



Investigation of the monocyte diapedesis-related *LFA-1* and *JAM-A* gene variants in Turkish coronary heart disease patients[☆]



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ABSTRACT

Background: LFA-1/JAM-A interaction plays a significant role in early steps of leukocyte transendothelial migration (diapedesis) which takes part in atherosclerosis pathogenesis. In this population-based case–control study, the frequencies of JAM-A rs790056 and LFA-1 rs8058823 gene polymorphisms in patients with coronary heart disease (CHD) and healthy subjects were investigated and the correlations between the different genotypes and cardiovascular risk factors were analyzed.

Methods: The JAM-A and LFA-1 genotypes were determined in 153 patients with CHD and 124 controls by PCR–RFLP assay.

Results: In CHD patient group, the frequency of JAM-A rs790056 TT genotype and the frequency of T allele were higher when compared with the control group ($p = 0.03$ and $p = 0.007$, respectively). In patient groups, the frequency of LFA-1 rs8058823 AA genotype was higher ($p = 0.000$), and the frequency of AG genotype was lower when compared with the control group ($p = 0.031$). In the control group,

Abbreviations: JAM-A, junctional adhesion molecule-A; LFA-1, leukocyte function-associated antigen-1; CHD, coronary heart disease; BMI, body mass index; TC, total cholesterol; TG, triglyceride; LDL-C, low density lipoprotein cholesterol; HDL-C, high density lipoprotein cholesterol; VLDL-C, very low density lipoprotein cholesterol; SBP, systolic blood pressure; DBP, diastolic blood pressure; T2DM, type 2 diabetes mellitus; LVH, left ventricular hypertrophy; OR, odds ratio; CI, confidence interval; HWE, Hardy-Weinberg Equilibrium; PCR-RFLP, polymerase chain reaction–restriction fragment length polymorphism; SNP, single nucleotide polymorphism; 3'UTR, 3'-untranslated region.

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LFA-1 rs8058823 G allele carriers had higher SBP than subjects with AA genotype ($p = 0.038$), whereas in the CHD patient group, G allele carriers had lower DBP than subjects with AA genotype ($p = 0.007$). The multivariate logistic regression analysis confirmed that the JAM-A rs790056 TT genotype (OR = 2.472, $p = 0.045$) and LFA-1 rs8058823 AA genotype (OR = 6.751, $p = 0.000$) were risk factors for CHD development.

Conclusion: These results suggest that the wild type genotypes and alleles of JAM-A rs790056 (TT genotype and T allele) and LFA-1 rs8058823 (AA genotype and A allele) were found to be risk factors for CHD, whereas rare genotypes and alleles were found to be higher in healthy controls thus being protective.

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Introduction

Atherosclerosis is a progressive inflammatory disorder underlying coronary heart disease (CHD) and stroke [1]. Monocytes transmigrate to arterial intima and differentiate into macrophages in the early step of atherosclerosis. Macrophages take up modified forms of low density lipoproteins (LDL) (acetyl-LDL, oxidized-LDL) and transform into foam cells, which contribute to the formation of fatty streaks known as early lesion of atherosclerosis [2].

Diapedesis (transendothelial migration) is defined as passage of monocytes through capillary wall and their entry into the subendothelial space [3]. In atherosclerosis, local expression of key adhesion molecules may mediate the recruitment of mononuclear cells to the plaque. Among these molecules, intercellular adhesion molecule-1 (ICAM-1) is an immunoglobulin-like cell adhesion molecule expressed by several cell types including leukocytes and endothelial cells, and one of the ligands for LFA-1 has been suggested to play an important role in atherogenesis [4]. In the studies using ICAM-1 deficient cell, it was observed that the transmigration was not completely inhibited. This indicates that the ICAM-1 is involved in the transmigration but not the most necessary [5,6].

Also, junctional adhesion molecule (JAM-A) plays an important role in leukocyte transmigration. JAM-A also called JAM-1 or F11 receptor (F11R) is a member of immunoglobulin superfamily and is expressed on the surface of epithelial and endothelial cells, monocytes, platelets, lymphocytes, neutrophils, erythrocytes, macrophages and dendritic cells [7–10]. JAM-A takes part in the interaction of adjacent cells, transendothelial migration (diapedesis) of neutrophils and mononuclear cells [8,9,11] and platelet adhesion on activated endothelial surface [12]. Ostermann et al. reported that the JAM-A upregulated on early atherosclerotic endothelium and they suggested that it had an important role in the initiation of atherosclerosis [13]. In addition, Martin-Padura et al. reported that the leukocyte transmigration was inhibited by a monoclonal antibody against JAM-A [8]. Since JAM-A/LFA-1 interaction is essential at the onset of leukocyte transendothelial migration [7], these proteins are thought to play a significant role in atherosclerosis pathogenesis.

Leukocyte function-associated antigen-1 (LFA-1) that is also called $\alpha\text{L}\beta\text{2}$ integrin, CD11a/CD18 or ITGAL, is a $\alpha\beta$ heterodimeric transmembrane glycoprotein expressed on the surface of leukocytes [14]. α subunit of LFA-1 (CD11a) has an N-terminal I-domain consisted of approximately 200 amino acid residues [15,16] which contains a binding site for JAM-A [17]. LFA-1 is expressed on the surface of the migrating leukocyte. During transendothelial migration, it binds to membrane-proximal Ig domain 2 (D2) of JAM-A and weakens JAM-A homophilic interaction. Weakened JAM-A homophilic interaction is disrupted and stronger LFA-1/JAM-A interaction establishes. In this way, leukocyte proceeds down the endothelial junction and transmigrates to intima [18].

Significant amounts of JAM-A protein and JAM-A mRNA were detected in atherosclerotic plaques and atherosclerotic animal models, this indicates that JAM-A involves in atherosclerosis pathogenesis [19]. There are few studies on the effects of JAM-A and LFA-1 gene variations on disease development risk and metabolic parameters [20,21]. Ong et al. [20] analyzed rs790056 T>C variation of JAM-A gene in subjects who had no anti-hypertensive medication, and found that C allele carriers had lower systolic blood pressure when compared to subjects with TT genotype. Fu et al. [21] analyzed rs8058823 A>G variation of

LFA-1 gene in Chinese women with sporadic infiltrative duct breast carcinoma, and found that AA genotype and A allele frequency were significantly lower in patients; whereas AG genotype was significantly higher in patient group. As of now, there is no study investigating individual and combined effects of JAM-A and LFA-1 gene variations in atherosclerotic heart diseases. Thus, the aim of this study was to investigate the association between JAM-A and LFA-1 gene variants and CHD.

Materials and methods

Patients selection

We investigated the JAM-A rs790056 variation and LFA-1 rs8058823 variation in 153 patients diagnosed with CHD who were in the follow-up of Istanbul University, Istanbul Faculty of Medicine, Department of Cardiology and 124 healthy controls. Because coronary angiography was not performed on these individuals, the presence of atherosclerotic coronary arteries could not be excluded. However, none of these individuals had any history of vascular event. All subjects were subjected to full history of questioning with special emphasis on coronary risk factors including smoking, family history of coronary heart disease, hypertension, diabetes mellitus and hyperlipidemia.

The patients with severe coronary vascular disease were documented by angiography. Angiographic inclusion criteria were, 50% stenosis of at least one major coronary vessel caused by atherosclerosis, and a vascular event, defined as myocardial infarction, percutaneous transluminal coronary angioplasty, or coronary artery by-pass grafting.

The study protocol was approved by both the Ethical Committee of the Istanbul Faculty of Medicine and The Scientific Research Projects Coordination Unit of Istanbul University. The protocol followed was consistent with the World Medical Association Declaration of Helsinki "Ethical Principles for Medical Research Involving Human Subjects". All participants received medical approval from their personal physicians and gave written, informed consent prior to giving their blood sample.

Genotyping

Peripheral blood samples were collected in tubes containing EDTA and genomic DNA samples were extracted with DNA extraction kit according to the kit procedures (Roche High Pure PCR Template Preparation Kit). Polymerase chain reaction–restriction fragment length polymorphism (PCR–RFLP) protocols were performed to detect rs790056 variation (in intron 6 T>C) of the JAM-A gene and rs8058823 variation (in 3'-UTR A>G) of the LFA-1 gene. Primer sequences used for PCR to amplify JAM-A gene fragment containing rs790056 variation were forward 5'-GCAGTACAAAGGAGAGCCTCT-3' and reverse 5'-TGGGACACCCATGACTTCA-3'. To amplify LFA-1 gene fragment containing rs8058823 variation primer sequences were forward 5'-CAGCTCACGTACACTTGGT-3' and reverse 5'-CCACGCTGGATTTTGTATT-3' [21]. PCR amplifications were performed in a thermal cycler (Applied Biosystems). PCR reactions were carried out with a total volume of 25 µl containing 150–200 ng genomic DNA, 10× Taq buffer (with KCl) (Fermentas), 25 mM MgCl₂ (Fermentas), 1 mM dNTPs (Fermentas), 50 pmol/µl of each primer, and 1.5 U Taq DNA polymerase (Fermentas). Thermal conditions for amplification of both JAM-A and LFA-1 gene fragments consisted of an initial denaturing step of 5 min at 94 °C followed by 30 cycles of denaturation at 94 °C for 45 s, annealing at 59 °C for 45 s and extension at 72 °C for 45 s with a final extension step for 5 min at 72 °C. The lengths of PCR products were 314 bp (rs790056) and 437 bp (rs8058823). The PCR products were digested with restriction endonucleases (KpnI (Fermentas) for rs790056 and BspHI (Fermentas) for rs8058823). Restriction fragments were separated by agarose gel electrophoresis, stained with ethidium bromide and visualized under UV light. In rs790056, restriction fragments were 195 and 119 bp with T allele and 314 bp with C allele. In rs8058823, restriction fragments were 232 and 205 bp with A allele and 437 bp with G allele.

Statistical analysis

Statistical analysis were performed using SPSS software for Windows, version 13.0. Allele frequencies were calculated by using gene counting method. The difference in the occurrence of the JAM-A rs790056

and LFA-1 rs8058823 genotypes in the case and control groups was evaluated with chi-square test. In order to determine the relative risks, odds ratios and 95% confidence intervals were used. Comparison of clinical and non-clinical parameters with alleles was performed with chi-square test and Student's *t* test. ANOVA test was used in the comparison of genotypes and in the case of more than two variables. Haploview program was used to determine linkage disequilibrium between variations and haplotype analysis [22]. Multivariate logistic regression analysis was performed between CHD risk factors with significance of $p < 0.05$ and then a p value less than 0.05 was considered to be statistically significant.

Results

Clinical investigation

There was no significant difference between the study groups in terms of age and sex distributions ($p > 0.05$). Smoking habit ($p = 0.000$; odds ratio (OR): 3.681 (95% CI): 2.093–6.472), DBP ($p = 0.003$), TC ($p = 0.003$), LDL-C ($p = 0.046$) and TC ≥ 5.18 mmol/L (%) ($p = 0.026$) were found to be higher in CHD patients than the control group, while HDL-C was found to be lower than the control group ($p = 0.007$).

In the control group, SBP ($p = 0.003$), DBP ($p = 0.011$), BMI ($p = 0.045$), HDL-C ($p = 0.000$) and ve BMI ≥ 27 kg/m² (%) ($p = 0.001$) were higher in women than in men; while HDL-C ≤ 0.90 mmol/L (%) ($p = 0.005$) was lower in women than in men.

In the CHD patients, BMI ($p = 0.05$), LDL-C ≥ 3.36 mmol/L (%) ($p = 0.03$), and prevalences of type 2 diabetes and hypertension ($p = 0.000$ and $p = 0.004$, respectively) were higher in women than in men, while smoking habit ($p = 0.000$) and alcohol use ($p = 0.014$) were lower in women than in men (Table 1).

JAM-A rs790056 and LFA-1 rs8058823 genotypes and allele distribution

In CHD patient group, the frequency of JAM-A rs790056 normal TT genotype ($p = 0.03$; OR: 1.33 (95% CI: 1.030–1.718) and the frequency of T allele ($p = 0.007$; OR: 3.041 (95% CI: 1.294–7.148) were higher when compared with the control group. The frequency of LFA-1 rs8058823 normal AA genotype ($p = 0.000$; OR: 2.842 (95% CI: 1.815–4.449) and the frequency of A allele ($p = 0.000$) were found to be higher than the control group; while the frequency of heterozygous AG genotype ($p = 0.031$; OR: 0.848 (95% CI: 0.728–0.987) and the frequency of mutant G allele ($p = 0.000$; OR: 0.602 (95% CI: 0.489–0.742) were higher in the control group than the CHD patient group. There was no mutant GG genotype in the CHD patient group.

No significant deviation from Hardy–Weinberg Equilibrium (HWE) was observed for JAM-A rs790056 and LFA-1 rs8058823 polymorphisms in the control group, while a significant deviation from HWE was observed for these polymorphisms in the patient group. If only genotype distribution of the patient group shows deviation from HWE, this may provide additional support for an association of the marker locus with the disease in question [23–25].

In the CHD patient group, JAM-A rs790056 TT genotype frequency was higher in women (70.4%) when compared with men (53.5%); whereas C allele frequency was higher in men (25.25%) than in women (17.59%) ($\chi^2 = 4.109$; $p = 0.043$) (Table 2).

Association of JAM-A and LFA-1 gene variants with metabolic parameters

In the control group, LFA-1 rs8058823 G allele carriers had higher SBP than subjects with AA genotype ($p = 0.038$), whereas in the CHD patient group, G allele carriers had lower DBP than subjects with AA genotype ($p = 0.007$) (Table 3).

In the CHD group, JAM-A rs790056 TT genotype ($p = 0.03$), LFA-1 rs8058823 AA genotype ($p = 0.000$), smoking habit ($p = 0.000$), DBP ($p = 0.003$) and TC ($p = 0.003$) were found to be higher in the CHD group than in the control group. In logistic regression analysis, we confirmed that rs790056 TT genotype, rs8058823 AA genotype, smoking habit, DBP ≥ 90 mm Hg and TC ≥ 5.18 mmol/L were risk factors for CHD development (Table 4).

Haplotype analysis revealed that there was no significant difference between patients and controls in terms of the frequencies of haplotypes ($p > 0.05$) (Data was not shown).

Table 1

Demographic, biochemical, and clinical data.

	Total control (n = 124)	Total CHD (n = 153)	p values	Control women (n = 41)	Control men (n = 83)	p values	CHD women (n = 54)	CHD men (n = 99)	p values
Age (year)	56.30 ± 8.03	57.82 ± 11.73	0.213	56.71 ± 8.30	56.10 ± 7.94	0.693	60.27 ± 12.87	56.47 ± 10.88	0.077
SBP (mm Hg)	125.53 ± 17.03	131.57 ± 31.59	0.083	133.86 ± 19.75	121.22 ± 13.74	0.003	137.00 ± 37.26	129.17 ± 28.67	0.274
DBP (mm Hg)	74.50 ± 12.34	80.74 ± 17.38	0.003	79.83 ± 15.12	71.74 ± 9.68	0.011	82.00 ± 17.78	80.18 ± 17.29	0.615
BMI (kg/m ²)	25.81 ± 3.66	25.66 ± 3.30	0.744	26.87 ± 4.48	25.25 ± 3.03	0.045	26.74 ± 3.54	25.22 ± 3.10	0.050
TC (mmol/L)	4.66 ± 1.36	5.21 ± 1.28	0.003	4.47 ± 1.15	4.75 ± 1.46	0.303	5.37 ± 1.35	5.14 ± 1.26	0.363
TG (mmol/L)	1.65 ± 0.86	1.75 ± 1.55	0.557	1.47 ± 0.47	1.74 ± 0.99	0.082	1.85 ± 1.08	1.71 ± 1.72	0.654
LDL-C (mmol/L)	2.99 ± 1.00	3.28 ± 1.01	0.046	2.97 ± 0.68	3.01 ± 1.15	0.828	3.38 ± 1.07	3.24 ± 0.99	0.509
HDL-C (mmol/L)	1.11 ± 0.29	1.01 ± 0.24	0.007	1.29 ± 0.32	1.02 ± 0.23	0.000	1.04 ± 0.24	0.99 ± 0.24	0.366
VLDL-C (mmol/L)	0.69 ± 0.26	0.74 ± 0.36	0.290	0.65 ± 0.21	0.70 ± 0.28	0.345	0.81 ± 0.43	0.70 ± 0.32	0.201
Smoking (%)	28.0	58.9	0.000	20.6	31.8	0.236	25.6	74.1	0.000
Alcohol use (%)	10.6	14.6	0.516	–	13.2	0.250	2.9	21.8	0.014
TC ≥ 5.18 mmol/L (%)	33	47.9	0.026	33.3	32.8	0.959	59.5	42.9	0.092
LDL-C ≥ 3.36 mmol/L (%)	32.6	43.5	0.111	36.4	30.5	0.566	58.3	36.7	0.030
TG ≥ 1.70 mmol/L (%)	41.5	40.8	0.923	32.3	46.0	0.203	45.9	38.6	0.447
HDL-C ≤ 0.90 mmol/L (%)	18.6	26.3	0.180	3	26.6	0.005	21.6	28.4	0.438
BMI ≥ 27 kg/m ² (%)	33	42	0.175	52.5	22.7	0.001	55.2	36.6	0.088
T2DM (%)	–	40	–	–	–	–	65.9	25.9	0.000
HT (%)	–	45.2	–	–	–	–	64.9	35.9	0.004
LVH (%)	–	27.3	–	–	–	–	42.9	22.4	0.066

BMI, body mass index; SBP, systolic blood pressure; DBP, diastolic blood pressure; TC, total cholesterol; TG, triglyceride; LDL-C, low density lipoprotein-cholesterol; HDL-C, high density lipoprotein-cholesterol; VLDL-C, very low density lipoprotein-cholesterol; T2DM, type 2 diabetes mellitus; HT, hypertension; LVH, left ventricular hypertrophy. Parametric results are shown as mean ± SD.

Table 2

The distribution of JAM-A rs790056 and LFA-1 rs8058823 genotypes and alleles in the study groups.

JAM-A rs790056 genotypes	Total control (n = 115)	Total CHD (n = 153)	p values	OR (CI%)
TT	53 (46.1%)	91 (59.5%)	0.03	1.33 (1.030–1.718)
CC	16 (13.9%)	7 (4.6%)	0.007	0.902 (0.832–0.979)
TC	46 (40.0%)	55 (35.9%)	0.498	
<i>JAM-A rs790056 alleles</i>				
T	152 (66.08%)	237 (77.45%)	0.007	3.041 (1.294–7.148)
C	78 (33.91%)	69 (22.55%)	0.03	0.775 (0.611–0.982)
<i>LFA-1 rs8058823 genotypes</i>				
AA	n = 109 54 (49.5%)	n = 107 88 (82.2%)	0.000	2.842 (1.815–4.449)
GG	22 (20.2%)	–	0.000	
AG	33 (30.3%)	19 (17.8%)	0.031	0.848 (0.728–0.987)
<i>LFA-1 rs8058823 alleles</i>				
A	141 (64.68%)	195 (91.12%)	0.000	
G	77 (35.32%)	19 (8.88%)	0.000	0.602 (0.489–0.742)

OR, odds ratio; CI, confidence interval. Chi-square test was used to compare genotypes in the study group. Bold values of *p* indicate statistical significance.

Discussion

Coronary heart disease (CHD), once considered the result of vessel occluding by deposition of lipids, is now considered a chronic inflammatory disease developing as response to injury or infection [26]. Atherosclerotic lesions involved in CHD development are due to the increase in inflammatory-fibroproliferative response to changes in endothelium and smooth muscle cells of artery wall. Atherosclerosis shares several characteristics of chronic inflammatory diseases and many growth factors, cytokines and vasoregulatory molecules contribute to atherosclerotic formation [2].

Macrophages are key cells responsible for the onset of connective tissue proliferation associated with chronic inflammatory response as they collect waste materials for cells and secrete growth factors. Macrophages are shown to deposit large amounts of lipid droplets consisted of cholesteryl esters and transform into foam cells in atherosclerotic lesions. Foam cells are main cells forming fatty streak in early lesions of atherosclerosis [27].

LFA-1/JAM-A interaction plays a significant role in early steps of leukocyte transendothelial migration [7]. LFA-1 allows the migrating leukocyte to be recruited into the endothelial cell junction, and it blocks the second domain of JAM-A, which is important for stabilizing the JAM-A homophilic interaction. Thus, LFA-1 loose the endothelial junctional contacts and allows leukocyte diapedesis by destabilizing the homophilic JAM-A interactions. Subsequently, the LFA-1/JAM-A interaction allows the leukocyte to proceed farther down the endothelial junction [18].

Taking into consideration the hypothesis that since LFA-1/JAM-A interaction has a role in monocyte migration in atherosclerosis pathogenesis [7], the variations in these genes might influence atherosclerosis development, thus we aimed to determine JAM-A rs790056 and LFA-1 rs8058823 variation distributions in CHD patients and their individual and combined effects on CHD development as a risk factor. JAM-A and LFA-1 gene variations are investigated in CHD for the first time with this study.

There are few studies investigating the effects of JAM-A and LFA-1 gene variations on disease development. Ong et al. [20] investigated JAM-A rs790056 gene variation in 509 Chinese subjects including

Table 4

Evaluation of risk factors associated with CHD patients in logistic regression analysis.

Variables	Exp (B) (OR)	p values	95% CI for exp (B)
Smoking	5.856	0.000	2.284–15.015
Nonsmoking (Ref.)	1		
TC \geq 5.18 mmol/L	2.865	0.023	1.156–7.100
TC < 5.18 mmol/L (Ref.)	1		
DBP \geq 90 mm Hg	7.135	0.003	1.938–26.265
DBP < 90 mm Hg (Ref.)	1		
rs790056 TT	2.472	0.045	1.019–5.999
rs790056 C (Ref.)	1		
rs8058823 AA	6.751	0.000	2.719–16.762
rs8058823 G (Ref.)	1		

TC, total cholesterol; DBP, diastolic blood pressure.

Fu et al. [21] investigated LFA-1 rs8058823 SNP in 537 Chinese female infiltrative duct breast carcinoma patients and 577 Chinese healthy women and reported that LFA-1 rs8058823 genotype and allele distributions showed statistically significant difference between study groups ($p = 0.0397$). They found [21] that rs8058823 minor allele frequency (G) was 2% in the patients with infiltrative duct breast carcinoma, while it was 0.09% in the control group. In our study, LFA-1 rs8058823 minor allele frequency (G) was 35.3% in the control group and 8% in the CHD patient group ($p = 0.000$, OR = 0.602). This difference might be due to different number of subjects and different ethnical/geographical populations.

Fu et al. reported that rs8058823 variation located in 3'-UTR homozygous major AA genotype and A allele frequencies were lower in patients with infiltrative duct breast carcinoma than control group ($p = 0.00000418$, OR = 0.041 and $p = 0.00000267$, OR = 0.040 respectively), so they concluded that AA genotype and A allele might be protective against infiltrative duct breast carcinoma. rs8058823 AG genotype was found to be higher in the patient group than the control group ($p = 0.00000747$, OR = 23.442) and they suggested that rs8058823 AG genotype might increase infiltrative duct breast carcinoma risk [21]. In our study, AA genotype and A allele were higher in the CHD patient group than the control group ($p = 0.000$ and $p = 0.000$ respectively); GG and AG genotypes and G allele were higher in the control group than the CHD patient group ($p = 0.000$, $p = 0.031$ and $p = 0.000$, respectively) and we observed that minor G allele might be protective against CHD. rs8058823 genotype and allele distributions were not different between women and men in the CHD patient group and the control group ($p > 0.05$).

3'-UTR gene region can regulate gene expression and mediate stability, degradation and subcellular localization of mRNA [34]. Therefore, it was suggested that the rs8058823 variation located in the 3' UTR might affect LFA-1 expression [21].

In the present study, we observed that, minor G allele frequency was lower and normal AA genotype frequency was higher in the CHD patient group than controls ($p = 0.000$). Moreover, the LFA-1 rs8058823 normal A allele and AA genotype had positive effect on blood pressure, whereas minor G allele and GG genotype might have negative effect on blood pressure in the control group. In the CHD patient group, unlike control group, negative effect of normal AA genotype and A allele on blood pressure was observed. Therefore, our findings indicated that LFA-1 rs8058823 normal AA genotype might create CHD risk by causing an increase in blood pressure thus a hypertensive phenotype that is independent of lipid profile in the CHD patient group.

We suggested that the normal genotypes and alleles of JAM-A rs790056 and LFA-1 236 rs8058823 might be associated with an increased CHD risk, whereas mutant genotypes and alleles might be protective.

A better understanding of the role of inflammation in atherogenesis is essential for new therapeutic attempts. Therefore, taking into account the hypothesis that blocking the interaction of adhesion molecules which take part in the inflammatory process and play key role in the junctions between cells can inhibit the very early steps of atherogenesis, our data suggested that rs790056 and rs8058823 SNPs of JAM-A and LFA-1 genes might have an association with CHD risk despite a relatively small study group.

Declaration of interests

Authors declare that no competing interests exist.

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