doi: 10.3325/cmj.2009.50.305

Genetic Polymorphism and Haplotype Analysis of 4 Tightly Linked X-STR Duos in Koreans

Eun Jin Lim[1*], Hwan Young Lee[1,2*], Jeong Eun Sim[1], Woo Ick Yang[1], Kyoung-Jin Shin[1,2]

[1]Department of Forensic Medicine and Brain Korea 21 Project for Medical Science, Yonsei University College of Medicine, Seoul, Korea

[2]Human Identification Research Center, Yonsei University, Seoul, Korea

*The first two authors equally contributed to this work

Aim To investigate genetic polymorphism and haplotypes of tightly linked X-chromosomal short tandem repeat (X-STR) clusters in Koreans.

Methods Four X-STR duos in the linkage group 1-4 (DXS10135-DXS8378, DXS7132-DXS10074, HPRTB-DXS10101, and DXS10134-DXS7423) were investigated in 450 unrelated Koreans (300 men and 150 women) using the Mentype Argus X-8 Polymerase Chain Reaction Amplification Kit.

Results No significant deviation from Hardy-Weinberg equilibrium was observed in any of the 8 loci. DXS10135 was the most polymorphic X-STRs, with 25 alleles and DXS7423 was the least informative, with 5 alleles. Eleven off-ladder alleles and a triallelic pattern were observed, and these alleles were characterized by cloning and sequencing analysis. In 300 Korean men, 38 to 59 haplotypes were observed for each linkage duo with 91.6-96.6% of haplotype diversities. However, due to the low genetic diversity of DXS7423, the X-STR duo in linkage group 4 (DXS10134-DXS7423), in comparison with other linkage duos, had considerably lower haplotype diversity values (91.6%) with 3 common haplotypes (35-15, 36-15, and 37-15) observed in 44.3% of Koreans.

Conclusion Four X-STR duos in the linkage group 1-4 will be able to provide a powerful tool for solving complex kinship cases in Koreans. However, to increase the haplotype diversity in the linkage group 4, it will be useful to discover a new marker for Asians that can serve as an adequate substitute for DXS7423 or at least complement the existing linkage duo of DXS10134-DXS7423.

Received: October 27, 2008.

Accepted: February 10, 2009.

Correspondence to:
Kyoung-Jin Shin
Department of Forensic Medicine
Yonsei University College of Medicine
250 Seongsanno, Seodaemun-Gu
Seoul 120-752, Korea
kjshin@yuhs.ac

Gonosomal markers have been efficiently used for solving deficiency cases (1,2). Due to hemizygosity in men and high mean exclusion chances, X-chromosomal short tandem repeats (X-STR) are particularly helpful in paternity testing and kinship analyses, such as father-daughter, mother-son, and grandmother-granddaughter kinship testing, or the kinship testing of putative sisters (1). However, when second and third degree kinships are investigated, extremely polymorphic STRs might be required (3). As the degree of polymorphism is limited in most STRs and highly polymorphic STRs like DXS10011 are prone to mutations (4,5), it has recently been suggested that stable haplotypes of closely linked loci are used in kinship testing instead of a single STR (2).

This approach of substituting single STRs with haplotypes consisting of clustered STRs resulted in the division of the chromosome X into the linkage groups 1-4 located at Xp22, Xq12, Xq26, and Xq28, each of which yields independent genotype information (2,6). Especially, 4 X-STR duos in the linkage groups 1-4 (DXS10135-DXS8378, DXS7132-DXS10074, HPRTB-DXS10101, and DXS10134-DXS7423) have been widely investigated in various population groups (6-12). Since each of the 4 STR clusters spans less than 0.5 cM, the clusters represent stable haplotypes, thereby providing highly informative tools for kinship testing (2,6).

In the present study, we investigated the polymorphisms and haplotypes of the 4 tightly linked X-STR duos in Koreans and evaluated their efficiency in forensic practice. In addition, we provided relevant information about population differences with respect to allele distribution patterns and haplotype diversities.

MATERIALS AND METHODS

DNA samples

Blood or buccal samples from 450 unrelated Koreans living in Seoul (300 men and 150 women), including 150 men and 150 women already typed for 9 X-STRs (13,14), were analyzed. Genomic DNA was extracted using a QIAamp DNA Mini Kit (Qiagen, Hilden, Germany) according to the manufacturer's instructions, and the DNA was quantitated using NanoDrop 1000 spectrophotometer (Thermo Fisher Scientific, Wilmington, DE, USA), following the manufacturer's recommendation. The study was performed in accordance with the ethical standards of the Declaration of Helsinki.

Polymerase chain reaction (PCR) amplification and genotyping

The genomic DNA was amplified using the Mentype Argus X-8 PCR Amplification Kit (Biotype AG, Dresden, Germany) and the PCR products were analyzed by capillary electrophoresis using an ABI PRISM 310 Genetic Analyzer (Applied Biosystems, Foster City, CA, USA) according to the Mentype Argus X-8 PCR Amplification Kit manual (15). The fragment sizes were determined using the GeneScan 3.7 software (Applied Biosystems) and the allele designations were carried out using Genotyper 3.7 software (Applied Biosystems) with the Argus X-8_v1.gta macro (Biotype AG).

Sequence analysis of off-ladder alleles

Sequence analyses were performed on samples which contained alleles that could not be designated using the allelic ladder of the Mentype Argus X-8 PCR Amplification Kit. Primers for PCR amplification of off-ladder alleles were designed using the Primer 3 software (http://frodo.wi.mit.edu/primer3/input.htm) (Table 1). Each PCR product was cloned using the TOPO TA Cloning Kit (Invitrogen, Carlsbad, CA, USA) following the manufacturer's recommendation. Then, at least two clones were chosen and sequenced on an ABI 3730 Genetic Analyzer using a BigDye Terminator Cycle Sequencing Ready Reaction Kit (Applied Biosystems) according to the manufacturer's instruction. The allele nomenclature followed the guidelines of the DNA commission of the International Society for Forensic Genetics (16).

TABLE 1. Polymerase chain reaction and sequencing primers for sequence analysis of the observed off-ladder alleles from the Mentype Argus X-8 kit

Locus	Sequence (5′ to 3′)
DXS7132-F	GGC TCC CCA TAT TCT CAG AC
DXS7132-R	CAC TCC TGG TGC CAA ACT CT
DXS8378-F	TTT CCA TCC TGG GAC AGT TC
DXS8378-R	TGG CAA AAC CCC ATC TCT AC
DXS10074-F	ACT TCC TAC TGC CCC ACC TT
DXS10074-R	CCT TCC TTC CCA TGT TCT CA
DXS10134-F	TGA GAC CAG GAG GTT GAA GC
DXS10134-R	TGA TGG ACA TTT GGG TTG TC
DXS10135-F	AGC CAA GAA CAT TTT TCA GTC A
DXS10135-R	AGC CTG AAG ACC ACA CAT GA

Statistical analysis

Polymorphism information content, heterozygosity, mean exclusion chances for trio and duo cases, and power of dis-

TABLE 2. Allele frequencies of 8 X-chromosomal short tandem repeat loci in 450 Koreans (300 men and 150 women)

Allele	DXS7132	DXS7423	DXS8378	HPRTB	DXS10074	DXS10101	DXS10134	DXS10135
7			0.0017					
9			0.0050					
10	0.0017		0.5767	0.0033				
11	0.0067		0.3000	0.0400				
12	0.0833		0.1117	0.3183	0.0033			
13	0.2017	0.0017	0.0050	0.4067	0.0017			
14	0.3133	0.2833		0.1917	0.0117			
15	0.2983	0.6583		0.0300	0.0617			
16	0.0717	0.0533		0.0100	0.1833			0.0100
17	0.0183	0.0033			0.3067			0.0100
17.3					0.0033			
18	0.0050				0.2750			0.0666
19					0.1267			0.0882
20					0.0250			0.1032
21					0.0017			0.1314
21.3								0.0033
22								0.1265
22.2								0.0017
23								0.0799
24								0.0765
25								0.0599
26								0.0333
26.2						0.0017		
27						0.0117		0.0499
28						0.0167		0.0516
28.2						0.0167		
29						0.0317		0.0349
29.2						0.0450		0.0017
30						0.1017	0.0017	0.0150
30.2						0.0917		
31						0.1767	0.0017	0.0166
31.1						0.0017		
31.2						0.1467		
32						0.1633	0.0250	0.0183
32.2						0.0783		
33						0.0683	0.0317	0.0100
33.2						0.0300		
34						0.0150	0.0717	0.0033
34.2						0.0033	0.0017	
35							0.1567	0.0033
35.3							0.0033	
36							0.2217	0.0033
37							0.2183	0.0017
37.1							0.0017	
37.3							0.0117	
38							0.1250	
38.3							0.0267	
39							0.0650	
39.3							0.0083	
40							0.0150	
41							0.0017	
41.3							0.0050	
42.3							0.0017	
43.3							0.0050	

crimination for men and women were calculated at the ChrX research homepage (http://www.chrx-str.org). Exact tests of the Hardy-Weinberg equilibrium and the population differentiation were carried out using the Arlequin 2.0 software (http://lgb.unige.ch/arlequin). Data from German (6), Ghanaian (11), and Japanese (12) populations were used for the exact test of population differentiation. Haplotypes of 4 closely linked STR duos were obtained from male genotypes and haplotype diversity was calculated using Arlequin 2.0 software.

RESULTS

Genetic polymorphism of 8 X-STR loci

Allele frequencies of 8 X-STR loci (DXS7132, DXS7423, DXS8378, HPRTB, DXS10074, DXS10101, DXS10134, and DXS10135) are shown in Table 2, and the values for polymorphism information content, heterozygosity, mean exclusion chance, and power of discrimination are shown in Table 3. DXS10135 was the most polymorphic X-STR, with 25 alleles, and DXS7423 was the least polymorphic one, with 5 alleles. In particular, the most frequently observed alleles of the DXS7423 and DXS8378 loci had 65.8% and 57.7% occurrences, respectively. Forensic efficiency parameters also demonstrated that the DXS7423 and DXS8378 loci were much less informative in Koreans than in Germans (6). No significant deviations from the Hardy-Weinberg equilibrium were observed in these 8 markers (Table 3).

The allele frequencies of the 8 X-STR loci in the Korean, German, Ghanaian, and Japanese populations were compared with the exact test of population differentiation (6,11,12). We found no significant differences between Korean and Japanese populations in all 8 loci; *P*-values of population comparison were 0.292 for DXS7132, 0.270 for DXS7423, 0.128 for DXS8378, 0.040 for HPRTB, 0.957 for DXS10074, 0.468 for DXS10101, 0.030 for DXS10134 and 0.019 for DXS10135. However, the German and Ghanaian populations showed significant differences from the Korean population ($P < 0.001$) in almost all loci. For the locus DXS7132, a significant difference could not be detected between the Korean and Ghanaian populations ($P = 0.026$).

Sequence structure of off-ladder alleles

At 5 X-STR loci, 11 off-ladder alleles were observed in 15 samples: in 4 samples at DXS7132 (allele 10 and 18), in 1 sample at DXS8378 (allele 7), in 2 samples at DXS10074 (allele 17.3), in 3 samples at DXS10134 (allele 30, 34.2, and 37.1), and in 5 samples at DXS10135 (allele 21.3, 22.2, 29.2, and 37). All these off-ladder alleles were confirmed by cloning and sequencing analysis and their repeat structures were described in Table 4. Alleles 10 and 18 at DXS7132, allele 7 at DXS8378, allele 30 at DXS10134, and allele 37 at DXS10135 were found to have a regular repeat motif, but the other apparent microvariant alleles contained an insertion/deletion of nucleotides within or beyond repeat motifs. Two microvariant alleles at DXS10074 (17.3 with different sequence structure) and 3 microvariant alleles at DXS10135 (21.3, 22.2, and 29.2) contained variations in core repeat units, while 2 microvariant alleles at DXS10134 (34.2 and 37.1) and 1 microvariant allele at DXS10135 (21.3) had variations in the non-core repeat units within or adjacent to the repeat motifs. The allele 34.2 at DXS10134 contained a 6 bp (gacaga) of non-core repeat unit deletion within the repeat motif (genuine allele of 36). The allele 37.1 at DXS10134 and the allele 21.3 at DXS10135 had a 1 bp insertion within the upstream flanking region and a 5 bp (agaga) deletion at the downstream flanking region, respectively (genuine alleles 37 and 23, respectively). In addition, at DXS10135, a triallelic pattern (24-26-28) was ob-

TABLE 3. Forensic statistical parameters of 8 X-chromosomal short tandem repeat loci calculated in a Korean population*

Parameter	DXS7132	DXS7423	DXS8378	HPRTB	DXS10074	DXS10101	DXS10134	DXS10135	Combined
PIC	0.722	0.412	0.494	0.639	0.742	0.875	0.834	0.914	
Het_{obs} †	0.767	0.433	0.573	0.653	0.840	0.920	0.887	0.913	
Het_{exp}	0.761	0.485	0.565	0.695	0.777	0.888	0.852	0.921	
MEC_{trio}	0.722	0.412	0.494	0.639	0.742	0.875	0.834	0.914	>0.9999
MEC_{duo}	0.586	0.276	0.350	0.494	0.610	0.788	0.729	0.847	0.9997
PD_{female}	0.904	0.662	0.740	0.852	0.916	0.976	0.961	0.988	>0.9999
PD_{male}	0.760	0.484	0.565	0.694	0.776	0.886	0.851	0.920	>0.9999
HWE†	0.618	0.200	0.199	0.567	0.386	0.264	0.246	0.016	

*Abbreviations: PIC – polymorphic information content; Het_{obs} – observed heterozygosity; Het_{exp} – expected heterozygosity; MEC_{trio} – mean exclusion chance in trios involving daughters; MEC_{duo} – mean exclusion chance in father/daughter or mother/son duos; PD_{female} – power of discrimination in women; PD_{male} – power of discrimination in men; HWE – Hardy-Weinberg equilibrium.
†*P* value calculated using the female data.

TABLE 4. Off-ladder alleles of 8 X-chromosomal short tandem repeat loci in a Korean population

Locus	Allele*	Repeat structure†	N‡
DXS7132	10	$(TCTA)_{10}$	1
	18	$(TCTA)_{18}$	3
DXS8378	7	$(CTAT)_{7}$	1
DXS10074	17.3	$(AAGA)_4AGA(AAGA)_{10}AAGG(AAGA)_2$	1
	17.3	$(AAGA)_{12}AAA(AAGA)_2AAGG(AAGA)_2$	1
DXS10134	30	$(GAAA)_3$-gaga-$(GAAA)_4$-aa-(GAAA)-gaga-$(GAAA)_4$-gaga-$(gacaga)_3$-(GAAA)-gtaa-$(GAAA)_3$-aaa-$(GAAA)_4$-aaa-$(GAAA)_{10}$	1
	34.2 (36)	$(GAAA)_3$-gaga-$(GAAA)_4$-aa-(GAAA)-gaga-$(GAAA)_4$-gaga-$(gacaga)_2$-~~gacaga~~-(GAAA)-gtaa-$(GAAA)_3$-aaa-$(GAAA)_4$-aaa-$(GAAA)_{16}$	1
	37.1 (37)	[a]$(GAAA)_3$-gaga-$(GAAA)_4$-aa-(GAAA)-gaga-$(GAAA)_4$-gaga-$(gacaga)_3$-(GAAA)-gtaa-$(GAAA)_3$-aaa-$(GAAA)_4$-aaa-$(GAAA)_{17}$	1
DXS10135	21.3	$(AAGA)_3$-gaaag-$(GAAA)_{15}GAA(GAAA)_3$	1
	21.3 (23)	$(AAGA)_3$-gaaag-$(GAAA)_{20}$-~~agaga~~	1
	22.2	$(AAGA)_3$-gaaag-$(GAAA)_{12}AA(GAAA)_7$	1
	29.2	$(AAGA)_3$-gaaag-$(GAAA)_{15}GA(GAAA)_5GGAA(GAAA)_3GGAA(GAAA)$	1
	37	$(AAGA)_3$-gaaag-$(GAAA)_{28}GGAA(GAAA)_3GGAA(GAAA)$	1

*The numbers in parentheses are genuine alleles identified by sequence analysis. The allele nomenclature follows the guidelines of the DNA commission of the International Society for Forensic Genetics (16).
†Deletion and insertion are indicated with strikethrough and in square brackets, respectively.
‡The number of samples showing off-ladder allele.

served in the female sample, and this characterization was confirmed by cloning and sequencing.

Haplotype analysis

Table 5 shows the haplotype frequencies of the 4 linkage groups in 300 Korean men. The 4 linkage duos of DXS10135-DXS8378, DXS7132-DXS10074, HPRTB-DXS10101, and DXS10134-DXS7423 revealed 56, 41, 59, and 38 haplotypes, respectively, and their haplotype diversity values were all higher than 0.9. Of all the observed haplotypes, 68% showed frequencies <0.02, and some haplotypes (35-15, 36-15, and 37-15 of DXS10134-DXS7423) showed very high frequencies >0.10 (0.12, 0.18, and 0.14, respectively).

DISCUSSION

Forensic efficiency parameters indicated that the 8 X-STRs in the present study were suitable for forensic applications in Koreans. These values were still generally lower than in Germans (6); moreover, the values for DXS7423 and DXS8378 in Koreans were particularly low. The test for population differentiation also indicated a significant difference between Korean and German populations (6). However, Korean and Japanese populations showed similar allele distribution patterns across all 8 loci, implying genetic similarity according to the geographic location (12).

Sequencing analysis of 11 off-ladder alleles indicated that most off-ladder alleles in the present study had similar sequence structure to those reported in the Mentype Argus X-8 kit manual and those studied in a previous report (6,7,15). However, alleles 34.2 and 37.1 at DXS10134 and allele 21.3 (genuine allele of 23) at DXS10135 were first observed here, and the microvariant alleles at DXS10134 and DXS10135 showed somewhat different sequence structures in Koreans. Particularly, 3 microvariant alleles at DXS10135 (21.3, 22.2, and 29.2) in Koreans were caused by the addition or deletion of partial core repeat units, but most microvariant alleles observed in Germans and Hungarians were caused by variation at the 3' flanking region (6,7). In addition, the triallelic pattern (24-26-28) observed at DXS10135 was assumed to be a type 1 triallelic pattern (17), which might have originated from a somatic mutation of one allele during an individual's development, since this pattern showed an imbalance in amounts between the 3 alleles.

Since stable haplotypes of closely linked X-STR loci were recently suggested for use in kinship testing instead of a single STR, the haplotype analysis of 4 linked X-STR duos was carried out in 300 Korean men. A total of 38 to 59 haplotypes for each linkage duo and 91.6 to 96.6% of haplotype diversities were observed, which are slightly lower values than those found in Germans (96.0 – 97.6%) (6). Although each linkage duo was proved to be high-

TABLE 5. Haplotype frequencies (F) of 4 linked X-chromosomal short tandem repeat duos in 300 Korean men

No	DXS10135	DXS8378	F	DXS7132	DXS10074	F	HPRTB	DXS10101	F	DXS10134	DXS7423	F
1	16	10	0.0067	10	17	0.0033	10	30	0.0033	32	14	0.0067
2	16	12	0.0033	11	17	0.0033	10	32	0.0033	32	15	0.0100
3	17	10	0.0067	11	18	0.0067	11	29	0.0033	33	14	0.0067
4	17	11	0.0067	12	15	0.0067	11	30.2	0.0133	33	15	0.0133
5	18	10	0.0367	12	16	0.0233	11	31	0.0233	33	16	0.0033
6	18	11	0.0167	12	17	0.0433	11	31.2	0.0033	34	14	0.0267
7	18	12	0.0033	12	18	0.0133	11	33	0.0033	34	15	0.0300
8	19	9	0.0033	12	19	0.0100	12	26.2	0.0033	34	16	0.0033
9	19	10	0.0533	12	20	0.0067	12	28	0.0067	35	14	0.0400
10	19	11	0.0467	13	14	0.0033	12	28.2	0.0033	35	15	0.1200
11	19	12	0.0167	13	15	0.0167	12	29.2	0.0100	35	16	0.0033
12	20	10	0.0533	13	16	0.0133	12	30	0.0233	35	17	0.0033
13	20	11	0.0333	13	17	0.0867	12	30.2	0.0267	35.3	14	0.0033
14	20	12	0.0100	13	18	0.0533	12	31	0.0400	36	13	0.0033
15	21	10	0.0633	13	19	0.0267	12	31.1	0.0033	36	14	0.0533
16	21	11	0.0333	13	20	0.0033	12	31.2	0.0533	36	15	0.1800
17	21	12	0.0100	14	14	0.0033	12	32	0.0600	36	16	0.0067
18	21.3	10	0.0033	14	15	0.0233	12	32.2	0.0267	36	17	0.0033
19	22	10	0.0767	14	16	0.0533	12	33	0.0433	37	14	0.0533
20	22	11	0.0567	14	17	0.1067	12	33.2	0.0033	37	15	0.1433
21	22	12	0.0067	14	18	0.0733	12	34	0.0067	37	16	0.0333
22	22	13	0.0067	14	19	0.0600	13	27	0.0033	37.1	16	0.0033
23	22.2	10	0.0033	14	20	0.0100	13	28	0.0100	37.3	15	0.0067
24	23	10	0.0767	14	21	0.0033	13	28.2	0.0133	38	14	0.0333
25	23	11	0.0033	15	12	0.0067	13	29	0.0167	38	15	0.0700
26	23	12	0.0100	15	13	0.0033	13	29.2	0.0133	38	16	0.0067
27	24	10	0.0333	15	15	0.0200	13	30	0.0433	38.3	14	0.0067
28	24	11	0.0133	15	16	0.0700	13	30.2	0.0267	38.3	15	0.0133
29	24	12	0.0100	15	17	0.0467	13	31	0.0700	39	14	0.0167
30	25	10	0.0467	15	18	0.0900	13	31.2	0.0833	39	15	0.0500
31	25	11	0.0100	15	19	0.0333	13	32	0.0567	39	16	0.0033
32	25	12	0.0067	15	20	0.0033	13	32.2	0.0367	39.3	14	0.0067
33	26	10	0.0167	16	15	0.0067	13	33	0.0100	39.3	15	0.0033
34	26	11	0.0133	16	16	0.0100	13	33.2	0.0067	40	14	0.0033
35	26	12	0.0033	16	17	0.0133	13	34	0.0033	40	15	0.0133
36	27	10	0.0333	16	18	0.0200	14	27	0.0033	41.3	15	0.0067
37	27	11	0.0167	16	19	0.0067	14	28	0.0033	42.3	15	0.0033
38	28	9	0.0033	17	17	0.0033	14	28.2	0.0033	43.3	15	0.0067
39	28	10	0.0233	17	18	0.0067	14	29	0.0033			
40	28	11	0.0233	18	18	0.0033	14	29.2	0.0167			
41	28	12	0.0133	18	19	0.0033	14	30	0.0200			
42	29	9	0.0033				14	30.2	0.0133			
43	29	10	0.0100				14	31	0.0267			
44	29	11	0.0200				14	31.2	0.0233			
45	29.2	11	0.0033				14	32	0.0167			
46	30	10	0.0033				14	32.2	0.0100			
47	30	11	0.0067				14	33	0.0333			
48	30	12	0.0033				14	33.2	0.0133			
49	31	10	0.0033				15	29.2	0.0033			
50	31	11	0.0033				15	30	0.0133			
51	32	10	0.0100				15	31	0.0067			
52	33	10	0.0067				15	31.2	0.0033			
53	34	10	0.0033				15	32	0.0100			
54	35	10	0.0033				15	33	0.0033			
55	36	10	0.0033				15	34	0.0033			
56	37	11	0.0033				16	29	0.0033			
57							16	31	0.0033			
58							16	33	0.0033			
59							16	33.2	0.0033			
h*			0.9640 ± 0.0029			0.9473 ± 0.0038			0.9662 ± 0.0029			0.9157 ± 0.0073

*Haplotype diversity ± standard deviation.

ly informative for forensic applications, the linkage group 4 (DXS10134-DXS7423), in comparison with other linkage duos, had considerably lower haplotype diversity values (91.6%) with 3 common haplotypes (35-15, 36-15, and 37-15) observed in 44.3% of Koreans. This finding may be explained by the very low genetic diversity of DXS7423 in Koreans; these haplotype distribution patterns were also observed in a Japanese population (6). Since Germans (6), Hungarians (7), and Ghanaians (6), however, showed high haplotype diversity values and relatively even haplotype distribution patterns across all 4 X-STR duos, there will be a need for discovering a new marker for Asians that can serve as an adequate substitute for DXS7423 or at least complement the existing linkage duo of DXS10134-DXS7423. A recent report has suggested that DXS10146 and DXS10147 are two additional candidates that could be included into this linkage group to increase discrimination capacity (18). However, two recombination events have been observed between DXS10146 and DXS10134, and DXS10147 has been shown to have only a fairly low degree of polymorphism (18). Therefore, to evaluate the efficiency of certain markers for use in haplotype complexes along with other markers, and to quantify the genetic distance between markers with greater precision, the investigation of a much greater number of checked meiosis should be conducted with regard to ethnic background.

To summarize, the 4 X-STR duos in the linkage group 1-4 can provide a powerful tool for solving complex kinship cases in Koreans. To verify the usefulness of these haplotypes in family tree reconstruction, however, linkage analysis, determination of mutation rates, and the accurate recombination frequency between these linked markers should be performed before introducing them into forensic practice.

Acknowledgments

This work was supported by the Korea Science and Engineering Foundation (KOSEF) grant funded by the Korean government (MEST) (No. M10740030002-07N4003-00210).

References

1 Szibor R, Krawczak M, Hering S, Edelmann J, Kuhlisch E, Krause D. Use of X-linked markers for forensic purposes. Int J Legal Med. 2003;117:67-74. Medline:12690502

2 Szibor R. X-chromosomal markers: past, present and future. Forensic Sci Int; Genet. 2007;1:93-9. Medline:19083736 doi:10.1016/j.fsigen.2007.03.003

3 Hering S, Augustin C, Edelmann J, Heidel M, Dressler J, Rodig H, et al. DXS10079, DXS10074 and DXS10075 are STRs located within a 280-kb region of Xq12 and provide stable haplotypes useful for complex kinship cases. Int J Legal Med. 2006;120:337-45. Medline:16344967 doi:10.1007/s00414-005-0061-y

4 Brinkmann B, Klintschar M, Neuhuber F, Huhne J, Rolf B. Mutation rate in human microsatellites: influence of the structure and length of the tandem repeat. Am J Hum Genet. 1998;62:1408-15. Medline:9585597 doi:10.1086/301869

5 Hering S, Brundirs N, Kuhlisch E, Edelmann J, Plate I, Benecke M, et al. DXS10011: studies on structure, allele distribution in three populations and genetic linkage to further q-telomeric chromosome X markers. Int J Legal Med. 2004;118:313-9. Medline:15248074 doi:10.1007/s00414-004-0467-y

6 Becker D, Rodig H, Augustin C, Edelmann J, Gotz F, Hering S, et al. Population genetic evaluation of eight X-chromosomal short tandem repeat loci using Mentype Argus X-8 PCR amplification kit. Forensic Sci Int; Genet. 2008;2:69-74. Medline:19083792 doi:10.1016/j.fsigen.2007.08.013

7 Zalan A, Volgyi A, Brabetz W, Schleinitz D, Pamjav H. Hungarian population data of eight X-linked markers in four linkage groups. Forensic Sci Int. 2008;175:73-8. Medline:17590298 doi:10.1016/j.forsciint.2007.05.012

8 Barbaro A, Cormaci P, Votano S, Barbaro A. Population data of 8 X-STRs in South Italy (Calabria) using the Mentype® Argus X-8 PCR Amplification Kit (Biotype). Forensic Science International: Genetics Supplement Series. 2008;1:135-9. doi:10.1016/j.fsigss.2007.10.109

9 Ruivo D, Ribeiro T, Espinheira R, Geada H. Use of eight X-chromosomal STRs in paternity investigation. Forensic Science International: Genetics Supplement Series. 2008;1:522-4. doi:10.1016/j.fsigss.2007.10.001

10 Branicki W, Wolanska-Nowak P, Parys-Proszek A, Kupiec T. Application of the Mentype Argus X-8 Kit to forensic casework. Problems of Forensic Sciences. 2008;73:53-64.

11 Thiele K, Loffler S, Loffler J, Gunthner F, Nitschke K, Edelmann J, et al. Population data of eight X-chromosomal STR markers in Ewe individuals from Ghana. Forensic Science International: Genetics Supplement Series. 2008;1:167-9. doi:10.1016/j.fsigss.2007.10.059

12 Hashiyada M, Itakura Y, Funayama M. Polymorphism of eight X-chromosomal STRs in a Japanese population. Forensic Science International: Genetics Supplement Series. 2008;1:150-2. doi:10.1016/j.fsigss.2007.10.020

13 Shin KJ, Kwon BK, Lee SS, Yoo JE, Park MJ, Chung U, et al. Five highly informative X-chromosomal STRs in Koreans. Int J Legal Med. 2004;118:37-40. Medline:14634833 doi:10.1007/s00414-003-0415-2

14 Lee HY, Park MJ, Jeong CK, Lee SY, Yoo JE, Chung U, et al. Genetic characteristics and population study of 4 X-chromosomal STRs in Koreans: evidence for a null allele at DXS9898. Int J Legal Med. 2004;118:355-60. Medline:15185093 doi:10.1007/s00414-004-0456-1

15 Biotype AG. Mentype Argus X-8 PCR amplification kit manual.

Dresden (Germany): Biotype AG; 2007.

16 Bar W, Brinkmann B, Budowle B, Carracedo A, Gill P, Lincoln P, et al. DNA recommendations. Further report of the DNA Commission of the ISFH regarding the use of short tandem repeat systems. International Society for Forensic Haemogenetics. Int J Legal Med. 1997;110:175-6. Medline:9274938 doi:10.1007/s004140050061

17 Clayton TM, Guest JL, Urquhart AJ, Gill PD. A genetic basis for anomalous band patterns encountered during DNA STR profiling. J Forensic Sci. 2004;49:1207-14. Medline:15568691 doi:10.1520/JFS2003145

18 Edelmann J, Hering S, Augustin C, Szibor R. Characterisation of the STR markers DXS10146, DXS10134 and DXS10147 located within a 79.1 kb region at Xq28. Forensic Sci Int; Genet. 2008;2:41-6. Medline:19083788 doi:10.1016/j.fsigen.2007.08.001