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Supplemental Data

Genome-wide Association Analysis of Blood-Pressure Traits in African-Ancestry Individuals Reveals Common Associated Genes in African and Non-African Populations

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Study Description and Populations

1. Discovery COGENT BP studies

BioVU: BioVU is a DNA biorepository linked to a database of de-identified electronic medical records (EMR), designed and implemented to support genetic association studies at Vanderbilt University (VU). BioVU is an ongoing study with rapid accrual of DNA specimen, accumulating ~26,000 participants per year, and with a current size of over 130,000. Studies in BioVU have demonstrated the validity of EMR-based phenotypes [1], clinical assessment of ancestry [2], investigated pharmacogenetic traits [3-5], and cardiovascular traits [6-8]. A detailed description of the human subjects protection applied to BioVU is described by Pulley *et al.* (2010)[9] The program is under continuous oversight by the institutional review board (IRB) and was reviewed in detail by the federal Office for Human Research Protections (OHRP). The BioVU DNA Repository is housed within the Center for Human Genetics Research DNA Resources Core (DNARC). Program planning for BioVU started in 2004, and sample accrual started in February 2007. Sample accrual is ongoing; there are over 126,676 DNA samples from adult clinic patients.

Traits are constructed for BioVU using the Synthetic Derivative (SD) database. This database is only accessible to Vanderbilt investigators and available by IRB approval. The SD database is a research tool developed to enable studies with de-identified clinical data. The SD collection includes information extracted from the EMR systems, and indexed by the same one-way Research Unique Identifier (RUI) used to track samples. The SD contains 1.7 million total records, with highly detailed longitudinal clinical data for approximately one million subjects. The database incorporates data from multiple sources and includes diagnostic and procedure codes (ICD 9 and CPT), basic demographics (age, gender, race), text from clinical care including discharge summaries, nursing notes, progress notes, history and physical, problem lists and multi-disciplinary assessments, laboratory values, echocardiogram (ECG) diagnoses, imaging reports, clinical text and electronically derived trace values, and inpatient medication orders.

For this blood pressure (BP) study, we used adult (age ≥ 21) African American BioVU participants with GWAS data. We used the first non-Emergency Department measured BP in the EMR, and excluded participants if there was a diagnosis of secondary hypertension (ICD-9 405), HIV infection (ICD-9 042), any cancer (ICD-9 140-239), end-stage renal disease (ICD-9 585.6), or heart failure (ICD-9 428) prior to, or on the date, of BP measurement. To define hypertension cases, participants' measured systolic BP (SBP) or diastolic BP (DBP) ≥ 140mmHg or 90 mmHg respectively, have a diagnosis of hypertension (ICD-9 401-404), or a prescription for antihypertensive medication prior to, or on the date, of BP measurement (57.3% of eligible participants). For hypertension controls, participants' measured SBP and DBP ≤ 125 mmHg and 80 mmHg, and no prior diagnoses of hypertension, or prescriptions for antihypertensive medications.

Bogalusa Heart Study: The Bogalusa Heart Study is an epidemiologic survey of cardiovascular disease risk factors from birth through mid-adulthood. Participants (n = 1,420, ~40% male, ~70% European ancestry, 18–38 years of age) were previously examined as children in this long-term survey. Details of screening and examination procedures, followed in the Bogalusa Heart

Study since its inception, are reported elsewhere [10 11]. All data were collected after obtaining informed consent.

The BP levels were measured from the right arm of the subjects, with the subjects in a sitting position by two trained observers (three replicates each). The SBP and DBP were recorded at the first and fifth Korotkoff phases, respectively, using a mercury sphygmomanometer. The average of the six BP readings was used for this analysis.

Candidate Gene Association Resource (CARe): CARe samples were collected from five NHLBI-funded cohort studies where GWAS African American samples were available. (http://public.nhlbi.nih.gov/GeneticsGenomics/home/care.aspx).

Atherosclerosis Risk Communities Study (ARIC): The ARIC study is a population-based, biracial prospective cohort study of cardiovascular disease and its risk factors sponsored by National Heart, Lung and Blood Institute (NHLBI) [12]. ARIC included 15,792 European ancestry and African American individuals aged 45-64 years at baseline (1987-89), chosen by probability sampling from four US communities. Cohort members completed four clinic examinations, conducted three years apart between 1987 and 1998. Follow-up for clinical events was annual. The current analysis included only African American individuals with BP measures at baseline examination. The IRB at each of the study sites approved the study protocols, and written informed consent was obtained from all participants.

BP was measured using a standardized Hawksley random-zero mercury column sphygmomanometer with participants in a sitting position after a resting period of 5 minutes. The size of the cuff was chosen according to the arm circumference. Three sequential recordings for SBP and DBP were obtained; the mean of the last two measurements was used in this analysis, discarding the first reading. BP lowering medication use was recorded from the medication history. Outliers (>4 SDs from the mean) with respect to the SBP and DBP distribution were excluded from the analysis.

The Coronary Artery Risk Development in Young Adults (CARDIA) Study: The CARDIA study is a population based, prospective cohort examining the development and determinants of clinical and subclinical cardiovascular disease and its risk factors [13]. The CARDIA study initial enrollment consisted of 5,115 European Americans and African American men and women between 18 and 30 years old (52% African American and 55% women). The study is multicenter with recruitment in Birmingham, AL; Chicago, IL; Minneapolis, MN; and Oakland, CA. The IRB at each of the study sites approved the study protocols, and written informed consent was obtained from all participants. Baseline measurements were repeated, and additional measurements performed, at Years 2, 5, 7, 10, 15, and 20[13]. The current analysis included data measured at Year 15 (2000-2001) and only African American male and females.

Seated BP was measured on the right arm following 5 minutes rest using a random-zero sphygmomanometer. SBP and DBP were recorded as Phase I and Phase V Korotkoff sounds. Three measurements were taken at 1 minute intervals with the average of the second and third

measurements taken for the BP values. Hypertension was defined if SBP ≥140 mmHg, DBP ≥90 mmHg, or reported use of antihypertensive medication.

The Cleveland Family Study (CFS): CFS participants consist of first or selected second-degree relatives of a proband with either laboratory diagnosed obstructive sleep apnea or neighborhood control of an affected proband. Families were selected for genotyping on the basis of genetic informativness, including multigenerational data or individuals from the extremes of the distribution of apnea phenotype[14]. These families include 59 African-American families with 176 individuals (100 females and 76 males) and 66 European-American families with 262 individuals (120 females and 142 males) with genotype and phenotype information. The IRB approved the study and written informed consent was obtained from all participants.

Participants had three supine BP measurements each performed after lying quietly for 10 minutes, before bed (10:00 P.M.) and upon awakening (7:00 A.M.), and another three sitting at 11 am, following standardized guidelines using a calibrated sphygmomanometer. Cuff size was determined by the circumference of the upper arm and the appropriate bladder size from a standard chart. BP phenotypes were determined from the average of the nine measurements.

Jackson Heart Study (JHS): JHS was initiated in 2000 to investigate prospectively the epidemiology and determinants of cardiovascular disease in African Americans [15]. JHS recruited 5,302 participants after completion of data adjustment, representing more than 5% of African Americans 35-84 years old living in the Jackson, Mississippi tri-county area. Of this number, ~30% were prior Jackson participants in the Atherosclerosis Risk in Communities Study. Of the remaining, 23% were recruited by random selection from a commercial listing that represents the overall tri-county population and an additional 23% volunteer sample, in which recruitment was distributed among defined demographic cells in proportions designed to mirror those in the overall population[16]. Those who were overlapping ARIC participants and those with previous MI were excluded from the GWAS. The IRB approved the study protocol, and written informed consent was obtained from all participants.

Seated BP was measured with a random-zero sphygmomanometer three times with the last two measurements averaged.

The Multi-Ethnic Study of Atherosclerosis (MESA): The MESA is a multicenter prospective cohort study initiated to study the development of subclinical cardiovascular disease. A total of 6,814 women and men between the age of 45 and 84 year were recruited for the first examination between 2000 and 2002. Participants were recruited in six US cities (Baltimore, MD; Chicago, IL; Forsyth County, NC; Los Angeles County, CA; Northern Manhattan, NY; and St. Paul, MN). Those with a history of CVD (defined as physician-diagnosed myocardial infarction, angina, heart failure, stroke, transient ischemic attack or history of invasive procedure for CVD) were excluded from participation. Thirty-eight % are of European ancestry, 28% African-American, 22% Hispanic, and 12% Asian, predominantly of Chinese descent. This study was approved by the IRB of each study site, and written informed consent was obtained from all

participants[17]. This manuscript utilizes data from African-American MESA participants, genotyped through the CARe project.

BP was measured three times at 1 minute intervals after a 5 minute initial rest using a Dinamap PRO 100 automated oscillometric device (Critikon, Tampa, FL) with the subject in seated, and the average of the second and third BP measurements was used in the analysis.

Cardiovascular Health Study (CHS): The CHS is a population-based cohort study of risk factors for CHD and stroke in adults ≥65 years conducted across four field centers[18]. The original cohort, predominantly Americans of European Ancestry, comprised 5,201 persons who were recruited in 1989-1990 from random samples of the Medicare eligibility lists. Additional 687 individuals, predominantly African-Americans, were enrolled subsequently for a total sample of 5,888. DNA was extracted from blood samples drawn on all participants at their baseline examination in 1989-90 (original cohort) or 1992-93 (African American cohort). A sample of 823 African-Americans satisfying study design criteria, and with genome-wide association data, were used for analysis.

Research staff with central training in BP measurement assessed repeated right-arm seated SBP and DBP levels at baseline with a Hawksley random-zero sphygmomanometer. The reported BP is the average of two measurements, which were taken after the participant had been sitting quietly for five minutes. First the technician determined the correct cuff size by measuring the arm circumference at the midpoint between the acromion and the olecranon. After applying the appropriate cuff, the maximum inflation level was determined by inflating the cuff until the radial pulse was no longer felt. The maximum inflation level was then determined to be the pulse obliteration pressure plus 30 mmHg plus the maximum zero level of the instrument. BP was measured by inflating the cuff to the maximum inflation level, waiting 5 seconds, then lowering by 2-3 mmHg per second. The first and fifth Korotkoff sounds were recorded. At least 30 seconds elapsed between each cuff inflation. Medication use was collected by interview. Information on prescription medication use in the previous two weeks was collected directly from the medications. A computer program developed by CHS was used to match the medication names with NDC numbers and then to group medications into analytic variables (e.g. beta blockers, lipid-lowering medications)[19]. Means of the repeated BP measurements from the baseline examination were used for the analyses.

Genetic Study of Atherosclerosis Risk (GeneSTAR): GeneSTAR is a 27 year prospective family-based study of incident CAD, diabetes, stroke, and other vascular diseases in initially healthy African American and European American adult relatives of probands with angiographically documented coronary disease prior to 60 years of age at the time of hospitalization for an acute CAD event in any of 10 Baltimore area hospitals [20]. The genotyped sample size is 3,200, with ~35 % African American (n= 1,132). Participants are siblings of the probands, offspring of the siblings and probands, and coparents of the offspring. All participants were under 60 years of age at the time of enrollment (from 1983 to 2006).

Demographic information, self-reported medical history, medication use, and smoking information were obtained from a standardized interview[21]. BP was measured using a standard mercury sphygmomanometer, following the American Heart Association [22] and JNC guidelines

[23]. The mean of three resting BP readings, taken early morning, midday, and late afternoon during the screening day was used to characterize BP measurements. Hypertension was defined as the subject having a mean SBP of ≥140 mmHg, a mean DBP of ≥90 mmHg, and/or currently taking an antihypertensive medication.

The Genetic Epidemiology Network of Arteriopathy (GENOA): GENOA is one of four networks in the Family Blood Pressure Program (FBPP) which recruited hypertensive African American and non-Hispanic white sibships for linkage and family-based association studies to investigate genetic contributions to BP in multiple racial groups [24]. Recruitment (Exam 1, 1995-2000 and Exam 2, 2000-2005) was population-based in two geographic locations: Jackson, Mississippi and Rochester, Minnesota. African Americans were recruited solely at the Jackson field center. Hypertensive probands were ascertained from the Jackson cohort of the ARIC study if they were in a sibship with two individuals with essential hypertension (SBP =140 mmHg or DBP =90 mmHg on the second and third clinic visit), diagnosed prior to age 60, and consented to participate. Index sib-pairs with possible secondary hypertension, including sib-pairs with previously diagnosed kidney disease (defined by serum creatinine level > 2 mg/dL), were excluded. After quality control procedures, and exclusion of all overlapping participants with ARIC, genotype data from a total of 996 African Americans was available for this study.

SBP and DBPs were measured using an automated oscillometric BP measurement device with a consistent protocol across the FBPP networks. BP was measured three times on each participant by trained and certified technicians and then averaged for use in this analysis.

The Healthy Aging in Neighborhoods of Diversity across the Life Span study (HANDLS): The Healthy Aging in Neighborhoods of Diversity across the Life Span study (HANDLS) is an interdisciplinary, community-based, prospective longitudinal epidemiologic study examining the influences of race and socioeconomic status (SES) on the development of age-related health disparities among socioeconomically diverse African Americans and European ancestry individuals in Baltimore, Maryland, USA [25]. The HANDLS design is an area probability sample of Baltimore based on the 2000 Census. The study protocol facilitated our ability to recruit 3,722 participants from Baltimore. Among those who completed their examinations, there were no age differences associated with sex and poverty status, but African Americans were negligibly younger than individuals of European descent. The study is currently conducting wave three designed as a re-examination wave of all participants seen between 2004-2009. This wave began in July of 2009 and will conclude in 2012. Genotyping was focused on a subset of participants self-reporting as African American was undertaken at the Laboratory of Neurogenetics, National Institute on Aging, National Institutes of Health.

BP was measured using a non-invasively using the brachial artery auscultation method with an aneroid manometer, a stethoscope, and an inflatable cuff in individuals resting for 5 minutes. The average of right and left sitting BP values was taken to represent each of SBP and DBP, respectively for analyses.

The Health, Aging and Body Composition (Health ABC) study: HealthABC is a prospective cohort study of 3,075 community-dwelling men and women of African American and American European ancestry living in Memphis, Tennessee, USA and Pittsburgh, Pennsylvania, USA, aged 70–79 years at recruitment in 1997 [26]. To identify potential participants, a random sample of European ancestry and African American Medicare-eligible elders, within designated zip code areas, were contacted. To be eligible, participants had to report no difficulty with activities of daily living, walking a quarter of a mile, or climbing ten steps without resting. They also had to be free of life-threatening cancer diagnoses and have no plans to move out of the study area for at least three years. The sample was approximately balanced for sex (51% women) and 42% of participants were African American. Participants self-designated race/ethnicity from a fixed set of options (Asian/Pacific Islander, black/African American, white/Caucasian, Latino/Hispanic, do not know, other). The study was designed to have sufficient numbers of African Americans to allow separate estimates of the relationship of body composition to functional decline. All eligible participants signed a written informed consent, approved by the IRBs at the clinical sites. This study was approved by the IRBs of the clinical sites and the coordinating center (University of California, San Francisco).

The baseline clinic visit included a drug inventory to assess pharmacological treatment, evaluation of body composition using dual energy x-ray absorptiometry (DEXA), BP measurements, electrocardiogram, physical performance tests, and strength measures. BP was calculated as the average of two seated measurements.

The Hypertension Genetic Epidemiology Network (HyperGEN): HyperGEN is a multicenter family-based study to research the genetic causes of hypertension and related conditions [27]. HyperGEN recruited African American and Caucasian participants at five field centers, with recruitment based largely on ongoing population-based studies. Study participants were recruited as one of three main types of subjects: 1) as part of a hypertensive sibship with at least two siblings diagnosed with hypertension; 2) random subjects, who were age-matched with hypertensive sibs; or 3) unmedicated adult offspring of one or more of the hypertensive siblings. Subjects were brought into the clinic for a one day exam, and data were collected from questionnaires, a physical exam, and blood and urine samples. This study obtained informed consent from participants and approval from the appropriate IRBs.

SBP and DBPs were measured using an automated oscillometric BP measurement device with a consistent protocol across the FBPP networks. BP was measured three times on each participant by trained and certified technicians and then averaged for use in this analysis.

Loyola-Maywood study: Participants were self-identified African Americans from a working class suburb of Chicago, Illinois, USA who were enrolled in studies of BP at the Loyola University Medical Center in Maywood, Illinois, USA as part of the International Collaborative Study on Hypertension in Blacks (ICSHIB) which is described in detail elsewhere [28]. Briefly, nuclear families were identified through middle-aged probands who were not ascertained based on any phenotype. Thereafter all available first-degree relatives 18 years old and above were enrolled into the study cohort of families. A screening exam was completed by trained and certified

research staff using a standardized protocol[28; 29]. Information was obtained on medical history, age, body weight and height. Protocols were reviewed and approved by the IRB at the Loyola University Chicago Stritch School of Medicine prior to recruitment activities. This present study included unrelated adults sampled and for whom information on anthropometrics, BP and use of antihypertensive medication was available.

BP measurements were obtained using an oscillometric device, previously evaluated in our field settings [29]. Three measurements were taken three minutes apart and the average of the final two was used in the analysis. Individuals with SBP ≥140 mmHg, DBP ≥90 mmHg or on anti-hypertensive medication at time of exam were defined as hypertensive. Participants with hypertension were offered treatment after detection at the screening exam.

Loyola-Nigeria study: The sampling frame for the Nigeria cohort was also provided by the (International Collaborative Study on Hypertension in Blacks) ICSHIB. Study participants were recruited from Igbo-Ora and Ibadan in southwest Nigeria as part of a long-term study on the environmental and genetic factors underlying hypertension [30]. The base cohort consists of over 15,000 participants with information available on anthropometrics, BP and use of antihypertensive medication. BP measurements followed the same protocol described in the Loyola-Maywood study. This present study included unrelated adults samples from the cohort and some hypertensive participants who were recruited as controls in the Africa-America Diabetes Mellitus (AADM) Study recruited from Ibadan in similar neighborhoods. Both projects were reviewed and approved by the sponsoring US institutions (Loyola University Chicago and Howard University) and the University of Ibadan. All participants signed informed consent administered in either English or Yoruba. Protocols for BP measurement are described under the Loyola-Maywood study.

Mount Sinai IPM Biobank Program: The Charles Bronfman Institute for Personalized Medicine (IPM) Biobank Program is a consented, Electronic Medical Record (EMR)-linked medical care setting biorepository of the Mount Sinai Medical Center (MSMC), drawing from a population of over 70,000 inpatients and 800,000 outpatient visits annually. The study design is described in detail elsewhere [31]. MSMC serves the diverse local communities of upper Manhattan, including Central Harlem (86% African American), East Harlem (88% Hispanic Latino), and Upper East Side (88% Americans of European ancestry) with broad health disparities. IPM Biobank populations include 28% African American, 38% Hispanic Latino predominantly of Caribbean origin, 23% of European ancestry. IPM Biobank disease burden is reflective of health disparities with broad public health impact. Since 2007, over 21,000 Mount Sinai patients have enrolled in the IPM Biobank program. Biobank operations are fully integrated in clinical care processes, including direct recruitment from clinical sites waiting areas and phlebotomy stations by dedicated Biobank recruiters independent of clinical care providers, prior to or following a clinician standard of care visit. Recruitment currently occurs at a broad spectrum of over 30 clinical care sites. This present study included only unrelated, adult, self-reported African Americans.

Information on anthropometrics, demographics, BP and use of antihypertensive medication was derived from participants EMR. The Mount Sinai Biobank Project (IRB # 07-0529 0001 02

ME) operates under an IRB-approved research protocol with IRB-approved informed consent forms. All study participants provided written informed consent. The Mount Sinai IPM Biobank Program is supported by The Andrea and Charles Bronfman Philanthropies.

SIGNET/ Reasons for Geographic and Racial Differences in Stroke (REGARDS): The Reasons for Geographic and Racial Differences in Stroke (REGARDS) Study is a national, population-based, longitudinal study of ~30,000 adult individuals of African American or European descent. Participants were randomly sampled with recruitment by mail then telephone. Individuals aged 45 years old and older were eligible for inclusion in the REGARDS cohort, for which enrollment began in February 2003. Exclusion criteria for REGARDS participation included active treatment for cancer; any serious medical condition which would prevent long-term participation; cognitive impairment as judged by the interviewer; living in a nursing home or on the waiting list for a nursing home; and a language barrier (speaks other than English). Samples from 2,398 SIGNET individuals with measures of BP and with GWAS data respectively were available for this study.

SBP and DBP were defined as the average of two measurements taken by a trained technician using a standard protocol and regularly tested aneroid sphygmomanometer (American Diagnostic Corporation, Hauppauge, NY), measured after the participant was seated for 5 minutes [32]. Briefly, BPs measurements were taken in the left arm (when possible) and a large size cuff was used if the arm circumference was greater than 13 inches. Both the cuff bladder width and pulse obliteration level were recorded. The cuff was inflated to 20 mmHg above the pulse obliteration level and slowly deflated (~ 2 mmHg/second) to obtain the BPs. This process was repeated to obtain the second BP on the same arm.

Women's Health Initiative SNP Health Association Resource (WHI-SHARe): Women's Health Initiative (WHI) is a long-term national health study that focuses on strategies for preventing common diseases such as heart disease, cancer and fracture in postmenopausal women. A total of 161,838 women aged 50–79 years old were recruited from 40 clinical centers in the US between 1993 and 1998. WHI consists of an observational study, two clinical trials of postmenopausal hormone therapy (estrogen alone or estrogen plus progestin), a calcium and vitamin D supplement trial, and a dietary modification trial [33]. Study recruitment and exclusion criteria have been described previously [33]. Study protocols and consent forms were approved by the IRB at all participating institutions. Medical history was updated annually (for women in the observational study) or semiannually (for women in the clinical trials) by mail and/or telephone questionnaires.

BP was measured by certified staff using standardized procedures and instruments [34]. Two BP measures were recorded after 5 minutes rest using a mercury sphygmomanometer. Appropriate cuff bladder size was determined at each visit based on arm circumference. Diastolic BP was taken from the phase V Korotkoff measures. The average of the two measurements, obtained 30 seconds apart, was used in analyses. Women were asked to bring all of their current prescription and over-the-counter medications to each visit. The WHI SNP Health Association Resource (SHARe) minority cohort includes 8,515 self-identified African American women from WHI who provided written informed consent for study participation and

DNA analysis. Demographic data, medical history and anthropometric measures were obtained at a baseline clinical visit.

The Howard University Family Study (HUFS): is a population-based family study of African Americans in the Washington DC metropolitan area [35]. Investigators enrolled a randomly recruited set of families in addition to a set of unrelated individuals to study genetic and environmental factors of common complex diseases including hypertension. The IRB approved the study protocol, and written informed consent was obtained from all participants. A total of 1,016 individuals were included in this analysis.

BP was measured in the sitting position using an oscillometric device (Omron). Three BP readings were taken with a 10 minute interval between readings. The reported SBP and DBP readings were the average of the second and third readings.

Replication African ancestry studies

Ghana study:

Participants, of homogeneous Gahanna ancestry were enrolled into the Ghana study between May 2002 and October 2003 through community recruitment in Sunyani, Ghana. Exclusion criteria were age less than 18, prior enrollment of a first or second degree relative, and any acute illness such as malaria that might affect levels of tissue-type plasminogen activator (t-PA) or plasminogen activator inhibitor-1 (PAI-1). Participants were examined at the Regional Hospital, Sunyani after a 10-hour fast. All participants provided written informed consent or fingerprint consent, and all forms were approved by the IRBs at Vanderbilt University and Regional Hospital, Sunyani. All participants provided medical history and standard demographic data including age, sex, education, smoking status, alcohol consumption, current medications, cardiovascular disease, diabetes, and cancers. Height, weight and BP were measured. Three tubes of blood were taken from each participant, stored in liquid nitrogen, and shipped to VU. Genotyping for this project was conducted using the Sequenom genotyping system at the Vanderbilt DNA Resources Core. A total of seven candidate SNPs were genotyped and analyzed according to the analytic protocol for the discovery GWAS analysis, with the exception that principal components summarizing ancestry were not adjusted for due to the fact that these participants are not admixed. Concordance rates among candidate SNP genotypes for duplicate QC samples from the HapMap were all 100%.

BPs measurements were measured using an Omron HEM-705c instrument (Omron Healthcare Corp., Bannockburn, Ill., USA). Participants were seated in a quiet room and two measures of BP were taken from the left arm. The average of the two measures was used in the analysis. All BP measures were taken prior to blood draws.

Family Blood Pressure Program-AXIOM. These 872 African-American subjects were included from the **HyperGEN** and **GENOA** studies but whom were not genotyped with conventional GWAS platforms. The sample schemes are the same as HyperGEN and GENOA. For BP measures see HyperGEN and GENOA descriptions. These African-Americans were genotyped using Affymetrix Axiom chips, which include 808,558 SNPs. SNPs were called using Affymetrix Genotyping Console (GTC) by analyzing CEL files from Affymetrix AXIOM arrays

(www.affymetrix.com). Samples with Dish QC(DQC)<=0.82 were excluded. Samples with call Rate <=0.97 were also dropped. Imputation was performed using MaCH 1.0.17 with parameter "--round 50 –greedy". Reference haplotypes were downloaded from (http://www.sph.umich.edu/csg/abecasis/MACH/download/HapMap-r21.html, with ratio of CEU and YRI 1:1). All the replication SNPs have Rsq>0.76.

The Health and Retirement Study (HRS): The HRS is a longitudinal survey of a representative sample of Americans over age 50 sponsored by the National Institute on Aging (NIA) and conducted by the University of Michigan's Institute for Social Research. The sample for this analysis includes 1,337 African Americans (N=483 males, 36.1%) interviewed in 2006 or 2008 with BP measured using a Omron HEM-780 Intellisense. Automated BP monitor with ComFit cuff. Participants that had missing values for both SBP and DBP, had missing values for covariates, and one individual that was > 5 SDs from the mean of BMI were excluded. Mean SBP and DBP from three measures, adjusted for anti-hypertensive medication use (+10 mmHg for SBP, +5 mmHg for DBP) were used as the final quantitative outcome variables. Hypertension was defined as having a mean SBP ≥140 mmHg, a mean DBP≥90 mmHg, or self-reported hypertension medication use. Mean SBP was 143.96 mmHg, mean DBP was 85.53 mmHg, and 1073 (80.25%) participants had hypertension. Genotyping was performed by the Center for Inherited Disease Research (CIDR) using Illumina's Human Omni2.5-Quad BeadChip methodology. Genotyping quality control was performed by the Genetics Coordinating Center, Department of Biostatistics, University of Washington, Seattle.

Mt Sinai IPM Biobank Program: The Institute for Personalized Medicine (IPM) Biobank Program is a consented, Electronic Medical Record (EMR)-linked medical care setting biorepository of the Mount Sinai Medical Center (MSMC), drawing from a population of over 70,000 inpatients and 800,000 outpatient visits annually. MSMC serves the diverse local communities of upper Manhattan, including Central Harlem (86% African American), East Harlem (88% Hispanic Latino), and Upper East Side (88% Caucasian/white) with broad health disparities. IPM Biobank populations include 28% African American, 38% Hispanic Latino predominantly of Caribbean origin, 23% Caucasian/White. IPM Biobank disease burden is reflective of health disparities with broad public health impact. Since 2007, over 23,000 Mount Sinai patients have enrolled in the IPM Biobank program. Biobank operations are fully integrated in clinical care processes, including direct recruitment from clinical sites waiting areas and phlebotomy stations by dedicated Biobank recruiters independent of clinical care providers, prior to or following a clinician standard of care visit. Recruitment currently occurs at a broad spectrum of over 30 clinical care sites. This present study included only unrelated, adult, self-reported African Americans. For the discovery analysis, participants genotyped on Affymerix 6.0 in 2010 were included. For the replication analysis, participants genotyped on Illumina OmniExpress in 2012 were included. Information on anthropometrics, demographics, blood pressure and use of antihypertensive medication was derived from participants EMR. The Mount Sinai Biobank Project (IRB # 07-0529 0001 02 ME) operates under an IRB-approved research protocol with IRB-approved informed consent forms. All study participants provided written informed consent. The Mount Sinai IPM Biobank Program is supported by The Andrea and Charles Bronfman Philanthropies.

The Seychelles TANDEM study: The TANDEM study is a family-based study conducted in the Republic of Seychelles between 1999 and 2002. The Seychelles islands are located in the Indian Ocean, approximately 2000 km east to Kenya; the majority of the population is of African descent. The study was approved by the ethical committee in Seychelles and at the University of Lausanne, Switzerland and participants provided written informed consent, including for genetic analyses. Methods and main findings have been published in a number of publications. Families were selected from a national hypertension register if the family was from predominantly African descent and one could identify ≥2 full siblings with hypertension (≥140/90 mm Hg, average of 3 office measures or on current antihypertensive treatment) and ≥2 other first-degree relatives (full siblings or parents) with or without hypertension [36; 37] . Seventy-six of the 135 screened families were found to be eligible. Only persons aged 18 years or older have been included. Three BP measurements were taken at the study center in the morning between 7:00 and 10:30 AM, for participants who had been sitting quietly for at least 10 minutes, by trained health professionals, using a standard mercury sphygmomanometer with a triple-bladder cuff (Tricuff) that automatically adjusts bladder width to arm circumference.

The Seychelles Heart Study III (2004): The Seychelles Heart Study III is a population-based survey conducted in 2004 under the auspices of the Ministry of Health of the Republic of Seychelles. The Seychelles islands are located in the Indian Ocean, approximately 2000 km east to Kenya; the majority of the population is of African descent. The survey was approved by the Ministry of Health after technical and ethical reviews. Participants were free to participate and gave written informed consent. Survey methods have been described elsewhere [38]and findings published in over 20 publications. The sampling frame consisted of a sex and age stratified random sample of the entire population aged 25-64 years, using computerized data of a national population census in 2002 thereafter updated by civil status authorities. The survey was attended by 1255 individuals, corresponding to a participation rate of 81% [39]. BP was measured 3 times, at a survey center, in the morning, at intervals of more than 2 minutes, after a participant had been seated for at least 15 minutes, by trained nurses, using a mercury sphygmomanometer and a cuff that automatically adapts width to the arm circumference (Tricuff). BP was based on the average of the last two of three readings.

Genotyping for both **TANDEM** and **Heart Study III** samples from the Seychelles was performed on an Illumina iSelect platform (CardioMetaboChip - http://www.sph.umich.edu/csg/kang/MetaboChip) according to standard protocols. Data was cleaned using completeness parameters per individual and per SNP, principal components calculated in the presence of HapMap genotypes, sex mismatch, cryptic family relationships, Mendelian error, and similar parameters as appropriate.

Justification for the Use of Statins in Prevention: an Intervention Trial Evaluating Rosuvastatin (JUPITER). The study population was derived from JUPITER, an international, randomized, placebo-controlled trial of rosuvastatin (20mg/day) in the primary prevention of cardiovascular disease conducted among apparently healthy men 50 year or older and women 60 years or older with LDL-C < 130 mg/dL and hsCRP > 2 mg/L [40]. Blood pressure measures were made by a

healthcare professional at baseline. Approximately 70% of JUPITER participants provided blood for DNA extraction at baseline and consent for genetic analysis, among whom approximate 13.7% were self-reported blacks from South Africa. A single BP measure was obtained at time of enrollment.

Genotyping was performed using the Omni 1M Quad platform (Illumina, San Diego). Briefly, raw genotype intensity data were reduced to genotype calls using the Illumina Genome Studio (v. 1.6.2) software (Illumina, San Diego)[41]. SNP clusters were initially defined automatically using data from the JUPITER sample. SNPs with poor automatically defined clusters, ~1%, were visually inspected, and annotated, removed, or clustered again with manual intervention. After these procedures, 99.71% of the loci yielded successful genotype information. All samples had successful genotyping for >98.5% of the final SNPs. Identity-by-state clustering in PLINK [42] applied to 1,435 JUPITER ancestry informative SNPs confirmed of a cluster of JUPITER participants who were strongly correlated with self-reported South African ancestry. In total, over 97.4% or 1,688 of the South African black JUPITER participants with consent for genetic analysis remained after successful genotyping and exclusions requiring that no pair of individuals was related more closely than second degree using identity-by-descent clustering procedures in PLINK. EIGENSTRAT [43] was applied on the South African black population to compute covariates for population sub-structure to adjust for potential confounding in association analysis. Analyses followed the standard protocol and included adjustments for age, sex, BMI and markers for population stratification

Multi-ethnic samples

ICBP European samples

Summary *P*-values results for ICBP European ancestry were obtained from www.igm.jhmi.edu/~gehret/icbp32413ahsfd134/icbp_088023401234-9812599.html.

East Asian samples: AGEN

The Asian Genetic Epidemiology Network (AGEN) is a consortium of genetic epidemiology studies of cardiovascular disease related phenotypes, including BP, diabetes, and obesity, conducted among Asian populations. AGEN-BP consists of 19,608 East Asian participants who underwent standardized collection of BP measurements in eight population-and family-based GWAS, including: the Cardio-metabolic Genome Epidemiology (CAGE) Network, Genetic Epidemiology Network of Salt-Sensitivity (GenSalt), Korean Association Resource (KARE) Project, Shanghai Hypertension Study, Singapore Malay Eye Survey (SiMES), Singapore Prospective Study (SP2) Program, Suita Study, and Taiwan Super Control Study. Each study established a consensus on phenotype harmonization and analytical plan for within-study GWAS and meta-analysis of results across studies. Each study received an approval from the IRB and all participants in each study provided written informed consent for participation in the study. Our study utilized results from selected SNPs from Stage 1, which was a meta-analysis of directly genotyped and imputed SNPs from individuals of East Asian descent, drawn from the population-based or control samples in case-control studies in AGEN-BP, described above. The

BP measures and quality control (QC) criteria for genetic data have been previously described by He *et al.* [44]. All BP measures were taken at least two times, and the average of measures was used for analysis.

Briefly, studies each performed genotyping QC separately, and removed participants that had missing data between 2% and 10%, SNPs with missing data between 5% and 2%, HWE *P*-values between 1×10^{-4} and 1×10^{-6}, and SSNP with MAF ≤ 1%. Ungenotyped SNPs were imputed to phased haplotypes from the International HapMap Consortium CHB (Chinese from Beijing) and JPT (Japanese from Tokyo) reference data using MACH, IMPUTE, or BEAGLE. Association between SNPs and measured quantitative BP traits was assessed with linear regression with adjustment for age, age^2, sex, BMI, and any study-specific covariates within each study. All within-study genomic control lambdas (λ) for tests of association with BP outcomes were between 1 and 1.05. Evidence across studies for associations between SNPs and BP was evaluated by inverse-variance weighted fixed-effects meta-analysis using METAL.

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Bogalusa Heart Study (BHS): NJS is supported in part by NIH/NCRR Grant Number UL1 RR025774. The BHS was supported by grants HD-061437 and HD-062783 from the National Institute of Child Health and Human Development, and AG-16592 from the National Institute on Aging**.**

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Atherosclerotic Risk in Communities (ARIC): University of North Carolina at Chapel Hill (N01-HC-55015), Baylor Medical College (N01-HC-55016), University of Mississippi Medical Center (N01-HC-55021), University of Minnesota (N01-HC-55019), Johns Hopkins University (N01-HC-55020), University of Texas, Houston (N01-HC-55017), University of North Carolina, Forsyth County (N01-HC-55018);

Cardiovascular Health Study (CHS): University of Washington (N01-HC-85079), Wake Forest University (N01-HC-85080), Johns Hopkins University (N01-HC-85081), University of Pittsburgh (N01-HC-85082), University of California, Davis (N01-HC-85083), University of California, Irvine (N01-HC-85084), New England Medical Center (N01-HC-85085), University of Vermont (N01-HC-85086), Georgetown University (N01-HC-35129), Johns Hopkins University (N01 HC-15103), University of Wisconsin (N01-HC-75150), Geisinger Clinic (N01-HC-45133), University of Washington (N01 HC-55222, U01 HL080295); **Cleveland Family Study (CFS)**: Case Western Reserve University (RO1 HL46380-01-16);

Coronary Artery Risk in Young Adults (CARDIA): University of Alabama at Birmingham (N01-HC-48047), University of Minnesota (N01-HC-48048), Northwestern University (N01-HC-48049), Kaiser Foundation Research Institute (N01-HC-48050), University of Alabama at Birmingham (N01-HC-95095), Tufts-New England Medical Center (N01-HC-45204), Wake Forest University (N01-HC-45205), Harbor-UCLA Research and Education Institute (N01-HC-05187), University of California, Irvine (N01-HC-45134, N01-HC-95100);

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Ghana study: The authors wish to acknowledge the support of the study investigators, field staff and study participants in creating this resource for biomedical research. The Ghana Study is funded by NLM grant LM010098.

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HyperGEN: The hypertension network is funded by cooperative agreements (U10) with NHLBI: HL54471, HL54472, HL54473, HL54495, HL54496, HL54497, HL54509, HL54515, and 2 R01 HL55673-12. The study involves: University of Utah (Network Coordinating Center, Field Center, and Molecular Genetics Lab); Univ. of Alabama at Birmingham (Field Center and Echo Coordinating and Analysis Center); Medical College of Wisconsin (Echo Genotyping Lab); Boston University (Field Center); University of Minnesota (Field Center and Biochemistry Lab); University of North Carolina (Field Center); Washington University (Data Coordinating Center); Weil Cornell Medical College (Echo Reading Center); National Heart, Lung, & Blood Institute. For a complete list of HyperGEN Investigators please see: www.biostat.wustl.edu/hypergen/Acknowledge.html

Loyola-Nigeria: The Loyola-Nigeria study was supported by NIH grant numbers R01-HL053353. The authors acknowledge the assistance of the research staff and participants in Ibadan and Igbo-Ora, Oyo State, Nigeria.

Loyola-Maywood: Maywood African-American study is supported by the National Institutes of Health grant number HL074166 from National Heart, Lung, Blood Institute.

Mt Sinai IPM Study: The Mt. Sinai IPM study was supported by The Andrea and Charles Bronfman Philanthropies. The authors would like to thank the participants from New York City, United States, for participating in the Mount Sinai IPM Biobank Program.

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HRS: HRS is supported by the National Institute on Aging (NIA U01AG009740). The genotyping was funded separately by the National Institute on Aging (RC2 AG036495, RC4 AG039029). Genotyping was conducted by the NIH Center for Inherited Disease Research (CIDR) at Johns Hopkins University. Genotyping quality control and final preparation of the data were performed by the Genetics Coordinating Center at the University of Washington.

JUPITER: Genetic analysis in the JUPITER study was funded by AstraZeneca.

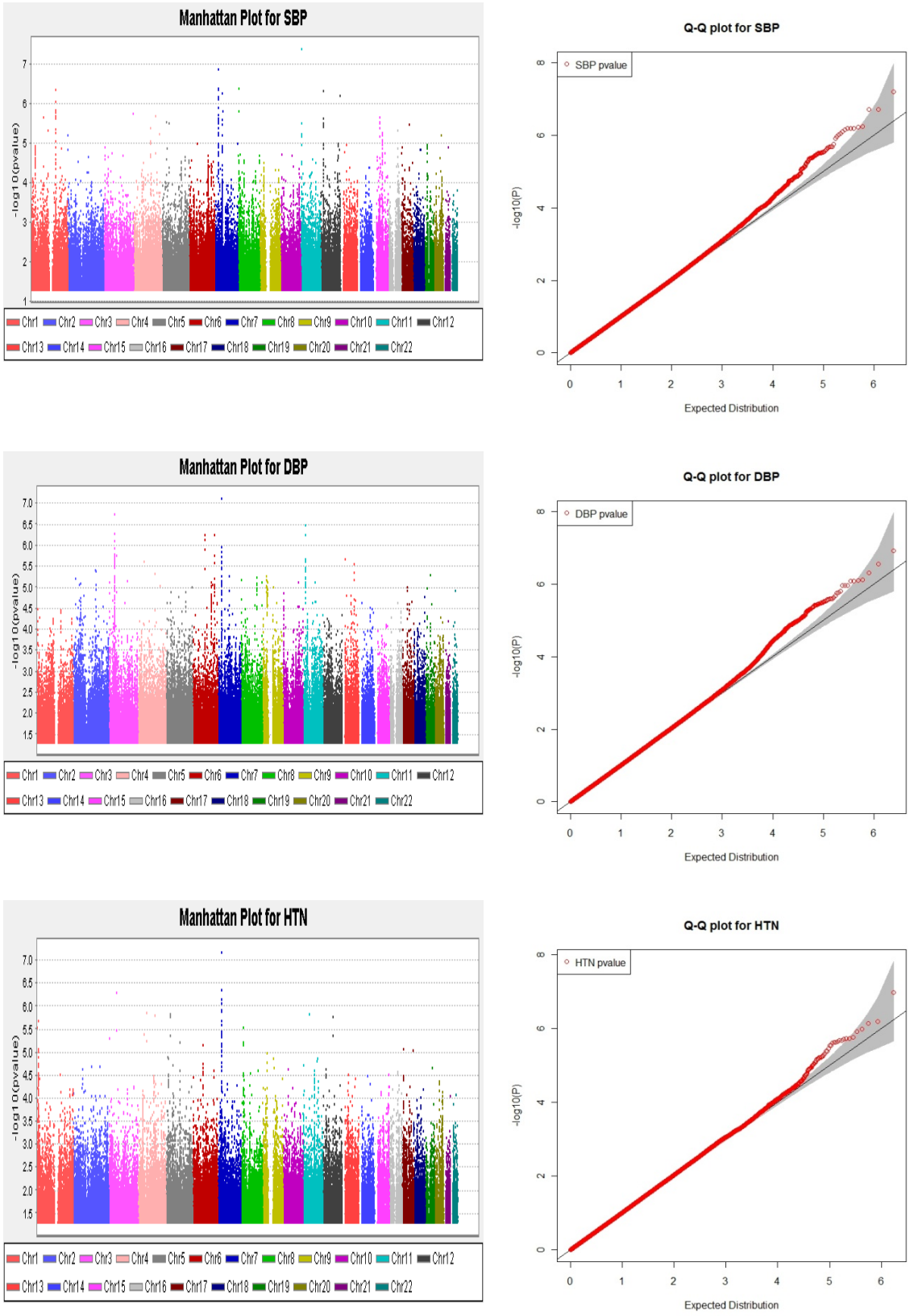

Figure S1. Genome-wide association Manhattan plots and Q-Q plots of SBP, DBP and HTN in the Continental Origins and Genetic Epidemiology Network (COGENT). GWAS Manhattan and Q-Q plots are illustrated for SBP, DBP and hypertension (HTN) in COGENT.

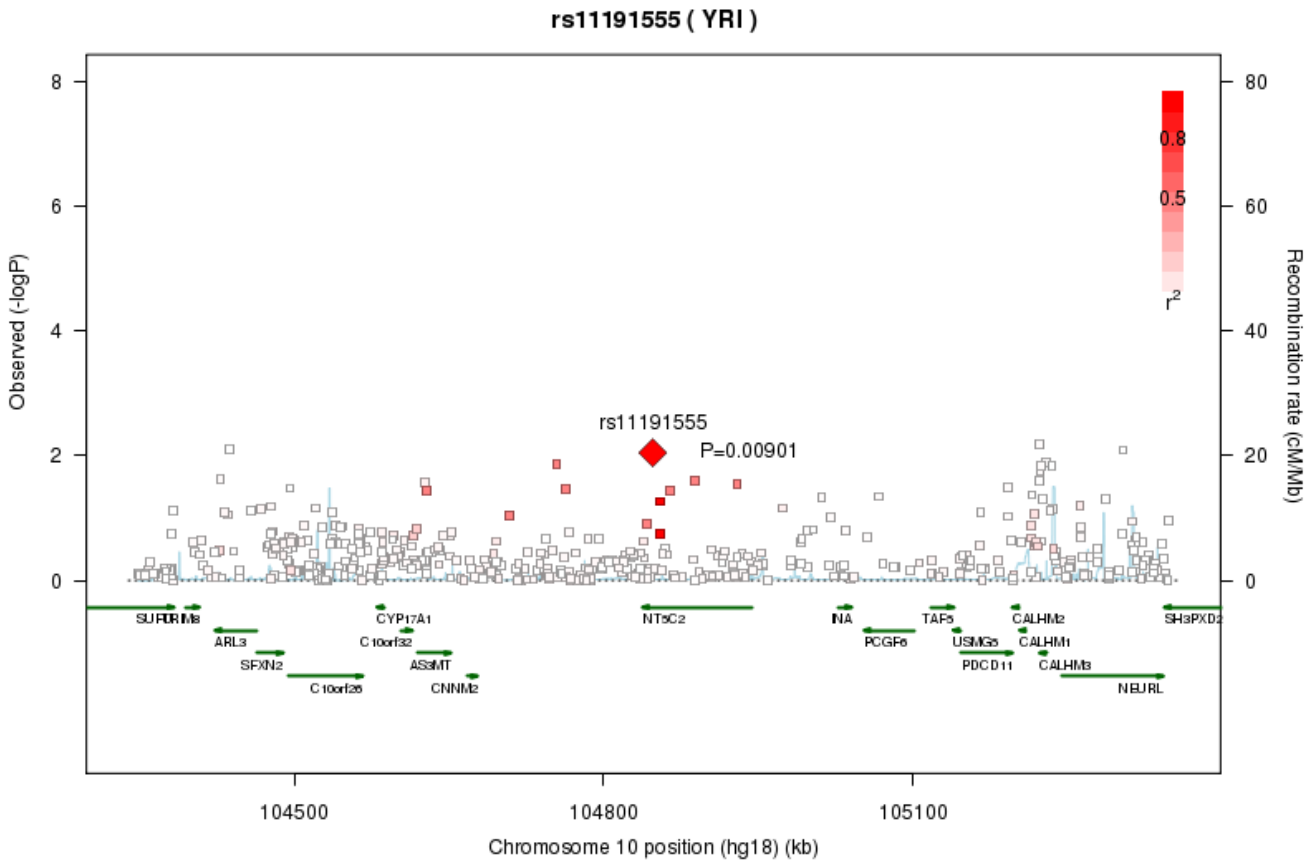

Figure S2. Regional plot of –log10(*P*-value) of *NT5C2* and SBP. The LD is based on YRI 1000G data. rs11191555 is the most significant SNP in this locus in COGENT AA data.

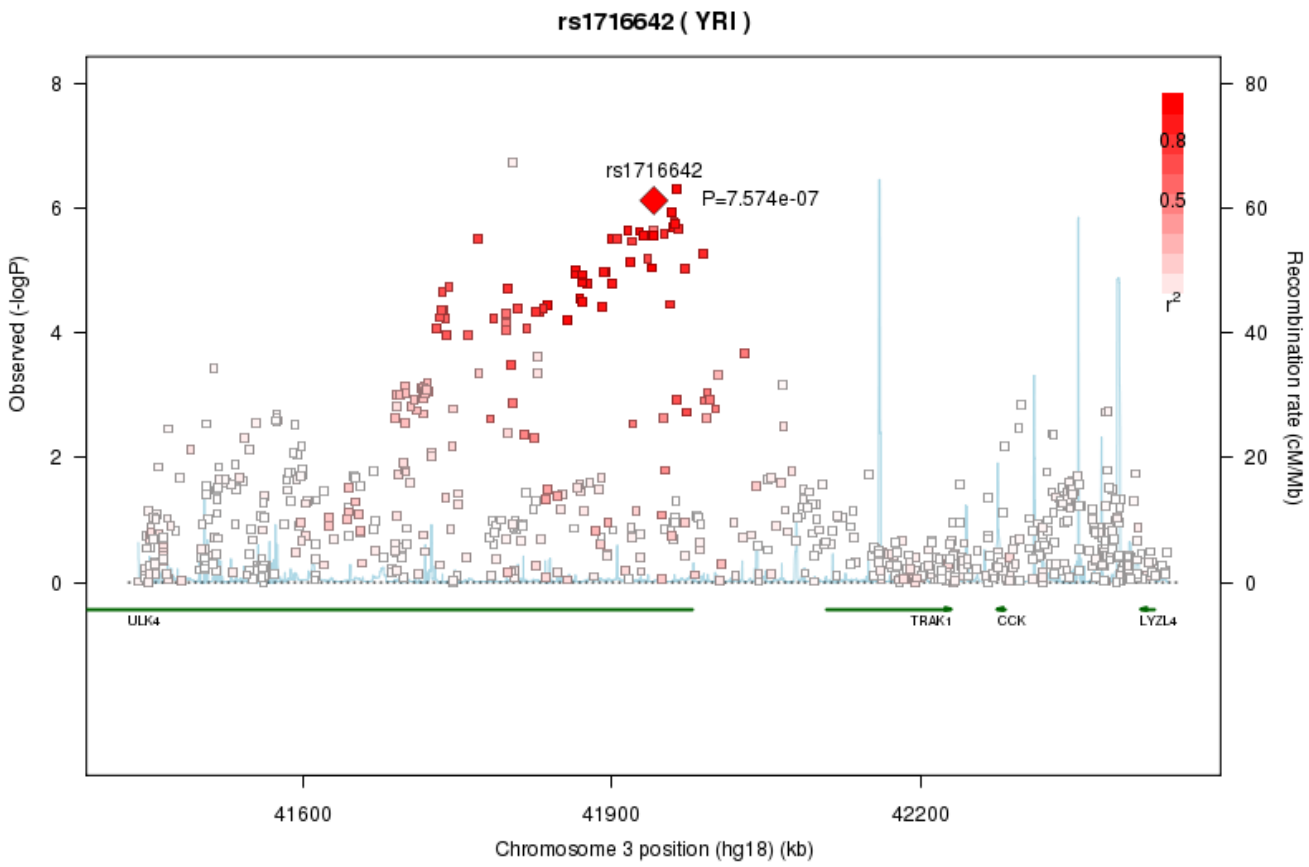

Figure S3. Regional plot of –log10(*P*-value) of *ULK4* and DBP. The LD is based on YRI 1000G data. rs1716642 is the most significant SNP in this locus in COGENT AA data.

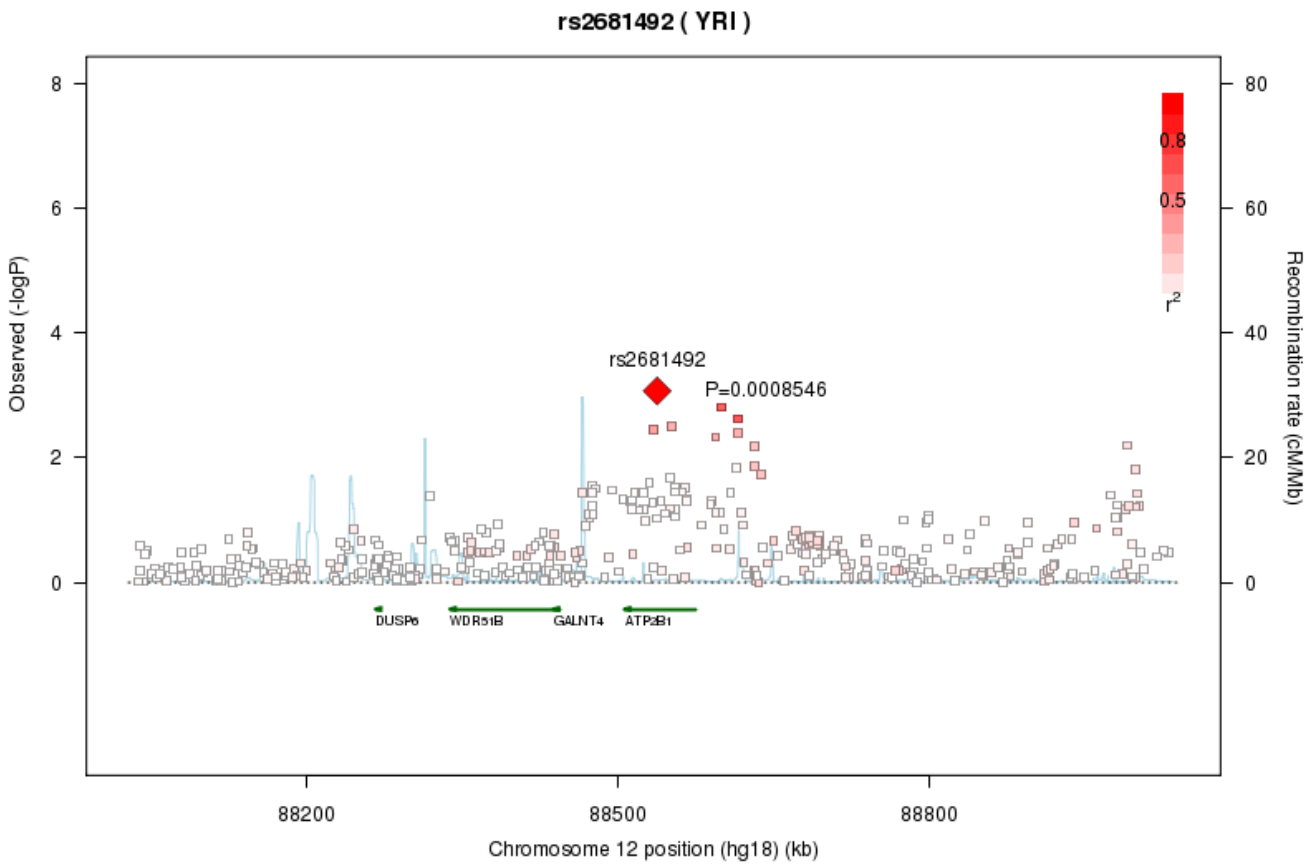

Figure S4. Regional plot of –log10(*P*-value) of *ATP2B1* and HTN. The LD is based on YRI 1000G data. rs2681492 is the most significant SNP in this locus in COGENT AA data.

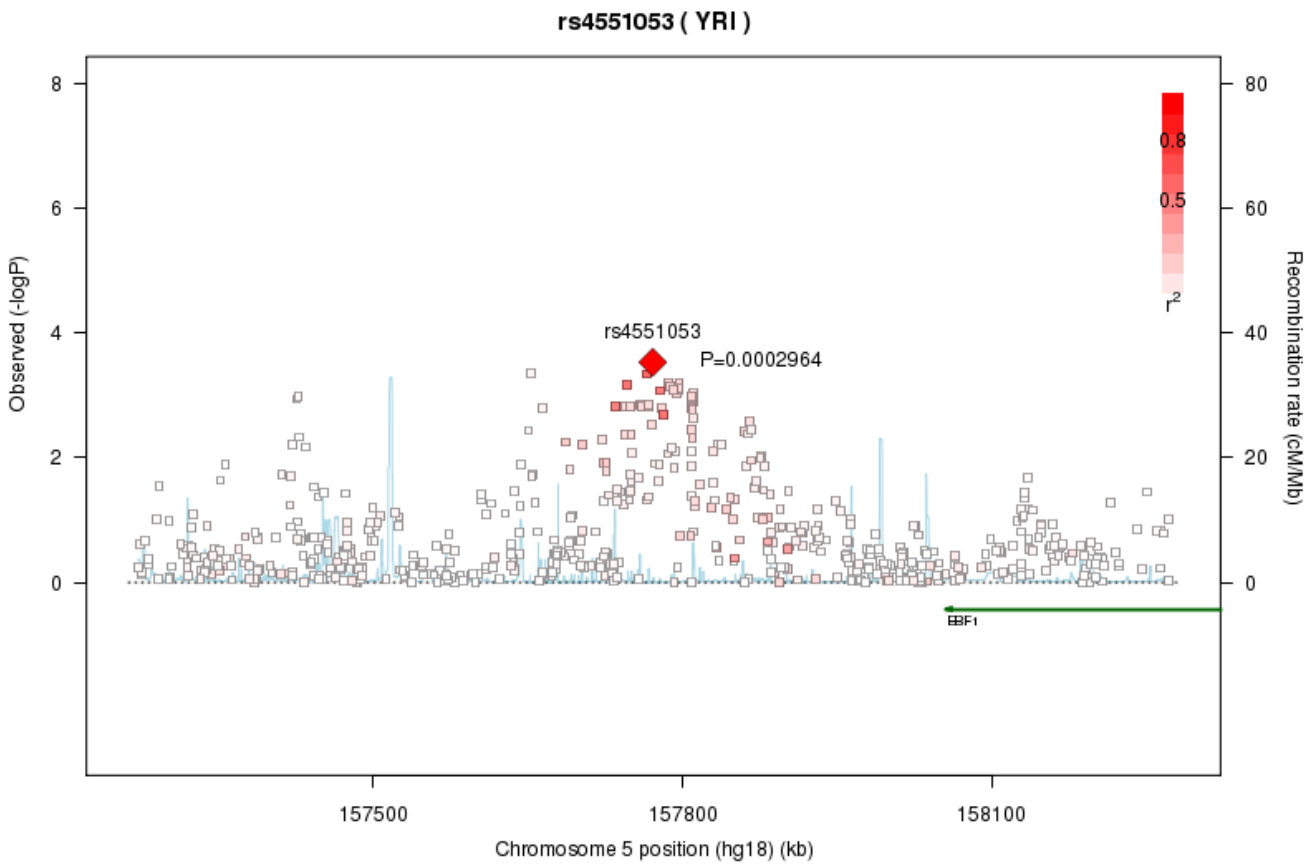

Figure S5. Regional plot of –log10(*P*-value) of *EBF1* and HTN. The LD is based on YRI 1000G data. rs4551053 is the most significant SNP in this locus in COGENT AA data.

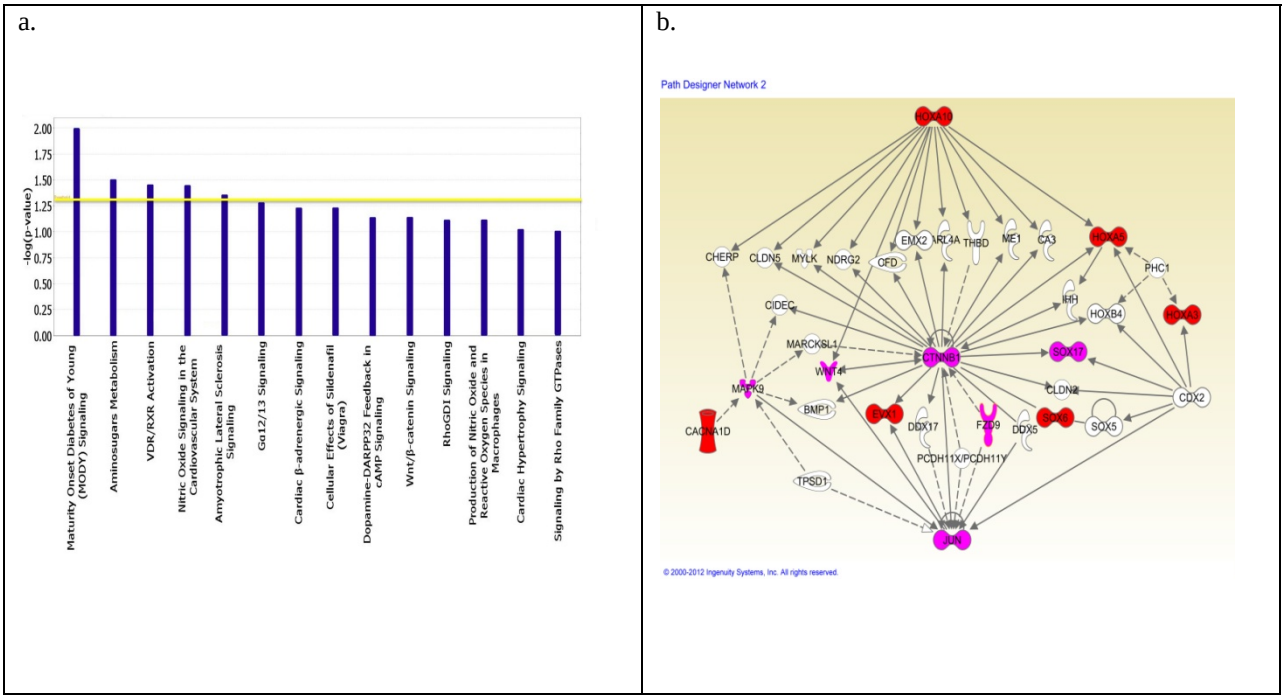

Figure S6. A. Canonical pathways and associated *p* -values identified by ingenuity pathway analysis (IPA). The yellow horizontal line is the threshold for *P* =0.05 with the names of the imputed genes shaded in red. B. Network constructed using the identified genes in GWAS by IPA. *CTNNB1* has the most connections in the network. Multiple genes including *SOX6*, *EVX1*, *HOXA* family genes and *CACNA1D* are present in this network.

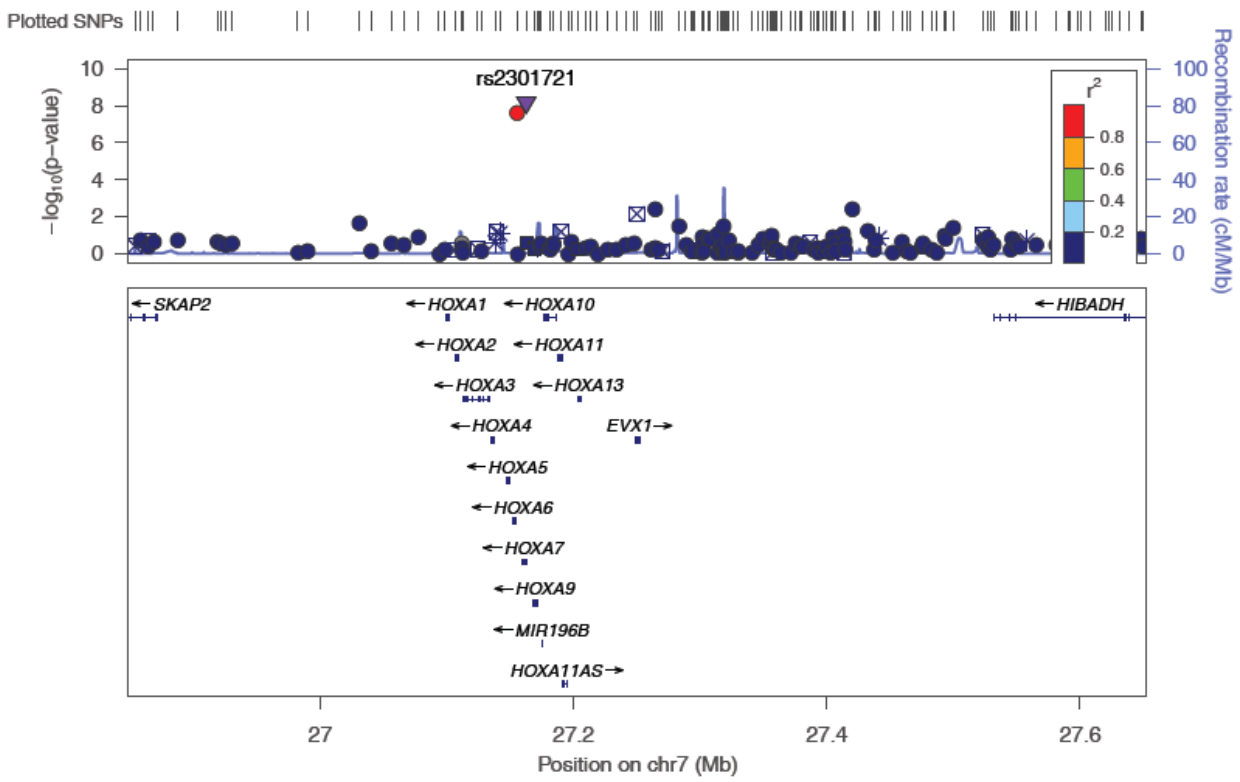

Figure S7. Regional plot of –log(*P*-values) from Treeselect analysis along the LWK branch of an unrooted tree with LWK, YRI and AA samples.

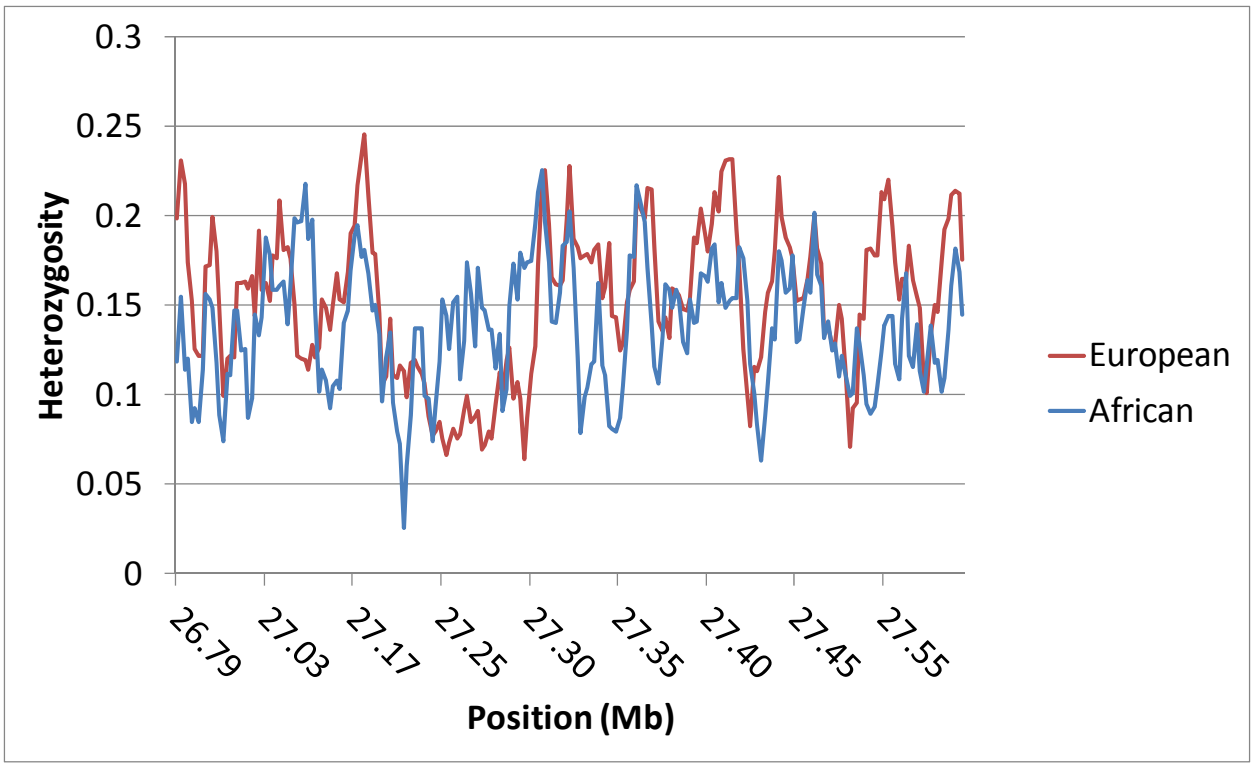

Figure S8. Regional heterozygosity in European and African Human Genome Diversity Project (HGDP) participants, with a decrease in heterozygosity in Europeans at the *HOX* gene cluster on chromosome 7 from 27.18 to 27.3 Mb.

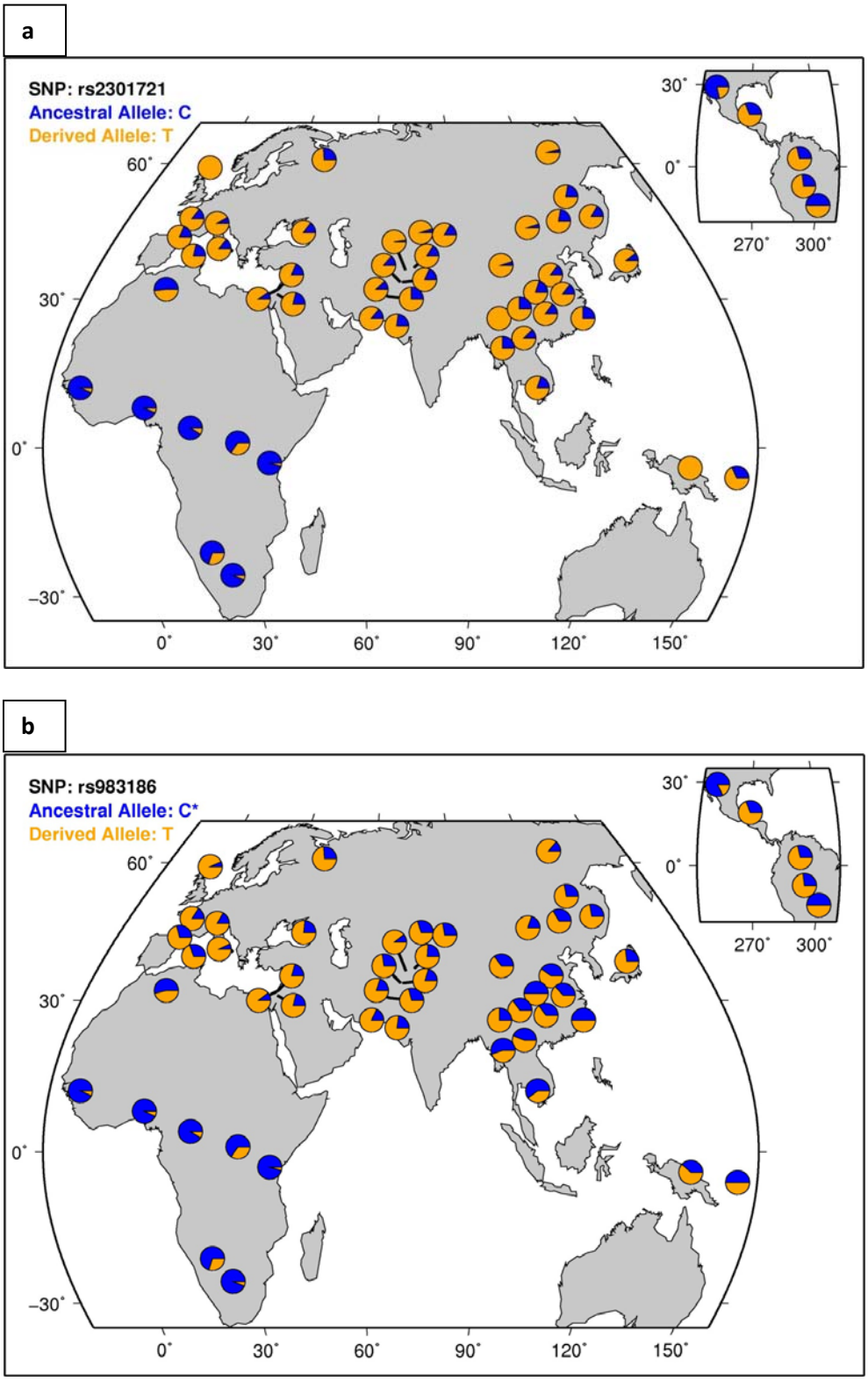

Figure S9.

(A) Map of allele frequencies from the Human Genome Diversity Project (HGDP) for the non-synonymous SNP rs2301721 in *HOXA7;*

(B) Map of allele frequencies from the HGDP for rs983186 near *EVX1.*

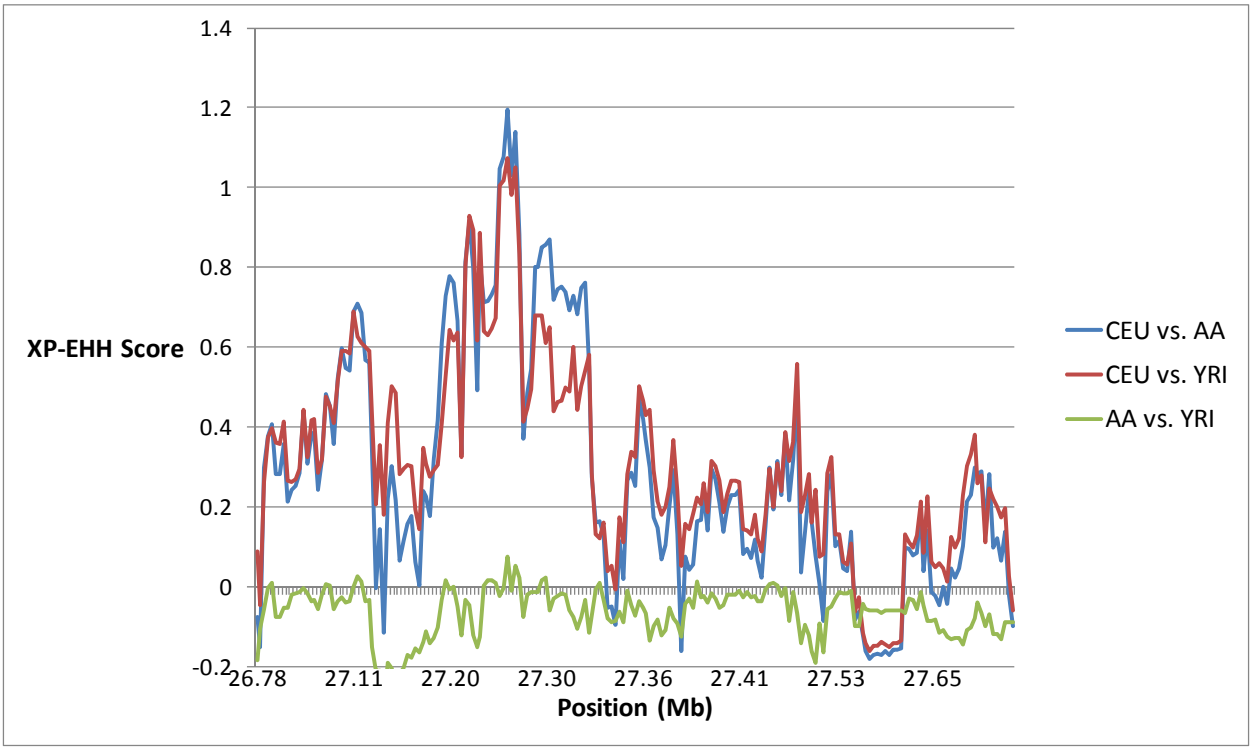

Figure S10. XP-EHH Scores for the *EVX1*/*HOXA* region for HapMap and African Ancestry samples. Signatures of recent positive selection across the *EVX1*/*HOXA* region in HapMap Phase III Yoruba (YRI) and European CEPH (CEU), and BioVU African Americans (AA) using the cross-population extended haplotype homozygosity statistic (XP-EHH).

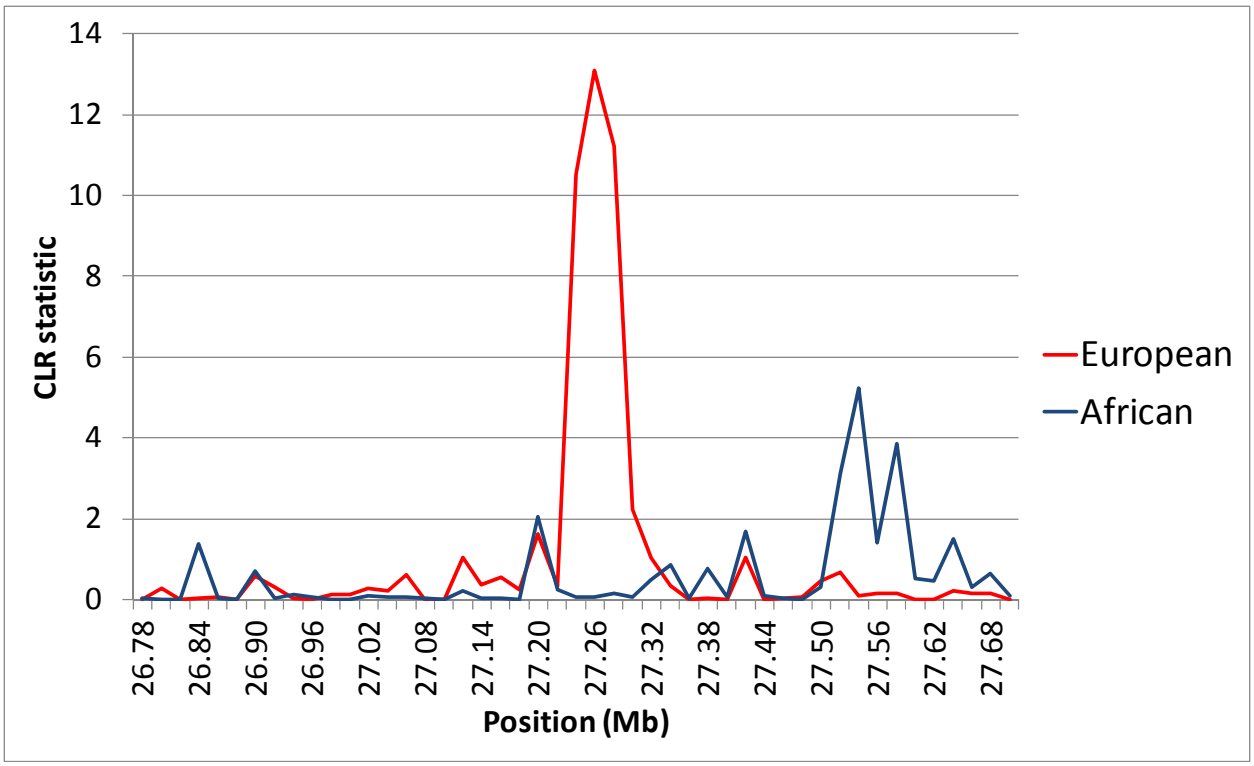

Figure S11. CLR statistics for Human Genome Diversity Project (HGDP) participants from Europe and Bantu-speaking Africans in the *HOXA*/*EVX1* region.

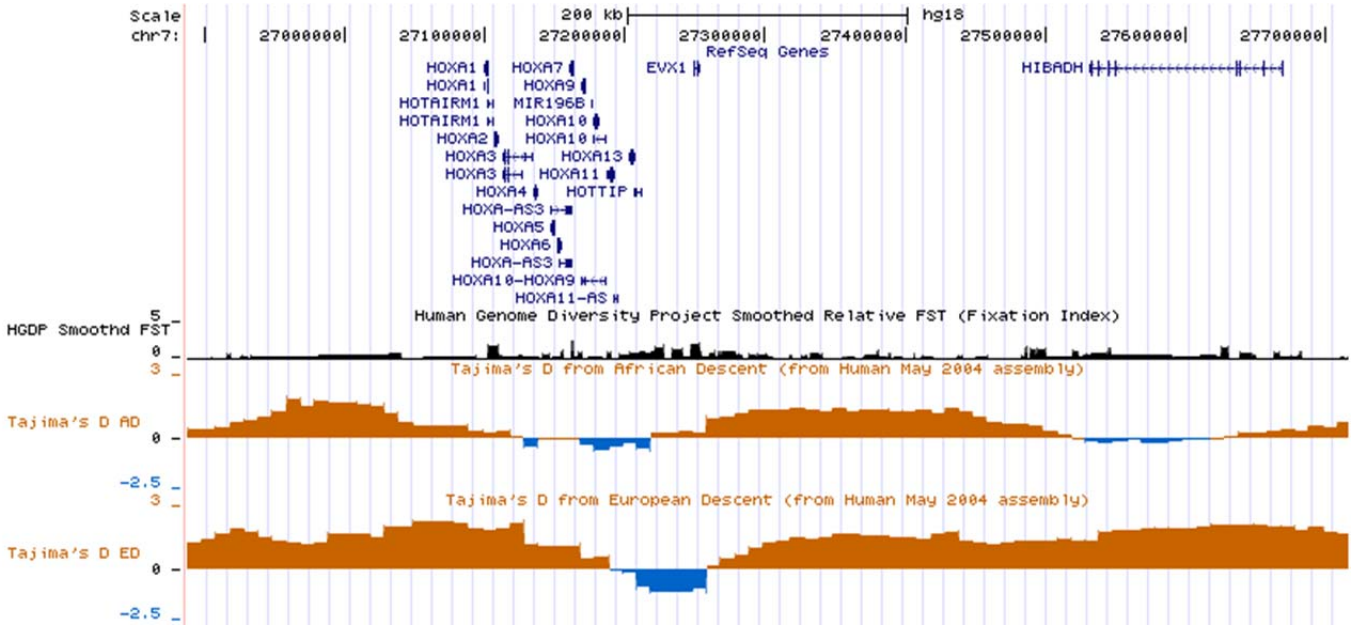

Figure S12. Calculations of Tajima's D from HapMap European (CEU) and African (YRI) participants, with negative values near the *HOX* gene cluster supporting recent positive selection at this locus.

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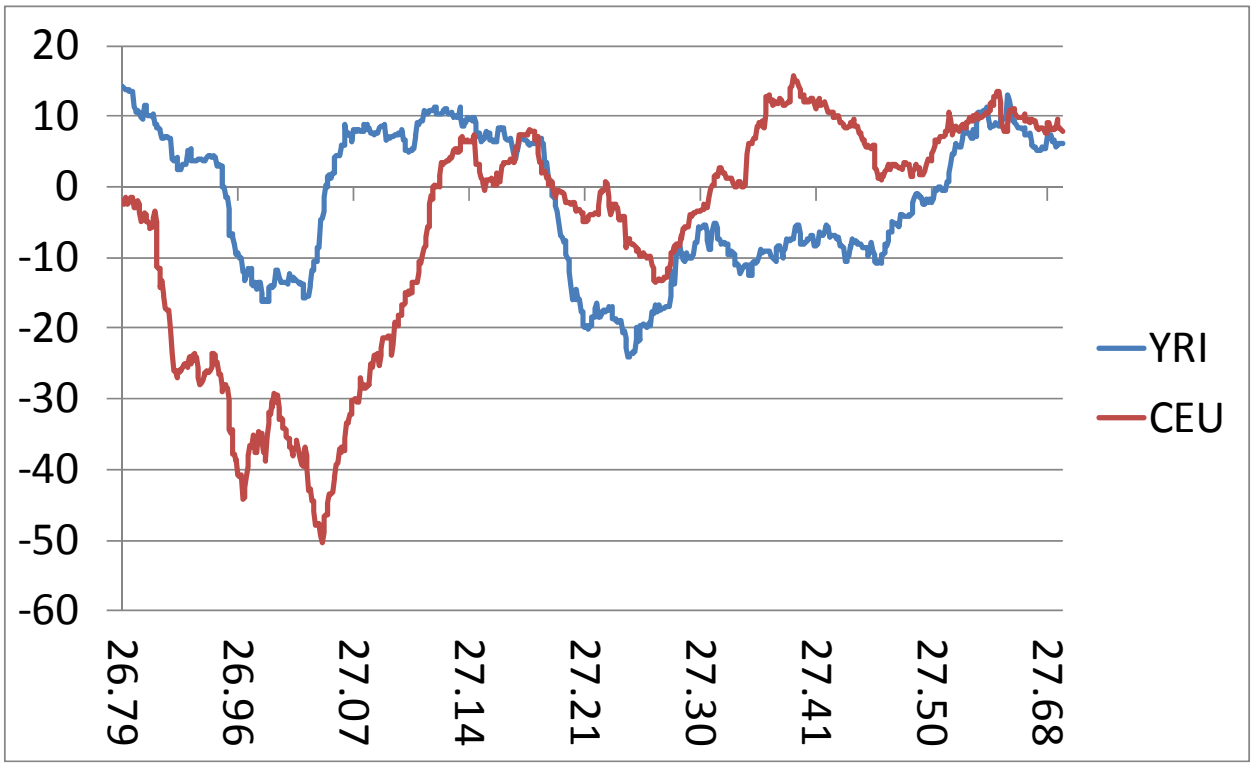

Figure S13. Calculation of Fay and Wu's H from European (CEU) and African HapMap (YRI) participants, with negative values nearby the *HOX* gene cluster.

Table S1. Genome-wide Genotyping and Imputation Information by Study

Study	Genotyping Platform	Genotyping calling algorithm	Genotype filter	Imputation	Imputation HapMap reference	Imputation NCBI version
BioVu	Illumina Human 1M-DuoV3 array	Illumina BeadStudio	No palindromic SNPs, Call rate < 95%, MAF < 0.01, HWE p < 0.0000001,	IMPUTE v2.1.2	YRI/CEU 1:1 ratio	b36
ARIC†	Affymetrix GeneChip SNP Array 6.0	BirdSeed	Call rates<95%, mapped to more than one locus	MACH	YRI/CEU 1:1 ratio	b36
CARDIA†	Affymetrix GeneChip SNP Array 6.0	BirdSeed	Call rates<90%, mapped to more than one locus	MACH	YRI/CEU 1:1 ratio	b36
CFS†	Affymetrix GeneChip SNP Array 6.0	BirdSeed	Call rates<90%, mapped to more than one locus, Mendelian inconsistence	MACH	YRI/CEU 1:1 ratio	b36
JHS†	Affymetrix GeneChip SNP Array 6.0	BirdSeed	Call rates<90%, mapped to more than one locus	MACH	YRI/CEU 1:1 ratio	b36
MESA†	Affymetrix GeneChip SNP Array 6.0	BirdSeed	Call rates<90%, mapped to more than one locus	MACH	YRI/CEU 1:1 ratio	b36
CHS	Illumina HumanOmni1-Quad_v1 BeadChip system	Illumina GenomeStudio software	Call rate < 97%, HWE P < 10-5, > 1 duplicate error or Mendelian inconsistency (for reference CEPH trios), heterozygote frequency = 0	BEAGLE v3.2.1	Imputation in 2 phases: HapMap III from ASW, YRI & CEU & HapMap II using CEU & YRI, & resulting 3 sets merged (final imputed data: 2,770,583 SNPs).	b36
GeneSTAR	Illumina Human 1Mv1_c Array	BeadStudio	Call rates <90%	MACH	YRI/CEU 1:1 ratio	HapMap2_r21_b36
GENOA	Affymetrix GeneChip SNP Array 6.0 & Illumina 1M array	BirdSeed and Beadstudio	Call rates < 95%	MACH	YRI/CEU 1:1 ratio	HapMap2_r22_b36
HANDLS	1M Illumina	Illumina GenomeStudio	Call rates<95%, mapped to more than one locus	MACH	YRI/CEU 1:1 ratio	HapMap2_r22_b36
HealthABC	Genotyping Platform 1M Illumina	Illumina GenomeStudio	Call rates < 97%	MACH	YRI/CEU 1:1 ratio	HapMap2_r22_b37
HyperGEN	Affymetrix GeneChip SNP Array 6.0	BirdSeed	Call rates < 95%	MACH	YRI/CEU 1:1 ratio	HapMap2_r22_b36
Maywood-Loyola	Affymetrix GeneChip SNP Array 6.0	BirdSeed	Call rates < 95%	MACH	YRI/CEU 1:1 ratio	HapMap2_r22_b36
Maywood-Nigeria	Affymetrix GeneChip SNP Array 6.0	BirdSeed	Call rates < 95%	MACH	YRI	HapMap2_r22_b36
Mt Sinai study	Affymetrix GeneChip SNP Array 6.0	BirdSeed	Call rates < 95%	MACH	CEU/YRI/JPT/CHB	HapMap2_r22_b36
WHI-SHARe	Affymetrix GeneChip SNP Array 6.0	Birdseed v2	Call rates < 95%	MACH	YRI/CEU 1:1 ratio	HapMap2_r22_b37

HUFS	Affymetrix GeneChip SNP Array 6.0	BirdSeed v2			Combined HapMap phase II+III YRI/CEU, 2 rounds of imputation, YRI then CEU, followed by merge	HapMap2+3_r28__b36
Bogalusa	Illumina Human 610 + Illumina CVD BeadChip	Illumina BeadStudio	Call rates < 95%, MAF<0.01, HWE ≥1.0×10-3	MACH		
			Call rates <90%	MACH	YRI/CEU 1:1 ratio	HapMap2_r22_b36
SIGNET	Affymetrix GeneChip SNP Array 6.0	BirdSeed v1.33	Call rates < 95%	MACH	YRI/CEU 1:1 ratio	HapMap2_r22_b36

† Members of the NHLBI Candidate gene Association Resource (CARe).

Genome-wide genotyping and imputation information by study within the Continental Origins and Genetic Epidemiology Network (COGENT). Abbreviations: Biological bank of Vanderbilt University (BioVU); Atherosclerosis Risk In Communities (ARIC); Coronary Artery Risk Development in Young Adults (CARDIA); Cleveland Family Study (CFS); Jackson Heart Study (JHS); Multi-Ethnic Study of Atherosclerosis (MESA); Cardiovascular Health Study (CHS); Genetic Study of Atherosclerosis Risk (GeneSTAR); Genetic Epidemiology Network of Arteriopathy (GENOA); The Healthy Aging in Neighborhoods of Diversity Across the Life Span Study (HANDLS); Health, Aging, and Body Composition (Health ABC) Study; The Hypertension Genetic Epidemiology Network (HyperGEN); Mount Sinai, New York City, USA study (Mt Sinai Study); Women's Health Initiative SNP Health Association Resource (WHI-SHARe); Howard University Family Study (HUFS); Bogalusa Heart Study (BHS); Sea Islands Genetic NETwork (SIGNET). MAF, minor allele frequency; HWE, Hardy Weinberg Equilibrium; SNP, single nucleotide polymorphism.

Table S2. Lambda (λ)values for the COGENT discovery genome-wide association studies.

Study	Number	Lambda HTN	Lambda SBP	Lambda DBP
BioVu	941	1.011	0.993	0.978
CARe-ARIC	2,511	1.033	1.027	1.023
CARe-CARDIA	833	1.051	1.003	0.999
CARe-CFS	489	1.048	1.038	1.044
CARe-JHS	2,017	1.022	1.025	1.04
CARe-MESA	1,623	1.004	0.998	1.025
CHS	815	1.025	1.027	1.023
GeneSTAR	1,132	1.052	1.02	1.011
GENOA	996	1.102	1.012	1.007
HANDLS	950	1.013	0.992	0.988
HealthABC	1,139	1.008	0.996	0.996
HyperGEN	1,252	1.058	1.016	1.018
Maywood-Loyola	743	1.031	1.008	1.001
Mt Sinai study	873	1.032	0.966	0.966
Nigeria-Loyola	1,188	1.118	1.107	1.091
WHI-SHARe	8,094	1.020	1.011	1.011
HUFS	1,017	1.031	1.041	1.056
Bogalusa	368	1.018	1.011	1.011
SIGNET-REGARDS	2,394	0.996	1.013	1.013
total	**29,375**			

Abbreviations: Biological bank of Vanderbilt University (BioVU); Atherosclerosis Risk In Communities (ARIC); Coronary Artery Risk Development in Young Adults (CARDIA); Cleveland Family Study (CFS); Jackson Heart Study (JHS); Multi-Ethnic Study of Atherosclerosis (MESA); Cardiovascular Health Study (CHS); Genetic Study of Atherosclerosis Risk (GeneSTAR); Genetic Epidemiology Network of Arteriopathy (GENOA); The Healthy Aging in Neighborhoods of Diversity Across the Life Span Study (HANDLS); Health, Aging, and Body Composition (Health ABC) Study; The Hypertension Genetic Epidemiology Network (HyperGEN); Mount Sinai, New York City, USA study (Mt Sinai Study); Women's Health Initiative SNP Health Association Resource (WHI-SHARe); Howard University Family Study (HUFS); Bogalusa Heart Study (BHS); Sea Islands Genetic NETwork (SIGNET).

Table S3. SNPs with P<1.0 x 10-5 in COGENT for Systolic Blood Pressure, Diastolic Blood Pressure or Hypertension.

						DBP					SBP					Hypertension							HapMap YRI		HapMap CEU	
SNPID	Chr	Position (build 36)	Coded allele	Other allele	Coded allele frequency	beta	SE	*P*	Het PVal	N	beta	SE	*P*	Het PVal	N	beta	SE	*P*	Het PVal	N	Gene nearby	GeneVariant	MAF	MAF	MAF	MAF
rs2745282	1	115528171	t	g	0.22	0.36	0.11	1.69E-03	6.55E-03	29090.9	0.64	0.19	9.22E-04	6.87E-01	29091.9	0.10	0.05	4.33E-02	6.87E-01	10860.9	*N/A*	INTERGENIC	T	0.03	G	0.28
rs351361	1	112844081	t	c	0.20	-0.45	0.14	1.84E-03	4.55E-01	27940.9	-1.11	0.24	4.60E-06	8.72E-01	27941.9	-0.07	0.03	1.75E-02	5.13E-01	27454.9	*WNT2B*	INTRONIC	T	0.14	T	0.19
rs7522390	1	165615309	a	g	0.27	0.25	0.10	1.65E-02	1.55E-01	28906	0.88	0.17	4.41E-07	1.68E-01	28907	0.08	0.04	7.70E-02	2.41E-01	8765	*POU2F1*	INTRONIC	A	0.29	A	0.27
rs10925060	1	245717763	t	c	0.16	0.35	0.13	7.13E-03	5.77E-01	28940	0.49	0.22	2.26E-02	5.00E-01	28941	0.10	0.03	6.91E-04	4.31E-01	27184	*N/A*	UPSTREAM	T	0.22	T	0.04
rs13405738	2	1929865	t	c	0.85	-0.28	0.14	4.71E-02	2.57E-01	29294	-1.05	0.23	5.94E-06	7.16E-01	29295	-0.13	0.03	7.69E-05	3.29E-01	27170	*MYT1L*	INTRONIC	C	0.12	C	0.16
rs17570579	2	50955087	t	c	0.07	0.85	0.19	8.07E-06	3.79E-01	29321	1.02	0.32	1.28E-03	4.07E-01	29322	0.09	0.04	4.35E-02	6.74E-01	27564	*NRXN1*	INTRONIC	T	0.01	T	0.22
rs1534260	2	156602790	t	c	0.36	-0.44	0.10	4.02E-06	1.62E-03	29303.7	-0.49	0.16	2.32E-03	1.30E-03	29304.7	-0.08	0.04	2.72E-02	2.77E-01	11401.7	*N/A*	INTERGENIC	T	0.40	T	0.09
rs234790	3	7055901	c	g	0.18	-0.41	0.13	1.78E-03	8.64E-01	29065.9	-0.96	0.22	1.26E-05	8.71E-01	29066.9	-0.02	0.04	6.55E-01	1.11E-01	13990.9	*GRM7*	INTRONIC	C	0.07	C	0.40
rs1449292	3	29906889	a	g	0.64	0.22	0.10	2.53E-02	3.50E-02	28948	0.49	0.16	2.46E-03	3.52E-02	28949	0.04	0.03	1.88E-01	1.19E-03	16865	*RBMS3*	INTRONIC	G	0.31	A	0.44
rs6802072	3	41002684	t	c	0.45	-0.42	0.09	6.17E-06	4.26E-01	29272.8	-0.43	0.16	6.17E-03	6.68E-01	29273.8	0.00	0.04	9.81E-01	2.29E-01	11035.8	*N/A*	INTERGENIC	T	0.34	C	0.07
rs1717027	3	41962924	t	c	0.64	0.49	0.10	5.07E-07	2.51E-01	29321.9	0.18	0.16	2.64E-01	5.04E-01	29322.9	0.05	0.02	1.15E-02	4.36E-02	29462.9	*ULK4*	INTRONIC	C	0.30	T	0.22
rs10049492	3	53571572	a	g	0.74	0.58	0.12	1.78E-06	5.07E-01	27878.9	0.86	0.20	1.74E-05	9.94E-02	27879.9	0.14	0.03	4.88E-07	1.40E-01	26184.8	*CACNA1D*	INTRONIC	G	0.08	G	0.45
rs7655423	4	112132084	t	c	0.51	-0.15	0.09	1.19E-01	2.98E-01	28955	-0.69	0.16	9.94E-06	4.62E-01	28956	-0.05	0.02	1.06E-02	9.87E-01	27175	*N/A*	INTERGENIC	T	0.40	C	0.03
rs7676999	4	117153528	t	c	0.10	-0.90	0.20	4.62E-06	8.18E-01	28933.7	-1.33	0.33	5.48E-05	6.14E-01	28934.7	-0.15	0.04	9.20E-04	7.17E-01	26173.7	*N/A*	INTERGENIC	T	0.03	T	0.26
rs4383597	4	148225110	a	g	0.51	-0.30	0.09	9.89E-04	7.23E-01	28944	-0.73	0.15	2.04E-06	8.76E-01	28945	-0.03	0.04	5.19E-01	3.19E-01	8747	*N/A*	INTERGENIC	G	0.41	A	0.44
rs12374234	4	150061158	t	c	0.25	0.48	0.11	8.85E-06	2.73E-01	28938	0.55	0.18	2.33E-03	5.49E-02	28939	0.06	0.02	2.10E-02	1.70E-01	27157	*N/A*	INTERGENIC	T	0.21	C	0.49
rs3828634	5	31496959	t	c	0.23	0.46	0.11	3.80E-05	8.80E-01	29131.8	0.88	0.19	2.81E-06	6.69E-01	29132.8	0.00	0.05	9.96E-01	4.62E-01	10862.8	*RNASEN*	INTRONIC	T	0.11	C	0.32
rs11963288	6	56443263	t	c	0.95	0.20	0.21	3.32E-01	2.88E-01	27373	1.55	0.35	9.73E-06	3.54E-01	27375	0.18	0.05	1.36E-04	7.19E-01	27877	*DST*	INTRONIC	C	0.03	C	0.03
rs6924906	6	82277271	t	c	0.71	-0.51	0.10	5.57E-07	5.93E-01	29111	-0.41	0.17	1.74E-02	7.68E-01	29112	-0.02	0.04	5.22E-01	7.57E-01	10860	*N/A*	INTERGENIC	C	0.32	C	0.07
rs13209747	6	127157147	t	c	0.17	0.56	0.12	8.84E-06	4.71E-01	28708	0.85	0.21	5.88E-05	6.10E-01	28709	0.04	0.05	3.25E-01	5.70E-01	12312	*N/A*	INTERGENIC	T	0.13	T	0.46
rs17080102	6	151046463	c	g	0.10	-0.74	0.15	5.45E-07	6.85E-01	29323	-1.02	0.25	3.42E-05	8.21E-01	29324	-0.10	0.03	1.32E-03	5.86E-02	29464	*PLEKHG1*	INTRONIC	C	0.11	C	0.05
rs17471520	7	27145315	t	c	0.69	-0.50	0.10	1.81E-06	6.04E-01	29232.7	-0.88	0.17	4.39E-07	9.54E-01	29233.7	-0.10	0.02	3.97E-06	9.92E-01	29373.7	*N/A*	DOWNSTREAM	C	0.34	C	0.11
rs11564022	7	27303571	t	c	0.23	-0.60	0.11	7.66E-08	7.95E-01	29321.9	-0.89	0.19	1.83E-06	4.99E-01	29322.9	-0.13	0.02	6.78E-08	1.46E-01	29462.9	*N/A*	INTERGENIC	T	0.18	T	0.42
rs17428471	7	27304392	t	g	0.12	0.61	0.14	1.23E-05	7.76E-01	29325.9	1.20	0.24	4.00E-07	7.48E-01	29326.9	0.15	0.03	1.32E-06	4.76E-01	29834.9	*N/A*	INTERGENIC	T	0.14	T	0.06
rs11972761	7	52858144	c	g	0.15	0.40	0.13	1.71E-03	6.99E-01	29321	1.09	0.22	5.39E-07	5.32E-01	29322	0.07	0.03	1.52E-02	7.66E-01	29830	*N/A*	INTERGENIC	C	0.19	C	0.03
rs12718983	7	55692246	t	g	0.85	0.39	0.14	4.58E-03	6.79E-01	29294.8	1.10	0.23	1.46E-06	8.48E-01	29295.8	0.06	0.03	3.81E-02	1.57E-01	29435.8	*N/A*	INTERGENIC	G	0.10	G	0.42

rs11768155	7	80203792	a	g	0.75	-0.48	0.11	5.40E-06	4.09E-01	29072.7	-0.41	0.18	2.13E-02	2.08E-01	29073.7	-0.12	0.04	2.87E-03	4.00E-01	10851.7	*N/A*	INTERGENIC	G	0.37	G	0.02
rs6997487	8	107034687	a	c	0.27	-0.48	0.11	5.62E-06	6.28E-01	29303	-0.31	0.18	8.37E-02	2.09E-01	29304	-0.04	0.02	8.92E-02	3.49E-01	27546	*N/A*	INTERGENIC	A	0.20	A	0.50
rs12339156	9	35905230	c	g	0.17	-0.56	0.12	7.73E-06	7.32E-01	29304.9	-0.61	0.21	3.30E-03	1.55E-01	29305.9	-0.07	0.03	1.42E-02	5.42E-01	29813.9	*N/A*	INTERGENIC	C	0.20	C	0.28
rs7868945	9	72704778	a	g	0.24	0.50	0.11	9.70E-06	7.42E-01	28881	0.53	0.19	5.84E-03	4.68E-01	28882	0.07	0.03	9.39E-03	6.19E-01	27126	*TRPM3*	INTRONIC	A	0.30	A	0.08
rs4918017	10	105234221	c	g	0.73	0.53	0.12	7.31E-06	6.08E-01	28308.9	0.48	0.20	1.45E-02	8.29E-01	28309.9	0.05	0.03	3.24E-02	8.79E-01	28818.8	*N/A*	INTERGENIC	G	0.06	C	0.33
rs11041530	11	7658079	c	g	0.11	-0.54	0.15	2.65E-04	9.21E-01	29173.9	-1.35	0.25	4.04E-08	3.45E-01	29174.9	-0.08	0.05	1.50E-01	4.66E-01	11002.9	*N/A*	INTERGENIC	C	0.09	C	0.01
rs16932474	11	16008731	t	c	0.83	-0.55	0.12	5.61E-06	7.12E-01	29313	-0.49	0.20	1.70E-02	1.89E-02	29314	-0.07	0.03	1.37E-02	9.29E-01	27557	*SOX6*	INTRONIC	C	0.28		monomorphic
rs1401454	11	16206759	t	c	0.46	0.45	0.10	2.11E-06	8.70E-01	27939	0.55	0.16	5.68E-04	8.25E-01	27940	0.05	0.02	1.10E-02	8.96E-01	26185	*SOX6*	INTRONIC	C	0.47	T	0.48
rs17142803	11	81104083	t	c	0.10	0.98	0.22	7.53E-06	6.24E-01	15897	0.58	0.35	9.60E-02	8.69E-01	15894	0.07	0.05	1.72E-01	6.68E-01	14161	*N/A*	INTERGENIC	T	0.13		monomorphic
rs12311091	12	19872394	t	c	0.20	-0.21	0.12	7.23E-02	1.71E-01	28308.9	-0.99	0.20	4.69E-07	8.22E-01	28309.9	-0.08	0.03	1.21E-03	1.98E-01	28818.9	*N/A*	INTERGENIC	T	0.22	T	0.17
rs10848279	12	130139844	a	c	0.10	-0.53	0.16	7.25E-04	6.15E-01	29131	-1.33	0.27	6.18E-07	7.89E-01	29132	-0.05	0.06	4.38E-01	6.30E-01	12691	*GPR133*	INTRONIC	A	0.05	A	0.23
rs9555689	13	109782559	a	g	0.67	0.20	0.10	4.87E-02	1.13E-02	28308.9	0.61	0.17	5.21E-04	5.12E-02	28309.9	0.08	0.02	8.08E-04	7.12E-02	27822.9	*COL4A2*	INTRONIC	G	0.42	G	0.22
rs6575454	14	94215314	t	g	0.14	-0.29	0.13	2.72E-02	1.56E-01	28661	-0.54	0.22	1.68E-02	2.78E-02	28662	-0.10	0.05	3.25E-02	3.00E-04	11335	*N/A*	INTERGENIC	T	0.19	T	0.20
rs11633456	15	62835692	t	c	0.32	0.34	0.10	6.65E-04	6.12E-01	28308.9	0.76	0.17	5.45E-06	8.71E-01	28310	0.07	0.02	9.41E-04	7.56E-01	28818.9	*RBPMS2*	INTRONIC	T	0.36	T	0.04
rs467649	16	64392242	t	g	0.02	0.74	0.31	1.88E-02	4.52E-01	26887	2.41	0.52	4.43E-06	9.21E-01	26889	0.05	0.08	5.19E-01	3.61E-01	26423	*N/A*	INTERGENIC	T	0.02	T	0.09
rs16958138	17	52697608	a	g	0.25	0.24	0.12	3.74E-02	7.24E-01	28308.9	0.90	0.19	3.14E-06	5.86E-01	28309.9	0.08	0.03	1.72E-03	2.33E-02	28818.9	*MSI2*	INTRONIC	A	0.25	A	0.05
rs1786784	18	33252486	a	g	0.31	-0.19	0.15	2.09E-01	1.79E-02	13840	-0.14	0.24	5.58E-01	3.11E-03	13838	-0.10	0.03	1.43E-03	2.19E-02	14343	*BRUNOL 4*	INTRONIC	A	0.44	A	monomorphic
rs11084566	19	36049889	t	c	0.71	0.47	0.10	5.13E-06	3.00E-01	28720	0.62	0.17	2.80E-04	7.27E-01	28722	0.01	0.02	5.10E-01	1.44E-01	26964	*N/A*	INTERGENIC	C	0.25	C	0.33
rs2064726	20	50149092	t	c	0.47	-0.24	0.09	8.23E-03	9.58E-01	28599	-0.70	0.15	6.02E-06	9.04E-01	28600	-0.02	0.04	5.65E-01	8.01E-01	8576	*ZFP64*	INTRONIC	C	0.44	T	0.37

SNPs association values with P<1.0 x 10-5 for SBP, DBP and hypertension (HTN) in the Continental Origins and Genetic Epidemiology Network (COGENT). Abbreviations: Chr, chromosome; MAF, minor allele frequency; HetPVal, P for heterogeneity; N/A, not available

Table S4. Comparison of the number of observed and expected signals in ICBP for the 43 independent SNPs in COGENT with P <1.0 x 10-5

Significance level	0.05	0.01	0.001	0.0001
Observed	18	14	11	5
Expected	4.5	0.9	0.09	0.009
P-value	2.2×10^{-7}	2.3×10^{-13}	2.3×10^{-20}	3.5×10^{-13}

Comparison observed and expected SBP or DBP signals in the International Consortium for Blood Pressure (ICBP) for 43 independent SNPs in Continental Origins and Genetic Epidemiology Network (COGENT) with *P* $<1.0 \times 10^{-5}$

Table S5. Statistical power of replicating the SNPs in Table 1 and 2 using African ancestry samples only.

SNP	Alleles	Trait	Estimated SNP specific variance	Total sample size in AA available for the SNP	Allele frequency	Sample size required for 80% power at alpha=0.05
rs13209747	T/C	SBP	5.85E-04	8686	0.1854	1.65E+04
		DBP	7.07E-04	8686	0.1854	1.36E+04
rs17080102	C/G	SBP	5.56E-04	10070	0.1016	1.73E+04
		DBP	8.19E-04	10070	0.1016	1.18E+04
rs6924906	T/C	SBP	1.98E-04	11770	0.7145	4.87E+04
		DBP	8.85E-04	11770	0.7145	1.09E+04
rs17428471	T/G	SBP	8.99E-04	6650	0.1432	1.07E+04
		DBP	6.70E-04	6650	0.1432	1.44E+04
rs1717027	T/C	SBP	4.44E-05	10070	0.6447	2.17E+05
		DBP	9.07E-04	10070	0.6447	1.06E+04
rs1401454	T/C	SBP	4.41E-04	10070	0.4615	2.18E+04
		DBP	8.35E-04	10070	0.4615	1.15E+04
rs11041530	C/G	SBP	1.07E-03	8686	0.1134	9000
		DBP	4.78E-04	8686	0.1134	2.02E+04

Table S6. Conditional analysis of SNPs in HOXA locus for SBP and DBP

Systolic blood pressure (SBP)					COGENT single-SNP meta-analysis				Conditional analysis, LD from 5 CARe studies*		
SNP	**Chr**	**Position (build 36)**	**Nearest gene**	**Allele 1**	**allele frequency**	**beta**	**se**	**pvalue**	**beta**	**se**	**pvalue**
rs11564022	7	27303571	*EVX1-HOXA*	T	0.2256	-0.8915	0.1868	1.83E-06	-0.88434	0.185832	1.95E-06
rs17471520	7	27145315	*EVX1-HOXA*	T	0.6945	-0.8786	0.1739	4.39E-07	-0.85691	0.16913	4.05E-07
rs11564022	7	27303571	*EVX1-HOXA*	T	0.2256	-0.8915	0.1868	1.83E-06	-0.89508	0.185545	1.41E-06
rs17428471	7	27304392	*EVX1-HOXA*	T	0.1225	1.1961	0.236	4.00E-07	1.17406	0.235888	6.45E-07
rs17471520	7	27145315	*EVX1-HOXA*	T	0.6945	-0.8786	0.1739	4.39E-07	-0.8851	0.172681	2.97E-07
rs17428471	7	27304392	*EVX1-HOXA*	T	0.1225	1.1961	0.236	4.00E-07	1.19066	0.241156	7.92E-07

Diastolic blood pressure (DBP)					COGENT single-SNP meta-analysis				Conditional analysis, LD from 5 CARe studies*		
SNP	**Chr**	**Position (build 36)**	**Nearest gene**	**Allele 1**	**allele frequency**	**beta**	**se**	**pvalue**	**beta**	**se**	**pvalue**
rs11564022	7	27303571	*EVX1-HOXA*	T	0.2256	-0.5969	0.111	7.66E-08	-0.59355	0.110236	7.27E-08
rs17471520	7	27145315	*EVX1-HOXA*	T	0.6945	-0.496	0.1039	1.81E-06	-0.47971	0.100524	1.82E-06
rs11564022	7	27303571	*EVX1-HOXA*	T	0.2256	-0.5969	0.111	7.66E-08	-0.59901	0.110113	5.33E-08
rs17428471	7	27304392	*EVX1-HOXA*	T	0.1225	0.6143	0.1405	1.23E-05	0.589174	0.140037	2.58E-05
rs17471520	7	27145315	*EVX1-HOXA*	T	0.6945	-0.496	0.1039	1.81E-06	-0.49819	0.103024	1.33E-06
rs17428471	7	27304392	*EVX1-HOXA*	T	0.1225	0.6143	0.1405	1.23E-05	0.609722	0.143636	2.19E-05

Conditional analysis of SNPs in the HOXA region performed for systolic blood pressure (SBP) and diastolic blood pressure (DBP) in the Continental Origins and Genetic Epidemiology Network (COGENT). *Estimates and p-values

Abbreviations: Chr, chromosome; LD, linkage disequilibrium; SNP, single nucleotide polymorphism

Table S7. Heterogeneity P-values for the top SNPs in main text Table 1

					Replication *P*								
		Effect	Effect		COGENT	COGENT	ICBP	African	East	Phase III+replication	All African	All African	All samples
Chr	SNP	Other Allele	Allele Freq	Trait	*P*	P_{HET}	*P*	Ancestry	Asian		*P*	P_{HET}	P_{HET}
				SBP	$2.6x10^{-1}$	0.5	$5.0x10^{-1}$	$6.0x10^{-1}$	$5.6x10^{-1}$	$3.00x10^{-1}$	0.218	0.3577	0.4657
3	rs1717027	T/C	0.64	DBP	$5.1x10^{-7}$	0.25	$2.5x10^{-7}$	**$2.2x10^{-2}$**	$1.5x10^{-1}$	**$4.62x10^{-13**}$**	**$3.40x10^{-8}$**	**0.9375**	0.6815
				SBP	**1.7x10-2**	**0.77**	**5.6x10-4**	**4.7x10-1**	**2.0x10-3***	**6.16x10-5**	**9.61x10-2**	**0.2483**	**0.07095**
6	**rs6924906**	**T/C**	**0.71**	**DBP**	**5.6x10-7**	**0.59**	**4.9x10-2**	**9.8x10-1**	**8.8x10-3**	**5.50x10-7**	**1.31x10-5**	**0.2013**	**0.215**
				SBP	$5.9x10^{-5}$	0.61	$5.4x10^{-4}$	**$5.0x10^{-4*}$**	**$2.6x10^{-3*}$**	**$2.56x10^{-10**}$**	$3.32x10^{-7}$	**0.366**	0.1698
6	rs13209747	T/C	0.19	DBP	$8.8x10^{-6}$	0.47	$1.5x10^{-3}$	**$2.2x10^{-2}$**	**$1.2x10^{-4*}$**	**$2.43x10^{-11**}$**	$6.37x10^{-7}$	**0.2151**	0.2296
				SBP	**3.4x10-5**	**0.82**	**9.2x10-4**	**2.3x10-1**	**3.4x10-2**	**4.75x10-8**	**2.54x10-5**	**0.7246**	**0.8165**
6	**rs17080102**	**C/G**	**0.1**	**DBP**	**5.4x10-7**	**0.69**	**1.5x10-4**	**4.1x10-1**	**8.5x10-4***	**1.90x10-11****	**1.15x10-6**	**0.294**	**0.3656**
				SBP	$4.0x10^{-7}$	0.75	$8.0x10^{-6*}$	$1.4x10^{-4*}$	$3.4x10^{-1}$	$2.1x10^{-12**}$	$9.15x10^{-10}$	0.2651	0.07015
7	rs17428471	T/G	0.14	DBP	$1.2x10^{-5}$	0.78	$2.8x10^{-5*}$	$1.1x10^{-2}$	$4.4x10^{-1}$	$1.6x10^{-9**}$	$7.07x10^{-7}$	0.7819	0.4949
				SBP	**5.7x10-4**	**0.83**	**2.2x10-4**	**9.7x10-4***	**6.7x10-1**	**9.50x10-7**	**3.79x10-6**	**0.4655**	**0.05645**
11	**rs1401454**	**T/C**	**0.46**	**DBP**	**2.1x10-6**	**0.87**	**3.1x10-5**	**5.0x10-3**	**5.5x10-1**	**5.12x10-10****	**3.82x10-8**	**0.5955**	**0.1655**
				SBP	$4.0x10^{-8}$	0.34	$2.9x10^{-2}$	$8.0x10^{-1}$	$9.3x10^{-1}$	$5.6x10^{-6}$	$2.89x10^{-6}$	0.03584	0.02305
11	rs11041530	C/G	0.11	DBP	2.6**$x10^{-4}$**	0.47	0.119	$6.5x10^{-1}$	$6.6x10^{-1}$	$7.6x10^{-4}$	$2.30x10^{-3}$	0.1446	0.2073

Abbreviations: SNP, single nucleotide polymorphisms; PHET, p for heterogeneity

Table S8. Conditional analysis of SNPs in SOX6 for SBP and DBP

Systolic blood pressure (SBP)

					COGENT single-SNP meta-analysis				Conditional analysis, LD from 5 CARe studies*		
SNP	**Chr**	**Position (build 36)**	**Nearest gene**	**Allele 1**	**allele frequency**	**beta**	**se**	**pvalue**	**beta**	**se**	**pvalue**
rs1401454	11	16206759	*SOX6*	T	0.46	0.5512	0.1599	5.68E-04	0.550958	0.158859	5.24E-04
rs381815	11	16858844	*SOX6*	T	0.2225	0.2765	0.1886	0.1427	0.301567	0.190844	1.14E-01
rs1401454	11	16206759	*SOX6*	T	0.46	0.5512	0.1599	5.68E-04	0.528509	0.159365	9.12E-04
rs2014408	11	16321858	*SOX6*	T	0.0718	0.5363	0.3106	0.08423	0.527856	0.307876	8.64E-02

Diastolic blood pressure (DBP)

					COGENT single-SNP meta-analysis				Conditional analysis, LD from 5 CARe cohorts*		
SNP	**Chr**	**Position (build 36)**	**Nearest gene**	**Allele 1**	**allele frequency**	**beta**	**se**	**pvalue**	**beta**	**se**	**pvalue**
rs1401454	11	16206759	*SOX6*	T	0.46	0.451	0.0951	2.11E-06	0.450111	0.094335	1.83E-06
rs381815	11	16858844	*SOX6*	T	0.2225	0.2517	0.1122	0.0249	0.303716	0.113146	7.27E-03
rs1401454	11	16206759	*SOX6*	T	0.46	0.451	0.0951	2.11E-06	0.434742	0.094648	4.36E-06
rs2014408	11	16321858	*SOX6*	T	0.0718	0.3731	0.1873	0.04636	0.388407	0.184351	3.51E-02

*Conditional analysis estimates and p-values were obtained when using two SNPs (marked in the same color) in a linear regresion models

We performed conditional analysis using summary statistics methods previously described by Yang et al (2012, Nat Genet) for SBP and DBP signals in the NHLBI Candidate gene Association Resource (CARe) GWAS data using rs1401454, rs381815, rs2014408 from the SOX6 locus. The CARe cohorts used were as follows: Atherosclerosis Risk In Communities (ARIC); Coronary Artery Risk Development in Young Adults (CARDIA); Cleveland Family Study (CFS); Jackson Heart Study (JHS); Multi-Ethnic Study of Atherosclerosis (MESA).

Table S9. Replication analysis in COGENT of 29 identified SNPs by ICBP

							Allele frequencies					COGENT Results		
trait	Chr	Position (build 36)	SNP	Nearby gene	Coded Allele	Other allele	EUR	AA	Asia	YRI	CEU	Beta	SE	pvalue
DBP	chr12	113872179	rs10850411	*TBX5–TBX3*	T	C	0.70	0.657782	0.408	0.653	0.683	-0.0087	0.1052	0.9344
SBP	chr12	113872179	rs10850411	*TBX5–TBX3*	T	C	0.70	0.657782	0.408	0.653	0.683	-0.114	0.1748	0.5142
DBP	chr10	104836168	rs11191548	CYP17A1	T	C	0.91	0.950721	0.808		0.917	0.2967	0.2065	0.1507
SBP	chr10	104836168	rs11191548	CYP17A1	T	C	0.91	0.950721	0.808		0.917	0.9017	0.3457	0.009086
DBP	chr5	32850785	rs1173771	*NPR3–*	G	A	0.60	0.772235	0.658	0.805	0.525	-0.0741	0.109	0.4966
SBP	chr5	32850785	rs1173771	*NPR3–*	G	A	0.60	0.772235	0.658	0.805	0.525	0.0369	0.1824	0.8397
DBP	chr5	157777980	rs11953630	EBF1	T	C	0.37	0.185074	0.058	0.127	0.342	-0.3209	0.1188	0.0069
SBP	chr5	157777980	rs11953630	EBF1	T	C	0.37	0.185074	0.058	0.127	0.342	-0.4194	0.1992	0.03523
DBP	chr17	44757806	rs12940887	*ZNF652*	T	C	0.38	0.103031	0.1	0.008	0.375	0.0985	0.1491	0.5089
SBP	chr17	44757806	rs12940887	*ZNF652*	T	C	0.38	0.103031	0.1	0.008	0.375	0.4184	0.2501	0.0944
DBP	chr3	27512913	rs13082711	SLC4A7	T	C	0.78	0.925671	0.942	0.958	0.775	-0.3236	0.1775	0.06822
SBP	chr3	27512913	rs13082711	SLC4A7	T	C	0.78	0.925671	0.942	0.958	0.775	-0.2767	0.2988	0.3544
DBP	chr4	103407732	rs13107325	*SLC39A8*	T	C	0.05	0.018869			0.092	-1.1784	0.5385	0.02865
SBP	chr4	103407732	rs13107325	*SLC39A8*	T	C	0.05	0.018869			0.092	-1.589	0.8346	0.05692
DBP	chr4	156864963	rs13139571	GUCY1A3–	C	A	0.76	0.839506	0.733	0.915	0.717	0.0889	0.1298	0.4933
SBP	chr4	156864963	rs13139571	GUCY1A3–	C	A	0.76	0.839506	0.733	0.915	0.717	-0.0929	0.2169	0.6684
DBP	chr20	10917030	rs1327235	*JAG1*	G	A	0.46	0.506287	0.492	0.551	0.508	0.2137	0.0919	0.0201
SBP	chr20	10917030	rs1327235	*JAG1*	G	A	0.46	0.506287	0.492	0.551	0.508	0.4864	0.1543	0.001621
DBP	chr15	72864420	rs1378942	CYP1A1–	C	A	0.35	0.882267	0.808		0.3	-0.2289	0.1472	0.12
SBP	chr15	72864420	rs1378942	CYP1A1–	C	A	0.35	0.882267	0.808		0.3	-0.042	0.2482	0.8655
DBP	chr4	81383747	rs1458038	*FGF5*	T	C	0.29	0.087862	0.283	0.059	0.267	0.5318	0.1821	0.003494
SBP	chr4	81383747	rs1458038	*FGF5*	T	C	0.29	0.087862	0.283	0.059	0.267	0.4195	0.305	0.169
DBP	chr12	88584717	rs17249754	ATP2B1	G	A	0.84	0.865644	0.667	0.873	0.9	0.039	0.1378	0.7773
SBP	chr12	88584717	rs17249754	ATP2B1	G	A	0.84	0.865644	0.667	0.873	0.9	0.5724	0.2306	0.01306
DBP	chr1	11785365	rs17367504	*MTHFR–*	G	A	0.15	0.108908	0.108	0.085	0.183	-0.0199	0.1465	0.8922
SBP	chr1	11785365	rs17367504	*MTHFR–*	G	A	0.15	0.108908	0.108	0.085	0.183	-0.2578	0.2472	0.2971
DBP	chr17	42368270	rs17608766	GOSR2	T	C	0.86	0.972944			0.908	0.0986	0.3985	0.8046
SBP	chr17	42368270	rs17608766	GOSR2	T	C	0.86	0.972944			0.908	-0.4198	0.6375	0.5102

DBP	chr6	26199158	rs1799945	*HFE*	G	C	0.14	0.028593				0.3771	0.3892	0.3326
SBP	chr6	26199158	rs1799945	*HFE*	G	C	0.14	0.028593				0.3962	0.6193	0.5223
DBP	chr10	18747454	rs1813353	CACNB2(39)	T	C	0.68	0.872536	0.833	0.856	0.633	-0.0392	0.1241	0.7523
SBP	chr10	18747454	rs1813353	CACNB2(39)	T	C	0.68	0.872536	0.833	0.856	0.633	0.3615	0.2072	0.08101
DBP	chr15	89238392	rs2521501	*FURIN–FES*	T	A	0.31	0.269298	0.075	0.169	0.383	0.1965	0.1276	0.1235
SBP	chr15	89238392	rs2521501	*FURIN–FES*	T	A	0.31	0.269298	0.075	0.169	0.383	0.0656	0.2113	0.7564
DBP	chr1	113018066	rs2932538	MOV10	G	A	0.75	0.821123	0.842	0.831	0.7	0.3786	0.1197	0.001561
SBP	chr1	113018066	rs2932538	MOV10	G	A	0.75	0.821123	0.842	0.831	0.7	0.3793	0.2008	0.05883
DBP	chr12	110368991	rs3184504	*SH2B3*	T	C	0.47	0.082043			0.45	0.5759	0.2384	0.01571
SBP	chr12	110368991	rs3184504	*SH2B3*	T	C	0.47	0.082043			0.45	1.29E+00	3.70E-01	5.05E-04
DBP	chr3	41852418	rs3774372	ULK4	T	C	0.83	0.796856	0.842	0.805	0.783	-0.2336	0.1126	0.03805
SBP	chr3	41852418	rs3774372	ULK4	T	C	0.83	0.796856	0.842	0.805	0.783	-0.1484	0.1883	0.4305
DBP	chr11	16858844	rs381815	*PLEKHA7*	T	C	0.26	0.218154	0.175	0.203	0.317	0.2517	0.1122	0.0249
SBP	chr11	16858844	rs381815	*PLEKHA7*	T	C	0.26	0.218154	0.175	0.203	0.317	0.2765	0.1886	0.1427
DBP	chr3	170583580	rs419076	MECOM	T	C	0.47	0.507554	0.133	0.593	0.467	0.0268	0.0915	0.7699
SBP	chr3	170583580	rs419076	MECOM	T	C	0.47	0.507554	0.133	0.593	0.467	0.1333	0.154	0.3868
DBP	chr10	18459978	rs4373814	*CACNB2(59)*	G	C	0.55	0.441108	0.508	0.415	0.667	-0.2097	0.0989	0.03399
SBP	chr10	18459978	rs4373814	*CACNB2(59)*	G	C	0.55	0.441108	0.508	0.415	0.667	-0.1033	0.1661	0.5342
DBP	chr10	63137559	rs4590817	C10orf107	G	C	0.84	0.83826		0.797	0.817	-0.2224	0.1266	0.07897
SBP	chr10	63137559	rs4590817	C10orf107	G	C	0.84	0.83826		0.797	0.817	0.1496	0.2134	0.4833
DBP	chr20	57184512	rs6015450	*GNAS–EDN3*	G	A	0.12	0.186073		0.178	0.058	0.3083	0.1231	0.01225
SBP	chr20	57184512	rs6015450	*GNAS–EDN3*	G	A	0.12	0.186073		0.178	0.058	0.1621	0.2059	0.4311
DBP	chr11	100098748	rs633185	FLJ32810–	G	C	0.28	0.210992	0.525	0.144	0.292	-0.0559	0.1164	0.6311
SBP	chr11	100098748	rs633185	FLJ32810–	G	C	0.28	0.210992	0.525	0.144	0.292	-0.1942	0.1937	0.3161
DBP	chr11	10307114	rs7129220	*ADM*	G	A	0.89	0.927608		0.941	0.883	-0.3187	0.1728	0.0651
SBP	chr11	10307114	rs7129220	*ADM*	G	A	0.89	0.927608		0.941	0.883	-0.9915	0.2879	0.000573
DBP	chr6	31724345	rs805303	BAT2–BAT5	G	A	0.61	0.401722				-0.0285	0.0945	0.7634
SBP	chr6	31724345	rs805303	BAT2–BAT5	G	A	0.61	0.401722				0.095	0.1588	0.5495
DBP	chr10	95885930	rs932764	*PLCE1*	G	A	0.44	0.193873	0.542	0.195	0.425	-0.1295	0.1157	0.2627
SBP	chr10	95885930	rs932764	*PLCE1*	G	A	0.44	0.193873	0.542	0.195	0.425	-0.0855	0.1944	0.6599

Replication analysis of the 29 genome-wide significant SNPs identified by the International Consortium for Blood Pressure (ICBP) study in the in Continental Origins and Genetic Epidemiology Network (COGENT). Significant associations ($P < 0.05$) are shown in red.

Table S10. Fine-mapping of four loci identified by ICBP

								European ancestry (EA)			African ancestry (AA)			Conditional analysis	Conditional SNP		
Gene/Chr	Trait	SNP	r^2 EUR	r^2 AFR	Alleles (effect/other)	Effect allele frequency (EA, AA)	Position (Build 36)	N	Beta	P-value	N	Beta (SE)	P-value	Explained variance (%)	P-value			HapMap CEU and YRI block sizes (bp) defined by r2>0.7
EBF1/chr5	DBP	rs11953630	0.928	0.499	T/C	0.342,0.127	157777980	203056	-0.281	3.80E-13	28308.9	-0.3209(0.1188)	0.0069	0.0189%	0.431005	rs4551053	CEU	75,779
	DBP	rs4551053			A/G	0.325,0.068	157771120	203056		2.37E-05	28309	-0.4973(0.14)	0.000384	0.0259%			YRI	24,249
	SBP	rs11953630			T/C	0.342,0.127	157777980	203056	-0.412	3.00E-11	28308.9	-0.4194(0.1992)	0.03523	0.0114%	0.804633	rs4551053		
	SBP	rs4551053			A/G	0.325,0.068	157771120	203056		2.72E-06	28309	-0.754(0.2321)	0.001161	0.0211%				
	HTN	rs11953630			T/C	0.342,0.127	157777980	203056	-0.052	1.70E-07	28308.9	-0.0867(0.026)	0.000847	0.0111%	0.115087	rs4551053		
	HTN	rs4551053			A/G	0.325,0.068	157771120	203056			28309	-0.1148(0.0317)	0.000296	0.0111%				
ATP2B1/chr12	DBP	rs17249754	0.915	0.703	A/G	0.1,0.1298	88584717	203056	0.522	1.20E-14	28925	-0.039(0.1378)	0.7773	0.0003%	0.617033	rs2681492	CEU	150,233
	DBP	rs2681492			T/C	0.892,0.87	88537220	203056		6.12E-08	29247.9	0.0853(0.1403)	0.5433	0.0014%			YRI	58,987
	SBP	rs17249754			A/G	0.1,0.1298	88584717	203056	0.928	1.80E-18	28925	-0.5724(0.2306)	0.01306	0.0216%	0.574338	rs2681492		
	SBP	rs2681492			T/C	0.892,0.87	88537220	203056		2.06E-11	29247.9	0.745(0.2349)	0.001517	0.0367%				
	HTN	rs17249754			A/G	0.1,0.1298	88584717	203056	0.126	1.10E-14	28925	-0.1159(0.0522)	0.02642	0.0202%	0.574623	rs2681492		
	HTN	rs2681492			T/C	0.892,0.87	88537220	203056			29247.9	0.1034(0.031)	0.000855	0.0161%				
NT5C2/chr10	DBP	rs11191548	1	0.496	T/C	0.917,0.949	104836168	203056	0.464	9.40E-13	28675	0.2967(0.2065)	0.1507	0.0070%	0.774123	rs11191555	CEU	422,828
	DBP	rs11191555			A/C	0.917,0.956	104847513	203056		3.74E-06	27823	0.4455(0.2292)	0.05192	0.0138%			YRI	400,148
	SBP	rs11191548			T/C	0.917,0.949	104836168	203056	1.095	6.90E-26	28675	0.9017(0.3457)	0.009086	0.0230%	0.418126	rs11191555		
	SBP	rs11191555			A/C	0.917,0.956	104847513	203056		9.49E-10	27823	1.0032(0.3841)	0.00901	0.0247%				
	HTN	rs11191548			T/C	0.917,0.949	104836168	203056	0.097	1.40E-05	28675	0.1199(0.0777)	0.1226	0.0093%	0.568881	rs11191555		
	HTN	rs11191555			A/C	0.917,0.956	104847513	203056			27823	0.1045(0.0525)	0.04634	0.0061%				
ULK4/chr3	DBP	rs3774372	1	0.098	T/C	0.783,0.797	41852418	203056	-0.367	9.00E-14	29317	-0.2336(0.1126)	0.03805	0.0146%	0.613398	rs1716642	CEU	314,745
	DBP	rs1716642			A/C	0.783,0.648	41940869	203056		2.60E-07	24185	0.5359(0.1084)	7.57E-07	0.1083%			YRI	221,195
	SBP	rs3774372			T/C	0.783,0.797	41852418	203056	-0.067	0.39	29317	-0.1484(0.1883)	0.4305	0.0021%	0.573685	rs1716642		
	SBP	rs1716642			A/C	0.783,0.648	41940869	203056		0.497	24185	0.1424(0.1805)	0.4301	0.0027%				
	HTN	rs3774372			T/C	0.783,0.797	41852418	203056	-0.017	0.18	29317	0.0487(0.0476)	0.3069	0.0051%	0.0741162	rs1716642		
	HTN	rs1716642			A/C	0.783,0.648	41940869	203056			24185	0.0781(0.0238)	0.001047	0.0186%				

Table S11. Cardiotoxicity and associated molecules and p-values from toxicology function analysis of IPA

Cardiotoxicity	Molecules	Pvalue
Cardiac stenosis	*HOXA3*	4.54×10^{-3}
Congenital heart anomaly	*HOXA3*	1.31×10^{-2}
Cardiac congestive cardiac failure	*CACNA1D*	4.16×10^{-2}
Heart failure	*CACNA1D*	4.16×10^{-2}

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