The Effects of Uncoupling Protein-1 Genotype on Lipoprotein Cholesterol Level in Korean Obese Subjects

Hyun Hee Oh, Kil Soo Kim, Sun Mi Choi, Hyun Sung Yang, and Yoosik Yoon

Uncoupling protein-1 (UCP-1) plays a major role in thermogenesis, and has been implicated in the pathogenesis of obesity and metabolic disorders. The purpose of this study was to estimate the effects of A-3826G polymorphism of the *UCP-1* gene on the plasma lipid profiles in 190 Korean obese subjects with a body mass index (BMI) more than 30 kg/m^2. Height, weight, BMI, wait-to-hip ratio (WHR), obesity index, and body composition were measured and genotype of *UCP-1* was analyzed by polymerase chain reaction (PCR) restriction fragment length polymorphism (RFLP) method. Serum concentrations of fasting glucose, total cholesterol, high-density lipoprotein (HDL) cholesterol, and triglyceride were measured. The frequencies of *UCP-1* genotypes were AA type, 22.1%; AG type, 53.7%; and GG type, 24.2%; and the frequency of G allele was 0.51. Among many parameters, diastolic blood pressure (DBP) ($P = .023$) and low-density lipoprotein (LDL) cholesterol ($P = .011$) were significantly higher in AG and GG types compared with AA type, whereas HDL cholesterol was significantly lower in GG type compared with other types ($P < .05$). Atherogenic index was significantly higher in GG type compared with AA type ($P = 0.027$). LDL-to-HDL cholesterol ratio was significantly increased in the order of AA < AG < GG types ($P = .001$). When the subjects were divided into a normal group and a hyper-LDL cholesterolemia group by LDL cholesterol level of 3.626 mmol/L (140 mg/dL), the frequency of hyper-LDL cholesterolemia was significantly higher in GG type compared with other types by Fisher's exact (chi-square) test ($P = .05$). When logistic regression analysis was conducted to find the risk factors of hyper-LDL cholesterolemia, the odds ratio was 4.115 ($P = .03$) for GG type of *UCP-1* gene. These results suggest that the GG type of the *UCP-1* gene has a strong association with increased LDL cholesterol level and might be a significant risk factor for hyper-LDL cholesterolemia among Korean obese subjects.

UNCOUPLING PROTEIN-1 (UCP-1) is a proton transporter that uncouples oxidative metabolism from adenosine triphosphate (ATP) synthesis and dissipates energy through heat. It was shown to be expressed in brown adipose tissue (BAT), which was reported to play important roles for energy homeostasis in rodents.[1-3] Although BAT plays a minor role in humans, it is still responsible for 1% to 2% of the energy expenditure, preventing weight gain of 1 to 2 kg/yr.[1] This small portion of energy expenditure can increase the risk for obesity and related metabolic disorders when accumulated for decades.[4]

UCP-1 has been thought to be expressed only in BAT, which almost disappears in adulthood in humans. Recently, however, it was reported that the expression of UCP-1 mRNA and protein was detected in adult human white adipose tissue and skeletal muscle.[5,6] Esterbauer et al measured UCP-1 mRNA level in adipose tissues obtained from fat biopsy of 153 morbid obese subjects, and found that UCP-1 mRNA expression levels in adipose tissues were significantly lower in morbidly obese individuals than in lean controls.[7]

The human *UCP-1* gene has been located on the long arm of chromosome 4 (q31), and its expression and activity is regulated by sympathetic nervous system through β_3-adrenergic receptor.[3,8-10] A→G polymorphism at position −3826 (A-3826G) in the 5′-flanking region of the *UCP-1* gene was found and shown to be associated with increased body weight and body fat gain over time in the Quebec Family Study.[8,11,12] This polymorphism was also related to the resistance to weight loss during a low-calorie diet.[13] Several other studies reported associations of *UCP-1* A-3826G polymorphism with obesity and related metabolic disorders.[8,11,12,14-20]

This study was conducted to investigate the effect of the A-3826G polymorphism of the *UCP-1* gene on the biochemical parameters of Korean obese subjects with a body mass index (BMI) greater than 30 kg/m^2 who were at very high risk of obesity-related metabolic complications.

MATERIALS AND METHODS

Subjects

One hundred ninety Korean obese subjects with a BMI greater than 30 kg/m^2 were recruited from a weight-loss program at Kirin Oriental Medical Hospital (Seoul, Korea). The clinical characteristics of the subjects are shown in Table 1. Genomic DNA was obtained with informed consent. The study subjects were divided into 3 groups by genotypes of *UCP-1:* AA type (wild-type), and AG and GG types (variant types). They were classified as hyper-LDL cholesterolemia by plasma low-density lipoprotein (LDL) cholesterol level of more than 3.626 mmol/L (140 mg/dL).[21] All clinical data were obtained before starting a weight-loss program. Blood pressure, height, weight, and waist and hip circumference were measured. BMI was calculated as weight (kg) divided by squared height (m), and waist-to-hip ratio (WHR) was calculated as waist circumference divided by hip circumference. Obesity index was calculated as (obesity index = real weight/ideal weight × 100, ideal weight = [height − 100] × 0.9). Body compositions were measured by bioimpedance analysis using a commercial device (Inbody 2.0; Biospace, Seoul, Korea).

Determination of the UCP-1 Genotype

Genomic DNA was extracted from whole blood using a Qiagen mini kit (Hilden, Germany). Polymerase chain reaction (PCR) was conducted to amplify a genomic DNA fragment containing A-3826G position of the *UCP-1* gene. Upstream primer (5′CCAGTGGCTAATGAGAGAA3′),

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Table 1. Clinical Characteristics of Study Subjects

Characteristic	No. of Subjects (N = 190)
Sex (n)	M:F = 44:146
Age (yr)	28.38 ± 0.72
Weight (kg)	90.15 ± 1.13
BMI (kg/m^2)	33.88 ± 0.28
SBP (mm Hg)	125.80 ± 1.03
DBP (mm Hg)	76.96 ± 0.87

NOTE. Values are means ± SE.

Abbreviations: SBP, systolic blood pressure; DBP, diastolic blood pressure.

downstream primer (5′GCACAAAGAAGAAG -CAGAGAGG3′), 3 μL dNTP mix (1 mmol/L), 0.2 μL Taq DNA polymerase (1 U), and 3 μL PCR buffer (10×) were added and adjusted to total volume of 30 μL with distilled water. The amplification protocol consisted of 35 cycles of denaturation at 94°C for 30 seconds, annealing at 60°C for 30 seconds, and extension at 72°C for 30 seconds. The amplified PCR products were checked for correct size of 279 bp by electrophoresis in a 3% agarose gel. The PCR products were subsequently digested with a restriction enzyme *Bcl*1 for 1 hour at 50°C and were subjected to electrophoresis in a 3% agarose gel. The resulting band patterns were GG type, single band of 279 bp; AG type, 3 bands of 279, 157, and 122 bp; and AA type, 2 bands of 157 and 122 bp (Fig 1).[7]

Biochemical Analysis

Blood samples obtained after fasting overnight for more than 12 hours were centrifuged at 2,000 rpm for 30 minutes. Serum samples were taken and concentrations of fasting glucose, total and high-density lipoprotein (HDL) cholesterol, triglyceride, ALT, AST, and total bilirubin were determined by autobiochemical analyzer. LDL cholesterol was calculated using the Friedewald equation: (LDL = total cholesterol − HDL cholesterol − triglycerides/5). The atherogenic index and LDL/HDL ratio were calculated.

Statistical Analysis

All values are presented as the mean ± SE. Age- and sex-adjusted univariate analysis of variance was performed by the general linear model (GLM) procedure to examine the independent effect of *UCP-1* genotypes on dependent variables. Fisher's exact (chi-square) test was used to compare *UCP-1* genotype frequencies among the hyper-LDL cholesterolemia group and normal group. Risk factors for hyper-LDL cholesterolemia were analyzed by logistic regression analysis. Statistical significance was established at the level of $P < .05$. All analyses were performed using SPSS version 10.0 (SPSS Inc, Chicago, IL).

RESULTS

The frequencies of *UCP-1* genotypes in the 190 obese subjects were AA type, 22.1%; AG type, 53.7%; and GG type, 24.2%; and the frequency of G allele was 0.51 (Table 2). The frequencies of variant types (AG, GG) of *UCP-1* found in this study were statistically identical to other Korean population studies and Japanese population studies ($P = 1.000$), but significantly higher than those in Caucasian population studies ($P = .016$), when compared by Fisher's exact test.

Table 3 shows the comparison of physical characteristics and body compositions of the subjects by *UCP-1* genotype. Diastolic blood pressure (DBP) was significantly higher in the AG/GG type compared with AA type ($P = .023$). However, weight, BMI, obesity index, WHR, systolic blood pressure (SBP), and body compositions were not significantly different by *UCP-1* genotype. Among all subjects, 85 finished a 1-month weight-reduction program consisting of a low-caloriie diet and aerobic exercise, and the mean reductions of body weight and BMI in all participants were 9.9 kg and 3.7 kg/m^2. The weight loss was 10.67 ± 1.16 kg in AA type and 10.25 ± 1.25 kg in AG type. In GG type, weight loss was 8.21 ± 0.61 kg, a 23.0% decrease compared with AA type, even though statistical significance was not found ($P > .05$). BMI change showed similar results (Fig 2).

Table 4 shows the comparison of serum biochemical characteristics of the subjects by the genotypes of *UCP-1*. LDL cholesterol level was significantly higher in AG and GG types compared with AA type ($P = .011$), whereas HDL cholesterol level was significantly lower in GG type compared with AA and AG types ($P = .042$). Total cholesterol, triglycerides, and blood glucose were not significantly different by *UCP-1* genotype. The atherogenic index was 22.8% higher in GG type compared with AA type ($P = .027$), and LDL/HDL was significantly increased in the order of AA < AG < GG type ($P = .001$), showing a 30.6% increase in GG type compared with AA type.

These results suggest that *UCP-1* genotype has significant effects on cholesterol and lipoprotein metabolism. The frequency of hyper-LDL cholesterolemia in relation to *UCP-1* genotype is shown in Table 5. When the subjects were divided into a normal group and a hyper-LDL cholesterolemia group by the criteria of LDL cholesterol level of 3.626 mmol/L, the distribution of *UCP-1* genotype was significantly different by Fisher's exact test ($P = .05$). The frequency of GG type was 43.9% in the normal group, and was significantly increased to 71.4% in the hyper-LDL cholesterolemia group. The frequency of hyper-LDL cholesterolemia was 9.8% (4 of 41) in AA type subjects, while it was significantly increased to 25.6% (10 of 39) in GG type subjects.

To find risk factors for hyper-LDL cholesterolemia in Korean obese subjects, stepwise logistic regression analysis was conducted (Table 6). Among many variables including age, sex, *UCP-1* GG type, SBP, DBP, fat mass, BMI, weight, and WHR, only 2 factors, GG type of *UCP-1* gene and body fat mass, were finally found to be statistically significant risk factors of hyper-LDL cholesterolemia. The odds ratios for hyper LDL cholesterolemia were 4.115 ($P = .03$) for GG type of *UCP-1* gene and 1.079 ($P = .03$) for body fat mass. This result suggests that the GG type of *UCP-1* gene can be a significant risk factor for hyper-LDL cholesterolemia among Korean adult obese subjects.

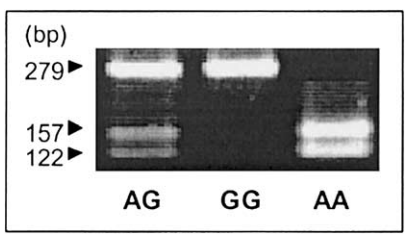

Fig 1. A-3826G polymorphism of the *UCP-1* gene.

Table 2. Frequencies of *UCP-1* Genotypes of the Current Study and Other Studies

Population	n	*UCP-1* Genotype (%)			
		AA	AG	GG	Frequency of G Allele
Korean*	429	27.2	46.3	26.1	0.49
1. Current study: obese women	190	22.1	53.7	24.2	0.51
2. Kim et al[36]					
Normal subjects	98	25.7	42.0	30.4	0.51
NIDDM	76	31.6	44.7	23.7	0.46
3. Kim et al[37]	65	29.2	44.6	26.2	0.49
Caucasians*	1950	55.6	38.2	6.2	0.25
4. Esterbauer et al[7]: Austrian	153	48.6	45.8	5.6	0.29
5. Urhammer et al[24]: Danish	379	56.2	36.9	6.9	0.25
6. Pihlajamaki et al[20]: Finnish	228	59.2	39.0	1.8	0.21
7. Valve et al[22]: Finnish	170	52.8	42.2	4.7	0.26
8. Schaffler et al[23]: German	1020	57.0	35.4	7.6	0.25
Japanese*	676	26.2	49.8	24.1	0.49
9. Shihara et al[9]: men	849	20.4	54.7	24.9	0.52
10. Hayakawa et al[16]: man	214	26.2	49.5	24.3	0.49
11. Kogure et al[12]: obese women	113	31.9	45.1	23.0	0.46

*Calculated by the summation of the result of studies 1-3 as total Korean population (n = 429), 4-8 as total Caucasian population (n = 1,950), and 9-11 as total Japanese population (n = 495).

DISCUSSION

Recently, numerous candidate genes were searched to determine the genetic factors implicated in the pathogenesis of obesity and related metabolic disorders. *UCP-1*, which plays a major role in thermogenesis, was suggested to be one of the candidates.

Until now many studies conducted in various populations suggested an association of the *UCP-1* G allele with higher weight gain, lower weight loss, and worse biochemical parameters. Oppert *et al*[11] reported that the G allele of *UCP-1* was associated with higher body weight gain over a 12-year period among 57 French Canadians. Clement et al[8] showed by logistic regression analysis that G allele of *UCP-1* was an independent factor associated with high weight gain for which the attributable risk was 25% in 238 French obese subjects. Fumeron et al[13] suggested an association of the G allele of *UCP-1* with lower weight loss after a low-calorie diet in 163 French obese subjects. Herrmann et al[18] reported that AG/GG type of *UCP-1* was associated with higher WHR compared with AA type (0.931 *v* 0.919, $P = .05$) in 162 Germans. Heilbronn et al[15] reported that the G allele of *UCP-1* was associated with higher BMI, type II diabetes, and increased serum glucose level in 526 overweight Australian women. Proenza et al[17] showed that BMI-related increase of cholesterol level was associated with *UCP-1* polymorphism in 271 Turkish subjects. Subjects with the GG type showed significantly more increase in cholesterol levels (5.6 mmol/L cholesterol increase per 1 U BMI increase) according to the degree of obesity than AA (2.0 mmol/L) and AG (1.9 mmol/L) types. Esterbauer et al[7] reported that AG/GG type of *UCP-1* gene was associated with significantly lower

Table 3. Comparisons of Physical Characteristics and Body Compositions by Genotype of UCP-1 in Korean Obese Subjects

	Genotype			*P* Value*
	AA (n = 42)	AG (n = 102)	GG (n = 46)	
Physical characteristics				
Weight (kg)	92.77 ± 2.57	88.40 ± 1.29	91.23 ± 1.94	.275
BMI (kg/m^2)	34.47 ± 0.56	33.41 ± 0.37	34.36 ± 0.55	.176
Obesity index (%)	158.99 ± 2.58	154.38 ± 1.68	159.01 ± 2.51	.174
WHR	0.99 ± 0.01	0.99 ± 0.01	1.00 ± 0.01	.354
SBP (mm Hg)	124.29 ± 1.98	126.64 ± 1.30	125.41 ± 1.94	.595
DBP (mm Hg)	73.20 ± 1.70[a]	78.80 ± 1.12[b]	76.49 ± 1.67[b]	.023
Body composition				
Water (kg)	37.90 ± 0.83	36.01 ± 0.54	36.90 ± 0.81	.159
Fat mass (kg)	37.68 ± 1.23	35.39 ± 0.80	36.75 ± 1.20	.265
Lean body mass (kg)	55.48 ± 1.14	53.01 ± 0.74	54.48 ± 1.10	.163
Protein mass (kg)	13.89 ± 0.44	13.62 ± 0.29	13.39 ± 0.43	.716
Percent body fat (%)	40.56 ± 0.70	40.02 ± 0.45	40.20 ± 0.68	.811

NOTE. Values are mean ± SE. Different superscript letters in the same row indicate significant difference at $P < .05$ among three GLM analyses adjusted for age and sex.

**P* values were obtained by GLM (covariance) analysis adjusted for age and sex.

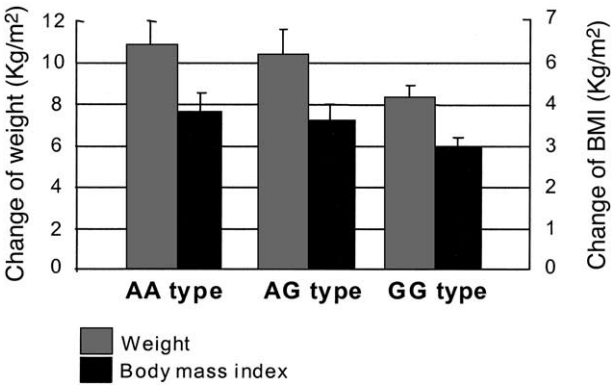

Fig 2. Reduction of body weight and BMI by 1-month weight-loss program in Korean obese subjects (mean ± SE).

HDL cholesterol level compared AA type, even though it was not significantly associated with BMI, SBP, DBP, glucose, total cholesterol, and triglycerides in 153 obese Austrian subjects, which is very similar to the result of the current study. Kogure et al[12] reported that 113 Japanese obese subjects (BMI, 31.0 ± 5.6 kg) were treated with a combined low-calorie diet and exercise for 3 months and the decrease in body weight was less in obese subjects with GG type than AA type (4.3 ± 2.6 kg *v* 7.4 ± 4.2 kg), although the food intake, exercise, and initial BMI were similar in these groups, which shows a similar tendency as the results of our study (Fig 2).

Some reports suggested a synergistic effect of the *UCP-1* G allele with β_3-adrenergic receptor gene Trp64Arg polymorphism. In the study of Valve et al,[22] the combination of *UCP-1* genotype and β_3-adrenergic receptor genotype was associated with lower basal metabolic rate in 170 obese Finns. Fogelholm et al[19] showed that the combination of *UCP-1* genotype and β_3-adrenergic receptor genotype was associated with weight loss during a very-low-calorie diet and subsequent weight gain among 77 obese Finnish women.

Even though significant role of *UCP-1* polymorphism in obesity and related metabolic disorders has been suggested in many studies, controversy remains because some reports do not support its role. For example, in the study of Schaffler et al,[23] G allele of *UCP-1* was not associated with obesity and metabolic parameters among 1,020 Germans. Urhammer et al[24] reported that *UCP-1* polymorphism was not associated with obesity in 380 Danes. Pihlajamaki et al[20] showed that BMI and serum biochemistry were not significantly different by *UCP-1* genotype in 238 Finnish with familial combined hyperlipidemia. In the report of Gagnon et al,[25] *UCP-1* genotype was not related to obesity indices in 985 Swedish subjects. Thus, the role of *UCP-1* polymorphism has been complex and controversial until now, because obesity and related metabolic disorders may be determined by environmental and life style factors as well as genetic factors in which many candidates genes and their interactions may be involved.

It should be considered that the relation between obesity and metabolic disorders shows ethnical differences. In Caucasian populations, risks of metabolic disorder begin to increase at BMI 25, are moderate at BMI 30, and are severe at BMI 35. In East Asian populations, however, metabolic risk begins to increase at BMI 23, is moderate at BMI 25, and is severe at BMI 30, so differential diagnosis and treatment for obesity-related metabolic disorders are required.[26] The different etiologies of obesity and metabolic disorders of the East Asian population may be related not only to differences in diet patterns, but also to differences in genetic characteristics, an example of which is the difference of allele frequencies of *UCP-1* gene (Table 2). G allele frequency is about 2-fold higher in East Asian than Caucasian populations. If the G allele of the *UCP-1* gene is associated with metabolic disorders rather than obesity itself as shown in this study, it may partly explain ethnical differences in the relation of obesity and metabolic disorders. The impact of *UCP-1* polymorphism on metabolic risk may not be identical in East Asian populations compared to Caucasian populations, and it can be hypothesized that higher

Table 4. Comparisons of Serum Biochemical Characteristics by Genotypes of *UCP-1* in Korean Obese Subjects

	Genotype			
	AA (n = 42)	AG (n = 102)	GG (n = 46)	*P* Value*
Lipid profiles				
Total cholesterol (mmol/L)	4.64 ± 0.16	4.75 ± 0.10	4.84 ± 0.16	.645
LDL cholesterol (mmol/L)	2.69 ± 0.12[a]	3.00 ± 0.08[b]	3.21 ± 0.12[b]	.011
HDL cholesterol (mmol/L)	1.12 ± 0.04[b]	1.10 ± 0.03[b]	1.06 ± 0.05[a]	.042
Triglyceride (mmol/L)	1.64 ± 0.12	1.56 ± 0.08	1.55 ± 0.12	.801
Atherogenic index†	3.16 ± 0.19[a]	3.54 ± 0.12[ab]	3.88 ± 0.19[b]	.027
LDL/HDL	2.43 ± 0.15[a]	2.82 ± 1.00[b]	3.24 ± 0.15[c]	.001
Fasting blood glucose				
Glucose (mmol/L)	5.93 ± 0.20	5.76 ± 0.13	5.67 ± 0.19	.610
Characteristics of liver function				
Total bilirubin (μmol/L)	0.63 ± 0.18	0.78 ± 0.12	1.05 ± 0.18	.228
AST (IU/L)	26.48 ± 4.22	33.60 ± 2.72	35.22 ± 4.19	.275
ALT (IU/L)	41.86 ± 6.77	52.64 ± 4.44	51.15 ± 6.72	.403

NOTE. Values are mean ± SE. Different superscript letters in the same row indicate significant difference at $P < .05$ among three GLM analyses adjusted for age and sex.

**P* values were obtained by GLM (covariance) analysis adjusted for age and sex.

†Atherogenic index = (total cholesterol-HDL)/HDL.

Table 5. Frequencies of *UCP-1* Genotypes Among Normal and Hyper-LDL Cholesterolemia Groups in Korean Obese Subjects

	UCP-1 Genotype			
	AA	GG	Total	*P* Value*
Normal, n (LDL < 3.626 mmol/L)	37 (56.1)	29 (43.9)	66 (100.0)	
Hyper-LDL cholesterolemia, n (LDL ≥ 3.626 mmol/L)	4 (28.6)	10 (71.4)	14 (100.0)	.05
Total, n	41 (51.3)	39 (48.8)	80 (100.0)	

*P values were obtained by Fisher's exact test (χ^2).

Table 6. Logistic Regression Model of Hyper-LDL Cholesterolemia in Korean Obese Subjects

Variable*	β	SE	*df*	*P* Value	Odds Ratio
UCP-1 genotype†	1.415	0.680	1	.03	4.115
Fat mass	0.076	0.036	1	.03	1.079/kg

NOTE. Hyper-LDL cholesterolemia was defined by the criteria of LDL cholesterol level > 3.626 mmol/L (140 mg/dL).

*Included variables were sex, age, variant type of *UCP-1* gene, SBP, DBP, fat mass, BMI, weight, and WHR.

†GG type of *UCP-1* gene compared with AA type.

G allele frequency of the East Asian population is one of the genetic factors that leads to increased susceptibility to obesity-related metabolic disorders compared with Caucasian populations.[9,15,27,28]

In this study, the effect of *UCP-1* polymorphism was examined in obese Korean subjects with a BMI greater than 30, who have second-level obesity or morbid obesity, with ensuing very high metabolic risks among East Asian populations. The results show that no significant effects of *UCP-1* genotypes were found in body weight or body composition (Table 2). The reduction of body weight and BMI by low-calorie diet combined with exercise was smaller in GG types compared with AA types, even though statistical significances were not found (Fig 2). LDL cholesterol was significantly higher and HDL cholesterol significantly lower in GG types. The atherogenic index and LDL/HDL ratio were also significantly higher in subjects with GG type, suggesting higher risks of cardiovascular disease. The values of liver function indicators such as total bilirubin, AST, and ALT showed increased tendencies by G allele, even though statistical significance was not observed (Table 4). *UCP-1* genotype was found to have a stronger effect on LDL cholesterol level than weight, BMI, WHR, or blood pressure and by logistic regression analysis (Table 6). Our results suggest that the G allele of *UCP-1* is strongly related to the increased risk of metabolic disorders such as hyper-LDL cholesterolemia among severely obese subjects in an East Asian population. In a study conducted among 182 postmenopausal Japanese women, although changes in body weight and BMI were not significantly different, HDL cholesterol was significantly decreased in the G allele carriers of the *UCP-1* gene, similar to the results of our study.[27]

Many studies have shown that HDL and LDL cholesterol levels are closely related to energy expenditure. Higuchi et al[29] conducted a study among 5 healthy male volunteers, aged 28 to 31 years, who joined in a treadmill exercise at 140 to 160 m/50 min, 5 times per week for a total of 4 weeks, equivalent to an energy expenditure of 9 kcal/kg/d. Subjects maintained their body weights by increasing calorie intake to match increased energy expenditure. The HDL cholesterol level was significantly increased without changes in body weight, total cholesterol, and triglyceride levels in response to the exercise. Ferguson et al[30] also reported that in 11 male subjects who ran on a treadmill at 70% Vo_2max and expended 1,500 kcal, LDL and total cholesterol were decreased and HDL cholesterol was increased immediately after exercise. These studies suggest that energy expenditure can be a potent factor for regulation of HDL and LDL cholesterol levels in the absence of alterations in body weight.

Thermogenesis as well as exercise is an important source of energy expenditure. It is well reported that the G allele of the *UCP-1* gene is associated with lower energy expenditure.[12,22] Lower energy expenditure among G allele carriers may explain the decreased HDL cholesterol and increased LDL cholesterol levels shown in this study. Decreased thermogenesis and energy expenditure among G allele carriers of *UCP-1* may lead to less efficient oxidation of free fatty acids in mitochondria and may cause an increase of tissue triglyceride levels, which may impair cholesterol transport from tissue.[31,32] Reduced tissue cholesterol transport may lead to a decrease of HDL cholesterol level and an increase of LDL cholesterol level,[31,33-35] providing some possible explanation; however, the elucidation of the relation between UCP-mediated thermogenesis and blood lipid profiles needs further study.

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