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Original Article

Association of the SPT2 chromatin protein domain containing 1 gene rs17579600 polymorphism and serum lipid traits

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Abstract: SPT2 chromatin protein domain containing 1 gene (*SPTY2D1*) is a candidate gene for dyslipidemia. The single nucleotide polymorphism (SNP) of rs7934205 near *SPTY2D1* locus was ethnic- and sex-specific associated with serum lipid levels in our previous study. Whether *SPTY2D1* rs17579600 SNP and several environmental factors are associated with serum lipid profiles is unknown. A total of 712 participants of Han and 689 unrelated individuals of Mulao were included. The genotype and allele frequencies of *SPTY2D1* rs17579600 SNP were different between the Han and Mulao populations (TT, 74.3% *vs*. 55.7%; TC, 17.6% *vs*. 31.2%, CC, 8.1% *vs*. 13.1%, $P = 0.028$; T, 83.1% *vs*. 71.3%; C, 16.9% *vs*. 28.7%, $P = 0.044$), and between males and females in the both ethnic groups. The levels of serum apolipoprotein (Apo) A1 in Han, triglyceride (TG) in Mulao, and total cholesterol (TC), low-density lipoprotein cholesterol (LDL-C), ApoA1 and ApoB in Mulao males were difference among the genotypes. The C allele carriers had higher ApoA1 in Han, lower TG in Mulao, and lower TC, LDL-C and ApoB and higher ApoA1 in Mulao males than the C allele non-carriers. Serum lipid parameters were also associated with several environmental factors in both ethnic groups. The differences suggesting there may be a racial/ethnic- and/or sex-specific association between the *SPTY2D1* rs17579600 SNP and serum lipid parameters in some ethnic groups.

Keywords: Lipids, SPT2 chromatin protein domain containing 1 gene, single nucleotide polymorphism, environmental factors

Introduction

Cardiovascular disease (CVD) is the world's leading cause of mortality, morbidity, disability, functional decline, and healthcare costs [1, 2]. The 2011 overall rate of death attributable to CVD was 229.6 per 100 000 Americans. The death rates were 275.7 for males and 192.3 for females. The rates were 271.9 for white males, 352.4 for black males, 188.1 for white females, and 248.6 for black females [3]. To establish risk status measurement of a standard lipid profile, including total cholesterol (TC) [4], triglycerides (TG) [5], LDL (low-density lipoprotein) cholesterol [6], apolipoprotein (Apo) B [7], HDL (high-density lipoproteins) cholesterol [8], ApoA1 [9] and the ratio ApoA1 to ApoB [10] is recommended from an integral component of approaches to cardiovascular risk prediction. This is well illustrated by the widespread popularity of the metabolic syndrome concept [11], a constellation of risk factors that confers an elevated risk of cardiometabolic anomalies and CVD. Decades of research on common CVD risk factors have established that they often differ between men and women [12], are influenced by age [13] and ethnicity [14], and are modulated by behavioral choices [15], including poor diet [16] and a sedentary lifestyle [17], environmental conditions [18], and one's genetic profile [19, 20]. Even though it is well recognized that all these risk factors taken individually are characterized by a significant genetic component, there are uncertainties about the true magnitude of risk factor clustering, as well as on the role of genetic factors in risk factor clustering in individuals.

Using several twin and family study designs, studies have revealed that there is a significant

genetic component to human variability in CVD risk factors when considered individually [21, 22]. These risks above mentioned factors are all characterized by familial resemblance and significant heritability estimates [23, 24]. All these CVD risk factors have been the target of genome-wide association studies (GWAS) aimed at identifying common single nucleotide polymorphisms (SNPs) and at quantifying how much of the phenotypic variance is actually captured by them [25].

Several GWAS have reported the association of many SNPs near the SPT2 chromatin protein domain containing 1 gene (SPTY2D1; previous symbols & names: SPT2, Suppressor of Ty, domain containing 1 (S. cerevisiae), Gene ID: 144108, HGNC ID: 26818, synonyms: DKFZp686I068, FLJ39441, Spt2, locus type: gene with protein product, chromosomal location: 11p15.1) with one or more lipid traits [26-28]. SPT2 is a DNA binding protein with HMG-like domains. Functional domains of the yeast chromatin protein SPT2 can bind four-way junction and crossing DNA structures [29]. It plays a role in chromatin modulations associated with transcription elongation in Saccharomyces cerevisiae [30]. Vertebrate SPT2 is a representative of a new class of nucleolar histone chaperones, which associate with chromatin by their DNA-binding activity and function as nucleosome assembly/disassembly factors in the regulation of rDNA transcription [31]. A previous GWAS on plasma-lipid levels has identified the rs10128711 SNP near the *SPTY2D1* as TC-related loci in European [28]. A sex-stratified analysis of other variant in *SPTY2D1*, rs7934205, in our previous study in Chinese has shown that the association between the *SPTY2D1* rs7934205 SNP and serum lipid levels might have ethnic- and/or sex-specificity [32]. Whether *SPTY2D1* rs17579600 SNP is associated with serum lipid levels or whether it exhibits ethnic and/or sex specific association like the previously reported *SPTY2D1* SNPs remains elusive.

Mulao nationality, as one of the minorities (Han is the largest one), 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 recent molecular anthropological data showed that Mulao has much closer genetic relationship with the other minorities in Guangxi than with the Han nationality [33]. Height, fat mass, and fat distribution differ substantially between men and women, and these differences may, in part, explain the sex-specific susceptibilities to certain diseases such as CAD [34]. 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 [35]. Sexual dimorphism has been demonstrated as the potential of dyslipidemia and CVD risk factors. This study, therefore, was undertaken to detect the association of *SPTY2D1* rs17579600 SNP and several environmental factors with serum lipid levels between males and females in the Mulao and Han populations.

Materials and methods

Subjects

The study populations including 712 unrelated subjects (248 males, 34.83% and 464 females, 65.17%) of Han and 689 unrelated participants (222 males, 33.22% and 467 females, 67.78%) of Mulao were randomly selected from our previous stratified randomized samples [36]. 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 49.02 ± 14.39 years in Han and 48.43 ± 14.58 years in Mulao; 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 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 [37]. 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 [38].

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-turbidimetric immunoassay [39].

Genotyping

Genomic DNA was isolated from peripheral blood leukocytes using the phenol-chloroform method [36-39]. The *SPTY2D1* rs17579600 SNP was genotyped by polymerase chain reaction and restriction fragment length polymorphism (PCR-RFLP). PCR amplification was performed using 5'-CAAAGAAATCTCTATCTCAC-3' as the forward and 5'-ACCAGCCTGGCCAACATGGT-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 7 min of pre-denaturing at 95°C and followed by 50 s of denaturing at 95°C, 45 s of annealing at 60°C and 1 min of elongation at 72°C for 33 cycles. The amplification was completed by a final extension at 72°C for 7 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 '*Mob* 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% agarose 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 [36-39].

Statistical analysis

The statistical analyses were performed with the statistical software package SPSS 17.0 (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 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 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 (TT = 1, TC = 2, CC = 3) or alleles (the C allele non-carrier = 1, the C allele carrier = 2) and several environmental factors with serum lipid levels in males and females of Han and Mulao 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 Han and Mulao

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

Parameter	Han	Mulao	*T* (x^2)	P
Number	712	689		
Male/female	248/464	222/467	1.071	0.301
Age (years)	49.02±14.39	48.43±14.58	0.762	0.446
Height (cm)	154.65±7.48	154.03±7.86	1.522	0.128
Weight (kg)	53.09±8.74	51.30±8.68	3.843	0.000
Body mass index (kg/m^2)	22.38±3.41	21.41±3.08	5.566	0.000
waist circumference (cm)	74.78±7.85	73.32±7.88	3.479	0.001
Cigarette smoking (n%)				
Nonsmoker	547 (76.8)	558 (81.0)		
< 20 cigarettes/day	137 (19.2)	113 (16.4)	4.211	0.122
≥ 20 cigarettes/day	28 (3.9)	18 (2.6)		
Alcohol consumption [n (%)]				
Nondrinker	577 (81.0)	577 (83.7)		
< 25 g/day	64 (9.0)	38 (5.5)	6.314	0.043
≥ 25 g/day	71 (10.0)	74 (10.7)		
Systolic blood pressure (mmHg)	127.03±18.35	116.86±11.79	12.380	0.000
Diastolic blood pressure (mmHg)	81.25±10.81	75.48±7.31	11.738	0.000
Pulse pressure (mmHg)	45.78±13.59	41.38±10.02	6.908	0.000
Blood glucose (mmol/L)	5.98±1.55	5.43±0.78	8.099	0.000
Total cholesterol (mmol/L)	4.96±1.09	4.95±1.27	0.045	0.964
Triglyceride (mmol/L)	1.02 (0.75)	1.01 (0.76)	-1.852	0.064
HDL-C (mmol/L)	1.75±0.59	1.78±0.45	-1.075	0.283
LDL-C (mmol/L)	2.90±0.89	2.85±0.85	1.230	0.219
Apolipoprotein (Apo) A1 (g/L)	1.34±0.26	1.34±0.38	-0.080	0.937
ApoB (g/L)	0.95±0.53	0.85±0.20	4.409	0.000
ApoA1/ApoB	1.66±0.48	1.67±0.77	-0.126	0.900

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.

populations is summarized in **Table 1**. The levels of body weight, BMI, waist circumference, systolic blood pressure, diastolic blood pressure, pulse pressure, blood glucose and the levels of ApoB were lower in Mulao than in Han (P < 0.05-0.001), whereas the percentage of excessive alcohol consumption were 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, serum TC, TG, HDL-C, LDL-C and ApoA1 levels and the ApoA1/ApoB ratio between the two ethnic groups (P > 0.05 for all).

Results of genotyping

After the genomic DNA of the samples was amplified by PCR, the purpose gene of 496-bp nucleotide sequences could be seen in all samples (**Figure 1**). 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 (496-bp), TC genotype is heterozygote for the presence and absence of the site (496-, 288- and 208-bp) and CC genotype is homozygote for the presence of the site (288- and 208-bp; **Figure 2**). The TT, CT and CC genotypes detected by PCR-RFLP were also confirmed by direct sequencing (**Figure 3**), respectively.

Genotypic and allelic frequencies

As shown in **Table 2**, the genotype and allele frequencies of *SPTY2D1* rs17579600 SNP were different between the Han and Mulao populations (TT, 74.3% *vs.* 55.7%; TC, 17.6% *vs.*

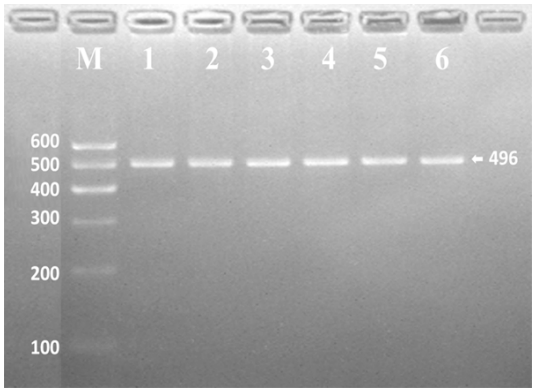

Figure 1. Electrophoresis of PCR products of the samples. Lane M is the 100 bp Marker ladder; lines 1-6 are samples, the 496 bp bands are the target genes.

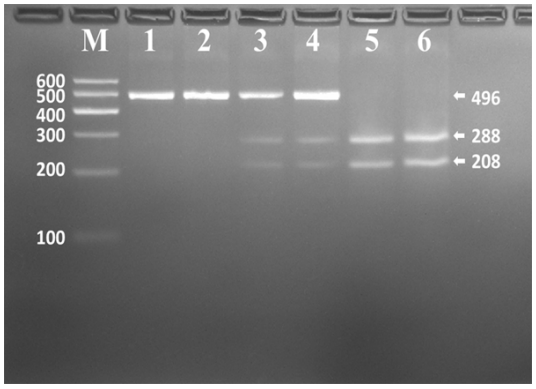

Figure 2. Genotyping of the *SPTY2D1* rs17579600 SNP. Lane M is the 100 bp Marker Ladder; lanes 1 and 2, TT genotype (496-bp); lanes 3 and 4, TC genotype (496-, 288- and 208-bp); and lanes 5 and 6, CC genotype (288- and 208-bp).

31.2%, CC, 8.1% *vs.* 13.1%, $P = 0.028$; T, 83.1% *vs.* 71.3%; C, 16.9% *vs.* 28.7%, P = 0.044). The genotype frequencies of rs17579600 SNP agreed with the Hardy-Weinberg equilibrium in both populations ($P > 0.05$ for each). Gender-subgroup analysis showed that the genotype and allele frequencies of *SPTY2D1* rs17579600 SNP between males and females were different in Han and Mulao. The genotype and allele frequencies were different between Han males and females (TT, 66.1% *vs.* 78.7%; TC, 27.8% *vs.* 12.1%, CC, 6.0% *vs.* 9.3%, $P = 0.017$; T, 80.0% *vs.* 84.7%; C, 20.0% *vs.* 15.3%, $P = 0.026$). The genotype and allele frequencies were significantly different between Mulao males and females (TT, 45.9% *vs.* 60.4%; TC, 31.5% *vs.* 31.0%, CC, 22.5% *vs.* 8.6%, $P = 0.018$; T, 61.7% *vs.* 75.9%; T, 38.3% *vs.* 24.1%, P = 0.032).

Genotypes and serum lipid levels

Tables 3 and **4** describe the association between genotypes and serum lipid levels. Serum ApoA1 levels in Han were different among the genotypes ($P < 0.05$), and the C allele carriers had higher ApoA1 levels than the C allele non-carriers. Serum TG levels in Mulao were different among the genotypes ($P < 0.05$), and the C allele carriers had lower TG levels than the C allele non-carriers. Subgroup analyses showed that serum levels of TC, LDL-C, ApoA1 and ApoB in Mulao males were different among the genotypes ($P < 0.05$ for all); the C allele carriers had higher serum ApoA1 level and lower serum TC, LDL-C and ApoB levels than the C allele non-carriers. In a word, he subjects with the minor C allele have more favorable lipid profiles than those with the C allele non-carriers.

Relative factors for serum lipid parameters

Several environmental factors such as age, gender, height, weight, waist circumference, alcohol consumption and cigarette smoking, and traditional cardiovascular risk factors such as BMI, fasting blood glucose and blood pressure levels were also correlated with serum lipid parameters in the Han and Mulao populations and in males and females of both ethnic groups ($P < 0.05$-0.001, **Tables 5** and **6**).

Discussion

In the current study, we showed that serum lipid profiles were significantly different between Han and Mulao ethnic groups. A significant difference in the genotype and allele frequencies of *SPTY2D1* rs17579600 SNP was also noted between the two ethnic populations. The minor C allele frequencies in Han and Mulao were 16.9% and 28.7% respectively, which were in close proximity to those of Chinese Han Beijing (14.0%) reported in international haplotype map (HapMap) project. According to HapMap data, the minor allele frequency of rs17579600 was 15.1% in Japanese, and 8.8% in Europeans. Apparently, the minor allele frequency was higher in Asian than the Western populations. These findings suggest that genotype and allele frequencies of

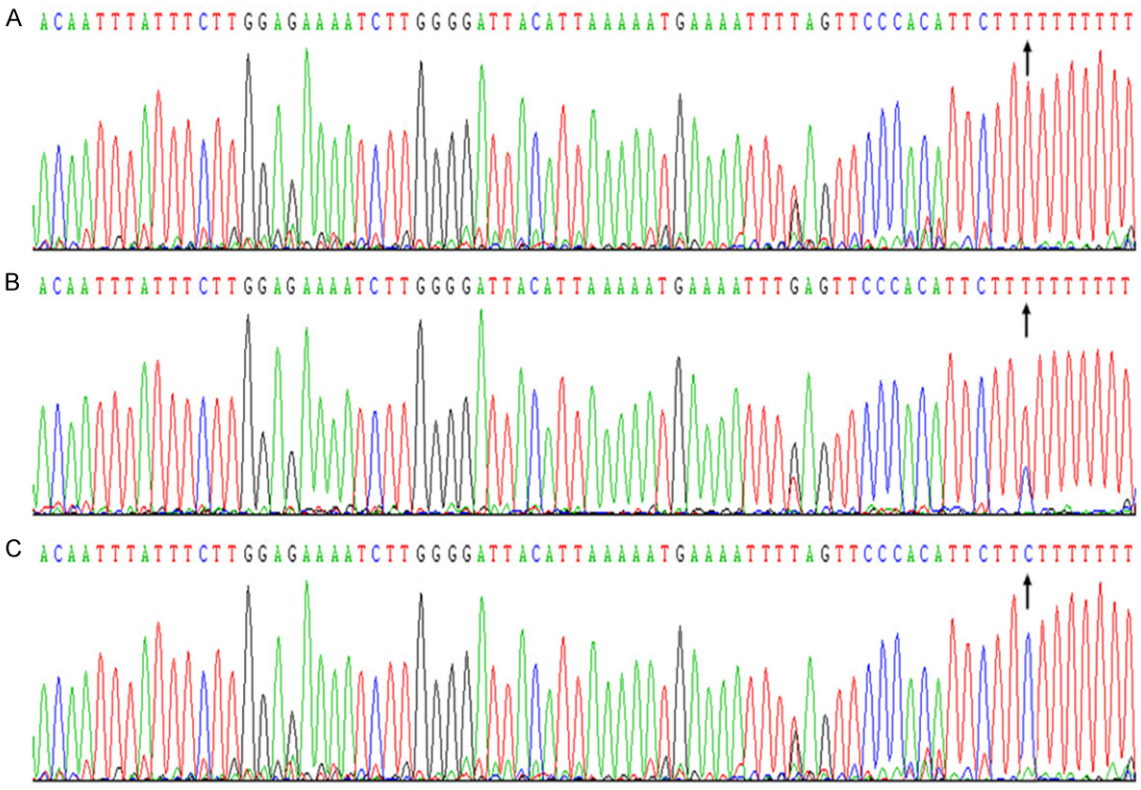

Figure 3. A part of the nucleotide forward sequence of the *SPTY2D1* rs17579600 SNP. A: TT genotype; B: TC genotype; C: CC genotype.

Table 2. Comparison of the genotype and allele frequencies of the *SPTY2D1* rs17579600 SNP between males and females of the Han and Mulao populations

Group	n	Genotype			Allele	
		TT	TC	CC	T	C
Han	712	529 (74.3)	125 (17.6)	58 (8.1)	1183 (83.1)	241 (16.9)
Mulao	689	384 (55.7)	215 (31.2)	90 (13.1)	983 (71.3)	395 (28.7)
x^2	-		7.132		4.065	
P	-		0.028		0.044	
Han						
Male	248	164 (66.1)	69 (27.8)	15 (6.0)	397 (80.0)	99 (20.0)
Female	464	365 (78.7)	56 (12.1)	43 (9.3)	786 (84.7)	142 (15.3)
x^2	-		8.166		4.988	
P	-		0.017		0.026	
Mulao						
Male	222	102 (45.9)	70 (31.5)	50 (22.5)	274 (61.7)	170 (38.3)
Female	467	282 (60.4)	145 (31.0)	40 (8.6)	709 (75.9)	225 (24.1)
x^2	-		7.985		4.582	
P	-		0.018		0.032	

SPTY2D1 rs17579600 SNP are inconsistent among diverse ethnic groups.

A recent GWAS reported that *SPTY2D1* rs10128711 SNP was the top association SNP with MetS in European ancestry [27, 28]. The minor allele was significantly associated with TC. Another our previous study shown that the *SPTY2D1* rs7934205 SNP minor allele was significantly associated with pleiotropic (one SNP influence many serum lipid traits) effects on serum lipid profiles. In the present study, the *SPTY2D1* rs17579600 SNP was correlated serum ApoA1 levels in Han and TG in Mulao. However, no association with TC was detected either in Han or Mulao population. The reason for this discrepancy is not fully understood. It might be due to the differences in genetic backgrounds, dietary habits, and environmental factors

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

Ethnic/ Genotype	N	TC (mmol/L)	TG (mmol/L)	HDL-C (mmol/L)	LDL-C (mmol/L)	ApoA1 (g/L)	ApoB (g/L)	ApoA1/ ApoB
Han								
TT	529	4.98±1.13	1.02 (0.74)	1.73±0.64	2.86±0.89	1.32±0.29	0.86±0.21	1.64±0.40
TC/CC	183	4.90±0.97	1.02 (0.75)	1.76±0.57	2.81±0.75	1.35±0.25	0.83±0.17	1.67±0.51
F		0.690	0.091	0.960	0.779	4.347	3.229	1.900
P		0.502	0.763	0.328	0.378	0.037	0.073	0.169
Mulao								
TT	384	4.98±1.38	1.14 (0.80)	1.78±0.47	2.94±0.93	1.34±0.41	0.96±0.55	1.65±0.74
TC/CC	305	4.92±1.13	1.07 (0.76)	1.79±0.41	2.88±0.86	1.35±0.35	0.93±0.50	1.68±0.80
F		2.292	4.172	0.041	0.017	0.000	0.671	1.278
P		0.131	0.041	0.839	0.896	0.996	0.413	0.259

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 4. Comparison between the *SPTY2D1* rs17579600 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
Han/Male								
TT	102	5.04±1.93	1.02 (0.76)	1.70±0.63	2.94±0.74	1.31±0.47	0.98±0.62	1.58±0.77
TC/CC	120	5.00±0.90	0.97 (0.74)	1.78±0.40	2.79±0.90	1.37±0.33	0.96±0.48	1.62±0.63
F		0.322	1.754	2.330	1.618	0.124	0.055	0.099
P		0.571	0.187	0.128	0.205	0.725	0.814	0.754
Han/Female								
TT	282	4.96±1.12	1.02 (0.78)	1.79±0.42	2.93±1.03	1.34±0.36	0.95±0.52	1.68±0.73
TC/CC	185	4.86±1.25	1.01 (0.73)	1.81±0.40	2.91±0.85	1.35±0.39	0.91±0.52	1.73±0.89
F		0.372	2.552	0.312	0.245	0.065	0.243	0.294
P		0.542	0.111	0.576	0.621	0.799	0.622	0.588
Mulao/Male								
TT	164	5.40±1.17	1.31 (0.93)	1.65±0.42	3.02±0.88	1.33±0.30	0.96±0.22	1.54±0.52
TC/CC	84	4.88±0.91	1.10 (0.83)	1.70±0.47	2.74±0.79	1.40±0.30	0.85±0.16	1.60±0.40
F		9.637	0.615	3.417	8.600	4.881	6.341	0.027
P		0.002	0.434	0.066	0.004	0.028	0.012	0.870
Mulao/Female								
TT	365	4.92±1.02	0.96 (0.69)	1.79±0.61	2.87±0.71	1.32±0.28	0.81±0.19	1.67±0.39
TC/CC	99	4.79±1.06	0.97 (0.75)	1.80±0.78	2.79±0.88	1.33±0.22	0.81±0.18	1.73±0.49
F		0.116	0.691	0.614	0.237	2.375	0.331	1.889
P		0.733	0.406	0.434	0.627	0.124	0.565	0.170

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 the difference between the TT and TC/CC genotypes was determined by the Wilcoxon-Mann-Whitney test.

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 [40]. Diet alone could account for up to 2.5% of the variability on

Table 5. The risk factors for serum lipid parameters in the Han and Mulao populations

Lipid parameter	Risk factor	*B*	*Std. error*	*Beta*	*t*	P
Han and Mulao						
TC	Ethnic group	0.137	0.067	0.058	2.037	0.042
	Age	0.011	0.002	-.136	4.554	0.000
	Alcohol consumption	0.219	0.060	0.118	3.665	0.000
	Waist circumference	0.027	0.006	0.180	4.199	0.000
	Diastolic blood pressure	0.008	0.003	0.065	2.293	0.022
TG	Alcohol consumption	0.301	0.100	0.097	3.021	0.003
	Waist circumference	0.071	0.011	0.281	6.605	0.000
	Waist circumference	0.070	0.009	0.297	7.779	0.000
	Diastolic blood pressure	0.013	0.006	0.064	2.300	0.022
	Glucose	0.091	0.043	0.058	2.121	0.034
HDL-C	Gender	0.150	0.047	0.135	3.171	0.002
	Age	0.004	0.001	0.108	3.589	0.000
	Alcohol consumption	0.124	0.027	0.151	4.652	0.000
	Height	0.018	0.009	0.257	2.044	0.041
	Weight	-0.028	0.012	-0.461	-2.377	0.018
	Waist circumference	-0.007	0.003	-0.103	-2.378	0.018
LDL-C	Ethnic group	0.132	0.050	0.075	2.646	0.008
	Gender	-0.210	0.078	-0.114	-2.686	0.007
	Age	0.009	0.002	0.145	4.852	0.000
	Cigarette smoking	-0.141	0.061	-0.081	-2.314	0.021
	Waist circumference	0.018	0.005	0.159	3.695	0.000
ApoA1	Gender	0.112	0.029	0.162	3.821	0.000
	Age	0.002	0.001	0.106	3.527	0.000
	Alcohol consumption	0.142	0.017	0.279	8.557	0.000
ApoB	Ethnic group	0.152	0.023	0.190	6.718	0.000
	Waist circumference	0.010	0.002	0.202	4.727	0.000
	Pulse pressure	0.002	0.001	0.075	2.727	0.006
	Glucose	0.021	0.009	0.065	2.373	0.018
ApoA1/ApoB	Gender	0.213	0.057	0.158	3.771	0.000
	Alcohol consumption	0.127	0.032	0.128	3.980	0.000
	Waist circumference	-0.015	0.003	-0.182	-4.267	0.000
	Pulse pressure	-0.003	0.001	-0.061	-2.211	0.027
Han						
TC	Gender	-0.394	0.131	-0.173	-3.018	0.003
	Age	0.010	0.003	0.127	2.978	0.003
	Alcohol consumption	0.294	0.076	0.172	3.887	0.000
	Waist circumference	0.041	0.009	0.295	4.708	0.000
	Diastolic blood pressure	0.013	0.004	0.134	3.583	0.000
TG	Age	-0.015	0.007	-0.098	-2.278	0.023
	Cigarette smoking	0.762	0.201	0.182	3.793	0.000
	Weight	0.092	0.040	0.916	2.303	0.022
	Waist circumference	0.102	0.018	0.365	5.758	0.000
	Diastolic blood pressure	0.023	0.008	0.113	2.997	0.003
	Glucose	0.177	0.053	0.125	3.326	0.001
HDL-C	Gender	0.164	0.075	0.132	2.177	0.030
	Age	0.005	0.002	0.125	2.745	0.006

	Alcohol consumption	0.131	0.044	0.141	3.011	0.003
LDL-C	Gender	-0.400	0.106	-0.223	-3.789	0.000
	Age	0.011	0.003	0.180	4.095	0.000
	Cigarette smoking	-0.342	0.079	-0.211	-4.310	0.000
	Waist circumference	0.027	0.007	0.251	3.890	0.000
ApoA1	Genotype	-0.044	0.021	-0.073	-2.085	0.037
	Age	0.002	0.001	0.085	1.988	0.047
	Cigarette smoking	0.063	0.023	0.128	2.713	0.007
	Alcohol consumption	0.146	0.018	0.359	8.138	0.000
	Weight	-0.021	0.007	-0.699	-3.039	0.002
ApoB	Gender	-0.087	0.023	-0.203	-3.802	0.000
	Age	0.001	0.001	0.084	2.107	0.035
	Alcohol consumption	0.036	0.013	0.111	2.689	0.007
	Waist circumference	0.009	0.002	0.357	6.094	0.000
	Diastolic blood pressure	0.002	0.001	0.099	2.823	0.005
	Glucose	0.015	0.005	0.111	3.196	0.001
ApoA1/ApoB	Gender	0.241	0.056	0.238	4.301	0.000
	Cigarette smoking	0.134	0.042	0.147	3.189	0.001
	Alcohol consumption	0.113	0.032	0.149	3.491	0.001
	Waist circumference	-0.014	0.004	-0.220	-3.625	0.000
Mulao						
TC	Age	0.014	0.004	0.163	3.879	0.000
	Height	-0.112	0.047	-0.655	-2.376	0.018
	Weight	0.174	0.071	1.186	2.455	0.014
	Body mass index	-0.383	0.168	-0.927	-2.278	0.023
TG	Genotype	-0.272	0.133	-0.078	-2.042	0.041
	Cigarette smoking	-0.363	0.182	-0.099	-1.996	0.046
	Alcohol consumption	0.378	0.123	0.140	3.065	0.002
	Height	-0.158	0.063	-0.679	-2.499	0.013
	Weight	0.252	0.095	1.260	2.643	0.008
	Body mass index	-0.582	0.226	-1.032	-2.571	0.010
	Waist circumference	0.040	0.013	0.182	3.182	0.002
	Glucose	-0.172	0.083	-0.077	-2.077	0.038
HDL-C	Gender	0.128	0.058	0.135	2.223	0.027
	Age	0.003	0.001	0.100	2.412	0.016
	Alcohol consumption	0.116	0.032	0.167	3.671	0.000
	Waist circumference	-0.007	0.003	-0.128	-2.245	0.025
LDL-C	Age	0.008	0.003	0.131	3.122	0.002
ApoA1	Gender	0.156	0.051	0.190	3.056	0.002
	Age	0.003	0.001	0.117	2.762	0.006
	Alcohol consumption	0.136	0.028	0.228	4.899	0.000
ApoB	Waist circumference	0.011	0.004	0.166	2.866	0.004
	Pulse pressure	0.005	0.002	0.104	2.750	0.006
ApoA1/ApoB	Alcohol consumption	0.140	0.055	0.117	2.537	0.011
	Waist circumference	-0.015	0.006	-0.159	-2.748	0.006
	Pulse pressure	-0.006	0.003	-0.079	-2.099	0.036

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.

Table 6. The risk factors for serum lipid parameters in the males and females of the Han and Mulao populations

Lipid parameter	Risk factor	*B*	*Std. error*	*Beta*	*t*	P
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

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

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.

serum lipid levels [41-45]. 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 Han and

Mulao ethnic groups partly contribute variability in the effect of *SPTY2D1* rs17579600 SNP on serum lipid levels.

It has been well-known that the males had higher serum levels of bad cholesterols and lower levels of good cholesterols than the females, especially in women before menopause [46]. On gender subgroup analysis, the genotype frequencies between males and females were different both in Han and Mulao. The minor allele frequency was higher in males than females. Here, we found that the minor C allele of *SPTY2D1* rs17579600 SNP had higher serum ApoA1 level and lower serum TC, LDL-C and ApoB levels than the C allele non-carriers just in Mulao males. In other words, the subjects with the minor C allele have more favorable lipid profiles than those with the C allele non-carriers but the minor C allele frequency was higher in males than females. The reason for this discrepancy mainly attributed to the role of gonadal steroid hormones, estrogen especially [47-49]. To the best of our knowledge, this study is the first attempt to report the gender specific association of *SPTY2D1* rs17579600 SNP. Therefore, further studies with larger sample size are still needed to confirm this association.

Several environmental factors were also correlated with serum lipid levels in males and females of both Han and Mulao populations. In the present study, The Han has significantly higher levels of body weight, BMI, waist circumference, systolic blood pressure, diastolic blood pressure, pulse pressure, blood glucose and the levels of ApoB and lower the percentage of excessive alcohol consumption compared to the Han counterparts. Garcia-Palmieri et al. stated that diet and relative weight could account for up to 6% of the variability in serum cholesterol levels [41]. 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 [50]. Rimm et al. 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 [51]. Yin et al. also showed that BMI 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 [52, 53]. 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.

This study has some limitations. The sample size was relatively small compared to many GWAS and replication studies. Hence, further studies with larger sample sizes are needed to confirm our results. Secondly, we were not able to alleviate the effect of diet and several environmental factors during the statistical analysis. Thirdly, although we have detected the effects of *SPTY2D1* rs17579600 SNP on serum lipid levels in this study, there are still many lipid-related SNPs and the interactions of SNP-SNP and/or SNP-environmental factors. What's more, the relevance of this finding has to be defined in further high caliber of studies including incorporating the genetic information of *SPTY2D1* rs17579600 SNP and in vitro functional studies to confirm the impact of a variant on a molecular level.

Conclusion

In conclusion, the minor C allele frequency of the *SPTY2D1* rs17579600 SNP is higher in Mulao than in Han but lower in females than in males. The minor C allele carriers in both ethnic groups and gender subgroups have more favorable serum lipid profiles than the C allele non-carriers. These findings suggest that the association between the *SPTY2D1* rs17579600 SNP and serum lipid levels might have ethnic- and/or sex-specificity.

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Disclosure of conflict of interest

None.

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