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No Association of the Human Y Chromosome with Blood Pressure in Korean Male Population

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ABSTRACT. It has been reported that the genetic variations in the Y chromosome has influence the blood pressure in some Caucasian male populations, but the effect in non-Caucasian population is unclear. In the present study, we examined the relationship between blood pressure and a *Hin*dIII RFLP of Y chromosome in 152 unrelated male individuals of ethnically homogeneous Korean origin. There were no significant differences in systolic and diastolic blood pressures between genotype groups, respectively. However, the frequency of A genotype in Korean population was much higher than those of Caucasian populations ($P < 0.05$). Therefore, the results of this study will contribute the better understanding the genetic characteristics of Y chromosome in Korean population.

Keywords: Blood pressure, Genotype and Y chromosome.

INTRODUCTION

The cardiovascular risk significantly differs between genders, and especially men indicate a higher prevalence of hypertension and ischemic heart disease compared with women. This is contributed, in part, by sex difference in blood pressure (BP) that occurs throughout their life span (Reckelhoff, 2001).

One of the obvious genetic determinants of sexual dimorphism is the Y chromosome. Y chromosome exists as a single chromosome, and the majority of this chromosome does not recombine (known as the recombining region [NRY]) and is inherited intact by sons from their fathers (Graves, 1995). Extensive studies using animal models demonstrate a significant association between the Y chromosome and BP. (Davidson *et al.*, 1995; Ely and Turner, 1990; Ely *et al.*, 2000; Kren *et al.*, 2001; Kreutz *et al.*, 1996; Negrin *et al.*, 2001).

Ellis *et al.* (2000) firstly reported a significant association between an increased risk of elevated diastolic blood pressure (DBP) and a genetic variation of the Y chromosome in human population. Later, this association has been replicated in two European population. (Charchar *et al.*, 2002).

However, these studies were mainly performed in Caucasian population, and this study in non-Caucasian population is scanty. In the present study, we tested the hypothesis that the genetic polymorphism of Y chromosome was associated with BP in ethnically homogeneous Korean population.

MATERIALS AND METHODS

Study Subjects

A total of 152 unrelated male individuals were randomly chosen from the students of the department of physical education, the Hanyang University, Seoul, and the outpatients of the department of clinical pathology, Seoul Hygiene Hospital, Seoul, Korea.

The body mass index (BMI) value was calculated by the body weight (kg) divided by the square of the height (m^2). BP was measured by carefully trained observers with a standard mercury sphygmomanometer. Systolic BP (SBP) was taken at the return of arterial sounds (Korotkoff phase I), and diastolic BP (DBP) was taken at the disappearance of sounds (Korotkoff phase V). The mean arterial pressure (MAP) was calculated by DBP-1/3(SBP-DBP) (mmHg). Also, pulse pressure (PP) was calculated as the difference between SBP and

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Table 1. Clinical parameters of the male population studied (n = 152)

	Mean±SD[1]	Range
Number	152	
Age (year)	34.3±17.5	19.0-80.0
BMI (kg/m^2)[2]	23.2±1.9	18.8-29.6
SBP (mmHg)[3]	119.4±7.8	105.0-142.0
DBP (mmHg)[4]	72.9±7.1	54.0-82.0
MAP (mmHg)[5]	87.0±7.8	67.0-102.0
PP (mmHg)[6]	46.5±7.9	30.0-80.0

Abbreviations: [1]SD, standard deviation; [2]BMI, body mass index; [3]SBP, systolic blood pressure; [4]DBP, diastolic blood pressure; [5]MAP, mean arterial pressure; [6]PP, pulse pressure.

DBP.

The general characteristics of the participants from Korean male population are displayed in Table 1.

DNA Analysis

Genomic DNA was isolated from buffy coat by the method of Kunkel *et al.* (1977). Polymerase Chain Reaction (PCR) techniques were used for *Hin*dIII RFLP of Y chromosome (Ellis *et al.*, 2000). Briefly, total 50 μl of the reaction mixture contained 200~400 ng of genomic DNA, 100 ng of each primer, 200 μM of each dNTP, and buffers recommended by the manufacturer. The sequences of the primer for *Hin*dIII RFLP studied were:

sense, 5'-TCTGAGACACTTCTTTGTGGTA-3',
nonsense 5-CGCTCAAAATATCCACTTTCAC-3.

Amplification was carried out with DNA thermocycler: one cycle at 95°C for 10 min, 35 cycles at 95°C for 30 sec, at 60°C for 30 sec and at 72°C for 1 min with a final polymerization at 72°C for 10 min.

Following amplification, 10 ul of the PCR product were digested by the addition of 10 units of restriction enzyme *Hin*dIII (Boeringer Mannheim, Germany) at 37°C for 18 hours. Digested PCR products were genotyped by the electrophoresis using 2% agarose gel with 0.5x TBE buffer.

Statistical Analysis

Allele frequencies were estimated by gene counting method. Student's t- test was performed to compare the mean levels of anthropometric parameters among different genotypes. Statistical significance was accepted at the $P = 0.05$ level. Statistical analysis were performed with the SPSS statistical software package (version 9.0).

RESULTS AND DISCUSSION

Two copies of the alphoid satellite are located in the NRY region of the Y chromosome (Santos *et al.*, 1995), but only one copy contains the *Hin*dIII RFLP. In the presence of the *Hin*dIII recognition site, this copy is cut into 2 fragments of 250 bp and 35 bp by PCR-RFLP analysis, whereas the additional copy remains uncut. Therefore, the presence of restriction site (which we designate A genotype) is indicated by 3 fragment bands of 285, 250 and 35 bp, whereas the absence of the restriction site (which we designate the B genotype) is indicated by a single 285 bp band (Fig. 1).

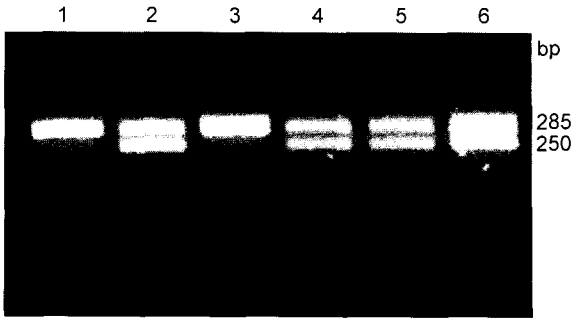

Fig. 1. *Hin*dIII RFLP patterns of human Y chromosome. Lane 1 and 3, B genotypes; lane 2 and 4~6, A genotypes.

Distribution of genotypes in 152 unrelated male individuals are presented in Table 2. As seen in Table 2, The A genotype was found in 93% of the men studied. There were no significant differences in any anthropometrical parameters between genotype groups. This result is opposite to that of previous studies with Caucasian populations (Charchar *et al.*, 2002; Ellis *et al.*, 2000). Because BP has the multifactorial and polygenic origin, in contrast to a disease that is transmitted according to simple Mendelian hereditary principles, it is possible that the mechanism altering the control of the BP associated with *Hin*dIII RFLP vary for different popu-

Table 2. Clinical characteristics of men grouped according to the presence (A genotype) or absence (B genotype) of the Y chromosome *Hin*dIII restriction site

Phenotype	A Genotype	B Genotype	Probability
Number	142	10	
Age (year)	34.5 (17.5)	31.0 (17.6)	0.599
BMI (kg/m^2)[1]	23.2 (1.9)	23.5 (2.1)	0.622
SBP (mmHg)[2]	119.4 (7.5)	119.0 (11.3)	0.422
DBP (mmHg)[3]	72.8 (7.2)	73.5 (6.0)	0.379
MAP (mmHg)[4]	86.9 (7.9)	88.8 (7.4)	0.653
PP (mmHg)[5]	46.6 (8.0)	45.5 (7.1)	0.706

Phenotypes are presented as mean values with SD (standard deviation) in parentheses.
Abbreviations: [1]BMI, body mass index; [2]SBP, systolic blood pressure; [3]DBP, diastolic blood pressure; [4]MAP, mean arterial pressure; [5]PP, pulse pressure.
Probability values are calculated by unpaired t-test.

Table 3. Genotype frequencies of Y chromosome *Hin*dIII RFLP in different populations

Population	Number	A genotype	B genotype	P[1]	Reference
Caucasian					
Australian	409	0.31	0.69	<0.05	Ellis *et al.*, 2000
Polish	155	0.33	0.67	<0.05	Charchar *et al.*, 2002
Scottish	762	0.28	0.72	<0.05	Charchar *et al.*, 2002
Mongolian					
Korean	152	0.93	0.07		*Present study*

[1]Probability.

lations and hence that the results from different ethnic groups may be quite different. Therefore, this study emphasizes the importance of interethnic comparisons in developing a more complete understanding of the relation between genetic variation of Y chromosome and BP.

The genotype distributions for *Hin*dIII RFLP in Mongoloid and Caucasian populations are given in Table 3. As seen in Table 3, Korean population has much higher A genotype frequency (0.93) than Caucasian populations ranging from 0.28 to 0.33. This discrepancy in the genotype distribution may be explained by differences in genetic background. That is, it might be due to genetic drift by a founder effect or a selective mechanism. Thus, the significant association between *Hin*dIII RFLP of Y chromosome and BP in Caucasian populations might be a consequence of linkage disequilibrium between neutral mutations and a significant allele of the Y chromosome. However, because there is no data on *Hin*dIII RFLP from Negroid populations and Asian populations such as Japanese and Chinese populations to compare with the present data, it was not possible to discuss about the genotype frequencies in worldwide ethnic populations. Therefore, studies in other racial or ethnic groups will be great interest.

REFERENCES

Charchar, F.J., Tomaszewski, M., Padmanabhan, S., Lacka, B., Upton, M.N., Inglis, G.C., Anderson, N.H., McConnachie, A., Zukowska-Szczechowska, E., Grzeszczak, W., Connell, J.M.C., Watt, G.C.M. and Dominiczak, A.F. (2002): The Y chromosome effect on blood pressure in two European populations, *Hypertension*, **39**, 353-356.

Davidson, A.O., Schork, N., Jaques, B.C., Kelman, A.W., Sutcliffe, R.G., Reid, J.L. and Dominiczak, A.F. (1995): Blood pressure in genetically hypertensive rats: influence of the Y chromosome, *Hypertension*, **26**, 452-459.

Ellis, J.A., Stebbing, M. and Harrap, S.B. (2000): Association of the Human Y chromosome with high blood pressure in the general population, *Hypertension*, **36**, 731-733.

Ely, D.L. and Turner, M.E. (1990): Hypertension in the spontaneously hypertensive rat is linked to the Y chromosome, *Hypertension*, **16**, 277-281.

Ely, D., Turner, M.E. and Milsted, A. (2000): A review of the Y chromosome and hypertension, *Braz. J. Med. Biol. Res.*, **33**, 679-691.

Graves, J.A. (1995): The origin and function of the mammalian Y chromosome and Y-borne genes: an evolving understanding, *Bioessays*, **17**, 311-320.

Kren, V., Qi, N., Krenova, D., Zidek, V., Sladka, M., Jachymova, M., Mikova, B., Horky, K., Bonne, A., Van Lith, H.A., Van Zutphen, B.F., Lau, Y.F., Pravenec, M. and St. Lezin, E. (2001): Y-chromosome transfer induces changes in blood pressure and blood lipids in SHR, *Hypertension*, **37**, 1147-1152.

Kreutz, R., Stock, P., Struk, B. and Lindpaintner, K. (1996): The Y chromosome: epistatic and ecogenetic interactions in genetic hypertension, *Hypertension*, **28**, 895-897.

Kunkel, L.M., Smith, K.D., Boyer, S.H., Borgaonkar, D.S., Wachtel, S.S., Miller, O.J., Breg, W.R., Jones, H.W. and Rary, J.M. (1977): Analysis of human Y chromosome-specific reiterated DNA in chromosome variants, *Proc. Natl. Acad. Sci. USA*, **74**, 1245-1249.

Negrin, C.D., McBride, M.W., Carswell, H.V., Graham, D., Carr, F.J., Clark, J.S., Jeffs, B., Anderson, N.H., Macrae, I.M. and Dominiczak, A.F. (2001): Reciprocal consomic strains to evaluate Y chromosome effects, *Hypertension*, **37**, 391-397.

Reckelhoff, J.F. (2001): Gender differences in the regulation of blood pressure, *Hypertension*, **37**, 1199-1208.

Santos, F.R., Pena, S.D.J. and Tyler-Smith, C. (1995): PCR haplotypes for the human Y chromosome based on alphoid satellite DNA variants and heteroduplex analysis, *Gene*, **165**, 191-198.