SUPPLEMENTARY FIGURE LEGENDS

Supplementary Figure 1: Kaplan-Meyer estimates measuring RFS probability over time in the BIOSTORM cohort.

Supplementary Figure 2: (A-C) Representative images demonstrating that tumors bearing pERK negative tumor hepatocytes have intact vascularization, stained by CD31, and are no proliferative as shown by the lack of Ki67 staining. (D-F) Representative images of tumors with tumor endothelial cells positive for pERK, characterized by positive CD31 staining and Ki67 negative. (G-I) Representative images of tumors with tumor hepatocytes pERK positive, with positive CD31 staining and Ki67.

Supplementary Figure 3: Predictive value of pERK staining in tumor hepatocytes (A) and tumor endothelial cells (B); of pVEGFR2 staining in tumor hepatocytes (C) and of VGFA measured by FISH (D) in the BIOSTORM cohort.

Supplementary Figure 4: Targeted Exome Sequencing of 143 HCC samples. (A) Summary statistics for targeted exome sequencing. (B) Average number of reads per gene in the whole cohort was 500X.

Supplementary Figure 5: (A) Estimation of the abundance of different immune cell types.[1] (B) Several MHC components are down-regulated in '*sorafenib RFS responders*', compared to '*non-responders*'. (C) Heatmap displaying up/down-regulation of immune-related molecules and down-regulation of AFP in '*sorafenib RFS responders*' vs. '*non-responders*'.

Supplementary Figure 6: (A) The pro-inflammatory kinase FAK1/PTK2 was globally down-regulated in '*sorafenib RFS responders*'. (B) mRNA levels of STAT proteins were lower in '*sorafenib RFS responders*' compared to '*non-responders*'.

REFERENCES

1. Newman AM, Liu CL, Green MR, et al. *Robust enumeration of cell subsets from tissue expression profiles.* Nat. Methods 2015;12:453–7.