

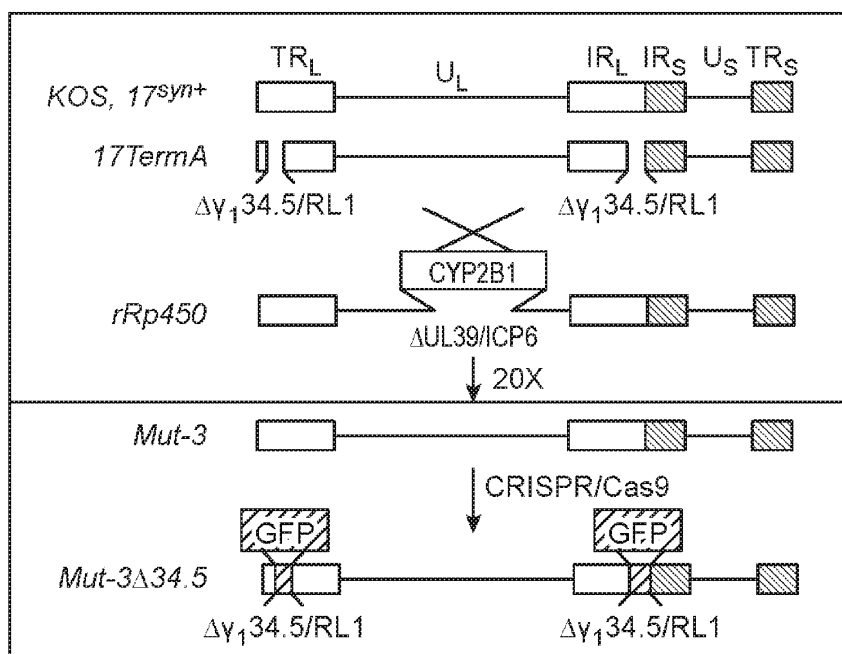


FIG. 1A

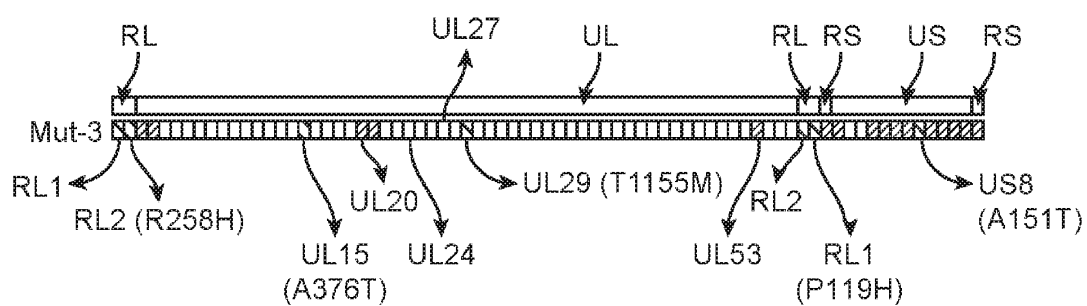


FIG. 1B

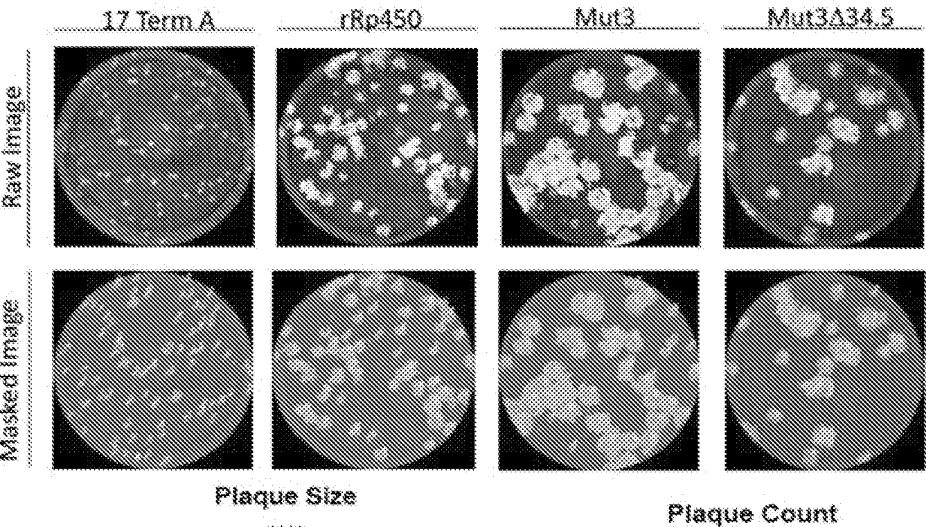


FIG. 2A

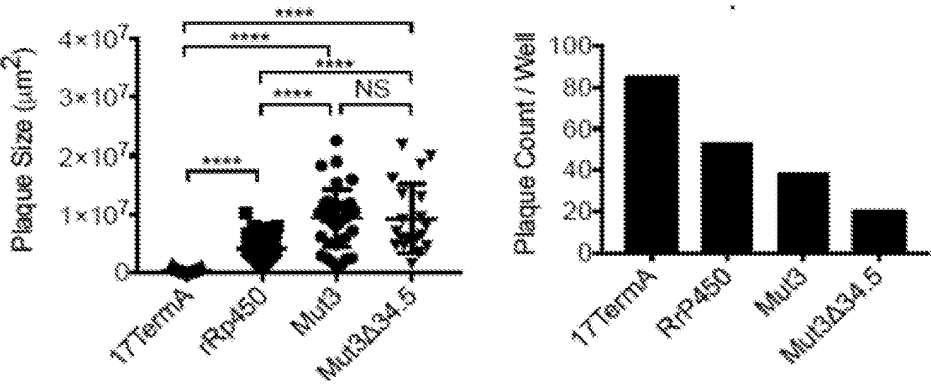


FIG. 2B

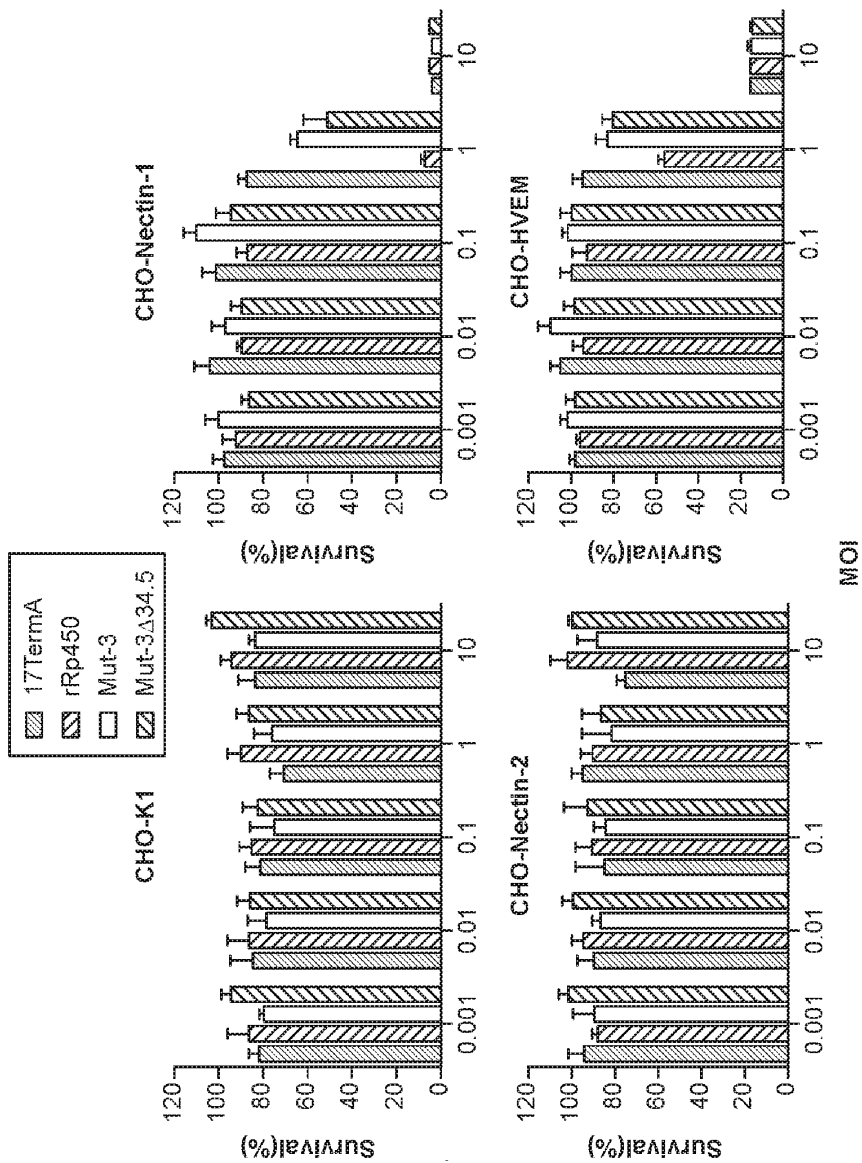


FIG. 2C

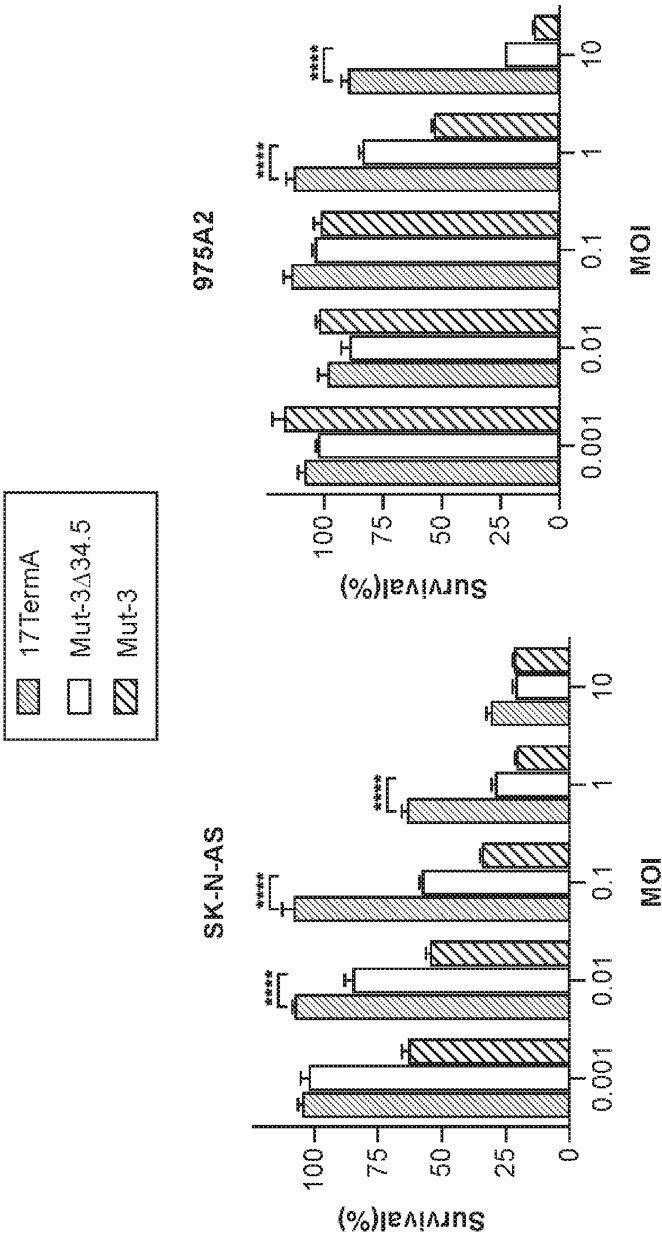


FIG. 3A

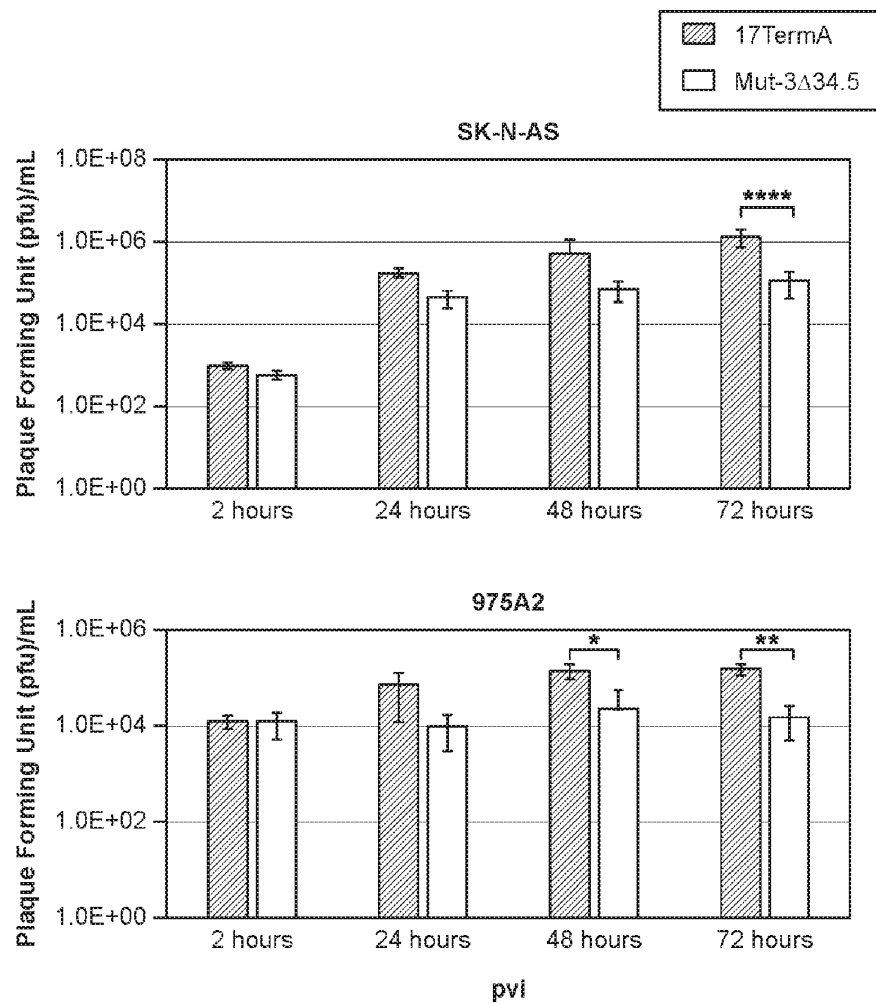


FIG. 3B

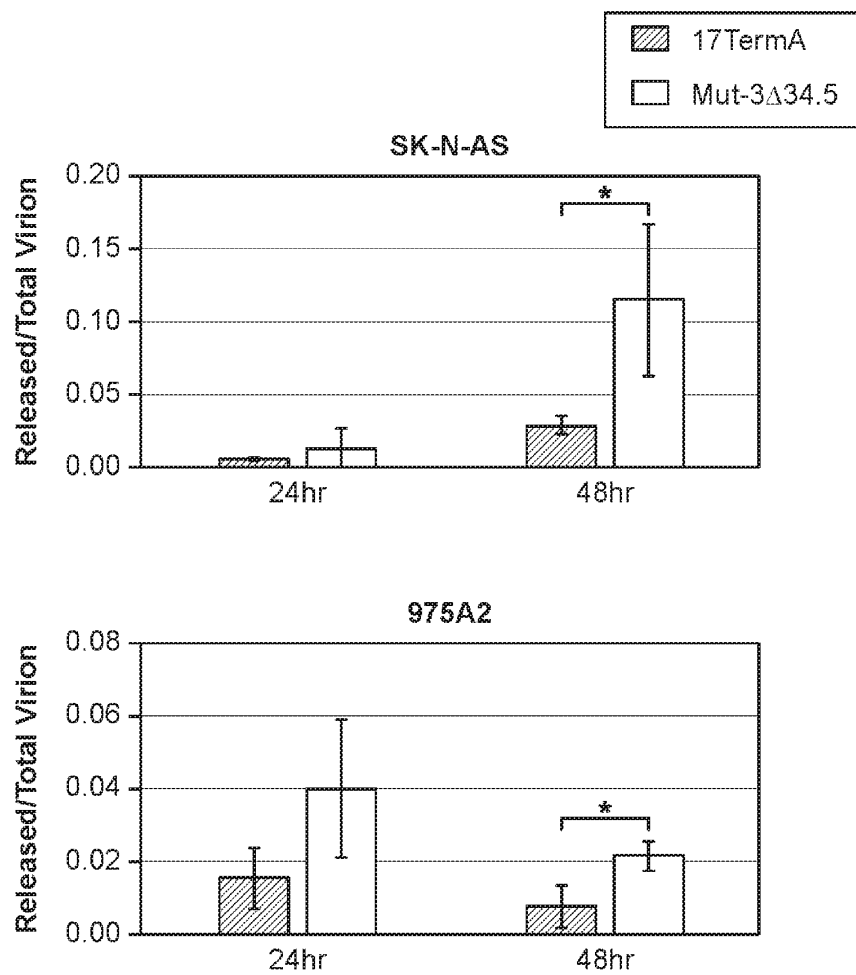
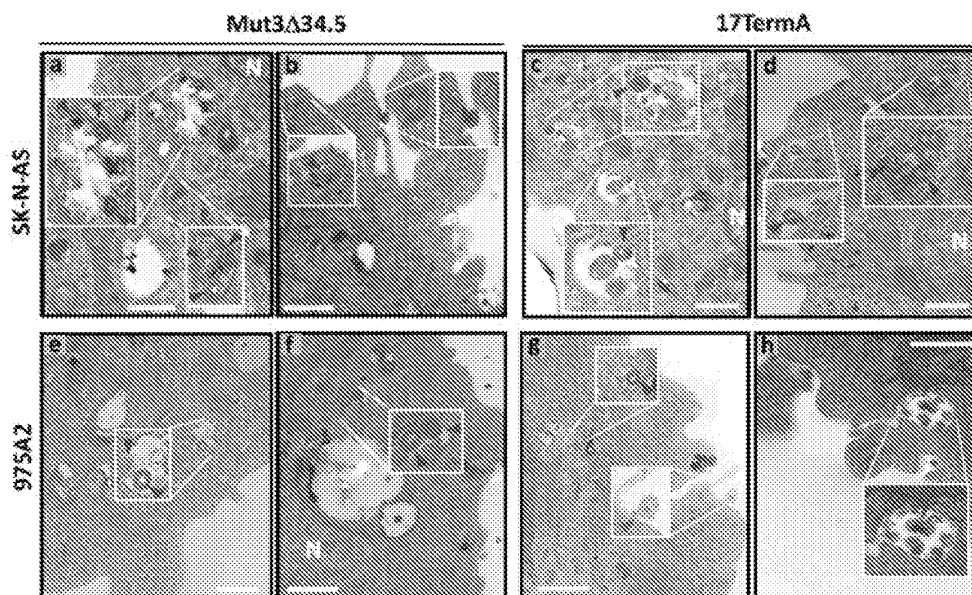


FIG. 3C



FIGS. 4A – 4H

a

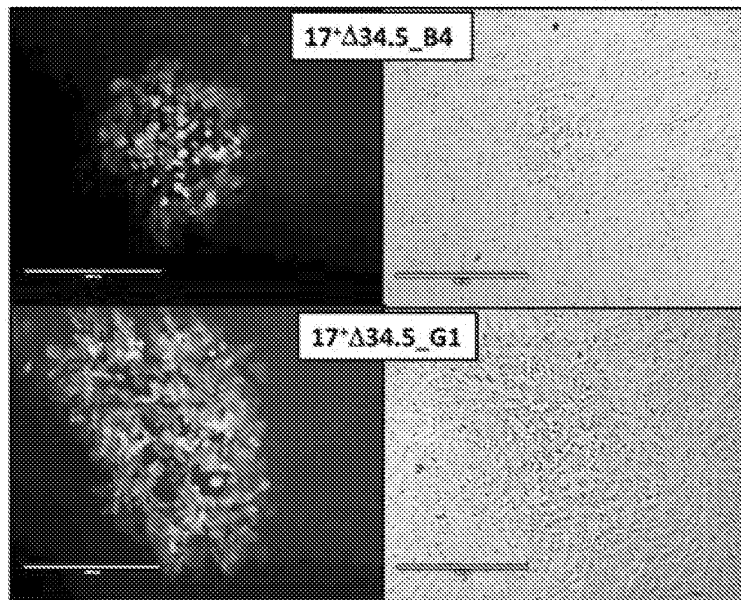


FIG. 5A

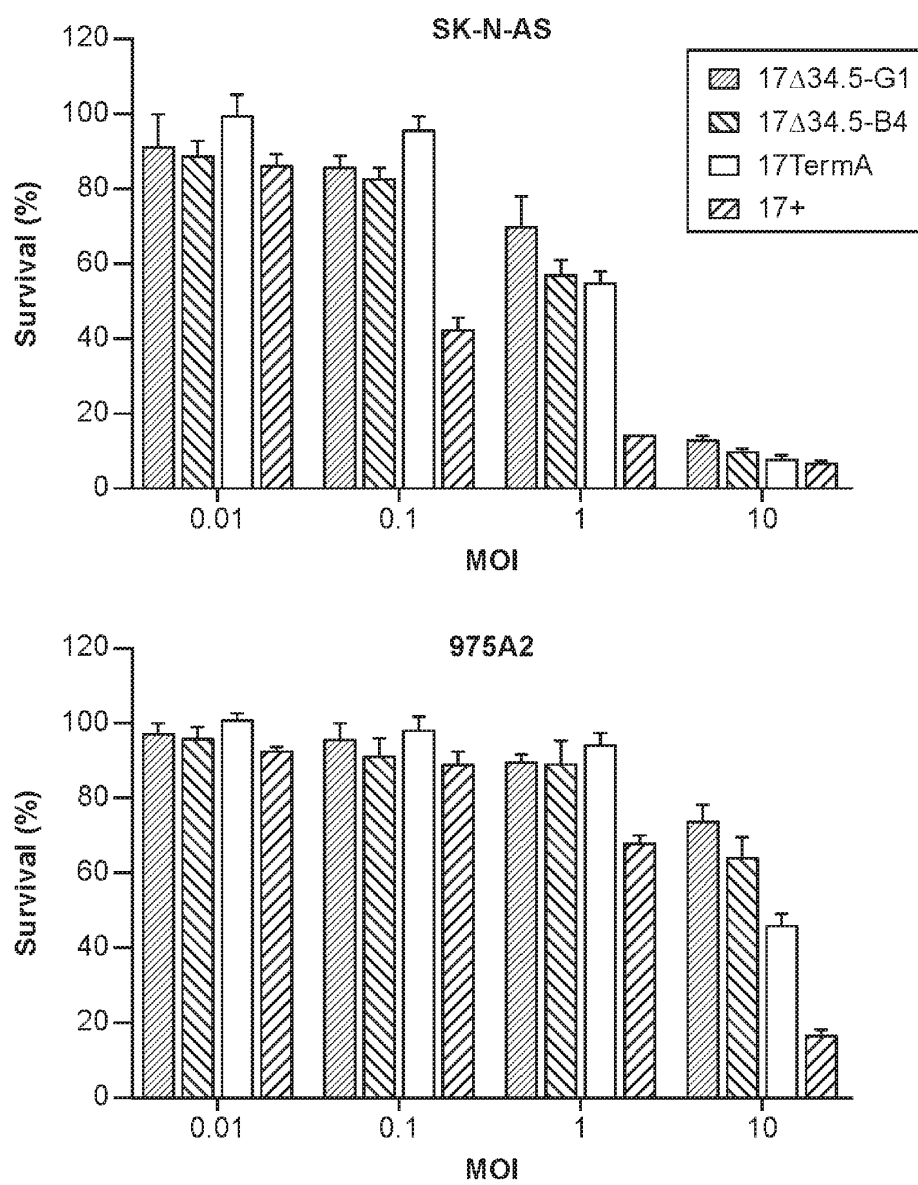


FIG. 5B

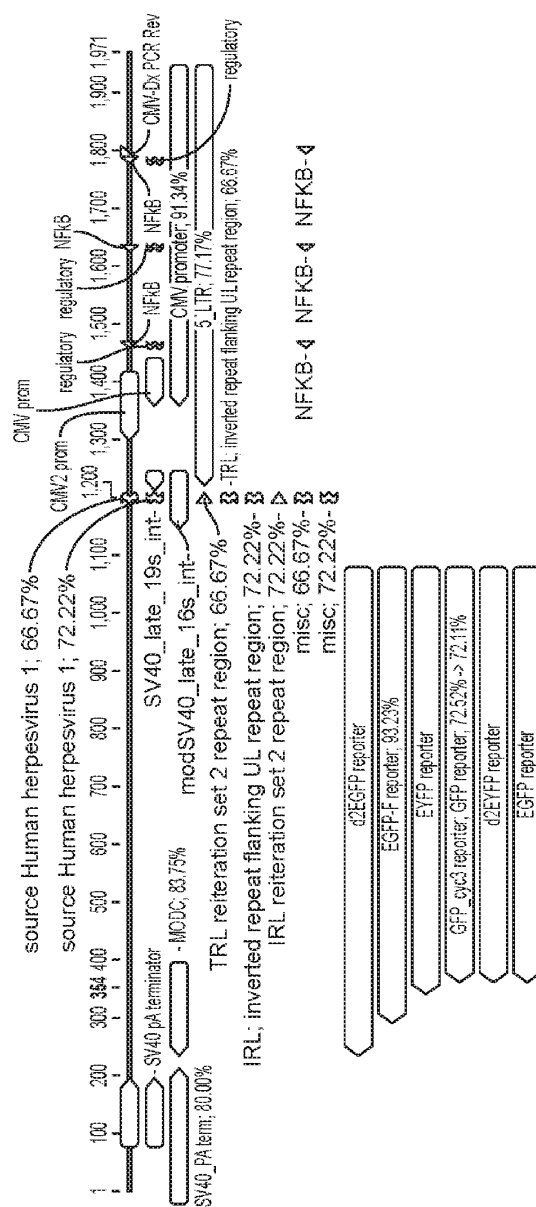


Fig. 50

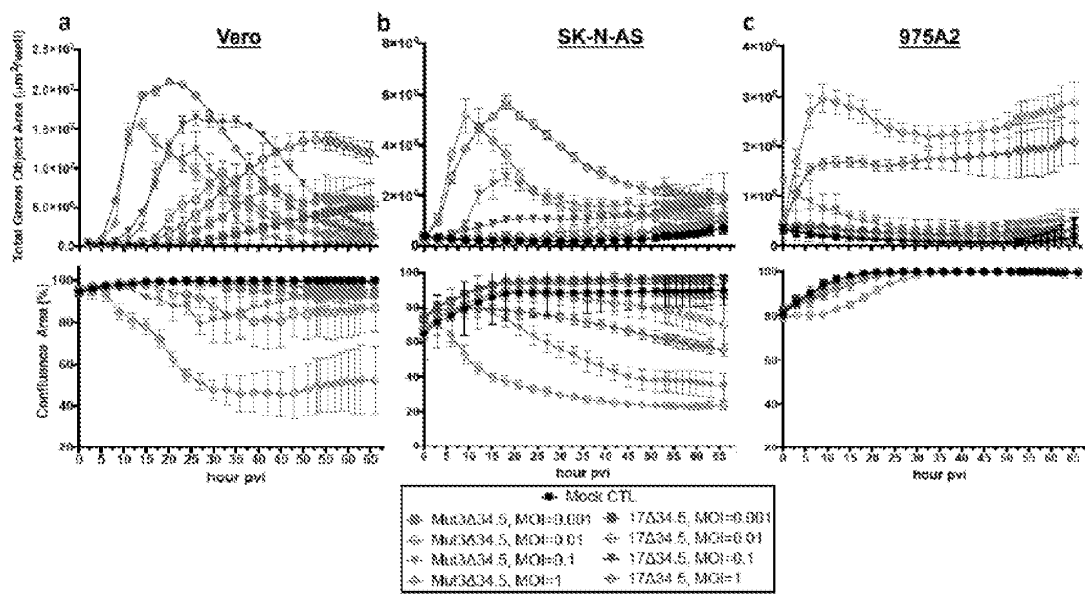
Sequence of EGFP cassette

AACACATTAATTAAAAACCTCCCACACCTCCCCCTGAACCTGAAACATA
AAATGAATGCAATTGTTGTTGTTAACTTGTTTATTGCAGCTTATAATGGT
TACAAATAAAGCAATAGCATCACAAATTCACAAATAAAGCATTTTTTTC
ACTGCATTCTAGTTGTGGTTTGTCCAACTCATCAATGTATCTTATCATG
TCTGCTCGAAGCGGCCGGCCGCCCGACTCTAGACTACACATTGATCCTA
GCAGAAGCACAGGCTGCAGGGTGACGGTCCATCCCGCTCTCCTGGGCACA
AGACATGGGCAGCGTGCCATCATCCTGCTCCTCCACCTCCGGCGGGAAGC
CATGGCTAAGCTTCTTGTTACAGCTCGTCCATGCCGAGAGTGATCCCGGCG
GCGGTACGAACTCCAGCAGGACCATGTGATCGCGCTTCTCGTTGGGGTC
TTTGCTCAGGGCGGACTGGGTGCTCAGGTAGTGGTTGTCGGGCAGCAGCA
CGGGGCCGTCGCCGATGGGGGTGTTCTGCTGGTAGTGGTCGGCGAGCTGC
ACGCTGCCGTCCTCGATGTTGTGGCGGATCTTGAAGTTCACCTTGATGCC
GTTCTTCTGCTTGTCGGCCATGATATAGACGTTGTGGCTGTTGTAGTTGT
ACTCCAGCTTGTCGCCCAGGATGTTGCCGTCCTCCTTGAAGTCGATGCCC
TTCAGCTCGATGCGGTTCAACAGGGTGTCGCCCTCGAACTTCACCTCGGC
GCGGGTCTTGTAAGTTGCCGTCGTCCTTGAAGAAGATGGTGCGCTCCTGGA
CGTAGCCTTCGGGCATGGCGGACTTGAAGAAGTCGTGCTGCTTCATGTGG
TCGGGGTAGCGGCTGAAGCACTGCACGCCGTAGGTGAGGGTGGTCACGAG
GGTGGGCCAGGGCACGGGCAGCTTGCCGGTGGTGCAGATGAACTTCAGGG

FIG. 5C (Cont. 1)

TCAGCTTGCCGTAGGTGGCATCGCCCTCGCCCTCGCCGGACACGCTGAAC
TTGTGGCCGTTTACGTGCGCGTCCAGCTCGACCAGGATGGGCACCACCCC
GGTGAACAGCTCCTCGCCCTTGCTCACCATCCGGGAATTGCGGCCGCGGG
TACAATTCCGCAGCTTTTAGAGCAGAAGTAACACTTCCGTACAGGCCTAG
AAGTAAAGGCAACATCCACTGAGGAGCAGTTCTTTGATTTGCACCACCAC
CGGATCCGGGACCTGAAATAAAAGACAAAAAGACTAAACTTACCAGTTAA
CTTTCTGGTTTTTTCAGTTCCTCGAGTAACCGGATCCTCTAGAGTCCGGAGG
CTGGATCGGTCCCGGTGTCTTCTATGGAGGTCAAAACAGCGTGGATGGCG
TCTCCAGGCGATCTGACGGTTCACTAAACGAGCTCTGCTTATATAGACCT
CCCACCGTACACGCCTACCGCCCATTTGCGTCAATGGGGCGGAGTTGTTA
CGACATTTTGGAAAGTCCCGTTGATTTTGGTGCCAAAACAAACTCCCATT
GACGTCAATGGGGTGGAGACTTGGAAATCCCCGTGAGTCAAACCGCTATC
CACGCCCATTTGATGTACTGCCAAAACCGCATCACCATGGTAATAGCGATG
ACTAATACGTAGATGTACTGCCAAGTAGGAAAGTCCCATAAGGTCATGTA
CTGGGCATAATGCCAGGCGGGCCATTTACCGTCATTGACGTCAATAGGGG
GCGTACTTGGCATATGATACACTTGATGTACTGCCAAGTGGGCAGTTTAC
CGTAAATACTCCACCCATTGACGTCAATGGAAAGTCCCTATTGGCGTTAC
TATGGGAACATACGTCATTATTGACGTCAATGGGCGGGGGTCGTTGGGCG
GTCAGCCAGGCGGGCCATTTACCGTAAGTTATGTAACGACCTGCAGGCAT
GCAAGCTCGAATTCGAACACGCAGATGCAGTCGGGGCGGCAGATCTTAAT
TAATGGCTGGTTGTTTGTGT

FIG. 5C (Cont. 2)



FIGS. 6A – 6C

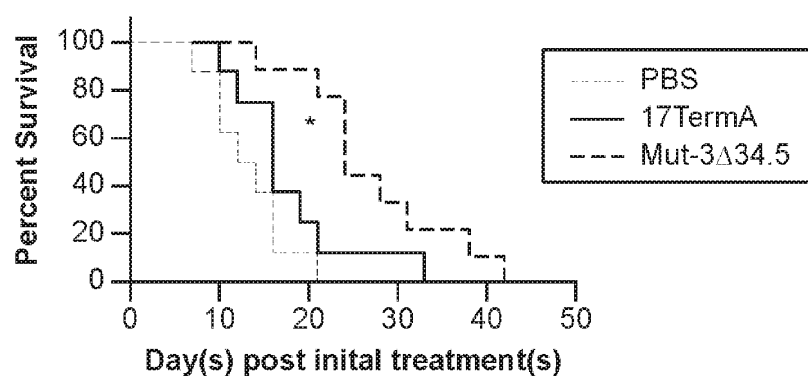
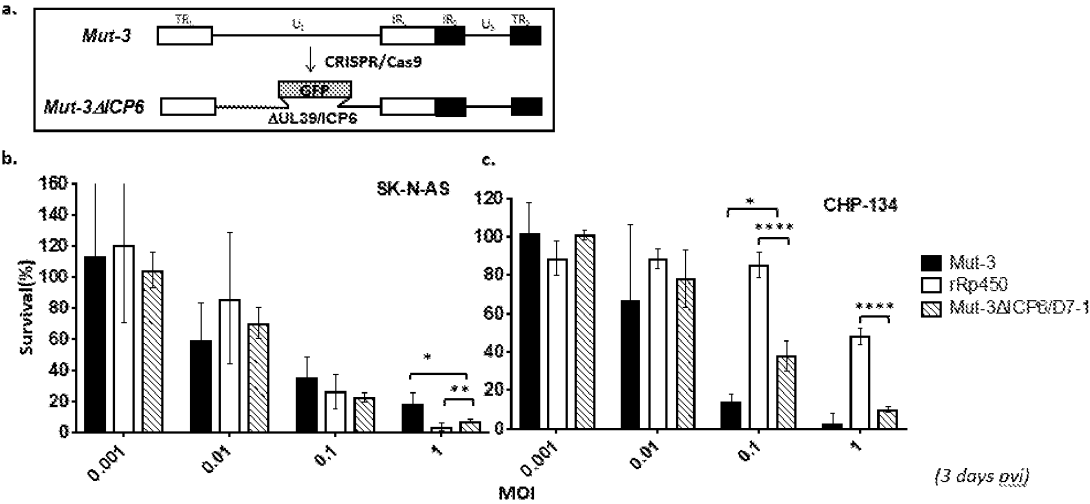


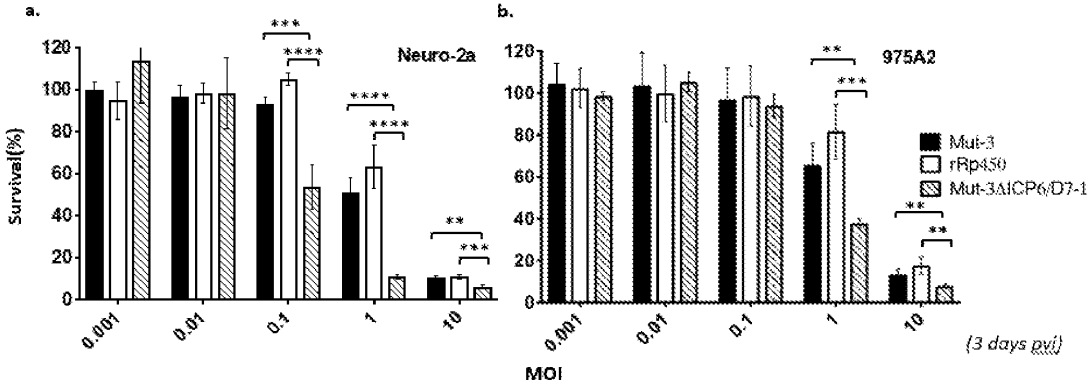
FIG. 7

Mut-3 Δ ICP6, an attenuated version of Mut-3, induces superior cytotoxicity in the human neuroblastoma cell line CHP-134 compared to oncolytic herpes virus rRp450



FIGS. 8A – 8C

Mut-3 Δ ICP6 induces superior cytotoxicity in the murine neuroblastoma cell lines Neuro-2a & 975A2 compared to rRp450



FIGS. 9A – 9B

Mut-3ΔICP6 produces a significantly higher virus yield than rRp450 in the murine neuroblastoma cell line 975A2 over 48 and 72hrs infection time periods

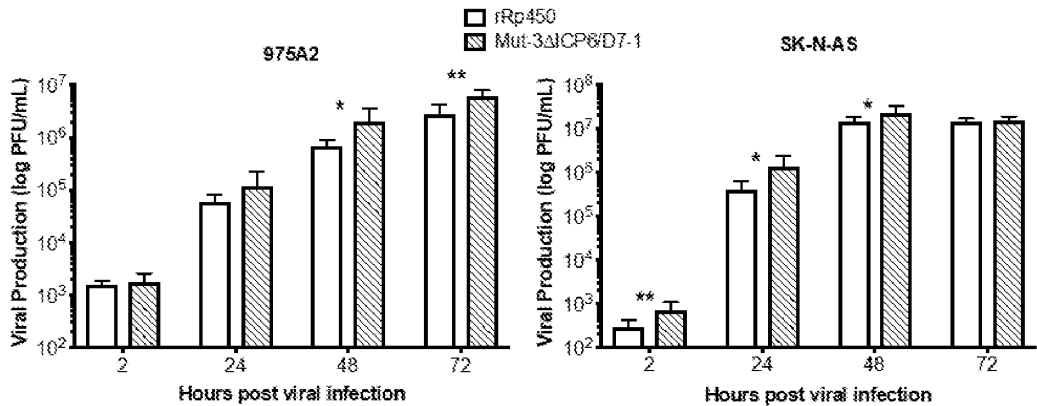


FIG. 10A

FIG. 10B

Mut-3Δ34.5 & Mut-3ΔICP6 are significantly less potent than the Mut-3 virus against differentiated human keratinocyte cells

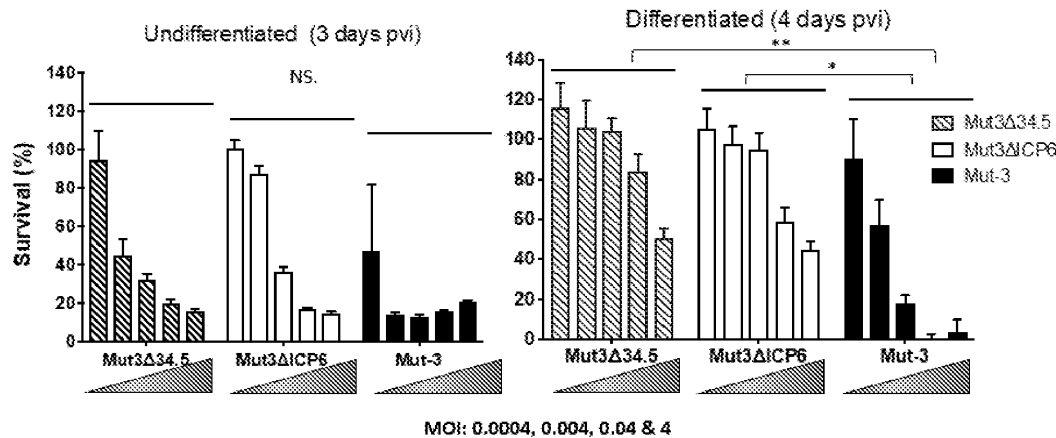


FIG. 11A

FIG. 11B

Intravenous injection of 1e6 pfu of wild-type strain KOS virus is lethal to naïve Balb/c mice

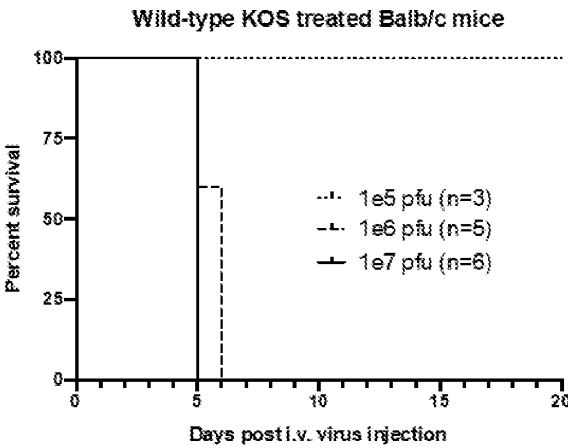
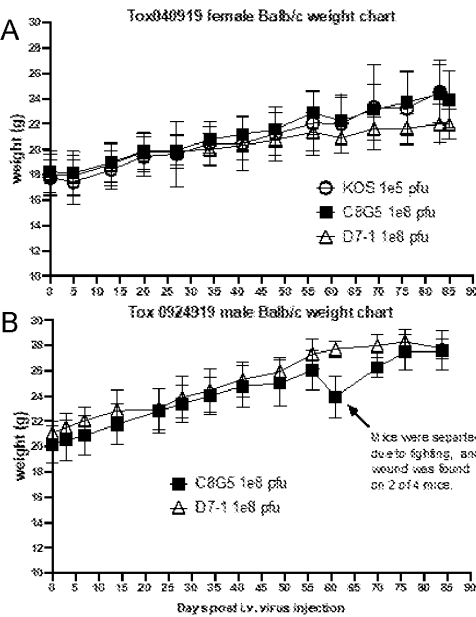


FIG. 12



FIGS. 13A – 13B

Wild-type KOS		Brain	Heart	Kidney	Liver	Lung	Ovary	Spleen
1e7_#1	plaque			-				-
1e7_#2	plaque	+	-	-	-	-	+	-
1e7_#3	plaque	+	-	+	-	-	+	-
1e7_#4	plaque	+	-	+	-	-	+	-
1e6_#1	plaque	+	-	+		-		-
1e6_#2	plaque	+	-	+	-	-	+	-
1e6_#3	plaque	-	-	+	-	-	+	-

FIG. 14

24hrs pvi		Brain	Heart	Kidney	Liver	Lung	Ovary	Spleen
C8G5 (Mut3-Δ34.5)								
#1	plaque	-	-	+	+	-	+	-
#2	plaque	-	+	-	-	-	-	-
#3	plaque	-	+	+	-	-	-	-
#4	plaque	-	-	+	-	-	-	-
D7-1 (Mut3-ΔICP6)								
#1	plaque	+	+	+	-		+	-
#2	plaque	-	+	+	+	-	+	-
#3	plaque	+	+	+	-	-	-	-
#4	plaque	-	-	+	+	-	+	-

FIG. 15

14 days pvi		Brain	Heart	Kidney	Liver	Lung	Ovary	Spleen
C8G5 (Mut3-Δ34.5)								
#1	plaque	-	-	-	-	-	-	-
#2	plaque	-	-	-	-	-	-	-
#3	plaque	-	-	-	-	-	-	-
#4	plaque	-	-	-	-	-	-	-
D7-1 (Mut3-ΔICP6)								
#1	plaque	-	-	-	-	-	-	-
#2	plaque	-	-	-	-	-	-	-
#3	plaque	-	-	-	-	-	-	-
#4	plaque	-	-	-	-	-	-	-

FIG. 16

28 days pvi		Brain	Heart	Kidney	Liver	Lung	Ovary	Spleen
C8G5 (Mut3-Δ34.5)								
#1	plaque	-	-					
#2	plaque	-	-	-	-	-	-	-
#3	plaque	-	-	-	-	-	-	-
#4	plaque	-	-	-	-	-	-	-
D7-1 (Mut3-ΔICP6)								
#1	plaque	-	-	-	-	-	-	-
#2	plaque	-	-	-	-	-	-	-
#3	plaque	-	-	-	-	-	-	-
#4	plaque	-	-	-	-	-	-	-

FIG. 17

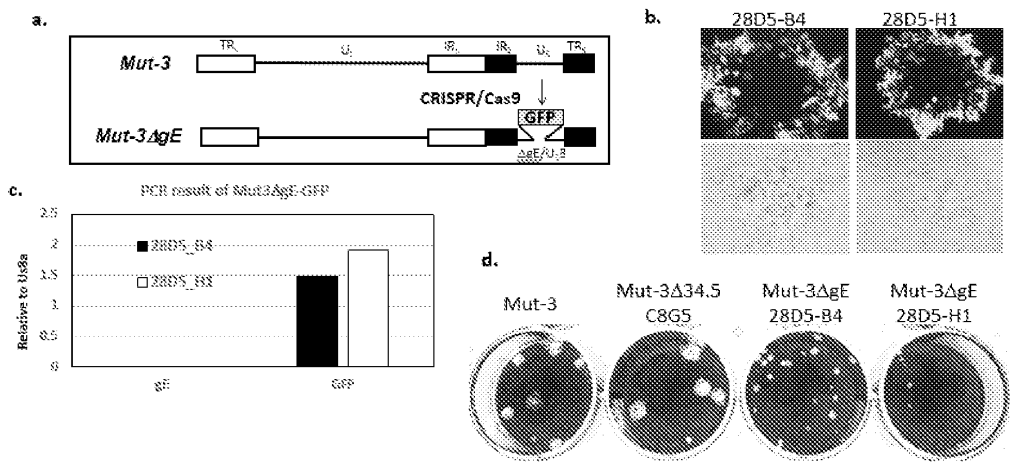
56 days pvi		Brain	Heart	Kidney	Liver	Lung	Ovary	Spleen
C8G5 (Mut3-Δ34.5)								
#1	plaque	-	-	-	-	-	-	-
#2	plaque	-	-	-	-	-	-	-
#3	plaque	-	-	-	-	-	-	-
#4	plaque	-	-	-	-	-	-	-
D7-1 (Mut3-ΔICP6)								
#1	plaque	-	-	-	-	-	-	-
#2	plaque	-	-	-	-	-	-	-
#3	plaque	-	-	-	-	-	-	-
#4	plaque	-	-	-	-	-	-	-

FIG. 18

85 days pvi		Brain	Heart	Kidney	Liver	Lung	Ovary	Spleen
C8G5 (Mut3-Δ34.5)								
#1	plaque	-	-	-	-	-	-	-
#2	plaque	-	-	-	-	-	-	-
#3	plaque	-	-	-	-	-	-	-
#4	plaque	-	-	-	-	-	-	-
D7-1 (Mut3-ΔICP6)								
#1	plaque	-	-	-	-	-	-	-
#2	plaque	-	-	-	-	-	-	-
#3	plaque	-	-	-	-	-	-	-
#4	plaque	-	-	-	-	-	-	-

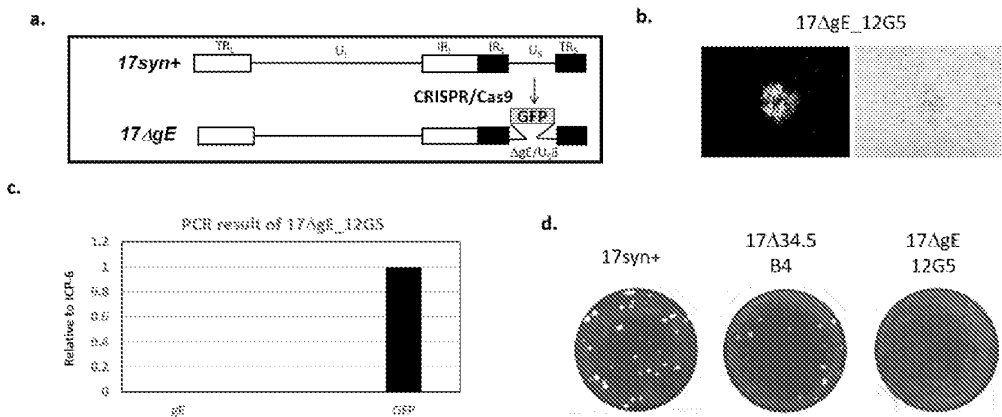
FIG. 19

Plaque size of Mut-3ΔgE is much smaller compare to Mut-3 or Mut-3Δ34.5(C8G5)



FIGS. 20A – 20D

Plaque size of 17ΔgE is much smaller compare to 17syn+ or 17Δ34.5



FIGS. 21A – 21D