```
Query  1    MELPILKANAITTILAAVTFCFASSQNITEEFYQSTCSAVSKGYLSALRTGWYTSVITIE  60
            MELPILKANAITTILAAVTFCFASSQNITEEFYQSTCSAVSKGYLSALRTGWYTSVITIE
Sbjct  1    MELPILKANAITTILAAVTFCFASSQNITEEFYQSTCSAVSKGYLSALRTGWYTSVITIE  60

Query  61   LSNIKKNKCNGTDAKVKLMKQELDKYKNAVTELQLLMQSTPAANNRARRELPRFMNYTLN  120
            LSNIKKNKCNGTDAKVKLMKQELDKYKNAVTELQLLMQSTPAANNRARRELPRFMNYTLN
Sbjct  61   LSNIKKNKCNGTDAKVKLMKQELDKYKNAVTELQLLMQSTPAANNRARRELPRFMNYTLN  120

Query  121  NTKKTNVTLSKKRKRRFLGFLLGVGSAIASGIAVSKVLHLEGEVNKIKSALLSTNKAVVS  180
            NTKKTNVTLSKKRKRRFLGFLLGVGSAIASGIAVSKVLHLEGEVNKIKSALLSTNKAVVS
Sbjct  121  NTKKTNVTLSKKRKRRFLGFLLGVGSAIASGIAVSKVLHLEGEVNKIKSALLSTNKAVVS  180

Query  181  LSNGVSVLTSRVLDLKNYIDKQLLPIVNKQSCRISNIETVIEFQQKNNRLLEITREFSVN  240
            LSNGVSVLTSRVLDLKNYIDKQLLPIVNKQSCRISNIETVIEFQQKNNRLLEITREFSVN
Sbjct  181  LSNGVSVLTSRVLDLKNYIDKQLLPIVNKQSCRISNIETVIEFQQKNNRLLEITREFSVN  240

Query  241  AGVTTPVSTYMLTNSELLSLINDMPITNDQKKLMSNNVQIVRQQSYSIMSIIKEEVLAYV  300
            AGVTTPVSTYMLTNSELLSLINDMPITNDQKKLMSNNVQIVRQQSYSIMSIIKEEVLAYV
Sbjct  241  AGVTTPVSTYMLTNSELLSLINDMPITNDQKKLMSNNVQIVRQQSYSIMSIIKEEVLAYV  300

Query  301  VQLPLYGVIDTPCWKLHTSPLCTTNTKEGSNICLTRTDRGWYCDNAGSVSFFPQAEKCKV  360
            VQLPLYGVIDTPCWKLHTSPLCTTNTKEGSNICLTRTDRGWYCDNAGSVSFFPQAEKCKV
Sbjct  301  VQLPLYGVIDTPCWKLHTSPLCTTNTKEGSNICLTRTDRGWYCDNAGSVSFFPQAEKCKV  360

Query  361  QSNRVFCDTMYSLTLPSEVNLCNVDIFNPKYDCKIMTSKTDVSSSVITSLGAIVSCYGKT  420
            QSNRVFCDTMYSLTLPSEVNLCNVDIFNPKYDCKIMTSKTDVSSSVITSLGAIVSCYGKT
Sbjct  361  QSNRVFCDTMYSLTLPSEVNLCNVDIFNPKYDCKIMTSKTDVSSSVITSLGAIVSCYGKT  420

Query  421  KCTASNKNRGIIKTFSNGCDYVSNKGVDTVSVGNTLYYVNKQEGKSLYVKGEPIINFYDP  480
            KCTASNKNRGIIKTFSNGCDYVSNKGVDTVSVGNTLYYVNKQEGKSLYVKGEPIINFYDP
Sbjct  421  KCTASNKNRGIIKTFSNGCDYVSNKGVDTVSVGNTLYYVNKQEGKSLYVKGEPIINFYDP  480

Query  481  LVFPSDEFDASISQVNEKINQSLAFIRKSDELLHNVNAGKSTTNIMITTIIIVIIVILLS  540
            LVFPSDEFDASISQVNEKINQSLAFIRKSDELLHNVNAGKSTTNIMITTIIIVIIVILLS
Sbjct  481  LVFPSDEFDASISQVNEKINQSLAFIRKSDELLHNVNAGKSTTNIMITTIIIVIIVILLS  540

Query  541  LIAVGLLLYCKARSTPVTLSKDQLSGINNIAFSN    (SEQ ID NO: 3)
            LIAVGLLLYCKARSTP+TLSKDQLSGINNIAFSN
Sbjct  541  LIAVGLLLYCKARSTPITLSKDQLSGINNIAFSN       (SEQ ID NO: 4)
```

FIG. 1

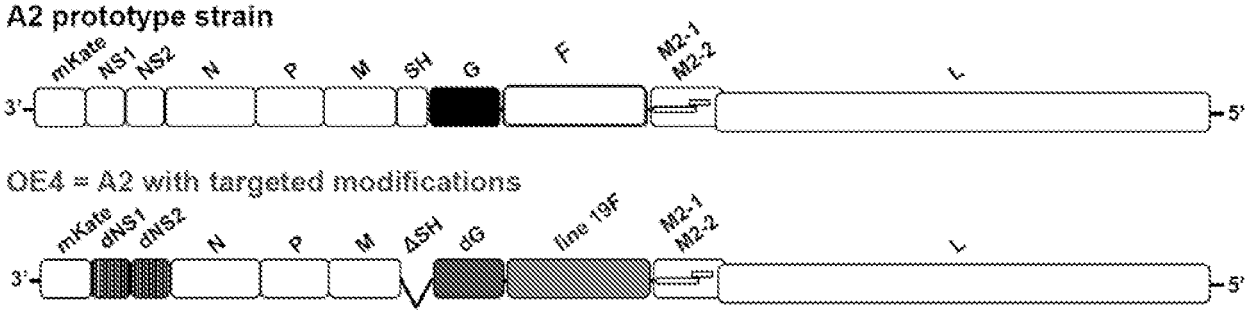
A2 prototype strain
mKate
NS1
NS2
N
P
M
SH
G
F
M2-1
M2-2
L
3'
5'
OE4 = A2 with targeted modifications
mKate
dNS1
dNS2
N
P
M
ΔSH
dG
line 19F
M2-1
M2-2
L
3'
5'

FIG. 2

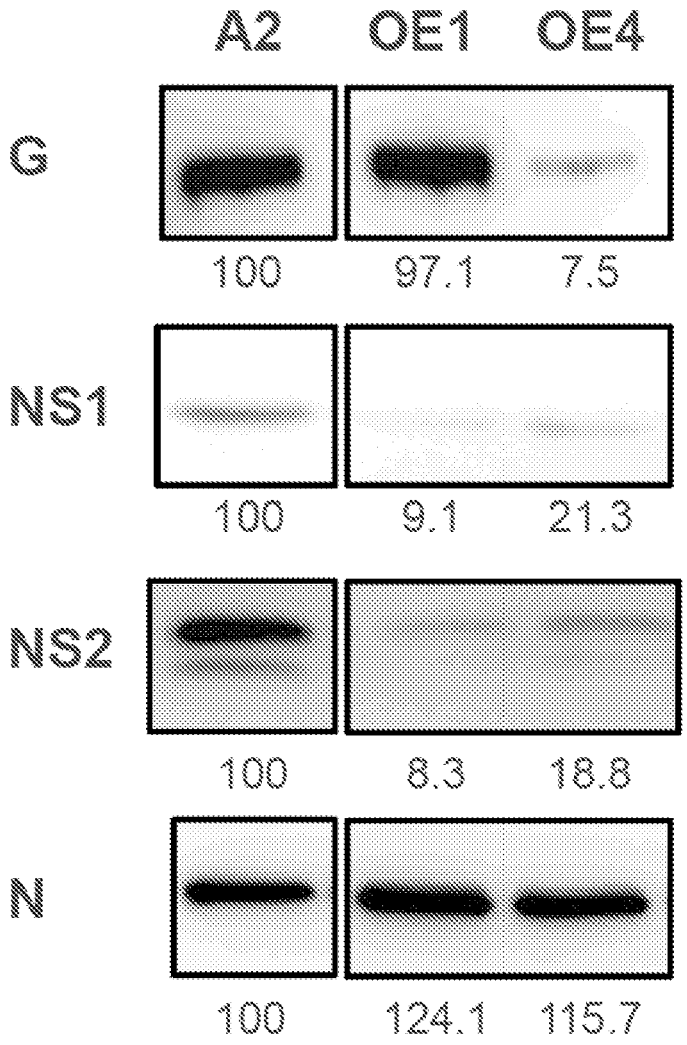
A2
OE1
OE4
G
100
97.1
7.5
NS1
100
9.1
21.3
NS2
100
8.3
18.8
N
100
124.1
115.7

FIG. 3

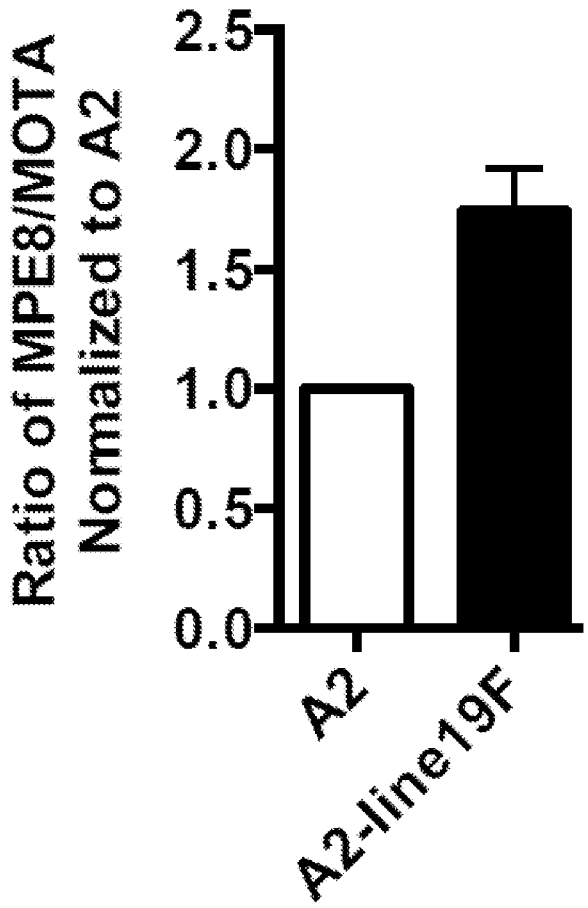
Ratio of MPE8/MOTA
Normalized to A2
2.5
2.0
1.5
1.0
0.5
0.0
A2
A2-line19F

FIG. 4

```
Query  1    MELLIHRSSAIFLTLAINALYLTSSQNITEEFYQSTCSAVSRGYLSALRTGWYTSVITIE  60
            MELLIHRSSAIFLTLAINALYLTSSQNITEEFYQSTCSAVSRGYLSALRTGWYTSVITIE
Sbjct  1    MELLIHRSSAIFLTLAINALYLTSSQNITEEFYQSTCSAVSRGYLSALRTGWYTSVITIE  60

Query  61   LSNIKETKCNGTDTKVKLMKQELDKYKNAVTELQLLMQNTPAANNRARREAPQYMNYTIN  120
            LSNIKETKCNGTDTKVKL+KQELDKYKNAVTELQLLMQNTPAANNRARREAPQYMNYTIN
Sbjct  61   LSNIKETKCNGTDTKVKLIKQELDKYKNAVTELQLLMQNTPAANNRARREAPQYMNYTIN  120

Query  121  TTKNLNVSISKKRKRRFLGFLLGVGSAIASGIAVSKVLHLEGEVNKIKNALLSTNKAVVS  180
            TTKNLNVSISKKRKRRFLGFLLGVGSAIASGIAVSKVLHLEGEVNKIKNALLSTNKAVVS
Sbjct  121  TTKNLNVSISKKRKRRFLGFLLGVGSAIASGIAVSKVLHLEGEVNKIKNALLSTNKAVVS  180

Query  181  LSNGVSVLTSRVLDLKNYINNQLLPIVNQQSCRISNIETVIEFQQKNSRLLEITREFSVN  240
            LSNGVSVLTS+VLDLKNYINNQLLPIVNQQSCRISNIETVIEFQQKNSRLLEITREFSVN
Sbjct  181  LSNGVSVLTSKVLDLKNYINNQLLPIVNQQSCRISNIETVIEFQQKNSRLLEITREFSVN  240

Query  241  AGVTTPLSTYMLTNSELLSLINDMPITNDQKKLMSSNVQIVRQQSYSIMSIIKEEVLAYV  300
            AGVTTPLSTYMLTNSELLSLINDMPITNDQKKLMSSNVQIVRQQSYSIMSIIKEEVLAYV
Sbjct  241  AGVTTPLSTYMLTNSELLSLINDMPITNDQKKLMSSNVQIVRQQSYSIMSIIKEEVLAYV  300

Query  301  VQLPIYGVIDTPCWKLHTSPLCTTNIKEGSNICLTRTDRGWYCDNAGSVSFFPQADKCKV  360
            VQLPIYGVIDTPCWKLHTSPLCTTNIKEGSNICLTRTDRGWYCDNAGSVSFFPQAD CKV
Sbjct  301  VQLPIYGVIDTPCWKLHTSPLCTTNIKEGSNICLTRTDRGWYCDNAGSVSFFPQADTCKV  360

Query  361  QSNRVFCDTMYSLTLPSEVSLCNTDIFNSKYDCKIMTSKTDISSSVITSLGAIVSCYGKT  420
            QSNRVFCDTM SLTLPSEVSLCNTDIFNSKYDCKIMTSKTDISSSVITSLGAIVSCYGKT
Sbjct  361  QSNRVFCDTMNSLTLPSEVSLCNTDIFNSKYDCKIMTSKTDISSSVITSLGAIVSCYGKT  420

Query  421  KCTASNKNRGIIKTFSNGCDYVSNKGVDTVSVGNTLYYVNKLEGKNLYVKGEPIINYYDP  480
            KCTASNKNRGIIKTFSNGCDYVSNKGVDTVSVGNTLYYVNKLEGKNLYVKGEPIINYYDP
Sbjct  421  KCTASNKNRGIIKTFSNGCDYVSNKGVDTVSVGNTLYYVNKLEGKNLYVKGEPIINYYDP  480

Query  481  LVFPSDEFDASISQVNEKINQSLAFIRRSDELLHNVNTGKSTTNIMITAIIIVIIVVLLS  540
            LVFPSDEFDASISQVNEKINQSLAFIRRSDELLHNVNTGKSTTNIMITAIIIVIIVVLLS
Sbjct  481  LVFPSDEFDASISQVNEKINQSLAFIRRSDELLHNVNTGKSTTNIMITAIIIVIIVVLLS  540

Query  541  LIAIGLLLYCKAKNTPVTLSKDQLSGINNIAFS    (SEQ ID NO:1)
            LIAIGLLLYCKAKNTPVTLSKDQLSGINNIAFS
Sbjct  541  LIAIGLLLYCKAKNTPVTLSKDQLSGINNIAFS     (SEQ ID NO: 2)
```

FIG. 5A

```
Query  1    MELLIHRSSAIFLTLAINALYLTSSQNITEEFYQSTCSAVSRGYLSALRTGWYTSVITIE  60
            MEL I +++AI   LA       SSQNITEEFYQSTCSAVS+GYLSALRTGWYTSVITIE
Sbjct  1    MELPILKANAITTILAAVTFCFASSQNITEEFYQSTCSAVSKGYLSALRTGWYTSVITIE  60

Query  61   LSNIKETKCNGTDTKVKLMKQELDKYKNAVTELQLLMQNTPAANNRARREAPQYMNYTIN  120
            LSNIK+ KCNGTD KVKLMKQELDKYKNAVTELQLLMQ+TPAANNRARRE P++MNYT+N
Sbjct  61   LSNIKKNKCNGTDAKVKLMKQELDKYKNAVTELQLLMQSTPAANNRARRELPRFMNYTLN  120

Query  121  TTKNLNVSISKKRKRRFLGFLLGVGSAIASGIAVSKVLHLEGEVNKIKNALLSTNKAVVS  180
             TK  NV++SKKRKRRFLGFLLGVGSAIASGIAVSKVLHLEGEVNKIK+ALLSTNKAVVS
Sbjct  121  NTKKTNVTLSKKRKRRFLGFLLGVGSAIASGIAVSKVLHLEGEVNKIKSALLSTNKAVVS  180

Query  181  LSNGVSVLTSRVLDLKNYINNQLLPIVNQQSCRISNIETVIEFQQKNSRLLEITREFSVN  240
            LSNGVSVLTSRVLDLKNYI+ QLLPIVN+QSCRISNIETVIEFQQKN+RLLEITREFSVN
Sbjct  181  LSNGVSVLTSRVLDLKNYIDKQLLPIVNKQSCRISNIETVIEFQQKNNRLLEITREFSVN  240

Query  241  AGVTTPLSTYMLTNSELLSLINDMPITNDQKKLMSSNVQIVRQQSYSIMSIIKEEVLAYV  300
            AGVTTP+STYMLTNSELLSLINDMPITNDQKKLMS+NVQIVRQQSYSIMSIIKEEVLAYV
Sbjct  241  AGVTTPVSTYMLTNSELLSLINDMPITNDQKKLMSNNVQIVRQQSYSIMSIIKEEVLAYV  300

Query  301  VQLPIYGVIDTPCWKLHTSPLCTTNIKEGSNICLTRTDRGWYCDNAGSVSFFPQADKCKV  360
            VQLP+YGVIDTPCWKLHTSPLCTTN KEGSNICLTRTDRGWYCDNAGSVSFFPQA+KCKV
Sbjct  301  VQLPLYGVIDTPCWKLHTSPLCTTNTKEGSNICLTRTDRGWYCDNAGSVSFFPQAEKCKV  360

Query  361  QSNRVFCDTMYSLTLPSEVSLCNTDIFNSKYDCKIMTSKTDISSSVITSLGAIVSCYGKT  420
            QSNRVFCDTMYSLTLPSEV+LCN DIFN KYDCKIMTSKTD+SSSVITSLGAIVSCYGKT
Sbjct  361  QSNRVFCDTMYSLTLPSEVNLCNVDIFNPKYDCKIMTSKTDVSSSVITSLGAIVSCYGKT  420

Query  421  KCTASNKNRGIIKTFSNGCDYVSNKGVDTVSVGNTLYYVNKLEGKNLYVKGEPIINYYDP  480
            KCTASNKNRGIIKTFSNGCDYVSNKGVDTVSVGNTLYYVNK EGK+LYVKGEPIIN+YDP
Sbjct  421  KCTASNKNRGIIKTFSNGCDYVSNKGVDTVSVGNTLYYVNKQEGKSLYVKGEPIINFYDP  480

Query  481  LVFPSDEFDASISQVNEKINQSLAFIRRSDELLHNVNTGKSTTNIMITAIIIVIIVVLLS  540
            LVFPSDEFDASISQVNEKINQSLAFIR+SDELLHNVN GKSTTNIMIT IIIVIIV+LLS
Sbjct  481  LVFPSDEFDASISQVNEKINQSLAFIRKSDELLHNVNAGKSTTNIMITTIIIVIIVILLS  540

Query  541  LIAIGLLLYCKAKNTPVTLSKDQLSGINNIAFS   (SEQ ID NO:1)

             LIA+GLLLYCKA++TP+TLSKDQLSGINNIAFS
Sbjct  541  LIAVGLLLYCKARSTPITLSKDQLSGINNIAFS   (SEQ ID NO:4)
```

FIG. 5B

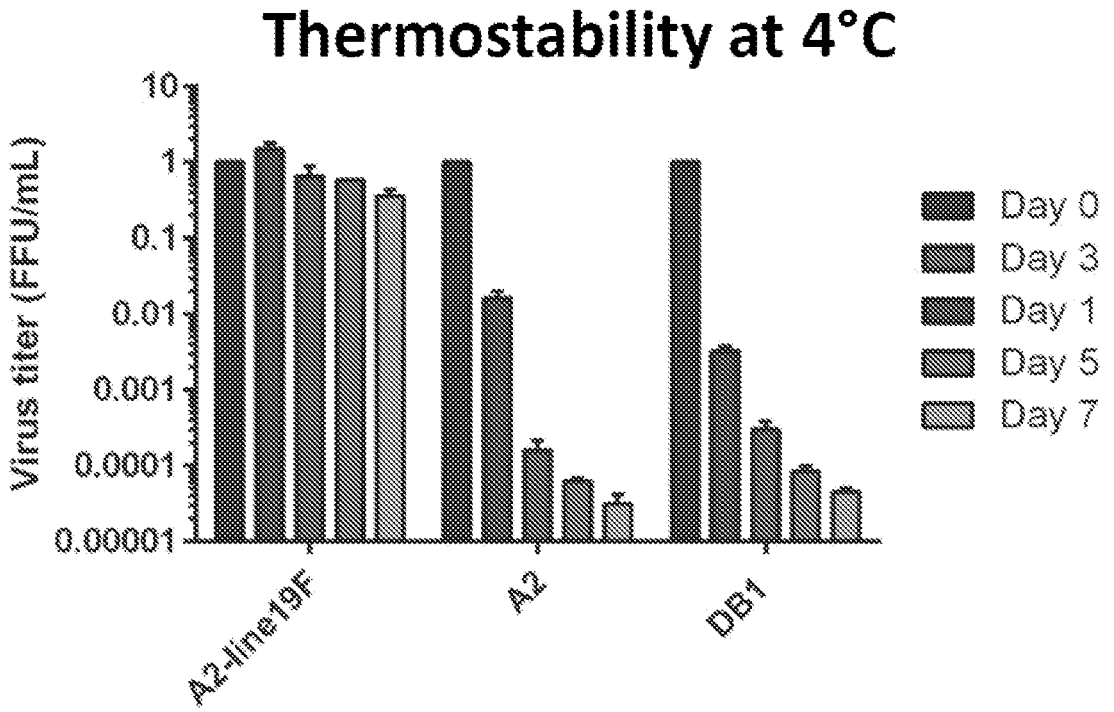
Thermostability at 4°C
Virus titer (FFU/mL)
10
1
0.1
0.01
0.001
0.0001
0.00001
A2-line19F
A2
DB1
Day 0
Day 3
Day 1
Day 5
Day 7

FIG. 6A

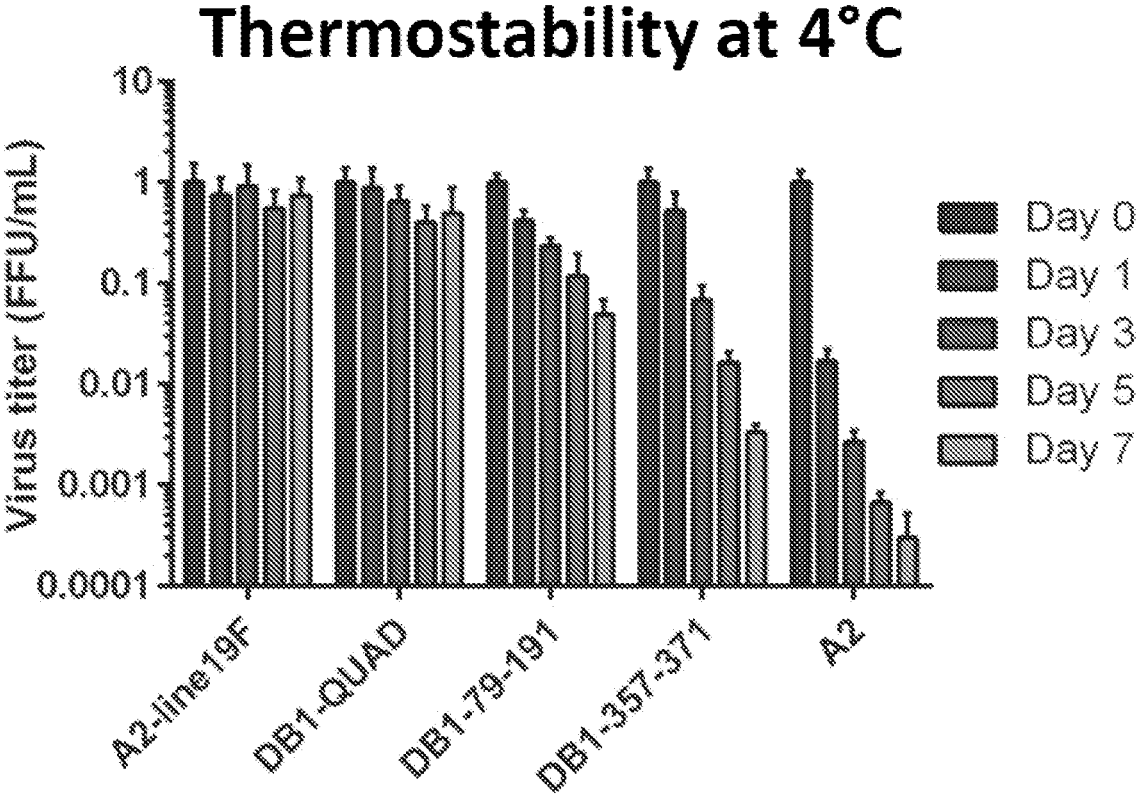
Thermostability at 4°C
Virus titer (FFU/mL)
10
1
0.1
0.01
0.001
0.0001
A2-line19F
DB1-QUAD
DB1-79-191
DB1-357-371
A2
Day 0
Day 1
Day 3
Day 5
Day 7

FIG. 6B

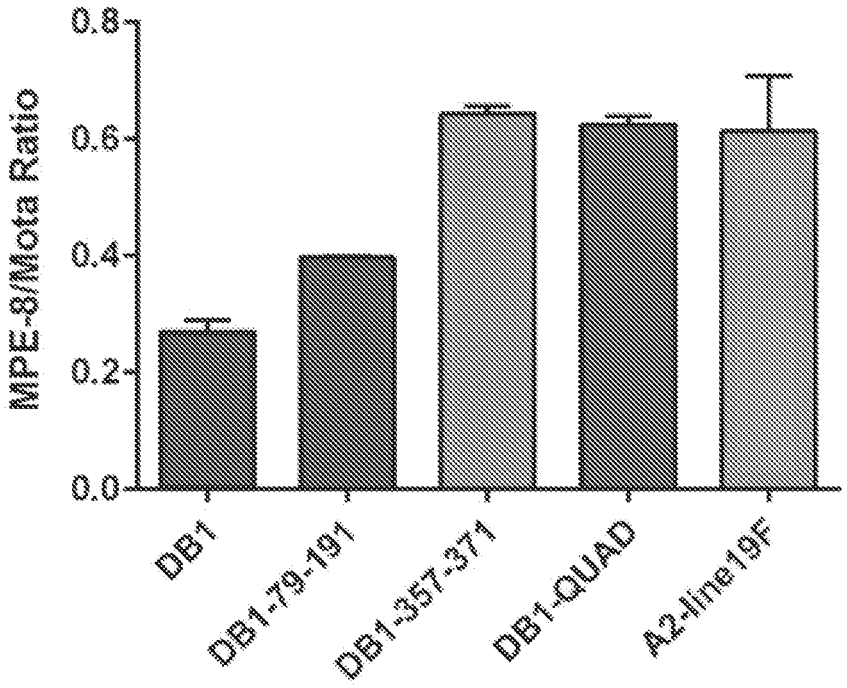
MPE-8/Mota Ratio
0.8
0.6
0.4
0.2
0.0
DB1
DB1-79-191
DB1-357-371
DB1-QUAD
A2-line19F

FIG. 6C

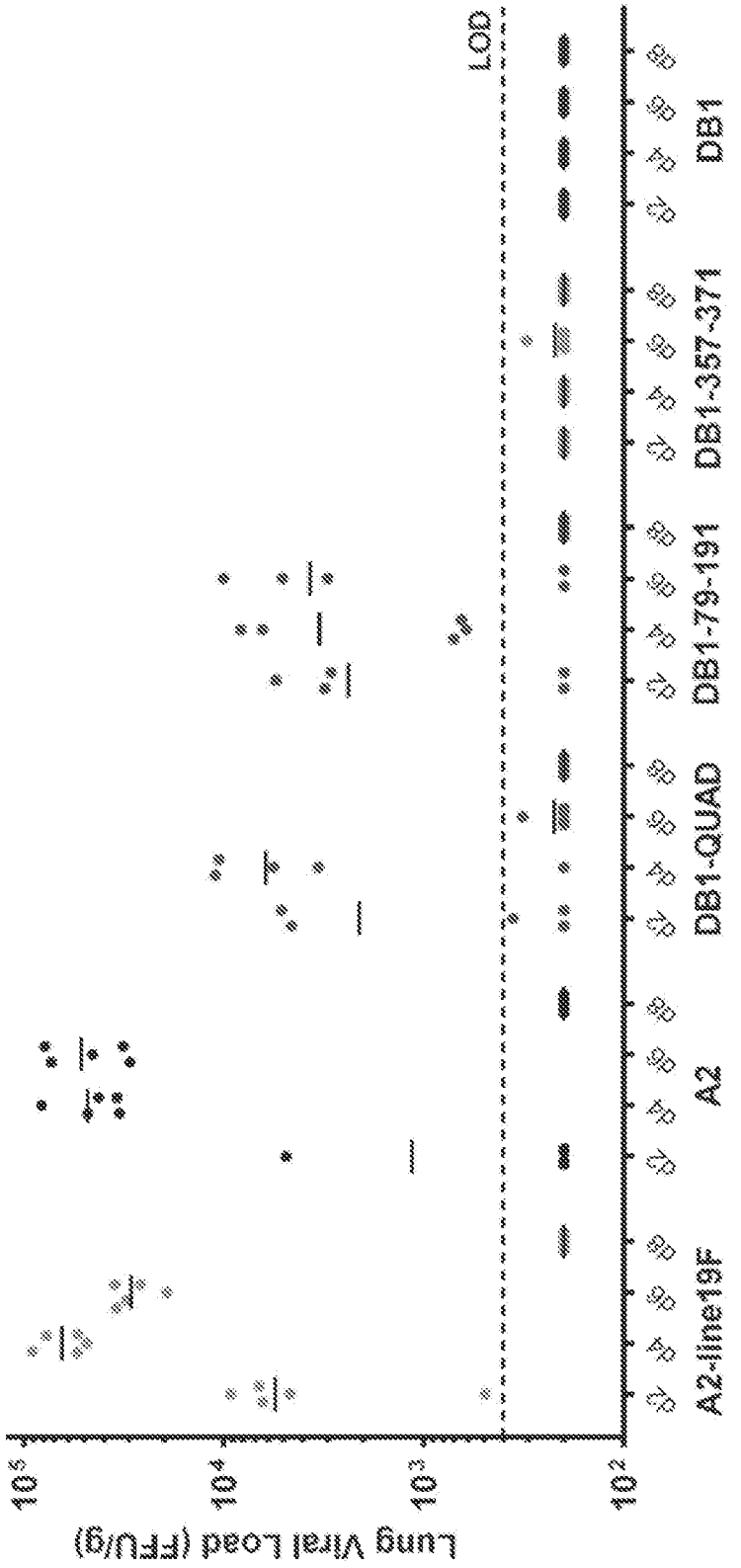
Lung Viral Load (FFU/g)
10^5
10^4
10^3
10^2
LOD
A2-line19F
A2
DB1-QUAD
DB1-79-191
DB1-357-371
DB1
Days Post Infection

FIG. 7A

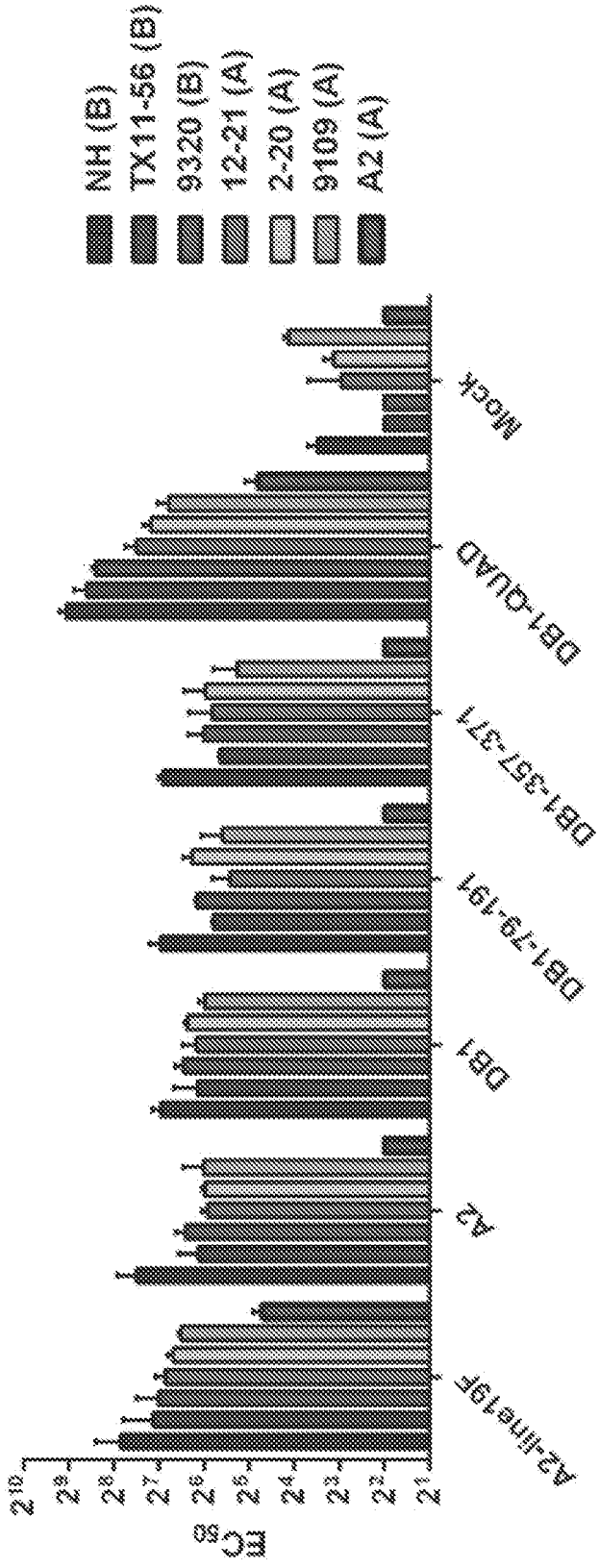
NH (B)
TX11-56 (B)
9320 (B)
12-21 (A)
2-20 (A)
9109 (A)
A2 (A)
Mock
DB1-QUAD
DB1-357-371
DB1-179-191
DB1
A2
A2-line19F
EC50
2^10
2^9
2^8
2^7
2^6
2^5
2^4
2^3
2^2
2^1

FIG. 7B