Lan Blood Group System

Number of antigens 1

High prevalence	Lan

Terminology

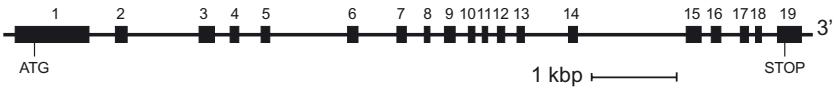
ISBT symbol (number)	LAN (033)
History	Lan, which stems from the name Langereis, was promoted from the 901 Series of High-Incidence antigens to a System in 2012 when it was shown that homozygosity for *ABCB6* null alleles define the Lan– phenotype.

Expression

Tissues	Widely expressed; high expression in heart, skeletal muscles, and fetal liver; also in mitochondrial membrane, eye, and Golgi apparatus

Gene

Chromosome	2q36
Name	*LAN* (*ABCB6*)
Organization	19 exons spread over approximately 9.2 kbp of gDNA
Product	Lan glycoprotein (ATP-binding cassette, sub-family B [MDR/TAP], member 6 [ABCB6])



Database accession numbers

GenBank	NM_005689.1 (DNA)
Entrez Gene ID	10058

The Blood Group Antigen (3/e). DOI: http://dx.doi.org/10.1016/B978-0-12-415849-8.00035-1

Molecular bases of LAN_{null} (Lan–, LAN:–1) phenotype[1]

The reference allele, *ABCB6* (Accession number NM_005689.1) encodes Lan (LAN1). Nucleotide differences from this reference allele, and amino acids affected, are given.

Allele name	Exon(intron)	Nucleotide	Amino acid	Ethnicity (prevalence)
*ABCB6*01N.01* or *LAN*01N.01*	1	197_198insG	Ala66Gly fs	Caucasian (Rare)
*ABCB6*01N.02* or *LAN*01N.02*	3	717G>A	Gln239Stop	Caucasian (Rare)
*ABCB6*01N.03* or *LAN*01N.03*	4	953_956delGTGG	Gly318Ala fs	Caucasian (Rare)
*ABCB6*01N.04* or *LAN*01N.04*	9	1533_1543 dupCGGCTCCCTGC	Leu515Pro fs	Caucasian (Rare)
*ABCB6*01N.05* or *LAN*01N.05*	11	1709_1710delAG	Glu570Gly fs	Caucasian (Rare)
*ABCB6*01N.06* or *LAN*01N.06*	11	1690_1691delAT	Met564Val fs	Caucasian (Rare)
*ABCB6*01N.07* or *LAN*01N.07*	14	1867 delinsAACAGGTGA	Gly623Asn fs	Caucasian (Few)
*ABCB6*01N.08* or *LAN*01N.08*	14	1942C>T	Arg648Stop	Caucasian (Few)
*ABCB6*01N.09* or *LAN*01N.09*	15	1985_1986delTC	Leu662Pro fs	Caucasian (Rare)
*ABCB6*01N.10* or *LAN*01N.10*	(16)	2256+2t>g	Splicing defect	Japanese (Rare)

Amino acid sequence

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MVTVGNYCEA  EGPVGPAWMQ  DGLSPCFFFT  LVPSTRMALG  TLALVLALPC   50
RRRERPAGAD  SLSWGAGPRI  SPYVLQLLLA  TLQAALPLAG  LAGRVGTARG  100
APLPSYLLLA  SVLESLAGAC  GLWLLVVERS  QARQRLAMGI  WIKFRHSPGL  150
LLLWTVAFAA  ENLALVSWNS  PQWWWARADL  GQQVQFSLWV  LRYVVSGGLF  200
VLGLWAPGLR  PQSYTLQVHE  EDQDVERSQV  RSAAQQSTWR  DFGRKLRLLS  250
GYLWPRGSPA  LQLVVLICLG  LMGLERALNV  LVPIFYRNIV  NLLTEKAPWN  300
SLAWTVTSYV  FLKFLQGGGT  GSTGFVSNLR  TFLWIRVQQF  TSRRVELLIF  350
SHLHELSLRW  HLGRRTGEVL  RIADRGTSSV  TGLLSYLVFN  VIPTLADIII  400
GIIYFSMFFN  AWFGLIVFLC  MSLYLTLTIV  VTEWRTKFRR  AMNTQENATR  450
ARAVDSLLNF  ETVKYYNAES  YEVERYREAI  IKYQGLEWKS  SASLVLLNQT  500
QNLVIGLGLL  AGSLLCAYFV  TEQKLQVGDY  VLFGTYIIQL  YMPLNWFGTY  550
YRMIQTNFID  MENMFDLLKE  ETEVKDLPGA  GPLRFQKGRI  EFENVHFSYA  600
DGRETLQDVS  FTVMPGQTLA  LVGPSGAGKS  TILRLLFRFY  DISSGCIRID  650
GQDISQVTQA  SLRSHIGVVP  QDTVLFNDTI  ADNIRYGRVT  AGNDEVEAAA  700
QAAGIHDAIM  AFPEGYRTQV  GERGLKLSGG  EKQRVAIART  ILKAPGIILL  750
DEATSALDTS  NERAIQASLA  KVCANRTTIV  VAHRLSTVVN  ADQILVIKDG  800
CIVERGRHEA  LLSRGGVYAD  MWQLQQGQEE  TSEDTKPQTM  ER         842
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Carrier molecule

In the RBC, ABCB6 is presumed to be a multipass membrane protein, with one nucleotide binding domain (NBD) oriented to the cytoplasm. In the mitochondria, ABCB6 passes through the membrane 11 times, with the Walker A, Walker B, and Signature motifs on the outer surface, i.e., oriented to the cytoplasm.

M_r (SDS-PAGE)	80,000
CHO: N-glycan	Four potential
Cysteine residues	10

Function

Binds heme and porphyrins, and functions in their ATP-dependent uptake into the mitochondria. Plays a crucial role in heme synthesis[2,3], although expression of ABCB6 does not appear to be required for normal erythropoiesis[1].

Disease association

The eye developmental defect coloboma is associated with changes in *ABCB6*, but Lan– individuals appear healthy[4].

References

[1] Helias, V., et al., 2012. ABCB6 is dispensable for erythropoiesis and specifies the new blood group system Langereis. Nat Genet 44, 170–173.

[2] Krishnamurthy, P.C., et al., 2006. Identification of a mammalian mitochondrial porphyrin transporter. Nature 443, 586–589.
[3] Mitsuhashi, N., et al., 2000. MTABC3, a novel mitochondrial ATP-binding cassette protein involved in iron homeostasis. J Biol Chem 275, 17536–17540.
[4] Wang, L., et al., 2012. ABCB6 mutations cause ocular coloboma. Am J Hum Genet 90, 40–48.

Lan Antigen

Terminology

ISBT symbol (number)	Lan (033001 or 33.1)
Obsolete names	Gn[a]; Gonsowski; So; 900003; 901002
History	Reported in 1961; named after the first antigen-negative proband (Langereis) to make anti-Lan.

Occurrence

All populations	>99%

The Lan– phenotype occurs in about 1 in 20,000 people; found in Blacks[1,2], Caucasians, and Japanese.

Expression

Cord RBCs	Expressed
Altered	A weak form of Lan has been reported[3]

Effect of enzymes and chemicals on Lan antigen on intact RBCs

Ficin/Papain	Resistant
Trypsin	Resistant
α-Chymotrypsin	Resistant
DTT 200 mM	Resistant
Acid	Resistant

In vitro characteristics of alloanti-Lan

Immunoglobulin class	IgG
Optimal technique	IAT
Complement binding	Some

Clinical significance of alloanti-Lan

Transfusion reaction	No to severe/hemolytic
HDFN	No to mild

Autoanti-Lan

One example in a patient with depressed Lan antigens.

References

[1] Ferraro, M.L., et al., 2000. The rare red cell phenotype, Lan–, in an African-American [abstract]. Transfusion 40 (Suppl.), 121S.

[2] Sturgeon, J.K., et al., 2000. Report of an anti-Lan in an African American [abstract]. Transfusion 40 (Suppl.), 115S.

[3] Storry, J.R., Øyen, R., 1999. Variation in Lan expression. Transfusion 39, 109–110.