The Distribution of IL-10 Promoter Polymorphism in Thais

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*IL-10 is a regulatory cytokine, which plays important roles in the pathogenesis of many diseases Polymorphism of IL-10 promoter influences the phenotypic expressions such as the variation of IL-10 production among individuals and is subjected to the genetic susceptibility study of many diseases. However, there is no information about the frequencies of IL-10 promoter polymorphism in a Thai population. To determine the distribution of IL-10 promoter polymorphism in unrelated healthy Thais, genomic-DNA from 160 unrelated healthy volunteers were analyzed by polymerase chain reaction-restriction fragment length polymorphism (PCR-RFLP) method. The functional single-nucleotide polymorphisms (SNPs) in IL-10 promoter (positions -1082 (G/A), -819 (C/T), -592 (C/A) were included. The allele frequencies of -1082*A (93.4%), -819*T (71.9%), and -592*A (71.9%) were significantly higher than the allele frequencies of -1082*G (6.6%), -819*C (28.1%), and -592*C (28.1%) respectively in a Thai population similar to other Asian populations (Korean, Japanese, Chinese). As for the haplotype analysis, the ATA haplotype (72%) was significantly higher in Thais and other Asian populations compared to non-Asian populations; whereas, GCC haplotype (6.6%) was significantly lower in Thais. Additionally, two rare haplotypes of IL-10 promoter (ATC and ACA) which were previously reported only in the Chinese Han people, were found with similar frequencies (0.6%) in the present study. In conclusion, the distribution of IL-10 promoter polymorphisms in Thais was comparable to other Asian populations but distinct from Non-Asian populations. At least five haplotypes existed in an unrelated healthy Thai population as ACC, GCC, ATA, ATC, and ACA haplotypes.*

Keywords : *IL-10, Single-nucleotide polymorphisms*

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Interleukin-10 (IL-10) has pleiotropic effects in immunoregulation and inflammation [1]. Initially, it was identified as a type 2 T-helper cell cytokine, which suppresses type 1 T-helper lymphocytes by decreasing IL-2 and interferon-γ production. It also down-regulates MHC class II, B7 expression, and the pro-inflammatory cytokines [2-4]. Contrary to its T cell and macrophage inhibitory actions, IL-10 has potent *in vitro* stimulatory effects on B lymphocytes leading to the production of immunoglobulin [5]. In summary, the level of IL-10 production is crucial for immune regulation, controlling the balance between inflammatory and humoral response.

Since promoter region is critical for the transcription regulation of the gene, it is known that genetic variations in the promoter region of cytokine genes can significantly influence the cytokine production levels, thus affecting the outcome of immune balance [6-8]. Recently, a polymorphism of IL-10 gene has been implicated in several autoimmune diseases in which IL-10 plays an important role in the pathogenesis, such as systemic lupus erythematosus [9], rheumatoid arthritis [10], Sjogren's syndrome [11], and psoriasis [12]. The gene-encoding IL-10 maps on the long arm of chromosome 1 in the q31-32 region and its 5' flanking region contains numerous polymorphism including two CA-repeated microsatellites designated as IL-10.R (-4 kb) and IL-10.G (-1.1 kb) [13-15]. However, the functional significance of these microsatellites in relation to the production of cytokine is controversial and unclear. Three biallelic polymorphisms within the IL-10 promoter region, at position -1082 (G/A), -819 (C/T) and -592 (C/A) from the transcription initiation site, have also been identified. Their functional role influencing the capacity of IL-10 production was largely proved by *in vitro* stimulation of PBMC and macrophage [16-18], *in vitro* transcription assay [19] and by differential nuclear-binding activity [20]. The present study was undertaken to identify the distribution of these 3 biallelic IL-10 polymorphisms in healthy Thai individuals.

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Material and Method

DNA Samples

One hundred and sixty unrelated healthy volun-teers were included in the present study. The genomic DNA was extracted from buffy coat of EDTA-anticoagulated blood by using a salting out method as previously described [21].

Polymerase Chain Reaction-Restriction fragment Length Polymorphism Analysis

The genomic DNA were analyzed by Polymerase Chain Reaction-Restriction fragment Length Polymorphism (PCR-RFLP) mothod for genotyping the polymorphism of IL-10 at position -1082 (G/A), -819 (C/T) and -592 (C/A) as previously described[17]. The reaction volume for the amplification reaction was 30 µl, containing 100 ng of genomic DNA, 0.15 µl of 5.0 unit/µl Taq polymerase (Promega), 3 µl of 10x PCR buffer (20mM Tris-HCL pH 8.0, 100 mM KCL), 1.8 µl of 25 mM $MgCl_2$, 0.6 ml of 10 mM dNTP and 1.5 µl (20 pmol) of each oligonucleotide primer. PCR was carried out under specific PCR conditions, consisting of an initiation denaturation at 94 C for 2 minutes, followed by 35 cycles of denaturation (94 C, 20 seconds), annealing (60 C, 50 seconds) and extension (72 C, 20 seconds) and final extension at 72 C for 7 minutes. The amplification PCR products were subjected to specific restriction endonuclease as previously described [17]. After digestion, the fragments were separated on 3% agarose gel electrophoresis, and were visualized by ethidium bromide staining.

DNA Sequencing

Selected samples representing different genotypes from each SNP were subjected to DNA sequencing to validate the results of PCR-RFLP method. Briefly, PCR products were purified by the QIAquick PCR purification Kit (QIAGEN Inc., USA) and sequenced with both forward and reverse direction of IL-10 promoter region. The sequencing was undertaken using an ABI Prism310 genetic Analyzer by cycle sequencing chemistry with base-specific fluorescence-labeled dideoxynucleotide termination reagents, BigDye Terminator Ready Reaction Mix (Applied Biosystems, USA).

Statistical Analysis

Allele and haplotype frequencies were calculated by direct counting. The statistical significance of the difference was tested by chi-square method. Fisher's exact tests were applied if the expected frequency was less than 5. A p value of < 0.05 were considered to be significant. The goodness of fit to Hardy-Weinberg equilibrium, calculating the expected frequencies of each genotype and comparing them with the observed values, was performed using a chi-square test. Estimated haplotype frequencies from genotypic data were analyzed by PHASE program [22]. The values of linkage disequilibrium (LD) were determined using LDPlotter (http://innateimmunity.net/IIPGA2/Bioinfor-matics/index_html).

Results

The genotype distribution of all 3 SNPs in IL-10 promoter was consistent with the assumption of Hardy-Weinberg equilibrium (data not shown). The allele, genotype and haplotype frequencies of the IL-10 promoter polymorphisms in Thais are shown in Table 1 and 2. The distribution of IL-10 SNPs comparing between the study group and previous report groups [23-31], that consist of Asian (Korean, Chinese, Japanese), Caucasian, Hispanic, and African-Americans are summarized in Table 2 and 3. The -1082A allele was the highest allele frequency (93.4%) in the Thai population. The -1082 G/G genotype could not be detected in this study. At the other 2 positions, linkage disequilibrium was observed between alleles similar to other populations (r^2 =0.9887; D'=0.9943). Allele -819T and -592A were seen together (71.9%) and were more frequent than -819C and -592C (28.1%). In haplotype analysis, five haplotypes were detected in a Thai population: ATA (71.6%), ACC (21.2%), GCC (6.6%), ACA (0.3%), and ATC (0.3%). When allele and haplotype frequencies were compared to other published data, they were found to be similar to other Asian populations but significantly different from Caucasian, Hispanic and African-American populations (Table 3, 4). In summary, allele frequencies of -1082*A, -819*T, and -592*A (ATA haplotype) were significantly higher than the allele frequencies of -1082*G, -819*C, and -592*C (GCG haplotype) in Thai population, compared to non-Asian populations.

Discussion

Knowledge of the frequencies of cytokine polymorphisms in particular populations is very useful for population genetic studies, which may contribute to a better understanding of the pathogenesis of inflammatory diseases. Population genetic studies either family-based or population-based studies aimed to determine disease susceptibility using genetic markers. SNP is a very powerful genetic marker used widely

nowadays. The selection of SNPs for a genetic study requires not only the knowledge of their biological significance but also their frequencies in the population of interest. In the present study, the authors focused on the IL-10 polymorphisms within the regulatory regions, which affect the express level of this gene. The DNA sequence surrounding the -592 was shown to include motifs specific for SP-1 and avian erythroblastosis virus (ETS) family binding sites [20]. The -592C allele lacking the ETS motif is a potential molecular mechanism for increased IL-10 production in PBMC [20]. This finding is consistent with other reports by *in vitro* stimulation assay that -1082, -819, -592 haplotype of GCC rather than ATA are associated with high IL-10 production [16-19].

In the present study, the authors analyzed the distribution of IL-10 promoter alleles and haplotypes in unrelated healthy Thais compared to various ethnic groups from previously published reports. The distribution pattern of these alleles and haplotypes frequencies are rather similar among Asian populations including Thai, Korean, Chinese and Japanese. In addition, two rare haplotypes of IL-10 gene promoter (ATC and ACA) only reported previously in Chinese Han [32], were also found in a Thai population indicating closely related genetic backgrounds between the Thais and Chinese. Nevertheless, the GTA haplotype found in the Chinese population, was not observed in the Thai population. The frequency of ATA haplotype, which determines decreased IL-10 production, was at the highest frequency in Asian populations (64-72%) including the presented study group when compared to Hispanic (41%), African-American (41%), and Caucasians (16-28%), respectively.

Table 1. Distribution of IL-10 promoter SNPs: The genotype and allele frequencies in 160 unrelated healthy Thais

Genotype	Genotype frequencies (%)	Allele	Allele frequencies (%)
IL-10 -1082			
GG	0 (0)	G	21 (6.6%)
GA	21 (13.1%)	A	299 (93.4%)
AA	139 (86.8%)		
IL-10 -819			
CC	10 (6.3%)	C	90 (28.1%)
CT	70 (43.7%)	T	230 (71.9%)
TT	80 (50%)		
IL-10 -592			
CC	10 (6.3%)	C	90 (28.1%)
CA	70 (43.7%)	A	230 (71.9%)
AA	80 (50%)		

Table 2. Distribution of IL-10 promoter SNPs : The genotype and haplotype frequencies in 160 unrelated healthy Thais

Genotype -1082/-819/ -592	Genotype frequencies (%)	Haplotype	Haplotype frequencies (%)
GCC/GCC	0 (0%)	ATA	229 (71.6%)
GCC/ACC	4 (2.5%)	ACC	68 (21.2%)
GCC/ATA	17 (10.6%)	GCC	21 (6.6%)
ACC/ACC	5 (3.1%)	ACA	1 (0.3%)
ACC/ATA	52 (32.5%)	ATC	1 (0.3%)
ATA/ATA	80 (50%)		
ATC/ACC	1 (0.6%)		
ACA/ACC	1 (0.6%)		

IL-10 is an immune-regulatory cytokine which is important for balance Th1/Th2 response in the immune system by inhibiting type1/proinflammatory cytokine formation which plays a role in many inflammatory and autoimmune diseases. Therefore, the polymorphisms of the cytokine gene are potentially important as genetic prediction of disease susceptibility or clinical outcome. The ethnic difference in distribution pattern of IL-10 promoter polymorphism may explain the ethnic differences in susceptibility or severity of many diseases. Further investigation is underway to elucidate the role of polymorphism of IL-10 promoter together with the phenotypic expression and the susceptibility to various diseases, in which IL-10 plays a role in the pathogenesis, in a Thai population.

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References

1. Lalani I, Bhol K, Ahmed AR. Interleukin-10: biology, role in inflammation and autoimmunity. Ann Allergy Asthma Immunol 1997; 79: 469-83.
2. Taga K, Tosato G. IL-10 inhibits human T cell proliferation and IL-2 production. J Immunol 1992; 148: 1143-8.
3. Ding L, Linsley PS, Huang LY, Germain RN, Shevach EM. IL-10 inhibits macrophage costimulatory activity by selectively inhibiting the up-regulation of B7 expression. J Immunol 1993; 151: 1224-34.
4. Fiorentino DF, Bond MW, Mosmann TR. Two types of mouse T helper cell. IV. Th2 clones secrete a factor that inhibits cytokine production by Th1 clones. J Exp Med 1989; 170: 2081-95.
5. Rousset F, Garcia E, Defrance T, Peronne C, Vezzio N,

Table 3. Allele frequencies of the IL-10 promoter polymorphisms in healthy Thais individuals compared with other groups

Position/ Allele	Thai n=320 (%)	Korea n=622 (%) [26]	China n=152 (%) [25]	Japan n=104 (%) [28]	White n=428 (%) [24]	Greek Crpriot n=200 (%) [30]	Italy n=144 (%) [31]	Southeast England n=152 (%) [27]	Northern England n=156 (%) [29]	Manchester England n=660 (%) [23]	Hispanic n=50 (%) [24]	Afican-American n=114 (%) [24]
-1082												
G	21(6.6)	46(7.4)	9(6.0)	4(3.8)	198(46.3)*	76(38)*	48(33)*	80(52.6)*	79(50.6)*	323(49.0)*	11(22.0)*	38(33.3)
A	299(93.4)	576(92.6)	143(94.0)	100(96.2)	230(53.7)*	124(62)*	96(67)*	2(47.4)*	77(49.4)*	337(51.0)*	76(66.7)*	39(78.0)*
-819												
C	90(28.1)	200(32.2)	50(33.0)	32(30.8)	330(77.1)*	153(76.5)*	104(72)*	127(83.6)*	115(73.7)*	508(77.0)*	30(60.0)*	67(58.8)*
T	230(71.9)	422(67.8)	102(67.0)	72(69.2)	98(22.9)*	47(23.5)*	40(28)*	25(16.4)*	41(26.3)*	152(23.0)*	20(40.0)*	47(41.2)*
-592												
C	90(28.1)	200(32.2)	50(33.0)	32(30.8)	330(77.1)*	153(76.5)*	104(72)*	127(83.6)*	115(73.7)*	508(77.0)*	30(60.0)*	67(58.8)*
A	230(71.9)	422(67.8)	102(67.0)	72(69.2)	98(22.9)*	47(23.5)*	40(28)*	25(16.4)*	41(26.3)*	152(23.0)*	20(40.0)*	47(41.2)*

* The corrected *p* value was lower than 0.05 when compared with Thais

Table 4. Haplotype frequencies of the IL-10 promoter polymorphisms in healthy Thais individuals compared with other groups

Haplotype	Thai n=320 (%)	Korea n=622 (%) [26]	China n=152 (%) [25]	Japan n=104 (%) [28]	White n=428 (%) [24]	Greek Crpriot n=200 (%) [30]	Italy n=144 (%) [31]	Southeast England n=152 (%) [27]	Northern England n=156 (%) [29]	Manchester England n=660 (%) [23]	Hispanic n=50 (%) [24]	African-American n=114 (%) [24]
GCC	21(6.6)	46(7.4)	3(2.0)	4(4)	173(46.7)*	70(35)*	47(33)*	80(52.6)*	77(49)*	326(49.4)*	9(18.8)	35(31.8)*
ACC	68(21.2)	154(24.8)	46(30.0)	28(27)	115(31.1)	83(41.5)	56(39)	47(30.9)	38(24)	190(28.8)	19(39.6)	29(26.4)
ATA	229(71.6)	422(67.8)	97(64.0)	72(69)	82(22.2)*	47(23.5)*	41(28)*	25(16.4)*	41(27)*	144(21.8)*	20(41.6)*	46(41.8)*
ATC	1(0.3)	0	0	0	0	0	0	0	0	0	0	0
ACA	1(0.3)	0	0	0	0	0	0	0	0	0	0	0
GTA	0	0	6(4.0)	0	0	0	0	0	0	0	0	0

* The corrected *p* value was lower than 0.05 when compared with Thais

Hsu DH, et al. Interleukin 10 is a potent growth and differentiation factor for activated human B lymphocytes. Proc Natl Acad Sci U S A 1992; 89: 1890-3.
6. Moser KL, Neas BR, Salmon JE, Yu H, Gray-McGuire C, Asundi N, et al. Genome scan of human systemic lupus erythematosus: evidence for linkage on chromo-some 1q in African-American pedigrees. Proc Natl Acad Sci USA 1998; 95: 14869-74.
7. Loughrey BV, Maxwell AP, Fogarty DG, Middleton D, Harron JC, Patterson CC, et al. An interluekin 1B allele, which correlates with a high secretor phenotype, is associated with diabetic nephropathy. Cytokine 1998; 10: 984-8.
8. Suarez A, Castro P, Alonso R, Mozo L, Gutierrez C. Interindividual variations in constitutive interleukin-10 messenger RNA and protein levels and their association with genetic polymorphisms. Trans-plantation 2003; 75: 711-7.
9. Lazarus M, Hajeer AH, Turner D, Sinnott P, Worthington J, Ollier WE, et al. Genetic variation in the interleukin 10 gene promoter and systemic lupus erythematosus. J Rheumatol 1997; 24: 2314-7.
10. Hajeer AH, Lazarus M, Turner D, Mageed RA, Vencovsky J, Sinnott P, et al. IL-10 gene promoter polymorphisms in rheumatoid arthritis. Scand J Rheumatol 1998; 27: 142-5.
11. Hulkkonen J, Pertovaara M, Antonen J, Lahdenpohja N, Pasternack A, Hurme M. Genetic association between interleukin-10 promoter region polymorphisms and primary Sjogren's syndrome. Arthritis Rheum 2001; 44: 176-9.
12. Asadullah K, Eskdale J, Wiese A, Gallagher G, Friedrich M, Sterry W. Interleukin-10 promoter polymorphism in psoriasis. J Invest Dermatol 2001; 116: 975-8.
13. Eskdale J, Gallagher G. A polymorphic dinucleotide repeat in the human IL-10 promoter. Immunogenetics 1995; 42: 444-5.
14. Eskdale J, Kube D, Gallagher G. A second polymorphic dinucleotide repeat in the 5' flanking region of the human IL10 gene. Immunogenetics 1996; 45: 82-3.
15. Eskdale J, Keijsers V, Huizinga T, Gallagher G. Micro-satellite alleles and single nucleotide polymorphisms (SNP) combine to form four major haplotype families at the human interleukin-10 (IL-10) locus. Genes Immun 1999; 1: 151-5.
16. Rosenwasser LJ, Borish L. Genetics of atopy and asthma: the rationale behind promoter-based candidate gene studies (IL-4 and IL-10). Am J Respir Crit Care Med 1997; 156: S152-5.
17. Edwards-Smith CJ, Jonsson JR, Purdie DM, Bansal A, Shorthouse C, Powell EE. Interleukin-10 promoter poly-morphism predicts initial response of chronic hepatitis C to interferon alfa. Hepatology 1999; 30(2): 526-30.
18. Turner DM, Williams DM, Sankaran D, Lazarus M, Sinnott PJ, Hutchinson IV. An investigation of polymorphism in the interleukin-10 gene promoter. Eur J Immunogenet 1997; 24(1): 1-8.
19. Crawley E, Kay R, Sillibourne J, Patel P, Hutchinson I, Woo P. Polymorphic haplotypes of the interleukin-10 5' flanking region determine variable interleukin-10 transcription and are associated with particular pheno-types of juvenile rheumatoid arthritis. Arthritis Rheum 1999; 42: 1101-8.
20. Shin HD, Winkler C, Stephens JC, Bream J, Young H, Goedert JJ, et al. Genetic restriction of HIV-1 patho-genesis to AIDS by promoter alleles of IL10. Proc Natl Acad Sci U S A 2000; 97: 14467-72.
21. Miller SA, Dykes DD, Polesky HF. A simple salting out procedure for extracting DNA from human nucleated cells. Nucleic Acids Res 1988; 16: 1215.
22. Stephens M, Donnelly P. A comparison of bayesian methods for haplotype reconstruction from population genotype data. Am J Hum Genet 2003; 73: 1162-9.
23. Perrey C, Pravica V, Sinnott PJ, Hutchinson IV. Genotyping for polymorphisms in interferon-gamma, interleukin-10, transforming growth factor-beta 1 and tumour necrosis factor-alpha genes: a technical report. Transpl Immunol 1998; 6: 193-7.
24. Hoffmann SC, Stanley EM, Cox ED, DiMercurio BS, Koziol DE, Harlan DM, et al. Ethnicity greatly influences cytokine gene polymorphism distribution. Am J Transplant 2002; 2: 560-7.
25. Mok CC, Lanchbury JS, Chan DW, Lau CS. Inter-leukin-10 promoter polymorphisms in Southern Chinese patients with systemic lupus erythematosus. Arthritis Rheum 1998; 41: 1090-5.
26. Pyo CW, Hur SS, Kim YK, Choi HB, Hong YS, Kim DW, et al. Polymorphisms of IL-1B, IL-1RN, IL-2, IL-4, IL-6, IL-10, and IFN-gamma genes in the Korean population. Hum Immunol 2003; 64: 979-89.
27. Reynard MP, Turner D, Navarrete CV. Allele frequencies of polymorphisms of the tumour necrosis factor-alpha, interleukin-10, interferon-gamma and interleukin-2 genes in a North European Caucasoid group from the UK. Eur J Immunogenet 2000; 27: 241-9.
28. Miyazoe S, Hamasaki K, Nakata K, Kajiya Y, Kitajima K, Nakao K, et al. Influence of interleukin-10 gene promoter polymorphisms on disease progression in patients chronically infected with hepatitis B virus. Am J Gastroenterol 2002; 97: 2086-92.
29. Donaldson PT, Norris S, Constantini PK, Bernal W, Harrison P, Williams R. The interleukin-1 and inter-leukin-10 gene polymorphisms in primary sclerosing cholangitis: no associations with disease susceptibility/ resistance. J Hepatol 2000; 32: 882-6.
30. Costeas PA, Koumas L, Koumouli A, Kyriakou-Giantsiou A, Papaloizou A. Cytokine polymorphism frequencies in the Greek Cypriot population. Eur J Immunogenet 2003; 30: 341-3.
31. Matsushita M, Tanaka A, Kikuchi K, Kitazawa E, Kawaguchi N, Kawashima Y, et al. Association of single nucleotide polymorphisms of the interleukin-10 promoter gene and susceptibility to primary biliary cirrhosis: immunogenetic differences in Italian and Japanese patients. Autoimmunity 2002; 35: 531-6.
32. Hu RC, Xu YJ, Zhang ZX, Xie JG. [Polymorphism of interleukin-10 gene promoter and its association with susceptibility to chronic obstructive pulmonary disease in Chinese Han people]. Zhonghua Yi Xue Yi Chuan Xue Za Zhi 2003; 20: 504-7.

การศึกษาการกระจายตัวของ IL-10 alleles ในประเทศไทย

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*IL-10 เป็นไซโตไคน์ที่มีบทบาทสำคัญในกลไกการเกิดโรคหลายอย่าง polymorphism ของยีน IL-10 มีผลต่อการแสดงออกของยีน (phenotypic expression) หลายอย่างเช่น เกี่ยวข้องระดับการสร้าง IL-10 ของแต่ละบุคคล และยังมีความสำคัญในการศึกษาความสัมพันธ์ระหว่างพันธุกรรมกับโอกาสเกิดโรคหลาย ๆ โรคอีกด้วย เนื่องจากยังไม่มีการศึกษาการกระจายตัวของ polymorphism ของยีน IL-10 ในคนไทย การศึกษานี้มีวัตถุประสงค์เพื่อศึกษาการกระจายตัวของ polymorphism ของยีนIL-10 ของคนไทย โดยศึกษา single-neucleotide polymorphisms ของ promoter ของยีน IL-10 ตำแหน่งที่ -1082 (G/A), -819 (C/T) และ -592 (C/A) ด้วยวิธี PCR-RFLP ในคนไทยปกติ 160 คน ผลการวิจัยพบว่าความถี่ของอัลลีล (allele) -1082*A (93.4%), -819*T (71.9%), และ -592*A (71.9%) สูงกว่าความถี่ของอัลลีล -1082*G (6.6%), -819*C (28.1%), และ -592*C (28.1%) อย่างมีนัยสำคัญทางสถิติในคนไทยเช่นเดียวกับคนเอเชียเชื้อชาติอื่น ๆ (เกาหลี ญี่ปุ่น จีน) จากการศึกษา haplotype ของยีน IL-10 พบว่าความถี่ของ ATA haplotype (71.6%) สูงขึ้นอย่างมีนัยสำคัญทางสถิติในคนไทยและคนเอเชียเชื้อชาติอื่น ๆ เมื่อเทียบกับกลุ่มซึ่งไม่ใช่คนเอเชีย ในทางตรงข้ามความถี่ของ GCC haplotype(6.6%) ลดลงอย่างมีนัยสำคัญทางสถิติเช่นกัน ในการศึกษานี้ยังพบ haplotype 2 แบบที่เคยมีรายงานเฉพาะในคนจีน คือ ATC และ ACA โดยพบความถี่เท่ากัน (0.6%) ในคนไทยปกติอีกด้วย โดยสรุปการกระจายตัวของ polymorphism ของยีน IL-10 ของประชากรไทยคล้ายคลึงกับคนเอเชียชาติอื่น ๆ แต่แตกต่างจากกลุ่มซึ่งไม่ใช่คนเอเชีย และมี haplotype อย่างน้อย 5 ชนิดในคนไทยปกติ คือ ACC, ATC, GCC, ATC และ ACA*