Figure 1

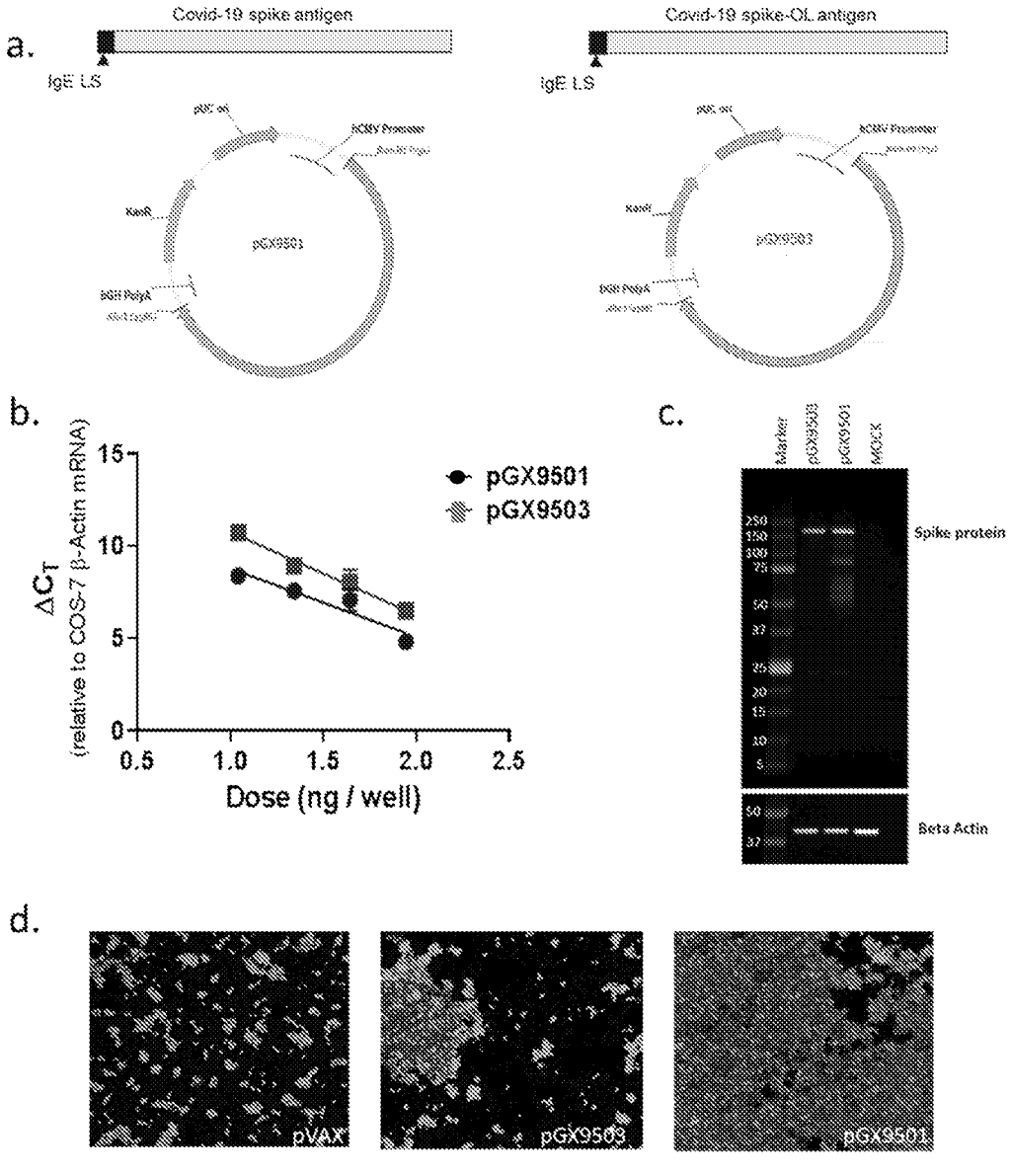

a.
Covid-19 spike antigen
IgE LS
Covid-19 spike-OL antigen
IgE LS
pGX9501
pGX9503
b.
ΔCT
(relative to COS-7 β-Actin mRNA)
15
10
5
0
0.5
1.0
1.5
2.0
2.5
Dose (ng / well)
pGX9501
pGX9503
c.
Marker
pGX9503
pGX9501
MOCK
250
150
100
75
50
37
25
20
15
10
5
Spike protein
50
37
Beta Actin
d.
pVAX
pGX9503
pGX9501

Figure 2

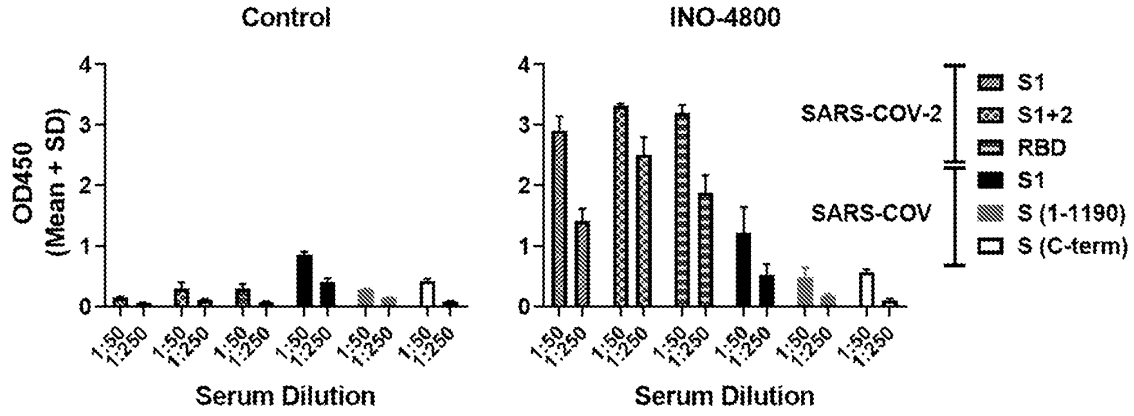

Control
INO-4800
OD450
(Mean + SD)
Serum Dilution
Serum Dilution
SARS-COV-2
SARS-COV
S1
S1+2
RBD
S1
S (1-1190)
S (C-term)

Figure 3

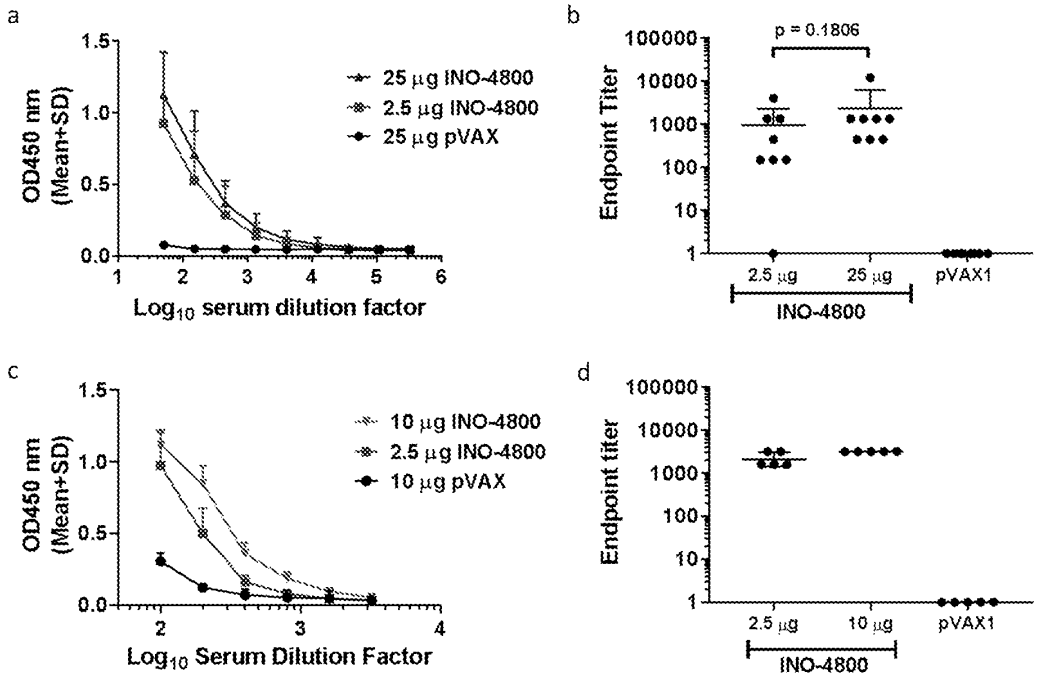

a
OD450 nm (Mean+SD)
1.5
1.0
0.5
0.0
1
2
3
4
5
6
Log10 serum dilution factor
25 µg INO-4800
2.5 µg INO-4800
25 µg pVAX
b
Endpoint Titer
100000
10000
1000
100
10
1
p = 0.1806
2.5 µg
25 µg
pVAX1
INO-4800
c
OD450 nm (Mean+SD)
1.5
1.0
0.5
0.0
2
3
4
Log10 Serum Dilution Factor
10 µg INO-4800
2.5 µg INO-4800
10 µg pVAX
d
Endpoint titer
100000
10000
1000
100
10
1
2.5 µg
10 µg
pVAX1
INO-4800

Figure 4A

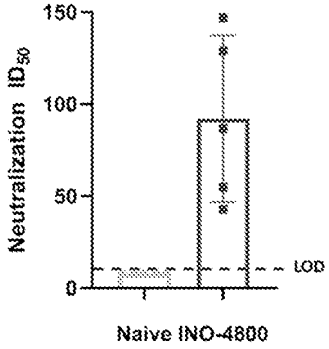


Figure 4B

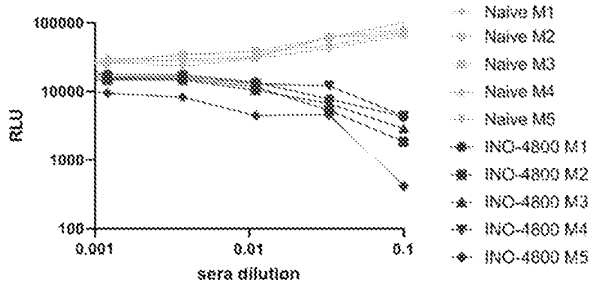


Figure 5

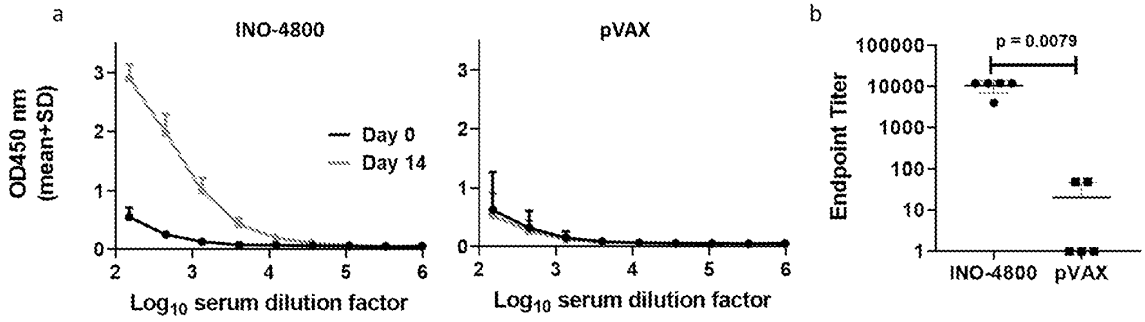

a
INO-4800
pVAX
OD450 nm (mean+SD)
Day 0
Day 14
Log10 serum dilution factor
Log10 serum dilution factor
b
Endpoint Titer
p = 0.0079
INO-4800
pVAX

Figure 6

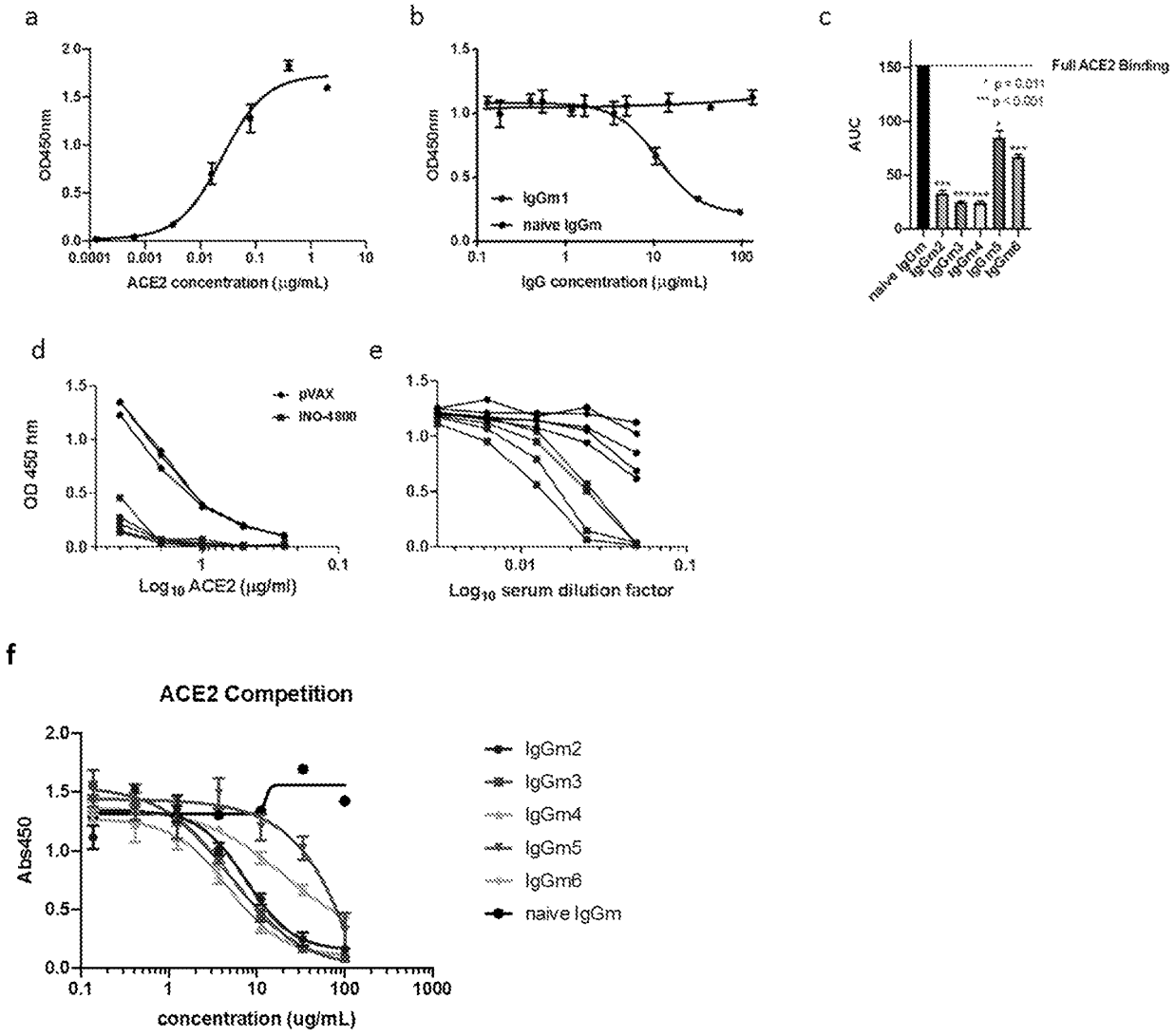

a
OD450nm
ACE2 concentration (μg/mL)
b
OD450nm
IgGm1
naive IgGm
IgG concentration (μg/mL)
c
AUC
Full ACE2 Binding
naive IgGm
IgGm2
IgGm3
IgGm4
IgGm5
IgGm6
d
OD 450 nm
pVAX
INO-4800
Log10 ACE2 (μg/ml)
e
Log10 serum dilution factor
f
ACE2 Competition
Abs450
concentration (ug/mL)
IgGm2
IgGm3
IgGm4
IgGm5
IgGm6
naive IgGm

Figure 7

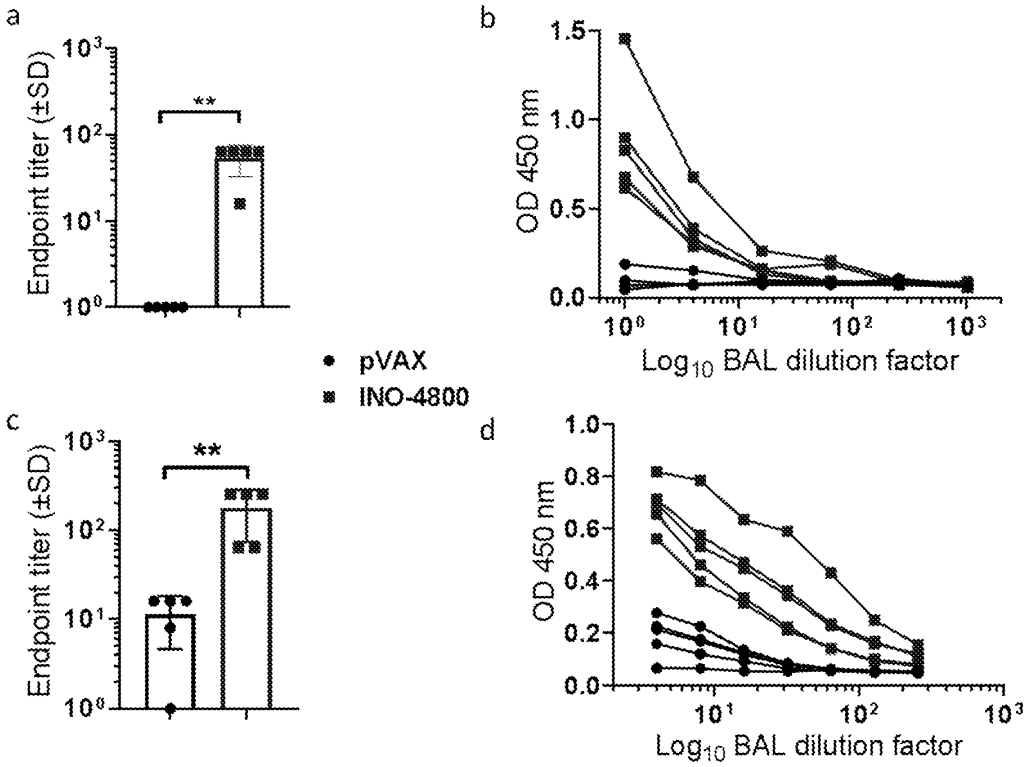

a
Endpoint titer (±SD)
**
b
OD 450 nm
Log10 BAL dilution factor
pVAX
INO-4800
c
Endpoint titer (±SD)
**
d
OD 450 nm
Log10 BAL dilution factor

Figure 8

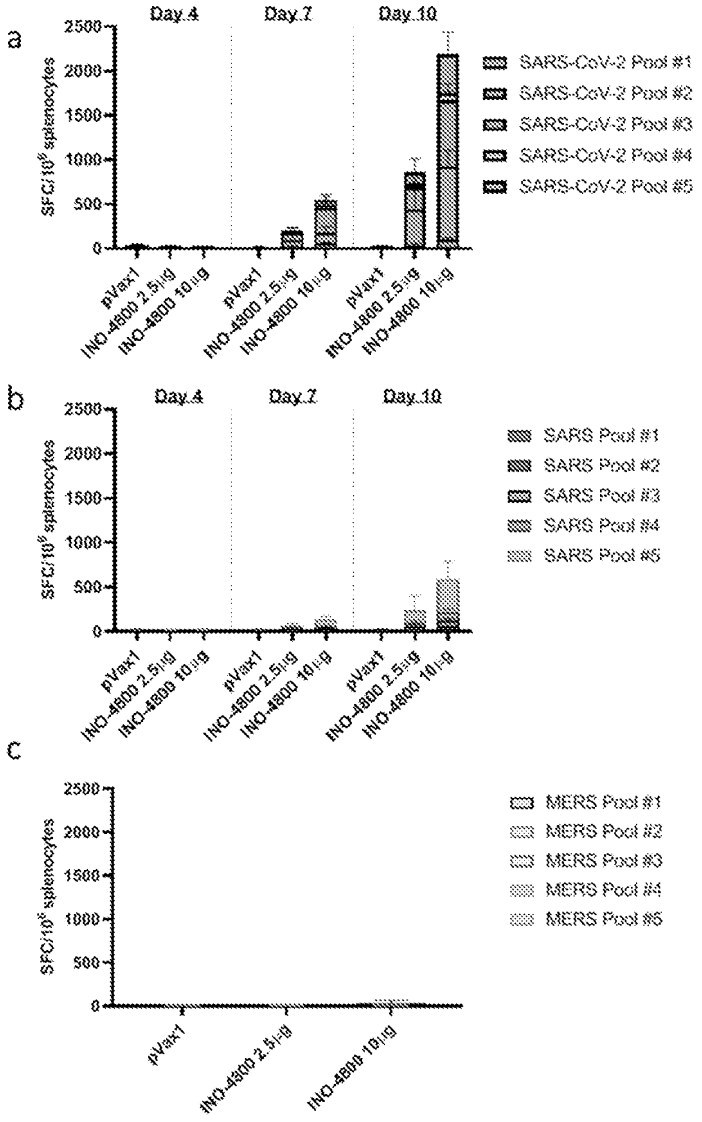

a
Day 4
Day 7
Day 10
SFC/10^6 splenocytes
2500
2000
1500
1000
500
0
pVax1
INO-4800 2.5mg
INO-4800 10mg
SARS-CoV-2 Pool #1
SARS-CoV-2 Pool #2
SARS-CoV-2 Pool #3
SARS-CoV-2 Pool #4
SARS-CoV-2 Pool #5
b
SARS Pool #1
SARS Pool #2
SARS Pool #3
SARS Pool #4
SARS Pool #5
c
MERS Pool #1
MERS Pool #2
MERS Pool #3
MERS Pool #4
MERS Pool #5

Figure 9

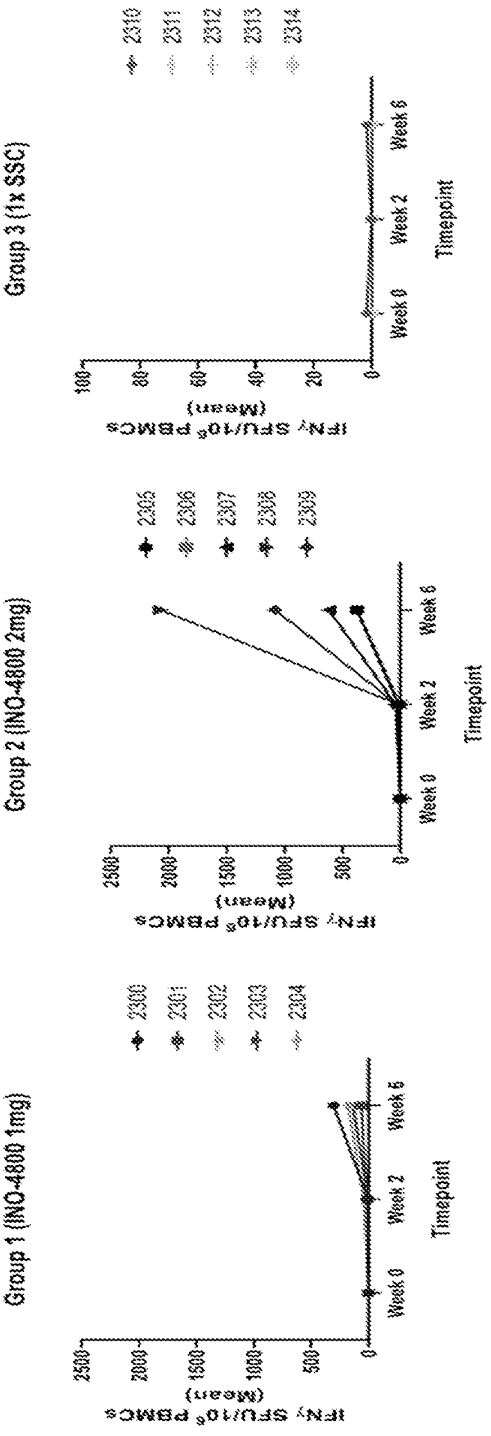

Group 1 (INO-4800 1mg)
Group 2 (INO-4800 2mg)
Group 3 (1x SSC)
IFNγ SFU/10^6 PBMCs (Mean)
Timepoint
Week 0
Week 2
Week 6
2300
2301
2302
2303
2304
2305
2306
2307
2308
2309
2310
2311
2312
2313
2314

Figure 10

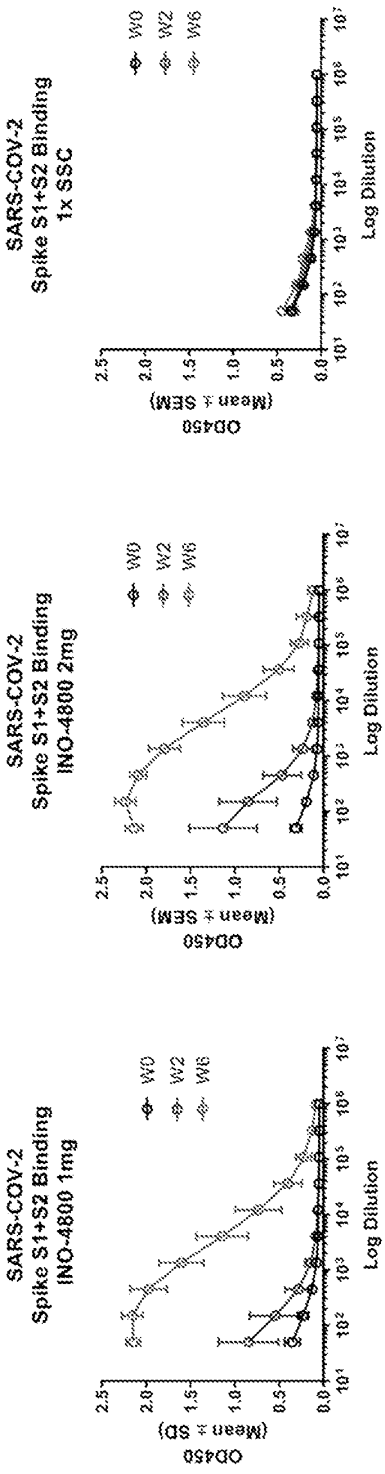

SARS-COV-2
Spike S1+S2 Binding
INO-4800 1mg
OD450
(Mean ± SD)
Log Dilution
W0
W2
W6
SARS-COV-2
Spike S1+S2 Binding
INO-4800 2mg
OD450
(Mean ± SEM)
Log Dilution
W0
W2
W6
SARS-COV-2
Spike S1+S2 Binding
1x SSC
OD450
(Mean ± SEM)
Log Dilution
W0
W2
W6

Figure 11A

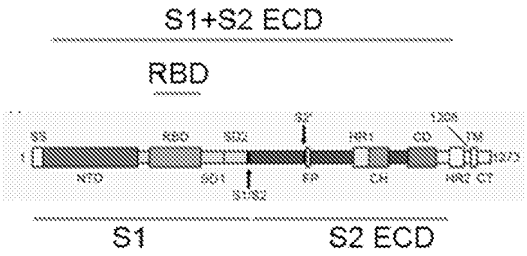


Figure 11B

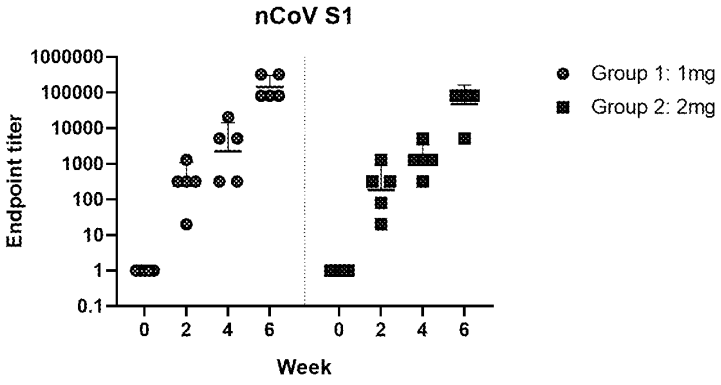


Figure 11C

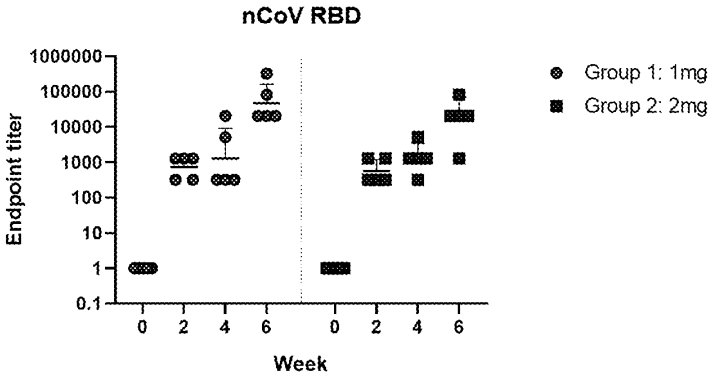


Figure 11D

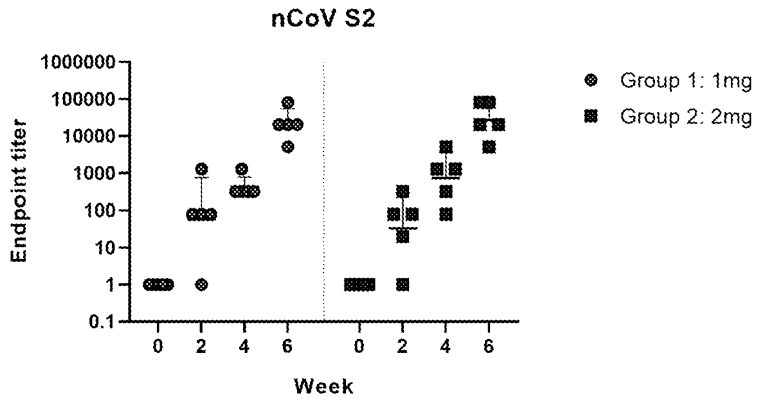


Figure 11E

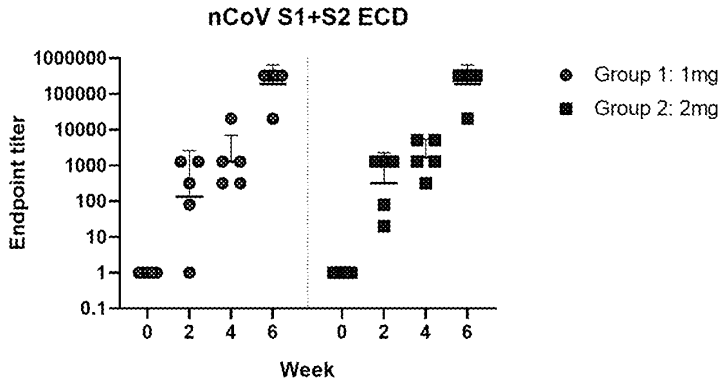


Figure 12A

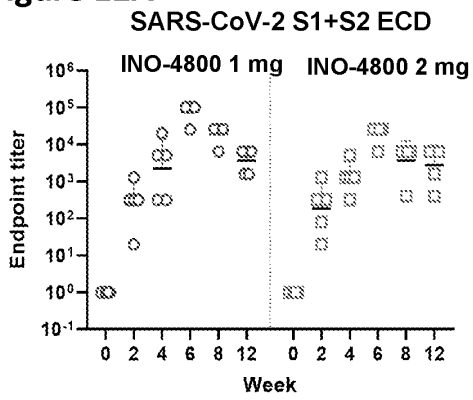


Figure 12B

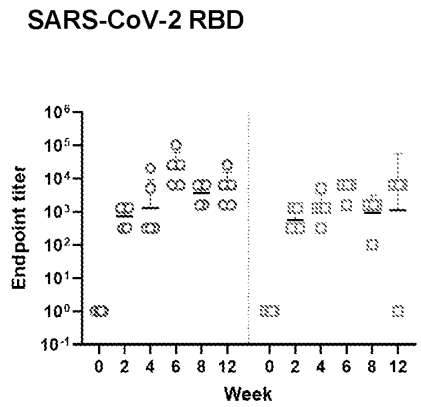


Figure 12C

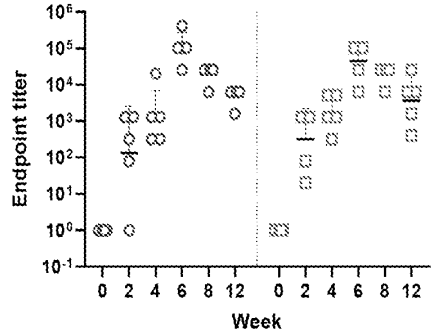


Figure 12D

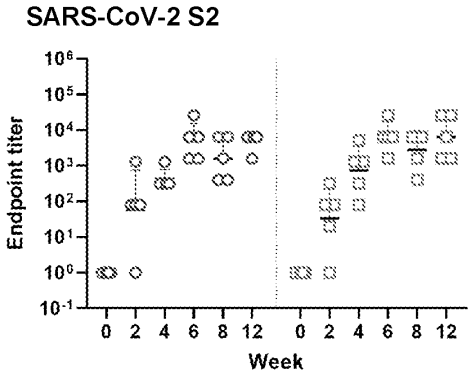


Figure 12E

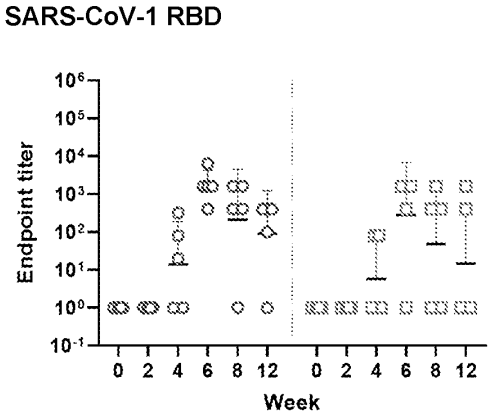


Figure 12F

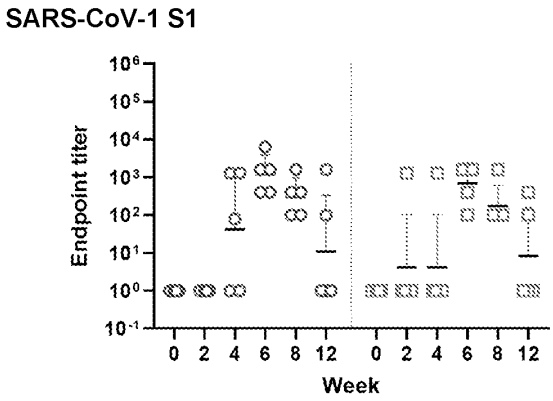


Figure 12G

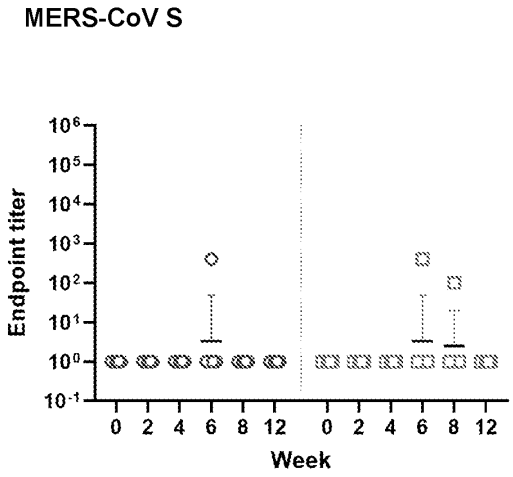

MERS-CoV S
Endpoint titer
10^6
10^5
10^4
10^3
10^2
10^1
10^0
10^{-1}
0 2 4 6 8 12 0 2 4 6 8 12
Week

Figure 13A

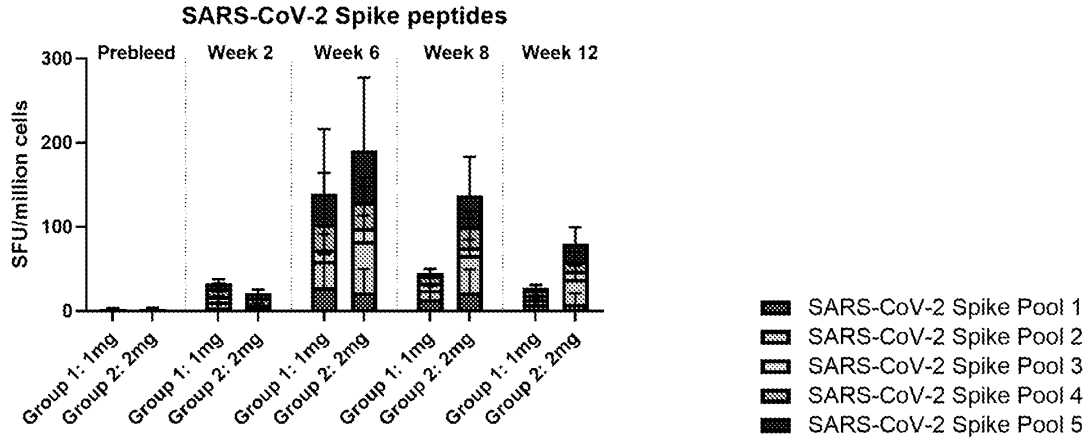


Figure 13B

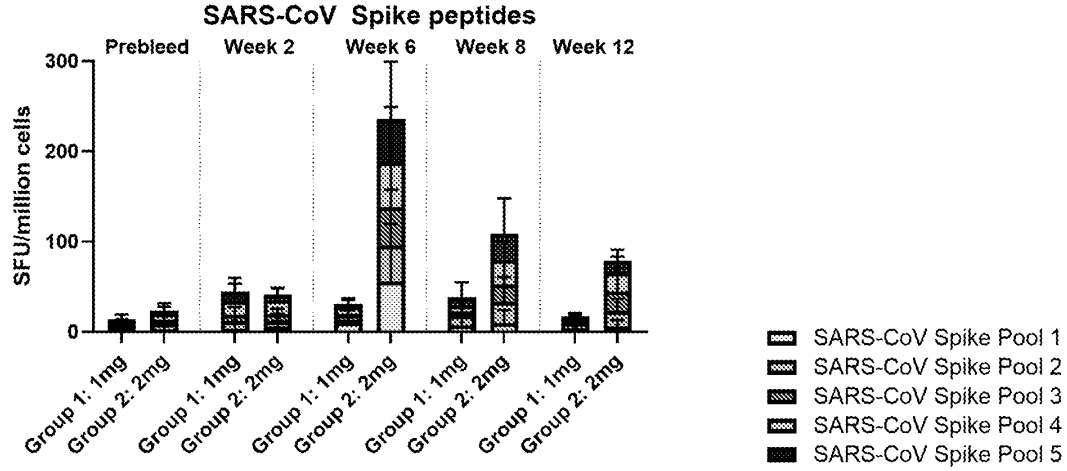


Figure 13C

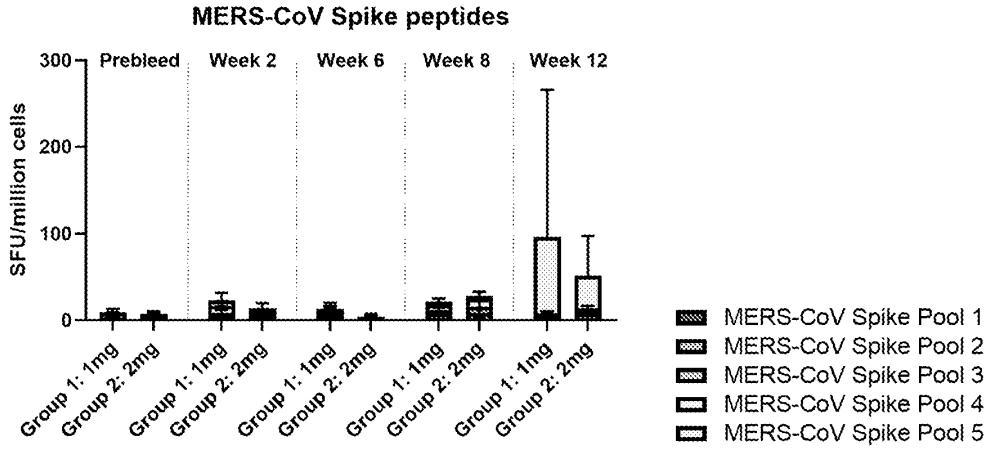

MERS-CoV Spike peptides
SFU/million cells
300
200
100
0
Prebleed
Week 2
Week 6
Week 8
Week 12
Group 1: 1mg
Group 2: 2mg
MERS-CoV Spike Pool 1
MERS-CoV Spike Pool 2
MERS-CoV Spike Pool 3
MERS-CoV Spike Pool 4
MERS-CoV Spike Pool 5

Figure 14

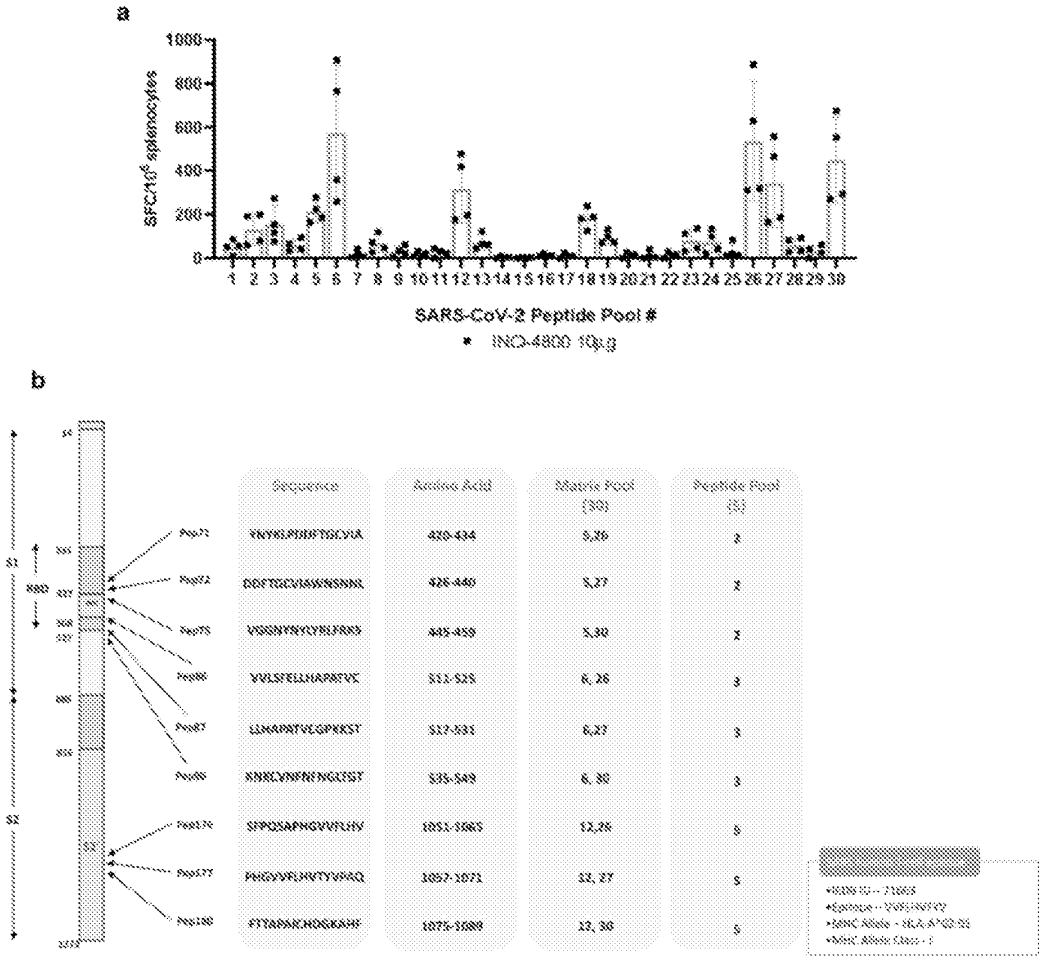

a
SFC/10^6 splenocytes
SARS-CoV-2 Peptide Pool #
INO-4800 10μg
b
Sequence
Amino Acid
Matrix Pool (3D)
Peptide Pool (2)

Figure 15

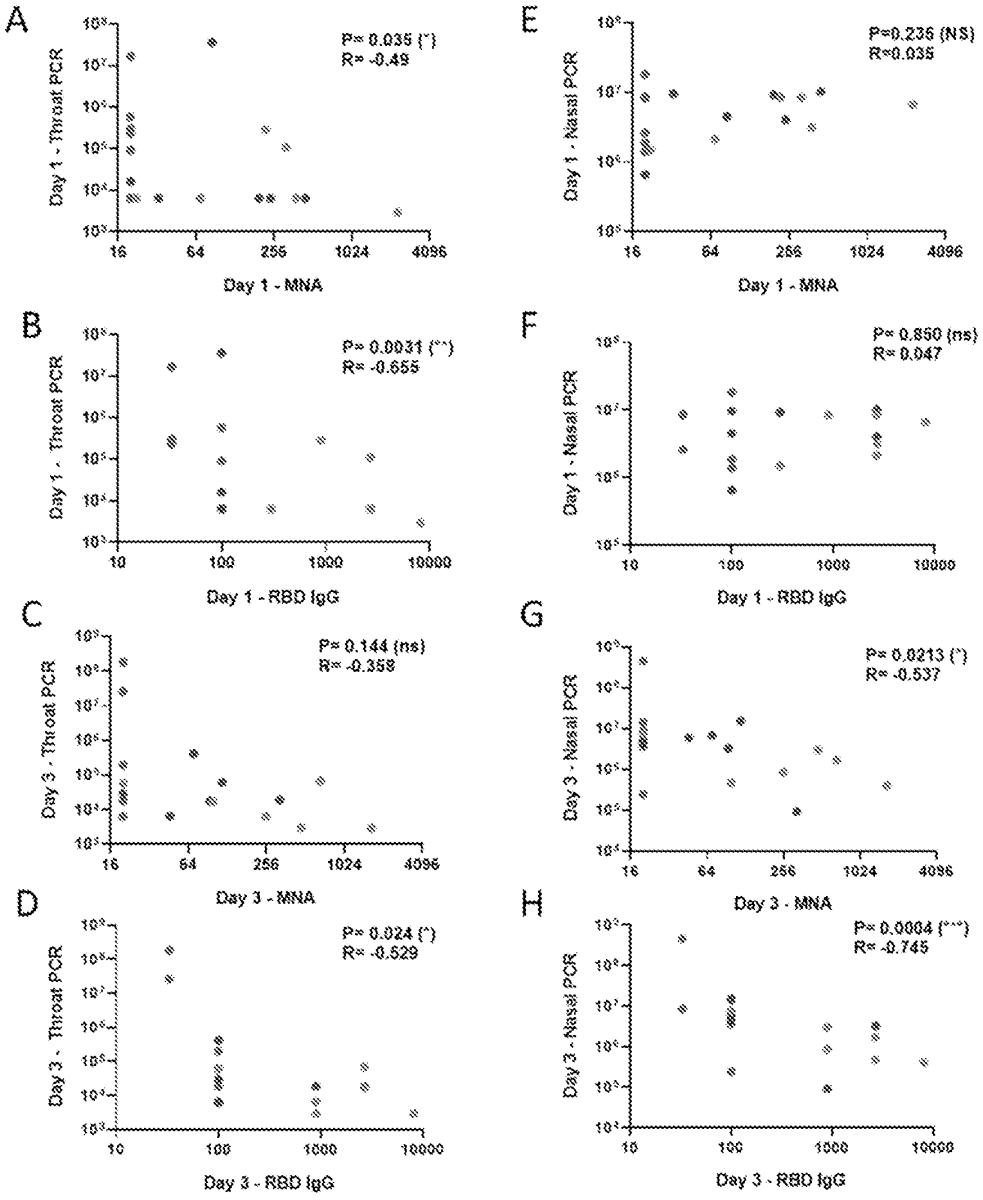
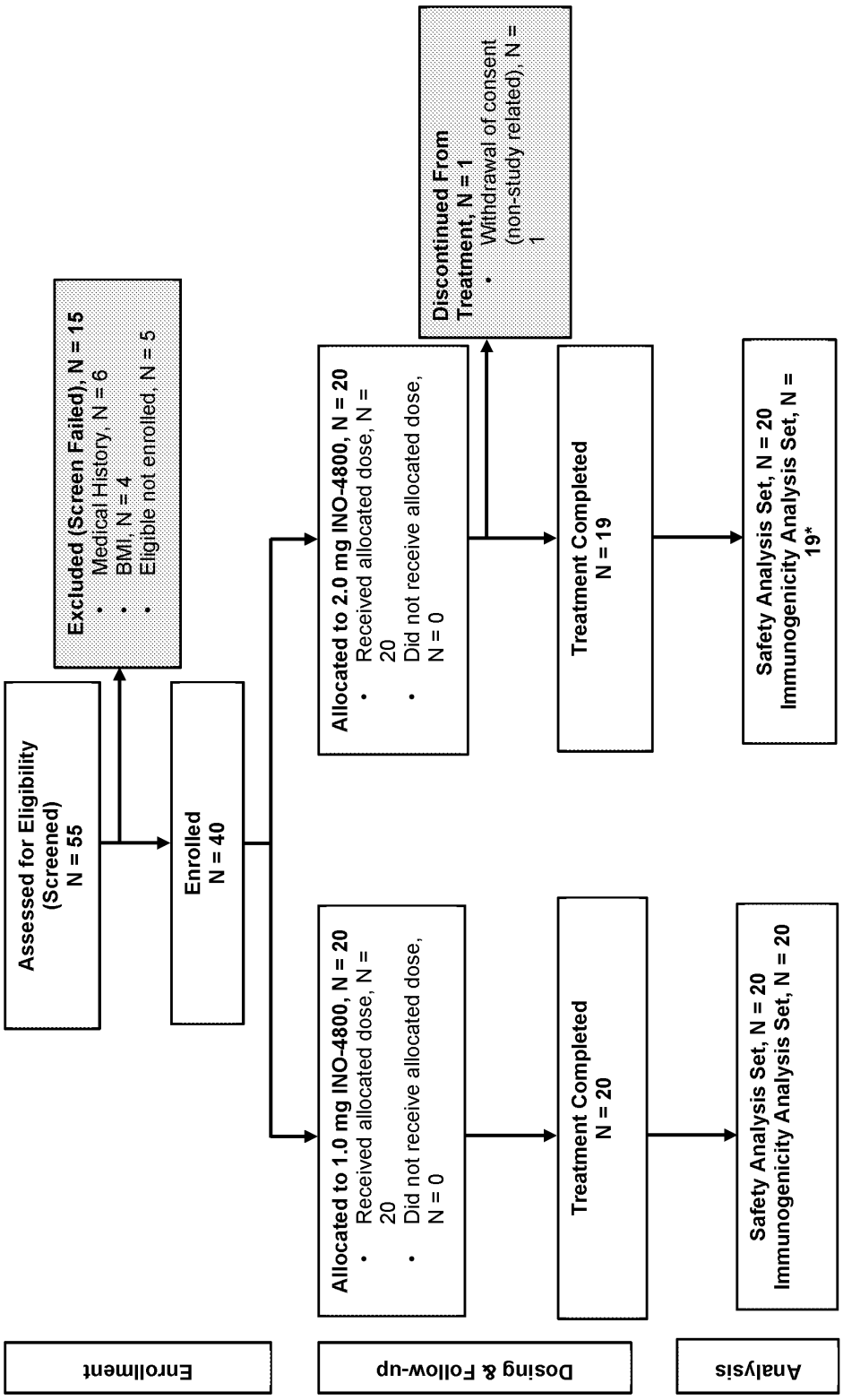

A
P= 0.035 (*)
R= -0.49
Day 1 - Throat PCR
Day 1 - MNA
B
P= 0.0031 (**)
R= -0.655
Day 1 - Throat PCR
Day 1 - RBD IgG
C
P= 0.144 (ns)
R= -0.358
Day 3 - Throat PCR
Day 3 - MNA
D
P= 0.024 (*)
R= -0.529
Day 3 - Throat PCR
Day 3 - RBD IgG
E
P=0.236 (NS)
R=0.035
Day 1 - Nasal PCR
Day 1 - MNA
F
P= 0.850 (ns)
R= 0.047
Day 1 - Nasal PCR
Day 1 - RBD IgG
G
P= 0.0213 (*)
R= -0.537
Day 3 - Nasal PCR
Day 3 - MNA
H
P= 0.0004 (***)
R= -0.745
Day 3 - Nasal PCR
Day 3 - RBD IgG

Figure 16



*one subject in the 2.0 mg dose group was not able to secure consistent transportation and therefore discontinued

Figure 17A

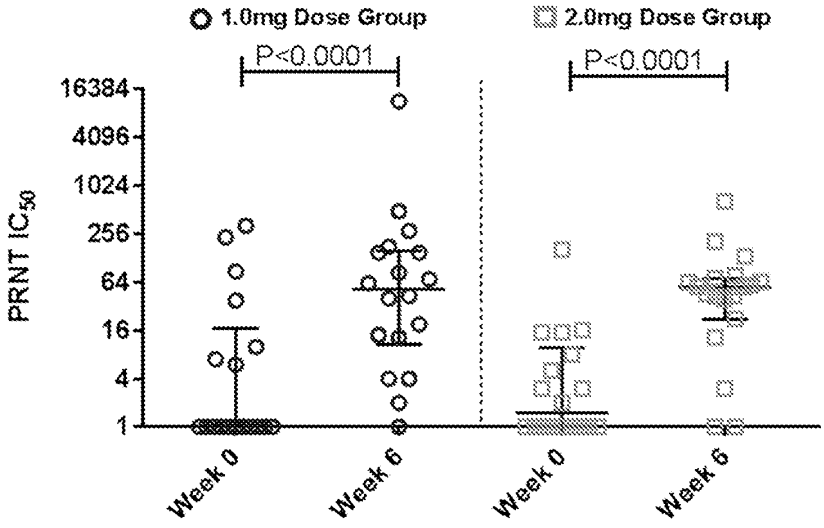


Figure 17B

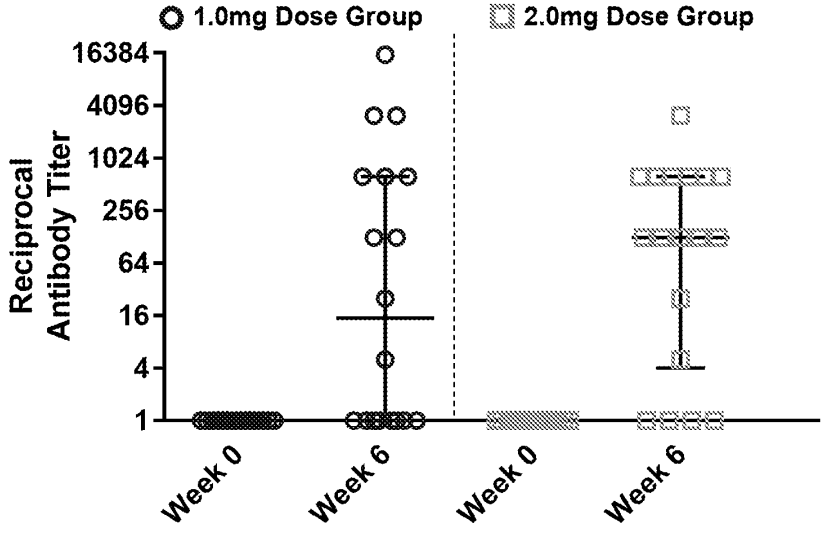


Figure 17C

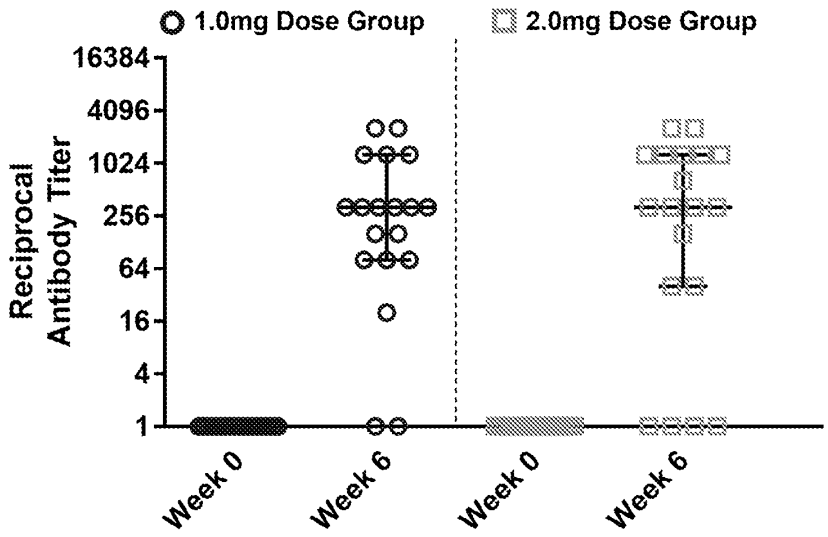


Figure 17D

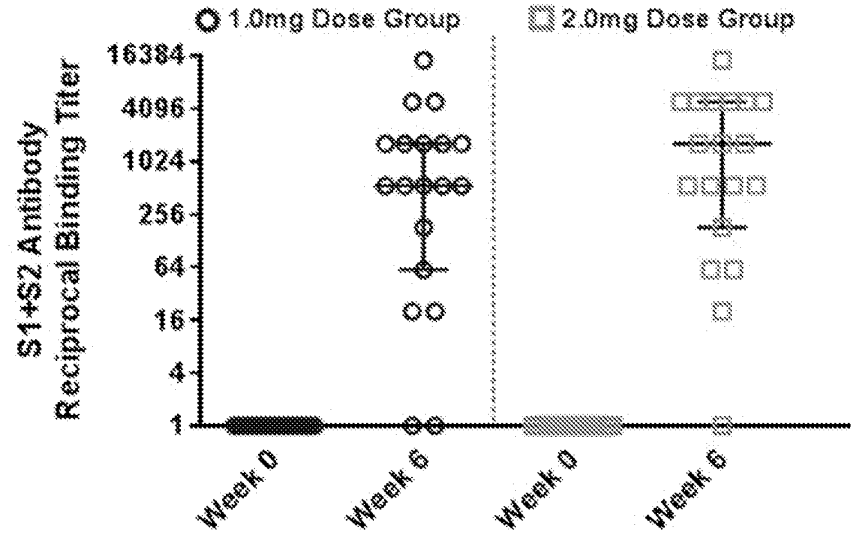


Figure 18A

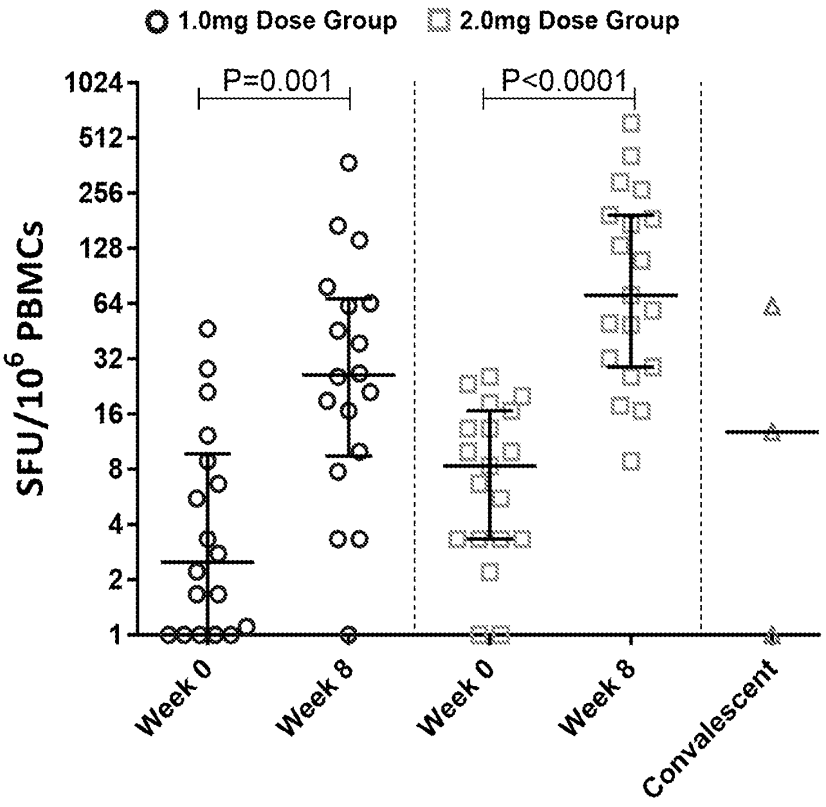

1.0mg Dose Group
2.0mg Dose Group
P=0.001
P<0.0001
SFU/10^6 PBMCs
1024
512
256
128
64
32
16
8
4
2
1
Week 0
Week 8
Week 0
Week 8
Convalescent

Figure 18B

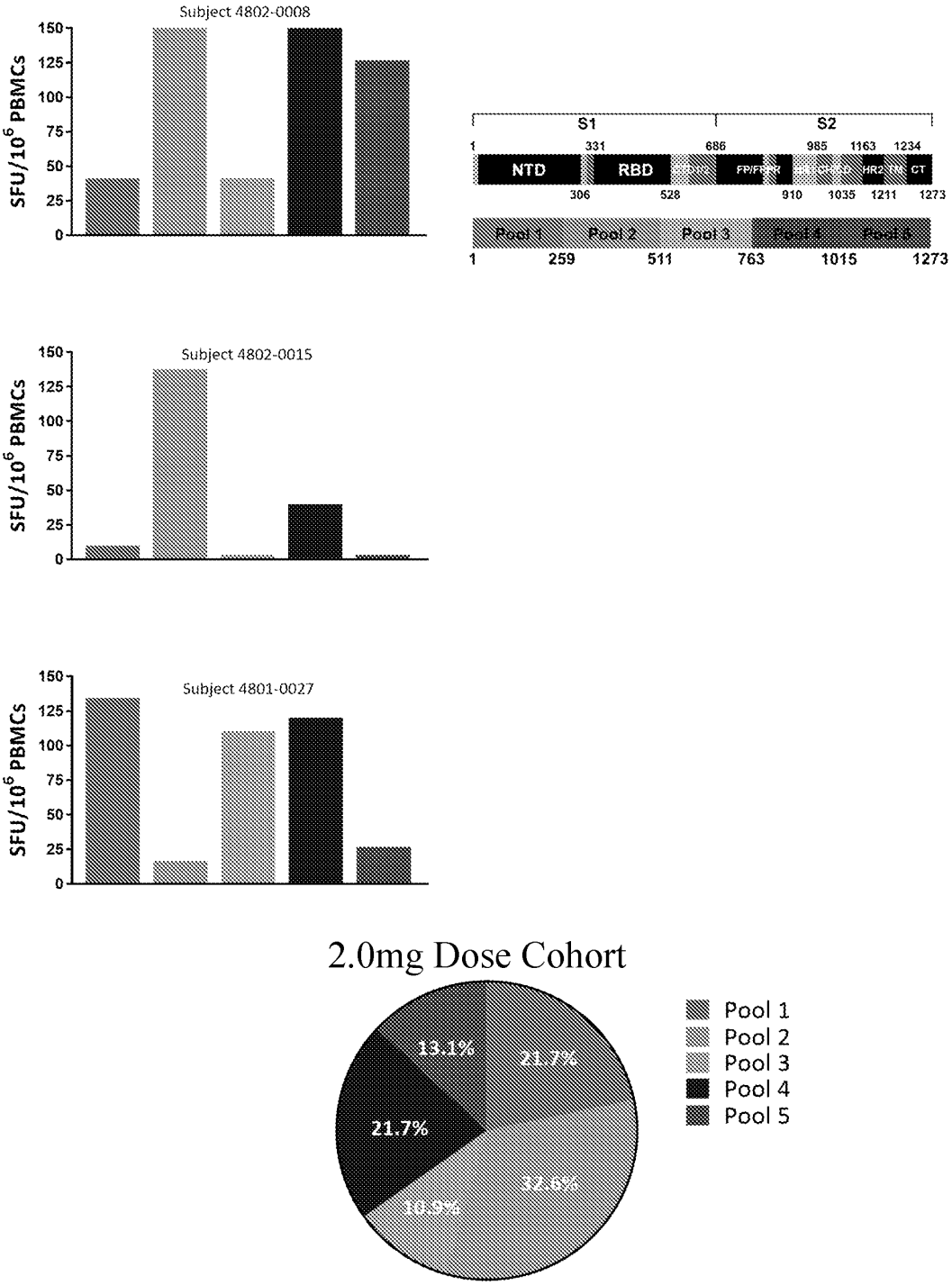

Subject 4802-0008
SFU/10^6 PBMCs
150
125
100
75
50
25
0
S1
S2
1
331
686
985
1163
1234
NTD
RBD
306
528
910
1035
1211
1273
Pool 1
Pool 2
Pool 3
Pool 4
Pool 5
1
259
511
763
1015
1273
Subject 4802-0015
Subject 4801-0027
2.0mg Dose Cohort
13.1%
21.7%
21.7%
32.6%
10.9%
Pool 1
Pool 2
Pool 3
Pool 4
Pool 5

Figure 18C

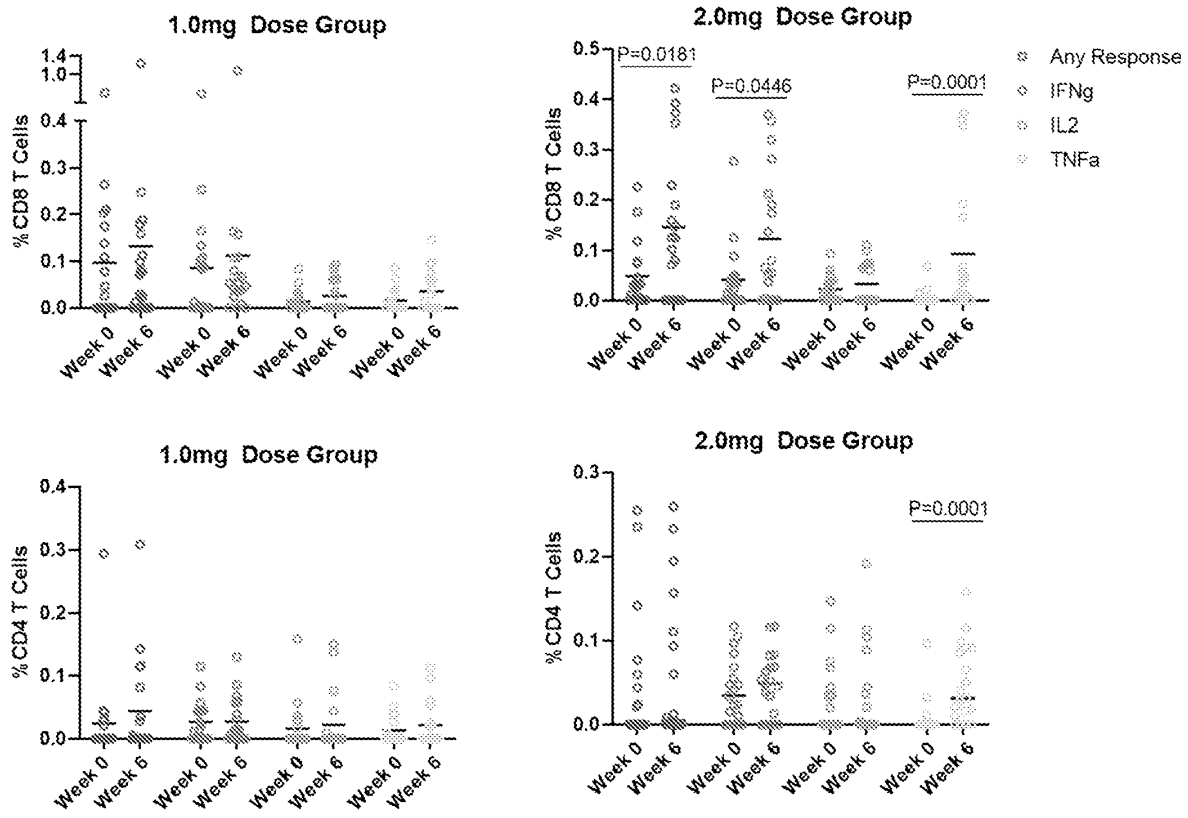

1.0mg Dose Group
% CD8 T Cells
Week 0
Week 6
2.0mg Dose Group
P=0.0181
P=0.0446
P=0.0001
Any Response
IFNg
IL2
TNFa
1.0mg Dose Group
% CD4 T Cells
2.0mg Dose Group
P=0.0001

Figure 18D

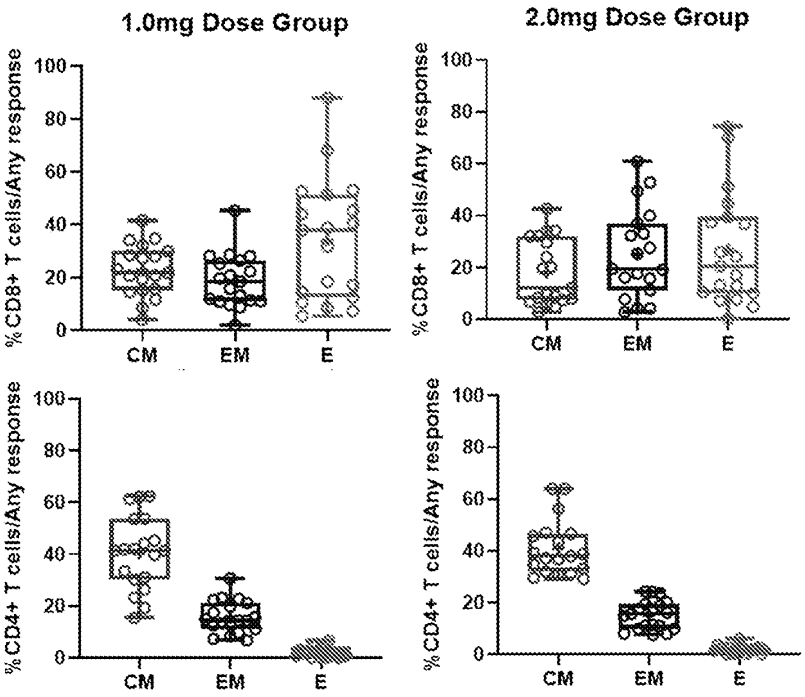

1.0mg Dose Group
2.0mg Dose Group
% CD8+ T cells/Any response
% CD4+ T cells/Any response
100
80
60
40
20
0
CM
EM
E

Figure 18E

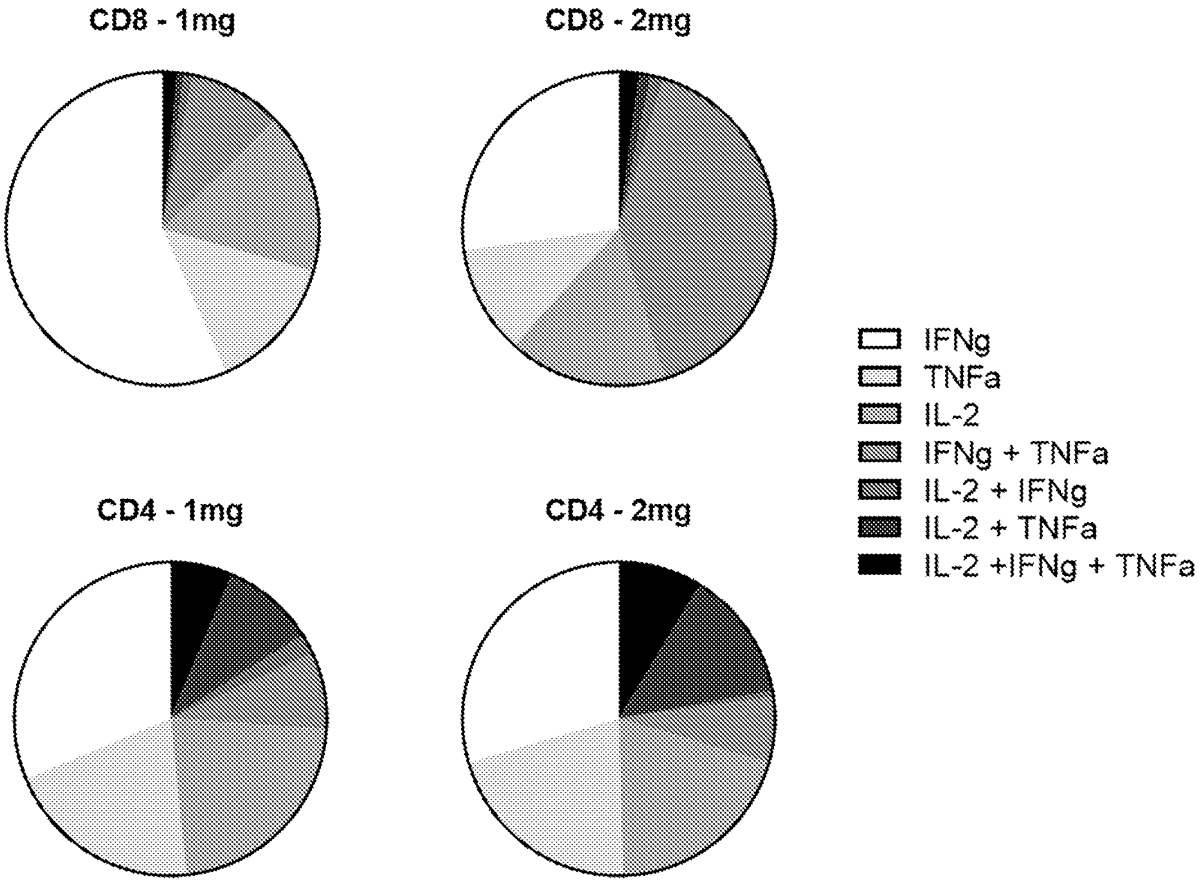
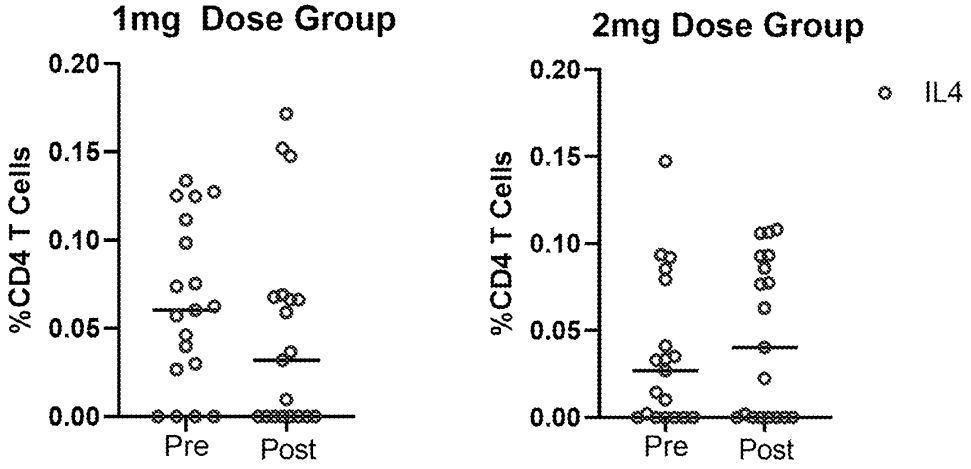

CD8 - 1mg
CD8 - 2mg
CD4 - 1mg
CD4 - 2mg
IFNg
TNFa
IL-2
IFNg + TNFa
IL-2 + IFNg
IL-2 + TNFa
IL-2 +IFNg + TNFa

Figure 18F



Updated:

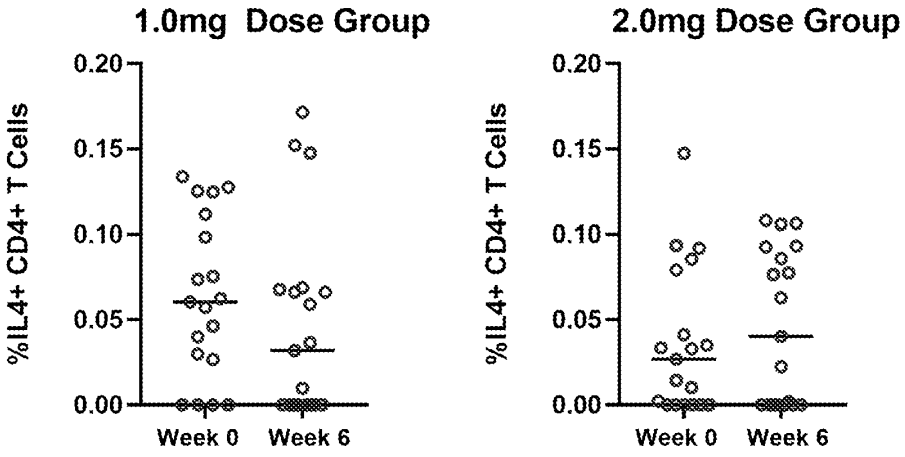


Figure 18G

2.0mg Dose Cohort

Subject ID	Pool 1	Pool 2	Pool 3	Pool 4	Pool 5
4801-0027	33.0%	4.1%	27.0%	29.4%	6.5%
4801-0028	3.3%	95.8%	0.0%	0.8%	0.0%
4801-0029	20.0%	0.0%	80.0%	0.0%	0.0%
4802-0013	4.7%	57.8%	4.7%	23.4%	9.4%
4802-0014	27.3%	31.8%	11.4%	13.6%	15.9%
4802-0015	5.1%	70.9%	1.7%	20.6%	1.7%
4801-0011	9.2%	62.2%	5.0%	20.2%	3.4%
4801-0016	24.2%	29.3%	3.0%	19.2%	24.2%
4801-0017	22.6%	17.0%	5.7%	30.2%	24.5%
4801-0026	31.3%	18.7%	18.7%	31.3%	0.0%
4802-0005	26.1%	34.8%	0.0%	26.1%	13.0%
4802-0012	10.3%	10.3%	37.9%	20.7%	20.7%
4802-0019	0.0%	50.0%	50.0%	0.0%	0.0%
4802-0018	11.5%	9.6%	3.2%	3.8%	71.8%
4802-0020	8.0%	6.1%	36.0%	5.3%	44.7%
4802-0021	0.0%	11.5%	53.8%	23.1%	11.5%
4802-0008	6.7%	34.7%	6.7%	31.4%	20.6%
4802-0016	16.3%	16.9%	10.2%	13.3%	43.4%
	Pool 1	Pool 2	Pool 3	Pool 4	Pool 5

Proportion of Response

100.00%	Highest
75.00%	
50.00%	Middle
25.00%	
0.00%	Lowest

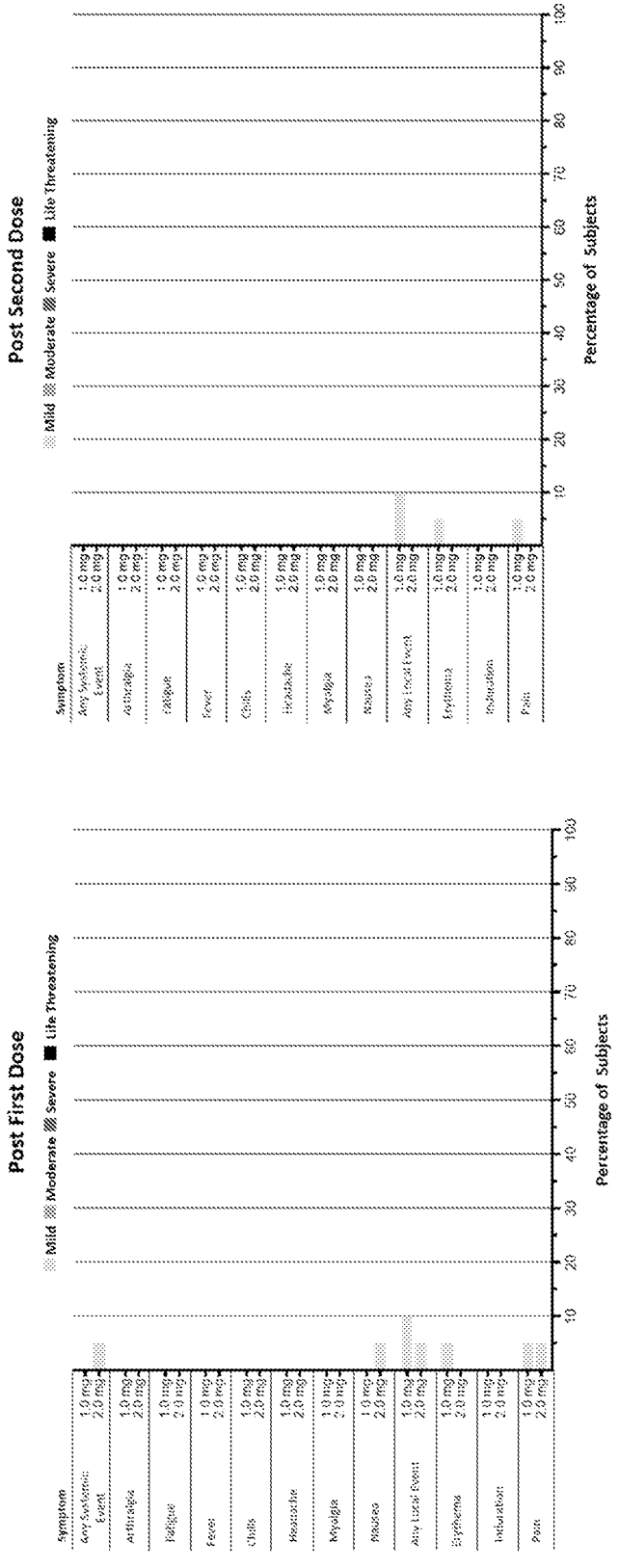

Post First Dose
Mild
Moderate
Severe
Life Threatening
Symptom
Any Systemic Event
Arthralgia
Fatigue
Fever
Chills
Headache
Myalgia
Nausea
Any Local Event
Erythema
Induration
Pain
1.0 mg
2.0 mg
Percentage of Subjects
Post Second Dose
Mild
Moderate
Severe
Life Threatening
Symptom
Any Systemic Event
Arthralgia
Fatigue
Fever
Chills
Headache
Myalgia
Nausea
Any Local Event
Erythema
Induration
Pain
1.0 mg
2.0 mg
Percentage of Subjects

Figure 19

Figure 20

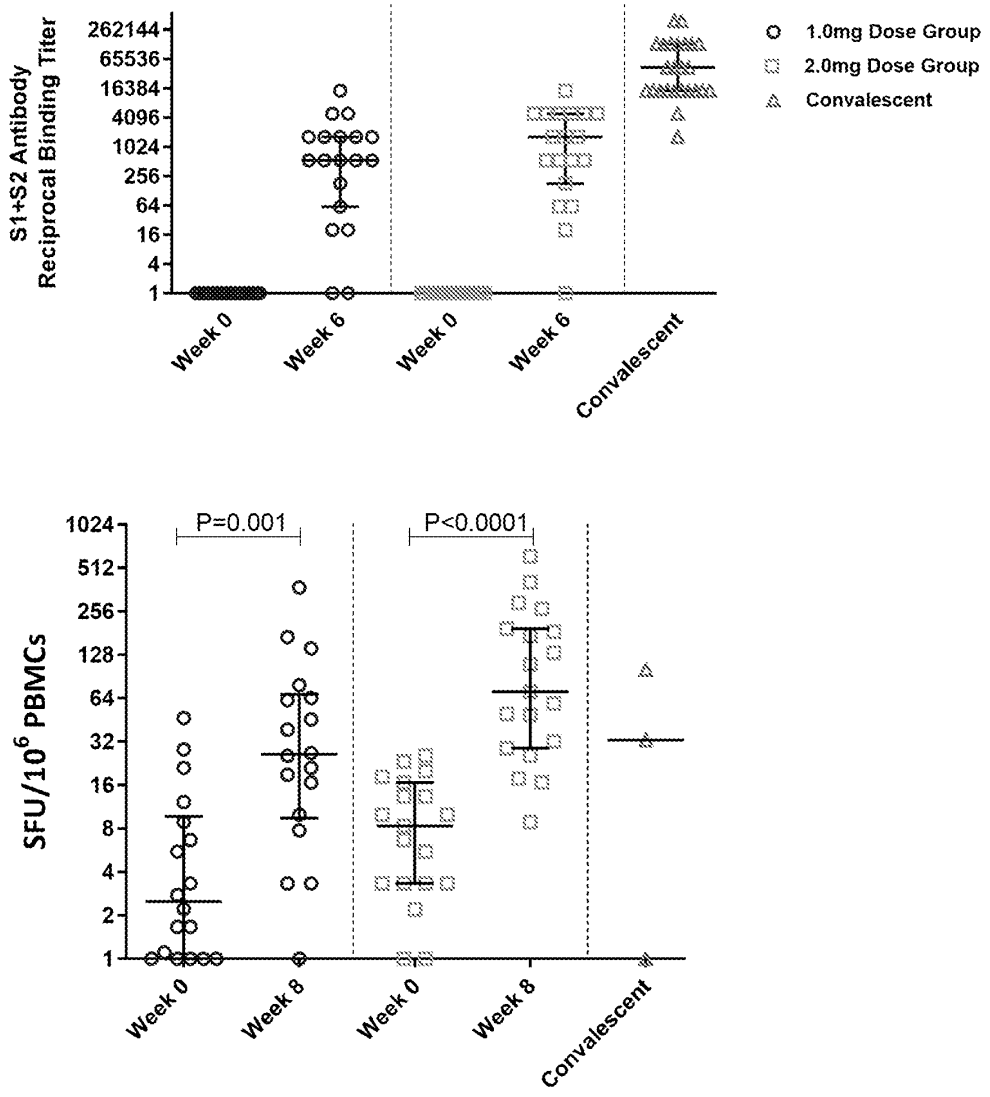
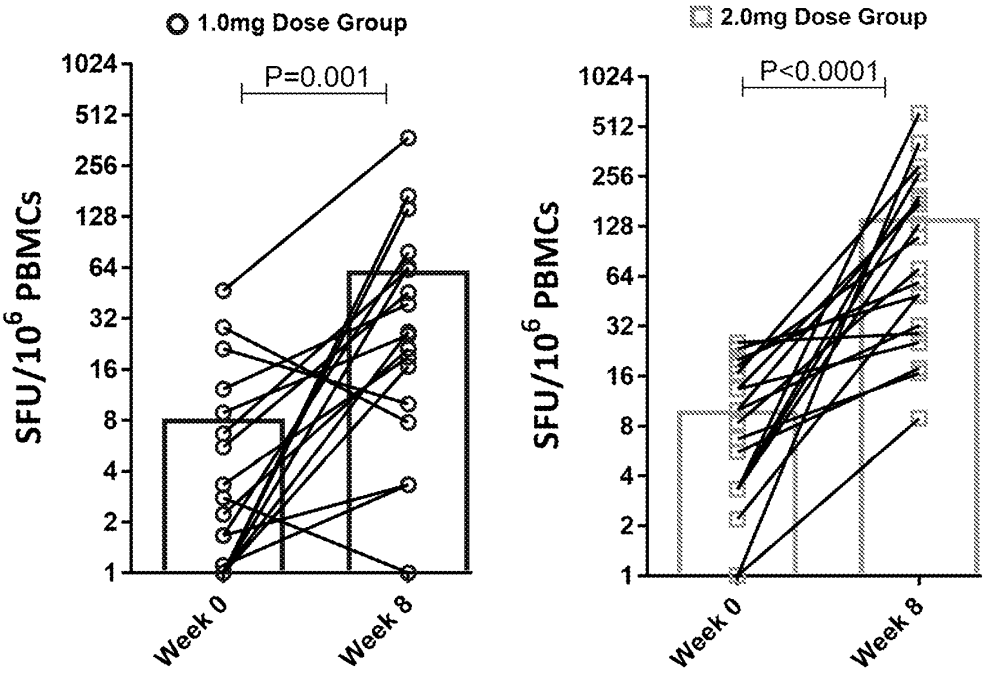

S1+S2 Antibody Reciprocal Binding Titer
262144
65536
16384
4096
1024
256
64
16
4
1
Week 0
Week 6
Week 0
Week 6
Convalescent
1.0mg Dose Group
2.0mg Dose Group
Convalescent
SFU/10^6 PBMCs
1024
512
256
128
64
32
16
8
4
2
1
P=0.001
P<0.0001
Week 0
Week 8
Week 0
Week 8
Convalescent

Figure 21


1.0mg Dose Group
2.0mg Dose Group
P=0.001
P<0.0001
SFU/10^6 PBMCs
1024
512
256
128
64
32
16
8
4
2
1
Week 0
Week 8

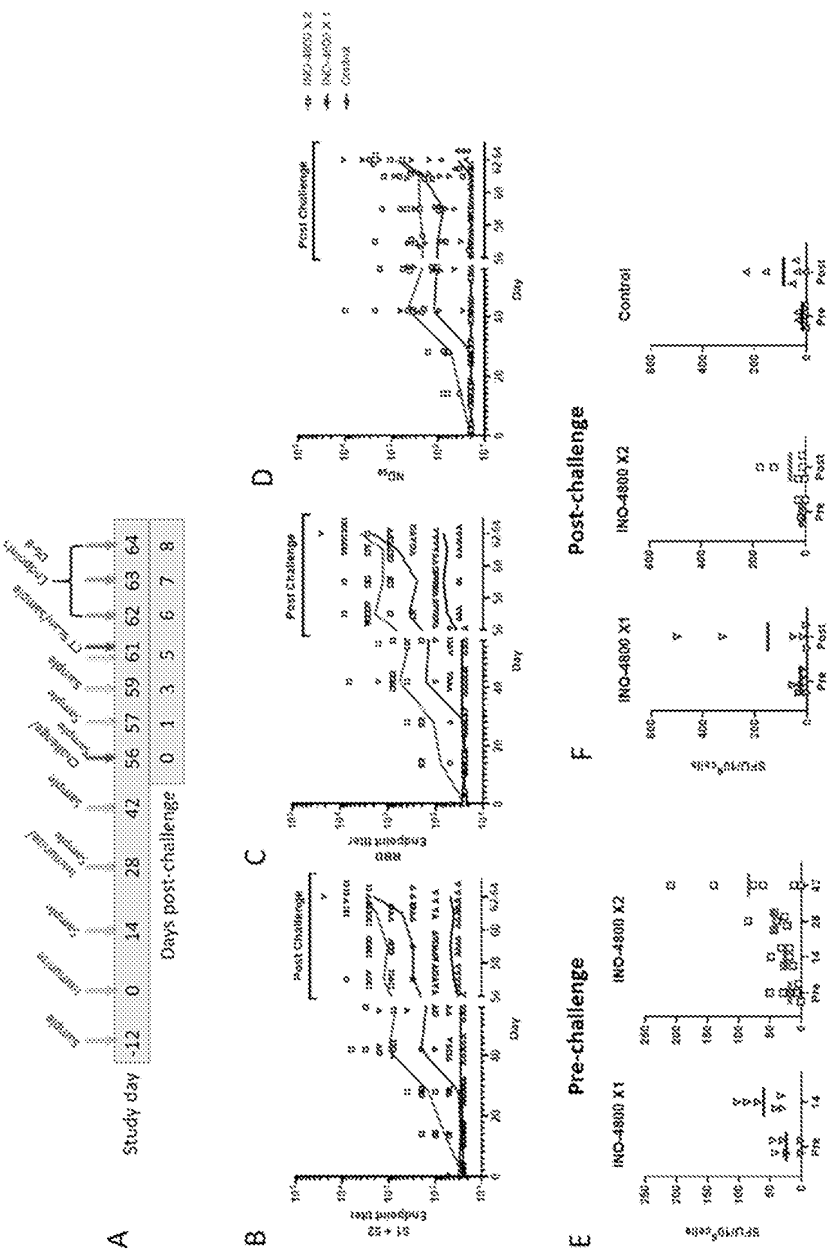

A
Study day
-12
0
14
28
42
56
57
59
61
62
63
64
0
1
3
5
6
7
8
Days post-challenge
B
C
D
Post Challenge
Day
INO-4800 X2
INO-4800 X1
Control
E
Pre-challenge
F
Post-challenge
INO-4800 X1
INO-4800 X2
Control
Pre
Post

Fig. 22

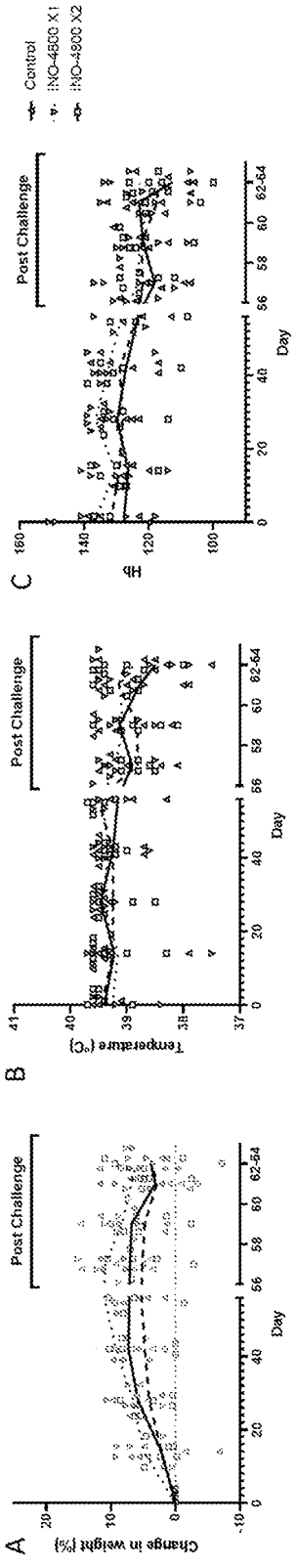
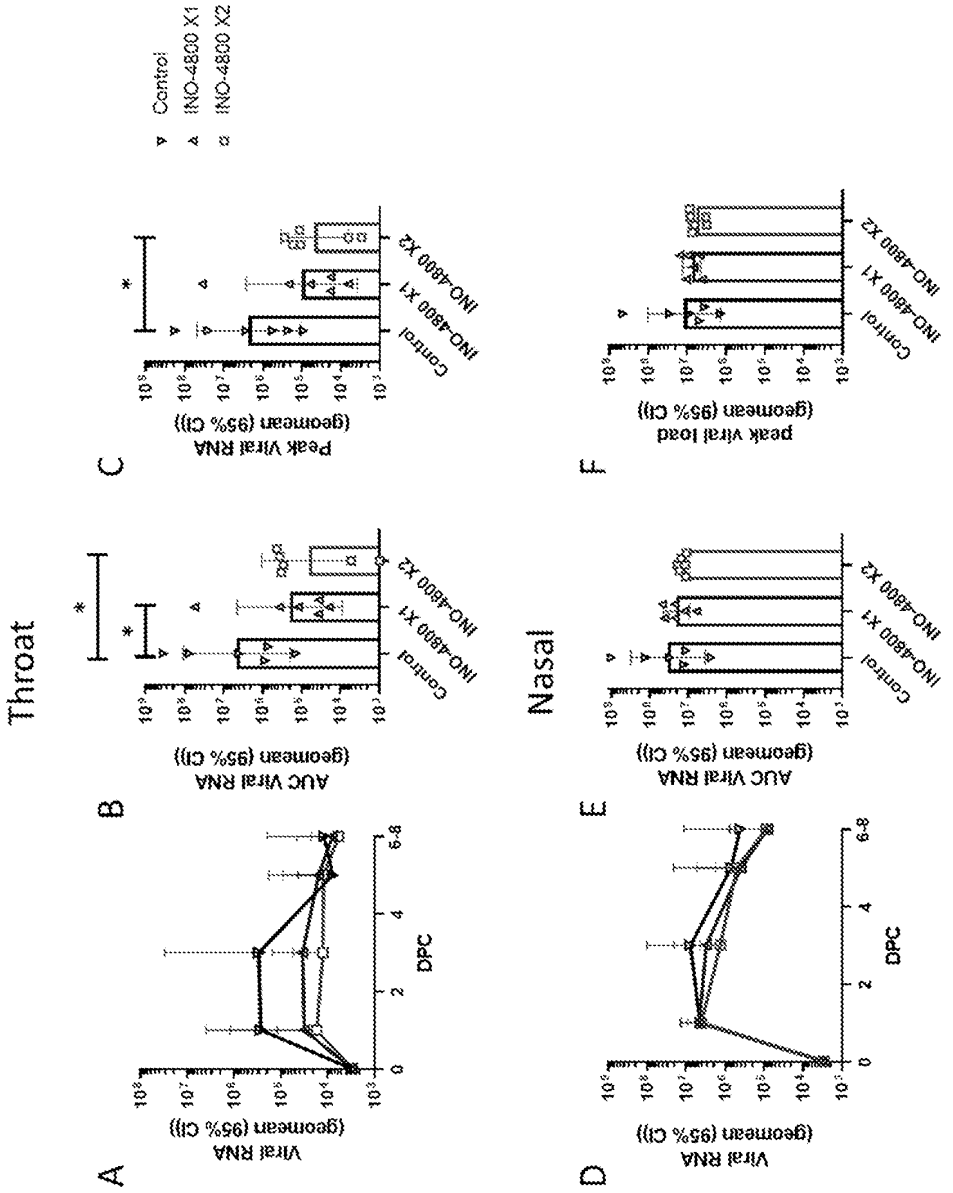

A
Change in weight (%)
Post Challenge
Day
B
Temperature (°C)
Post Challenge
Day
C
Hb
Post Challenge
Day
Control
iNO-4800 X1
iNO-4800 X2

Fig. 23

Figure 24


Throat
Nasal
A
B
C
D
E
F
Viral RNA (geomean (95% CI))
AUC Viral RNA (geomean (95% CI))
Peak Viral RNA (geomean (95% CI))
peak viral load (geomean (95% CI))
DPC
Control
INO-4800 X1
INO-4800 X2
*

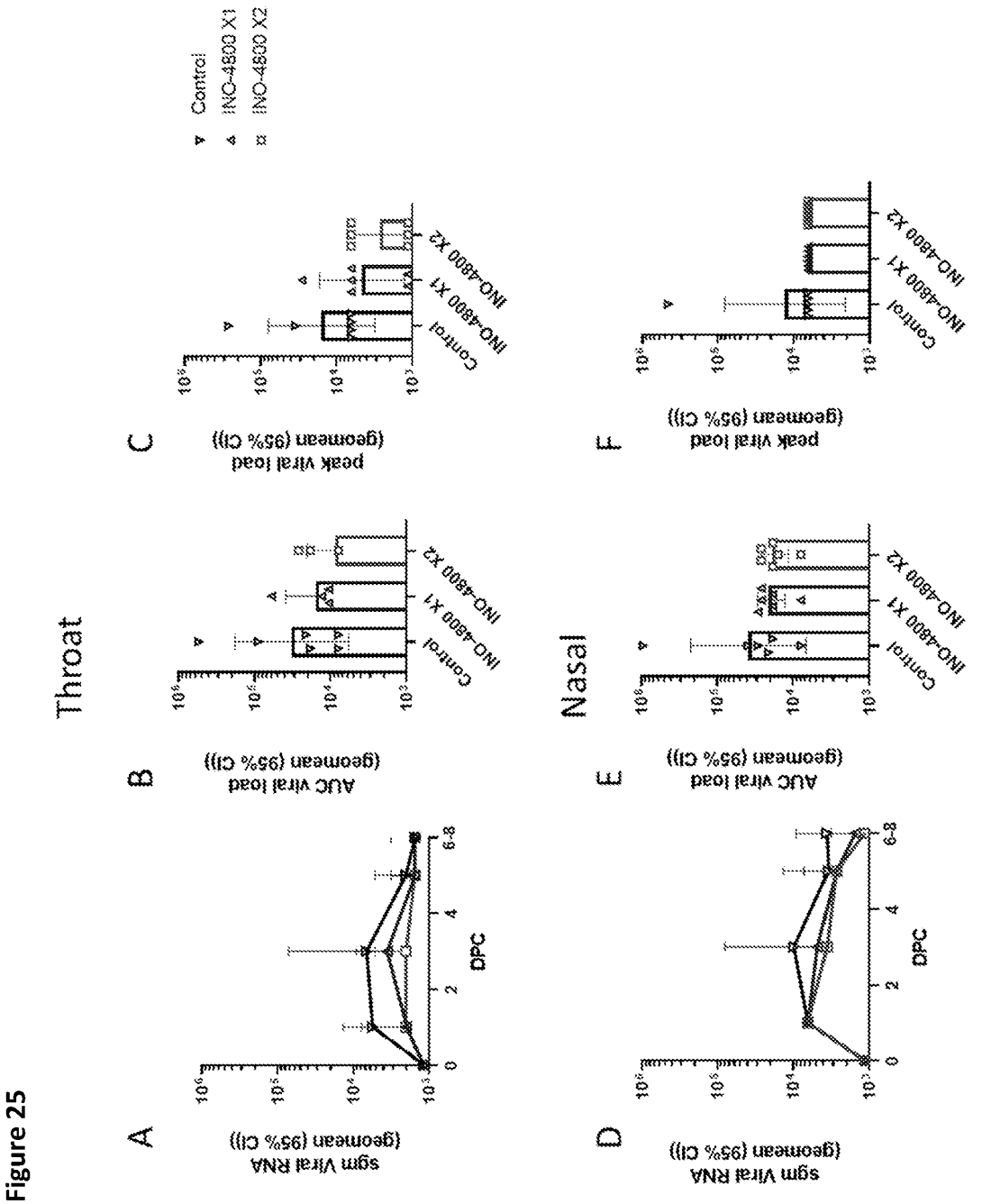

Throat
Nasal
A
B
C
D
E
F
sgm Viral RNA (geomean (95% CI))
AUC viral load (geomean (95% CI))
peak viral load (geomean (95% CI))
DPC
Control
INO-4800 X1
INO-4800 X2

Figure 25

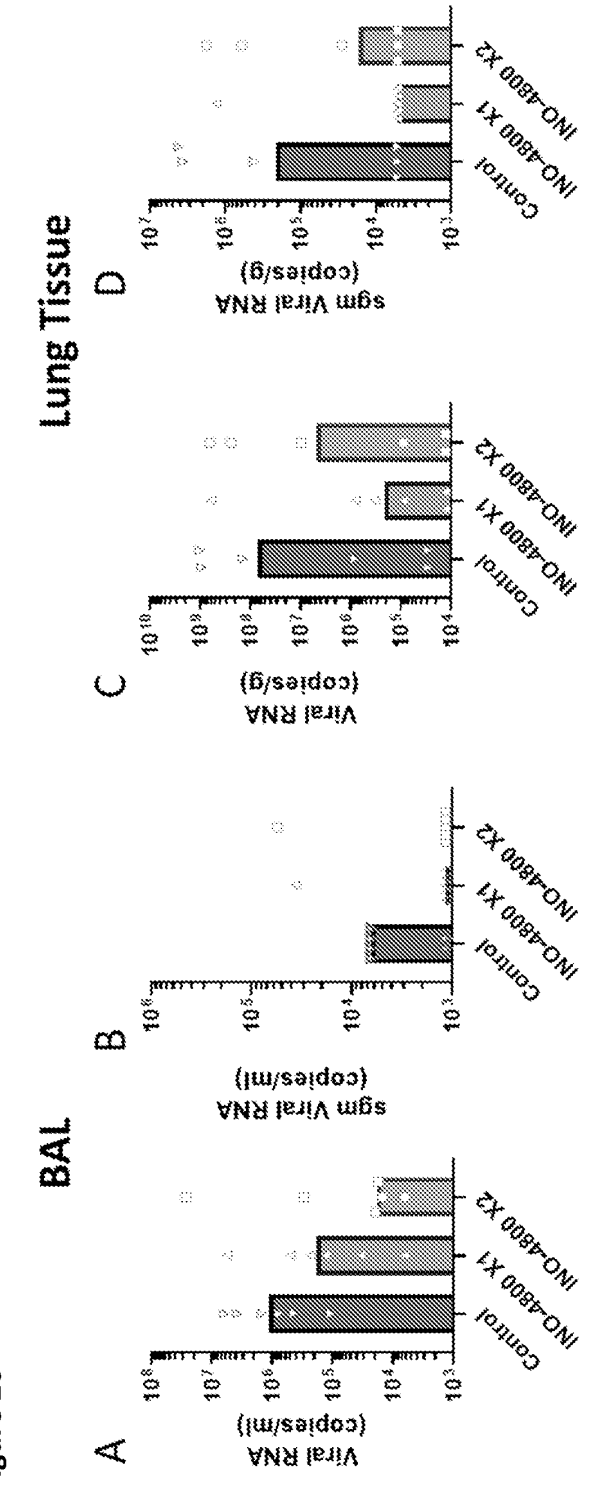

BAL
Lung Tissue
A
Viral RNA
(copies/ml)
B
sgm Viral RNA
(copies/ml)
C
Viral RNA
(copies/g)
D
sgm Viral RNA
(copies/g)
Control
INO-4800 X1
INO-4800 X2

Figure 26

Figure 27

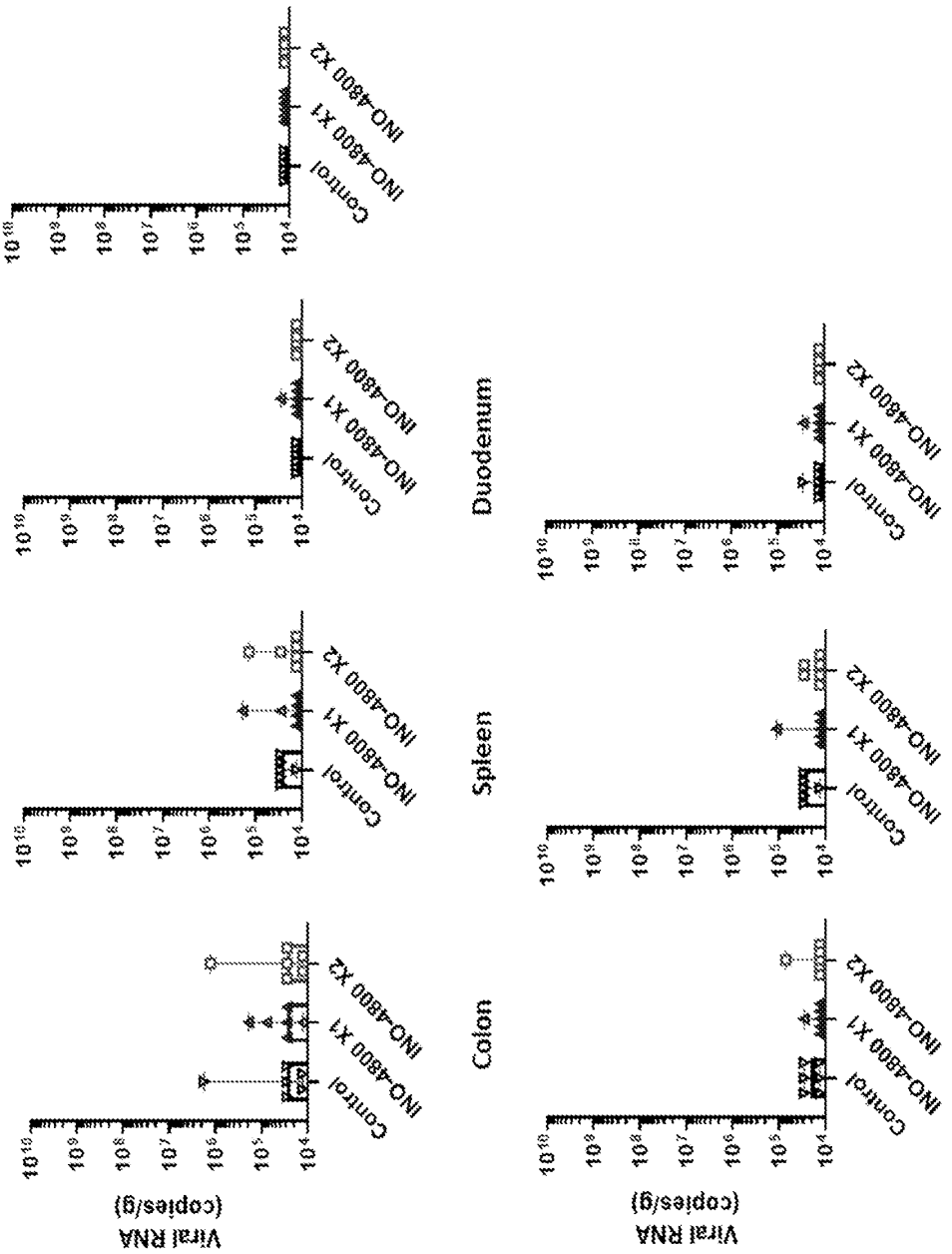

Tonsil
Trachea
Kidney
Liver
Colon
Spleen
Duodenum
Viral RNA (copies/g)
Control
INO-4800 X1
INO-4800 X2

Figure 28

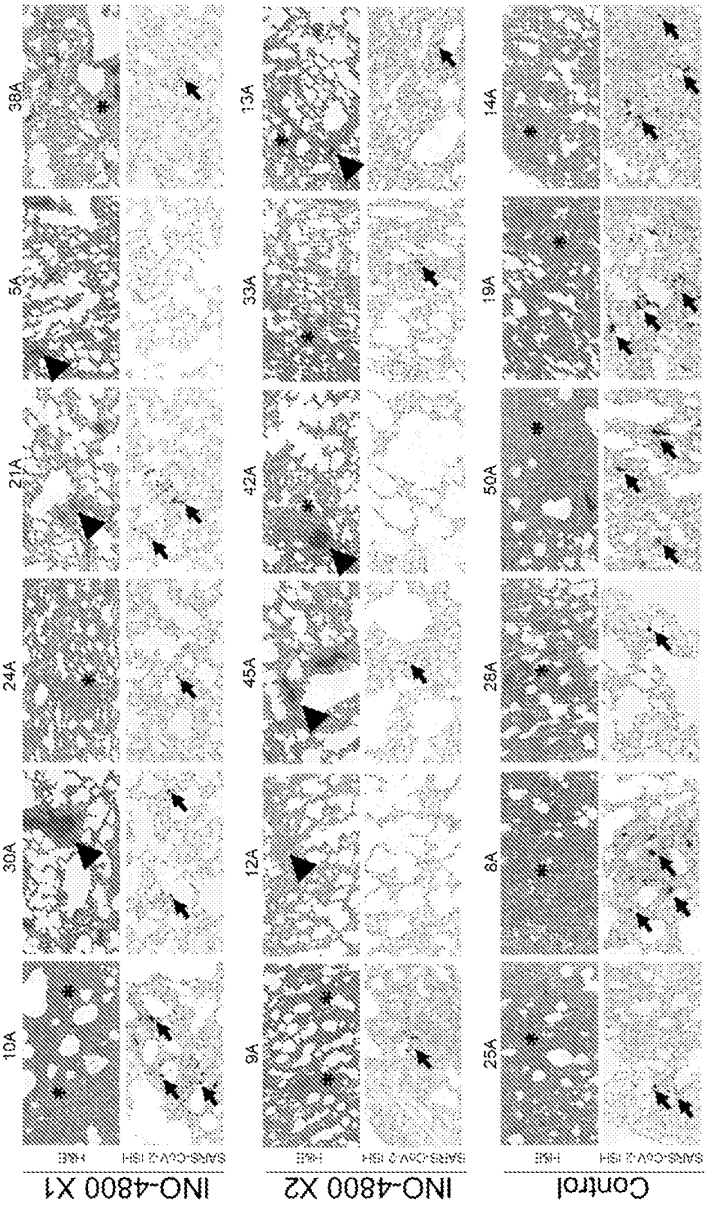

INO-4800 X1
INO-4800 X2
Control
H&E
SARS-CoV-2 ISH
10A
30A
24A
21A
5A
38A
9A
12A
45A
42A
33A
13A
25A
8A
28A
50A
19A
14A

Figure 29

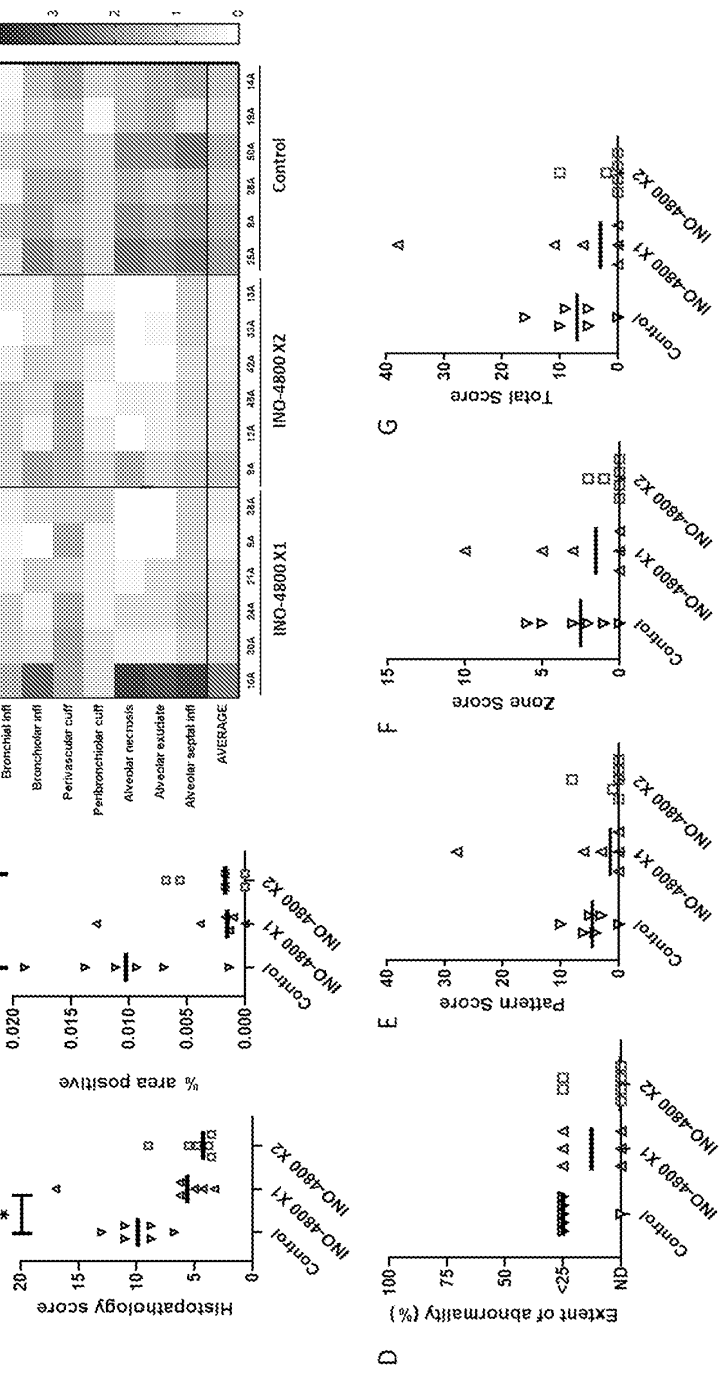

A
HP
Histopathology score
Control
INO-4800 X1
INO-4800 X2
B
ISH
% area positive
C
Lung histopathology score
Bronchial infl
Bronchiolar infl
Perivascular cuff
Peribronchiolar cuff
Alveolar necrosis
Alveolar exudate
Alveolar septal infl
AVERAGE
INO-4800 X1
INO-4800 X2
Control
D
Extent of abnormality (%)
ND
<25
E
Pattern Score
F
Zone Score
G
Total Score

Figure 30

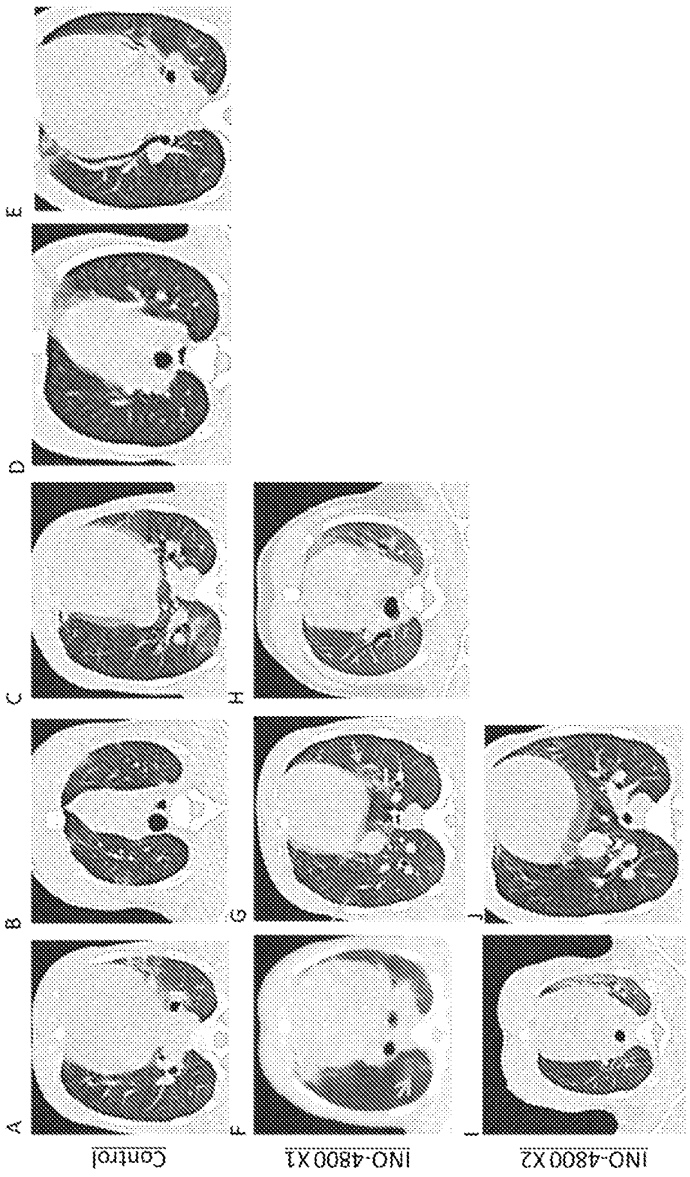


Figure 31

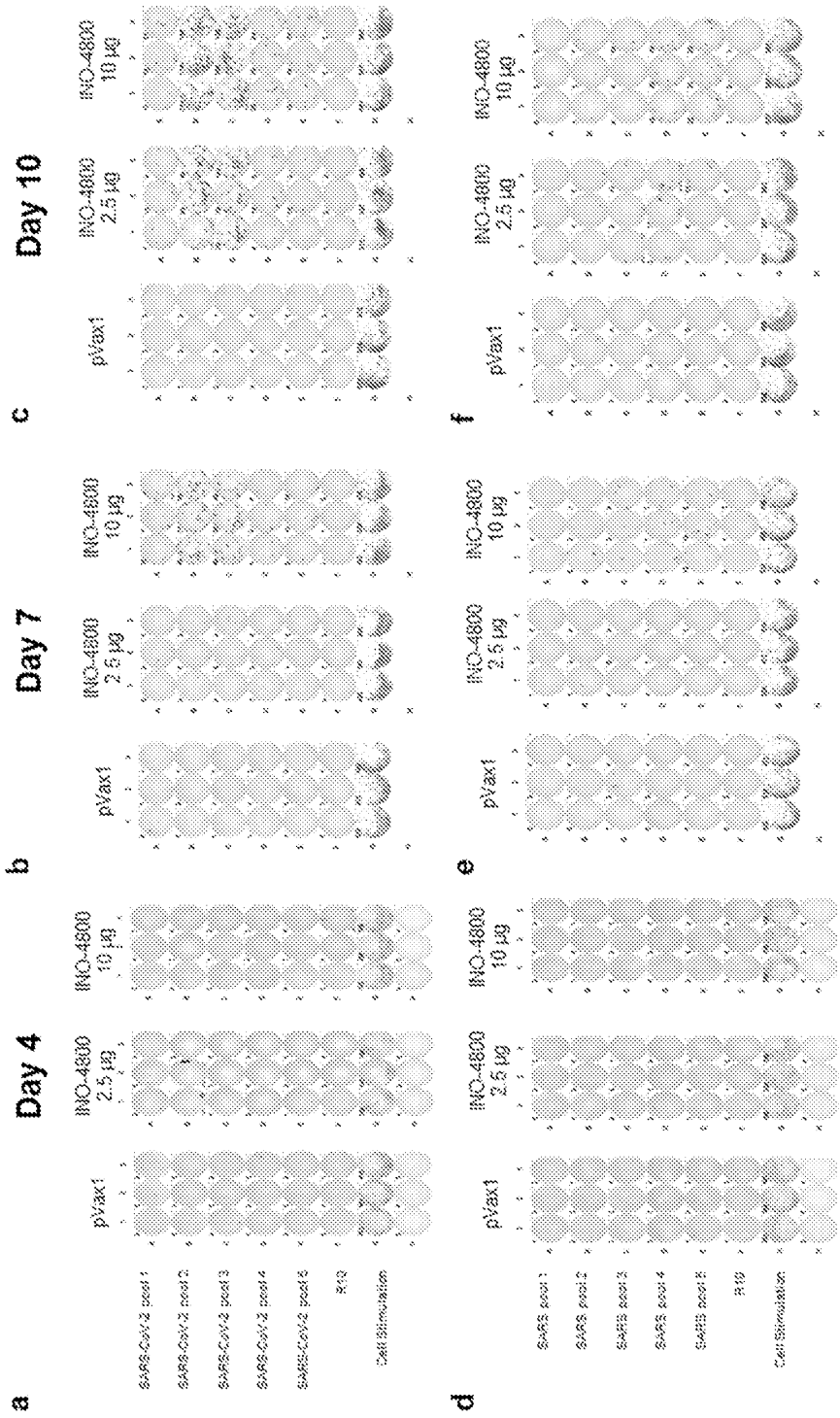
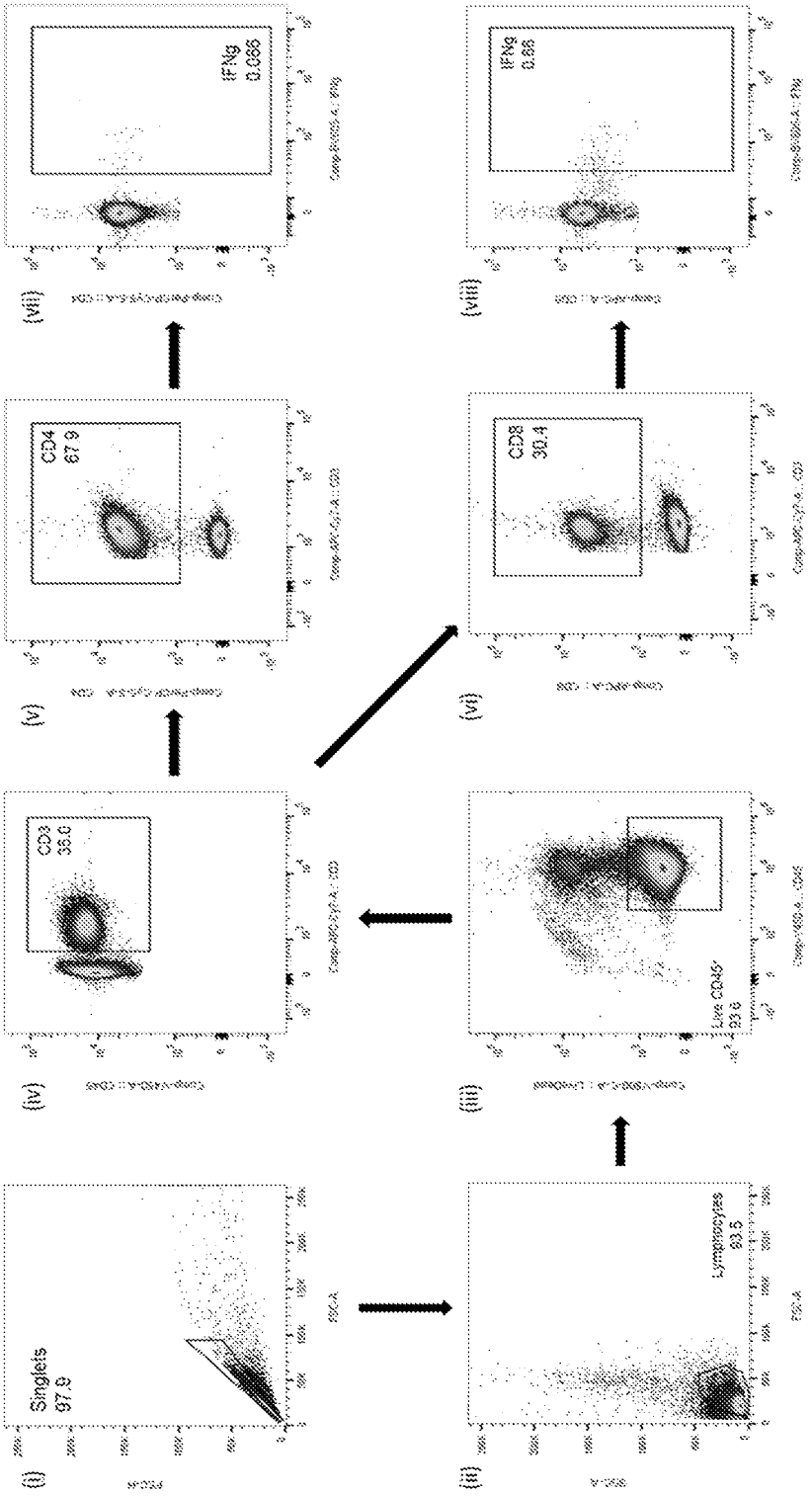

a
Day 4
pVax1
INO-4800 2.5 µg
INO-4800 10 µg
SARS-CoV-2 pool 1
SARS-CoV-2 pool 2
SARS-CoV-2 pool 3
SARS-CoV-2 pool 4
SARS-CoV-2 pool 5
S1S2
Cell Stimulation
b
Day 7
c
Day 10
d
SARS pool 1
SARS pool 2
SARS pool 3
SARS pool 4
SARS pool 5
e
f

Figure 32A
a


(i)
Singlets
97.9
(ii)
Lymphocytes
83.5
(iii)
Live CD45+
93.6
(iv)
CD3
38.6
(v)
CD4
67.9
(vi)
CD8
30.4
(vii)
IFNg
0.086
(viii)
IFNg
0.88

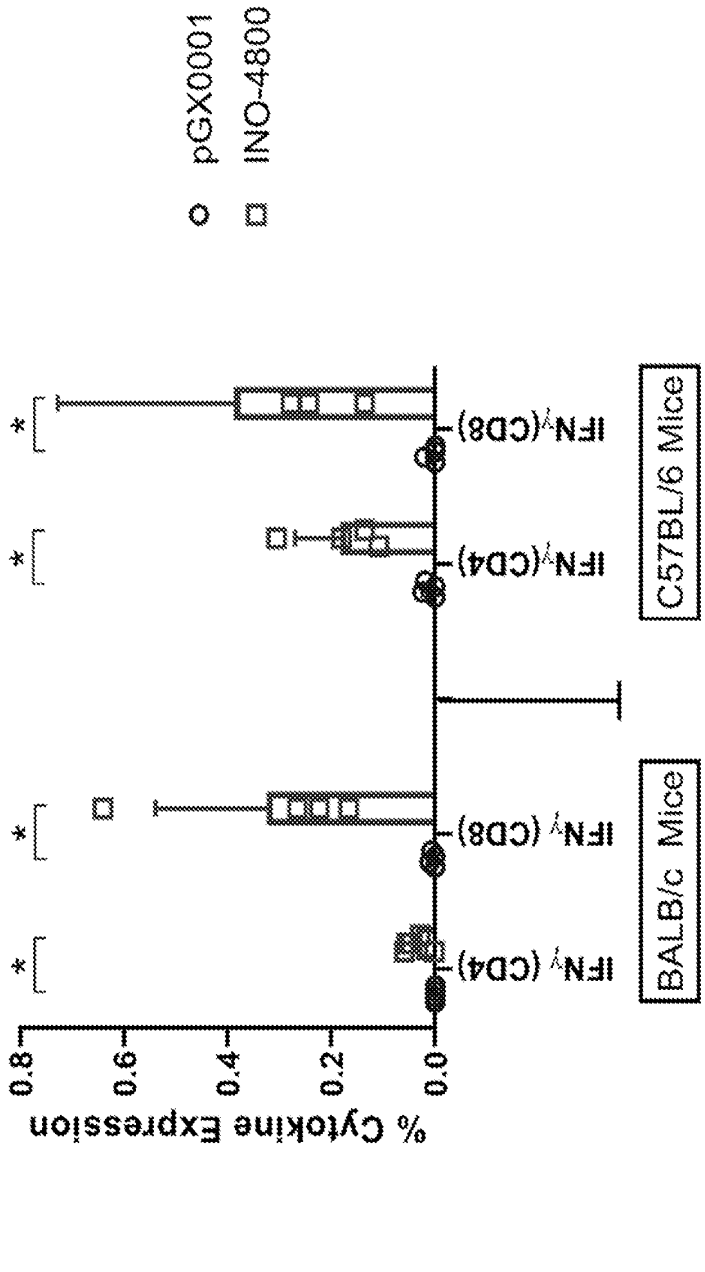

b
pGX0001
INO-4800
% Cytokine Expression
0.0
0.2
0.4
0.6
0.8
IFNγ (CD4)
IFNγ (CD8)
IFNγ (CD4)
IFNγ (CD8)
BALB/c Mice
C57BL/6 Mice
*
*
*
*

Figure 32B

Figure 33A

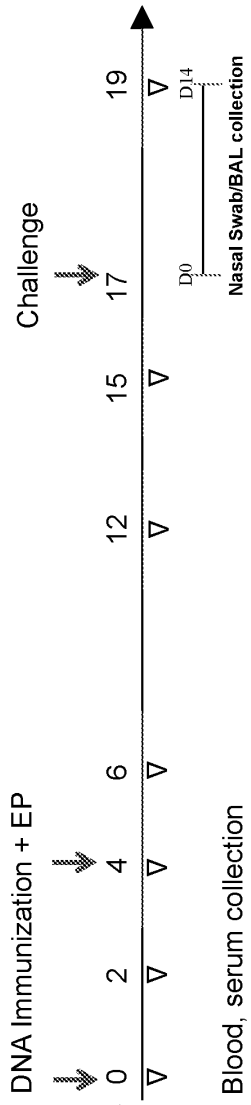


Figure 33B

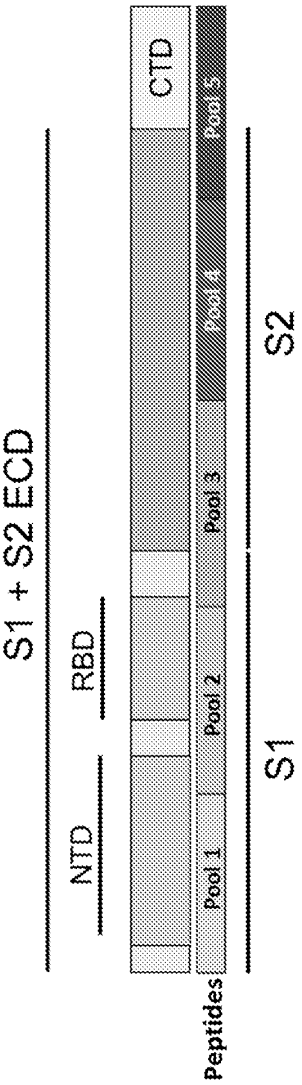


Figure 33C

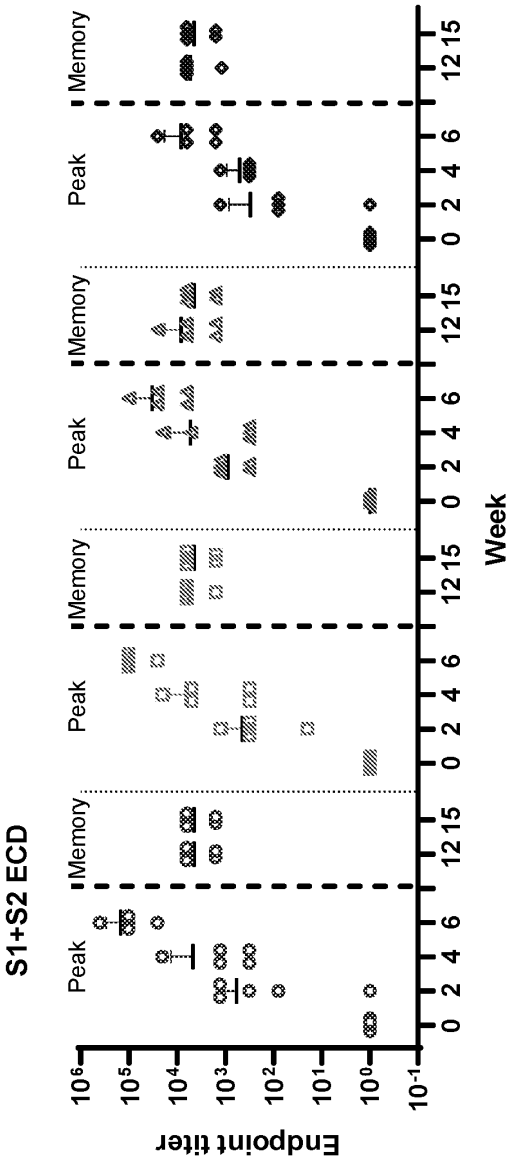

S1+S2 ECD
Endpoint titer
10^6
10^5
10^4
10^3
10^2
10^1
10^0
10^{-1}
Peak
Memory
Peak
Memory
Peak
Memory
0 2 4 6
12 15
Week

Figure 33D

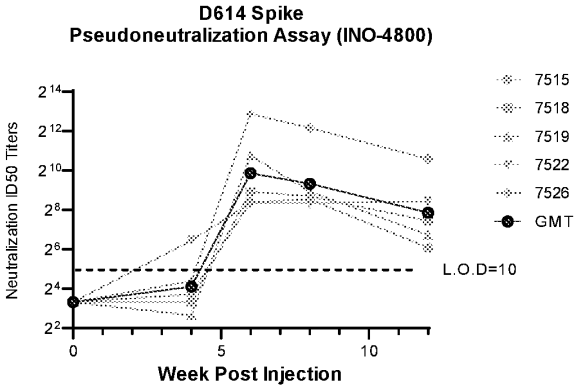


Figure 33E

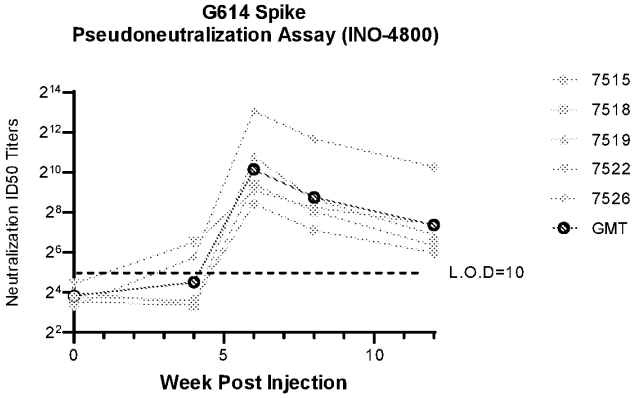


Figure 33F

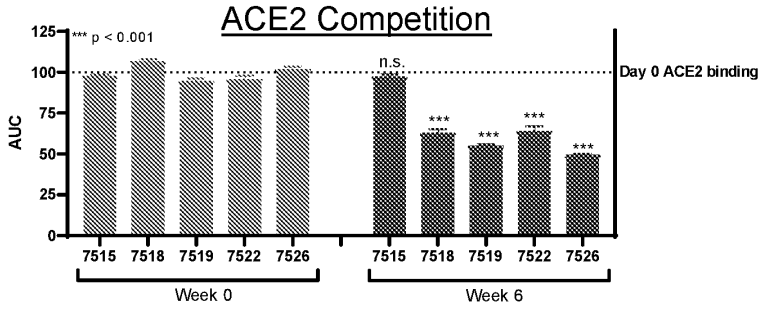


Figure 33G

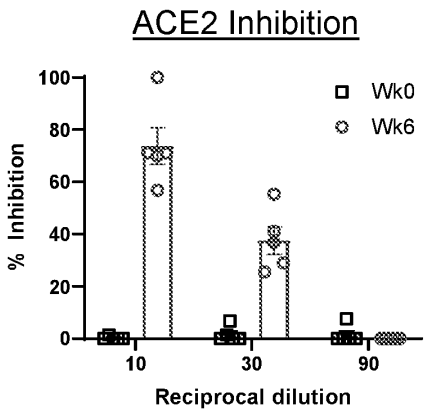


Figure 33H

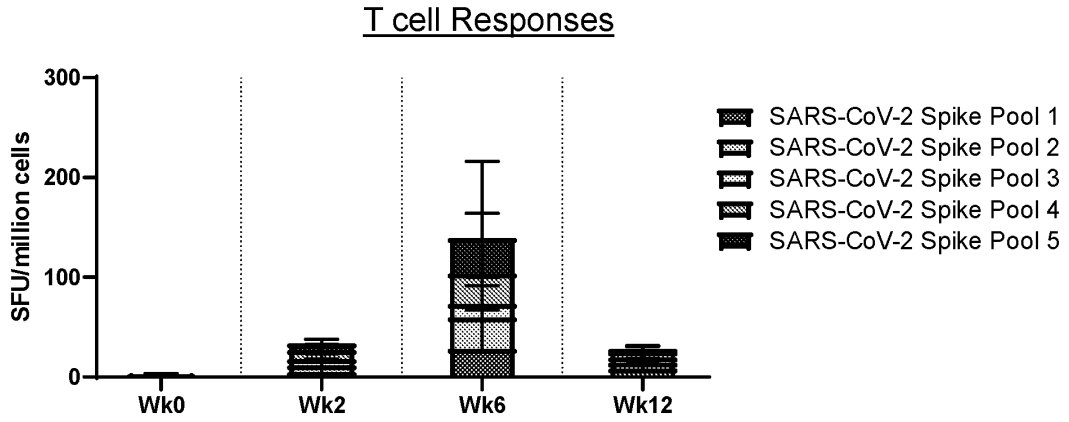


Figure 34

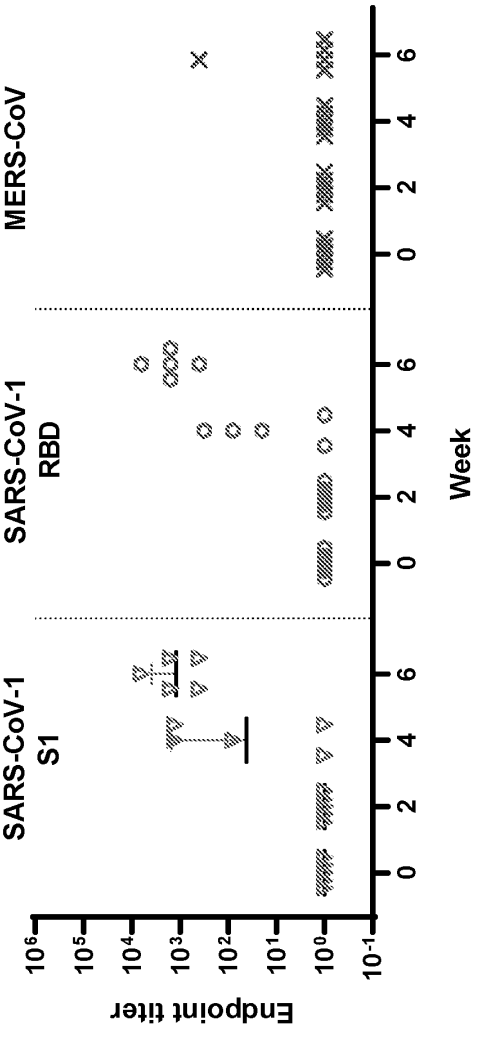

SARS-CoV-1
S1
SARS-CoV-1
RBD
MERS-CoV
Endpoint titer
Week
10^{6}
10^{5}
10^{4}
10^{3}
10^{2}
10^{1}
10^{0}
10^{-1}
0
2
4
6
0
2
4
6
0
2
4
6

Figure 35

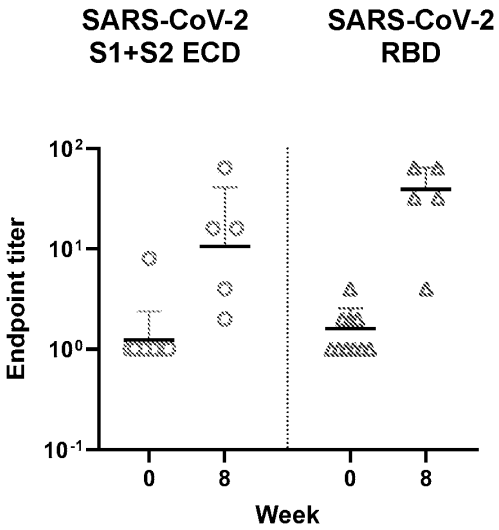

SARS-CoV-2
S1+S2 ECD
SARS-CoV-2
RBD
Endpoint titer
10^2
10^1
10^0
10^{-1}
0
8
0
8
Week

Figure 36A

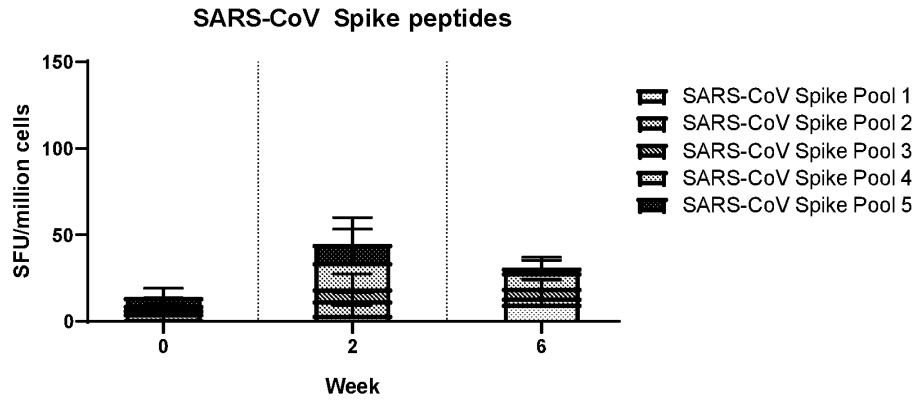


Figure 36B

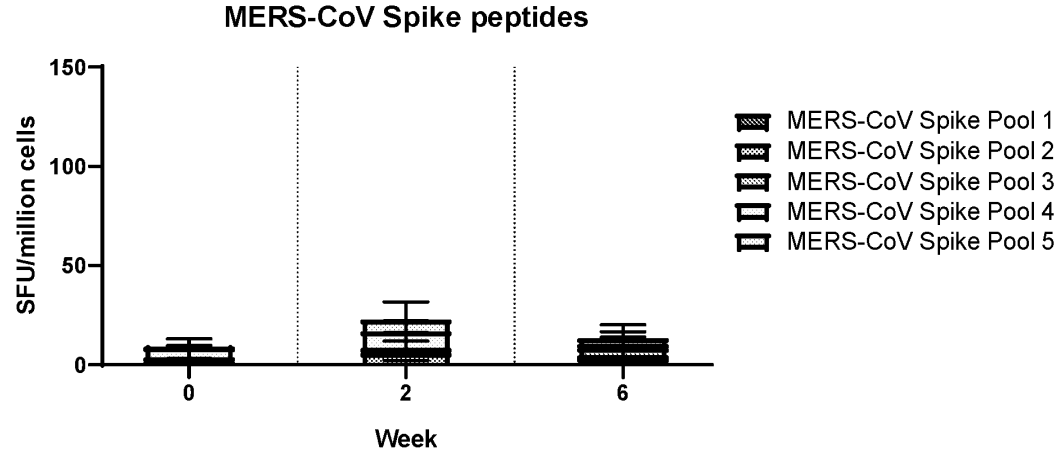


Figure 37A

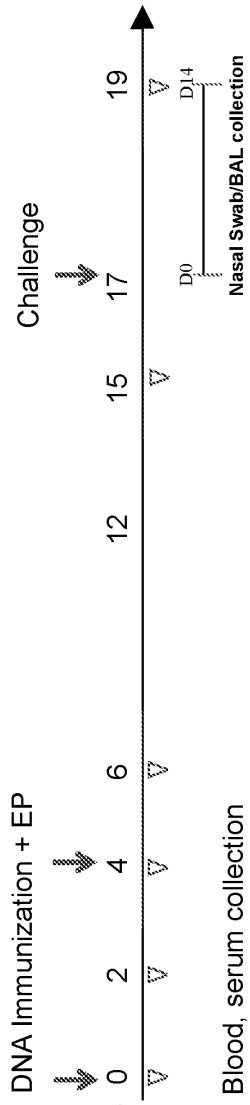

DNA Immunization + EP
Challenge
Weeks 0 2 4 6 12 15 17 19
D0
D14
Nasal Swab/BAL collection
Blood, serum collection

Figure 37B

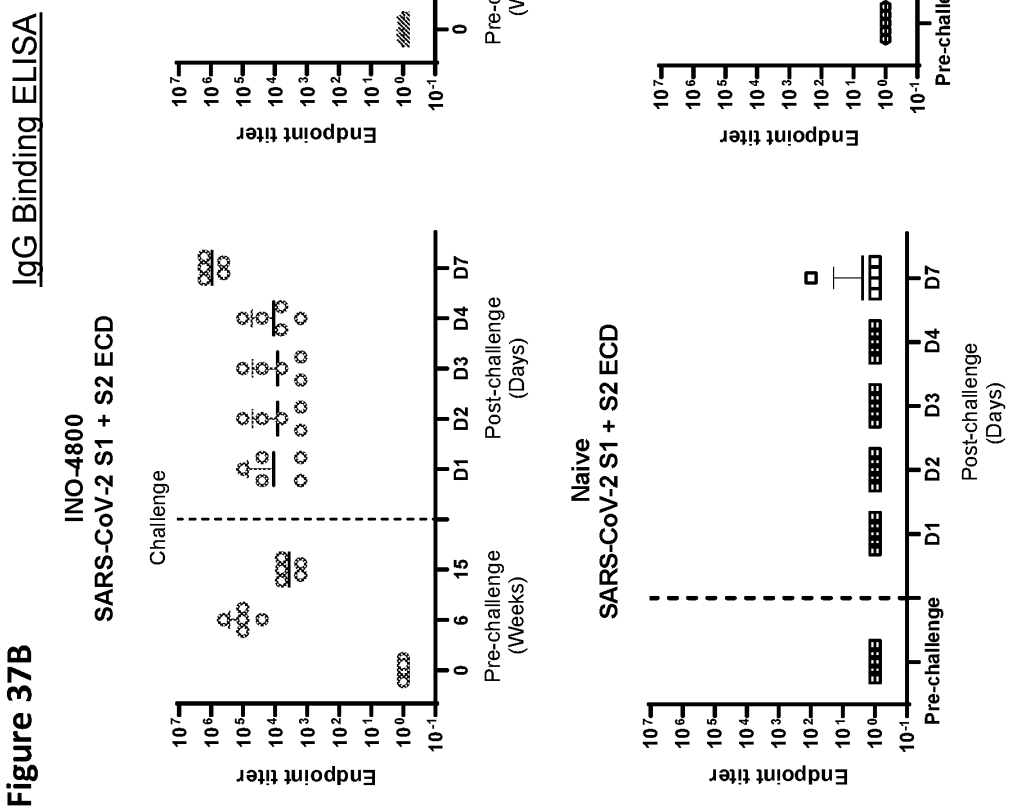

IgG Binding ELISA
INO-4800
SARS-CoV-2 S1 + S2 ECD
Challenge
Endpoint titer
Pre-challenge (Weeks)
Post-challenge (Days)
INO-4800
SARS-CoV-2 RBD
Naive
SARS-CoV-2 S1 + S2 ECD
SARS-CoV-2 RBD
Pre-challenge
Post-Challenge (Days)
D1
D2
D3
D4
D7

Figure 37C

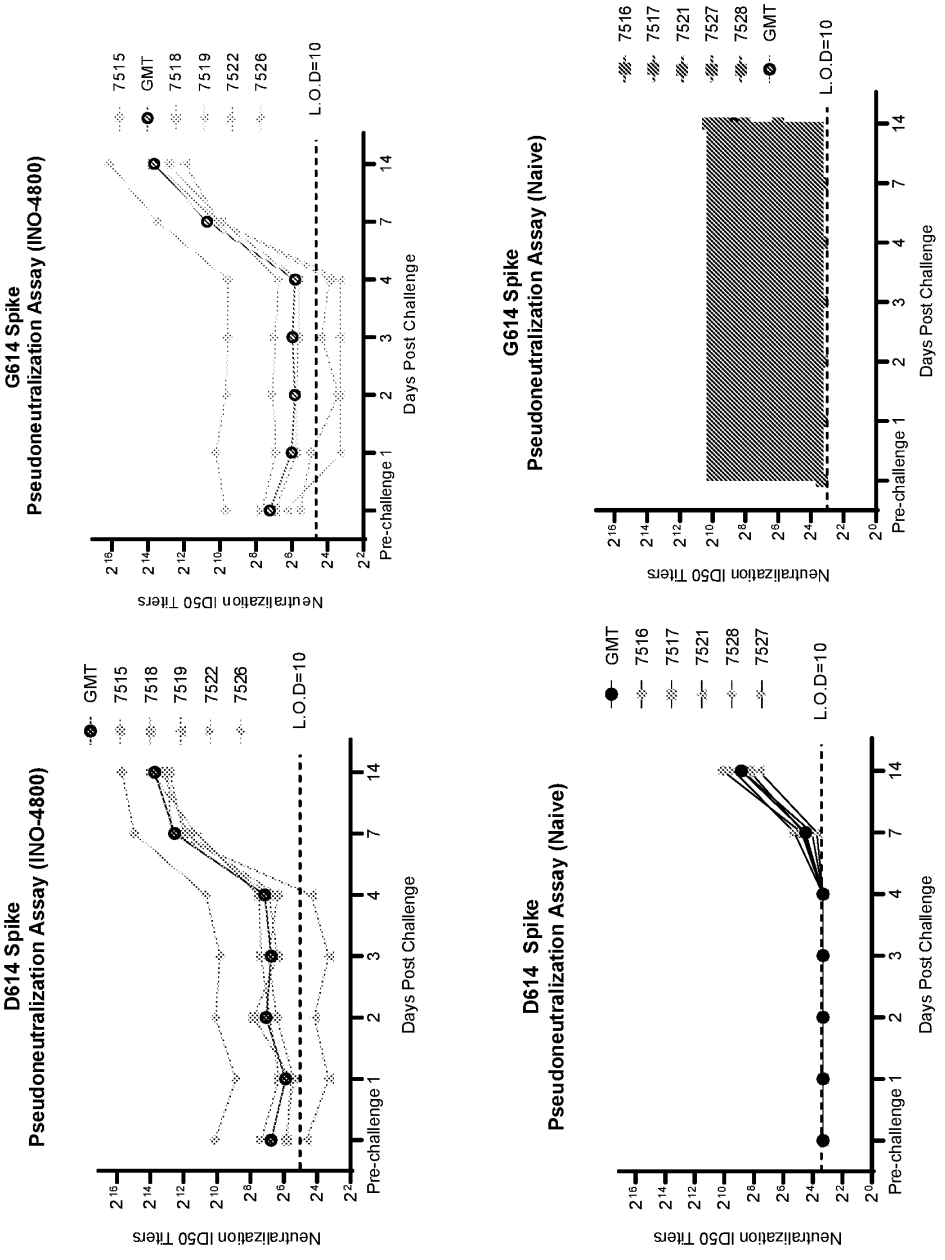

D614 Spike
Pseudoneutralization Assay (INO-4800)
G614 Spike
Pseudoneutralization Assay (INO-4800)
D614 Spike
Pseudoneutralization Assay (Naive)
G614 Spike
Pseudoneutralization Assay (Naive)
Neutralization ID50 Titers
Days Post Challenge
Pre-challenge 1
L.O.D=10
GMT
7515
7516
7517
7518
7519
7521
7522
7526
7527
7528

Figure 38

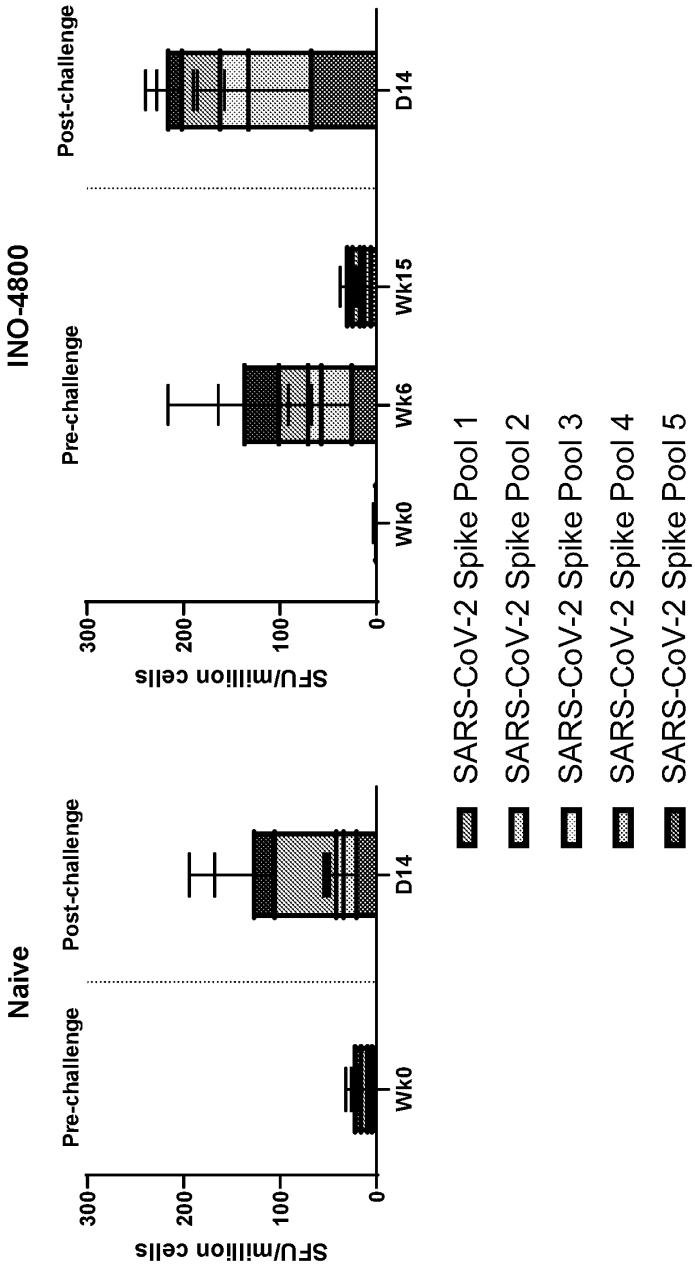
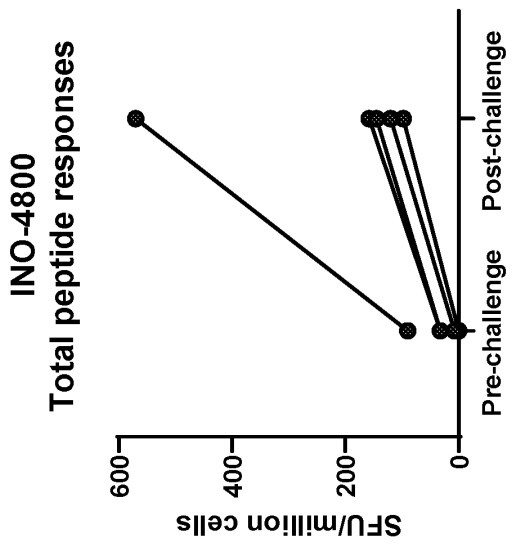

Naive
INO-4800
Pre-challenge
Post-challenge
SFU/million cells
300
200
100
0
Wk0
Wk6
Wk15
D14
SARS-CoV-2 Spike Pool 1
SARS-CoV-2 Spike Pool 2
SARS-CoV-2 Spike Pool 3
SARS-CoV-2 Spike Pool 4
SARS-CoV-2 Spike Pool 5

Figure 39


INO-4800
Total peptide responses
SFU/million cells
600
400
200
0
Pre-challenge
Post-challenge

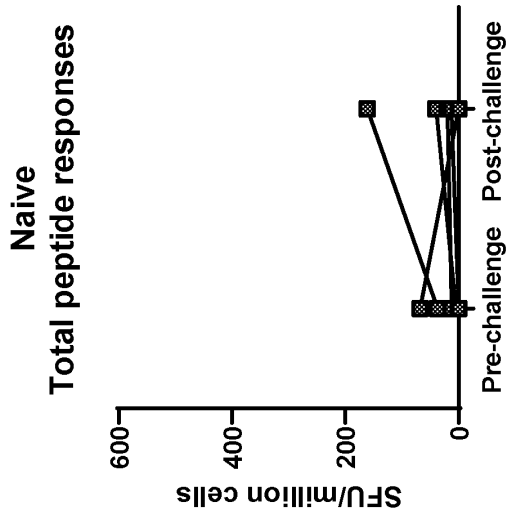
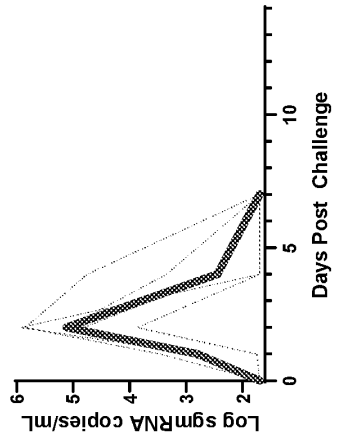

Naive
Total peptide responses
SFU/million cells
600
400
200
0
Pre-challenge
Post-challenge

Figure 40A



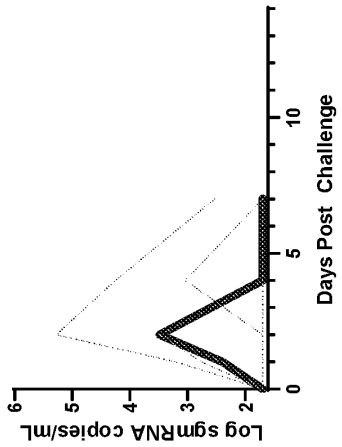


Figure 40B

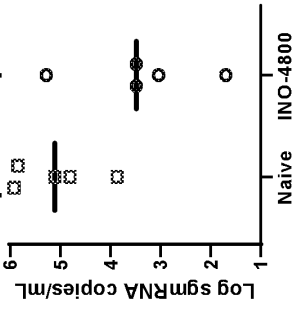


Figure 40C

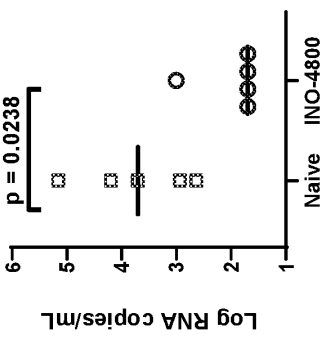


Figure 40D

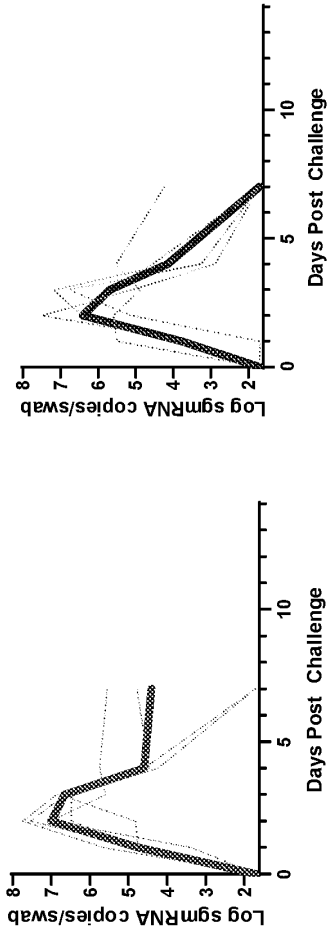


Figure 40E

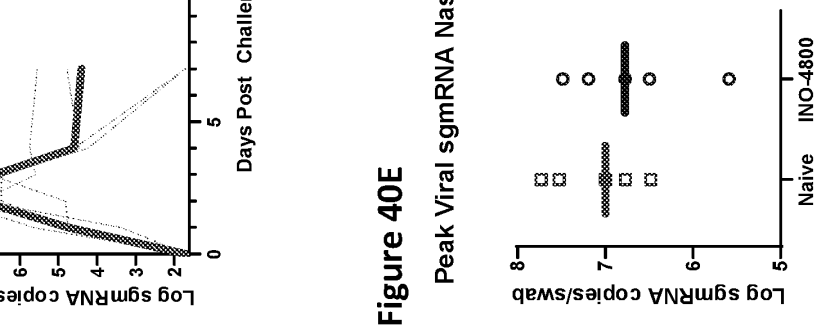


Figure 40F

