

## SUPPLEMENTARY ONLINE MATERIAL

### Table of Contents

<b>Supplementary Notes</b>		
Supplementary Note 1.	Replication cohort descriptions	2-3
Supplementary Note 2.	Investigator acknowledgements	3-4
Supplementary Note 3.	Study Acknowledgements	4-16
Supplementary Note 4	NHLBI TOPMed: NHLBI Trans-Omics for Precision Medicine (TOPMed) consortium banner authorship	16-23
Supplementary Note 5	References	23
<b>Supplementary Figures</b>		
Supplementary Figure 1	Scatter plots of PC1 vs. PC2 by population group	24-26
Supplementary Figure 2	QQ Plots primary BMI GWAS	27
Supplementary Figure 3	Regional association plots for primary BMI GWAS	28-36
Supplementary Figure 4	Manhattan plot of African HARE group BMI GWAS	37
Supplementary Figure 5	QQ Plot of African HARE group BMI GWAS	38
Supplementary Figure 6	Manhattan plot of European HARE group BMI GWAS	39
Supplementary Figure 7	QQ Plots of European HARE group BMI GWAS	40
Supplementary Figure 8	Regional association plots of secondary signals in discovery	41
Supplementary Figure 9	LD matrix heatmap for conditionally independent SNPs in known BMI-risk loci	42-43
Supplementary Figure 10	Fine-mapping regional plots	44-47
Supplementary Figure 11	PheWAS meta-analysis Manhattan plot	48
<b>Supplementary Data Tables</b>		
Supplementary Data 1	Participant counts by study and population group	49
Supplementary Data 2	BMI and percent female by study	50
Supplementary Data 3	BMI and percent female by population group	51
Supplementary Data 4	Study-specific descriptive statistics of age and BMI	52-55
Supplementary Data 5	Genome-wide significant (GWS) variants by locus with frequency by population group	56
Supplementary Data 6	GWS variants by locus from African and European population groups	57
Supplementary Data 7	Replication of rs111490516	58
Supplementary Data 8	Variant annotation from Variant Effect Predictor (VEP) for <i>MTMR3</i> locus	59-61
Supplementary Data 9	Association results after conditioning on top index variant	62
Supplementary Data 10	Association results after conditioning on known index variants	63
Supplementary Data 11	PAINTOR fine-mapping results assuming a single causal variant	64
Supplementary Data 12	PheWAS meta-analysis	65

## SUPPLEMENTARY NOTE

### Supplementary Note 1. REPLICATION COHORTS DESCRIPTIONS

**MEC** is a population-based prospective cohort study including approximately 215,000 men and women from Hawaii and California [Kolonel, L. N. et al. A multiethnic cohort in Hawaii and Los Angeles: baseline characteristics. *Am. J. Epidemiol.* 151, 346–357 (2000)]. All participants were 45-75 years of age at baseline, and primarily of five ancestries: Japanese Americans, African Americans, European Americans, Hispanic/Latinos, and Native Hawaiians. MEC was funded by the National Cancer Institute in 1993 to examine lifestyle risk factors and genetic susceptibility to cancer. All eligible cohort members completed baseline and follow-up questionnaires. Participants from the MEC sample in the current analyses included 3,825 women and 3,281 men who self-reported African American background, had measured height and weight available, and had genetic data available. Of these, 4,593 were genotyped on the MEGA chip and 2,513 were genotyped on the Illumina Human1M-Duo chip.

**MVP** participants were recruited from over 60 Veterans Health Administration medical centers nationwide since 2011. The design of MVP has been previously described <sup>1</sup>. A unique feature of MVP is the linkage of a large biobank to an extensive, national, database from 2003 onward that integrates multiple elements such as diagnosis codes, procedure codes, laboratory values, and imaging reports, which permits detailed phenotyping of this large cohort. MVP has received ethical and study protocol approval by the Veterans Affairs Central Institutional Review Board in accordance with the principles outlined in the Declaration of Helsinki. DNA extracted from participants' blood was genotyped using a customized Affymetrix Axiom® biobank array, the MVP 1.0 Genotyping Array. The array was enriched for both common and rare genetic variants of clinical significance in different ethnic backgrounds. Quality-control procedures used to assign ancestry, remove low-quality samples and variants, and perform genotype imputation were previously described <sup>2</sup>. We excluded: duplicate samples, samples with more heterozygosity than expected an excess (>2.5%) of missing genotype calls, or discordance between genetically inferred sex and phenotypic gender. In addition, one individual from each pair of related individuals (more than second degree relatedness as measured by the KING software) were removed. The MVP participants were assigned to mutually exclusive racial/ethnic groups using HARE (Harmonized Ancestry and Race/Ethnicity), a machine learning algorithm that integrates genetically inferred ancestry with self-identified race/ethnicity <sup>3</sup>. The present study included non-Hispanic African Americans with both genotypic and phenotypic data for genetic association analyses. The phenotyping and analytical details of body mass index in the MVP were previously described <sup>4</sup>. SNP rs111490516 was imputed with quality score of 0.7083.

**The UK Biobank** is a prospective cohort study with genetic and phenotypic data on more than 500,000 individuals, aged between 39–69 years. Study design, protocols, sample handling and quality control have been described in detail elsewhere (PMID: 25826379 and PMID: 30305743). African ancestry was determined using k-means clustering (PMID: 32692746). Briefly, clustering was performed by projecting the 1000 genomes reference panel dataset based on the PCA loadings from the UK Biobank. We performed k-means clustering with a pre-specified number of 4 clusters. Individuals from the UK Biobank that clustered with the AFR 1000G cluster were assigned African ancestry.

**REGARDS:** The Reasons for Geographic and Racial Differences in Stroke (REGARDS) project, sponsored by the National Institutes of Health (NIH), is a national study focusing on learning more about the factors that increase a person's risk of having a stroke. REGARDS is an observational study of risk factors for stroke in unrelated adults 45 years or older. 30,239 African American and European American participants were recruited between January 2003 and October 2007. The study design and objectives have been previously described <sup>5</sup>. MEGAEX genotype data is available for 8,837 African American and 1,716 European American REGARDS participants. The study is ongoing and will follow participants

for many years.

**BioMe** is an ongoing electronic medical record-linked biobank with more than 60,000 patients enrolled through the Mount Sinai Health System in New York. BioMe is a multiethnic biobank comprising individuals of African, Hispanic, European, Asian, and other ancestries <sup>6</sup>. Genotyping data is available on 32,595 individuals and was done using the Global Screening Array (GSA-24v1-0\_A1). The data was cleaned for duplicate samples, discordant sex, heterozygosity rate that exceeded 6 SD from the population mean, call rate < 95% at the site and individual level, and deviation from Hardy Weinberg equilibrium. Replication was conducted within self-reported African ancestry.

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**COPDGene® Investigators – Core Units:** Administrative Center: James D. Crapo, MD (PI); Edwin K. Silverman, MD, PhD (PI); Barry J. Make, MD; Elizabeth A. Regan, MD, PhD. **Genetic Analysis Center:** Terri Beaty, PhD; Ferdouse Begum, PhD; Peter J. Castaldi, MD, MSc; Michael Cho, MD; Dawn L. DeMeo, MD, MPH; Adel R. Boueiz, MD; Marilyn G. Foreman, MD, MS; Eitan Halper-Stromberg; Lystra P. Hayden, MD, MMSc; Craig P. Hersh, MD, MPH; Jacqueline Hetmanski, MS, MPH; Brian D. Hobbs, MD; John E. Hokanson, MPH, PhD; Nan Laird, PhD; Christoph Lange, PhD; Sharon M. Lutz, PhD; Merry-Lynn McDonald, PhD; Margaret M. Parker, PhD; Dmitry Prokopenko, Ph.D; Dandi Qiao, PhD; Elizabeth A. Regan, MD, PhD; Phuwanat Sakornsakolpat, MD; Edwin K. Silverman, MD, PhD; Emily S. Wan, MD; Sungho Won, PhD. **Imaging Center:** Juan Pablo Centeno; Jean-Paul Charbonnier, PhD; Harvey O. Coxson, PhD; Craig J. Galban, PhD; MeiLan K. Han, MD, MS; Eric A. Hoffman, Stephen Humphries, PhD; Francine L. Jacobson, MD, MPH; Philip F. Judy, PhD; Ella A. Kazerooni, MD; Alex Kluber; David A. Lynch, MB; Pietro Nardelli, PhD; John D. Newell, Jr., MD; Aleena Notary; Andrea Oh, MD; Elizabeth A. Regan, MD, PhD; James C. Ross, PhD; Raul San Jose Estepar, PhD; Joyce Schroeder, MD; Jered Sieren; Berend C. Stoel, PhD; Juerg Tschirren, PhD; Edwin Van Beek, MD, PhD; Bram van Ginneken, PhD; Eva van Rikxoort, PhD; Gonzalo Vegas Sanchez-Ferrero, PhD; Lucas Veitel; George R. Washko, MD; Carla G. Wilson, MS; **PFT QA Center, Salt Lake City, UT:** Robert Jensen, PhD. **Data Coordinating Center and Biostatistics, National Jewish Health, Denver, CO:** Douglas Everett, PhD; Jim Crooks, PhD; Katherine Pratte, PhD; Matt Strand, PhD; Carla G. Wilson, MS. **Epidemiology Core, University of Colorado Anschutz Medical Campus, Aurora, CO:** John E. Hokanson, MPH, PhD; Gregory Kinney, MPH, PhD; Sharon M. Lutz, PhD; Kendra A. Young, PhD. **Mortality Adjudication Core:** Surya P. Bhatt, MD; Jessica Bon, MD; Alejandro A. Diaz, MD, MPH;

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**NHLBI TOPMed: Multi-Ethnic Study of Atherosclerosis (MESA)**

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study coordination, were provided by the TOPMed Data Coordinating Center (3R01HL-120393-02S1), and TOPMed MESA Multi-Omics (HHSN2682015000031/HSN26800004). The MESA projects are conducted and supported by the National Heart, Lung, and Blood Institute (NHLBI) in collaboration with MESA investigators. Support for the Multi-Ethnic Study of Atherosclerosis (MESA) projects are conducted and supported by the National Heart, Lung, and Blood Institute (NHLBI) in collaboration with MESA investigators. Support for MESA is provided by contracts 75N92020D00001, HHSN268201500003I, N01-HC-95159, 75N92020D00005, N01-HC-95160, 75N92020D00002, N01-HC-95161, 75N92020D00003, N01-HC-95162, 75N92020D00006, N01-HC-95163, 75N92020D00004, N01-HC-95164, 75N92020D00007, N01-HC-95165, N01-HC-95166, N01-HC-95167, N01-HC-95168, N01-HC-95169, UL1-TR-000040, UL1-TR-001079, UL1-TR-001420, UL1TR001881, DK063491, and R01HL105756. The authors thank the other investigators, the staff, and the participants of the MESA study for their valuable contributions. A full list of participating MESA investigators and institutes can be found at <http://www.mesa-nhlbi.org>.

#### **NHLBI TOPMed: Massachusetts General Hospital Atrial Fibrillation Study (MGH\_AF)**

#### **NHLBI TOPMed: Outcome Modifying Genes in Sickle Cell Disease (OMG\_SCD)**

The OMG-SCD study was administrated by Marilyn J. Telen, M.D. and Allison E. Ashley-Koch, Ph.D. from Duke University Medical Center and collection of the data set was supported by grants HL068959 and HL079915 from the National Heart, Lung, and Blood Institute (NHLBI) of the National Institute of Health (NIH).

#### **NHLBI TOPMed: Partners Healthcare Biorepository (Partners)**

#### **NHLBI TOPMed: Whole Genome Sequencing to Identify Causal Genetic Variants Influencing CVD Risk - San Antonio Family Studies (SAFS)**

Collection of the San Antonio Family Study data was supported in part by National Institutes of Health (NIH) grants R01 HL045522, MH078143, MH078111 and MH083824; and whole genome sequencing of SAFS subjects was supported by U01 DK085524 and R01 HL113323. We are very grateful to the participants of the San Antonio Family Study for their continued involvement in our research programs.

#### **NHLBI TOPMed: Study of African Americans, Asthma, Genes and Environment (SAGE)**

The Study of African Americans, Asthma, Genes and Environments (SAGE) was supported by the National Heart, Lung, and Blood Institute of the National Institute of Health (NIH) grants R01HL117004 and X01HL134589; study enrollment supported by the Sandler Family Foundation, the American Asthma Foundation, the RWJF Amos Medical Faculty Development Program, Harry Wm. and Diana V. Hind Distinguished Professor in Pharmaceutical Sciences II. The SAGE study collaborators include Harold J. Farber, Texas Children's Hospital; Emerita Brigino-Buenaventura, Kaiser Permanente; Michael A. LeNoir, Bay Area Pediatrics; Kelley Meade, UCSF Benioff Children's Hospital, Oakland; Luisa N. Borrell, City University of New York; Adam Davis, UCSF Benioff Children's Hospital, Oakland and Fred Lurmann, Sonoma Technologies, Inc. The authors acknowledge the families and patients for their participation and thank the numerous health care providers and community clinics for their support and participation in SAGE. In particular, the authors thank study coordinator Sandra Salazar; the recruiters who obtained the data: Lisa Caine, Elizabeth Castellanos, Brenda Lopez, MD, Shahdad Saedi; and the lab researcher Celeste Eng who processed the biospecimens.

#### **NHLBI TOPMed: Samoan Adiposity Study (Samoan)**

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We would also like to acknowledge the Samoan Obesity, Lifestyle and Genetic Adaptations Study (OLaGA) Group: Ranjan Deka, Dept. of Environmental Health, University of Cincinnati; Nicola L. Hawley, Dept. of Chronic Disease Epidemiology, Yale University; Stephen T McGarvey, Dept. of Epidemiology and International Health Institute, and Dept. of Anthropology, Brown University; Ryan L Minster, Dept. of Human Genetics, University of Pittsburgh; Take Naseri, Ministry of Health, Government of Samoa; Muagututi'a Sefuiva Reupena, Lutia I Puava Ae Mapu I Fagalele; Daniel E. Weeks, Depts. of Human Genetics and Biostatistics, University of Pittsburgh.

**NHLBI TOPMed: Taiwan Study of Hypertension using Rare Variants (THRV)**

The Rare Variants for Hypertension in Taiwan Chinese (THRV) is supported by the National Heart, Lung, and Blood Institute (NHLBI) grant (R01HL11249) and its participation in TOPMed is supported by an NHLBI supplement (R01HL11249-04S1). THRV is a collaborative study between Washington University in St. Louis, LA BioMed at Harbor UCLA, University of Texas in Houston, Taichung Veterans General Hospital, Taipei Veterans General Hospital, Tri-Service General Hospital, National Health Research Institutes, National Taiwan University, and Baylor University. THRV is based (substantially) on the parent SAPPHERE study, along with additional population-based and hospital-based cohorts. SAPPHERE was supported by NHLBI grants (U01HL54527, U01HL54498) and Taiwan funds, and the other cohorts were supported by Taiwan funds.

**NHLBI TOPMed: Vanderbilt Atrial Fibrillation Ablation Registry (VAFAR)**

**NHLBI TOPMed: Vanderbilt Genetic Basis of Atrial Fibrillation (VU\_AF)**

**NHLBI TOPMed: Treatment of Pulmonary Hypertension and Sickle Cell Disease with Sildenafil Therapy (walk\_PHaSST)**

We thank Dr. Mark Gladwin and the investigators of the Walk-PHaSst study and the patients who participated in the study. We also thank the walk-PHaSST clinical site team: Albert Einstein College of Medicine: Jane Little and Verlene Davis; Columbia University: Robyn Barst, Erika Rosenzweig, Margaret Lee and Daniela Brady; UCSF Benioff Children's Hospital Oakland: Claudia Morris, Ward Hagar, Lisa Lavrisha, Howard Rosenfeld, and Elliott Vichinsky; Children's Hospital of Pittsburgh of UPMC: Regina McCollum; Hammersmith Hospital, London: Sally Davies, Gaia Mahalingam, Sharon Meehan, Ofelia Lebanto, and Ines Cabrita; Howard University: Victor Gordeuk, Oswaldo Castro, Onyinye Onyekwere, Vandana Sachdev, Alvin Thomas, Gladys Onojobi, Sharmin Diaz, Margaret Fadojutimi-Akinsiku, and Randa Aladdin; Johns Hopkins University: Reda Girgis, Sophie Lanzkron and Durrant Barasa; NHLBI: Mark Gladwin, Greg Kato, James Taylor, Wynona Coles, Catherine Seamon, Mary Hall, Amy Chi, Cynthia Breneman, Wen Li, and Erin Smith; University of Colorado: Kathryn Hassell, David Badesch, Deb McCollister and Julie McAfee; University of Illinois at Chicago: Dean Schraufnagel, Robert Molokie, George Kondos, Patricia Cole-Saffold, and Lani Krauz; National Heart & Lung Institute, Imperial College London: Simon Gibbs. Thanks also to the data coordination center team from Rho, Inc.: Nancy Yovetich, Rob Woolson, Jamie Spencer, Christopher Woods, Karen Kesler, Vickie Coble, and Ronald W. Helms. We also thank Dr. Yingze Zhang for directing the Walk-PHaSst repository and Dr. Mehdi Nouraie for maintaining the Walk-PHaSst database and Dr. Jonathan Goldsmith as a NIH program director for this study. Special thanks to the volunteers who participated in the Walk-PHaSST study. This project was funded with federal funds from the NHLBI, NIH, Department of Health and Human Services, under contract HHSN268200617182C. This study is registered at [www.clinicaltrials.gov](http://www.clinicaltrials.gov) as NCT00492531. Detail description of the study was published in Blood, 2011 118:855-864, Machado et al "Hospitalization for pain in patients with sickle cell disease treated with sildenafil for elevated TRV and low exercise capacity".

**NHLBI TOPMed: Women's Genome Health Study (WGHS)**

The WGHS is supported by the National Heart, Lung, and Blood Institute (HL043851 and HL080467) and the National Cancer Institute (CA047988 and UM1CA182913). The most recent cardiovascular endpoints were supported by ARRA funding HL099355.

**NHLBI TOPMed: Women's Health Initiative (WHI)**

The WHI program is funded by the National Heart, Lung, and Blood Institute, National Institutes of Health, U.S. Department of Health and Human Services through contracts 75N92021D00001, 75N92021D00002, 75N92021D00003, 75N92021D00004, 75N92021D00005.

**The Multiethnic Cohort (MEC)** is a population-based prospective cohort study including approximately 215,000 men and women from Hawaii and California. All participants were 45-75 years of age at baseline, and primarily of 5 ancestries: Japanese Americans, African Americans, European Americans, Hispanic/Latinos, and Native Hawaiians. (PMIDs: 10695593; 23449381) MEC was funded by the National Cancer Institute in 1993 to examine lifestyle risk factors and genetic susceptibility to cancer. All eligible cohort members completed baseline and follow-up questionnaires. Within the PAGE II investigation, MEC proposes to study: 1) diseases for which we have DNA available for large numbers of cases and controls (breast, prostate, and colorectal cancer, diabetes, and obesity); 2) common traits that are risk factors for these diseases (e.g., body mass index / weight, waist-to-hip ratio, height), and 3) relevant disease-associated biomarkers (e.g., fasting insulin and lipids, steroid hormones). The specific aims are: 1) to determine the population-based epidemiologic profile (allele frequency, main effect, heterogeneity by disease characteristics) of putative causal variants in the five racial/ethnic groups in MEC; 2) for variants displaying effect heterogeneity across ethnic/racial groups, we will utilize differences in LD to identify a more complete spectrum of associated variants at these loci; 3) investigate gene x gene and gene x environment interactions to identify modifiers; 4) examine the associations of putative causal variants with already measured intermediate phenotypes (e.g., plasma insulin, lipids, steroid hormones); and 5) for variants that do not fall within known genes, start to investigate their relationships with gene expression and epigenetic patterns in small genomic studies. The studies listed here are individuals of African and Latino American ancestry/ethnicity who were part of the breast cancer or prostate cancer case/controls substudies. (dbGaP study accession number: phs000220).

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*MVP Program Office*

- Sumitra Muralidhar, Ph.D., Program Director

US Department of Veterans Affairs, 810 Vermont Avenue NW, Washington, DC 20420

- Jennifer Moser, Ph.D., Associate Director, Scientific Programs  
US Department of Veterans Affairs, 810 Vermont Avenue NW, Washington, DC 20420
- Jennifer E. Deen, B.S., Associate Director, Cohort & Public Relations  
US Department of Veterans Affairs, 810 Vermont Avenue NW, Washington, DC 20420

*MVP Executive Committee*

- Co-Chair: Philip S. Tsao, Ph.D.  
VA Palo Alto Health Care System, 3801 Miranda Avenue, Palo Alto, CA 94304
- Co-Chair: Sumitra Muralidhar, Ph.D.  
US Department of Veterans Affairs, 810 Vermont Avenue NW, Washington, DC 20420
- J. Michael Gaziano, M.D., M.P.H.  
VA Boston Healthcare System, 150 S. Huntington Avenue, Boston, MA 02130
- Elizabeth Hauser, Ph.D.  
Durham VA Medical Center, 508 Fulton Street, Durham, NC 27705
- Amy Kilbourne, Ph.D., M.P.H.  
VA HSR&D, 2215 Fuller Road, Ann Arbor, MI 48105
- Shih-Wen Luoh, M.D., Ph.D.  
VA Portland Health Care System, 3710 SW US Veterans Hospital Rd, Portland, OR 97239
- Michael Matheny, M.D., M.S., M.P.H.  
VA Tennessee Valley Healthcare System, 1310 24<sup>th</sup> Ave. South, Nashville, TN 37212
- Dave Oslin, M.D.  
Philadelphia VA Medical Center, 3900 Woodland Avenue, Philadelphia, PA 19104

*MVP Co-Principal Investigators*

- J. Michael Gaziano, M.D., M.P.H.  
VA Boston Healthcare System, 150 S. Huntington Avenue, Boston, MA 02130
- Philip S. Tsao, Ph.D.  
VA Palo Alto Health Care System, 3801 Miranda Avenue, Palo Alto, CA 94304

*MVP Core Operations*

- Lori Churby, B.S., Director, MVP Regulatory Affairs  
VA Palo Alto Health Care System, 3801 Miranda Avenue, Palo Alto, CA 94304
- Stacey B. Whitbourne, Ph.D., Director, MVP Cohort Management  
VA Boston Healthcare System, 150 S. Huntington Avenue, Boston, MA 02130
- Jessica V. Brewer, M.P.H., Director, MVP Recruitment & Enrollment  
VA Boston Healthcare System, 150 S. Huntington Avenue, Boston, MA 02130
- Shahpoor (Alex) Shayan, M.S., Director, MVP Recruitment and Enrollment Informatics  
VA Boston Healthcare System, 150 S. Huntington Avenue, Boston, MA 02130
- Luis E. Selva, Ph.D., Executive Director, MVP Biorepositories  
VA Boston Healthcare System, 150 S. Huntington Avenue, Boston, MA 02130
- Saiju Pyarajan Ph.D., Director, Data and Computational Sciences  
VA Boston Healthcare System, 150 S. Huntington Avenue, Boston, MA 02130
- Kelly Cho, M.P.H, Ph.D., Director, MVP Phenomics Data Core  
VA Boston Healthcare System, 150 S. Huntington Avenue, Boston, MA 02130
- Scott L. DuVall, Ph.D., Director, VA Informatics and Computing Infrastructure (VINCI)  
VA Salt Lake City Health Care System, 500 Foothill Drive, Salt Lake City, UT 84148
- Mary T. Brophy M.D., M.P.H., Director, VA Central Biorepository  
VA Boston Healthcare System, 150 S. Huntington Avenue, Boston, MA 02130

- MVP Coordinating Centers
  - o MVP Coordinating Center, Boston - J. Michael Gaziano, M.D., M.P.H.  
VA Boston Healthcare System, 150 S. Huntington Avenue, Boston, MA 02130
  - o MVP Coordinating Center, Palo Alto – Philip S. Tsao, Ph.D.  
VA Palo Alto Health Care System, 3801 Miranda Avenue, Palo Alto, CA 94304
  - o MVP Information Center, Canandaigua – Brady Stephens, M.S.  
Canandaigua VA Medical Center, 400 Fort Hill Avenue, Canandaigua, NY 14424
  - o Cooperative Studies Program Clinical Research Pharmacy Coordinating Center,  
Albuquerque – Todd Connor, Pharm.D.; Dean P. Argyres, B.S., M.S.  
New Mexico VA Health Care System, 1501 San Pedro Drive SE, Albuquerque, NM 87108

*MVP Publications and Presentations Committee*

- Co-Chair: Tim Assimes, M.D.  
VA Palo Alto Health Care System, 3801 Miranda Avenue, Palo Alto, CA 94304
- Co-Chair: Adriana Hung, M.D.  
VA Tennessee Valley Healthcare System, 1310 24<sup>th</sup> Ave. South, Nashville, TN 37212
- Co-Chair: Henry Kranzler, M.D.  
Philadelphia VA Medical Center, 3900 Woodland Avenue, Philadelphia, PA 19104

*MVP Local Site Investigators*

- Samuel Aguayo, M.D., Phoenix VA Health Care System  
650 E. Indian School Road, Phoenix, AZ 85012
- Sunil Ahuja, M.D., South Texas Veterans Health Care System  
7400 Merton Minter Boulevard, San Antonio, TX 78229
- Kathrina Alexander, M.D., Veterans Health Care System of the Ozarks  
1100 North College Avenue, Fayetteville, AR 72703
- Xiao M. Androulakis, M.D., Columbia VA Health Care System  
6439 Garners Ferry Road, Columbia, SC 29209
- Prakash Balasubramanian, M.D., William S. Middleton Memorial Veterans Hospital  
2500 Overlook Terrace, Madison, WI 53705
- Zuhair Ballas, M.D., Iowa City VA Health Care System  
601 Highway 6 West, Iowa City, IA 52246-2208
- Jean Beckham, Ph.D., Durham VA Medical Center  
508 Fulton Street, Durham, NC 27705
- Sujata Bhushan, M.D., VA North Texas Health Care System  
4500 S. Lancaster Road, Dallas, TX 75216
- Edward Boyko, M.D., VA Puget Sound Health Care System  
1660 S. Columbian Way, Seattle, WA 98108-1597
- David Cohen, M.D., Portland VA Medical Center  
3710 SW U.S. Veterans Hospital Road, Portland, OR 97239
- Louis Dellitalia, M.D., Birmingham VA Medical Center  
700 S. 19th Street, Birmingham AL 35233
- L. Christine Faulk, M.D., Robert J. Dole VA Medical Center  
5500 East Kellogg Drive, Wichita, KS 67218-1607
- Joseph Fayad, M.D., VA Southern Nevada Healthcare System  
6900 North Pecos Road, North Las Vegas, NV 89086
- Daryl Fujii, Ph.D., VA Pacific Islands Health Care System  
459 Patterson Rd, Honolulu, HI 96819

- Saib Gappy, M.D., John D. Dingell VA Medical Center  
4646 John R Street, Detroit, MI 48201
- Frank Gesek, Ph.D., White River Junction VA Medical Center  
163 Veterans Drive, White River Junction, VT 05009
- Jennifer Greco, M.D., Sioux Falls VA Health Care System  
2501 W 22nd Street, Sioux Falls, SD 57105
- Michael Godschalk, M.D., Richmond VA Medical Center  
1201 Broad Rock Blvd., Richmond, VA 23249
- Todd W. Gress, M.D., Ph.D., Hershel "Woody" Williams VA Medical Center  
1540 Spring Valley Drive, Huntington, WV 25704
- Samir Gupta, M.D., M.S.C.S., VA San Diego Healthcare System  
3350 La Jolla Village Drive, San Diego, CA 92161
- Salvador Gutierrez, M.D., Edward Hines, Jr. VA Medical Center  
5000 South 5th Avenue, Hines, IL 60141
- John Harley, M.D., Ph.D., Cincinnati VA Medical Center  
3200 Vine Street, Cincinnati, OH 45220
- Kimberly Hammer, Ph.D., Fargo VA Health Care System  
2101 N. Elm, Fargo, ND 58102
- Mark Hamner, M.D., Ralph H. Johnson VA Medical Center  
109 Bee Street, Mental Health Research, Charleston, SC 29401
- Adriana Hung, M.D., M.P.H., VA Tennessee Valley Healthcare System  
1310 24th Avenue, South Nashville, TN 37212
- Robin Hurley, M.D., W.G. (Bill) Hefner VA Medical Center  
1601 Brenner Ave, Salisbury, NC 28144
- Pran Iruvanti, D.O., Ph.D., Hampton VA Medical Center  
100 Emancipation Drive, Hampton, VA 23667
- Frank Jacono, M.D., VA Northeast Ohio Healthcare System  
10701 East Boulevard, Cleveland, OH 44106
- Darshana Jhala, M.D., Philadelphia VA Medical Center  
3900 Woodland Avenue, Philadelphia, PA 19104
- Scott Kinlay, M.B.B.S., Ph.D., VA Boston Healthcare System  
150 S. Huntington Avenue, Boston, MA 02130
- Jon Klein, M.D., Ph.D., Louisville VA Medical Center  
800 Zorn Avenue, Louisville, KY 40206
- Michael Landry, Ph.D., Southeast Louisiana Veterans Health Care System  
2400 Canal Street, New Orleans, LA 70119
- Peter Liang, M.D., M.P.H., VA New York Harbor Healthcare System  
423 East 23rd Street, New York, NY 10010
- Suthat Liangpunsakul, M.D., M.P.H., Richard Roudebush VA Medical Center  
1481 West 10th Street, Indianapolis, IN 46202
- Jack Lichy, M.D., Ph.D., Washington DC VA Medical Center  
50 Irving St, Washington, D. C. 20422
- C. Scott Mahan, M.D., Charles George VA Medical Center  
1100 Tunnel Road, Asheville, NC 28805
- Ronnie Marrache, M.D., VA Maine Healthcare System  
1 VA Center, Augusta, ME 04330

- Stephen Mastorides, M.D., James A. Haley Veterans' Hospital  
13000 Bruce B. Downs Blvd, Tampa, FL 33612
- Elisabeth Mates M.D., Ph.D., VA Sierra Nevada Health Care System  
975 Kirman Avenue, Reno, NV 89502
- Kristin Mattocks, Ph.D., M.P.H., Central Western Massachusetts Healthcare System  
421 North Main Street, Leeds, MA 01053
- Paul Meyer, M.D., Ph.D., Southern Arizona VA Health Care System  
3601 S 6th Avenue, Tucson, AZ 85723
- Jonathan Moorman, M.D., Ph.D., James H. Quillen VA Medical Center  
Corner of Lamont & Veterans Way, Mountain Home, TN 37684
- Timothy Morgan, M.D., VA Long Beach Healthcare System  
5901 East 7th Street Long Beach, CA 90822
- Maureen Murdoch, M.D., M.P.H., Minneapolis VA Health Care System  
One Veterans Drive, Minneapolis, MN 55417
- James Norton, Ph.D., VA Health Care Upstate New York  
113 Holland Avenue, Albany, NY 12208
- Olaoluwa Okusaga, M.D., Michael E. DeBakey VA Medical Center  
2002 Holcombe Blvd, Houston, TX 77030
- Kris Ann Oursler, M.D., Salem VA Medical Center  
1970 Roanoke Blvd, Salem, VA 24153
- Ana Palacio, M.D., M.P.H., Miami VA Health Care System  
1201 NW 16th Street, 11 GRC, Miami FL 33125
- Samuel Poon, M.D., Manchester VA Medical Center  
718 Smyth Road, Manchester, NH 03104
- Emily Potter, Pharm.D., VA Eastern Kansas Health Care System  
4101 S 4th Street Trafficway, Leavenworth, KS 66048
- Michael Rauchman, M.D., St. Louis VA Health Care System  
915 North Grand Blvd, St. Louis, MO 63106
- Richard Servatius, Ph.D., Syracuse VA Medical Center  
800 Irving Avenue, Syracuse, NY 13210
- Satish Sharma, M.D., Providence VA Medical Center  
830 Chalkstone Avenue, Providence, RI 02908
- River Smith, Ph.D., Eastern Oklahoma VA Health Care System  
1011 Honor Heights Drive, Muskogee, OK 74401
- Peruvemba Sriram, M.D., N. FL/S. GA Veterans Health System  
1601 SW Archer Road, Gainesville, FL 32608
- Patrick Strollo, Jr., M.D., VA Pittsburgh Health Care System  
University Drive, Pittsburgh, PA 15240
- Neeraj Tandon, M.D., Overton Brooks VA Medical Center  
510 East Stoner Ave, Shreveport, LA 71101
- Philip Tsao, Ph.D., VA Palo Alto Health Care System  
3801 Miranda Avenue, Palo Alto, CA 94304-1290
- Gerardo Villareal, M.D., New Mexico VA Health Care System  
1501 San Pedro Drive, S.E. Albuquerque, NM 87108
- Agnes Wallbom, M.D., M.S., VA Greater Los Angeles Health Care System  
11301 Wilshire Blvd, Los Angeles, CA 90073

- Jessica Walsh, M.D., VA Salt Lake City Health Care System  
500 Foothill Drive, Salt Lake City, UT 84148
- John Wells, Ph.D., Edith Nourse Rogers Memorial Veterans Hospital  
200 Springs Road, Bedford, MA 01730
- Jeffrey Whittle, M.D., M.P.H., Clement J. Zablocki VA Medical Center  
5000 West National Avenue, Milwaukee, WI 53295
- Mary Whooley, M.D., San Francisco VA Health Care System  
4150 Clement Street, San Francisco, CA 94121
- Allison E. Williams, N.D., Ph.D., R.N, Bay Pines VA Healthcare System  
10,000 Bay Pines Blvd Bay Pines, FL 33744
- Peter Wilson, M.D., Atlanta VA Medical Center  
1670 Clairmont Road, Decatur, GA 30033
- Junzhe Xu, M.D., VA Western New York Healthcare System  
3495 Bailey Avenue, Buffalo, NY 14215-1199
- Shing Shing Yeh, Ph.D., M.D., Northport VA Medical Center  
79 Middleville Road, Northport, NY 11768

**Supplementary Note 4. NHLBI TOPMED: NHLBI TRANS-OMICS FOR  
PRECISION MEDICINE (TOPMED) CONSORTIUM BANNER AUTHORSHIP**

***Banner Authors (in alphabetical order by last name)***

Abe, Namiko, New York Genome Center, New York, New York, 10013, US; Abecasis, Gonçalo, University of Michigan, Ann Arbor, Michigan, 48109, US; Aguet, Francois, Broad Institute, Cambridge, Massachusetts, 02142, US; Albert, Christine, Cedars Sinai, Boston, Massachusetts, 02114, US; Almasy, Laura, Children's Hospital of Philadelphia, University of Pennsylvania, Philadelphia, Pennsylvania, 19104, US; Alonso, Alvaro, Emory University, Atlanta, Georgia, 30322, US; Ament, Seth, University of Maryland, Baltimore, Maryland, 21201, US; Anderson, Peter, University of Washington, Seattle, Washington, 98195, US; Anugu, Pramod, University of Mississippi, Jackson, Mississippi, 38677, US; Applebaum-Bowden, Deborah, National Institutes of Health, Bethesda, Maryland, 20892, US; Ardlie, Kristin, Broad Institute, Cambridge, Massachusetts, 02142, US; Arking, Dan, Johns Hopkins University, Baltimore, Maryland, 21218, US; Arnett, Donna K, University of Kentucky, Lexington, Kentucky, 40506, US; Ashley-Koch, Allison, Duke University, Durham, North Carolina, 27708, US; Aslibekyan, Stella, University of Alabama, Birmingham, Alabama, 35487, US; Assimes, Tim, Stanford University, Stanford, California, 94305, US; Auer, Paul, Medical College of Wisconsin, Milwaukee, Wisconsin, 53211, US; Avramopoulos, Dimitrios, Johns Hopkins University, Baltimore, Maryland, 21218, US; Ayas, Najib, Providence Health Care, Medicine, Vancouver, CA; Balasubramanian, Adithya, Baylor College of Medicine Human Genome Sequencing Center, Houston, Texas, 77030, US; Barnard, John, Cleveland Clinic, Cleveland, Ohio, 44195, US; Barnes, Kathleen, Tempus, University of Colorado Anschutz Medical Campus, Aurora, Colorado, 80045, US; Barr, R. Graham, Columbia University, New York, New York, 10032, US; Barron-Casella, Emily, Johns Hopkins University, Baltimore, Maryland, 21218, US; Barwick, Lucas, The Emmes Corporation, LTRC, Rockville, Maryland, 20850, US; Beaty, Terri, Johns Hopkins University, Baltimore, Maryland, 21218, US; Beck, Gerald, Cleveland Clinic, Quantitative Health Sciences, Cleveland, Ohio, 44195, US; Becker, Diane, Johns Hopkins University, Medicine, Baltimore, Maryland, 21218, US; Becker, Lewis, Johns Hopkins University, Baltimore, Maryland, 21218, US; Beer, Rebecca, National Heart, Lung, and Blood Institute, National Institutes of Health, Bethesda, Maryland, 20892, US; Beitelshes, Amber, University of Maryland, Baltimore, Maryland, 21201, US; Benjamin, Emelia, Boston University, Massachusetts General Hospital, Boston University School of Medicine, Boston, Massachusetts, 02114, US; Benos, Takis, University of Pittsburgh, Pittsburgh, Pennsylvania, 15260, US; Bezerra, Marcos, Fundação de Hematologia e Hemoterapia de Pernambuco -



Hemope, Recife, 52011-000, BR; Bielak, Larry, University of Michigan, Ann Arbor, Michigan, 48109, US; Bis, Joshua, University of Washington, Cardiovascular Health Research Unit, Department of Medicine, Seattle, Washington, 98195, US; Blackwell, Thomas, University of Michigan, Ann Arbor, Michigan, 48109, US; Blangero, John, University of Texas Rio Grande Valley School of Medicine, Human Genetics, Brownsville, Texas, 78520, US; Boerwinkle, Eric, University of Texas Health at Houston, Houston, Texas, 77225, US; Bowden, Donald W., Wake Forest Baptist Health, Department of Biochemistry, Winston-Salem, North Carolina, 27157, US; Bowler, Russell, National Jewish Health, National Jewish Health, Denver, Colorado, 80206, US; Brody, Jennifer, University of Washington, Seattle, Washington, 98195, US; Broeckel, Ulrich, Medical College of Wisconsin, Pediatrics, Milwaukee, Wisconsin, 53226, US; Broome, Jai, University of Washington, Seattle, Washington, 98195, US; Brown, Deborah, University of Texas Health at Houston, Pediatrics, Houston, Texas, 77030, US; Bunting, Karen, New York Genome Center, New York, New York, 10013, US; Burchard, Esteban, University of California, San Francisco, San Francisco, California, 94143, US; Bustamante, Carlos, Stanford University, Biomedical Data Science, Stanford, California, 94305, US; Butth, Erin, University of Washington, Biostatistics, Seattle, Washington, 98195, US; Cade, Brian, Brigham & Women's Hospital, Brigham and Women's Hospital, Boston, Massachusetts, 02115, US; Cardwell, Jonathan, University of Colorado at Denver, Denver, Colorado, 80204, US; Carey, Vincent, Brigham & Women's Hospital, Boston, Massachusetts, 02115, US; Carrier, Julie, University of Montreal, , US; Carson, April, University of Mississippi, Medicine, Jackson, Mississippi, 39213, US; Carty, Cara, Washington State University, Pullman, Washington, 99164, US; Casaburi, Richard, University of California, Los Angeles, Los Angeles, California, 90095, US; Casas Romero, Juan P, Brigham & Women's Hospital, , US; Casella, James, Johns Hopkins University, Baltimore, Maryland, 21218, US; Castaldi, Peter, Brigham & Women's Hospital, Medicine, Boston, Massachusetts, 02115, US; Chaffin, Mark, Broad Institute, Cambridge, Massachusetts, 02142, US; Chang, Christy, University of Maryland, Baltimore, Maryland, 21201, US; Chang, Yi-Cheng, National Taiwan University, Taipei, 10617, TW; Chasman, Daniel, Brigham & Women's Hospital, Division of Preventive Medicine, Boston, Massachusetts, 02215, US; Chavan, Sameer, University of Colorado at Denver, Denver, Colorado, 80204, US; Chen, Bo-Juen, New York Genome Center, New York, New York, 10013, US; Chen, Wei-Min, University of Virginia, Charlottesville, Virginia, 22903, US; Chen, Yii-Der Ida, Lundquist Institute, Torrance, California, 90502, US; Cho, Michael, Brigham & Women's Hospital, Boston, Massachusetts, 02115, US; Choi, Seung Hoan, Broad Institute, Cambridge, Massachusetts, 02142, US; Chuang, Lee-Ming, National Taiwan University, National Taiwan University Hospital, Taipei, 10617, TW; Chung, Mina, Cleveland Clinic, Cleveland Clinic, Cleveland, Ohio, 44195, US; Chung, Ren-Hua, National Health Research Institute Taiwan, Miaoli County, 350, TW; Clish, Clary, Broad Institute, Metabolomics Platform, Cambridge, Massachusetts, 02142, US; Comhair, Suzy, Cleveland Clinic, Immunity and Immunology, Cleveland, Ohio, 44195, US; Conomos, Matthew, University of Washington, Biostatistics, Seattle, Washington, 98195, US; Cornell, Elaine, University of Vermont, Burlington, Vermont, 05405, US; Correa, Adolfo, University of Mississippi, Population Health Science, Jackson, Mississippi, 39216, US; Crandall, Carolyn, University of California, Los Angeles, Los Angeles, California, 90095, US; Crapo, James, National Jewish Health, Denver, Colorado, 80206, US; Cupples, L. Adrienne, Boston University, Biostatistics, Boston, Massachusetts, 02115, US; Curran, Joanne, University of Texas Rio Grande Valley School of Medicine, Brownsville, Texas, 78520, US; Curtis, Jeffrey, University of Michigan, Internal Medicine, Ann Arbor, Michigan, 48109, US; Custer, Brian, Vitalant Research Institute, San Francisco, California, 94118, US; Damcott, Coleen, University of Maryland, Baltimore, Maryland, 21201, US; Darbar, Dawood, University of Illinois at Chicago, Chicago, Illinois, 60607, US; David, Sean, University of Chicago, Chicago, Illinois, 60637, US; Davis, Colleen, University of Washington, Seattle, Washington, 98195, US; Daya, Michelle, University of Colorado at Denver, Denver, Colorado, 80204, US; de Andrade, Mariza, Mayo Clinic, Health Quantitative Sciences Research , Rochester, Minnesota, 55905, US; de las Fuentes, Lisa, Washington University in St Louis, Department of Medicine, Cardiovascular Division, St. Louis, Missouri, 63110, US; de Vries, Paul, University of Texas Health at Houston, Human Genetics Center, Department of Epidemiology, Human Genetics, and Environmental Sciences, Houston, Texas, 77030,

US; DeBaun, Michael, Vanderbilt University, Nashville, Tennessee, 37235, US; Deka, Ranjan, University of Cincinnati, Cincinnati, Ohio, 45220, US; DeMeo, Dawn, Brigham & Women's Hospital, Boston, Massachusetts, 02115, US; Devine, Scott, University of Maryland, Baltimore, Maryland, 21201, US; Dinh, Huyen, Baylor College of Medicine Human Genome Sequencing Center, Houston, Texas, 77030, US; Doddapaneni, Harsha, Baylor College of Medicine Human Genome Sequencing Center, Houston, Texas, 77030, ; Duan, Qing, University of North Carolina, Chapel Hill, North Carolina, 27599, US; Dugan-Perez, Shannon, Baylor College of Medicine Human Genome Sequencing Center, Houston, Texas, 77030, US; Duggirala, Ravi, University of Texas Rio Grande Valley School of Medicine, Edinburg, Texas, 78539, US; Durda, Jon Peter, University of Vermont, Burlington, Vermont, 05405, US; Dutcher, Susan K., Washington University in St Louis, Genetics, St Louis, Missouri, 63110, US; Eaton, Charles, Brown University, Providence, Rhode Island, 02912, US; Ekunwe, Lynette, University of Mississippi, Jackson, Mississippi, 38677, US; El Boueiz, Adel, Harvard University, Channing Division of Network Medicine, Cambridge, Massachusetts, 02138, US; Ellinor, Patrick, Massachusetts General Hospital, Boston, Massachusetts, 02114, US; Emery, Leslie, University of Washington, Seattle, Washington, 98195, US; Erzurum, Serpil, Cleveland Clinic, Cleveland, Ohio, 44195, US; Farber, Charles, University of Virginia, Charlottesville, Virginia, 22903, US; Farek, Jesse, Baylor College of Medicine Human Genome Sequencing Center, Houston, Texas, 77030, US; Fingerlin, Tasha, National Jewish Health, Center for Genes, Environment and Health, Denver, Colorado, 80206, US; Flickinger, Matthew, University of Michigan, Ann Arbor, Michigan, 48109, US; Fornage, Myriam, University of Texas Health at Houston, Houston, Texas, 77225, US; Franceschini, Nora, University of North Carolina, Epidemiology, Chapel Hill, North Carolina, 27599, US; Frazar, Chris, University of Washington, Seattle, Washington, 98195, US; Fu, Mao, University of Maryland, Baltimore, Maryland, 21201, US; Fullerton, Stephanie M., University of Washington, Seattle, Washington, 98195, US; Fulton, Lucinda, Washington University in St Louis, St Louis, Missouri, 63130, US; Gabriel, Stacey, Broad Institute, Cambridge, Massachusetts, 02142, US; Gan, Weiniu, National Heart, Lung, and Blood Institute, National Institutes of Health, Bethesda, Maryland, 20892, US; Gao, Shanshan, University of Colorado at Denver, Denver, Colorado, 80204, US; Gao, Yan, University of Mississippi, Jackson, Mississippi, 38677, US; Gass, Margery, Fred Hutchinson Cancer Research Center, Seattle, Washington, 98109, US; Geiger, Heather, New York Genome Center, New York City, New York, 10013, US; Gelb, Bruce, Icahn School of Medicine at Mount Sinai, New York, New York, 10029, US; Geraci, Mark, University of Pittsburgh, Pittsburgh, Pennsylvania, US; Germer, Soren, New York Genome Center, New York, New York, 10013, US; Gerszten, Robert, Beth Israel Deaconess Medical Center, Boston, Massachusetts, 02215, US; Ghosh, Auyon, Brigham & Women's Hospital, Boston, Massachusetts, 02115, US; Gibbs, Richard, Baylor College of Medicine Human Genome Sequencing Center, Houston, Texas, 77030, US; Gignoux, Chris, Stanford University, Stanford, California, 94305, US; Gladwin, Mark, University of Pittsburgh, Pittsburgh, Pennsylvania, 15260, US; Glahn, David, Boston Children's Hospital, Harvard Medical School, Department of Psychiatry, Boston, Massachusetts, 02115, US; Gogarten, Stephanie, University of Washington, Seattle, Washington, 98195, US; Gong, Da-Wei, University of Maryland, Baltimore, Maryland, 21201, US; Goring, Harald, University of Texas Rio Grande Valley School of Medicine, San Antonio, Texas, 78229, US; Graw, Sharon, University of Colorado Anschutz Medical Campus, Aurora, Colorado, 80045, US; Gray, Kathryn J., Mass General Brigham, Obstetrics and Gynecology, Boston, Massachusetts, 02115, US; Grine, Daniel, University of Colorado at Denver, Denver, Colorado, 80204, US; Gross, Colin, University of Michigan, Ann Arbor, Michigan, 48109, US; Gu, C. Charles, Washington University in St Louis, St Louis, Missouri, 63130, US; Guan, Yue, University of Maryland, Baltimore, Maryland, 21201, US; Guo, Xiuqing, Lundquist Institute, Torrance, California, 90502, US; Gupta, Namrata, Broad Institute, Cambridge, Massachusetts, 02142, US; Haas, David M., Indiana University, OB/GYN, Indianapolis, Indiana, 46202, US; Haessler, Jeff, Fred Hutchinson Cancer Research Center, Seattle, Washington, 98109, US; Hall, Michael, University of Mississippi, Cardiology, Jackson, Mississippi, 39216, US; Han, Yi, Baylor College of Medicine Human Genome Sequencing Center, Houston, Texas, 77030, US; Hanly, Patrick, University of Calgary, Medicine, Calgary, CA; Harris, Daniel, University of Maryland, Genetics, Philadelphia, Pennsylvania, 19104, US; Hawley, Nicola L.,

Yale University, Department of Chronic Disease Epidemiology, New Haven, Connecticut, 06520, US; He, Jiang, Tulane University, New Orleans, Louisiana, 70118, US; Heavner, Ben, University of Washington, Biostatistics, Seattle, Washington, 98195, US; Heckbert, Susan, University of Washington, Epidemiology, Seattle, Washington, 98195, US; Hernandez, Ryan, University of California, San Francisco, San Francisco, California, 94143, US; Herrington, David, Wake Forest Baptist Health, Winston-Salem, North Carolina, 27157, US; Hersh, Craig, Brigham & Women's Hospital, Channing Division of Network Medicine, Boston, Massachusetts, 02115, US; Hidalgo, Bertha, University of Alabama, Birmingham, Alabama, 35487, US; Hixson, James, University of Texas Health at Houston, Houston, Texas, 77225, US; Hobbs, Brian, Brigham & Women's Hospital, Boston, Massachusetts, 02115, US; Hokanson, John, University of Colorado at Denver, Denver, Colorado, 80204, US; Hong, Elliott, University of Maryland, Baltimore, Maryland, 21201, US; Hoth, Karin, University of Iowa, Iowa City, Iowa, 52242, US; Hsiung, Chao (Agnes), National Health Research Institute Taiwan, Institute of Population Health Sciences, NHRI, Miaoli County, 350, TW; Hu, Jianhong, Baylor College of Medicine Human Genome Sequencing Center, Houston, Texas, 77030, US; Hung, Yi-Jen, Tri-Service General Hospital National Defense Medical Center, , TW; Huston, Haley, Blood Works Northwest, Seattle, Washington, 98104, US; Hwu, Chii Min, Taichung Veterans General Hospital Taiwan, Taichung City, 407, TW; Irvin, Marguerite Ryan, University of Alabama, Birmingham, Alabama, 35487, US; Jackson, Rebecca, Oklahoma State University Medical Center, Internal Medicine, Division of Endocrinology, Diabetes and Metabolism, Columbus, Ohio, 43210, US; Jain, Deepti, University of Washington, Seattle, Washington, 98195, US; Jaquish, Cashell, National Heart, Lung, and Blood Institute, National Institutes of Health, NHLBI, Bethesda, Maryland, 20892, US; Johnsen, Jill, Blood Works Northwest, Research Institute, Seattle, Washington, 98104, US; Johnson, Andrew, National Heart, Lung, and Blood Institute, National Institutes of Health, Bethesda, Maryland, 20892, US; Johnson, Craig, University of Washington, Seattle, Washington, 98195, US; Johnston, Rich, Emory University, Atlanta, Georgia, 30322, US; Jones, Kimberly, Johns Hopkins University, Baltimore, Maryland, 21218, US; Kang, Hyun Min, University of Michigan, Biostatistics, Ann Arbor, Michigan, 48109, US; Kaplan, Robert, Albert Einstein College of Medicine, New York, New York, 10461, US; Kardia, Sharon, University of Michigan, Ann Arbor, Michigan, 48109, US; Kelly, Shannon, University of California, San Francisco, San Francisco, California, 94118, US; Kenny, Eimear, Icahn School of Medicine at Mount Sinai, New York, New York, 10029, US; Kessler, Michael, University of Maryland, Baltimore, Maryland, 21201, US; Khan, Alyna, University of Washington, Seattle, Washington, 98195, US; Khan, Ziad, Baylor College of Medicine Human Genome Sequencing Center, Houston, Texas, 77030, US; Kim, Wonji, Harvard University, Cambridge, Massachusetts, 02138, US; Kimoff, John, McGill University, Montréal, QC H3A 0G4, CA; Kinney, Greg, University of Colorado at Denver, Epidemiology, Aurora, Colorado, 80045, US; Konkle, Barbara, Blood Works Northwest, Medicine, Seattle, Washington, 98104, US; Kooperberg, Charles, Fred Hutchinson Cancer Research Center, Seattle, Washington, 98109, US; Kramer, Holly, Loyola University, Public Health Sciences, Maywood, Illinois, 60153, US; Lange, Christoph, Harvard School of Public Health, Biostats, Boston, Massachusetts, 02115, US; Lange, Ethan, University of Colorado at Denver, Denver, Colorado, 80204, US; Lange, Leslie, University of Colorado at Denver, Medicine, Aurora, Colorado, 80048, US; Laurie, Cathy, University of Washington, Seattle, Washington, 98195, US; Laurie, Cecelia, University of Washington, Seattle, Washington, 98195, US; LeBoff, Meryl, Brigham & Women's Hospital, Boston, Massachusetts, 02115, US; Lee, Jiwon, Brigham & Women's Hospital, Boston, Massachusetts, 02115, US; Lee, Sandra, Baylor College of Medicine Human Genome Sequencing Center, Houston, Texas, 77030, US; Lee, Wen-Jane, Taichung Veterans General Hospital Taiwan, Taichung City, 407, TW; LeFaive, Jonathon, University of Michigan, Ann Arbor, Michigan, 48109, US; Levine, David, University of Washington, Seattle, Washington, 98195, US; Levy, Dan, National Heart, Lung, and Blood Institute, National Institutes of Health, Bethesda, Maryland, 20892, US; Lewis, Joshua, University of Maryland, Baltimore, Maryland, 21201, US; Li, Xiaohui, Lundquist Institute, Torrance, California, 90502, US; Li, Yun, University of North Carolina, Chapel Hill, North Carolina, 27599, US; Lin, Henry, Lundquist Institute, Torrance, California, 90502, US; Lin, Honghuang, Boston University, Boston, Massachusetts, 02215, US; Lin, Xihong, Harvard School of Public Health,

Boston, Massachusetts, 02115, US; Liu, Simin, Brown University, Epidemiology and Medicine, Providence, Rhode Island, 02912, US; Liu, Yongmei, Duke University, Cardiology, Durham, North Carolina, 27708, US; Liu, Yu, Stanford University, Cardiovascular Institute, Stanford, California, 94305, US; Loos, Ruth J.F., Icahn School of Medicine at Mount Sinai, The Charles Bronfman Institute for Personalized Medicine, New York, New York, 10029, US; Lubitz, Steven, Massachusetts General Hospital, Boston, Massachusetts, 02114, US; Lunetta, Kathryn, Boston University, Boston, Massachusetts, 02215, US; Luo, James, National Heart, Lung, and Blood Institute, National Institutes of Health, Bethesda, Maryland, 20892, US; Magalang, Ulysses, Ohio State University, Division of Pulmonary, Critical Care and Sleep Medicine, Columbus, Ohio, 43210, US; Mahaney, Michael, University of Texas Rio Grande Valley School of Medicine, Brownsville, Texas, 78520, US; Make, Barry, Johns Hopkins University, Baltimore, Maryland, 21218, US; Manichaikul, Ani, University of Virginia, Charlottesville, Virginia, 22903, US; Manning, Alisa, Broad Institute, Harvard University, Massachusetts General Hospital, , ; Manson, JoAnn, Brigham & Women's Hospital, Boston, Massachusetts, 02115, US; Martin, Lisa, George Washington University, cardiology, Washington, District of Columbia, 20037, US; Marton, Melissa, New York Genome Center, New York City, New York, 10013, US; Mathai, Susan, University of Colorado at Denver, Denver, Colorado, 80204, US; Mathias, Rasika, Johns Hopkins University, Baltimore, Maryland, 21218, US; May, Susanne, University of Washington, Biostatistics, Seattle, Washington, 98195, US; McArdle, Patrick, University of Maryland, Baltimore, Maryland, 21201, US; McDonald, Merry-Lynn, University of Alabama, University of Alabama at Birmingham, Birmingham, Alabama, 35487, US; McFarland, Sean, Harvard University, Cambridge, Massachusetts, 02138, US; McGarvey, Stephen, Brown University, Epidemiology, Providence, Rhode Island, 02912, US; McGoldrick, Daniel , University of Washington, Genome Sciences, Seattle, Washington, 98195, US; McHugh, Caitlin, University of Washington, Biostatistics, Seattle, Washington, 98195, US; McNeil, Becky, RTI International, , US; Mei, Hao, University of Mississippi, Jackson, Mississippi, 38677, US; Meigs, James, Massachusetts General Hospital, Medicine, Boston , Massachusetts, 02114, US; Menon, Vipin, Baylor College of Medicine Human Genome Sequencing Center, Houston, Texas, 77030, US; Mestroni, Luisa, University of Colorado Anschutz Medical Campus, Aurora, Colorado, 80045, US; Metcalf, Ginger, Baylor College of Medicine Human Genome Sequencing Center, Houston, Texas, 77030, US; Meyers, Deborah A, University of Arizona, Tucson, Arizona, 85721, US; Mignot, Emmanuel, Stanford University, Center For Sleep Sciences and Medicine, Palo Alto, California, 94304, US; Mikulla, Julie, National Heart, Lung, and Blood Institute, National Institutes of Health, Bethesda, Maryland, 20892, US; Min, Nancy, University of Mississippi, Jackson, Mississippi, 38677, US; Minear, Mollie, National Institute of Child Health and Human Development, National Institutes of Health, Bethesda, Maryland, 20892, US; Minster, Ryan L, University of Pittsburgh, Pittsburgh, Pennsylvania, 15260, US; Mitchell, Braxton D., University of Maryland, Baltimore, Maryland, 21201, US; Moll, Matt, Brigham & Women's Hospital, Medicine, Boston, Massachusetts, 02115, US; Momin, Zeineen, Baylor College of Medicine Human Genome Sequencing Center, Houston, Texas, 77030, US; Montasser, May E., University of Maryland, Baltimore, Maryland, 21201, US; Montgomery, Courtney, Oklahoma Medical Research Foundation, Genes and Human Disease, Oklahoma City, Oklahoma, 73104, US; Muzny, Donna, Baylor College of Medicine Human Genome Sequencing Center, Houston, Texas, 77030, US; Mychaleckyj, Josyf C, University of Virginia, Charlottesville, Virginia, 22903, US; Nadkarni, Girish, Icahn School of Medicine at Mount Sinai, New York, New York, 10029, US; Naik, Rakhi, Johns Hopkins University, Baltimore, Maryland, 21218, US; Naseri, Take, Ministry of Health, Government of Samoa, Apia, WS; Natarajan, Pradeep, Broad Institute, Cambridge, Massachusetts, 02142, US; Nekhai, Sergei, Howard University, Washington, District of Columbia, 20059, US; Nelson, Sarah C., University of Washington, Biostatistics, Seattle, Washington, 98195, US; Neltner, Bonnie, University of Colorado at Denver, Denver, Colorado, 80204, US; Nessner, Caitlin, Baylor College of Medicine Human Genome Sequencing Center, Houston, Texas, 77030, US; Nickerson, Deborah, University of Washington, Department of Genome Sciences, Seattle, Washington, 98195, US; Nkechinyere, Osuji, Baylor College of Medicine Human Genome Sequencing Center, Houston, Texas, 77030, US; North, Kari, University of North Carolina, Chapel Hill, North Carolina,

27599, US; O'Connell, Jeff, University of Maryland, Baltimore, Maryland, 21201, US; O'Connor, Tim, University of Maryland, Baltimore, Maryland, 21201, US; Ochs-Balcom, Heather, University at Buffalo, Buffalo, New York, 14260, US; Okwuonu, Geoffrey, Baylor College of Medicine Human Genome Sequencing Center, Houston, Texas, 77030, US; Pack, Allan, University of Pennsylvania, Division of Sleep Medicine/Department of Medicine, Philadelphia, Pennsylvania, 19104-3403, US; Paik, David T., Stanford University, Stanford Cardiovascular Institute, Stanford, California, 94305, US; Palmer, Nicholette, Wake Forest Baptist Health, Biochemistry, Winston-Salem, North Carolina, 27157, US; Pankow, James, University of Minnesota, Minneapolis, Minnesota, 55455, US; Papanicolaou, George, National Heart, Lung, and Blood Institute, National Institutes of Health, Bethesda, Maryland, 20892, US; Parker, Cora, RTI International, Biostatistics and Epidemiology Division, Research Triangle Park, North Carolina, 27709-2194, US; Peloso, Gina, Boston University, Department of Biostatistics, Boston, Massachusetts, 02118, US; Peralta, Juan Manuel, University of Texas Rio Grande Valley School of Medicine, Edinburg, Texas, 78539, US; Perez, Marco, Stanford University, Stanford, California, 94305, US; Perry, James, University of Maryland, Baltimore, Maryland, 21201, US; Peters, Ulrike, Fred Hutchinson Cancer Research Center, Fred Hutch and UW, Seattle, Washington, 98109, US; Peyser, Patricia, University of Michigan, Ann Arbor, Michigan, 48109, US; Phillips, Lawrence S, Emory University, Atlanta, Georgia, 30322, US; Pleiness, Jacob, University of Michigan, Ann Arbor, Michigan, 48109, US; Pollin, Toni, University of Maryland, Baltimore, Maryland, 21201, US; Post, Wendy, Johns Hopkins University, Cardiology/Medicine, Baltimore, Maryland, 21218, US; Powers Becker, Julia, University of Colorado at Denver, Medicine, Denver, Colorado, 80204, US; Preethi Boorgula, Meher, University of Colorado at Denver, Denver, Colorado, 80204, US; Preuss, Michael, Icahn School of Medicine at Mount Sinai, New York, New York, 10029, US; Psaty, Bruce, University of Washington, Seattle, Washington, 98195, US; Qasba, Pankaj, National Heart, Lung, and Blood Institute, National Institutes of Health, Bethesda, Maryland, 20892, US; Qiao, Dandi, Brigham & Women's Hospital, Boston, Massachusetts, 02115, US; Qin, Zhaohui, Emory University, Atlanta, Georgia, 30322, US; Rafaels, Nicholas, University of Colorado at Denver, CCPM, Denver, Colorado, 80045, US; Raffield, Laura, University of North Carolina, Genetics, Chapel Hill, North Carolina, 27599, US; Rajendran, Mahitha, Baylor College of Medicine Human Genome Sequencing Center, Houston, Texas, 77030, US; Ramachandran, Vasana S., Boston University, Boston, Massachusetts, 02215, US; Rao, D.C., Washington University in St Louis, St Louis, Missouri, 63130, US; Rasmussen-Torvik, Laura, Northwestern University, Chicago, Illinois, 60208, US; Ratan, Aakrosh, University of Virginia, Charlottesville, Virginia, 22903, US; Redline, Susan, Brigham & Women's Hospital, Medicine, Boston, Massachusetts, 02115, US; Reed, Robert, University of Maryland, Baltimore, Maryland, 21201, US; Reeves, Catherine, New York Genome Center, New York Genome Center, New York City, New York, 10013, US; Regan, Elizabeth, National Jewish Health, Denver, Colorado, 80206, US; Reiner, Alex, Fred Hutchinson Cancer Research Center, University of Washington, Seattle, Washington, 98109, US; Reupena, Muagututi'a Sefuiva, Lutia I Puava Ae Mapu I Fagalele, Apia, WS; Rice, Ken, University of Washington, Seattle, Washington, 98195, US; Rich, Stephen, University of Virginia, Charlottesville, Virginia, 22903, US; Robillard, Rebecca, University of Ottawa, Sleep Research Unit, University of Ottawa Institute for Mental Health Research, Ottawa, ON K1Z 7K4, CA; Robine, Nicolas, New York Genome Center, New York City, New York, 10013, US; Roden, Dan, Vanderbilt University, Medicine, Pharmacology, Biomedical Informatics, Nashville, Tennessee, 37235, US; Roselli, Carolina, Broad Institute, Cambridge, Massachusetts, 02142, US; Rotter, Jerome, Lundquist Institute, Pediatrics, Torrance, California, 90502, US; Ruczinski, Ingo, Johns Hopkins University, Baltimore, Maryland, 21218, US; Runnels, Alexi, New York Genome Center, New York City, New York, 10013, US; Russell, Pamela, University of Colorado at Denver, Denver, Colorado, 80204, US; Ruuska, Sarah, Blood Works Northwest, Seattle, Washington, 98104, US; Ryan, Kathleen, University of Maryland, Baltimore, Maryland, 21201, US; Sabino, Ester Cerdeira, Universidade de Sao Paulo, Faculdade de Medicina, Sao Paulo, 01310000, BR; Saleheen, Danish, Columbia University, New York, New York, 10027, US; Salimi, Shabnam, University of Maryland, Pathology, Seattle, Washington, 98195, US; Salvi, Sejal, Baylor College of Medicine Human Genome Sequencing Center, Houston, Texas, 77030, US; Salzberg, Steven, Johns Hopkins University,

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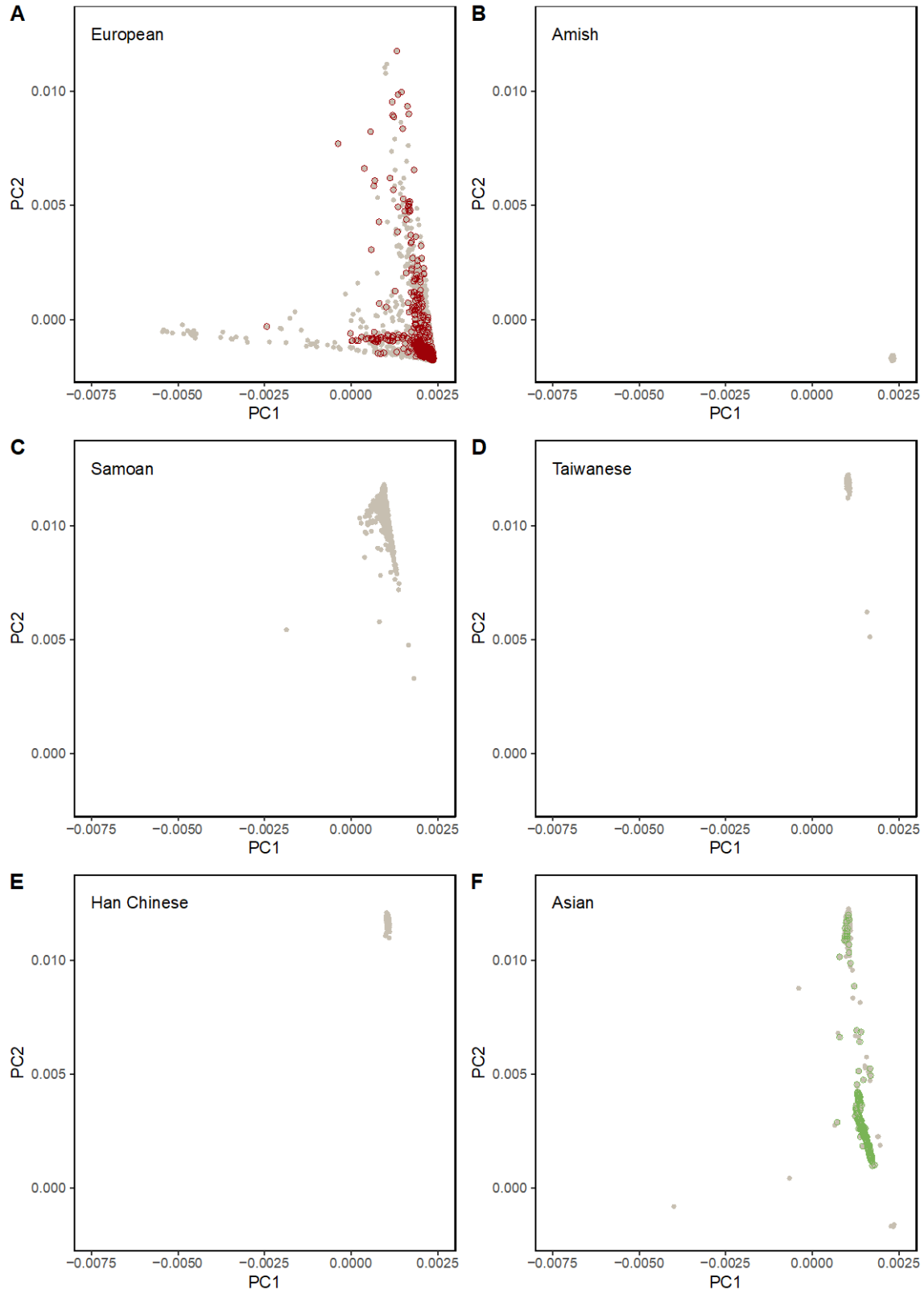
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## Supplementary Note 5. REFERENCES

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## Supplementary Figure 1. Scatter plots of PC1 vs. PC2 by population group

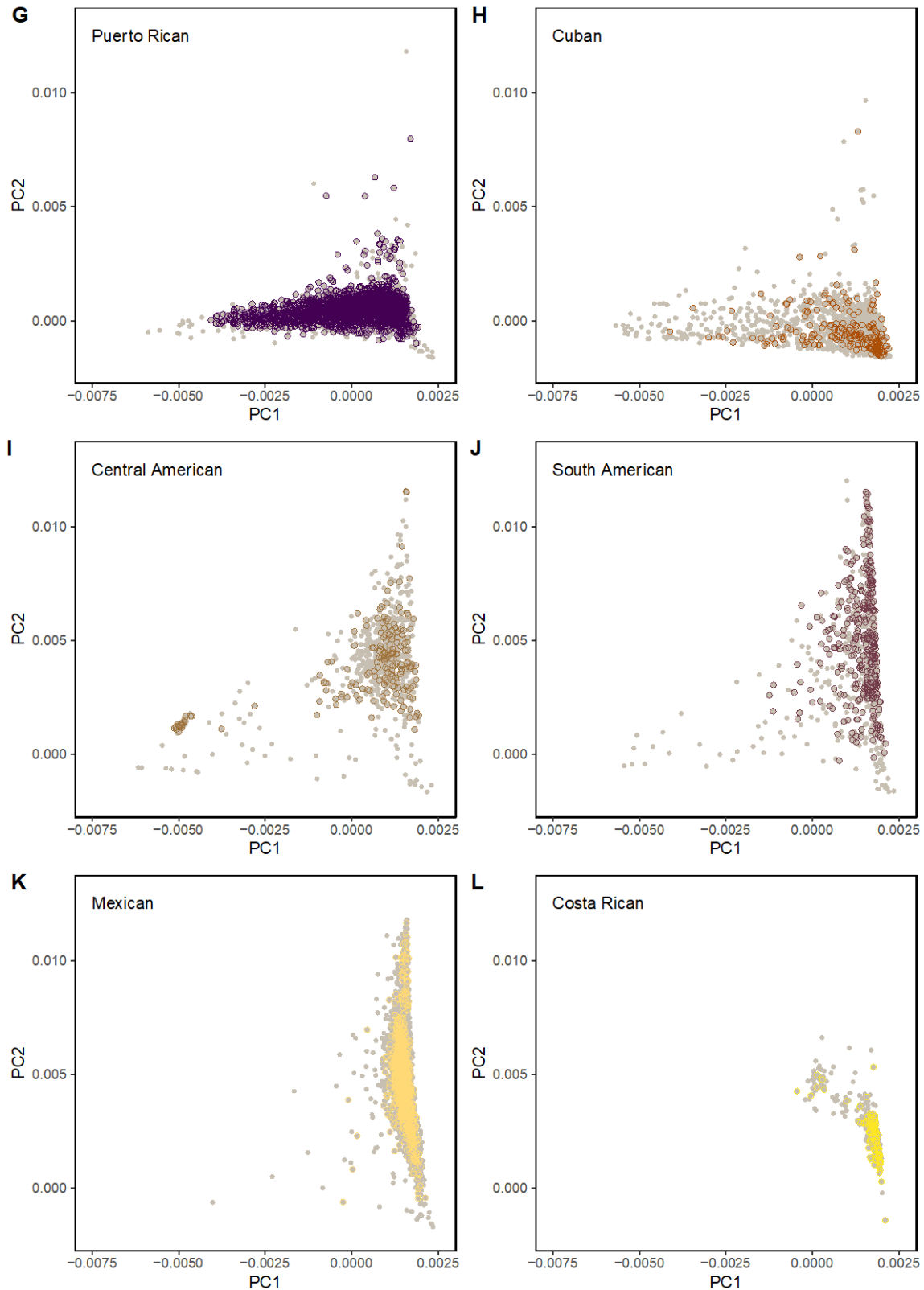
Individuals with reported population memberships in each population group are denoted by filled circles in grey. Unfilled circles in colors represent inferred population memberships (N = 8,015), using Harmonized Ancestry and Race/Ethnicity (HARE) method (see methods for details). A) European, B) Amish, C) Samoan, D) Taiwanese, E) Han Chinese, F) Asian, G) Puerto Rican, H) Cuban, I) Central American, J) South American, K) Mexican, L) Costa Rican, M) Dominican, N) Barbadian, O) African/African American/Black.





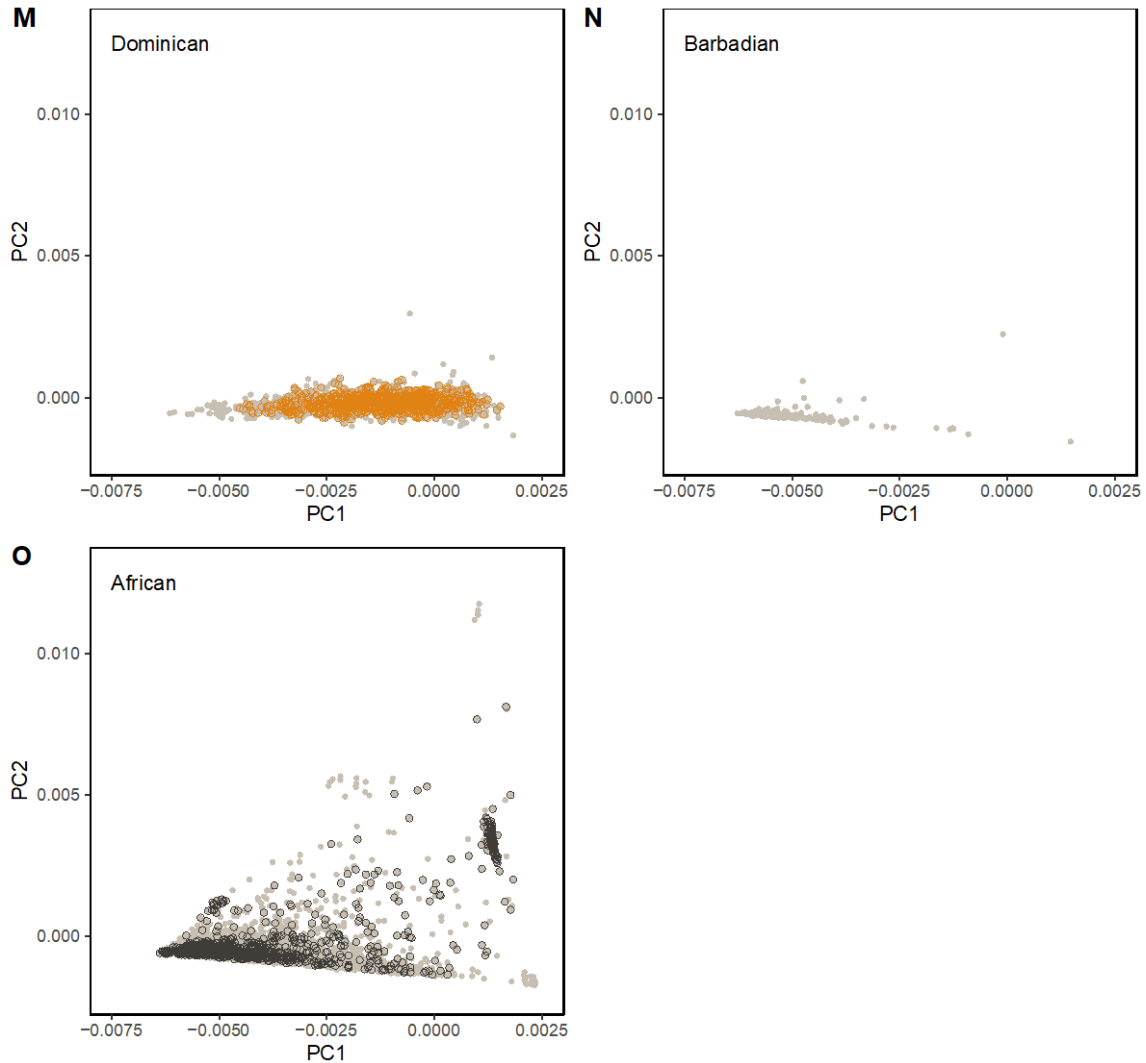
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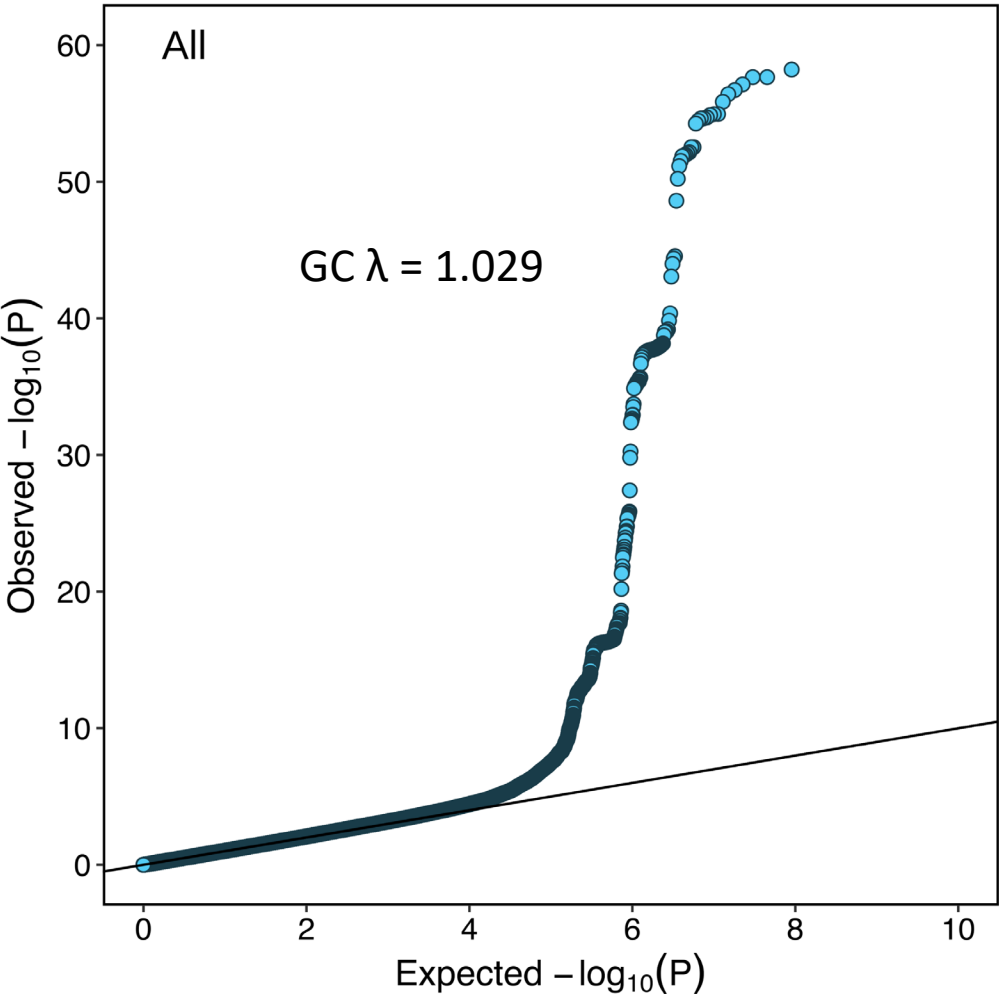
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**Supplementary Figure 2. QQ plot of primary BMI GWAS**

Quantile-quantile plot of multi-population, single variant analysis (N = 88,873 individuals, N = 90,142,062 variants).

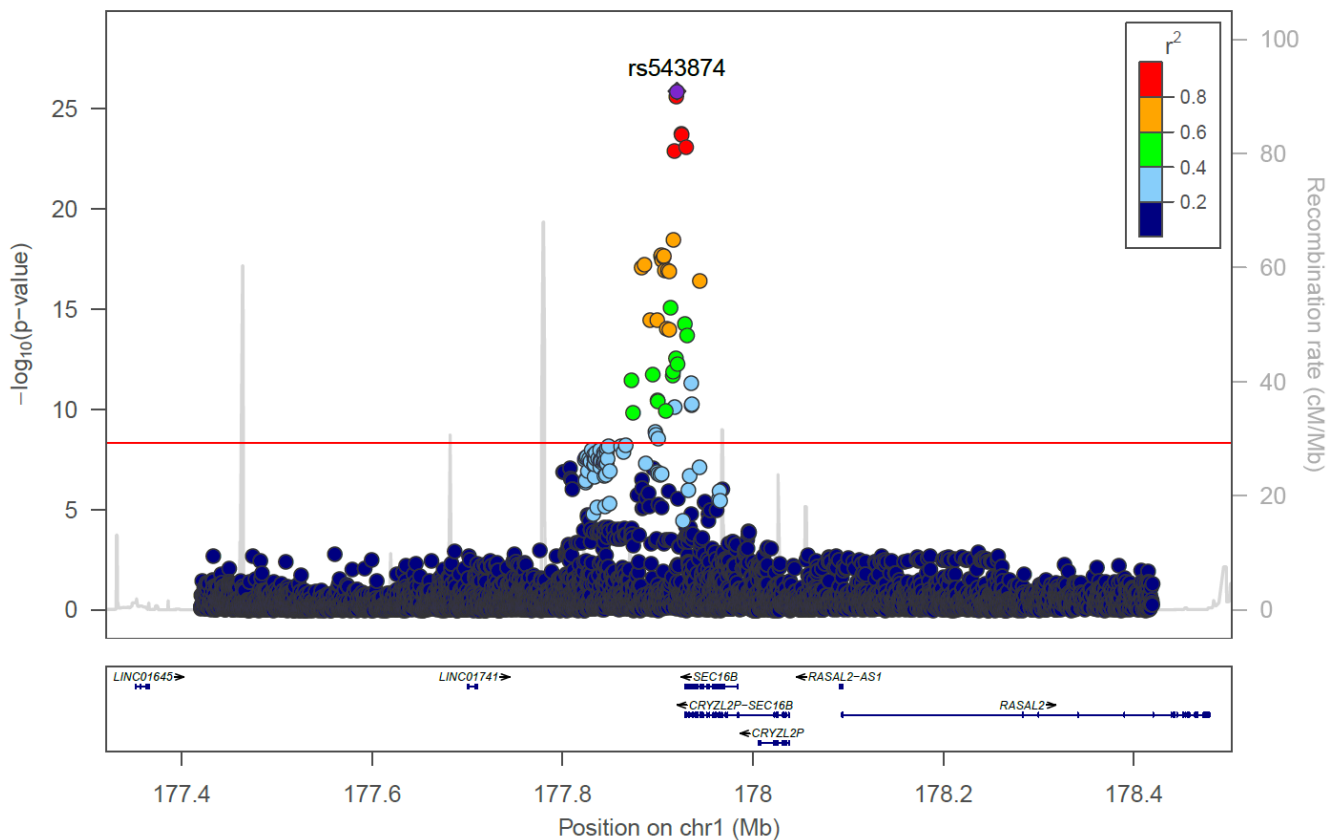


### Supplementary Figure 3. Regional association plots

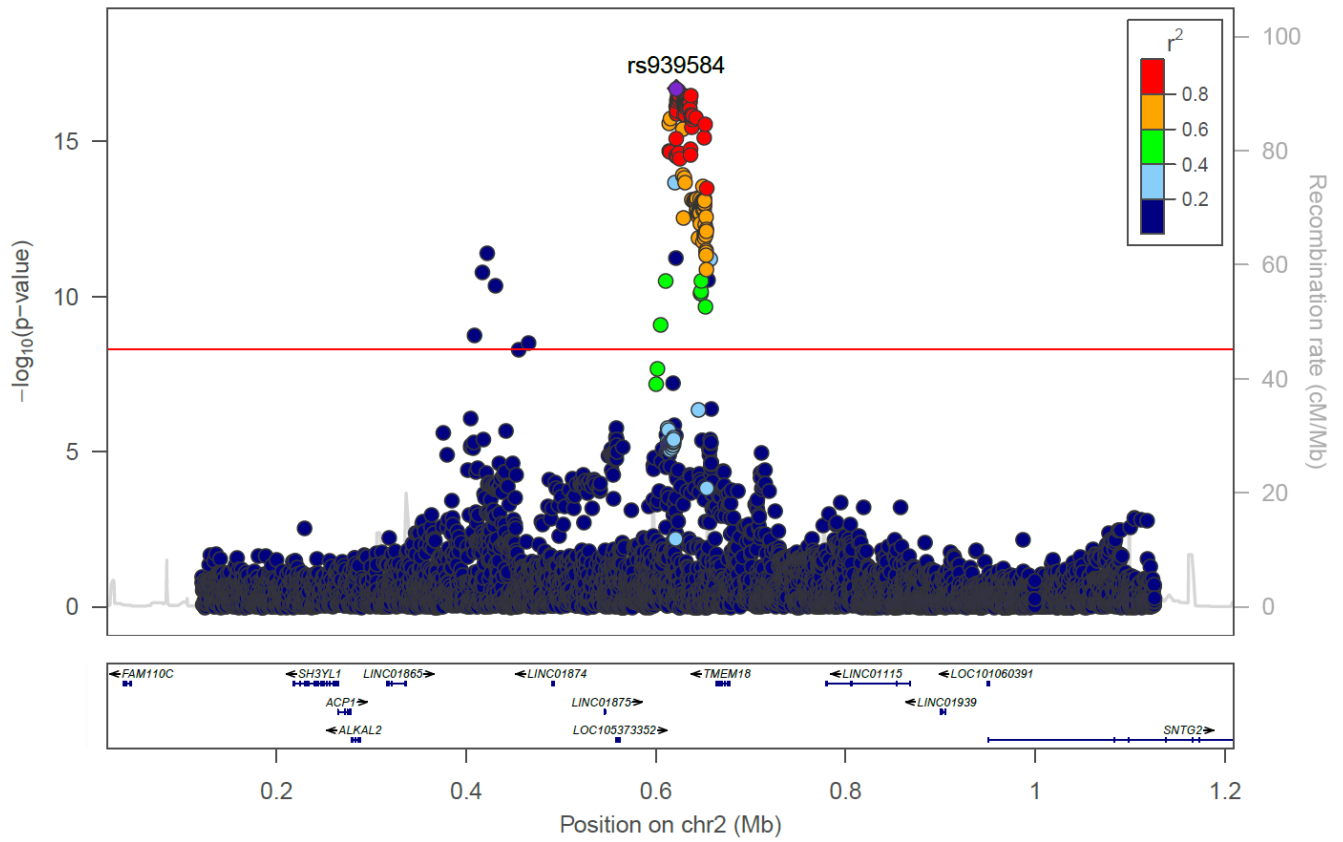
Regional association plots for each significant locus in the multi-population analysis, including all variants  $\pm 500$  kb from index variant. The plots appear in order of chromosomal location. TOPMed study populations were used to calculate linkage disequilibrium (LD). The red line indicates genome-wide significance threshold  $P = 5 \times 10^{-9}$ .

A) *SEC16B*, rs543874; B) *TMEM18*, rs939584; C) *ADCY3*, rs10182181; D) *ETV5*, rs869400; E) *GNPDA2*, rs12507026; F) *POC5*, rs2307111; G) *TFAP2B*, rs2206277; H) *HNF4G*, rs830463; I) *BDNF*, rs3838785; J) *BCDIN3D*, rs7138803; K) *OLFM4*, rs9568868; L) *FTO*, rs1421085; M) *MC4R*, rs6567160; N) *ZC3H4*, rs28590228; O) *MTMR3*, rs111490516; P) *DMD*, rs1379871.

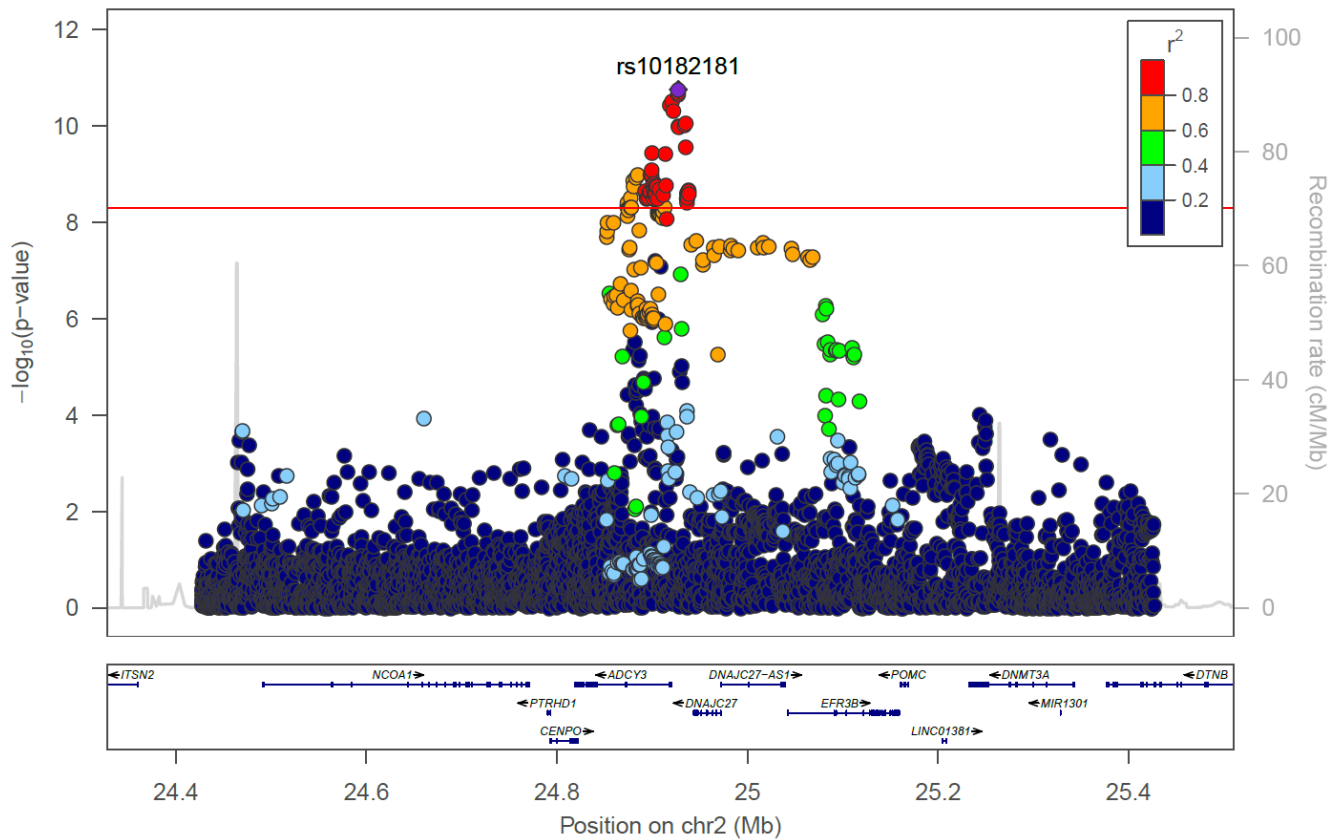
#### A) *SEC16B*, rs543874



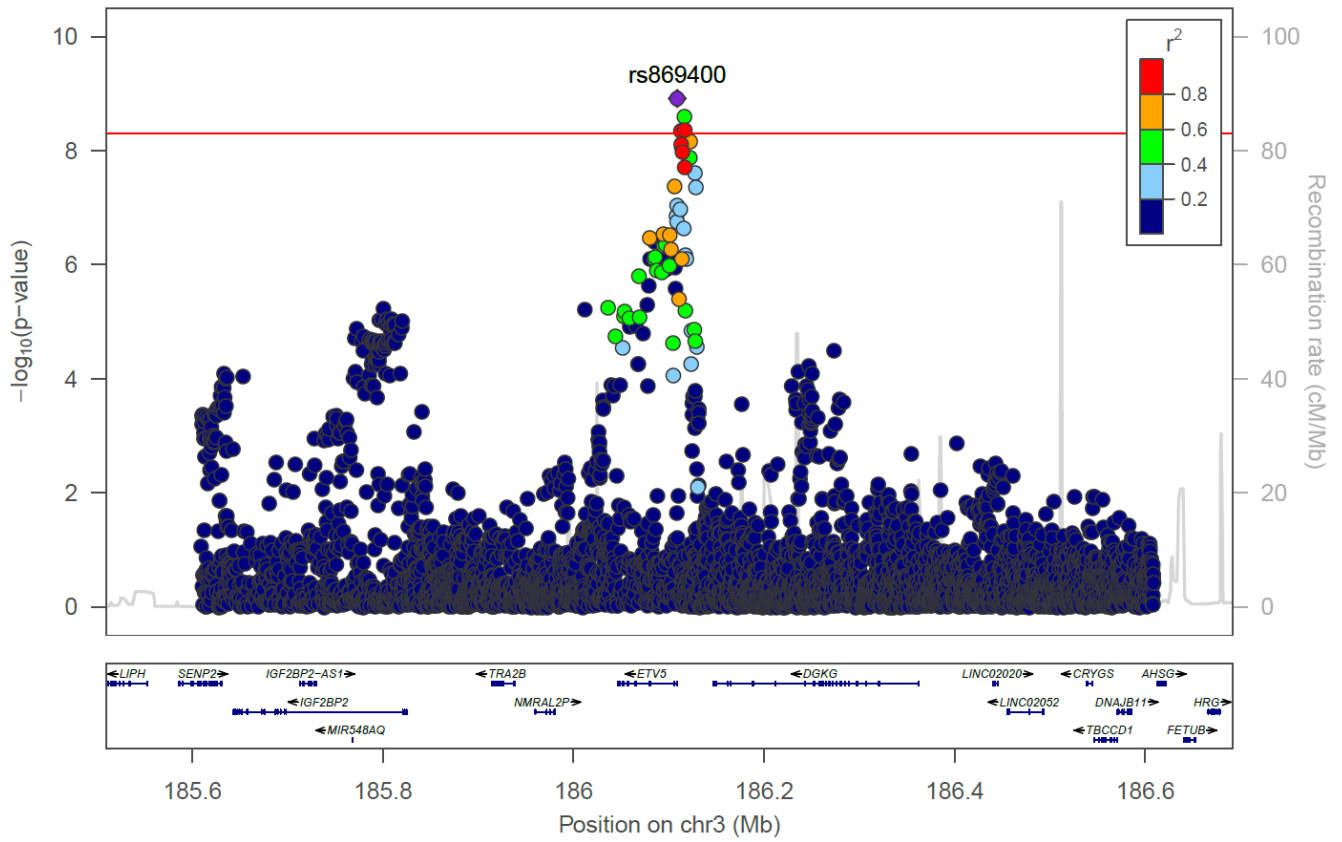
**B) *TMEM18*, rs939584**



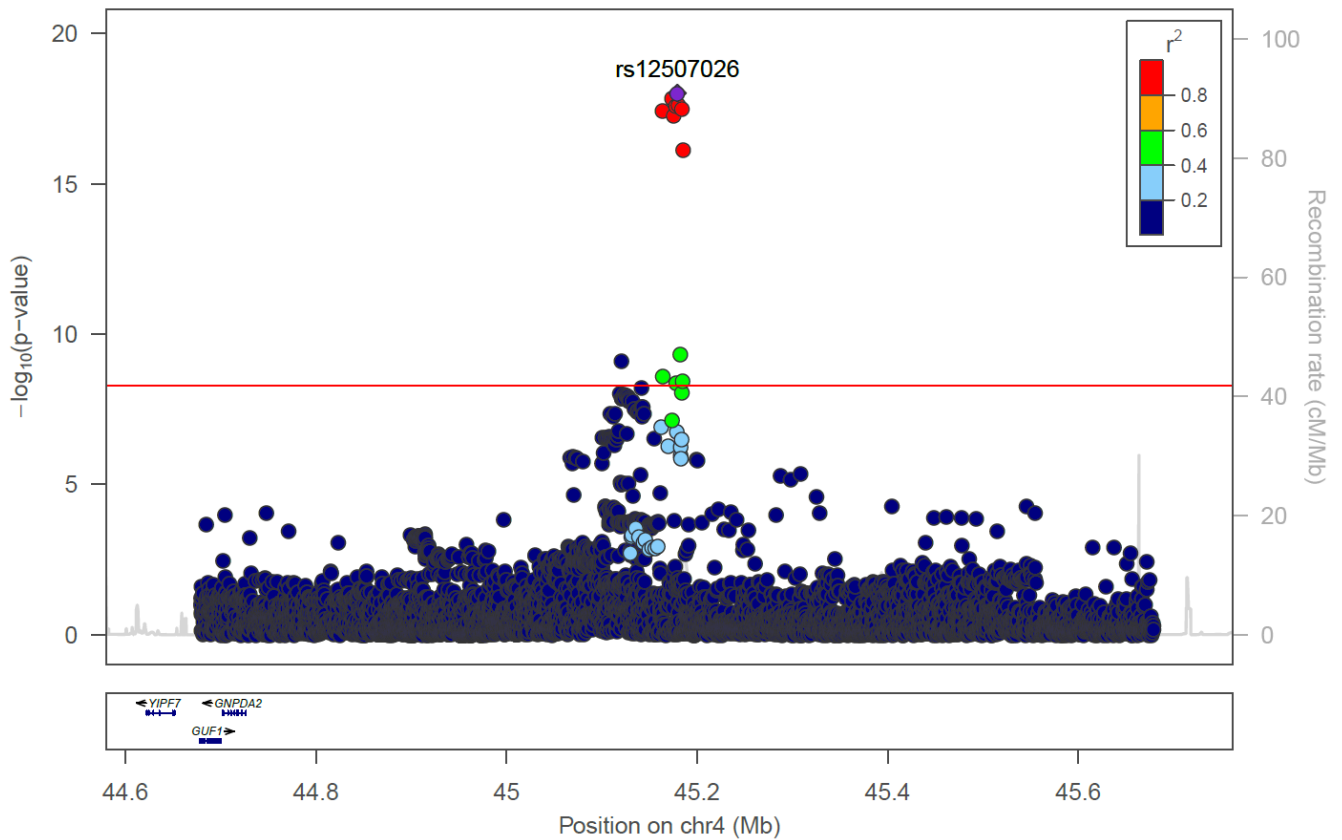
**C) *ADCY3*, rs10182181**



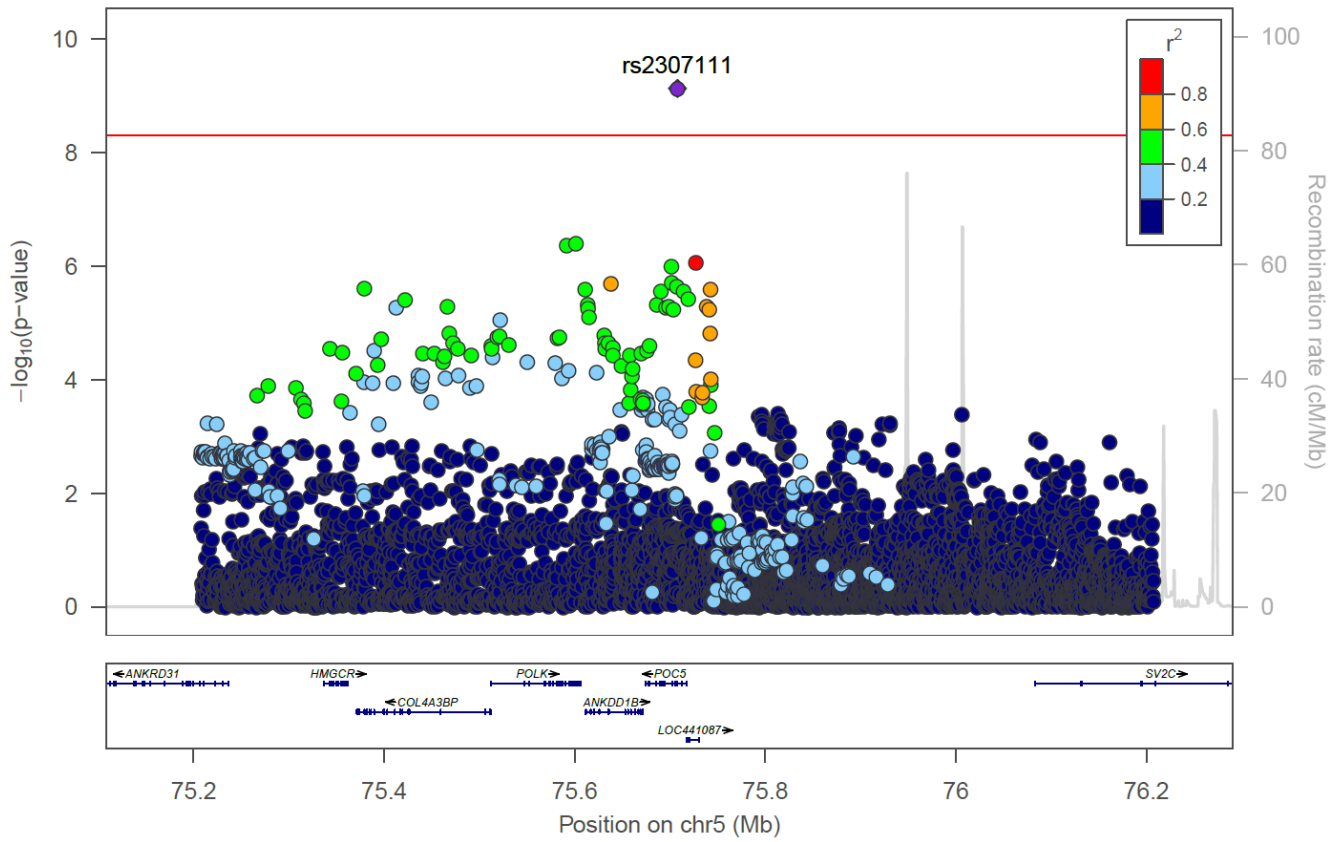
### D) *ETV5*, rs869400



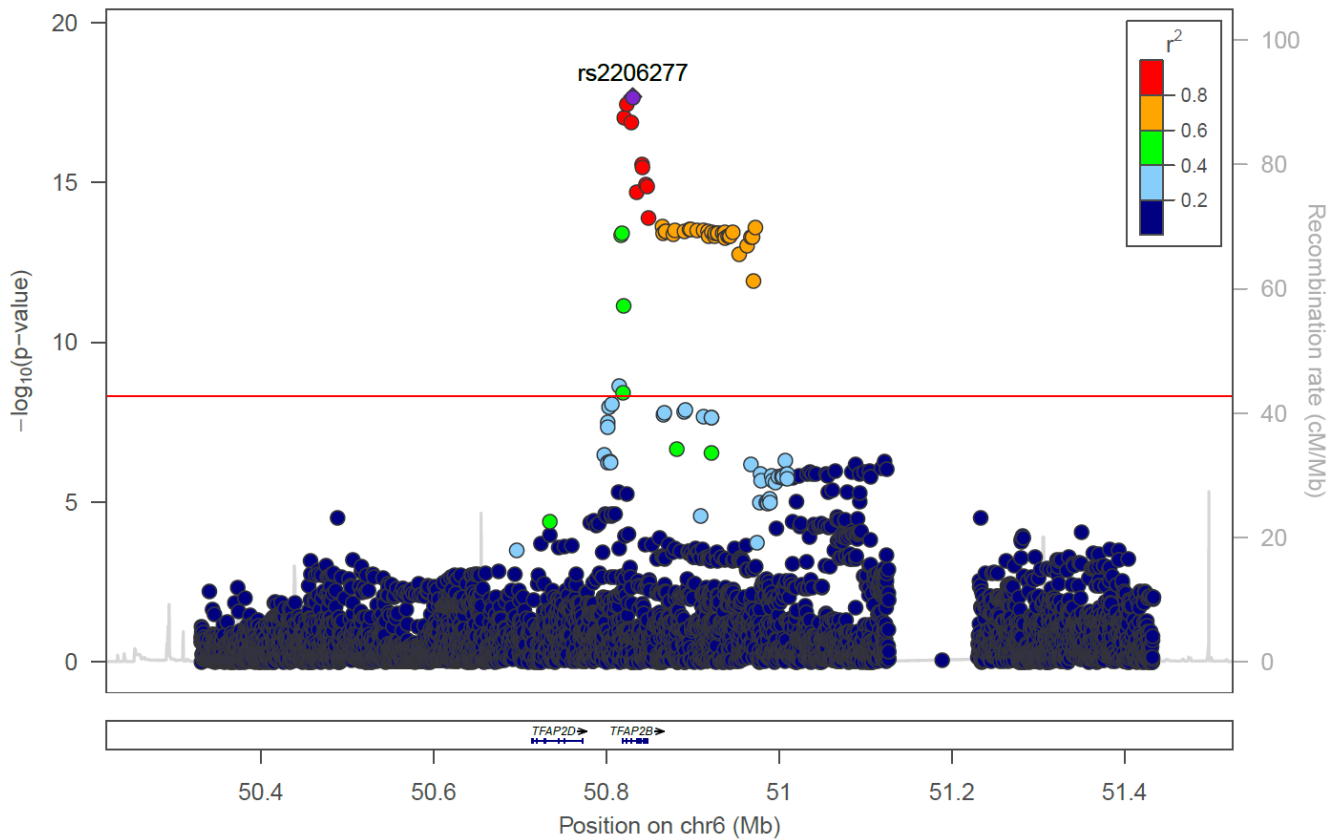
### E) *GNPDA2*, rs12507026



**F) *POC5*, rs2307111**

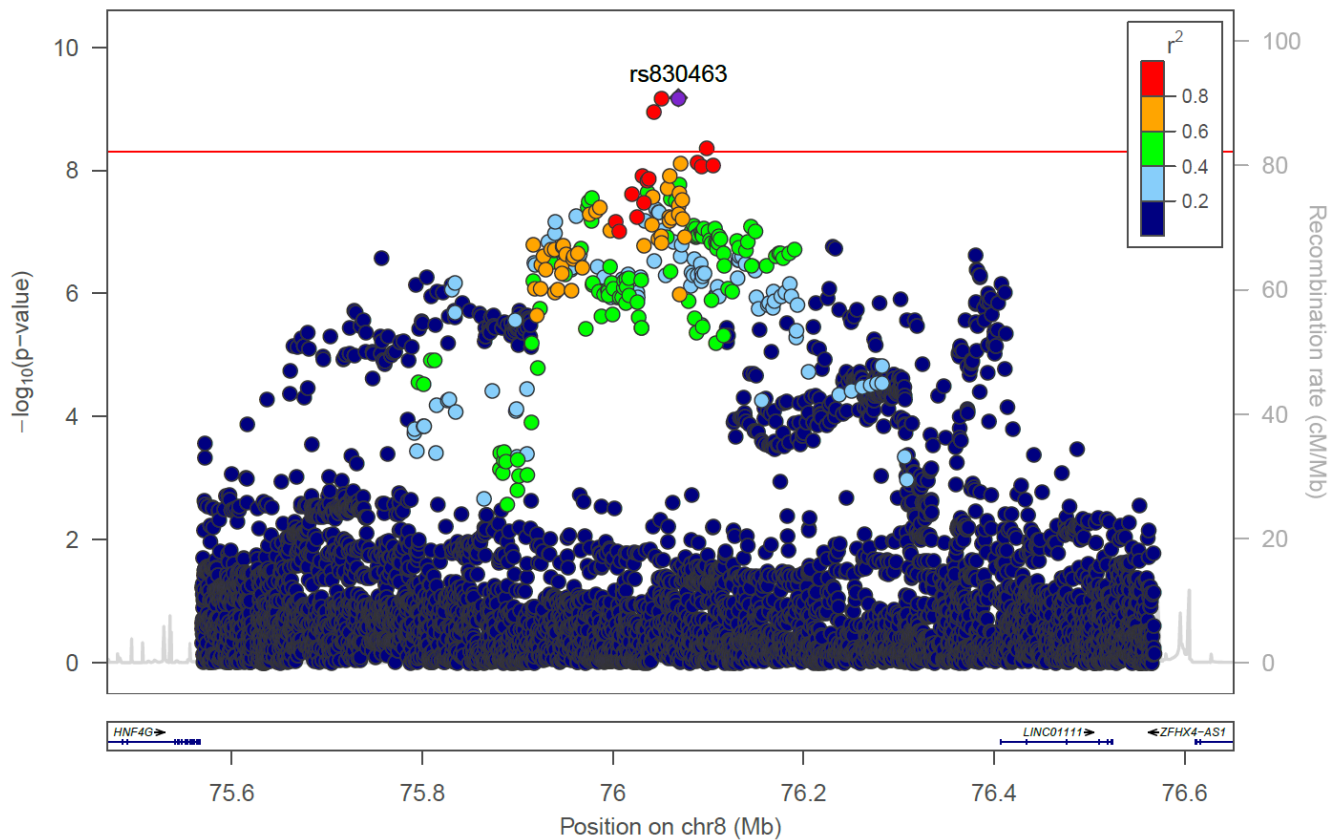


**G) *TFAP2B*, rs2206277**

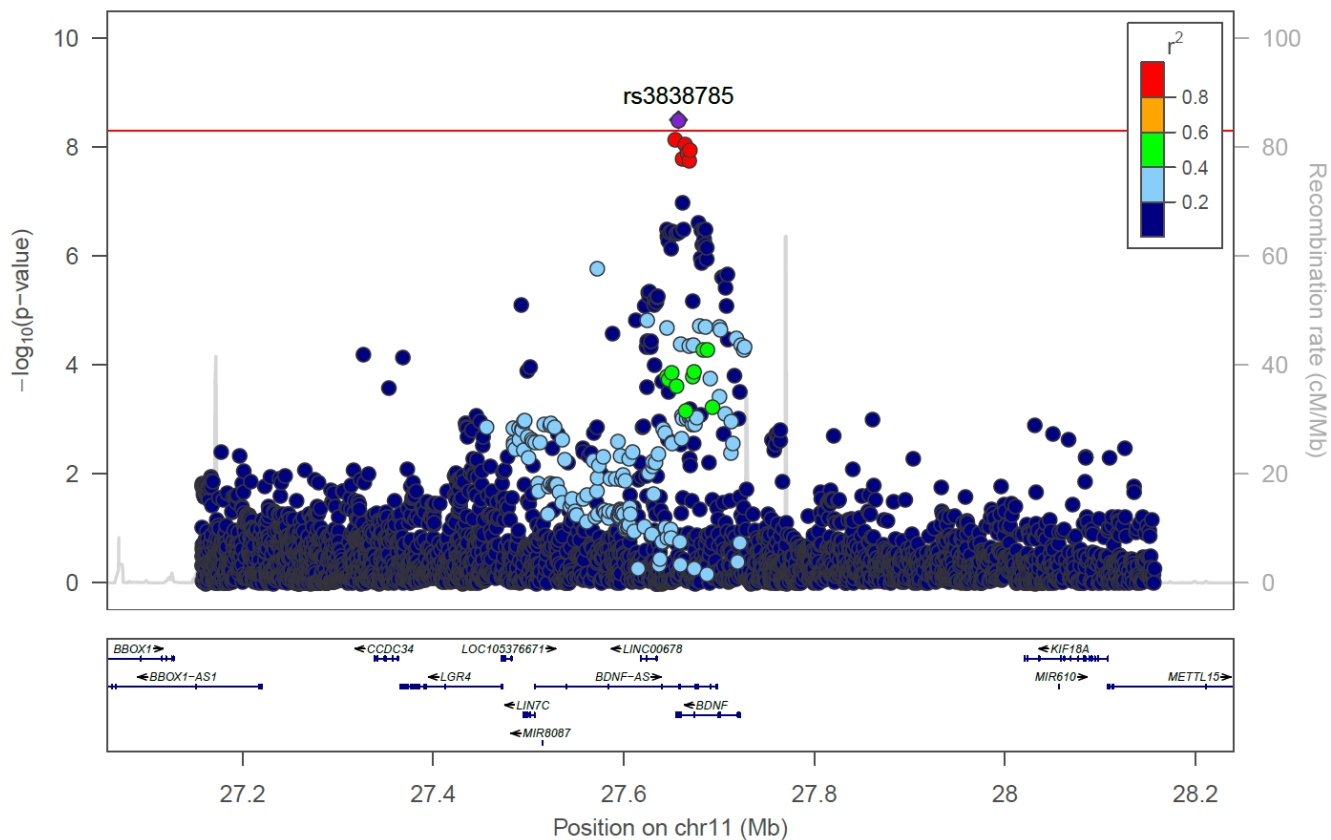




**H) *HNF4G*, rs830463**

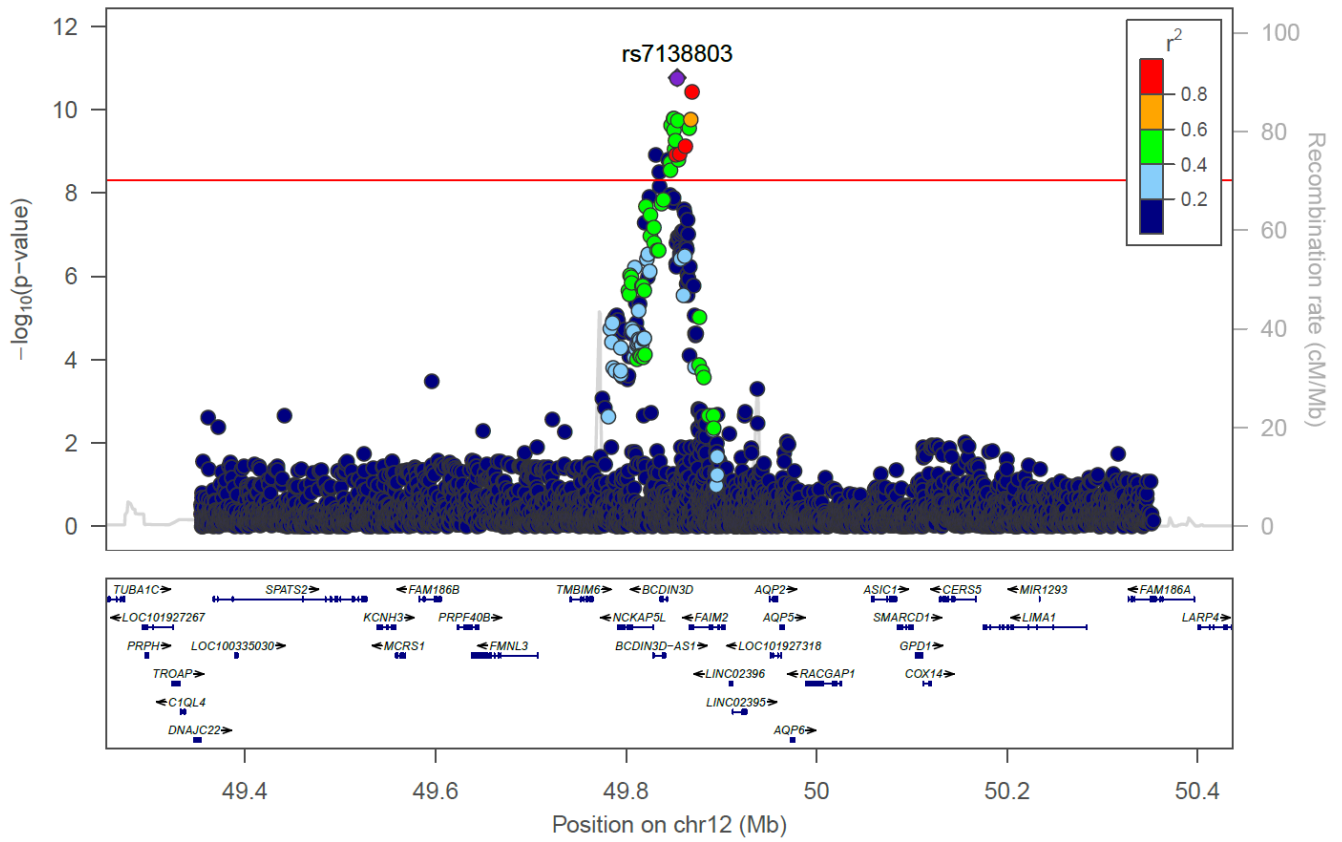


**I) *BDNF*, rs3838785**

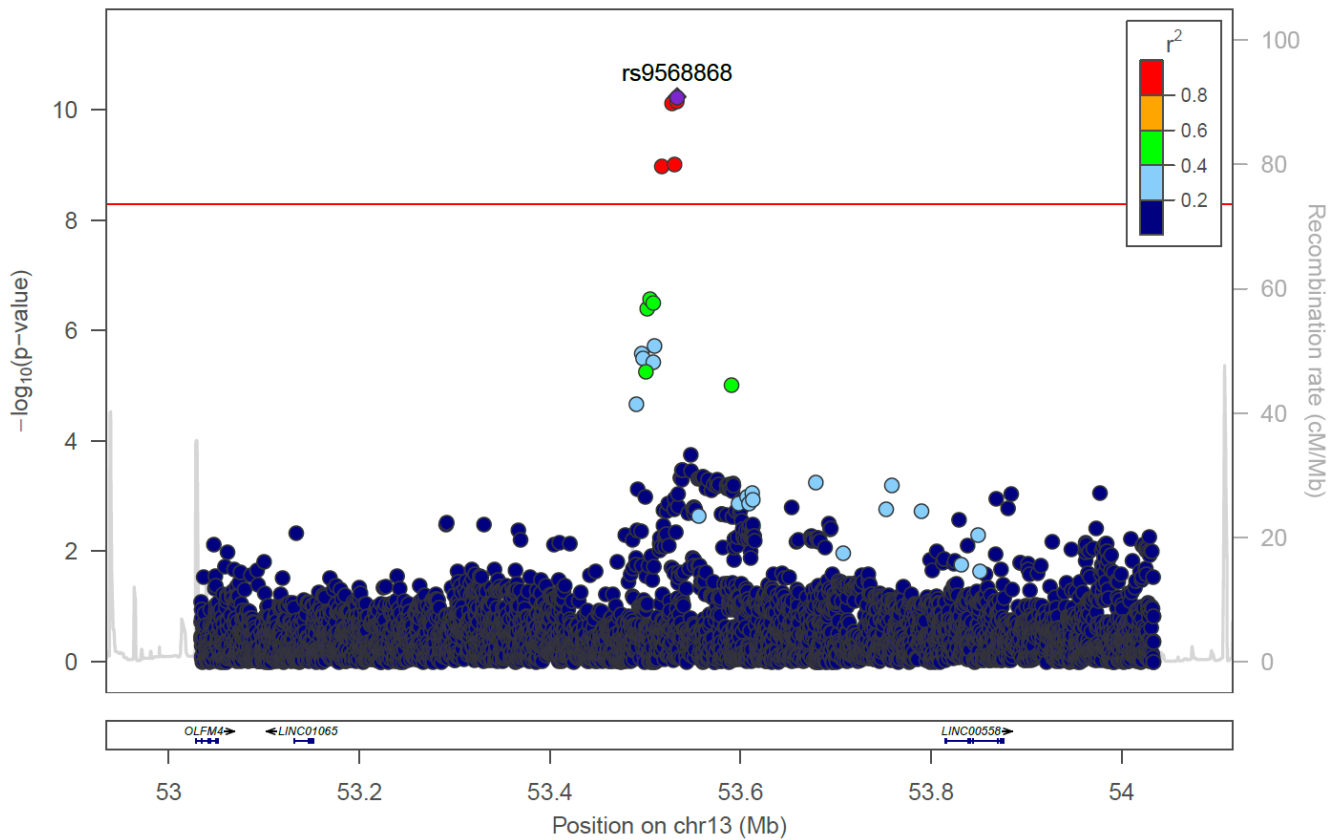




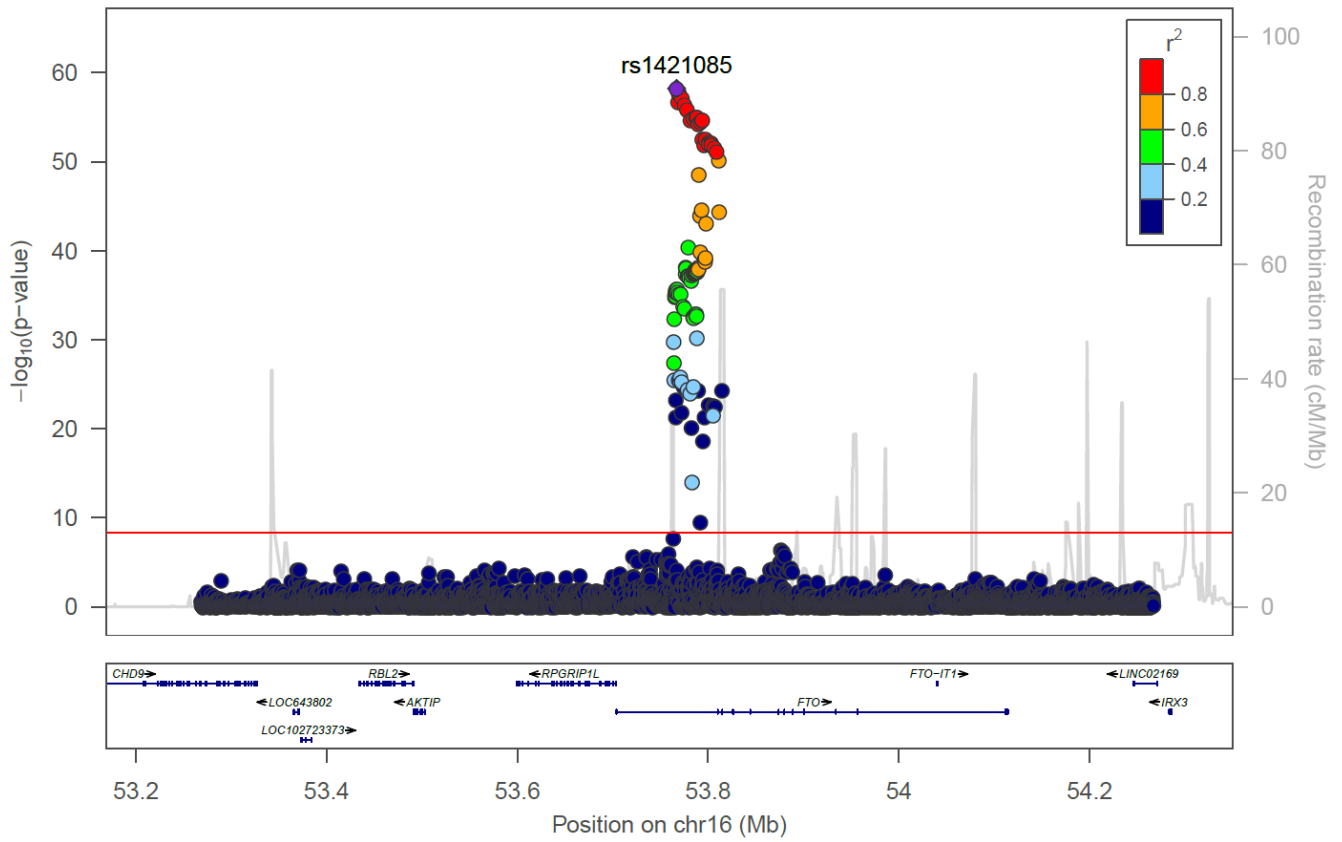
**J) *BCDIN3D*, rs7138803**



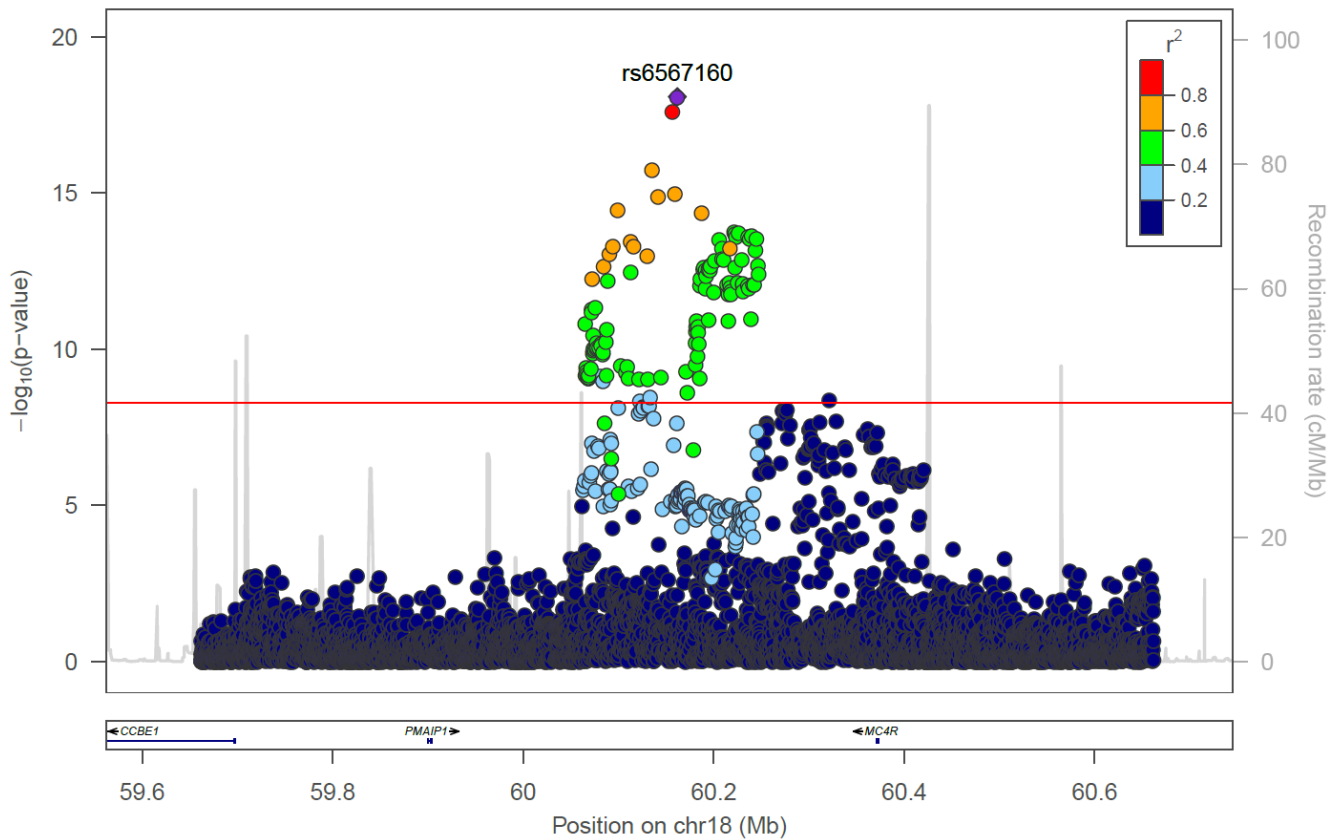
**K) *OLFM4*, rs9568868**



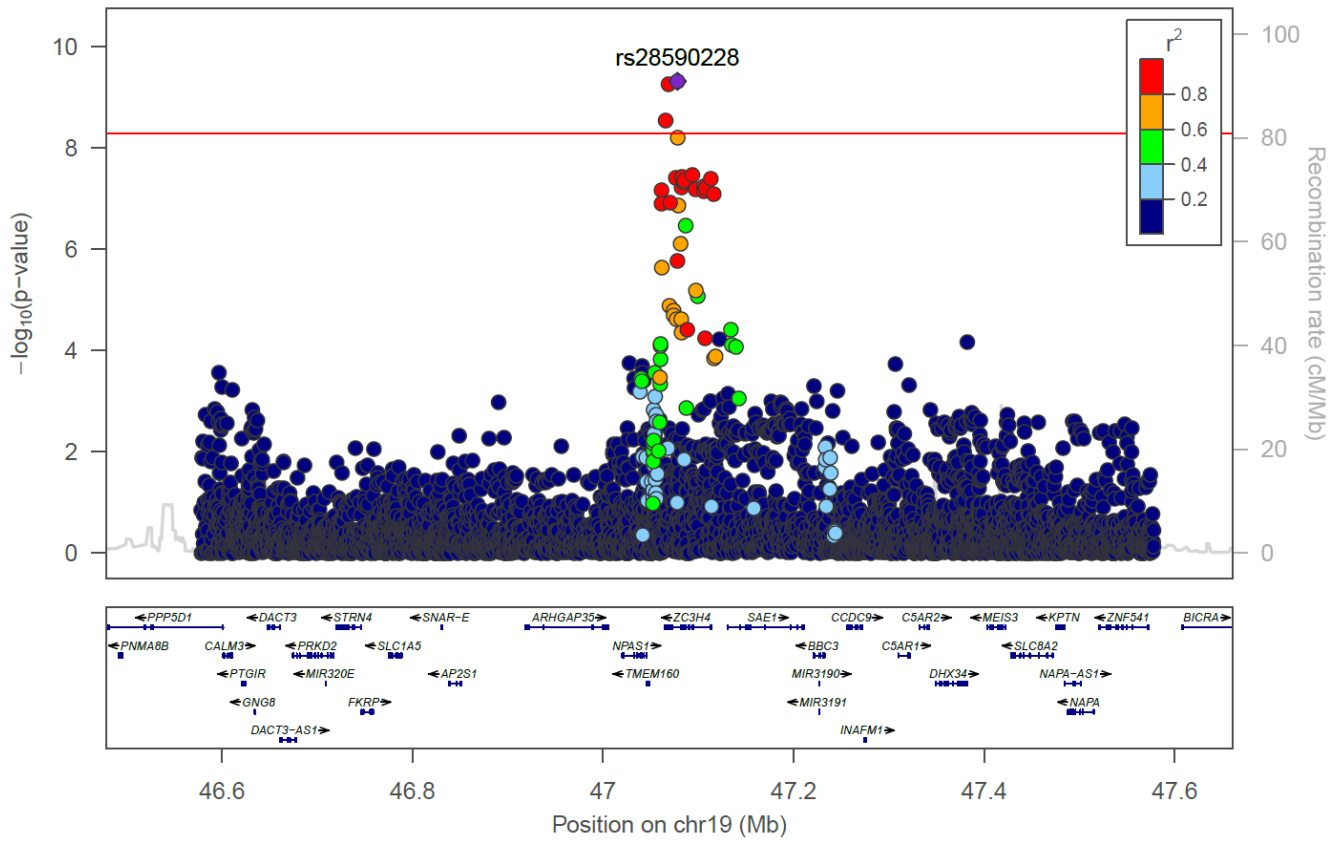
**L) *FTO*, rs1421085**



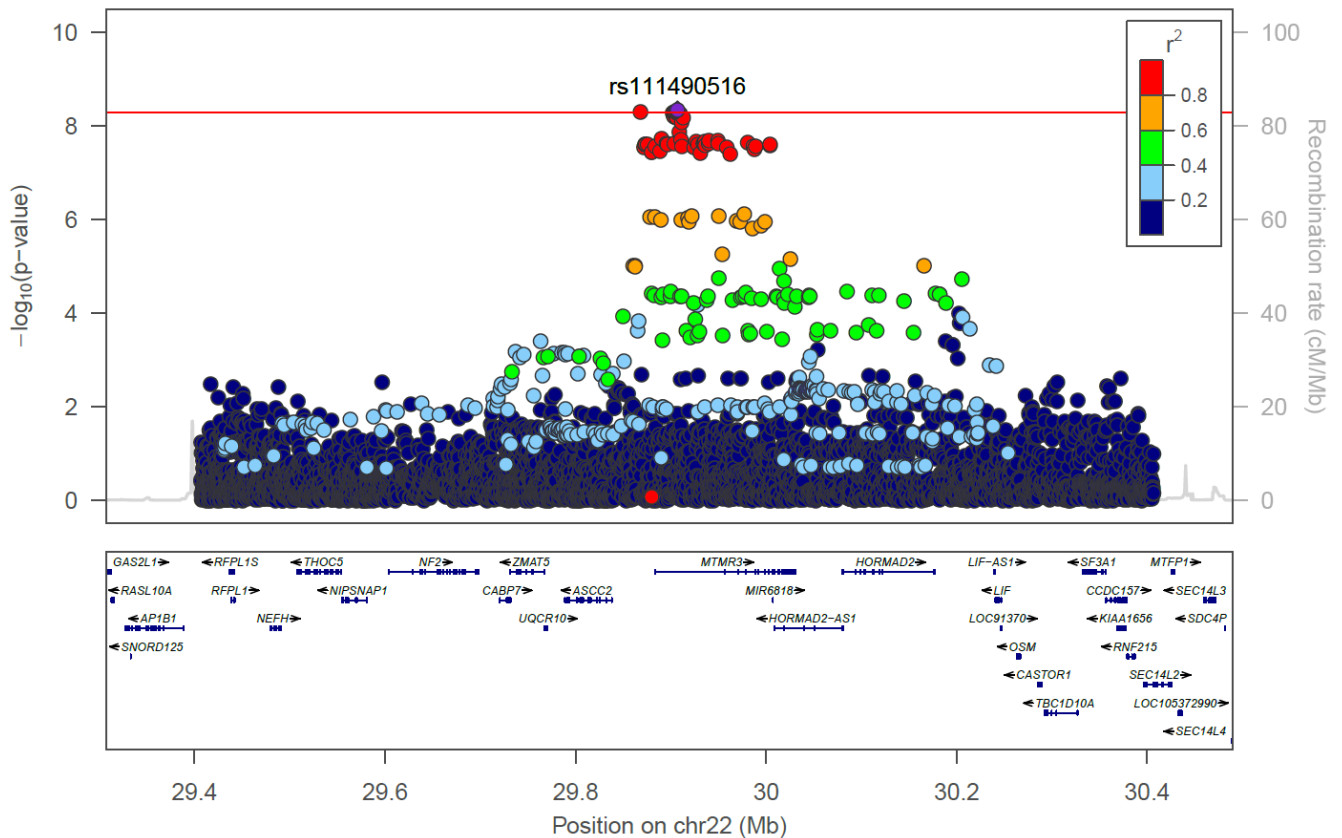
**M) *MC4R*, rs6567160**



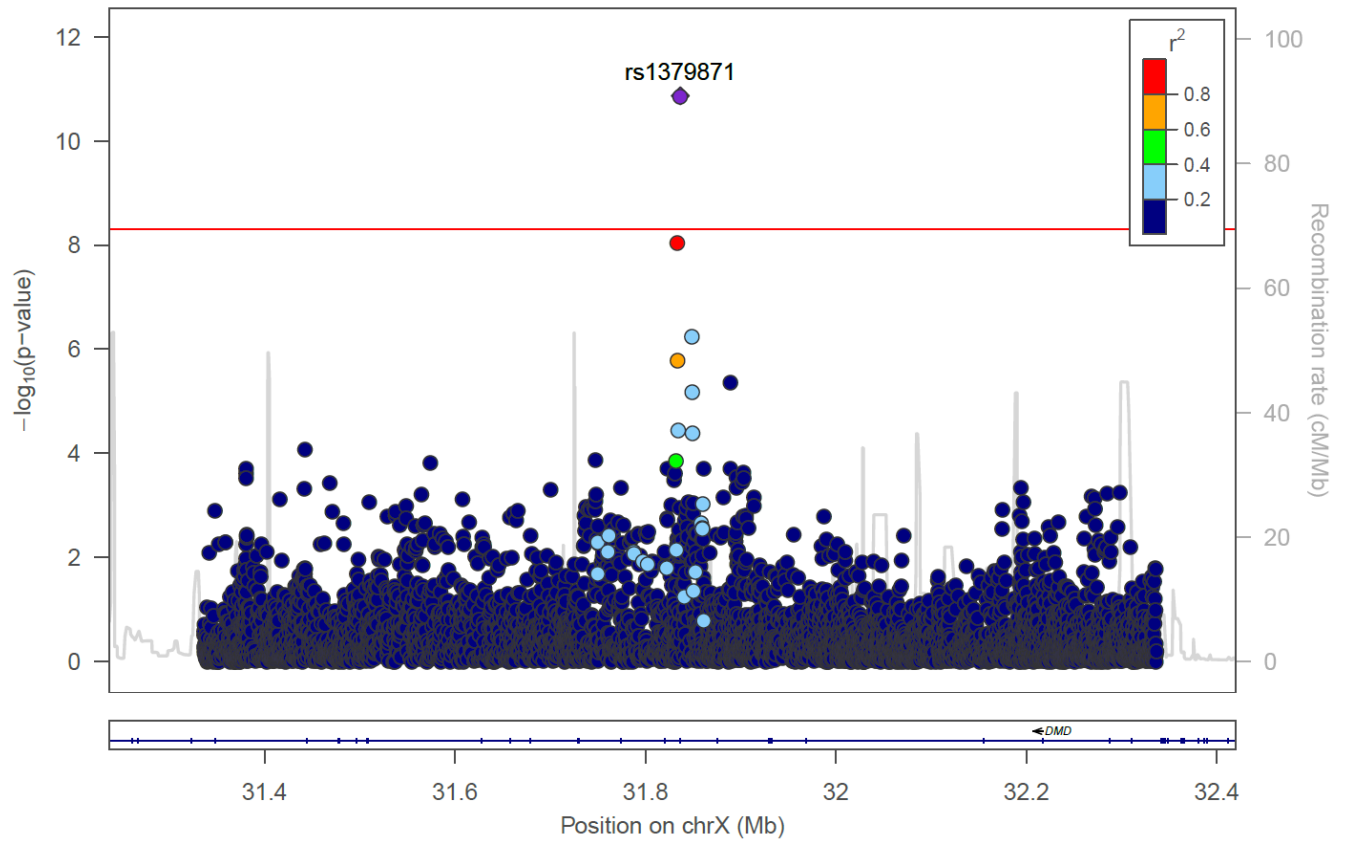
**N) *ZC3H4*, rs28590228**



**O) *MTMR3*, rs111490516**

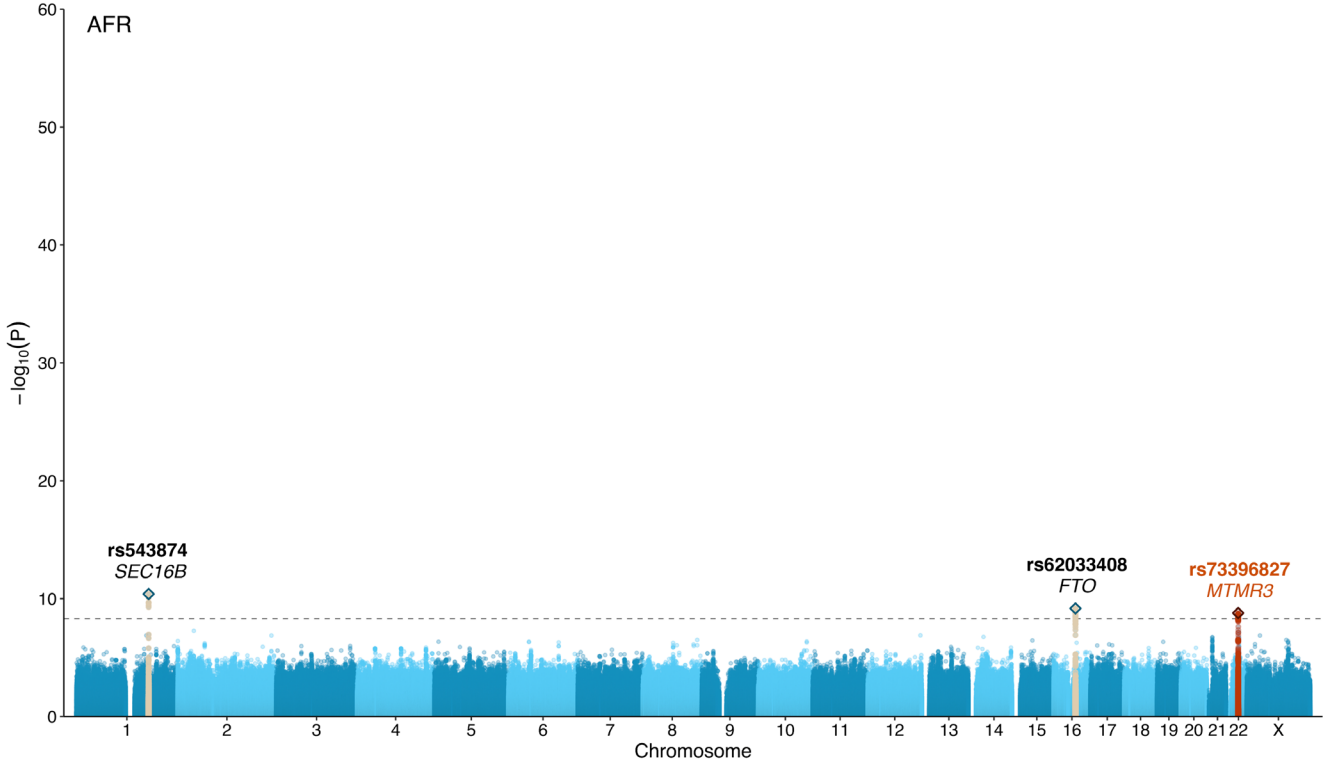


P) *DMD*, rs1379871



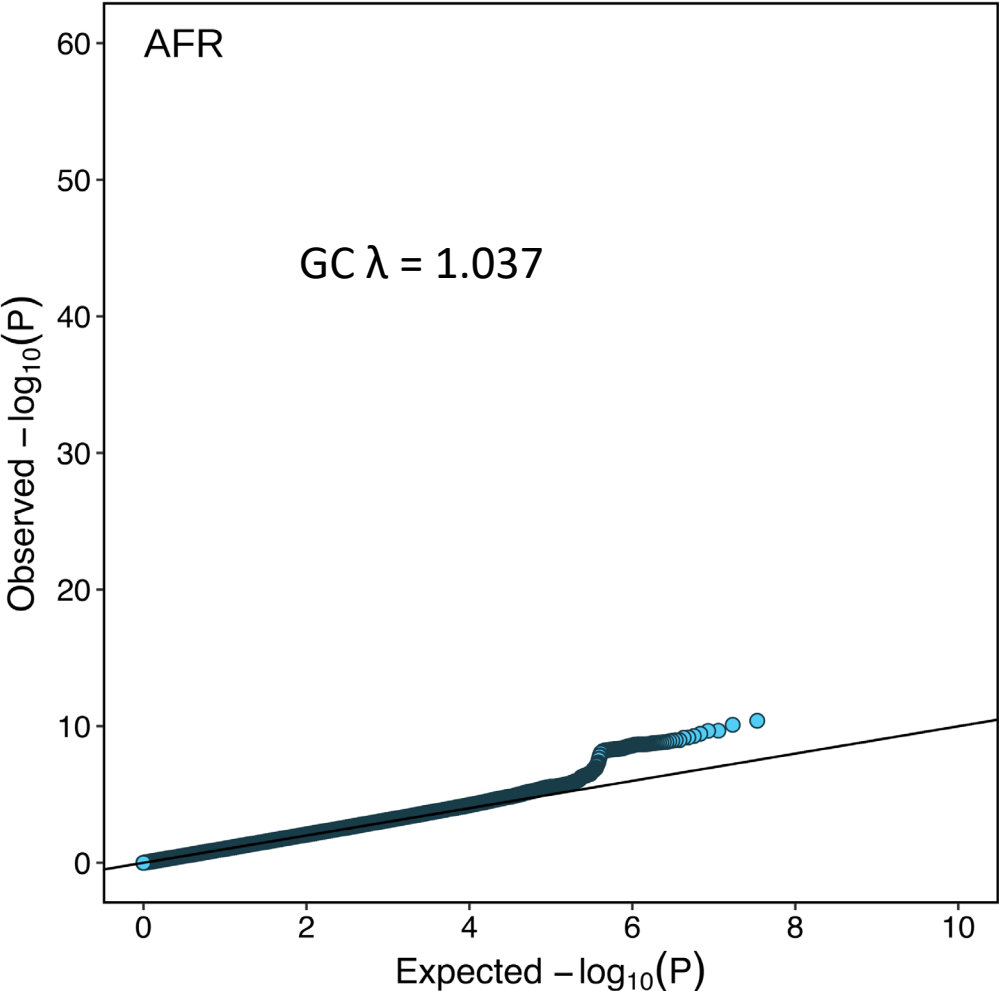
**Supplementary Figure 4. Manhattan plot of African population group BMI GWAS**

Manhattan plot of African population group, single variant analysis (N = 22,488 individuals). The novel locus (*MTMR3*) is highlighted in red. Previously reported BMI loci are in dark beige. The horizontal dashed line indicates genome-wide significant threshold  $P = 5 \times 10^{-9}$ .



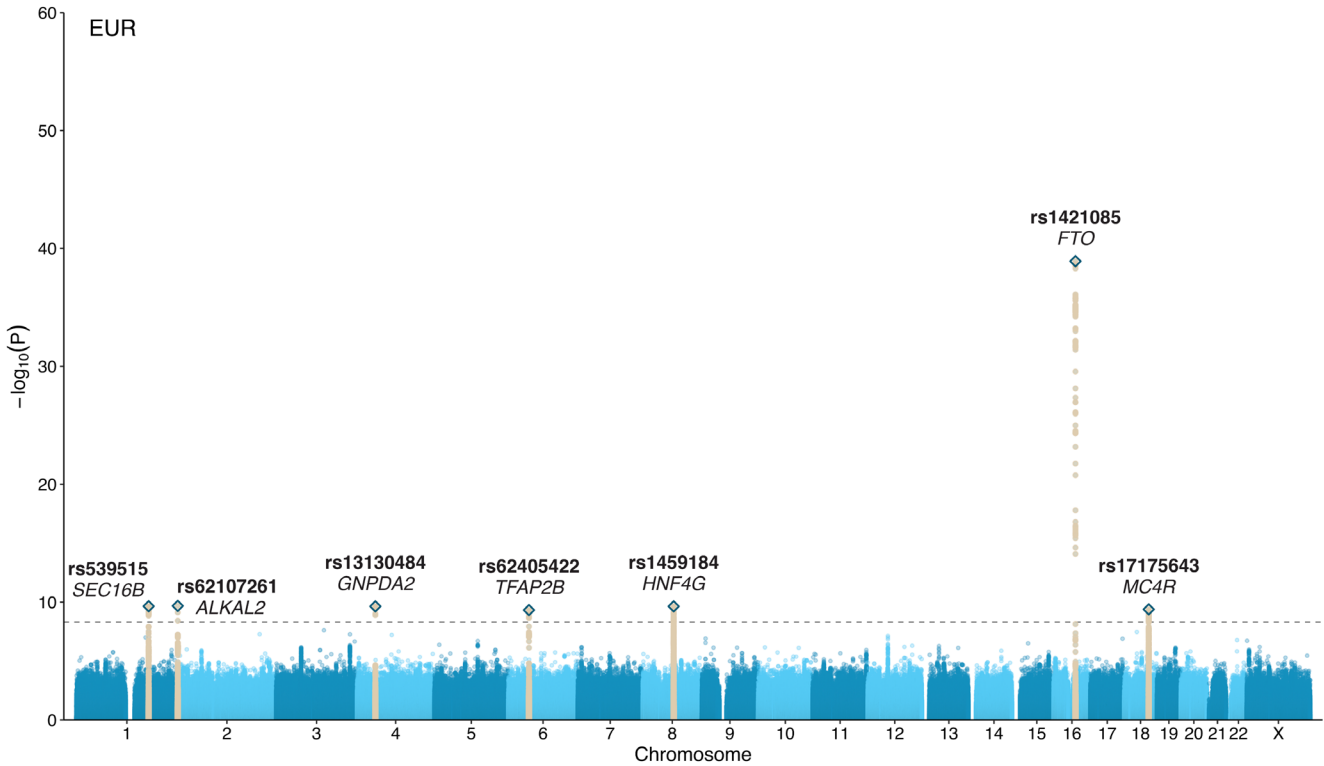
**Supplementary Figure 5. QQ plot of African population group BMI GWAS**

Quantile-quantile plot of African population group, single variant analysis (N = 22,488 individuals).



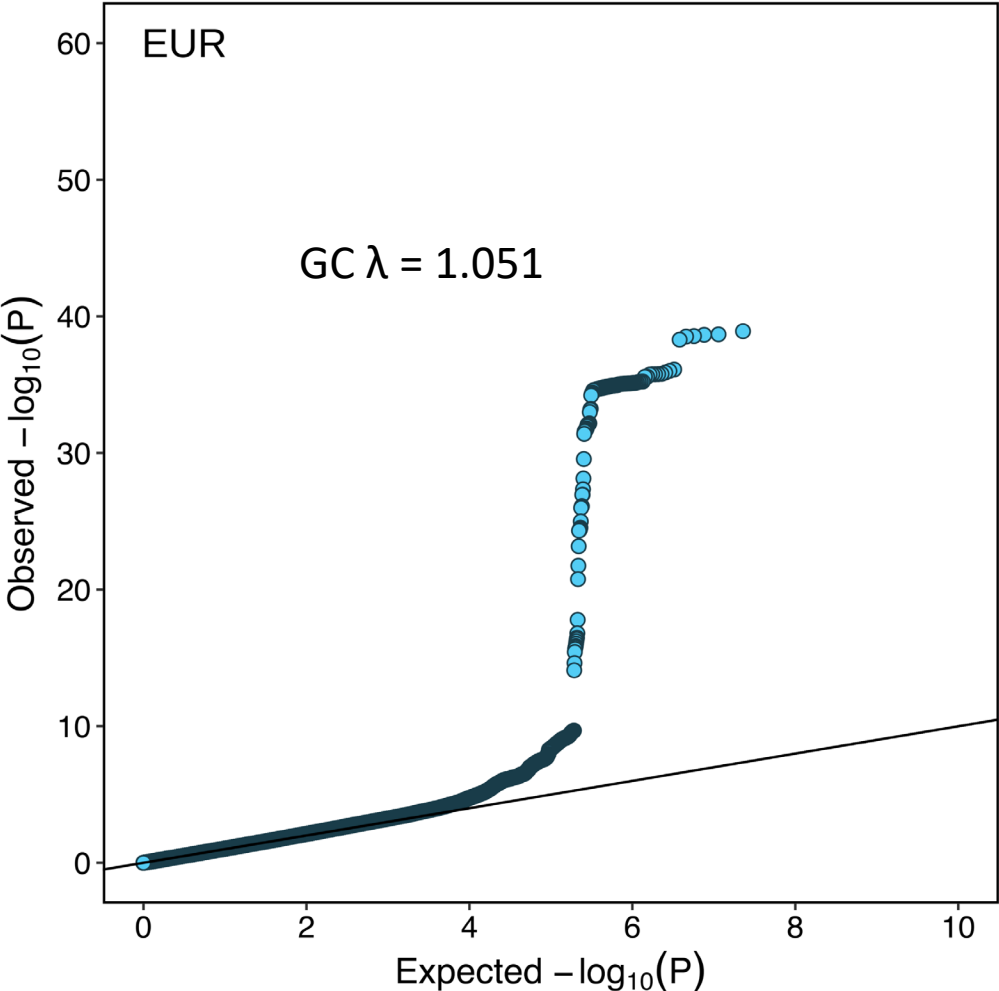
**Supplementary Figure 6. Manhattan plot of European population group BMI GWAS**

Manhattan plot of European population group, single variant analysis (N = 43,434 individuals). Previously reported BMI loci are in dark beige. The horizontal dashed line indicates genome-wide significant threshold  $P = 5 \times 10^{-9}$ .



**Supplementary Figure 7. QQ plot of European population group BMI GWAS**

Quantile-quantile plot of European population group, single variant analysis (N = 43,434 individuals).

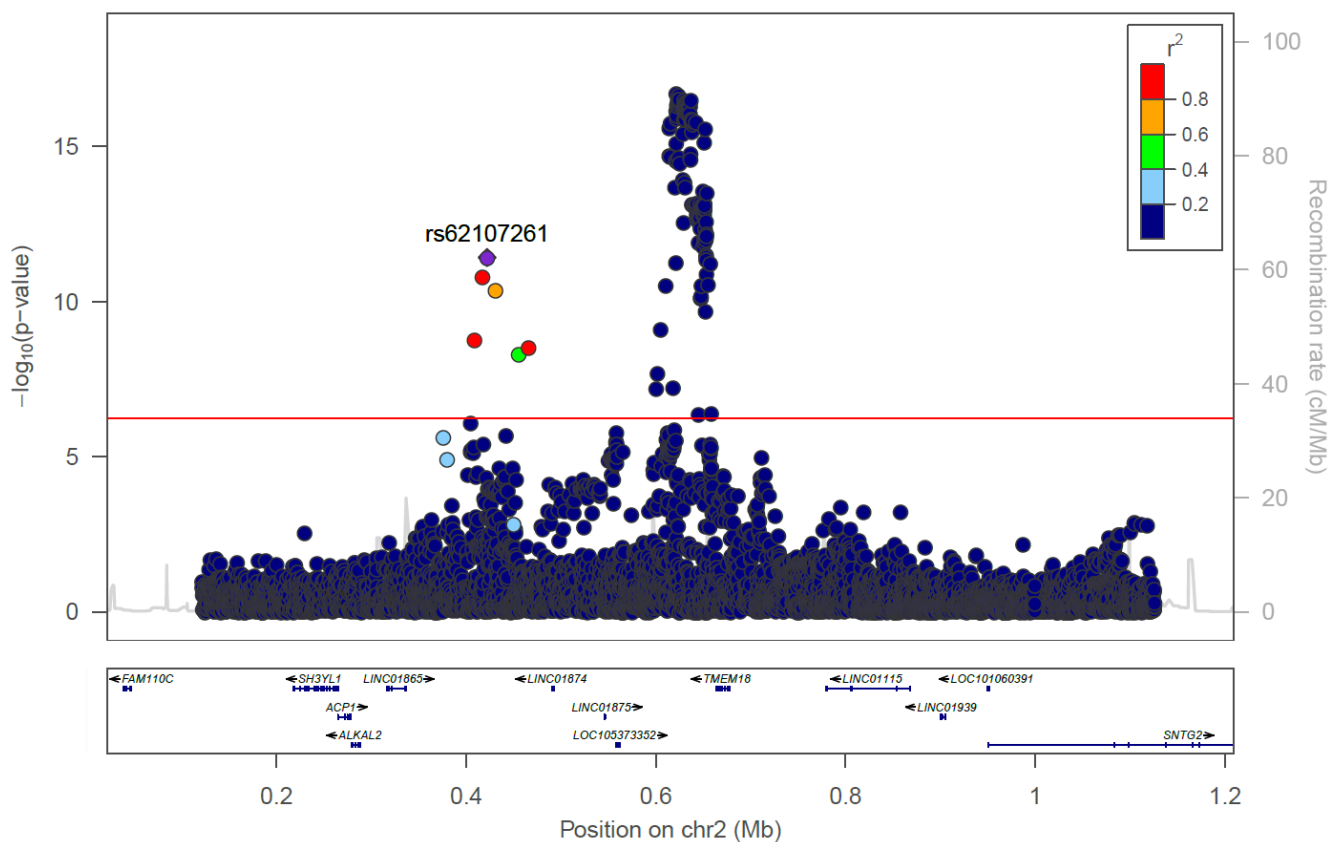




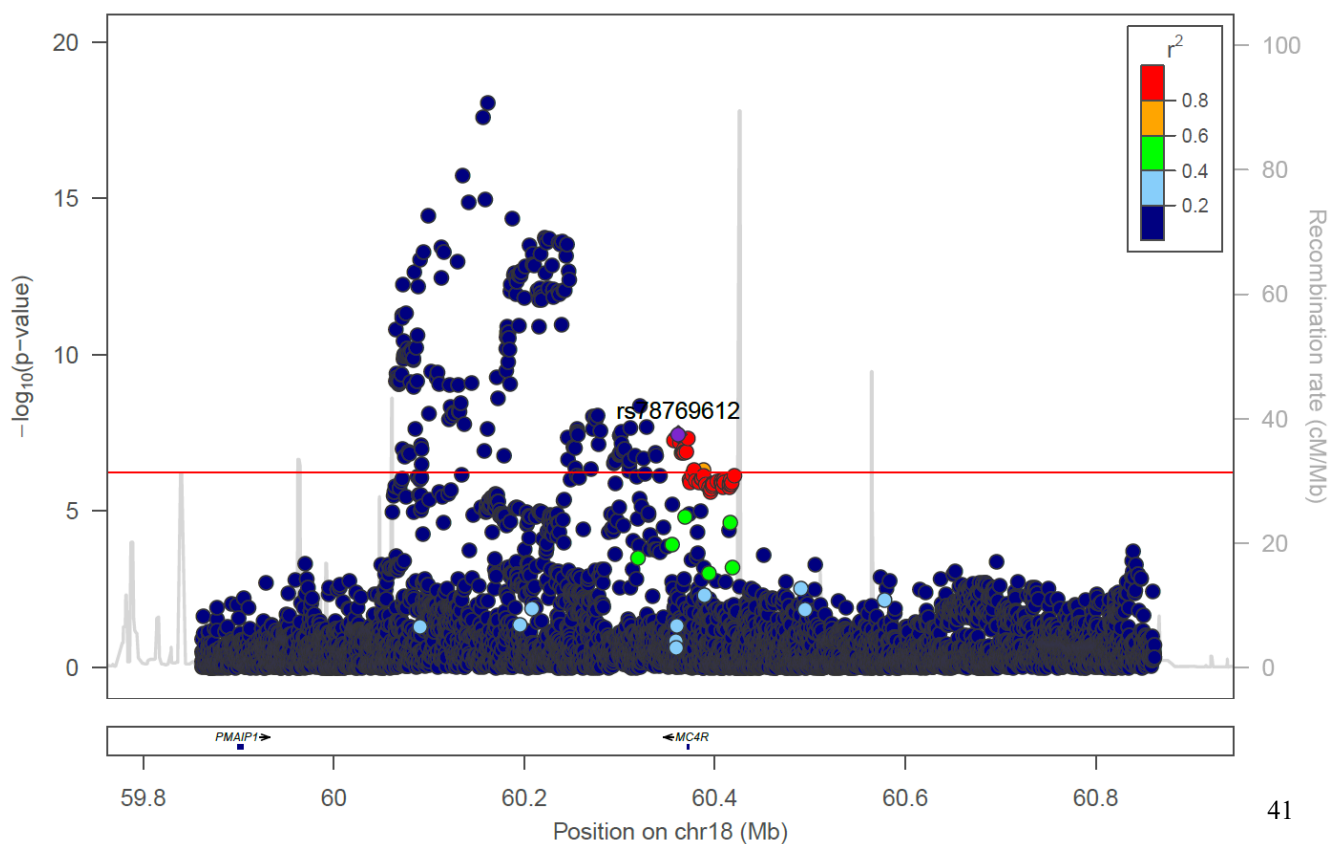
## Supplementary Figure 8. Regional association plots of secondary signals

Regional association plots for each significant secondary signal in the multi-population analysis following conditional analysis on top variant, including all variants  $\pm 500$  kb from index variant. TOPMed study populations were used to calculate LD. The red line indicates  $P = 5.67 \times 10^{-7}$ . A) *ALKAL2*, rs62107261; B) *MC4R*, rs78769612.

### A) *ALKAL2*, rs62107261

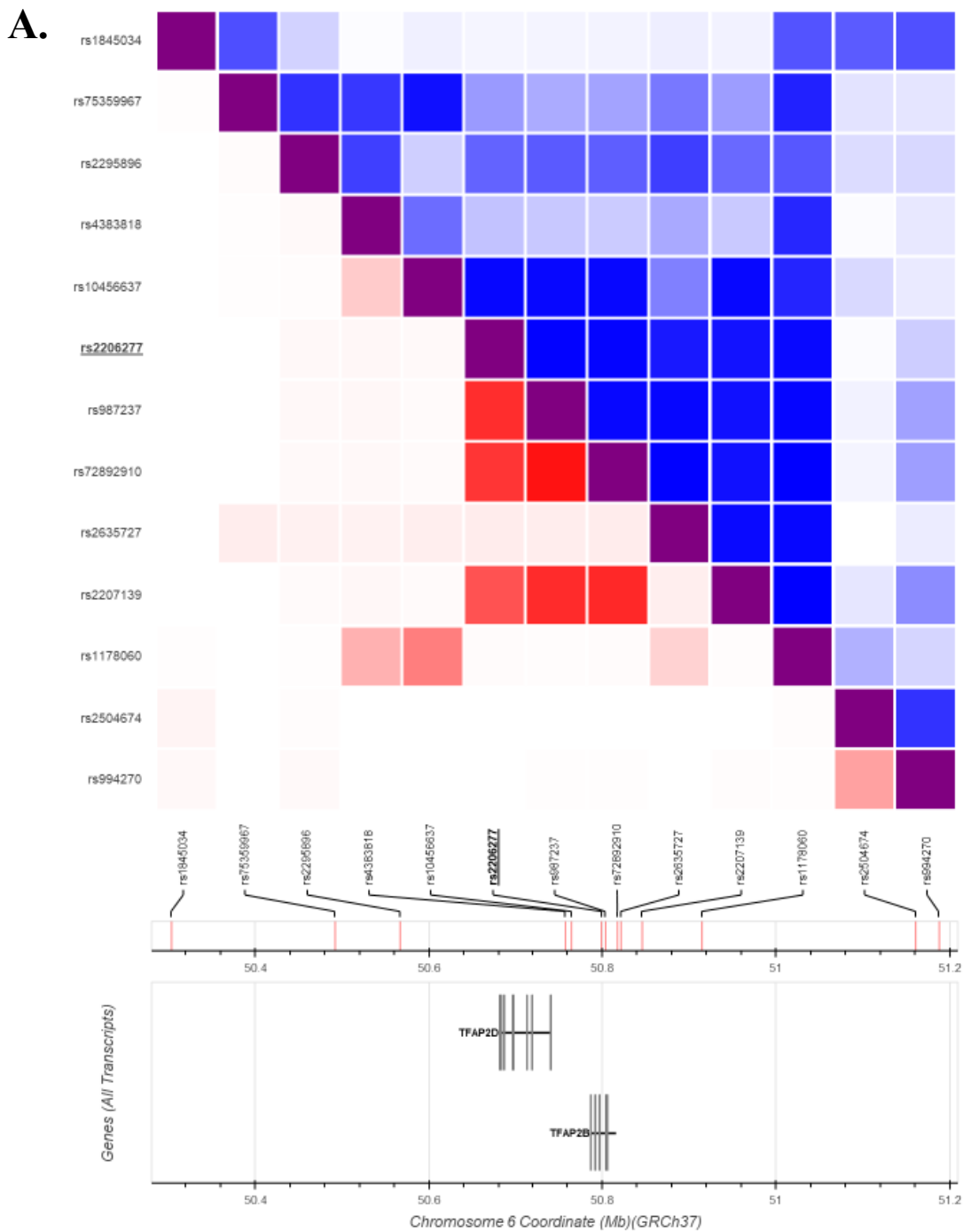


### B) *MC4R*, rs78769612



## Supplementary Figure 9. LD matrix heatmap for conditionally independent SNPs in known BMI-risk loci

Pairwise LD matrix heatmap for lead index SNP in discovery analyses (**bold and underlined**) and published BMI GWAS SNPs within 500 kb (+/-) of index SNPs. A) rs2206277 index SNP in *TFAP2B* locus; B) rs3838785 in *BDNF* locus.



### Correlation

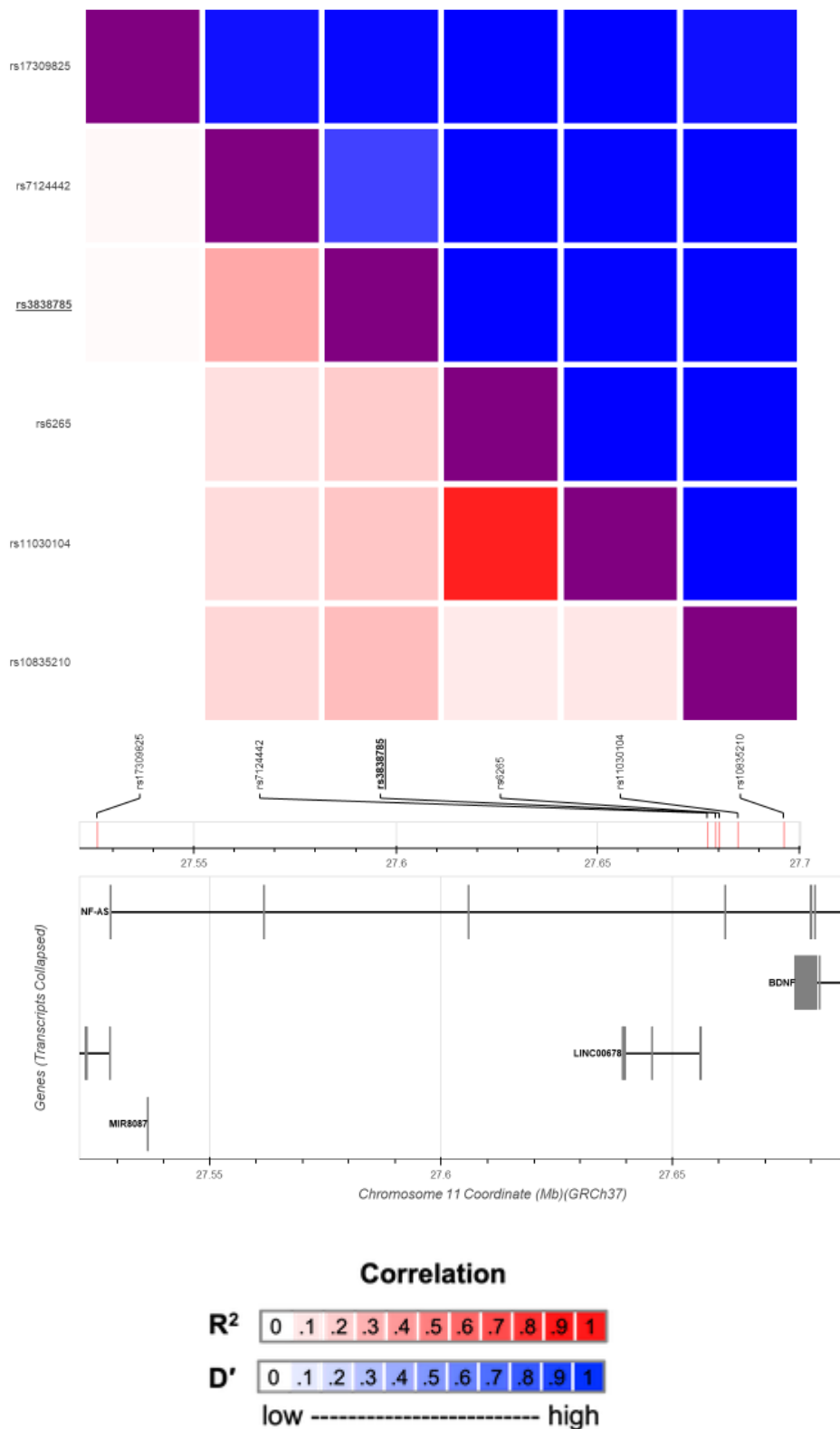


low ----- high

**Supplementary Figure 9. LD matrix heatmap for conditionally independent SNPs in known BMI-risk loci**

Pairwise LD matrix heatmap for lead index SNP in discovery analyses (**bold and underlined**) and published BMI GWAS SNPs within 500 kb (+/-) of index SNPs. A) rs2206277 index SNP in *TFAP2B* locus; B) rs3838785 in *BDNF* locus.

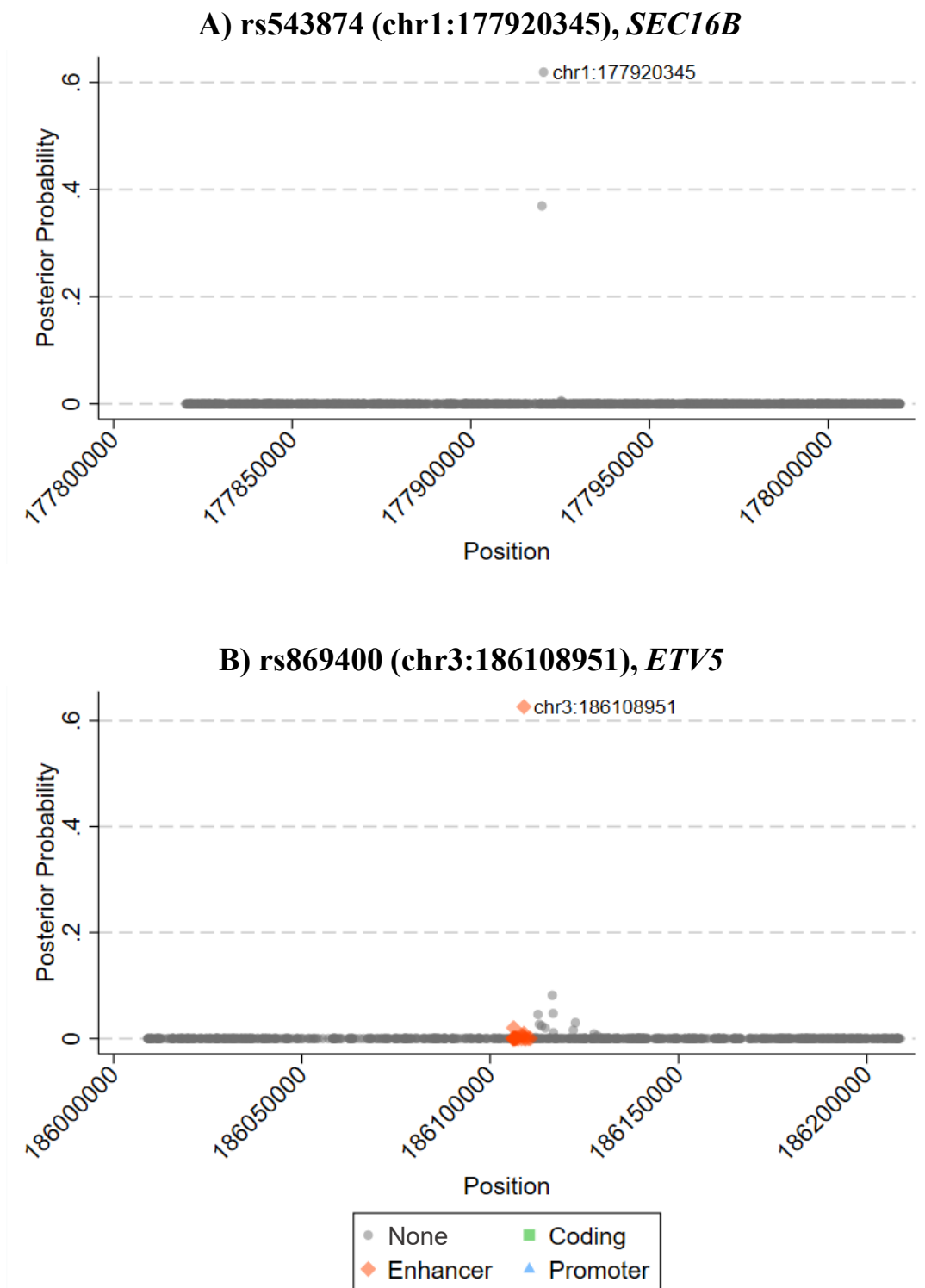
**B.**



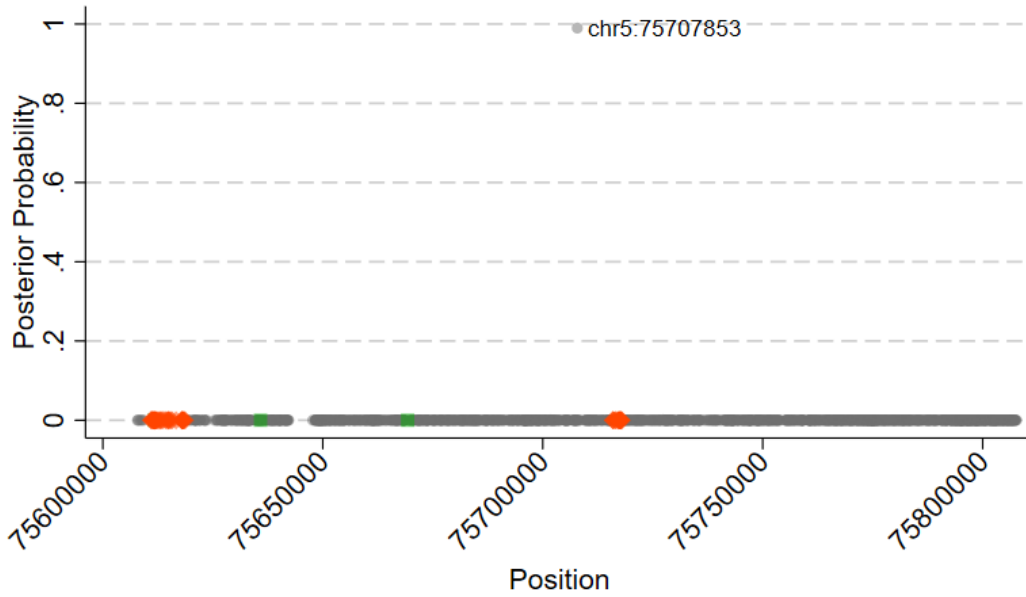
## Supplementary Figure 10. Fine-mapping regional plots

Regional plots of posterior probability (PP) from fine-mapping analysis in PAINTOR, including all variants  $\pm 100$  kb from index variant for each locus with any variant exhibiting a moderate PP  $> 0.5$ . The plots appear in order of chromosomal location. TOPMed study populations were used to calculate LD. Shape and color indicate potential functional consequence of each variant as reported in Variant Effect Prediction (VEP) tool or GeneHancer (see methods for details).

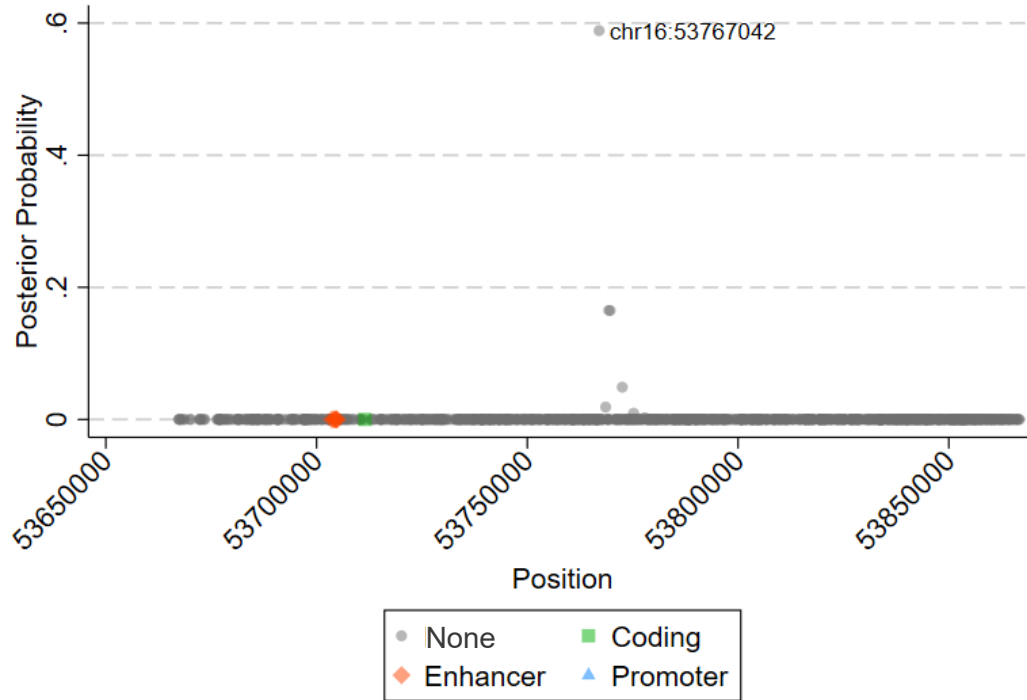
A) rs543874, *SEC16B*; B) rs869400, *ETV5*; C) rs2307111, *POC5*; D) rs1421085, *FTO*; E) rs6567160, *MC4R*; F) rs55731973, *ZC3H4*; G) rs1379871, *DMD*.



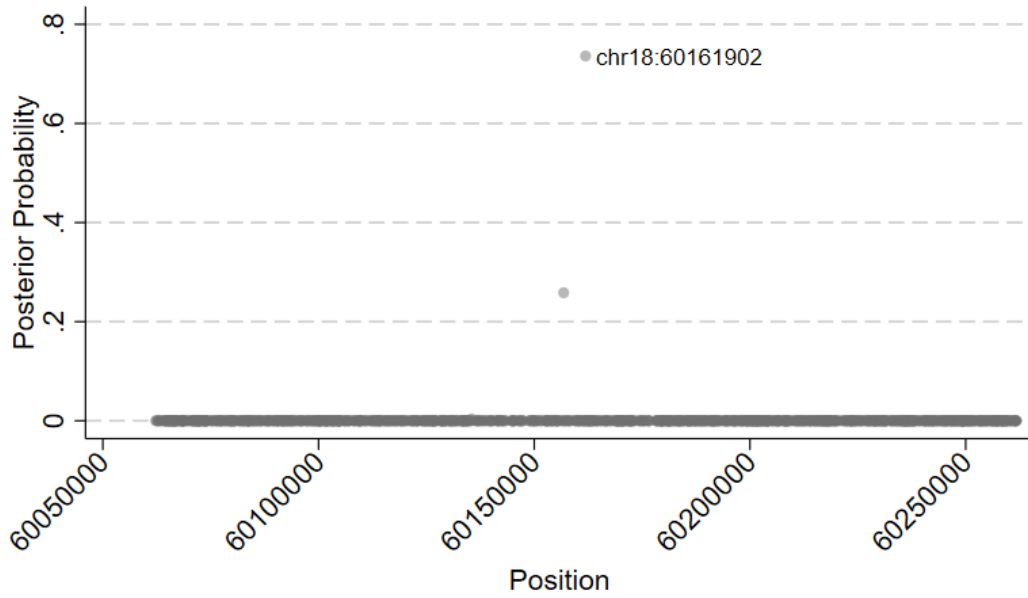
**C) rs2307111 (chr5: 75707853), *POC5***



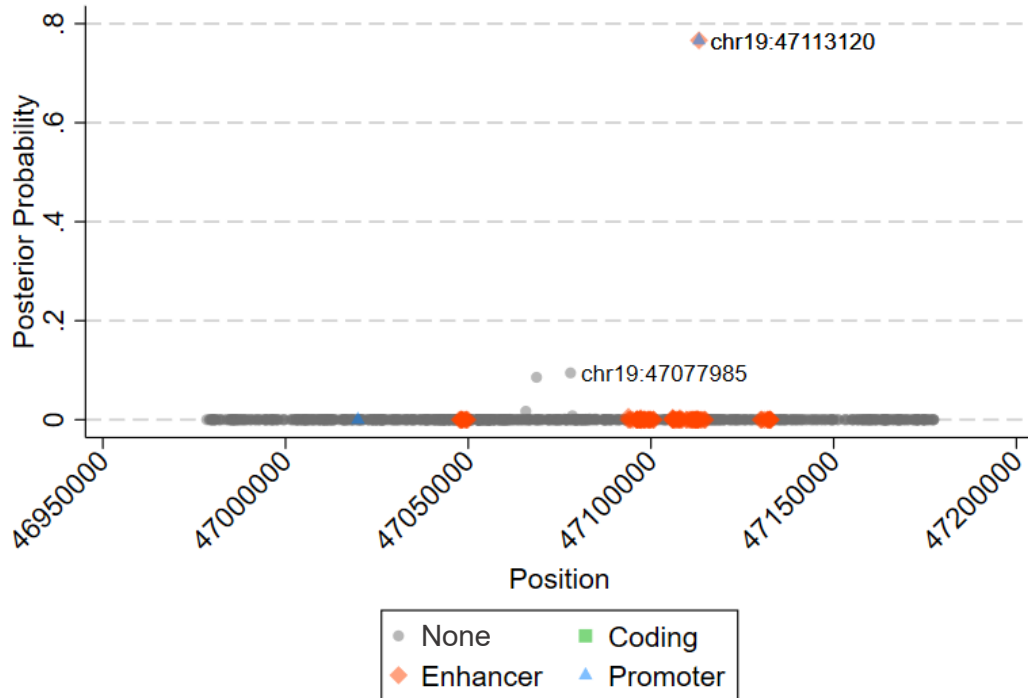
**D) rs1421085 (chr16:53767042), *FTO***



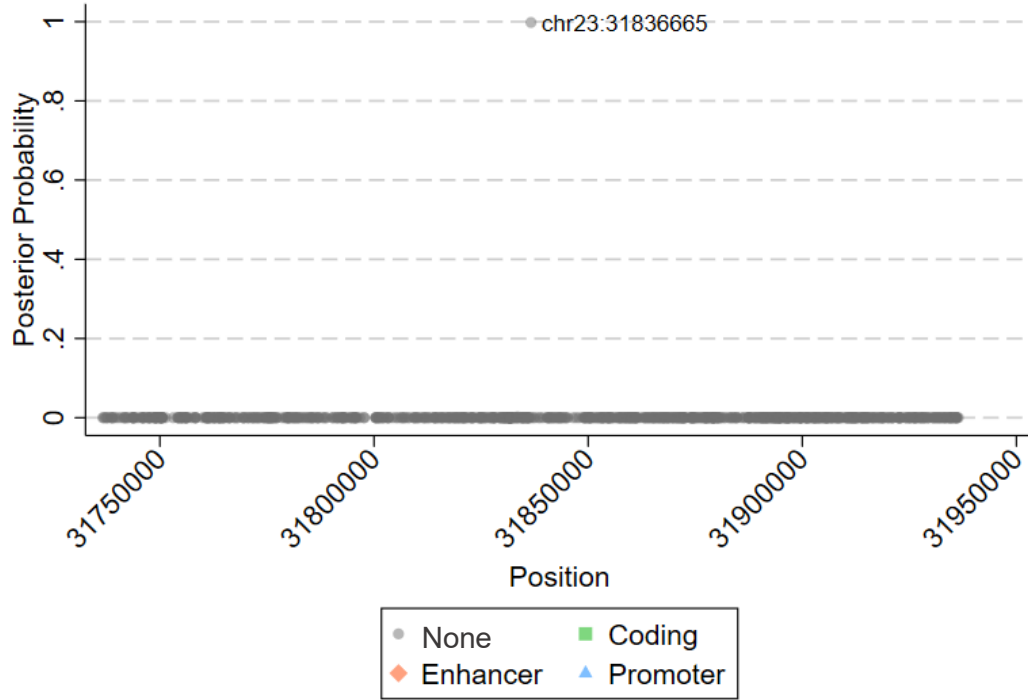
**E) rs6567160 (chr18:60161902), *MC4R***



**F) rs55731973 (chr19:47113120), *ZC3H4***

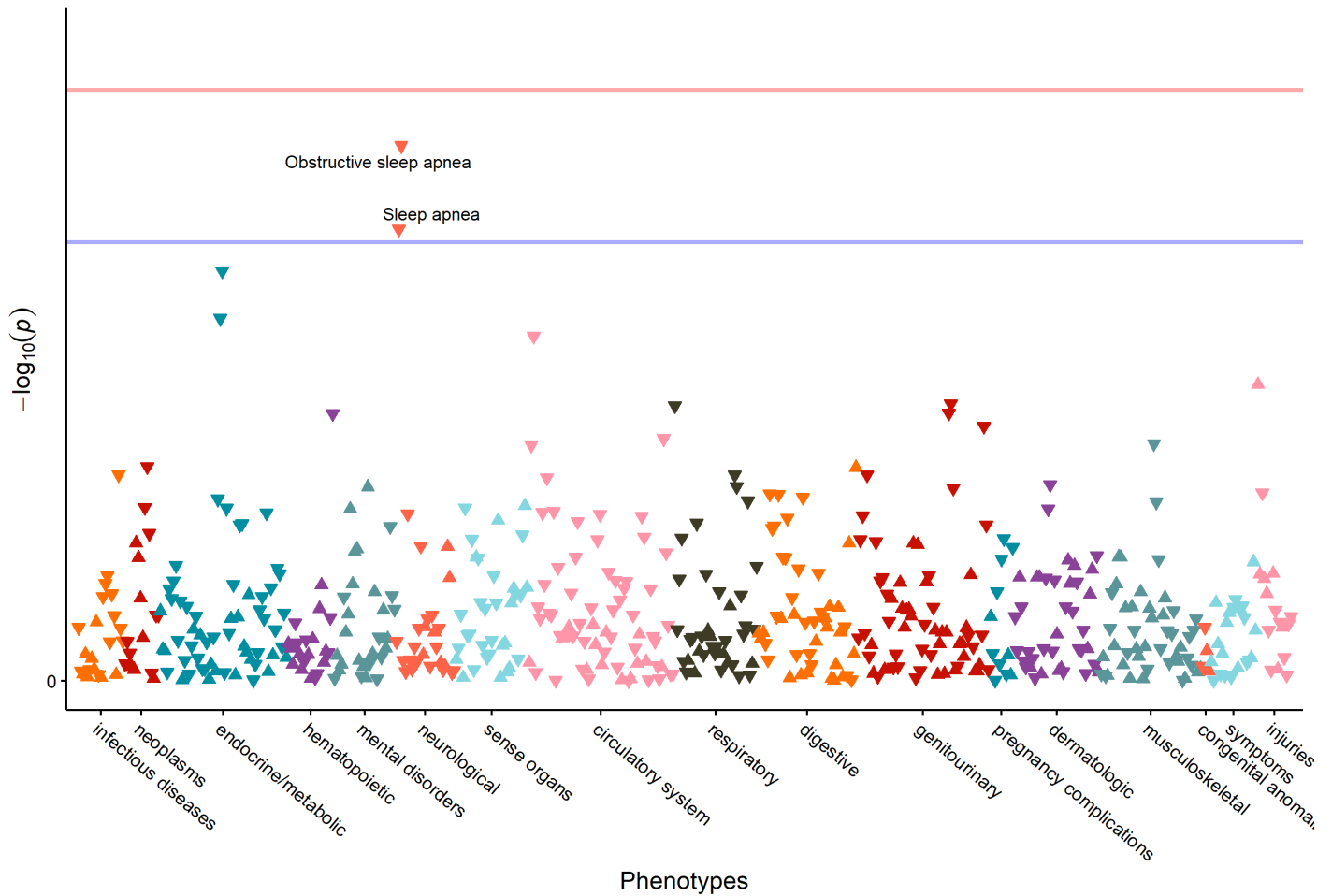


**G) rs1379871 (chrX:31836665), *DMD***



### Supplementary Figure 11. PheWAS meta-analysis Manhattan plot

Manhattan plot of the PheWAS meta-analysis results. The red line indicates phenome-wide significance threshold ( $P < 0.05/538$  PheCodes =  $9.3 \times 10^{-5}$ ), and the blue line indicates suggestive significance ( $P < 0.001$ ). Only suggestively significant PheCodes are annotated with their phenotype. Arrow indicates direction of effect.





Supplementary Data 1. Participant counts by study and population group

Study	Population groups															Total	Individuals with imputed population membership by study, n (%)
	African	Amish	Asian	Barbadian	Central American	Costa Rican	Cuban	Dominican	European	Han Chinese	Mexican	Puerto Rican	Samoan	South American	Taiwanese		
Amish	0	1106	0	0	0	0	0	0	0	0	0	0	0	0	0	1106	0 (0.0%)
ARIC	1503	0	0	0	0	0	0	0	6158	0	0	0	0	0	0	7661	0 (0.0%)
BAGS	0	0	0	248	0	0	0	0	0	0	0	0	0	0	0	248	0 (0.0%)
BioMe	3138	0	408	0	161	0	149	763	3200	0	101	2595	0	289	0	10804	5248 (48.6%)
CARDIA	1379	0	0	0	0	0	0	0	1684	0	0	0	0	0	0	3063	0 (0.0%)
CCAF	0	0	0	0	0	0	1	0	360	0	0	0	0	0	0	361	4 (1.1%)
CFS	493	0	2	0	0	0	0	0	450	0	1	2	0	0	0	948	14 (1.5%)
CHS	711	0	0	0	0	0	0	0	2788	0	12	0	0	0	0	3511	53 (1.5%)
COPDGene	3196	0	0	0	0	0	0	0	6661	0	0	0	0	0	0	9857	0 (0.0%)
CRA	0	0	0	0	0	341	0	0	0	0	0	0	0	0	0	341	123 (36.1%)
DHS (AA CAC)	384	0	0	0	0	0	0	0	0	0	0	0	0	0	0	384	0 (0.0%)
FHS	4	0	1	0	0	0	1	0	4092	0	0	0	0	0	0	4098	480 (11.7%)
GALAH	0	0	0	0	29	0	3	1	2	0	175	130	0	4	0	344	32 (9.3%)
GeneSTAR	777	0	0	0	0	0	0	0	971	0	0	0	0	0	0	1748	0 (0.0%)
GENOA	1193	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1193	0 (0.0%)
GenSalt	0	0	0	0	0	0	0	0	0	1787	0	0	0	0	0	1787	0 (0.0%)
GOLDN	0	0	0	0	0	0	0	0	914	0	0	0	0	0	0	914	0 (0.0%)
HCHS/SOL	23	0	0	0	509	0	1899	1124	33	0	1728	2073	0	297	0	7686	293 (3.8%)
HVH	26	0	8	0	0	0	0	0	650	0	3	2	0	0	0	689	24 (3.5%)
HyperGEN	1838	0	1	0	0	0	0	0	0	0	0	0	0	0	0	1839	0 (0.0%)
JHS	3121	0	0	0	0	0	0	0	0	0	0	0	0	0	0	3121	0 (0.0%)
LTRC	83	0	4	0	0	0	0	0	1276	0	12	8	0	0	0	1383	51 (3.7%)
Mayo_VTE	3	0	0	0	0	0	1	0	920	0	5	1	0	0	0	930	54 (5.8%)
MESA	1846	0	603	0	64	0	35	144	1861	0	544	140	0	81	0	5318	14 (0.3%)
MGH_AF	1	0	0	0	1	0	3	0	974	0	2	0	0	1	0	982	25 (2.5%)
OMG_SCD	443	0	0	0	0	0	0	0	0	0	0	1	0	0	0	444	444 (100.0%)
Partners	4	0	1	0	0	0	0	0	117	0	0	0	0	0	0	122	2 (1.6%)
SAFS	5	0	2	0	0	0	0	0	23	0	1504	0	0	0	0	1534	914 (59.6%)
SAGE	448	0	0	0	0	0	0	0	0	0	0	0	0	0	0	448	1 (0.2%)
Samoan	0	0	0	0	0	0	0	0	0	0	0	1274	0	0	0	1274	0 (0.0%)
THRV	0	0	0	0	0	0	0	0	0	0	0	0	0	0	2053	2053	0 (0.0%)
VAFAR	0	0	0	0	0	0	0	0	173	0	0	0	0	0	0	173	0 (0.0%)
VU_AF	46	0	5	0	1	0	1	0	1030	0	2	0	0	1	0	1086	6 (0.6%)
walk_PHaSST	373	0	0	0	3	0	1	11	1	0	0	0	0	2	0	391	29 (7.4%)
WGHS	0	0	0	0	0	0	0	0	111	0	0	0	0	0	0	111	0 (0.0%)
WHI	1450	0	206	0	8	0	34	3	8985	0	176	39	0	20	0	10921	204 (1.9%)
<b>Total</b>	<b>22488</b>	<b>1106</b>	<b>1241</b>	<b>248</b>	<b>776</b>	<b>341</b>	<b>2128</b>	<b>2046</b>	<b>43434</b>	<b>1787</b>	<b>4265</b>	<b>4991</b>	<b>1274</b>	<b>695</b>	<b>2053</b>	<b>88873</b>	<b>8015 (9.0%)</b>
<b>Individuals with imputed population membership by population group, n (%)</b>	1038 (4.6%)	0 (0.0%)	212 (17.1%)	0 (0.0%)	193 (24.9%)	123 (36.1%)	202 (9.5%)	834 (40.8%)	1249 (2.9%)	0 (0.0%)	1128 (26.4%)	2712 (54.3%)	0 (0.0%)	324 (46.6%)	0 (0.0%)	8015 (9.0%)	

**Supplementary Data 2. BMI and percent female by study**

<b>Study</b>	<b>N</b>	<b>Women, N (%)</b>	<b>BMI, mean (SD)</b>
Amish	1106	552 (49.91)	26.97 (4.65)
ARIC	7661	4230 (55.21)	27.35 (5.23)
BAGS	248	141 (56.85)	28.00 (6.87)
BioMe	10804	6242 (57.77)	29.12 (7.01)
CARDIA	3063	1739 (56.77)	24.45 (4.96)
CCAF	361	69 (19.11)	30.42 (6.34)
CFS	948	521 (54.96)	32.27 (8.75)
CHS	3511	2045 (58.25)	26.84 (4.73)
COPDGene	9857	4608 (46.75)	28.82 (6.26)
CRA	341	197 (57.77)	26.39 (4.30)
DHS (AA CAC)	384	220 (57.29)	33.92 (7.79)
FHS	4098	2224 (54.27)	25.82 (4.83)
GALAII	344	226 (65.70)	27.47 (6.90)
GeneSTAR	1748	1037 (59.32)	29.62 (7.17)
GENOA	1193	835 (69.99)	31.08 (6.66)
GenSalt	1787	843 (47.17)	23.44 (3.12)
GOLDN	914	481 (52.63)	28.33 (5.75)
HCHS/SOL	7686	4478 (58.26)	30.11 (6.40)
HVH	689	241 (34.98)	31.86 (7.90)
HyperGEN	1839	1165 (63.35)	32.01 (7.75)
JHS	3121	1952 (62.54)	31.89 (7.31)
LTRC	1383	664 (48.01)	28.32 (5.91)
Mayo_VTE	930	527 (56.67)	31.29 (8.02)
MESA	5318	2801 (52.67)	28.51 (5.48)
MGH_AF	982	202 (20.57)	28.65 (5.56)
OMG_SCD	444	243 (54.73)	25.22 (6.84)
Partners	122	43 (35.25)	30.80 (7.42)
SAFS	1534	899 (58.60)	31.19 (7.41)
SAGE	448	273 (60.94)	28.11 (7.51)
Samoan	1274	772 (60.60)	33.75 (6.84)
THRV	2053	1043 (50.80)	24.76 (3.47)
VAFAR	173	55 (31.79)	32.70 (6.78)
VU_AF	1086	300 (27.62)	31.19 (6.85)
walk_PHaSST	391	210 (53.71)	24.83 (4.86)
WGHS	111	111 (100.00)	28.20 (6.11)
WHI	10921	10920 (99.99)	28.73 (5.97)

**Supplementary Data 3. BMI and percent female by population group**

<b>Population group</b>	<b>N</b>	<b>Women, N (%)</b>	<b>BMI, mean (SD)</b>
African	22488	13903 (61.82)	30.22 (7.32)
Amish	1106	552 (49.91)	26.97 (4.65)
Asian	1241	711 (57.29)	24.79 (4.42)
Barbadian	248	141 (56.85)	28.00 (6.87)
Central American	776	466 (60.05)	29.98 (6.26)
Costa Rican	341	197 (57.77)	26.39 (4.30)
Cuban	2128	1119 (52.58)	29.20 (5.84)
Dominican	2046	1304 (63.73)	29.05 (5.63)
European	43434	26071 (60.02)	27.76 (5.83)
Han Chinese	1787	843 (47.17)	23.44 (3.12)
Mexican	4265	2555 (59.91)	30.52 (6.72)
Puerto Rican	4991	3027 (60.65)	30.47 (6.95)
Samoan	1274	772 (60.60)	33.75 (6.84)
South American	695	405 (58.27)	28.73 (5.67)
Taiwanese	2053	1043 (50.80)	24.76 (3.47)

Supplementary Data 4. Study-specific descriptive statistics of age and BMI

Study	Population group	Trait	Men						Women					
			N	Mean	SD	Median	Min	Max	N	Mean	SD	Median	Min	Max
<b>Discovery studies</b>														
Amish	Amish	Age (years)	554	49.39	17.29	49	20	90	552	51.63	16.29	53	20	90
		BMI (kg/m <sup>2</sup> )	554	26.16	3.55	25.93	18.43	43.6	552	27.78	5.42	27.47	16.91	46.85
ARIC	African	Age (years)	608	53.95	6.07	53	44	66	895	53.85	5.89	53	45	65
		BMI (kg/m <sup>2</sup> )	608	27.7	4.98	27.05	15.65	52.25	895	31.01	6.96	29.6	14.17	65.77
ARIC	European	Age (years)	2823	54.43	5.7	54	44	66	3335	53.71	5.74	53	44	66
		BMI (kg/m <sup>2</sup> )	2823	27.31	3.91	26.81	16.07	53.75	3335	26.34	5.27	25.26	14.35	54.61
BAGS	Barbadian	Age (years)	107	40.84	12.66	43	18	74	141	38.19	10.83	39	18	72
		BMI (kg/m <sup>2</sup> )	107	26.34	4.95	25.48	15.86	47.55	141	29.26	7.81	28.69	14.84	59.53
BioMe	Asian	Age (years)	212	53.12	13.47	54	23	81	196	46.77	14.42	44.5	21	91
		BMI (kg/m <sup>2</sup> )	212	26.59	5.51	25.43	14.35	49.46	196	24.19	4.61	23.27	17.01	43.41
BioMe	African	Age (years)	1074	52.06	12.63	51	19	90	2064	53.05	13.17	53	19	92
		BMI (kg/m <sup>2</sup> )	1074	28.63	6.36	27.79	15.29	65.61	2064	31.9	8.68	30.42	13.08	78.78
BioMe	Central American	Age (years)	73	52.58	14.4	54	19	77	88	52.45	13.99	55	23	77
		BMI (kg/m <sup>2</sup> )	73	28.59	5.34	28.19	17.54	45.33	88	30.16	5.51	29	17.95	52.48
BioMe	Cuban	Age (years)	76	59.08	12.92	59	27	84	73	57.96	14.01	58	27	89
		BMI (kg/m <sup>2</sup> )	76	29.56	5.44	28.32	20.8	44.94	73	27.28	6.45	25.13	17.14	47.26
BioMe	Dominican	Age (years)	290	61.16	13.47	63	24	97	473	54.34	13.31	55	19	89
		BMI (kg/m <sup>2</sup> )	290	27.92	4.98	27.41	16.17	52.97	473	29.27	5.79	28.26	18.16	58.31
BioMe	Mexican	Age (years)	45	43.87	10.64	42	27	77	56	43.88	10.2	42	31	68
		BMI (kg/m <sup>2</sup> )	45	28.64	4.28	29.07	21.45	37.48	56	27.89	3.97	27.92	19.31	36.33
BioMe	Puerto Rican	Age (years)	962	55.02	12.5	55	25	87	1633	55.22	13.63	55	19	97
		BMI (kg/m <sup>2</sup> )	962	29.36	6.65	28.22	13.31	86.81	1633	31.05	7.11	30.17	14.26	68.02
BioMe	South American	Age (years)	137	57.76	13.24	58	25	91	152	54.38	14.54	56.5	24	83
		BMI (kg/m <sup>2</sup> )	137	28.85	4.99	28.35	19.85	53.11	152	29.42	7	28.23	19.42	70.57
BioMe	European	Age (years)	1693	59.47	14.63	60	19	97	1507	55.31	14.86	56	19	90
		BMI (kg/m <sup>2</sup> )	1693	27.96	5.33	27.01	15.46	63.11	1507	25.97	6.08	24.57	14.15	57.08
CARDIA	African	Age (years)	550	24.15	3.65	24	18	30	829	24.49	3.82	25	18	31
		BMI (kg/m <sup>2</sup> )	550	24.63	4.3	23.94	15.76	44.11	829	26.04	6.56	24.31	14.51	53.42
CARDIA	European	Age (years)	774	25.6	3.27	26	18	30	910	25.59	3.32	26	18	30
		BMI (kg/m <sup>2</sup> )	774	24.35	3.54	23.76	16.81	43.17	910	22.98	4.17	21.96	16.28	46.84
CCAF	Cuban and European*	Age (years)	292	54.34	9.02	56	20	76	69	55.83	10.24	58	22	73
		BMI (kg/m <sup>2</sup> )	292	30.47	5.96	29.02	20.95	70.17	69	30.24	7.79	28.65	16.48	50.2
CFS	European	Age (years)	216	45.81	14.9	44.5	18	81	234	43.49	14.3	41	18	84
		BMI (kg/m <sup>2</sup> )	216	31.4	7.24	29.83	19.33	60.95	234	30.3	8.38	29.08	17.52	66.6
CFS	non-European <sup>1</sup>	Age (years)	211	43.14	14.95	42	18	81	287	44.23	15.13	43	18	86
		BMI (kg/m <sup>2</sup> )	211	31.83	8.28	30.92	12.71	58.86	287	34.86	9.78	32.72	16.09	84.8
CHS	European	Age (years)	1196	73.06	5.55	72	65	94	1592	72.24	5.17	71	65	98
		BMI (kg/m <sup>2</sup> )	1196	26.4	3.69	26.05	15.61	46.23	1592	26.31	4.8	25.75	14.65	48.05
CHS	non-European <sup>2</sup>	Age (years)	270	72.42	5.52	71	65	92	453	72.89	5.62	72	65	93
		BMI (kg/m <sup>2</sup> )	270	27.21	4.27	26.84	16.12	44.17	453	29.64	6.04	29.12	16.34	58.79
COPDGene	African	Age (years)	1765	54.41	6.84	53.1	39.9	80.8	1431	55.13	7.71	53.4	42.4	80.7
		BMI (kg/m <sup>2</sup> )	1765	27.71	5.71	26.76	14.78	55.27	1431	30.82	7.42	30.12	12.67	64.1
COPDGene	European	Age (years)	3484	62.35	8.83	62.5	45	81	3177	61.64	8.87	62	45	85
		BMI (kg/m <sup>2</sup> )	3484	28.85	5.52	28.09	13.75	58.65	3177	28.52	6.55	27.51	12.29	56.01
CRA	Costa Rican	Age (years)	144	41.15	15.02	38.91	18.11	91.62	197	39.3	13.53	36.62	18.07	72.07
		BMI (kg/m <sup>2</sup> )	144	26.02	4.04	25.54	17.25	38.02	197	26.66	4.48	26.43	13.63	40.37
DHS (AA CAC)	African	Age (years)	164	60.01	8.59	60.5	39	79	220	59.42	8.81	60	36	86
		BMI (kg/m <sup>2</sup> )	164	31.59	6.97	30.85	17.6	63.27	220	35.66	7.93	35.04	20.91	64.82
FHS	African, Cuban, European*	Age (years)	1874	38.97	9.95	38	18	83	2224	38.12	9.74	37	18	79
		BMI (kg/m <sup>2</sup> )	1874	27.13	4.14	26.62	16.91	52.15	2224	24.72	5.08	23.44	16.34	58.08
GALAH	Mexican	Age (years)	57	19.46	1.04	19	18	22	118	19.83	1.19	19.8	18.01	21.97

		BMI (kg/m <sup>2</sup> )	57	28.09	7.23	26.5	17.2	52.2	118	27.77	6.93	26.5	17.8	48.1
GALAI	Puerto Rican	Age (years)	48	19.64	0.9	19.79	18	21.21	82	19.34	0.94	19.14	18.02	21.86
		BMI (kg/m <sup>2</sup> )	48	27.2	6.22	25.9	17.6	44.4	82	26.75	7.3	25	17.5	67.5
GALAI	Other <sup>3</sup>	Age (years)	13	19.67	1.06	19.75	18.21	21.46	26	19.9	1.17	19.75	18.05	21.99
		BMI (kg/m <sup>2</sup> )	13	27.73	5.41	29.1	19.5	38.51	26	27.44	6.99	27.15	18.7	50.18
GeneSTAR	African	Age (years)	286	40.73	10.78	41	21	66	491	41.06	10.82	41	21	75
		BMI (kg/m <sup>2</sup> )	286	29.06	6.44	27.87	16.89	53.48	491	32.44	8.4	31.18	16.41	81.19
GeneSTAR	European	Age (years)	425	40.37	10.87	41	21	75	546	43.29	12.32	43	21	79
		BMI (kg/m <sup>2</sup> )	425	28.72	5.1	27.81	16.5	51.13	546	28.08	7.01	26.35	16.99	61.83
GENOA	African	Age (years)	358	57.37	10.2	56.7	29.4	86.1	835	56.46	10.76	56.7	21	90.3
		BMI (kg/m <sup>2</sup> )	358	28.4	4.76	28.24	15.24	50.32	835	32.23	7.02	31.52	17.58	61.37
GenSalt	Han Chinese	Age (years)	944	39.75	8.99	39	18	62	843	38.71	8.84	39	18	59
		BMI (kg/m <sup>2</sup> )	944	23.25	3.08	22.77	16.38	33.82	843	23.66	3.16	23.38	15.87	37.77
GOLDN	European	Age (years)	433	48.42	16.3	48	18	88	481	47.86	16.13	47	18	87
		BMI (kg/m <sup>2</sup> )	433	28.46	4.9	27.89	17.13	50.73	481	28.2	6.42	27.38	16.6	52.66
HCHS/SOL	Central American	Age (years)	201	43.27	13.95	44	18	74	308	45.69	13.4	47	18	74
		BMI (kg/m <sup>2</sup> )	201	29.61	5.74	28.89	17.34	47.3	308	30.87	7.06	29.58	16.64	62.37
HCHS/SOL	Cuban	Age (years)	911	49.33	13.19	51	18	74	988	48.91	12.97	50	18	75
		BMI (kg/m <sup>2</sup> )	911	28.75	5.18	28.33	14.9	50.91	988	29.81	6.37	29.03	14.28	63.78
HCHS/SOL	Dominican	Age (years)	386	45.01	14.78	47	18	75	738	45.74	13.98	47	18	74
		BMI (kg/m <sup>2</sup> )	386	28.61	4.89	28.61	17.3	55.3	738	29.91	6.15	29.13	15.23	60.57
HCHS/SOL	Mexican	Age (years)	680	42.76	14.26	44	18	74	1048	44.91	13.72	46	18	76
		BMI (kg/m <sup>2</sup> )	680	29.7	5.5	28.85	16.33	52.94	1048	31.28	7.14	29.86	17.73	70.35
HCHS/SOL	Puerto Rican	Age (years)	884	46.25	14.43	48	18	74	1189	48.4	14.07	50	18	75
		BMI (kg/m <sup>2</sup> )	884	29.53	6.36	28.56	17.67	55.87	1189	31.8	7.18	30.82	15.62	67.7
HCHS/SOL	South American	Age (years)	116	44.93	12.99	46.5	18	70	181	47.49	13.09	48	18	76
		BMI (kg/m <sup>2</sup> )	116	28.24	4.76	28	17.12	42.65	181	29.33	6.06	28.52	19.5	49.93
HCHS/SOL	Other <sup>4</sup>	Age (years)	30	47.93	14.36	48.5	21	74	26	45.12	17.59	42	20	74
		BMI (kg/m <sup>2</sup> )	30	28.75	6.28	27.27	17.65	48.49	26	31.94	8.48	31.39	19.04	61.32
HVH	European	Age (years)	423	61.36	11.1	60	31	89	227	63.86	13.67	64	21	90
		BMI (kg/m <sup>2</sup> )	423	30.89	6.69	29.53	17.07	74.34	227	33.34	8.99	31.64	18.71	67.49
HVH	non-European <sup>5</sup>	Age (years)	25	60	13.69	59	35	88	14	51.21	12.32	49.5	23	69
		BMI (kg/m <sup>2</sup> )	25	31.28	10.45	29.6	20.68	76.05	14	38.36	11.28	35.26	23.78	64.73
HyperGEN	African and Asian*	Age (years)	674	46.42	12.43	46	18	85	1165	47.01	13	47	18	84
		BMI (kg/m <sup>2</sup> )	674	29.6	6.31	28.55	16.51	56.66	1165	33.41	8.15	32.13	16.18	73.68
JHS	African	Age (years)	1169	53.58	12.91	54	21	89	1952	54.69	12.78	55	20	91
		BMI (kg/m <sup>2</sup> )	1169	30.06	6.31	29.03	16.35	66.09	1952	32.99	7.65	31.92	16.02	91.8
LTRC	European	Age (years)	665	64.09	10.44	65	25	87	611	62.65	10.55	64	21	88
		BMI (kg/m <sup>2</sup> )	665	28.74	4.97	28.39	16.37	58.63	611	27.74	6.61	27.17	13.28	52.28
LTRC	non-European <sup>6</sup>	Age (years)	54	61.3	9.66	61	40	83	53	56.77	12.25	57	24	80
		BMI (kg/m <sup>2</sup> )	54	27.17	5.85	26.57	17.37	40	53	30.77	7.16	29.62	19.18	51.01
Mayo_VTE	African, Cuban, European, Mexican, Puerto Rican*	Age (years)	403	58.47	15.33	60	18	91	527	52.42	17.05	53	19	95
		BMI (kg/m <sup>2</sup> )	403	31.13	6.6	29.94	18.21	70.53	527	31.42	8.95	29.71	17.14	69.63
MESA	Asian	Age (years)	302	61.44	10.2	61	44	84	301	60.95	10.11	60	44	83
		BMI (kg/m <sup>2</sup> )	302	24.19	3.09	23.86	16.09	33.48	301	23.96	3.31	23.82	16.63	35.35
MESA	African	Age (years)	815	59.43	9.61	58	39	84	1031	60.13	8.98	59	44	91
		BMI (kg/m <sup>2</sup> )	815	29	4.84	28.61	17.4	52.46	1031	31.07	6.25	30.12	15.68	53.45
MESA	Central American	Age (years)	25	56.2	6.95	56	46	68	39	58.46	8.87	59	46	77
		BMI (kg/m <sup>2</sup> )	25	28.73	4.73	27.96	23.01	45.64	39	30.33	5.38	30.41	20.44	47.46
MESA	Cuban	Age (years)	17	65.76	11.62	68	45	81	18	70.06	8.13	70	51	82
		BMI (kg/m <sup>2</sup> )	17	27.87	4.26	26.41	22.02	36.24	18	28.71	6.21	27.36	21.39	46.82
MESA	Dominican	Age (years)	63	57.4	9.65	55	45	80	81	59.33	9.64	59	45	79
		BMI (kg/m <sup>2</sup> )	63	27.4	3.85	26.89	18.91	39.34	81	28.17	4.47	27.48	19.95	38.5
MESA	Mexican	Age (years)	283	60.7	10.16	60	44	84	261	60.28	9.64	60	44	82
		BMI (kg/m <sup>2</sup> )	283	29.33	4.46	28.83	17.57	46.28	261	30.98	5.99	30.35	18.84	52.48

MESA	Puerto Rican	Age (years)	63	57.9	8.67	56	45	79	77	59.45	9.37	57	45	81	
		BMI (kg/m <sup>2</sup> )	63	28.8	4.21	28.75	21.89	43.9	77	30.73	6.51	28.67	20.13	51.56	
MESA	South American	Age (years)	34	60.68	9.85	60	45	80	47	61.83	11.1	61	45	84	
		BMI (kg/m <sup>2</sup> )	34	27.2	2.87	27.05	22.92	33.95	47	27.93	4.67	27.77	18.3	39.61	
MESA	European	Age (years)	915	61.63	9.67	62	45	83	946	61.4	9.95	61	44	84	
		BMI (kg/m <sup>2</sup> )	915	27.98	3.98	27.61	19.01	42.41	946	27.59	5.81	26.52	16.87	48.99	
MGH_AF	European, Mexican, South American*	Age (years)	780	53.81	10.69	55	19	82	202	56.77	10.27	58	18	80	
		BMI (kg/m <sup>2</sup> )	780	28.8	5.11	27.88	15.2	57.5	202	28.07	7.03	26.56	17.14	54.73	
OMG_SCD	African and Puerto Rican*	Age (years)	201	31.68	11.95	29	18	84	243	34.56	12.36	33	18	70	
		BMI (kg/m <sup>2</sup> )	201	24.22	5.88	23.2	13.8	59	243	26.04	7.45	24.3	16	58	
Partners	African, Asian, European*	Age (years)	79	48.46	9.47	51	23	60	43	50.16	8.97	53	21	63	
		BMI (kg/m <sup>2</sup> )	79	30.78	7.16	29.29	21.46	59.37	43	30.84	7.96	29.65	19.27	53.59	
SAFS	Mexican	Age (years)	620	42.14	17.28	40	18	90	884	44.74	16.74	44	18	97	
		BMI (kg/m <sup>2</sup> )	620	30.32	7.01	29.59	14.36	65.62	884	31.8	7.63	31.07	15.55	70.2	
SAFS	non-Mexican <sup>7</sup>	Age (years)	15	38.27	17.51	31	18	75	15	37.8	13.8	32	20	66	
		BMI (kg/m <sup>2</sup> )	15	28.99	6.36	30.02	19.5	39.67	15	33.72	7.68	33	20.81	49.13	
SAGE	African	Age (years)	175	20.87	4.45	19.7	18	40.9	273	22.2	5.91	20	18	40.7	
		BMI (kg/m <sup>2</sup> )	175	26.55	6.22	24.5	17.5	49.2	273	29.11	8.09	27	16.26	56.9	
Samoan	Samoan	Age (years)	502	45.04	11.54	46.13	24.62	64.96	772	44.2	11.16	43.78	24.53	65	
		BMI (kg/m <sup>2</sup> )	502	31.37	5.83	30.75	18.56	54.06	772	35.3	7	35.04	18.05	61.07	
THRIV	Taiwanese	Age (years)	1010	52.25	9.95	51	29	86	1043	51.71	9.63	51	18	86	
		BMI (kg/m <sup>2</sup> )	1010	25.35	3.35	25.24	15.87	42.45	1043	24.19	3.49	23.64	15.37	35.82	
VAFAR	European	Age (years)	118	57.07	8.63	58.5	32.53	78.21	55	60.49	8.22	61.54	25.68	74.78	
		BMI (kg/m <sup>2</sup> )	118	32.27	6.15	31.41	22.2	56.92	55	33.62	7.94	32.74	21.11	53.26	
VU_AF	European	Age (years)	750	53.17	10.69	55	19	80	280	53.72	11.76	56.5	18	81	
		BMI (kg/m <sup>2</sup> )	750	31.1	6.42	30.12	16.81	69.64	280	31.27	7.63	30.1	18.79	55.76	
VU_AF	non-European <sup>8</sup>	Age (years)	36	45.47	11.12	48	21	65	20	48.6	10.06	48	29	63	
		BMI (kg/m <sup>2</sup> )	36	31.36	8.36	29.79	20.36	66.29	20	32.75	8.16	30.57	22.08	52.87	
walk_PhaSST	African, Central American, Cuban, Dominican, European, South American*	Age (years)	181	35.59	12.23	33.2	18.3	72	210	39.91	13.13	39.5	18.3	84	
		BMI (kg/m <sup>2</sup> )	181	23.77	4.28	22.84	17.09	38.67	210	25.75	5.15	24.97	15.24	45.23	
WGHS	European	Age (years)	n/a	n/a	n/a	n/a	n/a	n/a	111	49.38	3.46	48	45	59	
		BMI (kg/m <sup>2</sup> )	n/a	n/a	n/a	n/a	n/a	n/a	111	28.2	6.11	27.37	18.88	57.61	
WHI	Asian	Age (years)	n/a	n/a	n/a	n/a	n/a	n/a	206	66.49	7.27	67.24	50	79.04	
		BMI (kg/m <sup>2</sup> )	n/a	n/a	n/a	n/a	n/a	n/a	206	25.18	4.5	24.5	16.83	42.33	
WHI	African	Age (years)	n/a	n/a	n/a	n/a	n/a	n/a	1450	63.58	7.04	63.21	50	80.84	
		BMI (kg/m <sup>2</sup> )	n/a	n/a	n/a	n/a	n/a	n/a	1450	31.55	6.19	30.63	17.73	60.91	
WHI	Cuban	Age (years)	n/a	n/a	n/a	n/a	n/a	n/a	34	64	8.28	64.04	51.05	78.55	
		BMI (kg/m <sup>2</sup> )	n/a	n/a	n/a	n/a	n/a	n/a	34	28.78	4.98	28.35	19.35	44.11	
WHI	Mexican	Age (years)	n/a	n/a	n/a	n/a	n/a	n/a	176	62.62	6.81	62.28	50.02	78.1	
		BMI (kg/m <sup>2</sup> )	n/a	n/a	n/a	n/a	n/a	n/a	176	29.07	5.37	28.16	18.63	45.55	
WHI	Puerto Rican	Age (years)	n/a	n/a	n/a	n/a	n/a	n/a	39	62.74	6.39	63.05	51.09	76.01	
		BMI (kg/m <sup>2</sup> )	n/a	n/a	n/a	n/a	n/a	n/a	39	28.78	6.03	27.88	20.53	48.68	
WHI	South American	Age (years)	n/a	n/a	n/a	n/a	n/a	n/a	20	63.73	7.84	64.53	50.18	75.2	
		BMI (kg/m <sup>2</sup> )	n/a	n/a	n/a	n/a	n/a	n/a	20	26.98	3.93	26.36	21.15	38.09	
WHI	European <sup>9</sup>	Age (years)	n/a	n/a	n/a	n/a	n/a	n/a	8985	67.37	6.54	68.07	49.92	80.07	
		BMI (kg/m <sup>2</sup> )	n/a	n/a	n/a	n/a	n/a	n/a	8985	28.36	5.83	27.34	15.59	60.91	
WHI	Other <sup>10</sup>	Age (years)	n/a	n/a	n/a	n/a	n/a	n/a	11	63.29	7.99	61.08	52.35	78.09	
		BMI (kg/m <sup>2</sup> )	n/a	n/a	n/a	n/a	n/a	n/a	11	27.02	7.62	24.98	20.84	47.59	
TOTAL		Age (years)	35764	52.16	14.98	53	18	97	53109	54.47	15.16	56	18	98	
		BMI (kg/m <sup>2</sup> )	35764	28.12	5.54	27.31	12.71	86.81	53109	28.98	7.02	27.73	12.29	91.8	
<b>Replication studies</b>															
Study	Population group	Trait	Men						Women						
			N	Mean	SD	Median	Min	Max	N	Mean	SD	Median	Min	Max	
MEC		Age (years)	3281	59.72	7.4	61	44	70	3825	57.65	7.61	57	44	70	
		BMI (kg/m <sup>2</sup> )	3281	27.64	4.31	27.18	10.87	54.16	3825	29.5	6.25	28.38	13.42	68.73	

MVP	African, African American, Black	Age (years)	69346	58.92	11.65	60	20	103		10543	48.59	11.37	50	20	94
		BMI (kg/m <sup>2</sup> )	69346	30.06	6.07	29.42	12.21	85.46		10543	31.42	6.32	30.83	14.18	66.8
BioMe		Age (years)	2492	48.63	13.92	49.56	18.01	83.24		4146	48.95	15.1	49.32	18.02	84.04
		BMI (kg/m <sup>2</sup> )	2492	28.47	6.55	27.46	14.13	69.09		4146	31.89	8.66	30.61	13.08	89.14
UKBB		Age (years)	3718	51.65	8.23	50	39	70		5148	52.05	7.95	51	40	70
		BMI (kg/m <sup>2</sup> )	3718	28.33	4.29	27.93	16.66	57.48		5148	30.34	5.98	29.59	16.02	68.13
REGARDS		Age (years)	3409	64.03	9.06	63	45	94		5312	63.37	9.27	62	45	96
		BMI (kg/m <sup>2</sup> )	3409	28.97	5.49	28.43	12.31	51.73		5312	32.02	7.14	31.09	12.16	89.44

BMI, body mass index; SD, standard deviation; n/a, not available

\*Combined because when stratified by sex, the number of participant is  $\leq 5$  in at least one of the population group.

1. CFS non-European: Collapsed African, Asian, Mexican, and Puerto Rican.
2. CHS non-European: Collapsed African and Mexican.
3. GALA II Other: Collapsed Central American, Cuban, Dominican, European, and South American.
4. HCHS\_SOL Other: Collapsed African and European.
5. HVH non-European: Collapsed African, Asian, Mexican, and Puerto Rican.
6. LTRC non-European: Collapsed African, Asian, Mexican, and Puerto Rican.
7. SAFS non-Mexican: Collapsed African, Asian, and European.
8. VU\_AF non-European: Collapsed African, Asian, South American, Central American, Cuban, and Mexican.
9. WHI European includes 1 participant who is biologically male.
10. WHI Other: Collapsed Central American and Dominican.

Supplementary Data 5. Genome-wide significant variants by locus and ALT frequency by population group

CHR	POS (hg38)	REF	ALT	ALT Freq	rsID	Beta	SE	P-value	PVE (%)	Known index variant <sup>a</sup>	OASIS annotation	Nearest gene	Novel locus <sup>b</sup>	ALT frequency by population group														
														African	Amish	Asian	Barbadian	Central American	Costa Rican	Cuban	Dominican	European	Han Chinese	Mexican	Puerto Rican	Samoan	South American	Taiwanese
1	177920345	A	G	20%	rs543874	0.0639	0.0060	1.38E-26	0.128	Yes	intergenic	<i>SEC16B</i>	No	25%	15%	15%	29%	26%	23%	19%	21%	19%	22%	18%	22%	5%	21%	16%
2	621558	C	T	85%	rs939584	0.0576	0.0068	1.99E-17	0.081	No	intergenic	<i>TMEM18</i>	No	12%	18%	10%	12%	12%	8%	15%	14%	18%	11%	11%	16%	1%	12%	8%
2	24927427	A	G	56%	rs10182181	0.0350	0.0052	1.76E-11	0.051	Yes	intergenic	<i>ADCY3</i>	No	16%	65%	54%	11%	63%	63%	52%	36%	53%	57%	67%	47%	47%	65%	56%
3	186108951	T	G	82%	rs869400	0.0383	0.0063	1.21E-09	0.042	No	UTR5	<i>ETV5</i>	No	23%	11%	7%	25%	11%	9%	18%	20%	18%	2%	10%	19%	5%	12%	7%
4	45179317	A	T	36%	rs12507026	0.0449	0.0051	9.55E-19	0.088	Yes	intergenic	<i>GNPDA2</i>	No	24%	32%	28%	27%	37%	48%	40%	34%	43%	32%	37%	37%	21%	41%	28%
5	75707853	T	C	55%	rs23071111	-0.0324	0.0053	7.43E-10	0.043	Yes	exonic, missense	<i>POC5</i>	No	15%	55%	43%	10%	53%	52%	52%	38%	59%	42%	61%	46%	55%	54%	44%
6	50830813	C	T	19%	rs2206277	0.0543	0.0062	2.05E-18	0.086	Novel	intronic	<i>TFAP2B</i>	No	14%	12%	25%	11%	30%	28%	18%	18%	18%	24%	39%	24%	10%	34%	21%
8	76068626	A	G	47%	rs830463	0.0305	0.0049	6.58E-10	0.043	No	intergenic	<i>HNF4G</i>	No	33%	60%	37%	30%	46%	50%	49%	43%	56%	35%	51%	48%	24%	48%	36%
11	27657463	GT	G	58%	rs3838785	-0.0303	0.0051	3.14E-09	0.040	Novel	ncRNA_intronic, deletion	<i>BDNF</i>	No	63%	21%	27%	63%	57%	55%	38%	52%	31%	26%	52%	48%	32%	53%	24%
12	49853685	G	A	30%	rs7138803	0.0363	0.0054	1.69E-11	0.051	Yes	intergenic	<i>BCDIN3D</i>	No	18%	40%	29%	17%	22%	15%	31%	23%	38%	29%	24%	26%	10%	23%	27%
13	53533448	G	T	14%	rs9568868	0.0472	0.0072	5.73E-11	0.048	No	intergenic	<i>OLFM4</i>	No	5%	28%	24%	2%	31%	33%	13%	11%	13%	25%	34%	19%	43%	33%	25%
16	53767042	T	C	29%	rs1421085	0.0901	0.0056	6.11E-59	0.295	Yes	intronic	<i>FTO</i>	No	11%	50%	19%	9%	21%	30%	35%	25%	42%	10%	22%	27%	20%	23%	14%
18	60161902	T	C	21%	rs6567160	0.0525	0.0059	8.22E-19	0.088	Yes	intergenic	<i>MC4R</i>	No	19%	31%	20%	25%	12%	14%	19%	20%	23%	24%	12%	19%	17%	12%	20%
19	47077985	C	T	50%	rs28590228	0.0332	0.0053	4.75E-10	0.044	No	intronic	<i>ZC3H4</i>	No	20%	66%	33%	18%	48%	59%	58%	40%	68%	29%	57%	46%	68%	51%	26%
22	29906934	C	T	4%	rs111490516	0.0783	0.0133	4.52E-09	0.039	Novel	intronic	<i>MTMR3</i>	Yes	13%	0%	0%	13%	2%	0%	2%	5%	0%	0%	1%	3%	0%	1%	0%
X	31836665	G	C	41%	rs1379871	0.0287	0.0042	1.35E-11	0.052	Yes	intronic	<i>DMD</i>	No	45%	18%	63%	52%	62%	53%	40%	42%	33%	70%	62%	47%	48%	64%	67%

CHR, chromosome; POS, position; REF, reference allele; ALT, alternative allele; ALT freq, alternative allele frequency; SE, standard error; PVE, percent variance explained; OASIS, Omics Analysis, Search & Information System

<sup>a</sup> Known index variant 'Yes' indicates previously published index variant from NHGRI-EBI GWAS Catalog; 'No' indicates index variant within 500 kb ± of the published lead variant, not independent of known signal in conditional analysis; 'Novel' indicates new lead variant either not published or conditionally independent.

<sup>b</sup> Novel locus 'Yes' was defined if there is no known index variant within 500 kb ± of the lead variant in current analysis.



**Supplementary Data 6. Genome-wide significant variants by locus from African and European population group-specific analyses**

Population group	rsID	CHR	POS (hg38)	REF/ALT	ALT Freq	Beta	SE	P- value	PVE (%)	Nearest Gene	Known index variant <sup>a</sup>	Novel locus <sup>b</sup>	Index SNP in discovery analysis	Distance from index SNP	R <sup>2</sup>
African	rs543874	1	177920345	A/G	25.0%	0.0731	0.0111	4.00E-11	0.194	<i>SEC16B</i>	Yes	No	rs543874 (self)	0	-
	rs62033408	16	53794050	A/G	10.6%	0.0982	0.0159	6.72E-10	0.170	<i>FTO</i>	No	No	rs1421085	27008	0.951
	rs73396827	22	29906123	C/T	12.6%	0.0873	0.0145	1.66E-09	0.162	<i>MTMR3</i>	No	Yes	rs111490516	811	0.997
European	rs539515	1	177919890	A/C	18.9%	0.0556	0.0088	2.22E-10	0.093	<i>SEC16B</i>	No	No	rs543874	455	0.997
	rs62107261	2	422144	T/C	4.8%	-0.1015	0.0160	2.08E-10	0.093	<i>ALKAL2</i>	Yes	No	rs939584	199414	0.000 <sup>c</sup>
	rs13130484	4	45173674	C/T	43.1%	0.0439	0.0069	2.28E-10	0.093	<i>GNPDA2</i>	No	No	rs12507026	5643	0.986
	rs62405422	6	50829192	T/C	18.5%	0.0552	0.0089	4.74E-10	0.089	<i>TFAP2B</i>	No	No	rs2206277	1621	0.997
	rs1459184	8	76032892	A/T	54.2%	0.0437	0.0069	2.28E-10	0.093	<i>HNF4G</i>	No	No	rs830463	35734	0.912
	rs1421085	16	53767042	T/C	41.9%	0.0917	0.0070	1.22E-39	0.400	<i>FTO</i>	Yes	No	rs1421085 (self)	0	-
	rs17175643	18	60229509	C/T	26.3%	0.0486	0.0078	4.11E-10	0.090	<i>MC4R</i>	No	No	rs6567160	67607	0.751

CHR, chromosome; POS, position; REF, reference allele; ALT, alternative allele; ALT freq, alternative allele frequency; SE, standard error; PVE, percent variance explained; SNP, single nucleotide polymorphism

<sup>a</sup> Known index variant 'Yes' indicates previously published index variant from NHGRI-EBI GWAS Catalog; 'No' indicates index variant within 500 kb ± of the published lead variant, not independent of known signal in conditional analysis; 'Novel' indicates new lead variant either not published or conditionally independent.

<sup>b</sup> Novel locus 'Yes' was defined if there is no known index variant within 500 kb ± of the lead variant in current analysis.

<sup>c</sup> Linkage disequilibrium was calculated using our own data in the total population. All other R<sup>2</sup> values were calculated using TOPLD (<http://topld.genetics.unc.edu/>).

**Supplementary Data 7. Replication of rs111490516**

<b>Study</b>	<b>N</b>	<b>Imputation reference panel</b>	<b>Imputation R<sup>2</sup></b>	<b>Freq</b>	<b>Beta</b>	<b>SE</b>	<b>P-value</b>
MEC	7,907	1000 Genomes	0.9910	0.113	0.0354	0.0236	0.1325
MVP	79,889	1000 Genomes Project phase 3, version 5	0.7083	0.109	0.0181	0.0090	0.0442
BioMe	4,413	TOPMed	0.9775	0.125	0.0439	0.0311	0.1939
UKBB	8,863	UK10K + HRC	0.9827	0.129	0.0260	0.0222	0.2414
REGARDS	8,676	TOPMed	0.9981	0.125	0.0521	0.0226	0.0213
<b>Meta-analysis</b>	<b>109,748</b>			<b>0.114</b>	<b>0.0253</b>	<b>0.0072</b>	<b>4.76E-04</b>
Discovery	88,873			0.037	0.0783	0.0133	4.52E-09
<b>Meta-analysis of Discovery + Replication</b>	<b>198,621</b>			<b>0.079</b>	<b>0.0372</b>	<b>0.0063</b>	<b>4.19E-09</b>

*Freq, frequency; SE, standard error*

*MEC, Multiethnic Cohort Study; MVP, Million Veteran Program; BioMe, BioMe BioBank; UKBB, United Kingdom BioBank; REGARDS, Reasons for Geographic And Racial Differences in Stroke Study*

Supplementary Data 8. Variant annotation from Variant Effect Predictor (VEP) for all SNPs in high LD ( $R^2 > 0.8$ ) with top SNP in novel *MTMR3* locus.

Uploaded_variation	Location	Allele	Consequence	IMPACT	Entrez Gene	SYMBOL	Feature_type	Feature	BIOTYPE	INTRON N	HGVSc	Existing_variation	DISTANCE	STRAND	AF	SOMATIC	PHENO	CADD_PHEU D	CADD_RAW	SpliceAI_pred_DS_AG	SpliceAI_pred_DS_AL	SpliceAI_pred_DS_DG	SpliceAI_pred_DS_DL	SpliceAI_pred_SYMBOL	
rs111490516	22:29906934-29906934	T	intron_variant	-	<i>MTMR3</i>	Transcript	ENST00000323630.9	protein coding	-	1/18	-	-	-	1	0.0397	-	-	-	-0.229	0.00	0.00	0.00	0.00	<i>MTMR3</i>	
		T	intron_variant	-	<i>MTMR3</i>	Transcript	ENST00000333027.7	protein coding	-	1/19	-	-	-	1	0.0397	-	-	-	-0.229	0.00	0.00	0.00	0.00	<i>MTMR3</i>	
		T	intron_variant	-	<i>MTMR3</i>	Transcript	ENST00000351488.7	protein coding	-	1/18	-	-	-	1	0.0397	-	-	-	-0.229	0.00	0.00	0.00	0.00	<i>MTMR3</i>	
		T	intron_variant	-	<i>MTMR3</i>	Transcript	ENST00000401950.7	protein coding	-	1/19	-	-	-	1	0.0397	-	-	-	-0.229	0.00	0.00	0.00	0.00	<i>MTMR3</i>	
		T	intron_variant,non_coding_transcript_variant	-	<i>MTMR3</i>	Transcript	ENST00000415511.1	protein_coding_CDS_not_defined	-	1/5	-	-	-	1	0.0397	-	-	-	-0.229	0.00	0.00	0.00	0.00	<i>MTMR3</i>	
		T	intron_variant	-	<i>MTMR3</i>	Transcript	ENST00000445401.5	protein coding	-	1/5	-	-	-	1	0.0397	-	-	-	-0.229	0.00	0.00	0.00	0.00	<i>MTMR3</i>	
		T	intron_variant,non_coding_transcript_variant	-	<i>MTMR3</i>	Transcript	ENST00000495098.5	protein_coding_CDS_not_defined	-	1/4	-	-	-	1	0.0397	-	-	-	-0.229	0.00	0.00	0.00	0.00	<i>MTMR3</i>	
rs6006286	22:29868401-29868401	C	regulatory_region_variant	-	-	RegulatoryFeature	ENSR00001059241	enhancer	-	-	-	-	-	-	-	-	-	-	1.44	0.0161	-	-	-	-	
		G	regulatory_region_variant	-	-	RegulatoryFeature	ENSR00001059241	enhancer	-	-	-	-	-	-	-	-	-	-	1.44	0.0161	-	-	-	-	
		C	intergenic_variant	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	0.421	-	-	-	-	-
rs73394881	22:29871862-29871862	G	regulatory_region_variant	-	-	RegulatoryFeature	ENSR00001059243	enhancer	-	-	-	-	-	-	-	-	-	-	1.648	0.0458	-	-	-	-	
		A	intergenic_variant	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	1.648	0.0458	-	-	-	-
		G	regulatory_region_variant	-	-	RegulatoryFeature	ENSR00001059243	enhancer	-	-	-	-	-	-	-	-	-	-	0.0351	-	-	-	-	-	
rs73394884	22:29872883-29872883	A	regulatory_region_variant	-	-	RegulatoryFeature	ENSR00001059243	enhancer	-	-	-	-	-	-	-	-	-	-	5.087	0.3697	-	-	-	-	
		T	regulatory_region_variant	-	-	RegulatoryFeature	ENSR00001059243	enhancer	-	-	-	-	-	-	-	-	-	-	5.593	0.4151	-	-	-	-	
		G	intergenic_variant	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	0.0353	-	-	-	-	-
rs74832232	22:29873682-29873682	G	regulatory_region_variant	-	-	RegulatoryFeature	ENSR00001059243	enhancer	-	-	-	-	-	-	-	-	-	-	17.07	1.7057	-	-	-	-	
		A	intergenic_variant	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	17.07	1.7057	-	-	-	-
		G	intergenic_variant	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	0.0353	-	-	-	-	-
rs73394885	22:29875581-29875581	A	intergenic_variant	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	4.218	0.2939	-	-	-	-
		T	upstream_gene_variant	-	<i>MTMR3</i>	Transcript	NM_021090.4	protein coding	-	-	-	-	-	3112	1	0.0012	-	-	0.255	-0.341	-	-	-	-	-
		C	upstream_gene_variant	-	<i>MTMR3</i>	Transcript	NM_021090.4	protein coding	-	-	-	-	-	3112	1	0.0012	-	-	0.214	-0.378	-	-	-	-	-
rs73394892	22:29880062-29880062	A	upstream_gene_variant	-	<i>MTMR3</i>	Transcript	NM_021090.4	protein coding	-	-	-	-	-	3112	1	0.0357	-	-	0.202	-0.39	-	-	-	-	
		T	upstream_gene_variant	-	<i>MTMR3</i>	Transcript	NM_153050.3	protein coding	-	-	-	-	-	3112	1	0.0012	-	-	0.255	-0.341	-	-	-	-	
		A	upstream_gene_variant	-	<i>MTMR3</i>	Transcript	NM_153050.3	protein coding	-	-	-	-	-	3112	1	0.0012	-	-	0.214	-0.378	-	-	-	-	
		T	upstream_gene_variant	-	<i>MTMR3</i>	Transcript	NM_153050.3	protein coding	-	-	-	-	-	3112	1	0.0357	-	-	0.202	-0.39	-	-	-	-	-
		A	upstream_gene_variant	-	<i>MTMR3</i>	Transcript	NM_153051.3	protein coding	-	-	-	-	-	3112	1	0.0012	-	-	0.255	-0.341	-	-	-	-	-
		C	upstream_gene_variant	-	<i>MTMR3</i>	Transcript	NM_153051.3	protein coding	-	-	-	-	-	3112	1	0.0012	-	-	0.214	-0.378	-	-	-	-	-
		T	upstream_gene_variant	-	<i>MTMR3</i>	Transcript	NM_153051.3	protein coding	-	-	-	-	-	3112	1	0.0357	-	-	0.202	-0.39	-	-	-	-	-
rs60573683	22:29883670-29883670	T	intron_variant	-	<i>MTMR3</i>	Transcript	NM_021090.4	protein coding	-	1/19	NM_021090.4:c.-138+311G>T	-	-	1	0.0353	-	-	-	3.147	0.2021	0.00	0.00	0.00	0.00	<i>MTMR3</i>
		T	intron_variant	-	<i>MTMR3</i>	Transcript	NM_153050.3	protein coding	-	1/19	NM_153050.3:c.-138+311G>T	-	-	1	0.0353	-	-	-	3.147	0.2021	0.00	0.00	0.00	0.00	<i>MTMR3</i>
		T	intron_variant	-	<i>MTMR3</i>	Transcript	NM_153051.3	protein coding	-	1/18	NM_153051.3:c.-138+311G>T	-	-	1	0.0353	-	-	-	3.147	0.2021	0.00	0.00	0.00	0.00	<i>MTMR3</i>
rs73394897	22:2988561-2988561	C	regulatory_region_variant	-	-	RegulatoryFeature	ENSR00000145133	promoter	-	-	-	-	-	-	-	-	-	-	3.147	0.2021	-	-	-	-	
		T	intron_variant	-	<i>MTMR3</i>	Transcript	NM_021090.4	protein coding	-	1/19	NM_021090.4:c.-138+5202T>C	-	-	1	0.0353	0.1	0.1	11.25	0.9703	0.00	0.00	0.00	0.00	<i>MTMR3</i>	
		C	intron_variant	-	<i>MTMR3</i>	Transcript	NM_153050.3	protein coding	-	1/19	NM_153050.3:c.-138+5202T>C	-	-	1	0.0353	0.1	0.1	11.25	0.9703	0.00	0.00	0.00	0.00	<i>MTMR3</i>	
rs112565384	22:29890308-29890308	A	intron_variant	-	<i>MTMR3</i>	Transcript	NM_021090.4	protein coding	-	1/19	NM_021090.4:c.-138+6949G>A	-	-	1	0.0353	-	-	-	1.965	0.0856	0.00	0.00	0.00	0.00	<i>MTMR3</i>
		A	intron_variant	-	<i>MTMR3</i>	Transcript	NM_153050.3	protein coding	-	1/19	NM_153050.3:c.-138+6949G>A	-	-	1	0.0353	-	-	-	1.965	0.0856	0.00	0.00	0.00	0.00	<i>MTMR3</i>
		T	intron_variant	-	<i>MTMR3</i>	Transcript	NM_153051.3	protein coding	-	1/18	NM_153051.3:c.-138+6949G>A	-	-	1	0.0353	-	-	-	1.965	0.0856	0.00	0.00	0.00	0.00	<i>MTMR3</i>
rs73396810	22:29895377-29895377	T	intron_variant	-	<i>MTMR3</i>	Transcript	NM_021090.4	protein coding	-	1/19	NM_021090.4:c.-138+12018G>T	-	-	1	0.0353	-	-	-	1.479	0.022	0.00	0.00	0.00	0.00	<i>MTMR3</i>
		T	intron_variant	-	<i>MTMR3</i>	Transcript	NM_153050.3	protein coding	-	1/19	NM_153050.3:c.-138+12018G>T	-	-	1	0.0353	-	-	-	1.479	0.022	0.00	0.00	0.00	0.00	<i>MTMR3</i>
		G	intron_variant	-	<i>MTMR3</i>	Transcript	NM_153051.3	protein coding	-	1/18	NM_153051.3:c.-138+12018G>T	-	-	1	0.0353	-	-	-	1.479	0.022	0.00	0.00	0.00	0.00	<i>MTMR3</i>
rs73396811	22:29896358-29896358	G	intron_variant	-	<i>MTMR3</i>	Transcript	NM_021090.4	protein coding	-	1/19	NM_021090.4:c.-138+12999A>G	-	-	1	0.0353	-	-	-	5.789	0.4329	0.00	0.00	0.00	0.00	<i>MTMR3</i>
		G	intron_variant	-	<i>MTMR3</i>	Transcript	NM_153050.3	protein coding	-	1/19	NM_153050.3:c.-138+12999A>G	-	-	1	0.0353	-	-	-	5.789	0.4329	0.00	0.00	0.00	0.00	<i>MTMR3</i>
		G	intron_variant	-	<i>MTMR3</i>	Transcript	NM_153051.3	protein coding	-	1/18	NM_153051.3:c.-138+12999A>G	-	-	1	0.0353	-	-	-	5.789	0.4329	0.00	0.00	0.00	0.00	<i>MTMR3</i>
rs73396818	22:29902155-29902155	T	intron_variant	-	<i>MTMR3</i>	Transcript	NM_021090.4	protein coding	-	1/19	NM_021090.4:c.-138+18796A>T	-	-	1	0.0397	-	-	-	0.366	-0.267	0.00	0.00	0.00	0.00	<i>MTMR3</i>
		T	intron_variant	-	<i>MTMR3</i>	Transcript	NM_153050.3	protein coding	-	1/19	NM_153050.3:c.-138+18796A>T	-	-	1	0.0397	-	-	-	0.366	-0.267	0.00	0.00	0.00	0.00	<i>MTMR3</i>
		T	intron_variant	-	<i>MTMR3</i>	Transcript	NM_153051.3	protein coding	-	1/18	NM_153051.3:c.-138+18796A>T	-	-	1	0.0397	-	-	-	0.366	-0.267	0.00	0.00	0.00	0.00	<i>MTMR3</i>
rs113463187	22:29902988-29902988	T	intron_variant	-	<i>MTMR3</i>	Transcript	NM_021090.4	protein coding	-	1/19	NM_021090.4:c.-138+19629C>T	-	-	1	0.0399	-	-	-	2.775	0.1688	0.00	0.00	0.00	0.00	<i>MTMR3</i>
		T	intron_variant	-	<i>MTMR3</i>	Transcript	NM_153050.3	protein coding	-	1/19	NM_153050.3:c.-138+19629C>T	-	-	1	0.0399	-	-	-	2.775	0.1688	0.00	0.00	0.00	0.00	<i>MTMR3</i>
		C	intron_variant	-	<i>MTMR3</i>	Transcript	NM_021090.4	protein coding	-	1/18	NM_021090.4:c.-138+19629C>T	-	-	1	0.0399	-	-	-	2.775	0.1688	0.00	0.00	0.00	0.00	<i>MTMR3</i>
rs57349783	22:29903544-29903544	C	intron_variant	-	<i>MTMR3</i>	Transcript	NM_021090.4	protein coding	-	1/19	NM_021090.4:c.-138+20185T>C	-	-	1	0.0395	-	-	-	1.297	-0.006	0.00	0.00	0.00	0.00	<i>MTMR3</i>
		C	intron_variant	-	<i>MTMR3</i>	Transcript	NM_153050.3	protein coding	-	1/19	NM_153050.3:c.-138+20185T>C	-	-	1	0.0395	-	-	-	1.297	-0.006	0.00	0.00	0.00	0.00	<i>MTMR3</i>
		C	intron_variant	-	<i>MTMR3</i>	Transcript	NM_153051.3	protein coding	-	1/18	NM_153051.3:c.-138+20185T>C	-	-	1	0.0395	-	-	-	1.297	-0.006	0.00	0.00	0.00	0.00	<i>MTMR3</i>
rs2158535	22:29903616-29903616</																								



rs58564057	22:29962609	T	intron_variant	MODIFIER	MTMR3	Transcript	NM_153050.3	protein_coding	2/19	NM_153050.3:c.-85+5521C>T	rs58564057	-	1	0.0353	-	-	0.64	-0.154	0.00	0.00	0.00	0.00	MTMR3	
		T	intron_variant		MTMR3	Transcript	NM_153051.3	protein_coding	2/18	NM_153051.3:c.-85+5521C>T		-	1	0.0353	-	-	0.64	-0.154	0.00	0.00	0.00	0.00	MTMR3	
rs73398654	22:29980789-29980789	G	intron_variant	MODIFIER	MTMR3	Transcript	NM_021090.4	protein_coding	5/19	NM_021090.4:c.210+1737C>G	rs73398654	-	1	0.0353	-	-	0.248	-0.347	0.00	0.00	0.00	0.00	MTMR3	
		G	intron_variant		MTMR3	Transcript	NM_153050.3	protein_coding	5/19	NM_153050.3:c.210+1737C>G		-	1	0.0353	-	-	0.248	-0.347	0.00	0.00	0.00	0.00	MTMR3	
		G	intron_variant		MTMR3	Transcript	NM_153051.3	protein_coding	5/18	NM_153051.3:c.210+1737C>G		-	1	0.0353	-	-	0.248	-0.347	0.00	0.00	0.00	0.00	MTMR3	
rs73398659	22:29986440-29986440	A	intron_variant	MODIFIER	MTMR3	Transcript	NM_021090.4	protein_coding	5/19	NM_021090.4:c.211-2040G>A	rs73398659	-	1	0.0353	-	-	0.062	-0.631	0.00	0.00	0.00	0.00	MTMR3	
		A	intron_variant		MTMR3	Transcript	NM_153050.3	protein_coding	5/19	NM_153050.3:c.211-2040G>A		-	1	0.0353	-	-	0.062	-0.631	0.00	0.00	0.00	0.00	MTMR3	
		A	intron_variant		MTMR3	Transcript	NM_153051.3	protein_coding	5/18	NM_153051.3:c.211-2040G>A		-	1	0.0353	-	-	0.062	-0.631	0.00	0.00	0.00	0.00	MTMR3	
		A	regulatory_region_variant		-	RegulatoryFeature	ENSR00000669742	enhancer	-	-		-	-	0.0353	-	-	0.062	-0.631	-	-	-	-	-	
rs73398662	22:29987780-29987780	G	intron_variant	MODIFIER	MTMR3	Transcript	NM_021090.4	protein_coding	5/19	NM_021090.4:c.211-700C>G	rs73398662	-	1	0.0353	-	-	1.504	0.0256	0.00	0.00	0.00	0.00	MTMR3	
		G	intron_variant		MTMR3	Transcript	NM_153050.3	protein_coding	5/19	NM_153050.3:c.211-700C>G		-	1	0.0353	-	-	1.504	0.0256	0.00	0.00	0.00	0.00	MTMR3	
		G	intron_variant		MTMR3	Transcript	NM_153051.3	protein_coding	5/18	NM_153051.3:c.211-700C>G		-	1	0.0353	-	-	1.504	0.0256	0.00	0.00	0.00	0.00	MTMR3	
		G	regulatory_region_variant		-	RegulatoryFeature	ENSR00000669742	enhancer	-	-		-	-	0.0353	-	-	1.504	0.0256	-	-	-	-	-	
rs73398664	22:29989196-29989196	T	intron_variant	MODIFIER	MTMR3	Transcript	NM_021090.4	protein_coding	6/19	NM_021090.4:c.293+634G>T	rs73398664	-	1	0.0355	-	-	3.82	0.2599	0.00	0.00	0.00	0.00	MTMR3	
		T	intron_variant		MTMR3	Transcript	NM_153050.3	protein_coding	6/19	NM_153050.3:c.293+634G>T		-	1	0.0355	-	-	3.82	0.2599	0.00	0.00	0.00	0.00	MTMR3	
		T	intron_variant		MTMR3	Transcript	NM_153051.3	protein_coding	6/18	NM_153051.3:c.293+634G>T		-	1	0.0355	-	-	3.82	0.2599	0.00	0.00	0.00	0.00	MTMR3	
		T	regulatory_region_variant		-	RegulatoryFeature	ENSR00001238990	enhancer	-	-		-	-	0.0355	-	-	3.82	0.2599	-	-	-	-	-	
rs112672347	22:30004075-30004076	A	intron_variant	MODIFIER	MTMR3	Transcript	NM_021090.4	protein_coding	9/19	NM_021090.4:c.671+1083del	rs112672347	-	1	0.0353	-	-	6.746	0.5233	0.00	0.00	0.00	0.00	MTMR3	
		A	intron_variant		MTMR3	Transcript	NM_153050.3	protein_coding	9/19	NM_153050.3:c.671+1083del		-	1	0.0353	-	-	6.746	0.5233	0.00	0.00	0.00	0.00	MTMR3	
		A	intron_variant		MTMR3	Transcript	NM_153051.3	protein_coding	9/18	NM_153051.3:c.671+1083del		-	1	0.0353	-	-	6.746	0.5233	0.00	0.00	0.00	0.00	MTMR3	
		A	upstream_gene_variant		MIR6618	Transcript	NR_106876.1	miRNA	-	-		-	2973	1	0.0353	-	-	6.746	0.5233	-	-	-	-	-
		A	downstream_gene_variant		HORMAD2-AS1	Transcript	NR_110541.2	lncRNA	-	-		-	4670	-1	0.0353	-	-	6.746	0.5233	-	-	-	-	-
rs73398683	22:30004230-30004230	A	intron_variant	MODIFIER	MTMR3	Transcript	NM_021090.4	protein_coding	9/19	NM_021090.4:c.671+1237G>A	rs73398683	-	1	0.0353	-	-	9.222	0.7828	0.00	0.00	0.02	0.00	MTMR3	
		A	intron_variant		MTMR3	Transcript	NM_153050.3	protein_coding	9/19	NM_153050.3:c.671+1237G>A		-	1	0.0353	-	-	9.222	0.7828	0.00	0.00	0.02	0.00	MTMR3	
		A	intron_variant		MTMR3	Transcript	NM_153051.3	protein_coding	9/18	NM_153051.3:c.671+1237G>A		-	1	0.0353	-	-	9.222	0.7828	0.00	0.00	0.02	0.00	MTMR3	
		A	upstream_gene_variant		MIR6618	Transcript	NR_106876.1	miRNA	-	-		-	2819	1	0.0353	-	-	9.222	0.7828	-	-	-	-	-
		A	downstream_gene_variant		HORMAD2-AS1	Transcript	NR_110541.2	lncRNA	-	-		-	4516	-1	0.0353	-	-	9.222	0.7828	-	-	-	-	-

**Supplementary Data 9. Summary of per locus association results after conditioning on top index variant**

CHR	POS (hg38)	rsID	REF	ALT	ALT Freq	Nearest Gene	Pre-conditioning			N SNPs in region <sup>a</sup>	Post-conditioning			Signif. <sup>b</sup>
							Beta	SE	P-value		Beta	SE	P-value	
1	178057912	rs111238523	C	T	2%	<i>RASAL2</i>	0.058	0.018	1.76E-03	5008	0.065	0.018	4.30E-04	
<b>2</b>	<b>422144</b>	<b>rs62107261</b>	<b>T</b>	<b>C</b>	<b>3%</b>	<b><i>ALKAL2</i></b>	<b>-0.095</b>	<b>0.014</b>	<b>3.83E-12</b>	<b>6640</b>	<b>-0.097</b>	<b>0.014</b>	<b>2.06E-12</b>	<b>Yes</b>
2	24881806	n/a	CCA	C	11%	<i>ADCY3</i>	0.042	0.009	2.94E-06	4187	0.038	0.009	2.63E-05	
3	185800743	rs73061097	T	A	32%	<i>IGF2BP2</i>	-0.024	0.005	5.70E-06	4848	-0.024	0.005	3.47E-06	
4	45308738	rs80129601	A	G	2%	<i>GNPDA2</i>	-0.087	0.019	4.24E-06	6131	-0.081	0.019	2.06E-05	
5	75750228	rs258502	G	T	57%	<i>POC5</i>	-0.001	0.005	8.27E-01	6179	-0.019	0.005	6.14E-04	
6	51174169	rs984697642	G	A	3%	<i>TFAP2B</i>	-0.072	0.014	3.07E-07	5184	-0.065	0.014	3.97E-06	
8	75725530	rs16939149	A	G	6%	<i>HNF4G</i>	-0.039	0.011	4.29E-04	5692	-0.051	0.011	8.10E-06	
11	27647068	rs3838785	A	G	2%	<i>BDNF</i>	0.071	0.020	3.06E-04	3667	0.080	0.020	5.76E-05	
12	49831467	rs4391887	A	G	74%	<i>NCKAP5L</i>	0.034	0.006	1.18E-09	4264	0.023	0.006	2.79E-04	
13	53367083	rs1036958	T	A	52%	<i>OLFM4</i>	-0.014	0.005	4.02E-03	5125	-0.018	0.005	2.70E-04	
16	53730708	rs117502563	G	A	4%	<i>FTO</i>	0.031	0.012	7.20E-03	5673	0.054	0.012	4.30E-06	
<b>18</b>	<b>60361739</b>	<b>rs78769612</b>	<b>G</b>	<b>T</b>	<b>2%</b>	<b><i>MC4R</i></b>	<b>-0.106</b>	<b>0.019</b>	<b>3.53E-08</b>	<b>6861</b>	<b>-0.100</b>	<b>0.019</b>	<b>2.17E-07</b>	<b>Yes</b>
19	47321406	rs149173729	C	T	1%	<i>C5AR1</i>	0.094	0.027	4.64E-04	4744	0.108	0.027	6.65E-05	
22	30035665	rs73400621	A	G	5%	<i>MTMR3</i>	0.029	0.012	1.23E-02	4814	0.042	0.012	4.80E-04	
X	32268401	rs147568648	A	G	11%	<i>DMD</i>	-0.023	0.007	6.50E-04	4911	-0.025	0.007	2.19E-04	

CHR, chromosome; POS, position; REF, reference allele; ALT, alternative allele; Freq, frequency; SE, standard error; Signif., significant; n/a, not available

<sup>a</sup> Region was defined as within  $\pm 500$ kb of each index variant.

<sup>b</sup> Significance threshold for secondary signals ( $P < 5.96 \times 10^{-7}$ ) was determined by Bonferroni correction for the number of variants across all regions

**Supplementary Data 10. Summary of association results after conditioning on all known index variants**

CHR	POS (hg38)	rsID	Nearest Gene	REF	ALT	ALT Freq	Pre-conditioning			Post-conditioning		
							Beta	SE	P-value	Beta	SE	P-value
2	621558	rs939584	<i>TMEM18</i>	C	T	85%	0.0576	0.0068	1.99E-17	0.0392	0.0282	0.1655
3	186108951	rs869400	<i>ETV5</i>	T	G	82%	0.0383	0.0063	1.21E-09	0.0330	0.0225	0.1439
<b>6</b>	<b>50830813</b>	<b>rs2206277</b>	<b><i>TFAP2B</i></b>	<b>C</b>	<b>T</b>	<b>19%</b>	<b>0.0543</b>	<b>0.0062</b>	<b>2.05E-18</b>	<b>0.0687</b>	<b>0.0182</b>	<b>1.59E-04</b>
8	76068626	rs830463	<i>HNF4G</i>	A	G	47%	0.0305	0.0049	6.58E-10	0.0237	0.0058	4.31E-05
<b>11</b>	<b>27657463</b>	<b>rs3838785</b>	<b><i>BDNF</i></b>	<b>GT</b>	<b>G</b>	<b>58%</b>	<b>-0.0303</b>	<b>0.0051</b>	<b>3.14E-09</b>	<b>-0.0324</b>	<b>0.0092</b>	<b>4.11E-04</b>
13	53533448	rs9568868	<i>OLFM4</i>	G	T	14%	0.0472	0.0072	5.73E-11	0.1990	0.1881	0.2900
19	47077985	rs28590228	<i>ZC3H4</i>	C	T	50%	0.0332	0.0053	4.75E-10	0.0410	0.0219	0.0617
<b>Secondary signal</b>												
18	60361739	rs78769612	<i>MC4R</i>	G	T	2%	-0.106	0.019	3.53E-08	-0.0722	0.0945	0.4450

*CHR, chromosome; POS, position; REF, reference allele; ALT, alternative allele; Freq, frequency; SE, standard error*

Known index variants curated from the following papers (PMIDs): 22344219, 22344221, 23563607, 23583978, 24094743, 24861553, 25673413, 26426971, 28391526, 28430825, 28443625, 28448500, 28552196, 28892062, 29273807, 29381148, 30108127, 30124842, 30595370, 31217584, 35399580

**Supplementary Data 11. PAINTOR results for top loci assuming one single causal variant at each locus**

Only index variants and those with posterior probability (PP) > 50% are shown. **Bold** identifies variants with > 95% PP.

Locus rsID	CHR	POS (hg38)	rsID	REF	ALT	EAF	MAF	Gene	PAINTOR Annotation	Beta	SE	P-value	PVE (%)	PP	Is Index highest PP?
rs543874	1	177920345	rs543874	A	G	0.2043	0.2043	<i>SEC16B</i>	-	0.0639	0.0060	1.38E-26	0.128	0.6192	Yes
rs939584	2	621558	rs939584	C	T	0.8518	0.1482	<i>TMEM18</i>	-	0.0576	0.0068	1.99E-17	0.081	0.0230	Yes
rs10182181	2	24927427	rs10182181	A	G	0.5608	0.4392	<i>ADCY3</i>	-	0.0350	0.0052	1.76E-11	0.051	0.1376	No
		24920780	rs6746013	C	G	0.5629	0.4371		genehancer	0.3462	0.0052	2.99E-11	0.050	0.3163	
rs869400	3	186108951	rs869400	T	G	0.8195	0.1805	<i>ETV5</i>	genehancer	0.0383	0.0063	1.21E-09	0.042	0.6263	Yes
rs12507026	4	45179317	rs12507026	A	T	0.3614	0.3614	<i>GNPDA2</i>	-	0.0449	0.0051	9.55E-19	0.088	0.3051	Yes
<b>rs2307111</b>	<b>5</b>	<b>75707853</b>	<b>rs2307111</b>	<b>T</b>	<b>C</b>	<b>0.5474</b>	<b>0.4526</b>	<b><i>POC5</i></b>	-	<b>-0.0324</b>	<b>0.0053</b>	<b>7.43E-10</b>	<b>0.043</b>	<b>0.9898</b>	<b>Yes</b>
rs2206277	6	50830813	rs2206277	C	T	0.1903	0.1903	<i>TFAP2B</i>	-	0.0543	0.0062	2.05E-18	0.086	0.4895	Yes
rs830463	8	76068626	rs830463	A	G	0.4700	0.4700	<i>HNF4G</i>	-	0.0305	0.0049	6.58E-10	0.043	0.2278	Yes
rs3838785	11	27657463	rs3838785	GT	G	0.5792	0.4208	<i>BDNF</i>	-	-0.0303	0.0051	3.14E-09	0.040	0.3310	Yes
rs7138803	12	49853685	rs7138803	G	A	0.2974	0.2974	<i>BCDIN3D</i>	-	0.0363	0.0054	1.69E-11	0.051	0.4231	Yes
rs9568868	13	53533448	rs9568868	G	T	0.1387	0.1387	<i>OLFM4</i>	-	0.0472	0.0072	5.74E-11	0.048	0.3631	Yes
rs1421085	16	53767042	rs1421085	T	C	0.2949	0.2949	<i>FTO</i>	-	0.0901	0.0056	6.11E-59	0.295	0.5887	Yes
rs6567160	18	60161902	rs6567160	T	C	0.2096	0.2096	<i>MC4R</i>	-	0.0525	0.0059	8.22E-19	0.088	0.7360	Yes
		47077985	rs28590228	C	T	0.5039	0.4961		-	0.0332	0.0053	4.76E-10	0.044	0.0945	
rs28590228	19	47113120	rs55731973	G	T	0.5196	0.4804	<i>ZC3H4</i>	promoter, genehancer	0.0297	0.0054	3.91E-08	0.034	0.7664	No
rs111490516	22	29906934	rs111490516	C	T	0.0368	0.0368	<i>MTMR3</i>	-	0.0783	0.0133	4.52E-09	0.039	0.0407	Yes
<b>rs1379871</b>	<b>X</b>	<b>31836665</b>	<b>rs1379871</b>	<b>G</b>	<b>C</b>	<b>0.4131</b>	<b>0.4131</b>	<b><i>DMD</i></b>	-	<b>0.0287</b>	<b>0.0042</b>	<b>1.35E-11</b>	<b>0.052</b>	<b>0.9980</b>	<b>Yes</b>

PAINTOR, Probabilistic Annotation INtegraTOR; CHR, chromosome; POS, position; REF, reference allele; ALT, alternative allele; EAF, effect allele frequency; MAF, minor allele frequency; SE, standard error; PVE, percent variance explained; PP, posterior probability



**Supplementary Data 12. Top associations meeting suggestive significance ( $P < 0.001$ ) in PheWAS meta-analysis**

PheCode	Phenotype Descriptions	Category	Meta					MyCode					BioMe				
			Beta	SE	OR	P	N	Beta	SE	OR	P	N	Beta	SE	OR	P	N
327.3	Sleep apnea	neurological	-0.2530	0.0755	0.7765	8.12E-04	7,600	-0.1436	0.1391	0.8663	3.02E-01	1,536	-0.2987	0.0900	0.7418	8.99E-04	6,064
327.32	Obstructive sleep apnea	neurological	-0.2903	0.0785	0.7480	2.19E-04	7,497	-0.1809	0.1455	0.8345	2.14E-01	1,486	-0.3352	0.0933	0.7152	3.26E-04	6,011