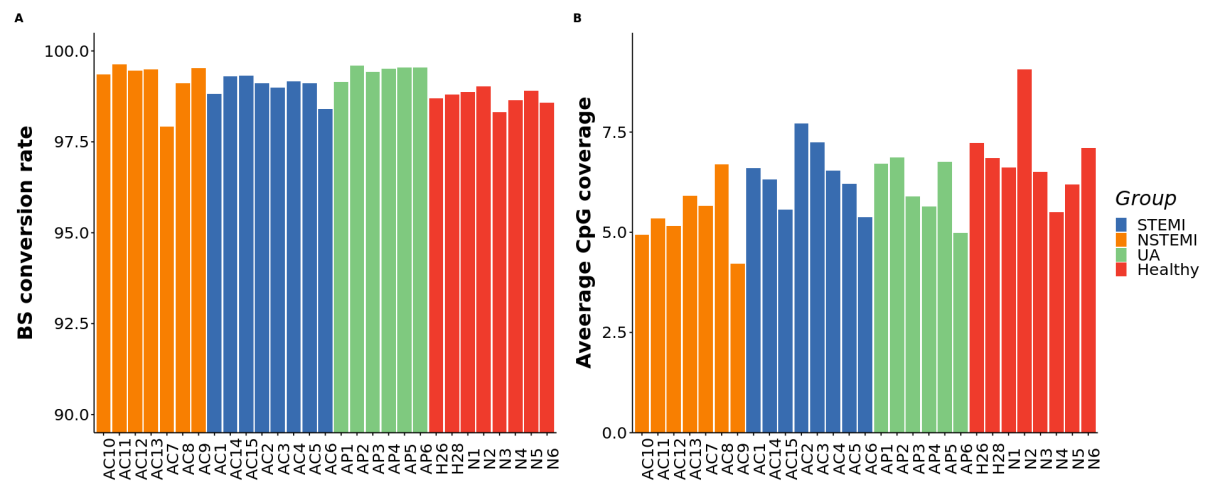
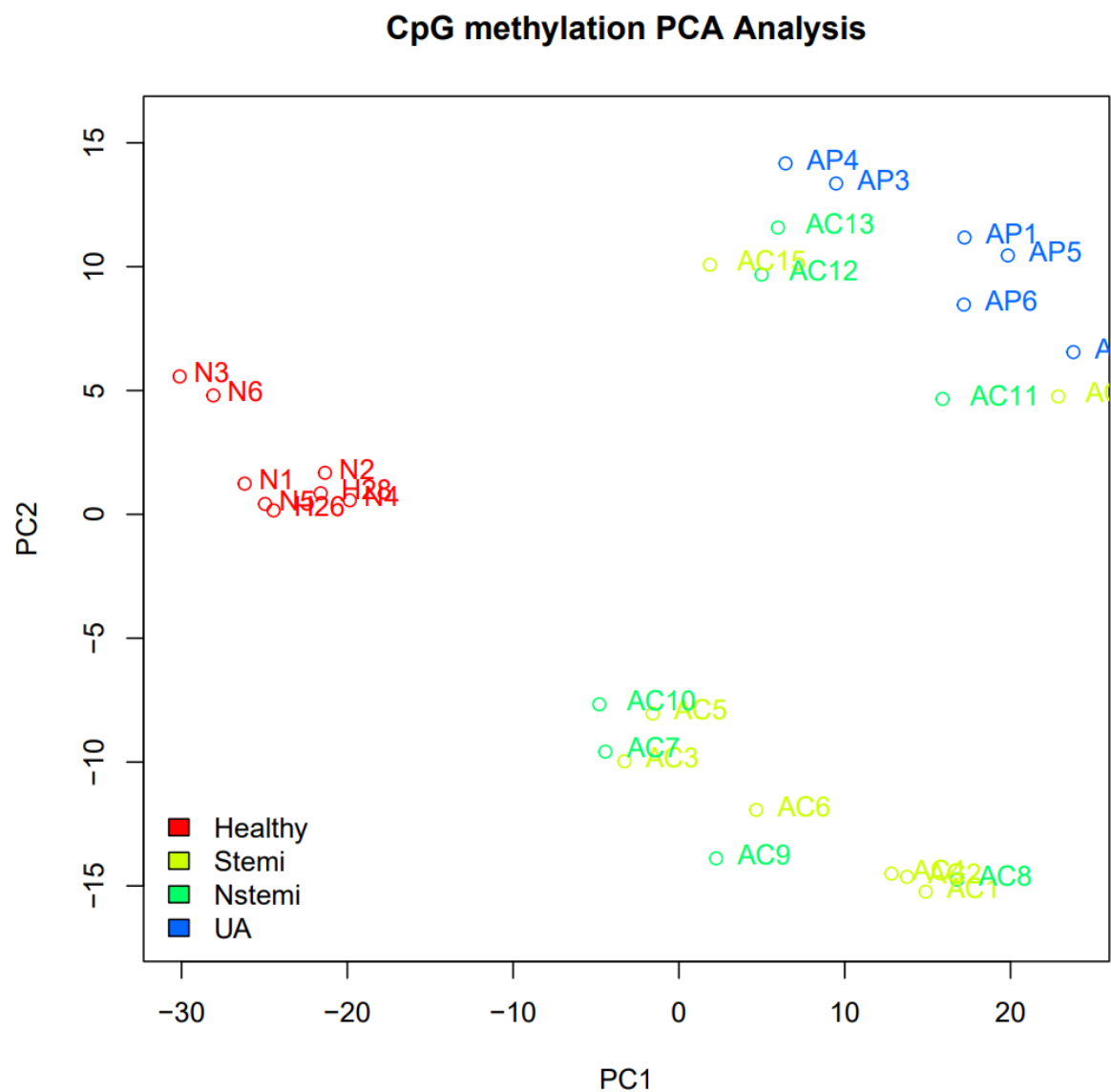


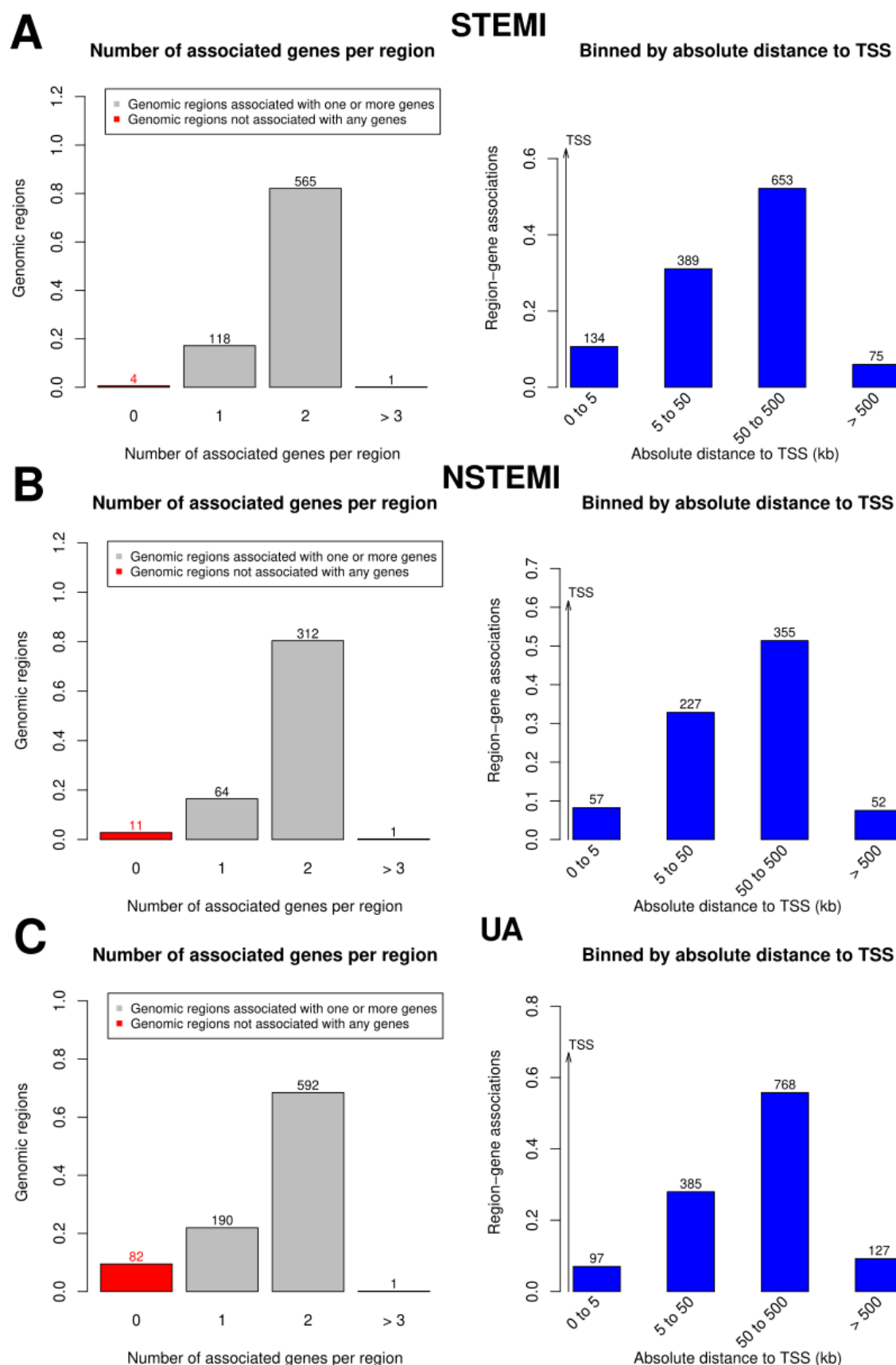
**Figure S1: Biomarker values for each patient group representing an ACS type or healthy subjects.**



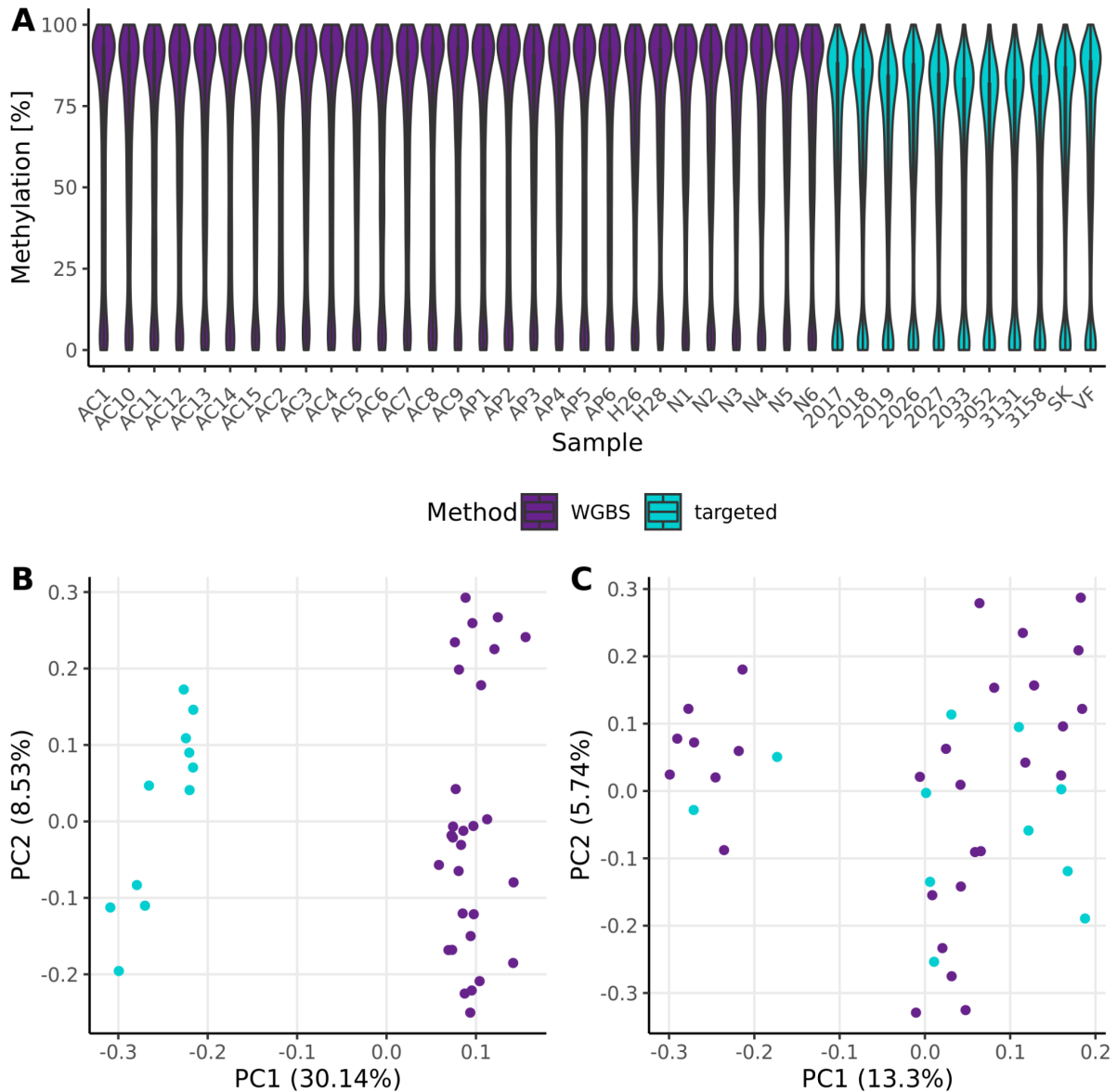
**Figure S2: A - BS conversion rate. B - Average CpG coverage for the cfDNA samples.**



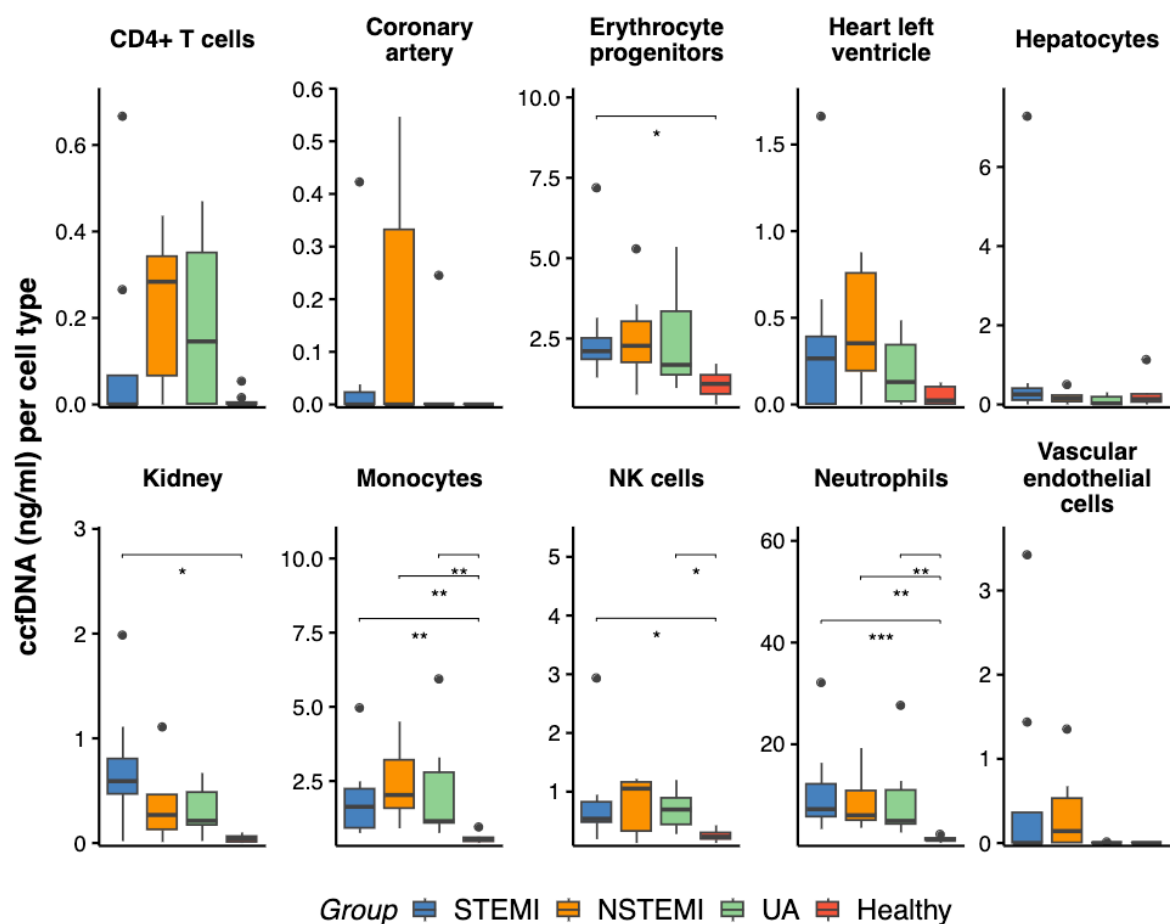
**Figure S3: PCA on CpG methylation percentage using all differentially methylated regions (DMRs with at least 25% difference among 2 groups, q-value smaller than 0.01) from discovery samples.**



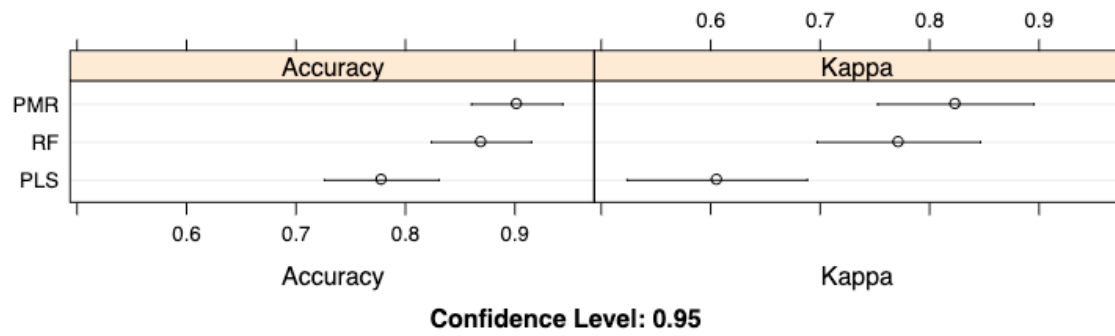
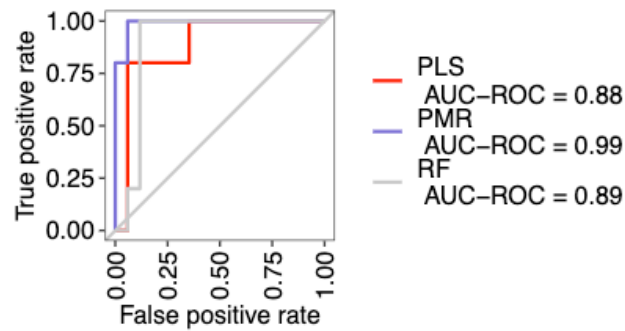
**Figure S4: DMRs associated with genes and their distances to transcription start sites (TSS).** The DMRs for each comparison were annotated by Genomic Regions Enrichment of Annotations Tool (GREAT) using the rGREAT package (release 3.12).



**Figure S5: Removal of systematic methylation bias. A - Systematic bias between targeted sequenced samples and WGBS samples.** Boxplots are depicted within the violin plots, showing hinges from 25th to 75th percentile with whiskers expanding from  $\pm 1.5^*$  interquartile range of the hinges. **B - PCA on log transformed percentages of methylation from all samples on all common methylation tiles ( $n = 9114$ ).** **C - PCA on log transformed, quantile normalized, ComBat adjusted and back transformed percentages of methylation from all samples on common methylation tiles ( $n = 9114$ ).**



**Figure S6:** Predicted cell/tissue-type proportions per group normalized by the concentration of the sample's ccfDNA. The stars indicate significance levels according to Wilcoxon Test (Significance Levels \*: P-Value < 0.05, \*\*: P-Value < 0.01, \*\*\*: P-Value < 0.001)

**A****B**

**Figure S7: Machine learning approaches on ccfDNA methylation data to determine ACS type.** A - Performance Metrics under Cross-Validation Resampling. B - ROC-Curve  
 PMR - Penalized Multinomial Regression, PLS - Partial Least Squares regression, RF - Random Forest, ROC - receiver operating characteristic, AUC-ROC - Area under the ROC curve for Cross-Validation resampling.