Significance of β_2-Adrenergic Receptor Gene Polymorphism in Obesity and Type 2 Diabetes Mellitus in Korean Subjects

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Catecholamines play a central role in the regulation of energy expenditure, in part stimulating lipid mobilization through lipolysis in fat cells. The β_2-adrenergic receptor (ADRB2) is a major lipolytic receptor in human fat cells, and a recent study has shown that common polymorphisms occurring in codons 16 and 27 of the ADRB2 gene are significantly associated with obesity and lipolytic ADRB2 function in adipose tissue. We investigated whether previously described human ADRB2 gene polymorphisms are associated with obesity and diabetes in Korean subjects. According to the World Health Organization (WHO) criteria for oral glucose tolerance testing, 57 subjects had normal glucose tolerance (NGT), 32 had impaired glucose tolerance (IGT), and 106 had diabetes mellitus. The nondiabetic group (including NGT and IGT) consisted of 46 obese (defined as those with body mass index [BMI] of $\geq$ 27 kg/m^2) and 43 nonobese subjects (BMI $<$ 27 kg/m^2). The subjects with diabetes consisted of 62 obese and 44 nonobese subjects. There was no significant difference between nonobese and obese subjects in the allele frequency of ADRB2 gene polymorphisms at codons 16 and 27. There were no significant differences in BMI, percentage body fat, waist–to-hip ratio (WHR), systolic blood pressure, diastolic blood pressure and concentrations of fasting plasma glucose, fasting serum insulin, serum low-density lipoprotein (LDL)-cholesterol, serum high-density lipoprotein (HDL)-cholesterol, serum triglyceride, and serum free fatty acids, according to ADRB2 gene polymorphisms at codons 16 and 27. The frequency of the Glu27 homozygote was 1.1%. These findings suggest that genetic variability in the ADRB2 gene may not be a major determinant for the development of obesity and diabetes in Koreans.

OBESITY IS A complex metabolic disorder resulting from the combined effects of genes and behavior.[1] The search for candidate genes for obesity has been active. However, the exact genes have not been identified, because obesity is determined not only by a number of different genes, but also by a large number of environmental factors. Genes that are involved in the regulation of catecholamine function may be of particular importance for human obesity, because catecholamine plays a central role in the regulation of energy expenditure.[2] β_1-, β_2-, and β_3-adrenoceptors stimulate lipolysis in human fat cells.[3,4] Genes encoding these receptors may constitute interesting candidates to explain part of the genetic predisposition to human obesity. Large et al[5] have reported that genetic variability in the human β_2-adrenergic receptor (ADRB2) gene could be of major importance for obesity, energy expenditure, and lipolytic ADRB2 function in adipose tissue. Other studies have also suggested an association between ADRB2 gene polymorphism and obesity.[6-9] However, there is still considerable debate on this association. Hayakawa et al[10] reported that Glu27Glu and Arg16Gly polymorphisms of the ADRB2 gene are not a major contributing factor to obesity in Japanese men. Some other studies reported a lack of association between polymorphisms of the ADRB2 gene and obesity in Caucasians,[11,12] and others have suggested that there may be differences between men and women in the effects of Gln27Glu β_2-adrenoceptor gene polymorphisms on obesity.[9,13] In this study, we investigated whether the previously described human ADRB2 gene polymorphisms are associated with obesity and type 2 diabetes in Korean subjects.

SUBJECTS AND METHODS

Subjects

A cohort of 195 unrelated Korean subjects was studied. Based on World Health Organization (WHO) criteria for oral glucose tolerance testing (OGTT),[14] 57 subjects had normal glucose tolerance (NGT), 32 had impaired glucose tolerance (IGT), and 106 had diabetes mellitus. Study subjects were subdivided into 2 groups according to their degree of obesity. The nondiabetic group (including those with NGT and IGT) consisted of 46 obese (defined as those with body mass index [BMI] of $\geq$ 27 kg/m^2) and 43 nonobese subjects (BMI $<$ 27 kg/m^2). The group with diabetes consisted of 62 obese and 44 nonobese subjects, and all of them were newly detected cases. All subjects were recruited from visitors to the Health Promotion Centre. Any subjects with previous diagnosis of heart or renal failure, chronic liver diseases, endocrine diseases, hypertension, dyslipidemia, or type 1 diabetes (ketonuria or anti-glutamic acid decarboxylase [anti-GAD] II antibody positivity) were excluded from the study. Informed consent was obtained from all the participants, and this study was approved by the Internal Review Board (IRB) of Samsung Medical Centre.

Phenotype Measurements

A complete physical examination, routine collection of biochemical data, and a 75-g OGTT were performed after an overnight fast of 12 to 14 hours. Subjects ingested 75 g of glucose, and blood samples were taken at 0, 30, 60, 90, and 120 minutes. Plasma and serum were stored at -20°C for later assay of plasma glucose and serum insulin. Plasma glucose was measured in duplicate with an autoanalyzer (Hitachi, Tokyo, Japan) by the hexokinase method. The interassay coefficient of variation was 1.6%. Serum insulin was measured in duplicate using an immunoradiometric assay (IRMA) method (Medgenix, Niveles, Belgium). Intra- and interassay coefficients of variation were 2.2% and

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Table 1. Clinical Characteristics of the Subjects

	Nondiabetic Subjects		Diabetic Subjects	
	Nonobese	Obese	Nonobese	Obese
Sex (M/F)	24/19	26/20	25/19	26/36
Age (yr)	45 ± 2	42 ± 2	51 ± 2	56 ± 1
BMI (kg/m^2)	22.3 ± 0.3*	29.9 ± 0.5	22.2 ± 0.4*	29.9 ± 0.4
Body fat (%)	22.3 ± 1.5*	30.9 ± 1.2	23.6 ± 1.2*	33.2 ± 1.3
WHR	0.83 ± 0.01*	0.89 ± 0.01	0.87 ± 0.01*	0.92 ± 0.01
Systolic BP (mm Hg)	125.1 ± 2.6†	134.4 ± 2.9	128.3 ± 2.2*	140.5 ± 2.5
Diastolic BP (mm Hg)	77.1 ± 1.9	82.0 ± 1.9	79.0 ± 1.6†	84.1 ± 1.8
FPG (mmol/L)	5.8 ± 0.1	5.5 ± 0.1	7.8 ± 0.4	9.5 ± 0.6
FSI (nmol/L)	52.4 ± 2.9*	104.0 ± 10.0	73.2 ± 7.2	101.2 ± 12.
LDL-cholesterol (mmol/L)	2.88 ± 0.16	3.17 ± 0.24	3.06 ± 0.33	2.95 ± 0.48
HDL-cholesterol (mmol/L)	1.19 ± 0.05	1.26 ± 0.07	1.67 ± 0.07	1.10 ± 0.16
Triglyceride (mmol/L)	1.26 ± 0.13	1.76 ± 0.22	1.67 ± 0.07	1.10 ± 0.16
Free fatty acid (μEq/L)	831 ± 69	880 ± 101	1,053 ± 224	1,007 ± 207

NOTE. Values are mean ± SEM.

Abbreviations: BMI, body mass index; WHR, waist hip ratio; FPG, fasting plasma glucose; FSI, fasting serum insulin.

*$P < .01$ *v* obese group; †$P < .05$ *v* obese group.

5.8%, respectively, in cases of serum insulin levels < 215 pmol/L, and 3.9% and 4.5%, respectively, in cases of serum insulin levels ≥ 215 pmol/L. Blood pressure, waist–to-hip ratio (WHR), percentage body fat, and BMI were measured. Serum low-density lipoprotein (LDL)-cholesterol and triglyceride levels were measured with an autoanalyzer (Hitachi).

Genotyping of ADRB2 Polymorphism

The genomic DNAs of 195 subjects were extracted from peripheral blood leukocytes. The DNA segment containing codon 16 of the ADRB2 gene was amplified by polymerase chain reaction (PCR) using a sense primer (5′-GGCCCATGACCAGATCAGCA-3′) and an antisense primer (5′-GAATGAGGCTTCCAGGC GTC-3′). With these primers, we obtained a PCR product of 353 bp. The PCR conditions consisted of an initial denaturation step at 94°C for 4 minutes, followed by 30 cycles of denaturation at 94°C for 1 minute, annealing at 63°C for 1 minute, and extension at 72°C for 1 minute, with a final extension of 10 minutes at 72°C. The PCR products were digested with *Ita*I (Boehringer-Mannheim, Germany) at 37°C for 60 minutes, electrophoresed on a 2% agarose gel (BIO-RAD, Hercules, CA), and stained with ethidium bromide. The expected products after digestion with *Ita*I were 27, 55, 97, and 174 bp for Gln27 homozygotes, 27, 55, 97, 174, and 229 bp for Gln27Glu27, and 27, 97, and 229 for Glu27 homozygotes. The DNA segment in codon 16 of ADRB2 gene was amplified by PCR using a sense primer (5′-CTTCTTGCTGGCACGCAAT-3′) and an antisense primer (5′-CCAGTGAAGTTGAAG TAGTTGG-3′). With these primers, we obtained a PCR product of 201 bp. The PCR conditions were an initial denaturation step at 94°C for 4 minutes, followed by 30 cycles of denaturation at 94°C for 1 minute, annealing at 56°C for 1 minute, and extension at 72°C for 1 minute, with a final extension of 10 minutes at 72°C. The PCR products were digested with *Bsr*DI (New England Biolabs, Beverly, MA) at 60°C for 60 minutes, electrophoresed on a 3% Meta-Phor agarose gel (FMC, Rockland, ME), and stained with ethidium bromide. The expected products after digestion with *Bsr*DI were 14, 56, and 131 bp for Arg16 homozygotes, 14, 23, 56, 108, and 131 bp for Arg16Gly16, and 14, 23, 56, and 108 for Gly16 homozygotes.

Statistical Analyses

Statistical analyses were performed using the SPSS/PC$^+$ software program (SPSS, Evanston, IL). The frequencies of mutations in each group were compared using a 2-tailed Fisher's exact test. Anthropometric and laboratory data were compared by Mann-Whitney *U* test or 1-way analysis of variance (ANOVA) with post hoc comparison (Bon-Feroni correction). Differences were considered statistically significant at the level of $P < .05$.

RESULTS

Subjects

The clinical features of the study subjects are presented in Table 1. In the nondiabetic group (including NGT and IGT), there were no significant differences in sex ratio, age, diastolic blood pressure, and concentrations of fasting plasma glucose, serum LDL-cholesterol, serum HDL-cholesterol, serum triglycerides, and serum free fatty acids between nonobese and obese subjects. However, BMI, percentage body fat, systolic blood pressure, and concentrations of fasting serum insulin in nonobese subjects were significantly lower than in obese subjects. In the diabetic group, there was also no significant difference in sex ratio, age, and concentrations of fasting plasma glucose, fasting serum insulin, serum LDL-cholesterol, serum HDL-cholesterol, serum triglycerides, and serum free fatty acids between nonobese and obese subjects. However, BMI, percentage body fat, and systolic and diastolic blood pressures in nonobese subjects were significantly lower than in obese subjects.

Frequency of ADRB2 Gene Polymorphism

The frequency of Arg16Gly substitution was not significantly different between obese and nonobese subjects ($\chi^2 = 2.09$, $P = .352$). In subgroup analysis, it was not significantly different between 2 groups in both the nondiabetic ($\chi^2 = 0.06$, $P = .970$) and the diabetic group ($\chi^2 = 4.47$, $P = .107$). We did not observe any difference in the frequency of the Arg16Gly substitution according to gender. There was no significant difference in the Gly16 allele frequency according to the degree of obesity, gender, and the presence of diabetes (Table 2). Because there was 1 case of Glu27Glu, this case was excluded

Table 2. Codon 16 and 27 Polymorphims of ADRB2 Gene

	Nondiabetic Subjects		Diabetic Subjects	
	Nonobese (n = 43)	Obese (n = 46)	Nonobese (n = 44)	Obese (n = 62)
Codon 16 (M/F)				
Arg16Arg16	17 (39.5%)	18 (39.1%)	15 (34.1%)	26 (41.9%)
Arg16Gly16	22 (51.2%)	23 (50.0%)	17 (38.6%)	29 (46.8%)
Gly16Gly16	4 (9.3%)	5 (10.9%)	12 (27.3%)	7 (11.3%)
Gly16 allele frequency	0.35 (0.38/0.32)	0.36 (0.29/0.45)	0.40 (0.52/0.39)	0.35 (0.50/0.34)
Codon 27 (M/F)				
Gln27Gln27	34 (79.1%)	34 (73.9%)	34 (77.3%)	53 (85.5%)
Gln27Glu27	9 (20.9%)	11 (23.9%)	10 (22.7%)	9 (14.5%)
Glu27Glu27	0	0	1 (2.3%)	0
Glu27 allele frequency	0.10 (0.13/0.08)	0.14 (0.08/0.18)	0.14 (0.15/0.13)	0.07 (0.12/0.06)

in the analysis of association between obesity and codon 27 polymorphism of ADRB2 gene. No difference in the frequency of Gln27Glu substitution could be identified between nonobese and obese subjects ($\chi^2 = 0.30$, $P = .594$) in both the nondiabetic ($\chi^2 = 0.16$, $P = .801$) and the diabetic group ($\chi^2 = 1.18$, $P = .312$). There was no significant difference in the Glu27 allele frequency according to the degree of obesity, gender, and the presence of diabetes (Table 2). The polymorphisms of codon 16 and of codon 27 were in Hardy-Weinberg expectations in nondiabetic subjects, whereas in diabetic subjects, the polymorphism of codon 16 were not.

Clinical Features According to Codon 16 Polymorphism of ADRB2 Gene

The clinical features according to codon 16 polymorphism of ADRB2 gene are presented in Table 3. In the nondiabetic group, there were no significant differences in sex ratio, age, BMI, percentage body fat, WHR, systolic and diastolic blood pressure, and concentrations of fasting plasma glucose, serum LDL-cholesterol, serum HDL-cholesterol, serum triglycerides, and serum free fatty acids between the Arg/Arg, Arg/Gly, and Gly/Gly groups. Concentrations of fasting serum insulin in the Arg/Gly group were significantly lower than in the Arg/Arg group (66.7 ± 4.3 pmol/L *v* 92.6 ± 12.9 pmol/L; $P < .05$). In the diabetic group, BMI in the Gly/Gly group was significantly lower than in the Arg/Arg group (24.3 ± 0.8 kg/m^2 *v* 27.7 ± 0.8 kg/m^2; $P < .05$). There were no significant differences in sex ratio, age, percentage body fat, WHR, systolic and diastolic blood pressure, and concentrations of fasting plasma glucose, fasting serum insulin, serum LDL-cholesterol, serum HDL-cholesterol, serum triglycerides, and serum free fatty acids between the Arg/Arg, Arg/Gly, and Gly/Gly groups.

Clinical Features According to Codon 27 Polymorphism of ADRB2 Gene

The clinical features according to codon 27 polymorphism of ADRB2 gene are presented in Table 4. In both the nondiabetic and diabetic groups, there were no significant differences in sex ratio, age, BMI, percent body fat, WHR, systolic and diastolic blood pressure, and concentrations of fasting plasma glucose, fasting serum insulin, serum LDL-cholesterol, serum HDL-cholesterol, serum triglycerides, and serum free fatty acids between the Gln/Gln, Gln/Glu, and Glu/Glu groups.

Table 3. Phenotypic Characteristics of Subjects According to ADRB2 Polymorphism at Codon 16

	Nondiabetic			Diabetic		
	Arg/Arg	Arg/Gly	Gly/Gly	Arg/Arg	Arg/Gly	Gly/Gly
Sex (M/F)	23/12	21/24	6/3	16/25	23/23	12/7
Age (yr)	41 ± 2	46 ± 2	45 ± 5	56 ± 2	53 ± 2	54 ± 3
BMI (kg/m^2)	26.8 ± 0.9	26.1 ± 0.6	27.3 ± 1.4	27.7 ± 0.8	26.7 ± 0.6	24.3 ± 0.8*
Body fat (%)	26.8 ± 1.6	27.6 ± 1.7	27.7 ± 2.4	31.1 ± 1.8	29.4 ± 1.5	25.2 ± 2.4
WHR	0.85 ± 0.01	0.85 ± 0.01	0.87 ± 0.01	0.91 ± 0.01	0.90 ± 0.01	0.92 ± 0.01
Systolic BP (mm Hg)	127.7 ± 2.9	133.1 ± 3.1	122.4 ± 3.8	134.0 ± 3.2	136.5 ± 2.4	134.5 ± 5.1
Diastolic BP (mm Hg)	78.9 ± 2.4	81.6 ± 1.6	72.7 ± 4.6	80.5 ± 12.7	82.5 ± 1.8	83.1 ± 3.1
FPG (mmol/L)	5.64 ± 0.12	5.62 ± 0.9	5.65 ± 0.21	9.06 ± 0.60	9.11 ± 0.62	7.73 ± 0.57
FSI (nmol/L)	92.6 ± 12.9	66.7 ± 4.3*	76.8 ± 9.3	85.0 ± 12.0	93.3 ± 12.1	71.8 ± 12.1
LDL-cholesterol (mmol/L)	2.90 ± 0.22	3.10 ± 0.20	2.79 ± 0.26	3.25 ± 0.34	3.00 ± 0.43	3.05 ± 0.26
HDL-cholesterol (mmol/L)	1.23 ± 0.07	1.21 ± 0.06	1.24 ± 0.14	1.42 ± 0.08	1.20 ± 0.09	1.03 ± 0.09
Triglyceride (mmol/L)	1.51 ± 0.26	1.43 ± 0.16	1.78 ± 0.34	1.90 ± 0.20	2.63 ± 0.29	1.71 ± 0.39
Free fatty acid (μEq/L)	785 ± 65	842 ± 81	1,205 ± 371	582 ± 144	1,132 ± 176	1,010 ± 250

NOTE. Values are mean ± SEM.

Abbreviations: BMI, body mass index; WHR, waist hip ratio; FPG, fasting plasma glucose; FSI, fasting serum insulin.

*$P < .05$ *v* Arg/Arg.

Table 4. Phenotypic Characteristics of Subjects According to ADRB2 Polymorphism at Codon 27

	Nondiabetic			Diabetes	
	Gln/Gln	Gln/Glu	Glu/Glu	Gln/Gln	Gln/Glu
Sex (M/F)	39/29	10/10	1/0	41/46	10/9
Age (yr)	43 ± 2	46 ± 2	49	55 ± 1	52 ± 3
BMI (kg/m^2)	26.4 ± 0.9	26.6 ± 0.9	27.9	27.0 ± 0.5	25.4 ± 0.9
Body fat (%)	26.6 ± 1.3	29.3 ± 2.1	30.8	29.5 ± 1.1	29.1 ± 3.1
WHR	0.85 ± 0.01	0.84 ± 0.01	0.87	0.91 ± 0.01	0.88 ± 0.01
Systolic BP (mm Hg)	132.0 ± 2.2	123.1 ± 4.5	123	135.9 ± 2.0	131.9 ± 4.1
Diastolic BP (mm Hg)	80.1 ± 1.6	78.1 ± 2.8	75	82.4 ± 1.4	79.6 ± 3.0
FPG (mmol/L)	5.64 ± 0.08	5.57 ± 0.13	5.93	8.71 ± 0.36	9.73 ± 1.38
FSI (nmol/L)	80.4 ± 7.3	67.4 ± 5.7	119.8	80.1 ± 7.5	118.0 ± 23.7
LDL-cholesterol (mmol/L)	2.92 ± 0.18	3.07 ± 0.18	3.00	2.90 ± 0.35	3.27 ± 0.37
HDL-cholesterol (mmol/L)	1.19 ± 0.05	1.35 ± 0.10	1.06	1.15 ± 0.07	1.15 ± 0.14
Triglyceride (mmol/L)	1.471 ± 0.14	1.59 ± 1.07	2.00	2.42 ± 0.33	1.69 ± 0.40
Free fatty acid (μEq/L)	833 ± 75	941 ± 92	1,100	1,030 ± 156	1,135 ± 170

NOTE. Values are mean ± SEM.

Abbreviations: BMI, body mass index; WHR, waist hip ratio; FPG, fasting plasma glucose; FSI, fasting serum insulin.

DISCUSSION

This is the first report on the relationship between obesity and ADRB2 polymorphisms in Korean subjects. ADRB2 polymorphism was not significantly associated with the degree of obesity or the presence of diabetes in either female or male Koreans. These results suggest that the Gln27Glu and Arg16Gly polymorphisms of the ADRB2 gene are not a major contributing factor to obesity in Korean subjects. Several studies have reported strong associations between ADRB2 gene polymorphism and obesity.[5-9] Large et al[5] have reported that ADRB2 gene polymorphisms were found more frequently in obese Caucasian women and had a close relationship with the amount of body fat. They showed that mutation in ADRB2 gene affected the functions of ADRB2 in fat cells.[5] Ishiyama et al[6] have suggested an association of polymorphisms in the ADRB2 receptor gene with obesity, hypertriglyceridemia, and diabetes mellitus in Japanese subjects. They observed that the Gln27Glu substitution was twice as common in obese subjects, and that the frequency of the Glu27 allele was also higher in patients with type 2 diabetes mellitus than in nondiabetic subjects.[6] Another Japanese study reported that the Gln27Glu ADRB2 receptor variant was associated with obesity in males.[8] Ukkola et al[7] reported that gene-to-gene interactions among the α_2-, β_2-, and β-adrenergic receptor genes contributed to the phenotypic variability in abdominal obesity and plasma lipid and lipoprotein in a family study in Québec. However, there is considerable debate on this association, because there have been several studies showing no significant association between ADRB2 gene polymorphism and obesity.[10-12] Hayakawa et al[10] reported that Gln27Glu and Arg16Gly polymorphisms of the ADRB2 gene are not a major contributing factor to obesity, blood pressure, serum lipid levels, uric acid, or free fatty acid levels in 210 Japanese men. Oberkofler et al[11] reported that Gln27Glu polymorphisms in the ADRB2 gene are not a major factor contributing to morbid obesity in Austrian women. On the other hand, there are a few reports about the gender-specific association between ADRB2 polymorphism and obesity. Hellstrom et al[13] suggested that a positive association between obesity and the Glu27 genetic variant in ADRB2 exists in females, whereas there is a negative correlation between Glu27 and obesity in Swedish male subjects.

Although the reasons for this discrepancy among studies are unclear, there are some possible explanations. First, the difference in the degree of obesity among study subjects should be considered. Our subjects were less obese than those in studies on Caucasian subjects. In the study of Large et al,[5] values of BMI in nonobese and obese subjects were 23.0 ± 0.3 kg/m^2 and 39.3 ± 0.8 kg/m^2, respectively. In the present study, values of BMI in nonobese and obese subjects were 22.5 ± 0.2 kg/m^2 and 29.9 ± 0.3 kg/m^2, respectively. However, it is not likely that the degree of obesity among study subjects can explain the different results. Values of BMI in nonobese and obese Japanese were 22.9 ± 2.0 kg/m^2 and 31.2 ± 3.5 kg/m^2 in the study of Ishiyama et al.[6] Although there was no difference compared with our subjects in the degree of obesity in that study, there was a significant association between ADRB2 gene polymorphism and obesity. This may imply that the difference in the degree of obesity is not the major factor that can explain the different results among studies. The Glu27 frequency in the Far East Asian studies is much lower than that in the Caucasian studies. In the present study, there was only 1 Glu27 homozygote (1/195, 0.5%), and the Glu27 allele frequency was 0.105. In the study of Ishiyama et al,[6] the frequency of the Glu27 homozygote was 1.3% (5/400) and that of the Glu27 allele was 0.108. By contrast, Large et al[5] reported that the frequency of the Glu27 homozygote was 15.7% (22/140), and the Glu27 allele frequency was 0.40. Several studies have shown strong linkage disequilibrium between the Gln27Glu and Arg16Gly polymorphisms. In our study, however, we did not observe this. The Glu27 allele was detected in 8 of 68 subjects homozygous for the Arg16 allele, and 8 of 19 subjects homozygous for the Gly16 allele also carried the Glu27 allele. Only 16.4% of all subjects had both the Gly16 and the Glu27 allele. One particular aspect of our study is that the Gly16 homozygote group had significantly lower BMI than did the Arg16 homozygote group, whereas the WHR between the 2 groups was not different in the diabetic subjects. This suggests that the codon 16 polymorphism might affect the distribution of body fat, but this

was not observed in the nondiabetic subjects. This hypothesis is, therefore, inconclusive and should be further studied.

One of the major limitations in this study was the relatively small number of subjects, especially in subgroup analysis. The allele frequency of the Glu27 variant was twice as high in nonobese diabetic subjects than obese diabetic subjects, yet the findings were not statistically significant. This implied that the number of our subjects was too small in subgroup analysis. However, in the comparison of the frequency of codon 16 polymorphism and codon 27 polymorphism between nonobese and obese groups, there was no significant difference between 2 groups; and values of χ^2 were markedly low (codon 16, $\chi^2 = 2.09$, $P = .352$ and codon 27, $\chi^2 = 0.30$, $P = .594$). We could not observe the effect of homozygocity in Glu27, because only 1 case was Glu27 homozygote. The effect of Glu27 homozygocity should be investigated in another future study. Numerous genetic and environmental factors may contribute to obesity, which is a complex metabolic disorder resulting from the combined effects of genes and behavior. Although the ADRB2 gene is one of the putative "obesity genes," we could not observe any significant association between polymorphisms of ADRB2 gene and obesity. Our results suggest that the Glu27Glu and Arg16Gly polymorphisms of the ADRB2 gene are not major contributing factors to obesity in Korean subjects.

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