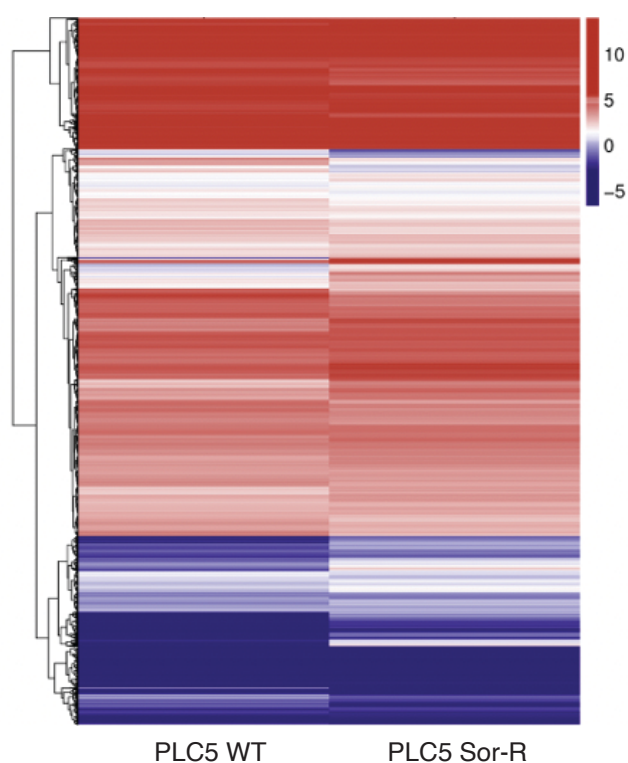
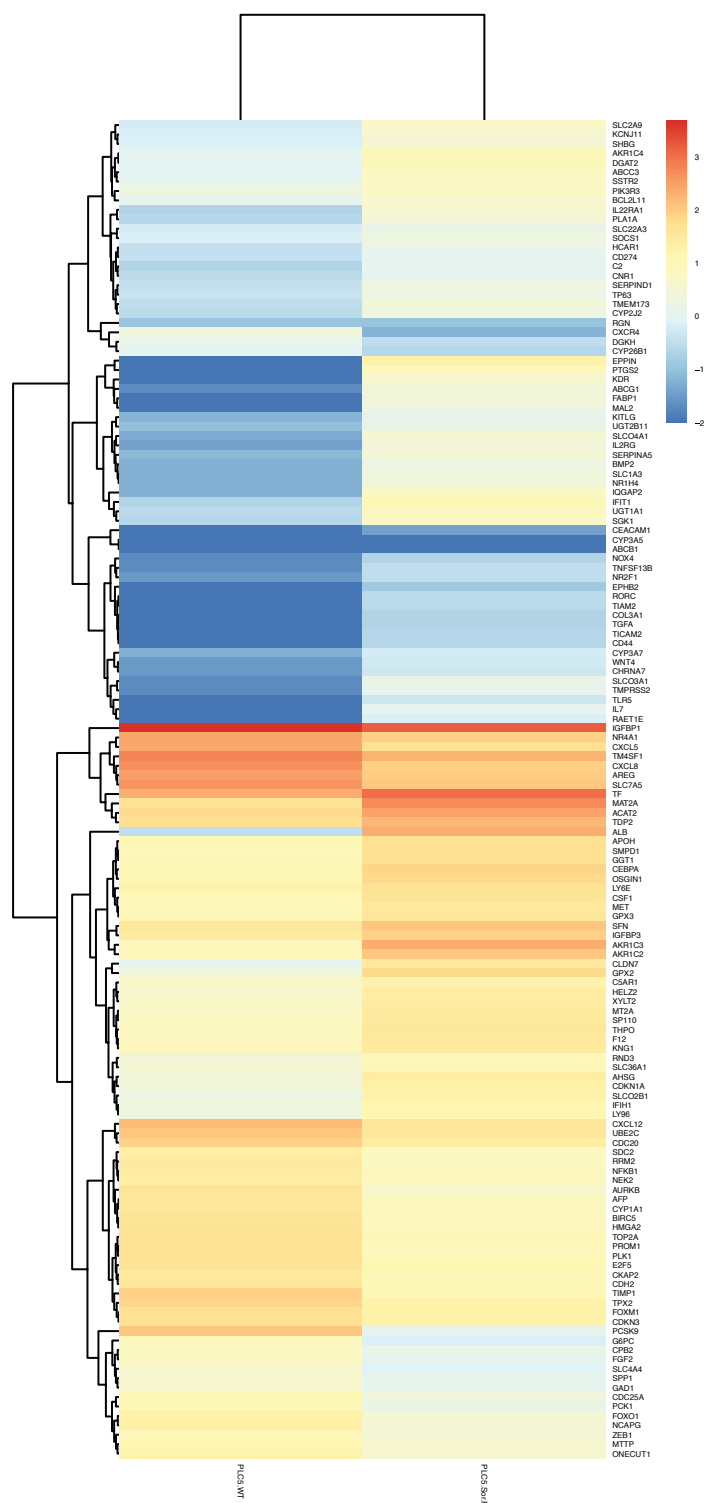


**A**

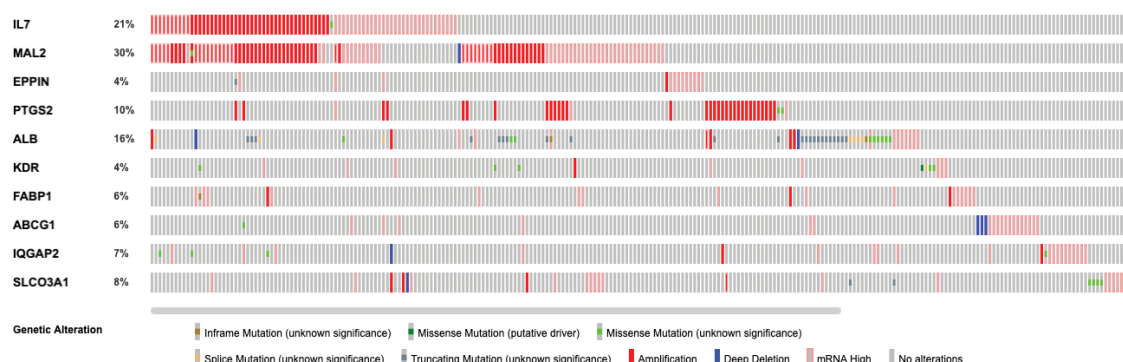


**B**

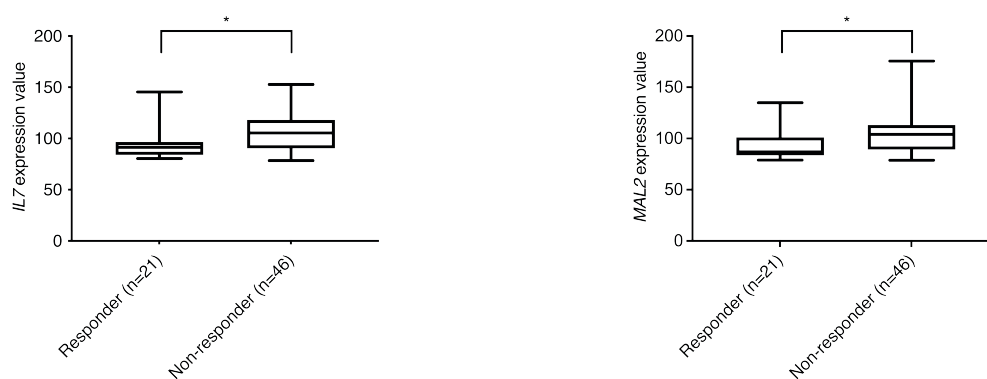


**Supplementary Figure S1** Identification of *IL7* and *MAL2* as candidate genes in HCC-associated Sorafenib resistance. **(A)** RNA-seq heatmap of 3,255 differentially expressed genes (DEGs) showing differences in gene expression profiles between PLC/PRF/5 wild-type (PLC5 WT) and Sorafenib resistant mutant (PLC5 Sor-R) cells – 2,240 genes were upregulated and 1,015 genes were downregulated. **(B)** Under further stringent selection criteria ( $P$ -value < 0.01, FDR < 0.02, Fold-change:  $\pm 1.5$ ), 142 candidate genes were identified in contributing to Sorafenib resistance – 96 upregulated genes and 46 downregulated genes.

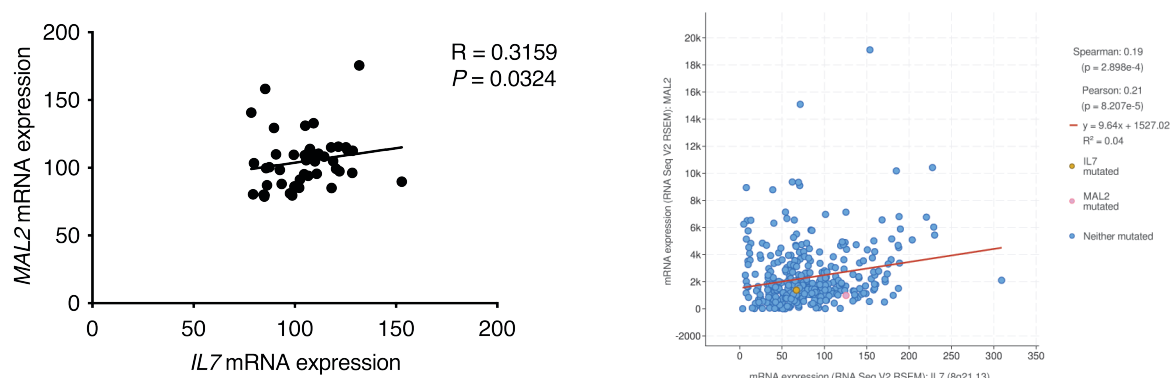
**A**



**B**



**C**



**Supplementary Figure S2** Clinical relevance of *IL7* and *MAL2* as candidate genes in HCC-associated Sorafenib resistance. (A) *IL7* and *MAL2* were either amplified or showed high mRNA expression in majority of affected HCC patients. Co-occurrence of *IL7* and *MAL2* was found in the TCGA liver cancer database. (B) Expression of *IL7* and *MAL2* in Sorafenib non-responding patients (GSE109211) were significantly higher than responding patients. \*,  $P < 0.05$ , two-tailed unpaired t-test. (C) Significant tendency for co-occurrence of *IL7* and *MAL2* was found in GSE109211 clinical study (left) and TCGA liver cancer database (right), based on their gene expression levels.