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Multiomics profiling of plasma and buffy coat unveils predictive biomarkers for immunotherapy responses in patients with hepatocellular carcinoma

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Immune checkpoint blockade (ICB) is now robustly applied to cancer treatment of patients with advanced hepatocellular carcinoma (HCC). However, the lack of stable biomarkers in prediction of immunotherapy impedes the effective patient stratification who will benefit from ICB treatment, highlighting the urgent need for the reliable blood-based predictive biomarkers for HCC immunotherapy. Here, we performed blood multiomics analysis, integrating targeted proteome data and methylome sequencing data from plasma and buffy coat samples of HCC patients. Differential expression and methylation analyses revealed a distinct landscape in gene regulation and expression between responders and non-responders at the blood level. A predictive gene signature constructed by machine learning algorithms exhibited promising performance, encouraging further validation. Extended investigation at the transcriptome level using in-house whole transcriptome data and publicly available single-cell RNA-seq data has corroborated the reliability of identified predictive biomarkers in determining the immunotherapy responses of HCC patients. Further validation and standardization would potentially contribute to the discovery of therapeutic targets, enhancing ICB treatment efficacy of HCC patients.