusion reaction	No to moderate/delayed
HDFN	Mild to moderate

Autoantibody

Yes. May appear as alloantibody on initial presentation due to suppression of Kp^b antigen.

Comments

Sera containing anti-Kp^b often contain anti-K (see **KEL1**).
Siblings of patients with anti-Kp^b should be tested for compatibility, and the patient urged to donate blood for cryogenic storage when his/her clinical state permits.

Reference

[1] Lee, S., et al., 1996. Point mutations characterize *KEL10*, the *KEL3*, *KEL4*, and *KEL21* alleles, and the *KEL17* and *KEL11* alleles. Transfusion 36, 490–494.

Ku Antigen

Terminology

ISBT symbol (number)	KEL5 (006005 or 6.5)
Obsolete names	Peltz; K5
History	Antibody in serum of K_0 [K–k–Kp(a–b–)] person identified in 1957; originally called anti-KkKp^a or anti-Peltz (after the proband); renamed anti-Ku (K for Kell, u for universal) in 1961.

Occurrence

All populations	100%

Expression

Cord RBCs	Expressed
Altered	See table showing Comparison of Kell phenotypes on System pages.

Molecular basis associated with Ku antigen

For the molecular basis associated with the K_0 phenotype, see Kell System pages.

Effect of enzymes and chemicals on Ku antigen on intact RBCs

Ficin/Papain	Resistant
Trypsin	Resistant
α-Chymotrypsin	Resistant (see K [**KEL1**])
DTT 200 mM/50 mM	Sensitive/sensitive (thus sensitive to WARM™ and ZZAP)
Acid	Sensitive (thus sensitive to EGA)

In vitro characteristics of alloanti-Ku

Immunoglobulin class	IgG
Optimal technique	IAT

Clinical significance of alloanti-Ku

Transfusion reaction	Mild to severe
HDFN	No to moderate

Autoantibody

Yes

Comments

Anti-Ku is made by K_0 people who may make additional antibodies directed at other Kell antigens and, rarely, make Kell system specificities without making anti-Ku. K_{mod} people make Ku-like antibodies that are not necessarily mutually compatible.

An antibody detected only in the presence of trimethoprim, found in co-trimoxazole (CTMX; a combination of two drugs, trimethoprim [the culprit] and sulfamethoxazole, present in the suspension medium of some reagent RBCs) was identified as anti-Ku[1].

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

Reference

[1] Le Pennec, P., et al., 1999. Sulfamethoxazole and trimethoprim dependent antibodies with respective anti-H (H1) and anti-Ku (KEL5) specificity [abstract]. Transfusion 39 (Suppl.), 81S.

Js^a Antigen

Terminology

ISBT symbol (number)	KEL6 (006006 or 6.6)
Obsolete names	Sutter; K6
History	Described in 1958; "J" is from the first name (John) and "s" is from the last name (Sutter) of the first producer of the antibody. Js^a was shown to belong to the Kell System in 1965.

Occurrence

Caucasians	<0.01%
Blacks	20%

Antithetical antigen

Js^b (**KEL7**)

Expression

Cord RBCs	Expressed
Altered	See table showing Comparison of Kell phenotypes on System pages

Molecular basis associated with Js^a antigen[1]

Amino acid	Pro597
Nucleotide	C at bp 1790 in exon 17 (previously reported as 1910)

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

Ficin/Papain	Resistant
Trypsin	Resistant
α-Chymotrypsin	Resistant (see K [**KEL1**])
DTT 200 mM/50 mM	Sensitive/sensitive (see Comments) (thus sensitive to WARM™ and ZZAP)
Acid	Sensitive (thus sensitive to EGA)

In vitro characteristics of alloanti-Js^a

Immunoglobulin class	IgG more common than IgM
Optimal technique	IAT

Clinical significance of alloanti-Js^a

Transfusion reaction	No to moderate/delayed
HDFN	Mild to severe

Comments

At least one example of "naturally-occurring" anti-Js^a has been reported in a Japanese woman.
Js^a is extremely sensitive to thiol reagents (it is sensitive to 2 mM DTT), most likely because it is located between two cysteine residues.

Reference

[1] Lee, S., et al., 1995. Molecular basis of the K:6, −7 [Js(a+b−)] phenotype in the Kell blood group system. Transfusion 35, 822–825.

Js^b Antigen

Terminology

ISBT symbol (number)	KEL7 (006007 or 6.7)
Obsolete names	Matthews; K7
History	Named in 1963 when it was found to be antithetical to Js^a; joined the Kell blood group system in 1965.

Occurrence

Caucasians	100%
Blacks	99%

Antithetical antigen

Js^a (**KEL6**)

Expression

Cord RBCs	Expressed
Altered	See table showing Comparison of Kell phenotypes on System pages

Molecular basis associated with Js^b antigen[1]

Amino acid	Leu597
Nucleotide	T at bp 1790 in exon 17 (previously reported as 1910)

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

Ficin/Papain	Resistant (some enhanced)
Trypsin	Resistant
α-Chymotrypsin	Resistant (see K [**KEL1**])
DTT 200 mM/50 mM	Sensitive/sensitive (see Comments) (thus sensitive to WARM™ and ZZAP)
Acid	Sensitive (thus sensitive to EGA)

In vitro characteristics of alloanti-Js^b

Immunoglobulin class	IgG
Optimal technique	IAT

Clinical significance of alloanti-Js^b

Transfusion reaction	Mild to moderate/delayed
HDFN	Mild to severe (1 fatality)[2,3]

Comments

Js^b is extremely sensitive to thiol reagents (it is sensitive to 2 mM DTT), most likely because it is located between two cysteine residues.
Siblings of patients with anti-Js^b should be tested for compatibility, and the patient urged to donate blood for cryogenic storage when his/her clinical state permits.

References

[1] Lee, S., et al., 1995. Molecular basis of the K:6,−7 [Js(a+b−)] phenotype in the Kell blood group system. Transfusion 35, 822–825.

[2] Gordon, M.C., et al., 1995. Severe hemolytic disease of the newborn due to anti-Js^b. Vox Sang 69, 140–141.

[3] Stanworth, S., et al., 2001. Severe haemolytic disease of the newborn due to anti-Js^b. Vox Sang 81, 134–135.

Ul^a Antigen

Terminology

ISBT symbol (number)	KEL10 (006010 or 6.10)
Obsolete names	Karhula; K10
History	Described in 1968, and shown to be part of the Kell system in 1969. Named after the last letters of the antibody producer (Karhula).

Occurrence

Most populations	<0.01%
Finns	2.6% (higher in some regions)
Japanese	0.46%

Expression

Cord RBCs	Expressed

Molecular basis associated with Ul^a antigen[1]

Amino acid	Val494
Nucleotide	T at bp 1481 in exon 13 (previously reported as 1601)
Ul(a–) (wild type)	A at bp 1481 and Glu494

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

Ficin/Papain	Resistant
Trypsin	Resistant
α-Chymotrypsin	Resistant (see K [**KEL1**])
DTT 200 mM/50 mM	Presumed sensitive

In vitro characteristics of alloanti-Ul^a

Immunoglobulin class	IgG
Optimal technique	IAT

Clinical significance of alloanti-Ul^a

Transfusion reaction	No data but anti-Ul^a has been stimulated by transfusion
HDFN	One case[2]. 19 Ul(a–) mothers with Ul(a+) children did not make anti-Ul^a

Comments

Only a few examples of anti-Ul^a have been reported: two in Finland and two in Japan.

References

[1] Lee, S., et al., 1996. Point mutations characterize *KEL10*, the *KEL3*, *KEL4*, and *KEL21* alleles, and the *KEL17* and *KEL11* alleles. Transfusion 36, 490–494.

[2] Sakuma, K., et al., 1994. First case of hemolytic disease of the newborn due to anti-Ula antibodies. Vox Sang 66, 293–294.

K11 Antigen

Terminology

ISBT symbol (number)	KEL11 (006011 or 6.11)
Obsolete name	Côté
History	Found in 1971 in the serum of Mrs. Côté; the first of a series of K–k+ people who made an antibody compatible only with K_0 RBCs; a para-Kell antigen until proven to belong to Kell in 1974.

Occurrence

All populations	100%

Antithetical antigen

K17 (**KEL17**)

Expression

Cord RBCs	Expressed
Altered	See table showing Comparison of Kell phenotypes on System pages

Molecular basis associated with K11 antigen[1]

Amino acid	Val302
Nucleotide	T at bp 905 in exon 8 (previously reported as 1025)

Effect of enzymes and chemicals on K11 antigen on intact RBCs

Ficin/Papain	Resistant
Trypsin	Resistant
α-Chymotrypsin	Resistant (see K [**KEL1**])
DTT 200 mM/50 mM	Sensitive/sensitive (thus sensitive to WARM™ and ZZAP)
Acid	Sensitive (thus sensitive to EGA)

In vitro characteristics of alloanti-K11

Immunoglobulin class	IgG
Optimal technique	IAT

Clinical significance of alloanti-K11

Transfusion reaction	Mild to moderate (not much data)
HDFN	No to mild (not much data)

Comments

Siblings of patients with anti-K11 should be tested for compatibility, and the patient urged to donate blood for cryogenic storage when his/her clinical state permits.

Reference

[1] Lee, S., et al., 1996. Point mutations characterize *KEL10*, the *KEL3*, *KEL4*, and *KEL21* alleles, and the *KEL17* and *KEL11* alleles. Transfusion 36, 490–494.

K12 Antigen

Terminology

ISBT symbol (number)	KEL12 (006012 or 6.12)
Obsolete names	Bøc (Bøckman); Spears
History	Described in 1973; given the next number in the series of K–k+ people who made an antibody compatible only with K_0 RBCs.

Occurrence

The KEL:–12 phenotype has been reported only in four Caucasian families.

Expression

Cord RBCs	Presumed expressed
Altered	See table showing Comparison of Kell phenotypes on System pages RBCs from a KELP– (see **KEL35**) person were KEL:–12

Molecular basis associated with K12 antigen[1]

Amino acid	His548
Nucleotide	A at bp 1643 in exon 15 (previously reported as 1763)
K12–	Arg548 and G at bp 1643

Effect of enzymes and chemicals on K12 antigen on intact RBCs

Ficin/Papain	Resistant
Trypsin	Resistant
α-Chymotrypsin	Resistant (see K [**KEL1**])
DTT 200 mM/50 mM	Sensitive/sensitive (thus sensitive to WARM™ and ZZAP)

In vitro characteristics of alloanti-K12

Immunoglobulin class	IgG
Optimal technique	IAT

Clinical significance of alloanti-K12

Transfusion reaction	K12+ blood transfused to two patients (DL, MS) did not cause a transfusion reaction
HDFN	No data, although Mrs. Bøckman had at least two children

Comments

Siblings of patients with anti-K12 should be tested for compatibility, and the patient urged to donate blood for cryogenic storage when his/her clinical state permits.

Reference

[1] Lee, S., 1997. Molecular basis of Kell blood group phenotypes. Vox Sang 73, 1–11.

K13 Antigen

Terminology

ISBT symbol (number)	KEL13 (006013 or 6.13)
Obsolete name	SGRO
History	Described in 1974, given the next Kell System number. The K13– proband is a K_{mod}, thereby explaining the weak expression of Kell antigens in this phenotype[1].

Occurrence

K13– has been found in only one family.

Expression

Cord RBCs	Presumed expressed
Altered	See table showing Comparison of Kell phenotypes on System pages

Molecular basis associated with K13 antigen[1]

Amino acid	Leu329
Nucleotide	T at bp 986 in exon 9 (previously reported as 1106)
K13–	C at bp 1106 and Pro329

Effect of enzymes and chemicals on K13 antigen on intact RBCs

Ficin/Papain	Resistant
Trypsin	Resistant
α-Chymotrypsin	Resistant (see K [**KEL1**])
DTT 200 mM/50 mM	Sensitive/sensitive (thus sensitive to WARM™ and ZZAP)

In vitro characteristics of alloanti-K13

Immunoglobulin class	IgG
Optimal technique	IAT

Clinical significance of alloanti-K13

Transfusion reaction	No data are available because only one anti-K13 has been reported
HDFN	The proband's KEL:–13 sister had seven children, without making anti-K13

Comments

K13– RBCs express Kell antigens weakly; it is a K_{mod} phenotype.
Siblings of patients with anti-K13 should be tested for compatibility, and the patient urged to donate blood for cryogenic storage when his/her clinical state permits.

Reference

[1] Lee, S., et al., 2003. Mutations that diminish expression of Kell surface protein and lead to the $Kell_{mod}$ red cell phenotype. Transfusion 43, 1121–1125.

K14 Antigen

Terminology

ISBT symbol (number)	KEL14 (006014 or 6.14)
Obsolete names	San; Santini; Dp
History	Described in 1973, given the next number in the series of K–k+ people who made an antibody compatible only with K_0 RBCs.

Occurrence

K14– has been found in only three French-Cajun families.

Antithetical antigen

K24 (**KEL24**)

Expression

Cord RBCs	Expressed
Altered	See table showing Comparison of Kell phenotypes on System pages

Molecular basis associated with K14 antigen[1,2]

Amino acid	Arg180
Nucleotide	G at bp 539 in exon 6 (previously reported as 659)

The presence of Cys, His or Pro at amino acid residue 180 has resulted in the K14– phenotype (see table "Molecular basis of Kell phenotypes").

Effect of enzymes and chemicals on K14 antigen on intact RBCs

Ficin/Papain	Resistant
Trypsin	Resistant
α-Chymotrypsin	Resistant (see K [**KEL1**])
DTT 200 mM/50 mM	Sensitive/sensitive (thus sensitive to WARM™ and ZZAP)

In vitro characteristics of alloanti-K14

Immunoglobulin class	IgG
Optimal technique	IAT

Clinical significance of alloanti-K14

Transfusion reaction	No data are available because only three anti-K14 have been reported
HDFN	Mild in one case[3]

Comments

Siblings of patients with anti-K14 should be tested for compatibility, and the patient urged to donate blood for cryogenic storage when his/her clinical state permits.

References

[1] Lee, S., 1997. Molecular basis of Kell blood group phenotypes. Vox Sang 73, 1–11.

[2] Lee, S., et al., 1997. The *KEL24* and *KEL14* alleles of the Kell blood group system. Transfusion 37, 1035–1038.

[3] Wallace, M.E., et al., 1976. Anti-K14: an antibody specificity associated with Kell blood group system. Vox Sang 30, 300–304.

K16 Antigen

Terminology

ISBT symbol (number)	KEL16 (006016 or 6.16)
Obsolete names	Weak k; k-like
History	When anti-k was absorbed with McLeod RBCs, an antibody remained that was non-reactive with McLeod RBCs and reactive with all other k+ RBCs. In 1976, this antibody was named anti-K16 and the antigen K16. No further studies have been performed.

K17 (Wk^a) Antigen

Terminology

ISBT symbol (number)	KEL17 (006017 or 6.17)
Obsolete names	Weeks
History	Reported in 1974; given a Kell System number because the antigen had linkage disequilibrium to K, and in 1975 was shown to be antithetical to K11.

Occurrence

All populations	0.3%

Antithetical antigen

K11 (**KEL11**)

Expression

Cord RBCs	Presumed expressed
Altered	See table showing Comparison of Kell phenotypes on System pages

Molecular basis associated with K17 antigen[1]

Amino acid	Ala302
Nucleotide	C at bp 905 in exon 8 (previously reported as 1025)

Effect of enzymes and chemicals on K17 antigen on intact RBCs

Ficin/Papain	Resistant
Trypsin	Resistant
α-Chymotrypsin	Presumed resistant (see K [**KEL1**])
DTT 200 mM/50 mM	Sensitive/sensitive (thus sensitive to WARM™ and ZZAP)

In vitro characteristics of alloanti-K17

Immunoglobulin class	IgG
Optimal technique	IAT

Clinical significance of alloanti-K17

No data because the antigen and antibody are rare.

Reference

[1] Lee, S., et al., 1996. Point mutations characterize *KEL10*, the *KEL3*, *KEL4*, and *KEL21* alleles, and the *KEL17* and *KEL11* alleles. Transfusion 36, 490–494.

K18 Antigen

Terminology

ISBT symbol (number)	KEL18 (006018 or 6.18)
Obsolete names	V.M.; Marshall
History	Described in 1975, given the next number in the series of K–k+ people who made an antibody compatible only with K_0 RBCs.

Occurrence

K18– has been found only in three families.

Expression

Cord RBCs	Expressed
Altered	See table showing Comparison of Kell phenotypes on System pages

Molecular basis associated with K18 antigen[1]

Amino acid	Arg130
Nucleotide	C at bp 388 and G at bp 389 in exon 4 (previously reported as 508 and 509)
K18–: Type 1	130Trp and T at bp 388
K18–: Type 2	130Gln and A at bp 389

Effect of enzymes and chemicals on K18 antigen on intact RBCs

Ficin/Papain	Resistant
Trypsin	Resistant
α-Chymotrypsin	Resistant (see K [**KEL1**])
DTT 200 mM/50 mM	Sensitive/sensitive (thus sensitive to WARM™ and ZZAP)

In vitro characteristics of alloanti-K18

Immunoglobulin class	IgG
Optimal technique	IAT

Clinical significance of alloanti-K18

Transfusion reaction	Clinical significance is largely unknown. Chromium survival studies showed accelerated RBC destruction in one case[2]. Transfusion of an incompatible unit to a woman with anti-K18 resulted in shortened survival of transfused RBCs[3].
HDFN	Mild in the only reported case. Positive DAT; only phototherapy was required[3].

Comments

Siblings of patients with anti-K18 should be tested for compatibility, and the patient urged to donate blood for cryogenic storage when his/her clinical state permits.

References

[1] Lee, S., 1997. Molecular basis of Kell blood group phenotypes. Vox Sang 73, 1–11.

[2] Barrasso, C., et al., 1983. *In vivo* survival of K:18 red cells in a recipient with anti-K18. Transfusion 23, 258–259.

[3] O'Leary, M.F., et al., 2011. Anti-K18 causing hemolytic disease of the fetus and newborn [abstract]. Transfusion 51 (Suppl.), 156A.

K19 Antigen

Terminology

ISBT symbol (number)	KEL19 (006019 or 6.19)
Obsolete names	Sub; Sublett
History	Described in 1979; given the next number in the series of K–k+ people who made an antibody compatible only with K_0 RBCs.

Occurrence

All populations	100%

Expression

Cord RBCs	Presumed expressed
Altered	See table showing Comparison of Kell phenotypes on System pages

Molecular basis associated with K19 antigen[1]

Amino acid	Arg492
Nucleotide	G at bp 1475 in exon 13 (previously reported as 1595)
K19–	Gln492 and A at bp 1475

Effect of enzymes and chemicals on K19 antigen on intact RBCs

Ficin/Papain	Resistant
Trypsin	Resistant
α-Chymotrypsin	Resistant (see K [**KEL1**])
DTT 200 mM/50 mM	Sensitive/sensitive (thus sensitive to WARM™ and ZZAP)

In vitro characteristics of alloanti-K19

Immunoglobulin class	IgG
Optimal technique	IAT

Clinical significance of alloanti-K19

Transfusion reaction	Moderate/delayed/hemolytic in one case
HDFN	No data

Comments

Only two examples of anti-K19 have been described, one made by a woman (ethnic origin unknown) probably as a result of pregnancy, the other made by a black, multiply-transfused man.
Siblings of patients with anti-K19 should be tested for compatibility, and the patient urged to donate blood for cryogenic storage when his/her clinical state permits.

Reference

[1] Lee, S., 1997. Molecular basis of Kell blood group phenotypes. Vox Sang 73, 1–11.

Km Antigen

Terminology

ISBT symbol (number)	KEL20 (006020 or 6.20)
Obsolete name	K20
History	Reported in 1979. The suffix “m” denotes the association with the McLeod phenotype[1].

Occurrence

All populations	100%

Expression

Cord RBCs	Presumed expressed
Altered	See table showing Comparison of Kell phenotypes on System pages

Effect of enzymes and chemicals on Km antigen on intact RBCs

Ficin/Papain	Resistant
Trypsin	Resistant
DTT 200 mM/50 mM	Not known but sensitive to AET

In vitro characteristics of alloanti-Km

Immunoglobulin class	IgG
Optimal technique	IAT

Clinical significance of alloanti-Km

Transfusion reaction	Delayed/hemolytic in one case[2]
HDFN	Not applicable; anti-Km has been made only by McLeod males

Comments

Anti-Km is made by non-CGD McLeod males. Both McLeod and K_0 phenotype blood will be compatible. Anti-Km+anti-Kx (sometimes called anti-KL) is made by CGD McLeod males, and only McLeod blood will be compatible[3].

References

[1] Marsh, W.L., 1979. Anti-KL. Vox Sang 36, 375.

[2] Marsh, W.L., et al., 1979. Delayed hemolytic transfusion reaction caused by the second example of anti-K19. Transfusion 19, 604–608.

[3] Marsh, W.L., Redman, C.M., 1990. The Kell blood group system: a review. Transfusion 30, 158–167.

Kp^c Antigen

Terminology

ISBT symbol (number)	KEL21 (006021 or 6.21)
Obsolete names	Levay; K21
History	First reported in 1945; joined the Kell System in 1979 when it was shown to be antithetical to Kp^a and Kp^b. Anti-Levay (anti-Kp^c) was the first antibody to a low-prevalence (“private”) antigen found.

Occurrence

Most populations	<0.01%
Japanese	Up to 0.32% (several *Kp*^{c} homozygotes reported)

Antithetical antigens

Kp^a (**KEL3**), Kp^b (**KEL4**)

Expression

Cord RBCs	Expressed
Altered	See table showing Comparison of Kell phenotypes on System pages

Molecular basis associated with Kp^c antigen[1]

Amino acid	Gln281
Nucleotide	A at bp 842 in exon 8 (previously reported as 962)

Effect of enzymes and chemicals on Kp^c antigen on intact RBCs

Ficin/Papain	Resistant
Trypsin	Resistant
DTT 200 mM/50 mM	Sensitive/sensitive (thus sensitive to WARM™ and ZZAP)

In vitro characteristics of alloanti-Kp^c

Immunoglobulin class	IgG; IgM
Optimal technique	IAT; saline RT

Clinical significance of alloanti-Kp^c

No data are available because the antigen and antibody are rare.

Comments

A Japanese Kp(a–b–) blood donor with anti-Kp^b was found to be Levay positive [Kp(c+)].

Reference

[1] Lee, S., et al., 1996. Point mutations characterize *KEL10*, the *KEL3*, *KEL4*, and *KEL21* alleles, and the *KEL17* and *KEL11* alleles. Transfusion 36, 490–494.

K22 Antigen

Terminology

ISBT symbol (number)	KEL22 (006022 or 6.22)
Obsolete names	N.I.; Ikar
History	Described in 1982; given the next number in the series of K–k+ people who made an antibody compatible only with K_0 RBCs.

Occurrence

K22– has been found in only two Iranian Jewish families.

Expression

Cord RBCs	Expressed
Altered	See table showing Comparison of Kell phenotypes on System pages

Molecular basis associated with K22 antigen[1]

Amino acid	Ala322
Nucleotide	C at bp 965 in exon 9 (previously reported as 1085)
K22–	Val322 and T at bp 965

Effect of enzymes and chemicals on K22 antigen on intact RBCs

Ficin/Papain	Resistant
Trypsin	Resistant
α-Chymotrypsin	Resistant (see K [**KEL1**])
DTT 200 mM/50 mM	Sensitive/sensitive (thus sensitive to WARM™ and ZZAP)

In vitro characteristics of alloanti-K22

Immunoglobulin class	IgG
Optimal technique	IAT

Clinical significance of alloanti-K22

Transfusion reaction	No data
HDFN	Mild to severe in one case

Comments

Siblings of patients with anti-K22 should be tested for compatibility, and the patient urged to donate blood for cryogenic storage when his/her clinical state permits.

Reference

[1] Lee, S., 1997. Molecular basis of Kell blood group phenotypes. Vox Sang 73, 1–11.

K23 Antigen

Terminology

ISBT symbol (number)	KEL23 (006023 or 6.23)
Obsolete name	Centauro
History	Reported in 1987; antibody identified in serum of a pregnant woman; assigned to Kell because the serum precipitated Kell glycoprotein from her husband's RBCs.

Occurrence

K23+ has been reported in only one Italian family.

Expression

Cord RBCs	Expressed

Molecular basis associated with K23 antigen[1]

Amino acid	Arg382
Nucleotide	G at bp 1145 in exon 10 (previously reported as 1265)
K23– (wild type)	Gln382 and A at bp 1145

Effect of enzymes and chemicals on K23 antigen on intact RBCs

Ficin/Papain	Resistant
Trypsin	Resistant
DTT 200 mM/50 mM	Sensitive/sensitive (thus sensitive to WARM™ and ZZAP)

In vitro characteristics of alloanti-K23

Immunoglobulin class	IgG
Optimal technique	IAT

Clinical significance of alloanti-K23

Transfusion reaction	No data because antigen and antibody are rare
HDFN	Positive DAT; no clinical HDFN

Reference

[1] Lee, S., 1997. Molecular basis of Kell blood group phenotypes. Vox Sang 73, 1–11.

K24 Antigen

Terminology

ISBT symbol (number)	KEL24 (006024 or 6.24)
Obsolete names	CL; Callais; Cls
History	Described in 1985 when it was shown to be antithetical to K14.

Occurrence

K24+ has been reported in only three French-Cajun families.

Antithetical antigen

K14 (**KEL14**)

Expression

Cord RBCs	Expressed
Altered	See table showing Comparison of Kell phenotypes on System pages

Molecular basis associated with K24 antigen[1]

Amino acid	Pro180
Nucleotide	C at bp 539 in exon 6 (previously reported as 659)

Effect of enzymes and chemicals on K24 antigen on intact RBCs

Ficin/Papain	Resistant
Trypsin	Resistant
α-Chymotrypsin	Presumed resistant (see K [**KEL1**])
DTT 200 mM/50 mM	Sensitive/sensitive (thus sensitive to WARM™ and ZZAP)

In vitro characteristics of alloanti-K24

Immunoglobulin class	IgG
Optimal technique	IAT

Clinical significance of alloanti-K24

Transfusion reaction	No data because only one example of anti-K24 has been reported
HDFN	Positive DAT; no clinical HDFN

Reference

[1] Lee, S., 1997. Molecular basis of Kell blood group phenotypes. Vox Sang 73, 1–11.

VLAN Antigen

Terminology

ISBT symbol (number)	KEL25 (006025 or 6.25)
History	Named in 1996 after the last name of the proband who's RBCs possessed the antigen.

Occurrence

VLAN+ has been reported in only one Dutch family[1].

Antithetical antigen

VONG (**KEL28**)

Expression

Cord RBCs	Presumed expressed

Molecular basis associated with VLAN antigen[2]

Amino acid	Gln248
Nucleotide	A at bp 743 in exon 8 (previously reported as 863)
VLAN– (wild type)	Arg248 and G at bp 743

Effect of enzymes and chemicals on VLAN antigen on intact RBCs

Ficin/Papain	Resistant
Trypsin	Presumed resistant
DTT 200 mM/50 mM	Sensitive/sensitive (thus sensitive to WARM™ and ZZAP)

In vitro characteristics of alloanti-VLAN

Immunoglobulin class	IgG
Optimal technique	IAT

Clinical significance of alloanti-VLAN

No data because only one example of anti-VLAN was found in a serum (named BUS) following an incompatible cross-match[1].

References

[1] Jongerius, J.M., et al., 1996. A new low-incidence antigen in the Kell blood group system: VLAN (KEL25). Vox Sang 71, 43–47.

[2] Lee, S., et al., 2001. Point mutations in KEL exon 8 determine a high incidence (RAZ) and a low incidence (KEL25, VLAN) antigen of the Kell blood group system. Vox Sang 81, 259–263.

TOU Antigen

Terminology

ISBT symbol (number)	KEL26 (006026 or 6.26)
History	Named in 1995 after the last name of the proband whose serum contained an antibody to a high-prevalence antigen; provisional assignment to Kell System ratified in 1998.

Occurrence

TOU– has been reported in only two families, one Native American and one Hispanic[1].

Expression

Cord RBCs	Presumed expressed
Altered	See table showing Comparison of Kell phenotypes on System pages

Molecular basis associated with TOU antigen[2]

Amino acid	Arg406
Nucleotide	G at bp 1217 in exon 11 (previously reported as 1337)
TOU–	Gln406 and A at bp 1217

Effect of enzymes and chemicals on TOU antigen on intact RBCs

Ficin/Papain	Resistant
Trypsin	Resistant
DTT 200 mM/50 mM	Sensitive/sensitive (thus sensitive to WARM™ and ZZAP)

In vitro characteristics of alloanti-TOU

Immunoglobulin class	IgG
Optimal technique	IAT

Clinical significance of alloanti-TOU

No data because only two examples of anti-TOU have been reported.

Comments

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

References

[1] Jones, J., et al., 1995. A novel common Kell antigen, TOU, and its spatial relationship to other Kell antigens. Vox Sang 69, 53–60.

[2] Lee, S., 1997. Molecular basis of Kell blood group phenotypes. Vox Sang 73, 1–11.

RAZ Antigen

Terminology

ISBT symbol (number)	KEL27 (006027 or 6.27)
History	Named in 1994 after the proband whose serum contained an antibody to a high-prevalence antigen; provisional Kell System assignment ratified in 2002.

Occurrence

RAZ– has been found in only one Indian family (from Gujarat)[1].

Expression

Cord RBCs	Presumed expressed
Altered	See table showing Comparison of Kell phenotypes on System pages

Molecular basis associated with RAZ antigen[2]

Amino acid	Glu249
Nucleotide	G at bp 745 in exon 8 (previously reported as 865)
K27–	Lys249 and A at bp 745

Effect of enzymes and chemicals on RAZ antigen on intact RBCs

Ficin/Papain	Resistant
Trypsin	Resistant
α-Chymotrypsin	Weakened
DTT 200 mM/50 mM	Sensitive/sensitive (thus sensitive to WARM™ and ZZAP)

In vitro characteristics of alloanti-RAZ

Immunoglobulin class	IgG
Optimal technique	IAT

Clinical significance of alloanti-RAZ

No data because only one example of anti-RAZ has been reported.

Comments

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

References

[1] Daniels, G.L., et al., 1994. Demonstration by the monoclonal antibody-specific immobilization of erythrocyte antigens assay that a new red cell antigen belongs to the Kell blood group system. Transfusion 34, 818–820.

[2] Lee, S., et al., 2001. Point mutations in KEL exon 8 determine a high incidence (RAZ) and a low incidence (KEL25, VLAN) antigen of the Kell blood group system. Vox Sang 81, 259–263.

VONG Antigen

Terminology

ISBT symbol (number)	KEL28 (006028 or 6.28)
History	Described in 2003 and named after the VONG+ proband's name.

Occurrence

VONG+ has been reported in only one Chinese family from Timor.

Antithetical antigen

VLAN (**KEL25**)

Molecular basis associated with VONG antigen[1]

Amino acid	Trp248
Nucleotide	T at bp 742 in exon 8 (previously reported as 862)
VONG– (wild type)	Arg248 and C at bp 742

Effect of enzymes and chemicals on VONG antigen on intact RBCs[1]

Ficin/Papain	Resistant
Trypsin	Resistant
α-Chymotrypsin	Resistant (see K [**KEL1**])
DTT 200 mM/50 mM	Sensitive/sensitive (thus sensitive to WARM™ and ZZAP)

In vitro characteristics of alloanti-VONG

Immunoglobulin class	IgG
Optimal technique	IAT

Clinical significance of alloanti-VONG

Transfusion reaction	No data, only one example of anti-VONG has been described
HDFN	Mild[1]

Reference

[1] Grey, D., et al., 2003. Haemolytic disease of the newborn caused by a new Kell antigen [abstract]. Transfus Med 13 (Suppl. 1), 30.

KALT Antigen

Terminology

ISBT symbol (number)	KEL29 (006029 or 6.29)
History	Named in 2006, "K" for the System and "ALT" from the KALT– proband's name.

Occurrence

Only one KALT– proband, a Mexican woman with a history of pregnancy, and her KALT– sister have been reported.

Molecular basis associated with KALT antigen[1]

Amino acid	Arg623
Nucleotide	G at bp 1868 in exon 17 (previously reported as 1988)
KALT–	Lys623 and A at bp 1868

Effect of enzymes and chemicals on KALT antigen on intact RBCs

Ficin/Papain	Resistant
Trypsin	Sensitive (see Comments below)
α-Chymotrypsin	Resistant
DTT 200 mM/50 mM	Sensitive/sensitive (thus sensitive to WARM™ and ZZAP)

In vitro characteristics of alloanti-KALT

Immunoglobulin class	IgG
Optimal technique	IAT

Clinical significance of alloanti-KALT

Transfusion reaction	No data because only one anti-KALT has been described
HDFN	Positive DAT but no clinical HDFN

Comments

The KALT antigen is currently the only Kell antigen that is sensitive to trypsin treatment of intact RBCs. Anti-KALT recognizes the presence of Arg623, which is located on the C-terminal side of the catalytic domain of the Kell glycoprotein.
Siblings of patients with anti-KALT should be tested for compatibility, and the patient urged to donate blood for cryogenic storage when his/her clinical state permits.

Reference

[1] Lee, S., et al., 2006. Molecular basis of two novel high prevalence antigens in the Kell blood group system, KALT and KTIM. Transfusion 46, 1323–1327.

KTIM Antigen

Terminology

ISBT symbol (number)	KEL30 (006030 or 6.30)
History	Named in 2006, "K" from the System name and "TIM" from the KTIM– proband's name.

Occurrence

Only one KTIM– proband, a White American woman with a history of transfusion and pregnancy, has been described.

Molecular basis associated with KTIM antigen[1]

Amino acid	Asp305
Nucleotide	G at bp 913 in exon 8 (previously reported as 1033)
KTIM–	Asn305 and A at bp 913

Effect of enzymes and chemicals on KTIM antigen on intact RBCs

Ficin/Papain	Resistant
Trypsin	Resistant
α-Chymotrypsin	Resistant (see K [**KEL1**])
DTT 200 mM/50 mM	Sensitive/sensitive (thus sensitive to WARM™ and ZZAP)

In vitro characteristics of alloanti-KTIM

Immunoglobulin class	IgG
Optimal technique	IAT

Clinical significance of alloanti-KTIM

No data have been described.

Comments

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

Reference

[1] Lee, S., et al., 2006. Molecular basis of two novel high prevalence antigens in the Kell blood group system, KALT and KTIM. Transfusion 46, 1323–1327.

KYO Antigen

Terminology

ISBT symbol (number)	KEL31 (006031 or 6.31)
History	Named in 2006; "K" for the System and "YO" from the KYO+ proband's name

Occurrence

Most populations	<0.1%
Japanese	1.5%

Molecular basis associated with KYO antigen[1]

Amino acid	Gln292
Nucleotide	A at bp 875 in exon 8 (previously reported as 995)
KYO– (wild type)	Arg292 and G at bp 875

Effect of enzymes and chemicals on KYO antigen on intact RBCs

Ficin/Papain	Resistant
Trypsin	Resistant
DTT 200 mM/50 mM	Sensitive/sensitive (thus sensitive to WARM™ and ZZAP)

In vitro characteristics of alloanti-KYO

Immunoglobulin class	IgG
Optimal technique	IAT

Clinical significance of alloanti-KYO

No data because anti-KYO is rare.

Reference

[1] Uchikawa, M., et al., 2006. Molecular basis for a novel low-frequency antigen in the Kell blood group system, KYO [abstract]. Vox Sang 91 (Suppl. 3), 136.

KUCI Antigen

Terminology

ISBT symbol (number)	KEL32 (006032 or 6.32)
History	Named in 2007, "K" for the System and "UCI" from the name of the KUCI– proband.

Occurrence

KUCI– has been found in only one American Indian family.

Molecular basis associated with KUCI antigen[1]

Amino acid	Ala424
Nucleotide	C at bp 1271 in exon 11 (previously reported as 1391)
KUCI–	Val424 and T at bp 1271

Effect of enzymes and chemicals on KUCI antigen on intact RBCs

Ficin/Papain	Resistant
Trypsin	Resistant
α-Chymotrypsin	Resistant (see K [**KEL1**])
DTT 200 mM/50 mM	Sensitive/sensitive (thus sensitive to WARM™ and ZZAP)

In vitro characteristics of alloanti-KUCI

Immunoglobulin class	IgG
Optimal technique	IAT

Clinical significance of alloanti-KUCI

No data because only one example of anti-KUCI has been described.

Comments

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

KUCI– RBCs were non-reactive with plasma from the KANT– proband [see KANT (**KEL33**)].

Reference

[1] Velliquette, R.W., et al., 2007. Two novel and related high-prevalence antigens in the Kell blood group system [abstract]. Transfusion 47 (Suppl.), 164A–165A.

KANT Antigen

Terminology

ISBT symbol (number)	KEL33 (006033 or 6.33)
History	Named in 2007, "K" for the System and "ANT" from the KANT– proband's name.

Occurrence

KANT– has been found in only one French proband.

Molecular basis associated with KANT antigen[1]

Amino acid	Arg428
Nucleotide	G at bp 1283 in exon 11 (previously 1403)
KANT–	Leu428 and T at bp 1283

Effect of enzymes and chemicals on KANT antigen on intact RBCs

Ficin/Papain	Resistant
Trypsin	Resistant
α-Chymotrypsin	Resistant (see K [**KEL1**])
DTT 200 mM/50 mM	Sensitive/sensitive (thus sensitive to WARM™ and ZZAP)

In vitro characteristics of alloanti-KANT

Immunoglobulin class	IgG
Optimal technique	IAT

Clinical significance of alloanti-KANT

No data because only one example of anti-KANT has been described.

Comments

KUCI– RBCs were non-reactive with anti-KANT, whereas KANT– RBCs reacted very weakly with anti-KUCI. The change in the KANT– proband is predicted to be just four amino acids from that found in the KUCI– proband; this may provide an explanation for partial serological compatibility between the KUCI– and KANT– probands. KANT– RBCs express K11 weakly and KETI very weakly [see KETI (**KEL36**)].

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

Reference

[1] Velliquette, R.W., et al., 2007. Two novel and related high-prevalence antigens in the Kell blood group system [abstract]. Transfusion 47 (Suppl.), 164A–165A.

KASH Antigen

Terminology

ISBT symbol (number)	KEL34 (006034 or 6.34)
History	Named in 2010, "K" for the System and "ASH" from the KASH– proband's name.

Occurrence

Only one KASH– proband and her KASH– brother have been reported.

Molecular basis associated with KASH antigen[1]

Amino acid	253Tyr
Nucleotide	A at bp 758 in exon 8
KASH–	Cys253 and G at bp 758

Effect of enzymes and chemicals on KASH antigen on intact RBCs

Ficin/Papain	Resistant
Trypsin	Resistant
DTT 200 mM/50 mM	Sensitive/sensitive (thus sensitive to WARM™ and ZZAP)

In vitro characteristics of alloanti-KASH

Immunoglobulin class	IgG
Optimal technique	IAT

Clinical significance of alloanti-KASH

No data, because only one example of anti-KASH has been described. The antibody maker had a history of pregnancy but no transfusions.

Comments

Lack of the KEL34 epitope prevents normal expression of the Kell antigens, and gives rise to a K_{mod} phenotype: the RBCs of the KASH– proband and those of her KASH– brother gave extremely weak reactions with some antibodies to high

prevalence Kell antigens, and were negative with the majority of them, but their cells absorbed and eluted anti-k and anti-Kp^b.

Reference

[1] Karamatic Crew, V., et al., 2010. KASH (KEL34): a novel high incidence antigen in the Kell blood group system [abstract]. Vox Sang 99 (Suppl. 1), 357.

KELP Antigen

Terminology

ISBT symbol (number)	KEL35 (006035 or 6.35)
History	Named in 2010, "KE" from the System, "L" for leucine and "P" for the first letter of phenylalanine.

Occurrence

Only one KELP– proband has been reported.

Molecular basis associated with KELP antigen[1]

Amino acid	Leu260 and Arg675
Nucleotide	G at bp 780 in exon 8 and G at bp 2024 in exon 18
KELP–	Phe260 and Gln675, with T at bp 780 and A at bp 2024

Effect of enzymes and chemicals on KELP antigen on intact RBCs

Ficin/Papain	Resistant
Trypsin	Resistant
DTT 200 mM/50 mM	Sensitive/sensitive (thus sensitive to WARM™ and ZZAP)

In vitro characteristics of alloanti-KELP

Immunoglobulin class	IgG
Optimal technique	IAT

Clinical significance of alloanti-KELP

No data, because only one example of anti-KELP in a pregnant woman has been described.

Comments

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

RBCs from the KELP– proband typed K12–, although DNA sequence analysis predicted the K12+ phenotype.

Reference

[1] Karamatic Crew, V., et al., 2010. KELP (KEL35): a new high incidence antigen in the Kell blood group defined by two homozygous missense mutations in KEL [abstract]. Transfus Med 20 (Suppl. 1), 30.

KETI Antigen

Terminology

ISBT symbol (number)	KEL36 (006036 or 6.36)
History	Named in 2011, "KE" from the System, "T" for Thr and "I" for Ile.

Occurrence

KETI– has been found in only a few European families.

Molecular basis associated with KETI antigen[1]

Amino acid	Thr464
Nucleotide	C at bp 1391 in exon 12
KETI–	Ile464 and T at bp 1391

Effect of enzymes and chemicals on KETI antigen on intact RBCs

Ficin/Papain	Resistant
Trypsin	Resistant
α-Chymotrypsin	Resistant
DTT 200 mM/50 mM	Sensitive/sensitive (thus sensitive to WARM™ and ZZAP)

In vitro characteristics of alloanti-KETI

Immunoglobulin class	IgG
Optimal technique	IAT

Clinical significance of alloanti-KETI

No data because anti-KETI is rare.

Comments

An example of KASH– RBCs was found to be compatible with the anti-KETI[1].
KETI– RBCs are K11+/− and KUCI+, KANT+.

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

Reference

[1] Karamatic Crew, V., et al., 2011. KETI, a novel high incidence antigen in the Kell blood group system: a serological and molecular study [abstract]. Vox Sang 101 (Suppl. 1), 19.

KHUL Antigen

Terminology

ISBT symbol (number)	KEL37 (006037 or 6.37)
History	Named in 2011, "K" from the System and "HUL" from the KHUL– proband's name.

Occurrence

KHUL– has been found in only one Asian proband and her sister.

Molecular basis associated with KHUL antigen[1]

Amino acid	Arg293
Nucleotide	C at bp 877 in exon 8
KHUL–	Trp293 and T at bp 877

Effect of enzymes and chemicals on KHUL antigen on intact RBCs

Ficin/Papain	Resistant
Trypsin	Resistant
α-Chymotrypsin	Resistant
DTT 200 mM/50 mM	Sensitive/sensitive (thus sensitive to WARM™ and ZZAP)

In vitro characteristics of alloanti-KHUL

Immunoglobulin class	IgG
Optimal technique	IAT

Clinical significance of alloanti-KHUL

No data because anti-KHUL is rare.

Comments

KHUL is, surprisingly, independent of the low-prevalence antigen, KYO, which is associated with the adjacent amino acid, Arg292Gln.

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

Reference

[1] Vege, S., et al., 2011. A new high prevalence antigen (KHUL) in the Kell blood group system [abstract]. Transfusion 51 (Suppl.), 25A–26A.