Table S1. Impact of NS5A Mutations associated with HCC on protein stability and their localization.

#	Mutation	$\Delta\Delta G^a$	Location in NS5A		Interacting Protein/Nucleic Acid
1	S3T	-0.36	Alpha-helix	N-terminal	p53, p85-PI3K, β-catenin
2	**C13S**	**-1.86**			
3	**C13R**	**-1.74**			
4	T122M	0.06	Beta-sheet	Domain-1	NS5B, p53, p85-PI3K, β-catenin
5	F127L	-0.43			
6	**F127S**	**-1.08**			
7	M133I	-0.31			
8	N137D	0.54	Coil-turn		
9	N137K	0.16			
10	Q181E	0.62	Beta-sheet		Viral RNA genome
11	Q181G	0.52			
12	Q181H	0.53			
13	Q181P	0.22			

^{a} $\Delta\Delta G$ (kcal/ mol) = (ΔG wt fold - ΔG mutant fold) was calculated by STRUM algorithm. A negative $\Delta\Delta G$ value indicates a decrease in protein stability.

The mutations with $\Delta\Delta G < -1.0$, indicating a relevant decrease in protein stability is reported in bold