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Genetic polymorphisms of CYP2C9, CYP2C19, CYP2D6, CYP3A4, and CYP3A5 in Vietnamese-Koreans

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ORIGINAL ARTICLE

The Vietnamese-Koreans, especially offspring between a Vietnamese mother and a Korean father constituted the highest proportion (64.2%) of total Kosian population according to a census in 2014. To evaluate genetic characteristics in the Vietnamese-Koreans, a total of 25 alleles from CYP2C9, CYP2C19, CYP2D6, CYP3A4, and CYP3A5 were genotyped using SNaPshot method with DNA samples of 127 Vietnamese-Koreans. The previous reports on the CYPs of Korean and Vietnamese populations were also analyzed for the comparative studies for the frequencies of *CYP* alleles. The statistical significances in allele and genotype frequencies among the ethnics were analyzed by Chi-square or Fisher's exact probability test. Although most of variants analyzed in 5 CYPs did not reach the statistically significant difference between the Vietnamese-Koreans and Vietnamese, some alleles were only found in Vietnamese-Koreans. Compared with Korean population, frequencies of *CYP2D6*1* and *CYP2D6*10B* were statistically different from Vietnamese-Koreans ($p<0.05$). This is the first report to describe the CYP genotype profiles of Vietnamese-Koreans, which may provide important insight for the genotype based prediction of CYP activities of this admixture of Korean and Vietnamese.

Introduction

There has been a significant increase in the number of South-east Asians in Korea due to employment programs of foreign workers and marriage between female immigrants and Korean men over the last decade. A new word, 'Kosian' was made in 1997 during researching for problems of the foreign workers. The Kosian is a compound word of 'Korean' and 'Asian'. Originally, the meaning had been used as 'Asian living in Korea', but it was changed to 'admixture of a Korean and a South-east Asian'. [1]

According to a census by Korea Ministry of Public Administration and Security in 2014, the population of foreign residents in Korea was estimated to 1,569,470 (3.1% of total Korea population) which was 2.8% increased ratio compared to the value counted in 2013 (1,445,631). Looking into national distribution, North-east Asians were the highest (59.5%), followed by South-east Asians (23.6%), South Asians (4.8%), and Americans (4.5%). Of them, Vietnamese accounts for 50.1% of total South-east Asian population. Total Kosian population was 85,250, and among them, population whose one parent is Vietnamese was 54,737. They had the highest percentage of the total Kosians (64.2%).[2] It is expected that upcoming Korean society will have considerable proportion of multi-cultural families and the Kosians. Understanding the Kosian pharmacogenetic information would be important to provide them better medical services. Many countries such as United States, Unites Kingdom, and some European countries have been experienced the multi-ethnicities and multi-cultures in their countries and have already launched pharmacogenetic research program for their nationals.[3-6]

Individual differences in capacity to metabolize drugs can be

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affected by genetic polymorphisms in drug metabolizing enzymes such as phase I and phase II enzymes. Cytochrome P450 (CYP) is accounted as a major phase I enzyme consisting of about 75 percent of the phase I enzyme.[7] The polymorphisms of CYPs are important for drug metabolism and pharmacokinetics which often influence drug efficacy or toxicity (Appendix 1).[8]

Among the 57 CYPs in humans, the liver expression levels of CYP2C, CYP2D6, and CYP3A4/5 are estimated to about 18.2%, 1.5%, and 28.8%, respectively. However, theses CYPs contribute to commonly used drugs' metabolism about 19%, 24%, and 51%, respectively.[9]

The CYP2C9 involves the metabolism of phenytoin, amitryptiline, S-warfarin, tolbutamide, and several nonsteroidal anti-inflammatory drugs.[10] The major variants of *CYP2C9* are *CYP2C9*2* and *CYP2C9*3* which have been exhibited impaired metabolic activity both in vitro and in vivo, and their frequencies are apparently different among ethnic groups.[11] *CYP2C9*2* has not been found in both Korean and Vietnamese populations and the frequencies of *CYP2C9*3* in both populations have been reported as similar frequency.[12] CYP2C19 metabolizes anticonvulsants, proton pump inhibitors, and psychotropic drugs.[13] The proportions of poor metabolizer of the CYP2C19 are different between ethnicities; 2-5% in Caucasian but 13-23% in Asian.[14] In case of *CYP2C19*17*, it was identified in several Korean studies.[15,16] but there was no report in Vietnamese population. The CYP2D6 exists as a small proportion of drug metabolizing enzymes in liver (about 2%), but it is very important on drug metabolism (20-25% of total drugs in market).[17] There are about 90 alleles in *CYP2D6* and the major variants are *CYP2D6*2, CYP2D6*3, CYP2D6*4, CYP2D6*5, CYP2D6*6, CYP2D6*10, CYP2D6*17*, and *CYP2D6*41*.[18] The polymorphism of CYP2D6 was well established in Korean population, but not in Vietnamese population. The substrates of CYP2D6 are analgesics, antiarrhythmics, β-Adrenoceptor antagonists, and psychotropic drugs.[19] The CYP3A subfamily is one of the most important enzymes due to its high expression in liver and intestine, and metabolizing about half of all commonly used drugs.[9] The *CYP3A4* alleles were reported to exhibit large ethnic differences in their distributions. Among the *CYP3A4* alleles, *CYP3A4*18* is commonly distributed among the East Asians.[20-22] The CYP3A5 polymorphism is more prevalent and shows marked differences in protein expression and catalytic activity among the ethnic groups. In case of *CYP3A5,* the splicing variant *CYP3A5*3*, as known as defective allele, is the most common allele in most ethnic groups including Caucasians, African-American, and Asians.[23]

Although the frequencies of genetic polymorphisms in CYP alleles are different in various ethnicities, there have been no screening studies for major CYP variants in Kosian population. To determine the distribution of major CYP variants in Vietnamese-Korean which is percentage of the total Kosians, we conducted genotyping for 25 important CYP alleles and compared them with those of Vietnamese and Korean for the first time. It is believed that the present data are highly imperative to establish a comprehensive pharmacogenomic database of Vietnamese-Koreans and would be an important resource for studying individual variations in drug metabolism in Vietnamese-Korean population in the future.

Methods

Subjects

This study included Vietnamese-Koreans which are offspring between a Vietnamese woman and a Korean man. Total 127 samples from Vietnamese-Koreans (62 males, 65 females; average age, 17.5 months) were genotyped for analyzing the genetic alleles. Of them, the 4 samples from Vietnamese-Koreans were recruited at Department of Clinical Pharmacology, Inje University Busan Paik Hospital. Written informed consent was obtained from the legal representatives of these subjects prior to participation of this study which was approved by the Institutional Review Boards of Busan Paik Hospital (Busan, Korea). The 100 biospecimens of Vietnamese-Koreans for this study were provided by National Biobank of Korea, supported by the Ministry of Health, Welfare and Family Affairs. All samples derived from the National Biobank of Korea were obtained with informed consent under institutional review board-approved protocols (KOBB-2012-17). The 23 biospecimens of Vietnamese-Koreans for this study were provided by the Gyeongsang National University Hospital, a member of the National Biobank of Korea, which is supported by the Ministry of Health, Welfare and Family Affairs. All samples derived from the National Biobank of Korea were obtained with informed consent under institutional review board-approved protocols.

Genotyping

The genomic DNA was extracted from peripheral whole blood using QIAamp Blood Mini Kit (QIAGEN, Hilden, Germany).

The multiplex PCR conditions were optimized in order to develop a SNaPshot reaction. A premixture for *CYP2C9*14, CYP2C19*2, *3, *17, CYP3A4*18,* and *CYP3A5*3* was amplified in a total volume of 30 μL containing 100 ng of genomic DNA, 3 μL of 10X PCR buffer containing Mg^{2+}, 250 μM of each dNTP, 0.13 μM of each primer, and 5 U/μL of rTaq DNA polymerase (TaKaRa, Shiga, Japan). A premixture for *CYP2C9*3* and *13 was amplified in a total volume of 30 μL containing 100 ng of genomic DNA, 3 μL of 10X PCR buffer containing Mg^{2+}, 250 μM of each dNTP, 0.13 μM of each primer, and 5 U/μL of rTaq DNA polymerase (TaKaRa, Shiga, Japan). A premixture with *CYP2D6* 6.4 kb product for *CYP2D6*1XN, *2, *2XN, *3, *4, *5, *6, *9X2, *10B, *10BX2, *14B, *17, *17XN, *18, *21B, *29, *41, *49, *52,* and **60* was amplified in a total volume of 20 μL containing 100 ng of genomic DNA, 2 μL of 10X LA Taq PCR buffer, 250 μM of each dNTP, 2 μL of 25 mM $MgCl_2$, 2 μL 5X Band doctor (SolGent, Daejeon, South Korea), 0.25 μM of each

primer, and 5 U/μL of LA Taq DNA polymerase (TaKaRa, Shiga, Japan). A premixture for *CYP2D6* deletion was amplified in a total volume of 20 μL containing same components to the premixture with *CYP2D6* 6.4 kb except the primers. A premixture for *CYP2D6* duplication was amplified in a total volume of 20 μL containing same components to the premixture with *CYP2D6* 6.4 kb except the primers. The PCR was set up using GeneAmp PCR system 9700 (Applied Biosystems, Foster City, CA, USA) under the previous reported methods by our center.[15,24-26] The PCR products were purified to remove the remaining primers and dNTPs by ExoSAP-IT. The PCR products were mixed with ExoSAP-IT (USB®, Ohio, USA) at 37°C for 30 min, and then incubated at 80°C for 15 min to inactivate the enzyme. Multiplex and singleplex single-base extension (SBE) were performed using by SNaPshot® (Applied Biosystems, CA, USA) based on single-base primer with fluorescent labeled dideoxynucleotide triphosphate (ddNTP) to detect SNPs as showing four different colors according to a nucleotide.

The SNaPshot analysis was divided 3 sets; set 1 for *CYP2C9, CYP2C19, CYP3A4, CYP3A5,* and *CYP2D6* duplication, set 2 *for CYP2D6*2, *2XN, *5, *10B, *10BX2, *14B, *18, *21B, *41, *49, *52, *60* (using 6.4 kb template), and deletion, and set 3 *for CYP2D6 *3, *4, *6, *9X2, *17, *17XN, and *29.* Briefly, 4.5 μL (set 1) or 4 μL (set 2 and set 3) aliquots of purified PCR product were mixed with 1 μL of SNaPshot Multiplex Ready Reaction Mix, 4 μL of half-term buffer (200 mmol/L Tris–HCl, 5 mmol/L $MgCl_2$, pH 9), and 0.5 μL of 2X primer mix (set 1) or 1 μL of primer mix (set 2 and set 3). The SBE reactions were performed in GeneAmp PCR system 9700 as following conditions; 40 cycles of 96°C for 10 s, 50°C for 5 s, and 60°C for 30 s. The products were treated with 1 μL of SAP (USB®, Ohio, USA) at 37°C for 60 min to remove fluorescently labeled ddNTP, and then incubated at 65°C for 15 min to inactivate the SAP. When SNaPshot reactions were completed, 1 μL of the SNaPshot product was mixed with 0.25 μL of Genescan™-120 LIZ™ size standard (Applied Biosystems, CA, USA) and 8.75 μL of Hi-Di™ formamide (Applied Biosystems, CA, USA). The samples were denatured at 95°C for 5 min and separated by an ABI-Prism 3100 genetic analyzer (Applied Biosystems, CA, USA) using a 36-cm capillary array and POP-7 polymer. The SNaPshot results were analyzed by GeneMapper® version 3.7 software (Applied Biosystems, CA, USA).

Data collection from previous studies

The previous reports on the CYP genetic polymorphism of Korean and Vietnamese populations were collected to compare with the Vietnamese-Koreans results. For Korean population, referred data were gathered in *CYP2C9* reported by Lee et al,[27] *CYP2C19* reported by Kim et al,[16] *CYP2D6* reported by Lee et al,[28] *CYP3A4* reported by Lee et al,[21] and *CYP3A5* reported by Yoo et al.[29] For Vietnamese population, referred data were gathered in *CYP2C9* reported by Lee et al,[12] *CYP2C19* reported by Lee et al,[30] *CYP2D6* reported by Kim et al,[25] *CYP3A4* and *CYP3A5* reported by Veiga et al.[31]

Data analysis

The genotyped allele frequencies with 95% confidence intervals (CIs) of Vietnamese-Koreans were calculated from the observed numbers of alleles using frequency analysis. The Korean and Vietnamese data which were collected from literatures were compared with the Vietnamese-Korean data by the Chi-square or Fisher's exact probability test as necessary. If the p-value is less than 0.05, the results were considered to be statistically significant in the comparison. The statistical analysis was conducted by SAS® version 9.1.3 (SAS Institute Inc., Cary, NC, USA).

Results

Genotyping of Vietnamese-Koreans

The frequencies of CYP alleles in the 127 Vietnamese-Koreans are shown in Table 1. One sample was excluded in CYP2D6 genotyping due to inadequateness for PCR amplification. The identified alleles were 3 in *CYP2C9 (*1, *3, and *13),* 4 alleles in *CYP2C19 (*1, *2, *3, and *17)*, 10 in *CYP2D6 (*1, *2, *5, *10B, *14B, *21B, *41, *49, *1XN, and *10BX2)*, 2 in *CYP3A4 (*1 and *18)*, and 2 in *CYP3A5 (*1 and *3)*. The most frequent allele on each *CYP* was *CYP2C9*1* (96.1%), *CYP2C19*1* (66.9%), *CYP2D6*10B* (56.0%), *CYP3A4*1* (99.2%), and *CYP3A5*3* (78.4%).

Total 33 genotypes were detected; 3 genotypes of *CYP2C9, 7* genotypes of *CYP2C19,* 18 genotypes of *CYP2D6,* 2 genotypes of *CYP3A4*, and 3 genotypes of *CYP3A5* (Table 2).

Comparative analysis among Vietnamese-Korean, Vietnamese, and Korean data

Comparing with previous reported Korean data, the frequencies of *CYP* alleles were not significantly different between the Vietnamese-Koreans and Koreans (p>0.05) except *CYP2D6*. The frequency of *CYP2D6*1* was significantly lower in Vietnamese-Koreans (21.8%) than that reported for the Korean population (32.3%, p=0.0126, used bonferroni correction for the adjustment of p-value). However, the frequency of *CYP2D6*10B* was significantly higher in Vietnamese-Koreans (56.0%) than that reported for the Korean population (45.6%, p=0.0322, used bonferroni correction for the adjustment of p-value). The frequency of *CYP2D6*41* showed higher in Vietnamese-Koreans (4.4%) than the Korean population (2.2%). However, the frequency of *CYP2C19*3* showed lower in Vietnamese-Koreans (5.5%) than the Korean population (10.1%). The allele frequencies of the Vietnamese-Koreans and the Korean were showed in Table 1 which also included the *CYP* allele frequencies in Vietnamese. Comparing with previous reported Vietnamese data, the frequencies of *CYP* alleles were not statistically different between Vietnamese-Koreans and Vietnamese (p>0.05). However, *CYP2D6*21B, CYP2D6*1XN,* and *CYP2D6*10BX2* were only found in Vietnamese-Korean population (Table 1). In frequen-

Table 1. The allele frequencies of Vietnamese-Korean, Korean, and Vietnamese populations

Gene	Allele	Vietnamese-Korean[a]			Korean		Vietnamese	
		N[b]	(%)	95% CI[c]	N[d]	(%)	N[d]	(%)
CYP2C9	*1	244	96.1	93.7 - 98.5	295 [27]	94.7	157 [12]	97.8
	*3	8	3.2	1.0 - 5.3		5.1		2.2
	*13	2	0.8	0.0 - 1.9		0.2		0
CYP2C19	*1	170	66.9	61.1 - 72.7	271 [16]	60	165 [30]	68.8
	*2	65	25.6	20.2 - 31		28.4		26.4
	*3	14	5.5	2.7 - 8.3		10.1		4.9
	*17	5	2	0.3 - 3.7		1.5		ND
CYP2D6	*1	55	21.8	16.7 - 26.9	758 [28]	32.3	122 [25]	24.6
	*2	20	7.9	4.6 - 11.3		10.1		7.8
	*5	17	6.8	3.7 - 9.8		5.6		6.1
	*10B	141	56	49.8 - 62.1		45.6		57.0
	*14B	2	0.8	0.0 - 1.9		0.3		1.2
	*18	0	0	0.0 - 0.0		0.3		0
	*21B	1	0.4	0.0 - 1.2		0.3		0
	*41	11	4.4	1.8 - 6.9		2.2		2.7
	*49	3	1.2	0.0 - 2.5		1.4		0.4
	*52	0	0	0.0 - 0.0		0.3		0
	*60	0	0	0.0 - 0.0		0.1		0
	*1XN	1	0.4	0.0 - 1.2		0.1		0
	*2XN	0	0	0.0 - 0.0		1		0
	*10BX2	1	0.4	0.0 - 1.2		0.4		0
CYP3A4	*1	252	99.2	98.1 - 100.0	298 [21]	98.3	72 [31]	97.9
	*1B	ND	ND			ND		2.1
	*18	2	0.8	0.0 - 1.9		1.7		ND
CYP3A5	*1	55	21.7	16.6 - 26.7	104 [29]	26	72 [31]	33.3
	*3	199	78.4	73.3 - 83.4v		74		66.7

a) 126 subjects for *CYP2D6*, 127 subjects for *CYP2C9, CYP2C19, CYP3A4, and CYP3A5,* b) Number of alleles, c) CI: confidence interval, d) Number of studied subjects

cies of *CYP* genotypes, there were little differences between the ethnics, but it is a result from low frequency of each allele (Table 2).

Discussion

The population of Kosian who is admixture of a South-east Asian mother and a Korean father has been recently increasing in Korea. Among them, the population of Vietnamese-Koreans whose mother is Vietnamese has the highest proportion. CYP enzymes are very important for drug metabolism and their therapeutic effects. Among the CYPs, CYP2C9, CYP2C19, CYP2D6, CYP3A4, and CYP3A5 contribute to metabolizing over 90% of commonly used drugs.[9] Genetic polymorphisms of the CYPs have been studied in various ethnic groups. The present study provided the comprehensive pharmacogenetic

Table 2. The frequencies of genotypes in Vietnamese-Korean, Korean, and Vietnamese populations

Genotype	Vietnamese-Korean[a]			Korean		Vietnamese	
	No.[b]	(%)	95% CI[c]	N[d]	(%)	N[d]	(%)
CYP2C9				295 [27]		157 [12]	
**1/*1*	117	92.1	87.4 - 96.8		88.7		95.5
**1/*3*	8	6.3	2.1 - 10.5		10.6		7.0
**1/*13*	2	1.6	0.0 - 3.7		0.4		0.0
CYP2C19				271 [16]		165 [30]	
**1/*1*	56	44.1	35.5 - 52.7		35.7		44.9
**1/*2*	45	35.4	27.1 - 43.7		36.5		41.8
**1/*3*	9	7.1	2.6 - 11.6		10.7		6.1
**1/*17*	4	3.2	0.1 - 6.2		1.1		ND
**2/*2*	7	5.5	1.5 - 9.5		5.9		4.2
**2/*3*	5	3.9	0.6 - 7.3		7.0		2.4
**2/*17*	1	0.8	0.0 - 2.3		1.4		ND
**3/*3*	0	0.0	0.0 - 0.0		1.1		0.6
**3/*17*	0	0.0			0.3		ND
CYP2D6				758 [28]			
**1/*1*	6	4.8	1 - 8.5		12.4		ND
**1/*2*	8	6.4	2.1 - 10.6		5.9		ND
**1/*5*	3	2.4	0.0 - 5.0		3.6		ND
**1/*10B*	30	23.8	16.4 - 31.2		26.8		ND
**1/*14B*	0	0.0	0.0 - 0.0		0.0		ND
**1/*21B*	1	0.8	0.0 - 2.3		0.1		ND
**1/*41*	0	0.0	0.0 - 0.0		1.1		ND
**1/*49*	1	0.8	0.0 - 2.3		1.1		ND
**1XN/*1*	0	0.0	0.0 - 0.0		0.3		ND
**1XN/*10B*	1	0.8	0.0 - 2.3		0.0		ND
**2/*2*	0	0.0	0.0 - 0.0		1.19		ND
**2/*5*	2	1.6	0.0 - 3.8		1.2		ND
**2/*10B*	7	5.6	1.6 - 9.6		9.9		ND
**2/*14*	0	0.0	0.0 - 0.0		0.1		ND
**2/*18*	0	0.0	0.0 - 0.0		0.1		ND
**2/*21*	0	0.0	0.0 - 0.0		0.1		ND
**2/*41*	3	2.4	0.0 - 5.0		0.1		ND
**2/*52*	0	0.0	0.0 - 0.0		0.3		ND
**2XN/*1*	0	0.0	0.0 - 0.0		0.92		ND
**2XN/*5*	0	0.0	0.0 - 0.0		0.1		ND
**2XN/*10B*	0	0.0	0.0 - 0.0		0.9		ND
**5/*5*	0	0.0	0.0 - 0.0		0.3		ND
**5/*10B*	9	7.1	2.6 - 11.6		5.5		ND
**5/*10BX2*	1	0.8	0.0 - 2.3		0.0		ND
**5/*14*	0	0.0	0.0 - 0.0		0.1		ND

Table 2. Continued

Genotype	Vietnamese-Korean[a]			Korean		Vietnamese	
	No.t[b]	(%)	95% CI[c]	N[d]	(%)	N[d]	(%)
**5/*41*	1	0.8	0.0 - 2.3		0.13		ND
**5/*49*	1	0.8	0.0 - 2.3		0.0		ND
**10B/*10B*	42	33.3	25.1 - 41.6		20.8		ND
**10B/*14B*	2	1.6	0.0 - 3.8		0.3		ND
**10B/*18*	0	0.0	0.0 - 0.0		0.4		ND
**10B/*21*	0	0.0	0.0 - 0.0		0.4		ND
**10B/*41*	7	5.6	1.6 - 9.6		2.5		ND
**10B/*49*	1	0.8	0.0 - 2.3		1.6		ND
**10B/*52*	0	0.0	0.0 - 0.0		0.3		ND
**10B/*60*	0	0.0	0.0 - 0.0		0.1		ND
**10/*10XN*	0	0.0	0.0 - 0.0		0.8		ND
**14/*41*	0	0.0	0.0 - 0.0		0.1		ND
**41/*41*	0	0.0	0.0 - 0.0		0.3		ND
**49/*52*	0	0.0	0.0 - 0.0		0.1		ND
CYP3A4							
**1/*1*	125	98.4	96.3 - 100.0		ND		ND
**1A/*1A*	ND	ND			ND		95.9
**1A/*1B*	ND	ND			ND		4.1
**1/*18*	2	1.6	0.0 - 3.7		ND		ND
CYP3A5				104 [29]		74 [31]	
**1/*1*	5	3.9	0.6 - 7.3		5.8		9.5
**1/*3*	45	35.4	27.1 - 43.7		40.4		44.6
**3/*3*	77	60.6	52.1 - 69.1		53.8		45.9

a) 126 subjects for CYP2D6, 127 subjects for CYP2C9, CYP2C19, CYP3A4, and CYP3A5, b) Number of detected subjects, c) CI: confidence interval, d) Number of studied subjects

information on Vietnamese-Koreans.

To identify the differences of CYP polymorphisms between Vietnamese-Korean, Vietnamese, and Korean population, the Vietnamese-Korean data from the present study were compared with formerly researched data on Korean and Vietnamese population.

The observed *CYP* allele frequencies of Vietnamese-Koreans were similar to Koreans,[12,28-31] except *CYP2D6*1* which showed less frequent in Vietnamese-Koreans, and *CYP2D6*10B* which showed more frequent in Vietnamese-Koreans. In the Vietnamese-Koreans, the alleles which can decrease the CYP2D6 enzyme activity such as *CYP2D6*10B, *14B, *41, *49* and **10BX2* were higher than in Korean population; 62.8% in Vietnamese-Koreans and 49.9% in Koreans. The frequency of those decreased activity alleles was 69.0% in Vietnamese which was higher than Vietnamese-Koreans. It means that the capability of drug metabolism under CYP2D6 might be the lowest in Vietnamese population, followed by Vietnamese-Korean and Korean population.

The allele frequencies of *CYPs* did not show statistically significant differences between Vietnamese-Koreans and Vietnamese (P>0.05). However, the *CYP2D6*1XN, CYP2D6*10BX2,* and *CYP2D6*21B* were only found in Vietnamese-Koreans. The proportions of total alleles which decreased activity enzyme were similar in the Vietnamese-Koreans and Vietnamese although the frequencies of each allele were different between them.

The ethnic difference of CYP polymorphisms was reviewed through published reports to compare them with the Vietnamese-Korean data. In case of *CYP2C9,* the frequency of *CYP2C9*2* allele showed differences by ethnicities. The *CYP2C9*2* was not detected in Vietnamese-Koreans as same as Asians, however approximately 15% of Caucasians and 0-4.3% of Afri-

cans have been reported to contain the allele. Furthermore, the frequencies of *CYP2C9*3* allele were similar between the Vietnamese-Koreans and Africans (3.2% and 0.5-2.3%) but Caucasians exhibited high proportion of this allele (3.3-17%). This suggests that Vietnamese-Koreans have less clinical significance caused by CYP2C9 genotype than Caucasian population [32]. Second, in the distribution of *CYP2C19*, the Vietnamese-Koreans have low frequency of **17* (2.0%) compared to Caucasians and African-Americans (~20% and 17-18%). In addition, the proportion of poor metabolizers (PMs) is 9.4% of Vietnamese-Koreans, 12-23% of Asians, 1-8% of Europeans, and 1-8% of Black Africans,[33] suggesting that the Vietnamese-Koreans exhibit higher frequency of PM alleles than Caucasians and Black Africans. Third, the *CYP2D6* showed various allele distributions through ethnic groups. There were no PMs in Vietnamese-Koreans but 5-10% in Caucasians and 0-19% in Black Africans. [34] The major reason for these differences would be from the result that Vietnamese-Koreans don't have *CYP2D6*3* and **4*, which were the most abundant null alleles in Caucasians.[35] The *CYP2D6*4* is more common in the Caucasian population, *CYP2D6*17* is more frequently observed in Africans, and *CYP2D6*10* is most common in Asians.[3] Finally, the frequency of *CYP3A5*3* which is decreased activity allele also showed ethnic differences; Vietnamese-Koreans (78.4%), African-Americans (32%), Caucasians (90-93%), Hispanics (65%), and South Asians (60%).[36,37]

There are some limitations of the present study. First, only few Vietnamese-Korean subjects were genotyped for this study because it was hard to enroll that population. In case of *CYP2D6,* there are lots of low-frequency alleles such as *CYP2D6*18, *52, *60,* and duplications. For detecting them, further large-scale studies are required. Second, there was lack of pharmacogenomics study for Vietnamese population to compare with the Vietnamese-Koreans. Thus, more pharmacogenomics research is needed in Vietnamese population. Third, this study only defined genetic polymorphisms of Vietnamese-Koreans. For gathering more pharmacogenetic information, more studies need to investigate functional effects of the genetic polymorphisms which were identified in this study.

This research is the first paper to evaluate polymorphisms of major CYPs in Vietnamese-Koreans. The present study describing genetic polymorphisms in major CYPs could serve as an important resource for studying individual variations in drug metabolism in Vietnamese-Korean population in the future.

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Conflict of Interest

The authors declared no conflict of interest.

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