Names for Lewis (ISBT 007) Blood Group Alleles

Intro

General description:

The Lewis blood group antigens, e.g. Lea and Leb, are part of carbohydrate moieties attached to lipids (fucosylated glycosphingolipids) and glycoproteins. These antigens are not intrinsic to red blood cells. Instead, they are enzymatically added to precursor molecules inside exocrine epithelial cells and, following synthesis, are excreted into various bodily fluids such as plasma from which the Lewis glycolipids are adsorbed onto the red cell membrane giving rise to the Lewis phenotypes. The glycoprotein forms mainly remain in plasma and other fluids. Lewis structures also appear on other cell surfaces and have functions in embryogenesis, tissue differentiation, tumour metastasis, inflammation, and bacterial as well as viral adhesion.

The biosynthesis of the Lewis antigens is dependent on the *FUT3* gene that encodes an α(1,3/4)-fucosyltransferase protein (UniProt ID P21217) which catalyses the addition of fucose to a precursor polysaccharide. The biochemistry underpinning Lewis antigen synthesis is complex and cannot be detailed fully here – for more detail, please see Kukowska-Latallo et al., 1990 (PMID: 1977660) and Henry, 1996 (PMID:15387741). The type of Lewis antigen produced in this reaction depends on the type of precursor molecule the enzyme (Fuc-TIII) interacts with.

In individuals with an active *FUT2* (Secretor or SE) gene, which encodes a fully active α(1,2)-fucosyltransferase (see H Blood Group System), predominantly Leb (and related Lewis antigens depending on ABO group, e.g. ALeb in group A) is made alongside trace amounts of Lea. The trace amounts of Lea produced are typically undetectable using serological methods, and usually, a Le(a–b+) phenotype is reported.

In individuals without an active FUT2 (Secretor or SE) gene, only Lea can be made as these “non-secretor” individuals cannot produce the precursor H type 1 antigen - this results in a Le(a+b–) phenotype.
In individuals with a partially functional FUT2 (Secretor) gene, the biosynthesis of the H type 1 precursor is hampered, and much more Lea can be made, resulting in a Le(a+b+) phenotype in “secretor-weak” individuals. This is because the enzymes produced by the FUT2 (Secretor) and FUT3 (Lewis) genes compete for access to the same unfucosylated precursor molecules, and the Lea antigen, once formed, cannot be converted into Leb. Although FUT2 (Secretor) generally outcompetes FUT3 (Lewis), some Lea is made, and hence Leb positive individuals always have trace amounts of Lea.
In individuals without a functional FUT3 gene, their RBC phenotype will have the Le(a–b–) regardless of the FUT2 status.

IMPORTANT: Given the above information, the phenotype column in this table will report on the ACTIVITY status of the FUT3 enzyme, therefore, the ability to synthesise Lewis antigens. Inference of Lewis antigen phenotypes using the variants contained in this table should be done with regard also to the individual’s Secretor/H antigen status (i.e. the functionality of their FUT2 gene) as they are dependent on one another's functionality.

Gene name:	*FUT3*
Number of exons:	3
Initiation codon:	Beginning of exon 3
Stop codon:	Within exon 3
Entrez Gene ID:	2525
LRG:	LRG_800
LRG sequence:	NG_007482.2 (genomic) NM_000149.4 (transcript) NP_000140.1 (protein)
Reference allele *FUT3* encodes:	Reference allele encodes an ACTIVE *FUT3* gene.
Antithetical antigens:	Does not apply in traditional sense
Antigens:	Lea, Leb. Variations: Leab, LebH, ALeb, Bleb

Annotation category:	The reference transcript, NM_000149.4, differs in two places from the GRCh38 reference genome: GRCh38 chr19:5844638 is G at this position, NM_000149.4 is A GRCh38 chr19:5844526 is A at this position, NM_000149.4 is G Note 1: The above mismatched bases for NM_000149.4, are reported after alignment to GRCh38 and conversion of transcript bases to the forward genomic strand (as the *FUT3* is reverse transcribed). More information on this mapping can be found here - http://ftp.ebi.ac.uk/pub/databases/lrgex/LRG_800.xml#assembly_mapping. Note 2: This gene has been reviewed for its involvement in coronavirus biology, and is relevant for disease process.

Phenotype	Allele Name	Nucleotide change	Exon Intron	Predicted amino acid change	(Reference No.) PMID	Accession number	rs number
FUT3 Active - can make Lewis antigens	*FUT3*01.01*	No change listed below	N/A			NM_000149.4	
FUT3 Active - can make Lewis antigens	*FUT3*01.02*	c.104G>A	2	p.Arg35His	PMID: 15383031		rs760467123
FUT3 Active - can make Lewis antigens	*FUT3*01.03*	c.304C>A	2	p.Gln102Lys	PMID: 9703429		rs59796499
FUT3 Active - can make Lewis antigens	*FUT3*01.04*	c.314C>T	2	p.Thr105Met	PMID: 9268337		
FUT3 Active - can make Lewis antigens	*FUT3*01.05*	c.370T>G	2	p.Ser124Ala	PMID: 9703429		rs1175404919
FUT3 Active - can make Lewis antigens	*FUT3*01.06*	c.478C>T	2	p.Arg160Cys	PMID: 15383031		rs28362462
FUT3 Active - can make Lewis antigens	*FUT3*01.07*	c.612A>G	3	p.Ser204=	PMID: 15383031		rs28362465
FUT3 Active - can make Lewis antigens	*FUT3*01.08.01*	c.732C>T	3	p.Tyr244=	PMID: 15383031		rs565590532
FUT3 Active - can make Lewis antigens	*FUT3*01.08.02*	c.732C>T c.858A>G	3 3	p.Tyr244= p.Pro286=	PMID: 15383031		rs565590532 rs139326855
FUT3 Active - can make Lewis antigens, however there is a 90% reduction in enzyme functionality.	*FUT3*01.10*	c.1067T>A	3	p.Ile356Lys	PMID: 7961897		rs3894326
FUT3 Active - can make Lewis antigens	*FUT3*01.11*	c.381G>A	2	p.Pro127=	PMID: 32218479		rs144354196
FUT3 Active - can make Lewis antigens	*FUT3*01.12*	c.561G>A	2	p.Ser187=	PMID: 32218479		rs747036561
FUT3 Active - can make Lewis antigens	*FUT3*01.13*	c.645T>C	3	p.Ala215=	PMID: 32218479		rs148170391
FUT3 Active - can make Lewis antigens	*FUT3*01.14*	c.876C>T	3	p.His292=	PMID: 32218479		rs773934140
FUT3 Active - can make Lewis antigens, however there is a 90% reduction in enzyme functionality.	*FUT3*01.15*	c.484G>A c.667G>A	2 3	p.Asp162Asn p.Gly223Arg	PMID: 9703429		rs28362463 rs28362466
FUT3 Active - can make Lewis antigens, however there is a 90% reduction in enzyme functionality.	*FUT3*01.16*	c.484G>A c.667G>A c.808G>A	2 3 3	p.Asp162Asn p.Gly223Arg p.Val270Met	PMID: 9703429		rs28362463 rs28362466 rs28381968

Phenotype	Allele Name	Nucleotide change	Exon Intron	Predicted amino acid change	(Reference No.) PMID	Accession number	rs number
FUT3 Active - can make Lewis antigens, however there is a 90% reduction in enzyme functionality.	*FUT3*01.17.01*	c.59T>G	1	p.Leu20Arg	PMID: 8240337		rs28362459
Null allele							
FUT3 Inactive - Le(a-b-)	*FUT3*01N.01.01*	c.13G>A c.484G>A	1 2	p.Gly5Ser p.Asp162Asn	PMID: 14674375		rs28362458 rs28362463
FUT3 Inactive - Le(a-b-)	*FUT3*01N.01.02*	c.13G>A c.484G>A c.667G>A	1 2 3	p.Gly5Ser p.Asp162Asn p.Gly223Arg	PMID: 14674375		rs28362458 rs28362463 rs28362466
FUT3 Inactive - Le(a-b-)	*FUT3*01N.01.03*	c.13G>A c.59T>G c.484G>A c.667G>A	1 1 2 3	p.Gly5Ser p.Leu20Arg p.Asp162Asn p.Gly223Arg	PMID: 14674375		rs28362458 rs28362459 rs28362463 rs28362466
FUT3 Inactive - Le(a-b-)	*FUT3*01N.01.04*	c.13G>A c.59T>G c.667G>A	1 1 3	p.Gly5Ser p.Leu20Arg p.Gly223Arg	PMID: 14674375		rs28362458 rs28362459 rs28362466
FUT3 Inactive - Le(a-b-)	*FUT3*01N.01.05*	c.13G>A c.59T>G c.508G>A	1 1 2	p.Gly5Ser p.Leu20Arg p.Gly170Ser	PMID: 14674375		rs28362458 rs28362459 rs3745635
FUT3 Inactive - Le(a-b-)	*FUT3*01N.01.06*	c.13G>A c.179G>A c.484G>A c.808G>A	1 2 2 3	p.Gly5Ser p.Arg60His p.Asp162Asn p.Val270Met	PMID: 19175549		rs28362458 rs148881389 rs28362463 rs28381968
FUT3 Inactive - Le(a-b-)	*FUT3*01N.01.07*	c.13G>A c.484G>A c.522G>A c.667G>A	1 2 2 3	p.Gly5Ser p.Asp162Asn p.Pro174= p.Gly223Arg	PMID: 19175549		rs28362458 rs28362463 rs757770735 rs28362466

Phenotype	Allele Name	Nucleotide change	Exon Intron	Predicted amino acid change	(Reference No.) PMID	Accession number	rs number
FUT3 Inactive - Le(a-b-)	*FUT3*01N.01.08*	c.13G>A c.484G>A c.667G>A c.808G>A	1 2 3 3	p.Gly5Ser p.Asp162Asn p.Gly223Arg p.Val270Met	PMID: 19175549		rs28362458 rs28362463 rs28362466 rs28381968
FUT3 Inactive - Le(a-b-)	*FUT3*01N.01.09*	c.13G>A c.484G>A c.667G>A c.962G>A	1 2 3 3	p.Gly5Ser p.Asp162Asn p.Gly223Arg p.Arg321His	PMID: 19175549		rs28362458 rs28362463 rs28362466 rs567372133
FUT3 Inactive - Le(a-b-)	*FUT3*01N.01.10*	c.13G>A c.484G>A c.667G>A c.974C>T	1 2 3 3	p.Gly5Ser p.Asp162Asn p.Gly223Arg p.Thr325Met	PMID: 19175549		rs28362458 rs28362463 rs28362466 rs28381969
FUT3 Inactive - Le(a-b-)	*FUT3*01N.01.11*	c.13G>A c.484G>A c.808G>A c.968G>C	1 2 3 3	p.Gly5Ser p.Asp162Asn p.Val270Met p.Arg323Pro	PMID: 19175549		rs28362458 rs28362463 rs28381968 rs150418165
FUT3 Inactive - Le(a-b-)	*FUT3*01N.01.12*	c.13G>A c.484G>A c.968G>C	1 2 3	p.Gly5Ser p.Asp162Asn p.Arg323Pro	PMID: 19175549		rs28362458 rs28362463 rs150418165
FUT3 Inactive - Le(a-b-)	*FUT3*01N.03.01*	c.202T>C	2	p.Trp68Arg	PMID: 9268337		
FUT3 Inactive - Le(a-b-)	*FUT3*01N.03.02*	c.202T>C c.314C>T	2 2	p.Trp68Arg p.Thr105Met	PMID: 9987874		
FUT3 Inactive - Le(a-b-)	*FUT3*01N.03.03*	c.202T>C c.314C>T c.484G>A	2 2 2	p.Trp68Arg p.Thr105Met p.Asp162Asn	PMID: 9703429		rs28362463
FUT3 Inactive - Le(a-b-)	*FUT3*01N.03.04*	c.202T>C c.1067T>A	2 3	p.Trp68Arg p.Ile356Lys	PMID: 12424536		rs3894326

Phenotype	Allele Name	Nucleotide change	Exon Intron	Predicted amino acid change	(Reference No.) PMID	Accession number	rs number
FUT3 Inactive - Le(a-b-)	*FUT3*01N.03.05*	c.202T>C c.314C>T c.451A>G	2 2 2	p.Trp68Arg p.Thr105Met p.Arg151Gly	PMID: 19175549		rs417341
FUT3 Inactive - Le(a-b-)	*FUT3*01N.03.06*	c.202T>C c.314C>T c.560C>T	2 2 2	p.Trp68Arg p.Thr105Met p.Ser187Leu	PMID: 19175549		rs144130818
FUT3 Inactive - Le(a-b-)	*FUT3*01N.03.07*	c.202T>C c.314C>T c.612A>G	2 2 3	p.Trp68Arg p.Thr105Met p.Ser204=	PMID: 19175549		rs28362465
FUT3 Inactive - Le(a-b-)	*FUT3*01N.03.08*	c.202T>C c.314C>T c.858A>G	2 2 3	p.Trp68Arg p.Thr105Met p.Pro286=	PMID: 19175549		rs139326855
FUT3 Inactive - Le(a-b-)	*FUT3*01N.03.09*	c.202T>C c.314C>T c.882C>T	2 2 3	p.Trp68Arg p.Thr105Met p.Asp294=	PMID: 32218479		rs778985
FUT3 Inactive - Le(a-b-)	*FUT3*01N.03.10*	c.113G>A c.202T>C c.314C>T	2 2 2	p.Arg38Gln p.Trp68Arg p.Thr105Met	PMID: 32218479		rs147046153
FUT3 Inactive - Le(a-b-)	*FUT3*01N.03.11*	c.47G>C c.202T>C c.314C>T	1 2 2	p.Cys16Ser p.Trp68Arg p.Thr105Met	PMID: 15383031		rs145362171
FUT3 Inactive - Le(a-b-)	*FUT3*01N.03.12*	c.47G>C c.202T>C c.314C>T c.655G>A c.1029A>G	1 2 2 3 3	p.Cys16Ser p.Trp68Arg p.Thr105Met p.Val219Met p.Lys343=	PMID: 19175549		rs145362171 rs199931170
FUT3 Inactive - Le(a-b-)	*FUT3*01N.17.02*	c.55G>A c.59T>G	1 1	p.Ala19Thr p.Leu20Arg	PMID: 19175549		rs146199130 rs28362459
FUT3 Inactive - Le(a-b-)	*FUT3*01N.17.03*	c.59T>G c.1067T>A	1 3	p.Leu20Arg p.Ile356Lys	PMID: 8801770		rs28362459 rs3894326

Phenotype	Allele Name	Nucleotide change	Exon Intron	Predicted amino acid change	(Reference No.) PMID	Accession number	rs number
FUT3 Inactive - Le(a-b-)	*FUT3*01N.17.04*	c.59T>G c.445C>A	1 2	p.Leu20Arg p.Leu149Met	PMID: 19175549		rs28362459 rs143012663
FUT3 Inactive - Le(a-b-)	*FUT3*01N.17.05*	c.59T>G c.508G>A	1 2	p.Leu20Arg p.Gly170Ser	PMID: 8240337		rs28362459 rs3745635
FUT3 Inactive - Le(a-b-)	*FUT3*01N.17.06*	c.59T>G c.1007A>C c.1029A>G	1 3 3	p.Leu20Arg p.Asp336Ala p.Lys343=			rs28362459 rs151218854 rs199931170
FUT3 Inactive - Le(a-b-)	*FUT3*01N.17.07*	c.59T>G c.202T>C c.1067T>A	1 2 3	p.Leu20Arg p.Trp68Arg p.Ile356Lys	PMID: 19175549		rs28362459 rs3894326
FUT3 Inactive - Le(a-b-)	*FUT3*01N.17.08*	c.59T>G c.258C>T c.1067T>A	1 2 3	p.Leu20Arg p.Pro86= p.Ile356Lys	PMID: 19175549		rs28362459 rs373337765 rs3894326
FUT3 Inactive - Le(a-b-)	*FUT3*01N.17.09*	c.59T>G c.508G>A c.548C>T	1 2 2	p.Leu20Arg p.Gly170Ser p.Pro183Leu	PMID: 19175549		rs28362459 rs3745635 rs146519599
FUT3 Inactive - Le(a-b-)	*FUT3*01N.17.10*	c.59T>G c.508G>A c.612A>G	1 2 3	p.Leu20Arg p.Gly170Ser p.Ser204=	PMID: 19175549		rs28362459 rs3745635 rs28362465
FUT3 Inactive - Le(a-b-)	*FUT3*01N.17.11*	c.59T>G c.508G>A c.732C>T	1 2 3	p.Leu20Arg p.Gly170Ser p.Tyr244=	PMID: 19175549		rs28362459 rs3745635 rs565590532
FUT3 Inactive - Le(a-b-)	*FUT3*01N.17.12*	c.59T>G c.508G>A c.858A>G	1 2 3	p.Leu20Arg p.Gly170Ser p.Pro286=	PMID: 19175549		rs28362459 rs3745635 rs139326855
FUT3 Inactive - Le(a-b-)	*FUT3*01N.17.13*	c.59T>G c.548C>T c.612A>G c.1067T>A	1 2 3 3	p.Leu20Arg p.Pro183Leu p.Ser204= p.Ile356Lys	PMID: 19175549		rs28362459 rs146519599 rs28362465 rs3894326

Phenotype	Allele Name	Nucleotide change	Exon Intron	Predicted amino acid change	(Reference No.) PMID	Accession number	rs number
FUT3 Inactive - Le(a-b-)	*FUT3*01N.17.14*	c.59T>G c.571G>A c.1067T>A	1 2 3	p.Leu20Arg p.Glu191Lys p.Ile356Lys	PMID: 19175549		rs28362459 rs779363554 rs3894326
FUT3 Inactive - Le(a-b-)	*FUT3*01N.17.15*	c.59T>G c.61C>T c.508G>A	1 2 2	p.Leu20Arg p.Leu21= p.Gly170Ser	PMID: 19175549		rs28362459 rs28362460 rs3745635
FUT3 Inactive - Le(a-b-)	*FUT3*01N.17.16*	c.59T>G c.61C>T c.508G>A c.980G>A	1 2 2 3	p.Leu20Arg p.Leu21= p.Gly170Ser p.Arg327Gln	PMID: 19175549		rs28362459 rs28362460 rs3745635 rs28381970
FUT3 Inactive - Le(a-b-)	*FUT3*01N.17.17*	c.59T>G c.1022G>T c.1067T>A	1 3 3	p.Leu20Arg p.Cys341Phe p.Ile356Lys	PMID: 14674375		rs28362459 rs61737304 rs3894326
FUT3 Inactive - Le(a-b-)	*FUT3*01N.17.18*	c.59T>G c.146G>A c.508G>A	1 2 2	p.Leu20Arg p.Ser49Asn p.Gly170Ser	PMID: 32218479		rs28362459 rs1263565737 rs3745635
FUT3 Inactive - Le(a-b-)	*FUT3*01N.17.19*	c.59T>G c.508G>A c.1061G>A	1 2 3	p.Leu20Arg p.Gly170Ser p.Arg354His	PMID: 32218479		rs28362459 rs3745635 rs144953440
FUT3 Inactive - Le(a-b-)	*FUT3*01N.17.20*	c.47G>C c.59T>G c.202T>C c.490G>A	1 1 2 2	p.Cys16Ser p.Leu20Arg p.Trp68Arg p.Asp164Asn	PMID: 32218479		rs145362171 rs28362459 rs767305253
FUT3 Inactive - Le(a-b-)	*FUT3*01N.17.21*	c.24G>C c.59T>G c.508G>A	1 1 2	p.Lys8Asn p.Leu20Arg p.Gly170Ser	PMID: 32218479		 rs28362459 rs3745635
FUT3 Inactive - Le(a-b-)	*FUT3*01N.17.22*	c.59T>G c.959T>C c.1067T>A	1 3 3	p.Leu20Arg p.Phe320Ser p.Ile356Lys	PMID: 32218479		rs28362459 rs762649552 rs3894326

References

PMID 1977660 Kukowska-Latallo JF, Larsen RD, Nair RP, Lowe JB. A cloned human cDNA determines expression of a mouse stage-specific embryonic antigen and the Lewis blood group alpha(1,3/1,4)fucosyltransferase. Genes Dev. 1990 Aug;4(8):1288-303. doi: 10.1101/gad.4.8.1288.

PMID 7961897 Nishihara S, Narimatsu H, Iwasaki H, Yazawa S, Akamatsu S, Ando T, Seno T, Narimatsu I. Molecular genetic analysis of the human Lewis histo-blood group system. J Biol Chem. 1994 Nov 18;269(46):29271-8.

PMID 8063716 Mollicone R, Reguigne I, Kelly RJ, Fletcher A, Watt J, Chatfield S, Aziz A, Cameron HS, Weston BW, Lowe JB. Molecular basis for Lewis alpha(1,3/1,4)-fucosyltransferase gene deficiency (FUT3) found in Lewis-negative Indonesian pedigrees. J Biol Chem. 1994 Aug 19;269(33):20987-94.

PMID 8219240 Koda Y, Kimura H, Mekada E. Analysis of Lewis fucosyltransferase genes from the human gastric mucosa of Lewis-positive and -negative individuals. Blood. 1993 Nov 1;82(9):2915-9.

PMID 8240337 Nishihara S, Yazawa S, Iwasaki H, Nakazato M, Kudo T, Ando T, Narimatsu H. Alpha (1,3/1,4)fucosyltransferase (FucT-III) gene is inactivated by a single amino acid substitution in Lewis histo-blood type negative individuals. Biochem Biophys Res Commun. 1993 Oct 29;196(2):624-31. doi: 10.1006/bbrc.1993.2295.

PMID 8801770 Elmgren A, Börjeson C, Svensson L, Rydberg L, Larson G. DNA sequencing and screening for point mutations in the human Lewis (FUT3) gene enables molecular genotyping of the human Lewis blood group system. Vox Sang. 1996;70(2):97-103. doi: 10.1111/j.1423-0410.1996.tb01300.x.

PMID 9268337 Significance of individual point mutations, T202C and C314T, in the human Lewis (FUT3) gene for expression of Lewis antigens by the human alpha(1,3/1,4)-fucosyltransferase, Fuc-TIII

PMID 9268337 Elmgren A, Mollicone R, Costache M, Börjeson C, Oriol R, Harrington J, Larson G. Significance of individual point mutations, T202C and C314T, in the human Lewis (FUT3) gene for expression of Lewis antigens by the human alpha(1,3/1,4)-fucosyltransferase, Fuc-TIII. J Biol Chem. 1997 Aug 29;272(35):21994-8. doi: 10.1074/jbc.272.35.21994.

PMID 9703429 Pang H, Liu Y, Koda Y, Soejima M, Jia J, Schlaphoff T, Du Toit ED, Kimura H. Five novel missense mutations of the Lewis gene (FUT3) in African (Xhosa) and Caucasian populations in South Africa. Hum Genet. 1998 Jun;102(6):675-80. doi: 10.1007/s004390050760.

PMID 9987874 Lewis (FUT3) genotypes in two different Chinese populations

PMID 10211701 Pang H, Koda Y, Soejima M, Kimura H. Significance of each of three missense mutations, G484A, G667A, and G808A, present in an inactive allele of the human Lewis gene (FUT3) for alpha(1,3/1,4)fucosyltransferase inactivation. Glycoconj J. 1998 Oct;15(10):961-7. doi: 10.1023/a:1006981724233.

PMID 12424536 Distribution of Lewis (FUT3)genotype and allele: frequencies in a biethnic United States population_Cakir B, Pankow JS, Salomaa V, Couper D, Morris TL, Brantley KR, Hiller KM, Heiss G, Weston BW. Distribution of Lewis (FUT3)genotype and allele: frequencies in a biethnic United States population. Ann Hematol. 2002 Oct;81(10):558-65. doi: 10.1007/s00277-002-0508-x. Epub 2002 Oct 11.

PMID 14674375 Cooling L, Gu Y. Identification of two new single-nucleotide polymorphisms in FUT3 associated with the Lewis-null phenotype. Transfusion. 2003 Dec;43(12):1760-1. doi: 10.1111/j.0041-1132.2003.00593.x.

PMID 15383031 Two novel FUT3 alleles responsible for Lewis-null phenotypes in Sri Lanka

PMID 19175549 Soejima M, Munkhtulga L, Iwamoto S, Koda Y. Genetic variation of FUT3 in Ghanaians, Caucasians, and Mongolians. Transfusion. 2009 May;49(5):959-66. doi: 10.1111/j.1537-2995.2008.02069.x. Epub 2009 Jan 21.

PMID 32218479 Systematic sequence analysis of the FUT3 gene identifies 11 novel alleles in the Sindhi and Punjabi populations from Pakistan

Notes

Allele Name	Note #	
*FUT3*01.04*	n010	This is not a variant in grch38 - nor has anything at this site been reported in gnomAD. Reference genome has T>C.
*FUT3*01.10*	n020	In "Nishihara S, Narimatsu H, Iwasaki H, Yazawa S, Akamatsu S, Ando T, Seno T, Narimatsu I. Molecular genetic analysis of the human Lewis histo-blood group system. J Biol Chem. 1994 Nov 18;269(46)29271-8. PMID 7961897." and in "Mollicone R, Reguigne I, Kelly RJ, Fletcher A, Watt J, Chatfield S, Aziz A, Cameron HS, Weston BW, Lowe JB. Molecular basis for Lewis alpha(1,3/1,4)-fucosyltransferase gene deficiency (FUT3) found in Lewis-negative Indonesian pedigrees. J Biol Chem. 1994 Aug 19;269(33):20987-94. PMID: 8063716." the reduced activity is described...and in "Pang H, Liu Y, Koda Y, Soejima M, Jia J, Schlaphoff T, Du Toit ED, Kimura H. Five novel missense mutations of the Lewis gene (*FUT3*) in African (Xhosa) and Caucasian populations in South Africa. Hum Genet. 1998 Jun;102(6):675-80. doi: 10.1007/s004390050760. PMID: 9703429" describes the le1067 allele frequencies in different populations. These data are extended in "Liu YH, Koda Y, Soejima M, Pang H, Wang B, Kimura H. Lewis (*FUT3*) genotypes in two different Chinese populations. J Forensic Sci. 1999 Jan;44(1):82-6. PMID: 9987874." and in "Guo M, Luo G, Lu R, Shi W, Cheng H, Lu Y, Jin K, Yang C, Wang Z, Long J, Xu J, Ni Q, Liu C, Yu X. Distribution of Lewis and Secretor polymorphisms and corresponding CA19-9 antigen expression in a Chinese population. FEBS Open Bio. 2017 Oct 4;7(11):1660-1671. doi: 10.1002/2211-5463.12278. PMID: 29123975; PMCID: PMC5666394 " again showing allele frequencies in different chinese populations.
*FUT3*01.15*	n030	It is currently unclear if this allele is null - for safety Nick Gleadall has decided to opt for active but with reduced activity
*FUT3*01.15*	n031	The 484 mutation was first described in "Pang H, Liu Y, Koda Y, Soejima M, Jia J, Schlaphoff T, Du Toit ED, Kimura H. Five novel missense mutations of the Lewis gene (FUT3) in African (Xhosa) and Caucasian populations in South Africa. Hum Genet. 1998 Jun;102(6):675-80. doi: 10.1007/s004390050760. PMID: 9703429." but then in combination with other mutations; le484,667, le484,667,808 (inactive) and le202,314,484 (not expressed?). In the publication "Pang H, Koda Y, Soejima M, Kimura H. Significance of each of three missense mutations, G484A, G667A, and G808A, present in an inactive allele of the human Lewis gene (*FUT3*) for alpha(1,3/1,4)fucosyltransferase inactivation. Glycoconj J. 1998 Oct;15(10):961-7. doi: 10.1023/a:1006981724233. PMID: 10211701." expression data say tha the G484A mutation results in only a 80% reduction of transferase activity and could thus be reported as a weak genotype if such an allele was found.
*FUT3*01.16*	n040	It is currently unclear if this allele is null - for safety I have decided to opt for active but with reduced activity

Notes

Allele Name	Note #	
*FUT3*01.17.01*	n050	According to "Koda Y, Kimura H, Mekada E. Analysis of Lewis fucosyltransferase genes from the human gastric mucosa of Lewis-positive and negative individuals. Blood. 1993 Nov 1;82(9)2915-9. PMID 8219240." and to "Mollicone R, Reguigne I, Kelly RJ, Fletcher A, Watt J, Chatfield S, Aziz A, Cameron HS, Weston BW, Lowe JB. Molecular basis for Lewis alpha(1,31,4)-fucosyltransferase gene deficiency (FUT3) found in Lewis-negative Indonesian pedigrees. J Biol Chem. 1994 Aug 19;269(33)20987-94. PMID 8063716." and to "Nishihara S, Yazawa S, Iwasaki H, Nakazato M, Kudo T, Ando T, Narimatsu H. Alpha (1,3/1,4)fucosyltransferase (FucT-III) gene is inactivated by a single amino acid substitution in Lewis histo-blood type negative individuals. Biochem Biophys Res Commun. 1993 Oct 29;196(2):624-31. doi: 10.1006/bbrc.1993.2295. PMID: 8240337." this is not an inactivating mutation but rather gives a weak phenotype.
*FUT3*01N.03.01*	n060	This is not actually a variant in grch38 - nor has anything at this site been reported in gnomAD. Reference genome has C>T? According to expression experiments the 202 mutation is a null (<1%) allele (Elmgren et al. 1997) which was also confirmed as a null allele in African Xhosa population Tables 3 and 4 "Pang H, Liu Y, Koda Y, Soejima M, Jia J, Schlaphoff T, Du Toit ED, Kimura H. Five novel missense mutations of the Lewis gene (FUT3) in African (Xhosa) and Caucasian populations in South Africa. Hum Genet. 1998 Jun;102(6):675-80"
*FUT3*01N.03.01*	n061	There is one publication (Nanakorn, Natthaphon, et al. "Prevalence of Lewis Blood Group Polymorphisms in Southern Thai Blood Donors." Journal of Health Science and Medical Research 40.4 (2022): 391-400.; NOT FOUND IN PUBMED) that describes Lewis alleles in Thailand population, which conflicts the accepted knowledge that 202T>C is an inactivating mutation. However, in this publication no data are presented on *FUT3* or *FUT2* sequences (only *FUT3* genotypes) and only hemagglutination but no phenotyping of saliva was done. Thus, much more work should be published on this population and presently we feel that the data are too weak to motivate reference to this conflicting and preliminary work.
*FUT3*01N.03.11*	n070	Contradictory inbetween "Soejima M, Munkhtulga L, Iwamoto S, Koda Y. Genetic variation of FUT3 in Ghanaians, Caucasians, and Mongolians. Transfusion. 2009 May;49(5):959-66. doi: 10.1111/j.1537-2995.2008.02069.x. Epub 2009 Jan 21. PMID: 19175549" where the freqency of the le47,202,314 allele is described, in "Zhao M, Adnan A, Rakha A, Nazir S, Tian M, Zhang S, Pang H. Systematic sequence analysis of the *FUT3* gene identifies 11 novel alleles in the Sindhi and Punjabi populations from Pakistan. Sci Rep. 2020 Mar 26;10(1):5543. doi: 10.1038/s41598-020-62524-8. PMID: 32218479; PMCID: PMC7099025." the le47,202,314 allele is described but only as such and not any allele with only the G47C mutation.

Notes

Allele Name	Note #	
*FUT3*01N.17.03*	n080	"Elmgren A, Börjeson C, Svensson L, Rydberg L, Larson G. DNA sequencing and screening for point mutations in the human Lewis (*FUT3*) gene enables molecular genotyping of the human Lewis blood group system. Vox Sang. 1996;70(2):97-103. doi: 10.1111/j.1423-0410.1996.tb01300.x. PMID: 8801770." associates le202/314; le59/1067 as inactive alleles.

Track of changes

1	**Version**		**v1.0 31-DEC-2022**	**v1.1 26-FEB-2024**
2	Author	created	Nick Gleadall, December 2022	Nick Gleadall, February 2024
3	Reviewer	reviewed	Martin Olsson, December 2022	Martin Olsson, February 2024
4	General	Document created	Spread-sheets "Intro", "Allele Table", "References", "Notes" and "Versioning" created	
5	Allele	Visibility		*FUT3*01.01* until *FUT3*01.08.02* are visible now
6	**End Version**		**v1.0 31-DEC-2022**	**v1.1 26-FEB-2024**