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Association of the A/T54 polymorphism in the intestinal fatty acid binding protein with variations in plasma lipids in The Framingham Offspring Study

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Abstract

We investigated the potential role of the genetic variation at the intestinal fatty acid binding protein gene (*FABP2*) in influencing lipid levels in a representative sample of the Framingham Offspring Study participants ($n = 1930$). In men, the T54 allele was associated with significantly higher LDL-cholesterol (3.47 ± 0.83 vs 3.36 ± 0.83 mmol/l; $P < 0.047$), and ApoB (1.04 ± 0.23 vs 1.01 ± 0.24 g/l; $P < 0.020$) after adjustment for familial relationship, age, BMI, smoking, alcohol intake and the use of beta-blockers compared with the A54 allele. This relationship with ApoB continued to be significant after adjustment for *APOE* genotype ($P < 0.034$). In women, the T54 allele was associated with significantly higher total-cholesterol (5.32 ± 1.01 vs 5.17 ± 0.98 mmol/l; $P < 0.049$) and LDL-cholesterol (3.31 ± 0.93 vs 3.18 ± 0.85 mmol/l; $P < 0.023$) after adjustment for covariates and menopausal status, estrogen therapy and *APOE* genotype. In men, the T54 allele was associated with significantly higher levels of small VLDL and lower levels of large HDL. Moreover, there was no significant relationship between *FABP2* alleles and lipoprotein diameter or the prevalence of coronary heart disease in both genders. Our data are consistent with the T54 IFABP increasing the flux of lipids through the enterocyte leading to an increase in chylomicron secretion. © 2001 Elsevier Science Ireland Ltd. All rights reserved.

Keywords: FABP2; Cholesterol; Polymorphism; Framingham

1. Introduction

The development and progression of coronary heart disease (CHD) is complex, and includes diet, environment and genetic influences [1]. Genetic variation at candidate genes is becoming increasingly important in the study of the development of CHD [1–3]. One of the most common phenotypes associated with CHD is syndrome X (or pluri-metabolic syndrome) which is characterized by dyslipidemia, obesity, hypertension, and insulin resistance [4,5]. A common genetic variant at *FABP2*, the gene coding for the intestinal fatty acid binding protein (IFABP), has shown associations with components of syndrome X [6–8].

The 15 kDa IFABP is a member of the family of cytoplasmic fatty acid binding proteins. The structure and ligand binding of the IFABP have been well studied and reviewed [9–15]. However, the precise function of the IFABP and other FABPs within the cell remains to be discerned. The IFABP is located only in the intestine and is believed to be involved with the transport and metabolism of saturated and unsaturated long-chain fatty acids (LCFA).

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A transition (G → A) at codon 54 of *FABP2* results in an amino acid substitution (A54 → T54) [6]. In vitro studies have found that the mutated (T54) IFABP has greater affinity for LCFA than the wild-type (A54) IFABP and it transports LCFA and secretes triglycerides (TG), and cholesterol esters to a greater degree than wild-type IFABP [6,16]. Also, amino acid 54 of the IFABP is believed to be a component of the portal where the fatty acids pass for entry into the protein [17,18].

Recently, genetic variation at this locus has been reviewed in terms of plasma lipid response to diet [19]. The current evidence indicates that the IFABP T54 variant is often associated with a more deleterious phenotypic expression, i.e. impaired glucose tolerance, obesity, and altered lipid and lipoprotein profiles [19]. The IFABP mutation appears to influence post-prandial lipemic responses. It was found that T54 homozygotes had significantly greater increases in plasma chylomicron TG, very low-density lipoprotein TG, and chylomicron cholesterol levels after an oral fat load compared to A54 homozygotes [8]. These findings are important because post-prandial lipemia has been found to be significantly associated with CHD [20]. Also, Hegele et al. found that the A54thr mutation was associated with variation in the response of plasma lipoproteins to dietary fiber [7].

In vivo studies have found that subjects with the T54 mutation, compared with A54, have a higher fasting plasma cholesterol level [21], mean fasting fat oxidation rate [6,22] and higher fasting plasma TG [21,23,24]. However, other studies, mostly with small numbers of subjects, have failed to find a relationship between *FABP2* genotype and fasting lipids [25–31].

Since evidence indicates that the T54 IFABP is functionally different from the A54 IFABP, it is a good candidate for studying the potential impact of this genetic variation on plasma lipids and lipoproteins in a large free-living population. We hypothesize that the T54 mutation leads to accelerated flux of lipids through the enterocyte, which may lead to lipid related phenotypes. The aim of the present study was to examine the associations of the *FABP2* genetic polymorphism with variations in plasma lipid levels, lipoprotein subclass profiles and CHD in Framingham Offspring Study participants.

2. Methods

2.1. Population subjects

Subjects were participants in the Framingham Offspring Study, a long-term, community-based, prospective observational study of risk factors for cardiovascular disease in which participants are the offspring of the subjects of the original Framingham Heart Study cohort and their spouses. The details of the design of the Framingham Offspring Study have been reported elsewhere [32]. Starting in 1971, a total of 5124 subjects were enrolled [33]. Lipid, lipoprotein, and apolipoprotein measurements as well as DNA, and information on CHD risk factors were available for 907 men and 1023 women who attended the fourth and fifth examination visits of the Framingham Offspring Study conducted between 1987 and 1995. Almost all subjects were Caucasians. Data on smoking, blood pressure, height, weight, and diabetes were obtained on these subjects as previously described [33]. CHD cases were adjudicated up to 1994, by criteria established for the analysis of Framingham Offspring Study, as described elsewhere [34]. CHD included the presence of myocardial infarction, angina pectoris, coronary insufficiency, and coronary death. Subjects taking a lipid-lowering medication were included for the calculation of CHD prevalence at exam 5.

2.2. Plasma lipid, lipoprotein and apolipoprotein measurements

Plasma was isolated from venous blood drawn in EDTA containing tubes after a twelve hour fast. Plasma total cholesterol, high density (HDL) cholesterol and TG levels were measured as previously described [35]. Friedwald et al.'s equation was used to estimate low-density (LDL) cholesterol concentrations [36]. Non-competitive enzyme-linked immunosorbent assay (ELISA), using affinity-purified polyclonal antibodies was used to measure plasma levels of ApoAI and ApoB [37,38].

Plasma lipoprotein concentrations and subclasses distributions were determined by proton nuclear magnetic resonance (NMR) spectroscopy as described by Otvos et al. [39]. The 10 lipoprotein subclass categories used were the following: large VLDL and remnants (40–220 nm), intermediate VLDL (31–40 nm), small VLDL (27–31 nm), large LDL (21.3–27.0 nm), intermediate LDL (19.8–21.2), small LDL (18.3–19.7 nm), large HDL (8.8–13.0 nm), intermediate HDL (7.8–8.8 nm), and small HDL (7.3–7.7 nm). Levels of VLDL subclasses are expressed in units of TG (mg/dl), and those of LDL and HDL subclasses in units of cholesterol (mg/dl).

2.3. DNA analysis

Genomic DNA was isolated from peripheral blood leukocytes by standard methods [40]. Genotyping for the *FABP2* polymorphism was performed using the Perkin Elmer/Applied Biosystems 7700 Sequence Detection Systems and Taqman® reagents as previously described [41].

2.4. Statistical analyses

Female and male participants were compared by using χ^2 tests for categorical measures and two-sample t-test for continuous measures. Frequencies of the *FABP2* and *APOE* alleles were estimated with the chromosome counting method and a χ^2 test was used to compare frequencies between men and women. For the analyses with lipid variables, carriers of the T54 allele were grouped together. Subjects with the GG genotype (A54) were compared with subjects with either the GA (heterozygotes) or AA genotypes (T54). The relationship between the carriers and non-carriers of the *FABP2* T54 allele and lipid levels was evaluated by analysis of covariance techniques which accounted for the familial relationships among the study participants (mostly siblings and cousins). A repeated measures approach was used which assumed an exchangeable correlation structure among all members of a family, using PROC MIXED in SAS. Since this approach does not accurately represent the true correlation structure within these pedigrees, we also employed a measured genotype approach [42] as implemented in SOLAR, a variance component analysis computer package for quantitative traits measured in pedigrees of arbitrary size [43]. The measured genotype approach fully accounts for the different types of relationships within a pedigree in performing an analysis of variance on the defined genotypes. In these analyses, several different models were used to adjust for possible confounders. First, we obtained raw results which accounted only for the family structure; second, we adjusted for age, BMI, smoking, alcohol consumption, beta-blockers, and menopausal status and hormonal replacement therapy in women. In our final analysis, we added *APOE* genotypes to the model with E2/E2 and E2/E3 in one group, E3/E4 and E4/E4 in a second group and E3/E3 as the reference group. Five subjects with the very rare *APOE* E2/E4 genotype were excluded. We report our results without adjustment for multiple testing across outcomes. Since we report p values, one can use their own judgement as to what is significant and what is not.

3. Results

3.1. Demographic, genotypic, and biochemical characteristics

A total of 1930 subjects (907 men and 1023 women) from the Framingham Offspring study, who were not taking lipid-lowering medications, were analyzed. The demographic, genotypic, and biochemical characteristics of subjects according to gender are presented in Table 1. There were no significant differences in the frequency of the T54 allele between men and women, and the genotypic frequencies were in Hardy–Weinberg equilibrium. The mean ages of men and women were 53.6 ± 10.2 and 52.2 ± 9.9 years ($P < 0.003$), respectively, and over one-half of the female subjects (56.4%) were post-menopausal. Men had significantly higher BMI, LDL-cholesterol, ApoB, TG, as well as, glucose levels, alcohol consumption, and number of cigarettes smoked compared with women. Women had significantly higher total cholesterol, ApoAI, HDL, HDL2, and HDL3 cholesterol levels compared with men. The distribution of *APOE* genotypes was similar in men and women.

3.2. Association of the *FABP2* alleles with lipid, lipoprotein, and apolipoprotein levels

Table 2 shows that in men and women there was no difference in age or BMI between carriers and non-carriers of the T54 allele. Linear regression was performed to test for possible associations of the *FABP2* alleles with lipid and apolipoprotein profiles. In men, the carriers of the T54 allele had significantly higher LDL-cholesterol (3.47 ± 0.83 vs 3.36 ± 0.83 mmol/l; $P < 0.047$), and ApoB levels (1.04 ± 0.23 vs 1.01 ± 0.24 g/l;

Table 1
Demographic, genotypic and biochemical characteristics of FOS participants according to gender[a]

	Men	Women	p
n (Total)	907	1023	
FABP2 alleles			
A54 homozygotes (%)	478 (52.7)	541 (52.9)	
T54 carriers (%)	429 (47.3)	482 (47.1)	0.9360
APOE alleles[b]	870	964	0.6230
E2 (%)	116 (13.3)	147 (15.2)	
E3 (%)	574 (66.0)	616 (63.9)	
E4 (%)	180 (20.7)	201 (20.9)	
Age (years)	53.6 ± 10.2	52.2 ± 9.9	0.0025
BMI (kg/m^2)	27.9 ± 4.0	26.1 ± 5.2	0.0001
TC (mmol/l)	5.22 ± 0.93	5.25 ± 0.98	0.0216
LDL-C (mmol/l)	3.44 ± 0.83	3.23 ± 0.90	0.0205
HDL-C (mmol/l)	1.12 ± 0.30	1.44 ± 0.39	0.0001
HDL2-C (mmol/l)	0.13 ± 0.09	0.24 ± 0.15	0.0001
HDL3-C (mmol/l)	0.98 ± 0.23	1.19 ± 0.29	0.0001
TG (mmol/l)	1.56 ± 1.12	1.23 ± 0.99	0.0001
ApoAI (g/l)	1.34 ± 0.23	1.54 ± 0.29	0.0001
ApoB (g/l)	1.02 ± 0.24	0.95 ± 0.25	0.0001
TC/HDL-C	4.97 ± 1.55	3.93 ± 1.42	0.0086
Glucose (mmol/l)	5.77 ± 1.87	5.39 ± 1.48	0.0001
Alcohol (g/day)	16.1 ± 19.6	7.2 ± 11.6	0.0001
Cigarette/day	5.7 ± 12.1	4.6 ± 10.1	0.0463
Post-menopausal (%)		56.4	
On estrogen Rx (%)[c]		10.2	

[a] Results are listed as means ± S.D.

[b] E2: E2/2 + E2/3; E3: E3/3; E4: E3/4 + E4/4.

[c] Includes hormonal replacement therapy and the use of oral contraceptives.

Table 2
Plasma levels of lipids, lipoproteins and apoproteins of FOS subjects according to *FABP2* genotypes at codon 54[a]

	GG	GA/AA	P^b	P^c	P^d
Men					
N	478	429			
Age (years)	53.3 ± 10.1	53.8 ± 10.3	0.4128		
BMI (kg/m^2)	28.2 ± 4.0	27.7 ± 3.8	0.0963		
TC (mmol/l)	5.17 ± 0.88	5.28 ± 0.96	0.0956	0.0886	0.1206
LDL-C (mmol/l)	3.36 ± 0.83	3.47 ± 0.83	0.0793	0.0466*	0.0659
HDL-C (mmol/l)	1.13 ± 0.33	1.11 ± 0.27	0.5446	0.0704	0.0650
HDL2-C (mmol/l)	0.14 ± 0.09	0.13 ± 0.09	0.8959	0.4029	0.3554
HDL3-C (mmol/l)	0.99 ± 0.26	0.98 ± 0.21	0.4847	0.0668	0.0658
TG (mmol/l)	1.55 ± 1.17	1.56 ± 1.07	0.8620	0.5066	0.4108
ApoAI (g/l)	1.35 ± 0.27	1.33 ± 0.22	0.5513	0.1632	0.1606
ApoB (g/l)	1.01 ± 0.24	1.04 ± 0.23	0.1102	0.0197*	0.0336*
TC/HDL-C	4.94 ± 1.65	5.02 ± 1.45	0.6397	0.2030	0.2057
Women					
N	541	482			
Age (years)	51.7 ± 10.7	52.7 ± 9.8	0.1235		
BMI (kg/m^2)	26.2 ± 5.5	26.0 ± 5.1	0.5131		
TC (mmol/l)	5.17 ± 0.98	5.32 ± 1.01	0.0203*	0.0637	0.0486*
LDL-C (mmol/l)	3.18 ± 0.85	3.31 ± 0.93	0.0332*	0.0320*	0.0223*
HDL-C (mmol/l)	1.42 ± 0.38	1.46 ± 0.40	0.1358	0.5072	0.5429
HDL2-C (mmol/l)	0.25 ± 0.14	0.25 ± 0.16	0.8758	0.6891	0.6799
HDL3-C (mmol/l)	1.17 ± 0.28	1.21 ± 0.30	0.0678	0.2942	0.3215
TG (mmol/l)	1.24 ± 1.14	1.22 ± 0.77	0.4620	0.8313	0.8104
ApoAI (g/l)	1.54 ± 0.30	1.55 ± 0.30	0.2939	0.9460	0.9855
ApoB (g/l)	0.94 ± 0.25	0.97 ± 0.26	0.0626	0.1364	0.1001
TC/HDL-C	3.92 ± 1.50	3.94 ± 1.33	0.8473	0.9831	0.9251

[a] Results are listed as means ± S.D.
[b] After adjustment for familial relationship.
[c] After adjustment for familial relationship, age, BMI, smoking, alcohol intake and the use of beta-blockers, (menopausal status and estrogen therapy in women).
[d] After adjustment for familial relationship, age, BMI, smoking, alcohol intake, use of beta-blockers, (menopausal status and estrogen therapy in women) and *APOE* genotype.

$P < 0.020$) than non-carriers after adjustment for familial relationship, age, BMI, smoking, alcohol intake and the use of beta-blockers. This relationship with ApoB continued to be significant after adjustment for APOE genotype ($P < 0.034$). In women, carriers of the T54 allele had significantly higher total-cholesterol (5.32 ± 1.01 vs 5.17 ± 0.98 mmol/l; $P < 0.049$) and LDL-cholesterol (3.31 ± 0.93 vs 3.18 ± 0.85 mmol/l; $P < 0.023$) than non-carriers after adjustment for familial relationship, age, BMI, smoking, alcohol intake, use of beta-blockers, menopausal status, estrogen therapy and *APOE* genotype.

3.3. Association with the FABP2 alleles with lipoprotein subclass profiles

Lipoprotein subclass profiles were characterized by automated NMR spectroscopy. Table 3 shows that male carriers of the T54 allele had significantly higher levels of small VLDL and lower levels of large HDL than noncarriers, after adjustment for familial relationship and other covariables. In women, no significant relationship was found between the *FABP2* alleles and lipoprotein subclass profiles. Also, as shown in Table 4, there was no significant relationship between *FABP2* alleles and lipoprotein diameter in men or women.

3.4. FABP2 polymorphism and association with CHD

CHD was present in 91 men (10.7%) and 42 women (4.3%). Of the 445 males who did not carry the T54 allele, 49 (11.0%) had a history of CHD compared with 42 (10.4%) of 403 subjects who were carriers of the T54 allele. The *FABP2* polymorphism was not associated with CHD in a logistic regression model adjusting for age, BMI, smoking, alcohol, beta-blockers, systolic blood pressure, and diabetes ($P = 0.294$).

In women, 22 (4.3%) of the 513 noncarriers of the T54 allele had a history of CHD compared with 20 (4.3%) of 465 carriers. As observed in men, this association was not significant after adjustment for covariates including menopausal status and hormonal replacement therapy ($P = 0.789$).

4. Discussion

We report significant associations between the *FABP2* T54 variant and LDL-cholesterol and ApoB in men and total cholesterol and LDL-cholesterol in women. Similar trends were seen in both men and women. Our data is consistent with the T54 IFABP increasing the flux of lipids through the enterocyte leading to an increase in chylomicron secretion of TG and cholesterol.

We did not find a significant relationship between fasting plasma TG levels and the *FABP2* alleles, which is consistent with the results of some other studies [25–31]. Two studies conducted in an aboriginal Canadian population found a relationship between the T54 allele and higher fasting plasma TG [23,24]. This aboriginal Canadian population had a much lower T54 allele frequency (0.14) than any other study population, which was thought due to a founder effect. In the present study, the carrier frequency of the T54 IFABP variant (0.27) was similar to that of other studies [7].

Although the T54 allele was not associated with fasting TG levels, we did find a relationship with fasting LDL-cholesterol, and ApoB levels in men and total cholesterol and LDL-cholesterol levels in women. Our results are consistent with those of Carlsson et al., who found that siblings with an excess of the T54 allele had higher cholesterol concentrations than those with the A54 allele [21]. Some other studies did not find an association between A/T54 alleles and fasting cholesterol and apolipoprotein levels [23–31].

The T54 allele in men was also associated with an increase in the levels of small VLDL, which has a positive association with CHD, and a decrease in large HDL, which has a negative association with CHD, as measured by NMR spectroscopy [44]. This further supports that the T54 allele is associated with a more deleterious lipid profile than that of the A54 allele. In the present study we did not find an association between the *FABP2* polymorphism and CHD. This may be due to the small numbers of CHD patients in this young cohort. However, a previous study in a Finnish population also found that the T54 allele was not significantly associated with CHD [45].

Table 3
Lipoprotein subclass distributions of FOS subjects according to *FABP2* genotypes at Codon 54[a]

	GG	GA/AA	P^b	P^c	P^d
Men					
VLDL					
Large	11.3 ± 20.1	11.0 ± 19.3	0.8027	0.7572	0.7169
Intermediate	75.7 ± 63.3	77.5 ± 65.3	0.7136	0.2838	0.2328
Small	19.8 ± 13.2	22.8 ± 14.1	0.0019*	0.0043*	0.0062*
LDL					
Large	69.6 ± 32.3	72.4 ± 34.7	0.1861	0.2624	0.3800
Intermediate	35.3 ± 24.4	37.9 ± 23.8	0.1346	0.0767	0.0863
Small	32.8 ± 25.8	32.5 ± 24.1	0.7503	0.8936	0.9058
HDL					
Large	15.9 ± 12.9	14.5 ± 10.9	0.1394	0.0051*	0.0064*
Intermediate	21.1 ± 6.5	21.1 ± 6.4	0.9931	0.8653	0.8913
Small	8.5 ± 5.1	8.8 ± 5.2	0.4934	0.2643	0.3213
Women					
VLDL					
Large	6.4 ± 19.4	6.0 ± 12.0	0.7321	0.5609	0.5621
Intermediate	50.4 ± 53.7	52.3 ± 50.0	0.5390	0.7851	0.7849
Small	22.2 ± 13.4	23.2 ± 13.1	0.2435	0.4347	0.4451
LDL					
Large	83.8 ± 32.1	84.8 ± 31.9	0.6615	0.4333	0.3722
Intermediate	29.6 ± 22.5	31.8 ± 24.1	0.1573	0.2843	0.2751
Small	19.2 ± 20.1	18.5 ± 17.7	0.5545	0.4687	0.4724
HDL					
Large	31.1 ± 15.9	31.5 ± 16.7	0.7556	0.8165	0.7958
Intermediate	20.6 ± 6.2	21.0 ± 6.6	0.3191	0.3232	0.3210
Small	5.4 ± 4.6	5.4 ± 4.4	0.9097	0.9257	0.9376

[a] Results are listed as means ± S.D. Levels of VLDL subclasses are expressed in units of triglyceride (mg/dl), and those of LDL and HDL subclasses in units of cholesterol (mg/dl).

[b] After adjustment for familial relationship.

[c] After adjustment for familial relationship, age, BMI, smoking, alcohol intake and the use of beta-blockers, (menopausal status and estrogen therapy in women).

[d] After adjustment for familial relationship, age, BMI, smoking, alcohol intake, use of beta-blockers, (menopausal status and estrogen therapy in women) and *APOE* genotype.

Table 4
Lipoprotein diameters (nm) of FOS subjects according to *FABP2* genotype at codon 54[a]

	GG	GA/AA	P^b	P^c	P^d
Men					
VLDL	48.94 ± 9.79	48.10 ± 9.36	0.2186	0.5684	0.6571
LDL	20.71 ± 0.56	20.72 ± 0.54	0.6341	0.9311	0.8352
HDL	8.96 ± 0.40	8.94 ± 0.39	0.5656	0.0799	0.0756
Women					
VLDL	44.08 ± 8.63	44.32 ± 8.65	0.6328	0.7780	0.7611
LDL	21.07 ± 0.46	21.07 ± 0.42	0.9480	0.7315	0.7029
HDL	9.40 ± 0.41	9.42 ± 0.45	0.4709	0.8840	0.8925

[a] Results are listed as means ± S.D.
[b] After adjustment for familial relationship.
[c] After adjustment for familial relationship, age, BMI, smoking, alcohol intake and the use of beta-blockers, (menopausal status and estrogen therapy in women).
[d] After adjustment for familial relationship, age, BMI, smoking, alcohol intake, use of beta-blockers, (menopausal status and estrogen therapy in women), and *APOE* genotype.

Other studies have found a relationship between the A/T54 mutation and hyperresponsive cholesterol levels to diet. A study by Agren et al. found that those with the T54 allele had significantly elevated chylomicron cholesterol levels, as well as TG levels, compared with A54 subjects, after an oral fat load [8]. A similar trend was seen in VLDL cholesterol, but the difference was not statistically significant [8]. Also, in a separate study, Hegele et al. found that the T54 allele modified the lipid response to fiber-fed diets. They found that subjects with the T54 allele had significantly greater decreases in plasma total and LDL cholesterol and ApoB when consuming a high soluble fiber diet compared to a high insoluble fiber diet [7].

In vitro data show that the T54 IFABP increases that secretion of cholesterol as well as TG. The IFABP is abundant and represents 2–3% of an enterocyte's cytoplasmic mass [46]. Baier et al. found that the secretion of cholesterol esters consistently differed between the A54 and T54 transfected Caco-2 cells (1.4% and 6% of the total secreted lipids for A54 and T54, respectively). Also, it was found that T54 IFABP transports LCFA and secretes TG to 5-6 fold greater degree than A54 IFABP in transfected Caco-2 cells [16].

We hypothesize that since TG and cholesterol are packaged together into chylomicrons in the enterocyte, then a change in TG transport affects cholesterol transport as well. If the T54 mutation increases the transport of LCFA through the enterocyte, then it may tip the equilibrium by removing more cholesterol esters from the cell by being packaged together with TG into chylomicrons. This removal of cholesterol from the cell may lead to more being absorbed and transported into the lymph with the flux of TG. There is an excess of cholesterol that is available for absorption, because it is estimated that only 50% of the cholesterol in the intestinal lumen is absorbed [47]. It has also been shown in Finnish men that cholesterol absorption efficiency is correlated with plasma cholesterol concentrations [48,49]. Future studies should examine cholesterol absorption in subjects with the T54 and A54 IFABP alleles. Our study suggests that subjects with the T54 allele may have increased intestinal absorption of cholesterol.

In conclusion, the results of the present study show that the T54 IFABP allele is associated with small, but significant variations in fasting plasma cholesterol, ApoB, and lipoprotein subclass distributions. Our results suggest that the T54 allele is associated with a more proatherogenic lipoprotein profile than the A54 allele.

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