

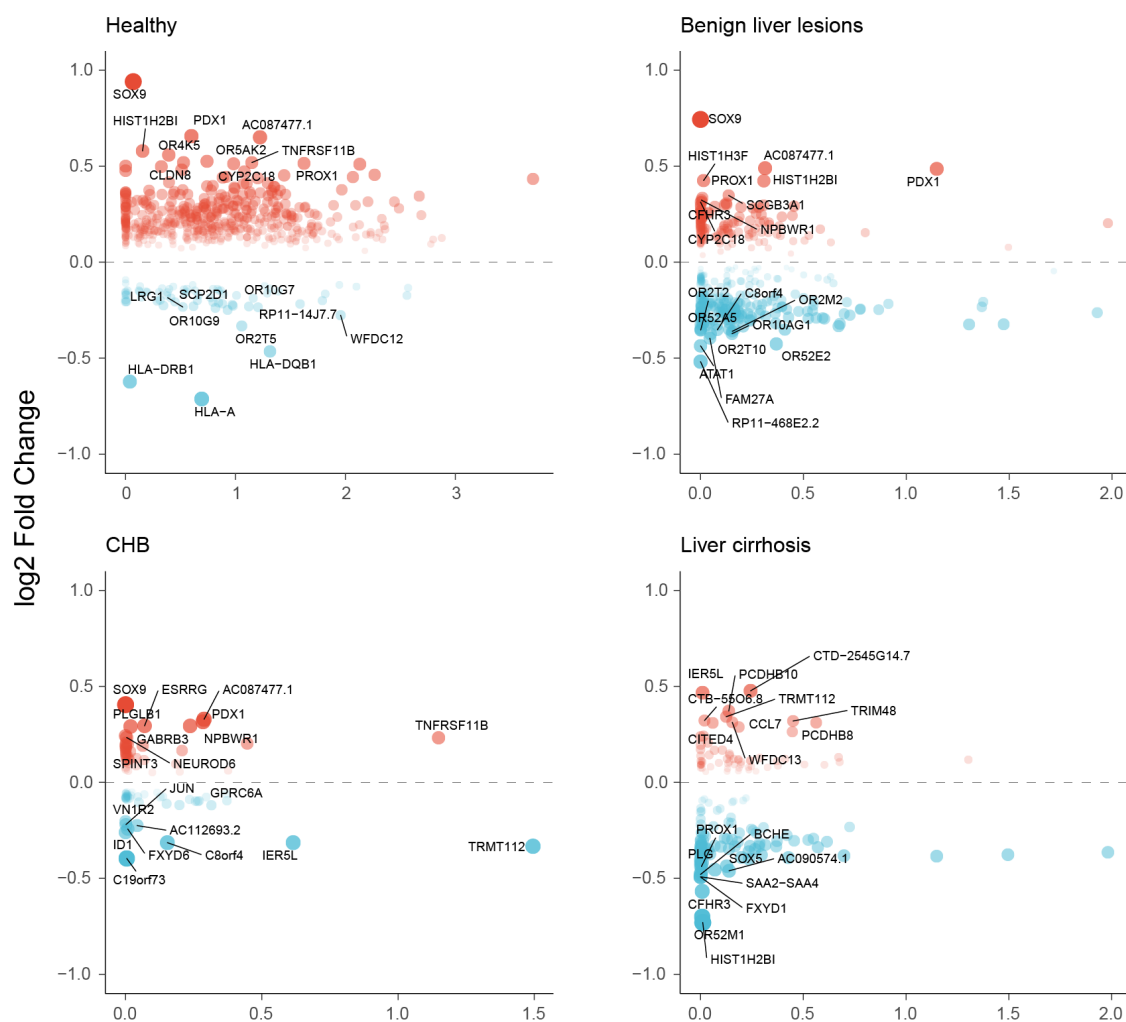


Figure S1 Scatter plot showing the DHGs between early HCC and non-HCC samples in cfDNA. Red and blue represent the up- and down-regulation in HCC, respectively. Top 10 up- and down-regulated genes are labeled.

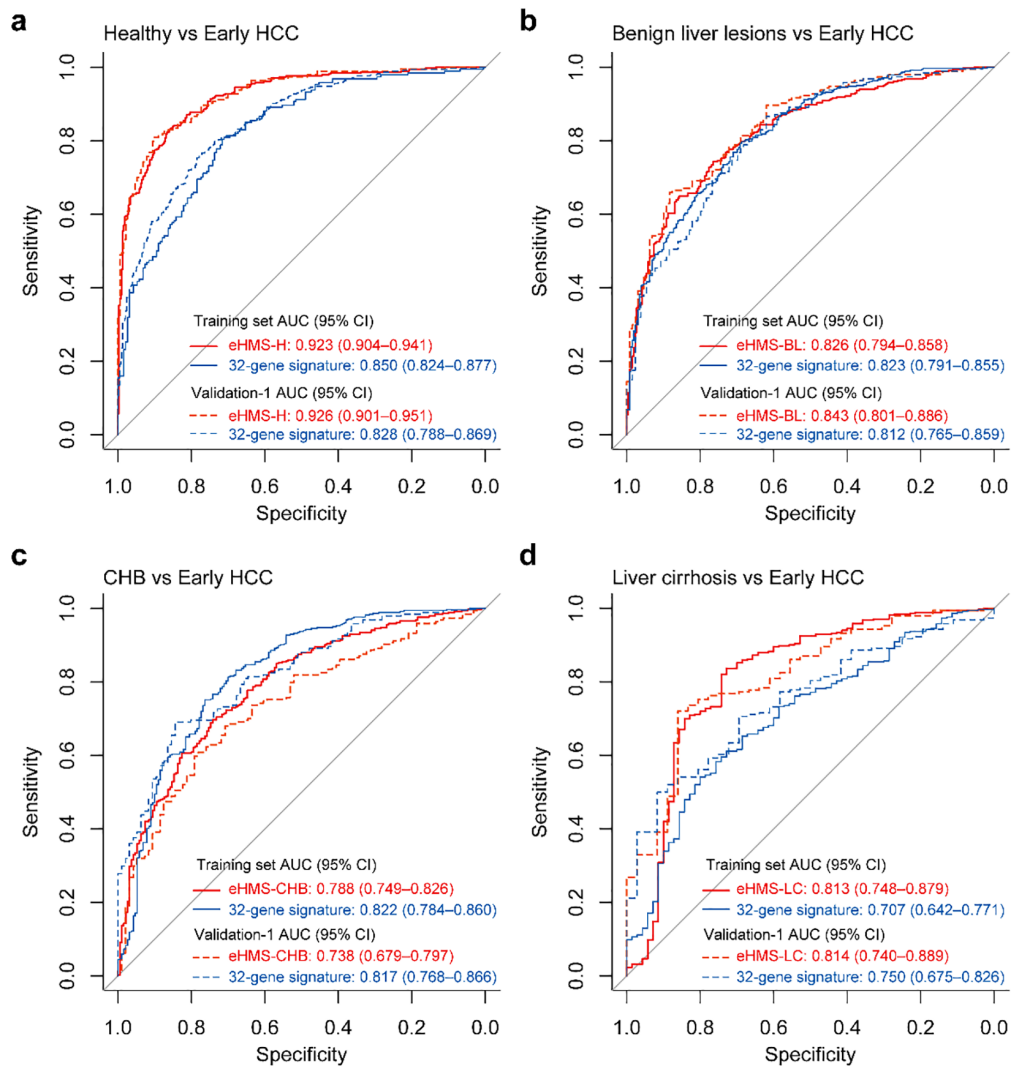


Figure S2 The performance of eHMS for distinguishing the HCC and non-HCC samples based on the score of (A) eHMS-H, (B) eHMS-CHB, (C) eHMS-CHB, and (D) eHMS-LC.

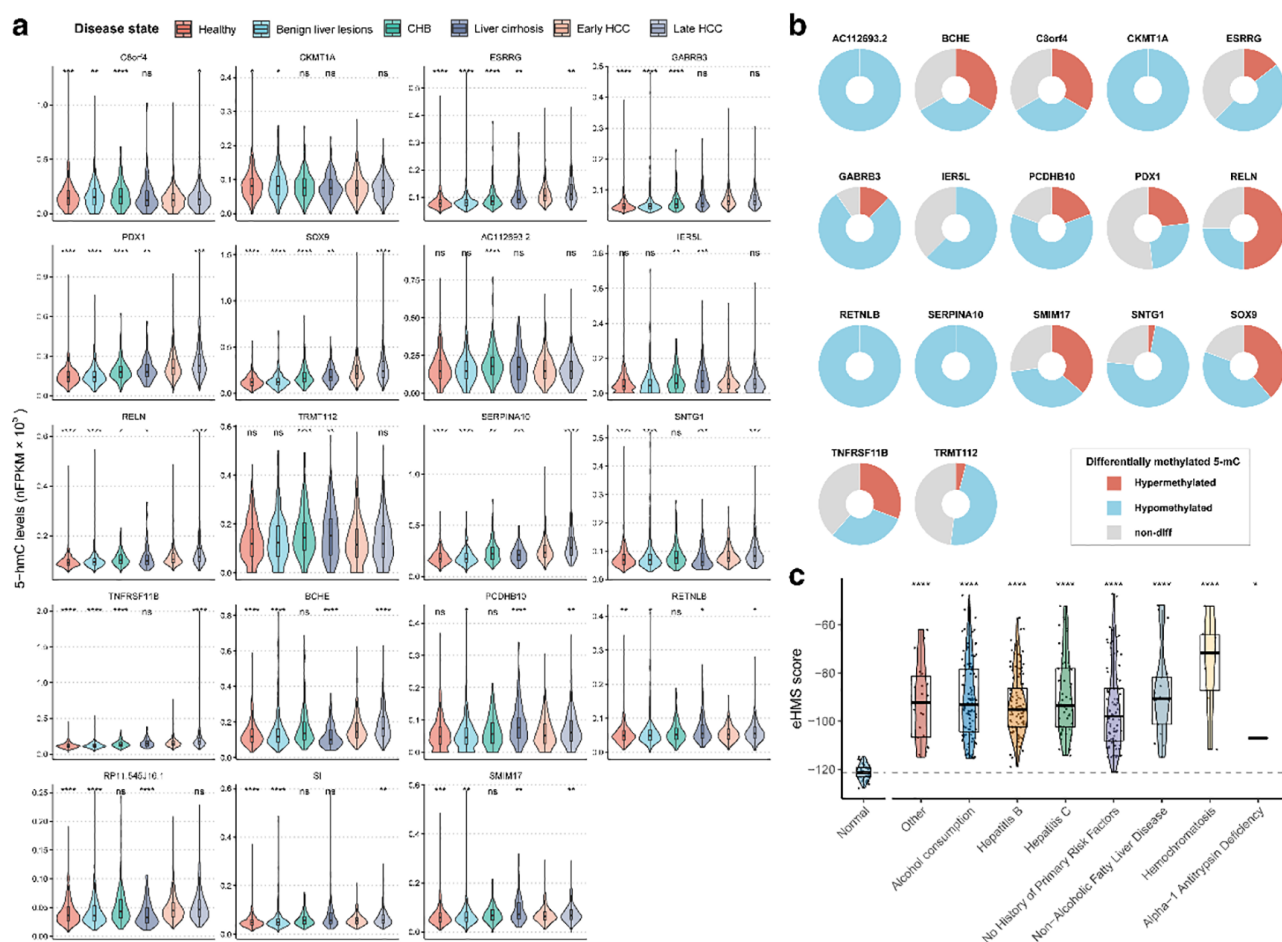


Figure S3 5-HmC and 5-mC levels of genes in eHMS. (A) Violin plot showing the 5-hmC levels of eHMS gene across different disease states. The significance label marks the difference between early HCC and other case state. (B) Percentage of differentially methylated 5-mC sites in eHMS gene regions. (C) Box plot showing the MeHMS score across HCCs with different disease history. The significance label marks the difference between normal and HCC tissues. NS, not significant; *, $P < 0.05$; **, $P < 0.01$; ***, $P < 0.001$; ****, $P < 0.0001$, as calculated by the Mann-Whitney U test (A) and (C).

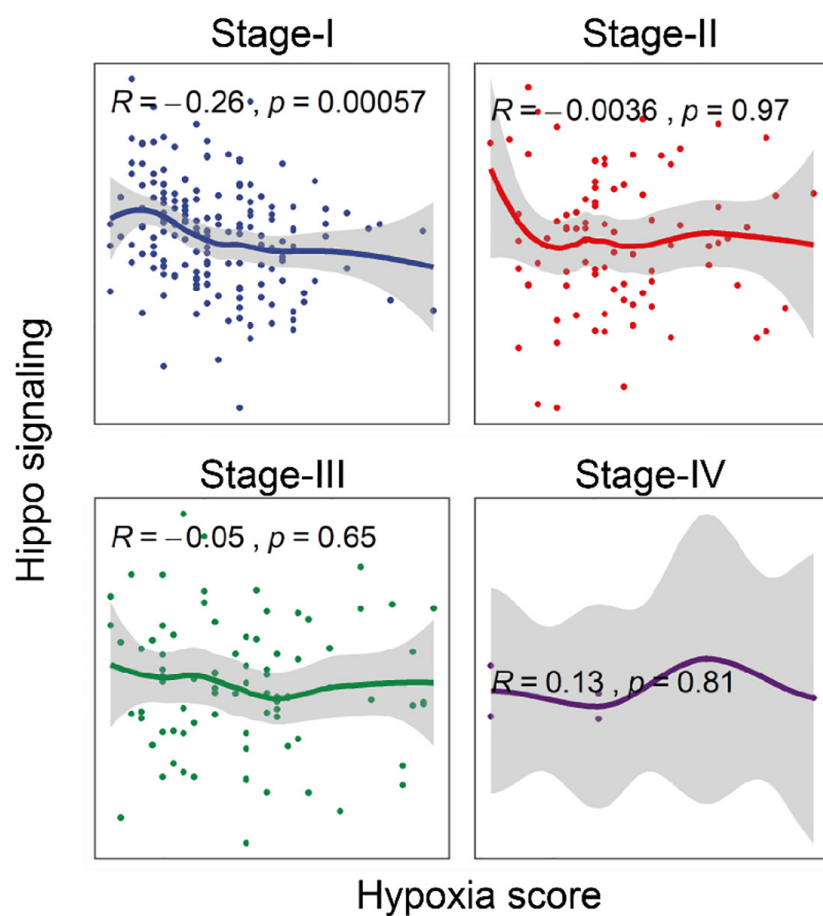


Figure S4 Scatter plot showing the correlation between Hypoxia score and Hippo signaling score in different tumor stages in TCGA-HCC cohort, respectively. P value was calculated by Spearman's correlation test. Dots colored by normal and different tumor stages.

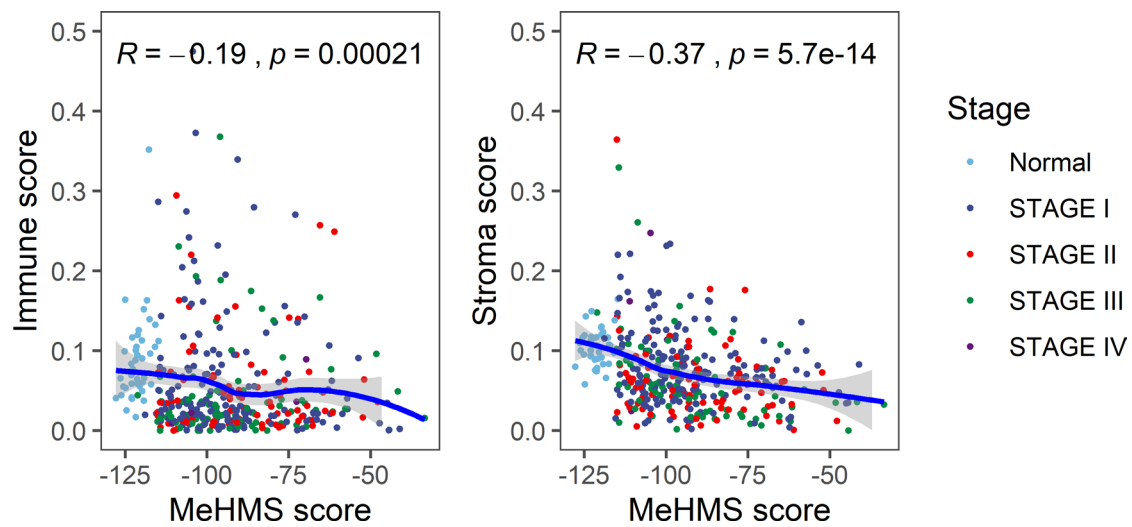


Figure S5 Scatter plot showing the correlation between MeHMS score and Immune score (left) and Stroma score (right), respectively. P value was calculated by Spearman's correlation test. Dots colored by normal and different tumor stages.