Names for KN (ISBT 022) Blood Group Alleles

Intro

General Description	The Knops blood group system consists of 9 antigens carried on a glycoprotein of **2039** amino acids and called the Complement Receptor I (CR1). It has a leader sequence of 41 to 46 amino acids, depending on translation initiation site, which is cleaved from the membrane protein. The coding sequence starts at nucleotide 28. The Helg**e**son phenotype, initially thought to be a KN serologic null, may be more likely the result of lower-level CR1 density and may also involve lack of a high-prevalence KN antigen [Pham Transfusion 2010 50(7):1435-43].
General Description (from GeneCards)	*CR1* (Complement C3b/C4b Receptor 1 (Knops Blood Group)) is a **p**rotein **c**oding gene **that is a member of the receptors of complement activiation (RCA) family and is located in the "cluster RCA" region of chromosome 1.** Diseases associated with *CR1* include **m**alaria and Plasmodium **f**alciparum **m**alaria. Among its related pathways are **immune response, lectin-induced complement pathway and innate immune system**. Gene Ontology (GO) annotations related to this gene include complement component C3b binding and complement component C4b receptor activity. An important paralog of this gene is *CR1L* .
Gene name:	*CR1* (aliases CD35, KN, C3BR, C4BR)
RefGene Name	LRG_814
Number of exons:	39
Initiation codon:	beginning of exon 1
Stop codon:	end of exon 38
Entrez Gene ID:	1378
LRG sequence:	NG_007481.1 (genomic) NM_000573.3 (transcript)
Reference allele *KN*01* encodes:	KN1, KN3, KN4, KN5, KN8, KN9, KN11 Acceptable: *KN*A* , or Kn^a if inferred by haemagglutination
Antithetical antigens:	[KN1 KN2]; [KN3 KN6]; [KN4 KN7]; [KN9 KN10]; [KN11 KN12]
Comment:	The antithetical KN antigens KN9/KN10 (KCAM/KDAS) and KN 11/12 (DACY/YCAD) are adding additional polymorphism to almost all *KN** alleles known so far and listed in the Allele Table.

Phenotype	Allele name	Nucleotide change	Exon Intron	Predicted amino acid change	(Reference No.) PMID	Accession number	rs number
KN:1 or Kn(a+) KN:3 or McC(a+) KN:4 or Sl1+ KN:5 or Yk(a+) KN:8 or Sl3+ KN:9 or KCAM+ KN:11 or DACY+	***KN*01* or *KN*A***	c.4681G c.4768A c.4801A c.4223C c.4828T c.4843A c.3623A	29 29 29 26 29 29 22	p.Val1561 p.Lys1590 p.Arg1601 p.Thr1408Met p.Ser1610 p.Ile1615 p.His1208		n.a.	n.a.
KN:2 or Kn(a-b+)	***KN*02* or *KN*B***	c.4681G>A	29	p.Val1561Met	PMID: 14962306	n.a.	rs41274768
KN:2 or Kn(a-b+) KN:-9 or KCAM- KN:10 or KDAS+	***KN*02.10***	c.4681G>A c.4843A>G	29 29	p.Val1561Met p.Ile1615Val	PMID: 14962306 PMID: 32870515	n.a.	rs41274768 rs6691117
KN:–5 or Yk(a–)	***KN*01.-05***	c.4223C>T	26	p.Thr1408Met	PMID: 21214579	n.a.	rs3737002
KN:-4 or Sl1- KN:-3,6 or McC(a-b+) KN:7 or Vil+ KN:-9 or KCAM- KN:10 or KDAS+	***KN*01.06***	c.4768A>G c.4801A>G c.4843A>G	29 29 29	p.Lys1590Glu p.Arg1601Gly p.Ile1615Val	PMID: 11313284 PMID: 32870515	n.a.	rs17047660 rs17047661 rs6691117
KN:7 or Vil+ KN:-9 or KCAM- KN:10 or KDAS+	***KN*01.07***	c.4801A>G c.4843A>G	29 29	p.Arg1601Gly p.Ile1615Val	(1), Abstract PMID: 6865671	n.a.	rs17047661 rs6691117
KN:–8 or Sl3–	***KN*01.-08***	c.4828T>A	29	p.Ser1610Thr	PMID: 11896343	n.a.	rs4844609
KN:-9 or KCAM- KN:10 or KDAS+	***KN*01.10***	c.4843A>G	29	p.Ile1615Val	(2), Abstract PMID: 32589271	n.a.	rs6691117
KN:-11 or DACY- KN:12 or YCAD+	***KN*01.12***	c.3623A>G	22	p.His1208Arg	PMID: 32870515	n.a.	rs2274567
KN:-13 or KNMB-	***KN*01.-13***	c.3290T>C c.3298A>G	21	p.Leu1097Pro p.Arg1100Gly	(3), Abstract		rs200111726 rs202070239
Helgeson Phenotype	***KN*01W***	c.488-2599T>C	IVS4	abolished GATA-1 site	PMID: 37591894		rs11117991

Note: Nucleotides are numbered from the initiation codon, so numbering will differ from publications prior to 2012 by –27 nucleotides.

‡ KN:4 was listed in older literature with the alias Sl^a or S1 and KN:7 with the alias Sl2.

† Arg1601 and Ser1610 are required for KN:8 (Sl3) expression

All *KN*01.06* alleles known so far are KDAS (KN10) positive and KCAM (KN9) negative and express almost exclusively DACY (KN11). PMID: 32870515

Almost all *KN*01.05* alleles known so far are KCAM positive (KN9) and KDAS (KN10) negative and express almost exclusively DACY (KN11). PMID: 32870515

The *KN*01.07* known so far usually express KDAS (KN10) and are DACY (KN11) positive. PMID: 32870515

The *KN*01.10* known so far usually express KDAS (KN10) and are YCAD (KN12) positive. PMID: 32870515. **See above. The allele is found without KN10**

References

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Abstract (1) Lacey P, Laird-Fryer B, Block U, Lar J, Guilbeau L and JJ Moulds. A New High Incidence Blood Group Factor, Sla and its hyothetical allele. Transfusion 1980 20(5):632.

PMID 6865671 Molthan L. The status of the Mccoy/Knops antigens. Med Lab Sci. 1983 Jan;40(1):59-63.

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Abstract (2) Moulds JM, Pierce S, Peck KB, Tulley ML, Doumbo O, JJ Moulds. KCAM: A New Allele in the Knops Blood Group System. Transfusion 2005 45(S3): 27A.

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PMID 37591894 Wu PC, Lee YQ, Möller M, Storry J, ML Olsson. Elucidation of the low-expressing erythroid CR1 phenotype by bioinformatic mining of the GATA1-driven blood-group regulome. Nature Communications 2023;14:5001.

Abstract (3) E Scharberg, S Seyboth, J Küthe-Rieger, N Kömürcü, A Stürtzel, E Weinig, D Grüger, C Schneeweiss, C Weinstock, G Rink, P Bugert. A New Knops Antigen Located on the Long Homologous Repeat C. Vox Sanguinis. 2023;118(Suppl. 1):23.

Abstract (4) P Wu, E McGowan, M Möller, Y Lee, J Storry, M Olsson. Elucidating the blood group regulome. Vox Sanguinis. 2023;118(Suppl. 1):64.

Track of changes

			from	to
1	**Version**		**v4.1 31-JUL-2023**	**v4.2 30-JUN-2024**
2	Author	created	Margaret Keller, July 2023	Margaret Keller, May 2024
3	Review	reviewed	Christoph Gassner, July 2023	Jill Storry, Gloria Wu, June 2024
4	Intro	added		KN5 was added to reference allele. Helgeson phenotype is described.
5	Allele Table	Nucleotide additions		KN c.4223C and c.3623A added to *KN*01* reference allele. Added KN:11 to reference allele.
6	Allele Table	Nucleotide correction		*KN*02* c.4681 variant corrected to G>A.
7	Allele Table	Allele changed		*KN*02.10* updated to show loss of KN9; c.4681 variant corrected to G>A
8	Allele Table	Allele changed		*KN*01.06* updated to show loss of KN4 and KN9; Added KN:-3,6 to phenotype
9	Allele Table	Allele changed		*KN*01.07,* added KN:10 or KDAS+, KN:11 or DACY+
10	Allele Table	Allele changed		*KN*01.10,* added KN:-9 or KCAM-
11	Allele Table	Allele changed		*KN*01.12,* added KN:-11 or DACY-
12	Allele Table	Alleles added		*KN*01.-13* added KN:-13 or KNMB-
13	Allele Table	Alleles added		*KN*01W* allele added
14	Tab Sheet	Removed "Proposal and AG per Allele" tab		Proposal and AG per Allele removed until after Nomenclature Decision by WP
15	**End Version**		**v4.1 31-JUL-2023**	**v4.2 30-JUN-2024**

Track of changes

			from	to
1	**Version**		**v4.0 31-MAR-2022**	**v4.1 31-JUL-2023**
2	Author	created	Margaret Keller, March 2022	Margaret Keller, July 2023
3	Review	reviewed	Christoph Gassner, March 2022	Christoph Gassner, July 2023
4	Intro	added		KN5
5	Allele Table	Nucleotide changed		*KN*02 or KN*B* , c.4681G>A
6	Allele Table	Allele changed		*KN*01.06,* added KN:9 or KCAM+
7	Allele Table	Allele changed		*KN*01.07,* added KN:10 or KDAS+, KN:11 or DACY+
8	Allele Table	Allele changed		*KN*01.10,* added KN:12 or YCAD+
9	Allele Table	Alleles added		KN*01.-13 added KN:-13 or KNMB-
10	**End Version**		**v4.0 31-MAR-2022**	**v4.1 31-JUL-2023**

Track of changes

			from	to
1	**Version**		**v3.0 160903**	**v4.0 31-MAR-2022**
2	Author	created	Joanne Moulds, 2016	Margaret Keller, March 2022
3	Review	reviewed	n.a.	Christoph Gassner, March 2022
4	General	Formatting		Updated to newest project-2-excel format with addition of columns for rs number, PMID. Added tab with reference details.
5	Allele Table	Allele removed		In the allele table, entries KN:–9 or KCAM–, *KN*01.–09* will become obsolete and be replaced by KN:10, KDAS, *KN*01.10* , defined by the SNV c.4843A>G (rs 6691117). KDAS (=KCAM-) is antithetical to KCAM.
6	Allele Table	Allele		Allele KN:10 and KDAS added as antithetical to KCAM based on PMID 32589271.
7	Allele Table	Allele		Allele KN:12 and DACY/YCAD added as antithetical pair, based on PMID 32870515.
8	Allele Table	negative signs		Continued use of negative signs according to genomics meetings and reviewer Christoph Gassner
9	References	numbering changed		References numbering changed and additional references (PMID 32589271 and 32870515) added
10	Tab sheet	Tab sheet added		Tab sheet 'Proposal & AG per Allele' added.
11	**End Version**		**v3.0 160903**	**v4.0 31-MAR-2022**