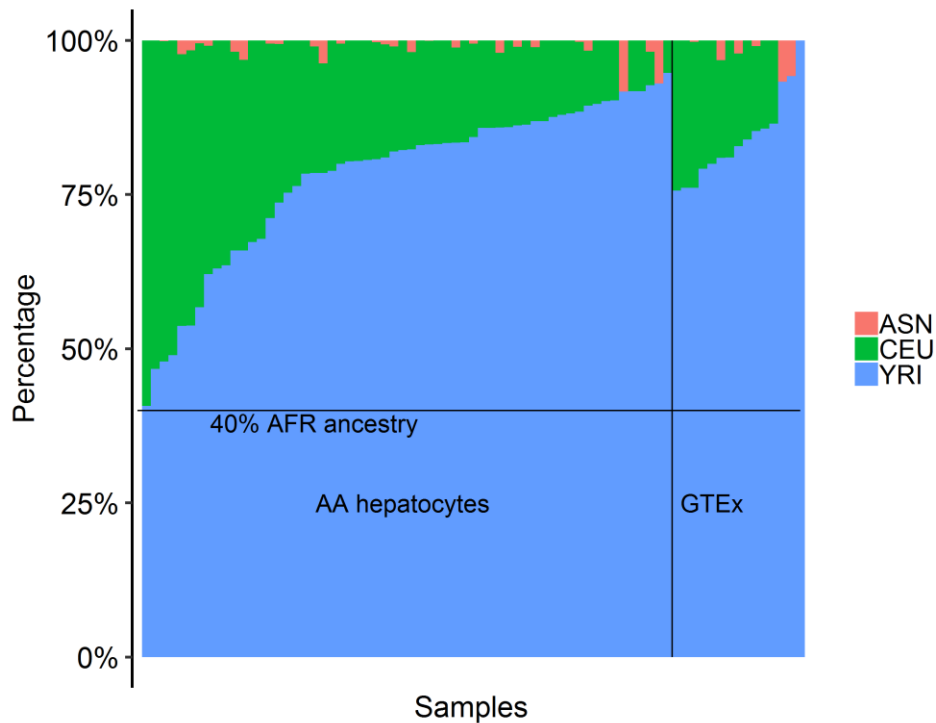
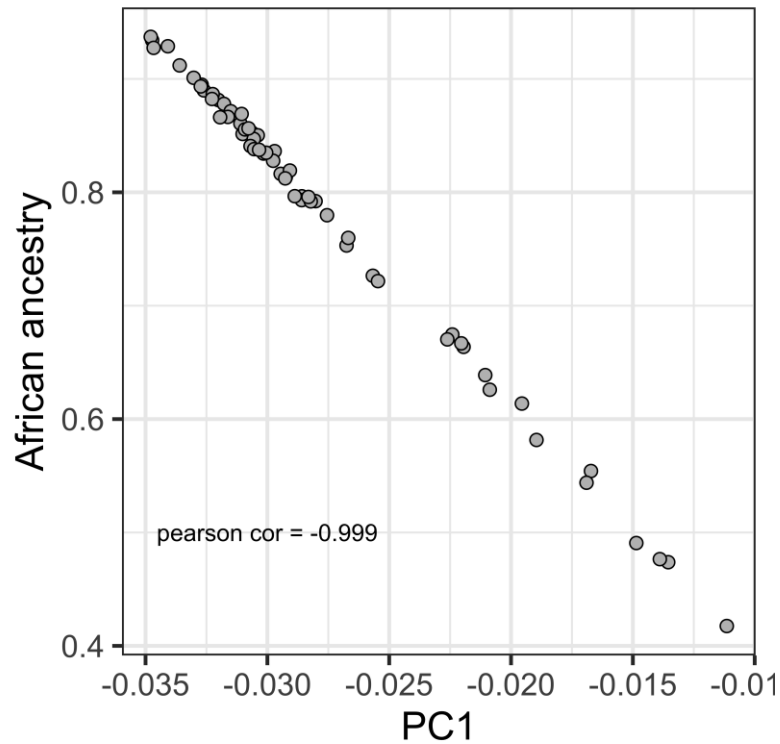


## Supplemental Figure

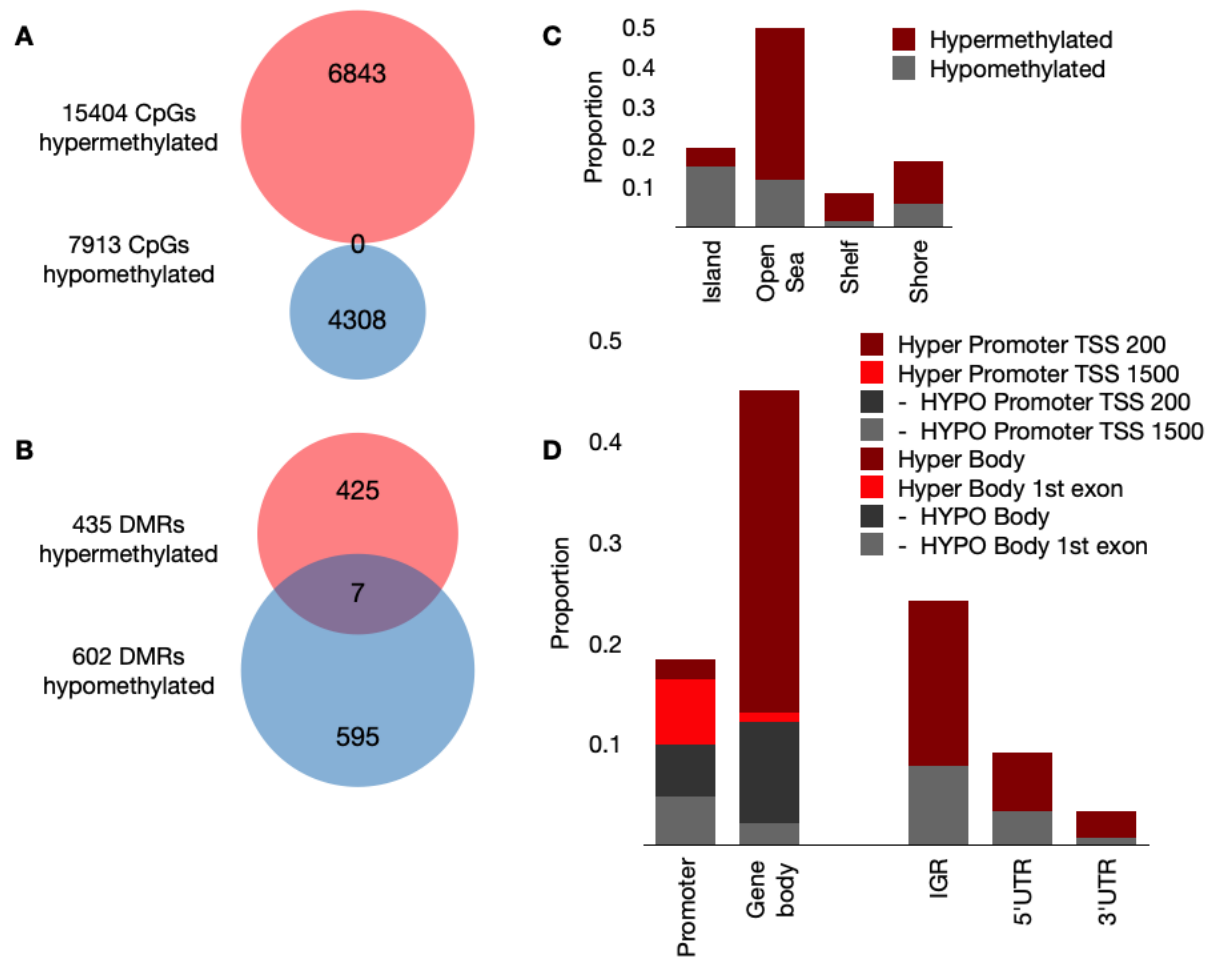


**Fig. S1: West African ancestry estimation in the AA Hepatocyte Discovery and GTEx cohorts.**

An admixture plot showing the ancestry components of the 60 African-American hepatocyte and 15 GTEx cohorts was calculated using fastStructure v1.3. A model with three parental ancestral components ( $K = 3$ ) was used to estimate from three populations from HapMap phase 3 reference data: Han Chinese in Beijing, China (CHB) and Japanese in Tokyo, Japan (JPT) combined as Asian (ASN, pink); Utah residents with Northern and Western European ancestry (CEU, green); Yoruba in Ibadan, Nigeria (YRI) as African (AFR, blue). Percent WAA is plotted on the y-axis. Each sample is represented individually on the x-axis and partitioned into segments proportional to the contributions of the ancestral components to the individual's genome. The black line identified the threshold use for inclusion in the study.



**Fig. S2: Correlation plot of proportion of WAA and Principal Component 1 (PC1).** A correlation plot of admixture proportion and principal component 1 (PC1) in the 60 African-American hepatocyte samples used in this study (Pearson correlation = -0.999). African ancestry for each sample is represented on the y-axis on a scale of 40% – 100% WAA. Principal component 1 for each sample is represented on the x-axis, in a range between -0.035 and -0.01.



**Fig. S3: DNA methylation by genomic features and regions associated with West African ancestry.** **A.** Venn diagrams of unique genes comprised of 15,404 hyper- (pink) and 7913 hypomethylated (blue) CpG sites associated with WAA, and **B.** unique genes comprised of 435 hyper- (pink) and 602 hypomethylated (blue) differentially methylated regions (DMRs) associated with WAA, **C.** Bar graphs showing the proportion of hyper- and hypomethylated CpG sites by genomic features (islands, open sea, shelf and shore), and **D.** proportion of hyper- and hypomethylated CpG sites by transcriptionally-regulated regions: promoter, gene body (with 200 or 1500 bp from the gene transcriptional start site [TSS]), intergenic region (IGR), and 5' and 3' untranslated regions (UTR).

**Supplementary Data S1. Genes associated with WAA replicated in Innocenti and GTEx validation cohorts**

List of 131 West African Ancestry-associated genes with p-values from the validation of DE gene analysis in the Innocenti Validation Liver Cohort of AAs and EAs and in the AA GTEx Liver cohort.

**Supplementary Data S2. GWAS traits and diseases associated with replicated genes**

Phenotypic traits associated with replicated genes in the GWAS Catalog.

**Supplementary Data S3. WAA-associated genes mediated by methylation**

- A. Differential methylation analysis results of the ten significant DMRs overlapping the 131 significant WAA-associated genes.
- B. Effect size of the ancestry association to gene expression of the five genes containing significant DMRs overlapping the 131 significant WAA-associated genes and with concordant direction of effect.
- C. Mediation effects of the five overlapping genes after performing mediation analysis to determine the indirect effect of methylation on gene expression.