Original Article Association of the BTNL2 rs9268480 SNP and several environmental factors with serum lipid profiles in the Jing and Han populations

Tao Guo, Rui-Xing Yin, Xia Chen, Ling Pan, Yuan Bin, Wu-Xian Chen

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

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Abstract: Hyperlipidemia-related mechanisms have been associated with damage to the cardiovascular disease (CVD). Here, we discuss potential explanations for the higher prevalence of hyperlipidemia in the Jing and Han populations. Although genetic and environmental factors are the triggers, the search for the ethnic and gender related factors that explain the increased susceptibility of hyperlipidemia is a promising area for research. Ethnicity and gender differences could be the major confounding variable to prove genetic associations. Despite that, we investigated the ethnic and sex-specific association between the butyrophilin-like 2 gene (BTNL2) rs9268480 single nucleotide polymorphism (SNP) and several environmental factors with serum lipid profiles in the Jing and Han populations. Genotypes of the rs9268480 SNP, clinical and biochemical measurements were characterized in a total of 2503 subjects (1148 Jing and 1355 Han). Jing populations had higher serum total cholesterol (TC), triglyceride (TG) and low-density lipoprotein cholesterol (LDL-C) levels and lower apolipoprotein (Apo) A1 levels and the ratio of ApoA1 to ApoB than in Han. The frequency of susceptibility alleles of rs9268480 C > T were significantly different between the two populations (20.86% vs. 18.16%; P = 0.016), and between males and females in Jing (17.18% vs. 24.65%; P < 0.001) and Han (16.57% vs. 19.88%; P = 0.026) populations. The minor T allele carriers of BTNL2 rs9268480 SNP was a risk allele for dyslipidemia, especially higher serum TG levels in ethnic and sexually dimorphic subgroup. These results suggested that the genetic variant of rs9268480 C > T and several environmental factors were associated with hyperlipidemia, and there may be a ethnic- and/or sex-specific association of this SNP.

Keywords: Ethnic and sexual dimorphic association, butyrophilin-like 2 gene (*BTNL2*), single nucleotide polymorphism, lipids, environmental factors

Introduction

Serum lipid and lipoprotein levels [1-3] have proven among the most potent and best substantiated risk for atherosclerosis [4] in cardiovascular diseases (CVD) in particular [5, 6], which leading causes of morbidity and mortality worldwide [7-9]. Several large statin trials and meta-analyses have demonstrated a reduction in low-density lipoprotein cholesterol (LDL-C) and cardiovascular morbidity and mortality [10-15]. Some same statin-trials have also highlighted the significance of residual cardiovascular risk after treatment of LDL-C to target levels. This reflects the complex nature of residual cardiovascular risk. This residual risk is partially due to high triglyceride (TG) despite achievement of LDL-C goals with statin therapy. In subjects with the metabolic syndrome, elevation of plasma TG levels occurs most often in the presence of several environmental factors such as visceral (abdominal) obesity and a diet rich in calories, carbohydrates, and saturated fats [16-18]. Severe elevation of plasma TG levels can result from heritability [19-21]. Although both environmental and genetic factors are the triggers, the search for the ethnic and gender related factors that explain the increased susceptibility of hyperlipidemia is a promising area for research [22-24]. Ethnicity and gender differences could be a major confounding variable to prove genetic associations.

Butyrophilin-like 2 gene (*BTNL2*; Gene ID: 562-44; MIM: 606000; Cytogenetic location: 6p21.-

32; Genomic coordinates (GRCh38):6:32, 393, 338-32, 408, 878), a member of the immunoglobulin gene superfamily with homology to butyrophilin genes (e.g., BTN1A1; 601610) [25]. The BTNL2 protein contains a small hydrophobic sequence that may be a signal peptide, 2 immunoglobulin domains, a 7-amino acid heptad repeat, and 2 more immunoglobulin domains. Unlike other butyrophilins, BTNL2 lacks a C-terminal B30-2 domain. RT-PCR analysis detected BTNL2 expression in mouse skeletal muscle, duodenum, ileum, cecum, ascending colon, descending colon, and appendix. Nguyen et al. found that a putative receptor for mouse BTNL2, distinct from Cd28 (186760) and Ctla4 (123890), was expressed on activated B and T cells. BTNL2 appeared to regulate T-cell activation, a finding with implications for the role of BTNL2 in inflammatory autoimmune diseases [26]. Valentonyte et al. identified a G-to-A transition at position-1 of a splice donor site (rs2076530) in the BTNL2 gene. The change resulted in the use of an alternative splice site located 4 bp upstream. The loss of 4 bases from the cDNA transcribed from the A allele resulted in a frameshift and a premature stop in the downstream exon. In the corresponding protein product, the 118 C-terminal residues in the nontruncated protein were replaced by 5 different amino acids. The mutant protein lacks the C-terminal IgC domain and transmembrane helix, thereby disrupting localization of the protein [27]. However, the effect of this rs9268480 SNP on lipid profiles was not functionally validated and the mechanism was yet unclear. Furthermore, the reproducibility of this association has not been detected in the Jing and Han populations so far.

China has a majority population of Han ethnicity and 55 officially recognized ethnic minorities [28]. The Jing ethnic group is an isolated minority in the Guangxi Zhuang Autonomous Region, China. The Jing population is the only oceanic ethnic group in China, with a very small population size of 28,199 reported in 2010 [29]. In the early 16th century, the Jing ancestors emigrated from Vietnam to China to first settle on the three islands of Wanwei, Wutou and Shanxin in Dongxing City, where almost all of the Jing population now live [29]. The recent molecular anthropological data showed that Jing has much closer genetic relationship with the other minorities in Guangxi than with the Han nationality [30]. In addition, several previous studies have revealed that the associations of variants in several lipid-related genes and lipid profiles are significantly different between the Jing and Han populations and their gender subgroups [31, 32]. Despite that, we investigated the ethnic and sex-specific association between *BTNL2* rs9268480 mutant and several environmental factors with serum lipid profiles in the Jing and Han populations.

Materials and methods

Ethical approval

The study design was approved by the Ethics Committee of the First Affiliated Hospital, Guangxi Medical University. Informed consent was taken from all participants.

Subjects

A total of 2503 subjects including 1148 unrelated subjects of Jing nationality comprising 582 males and 566 females and 1355 unrelated participants of Han nationality including 706 men and 649 women were randomly selected from our previous stratified randomized samples. All of them were rural agricultural and/or fishery workers residing in three islands of Wanwei, Wutou and Shanxin, Dongxing City, Guangxi Zhuang Autonomous Region, People's Republic of China. The age ranged from 15 to 80 years. The mean age of Jing participants was 57.28±13.52 years, whereas that of Han subjects was 56.92±12.95 years. All participants were essentially healthy and had no evidence of diseases related to atherosclerosis, CVD and diabetes. Any participant had a history of taking medications known to affect lipid profiles (lipid-lowering drugs such as statins or fibrates, beta blockers, diuretics, or hormones) was excluded before the blood sample was taken.

Epidemiological survey

The survey was carried out using internationally standardized methods, following a common protocol [33, 34]. Information on demographics, socioeconomic status, and lifestyle factors was collected with standardized questionnaires. The intake of alcohol was quantified as the number of liang (about 50 g) of rice wine,

| | 0 | • | | |
|-------------------------------|--------------|--------------|---------------------|-------|
| Parameter | Jing | Han | $t(x^2)$ | D |
| | (n = 1148) | (n = 1355) | L (X ⁻) | P |
| Male/Female | 582/566 | 706/649 | 0.492 | 0.483 |
| Age (year) | 57.28±13.52 | 56.92±12.95 | 0.680 | 0.497 |
| Height (cm) | 158.17±7.96 | 157.97±7.98 | 0.621 | 0.535 |
| Weight (kg) | 58.76±10.15 | 57.06±9.41 | 4.340 | 0.000 |
| Body mass index (kg/m²) | 23.42±3.20 | 22.83±3.16 | 4.611 | 0.000 |
| Waist circumference (cm) | 80.42±9.30 | 77.93±8.72 | 6.853 | 0.000 |
| Cigarette smoking [n (%)] | | | | |
| Non-smoker | 933 (81.3) | 1028 (75.9) | | |
| < 20 cigarettes/day | 55 (4.8) | 67 (4.9) | | |
| ≥ 20 cigarettes/day | 160 (13.9) | 260 (19.2) | 12.559 | 0.002 |
| Alcohol consumption [n (%)] | | | | |
| Non-drinker | 884 (77.0) | 911 (67.2) | | |
| < 25 g/day | 138 (12.0) | 98 (7.2) | | |
| ≥ 25 g/day | 126 (11.0) | 346 (25.5) | 93.247 | 0.000 |
| Systolic BP (mmHg) | 131.62±21.46 | 134.68±57.62 | -1.701 | 0.089 |
| Diastolic BP (mmHg) | 80.53±10.56 | 81.39±10.45 | -2.036 | 0.042 |
| Pulse pressure (mmHg) | 51.09±17.20 | 53.29±16.11 | -1.279 | 0.201 |
| Glucose (mmol/L) | 6.70±1.75 | 6.63±1.10 | 1.262 | 0.207 |
| Total cholesterol (mmol/L) | 5.15±0.91 | 4.89±0.86 | 7.391 | 0.000 |
| Triglyceride (mmol/L) | 1.43 (1.13) | 1.31 (1.07) | -4.673 | 0.000 |
| HDL-cholesterol (mmol/L) | 1.78±0.53 | 1.80±0.45 | -0.947 | 0.344 |
| LDL-cholesterol (mmol/L) | 2.86±0.43 | 2.82±0.43 | 2.168 | 0.030 |
| Apolipoprotein (Apo) A1 (g/L) | 1.31±0.24 | 1.33±0.20 | -3.024 | 0.003 |
| ApoB (g/L) | 1.06±0.25 | 1.04±0.24 | 1.737 | 0.083 |
| ApoA1/ApoB | 1.30±0.39 | 1.35±0.38 | -3.000 | 0.003 |

Table 1. Demographic, clinical and anthropometric parameters and

 lipid profiles between the Jing and Han populations

BP, blood pressure; HDL, high-density lipoprotein; LDL, low-density lipoprotein.

corn wine, rum, beer, or liquor consumed during the preceding 12 months. Alcohol consumption was categorized into groups of grams of alcohol per day: < 25 and \geq 25. Smoking status was categorized into groups of cigarettes per day: < 20 and \geq 20. In the physical examination, several parameters such as height, weight, and waist circumference were measured. Sitting blood pressure was measured three times with the use of a mercury sphygmomanometer after a 5-minute rest, and the average of the three measurements was recorded. Systolic blood pressure was determined by the first Korotkoff sound, and diastolic blood pressure by the fifth Korotkoff sound. Body weight, to the nearest 50 grams, was measured using a portable balance scale. Subjects were weighed in a minimum of clothing with shoes off. Height was measured, to the nearest 0.5 cm, using a stadiometer. From these two measurements body mass index (BMI, kg/m²) was calculated.

Biochemical measurements

A venous blood sample of 5 mL was obtained from all subjects after at least 12 hours of fasting. A two fifth of the sample (2 mL) was collected into glass tubes and used to determine lipid profiles. The remaining three fifth of the sample (3 mL) was transferred to the tubes contained anticoagulants (4.80 g/L citric acid, 14.70 g/L glucose, and 13.20 g/L tri-sodium citrate) and was used to extract deoxyribonucleic acid (DNA). Measurements of serum total cholesterol (TC), TG, high-density lipoproteincholesterol (HDL-C), and LDL-C levels in the samples were performed by enzymatic methods with commercially available kits (RANDOX Laboratories Ltd., Ardmore, Diamond Road, Crumlin Co. Antrim, United Kingdom, BT29 4QY; Daiichi Pure Chemi-

cals Co., Ltd., Tokyo, Japan). Serum apolipoprotein (Apo) A1 and ApoB levels were detected by the immunoturbidimetric immunoassay using a commercial kit (RANDOX Laboratories Ltd.). All determinations were performed with an autoanalyzer (Type 7170A; Hitachi Ltd., Tokyo, Japan) in the Clinical Science Experiment Center of the First Affiliated Hospital, Guangxi Medical University [34, 35].

DNA amplification and genotyping

Genomic DNA was isolated from peripheral blood leukocytes using the phenol-chloroform method [37, 38]. The extracted DNA was stored at 4°C until analysis. Genotyping of the *BTNL2* rs9268480 SNP was performed by polymerase chain reaction and restriction fragment length polymorphism (PCR-RFLP). PCR amplification was performed using 5'-GTGGCAGGAGCAGG-TATT-3' and 5'-TCGTCAGAGTGGGAGAAG-3' (Sangon, Shanghai, People's Republic of China) as



Figure 1. Electrophoresis of PCR products of the samples. Lane M is the 100 bp Marker ladder; Lane 1-6 are samples, the 360-bp bands are the target genes.



Figure 2. Genotyping of the *BTNL2* rs9268480 SNP. Lane M is the 100 bp Marker Ladder; Lanes 1 and 2, TT genotype (360-bp); Lanes 3 and 4, CT genotype (360-, 283- and 77-bp); and lanes 5 and 6, CC genotype (283- and 77-bp).

the forward and reverse primer pairs; respectively. Each amplification reaction was performed in a total volume of 25 µL, containing 10 × PCR buffer (1.8 mM MgCl_o) 2.5 µL, 1 U Tag polymerase, 2.5 mmol/L of each dNTP (Tiangen, Beijing, People's Republic of China) 2.0 µL, 20 pmol/L of each primer and 50 ng of genomic DNA, processing started with 95°C for 7 min 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 10 U of enzyme Mval was added directly to the PCR products (10 µL) and digested at 37°C overnight. After restriction enzyme digestion of the amplified DNA, genotypes were identified by electrophoresis on 2% ethidiumbromide stained agarose gels and visualizing with ultraviolet illumination. Genotypes were scored by an experienced reader blinded to the epidemiological and lipid results. Six samples (CC, CT and TT genotypes in two; respectively) detected by the PCR-RFLP were also confirmed by direct sequencing. The PCR product was purified by low melting point gel electrophoresis and phenol extraction, and then the DNA sequences were analyzed 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. The individuals with TC > 5.17 mmol/L and/or TG > 1.70mmol/L were defined as hyperlipidemic [39]. Hypertension was diagnosed according to the criteria of 1999 World Health Organization-International Society of Hypertension Guidelines for the management of hypertension [40, 41]. The diagnostic criteria of overweight and obesity were according to the Cooperative Meta-analysis Group of China Obesity Task Force. Normal weight, overweight and obesity were defined as a BMI < 24, 24-28, and > 28 kg/m²; respectively [42].

Statistical analyses

Epidemiological data were recorded on a predesigned form and managed with Excel software. Data analysis was performed using the software SPSS version 19.0 (SPSS Inc., Chicago, Illinois). Quantitative variables were expressed as mean ± standard deviation (serum TG levels were presented as medians and interquartile ranges). Qualitative variables were expressed as percentages. Allele frequency was determined via direct counting, and the standard goodness-of-fit test was used to test the Hardy-Weinberg equilibrium. Difference in genotype distribution between the groups was obtained using the chi-square test. The difference in general characteristics between Jing and Han was tested by the Student's unpaired *t*-test. The association of genotypes and serum lipid parameters was tested by analysis of covariance (ANCOVA). Sex, age, BMI, blood pressure, alcohol consumption, cigarette smok-

| Group | n | | Genotype Allele | | Allele | | |
|----------------|------|-------------|-----------------|-----------|--------------|-------------|-------|
| | | CC | СТ | TT | С | Т | HWP |
| Jing | 1148 | 718 (62.54) | 381 (33.19) | 49 (4.27) | 1817 (79.14) | 479 (20.86) | 0.863 |
| Han | 1355 | 915 (67.53) | 388 (28.63) | 52 (3.84) | 2218 (81.84) | 492 (18.16) | 0.180 |
| X ² | | | 6.846 | | 5.8 | | |
| Р | | | 0.033 | | 0.0 | | |
| Jing | 1148 | | | | | | |
| Male | 582 | 404 (69.42) | 156 (26.80) | 22 (3.78) | 964 (82.82) | 200 (17.18) | 0.161 |
| Female | 566 | 314 (55.48) | 225 (39.75) | 27 (4.77) | 853 (75.35) | 279 (24.65) | 0.095 |
| X ² | | | 24.069 | | 19.3 | | |
| Р | | | 0.000 | | 0.0 | 00 | |
| Han | 1355 | | | | | | |
| Male | 706 | 498 (70.54) | 182 (25.78) | 26 (3.68) | 1178 (83.43) | 234 (16.57) | 0.072 |
| Female | 649 | 417 (64.25) | 206 (31.74) | 26 (4.01) | 1040 (80.12) | 258 (19.88) | 0.929 |
| X ² | | | 6.268 | | 4.9 | | |
| Р | | 0.044 0.026 | | 26 | | | |

Table 2. Comparison of the genotype and allele frequencies of *BTNL2* rs9268480 SNP in the Jing and Han populations [n (%)]

ing were adjusted for the statistical analysis. Multivariate linear regression analysis with stepwise modeling was performed to evaluate the association of lipid profiles with genotypes (CC = 1, CT = 2 and TT = 3) and several environment factors in the combined population of Jing and Han, Jing, Han, males and females; respectively. A *P* value of less than 0.05 was considered statistically significant.

Results

General characteristics and lipid profiles

The general characteristics and lipid profiles between the Jing and Han populations are summarized in **Table 1**. The values of weight, body mass index, waist circumference, and the levels of TC, TG and LDL-C were higher in Jing than in Han (P < 0.05-0.001), whereas the percentage of cigarette smoking, alcohol consumption, the levels of diastolic blood pressure, Apo A1 and the ratio of ApoA1 to Apo B were lower in Jing than in Han (P < 0.05-0.001). There were no significant differences in the gender ratio, age structure, height, systolic blood pressure, pulse pressure, blood glucose, HDL-C and Apo B levels between the two ethnic groups (P >0.05 for all).

Results of electrophoresis and genotyping

After the genomic DNA of the samples were amplified by 2% agarose gel electrophoresis, the products of 360 bp nucleotide sequences were found in all samples (**Figure 1**). The genotypes identified were named according to the presence (C allele) or absence (T allele) of the enzyme restriction sites. Thus CC genotype was homozygote for the presence of the sites (bands at 283- and 77-bp). CT genotype was heterozygote for the presence and absence of the site (bands at 360-, 283- and 77-bp), and TT genotype was homozygote for the absence of the site (bands at 360-bp; **Figure 2**). The genotypes of the rs9268480 SNP were followed by the Hardy-Weinberg equilibrium.

Genotypic and allelic frequencies

The genotypic and allelic frequencies of *BTNL2* rs9268480 SNP are shown in Table 2. The frequency of susceptibility genotype and allele of rs9268480 (C > T) were significantly different between the two populations (CC, 62.54% vs. 67.53%; CT, 33.19% vs. 28.63%; TT, 4.27% vs. 3.84%; P = 0.033; C, 79.14% vs. 81.84%; T, 20.86% vs. 18.16%; P = 0.016) and between males and females in Jing (CC, 69.42% vs. 55.48%; CT, 26.80% vs. 39.75%; TT, 3.78% vs. 4.77%; P < 0.001; C, 82.82% vs. 75.35%; T, 17.18% vs. 24.65%; P < 0.001) and Han (CC, 70.54% vs. 64.25%; CT, 25.78% vs. 31.74%; TT, 3.68% vs. 4.01%; P = 0.044; C, 83.43% vs. 80.12%; T, 16.57% vs. 19.88%; P = 0.026) populations; respectively.

Results of sequencing

The results were shown as CC, CT and TT genotypes by PCR-RFLP, the CC, CT and TT geno-



Figure 3. A part of the nucleotide forward sequence of the *BTNL2* rs9268480 SNP. A. TT genotype; B. CT genotype; C. CC genotype.

| Table 3. | Comparison | of the genotypes | and lipid p | profiles in the Jing | g and Han p | populations |
|----------|------------|------------------|-------------|----------------------|-------------|-------------|
|----------|------------|------------------|-------------|----------------------|-------------|-------------|

| Genotype | Ν | TC (mmol/L) | TG (mmol/L) | HDL-C (mmol/L) | LDL-C (mmol/L) | ApoA1 (g/L) | ApoB (g/L) | ApoA1/ApoB |
|----------|------|----------------|----------------|-------------------|-------------------|----------------|---------------|------------|
| Jing | 1148 | | | | | | | |
| CC | 718 | 5.10±0.87 | 1.40 (1.10) | 1.81±0.45 | 2.79±0.44 | 1.31±0.24 | 0.99±0.20 | 1.36±0.41 |
| CT | 381 | 5.21±0.96 | 1.48 (1.20) | 1.79±0.47 | 2.86±0.42 | 1.30±0.23 | 1.06±0.24 | 1.30±0.39 |
| TT | 49 | 5.30±0.96 | 1.50 (1.23) | 1.71±0.40 | 2.91±0.40 | 1.28±0.20 | 1.06±0.26 | 1.29±0.38 |
| F | | 1.919 | 18.767 | 1.679 | 3.661 | 0.534 | 1.400 | 0.267 |
| Р | | 0.147 | 0.000 | 0.187 | 0.026 | 0.587 | 0.247 | 0.766 |
| Han | 1355 | | | | | | | |
| CC | 915 | 4.87±0.87 | 1.29 (1.03) | 1.85±0.68 | 2.85±0.43 | 1.35±0.20 | 1.04±0.25 | 1.35±0.39 |
| СТ | 388 | 4.90±0.84 | 1.39 (1.11) | 1.79±0.56 | 2.87±0.42 | 1.33±0.20 | 1.04±0.23 | 1.35±0.37 |
| TT | 52 | 4.93±0.82 | 1.43 (1.13) | 1.77±0.51 | 2.92±0.42 | 1.32±0.20 | 1.05±0.22 | 1.30±0.28 |
| F | | 0.171 | 16.783 | 1.422 | 0.523 | 0.868 | 0.135 | 0.236 |
| Р | | 0.843 | 0.000 | 0.242 | 0.593 | 0.420 | 0.874 | 0.790 |

types were also confirmed by direct sequencing (**Figure 3**); respectively.

Genotypes and lipid profiles

As shown in **Table 3**, serum TG and LDL-C levels in Jing were different among the genotypes (*P* < 0.05-0.001). The T allele carriers had higher serum TG and LDL-C levels than the T allele non-carriers. Serum TG levels was different among the genotypes in Han (P < 0.001). The T allele carriers had higher serum TG levels than the T allele non-carriers. Subgroup analyses showed that serum TC and TG levels in Jing

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| Ethnic/ Genotype | N | TC (mmol/L) | TG (mmol/L) | HDL-C | LDL-C | ApoA1 | ApoB | ApoA1/ |
|---------------------|-----|----------------|----------------|--------------|-----------|-----------|-----------|-----------|
| Jing/Male | 582 | | | (1111101/ L) | | (8/ -) | (8/ =) | Лров |
| CC | 404 | 5.05±0.79 | 1.42 (1.10) | 1.78±0.45 | 2.79±0.37 | 1.30±0.22 | 1.02±0.19 | 1.30±0.43 |
| СТ | 156 | 5.20±0.89 | 1.50 (1.20) | 1.78±0.51 | 2.84±0.39 | 1.28±0.24 | 1.06±0.24 | 1.29±0.36 |
| TT | 22 | 5.55±0.48 | 1.51 (1.23) | 1.69±0.42 | 2.91±0.21 | 1.26±0.18 | 1.07±0.25 | 1.28±0.41 |
| F | | 4.088 | 6.330 | 0.930 | 0.779 | 0.090 | 0.473 | 0.024 |
| Р | | 0.017 | 0.002 | 0.395 | 0.460 | 0.914 | 0.624 | 0.976 |
| Jing/Female | 566 | | | | | | | |
| CC | 314 | 5.11±0.96 | 1.32 (1.09) | 1.86±0.44 | 2.79±0.51 | 1.33±0.27 | 0.97±0.21 | 1.41±0.44 |
| СТ | 225 | 5.16±0.96 | 1.40 (1.18) | 1.80±0.45 | 2.88±0.44 | 1.31±0.22 | 1.06±0.24 | 1.31±0.34 |
| TT | 27 | 5.22±1.00 | 1.42 (1.24) | 1.72±0.39 | 2.91±0.50 | 1.29±0.22 | 1.06±0.27 | 1.30±0.37 |
| F | | 0.314 | 9.862 | 2.429 | 1.777 | 0.773 | 1.504 | 0.832 |
| Р | | 0.730 | 0.000 | 0.089 | 0.170 | 0.462 | 0.223 | 0.436 |
| Han/Male | 706 | | | | | | | |
| CC | 498 | 4.84±0.91 | 1.27 (0.99) | 1.73±0.55 | 2.83±0.44 | 1.36±0.22 | 1.05±0.25 | 1.35±0.40 |
| СТ | 182 | 4.84±0.76 | 1.38 (1.07) | 1.73±0.54 | 2.89±0.45 | 1.33±0.20 | 1.06±0.20 | 1.33±0.40 |
| TT | 26 | 4.85±0.82 | 1.43 (1.07) | 1.69±0.57 | 2.91±0.38 | 1.29±0.14 | 1.08±0.22 | 1.22±0.21 |
| F | | 0.249 | 8.148 | 0.051 | 1.321 | 0.417 | 0.053 | 0.326 |
| Р | | 0.780 | 0.000 | 0.950 | 0.267 | 0.659 | 0.949 | 0.722 |
| Han/Female | 649 | | | | | | | |
| CC | 417 | 4.91±0.82 | 1.31 (1.06) | 2.00±0.74 | 2.83±0.45 | 1.36±0.24 | 1.02±0.23 | 1.38±0.33 |
| СТ | 206 | 4.95±0.90 | 1.43 (1.12) | 1.84±0.57 | 2.86±0.43 | 1.34±0.19 | 1.02±0.25 | 1.37±0.34 |
| TT | 26 | 5.00±0.83 | 1.47 (1.13) | 1.83±0.48 | 2.95±0.39 | 1.32±0.20 | 1.03±0.24 | 1.35±0.38 |
| F | | 0.378 | 7.806 | 2.624 | 1.438 | 1.803 | 1.169 | 2.927 |
| Р | | 0.685 | 0.000 | 0.073 | 0.238 | 0.166 | 0.311 | 0.054 |

Table 4. Comparison of the genotypes and lipid profiles between males and females in the Jing andHan populations

males and TG levels in Jing females were different among the genotypes (P < 0.05-0.001), the T allele carrier had higher serum TC, TG levels than the T allele non-carriers. Serum TG levels in Hanmales and Han females were different among the genotypes (P < 0.001 for each), the T allele carriers had higher serum TG levels than the T allele non-carriers (**Table 4**).

Relative factors for serum lipid parameters

Multiple linear regression analysis showed that serum TC, TG and LDL-C levels in the combined population of Jing and Han; TC, TG and LDL-C levels in Jing; and TG levels in Han were correlated with the genotypes of the *BTNL2* rs9268480 SNP (P < 0.05-0.001; **Table 5**). When the correlation of serum lipid parameters and the genotypes was analyzed according to sex, we showed that serum TC and TG levels in Jing males; serum TG, HDL-C and LDL-C levels in Jing females; serum TG levels in Han males; and TG and ApoA1 levels and the ratio of ApoA1 to ApoB in Han females were correlated with the genotypes (P < 0.05-0.001; Table 6).

Serum lipid parameters were also associated with gender, age, BMI, systolic and diastolic blood pressure, pulse pressure, fasting blood glucose levels, cigarette smoking and alcohol consumption in both ethnic groups or in males and females (P < 0.05-0.001; **Tables 5** and **6**).

Discussion

Earlier questions regarding the generalizability of CVD risk and lipid traits to a more heterogeneous populace (i.e., varied populations) have been quelled by the replication of similar risk and lipid profiles and features in contemporary racially and ethnically diverse population surveys. Several reports have suggested that blacks have lower LDL-C concentrations and less hypercholesterolemia than whites. The

| | Risk factor | В | Std. | Beta | t | P |
|-----------------|---------------------|--------|-------|--------|-----------------|-------|
| | | | error | | | |
| Jing and Han | Construct | 0.000 | 0.000 | 0.000 | 1 074 | 0.040 |
| IC | Genotype | 0.060 | 0.030 | 0.038 | 1.974 | 0.048 |
| | Ethnic group | -0.255 | 0.034 | -0.143 | -7.502 | 0.000 |
| | Age | 0.007 | 0.001 | 0.110 | 5.577 | 0.000 |
| | Height | -0.009 | 0.002 | -0.085 | -4.375 | 0.000 |
| | Diastolic BP | 0.005 | 0.002 | 0.057 | 2.960 | 0.003 |
| | Glucose | 0.127 | 0.012 | 0.205 | 10.640 | 0.000 |
| TG | Genotype | 0.253 | 0.030 | 0.151 | 8.311 | 0.000 |
| | Gender | -0.150 | 0.049 | -0.079 | -3.035 | 0.002 |
| | Age | -0.009 | 0.001 | -0.123 | -5.949 | 0.000 |
| | Height | -0.026 | 0.003 | -0.217 | -7.889 | 0.000 |
| | Waist circumference | 0.042 | 0.004 | 0.403 | 10.617 | 0.000 |
| | Body mass index | -0.044 | 0.011 | -0.149 | -4.080 | 0.000 |
| | Cigarette smoking | 0.270 | 0.026 | 0.216 | 10.282 | 0.000 |
| | Diastolic BP | 0.009 | 0.002 | 0.099 | 5.329 | 0.000 |
| | Glucose | 0.109 | 0.012 | 0.165 | 9.039 | 0.000 |
| HDL-cholesterol | Ethnic group | -0.081 | 0.020 | -0.081 | -4.147 | 0.000 |
| | Gender | 0.102 | 0.023 | 0.102 | 4.476 | 0.000 |
| | Waist circumference | -0.016 | 0.001 | -0.291 | -14.559 | 0.000 |
| | Cigarette smoking | -0.076 | 0.015 | -0.115 | -5.155 | 0.000 |
| | Alcohol consumption | 0.119 | 0.015 | 0.189 | 8.044 | 0.000 |
| | Diastolic BP | 0.003 | 0.001 | 0.055 | 2.830 | 0.005 |
| LDL-cholesterol | Genotype | 0.041 | 0.015 | 0.054 | 2.766 | 0.006 |
| | Ethnic group | 0.038 | 0.017 | 0.045 | 2.281 | 0.023 |
| | Age | 0.003 | 0.001 | 0.078 | 3.863 | 0.000 |
| | Height | -0.003 | 0.001 | -0.056 | -2.816 | 0.005 |
| | Diastolic BP | 0.003 | 0.001 | 0.081 | 4.100 | 0.000 |
| | Glucose | 0.044 | 0.006 | 0.147 | 7.439 | 0.000 |
| ApoA1 | Gender | 0.033 | 0.011 | 0.075 | 3.110 | 0.002 |
| | Weight | -0.003 | 0.001 | -0.116 | -3.022 | 0.003 |
| | Waist circumference | -0.002 | 0.001 | -0.096 | -2 621 | 0.000 |
| | Alcohol consumption | 0.062 | 0.006 | 0.225 | 10 116 | 0.000 |
| | Diastolic RP | 0.002 | 0.000 | 0.220 | 2 805 | 0.000 |
| | | 0.001 | 0.000 | 0.007 | 2.000 | 0.004 |
| | Fuise pressure | 0.000 | 0.000 | 0.041 | ∠.113 E 043 | 0.030 |
| AnoP | Ado | -0.010 | 0.003 | -0.102 | -0.243 5 040 | 0.000 |
| Ahop | nge Hoight | 0.002 | 0.000 | 0.104 | 0.248 | 0.000 |
| | | -0.002 | 0.001 | -0.049 | -2.429 | 0.015 |
| | waist circumference | 0.006 | 0.001 | 0.214 | 10.430 | 0.000 |
| | | 0.001 | 0.000 | 0.052 | 2.588 | 0.010 |
| АроА1/АроВ | Gender | 0.073 | 0.021 | 0.094 | 3.434 | 0.001 |
| | Age | -0.001 | 0.001 | -0.044 | -2.094 | 0.036 |
| | Height | 0.003 | 0.001 | 0.065 | 2.452 | 0.014 |
| | Waist circumference | -0.012 | 0.001 | -0.282 | -14.228 | 0.000 |
| | Alcohol consumption | 0.072 | 0.011 | 0.148 | 6.720 | 0.000 |
| | Glucose | -0.021 | 0.005 | -0.080 | -4.118 | 0.000 |

Table 5. Correlations between lipid profiles and relative risk factors inthe Jing and Han populations

the prevalence of high LDL-C levels in young adults; LDL-C exceeded 160 mg/dl in 10% and 5% of young black men and women, respectively, compared with 9% and 4% of young white men and women. HDL-C levels were higher in black men than in white men. ApoA1, as known risk factor for CVD, and levels are two- to threefold higher in blacks [43]. In the present study, we showed that Jing population had higher serum TC, TG and LDL-C levels and lower ApoA1 levels and the ratio of ApoA1 to ApoB than in Han. Jing is the only Chinese minority for coastal fisheries, meanwhile is the only sea people in China. In this case, it has a very special lifestyle and dietary habits compared with the other landlocked nationalities. Their marriages were family-arranged in the old days when they sing antiphonal songs to look for the other half. After antiphonal singing, if the boy's into the girl he would kick sand toward her while approaching her. If the girl feel the same she would kick back, which means engagement. While the formal engagement ceremony and wedding they need pork, cake, tea, wine, glutinous rice as gifts. Jing stays endogamy, intermarriage with Han or Zhuang people is seldom happened. Jing people don't get married with someone sharing the same last name, also cross-cousin marriage is

CARDIA study identified

| Jing | | | | | | |
|-----------------|---------------------|--------|-------|--------|--------|-------|
| TC | Genotype | 0.091 | 0.044 | 0.058 | 2.065 | 0.039 |
| | Gender | 0.262 | 0.064 | 0.145 | 4.087 | 0.000 |
| | Age | 0.019 | 0.002 | 0.290 | 9.183 | 0.000 |
| | Body mass index | 0.069 | 0.014 | 0.243 | 4.784 | 0.000 |
| | Waist circumference | -0.017 | 0.005 | -0.171 | -3.260 | 0.001 |
| | Cigarette smoking | 0.103 | 0.042 | 0.080 | 2.422 | 0.016 |
| | Alcohol consumption | 0.153 | 0.044 | 0.113 | 3.503 | 0.000 |
| | Pulse pressure | -0.008 | 0.002 | -0.147 | -4.836 | 0.000 |
| | Glucose | 0.101 | 0.015 | 0.195 | 6.898 | 0.000 |
| TG | Genotype | 0.254 | 0.041 | 0.165 | 6.237 | 0.000 |
| | Gender | -0.242 | 0.069 | -0.138 | -3.508 | 0.000 |
| | Age | -0.006 | 0.002 | -0.096 | -3.113 | 0.002 |
| | Height | -0.027 | 0.004 | -0.242 | -6.172 | 0.000 |
| | Waist circumference | 0.031 | 0.003 | 0.330 | 11.218 | 0.000 |
| | Cigarette smoking | 0.247 | 0.038 | 0.198 | 6.425 | 0.000 |
| | Diastolic BP | 0.008 | 0.002 | 0.091 | 3.300 | 0.001 |
| | Glucose | 0.085 | 0.013 | 0.169 | 6.349 | 0.000 |
| HDL-cholesterol | Gender | 0.162 | 0.032 | 0.179 | 5.064 | 0.000 |
| | Age | 0.003 | 0.001 | 0.090 | 3.012 | 0.003 |
| | Weight | 0.006 | 0.003 | 0.126 | 2.147 | 0.032 |
| | Waist circumference | -0.022 | 0.003 | -0.452 | -8.376 | 0.000 |
| | Alcohol consumption | 0.184 | 0.021 | 0.270 | 8.747 | 0.000 |
| LDL-cholesterol | Genotype | 0.066 | 0.022 | 0.089 | 3.048 | 0.002 |
| | Age | 0.004 | 0.001 | 0.135 | 4.635 | 0.000 |
| | Diastolic BP | 0.003 | 0.001 | 0.061 | 2.102 | 0.036 |
| | Glucose | 0.025 | 0.007 | 0.102 | 3.509 | 0.000 |
| ApoA1 | Weight | -0.004 | 0.001 | -0.190 | -6.451 | 0.000 |
| | Alcohol consumption | 0.043 | 0.010 | 0.120 | 4.079 | 0.000 |
| | Systolic BP | 0.001 | 0.000 | 0.071 | 2.436 | 0.015 |
| | Glucose | -0.018 | 0.004 | -0.132 | -4.517 | 0.000 |
| АроВ | Age | 0.003 | 0.001 | 0.165 | 5.788 | 0.000 |
| | Body mass index | 0.016 | 0.002 | 0.204 | 7.138 | 0.000 |
| ApoA1/ApoB | Age | -0.004 | 0.001 | -0.148 | -4.815 | 0.000 |
| | Waist circumference | -0.011 | 0.001 | -0.272 | -9.500 | 0.000 |
| | Alcohol consumption | 0.077 | 0.017 | 0.132 | 4.596 | 0.000 |
| | Pulse pressure | 0.001 | 0.001 | 0.063 | 2.042 | 0.041 |
| Han | | | | | | |
| TC | Height | -0.008 | 0.003 | -0.070 | -2.485 | 0.013 |
| | Cigarette smoking | -0.084 | 0.030 | -0.078 | -2.802 | 0.005 |
| | Systolic BP | 0.001 | 0.000 | 0.079 | 2.951 | 0.003 |
| | Diastolic BP | 0.004 | 0.002 | 0.053 | 2.004 | 0.045 |
| | Glucose | 0.218 | 0.020 | 0.279 | 10.773 | 0.000 |
| TG | Genotype | 0.254 | 0.045 | 0.141 | 5.678 | 0.000 |
| | Age | -0.011 | 0.002 | -0.148 | -5.676 | 0.000 |
| | Weight | -0.025 | 0.005 | -2.234 | -5.020 | 0.000 |
| | Waist circumference | 0.045 | 0.005 | 0.391 | 8.626 | 0.000 |
| | Cigarette smoking | 0.286 | 0.033 | 0.228 | 8.694 | 0.000 |
| | Diastolic BP | 0.009 | 0.002 | 0.097 | 3.833 | 0.000 |

strictly forbidden. This kind of breeding with exclusive indicates that some hereditary characteristics and genotypes of lipid metabolism-related genes in this population may be different from those in Han people. The Human Project has failed to identify any genotype clearly identifies race and the similarity of the genetic code for all persons is > 99% [44]. Thus, race is poor proxy for genotypes. and exists only as a sociopolitical construct. Ultimately, race and ethnicity are less risk factors and more risk markers, placeholders for more physiologic risks. The continued elucidation of nuances in CVD as a function of varied populations and the discovery of more precise pathophysiologic considerations are appropriate, but discussion of race and ethnicity in medicine must rigorously avoid polarization and the further perpetuation of disparate health care.

The frequency spectrum of BTNL2 rs9268480 mutation varied significantly among different races/ ethnicities. According to the Hap Map data, the minor allele T frequency of the SNP was 17.07% in Peking Chinese, 9.88% in Japanese, 12.50% in Yoruba, 34.07% in European population, 73.3% in Italy. In the current study, we showed that the frequency of susceptibility alleles of rs9268480 C > T were significantly different between the two populations

BTNL2 rs9268480 SNP and serum lipid profiles

| | Glucose | 0.173 | 0.023 | 0.191 | 7.474 | 0.000 |
|-----------------|---------------------|--------|-------|--------|---------|-------|
| HDL-cholesterol | Gender | 0.114 | 0.034 | 0.107 | 3.396 | 0.001 |
| | Waist circumference | -0.014 | 0.002 | -0.233 | -8.684 | 0.000 |
| | Cigarette smoking | -0.112 | 0.021 | -0.167 | -5.279 | 0.000 |
| | Alcohol consumption | 0.095 | 0.021 | 0.155 | 4.599 | 0.000 |
| | Systolic BP | 0.001 | 0.000 | 0.056 | 2.072 | 0.038 |
| | Diastolic BP | 0.004 | 0.001 | 0.080 | 2.918 | 0.004 |
| | Glucose | -0.032 | 0.013 | -0.066 | -2.524 | 0.012 |
| LDL-cholesterol | Height | -0.006 | 0.002 | -0.120 | -4.001 | 0.000 |
| | Body mass index | -0.021 | 0.007 | -0.158 | -2.922 | 0.004 |
| | Waist circumference | 0.010 | 0.003 | 0.196 | 3.579 | 0.000 |
| | Systolic BP | 0.000 | 0.000 | 0.054 | 1.987 | 0.047 |
| | Diastolic BP | 0.004 | 0.001 | 0.089 | 3.264 | 0.001 |
| | Glucose | 0.087 | 0.010 | 0.223 | 8.484 | 0.000 |
| ApoA1 | Weight | -0.005 | 0.001 | -0.225 | -8.185 | 0.000 |
| | Cigarette smoking | -0.015 | 0.008 | -0.061 | -1.983 | 0.048 |
| | Alcohol consumption | 0.069 | 0.007 | 0.293 | 9.355 | 0.000 |
| | Diastolic BP | 0.001 | 0.001 | 0.072 | 2.714 | 0.007 |
| | Glucose | -0.016 | 0.005 | -0.085 | -3.253 | 0.001 |
| АроВ | Gender | -0.030 | 0.014 | -0.063 | -2.104 | 0.036 |
| | Weight | -0.004 | 0.001 | -0.152 | -2.862 | 0.004 |
| | Waist circumference | 0.009 | 0.001 | 0.325 | 6.510 | 0.000 |
| | Diastolic BP | 0.002 | 0.001 | 0.091 | 3.396 | 0.001 |
| | Glucose | 0.022 | 0.006 | 0.099 | 3.739 | 0.000 |
| ApoA1/ApoB | Gender | 0.060 | 0.023 | 0.079 | 2.605 | 0.009 |
| | Waist circumference | -0.012 | 0.001 | -0.285 | -10.977 | 0.000 |
| | Alcohol consumption | 0.072 | 0.013 | 0.164 | 5.394 | 0.000 |
| | Glucose | -0.050 | 0.009 | -0.144 | -5.599 | 0.000 |

TC, total cholesterol; TG, triglyceride; HDL, high-density lipoprotein; LDL, low-density lipoprotein; Apo, apolipoprotein; BP, blood pressure.

| Table 6. Correlations betwee | en lipid profile | s and relative | risk factors in |
|------------------------------|------------------|----------------|-----------------|
| the males and females of Jir | ng and Han po | opulations | |

| Lipid | Risk factor | В | Std. error | Beta | t | Р |
|-----------|---------------------|--------|---------------|--------|--------|-------|
| Jing/Male | | | | | | |
| TC | Genotype | 0.152 | 0.059 | 0.102 | 2.595 | 0.010 |
| | Age | 0.015 | 0.002 | 0.255 | 5.978 | 0.000 |
| | Body mass index | 0.104 | 0.021 | 0.388 | 4.981 | 0.000 |
| | Waist circumference | -0.028 | 0.007 | -0.329 | -4.121 | 0.000 |
| | Alcohol consumption | 0.175 | 0.040 | 0.173 | 4.335 | 0.000 |
| | Pulse pressure | -0.013 | 0.002 | -0.248 | -5.757 | 0.000 |
| | Glucose | 0.080 | 0.018 | 0.183 | 4.529 | 0.000 |
| TG | Genotype | 0.234 | 0.063 | 0.134 | 3.712 | 0.000 |
| | Age | -0.014 | 0.003 | -0.199 | -4.638 | 0.000 |
| | Height | -0.031 | 0.006 | -0.222 | -5.135 | 0.000 |
| | Waist circumference | 0.037 | 0.004 | 0.372 | 9.098 | 0.000 |
| | Cigarette smoking | 0.218 | 0.043 | 0.199 | 5.067 | 0.000 |
| | Diastolic BP | 0.008 | 0.003 | 0.087 | 2.289 | 0.022 |
| | Glucose | 0.107 | 0.019 | 0.207 | 5.711 | 0.000 |
| | | | | | | |

(20.86% vs. 18.16%; P = 0.016) and between males and females in Jing (17.18% vs. 24.65%; P < 0.001) and Han (16.57% vs. 19.88%; P = 0.026) populations. The minor T allele carriers of BTNL2 rs9268480 SNP was a risk allele for dyslipidemia, especially higher serum TG levels in ethnic and sexually dimorphic subgroup. These findings may also partly explain why the prevalence of CVD is higher in females than in males in some ethnic groups.

The relative risk for CVD events associated with elevation of various lipid variables was determined in a nested case-control study from the Nurses' Hea-Ith Study. Among 32,826 healthy women who provided blood samples at baseline, the multivariable adjusted relative risks (homocysteine and other traditional cardiac risk factors) for the highest quintiles of lipid variables were ApoB (RR, 4.1; 95% CI, 2 to 8.3), LDL-C (RR, 3.1; 95% Cl, 1.7 to 5.8), TG (RR, 1.9; 95% CI, 1.0 to 3.9) and low levels of HDL-C (RR, 2.6; 95% CI, 1.4 to 5) [45]. Adverse changes in lipid profiles accompany menopause [46]. Perimenopausal TG levels are the most erratic but follow roughly the same pattern of increase as TC and LDL-C, which increase on average by an absolute 10% from levels at6monthsbeforemenopause. Menopause influences HDL-C less dramatical-

BTNL2 rs9268480 SNP and serum lipid profiles

| | HDL-cholesterol | Age | 0.004 | 0.001 | 0.123 | 3.163 | 0.002 | ly. HDL-C declines gradu- |
|----|------------------|---------------------|---------|-------|--------|--------|-------|-------------------------------|
| | | Body mass index | 0.024 | 0.011 | 0.160 | 2.231 | 0.026 | ally in the two years pre- |
| | | Waist circumference | -0.024 | 0.003 | -0.512 | -7.066 | 0.000 | ceding menopause and |
| | | Alcohol consumption | 0.201 | 0.021 | 0.352 | 9.406 | 0.000 | then levels off after men- |
| | | Systolic BP | -0.003 | 0.001 | -0 109 | -2 753 | 0.006 | opause. The postmenop- |
| | I DI-cholesterol | Age | 0.003 | 0.001 | 0.116 | 2 599 | 0.010 | ausal increase in CVD risk |
| | EDE ONOICOLOIO | Rody mass index | 0.000 | 0.001 | 0.346 | 4 244 | 0.000 | may result partly from |
| | | Waist circumference | -0.010 | 0.003 | -0.264 | -3 149 | 0.002 | these lipid alterations. |
| | | Alcohol consumption | 0.010 | 0.000 | 0.204 | 2 3/6 | 0.002 | It is well realized that onvi |
| | | | -0.0043 | 0.013 | -0.190 | -1 211 | 0.013 | ronmental factors such as |
| | | Glucoso | 0.004 | 0.001 | 0.120 | 3 060 | 0.000 | dietary natterns life style |
| | Apo 1 | Hoight | 0.025 | 0.008 | 0.129 | 2 107 | 0.002 | nhysical inactivity ciga- |
| | APOAL | Maist aircumfaranaa | -0.003 | 0.001 | -0.091 | 5 277 | 0.028 | rette smoking and alcohol |
| | | Maist circumierence | -0.005 | 0.001 | -0.222 | -5.211 | 0.000 | consumption are all stro- |
| | | | 0.001 | 0.011 | 0.219 | 2.544 | 0.000 | ngly correlated with linid |
| | Are a D | Giucose | -0.015 | 0.005 | -0.124 | -3.143 | 0.002 | profiles. In the present |
| | Аров | Age | 0.003 | 0.001 | 0.152 | 3.465 | 0.001 | study. multivariate linear |
| | | Body mass index | 0.021 | 0.003 | 0.262 | 6.575 | 0.000 | regression analysis also |
| | | Pulse pressure | -0.002 | 0.001 | -0.109 | -2.475 | 0.014 | showed that age, sex. |
| | ApoA1/ApoB | Age | -0.003 | 0.001 | -0.088 | -2.237 | 0.026 | BMI, waist circumference, |
| | | Waist circumference | -0.014 | 0.002 | -0.313 | -7.927 | 0.000 | alcohol consumption, cig- |
| | | Alcohol consumption | 0.096 | 0.020 | 0.185 | 4.691 | 0.000 | arette smoking, and blood |
| Ji | ng/Female | | | | | | | pressure were involved in |
| | TC | Age | 0.025 | 0.003 | 0.318 | 7.455 | 0.000 | determining serum lipid |
| | | Weight | 0.025 | 0.008 | 0.228 | 3.065 | 0.002 | parameters in both ethnic |
| | | Waist circumference | -0.019 | 0.008 | -0.164 | -2.277 | 0.023 | groups. The values of |
| | | Glucose | 0.135 | 0.024 | 0.222 | 5.620 | 0.000 | weight, BMI, waist circum- |
| | TG | Genotype | 0.243 | 0.051 | 0.184 | 4.751 | 0.000 | ference were higher in |
| | | Height | -0.028 | 0.005 | -0.204 | -5.059 | 0.000 | Jing than in Han, whereas |
| | | Waist circumference | 0.026 | 0.004 | 0.291 | 7.227 | 0.000 | the percentage of ciga- |
| | | Cigarette smoking | 0.660 | 0.241 | 0.107 | 2.735 | 0.006 | rette smoking, alcohol |
| | | Glucose | 0.059 | 0.019 | 0.123 | 3.144 | 0.002 | consumption, the levels |
| | HDL-cholesterol | Genotype | -0.062 | 0.030 | -0.082 | -2.049 | 0.041 | of diastolic blood pres- |
| | | Waist circumference | -0.017 | 0.002 | -0.324 | -7.893 | 0.000 | sure were lower in Jing |
| | | Diastolic BP | 0.005 | 0.002 | 0.110 | 2.685 | 0.007 | than in Han. These data |
| | LDL-cholesterol | Genotype | 0.065 | 0.033 | 0.079 | 1.968 | 0.050 | suggest that the environ- |
| | | Age | 0.009 | 0.002 | 0.230 | 5.687 | 0.000 | mental factors also play |
| | | Glucose | 0.043 | 0.012 | 0.145 | 3.587 | 0.000 | an important role in deter- |
| | ApoA1 | Body mass index | -0.008 | 0.003 | -0.105 | -2.508 | 0.012 | mining lipid profiles in our |
| | | Pulse pressure | 0.001 | 0.001 | 0.095 | 2.242 | 0.025 | sludy populations. when |
| | | Glucose | -0.015 | 0.007 | -0.099 | -2.323 | 0.021 | taiking about thet pattern, |
| | АроВ | Age | 0.005 | 0.001 | 0.230 | 5.675 | 0.000 | food cumplemented with |
| | | Body mass index | 0.012 | 0.003 | 0.162 | 3.992 | 0.000 | corp sweet potato taro |
| | ApoA1/ApoB | Age | -0.05 | 0.001 | -0.162 | -3.977 | 0.000 | and other grains They |
| | | Body mass index | -0.023 | 0.004 | -0.213 | -5.216 | 0.000 | prefer dutinous rice and |
| Н | an/Male | | | | | | | seafood like fish shrimn |
| | TC | Cigarette smoking | -0.091 | 0.033 | -0.097 | -2.755 | 0.006 | crabs shellfish and sand- |
| | | Diastolic BP | 0.011 | 0.003 | 0.130 | 3.732 | 0.000 | worm. Also nigs chickens |
| | | Pulse pressure | 0.001 | 0.000 | 0.089 | 2.556 | 0.011 | and ducks are the main |
| | | Glucose | 0.248 | 0.027 | 0.319 | 9.069 | 0.000 | sources of meat. Jing peo- |
| | TG | Genotype | 0.273 | 0.070 | 0.135 | 3.884 | 0.000 | ple prefer sweet food |
| | | Age | -0.020 | 0.003 | -0.238 | -6.109 | 0.000 | such as sweet glutinous |
| | | - | | | | | | 0 |

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BTNL2 rs9268480 SNP and serum lipid profiles

| | Weight | -0.036 | 0.009 | -0.288 | -4.236 | 0.000 |
|-----------------|----------------------------|--------|-------|--------|-----------------|-------|
| | Waist circumference | 0.057 | 0.009 | 0.425 | 6.495 | 0.000 |
| | Cigarette smoking | 0.233 | 0.043 | 0.196 | 5.409 | 0.000 |
| | Diastolic BP | 0.013 | 0.004 | 0.128 | 3.664 | 0.000 |
| | Glucose | 0.189 | 0.034 | 0.191 | 5.499 | 0.000 |
| HDL-cholesterol | Waist circumference | -0.018 | 0.002 | -0.271 | -7.382 | 0.000 |
| | Cigarette smoking | -0.106 | 0.022 | -0.182 | -4.772 | 0.000 |
| | Alcohol consumption | 0.100 | 0.022 | 0.173 | 4.471 | 0.000 |
| | Diastolic BP | 0.006 | 0.002 | 0.122 | 3.367 | 0.001 |
| | Pulse pressure | 0.001 | 0.000 | 0.078 | 2.175 | 0.030 |
| LDL-cholesterol | Diastolic BP | 0.006 | 0.001 | 0.141 | 3.944 | 0.000 |
| | Glucose | 0.111 | 0.014 | 0.289 | 8.104 | 0.000 |
| ApoA1 | Waist circumference | -0.006 | 0.001 | -0.260 | -7.351 | 0.000 |
| | Cigarette smoking | -0.018 | 0.008 | -0.083 | -2 248 | 0.025 |
| | Alcohol consumption | 0.081 | 0.008 | 0.368 | 9 846 | 0.000 |
| AnoB | Waist circumference | 0.006 | 0.001 | 0.219 | 6.083 | 0.000 |
| Аров | | 0.000 | 0.001 | 0.210 | 1 284 | 0.000 |
| | Glucoso | 0.003 | 0.001 | 0.173 | 1 860 | 0.000 |
| ΔροΔ1/ΔροΒ | Aro | 0.037 | 0.008 | 0.173 | 4.009 | 0.000 |
| ADOAT/ ADOR | Age Waist aircumfaranaa | 0.003 | 0.001 | 0.094 | 2.507 | 0.010 |
| | Alashal concumption | -0.014 | 0.002 | -0.291 | -0.112 5 200 | 0.000 |
| | Disetelia BD | 0.079 | 0.015 | 0.100 | 0.200 | 0.000 |
| | | -0.003 | 0.001 | -0.083 | -2.339 | 0.020 |
| Hen (Female | Glucose | -0.062 | 0.013 | -0.173 | -4.761 | 0.000 |
| | lloidht | 0.010 | 0.005 | 0.005 | 0 400 | 0.012 |
| 10 | Height | -0.012 | 0.005 | -0.095 | -2.499 | 0.013 |
| то | Giucose | 0.201 | 0.050 | 0.257 | 0.770 | 0.000 |
| IG | Genotype | 0.206 | 0.056 | 0.135 | 3.680 | 0.000 |
| | weight | -0.021 | 0.007 | -0.223 | -3.124 | 0.002 |
| | Waist circumference | 0.041 | 0.007 | 0.435 | 6.116 | 0.000 |
| | Cigarette smoking | 0.404 | 0.088 | 0.170 | 4.568 | 0.000 |
| | Pulse pressure | -0.006 | 0.002 | -0.103 | -2.735 | 0.006 |
| | Glucose | 0.175 | 0.030 | 0.219 | 5.904 | 0.000 |
| HDL-cholesterol | Waist circumference | -0.010 | 0.002 | -0.178 | -4.600 | 0.000 |
| | Glucose | -0.038 | 0.019 | -0.078 | -2.014 | 0.044 |
| LDL-cholesterol | Age | 0.004 | 0.001 | 0.101 | 2.448 | 0.015 |
| | Height | -0.005 | 0.003 | -0.083 | -2.080 | 0.038 |
| | Glucose | 0.064 | 0.016 | 0.160 | 4.054 | 0.000 |
| ApoA1 | Genotype | 0.031 | 0.014 | 0.086 | 2.189 | 0.029 |
| | Body mass index | -0.011 | 0.002 | -0.181 | -4.527 | 0.000 |
| | Alcohol consumption | 0.040 | 0.017 | 0.088 | 2.289 | 0.022 |
| | Diastolic BP | 0.002 | 0.001 | 0.089 | 2.228 | 0.026 |
| | Glucose | -0.022 | 0.007 | -0.117 | -2.985 | 0.003 |
| АроВ | Age | 0.003 | 0.001 | 0.130 | 3.306 | 0.001 |
| | Weight | -0.007 | 0.002 | -0.247 | -3.316 | 0.001 |
| | Waist circumference | 0.011 | 0.002 | 0.413 | 5.625 | 0.001 |
| ApoA1/ApoB | Genotype | 0.058 | 0.024 | 0.090 | 2.389 | 0.017 |
| | Height | 0.009 | 0.002 | 0.178 | 4.710 | 0.000 |
| | Waist circumference | -0.012 | 0.002 | -0.294 | -7.683 | 0.000 |
| | Glucose | -0.044 | 0.012 | -0.131 | -3.518 | 0.000 |

rice porridge, mung bean syrup, because they believe sweet food is a symbol for happiness. A kind of fish sauce called nuocmam is also popular on Jing people's dinner table, which contains 17 amino acids (8 essential amino acids included of course). Furthermore, the joint effects of different dietary habits and environmental factors probably further modify the association of genetic variations and lipid profiles in our study populations.

Several potential limitations in our study should be considered. First, the number of participants available for MAF of this SNP was not high enough to calculate a strong power as compared with many previous GWAS and replication studies. Second, there are still many unmeasured environmental and genetic factors including omega-3 and/or omega-6 polyunsaturated fatty acids that needed to be considered. Third, the relevance of this finding has to be defined in further high caliber of studies including incorporating the genetic information of this SNP and in vitro functional studies to confirm the impact of a variant on a molecular level.

Conclusions

In conclusion, this study showed that the associations of the *BTNL2* rs926-8480 SNP and lipid profiles were different bet-

TC, total cholesterol; TG, triglyceride; HDL, high-density lipoprotein; LDL, low-density lipoprotein; Apo, apolipoprotein; BP, blood pressure.

ween the Jing and Han populations and between males and females in the both ethnic groups. There may be a racial/ethnic- and/ or sex-specific association of the *BTNL2* rs9268480 SNP and lipid profiles.

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Disclosure of conflict of interest

The authors have nothing to disclose.

Address correspondence to: Wu-Xian Chen, Department of Cardiology, Institute of Cardiovascular Diseases, The First Affiliated Hospital, Guangxi Medical University, 22 Shuangyong Road, Nanning 530021, Guangxi, People's Republic of China. Tel: +86-771-5316206; E-mail: nncwx@163.com

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