Hepatocellular carcinoma (HCC) is heterogeneous lethal disease in genomic and clinical level. By integrating 15 previously established genomic signatures for HCC subtypes, we identified 5 clinically and molecularly distinct consensus subtypes. STM (STeM) is characterized by high stem cell features, vascular invasion, and poor prognosis. CIN (Chromosomal INstability) has moderate stem cell features but high genomic instability and low immune activity. IMH (IMmune High) is characterized by high immune activity. BCM (Beta-Catenin with high Male predominance) is characterized by prominent b-catenin activation, low miRNA expression, hypomethylation, and high sensitivity to sorafenib. DLP (Differentiated and Low Proliferation) is differentiated with high HNF4A activity. We developed and validated a robust predictor of consensus subtype with 100 genes (PICS100). We also identified potential serum biomarkers that can stratify patients into 5 subtypes. Because these subtypes are highly associated with currently available treatments, our findings may provide the foundation for rationalized biomarker-based clinical trials.