

Table S1. Mutations predicted by energy-based and evolution-based approach

Combined mutant: -14.23 kcal/mol (18 mutations)							
Chain	Mutation	Conserved	Correlated	BTC by majority	BTC by ratio	FoldX (kcal/mol)	Rosetta (kcal/mol)
A	T41V	N	N	N	N	-1.64	-2.05
A	E49T	N	N	Y	Y	0.37	-
A	N54A	N	N	Y	N	-0.18	-
A	N63S	N	N	N	Y	-0.27	-
A	S66G	N	N	Y	Y	0.26	-
A	A79Y	N	N	N	N	-1.28	-2.11
A	T81Q	N	N	N	N	-1.23	-2.81
A	T89N	N	N	N	Y	0.43	-
A	S90P	N	N	Y	Y	-1.14	0.25
A	S94G	N	N	Y	Y	0.11	-
A	S106N	N	N	Y	N	—2	-
A	L114V	N	N	Y	Y	0.22	-
A	A125G	N	N	Y	N	0.00	-
A	G126A	N	N	Y	N	-0.84	-
A	S131T	N	N	Y	N	0.27	-
A	Y133T	N	N	Y	Y	0.40	-
A	T143M	N	N	N	N	-1.27	-6.55
A	T145Y	N	N	N	N	-1.20	-3.14

Table S2. sequences of mutated primers

primer	Sequence (5' - 3')
T41V-F	TACTACTCCTTCTGG <u>GT</u> TGATGGTGCAAGCGGA
T41V-R	TCCGCTTGCACCATCA <u>AAC</u> CCAGAAGGAGTA GTA
A79Y-F	TGGAATCCGGGCAGTT <u>TAT</u> AGAACCATCACGTAC
A79Y-R	GTACGTGATGGTTCT <u>ATA</u> ACTGCCCCGGATTCCA
T81Q-F	CCGGGCAGTGCCAGAC <u>AG</u> ATCACGTACTCCGGC
T81Q-R	GCCGGAGTACGTGATC <u>TGT</u> CTGGCACTGCCCCGG
A79Y/T81Q-F	TGGAATCCGGGCAGTT <u>TAT</u> AGAC <u>AG</u> ATCACGTACTCCGGC
A79Y-T81Q-R	GCCGGAGTACGTGATC <u>TGT</u> CT <u>ATA</u> ACTGCCCCGGATTCCA

The underline indicates the mutated sites