

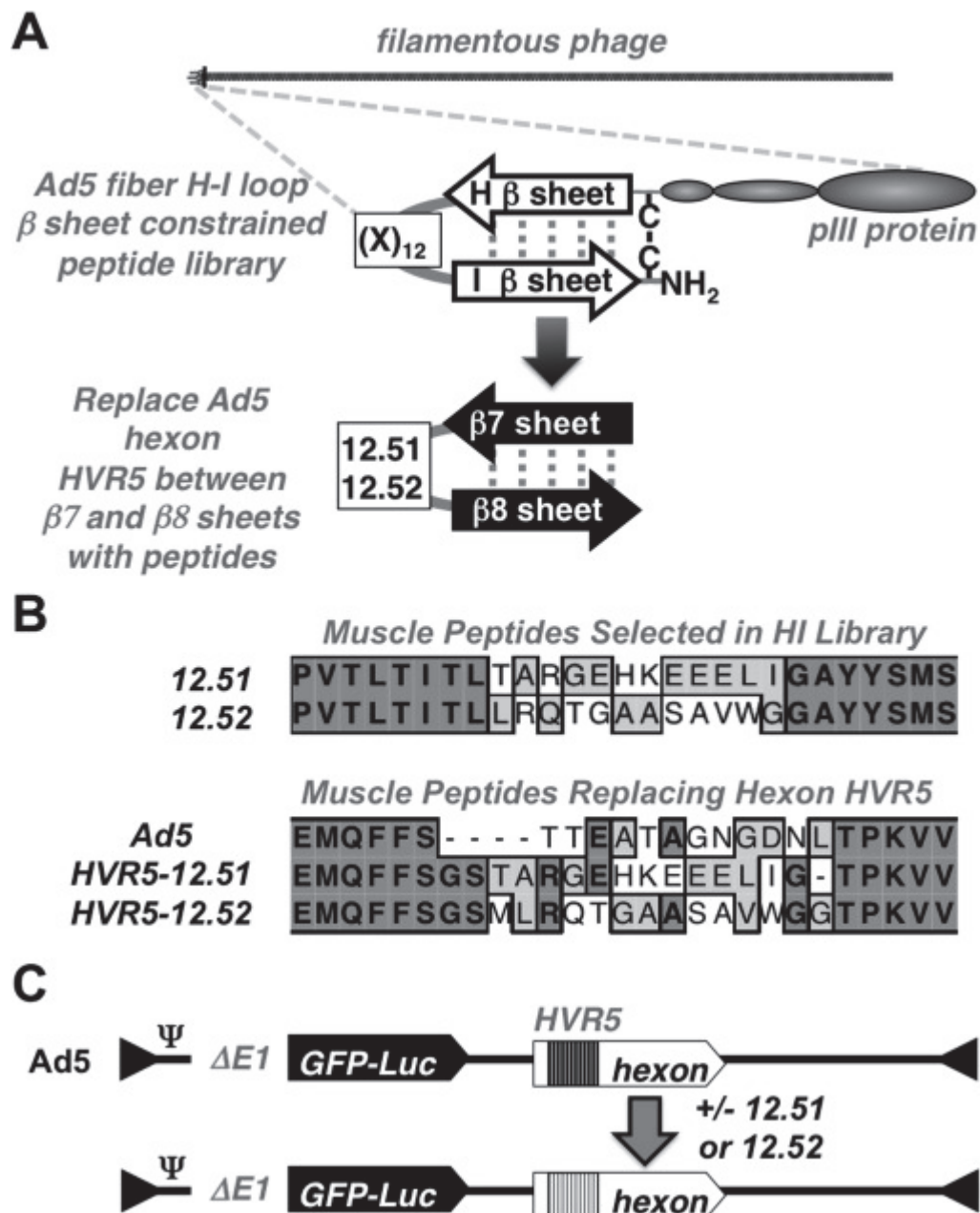


FIG. 1

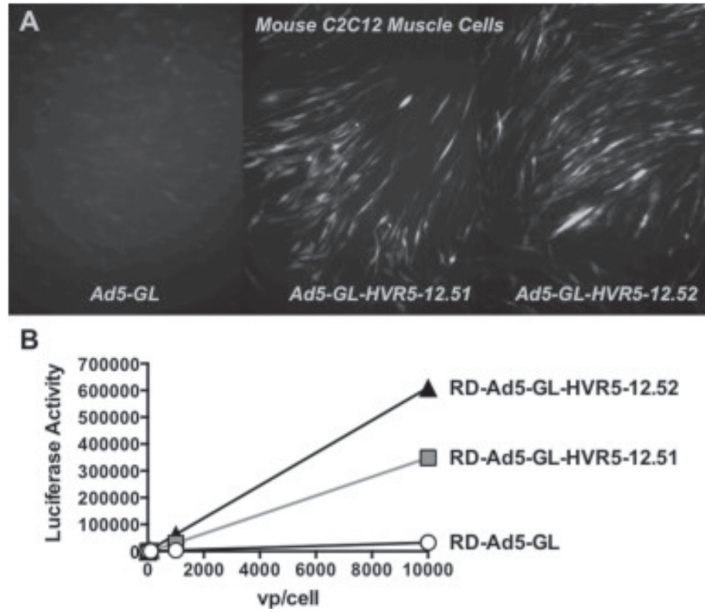


FIG. 2

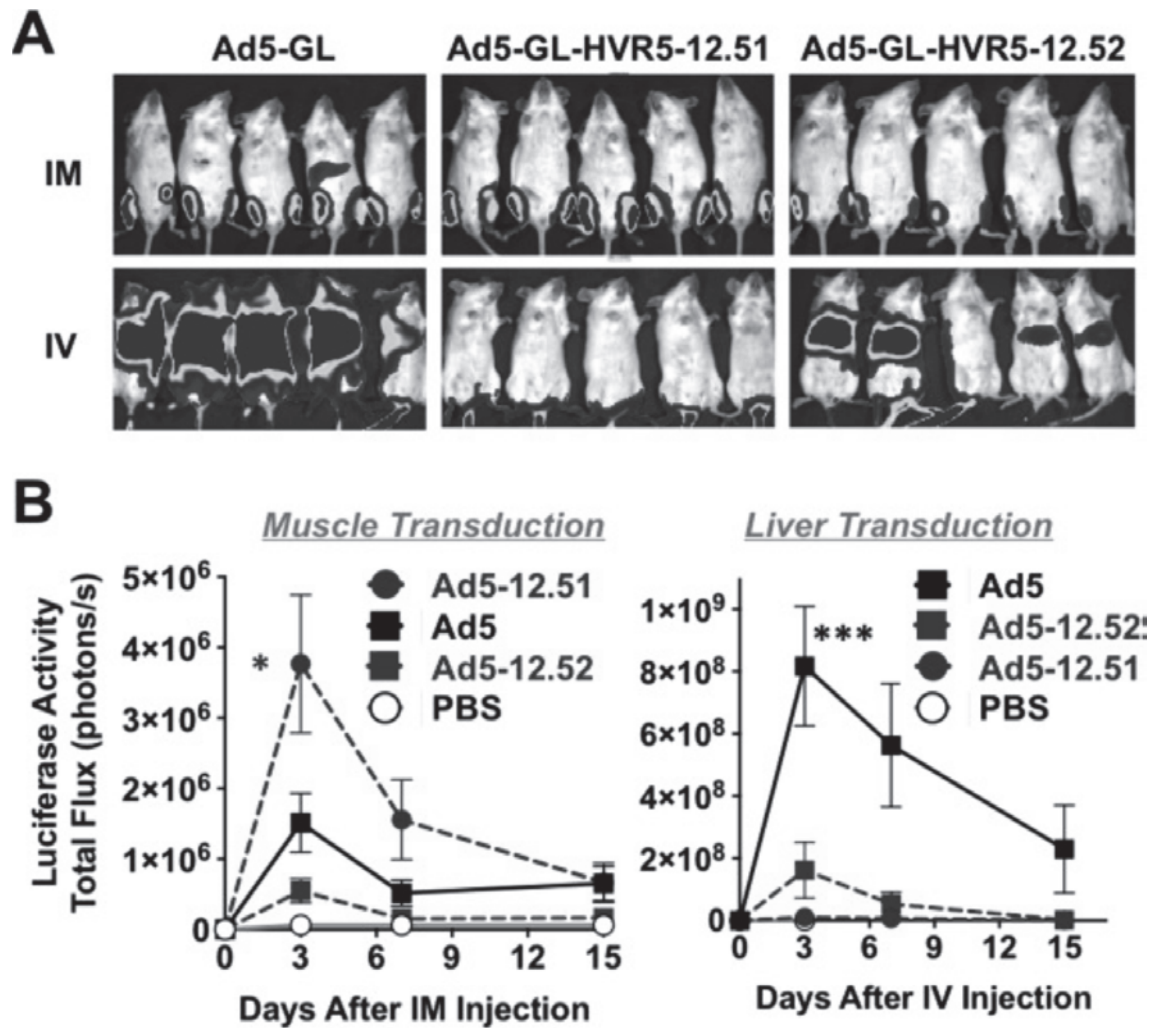


FIG. 3

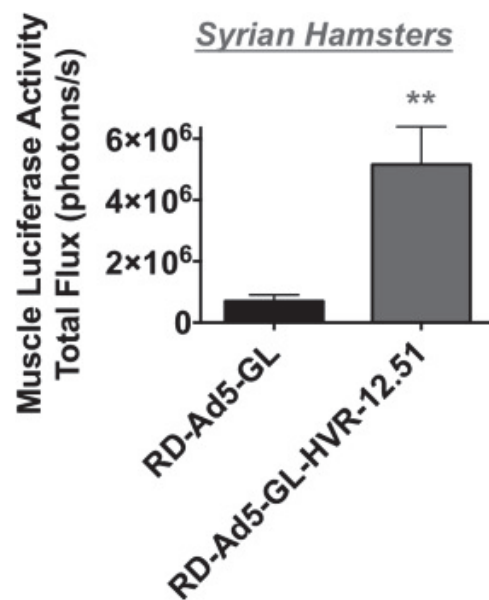


FIG. 4

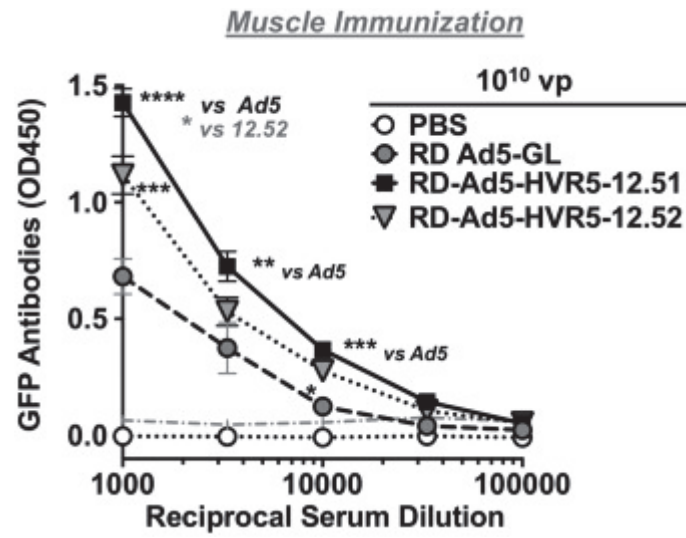


FIG. 5

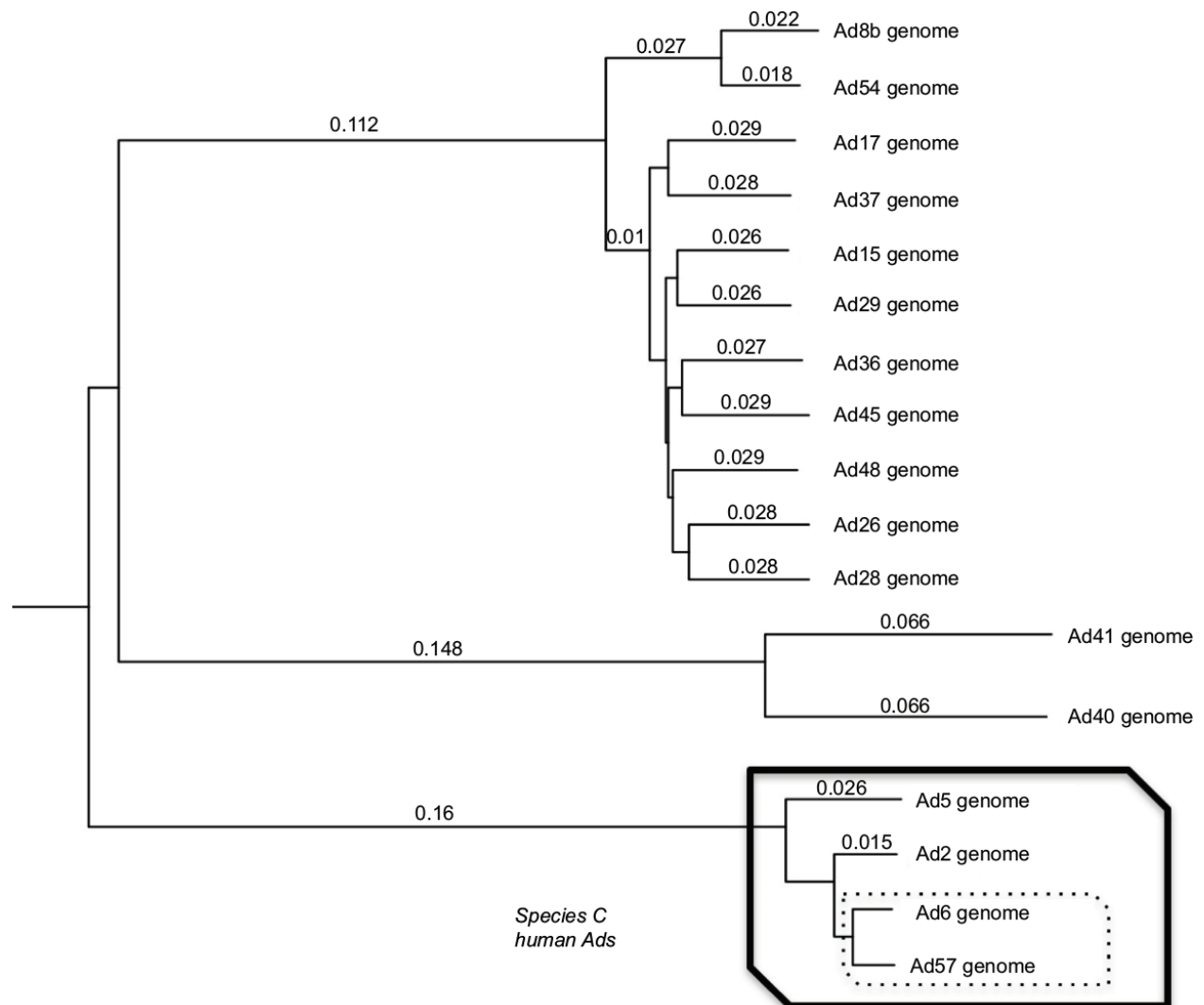


FIG. 6

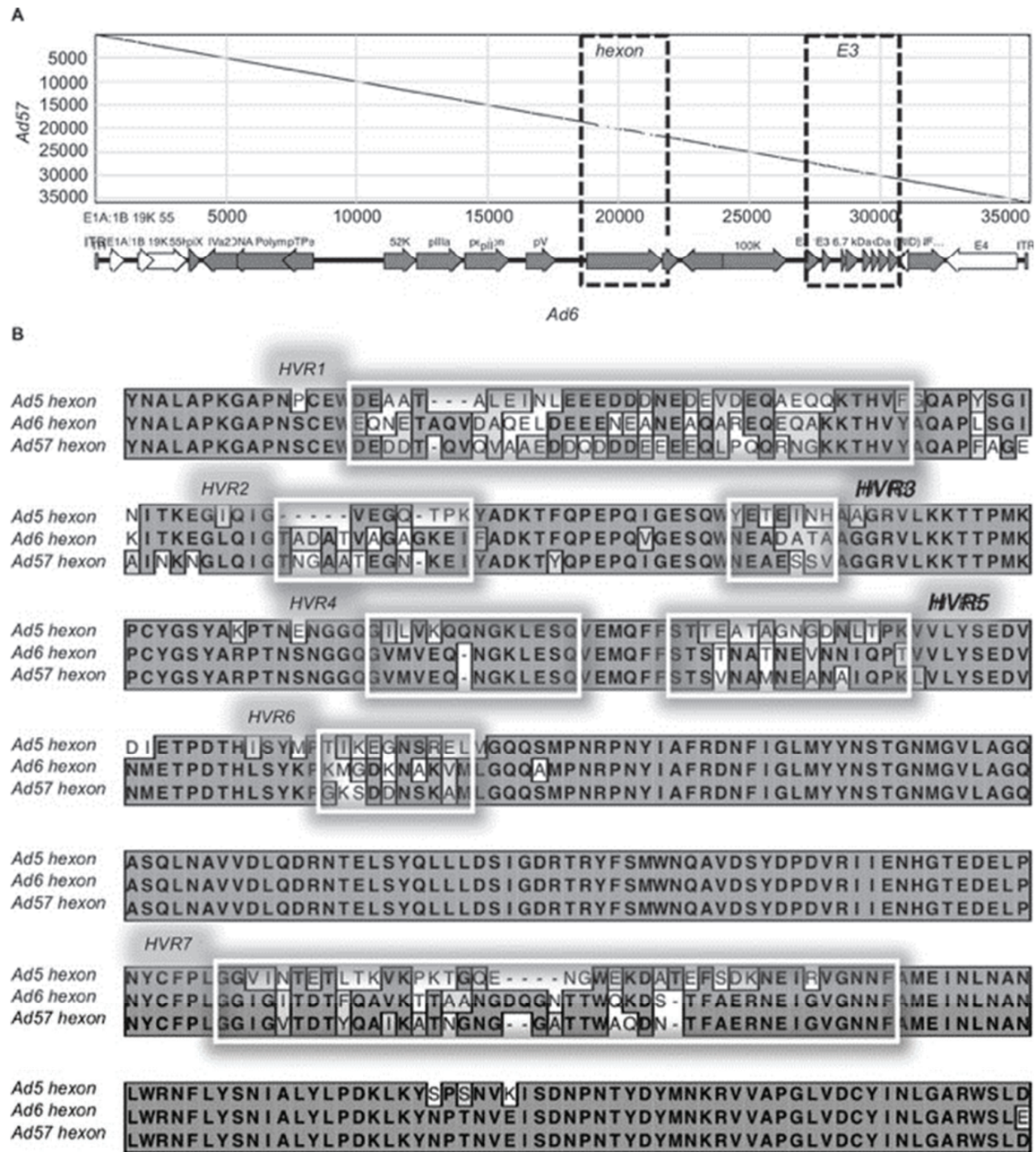


FIG. 7

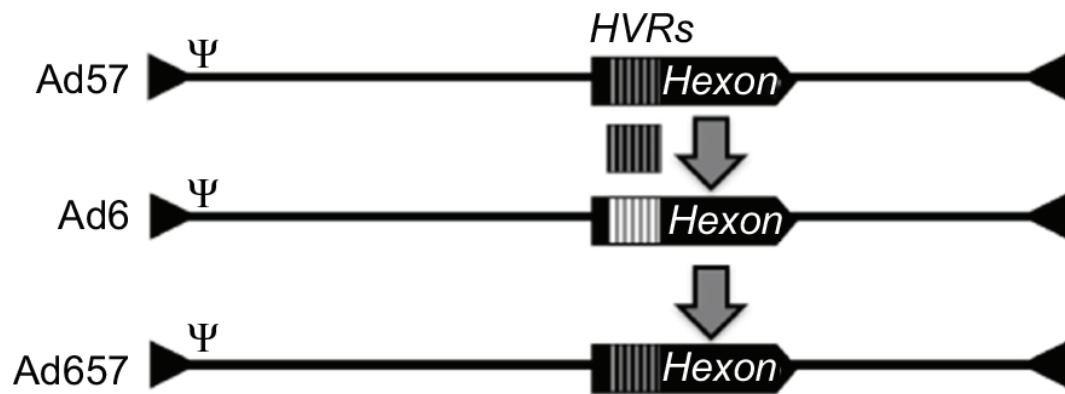


FIG. 8

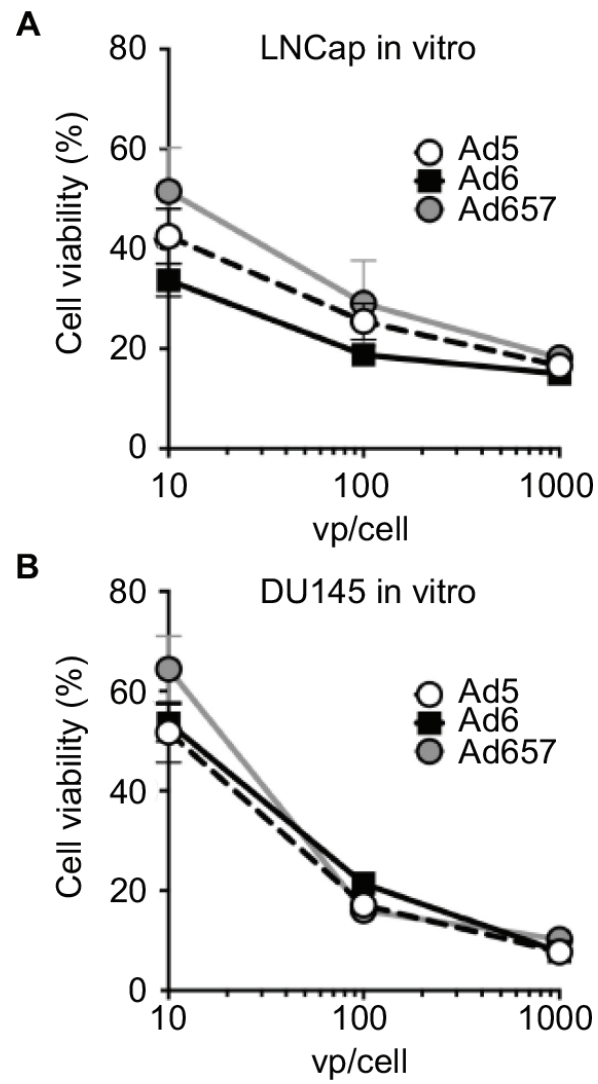


FIG. 9

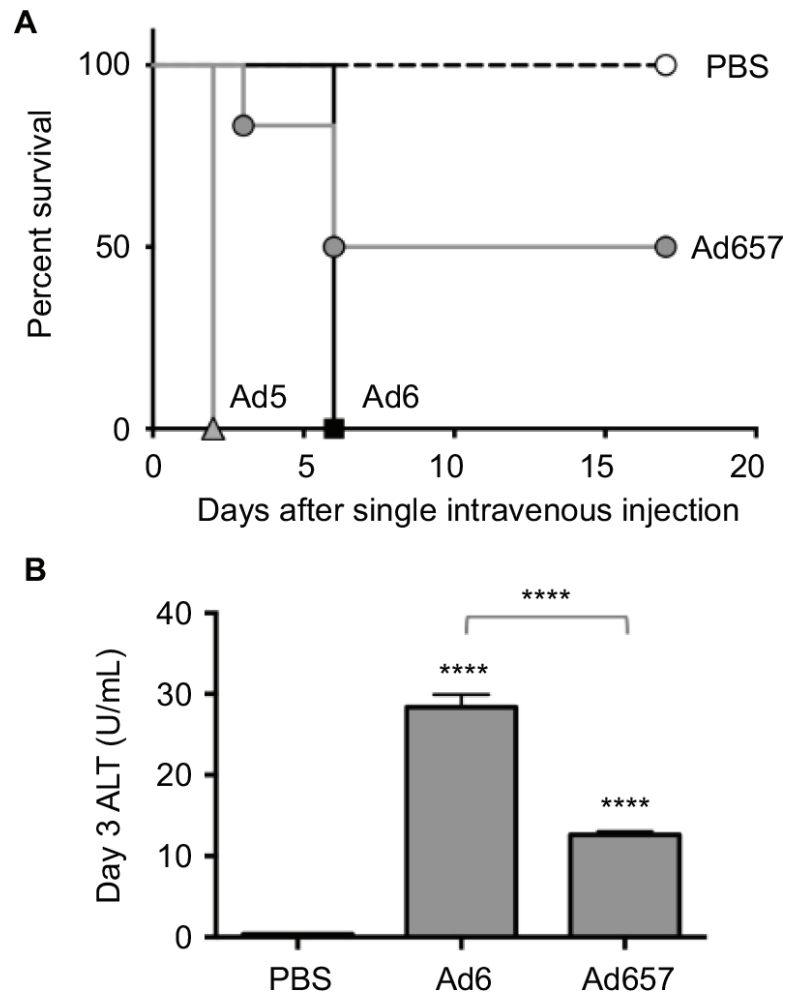


FIG. 10

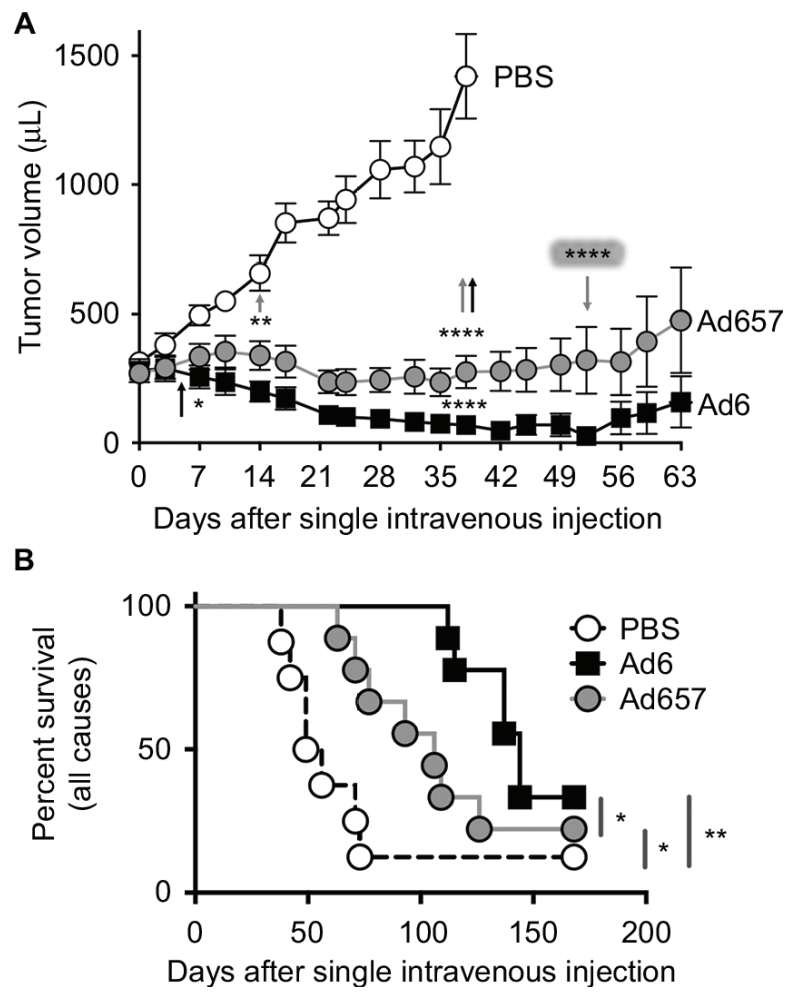
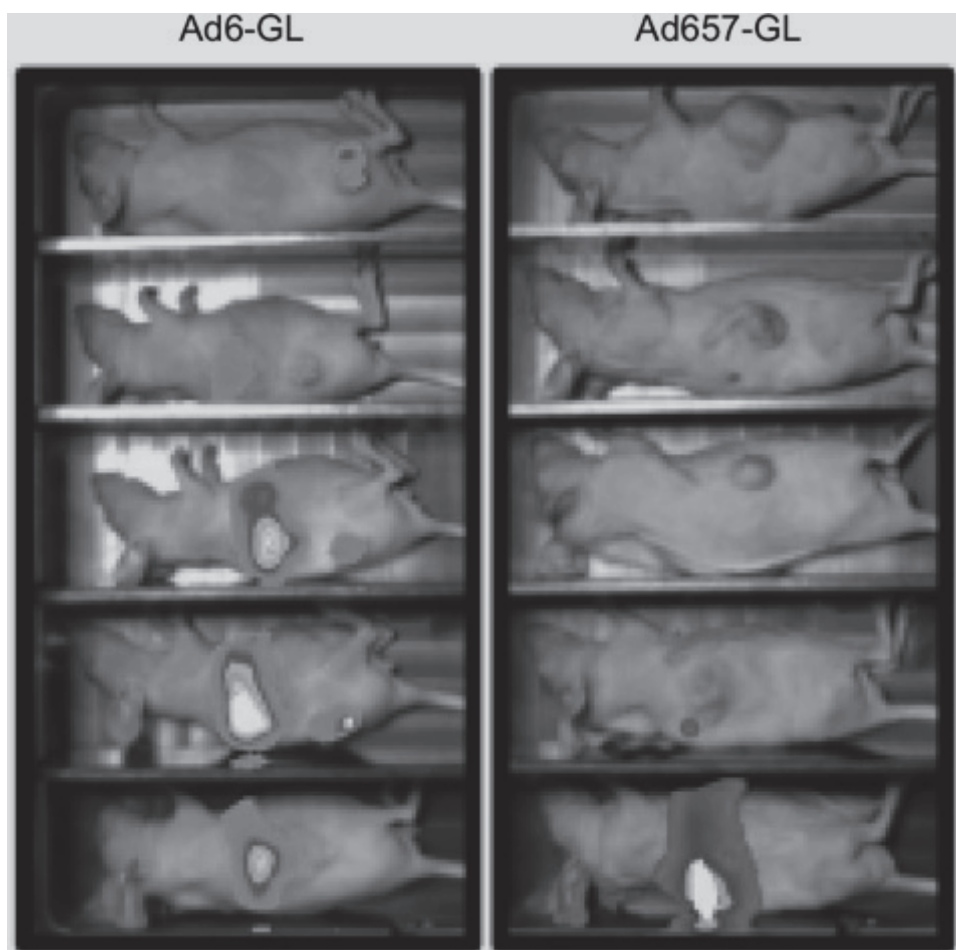


FIG. 11



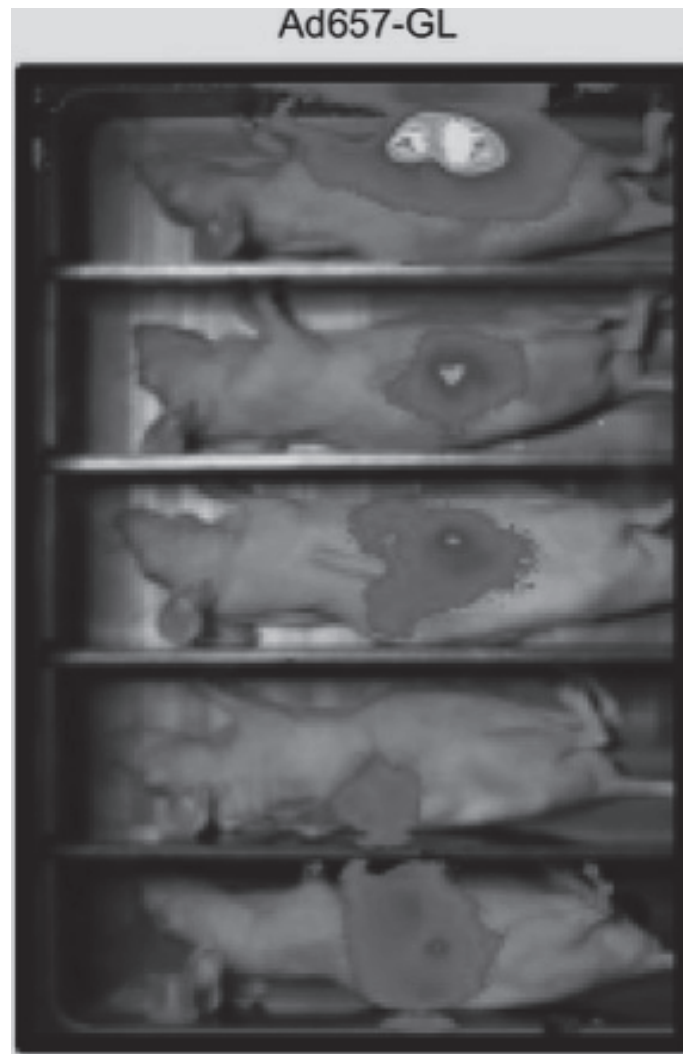
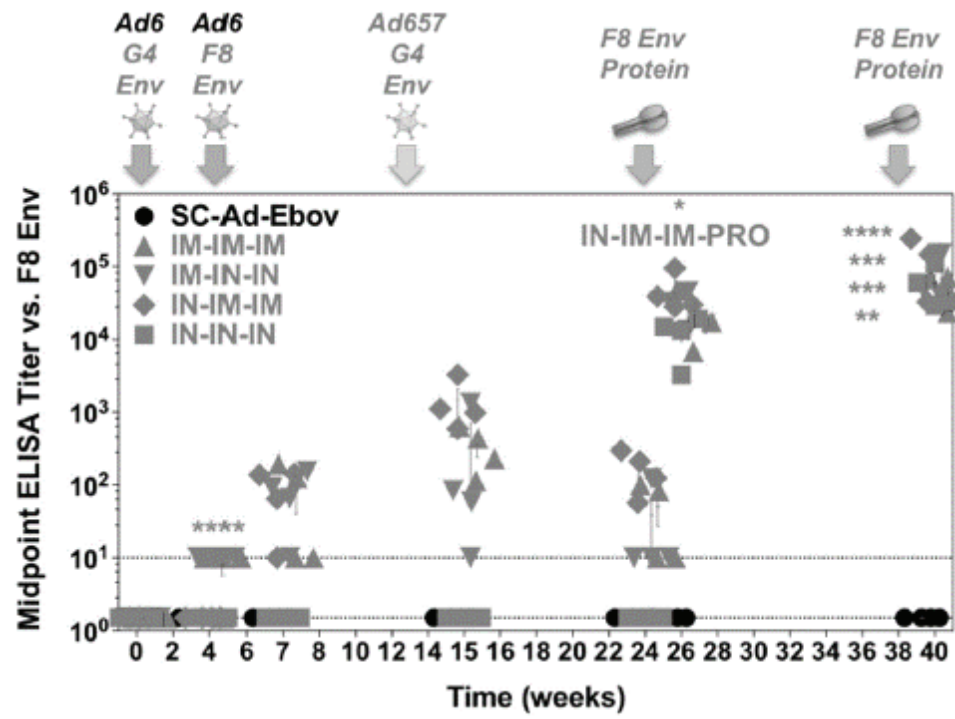


FIG. 13



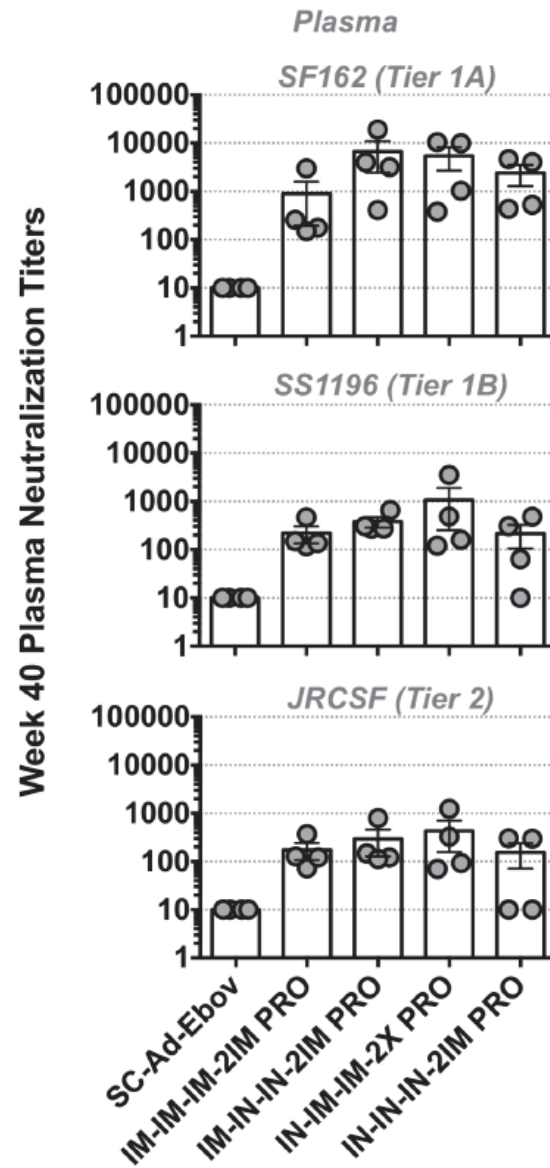


FIG. 15

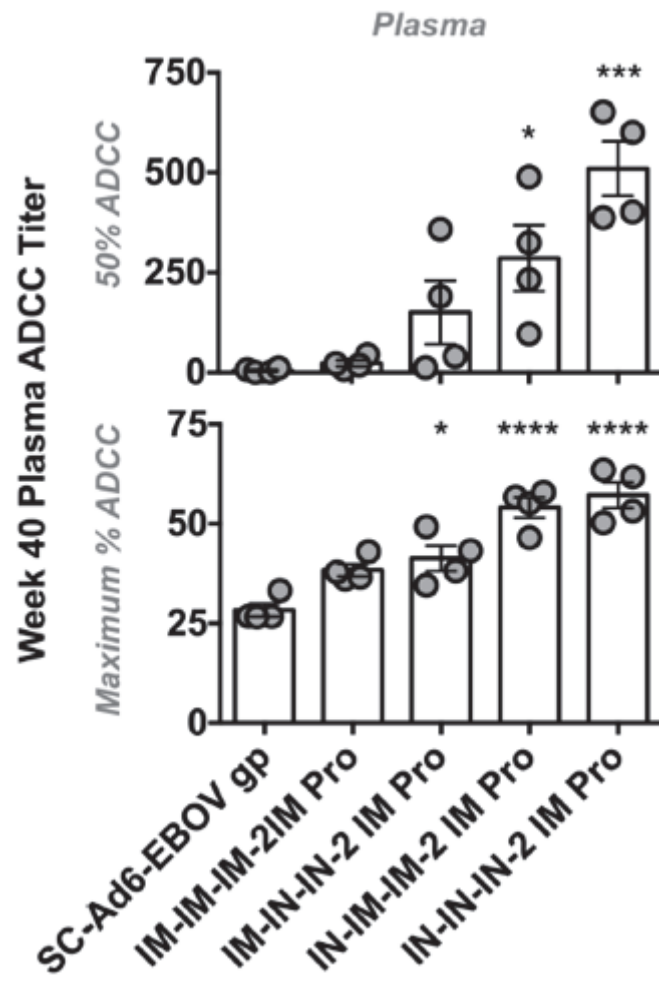


FIG. 16

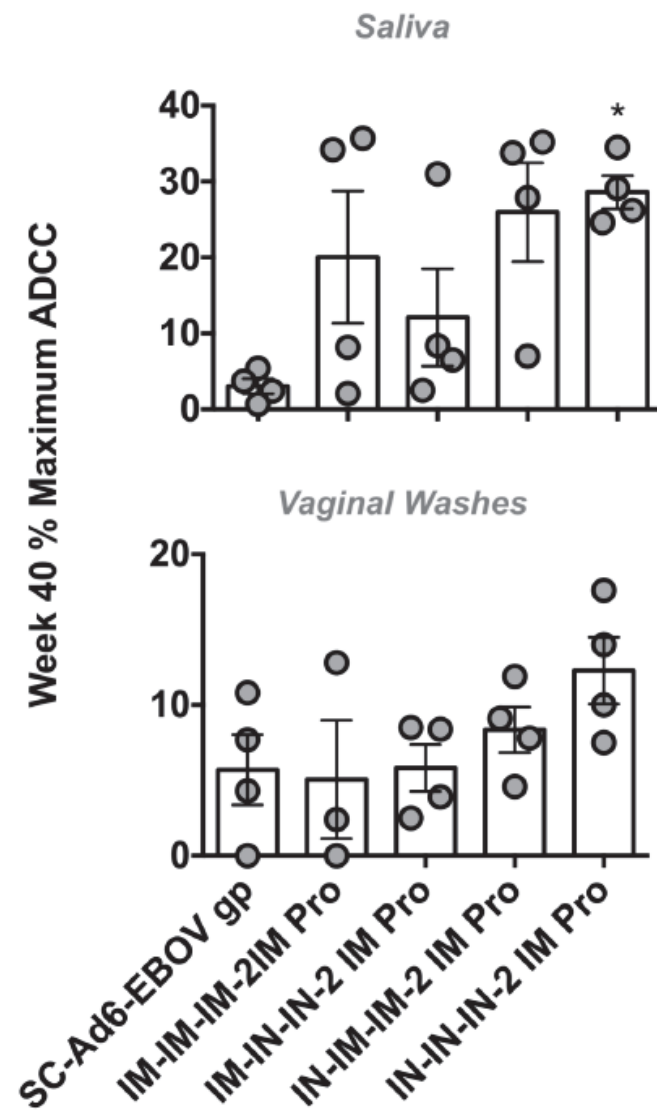


FIG. 17

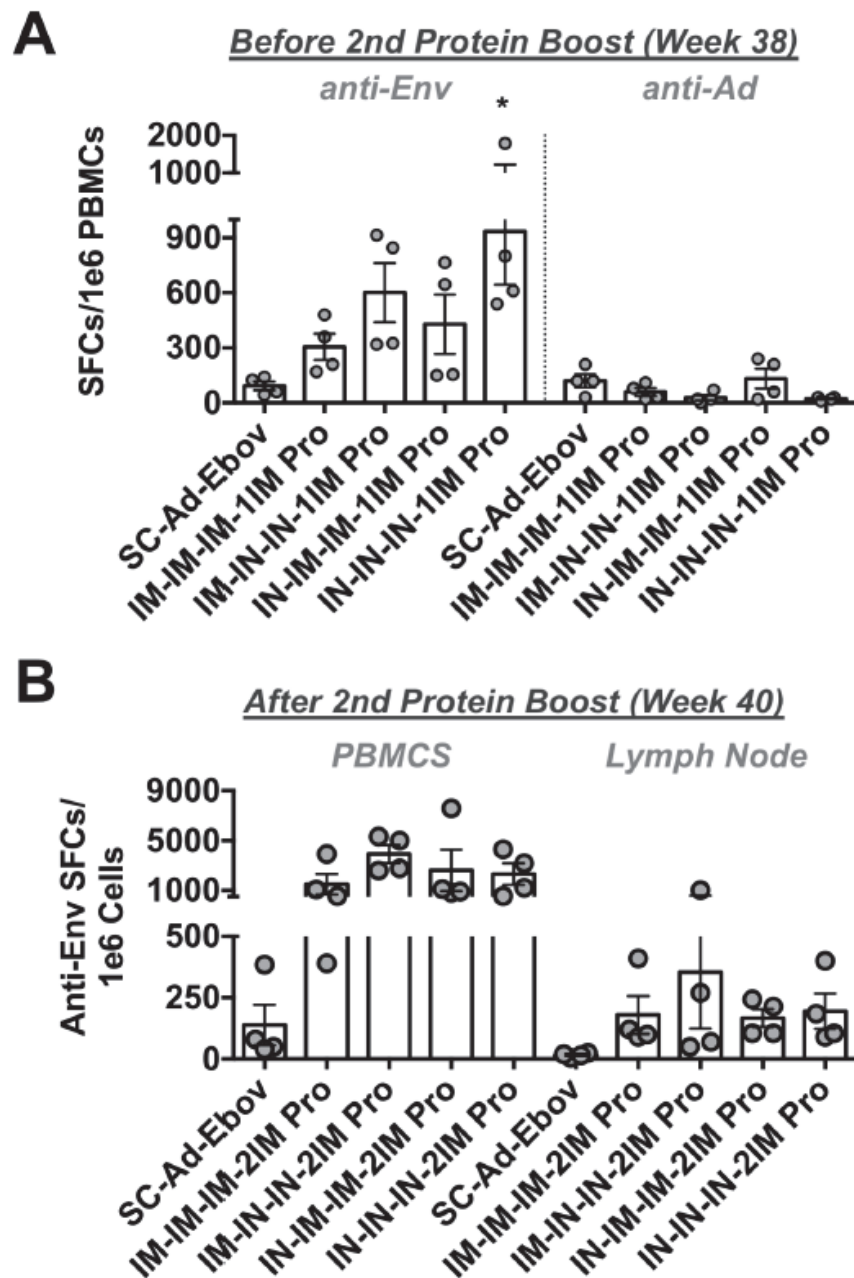


FIG. 18

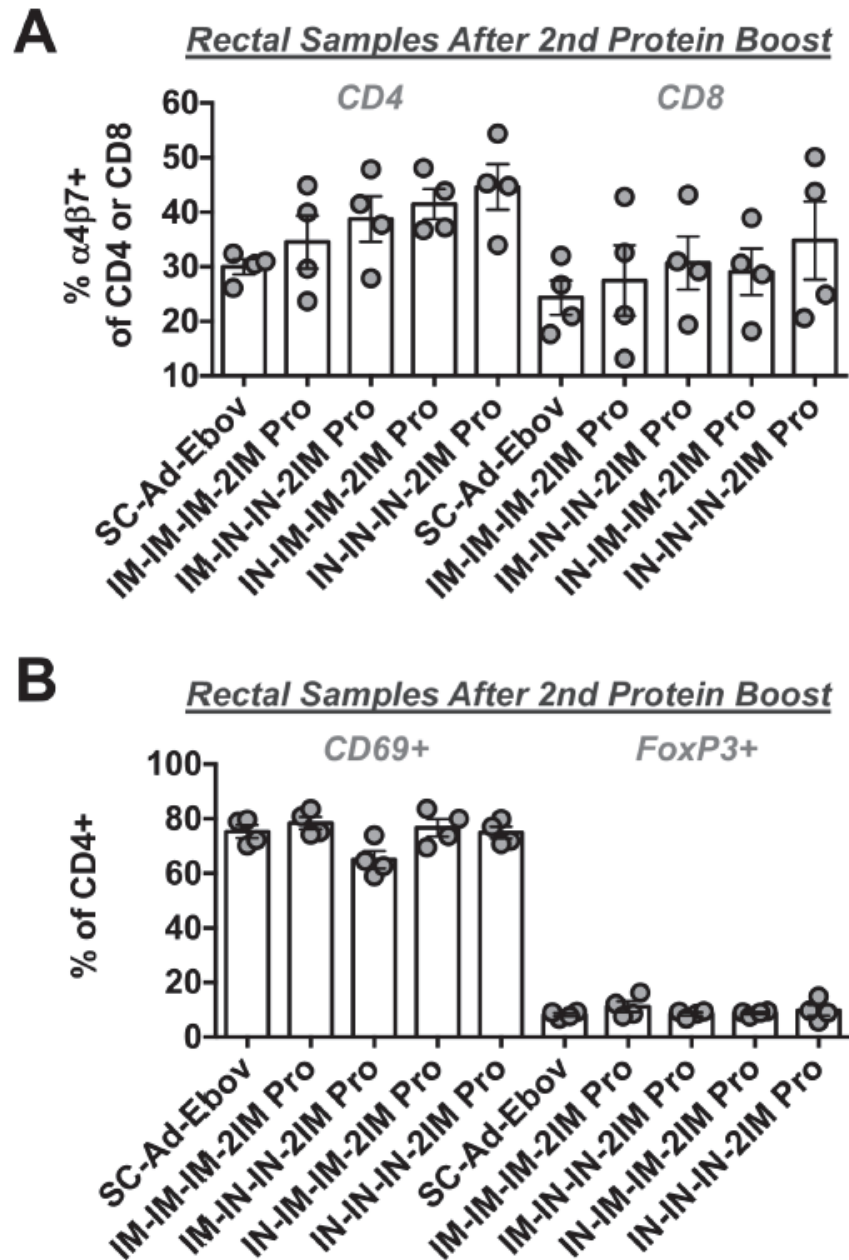


FIG. 19

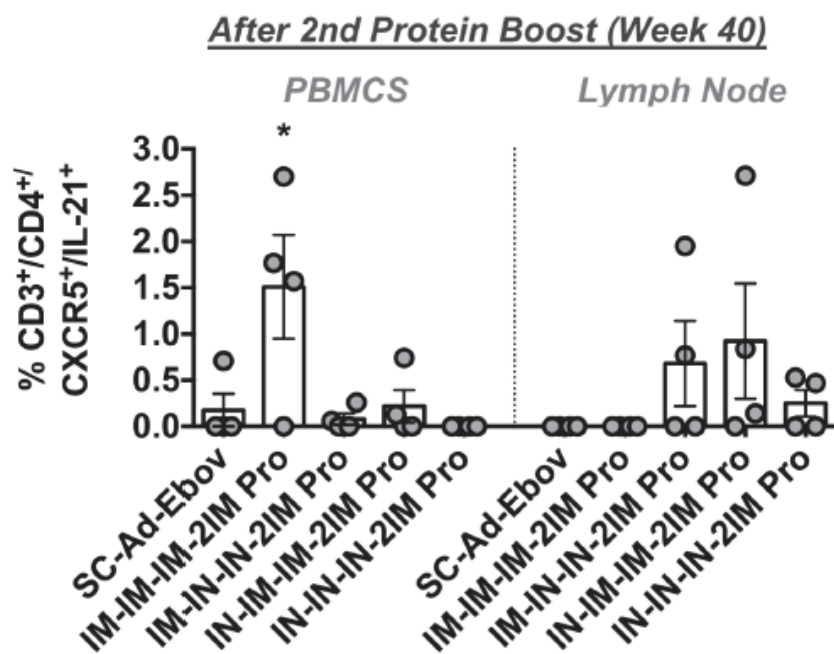


FIG. 20

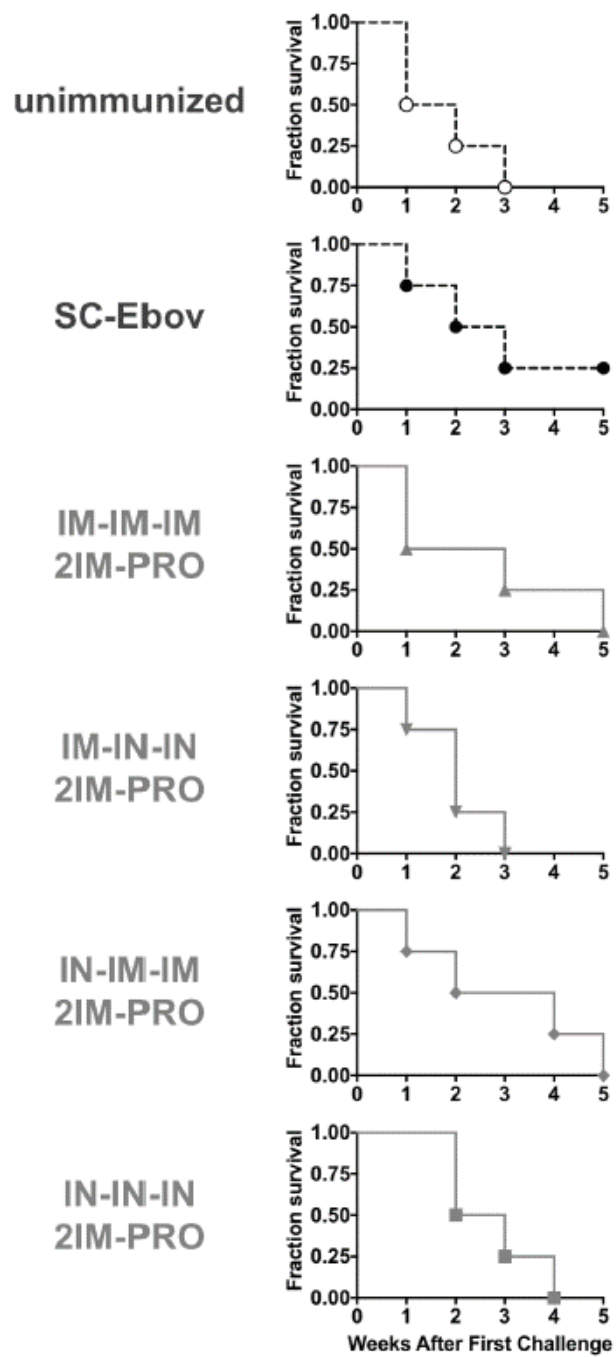


FIG. 21

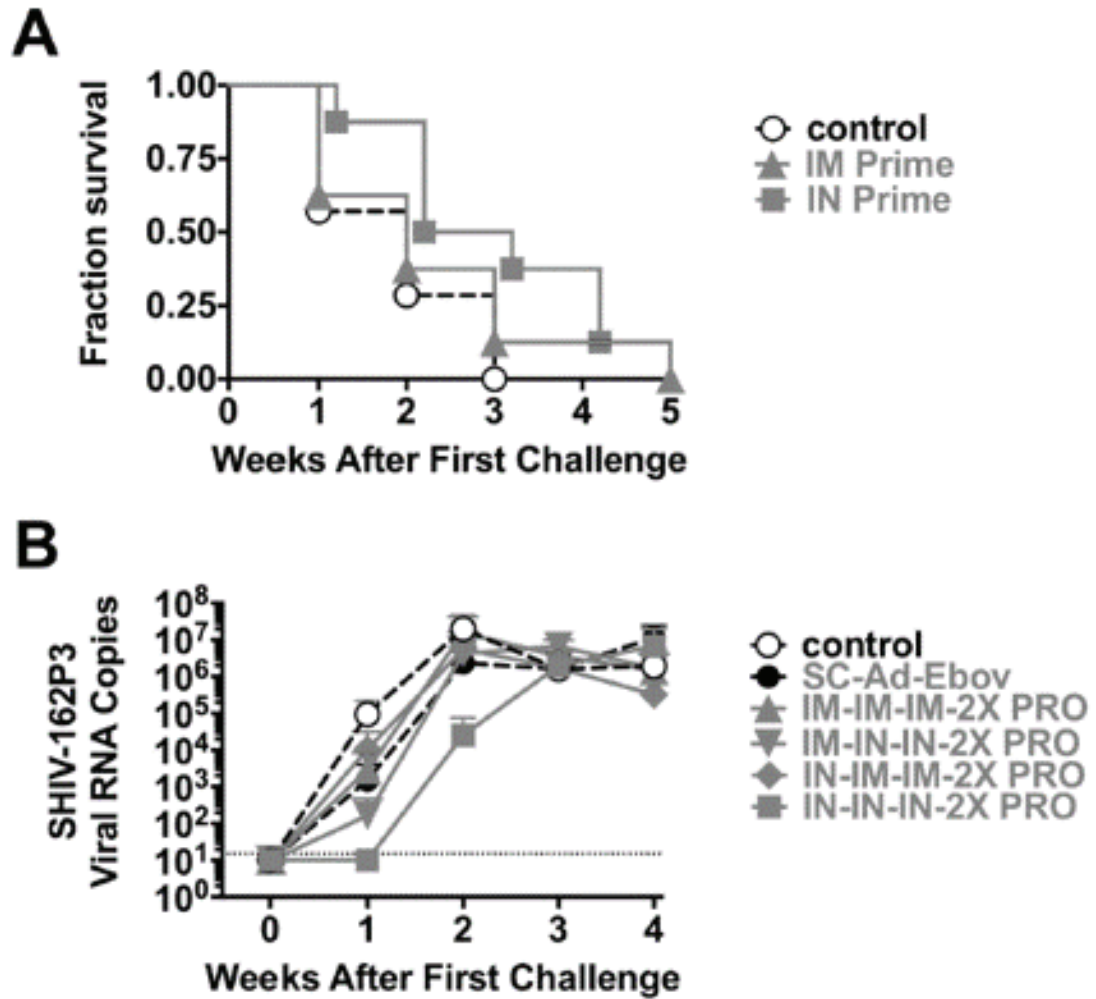


FIG. 22

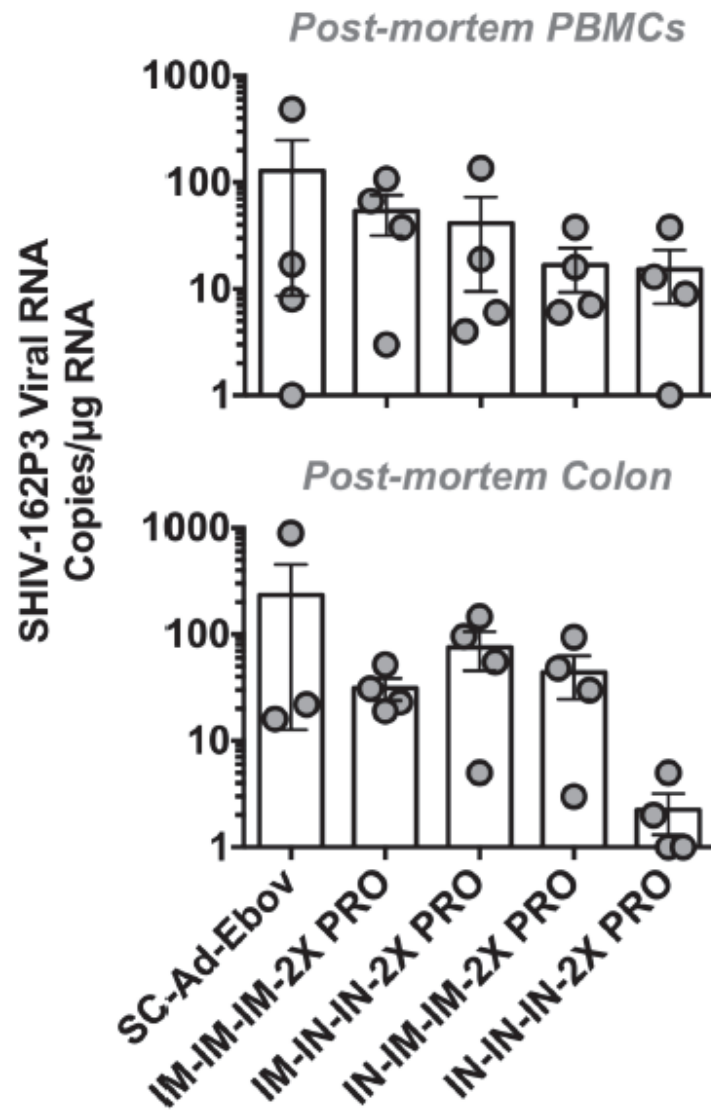


FIG. 23

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

	HVR1	
Ad1 hexon	YNALAPKGPAPNSCEVEQEETPTQEMAELEDEEEAEEEEAEAEAPQADQKVKKTHVYAQ	
Ad2 hexon	YNALAPKGPAPNSCEVEQTEDSGRAVAEDEEEDEDEEEEEEQNAR--DQATKKTHVYAQ	
Ad5 hexon	YNALAPKGPAPNCEVEDEAAALEINLEEDDDNEDEVDE-----QAEQKTHVYFQ	
Ad6 hexon	YNALAPKGPAPNSCEVEQNETAQVDAQELDEEENEANEQAQARE-----QEQAkkTHVYAQ	
Ad57 hexon	YNALAPKGPAPNSCEVEDDDTQVQVAEDDQDDDEEEQLPQ-----QRNGKKTHVYAQ	
	HVR2	HVR3
Ad1 hexon	APLAGERKITANGIQI-VSDTQTEG--NPVFADPTYQPEPQVGESQVNEAEATASGGRVLK	
Ad2 hexon	APLSGETITKSGIQIGSDNAETQA--KPYVADPSYQPEPQIGESQVNEADANAAGGRVLK	
Ad5 hexon	APYSGINITKEGQIGVEGQ-----TPKYADKTFQPEPQIGESQVYETEINHAGGRVLK	
Ad6 hexon	APLSGIKITKEGQIGTADATVAGAGKEIFADKTFQPEPQVGESQVNEADANAAGGRVLK	
Ad57 hexon	APFAGEAINKNGIQIGTNGAATEG-NKEIYADKTYQPEPQIGESQVNEAESVAGGRVLK	
	HVR4	HVR5
Ad1 hexon	KTTMPMKPCYGSYARPTNKNGGQGILVANNQGALESKVEMQFFAPSGTAMN-ERNVOPPSI	
Ad2 hexon	KTTMPMKPCYGSYARPTNPFGGQSVLVPDEKGVPLPKVDLQFFSNITSLNDROGNATKPKV	
Ad5 hexon	KTTMPMKPCYGSYAKPTNENGGQGILVKQNGKLESQVEMQFFSTTEATAG-NGDNLTPKV	
Ad6 hexon	KTTMPMKPCYGSYARPTNSNGGQGVMMV-EQNGKLESQVEMQFFSTSTINATN-EVNNIQPTV	
Ad57 hexon	KTTMPMKPCYGSYARPTNSNGGQGVMMV-EQNGKLESQVEMQFFSTSVNAMN-EANAIQPKL	
	HVR6	
Ad1 hexon	VLYSEDVNMETPDTHISYKPKSKTDENSKAMLGQQAAMPNRPNYIAFRDNF IGLMYNSTGN	
Ad2 hexon	VLYSEDVNMETPDTHLSYKPKGKGDENSKAMLGQQSMPNRPNYIAFRDNF IGLMYNSTGN	
Ad5 hexon	VLYSEDVDIETPDTHISYMTIKEGNSREL MGQQSMPNRPNYIAFRDNF IGLMYNSTGN	
Ad6 hexon	VLYSEDVNMETPDTHLSYKPKMGDKNAKVM LGQQAAMPNRPNYIAFRDNF IGLMYNSTGN	
Ad57 hexon	VLYSEDVNMETPDTHLSYKPKKSSDDNSKAMLGQQSMPNRPNYIAFRDNF IGLMYNSTGN	
	HVR7	
Ad1 hexon	GTEDELPNYCFPLGGIGVTDITYQGIRK--NGNG--NPQNMTKND-FAARNEIGVGN	
Ad2 hexon	GTEDELPNYCFPLGGIGVTDITYQAIAK--NGNGSGDNGDITWTKDET-FATRNEIGVGN	
Ad5 hexon	GTEDELPNYCFPLGGVINETETLTQVVKPKTGOENG-----WEKDATEFSQKNEIRVGN	
Ad6 hexon	GTEDELPNYCFPLGGIGITDTFQAVKTTAAANGDQ---GNTTWQKDSI-FAERNEIGVGN	
Ad57 hexon	GTEDELPNYCFPLGGIGVTDITYQAIAKAT--NGNG--GATTWAQDNT-FAERNEIGVGN	

FIG. 24

Week 40 F8 Binding Antibodies (OD450)

SC-Ebov

IM-IM-IM
2IM-PRO

IM-IN-IN
2IM-PRO

IN-IM-IM
2IM-PRO

IN-IN-IN
2IM-PRO

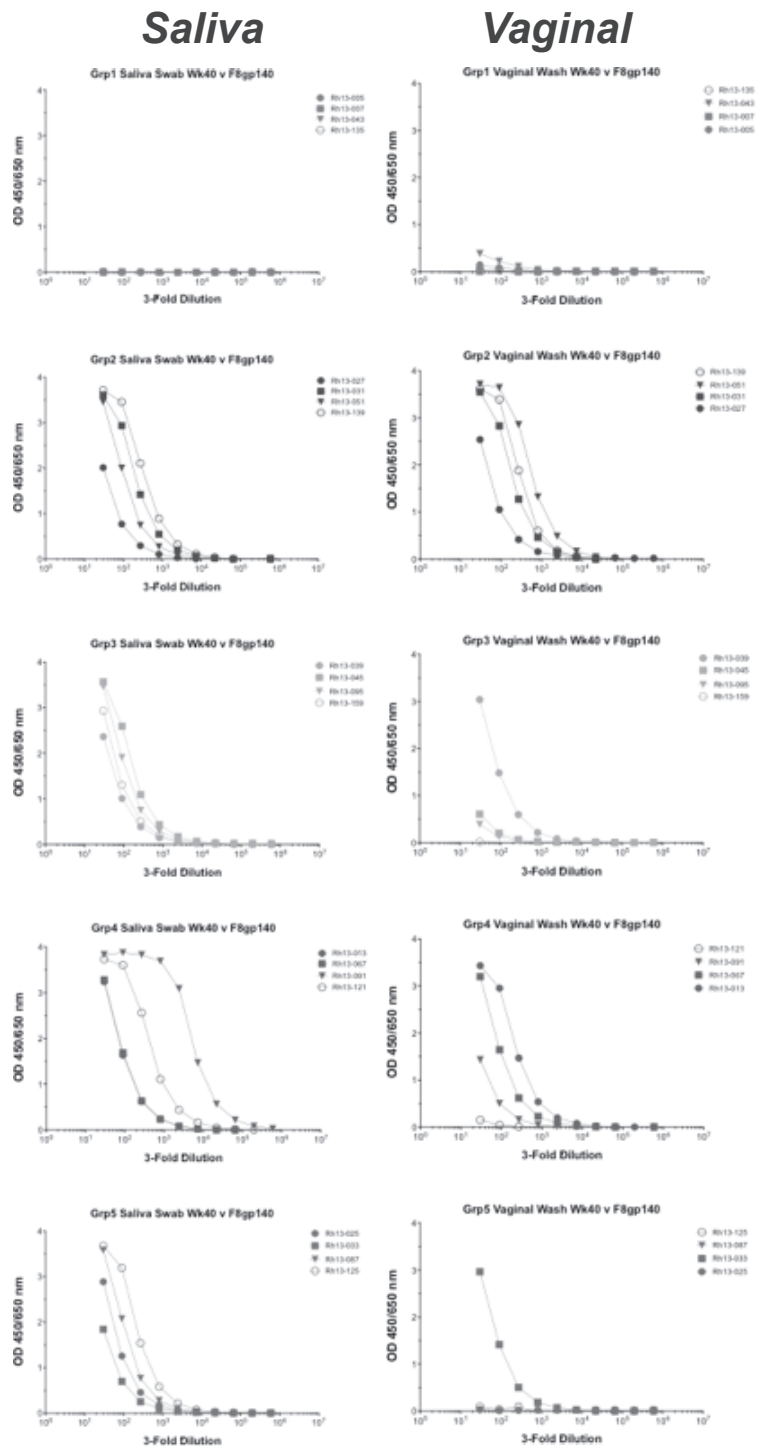


FIG. 25

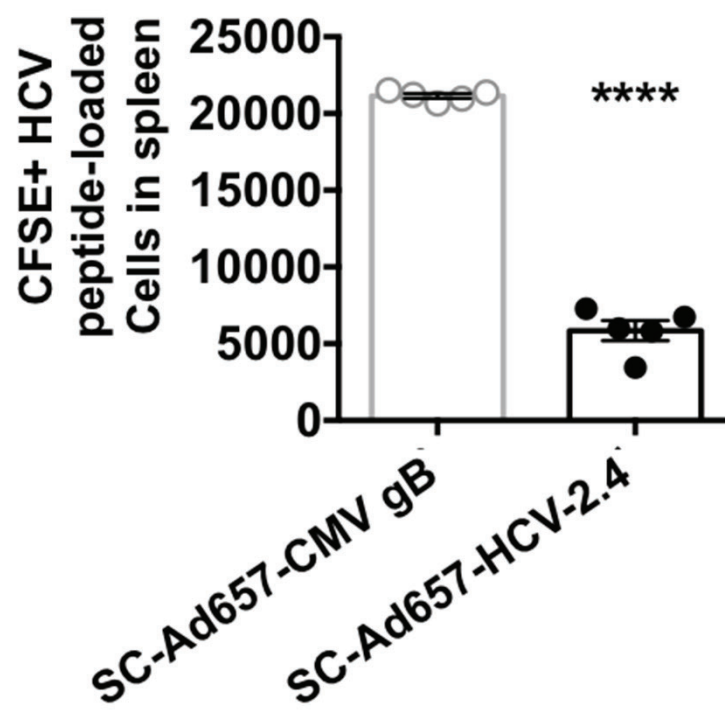


FIG. 26

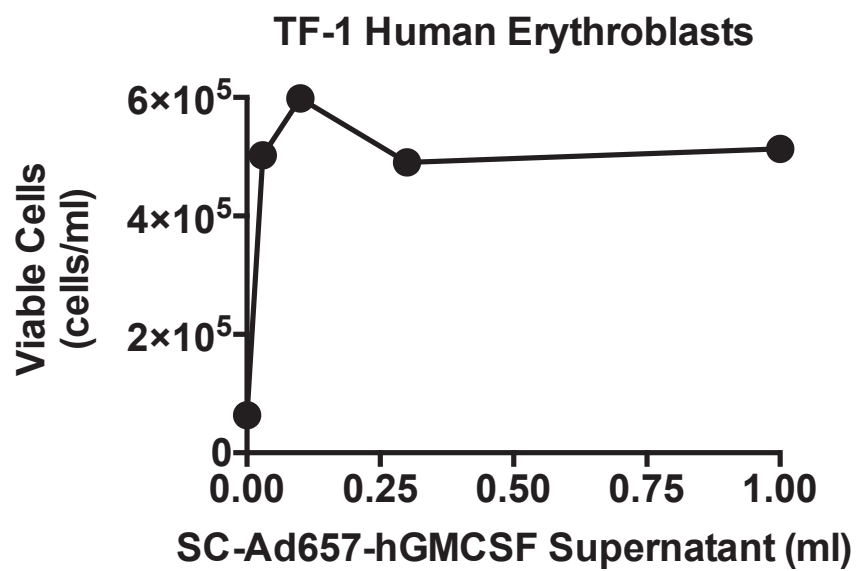


FIG. 27

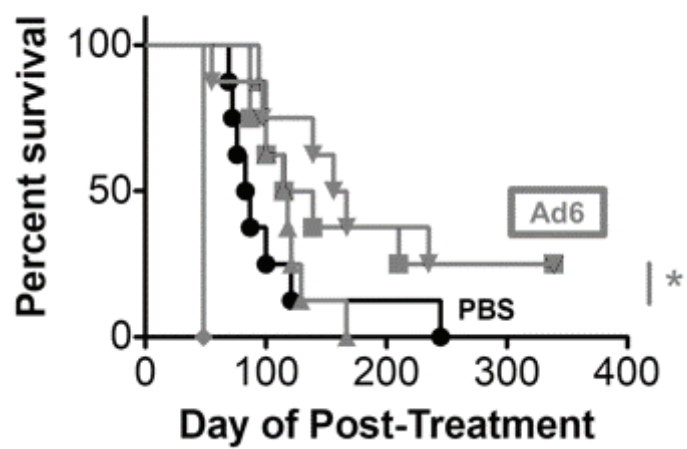


FIG. 28

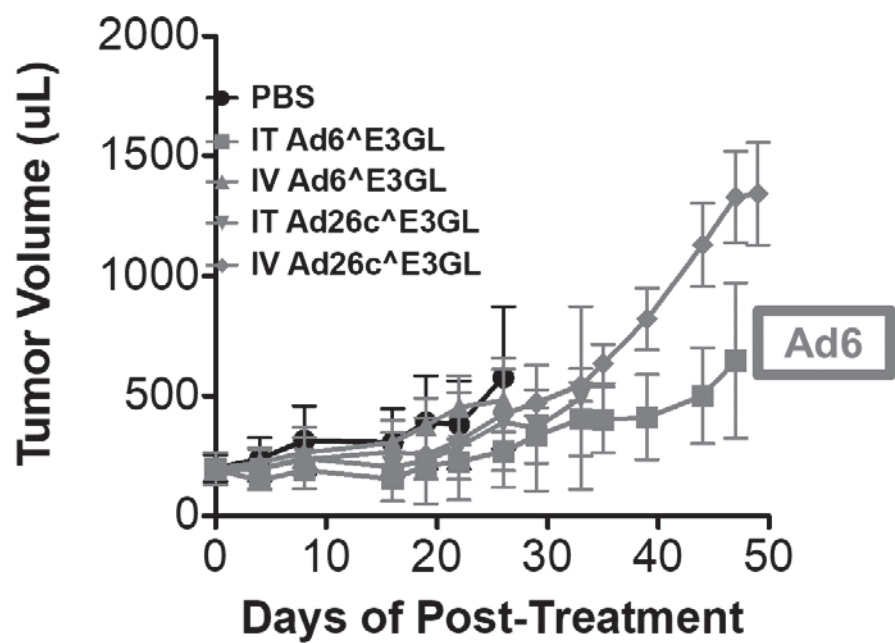


FIG. 29

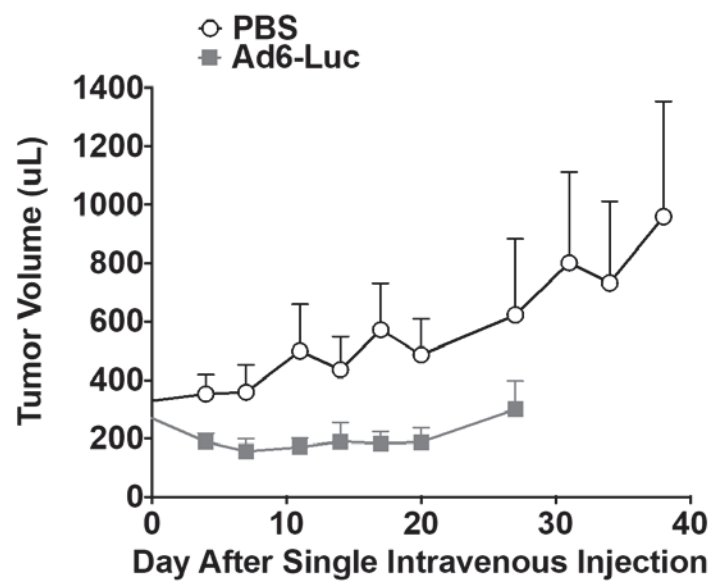


FIG. 30

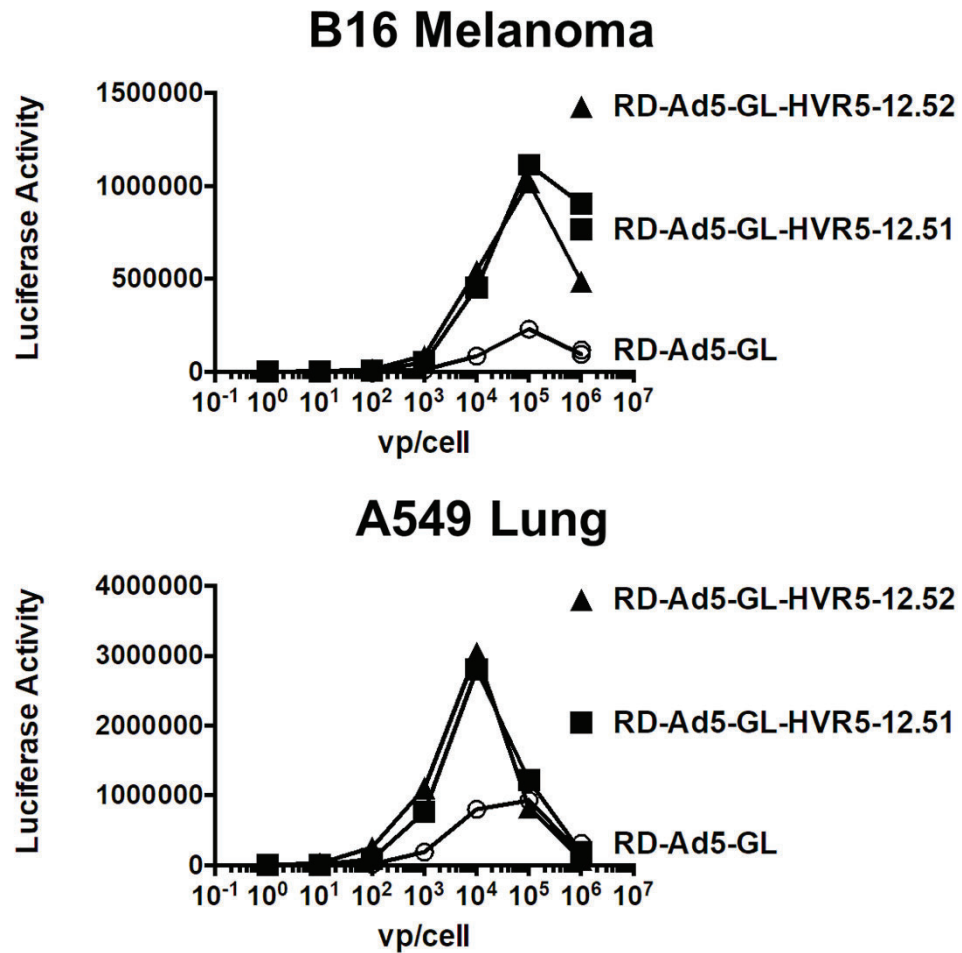


FIG. 31

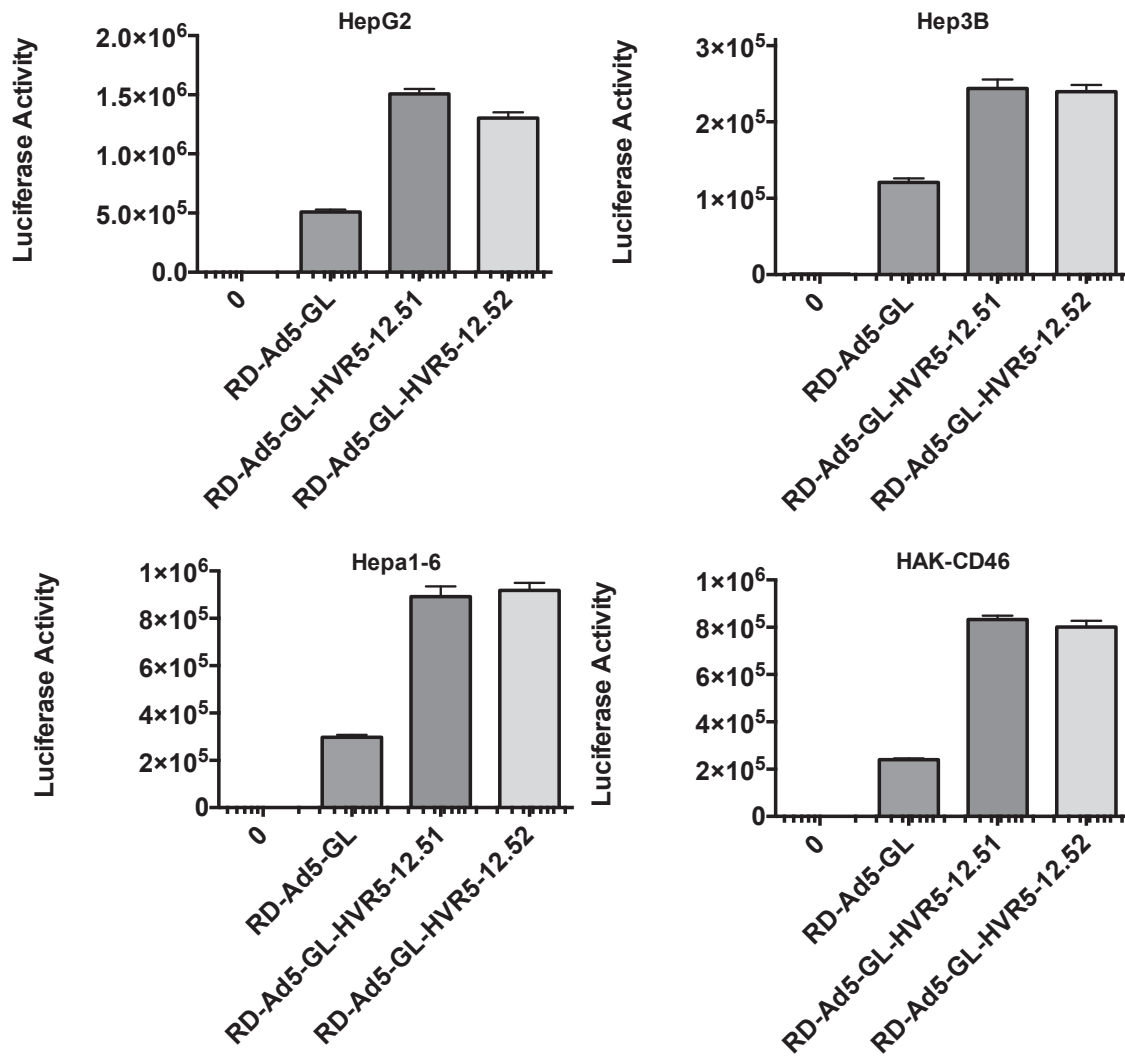


FIG. 32

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

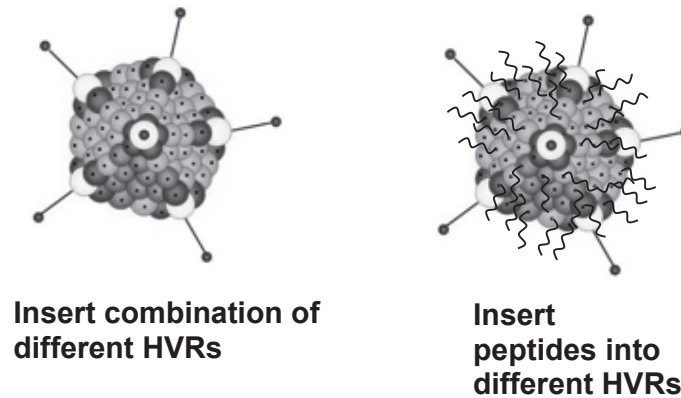


FIG. 33

Figure 33 (continued)

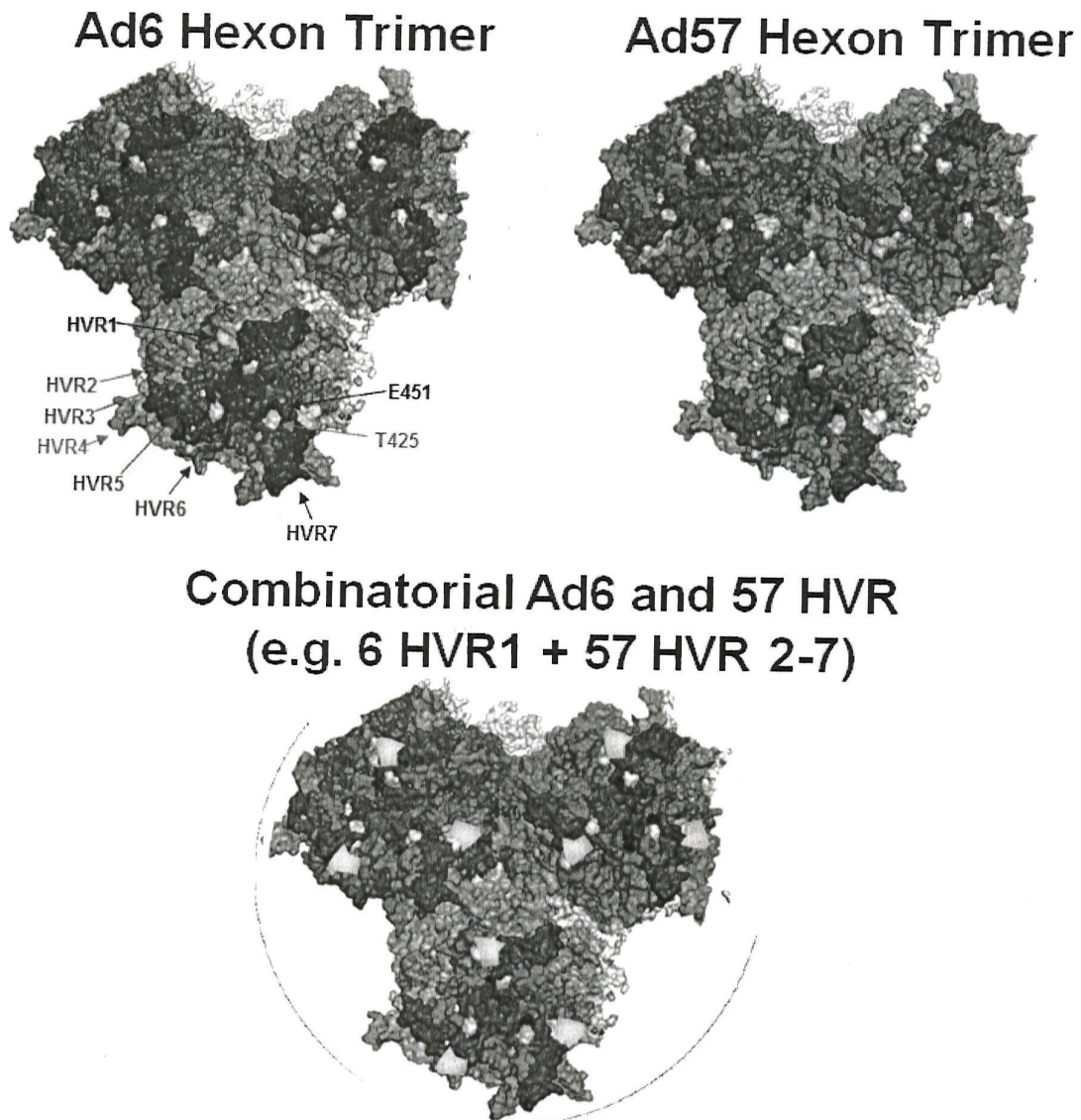
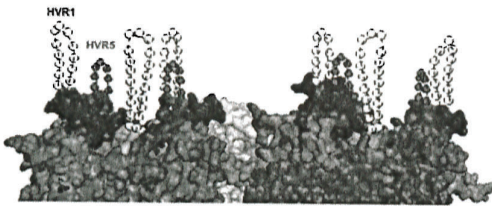
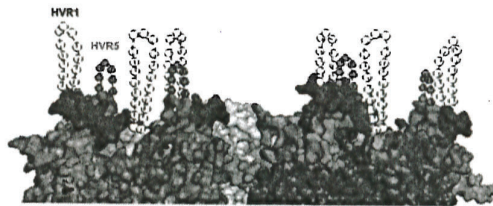
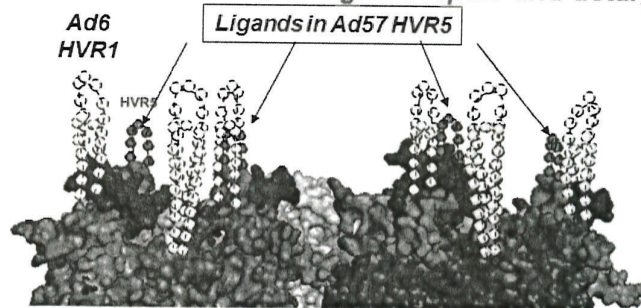


Figure 33 (continued)

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)*

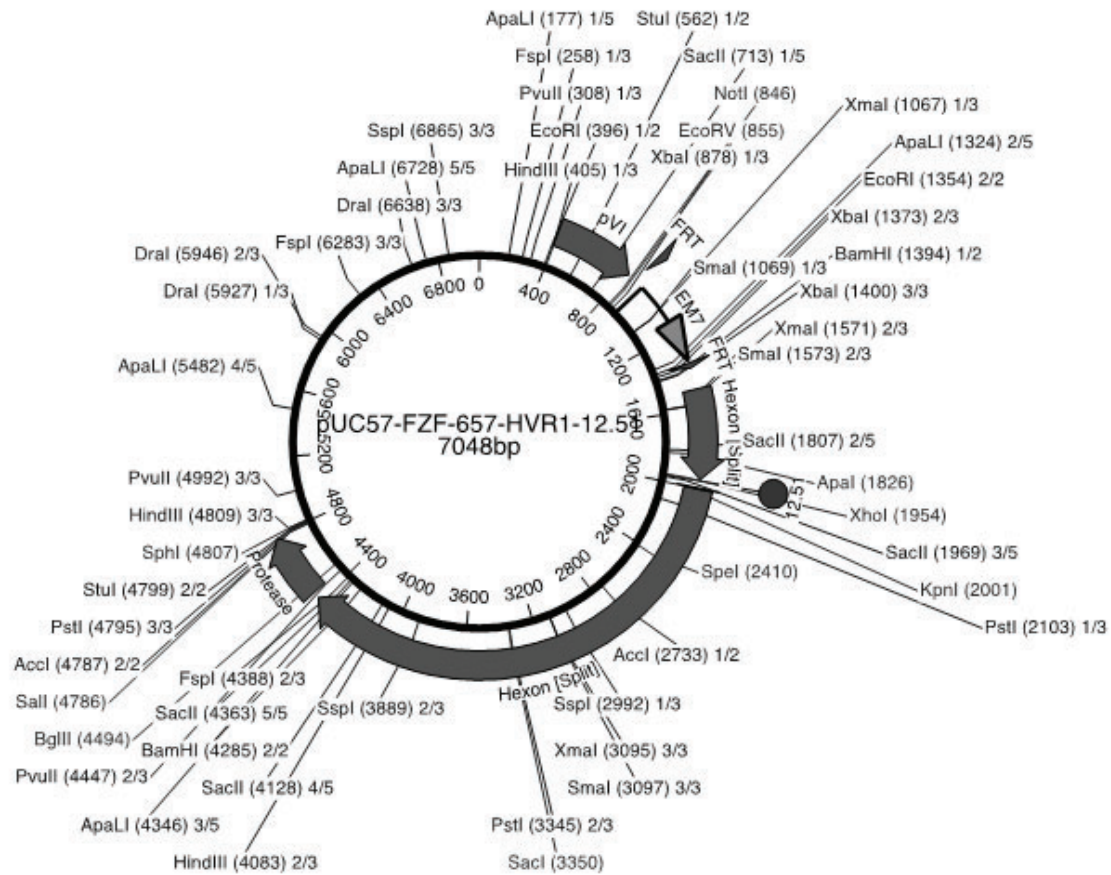


FIG. 34

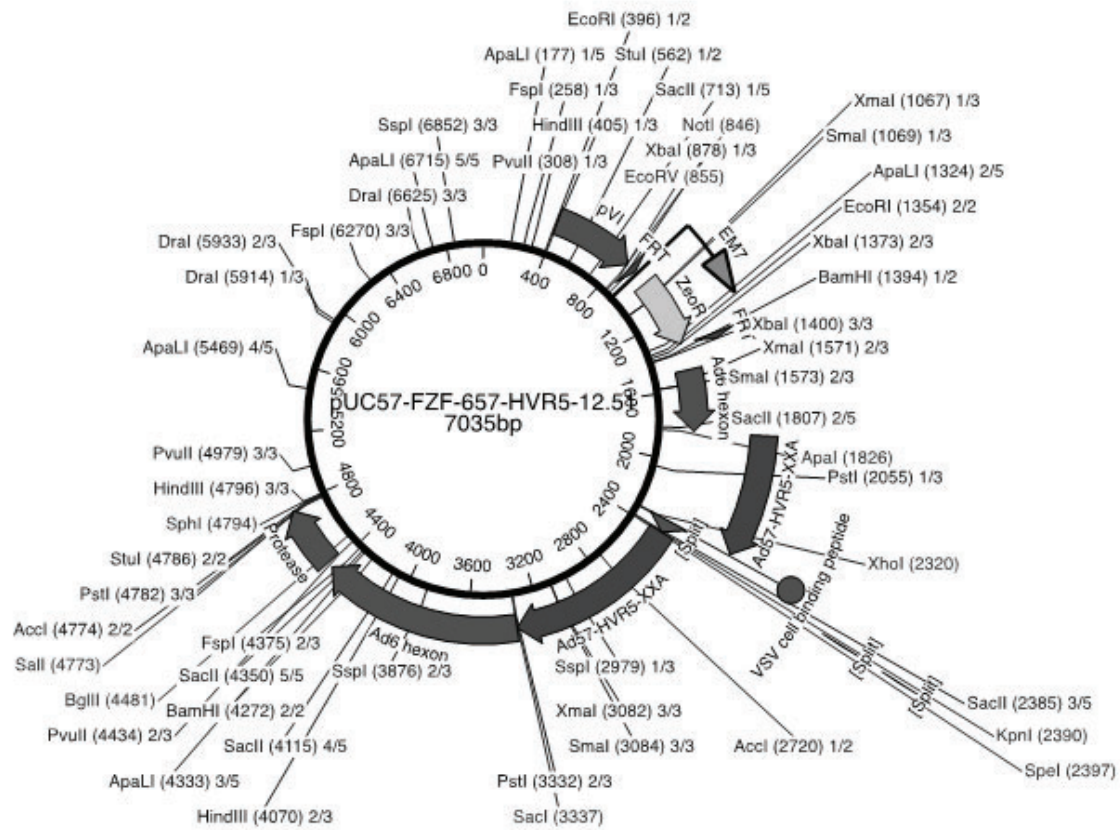


FIG. 34 (continued)

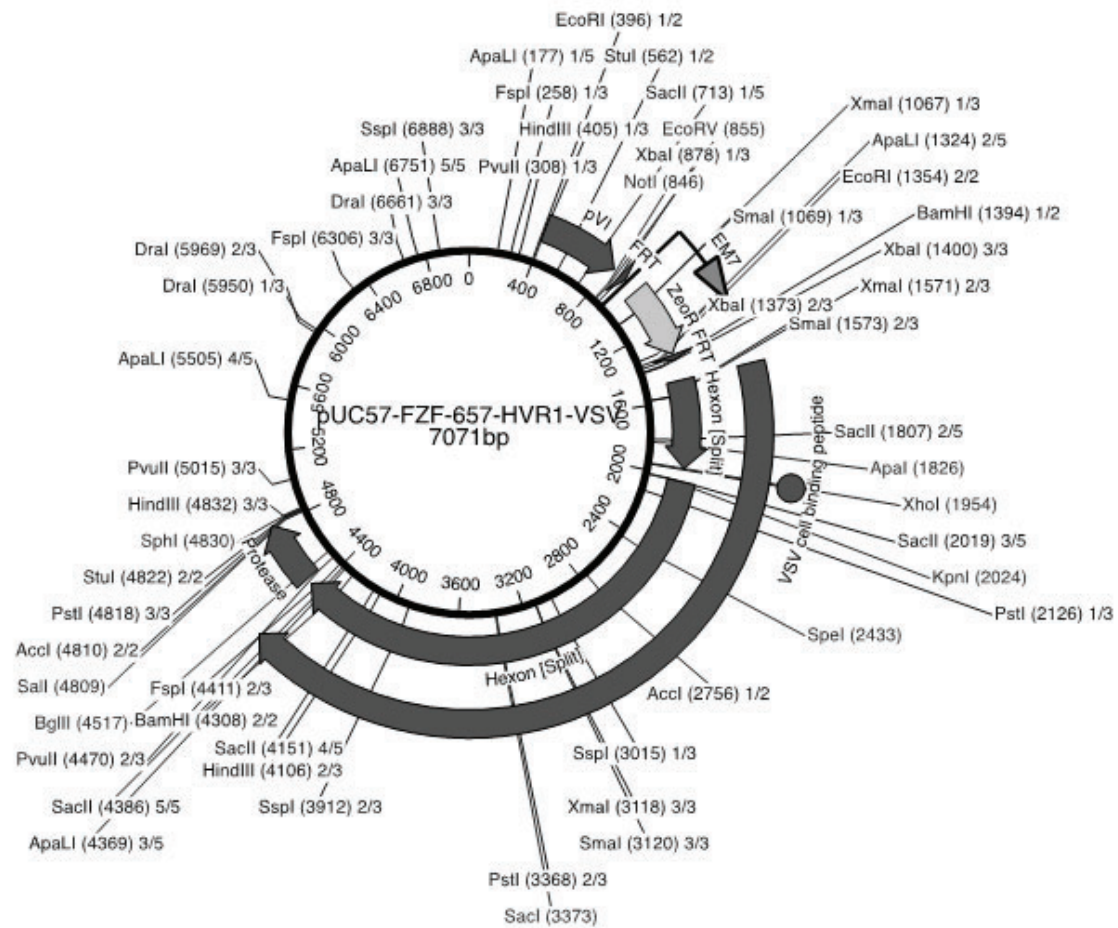


FIG. 34 (continued)

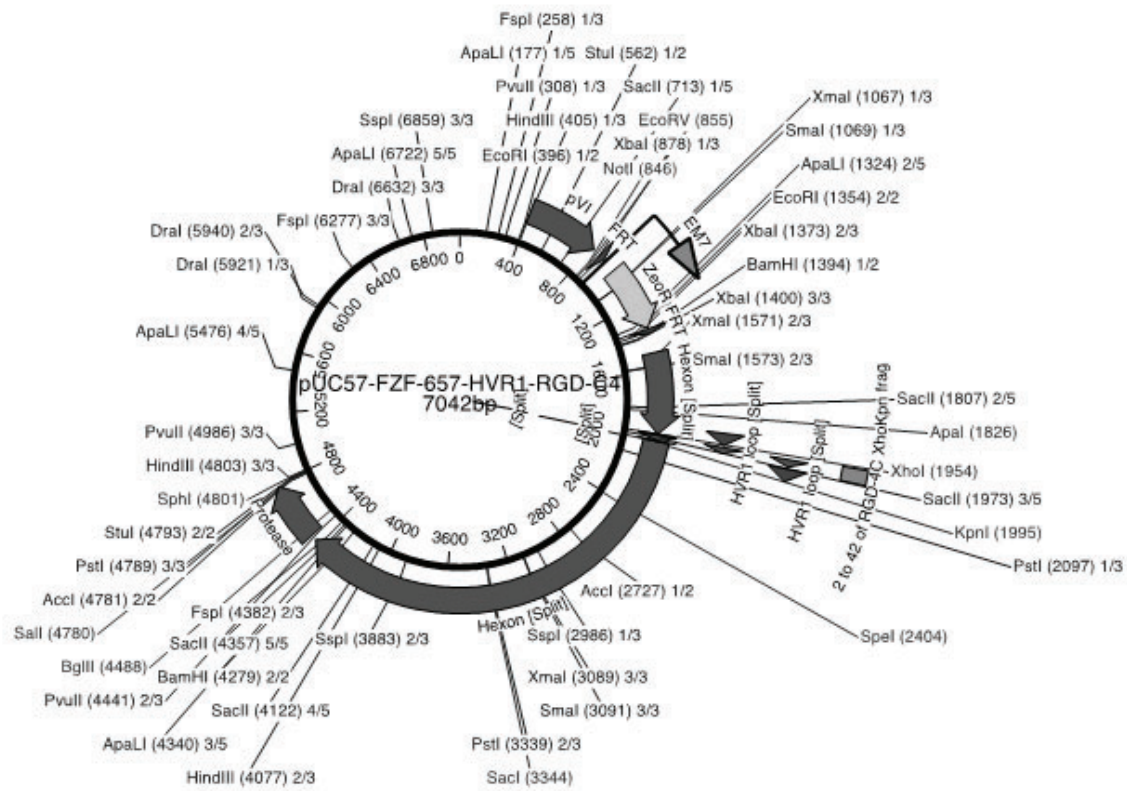


FIG. 34 (continued)

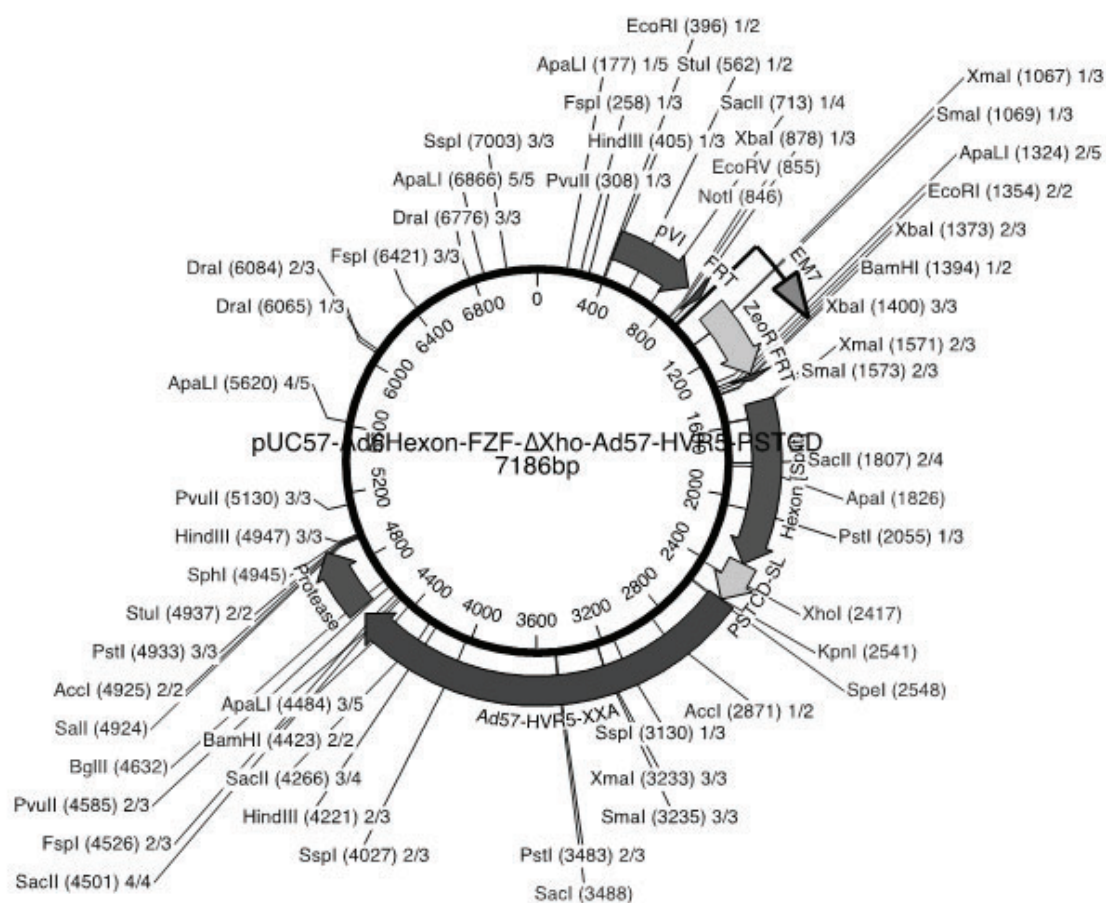


FIG. 34 (continued)

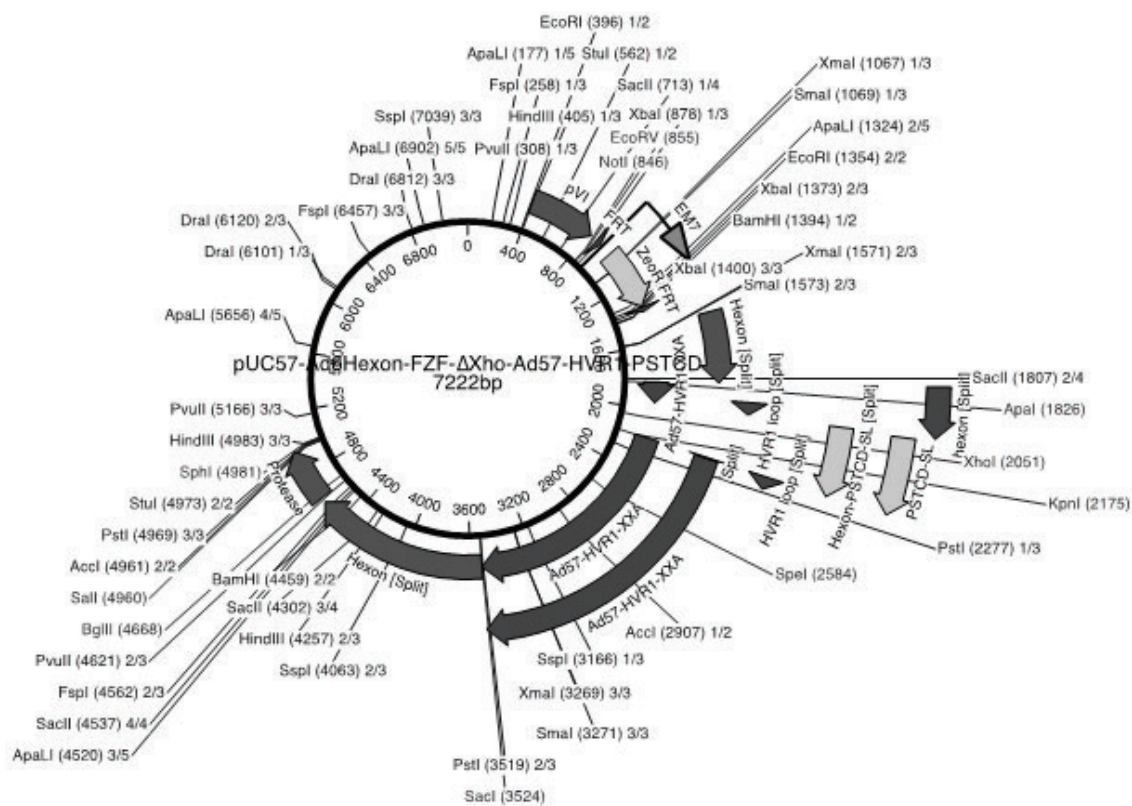


FIG. 34 (continued)

FIG. 34 (continued)

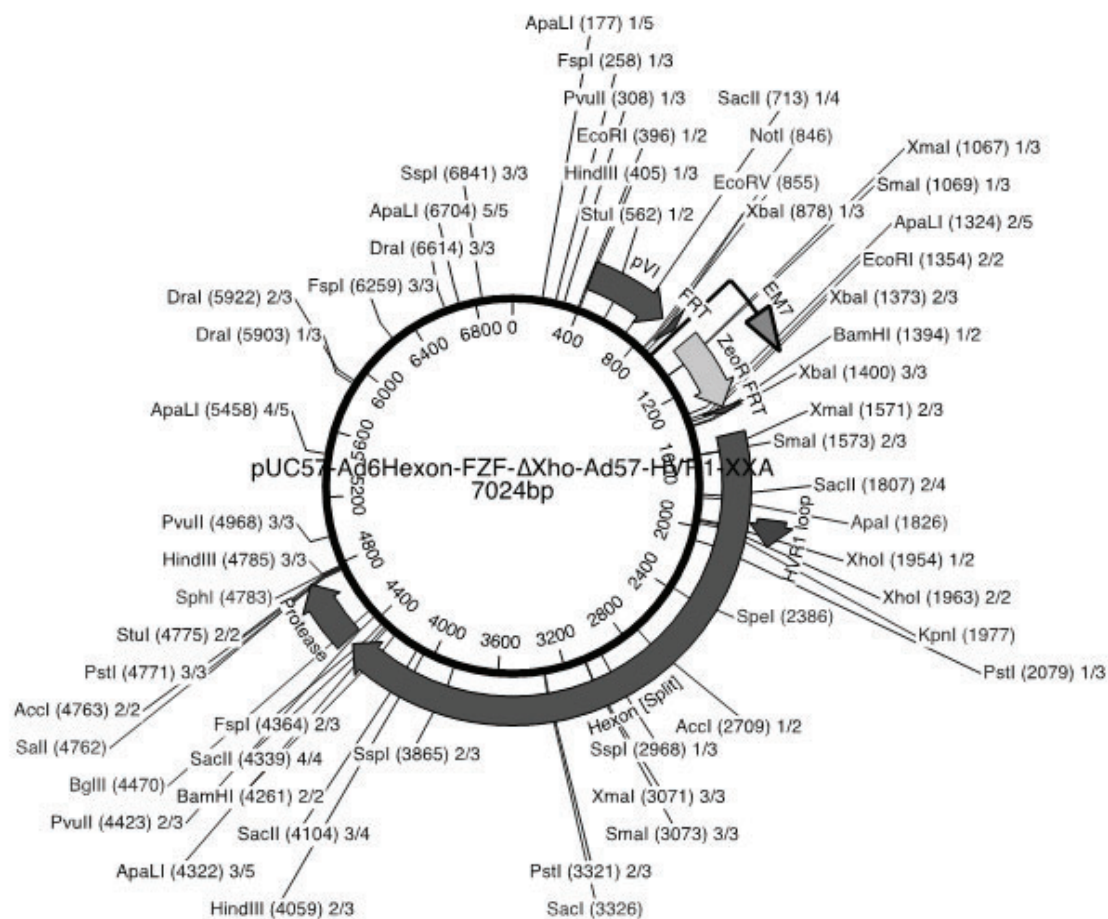


FIG. 34 (continued)

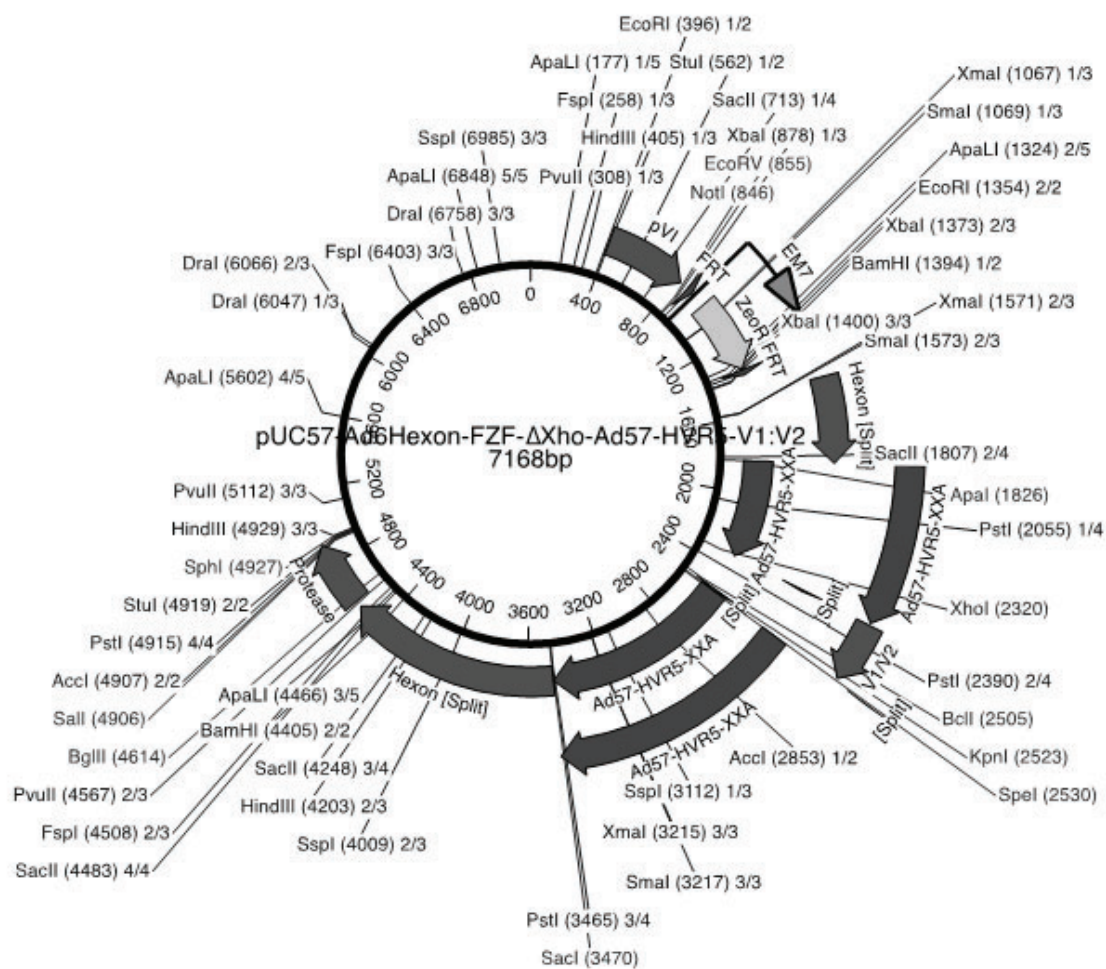


FIG. 34 (continued)

cysteine-insertions into Ad657 HVRs

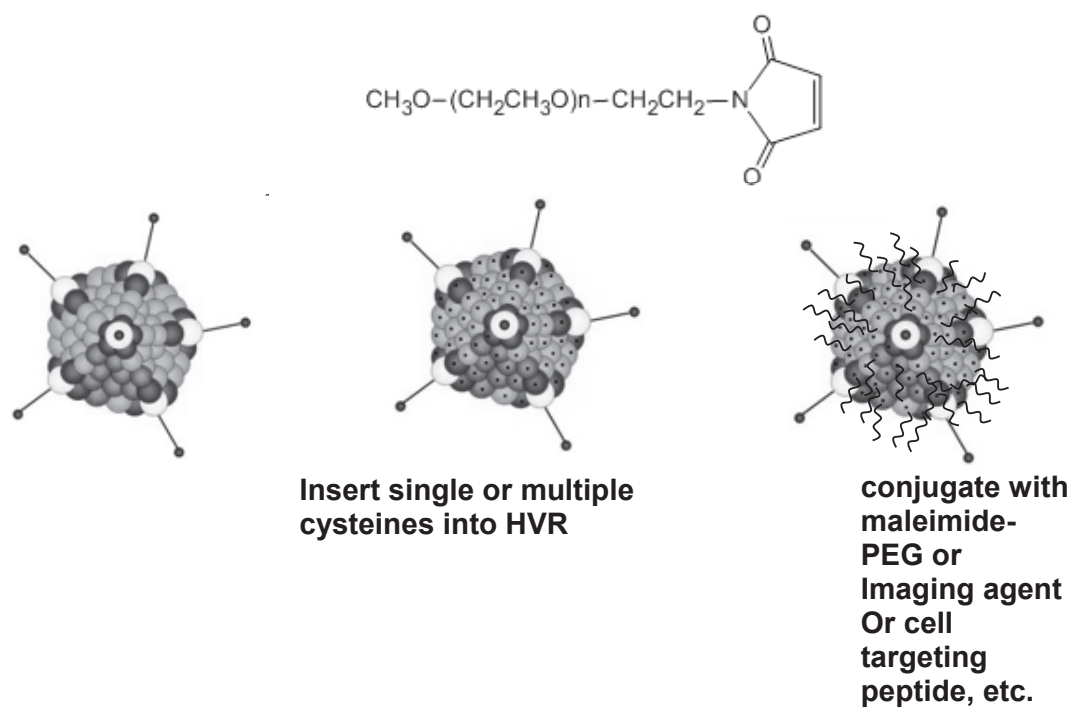
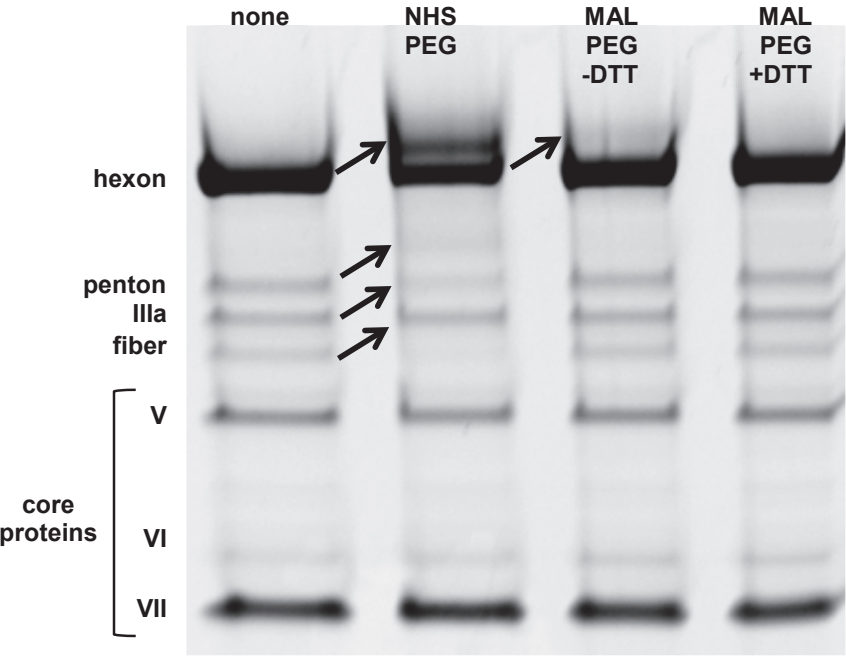


FIG. 35

A



B

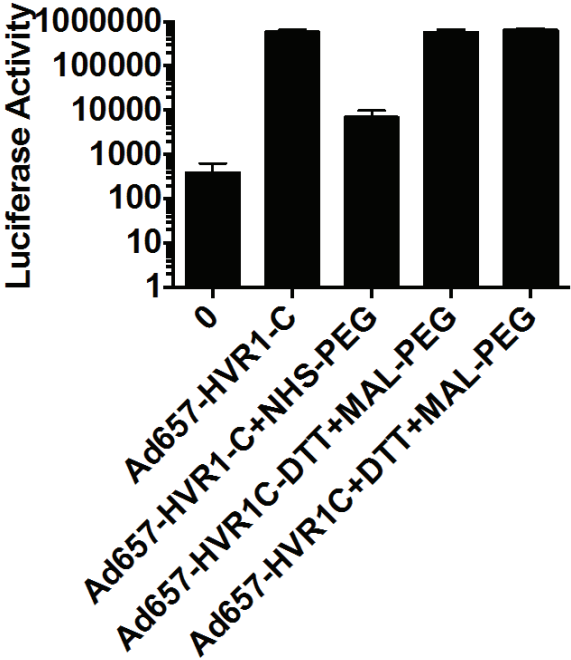


FIG. 36

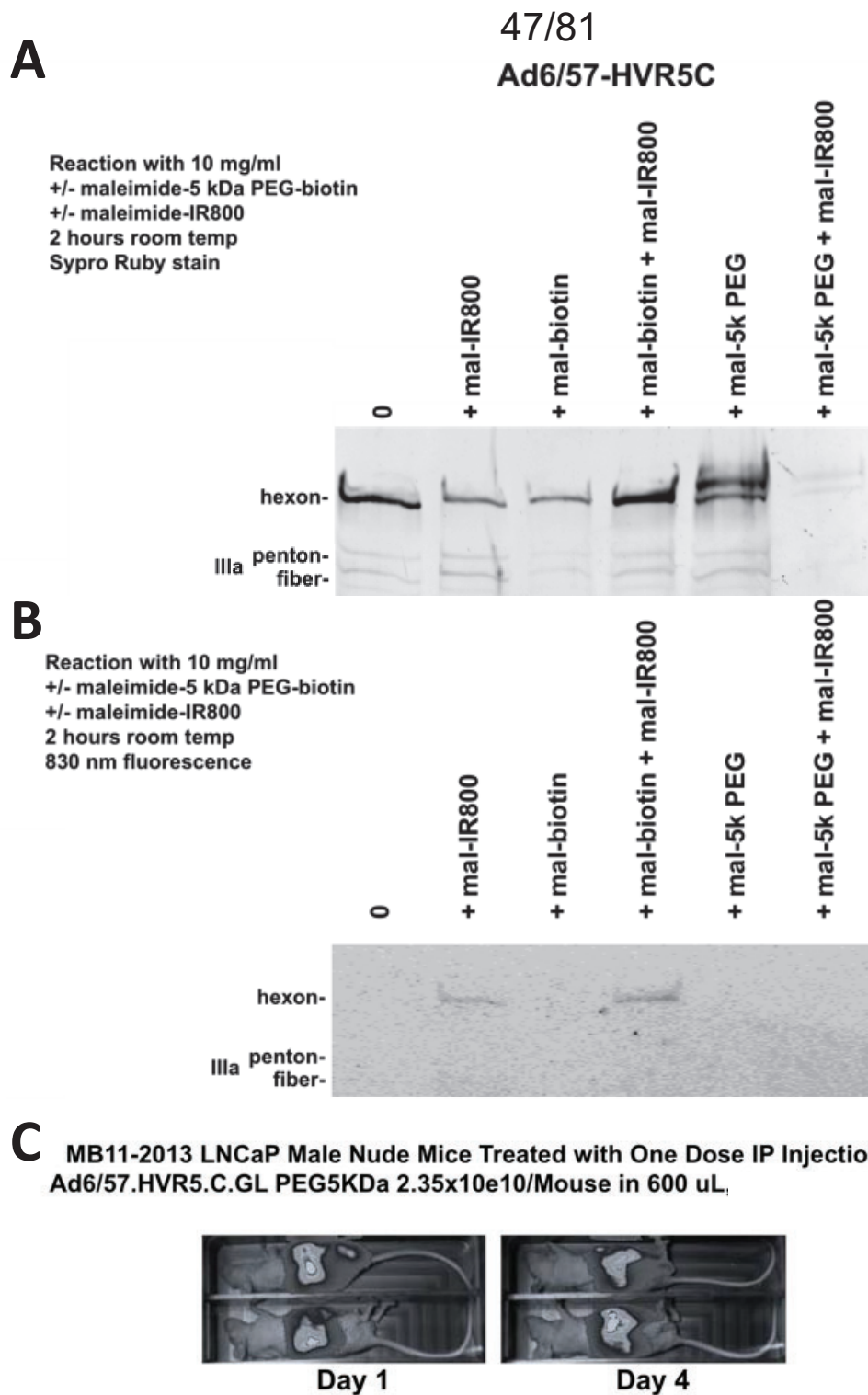


FIG. 37

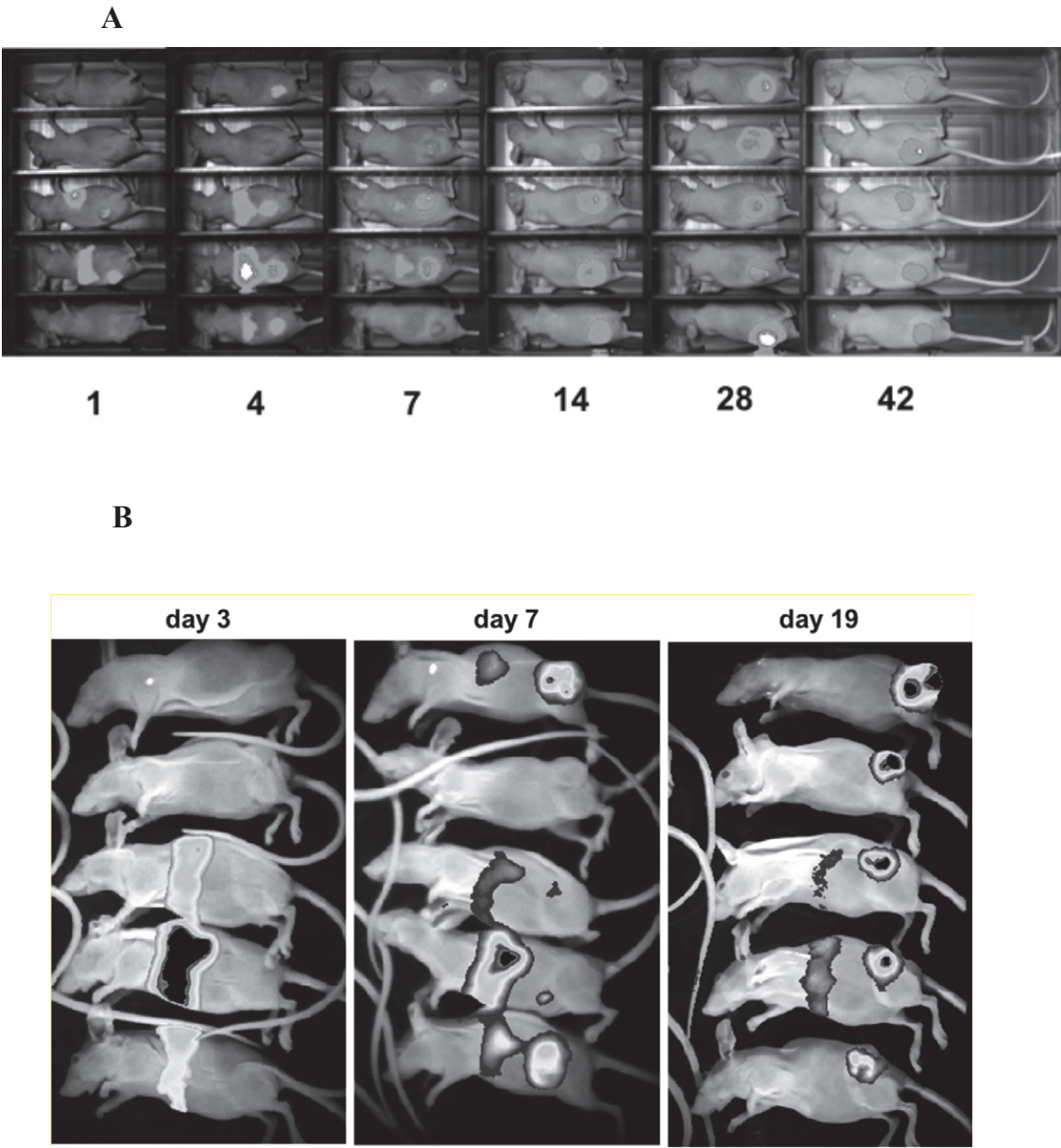


FIG. 38

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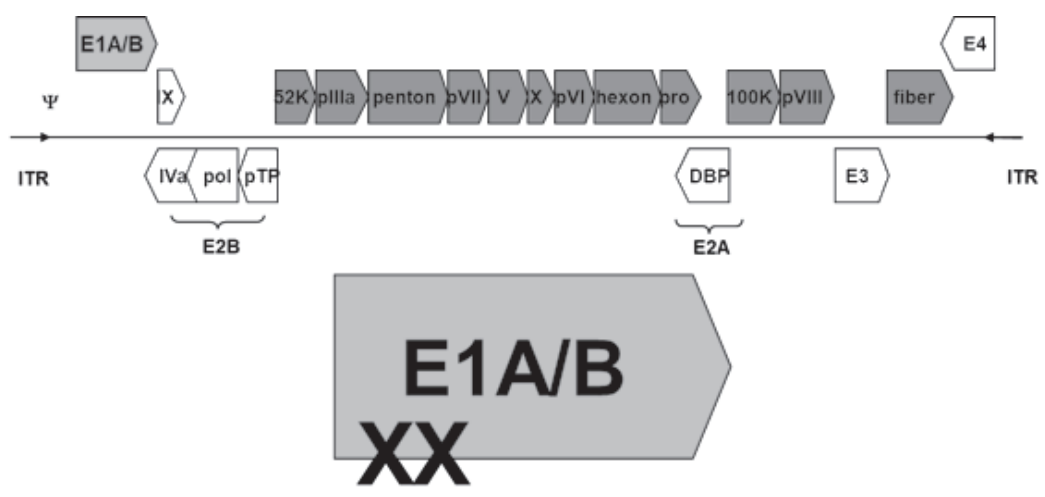


FIG. 39

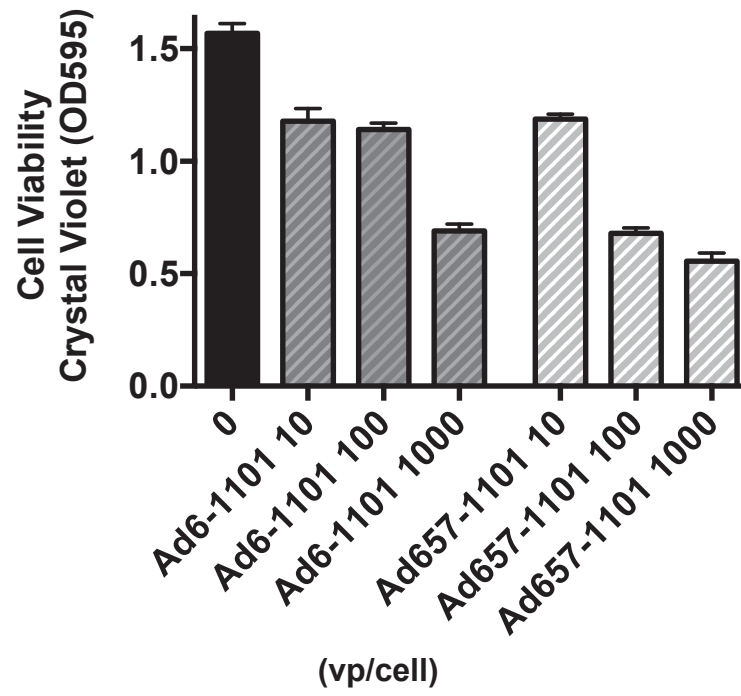


FIG. 40

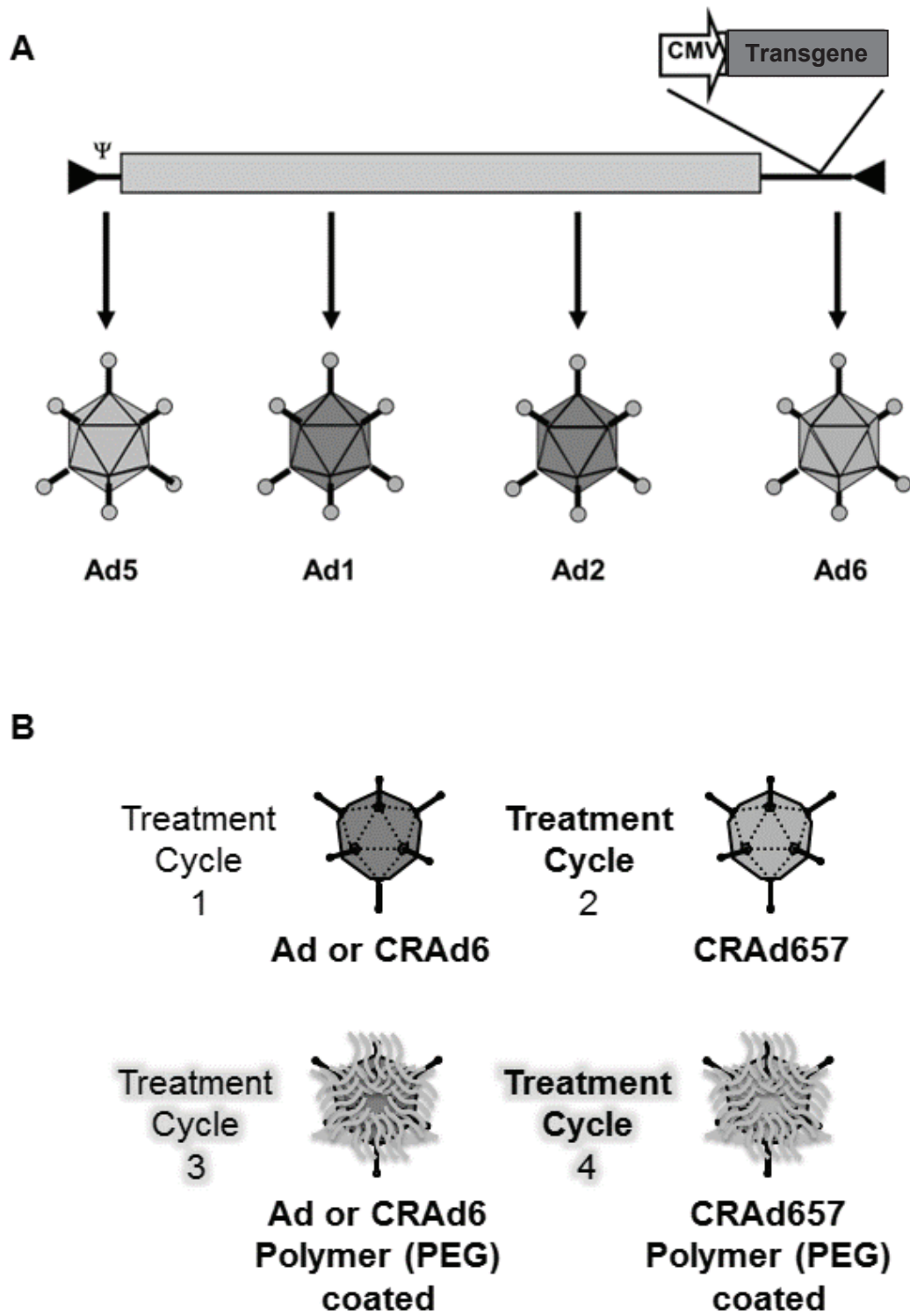


FIG. 41

Prostate Tumor Targeting After Serotype Switching

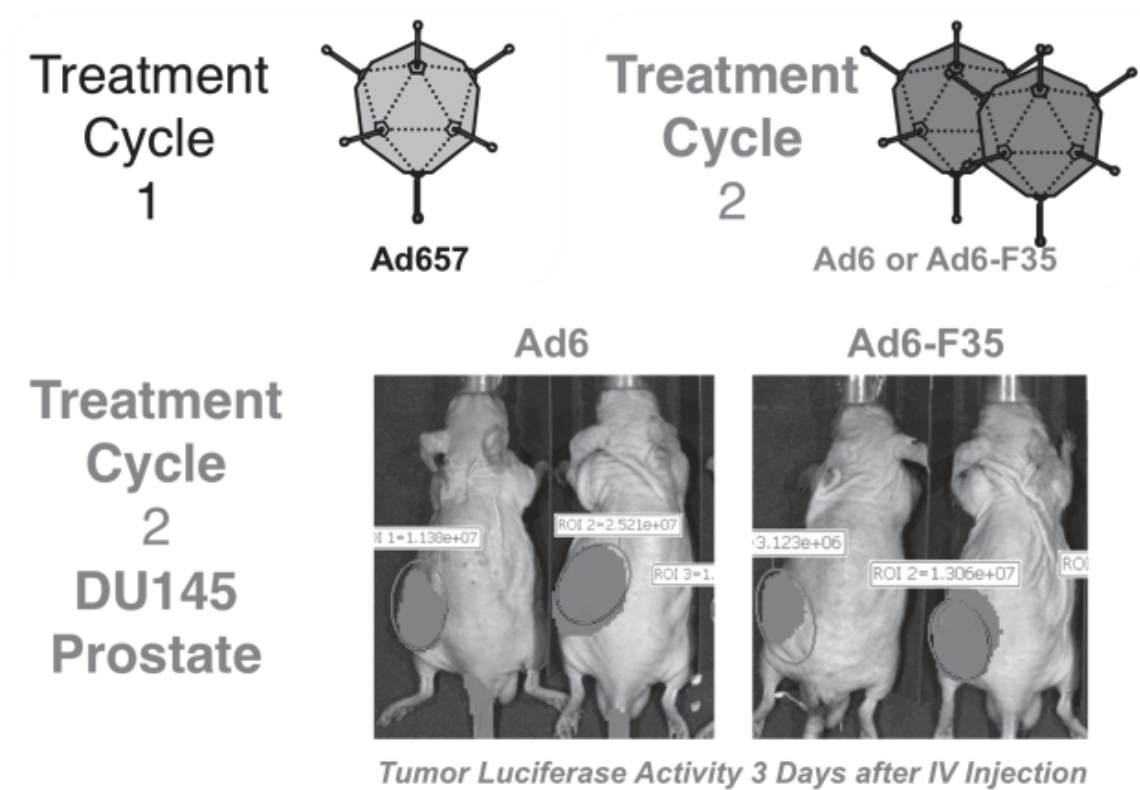


Figure 42

RC-Ad

E1 expression controlled by native E1 promoter

CRAd-Probasin-E1A (Ad-PB)

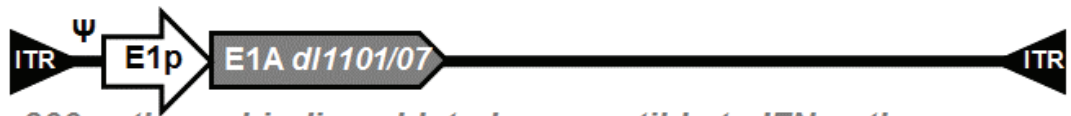
*E1 expression
controlled by prostate-specific probasin promoter*

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.*

Figure 43

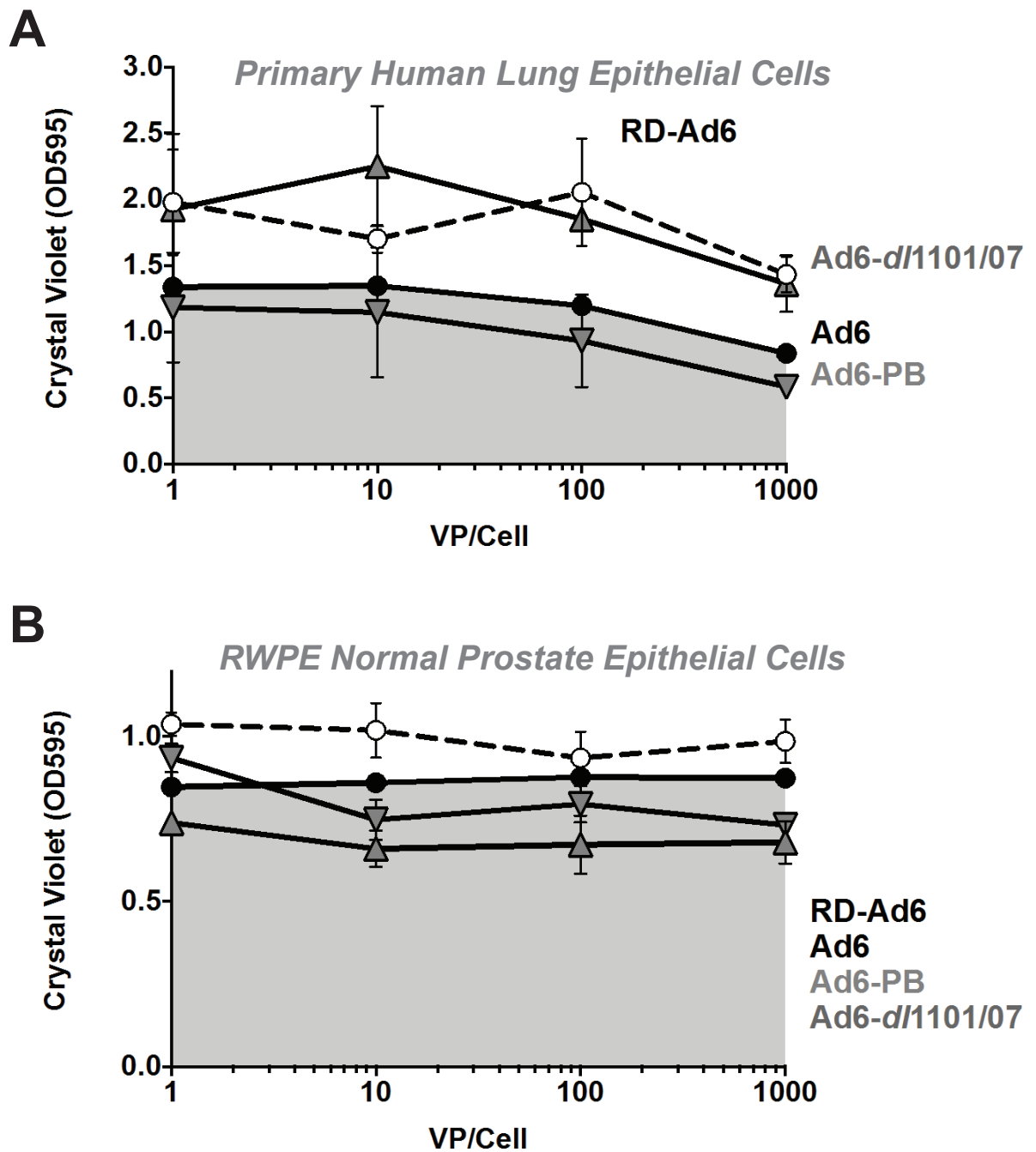


Figure 44

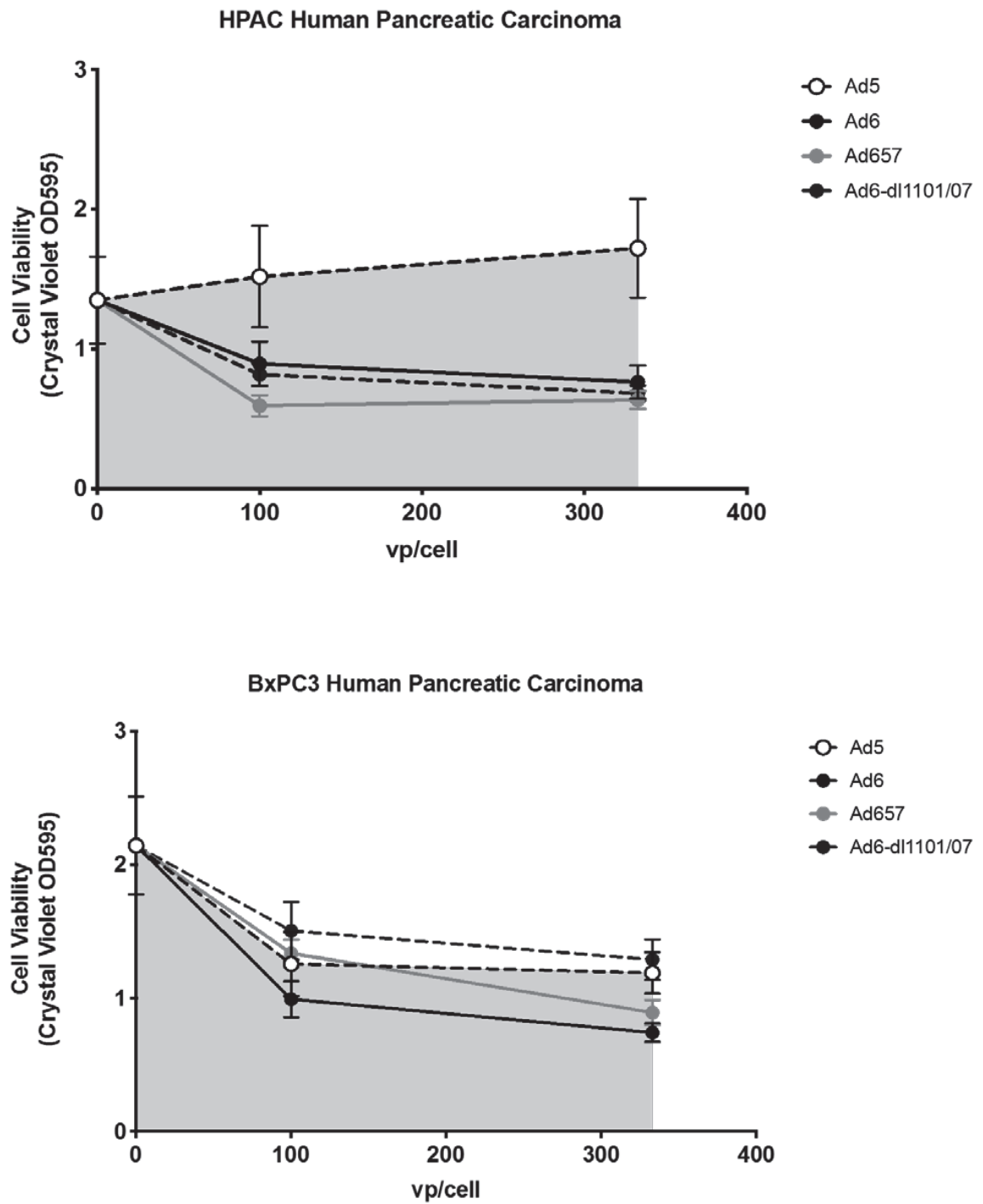


FIGURE 45

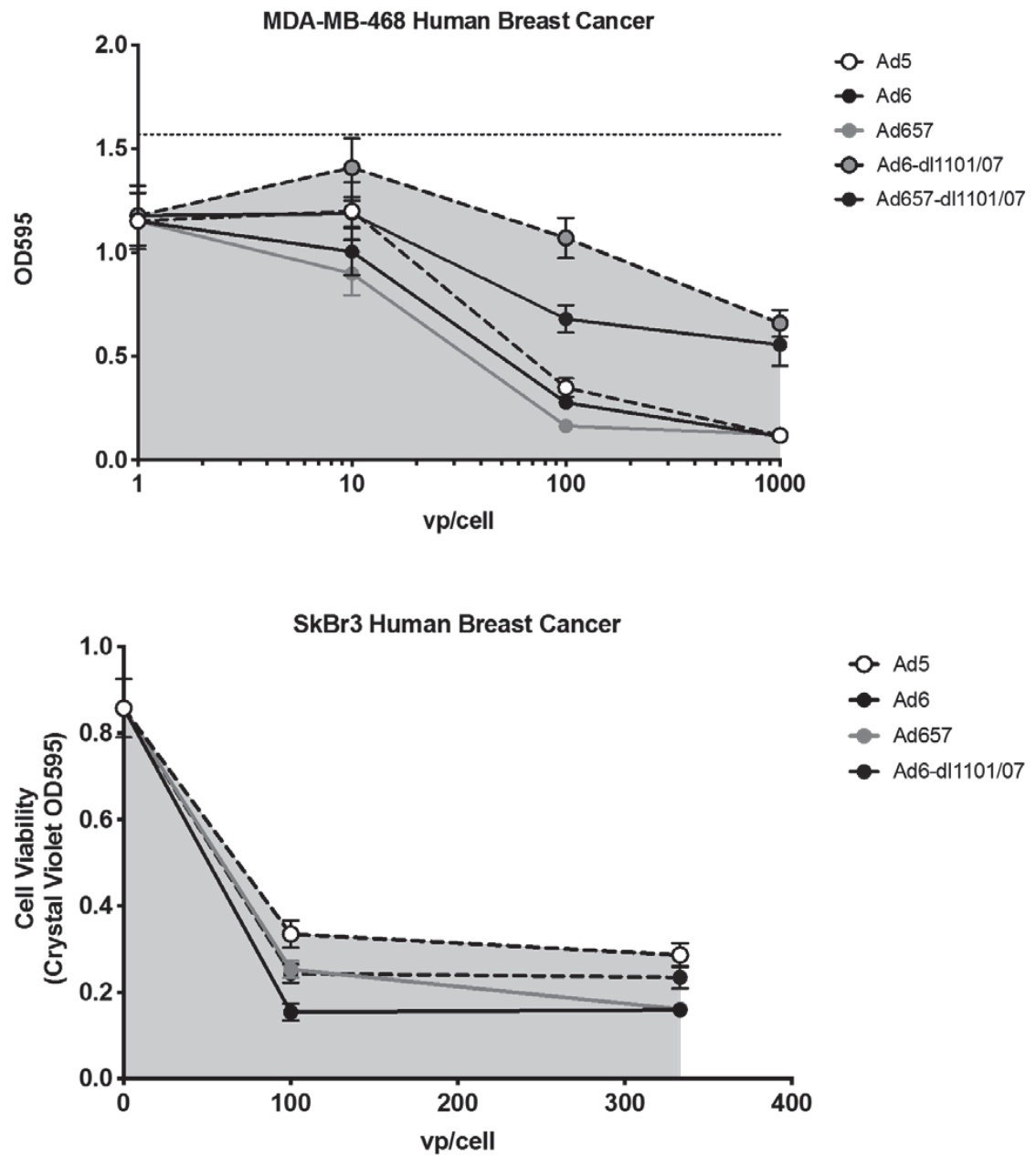


Figure 46

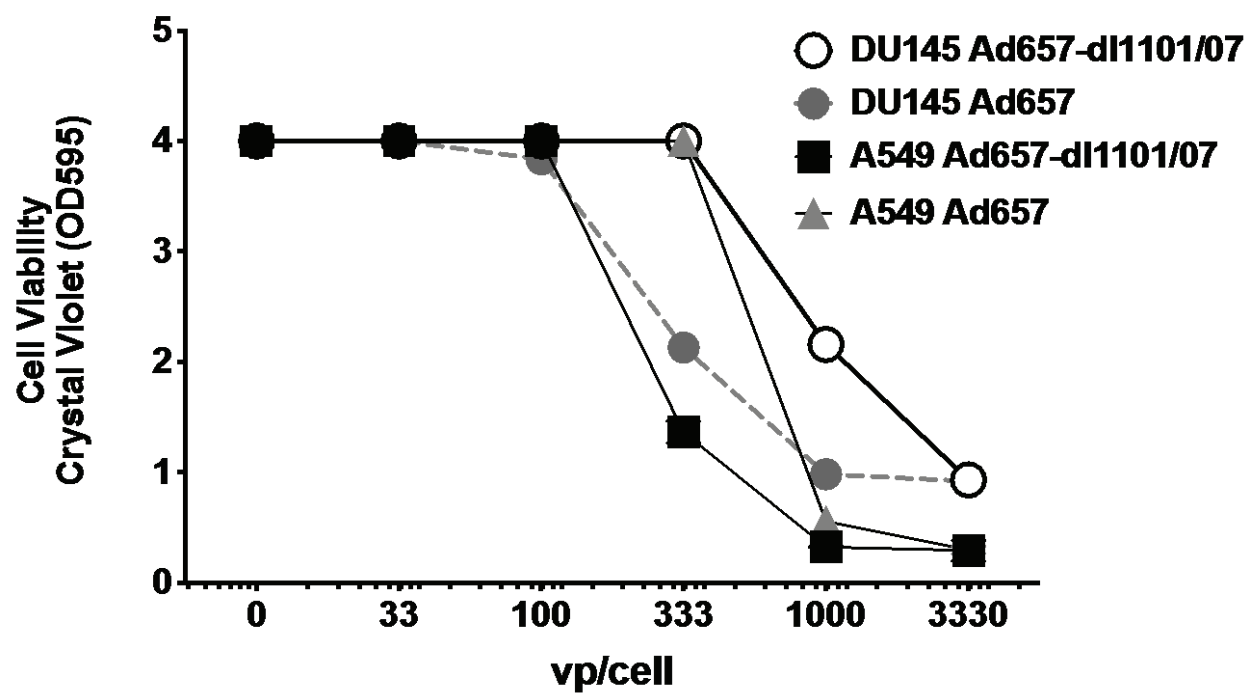


Figure 47

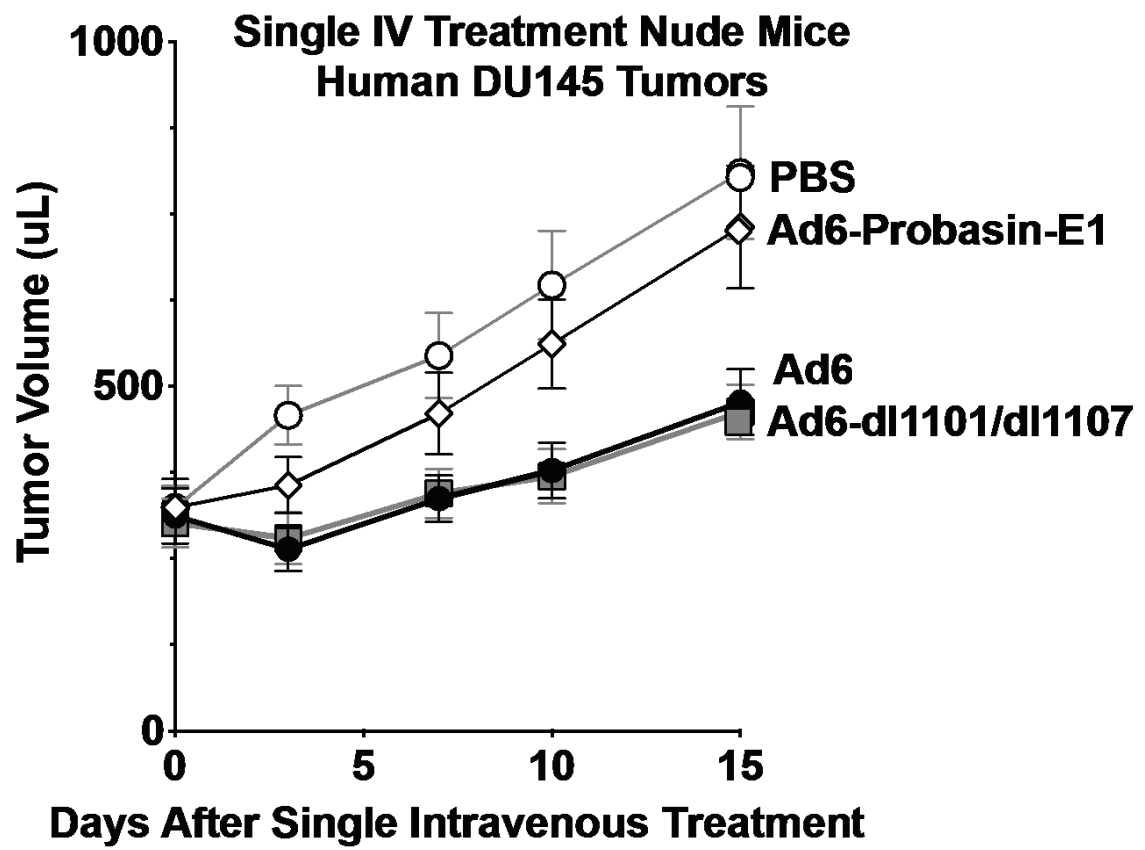


Figure 48

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DU145 Ad Single IV Treatment Survival

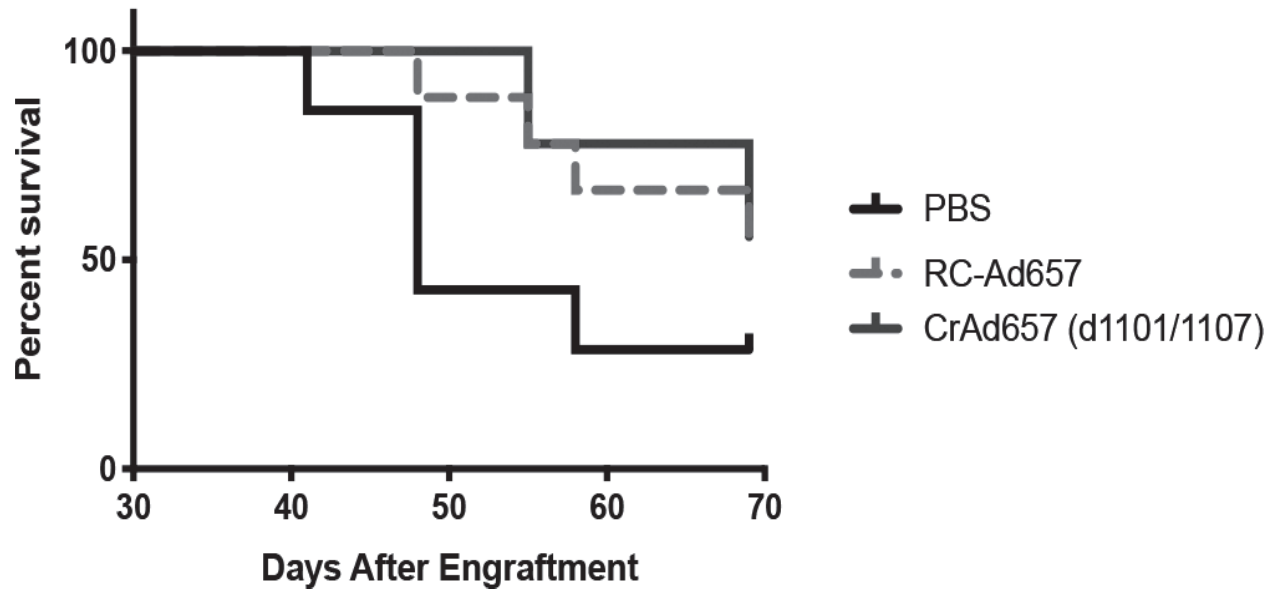
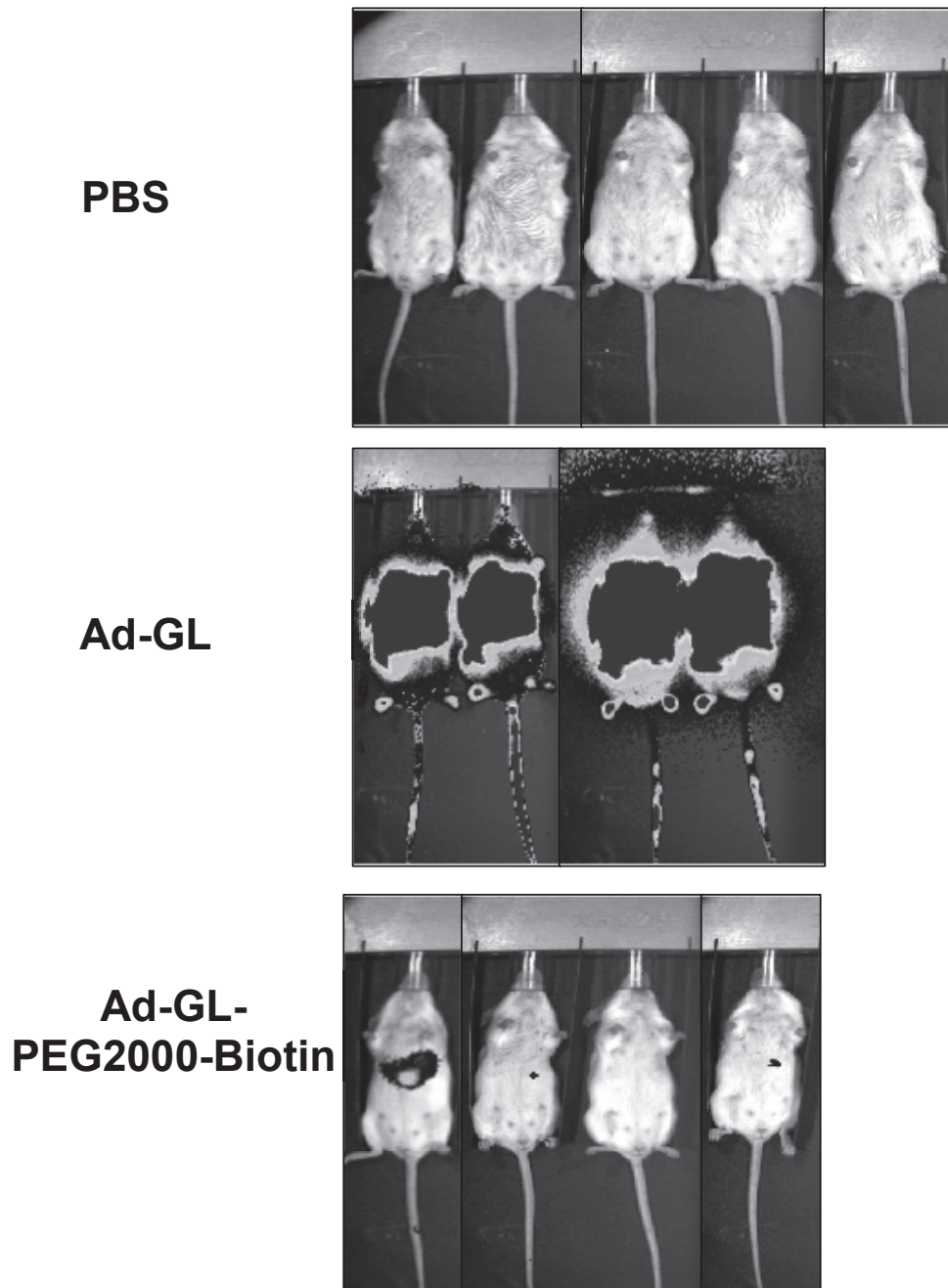


Figure 49

Figure 50

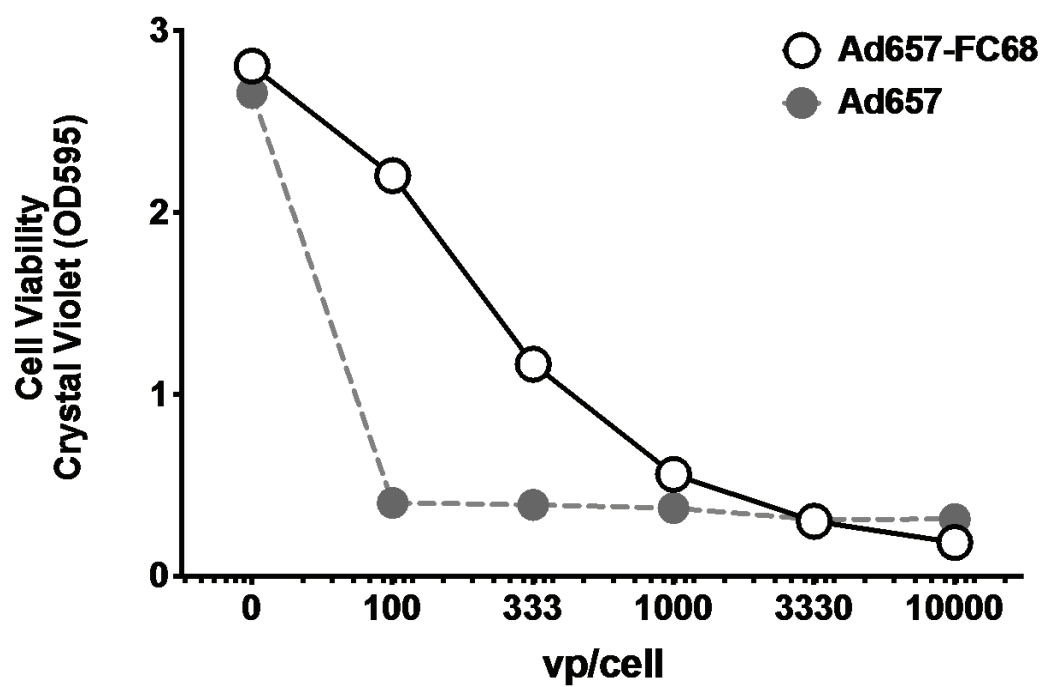


Figure 51

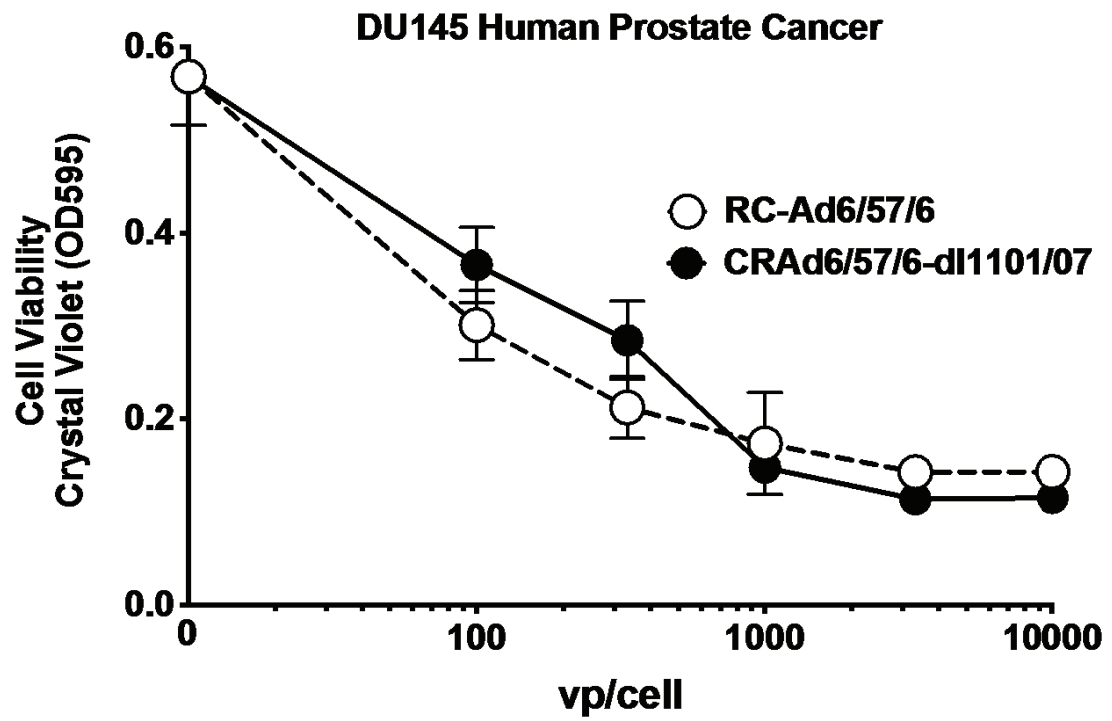


Figure 52

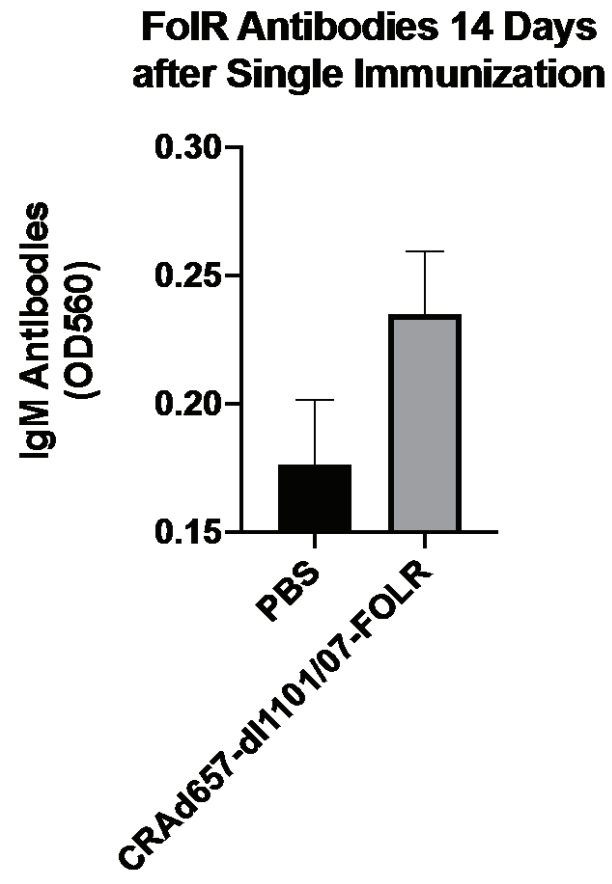


Figure 53

Figure 54

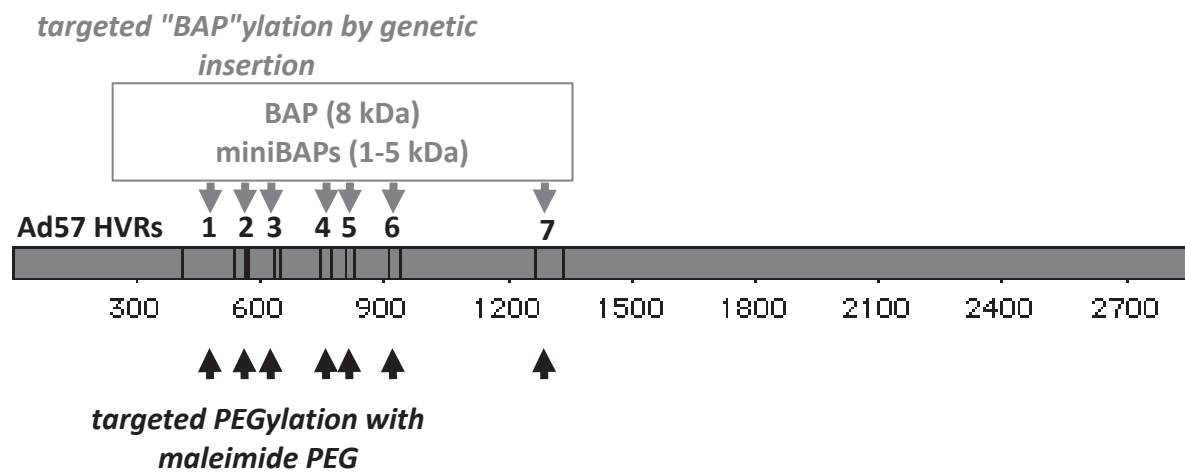
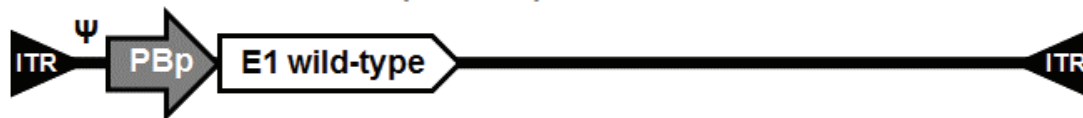


Figure 55

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

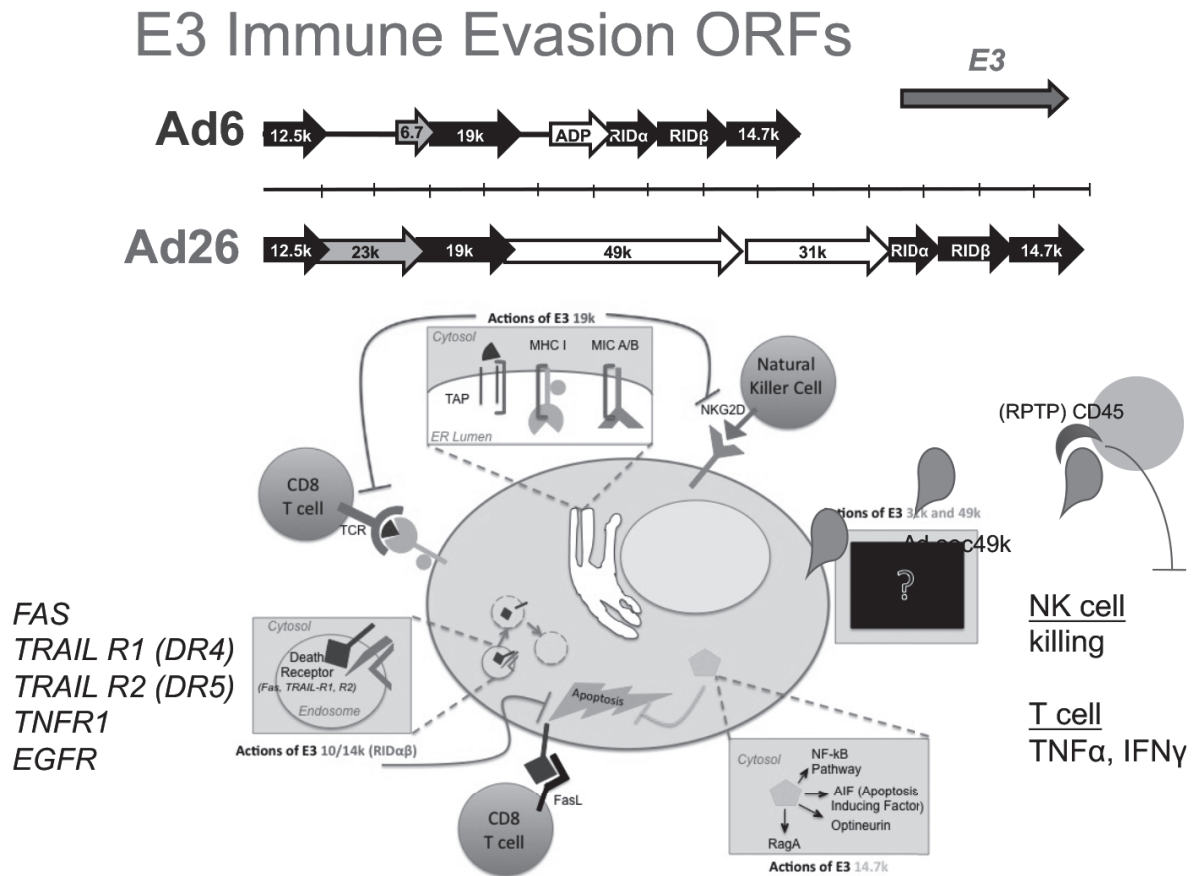
MRHIICHGGVITEEMAASLLDQLIEEV LADNLPPPSHFEPPTLHEL YDLDVT
APEDPNEEAVSQIFPESV MLAVQEGIDLFTFPPAPGSPEPPHLSRQPEQP
EQRALGPVCHEAGFPPS (SEQ ID NO:44)

E1A dl1101/1107 N-terminus

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

Figure 56

Figure 57



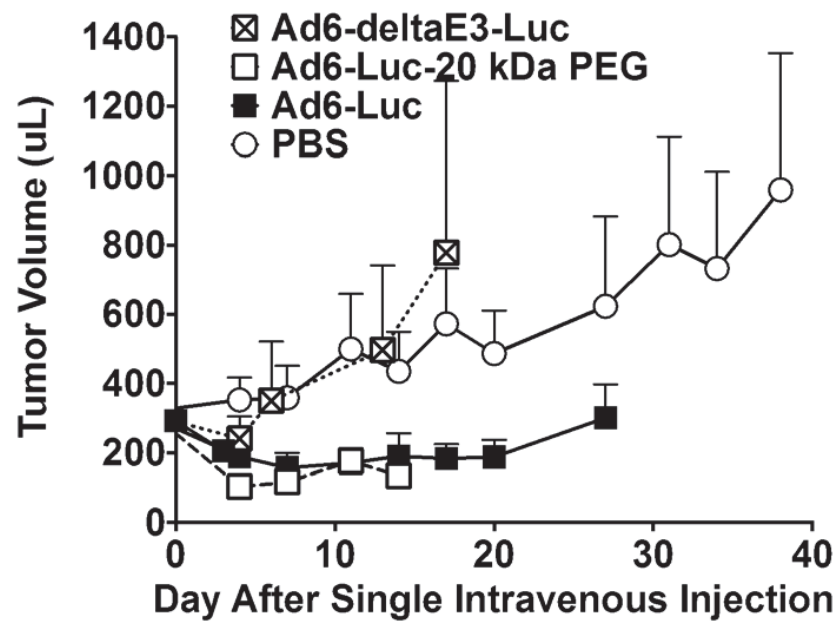
Ad6-Luc Viruses in Immunocompetent Hamsters

Figure 58

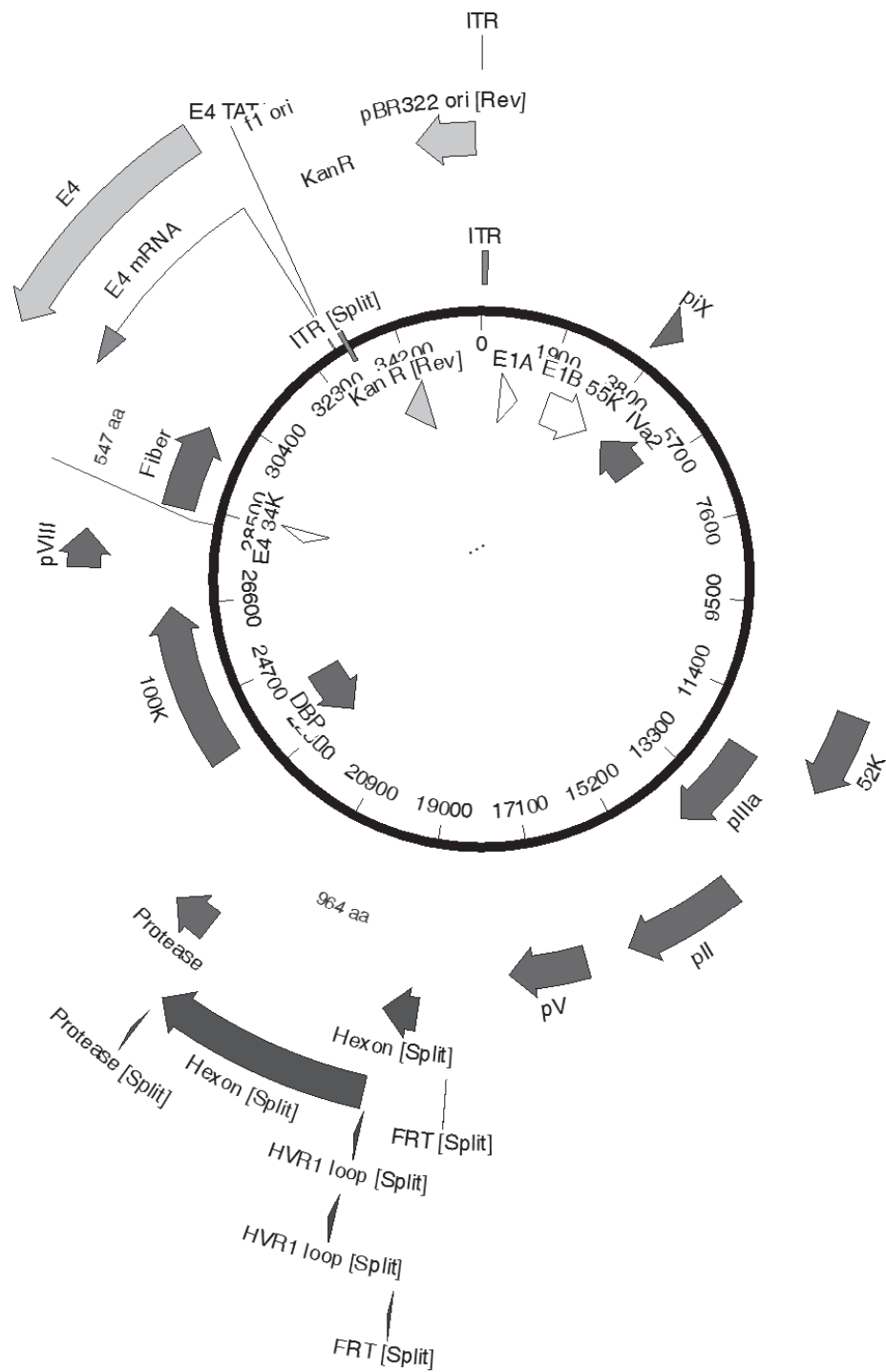


Figure 59

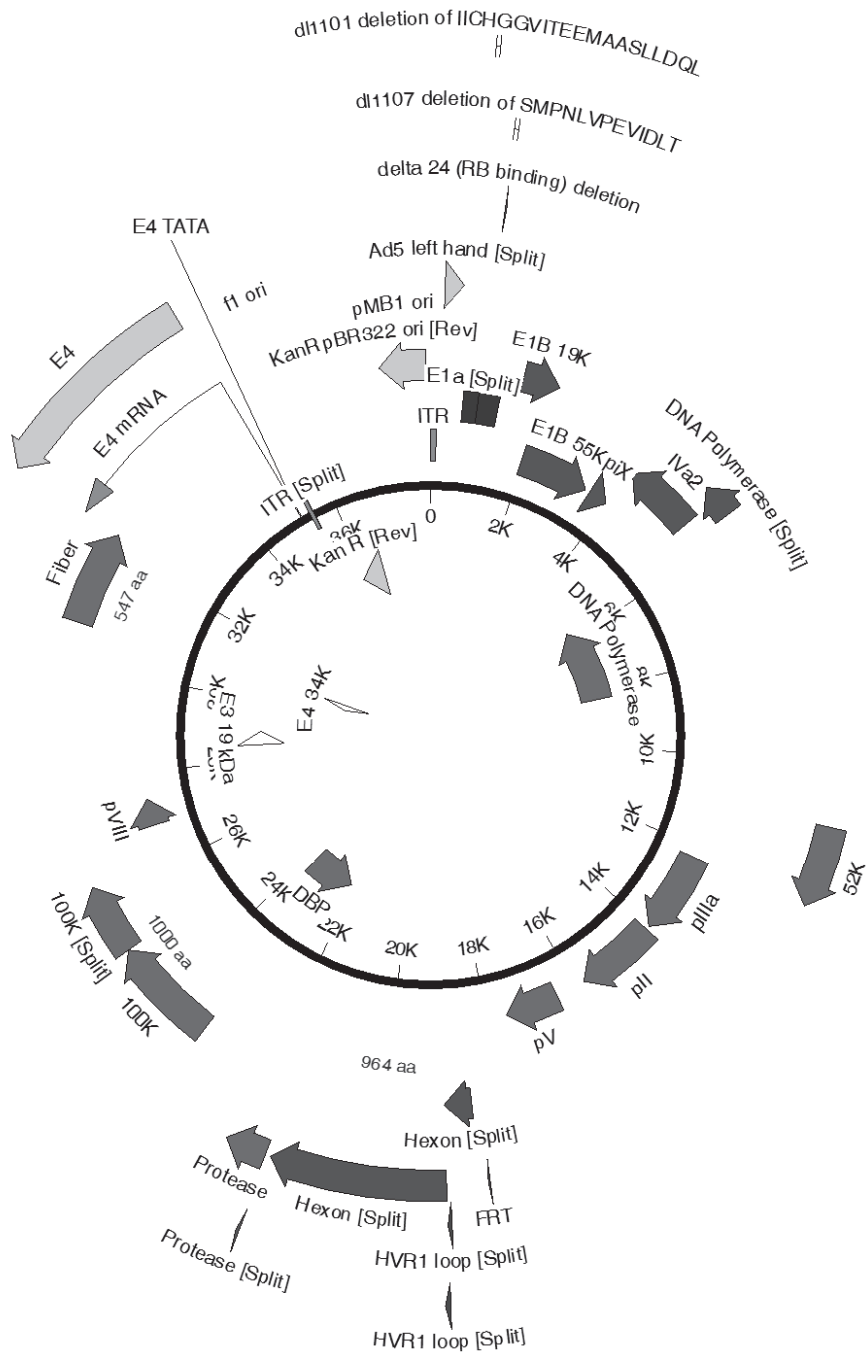


Figure 60

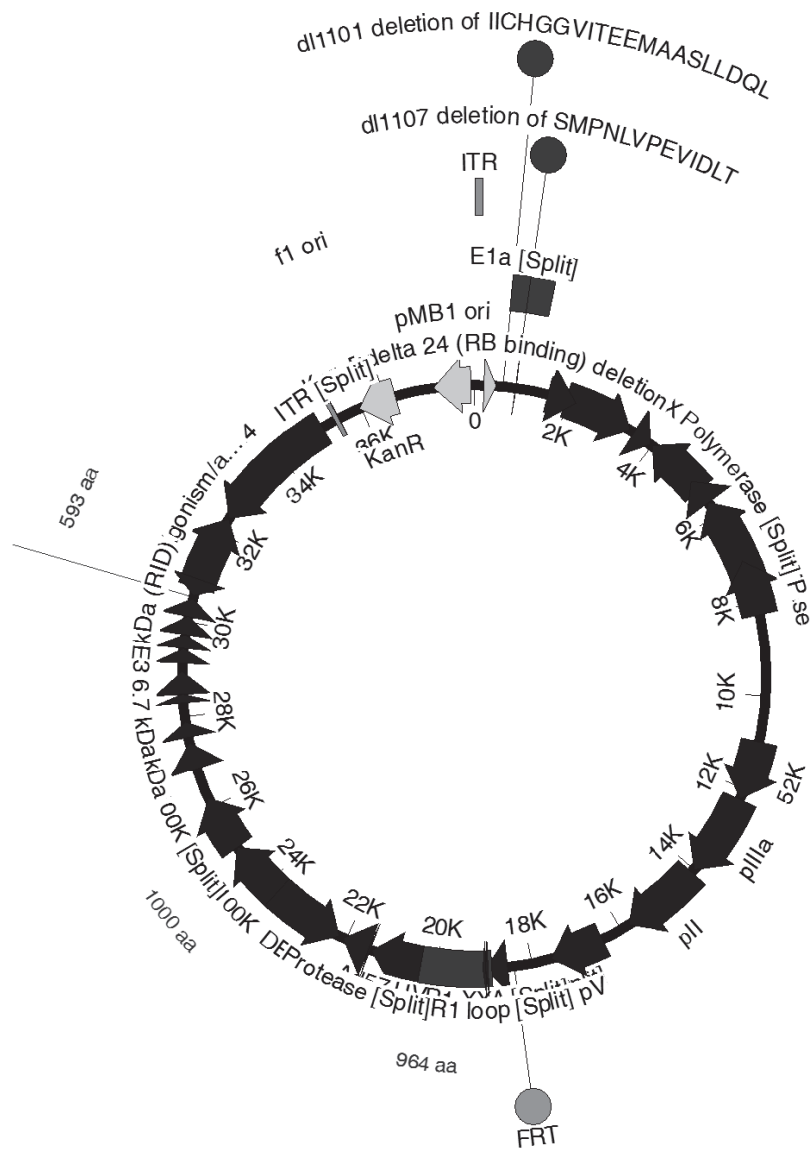


Figure 61

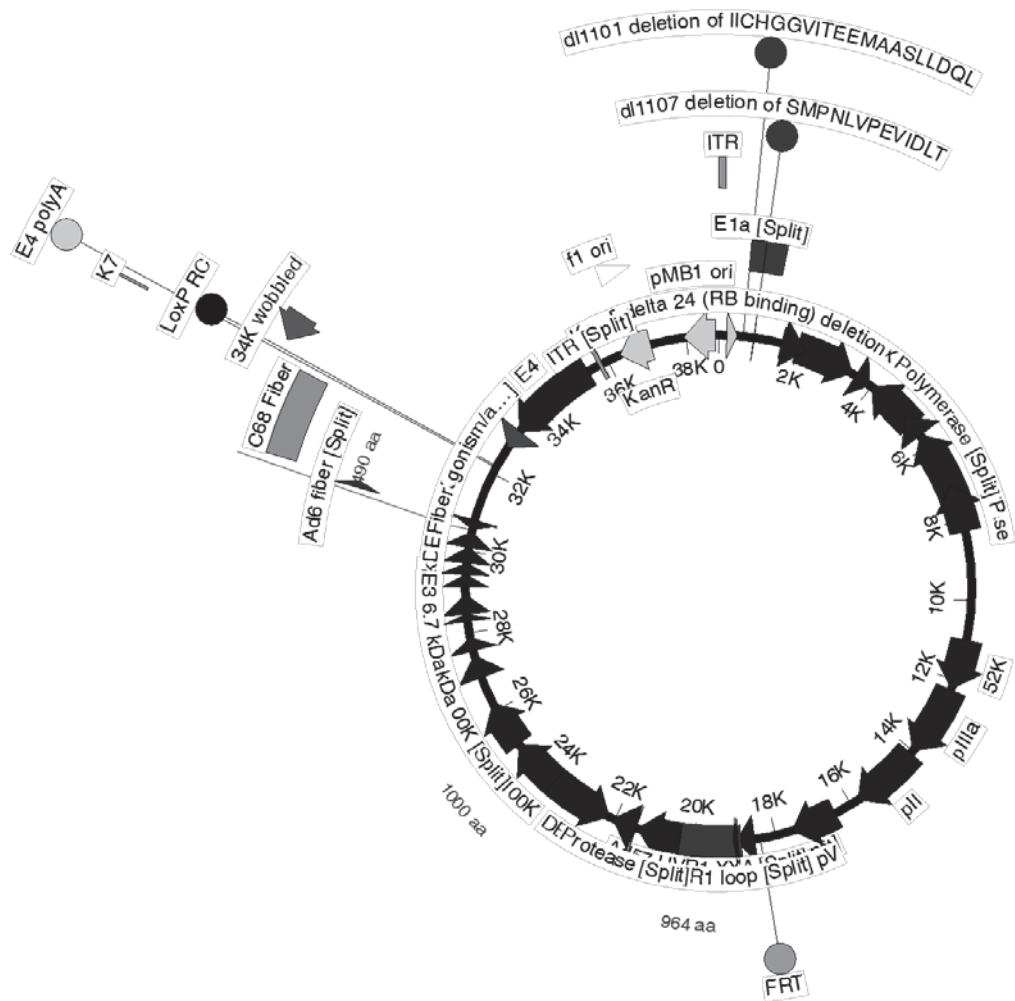


Figure 62

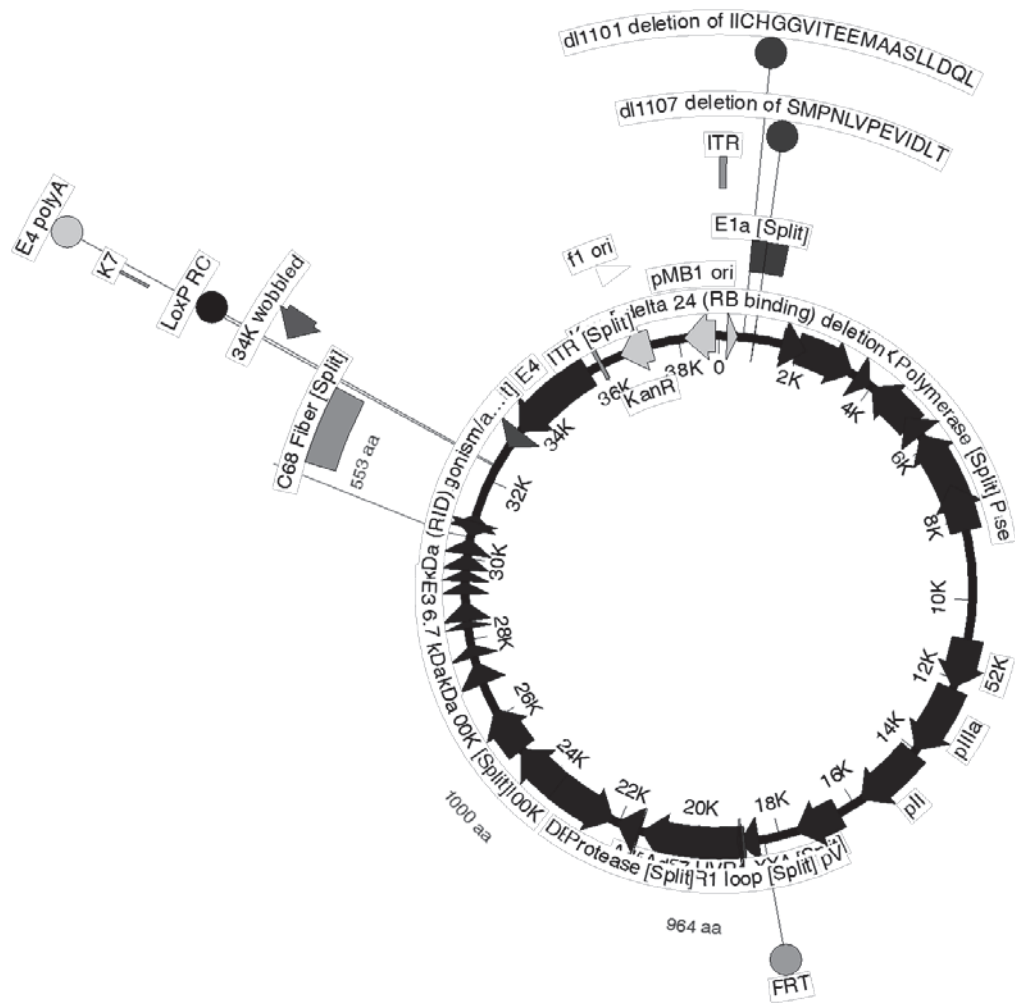


Figure 63

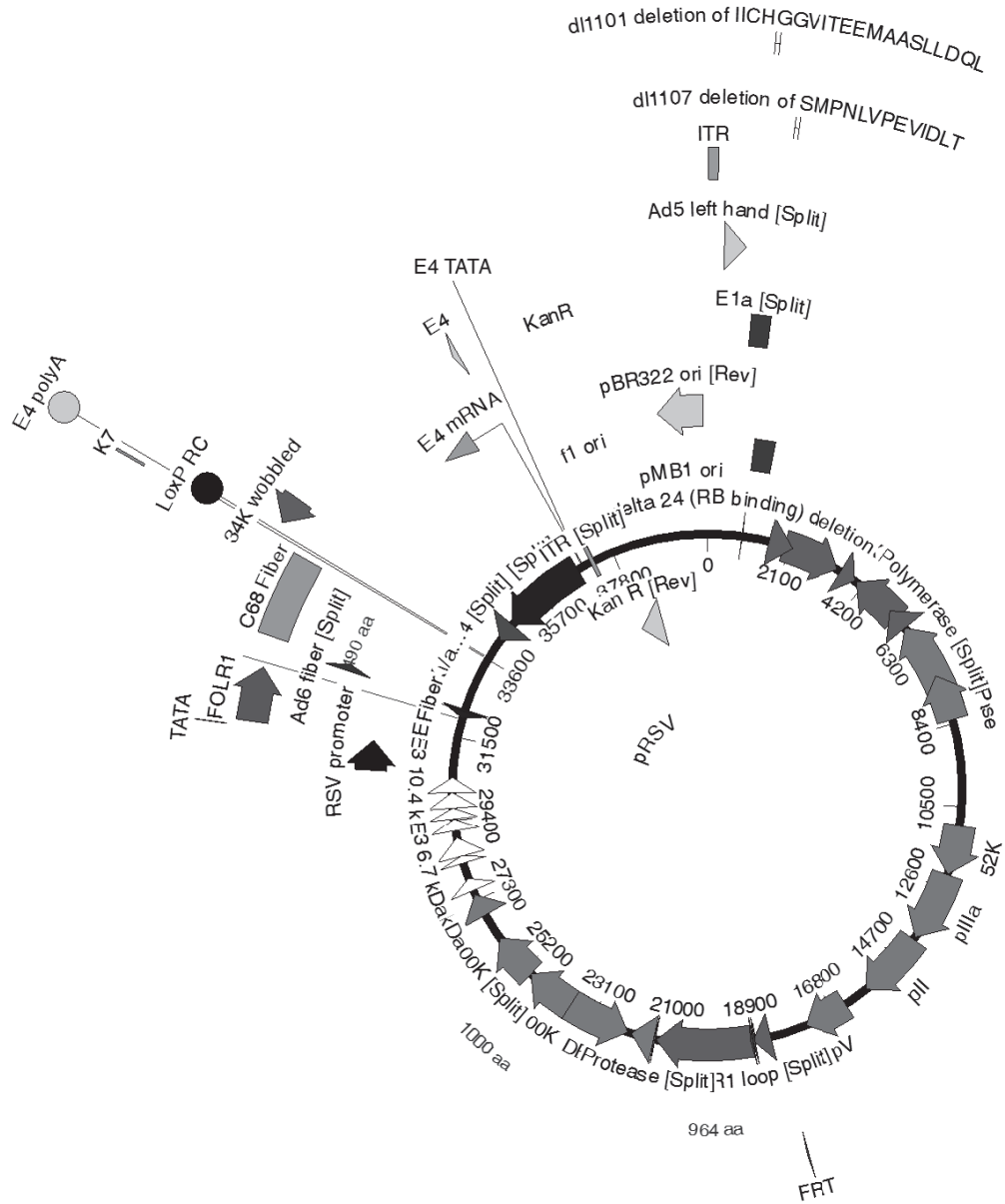


Figure 64

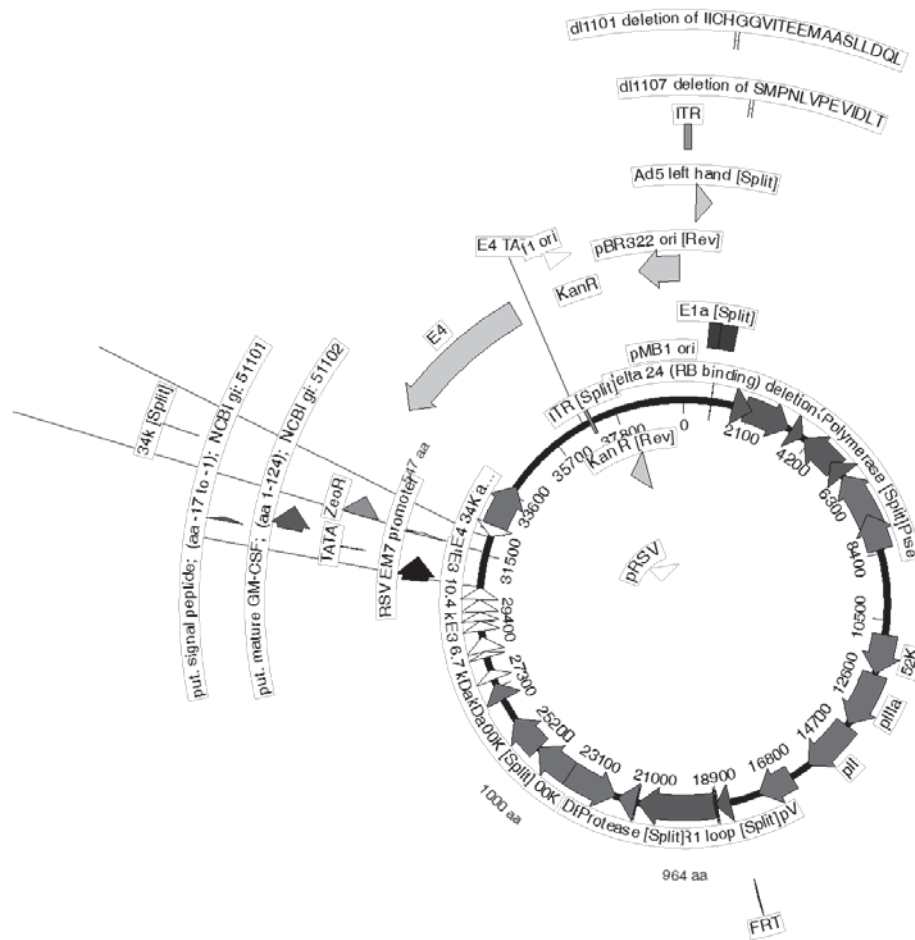


Figure 65

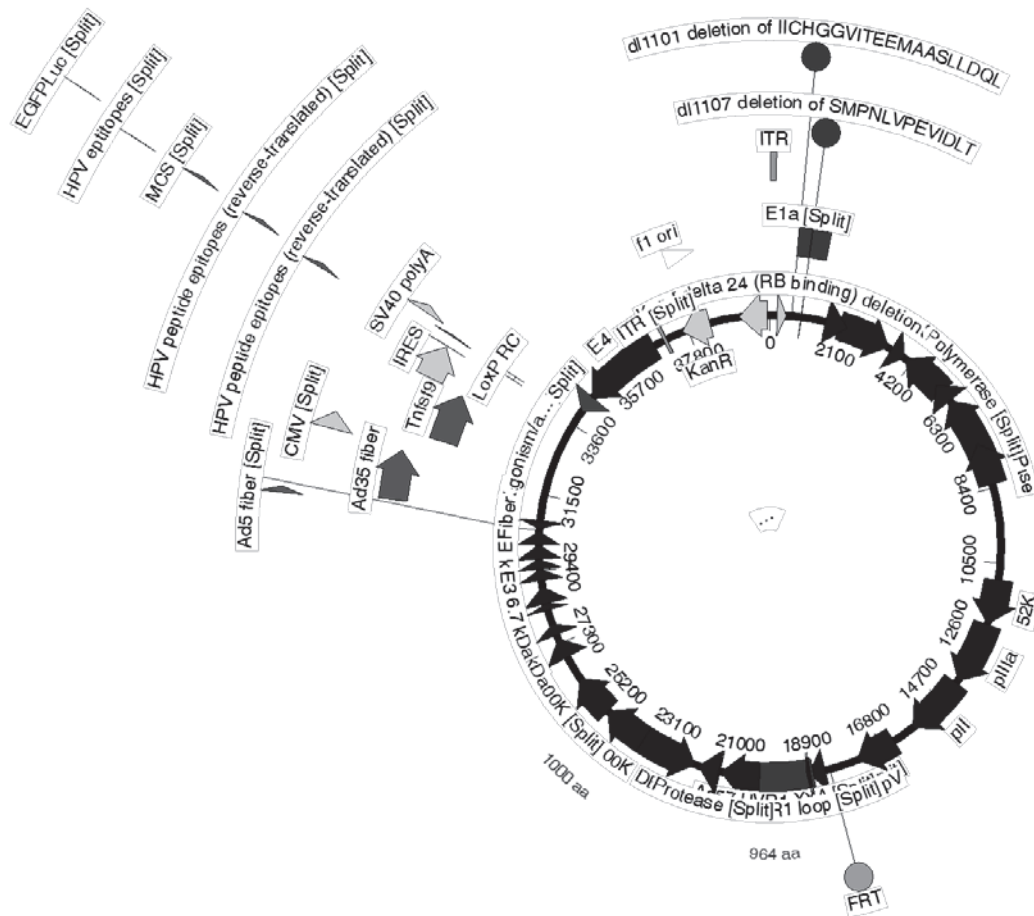


Figure 66

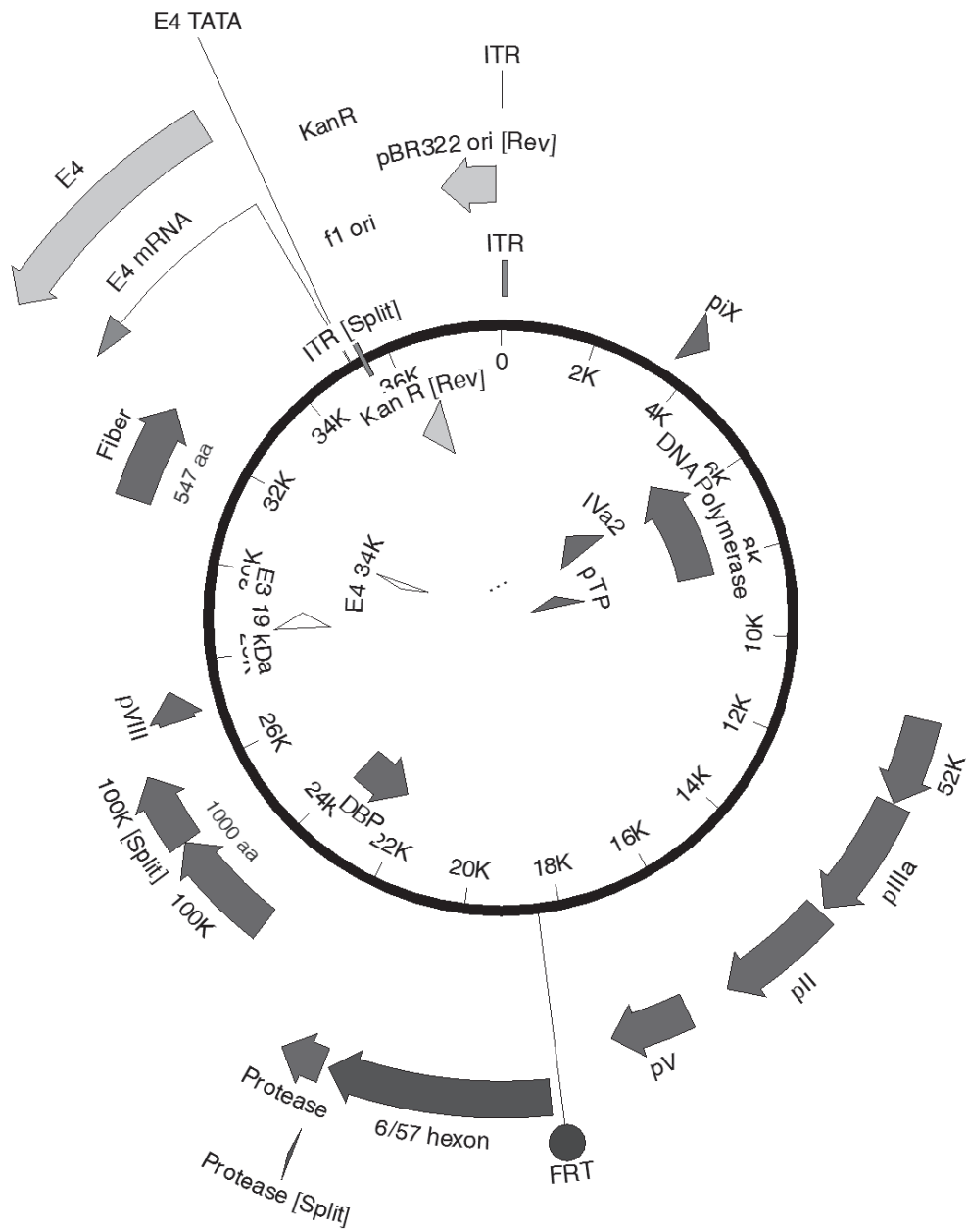


Figure 67

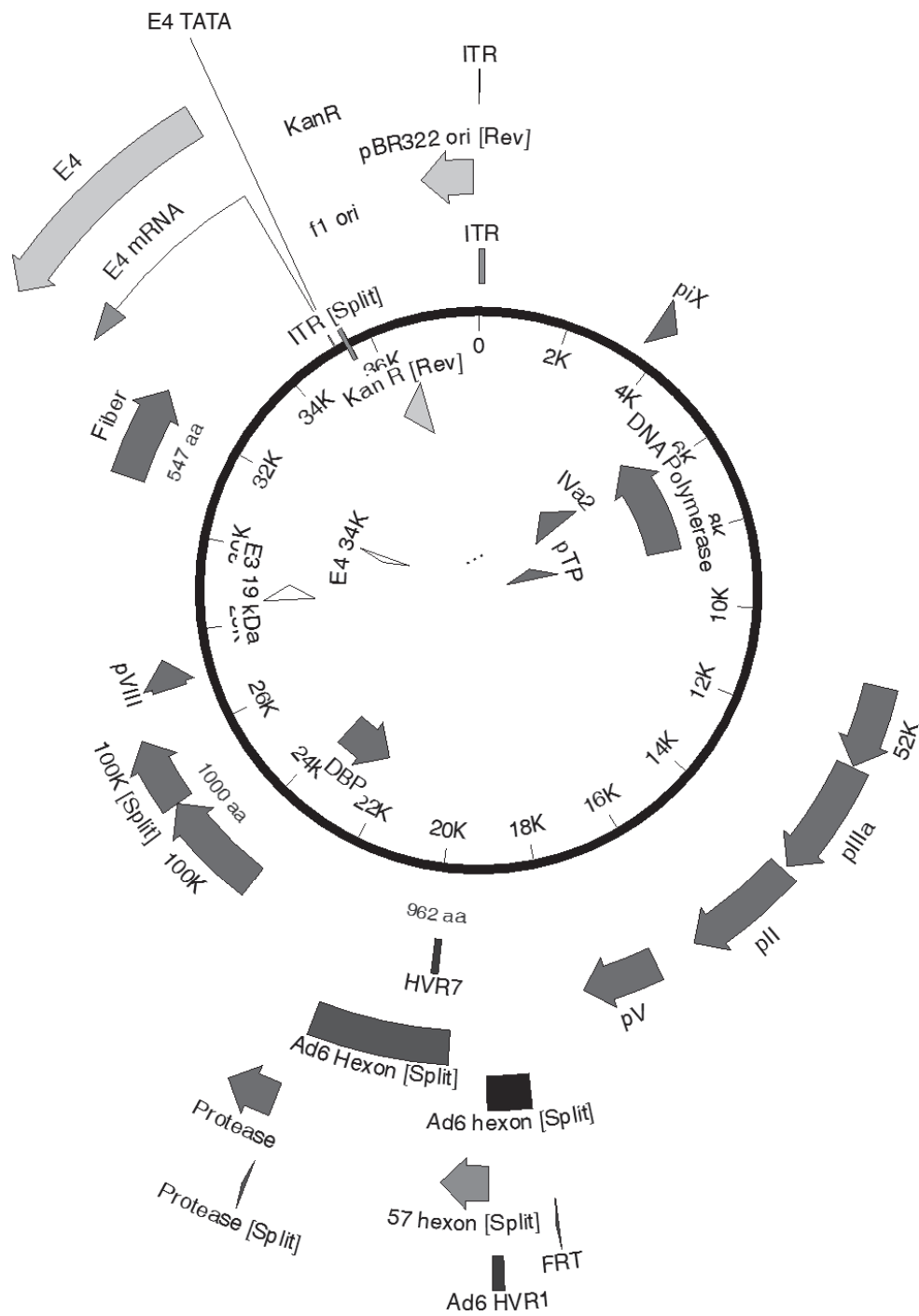


Figure 68

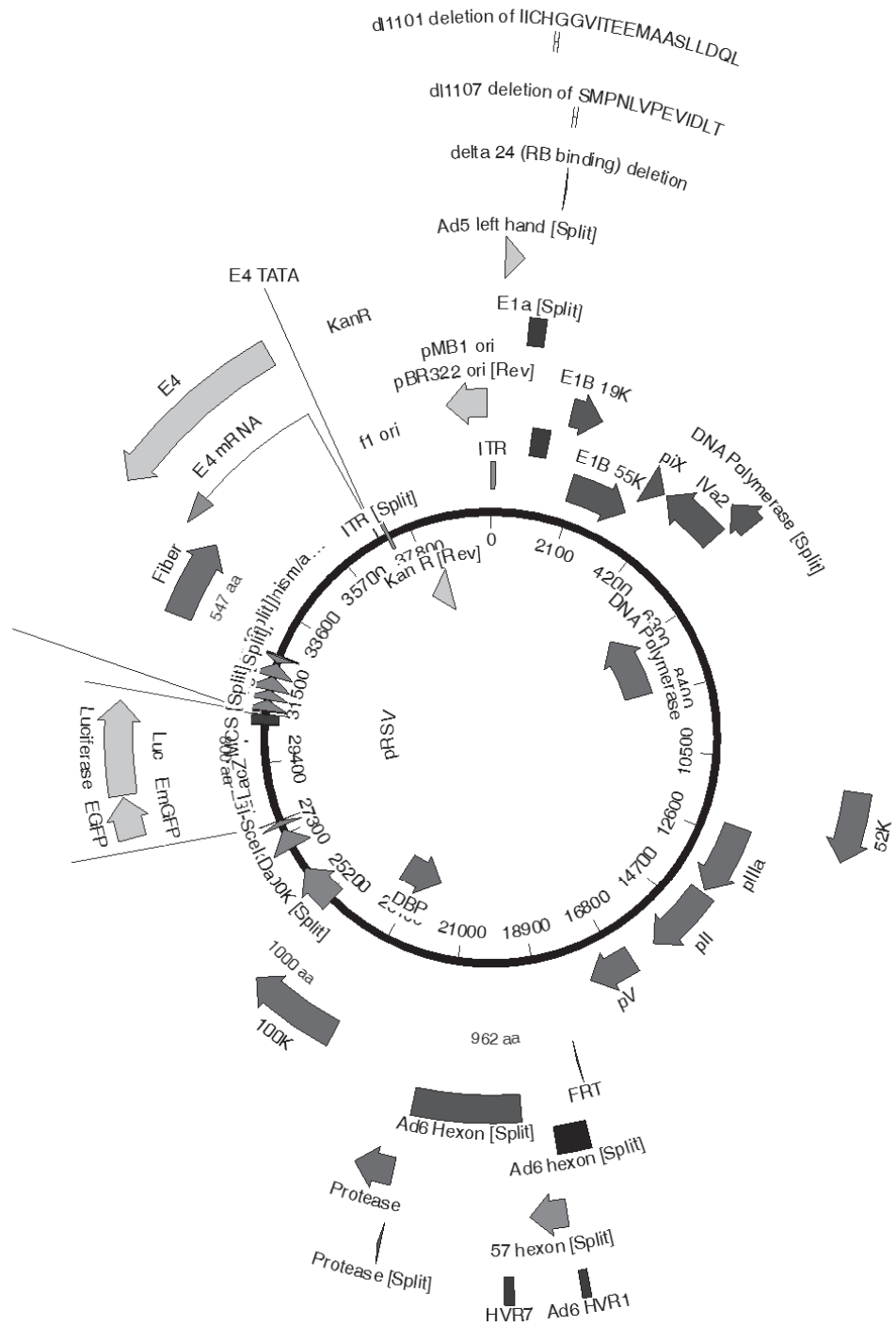
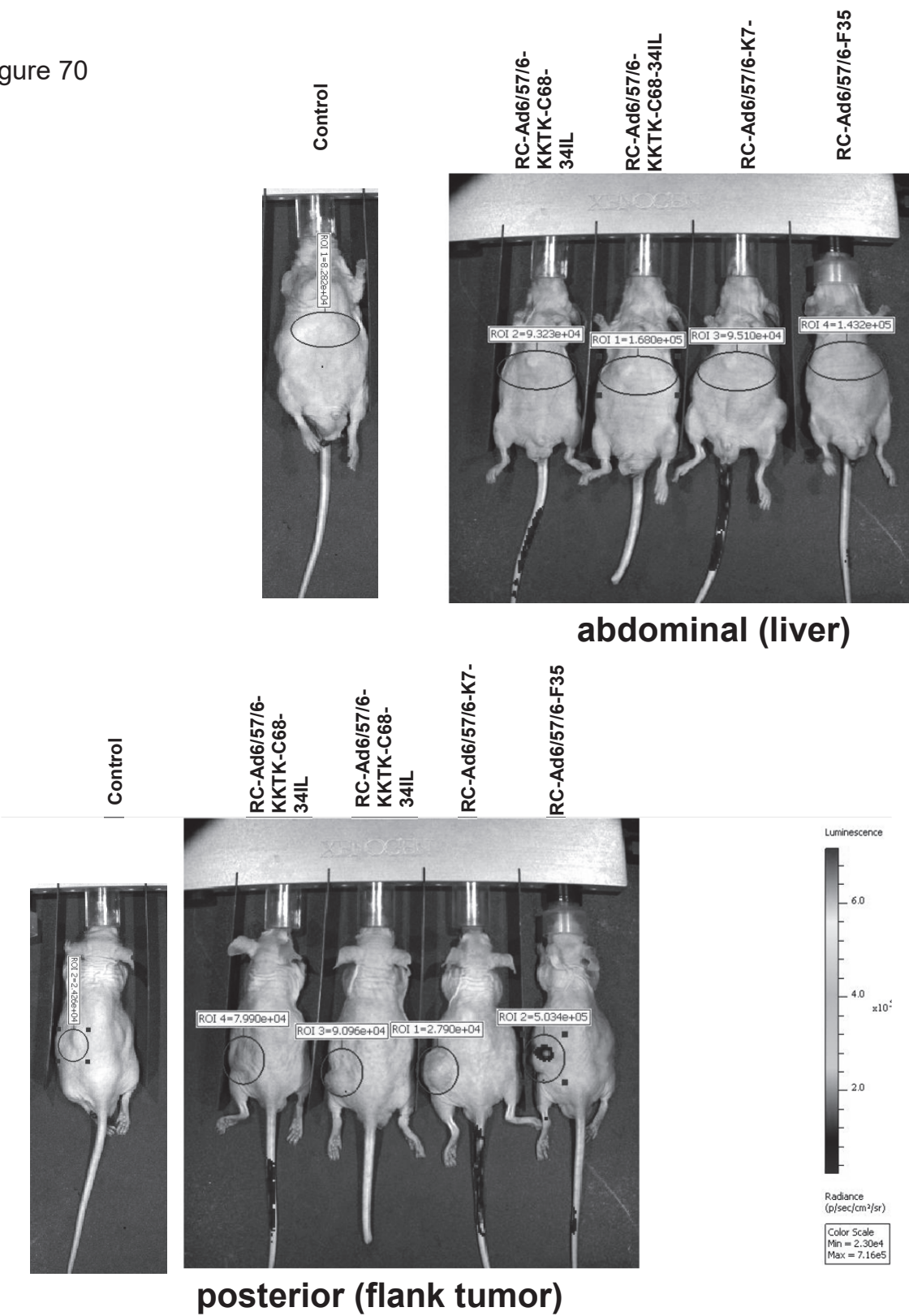


Figure 69

Figure 70



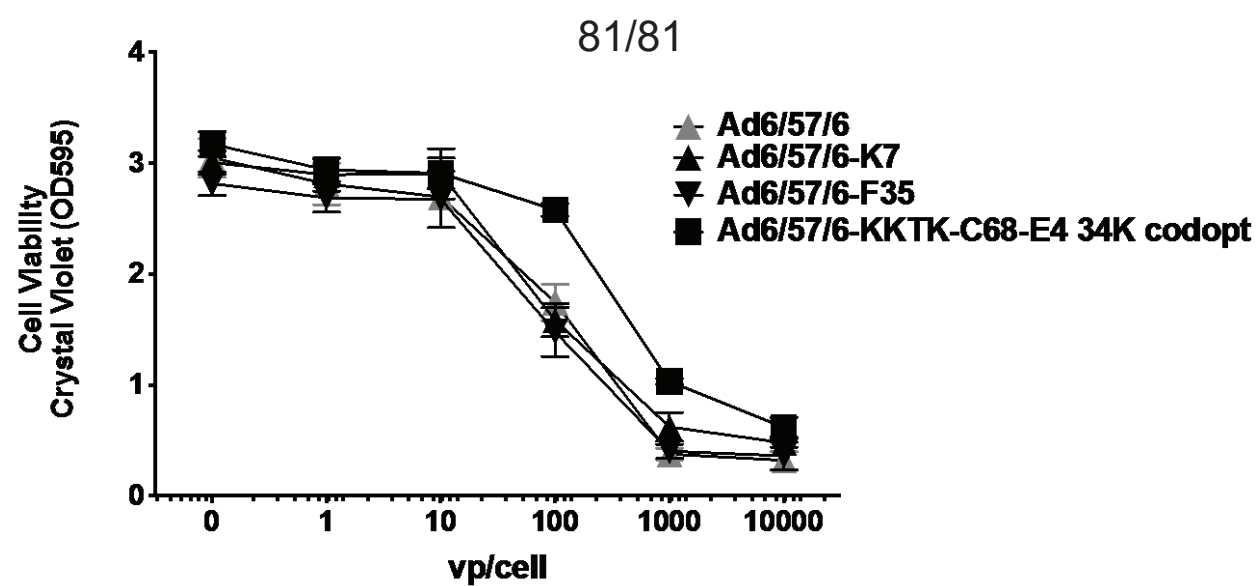


Figure 71