Lack of Association between *FTO* Gene Variations and Metabolic Healthy Obese (MHO) Phenotype: Tehran Cardio-Metabolic Genetic Study (TCGS)

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movement of cholesteryl ester from high-density lipoproteins/HDL to triglyceride-rich very low-density lipoproteins/VLDL, and the equimolar transport of triglyceride from VLDL to HDL [12,13].

Given the scarcity of data in genetic studies on diwerent obesity phenotypes, we aimed to examine the interaction of 9 remarkable single nucleotide polymorphisms (SNP) in FTO and CETP with lipid proŽles among these mentioned phenotypes in the Tehran Cardio-metabolic Genetics Study (TCGS).

Materials and Methods

Population

Subjects were selected from the ongoing Tehran Cardio-metabolic Genetics Study (TCGS) which is an ongoing genetic study involving a cohort designed to determine the risk factors for major non-communicable disorders in the Tehran population referred to as the Tehran lipid and glucose study [14,15]. Written consent was obtained from each subject and the research council of the Research Institute of Endocrine Sciences of the Shahid Beheshti University of Medical sciences approved the study.

Demographic information and biochemical analysis

Information for age, sex and history of using medication for diabetes, hypertension and lipid disorders were collected with a standardized questionnaire. Weight and height were recorded using standard protocols [16]. Body mass index (BMI) was calculated as weight in kilograms divided by height in square meters. Systolic blood pressure (SBP), Diastolic blood pressure (DBP) and anthropometric variables such as Waist circumference (WC) and Hip circumference (HC) were measured as described previously [17]. Fasting plasma glucose (FPG), Triglycerides (TG), Total cholesterol (TC) and High-density lipoprotein cholesterol (HDL-C) levels were measured by Pars AzmunCo (Iran); in addition, CoeŸcients of variation (CV) for total cholesterol, HDL-C and triglyceride measurements were below 5% [18]. Non-HDL-C was calculated by subtracting HDL-C from TC [19]. LDL-C concentrations were calculated using modiŽed Friedewald's equation [20].

Genetic analysis

Genomic DNA from 954 subjects was extracted from peripheral blood using the standard Proteinase K, salting-out method [21]. Nine selected polymorphisms (FTO polymorphisms located in intron: rs6499640, rs1421085, rs1558902, rs1121980, rs8050136, rs7202116; CETP polymorptahisms located in upstream and intron: rs3764261, rs1800775, rs1864163) were studied with the T-ARMS assay. In each d in !

rs17817449	T>G	OF	ACGGTGAAGAGGAGGAGATTGTGTAACT	66.5	28	TT:568,128	TG:568,489,128	GG:568,489
		OR	TGTAGTAGTAGTGACAGAAGTGGAGAAA	58.7	28			
		IF	GTTTCAGCTTGGCACACAGAATCG	65.4	24			
		IR	AGGAGCGGGACTGTTAAATTAAAGCA	66.5	26			
rs8050136	C>A	OF	CCAACCAAGGTCATTATAGGAAGAGCT	62.5	27	CC:530,342	CA:530,342,237	AA:530,237
		OR	TACATCCTGAGCTCTGCCACTATACCA	64.6	27			
		IF	ATGCAAGTTGACCACTGTGGCTATC	63.6	25			
		IR	GCAAAAACCACAGGCTCAGATACTT	62	25			
rs9939609	T>A	OF	GGTGGTACGCTGCTATGGTTCTACA	64.4	25	TT:455,306	TA: 455,306,200	AA: 455,200
		OR	TCAGCCTCTCTACCATCTTATGTCCAA	62.9	27			
		IF	GGTTCCTTGCGACTGCTGTGAATATA	63.3	26			
		IR	AACAGAGACTATCCAAGTGCATCGCA	64.4	26			
rs9939973	G>A	OF	CTCAAGTGATTTACCCATTTCAGTGCTCCAA	65.5	31	GG:479,227	GA:479,227,301	AA:479,301
		OR	CTGGCTCATGGTGTGTGTCATCTCCTG	67	27			
		IF	AGCACCCAAGGGACCATCAAACAGA	66.2	25			
		IR	CTTCGCATTCCCTCTCCACAACTGC	66	25			
rs6499640	G>A	OF	ATCTGCTCTTAATGTGGAAACTGTGG	61.5	26	GG:577,206	GA:577,206	AA:577,424
		OR	ATATTCAAACCCTCAACTCTACCAGCT	62	27			
		IF	TGTGTAAGGAACAGGGTTTATCTAAAG	59.1	27			
		IR	CTGATGGTAGAGTATTTCAAAGATGCT	59.3	27			

OF: Outer Forward Primer; OR: Outer Reverse Primer; IF: Inner Forward Primer; IR: Inner Reverse Primer.

		HDL-C (mg/dl)	LDL-C (mg/dl)	non-HDL-C (mg/dl)	Cholesterol (mg/dl)	Triglyceride (mg/dl)	Hip circumference	Waist circumference
Statistic								
		SE,β (95% CI)	SE,β (95% CI)	SE,β (95% CI)	SE,β (95% CI)	SE,β (95% CI)	SE,β (95% CI)	SE,β (95% CI)
	Total population	0.09,-0.05(-0.22;0.12)	0.09,-0.11(-0.28;0.07)	0.09,-0.08(-0.25;0.09)	0.09,-0.1(-0.28;0.07)	0.08,0.08(-0.08;0.25)	0.08,0.05(-0.11;0.21)	0.08,0.09(-0.07;0.24)
rs6499640	Overweight	0.13,0.01(-0.25;0.26)	0.13,-0.13(-0.39;0.14)	0.13,-0.08(-0.33;0.17)	0.13,-0.08(-0.34;0.19)	0.12,0.13(-0.12;0.37)	0.09,0.04(-0.14;0.21)	0.08,0.06(-0.1;0.22)
	Obese	0.16,0.1(-0.22;0.41)	0.18,-0.24(-0.59;0.11)	0.16,-0.22(-0.53;0.1ز 0.14)				

	Overweight	0.11,0.34(0.12;0.56)*	0.11,0.25(0.03;0.47)	0.11,0.15(-0.07;0.36)	0.11,0.23(0;0.45)*	0.11,-0.09(-0.3;0.12)	0.08,0.01(-0.14;0.16)	0.07,-0.03(-0.17;0.1)
	Obese	0.13,0.51(0.25;0.77)*	0.15,0.15(-0.15;0.44)	0.14,0.05(-0.22;0.32)	0.15,0.19(-0.1;0.48)	0.13,-0.1(-0.35;0.15)	0.1,-0.02(-0.21;0.18)	0.11,0(-0.21;0.2)
rs1864163	General population	0.07,0.3(0.16;0.43)*	0.07,0.04(-0.11;0.18)	0.07,-0.03(-0.17;0.1)	0.07,0.05(-0.09;0.19)	0.07,-0.15(-0.28;-0.02)*	0.07,-0.16(-0.29;-0.03)*	0.06,-0.08(-0.21;0.04)
	Overweight	0.1,0.11(-0.09;0.31)	0.11,0.01(-0.2;0.22)	0.1,-0.05(-0.25;0.15)	0.11,-0.03(-0.23;0.18)	0.1,-0.11(-0.3;0.08)	0.07,-0.16(-0.3;-0.02)*	0.06,-0.08(-0.21;0.04)
	Obese	0.12,0.5(0.26;0.74)*	0.14,0.18(-0.1;0.46)	0.13,0.08(-0.18;0.33)	0.14,0.21(-0.06;0.49)	0.12,-0.19(-0.42;0.05)	0.1,0.01(-0.18;0.19)	0.1,-0.03(-0.23;0.16)

*p<0.01

12. Kuivenhoven