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# Characteristics of Mitochondrial DNA Sequence Polymorphisms and Haplogroups in Korean Population

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## ABSTRACT

We examined sequence variations in the mitochondrial DNA (mtDNA) *control region*, *tRNA leucine1* (*tRNA leu1*) and *cytochrome b* (*CYTB*) genes in order to investigate the characteristics of mtDNA polymorphisms and haplogroups in Korean population. Seventy maternally unrelated healthy Korean donors provided blood samples for the present study. The small deletion mutations exist only in the *hypervariable region* (*HV*) region. The Korean population exhibited a high level of length heteroplasmy in the 16184-16193 and 303-315 poly-C regions from the mtDNA control region. Some of the most common polymorphisms found in all subjects were 73A > G, 263A > G, 3107delC and 15326A > G from *HV2, HV1, tRNA leu1* and *CYTB* genes, respectively. The most common haplogroup in the Korean population was D4 which was found in 16% of the population, followed by A, B, B4a, D5, G1a and M10 (each of 6%). Several haplogroups appear to be restricted to the Japanese and Korean populations. However, the current study revealed different distribution of some haplogroups in the Korean population in comparison with a previous study. The overall pattern and frequency of haplogroups among Koreans in the current study were closer to those of a Japanese population than to a Han Chinese population.

**Key words:** mtDNA, polymorphism, haplogroup, Korean.

## INTRODUCTION

Human mitochondrial DNA (mtDNA) is a closed circular duplex molecule, composed of 16,569 bp, and is present in high cellular copy numbers that vary depending on the tissue type (Mambo et al., 2003; Shin et al., 2004; Lee et al., 2004a). mtDNA molecules have a non-coding control region that includes a unique displacement loop (D-loop) containing replication and transcription control elements. This control region of human mtDNA has been studied extensively with an aim toward the elucidation of both its evolutionary status and its use in the area of forensics

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and human identity. Its high degree of polymorphisms is apparently due to its high mutation rate (Wilson et al., 1997). The control region includes two *hypervariable* (*HV*) regions (*HV1* and *HV2*), so-called because of their high incidence of nucleotide variations. Many mtDNA length heteroplasmies are localized in the *HV2* homopolymeric C (poly-C) tract that lies between nucleotide positions (np) 303–315. Recent studies have revealed a high level of mtDNA length heteroplasmies in the poly-C tracts from Korean donors using size-based PCR product separation by capillary electrophoresis (Lee et al., 2004b; Shin et al., 2006).

Knowledge of the frequencies with which certain mtDNA sequences occur in a given population is of crucial importance for the application of mitochondrial markers for forensic and phylogenetic studies. However, there are a limited number of studies on mtDNA polymorphisms and haplogroups in the Korean population. Therefore, the analysis of mtDNA *control region*, *tRNA leucine1* (*tRNA leu1*) and *cytochrome b* (*CYTB*) genes was carried out to study the characteristics and distribution of mtDNA polymorphisms and haplogroups in Korean population. We further examined differences of haplogroup distribution among East Asian populations including Korean, Japanese and Chinese.

## MATERIALS AND METHODS

### Samples

Seventy maternally unrelated healthy Korean donors were enrolled in the current study. Fourteen samples came from each of the following age groups: cord blood (CB), 1 to 20 years, 21 to 40 years, 41 to 60 years, 61 years and older. Five mililiters of heparinized peripheral blood (PB) and CB was drawn from the donors that had provided informed consent. The Institutional Review Board of the Chonnam National University Hwasun Hospital (Hwasun, Korea) approved the present study protocols.

### Sequencing of the mtDNA control and coding regions

Total DNA was extracted from the collected PB and CB samples with an AccuPrep Genomic DNA Extraction Kit (Bioneer, Daejon, Korea). We used a set of designated primer pairs (**Table 1**) and PCR conditions based on a published protocol in order to amplify and sequence the *control region* (np 16024 to 16569 and 1 to 576), *tRNA leu1* and *CYTB* coding genes of the mtDNA (Shin et al., 2006). Each amplified mtDNA product was then purified with an AccuPrep PCR Purification Kit (Bioneer) and sequenced with the BigDye Terminator v3.1 Ready Reaction Kit (Applied Biosystems, Foster City, CA) and the ABI Prism 3100 Genetic Analyzer (Applied Biosystems). The mtDNA sequence results were compared to the Revised Cambridge Reference Sequence (RCRS) (http://www.mitomap.org/) with the database search tool, MitoAnalyzer (http://www.cstl. nist.gov/biotech/strbase/mitoanalyzer.html), in order to determine the polymorphisms and mutations differing from the RCRS.

**Table 1.** Primer sets of the mtDNA control and coding region for PCR and direct sequencing.

| Primer set No | mtDNA segment | PCR primers (5' to 3') | | Sequencing primers (5' to 3') | |
|---|---|---|---|---|---|
| 1 (1.12 kb) | *Control region* (np 16024-16569; np 1-576) | F15971 | TTAACTCCACCATTAGCACC | F15971 | TTAACTCCACCATTAGCACC |
| | | | | R48 | GCATGGAGAGCTCCCGTGAGTGG |
| | | R611 | CAGTGTATTGCTTTGAGGAGG | F15 | CACCCTATTAACCACTCACG |
| | | | | R611 | CAGTGTATTGCTTTGAGGAGG |
| 2 (586 bp) | *tRNA leu1, ND1* (np 2972-3557) | F2972 | ATAGGGTTTACGACCTCGATG | F2972 | ATAGGGTTTACGACCTCGATG |
| | | R3557 | AGAAGAGCGATGGTGAGAGC | R3557 | AGAAGAGCGATGGTGAGAGC |
| 3 (488 bp) | *Cytochrome b* (np 14909-15396) | F14909 | TACTCACCAGACGCCTCAACCG | F14909 | TACTCACCAGACGCCTCAACCG |
| | | R15396 | TTATCGGAATGGGAGGTGATTC | R15396 | TTATCGGAATGGGAGGTGATTC |

ND, NADH dehydrogenase.