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The Relationship between *Lewis/Secretor* Genotypes and Serum Carbohydrate Antigen 19-9 Levels in a Korean Population

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Background : The Lewis histo-blood group system consists of 2 major antigens-Le^a and Le^b-and a sialyl Lewis antigen-carbohydrate antigen (CA) 19-9. We investigated the distribution of *Lewis* genotypes and evaluated the relationship between the *Lewis/Secretor* genotypes and the serum level of CA 19-9 in a Korean population to identify whether the serum CA 19-9 levels are influenced by the *Lewis/Secretor* genotypes.

Methods : The study included 242 individuals who had no malignancies. *Lewis* genotyping was performed for the 59T>G, 508G>A and 1067T>A polymorphic sites. The *Secretor* genotype was determined through analysis of the 357C>T and 385A>T polymorphic sites and the fusion gene. Serum CA 19-9 level was analyzed using an electrochemiluminescence immunoassay.

Results : Individuals carrying the 3 common genotypes-*Le/Le, Le/le*^{59,508}, and *Le/le*^{59,1067}-accounted for 95% of the study population. In the Korean population, the allelic frequencies of *Le, Le*^{59}, *le*^{59,508}, and *le*^{59,1067} were 0.731, 0.010, 0.223, and 0.035, respectively. We found a significant difference in serum CA 19-9 concentrations among the 9 *Lewis/Secretor* genotype groups (P<0.001). The serum CA 19-9 levels in subjects with genotype groups 1 and 2 (*Le/-* and *se/se*) were higher than those with genotype groups 3-6 (*Le/-* and *Se/-*; 15.63 vs 6.64 kU/L, P<0.001).

Conclusions : *Le/Le, Le/le*^{59,508}, and *Le/le*^{59,1067} are frequent *Lewis* genotypes in Koreans. Because serum CA 19-9 levels are significantly influenced by the *Lewis/Secretor* genotypes, caution is suggested when interpreting the serum CA 19-9 levels. *(Korean J Lab Med 2010;30:51-7)*

Key Words : *Lewis genotype, Lewis/Secretor genotype, CA 19-9, Korean population*

INTRODUCTION

The Lewis histo-blood group system consists of 2 major antigens-Le^a and Le^b-and 3 common phenotypes-Le(a-b-), Le(a+b-), and Le(a-b+). The Le^a antigen is synthesized from a type 1 precursor substrate by the *Lewis*-encoded α-(1,3/1,4)-fucosyltransferase, while the Le^b antigen is synthesized from a type 1 H substrate. There are 2 alleles at the *Lewis* locus, *Le*, which encodes a functional fucosyltransferase, and *le*, which encodes a nonfunctional enzyme. The *Le*^{59} allele confers approximately the same level of enzymatic activity as the *Le* allele [1]. The *le*^{59,508} and *le*^{59,1067} alleles confer very low enzymatic activity as compared to the *Le* and *Le*^{59} alleles [2]. *Lewis* phenotype is determined by the combination of the *Lewis/Secretor* genotype. An individual homozygous for *le* expression has neither the Le^a nor the Le^b antigen. Secretors have at least 1 functional *Se* allele, while non-secretors are homozygous for nonfunctional *se* alleles. Several polymorphisms in the *Lewis* and *Secretor* genes have been reported [1-7]. Frequent polymorphisms in Koreans were 357C>T and 385A>T in the *Secretor* gene and 59T>G and 508G>A in the *Lewis*

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gene [8, 9].

Carbohydrate antigen 19-9 (CA 19-9), which is equivalent to the sialyl *Lewis* antigen, is a well-known tumor marker for pancreatic cancer [10]. Healthy individuals with an Le^a-positive secretor status may show physiologically elevated CA 19-9 concentrations in all types of secretions (e.g. sputum, saliva, bronchial/gastric secretions, bile juice, etc), in contrast to patients with a *Lewis*(a-b-) status, who have little or no CA 19-9 in their serum [11]. Usually, CA 19-9 is detected at low concentrations (<40 kU/L) in the serum of healthy individuals.

In this study, we examined the *Lewis/Secretor* genotypes and serum CA 19-9 levels, and evaluated the relationship between these 2 factors in a Korean population. We aimed to identify whether serum CA19-9 levels are influenced by the *Lewis/Secretor* genotypes.

MATERIALS AND METHODS

1. Subjects

A total of 242 individuals (161 men and 81 women) without any malignancy who had visited the health promotion center at Seoul National University Bundang Hospital, Korea, between January 1, and March 8, 2004 were enrolled in this study. The Seoul National University Bundang Hospital institutional review board approved this study. The DNA used to determine the *Lewis* and *Secretor* genotypes was extracted using a Puregene DNA Kit (Gentra, Minneapolis, MN, USA).

2. Genotyping for the *Lewis* gene

The *Lewis* genotyping was performed for the 59T>G, 508G>A, and 1067T>A polymorphic sites. The 59T>G mutation was determined by PCR with confronting two-pair primers (PCR-CTPP) [12]. In brief, PCR-CTPP is a genotyping method that uses 4 primers with similar melting temperatures. By changing the annealing temperature, different sized products are amplified on the basis of allele specificity, which can easily be visualized by gel electrophoresis. This lowers the cost and shortens genotyping times because enzymatic digestion is not required [12]. The oligonucleotide primer sequences (Bioneer Corporation, Daejeon, Korea) and experimental conditions used in the PCR-CTPP have been previously reported [13]. The 508G>A and 1067T>A mutations were determined by PCR and restriction fragment length polymorphism (PCR-RFLP) anal-

Table 1. Primer sequences for *Lewis/Secretor* genotyping by PCR-RFLP

Gene	Forward/reverse	Primer sequence
Lewis	Le59-F1	5′-CCA TGG ATC CCC TGG GTG-3′
	Le59-R1	5′-CCA CCA GCA GCT GAA ATA GCC-3′
	Le59-F2	5′-CGC TGT CTG GCC GCA CT-3′
	Le59-R2	5′-GAA GGT GGG AGG CGT GAC TTA-3′
	Le508-F	5′-ACT TGG AGC CAC CCC CTA ACT GCC A-3′
	Le508-R	5′-TGA GTC CGG CTT CCA GTT GGA CAC C-3′
	Le1067-F1	5′-CTC CCG ACA GGA CAC CAC TCC CA-3′
	Le1067-R1	5′-CTC AAG CTT CGT GCC GTG ATG ATC TCT CTG CAC-3′
	Le1067-F2	5′-CGC TCC TTC AGC TGG GCA CTG GA-3′
	Le1067-R2	5′-CGG CCT CTC AGG TGA ACC AAG AAG CT-3′
Secretor	Se357-F1	5′-CTC GAA TTC GGG CCT CCA TCT CCC AGC TAA C-3′
	Se357-R1	5′-CTC AAG CTT GCT TCT CAT GCC CGG GCA CTC-3′
	Se357-F2	5′-CAG GAT CCC CTG GCA GAA CTA CCA CAT TAA-3′
	Se357-R2	5′-AGC AGG GGT AGC CGG TGA AGC GGA CGT ACT-3′
	Se385-F0	5′-TTT CAC TGC CAC CAG CAC CTG-3′
	Se385-F1	5′-ATC AAA GGC ACT GGG ACC CAG-3′
	Se385-R1	5′-GGA CGT ACT CCC CCG GGA T-3′
	Se385-F2	5′-TGG AGG AGG AAT ACC GCC ACT-3′
	Se385-R2	5′-GTC CCC TCG GCG AAC ATG G-3′

ysis. The primer sequences for determining the 508G>A and 1067T>A mutations were reported previously [2, 4].

3. Genotyping for the *Secretor* gene

The *Secretor* genotype was determined for the 357C>T and 385A>T mutations and the fusion gene. The se^{fus} allele is due to the fusion of the *Secretor* gene and a pseudogene. The 357C>T mutation was determined by PCR-RFLP. The 357C>T mutation was detected by performing the first PCR amplification with the primers previously reported [4]. The 385A>T mutation and fusion gene were detected by PCR-CTPP genotyping [12], using primers that have been previously reported [14]. The methods for detecting mutations

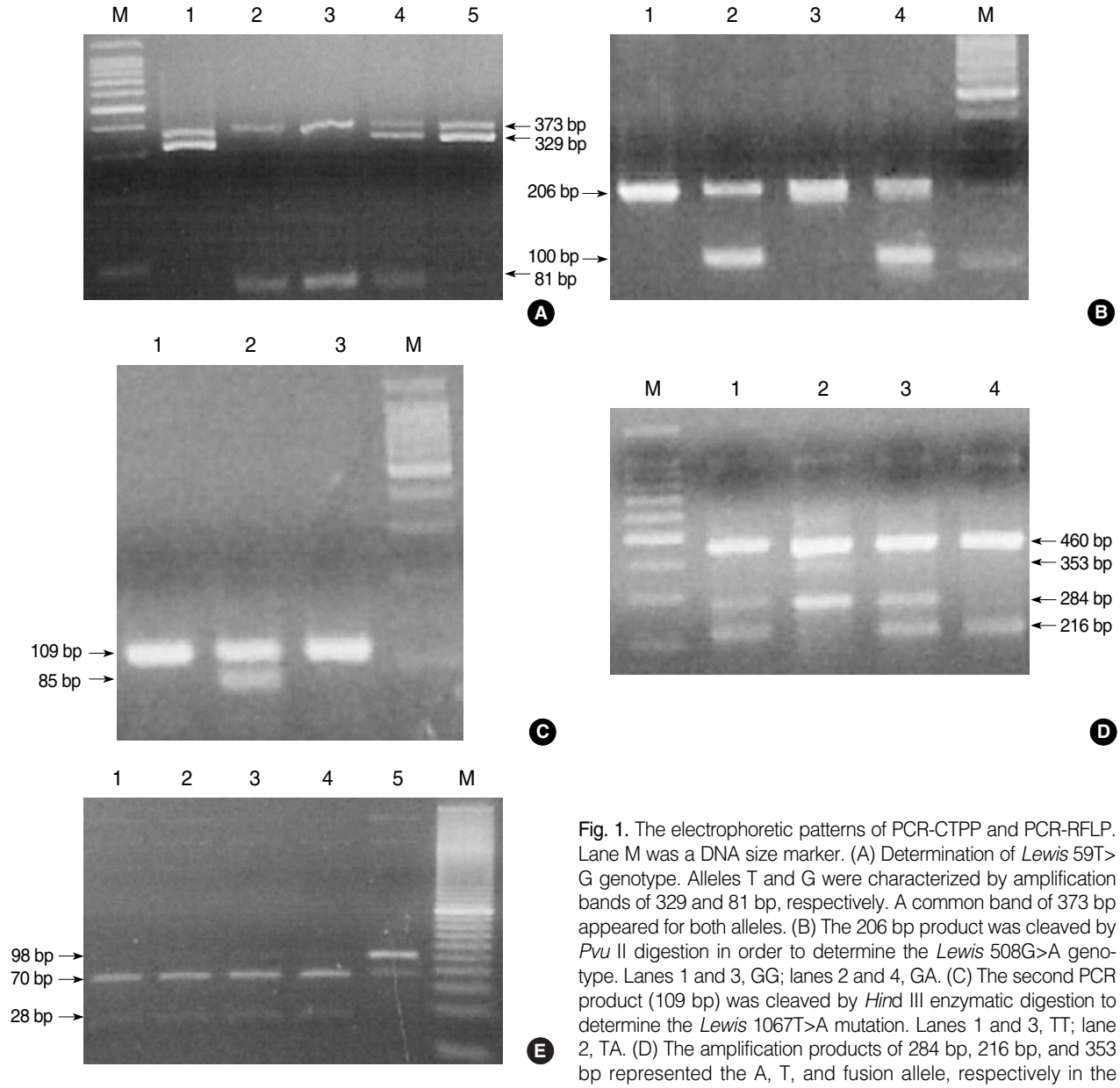

Fig. 1. The electrophoretic patterns of PCR-CTPP and PCR-RFLP. Lane M was a DNA size marker. (A) Determination of *Lewis* 59T>G genotype. Alleles T and G were characterized by amplification bands of 329 and 81 bp, respectively. A common band of 373 bp appeared for both alleles. (B) The 206 bp product was cleaved by *Pvu* II digestion in order to determine the *Lewis* 508G>A genotype. Lanes 1 and 3, GG; lanes 2 and 4, GA. (C) The second PCR product (109 bp) was cleaved by *Hin*d III enzymatic digestion to determine the *Lewis* 1067T>A mutation. Lanes 1 and 3, TT; lane 2, TA. (D) The amplification products of 284 bp, 216 bp, and 353 bp represented the A, T, and fusion allele, respectively in the *Secretor* 385A>T genotyping. A common band of 460 bp appeared for the A and T alleles. (E) Determination of C and T alleles for the *Secretor* 357C>T genotype. The second PCR product (98 bp) was cleaved by *Ase* I digestion to confirm *Secretor* 357C>T genotype. Lanes 1-4, TT; lane 5, CT.

Abbreviations: PCR-CTPP, PCR with the confronting two-pair primers; PCR-RFLP, PCR and restriction fragment length polymorphism.

in the *Se* gene using these primer sets have been described previously [15]. Primer sequences are listed in Table 1, and the representative electrophoretic patterns of PCR-RFLP and PCR-CTPP are shown in Fig. 1.

4. Determination of serum CA 19-9 concentrations

The serum CA 19-9 concentrations were analyzed using an electrochemiluminescence immunoassay kit on the Modular Analytics E 170 module (Roche Diagnostics Corporation, Indianapolis, IN, USA), according to the manufacturer's instructions.

5. Statistical analysis

The data were analyzed by Mann-Whitney U test and Kruskal-Wallis test. All significance tests performed were two-tailed, and P values <0.05 were considered statistically significant. All statistical analyses were carried out using the SPSS 12.0 statistical software program (SPSS, Chicago, IL, USA).

RESULTS

The individuals enrolled in this study consisted of 161 men and 81 women with a mean age of 50.7 yr (range, 26-72 yr). The distribution of *Lewis* genotypes within the study group is described in Table 2. Individuals carrying the 3 common genotypes-*Le/Le*, *Le/le*^{59,508}, and *Le/le*^{59,1067}-accounted for 95% of the study population. Five individuals (2.1%) were heterozygous for *Le*^{59} (*Le/Le*^{59}) and 7 (2.9%) were homozygous for *le*^{59,508} or *le*^{59,10677}, the *Lewis* genotypes with little enzymatic activity. Table 3 shows the differences in the allelic frequencies of the *Lewis* gene among various populations-Korean, African, Caucasian, Japanese, Chinese, and Taiwanese. In the Korean population, the allelic frequencies of *Le*, *Le*^{59}, *le*^{59,508}, and *le*^{59,1067} were 0.731, 0.010, 0.223, and 0.035, respectively.

The 242 subjects were classified into 9 genotype groups according to their *Lewis/Secretor* genotypes (Table 4). There was a significant difference in the serum CA 19-9 concentrations among the 9 genotype groups (P<0.001).

Serum CA 19-9 was not detected in any of the subjects that were homozygous for *le* (genotype groups 7-9; 2.9%,

Table 2. Distribution of *Lewis* genotypes in a Korean population

Genotypes	Number	%
Le/Le	119	49.2
Le/Le^{59}	5	2.1
Le/le^{59,508}	96	39.7
Le/le^{59,1067}	15	6.2
le^{59,508}/*le*^{59,508}	6	2.5
le^{59,1067}/*le*^{59,1067}	1	0.4
Total	242	100.0

Table 3. Comparison of *Lewis* allele frequencies among different populations

Allele	Korean (N=242)	Xhosa* (African) (N=100)	Caucasian* (N=100)	Japanese† (N=149)	Shenyang‡ (Chinese) (N=138)	Guangzhou† (Chinese) (N=154)	Taiwanese§ (N=137)
Le	0.731	0.500	0.675	0.607	0.750	0.675	0.682
Le^{59}	0.010	0.000	0.020	0.000	0.011	0.026	-
le^{59,508}	0.223	0.310	0.010	0.275	0.145	0.140	-
le^{59,1067}	0.035	0.025	0.130	0.114	0.054	0.123	-
le^{508}	0.000	0.000	0.000	0.000	0.000	0.000	0.128
le^{1067}	0.000	0.000	0.005	0.003	0.004	0.010	0.139
Le^{304}	-	0.020	0.005	-	-	-	-
Le^{370}	-	0.005	0.000	-	-	-	-
le^{202}	-	0.015	0.010	-	0.000	0.000	0.000
le^{202,314}	-	0.080	0.140	-	0.036	0.026	0.051
le^{202,314,484}	-	0.000	0.005	-	-	-	-
le^{484,667}	-	0.025	0.000	-	-	-	-
le^{484,667,808}	-	0.020	0.000	-	-	-	-

The allele *Le* indicates a functional allele and *le* a nonfunctional allele (-, not examined).
*Data from Pang et al. [16]; †Data from Liu et al. [7]; ‡Data from Liu et al. [22]; §Data from Liu et al. [17].

Table 4. *Lewis/Secretor* genotype-specific values for serum CA 19-9*

	Genotype groups		N	CA 19-9 (kU/L)		
	Lewis	*Secretor*		Median	Range	URL
1	*Le/Le*	*se/se*	33	16.21	5.87-79.25	15.01
2	*Le/le*	*se/se*	32	13.88	<0.60-35.09	48.06
3	*Le/Le*	*Se/se*	88	7.13	0.78-31.03	6.65
4	*Le/le*	*Se/se*	77	5.95	<0.60-27.79	18.02
5	*Le/Le*	*Se/Se*	3	13.21	12.52-25.15	-
6	*Le/le*	*Se/Se*	2	1.99	<0.60-3.38	-
7	*le/le*	*Se/Se*	1	<0.60	-	-
8	*le/le*	*Se/se*	5	<0.60	-	-
9	*le/le*	*se/se*	1	<0.60	-	-

*There was a significant difference in the serum CA 19-9 concentrations among the 9 genotype groups (P<0.001).
URL, Upper reference limit is the nonparametrically calculated 0.975 fractile.

7/242 subjects). Among the individuals with at least 1 functional *Le* allele, there were only 5 (2.1%) subjects homozygous for the functional *Se* allele (genotype groups 5 and 6). The remaining subjects (95.0%, 230/242 subjects) were in genotype groups 1–4 (*Le*/− and *se*/−). The 9 genotypes were grouped into 3 groups according to the combination of functional genotypes of the *Lewis* and *Secretor* genes: *Le*/− and *se/se* (genotype groups 1 and 2), *Le*/− and *Se*/− (genotype groups 3–6), and *le/le* and −/− (genotype groups 7–9). The serum CA 19–9 levels in subjects from genotype groups 1 and 2 (*Le*/− and *se/se*) were higher than those from genotype groups 3–6 (*Le*/− and *Se*/−; P<0.001) (Table 5).

DISCUSSION

The majority (97.1%) of Korean subjects had at least 1 functional *Le* allele (*Le*/− or Le^{59}/−). Seven individuals (2.9%) were homozygous for the nonfunctional *le* allele (*le/le*), which is a low proportion when compared with that from other ethnic populations: 22.0% in Xhosa, 9.0% in Caucasians, 8.6% in Taiwanese, 15.5% in Thai, and 12.0% in Filipinos [16, 17]. In Koreans patients with gastric cancer, approximately 10.5% (6/57 patients) have been reported to be homozygous for the *le/le* genotype [9]; however, our data, which includes the *Lewis/Secretor* genotyping, were derived from a large number of subjects who did not have any malignancy. For the *Secretor* gene, 6 alleles–*Se*, Se^{357}, se^{385}, $se^{357/385}$, se^{428}, and se^{fus}–have been reported in the Korean population [15, 18]. The nonfunctional se^{428} (428G>A) allele accounted for the majority of the Secretor gene polymorphisms in Caucasian and African populations [3, 19]. However, it was previously reported that this mutation is extremely rare in Koreans [15]. Therefore, this study did not investigate the 428G>A mutation in the *Secretor* gene.

Table 5. Comparison of the serum CA 19-9 concentrations according to *Lewis/Secretor* genotype groups

Genotype groups*	Genotype	N	CA 19-9 (kU/L)		
			Median	Range	URL
7, 8, 9	*le/le* and -/-	7	<0.60	-	-
1, 2	*Le/-* and *se/se*	65	15.63	<0.60-79.25	36.65
3, 4, 5, 6	*Le/-* and *Se/-*	170	6.64	<0.60-31.03	20.30

*Genotype groups are same as in Table 1.
URL, Upper reference limit is the nonparametrically calculated 0.975 fractile.

The serum CA 19–9 levels in the 9 genotype groups were compared to the *Lewis/Secretor* genotypes. Previous reports suggest that the status of *Lewis/Secretor* genotypes can be determined by serum CA 19–9 levels [20, 21]. Nonparametric statistical methods were used to investigate the distribution of CA 19–9 concentrations, since these concentrations were not distributed in a Gaussian manner. With the exception of genotype group 5, the CA 19–9 levels decreased in the 9 genotype groups, with the highest levels observed in group 1 and the lowest levels observed in group 9. This is similar to the results of other studies [20, 21]. The CA 19–9 levels in genotype group 5 were higher than the values inferred from a previous study [21]. Genotype group 5 only consisted of 3 subjects (1.2%); however, the cause of the elevated CA 19–9 levels is unknown. These results may be outliers or a genotype–specific result within the Korean population. Further studies should recruit more subjects belonging to genotype group 5 to identify the cause of these results. In this study, only 2.1% (5/242) of the subjects were in genotype groups 5 and 6 (*Le*/− and *Se/Se*), which when compared with the 32.6% reported in Caucasians, is very a low percentage of study participants [21]. The difference in the genotype distribution of the *Lewis/Secretor* genes may be due to ethnic specificities.

Seven subjects with the *le/le* genotype (genotype groups

7–9) showed undetectable serum levels of CA 19–9. This suggests that CA 19–9 serum levels are influenced by the homozygous *Lewis* genotype (*le/le*), which has little enzymatic activity. Although most serum CA 19–9 levels fell within the reference range, there was a significant difference between the genotype groups *Le*/– and *se/se* and *Le*/– and *Se*/–, with significantly higher CA 19–9 serum levels in the *Le*/– and *se/se* genotype group.

We should also consider the fact that subjects with at least 1 functional *Le* allele and 1 functional *Se* allele (genotype groups 3–6, 170 persons) expressed low levels of CA 19–9 in serum, with the median and the 0.975 fractile value as 6.64 and 20.30 kU/L, respectively.

This study examined the genotypes of the *Lewis/Secretor* genes and the serum CA 19–9 levels. Because serum CA 19–9 levels are significantly influenced by the *Lewis/Secretor* genotypes, caution is suggested when interpreting the serum CA 19–9 levels.

REFERENCES

1. Mollicone R, Reguigne I, Kelly RJ, Fletcher A, Watt J, Chatfield S, et al. Molecular basis for Lewis alpha(1,3/1,4)-fucosyltransferase gene deficiency (FUT3) found in Lewis-negative Indonesian pedigrees. J Biol Chem 1994;269:20987-94.
2. Nishihara S, Narimatsu H, Iwasaki H, Yazawa S, Akamatsu S, Ando T, et al. Molecular genetic analysis of the human Lewis histo-blood group system. J Biol Chem 1994;269:29271-8.
3. Kelly RJ, Rouquier S, Giorgi D, Lennon GG, Lowe JB. Sequence and expression of a candidate for the human Secretor blood group alpha (1,2)fucosyltransferase gene (FUT2). Homozygosity for an enzyme-inactivating nonsense mutation commonly correlates with the non-secretor phenotype. J Biol Chem 1995;270:4640-9.
4. Kudo T, Iwasaki H, Nishihara S, Shinya N, Ando T, Narimatsu I, et al. Molecular genetic analysis of the human Lewis histo-blood group system. II. Secretor gene inactivation by a novel single missense mutation A385T in Japanese nonsecretor individuals. J Biol Chem 1996; 271:9830-7.
5. Koda Y, Soejima M, Liu Y, Kimura H. Molecular basis for secretor type alpha(1,2)-fucosyltransferase gene deficiency in a Japanese population: a fusion gene generated by unequal crossover responsible for the enzyme deficiency. Am J Hum Genet 1996;59:343-50.
6. Rouquier S, Lowe JB, Kelly RJ, Fertitta AL, Lennon GG, Giorgi D. Molecular cloning of a human genomic region containing the H blood group alpha(1,2)fucosyltransferase gene and two H locus-related DNA restriction fragments. Isolation of a candidate for the human Secretor blood group locus. J Biol Chem 1995;270:4632-9.
7. Liu Y, Koda Y, Soejima M, Uchida N, Kimura H. PCR analysis of Lewis-negative gene mutations and the distribution of Lewis alleles in a Japanese population. J Forensic Sci 1996;41:1018-21.
8. Song SY, An SS, Ryu SW, Kim JS, Suh IB. Evaluation of the genotypes of the Lewis blood group in a Korean population using direct sequencing. Korean J Hematol 2008;43:34-42.
9. Kim MJ, Kim HS, Song KS, Noh SH, Kim HG, Paik YK, et al. Altered expression of Lewis antigen on tissue and erythrocytes in gastric cancer patients. Yonsei Med J 2002;43:427-34.
10. Hayashi N, Nakamori S, Okami J, Nagano H, Dono K, Umeshita K, et al. Association between expression levels of CA 19-9 and N-acetylglucosamine-beta;1,3-galactosyltransferase 5 gene in human pancreatic cancer tissue. Pathobiology 2004;71:26-34.
11. Lamerz R. Role of tumour markers, cytogenetics. Ann Oncol 1999; 10:145-9.
12. Hamajima N, Saito T, Matsuo K, Tajima K. Competitive amplification and unspecific amplification in polymerase chain reaction with confronting two-pair primers. J Mol Diagn 2002;4:103-7.
13. Shibata A, Hamajima N, Ikehara Y, Saito T, Matsuo K, Katsuda N, et al. ABO blood type, Lewis and Secretor genotypes, and chronic atrophic gastritis: a cross-sectional study in Japan. Gastric Cancer 2003;6:8-16.
14. Hamajima N, Shibata A, Ikehara Y, Katsuda N, Mori S, Ito H, et al. Lack of consistency in the associations of Helicobacter pylori seropositivity with Se and Le polymorphisms among Japanese. Gastric Cancer 2002;5:194-200.
15. Park KU, Song J, Han KS, Kim JQ. The fusion allele of the FUT2 (secretor type alpha(1,2)-fucosyltransferase) gene at a high frequency and a new se385 allele in a Korean population. Ann Hematol 2005; 84:656-60.
16. Pang H, Liu Y, Koda Y, Soejima M, Jia J, Schlaphoff T, et al. Five novel missense mutations of the Lewis gene (FUT3) in African (Xhosa) and Caucasian populations in South Africa. Hum Genet 1998;102: 675-80.
17. Liu TC, Chang JG, Lin SF, Chang WC, Yang TY, Lin CL, et al. Lewis

(FUT3) genotypes in Taiwanese, Thai, and Filipino populations. Ann Hematol 2000;79:599-603.

18. Liu YH, Koda Y, Soejima M, Pang H, Wang BJ, Kim DS, et al. The fusion gene at the ABO-secretor locus (FUT2): absence in Chinese populations. J Hum Genet 1999;44:181-4.
19. Liu Y, Koda Y, Soejima M, Pang H, Schlaphoff T, du Toit ED, et al. Extensive polymorphism of the FUT2 gene in an African (Xhosa) population of South Africa. Hum Genet 1998;103:204-10.
20. Narimatsu H, Iwasaki H, Nakayama F, Ikehara Y, Kudo T, Nishihara S, et al. Lewis and secretor gene dosages affect CA19-9 and DUPAN-2 serum levels in normal individuals and colorectal cancer patients. Cancer Res 1998;58:512-8.
21. Vestergaard EM, Hein HO, Meyer H, Grunnet N, Jorgensen J, Wolf H, et al. Reference values and biological variation for tumor marker CA 19-9 in serum for different Lewis and secretor genotypes and evaluation of secretor and Lewis genotyping in a Caucasian population. Clin Chem 1999;45:54-61.
22. Liu YH, Koda Y, Soejima M, Pang H, Wang B, Kimura H. Lewis (FUT3) genotypes in two different Chinese populations. J Forensic Sci 1999;44:82-6.