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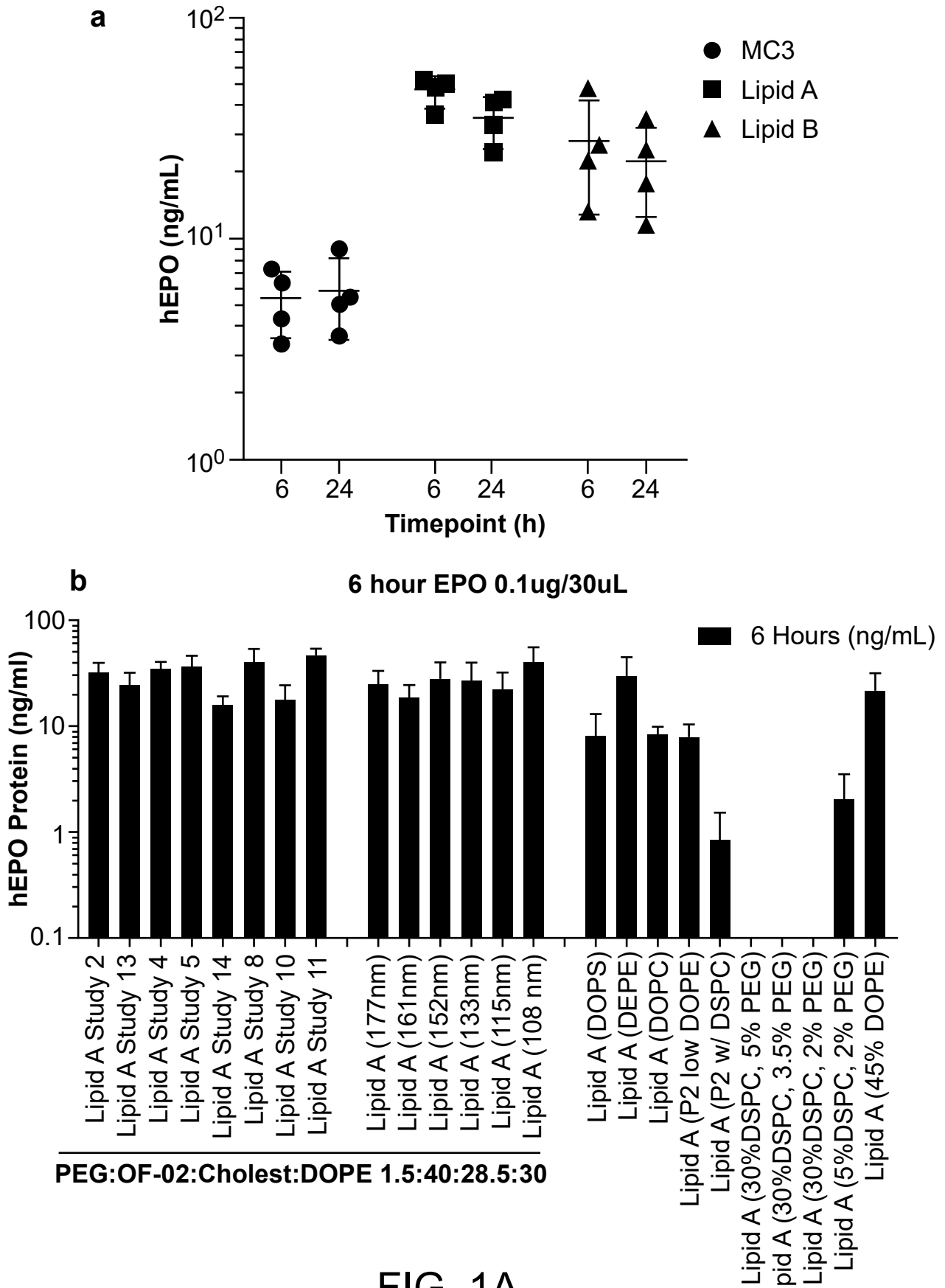
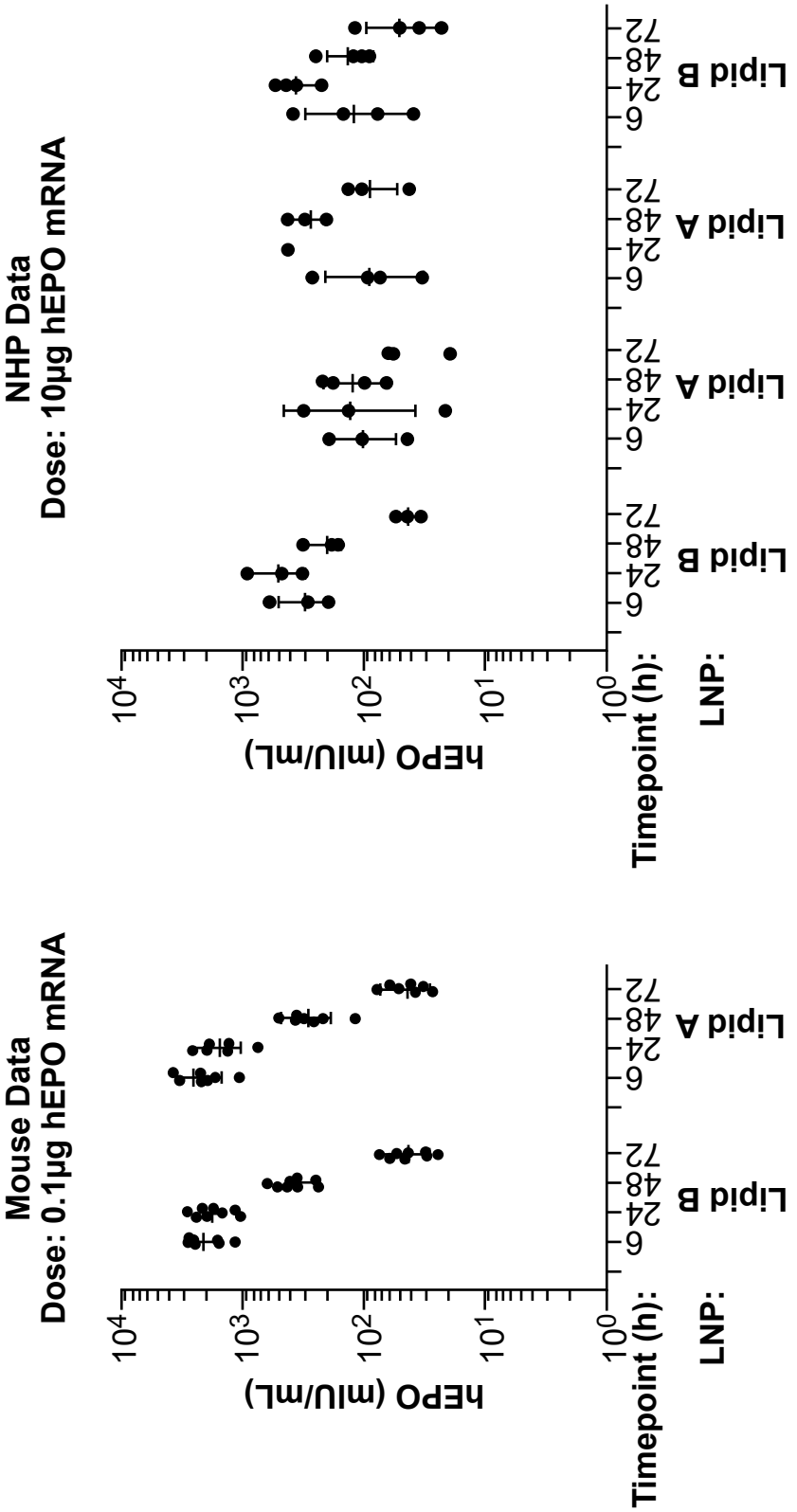
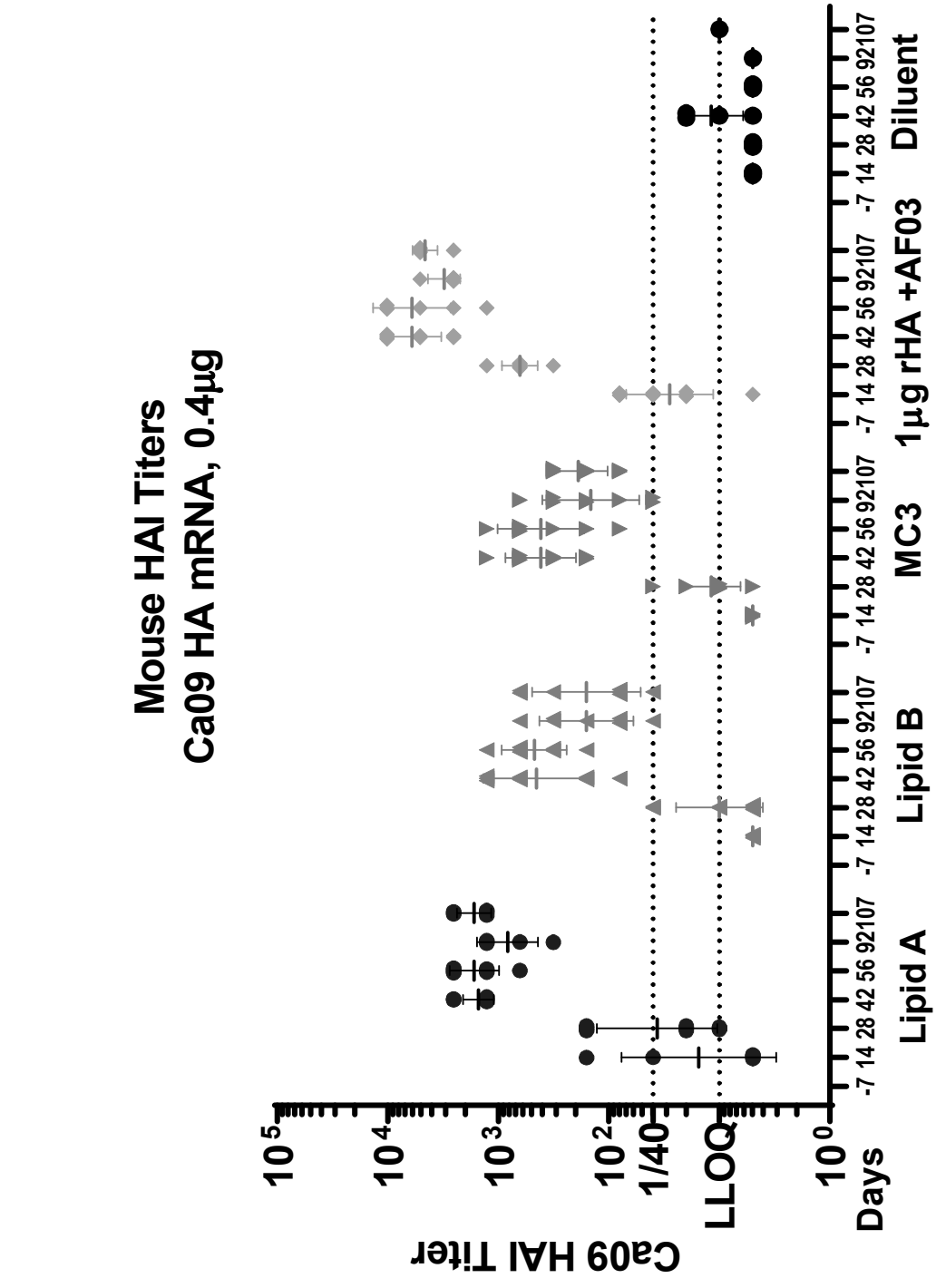

a
10^2
10^1
10^0
hEPO (ng/mL)
MC3
Lipid A
Lipid B
6
24
6
24
6
24
Timepoint (h)
b
6 hour EPO 0.1ug/30uL
100
10
1
0.1
hEPO Protein (ng/ml)
6 Hours (ng/mL)
Lipid A Study 2
Lipid A Study 13
Lipid A Study 4
Lipid A Study 5
Lipid A Study 14
Lipid A Study 8
Lipid A Study 10
Lipid A Study 11
Lipid A (177nm)
Lipid A (161nm)
Lipid A (152nm)
Lipid A (133nm)
Lipid A (115nm)
Lipid A (108 nm)
Lipid A (DOPS)
Lipid A (DEPE)
Lipid A (DOPC)
Lipid A (P2 low DOPE)
Lipid A (P2 w/ DSPC)
Lipid A (30%DSPC, 5% PEG)
Lipid A (30%DSPC, 3.5% PEG)
Lipid A (30%DSPC, 2% PEG)
Lipid A (5%DSPC, 2% PEG)
Lipid A (45% DOPE)
PEG:OF-02:Cholest:DOPE 1.5:40:28.5:30

FIG. 1A



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

FIG. 1B



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

FIG. 2A

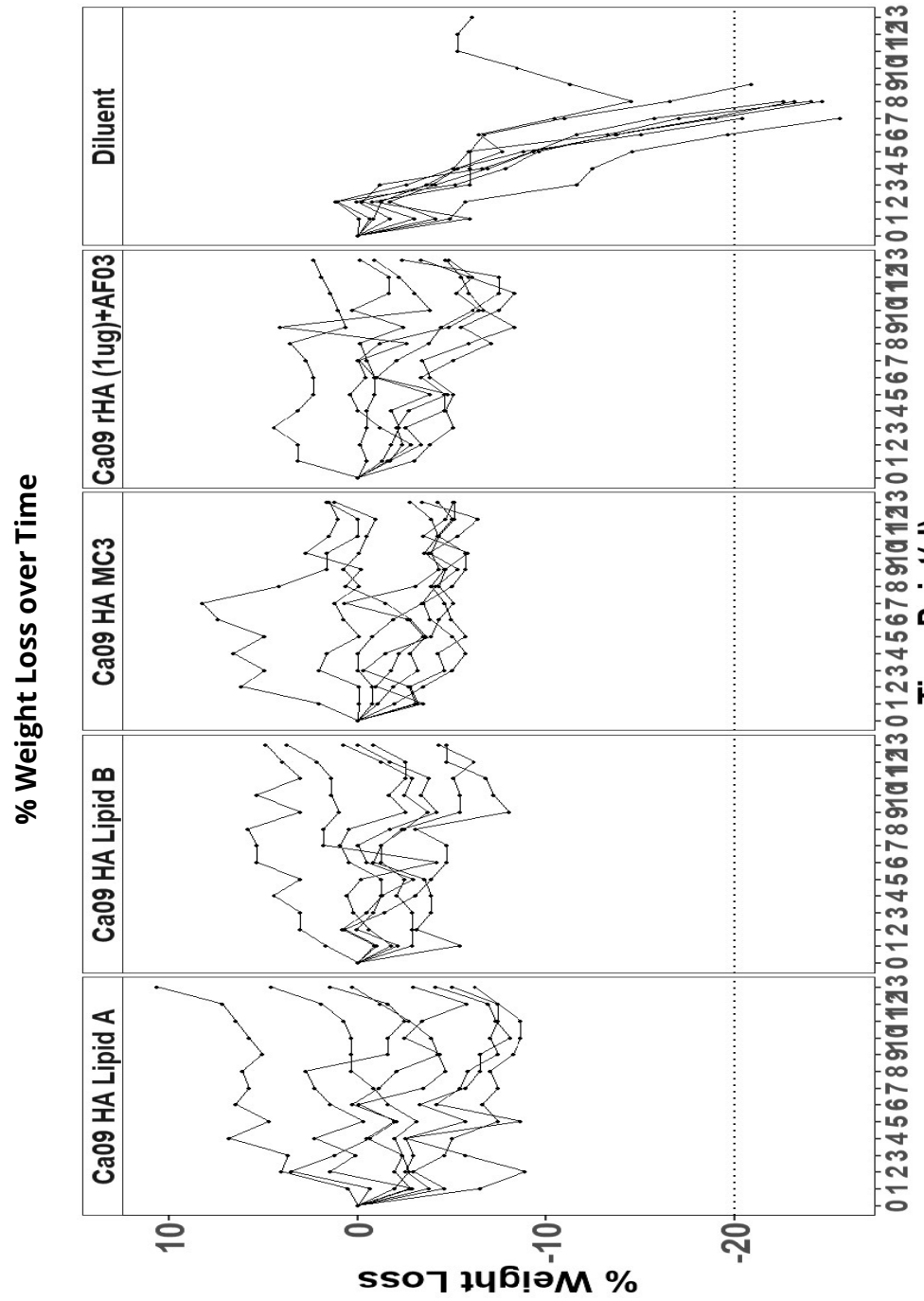
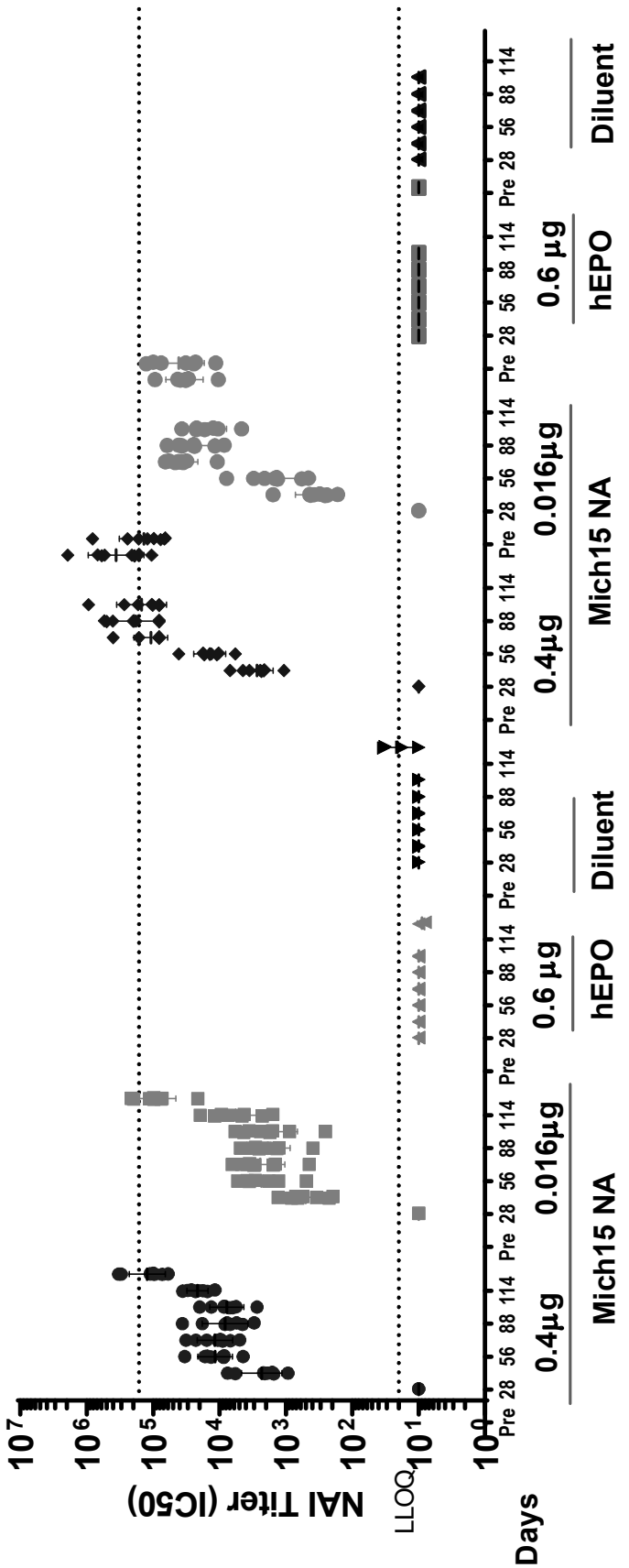

% Weight Loss over Time
Ca09 HA Lipid A
Ca09 HA Lipid B
Ca09 HA MC3
Ca09 rHA (1ug)+AF03
Diluent
% Weight Loss
10
0
-10
-20
Time-Point(d)

FIG. 2B



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

FIG. 3A

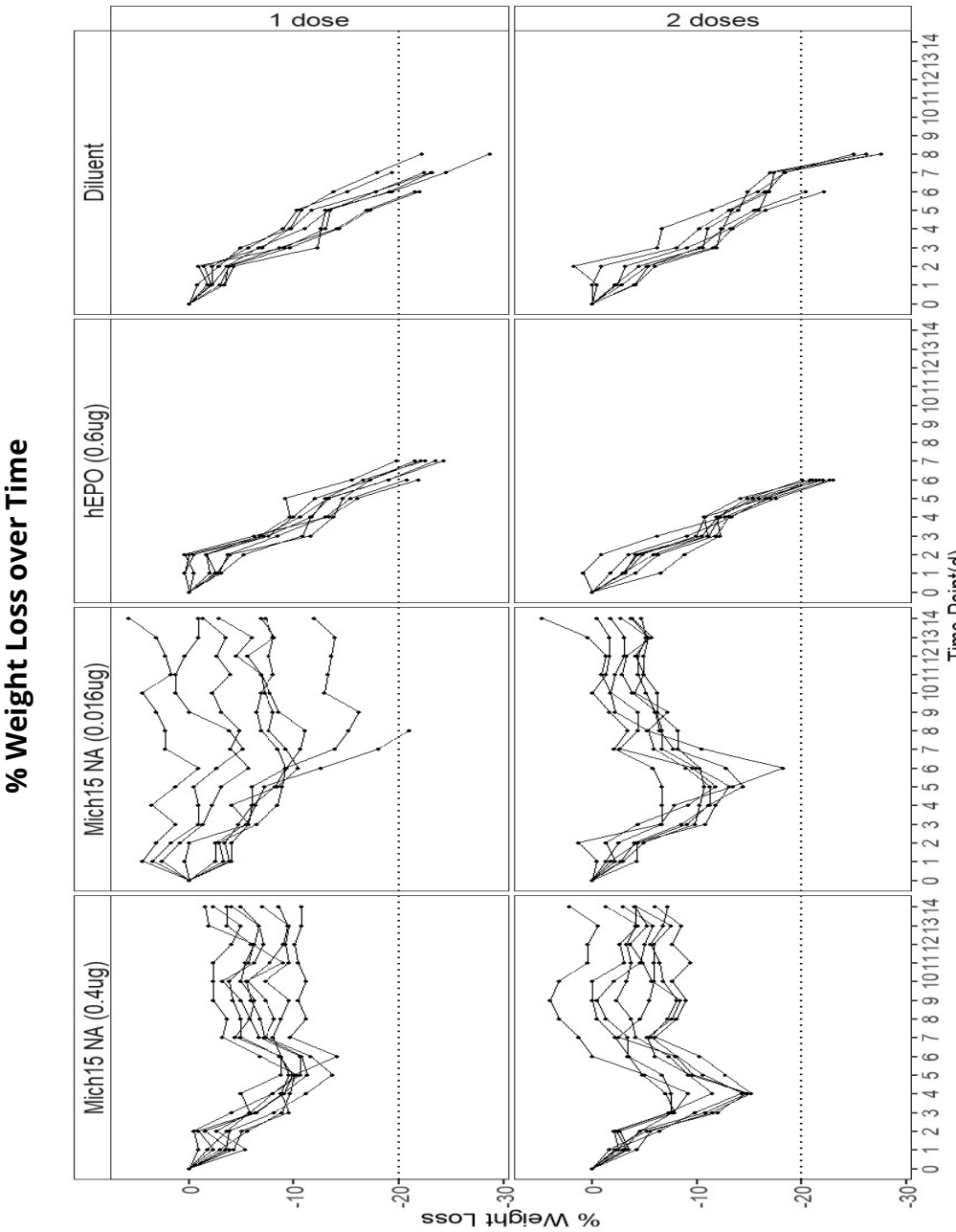
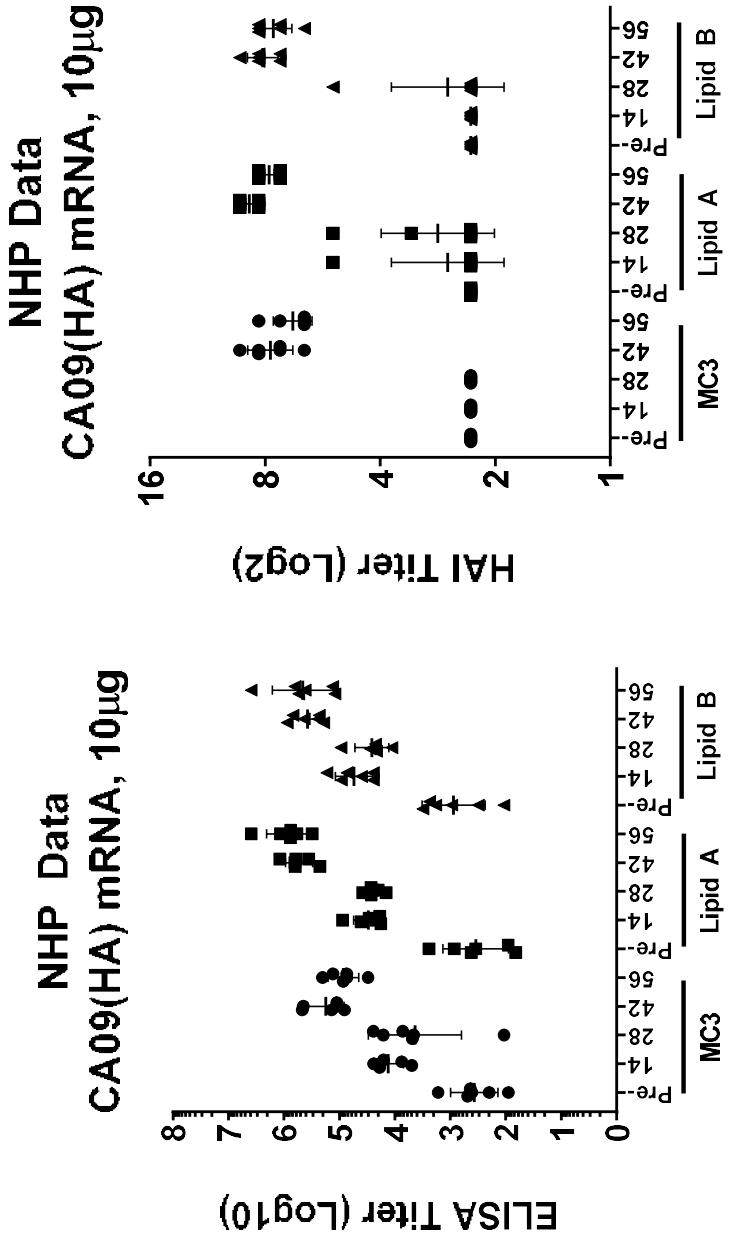

% Weight Loss over Time
Mich15 NA (0.4ug)
Mich15 NA (0.016ug)
hEPO (0.6ug)
Diluent
1 dose
2 doses
% Weight Loss
Time-Point(d)

FIG. 3B



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

FIG. 4

ATGAAAACCATAATCGCGCTCTCATACATACTTTGCCTGGTCTTTGCCCAAAAGATCCCTGGCAACGACAACTCAACCGCGACCCTTTGCCTCGGCCATCACGCCGTGCCGAACGG
CACTATCGTCAAGACCATCACAAACGACCGCATCGAAGTGACCAACGCGACTGAGCTAGTGCAGAACTCCAGCATTGGAGAGATTTGCGATTCTCCACACCAAATCCTGGACGGAG
AGAATTGTACCTTGATCGACGCGCTGCTGGGGGATCCGCAGTGCGACGGATTCCAGAACAAGAAATGGGACCTTTTCGTGGAACGGAGCAAGGCATACTCGAATTGCTACCCCTAC
GATGTGCCCGACTACGCCTCGCTGCGGTCCTTGGTCGCTTCCTCCGGGACCCTGGAATTCAAAAACGAGAGCTTTAATTGGACCGGAGTGACCCAGAATGGCACCTCGAGCGCCTG
CATTCGGGGCTCCTCCTCGAGCTTCTTCAGCCGCCTGAACTGGCTCACTCACCTCAACTACACCTACCCGGCACTGAACGTGACCATGCCGAACAAGGAACAATTCGACAAGCTCT
ACATTTGGGGGGTGCATCACCCGGGTACCGATAAGGACCAGATCTTCCTCTACGCCCAATCCTCGGGCCGGATCACCGTGTCCACTAAGCGCTCGCAGCAGGCCGTGATCCCGAAC
ATTGGAAGCAGACCCCGCATTCGCGACATTCCATCGAGGATCTCGATCTACTGGACGATTGTCAAGCCTGGCGACATCCTCCTCATTAACTCCACCGGGAACCTCATCGCCCCTCG
GGGTTATTTCAAGATCCGCAGCGGGAAGTCCTCCATCATGAGAAGCGATGCCCCCATTGGAAAGTGCAAGTCCGAGTGTATCACACCTAACGGAAGCATTCCCAATGACAAGCCAT
TCCAGAACGTGAACAGAATTACCTACGGAGCTTGCCCTCGCTACGTCAAACATTCGACCCTCAAGTTGGCGACTGGAATGCGCAACGTGCCGGAGAAGCAAACCCGGGGGATCTTC
GGGGCTATCGCGGGATTCATCGAAAATGGATGGGAAGGAATGGTCGATGGTTGGTACGGTTTCAGACACCAGAACTCCGAGGGGCGGGGCCAGGCCGCAGACCTGAAGTCCACTCA
GGCCGCGATTGACCAGATCAACGGAAAGCTCAACAGACTCATTGGAAAGACCAACGAAAAGTTCCACCAAATCGAAAAGGAATTCTCCGAAGTGGAGGGCCGGGTGCAAGACCTGG
AGAAGTACGTGGAGGACACTAAGATCGACCTTTGGAGCTATAACGCAGAACTCCTTGTGGCCCTGGAAAACCAGCACACCATCGACCTGACCGATTCAGAGATGAACAAGCTCTTT
GAGAAAACTAAGAAGCAACTCCGGGAAAACGCTGAGGACATGGGAAATGGATGCTTTAAGATCTACCACAAGTGCGACAACGCCTGCATTGAGTCCATACGGAACGAAACTTACGA
CCATAACGTCTACCGGGATGAAGCCCTGAACAACAGATTCCAGATCAAGGGCGTGGAGCTGAAGTCCGGCTACAAAGATTGGATCCTGTGGATTTCCTTCGCGATTTCATGCTTCT
TGCTCTGCGTGGCCCTCCTGGGATTCATAATGTGGGCCTGTCAGAAGGGCAACATTAGGTGCAACATATGCATATAA

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

MRT10279        GGCAACGACAACTCAACCGCGACCCTTTGCCTCGGCCATCACGCCGTGCCGAACGGCACT
H3_WT           GGAAATGACAATAGCACGGCAACGCTGTGCCTTGGGCACCATGCAGTACCAAACGGAACG
                ** ** *****    ** ** ** ** ***** ** ** ** ** ** ** ***** **

MRT10279        ATCGTCAAGACCATCACAAACGACCGCATCGAAGTGACCAACGCGACTGAGCTAGTGCAG
H3_WT           ATAGTGAAAACAATCACAAATGACCGAATTGAAGTTACTAATGCTACTGAGTTGGTTCAG
                ** ** ** ** ******** ***** ** ***** ** ** ** ****** * ** ***

MRT10279        AACTCCAGCATTGGAGAGATTTGCGATTCTCCACACCAAATCCTGGACGGAGAGAATTGT
H3_WT           AATTCCTCAATAGGTGAAATATGCGACAGTCCTCATCAGATCCTTGATGGAGAGAACTGC
                ** ***   ** ** ** ** *****   *** ** ** ***** ** ******** **

MRT10279        ACCTTGATCGACGCGCTGCTGGGGGATCCGCAGTGCGACGGATTCCAGAACAAGAAATGG
H3_WT           ACACTAATAGATGCTCTATTGGGAGACCCTCAGTGTGATGGCTTTCAAAATAAGAAATGG
                **  * ** ** ** **  **** ** ** ***** ** ** ** ** ** *********

MRT10279        GACCTTTTCGTGGAACGGAGCAAGGCATACTCGAATTGCTACCCCTACGATGTGCCCGAC
H3_WT           GACCTTTTTGTTGAACGAAGCAAAGCCTACAGCAACTGTTACCCTTATGATGTGCCGGAT
                ******** ** ***** ***** ** ***   ** ** ***** ** ******** **

MRT10279        TACGCCTCGCTGCGGTCCTTGGTCGCTTCCTCCGGGACCCTGGAATTCAAAAACGAGAGC
H3_WT           TATGCCTCCCTTAGGTCACTAGTTGCCTCATCCGGCACACTGGAGTTTAAAAATGAAAGC
```

FIG. 5A

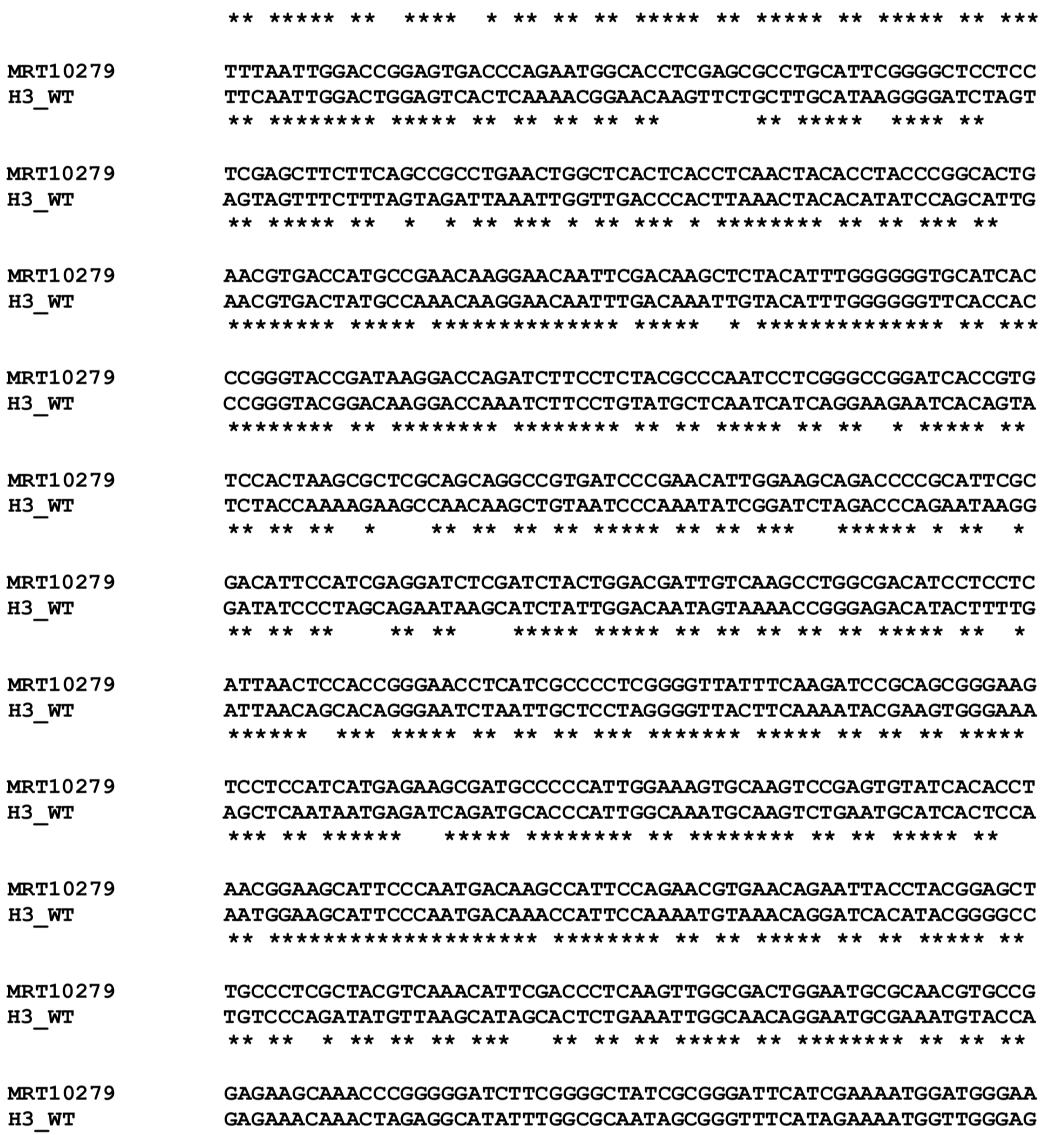

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H3_WT TTCAATTGGACTGGAGTCACTCAAAACGGAACAAGTTCTGCTTGCATAAGGGGATCTAGT
MRT10279 TCGAGCTTCTTCAGCCGCCTGAACTGGCTCACTCACCTCAACTACACCTACCCGGCACTG
H3_WT AGTAGTTTCTTTAGTAGATTAAATTGGTTGACCCACTTAAACTACACATATCCAGCATTG
MRT10279 AACGTGACCATGCCGAACAAGGAACAATTCGACAAGCTCTACATTTGGGGGGTGCATCAC
H3_WT AACGTGACTATGCCAAACAAGGAACAATTTGACAAATTGTACATTTGGGGGGTTCACCAC
MRT10279 CCGGGTACCGATAAGGACCAGATCTTCCTCTACGCCCAATCCTCGGGCCGGATCACCGTG
H3_WT CCGGGTACGGACAAGGACCAAATCTTCCTGTATGCTCAATCATCAGGAAGAATCACAGTA
MRT10279 TCCACTAAGCGCTCGCAGCAGGCCGTGATCCCGAACATTGGAAGCAGACCCCGCATTCGC
H3_WT TCTACCAAAAGAAGCCAACAAGCTGTAATCCCAAATATCGGATCTAGACCCAGAATAAGG
MRT10279 GACATTCCATCGAGGATCTCGATCTACTGGACGATTGTCAAGCCTGGCGACATCCTCCTC
H3_WT GATATCCCTAGCAGAATAAGCATCTATTGGACAATAGTAAAACCGGGAGACATACTTTTG
MRT10279 ATTAACTCCACCGGGAACCTCATCGCCCCTCGGGGTTATTTCAAGATCCGCAGCGGGAAG
H3_WT ATTAACAGCACAGGGAATCTAATTGCTCCTAGGGGTTACTTCAAAATACGAAGTGGGAAA
MRT10279 TCCTCCATCATGAGAAGCGATGCCCCCATTGGAAAGTGCAAGTCCGAGTGTATCACACCT
H3_WT AGCTCAATAATGAGATCAGATGCACCCATTGGCAAATGCAAGTCTGAATGCATCACTCCA
MRT10279 AACGGAAGCATTCCCAATGACAAGCCATTCCAGAACGTGAACAGAATTACCTACGGAGCT
H3_WT AATGGAAGCATTCCCAATGACAAACCATTCCAAAATGTAAACAGGATCACATACGGGGCC
MRT10279 TGCCCTCGCTACGTCAAACATTCGACCCTCAAGTTGGCGACTGGAATGCGCAACGTGCCG
H3_WT TGTCCCAGATATGTTAAGCATAGCACTCTGAAATTGGCAACAGGAATGCGAAATGTACCA
MRT10279 GAGAAGCAAACCCGGGGGATCTTCGGGGCTATCGCGGGATTCATCGAAAATGGATGGGAA
H3_WT GAGAAACAAACTAGAGGCATATTTGGCGCAATAGCGGGTTTCATAGAAAATGGTTGGGAG

FIG. 5A (Cont.)

```
                ***** *****  * ** ** ** ** ** ** ***** ***** ******** *****

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

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

MRT10279        ATTGGAAAGACCAACGAAAAGTTCCACCAAATCGAAAAGGAATTCTCCGAAGTGGAGGGC
H3_WT           ATCGGAAAAACCAACGAGAAATTCCATCAGATTGAAAAAGAATTCTCAGAAGTAGAAGGA
                ** ***** ******** ** ***** ** ** ***** ******** ***** ** **

MRT10279        CGGGTGCAAGACCTGGAGAAGTACGTGGAGGACACTAAGATCGACCTTTGGAGCTATAAC
H3_WT           AGAGTTCAAGACCTTGAGAAATATGTTGAGGACACTAAAATAGATCTCTGGTCATACAAC
                * ** ******** ***** ** ** ********** ** ** ** ***   ** ***

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

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

MRT10279        GGATGCTTTAAGATCTACCACAAGTGCGACAACGCCTGCATTGAGTCCATACGGAACGAA
H3_WT           GGTTGTTTCAAAATATACCACAAATGTGACAATGCCTGCATAGAATCAATAAGAAATGAA
                ** ** ** ** ** ******** ** ***** ******** ** ** *** * ** ***

MRT10279        ACTTACGACCATAACGTCTACCGGGATGAAGCCCTGAACAACAGATTCCAGATCAAGGGC
H3_WT           ACTTATGACCACAATGTGTACAGGGATGAAGCATTGAACAACCGGTTCCAGATCAAGGGA
                ***** ***** ** ** *** **********  ******** * **************

MRT10279        GTGGAGCTGAAGTCCGGCTACAAAGATTGGATCCTGTGGATTTCCTTCGCGATTTCATGC
H3_WT           GTTGAGCTGAAGTCAGGATACAAAGATTGGATCCTATGGATTTCCTTTGCCATATCATGT
                ** *********** ** ***************** *********** ** ** *****

MRT10279        TTCTTGCTCTGCGTGGCCCTCCTGGGATTCATAATGTGGGCCTGTCAGAAGGGCAACATT
H3_WT           TTTTTGCTTTGTGTTGCTTTGTTGGGGTTCATCATGTGGGCCTGCCAAAAGGGCAACATT
                ** ***** ** ** **  *  **** ***** *********** ** ************

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

FIG. 5A (Cont.)


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

FIG. 5B

5′UTR

GGACAGAUCGCCUGGAGACGCCAUCCACGCUGUUUUGACCUCCAUAGAAGACACCGGGACCGAUCCAGCCUCCGCGGCCGGGAACGGUGCAUUGGAACGCGGAUUCCCCGUGCCAA
GAGUGACUCACCGUCCUUGACACG

CDS (coding Sequence)

AUGAAAACCAUAAUCGCGCUCUCAUACAUACUUUGCCUGGUCUUUGCCCAAAAGAUCCCUGGCAACGACAACUCAACCGCGACCCUUUGCCUCGGCCAUCACGCCGUGCCGAACGG
CACUAUCGUCAAGACCAUCACAAACGACCGCAUCGAAGUGACCAACGCGACUGAGCUAGUGCAGAACUCCAGCAUUGGAGAGAUUUGCGAUUCUCCACACCAAAUCCUGGACGGAG
AGAAUUGUACCUUGAUCGACGCGCUGCUGGGGGAUCCGCAGUGCGACGGAUUCCAGAACAAGAAAUGGGACCUUUUCGUGGAACGGAGCAAGGCAUACUCGAAUUGCUACCCCUAC
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CAUUCGGGGCUCCUCCUCGAGCUUCUUCAGCCGCCUGAACUGGCUCACUCACCUCAACUACACCUACCCGGCACUGAACGUGACCAUGCCGAACAAGGAACAAUUCGACAAGCUCU
ACAUUUGGGGGGUGCAUCACCCGGGUACCGAUAAGGACCAGAUCUUCCUCUACGCCCAAUCCUCGGGCCGGAUCACCGUGUCCACUAAGCGCUCGCAGCAGGCCGUGAUCCCGAAC
AUUGGAAGCAGACCCCGCAUUCGCGACAUUCCAUCGAGGAUCUCGAUCUACUGGACGAUUGUCAAGCCUGGCGACAUCCUCCUCAUUAACUCCACCGGGAACCUCAUCGCCCCUCG
GGGUUAUUUCAAGAUCCGCAGCGGGAAGUCCUCCAUCAUGAGAAGCGAUGCCCCCAUUGGAAAGUGCAAGUCCGAGUGUAUCACACCUAACGGAAGCAUUCCCAAUGACAAGCCAU
UCCAGAACGUGAACAGAAUUACCUACGGAGCUUGCCCUCGCUACGUCAAACAUUCGACCCUCAAGUUGGCGACUGGAAUGCGCAACGUGCCGGAGAAGCAAACCCGGGGGAUCUUC
GGGGCUAUCGCGGGAUUCAUCGAAAAUGGAUGGGAAGGAAUGGUCGAUGGUUGGUACGGUUUCAGACACCAGAACUCCGAGGGGCGGGGCCAGGCCGCAGACCUGAAGUCCACUCA
GGCCGCGAUUGACCAGAUCAACGGAAAGCUCAACAGACUCAUUGGAAAGACCAACGAAAAGUUCCACCAAAUCGAAAAGGAAUUCUCCGAAGUGGAGGGCCGGGUGCAAGACCUGG
AGAAGUACGUGGAGGACACUAAGAUCGACCUUUGGAGCUAUAACGCAGAACUCCUUGUGGCCCUGGAAAACCAGCACACCAUCGACCUGACCGAUUCAGAGAUGAACAAGCUCUUU
GAGAAAACUAAGAAGCAACUCCGGGAAAACGCUGAGGACAUGGGAAAUGGAUGCUUUAAGAUCUACCACAAGUGCGACAACGCCUGCAUUGAGUCCAUACGGAACGAAACUUACGA
CCAUAACGUCUACCGGGAUGAAGCCCUGAACAACAGAUUCCAGAUCAAGGGCGUGGAGCUGAAGUCCGGCUACAAAGAUUGGAUCCUGUGGAUUUCCUUCGCGAUUUCAUGCUUCU
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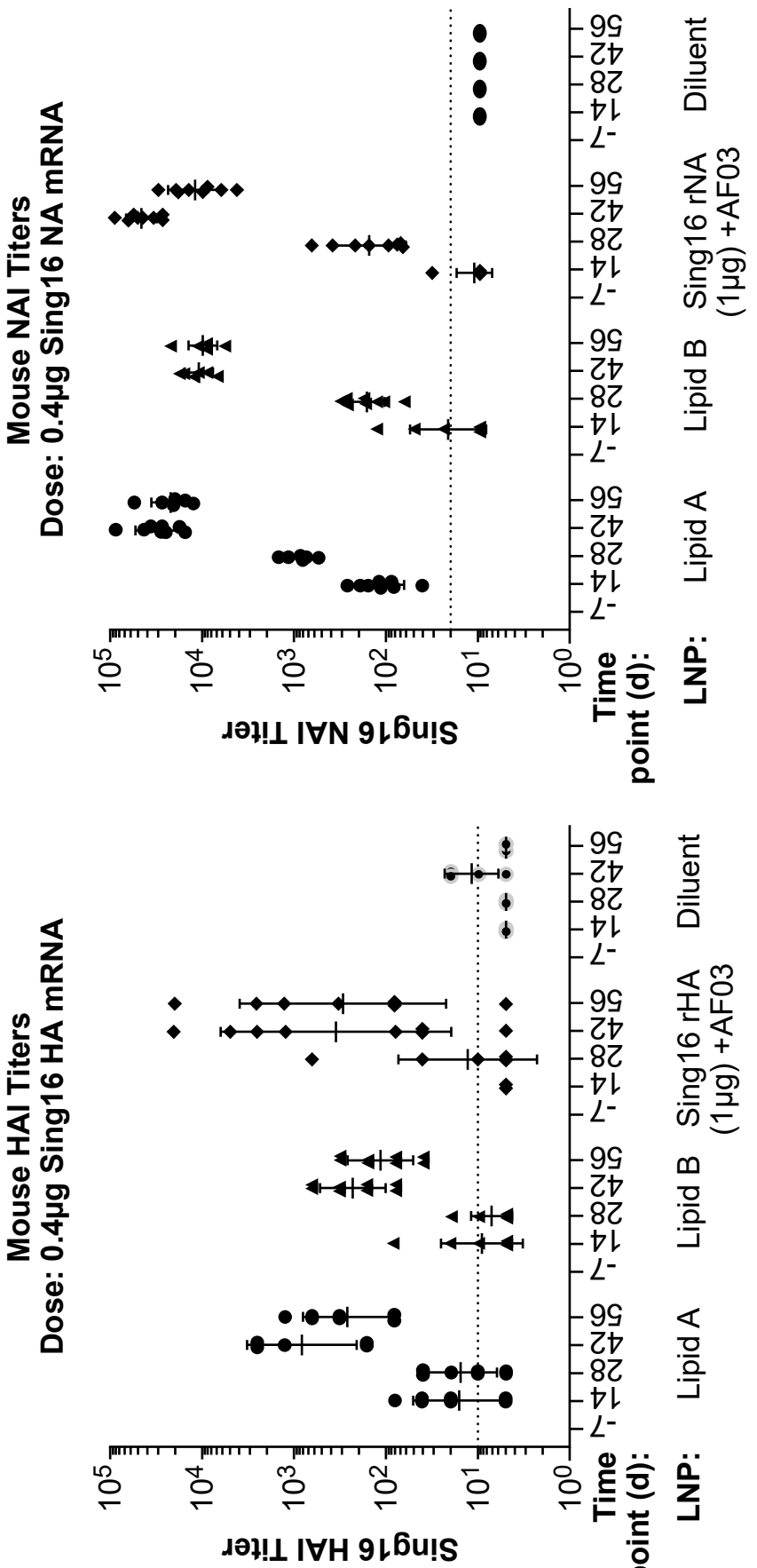
3′UTR

CGGGUGGCAUCCCUGUGACCCCUCCCCAGUGCCUCUCCUGGCCCUGGAAGUUGCCACUCCAGUGCCCACCAGCCUUGUCCUAAUAAAAUUAAGUUGCAUC

+ Poly A Tail

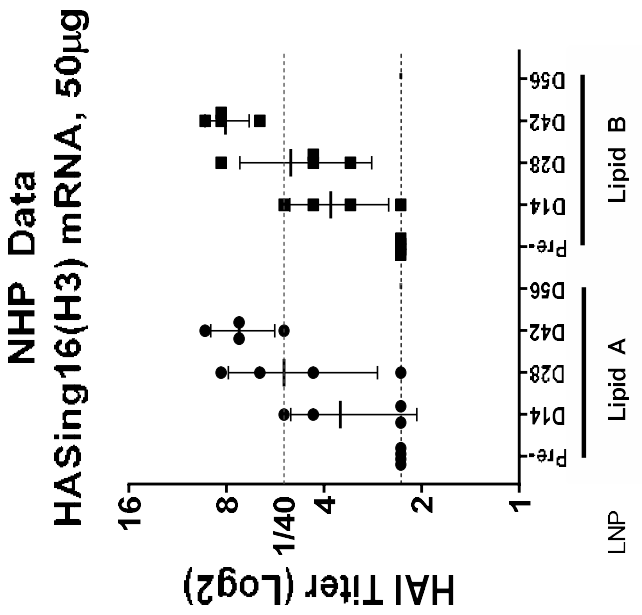
(SEQ ID NO:4)

FIG. 5C



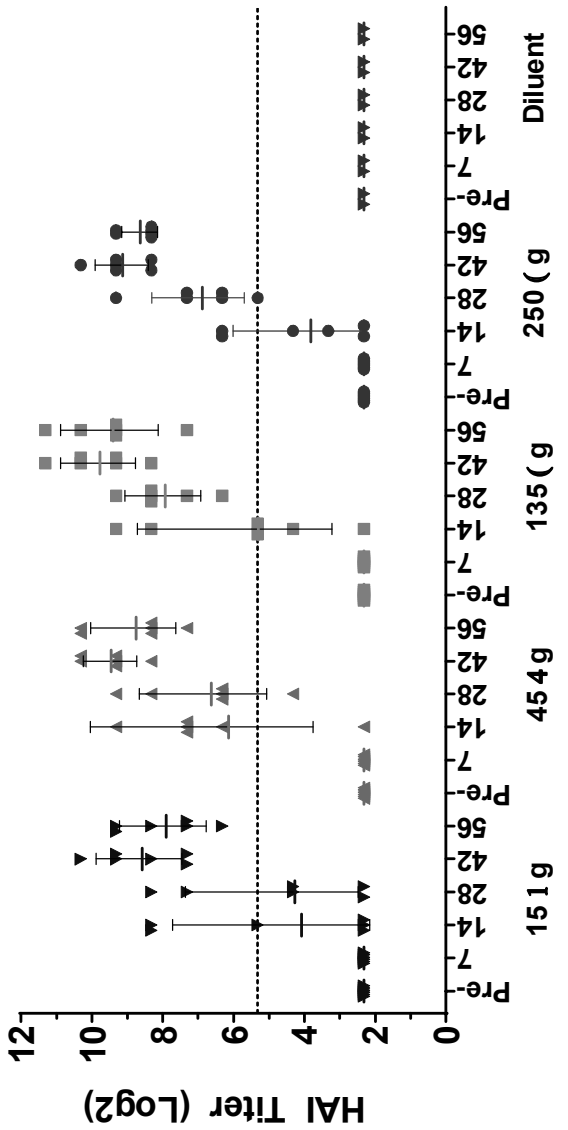
Lipid	Composition (Molar Ratio)
Lipid A	Cationic lipid: DMG-PEG2000: Cholesterol: DOPE 40:1.5:28.5:30
Lipid B	Cationic lipid: DMG-PEG2000: Cholesterol: DOPE 40:1.5:28.5:30

FIG. 6



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

FIG. 7A



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

FIG. 7B

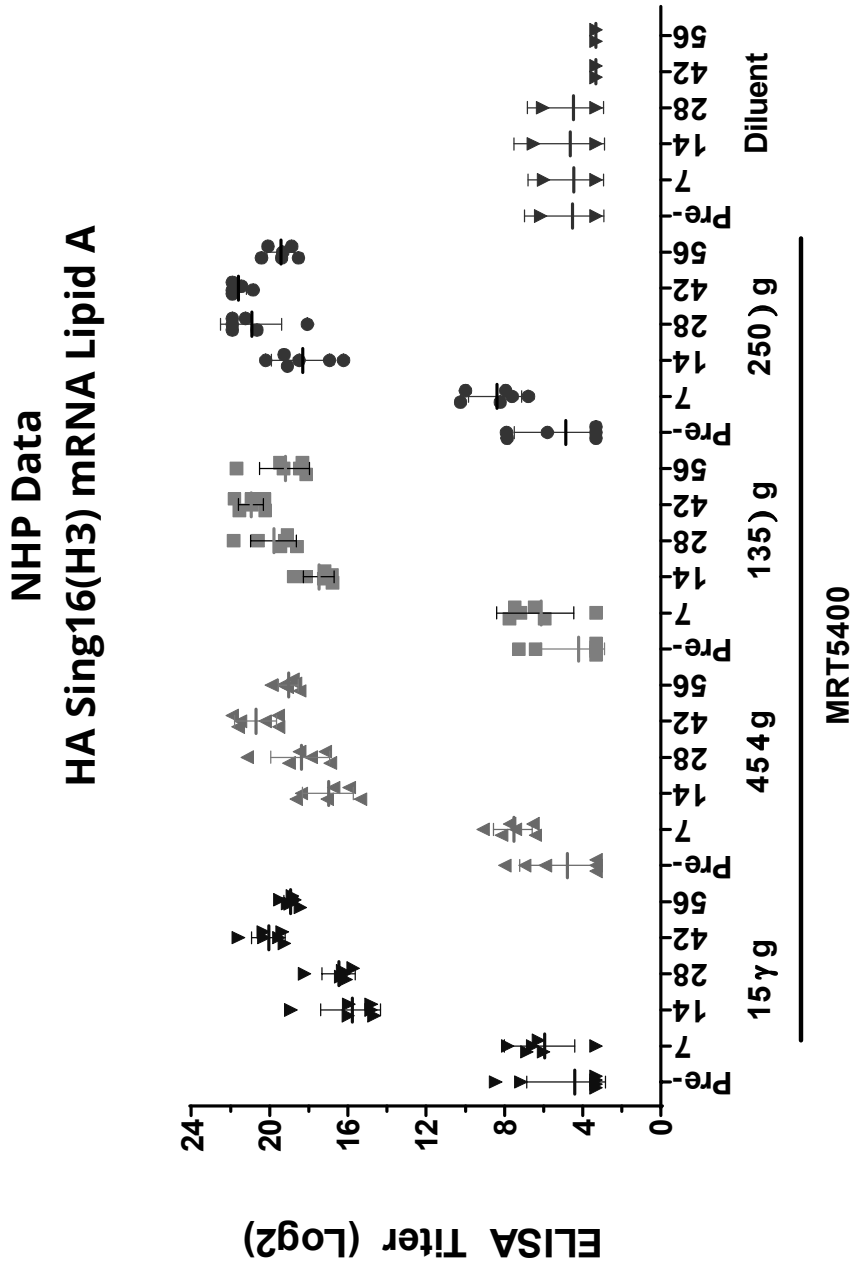
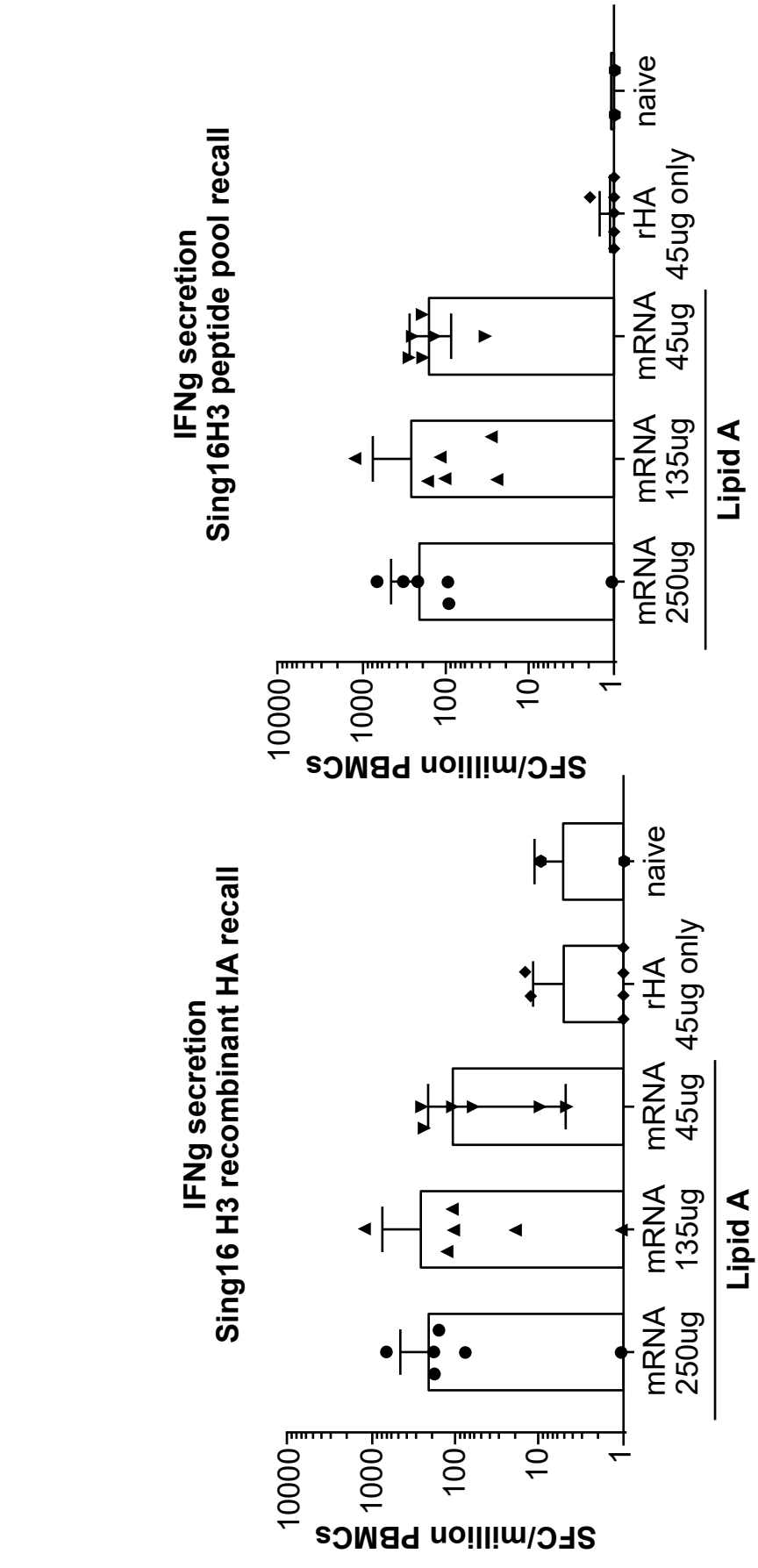
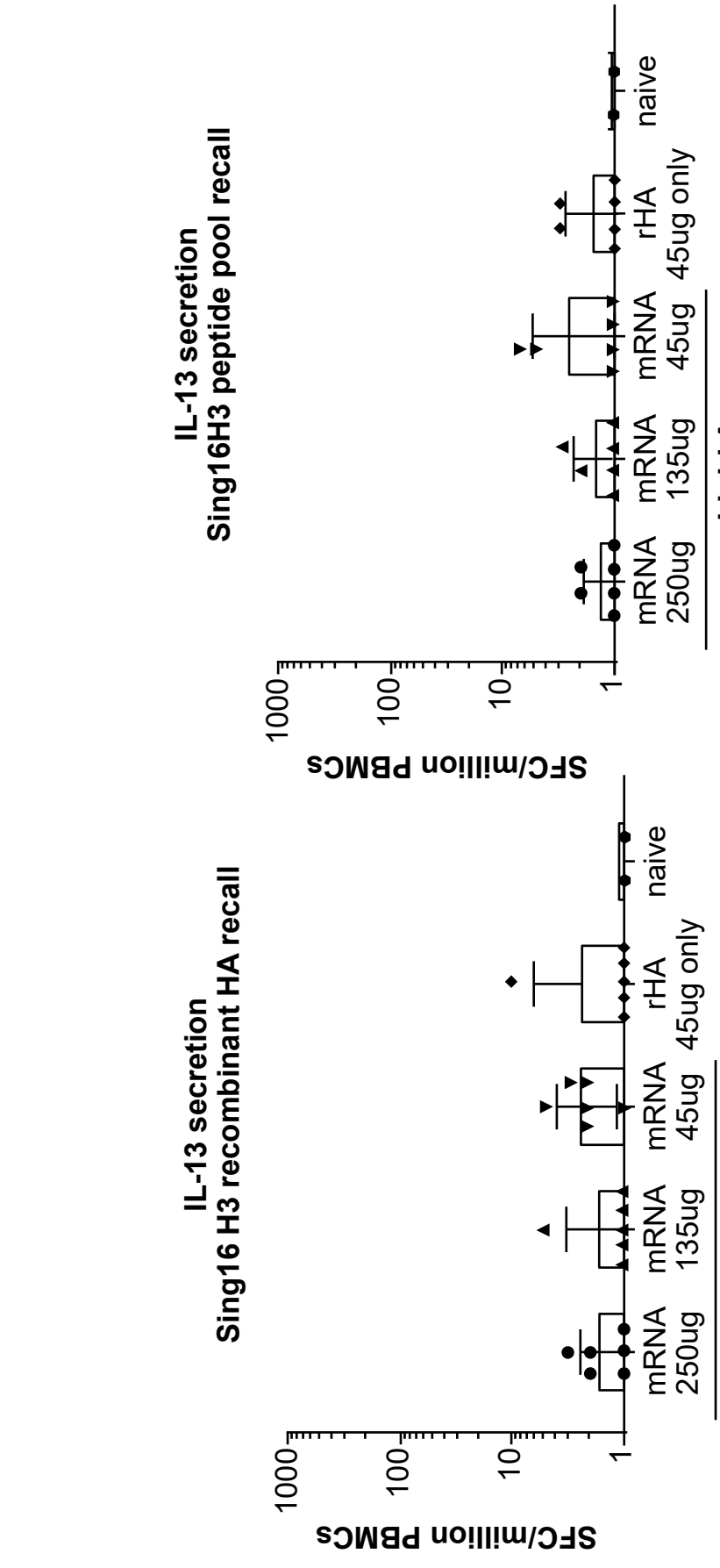

NHP Data
HA Sing16(H3) mRNA Lipid A
ELISA Titer (Log2)
0
4
8
12
16
20
24
Pre-
7
14
28
42
56
15γ g
45 4 g
135) g
250) g
Diluent
MRT5400

FIG. 7C



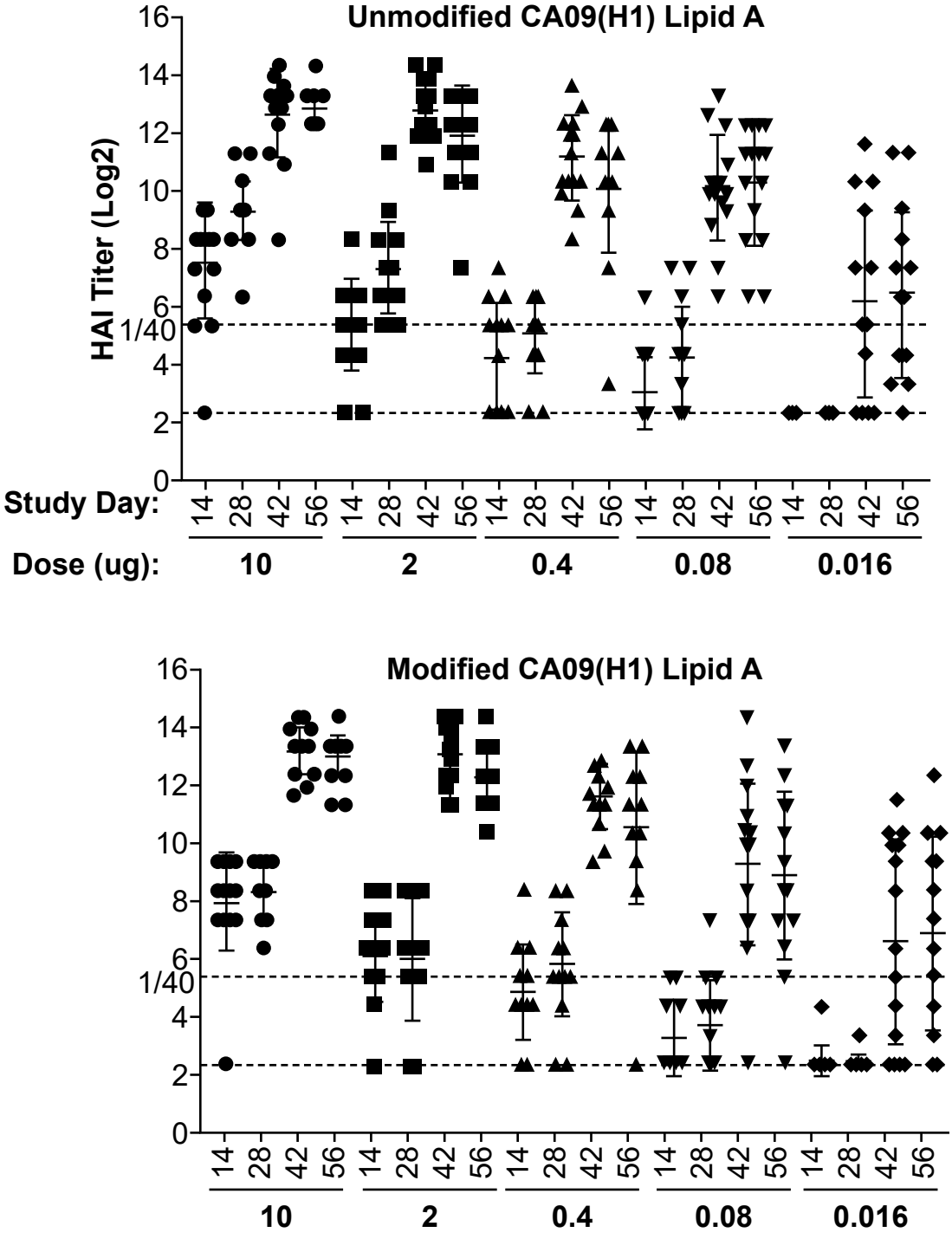
Lipid	Composition (Molar Ratio)
Lipid A	Cationic lipid: DMG-PEG2000: Cholesterol: DOPE 40:1.5:28.5:30

FIG. 8A



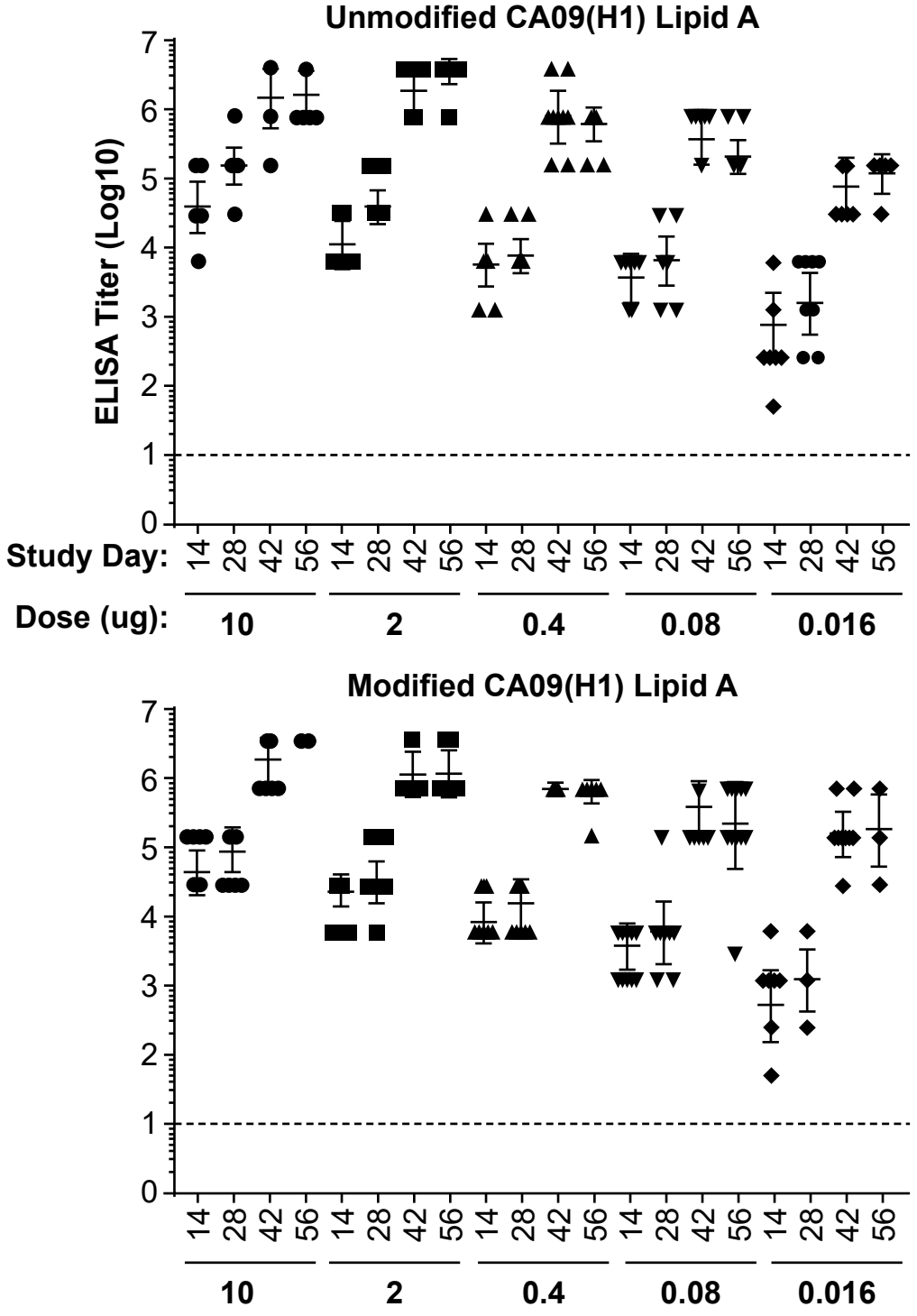
Lipid	Composition (Molar Ratio)
Lipid A	Cationic lipid: DMG-PEG2000: Cholesterol: DOPE 40:1.5:28.5:30

FIG. 8B



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

FIG. 9A



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

FIG. 9B

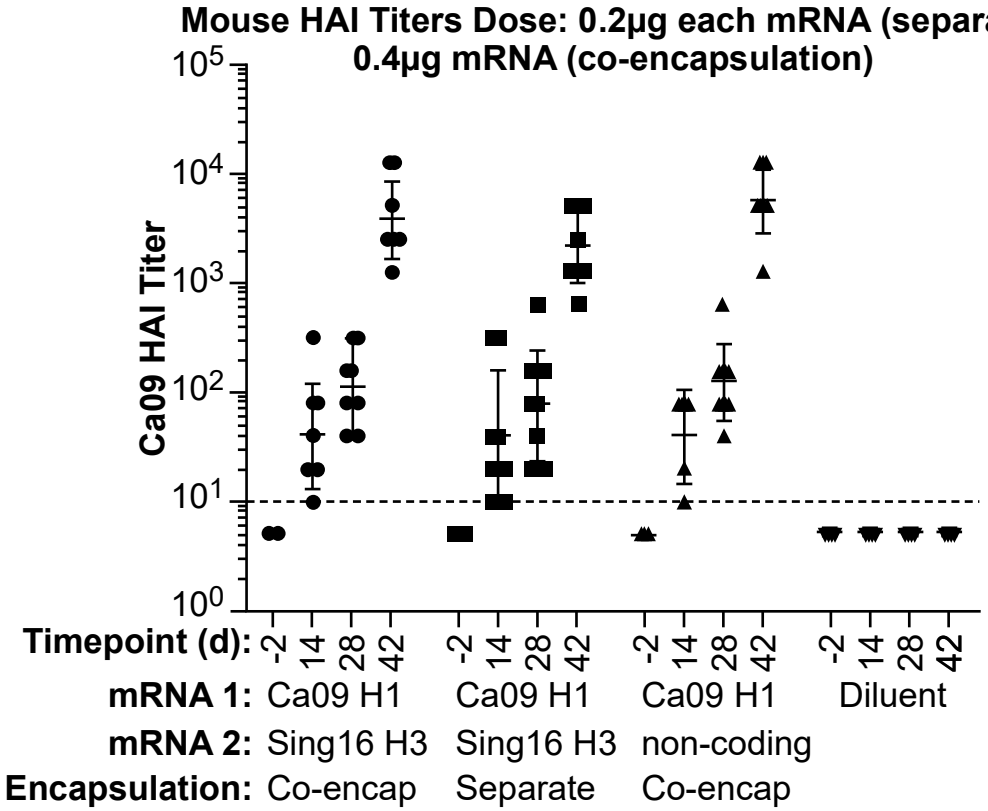


FIG. 10A

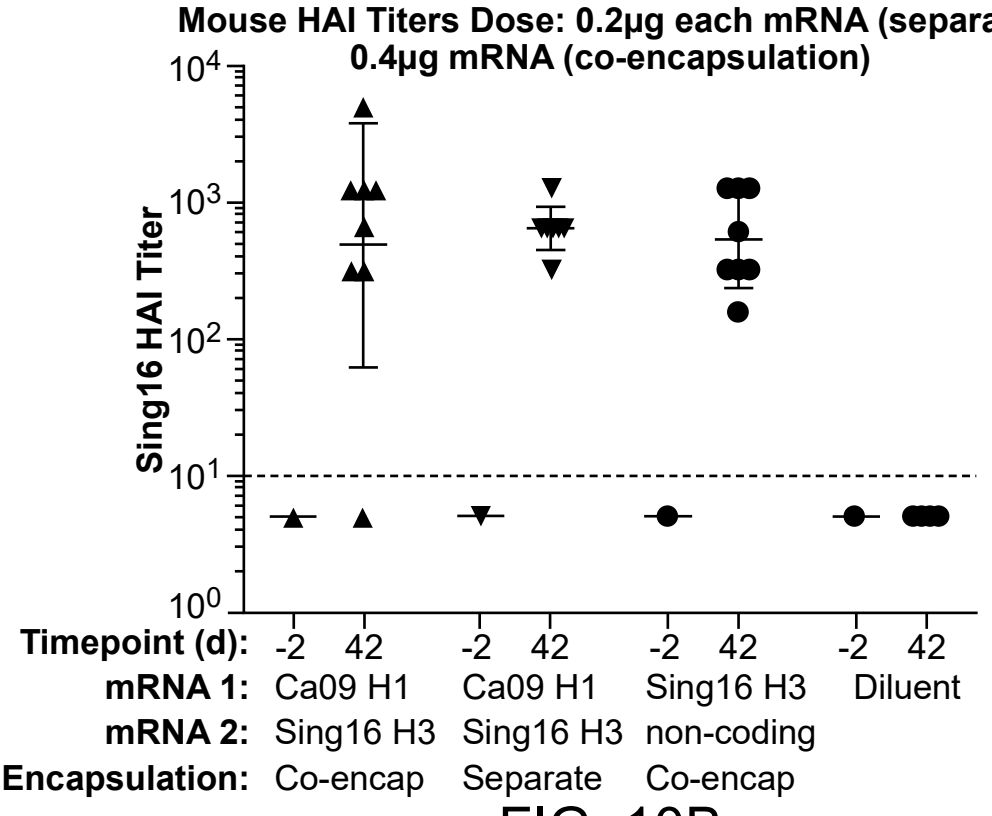


FIG. 10B

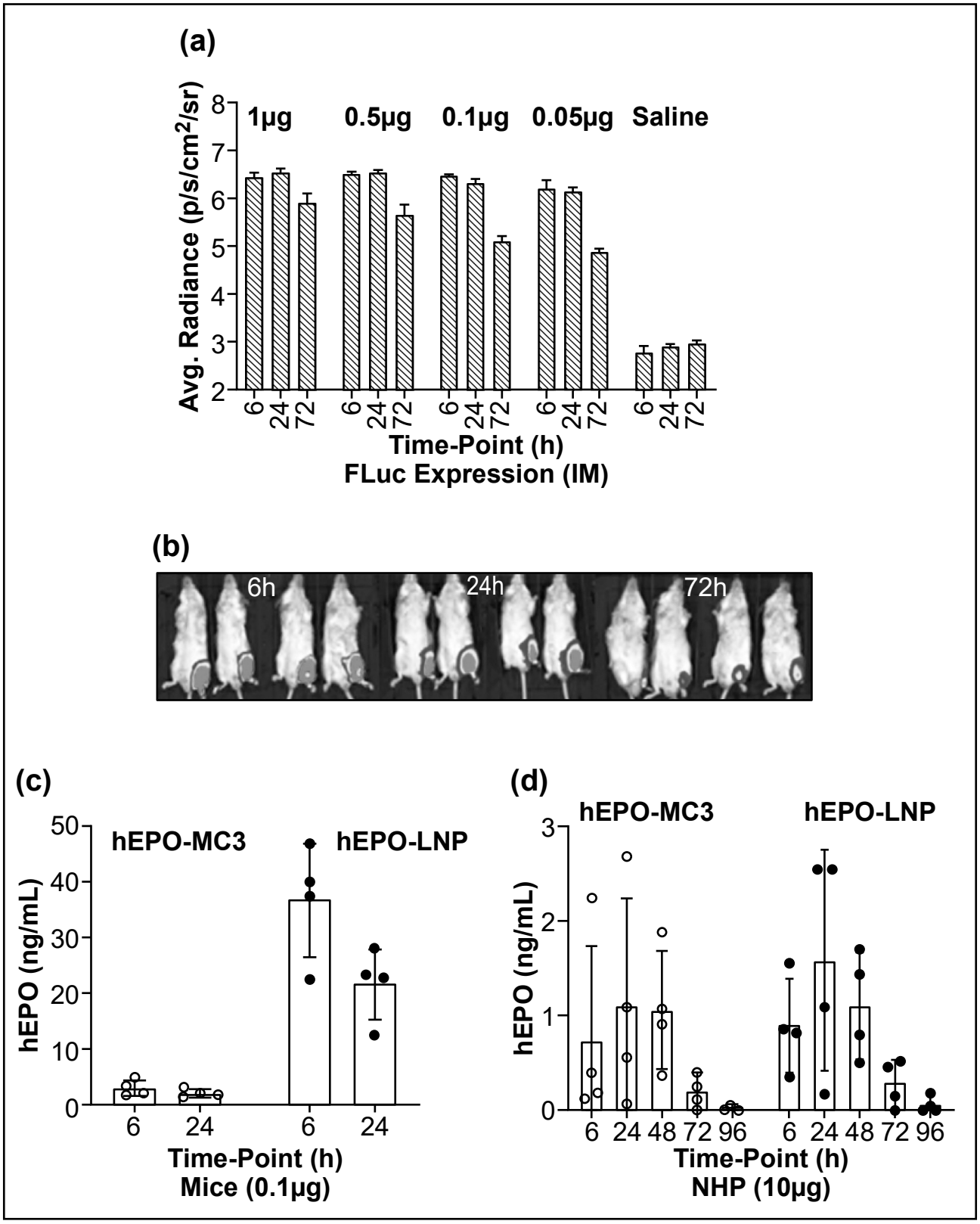
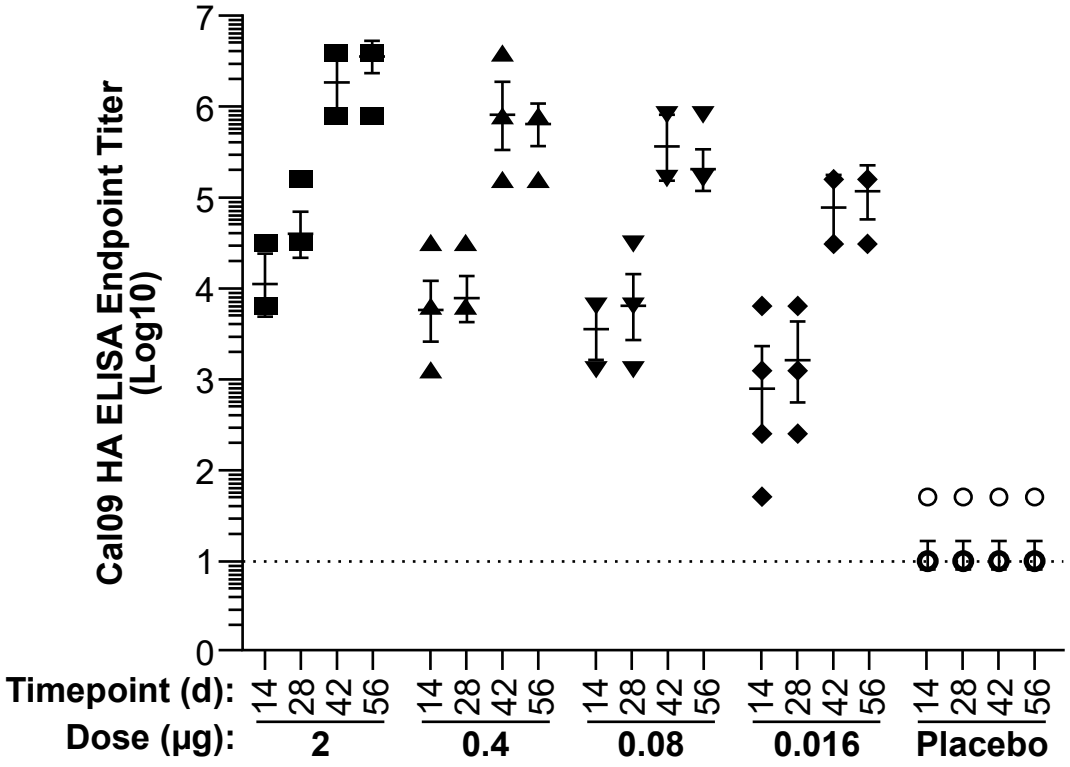

(a)
1µg
0.5µg
0.1µg
0.05µg
Saline
Avg. Radiance (p/s/cm²/sr)
Time-Point (h)
FLuc Expression (IM)
(b)
6h
24h
72h
(c)
hEPO-MC3
hEPO-LNP
hEPO (ng/mL)
Time-Point (h)
Mice (0.1µg)
(d)
hEPO-MC3
hEPO-LNP
hEPO (ng/mL)
Time-Point (h)
NHP (10µg)

FIG. 11


Cal09 HA ELISA Endpoint Titer (Log10)
0
1
2
3
4
5
6
7
Timepoint (d):
14
28
42
56
Dose (µg):
2
0.4
0.08
0.016
Placebo

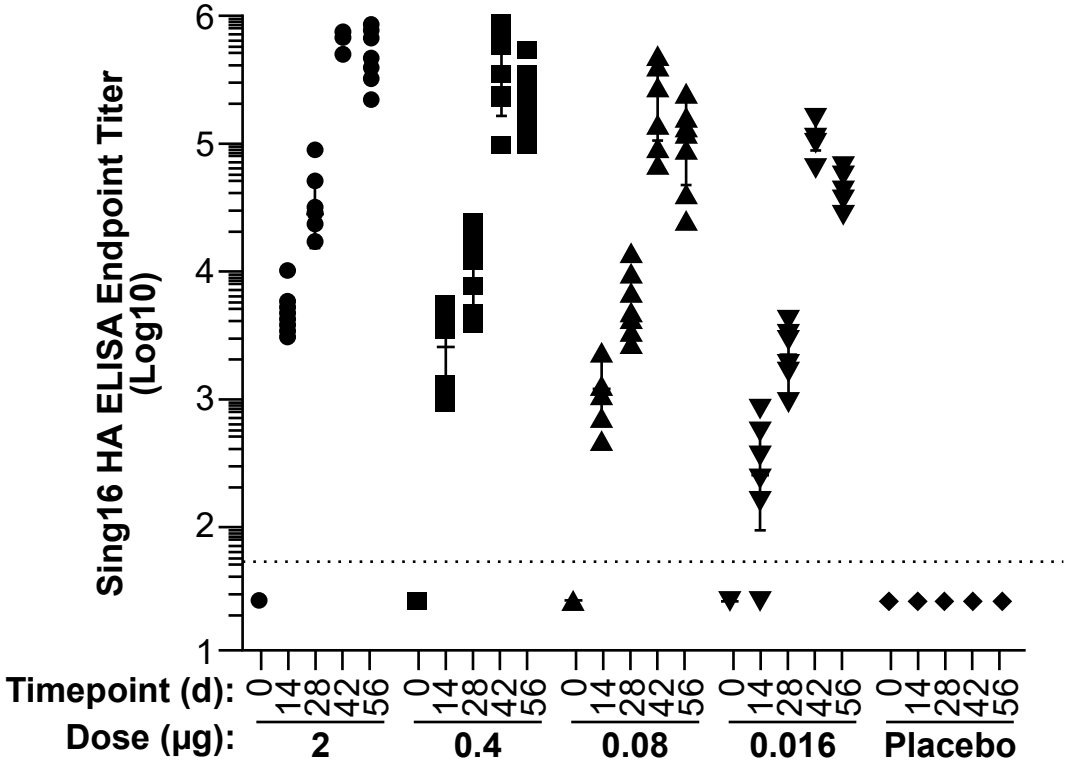

Sing16 HA ELISA Endpoint Titer (Log10)
1
2
3
4
5
6
Timepoint (d):
0
14
28
42
56
Dose (µg):
2
0.4
0.08
0.016
Placebo

FIG. 12

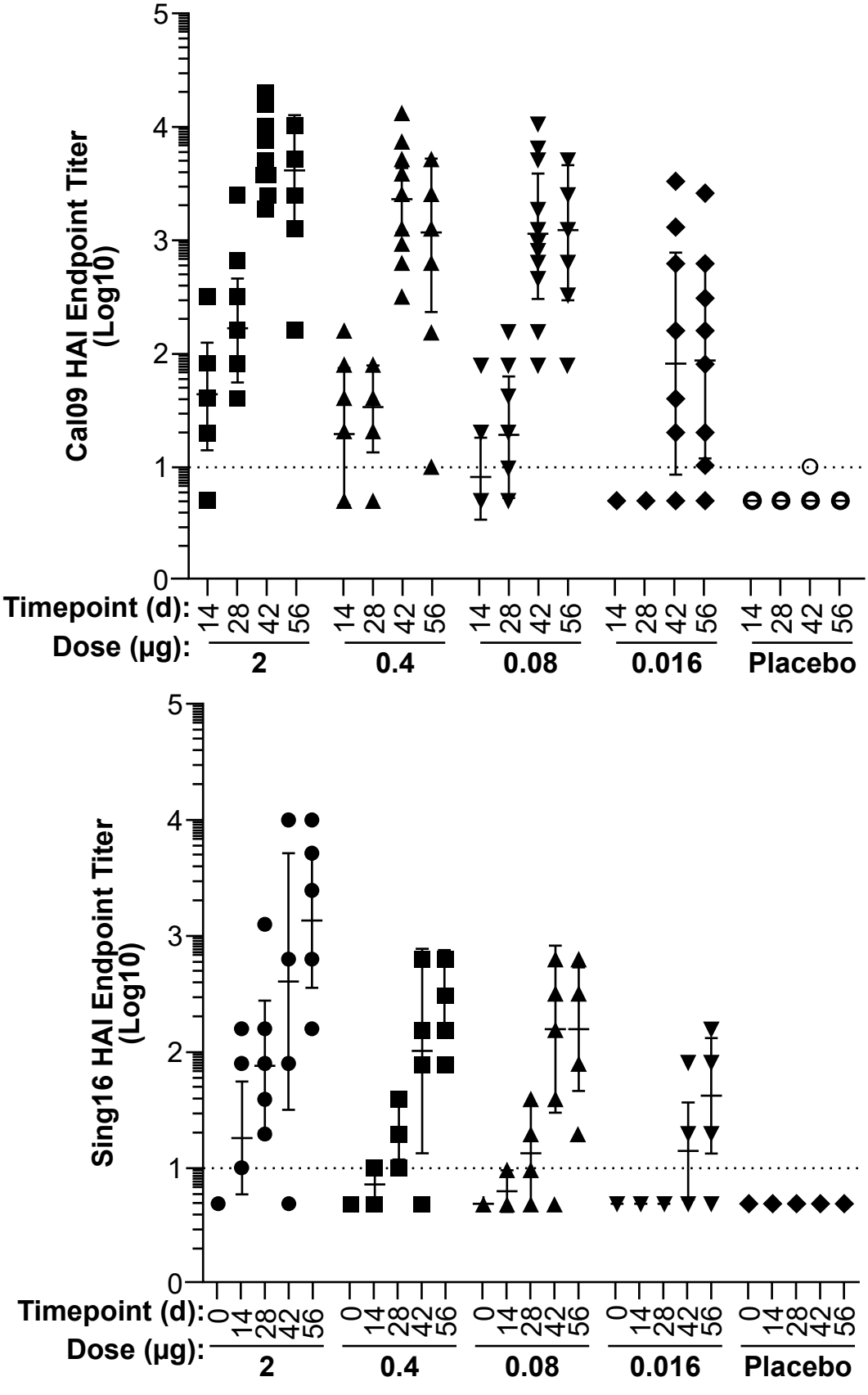

Cal09 HAI Endpoint Titer (Log10)
Timepoint (d):
Dose (µg):
2
0.4
0.08
0.016
Placebo
Sing16 HAI Endpoint Titer (Log10)
Timepoint (d):
Dose (µg):
2
0.4
0.08
0.016
Placebo

FIG. 13

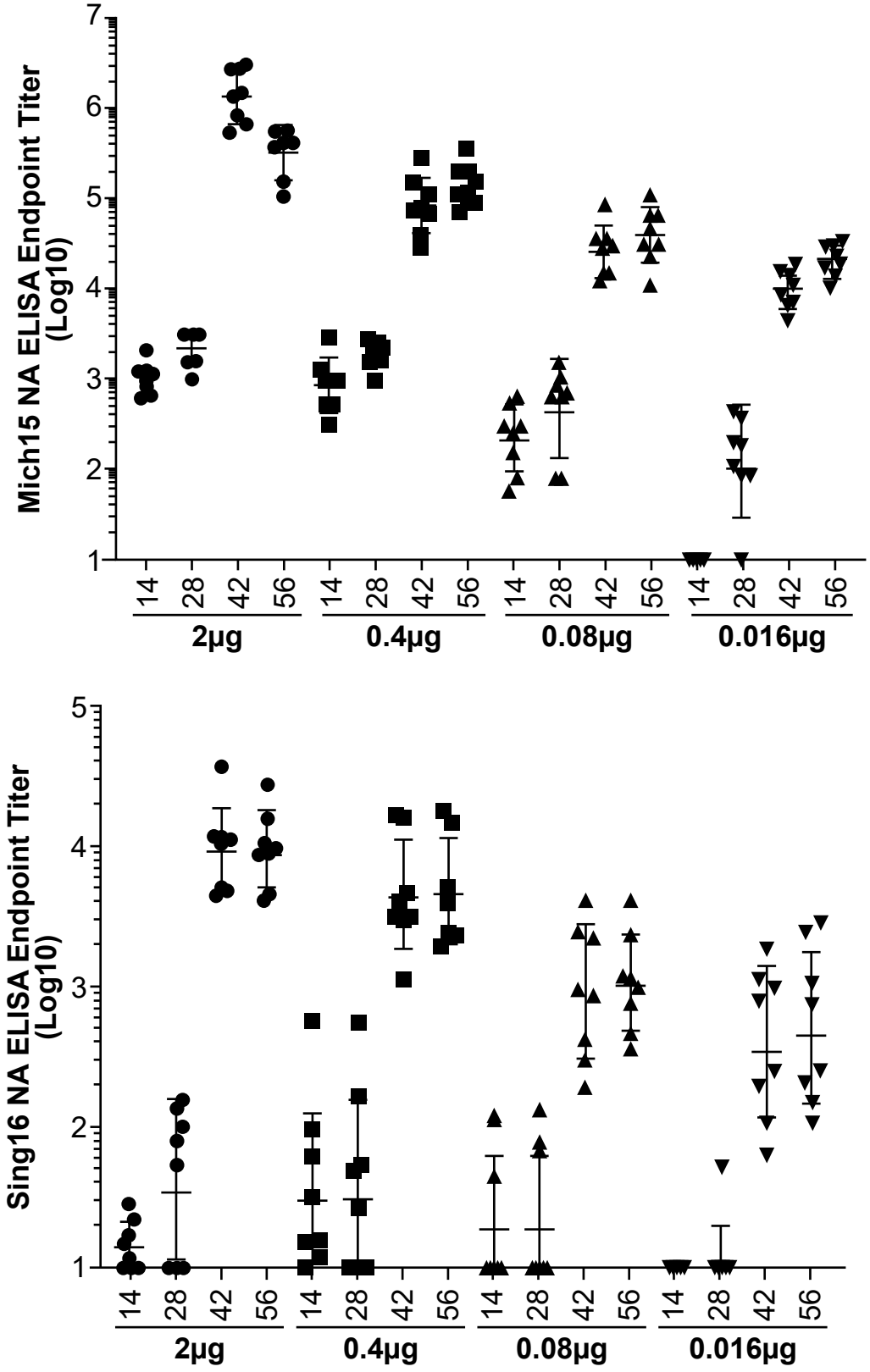

Mich15 NA ELISA Endpoint Titer (Log10)
7
6
5
4
3
2
1
14
28
42
56
2μg
0.4μg
0.08μg
0.016μg
Sing16 NA ELISA Endpoint Titer (Log10)
5
4
3
2
1
14
28
42
56
2μg
0.4μg
0.08μg
0.016μg

FIG. 14

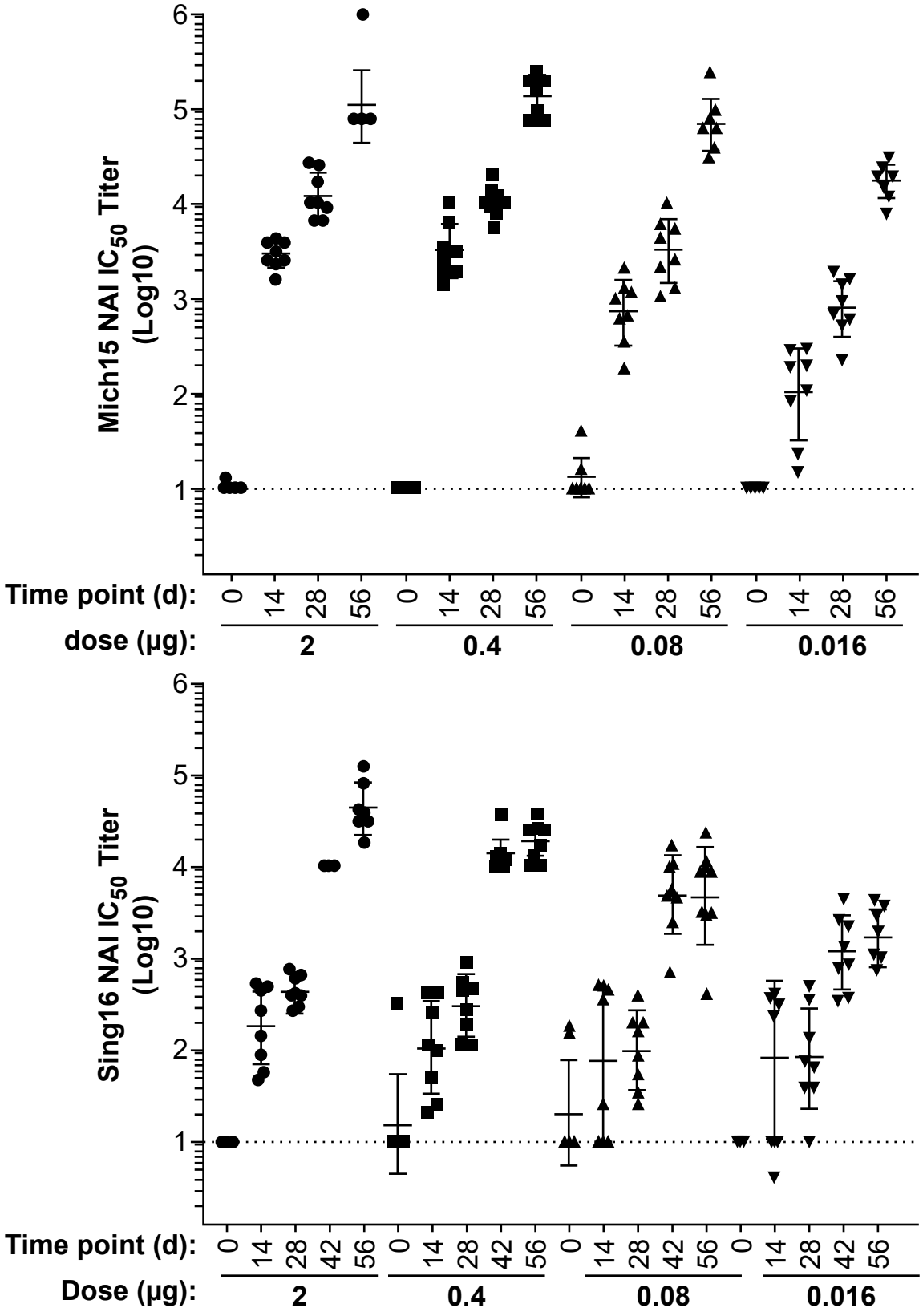

Mich15 NAI IC50 Titer (Log10)
6
5
4
3
2
1
Time point (d):
0
14
28
56
dose (µg):
2
0.4
0.08
0.016
Sing16 NAI IC50 Titer (Log10)
6
5
4
3
2
1
Time point (d):
0
14
28
42
56
Dose (µg):
2
0.4
0.08
0.016

FIG. 15

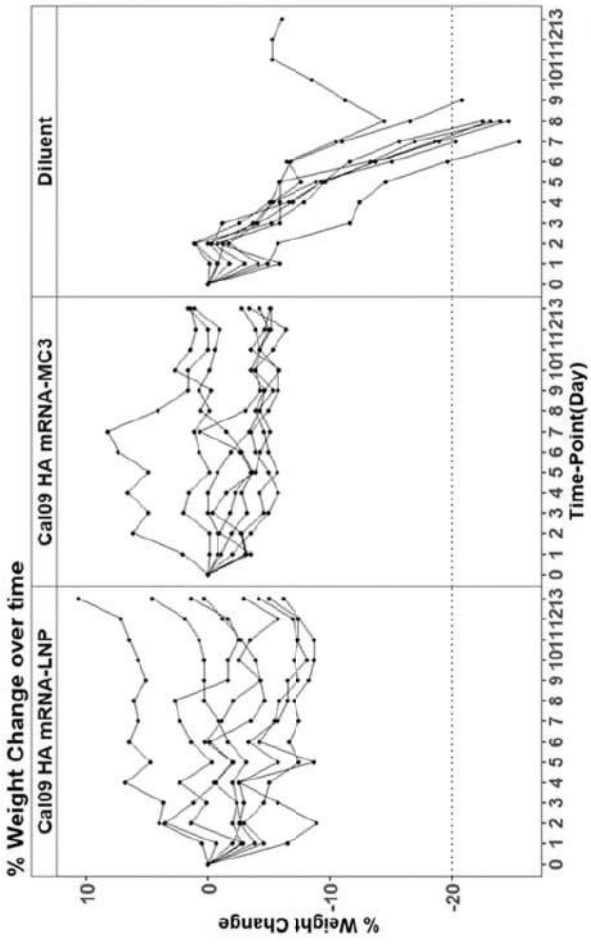


FIG. 16B

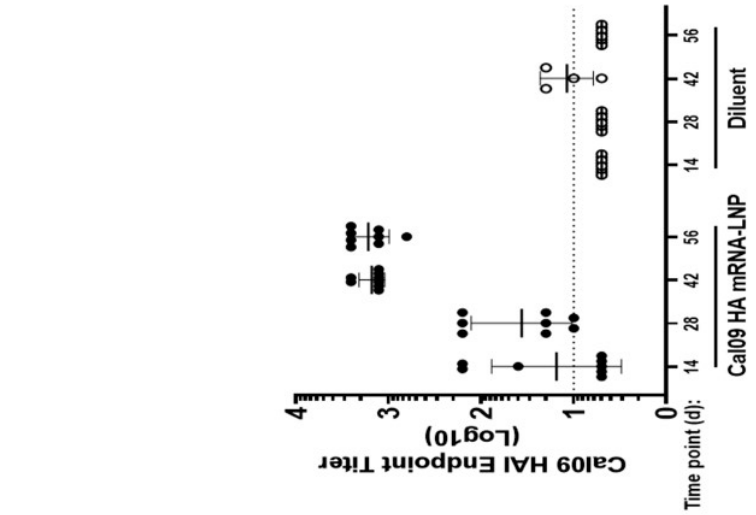


FIG. 16A

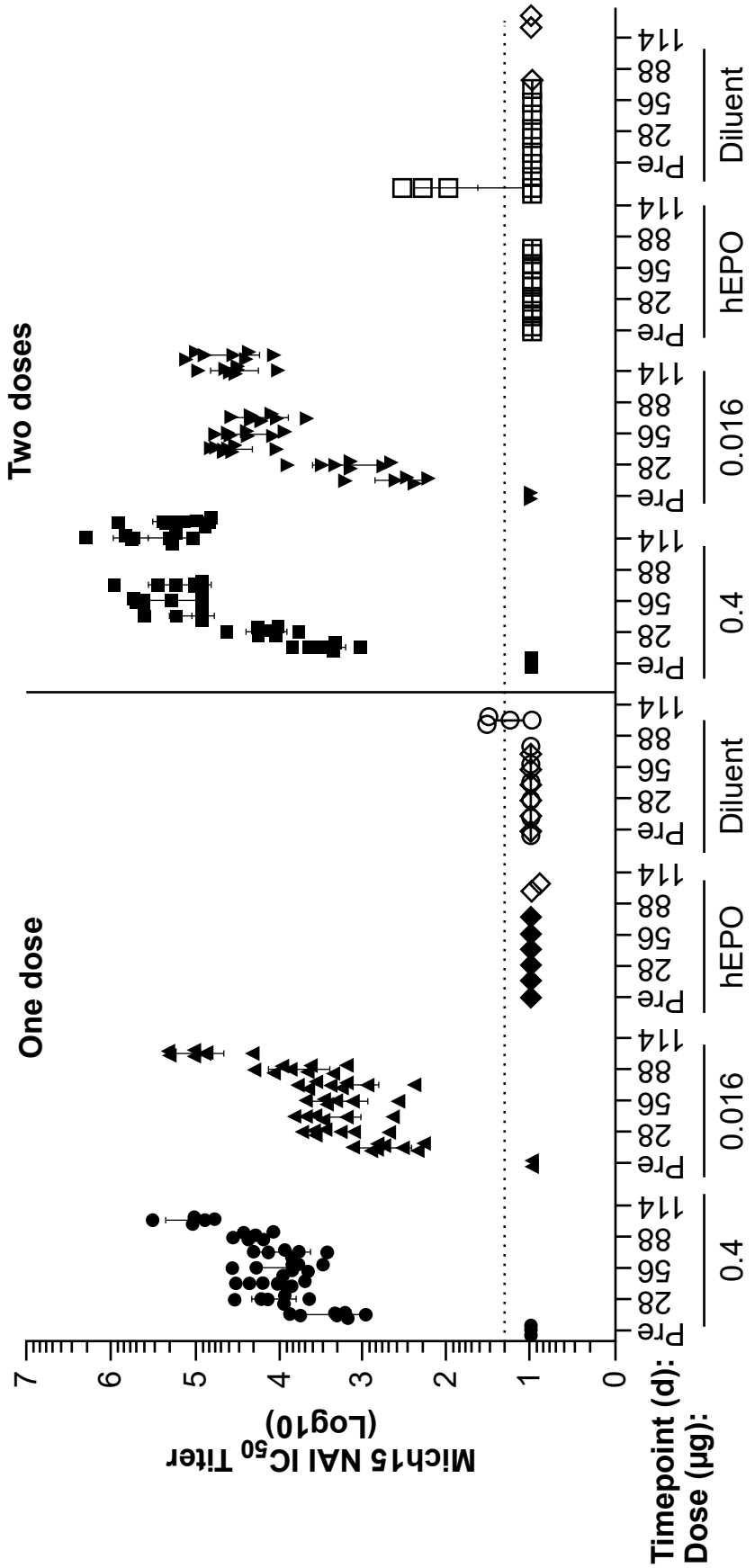

Mich15 NAI IC50 Titer
(Log10)
7
6
5
4
3
2
1
0
One dose
Two doses
Timepoint (d):
Dose (µg):
Pre
28
56
88
114
0.4
0.016
hEPO
Diluent

FIG. 17A

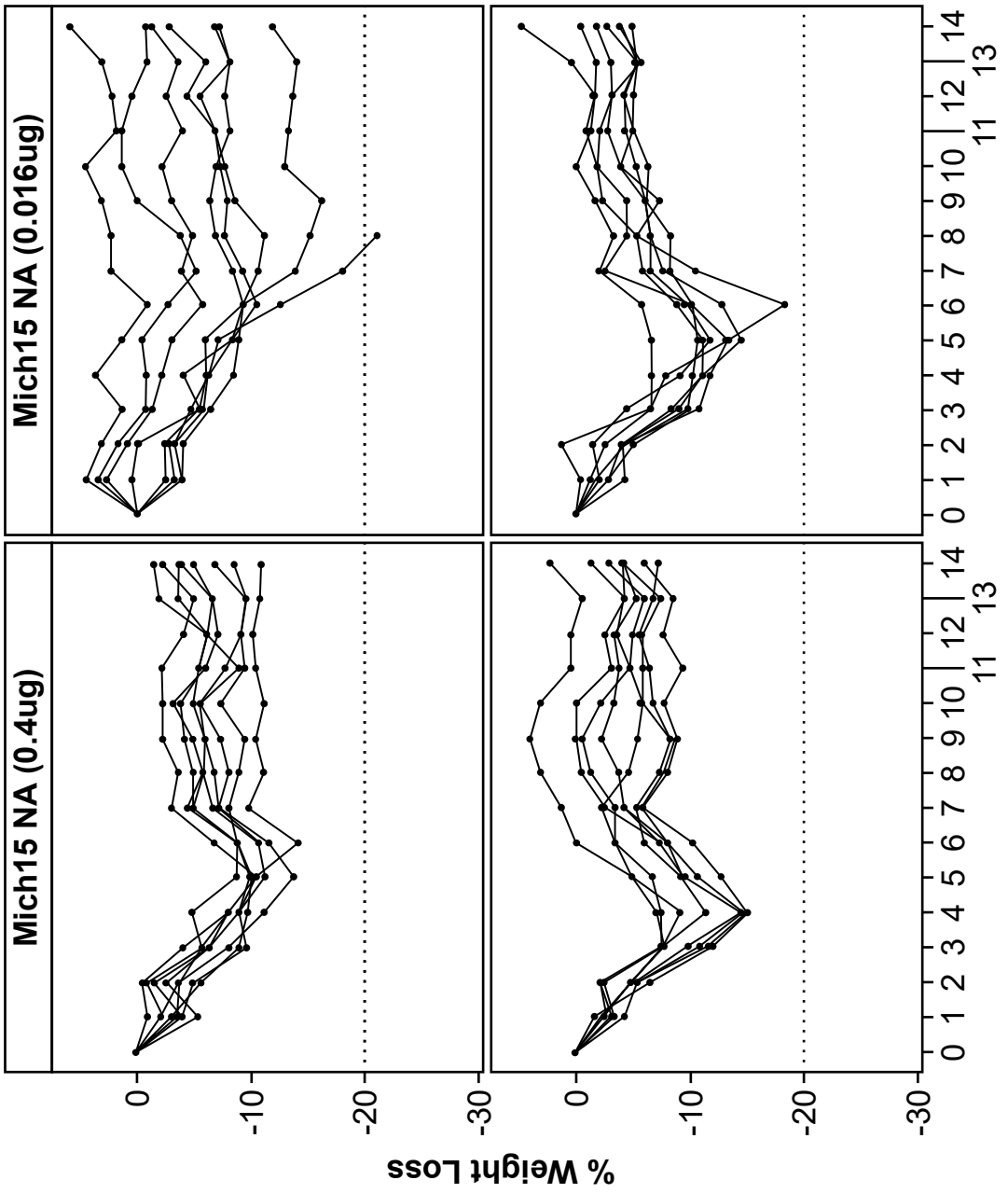

Mich15 NA (0.4ug)
Mich15 NA (0.016ug)
% Weight Loss
0
-10
-20
-30
0 1 2 3 4 5 6 7 8 9 10 11 12 13 14
Time-Point(d)

FIG. 17B

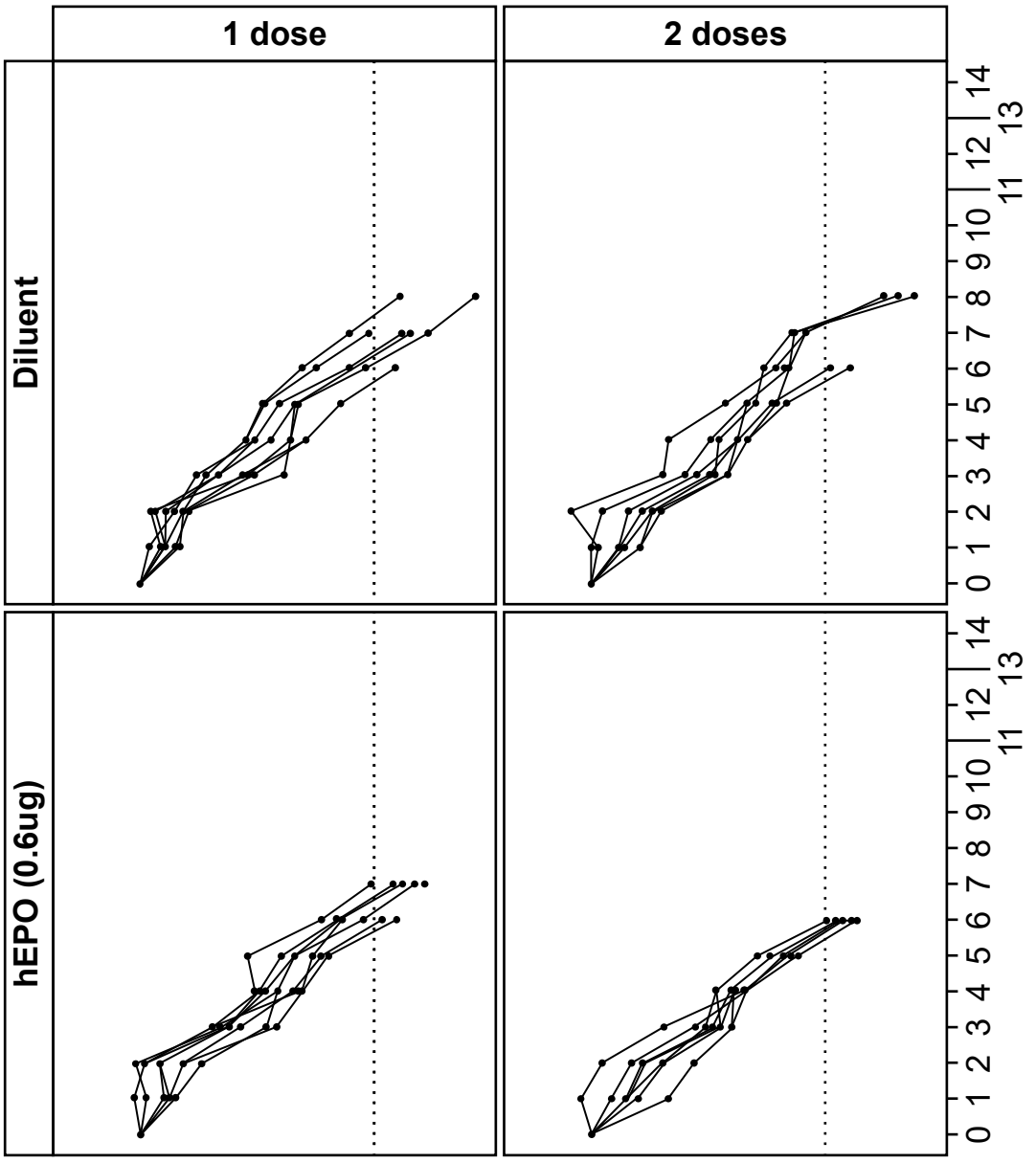


FIG. 17B (cont'd)

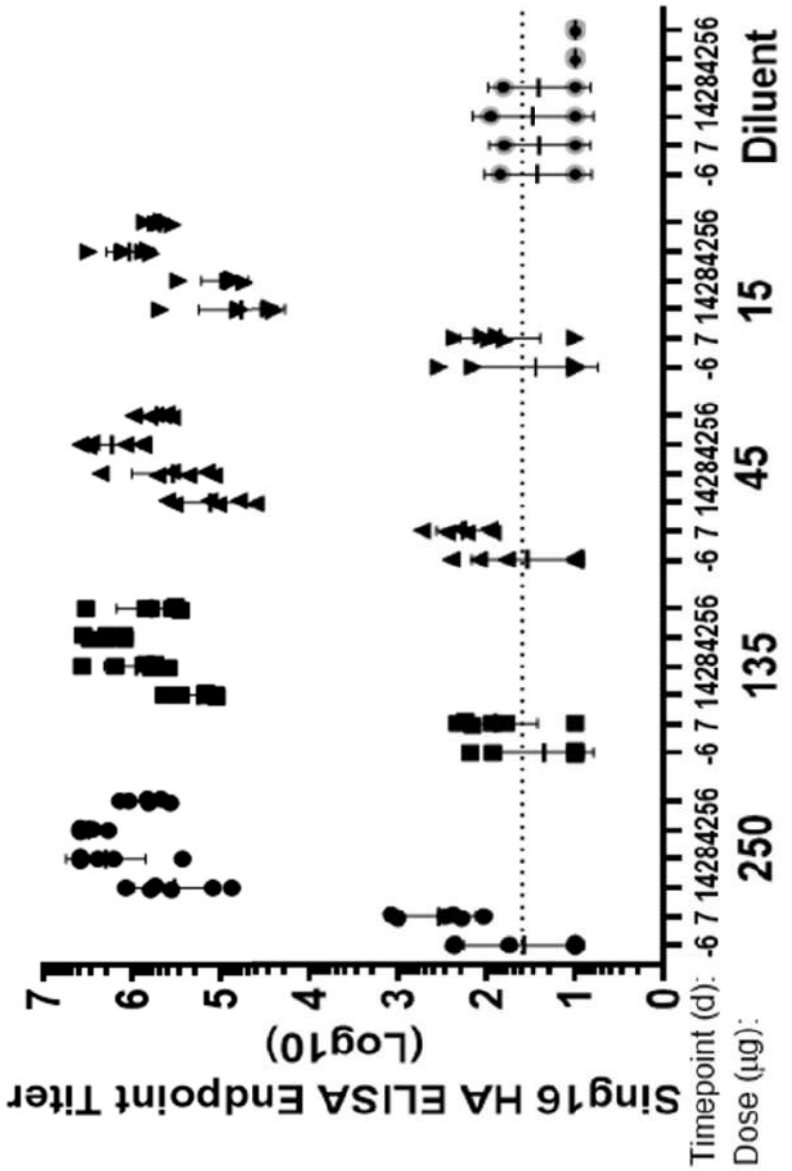

Sing16 HA ELISA Endpoint Titer
(Log10)
0
1
2
3
4
5
6
7
Timepoint (d): -6 7 14284256 -6 7 14284256 -6 7 14284256 -6 7 14284256 -6 7 14284256
Dose (µg): 250 135 45 15 Diluent

FIG. 18

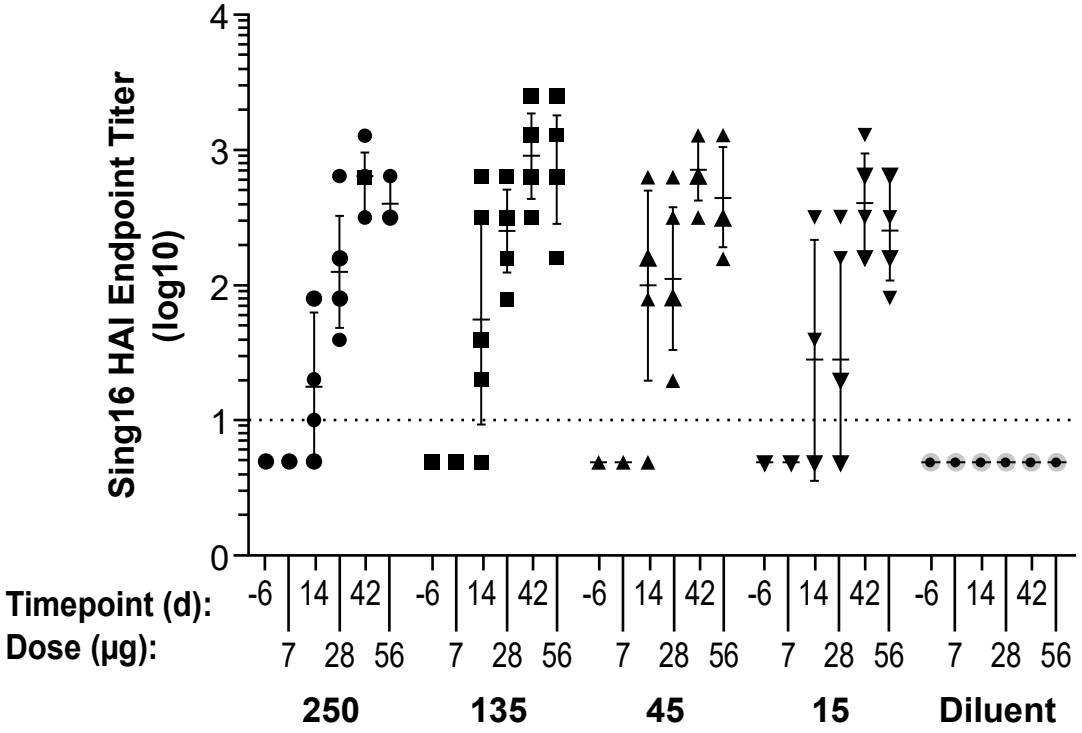


FIG. 19A

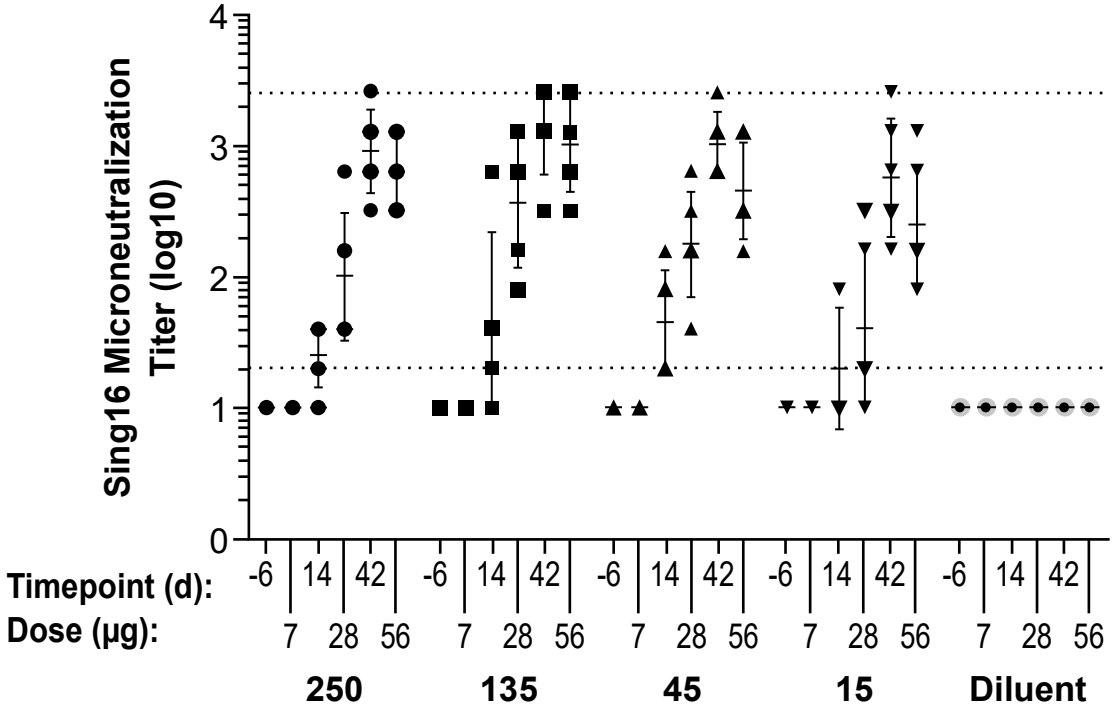


FIG. 19B

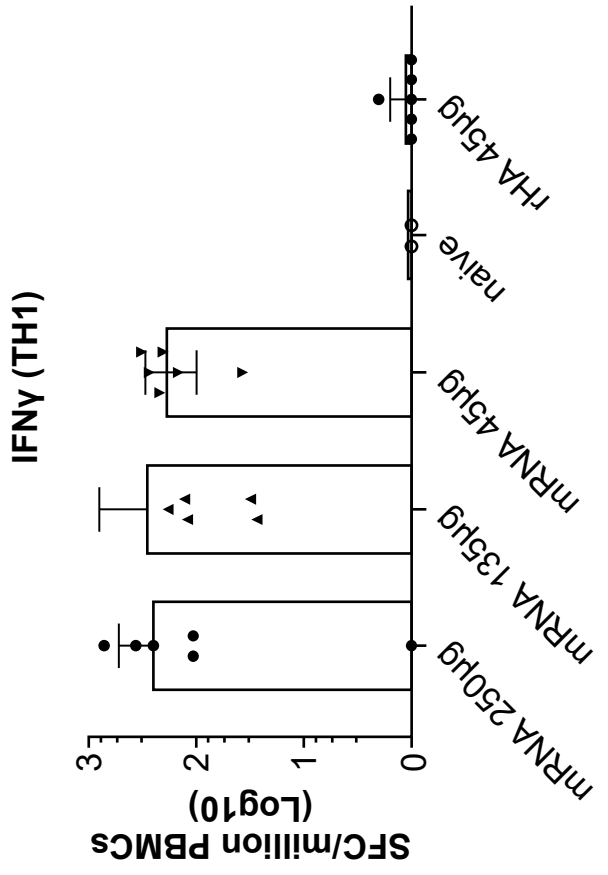


FIG. 20A

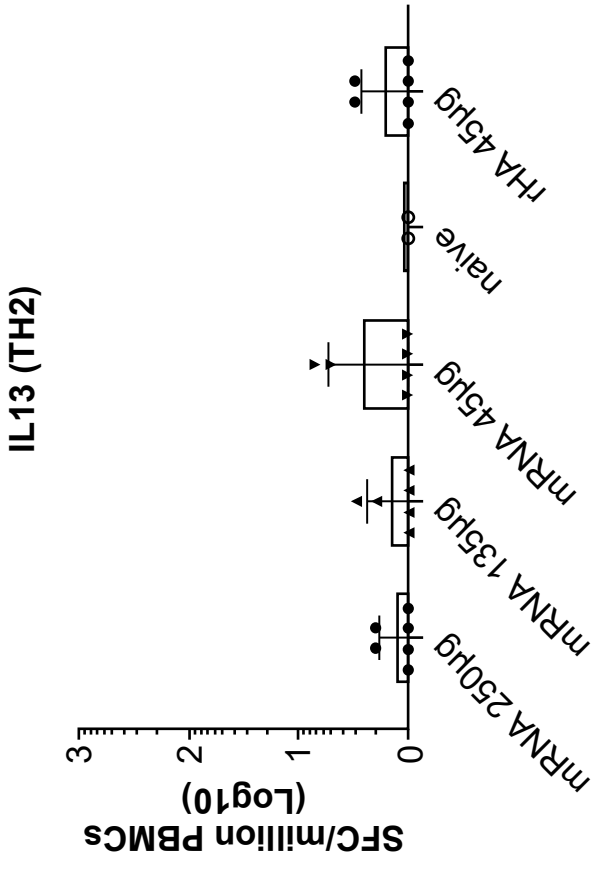


FIG. 20B

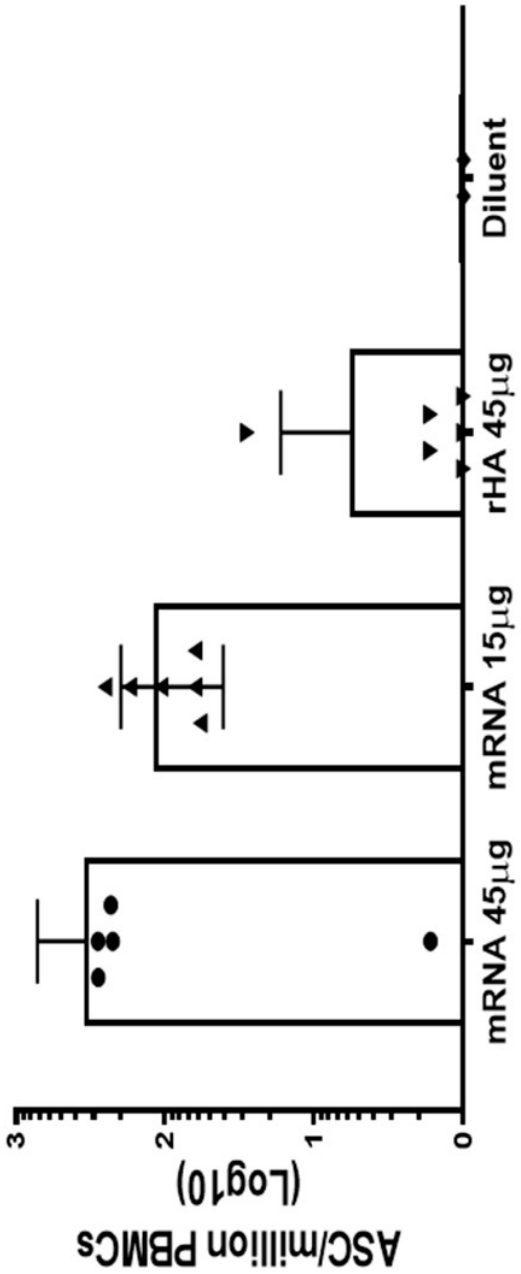

ASC/million PBMCs
(Log10)
3
2
1
0
mRNA 45μg
mRNA 15μg
rHA 45μg
Diluent

FIG. 21

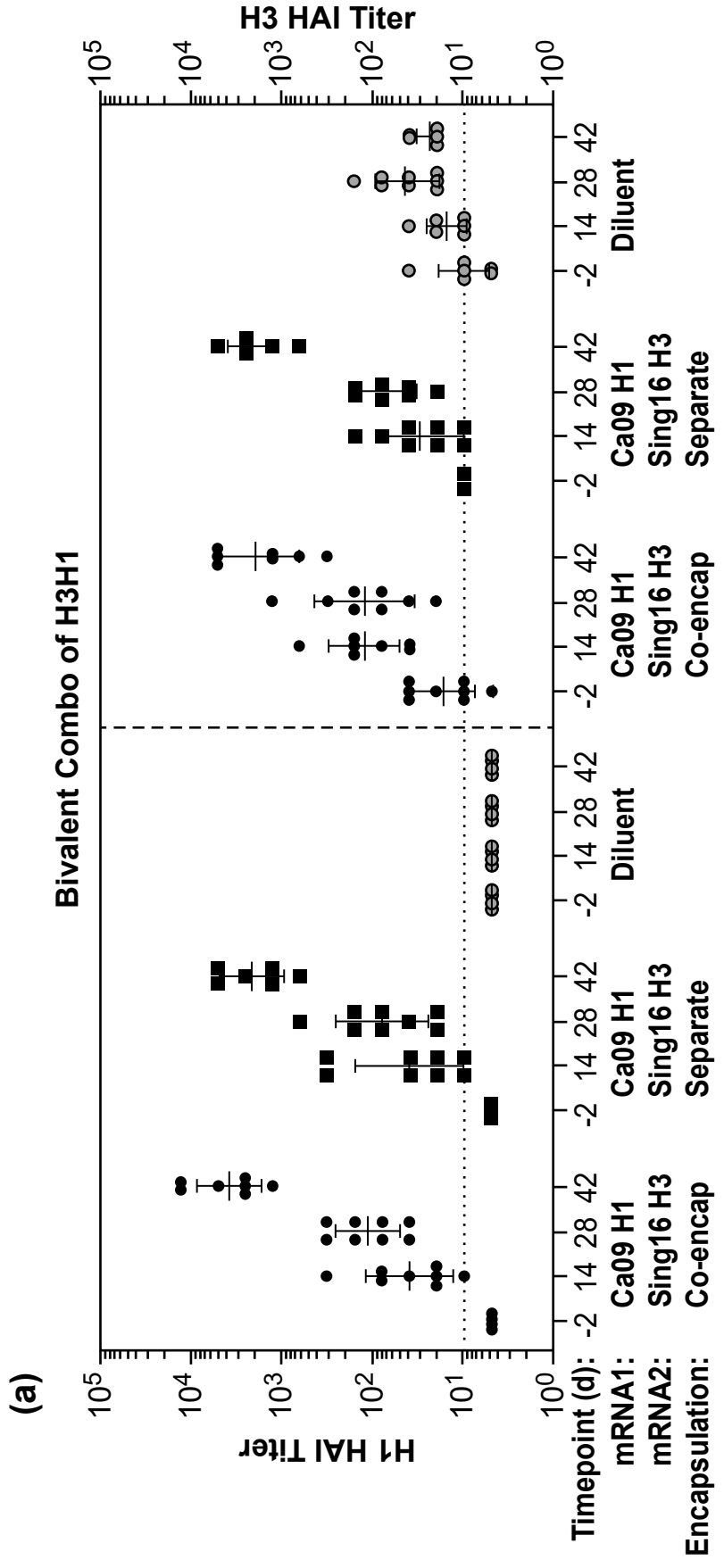

(a)
Bivalent Combo of H3H1
H1 HAI Titer
H3 HAI Titer
10^5
10^4
10^3
10^2
10^1
10^0
Timepoint (d): -2 14 28 42 -2 14 28 42 -2 14 28 42 -2 14 28 42
mRNA1: Ca09 H1 Ca09 H1 Ca09 H1 Diluent
mRNA2: Sing16 H3 Sing16 H3 Sing16 H3 Diluent
Encapsulation: Co-encap Separate Co-encap Separate

FIG. 22

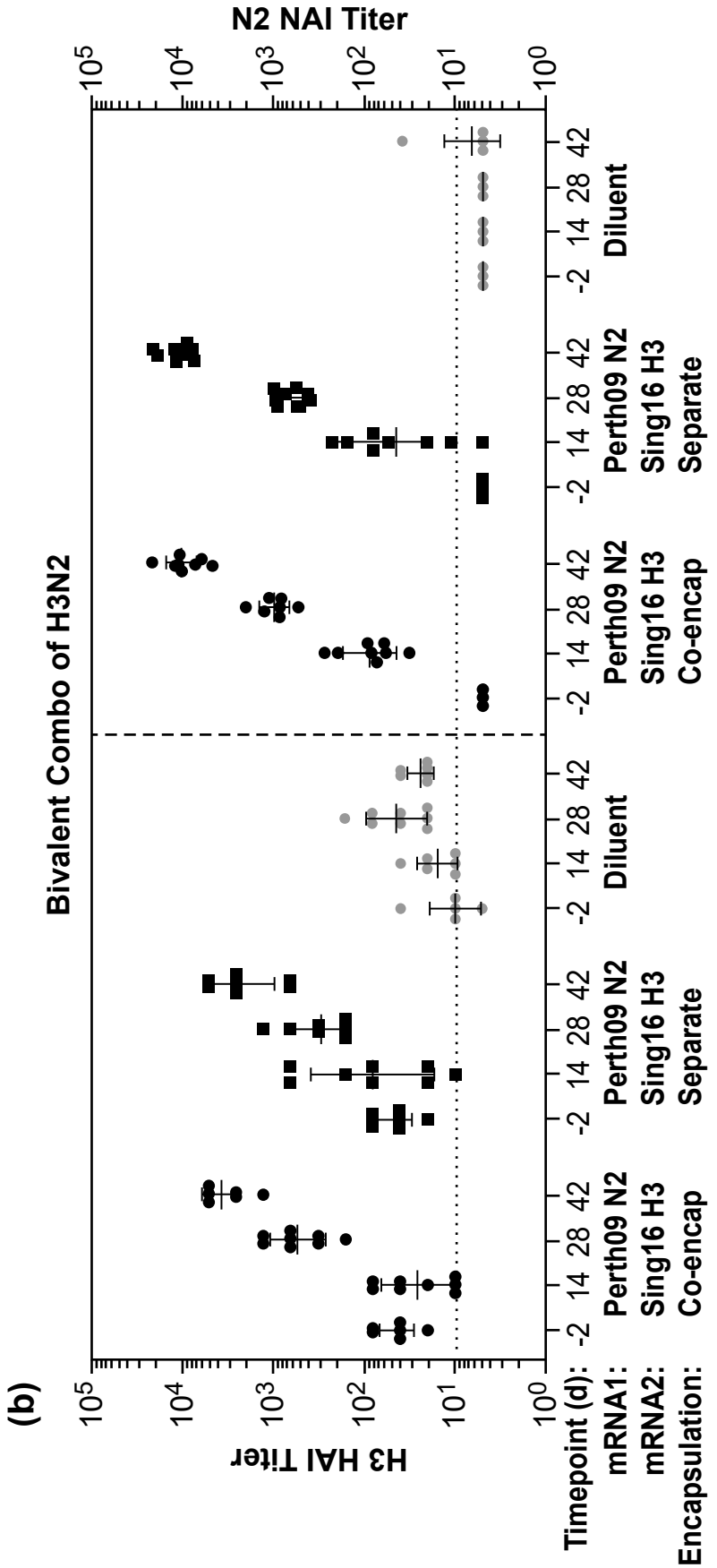

(b)
Bivalent Combo of H3N2
H3 HAI Titer
N2 NAI Titer
10^0
10^1
10^2
10^3
10^4
10^5
Timepoint (d): -2 14 28 42 -2 14 28 42 -2 14 28 42 -2 14 28 42
mRNA1: Perth09 N2 Perth09 N2 Diluent Diluent
mRNA2: Sing16 H3 Sing16 H3
Encapsulation: Co-encap Separate

FIG. 22 (cont'd)

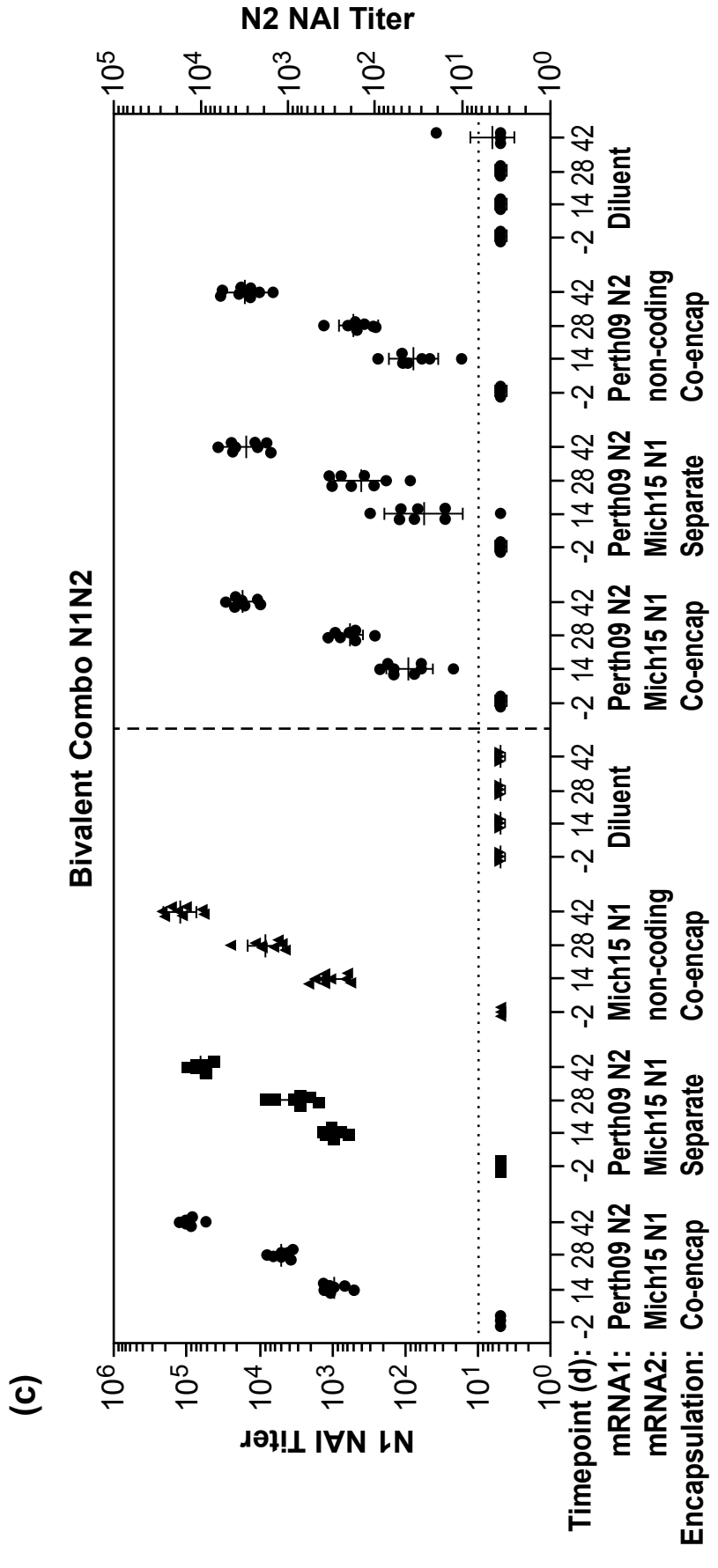

(c)
Bivalent Combo N1N2
N1 NAI Titer
N2 NAI Titer
10^6
10^5
10^4
10^3
10^2
10^1
10^0
Timepoint (d): -2 14 28 42 -2 14 28 42 -2 14 28 42 -2 14 28 42
mRNA1: Perth09 N2 Perth09 N2 Mich15 N1 Diluent Perth09 N2 Perth09 N2 Mich15 N1 Diluent
mRNA2: Mich15 N1 Mich15 N1 non-coding Mich15 N1 non-coding
Encapsulation: Co-encap Separate Co-encap Co-encap Separate Co-encap

FIG. 22 (cont'd)

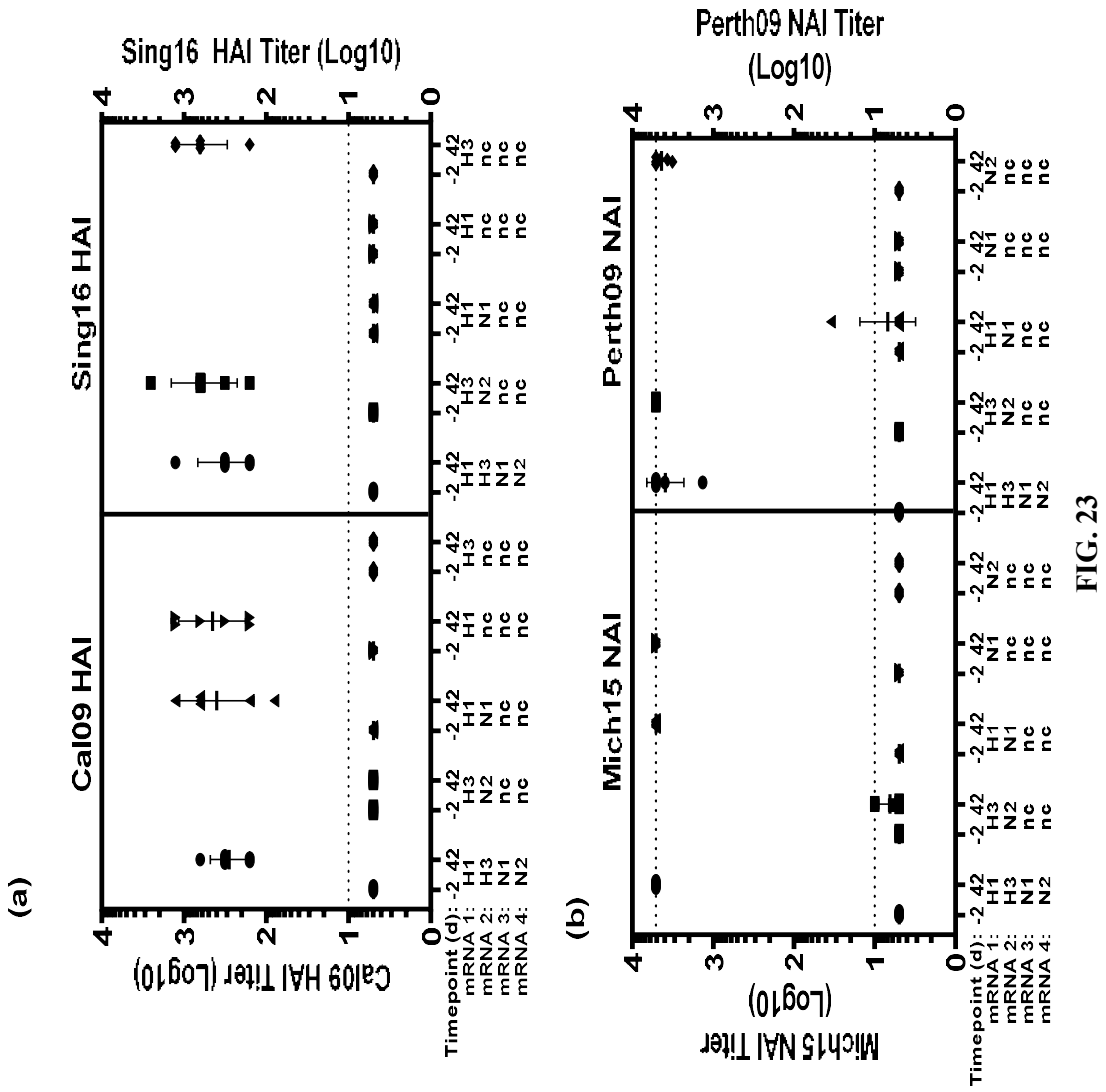

(a)
Sing16 HAI Titer (Log10)
Sing16 HAI
Cal09 HAI
Cal09 HAI Titer (Log10)
(b)
Perth09 NAI Titer
(Log10)
Perth09 NAI
Mich15 NAI
Mich15 NAI Titer
(Log10)
Timepoint (d):
mRNA 1:
mRNA 2:
mRNA 3:
mRNA 4:

FIG. 23

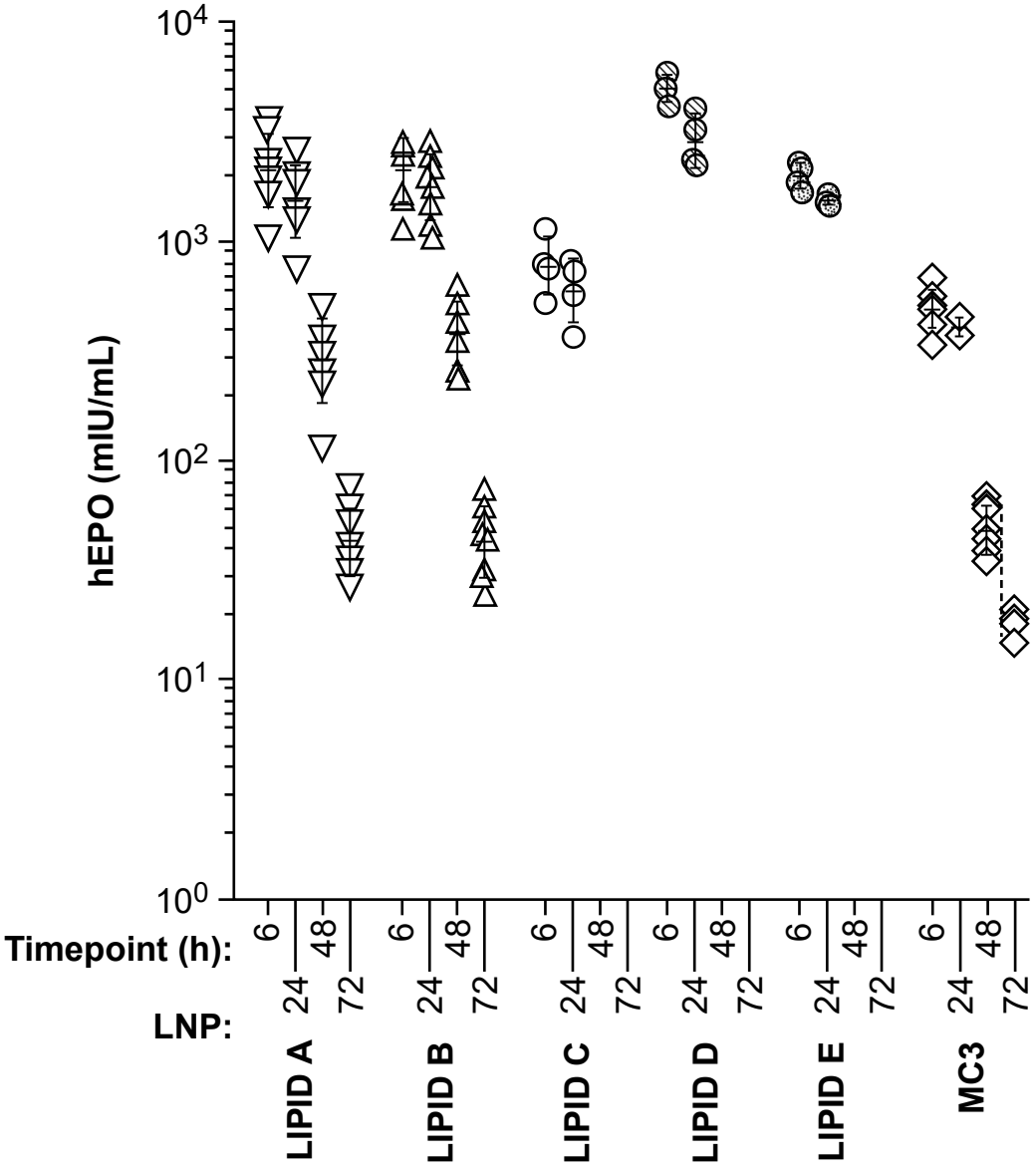

hEPO (mIU/mL)
10^4
10^3
10^2
10^1
10^0
Timepoint (h):
6
24
48
72
LNP:
LIPID A
LIPID B
LIPID C
LIPID D
LIPID E
MC3

FIG. 24

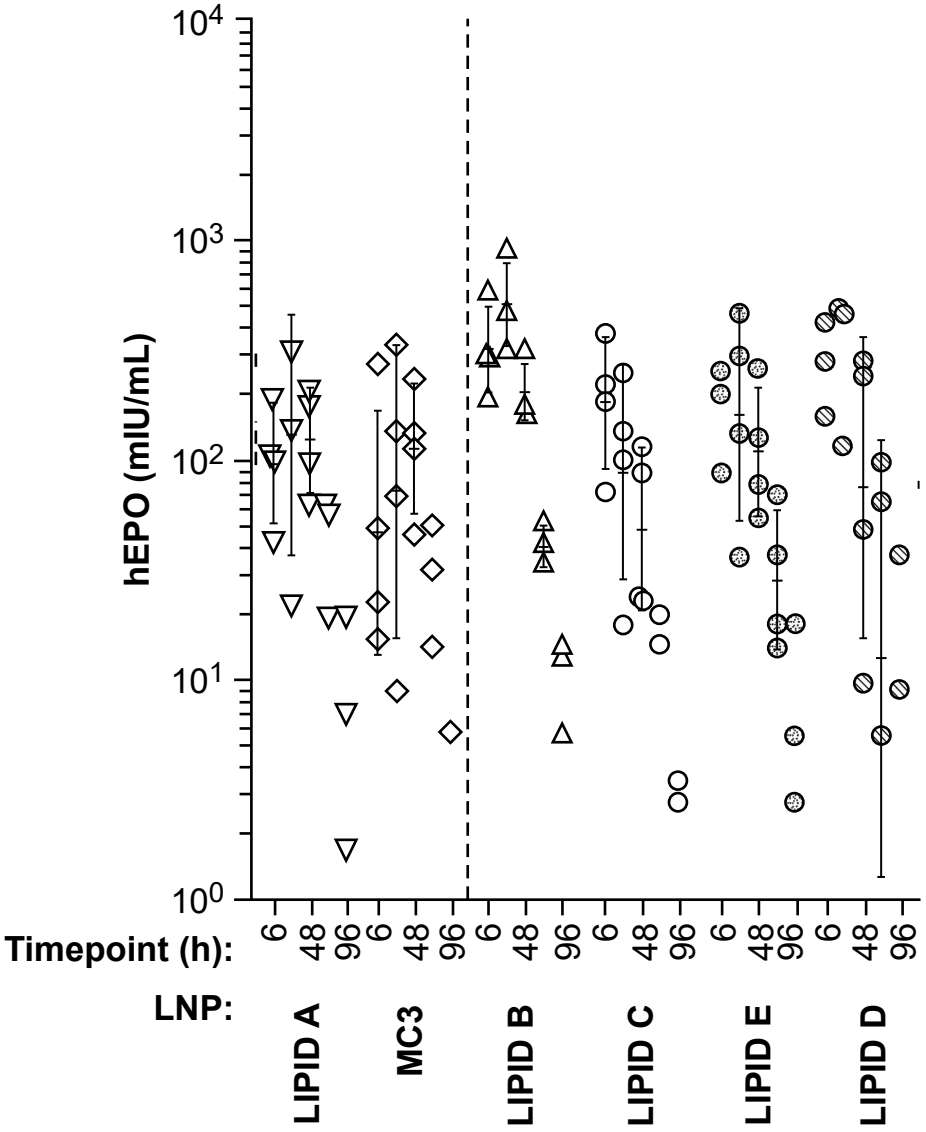

hEPO (mIU/mL)
10^4
10^3
10^2
10^1
10^0
Timepoint (h):
6
48
96
LNP:
LIPID A
MC3
LIPID B
LIPID C
LIPID E
LIPID D

FIG. 25

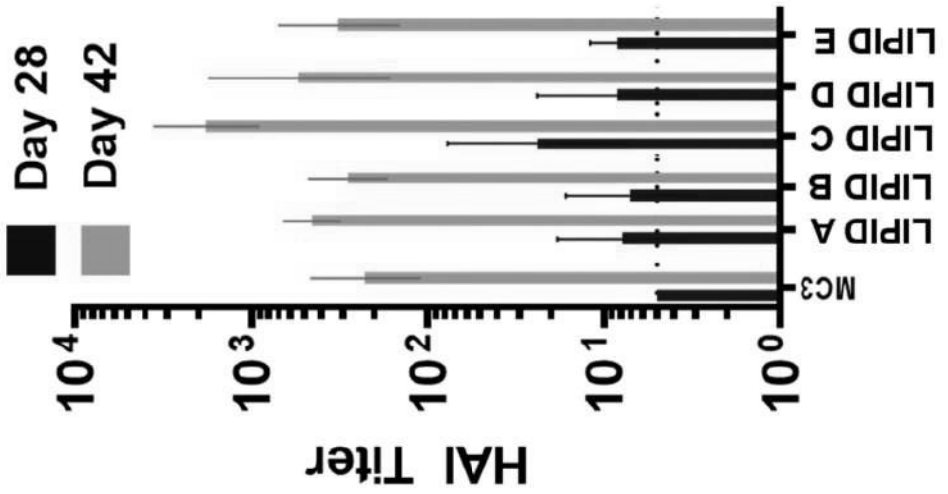

Day 28
Day 42
HAI Titer
10^4
10^3
10^2
10^1
10^0
MC3
LIPID A
LIPID B
LIPID C
LIPID D
LIPID E

FIG. 26

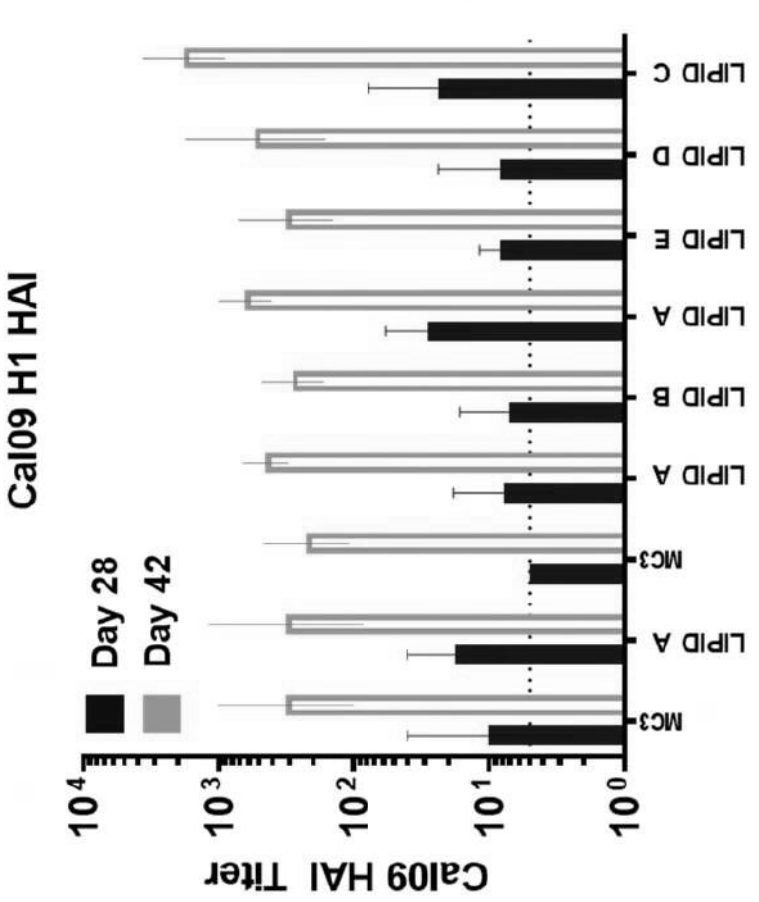

Cal09 H1 HAI
Day 28
Day 42
Cal09 HAI Titer
10^4
10^3
10^2
10^1
10^0
MC3
LIPID A
MC3
LIPID A
LIPID B
LIPID A
LIPID E
LIPID D
LIPID C

FIG. 27

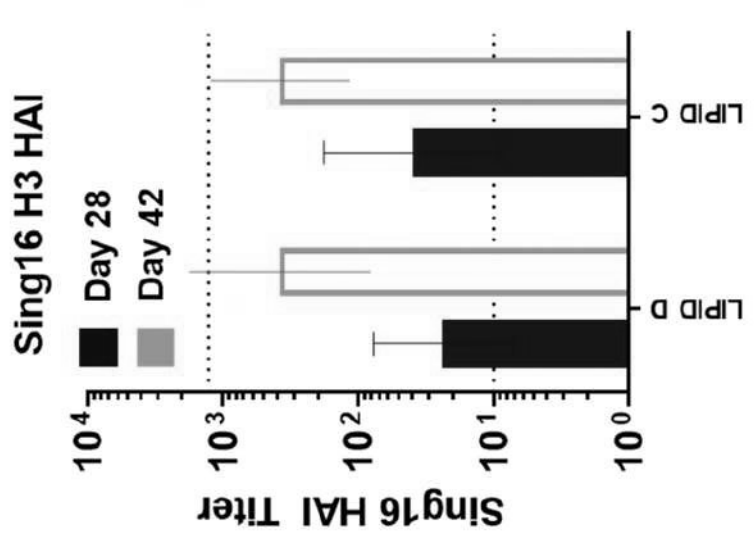

Sing16 H3 HAI
Day 28
Day 42
Sing16 HAI Titer
10^4
10^3
10^2
10^1
10^0
LIPID D
LIPID C

FIG. 28

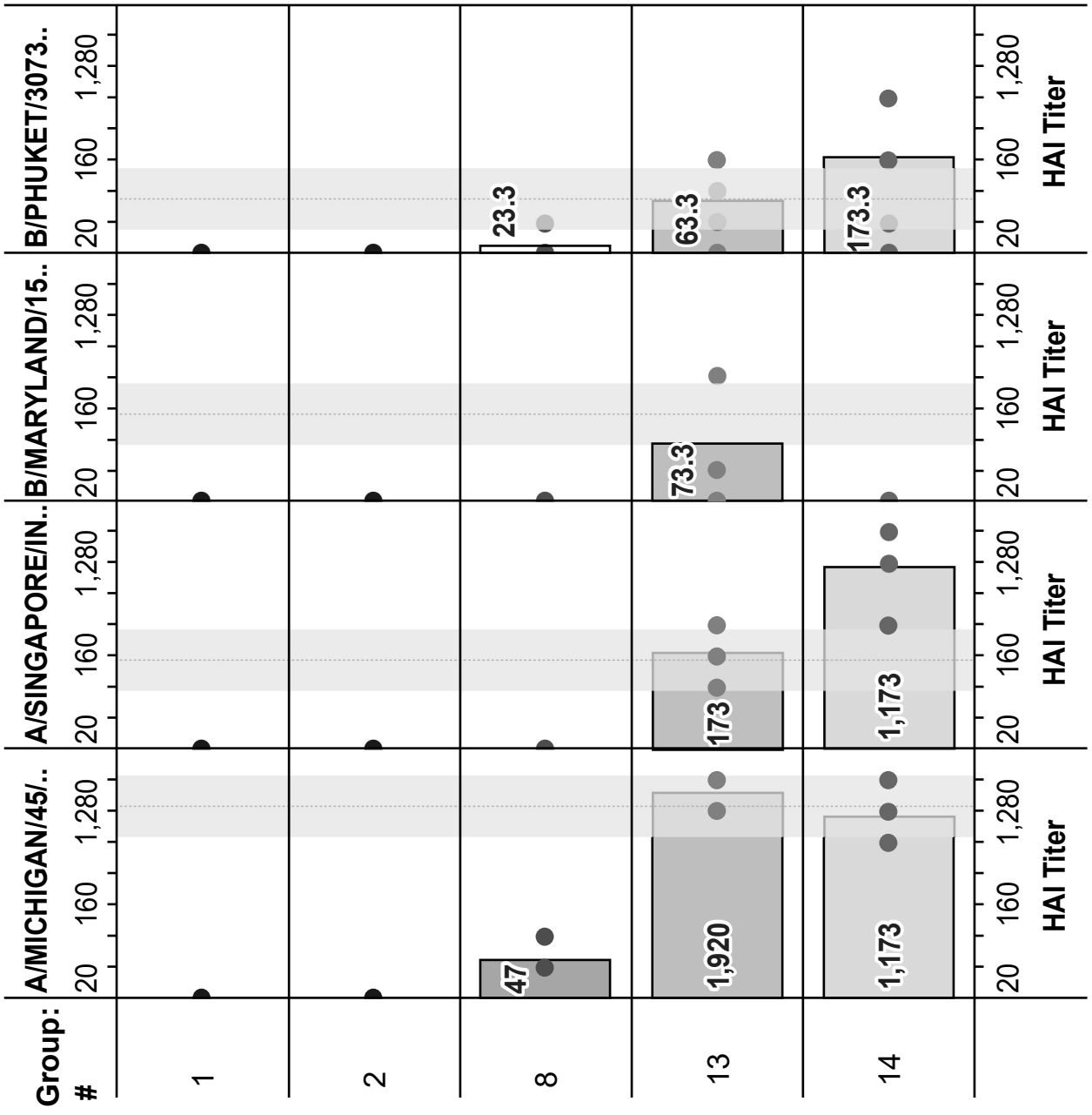

Group:
#
A/MICHIGAN/45/..
A/SINGAPORE/IN..
B/MARYLAND/15..
B/PHUKET/3073..
20
160
1,280
HAI Titer
1
2
8
13
14
Naive
Naive
Quadrivalent NA mRNA
Quadrivalent HA mRNA
Octavalent mRNA
47
1,920
1,173
23.3
73.3
173
63.3
1,173
173.3

FIG. 29

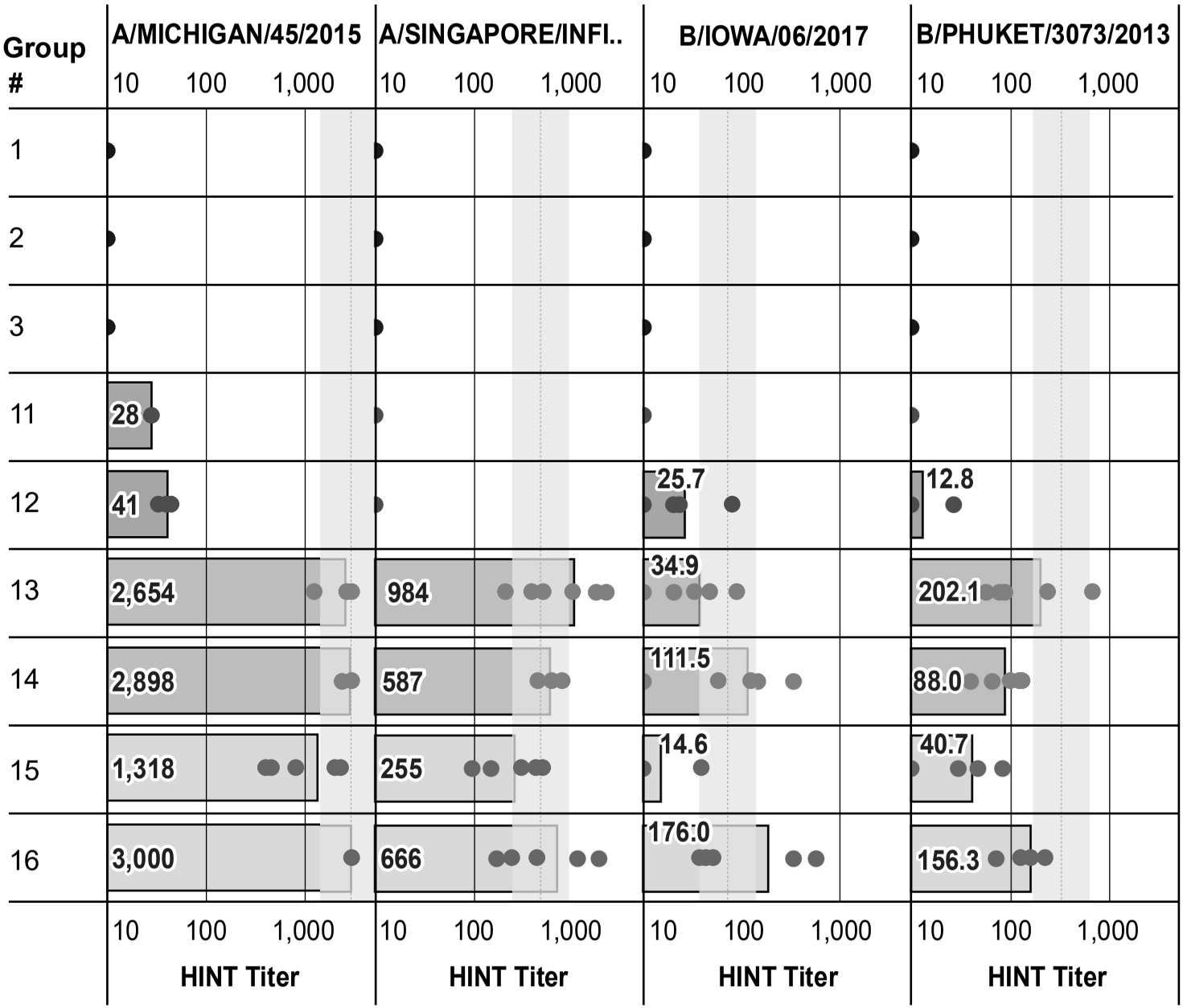

Group #
A/MICHIGAN/45/2015
A/SINGAPORE/INFl..
B/IOWA/06/2017
B/PHUKET/3073/2013
10
100
1,000
1
2
3
11
12
13
14
15
16
28
41
2,654
2,898
1,318
3,000
984
587
255
666
25.7
34.9
111.5
14.6
176.0
12.8
202.1
88.0
40.7
156.3
HINT Titer

FIG. 30

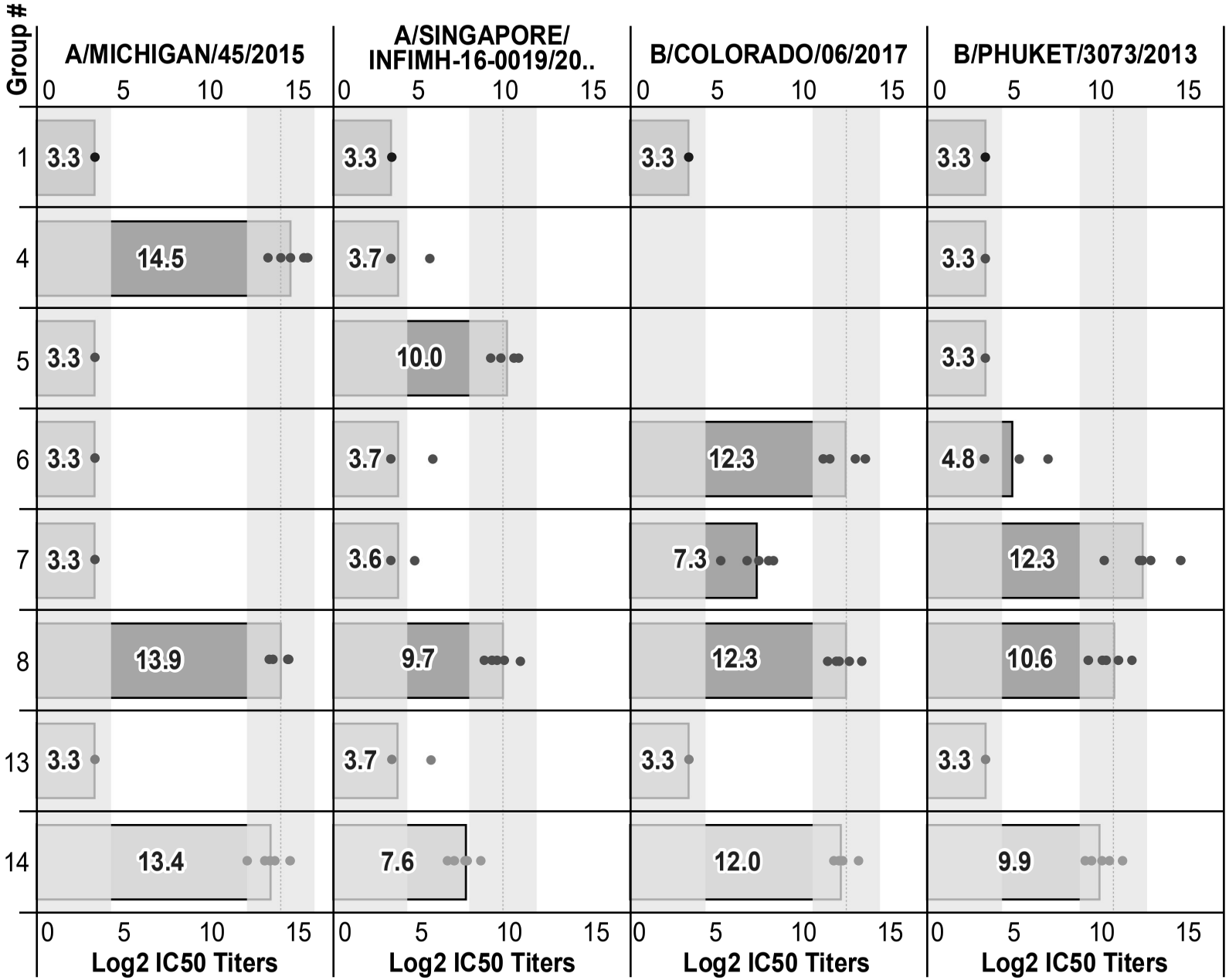

Group #
A/MICHIGAN/45/2015
A/SINGAPORE/ INFIMH-16-0019/20..
B/COLORADO/06/2017
B/PHUKET/3073/2013
0 5 10 15
1 3.3 3.3 3.3 3.3
4 14.5 3.7 3.3
5 3.3 10.0 3.3
6 3.3 3.7 12.3 4.8
7 3.3 3.6 7.3 12.3
8 13.9 9.7 12.3 10.6
13 3.3 3.7 3.3 3.3
14 13.4 7.6 12.0 9.9
Log2 IC50 Titers

FIG. 31

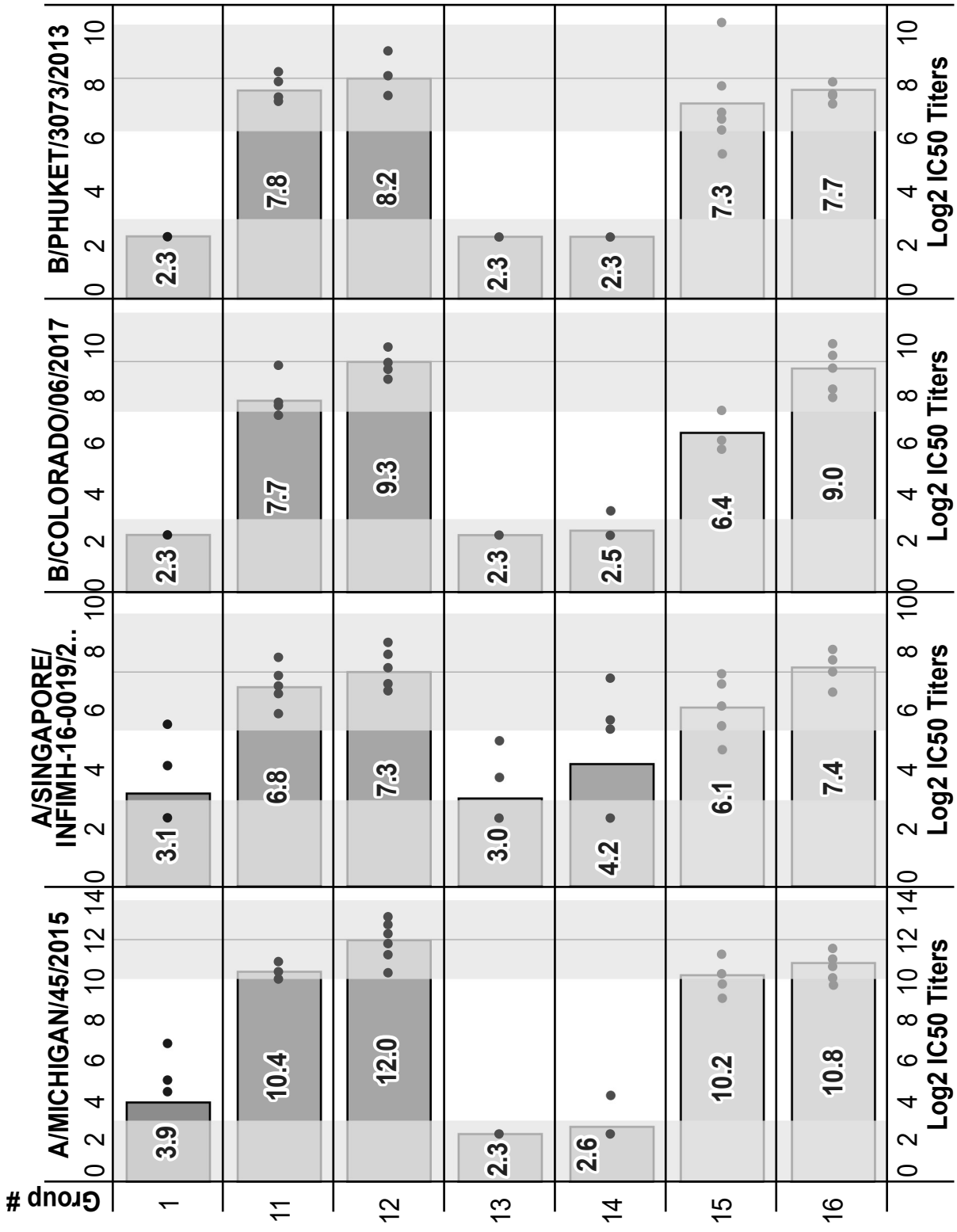

Group #
A/MICHIGAN/45/2015
A/SINGAPORE/INFIMH-16-0019/2..
B/COLORADO/06/2017
B/PHUKET/3073/2013
Log2 IC50 Titers
1
11
12
13
14
15
16
3.9
3.1
2.3
2.3
10.4
6.8
7.7
7.8
12.0
7.3
9.3
8.2
2.3
3.0
2.3
2.3
2.6
4.2
2.5
2.3
10.2
6.1
6.4
7.3
10.8
7.4
9.0
7.7

FIG. 32

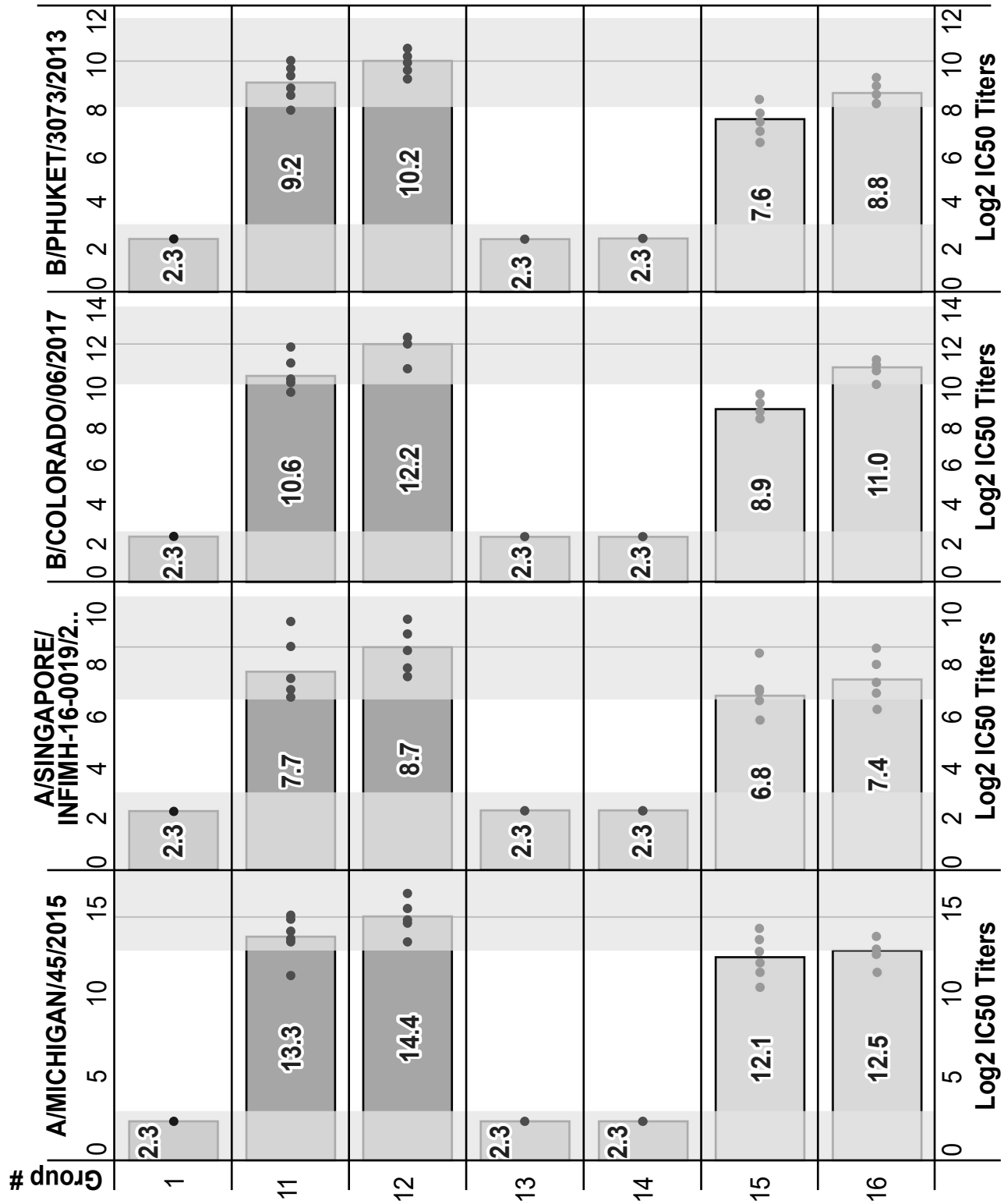

Group #
A/MICHIGAN/45/2015
A/SINGAPORE/ INFIMH-16-0019/2..
B/COLORADO/06/2017
B/PHUKET/3073/2013
1
11
12
13
14
15
16
2.3
13.3
14.4
12.1
12.5
7.7
8.7
6.8
7.4
10.6
12.2
8.9
11.0
9.2
10.2
7.6
8.8
Log2 IC50 Titers

FIG. 33