Names for LAN (ISBT 033) Blood Group Alleles

Intro

General description: The LAN blood group system consists of one antigen, Lan, carried on a multipass membrane protein ATP binding cassette subfamily B member 6 (ABCB6) of 842 amino acids, encoded by the *ABCB6* gene located on 2q35. ABCB6 is an ATP-dependent transporter of porphyrins (including heme) and is localized in the golgi apparatus, lysosomes, and plasma membranes. The biologically active protein is a homodimer. ABCB6 is up regulated during erythroid maturation. Mutations in *ABCB6* underlie Lan null and variant phenotypes and are associated with familial pseudohyperkalemia and dyschromatosis universalis hereditaria.

Gene name:	*ABCB6*
Number of exons:	19
Initiation codon:	Within exon 1
Stop codon:	Within exon 19
Entrez Gene ID:	10058
LRG:	LRG_824
LRG sequence:	NG_032110.1 (genomic) NM_005689.4 (transcript) NP_005680.1 (protein)
Reference allele:	*ABCB6*01* (shaded) Acceptable: *Lan* , if inferred by haemagglutination

Phenotype	Allele name	Nucleotide change	Exon Intron	Predicted amino acid change	(Reference No.) PMID	Accession number	rs number
Lan+	*ABCB6*01*						
Null phenotypes							
Lan-	*ABCB6*01N.01*	c.196dupG	1	p.Ala66GlyfsTer96	PMID: 22246506	N/A	rs781146478
Lan-	*ABCB6*01N.02*	c.717G>A	3	p.Trp239Ter* *see note in v.5.0	PMID: 22246506	N/A	rs148458820
Lan-	*ABCB6*01N.03*	c.953_956delGTGG	4	p.Gly318AlafsTer8	PMID: 22246506	N/A	rs755885095
Lan-	*ABCB6*01N.04*	c.1533_1543dupCGGCTCCCTGC	9	p.Leu515ProfsTer43	PMID: 22246506	N/A	rs772078524
Lan-	*ABCB6*01N.05*	c.1709_1710delAG	11	p.Glu570GlyfsTer21	PMID: 22246506	N/A	rs867157424
Lan-	*ABCB6*01N.06*	c.1690_1691delAT	11	p.Met564ValfsTer2	PMID: 22246506	N/A	N/A
Lan-	*ABCB6*01N.07*	c.1867delinsAACAGGTGA	14	p.Gly623AsnfsTer3	PMID: 22246506	N/A	N/A
Lan-	*ABCB6*01N.08*	c.1942C>T	14	p.Arg648Ter	PMID: 22246506	N/A	rs376664522
Lan-	*ABCB6*01N.09*	c.1985_1986delTC	15	p.Leu662ProfsTer15	PMID: 22246506	N/A	rs387906909
Lan-	*ABCB6*01N.10*	c.2256+2t>g	i16	Altered splicing	PMID: 22246506	N/A	rs1559234527
Lan-	*ABCB6*01N.11*	c.1236G>A	6	p.Trp412Ter	PMID: 23763549	N/A	rs772387819
Lan-	*ABCB6*01N.12*	c.1557dupT	9	p.Val520CysfsTer3	PMID: 23763549	N/A	rs749201224
Lan-	*ABCB6*01N.13*	c.574C>T	2	p.Arg192Trp	PMID: 22958180, PMID: 23763549	N/A	rs149202834
Lan-	*ABCB6*01N.14*	c.85_87delTTC	1	p.Phe29del	PMID: 22958180	N/A	rs748337351
Lan-	*ABCB6*01N.15*	c.376delG	1	p.Val126SerfsTer124	PMID: 23763549	N/A	rs377591749
Lan-	*ABCB6*01N.16*	c.459delC	1	p.Trp154GlyfsTer96	PMID: 24400966	AB844675	rs755723161
Lan-	*ABCB6*01N.17*	c.2256+1g>a	i16	Altered splicing	PMID: 24400966	N/A	N/A

Phenotype	Allele name	Nucleotide change	Exon Intron	Predicted amino acid change	(Reference No.) PMID	Accession number	rs number
Lan-	*ABCB6*01N.18*	c.301dupG	1	p.Ala101GlyfsTer61	PMID: 24400966	AB844676	rs768732686
Lan-	*ABCB6*01N.19*	c.718C>T	3	p.Arg240Ter	PMID: 24400966	AB844677	rs766607263
Lan-	*ABCB6*01N.20*	c.869-2a>g	i3	Altered splicing	PMID: 24400966	N/A	rs1574816150
Lan-	*ABCB6*01N.21*	c.1199_1210delTTGG CATCATCT	6	p.Ile400_Tyr404delinAsn	PMID: 24400966	AB844679	N/A
Lan-	*ABCB6*01N.22*	c.2383_2385delCTC	18	p.Leu795del	PMID: 24400966	AB844682	rs1950559481
Lan-	*ABCB6*01N.23*	c.20A>G* c.403C>A	1	p.Tyr7Cys p.Arg135Ser	(2) Abstract, PMID: 24400966	N/A	rs1401023454 rs202232534
Lan-	*ABCB6*01N.24*	c.301dupG c.459delC* *see note in v5.0	1	p.Ala101GlyfsTer61 p.Trp154GlyfsTer96	Abstract (2), PMID: 24400966	N/A	rs768732686 rs755723161
Lan-	*ABCB6*01N.25*	c.881_884delCTGA	4	p.Thr294ArgfsTer32	Abstract (2), PMID: 24400966	AB844678	N/A
Lan-	*ABCB6*01N.26*	c.1617delG	10	p.Gln539HisfsTer15	Abstract (2), PMID: 24400966	AB844680	rs769584110
Lan-	*ABCB6*01N.27*	c.459delC c.2256+1g>a* *see note in v5.0	1 i16	p.Trp154GlyfsTer96 Altered splicing	Abstract (2), PMID: 24400966	N/A	rs755723161 N/A
Lan-	*ABCB6*01N.28*	c.1A>C	1	p.0	PMID: 24456066	KF831582	rs770340675
Lan-	*ABCB6*01N.29*	c.827G>A	3	p.Arg276Gln	PMID: 24456066	KF831583	rs200125320
Lan-	*ABCB6*01N.30*	c.971-1g>a	i4	Altered splicing	PMID: 24456066	KF831584	rs1450661565
Lan-	*ABCB6*01N.31*	c.1825G>A	13	p.Val609Met	PMID: 24456066	KF831585	rs374541848
Lan-	*ABCB6*01N.32*	c.1912C>T	14	p.Arg638Cys	PMID: 24456066	KF831586	rs761968111
Lan-	*ABCB6*01N.33*	c.2155C>T	16	p.Gln719Ter	PMID: 24456066	KF831587	N/A
Lan-	*ABCB6*01N.34*	c.2351+1g>a	i17	Altered splicing	PMID: 24456066	KF831588	rs150574070

Phenotype	Allele name	Nucleotide change	Exon Intron	Predicted amino acid change	(Reference No.) PMID	Accession number	rs number
Lan-	*ABCB6*01N.35*	c.1118_1124delCGGATCG	5	p.Ala373GlyfsTer47	PMID: 29119571	N/A	rs765925019
Lan-	*ABCB6*01N.36*	c.1656-1g>a	i10	Altered splicing	PMID: 29119571	N/A	rs879255549
Lan-	*ABCB6*01N.37*	c.1463G>A	9	p.Trp488Ter	(1) Abstract	N/A	N/A
Lan-	*ABCB6*01N.38*	c.829delG	3	p.Ala277HisfsTer14	(3) Abstract	MK965668.1	rs747139680
Lan-	*ABCB6*01N.39*	c.589G>T	2	p.Gly197Ter	(3) Abstract	MK965669.1	N/A
Altered phenotypes							
Lan(+^{wk})	*ABCB6*01W.01*	c.826C>T	3	p.Arg276Trp	PMID: 23763549, PMID: 22958180	N/A	rs57467915
Lan(+^{wk})	*ABCB6*01W.02*	c.1028G>A	5	p.Arg343Gln	PMID: 23763549	N/A	rs60322991
Lan(+^{wk})	*ABCB6*01W.03*	c.1762G>A	12	p.Gly588Ser	PMID: 23763549, PMID: 22958180	N/A	rs145526996
Lan(+^{wk})	*ABCB6*01W.04*	c.2216G>A	16	p.Arg739His	PMID: 23763549	N/A	rs192931087
Lan(+^{wk})	*ABCB6*01W.05*	c.317A>G	1	p.Tyr106Cys	(1), Abstract	N/A	rs377474593
Lan(+^{wk})	*ABCB6*01W.06*	c.2206G>C	16	p.Ala736Pro	(1), Abstract	N/A	rs1456564537
Lan(+^{wk})	*ABCB6*01W.07*	c.403C>A c.575G>A	1	p.Arg135Ser p.Arg192Gln	(1), Abstract	N/A	rs202232534 rs150221689

References

PMID 22246506 Helias V, Saison C, Ballif BA, et al.: ABCB6 is dispensable for erythropoiesis and specifies the new blood group system Langereis. *Nat Genet* 2012; 44: 170-3. doi: 10.1038/ng.1069.

PMID 23763549 Reid ME, Hue-Roye K, Huang A, et al.: Alleles of the LAN blood group system: molecular and serologic investigations. *Transfusion* 2014; 54: 398-404. doi: 10.1111/trf.12285.

PMID 22958180 Saison C, Helias V, Peyrard T, et al.: The ABCB6 mutation p.Arg192Trp is a recessive mutation causing the Lan- blood type. *Vox Sang* 2013; 104: 159-65. doi: 10.1111/j.1423-0410.2012.01650.x.

PMID 24400966 Tanaka M, Yamamuro Y, Takahashi J, et al.: Novel alleles of Lan- in Japanese populations. *Transfusion* 2014; 54: 1438-9. doi: 10.1111/trf.12540.

PMID 24456066 Haer-Wigman L, Ait Soussan A, Ligthart P, et al.: Molecular analysis of immunized Jr(a-) or Lan- patients and validation of a high-throughput genotyping assay to screen blood donors for Jr(a-) and Lan- phenotypes. *Transfusion* 2014; 54: 1836-46. doi: 10.1111/trf.12544.

PMID 29119571 Schoeman EM, Roulis EV, Liew YW et al. Targeted exome sequencing defines novel and rare variants in complex blood group serology cases for a red blood cell reference laboratory setting. *Transfusion* 2018; 58: 284-293. doi: 10.1111/trf.14393.

Abstract (1) Yamamuro Y, Isa K, Ogasawara K, et al.: The mutations of ABCB6 gene in Japanese blood donors with weak expression of Lan antigen. *Vox Sanguinis* 2014; 107: 186-7.

Abstract (2) Yamamuro Y, Isa K, Ogasawara K, et al.: The new mutations of ABCB6 gene in Lan- Japanese. *Vox Sanguinis* 2013; 105: 230-1.

Abstract (3) Karamatic Crew V, Jones B, McNeill A, et al. Two Lan null individuals with a novel ABCB6 null alleles and a compound heterozygote with a rare combination of known null and weak ABCB6 alleles. Vox Sanguinis 2019; 114: 191-192.

Track of changes

			from	to
1	**Version**		**v4.0 08-APR-2019**	**v5.0 31-JUL-2023**
2	Author	created:	Thierry Peyrard, September 2019	Vanja Crew, supp. Louise Tilly, July 2023
3	Review	reviewed:	Slim Azouzi, September 2019	Silvano Wendel, supp. Mayra Altobelli Brito, July 2023
4	General	All	v4.0 Word-document	First Excel map version. Spread-sheets "Intro", "Allele Table", "References", "Versioning (v4.1)" created.
5	Introduction	Intro updated		General description updated: The LAN blood group system consists of one antigen, Lan, carried on a multipass membrane protein ATP binding cassette subfamily B member 6 (ABCB6) of 842 amino acids, encoded by the *ABCB6* gene located on 2q35. ABCB6 is an ATP-dependent transporter of porphyrins (including heme) and is localized in the golgi apparatus, lysosomes, and plasma membranes. The biologically active protein is a homodimer. ABCB6 is up regulated during erythroid maturation. Mutations in *ABCB6* underlie Lan null and variant phenotypes and are associated with familial pseudohyperkalemia and dyschromatosis universalis hereditaria.
6		LRG ID and reference sequences updated		LRG_824 added, transcript reference sequence updated from NM_005689.2 to NM_005689.4, protein reference NP_005680.1 added
7	Allele table	Table updated		Nucleotide change and predicted amino acid change sections updated for a number of variants to reflect current nomenclature. References changed from numbers to PMID. GenBank accession numbers and dbSNP rs numbers added where available.
8	Allele table	*ABCB6*01N.01* updated		c.197_198insG (also in Helias et al, 2012) changed to c.196dupG. Note: with c.197_198insG, amino acid change is p.Gly67ArgfsTer95, not Ala66GlyfsTer66, as recorded in v4.0 and in the original paper.

1	**Version**		**v4.0 08-APR-2019**	**v5.0 31-JUL-2023**
9	Allele table	*Note for *ABCB6*01N.02*		c.717G>A encodes p.Trp39Ter in NM_005689.4. In v4.0 and Helias et al, 2012, it was wrongly reported as Gln239Ter.
10	Allele table	*ABCB6*01N.04* updated		p.Leu515Profs*17 (also in Helias et al, 2012) corrected to p.Leu515ProfsTer43
11	Allele table	*ABCB6*01N.12* updated		c.1558_1559insT changed to c.1557dupT to agree with p.Val520CysfsTer3, as reported in Reid et al, 2014.
12	Allele table	*ABCB6*01N.16* updated		p.Leu154SerfsTer97 (also in Tanaka et al, 2014) changed to p.Trp154GlyfsTer96
13	Allele table	*ABCB6*01N.18* updated		c.296_301insG (also in Tanaka et al, 2014) changed to c.301dupG
14	Allele table	*ABCB6*01N.21* updated		p.Ile400_Gly401_Ile402_Ile403_Tyr404delinsAsn changed to p.Ile400_Tyr404delinAsn.
15	Allele table	*ABCB6*01N.23* updated		Removed c.459delC (also in Tanaka et al, 2014), because it was reported in trans with this allele (Yamamuro et al, 2013)
16	Allele table	*ABCB6*01N.24* updated		Note: c.301dupG and c.459delC were reported in trans (Yamamuro et al, 2013)
17	Allele table	*ABCB6*01N.25* updated		Removed c.459delC (also in Tanaka et al, 2014), because it was reported in trans with this allele (Yamamuro et al, 2013)
18	Allele table	*ABCB6*01N.26* updated		Removed c.459delC (also in Tanaka et al, 2014), because it was reported in trans with this allele (Yamamuro et al, 2013)
19	Allele table	*ABCB6*01N.27* updated		Note: c.2256+1g>a and c.459delC were reported in trans (Yamamuro et al, 2013)
20	Allele table	ABCB6*01N.29 updated		A typo in p.Arg276Glu (also in Haer-Wigman et al, 2014) amended to p.Arg276Gln
21	Allele table	*ABCB6*01N.33* updated		A typo in p.Glu719Ter (also in Haer-Wigman et al, 2014) amended to p.Gln719Ter
22	Allele table	*ABCB6*01N.35* updated		Exon 6 changed to 5; Shoeman et al, 2018, used NM_001349828.2 as a reference
23	Allele table	*ABCB6*01N.36* updated		Intron i9 changed to i10; Shoeman et al, 2018, used NM_001349828.2 as a reference

1	**Version**		**v4.0 08-APR-2019**	**v5.0 31-JUL-2023**
24	Allele table	Alleles added		*ABCB6*01N.37* to *ABCB6*01N.39*
25	Allele table	*ABCB^6*01W.07* updated		c.575G>A added, because it was reported in cis with c.403C>A (Abstract 1)
26	Allele table	Lan phenotype unconfirmed section removed		Removed alleles [c.869-2A>G], [c.1199_1210del], [c.2383_2385del], [c.2256+1G>A], and [c.20A>G], as these are the same as *ABCB6*01N.20* , *ABCB6*01N.21* , *ABCB6*01N.22* , *ABCB6*01N.17* , and *ABCB6*01N.23* . Allele [c.55A>T] removed because it was deemed highly unlikely that it contributes to the Lan phenotype (Haer-Wigman et al, 2014)
27	References	PMID		Added PMIDs.
28	References	Abstract		Changed Reference (6) to Abstract (1).
29	References	Abstract		Changed Reference (7) to Abstract (2).
30	References	rs-numbers		Added rs-numbers.
31	References	Abstract added		Abstract (3) added
32	**End Version**		**v4.0 08-APR-2019**	**v5.0 31-JUL-2023**