Kx Blood Group System

Number of antigens 1

High prevalence	Kx

Terminology

ISBT symbol (number)	XK (019)
History	Named in 1990 when the Kx antigen was assigned system status. XK was used as the ISBT symbol after the gene name.

Expression

Tissues	Fetal liver, adult skeletal muscle, brain, pancreas, heart, low levels in adult liver, kidney, spleen

Gene

Chromosome	Xp21.1
Name	*XK*
Organization	3 exons; sizes of introns have not been determined
Product	Xk protein

Database accession numbers

GenBank	NM_021083 (mRNA); Z32684 (gene)
Entrez Gene ID	7504

Molecular bases of silencing of *XK* (McLeod phenotype)

Homozygosity or compound heterozygosity leads to the Kx– phenotype (McLeod phenotype). Reference allele *XK*01* (Accession number

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NM_021083) encodes XK1 (Kx). Nucleotide differences from reference allele, and amino acids affected, are given.

Allele name	Exon (intron)	Nucleotide change†	Amino acid change	Ethnicity (prevalence)
*XK*01N.01*	1–3	Deletion of gene	del exons 1–3	(Rare)
*XK*01N.02*	1	del exon 1	del exon 1	(Rare)
*XK*01N.03*	1	del promoter + exon 1	del exon 1	(Rare)
*XK*01N.04*	2	del exon 2	del 82–170	(Rare)
*XK*01N.05*	3	del intron 2 & exon 3	del 170–444	(Rare)
*XK*01N.06*	1	−272_119del	del 1–40fs	(Rare)
*XK*01N.07*	1	172delG	Val58fs+Leu129X	(Rare)
*XK*01N.08*	2	269delA	Tyr90fs	(Rare)
*XK*01N.09*	2	268delT	Tyr90fs	(Rare)
*XK*01N.10*	2	451insC	Pro150fs	(Rare)
*XK*01N.11*	3	686_687delTT	Phe229fs+Pro264X	(Rare)
*XK*01N.12*	3	771delG	Trp257fs+Ile267X	(Rare)
*XK*01N.13*	3	856_860delCTCTA	Leu286fs+Lys301X	(Rare)
*XK*01N.14*	3	938_951del	Asn313fs+Tyr336X	(Rare)
*XK*01N.15*	3	1013delT	Phe338fs+Ile408X	Japanese (Rare)
*XK*01N.16*	1	107G>A	Trp36X	(Rare)
*XK*01N.17*	2	397C>T	Arg133X	(Rare)
*XK*01N.18*	2	463C>T	Gln155X	(Rare)
*XK*01N.19*	3	707G>A	Trp236X	(Rare)
*XK*01N.20*	3	895C>T	Gln299X	(Rare)
*XK*01N.21*	3	941G>A	Trp314X	(Rare)
*XK*01N.22*	Intron 1	IVS1+1g>c	Alternative splicing	(Rare)
*XK*01N.23*	Intron 1	IVS1–1g>a	Alternative splicing	(Rare)
*XK*01N.24*	Intron 2	IVS2+1g>a	Alternative splicing	(Rare)
*XK*01N.25*	Intron 2	IVS2+5g>a	Alternative splicing	(Rare)
*XK*01N.26*	Intron 2	IVS2−1g>a	Alternative splicing	(Rare)
*XK*01N.27*	3	664C>G	Arg222Gly	(Rare)
*XK*01N.28*	3	880T>C	Cys294Arg	(Rare)
*XK*01N.29*	3	979G>A	Glu327Lys	(Rare)
*XK*01N.30*	2	452insC	151fs	Japanese (Rare)

†Nucleotide 1 is the first nucleotide of the translation-initiation codon, which is 82 bp downstream of the first nucleotide in earlier reports.

Amino acid sequence[1]

Note: the amino acid residues 204 and 205 listed here are the corrected data from those that are in GenBank accession number Z32684.

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MKFPASVLAS  VFLFVAETTA  ALSLSSTYRS  GGDRMWQALT  LLFSLLPCAL   50
VQLTLLFVHR  DLSRDRPLVL  LLHLLQLGPL  FRCFEVFCIY  FQSGNNEEPY  100
VSITKKRQMP  KNGLSEEIEK  EVGQAEGKLI  THRSAFSRAS  VIQAFLGSAP  150
QLTLQLYISV  MQQDVTVGRS  LLMTISLLSI  VYGALRCNIL  AIKIKYDEYE  200
VKVKPLAYVC  IFLWRSFEIA  TRVVVLVLFT  SVLKTWVVVI  ILINFFSFFL  250
YPWILFWCSG  SPFPENIEKA  LSRVGTTIVL  CFLTLLYTGI  NMFCWSAVQL  300
KIDSPDLISK  SHNWYQLLVY  YMIRFIENAI  LLLLWYLFKT  DIYMYVCAPL  350
LVLQLLIGYC  TAILFMLVFY  QFFHPCKKLF  SSSVSEGFQR  WLRCFCWACR  400
QQKPCEPIGK  EDLQSSRDRD  ETPSSSKTSP  EPGQFLNAED  LCSA       444
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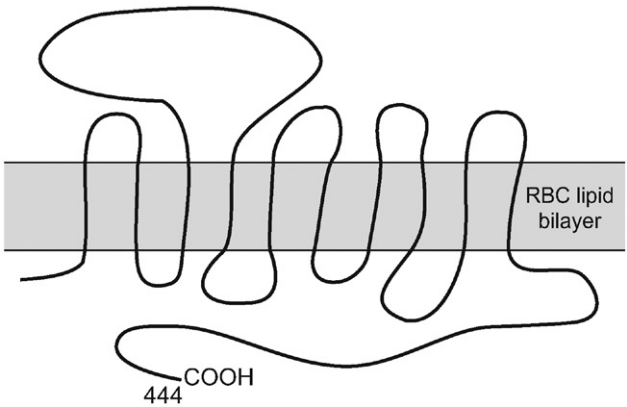
Carrier molecule[1]

A multipass membrane protein.



In the RBC membrane, XK protein is covalently linked at Cys72 to Cys347 of the Kell glycoprotein.

M_r (SDS-PAGE)	37,000
Glycosylation	None
Cysteine residues	16
Copies per RBC	1,000

Function

Not known, but XK has structural characteristics of a membrane transport protein, and a homolog, ced-8, is involved in regulating cell death in *C. elegans*[2]. Involved in maintenance of normal cell membrane integrity.

Disease association

Absence of XK protein is associated with acanthocytosis and the McLeod syndrome, which manifests a compensated hemolytic anemia, elevated serum creatinine kinase, and neuromuscular disorders including chorea, areflexia, skeletal muscle atrophy, and cardiomyopathy[3,4].
Some males with the McLeod phenotype have X-linked CGD.

Phenotypes

Null	McLeod (RBCs express Kell antigens weakly)
Unusual	Kx antigen has an increased expression on RBCs that lack or have a reduced expression of Kell antigens; see tables in Kell blood group system section

Comments

Very weak expression of Kx antigen (resembling a McLeod phenotype) together with extreme depression of Kell system antigens on the RBCs of a German proband were caused by the simultaneous presence of a single base change in the donor splice site of *XK*, and homozygosity for *KEL*02.03* (Kp^a at the *KEL* locus)[5].

References

[1] Ho, M., et al., 1994. Isolation of the gene for McLeod syndrome that encodes a novel membrane transport protein. Cell 77, 869–880.

[2] Stanfield, G.M., Horvitz, H.R., 2001. The ced-8 gene controls the timing of programmed cell deaths in *C. elegans*. Mol Cell 5, 423–433.

[3] Danek, A., et al., 2001. McLeod neuroacanthocytosis: genotype and phenotype. Ann Neurol 50, 755–764.

[4] Lee, S., et al., 2000. The Kell blood group system:Kell and XK membrane proteins. Semin Hematol 37, 113–121.

[5] Daniels, G.L., et al., 1996. A combination of the effects of rare genotypes at the *XK* and *KEL* blood group loci results in absence of Kell system antigens from the red blood cells. Blood 88, 4045–4050.

Kx Antigen

Terminology

ISBT symbol (number)	XK1 (019001 or 19.1)
Obsolete names	006015; K15
History	Named in 1975 when Kx was shown to be associated with the Kell blood group system, but controlled by a gene on the X chromosome.

Occurrence

All populations	100%

Expression

Cord RBCs	Expressed
Altered	Weak on RBCs of common Kell phenotype Expression of Kx antigen is enhanced on RBCs with reduced expression of Kell [K_0, K_{mod}, thiol-treated RBCs, Kp(a+b–)], even though levels of XK protein may be reduced[1]

Molecular basis associated with Kx antigen

For molecular basis associated with a lack of Kx antigen, see table in System pages.

Effect of enzymes and chemicals on Kx antigen on intact RBCs

Ficin/Papain	Resistant
Trypsin	Resistant
α-Chymotrypsin	Resistant
DTT 200 mM	Resistant (enhanced)

In vitro characteristics of alloanti-Kx

Immunoglobulin class	IgG
Optimal technique	IAT

Clinical significance of alloanti-Kx

Transfusion reaction	Mild/delayed

Autoanti-Kx

One example reported in a man with common Kell phenotype.

Comments

Anti-Km is made by non-CGD McLeod males; both McLeod and K_0 blood will be compatible.
Anti-Kx+anti-Km (sometimes called anti-KL) is made by males with the McLeod phenotype and CGD; only McLeod blood will be compatible.
Anti-Kx has been made by one non-CGD McLeod male[2].
Anti-Kx can be prepared by adsorption of anti-Kx+anti-Km (anti-KL) onto, and elution from, K_0 RBCs.

XK is subject to X chromosome inactivation, and female carriers of alleles that encode CGD have a mixed population of normal and acanthocytic RBCs. The range has been as much as 99%, and as few as 1% McLeod RBCs.

References

[1] Lee, S., et al., 2000. The Kell blood group system: Kell and XK membrane proteins. Semin Hematol 37, 113–121.

[2] Russo, D.C., et al., 2000. First example of anti-Kx in a person with McLeod phenotype and without chronic granulomatous disease. Transfusion 40, 1371–1375.