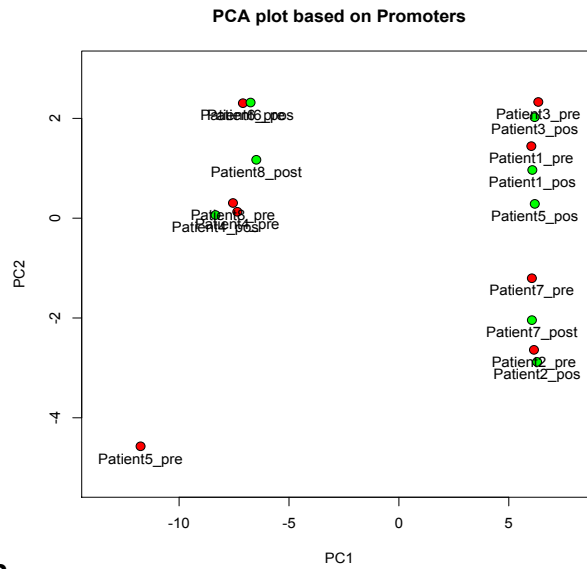
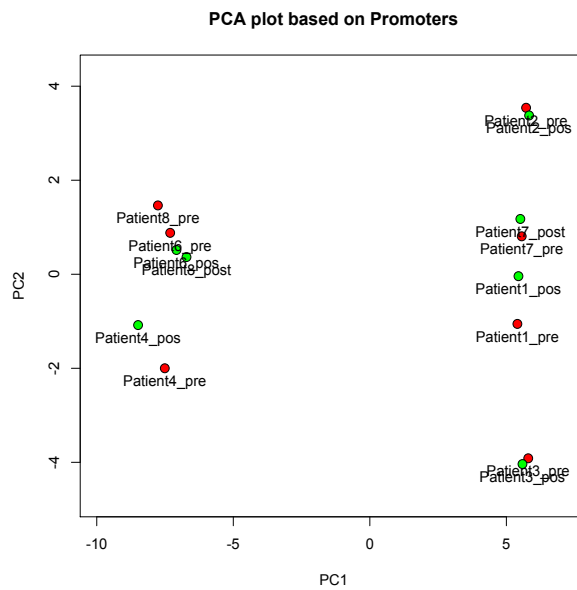


## Supplementary Figures

**A**

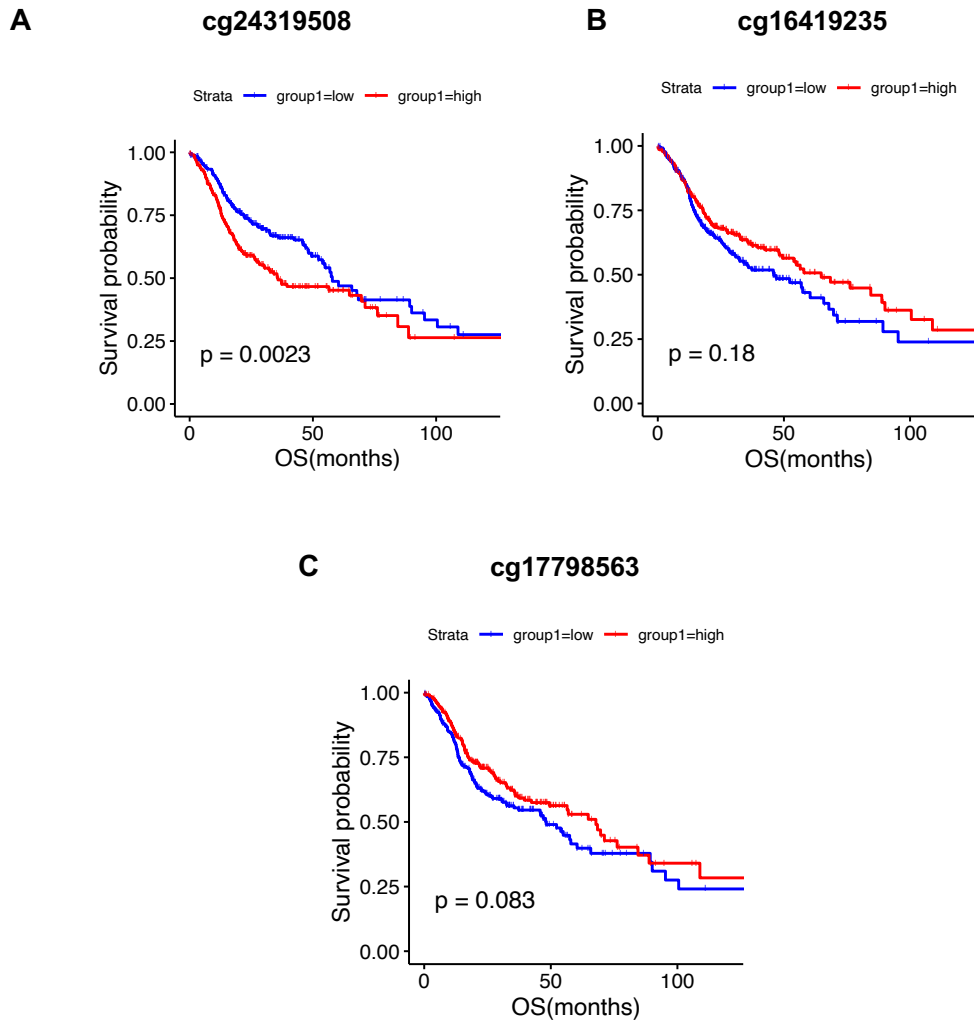


**B**



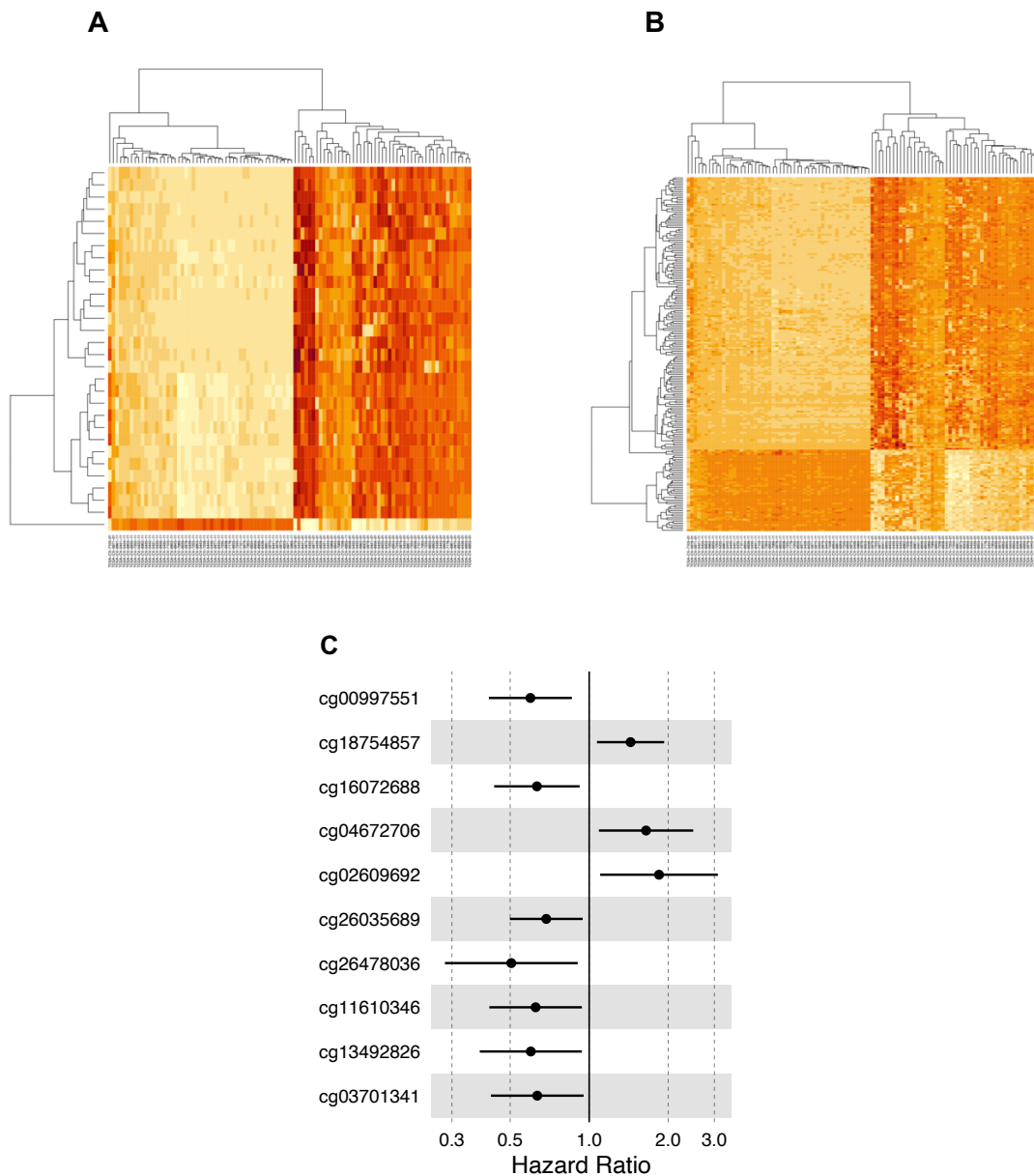
### Supplementary Figure S1.

Genome-wide PCA of cfDNA methylation profiles (promoter regions only) using (A) all pre- and post-treatment plasma samples; (B) all patients but Patient 5.



**Supplementary Figure S2.**

The prognostic significance of cg24319508 (in gene *IRF4*), cg16419235 (in *PENK*) and cg17798563 (in *ZIK1*) in the TCGA-HNSC cohort. The patient groups are stratified by the medium methylation level of the CpG site.



**Supplementary Figure S3.**

(A-B) The unsupervised clustering results of TCGA-HNSC tissue samples based on the top 30 DMRs (A) and top 300 DMRs (B) identified from the cfDNA data showing successful separation of tumor and normal tissue samples. The tissue samples are from 100 paired tumor and normal tissue methylation data collected from 50 patients in TCGA cohort. (C) The top 10 CpGs (in the top DMRs) that are significantly associated with patient overall survival in the TCGA data.