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ASSOCIATION BETWEEN *ADIPOQ* SNPS WITH PLASMA ADIPONECTIN AND GLUCOSE HOMEOSTASIS AND ADIPOSITY PHENOTYPES IN THE IRAS FAMILY STUDY

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Abstract

Context—Adiponectin is an adipocytokine associated with a variety of metabolic traits. These associations in human studies, in conjunction with functional studies in model systems, have implicated adiponectin in multiple metabolic processes.

Objective—We hypothesize that genetic variants associated with plasma adiponectin would also be associated with glucose homeostasis and adiposity phenotypes.

Design and Setting—The Insulin Resistance Atherosclerosis Family Study was designed to identify the genetic and environmental basis of insulin resistance and adiposity in the Hispanic- (n=1,424) and African-American (n=604) population.

Main Outcome Measures—High quality metabolic phenotypes, e.g. insulin sensitivity (S_I), acute insulin response (AIR), disposition index (DI), fasting glucose, body mass index (BMI),

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visceral adipose tissue (VAT), subcutaneous adipose tissue (SAT), and waist circumference, were explored.

Results—Based on association analysis of more than 40 genetic polymorphisms in the adiponectin gene (*ADIPOQ*), we found no consistent association of *ADIPOQ* variants with plasma adiponectin levels and adiposity phenotypes. However, there were two promoter variants, rs17300539 and rs822387, associated with plasma adiponectin levels ($P=0.0079$ and 0.021 , respectively) in the Hispanic-American cohort that were also associated with S_1 ($P=0.0067$ and 0.013 , respectively). In contrast, there was only a single promoter SNP, rs17300539, associated with plasma adiponectin levels ($P=0.0018$) and fasting glucose ($P=0.042$) in the African-American cohort. Strikingly, high impact coding variants did not show evidence of association.

Conclusions—The lack of consistent patterns of association between variants, adiponectin levels, glucose homeostasis, and adiposity phenotypes suggests a reassessment of the influence of adiponectin in these pathways.

Keywords

adiponectin; single nucleotide polymorphisms; glucose homeostasis; adiposity; African Americans; Hispanic Americans

1. Introduction

Adiponectin is an adipocytokine that has been implicated in glucose homeostasis and fatty acid oxidation [1, 2]. It is the most abundant adipocytokine found in plasma, accounting for 0.01% of plasma protein. Unlike other well-known adipocytokines such as leptin which increases in circulation with body mass, adiponectin levels are inversely correlated with body mass. Lower levels of adiponectin have been correlated with a variety of conditions including obesity [3, 4], type 2 diabetes (T2D) [2, 5], hypertension [6, 7], dyslipidemia [8], and metabolic syndrome [9]. In addition to these correlations, there have been multiple reports of a negative correlation between adiponectin levels and insulin resistance [10–12], a trait frequently observed in metabolic syndrome and T2D.

Plasma adiponectin levels have been genetically linked to many loci [9, 13–16] in various populations. However, chromosome 3q27 the location of the *ADIPOQ* gene encoding adiponectin remains the strongest signal identified from genome-wide association studies (GWAS) [16, 17]. In addition, this locus has been implicated in genetic studies of T2D [18–20] and metabolic syndrome [21], making *ADIPOQ* a candidate gene of interest in studies of insulin resistance, adiposity, and T2D.

The purpose of this study was to explore the relationship between adiponectin and glucose homeostasis and adiposity phenotypes. We sought to examine this relationship through association analysis of *ADIPOQ* single nucleotide polymorphisms (SNPs) with plasma adiponectin levels, glucose homeostasis, and adiposity measures such as insulin sensitivity, fasting glucose, and body mass index (BMI).

2. Materials and Methods

2.1 Insulin Resistance Atherosclerosis Family Study (IRASFS)

The study design, recruitment, and phenotyping for IRASFS have been described in detail [22]. Briefly, the IRASFS was designed to identify the genetic and environmental basis of insulin resistance and adiposity. Hispanic-American subjects included in this report were recruited from clinical centers in San Luis Valley, Colorado and San Antonio, Texas while African Americans were recruited from Los Angeles, California. The IRAS-FS protocol was

approved by local institutional review committees and all participants gave informed consent. While a diagnosis of diabetes was not a requirement to participate, approximately 12% of the subjects had diabetes. Families were recruited to obtain an average of 12–13 members. The exam included a fasting blood draw and medical history interview. The clinical examination included an insulin-modified frequently sampled glucose tolerance test (FSIGT) using the reduced sampling protocol [23]. Measures of glucose homeostasis, fasting glucose, insulin sensitivity (S_I), acute insulin response (AIR), and disposition index (DI), were computed using the results of the FSIGT combined with the MINMOD analysis program [24]. Height, weight, and waist circumference were measured and computed tomography was used to estimate visceral and subcutaneous fat (VAT and SAT, respectively). The characteristics of the IRASFS cohort are summarized in Table 1.

2.2 Laboratory Methods

Biomarkers—Total plasma adiponectin levels were measured by radioimmunoassay (RIA; Linco Research, St. Charles, MO). This RIA uses a polyclonal anti-adiponectin antibody which recognizes trimers and higher multimers of adiponectin and includes recognition of the globular domain. In addition, a subset of 200 samples has been measured with a monoclonal antibody-based enzyme-linked immunosorbent assay (ELISA), with good correlation ($r=0.88$) with the RIA [25].

DNA Isolation—Genomic DNA was purified using PUREGENE DNA isolation kits (Gentra Inc., Minneapolis, MN, USA). Total genomic DNA was quantified using a fluorometric assay by Hoefer DyNA Quant 200 fluorometer (Hoefer Pharmacia Biotech Inc., San Francisco, CA, USA).

ADIPOQ SNP Genotyping—In addition to database searches, SNPs identified by direct sequencing of *ADIPOQ* were evaluated in this study. Sequencing and analysis have been described (An, submitted). Briefly, *ADIPOQ* sequencing targeted promoter (region as defined by Kita *et al* [26]) and exonic sequences of *ADIPOQ* in Hispanic and African Americans. In addition to novel variants identified from sequencing, common SNPs across the *ADIPOQ* gene and the surrounding ± 50 kb region were selected using HapMap YRI and CEU populations (www.hapmap.org). Thirty-eight haplotype tagging SNPs were selected with an r^2 threshold of 0.8 and MAF $>5\%$. In addition, SNPs identified in prior GWAS studies [10, 27], functional studies [28], low frequency (LF) and rare variants identified from DNA sequencing described above, and studies in diverse populations as summarized in Waki *et al* [28] were also identified for genotyping, resulting in a total of 43 and 44 SNPs genotyped in the IRASFS Hispanic- and African-American samples, respectively. In addition, data from analysis of the previously described G45R mutation in Hispanic Americans, a high impact, low frequency coding variant [25] was included for completeness. SNP genotyping was performed on a Sequenom MassARRAY Genotyping System (Sequenom, San Diego, CA) using methods previously described [29]. The genotyping efficiency was $>90\%$ and 134 blind duplicate samples included to evaluate genotyping accuracy were 100% concordant.

2.3 Statistical Analysis

All variants were examined for Mendelian inconsistencies using PedCheck [30] in the IRASFS cohorts, resulting in $<0.05\%$ discrepancies which were converted to missing. In the Hispanic-American sample, there were five SNPs found to be monomorphic (T31I, C36S, G51G, R55C, and rs1865762) and thus excluded from further analysis. In the African-American cohort, there were four variants found to be monomorphic (C36S, G45R, G84R, and G90S) and thus excluded from further analysis. All SNPs were consistent with Hardy-Weinberg equilibrium. To best approximate the distributional assumptions of the tests (i.e.,

conditional normality given age, gender, BMI, recruitment center, and admixture and homogeneity of variance), each trait was examined for most appropriate transformations. Specifically, plasma adiponectin levels, BMI, and waist measures were natural log transformed, insulin sensitivity was natural log transformed after the addition of 1, acute insulin response and disposition index were sign square root, and visceral and subcutaneous adipose tissue were square root transformed. No transformation was required for fasting glucose.

Tests of association between the variants and quantitative traits were computed using a variance component model as implemented in Sequential Oligogenic Linkage Analysis Routines (SOLAR) [31]. For the tests of association, the inference was based on the additive genetic model adjusting for age, gender, BMI, recruitment center and admixture, except in the analysis with BMI. Admixture in the IRASFS African Americans was calculated with principle component analysis based on 36 ancestry informative markers (AIMs) [32]. In the IRASFS Hispanic Americans, admixture was estimated using a principal component analysis of 80 AIMs [33]. Multiple comparison correction was not performed owing to the a priori hypothesis of association between the variants examined and adiponectin levels and the primary hypothesis that *ADIPOQ* SNPs are associated with glucose homeostasis and adiposity as a consequence of these metabolic derangements.

3. Results

There were a total of 38 and 40 SNPs analyzed in the Hispanic- and African-American cohorts, respectively. In the Hispanic-American cohort, minor allele frequencies for the genotyped SNPs ranged from 0 to 49%. Six SNPs (excluding G45R) were nominally associated ($P < 0.05$) with plasma adiponectin levels (Table 2A) with p-values ranging from 0.0072 to 0.025. In addition to the previously described G45R variant, only one of these SNPs, rs62625753 was a coding variant (G90S; located in exon 3). The remaining SNPs associated with adiponectin levels were found 5' of the gene or in intron 1. The SNP with the strongest association with plasma adiponectin was rs822391, with a p-value of 0.0072. Individuals with zero ($13.57 \pm 7.84 \mu\text{g/mL}$), one ($13.49 \pm 6.67 \mu\text{g/mL}$), and two ($15.59 \pm 7.09 \mu\text{g/mL}$) copies of the minor allele had modest differences in plasma adiponectin levels (An *et al* submitted). In the African-American cohort, minor allele frequencies for the genotyped SNPs ranged from 0 to 44% (Table 3A). There were seven SNPs associated with plasma adiponectin levels, with a coding variant, R55C, being the most strongly associated ($p = 0.00030$). Individuals with this variant ($1.20 \pm 0.37 \mu\text{g/mL}$) had significantly lower levels of plasma adiponectin levels compared to those without the variant ($9.06 \pm 5.01 \mu\text{g/mL}$) (An *et al* submitted). The remaining associated variants were found 5' of the gene, in intron 1, or 3' of the gene.

Since adiponectin has been associated in the literature with insulin sensitivity and other metabolic derangements, *ADIPOQ* SNPs were evaluated for association with glucose homeostasis (insulin sensitivity (S_I), acute insulin response (AIR), disposition index (DI), and fasting glucose) and adiposity (body mass index (BMI), visceral adipose tissue (VAT), subcutaneous adipose tissue (SAT), and waist circumference) traits. When *ADIPOQ* variants were tested with these traits (Tables 2A, 2B, 3A and 3B) there was no consistent evidence of association between SNPs associated with plasma adiponectin levels and association with glucose homeostasis phenotypes in either cohort. Within the Hispanic-American sample, a single SNP, rs12495941 located in intron 1, was nominally associated with fasting glucose ($P = 0.022$) and trending toward association with adiponectin ($P = 0.090$). Four SNPs were associated with insulin sensitivity ($P = 0.013$ – 0.0013) with two of the variants, rs822387 and rs17300539, associated with plasma adiponectin levels ($P = 0.021$ and 0.0079 , respectively). There were 10 SNPs associated with AIR, which is a measure of the

first phase insulin response. However, only the *ADIPOQ* G45R variant was associated with AIR ($P=0.047$) and adiponectin levels ($P=5.0E-40$). There were no SNPs associated with disposition index, which is the product of S_I and AIR. There were three variants associated with BMI ($P=0.032-0.0071$), none of which were associated with adiponectin levels and two variants associated with VAT, one of which, rs2036373, was also associated with BMI ($P=0.032$) and S_I ($P=0.010$). Three variants were associated with SAT, but none were associated with adiponectin. One of these SNPs, rs12495941, was also associated with fasting glucose ($P=0.022$). Finally, there were five variants associated with waist circumference ($P=0.042-9.5E-04$). Two of the five variants were also associated with SAT ($P<0.039$) and one of the two was associated with fasting glucose (rs12495941, $P=0.022$). A 3' variant (rs13085499) associated with waist circumference ($P=0.0034$) was also associated with VAT ($P=0.035$).

In the African-American cohort, results were broadly similar to those observed in the Hispanic-American sample. There were a total of seven SNPs associated with plasma adiponectin levels (Table 3A; $P<0.034$). One was the coding variant, R55C, which was also the most strongly associated variant ($P=3.0E-04$) within the 40 SNPs analyzed. There were no *ADIPOQ* SNPs associated with S_I , DI, BMI, VAT, SAT, or waist circumference although four SNPs associated with fasting glucose ($P<0.042$). However, rs17300539 was the only SNP associated with fasting glucose ($P=0.042$) that was also associated with plasma adiponectin levels ($P=0.0018$). Only a single SNP located in intron 1 was associated with AIR, rs9877202 ($P=0.042$) and was not associated with plasma adiponectin levels ($P=0.21$).

4. Discussion

The purpose of this study was to evaluate whether *ADIPOQ* SNPs were associated with plasma adiponectin levels as well as glucose homeostasis and adiposity measures. There is an abundant literature investigating the association between adiponectin variants and glucose homeostasis and adiposity measures [10, 11, 20, 21, 34, 35]. Much of this literature has been inconclusive, but if adiponectin actively participates in metabolic disease, we would hypothesize that variants that alter circulating adiponectin levels should be associated with metabolic measures. Overall, our results were not consistent with this hypothesis: no consistent pattern of association was observed between SNPs, adiponectin levels, and metabolic traits. The few nominal associations, e.g. rs17300539 and rs822387, that followed from adiponectin levels into metabolic traits are less convincing when strict corrections for multiple comparisons (for Hispanic Americans, 40 SNPs; $P=0.0013$ and for African Americans, 42 SNPs; $P=0.0012$) were made.

Recently Hivert *et al* [10] observed association with two *ADIPOQ* promoter SNPs, rs17300539 and rs822387, with plasma adiponectin levels in the Framingham Offspring Study, a study which is comprised almost exclusively of individuals of European descent. We observed similar association with plasma adiponectin levels in the IRASFS Hispanic-American cohort with p-values of 0.0079 (rs17300539) and 0.021 (rs822387) for the two correlated SNPs ($r^2=0.69$). In addition, in the IRASFS African-American cohort, rs17300539 was also associated with plasma adiponectin levels ($P=0.0018$), while rs822387 was not associated ($P=0.23$) potentially due to decreased correlation among the variants ($r^2=0.06$). Interestingly, Hivert *et al* did not find association with glucose homeostasis and adiposity measures with either of these variants whereas in the IRASFS, there was association of rs17300539 and rs822387 with S_I in the Hispanic-American cohort ($P=0.0067$ and 0.013 , respectively) and association of rs17300539 with fasting glucose in the African-American cohort ($P=0.042$). The association of rs17300539 and rs822387 with S_I did not result in dramatic differences in S_I in individuals with zero ($2.16 \pm 1.86 \times 10^{-5} \text{ min}^{-1}[\text{pmol/L}]^{-1}$; $2.14 \pm 0.84 \times 10^{-5} \text{ min}^{-1}[\text{pmol/L}]^{-1}$), one ($2.08 \pm 1.85 \times 10^{-5}$

$\text{min}^{-1}[\text{pmol/L}]^{-1}$; $2.26 \pm 2.11 \times 10^{-5} \text{ min}^{-1}[\text{pmol/L}]^{-1}$), and two ($1.94 \times 10^{-5} \text{ min}^{-1}[\text{pmol/L}]^{-1}$; $1.94 \times 10^{-5} \text{ min}^{-1}[\text{pmol/L}]^{-1}$) copies of the minor allele, respectively (Appendix Table 1). The association of rs17300539 with fasting glucose in the African Americans yielded similar modest differences in the genotypic means for 0 ($94.77 \pm 9.74 \text{ mg/dL}$) and 1 ($91.91 \pm 8.38 \text{ mg/dL}$) copy of the minor allele. We explored the rs17300539 SNP further. Although the SNP was associated with fasting glucose in the independent African-American and Hispanic-American cohorts, the beta coefficients were in the opposite direction and in a meta-analysis there was no evidence for association ($P=0.51$, data not shown). Hivert *et al* was able to find association between the coding variant rs17366743 and fasting glucose ($P=0.0004$) and diabetes risk ($P=0.01$) [10]. However, in the IRASFS Hispanic- and African-American cohorts, there was no evidence of association of rs17366743 with glucose homeostasis or adiposity measures. Dastani *et al* [13] recently reported evidence for nominal association ($P=0.003\text{--}0.048$) between T2D and a collection of adiponectin-associated variants across the genome in a large European sample, however, the promoter SNP, rs17300539, was not found to be associated with T2D, only associated with high molecular weight adiponectin in the Cardiovascular Health Study ($P=3.0 \times 10^{-16}$) [13].

In addition to common variants we evaluated multiple low frequency coding variants. Similar to the G45R mutation which we have previously described [25], the R55C coding variant in African Americans corresponds to very low adiponectin levels and no evidence of association with the glucose homeostasis and adiposity phenotypes studied here (Table 3A and 3B). The frequency of the R55C is low (1.0%) which limits power to assess association, but one would suspect that a mutation that reduces the amount of circulating adiponectin 80–85% would result in a difference in metabolic measures. It is noteworthy that in a cross-ethnic (Hispanic American and African American) analysis, cross-SNP (R55C and G45R) meta-analysis of these high impact variants, there was no evidence of association with any of the metabolic and adiposity traits evaluated here (data not shown).

While there are reports of association between S_I and plasma adiponectin levels [36, 37], it is difficult to discern the exact relationship between the two due to a lack of consistent association between variants associated with plasma adiponectin levels and S_I . Within the IRASFS, there were only two SNPs that were associated with both plasma adiponectin and S_I in the Hispanic-American cohort, and none within the African-American cohort. There are also some mixed reports of association between fasting glucose and plasma adiponectin levels [4, 38]. These inconclusive findings across ancestries could be attributed to reduced power in the IRASFS African American cohort in comparison to the Hispanic American cohort as a result of sample size differences (Appendix Table 2) and compounded by LD differences between the two ethnicities. Therefore, it is not possible to draw firm conclusions based on these results, but we hypothesize that if adiponectin and fasting glucose are associated with one another, there may be factors other than *ADIPOQ* variants that drive the association.

As an adipocytokine, adiponectin has been reported to be associated with adiposity phenotypes [3, 36, 39]. In the IRASFS Hispanic-American cohort, there were several SNPs associated with adiposity phenotypes such as BMI, visceral and subcutaneous adipose tissue, and waist circumference. However, none of the variants were concomitantly associated with plasma adiponectin levels. This finding leads us to speculate that variants associated with plasma adiponectin levels are not similarly related to adipose tissue distribution or overall body mass, unlike many other reports. Interestingly, in the African-American cohort of the IRASFS, there were no *ADIPOQ* variants associated with adiposity phenotypes.

Within the IRASFS Hanley *et al* [40] previously reported strong correlations between plasma adiponectin levels and S_I , fasting glucose, fasting insulin, BMI, waist circumference,

and visceral adipose tissue. The current study failed to find consistent association between variants associated with plasma adiponectin and glucose homeostasis and adiposity phenotypes. One of the greatest strengths of the IRASFS is a unique study design with well phenotyped and comprehensively genotyped samples of African and Hispanic Americans. These results are limited in the number of individuals available within the sample, 1183 Hispanic and 566 African Americans. Due to the high quality phenotyping performed in the IRASFS, this also limits replication samples since this type of phenotyping is unavailable in most other cohorts. In spite of this, this study performed a comprehensive tagging of the *ADIPOQ* gene to assess the association of adiponectin variants with glucose homeostasis and adiposity phenotypes.

5. Conclusions

We evaluated approximately 40 *ADIPOQ* variants for association with plasma adiponectin levels, glucose homeostasis and adiposity phenotypes in a Hispanic- and African-American cohort. We were able to identify two promoter variants associated with plasma adiponectin and S_1 within the Hispanic-American cohort and one promoter variant associated with plasma adiponectin and fasting glucose within the African-American cohort. We did not find any consistent association of *ADIPOQ* variants with plasma adiponectin and other glucose homeostasis or adiposity phenotypes. These results question the role of adiponectin in glucose homeostasis and adiposity; whether it plays a causative role as previously reported or whether it is more a consequence of these metabolic derangements.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

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Highlights

- Focus on the Hispanic- and African-American population, an ethnic minority disproportionately affected by T2D and obesity and under-represented in genetic studies of common, complex disease.
- This study utilizes high quality metabolic phenotypes, e.g. insulin sensitivity (S_I), acute insulin response (AIR), disposition index (DI), fasting glucose, body mass index (BMI), visceral adipose tissue (VAT), subcutaneous adipose tissue (SAT), and waist circumference.
- Evaluation of quantitative measures of glucose homeostasis, S_I , AIR and DI, contributes to the understanding of the physiological architecture of T2D and obesity.
- The lack of consistent patterns of association between variants, adiponectin levels, glucose homeostasis, and adiposity phenotypes suggests a reassessment of the influence of adiponectin in these pathways.

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Summary statistics for Insulin Resistance Atherosclerosis Family Study participants.

Table 1

Trait Class	Trait	Hispanic Americans			African Americans		
		n*	mean	standard deviation	n*	mean	standard deviation
	Gender (n, female, %)	1183	691	58.4	566	337	59.5
	Age (years)	1183	42.9	14.5	566	42.8	13.9
	T2D (n, affected, percent total)	1180	146	12.4	566	64	11.3
	Adiponectin (ug/mL)	1073	13.5	6.9	555	9.01	5.24
Glucose Homeostasis	Insulin Sensitivity (S _I ; x10 ⁻⁵ min ⁻¹ [pmol/L] ⁻¹)	975	2.45	1.87	490	1.63	1.17
	Acute Insulin Response (AIR; pmol/L)	975	765	657	489	1007	822
	Fasting Glucose (mg/dL)	1032	93.5	9.5	501	94.6	9.7
	Disposition Index (DI; x10 ⁻⁵ min ⁻¹)	975	1317	1233	489	1432	1276
Adiposity	Body Mass Index (BMI; kg/m ²)	1183	29	6.2	566	30.1	6.8
	Visceral Adipose Tissue (VAT; cm ²)	1132	115	61	520	93.3	58
	Subcutaneous Adipose Tissue (SAT; cm ²)	1132	340	155	520	358	191
	Visceral Subcutaneous Ratio (VSR)	1091	0.38	0.21	502	0.3	0.18
	Waist Circumference (cm)	1182	90.1	14.3	565	91.8	15.1

* Sample sizes range from 964 to 1151 due to incomplete data for some measures. Specifically, the FSGT was not performed in those with diabetes, reducing the sample size for SI and AIR.

Table 2A

ADIPOQ SNP associations with glucose homeostasis phenotypes in Hispanic Americans.

SNP	Position (hg18)	Alleles (Major/Minor)	MAF	AA change	Location	Adiponectin		S _I		AIR		DI		Fasting Glucose	
						beta	P-value	beta	P-value	beta	P-value	beta	P-value	beta	P-value
rs7648121	68183280	C/T	0.060		5'	-1.04	0.25	0.073	0.082	-2.26	0.030	-1.18	0.43	-1.04	0.21
rs6810075	188031259	T/C	0.44		5'	0.39	0.74	-0.0010	0.96	-0.60	0.25	-0.41	0.58	0.39	0.33
rs10937273	188032389	G/A	0.33		5'	-0.47	0.062	0.012	0.60	0.95	0.090	0.95	0.23	-0.47	0.28
rs1648707	188034405	A/C	0.42		5'	0.21	0.66	-0.0014	0.95	-0.36	0.49	-0.22	0.76	0.21	0.61
rs864265	188036986	G/T	0.19		5'	0.20	0.25	0.022	0.39	-0.58	0.38	-0.09	0.92	0.20	0.69
rs822387	188038731	T/C	0.060		5'	0.36	0.021	-0.12	0.013	0.31	0.79	-1.37	0.41	0.36	0.68
rs16861194	188042119	A/G	0.14		5'	-0.041	0.67	-0.017	0.54	0.066	0.93	-1.01	0.31	-0.041	0.94
rs17300539	188042154	G/A	0.047		5'	0.18	0.0079	-0.13	0.0067	1.43	0.23	-1.92	0.25	0.18	0.84
rs266729	188042168	C/G	0.28		5'	0.42	0.72	0.0039	0.86	-0.45	0.43	0.14	0.86	0.42	0.33
rs710445	188044212	A/G	0.44		intron 1	0.24	0.67	0.0055	0.79	-0.57	0.27	-0.50	0.50	0.24	0.55
rs16861205	188044328	G/A	0.13		intron 1	-0.54	0.64	0.0013	0.96	0.39	0.60	-0.22	0.84	-0.54	0.36
rs16861209	188045808	C/A	0.064		intron 1	-0.0049	0.068	-0.14	0.0013	1.29	0.25	-2.34	0.14	-0.0049	1.00
rs822391	188046497	T/C	0.19		intron 1	0.23	0.0072	0.0044	0.86	-0.42	0.51	-0.60	0.50	0.23	0.63
rs822394	188049422	C/A	0.19		intron 1	0.33	0.013	0.0079	0.75	-0.53	0.40	-0.57	0.52	0.33	0.50
rs822396	188049571	A/G	0.20		intron 1	0.27	0.025	0.0064	0.79	-0.43	0.49	-0.46	0.60	0.27	0.59
rs12495941	188050874	G/T	0.32		intron 1	-1.01	0.090	0.016	0.47	0.49	0.38	1.08	0.18	-1.01	0.022
rs9877202	188052301	A/G	0.0066		intron 1	-0.19	0.81	0.15	0.37	3.24	0.44	10.23	0.091	-0.19	0.95
rs2036373	188052885	T/G	0.044		intron 1	-1.26	0.67	0.12	0.010	0.12	0.92	3.25	0.051	-1.26	0.18
rs17366568	188053147	G/A	0.066		intron 1	0.025	0.24	0.086	0.056	-1.97	0.078	0.34	0.83	0.025	0.98
rs2241766	188053586	T/G	0.18	G15G	exon 2	-0.33	0.32	-0.0051	0.84	1.44	0.026	1.56	0.090	-0.33	0.52
G45R *	188053674	G/C	0.011	G45R	exon 2	-1.17	5.0E-40	0.0049	0.96	-4.97	0.047	-3.75	0.29	3.69	0.058
rs2241767	188053890	A/G	0.18		intron 2	-0.40	0.30	-0.0051	0.84	1.58	0.016	1.66	0.072	-0.40	0.43
rs3774261	188054253	G/A	0.43		intron 2	-0.25	0.85	-0.0025	0.90	1.10	0.034	0.61	0.40	-0.25	0.53
rs3774262	188054508	G/A	0.18		intron 2	-0.38	0.48	-0.010	0.72	1.54	0.019	1.51	0.11	-0.38	0.46
rs62625753	188054720	G/A	0.0044	G90S	exon 3	0.91	0.025	-0.21	0.21	1.62	0.70	-2.23	0.70	0.91	0.78
rs17366743	188054783	T/C	0.016	Y111H	exon 3	3.67	0.77	-0.17	0.092	-0.83	0.74	-3.72	0.30	3.67	0.062
rs6444174	188055883	T/C	0.029		3' UTR	-0.80	0.97	0.11	0.061	-3.29	0.030	-1.47	0.50	-0.80	0.51

SNP	Position (hg18)	Alleles (Major/Minor)	MAF	AA change	Location	Adiponectin		S _I		AIR		DI		Fasting Glucose	
						beta	P-value	beta	P-value	beta	P-value	beta	P-value	beta	P-value
rs6773957	188056399	G/A	0.43		3' UTR	-0.25	0.90	-0.0024	0.91	1.11	0.032	0.67	0.36	-0.25	0.53
rs2082940	188056858	C/T	0.19		3' UTR	-0.33	0.35	-0.0030	0.91	1.27	0.050	1.34	0.14	-0.33	0.51
rs9842733	188058176	A/T	0.0044		3' UTR	0.69	0.77	0.029	0.94	1.28	0.90	3.02	0.83	0.69	0.93
rs1403697	188059387	A/G	0.0045		3'	0.69	0.77	0.029	0.94	1.28	0.90	3.02	0.83	0.69	0.93
rs7639352	188061168	C/T	0.24		3'	-0.081	0.44	-0.0060	0.80	0.30	0.62	-0.46	0.60	-0.081	0.87
rs7641507	188061267	C/T	0		3'	0.41	0.53	0.058	0.81	-6.98	0.26	-1.74	0.84	0.41	0.93
rs6444175	188062438	G/A	0.25		3'	-0.017	0.54	-0.011	0.66	0.20	0.75	-0.74	0.39	-0.017	0.97
rs1403696	188062560	C/T	0.024		3'	-2.07	0.17	0.13	0.067	-3.66	0.037	-0.53	0.83	-2.07	0.14
rs13085499	188063534	G/A	0.49		3'	0.39	0.78	-0.014	0.49	-0.24	0.64	-0.33	0.65	0.39	0.32
rs7628649	188068075	C/T	0.21		3'	-0.29	0.36	0.022	0.39	0.56	0.38	1.46	0.11	-0.29	0.57
rs17373414	188068221	C/T	0.051		3'	-1.66	0.052	-0.050	0.37	0.086	0.95	-1.58	0.42	-1.66	0.12

SNPs are ordered by position (hg18) and annotated with alleles (major/minor), minor allele frequency (MAF) determined in the largest set of unrelated individuals (n=229), amino acid (AA) change and location relative to the *ADIPOQ* gene. For each phenotype, adiponectin, insulin sensitivity (S_I), acute insulin response (AIR), disposition index (DI), and fasting glucose, the effect size and direction (beta) and additive P-values are given.

* G45R data was previously published by Bowden *et al.* in Hum Mol Genet. 2010 Oct 15;19(20):4112-20. Epub 2010 Aug 5.

Table 2B

ADIPOQ SNP associations with adiposity phenotypes in Hispanic Americans.

SNP	Position (hg18)	Alleles (Major/Minor)	MAF	AA change	Location	BMI		VAT		SAT		WAIST	
						beta	P-value	beta	P-value	beta	P-value	beta	P-value
rs7648121	68183280	C/T	0.060		5'	-0.0084	0.23	-0.29	0.073	-1.04	0.38	-0.0026	0.64
rs6810075	188031259	T/C	0.44		5'	0.0019	0.29	0.079	0.32	0.39	0.52	0.0033	0.23
rs10937273	188032389	G/A	0.33		5'	-0.0018	0.30	-0.054	0.53	-0.47	0.021	-0.0037	0.20
rs1648707	188034405	A/C	0.42		5'	0.0021	0.40	0.11	0.16	0.21	0.52	0.0045	0.093
rs864265	188036986	G/T	0.19		5'	0.0011	0.98	-0.031	0.75	0.20	0.64	0.0011	0.76
rs822387	188038731	T/C	0.060		5'	-0.0081	0.22	-0.29	0.10	0.36	0.10	-0.010	0.12
rs16861194	188042119	A/G	0.14		5'	0.0028	0.42	-0.023	0.84	-0.041	0.96	-0.0006	0.87
rs17300539	188042154	G/A	0.047		5'	-0.0062	0.26	-0.23	0.21	0.18	0.11	-0.0058	0.37
rs266729	188042168	C/G	0.28		5'	0.00083	0.51	0.14	0.090	0.42	0.17	0.0060	0.042
rs710445	188044212	A/G	0.44		intron 1	0.0011	0.27	0.059	0.46	0.24	0.44	0.0044	0.11
rs16861205	188044328	G/A	0.13		intron 1	-0.0011	0.19	-0.12	0.30	-0.54	0.41	-0.0026	0.51
rs16861209	188045808	C/A	0.064		intron 1	-0.0076	0.55	0.0052	0.98	-0.0049	0.091	-0.0049	0.40
rs822391	188046497	T/C	0.19		intron 1	0.0028	0.77	-0.068	0.47	0.23	0.28	0.0051	0.13
rs822394	188049422	C/A	0.19		intron 1	0.0027	0.75	-0.055	0.57	0.33	0.30	0.0046	0.17
rs822396	188049571	A/G	0.20		intron 1	0.0031	0.95	-0.041	0.67	0.27	0.27	0.0057	0.085
rs12495941	188050874	G/T	0.32		intron 1	-0.00063	0.067	-0.10	0.25	-1.01	0.039	-0.0063	0.034
rs9877202	188052301	A/G	0.066		intron 1	0.0029	0.72	-0.061	0.92	-0.19	0.68	0.010	0.62
rs2036373	188052885	T/G	0.044		intron 1	-0.0016	0.032	-0.42	0.022	-1.26	0.19	-0.015	0.023
rs17366568	188053147	G/A	0.066		intron 1	-0.0066	0.51	0.012	0.95	0.025	0.012	-0.020	9.5E-04
rs2241766	188053586	T/G	0.18	G15G	exon 2	0.00036	0.17	-0.15	0.12	-0.33	0.41	-0.0021	0.55
G45R [*]	188053674	G/C	0.011	G45R	exon 2	0.040	0.35	-0.22	0.57	-0.77	0.064	0	0.72
rs2241767	188053890	A/G	0.18		intron 2	-0.00086	0.24	-0.16	0.11	-0.40	0.58	-0.0025	0.48
rs3774261	188054253	G/A	0.43		intron 2	-0.0023	0.85	-0.13	0.11	-0.25	0.66	-0.0046	0.091
rs3774262	188054508	G/A	0.18		intron 2	-0.00079	0.26	-0.18	0.081	-0.38	0.39	-0.0032	0.36
rs62625753	188054720	G/A	0.0044	G90S	exon 3	0.013	0.88	-0.10	0.86	0.91	0.15	-0.015	0.49
rs17366743	188054783	T/C	0.016	Y111H	exon 3	0.0063	0.19	0.36	0.32	3.67	0.56	0.014	0.28
rs6444174	188055883	T/C	0.029		3' UTR	-0.00014	0.45	0.15	0.52	-0.80	0.84	-0.0063	0.44

SNP	Position (hg18)	Alleles (Major/Minor)	MAF	AA change	Location	BMI		VAT		SAT		WAIST	
						beta	P-value	beta	P-value	beta	P-value	beta	P-value
						beta	P-value	beta	P-value	beta	P-value	beta	P-value
rs6773957	188056399	G/A	0.43		3' UTR	-0.0020	0.96	-0.12	0.13	-0.25	0.61	-0.0045	0.094
rs2082940	188056858	C/T	0.19		3' UTR	-0.0010	0.23	-0.17	0.086	-0.33	0.74	-0.0038	0.27
rs9842733	188058176	A/T	0.0044		3' UTR	-0.074	0.0072	1.25	0.32	0.69	0.19	0.0091	0.79
rs1403697	188059387	A/G	0.0045		3'	-0.074	0.0071	1.25	0.32	0.69	0.19	0.0078	0.82
rs7639352	188061168	C/T	0.24		3'	-0.0015	0.32	-0.026	0.78	-0.081	0.34	-0.0034	0.29
rs7641507	188061267	C/T	0		3'	-0.029	0.15	-1.52	0.13	0.41	0.49	-0.0067	0.85
rs6444175	188062438	G/A	0.25		3'	-0.0018	0.30	-0.035	0.70	-0.017	0.44	-0.0029	0.37
rs1403696	188062560	C/T	0.024		3'	-0.0056	0.72	0.13	0.63	-2.07	0.49	-0.0049	0.60
rs13085499	188063534	G/A	0.49		3'	0.0022	0.70	0.16	0.035	0.39	0.36	0.0079	0.0034
rs7628649	188068075	C/T	0.21		3'	-0.0015	0.13	-0.14	0.14	-0.29	0.81	-0.0058	0.085
rs17373414	188068221	C/T	0.051		3'	-0.0027	0.13	0.034	0.87	-1.66	0.12	-0.0046	0.53

SNPs are ordered by position (hg18) and annotated with alleles (major/minor), minor allele frequency (MAF) determined in the largest set of unrelated individuals (n=229), amino acid (AA) change and location relative to the *ADIPOQ* gene. For each phenotype, adiponectin, body mass index (BMI), visceral adipose tissue (VAT), subcutaneous adipose tissue (SAT), and waist circumference (WAIST), the number of observations (n), effect size and direction (beta) and additive P-values are given.

* G45R data was previously published by Bowden *et al.* in Hum Mol Genet. 2010 Oct 15;19(20):4112-20. Epub 2010 Aug 5.

Table 3A

ADIPOQ SNP associations with glucose homeostasis phenotypes in African Americans.

SNP	Position (hg18)	Alleles (Major/Minor)	MAF	AA change	Location	Adiponectin		S ₁		AIR		DI		Fasting Glucose	
						beta	P-value	beta	P-value	beta	P-value	beta	P-value	beta	P-value
rs7648121	68183280	C/T	0.061		5'	0.15	0.0052	-0.072	0.12	0.66	0.66	-1.19	0.55	0.15	0.90
rs6810075	188031259	T/C	0.43		5'	0.011	0.72	-0.016	0.54	-0.16	0.85	-0.82	0.46	-0.29	0.65
rs10937273	188032389	G/A	0.13		5'	0.063	0.15	0.040	0.28	-0.27	0.82	0.66	0.68	1.26	0.15
rs1648707	188034405	A/C	0.39		5'	-0.072	0.017	-0.027	0.30	0.11	0.90	-1.05	0.35	-0.69	0.26
rs864265	188036986	G/T	0.065		5'	-0.0060	0.89	0.031	0.42	-1.41	0.26	-0.55	0.74	0.71	0.44
rs822387	188038731	T/C	0.33		5'	-0.042	0.23	-0.046	0.13	1.43	0.14	1.21	0.35	-0.54	0.46
rs16861194	188042119	A/G	0.32		5'	0.010	0.79	-0.0067	0.83	0.36	0.71	-0.49	0.71	-1.11	0.13
rs17300539	188042154	G/A	0.028		5'	0.32	0.0018	0.12	0.16	2.46	0.37	6.71	0.061	-4.12	0.042
rs266729	188042168	C/G	0.11		5'	-0.040	0.44	0.034	0.46	-1.69	0.25	-1.17	0.55	0.58	0.59
rs710445	188044212	A/G	0.44		intron 1	0.0054	0.86	0.014	0.61	0.19	0.83	-0.38	0.74	-1.11	0.085
rs16861205	188044328	G/A	0.26		intron 1	0.011	0.76	0.010	0.76	0.82	0.43	0.19	0.89	-0.70	0.35
rs16861209	188045808	C/A	0.14		intron 1	0.086	0.034	-0.013	0.71	0.31	0.78	0.21	0.89	-0.81	0.32
rs822391	188046497	T/C	0.031		intron 1	-0.031	0.67	-0.024	0.69	-1.56	0.44	-1.83	0.49	1.37	0.35
rs822394	188049422	C/A	0.029		intron 1	-0.010	0.88	0.017	0.76	1.50	0.41	3.59	0.13	-0.22	0.87
rs822396	188049571	A/G	0.19		intron 1	-0.071	0.060	-0.015	0.63	0.34	0.74	0.24	0.86	0.79	0.29
rs12495941	188050874	G/T	0.39		intron 1	-0.0091	0.77	-0.032	0.23	0.13	0.88	-0.63	0.58	-0.052	0.94
rs9877202	188052301	A/G	0.13		intron 1	-0.059	0.21	-0.053	0.20	2.71	0.042	1.43	0.41	0.54	0.58
rs2036373	188052885	T/G	0.083		intron 1	-0.0092	0.88	-0.025	0.62	-2.05	0.21	-1.41	0.52	1.75	0.15
rs17366568	188053147	G/A	0.037		intron 1	0.052	0.56	0.12	0.11	-0.33	0.89	1.20	0.71	-0.41	0.82
rs2241766	188053586	T/G	0.031	G15G	exon 2	0.043	0.62	-0.0071	0.92	2.11	0.37	4.30	0.17	0.30	0.86
G38D	188053654	G/A	0.0185	G38D	exon 2	-0.041	0.76	-0.19	0.075	-1.43	0.68	-4.94	0.27	4.05	0.11
R55C	188053704	C/T	0.010	R55C	exon 2	-1.00	3.0E-04	-0.369	0.16	9.73	0.26	2.43	0.83	9.71	0.13
rs2241767	188053890	A/G	0.028		intron 2	0.087	0.31	-0.0018	0.98	2.08	0.37	4.62	0.13	0.34	0.84
rs3774261	188054253	G/A	0.40		intron 2	0.041	0.16	0.018	0.46	-0.61	0.44	0.018	0.99	1.05	0.076
rs3774262	188054508	G/A	0.028		intron 2	0.088	0.30	-0.0034	0.96	2.13	0.35	4.63	0.13	0.32	0.85
rs17366743	188054783	T/C	0.010	Y111H	exon 3	-0.20	0.35	0.014	0.94	-11.12	0.061	-13.15	0.088	2.49	0.57
I164T	188054943	T/C	0	I164T	exon 3	-0.0019	0.996	0.31	0.38	-3.66	0.74	7.17	0.61	-10.93	0.20

SNP	Position (hg18)	Alleles (Major/Minor)	MAF	AA change	Location	Adiponectin		S _I		AIR		DI		Fasting Glucose	
						beta	P-value	beta	P-value	beta	P-value	beta	P-value	beta	P-value
						beta	P-value	beta	P-value	beta	P-value	beta	P-value	beta	P-value
rs6444174	188055883	T/C	0.21		3' UTR	-0.056	0.16	0.0041	0.91	-0.15	0.89	-0.89	0.54	2.13	0.010
rs6773957	188056399	G/A	0.40		3' UTR	0.041	0.16	0.018	0.46	-0.61	0.44	0.018	0.99	1.05	0.076
rs2082940	188056858	C/T	0.23		3' UTR	-0.047	0.20	0.0037	0.90	0.16	0.87	0.056	0.97	1.76	0.019
rs9842733	188058176	A/T	0.13		3' UTR	0.015	0.78	0.019	0.68	1.45	0.33	1.02	0.60	1.52	0.17
rs1403697	188059387	A/G	0.18		3'	0.0055	0.90	-0.0092	0.81	0.46	0.71	-0.20	0.90	1.85	0.042
rs7639352	188061168	C/T	0.33		3'	0.072	0.026	0.0079	0.77	-0.48	0.57	0.083	0.94	-0.19	0.76
rs7641507	188061267	C/T	0.094		3'	-0.030	0.61	0.051	0.30	1.21	0.45	2.14	0.31	-1.33	0.25
rs1865762	188062094	A/G	0.010		3'	0.19	0.17	0.074	0.56	-0.69	0.87	2.27	0.67	-1.57	0.61
rs6444175	188062438	G/A	0.33		3'	0.076	0.024	0.013	0.64	-0.95	0.30	-0.013	0.99	-0.044	0.95
rs1403696	188062560	C/T	0.26		3'	-0.032	0.39	-0.010	0.76	0.058	0.95	-1.01	0.44	0.97	0.19
rs13085499	188063534	G/A	0.34		3'	-0.054	0.072	0.011	0.67	0.19	0.82	0.36	0.74	-0.69	0.25
rs7628649	188068075	C/T	0.33		3'	-0.023	0.48	-0.028	0.29	0.79	0.35	-0.030	0.98	0.54	0.40
rs17373414	188068221	C/T	0.020		3'	0.096	0.47	0.10	0.36	3.12	0.39	7.05	0.13	-0.59	0.83

SNPs are ordered by position (hg18) and annotated with alleles (major/minor), minor allele frequency (MAF) as determined in the largest set of unrelated individuals (n=58), amino acid (AA) change and location relative to the *ADIPOQ* gene. For each phenotype, adiponectin, insulin sensitivity (S_I), acute insulin response (AIR), disposition index (DI), fasting glucose, effect size and direction (beta) and additive P-values are given.

Table 3B

ADIPOQ SNP associations with adiposity phenotypes in African Americans.

SNP	Position (hg18)	Alleles (Major/Minor)	MAF	AA change	Location	Adiponectin		BMI		VAT		SAT		WAIST	
						beta	P-value	beta	P-value	beta	P-value	beta	P-value	beta	P-value
rs7648121	68183280	C/T	0.061		5'	0.15	0.0052	0.0039	0.76	0.38	0.076	-0.17	0.53	0.0016	0.82
rs6810075	188031259	T/C	0.43		5'	0.011	0.72	-0.00014	0.36	0.071	0.57	0.0071	0.96	0.0028	0.47
rs10937273	188032389	G/A	0.13		5'	0.063	0.15	-0.0014	0.21	-0.086	0.63	-0.050	0.83	-0.0010	0.86
rs1648707	188034405	A/C	0.39		5'	-0.072	0.017	0.0022	0.45	0.094	0.44	0.032	0.84	0.00051	0.89
rs864265	188036986	G/T	0.065		5'	-0.0060	0.89	0.021	0.50	0.17	0.36	-0.27	0.21	-0.0032	0.57
rs822387	188038731	T/C	0.33		5'	-0.042	0.23	0.0029	0.70	0.17	0.22	0.16	0.36	0.0064	0.16
rs16861194	188042119	A/G	0.32		5'	0.010	0.79	-0.00064	0.31	-0.076	0.58	-0.24	0.18	-0.0031	0.49
rs17300539	188042154	G/A	0.028		5'	0.32	0.0018	0.0068	0.25	-0.23	0.58	-0.35	0.50	0.0025	0.85
rs266729	188042168	C/G	0.11		5'	-0.040	0.44	0.0023	0.95	-0.065	0.76	0.47	0.076	-0.0026	0.70
rs710445	188044212	A/G	0.44		intron 1	0.0054	0.86	-0.00039	0.24	-0.14	0.26	0.010	0.95	-0.0045	0.26
rs16861205	188044328	G/A	0.26		intron 1	0.011	0.76	-0.0017	0.47	-0.20	0.17	-0.25	0.18	-0.0022	0.64
rs16861209	188045808	C/A	0.14		intron 1	0.086	0.034	0.00048	0.97	-0.023	0.89	0.23	0.27	-0.00042	0.94
rs822391	188046497	T/C	0.031		intron 1	-0.031	0.67	-0.0060	0.91	0.077	0.79	0.27	0.46	0.0031	0.74
rs822394	188049422	C/A	0.029		intron 1	-0.010	0.88	-0.0053	0.87	-0.14	0.61	0.094	0.78	-0.0026	0.77
rs822396	188049571	A/G	0.19		intron 1	-0.071	0.060	-0.00076	0.99	0.15	0.29	-0.071	0.69	0.00092	0.84
rs12495941	188050874	G/T	0.39		intron 1	-0.0091	0.77	0.00033	0.15	0.092	0.47	0.0061	0.97	0.0044	0.27
rs9877202	188052301	A/G	0.13		intron 1	-0.059	0.21	-0.0013	0.95	0.35	0.061	0.14	0.56	0.0071	0.24
rs2036373	188052885	T/G	0.083		intron 1	-0.0092	0.88	-0.000074	0.98	0.27	0.25	0.061	0.83	-0.00051	0.95
rs17366568	188053147	G/A	0.037		intron 1	0.052	0.56	0.0087	0.17	-0.067	0.85	0.50	0.25	0.0033	0.76
rs2241766	188053586	T/G	0.031	G15G	exon 2	0.043	0.62	0.00011	0.80	-0.26	0.45	-0.41	0.34	-0.0035	0.75
G38D	188053654	G/A	0.0185	G38D	exon 2	-0.041	0.76	0.0034	0.96	0.40	0.46	-0.95	0.15	0.0021	0.90
R55C	188053704	C/T	0.010	R55C	exon 2	-1.00	3.0E-04	0.015	0.62	0.33	0.74	0.83	0.50	0.057	0.081
rs2241767	188053890	A/G	0.028		intron 2	0.087	0.31	0.0019	0.90	-0.16	0.64	-0.45	0.28	0.00077	0.94
rs3774261	188054253	G/A	0.40		intron 2	0.041	0.16	0.00022	0.37	0.013	0.91	-0.26	0.067	-0.00033	0.93
rs3774262	188054508	G/A	0.028		intron 2	0.088	0.30	0.0021	0.87	-0.16	0.64	-0.45	0.28	0.00081	0.94
rs17366743	188054783	T/C	0.010	Y111H	exon 3	-0.20	0.35	0.0012	0.66	-0.74	0.39	0.86	0.43	-0.051	0.070
I164T	188054943	T/C	0	I164T	exon 3	-0.0019	0.996	0.0034	0.96	-2.24	0.18	-0.22	0.92	-0.054	0.31

SNP	Position (hg18)	Alleles (Major/Minor)	MAF	AA change	Location	Adiponectin		BMI		VAT		SAT		WAIST	
						beta	P-value	beta	P-value	beta	P-value	beta	P-value	beta	P-value
rs6444174	188055883	T/C	0.21		3' UTR	-0.056	0.16	0.00060	0.33	-0.13	0.42	0.16	0.43	-0.0030	0.56
rs6773957	188056399	G/A	0.40		3' UTR	0.041	0.16	0.00022	0.37	0.013	0.91	-0.26	0.067	-0.00033	0.93
rs2082940	188056858	C/T	0.23		3' UTR	-0.047	0.20	0.0017	0.52	-0.17	0.26	-0.031	0.86	-0.0032	0.48
rs9842733	188058176	A/T	0.13		3' UTR	0.015	0.78	0.023	0.37	-0.20	0.38	0.24	0.39	0.0055	0.42
rs1403697	188059387	A/G	0.18		3'	0.0055	0.90	0.0019	0.65	-0.058	0.75	0.13	0.57	0.0035	0.54
rs7639352	188061168	C/T	0.33		3'	0.072	0.026	-0.00069	0.81	0.14	0.27	-0.21	0.18	-0.00031	0.94
rs7641507	188061267	C/T	0.094		3'	-0.030	0.61	0.0012	0.15	0.36	0.13	-0.32	0.30	-0.0073	0.32
rs1865762	188062094	A/G	0.010		3'	0.19	0.17	-0.0049	0.093	-0.45	0.42	-1.03	0.14	-0.023	0.21
rs6444175	188062438	G/A	0.33		3'	0.076	0.024	-0.0012	0.77	0.077	0.57	-0.30	0.071	-0.0021	0.62
rs1403696	188062560	C/T	0.26		3'	-0.032	0.39	0.0022	0.43	-0.097	0.52	0.074	0.69	0.0026	0.57
rs13085499	188063534	G/A	0.34		3'	-0.054	0.072	-0.0017	0.26	-0.073	0.54	0.090	0.54	-0.0021	0.57
rs7628649	188068075	C/T	0.33		3'	-0.023	0.48	0.0015	0.79	-0.071	0.58	0.0075	0.96	0.0025	0.53
rs17373414	188068221	C/T	0.020		3'	0.096	0.47	0.0077	0.93	0.27	0.61	0.051	0.94	0.027	0.11

SNPs are ordered by position (hg18) and annotated with alleles (major/minor), minor allele frequency (MAF) as determined in the largest set of unrelated individuals (n=58), amino acid (AA) change and location relative to the *ADIPOQ* gene. For each phenotype, adiponectin, body mass index (BMI), visceral adipose tissue (VAT), subcutaneous adipose tissue (SAT), and waist circumference (WAIST), effect size and direction (beta) and additive P-values are given.