

Original Article

Association of the *LIPC* rs1532085 SNP and serum lipid traits in the Chinese Maonan and Han populations

Eksavang Khounphinit, Rui-Xing Yin, Ling Qiu, Fen-Han Zhang, Rong-Qin Yan, Li Lu, Yuan Su

Department of Cardiology, Institute of Cardiovascular Diseases, The First Affiliated Hospital, Guangxi Medical University, Nanning, Guangxi, China

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Abstract: The hepatic lipase gene (*LIPC*) is known to play an important role in lipid and lipoprotein metabolism pathways, but the association of the *LIPC* rs1532085 single nucleotide polymorphism (SNP) and serum lipid profiles has not been previously reported in different racial/ethnic groups. The present study was to detect the association of the *LIPC* rs1532085 SNP and several environmental factors with serum lipid levels in the Maonan and Han populations. Genotypes of the *LIPC* rs1532085 SNP in 833 individuals of Maonan nationality and 801 participants of Han nationality were determined by polymerase chain reaction and restriction fragment length polymorphism. The frequencies of AA, AG, and GG genotypes were 22.34%, 47.70%, and 29.96% in Han, and 24.96%, 51.38%, and 23.64% in Maonan populations ($P < 0.05$). The frequency of the G allele was 53.80% in Han and 49.33% in Maonan individuals ($P < 0.05$). The G allele carriers had lower total cholesterol (TC), triglyceride (TG), low-density lipoprotein cholesterol (LDL-C), Apolipoprotein (Apo) A1 and ApoB levels in Han than the G allele non-carriers, but not in Maonan. Subgroup analyses indicated that the G allele carriers had lower TC, TG, LDL-C and ApoA1 levels in Han females than the G allele non-carriers ($P < 0.05-0.001$). Serum lipid parameters in the two ethnic groups were also associated with several environmental factors. These findings revealed that there might be a racial/ethnic- and/or sex-specific association between the *LIPC* rs1532085 SNP and serum lipid parameters in some populations.

Keywords: Lipids, hepatic lipase, single nucleotide polymorphism, environmental factors

Introduction

Previous studies have found that cardiovascular disease (CVD) is the leading cause of mortality, morbidity, disability, functional decline, and healthcare costs [1, 2]. The increased incidence of CVD in the world has been linked to dyslipidemia [3, 4]. Unfavorable lipid profiles including high levels of serum total cholesterol (TC) [5], triglyceride (TG) [6], low-density lipoprotein cholesterol (LDL-C) [7], apolipoprotein (Apo) B [8], low levels of high-density lipoprotein cholesterol (HDL-C) [9], and ApoA1 [8] play a significant role for CVD, and are the main target for therapeutic intervention. Epidemiological studies have consistently showed that dyslipidemia is a complex trait resulted from the joint effects of multiple genetic and environmental factors [10, 11]. The heritability estimates of the inter-individual variations in serum lipid levels from both twin and family studies are in the range of 40-70%, suggesting a con-

siderable genetic contribution [12, 13]. Therefore, understanding the association of single nucleotide polymorphisms (SNPs) and serum lipid levels has become crucial in the pursuit of reducing CVD [14].

Several genome-wide association studies (GWASes) have reported the association of many SNPs near the hepatic lipase gene (*LIPC*; Also known as: HL, HTGL, LIPH, HDLCQ12; Gene ID: 3990; HGNC ID: 6619; OMIM: 151670; chromosomal location: 15p12.3) with serum lipid levels and the risk of Alzheimer's disease [15, 16]. So far, the well-known function of *LIPC* is that it encodes hepatic lipase which is an important enzyme in HDL metabolism [17], and has been previously associated with HDL-C levels [18]. To the best of our knowledge, however, the association between the *LIPC* rs1532085 SNP and serum lipid levels has not been reported previously. Therefore, the present study was evaluated the association between the *LIPC*

rs1532085 SNP and several environmental factors with serum lipid levels in the Han and Maonan populations.

China is a multi-ethnic country of 56 ethnic groups. Han is the largest ethnic group and Maonan nationality is a relatively conservative and isolated minority, and preserves their custom of intra-ethnic marriage as one of the minorities. According to the statistics in 2010, the numbers of Maonan population were 101,192. Divertingly, they have their culture of consanguineous marriage to cousins of maternal side, suggesting that the genetic background of Maonan population may be less heterogeneous within the population. Local people widely utilize endemic species, and they have developed their own traditional medicinal knowledge [19]. Height, fat mass, and fat distribution differs substantially between men and women, and these differences may, in part, explain the sex-specific susceptibilities to certain diseases such as coronary artery disease [20]. These considerable differences in anthropometry may reflect sex-specific differences in steroid hormone regulation, adipogenesis, lipid storage, muscle metabolism, composition, and contractile speed, skeletal growth, and maturation, or lipolysis, and suggest a genetic underpinning [21]. Sexual dimorphism has been demonstrated as the potential of dyslipidemia and CVD risk factors. This study, therefore, was undertaken to detect the association of the LIPC rs1532085 SNP and several environmental factors with serum lipid levels between males and females in the Maonan and Han populations.

Materials and methods

Subjects

The study populations included 801 unrelated subjects (305 males, 38.07% and 496 females, 61.92%) of Han and 833 unrelated participants (335 males, 40.21% and 498 females, 59.78%) of Maonan. They were randomly selected from our previous stratified randomized samples [22]. The participants were all agricultural workers from Huanjiang Maonan Autonomous County, Guangxi Zhuang Autonomous Region, People's Republic of China. The participants' age ranged from 25 to 75 years with the mean age of 57.17±14.70 years in Han and

57.19±15.01 years in Maonan, respectively. The age distribution and gender ratio were matched between the two groups. All participants were essentially healthy with no history of CVD such as coronary artery disease, stroke, diabetes, hyper- or hypo-thyroids, and chronic renal disease. They were free from medications known to affect serum lipid levels. Informed consent was taken from all participants. The Ethics Committee of the First Affiliated Hospital, Guangxi Medical University, approved the study design (No. Lunshen-2014-KY-Guoji-001, Mar. 7, 2014). Informed consent was taken from all participants.

Epidemiological survey

The epidemiological survey was carried out using internationally standardized methods, following a common protocol [23]. Information on demographics, socioeconomic status, and lifestyle factors was collected with standardized questionnaires. Alcohol consumption was categorized into groups of grams of alcohol per day: 0 (non-drinker), ≤ 25 and > 25. Smoking status was categorized into groups of cigarettes per day: 0 (non-smoker), ≤ 20 and > 20. Several parameters such as blood pressure, height, weight, waist circumference, and body mass index (BMI) were measured. The methods of measuring above parameters were referred to previous studies [24].

Biochemical measurements

A fasting venous blood sample of 5 ml was drawn from the participants. A part of the sample (2 mL) was collected into glass tubes and used to determine serum lipid levels. Another part of the sample (3 mL) was transferred to tubes with anticoagulants (4.80 g/L citric acid, 14.70 g/L glucose and 13.20 g/L tri-sodium citrate) and used to extract deoxyribonucleic acid (DNA). Measurements of serum TC, TG, HDL-C, and LDL-C levels in the samples were performed by enzymatic methods with commercially available kits (RANDOX Laboratories Ltd., Ardmore, Diamond Road, and Crumlin Co. Antrim, United Kingdom, BT29 4QY; Daiichi Pure Chemicals Co., Ltd., Tokyo, Japan). Serum ApoA1 and ApoB levels were detected by the immunoturbidimetric immunoassay using a commercial kit (RANDOX Laboratories Ltd.). All determinations were performed with an auto-analyzer (Type 7170A; Hitachi Ltd., Tokyo,

LIPC rs1532085 SNP and serum lipid levels

Table 1. Comparison of demographic, lifestyle characteristics and serum lipid levels between the Han and Maonan populations

Parameter	Han	Maonan	t (χ^2)	P
Number	801	833		
Male/female	305/496	335/498	0.885	0.077
Age (years)	57.17±14.70	57.19±15.01	-0.031	0.481
Height (cm)	153.90±7.69	153.80±8.06	0.249	0.079
Weight (kg)	52.52±8.56	53.17±10.78	-1.329	0.000
Body mass index (kg/m ²)	22.15±3.23	22.36±3.66	-1.178	0.049
Waist circumference (cm)	74.85±7.72	76.70±9.57	-4.289	0.000
Smoking status [n (%)]				
Non-smoker	636 (79.40)	701 (84.15)		
≤ 20 cigarettes/day	145 (18.10)	110 (13.20)	7.435	0.024
> 20 cigarettes/day	20 (2.50)	22 (2.64)		
Alcohol consumption [n (%)]				
Non-drinker	646 (80.64)	661 (79.35)		
≤ 25 g/day	62 (7.74)	93 (11.16)	6.888	0.032
> 25 g/day	93 (11.61)	79 (9.48)		
Systolic blood pressure (mmHg)	128.23±19.75	135.84±24.75	-6.844	0.000
Diastolic blood pressure (mmHg)	80.26±11.35	82.83±12.54	-4.327	0.002
Pulse pressure (mmHg)	47.97±15.23	53.00±18.49	-5.983	0.000
Glucose (mmol/L)	5.99±1.43	6.12±1.33	-1.812	0.085
Total cholesterol (mmol/L)	4.94±1.09	5.00±1.06	-1.080	0.870
Triglyceride (mmol/L)	0.97 (0.73)	1.30 (0.88)	-8.932	0.000
HDL-C (mmol/L)	1.78±0.54	1.59±0.40	7.752	0.005
LDL-C (mmol/L)	2.85±0.85	2.86±0.83	-0.189	0.431
ApoA1 (g/L)	1.38±0.27	1.38±0.30	-0.220	0.560
ApoB (g/L)	0.83±0.19	0.88±0.20	-4.623	0.000
ApoA1/ApoB	1.73±0.50	1.65±0.56	3.053	0.002

HDL-C, high-density lipoprotein cholesterol; *LDL-C*, low-density lipoprotein cholesterol; *Apo*, Apolipoprotein. The value of triglyceride was presented as median (interquartile range); the difference between the two ethnic groups was determined by the Wilcoxon-Mann-Whitney test.

Japan) in the Clinical Science Experiment Center of the First Affiliated Hospital, Guangxi Medical University [25, 26].

DNA amplification and genotyping

Genomic DNA of the samples was isolated from peripheral blood leucocytes according to the phenol-chloroform method [27, 28]. The extracted DNA was stored at 4°C until analysis. Genotyping of the *LIPC* rs1532085 SNP was performed by polymerase chain reaction and restriction fragment length polymorphism (PCR-RFLP). PCR amplification was performed using 5'-ACATGCTTCTCCTTCCCCAA-3' as the left primer and 5'-ACCCAGTCGTGATCATCAAA-3' as right primer pair (Sangon, Shanghai, People's Republic of China), respectively. Each 25 µL

PCR reaction mixture consisted of 2.0 µL genomic DNA, 1.0 µL each primer (10 µmol/L), 12.5 µL of 2 × *Taq*PCR Master Mix (constituent: 0.1 U *Taq* polymerase/µL, 500 µM dNTP each and PCR buffer.), and 8.5 µL of ddH₂O (DNase/RNase-free). PCR was performed with an initialization step of 95°C for 5 min, followed by 45 s denaturing at 95°C, 30 s of annealing at 58°C and 45 s of elongation at 72°C for 32 cycles. The amplification was completed by a final extension at 72°C for 7 min. Following electrophoresis on a 2.0% agarose gel with 0.5 µg/mL ethidium bromide, the amplification products were visualized under ultraviolet light. Subsequently, each restriction enzyme reaction was performed with 5.0 µL amplified DNA, 8.8 µL nuclease-free water, 1.0 µL of 10 × buffer solution and 0.2 µL *Rsa*I restriction enzyme

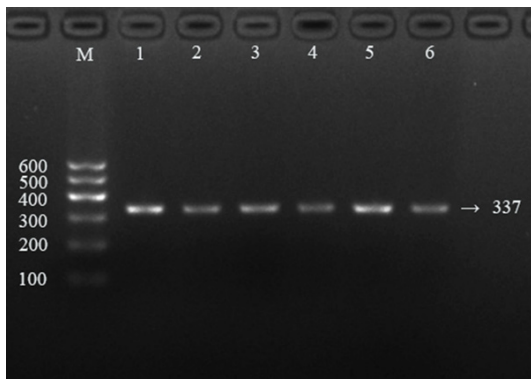


Figure 1. Electrophoresis of polymerase chain reaction products of the samples. Lane M is the 100-bp marker ladder; Lanes 1-6 are samples, the 337-bp bands are the target genes.

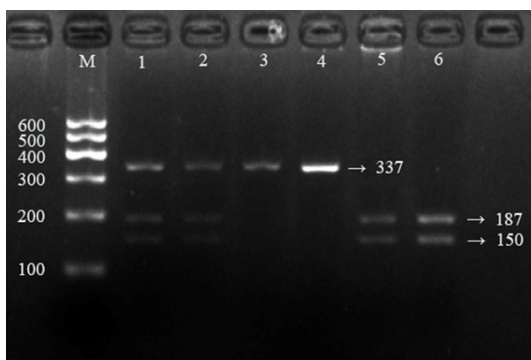


Figure 2. Genotyping of the *LIPC* rs1532085 SNP. Lane M is the 100-bp Marker Ladder; lanes 3 and 4, AA genotype (337-bp); lanes 1 and 2, AG genotype (337-, 187- and 150-bp); and lanes 5 and 6, GG genotype (187- and 150-bp).

in a total volume of 15 μ L digested at 37°C overnight. After restriction enzyme digestion of the amplified DNA, genotypes were identified by electrophoresis on 2% ethidium-bromide stained agarose gels and visualized with UV illumination. An experienced reader blinded to the epidemiological and serum lipid results scored genotypes. Six samples (AA, AG, and GG genotypes in two; respectively) detected by the PCR-RFLP were also confirmed by direct sequencing with an ABI Prism 3100 (Applied Biosystems) in Shanghai Sangon Biological Engineering Technology & Services Co., Ltd., People's Republic of China.

Diagnostic criteria

The normal values of serum TC, TG, HDL-C, LDL-C, ApoA1, ApoB levels and the ApoA1/ApoB

ratio in our Clinical Science Experiment Center were 3.10-5.17, 0.56-1.70, 1.16-1.42, 2.70-3.10 mmol/L, 1.20-1.60, 0.80-1.05 g/L and 1.00-2.50, respectively. The individuals with TC > 5.17 mmol/L and/or TG > 1.70 mmol/L were defined as hyper-lipidaemic [34]. Hypertension was diagnosed according to the 1999 and 2003 criteria of the World Health Organization-International Society of Hypertension Guidelines for the management of hypertension [29]. The diagnostic criteria of overweight and obesity were according to the Cooperative Meta-analysis Group of China Obesity Task Force. Normal weight, overweight and obesity were defined as a BMI < 24, 24-28 and > 28 kg/m², respectively [30].

Statistical analyses

Statistical analyses were performed with the statistical software package SPSS 24.0 (SPSS Inc., Chicago, Illinois). The quantitative variables were presented as mean \pm standard deviation (serum TG levels are presented as medians and interquartile ranges). Allele frequency was determined via direct counting, and the Hardy-Weinberg equilibrium was verified with the standard goodness-of-fit test. The genotype distribution between the two groups was analyzed by the Chi-square test. General characteristics between two ethnic groups were compared by the Student's unpaired *t*-test. The association between genotypes and serum lipid parameters was tested by covariance analysis (ANCOVA). Gender, age, BMI, blood pressure, alcohol consumption, and cigarette smoking were adjusted for the statistical analysis. Multivariable linear regression analyses with stepwise modeling were used to determine the correlation between the genotypes (AA=1, AG=2 and GG=3) and several environmental factors with serum lipid levels in males and females of Han and Maonan populations. Two sided *P* value < 0.05 was considered statistically significant.

Results

General and biochemical characteristics of the subjects

Table 1 shows the general characteristics and serum lipid levels between the Han and Maonan populations. The percentages of cigarette smoking, the levels of waist circumfer-

LIPC rs1532085 SNP and serum lipid levels

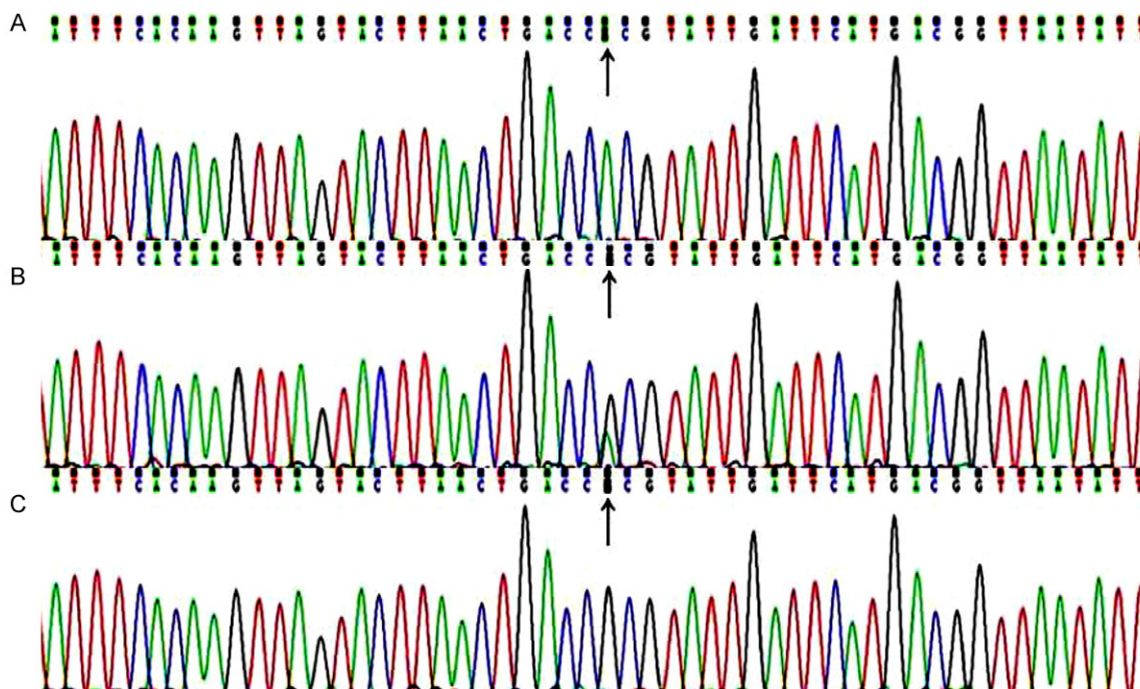


Figure 3. A part of the nucleotide sequence of the *LIPC* rs1532085 SNP. A: AA genotype; B: AG genotype; C: GG genotype.

Table 2. Comparison of the genotype and allele frequencies of *LIPC* rs1532085 SNP in the Han and Maonan populations [*n* (%)]

Group	n	Genotype			Allele	
		AA	AG	GG	A	G
Han	801	179 (22.34)	382 (47.70)	240 (29.96)	740 (46.19)	862 (53.80)
Maonan	833	208 (24.96)	428 (51.38)	197 (23.64)	844 (50.66)	822 (49.33)
χ^2			8.393			6.528
<i>P</i>			0.015			0.011
Han						
Male	305	79 (25.90)	155 (50.81)	71 (23.27)	310 (51.07)	297 (48.92)
Female	496	100 (20.16)	227 (45.76)	169 (34.07)	427 (43.04)	565 (56.95)
χ^2			11.140			9.764
<i>P</i>			0.004			0.002
Maonan						
Male	335	84 (25.07)	174 (51.94)	77 (22.98)	342 (51.04)	328 (48.95)
Female	498	124 (24.89)	254 (51.00)	120 (24.09)	502 (50.40)	494 (49.59)
χ^2			0.141			0.066
<i>P</i>			0.932			0.797

ence, systolic blood pressure, diastolic blood pressure, pulse pressure, TG and ApoB were higher in Maonan than in Han ($P < 0.05-0.001$), but the percentages of alcohol consumption, HDL-C levels and ApoA1/ApoB ratio were lower in Maonan than in Han ($P < 0.05-0.001$). The values of gender ratio, age structure, body height, weight, BMI, TC, LDL-C, and ApoA1 were

not different between the two ethnic groups ($P > 0.05$ for all).

Results of electrophoresis and genotyping

After the genomic DNA of the samples was amplified using PCR and visualized with 2% agarose gel electrophoresis, the products of

LIPC rs1532085 SNP and serum lipid levels

Table 3. Comparison of the genotypes and serum lipid levels in the Han and Maonan populations

Genotype	<i>n</i>	TC (mmol/L)	TG (mmol/L)	HDL-C (mmol/L)	LDL-C (mmol/L)	ApoA1 (g/L)	ApoB (g/L)	ApoA1/ApoB
Han								
AA	179	5.22±1.23	1.11 (0.77)	1.82±0.46	2.98±0.93	1.42±0.27	0.86±0.21	1.72±0.47
AG/GG	622	4.86±1.04	0.95 (0.72)	1.77±0.56	2.81±0.82	1.36±0.26	0.82±0.19	1.74±0.50
<i>F</i>		14.188	-2.464	1.055	4.821	5.042	4.709	0.223
<i>P</i>		0.000	0.014	0.305	0.028	0.025	0.030	0.637
Maonan								
AA	208	5.03±0.95	1.34 (0.82)	1.59±0.39	2.87±0.84	1.40±0.45	0.88±0.19	1.67±0.71
AG/GG	625	4.99±1.09	1.29 (0.89)	1.59±0.41	2.85±0.82	1.37±0.24	0.88±0.20	1.64±0.50
<i>F</i>		0.183	-1.226	0.000	0.053	1.549	0.001	0.418
<i>P</i>		0.669	0.220	0.985	0.817	0.214	0.982	0.518

TC, total cholesterol; TG, triglyceride; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; ApoA1, apolipoprotein A1; ApoB, apolipoprotein B; ApoA1/ApoB, the ratio of apolipoprotein A1 to apolipoprotein B. The value of triglyceride was presented as median (interquartile range); the difference between the AA and AG/GG genotypes was determined by the Kruskal-Wallis test.

337 bp nucleotide sequences were observed in all samples (**Figure 1**). The genotypes identified were termed according to the presence (G allele) or absence (A allele) of the enzyme restriction sites. Thus, the GG genotype is homozygous for the presence of the site (bands at 187- and 150-bp), the AG genotype is heterozygous for the presence and absence of the site (bands at 337-, 187- and 150-bp) and the AA genotype is homozygous for the absence of the site (bands at 337-bp; **Figure 2**). The AA, AG, and GG genotypes detected by PCR-RFLP were also confirmed by direct sequencing (**Figure 3**), respectively.

Genotypic and allelic frequencies

The genotypic and allelic frequencies of the LIPC rs1532085 SNP are shown in **Table 2**. The genotypic distribution was followed Hardy-Weinberg equilibrium (HWE). The frequencies of A and G alleles were 46.19% and 53.80% in Han and 50.66% and 49.33% in Maonan populations ($P < 0.05$), respectively. The frequencies of AA, AG, and GG genotypes were 22.34%, 47.70% and 29.96% in Han and 24.96%, 51.38% and 23.64% in Maonan ($P < 0.05$); respectively. The genotypic and allelic frequencies of the SNP were also different between Han males and females ($P < 0.01$ for each) but not between Maonan males and females.

Genotypes and serum lipid levels

Tables 3 and **4** describe the association between genotypes and serum lipid levels. The

levels of TC, TG, LDL-C, ApoA1, and ApoB were different between the AA and AG/GG genotypes ($P < 0.05-0.001$) in Han but not in Maonan, the G allele carriers had lower TC, TG, LDL-C, ApoA1, and ApoB levels than the G allele non-carriers. In the sex subgroup analyses, the G allele carriers had lower TC, TG, LDL-C, and ApoA1 levels in Han females but not in males ($P < 0.05-0.001$).

Relative factors for serum lipid parameters

The risk factors for serum lipid parameters in Han and Maonan are shown in **Tables 5** and **6**. Multiple linear regression analyses showed that serum TC and LDL-C levels in Han were correlated with genotypes of the LIPC rs1532085 SNP ($P < 0.05$ for each; **Table 5**). When the correlation of serum lipid parameters and the genotypes was analyzed according to two genders, we found that serum TC, LDL-C, and ApoA1 in Han females were correlated with genotypes ($P < 0.05$ for all; **Table 6**). Several environmental factors such as ethnic group, gender, age, height, weight, BMI, waist circumference, systolic and diastolic blood pressure, pulse pressure, fasting blood glucose, alcohol consumption, and cigarette smoking in both ethnic groups or in males and females were also correlated with serum lipid parameters ($P < 0.05-0.001$, **Tables 5** and **6**).

Discussion

The results of the present study showed that the serum lipid profiles were different between

LIPC rs1532085 SNP and serum lipid levels

Table 4. Comparison of the genotypes and serum lipid levels between males and females in the Han and Maonan populations

Genotype	<i>n</i>	TC (mmol/L)	TG (mmol/L)	HDL-C (mmol/L)	LDL-C (mmol/L)	ApoA1 (g/L)	ApoB (g/L)	ApoA1/ ApoB
Han/male								
AA	79	5.23±1.15	1.14 (0.69)	1.73±0.39	2.86±0.74	1.37±0.20	0.90±0.21	1.58±0.40
AG/GG	226	5.15±1.05	1.08 (0.98)	1.76±0.45	2.95±0.86	1.43±0.30	0.88±0.20	1.69±0.52
<i>F</i>		0.268	-0.061	0.389	0.744	2.330	0.551	2.662
<i>P</i>		0.605	0.951	0.534	0.389	0.128	0.458	0.104
Han/female								
AA	100	5.21±1.30	1.07 (0.80)	1.90±0.49	3.07±1.05	1.45±0.31	0.83±0.20	1.82±0.50
AG/GG	396	4.69±0.99	0.87 (0.59)	1.78±0.61	2.73±0.78	1.33±0.23	0.79±0.18	1.77±0.49
<i>F</i>		18.001	-3.014	2.927	11.921	18.149	3.292	0.980
<i>P</i>		0.000	0.003	0.088	0.001	0.000	0.070	0.323
Maonan/male								
AA	84	5.06±0.99	1.38 (0.94)	1.55±0.40	2.77±0.87	1.43±0.65	0.90±0.18	1.67±0.97
AG/GG	251	4.94±0.94	1.37 (0.98)	1.54±0.44	2.79±0.83	1.36±0.27	0.88±0.20	1.63±0.57
<i>F</i>		0.875	-0.909	0.008	0.033	1.755	0.376	0.260
<i>P</i>		0.350	0.363	0.930	0.856	0.186	0.540	0.611
Maonan/female								
AA	124	5.02±0.92	1.30 (0.65)	1.62±0.38	2.94±0.82	1.39±0.22	0.86±0.19	1.67±0.46
AG/GG	374	5.03±1.18	1.21 (0.84)	1.63±0.38	2.90±0.81	1.38±0.21	0.87±0.20	1.65±0.45
<i>F</i>		0.017	-0.898	0.009	0.219	0.066	0.225	0.158
<i>P</i>		0.898	0.369	0.925	0.640	0.797	0.636	0.691

TC, total cholesterol; TG, triglyceride; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; ApoA1, apolipoprotein A1; ApoB, apolipoprotein B; ApoA1/ApoB, the ratio of apolipoprotein A1 to apolipoprotein B. The value of triglyceride was presented as median (interquartile range); the difference between the AA and AG/GG genotypes was determined by the Kruskal-Wallis test.

the Maonan and Han populations. The levels of TG and ApoB were higher in Maonan than in Han ($P < 0.01$), whereas the levels of HDL-C and the ratio of ApoA1 to ApoB were lower in Maonan than in Han ($P < 0.01$). There were no significant differences in the levels of serum TC, LDL-C, and ApoA1 between the two ethnic groups ($P > 0.05$). It is widely realized that dyslipidemia as a serious risk factor for CVD is a multifactorial and complicated disease caused by genetic factors, including lipid-associated gene variants and environmental factors and their interactions [31, 32]. Maonan nationality belongs to a mountain ethnic minority and is mainly occupied with cereal and miscellaneous grain crops. The history of Maonan can retrospect to the 11th century. Maonan peoples mainly engaged in agriculture and were good at raising beef cattle and prepare the bamboo hat. The main food for them was rice, along with corn, sorghum, millet, sweet potatoes, and pumpkin which are also important complements. Thus, they enjoy a very special

lifestyle and dietary habits compared with the other nationalities. Maonan people are keen on spicy and acidic food. Parents usually take charge of their children's marriages. Maonan stays endogamy and thus inter-marriage with Han or Zhuang people seldom occurs. Therefore, it is considered that the hereditary characteristics and genotypes of certain lipid metabolism-related genes in this population might be different from those in the Han population.

To the best of our knowledge, the genotypic and allelic frequencies of the LIPC rs1532085 SNP have not been reported previously in different ethnic groups. In the present study, we first showed that the G allele frequency of the LIPC rs1532085 SNP was higher in Han than in Maonan populations (53.80% vs. 49.33%; $P < 0.05$). The genotype distribution of the SNP was different between the two ethnic groups ($P < 0.05$). The genotypic and allelic frequencies of the SNP in Han but not in Maonan were also different between males and females ($P < 0.01$

LIPC rs1532085 SNP and serum lipid levels

Table 5. Relationship between serum lipid parameters and relative factors in the Han and Maonan populations

Lipid	Risk factor	B	Std.error	Beta	t	P
Han and Maonan						
TC	Age	0.007	0.002	0.101	3.340	0.001
	Height	-0.035	0.016	-0.260	-2.154	0.031
	Waist circumference	0.021	0.006	0.173	3.884	0.000
TG	Cigarette smoking	0.018	0.007	0.085	2.612	0.009
	Alcohol consumption	0.004	0.002	0.084	2.773	0.006
	Height	-0.061	0.027	-0.270	-2.296	0.022
	Weight	0.081	0.081	0.446	2.289	0.022
	Body mass index	-0.174	0.075	-0.341	-2.299	0.022
	Waist circumference	0.050	0.009	0.244	5.623	0.000
	Glucose	0.076	0.034	0.059	2.216	0.027
HDL-C	Ethnic group	-0.155	0.026	-0.159	-6.086	0.000
	Gender	0.116	0.039	0.114	3.011	0.003
	Age	0.003	0.001	0.089	2.988	0.003
	Alcohol consumption	0.002	0.000	0.153	5.069	0.000
	Waist circumference	-0.009	0.002	-0.158	-3.623	0.000
LDL-C	Age	0.007	0.002	0.114	3.756	0.000
	Alcohol consumption	-0.003	0.001	-0.113	-3.668	0.000
	Waist circumference	0.019	0.004	0.192	4.316	0.000
	Pulse pressure	0.003	0.001	0.060	2.044	0.041
ApoA1	Gender	0.048	0.023	0.080	2.068	0.039
	Age	0.001	0.001	0.067	2.213	0.027
	Cigarette smoking	0.004	0.001	0.107	3.199	0.001
	Alcohol consumption	0.002	0.000	0.206	6.645	0.000
	Waist circumference	-0.003	0.001	-0.087	-1.960	0.050
ApoB	Ethnic group	0.031	0.010	0.078	3.052	0.002
	Age	0.001	0.000	0.058	2.023	0.043
	Waist circumference	0.007	0.001	0.290	6.831	0.000
	Pulse pressure	0.001	0.000	0.061	2.165	0.031
	Glucose	0.008	0.004	0.056	2.157	0.031
ApoA1/ApoB	Gender	0.128	0.041	0.116	3.116	0.002
	Cigarette smoking	0.004	0.002	0.066	2.028	0.043
	Alcohol consumption	0.002	0.000	0.156	5.239	0.000
	Waist circumference	-0.016	0.003	-0.270	-6.287	0.000
	Glucose	-0.022	0.010	-0.058	-2.202	0.028
Han						
TC	Genotype	-0.137	0.050	-0.102	-2.737	0.006
	Gender	-0.297	0.126	-0.132	-2.360	0.019
	Waist circumference	0.035	0.009	0.249	3.770	0.000
TG	Age	-0.011	0.005	-0.083	-2.050	0.041
	Cigarette smoking	0.038	0.010	0.171	3.640	0.000
	Waist circumference	0.094	0.016	0.381	5.867	0.000
HDL-C	Age	0.004	0.002	0.095	2.234	0.026
	Alcohol consumption	0.002	0.001	0.104	2.346	0.019
LDL-C	Genotype	-0.081	0.041	-0.075	-1.992	0.047
	Gender	-0.208	0.102	-0.115	-2.034	0.042

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	Age	0.005	0.002	0.089	2.139	0.033
	Waist circumference	0.025	0.007	0.220	3.291	0.001
ApoA1	Age	0.002	0.001	0.102	2.498	0.013
	Cigarette smoking	0.004	0.001	0.116	2.427	0.016
	Alcohol consumption	0.002	0.000	0.238	5.564	0.000
	Diastolic blood pressure	-0.002	0.001	-0.076	-1.967	0.050
ApoB	Gender	-0.059	0.022	-0.143	-2.704	0.007
	Waist circumference	0.007	0.002	0.290	4.642	0.000
	Diastolic blood pressure	0.001	0.001	0.077	2.100	0.036
	Glucose	0.017	0.005	0.124	3.396	0.001
ApoA1/ApoB	Gender	0.135	0.055	0.133	2.453	0.014
	Alcohol consumption	0.002	0.001	0.139	3.335	0.001
	Waist circumference	-0.010	0.004	-0.157	-2.432	0.015
	Diastolic blood pressure	-0.003	0.002	-0.082	-2.174	0.030
	Glucose	-0.035	0.013	-0.103	-2.724	0.007
Maonan						
TC	Gender	0.254	0.124	0.112	2.048	0.041
	Age	0.011	0.003	0.151	3.354	0.001
	Height	-0.055	0.024	-0.409	-2.298	0.022
	Weight	0.077	0.033	0.767	2.352	0.019
	Body mass index	-0.161	0.071	-0.549	-2.274	0.023
TG	Alcohol consumption	0.010	0.002	0.195	4.543	0.000
	Height	-0.124	0.036	-0.594	-3.479	0.001
	Weight	0.181	0.049	1.158	3.704	0.000
	Body mass index	-0.349	0.105	-0.769	-3.324	0.001
	Waist circumference	0.026	0.010	0.149	2.546	0.011
HDL-C	Gender	0.167	0.044	0.198	3.805	0.000
	Age	0.002	0.001	0.086	2.003	0.046
	Alcohol consumption	0.003	0.001	0.239	5.603	0.000
	Waist circumference	-0.011	0.002	-0.249	-4.291	0.000
	Pulse pressure	-0.002	0.001	-0.087	-2.128	0.034
LDL-C	Age	0.008	0.002	0.144	3.261	0.001
	Alcohol consumption	-0.004	0.001	-0.176	-3.990	0.000
	Waist circumference	0.015	0.005	0.171	2.840	0.005
ApoA1	Gender	0.095	0.035	0.148	2.726	0.007
	Cigarette smoking	0.004	0.002	0.097	2.040	0.042
	Alcohol consumption	0.002	0.000	0.184	4.151	0.000
	Waist circumference	-0.005	0.002	-0.168	-2.763	0.006
ApoB	Age	0.002	0.001	0.143	3.318	0.001
	Waist circumference	0.006	0.001	0.278	4.753	0.000
ApoA1/ApoB	Alcohol consumption	0.003	0.001	0.176	4.124	0.000
	Waist circumference	-0.018	0.003	-0.309	-5.299	0.000

TC, total cholesterol; TG, triglyceride; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; ApoA1, apolipoprotein A1; ApoB, apolipoprotein B; ApoA1/ApoB, the ratio of apolipoprotein A1 to apolipoprotein B; B, unstandardized coefficient; Beta, standardized coefficient.

for each). These results indicate that the prevalence of *LIPC* rs1532085 SNP may have racial/ethnic specificity.

The potential association of the *LIPC* rs1532085 SNP and serum lipid levels has not been previously reported in different racial/ethnic

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Table 6. Relationship between serum lipid parameters and relative factors in the males and females of the Han and Maonan populations

Lipid	Risk factor	B	Std.error	Beta	t	P
Han/male						
TC	Waist circumference	0.036	0.016	0.291	2.298	0.022
TG	Cigarette smoking	0.036	0.017	0.143	2.154	0.032
	Waist circumference	0.180	0.042	0.523	4.272	0.000
HDL-C	Age	0.004	0.002	0.159	2.349	0.020
	Alcohol consumption	0.001	0.001	0.170	2.724	0.007
	Height	0.042	0.013	0.013	3.130	0.002
	Weight	-0.054	0.016	-1.174	-3.424	0.001
ApoA1	Body mass index	0.093	0.032	0.887	2.918	0.004
	Age	0.002	0.001	0.140	2.097	0.037
	Alcohol consumption	0.002	0.000	0.320	5.225	0.000
	Height	0.019	0.008	0.556	2.279	0.024
ApoB	Weight	-0.028	0.010	-0.946	-2.803	0.006
	Body mass index	0.044	0.020	0.640	2.143	0.033
	Waist circumference	0.006	0.003	0.250	2.126	0.035
ApoA1/ApoB	Glucose	0.020	0.008	0.156	0.156	0.015
	Alcohol consumption	0.002	0.001	0.185	3.113	0.002
	Height	0.033	0.014	0.543	2.294	0.023
	Weight	-0.047	0.017	-0.896	-2.738	0.007
	Glucose	-0.053	0.018	-0.178	-2.899	0.004
Han/female						
TC	Genotype	-0.251	0.065	-0.180	-3.878	0.000
TG	Age	-0.009	0.004	0.126	-2.451	0.015
	Waist circumference	0.043	0.011	0.299	3.810	0.000
	Diastolic blood pressure	0.015	0.005	0.153	3.100	0.002
	Glucose	0.099	0.036	0.130	2.749	0.006
	Genotype	-0.149	0.051	-0.135	-2.890	0.004
LDL-C	Age	0.007	0.003	0.113	2.150	0.032
	Waist circumference	0.022	0.010	0.178	2.221	0.027
	Pulse pressure	0.009	0.003	0.142	2.796	0.005
	Genotype	-0.047	0.016	-0.141	-2.962	0.003
ApoA1	Diastolic blood pressure	-0.003	0.001	-0.117	-2.284	0.023
	Genotype	-0.047	0.016	-0.141	-2.962	0.003
ApoB	Waist circumference	0.007	0.002	0.276	3.523	0.000
	Glucose	0.013	0.007	0.094	2.007	0.045
	Pulse pressure	0.002	0.001	0.134	2.696	0.007
ApoA1/ApoB	Waist circumference	-0.015	0.006	-0.226	-2.806	0.005
Maonan/male						
TC	Glucose	0.105	0.047	0.139	2.245	0.026
TG	Alcohol consumption	0.010	0.003	0.195	3.019	0.003
HDL-C	Alcohol consumption	0.003	0.001	0.344	5.605	0.000
	Waist circumference	-0.023	0.005	-0.493	-4.661	0.000
LDL-C	Alcohol consumption	-0.005	0.001	-0.287	-4.352	0.000
ApoA1	Alcohol consumption	0.002	0.001	0.205	3.091	0.002
	Waist circumference	-0.016	0.005	-0.363	-3.159	0.002
ApoB	Glucose	0.019	0.009	0.122	2.048	0.042
ApoA1/ApoB	Alcohol consumption	0.003	0.001	0.218	3.399	0.001

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	Waist circumference	-0.026	0.008	-0.339	-3.046	0.003
Maonan/female						
TC	Age	0.013	0.004	0.165	2.962	0.003
	Waist circumference	0.019	0.009	0.147	2.125	0.034
TG	Waist circumference	0.021	0.006	0.239	3.571	0.000
	Systolic blood pressure	0.005	0.002	0.148	2.121	0.035
HDL-C	Age	-0.007	0.003	-0.145	-2.182	0.030
	Systolic blood pressure	-0.003	0.001	-0.185	-2.601	0.010
	Diastolic blood pressure	0.004	0.002	0.129	1.965	0.050
LDL-C	Age	0.009	0.003	0.169	3.096	0.002
	Alcohol consumption	0.013	0.006	0.099	2.159	0.031
	Waist circumference	0.019	0.006	0.213	3.149	0.002
ApoA1	Systolic blood pressure	-0.002	0.001	-0.171	-2.349	0.019
ApoB	Age	0.002	0.001	0.164	3.099	0.002
	Waist circumference	0.007	0.001	0.318	4.832	0.000
	Systolic blood pressure	0.001	0.001	0.170	2.484	0.013
ApoA1/ApoB	Waist circumference	-0.016	0.003	-0.312	-4.726	0.000
	Systolic blood pressure	-0.004	0.001	-0.211	-3.071	0.002
	Diastolic blood pressure	0.005	0.002	0.136	2.133	0.034

TC, total cholesterol; TG, triglyceride; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; ApoA1, apolipoprotein A1; ApoB, apolipoprotein B; ApoA1/ApoB, the ratio of apolipoprotein A1 to apolipoprotein B; B, unstandardized coefficient; Beta, standardized coefficient.

groups. A previous associated study indicated that the *LIPC* gene encodes hepatic triglyceride lipase, which has been shown to catalyze the hydrolysis of phospholipids, monoglycerides, diglycerides, triglycerides, and acyl-CoA thioesters, and it is a critical enzyme in HDL metabolism [33]. Recently, another GWAS has also identified that genetic variant of the *LIPC* rs1532085 was associated with serum HDL-C and TG levels [34]. Moreover, Women's Genome Health Study (WGHS) found that the *LIPC* rs1532085 SNP in 6382 white women was associated with serum HDL-C and ApoA1 levels [35]. In the current study, we showed that the G allele carriers in Han had lower TC, TG, LDL-C, ApoA1, and ApoB levels than the G allele non-carriers. Subgroup analyses showed that the G allele carriers in Han females had lower TC, TG, LDL-C, and ApoA1 levels than the G allele non-carriers. In the present study, we found that the *LIPC* rs1532085 SNP was significant associated with multiple serum lipid parameters but not HDL-C levels in the Han population. It is difficult to explain these contradictory findings. The possible reasons might be different in study designs, sample size, genetic background, environmental factors, as well as gene-environmental interactions. These findings also suggest that there may be an ethnic-, gender-

specific association of the *LIPC* rs1532085 SNP and serum lipid levels.

It is widely known that environmental factors such as dietary patterns, lifestyle, and physical inactivity are all strongly related with serum lipid levels [36]. In the present study, multivariate linear regression analysis also showed that serum lipid parameters were correlated to age, sex, waist circumference, BMI, blood pressure, blood glucose, alcohol consumption, and cigarette smoking in both ethnic groups. These findings suggest that environmental factors also play a key role in determining serum lipid levels in our study populations. The dietary habits are different between the Han and Maonan populations. Rice is the Maonan people's staple food supplemented with corn, sweet potato, and other grains. Maonan people prefer to eat spicy and acidic food with lots of oil and salt. This preference of high in carbohydrates may be related to the higher blood glucose levels, weight, BMI and waist circumference in Maonan than in Han people. Whereas, rich oil and salt can give rise to higher blood pressure, serum TC, LDL-C, and ApoB levels in Maonan than in Han people. Many past studies proved that diet alone could account for the variability on serum lipid levels [37, 38].

In addition, we also noticed that the percentage of cigarette smoking was higher in Maonan than in Han and the percentage of alcohol consumption was lower in Maonan than in Han. In multiple linear regression analysis, we could find that alcohol consumption and cigarette smoking may influence serum TG, HDL-C, LDL-C, ApoA1 levels, and ApoA1/ApoB ratio ($P < 0.05$). Several case-control and cohort studies have described a J- or U-shaped association between alcohol intake and atherogenesis [39]. A moderate intake of alcohol when taken on a regular basis has been showed to protect against CVD death, which has been attributed to the changes in serum HDL-C, TG and ApoA1 levels [40]. However, alcohol consumption was also associated with worse hematological values of TC and LDL-C levels. Another study showed that there was difference between two cigarette smoking habits: the length period of smoking and a number of cigarettes smoked daily, and made a conclusion that more reflection to the status of lipids has the bigger number of smoked cigarettes daily than the length of the period of cigarette smoking [41]. At the same time, an increase in HDL-C through lifestyle changes just as smoking cessation and physical exercise has positive effects [42]. Nevertheless, another research study indicated that the effects of alcohol consumption on LDL-C appear to vary by specific patient types or patterns of alcohol intake, and sex as well as genetic variants [43]. Therefore, the results of exposure to different lifestyle and environmental factors probably further modify the association of genetic variations and serum lipid levels in our study populations.

Limitations

There are several potential limitations in our study. First, we were not able to alleviate the effect of diet and several environmental factors during the statistical analysis. Second, we could not completely exclude asymptomatic disorders such as atherosclerosis that may create a potentially significant bias due to poor field study condition. Third, although we observed significant association of the LIPC rs1532085 SNP and serum lipid levels, there are still many unmeasured environmental and genetic factors that needed to be considered. The interactions of gene-gene, gene-environment, and environment-environment on serum lipid levels remain to be determined.

Furthermore, the relevance of this finding has to be defined in future studies, including incorporating the genetic information of the LIPC rs1532085 SNP and *in vitro* functional studies to confirm the impact of a variant on a molecular level.

Conclusions

This study showed that the association of the LIPC rs1532085 SNP and serum lipid profiles is different between the Maonan and Han populations and between males and females in the both ethnic groups. These results suggest that there may be a racial/ethnic- and/or sex-specific association of the LIPC rs1532085 SNP and serum lipid levels.

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Disclosure of conflict of interest

None.

Address correspondence to: Rui-Xing Yin, Department of Cardiology, Institute of Cardiovascular Diseases, The First Affiliated Hospital, Guangxi Medical University, 22 Shuangyong Road, Nanning 530021, Guangxi, China. E-mail: yinruixing@163.com

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LIPC rs1532085 SNP and serum lipid levels

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