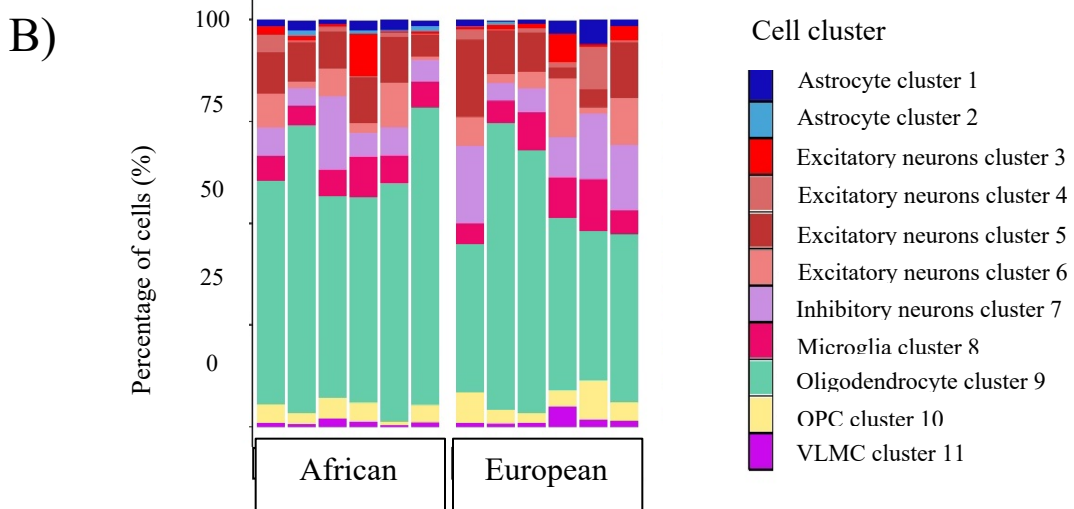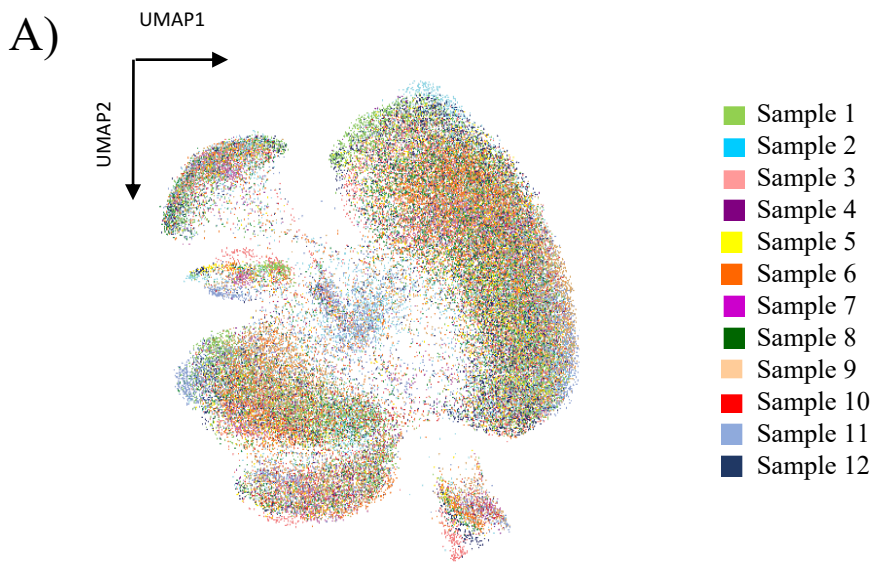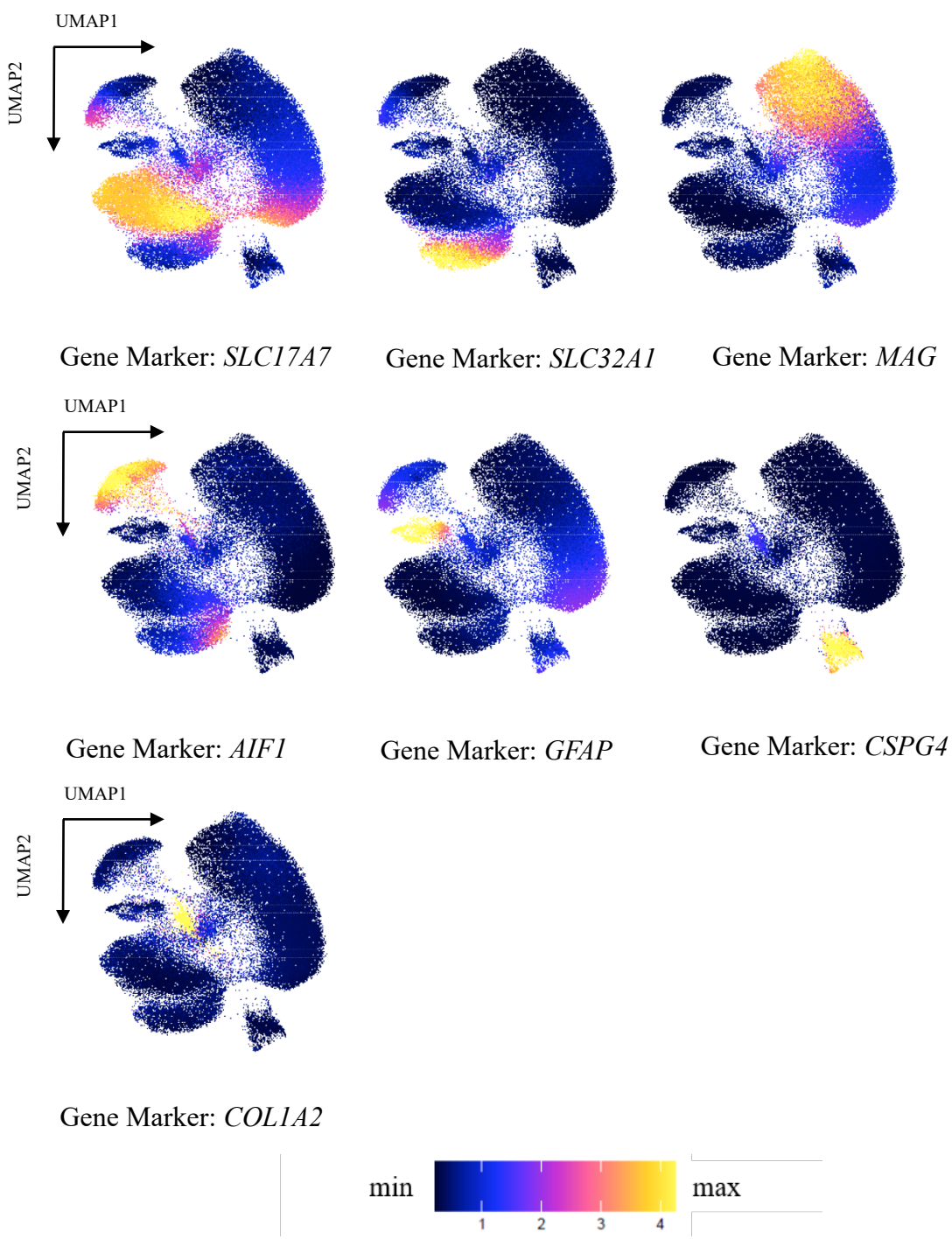**Supplementary Figure 1.** snATAC-seq data analysis clustering quality control.

A)

B)

Key: A) Integrated UMAP snATAC-seq representation of individual samples across all clusters, each color represents a sample; B) Ancestry distribution of percentage of cells per cluster from snATAC-seq data.

Supplementary Figure 2. SnATAC-seq cell marker cluster identification by chromatin accessibility.

Gene Marker: *SLC17A7*   Gene Marker: *SLC32A1*   Gene Marker: *MAG*

Gene Marker: *AIF1*   Gene Marker: *GFAP*   Gene Marker: *CSPG4*
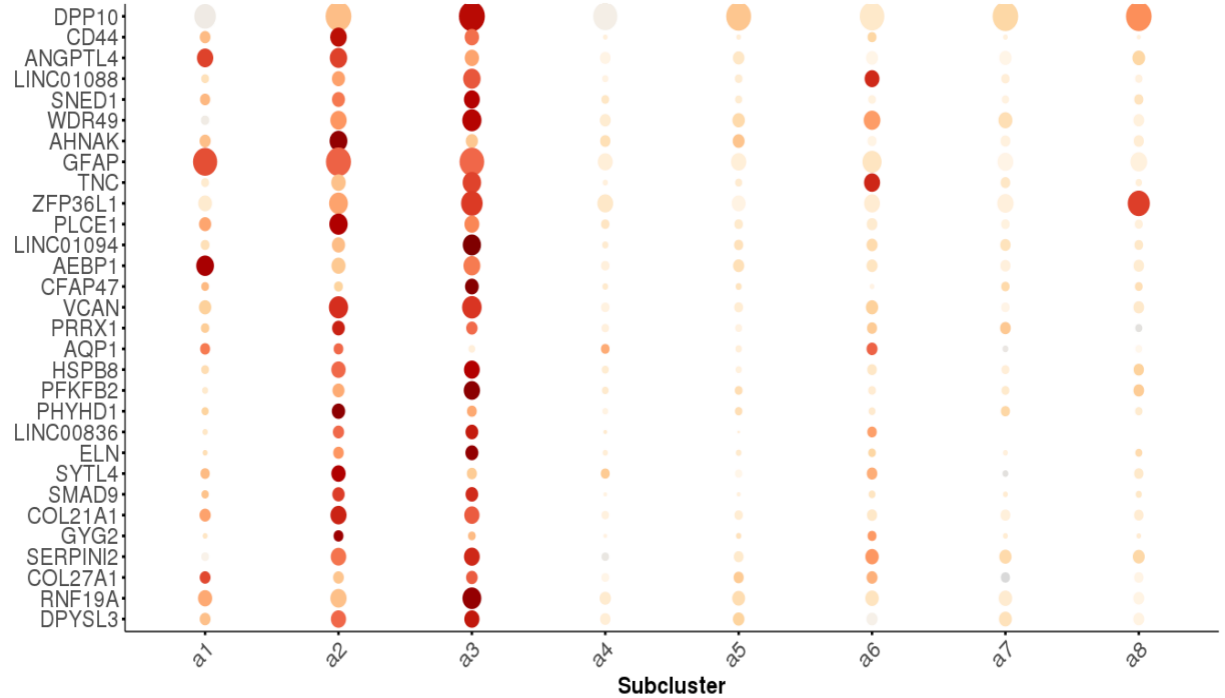
Gene Marker: *COL1A2*

Key: Marker genes used for cell type identification: *SLC1717* for excitatory neurons; *SLC32A1* for inhibitory neurons; *MAG* for oligodendrocytes; *AIF1* for microglia; *GFAP* for astrocytes, *CSPG4* for OPCs and *COL1A2* for VLMC.

**Supplementary Figure 3.** Astrocyte subtype classification.
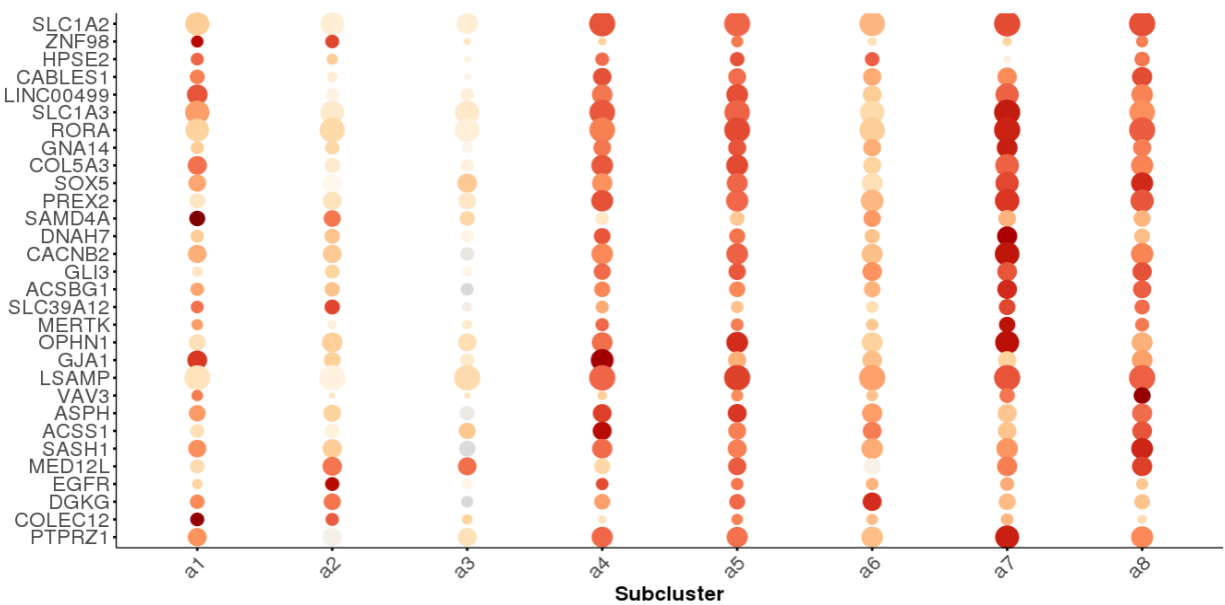
Key: Bubble plot showing the top 30 differentially expressed genes (DEGs) within the astrocyte clusters. The color represents the relative gene expression and the bubble size is the proportion of cells in the group expressing the gene.

Supplementary Figure 4. *APOE* chromatin accessibility in the other cell clusters where *APOE* is highly expressed but not differentially accessible between the ancestries.
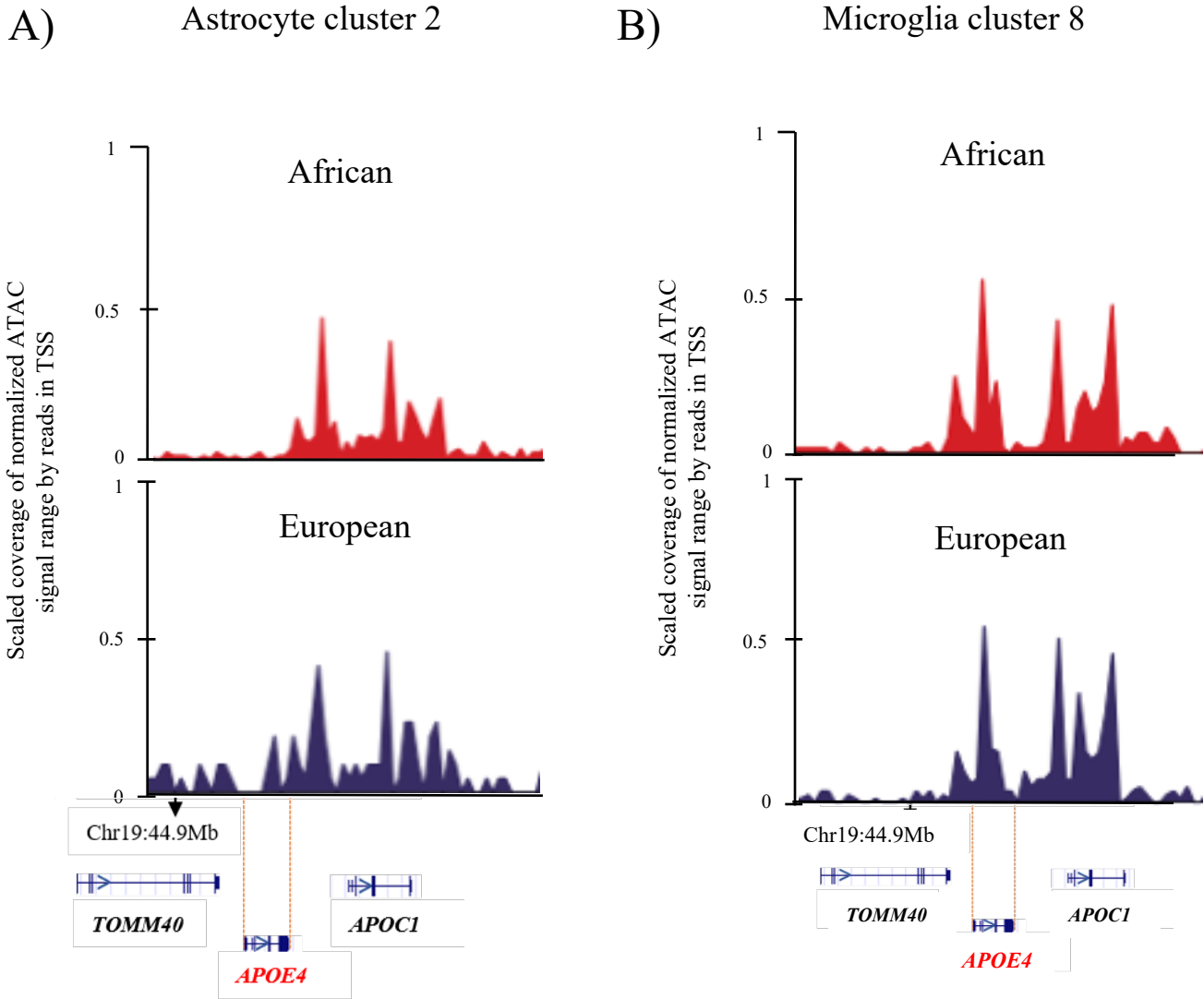
Key: Visualization of chromatin accessible peaks in the *APOE* local ancestry region between ancestries from Astrocyte cluster 2 (A) and Microglia cluster 8 (B). No significant differentially accessible peaks were observed between ancestries in either cluster.

Supplementary Figure 5. Visualization of local ancestry across all chromosomes per individual sample.

A)
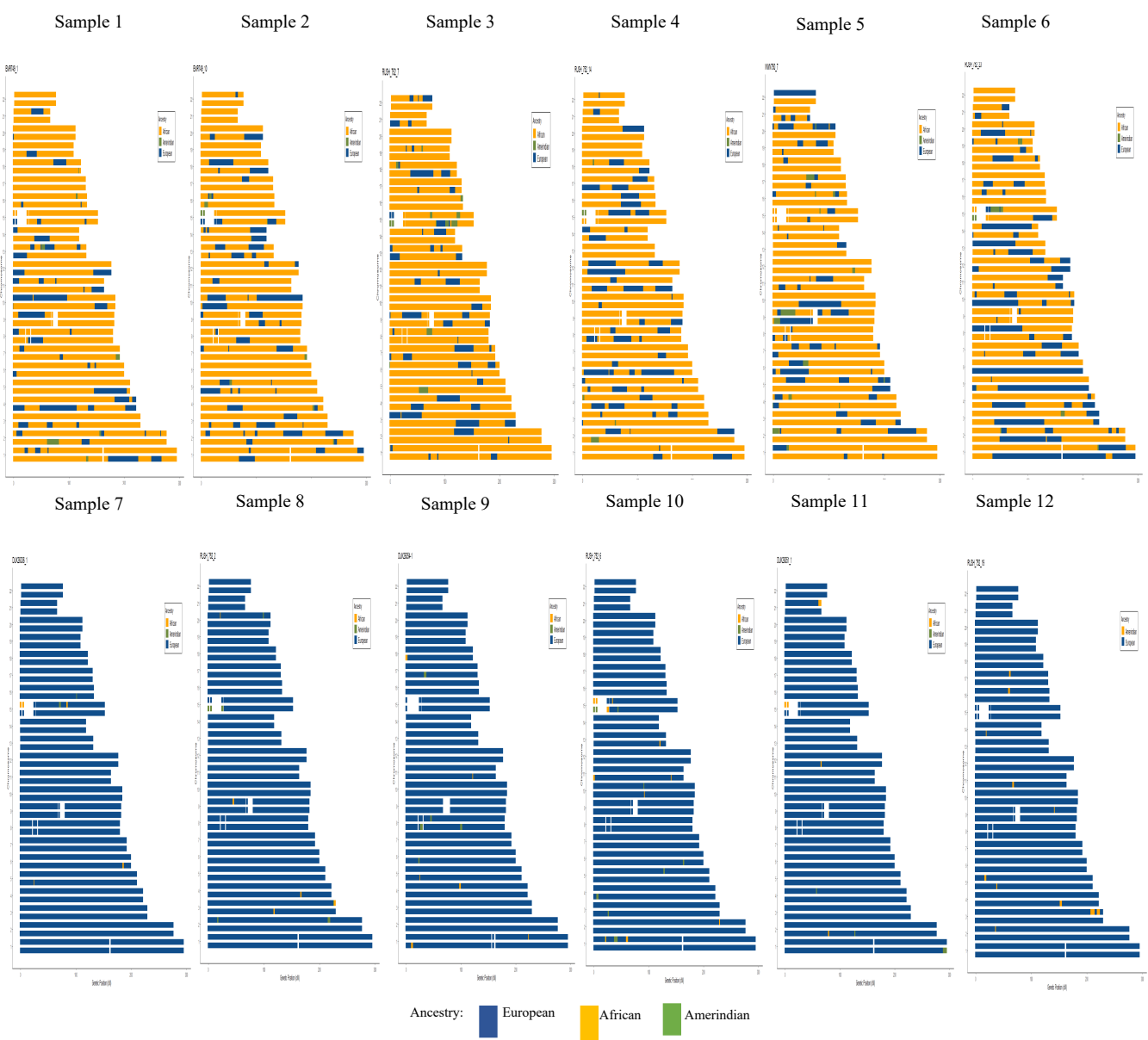
Key:A) Bar-plot showing the local ancestry across the genome. The y-axis represent the chromosomes and the x-axis represent the chromosomal position. Ancestries are represented by colors Blue (European), Yellow (African) and Green (Amerindian).

Supplementary Figure 5. Visualization of local ancestry across all chromosomes per individual sample.

B)
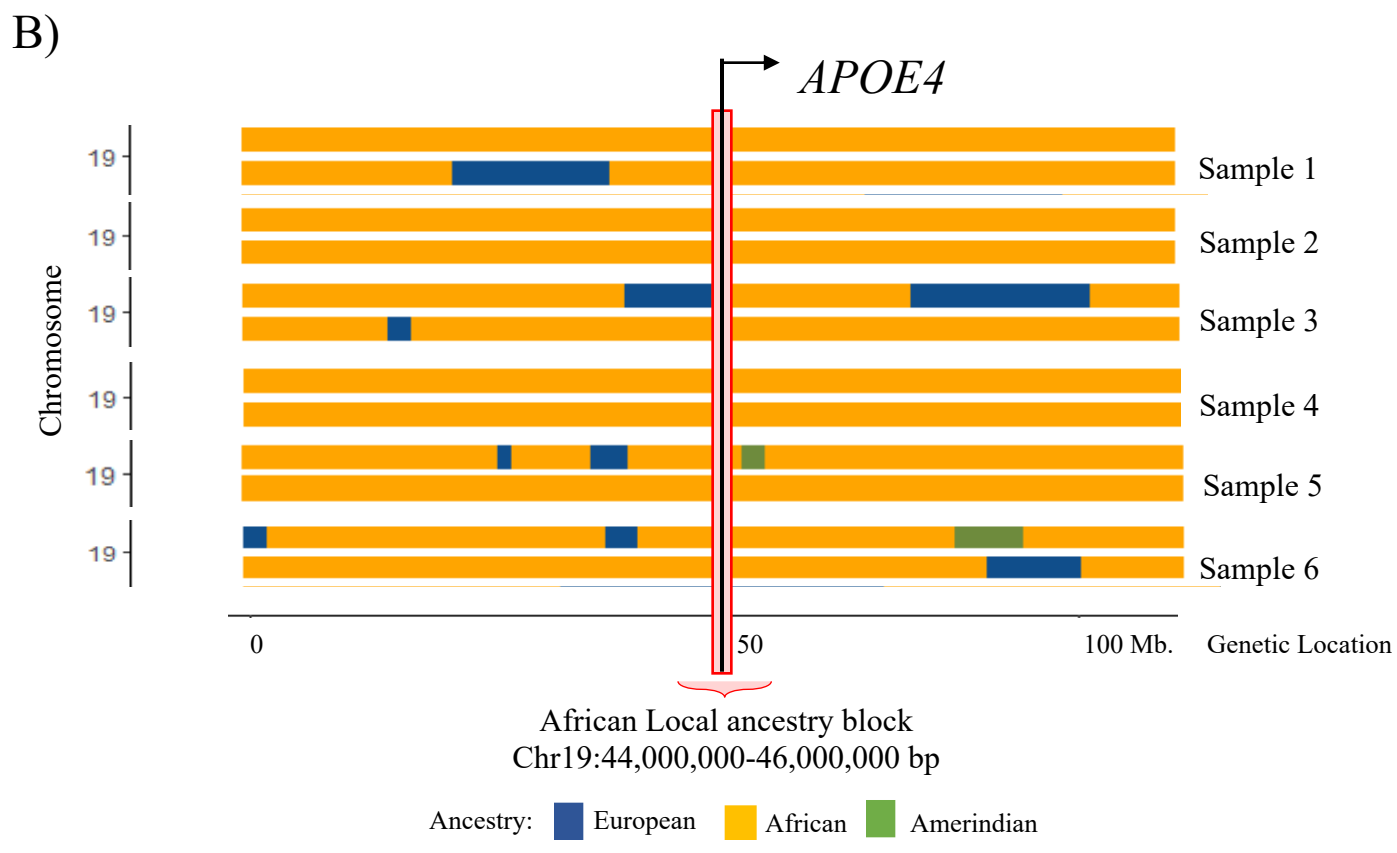
Key: B) Chromosome 19 Local Ancestry plots from African American samples. Light pink column shows local ancestry boundaries used for ancestry assignments in the *APOE* region.

Supplementary Figure 6. Enrichment of differentially accessible peak between ancestries in chromosome 19.
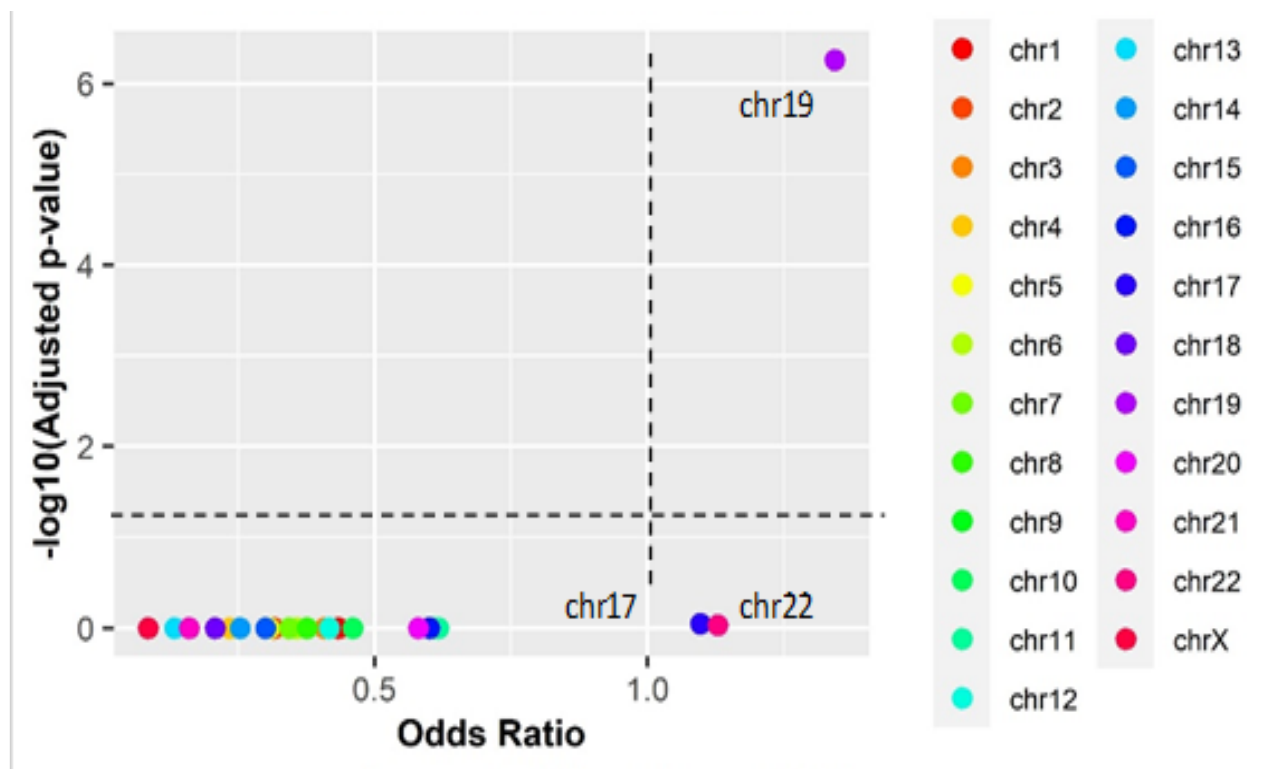
Key: The plot shows the significance of each gene set (genes associated to differentially accessible peaks by GREAT and HOMER software, located in a given chromosome) versus its odds ratio. Each point represents a single gene set (chromosome); the x-axis measures the odds ratio (0, inf) calculated for the gene set, while the y-axis gives the -log10 (adjusted *p*-value) of the gene set. The colored points represent each chromosome. The dotted lines represent statistical significance thresholds, the horizontal line represents the -log10 of an adjusted *p*-value <0.05. The -log10 values >1.3 show statistical significance. The vertical line represents that Odds ratios higher than 1 can be considered significant.