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# Relationship of the *APOA5*/*A4*/*C3*/*A1* gene cluster and *APOB* gene polymorphisms with dyslipidemia

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**ABSTRACT.** We determined the alleles of ten single nucleotide polymorphisms (SNPs) in the *APOA5*/*A4*/*C3*/*A1* gene cluster and in *APOB* in Han Chinese from Xinjiang Shihezi, China using MALDI-TOF mass spectrometry, and explored the correlation between these SNPs and dyslipidemia through a case-control study design with 250 patients and 250 normal controls. All SNPs except for *APOA5* rs2072560 conformed to Hardy-Weinberg equilibrium (all $P > 0.05$). *APOA5* rs651821, *APOA4* rs5104, *APOC3* rs734104, and *APOC3* rs5128 genotype and allele frequencies were significantly different between groups (all $P < 0.01$). For rs651821, the risks of dyslipidemia for the CC or

 

CC+CT genotypes were 9.917 or 1.859 times that of TT, and the risk of the C *vs* T allele was 2.027. For rs5104, the AG, GG, or AG+GG risks were 1.797, 1.861, and 1.809 times AA, and the G *vs* A risk was 1.427. For rs734104, the CT, CC, or CC+CT risks were 1.851, 2.570, and 1.958 times TT, and the C *vs* T risk was 1.610. For rs5128, the GC or CC+GC risks were 1.738 or 1.749 times GG, and the C *vs* G risk was 1.477. Compared with the wild-type haplotype TATG, the risks of dyslipidemia with CGCC, TGCC, or CATG haplotypes (odds ratios = 2.434, 1.503, and 2.740, respectively) were significantly higher. Our results suggested that these four SNPs were significantly associated with dyslipidemia in Xinjiang Shihezi Han Chinese, and might serve as risk factors for dyslipidemia. Individuals carrying the CGCC, TGCC, or CATG haplotypes were prone to dyslipidemia.

**Key words:** *APOA5*/*A4*/*C3*/*A1* gene cluster; Apolipoprotein B; Dyslipidemia; Gene polymorphism

## INTRODUCTION

Supernormal increase of one or more of lipids in plasma is called hyperlipidemia (Zheng and Zhu 2007), and can include total cholesterol (TC), triglycerides (TG), low density lipoprotein cholesterol (LDL-C), and high density lipoprotein cholesterol (HDL-C). The first three are characterized by increased levels, whereas the latter becomes reduced. Recently, studies have found that the *APOA5*/*A4*/*C3*/*A1* gene cluster and *APOB* gene polymorphisms were associated with dyslipidemia, but these findings have been controversial (Dallongeville et al., 2006; Chien et al., 2008; Yin et al., 2011; Zhang et al., 2011). Important reasons for the discrepancies might be related to the limitations of the research studies to a single or a small number of single nucleotide polymorphisms (SNPs), and the relatively weak associations detected. Xinjiang Shihezi Han Chinese originate from all over China, and represent the Han people. We chose ten SNPs that had controversial results as well as relatively high mutation rates within the *APOA5*/*A4*/*C3*/*A1* gene cluster and the *APOB* gene. The purpose of our analysis was to reveal the genetic correlation of dyslipidemia, and to provide new opportunities for the prevention and treatment of cardiovascular disease.

## MATERIAL AND METHODS

### Ethical approval

This study was approved by the Ethics Committee of The First Affiliated Hospital of Shihezi University and adhered to the standards of the Declaration of Helsinki. All participants provided written informed consent.

### Subjects

The patients and controls were recruited from the First Affiliated Hospital of Medical College, Shihezi University (ShiHeZi, China); after obtaining informed consent and ethical

approval, 500 subjects participated in this study. Inclusion criteria were taken from China's Prevention and Cure Guide of Hypertension (Joint Committee for Developing Chinese Guidelines on Prevention and Treatment of Dyslipidemia in Adults, 2007). Characteristics of the dyslipidemia group were: TG ≥ 2.26 mM, TC ≥ 6.22 mM, LDL-C ≥ 4.14 mM, and HDL-C < 1.04 mM; and of the control group were: TG < 1.7 mM, TC < 5.18 mM, LDL-C < 3.37 mM, and HDL-C ≥ 1.04 mM. Individuals who had thyroid disease, malignant tumor, tuberculosis, multiple organ failure, or had used lipid-lowering drugs within one week prior to admission were excluded from the study.

## Biochemical analyses

Venous blood samples (3 mL) were collected from each subject into tubes containing Heparin after 12 h overnight fasting. TC, TG, LDL-C, and HDL-C levels were measured using standard methods using an OLYAMPUS2700 automatic biochemical analyzer (Olympus Co. Ltd., Tokyo, Japan).

## Selection of SNPs and primer design

A total of ten SNPs from five genes were selected using the HapMap database as a reference. Based on the specific RS number of each SNP locus, 10 groups of primers with a perfect match were designed using the MassARRAY Assay Design software (Sequenom Inc., San Diego, CA, USA). To avoid cross hybridization, no short tandem repeats were included within the hybridization sequence. Three primers were designed for each SNP, including a pair of primers for polymerase chain reaction (PCR) amplification and a single-base extension primer (Table 1). The primers were synthesized by the Shanghai Sangon Biological Engineering Technology Corporation (Shanghai, China).

## Genotyping

DNA extraction: To determine the allele frequencies of the SNPs, blood samples were collected from 487 unrelated Han Chinese individuals. DNA was extracted from 0.3 mL blood using the RelaxGene Blood DNA System (BeiJing TIANGEN Co. Ltd., Beijing, China). The extracted DNA was qualitatively assessed using 1% agarose gel electrophoresis and quantified using UV spectrophotometry; concentrations were in the range of 10-30 ng/mL.

Multiplex PCR: PCRs were performed in 5 mL total volume, containing 1.6 μL nuclease free water, 0.5 μL 10X PCR buffer with 20 mM $MgCl_2$, 0.4 μL 25 mM $MgCl_2$, 0.1 μL 25 mM dNTP mix, and 0.2 μL 5 U/μL PCR enzyme (all from Sequenom Inc.). The PCR conditions were as follows: 94°C for 4 min, followed by 45 cycles of 94°C for 20s, 56°C for 30s, 72°C for 1 min, and a final step of 72°C for 3 min. The samples were kept at 4°C until further analysis.

Shrimp alkaline phosphatase (SAP) dephosphorylation: After the PCRs were performed, the products of three reactions were treated with SAP to remove excess dNTPs. This reaction contained 0.3 μL 1.7 U/μL SAP enzyme, 0.17 μL 10X SAP buffer, and 1.53 μL nuclease free water (all from Sequenom Inc.). The reaction conditions were 37°C for 40 min and 85°C for 5 min, and the samples were kept at 4°C until further analysis.

**Table 1.** Primers used for SNP genotyping.

| SNP | Primer (5'→3') | Sequence |
|---|---|---|
| APOA5 rs651821 | F | ACG TTG GAT GTG AAA GAA GAG CCA GAG CCC |
| | R | ACG TTG GAT GCT CCT TCT TCC CCT AAC CAG |
| | Extension | GCA GCC ATG CTT GCC ATT A |
| APOA5 rs2072560 | F | ACG TTG GAT GAC AGA TAT CCA GGC CGT CAG |
| | R | ACG TTG GAT GAT CAG TGC GCG ATG ACT TGG |
| | Extension | ctC CGT CAG ACT GCT AGC C |
| APOA5 rs619054 | F | ACG TTG GAT GAC CCC TGA GGA TCT ACC TG |
| | R | ACG TTG GAT GAA CCA TGC TAG AGG CTC AGA |
| | Extension | GGC TCC CCA GAC AAG |
| APOA4 rs5104 | F | ACG TTG GAT GTA CGC GGA CCA GCT GCG CAC |
| | R | ACG TTG GAT GAC TCT CTC CAT GCG CTG TG |
| | Extension | tCT GCG CAC CCA GGT CA |
| APOC3 rs734104 | F | ACG TTG GAT GCC CCT CAT CAT AAC CTG AAG |
| | R | ACG TTG GAT GAC CTG CAC TTG GAG CCA CTT |
| | Extension | ACT TGC CCA AAG CTA CA |
| APOC3 rs2070669 | F | ACG TTG GAT GAT ACG GGC TCT CAG AAG GG |
| | R | ACG TTG GAT GGT GGG TTT TCT GCT CCA TCC |
| | Extension | cCC TCG ATC CCT CGC C |
| APOC3 rs5128 | F | ACG TTG GAT GCT TTT AAG CAA CCT ACA GGG |
| | R | ACG TTG GAT GAG ACC TCA ATA CCC CAA GTC |
| | Extension | cac ccG CCT ATC CAT CCT GC |
| APOA1 rs5069 | F | ACG TTG GAT GTC CCC AGC TCA AGG TTC AG |
| | R | ACG TTG GAT GAG AAG ACC TCA GGT ACC CAG |
| | Extension | gGG TAC CCA GAG GCC C |
| APOB rs693 | F | ACG TTG GAT GCA CAT GAA GGC CAA ATT CCG |
| | R | ACG TTG GAT GGG TAT CGT TGA AGT TCC TGC |
| | Extension | AAG GCC AAA TTC CGA GAG AC |
| APOB rs1042031 | F | ACG TTG GAT GGT GTT TGA TGG CTT GGT ACG |
| | R | ACG TTG GAT GTG AGT GAG TCA ATC AGA TGC |
| | Extension | Tta TTG GTA CGA GTT ACT CAA |

SNP = single nucleotide polymorphism; PCR = polymerase chain reaction.

Primer extension reactions: The PCR products were then used as templates for primer extension reactions using the iPlex1 Gold reagent kit (Sequenom Inc.). The extension reactions were performed in 9 mL final volume, which contained 0.2 µL 10X iPlex Buffer plus, 0.2 µL iPlex terminator, 0.041 µL iPlex enzyme (Sequenom Inc.), 0.94 µL primer mix, and 0.619 µL nuclease free water. The extension reaction conditions were as follows: 94°C for 30 s, followed by 40 cycles of 94°C for 5 s, followed by 5 cycles of 52°C for 5 s and 80°C for 5 s and a final step of 72°C for 3 min. The samples were kept at 4°C until further analysis.

MALDI-TOF mass spectrometry (MS): Cleaned PCR products were spotted onto a MassARRAY SpectroCHIP with an auto-spot arm (Sequenom Inc.) and air-dried. The target plate was then inserted into the MALDI-TOF mass spectrometer of the MassARRAY Compact System (Sequenom Inc.), and the analysis was performed using 1800 nitrogen laser shots for each sample. The mass range of the MS instrument was set at 3920-12,023 Da.

## Statistical analysis

The data were analyzed with the statistical software package SPSS 17.0 (SPSS, Chicago, IL, USA). Quantitative variables are reported as means ± standard deviation, and differences among two groups were analyzed with an independent sample *t*-test. Qualitative variables are reported as percentages. Hardy-Weinberg equilibrium was assessed by $\chi^2$ analysis. Analyses of genotype and allele distributions were obtained using the $\chi^2$ test or single factor

logistic regression analysis. Haplotype analysis used the SHEsis software (http://analysis.bio-x.cn/SHEsisMain.htm). A P value < 0.05 was considered to be statistically significant.

## RESULTS

### Subject characteristics

According to inclusion and exclusion criteria, 500 subjects were selected for the research program, and experimental results of 487 people were completed. There was no difference in age, gender, body mass index (BMI), smoking, drinking, hypertension, or diabetes between the two groups. Serum TC, TG, LDL-C, and HDL-C levels were significantly different between dyslipidemia and control groups (P < 0.05). General data are shown in Table 2.

**Table 2.** Baseline characteristics of two goups.

| Characteristics | | Dyslipidemia (N = 241) | Control (N = 246) | Statistic | P |
|---|---|---|---|---|---|
| Gender (men/women, N) | | 130/111 | 118/128 | 1.739 | 0.187 |
| Age (years) | | 49.07 ± 0.74 | 48.31 ± 0.78 | 0.704 | 0.376 |
| BMI (kg/m$^2$) | | 24.25 ± 0.31 | 24.48 ± 0.29 | -0.540 | 0.590 |
| Smoker | Never (N) | 122 | 130 | | |
| | Past (N) | 51 | 34 | 4.910 | 0.086 |
| | Now (N) | 68 | 82 | | |
| Drinker | Never (N) | 95 | 120 | | |
| | Past (N) | 11 | 9 | 4.342 | 0.114 |
| | Now (N) | 135 | 117 | | |
| Hypertension (yes/no, N) | | 78/163 | 84/162 | 0.174 | 0.677 |
| Diabetes (yes/no, N) | | 28/213 | 21/225 | 1.278 | 0.258 |
| TG (mM) | | 3.07 ± 1.28 | 1.17 ± 0.44 | -15.090 | 0.001* |
| TC (mM) | | 6.60 ± 1.20 | 4.22 ± 0.71 | 26.704 | 0.001* |
| LDL-C (mM) | | 3.58 ± 1.09 | 2.65 ± 0.68 | 11.351 | 0.001* |
| HDL-C (mM) | | 1.21 ± 0.43 | 1.36 ± 0.40 | -4.965 | 0.001* |

BMI, body mass index. Continuous variables are reported as means ± SD. *P < 0.05 *vs* control, using the *t* test for continuous variables and $\chi^2$-test for categorical variables.

### Hardy-Weinberg equilibrium

We utilized the TYPER 4.0 software (Sequenom) to automatically output classification results. The observed allele frequencies for the Han Chinese population are presented in Figures 1-10. In the dyslipidemia and control groups, only rs2072560 deviated from Hardy-Weinberg equilibrium (P < 0.05).

### Genotype and allele frequencies

The genotype and allele frequencies observed for the dyslipidemia and control groups are presented in Table 3. Only four (*APOA5* rs651821, *APOA4* rs5104, *APOC3* rs734104, *APOC3* rs5128) SNPs showed differences in distributions between the two groups.

### Relationship between rs651821, rs5104, rs734104, rs5128, and dyslipidemia

For *APOA5* rs651821, the risks of dyslipidemia associated with carrying the CC or CC+CT genotypes were 9.917 or 1.859 times than of the TT genotype, respectively, and the

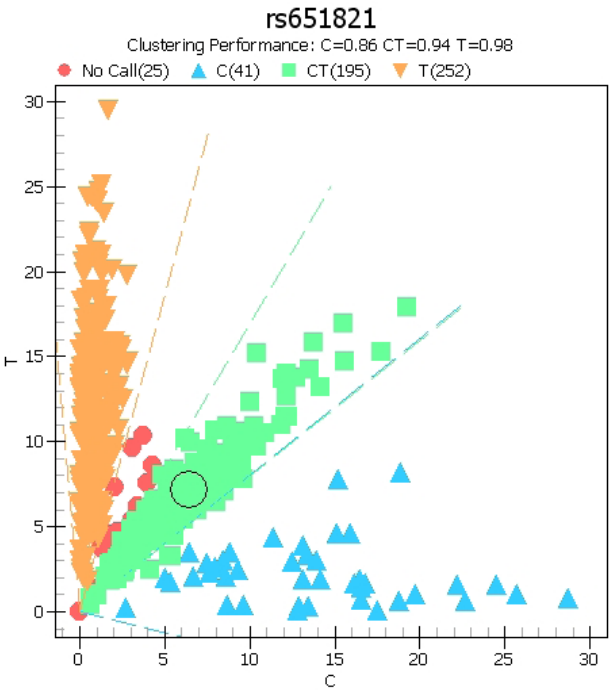


**Figure 1.** rs651821 scatter plot.

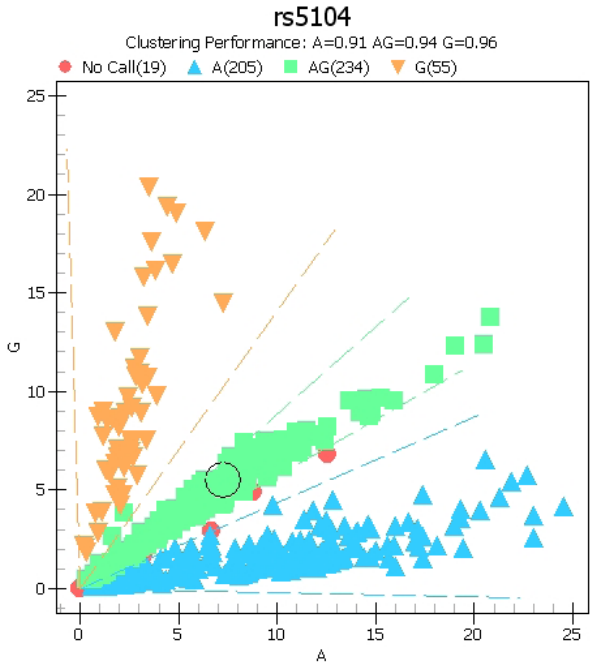


**Figure 2.** rs5104 scatter plot.

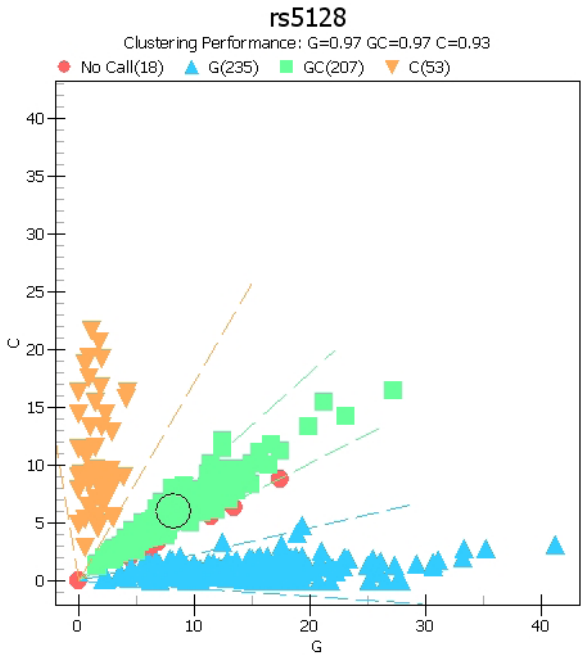


**Figure 3.** rs5128 scatter plot.

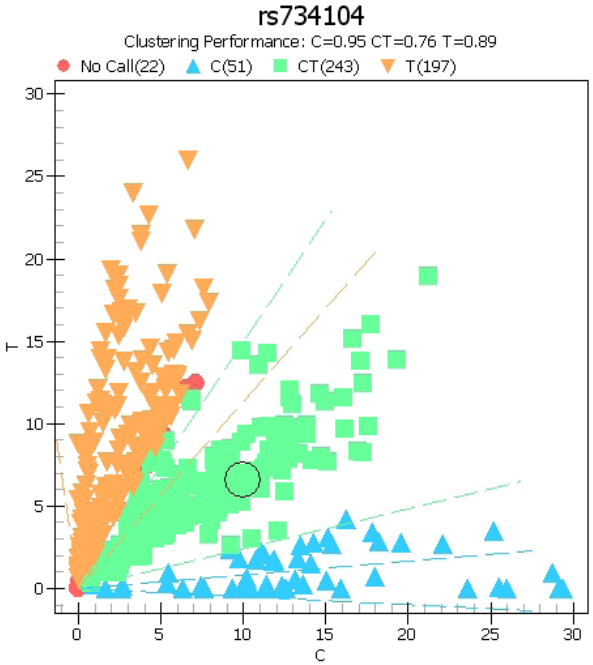


**Figure 4.** rs734104 scatter plot.

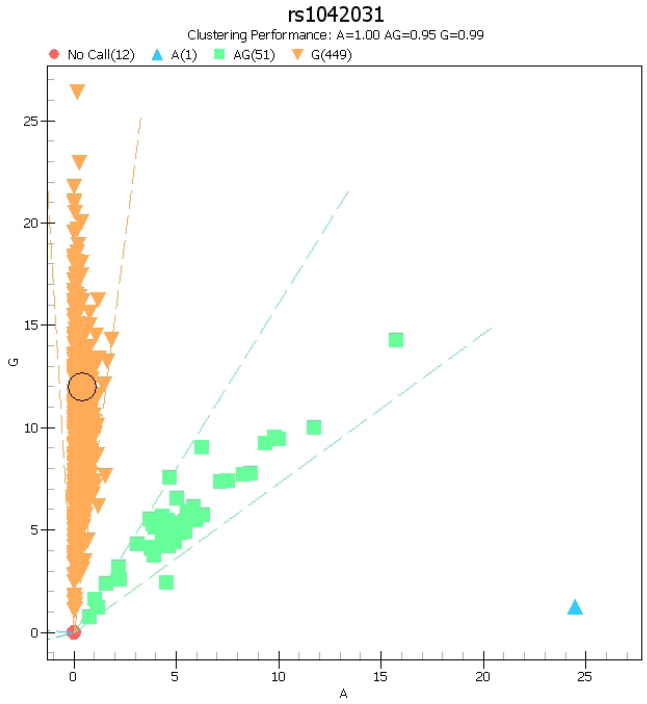


**Figure 5.** rs1042031 scatter plot.

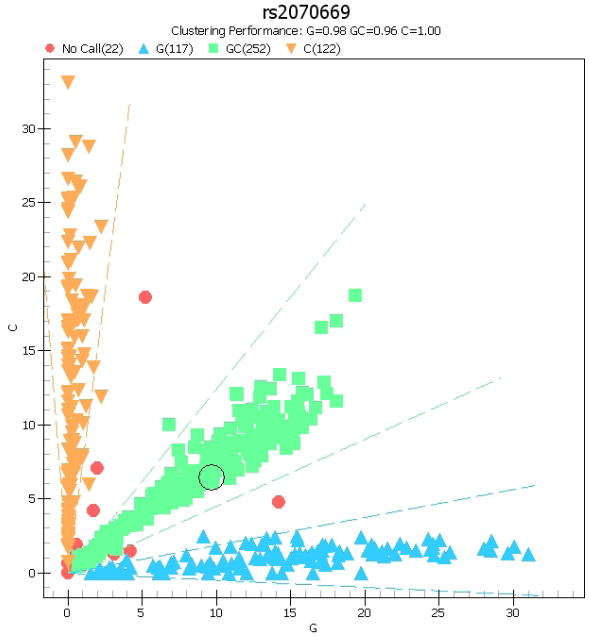


**Figure6.** rs2070669 scatter plot.

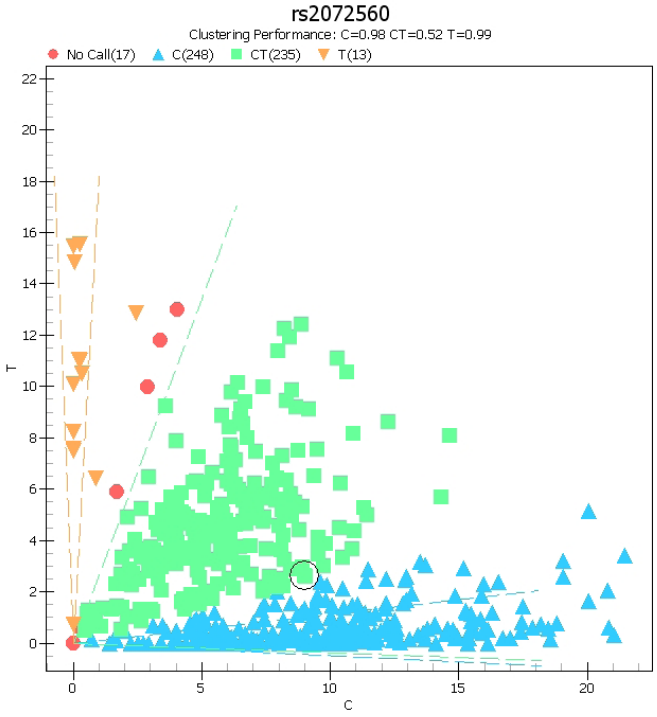


**Figure 7.** rs2072560 scatter plot.

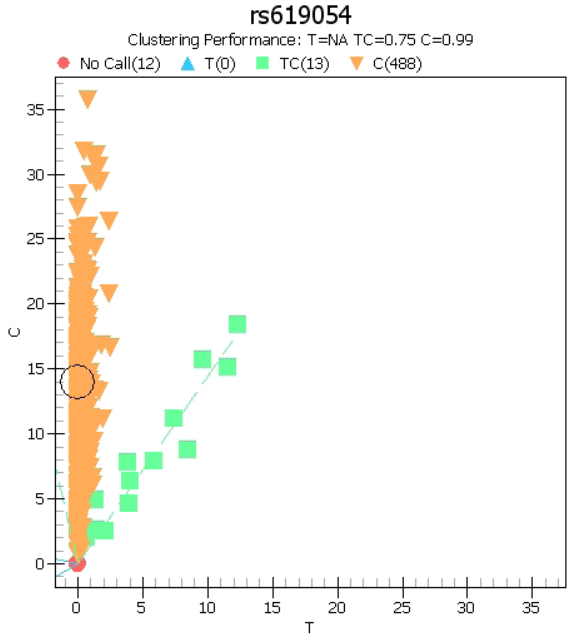


**Figure 8.** rs619054 scatter plot.

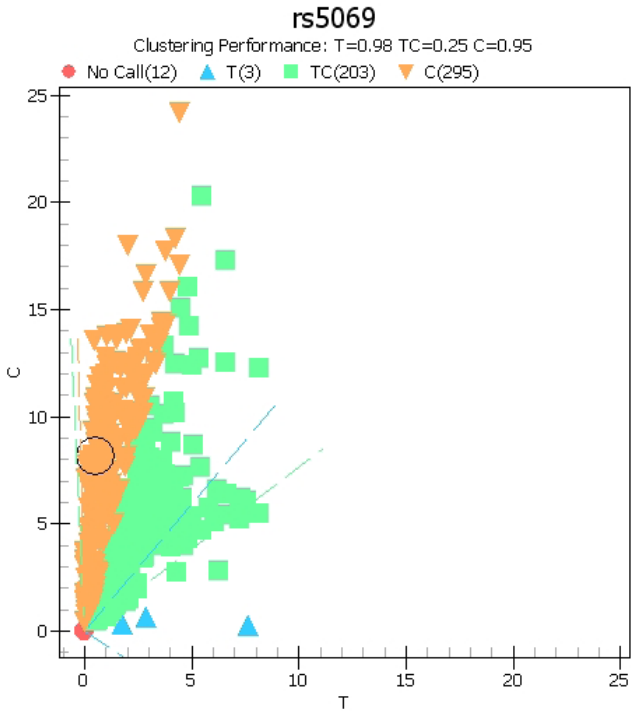


**Figure 9.** rs5069 scatter plot.

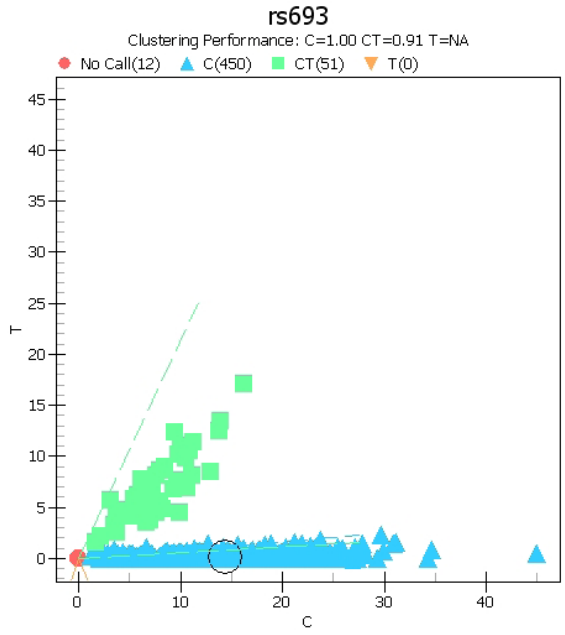


**Figure 10.** rs693 scatter plot.

risk of dyslipidemia for carriers of the C allele was 2.027 times that of the T allele. For *APOA4* rs5104, the risks of dyslipidemia for the AG, GG, or AG+GG genotypes were 1.797, 1.861 or 1.809 times that of the AA genotype, and the risk of dyslipidemia for the G allele was 1.427 times that of the A allele. For *APOC3* rs734104, the risks of dyslipidemia for the CT, CC, or CC+CT genotypes were 1.851, 2.570, or 1.958 times that of the TT genotype, and the risk of dyslipidemia from the C allele was 1.610 times that of the T allele. For *APOC3* rs5128, the risks of dyslipidemia for the GC or CC+GC genotypes were 1.738 or 1.749 times that of the GG genotype, and the risk of dyslipidemia for the C allele was 1.477 times that of the G allele (Table 4).

**Table 3.**Genotype and allele frequencies for dyslipidemia and control groups.

| SNP | | Dyslipidemia group | | Control group | | $\chi^2$ | P |
|---|---|---|---|---|---|---|---|
| | | N | Frequencies (%) | N | Frequencies (%) | | |
| rs651821 | TT | 106 | 43.98 | 146 | 59.35 | 29.823 | 0.001* |
| | CT | 99 | 41.08 | 95 | 38.62 | | |
| | CC | 36 | 14.94 | 5 | 2.03 | | |
| | T | 311 | 64.52 | 387 | 78.66 | 23.958 | 0.001# |
| | C | 171 | 35.48 | 105 | 21.34 | | |
| rs619054 | CC | 236 | 97.93 | 238 | 96.75 | 0.649 | 0.420 |
| | TC | 5 | 2.07 | 8 | 3.25 | | |
| | TT | 0 | 0.00 | 0 | 0.00 | | |
| | C | 477 | 98.96 | 484 | 98.37 | 0.641 | 0.423 |
| | T | 5 | 1.04 | 8 | 1.63 | | |
| rs5104 | AA | 84 | 34.85 | 121 | 49.19 | 10.272 | 0.006* |
| | AG | 126 | 52.28 | 101 | 41.06 | | |
| | GG | 31 | 12.87 | 24 | 9.75 | | |
| | A | 294 | 61.00 | 343 | 69.72 | 8.181 | 0.004# |
| | G | 188 | 39.00 | 149 | 30.28 | | |
| rs734104 | TT | 78 | 32.36 | 119 | 48.38 | 14.010 | 0.001* |
| | CT | 131 | 54.36 | 108 | 43.9 | | |
| | CC | 32 | 13.28 | 19 | 7.72 | | |
| | T | 287 | 59.54 | 346 | 70.33 | 12.439 | 0.001# |
| | C | 195 | 40.46 | 146 | 29.67 | | |
| rs2070669 | GG | 66 | 27.39 | 51 | 20.73 | 3.029 | 0.220 |
| | GC | 117 | 48.55 | 133 | 54.07 | | |
| | CC | 58 | 24.06 | 62 | 25.20 | | |
| | G | 249 | 51.66 | 235 | 47.76 | 1.478 | 0.224 |
| | C | 233 | 48.34 | 257 | 52.24 | | |
| rs5128 | GG | 96 | 39.83 | 132 | 53.66 | 9.355 | 0.009* |
| | GC | 115 | 47.72 | 91 | 36.99 | | |
| | CC | 30 | 12.45 | 23 | 9.35 | | |
| | G | 307 | 63.69 | 355 | 72.15 | 8.007 | 0.005# |
| | C | 175 | 36.31 | 137 | 27.85 | | |
| rs5069 | CC | 160 | 66.39 | 171 | 69.51 | 0.968 | 0.616 |
| | TC | 80 | 33.20 | 73 | 29.67 | | |
| | TT | 1 | 0.41 | 2 | 0.82 | | |
| | C | 400 | 82.99 | 415 | 84.35 | 0.331 | 0.565 |
| | T | 82 | 17.01 | 77 | 15.65 | | |
| rs693 | CC | 222 | 92.12 | 214 | 86.99 | 3.410 | 0.065 |
| | CT | 19 | 7.88 | 32 | 13.01 | | |
| | TT | 0 | 0.00 | 0 | 0.00 | | |
| | C | 463 | 96.06 | 460 | 93.50 | 3.221 | 0.073 |
| | T | 19 | 3.94 | 32 | 6.50 | | |
| rs1042031 | GG | 211 | 87.55 | 224 | 91.06 | 2.298 | 0.317 |
| | AG | 29 | 12.04 | 22 | 8.94 | | |
| | AA | 1 | 0.41 | 0 | 0.00 | | |
| | G | 451 | 93.57 | 470 | 95.53 | 1.818 | 0.178 |
| | A | 31 | 6.43 | 22 | 4.47 | | |

*P value shows genotype frequency differences in the distribution of the two groups. #P value shows allele frequency differences in the distributions of the two groups. SNP = single nucleotide polymorphism.

**Table 4.** Risk analysis of dyslipidemia.

| | | P | OR | 95%CI |
|---|---|---|---|---|
| rs651821 | TT | - | - | - |
| | CT | 0.060 | 1.435 | 0.985-2.092 |
| | CC | 0.001* | 9.917 | 3.766-26.715 |
| | CT+CC | 0.001* | 1.859 | 1.298-2.665 |
| | T | 0.001[#] | 2.027 | 1.524-2.695 |
| | C | | | |
| rs5104 | AA | - | - | - |
| | AG | 0.003[a] | 1.797 | 1.226-2.633 |
| | GG | 0.043[a] | 1.861 | 1.020-3.394 |
| | AG+GG | 0.001[a] | 1.809 | 1.257-2.604 |
| | A | 0.004[b] | 1.472 | 1.129-1.920 |
| | G | | | |
| rs734104 | TT | - | - | - |
| | CT | 0.002** | 1.851 | 1.262-2.713 |
| | CC | 0.004** | 2.570 | 1.361-4.851 |
| | CT+CC | 0.001** | 1.958 | 1.355-2.829 |
| | T | 0.001*** | 1.610 | 1.235-2.100 |
| | C | | | |
| rs5128 | GG | - | - | - |
| | GC | 0.004[c] | 1.738 | 1.188-2.542 |
| | CC | 0.058 | 1.793 | 0.981-3.279 |
| | GC+CC | 0.002[c] | 1.749 | 1.221-2.506 |
| | G | 0.005[d] | 1.477 | 1.127-1.936 |
| | C | | | |

rs651821, *Compared with TT, [#]C compared with T. rs5104, [a]Compared with AA, [b]G compared with A. rs734104, **Compared with TT, ***C compared with T. rs5128, [c]Compared with GG, [d]C compared with G. OR = odds ratio; CI = confidence interval.

**Table 5.** Haplotype analysis of dyslipidemia and control groups.

| Haplotype | Dyslipidemia group | | Control group | | $\chi^2$ | P | OR | 95%CI |
|---|---|---|---|---|---|---|---|---|
| | N | % | N | % | | | | |
| TATG | 195 | 40.45 | 293 | 59.55 | - | - | - | - |
| CGCC | 81 | 16.80 | 50 | 10.16 | 19.998 | 0.001* | 2.434 | 1.638-3.168 |
| TGCC | 73 | 15.15 | 73 | 14.84 | 4.643 | 0.032* | 1.503 | 1.036-2.179 |
| CATG | 62 | 12.86 | 34 | 6.91 | 17.940 | 0.001* | 2.740 | 1.737-4.322 |
| TACC | 9 | 1.87 | 5 | 1.02 | 3.339 | 0.078 | 2.705 | 0.893-8.191 |
| TGTG | 6 | 1.24 | 9 | 1.83 | 0.000 | 0.997 | 1.002 | 0.351-2.859 |
| CGCG | 4 | 0.83 | 10 | 2.03 | 0.738 | 0.395 | 0.601 | 0.186-1.943 |
| TATC | 4 | 0.83 | 5 | 1.02 | 0.074 | 0.786 | 1.202 | 0.319-4.532 |

TATG: rs651821T, rs5104A, rs734104T, rs5128G. CGCC: rs651821C, rs5104G, rs734104C, rs5128C. TGCC: rs651821T, rs5104G, rs734104C, rs5128C. CATG: rs651821C, rs5104A, rs734104T, rs5128G. TACC: rs651821T, rs5104A, rs734104C, rs5128C. TGTG: rs651821T, rs5104G, rs734104T, rs5128G. TATG: rs651821T, rs5104A, rs734104T, rs5128G. TATG: rs651821T, rs5104A, rs734104T, rs5128G. CGCG: rs651821C, rs5104G, rs734104C, rs5128G. TATC: rs651821T, rs5104A, rs734104T, rs5128C. *Compared with TATG. OR = odds ratio; CI = confidence interval.

## Haplotype analysis

To examine the combined effect of the four SNPs (in the order of rs651821, rs5104, rs734104, and rs5128) in dyslipidemia, we conducted haplotype analysis with these SNPs on the serum lipid traits shown in Table 5. There were 16 haplotypes in our population. We combined the eight haplotypes with frequencies less than 4 into one group; the other eight

haplotype analyses are shown in Table 5. The risks of dyslipidemia with the CGCC [odds ratio (OR) = 2.434], TGCC (OR = 1.503), or CATG (OR = 2.740) haplotypes were significantly higher than that of the wild-type haplotype TATG ($P < 0.05$).

## DISCUSSION

Recently, researchers across the world have examined the relationship between single SNPs in the *APOA5*/*A4*/*C3*/*A1* gene cluster or the *APOB* gene and dyslipidemia, but the results have not been completely compatible.

Tan et al. (2012) found that the rs651821 C allele frequency was 27% in Han male of Guigang, China. The result of this study suggested that the C allele presented a risk factor for dyslipidemia; these results were consistent to those from our research study. Our results suggested that the rs651821 C allele frequencies in the dyslipidemia and control groups were 35.48 and 25.34%, respectively, and that the C allele posed a risk factor for dyslipidemia, as the risk incidence increased 2.027 times in individuals carrying the C allele. Brautbar et al. (2011) found that the rs651821 C allele frequency was 9% in 2228 patients with mixed dyslipidemia in the United States; this finding was inconsistent with our results, most likely due to racial diversity between studies.

Liu et al. (2009) found that the rs5104 G allele frequency was 13% in a population of European descent, and that this allele was associated with serum TG levels. We found that the rs5104 G allele frequencies were 39 and 30.28% in the dyslipidemia and control groups, respectively, and that the risk incidence increased 1.861 times in individuals with the GG genotype.

In 553 Inuit people, Rudkowska et al. (2013) found that the rs5128 C allele frequency was 56.05%; however, we found that the rs5128 C allele frequency was 36.31%. Bhanushali and Das (2010) found that rs5128 was associated with dyslipidemia from a study in the Indian population. The result of our research were identical to theirs. We suggest that the detected allele frequencies differed as a result of different ethnic groups, but that the effects on blood lipid mechanism is likely to be consistent.

Worldwide, there have been few reports about the correlation of rs734104 C alleles and dyslipidemia. It is therefore very important and necessary to examine many SNPs, and especially to perform haplotype analysis to determine the association of the APO genes with dyslipidemia. Relative to the results obtained from examination of a single SNP, the relationships detected between haplotypes and blood lipids appear to be stronger and of higher significance.

This study found that the relative risk of dyslipidemia associated with the CGCC, TGCC, and CATG haplotypes was particularly high. Considering that only rare reports exist regarding the correlation of these haplotypes with dyslipidemia, further research should be performed in this area and on different populations.

### Conflicts of interest

The authors declare no conflict of interest.

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