A genetic variant in the promoter of lncRNA MALAT1 is related to susceptibility of ischemic stroke

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Abstract

Metastasis-associated lung adenocarcinoma transcript-1 (MALAT1) was aberrantly expressed in diverse diseases including ischemic stroke (IS). This study aimed to investigate the association between MALAT1 polymorphism and IS risk. We performed the genotyping of rs600231, rs1194338, rs4102217 and rs591291 in the promoter of MALAT1 by SNPscan method. Quantitative PCR was used to determine the levels of MALAT1 relative expression. We found the rs1194338 C>A variant in MALAT1 promoter was associated with IS risk (AC vs. CC: adjusted OR = 0.623, 95% CI, 0.417-0.932, P = 0.021; AA vs. CC: adjusted OR = 0.474, 95% CI, 0.226-0.991, P = 0.047; AC/AA vs. CC: adjusted OR = 0.596, 95% CI, 0.406-0.874, P = 0.008; A vs. C adjusted OR = 0.658, 95% CI, 0.487-0.890, P = 0.007). The IS patients showed higher expression levels of MALAT1 compared with the control group ($P < 0.05$), but patients with AC/AA genotypes of rs1194338 have no significant difference compared to CC genotype ($P > 0.05$). In addition, no significant differences were observed in blood lipid levels among SNPs of MALAT1 ($P > 0.05$). These results suggest that the rs1194338 AC/AA genotypes may be a protective factor for IS, which mechanism needs to be further explored.

Introduction

Stroke is a nervous system disease caused by cerebral blood circulation disorder and brain tissue damage with high fatality, disability and recurrence rate worldwide. Stroke has become the first cause of death In China, along with approximately 2.5 million new cases and 1.5 million deaths each year [1, 2]. The ischemic stroke (IS) accounts for about 87% of total cases [3]. Therefore, it is urgently required to explore etiology for meaningful targets. As we all known, the IS was a multifactorial complex disease. Traditional factors such as age, gender, obesity, hypertension, diabetes and smoking can only explain part of the IS risk [4-7]. Twins, familial aggregation and genome-wide association studies (GWAS) revealed that heredity was also a powerful factor in progression of IS [8-12].

Long non-coding RNAs (lncRNAs), with a length of more than 200 nucleotides, are emerging as key regulators of physiological and pathological processes [13-15]. Using RNA sequencing technology, a lot of lncRNAs were abnormally expressed after 16h under oxygen-glucose deprivation (OGD) condition [16]. MALAT1, one of the most highly upregulated lncRNAs, was further confirmed to promote angiogenesis and autophagy while reduce apoptosis and inflammation both in vitro and in vivo [17-19]. For example, MALAT1 reduced ischemic cerebral damages by regulating 15-LOX1, VEGF and STAT3 related to angiogenesis[17], and acting a competing endogenous RNA for miR-26b to upregulate autophagy factor ULK2 expression directly [18]. Silencing of MALAT1 obviously increased expression of the proapoptotic and proinflammatory cytokines including Bim, IL-6, MCP -1and E-selectin [19]. Taken together, MALAT1 may plays a protective role in IS, but the exact mechanism is still not fully known.

Currently, single nucleotide polymorphism (SNP) of lncRNAs have been proved to be associated with IS susceptibility, such as the rs217727 C>T and rs4929984 C>A in lncRNA H19, the rs2240183 C allele in promoter of lncRNA TUG1 [20-22]. It was reported that genetic variants in the promoter region can affect

disease occurrence by involving in transcription efficiency, genetic stability and function [23, 24]. At the same time, studies also showed that polymorphisms in MALAT1 affect susceptibility and progression of some diseases [25-27], but the impacts on IS have rarely been explored. To date, no study was conducted for the SNPs (rs600231, rs1194338, rs591291 and rs4102217) in promoter of MALAT1 with IS risk. Given the above, we performed SNPs of MALAT1 gene from 636 samples (320 controls and 316 IS patients) in Chinese southwestern population, attempting to identify new candidates for the etiology of IS.

Methods

Study population

A total of 316 patients with IS and 320 controls were consecutively recruited from the Affiliated Hospital of Youjiang Medical University for Nationalities, Guangxi, China, between March 2015 and July 2018. All subjects were native people living in Guangxi province who were unrelated with Han Chinese. The IS patients were diagnosed based on clinical manifestations, physical examination and cranial computed tomography (CT) or magnetic resonance imaging (MRI). Exclusion criteria were as follows: hemorrhagic stroke, craniocerebral trauma, cardiogenic thrombosis and tumors. Controls matched the cases at the age and gender frequency were selected from the hospital's health care center during the same period. Individuals with autoimmune diseases, liver diseases, genetic diseases, blood disorders and tumors were excluded. The clinical data such as age, gender, hypertension, diabetes, smoking status, total cholesterol (TC), triglyceride (TG) , high-density lipoprotein cholesterol (HDL-C), low-density lipoprotein cholesterol (LDL-C), apolipoprotein A1 (Apo-A1), apolipoprotein B (Apo-B) and non-esterified fatty acid (NEFA) were collected from our medical records. The interval time was within 24 hours between IS onset and biochemical test.

SNPs selection

The selection criteria for SNP are as follows: (i) tagSNPs in lncRNA MALAT 1; (ii) in silico analysis predicted potentially functional SNPs in the promoter region of MALAT1; (iii) the frequency of minor allele > 5% in Chinese Han population. Finally, four SNPs of rs600231 A>G, rs1194338 C>A, rs4102217 G>C and rs591291 C>T were selected for further analysis.

Genotyping

Genomic DNA was extracted from peripheral blood mononuclear cells by a salting-out method. About 3-5ml blood samples was taken into ethylene diamine tetra acetic acid (EDTA) tubes from each subject before treatment. Genotyping was performed on an ABI 3500 Genetic Analyzer (Applied Biosystems, CA, USA) using the custom-by-design 86-Plex SNPscan kit (Genesky Biotechnologies Inc, Shanghai, China). Genotypic primers for rs600231, rs1194338, rs4102217and rs591291 were showed in Table1. Meanwhile, about 10% of all samples were selected at random for Sanger sequencing and reached a 100% consistent rate.

Quantitative PCR (qPCR)

The relative expression of lncRNA MALAT1 was measured using qPCR among 40 IS patients and 40 normal controls. According to manufacturer's manual from a commercial kit (Takara, Beijing, China), qPCR was performed using SYBR Master Mix on the ABI 7500 real-time PCR machine (Applied Biosystems, CA, USA). The relative expression levels were calculated using the −ΔCT method.

Statistical analysis

The Student's t-test was used to compare continuous data (Mean ± SD) such as clinical data between IS cases and controls. The chi-squared test was chosen to analyze Hardy-Weinberg equilibrium (HWE) and categorical data (proportions) such as sex, hypertension, diabetes mellitus and smoker data. Logistic regression was used to assess the risk of IS by odds ratios (OR), 95% confidence intervals (CIs) and *P* value after adjustment of age, gender, diabetes mellitus, hypertension, smoker, TC, TG, HDL-C, LDL-C, Apo-A1, Apo-B and NEFA. Linkage disequilibrium (LD) and haplotype analysis were carried out by SHEsis software (http://analysis.bio-x.cn/myAnalysis.php). The SPSS statistical software package version 20.0 (SPSS, Chicago, USA) was used for all of the statistical analysis. $P < 0.05$ was considered as significant statistically.

Results

Characteristics of the study population

The results are exhibited in Table 2. No significant difference was observed in distributions of age and gender between cases and controls. The frequencies of hypertension, diabetes mellitus and smoker in IS patients were obviously higher than those in controls ($P < 0.05$). In addition, IS patients displayed higher levels of TC, TG, LDL-C and Apo-B while lower levels of HDL-C, Apo-A1, and NEFA (all $P < 0.05$).

Association of MALAT1 polymorphisms with IS risk

The analysis of SNPs of MALAT1 for IS risk are revealed in Table 3. The genotype distributions in controls conformed to HWE ($P = 0.780$ for rs600231, $P = 0.858$ for rs1194338, $P = 0.569$ for rs4102217, $P = 0.582$ for rs591291). Among these SNPs of MALAT1 , a decrease risk of IS was associated with the rs1194338 AC, AA and AC/AA genotype along with adjusted OR of 0.623, 0.474 and 0.596 respectively (AC vs. CC: 95% CI, 0.417-0.932, $P = 0.021$; AA vs. CC: 95% CI, 0.226-0.991, $P = 0.047$; AC/AA vs. CC: 95% CI, 0.406-0.874, $P = 0.008$). Similarly, IS risk of carriers with A allele was reduced than C allele (AOR = 0.658, 95% CI, 0.487-0.890, $P = 0.007$). No significant association was found between other SNPs (rs600231, rs4102 217, rs591291) and IS risk.

Haplotype analysis of the MALAT1 gene

To further estimated the association between MALAT1 polymorphism and IS risk, we performed Haplotype analysis. LD analysis showed that the rs600231 was in strong linkage disequilibrium (LD) with

rs591291 (D'= 0.94, r^2 = 0.83). As summarized in Table 4, possible four haplotypes were listed, rs600231-rs1194338-rs4102217-rs591 291 (A-C-G-C) haplotype had a 1.3-fold increase of IS risk (95% CI, 1.029-1.644, *P* = 0.028).

Multivariate logistic regression analysis

As shown in Table 5, the rs1194338 AC/AA affect the IS risk together with blood lipid index. The specific data were as follows: TC (OR = 1.607; 95%CI, 1.356-1.903), TG (OR = 1.482; 95%CI, 1.242-1.770), HDL-C (OR = 0.020; 95%CI, 0.010-0.040), LDL-C (OR = 2.181; 95%CI, 1.764-2.697), Apo-A1 (OR = 0.006; 95%CI, 0.002-0.013), Apo-B (OR = 23.315; 95%CI, 11.576-46.959), NEFA (OR = 0.092; 95%CI, 0.048-0.177) and rs1194338AC/AA (OR = 0.632; 95%CI, 0.461-0.865) (all $p < 0.05$).

The SNPs of MALAT1 and blood lipid levels analysis

The analysis was performed between the MALAT1 polymorphisms and blood lipid levels of cases (Table 6). Unfortunately, no evidence of association was observed between SNPs of MALAT1 and clinical blood lipid levels ($P > 0.05$).

MALAT1 expression levels analysis

The results revealed that patients with IS had a higher expression of MALAT1 than normal controls ($P < 0.001$), which suggested that MALAT1 might be a key in the pathogenesis of IS (Figure 1). However, regarding to the levels of MALAT1 expression, no significant difference was found between AC/AA and CC genotype of rs1194338 ($p = 0.206$).

Discussion

In the current study, main findings are listed as blow. Firstly, MALAT1 rs1194338 A allele, AA, AC genotype and the dominant model were associated with decreasing IS risk (Table 3). Secondly, the IS patients had a higher expression of lncRNA MALAT1 than controls, but did not find significant expression difference between the AC/AA and CC genotype of rs1194338 (Figure 1). In the clinical characteristics study, blood lipids levels were significantly different between controls and IS patients (Table 2). Unfortunately, there were no obvious differences in blood lipid levels of the rs1194338 SNPs in IS group (Table 6). Hence, analysis of rs1194338 may reveal the roles of MALAT1 in the etiology of IS in the future.

MALAT1, an 8.1 kb lncRNA, located on human chromosome 11q13. In 2003, Ji et al discovered firstly and named from tumor cells of patients with early stage non-small cell lung cancer [28]. New evidences show that MALAT1 participated in alternative splicing, transcriptional regulation, epigenetic modification, and aroused gradually interest in cancer and other diseases [29-32]. In atherosclerosis (AS), MALAT1 regulated the number and function of inflammatory cells and relieved persistent inflammation [33, 34]. Generally, the AS is considered to be the pathological basis of IS, thus the above results supported anti-inflammatory effect of MALAT1 on IS. In addition, cumulative studies have shown that MALAT1 was

obviously increased under hypoxia and regulated proliferation and migration of endothelial cells. Especially, MAlAT1 inhibition significantly lowered the expression of endothelial cyclins CCNA2 and CCNB1/2, all of which are important in the S-phase of cell cycle [35, 36]. Notably, animal model showed that mice with knocking down of MALAT1 had larger brain infarct size, lower neurological scores and damaged sensorimotor functions [19]. The above indicates that MALAT1 plays an important role in ischemic stroke.

The ischemic stroke is one of diseases threatening human health, which underlying mechanism are less well understood. Actually, increasing association studies focused on SNPs of lncRNA involved in process of IS. For example, the rs2240183 C allele of lncRNA TUG1 was associated with a higher risk of IS possibly by binding to GATA-1 and elevating TUG1 levels [20], the ANRIL rs2383207 increased the risk of IS by 1.52-fold under the recessive mode [21], the rs217727 TT and rs4929984 AA in the H19 increase the risk of IS, with adjusted OR 4.288, 3.020 respectively [22]. Those provide a new perspective on the genetic mechanism of IS. Thus, we hypothesized that the MALAT1 gene polymorphism is associated with IS risk. Our results supported the above assumptions. As shown in Table 3, case-control studies indicated the rs1194338 A allele, AC and AA genotype of MALAT1 contributed to the decrease of IS susceptibility, and A-C-A-G haplotype increased IS risk (Table 4). logistic regression also validated effect of the rs1194338 AC/AA for IS risk (Table 5).

The rs1194338, a functional site, located in the promoter region of the MALAT1. Recently, several studies reported the relationship between rs1194338 variant and human diseases. Zhao et al found carriers with AA and AC genotype of the rs1194338 were lower risk of colorectal cancer (CRC) than CC genotype [37]. In addition, the study from Li et al also confirmed the rs1194338 polymorphism (C>A) was significantly associated with a reduced risk of CRC, which is more obvious protection in the subgroup. Further analysis showed that although MALAT1 was over-expressed in CRC tissues, the expression difference was not significant between CC and AA genotype of rs1194338 in CRC tissues[38]. Similar to Li's study, we observed the expression of the MALAT1 in IS group was higher significantly than normal group, but expression difference between the AC/AA and CC genotype were not significant (figure 1). It was reported that MALAT1 can serve as miRNA sponges influencing the expression level, structure, function, and ultimately affect disease progression [39, 40]. Whether rs1194338 C>A binding directly to miRNA affect risk of IS needs to be further investigated. Collectively, our study indicated firstly that the rs1194338 C>A variant in the promoter of MALAT1 has a reduced risk for IS, the underlying mechanisms need to be further explored.

Studies on rs600231 polymorphism (A>G) with disease have not been reported, but rs4102217 was evaluated in hepatocellular cancer (HCC), with1.32-fold risk in the dominant model. In addition, rs591291 highlighted better prognosis in female and HBV negative subgroups. The association between MALAT1 haplotype (rs4102217-rs591291-rs11227209- rs619586) and HCC risk were not found [25]. In contrast to HCC, we found that A-C-A-G (rs600231-rs1194338-rs4102217-rs591291) haplotype had a 1.3-fold IS risk (Table 4) although SNPs (rs600231, rs4102217, rs591291) did not correlate with IS susceptibility. A recent result indicated that interaction model (rs4102217 polymorphism- smoking-drinking) has higher

risk of coronary artery disease, and there was no obvious difference in TC, TG, HDL and LDL levels between G and C allele of rs4102217 [41]. Similarly, we did not observe MALAT1 polymorphism affect blood lipid levels. However, the above results suggest that interaction analysis of SNP-SNP, SNP-environment may take part in IS susceptibility, which need to be further investigated.

There are few limitations in our research. Firstly, a relatively small sample may limit the statistical analysis of our research. Secondly, there is distribution differences of polymorphism in different races according to the 1000 Genomes Project Data. The population we studied came from the southwest of China. It was a hospital-based case-control study, which may have a choice bias. Thirdly, there may be subtype specificity between SNPs and IS risk. Therefore, the results vary possibly among different races and ethnic groups.

In conclusion, it is just beginning that functional analysis of lncRNA MALAT1 for IS risk. Our study provides a link between rs1194338 of MALAT1 promoter region and IS risk, which help to identify the potential molecular mechanisms. In the future, large- scale samples study can be performed among ischemic stroke subtypes and different populations.

Declarations

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Availability of data and materials

The data used in our study are available from the authors on reasonable request.

Authors' contributions

Ye-Sheng Wei guided and participated in experiment. Yan Wang and Xi-Xi Gu designed and wrote the manuscript. Hua-Tuo Huang, Chun-Hong Liu helped to perform experiments. Gui-Jiang Wei performed the statistical analysis and figures. All authors reviewed the manuscript.

Ethics approval and consent to participate

The procedure was reviewed and approved by the Institutional Ethical Committee of the Affiliated Hospital of Youjiang Medical University for Nationalities, in accordance with the principles of the Helsinki Declaration. Each subject signed informed consent and agreed to make the data public.

Consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing.

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Tables

Table 1 The primer sequences used for detecting four SNPs of the MALAT1 gene

SNPs	allele A1	allele A2	universal primer
rs600231	5'-TGAAACCCAGCAGACAGGACT-3'	5'-TGAAACCCAGCAGACAGGACC-3'	5'-GTCACTTCACAGAGAGCTGAGGGC-3'
rs1194338	5'-GGCTCCAGGGCCGTAGATCAA-3'	5'-GGCTCCAGGGCCGTAGATCAC-3'	5'-GGATCTCTCAGAAGCTTGTCTCTTGA-3'
rs4102217	5'-CCTGCTGCCTCCCTTCCTGTG-3'	5'-CCTGCTGCCTCCCTTCCTGTC-3'	5'-CAGCACTTCTGTCAGTCTCTCCAA-3'
rs591291	5'-CCCTCACCCCCGGGTCTGTG-3'	5'-CCCTCACCCCCGGGTCTGTA-3'	5'-GAACCTGTATCCATGGCTTGTTTTT-3'

Table 2 Clinical characteristics of the study population

Variables	Controls, n=320	IS patients, n=316	*P* value
Age, years (Mean ± SD)	60.72 ± 10.77	62.23 ± 11.36	0.087
Gender (M / F)	204 / 116	216 / 100	0.220
Hypertension (%)	59 (18.4%)	126 (39.9)	< 0.001
Diabetes mellitus (%)	30 (9.4%)	50 (15.8%)	< 0.001
Smoker (%)	50 (15.6%)	98 (31.0%)	< 0.001
TCH (mmol/L)	4.19 ± 0.79	4.64 ± 1.16	< 0.001
TG (mmol/L)	1.37 ± 0.99	1.81 ± 1.31	< 0.001
HDL-C (mmol/L)	1.50 ± 0.31	1.13 ± 0.32	< 0.001
LDL -C (mmol/L)	2.39 ± 0.66	2.92 ± 0.98	< 0.001
Apo-A1(g/L)	1.73 ± 1.10	1.23 ± 0.26	< 0.001
Apo-B (g/L)	0.77 ± 0.31	1.00 ± 0.31	< 0.001
NEFA (mmol/L)	0.71 ± 0.30	0.53 ± 0.28	< 0.001

IS, ischemic stroke; SD, standard deviation; M, male; F, female; TC, total cholesterol; TG, triglyceride; HDL-C, high density lipoprotein-cholesterol; LDL-C, low density lipoprotein-cholesterol; Apo-A1, apolipoprotein A1; Apo-B, apolipoprotein B; NEFA, non-esterified fatty acid.

Table 3 Association between the MALAT1 polymorphisms and risk of IS

SNPs	Controls n=320(n%)	IS patient n=316(n%)	OR (95%CI)	*P* value	AOR†(95%CI)	*P*† value
rs600231						
AA	117 (36.6)	120 (38.0)	1.000 (ref)		1.000 (ref)	
AG	151 (47.2)	154 (48.7)	0.994 (0.708-1.396)	0.974	0.987 (0.651-1.496)	0.950
GG	52 (16.2)	42 (13.3)	0.788 (0.487-1.272)	0.329	0.778 (0.434-1.395)	0.399
Dominant			0.941 (0.683-1.298)	0.713	0.933 (0.629-1.386)	0.733
Recessive			1.266 (0.815-1.966)	0.294	1.276 (0.750-2.171)	0.369
A	385 (60.2)	394 (62.3)	1.000 (ref)		1.000 (ref)	
G	255 (39.8)	238 (37.7)	0.912 (0.728-1.143)	0.424	0.906 (0.688-1.192)	0.481
rs1194338						
CC	154 (48.1)	188 (59.5)	1.000 (ref)		1.000 (ref)	
AC	135 (42.2)	106 (33.5)	0.643 (0.462-0.896)	**0.009**	0.623 (0.417-0.932)	**0.021**
AA	31 (9.7)	22 (7.0)	0.581 (0.323-1.045)	0.070	0.474 (0.226-0.991)	**0.047**
Dominant			0.632 (0.461-0.865)	**0.004**	0.596 (0.406-0.874)	**0.008**
Recessive			1.433 (0.811-2.535)	0.216	1.721 (0.841-3.523)	0.137
C	443 (69.2)	482 (76.3)	1.000 (ref)		1.000 (ref)	
A	197 (30.8)	150 (23.7)	0.700 (0.546-0.897)	**0.005**	0.658 (0.487-0.890)	**0.007**
rs4102217						
GG	243 (75.9)	237 (75.0)	1.000 (ref)		1.000 (ref)	
CG	73 (22.8)	69 (21.8)	0.969 (0.666-1.409)	0.870	1.186 (0.753-1.868)	0.463
CC	4 (1.3)	10 (3.2)	2.563 (0.793-8.286)	0.116	2.322 (0.605-8.906)	0.219
Dominant			1.052 (0.733-1.510)	0.784	1.254 (0.807-1.947)	0.314
Recessive			0.387 (0.120-1.248)	0.112	0.452 (0.119-1.721)	0.244
G	559 (87.3)	543 (85.9)	1.000 (ref)		1.000 (ref)	
C	81(12.7)	89 (14.1)	1.131 (0.819-1.563)	0.455	1.280 (0.869-1.886)	0.212
rs591291						
CC	123 (38.5)	129 (40.8)	1.000 (ref)		1.000 (ref)	
CT	147 (45.9)	144 (45.6)	0.934 (0.667-1.309)	0.692	0.916 (0.607-1.384)	0.678
TT	50 (15.6)	43 (13.6)	0.820 (0.509-1.321)	0.414	0.752 (0.421-1.343)	0.336
Dominant			0.905 (0.659-1.244)	0.539	0.873 (0.592-1.289)	0.495
Recessive			1.176 (0.756-1.827)	0.472	1.268 (0.743-2.163)	0.384
C	393 (61.4)	402 (63.6)	1.000 (ref)		1.000 (ref)	
T	247 (38.6)	230 (36.4)	0.910 (0.725-1.142)	0.418	0.877 (0.665-1.155)	0.350

IS, ischemic stroke; OR, odds ratio; 95% CI, 95% confidence interval. †Adjusted by age, gender, hypertension, diabetes mellitus, smoker, TCH, TG, HDL-C, LDL-C, Apo-A1, Apo-B, NEFA.

Table 4 Haplotype analysis of the MALAT1 polymorphisms with risk of IS

Haplotype	Controls (n %)	IS (n %)	OR (95%CI)	*P* value
ACGC	351 (54.9)	373 (59.1)	1.301 (1.029-1.644)	**0.027**
GAGT	91 (15.3)	86 (13.6)	0.903 (0.659-1.238)	0.527
GACT	71(11.1)	57 (9.1)	0.822 (0.569-1.187)	0.296
GCGT	61(9.6)	62 (9.9)	1.076 (0.742-1.561)	0.699

IS, ischemic stroke; OR, odds ratio; 95% CI, 95% confidence interval. Only frequency greater than 1% is listed.

Table 5 Logistic regression analysis for independent factors of IS susceptibility

Variables	B	OR (95%CI)	*P* value
TC	0.47	1.607 (1.356-1.903)	**< 0.001**
TG	0.39	1.482 (1.242-1.770)	**< 0.001**
HDL-C	-3.89	0.020 (0.010-0.040)	**< 0.001**
LDL-C	0.78	2.181 (1.764-2.697)	**< 0.001**
Apo-A1	-5.193	0.006 (0.002-0.013)	**< 0.001**
Apo-B	3.149	23.315 (11.576-46.959)	**< 0.001**
NEFA	-2.389	0.092 (0.048-0.177)	**< 0.001**
rs1194338AC/AA	-0.459	0.632 (0.461-0.865)	**0.004**

TC, total cholesterol; TG, triglyceride; HDL-C, high density lipoprotein-cholesterol; LDL-C, low density lipoprotein-cholesterol; Apo-A1, apolipoprotein A1; Apo-B, apolipoprotein B; NEFA, non-esterified fatty acid.

Table 6 Association between the MALAT1 SNPs and Blood lipid levels in IS

SNPs	TC, mmol/L	TG, mmol/L	HDL-C, mmol/L	LDL-C, mmol/L	Apo-A1, g/L	Apo-B, g/L	NEFA, mmol/L
rs600231							
AA	4.65 ± 1.20	1.79 ± 1.34	1.13 ± .33	2.94 ± 1.03	1.23 ± 0.26	1.00 ± 0.32	0.53 ± 0.28
AG/GG	4.64 ± 1.08	1.83 ± 1.27	1.12 ± .31	2.88 ± 0.90	1.23 ± 0.25	1.00 ± 0.30	0.55 ± 0.28
t	0.090	-0.245	0.384	0.462	-0.138	0.007	-0.620
p	0.928	0.806	0.701	0.645	0.890	0.995	0.535
rs1194338							
CC	4.68 ± 1.11	1.79 ± 1.38	1.14 ± 0.32	2.94 ± 0.97	1.23 ± 0.23	0.99 ± 0.30	0.52 ± 0.27
AC/AA	4.62 ± 1.19	1.82 ± 1.27	1.12 ± 0.32	2.90 ± 0.99	1.23 ± 0.28	1.01 ± 0.31	0.54 ± 0.29
t	0.478	-0.170	0.519	0.434	-0.032	-0.382	0.498
p	0.633	0.865	0.604	0.664	0.974	0.703	0.619
rs4102217							
GG	4.52 ± 1.21	1.72 ± 1.20	1.12 ± 0.30	2.80 ± 0.99	1.21 ± 0.26	0.98 ± 0.30	0.55 ± 0.29
CG/CC	4.68 ± 1.14	1.83 ± 1.35	1.13 ± 0.33	2.96 ± .98	1.24 ± 0.26	1.01 ± 0.31	0.53 ± 0.28
t	-1.079	-0.677	-0.374	-1.274	-0.642	-0.861	0.562
p	0.281	0.499	0.708	0.204	0.522	0.390	0.574
rs591291							
CC	4.64 ± 1.22	1.82 ± 1.40	1.13 ± 0.33	2.93 ± 1.05	1.23 ± 0.27	1.00 ± 0.32	0.53 ± 0.28
CT/TT	4.63 ± 1.07	1.78 ± 1.19	1.12 ± 0.31	2.89 ± 0.88	1.24 ± 0.25	1.00 ± 0.29	0.54 ± 0.28
t	0.072	0.262	0.124	0.460	-0.447	0.083	-0.550
p	0.943	0.794	0.902	0.646	0.655	0.934	0.583

TC, total cholesterol; TG, triglyceride; HDL-C, high density lipoprotein-cholesterol; LDL-C, low density lipoprotein-cholesterol; Apo-A1, apolipoprotein A1; Apo-B, apolipoprotein B; NEFA, non-esterified fatty acid.

Figures

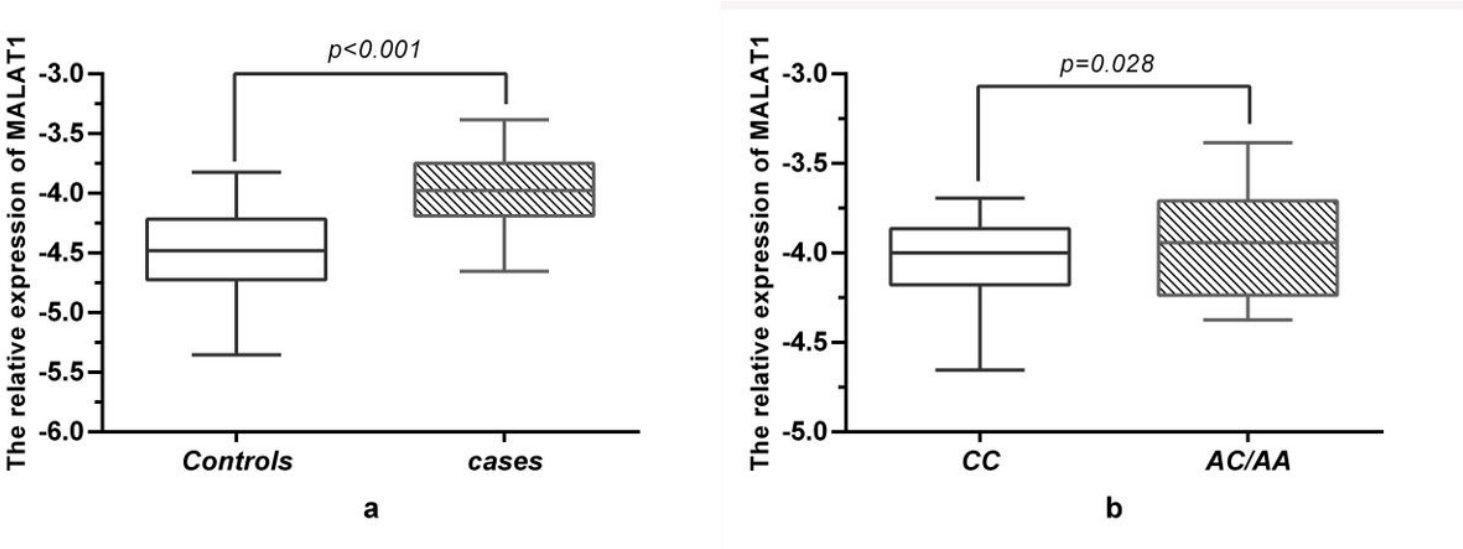

Figure 1

The relative expression of MALAT1 a, the expression of MALAT1 was higher in cases than controls (P < 0.001); b, the expression of MALAT1 was not significant between CC and AC/AA genotype of rs1194338 in cases (P = 0.028).