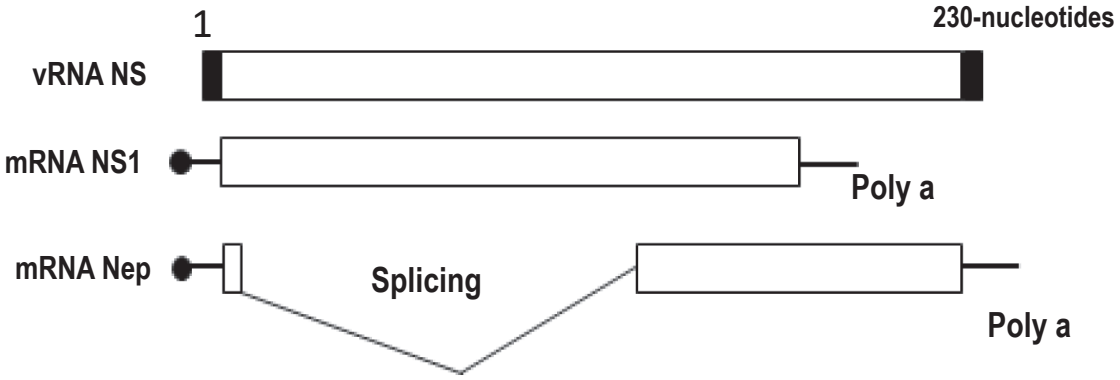
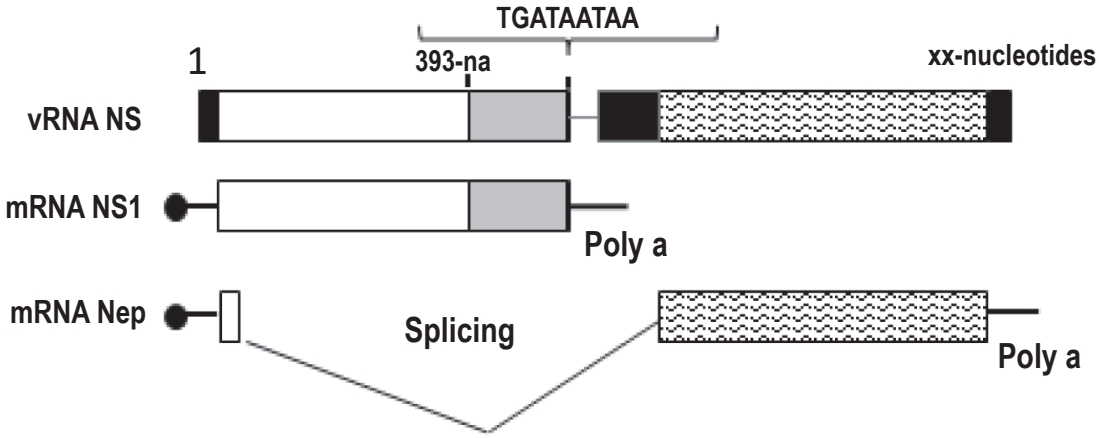
FIG. 1

(A)


1
230-nucleotides
vRNA NS
mRNA NS1
Poly a
mRNA Nep
Splicing
Poly a

(B)


TGATAATAA
1
393-na
xx-nucleotides
vRNA NS
mRNA NS1
Poly a
mRNA Nep
Splicing
Poly a

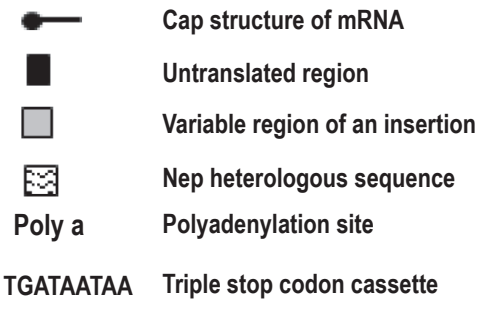

Cap structure of mRNA
Untranslated region
Variable region of an insertion
Nep heterologous sequence
Poly a
Polyadenylation site
TGATAATAA
Triple stop codon cassette

FIG. 2

(A)

AGCAAAAGCAGGGTGACAAAGACATAATGGATCCAAACACTGTGTCAAGCTTTCAGGTAGA
TTGCTTTCTTTGGCATGTCCGCAAACGAGTTGCAGACCAAGAACTAGGTGATGCCCCATTC
CTTGATCGGCTTCGCCGAGATCAGAAATCCCTAAGAGGAAGGGGCAGCACTCTTGGTCTG
GACATCGAGACAGCCACACGTGCTGGAAAGCAGATAGTGGAGCGGATTCTGAAAGAAGAA
TCCGATGAGGCACTTAAAATGACCATGGCCTCTGTACCTGCGTCGCGTTACCTAACCGACA
TGACTCTTGAGGAAATGTCAAGGGAATGGTCCATGCTCATACCCAAGCAGAAAGTGGCAG
GCCCTCTTTGTATCAGAATGGACCAGGCGATCATG**GATAAAAACATCATACTGAAAGCGA**
ACTTCAGTGTGATTTTTGACCGGCTGGAGACTCTAATATTGCTAAGGGCTTTCACCGAAGA
GGGAGCAATTGTTGGCGAAATTTCACCATTGCCTTCTCTTCCAG**GACATACTGCTGAGGAT**
GTCAAAAATGCAGTTGGAGTCCTCATCGGAGGACTTGAATGGAATGATAACACAGTTCG
AGTCTCTGAAACTCTACAGAGATTCGCTTGGAGAAGCAGTAATGAGAATGGGAGACCTC
CACTCACTCCAAAACAGAAACGAGAAATGGCGGGAACAATTAGGTCAGAAGTTTGAAGA
AATAAGATGGTTGATTGAAGAAGTGAGACACAAACTGAAGGTAACAGAGAATAGTTTTG
AGCAAATAACATTTATGCAAGCCTTACATCTATTGCTTGAAGTGGAGCAAGAGATAAGAA
CTTTCTCATTTCAGCTTATTTAATAATAAAAAACACCCTTGTTTCTACT (SEQ ID NO:1)

(B)

AGCAAAAGCAGGGTGACAAAGACATAATGGATCCAAACACTGTGTCAAGCTTTCAGGTAGA
TTGCTTTCTTTGGCATGTCCGCAAACGAGTTGCAGACCAAGAACTAGGTGATGCCCCATTC
CTTGATCGGCTTCGCCGAGATCAGAAATCCCTAAGAGGAAGGGGCAGCACTCTTGGTCTG
GACATCGAGACAGCCACACGTGCTGGAAAGCAGATAGTGGAGCGGATTCTGAAAGAAGAA
TCCGATGAGGCACTTAAAATGACCATGGCCTCTGTACCTGCGTCGCGTTACCTAACCGACA
TGACTCTTGAGGAAATGTCAAGGGAATGGTCCATGCTCATACCCAAGCAGAAAGTGGCAG
GCCCTCTTTGTATCAGAATGGACCAGGCGATCATG**TGATAATAA**AGTGTGATTTTTGACCG
GCTGGAGACTCTAATATTGCTAAGGGCTTTCACCGAAGAGGGAGCAATTGTTGGCGAAATT
TCACCATTGCCTTCTCTTCCAG**GACATACTAATGAGGATGTCAAAAATGCAATTGGGGTC**
CTCATCGGAGGACTTGAATGGAATGATAACACAGTTCGAGTCTCTAAAACTCTACAGAGA
TTCGCTTGGTGAAACAGTAATGAGAATGGGAGACCTCCACTCACTCCAAAACAGAAACG
GAAAATGGCGAGAACAATTAGGTCAAAAGTTCGAAGAAATAAGATGGCTGATTGAAGAA
GTGAGACACAAATTGAAGATAACAGAGAATAGTTTTGAGCAAATAACATTTATGCAAGCC
TTACAGCTACTATTTGAAGTGGAACAAGAGATAAGAACTTTCTCGTTTCAGCTTATTTAAT
AATAAAAAACACCCTTGTTTCTACT (SEQ ID NO:2)

(C)

AGCAAAAGCAGGGTGACAAAGACATAATGGATCCAAACACTGTGTCAAGCTTTCAGGTAGA
TTGCTTTCTTTGGCATGTCCGCAAACGAGTTGCAGACCAAGAACTAGGTGATGCCCCATTC
CTTGATCGGCTTCGCCGAGATCAGAAATCCCTAAGAGGAAGGGGCAGCACTCTTGGTCTG
GACATCGAGACAGCCACACGTGCTGGAAAGCAGATAGTGGAGCGGATTCTGAAAGAAGAA
TCCGATGAGGCACTTAAAATGACCATGGCCTCTGTACCTGCGTCGCGTTACCTAACCGACA
TGACTCTTGAGGAAATGTCAAGGGAATGGTCCATGCTCATACCCAAGCAGAAAGTGGCAG
GCCCTCTTTGTATCAGAATGGACCAGGCGATCATG**TGATAATAA**AGTGTGATTTTTGACCG
GCTGGAGACTCTAATATTGCTAAGGGCTTTCACCGAAGAGGGAGCAATTGTTGGCGAAATT
TCACCATTGCCTTCTCTTCCAG**GACATACTAATGAGGATGTCAAAAATGCAATTGGGGTC**
CTCATCGGAGGACTTGAATGGAATGATAACACAGTTCGAGTCTCTAAAACTCTACAGAGA
TTCGCTTGGAGAAGCAGTAATGAGAATGGGAGACCTCCACTCACTCCAAAACAGAAACG
GAAAATGGCGAGAACAATTAGGTCAAAAGTTCGAAGAAATAAGATGGCTGATTGAAGAA
GTGAGACACAAATTGAAGATAACAGAGAATAGTTTTGAGCAAATAACATTTATACAAGCC
TTACAGCTACTATTTGAAGTGGAACAAGAGATAAGAACTTTCTCGTTTCAGCTTATTTAAT
AATAAAAAACACCCTTGTTTCTACT (SEQ ID NO:3)

FIG. 3

NS124/Nep-Len

MDPNTVSSFQVDCFLWHVRKRVADQELGDAPFLDRLRRDQKSLRGRGSTLGLDIETATRAGKQIVERILKEESDEALKMTMASVPA SRYLTDMTLEEMSREWSMLIPKQKVAGPLCIRMDQAIM (SEQ ID NO:4)

NS124-HA2(A)-185

MDPNTVSSFQVDCFLWHVRKRVADQELGDAPFLDRLRRDQKSLRGRGSTLGLDIETATRAGKQIVERILKEESDEALKMTMASVPA SRYLTDMTLEEMSREWSMLIPKQKVAGPLCIRMDQAIM-GG-**GLFGAIAGFIEGGWTGMIDGWYGYHH QNEQGSGYAADQKSTQNAINGITNKVNTVIEKMNIQFTAVGKEFNKLEKRMENLNKKVDDGFLDIWTYNAELLVLLENERTLDF HDSNVKNLYEKVKSQLKNNAKEIGNGCFEFYHKCDNECMESVRNGTYDYPKYSEESKLNREKVDGVKLESMGIYQ** (SEQ ID NO:5)

NS124-HA2(A)-65-222

MDPNTVSSFQVDCFLWHVRKRVADQELGDAPFLDRLRRDQKSLRGRGSTLGLDIETATRAGKQIVERILKEESDEALKMTMASVPA SRYLTDMTLEEMSREWSMLIPKQKVAGPLCIRMDQAIM-*GG*-**AVGKEFNKLEKRMENLNKKVDDGFLDI WTYNAELLVLLENERTLDFHDSNVKNLYEKVKSQLKNNAKEIGNGCFEFYHKCDNECMESVRNGTYDYPKYSEESKLNREKVDG VKLESMGIYQILAIYSTVASSLVLLVSLGAISFWMCSNGSLQCRICI** (SEQ ID NO:6)

NS124-HA2(A)-23-185

MDPNTVSSFQVDCFLWHVRKRVADQELGDAPFLDRLRRDQKSLRGRGSTLGLDIETATRAGKQIVERILKEESDEALKMTMASVPA SRYLTDMTLEEMSREWSMLIPKQKVAGPLCIRMDQAIM-GG-**GYHHQNEQGSGYAADQKSTQNAINGI TNKVNTVIEKMNIQFTAVGKEFNKLEKRMENLNKKVDDGFLDIWTYNAELLVLLENERTLDFHDSNVKNLYEKVKSQLKNNAKEI GNGCFEFYHKCDNECMESVRNGTYDYPKYSEESKLNREKVDGVKLESMGIYQ** (SEQ ID NO:7)

NS124-HA2(B)-186

MDPNTVSSFQVDCFLWHVRKRVADQELGDAPFLDRLRRDQKSLRGRGSTLGLDIETATRAGKQIVERILKEESDEALKMTMASVPA SRYLTDMTLEEMSREWSMLIPKQKVAGPLCIRMDQAIM-GG- **GFFGAIAGFLEGGWEGMIAGWHGYT SHGAHGVAVAADLKSTQEAINKITKNLNSLSELEVKNLQRLSGAMNGLHDEILELDEKVDDLRADTISSQIELAVLLSNEGIINSEDE HLLALERKLKKMLGPSAVEIGNGCFETKHKCNQTCLDRIAAGTFNAGDFSLPTFD** (SEQ ID NO:8)

NS124-Fus(A)-NP

MDPNTVSSFQVDCFLWHVRKRVADQELGDAPFLDRLRRDQKSLRGRGSTLGLDIETATRAGKQIVERILKEESDEALKMTMASVPA SRYLTDMTLEEMSREWSMLIPKQKVAGPLCIRMDQAIM-*GG*-**GLFGAIAGFIEGGWTGMIDGW**-*GG*-**RESRNPGNA** (SEQ ID NO:9)

NS124-Fus(B)-NP

MDPNTVSSFQVDCFLWHVRKRVADQELGDAPFLDRLRRDQKSLRGRGSTLGLDIETATRAGKQIVERILKEESDEALKMTMASVPA SRYLTDMTLEEMSREWSMLIPKQKVAGPLCIRMDQAIM-GG- **GFFGAIAGFLEGGWEGMIAGW** -GG-**RESRNPGNA** (SEQ ID NO:10)

NS124-Esat6

MDPNTVSSFQVDCFLWHVRKRVADQELGDAPFLDRLRRDQKSLRGRGSTLGLDIETATRAGKQIVERILKEESDEALKMTMASVPA SRYLTDMTLEEMSREWSMLIPKQKVAGPLCIRMDQAIM-*GG*-**MTEQQWNFAGIEAAASAIQGNV TSIHSLLDEGKQSLTKLAAAWGGSGSEAYQGVQQKWDATATELNNALQNLARTISEAGQAMASTEGNVTGMFA** (SEQ ID NO:11)

NS124-2A-Esat6

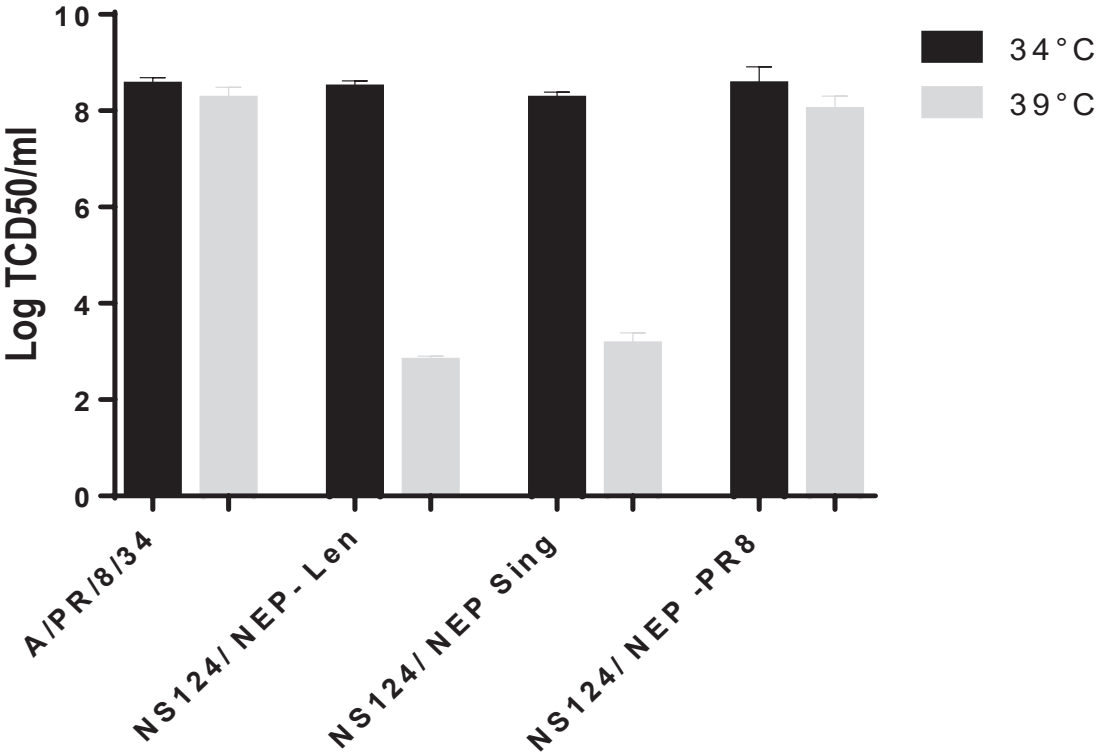
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NS124-HSV-2ASY

MDPNTVSSFQVDCFLWHVRKRVADQELGDAPFLDRLRRDQKSLRGRGSTLGLDIETATRAGKQIVERILKEESDEALKMTMASVPA SRYLTDMTLEEMSREWSMLIPKQKVAGPLCIRMDQAIM-AAA-**NLLTTPKFT**-AAA-**RMLGDVMAV**-AAA-**NLLTTPKFT**-AAA-**RMLGDVMAV** (SEQ ID NO:13)

FIG. 4

(A)


Log TCD50/ml
10
8
6
4
2
0
34°C
39°C
A/PR/8/34
NS124/NEP-Len
NS124/NEP Sing
NS124/NEP -PR8

(B)

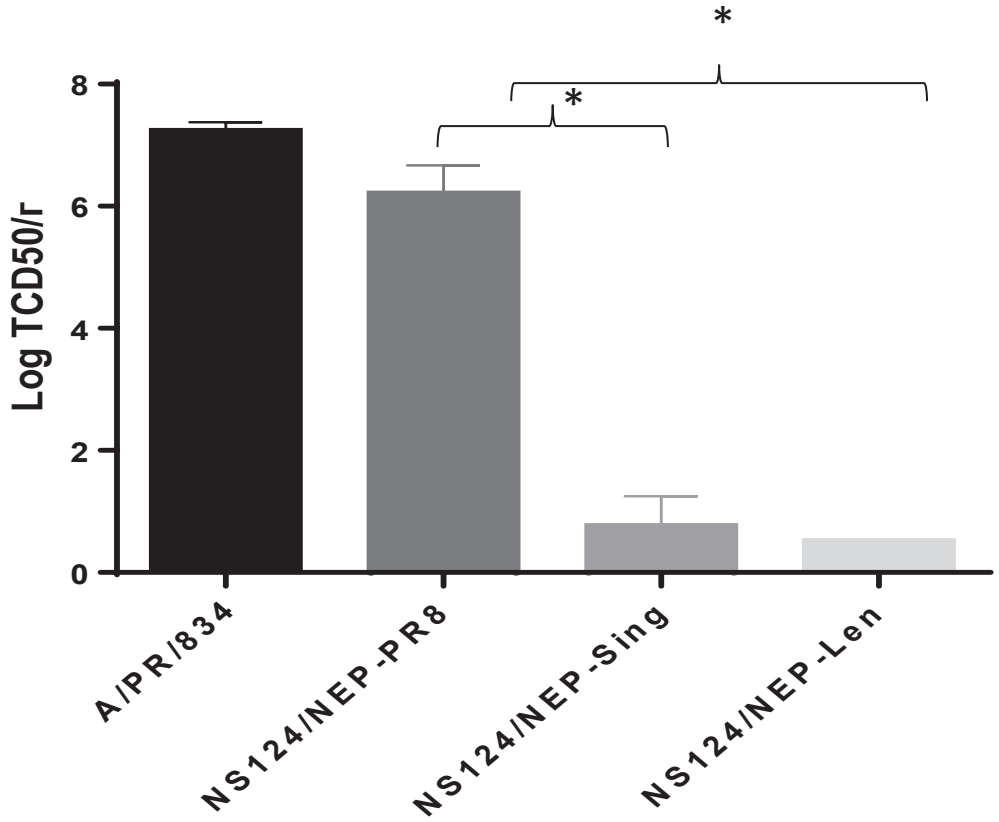
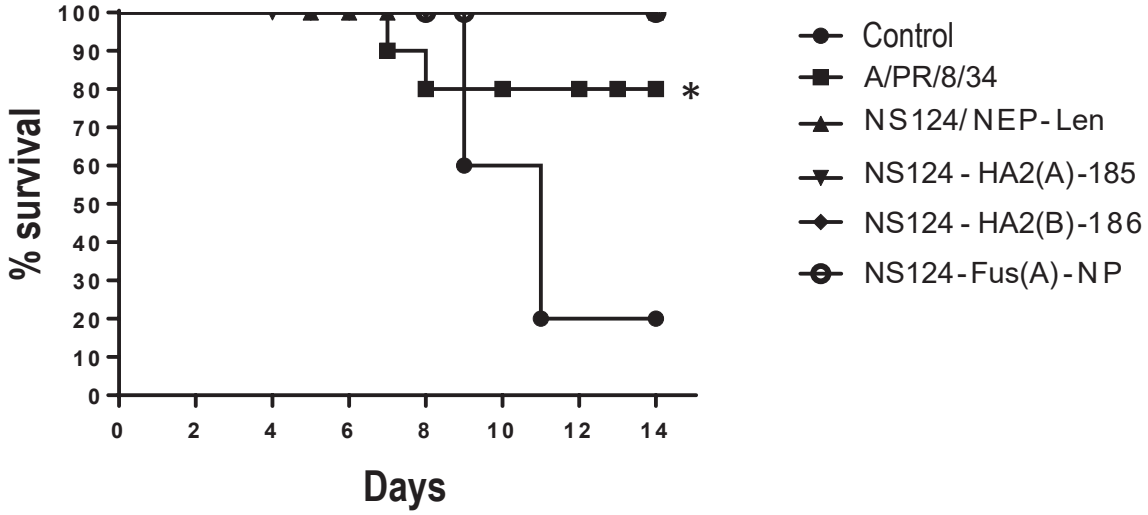

Log TCD50/r
8
6
4
2
0
*
*
A/PR/834
NS124/NEP-PR8
NS124/NEP-Sing
NS124/NEP-Len

FIG. 5

(A)


% survival
Days
*
Control
A/PR/8/34
NS124/NEP-Len
NS124 - HA2(A)-185
NS124 - HA2(B)-186
NS124-Fus(A)-NP

(B)

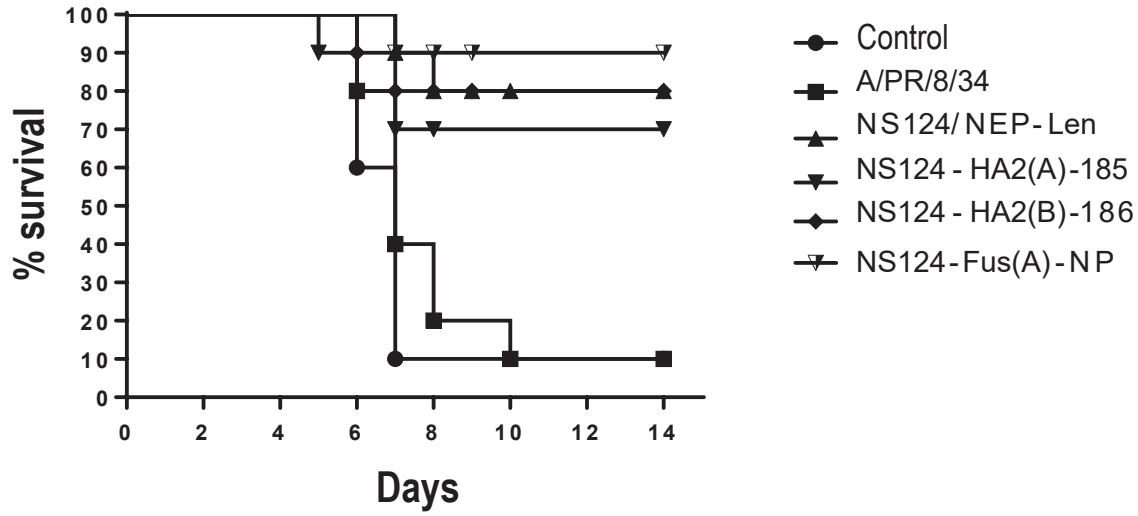
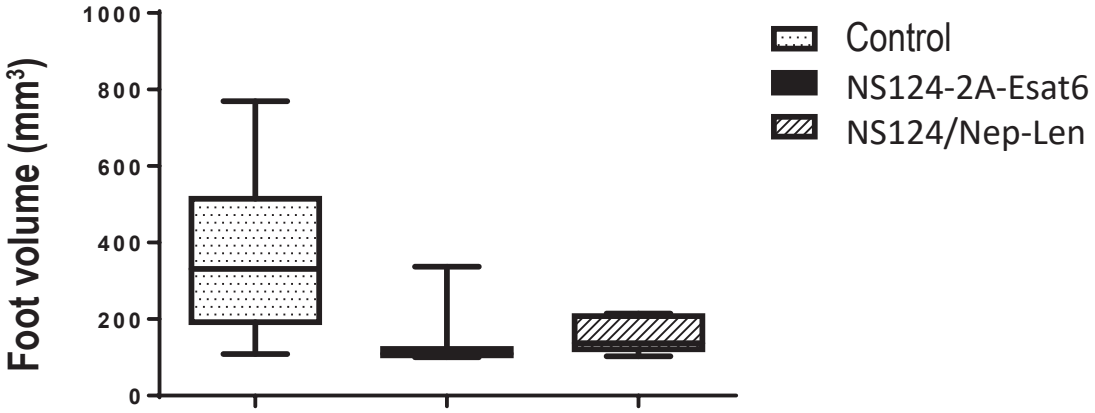

% survival
Days
Control
A/PR/8/34
NS124/NEP-Len
NS124 - HA2(A)-185
NS124 - HA2(B)-186
NS124-Fus(A)-NP

FIG. 6

(A)


1000
800
600
400
200
0
Foot volume (mm3)
Control
NS124-2A-Esat6
NS124/Nep-Len

(B)

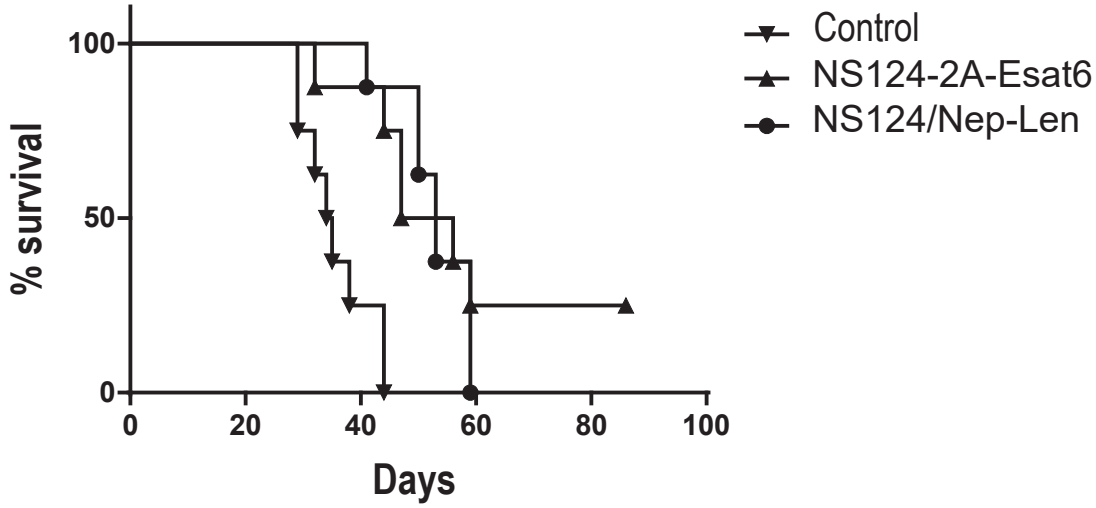

100
50
0
% survival
0
20
40
60
80
100
Days
Control
NS124-2A-Esat6
NS124/Nep-Len

FIG. 7

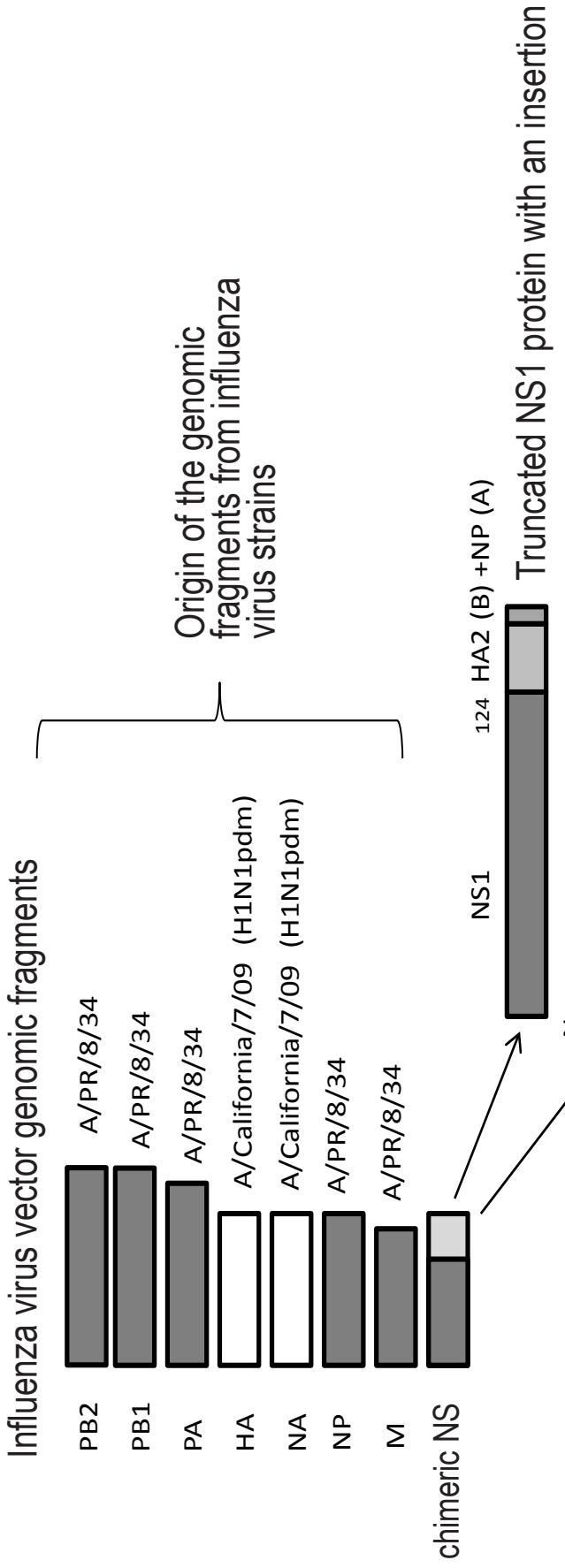

Influenza virus vector genomic fragments
PB2
PB1
PA
HA
NA
NP
M
chimeric NS
A/PR/8/34
A/PR/8/34
A/PR/8/34
A/California/7/09 (H1N1pdm)
A/California/7/09 (H1N1pdm)
A/PR/8/34
A/PR/8/34
Origin of the genomic fragments from influenza virus strains
NS1
124 HA2 (B) +NP (A)
Truncated NS1 protein with an insertion
Nep
Nep protein from H2N2 heterologous strain

FIG. 8

PB2

agcgaaagcaggtcaattatattcaatatggaaagaataaaagaactacgaaatctaatgtcgcagtctcgcacccgcgagatact
cacaaaaaccaccgtggaccatatggccataatcaagaagtacacatcaggaagacaggagaagaacccagcacttaggatga
aatggatgatggcaatgaaatatccaattacagcagacaagaggataacggaaatgattcctgagagaaatgagcaaggacaaa
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catcaatgaactgagcaaccttgcgaaaggagagaaggctaatgtgctaattgggcaaggagacgtggtgttggtaatgaaacgg
aaacgggactctagcatacttactgacagccagacagcgaccaaaagaattcggatggccatcaattagtgtcgaatagtttaaaa
acgaccttgtttctact

SEQ ID NO: 14

PB1

agcgaaagcaggcaaaccatttgaatggatgtcaatccgaccttacttttcttaaaagtgccagcacaaaatgctataagcacaactttcccttatact
ggagaccctccttacagccatgggacaggaacaggatacaccatggatactgtcaacaggacacatcagtactcagaaaagggaagatggacaac
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agagttcactgagatcatgaagatctgttccaccattgaagagctcagacggcaaaaatagtgaatttagcttgtccttcatgaaaaaatgccttgttt
ctact

SEQ ID NO: 15

FIG. 8 (cont.)

PA

agcgaaagcaggtactgatccaaaatggaagattttgtgcgacaatgcttcaatccgatgattgtcgagcttgcggaaaaaacaatgaaagagtat
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SEQ ID NO: 16

NP

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SEQ ID NO: 17

FIG. 8 (cont.)

M

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SEQ ID NO: 18

HA

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SEQ ID NO: 19

FIG. 8 (cont.)

NA

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SEQ ID NO: 20

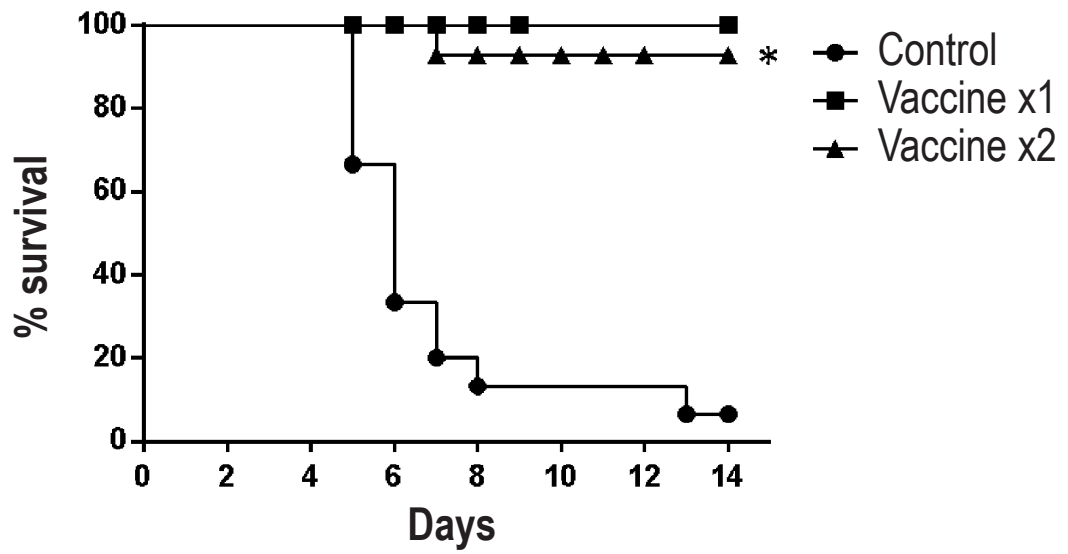
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SEQ ID NO: 21

FIG. 9

(A) A/California/07/09pdm



(B) A/Aichi/2/68 (H3N2)

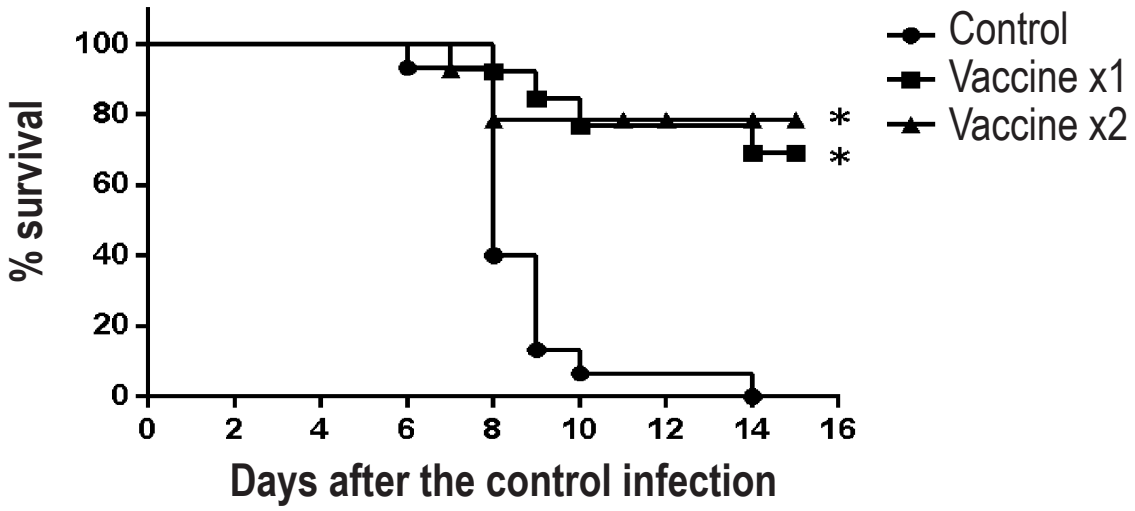
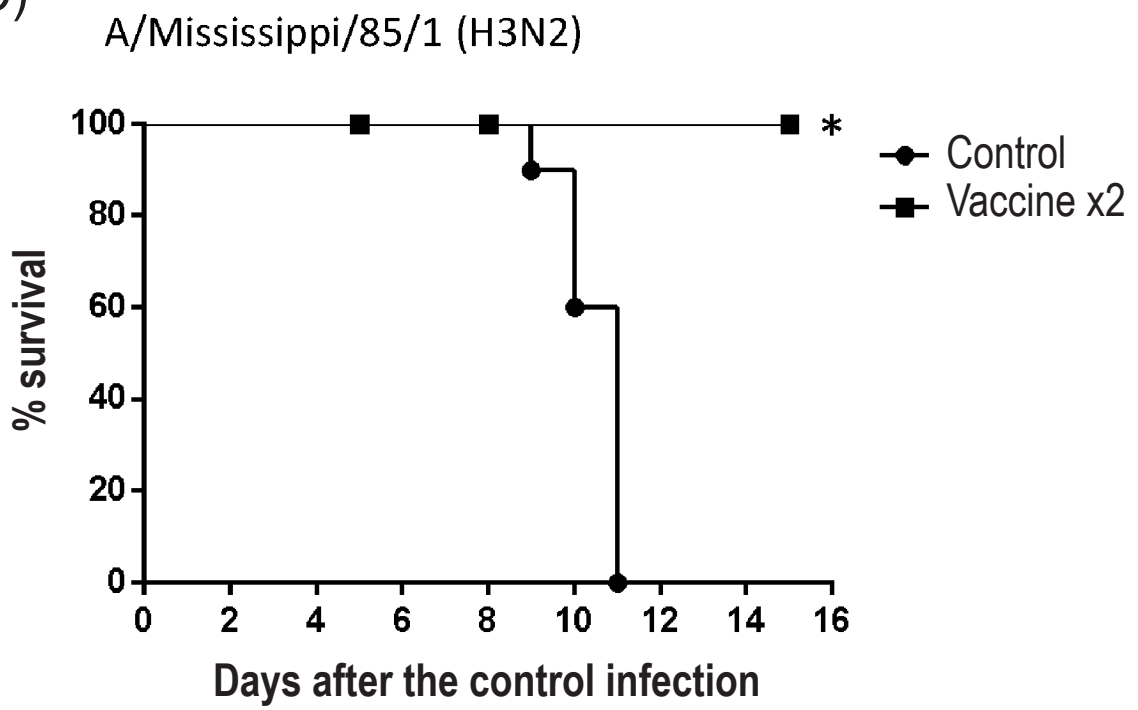


FIG. 9 (cont.)

(C)


A/Mississippi/85/1 (H3N2)
100
80
60
40
20
0
% survival
0
2
4
6
8
10
12
14
16
Days after the control infection
*
Control
Vaccine x2

(D)

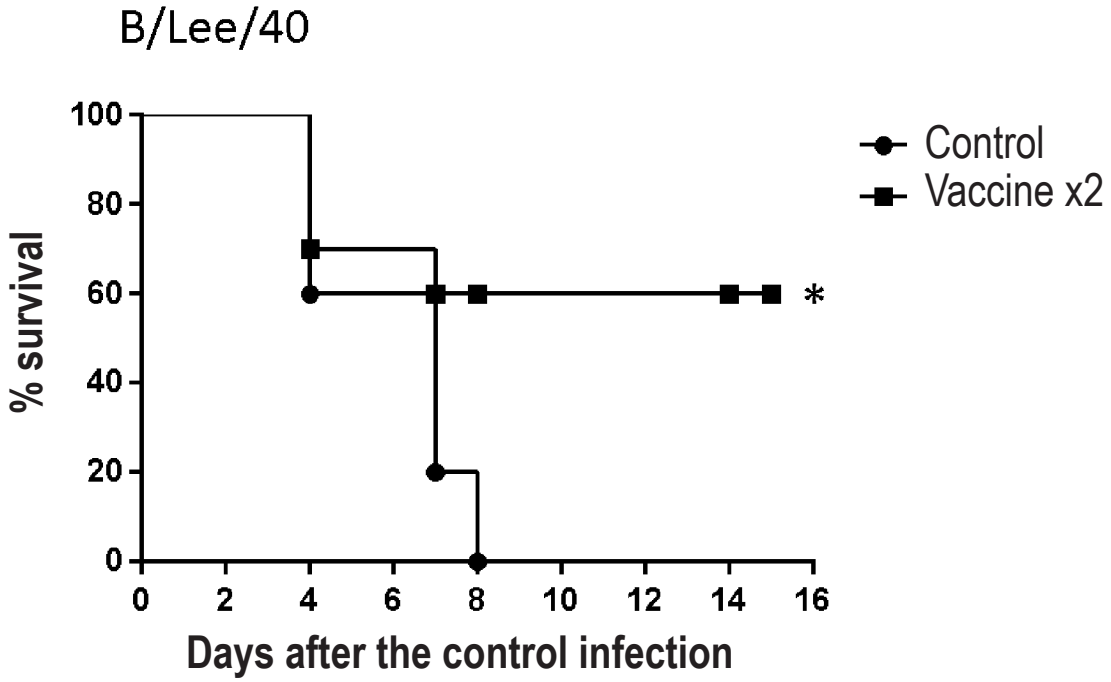
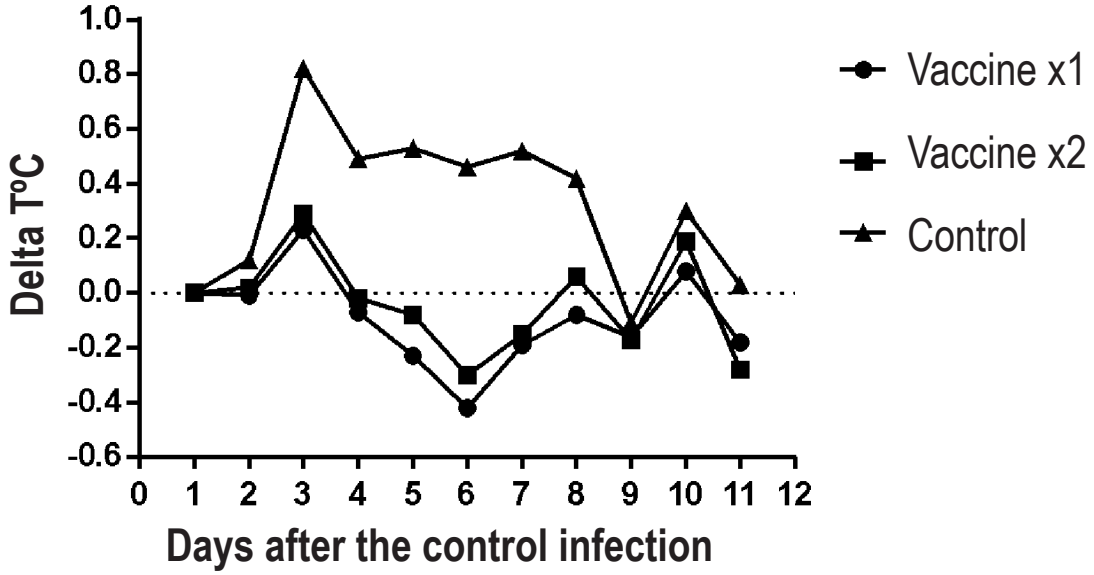
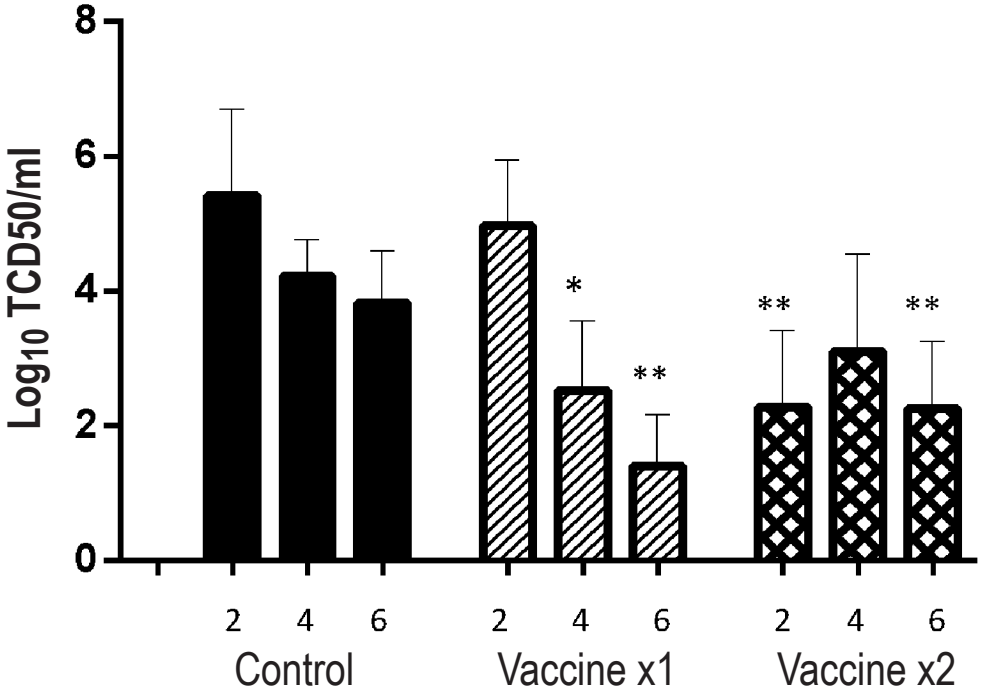

B/Lee/40
100
80
60
40
20
0
% survival
0
2
4
6
8
10
12
14
16
Days after the control infection
*
Control
Vaccine x2

FIG. 10

(A)


1.0
0.8
0.6
0.4
0.2
0.0
-0.2
-0.4
-0.6
Delta T°C
0 1 2 3 4 5 6 7 8 9 10 11 12
Days after the control infection
Vaccine x1
Vaccine x2
Control

(B)


8
6
4
2
0
Log10 TCD50/ml
*
**
**
**
2 4 6 2 4 6 2 4 6
Control
Vaccine x1
Vaccine x2