Supplement Material

Supplemental Table I. Associations of clinical covariates with SDF-1 levels after multivariable adjustment*

	Estimated β-Coefficient	Standard Error	P-value
Age	0.31	0.019	<0.0001
Sex (female)	0.09	0.036	0.013
BMI (kg/m^2)†	-0.048	0.018	0.007
HDL cholesterol (mg/dl)	-0.011	0.0012	<0.0001
Smoking status (yes)	0.11	0.046	0.017
Systolic blood pressure (mmHg)	-0.049	0.018	0.009

*SDF-1 levels were natural log-transformed. Regression coefficients represent change in ln(SDF-1) per one standard deviation change in independent variables (age, BMI, HDL, systolic blood pressure). Results represent full multivariable adjustment for all covariates jointly.
†BMI and waist circumference were highly correlated r=0.92 in men and r= 0.92 in women (adjusted for age). When waist circumference was substituted for BMI in the multivariable model, p-values for age, sex, waist circumference, HDL cholesterol, smoking status, and systolic blood pressure were: <0.0001, 0.077, 0.048, <0.0001, 0.011, and 0.016, respectively. Additionally, the estimated β-coefficients demonstrated the same directionality when waist circumference replaced BMI in the model.

Supplemental Table II. Risk of three causes of death according to levels of SDF-1

	HR [95% CI] per 1 SD* increment in ln(SDF-1)	P-value†
Death Due to CVD, n=110‡		
Model 1	5.3 [2.2-13.1]	0.0003
Model 2	3.0 [1.2-7.7]	0.02
Deaths Due to Cancer, n=199		
Model 1	1.8 [0.96-3.2]	0.07
Model 2	1.5 [0.79-2.8]	0.22
Deaths Due to Other or Unknown Causes, n=176		
Model 1	3.7 [1.8-7.5]	0.0003
Model 2	3.0 [1.5-6.0]	0.003

*1 standard deviation of ln(SDF-1): 0.26
†P-value for the association of ln(SDF-1) as a continuous variable with clinical outcomes
‡CVD Death – CHD sudden and non-sudden CHD deaths, cerebral vascular accidents (strokes), and other CVD deaths
Model 1: Adjusted for age and sex
Model 2: Adjusted for age, sex, systolic blood pressure, hypertension treatment, total cholesterol, HDL, diabetes, smoking status, angina, HF

Supplemental Table III. Association of coronary artery disease Risk Alleles from published genome-wide association studies with plasma ln(SDF-1) levels in Framingham

SNP	Risk allele frequency	Risk allele	β	SE	P-value
rs501120*	0.854	T	0.032	0.009	0.0005
rs1746048†	0.857	C	0.032	0.009	0.0006

*Samani, N.J., et al. *Genomewide association analysis of coronary artery disease. N Engl J Med* 2007;357: 443-453.
†*Schunkert, H., et al. Large-scale association analysis identifies 13 new susceptibility loci for coronary artery disease.* Nature Genetics. 2011; 43: 333–338.

Genotyping Methods

We used genome-wide genotype data from 3008 offspring participants to conduct genome-wide association analysis of plasma SDF-1 level. Genotypes were obtained from the Affymetrix GeneChip Human Mapping 500K Array Set (SNP Health Association Resource at http://www.ncbi.nlm.nih.gov/projects/gap/cgi-bin/study.cgi?study_id=phs000007.v2.p1). An Affymetrix 50K Array with gene-centric and coding SNPs was additionally genotyped; in total, the array set measured approximately 550,000 SNPs. To increase coverage to 2,540,223 HapMap SNPs, we imputed genotypes based on the CEU reference panel in HapMap release 22, build 26 using MACH software (http://www.sph.umich.edu/csg/abecasis/MACH/). For genotype and phenotype data, refer to publicly available dataset through the NHLBI's SNP Health Association Resource (SHARe) initiative (http://public.nhlbi.nih.gov/GeneticsGenomics/home/share.aspx).

In analyses, we used an additive genetic model to analyze log-transformed SDF-1 concentration (ln[SDF-1]) with allele dose for each of the imputed genotypes, and age and sex were included as covariates in the linear mixed-effects model.