Allele frequencies of human leukocyte antigen-G in Korean population

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The Doctoral Dissertation
submitted to the Department of Medicine,
the Graduate School of Yonsei University
in partial fulfillment of the requirements for the degree of
Doctor of Philosophy

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December 2011

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December 2011

Acknowledgements

I am heartly thankful to my supervisor, Hyon-Suk Kim, whose encouragement, guidance and support from the initial to the final level enabled me to develop an understanding of the subject. I am also grateful to professors of thesis committee, Yu Seun Kim, Chuhl Joo Lyu, Jongsun Kim and Oh-Joong Kwon, for their advice and help. Lastly, I offer my regards and blessing to all of those who supported me in any respect during the completion of this project.

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The human leukocyte antigen (HLA)-G is a nonclassical major histocompatibility complex class I molecule with relatively limited polymorphism. The differences in allele frequency according to ethnicity and country have not been studied enough, so far. Therefore, fundamental data including allele frequencies and polymorphism are needed for studies on immunological function of HLA-G in each population.

We investigated allele frequencies and 14-bp polymorphism of the *HLA-G* in Koreans. *HLA-G* alleles and 14-bp polymorphisms were determined by sequence-based typing analysis of exons 2–4 and polymerase chain reaction of the 3'-UTR region in 200 unrelated individuals.

Genotyping analysis identified eight different *HLA-G* alleles, which indicates that the Korean population presents limited *HLA-G* allelic polymorphism. *HLA-G*01:01:01:01* and *G*01:04:01* were frequent alleles (42.5% and 34.0%), and allelic frequencies were similar to those of other Asian populations. The 14-bp deletion alleles are higher (78%) in Koreans, although the frequencies of the 14-bp insertion/deletion polymorphism have been known to be nearly equal in many Caucasian populations. *HLA-G*01:01:08* was reported strong linkage disequilibrium with the 14-bp deletion in a previous report; the

same allele was accompanied with 14-bp insertion in our study.

There are a few studies investigating allele frequencies, and most of them were studied before high resolution method era. This is the first study regarding *HLA-G* genotypes in Korean, which were identified by high-resolution method. From this study, we identified *HLA-G* frequencies of a Korean population and expect this study could help further investigations for immunological and clinical implications of HLA-G.

Key words : human leukocyte antigen-G, sequence based typing, Korean, allele frequency

Allele frequencies of human leukocyte antigen-G in Korean population

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I. Introduction

Human leukocyte antigen (HLA)-G is one of the major histocompatibility complex (MHC) class I antigens[1]. HLA-G is called nonclassical because of its limited polymorphism, restricted tissue distribution, immunomodulatory function and the alternative splicing of its primary transcript that encodes seven protein isoforms[1]. The promoter and the 3'-untranslated region (UTR) of the *HLA-G* gene are highly polymorphic, and the variations in the last region were associated with HLA-G expression level. The *HLA-G* gene encodes seven proteins including four membrane-bound (HLA-G1 to HLA-G4) and three soluble isoforms (HLA-G5 to HLA-G7)[2]. Soluble HLA-G1, which is generated by the proteolytic cleavage of the membrane-bound HLA-G1, and HLA-G5 are major isoforms described in healthy tissues comprising trophoblast, thymus, cornea, erythroid and endothelial precursors. HLA-G expression can also be induced in the pathological situations such as autoimmune, inflammatory and viral infectious diseases, cancer and transplantation[1,3]. HLA-G molecules may protect cells from natural killer (NK) cell-mediated cytolysis through interactions with specific killer immunoglobulin- like receptors expressed on NK cells and T lymphocytes[4,5].

The *HLA-G* allele has relatively limited polymorphism, and low variability has been observed in different populations[6-17]. Caucasian, African and Asian populations have much less sequence variations within the *HLA-G* locus than other classical *HLA* loci, which are known as the most polymorphic loci in the human genome. To date, 47 alleles

have been assigned to the *HLA-G* gene, and the polymorphism sites are observed in coding and noncoding regions (http://hla.alleles.org/nomenclature/stats.html), primarily sequenced in exons 2, 3 and 4. The *HLA-G* gene also presents a 14-bp insertion/deletion polymorphism at the 3'-UTR region, with both exhibiting nearly equal frequencies (insertion frequency of about 45%) in the Caucasian populations analysed so far[14]. *HLA-G* 01:01:01*, *G*01:01:08*, *G*01:04:01* and *G*01:04:03* alleles are in strong linkage disequilibrium (LD) with the 14-bp deletion in European and Asian populations[14,15]. *HLA-G* polymorphism has been associated with several disorders, including recurrent spontaneous abortion, preeclampsia, asthma and pemphigus vulgaris[13,14,18-22]. In addition, *HLA-G* alleles presenting the 14-bp insertion at exon 8 have been associated with a lower *HLA-G* mRNA production for most membrane-bound and soluble isoforms[14]. In several studies, the relations between the 14-bp insertion/deletion and some clinical situations such as recurrent miscarriages, preeclampsia and pregnancy development, including increased birth weight, placental weight and placental ratio, have been reported[20,23-25]. These findings imply that HLA-G plays an important role in the outcome of pregnancy.

Data of *HLA-G* allele frequencies and 14-bp polymorphism from each population are needed for studies on the function of HLA-G. Although HLA-G has been reported to have limited polymorphism, differences in allele frequencies among populations have also been reported. However, the polymorphism of the *HLA-G* locus has not been characterized in a Korean population so far, and there are also only few reports of *HLA-G* polymorphisms at the allele level. In this study, we investigated the *HLA-G* allele frequencies, 14-bp insertion/deletion polymorphism and their relationship in Koreans using a sequence-based typing.

Table 1. *HLA-G* allele frequencies (%) in the present study compared with different studies

HLA-G alleles	Korean* (n=200)	Japanese (n=82)	Chinese, Han (n=292)	Danish (n=198)	Finnish (n=194)	German (n=344)	Portuguese (n=117)	Spanish (n=228)	Brazilian (n=103)	North Indian (n=120)	Iranian (n=102)	African Shona (n=108)	African American (n=84)	African Ghanaian (n=84)
*G*01:01:01:01*	42.5	43.0	37.3	58.0	58.0	32.0	37.0	38.0	39.8	10.0	3.9	39.3	70.0	83.0
*G*01:01:02:01*	10.8	14.0	11.6	25.0	38.0	36.0	31.0	22.0	19.9	16.3	29.9	14.4	6.0	2.4
*G*01:01:03:01*	5.0	5.0	20.2	4.7	5.0	7.0	17.0	7.0	5.3	5.0	10.8	0.0	2.4	0.0
*G*01:01:04*	0.0	-†	-	0.0	-	-	-	-	0.5	7.5	-	0.0	-	-
*G*01:01:05*	0.0	-	-	0.0	-	-	-	-	0.0	0.0	1.5	0.0	-	-
*G*01:01:06*	0.0	-	-	-	-	-	-	-	1.0	-	-	0.0	-	-
*G*01:01:07*	0.0	-	-	0.0	-	-	-	-	0.0	0.0	2.0	0.0	-	-
*G*01:01:08*	3.3	-	5.5	0.5	-	9.1	-	-	4.4	0.0	2.5	14.4	-	-
*G*01:01:09*	0.0	-	-	-	-	-	-	-	0.0	-	-	-	-	-
*G*01:02*	0.0	-	-	0.0	-	-	-	-	0.0	1.2	-	0.0	-	-
*G*01:03*	0.5	-	0.3	2.0	-	2.3	2.0	0.0	8.7	24.2	-	0.0	-	-
*G*01:04:01*	34.0	38.0	18.5	7.0	-	6.0	13.0	11.0	8.3	17.5	29.4	20.4	13.0	9.5
*G*01:04:02*	0.0	-	2.4	-	-	-	-	-	0.0	-	-	-	-	-
*G*01:04:03*	0.0	-	2.7	0.0	-	-	-	-	0.0	-	2.0	0.4	-	-
*G*01:04:04*	0.0	-	-	-	-	-	-	-	3.9	-	-	-	-	-
*G*01:05N*	2.3	0.0	1.4	0.8	-	2.3	0.0	3.0	1.0	15.4	18.1	11.1	8.3	4.8
*G*01:06*	0.8	-	-	2.0	-	-	-	-	4.9	2.9	-	-	-	-
*G*01:07*	0.0	-	-	-	-	-	-	-	0.0	-	-	-	-	-

* This study.

† not determined.

II. Materials and Methods

1. Subjects

A total of 200 healthy unrelated individuals were recruited. The genomic DNA was extracted from peripheral blood using QuickGene-Mini80 (Fuji, Tokyo, Japan). Age and gender of the subjects were random.

2. *HLA-G* allele assignment

HLA-G alleles were defined by nucleotide sequence variations at exons 2, 3 and 4. Briefly, exons 2, 3 and 4 were individually amplified, resulting in polymerase chain reaction (PCR) products of 361, 457 and 364 bp, respectively, using the following sets of primers[23]: HLAGEX2A (GGGTCGGGCGGGTCTCAA) and BHLAGEX2 (TCCGTGGGGCATGGAGGT) for exon 2, 5HLGIN2 (CCCAGACCCTCTACCTGGGAG) and NYGI3 (CTCTCCTTGTGCTAGGCCAGGCTGAGAGG) for exon 3, and HLAGEX4A (CCATGAGAGATGCAAAGTGCT) and BHLAGEX4 (TGCTTTCCCTAACAGACATGAT) for exon 4. PCR was performed in a final volume of 30 μL containing 1 x PCR buffer (70 mM Tris-HCl pH 8.8, 20 mM $(NH_4)_2SO_4$, 3 mM $MgCl_2$, 1 mM dithiothreitol, 1% Triton X-100, 50 μg bovine serum albumin), 0.2 mM of each dNTP, 10 pmol of each primer, 1.1 units of Taq DNA polymerase Platinum (Invitrogen, Carlsbad, CA, USA) and 200 ng of genomic DNA. The initial denaturation cycle was carried out at 94℃ for 3 min followed by 35 cycles of 94℃ for 30 s, 64℃ (exons 2 and 3) or 60℃ (exon 4) for 30 s and 72℃ for 60 s and by a final extension step at 72℃ for 7 min. PCR products were sequenced using the primers HLAGEX2A (GGGTCGGGCGGGTCTCAA) for exon 2, SEKHGEX3 (GGTGGGTCCGGGCGAGGGCGAGGCT) for exon 3 and HLAGEX4A (CCATGAGAGATGCAAAGTGCT) for exon 4 by ABI PRISM 3130 Genetic analyzer (Applied Biosytems, Tokyo, Japan) as previously described[23]. All the sequences obtained from each sample were aligned with the genomic sequences of the official alleles (recognized by the WHO and International Immunogenetics Information System (IMGT)). The methodology used in this study allowed the discrimination of all official *HLA-G* alleles determined by exon polymorphism, but not the alleles with intron variation. On this basis, in this study, the alleles *G*01:01:01:01* to *G*01:01:01:06* were considered *G*01:01:01:01* and the alleles *G*01:01:02:01* and *G*01:01:02:02* were considered *G*01:01:02:01* according to frequencies.

3. Detection of the 14-bp insertion/deletion polymorphism

HLA-G 3'-UTR region was amplified with the primers GE14HLAG (GTGATGGGCTGTTTAAAGTGTCACC) and RHG4 (GGAAGGAATGCAGTTCAGCATGA) for

the *HLA-G* 14-bp polymorphism analysis[16]. Amplification was performed with the following conditions: HF PCR premix (Bioneer Corporation, Daejeon, Korea), 10 pmol of each primer and 1 μL of genomic DNA in a final volume of 20 μL. The PCR was performed with initial denaturation at 95℃ for 5 min, 35 cycles at 95℃ for 30 s, 60℃ for 30 s and 72℃ for 30 s and the final extension at 72℃ for 5 min. The *HLA-G* 14-bp deletion/insertion polymorphism was detected by electrophoresis on 3% agarose gel: deleted and inserted allele generated a 210 and a 224-bp PCR fragment, respectively.

4. *HLA-A*, *HLA-B*, *HLA-C* and *HLA-DRB1* allele assignment

HLA-A, *HLA-B* and *HLA-C* alleles were defined by nucleotide sequence variations at exons 2, 3 and 4, respectively. *HLA-DRB1* alleles were defined by nucleotide sequence variations at exon 2. We performed sequence-based typing using Abbott reagents (Atria Genetics, CA, USA) and ABI PRISM 3100 Genetic analyzer (Applied Biosystems). Assign v3.5 software (Conexio Genomics, Applecross, Australia) was used for the interpretation of *HLA* allele assignment.

5. Statistical Analysis

The allelic and genotypic frequencies were obtained by allele and haplotype procedure of SAS version 10 (SAS Institute Inc., Cary, NC, USA) based on maximum likelihood and expectation-maximization algorithm. Relative values of LD (D') were also calculated.

III. Results

Based on nucleotide sequence variations in *HLA-G* exons 2 to 4, we identified eight different alleles in a Korean population (Table 1). The *HLA-G*01:01:01:01* allele was most frequent in our study population with a frequency of 42.5% followed by *G*01:04:01* (34.0%). Table 2 shows the frequencies of 22 *HLA-G* genotypes observed.

The frequencies of the 14-bp insertion/deletion alleles were nearly equal (insertion frequency of about 44.1%) in many Caucasian populations analysed so far[14]. The likelihood ratio test of LD indicated the presence of a significant association between the assigned *HLA-G* alleles and the 14-bp insertion or deletion[15]. In the Korean population of this study, 14-bp deletion alleles were common (78.0%; Table 3), and discrepancies between our results and previous reports were observed[14,15,18,21,26]. The *G*01:01:08* allele has been mostly associated with the 14-bp deletion; only one exception was observed in one of the nine Brazilian *G*01:01:08*[15], while 14-bp insertion accompanied in more than half of the Korean *HLA-G*01:01:08*.

Table 2. *HLA-G* genotype frequencies (%) in a Korean population (n=200)

Genotype	No. (%)
*G*01:01:01:01/*01:04:01*	51 (25.5)
*G*01:01:01:01/*01:01:01:01*	44 (22.0)
*G*01:04:01/*01:04:01*	23 (11.5)
*G*01:01:01:01/*01:01:02:01*	19 (9.5)
*G*01:01:02:01/*01:04:01*	17 (8.5)
*G*01:01:03:01/*01:04:01*	9 (4.5)
*G*01:01:08/*01:04:01*	7 (3.5)
*G*01:01:01:01/*01:01:03:01*	6 (3.0)
*G*01:04:01/*01:06*	3 (1.5)
*G*01:01:01:01/*01:05N*	2 (1.0)
*G*01:01:01:01/*01:06*	2 (1.0)
*G*01:01:02:01/*01:01:03:01*	2 (1.0)
*G*01:01:02:01/*01:05N*	2 (1.0)
*G*01:01:02:01/*01:06*	2 (1.0)
*G*01:01:03:01/*01:01:08*	2 (1.0)
*G*01:01:08/*01:05N*	2 (1.0)
*G*01:04:01/*01:05N*	2 (1.0)
*G*01:01:01:01/*01:01:08*	1 (0.5)
*G*01:01:01:01/*01:03*	1 (0.5)
*G*01:01:02:01/*01:01:08*	1 (0.5)
*G*01:01:03:01/*01:05N*	1 (0.5)
*G*01:03/*01:04:01*	1 (0.5)

Table 3. The 14-bp insertion/deletion polymorphisms associated with each allele found in a Korean population

HLA-G alleles	14-bp allele	Occurrence (%)
*G*01:01:01:01*	Del*	170 (42.5)
*G*01:01:02:01*	Ins†	43 (10.8)
*G*01:01:03:01*	Ins	20 (5.0)
*G*01:01:04*	NA‡	0 (0.0)
*G*01:01:05*	NA	0 (0.0)
*G*01:01:06*	NA	0 (0.0)
*G*01:01:08*	Del	6 (1.5)
	Ins	7 (1.8)
*G*01:02*	NA	0 (0.0)
*G*01:03*	Ins	2 (0.5)
*G*01:04:01*	Del	136 (34.0)
*G*01:04:03*	NA	0 (0.0)
*G*01:04:04*	NA	0 (0.0)
*G*01:05N*	Ins	9 (2.3)
*G*01:06*	Ins	7 (1.8)

* deletion

† insertion

‡ not available

HLA-G is located near *HLA-A* on chromosome 6. In our data, *HLA-G* alleles showed associations with some specific *HLA-A* alleles. Linkage disequilibrium (D') between *HLA-A* and *HLA-G* alleles determined in this study are described in Table 4. A $r^2 > 0.5$ was also found between the following allelic groups: *HLA-A*01:01-G*01:06* (D' = 1.0000, r^2 = 1.0000), *HLA-A*02:01-G*01:01:01:01* (D' = 1.0000, r^2 = 0.5076), *HLA-A*26:01-G*01:01:02:01* (D' = 1.0000, r^2 = 0.5687), *HLA-A*30:01-G*01:05N* (D' = 1.0000, r^2 = 1.0000), *HLA-A*30:04-G*01:01:08* (D' = 1.0000, r^2 = 0.7282), *HLA-A*11:01-G*01:01:03:01* (D' = 0.8857, r^2 = 0.6666), *HLA-A*31:01-G*01:01:02:01* (D' = 0.8794, r^2 = 0.5813) and *HLA-A*24:02-G*01:04:01* (D' = 0.8653, r^2 = 0.6542).

Table 4. Frequencies and linkage disequilibrium (D') between *HLA-A* and *HLA-G* alleles

HLA-A/*HLA-G* haplotype	Frequency	D'
*A*01:01-G*01:01:02:01*	0.0033	0.09
*A*01:01-G*01:06*	0.0175	1.00
*A*02:01-G*01:01:01:01*	0.1600	1.00
*A*02:03-G*01:01:01:01*	0.0100	1.00
*A*02:04-G*01:01:01:01*	0.0025	1.00
*A*02:04-G*01:05N*	0.0025	1.00
*A*02:06-G*01:01:01:01*	0.1000	1.00
*A*02:07-G*01:01:01:01*	0.0450	1.00
*A*02:10-G*01:01:01:01*	0.0025	1.00
*A*03:01-G*01:01:01:01*	0.0225	1.00
*A*03:01-G*01:01:02:01*	0.0055	0.15
*A*11:01-G*01:01:01:01*	0.0293	-0.19
*A*11:01-G*01:01:03:01*	0.0448	0.89
*A*11:01-G*01:01:08*	0.0050	0.08
*A*11:02-G*01:01:01:01*	0.0025	1.00
*A*11:02-G*01:01:03:01*	0.0025	1.00
*A*11:20-G*01:01:01:01*	0.0025	1.00
*A*11:20-G*01:01:03:01*	0.0025	1.00
*A*24:02-G*01:01:01:01*	0.0069	-0.93
*A*24:02-G*01:01:03:01*	0.0149	0.09
*A*24:02-G*01:01:08*	0.0161	0.35
*A*24:02-G*01:04:01*	0.2073	0.87
*A*24:02-G*01:05N*	0.0048	-0.07
*A*24:20-G*01:04:01*	0.0025	1.00
*A*26:01-G*01:01:02:01*	0.0375	1.00
*A*26:02-G*01:01:01:01*	0.0150	1.00
*A*26:02-G*01:01:02:01*	0.0150	1.00
*A*26:03-G*01:01:02:01*	0.0075	1.00
*A*29:01-G*01:01:01:01*	0.0075	1.00
*A*30:01-G*01:01:02:01*	0.0026	0.01
*A*30:01-G*01:01:08*	0.0045	0.17
*A*30:01-G*01:05N*	0.0225	1.00
*A*30:04-G*01:01:08*	0.0175	1.00
*A*30:04-G*01:04:01*	0.0073	0.11
*A*31:01-G*01:01:02:01*	0.0446	0.88
*A*31:01-G*01:01:03:01*	0.0025	–*

*A*31:01-G*01:03*	0.0050	1.00
*A*31:01-G*01:06*	0.0044	0.21
*A*33:03-G*01:01:01:01*	0.0403	-0.41
*A*33:03-G*01:01:08*	0.0047	-0.10
*A*33:03-G*01:04:01*	0.1228	0.65
*A*33:03-G*01:06*	0.0052	0.16
*A*68:01-G*01:01:01:01*	0.0025	1.00
*A*68:01-G*01:01:02:01*	0.0025	1.00

* no association was observed.

IV. Discussion

In a Korean population, we observed the presence of only eight of the 47 known *HLA-G* alleles. The data presented here indicate that the Korean population contains limited allelic polymorphism. *HLA-G* allele frequencies in Koreans were more similar to those reported in Japanese than Chinese and other populations (Table 1). *G*01:01:01:01* in our data had relatively lower frequency than those of European and African, and *G*01:04:01* had higher frequency than those of most populations. *G*01:01:05*, *G*01:01:06*, *G*01:01:07*, *G*01:01:09*, *G*01:02*, *G*01:04:04* and *G*01:07* alleles, described only in a few reports, were also not observed in the present study[6-16]. Because there have been not many reports on the data of *HLA-G* frequencies at a high-resolution level from worldwide populations and each study was performed at different time, it is difficult to compare the exact frequencies in the populations or ethnic groups. Our data were obtained by direct sequencing analysis of exons 2, 3 and 4. These are official alleles that can be easily approached; thus, most previous studies based on these three exons' sequences. However, there still was ambiguity of heterozygous allele in interpreting the sequencing data of exons 2, 3 and 4. Therefore, investigations with more exons and haplotype sequencing are needed.

*HLA-G*01:04:01* allele (34.0%) seems to be a common allele in Korean, Japanese, Chinese Han and African Shona than other populations[11,15,16]. Although the *G*01:04:01* has a nonsynonymous leucine-to-isoleucine substitution at the first base of codon 110 (exon 3), this codon did not interact with the processed antigens or T-cell receptors[27]. Currently, it is unclear that this common allele in Korean population has some immunological implications. Relations between this allele and immune responses, susceptibilities to certain diseases and ethnic implication should be studied.

In the present study, the *G*01:05N* allele was found with a frequency of 2.3%, which is higher than other Asian populations reported. The *G*01:05N* allele encodes for a truncated nonfunctional HLA-G protein[27]. This null allele has been found with higher frequencies in African populations and lower in

European populations (Table 1). This allele was not found in Japanese or Portuguese populations. The relatively high frequency of this null allele in African populations with historically high pathogen loads tempts us to speculate that reduced expression of the HLA-G proteins may be associated with increased numbers of maternal uterine T cells, which could be beneficial in the presence of intrauterine infections[12]. Because we cannot expect significant difference between the frequencies of 2.3% and 0.0%, *HLA-G*01:05N* of a Korean population may not have clinical implications like that of African populations.

Although most studies reported nearly equal frequencies of the 14-bp insertion/deletion polymorphism[14,15,18,21,26], 14-bp deletion alleles were frequent as 78% in a Korean population of our study. This seems to be caused from the high frequencies of *HLA-G*01:01:01:01* and *G*01:04:01* (42.5% and 34.0%) in Korean population and their association with 14-bp deletion (Table 3). In addition, it is interesting that 7 of 13 *HLA-G* 01:01:08* had 14-bp insertion. *HLA-G*01:01:08* has been reported to have a strong linkage disequilibrium with 14-bp deletion in exon 8. One previous study reported 14-bp insertion allele, but it was only one case among 9 *HLA-G*01:01:08*[15]. In our study, over half of *HLA-G*01:01:08* showed 14-bp insertion alleles. In relation to other *HLA-G* alleles, 6 of 8 *HLA-G*01:01:08* with *G*01:01:01:01* and *G*01:04:01*, which are known to have strong linkage disequilibrium with 14-bp deletion, had 14-bp insertion, while four of five *HLA-G*01:01:08* with *G*01:01:02:01*, *G*01:01:03:01* and *G*01:05N*, which have been reported to have strong linkage disequilibrium with 14-bp insertion, had 14-bp deletion in exon 8. Therefore, 14-bp insertion/deletion polymorphism related to *HLA-G*01:01:08* in Korean population was considered to be affected by coexisting *HLA-G* alleles.

Our results showed strong linkage disequilibrium between *HLA-G* and other *HLA* alleles. *HLA-A* had stronger linkage disequilibrium with *HLA-G* than others (Table 4). The distance between these two *HLA* loci on the chromosome could affect this association, and further evaluations with a larger number of subjects are needed for exact investigations.

In our data and previous reports, *HLA-G* coding region in human showed relatively low polymorphism. This region was also well conserved in apes, and this may indicate a strong selective pressure for invariance from an evolutionary perspective[28]. On the other hand, *HLA-G* noncoding regions in human, which are known to regulate the expression of HLA-G proteins, would have been maintained in worldwide population by balancing selection. Human lineages may have different promoter activity owing to the polymorphism of the noncoding regions, and they may have modulated the balance between high- and low-expressing *HLA-G* haplotypes[29]. Future understandings of *HLA-G* gene regulation and the impact of polymorphisms on gene function might facilitate the use of HLA-G for therapeutic purposes.

V. Conclusion

We firstly analysed *HLA-G* polymorphism in a Korean population using a sequence-based HLA typing method with high resolution. From comparison with previous results on other populations, similarities and differences between *HLA-G* allele frequencies and 14-bp polymorphism could be identified. Immunological and clinical implications of HLA-G could be different as allele frequencies and polymorphism in each population. Thus, this study will be basic data for further studies about HLA-G.

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Abstract (In Korean)

한국인의 HLA-G 대립유전자 빈도

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Human leukocyte antigen (HLA)-G는 상대적으로 제한된 다형성을 가진 비고전적 class I 주조직적합복합체이다. 현재까지 인종 및 나라에 따른 대립유전자 빈도의 차이에 충분한 연구 결과는 부족한 실정이다. 따라서, 각각의 인구집단에서 HLA-G의 면역학적 기능에 대한 연구를 위해서는 대립유전자의 빈도와 다형성에 대한 연구 등 기초적인 자료가 필요하다.

본 연구에서는 비혈연 관계인 200명의 한국인을 대상으로 HLA-G의 대립유전자 빈도와 14-bp 다형성에 대해 조사하였다. *HLA-G* 대립유전자 분석은 exon 2, 3, 4의 염기서열분석을 통해, 14-bp 다형성은 exon 8의 PCR을 통해 시행하였다.

유전형 분석 결과 8가지의 다른 *HLA-G* 대립유전자가 관찰되어, 한국인에서 *HLA-G* 대립유전자의 다형성은 높지 않음을 알 수 있었다. *HLA-G*01:01:01:01*과 *G*01:04:01*이 우세한 대립유전자였으며(42.5%, 34.0%), 대립유전자의 빈도는 다른 아시아국가의 대립유전자 빈도와 유사하였다. 여러 백인 민족을 대상으로 한 연구에서는 14-bp 삽입/결실 다형성은 거의 유사한 빈도로 나타나는 반면 한국인에서는 14-bp 결실 다형성이 우세하였다(78%). 이전의 연구에서 *G*01:01:08* 대립유전자는 14-bp 결실 다형성과 관련되어 있음이 알려져 있었으나, 이 연구에서는 14-bp 삽입 다형성이 흔히 동반되는 것으로 나타났다.

*HLA-G*의 대립유전자 빈도에 관한 연구는 많지 않으며, 그 연구의 대부분은 고해상도 분석 방법이 보편화되기 이전에 연구된 결과였다. 이 연구는 한국인에 고해상도 HLA

분석 방법을 이용하여 *HLA-G*의 유전형에 대한 최초의 연구이다. 이 연구를 통해 한국인에서의 *HLA-G* 대립유전자 빈도를 알 수 있었으며, 이 연구 결과를 바탕으로 한국인에서 HLA-G의 면역학적 역할, 임상적인 의미에 관해 연구를 진행할 수 있을 것으로 기대된다.

핵심되는 말 : human leukocyte antigen-G, 고해상도 분석법, 한국인, 대립유전자 빈도