

## **Supplemental Methods:**

### ***Covariates:***

Smoking and alcohol use were categorized into current versus never/former. Education was categorized as  $\geq$  college education versus  $<$  college education and income was represented as  $\geq$  \$40,000 versus  $<$ \$40,000. Height was measured by a stadiometer to the nearest 0.1 of a centimeter. Weight was measured to the nearest pound using a platform balance scale. Body mass index (BMI) was calculated as weight in kilograms per height in meters squared. Waist circumference was measured using a Gulick II anthropometric tape and was rounded to the nearest centimeter. Medication use was obtained via medication inventory. Estimated glomerular filtration rate (eGFR) was calculated using the equation  $186 * \text{creatinine}^{-1.154} * \text{age}^{-0.203} * 0.742(\text{if female}) * 1.21(\text{if African-American})$ , and prevalent chronic kidney disease was defined as an  $\text{eGFR} \leq 60 \text{ ml/min/1.73m}^2$ . Prevalent diabetes was defined as fasting glucose  $\geq 126 \text{ mg/dL}$ , use of insulin/oral diabetes medications, or a self-report of physician diagnosed diabetes. Prevalent hypertension was defined based on self-report of physician-diagnosed hypertension, diastolic blood pressure  $\geq 90 \text{ mmHg}$ , systolic blood pressure  $\geq 140 \text{ mmHg}$ , or use of anti-hypertensive medications. Systolic and diastolic blood pressures were determined by averaging the last two of three measurements taken with the Dinamap automated blood pressure device (GE Healthcare). Plasma HDL-cholesterol, plasma triglycerides, fasting plasma glucose, and C-reactive protein were measured at a central laboratory after a 12 hour fast. LDL-cholesterol was calculated using the Friedewald formula.

### ***Participant selection into the MESA candidate gene substudy:***

A subcohort of 2880 MESA subjects were selected for genetic studies from subjects who: (1) gave informed consent for DNA extraction and genetic sub-study; 2) had samples in the study DNA laboratory with sufficient DNA. Priority was given to subjects who participated in the MESA Examination 3 additional blood biomarker collection, supplemented by random selection from remaining participant samples to fulfill balanced ethnic group representation (720 African American, 720 Hispanic, 720 Chinese, and 720 Caucasian) and equality by gender. A total of 2847 participants had adequate genotype information and were used in the present study.

***SNP selection:***

SNPs were selected in candidate gene loci according to the following criteria: (1) within the proximal and distal 10 kb regions 5' and 3' to the given candidate gene (NCBI Build 35) ; (2) compatibility with the Illumina GoldenGate technology (Gunderson et al. 2004; Fan et al. 2006) as determined by the Assay Design Tool (TechSupport, Illumina, San Diego, CA); (3) minor allele frequency (MAF) > 0.05 or a tag ( $r^2$  value > 0.8) for another SNP with MAF>0.05 as determined by applying the multilocus or aggressive Tagger option of Haploview v3 (de Bakker 2004; Barrett et al. 2005) using International HapMap project data for CEPH and Yoruban populations (release 19), (International HapMap Consortium 2003). In some cases a complete set of tagSNPs for a given candidate gene was not possible due to these competing criteria.

Additional SNPs were added from (1) LDselect analysis of resequencing information from the Seattle SNPs project if available, (Carlson et al. 2004; SeattleSNPs 2007); (2) non-synonymous SNPs from dbSNP (release 124) (Wheeler et al. 2007); and (3) SNPs with prior report of association with a phenotype similar or identical to one measured in MESA and proposed by a MESA investigator. When a gene required >20-25 tagSNPs, the number was reduced by

selecting tagSNPs for: (1) Caucasian-American population only or (2) for other SNPs with  $MAF > 0.2$ . (*ADIPOQ* did not require  $> 20-25$  tagSNPs so was not affected by this last criterion.)

***References for SNP selection:***

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Fan JB, Gunderson KL, Bibikova M, Yeakley JM, Chen J, Garcia EW, Lebruska LL, Laurent M, Shen R, Barker D (2006) Illumina Universal Bead Arrays. *Methods in Enzymology* 410:57-73

Gunderson KL, Kruglyak S, Graige MS, Garcia F, Kermani BG, Zhao C, Che D, Dickinson T, Wickham E, Bierle J, Doucet D, Milewski M, Yang R, Siegmund C, Haas J, Zhou L, Oliphant A, Fan JB, Barnard S, Chee MS (2004) Decoding randomly ordered DNA arrays. *Genome Res* 14:870-877

International HapMap Consortium (2003) The International HapMap Project. *Nature* 426:789-796

SeattleSNPs (2007) <http://pgambtwashingtonedu/welcomehtml>

Wheeler DL, Barrett T, Benson DA, Bryant SH, Canese K, Chetvernin V, Church DM, et al. (2007) Database resources of the National Center for Biotechnology Information. *Nucleic Acids Res* 35:D5-12

**Supplemental Table 1. Summary of adiponectin gene (*ADIPOQ*) single nucleotide polymorphisms (SNPs) among Caucasians (EUA), African Americans (AFA), Hispanics (HIS), and Chinese (CHN) MESA participants**

<i>ADIPOQ</i>	Position	Position	Minor	MAF	HWE <sup>a</sup>	MAF	HWE <sup>a</sup>	MAF	HWE <sup>a</sup>	MAF	HWE <sup>a</sup>
SNP	(base pairs)	in	allele	EUA <sup>b</sup>	p-value	AFA <sup>b</sup>	p-value	HIS <sup>b</sup>	p-value	CHN <sup>b</sup>	p-value
		<i>ADIPOQ</i>			EUA		AFA		HIS		CHN
rs11711353	188039326	5' UTR	A	0.41	0.76	0.17	0.79	0.31	0.79	0.42	0.49
rs822396	188047725	intron	G	0.18	0.08	0.20	0.35	0.17	1	0.11	0.45
rs12495941	188049571	intron	A	0.34	0.87	0.36	0.81	0.32	0.66	0.42	0.70
rs7649121	188050874	intron	T	0.18	0.46	0.13	1	0.23	0.67	0.21	0.43
rs9877202	188051479	intron	G	0.0007 <sup>c</sup>	--	0.15	0.77	0.03	0.17	0†	--
rs9882205	188052301	intron	A <sup>d</sup>	0.30	0.05	0.23	0.24	0.27	0.51	0.40	0.94
rs2241767	188053890	intron	G	0.14	0.16	0.05	1	0.15	0.77	0.30	0.16
rs1063537	188054508	3' UTR	A	0.14	0.12	0.03	0.54	0.15	0.46	0.30	0.16
rs1063538	188056769	3' UTR	G <sup>d</sup>	0.43	0.59	0.44	0.08	0.48	0.55	0.42	0.28
rs1063539	188058086	3' UTR	G	0.15	0.07	0.05	1	0.16	0.89	0.29	0.24
rs1403697	188059387	3' UTR	G	0.0007 <sup>c</sup>	--	0.13	1	0.02	0.02	0†	--

<sup>a</sup> Hardy-Weinberg Equilibrium, by exact test

<sup>b</sup> Minor Allele Frequency

<sup>c</sup> Not polymorphic among CHN; no EUA homozygous GG participants and only 1 heterozygous EUA participant

<sup>d</sup> rs9882205 minor allele is G for CHN; rs1063538 minor allele is A for HIS and EUA

Supplemental Figure 1.

