Int J Clin Exp Pathol 2015;8(1):665-681
www.ijcep.com /ISSN:1936-2625/IJCEP0003708

Original Article

Sex-specific association of the *SPTY2D1* rs7934205 polymorphism and serum lipid levels

Tao Guo[1], Rui-Xing Yin[1], Xia Chen[1], Yuan Bin[1], Rong-Jun Nie[1], Hui Li[2]

[1]*Department of Cardiology, Institute of Cardiovascular Diseases, The First Affiliated Hospital, Guangxi Medical University, Nanning 530021, Guangxi, China;* [2]*Clinical Laboratory of The Affiliated Cancer Hospital, Guangxi Medical University, Nanning 530021, Guangxi, China*

Received November 8, 2014; Accepted December 24, 2014; Epub January 1, 2015; Published January 15, 2015

Abstract: The objective of the present study was to detect the association of the rs7934205 single nucleotide polymorphism (SNP) near the Suppressor of Ty, domain containing 1 gene (*SPTY2D1*) and serum lipid levels between males and females in the Mulao and Han populations. Genotyping of *SPTY2D1* rs7934205 SNP was performed in 933 of Mulao and 865 of Han participants using polymerase chain reaction and restriction fragment length polymorphism. The T allele frequency was different between Mulao males and females (23.2% *vs.* 27.9%, $P = 0.018$). The genotype and allele frequencies were also different between Han males and females ($P = 0.020$ and $P = 0.004$; respectively). Serum levels of apolipoprotein (Apo) A1 in Mulao males; and total cholesterol (TC), triglyceride (TG), low-density lipoprotein cholesterol (LDL-C), ApoA1 and ApoB in Mulao females were different between the CC and CT/TT genotypes ($P < 0.05$). Serum TC, ApoB levels in Han males, and ApoB levels in Han females were different between the CC and CT/TT genotypes ($P < 0.05$). The subjects with CT/TT genotype in both Mulao and Han males and females have more favorable lipid profiles than those with CC genotype. These findings suggest that the association between the *SPTY2D1* rs7934205 SNP and serum lipid levels might have ethnic- and/or sex-specificity.

Keywords: Lipids, sex-specific association, *SPTY2D1*, single nucleotide polymorphism, environmental factors

Introduction

Since the beginning of the 21st century, China has made progress in prevention and control of chronic non-communicable diseases, however there are still large action gaps in implementation [1] especially cardiovascular diseases (CVD), and the leading cause of mortality is increasing at an alarming rate in China [2]. Both dyslipidemia and sex have been demonstrated as the potential of CVD risk factors for a long time [3, 4]. Dyslipidemia management is one of the most important strategies for the prevention of CVD and has been shown to reduce cardiovascular risk in both men and women [5, 6]. However, the striking differences in lipid and lipoprotein metabolism between men and women bring a significant issue to the management and prognosis of CVD [7, 8]. Previous studies suggest that when their access to lipid-lowering treatment is similar to that of men, women are more likely to reach their lipid treatment goal than men especially in high risk groups [9-12]. The relative risk of CVD in subjects with high plasma triglyceride (TG) levels is higher in women than in men. Moreover, changes of TG or high-density lipoprotein cholesterol (HDL-C) in women are better predicators of CVD risk than those of total cholesterol (TC) or low-density lipoprotein cholesterol (LDL-C) [13]. It has also reported that regulating serum TG and HDL-C level is more essential in women than in men [14]. However, the reason for these differences concerned with gender is not yet fully understood. It may be due to 1) certain genes which are expressed in sexually dimorphic manner; 2) sexual hormones which determine phenotypic variations; and/or 3) difference in environmental factors [7, 8, 15]. Therefore, the understanding of sex-specific association between SNPs and serum lipid levels is crucial for improving lipid control in personalized medicine.

Recently, several genome wide association studies (GWAS) have reported the association

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

Parameter	Mulao	Han	t (X^2)	P
Number	933	865		
Male/female	466/467	436/429	0.038	0.846
Age (years)	47.63 ± 12.72	47.58 ± 13.37	0.088	0.930
Height (cm)	156.52 ± 7.46	156.62 ± 7.52	-0.290	0.772
Weight (kg)	52.65 ± 8.41	55.20 ± 9.51	-5.993	0.000
Body mass index (kg/m^2)	21.45 ± 2.83	22.43 ± 3.04	-7.064	0.000
Waist circumference	73.89 ± 7.93	76.21 ± 8.19	-6.109	0.000
Cigarette smoking (n %)				
Nonsmoker	651 (69.77)	590 (68.21)		
< 20 cigarettes/day	238 (25.51)	219 (25.32)	2.660	0.264
≥ 20 cigarettes/day	44 (4.72)	56 (6.47)		
Alcohol consumption [n (%)]				
Nondrinker	685 (73.42)	608 (70.29)		
< 25 g/day	172 (18.43)	188 (21.73)	3.067	0.216
≥ 25 g/day	76 (8.15)	69 (7.98)		
Systolic blood pressure (mmHg)	117.15 ± 11.67	128.16 ± 18.55	-14.927	0.000
Diastolic blood pressure (mmHg)	75.99 ± 7.32	82.26 ± 11.07	-14.054	0.000
Pulse pressure (mmHg)	41.16 ± 9.82	45.90 ± 13.58	-8.418	0.000
Glucose	5.44 ± 0.76	5.83 ± 1.50	-6.899	0.000
Total cholesterol (mmol/L)	4.91 ± 1.09	5.06 ± 1.12	-2.715	0.007
Triglyceride (mmol/L)	1.01 (0.75)	1.11 (0.78)	-4.207	0.000
HDL-C (mmol/L)	1.80 ± 0.45	1.73 ± 0.53	3.283	0.001
LDL-C (mmol/L)	2.93 ± 0.79	2.89 ± 0.86	1.097	0.273
Apolipoprotein (Apo) A1 (g/L)	1.37 ± 0.39	1.36 ± 0.25	0.531	0.595
ApoB (g/L)	0.94 ± 0.52	0.87 ± 0.21	4.024	0.000
ApoA1/ApoB	1.72 ± 1.11	1.78 ± 2.45	-0.730	0.466

HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol. 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.

of many single nucleotide polymorphisms (SNPs) near the Suppressor of Ty, domain containing 1 (S. cerevisiae) gene (*SPTY2D1*) located in chromosome 11 coding Protein SPT2 homolog with one or more lipid traits [16-18] though the biological function of SPT2 in lipid metabolism is unknown. The common variant of *SPTY2D1* is a new studied genetic variant in humans. The interest in this polymorphism is two-fold. First, the functional diversity of the *SPTY2D1* polymorphism appears to be a unique signature of humans. Understanding the functional diversity of the *SPTY2D1* gene, thus, can help in gaining insights on human evolution. Second, the *SPTY2D1* polymorphism may be of potential fundamental interest for geriatrics and gerontology because of its potential profound role in human diseases in late (post-reproductive) life and lifespan. Previous study has identified the rs10128711 SNP in the introns region of *SPTY2D1* as LDL-C-related loci in European populations [16, 17]. However, whether *SPTY2D1* rs7934205 SNP is associated with serum lipid levels or whether it exhibits sex specific association like the previously reported *SPTY2D1* SNPs remains elusive.

Among 56 ethnic groups in China, Han is the largest one. Mulao, on the other hand, is one of the minorities with a population of 207, 352 according to the China's fifth national census in 2000. Approximately ninety percent of Mulao peoples are dwelling in the Luocheng Mulao Autonomous County, Guangxi Zhuang Autonomous Region. "Ling", "Jin" and "Bendiren" are local alternative names for Mulao ethnic group. Historical data trace the history of this ethnic minority back to the Jin Dynasty (AD 265-420). Mulao nationality is a relatively conservative and isolated minority, and preserves their custom of intra-ethnic marriage. Interestingly, they have their culture of consanguineous marriage to cousins of maternal side, suggesting that the genetic background of Mulao population may be less heterogeneous within the population. The Mulao peoples are the descendants of the ancient "Baiyue tribe" in southern China and ethnically related to the neighboring ethnic groups. The recent molecular anthropological data showed that Mulao has much closer genetic relationship with the other minorities in Guangxi than with the Han nationality [19]. In addition, several previous studies have revealed that the

Table 2. Comparison of demographic, lifestyle characteristics and serum lipid levels between males and females of the Mulao and Han populations

Parameter	Mulao (n = 933)		Han (n = 865)	
	Male	Female	Male	Female
Number [n (%)]	466 (49.9)	467 (50.1)	436 (50.4)	429 (49.6)
Age (years)	47.32 ± 12.33	47.94 ± 13.11	47.05 ± 13.11	48.11 ± 13.63
Height (cm)	161.20 ± 5.90	151.84 ± 5.73[a]	161.46 ± 6.03	151.70 ± 5.39[a]
Weight (kg)	56.35 ± 7.73	48.97 ± 7.37[a]	59.95 ± 9.32	50.37 ± 6.90[a]
Body mass index (kg/m^2)	21.68 ± 2.70	21.23 ± 2.94[c]	22.96 ± 3.04	21.90 ± 2.95[a]
Waist circumference (cm)	75.30 ± 8.04	72.47 ± 7.57[a]	78.86 ± 8.32	73.52 ± 7.12[a]
Systolic blood pressure (mmHg)	118.23 ± 11.16	116.08 ± 12.08[b]	132.31 ± 18.183	123.94 ± 17.97[a]
Diastolic blood pressure (mmHg)	77.29 ± 7.05	74.70 ± 7.36[a]	84.41 ± 10.99	80.08 ± 10.73[a]
Pulse pressure (mmHg)	40.94 ± 9.33	41.38 ± 10.30	47.90 ± 14.29	43.86 ± 12.50[a]
Cigarette smoking [n (%)]				
Nonsmoker	185 (39.7)	466 (99.8)	169 (38.8)	421 (98.1)
≤ 20 cigarettes/day	237 (50.9)	1 (0.2)	211 (48.4)	8 (1.9)
> 20 cigarettes/day	44 (9.4)	0 (0)[a]	56 (12.8)	0 (0)[a]
Alcohol consumption [n (%)]				
Nondrinker	223 (47.9)	462 (98.9)	184 (42.2)	424 (98.8)
≤ 25 g/day	169 (36.3)	3 (0.6)	184 (42.2)	4 (0.9)
> 25 g/day	74 (15.9)	2 (0.4)	68 (15.6)	1 (0.2)
Blood glucose (mmol/L)	5.45 ± 0.75	5.43 ± 0.77	5.81 ± 1.66	5.85 ± 1.32
Total cholesterol (mmol/L)	5.02 ± 1.04	4.81 ± 1.14[b]	5.31 ± 1.13	4.80 ± 1.06[a]
Triglyceride (mmol/L)	1.01 (0.77)	1.00 (0.74)[c]	1.28 (0.85)	0.97 (0.71)[a]
HDL-C (mmol/L)	1.77 ± 0.49	1.83 ± 0.40[c]	1.68 ± 0.45	1.77 ± 0.60[c]
LDL-C (mmol/L)	2.96 ± 0.79	2.90 ± 0.80	2.99 ± 0.85	2.78 ± 0.86[a]
Apolipoprotein (Apo) A1 (g/L)	1.34 ± 0.41	1.39 ± 0.36[c]	1.34 ± 0.26	1.38 ± 0.24[c]
ApoB (g/L)	0.98 ± 0.55	0.91 ± 0.49	0.93 ± 0.21	0.80 ± 0.19[a]
ApoA1/ApoB	1.60 ± 0.71	1.83 ± 1.39[b]	1.50 ± 0.45	2.06 ± 3.43[b]

HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol. The quantitative variables were presented as mean ± standard deviation and the difference between the groups was determined by the *t*-test. The values of triglyceride were presented as median (interquartile range), and the difference between the groups was determined by the Wilcoxon-Mann-Whitney test. The difference in percentage of cigarette smoking and alcohol consumption between the groups was determined by χ^2-test. [a]$P < 0.001$ in comparison with males from the same ethnic group. [b]$P < 0.01$ in comparison with males from the same ethnic group. [c]$P < 0.05$ in comparison with males from the same ethnic group.

associations of variants in several lipid-related genes and serum lipid levels are significantly different between the Mulao and Han populations and their gender subgroups [20-22]. This study, therefore, was undertaken to detect the association of *SPTY2D1* rs7934205 SNP and several environmental factors with serum lipid levels between males and females in the Mulao and Han populations.

Materials and methods

Subjects

Two groups of study population including 933 unrelated participants (466 males, 49.9% and 467 females, 50.1%) of Mulao and 865 unrelated subjects (436 males, 50.45% and 429 females, 49.6%) of Han were randomly selected from our previous stratified randomized samples [13, 14]. All participants were agricultural workers from Luocheng Mulao Autonomous County, Guangxi Zhuang Autonomous region, People's Republic of China. The participants' age ranged from 15 to 80 years with the mean age of 47.32 ± 12.33 years in Mulao males and 47.94 ± 13.11 years in Mulao females, and 47.05 ± 13.11 years in Han males and 48.11 ± 13.63 years in Han females; respectively. The age distribution and gender ratio were matched between the two groups. All participants were essentially healthy with no

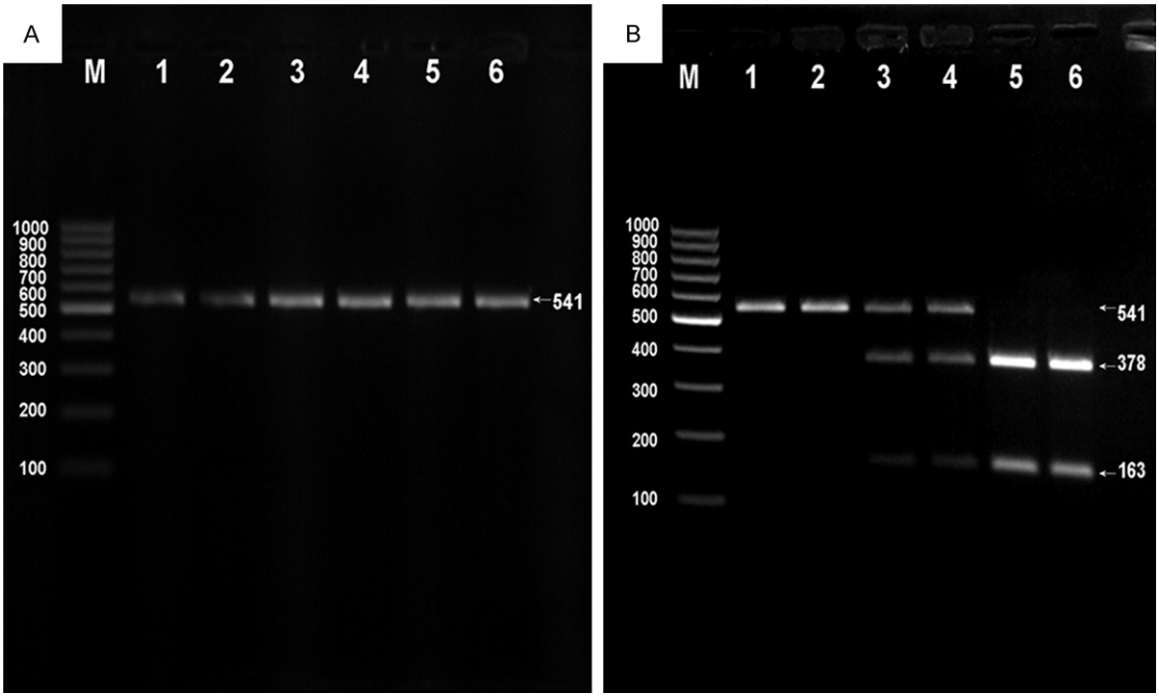

Figure 1. Electrophoresis of PCR products and genotyping of the *SPTY2D1* rs7934205 SNP. A. Lane M, 100 bp marker ladder; lanes 1-6, 541-bp band of PCR products. B. Lane M, 100 bp marker ladder; lanes 1 and 2, TT genotype (541-bp); lanes 3 and 4, CT genotype (541-, 378- and 163-bp); and lanes 5 and 6, CC genotype (378- and 163-bp).

history of CVD such as coronary artery disease (CAD) and 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 study design was approved by the Ethics Committee of the First Affiliated Hospital, Guangxi Medical University.

Epidemiological survey

The epidemiological survey was carried out using internationally standardized methods, following a common protocol [13, 14]. 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: ≤ 25 and > 25. Smoking status was categorized into groups of cigarettes per day: ≤ 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 [20-22].

Biochemical measurements

A fasting venous blood sample of 5 ml was drawn from the participants. The levels of TC, TG, HDL-C and LDL-C in the samples were determined by enzymatic methods with commercially available kits. Serum apolipoprotein (Apo) A1 and ApoB levels were assessed by the immune turbid metric immunoassay [23, 24].

Genotyping

Genomic DNA was isolated from peripheral blood leukocytes using the phenol-chloroform method [20-22]. The *SPTY2D1* rs7934205 SNP was genotyped by polymerase chain reaction and restriction fragment length polymorphism (PCR-RFLP). PCR amplification was performed using 5'-GCCTACTCCAGTTTCTTCA-3' as the forward and 5'-CACCCATTTCAGATACCTTCA-3' as reversed primer pair. Each amplification reaction was performed in a total volume of 25 μl, 12.5 μl of 2 × Taq PCR MasterMix (constituent: 0.1 U *Taq* polymerase/μl, 500 μM dNTP each and PCR buffer) and nuclease-free water 8.5 μl, 20 pmol/L of each primer and 100 ng of genomic DNA, processing started with 5 min of

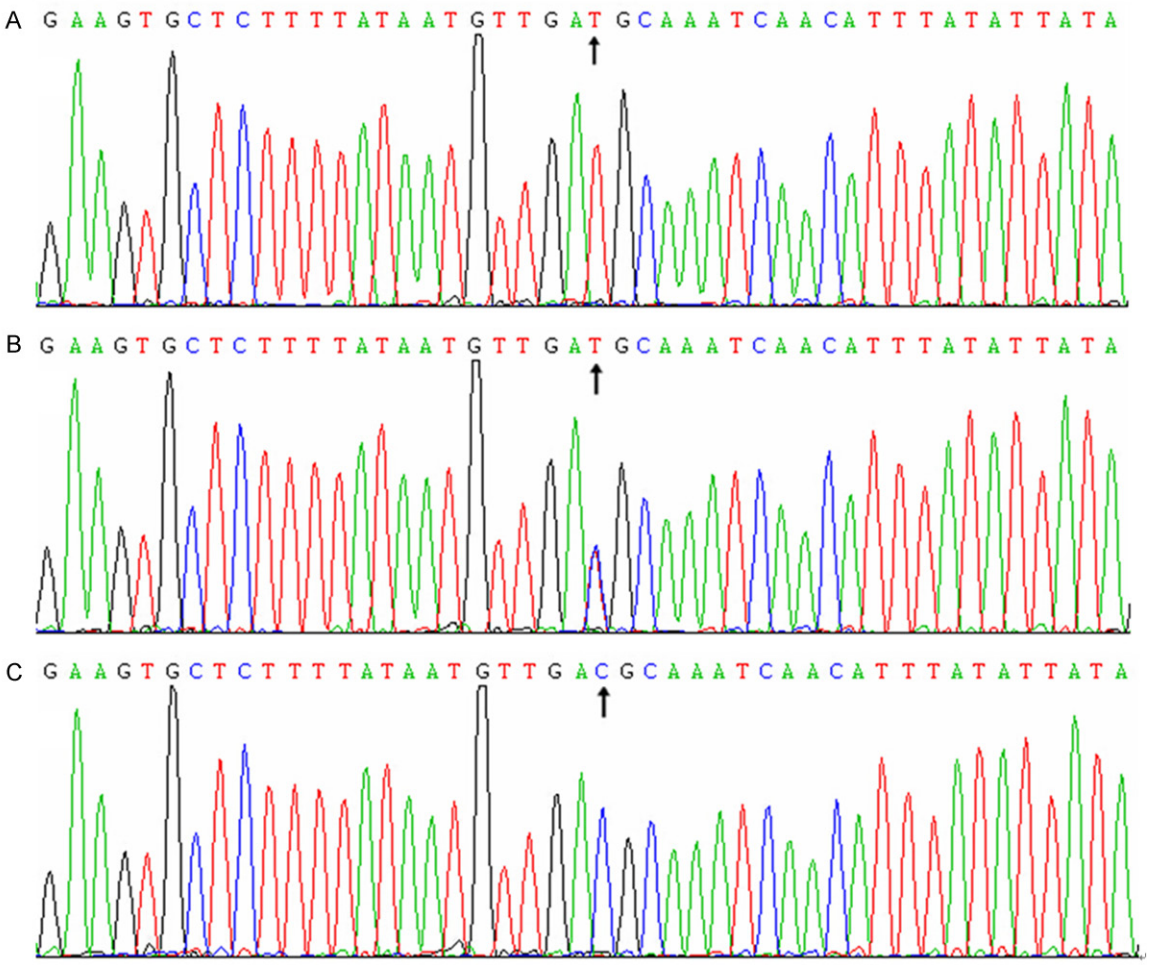

Figure 2. A part of the nucleotide sequences of the *SPTY2D1* rs7934205 SNP by direct sequencing. A. TT genotype. B. CT genotype. C. CC genotype.

pre-denaturing at 95°C and followed by 45 s of denaturing at 94°C, 30 s of annealing at 60°C and 1 min of elongation at 72°C for 35 cycles. The amplification was completed by a final extension at 72°C for 10 min. Then each restriction enzyme reaction was performed with 10 μl of amplified DNA, 8 μl of nuclease-free water, 1 μl of 10 × buffer solutions, and 10 U of '*Hinc* II' enzyme in a total volume of 20 μl digested at 37°C overnight. After restriction enzyme digestion of the amplified DNA, the digestive products were separated by electrophoresis on 2% agrose gel. The length of each digested DNA fragment was determined by comparing migration of a sample with that of standard DNA marker. Genotypes were scored by an experienced reader blinded to the epidemiological and lipid results. Six samples (each genotype in two; respectively) detected by the PCR-RFLP were also confirmed by direct sequencing. The PCR products were purified by low melting point gel electrophoresis and phenol extraction, and then the DNA sequences were analyzed using 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 and ApoB levels, and the ratio of ApoA1 to ApoB 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 [25, 26].

Statistical analysis

The statistical analyses were performed with the statistical software package SPSS 17.0

Table 3. Comparison of the genotype and allele frequencies of the *SPTY2D1* rs7934205 SNP between males and females of the Mulao and Han populations

Group	n	Genotype			Allele	
		CC	CT	TT	C	T
Mulao	933	551 (59.1)	287 (30.8)	95 (10.2)	1389 (74.4)	477 (25.6)
Han	865	482 (55.7)	301 (34.8)	82 (9.5)	1265 (73.1)	465 (26.9)
X^2	–		3.330		0.804	
P			0.189		0.370	
Mulao						
Male	466	288 (61.8)	140 (30.0)	38 (8.2)	716 (76.8)	216 (23.2)
Female	467	263 (56.3)	147 (31.5)	57 (12.2)	673 (72.1)	261 (27.9)
X^2			5.104		5.574	
P			0.078		0.018	
Han						
Male	436	263 (60.3)	138 (31.7)	35 (8.0)	664 (76.1)	208 (23.9)
Female	429	219 (51.0)	163 (38.0)	47 (11.0)	601 (70.0)	257 (30.0)
X^2			7.793		8.188	
P			0.020		0.004	

(SPSS Inc., Chicago, Illinois). The quantitative variables were presented as mean ± standard deviation (serum TG levels were 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 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 analysis of covariance (ANCOVA). Age, sex, BMI, smoking, and alcohol consumption were adjusted for the statistical analysis. Multivariable linear regression analyses with stepwise modeling were used to determine the correlation between genotypes (CC = 1, CT = 2, TT = 3) or alleles (the T allele non-carrier = 1, the T allele carrier = 2) and several environmental factors with serum lipid levels in males and females of Mulao and Han populations. Two sided *P* value < 0.05 was considered statistically significant.

Results

General and biochemical characteristics of the subjects

The comparison of general characteristics and serum lipid levels between the Mulao and Han populations is summarized in **Table 1**. The levels of body weight, BMI, waist circumference, systolic blood pressure, diastolic blood pressure, pulse pressure, glucose, serum TC and TG levels were lower in Mulao than in Han ($P < 0.05$-0.001), whereas the levels of HDL-C and ApoB was higher in Mulao than in Han ($P < 0.05$-0.001). There were no significant differences in the gender ratio, age structure, body height, the percentage of cigarette smoking and alcohol consumption, serum LDL-C and ApoA1 levels and the ApoA1/ApoB ratio between the two ethnic groups ($P > 0.05$ for all).

Table 2 compares the general characteristics and serum lipid profiles between males and females in Mulao and Han ethnic groups. The values of height, weight, BMI, waist circumference, systolic blood pressure, diastolic blood pressure, and the percentages of subjects cigarette smoking were different between men and women in both ethnic groups ($P < 0.05$-0.001). The values of pulse pressure were different between men and women in Han ($P < 0.001$) but not in Mulao. Overall, men had higher values of general characteristic parameters than women in both ethnic groups. In Mulao, men had higher serum TC and TG levels, and lower HDL-C and ApoA1 levels and ApoA1/ApoB ratio than the women ($P < 0.05$-0.01). In Han, males had higher TC, TG, LDL-C and ApoB levels, and lower LDL-C and ApoB levels and ApoA1/ApoB ratio than the females ($P < 0.05$-0.001).

Results of genotyping

After the genomic DNA of the samples was amplified by PCR, the purpose gene of 541-bp nucleotide sequences could be seen in all samples (**Figure 1A**). The genotypes identified were labeled according to the presence or absence of the enzyme restriction sites. Thus, TT genotype is homozygote for the absence of the site (541-bp), CT genotype is heterozygote for the presence and absence of the site (541-, 378- and 163-bp) and CC genotype is homozygote

Table 4. Comparison of the genotypes and serum lipid levels in the Mulao and Han populations

Ethnic Genotype	N	TC (mmol/L)	TG (mmol/L)	HDL-C (mmol/L)	LDL-C (mmol/L)	Apo A1 (g/L)	ApoB (g/L)	ApoA1/ ApoB
Mulao								
CC	551	4.98 ± 1.08	1.03 (0.77)	1.82 ± 0.49	2.96 ± 0.82	1.39 ± 0.40	0.96 ± 0.52	1.74 ± 1.30
CT/TT	382	4.82 ± 1.10	0.99 (0.73)	1.78 ± 0.38	2.88 ± 0.75	1.33 ± 0.38	0.92 ± 0.52	1.63 ± 0.78
F		2.127	-1.078	1.190	1.427	2.343	0.938	0.731
P		0.034	0.281	0.234	0.154	0.019	0.348	0.465
Han								
CC	482	5.11 ± 1.21	1.14 (0.80)	1.75 ± 0.59	2.90 ± 0.88	1.37 ± 0.26	0.88 ± 0.23	1.69 ± 0.84
CT/TT	383	4.98 ± 1.00	1.07 (0.76)	1.70 ± 0.45	2.86 ± 0.84	1.35 ± 0.24	0.86 ± 0.19	1.89 ± 0.56
F		1.677	-1.279	1.202	0.748	1.109	1.197	-1.151
P		0.094	0.201	0.230	0.455	0.268	0.232	0.250

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 TG was presented as median (interquartile range). The difference between the genotypes was determined by the Wilcoxon-Mann-Whitney test.

Table 5. Comparison between the *SPTY2D1* rs7934205 genotypes and serum levels in the males and females of the Mulao and Han populations

Genotype	n	TC (mmol/L)	TG (mmol/L)	HDL-C (mmol/L)	LDL-C (mmol/L)	ApoA1 (g/L)	ApoB (g/L)	ApoA/ApoB
Mulao/Male								
CC	288	5.05 ± 1.06	1.03 (0.78)	1.76 ± 0.36	2.96 ± 0.69	1.30 ± 0.41	0.99 ± 0.56	1.54 ± 0.69
CT/TT	178	4.97 ± 1.01	1.00 (0.75)	1.78 ± 0.56	2.95 ± 0.84	1.37 ± 0.41	0.97 ± 0.53	1.64 ± 0.73
F		1.209	0.024	0.005	0.043	4.761	0.029	1.076
P		0.272	0.877	0.945	0.836	0.030	0.865	0.300
Mulao/Female								
CC	263	4.90 ± 1.11	1.03 (0.74)	1.81 ± 0.40	2.96 ± 0.81	1.36 ± 0.35	0.94 ± 0.51	1.81 ± 0.83
CT/TT	204	4.69 ± 1.16	0.99 (0.73)	1.85 ± 0.41	2.82 ± 0.79	1.42 ± 0.38	0.87 ± 0.44	1.85 ± 1.71
F		7.428	8.315	2.577	8.151	4.409	4.175	0.007
P		0.007	0.004	0.109	0.005	0.036	0.042	0.935
Han/Male								
CC	263	5.41 ± 1.27	1.37 (0.94)	1.67 ± 0.45	3.06 ± 0.91	1.34 ± 0.28	0.96 ± 0.23	1.48 ± 0.44
CT/TT	173	5.16 ± 0.86	1.15 (0.78)	1.69 ± 0.46	2.88 ± 0.74	1.34 ± 0.24	0.90 ± 0.17	1.54 ± 0.48
F		7.027	2.014	0.729	3.269	0.194	7.449	2.214
P		0.008	0.157	0.394	0.071	0.660	0.007	0.138
Han/Female								
CC	219	4.84 ± 1.08	1.00 (0.75)	1.73 ± 0.45	2.84 ± 0.91	1.36 ± 0.24	0.82 ± 0.19	2.17 ± 4.78
CT/TT	210	4.76 ± 1.04	0.95 (0.67)	1.81 ± 0.71	2.72 ± 0.80	1.40 ± 0.24	0.78 ± 0.19	1.96 ± 1.10
F		0.146	0.002	2.655	0.927	2.396	4.118	0.487
P		0.702	0.960	0.104	0.336	0.122	0.043	0.486

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 values of triglyceride were presented as median (interquartile range), and their difference among the genotypes was determined by the Kruskal-Wallis test or the Wilcoxon-Mann-Whitney test.

for the presence of the site (378- and 163-bp; **Figure 1B**). The TT, CT and CC genotypes detected by PCR-RFLP were also confirmed by direct sequencing (**Figure 2**).

Genotypic and allelic frequencies

As shown in **Table 3**, the genotype and allele frequencies of *SPTY2D1* rs7934205 SNP were

Table 6. Correlation between the genotypes/alleles of the *SPTY2D1* rs7934205 SNP and serum lipid levels between males and females of the Mulao and Han populations

Lipid	Genotype /allele	Unstandardized coefficient	Standard error	Standardized coefficient	*t*	*P*
Mulao plus Han						
ApoA1	Allele	-0.085	0.042	-0.057	-2.013	0.044
Mulao/Male						
TC	Genotype	-0.181	0.088	-0.293	-2.052	0.041
HDL-C	Genotype	0.200	0.099	0.153	2.019	0.044
LDL-C	Genotype	0.186	0.084	0.227	2.200	0.028
TC	Allele	-0.140	0.067	-0.300	-2.102	0.036
Mulao/Female						
TG	Genotype	-0.128	0.057	-0.116	-2.262	0.024
TG	Allele	-0.090	0.040	-0.115	-2.258	0.024
Han						
ApoA1/ApoB	Genotype	0.025	0.010	0.091	2.369	0.018
Han/Female						
ApoB	Genotype	1.348	0.395	0.385	3.412	0.001
ApoA1/ApoB	Genotype	0.037	0.011	0.189	3.356	0.001
ApoB	Allele	0.715	0.296	0.277	2.419	0.016

TC, total cholesterol; TG, triglyceride; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; ApoA1, apolipoprotein A1; ApoB, apolipoprotein B.

not different between the Mulao and Han populations ($P > 0.05$ for each). The genotype frequencies of rs7934205 SNP agreed with the Hardy-Weinberg equilibrium in both populations ($P > 0.05$ for each). Gender-subgroup analysis showed that the genotype frequencies of rs7934205 SNP between males and females were different in Han ($P < 0.005$) but not in Mulao. The allele frequencies were different between Mulao males and females (C, 76.8% *vs.* 72.1%; T, 23.2% *vs.* 27.9%, $P = 0.018$). The genotype and allele frequencies were significantly different between Han males and females (CC, 60.3% *vs.* 51.0%; CT, 31.7% *vs.* 38.0%, TT, 8.0% *vs.* 11.0%, $P = 0.020$; C, 76.1% *vs.* 70.0%; T, 23.9% *vs.* 30.0%, $P = 0.004$).

Genotypes and serum lipid levels

Tables 4 and **5** describe the association between genotypes and serum lipid levels. Serum TC and ApoA1 levels in Mulao were different among the genotypes ($P < 0.05$ for each), the T allele carriers had lower serum TC and ApoA1 levels than the T allele non-carriers. There were no differences between genotypes and serum lipid levels in Han population. Subgroup analyses showed that serum levels of ApoA1 in Mulao males, and TC, TG, LDL-C, ApoA1 and ApoB in Mulao females were different between the CC and CT/TT genotypes ($P < 0.05$ for all); the subjects with CT/TT genotypes had higher serum TC, TG, LDL-C and ApoB levels than those with AA genotype. Serum TC and ApoB levels in Han males and ApoB levels in Han females were different between the CC and CT/TT genotypes ($P < 0.05$ for all); the CT/TT genotype subjects in Han males had lower TC and ApoB levels.

Relative factors for serum lipid parameters

Multiple linear regression analyses showed that the levels of ApoA1 in Mulao plus Han were correlated with allele ($P < 0.05$), and ApoA1/ApoB ratio in Han was correlated with genotypes ($P < 0.05$; **Table 4**). In gender subgroups, the levels of TC, HDL-C and LDL-C in Mulao males, the levels of TG in Mulao females, and the levels of ApoB and ApoA1/ApoB ratio in Han females were correlated with genotypes ($P < 0.05$-0.001). The levels of TC in Mulao males, the levels of TG in Mulao females, and the levels of ApoB in Han females were correlated with alelle ($P < 0.05$ for all; **Table 6**). Several environmental factors such as age, gender, height, weight, waist circumference, alcohol consumption and cigarette smoking, and traditional car-

Table 7. Relationship between serum lipid parameters and relative factors in the Mulao and Han populations

Lipid parameter	Risk factor	*B*	*Std. error*	*Beta*	*t*	*P*
Mulao and Han						
TC	Ethnic group	0.084	0.030	0.038	2.797	0.005
	Cigarette smoking	0.091	0.030	0.048	3.088	0.002
	Alcohol consumption	0.089	0.027	0.050	3.344	0.001
	Diastolic blood pressure	0.006	0.002	0.054	3.964	0.000
TG	Ethnic group	0.218	0.093	0.057	2.345	0.019
	Age	-0.007	0.004	-0.050	-2.013	0.044
	Cigarette smoking	0.426	0.092	0.130	4.634	0.000
	Height	-0.089	0.039	-0.349	-2.291	0.022
	Weight	0.108	0.056	0.511	1.941	0.052
	Body mass index	-0.322	0.138	-0.501	-2.342	0.019
	Waist circumference	0.070	0.009	0.297	7.779	0.000
	Diastolic blood pressure	0.019	0.005	0.099	4.020	0.000
	Glucose	0.168	0.037	0.104	4.513	0.000
HDL-C	Gender	0.122	0.036	0.114	3.109	0.002
	Age	0.003	0.001	0.087	3.432	0.001
	Alcohol consumption	0.129	0.021	0.164	6.014	0.000
	Weight	-0.029	0.015	-0.528	-1.978	0.048
LDL-C	Ethnic group	-0.124	0.041	-0.075	-3.035	0.002
	Gender	-0.258	0.061	-0.156	-4.228	0.000
	Age	0.010	0.002	0.155	6.052	0.000
	Cigarette smoking	-0.121	0.040	-0.086	-2.994	0.003
	Waist circumference	0.012	0.004	0.120	3.091	0.002
ApoA1	Gender	0.130	0.025	0.196	5.245	0.000
	Age	0.002	0.001	0.084	3.250	0.001
	Genotype	-0.043	0.015	-0.064	-2.764	0.006
	Alcohol consumption	0.109	0.015	0.207	7.449	0.000
ApoB	Ethnic group	-0.139	0.020	-0.172	-6.957	0.000
	Cigarette smoking	0.041	0.020	0.060	2.077	0.038
	Waist circumference	0.009	0.002	0.179	4.597	0.000
	Pulse pressure	0.003	0.001	0.101	4.232	0.000
	Glucose	0.024	0.008	0.072	3.043	0.002
ApoA1/ApoB	Ethnic group	0.197	0.097	0.052	2.038	0.042
	Gender	0.391	0.144	0.104	2.716	0.007
Mulao						
TC	Genotype	-0.192	0.071	-0.086	-2.704	0.007
	Age	0.017	0.003	0.195	5.704	0.000
	Cigarette smoking	0.194	0.077	0.101	2.506	0.012
	Pulse pressure	0.008	0.004	0.071	2.207	0.028
TG	Height	-0.055	0.027	-0.490	-2.055	0.040
	Weight	0.092	0.040	0.916	2.303	0.022
	Waist circumference	0.018	0.005	0.174	3.539	0.000
	Pulse pressure	0.005	0.003	0.063	1.968	0.049
HDL-C	Gender	0.099	0.046	0.111	2.172	0.030
	Age	0.003	0.001	0.088	2.624	0.009
	Alcohol consumption	0.130	0.027	0.181	4.879	0.000

LDL-C	Genotype	-0.110	0.051	-0.068	-2.157	0.031
	Age	0.013	0.002	0.207	6.102	0.000
	Height	-0.052	0.025	-0.493	-2.064	0.039
ApoA1	Genotype	-0.069	0.025	-0.087	-2.723	0.007
	Gender	0.173	0.040	0.222	4.282	0.000
	Age	0.004	0.001	0.128	3.742	0.000
	Alcohol consumption	0.144	0.024	0.231	6.111	0.000
ApoB	Cigarette smoking	0.095	0.037	0.104	2.581	0.010
	Waist circumference	0.009	0.003	0.135	2.711	0.007
	Pulse pressure	0.007	0.002	0.137	4.231	0.000
ApoA1/ApoB	Cigarette smoking	-0.175	0.080	-0.089	-2.194	0.028
	Alcohol consumption	0.153	0.068	0.086	2.248	0.025
	Pulse pressure	-0.009	0.004	-0.083	-2.545	0.011
Han						
TC	Gender	-0.461	0.114	-0.205	-4.055	0.000
	Alcohol consumption	0.242	0.069	0.135	3.485	0.001
	Waist circumference	0.038	0.008	0.276	4.676	0.000
	Diastolic blood pressure	0.021	0.003	0.209	6.264	0.000
	Glucose	0.063	0.024	0.084	2.611	0.009
TG	Age	-0.019	0.007	-0.098	-2.575	0.010
	Cigarette smoking	0.907	0.173	0.212	5.255	0.000
	Waist circumference	0.137	0.019	0.433	7.198	0.000
	Diastolic blood pressure	0.026	0.008	0.112	3.304	0.001
	Glucose	0.223	0.057	0.129	3.936	0.000
HDL-C	Gender	0.122	0.057	0.114	2.142	0.032
	Age	0.004	0.002	0.095	2.422	0.016
	Cigarette smoking	0.078	0.037	0.088	2.104	0.036
	Alcohol consumption	0.120	0.035	0.142	3.467	0.001
	Height	0.040	0.015	0.560	2.580	0.010
	Weight	-0.062	0.021	-1.101	-2.908	0.004
	Body mass index	0.127	0.053	0.727	2.402	0.017
LDL-C	Gender	-0.467	0.090	-0.271	-5.178	0.000
	Age	0.008	0.002	0.120	3.114	0.002
	Cigarette smoking	-0.345	0.059	-0.243	-5.900	0.000
	Waist circumference	0.020	0.006	0.193	3.146	0.002
	Diastolic blood pressure	0.005	0.003	0.068	1.979	0.048
ApoA1	Gender	0.082	0.027	0.163	3.026	0.003
	Cigarette smoking	0.066	0.018	0.159	3.769	0.000
	Alcohol consumption	0.057	0.017	0.143	3.450	0.001
ApoB	Gender	-0.106	0.020	-0.251	-5.299	0.000
	Alcohol consumption	0.038	0.012	0.113	3.114	0.002
	Waist circumference	0.008	0.001	0.316	5.713	0.000
	Diastolic blood pressure	0.003	0.001	0.151	4.830	0.000
	Pulse pressure	0.001	0.000	0.064	2.031	0.043
	Glucose	0.023	0.004	0.162	5.369	0.000
ApoA1/ApoB	Gender	0.638	0.273	0.130	2.334	0.020

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.

diovascular risk factors such as BMI, fasting blood glucose and blood pressure levels were also correlated with serum lipid parameters in the Mulao and Han populations and in males and females of both ethnic groups ($P < 0.05$-0.001, **Tables 7**, **8**).

Discussion

To the best of our knowledge, this is the first study to detect the association of the *SPTY2D1* rs7934205 polymorphism and serum lipid levels in the Chinese population. The current study demonstrated that serum lipid profiles were significantly different between males and females in both Mulao and Han ethnic groups. As expected, the males had higher serum levels of bad cholesterols and lower levels of good cholesterols than the females in both ethnic groups.

A significant difference in the genotype or allele frequencies of *SPTY2D1* rs7934205 SNP was also noted between the two ethnic populations. The minor T allele frequency in Mulao and Han were 25.6% and 26.9% respectively, which were extraordinary different to those of Chinese Han Beijing (42.7%) reported in international haplotype map (HapMap) project. On gender subgroup analysis, the genotype frequencies between males and females were different in Han but not in Mulao. According to HapMap data, the minor allele frequency of rs7934205 was 47.3% in European, 22.0% in Japanese, and 42.9% in Inbadan Yoruba and Utahns. Apparently, the minor allele frequency was lower in Asian than the Western populations. These findings suggest that genotype and allele frequencies of *SPTY2D1* rs7934205 SNP are inconsistent among diverse ethnic groups or between males and females.

The previous studies reported that minor allele of *SPTY2D1* SNP was significantly associated with pleiotropic (one SNP influence many traits) effects on decreased LDL-C [16-18]. Our study indicates that the *SPTY2D1* rs7934205 SNP was correlated with TC, LDL-C and ApoA1 in the combined Mulao. However, no association with LDL-C was detected in Han. The reason for this discrepancy is not fully understood. It might be due to the differences in genetic backgrounds, dietary habits, and environmental factors between the two ethnic populations and/or simply due to the low power of this study. It is well accepted that ethnic differences in serum lipid levels were partly due to the differences in the dietary intakes [27]. Diet alone could account for up to 2.5% of the variability on serum lipid levels [28-32]. Although rice and corn are the staple foods for both ethnic groups; Mulao peoples have a typical habit of eating cold foods along with acidic and spicy dishes, local bean soy sauce, pickled vegetables and animal offal's which contain abundant saturated fatty acid. Therefore, it is possible that the difference in dietary habit between Mulao and Han ethnic groups partly contribute variability in the effect of *SPTY2D1* rs7934205 SNP on serum lipid levels. The sex-specific association of *SPTY2D1* rs7934205 SNP and serum lipid levels has not been previously reported. Here, we found that the minor T allele of *SPTY2D1* rs7934205 SNP was associated with higher serum ApoA1 levels in Mulao males, higher ApoA1 and lower TC, TG, LDL-C and ApoB levels in Mulao females. On the other hand, the minor T allele was associated with lower TC and ApoB levels in Han males, and lower ApoB levels in Han females. Therefore, the minor T allele carriers in Mulao and males and females both in two nationalities have more favorable lipid profiles than the minor T allele non-carriers. This phenomenon might in part be explained by the presence of endogenous sex hormones such as estrogen, which mediate cholesterol metabolism in a sexually dimorphic manner [8], and it is associated with lowering cholesterol by reducing the LDL-C level through decreased LDL receptors [33] and an increased LDL clearance rate [34]. Majority of the females were pre-menopausal and thus could have benefited from protective effects of estrogen on cardiovascular risks [35]. Moreover, males have more visceral adipose tissue that increases over expression of inflammatory markers associated with increased cardiovascular risks [36]. Other plausible factors may include dietary habits, known CVD risk factors such as cigarette smoking and alcohol consumption common in Chinese men than women [37, 38]. Of remarkable interest is the high prevalence of *SPTY2D1* rs7934205 polymorphism in women which may suggest it as the main determinant for lipid levels. To the best of our knowledge, this study is the first attempt to report the gender specific association of *SPTY2D1* rs7934205 SNP. Therefore, further studies with larger sample size and well-designed studies are still needed to confirm this association.

Table 8. Relationship between serum lipid parameters and relative factors in the males and females of the Mulao and Han populations

Lipid parameter	Risk factor	*B*	*Std. error*	*Beta*	*t*	*P*
Mulao/male						
TC	Age	0.014	0.004	0.160	3.348	0.001
	Cigarette smoking	0.174	0.075	0.106	2.330	0.020
	Glucose	-0.146	0.064	-0.105	-2.280	0.023
TG	Waist circumference	0.019	0.008	0.150	2.337	0.020
HDL-C	Age	0.004	0.002	0.095	2.044	0.042
	Alcohol consumption	0.144	0.030	0.215	4.807	0.000
	Body mass index	-0.216	0.108	-1.187	-1.992	0.047
	Glucose	-0.069	0.029	-0.105	-2.335	0.020
LDL-C	Age	0.008	0.003	0.118	2.440	0.015
	Glucose	-0.100	0.049	-0.095	-2.039	0.042
ApoA1	Gender	-0.083	0.038	-0.098	-2.182	0.030
	Age	0.006	0.002	0.164	3.519	0.000
	Alcohol consumption	0.145	0.025	0.256	5.731	0.000
	Diastolic blood pressure	0.006	0.003	0.110	2.342	0.020
ApoB	Cigarette smoking	0.091	0.039	0.105	2.340	0.020
	Pulse pressure	0.011	0.003	0.180	3.960	0.000
ApoA1/ApoB	Cigarette smoking	-0.158	0.050	-0.141	-3.166	0.002
	Alcohol consumption	0.145	0.044	0.148	3.316	0.001
	Body mass index	-0.339	0.157	-1.282	-2.151	0.032
	Diastolic blood pressure	0.011	0.005	0.113	2.400	0.017
Mulao/female						
TC	Genotype	-0.283	0.104	-0.123	-2.725	0.007
	Age	0.020	0.004	0.231	4.660	0.000
	Pulse pressure	0.013	0.005	0.119	2.562	0.011
TG	Gender	-0.164	0.057	-0.129	-2.884	0.004
	Waist circumference	0.015	0.006	0.179	2.319	0.021
HDL-C	Waist circumference	-0.005	0.004	-0.053	-1.136	0.025
	Genotype	0.167	0.043	0.182	3.874	0.000
LDL-C	Genotype	-0.200	0.070	-0.124	-2.855	0.005
	Age	0.018	0.003	0.290	6.080	0.000
	Pulse pressure	0.007	0.003	0.089	2.001	0.046
ApoA1	Genotype	-0.072	0.034	-0.098	-2.100	0.036
	Age	0.003	0.001	0.101	1.981	0.048
ApoB	Genotype	-0.091	0.045	-0.093	-2.043	0.042
	Waist circumference	0.012	0.005	0.185	2.343	0.020
	Glucose	0.072	0.029	0.115	2.470	0.014
ApoA1/ApoB	Body mass index	-0.036	0.008	-0.206	-4.460	0.000
	Cigarette smoking	0.345	0.112	0.144	3.093	0.002
	Systolic blood pressure	-0.002	0.001	-0.070	-1.373	0.017
	Age	-0.008	0.002	-0.197	-3.765	0.000
	Genotype	0.057	0.032	-0.080	1.754	0.008
Han/male						
TC	Genotype	-0.268	0.101	-0.116	-2.651	0.008
	Alcohol consumption	0.222	0.074	0.140	2.998	0.003
	Waist circumference	0.050	0.012	0.370	4.255	0.000
	Diastolic blood pressure	0.032	0.005	0.311	6.842	0.000

	Glucose	0.102	0.031	0.150	3.262	0.001
TG	Cigarette smoking	0.862	0.236	0.172	3.650	0.000
	Waist circumference	0.227	0.036	0.562	6.344	0.000
	Diastolic blood pressure	0.035	0.014	0.116	2.503	0.013
	Glucose	0.300	0.095	0.148	3.174	0.002
HDL-C	Age	0.004	0.002	0.115	2.264	0.024
	Cigarette smoking	0.081	0.031	0.120	2.646	0.008
	Alcohol consumption	0.113	0.029	0.179	3.919	0.000
	Height	0.077	0.023	1.027	3.379	0.001
	Weight	-0.105	0.030	-2.163	-3.472	0.001
	Body mass index	0.226	0.080	1.520	2.835	0.005
	Diastolic blood pressure	0.006	0.002	0.148	3.341	0.001
	Pulse pressure	-0.003	0.001	-0.105	-2.259	0.024
LDL-C	Cigarette smoking	-0.318	0.062	-0.250	-5.164	0.000
	Waist circumference	0.007	0.004	0.094	1.974	0.049
ApoA1	Cigarette smoking	0.075	0.019	0.190	3.930	0.000
	Alcohol consumption	0.047	0.018	0.128	2.629	0.009
	Height	0.040	0.014	0.928	2.851	0.005
	Weight	-0.057	0.019	-2.026	-3.035	0.003
	Body mass index	0.126	0.050	1.456	2.534	0.012
ApoB	Genotype	-0.049	0.018	-0.115	2.729	0.007
	Alcohol consumption	0.034	0.013	0.116	2.580	0.010
	Waist circumference	0.009	0.002	0.355	4.234	0.000
	Diastolic blood pressure	0.004	0.001	0.230	5.262	0.000
	Glucose	0.028	0.006	0.222	5.027	0.000
ApoA1/ApoB	Cigarette smoking	0.111	0.031	0.164	3.545	0.000
Han/female						
TC	Age	0.019	0.005	0.246	4.139	0.000
TG	Waist circumference	0.047	0.014	0.266	3.288	0.001
	Diastolic blood pressure	0.020	0.006	0.168	3.293	0.001
HDL-C	Body mass index	-0.034	0.007	-0.233	-5.149	0.000
	Genotype	0.080	0.028	0.128	2.831	0.005
LDL-C	Body mass index	0.059	0.013	0.203	4.495	0.000
	Age	0.020	0.004	0.314	5.284	0.000
ApoA1	Height	-0.029	0.013	-0.642	-2.120	0.035
	Body mass index	-0.106	0.049	-1.296	-2.168	0.031
ApoB	Genotype	0.034	0.017	0.088	2.029	0.043
	Age	0.002	0.001	0.130	2.262	0.024
	Waist circumference	0.005	0.002	0.200	2.631	0.009
	Glucose	0.015	0.007	0.099	2.153	0.032
ApoA1/ApoB	Age	-0.011	0.004	-0.133	-2.886	0.004
	Waist circumference	-0.024	0.010	-0.156	-2.386	0.017

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.

Several environmental factors were also correlated with serum lipid levels in males and females of both Mulao and Han populations. In the current study, the males had significantly higher values of weight, height, BMI, waist circumference compared to the female counterparts in both ethnic groups. Garcia-Palmieri et al. [28] stated that diet and relative weight could account for up to 6% of the variability in serum cholesterol levels. In particular, for every

1-kg decrease in body weight, TG decreased by 0.011 mmol/L and HDL-C increased by 0.011 mmol/L [39]. In addition, in this study, the males' percentages of subjects consuming alcohol and cigarette smoking were significantly higher than the females' in both ethnic groups. Rimm et al. [40] documented that consuming of 30 g of ethanol per day increased the concentrations of HDL-C by 3.99 mg/dl, ApoA1 by 8.82 mg/dl, and TG by 5.69 mg/dl. Yin et al. [41, 42] also showed that BMI, cigarette smoking and alcohol consumption could interact with certain lipid-related gene variants to modify the serum lipid levels in Bai Ku Yao and Han Chinese ethnic groups. Therefore, the results of exposure to different environmental factors may further modify the effect of genetic variation on serum lipid levels in our study populations.

There are some potential limitations in our study. First, it is undeniable that this study has insufficient power to produce a robust conclusion; therefore, such a small-scale study needs to replicate in independent cohorts. Second, the study is the cross-sectional nature of the design which may not allow causal or directional inferences, and thus the need for a longitudinal study. Third, This led to the hypothesis may be partly attributable to gender differences in physical activity, daily diet, socioeconomic status, education level, occupation, and medical insurance coverage. Optimistic point of view, our results may have significant implications for clinical practice. In the future, genetic factors are either modifiable or potentially amenable to interventions. At the policy level, possible interventions include enhancing the coverage rate of medical insurance and improving the healthcare environment for female patients. Patient-level interventions include reducing and controlling cardiovascular risk factors and improving compliance to lipid-lowering treatment. Physicians should promote an attitude of knowledge informing practice for the treatment of dyslipidemia in women, pay more attention to female patients who are postmenopausal and have high LDL-C levels, and provide an adequate and intensive treatment strategy to female patients. Gene-gender interaction may be a potential contributor to gender disparities in lipid-lowering treatment goal attainment. As far as other potential explanatory factors, more studies need to be done to discover them and elaborate on their effects in the future.

In conclusion, T allele frequency of the *SPTY2D1* rs7934205 SNP in both Mulao and Han is higher in females than in males. The minor T allele carriers in both ethnic groups have more favorable serum lipid profiles than the T allele non-carriers. These findings suggest that the association between the *SPTY2D1* rs7934205 SNP and serum lipid levels might have ethnic- and/or sex-specificity.

Acknowledgements

This study was supported by the National Natural Science Foundation of China (No: 30960130).

Disclosure of conflict of interest

None.

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

References

[1] Lv J, Liu M, Jiang Y and Li LM. Prevention and control of major non-communicable diseases in China from 1990 to 2009: results of a two-round Delphi survey. Glob Health Action 2013; 6: 20004.

[2] Yang ZJ, Liu J, Ge JP, Chen L, Zhao ZG, Yang WY; China National Diabetes and Metabolic Disorders Study Group. Prevalence of cardiovascular disease risk factor in the Chinese population: the 2007-2008 China National Diabetes and Metabolic Disorders Study. Euro Heart J 2012; 33: 213-220.

[3] Ginsberg HN and Stalenhoef AF. The metabolic syndrome targeting dyslipidaemia to reduce coronary risk. J Cardiovasc Risk 2003; 10: 121-128.

[4] Zhang R, Zhao L, Liang L, Xie G and Wu Y. Factors explaining the gender disparity in lipid-lowering treatment goal attainment rate in Chinese patients with statin therapy. Lipids Health Dis 2012; 11: 59.

[5] Randomised trial of cholesterol lowering. Randomised trial of cholesterol lowering in 4444 patients with coronary heart disease: the Scandinavian Simvastatin Survival Study (4S). Lancet 1994; 344: 1383-1389.

[6] Baigent C, Keech A, Kearney PM, Blackwell L, Buck G, Pollicino C, Kirby A, Sourjina T, Peto R, Collins R, Simes R; Cholesterol Treatment

Trialists' (CTT) Collaborators. Efficacy and safety of cholesterol-lowering treatment: prospective meta-analysis of data from 90,056 participants in 14 randomised trials of statins. Lancet 2005; 366: 1267-1278.

[7] Mittendorfer B. Sexual dimorphism in human lipid metabolism. J Nutr 2005; 135: 681-686.

[8] Wang X, Magkos F and Mittendorfer B. Sex differences in lipid and lipoproteinmetabolism: it's not just about sex hormones. J Clin Endocrinol Metab 2011; 96: 885-893.

[9] Ansell BJ, Fonarow GC, Maki KC, Dicklin MR, Bell M, Davidson MH; NEPTUNE II Steering Committee. Reduced treatment success in lipid management among women with coronary heart disease or risk equivalents: results of a national survey. Am Heart J 2006; 152: 976-981.

[10] Santos RD, Waters DD, Tarasenko L, Messig M, Jukema JW, Ferrières J, Verdejo J, Chiang CW; L-TAP 2 Investigators. Low- and high-density lipoprotein cholesterol goal attainment in dyslipidemic women: The Lipid Treatment Assessment Project (L-TAP) 2. Am Heart J 2009; 158: 860-866.

[11] Dallongevillle J, De Bacquer D, Heidrich J, De Backer G, Prugger C, Kotseva K, Montaye M, Amouyel P; EUROASPIRE Study Group. Gender differences in the implementation of cardiovascular prevention measures after an acute coronary event. Heart 2010; 96: 1744-1749.

[12] Pearson TA, Laurora I, Chu H and Kafonek S. The lipid treatment assessment project (L-TAP): a multicenter survey to evaluate the percentages of dyslipidemic patients receiving lipid-lowering therapy and achieving low-density lipoprotein cholesterol goals. Arch Intern Med 2000; 160: 459-467.

[13] Cullen P. Evidence that triglycerides are an independent coronary heart disease risk factor. Am J Cardiol 2000; 86: 943-949.

[14] Meagher EA. Addressing cardiovascular disease in women: focus on dyslipidemia. J Am Board Fam Pract 2004; 17: 424-437.

[15] Teo YY and Sim X. Patterns of linkage disequilibrium in different populations implications and opportunities for lipid-associated loci identified from genome-wide association studies. Curr Opin Lipidol 2010; 21: 104-115.

[16] Teslovich TM, Musunuru K, Smith AV, Edmondson AC, Stylianou IM, Koseki M, Pirruccello JP, Ripatti S, Chasman DI, Willer CJ, Johansen CT, Fouchier SW, Isaacs A, Peloso GM, Barbalic M, Ricketts SL, Bis JC, Aulchenko YS, Thorleifsson G, Feitosa MF, Chambers J, Orho-Melander M, Melander O, Johnson T, Li X, Guo X, Li M, Shin Cho Y, Jin Go M, Jin Kim Y, Lee JY, Park T, Kim K, Sim X, Twee-Hee Ong R, Croteau-Chonka DC, Lange LA, Smith JD, Song K, Hua Zhao J, Yuan X, Luan J, Lamina C, Ziegler A, Zhang W, Zee RY, Wright AF, Witteman JC, Wilson JF, Willemsen G, Wichmann HE, Whitfield JB, Waterworth DM, Wareham NJ, Waeber G, Vollenweider P, Voight BF, Vitart V, Uitterlinden AG, Uda M, Tuomilehto J, Thompson JR, Tanaka T, Surakka I, Stringham HM, Spector TD, Soranzo N, Smit JH, Sinisalo J, Silander K, Sijbrands EJ, Scuteri A, Scott J, Schlessinger D, Sanna S, Salomaa V, Saharinen J, Sabatti C, Ruokonen A, Rudan I, Rose LM, Roberts R, Rieder M, Psaty BM, Pramstaller PP, Pichler I, Perola M, Penninx BW, Pedersen NL, Pattaro C, Parker AN, Pare G, Oostra BA, O'Donnell CJ, Nieminen MS, Nickerson DA, Montgomery GW, Meitinger T, McPherson R, McCarthy MI, McArdle W, Masson D, Martin NG, Marroni F, Mangino M, Magnusson PK, Lucas G, Luben R, Loos RJ, Lokki ML, Lettre G, Langenberg C, Launer LJ, Lakatta EG, Laaksonen R, Kyvik KO, Kronenberg F, König IR, Khaw KT, Kaprio J, Kaplan LM, Johansson A, Jarvelin MR, Janssens AC, Ingelsson E, Igl W, Kees Hovingh G, Hottenga JJ, Hofman A, Hicks AA, Hengstenberg C, Heid IM, Hayward C, Havulinna AS, Hastie ND, Harris TB, Haritunians T, Hall AS, Gyllensten U, Guiducci C, Groop LC, Gonzalez E, Gieger C, Freimer NB, Ferrucci L, Erdmann J, Elliott P, Ejebe KG, Döring A, Dominiczak AF, Demissie S, Deloukas P, de Geus EJ, de Faire U, Crawford G, Collins FS, Chen YD, Caulfield MJ, Campbell H, Burtt NP, Bonnycastle LL, Boomsma DI, Boekholdt SM, Bergman RN, Barroso I, Bandinelli S, Ballantyne CM, Assimes TL, Quertermous T, Altshuler D, Seielstad M, Wong TY, Tai ES, Feranil AB, Kuzawa CW, Adair LS, Taylor HA Jr, Borecki IB, Gabriel SB, Wilson JG, Holm H, Thorsteinsdottir U, Gudnason V, Krauss RM, Mohlke KL, Ordovas JM, Munroe PB, Kooner JS, Tall AR, Hegele RA, Kastelein JJ, Schadt EE, Rotter JI, Boerwinkle E, Strachan DP, Mooser V, Stefansson K, Reilly MP, Samani NJ, Schunkert H, Cupples LA, Sandhu MS, Ridker PM, Rader DJ, van Duijn CM, Peltonen L, Abecasis GR, Boehnke M and Kathiresan S. Biological, clinical and population relevance of 95 loci for blood lipids. Nature 2010; 466: 707-713.

[17] Jeemon P, Pettigrew K, Sainsbury C, Prabhakaran D, Padmanabhan S. Implications of discoveries from genome-wide association studies in current cardiovascular practice. World J Cardiol 2011; 3: 230-247.

[18] Asselbergs FW, Guo Y, van Iperen EP, Sivapalaratnam S, Tragante V, Lanktree MB, Lange LA, Almoguera B, Appelman YE, Barnard J, Baumert J, Beitelshees AL, Bhangale TR, Chen YD, Gaunt TR, Gong Y, Hopewell JC, Johnson T, Kleber ME, Langaee TY, Li M, Li YR,

Liu K, McDonough CW, Meijs MF, Middelberg RP, Musunuru K, Nelson CP, O'Connell JR, Padmanabhan S, Pankow JS, Pankratz N, Rafelt S, Rajagopalan R, Romaine SP, Schork NJ, Shaffer J, Shen H, Smith EN, Tischfield SE, van der Most PJ, van Vliet-Ostaptchouk JV, Verweij N, Volcik KA, Zhang L, Bailey KR, Bailey KM, Bauer F, Boer JM, Braund PS, Burt A, Burton PR, Buxbaum SG, Chen W, Cooper-Dehoff RM, Cupples LA, deJong JS, Delles C, Duggan D, Fornage M, Furlong CE, Glazer N, Gums JG, Hastie C, Holmes MV, Illig T, Kirkland SA, Kivimaki M, Klein R, Klein BE, Kooperberg C, Kottke-Marchant K, Kumari M, LaCroix AZ, Mallela L, Murugesan G, Ordovas J, Ouwehand WH, Post WS, Saxena R, Scharnagl H, Schreiner PJ, Shah T, Shields DC, Shimbo D, Srinivasan SR, Stolk RP, Swerdlow DI, Taylor HA Jr, Topol EJ, Toskala E, van Pelt JL, van Setten J, Yusuf S, Whittaker JC, Zwinderman AH; LifeLines Cohort Study, Anand SS, Balmforth AJ, Berenson GS, Bezzina CR, Boehm BO, Boerwinkle E, Casas JP, Caulfield MJ, Clarke R, Connell JM, Cruickshanks KJ, Davidson KW, Day IN, de Bakker PI, Doevendans PA, Dominiczak AF, Hall AS, Hartman CA, Hengstenberg C, Hillege HL, Hofker MH, Humphries SE, Jarvik GP, Johnson JA, Kaess BM, Kathiresan S, Koenig W, Lawlor DA, März W, Melander O, Mitchell BD, Montgomery GW, Munroe PB, Murray SS, Newhouse SJ, Onland-Moret NC, Poulter N, Psaty B, Redline S, Rich SS, Rotter JI, Schunkert H, Sever P, Shuldiner AR, Silverstein RL, Stanton A, Thorand B, Trip MD, Tsai MY, van der Harst P, van der Schoot E, van der Schouw YT, Verschuren WM, Watkins H, Wilde AA, Wolffenbuttel BH, Whitfield JB, Hovingh GK, Ballantyne CM, Wijmenga C, Reilly MP, Martin NG, Wilson JG, Rader DJ, Samani NJ, Reiner AP, Hegele RA, Kastelein JJ, Hingorani AD, Talmud PJ, Hakonarson H, Elbers CC, Keating BJ and Drenos F. Large-scale gene-centric meta-analysis across 32 studies identifies multiple lipid loci. Am J Hum Genet 2012; 91: 823-838.

[19] Xu L, Deng QY, Li SF, Zhou LN, Gong JC and Wei BY. Genetic analysis of Mulao nationality using 15 short tandem repeats. Zhonghua Yi Xue Yi Chuan Xue Za Zhi 2008; 25: 96-100.

[20] Guo T, Yin RX, Lin QZ, Wu J, Shen SW, Sun JQ, Shi GY, Wu JZ, Li H and Wang YM. Polymorphism of rs873308 near the transmembrane protein 57 gene is associated with serum lipid levels. Biosci Rep 2014; 34: e00095.

[21] Lin QZ, Yin RX, Guo T, Wu J, Sun JQ, Shen SW, Shi GY, Wu JZ, Liu CW and Pan SL. Association of the ST3GAL4 rs11220462 polymorphism and serum lipid levels in the Mulao and Han populations. Lipids Health Dis 2014; 13: 123.

[22] Aung LH, Yin RX, Wu DF, Wang W, Wu JZ and Liu CW. Sex-specific Association of the Zinc Finger Protein 259 rs2075290 Polymorphism and Serum Lipid Levels. Int J Med Sci 2014; 11: 471-478.

[23] Ruixing Y, Qiming F, Dezhai Y, Shuquan L, Weixiong L, Shangling P, Hai W, Yongzhong Y, Feng H and Shuming Q. Comparison of demography, diet, lifestyle, and serum lipid levels between the Guangxi Bai Ku Yao and Han populations. J Lipid Res 2007; 48: 2673-2681.

[24] Ruixing Y, Dezhai Y, Shuquan L, Yuming C, Hanjun Y, Qiming F, Shangling P, Weixiong L, Jing T and Yiyang L. Hyperlipidaemia and its risk factors in the Guangxi Bai Ku Yao and Han populations. Public Health Nutr 2009; 12: 816-824.

[25] Aung LH, Yin RX, Wu JZ, Wu DF, Wang W and Li H. Association between the MLX interacting protein-like, BUD13 homolog and zinc finger protein 259 gene polymorphisms and serum lipid levels. Sci Rep 2014; 4: 5565.

[26] Aung LH, Yin RX, Wu DF, Wang W, Liu CW and Pan SL. Association of the variants in the BUD13-ZNF259 genes and the risk of hyperlipidaemia. J Cell Mol Med 2014; 18: 1417-1428.

[27] Bermudez OI, Velez-Carrasco W, Schaefer EJ and Tucker KL. Dietary and plasma lipid, lipoprotein, and apolipoprotein profiles among elderly Hispanics and non-Hispanics and their association with diabetes. Am J Clin Nutr 2002; 76: 1214-1221.

[28] Garcia-Palmieri MR, Tillotson J, Cordero E, Costas R Jr, Sorlie P, Gordon T, Kannel WB and Colon AA. Nutrient intake and serum lipids in urban and rural Puerto Rican men. Am J Clin Nutr 1977; 30: 2092-2100.

[29] Sola R, Fito M, Estruch R, Salas-Salvadó J, Corella D, de La Torre R, Muñoz MA, López-Sabater Mdel C, Martínez-González MA, Arós F, Ruiz-Gutierrez V, Fiol M, Casals E, Wärnberg J, Buil-Cosiales P, Ros E, Konstantinidou V, Lapetra J, Serra-Majem L and Covas MI. Effect of a traditional Mediterranean diet on apolipoproteins B, A-I, and their ratio a randomized, controlled trial. Atherosclerosis 2011; 218: 174-180.

[30] Valente EA, Sheehy ME, Avila JJ, Gutierres JA, Delmonico MJ and Lofgren IE. The effect of the addition of resistance training to a dietary education intervention on apolipoproteins and diet quality in overweight and obese older adults. Clin Interv Aging 2011; 6: 235-241.

[31] Watts GF, Jackson P, Burke V and Lewis B. Dietary fatty acids and progression of coronary

artery disease in men. Am J Clin Nutr 1996; 64: 202-209.
[32] Grundy SM and Denke MA. Dietary influences on serum lipids and lipoproteins. J Lipid Res 1990; 31: 1149-1172.
[33] Arca M, Vega GL and Grundy SM. Hypercholesterolemia in postmenopausal women. Metabolic defects and response to low-dose lovastatin. JAMA 1994; 271: 453-459.
[34] Karjalainen A, Heikkinen J, Savolainen MJ, Bäckström AC and Kesäniemi YA. Mechanisms regulating LDL metabolism in subjects on peroral and transdermal estrogen replacement therapy. Arterioscler Thromb Vasc Biol 2000; 20: 1101-1106.
[35] Gouva L and Tsatsoulis A. The role of estrogens in cardiovascular disease in the aftermath of clinical trials. Hormones 2004; 3: 171-183.
[36] Weiss TW, Seljeflot IS, Hjerkinn EM and Arnesen H. Adipose tissue pro-inflammatory gene expression is associated with cardiovascular disease. Int J Clin Pract 2011; 65: 939-944.
[37] Von Deneen KM, Wei Q, Tian J and Liu Y. Obesity in China: What are the Causes? Curr Pharm Des 2011; 17: 1132-1139.
[38] Jin L, Huang Y, Bi Y, Zhao L, Xu M, Xu Y, Chen Y, Gu L, Dai M, Wu Y, Hou J, Li X and Ning G. Association between alcohol consumption and metabolic syndrome in 19,215 middle-aged and elderly Chinese. Diabetes Res Clin Pract 2011; 92: 386-392.
[39] Yu-Poth S, Zhao G, Etherton T, Naglak M, Jonnalagadda S and Kris-Etherton PM. Effects of the National Cholesterol Education Program's Step I and Step II dietary intervention programs on cardiovascular disease risk factors: a meta-analysis. Am J Clin Nutr 1999; 69: 632-646.
[40] Rimm EB, Williams P, Fosher K, Criqui M and Stampfer MJ. Moderate alcohol intake and lower risk of coronary heart disease: meta-analysis of effects on lipids and haemostatic factors. BMJ 1999; 319: 1523-1528.
[41] Yin RX, Wu DF, Miao L, Htet Aung LH, Cao XL, Yan TT, Long XJ, Liu WY, Zhang L and Li M. Interactions of several single nucleotide polymorphisms and high body mass index on serum lipid traits. Biofactors 2013; 39: 315-325.
[42] Yin RX, Wu DF, Miao L, Aung LH, Cao XL, Yan TT, Long XJ, Liu WY, Zhang L and Li M. Several genetic polymorphisms interact with overweight/obesity to influence serum lipid levels. Cardiovasc Diabetol 2012; 11: 123.