

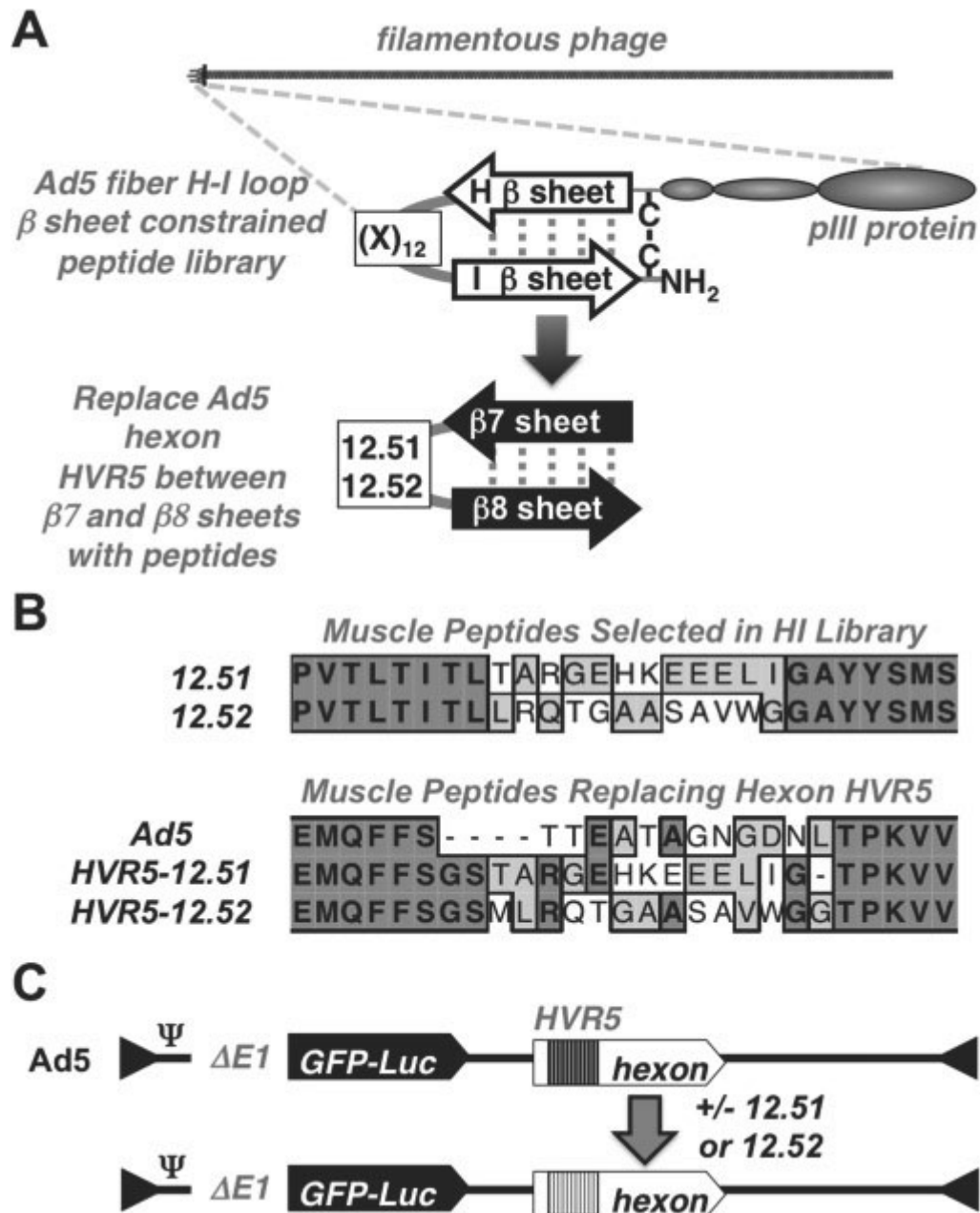


FIG. 1

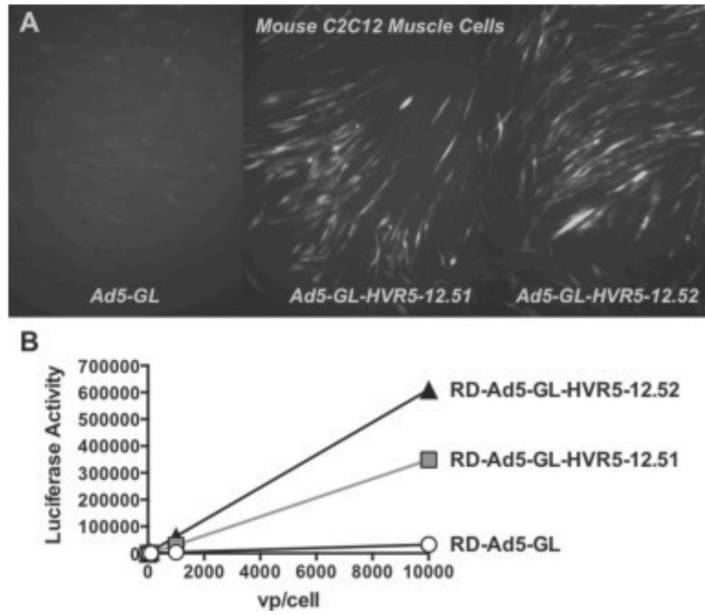


FIG. 2

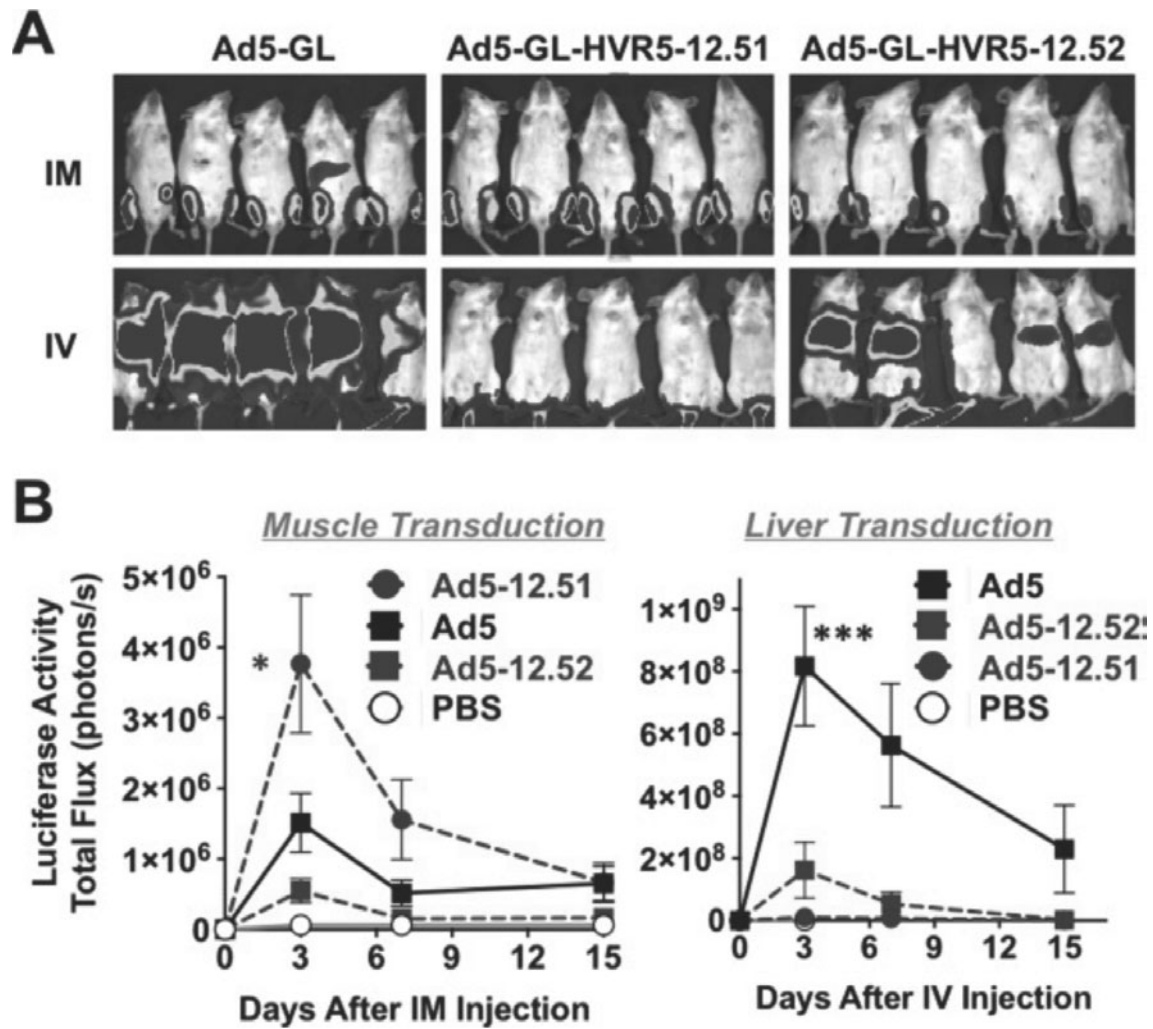


FIG. 3

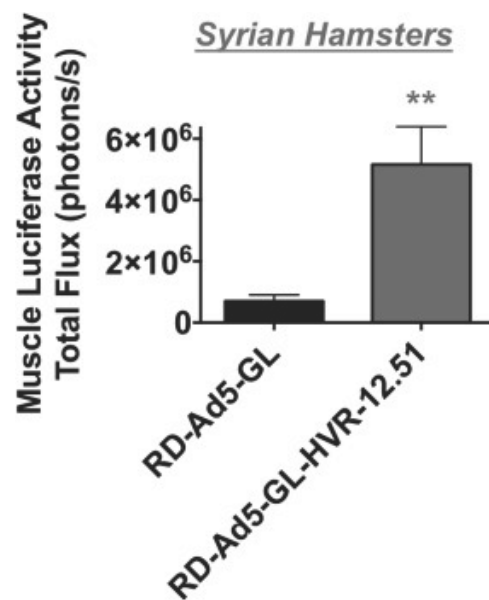


FIG. 4

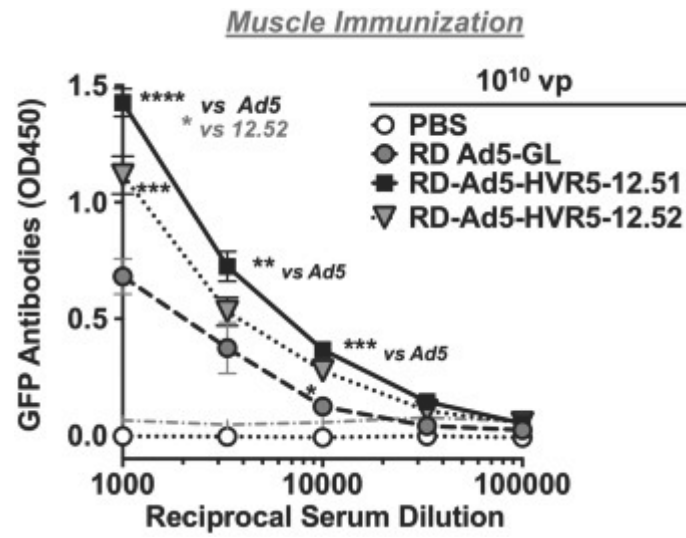


FIG. 5

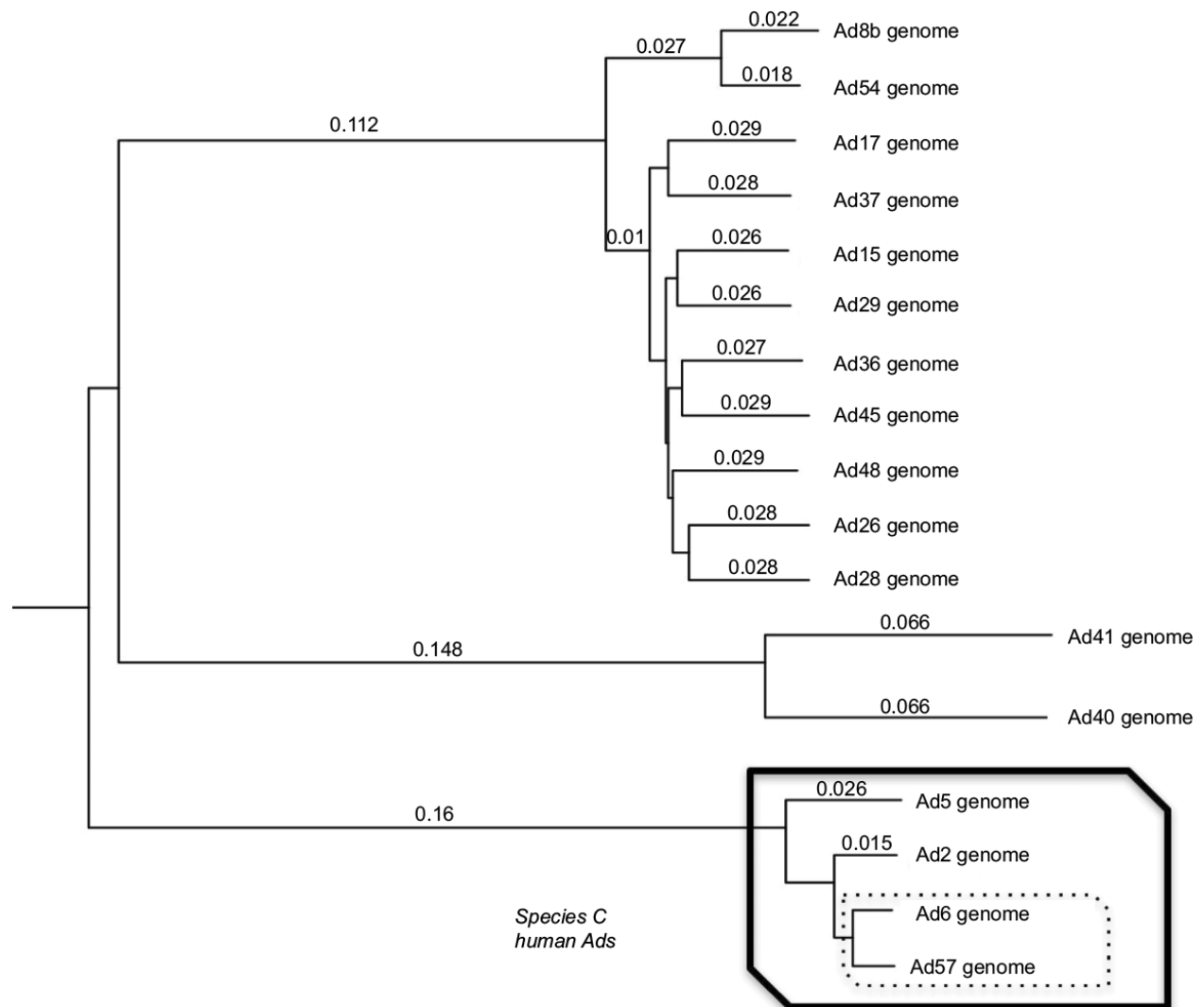


FIG. 6

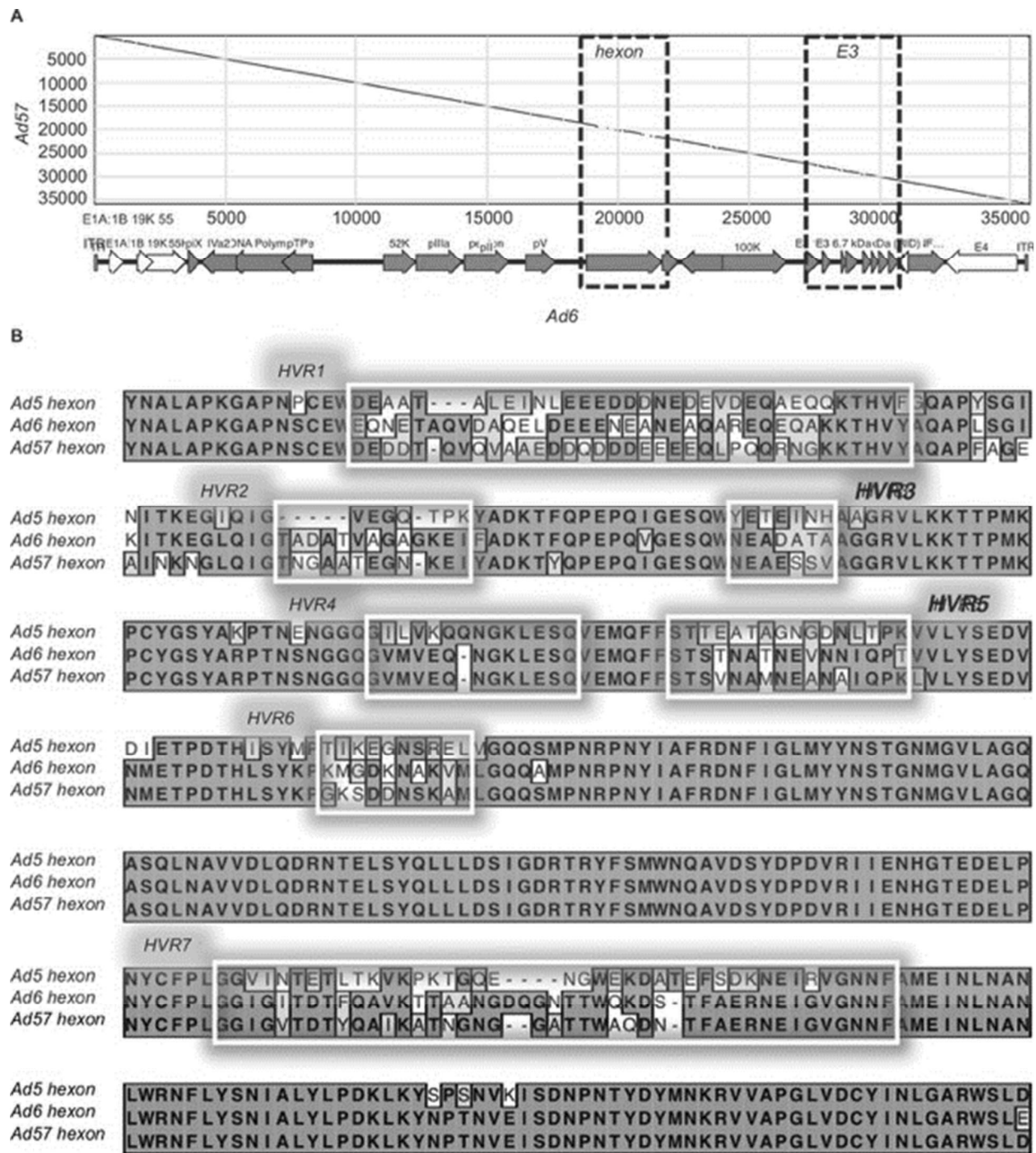


FIG. 7

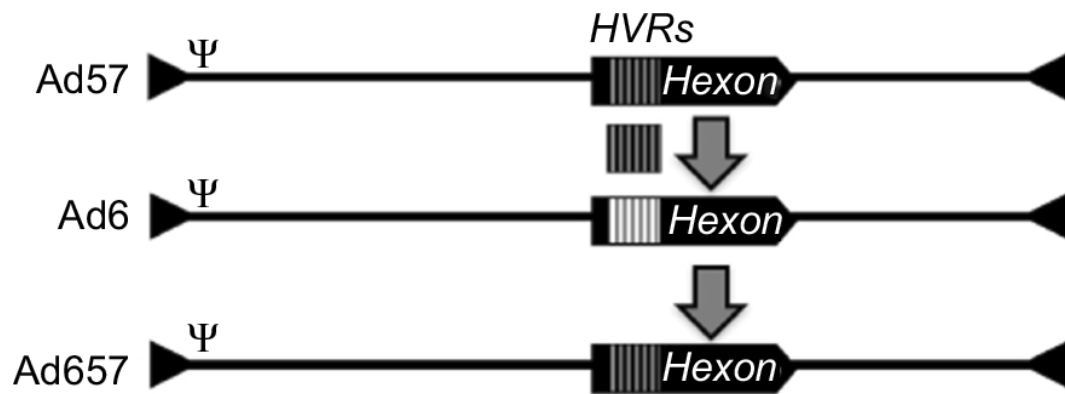


FIG. 8

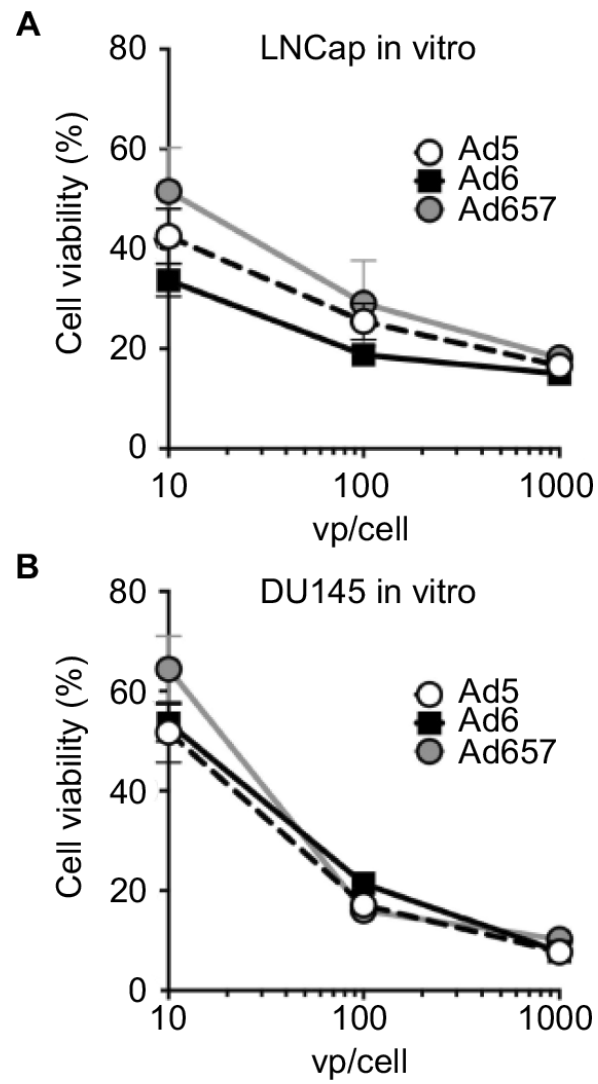


FIG. 9

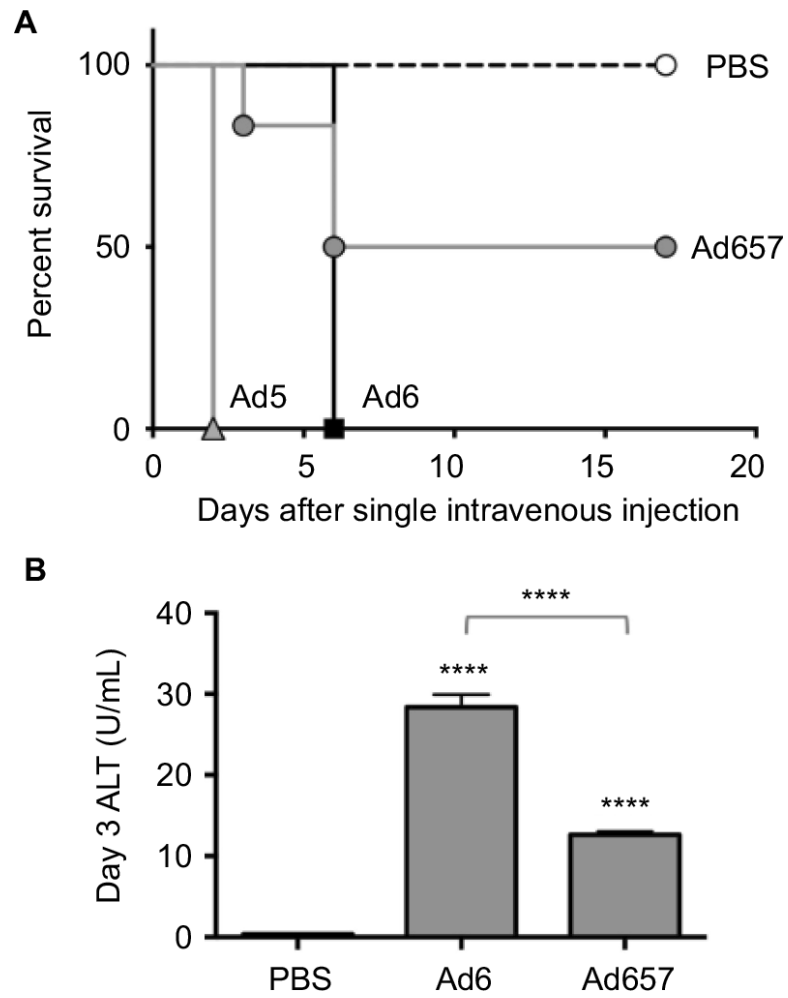


FIG. 10

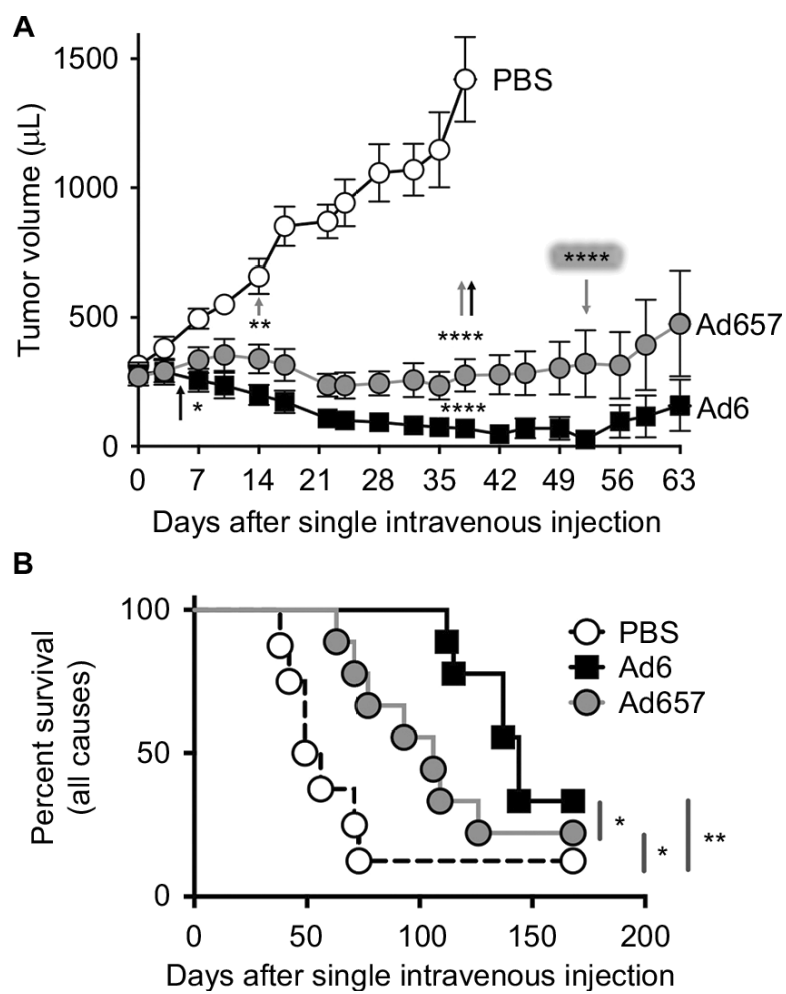


FIG. 11

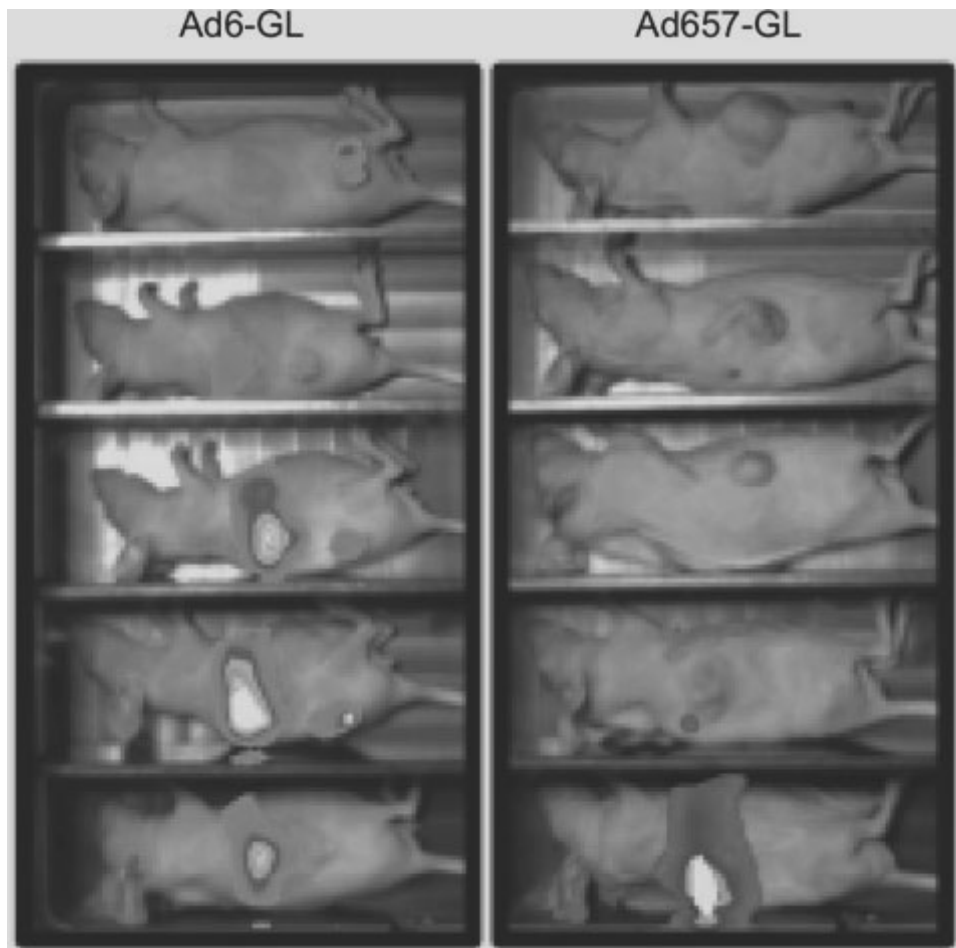


FIG. 12

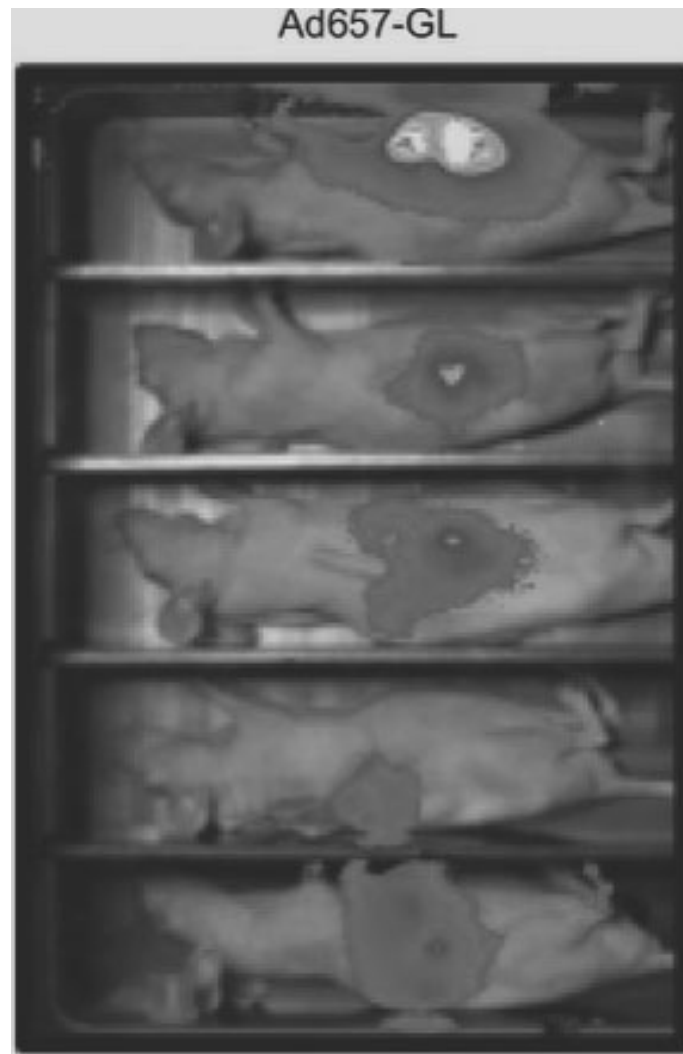


FIG. 13

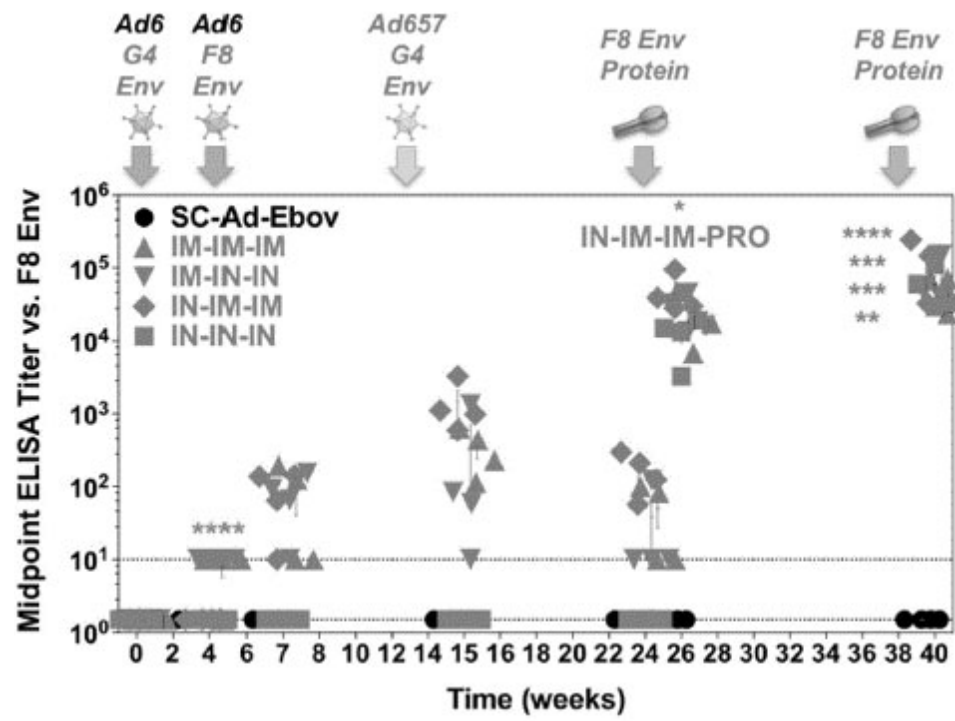


FIG. 14

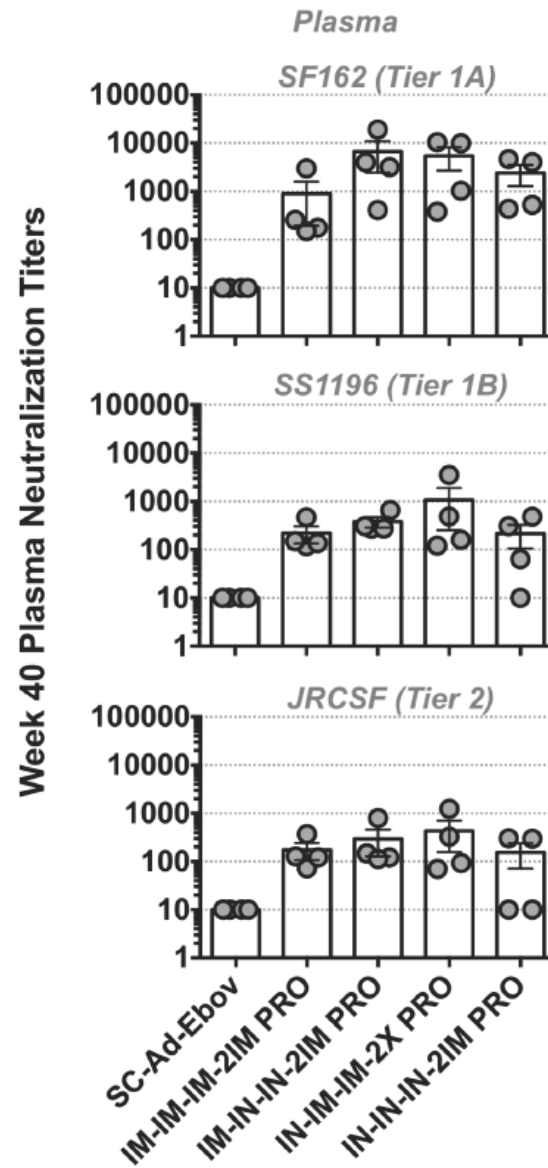


FIG. 15

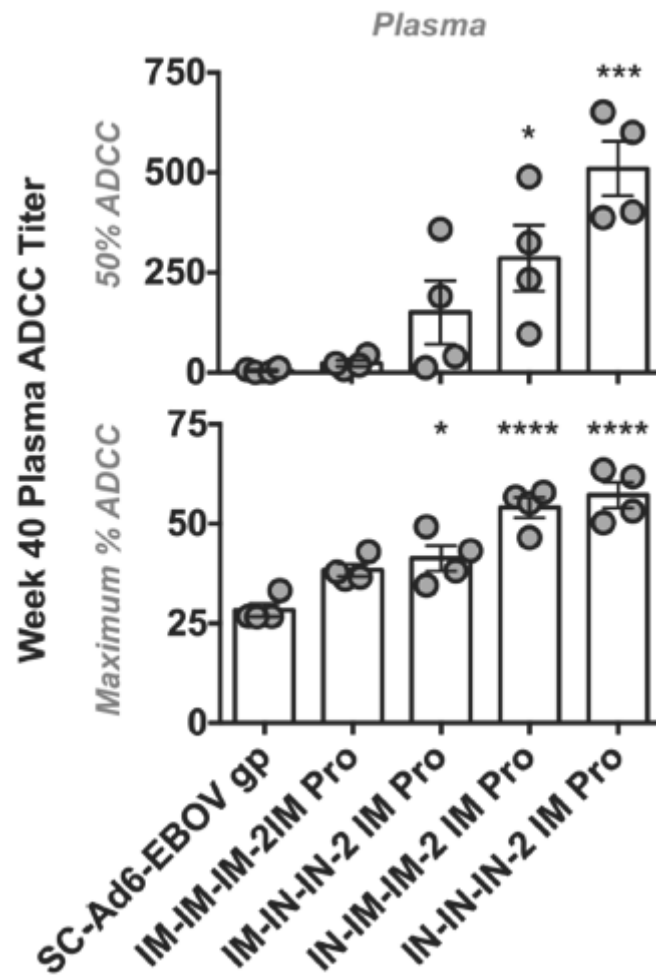


FIG. 16

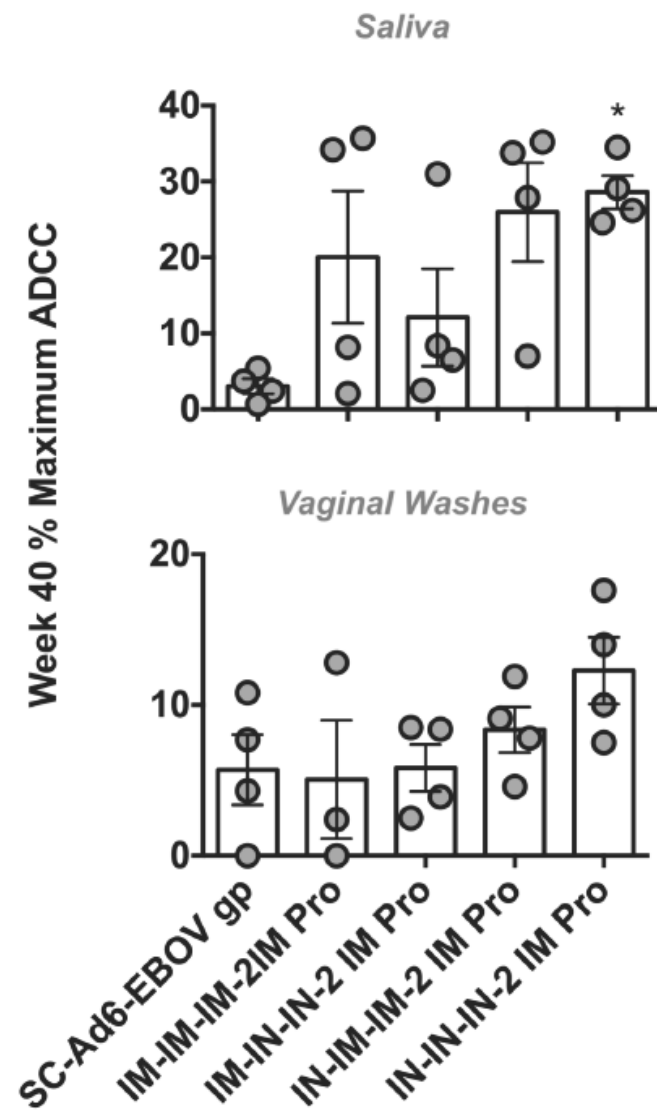


FIG. 17

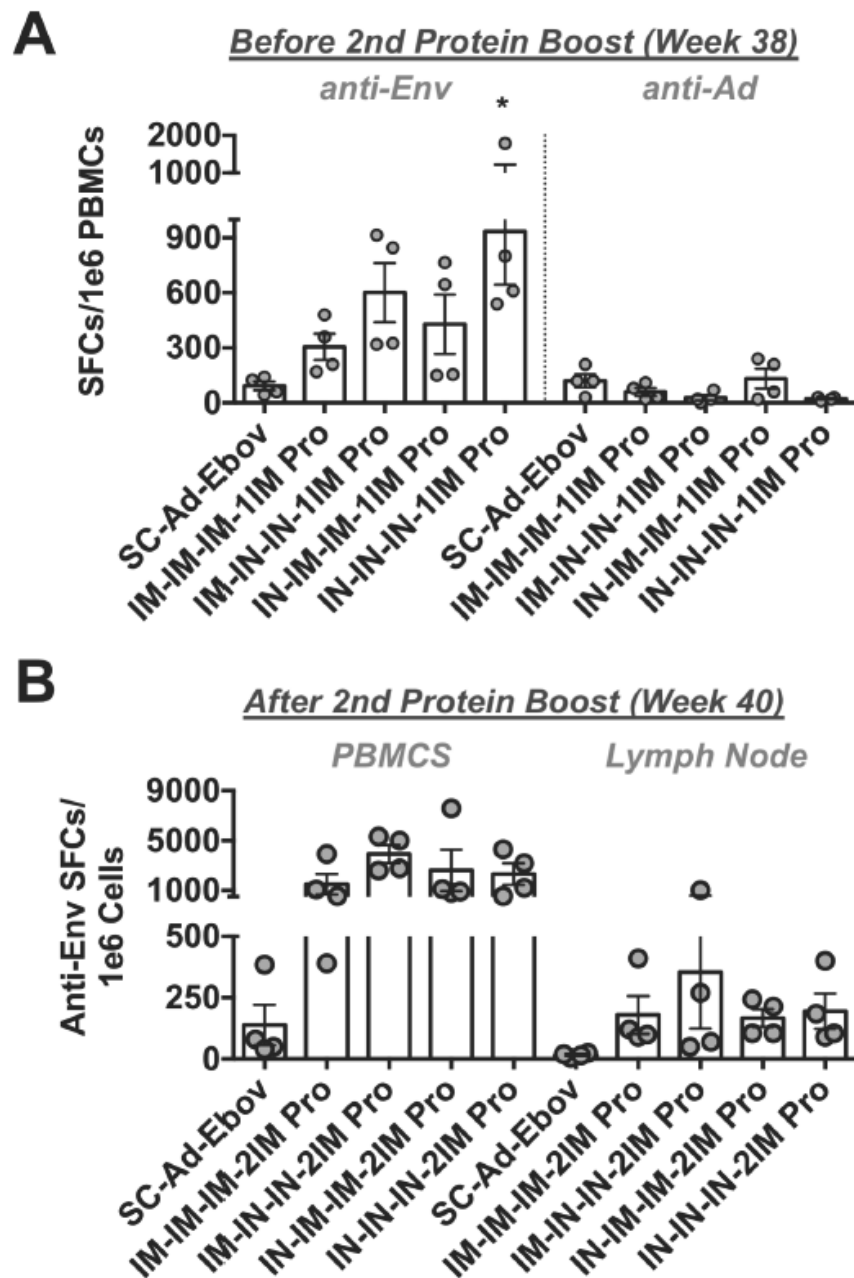


FIG. 18

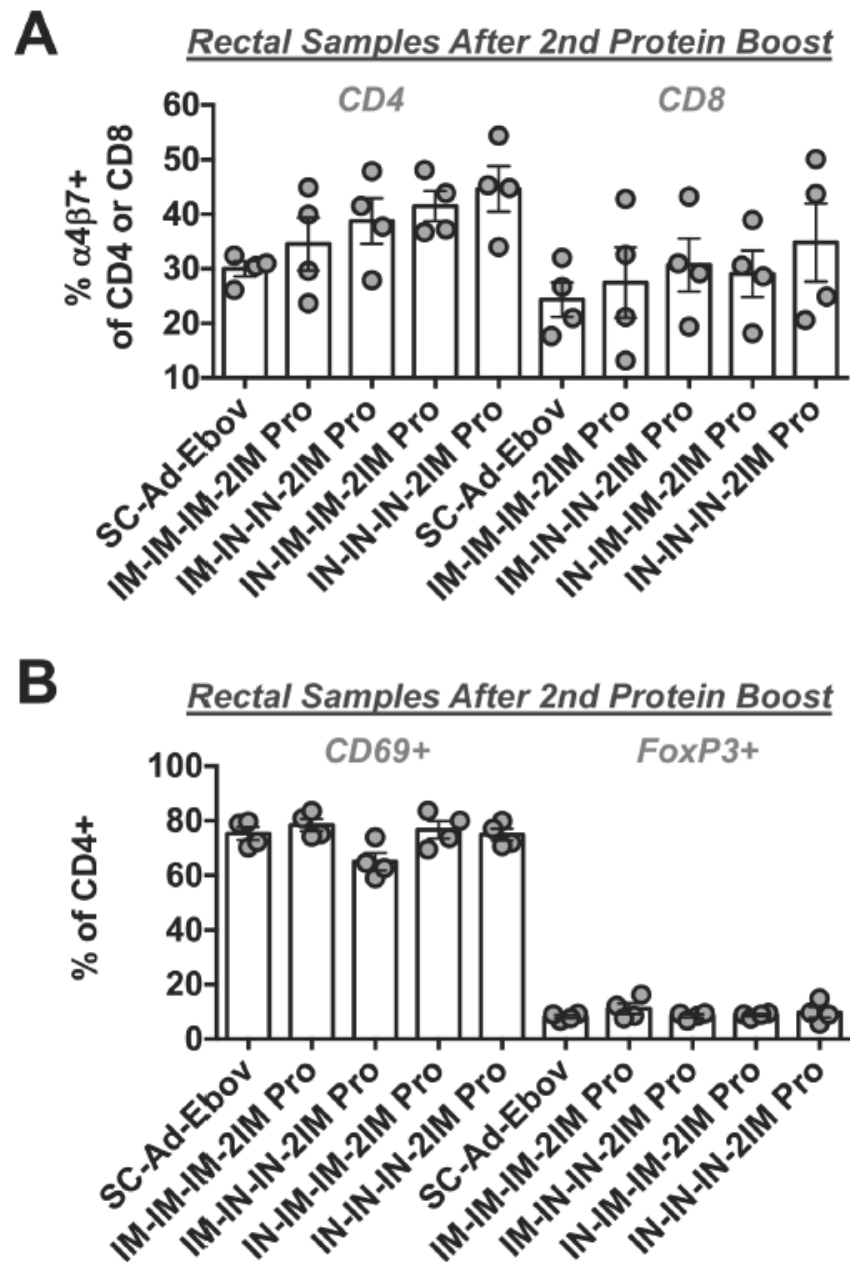


FIG. 19

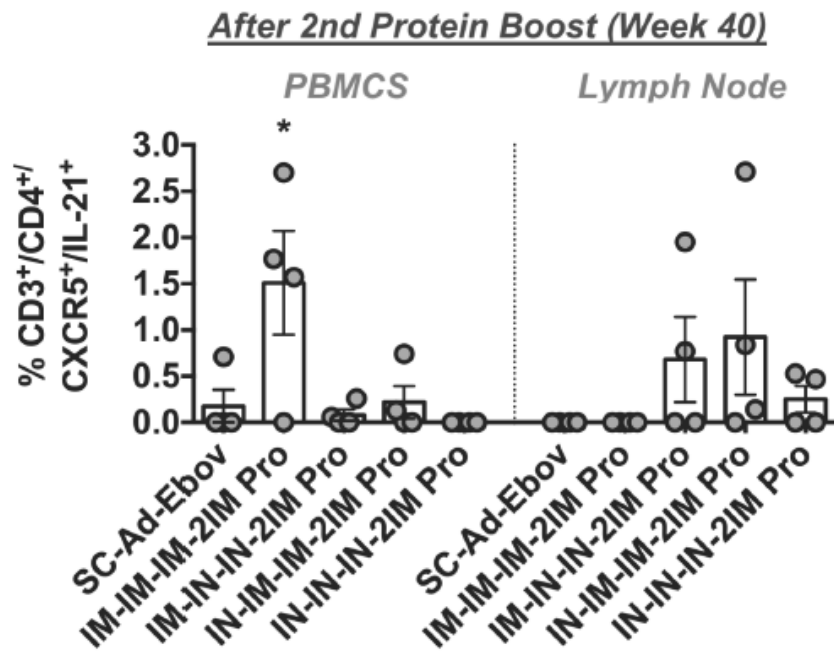


FIG. 20

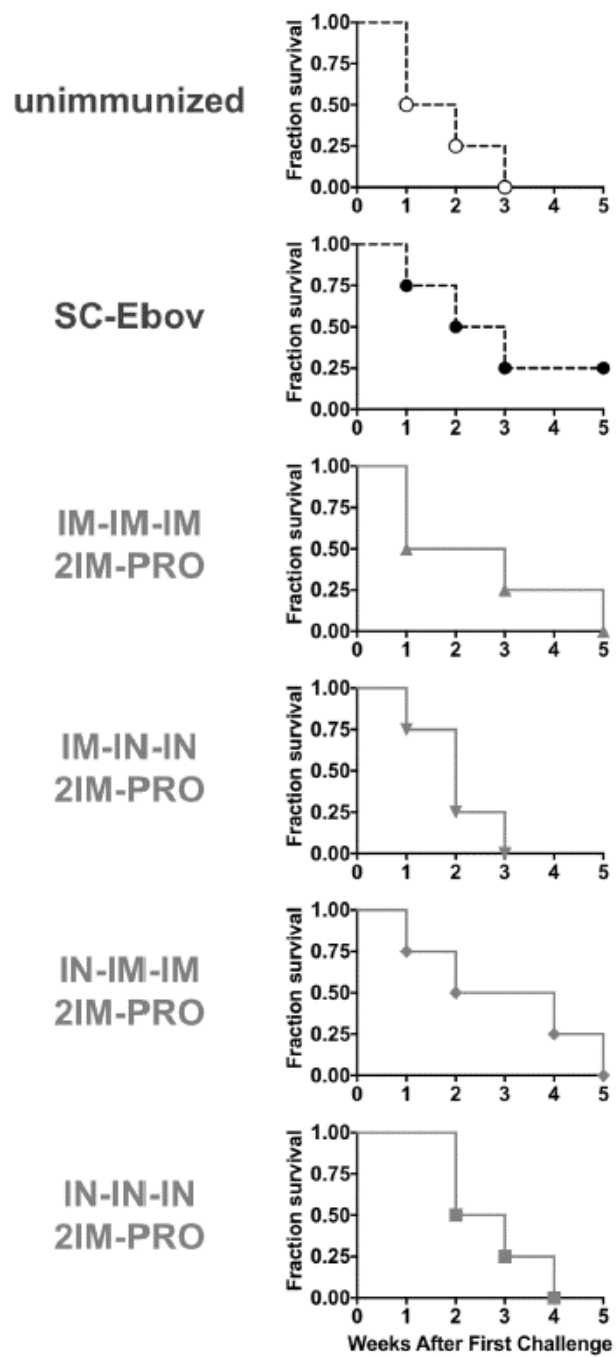


FIG. 21

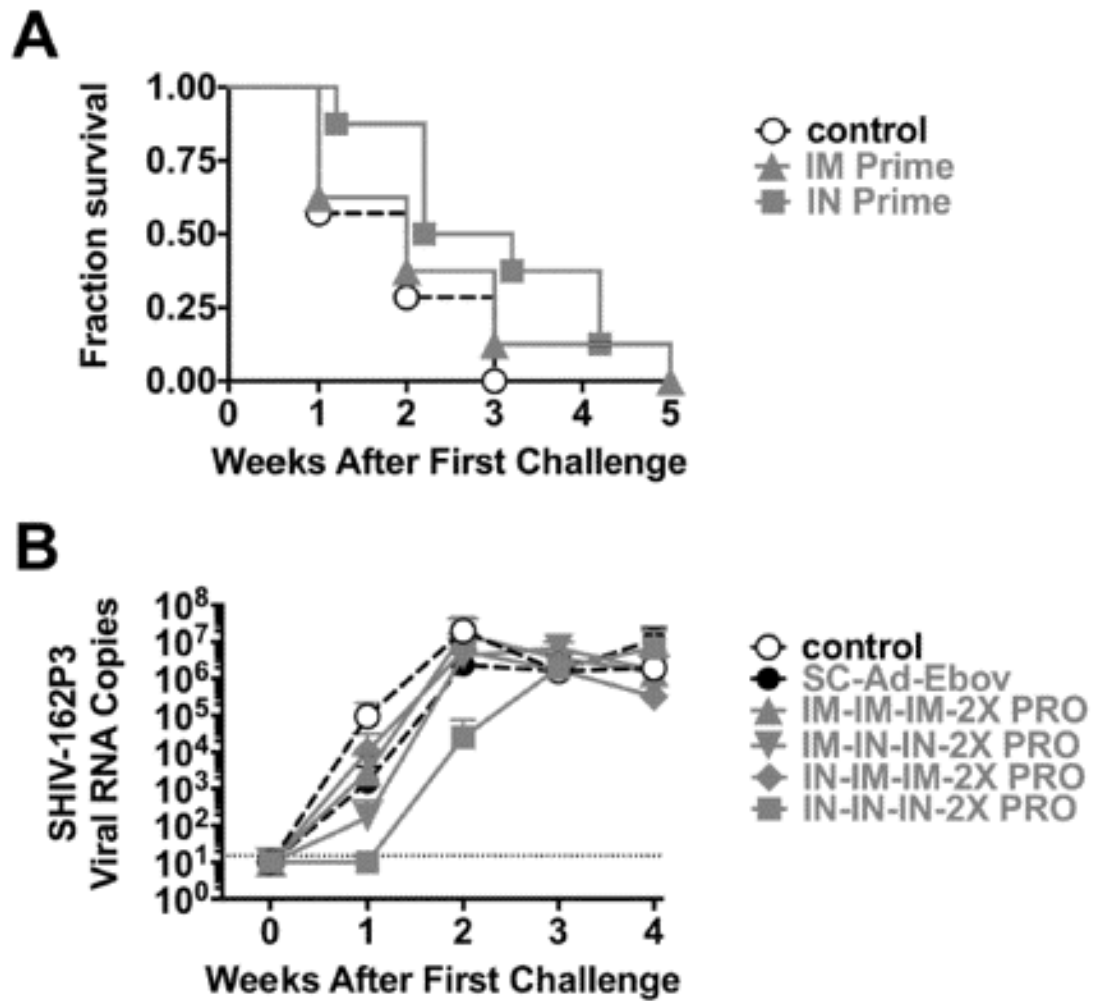


FIG. 22

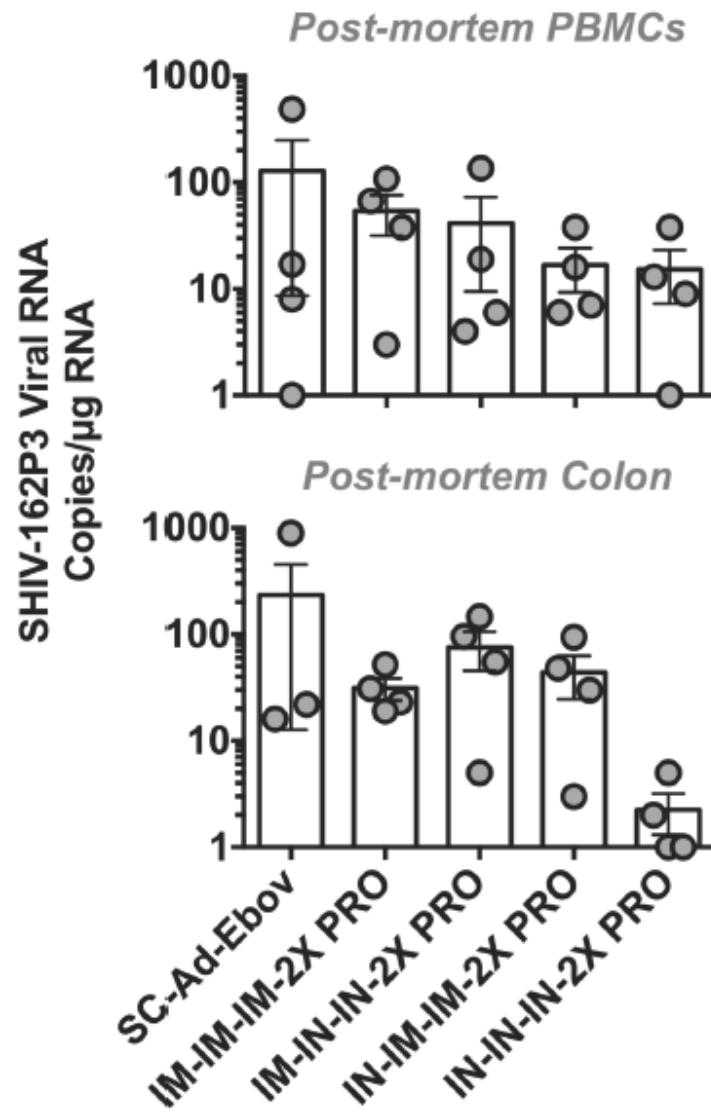


FIG. 23

A**SC-Ad6****SC-Ad657****B**

	HVR1	
Ad1 hexon	YNALAPKGPNSCEV	EQEEPTQEMAELEDEEEAEAAAAEAEAPQADQKVKKTHVYAQ
Ad2 hexon	YNALAPKGPNSCEV	EQTEDSGRAVAEDEEEDEDEEEEEEQNAR--DQATKKTHVYAQ
Ad5 hexon	YNALAPKGPNSCEV	DEAATALEINLEEEEDDNEDEVDE-----QAEQKTHVYFQ
Ad6 hexon	YNALAPKGPNSCEV	EQNETAQVDAQELDEEENEANEQAQARE-----QEQAKKTHVYAQ
Ad57 hexon	YNALAPKGPNSCEV	DEDDTQVQVAAEDDQDDDEEEELPQ-----QRNGKKTHVYAQ
	HVR2	HVR3
Ad1 hexon	APLAGERKITANGI	QI-VSDTQTEG--NPVFADPTYQPEPQVGESQVNEAEATASGGRVLK
Ad2 hexon	APLSGETITKSGI	QIGSDNAETQA--KPVYADPSYQPEPQIGESQVNEADANAAGGRVLK
Ad5 hexon	APYSGINITKEGI	QIGVEGQ-----TEKYADKTFQPEPQIGESQVYETEINHAGGRVLK
Ad6 hexon	APLSGIKITKEGI	QIGTADATVAGAGKEIFADKTFQPEPQVGESQVNEADANAAGGRVLK
Ad57 hexon	APFAGEAINKNGI	QIGTNGAATEG-NKEIYADKTYQPEPQIGESQVNEAESVAGGRVLK
	HVR4	HVR5
Ad1 hexon	KTTMPMKPCYGSYARPTNK	NGGQGILVANNQGALESKVEMQFFAPSGTAMN-ERNVQPSI
Ad2 hexon	KTTMPMKPCYGSYARPTNP	FGGQSVLVPDEKGVPLPKVDLQFFSNITSLNDROGNATKPKV
Ad5 hexon	KTTMPMKPCYGSYAKPTN	ENGGQGILVKQNGKLESQVEMQFFSTTEATAG-NGDNLTPKV
Ad6 hexon	KTTMPMKPCYGSYARPTNS	NGGQGVMM-EQNGKLESQVEMQFFSTSTINATN-EVNNIQPTV
Ad57 hexon	KTTMPMKPCYGSYARPTNS	NGGQGVMM-EQNGKLESQVEMQFFSTSVNAMN-EANAIQPKL
	HVR6	
Ad1 hexon	VLYSEDVNMETPDTHISYKFS	SKTDENSKAMLGQQAAMPNRPNYIAFRDNF IGLMYNSTGN
Ad2 hexon	VLYSEDVNMETPDTHLSYKPK	CKGDENSKAMLGQQSMPNRPNYIAFRDNF IGLMYNSTGN
Ad5 hexon	VLYSEDEVDIETPDTHISYMT	TIKEGNSRELNGQSMNRPNYIAFRDNF IGLMYNSTGN
Ad6 hexon	VLYSEDVNMETPDTHLSYKPK	KMGDKNAKVM LGQQAAMPNRPNYIAFRDNF IGLMYNSTGN
Ad57 hexon	VLYSEDVNMETPDTHLSYKPK	SKSDENSKAMLGQQSMPNRPNYIAFRDNF IGLMYNSTGN
	HVR7	
Ad1 hexon	GTEDELPNYCFPLG	GIGVTDTYQGIKS--NGNG---NPQNWKND-FAARNEIGVGN
Ad2 hexon	GTEDELPNYCFPLG	GIGVTDTYQAIAK--NGNGSGDNGDITWTKDET-FATRNEIGVGN
Ad5 hexon	GTEDELPNYCFPLG	GVINTEITLTKVKPKTGOENG-----WEKDATEFSDKNEIRVGN
Ad6 hexon	GTEDELPNYCFPLG	GIGITDTFQAVKTTAAANGDQ---GNTTWQKDSI-FAERNEIGVGN
Ad57 hexon	GTEDELPNYCFPLG	GIGVTDTYQAIAKAT--NGNG---GATTWAQDNT-FAERNEIGVGN

FIG. 24

Figure 25

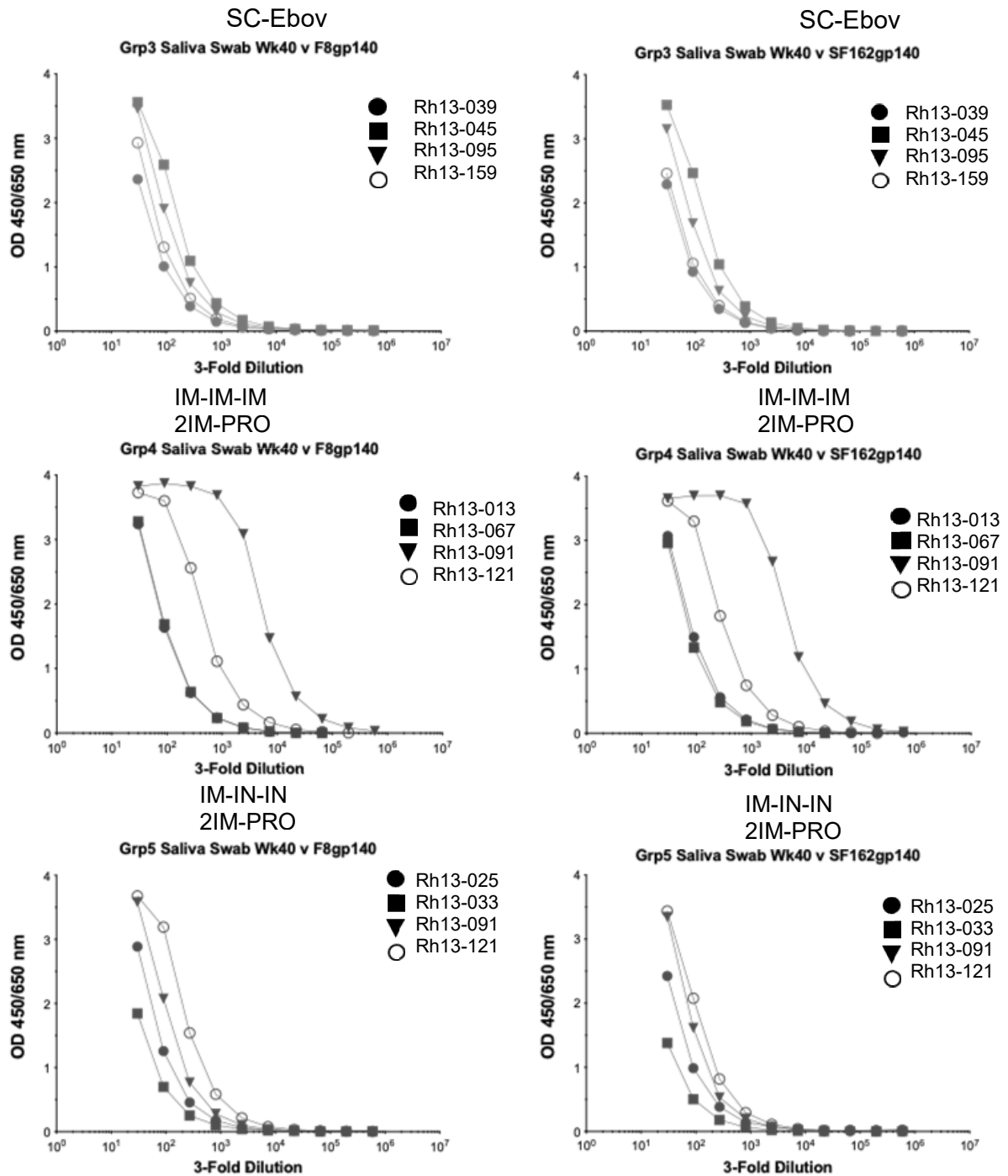
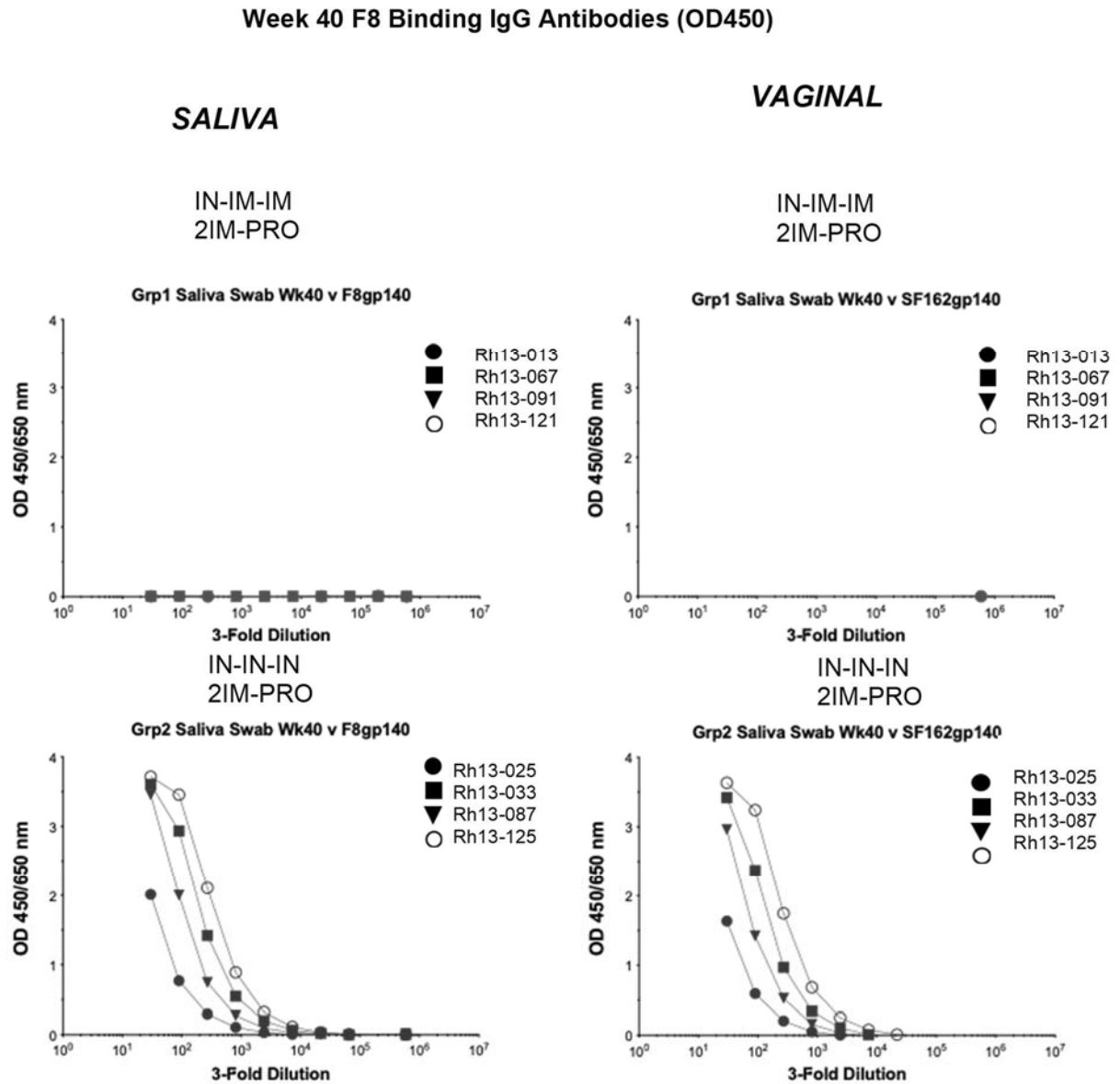
Week 40 F8 Binding IgG Antibodies (OD450)**SALIVA****VAGINAL**

Figure 25, continued



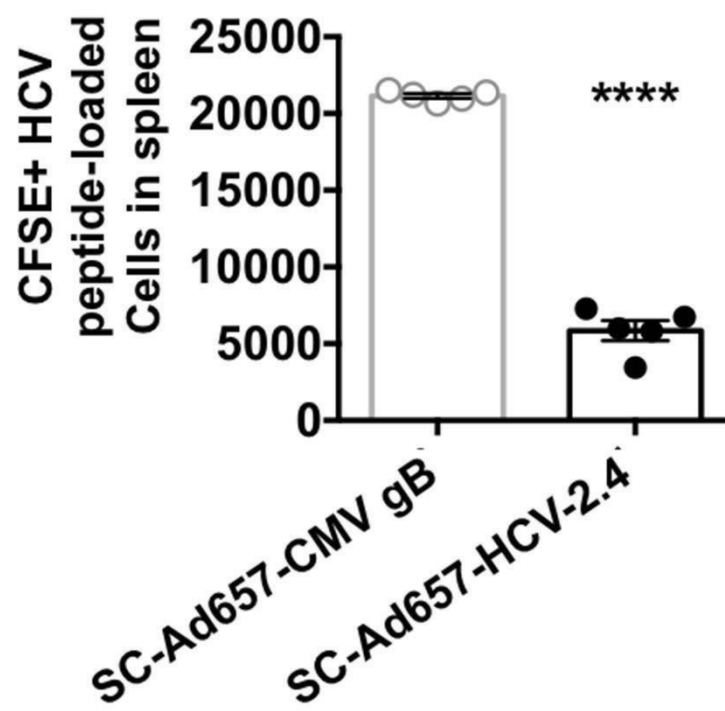


FIG. 26

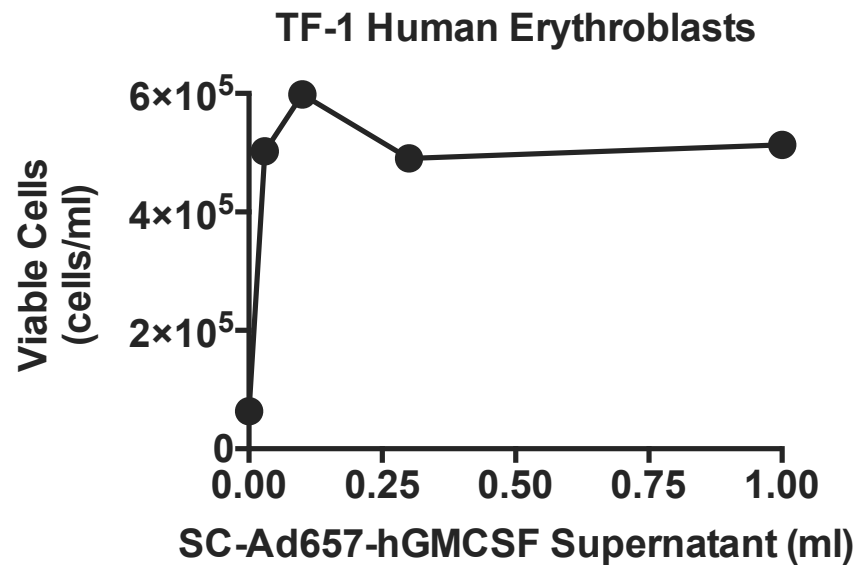


FIG. 27

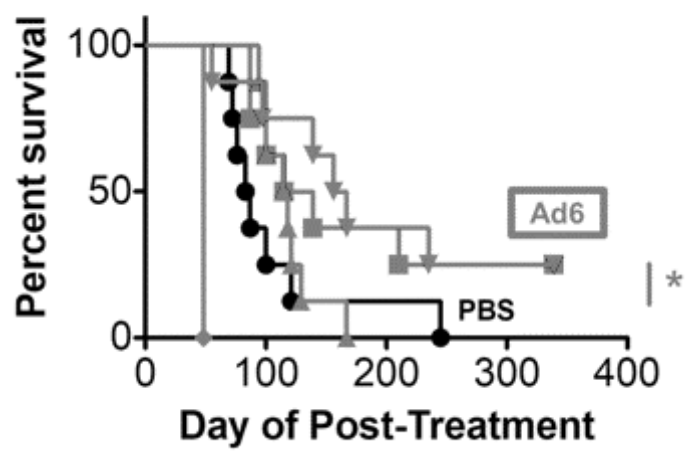


FIG. 28

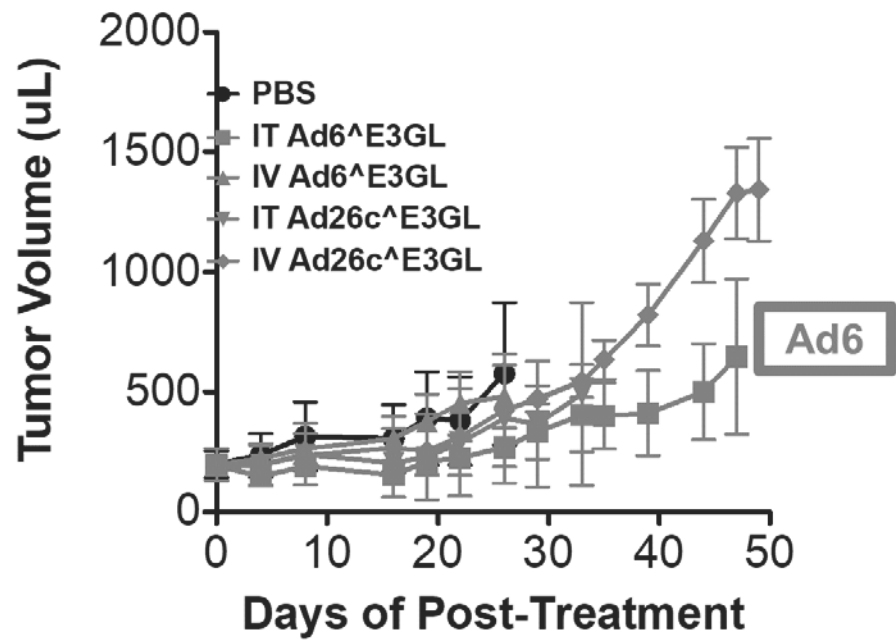


FIG. 29

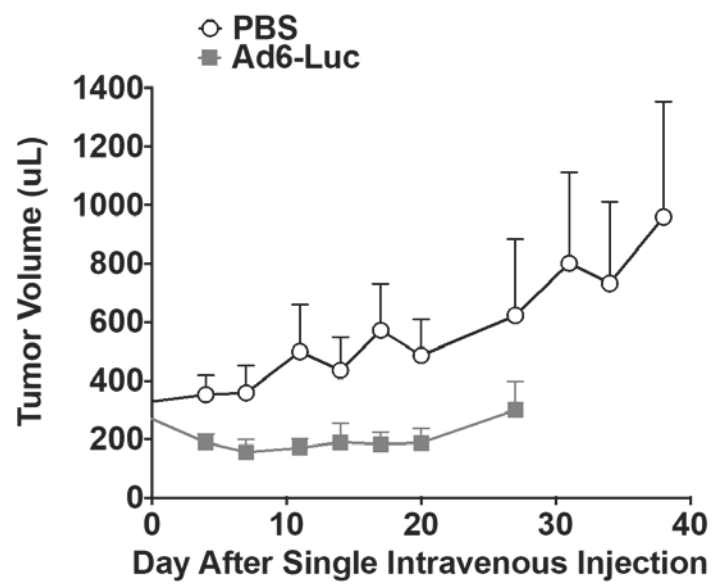


FIG. 30

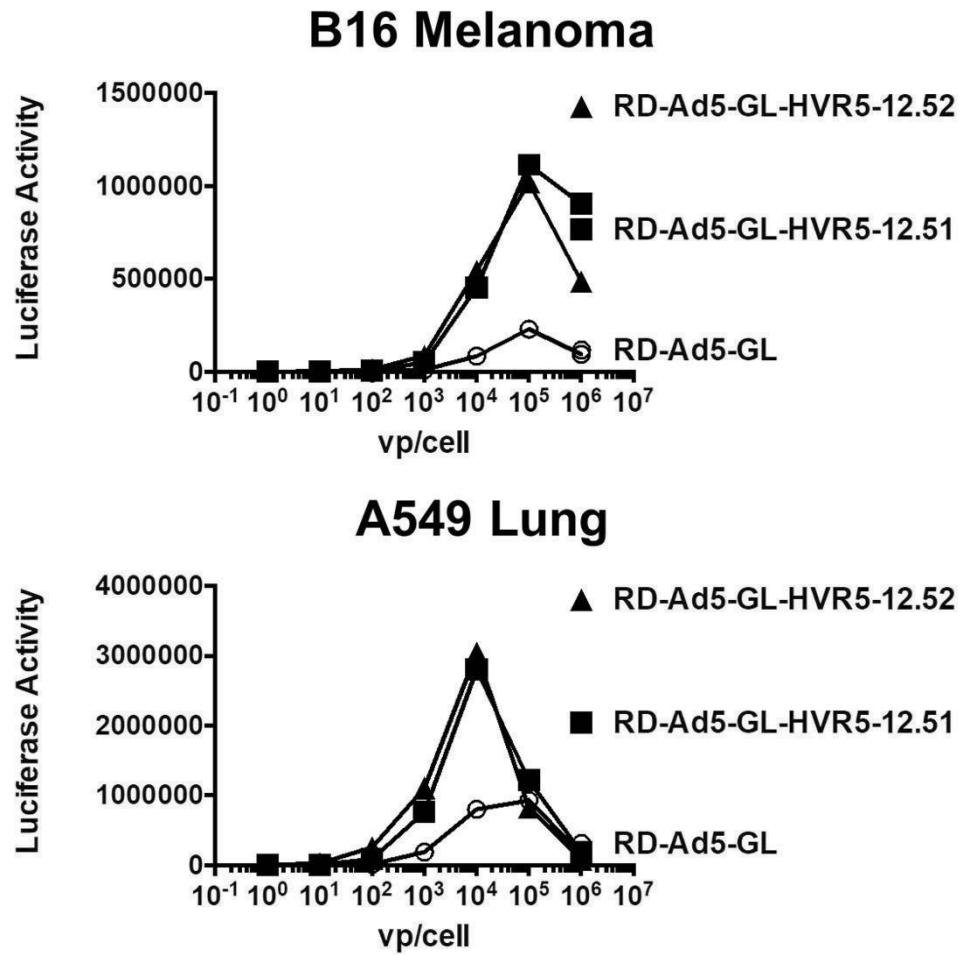


FIG. 31

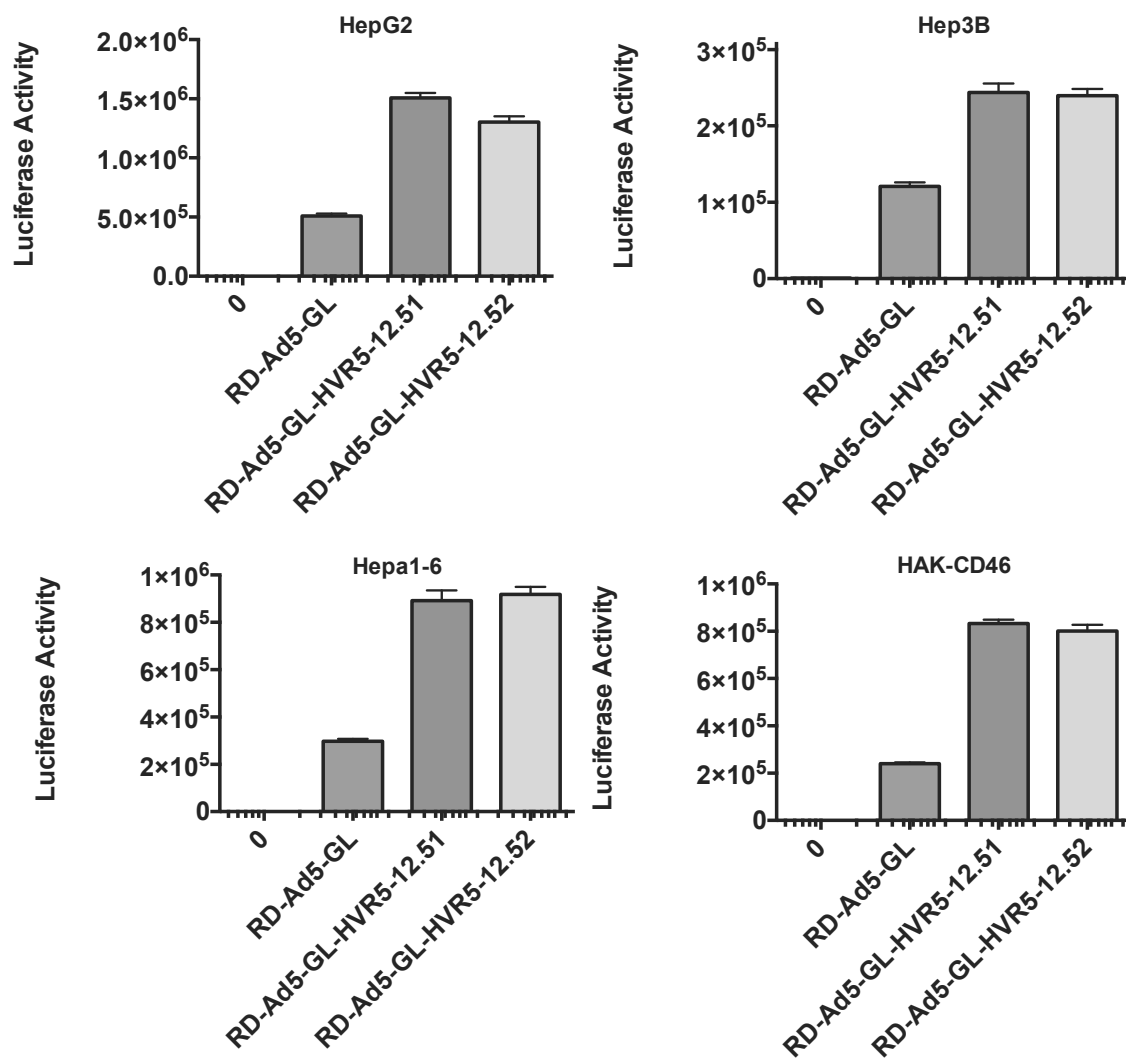
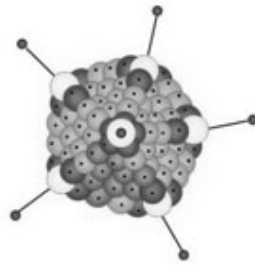
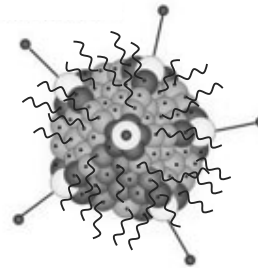


FIG. 32

Combining different HVRs from Ad6 and Ad657 and inserting cell targeting and detargeting ligands



**Insert combination of
different HVRs**



**Insert
peptides into
different HVRs**

FIG. 33

Figure 33 (continued)

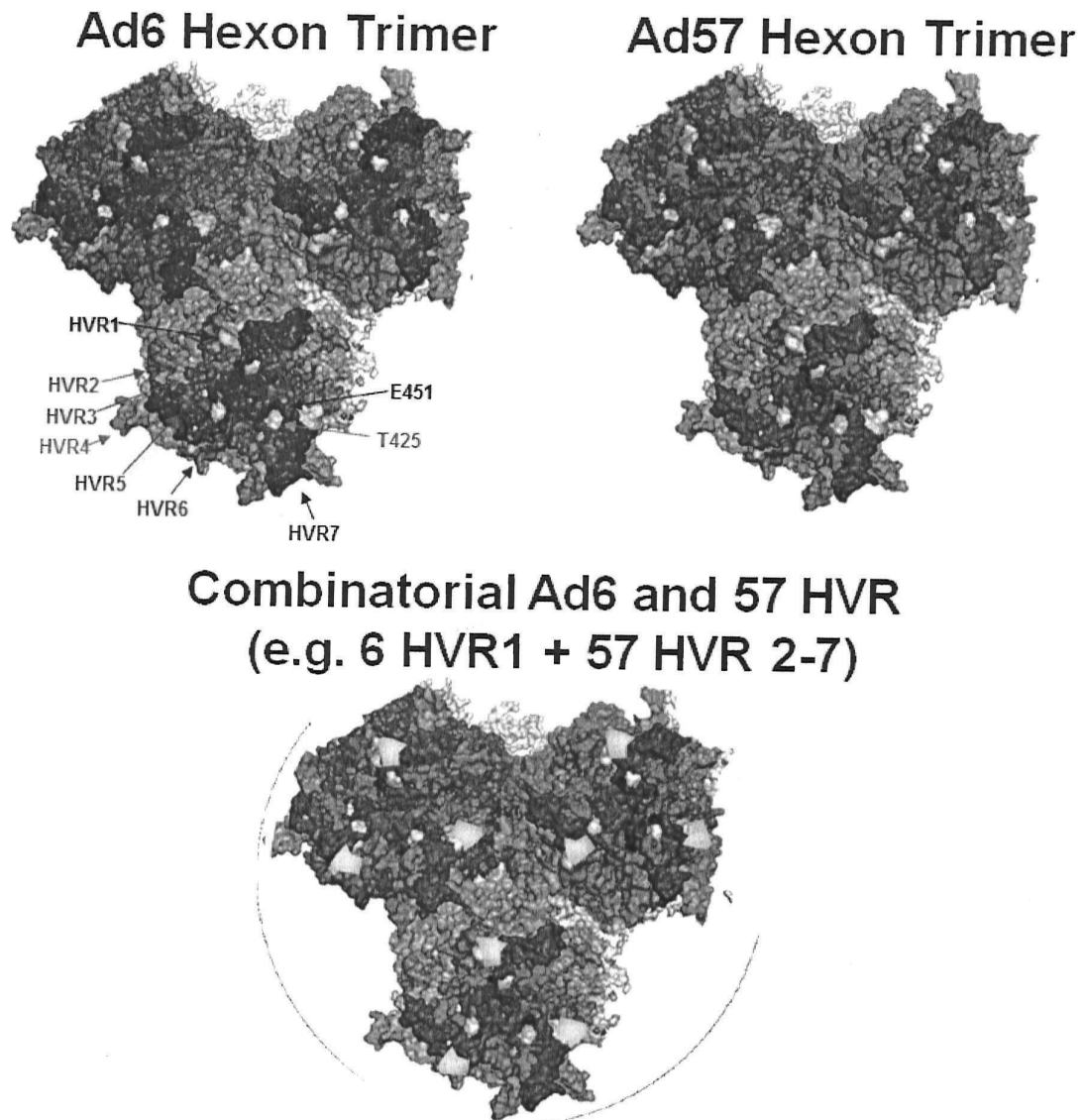
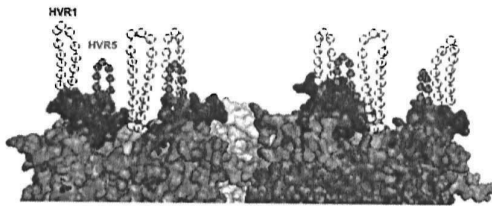
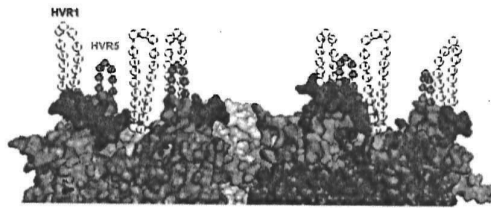
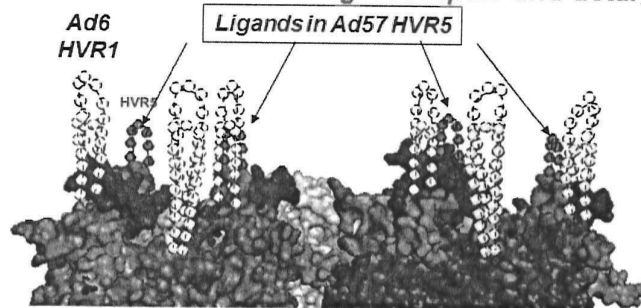


Figure 33 (continued)

Ad6 Hexon Trimer Surface**Ad57 Hexon Trimer Surface****Combinatorial Ad6 and 57 HVR***(e.g. 6 HVR1 + 57 HVR 2-7)***+/- Combinatorial Targeting/Detargeting Insertions***(e.g. Ad6 HVRs to avoid macrophages,**Peptides inserted in Ad57 HVR5 to target receptor and detarget hepatocytes)*

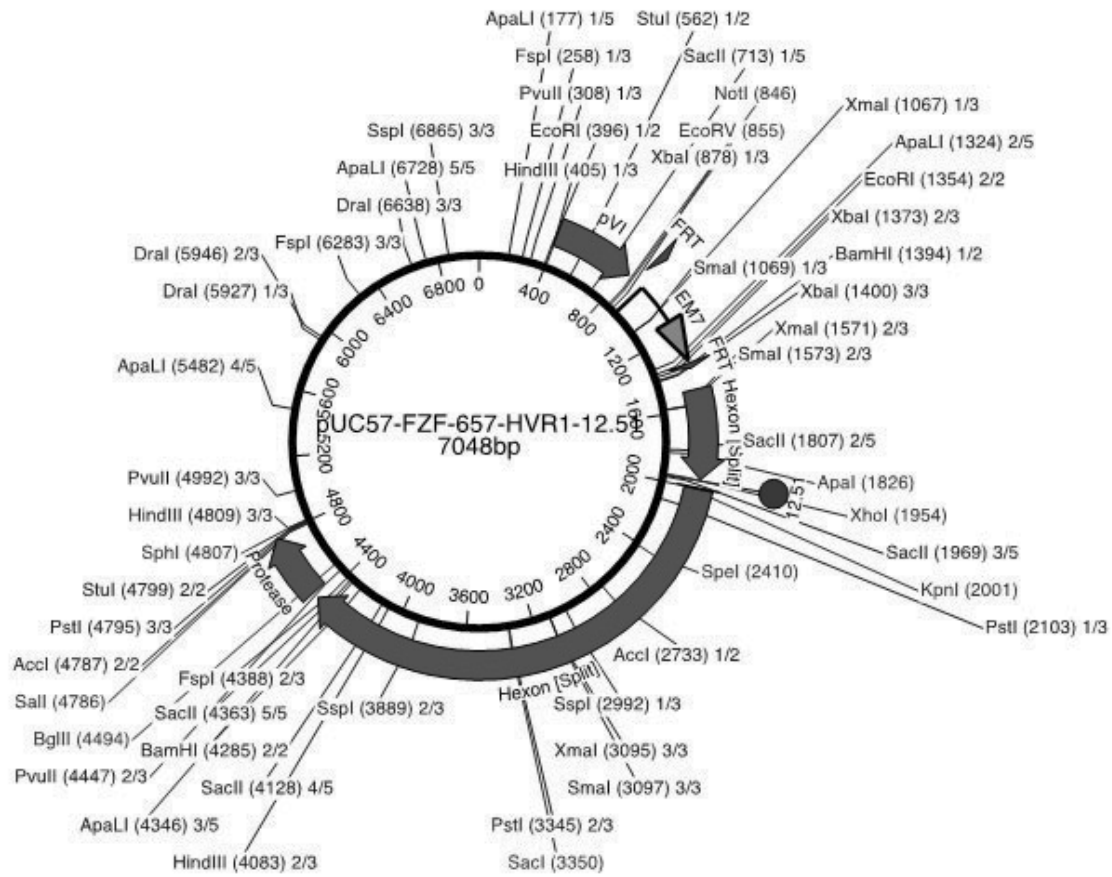


FIG. 34

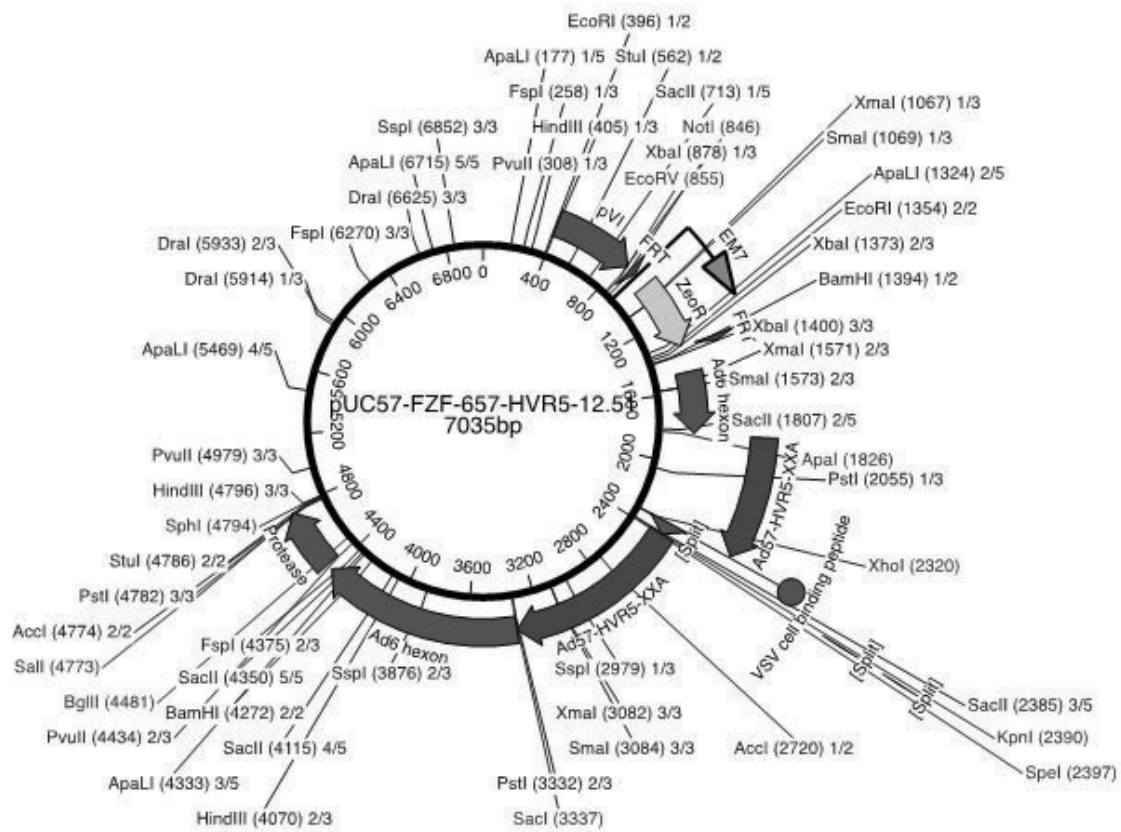


FIG. 34 (continued)

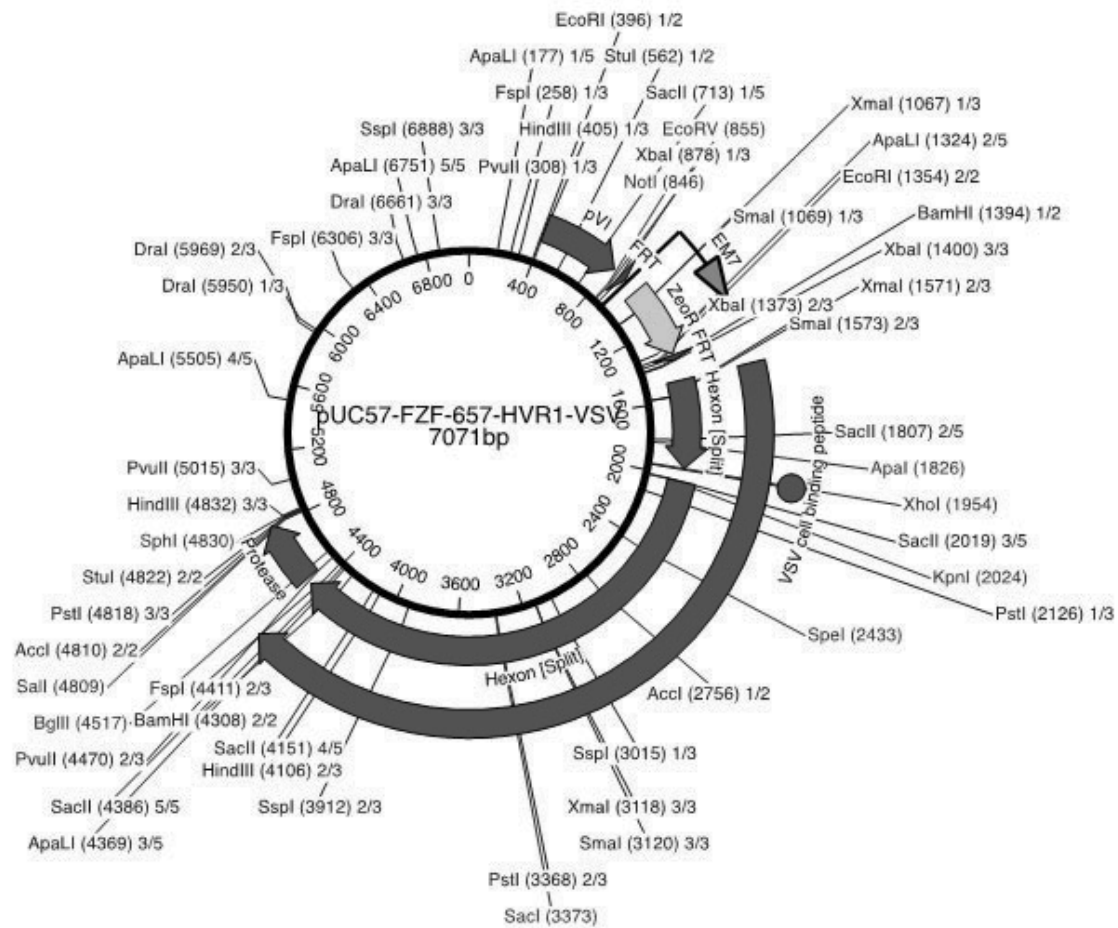


FIG. 34 (continued)

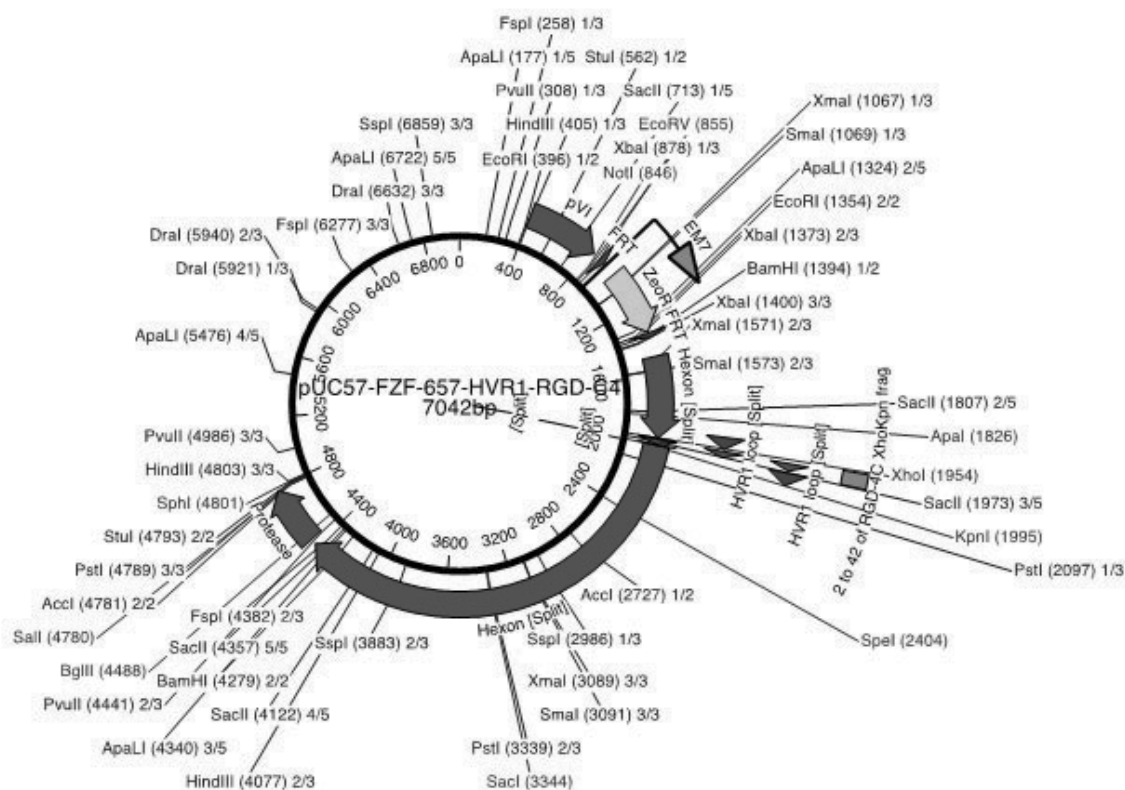


FIG. 34 (continued)

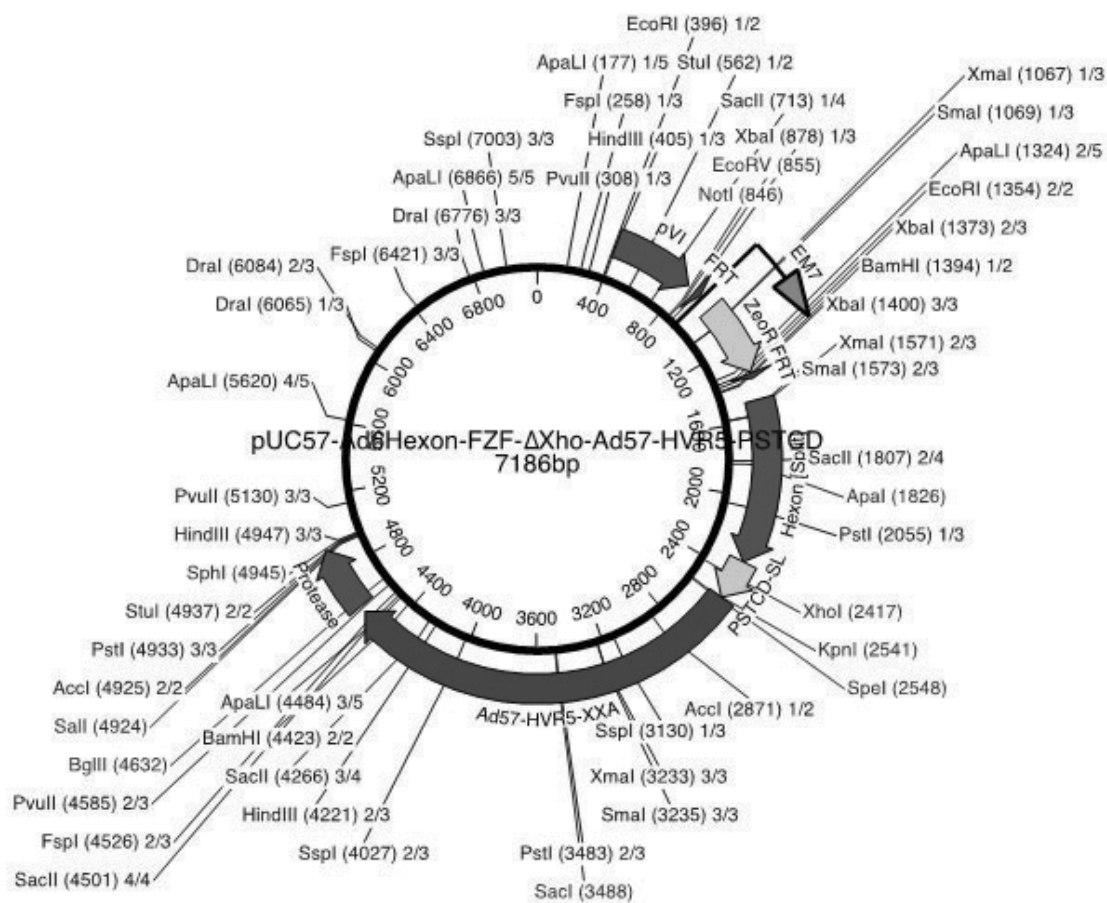


FIG. 34 (continued)

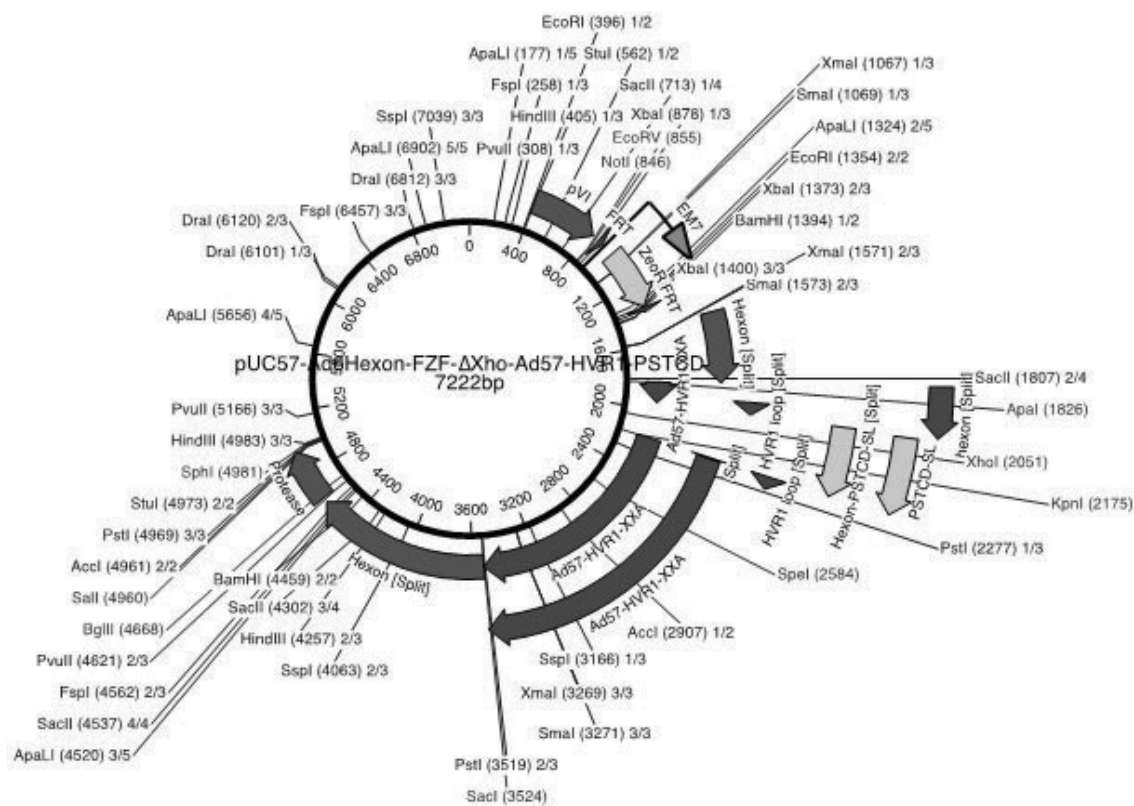


FIG. 34 (continued)

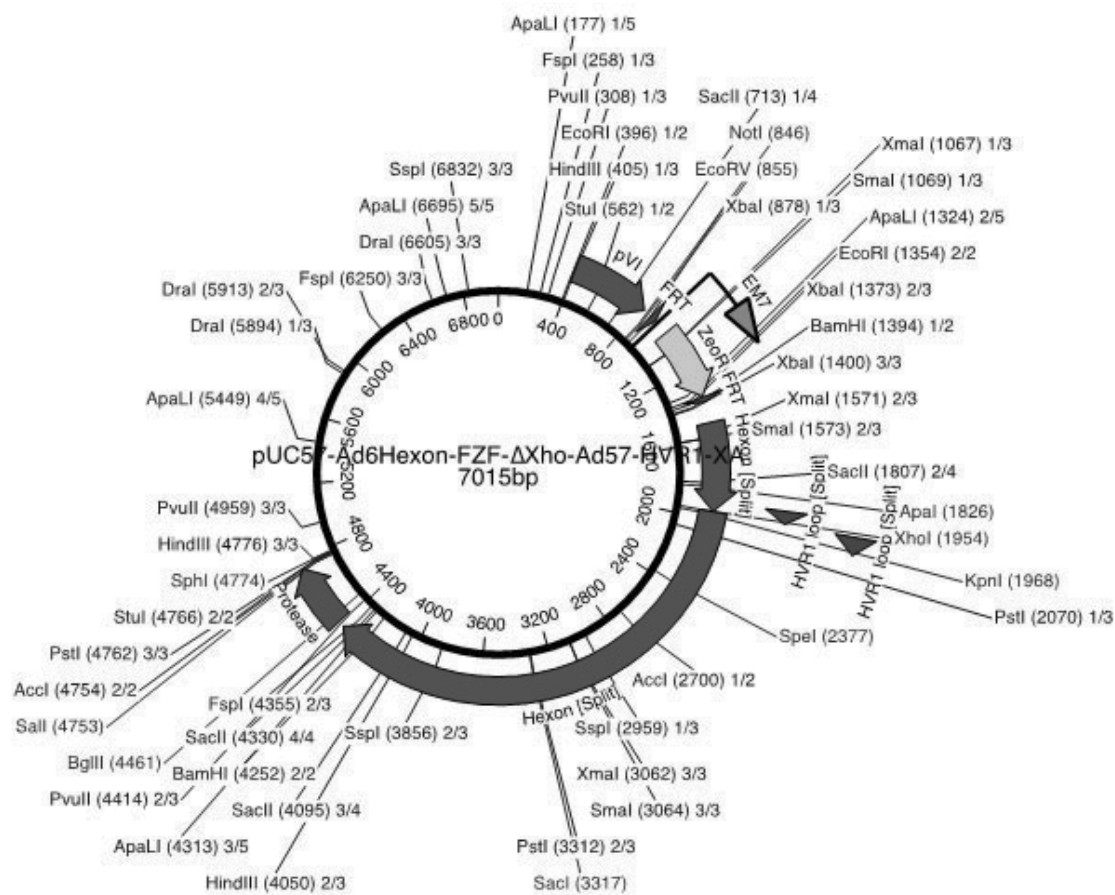


FIG. 34 (continued)

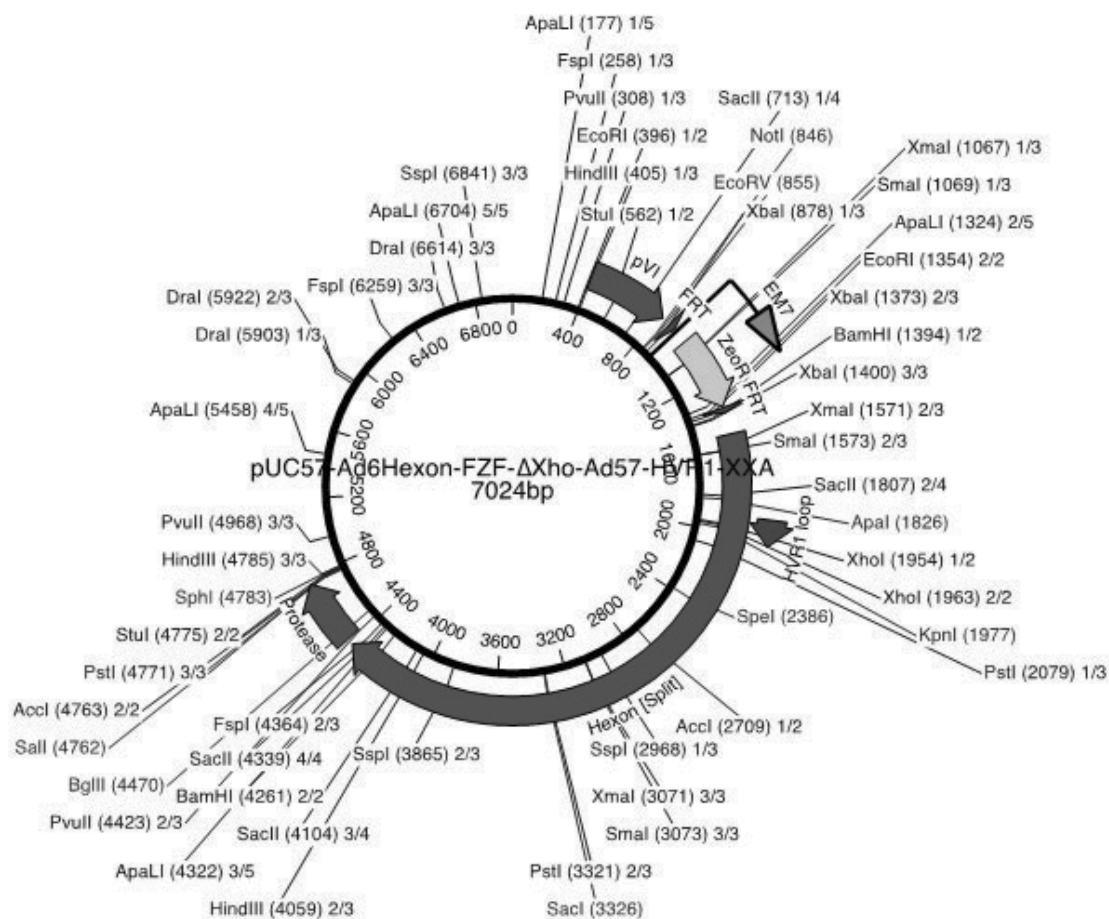


FIG. 34 (continued)

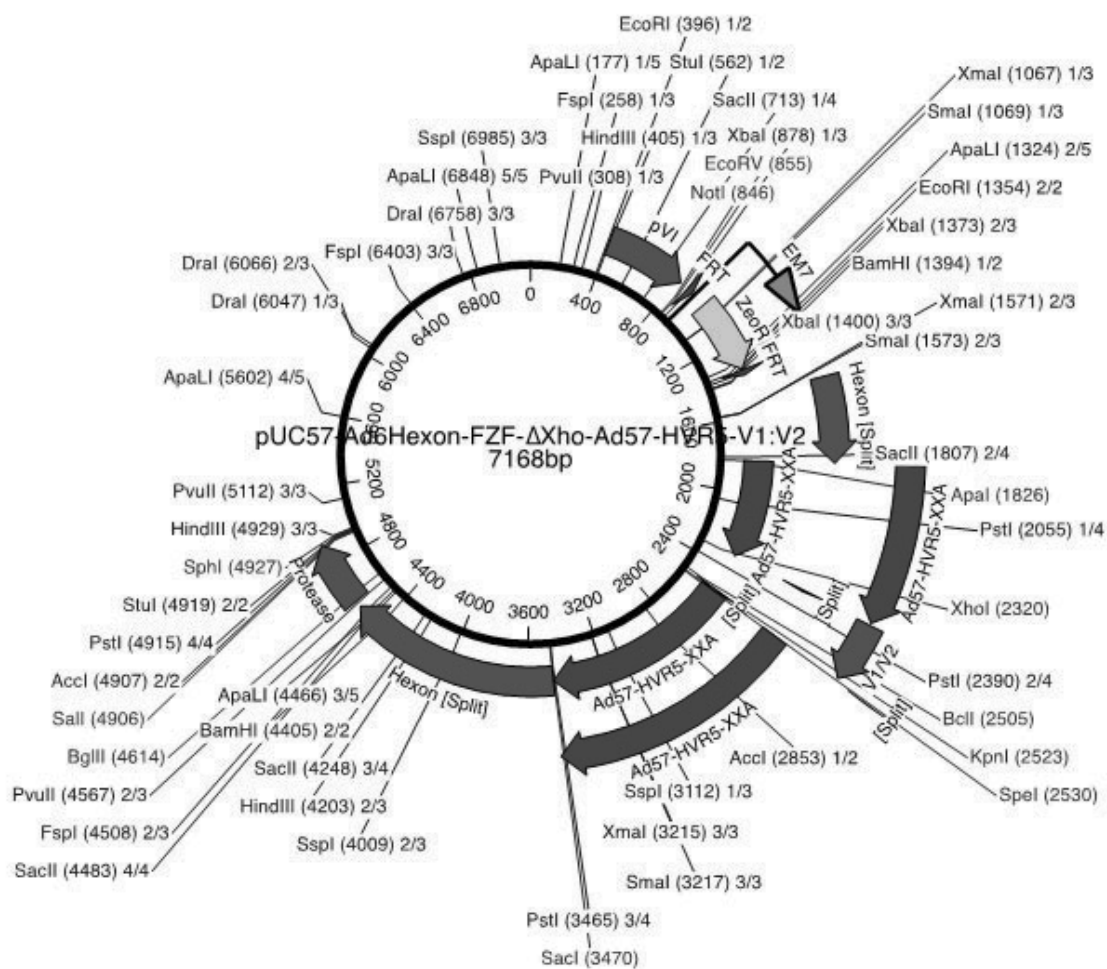


FIG. 34 (continued)

cysteine-insertions into Ad657 HVRs

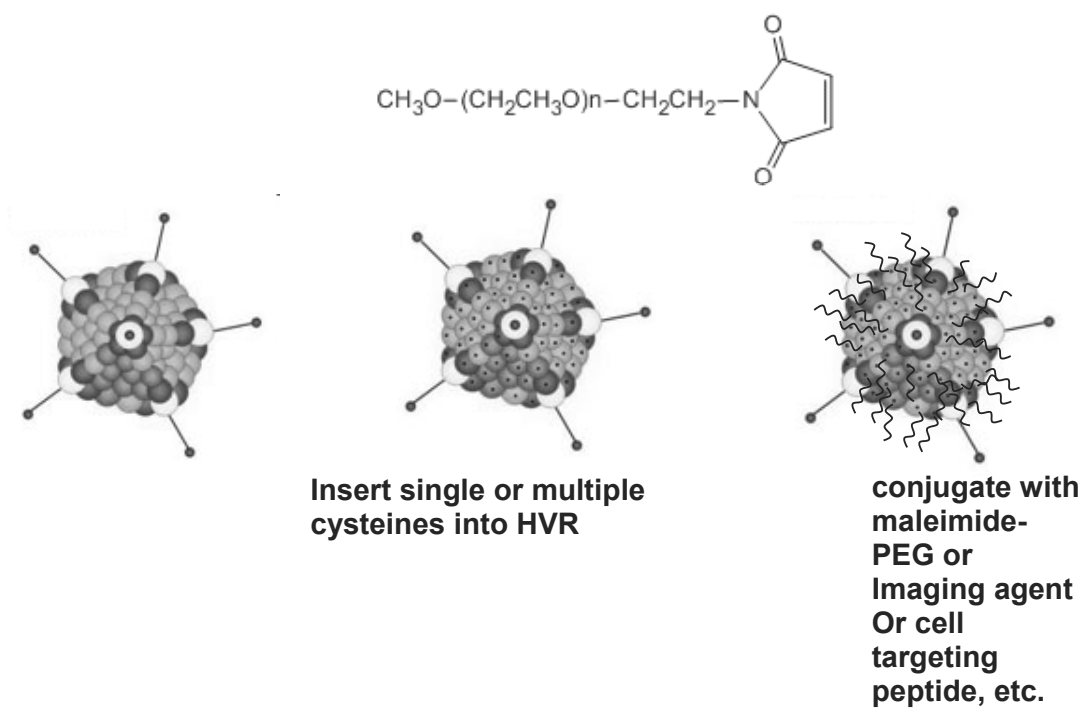
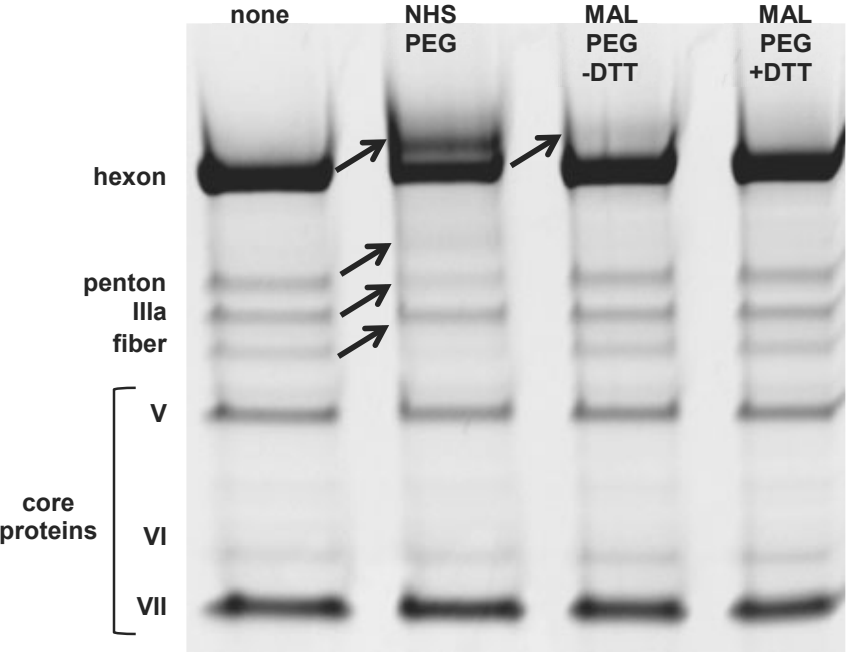


FIG. 35

A



B

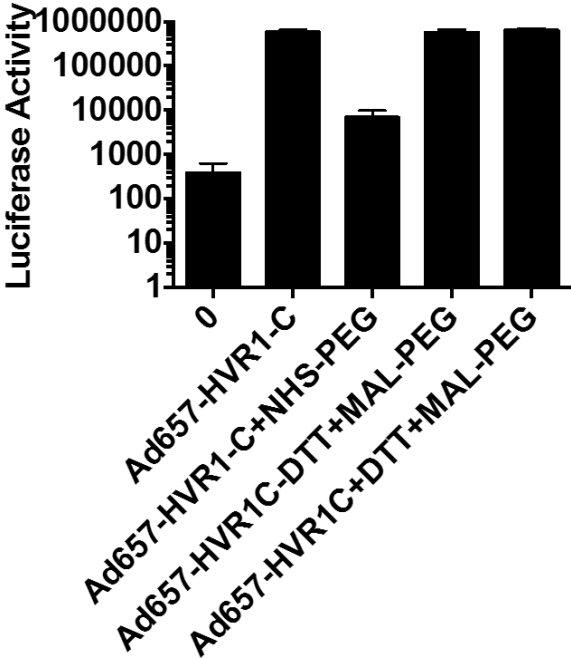


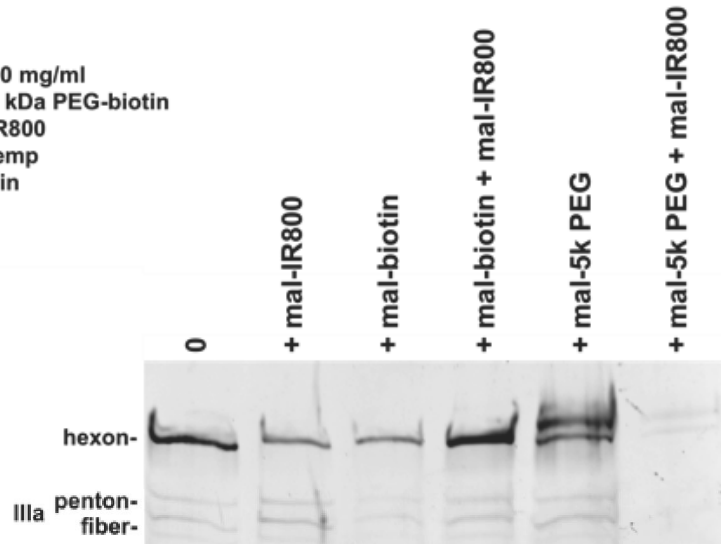
FIG. 36

48/82

A

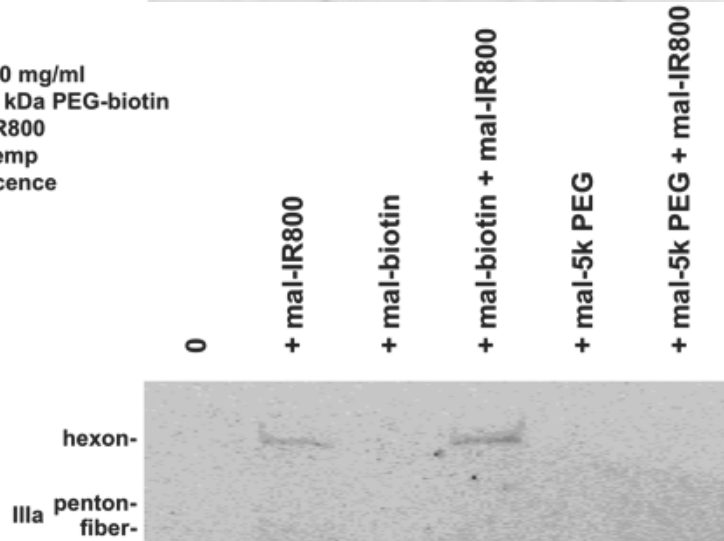
Ad6/57-HVR5C

Reaction with 10 mg/ml
+/- maleimide-5 kDa PEG-biotin
+/- maleimide-IR800
2 hours room temp
Sypro Ruby stain



B

Reaction with 10 mg/ml
+/- maleimide-5 kDa PEG-biotin
+/- maleimide-IR800
2 hours room temp
830 nm fluorescence



C

MB11-2013 LNCaP Male Nude Mice Treated with One Dose IP Injection
Ad6/57.HVR5.C.GL PEG5KDa 2.35x10¹⁰/Mouse in 600 uL

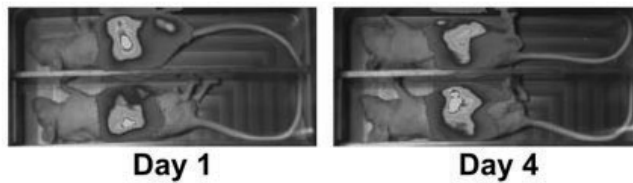
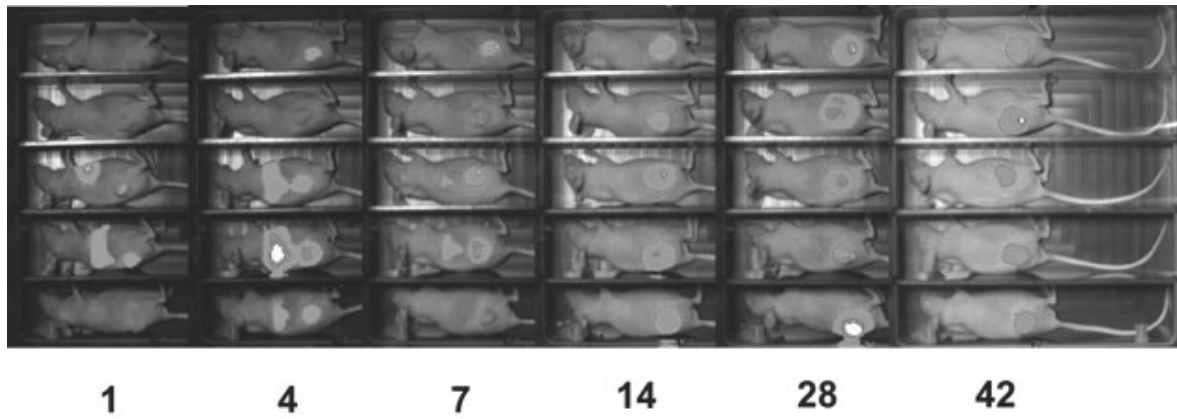


FIG. 37

A



B

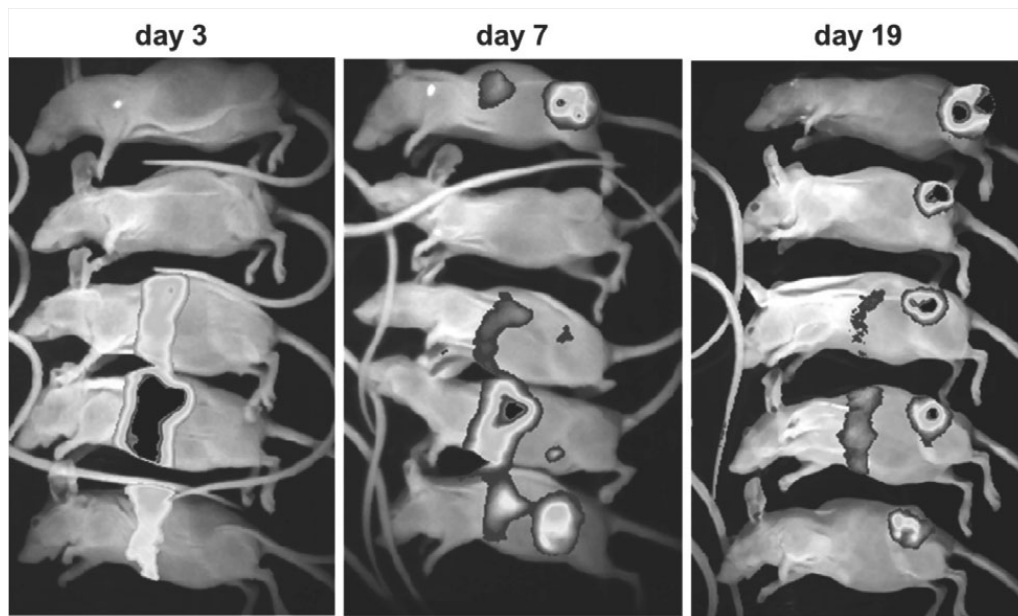


FIG. 38

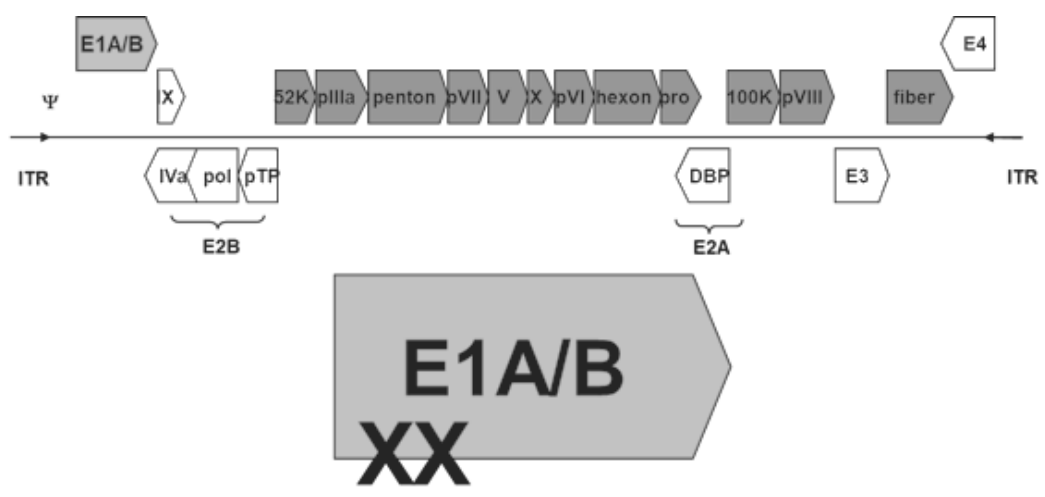


FIG. 39

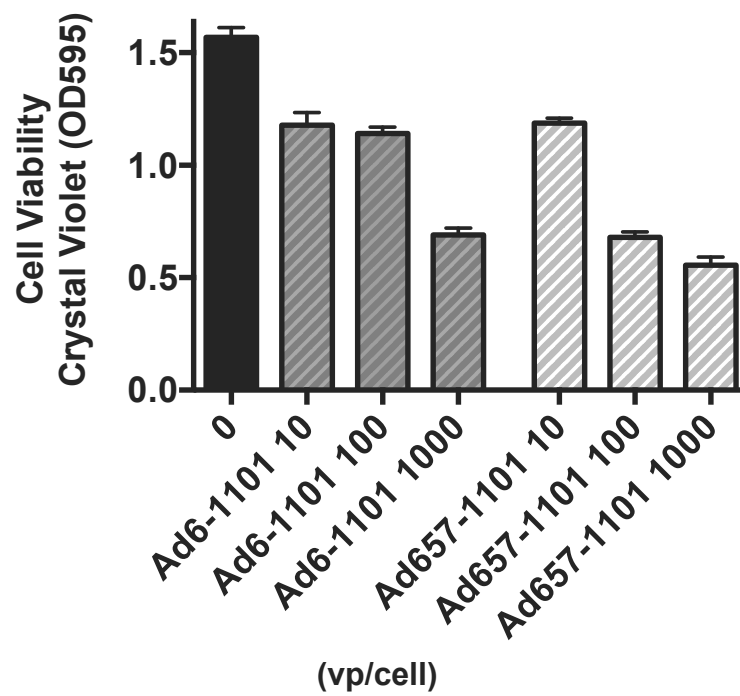


FIG. 40

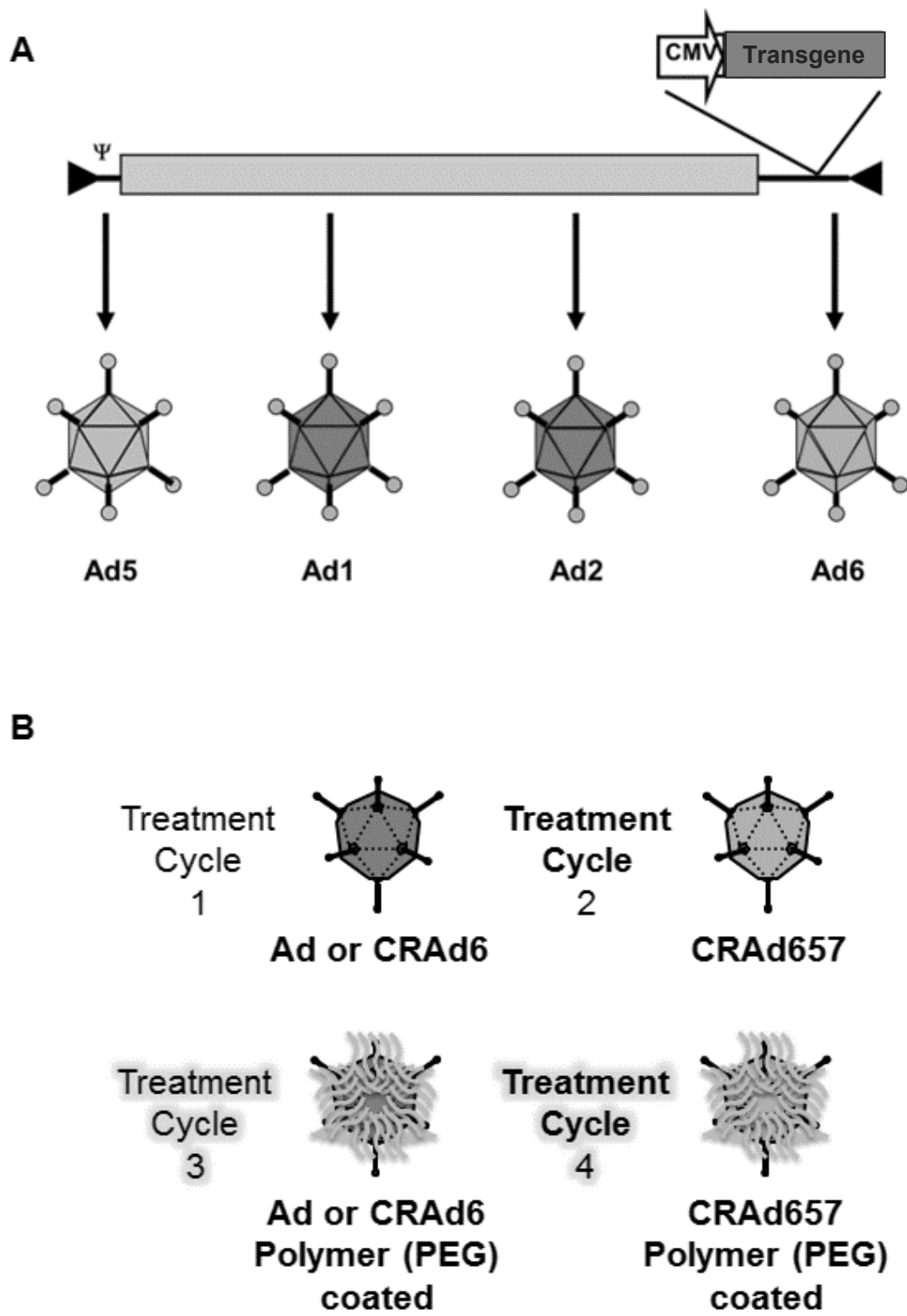


FIG. 41

Prostate Tumor Targeting After Serotype Switching

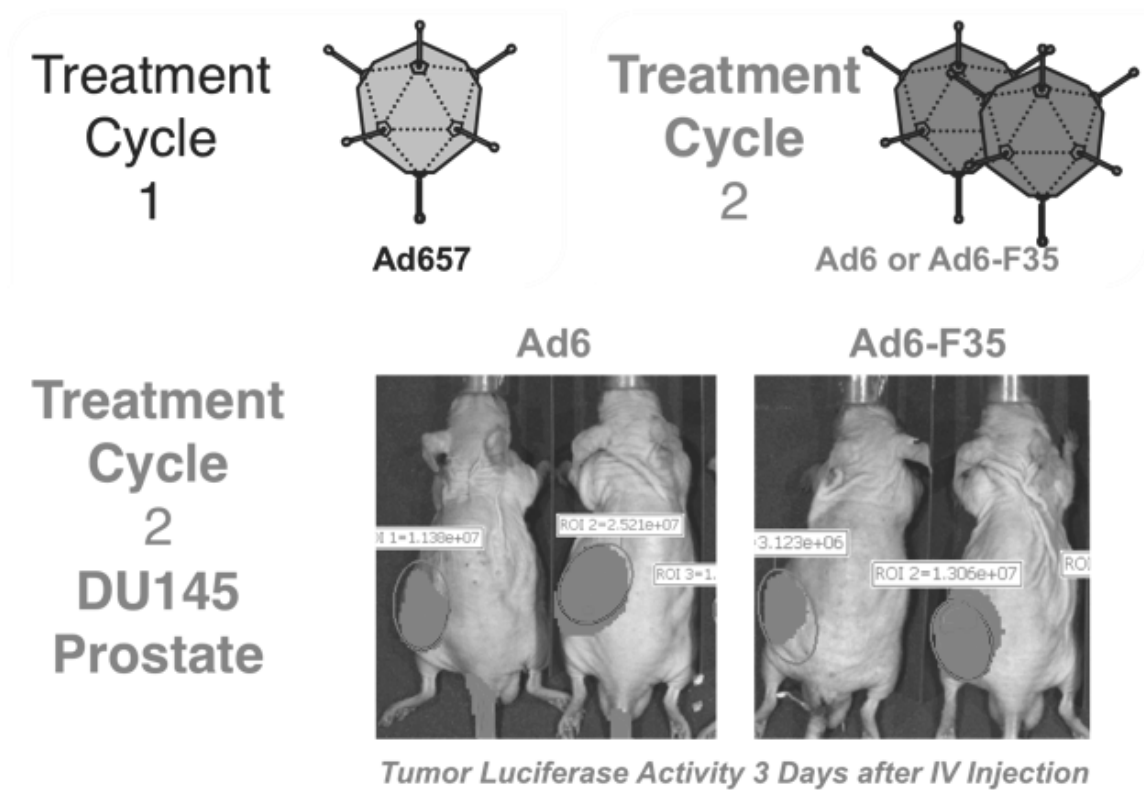


Figure 42

RC-Ad

E1 expression controlled by native E1 promoter

CRAAd-Probasin-E1A (Ad-PB)

*E1 expression
controlled by prostate-specific probasin promoter*

CRAAd-d/1101

*p300 pathway binding ablated, susceptible to IFN pathway
in normal cells*

CRAAd-d/1107

*pRB binding ablated allows virus to kill cancer cells with RB
pathway disruptions, but repressed in RB+ normal cells.*

CRAAd-d/1101/07

*p300 pathway binding ablated, susceptible to IFN pathway
pRB binding ablated allows virus to kill cancer cells with
RB pathway disruptions, but repressed in RB+
normal cells.*

Figure 43

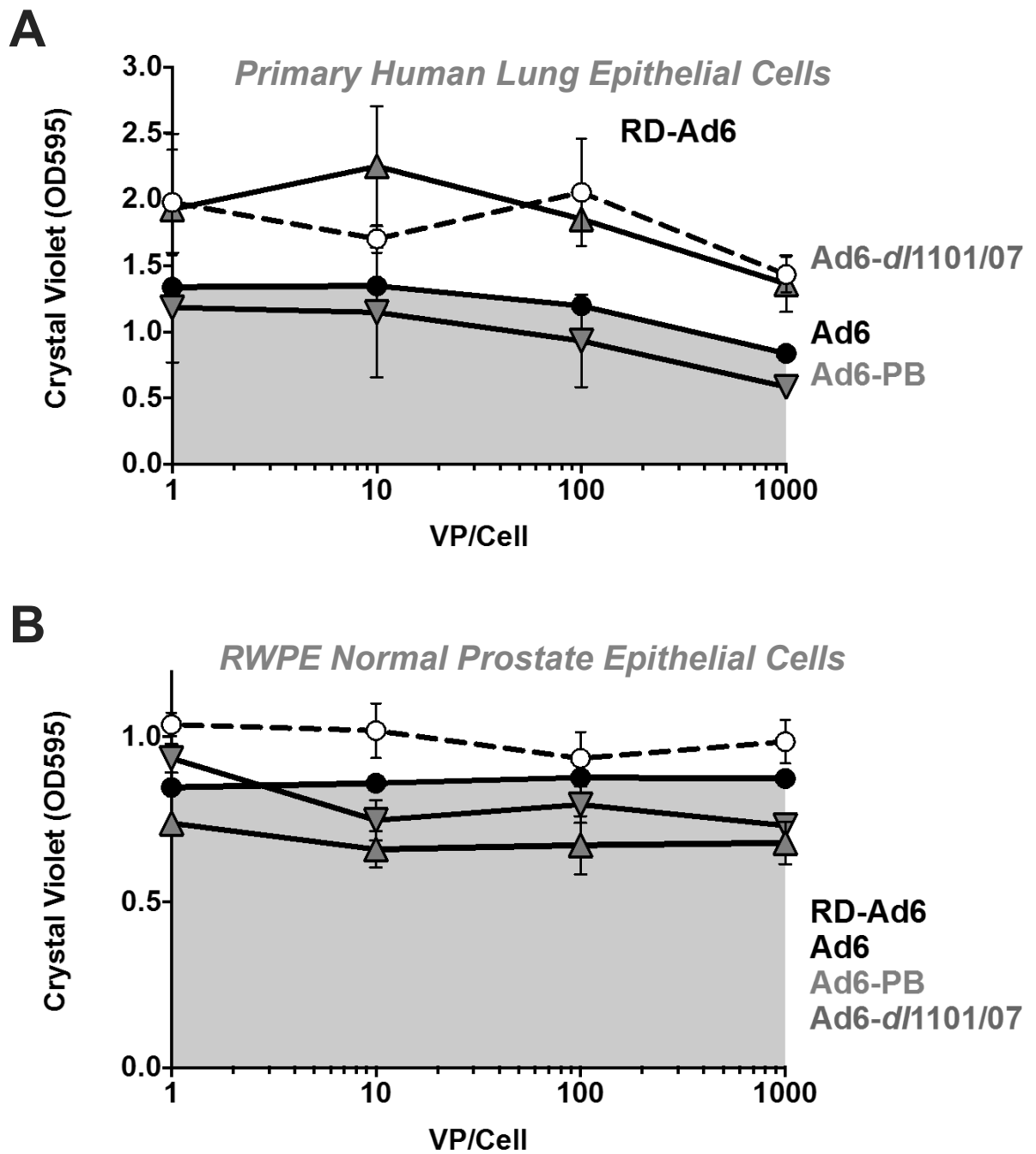


Figure 44

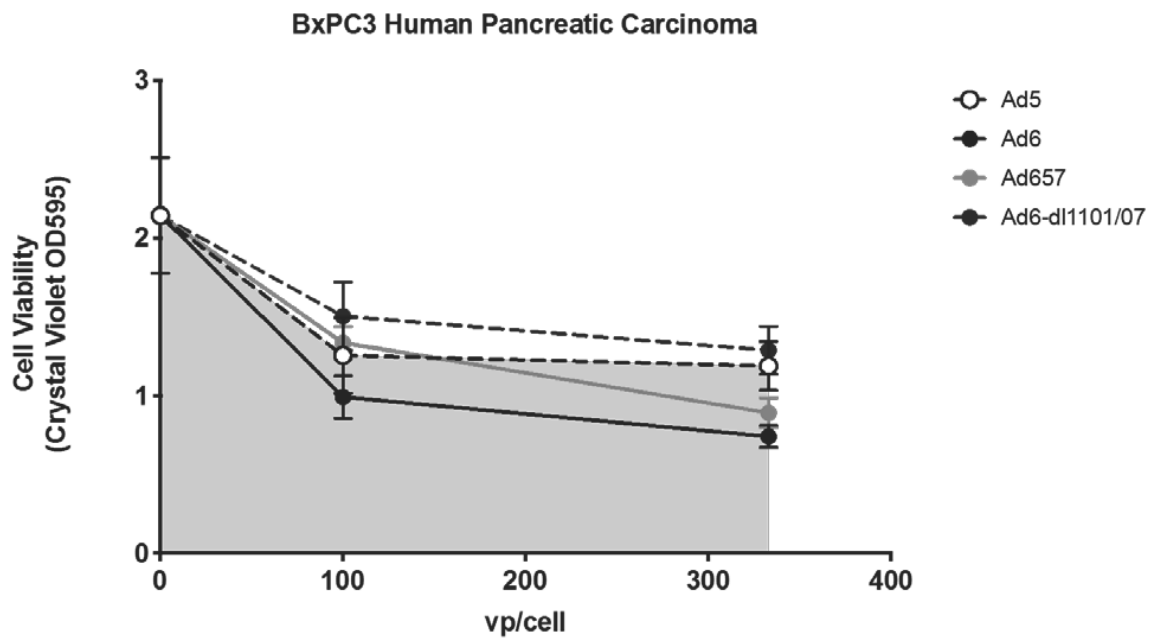
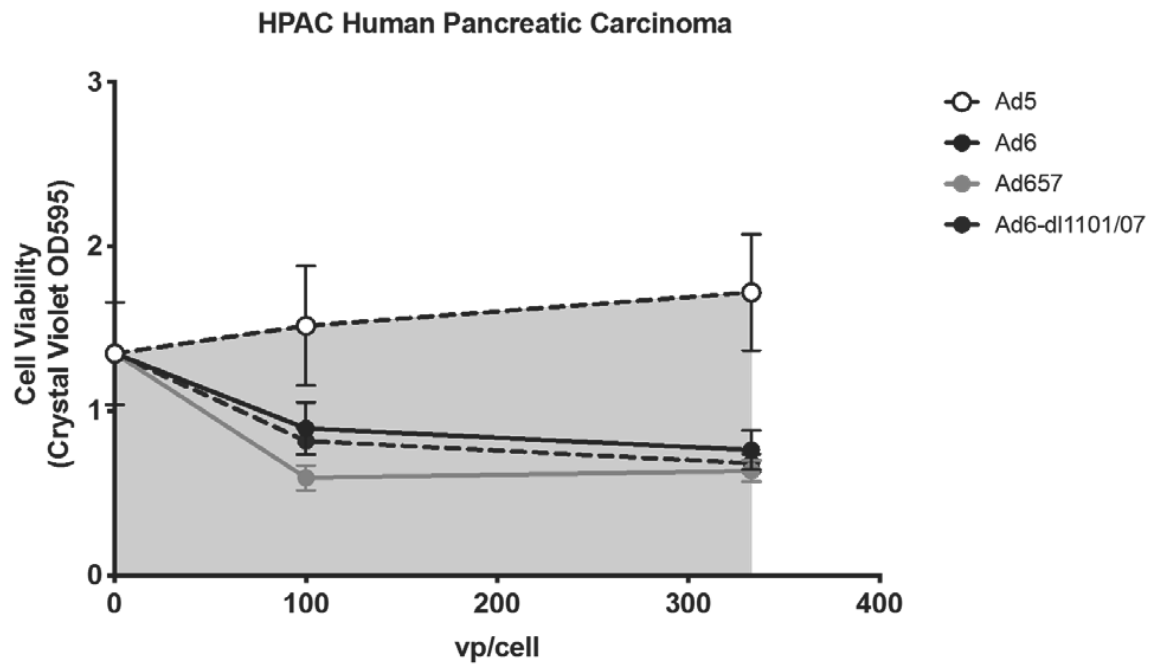


FIGURE 45

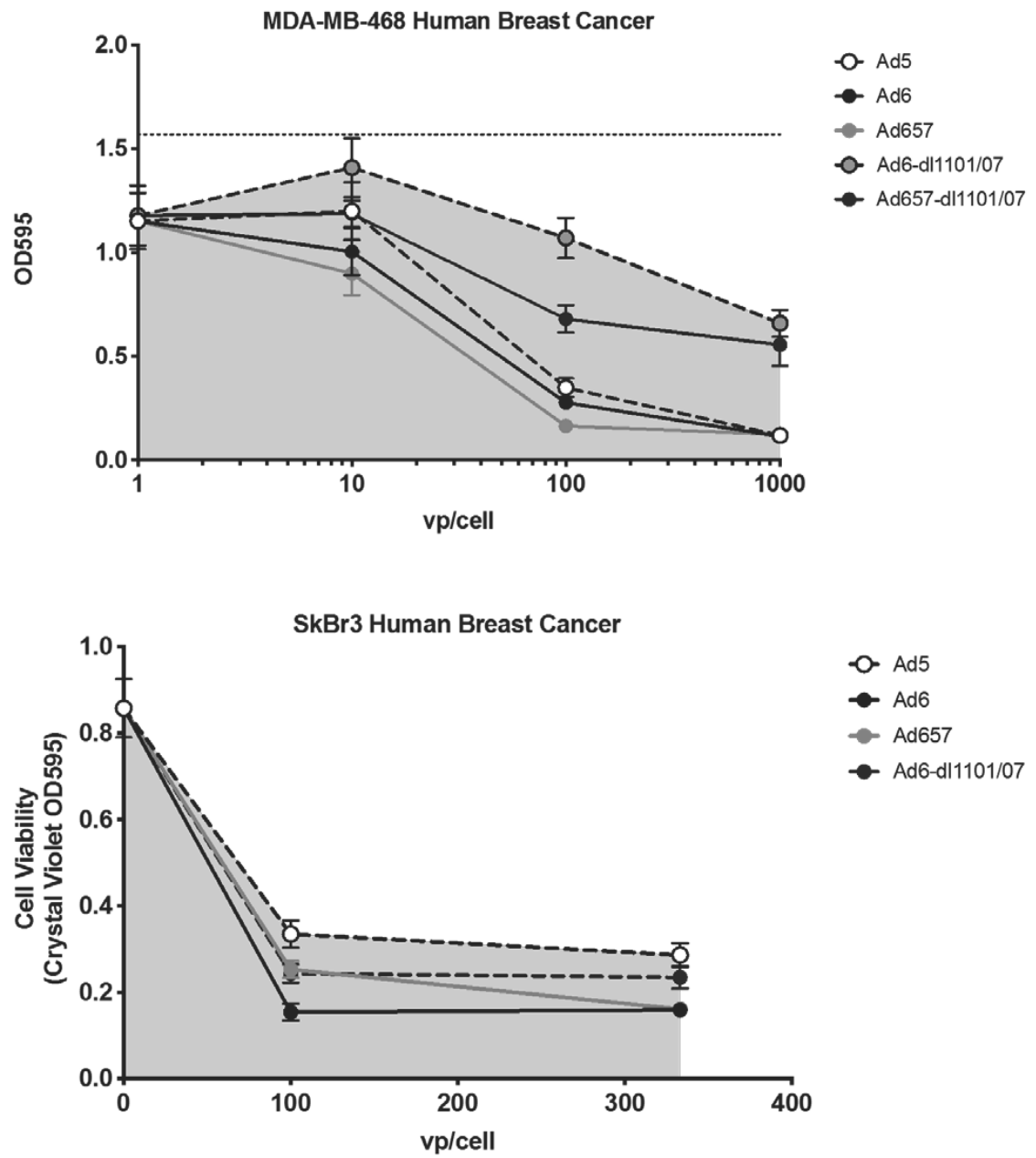


Figure 46

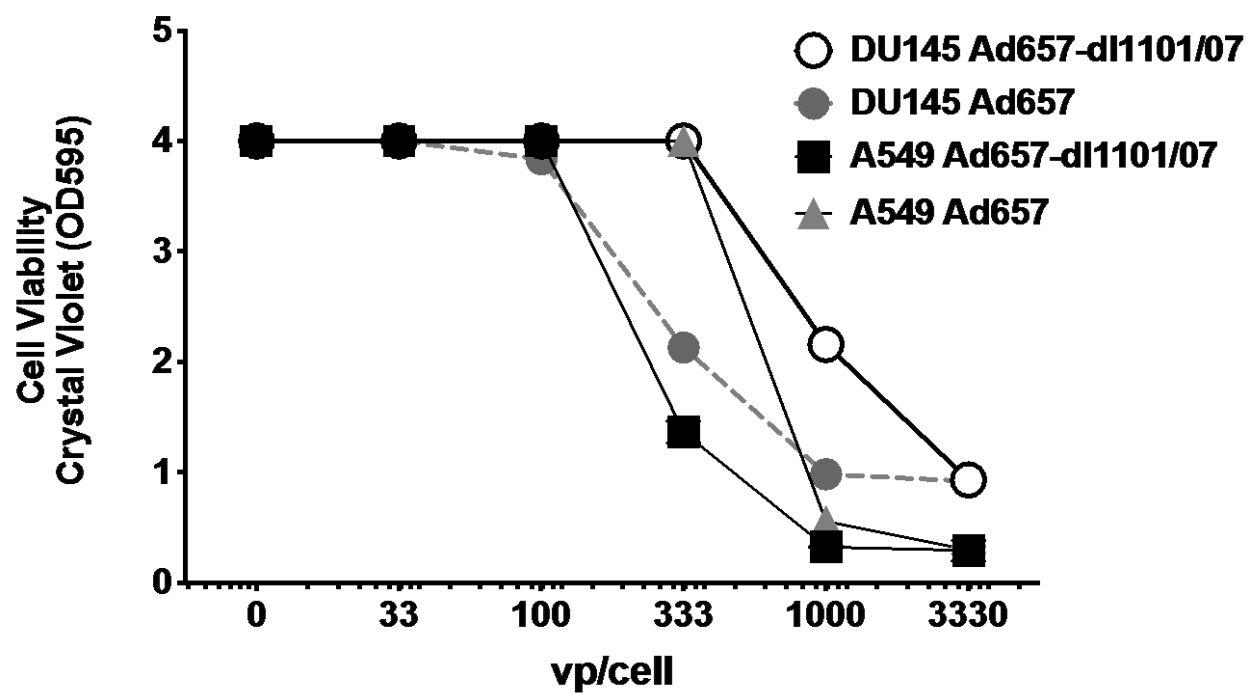


Figure 47

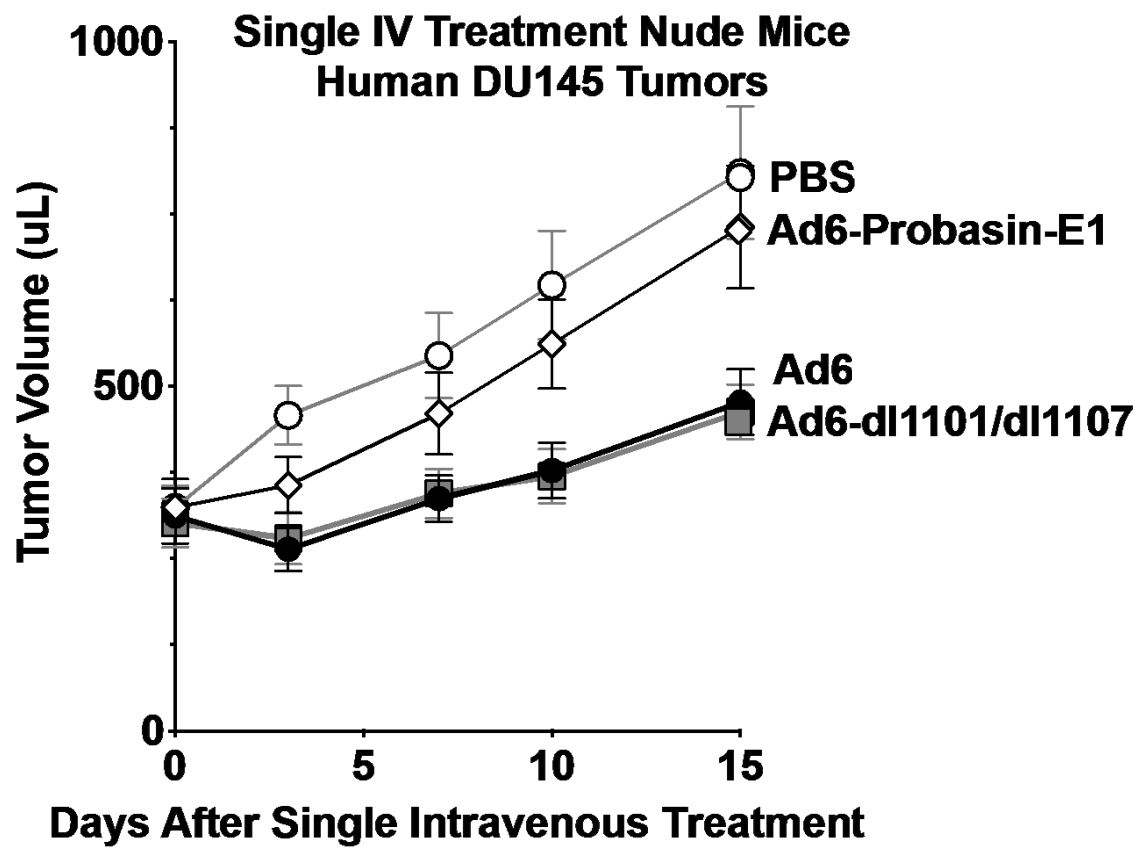


Figure 48

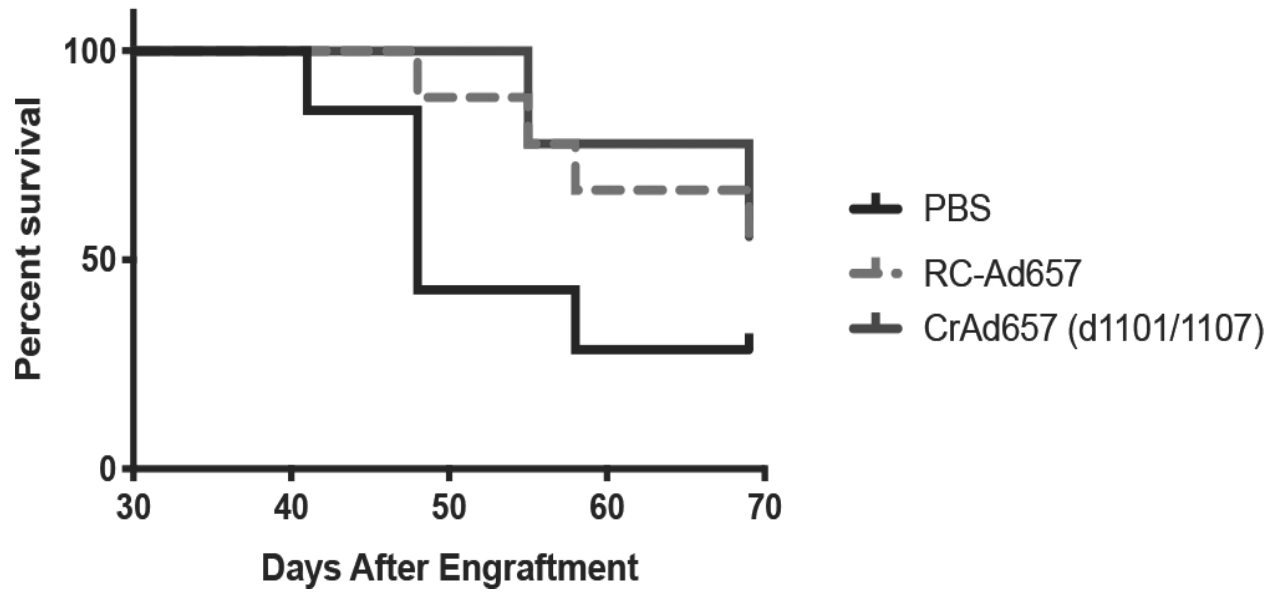
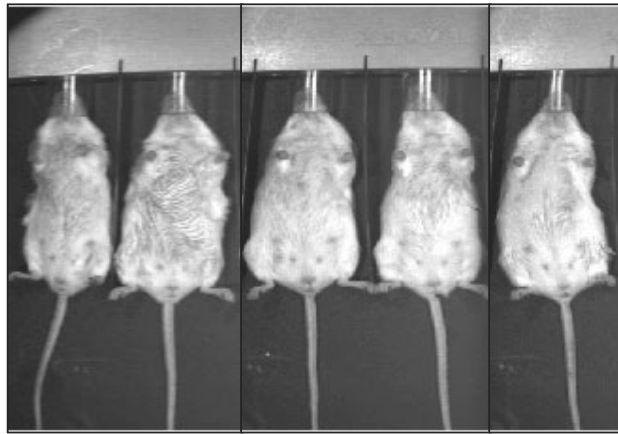
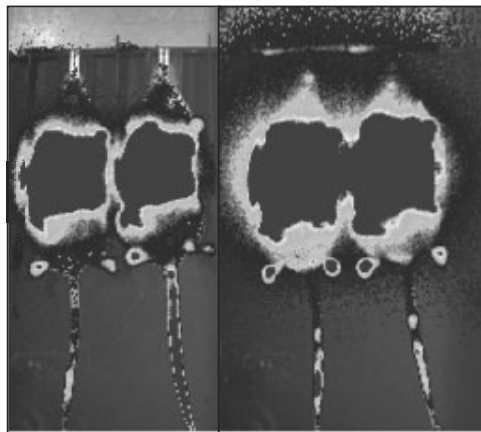
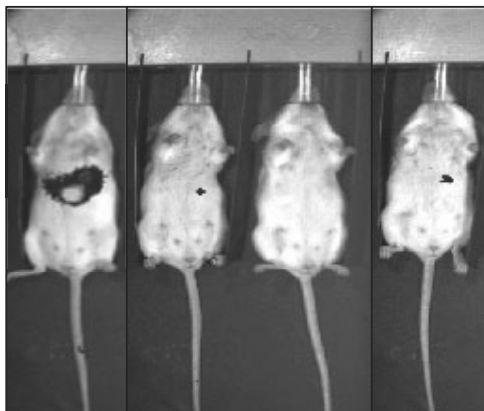
DU145 Ad Single IV Treatment Survival**Figure 49**

Figure 50**PBS****Ad-GL****Ad-GL-
PEG2000-Biotin**

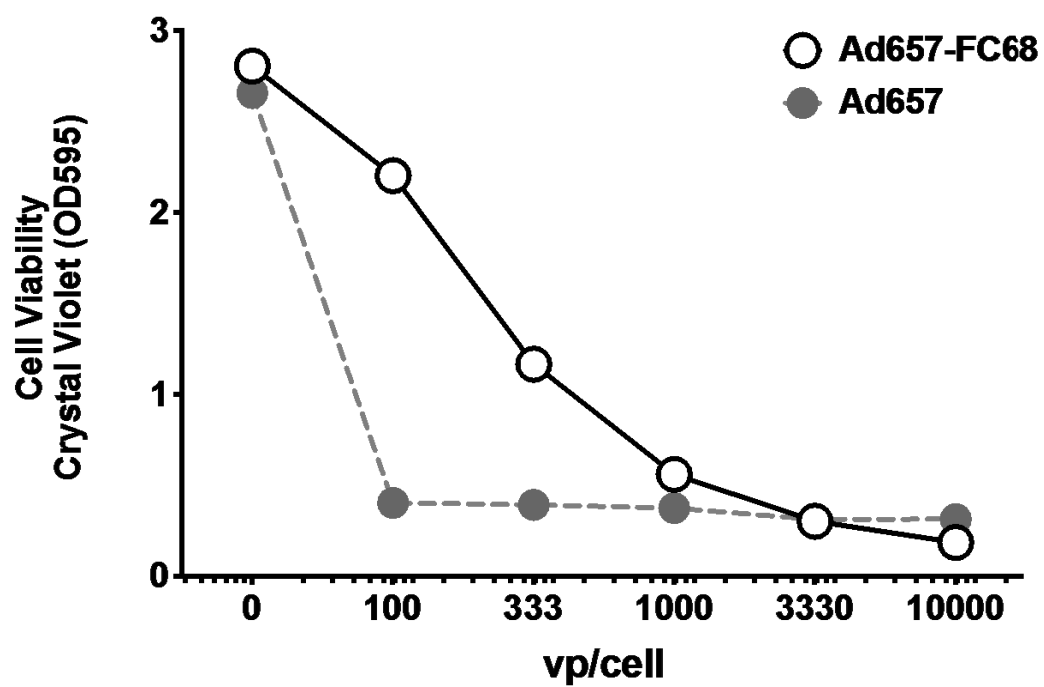


Figure 51

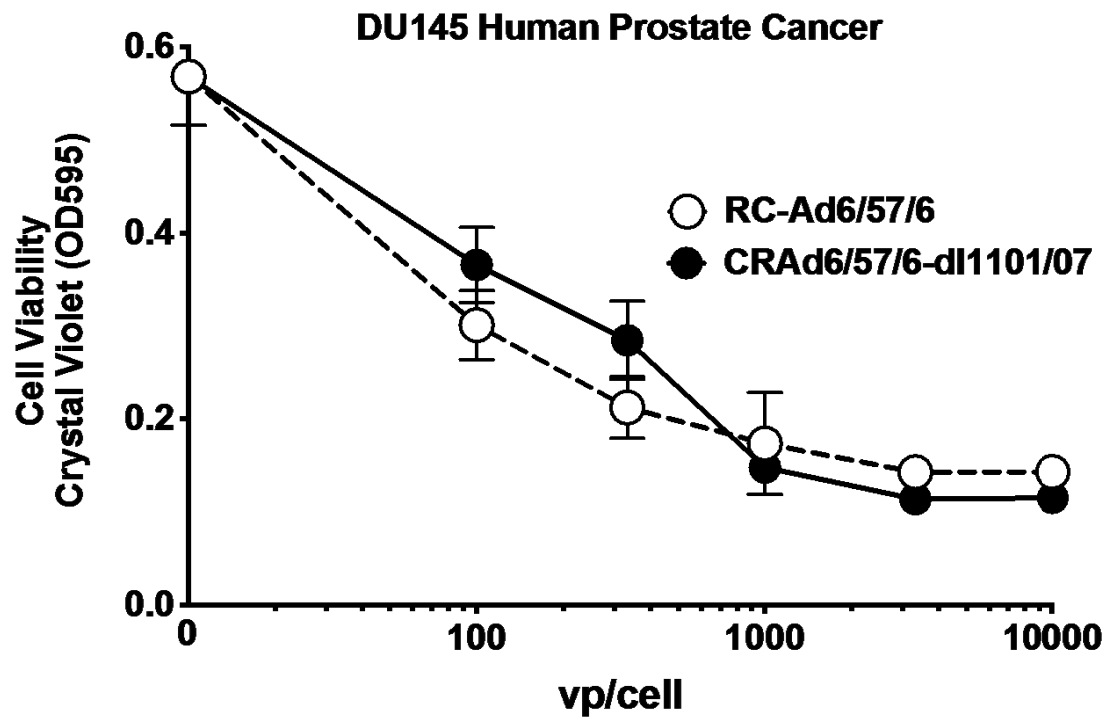


Figure 52

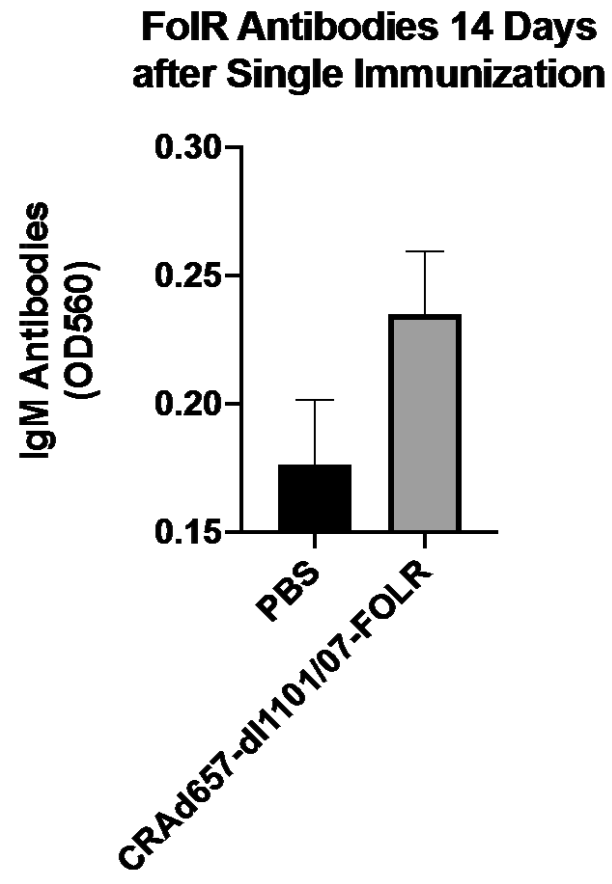


Figure 53

Figure 54

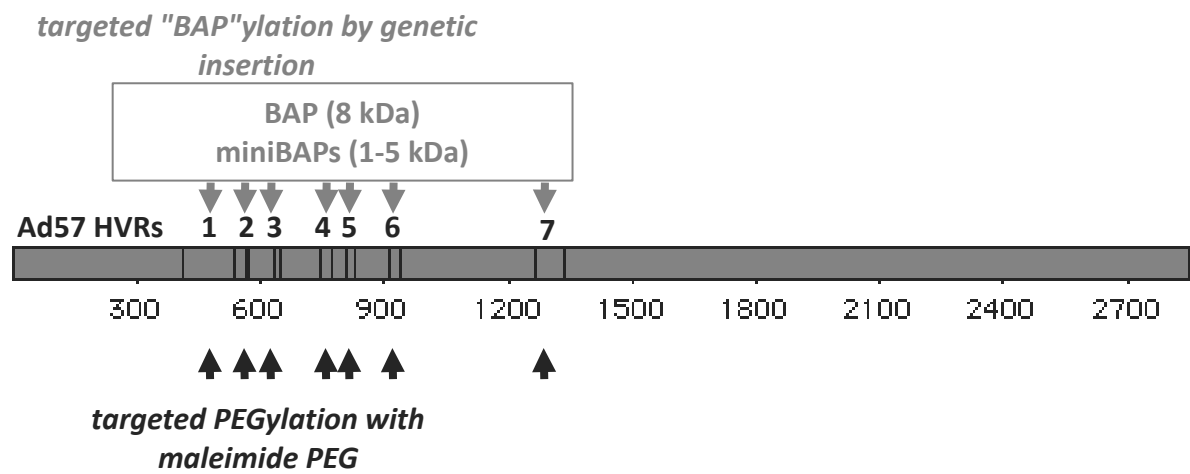
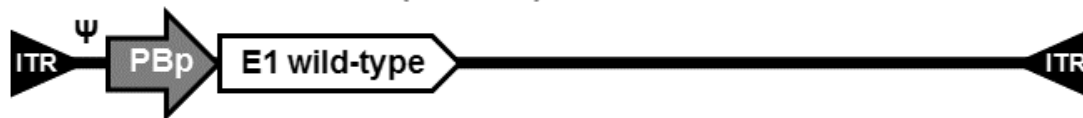


Figure 55

RC-Ad

E1 expression controlled by native E1 promoter

CRAd-Probasin-E1A (Ad-PB)

*E1 expression
controlled by prostate-specific probasin promoter*

CRAd-d/1101

*p300 pathway binding ablated, susceptible to IFN pathway
in normal cells*

CRAd-d/1107

*pRB binding ablated allows virus to kill cancer cells with RB
pathway disruptions, but repressed in RB+ normal cells.*

CRAd-d/1101/07

*p300 pathway binding ablated, susceptible to IFN pathway
pRB binding ablated allows virus to kill cancer cells with
RB pathway disruptions, but repressed in RB+
normal cells.*

wild-type E1A N-terminus

MRHIICHGGVITEEMAASLLDQLIEEV LADNLPPPSHFEPPTLHEL YDLDVT
APEDPNEEAVSQIFPESV MLAVQEGIDLFTFPPAPGSPEPPHLSRQPEQP
EQRALGPVSMPNLVPEVIDLTCHEAGFPPS (SEQ ID NO:42)

E1A dl1101 N-terminus

MRHIEEV LADNLPPPSHFEPPTLHEL YDLDVTAPEDPNEEAVSQIFPESV
MLAVQEGIDLFTFPPAPGSPEPPHLSRQPEQP EQRALGPVSMPNLVPEVI
DLTCHEAGFPPS (SEQ ID NO:43)

E1A dl1107 N-terminus

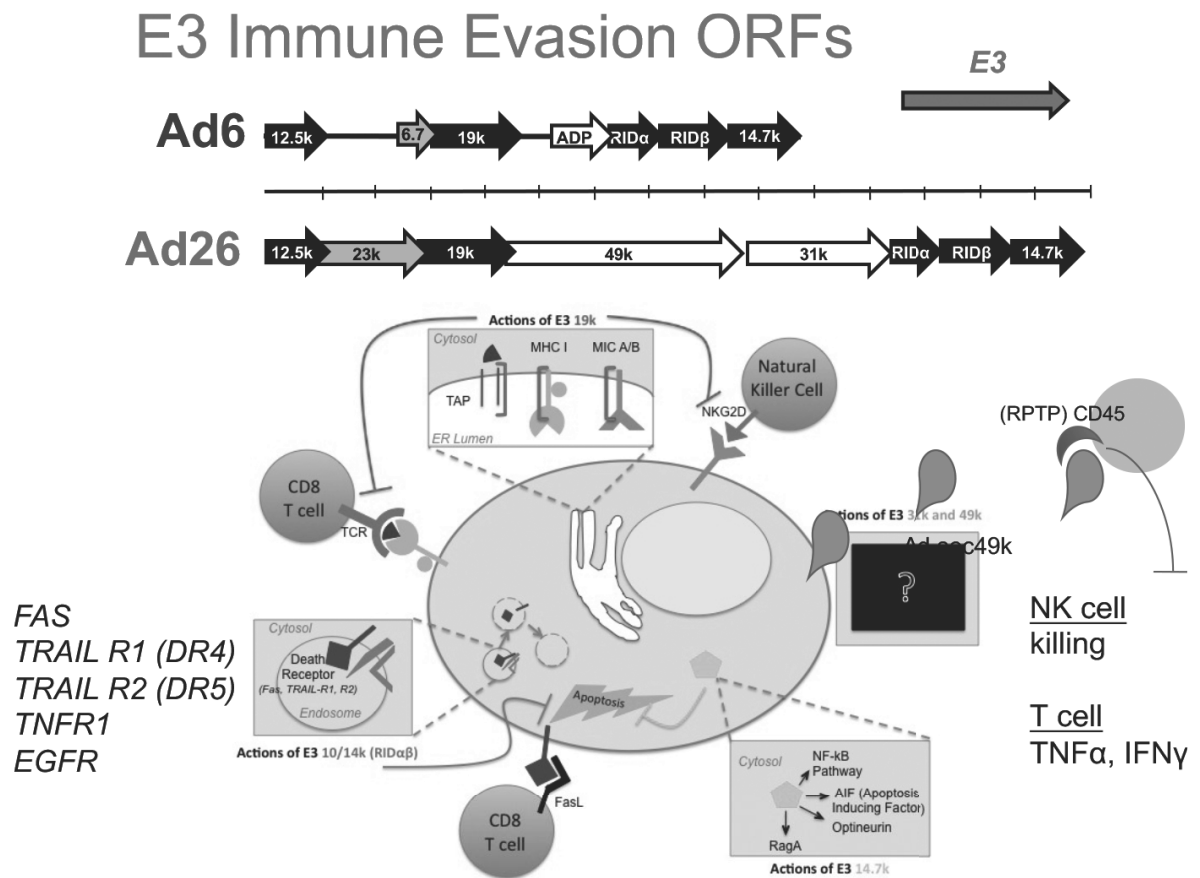
MRHIICHGGVITEEMAASLLDQLIEEV LADNLPPPSHFEPPTLHEL YDLDVT
APEDPNEEAVSQIFPESV MLAVQEGIDLFTFPPAPGSPEPPHLSRQPEQP
EQRALGPVCHEAGFPPS (SEQ ID NO:44)

E1A dl1101/1107 N-terminus

MRHIEEV LADNLPPPSHFEPPTLHEL YDLDVTAPEDPNEEAVSQIFPESV
MLAVQEGIDLFTFPPAPGSPEPPHLSRQPEQP EQRALGPVCHEAGFPPS
(SEQ ID NO:45)

Figure 56

Figure 57



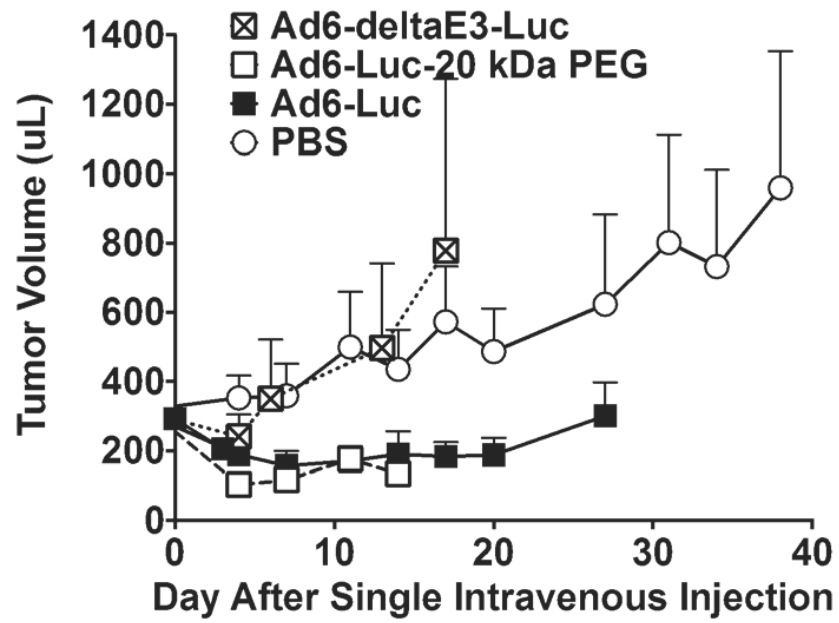
Ad6-Luc Viruses in Immunocompetent Hamsters

Figure 58

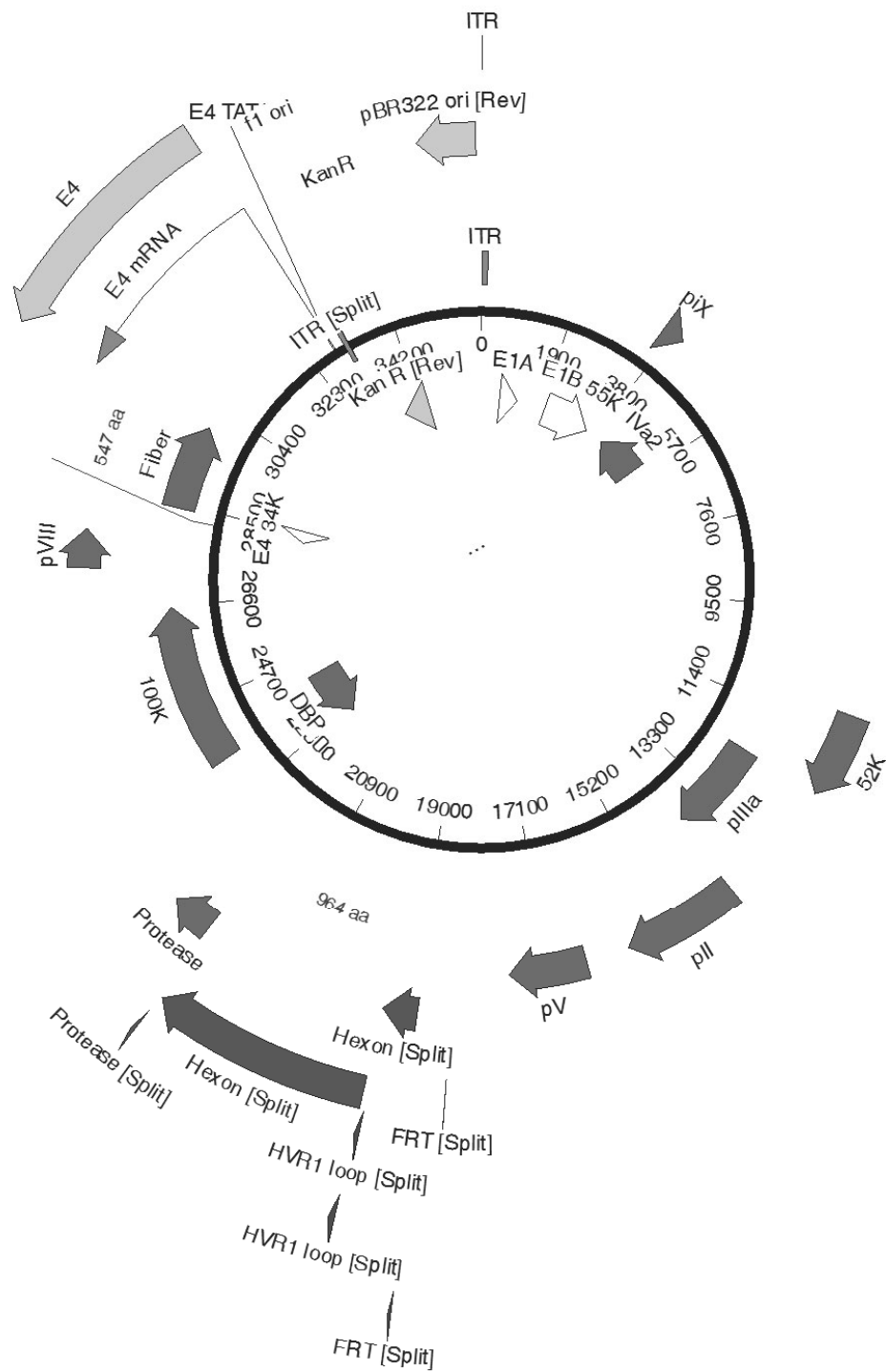


Figure 59

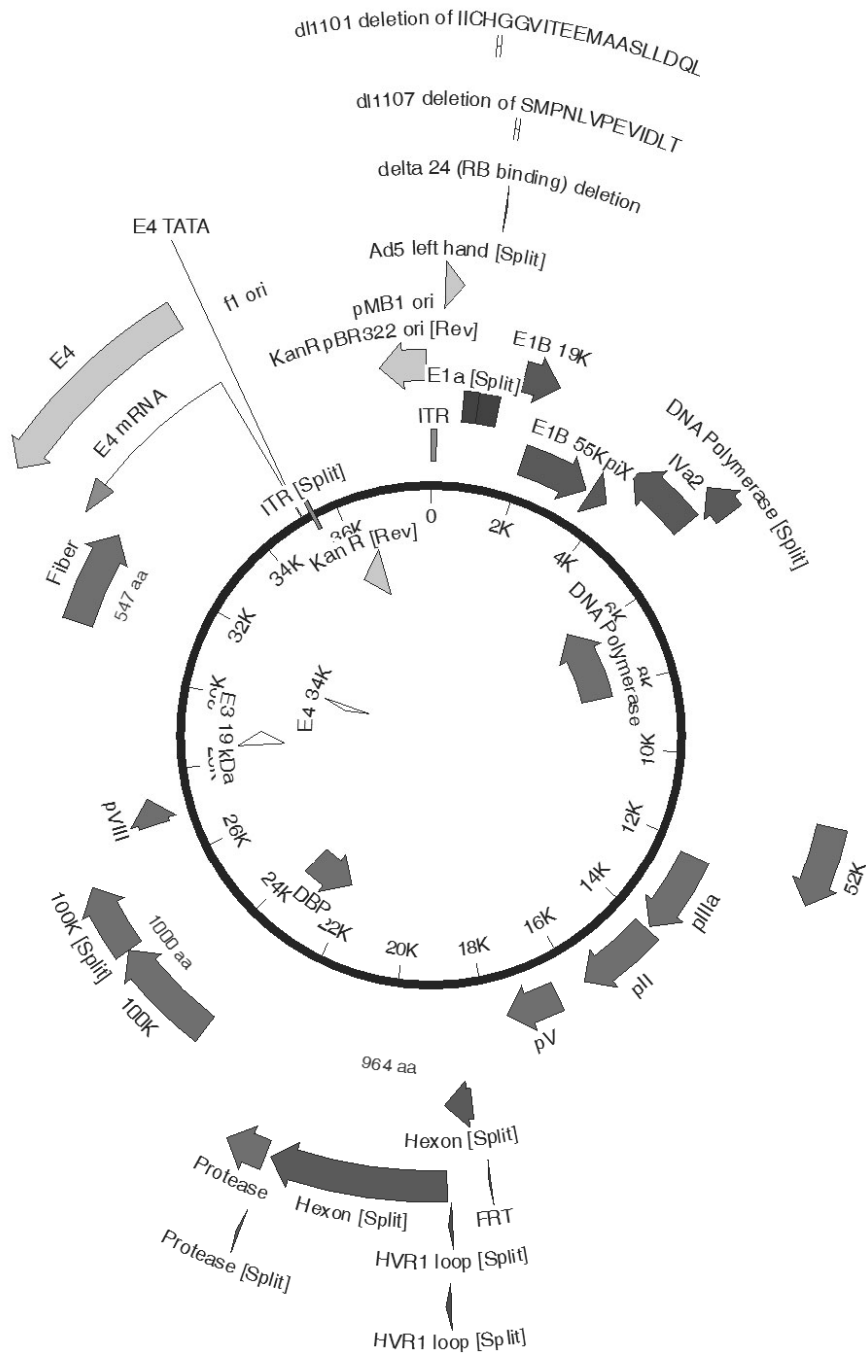


Figure 60

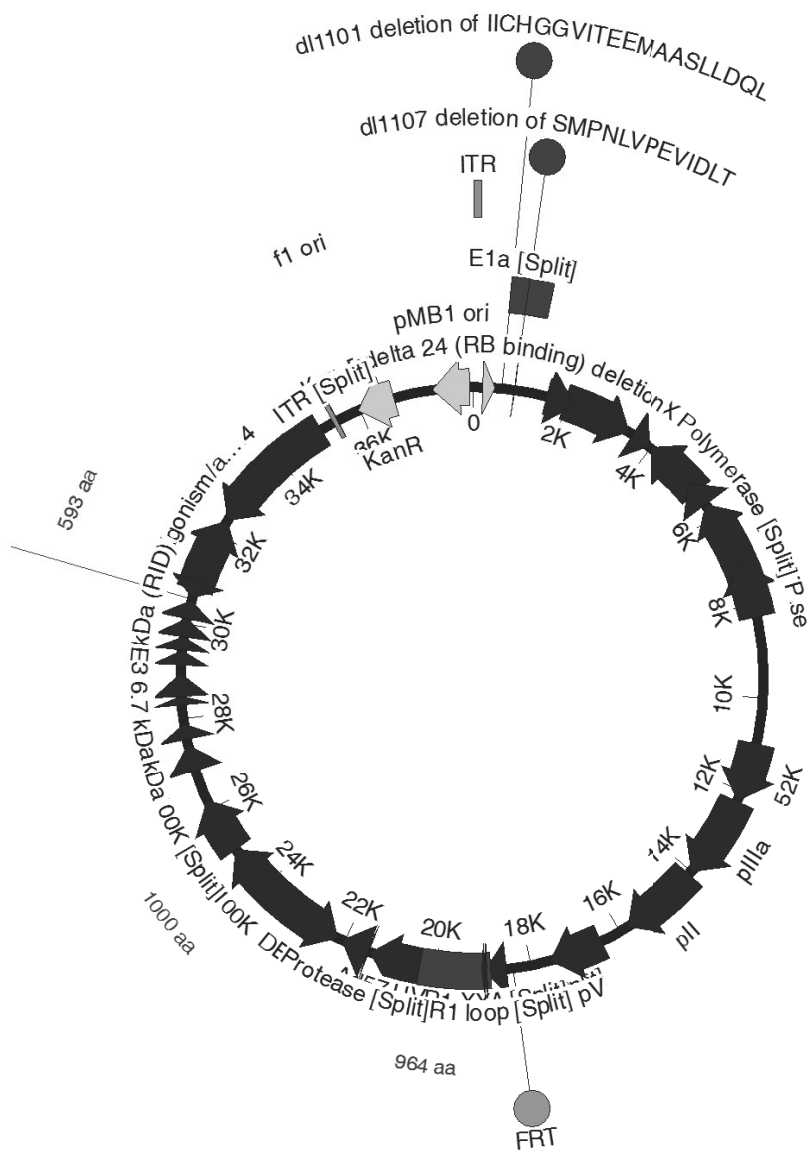


Figure 61

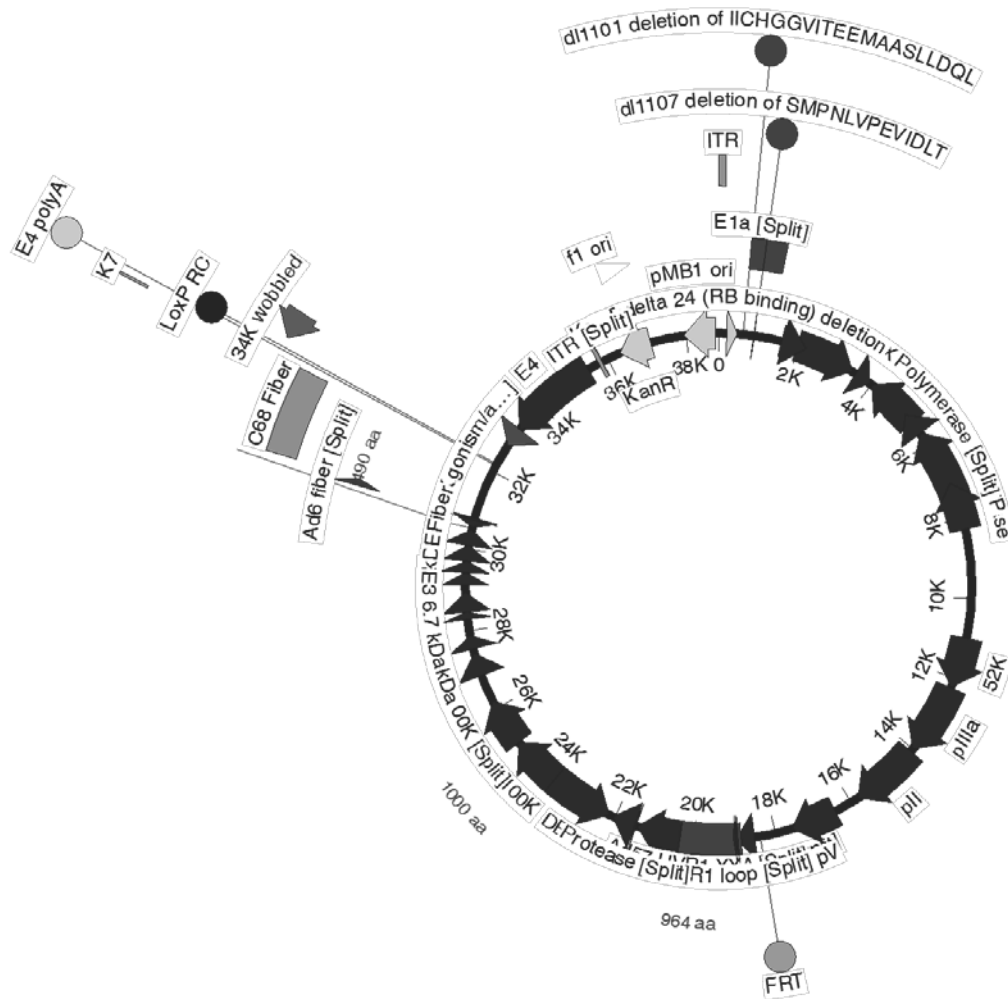


Figure 62

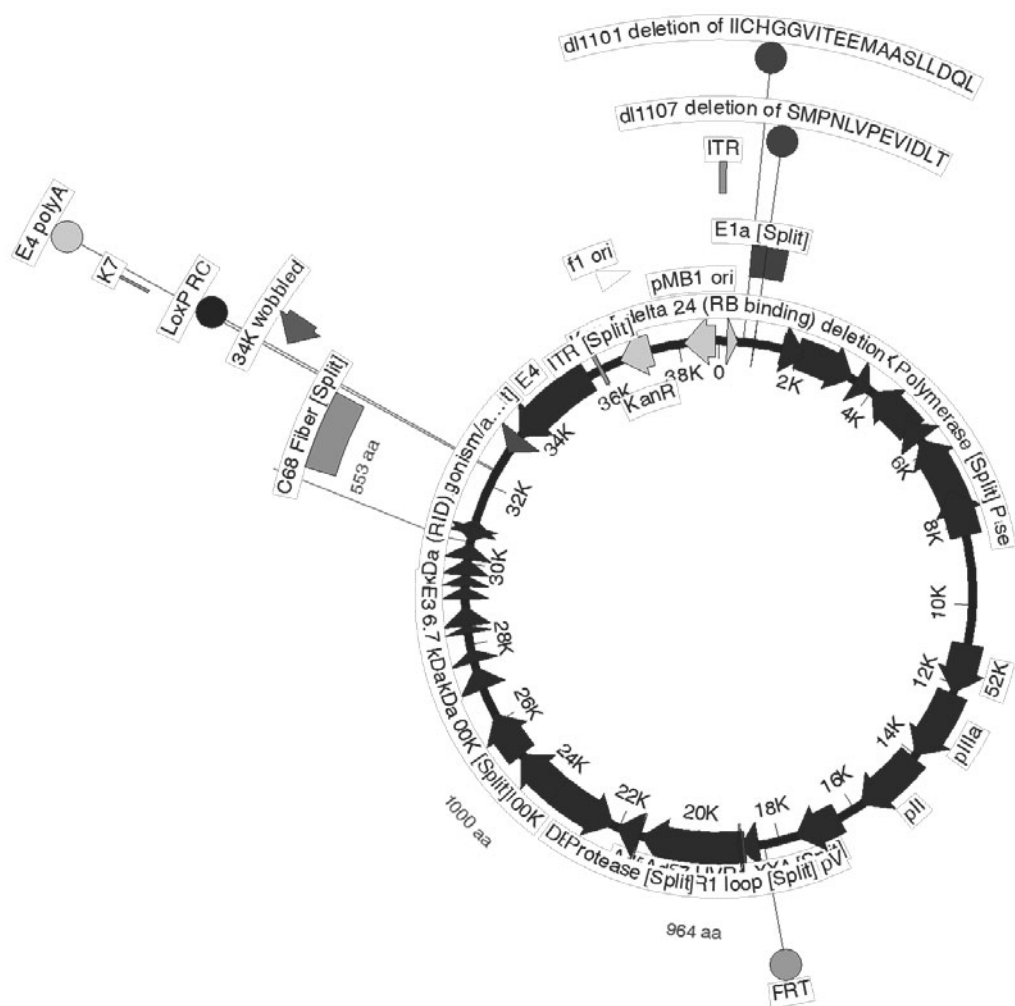


Figure 63

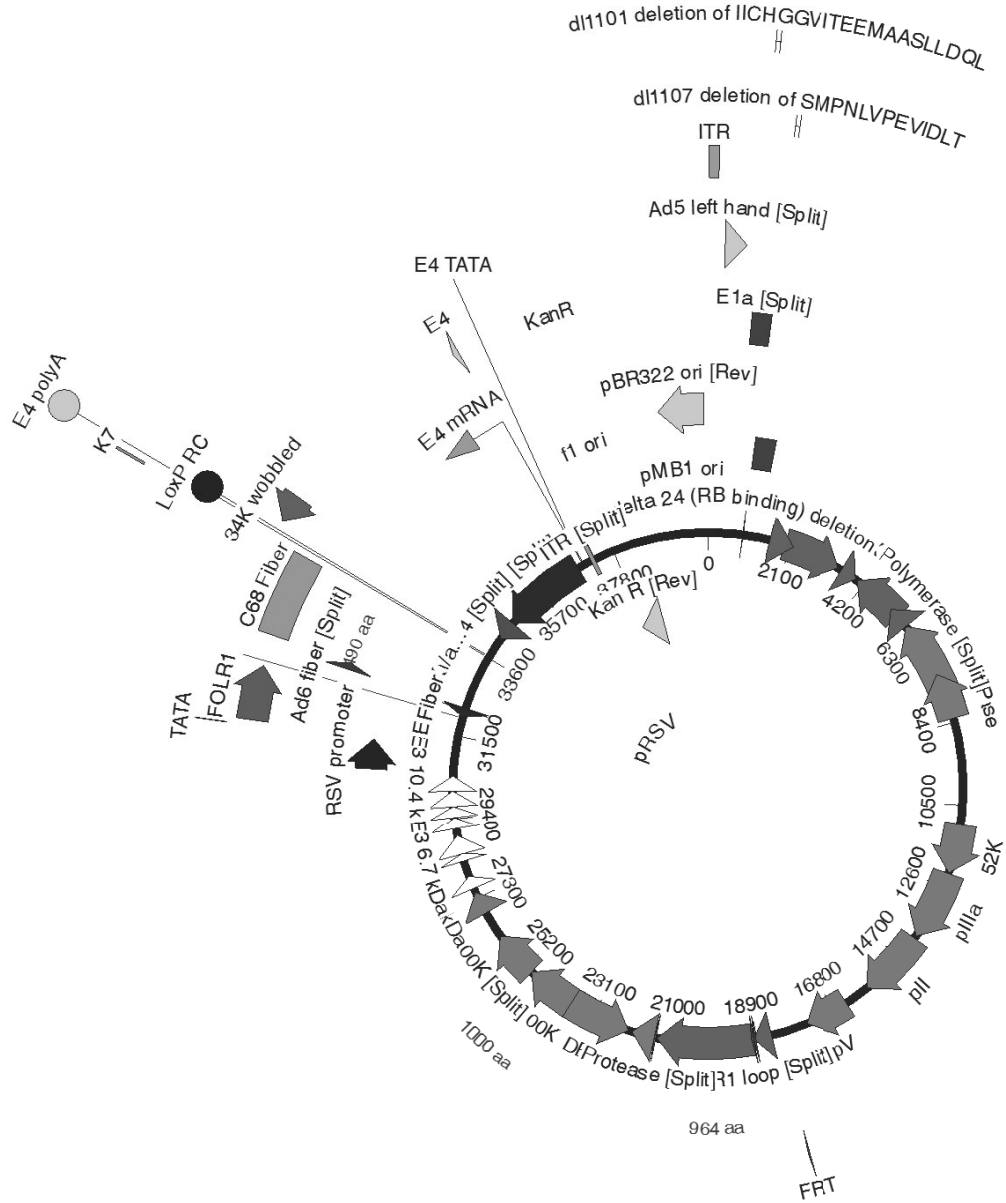


Figure 64

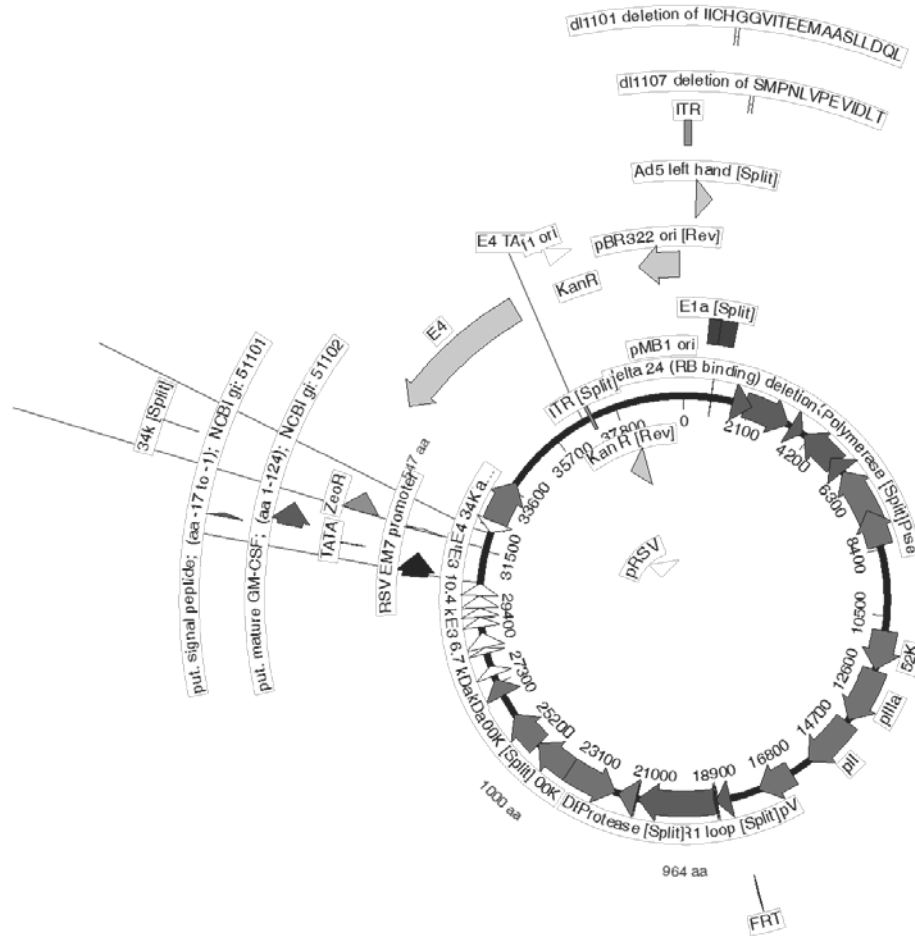


Figure 65

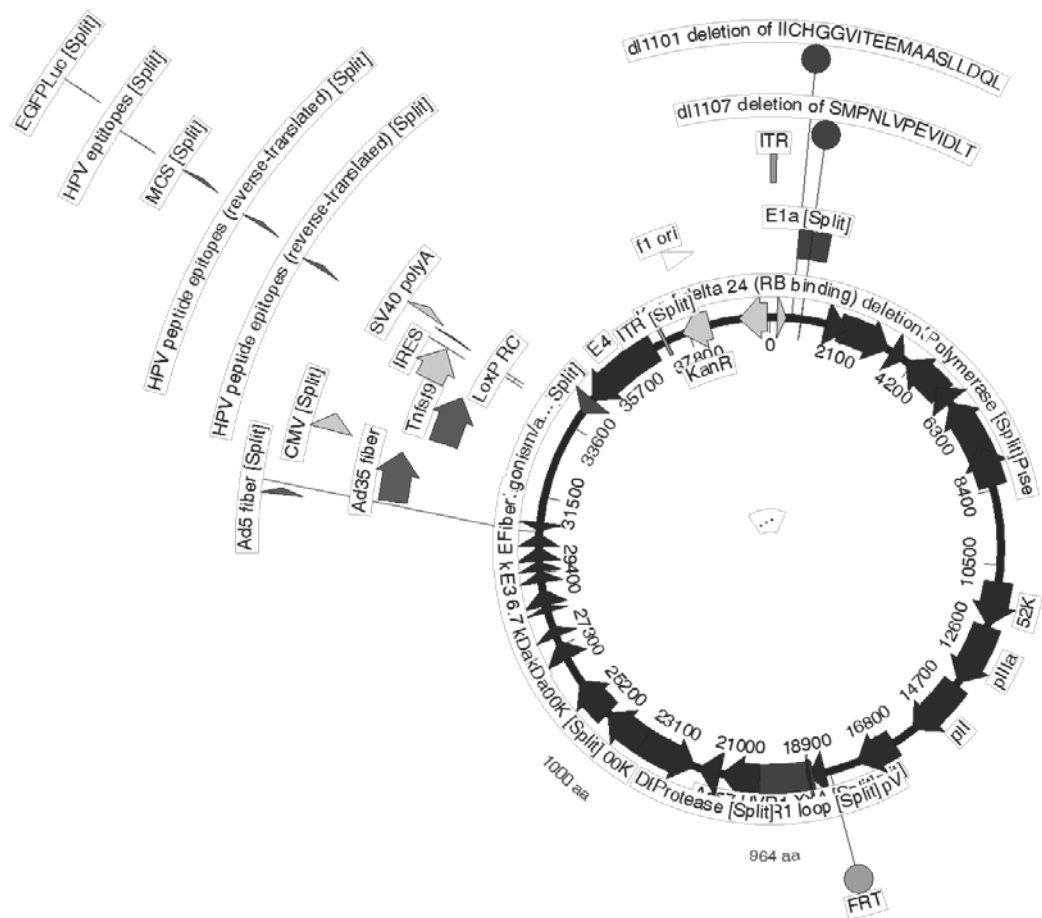


Figure 66

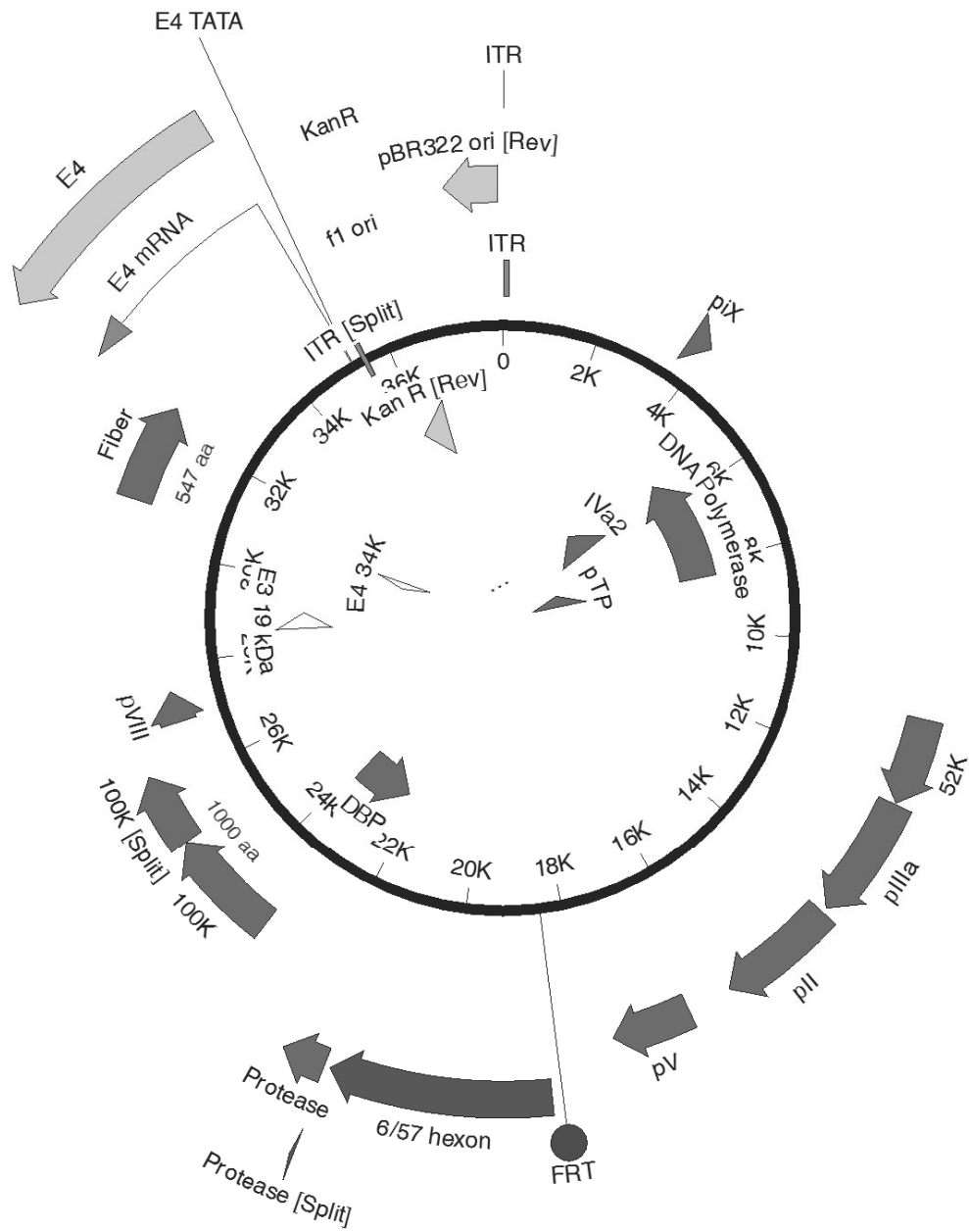


Figure 67

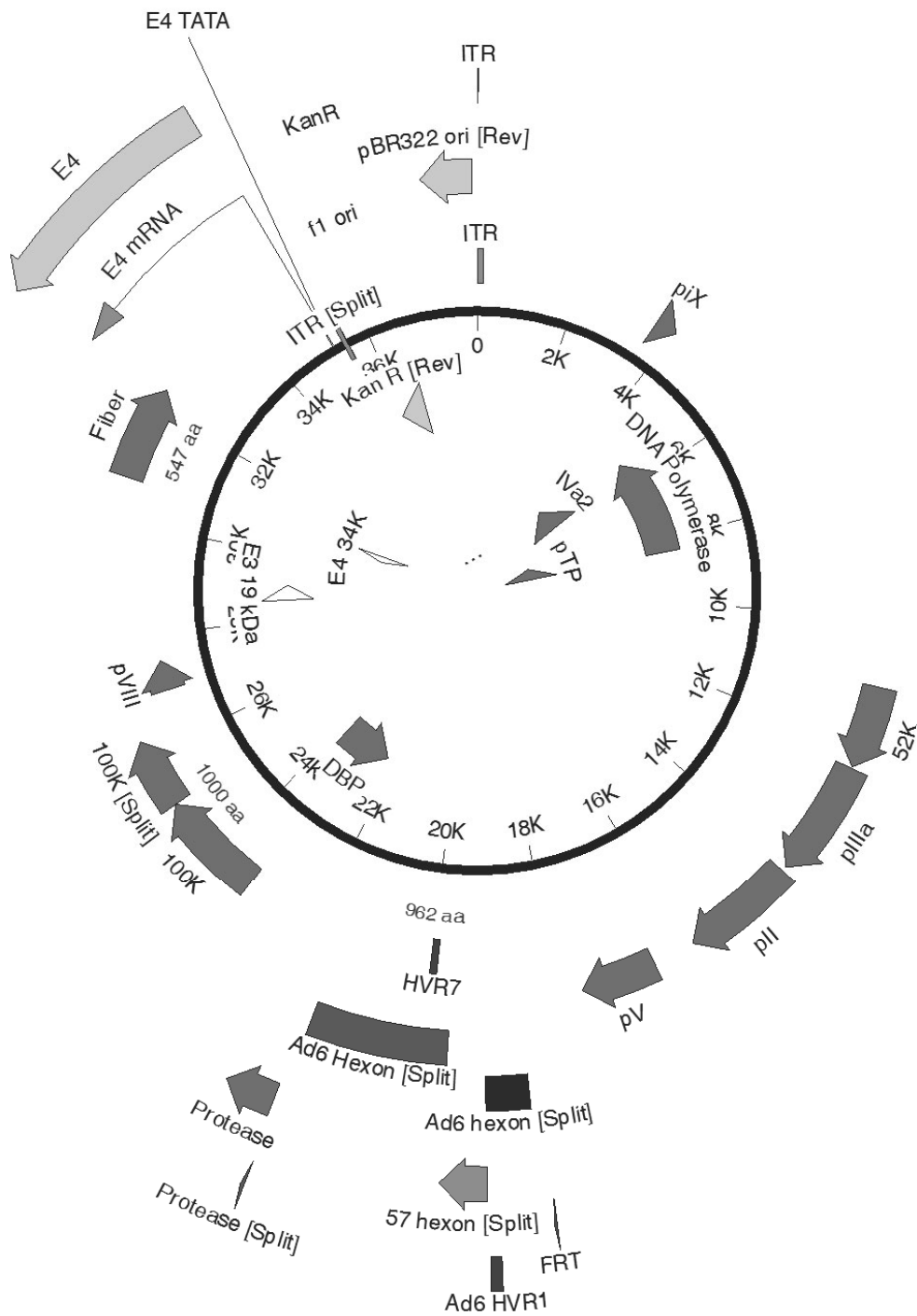


Figure 68

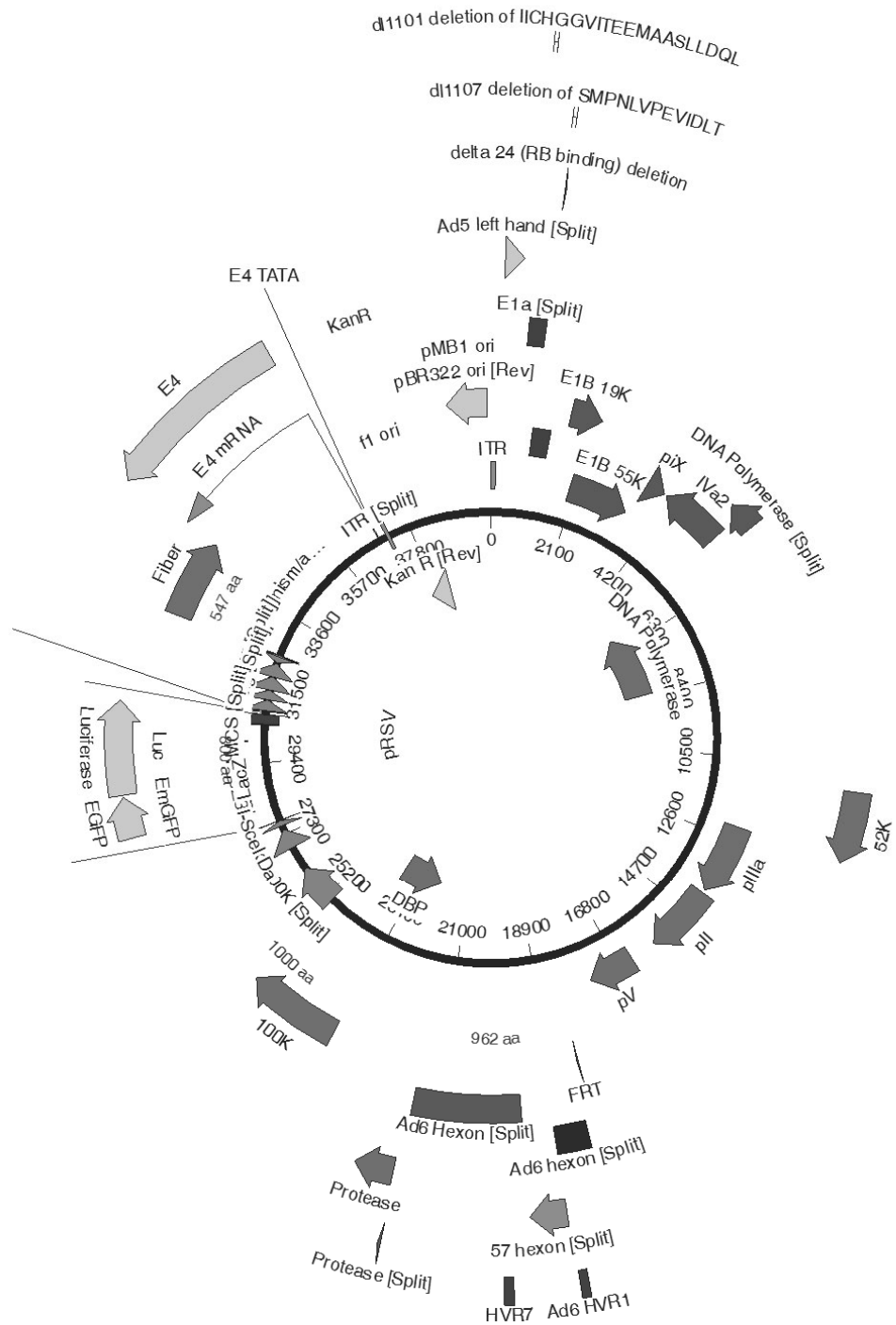
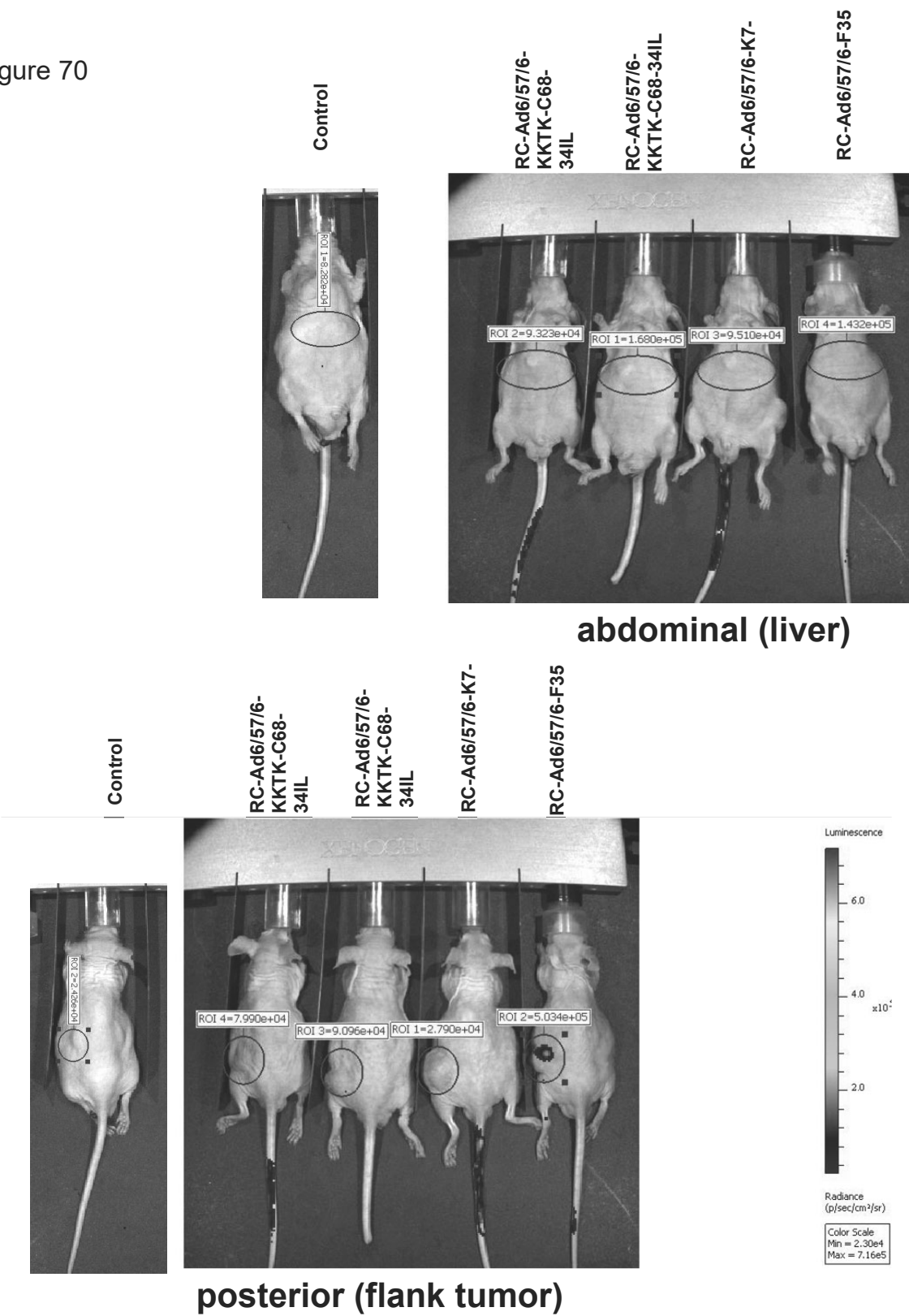


Figure 69

Figure 70



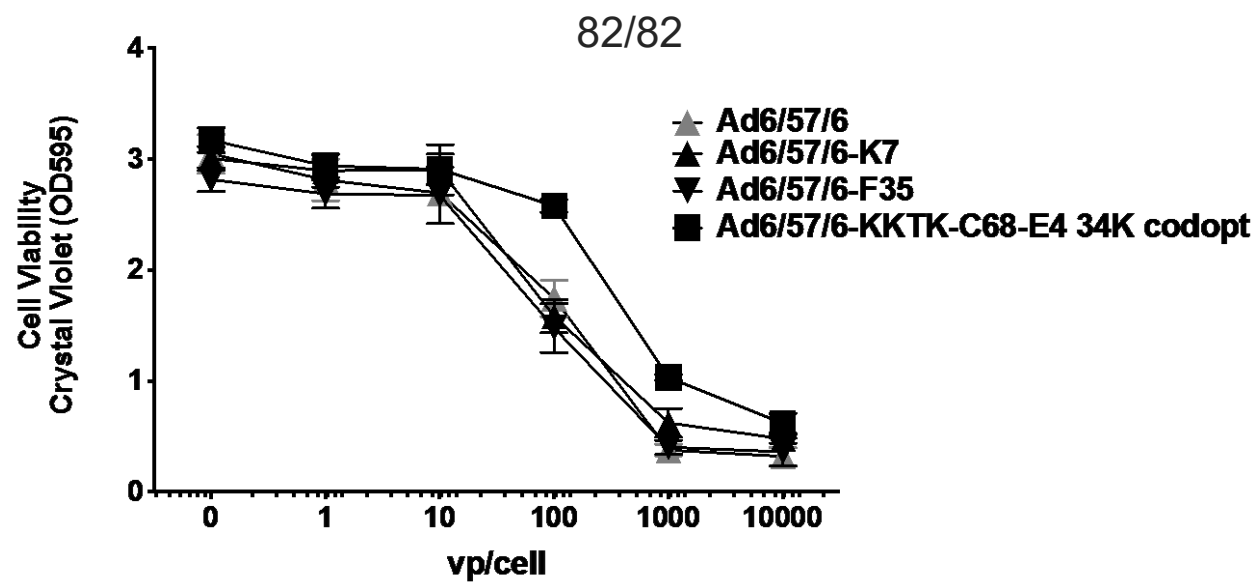


Figure 71