

FIG. 1A

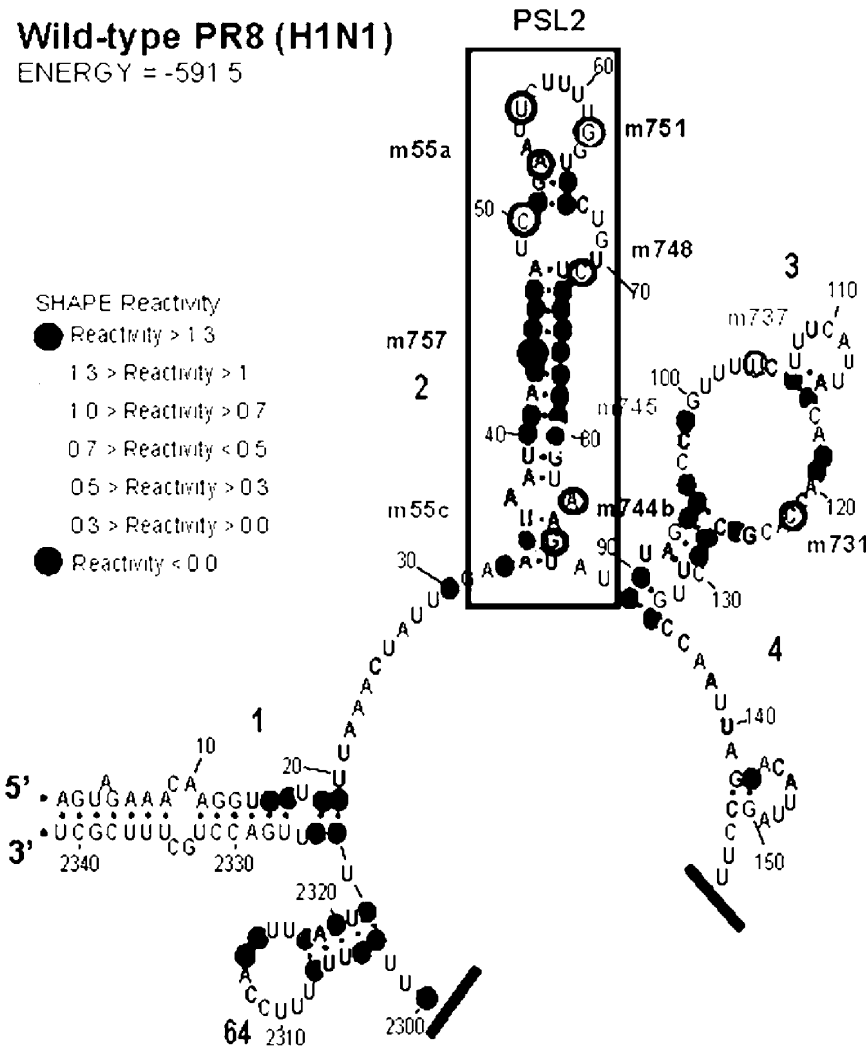
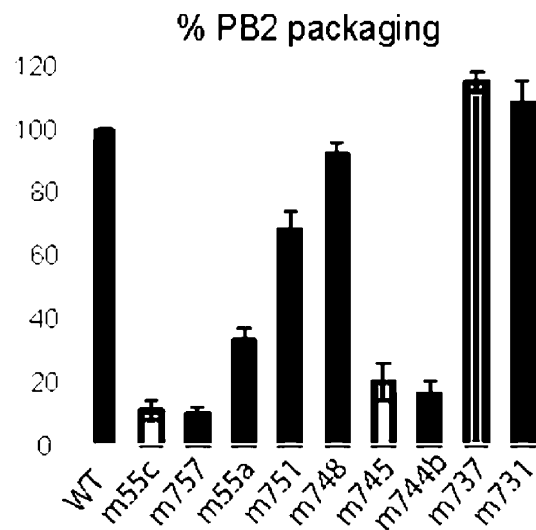


FIG. 1B



Mutant Name	Mutation Site(s)
m55c	CU35,36UC
m757	G44C
m55a	CAU50,53,56
m751	G62C
m748	C71U
m745	A80U
m744b	AG83,85UA
m737	U104A
m731	C122G

FIG. 1C

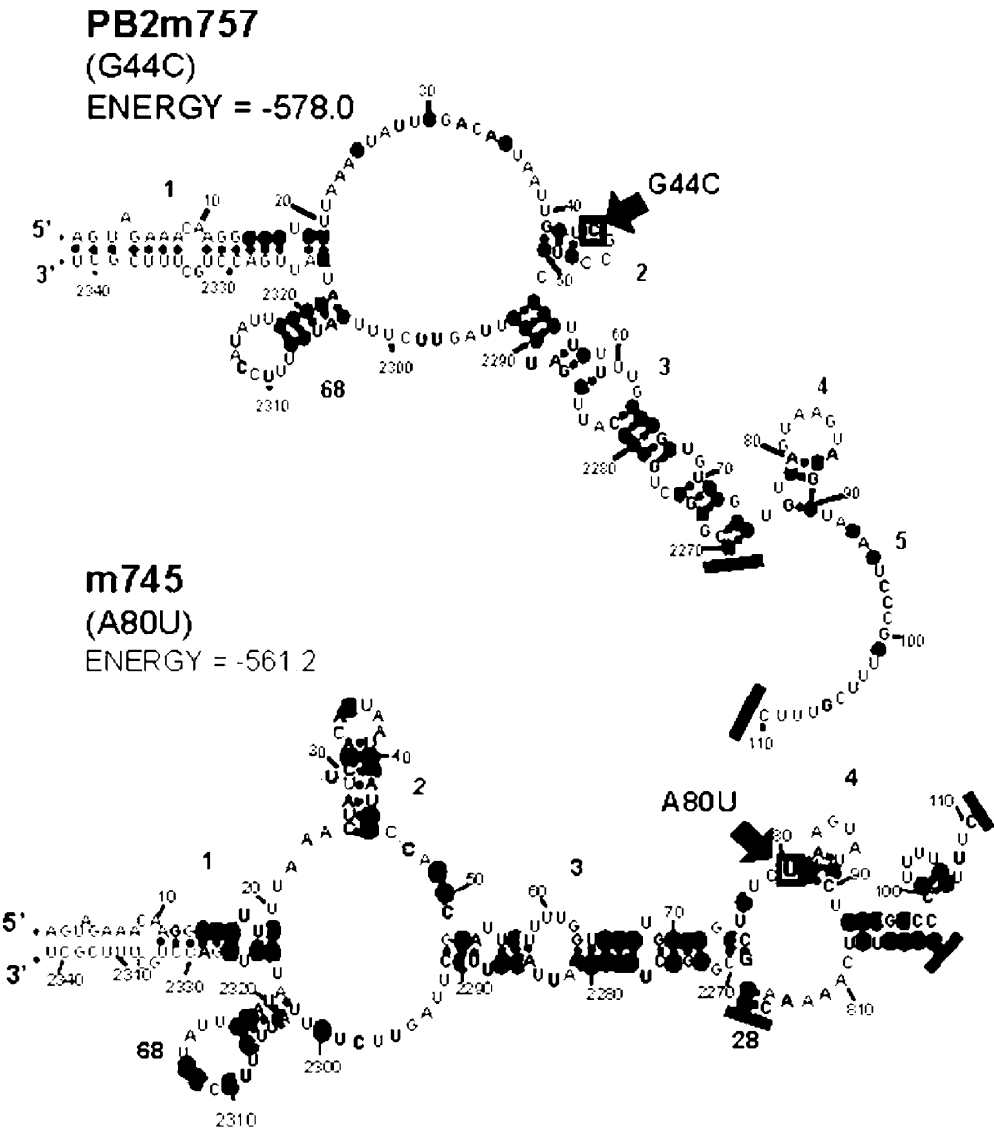


FIG. 1D

1918 pandemic (H1N1)
ENERGY = -593.6



FIG. 1E

High-path avian (H5N1)
ENERGY = -619.8

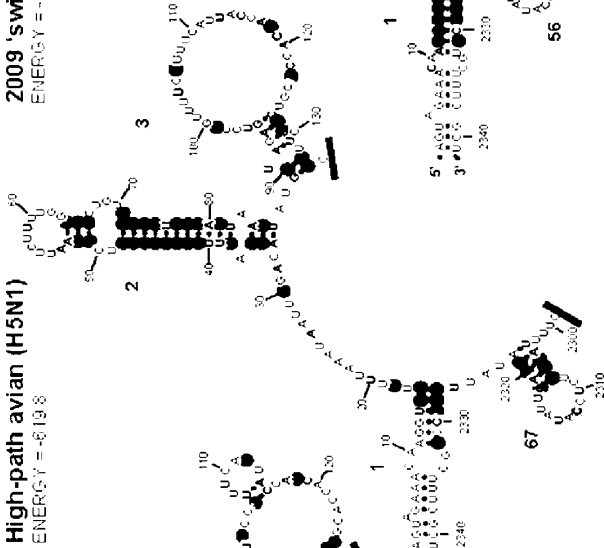


FIG. 1F

2009 'swine' (H1N1)
ENERGY = -628.4

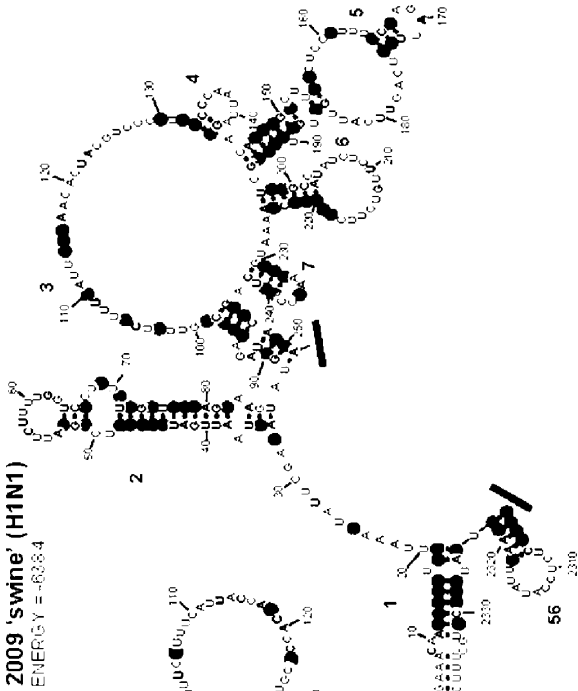


FIG. 1G

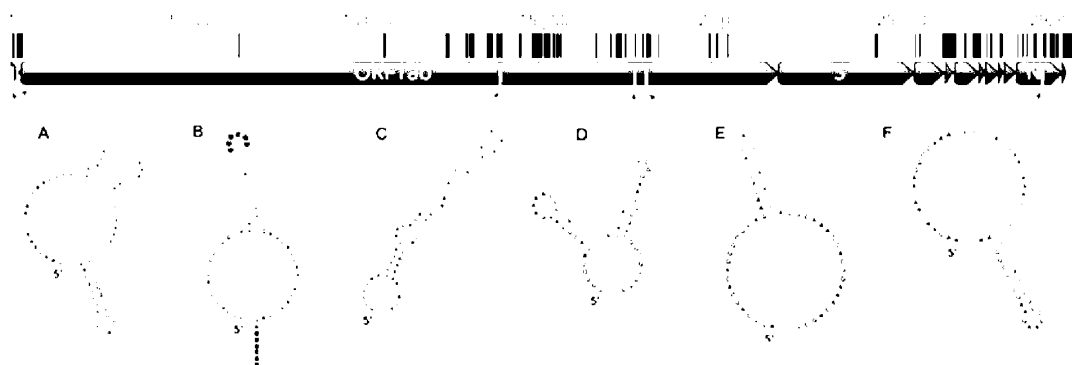


FIG. 2

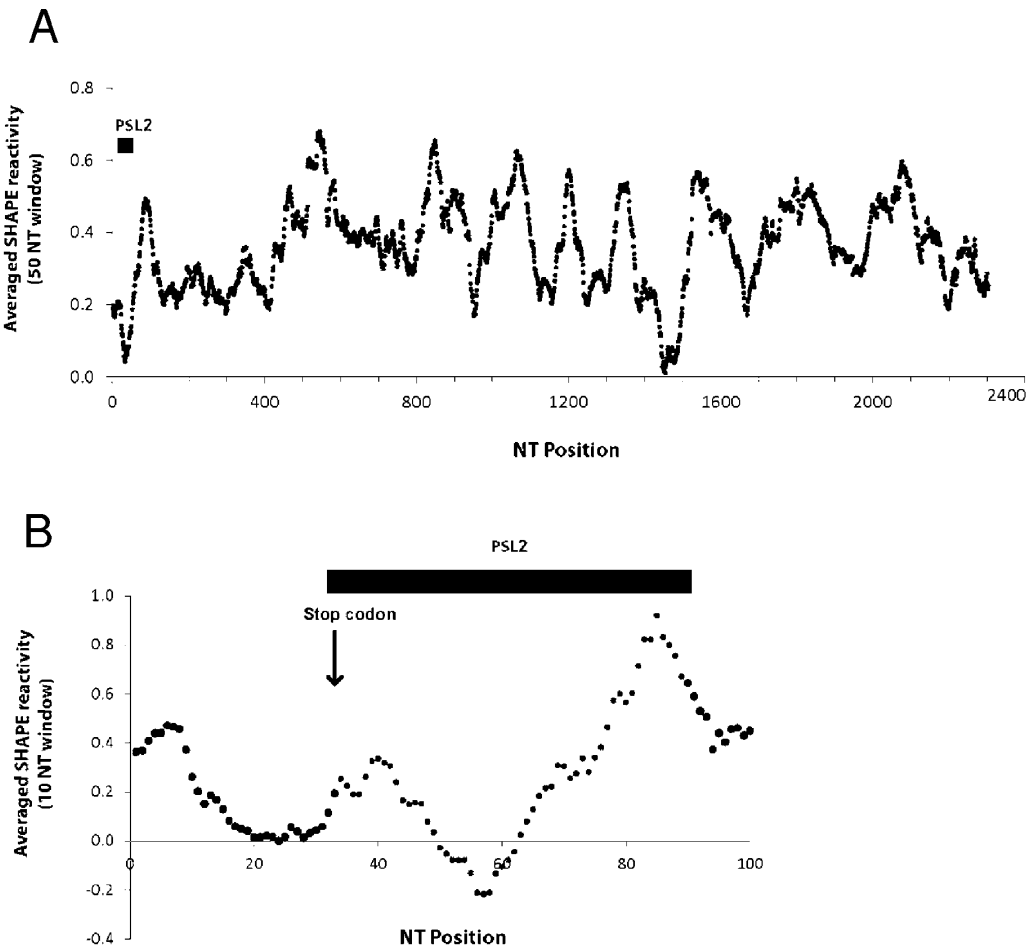


FIG. 3A

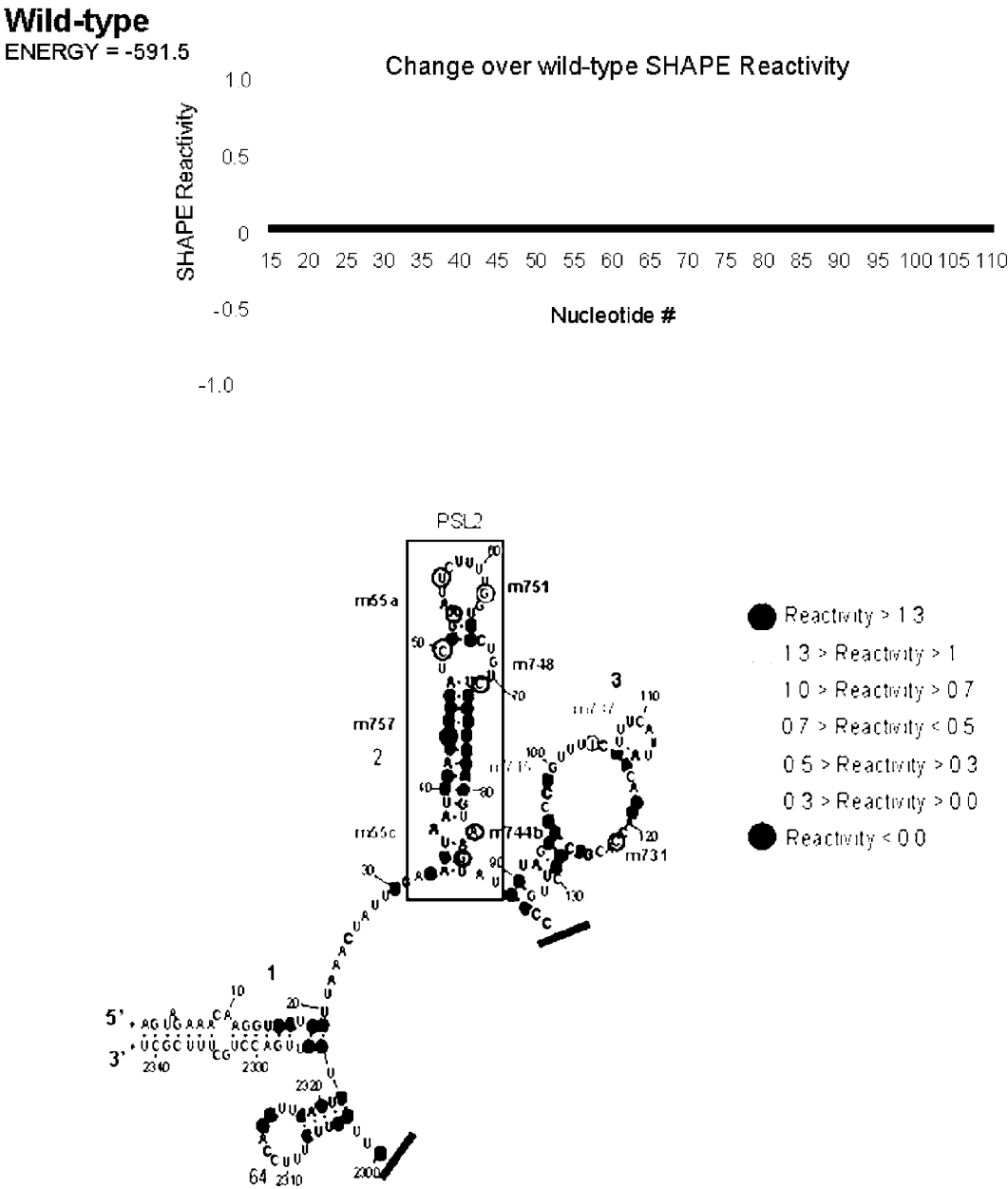


FIG. 3B**PB2m744b**

ENERGY = -553.0

% Packaging = 17%

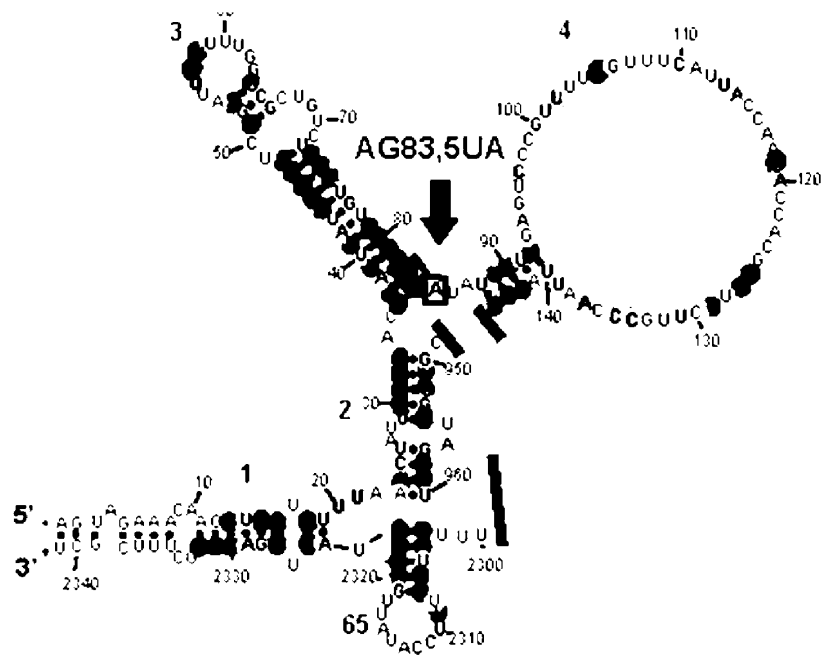
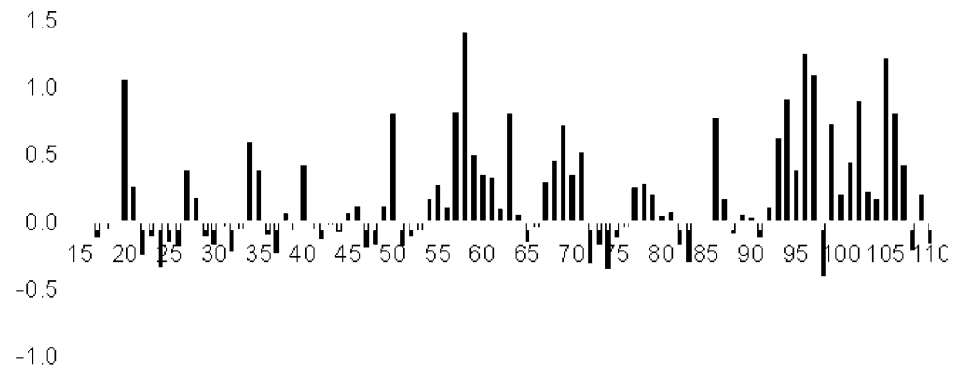
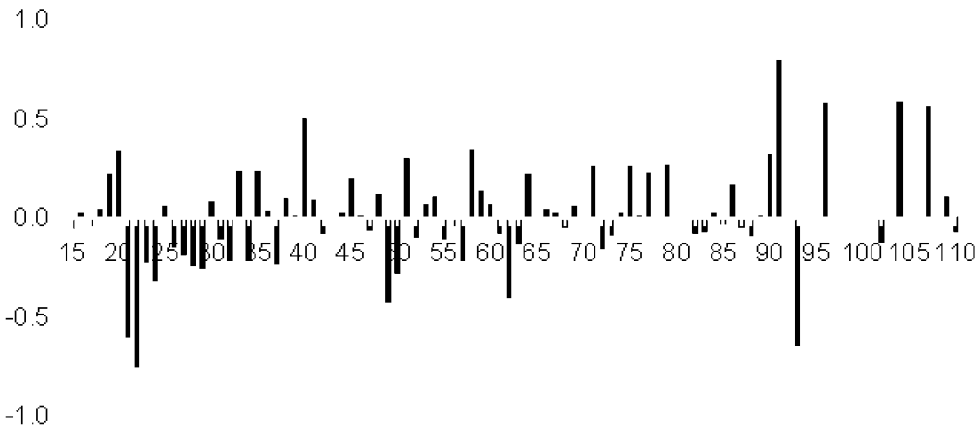


FIG. 3C

PB2m745

ENERGY = -561.2

% Packaging = 20%



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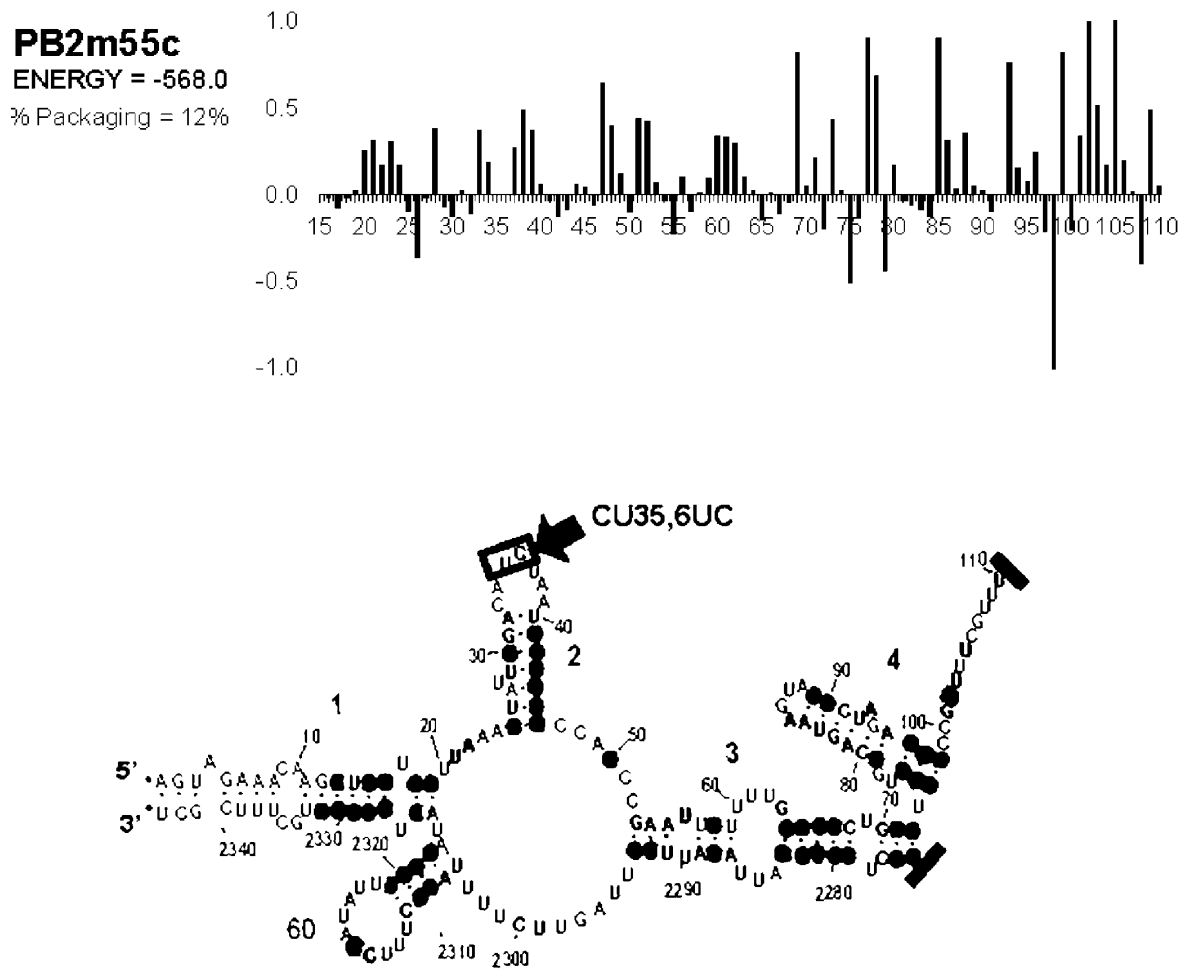
FIG. 3D

FIG. 3E

PB2m757
ENERGY = -578.0
% Packaging = 9%

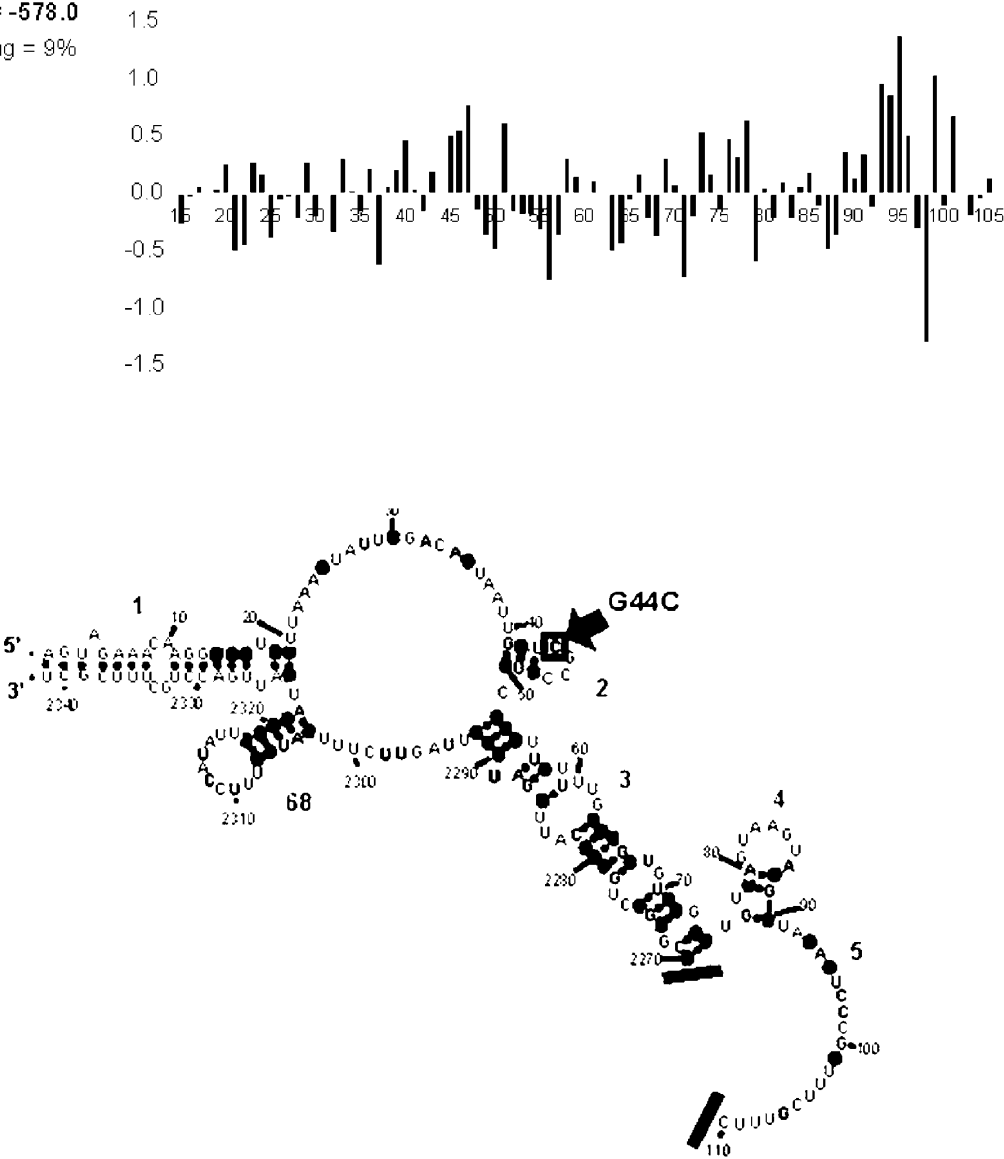


FIG. 4

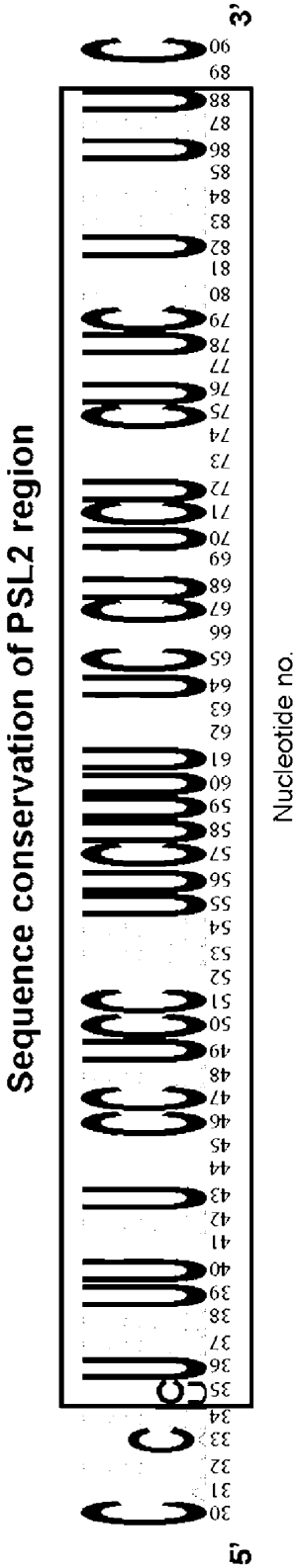


FIG. 5A

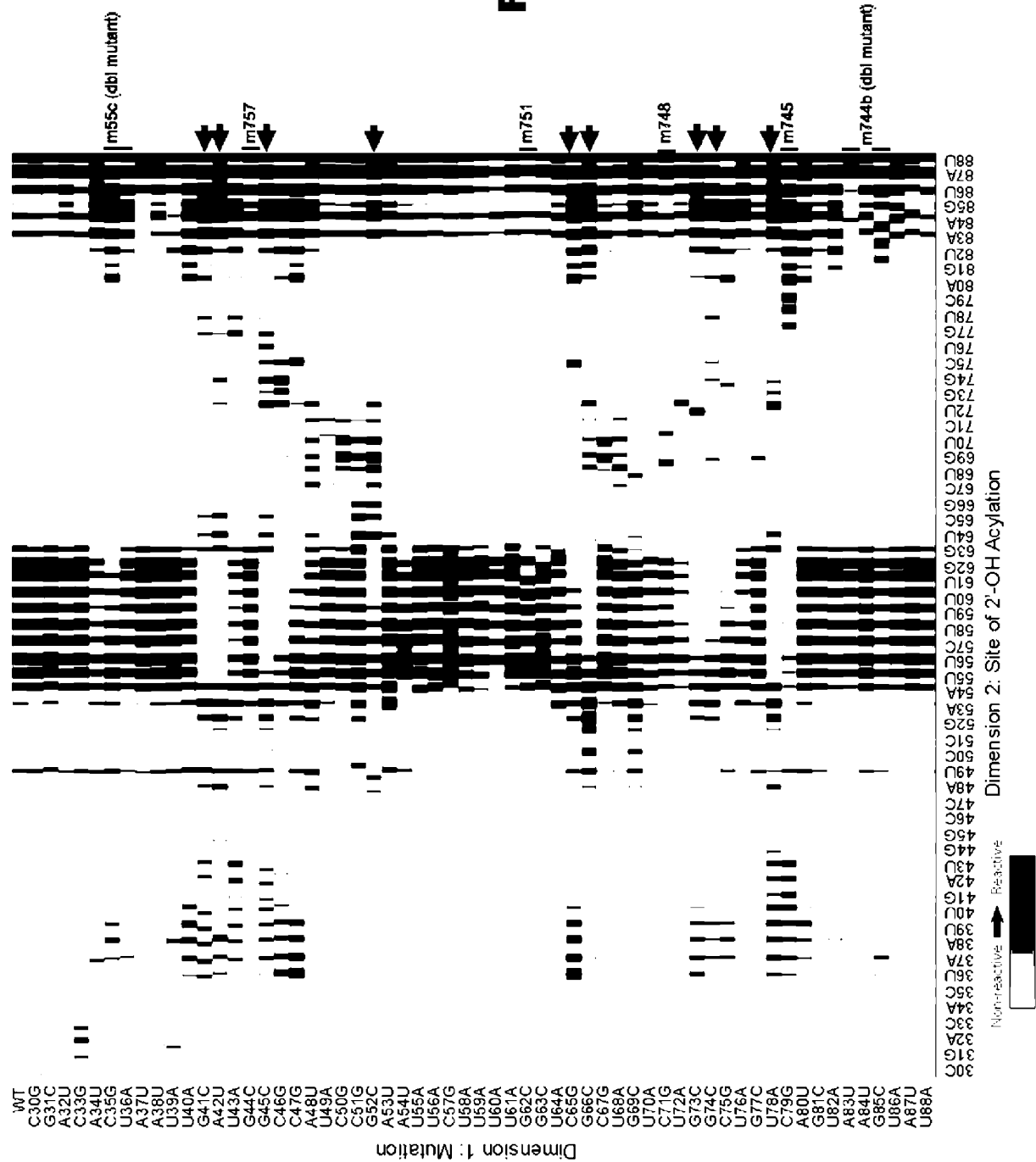


FIG. 5B

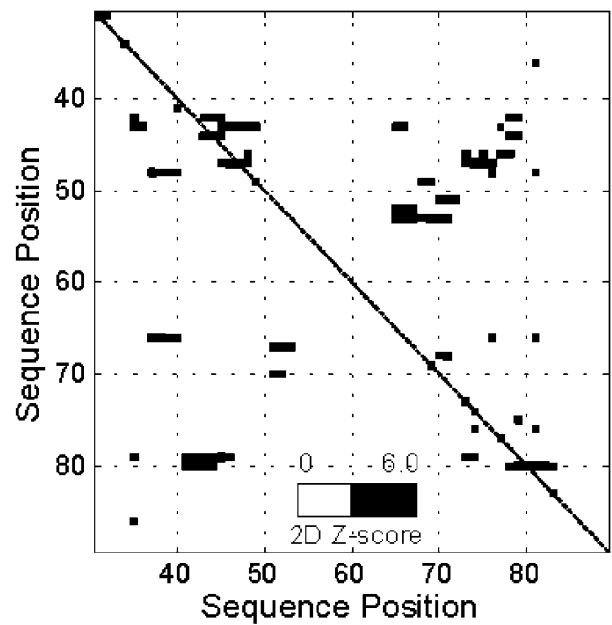


FIG. 5C

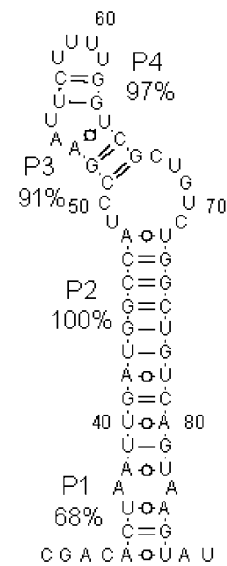


FIG. 5D

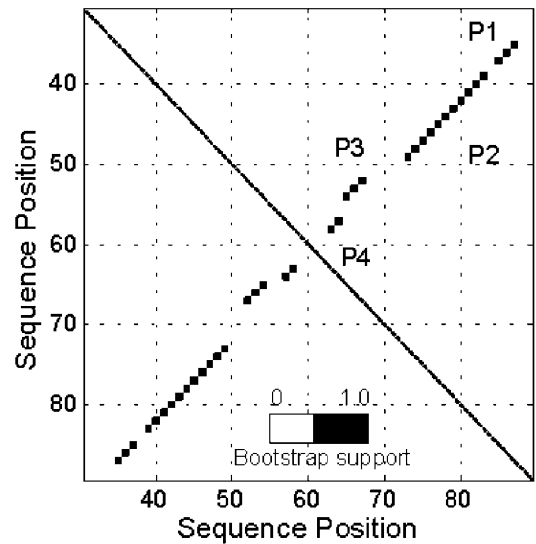


FIG. 6

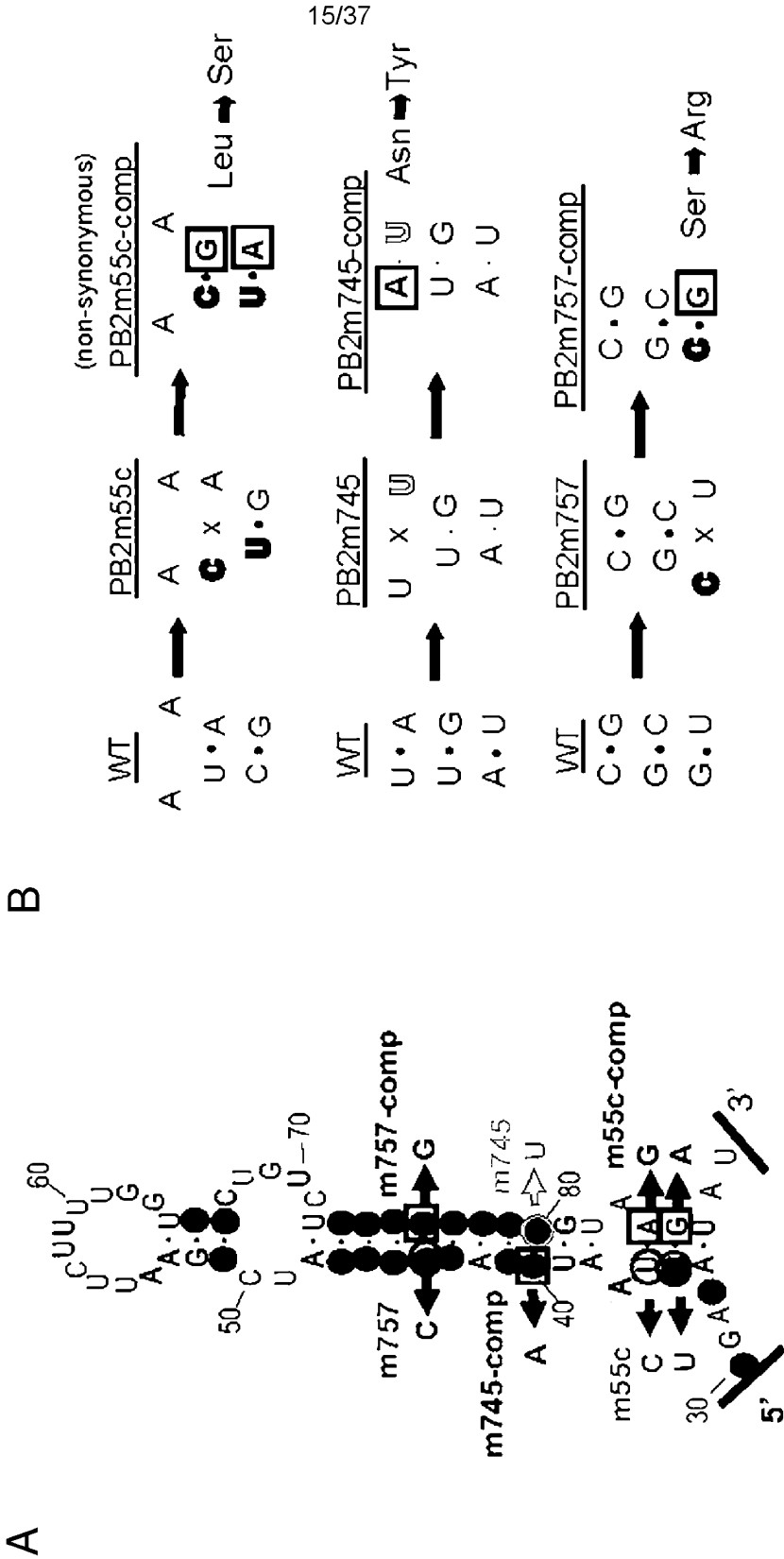


FIG. 7

A

2203 2215 2227
ATT GGG CAA GGA GAC GTG GTG TTG GTA ATG AAA CGG
ATT GGG CAA GGA GAC GTC GTG TTG GTA ATG AAA CGG
m731

2239 2251 2263
AAA CGG AAC TCT AGC ATA CTT ACT GAC AGC CAG ACA
AAA CGG AAC TCT AGC ATA TTA ACA GAC AGC CAA ACA
m744b m745 m748

2275 2287 2299
GCG ACC AAA AGA ATT CGG ATG GCC ATC AAT TAG TGT
GCG ACG AAA AGA ATT CGG ATG GCG ATC AAT TGA TGT
m751 m757 m55c

B

Mutate-and-Map predicted PB2 mutations

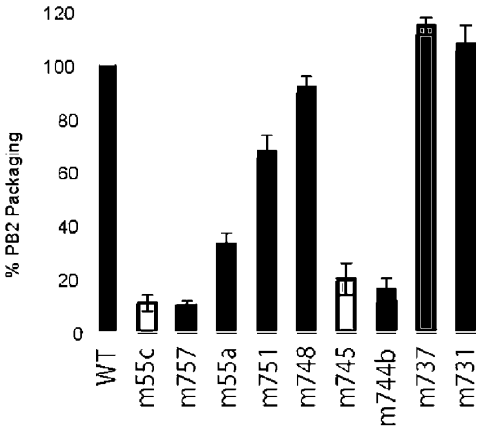
(Syn.) m74-1 (C2268T)-F: TAC TTA CTG ACA GTC AGA CAG CG
(Syn.) m74-1 (C2268T)-RC: CGC TGT CTG ACT GTC AGT AAG TA

(Syn.) m74-2 (AGC2266-8UCG)-F: TAC TTA CTG ACT CGC AGA CAG CG
(Syn.) m74-2 (AGC2266-8UCG)-RC: CGC TGT CTG CGA GTC AGT AAG TA

(Syn.) m68-1 (A2262T)-F: TGA CAG CCA GAC TGC GAC CAA AAG AAT TCG
(Syn.) m68-1 (A2262T)-RC: CGA ATT CTT TTG GTC GCA GTC TGG CTG TCA

(Syn.) m56 (A2286C)-F: AGC GAC CAA AAG CAT TCG GAT GGC
(Syn.) m56 (A2286C)-RC: GCC ATC CGA ATG CTT TTG GTC GCT

C



D

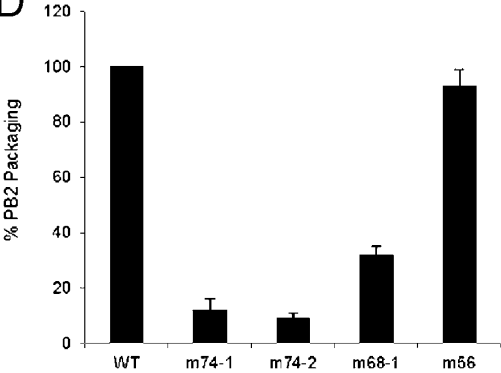


FIG. 8

Mutant Nomenclature and Mutation Sites

Previously-described Mutants	Mutant Name	Mutation Site(s) [(-)-sense orientation]	SYN or Non-SYN	Notes
	m55c	CU35,36UC	SYN	
	m757	G44C	SYN	
	m55a	CAU50,53,56	SYN	
	m751	G62C	SYN	
	m748	C71U	SYN	
	m745	A80U	SYN	
	m744b	AG83,85UA	SYN	
	m737	U104	SYN	
	m731	C122G	SYN	
Novel PSL2-informed Mutants	m83,84	AG83,84GA	Non-SYN	
	m55c-comp	CU35,36UC / AG83,84GA	Non-SYN	Dbl Mutant
	m76	U76G	Non-SYN	
	m757-comp	G44C / U76G	Non-SYN	Dbl Mutant
	m40	U40A	Non-SYN	
	m745-comp	A80U / U40A	Non-SYN	Dbl Mutant
	m74-1	G74A	SYN	
	m74-2	UCG74AGC	SYN	
	m68	U68A	SYN	
	m56	U56G	SYN	
	m41	G41C	Non-SYN	
	m79	C79G	Non-SYN	
	m41/79-comp	GC41,79CG	Non-SYN	Dbl Mutant
	m45	G45C	Non-SYN	
	m75	C75G	Non-SYN	
	m45/75-comp	GC45,75CG	Non-SYN	Dbl Mutant
	m46	C46G	Non-SYN	
	m74	G74C	Non-SYN	
	m46/74-comp	CG46,74GC	Non-SYN	Dbl Mutant
	m52	G52U	SYN	
	m65	C65A	SYN	
	m52/65-comp	GC52,65UA	SYN	Dbl Mutant

SYN = Synonymous mutation, Non-SYN = non-synonymous mutation

FIG. 9A

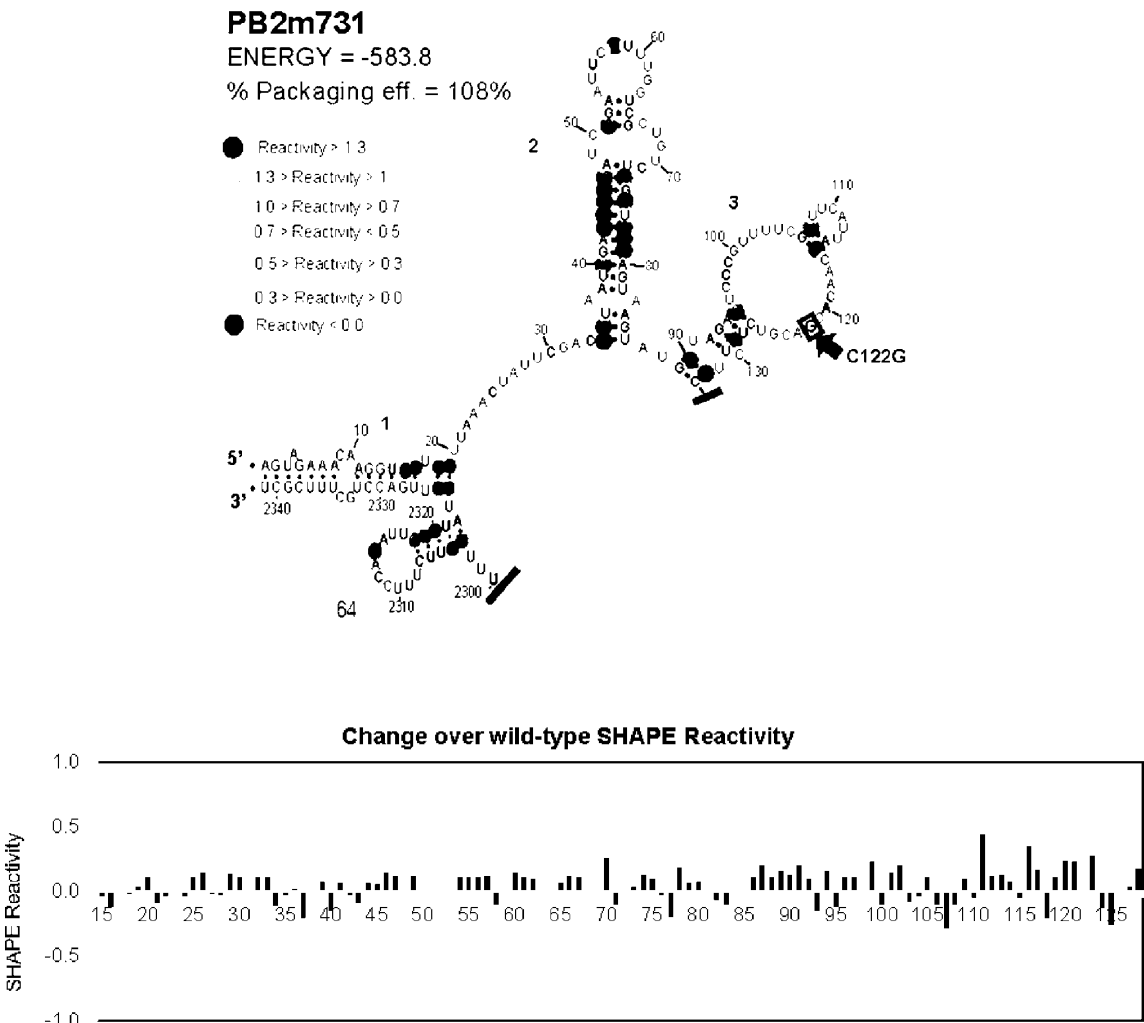


FIG. 9B

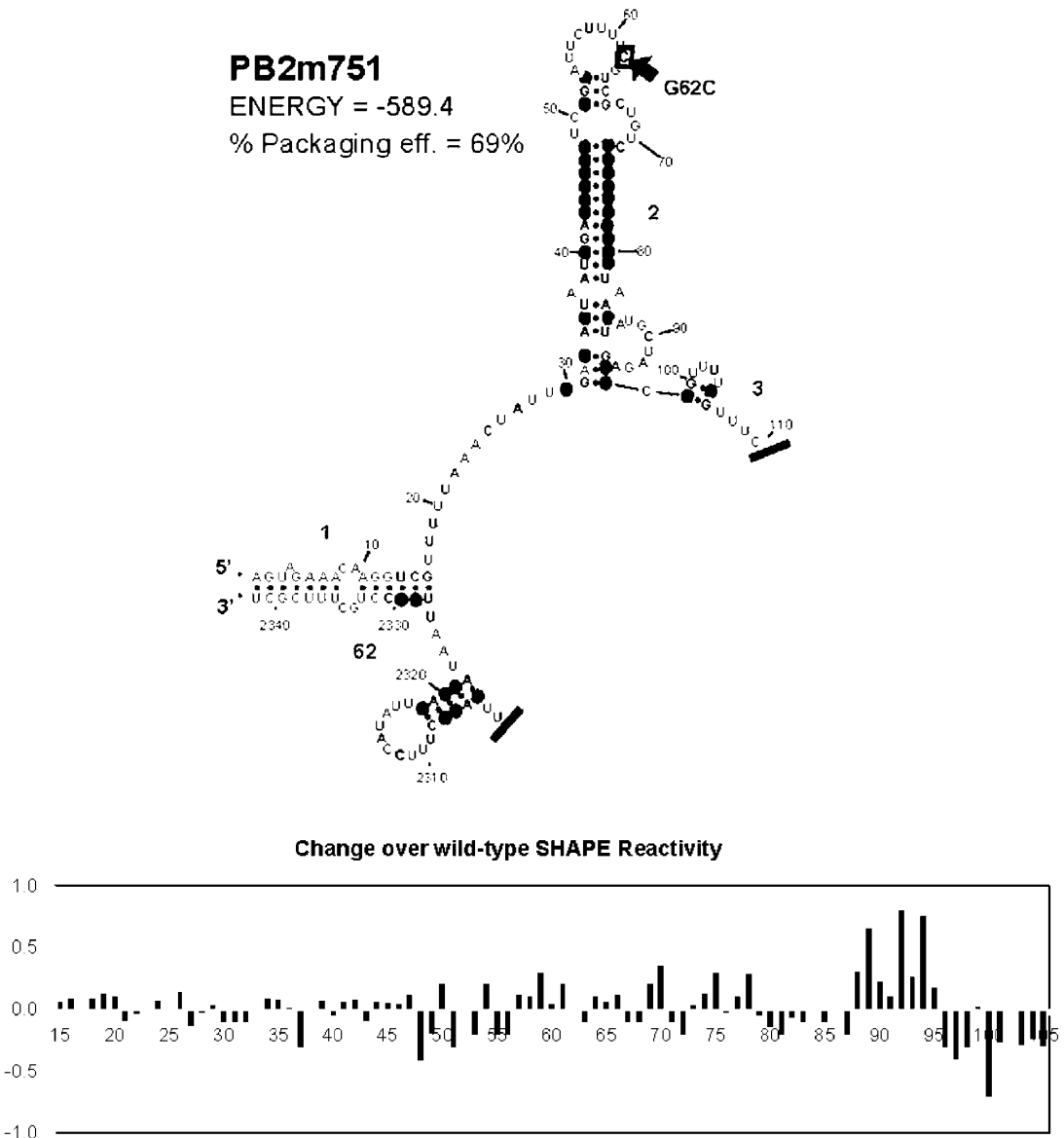


FIG. 9C

PB2m748
ENERGY = -593.9
% Packaging eff. = 92%

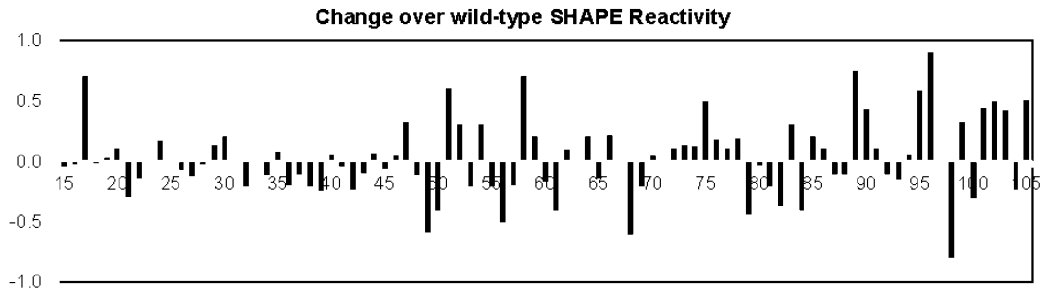
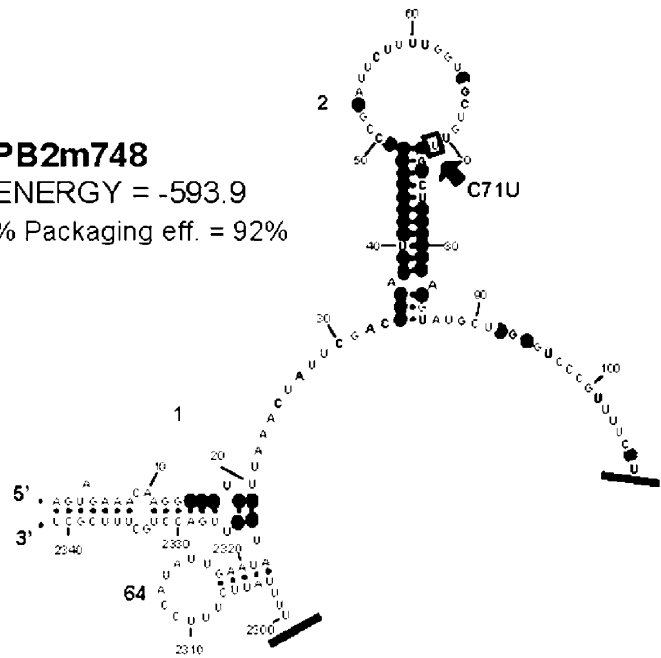


FIG. 10

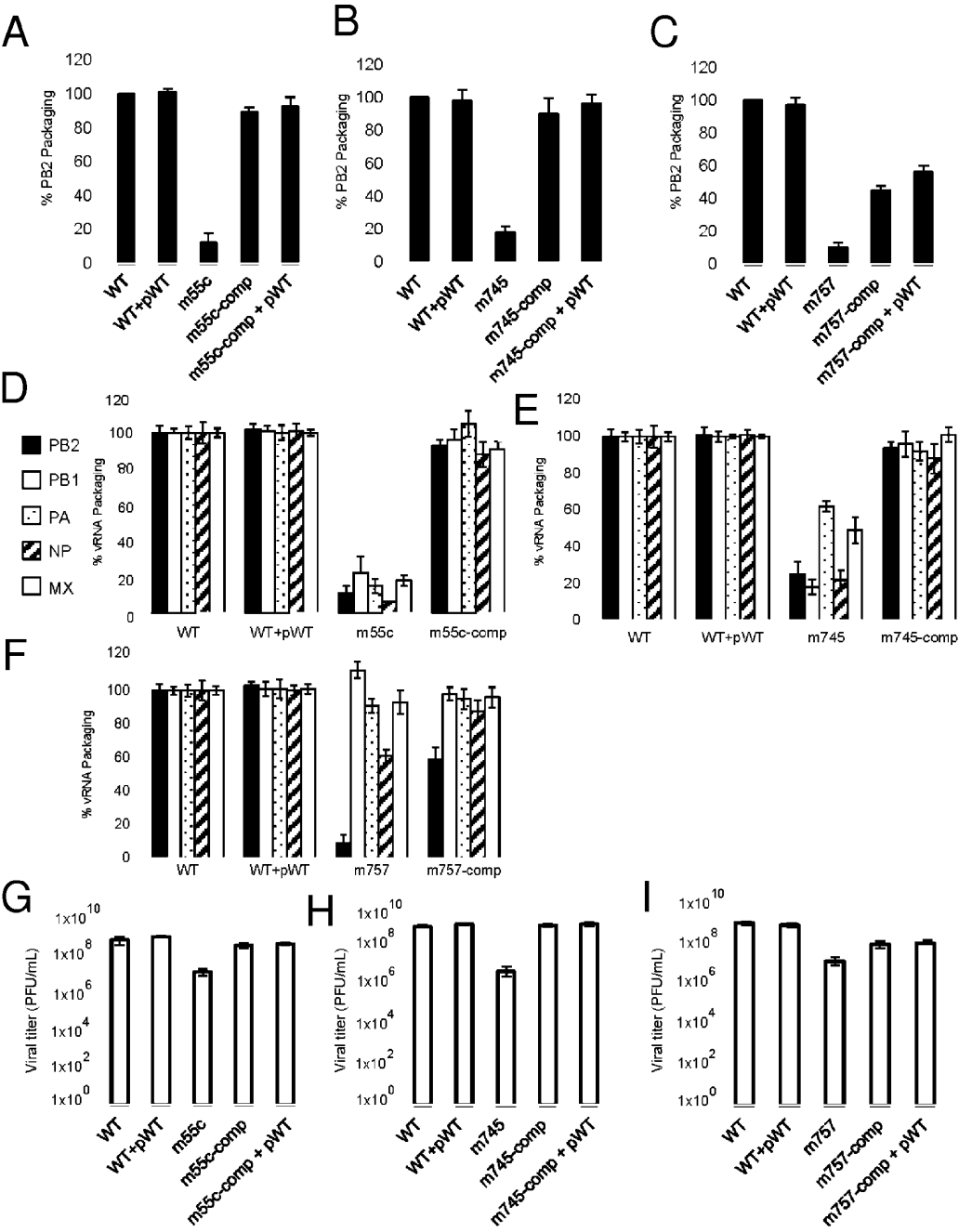


FIG. 11

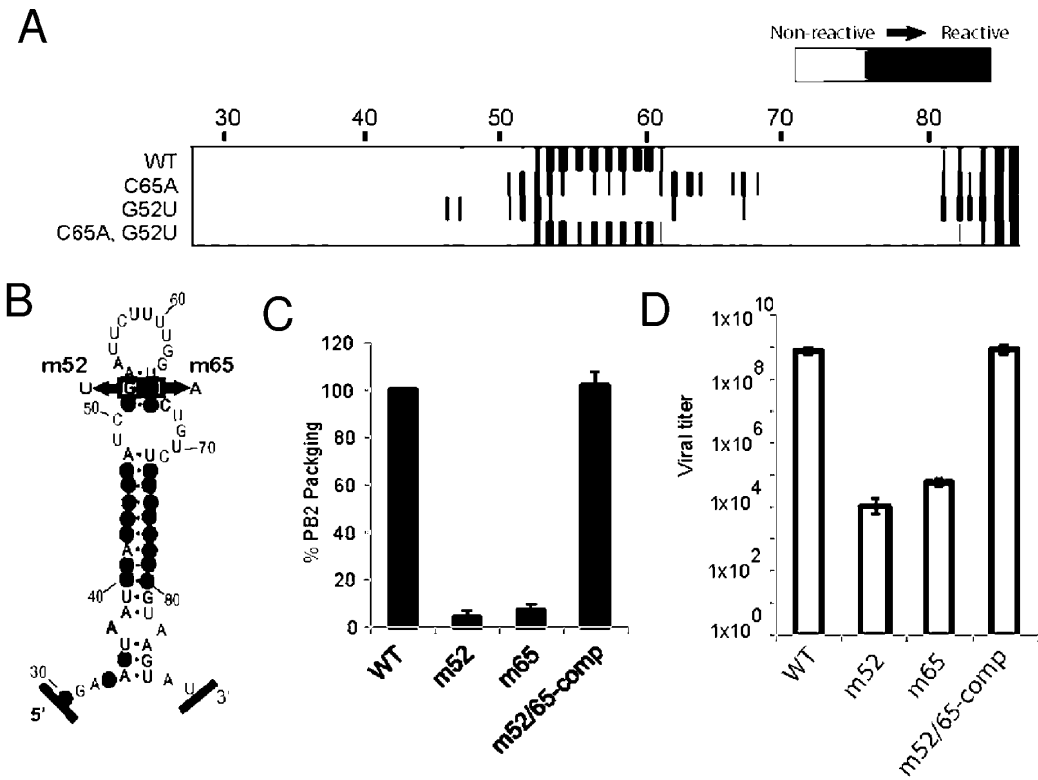


FIG. 12

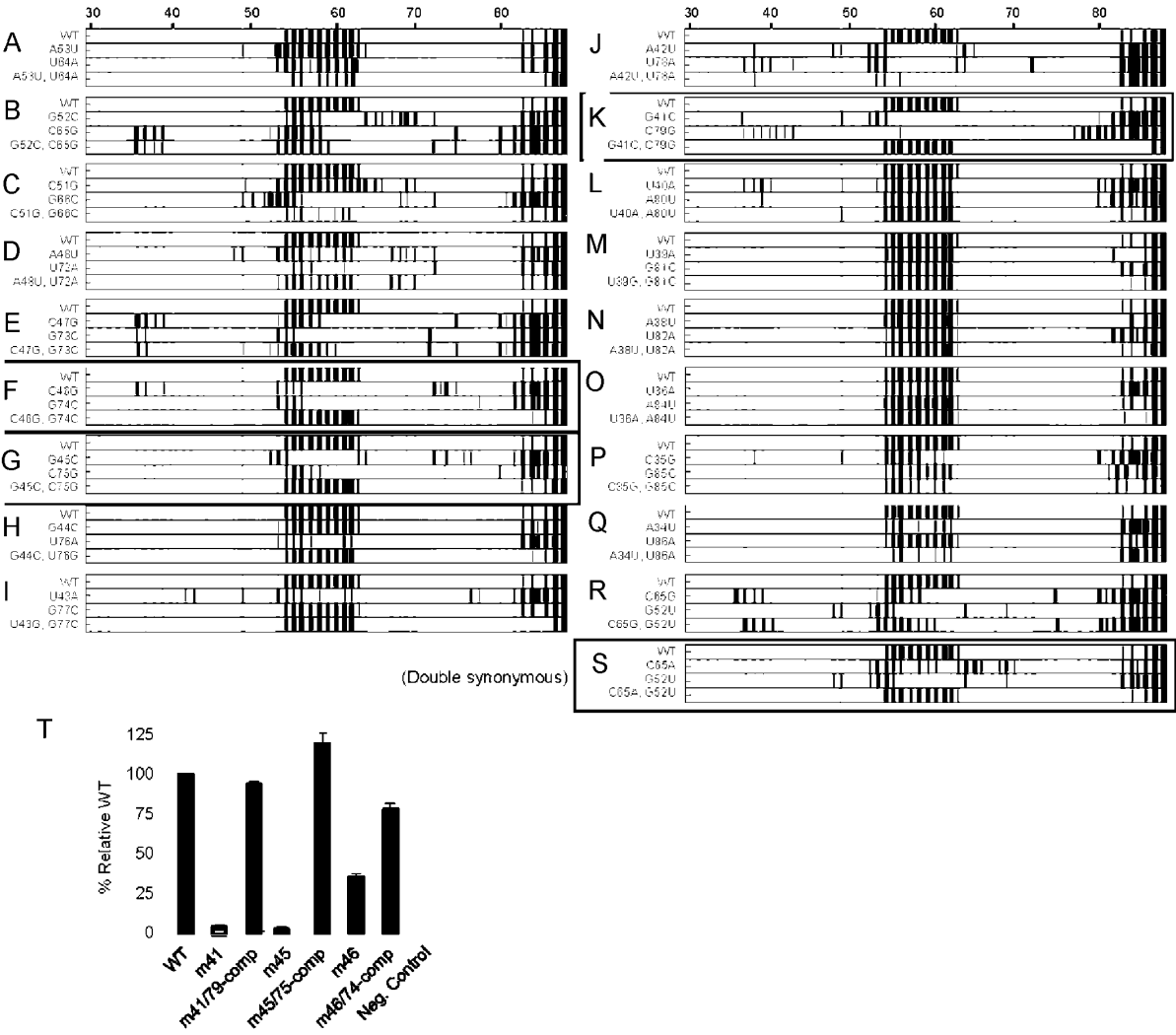


FIG. 13

(Non-syn.) m46-F (G2296C):	AGA ATT CGG ATG CCC ATC AAT TAG TGT CG
(Non-syn.) m46-RC (G2296C):	CGA CAC TAA TTG ATG GGC ATC CGA ATT CT
(Syn.) m46/74-comp (C2268G)-F:	TAC TTA CTG ACA GGC AGA CAG CG
(Syn.) m46/74-comp (C2268G)-RC:	CGC TGT CTG CCT GTC AGT AAG TA
(Non-syn.) m45-F (G2297C):	TTC GGA TGG GCA TCA ATT AGT GTC G
(Non-syn.) m45-RC (G2297C):	CGA CAC TAA TTG ATG CCC ATC CGA A
(Non-syn) m45/75-comp (G2267C)-F:	ATA CTT ACT GAC ACC CAG ACA GCG
(Non-syn) m45/75-comp (G2267C)-RC:	CGC TGT CTG GGT GTC AGT AAG TAT
(Non-syn.) m41-F (C2301G):	TCG GAT GGC CAT GAA TTA GTG TCG
(Non-syn.) m41-RC (C2301G):	CGA CAC TAA TTC ATG GCC ATC CGA
(Syn.) m41/79-comp (G2263C)-F:	AGC ATA CTT ACT CAC AGC CAG ACA GC
(Syn.) m41/79-comp (G2263C)-RC:	GCT GTC TGG CTG TGA GTA AGT ATG CT
(Syn.) m52-F (C2290A):	CCA AAA GAA TTA GGA TGG CCA TCA ATT AGT GTC G
(Syn.) m52-RC (C2290A):	CGA CAC TAA TTG ATG GCC ATC CTA ATT CTT TTG G
(Syn.) m65-F (G2277T):	GAC AGC CAG ACA GCT ACC AAA AGA ATT CG
(Syn.) m65-RC (G2277T):	CGA ATT CTT TTG GTA GCT GTC TGG CTG TC

Double synonymous mutant pair

FIG. 14

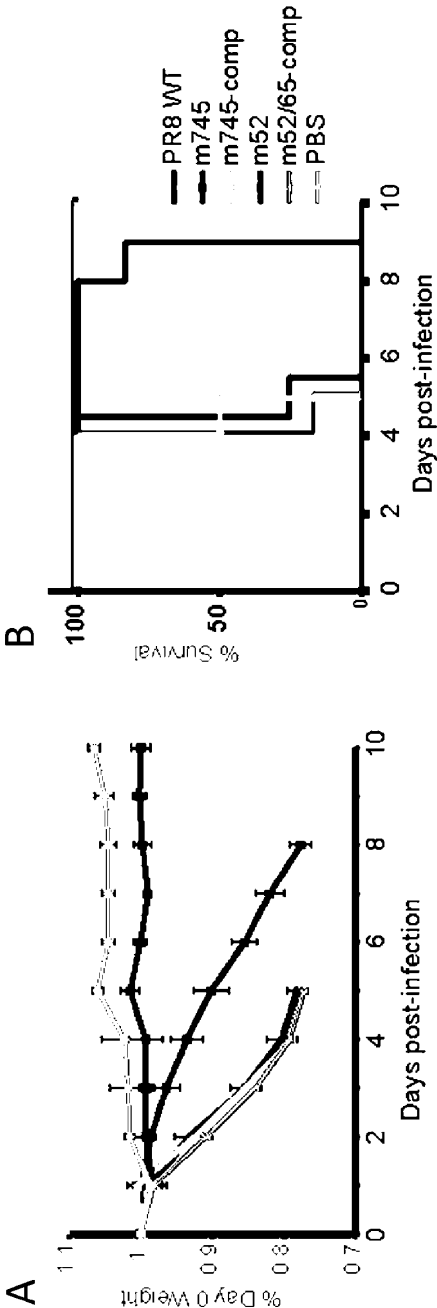


FIG. 15

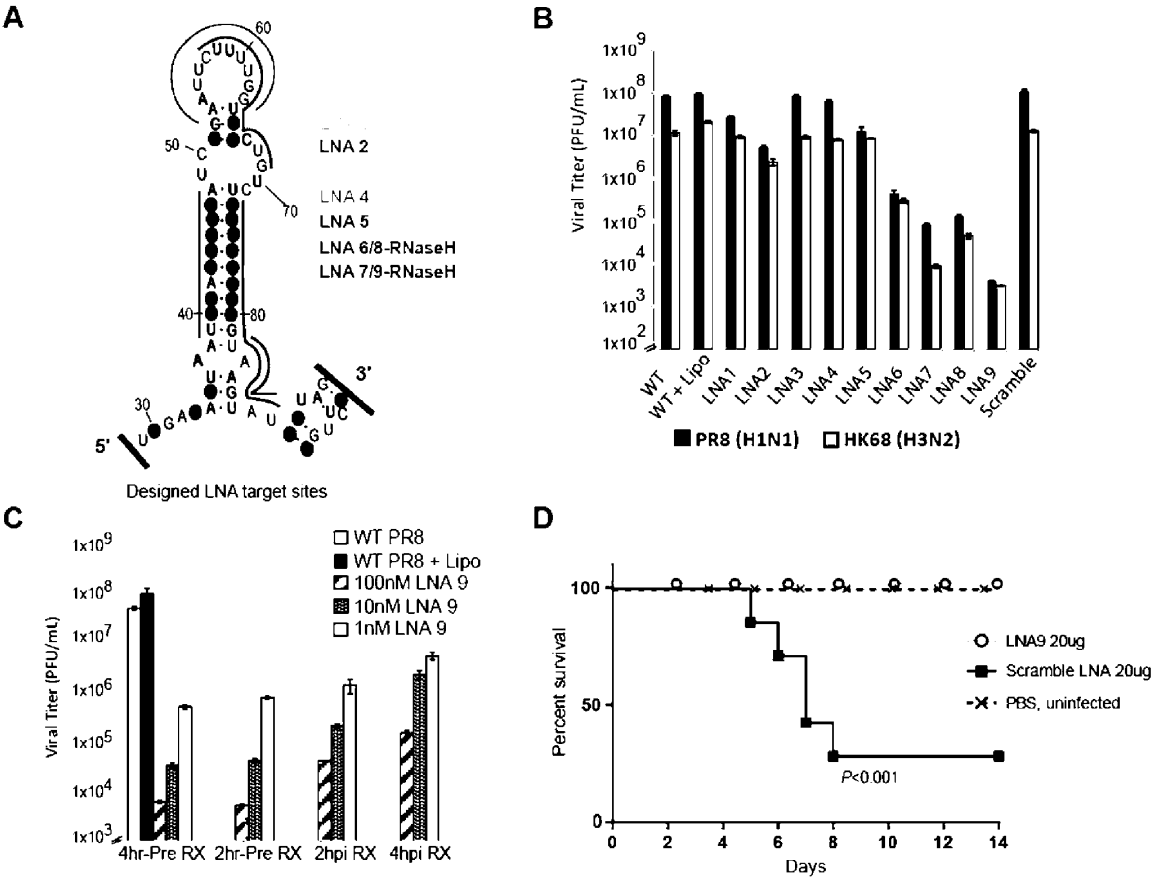


FIG. 16A

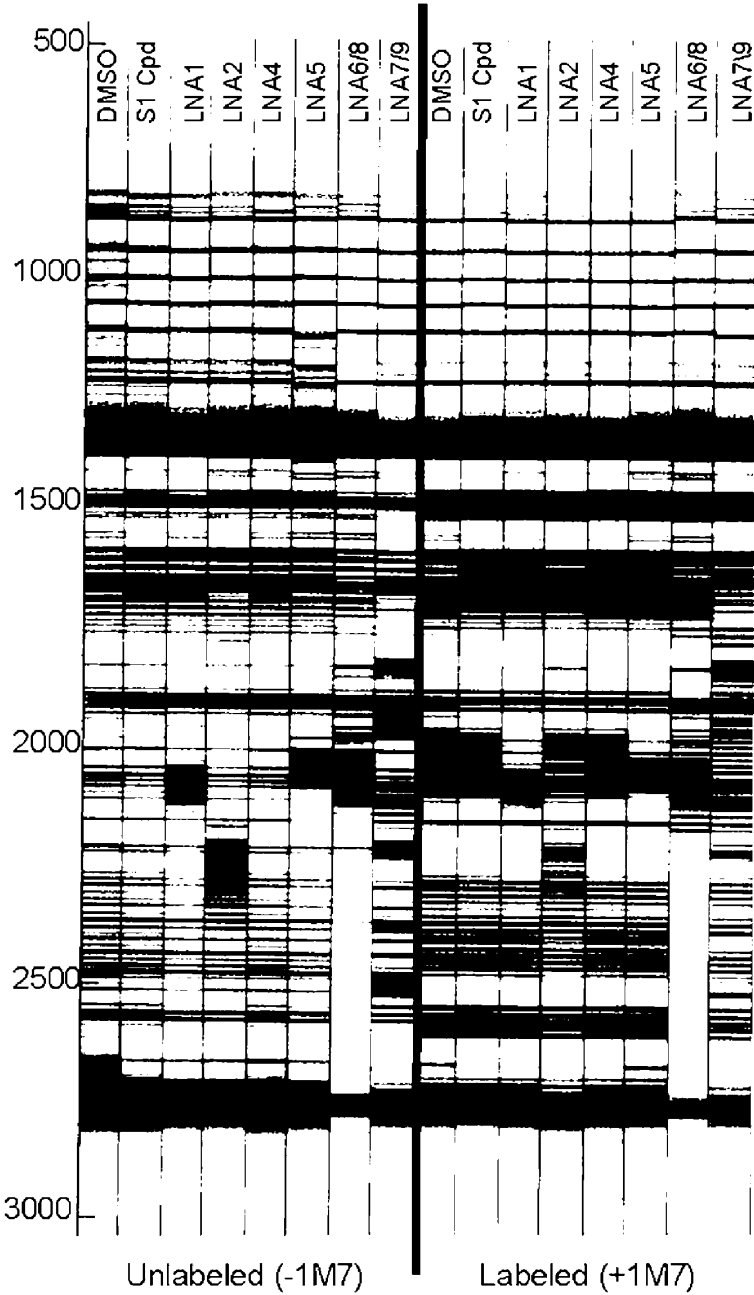


FIG. 16B

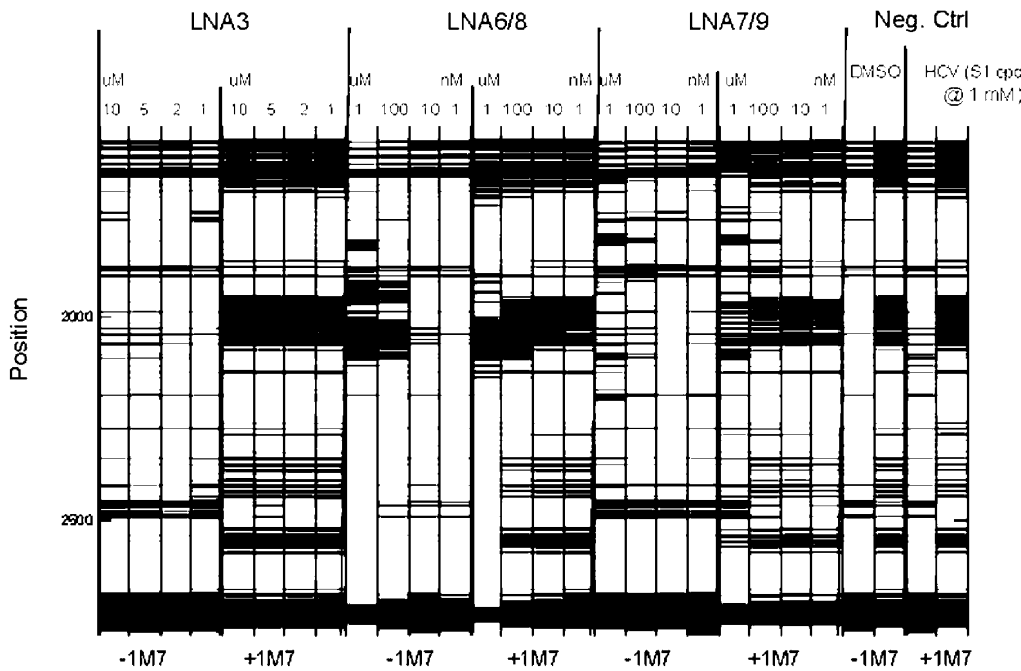


FIG. 17

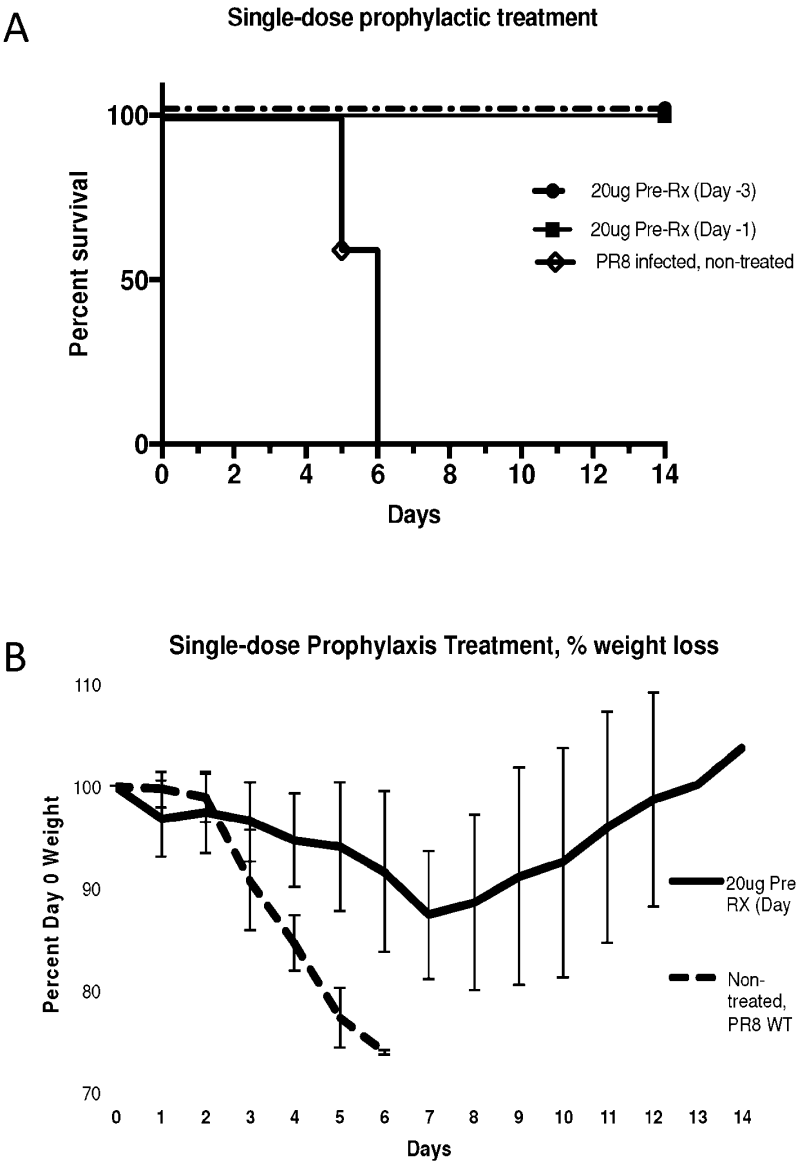


FIG. 18

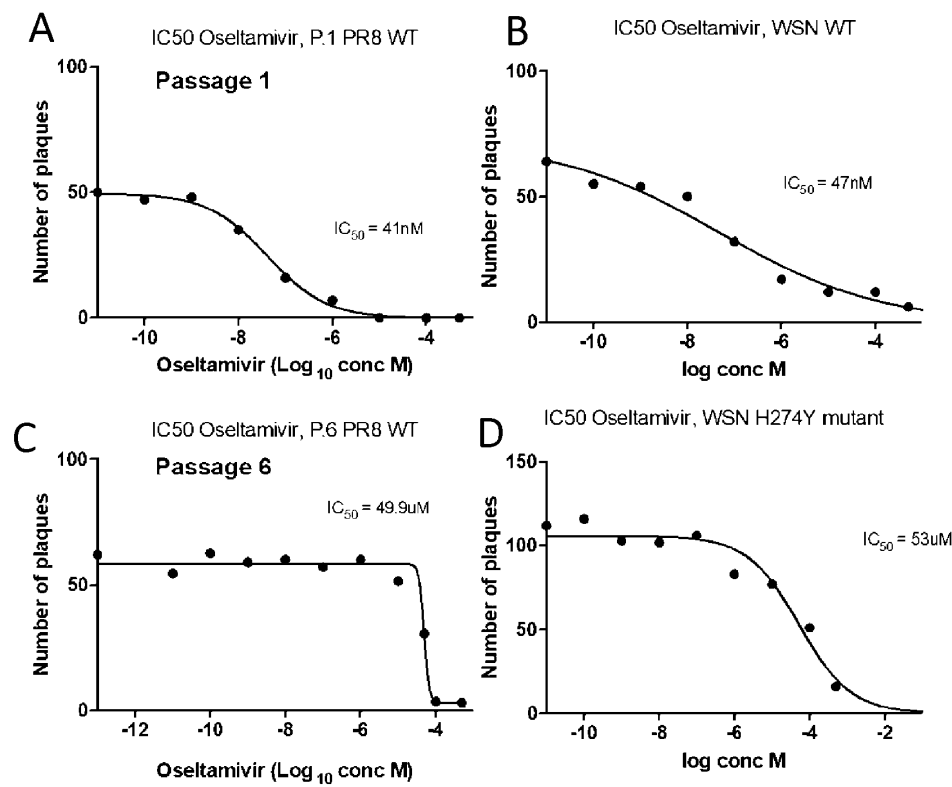


FIG. 19

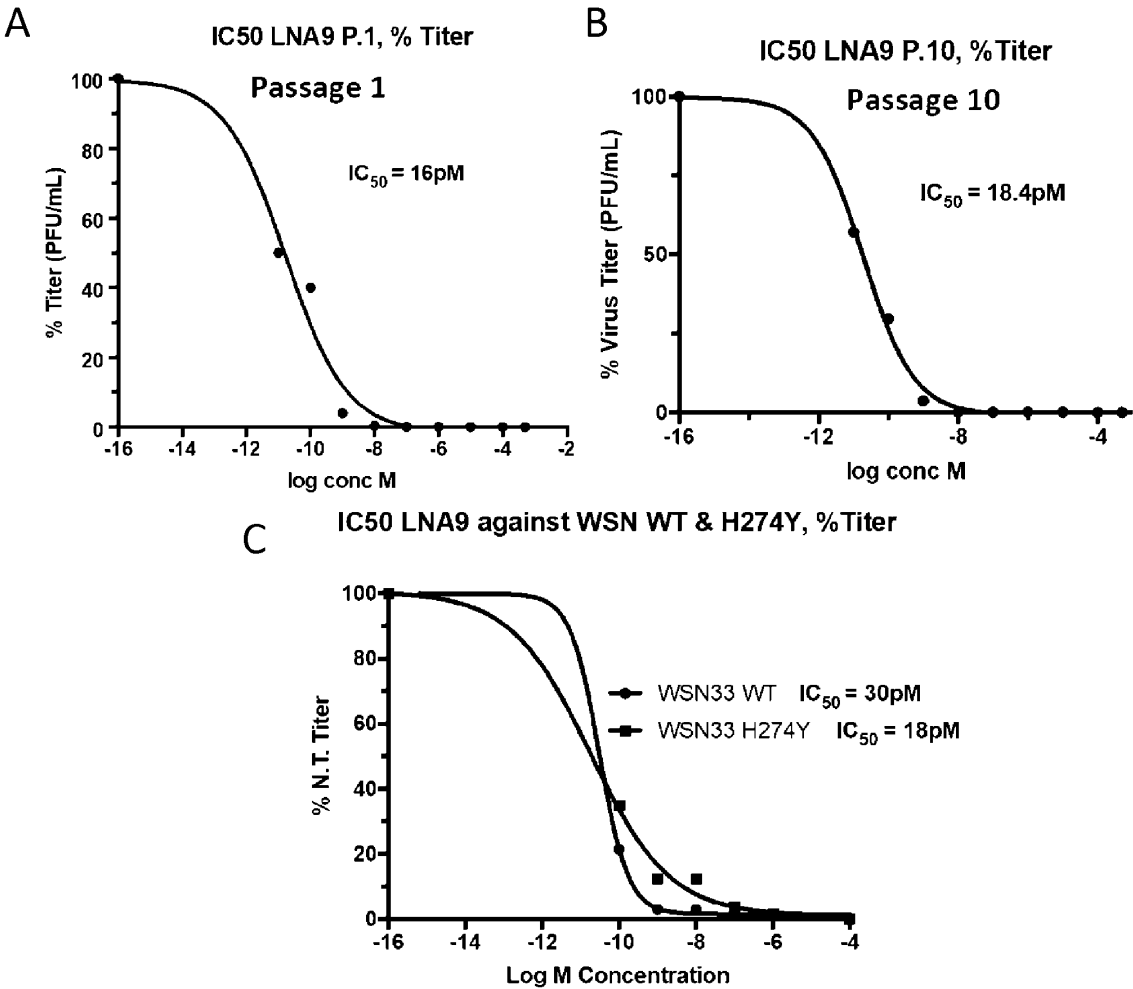
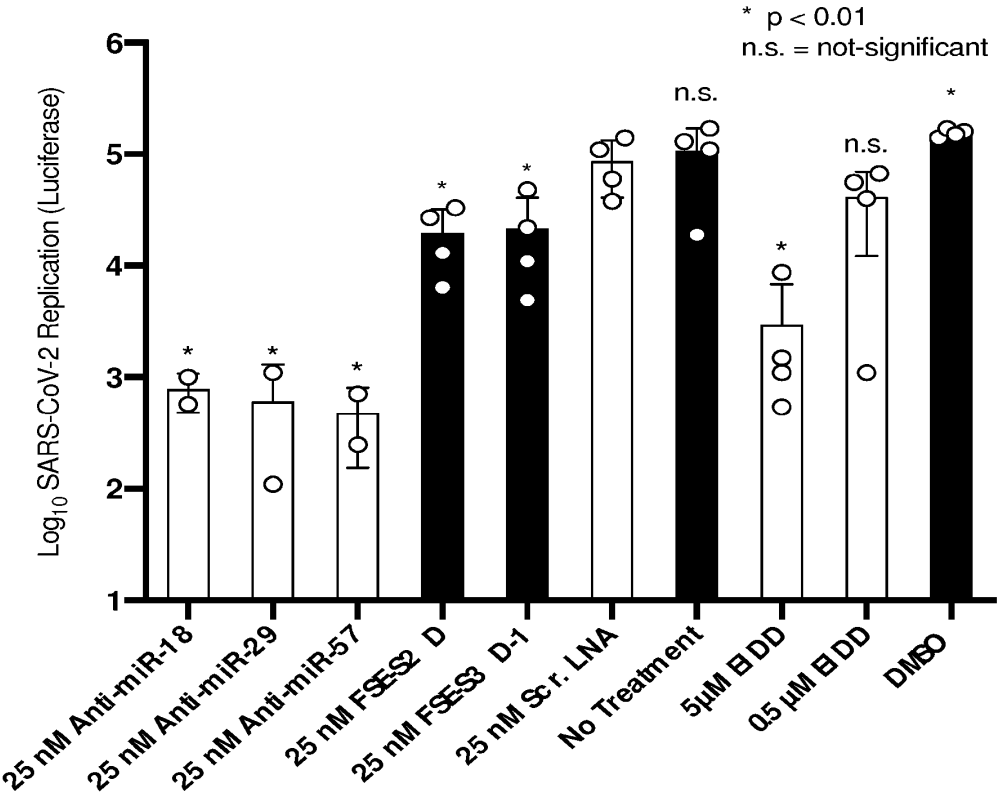
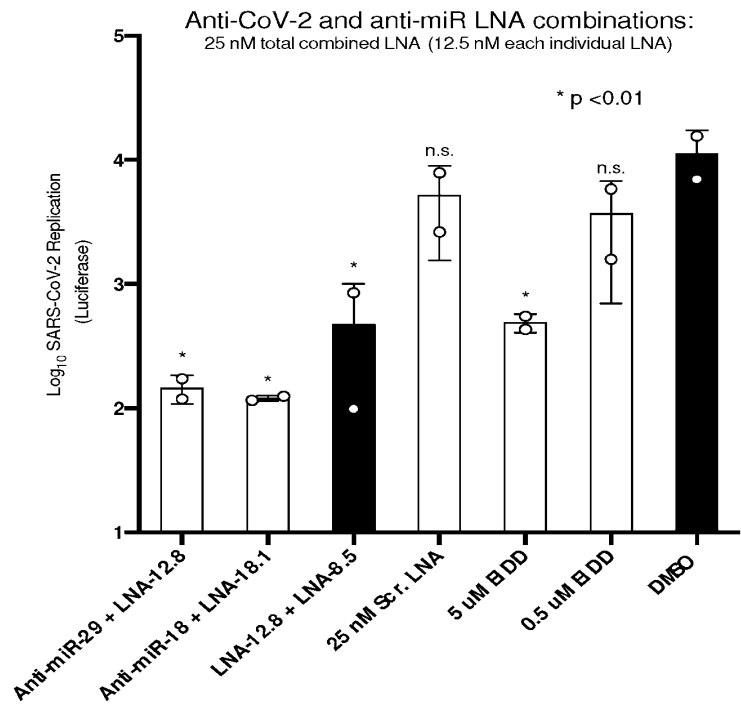


FIG. 20



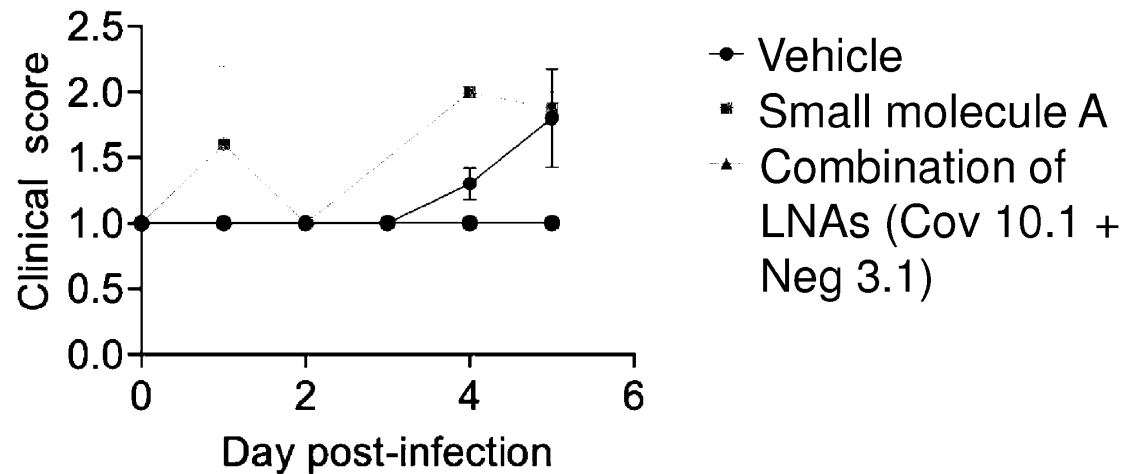
Anti-miR-29 is LNA-191.12
Anti-miR-57 is LNA-6810.2

FIG. 21



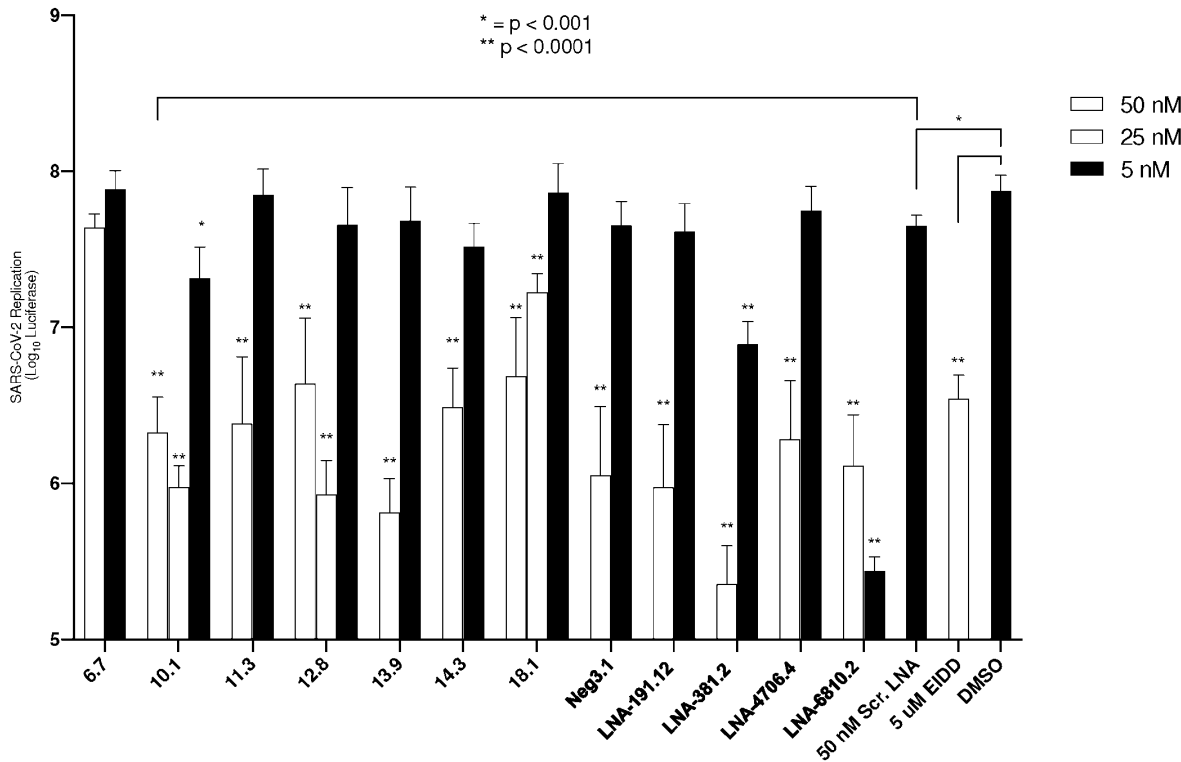
LNA-12.8 is Cov 12.8
LNA-8.5 is Cov 8.5
LNA-18.1 is Cov 18.1
Anti-miR-29 is LNA-191.12

FIG. 22



Vehicle:
Glyceryltri octanoate:octanoic
acid:NMP (80:10:10)

FIG. 23



6.7 is Cov 6.7; 12.8 is Cov 12.8
10.1 is Cov 10.1; 13.9 is Cov
13.9
11.3 is Cov 11.3; 14.3 is Cov 14.3
18.1 is Cov 18.1;

FIG. 24

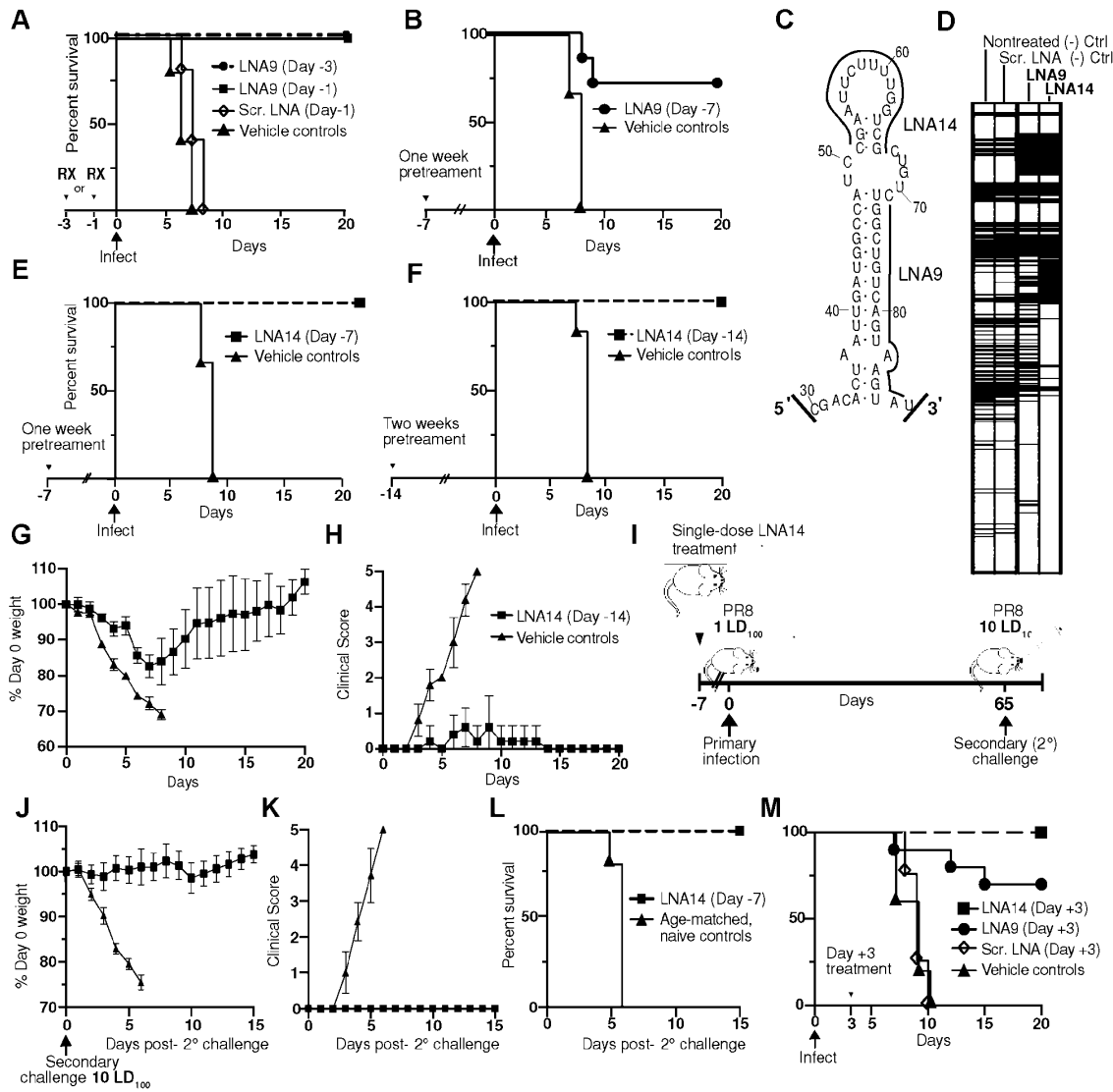


FIG. 25

