

Genetic Relationship Between Korean and Mongolian Populations Based on the Y Chromosome DNA Variation

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We analyzed seven Y chromosome binary markers (YAP, RPS4Y₇₁₁, M9, M175, LINE1, SRY₊₄₆₅ and 47z) in samples from a total of 254 males from Koreans and two Mongolian ethnic groups (Buryat and Khalkh) to study the genetic relationship among these populations. We found eight distinct Y haplogroups constructed from the seven binary markers. Haplogroup DE-YAP was present at extremely low frequencies (~2%) in the Korean and Mongolian populations. This result is consistent with earlier reports that showed the YAP+ chromosomes to be highly polymorphic only in populations from Japan and Tibet in east Asia. The observed high frequency of haplogroup C-RPS4Y₇₁₁ in the Mongolian populations (~40%) is concordant with recent findings, showing that the RPS4Y₇₁₁-T chromosomes were distributed at high frequencies in Siberian and Mongolian populations compared with most other populations from east Asia. Thus, the relatively moderate frequency of haplogroup C-RPS4Y₇₁₁ in Koreans (~15%) can be seen as genetic evidence for probable interaction with Mongolian and/or Siberian populations. In contrast, the majority (~75%) of modern Koreans studied here had high frequencies of Y chromosome lineages of haplogroup O-M175 and additional haplogroups that define sublineage of O-M175, which are most likely related with modern populations in China. In conclusion, our data on the Y chromosome haplogroup distribution may provide evidence for interaction between Korean and Mongolian populations, but Koreans tend to be much more related with those from southern-to-northern populations of China than to Mongolians in east Asia.

Although it is generally accepted that Koreans are considered a northeast Asian group, the peopling of Korea is not clearly understood based on the data of molecular physical anthropology. Studies of classic genetic markers of protein and nuclear DNA show that Koreans tend to have a close genetic affinity with Mongolians among northeast Asians (Goedde et al., 1987; Saha and Tay, 1992; Hong et al., 1993). In contrast, genetic surveys of mitochondrial DNA (mtDNA) variation indicate that Koreans are more closely related with Chinese and Japanese among east Asian populations (Harihara et al., 1988; Horai et al., 1996; Jin et al., 1999). Recent findings from Y chromosome DNA studies imply that Koreans possess lineages from both the southern (China) and the northern (southeastern Siberia) haplogroup complex (Kim et al., 2000; Kwak and Kim, 2001; Karafet et al., 2001; Kayser et al., 2003). These results indicate that the peopling of Korea can be seen as a complex process depending on molecular genetic markers and DNA samples.

Based on archaeological and anthropological data, the earliest modern human lithic cultures were found from 25,000 to 45,000 years ago in the Altai Mountains and southeast Siberia as well as the Korean peninsula (Vasil'ev, 1993; Choi, 1993). These results suggest that the early Korean population might be closely related with Mongolian ethnic groups who inhabited the general area of the Altai Mountains and southeastern Siberia. In addition, the Mongol Empires extended their power over other peoples in most Asia including the Korean peninsula in around 13 C (Roberts, 1993). This historical evidence would lead us to suspect that Koreans may share a common gene pool with the Mongolian population. Thus, further genetic markers and DNA samples from diverse regions of Mongolia are required to better understand the genetic relationship between Korean and Mongolian ethnic groups.

Due to genetic nature of the Y chromosome DNA, its survey can be of great benefit toward providing information on population history of modern humans. The non-recombining portions of the human Y-chromosome (NRPY) have special features of haploid transmission pattern and father-to-son transmission. The DNA sequence of the NRPY contains

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a genetic record only of the mutational events that occurred in the past. As a consequence, haplotypes constructed from Y-chromosomal alleles at multiple polymorphic sites can be used to study paternal lineages (Hammer, 1995) and to differentiate human population groups (Su et al., 1999, Karafet et al., 2001). Studies of ancient divergences in human evolution require polymorphisms with low probabilities of back and parallel mutation, and for which ancestral states can be determined (Hammer and Zegura, 1996). Binary markers, single nucleotide polymorphisms (SNPs) and small insertions or deletions (indels) are best suited for this purpose.

To further investigate the genetic relationship between Korean and Mongolian ethnic groups, we analyzed seven Y chromosome binary markers (YAP, RPS4Y₇₁₁, M9, M175, LINE1, SRY₊₄₆₅ and 47z) in samples from a total of 254 males from Korean and two Mongolian populations (Buryat and Khalkh). We report that the Y chromosome DNA variation may provide evidence for interaction between Korean and Mongolian populations, but Koreans tend to be much more related with those from southern-to-northern populations of China than to Mongolians in east Asia.

Materials and Methods

Subjects

We analyzed a total of 254 males from Korean and two Mongolian ethnic groups in northeast Asia (Table 1). DNA samples were obtained from volunteers living in Korea (south Korea, n = 156) and Mongolia (Buryat, n = 49; Khalkh, n = 49). Genomic DNAs from Buryat and Khalkh were kindly provided by Shinji Harihara and Suren Ganbold, respectively. Whole blood DNA was extracted using the standard method (Sambrook et al., 1989). Many of the DNA samples were also extracted from buccal cells according to the procedure of Richards et al. (1993).

Genotyping of DNA variations

The seven Y chromosome binary markers were chosen

to genotype all individuals sampled, including YAP (Hammer, 1994), RPS4Y₇₁₁ (Bergen et al., 1999), M9 (Underhill et al., 1997), M175 (Underhill et al., 2001), LINE1 (Santos et al., 2000), SRY₊₄₆₅ (Shinka et al., 1999) and 47z (Nakagome et al., 1992), which were known to be polymorphic in east Asia. The YAP Alu insertion was checked using the primer set and conditions reported by Hammer and Horai (1995). The RPS4Y₇₁₁ (C to T substitution), M9 (C to G substitution) and M175 (-5 bp) markers were amplified using the following primer sets and modifications reported by Bergen et al. (1999), Underhill et al. (1997) and Underhill et al. (2001), respectively: RPS4Y₇₁₁, 5'-TATCTCCTCTTCTATTGCAG-3' and 5'-CCACAAGGGGGAAAAACAC-3'; M9, 5'-GCAGCATATAAACTTTTCAG-3' and 5'-CTCAAGCGTAAATGTACTGT-3'; M175, 5'-TTGAGCAAGAAAAATAGTACCCA-3' and 5'-CTCCATTCTTA ACTATCTCAGGGA-3'; each PCR reaction was performed in a total volume of 25 µl containing 25 ng of genomic DNA, 10 pM each primer, 0.2 mM dNTPs, 2.0 mM MgCl₂, 50 mM KCl, 10 mM Tris-HCl (pH 8.3) and 1.5 U AmpliTaq DNA polymerase (Perkin-Elmer). The PCR cycling condition for the RPS4Y₇₁₁ marker was: the first denaturation step at 94°C for 5 min, and then 35 cycles at 94°C for 45 sec, 50°C for 45 sec, and 72°C for 1 min, and final extension at 72°C for 3 min. The cycling condition for M9 was: 94°C for 5 min, and then 35 cycles at 94°C for 45 sec, and 42°C for 45 sec, and 72°C for 1 min, and final extension at 72°C for 3 min. The M175 was amplified with the PCR condition at 95°C for 10 min, and then 35 cycles at 94°C for 45 sec, 55°C for 45 sec, 72°C for 1 min, and a final extension at 72°C for 10 min. The PCR products for RPS4Y₇₁₁ and M9 were digested with *BstI* and *HinfI* and their respective alleles were determined their alleles on 2% agarose gels. For typing the M175 allele, the PCR products were separated on a 6% denaturing polyacrylamide gel containing 8 M Urea, by electro-phoresis in 1×TBE buffer for 2.5 h at a constant 50 W with a separation distance of 40 cm. Bands were visualized by silver staining as described elsewhere (Rabilloud et al., 1988).

The LINE1 insertion was scored as described by

Table 1. Allele frequencies of seven Y chromosome binary markers in the Korean and Mongolian populations

Population (n)	No.(%)of													
	RPS4Y ₇₁₁		YAP		M9		M175		LINE1		SRY ₊₄₆₅		47z	
DNA type	C	T	+	-	C	G	+	-	+	-	C	T	Y1	Y2
Korean (156)	132 (84.6)	24 (15.4)	3 (1.9)	153 (98.1)	28 (17.9)	128 (82.1)	38 (24.4)	118 (75.6)	19 (12.2)	137 (87.8)	125 (80.1)	31 (19.9)	147 (94.2)	9 (5.8)
Mongolian														
Buryats (49)	30 (61.2)	19 (38.8)	2 (4.1)	47 (95.9)	23 (46.9)	26 (53.1)	39 (79.6)	10 (20.4)	3 (6.1)	46 (93.9)	48 (98.0)	1 (2.0)	49 (100.0)	0
Khakhs (49)	28 (57.1)	21 (42.9)	1 (2.0)	48 (98.0)	24 (49.0)	25 (51.0)	36 (73.5)	13 (26.5)	3 (6.1)	46 (93.9)	49 (100.0)	0	49 (100.0)	0

Table 2. A comparison of Y chromosome haplogroup frequencies between the Korean and Mongolian populations

Population (n)	No. (%) of							
	Y*	C-RPS4Y ₇₁₁	DE-YAP	K-M9	O-M175	O-LINE1	O-SRY ₊₄₆₅	O-47z
Korean (156)	1 (0.6)	24 (15.4)	3 (1.9)	10 (6.4)	68 (43.6)	19 (12.2)	22 (14.1)	9 (5.8)
Mongolian								
Euryats (49)	2 (4.1)	19 (38.8)	2 (4.1)	16 (32.7)	6 (12.2)	3 (6.1)	1 (2.0)	0
Khakhs (49)	2 (4.1)	21 (42.9)	1 (2.0)	12 (24.5)	10 (20.4)	3 (6.1)	0	0

Santos et al. (2000). The allele-specific PCR amplification method was performed to genotype the SRY₊₄₆₅ (C to T substitution), as described by Kim et al. (2000). The allelic variation of the 47 z was analyzed using a PCR-RFLP method reported by Shin et al. (1998). The PCR product amplified from the Y2 allele has the recognition sequence for the restriction enzyme *StuI* only

Nomenclature

We followed the terminology and nomenclature proposed by The Y Chromosome Consortium (YCC) (YCC, 2002). The terms “haplogroup” and “haplotype” are used according to de Knijff (2000): “haplogroup” refers to the NRPY lineages defined by binary polymorphisms and “haplotype” is reserved for all sublineages of haplogroups that are defined by variation at short tandem repeats (STRs) on the NRY.

Statistical analyses

The allele frequencies were calculated by counting the observed phenotypes. We used the PHYLIP Package program (Felsenstein, 1993) to compute genetic distances for use in distance matrix programs based on Y chromosome haplogroup frequencies. Genetic distance

was estimated by Nei genetic distance (*D*) (Nei 1972). The neighbor-joining (NJ) (Saitou and Nei 1987) was used to construct branching diagrams from matrices of pairwise distances.

Results and Discussion

The allele frequency distribution of seven Y chromosome binary markers in samples from the Korean and Mongolian populations are listed in Table 1. According to the new Y haplogroup nomenclature (YCC, 2002), a total of eight different Y haplogroups were characterized in this survey (Table 2). Thus, a single most parsimonious phylogeny based on The YCC (2002) could be constructed for the eight NRPY binary haplogroups (Fig. 1). Two Y chromosomal lineages (haplogroups C-RPS4Y₇₁₁ and K-M9/additional sublineages of K-M9) account for 95.7% of the Korean and Mongolian Y chromosomes (Table 2). These results are consistent with previous findings, showing that the east Asian Y chromosome gene pool is almost completely covered by these two Y lineages and DE-YAP lineages (Underhill et al., 2000; Ke et al., 2001; Tajima et al., 2002). The observed low frequencies of haplogroup DE-YAP in the Koreans and Mongolian ethnic groups provide additional data, showing that YAP+ chromosomes appeared only in populations from Japan and Tibet in east Asia (Hammer and Horai, 1995; Hammer et al., 1997; Tajima et al., 2002).

The observed high frequency of haplogroup C-RPS4Y₇₁₁ in the Mongolian populations (~40%) is concordant with recent findings, showing that the RPS4Y₇₁₁-T chromosomes were distributed at high frequencies in Siberian and Mongolian populations compared with most other populations from southeast Asia (Karafet et al., 2001; Tajima et al., 2002). The two Mongolian ethnic groups appeared to have nearly the same allele frequencies of eight haplogroups in their populations (Table 2). There are 20 ethnic Mongolian groups, and many people are of mixed ethnic origin; the population of Mongolia is known to be homogeneous, with Mongol speaking people are constituting ~95% of the total; the largest subgroup is the Khalkh, accounting for ~80% of the total population. The only substantial non-Mongol group, representing over 5% of the population, are the Khazakhs, a Turkish-speaking people

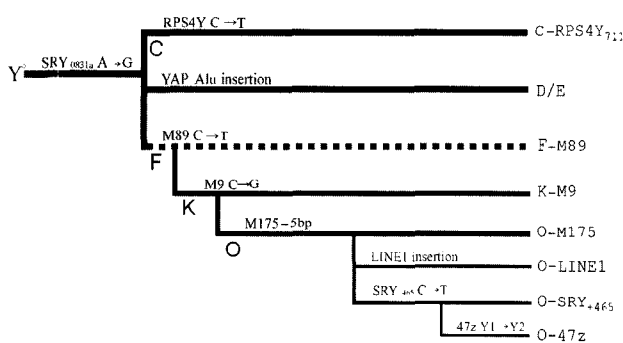


Fig. 1. Y chromosome parsimonious tree for the origin and evolutionary relationship based on eight haplogroups constructed from the seven binary markers. When the haplogroup Y is considered the probable ancestral, haplogroups can be created by mutation steps. Dashed line indicates haplogroup not analyzed in this survey. Nomenclature is according to the YCC (2002).

Table 3. Combined data for the Y chromosome haplogroup distribution in several northeast Asian populations

Population (n)	No. (%) of							
	Y*	C-RPS4Y ₇₁₁	DE-YAP	K-M9	O-M175	O-LINE1	O-SRY ₊₄₆₅	O-47z
Chinese								
Manchurian ^a (52)	1(1.9)	14 (26.9)	0	7 (13.5)	23 (44.2)	5 (9.6)	2 (3.8)	0
Taiwanese-Han ^a (82)	0	6 (7.3)	1 (1.2)	5 (6.1)	48 (58.5)	22 (26.8)	0	0
Miao ^a (57)	0	3 (5.3)	4 (7.0)	0	28 (49.1)	22 (38.6)	0	0
Korean ^b (156)	1 (0.6)	24 (15.4)	3 (1.9)	10 (6.4)	68 (43.6)	19 (12.2)	22 (14.1)	9 (5.8)
Mongolian								
Buryats ^b (49)	2 (4.1)	19 (38.8)	2 (4.1)	16 (32.7)	6 (12.2)	3 (6.1)	1 (2.0)	0
Khakhs ^b (49)	2 (4.1)	21 (42.9)	1 (2.0)	12 (24.5)	10(20.4)	3 (6.1)	0	0

^aKarafet et al. (2001); ^bPresent study.

dwelling in the far west (<http://www.un-mongolia.mn>).

Archaeological and anthropological data revealed that the early Korean population might have shared a common gene pool with Mongolian ethnic groups who inhabited the general area of the Altai Mountains and southeastern Siberia (Vasil'ev, 1993; Choi, 1993). In addition, the Mongol Empire stretched from Korea to Hungary and as far south as Vietnam around 13 C, making it the largest empire the world has ever known (Roberts, 1993). This historical evidence would lead us to suspect that the Koreans genetically interacted with the Mongolian population. Thus, the relatively moderate frequency of haplogroup C-RPS4Y₇₁₁ in Koreans (~15%) can be seen as genetic evidence for probable interaction with Mongolian and/or Siberian populations.

In contrast, the majority (~75%) of modern Koreans studied here had high frequencies of Y chromosome lineages of haplogroup O-M175 and additional haplogroups that define sublineage of O-M175 (O-LINE1, O-SRY₊₄₆₅ and O-47z), which are most likely related with Chinese populations (Table 2). There are population data related to the Chinese lineages, showing that haplogroup O-LINE1 is present at high frequencies in samples of the Han Chinese and two minority populations, the Tujia and Miao from Hunan located in the southern areas of the Yangtze River (Santos et al., 2000; Kwak and Kim, 2001). Santos et al. (2000) also pointed that this genetic variation might have emerged in China (southern China) and was carried south and east, and eventually distributed in its surrounding regions. The relatively moderate frequency of haplogroup O-LINE1 in the Korean population (12.2%) may have resulted from its interaction with the Chinese populations.

Koreans are characterized by a high frequency of haplogroups O-SRY₊₄₆₅ and additional sublineage of O-SRY₊₄₆₅. The haplogroup carrying the 47z-Y2 mutation are direct descendant of the haplogroup O-SRY₊₄₆₅ (Fig. 1). Recently, Shinka et al. (1999) reported that the chromosomes carrying SRY₊₄₆₅-T mutation were not found in most Caucasian and Negroid males examined in their survey, but were observed at high frequencies in

the Korean and Japanese populations. Lin et al. (1994) suggested that Y chromosomes carrying the 47z-Y2 mutation may have originated from an ancestral population of Henan or southern parts of Shanxi near the Yellow River in China. Many ancient Chinese moved from the estuary of the Yellow River to the mid and downstream regions of the Yangtze River ~4,000 years ago (Ruofu and Yip, 1993; Su et al., 2000). With increasing political chaos in Chinese mainland during its Warring Period (476-221 BC), many Chinese further moved southward and eastward, and eventually inhabited all of China (Choi and Rhee, 2001). There is also historical evidence that many Chinese fled and sought refuge in the Korean Ancient Chosun during the Warring Period (Yun, 1998; Choi and Rhee, 2001). In addition, archaeological evidence implied that rice cultivation had already spread to all parts of the Korean peninsula around 1,000 BC, introduced from the Yangtze River

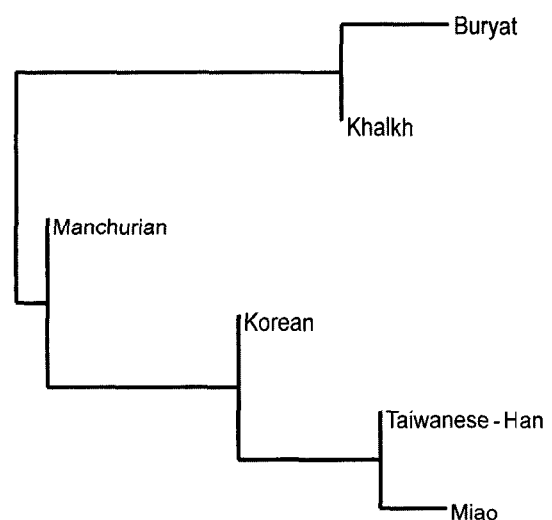


Fig. 2. Neighbor-joining (NJ) tree for six east Asian populations. This network was produced by the NJ unrooted method (Saitou and Nei 1987) based on the Nei genetic distance (D) (Nei 1972), calculated from frequencies of eight Y haplogroups in Table 3.

basin in central China (Choi and Rhee 2001). It postulates that the recent range expansion and introduction of rice cultivation from central China has resulted in the moderate appearance of Y chromosome lineages of haplogroup O-M175 and additional sublineage of O-M175.

Based on the results of combined data (Table 3 and Fig. 2), Koreans seemed to be more likely related to the Chinese than to the Mongolian ethnic groups, although they possess lineages from both the northeast and southeast Asia. However, this does not rule out the possibility of occurrence of the founder effect and different settlement processes of these Y lineages in east Asia, especially in the Korean population. Additional genetic markers and populations from diverse regions of east Asia are required to verify this hypothesis.

In conclusion, our data on the Y chromosome haplogroup distribution may provide evidence for an interaction between Korean and Mongolian populations, but the Koreans tend to be much more related with those from southern-to-northern populations of China than to the Mongolians in east Asia.

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