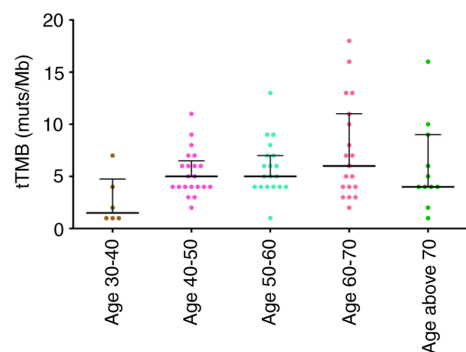


Figure S1. tTMB distribution in age-stratified HCC groups. HCC patients were stratified by age into four groups, and tTMB distribution was compared in each group. Long-horizontal line indicates the median TMB; short-horizontal line indicates the top quartile of tTMB. TMB, tumor mutation burden; tTMB, tissue TMB; HCC, hepatocellular carcinoma.



Scatter plot showing tTMB (mut/Mb) for Male and Female groups. The y-axis ranges from 0 to 20. The Male group (blue circles) has a mean of approximately 5.0 and a range from 1 to 16. The Female group (orange squares) has a mean of approximately 4.0 and a range from 2 to 18. A P-value of 0.6917 is indicated.

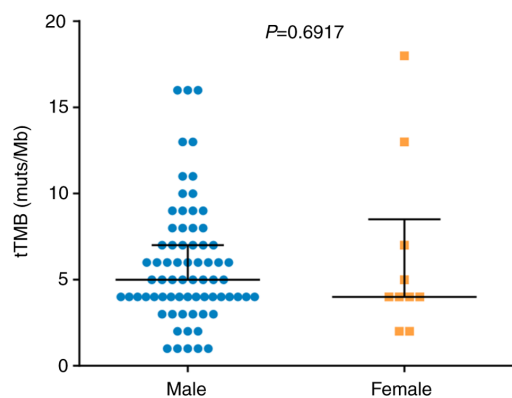


Figure S3. tTMB Distribution in hepatocellular carcinoma samples classified according to gene mutation status for (A) TP53, (B) ARID1A, (C) CTNNB1, (D) MLL and (E) NCOR1. Mann Whitney test was used to test the significance; non-parametric, double tail test.  $P < 0.05$  shows significant difference between two groups. Wild type, gene wild-type samples; mutation, gene mutated samples. Long line indicates median tTMB, and short line indicates the top quartile of tTMB. tTMB, tissue tumor mutation burden.

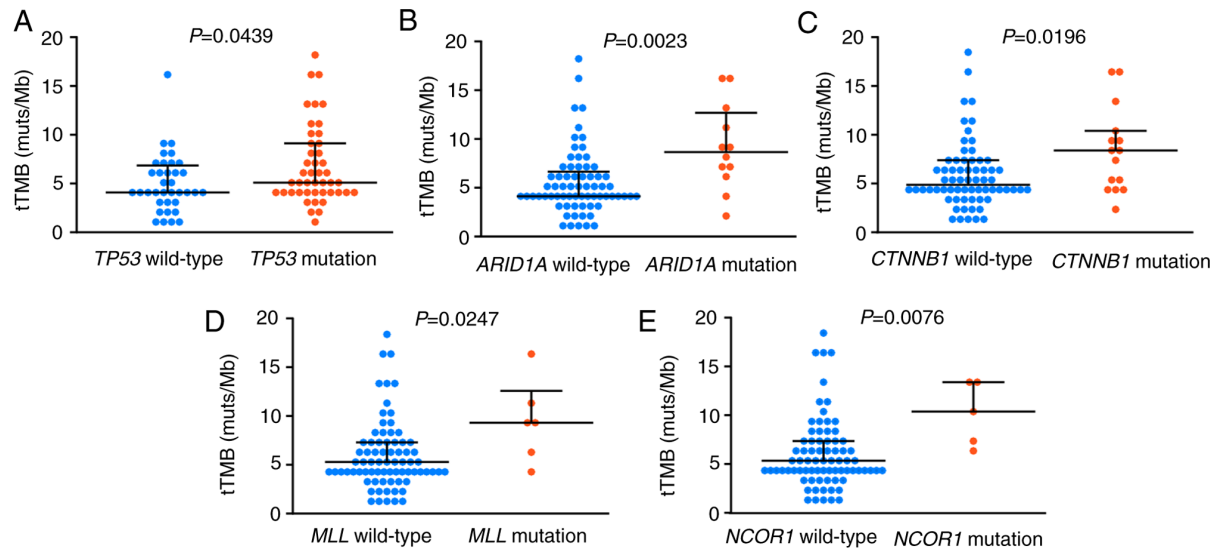


Figure S4. Kaplan-Meier analysis of OS and RFS based on gene mutation status. No statistically significant differences were observed in OS for (A) CTNNB1, (B) MLL, and (C) NCOR1 mutations, in RFS for (D) TP53, (E) ARID1A, (F) CTNNB1, and (G) NCOR1 mutations compared with the wild-type genotypes in the The Cancer Genome Atlas hepatocellular carcinoma cohort. OS, overall survival; RFS, recurrence-free survival.

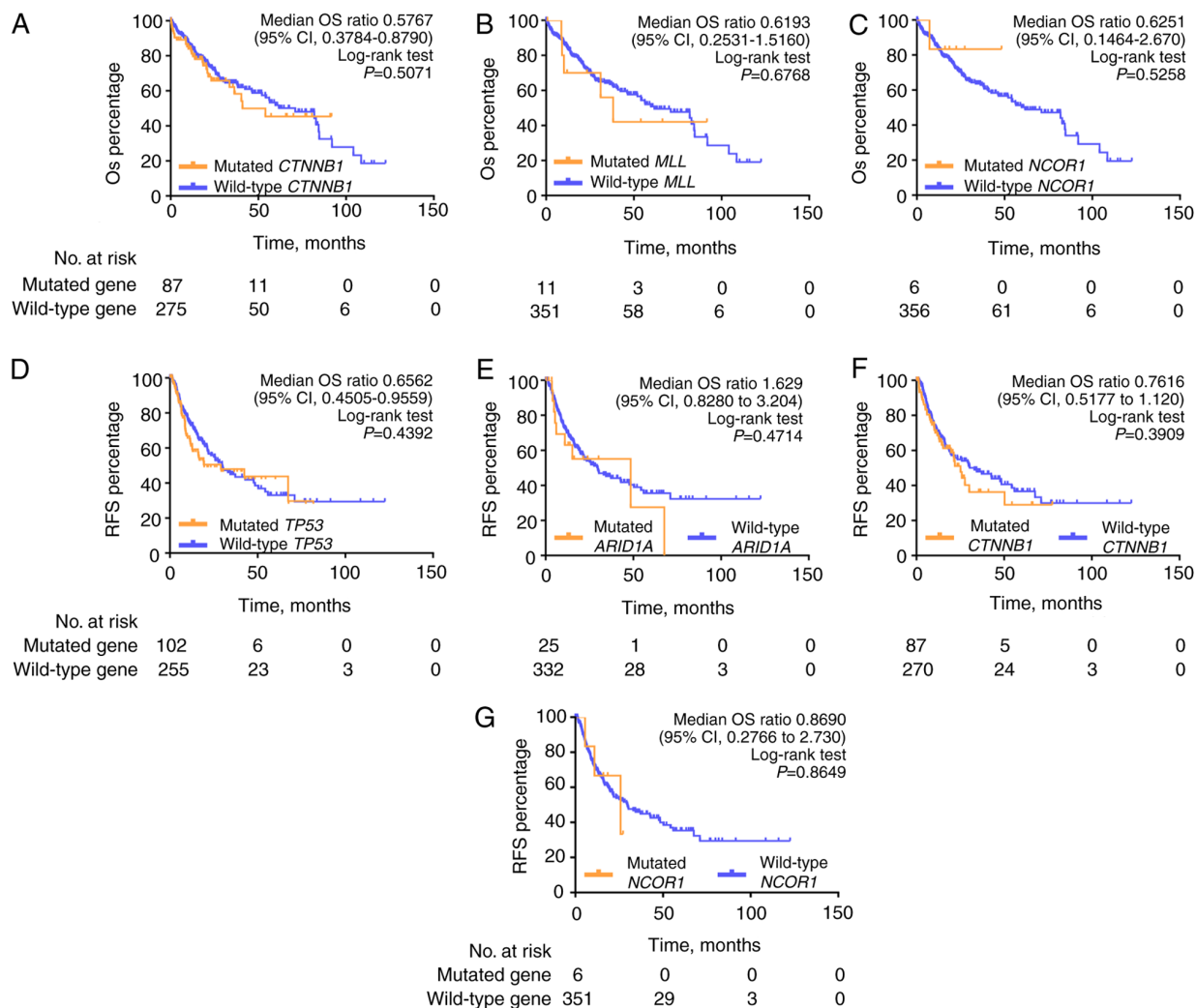


Table SI. Mutation rates of genes that predict response to immunotherapy efficacy in patients with hepatocellular carcinoma.

A, Positive response				
Gene, mutation rate	Sample IDs	c.HGVs	Alteration frequency (%)	Clone proportion (%)
<i>POLE</i> , 2.47%	GP012	c.3971G>A	24.49	50.94
	GP078	c.1434C>G	6.16	58.52
B, Resistance response				
Gene, mutation rate	Sample IDs	c.HGVs	Alteration frequency (%)	Clone proportion
<i>PTEN</i> , 2.47%	GP078	c.956delC	6.67	63.37
	GP014	c.871_879delGAAAATGGA	19.91	67.58
C, Hyper-progressive response				
<i>DNMT3A</i> , 1.23%	GP001	c.1522C>T	23.57	34.59