Names for Kx (ISBT 019) Blood Group Alleles

General description: The Kx blood group system contains one antigen carried on a multipass protein of 444 amino acids, which is linked to the Kell glycoprotein through a disulphide bond.
Gene name: *XK*
Gene label: *XK* (for use in allele names)
Number of exons: 3
Initiation codon: Within exon 1
Stop codon: Within exon 3
Genbank: Z32684
Entrez Gene ID: 7504
LRG sequence: NG_007473.2 (genomic)
NM_021083.3 (transcript)
NP_066569.1 (protein)
LRG_812 (LRG identifier)
Reference allele: *XK*01* (shaded)

Reference allele *XK*01* encodes Kx+

Phenotype	Allele name	Nucleotide change	Exon	Predicted amino acid change	dbSNP rs number	Authors and PubMed ID
XK:1 or Kx+	*XK*01*					Ho et al. PMID 8004674
Null phenotypes						
XK:-1 kx-	XK*N.01	Deletion of XK gene	1 -3			Multiple authors – see XK*N.01 series
XK:-1 kx-	XK*N.02	Del exon 1	1	del AA 1 to 82		Danek et al. PMID 11761473
XK:-1 kx-	XK*N.03	Del promoter + exon 1	1	del AA 1 - 82		Wendel et al. PMID 15504163
XK:-1 kx-	XK*N.04	Del exon 2	2	Del AA 82 to 170		Singleton et al. PMID 12899725

Phenotype	Allele name	Nucleotide change	Exon	Predicted amino acid change	dbSNP rs number	Authors and PubMed ID
XK:-1 kx-	XK*N.05	del intron 2 + exon 3	3	del AA 170 - 444		
XK:-1 kx-	XK*N.06	del -272 to 119	1 + 2	del 1 to 40 + fs 45X		
XK:-1 kx-	XK*N.07	172delG	1 + 2	V58Y + fs 129X		Zeman et al. PMID 16314760
XK:-1 kx-	XK*N.08	269delA	2	Y90S + fs 129X		
XK:-1 kx-	XK*N.09	268delT	2	Y90T + fs 129X		Ho et al. PMID 8619554
XK:-1 kx-	XK*N.10	450-451 insC	2 + 3	Q151P + fs 198X		Ueyama et al. PMID 10930599, Starling et al. PMID 16344536
XK:-1 kx-	XK*N.11	686+687delTT	3	F229Y + fs 264X		Danek et al. PMID 11761473
XK:-1 kx-	XK*N.12	771delG	3	W257C + fs 264X		Danek et al. PMID 11761473
XK:-1 kx-	XK*N.13	856-860delCTCTA	3	delL + L286Y + fs 301X		Danek et al. PMID 11761473 Man et al. PMID 23943810
XK:-1 kx-	XK*N.14	938-951del	3	del WYQL + N313T + fs 336X		Danek et al. PMID 11761473
XK:-1 kx-	XK*N.15	1013delT	3	F338S + fs 408X		Hanaoka et al. PMID 10426139
XK:-1 kx-	XK*N.16	107G>A	1	W36X		Danek et al. PMID 11761473
XK:-1 kx-	XK*N.17	397C>T	2	R133X		Danek et al. PMID 11761473, Bansal et al. PMID 18167163, Klempir et al. PMID 17870653
XK:-1 kx-	XK*N.18	463C>T	2	Q155X		Danek et al. PMID 11761473
XK:-1 kx-	XK*N.19	707G>A	3	W236X		Danek et al. PMID 11761473
XK:-1 kx-	XK*N.20	799C>T	3	Q299X	rs104894954	Jung et al. PMID 11261514

Phenotype	Allele name	Nucleotide change	Exon	Predicted amino acid change	dbSNP rs number	Authors and PubMed ID
XK:-1 kx-	XK*N.21	941G>A	3	W314X	rs104894953	Supple et al. PMID 11703337
XK:-1 kx-	XK*N.22	245+1G>C	1	Alt. splice		Russo et al. PMID 11961232, Russo et al. PMID 11099667
XK:-1 kx-	XK*N.23	246-1G>A	1	Alt. splice		Arnaud et al. PMID 19040496
XK:-1 kx-	XK*N.24	508+1G>A	2	Alt. splice		Ho et al. PMID 8004674, Russo et al. PMID 11961232
XK:-1 kx-	XK*N.25	508+5G>A	2	Alt. splice		Daniels et al. PMID 8916972, Walker et al. PMID 17302777
XK:-1 kx-	XK*N.26	509-1G>A	2	Alt. splice		Ho et al. PMID 8004674
XK:-1 kx-	XK*N.27	664C>G	3	R222G		Russo et al. PMID 11961232, Walker et al. PMID 17302777
XK:-1 kx-	XK*N.28	880T>C	3	C294R	rs28933690	Danek et al. PMID 11761473
XK:-1 kx-	XK*N.29	979G>A	3	E327K		Jung et al. PMID 12823753 *(a)

New, or not previously included variants

Predicted phenotype	Nominated Allele name	Nucleotide change	Exons	Amino acid change	Authors and PubMed ID	Clinical presentation
XK:-1 kx-	XK*N.30	1124G>C	3	R375P	Shizuka et al. PMID 9268240 *(b)	Neuroacanthocytosis, normal unaffected patients in control group
XK:-1 kx-	XK*N.31	1134C>G	3	N378K	Shizuka et al. PMID 9268240 *(b)	Neuroacanthocytosis, normal unaffected patients in control group
XK:-1 kx-	XK*N.32	962A>G	3	Y321C	Shimo et al. PMID 21145924	Mood disorder
XK:-1 kx-	XK*N.33	IVS3-13C>G	3	Alt. splice site	Shimo et al. PMID 21145924	Schizophrenia
XK:-1 kx-	XK*N.34	523insA	3	I175N + fs 198X	Dubielecka et al. PMID 21463873	Late onset MLS
XK:-1 kx-	XK*N.35	IVS2 - 2A>G		Alt. splice site	Dubielecka et al. PMID 21463873	Late onset MLS
XK:-1 kx-	XK*N.36	229delC	1 + 2	fs 125X	Wiethoff et al. PMID 24529944	Choreic movements, acanthocytosis
XK:-1 kx-	XK*N.37	154 C>T	1	Q52X	Chen et al. PMID 24635891	Movement disorders, psychotic disorder
XK:-1 kx-	XK*N.38	724-729del5ins13 (delTGTAGinsGGT CCTCTTTACC)	3	Frameshift causes X 36bp (12AA) upstream	Narumi et al. 2016 (doi: 10.1111/ncn3.12042)	MLS – dyskinesia, choreic movements, muscular weakness, insomnia
XK:-1 kx-	XK*N.39	195-198delCCGC	1	Frameshift causes X 187bp upstream (fs128X)	Gassner et al. 2017 PMID 28555782	Chorea, seizures, cognitive decline. Mildly elevated CK, occasional acanthocytes

Notes:

*(a) Study of two brothers with this allele uncovered no subclinical symptoms associated with Mcleod (No haematologic abnormalities, no neurological or muscular abnormalities) – protein appears to be functional.

*(b) Authors describe two transversions (C>G and G>C respectively) at exon 3 codons 204 and 205, however - nucleotides and amino acids at these positions do not correspond to those reported by the authors - the reference sequence already has nucleotides C and G at the respective positions, K and P as the respective amino acids. Authors note that these mutations were also found in healthy control subjects without neuroacanthocytosis. Danek et al 2001 (11761473) has noted that the original nucleotide sequence AACCGT at this locus has been updated to AAGCCT after the findings of Shizuka et al.

XK*N.01 series alleles – large scale and contiguous gene deletions presenting with McLeod phenotype or investigations delineating involvement of XK gene

XK*N.01.001 through XK*N.01.099 are large scale deletions **without specific nucleotide breakpoints identified**
XK*N.01.100 onwards are large scale deletions with **breakpoints defined** to the nucleotide level

XK*N.01.001 – XK*N.01.099 series

XK*N.01 Allele designation	telomeric	centromeric	Size of deletion	Authors and PubMed ID	Clinical presentation
XK*N.01.001	Xg(?)	OTC	Xp22.3 – 21.1	Franke U – 1984 PMID 6510024	Female patient – partial OTC deficiency reported – no reported associated McLeod phenotype due to X-inactivation.
XK*N.01.002	DMD	TX-IL5	Xp21.3 – 21.1 5-10mbp	Franke et al. 1985 PMID 4039107	DMD, CGD, McLeod syndrome, RP
XK*N.01.003	DMD	CGD	Xp21.2-21.1	Bertelson et al – 1988 PMID 3358422	Elevated CK, McLeod syndrome, muscular wasting
XK*N.01.004	XK	RP	Xp21.2-21.1	Bertelson et al – 1988 PMID 3358422	McLeod syndrome
XK*N.01.005	XK	XK	Xp21.2	Ho et al. 1994 PMID 8004674 (patient first reported by Danek et al. 1990 PMID 11761473)	McLeod syndrome, dilated cardiomyopathy, fluctuation/elevated serum CK
XK*N.01.006	XK	CGD	Xp21.2-21.1	Frey et al. 1998 PMID 3334897	CGD, McLeod syndrome

XK*N.01 series alleles – large scale and contiguous gene deletions presenting with McLeod phenotype or investigations delineating involvement of XK gene **XK*N.01.001 through XK*N.01.099** are large scale deletions **without specific nucleotide breakpoints identified** **XK*N.01.100 onwards** are large scale deletions with **breakpoints defined** to the nucleotide level					
XK*N.01.007	XK	RP	Xp21.2-21.1	De Saint-Basille et al. 1998 PMID 3417309	RP, CGD, Mcleod syndrome
XK*N.01.008	DXS84	ETX1	Xp21.2-21.1	El nemer et al. 2000 PMID 10651848	CGD, Mcleod Syndrome, DMD
XK*N.01.009	XK	RPGR	Xp21.2-21.1	El nemer et al. 2000 PMID 10651848	CGD, McLeod syndrome, RP
XK*N.01.010	DXS709	CYBB	Xp21.2-21.1	El nemer et al. 2000 PMID 10651848	CGD, Mcleod syndrome
XK*N.01.011	PRRG1	TCTE1L		Al-Zadjali et al. – 2015 PMID 24446915	Diagnosis at 10y/o Pyoderma, chest infections, gluteal abscess, bowel granuloma Salmonella infections

XK*N.01 series alleles – large scale and contiguous gene deletions presenting with McLeod phenotype or investigations delineating involvement of XK gene

XK*N.01.001 through XK*N.01.099 are large scale deletions **without specific nucleotide breakpoints identified**

XK*N.01.100 onwards are large scale deletions with **breakpoints defined** to the nucleotide level

XK*N.01.100 – onwards

XK*N.01 Allele designation	telomeric	centromeric	Size of deletion	Authors and PubMed ID	Clinical presentation
XK*N.01.100	LOC441488	XK intron 2	1.12mbp	Peng et al. 2007 PMID 17300882	Acanthocytosis, McLeod syndrome, mild chorea
XK*N.01.101	TCTE1L	DMD	5.65mbp	Peng et al. 2007 PMID 17300882	CGD (diagnosed at 4 months of age) – absence of DMD and McLeod symptoms due to age.
XK*N.01.102	LANCL3	DYNLT3	0.59mbp	Arai et al – 2012 PMID 22383943	CGD, reduced Kell antigen, acanthocytosis and high serum CK
XK*N.01.103	CXorf22	DYNLT3	1.94mbp	Arai et al – 2012 PMID 22383943	CGD, reduced Kell antigen, acanthocytosis and high serum CK
XK*N.01.104	DMD	DYNLT3	5.71mbp	Arai et al – 2012 PMID 22383943	Female patient - Increased susceptibility to infection (from age 11) and reduced ROS reactivity
XK*N.01.105	LANCL3	CYBB	0.151mpb	Gassner et al. - 2017 PMID 28555782	CGD diagnosis by age of 10, received CYBB gene corrected stem cell transplantation.