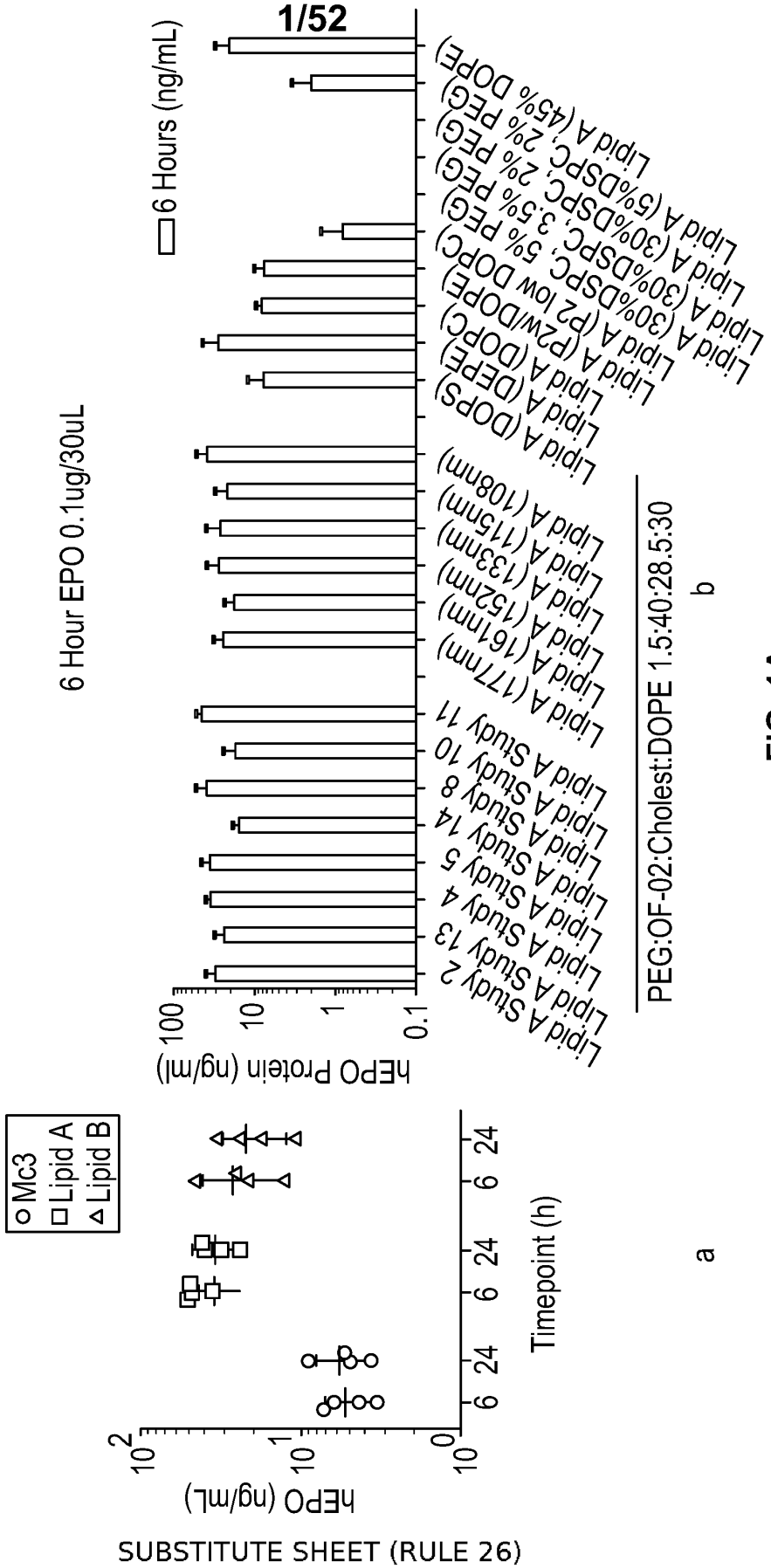
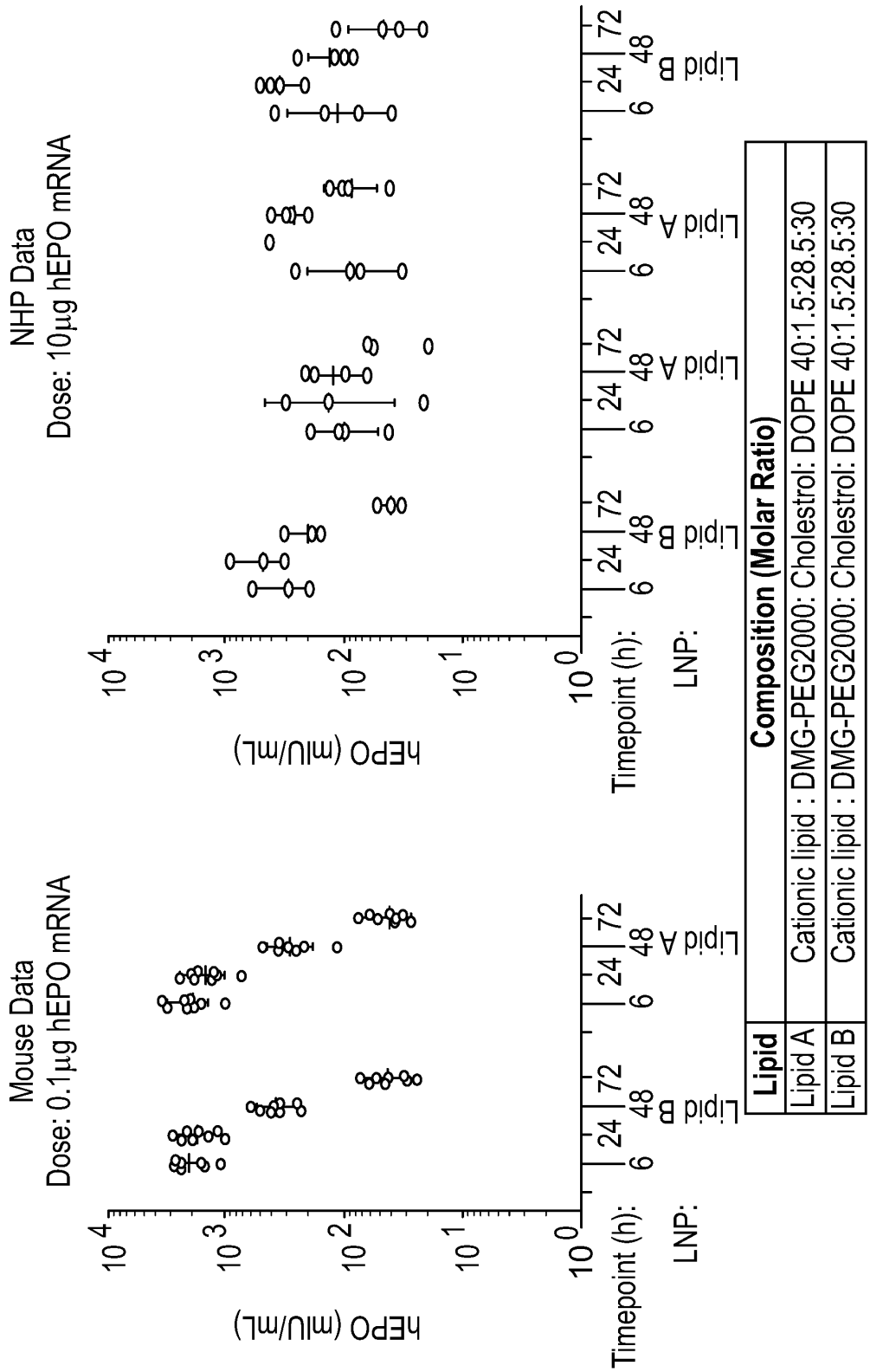
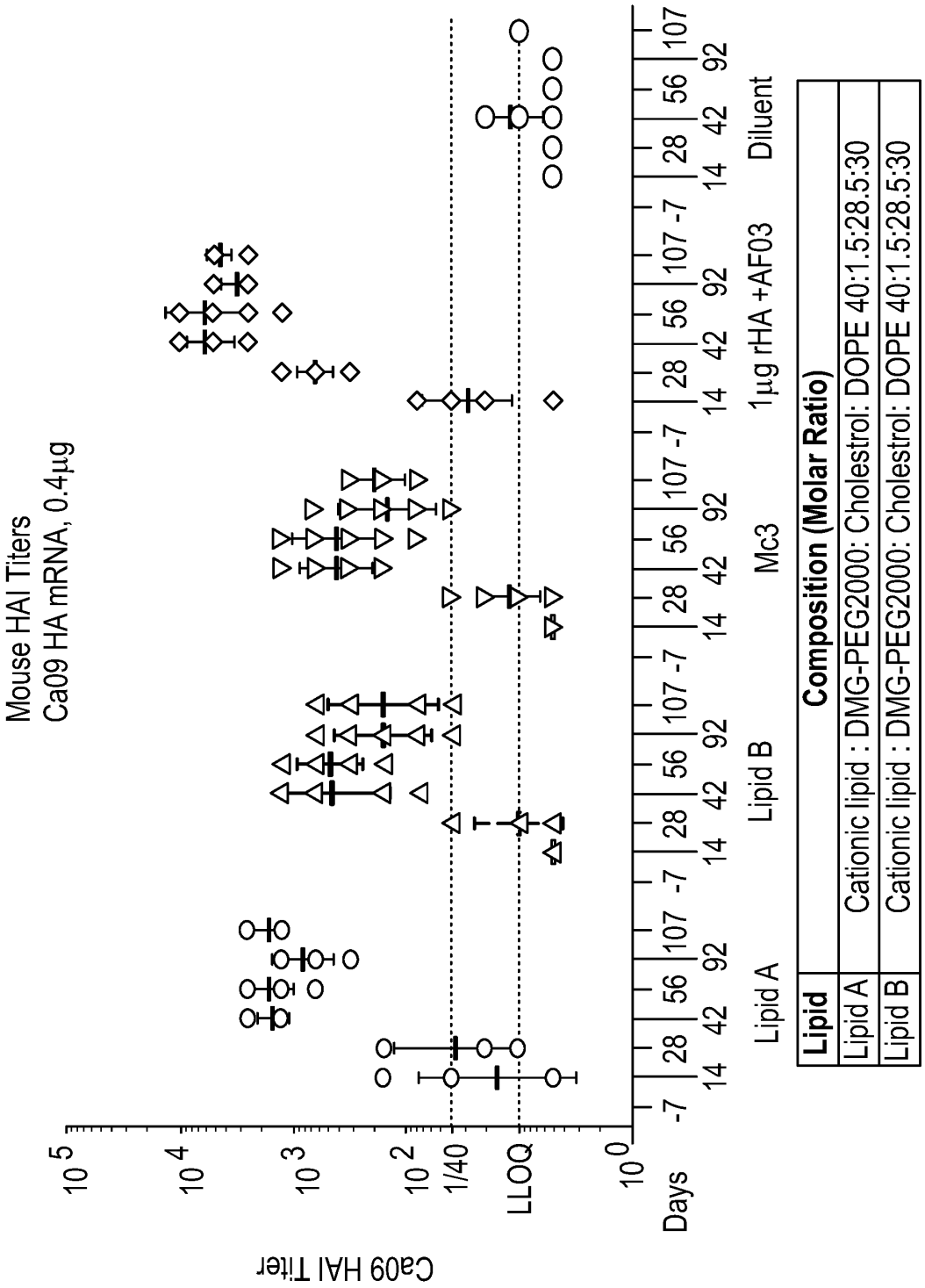

6 Hour EPO 0.1ug/30uL
6 Hours (ng/mL)
hEPO Protein (ng/ml)
100
10
1
0.1
Lipid A Study 2
Lipid A Study 13
Lipid A Study 4
Lipid A Study 5
Lipid A Study 14
Lipid A Study 8
Lipid A Study 10
Lipid A Study 11
Lipid A (177nm)
Lipid A (161nm)
Lipid A (152nm)
Lipid A (133nm)
Lipid A (115nm)
Lipid A (108nm)
Lipid A (DOPS)
Lipid A (DEPE)
Lipid A (DOPC)
Lipid A (P2w/DOPE)
Lipid A (P2 low DOPC)
Lipid A (30%DSPC, 5% PEG)
Lipid A (30%DSPC, 3.5% PEG)
Lipid A (5%DSPC, 2% PEG)
Lipid A (45% DOPE)
PEG:OF-02:Cholest:DOPE 1.5:40:28.5:30
b
hEPO (ng/mL)
Timepoint (h)
Mc3
Lipid A
Lipid B
a

FIG. 1A



Lipid	Composition (Molar Ratio)
Lipid A	Cationic lipid : DMG-PEG2000: Cholestrol: DOPE 40:1.5:28.5:30
Lipid B	Cationic lipid : DMG-PEG2000: Cholestrol: DOPE 40:1.5:28.5:30

FIG. 1B



Lipid	Composition (Molar Ratio)
Lipid A	Cationic lipid : DMG-PEG2000: Cholestrol: DOPE 40:1.5:28.5:30
Lipid B	Cationic lipid : DMG-PEG2000: Cholestrol: DOPE 40:1.5:28.5:30

FIG. 2A

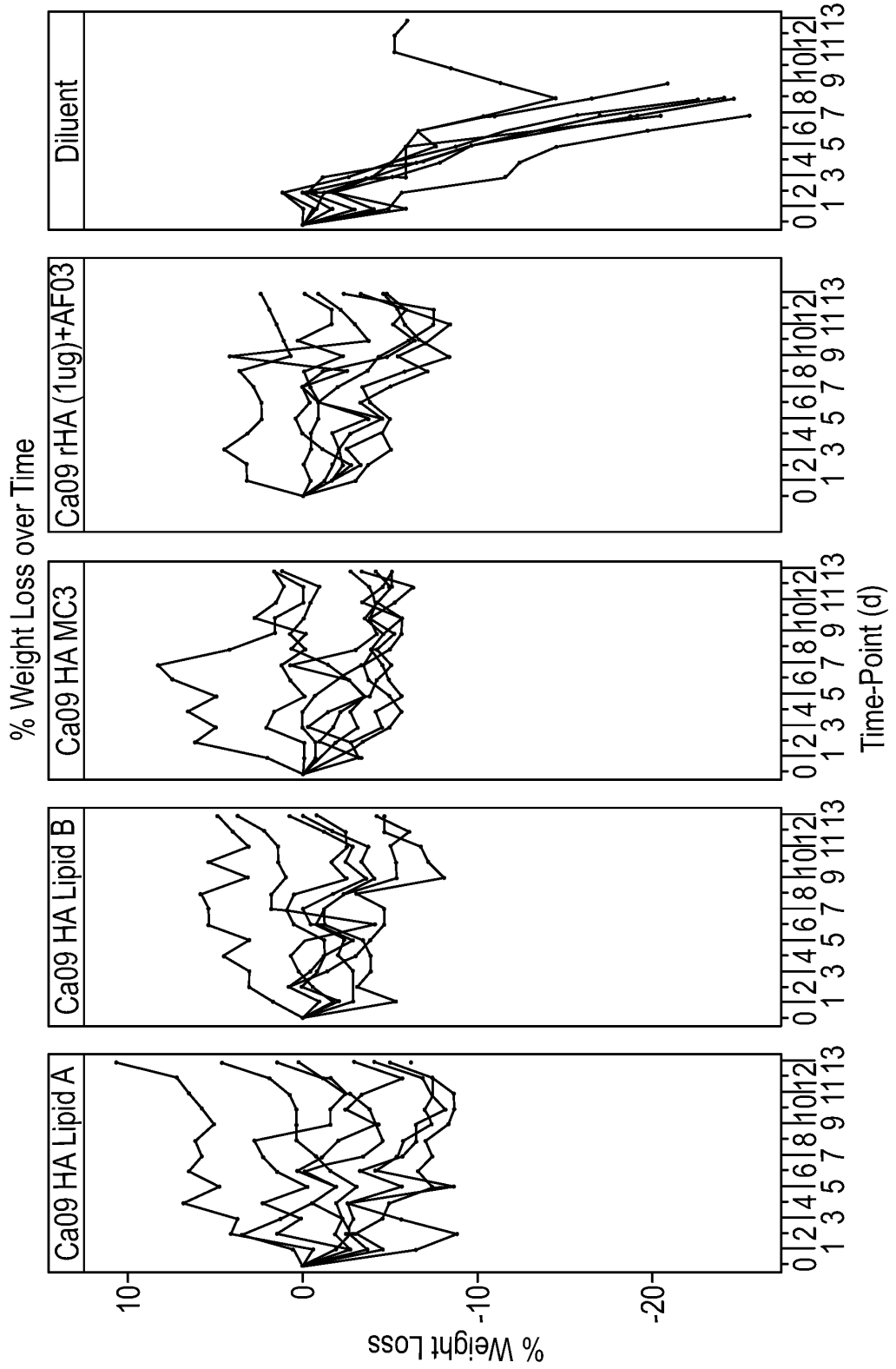
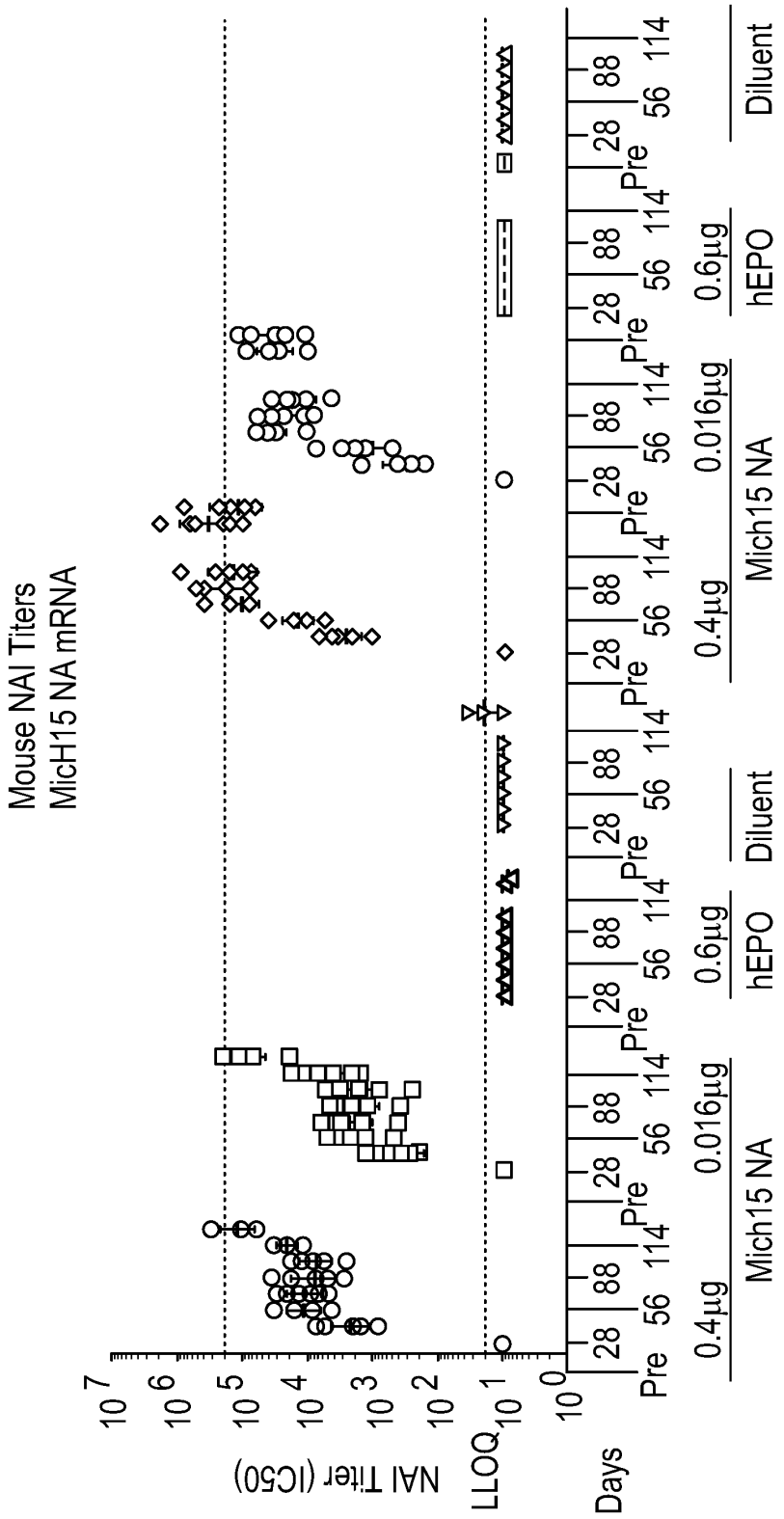

% Weight Loss over Time
Ca09 HA Lipid A
Ca09 HA Lipid B
Ca09 HA MC3
Ca09 rHA (1ug)+AF03
Diluent
% Weight Loss
10
0
-10
-20
0 2 4 6 8 10 12
1 3 5 7 9 11 13
Time-Point (d)

FIG. 2B



Lipid	Composition (Molar Ratio)
Lipid A	Cationic lipid : DMG-PEG2000: Cholestrol: DOPE 40: 1.5:28.5:30

FIG. 3A

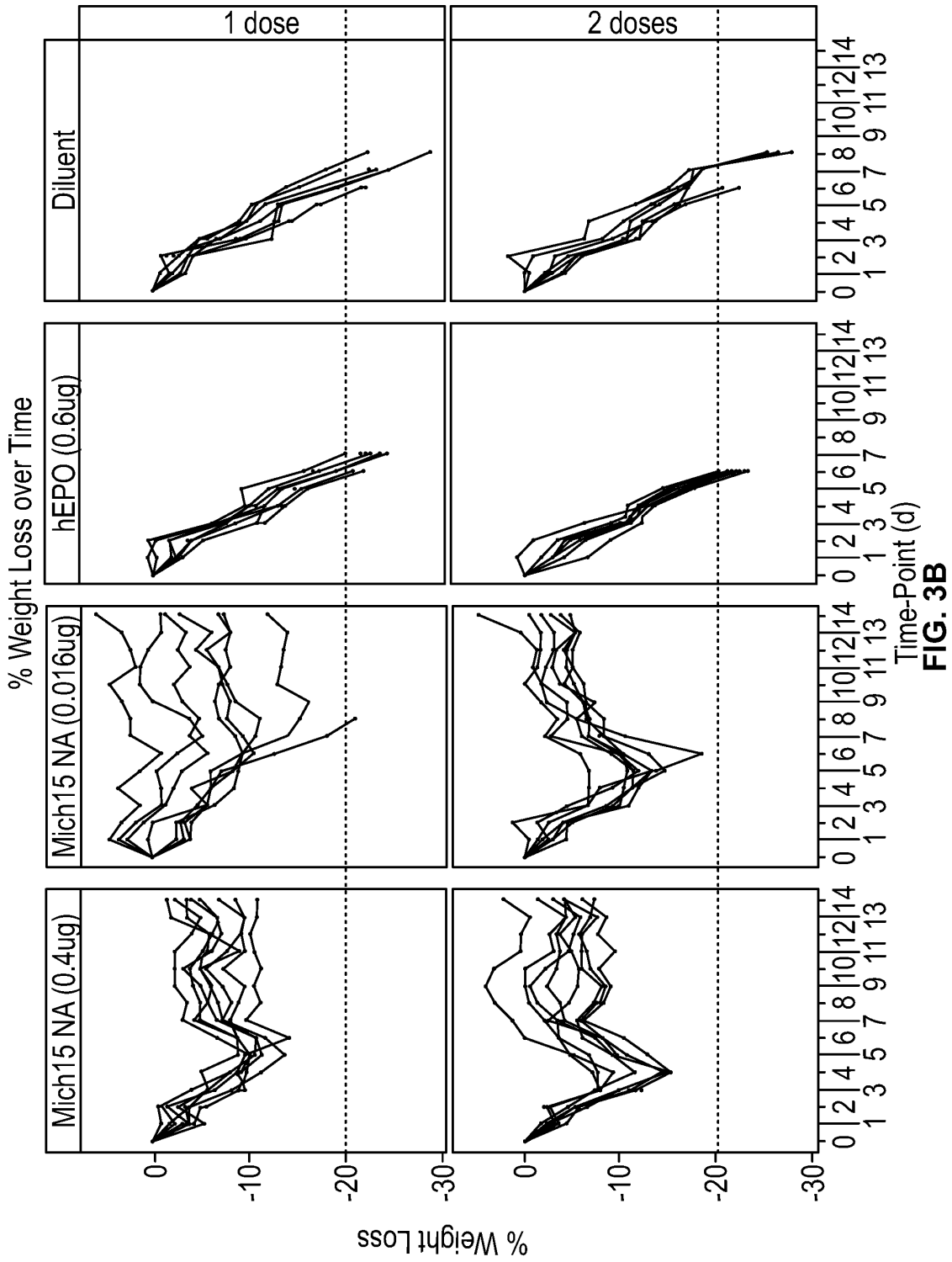
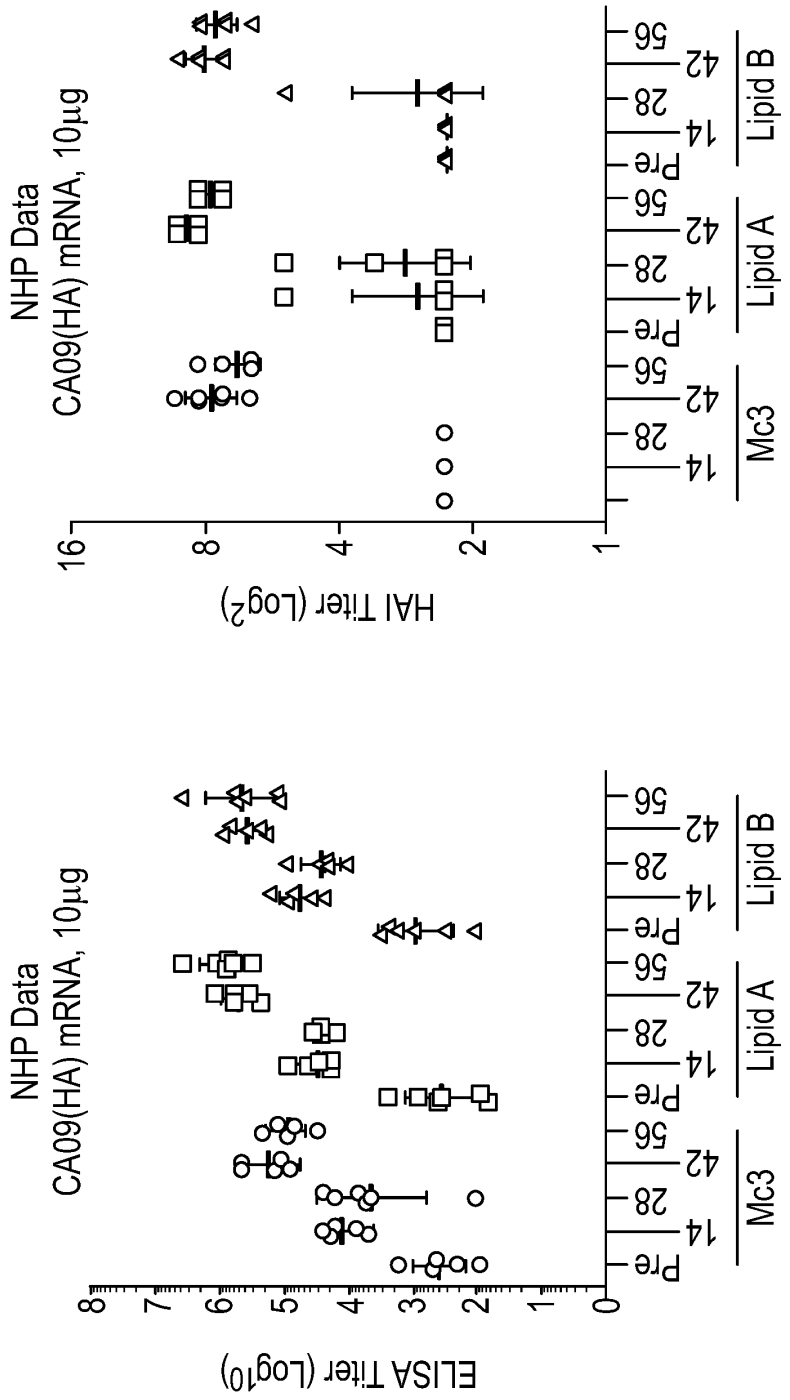

% Weight Loss over Time
1 dose
2 doses
Diluent
hEPO (0.6ug)
Mich15 NA (0.016ug)
Mich15 NA (0.4ug)
% Weight Loss
0
-10
-20
-30
Time-Point (d)
0 1 2 3 4 5 6 7 8 9 10 11 12 13 14

FIG. 3B



Lipid	Composition (Molar Ratio)
Lipid A	Cationic lipid : DMG-PEG2000: Cholestrol: DOPE 40:1.5:28.5:30
Lipid B	Cationic lipid : DMG-PEG2000: Cholestrol: DOPE 40:1.5:28.5:30

FIG. 4

ATGAAAACCATAATCGCGCTCTCATACATACTTTGCCTGGTCTTTGCCCAAAAGATCCCTGGCAACGACAA
CTCAACCGCGACCCTTTGCCTCGGCCATCACGCCGTGCCGAACGGCACTATCGTCAAGACCATCACAAACG
ACCGCATCGAAGTGACCAACGCGACTGAGCTAGTGCAGAACTCCAGCATTGGAGAGATTTGCGATTCTCCA
CACCAAATCCTGGACGGAGAGAATTGTACCTTGATCGACGCGCTGCTGGGGGATCCCGCAGTGCGACGGATT
CCAGAACAAGAAATGGGACCTTTTCGTGGAACGGAAGGCATACTCGAATTGCTACCCCTACGATGTGC
CCGACTACGCCTCGCTGCGGTCCTTCCTCCGGGACCCCTGGAATTCAAAAACGAGAGCTTTAAT
TGGACCGGAGTGACCCAGAATGGCACCTCGAGCGCCTGCATTCGGGGCTCCTCCTCGAGCTTCTTCAGCCG
CCTGAACTGGCTCACTCACCTCAACTACACCCGGCACTGAACGTGACCATGCCGAACAAGGAACAAT
TCGACAAGCTCTACATTTGGGGGGTGCATCACCCGGGTACCGATAAGGACCAGATCTTCCTCTACGCCCAA
TCCTCGGGCCGGATCACCGTGTCCACTAAGCGCTCGCAGGCCGTGATCCCGAACATTGGAAGCAGACC
CCGCATTCGCGACATTCCATCGAGGATCTCGATCTACTGGACGATTGTCAAGCCTGGCGACATCCTCCTCA
TTAACTCCACCGGGAACCTCATCGCCCCTCGGGGTTATTTCAAGATCCGCAGCGGGAAGTCCTCCATCATG
AGAAGCGATGCCCCCATTGGAAAGTGCAAGTCCGAGTGTATCACACCTAACGGAAGCATTCCCAATGACAA
GCCATTCCAGAACGTGAACACAGAATTACCTACGGAGCTTGCCCTCGCTACGTCAAACATTCGACCCTCAAGT
TGGCGACTGGAATGCGCAACGTGCCGGAGAAGCAAACCCGGGGGGATCTTCGGGGCTATCGCGGGATTCATC
GAAAATGGATGGGAAGGAATGGTCGATGGTTGGTACGGTTTCAGACACCAGAACTCCGAGGGGCGGGGCCA
GGCCGCAGACCTGAAGTCCACTCAGGCCGCGATTGACCAGATCAACGGAAAGCTCAACACAGACTCATTGGAA
AGACCAACGAAAAGTTCCACCAAATCGAAAAGGAATTCTCCCGAAGTGGAGGGCCCGGGTGCAAGACCTGGAG
AAGTACGTGGAGGACACTAAGATCGACCTTTGGAGCTATAACGCAGAACTCCTTGTGGCCCTGGAAAACCA
GCACACCATCGACCTGACCGATTCAGAGATGAACACAAGCTCTTTGAGAAAACTAAGAAGCAACTCCGGGAAA
ACGCTGAGGACATGGGAAATGGATGCTTTAAGATCTACCACAAGTGCGACAACGCCTGCATTGAGTCCATA
CGGAACGAAACTTACGACCATAACGTCTACCGGGATGAAGCCCTGAACACAACAGATTCCAGATCAAGGGCGT
GGAGCTGAAGTCCGGCTACAAAGATTGGATCCTGTGGATTTCCTTCGCGATTTCATGCTTCTTGCTCTGCG
TGGCCCTCCTGGGATTCATAATGTGGGCCTGTCAGAAGGGCAACATTAGGTGCAACATATGCATATAA

```
MRT10279  ATGAAAACCATAATCGCGCTCTCATACATACTTTGCCTGGTCTTTGCCCAAAAGATCCCT
H3_WT     ATGAAGACTATCATTGCTTTGAGCTACATTCTATGTCTGGTTTTCGCTCAAAAAATTCCT
          ****** ** ** **  *     ****** ** ** ****** ** ** ****** ** ***

MRT10279  GGCAACGACAACTCAACCGCGACCCTTTGCCTCGGCCATCACGCCGTGCCGAACGGCACT
H3_WT     GGAAATGACAATAGCACGGCAACCGCTGTGCCTTGGGCACCATGCAGTACCAAACGGAACG
          ** ***** ******     ** ** ** ****** ** ** ** ** ** ****** **

MRT10279  ATCGTCAAGACCATCACAAACGACCGCATCGAAGTGACCAACGCGACTGAGCTAGTGCAG
H3_WT     ATAGTGAAAACAATCACAAATGACCGAATTGAAGTTACCTAATGCTACTGAGTTGGTTCAG
          ** ** ** ** ********** ****** ** ****** ** ** ******* * ** ***

MRT10279  AACTCCAGCATTGGAGAGATTTGCGATTCTCCACACCAAATCCTGGACGGAGAGAAATTGT
H3_WT     AATTCCTCAATAGGTGAAATATGCGACAGTCCCTCATCAGATCCTTGATGGAGAGAACTGC
          ** **** ** ** ** ** ******    *** ** ** ****** *** ********** **

MRT10279  ACCTTGATCGACGCGCTGCTGGGGGATCCGCAGTGCGACGGATTCCAGAACAAGAAATGG
H3_WT     ACACTAATAGATGCTCTATTGGGAGACCCTCAGTGTGATGGCTTTTCAAAATAAGAAATGG
          **  * ** ** ** **  **** ** ** ****** ** ** ** ** ** ********** **

MRT10279  GACCTTTTTCGTGGAACGGAGCAAGGCATACTCGAATTGCTACCCCTACGATGTGCCCGAC
H3_WT     GACCTTTTTTGTTGAACGAAAGCCTACAGCAACTGTTACCCTTATGATGTGCCGGAT
          ********** ** ****** ** ****** ** ** ** ****** ** ********** **

MRT10279  TACGGCCTCGCTGCGGTCCTTGGTCGCTTCCTTCCGGGACCCCTGGAATTCAAAAACGAGAGC
H3_WT     TATGCCCTCCCTTAGGTCACTAGTTGCCCTCATCCGGCACACTGGAGTTTAAAAATGAAAGC
          ** ****** **  **** * ** ** ** ****** ** ****** ** ** ****** ***

MRT10279  TTTTAATTTGGACCGGAGTGACCCAGAATGGCACCTCGAGCGCCTGCATTTCGGGGCTCCTCC
H3_WT     TTCAATTTGGACTGGAGTCACTCAAAACGGAACAAGTTCTGCTTGCATAAGGGGATCTAGT
          ** ********** ****** ** ** ** **          ** ******  **** **

MRT10279  TCGAGCTTCTTCAGCCGCCTGAACTGGCTCACTCACCTCAACTACACCTACCCGGCACTG
H3_WT     AGTAGTTTCTTTAGATTAAATTGGTTGACCCACTTAAACTACACATATCCAGCATTG
          ** ****** **  *  * ** **** * ** **** * ********** ** ** *** **
```

```
MRT10279  AACGTGACCATGCCGAACAAGGAACACAATTCGACAAGCTCTACATTTGGGGGGTGCATCAC
H3_WT     AACGTGACTATGCCAAACAAGGAACACAATTTGACAAATTGTACATTTGGGGGGTTCACCAC
          ********** ********** ********** ******  * ********** ** ***

MRT10279  CCGGGTACCGATAAGGACCAGATCTTCCTCTACGCCCAATCCTCGGGCCGGATCACCGTG
H3_WT     CCGGGTACGGACAAGGACCAAAATCTTCCTGTATTGCTCAATCATCAGGAAGAATCACAGTA
          ********** ** ********** ********** ** ** ****** ** **  * ****** **

MRT10279  TCCACTAAGCGCTCGCAGGCGCCGTGATCCCGAACATTGGAAGCAGACCCCGCATTCGC
H3_WT     TCTACCAAAAGAAGCCAACAAGCTGTAATCCCAAATATCGGATCTAGACCCAGAATAAGG
          ** ** **  *    ** ** ** ** ****** ** ** ***     ******* * ** *

MRT10279  GACATTCCATCGAGGATCTCGATCTACTGGACGATTGTCAAGCCTGGCGACATCCTCCTC
H3_WT     GATATCCCTAGCAGAATAAGCATCTATTGGACAATAGTAAAACCGGGAGACATACTTTTG
          ** ** **    ** **      ****** ****** ** ** ** ** ******* ** *

MRT10279  ATTAACTCCCACCGGGAACCTCATCGCCCCTCGGGGTTATTTCAAGATCCGCAGCGGGAAG
H3_WT     ATTAACAGCACAGGGAATCTAATTGCTCCCTAGGGGTTACTTCAAAATACGAAGTGGGAAA
          ******* ***** ****** ** ** ** *** ********* ****** ** ** ** ******

MRT10279  TCCTCCATCATGAGAAGCGATGCCCCCCATTGGAAAGTGCAAGTCCGAGTGTATCACACCT
H3_WT     AGCTCAATAATGAGATCAGATGCCACCCATTGGCAAAATGCAAGTCTGAATGCATCACTCCA
          ***  ** ******* ******  ********** ** ********** ** ** ****** **

MRT10279  AACGGGAAGCATTCCCCAATGACAAGCCATTCCAGAACGTGAACAGAATTACCTACGGAGCT
H3_WT     AATGGGAAGCATTCCCCAATGACAAACCATTCCAAAATGTAAACAGGATCACATACGGGGCC
          ** ********** ********** ********** ** ** ****** ** ** ****** **

MRT10279  TGCCCCTCGCTACGTCAAACATTCGACCCCTCAAGTTGGCGCGACTGGAATGCGCAACGTGCCG
H3_WT     TGTCCCAGATATGTTAAGCATAGCACTCTCTGAAATTGGCAACAGGAATGCGAAATGTACCA
          ** **  * ** ** ** ***     ** ** ** ****** ** ********** ** ** **

MRT10279  GAGAAGCAAACCCGGGGGATCTTCGGGGCTATCGCGGGATTCATCGAAAATGGATGGGAA
H3_WT     GAGAAACAAACTAGAGGCATATTTGGCGCAATAGCGGGTTTCATAGAAAATGGTTGGGAG
          ****** ******  * ** ** ** ** ** ** ****** ********** ******
```

```
MRT10279  GGAATGGTCGATGGTTGGTACGGTTTCAGACACCAGAACTCCGAGGGGCGGGGCCAGGCC
H3_WT     GGAATGGTGGATGGTTGGTACGGTTTCAGGCATCAAAATTCTGAGGGAAGAGGACAAGCA
          ********** ********** ** ** ** ** ****** *  ** ** ** **

MRT10279  GCAGACCTGAAGTCCACTCAGGCCGCGATTGACCAGATCAACGGAAAGCTCAACAGACTC
H3_WT     GCAGATCTCAAAAGCACTCAAGCAGCAATCGATCAAATCAATGGGAAGCTGAATAGGTTG
          ***** **  **    ******* ** ** ** ** ****** ** ****** ** **  *

MRT10279  ATTGGAAAGACCAACGAAAAGTTCCACCAAATCGAAAAGGAATTCTCCGAAGTGGAGGGC
H3_WT     ATCGGAAAACCAACGAGAATTCCATCAGATTGAAAAAGAATTCTCAGAAGTAGAAGGA
          ** ********** ********** ** ** ****** ********** ****** ** **

MRT10279  CGGGTGCAAGACCTGGAGAAGTACGTTGGAGGACACTAAGATCGACCTTTGGAGCTATAAC
H3_WT     AGAGTTCAAGACCTTGAGAAATATGTTGAGGACACTAAAAATAGATCTCTGGTCATACAAC
          * ** ********** ****** ** ** ********** ** ** ** ***    ** ***

MRT10279  GCAGAACTCCTTGTGGCCCTGGAAAACCAGCACACCATCGACCTGACCGATTCAGAGATG
H3_WT     GCGGAGCTTCTTGTTGCCCTGGAGAACCAACATACAATTGATCTAACTGACTCAGAAATG
          ** ** ** ****** ********** ****** ** ** ** ** ** ****** ***

MRT10279  AACAAGCTCTTTGAGAAAACTAAGAAGCAACTCCGGGAAAACGCTGAGGACATGGGAAAT
H3_WT     AACAAACTGTTTGAAAAAACAAAGAAGCAACTGAGGGAAAATGCTGAGGATATGGGAAAT
          ***** ** ** ****** ****** ********** ********** ** ** ** ***

MRT10279  GGATGCTTTTAAGATCTACCACAAGTGCGACAACGCCTGCATTGAGTCCATACGGAACGAA
H3_WT     GGTTGTTTCAAAATATACCCACAAATGTGACAATGCCTGCATAGAATCAATAAGAAATGAA
          ** ** ** ** ** ********** ** ****** ********** ** ** *** * ** ***

MRT10279  ACTTTACGACCATAACGTCTACCGGGATGAAGCCCTGAACAACAGATTCCAGATCAAGGGC
H3_WT     ACTTTATGACCACAATGTGTACAGGGATGAAGCATTGAACAACCGGTTCCAGATCAAGGGA
          ****** ****** ** ** *** ********** ********** * ** ** ** ***
```

```
MRT10279  GTGGAGCTGAAGTCCGGCTACAAAGATTGGATCCTGTGGATTTCCTTCGGCGATTTCATGC
H3_WT     GTTGAGCTGAAGTCAGGATACAAAGATTGGATCCTATGGATTTCCTTTGGCCATATCATGT
          ** ********** ** ********** ********** ** ** ** ******

MRT10279  TTCTTTGCTCTGCGTGGCCCTCCTGGGATTCATAATGTGGGCCTGTCAGAAGGGCAACATT
H3_WT     TTTTTGCTTTGTGTTGGGGTTCATCATGTGGGCCTGCCAAAAGGGCAACATT
          ** ****** ** ** **  *  ***** ****** ********** ** ************

MRT10279  AGGTGCAACATATGCATATAA (SEQ ID NO:2)
H3_WT     AGATGCAACATTTGCATTTGA (SEQ ID NO:3)
          ** ********** ****** * *
```

FIG. 5A


Cap
3
5'UTR
141
142
Start HA-H3 Coding Sequence Stop
1842
1843
3'UTR
1942
PolyA Tail
~2242

FIG. 5B

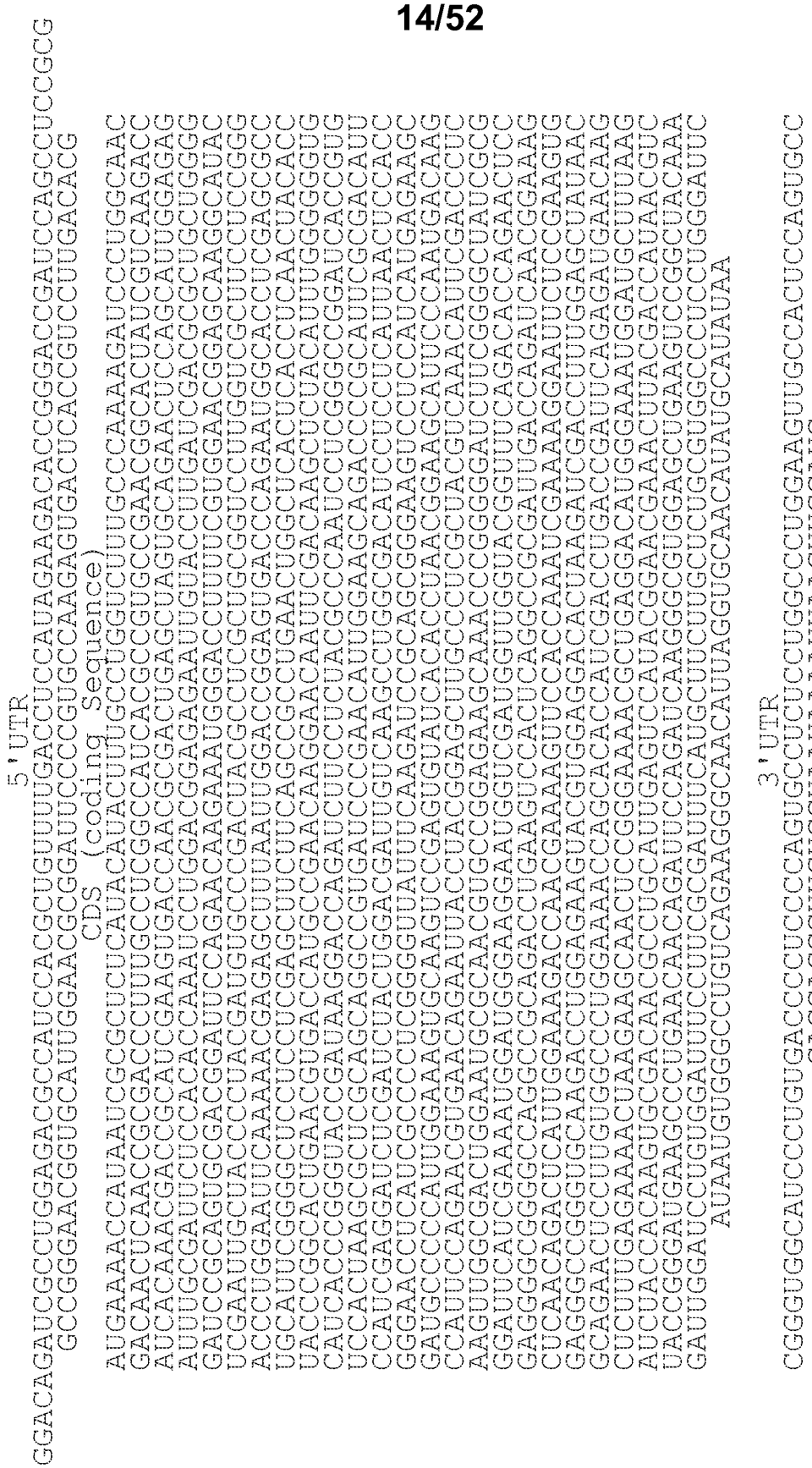
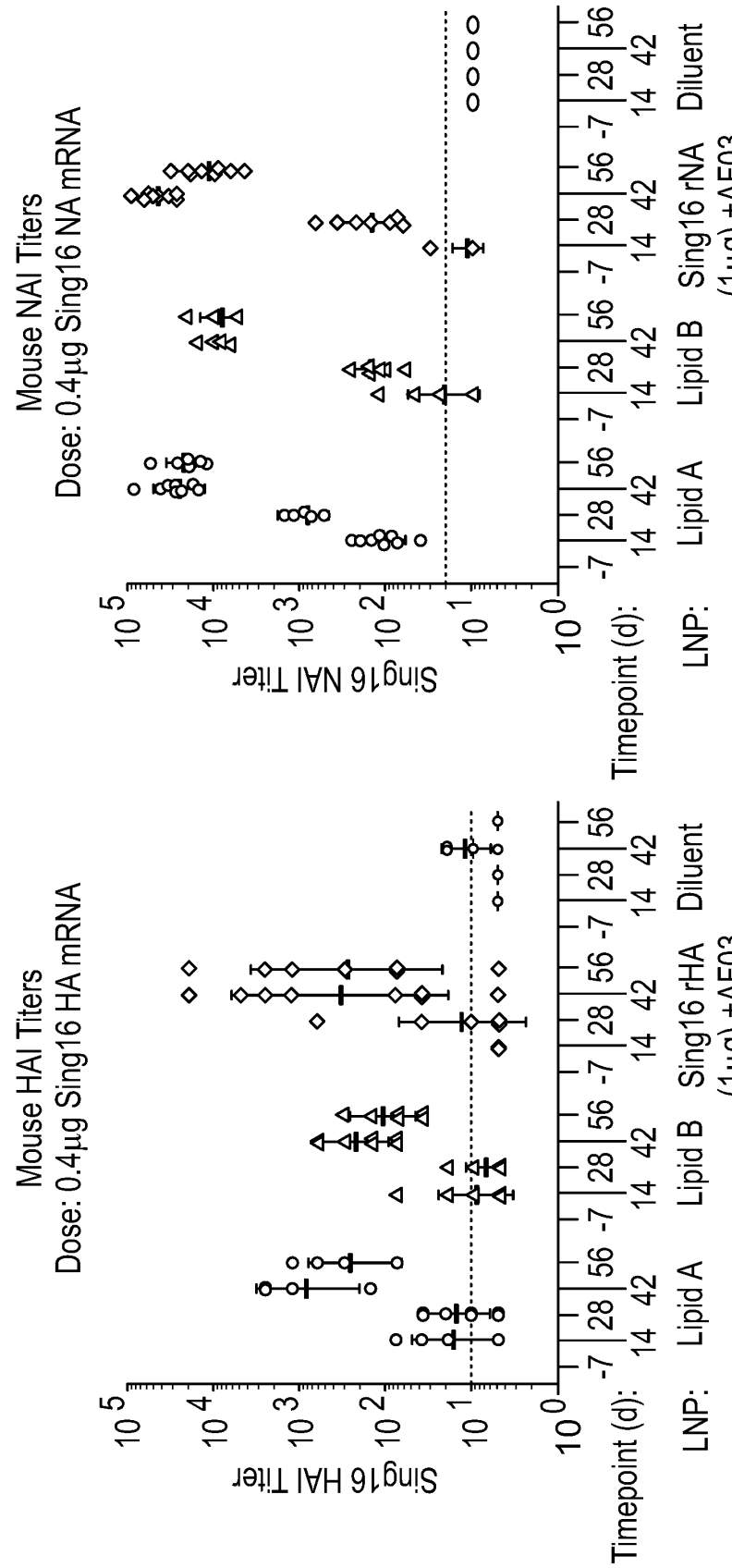
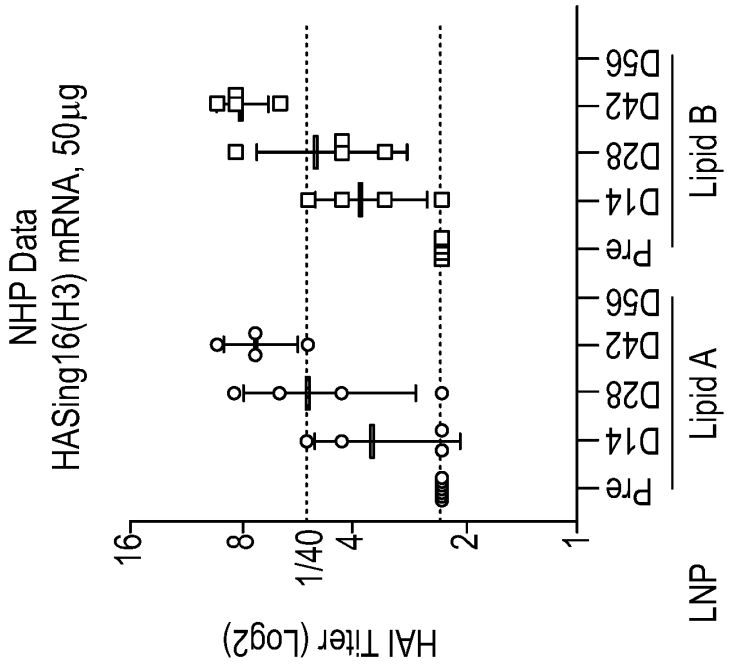

5'UTR
GGACAGAUCGCCUGGAGACGCCAUCCACGCUGUUUUGACCUCCAUAGAAGACACCGGGACCGAUCCAGCCUCCGCG
GCCGGGAACGGUGCAUUGGAACGCGGAUUCCCCGUGCCAAGAGUGACCUCACCGUCCUUGACACG
CDS (coding Sequence)
AUGAAAACCAUAAUCGCGCUCUCAUACAUACUUUGCCUGGUCUUUGCCCAAAAGAUCCCCUGGCAAC
GACAACUCAACCGCGACCCUUUGGCCAUCACGCCGUGCCGAACGGCACUAUCGUCAAGACC
AUCACAAACGACCGCGCAUCGAAGUGACCAACGCGACUGAGCUAGUGGCAGAACUCCAGCAUUGGAGAG
AUUUGGCGAUUCUCCACACCAAAAUCCUGGACGGAGAAAUUGUACCCUUGAUCGACGCGCUGCUGGGG
GAUCCGCAGUGCGACGGAUUCCAGAACAAGAAAUGGGACCUUUUCGUGGGAACGGAGCAAGGCAUAC
UCGAAUUGCUACCCCUACGACUACGCCUCGCUGCGGUCCUUGGUCGCUUCCUCCGGG
ACCCUGGAAUUCAAAAACGAGAGCUUUUAAUUGGACCCGGAGUGACCCAGAAUGGGCACCUCGAGCGCCC
UGCAUUCGGGGCUCCUCCUCGAGCCUUCAGCCGCCUGAACUGGGCUCACACCUCAACUACACCC
UACCCGGGCACUGAACGUGACCAUGCCCGAACACAAGGAACACAAUUCGACACAAGCUCUACAUUUGGGGGGUG
CAUCACCCGGGUACCGAUAAGGACCAGAUCUUUCCCUCUACGCCCCAAUCCUCGGGCGCGAUCACCGUG
UCCACUAAGCGCUCAGCAGGCCGUGAUCCCCGAACAUUGGAAGCAGACCCCCGCGCAUUCGACGACAUU
CCAUUCCCAGAACGUGGCCAAGAAUUACCUUACGGAGCUUUGCCCCUCGCUACGUCAAACAUUCGACCCCUC
AAGUUGGCGACUGGAAUGCGCAACGUGCCGGAGAAGCAAACCCCGGGGGAUCUUCGGGGCUAUCGCCG
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CUCAACAGACUCGGGAAAGACCAAGAAAGUCCACCAAAUCGAAAGGAAUUCCUCCGAAGGC
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CUCUUUGAGAAAACUAAGAAGCAACUCCGGGAAAACGCUGAGGACAUGGGAAAUGGAUGCUUUAAG
AUCCUACCACAAGUGCGACAACGCCUGCAUUGAGUCCAUACGGAACGAAACUUACGACCAUAACGUC
UACCGGGAUGAAGCCCUGAACACAACAGAUUCCAGAUCAAGGGCGUGGAGCUGAAGUCCGGCUACAAA
GAUUGGAUCCUGUGGAUUUCCUUCGCGAUUUCAUGCUUCUUGCUCUCGUGGGCCCUCCUGGGAUUC
AUAAUGUGGGCCUGUCAGAAGGGCAACAUUAGGUGCAACAUAUGCAUAUAA
3'UTR
CGGGUGGCAUCCCCUGUGACCCCUCCCCCAGUGCCUCUCCUGGCCCCUGGAAGUUGCCACUCCAGUGCCC
CACCAGCCUUGUCCUAAUAAAAUUAAGUUGCAUC
+ Poly A Tail
(SEQ ID NO:4)

FIG. 5C



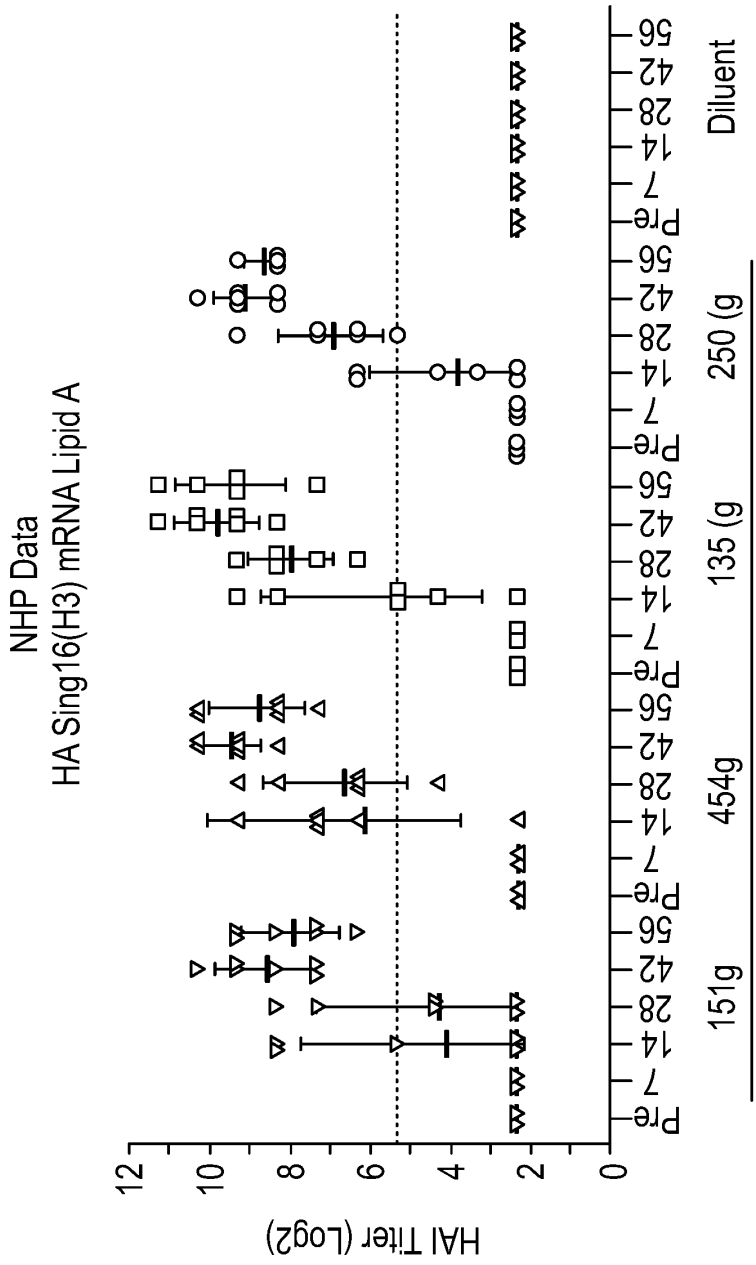
Lipid	Composition (Molar Ratio)
Lipid A	Cationic lipid : DMG-PEG2000: Cholestrol: DOPE 40:1.5:28.5:30
Lipid B	Cationic lipid : DMG-PEG2000: Cholestrol: DOPE 40:1.5:28.5:30

FIG. 6



Lipid	Composition (Molar Ratio)
Lipid A	Cationic lipid : DMG-PEG2000: Cholestrol: DOPE 40:1.5:28.5:30
Lipid B	Cationic lipid : DMG-PEG2000: Cholestrol: DOPE 40:1.5:28.5:30

FIG. 7A



Lipid	Composition (Molar Ratio)
Lipid A	Cationic lipid : DMG-PEG2000: Cholestrol: DOPE 40:1.5:28.5:30

FIG. 7B

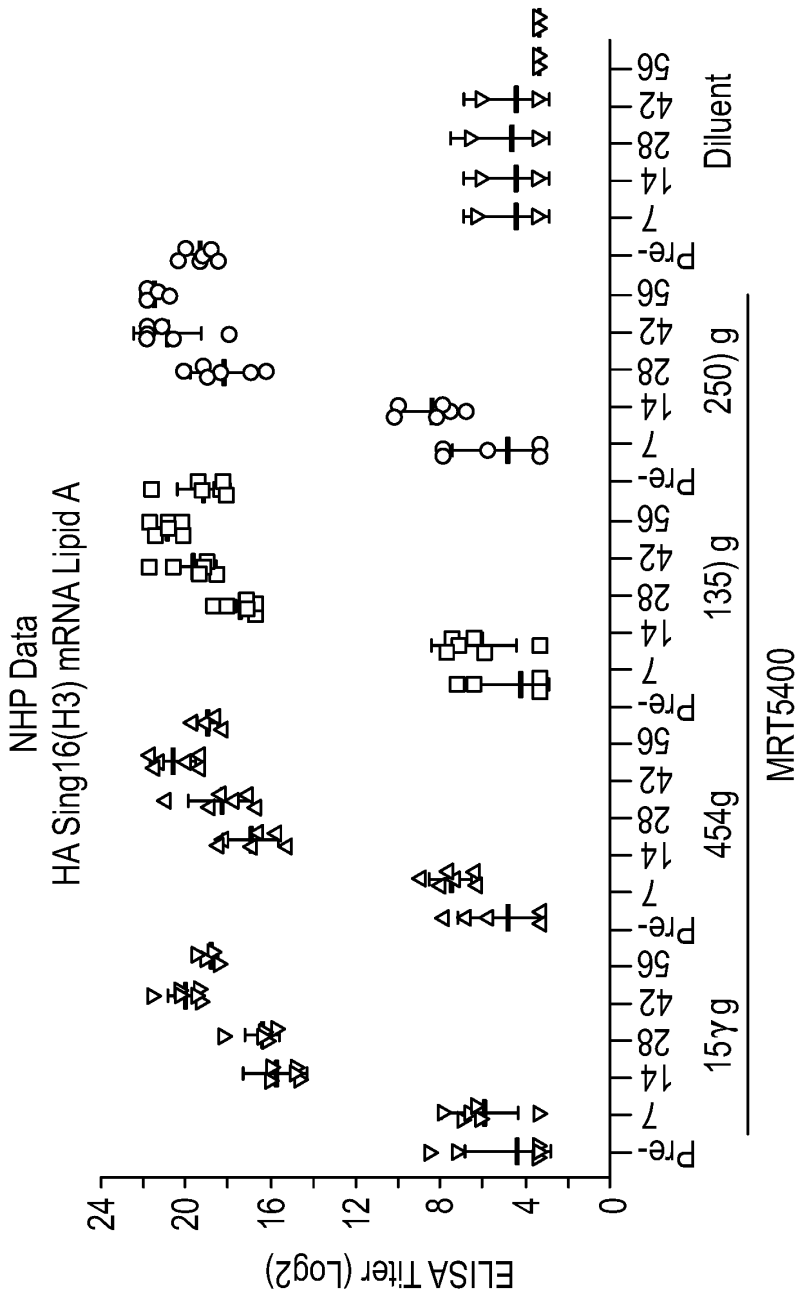
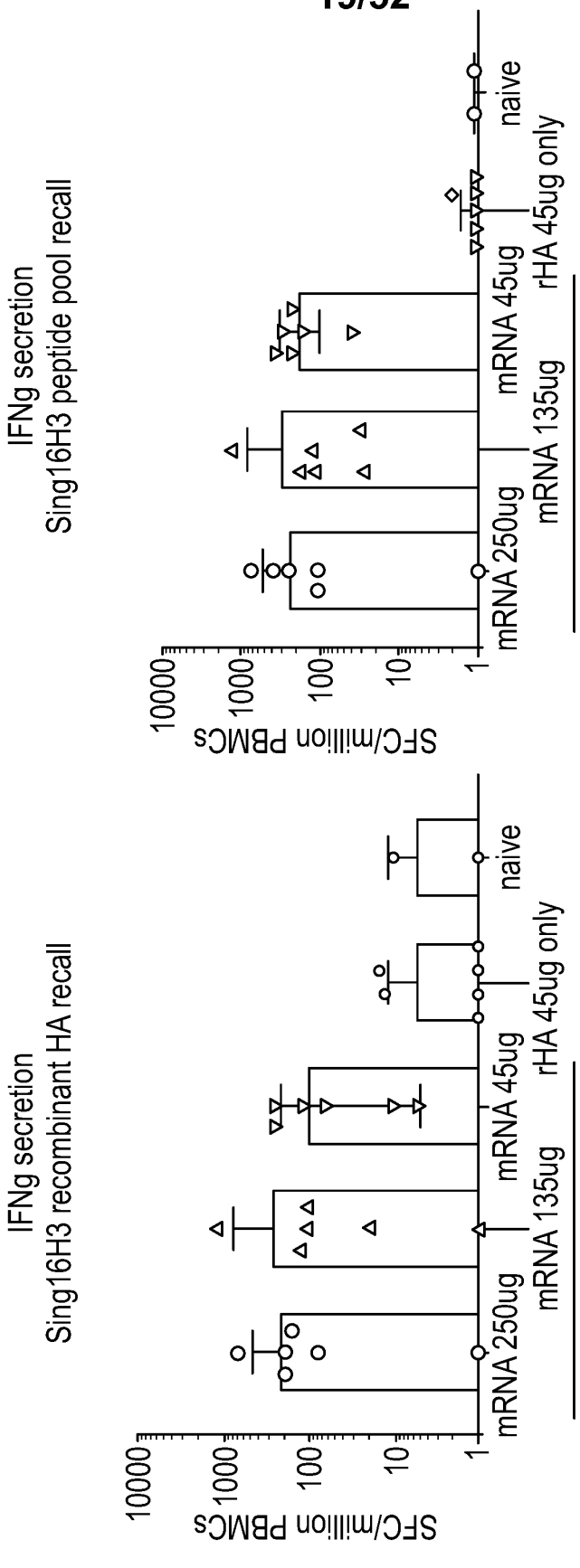
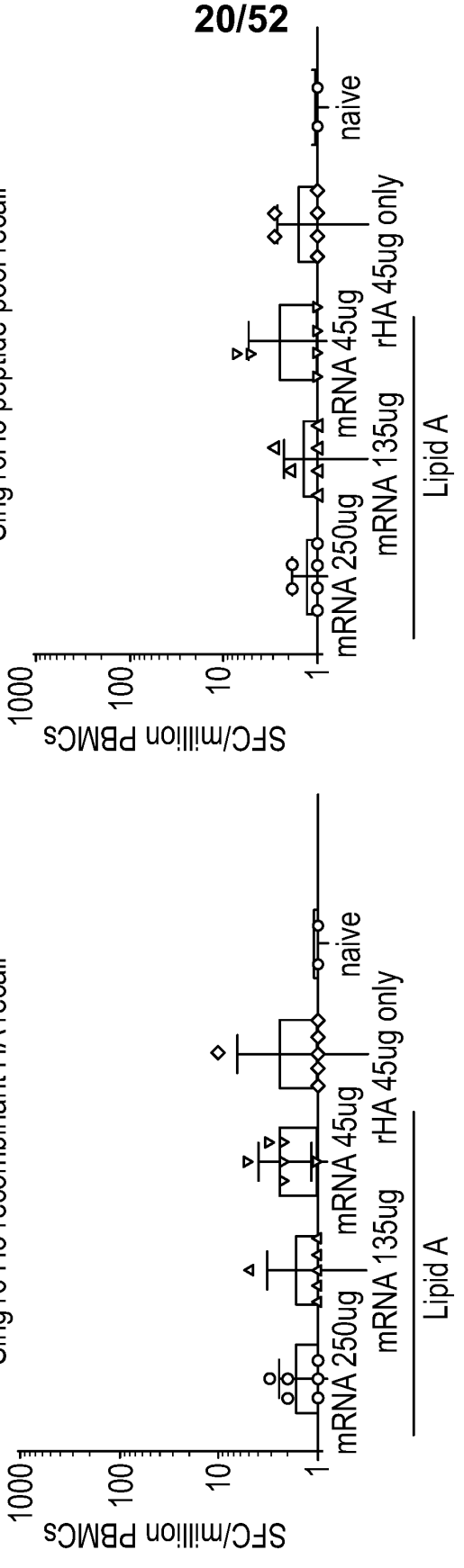

NHP Data
HA Sing16(H3) mRNA Lipid A
ELISA Titer (Log2)
24
20
16
12
8
4
0
Pre-
7
14
28
42
56
15γg
454g
135) g
250) g
Diluent
MRT5400

FIG. 7C



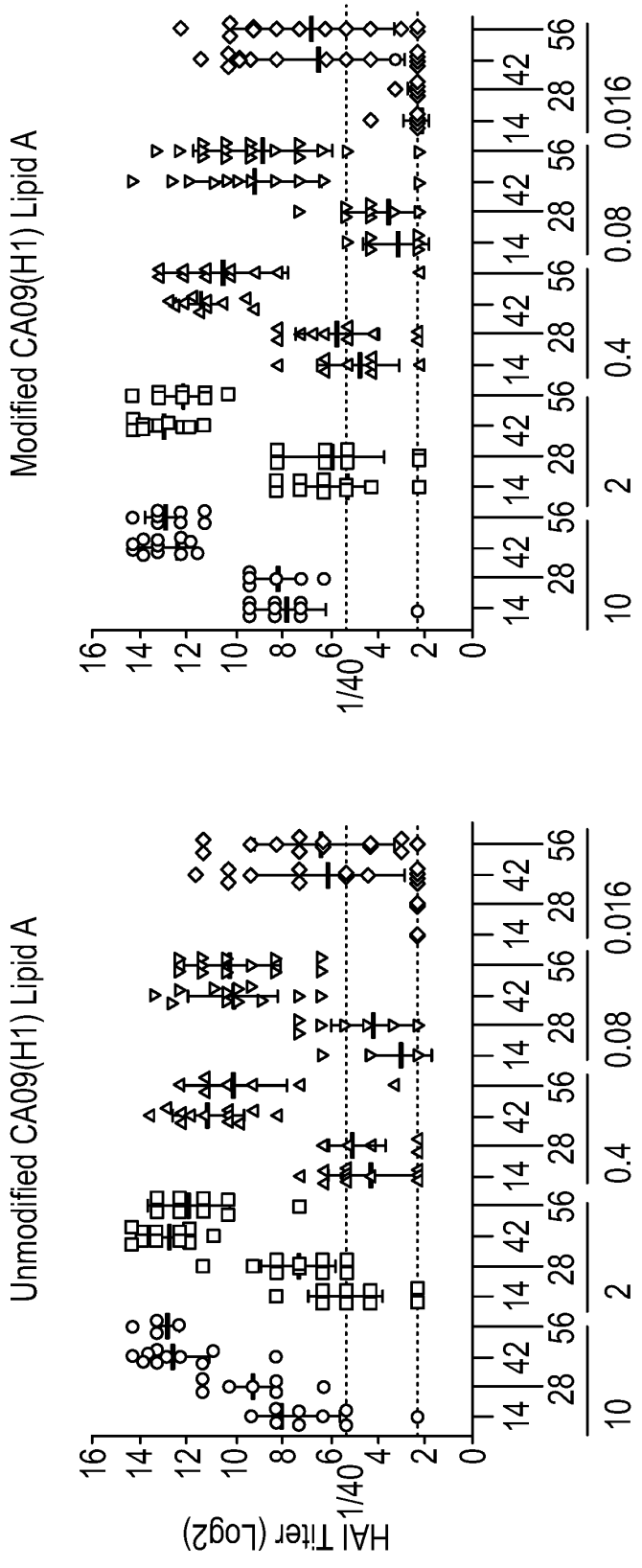
Lipid	Composition (Molar Ratio)
Lipid A	Cationic lipid : DMG-PEG2000: Cholestrol: DOPE 40:1.5:28.5:30

FIG. 8A



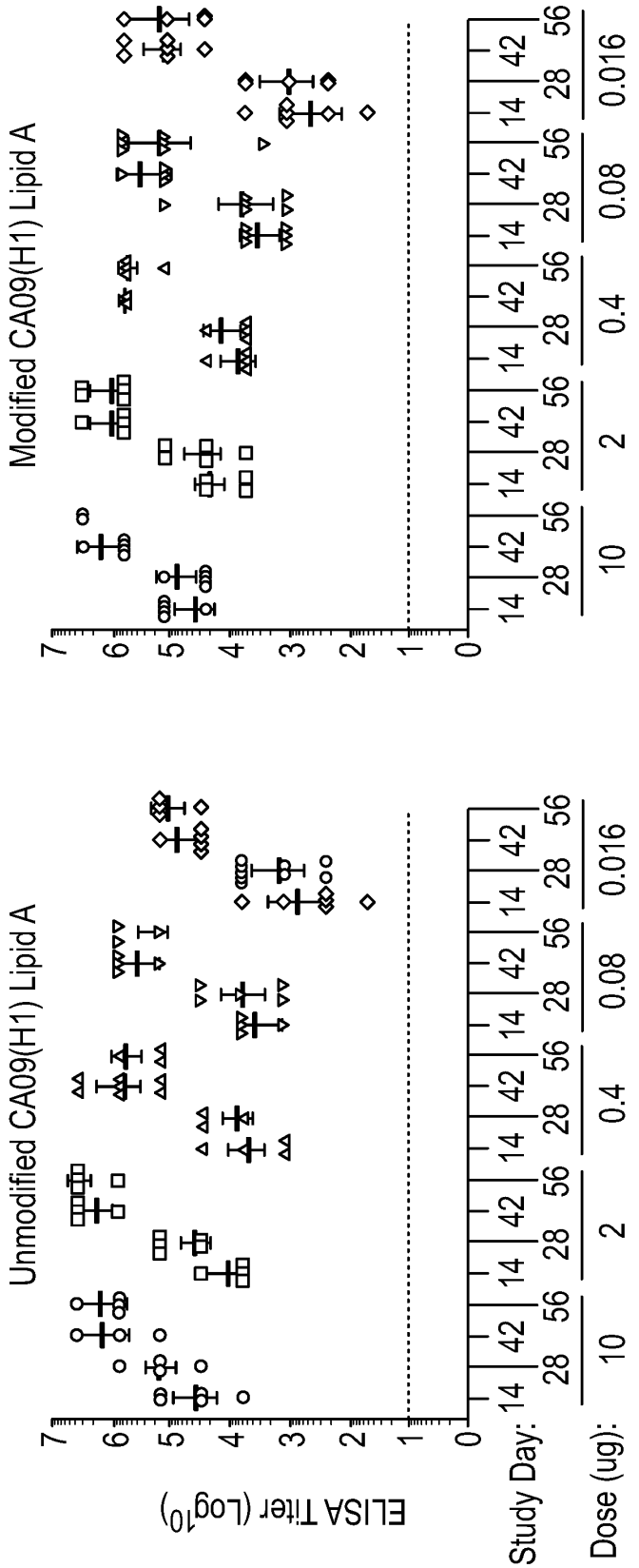
Lipid	Composition (Molar Ratio)
Lipid A	Cationic lipid : DMG-PEG2000: Cholestrol: DOPE 40:1.5:28.5:30

FIG. 8B



Lipid	Composition (Molar Ratio)
Lipid A	Cationic lipid : DMG-PEG2000: Cholestrol: DOPE 40:1.5:28.5:30

FIG. 9A



Lipid	Composition (Molar Ratio)
Lipid A	Cationic lipid : DMG-PEG2000: Cholestrol: DOPE 40:1.5:28.5:30

FIG. 9B

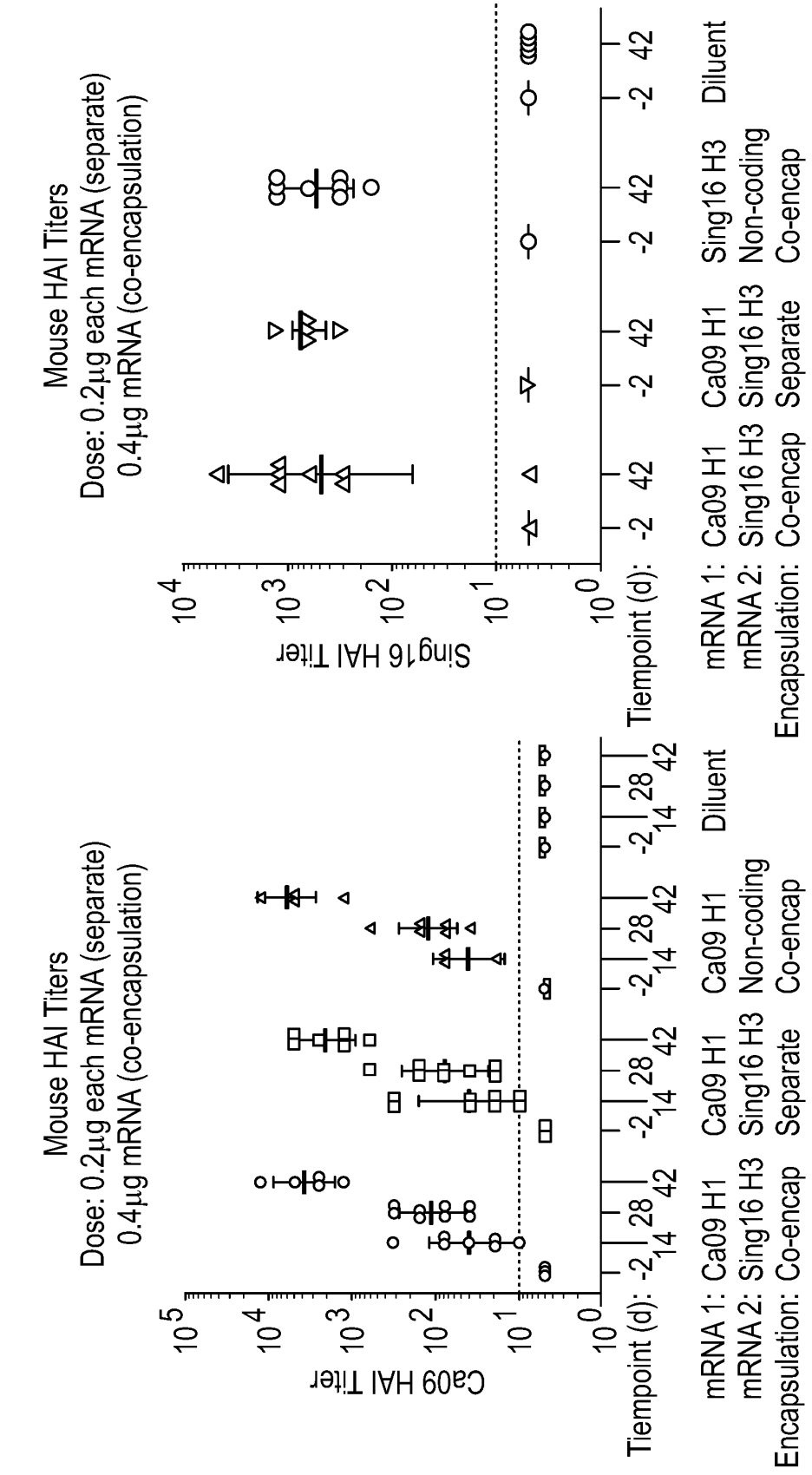


FIG. 10A

FIG. 10B

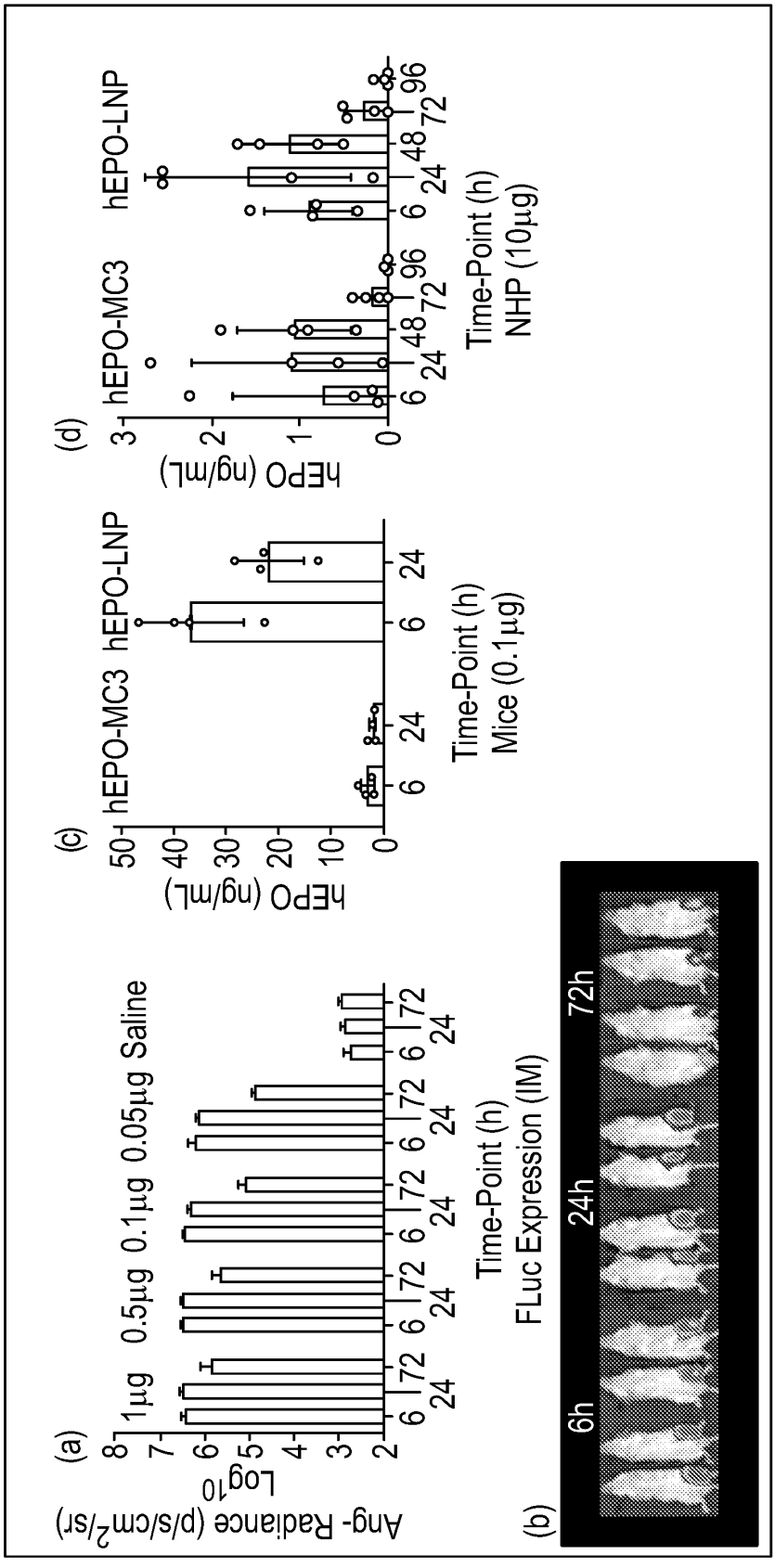

(a)
Ang- Radiance (p/s/cm²/sr)
Log10
1µg 0.5µg 0.1µg 0.05µg Saline
Time-Point (h)
FLuc Expression (IM)
(b)
6h
24h
72h
(c)
hEPO (ng/mL)
hEPO-MC3 hEPO-LNP
Time-Point (h)
Mice (0.1µg)
(d)
hEPO (ng/mL)
hEPO-MC3 hEPO-LNP
Time-Point (h)
NHP (10µg)

FIG. 11

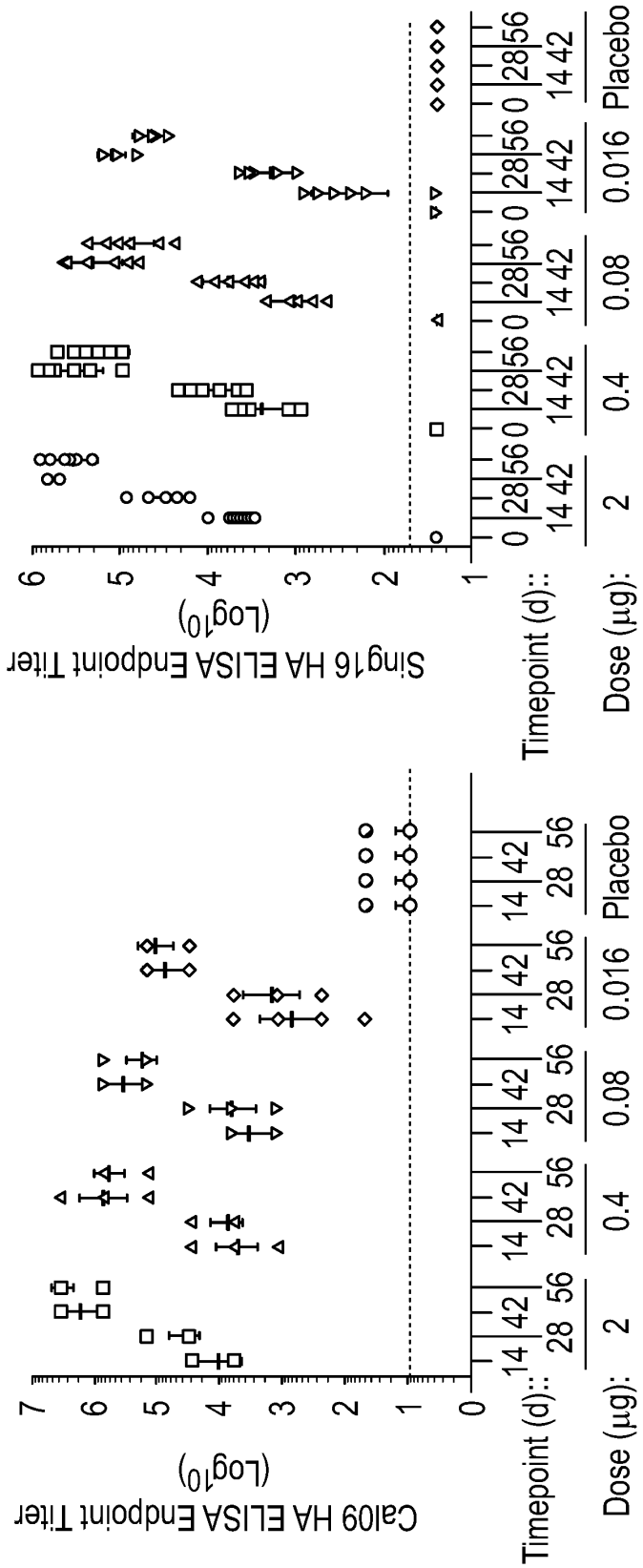

Sing16 HA ELISA Endpoint Titer
(Log10)
Timepoint (d)::
Dose (µg):
Placebo
Cal09 HA ELISA Endpoint Titer
(Log10)
Timepoint (d)::
Dose (µg):
Placebo

FIG. 12

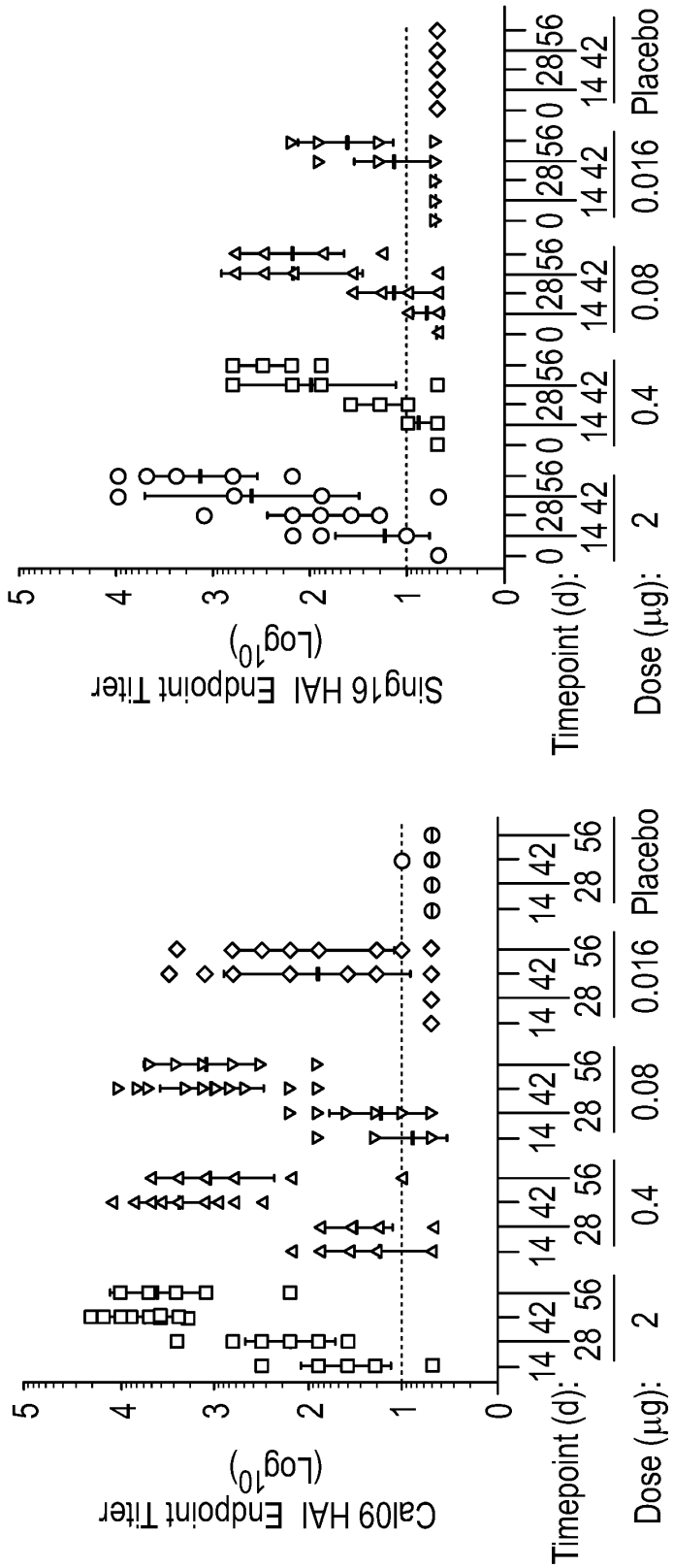
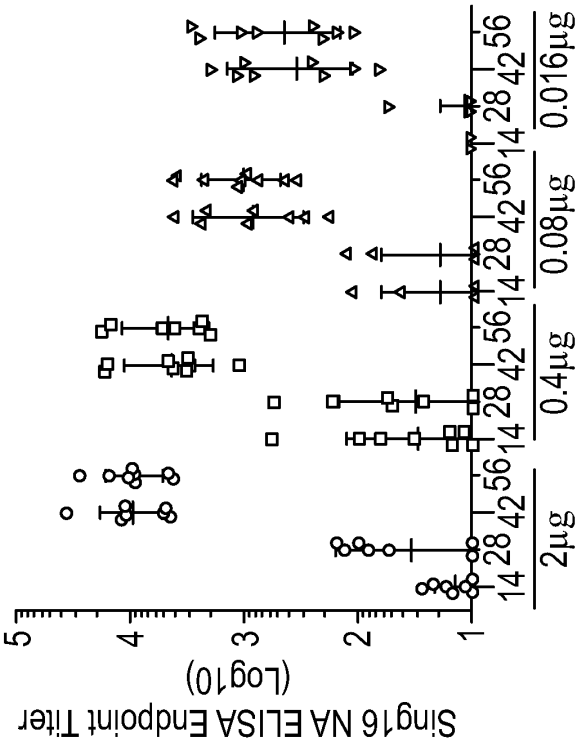

Sing16 HAI Endpoint Titer
(Log10)
Timepoint (d):
Dose (µg):
Placebo
Cal09 HAI Endpoint Titer
(Log10)
Timepoint (d):
Dose (µg):
Placebo

FIG. 13


Sing16 NA ELISA Endpoint Titer
(Log10)
1
2
3
4
5
14 28 42 56 14 28 42 56 14 28 42 56 14 28 42 56
2μg
0.4μg
0.08μg
0.016μg

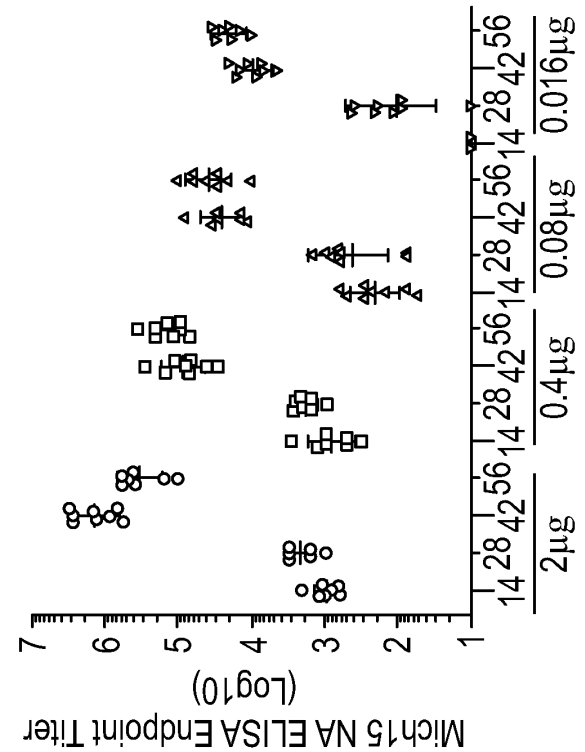

Mich15 NA ELISA Endpoint Titer
(Log10)
1
2
3
4
5
6
7
14 28 42 56 14 28 42 56 14 28 42 56 14 28 42 56
2μg
0.4μg
0.08μg
0.016μg

FIG. 14

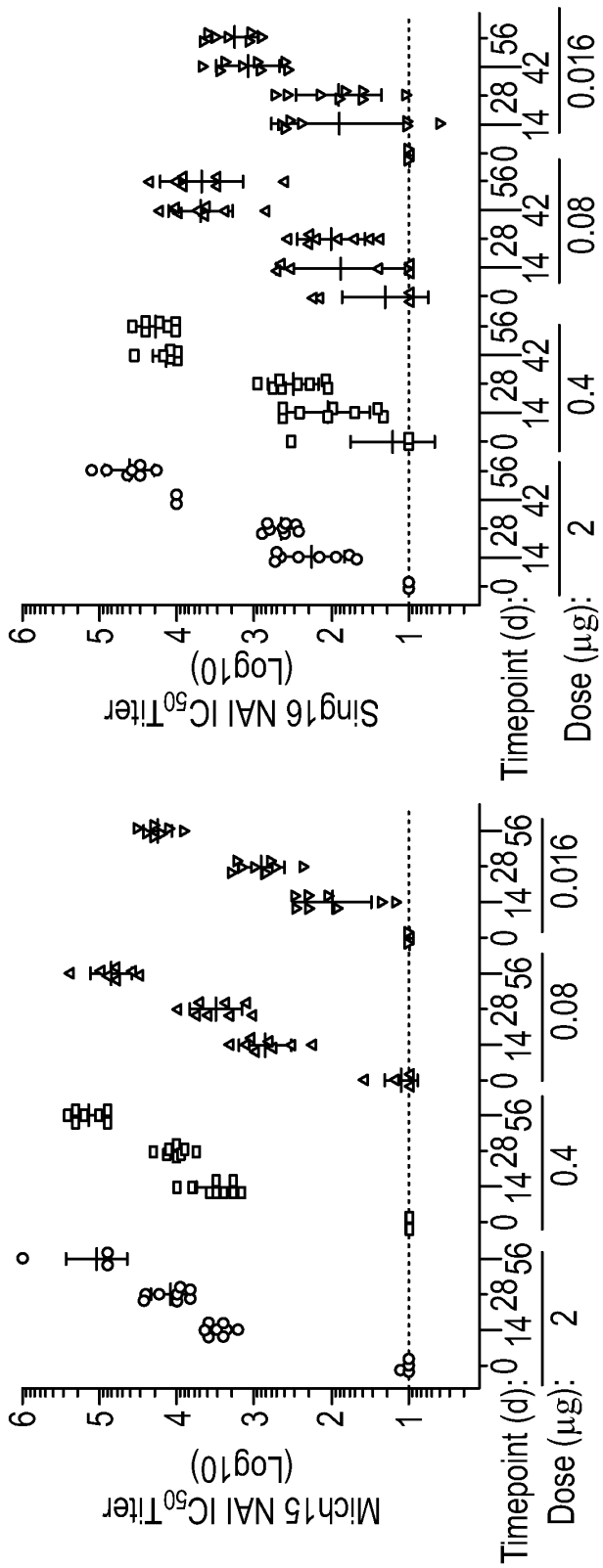

Sing16 NAI IC50Titer
(Log10)
Timepoint (d): 0 14 28 42 56 0 14 28 42 56 0 14 28 42 56 0 14 28 42 56
Dose (µg): 2 0.4 0.08 0.016
Mich15 NAI IC50Titer
(Log10)
Timepoint (d): 0 14 28 56 0 14 28 56 0 14 28 56 0 14 28 56
Dose (µg): 2 0.4 0.08 0.016

FIG. 15

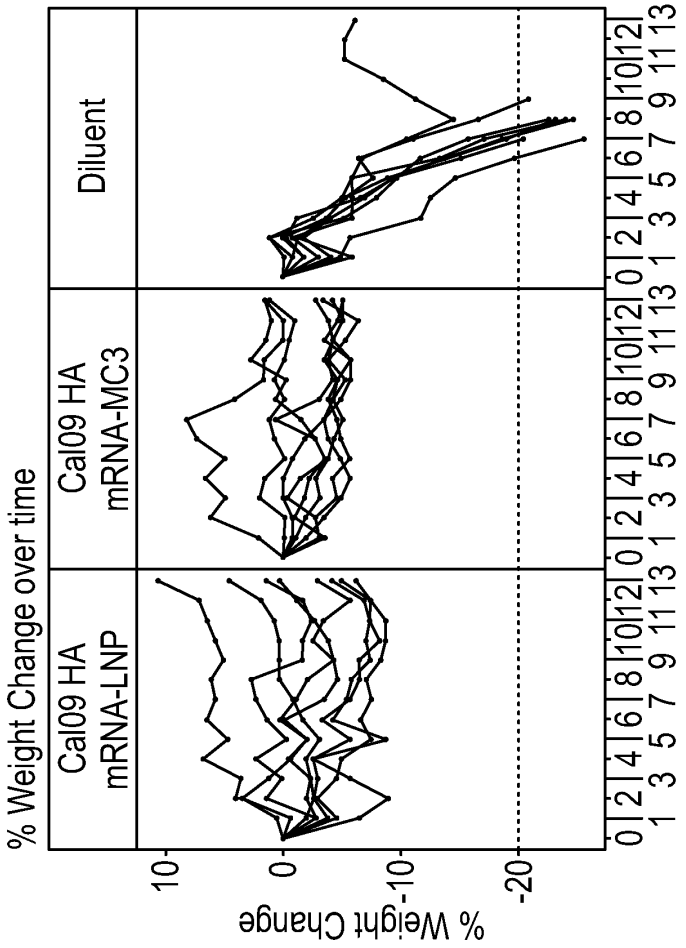


FIG. 16B

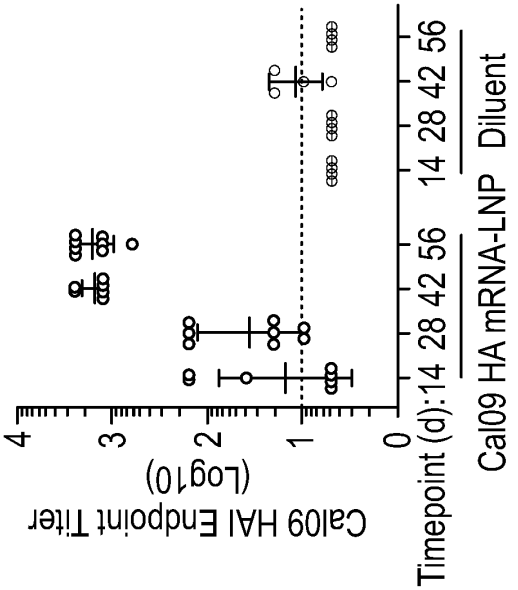


FIG. 16A

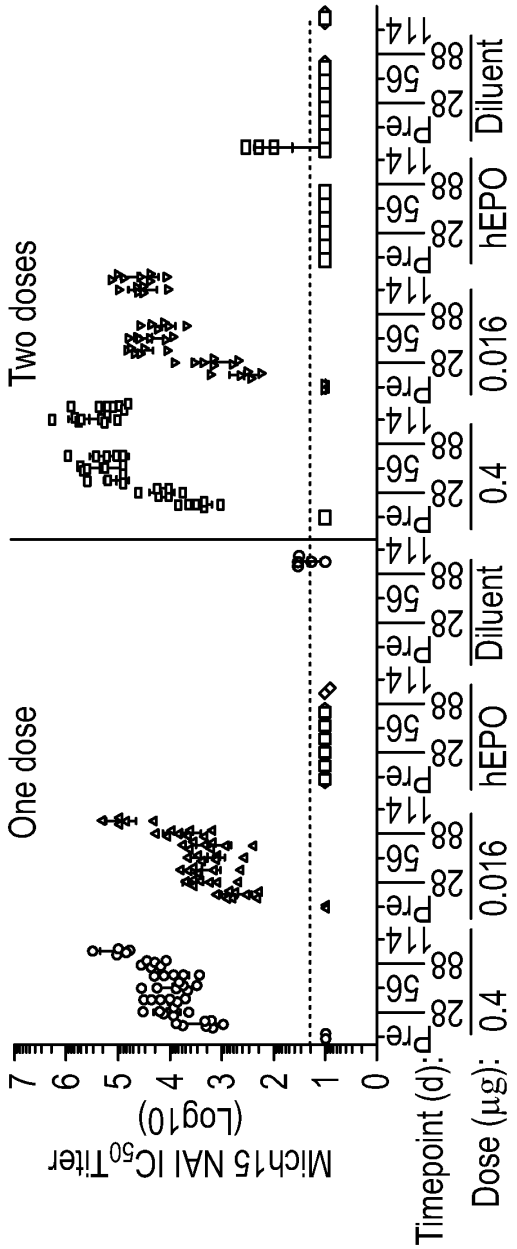

Mich15 NAI IC50 Titer (Log10)
0
1
2
3
4
5
6
7
One dose
Two doses
Timepoint (d):
Dose (µg):
Pre
28
56
88
114
0.4
0.016
hEPO
Diluent

FIG. 17A

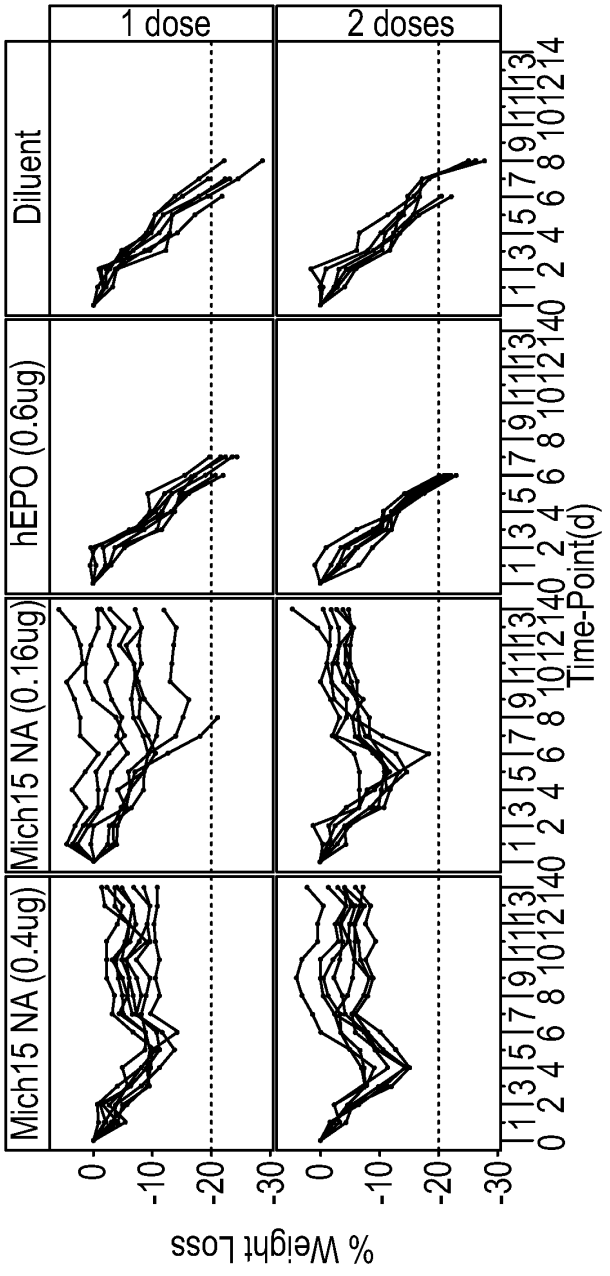

1 dose
2 doses
Diluent
hEPO (0.6ug)
Mich15 NA (0.16ug)
Mich15 NA (0.4ug)
% Weight Loss
0
-10
-20
-30
Time-Point(d)

FIG. 17B

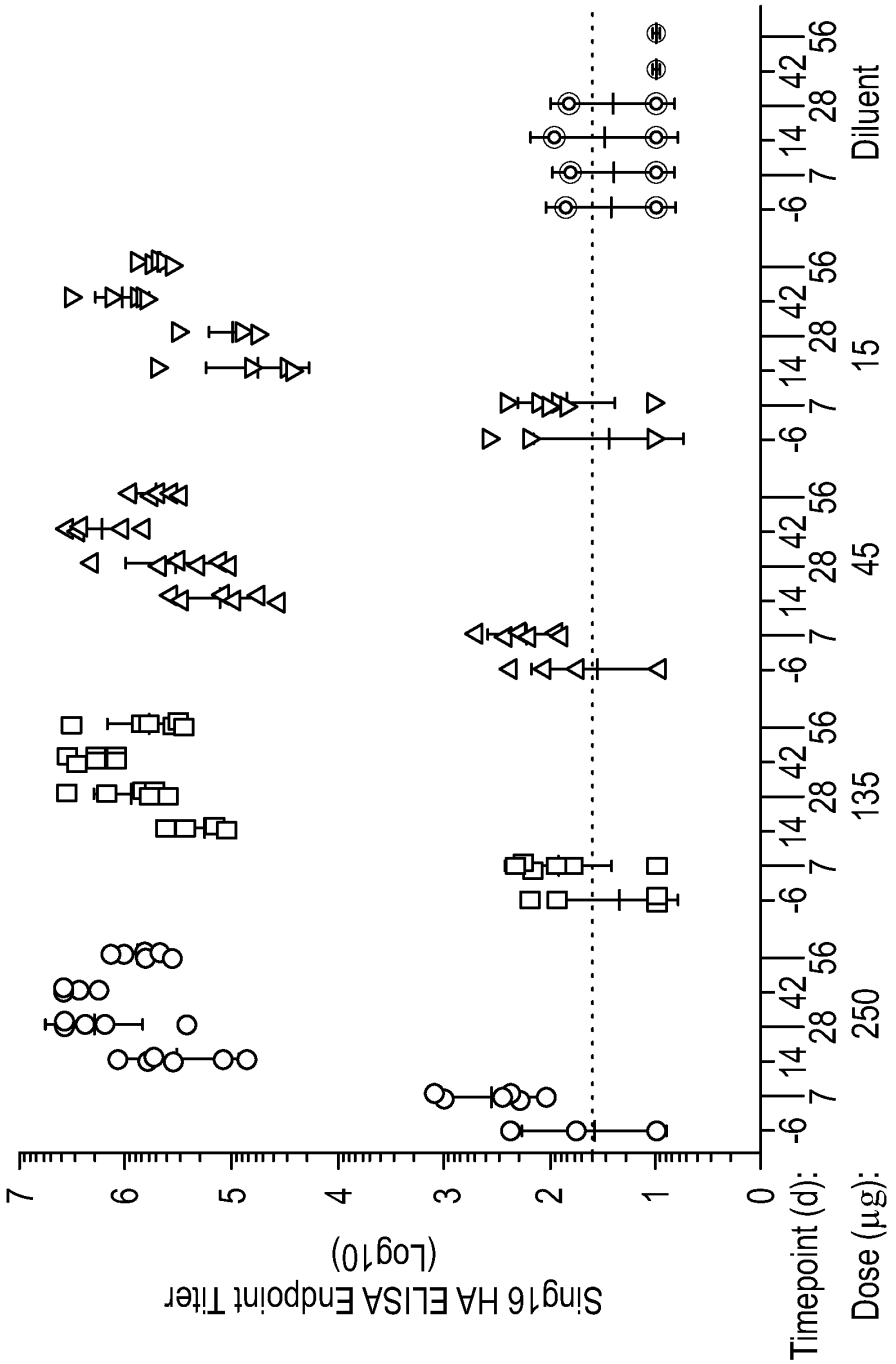

Sing16 HA ELISA Endpoint Titer
(Log10)
0
1
2
3
4
5
6
7
Timepoint (d):
Dose (µg):
-6
7
14
28
42
56
250
135
45
15
Diluent

FIG. 18

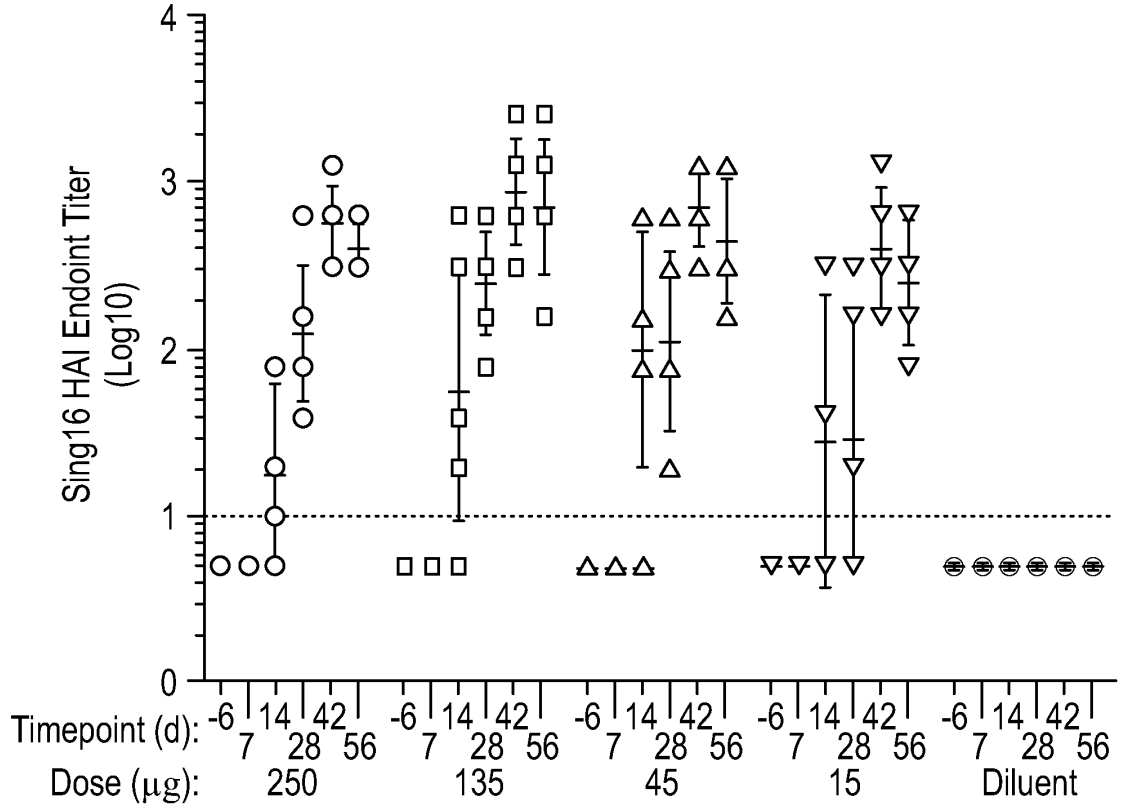


FIG. 19A

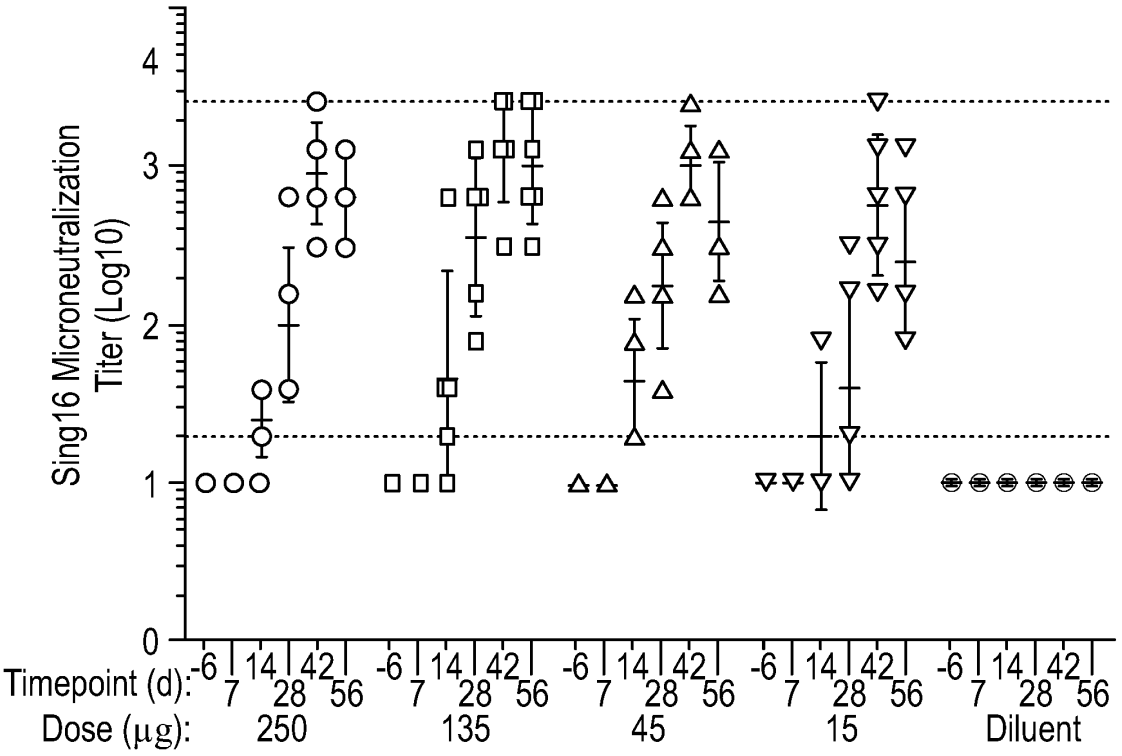


FIG. 19B

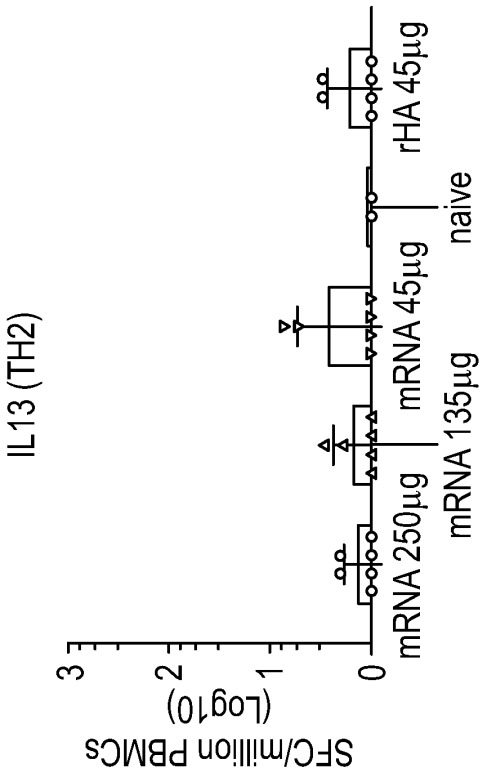


FIG. 20B

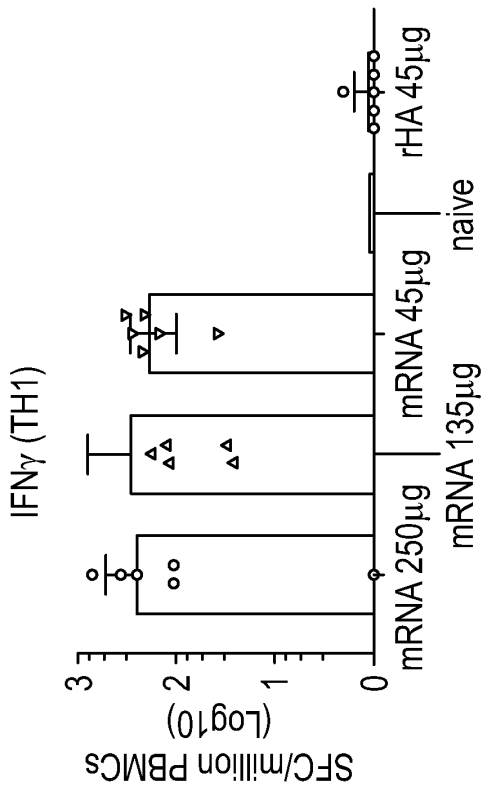


FIG. 20A

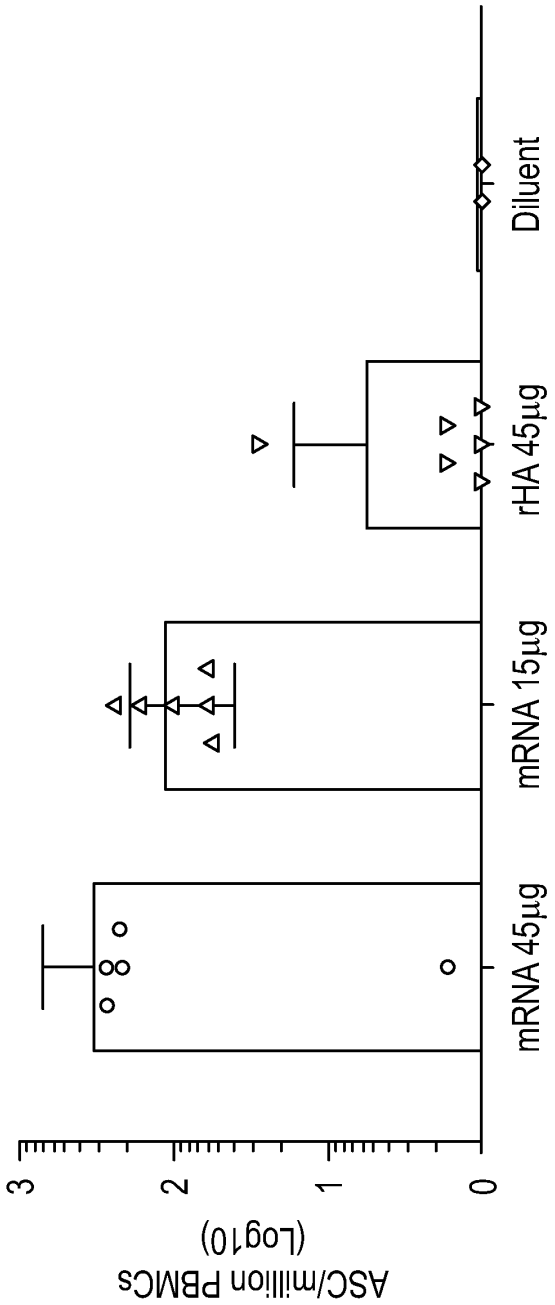

ASC/million PBMCs
(Log10)
3
2
1
0
mRNA 45µg
mRNA 15µg
rHA 45µg
Diluent

FIG. 21

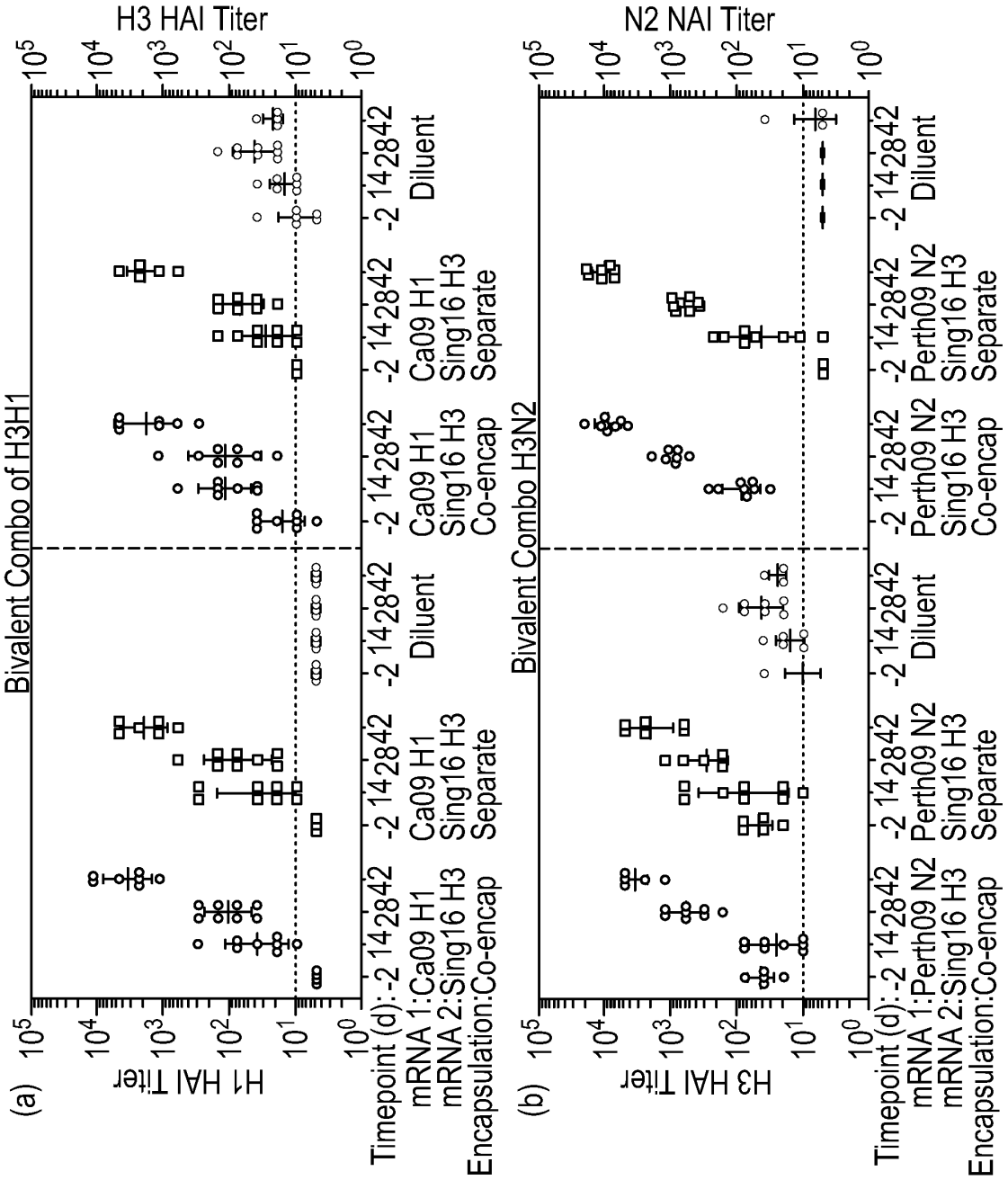

(a)
H1 HAI Titer
H3 HAI Titer
Bivalent Combo of H3H1
(b)
N2 NAI Titer
Bivalent Combo H3N2
Timepoint (d): -2 1 4 28 42
mRNA 1:Ca09 H1
mRNA 2:Sing16 H3
Encapsulation:Co-encap
Diluent
Ca09 H1
Sing16 H3
Co-encap
Separate
mRNA 1:Perth09 N2
mRNA 2:Sing16 H3
Encapsulation:Co-encap
Diluent
Perth09 N2
Sing16 H3
Co-encap
Separate

FIG. 22

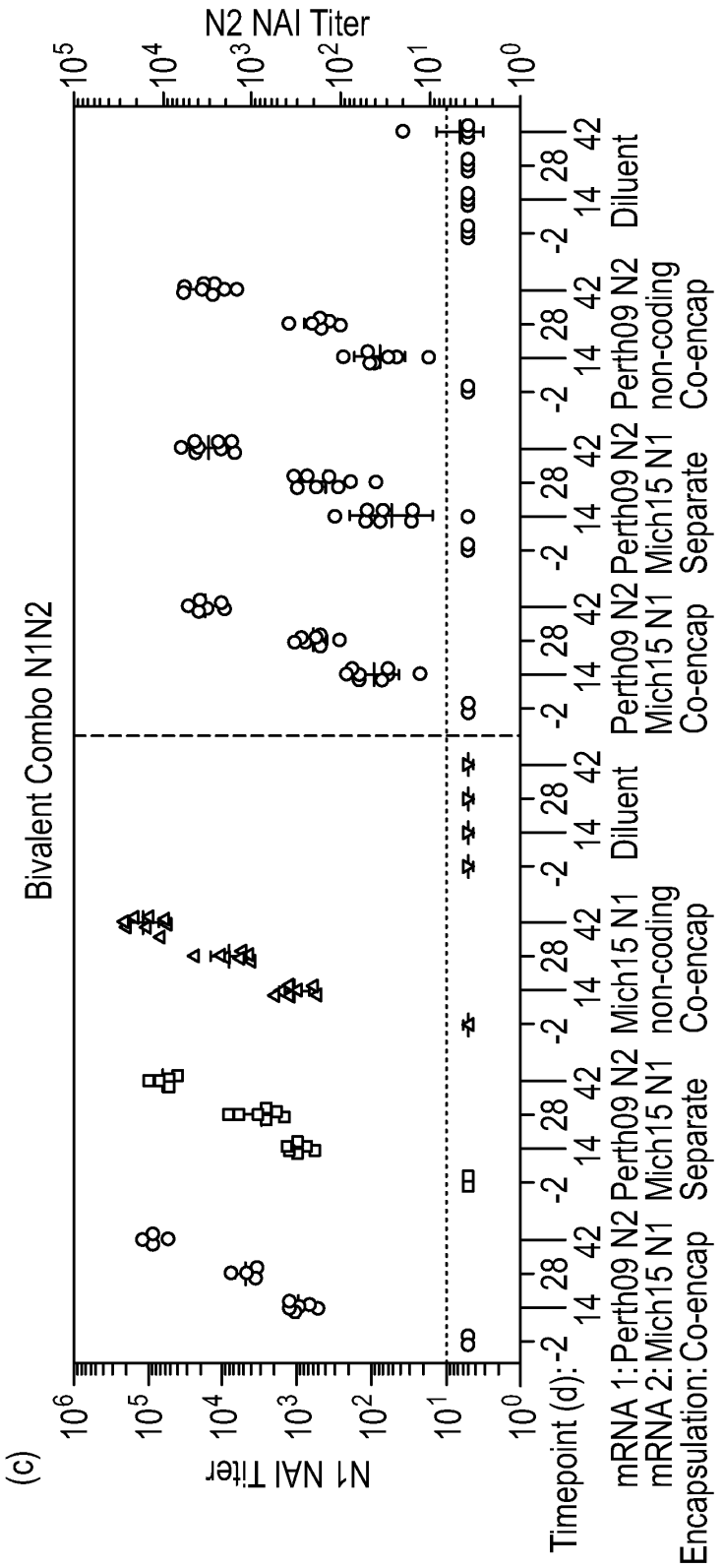

(c)
Bivalent Combo N1N2
N1 NAI Titer
N2 NAI Titer
Timepoint (d): -2 14 28 42 -2 14 28 42 -2 14 28 42 -2 14 28 42
mRNA 1: Perth09 N2 Perth09 N2 Mich15 N1 Diluent Perth09 N2 Perth09 N2 Diluent
mRNA 2: Mich15 N1 Mich15 N1 non-coding Mich15 N1 Mich15 N1 non-coding
Encapsulation: Co-encap Separate Co-encap Co-encap Separate Co-encap

FIG. 22 (cont'd)

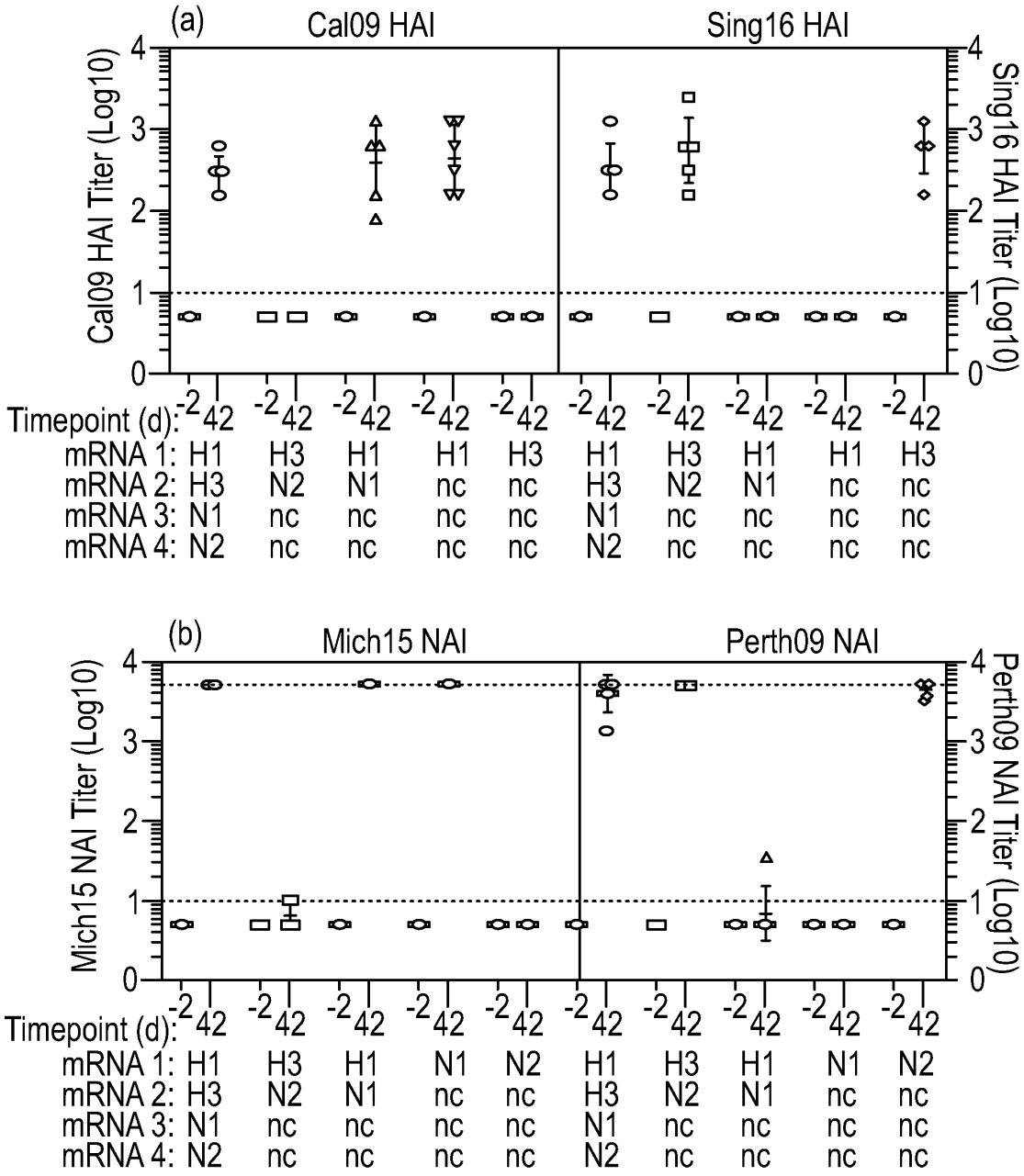

(a)
Cal09 HAI
Sing16 HAI
Cal09 HAI Titer (Log10)
Sing16 HAI Titer (Log10)
0
1
2
3
4
Timepoint (d): -2 4 2
mRNA 1: H1 H3 H1 H1 H3 H1 H3 H1 H1 H3
mRNA 2: H3 N2 N1 nc nc H3 N2 N1 nc nc
mRNA 3: N1 nc nc nc nc N1 nc nc nc nc
mRNA 4: N2 nc nc nc nc N2 nc nc nc nc
(b)
Mich15 NAI
Perth09 NAI
Mich15 NAI Titer (Log10)
Perth09 NAI Titer (Log10)
Timepoint (d): -2 4 2
mRNA 1: H1 H3 H1 N1 N2 H1 H3 H1 N1 N2
mRNA 2: H3 N2 N1 nc nc H3 N2 N1 nc nc
mRNA 3: N1 nc nc nc nc N1 nc nc nc nc
mRNA 4: N2 nc nc nc nc N2 nc nc nc nc

FIG. 23

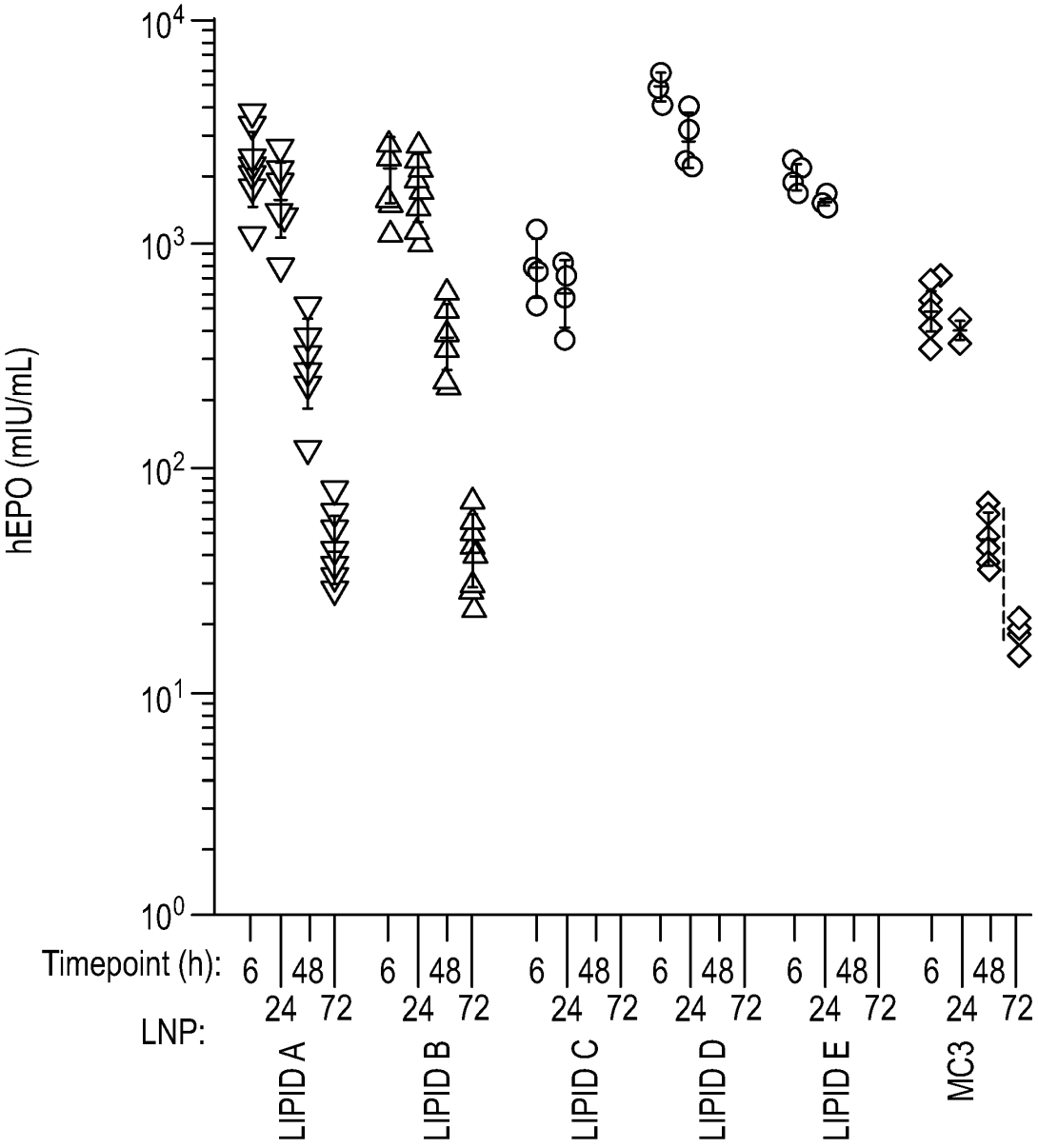

hEPO (mIU/mL)
10^4
10^3
10^2
10^1
10^0
Timepoint (h):
6
24
48
72
LNP:
LIPID A
LIPID B
LIPID C
LIPID D
LIPID E
MC3

FIG. 24

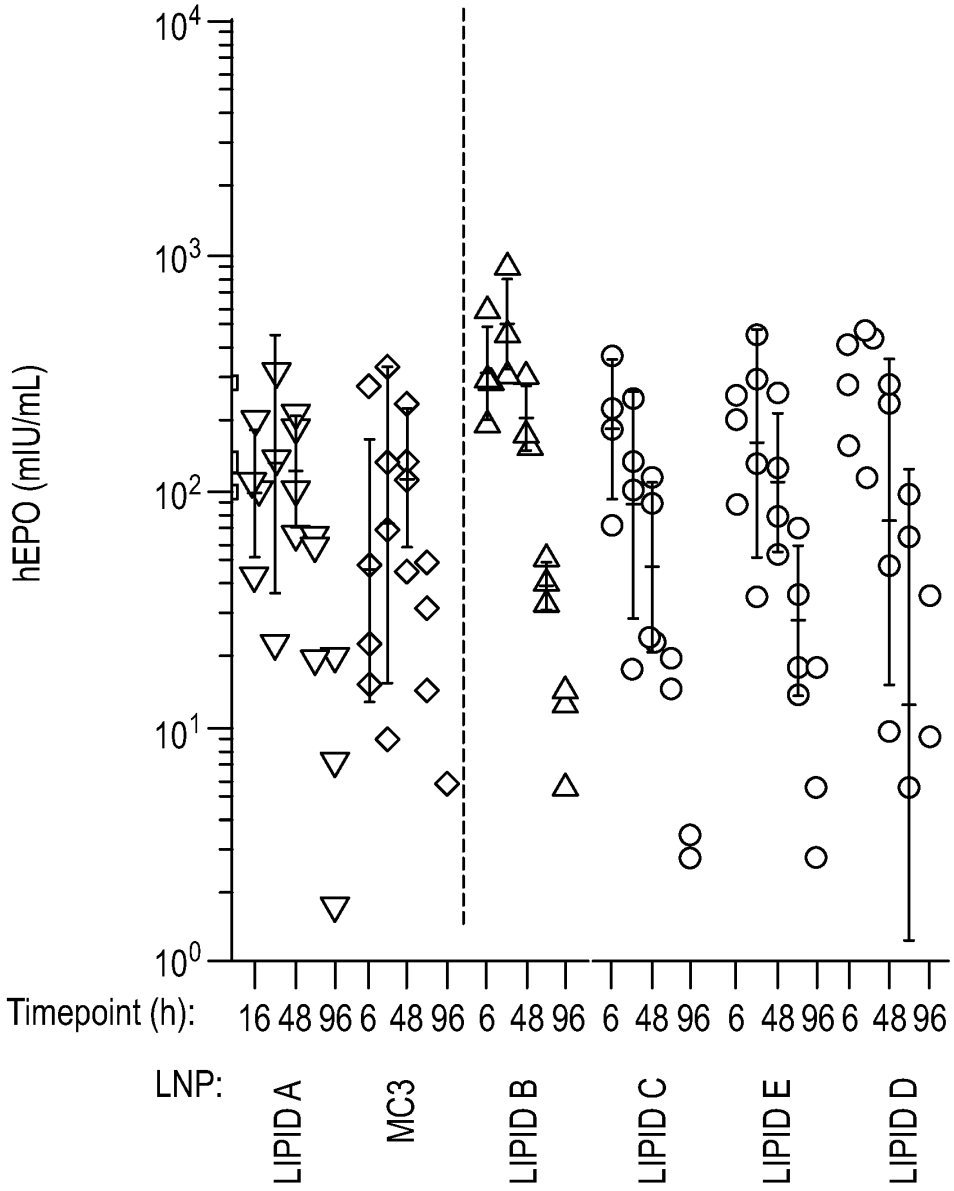

hEPO (mIU/mL)
10^4
10^3
10^2
10^1
10^0
Timepoint (h):
16 48 96 6 48 96 6 48 96 6 48 96 6 48 96 6 48 96
LNP:
LIPID A
MC3
LIPID B
LIPID C
LIPID E
LIPID D

FIG. 25

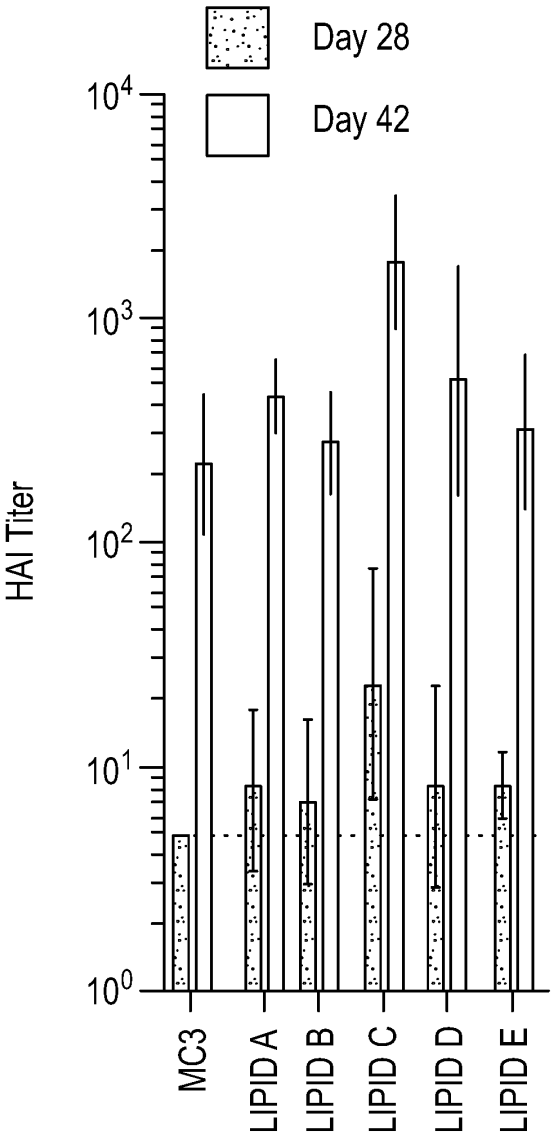

Day 28
Day 42
HAI Titer
10^4
10^3
10^2
10^1
10^0
MC3
LIPID A
LIPID B
LIPID C
LIPID D
LIPID E

FIG. 26

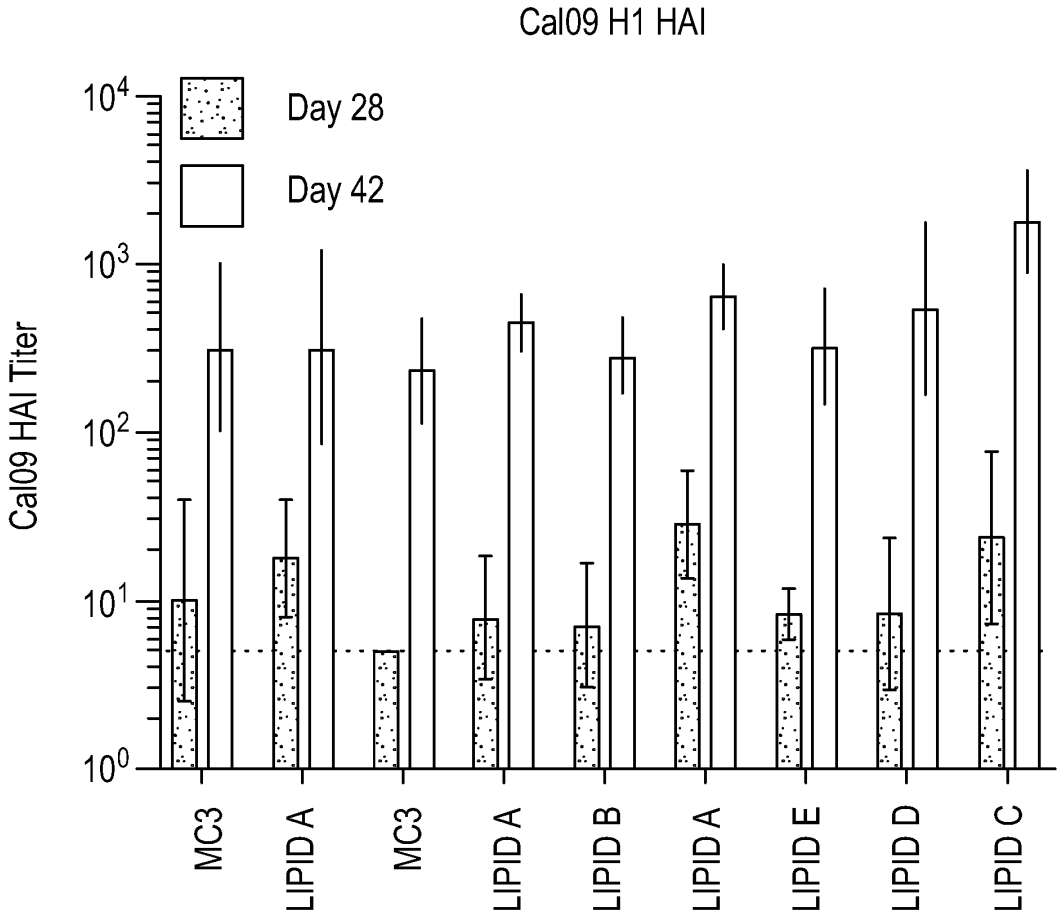

Cal09 H1 HAI
Day 28
Day 42
Cal09 HAI Titer
10^4
10^3
10^2
10^1
10^0
MC3
LIPID A
MC3
LIPID A
LIPID B
LIPID A
LIPID E
LIPID D
LIPID C

FIG. 27

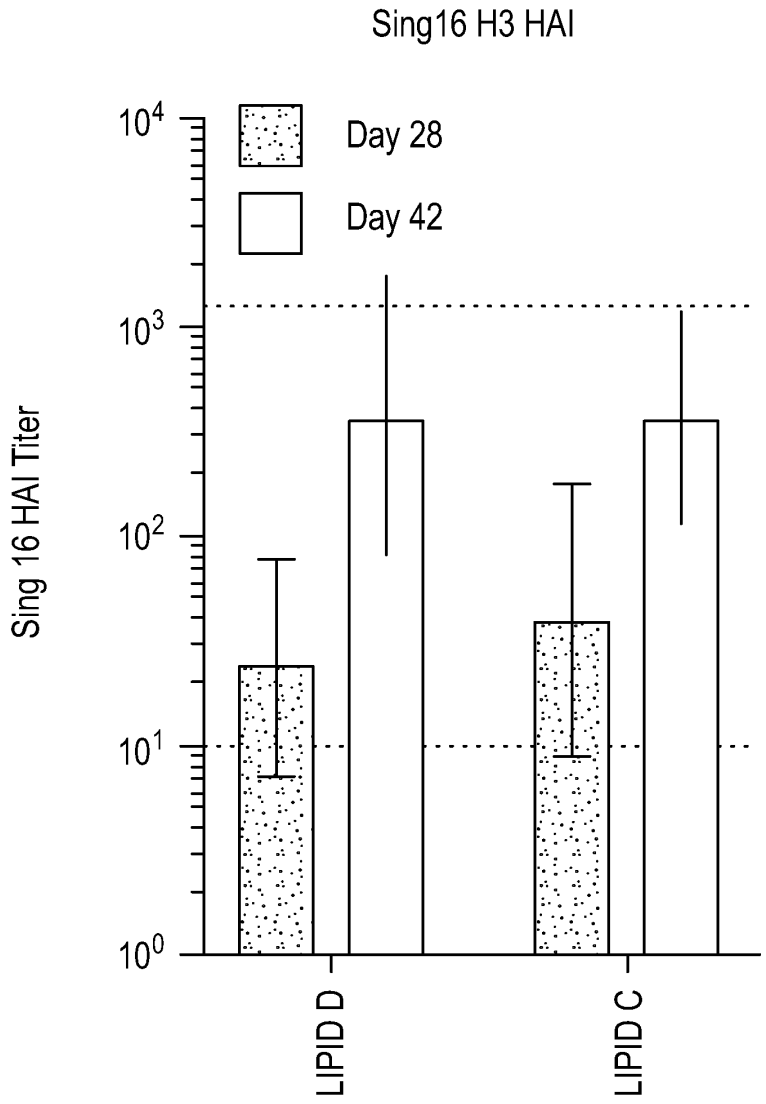

Sing16 H3 HAI
Day 28
Day 42
Sing 16 HAI Titer
10^4
10^3
10^2
10^1
10^0
LIPID D
LIPID C

FIG. 28

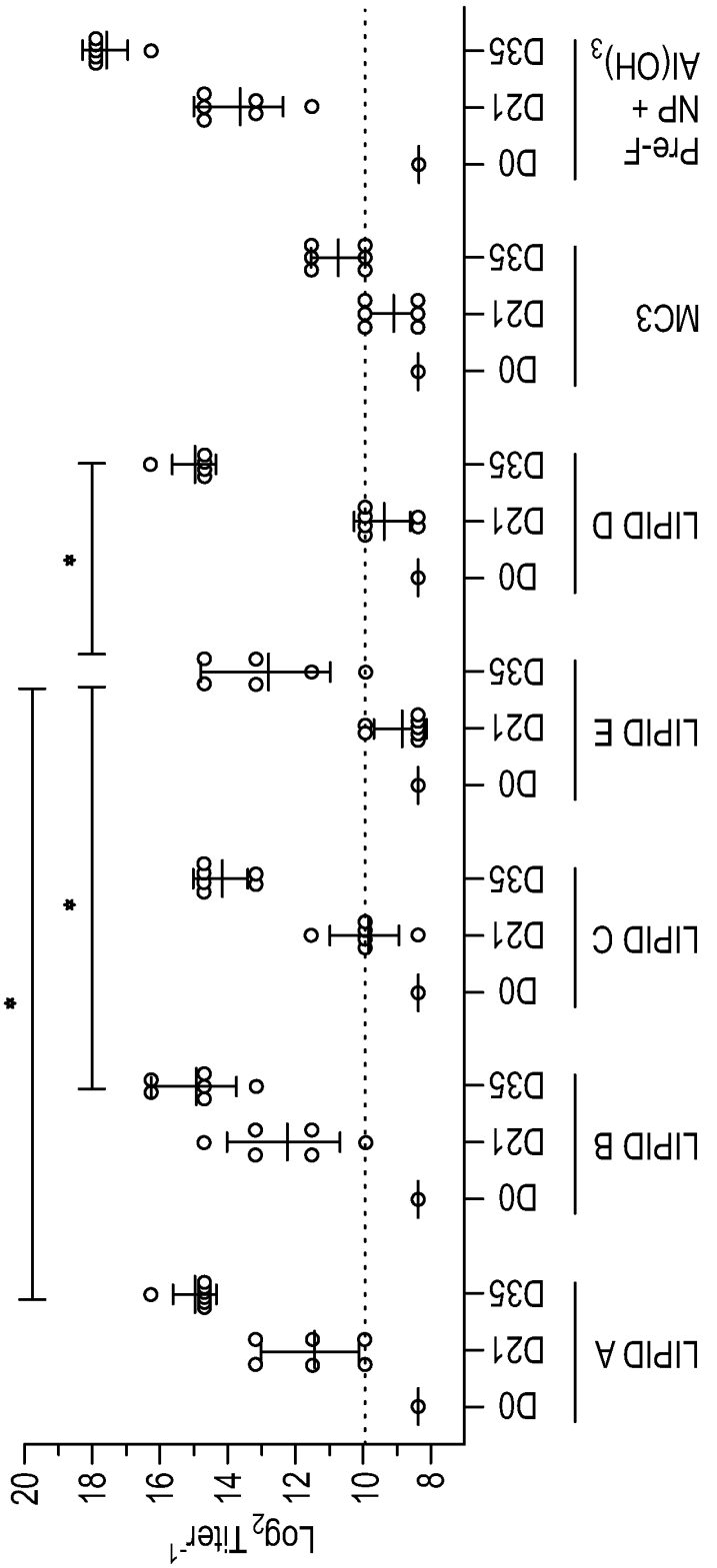

Log2 Titer-1
20
18
16
14
12
10
8
LIPID A
LIPID B
LIPID C
LIPID E
LIPID D
MC3
Pre-F NP + Al(OH)3
D0
D21
D35
*
*
*

FIG. 29

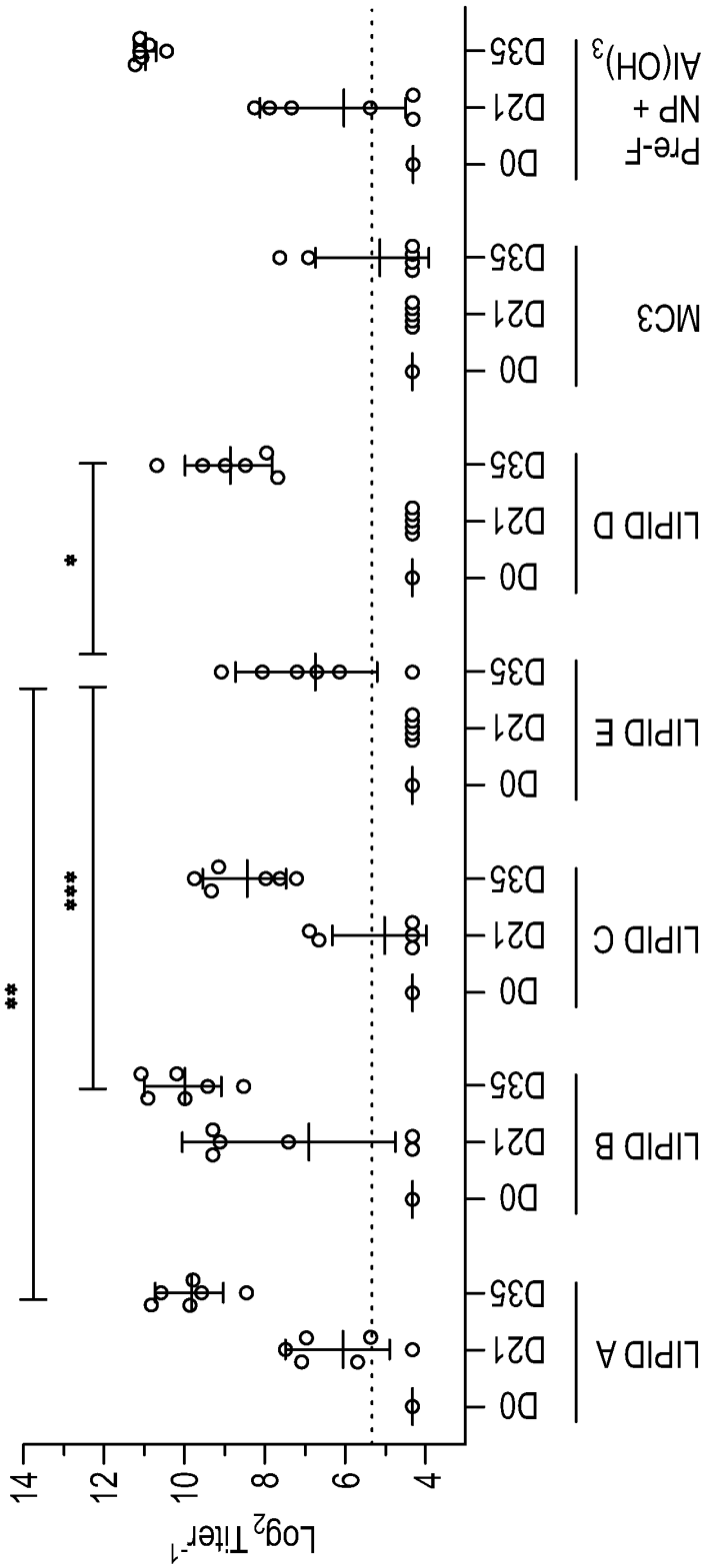

Log2 Titer-1
14
12
10
8
6
4
LIPID A
LIPID B
LIPID C
LIPID E
LIPID D
MC3
Pre-F NP + Al(OH)3
D0
D21
D35
**
***
*

FIG. 30

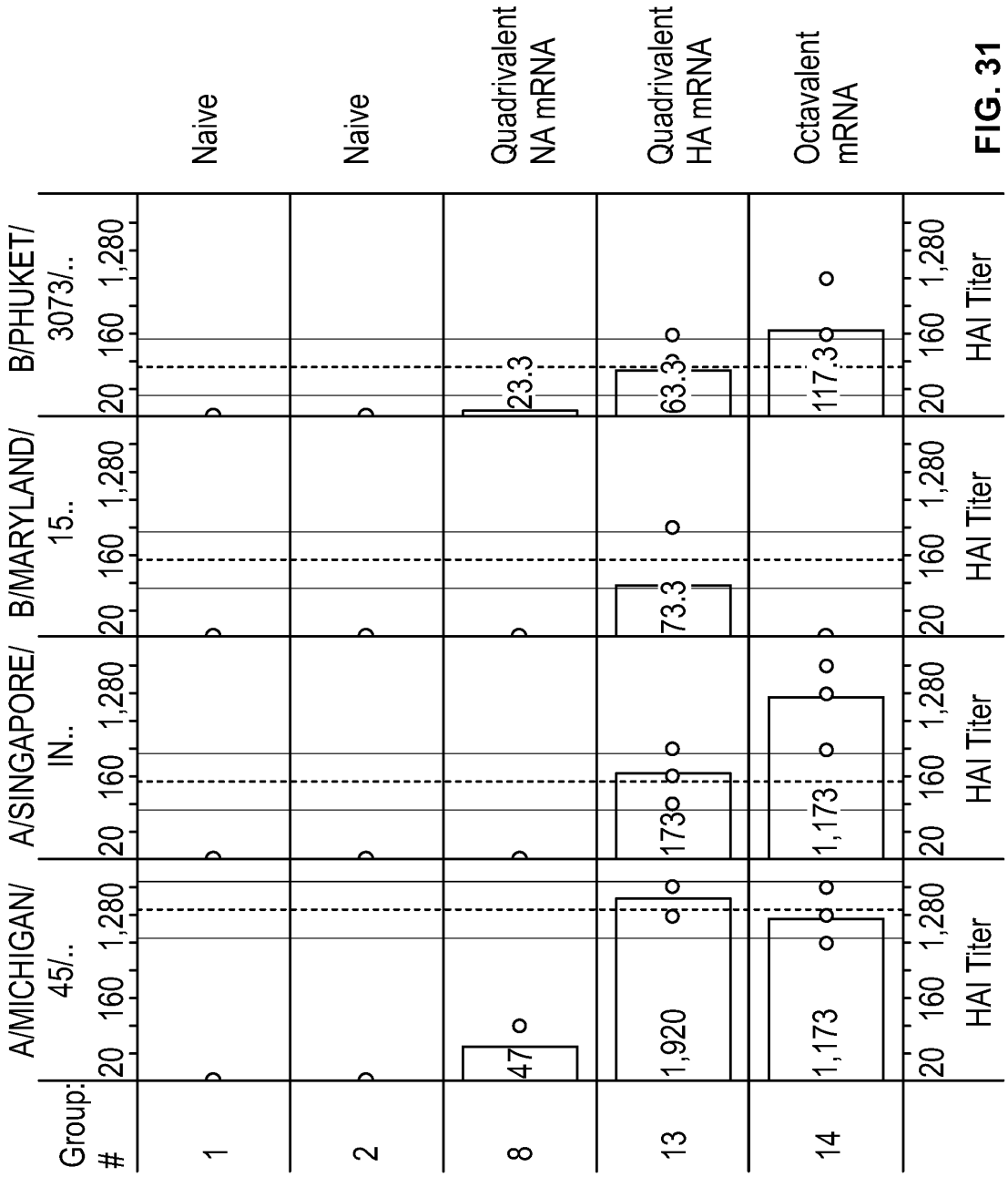

Group: #
A/MICHIGAN/ 45/..
A/SINGAPORE/ IN..
B/MARYLAND/ 15..
B/PHUKET/ 3073/..
20
160
1,280
HAI Titer
1
Naive
2
Naive
8
Quadrivalent NA mRNA
47
23.3
13
Quadrivalent HA mRNA
1,920
173
73.3
63.3
14
Octavalent mRNA
1,173
1,173
117.3

FIG. 31

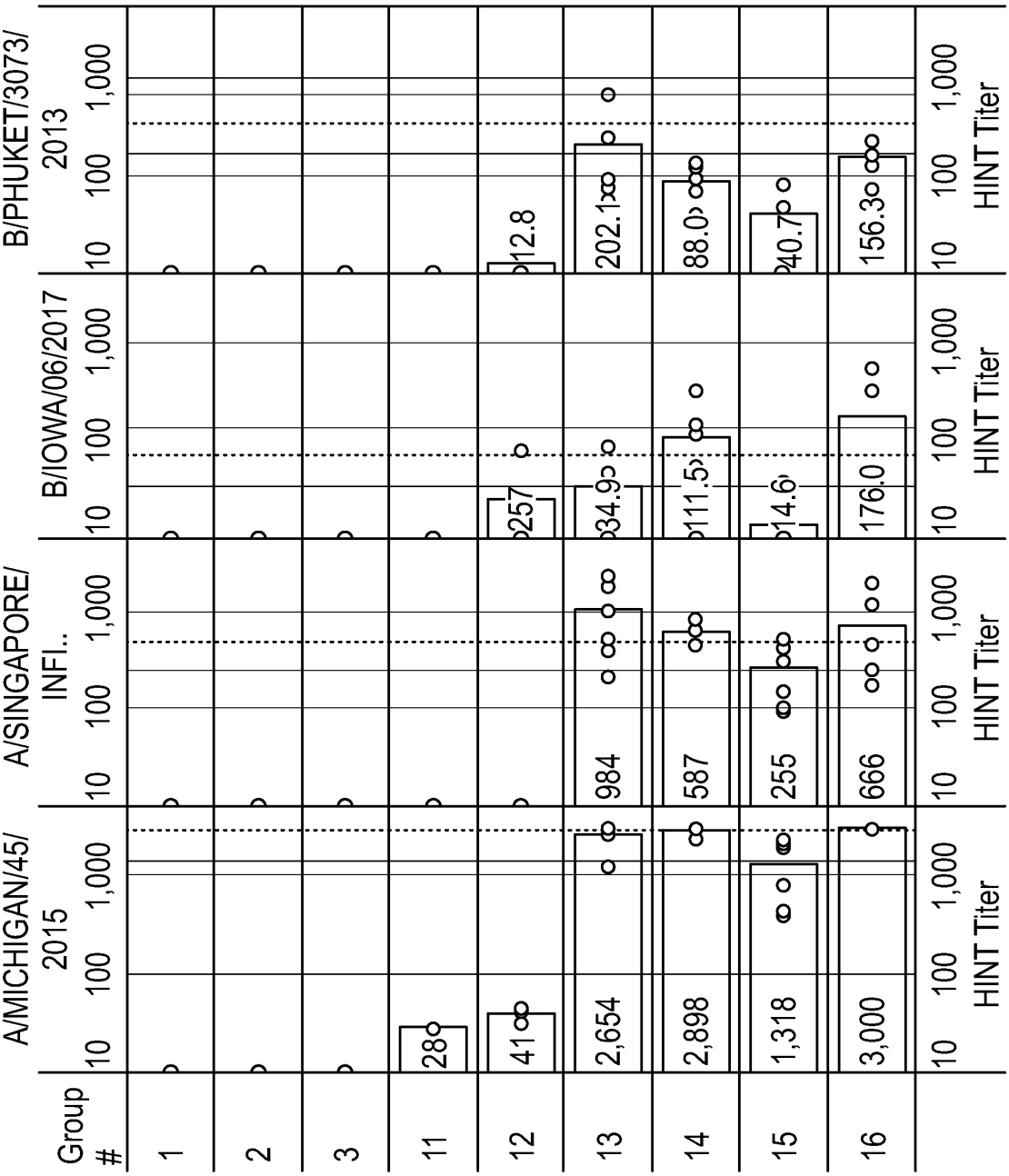

Group #
A/MICHIGAN/45/2015
A/SINGAPORE/INFl..
B/IOWA/06/2017
B/PHUKET/3073/2013
10
100
1,000
HINT Titer
1
2
3
11
12
13
14
15
16
28
41
2,654
2,898
1,318
3,000
257
984
587
255
666
12.8
34.9
202.1
111.5
88.0
14.6
40.7
176.0
156.3

FIG. 32

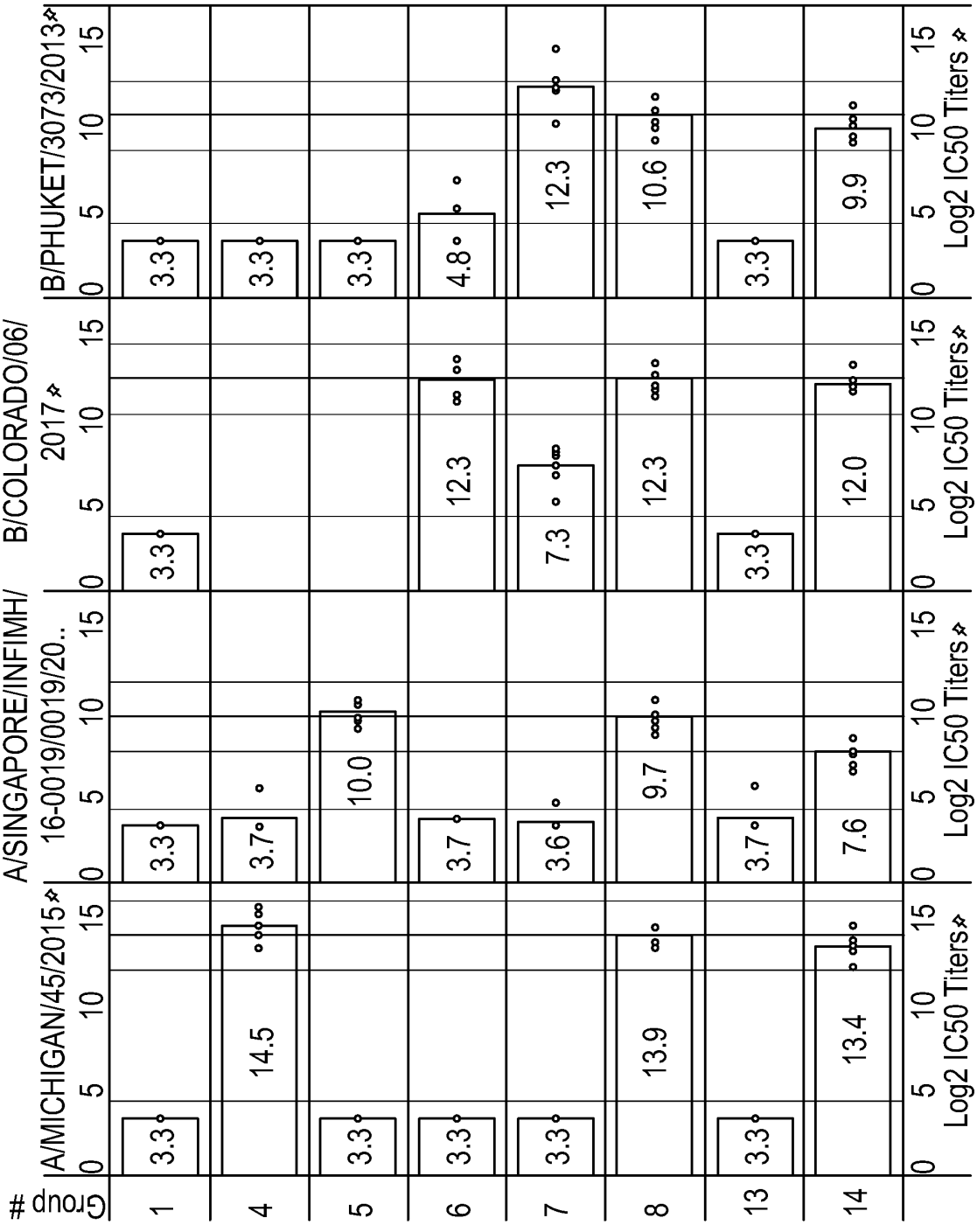

Group #
A/MICHIGAN/45/2015*
A/SINGAPORE/INFIMH/16-0019/0019/20..
B/COLORADO/06/2017*
B/PHUKET/3073/2013*
Log2 IC50 Titers*
1
4
5
6
7
8
13
14
3.3
14.5
10.0
3.7
7.3
12.3
9.7
13.9
13.4
7.6
12.0
9.9
10.6
4.8
0
5
10
15

FIG. 33

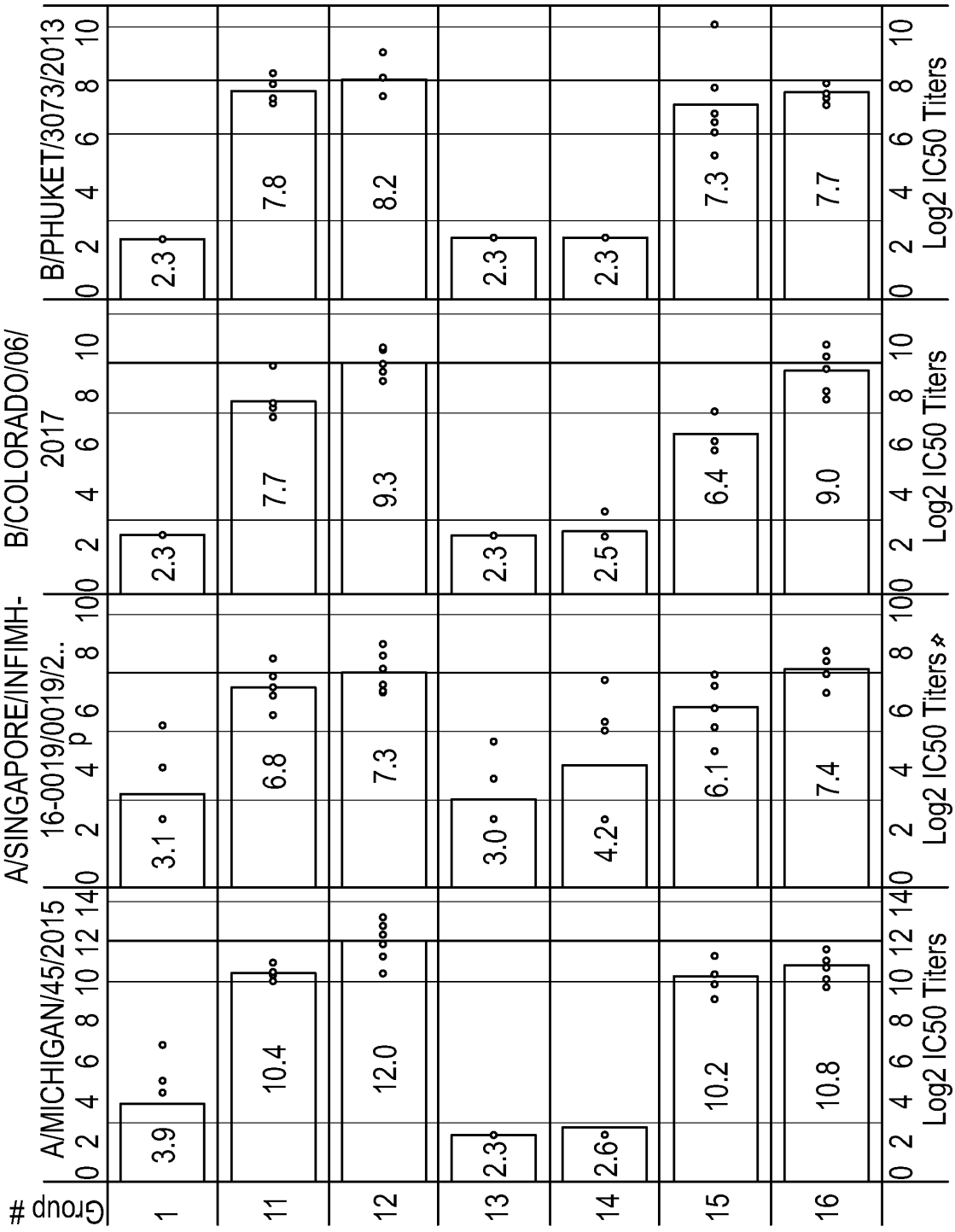

Group #
A/MICHIGAN/45/2015
A/SINGAPORE/INFIMH-16-0019/0019/2..
B/COLORADO/06/2017
B/PHUKET/3073/2013
Log2 IC50 Titers
1
11
12
13
14
15
16
3.9
10.4
12.0
2.3
2.6
10.2
10.8
3.1
6.8
7.3
3.0
4.2
6.1
7.4
2.3
7.7
9.3
2.3
2.5
6.4
9.0
2.3
7.8
8.2
2.3
2.3
7.3
7.7

FIG. 34

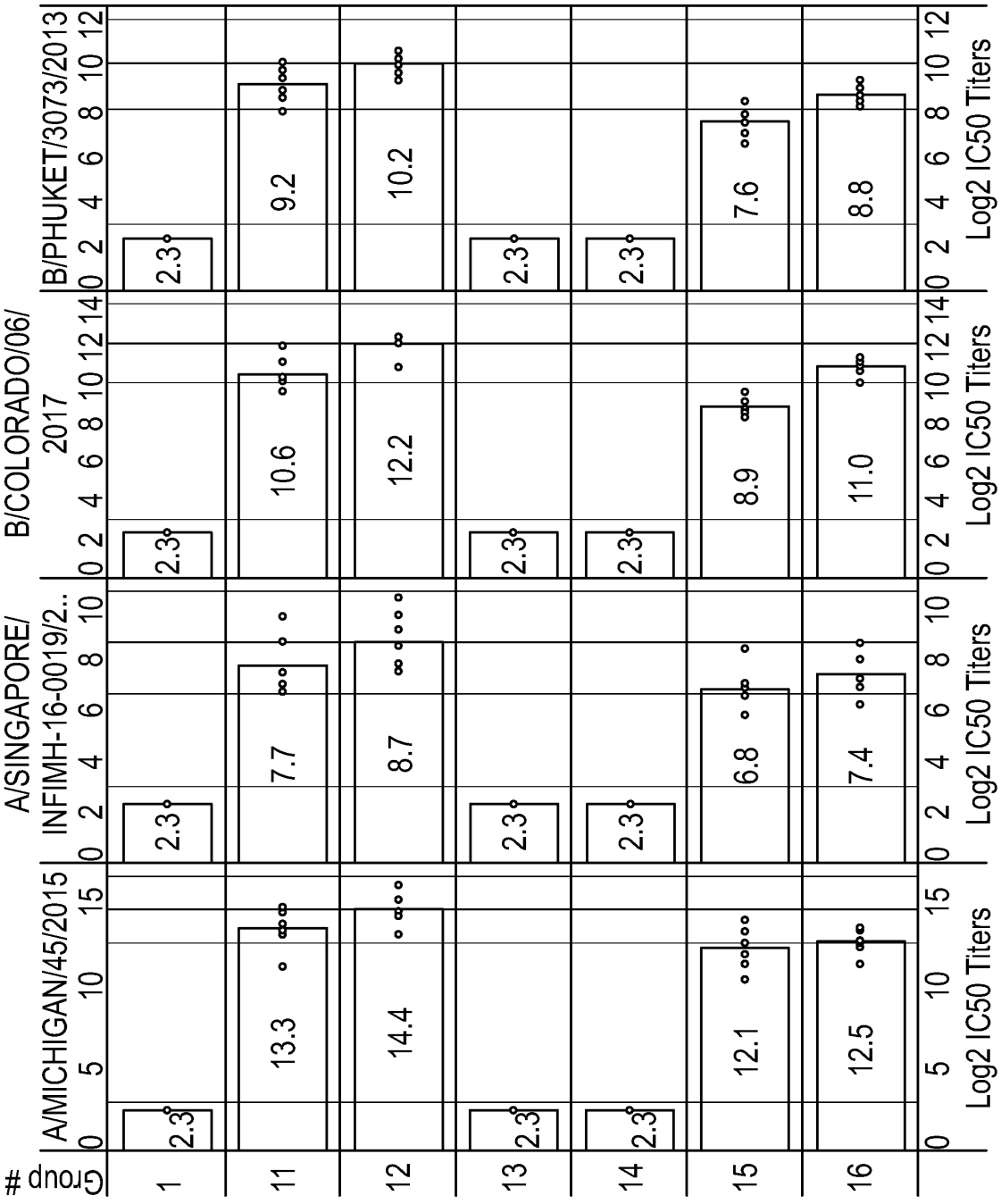

A/MICHIGAN/45/2015
A/SINGAPORE/ INFIMH-16-0019/2..
B/COLORADO/06/ 2017
B/PHUKET/3073/2013
Group #
1
11
12
13
14
15
16
2.3
13.3
14.4
12.1
12.5
7.7
8.7
6.8
7.4
10.6
12.2
8.9
11.0
9.2
10.2
7.6
8.8
Log2 IC50 Titers

FIG. 35

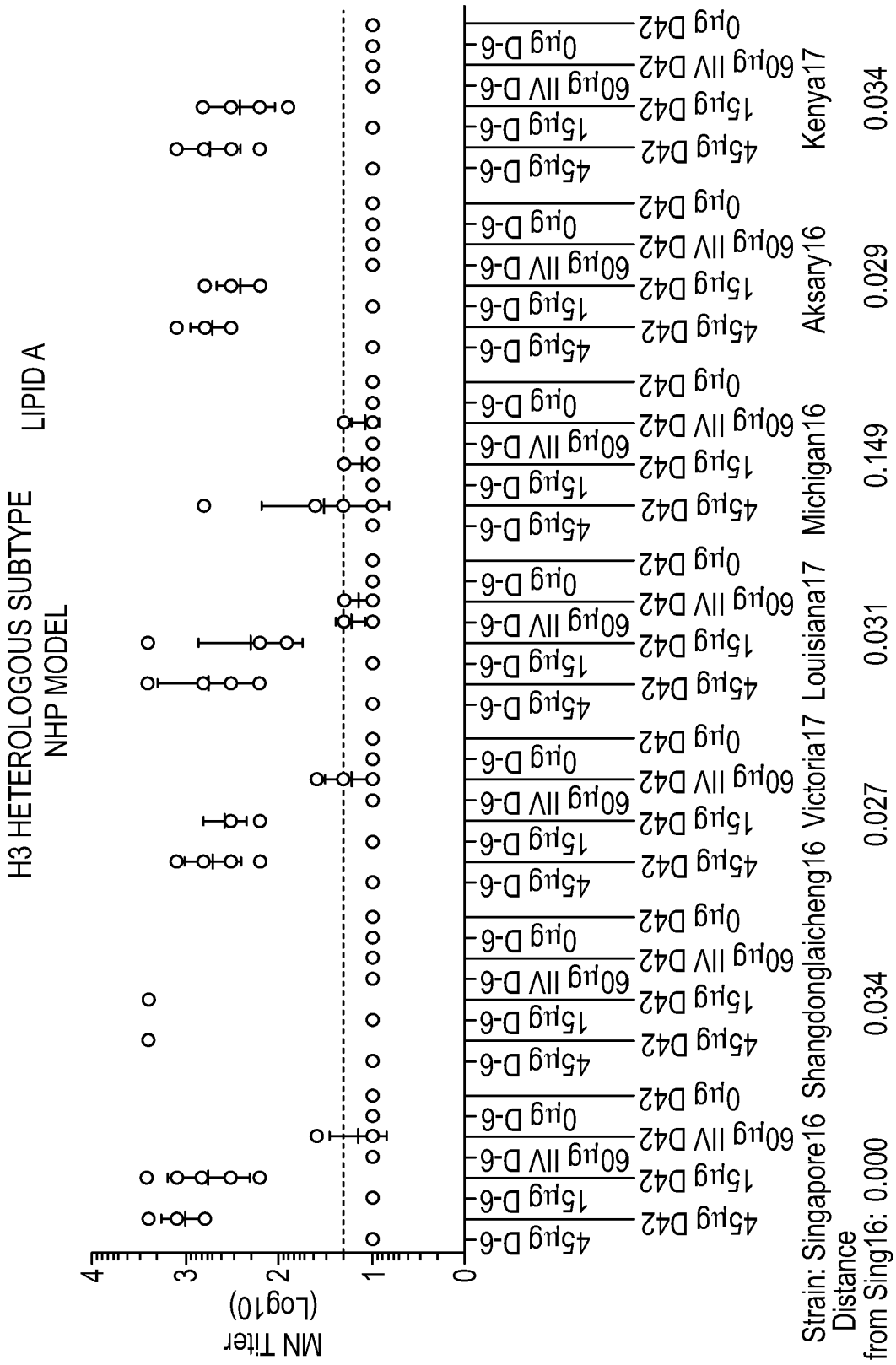

H3 HETEROLOGOUS SUBTYPE
NHP MODEL
LIPID A
MN Titer
(Log10)
0
1
2
3
4
Strain: Singapore16 Shangdonglaicheng16 Victoria17 Louisiana17 Michigan16 Aksary16 Kenya17
Distance
from Sing16: 0.000 0.034 0.027 0.031 0.149 0.029 0.034
0µg D42
0µg D-6
60µg IIV D42
60µg IIV D-6
15µg D42
15µg D-6
45µg D42
45µg D-6

FIG. 36

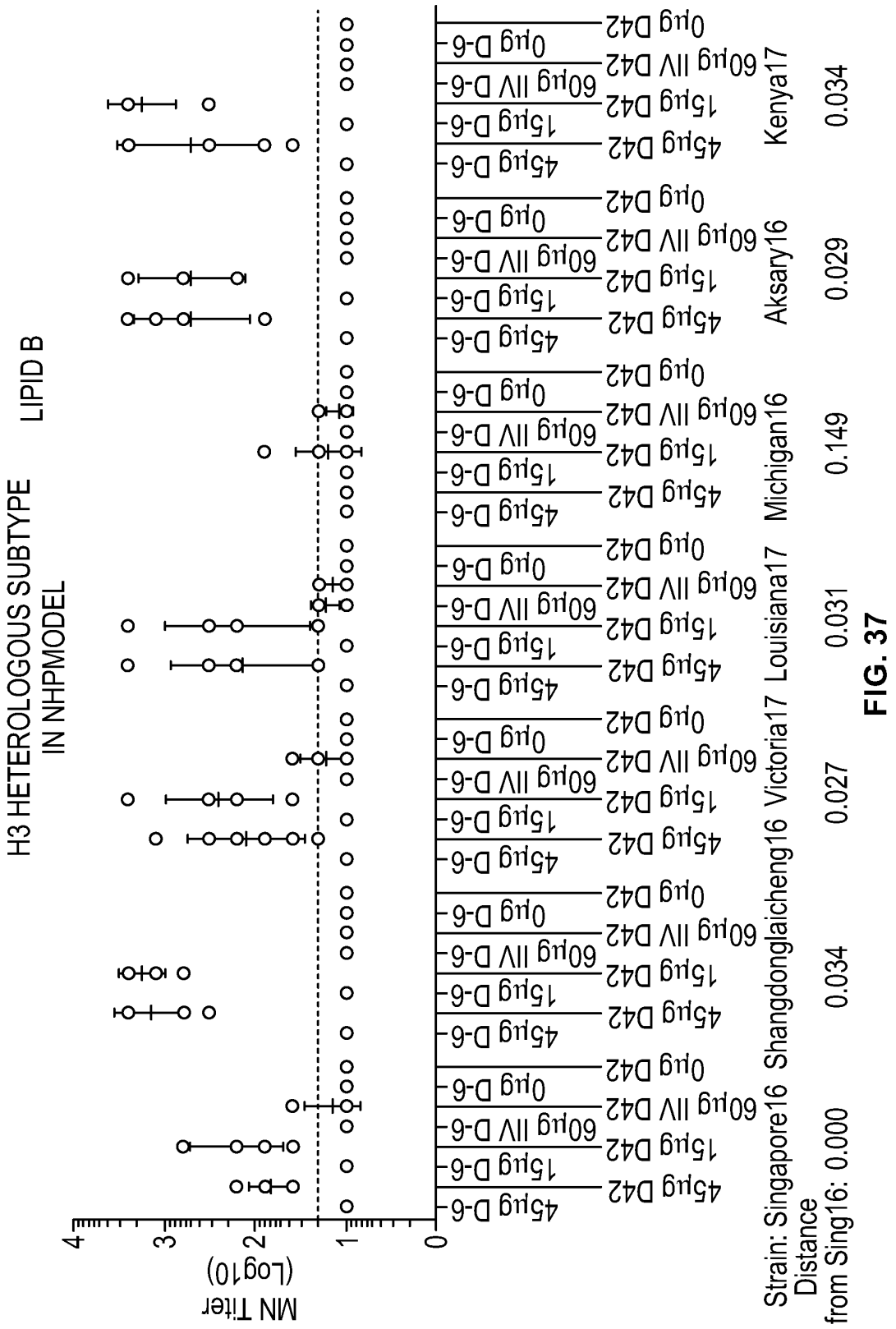

H3 HETEROLOGOUS SUBTYPE
IN NHPMODEL
LIPID B
MN Titer
(Log10)
0
1
2
3
4
0µg D-6
45µg D-6
15µg D-6
60µg IIV D-6
0µg D42
45µg D42
15µg D42
60µg IIV D42
Strain: Singapore16 Shangdonglaicheng16 Victoria17 Louisiana17 Michigan16 Aksary16 Kenya17
Distance
from Sing16: 0.000 0.034 0.027 0.031 0.149 0.029 0.034

FIG. 37