
ABCA1 Polymorphisms are Associated with Serum Levels of IL-6 and CRP

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INTRODUCTION: Preliminary evidence suggests that the ATP-binding cassette transporter A1 (ABCA1) participates in cell-mediated inflammation separate from its role in lipid metabolism. Although the -477T allele has been positively associated with atherosclerosis, the 1051A allele has been associated with higher HDL levels and less atherosclerosis. Associations between these single nucleotide polymorphisms (SNPs) and serum inflammatory markers have not been previously reported.

METHODS: Genotyping at the ABCA1 -477C/T and G1051A loci was performed in 1000 randomly-selected subjects from the Multi-Ethnic Study of Atherosclerosis. A total of 969 subjects were successfully genotyped at both loci, including 205 African-Americans, 97 Chinese, 219 Hispanics, and 448 Caucasians. Associations between the SNPs and plasma concentrations of IL-6 and high-sensitivity CRP were assessed by multivariate linear regression modeling after adjustment for potential confounders.

RESULTS: The two SNPs were not in linkage disequilibrium ($D'=0.09$ in Caucasians and $D'=0.009$ in African Americans). African-Americans with the -477TT genotype had significantly higher levels of both IL-6 and CRP than carriers of the C allele (**See Table**). In Caucasians, IL-6 levels did not differ by -477 genotype (race*genotype interaction term $p=0.008$). The 1051A allele was positively associated with IL-6 levels among Caucasians. A similar, although not statistically significant, trend was seen in African Americans and Chinese subjects. This association persisted in the overall study sample ($p=0.02$, race-adjusted). No significant IL-6 or CRP associations were present in Chinese or Hispanic subjects.

CONCLUSION: The ABCA1 -477T and 1051A alleles are associated with serum CRP and IL-6 independent of effects on HDL and LDL levels. These findings warrant further investigation into the role of ABCA1 variants in inflammatory aspects of atherosclerosis independent of cholesterol metabolism.

Table: Effects of ABCA1 Single Nucleotide Polymorphisms on Serum Levels of IL-6 and CRP

ABCA1 Locus	Race/Eth n.	Genotype	N (%)	IL-6 pg/mL	p-value	CRP mg/L	p-value
-477C/T	African American n=205	CC	60 (29)	1.59 ± 1.02	0.041*	5.71 ± 6.40	0.008*
		CT	93 (45)	1.65 ± 1.12		4.51 ± 4.90	
		TT	52 (25)	2.23 ± 2.27		7.76 ± 13.15	
	Caucasia n=448	CC	105 (23)	1.34 ± 0.80	ns	3.21 ± 3.88	ns
		CT	249 (56)	1.51 ± 1.50		4.00 ± 6.58	
		TT	94 (21)	1.22 ± 0.97		3.61 ± 4.75	
G1051A	African American n=205	GG	33 (16)	1.58 ± 1.31	ns	5.03 ± 5.05	ns
		GA	83 (40)	1.79 ± 1.39		5.70 ± 8.49	
		AA	89 (43)	1.82 ± 1.62		5.92 ± 8.95	
	Caucasia n=448	GG	230 (51)	1.31 ± 1.11	0.015†	4.07 ± 6.58	ns
		GA	186 (42)	1.48 ± 1.39		3.45 ± 4.73	
		AA	32 (7)	1.62 ± 1.55		3.01 ± 3.49	

* recessive model, † dominant model

Plasma concentrations shown are crude mean ± SD. P-values are from a regression model using log-transformed CRP and IL-6 levels, adjusted for age, gender, BMI, hypertension history, tobacco use, diabetes, LDL, and HDL.