Description of Additional Supplementary Files

File Name: Supplementary Data 1-27

Supplementary Data 1
Contribution of each LD score-MAF bin to the observed heritability h^2 of CAD in the European genetic ancestry sample. GRMs are estimated by ratio of averages (RoA) and variances by REML EM algorithm in GCTA. Low (High) represents SNVs with LD scores below (above) the median, respectively.
CAD, coronary artery disease; GRM, genomic relatedness matrix; LD, linkage disequilibrium; MAF, minor allele frequency; SE, standard error; SNV, single nucleotide variant.

Supplementary Data 2
Contribution of each LD score-MAF bin to the observed heritability h^2 of CAD in the European genetic ancestry sample. GRMs are estimated by ratio of averages (RoA) and variances by REML AI algorithm in GCTA. Low (High) represents SNVs with LD scores below (above) the median, respectively.
CAD, coronary artery disease; GRM, genomic relatedness matrix; LD, linkage disequilibrium; MAF, minor allele frequency; SE, standard error; SNV, single nucleotide variant.

Supplementary Data 3
Contribution of each LD score-MAF bin to the observed heritability h^2 of CAD in the European genetic ancestry sample. GRMs are estimated by average of ratios and variances by REML EM algorithm in GCTA. The first, second, third and fourth quartiles of LD scores are denoted Q1, Q2, Q3, and Q4, respectively.
CAD, coronary artery disease; GRM, genomic relatedness matrix; LD, linkage disequilibrium; MAF, minor allele frequency; SE, standard error.

Supplementary Data 4
Contribution of each LD score-MAF bin to the observed heritability h^2 of CAD in the European genetic ancestry sample. GRMs are estimated by average of ratios (AoR) and variances by REML AI algorithm in GCTA. Low (High) represents SNVs with LD scores below (above) the median, respectively.
CAD, coronary artery disease; GRM, genomic relatedness matrix; LD, linkage disequilibrium; MAF, minor allele frequency; SE, standard error; SNV, single nucleotide variant.

Supplementary Data 5
Comparison of each LD score-MAF bin contribution to the observed heritability h^2 of CAD between the TOPMed European sample (this study) and the non-Hispanic White sample of the Million Veteran Program (Tcheandjieu et al., Nature Medicine 2022). GRMs are estimated by ratio of averages (RoA) and variances by REML EM algorithm in GCTA. The first, second, third and fourth quartiles of LD scores are denoted Q1, Q2, Q3, and Q4, respectively.
CAD, coronary artery disease; GRM, genomic relatedness matrix; LD, linkage disequilibrium; MAF, minor allele frequency; SE, standard error.

Supplementary Data 6
Contribution of each LD score-MAF bin to the observed heritability h^2 of CAD in the African genetic ancestry sample. GRMs are estimated by ratio of averages (RoA) and variances by REML EM algorithm in GCTA. Low (High) represents SNVs with LD scores below (above) the median, respectively.
CAD, coronary artery disease; GRM, genomic relatedness matrix; LD, linkage disequilibrium; MAF, minor allele frequency; SE, standard error; SNV, single nucleotide variant.

Supplementary Data 7
Distribution of the number of SNVs in each MAF bin for the European and African genetic ancestry samples, respectively. 'X' indicate SNVs used by GCTA in one ancestry, but not in the other.
MAF, minor allele frequency; SNV, single nucleotide variant.

Supplementary Data 8
Proportion of SNVs used by GCTA in the TOPMed European genetic ancestry sample shared with the gnomAD v4.1.0 genetically inferred ancestry groups.
MAF, minor allele frequency; SNV, single nucleotide variant.

Supplementary Data 9
Distribution of the number of SNVs by MAF, LD score and constraint. SNV is considered constrained if its phyloP score ≥ 2.27. Low (High) represents SNVs with LD scores below (above) the median, respectively.
LD, linkage disequilibrium; MAF, minor allele frequency; SE, standard error; SNV, single nucleotide variant.

Supplementary Data 10
Absolute and relative (per variant) contribution of each LD score-MAF-Constrained bin to the observed heritability h^2 of CAD. SNV is considered constrained if its phyloP score ≥ 2.27. Low (High) represents SNVs with LD scores below (above) the median, respectively. Variance (SE) per SNV equals variance (SE) divided by the number of SNVs in the respective LD score-MAF-Constrained bin.
CAD, coronary artery disease; LD, linkage disequilibrium; MAF, minor allele frequency; SE, standard error; SNV, single nucleotide variant.

Supplementary Data 11
Log enrichment ratio of constrained variants in each LD score-MAF bin. SNV is considered constrained if its phyloP score ≥ 2.27. Low (High) represents SNVs with LD scores below (above) the median, respectively.
LD, linkage disequilibrium; MAF, minor allele frequency; SE, standard error; SNV, single nucleotide variant.

Supplementary Data 12
Distribution of the number of SNVs by MAF, LD score, and SnpEff functional annotation (sequence ontology term) and predicted impact. SnpEff predicted impacts are High, Low, Moderate and Modifier.
LD, linkage disequilibrium; MAF, minor allele frequency; SE, standard error.

Supplementary Data 13
Absolute and relative (per variant) contribution of each LD score-MAF-Impact bin to the observed heritability h^2 of CAD. Low (High) represents SNVs with LD scores below (above) the median, respectively. SnpEff predicted impact is High (protein-altering variants) or Low (non-protein-altering variants). Variance (SE) per SNV equals variance (SE) divided by the number of SNVs in the respective LD score-MAF-Impact bin.
CAD, coronary artery disease; LD, linkage disequilibrium; MAF, minor allele frequency; SE, standard error; SNV, single nucleotide variant.

Supplementary Data 14
Log impact ratio of contribution per variant from protein-altering over non-protein-altering SNVs in each LD score-MAF bin. Low (High) represents SNVs with LD scores below (above) the median, respectively.
LD, linkage disequilibrium; MAF, minor allele frequency; SE, standard error; SNV, single nucleotide variant.

Supplementary Data 15
Distribution of the number of SNVs by MAF, LD score and snATAC-seq peak bins for the 13 cell types. Proportion (Prop) of SNVs is calculated inside (IN) and outside (OUT) peaks in each LD score-MAF bin.
CAD, coronary artery disease; LD, linkage disequilibrium; MAF, minor allele frequency; Endo, endothelial cells; Fibrobl, fibroblasts; Fibromyo, fibromyocytes; Macro, macrophages, NK, natural killer cells; Peri, Pericytes, SMC, smooth muscle cells; snATAC-seq, single-nucleus assays for transposase accessible chromatin with sequencing; SNV, single nucleotide variant.

Supplementary Data 16
Contribution of each LD score-MAF-Peak bin to the observed heritability h^2 of CAD for the 13 snATAC-seq cell types. Low (High) represents SNVs with LD scores below (above) the median, respectively. SNVs lie inside (IN) or outside (OUT) peaks in each LD score-MAF bin.
CAD, coronary artery disease; LD, linkage disequilibrium; MAF, minor allele frequency; snATAC-seq, single-nucleus assays for transposase accessible chromatin with sequencing; SE, standard error; SNV, single nucleotide variant.

Supplementary Data 17
Proportion of SNVs and proportion of observed heritability in each LD score-MAF-Peak for all 13 snATAC-seq cell types. Low (High) represents SNVs with LD scores below (above) the median, respectively. SNVs lie inside (IN) or outside (OUT) peaks in each LD score-MAF bin.

LD, linkage disequilibrium; MAF, minor allele frequency; snATAC-seq, single-nucleus assays for transposase accessible chromatin with sequencing; SNV, single nucleotide variant.

Supplementary Data 18
Contribution on a per-variant basis of each LD score-MAF-Peak bin to the observed heritability for the 13 snATAC-seq cell types. Low (High) represents SNVs with LD scores below (above) the median, respectively. SNVs lie inside (IN) or outside (OUT) peaks in each LD score-MAF bin.
LD, linkage disequilibrium; MAF, minor allele frequency; snATAC-seq, single-nucleus assays for transposase accessible chromatin with sequencing; SNV, single nucleotide variant.

Supplementary Data 19
Log enrichment ratio of snATAC-seq peaks in each LD score-MAF bin for the 13 snATAC-seq cell types. Low (High) represents SNVs with LD scores below (above) the median, respectively.
LD, linkage disequilibrium; MAF, minor allele frequency; SE, standard error; snATAC-seq, single-nucleus assays for transposase accessible chromatin with sequencing; SNV, single nucleotide variant.

Supplementary Data 20
Distribution of the number of SNVs by MAF, LD score and aPC-Conservation functionality. Low (High) represents SNVs with LD scores below (above) the median, respectively. Functionality is High if Phred score ≥ 14.7.
LD, linkage disequilibrium; MAF, minor allele frequency; SNV, single nucleotide variant.

Supplementary Data 21
Absolute and relative (per variant) contribution of each LD score-MAF-aPC-Conservation bin to the observed heritability h^2 of CAD. Low (High) represents SNVs with LD scores below (above) the median, respectively. Functionality is High if Phred score ≥ 14.7. Variance (SE) per SNV equals variance (SE) divided by the number of SNVs in the respective LD score-MAF-aPC-Conservation bin.
CAD, coronary artery disease; LD, linkage disequilibrium; MAF, minor allele frequency; SE, standard error; SNV, single nucleotide variant.

Supplementary Data 22
Log enrichment ratio of conserved (Phred score ≥ 14.7) over non-conserved (Phred score < 14.7) variants (aPC-Conservation) in each LD score-MAF bin. Low (High) represents SNVs with LD scores below (above) the median, respectively.
LD, linkage disequilibrium; MAF, minor allele frequency; SE, standard error; SNV, single nucleotide variant.

Supplementary Data 23
Distribution of the number of SNVs by MAF, LD score and aPC-Protein-Function functionality. Low (High) represents SNVs with LD scores below (above) the median, respectively. Functionality is High if Phred score ≥ 3.

LD, linkage disequilibrium; MAF, minor allele frequency; SNV, single nucleotide variant.

Supplementary Data 24
Absolute and relative (per variant) contribution of each LD score-MAF-aPC-Protein-Function bin to the observed heritability h^2 of CAD. Low (High) represents SNVs with LD scores below (above) the median, respectively. Functionality is High if Phred score ≥ 3. Variance (SE) per SNV equals variance (SE) divided by the number of SNVs in the respective LD score-MAF-aPC-Protein-Function bin.
CAD, coronary artery disease; LD, linkage disequilibrium; MAF, minor allele frequency; SE, standard error; SNV, single nucleotide variant.

Supplementary Data 25
Log enrichment ratio of high (Phred score ≥ 3) over low (Phred score < 3) functionality (aPC-Protein-Function) variants in each LD score-MAF bin. Low (High) represents SNVs with LD scores below (above) the median, respectively.
LD, linkage disequilibrium; MAF, minor allele frequency; SE, standard error; SNV, single nucleotide variant.

Supplementary Data 26
Contribution of each LD score-MAF-Functionality bin to the observed heritability h^2 of CAD for aPCs at Phred score = 10 or 20. Functionality is denoted as High (Phred score ≥ 10 or 20) or Low (Phred score < 10 or 20). Low (High) represents SNVs with LD scores below (above) the median, respectively.
CAD, coronary artery disease; epiact10, aPC-Epigenetics-Active (Phred = 10); epiact20, aPC-Epigenetics-Active (Phred = 20); epirep10, aPC-Epigenetics-Repressed (Phred = 10); epirep20, aPC-Epigenetics-Repressed (Phred = 20); epitrans10, aPC-Epigenetics-Transcription (Phred = 10); epitrans20, aPC-Epigenetics-Transcription (Phred = 20); Funct, functionality; LD, linkage disequilibrium; MAF, minor allele frequency; map10, aPC-Mappability (Phred = 10); map20, aPC-Mappability (Phred = 20); mutdens10, aPC-Mutation-Density (Phred = 10); nucdiv10, aPC-Local-Nucleotide-Diversity (Phred = 10); prox10, aPC-Proximity-To-TSS-TES (Phred = 10); prox20, aPC-Proximity-To-TSS-TES (Phred = 20); SNV, single nucleotide variant; trans10, aPC-Transcription-Factor (Phred = 10); trans20, aPC-Transcription-Factor (Phred = 20).

Supplementary Data 27
Log enrichment ratio of high over low functionality variants in each LD score-MAF bin for aPCs at Phred score = 10 or 20. Functionality is denoted as High (Phred score ≥ 10 or 20) or Low (Phred score < 10 or 20). Low (High) represents SNVs with LD scores below (above) the median, respectively.
aPC-Epigenetics-Active (Phred = 10); epiact20, aPC-Epigenetics-Active (Phred = 20); epirep10, aPC-Epigenetics-Repressed (Phred = 10); epirep20, aPC-Epigenetics-Repressed (Phred = 20); epitrans10, aPC-Epigenetics-Transcription (Phred = 10); epitrans20, aPC-Epigenetics-Transcription (Phred = 20); LD, linkage disequilibrium; MAF, minor allele frequency; map10, aPC-Mappability (Phred = 10); map20, aPC-Mappability (Phred = 20); mutdens10, aPC-Mutation-Density (Phred = 10); nucdiv10, aPC-Local-Nucleotide-Diversity (Phred = 10); prox10,

aPC-Proximity-To-TSS-TES (Phred = 10); prox20, aPC-Proximity-To-TSS-TES (Phred = 20); SNV, single nucleotide variant; trans10, aPC-Transcription-Factor (Phred = 10); trans20, aPC-Transcription-Factor (Phred = 20).