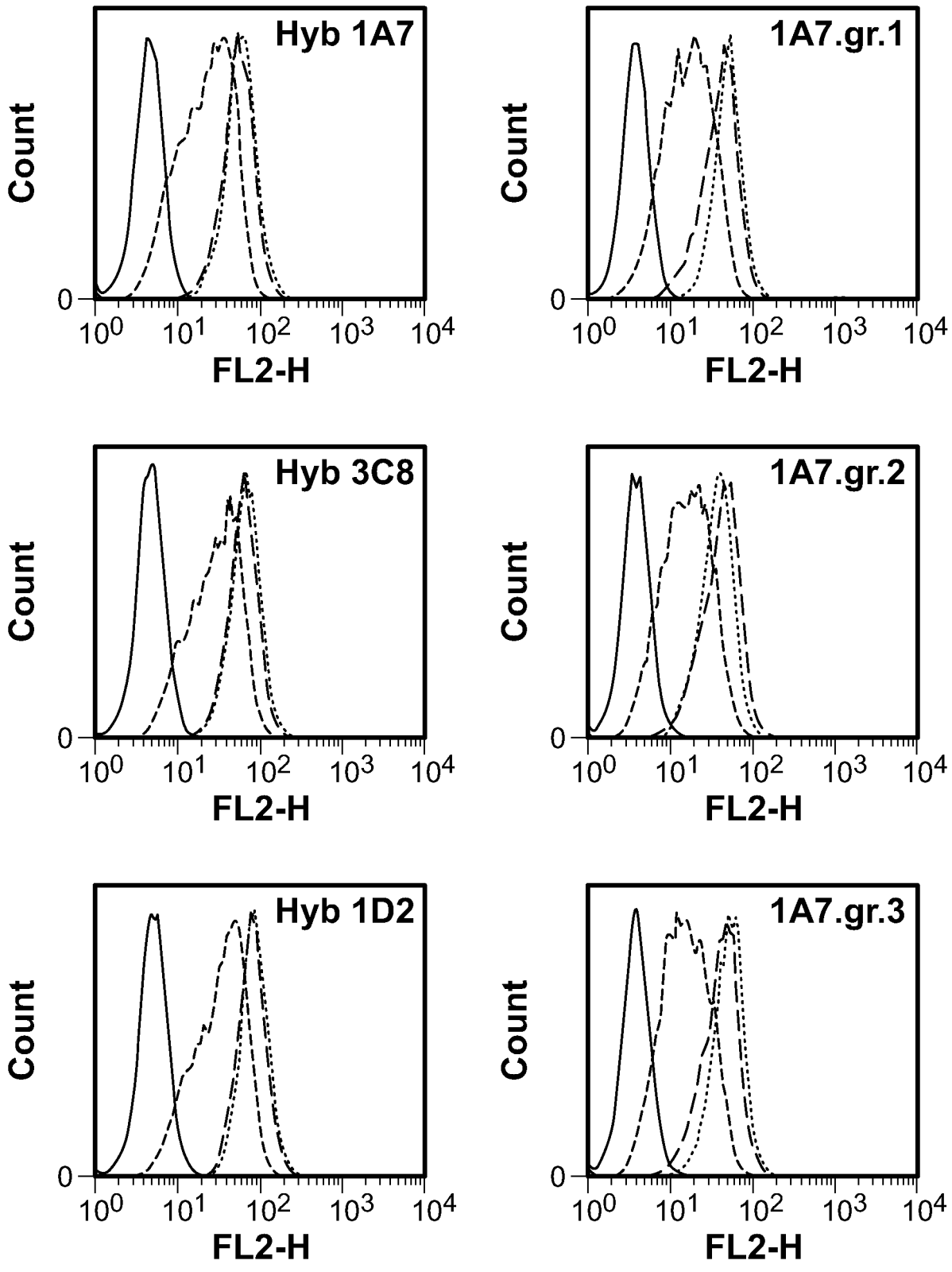

Hyb 1A7
1A7.gr.1
Hyb 3C8
1A7.gr.2
Hyb 1D2
1A7.gr.3
Count
0
10^0 10^1 10^2 10^3 10^4
FL2-H

FIG. 1

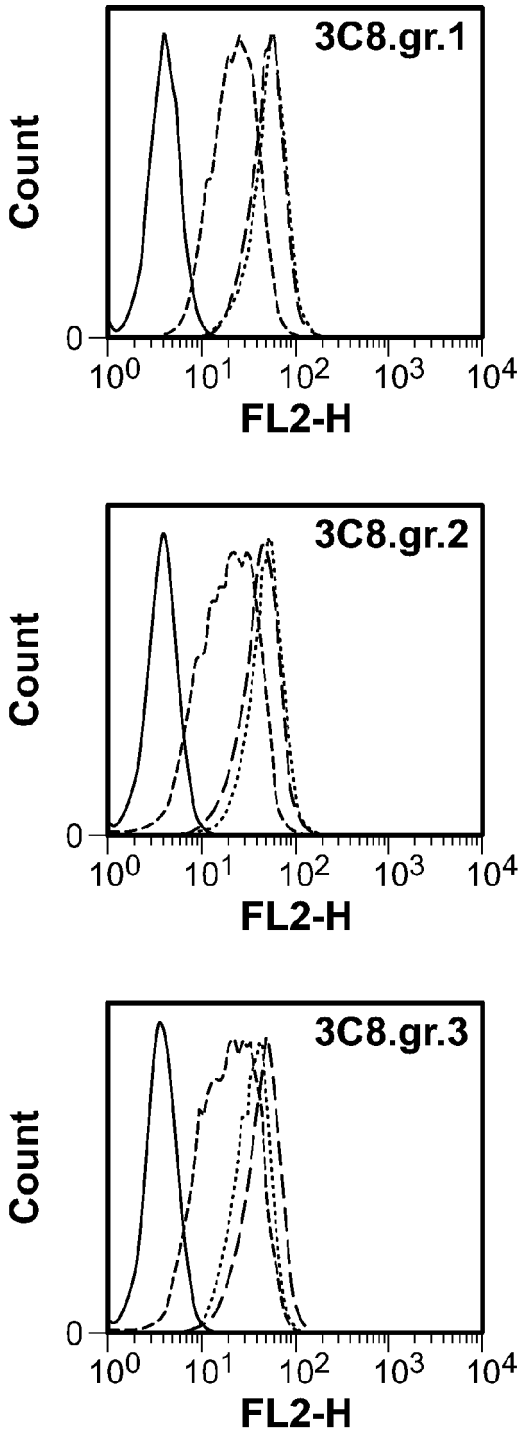

3C8.gr.1
Count
0
10^0 10^1 10^2 10^3 10^4
FL2-H
3C8.gr.2
Count
0
10^0 10^1 10^2 10^3 10^4
FL2-H
3C8.gr.3
Count
0
10^0 10^1 10^2 10^3 10^4
FL2-H

FIG. 1 (Cont.)

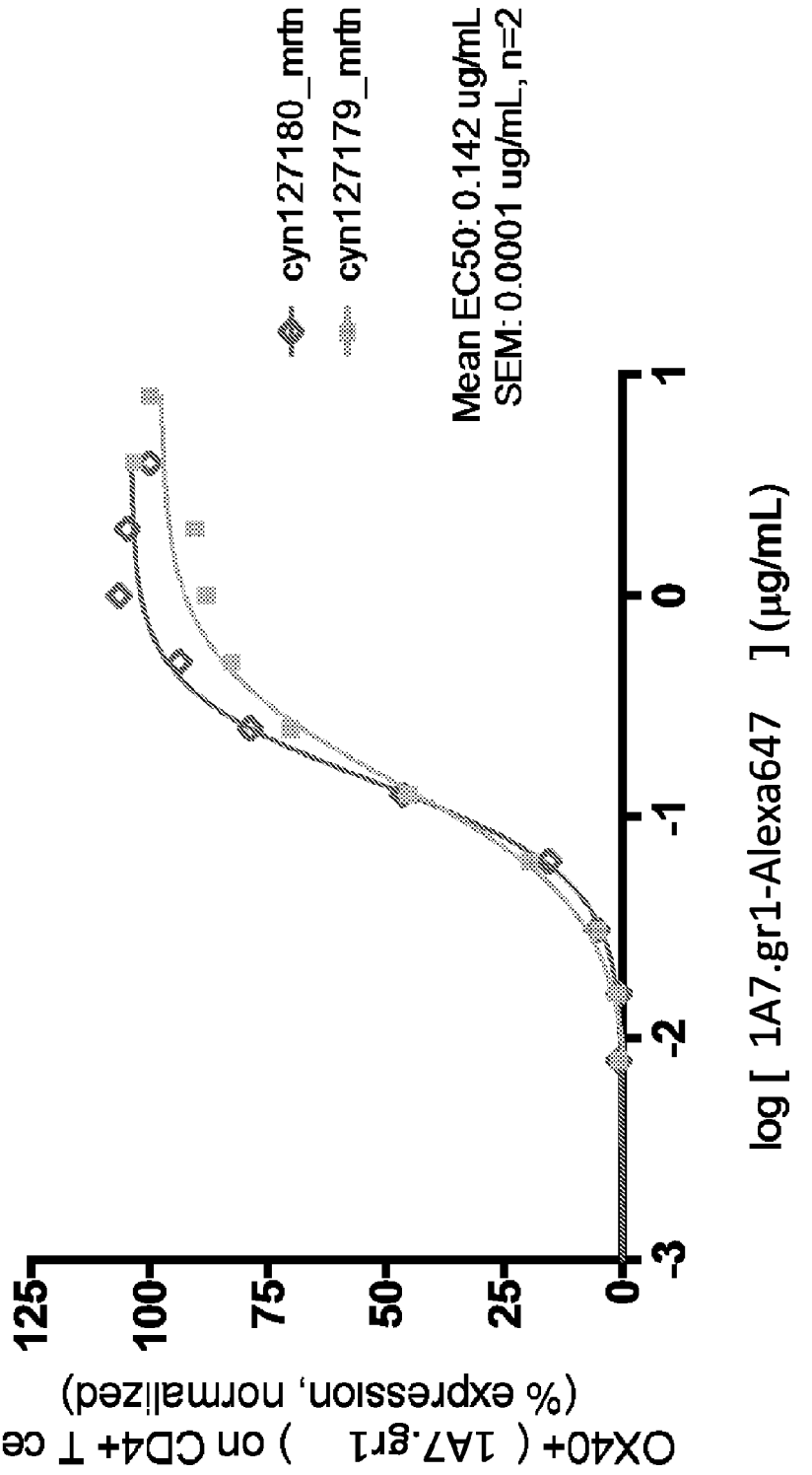

cyn127180_mrtn
cyn127179_mrtn
Mean EC50: 0.142 ug/mL
SEM: 0.0001 ug/mL, n=2
OX40+ (1A7.gr1) on CD4+ T cells
(% expression, normalized)
125
100
75
50
25
0
-3
-2
-1
0
1
log [1A7.gr1-Alexa647] (µg/mL)

FIG. 2

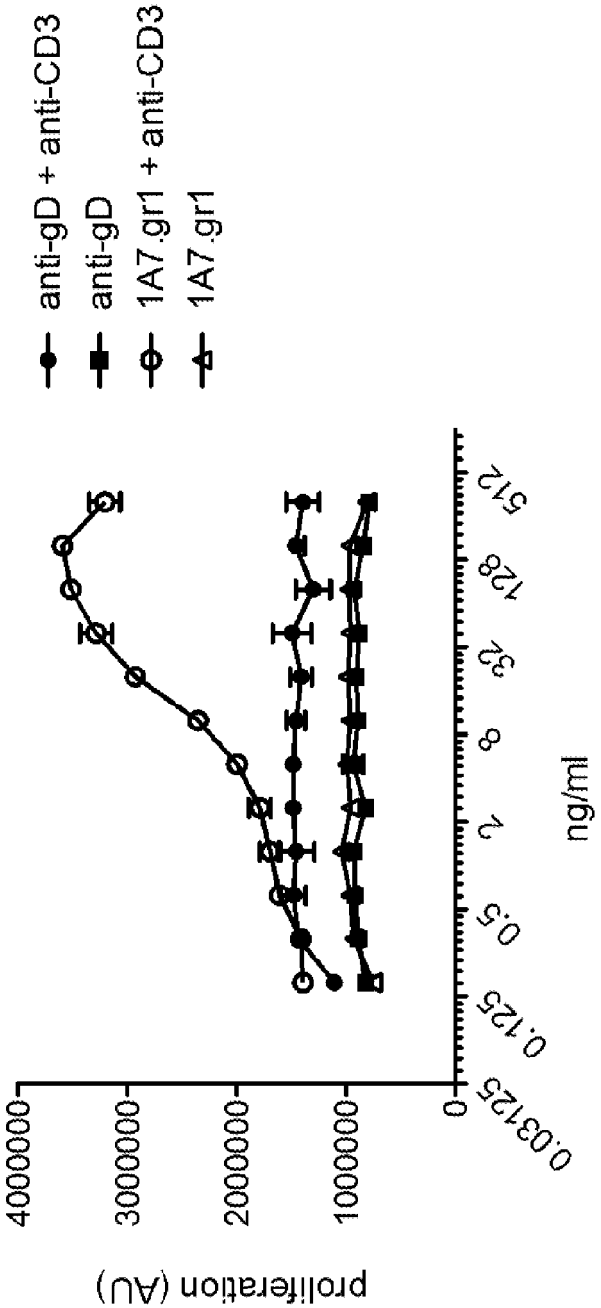


FIG. 3A

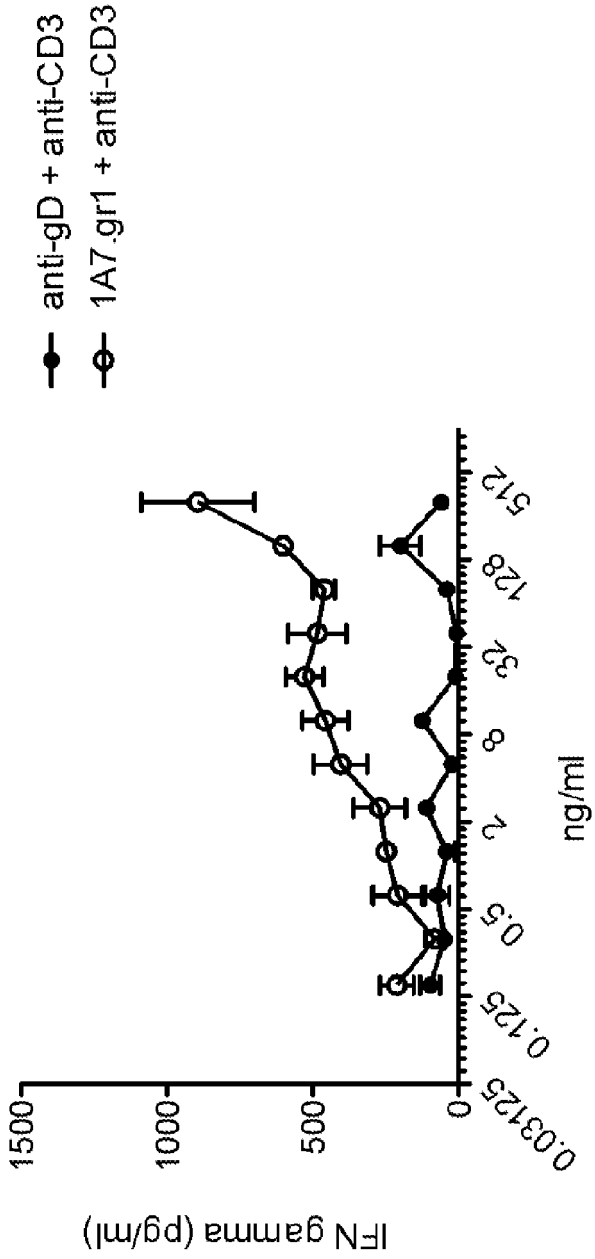


FIG. 3B

FIGS. 3A and 3B

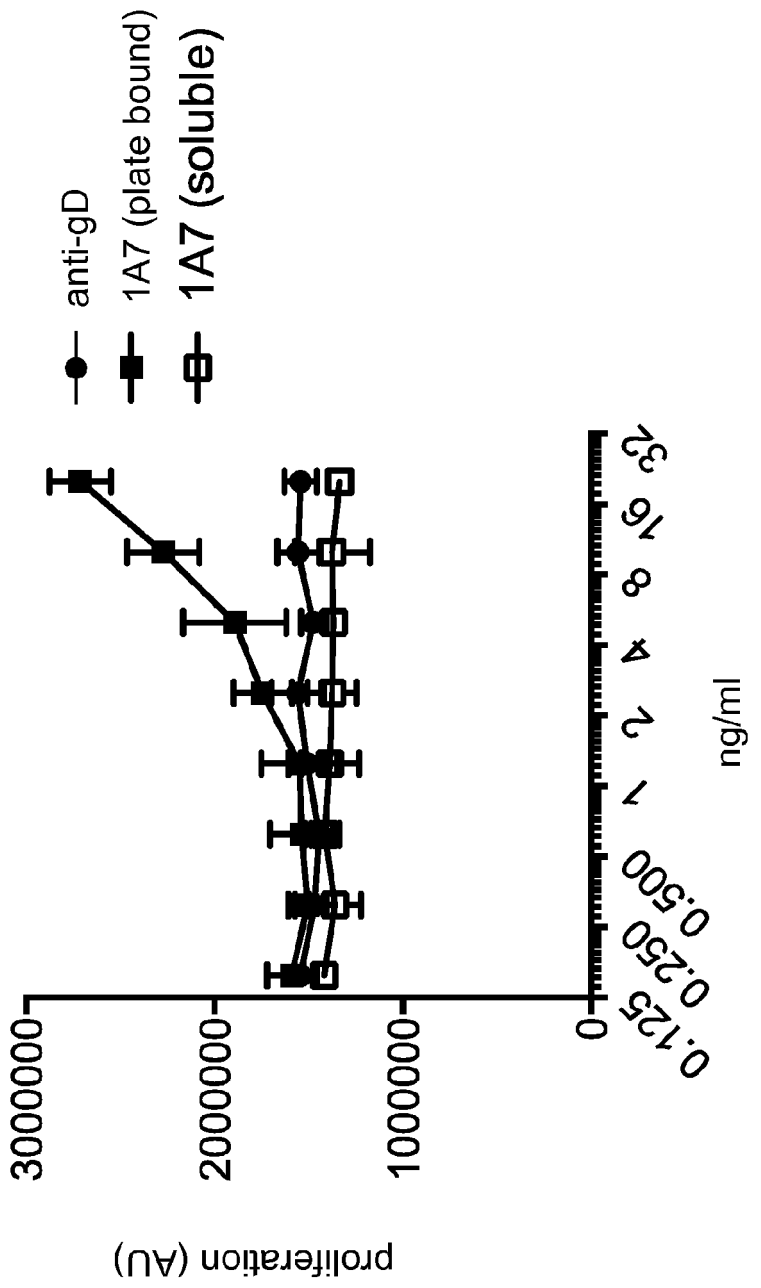

anti-gD
1A7 (plate bound)
1A7 (soluble)
proliferation (AU)
3000000
2000000
1000000
0
0.125
0.250
0.500
1
2
4
8
16
32
ng/ml

FIG. 4A

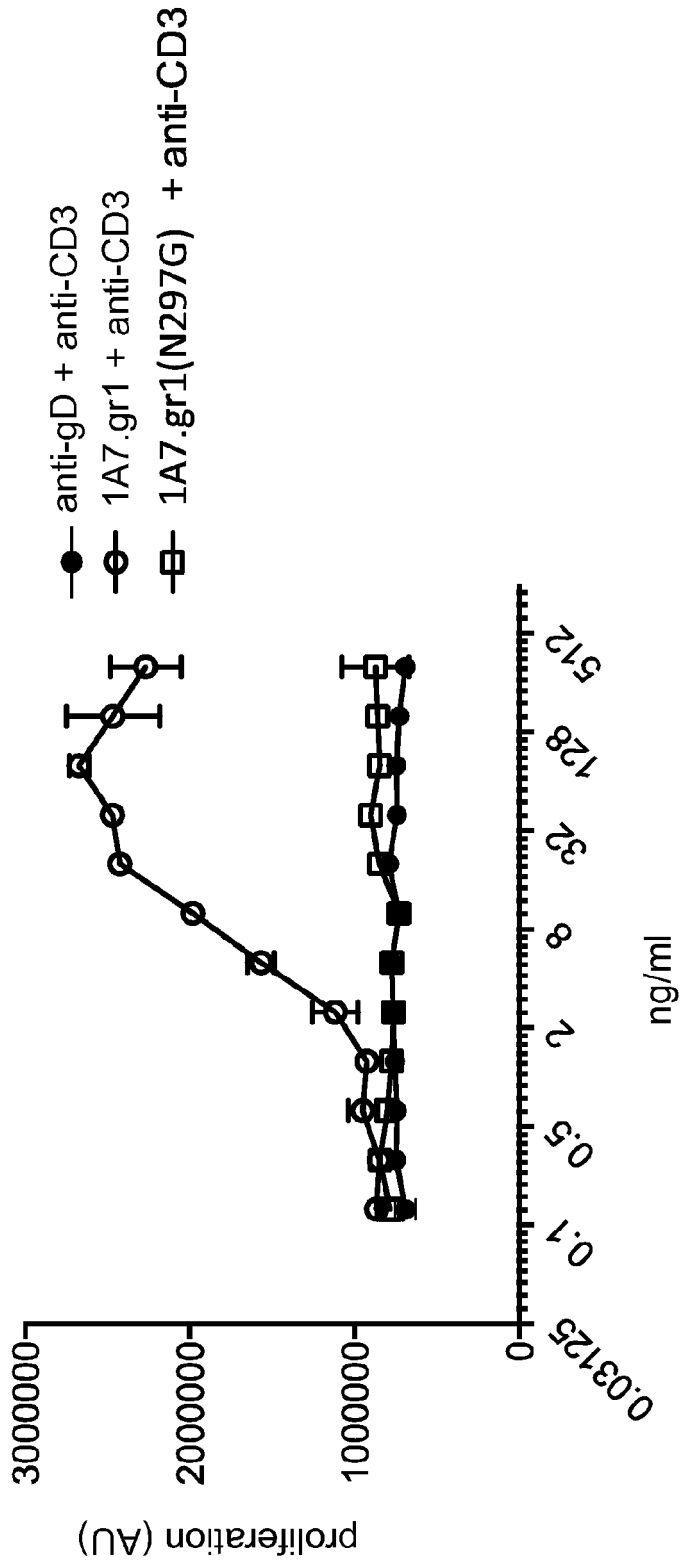

anti-gD + anti-CD3
1A7.gr1 + anti-CD3
1A7.gr1(N297G) + anti-CD3
proliferation (AU)
3000000
2000000
1000000
0
0.03125
0.1
0.5
2
8
32
128
512
ng/ml

FIG. 4B

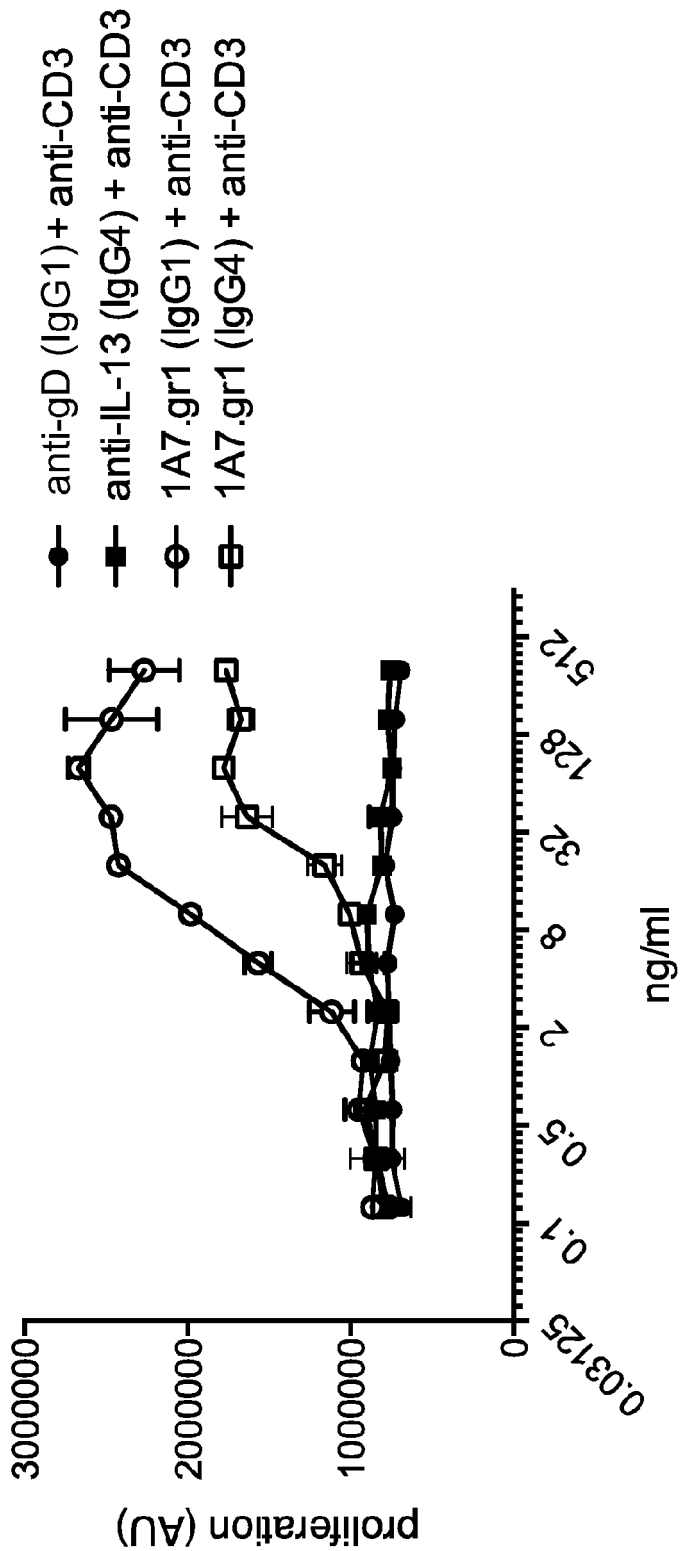

anti-gD (IgG1) + anti-CD3
anti-IL-13 (IgG4) + anti-CD3
1A7.gr1 (IgG1) + anti-CD3
1A7.gr1 (IgG4) + anti-CD3
proliferation (ΔU)
3000000
2000000
1000000
0
0.03125
0.1
0.5
2
8
32
128
512
ng/ml

FIG. 5

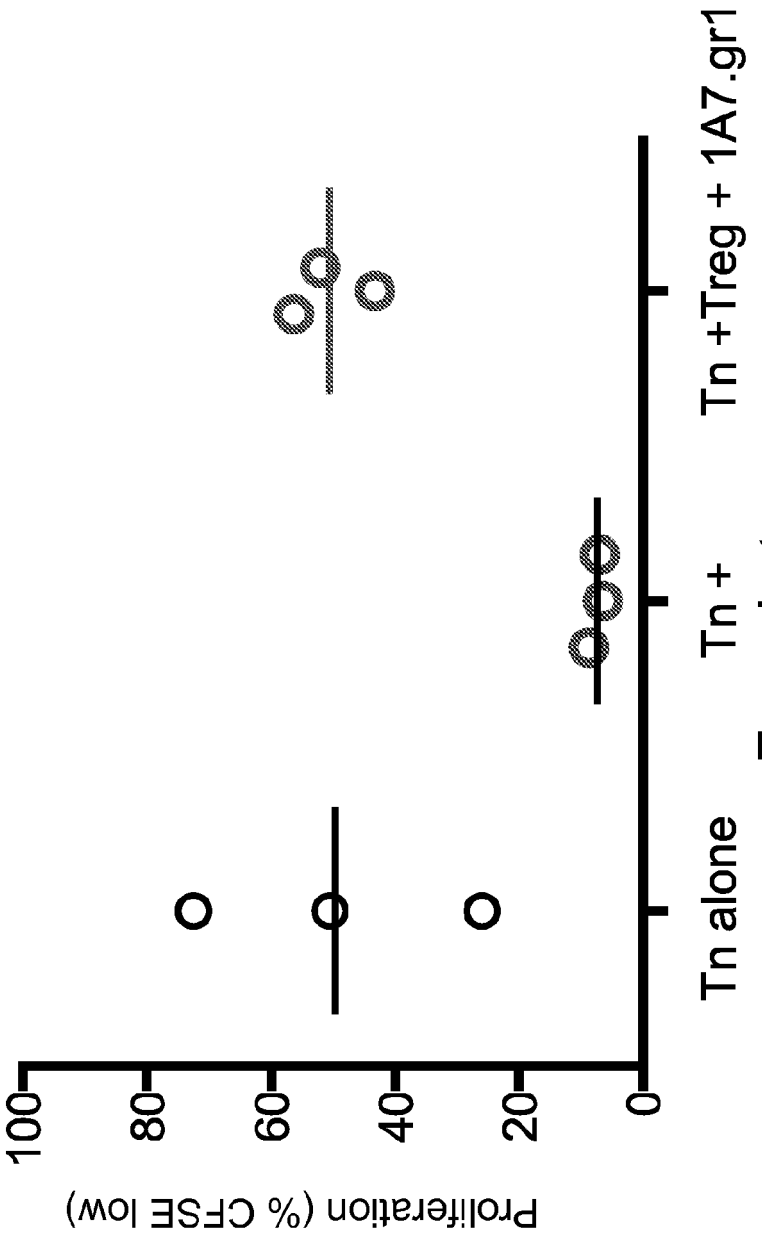

Proliferation (% CFSE low)
100
80
60
40
20
0
Tn alone
Tn + Treg + isotype
Tn +Treg + 1A7.gr1

FIG. 6

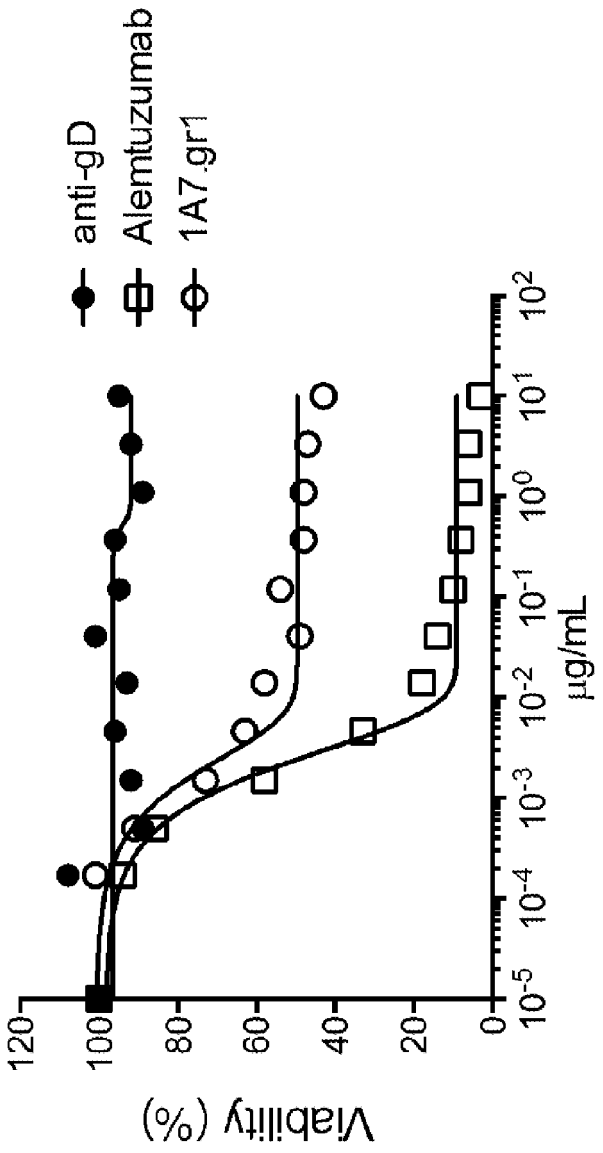
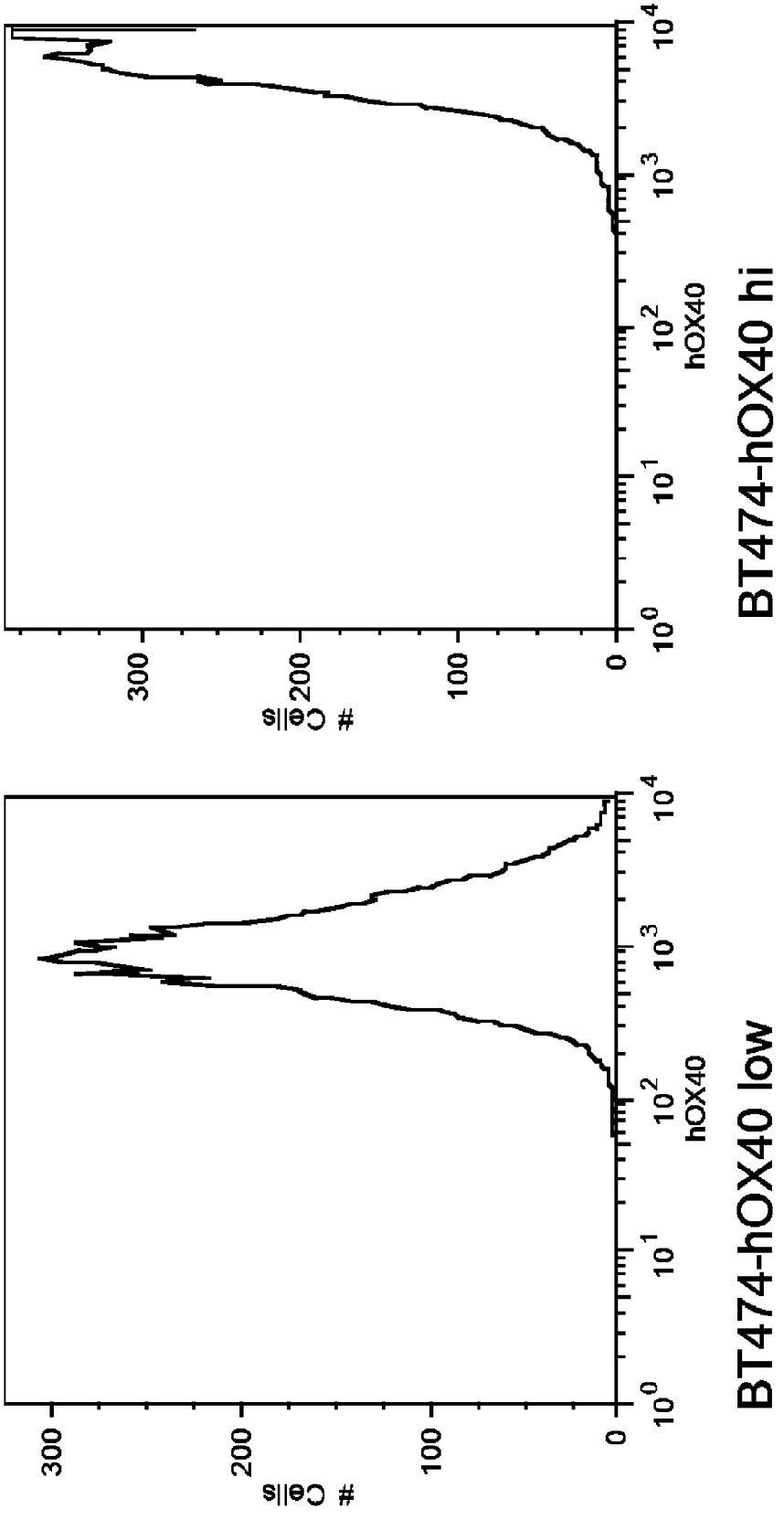


FIG. 7A

FIG. 7B

FIGS. 7A and 7B



FIGS. 8A and 8B

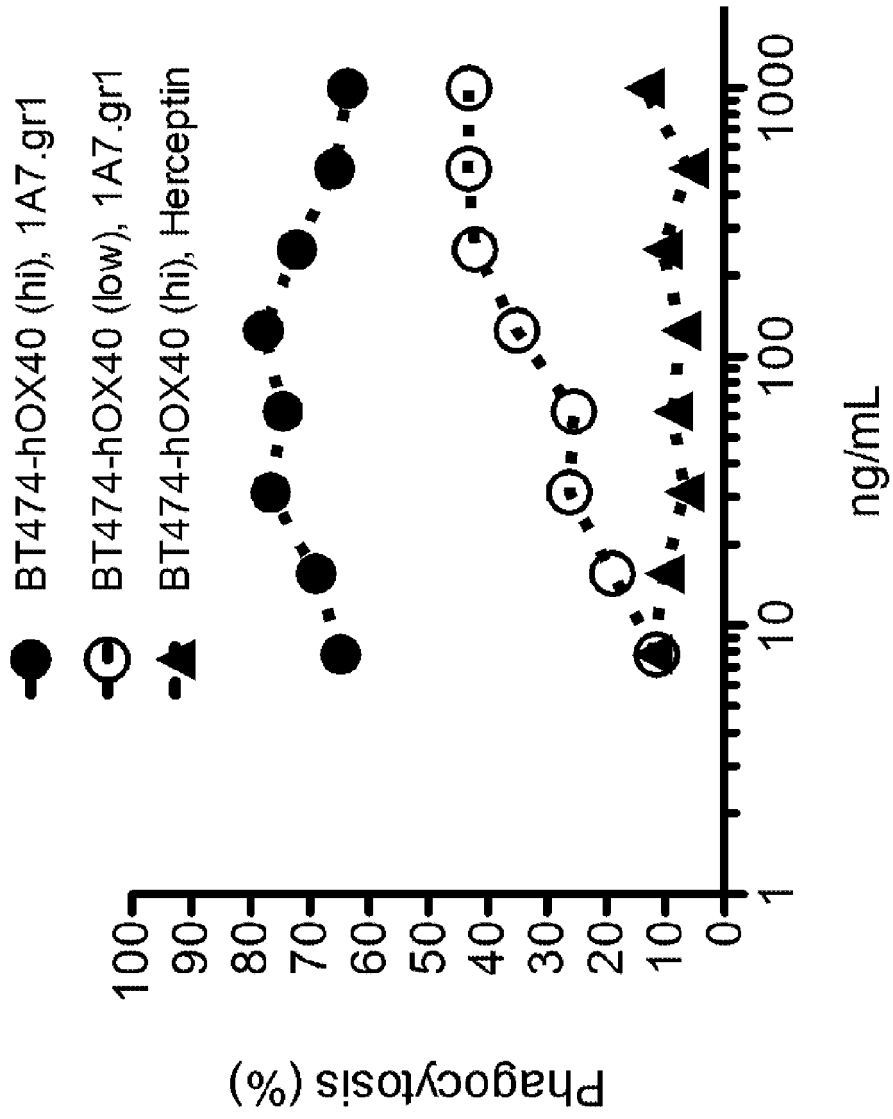

BT474-hOX40 (hi), 1A7.gr1
BT474-hOX40 (low), 1A7.gr1
BT474-hOX40 (hi), Herceptin
Phagocytosis (%)
100
90
80
70
60
50
40
30
20
10
0
1
10
100
1000
ng/mL

FIG. 9

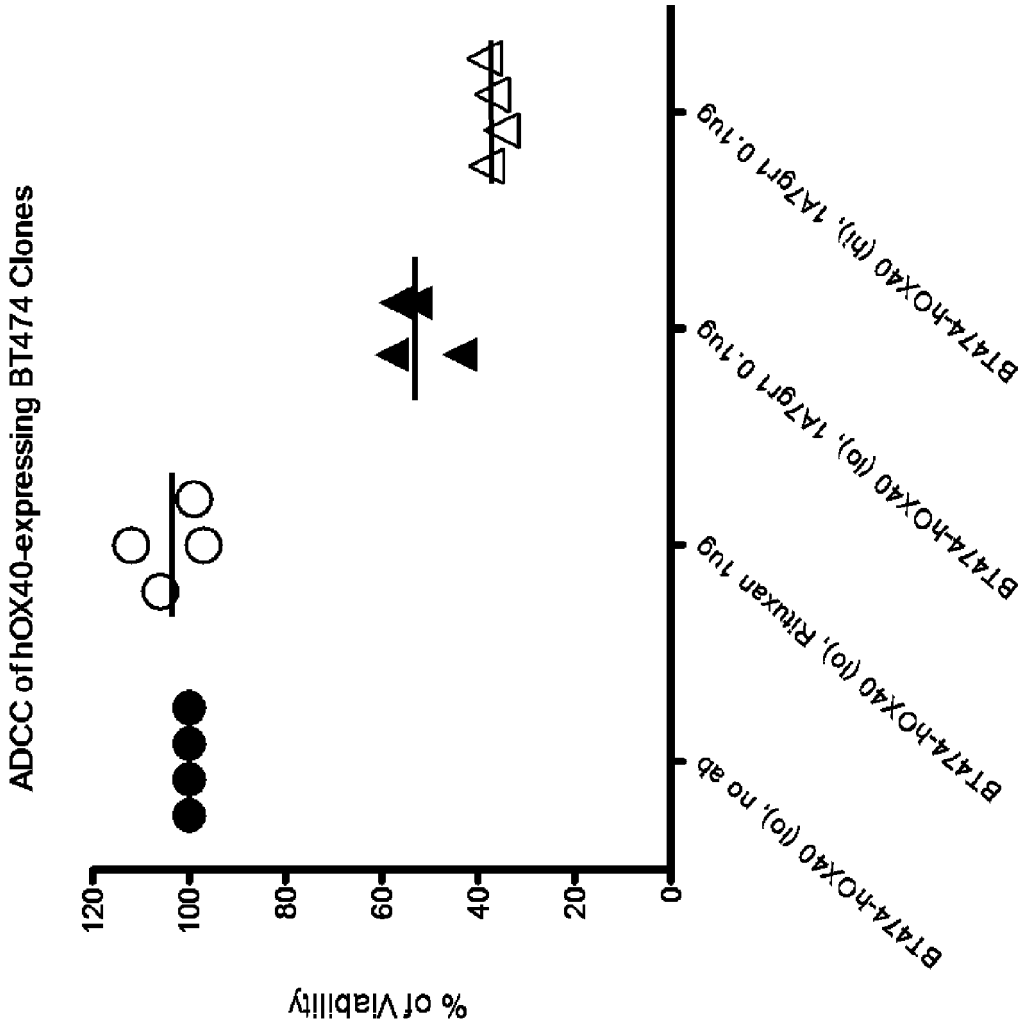

ADCC of hOX40-expressing BT474 Clones
% of Viability
120
100
80
60
40
20
0
BT474-hOX40 (lo), no ab
BT474-hOX40 (lo), Rituxan 1ug
BT474-hOX40 (lo), 1A7gr1 0.1ug
BT474-hOX40 (hi), 1A7gr1 0.1ug

FIG. 10

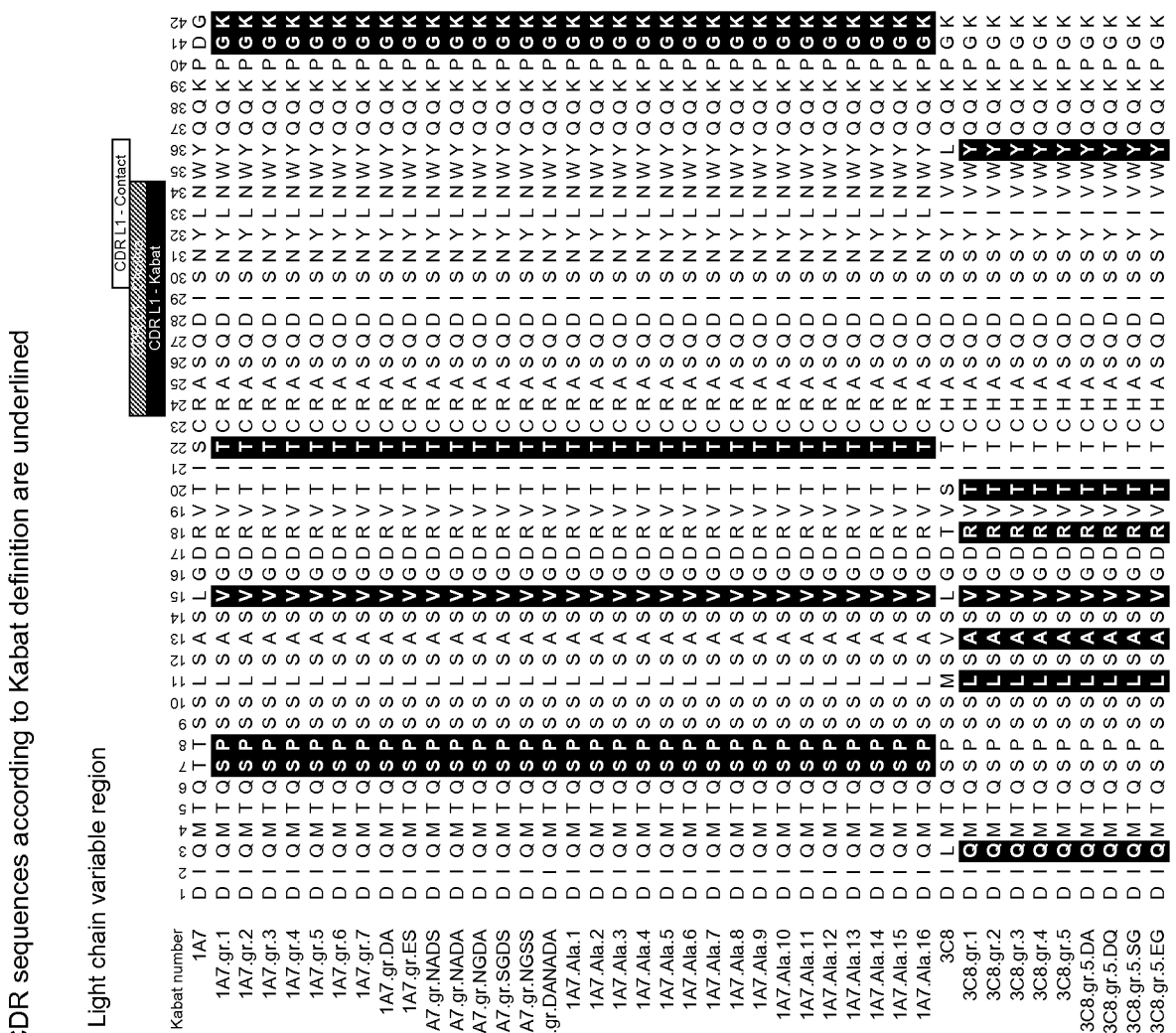

CDR sequences according to Kabat definition are underlined
Light chain variable region
CDR L1 - Contact
CDR L1 - Kabat
Kabat number

FIG. 11A

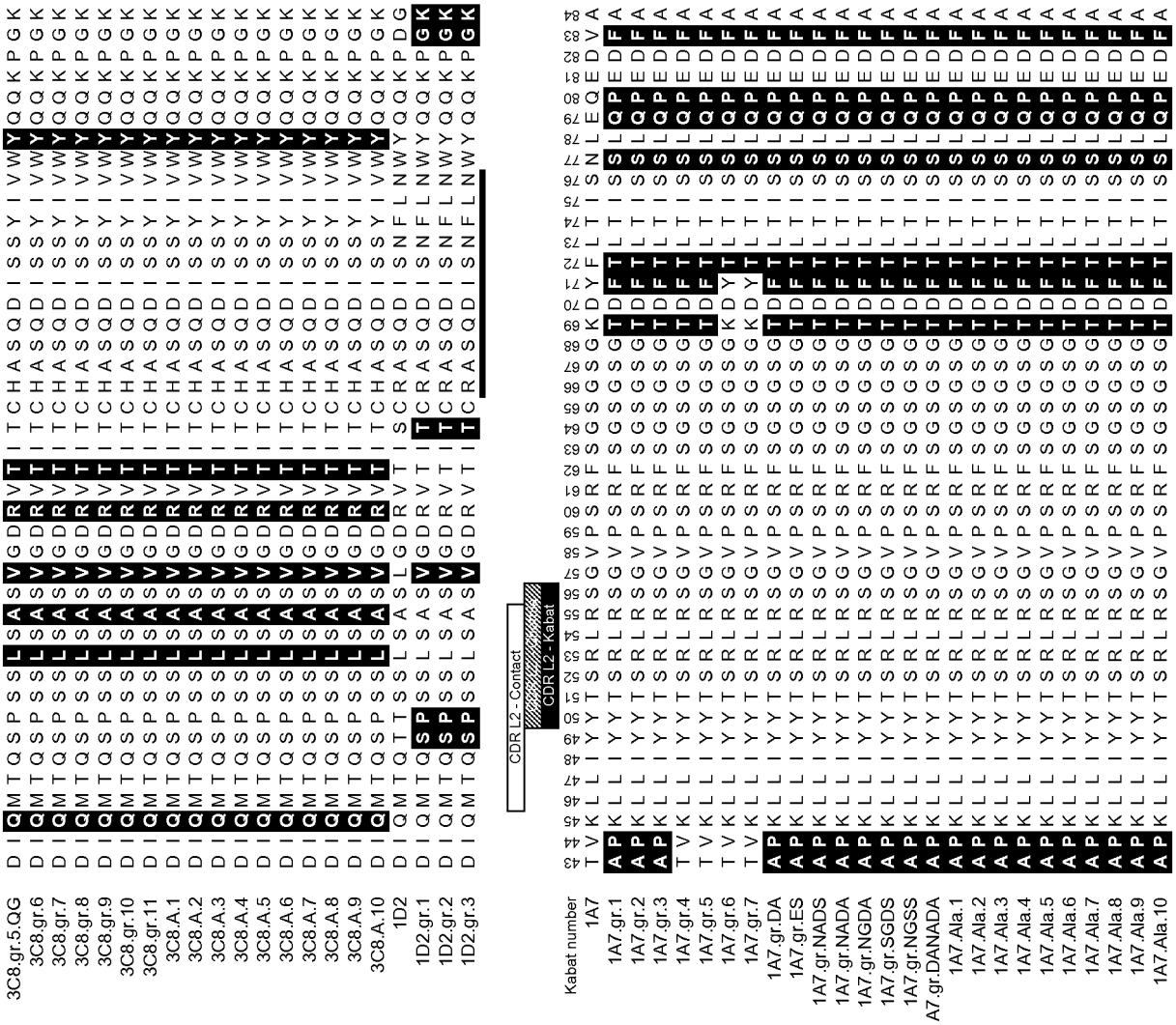


FIG. 11B

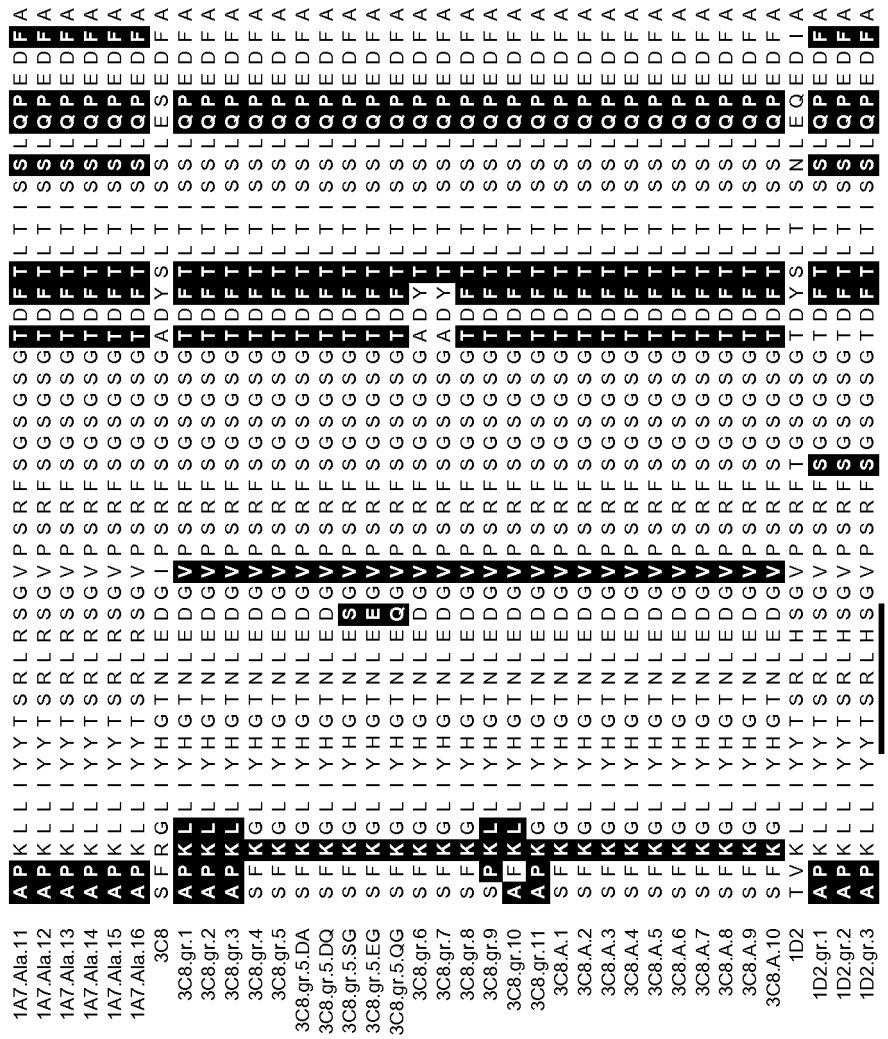


FIG. 11C

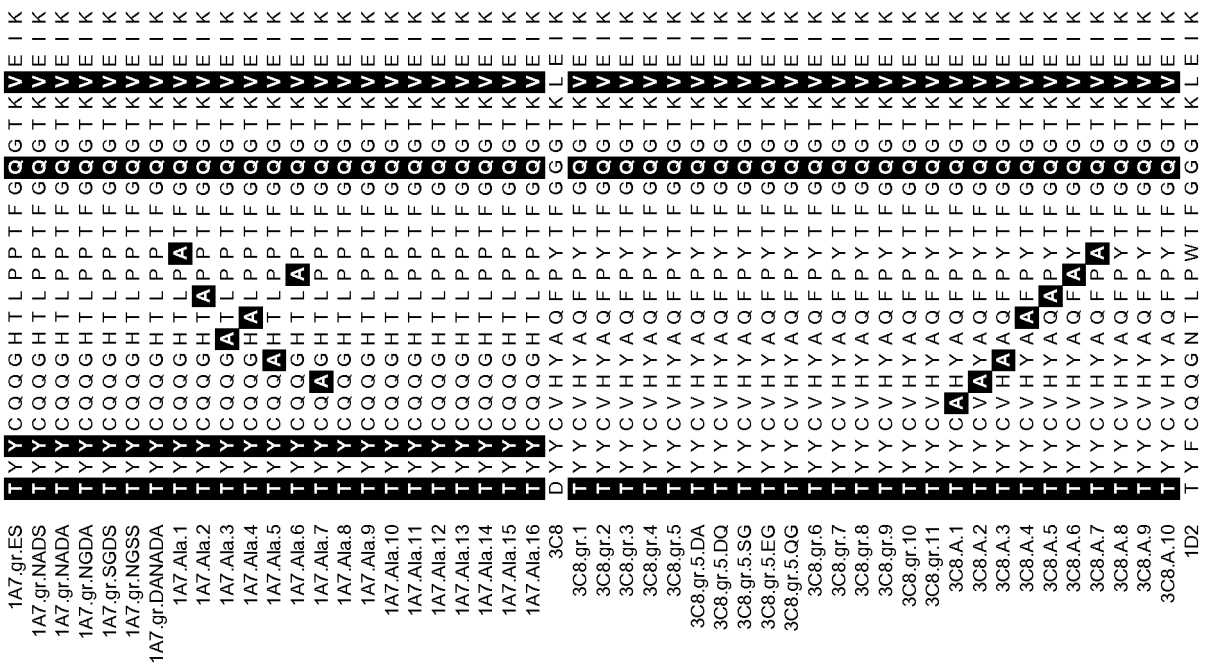

1A7.gr.ES
1A7.gr.NADS
1A7.gr.NADA
1A7.gr.NGDA
1A7.gr.SGDS
1A7.gr.NGSS
1A7.gr.DANADA
1A7.Ala.1
1A7.Ala.2
1A7.Ala.3
1A7.Ala.4
1A7.Ala.5
1A7.Ala.6
1A7.Ala.7
1A7.Ala.8
1A7.Ala.9
1A7.Ala.10
1A7.Ala.11
1A7.Ala.12
1A7.Ala.13
1A7.Ala.14
1A7.Ala.15
1A7.Ala.16
3C8
3C8.gr.1
3C8.gr.2
3C8.gr.3
3C8.gr.4
3C8.gr.5
3C8.gr.5.DA
3C8.gr.5.DQ
3C8.gr.5.SG
3C8.gr.5.EG
3C8.gr.5.QG
3C8.gr.6
3C8.gr.7
3C8.gr.8
3C8.gr.9
3C8.gr.10
3C8.gr.11
3C8.A.1
3C8.A.2
3C8.A.3
3C8.A.4
3C8.A.5
3C8.A.6
3C8.A.7
3C8.A.8
3C8.A.9
3C8.A.10
1D2

FIG. 11D

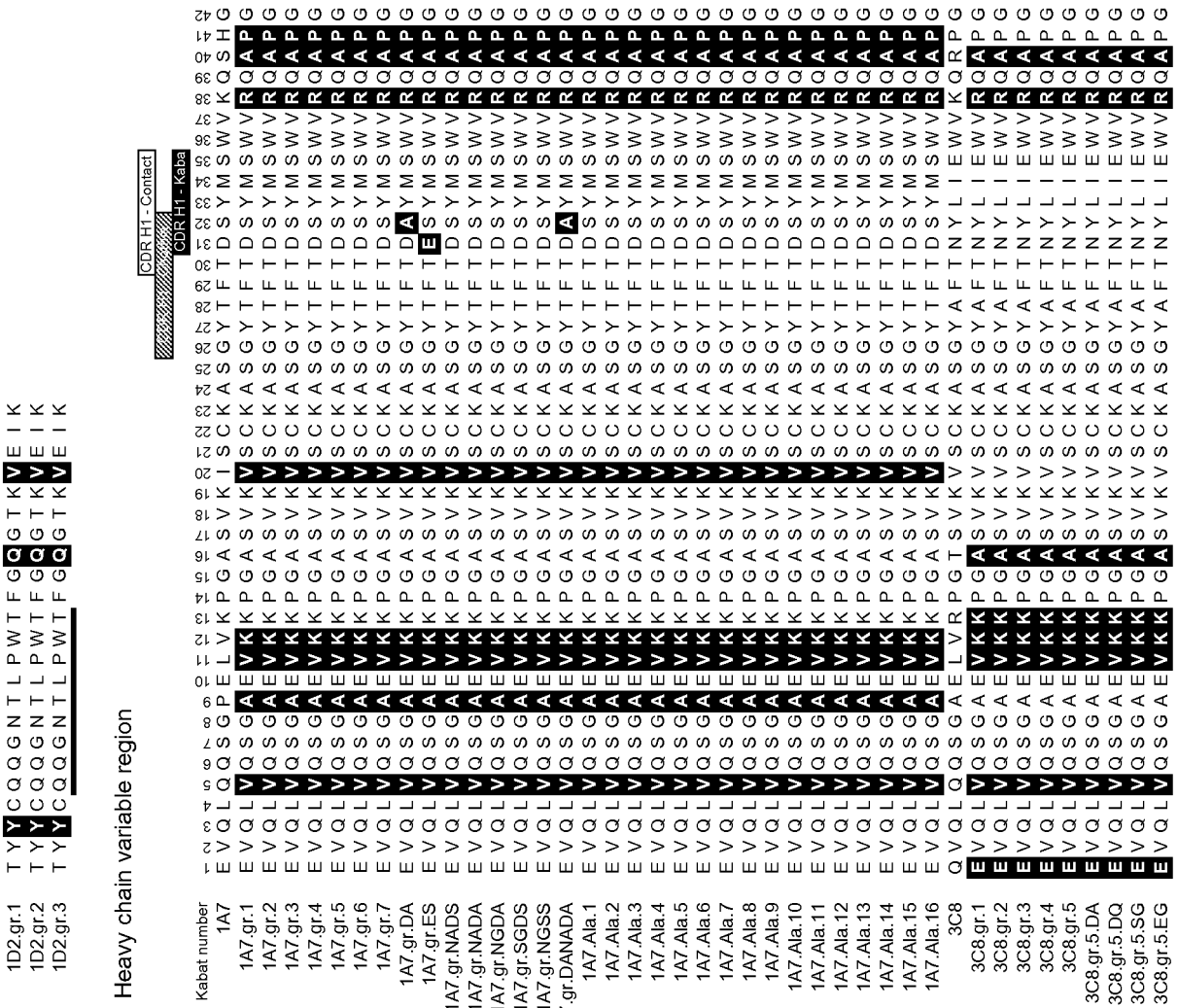

1D2.gr.1 T Y Y C Q Q G N T L P W T F G Q G T K V E I K
1D2.gr.2 T Y Y C Q Q G N T L P W T F G Q G T K V E I K
1D2.gr.3 T Y Y C Q Q G N T L P W T F G Q G T K V E I K
Heavy chain variable region
CDR H1 - Contact
CDR H1 - Kabat
Kabat number
1A7
1A7.gr.1
1A7.gr.2
1A7.gr.3
1A7.gr.4
1A7.gr.5
1A7.gr.6
1A7.gr.7
1A7.gr.DA
1A7.gr.ES
1A7.gr.NADS
1A7.gr.NADA
1A7.gr.NGDA
1A7.gr.SGDS
1A7.gr.NGSS
1A7.gr.DANADA
1A7.Ala.1
1A7.Ala.2
1A7.Ala.3
1A7.Ala.4
1A7.Ala.5
1A7.Ala.6
1A7.Ala.7
1A7.Ala.8
1A7.Ala.9
1A7.Ala.10
1A7.Ala.11
1A7.Ala.12
1A7.Ala.13
1A7.Ala.14
1A7.Ala.15
1A7.Ala.16
3C8
3C8.gr.1
3C8.gr.2
3C8.gr.3
3C8.gr.4
3C8.gr.5
3C8.gr.5.DA
3C8.gr.5.DQ
3C8.gr.5.SG
3C8.gr.5.EG

FIG. 11E

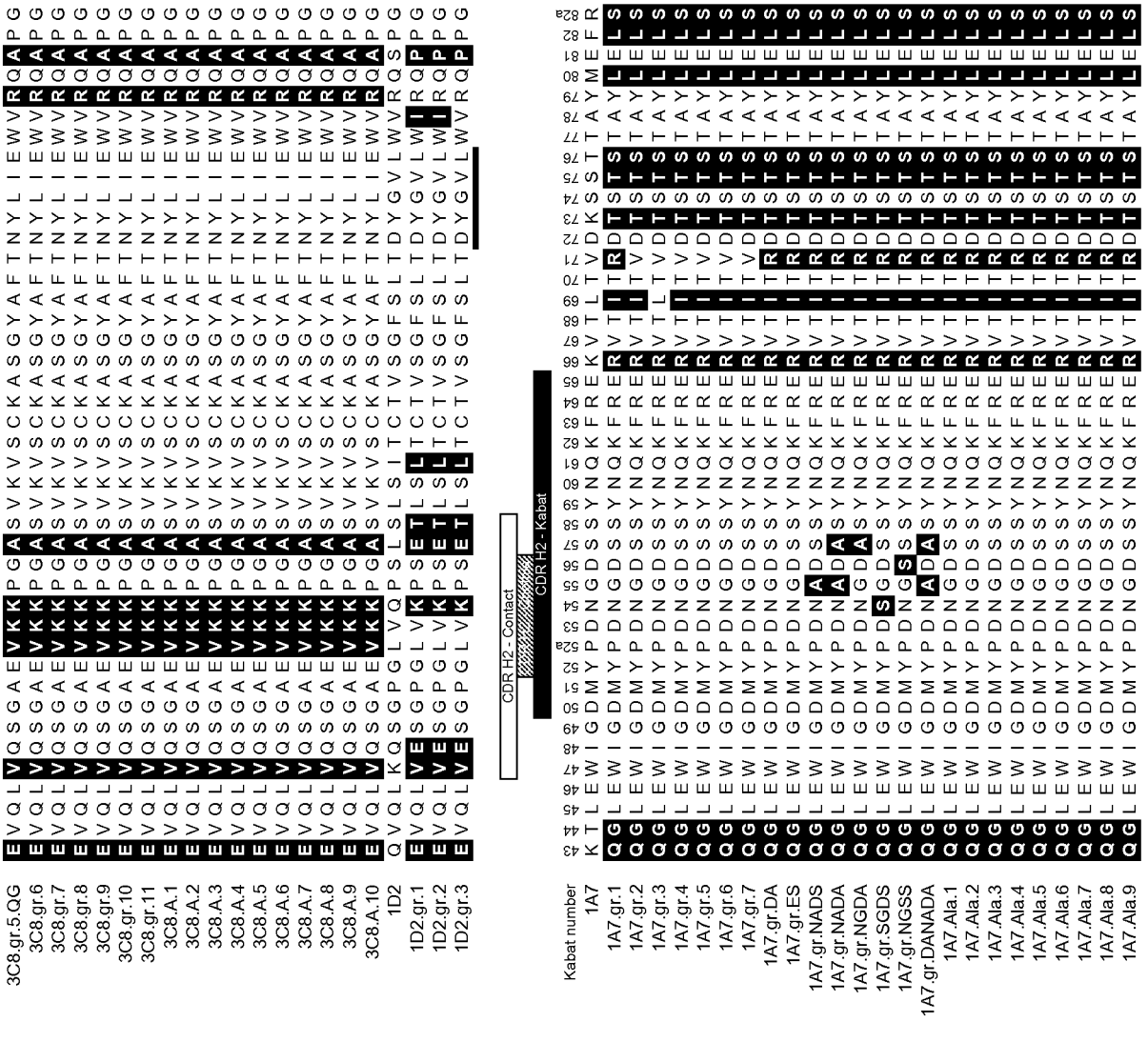


FIG. 11F

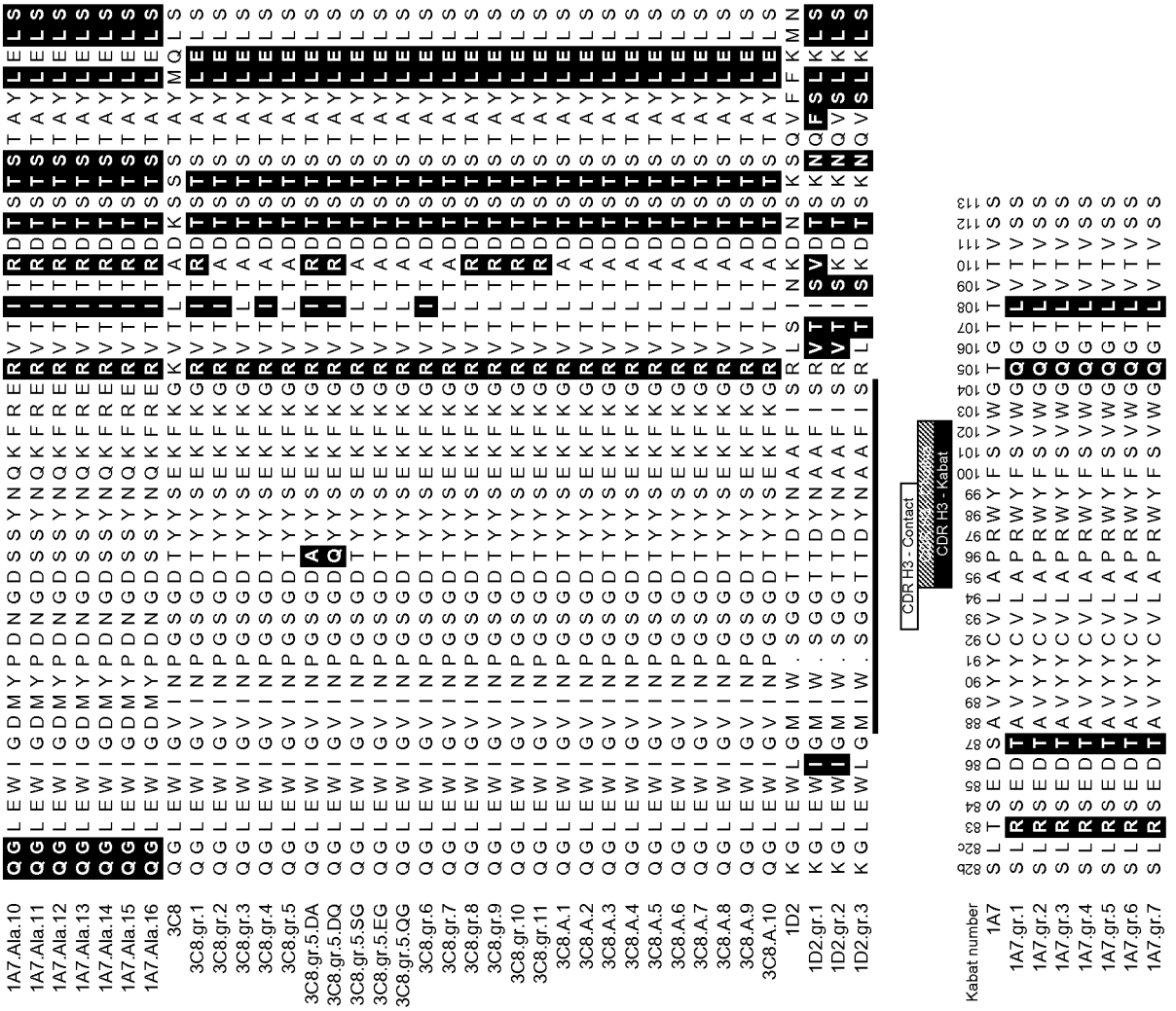


FIG. 11G

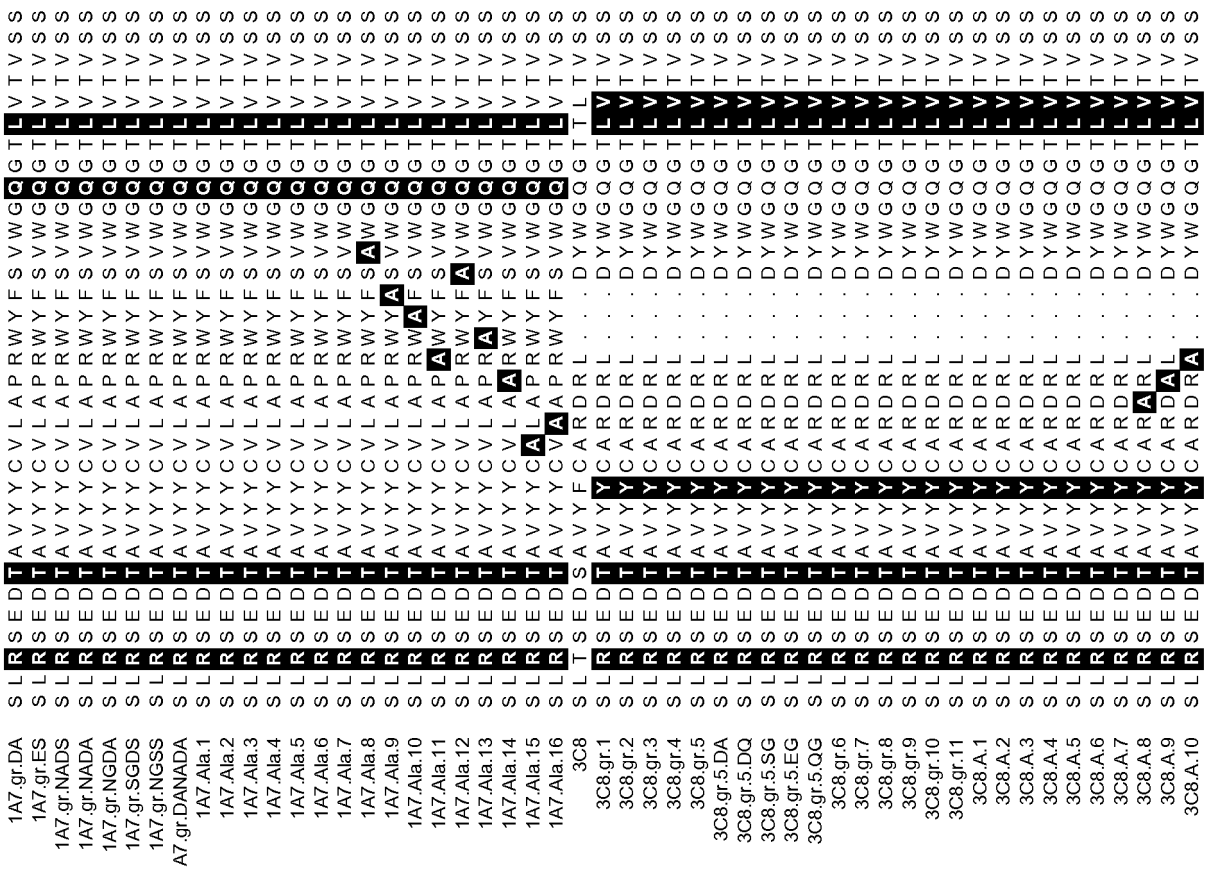

1A7.gr.DA
1A7.gr.ES
1A7.gr.NADS
1A7.gr.NADA
1A7.gr.NGDA
1A7.gr.SGDS
1A7.gr.NGSS
1A7.gr.DANADA
1A7.Ala.1
1A7.Ala.2
1A7.Ala.3
1A7.Ala.4
1A7.Ala.5
1A7.Ala.6
1A7.Ala.7
1A7.Ala.8
1A7.Ala.9
1A7.Ala.10
1A7.Ala.11
1A7.Ala.12
1A7.Ala.13
1A7.Ala.14
1A7.Ala.15
1A7.Ala.16
3C8
3C8.gr.1
3C8.gr.2
3C8.gr.3
3C8.gr.4
3C8.gr.5
3C8.gr.5.DA
3C8.gr.5.DQ
3C8.gr.5.SG
3C8.gr.5.EG
3C8.gr.5.QG
3C8.gr.6
3C8.gr.7
3C8.gr.8
3C8.gr.9
3C8.gr.10
3C8.gr.11
3C8.A.1
3C8.A.2
3C8.A.3
3C8.A.4
3C8.A.5
3C8.A.6
3C8.A.7
3C8.A.8
3C8.A.9
3C8.A.10

FIG. 11H

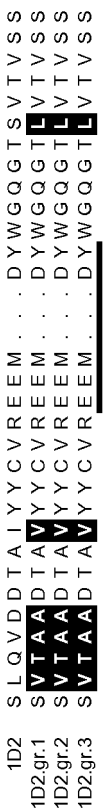

1D2 S L Q V D D T A I Y Y C V R E E M . . . D Y W G Q G T S V T V S S
1D2.gr.1 S V T A A D T A V Y Y C V R E E M . . . D Y W G Q G T L V T V S S
1D2.gr.2 S V T A A D T A V Y Y C V R E E M . . . D Y W G Q G T L V T V S S
1D2.gr.3 S V T A A D T A V Y Y C V R E E M . . . D Y W G Q G T L V T V S S

FIG. 11I

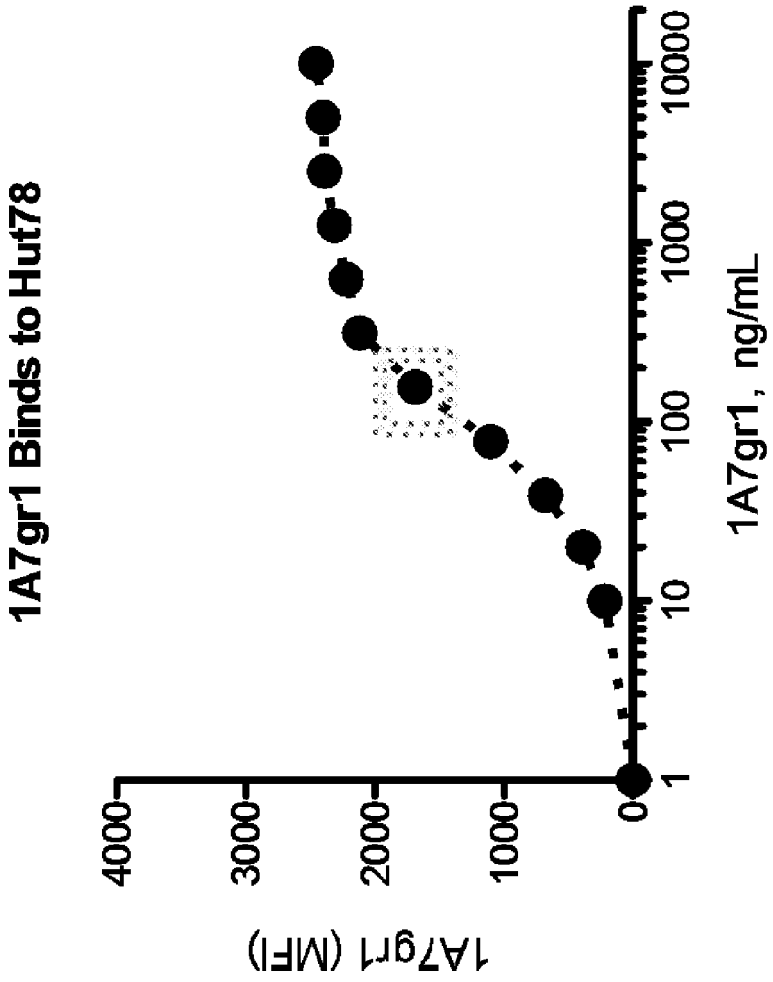

1A7gr1 Binds to Hut78
1A7gr1 (MFI)
4000
3000
2000
1000
0
1
10
100
1000
10000
1A7gr1, ng/mL

FIG. 12A

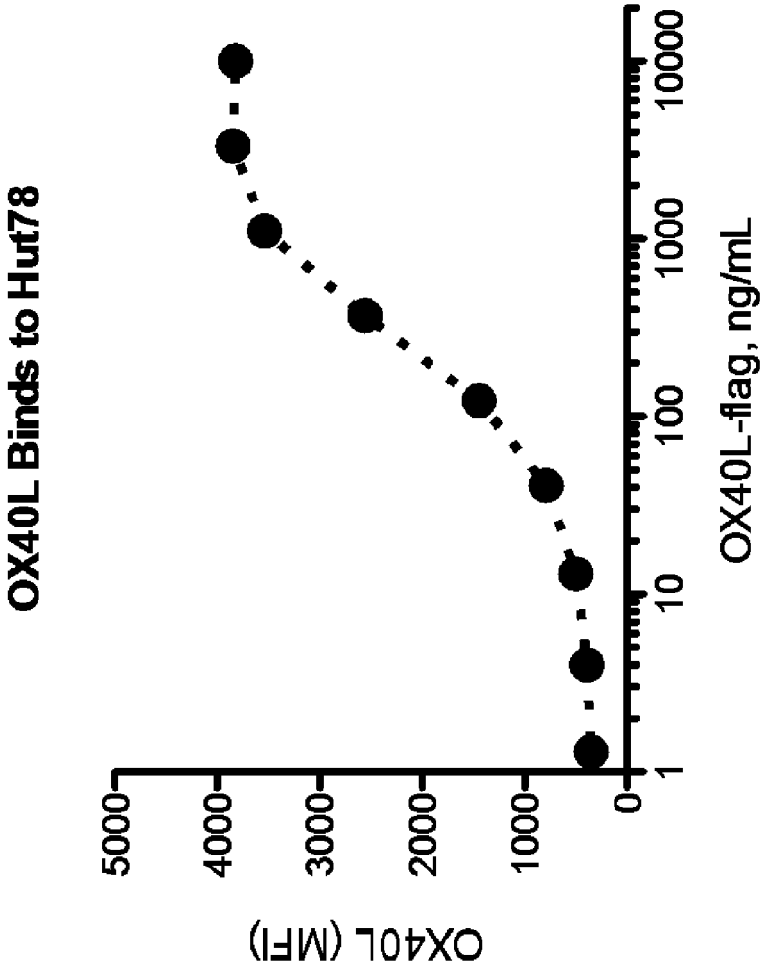

OX40L Binds to Hut78
OX40L (MFI)
5000
4000
3000
2000
1000
0
1
10
100
1000
10000
OX40L-flag, ng/mL

FIG. 12B

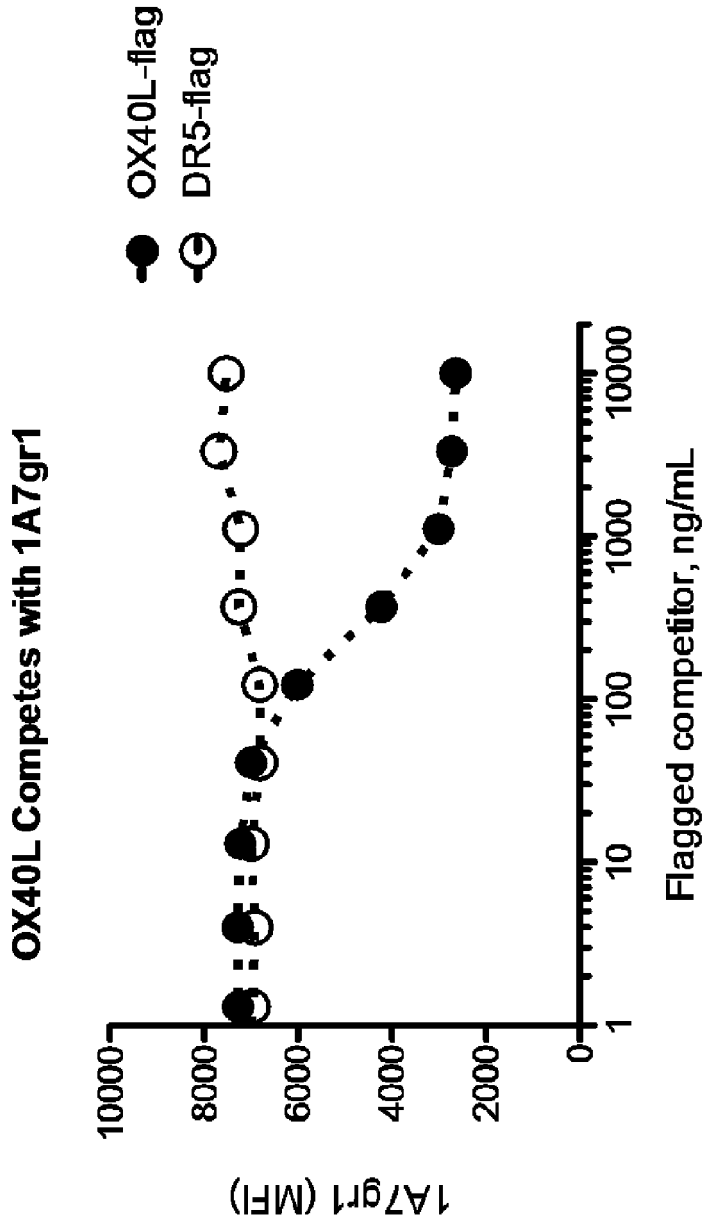

OX40L Competes with 1A7gr1
OX40L-flag
DR5-flag
1A7gr1 (MFI)
10000
8000
6000
4000
2000
0
1
10
100
1000
10000
Flagged competitor, ng/mL

FIG. 12C

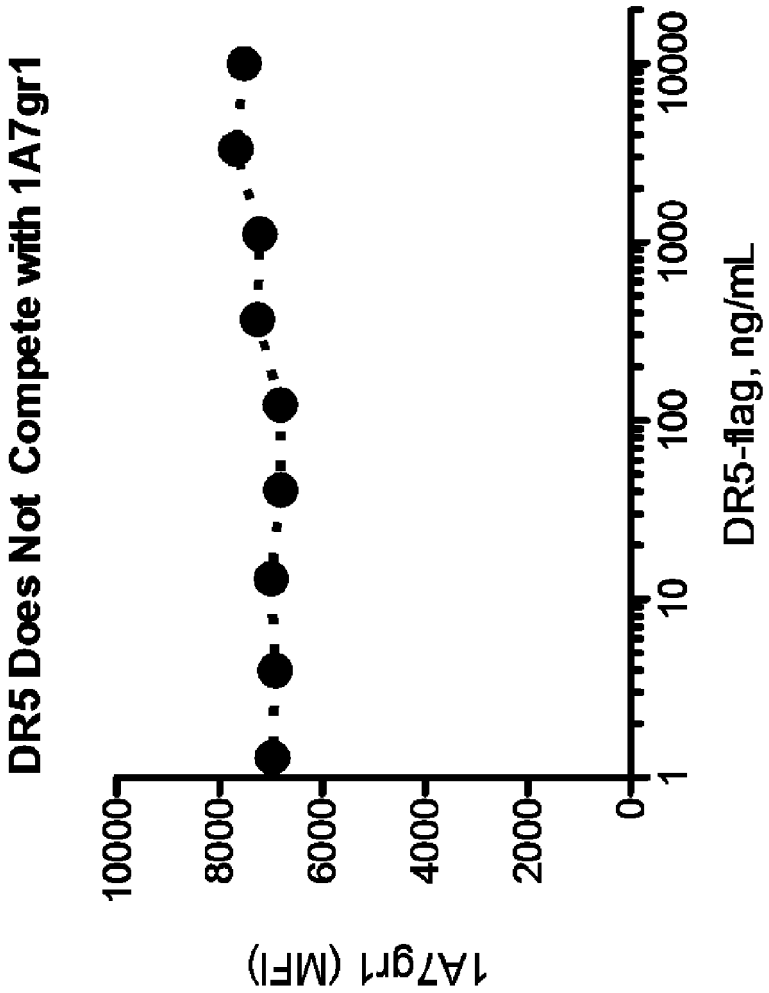

DR5 Does Not Compete with 1A7gr1
1A7gr1 (MFI)
10000
8000
6000
4000
2000
0
1
10
100
1000
10000
DR5-flag, ng/mL

FIG. 12D

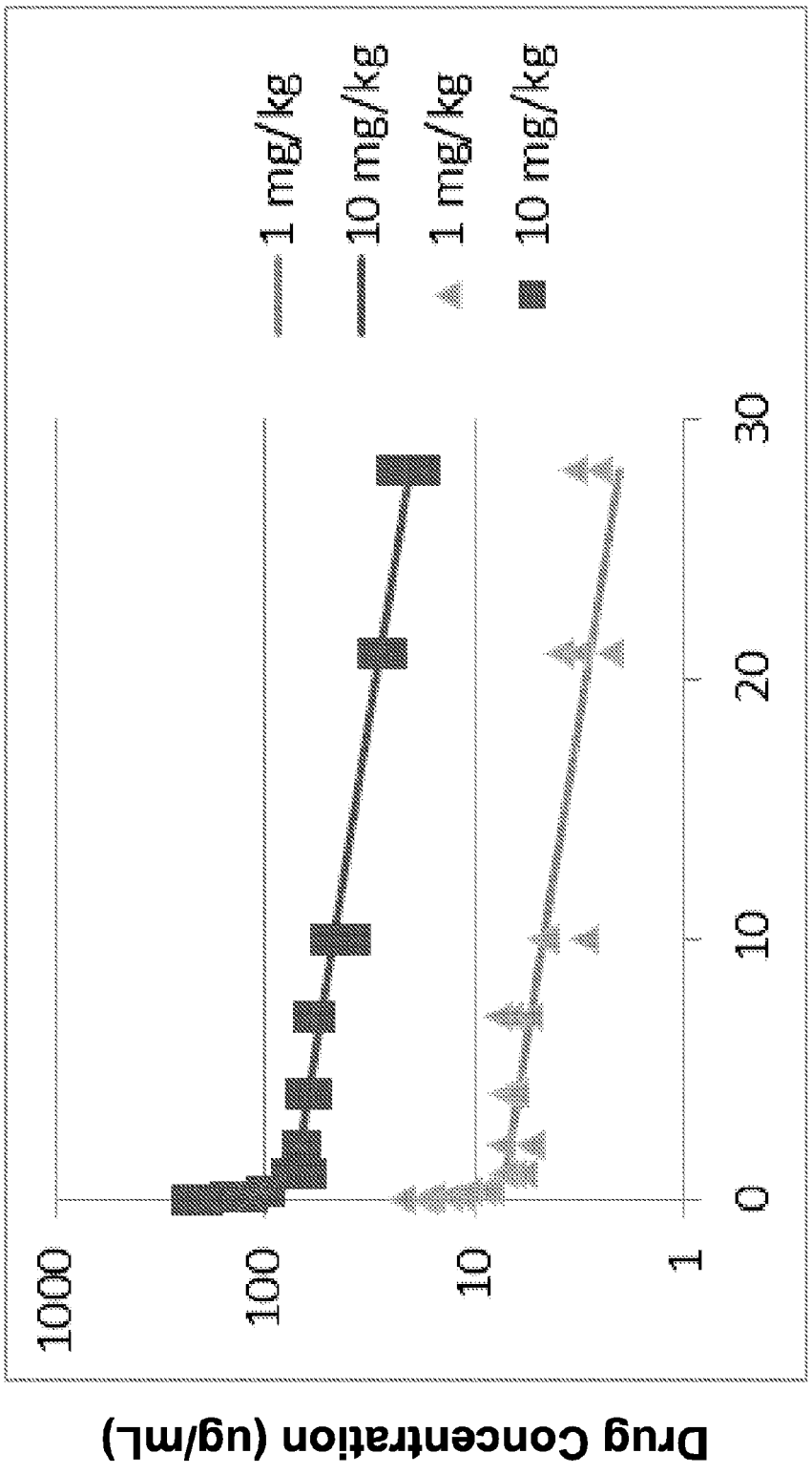

1 mg/kg
10 mg/kg
1 mg/kg
10 mg/kg
1000
100
10
1
0
10
20
30
Time (d)
Drug Concentration (ug/mL)

FIG. 13

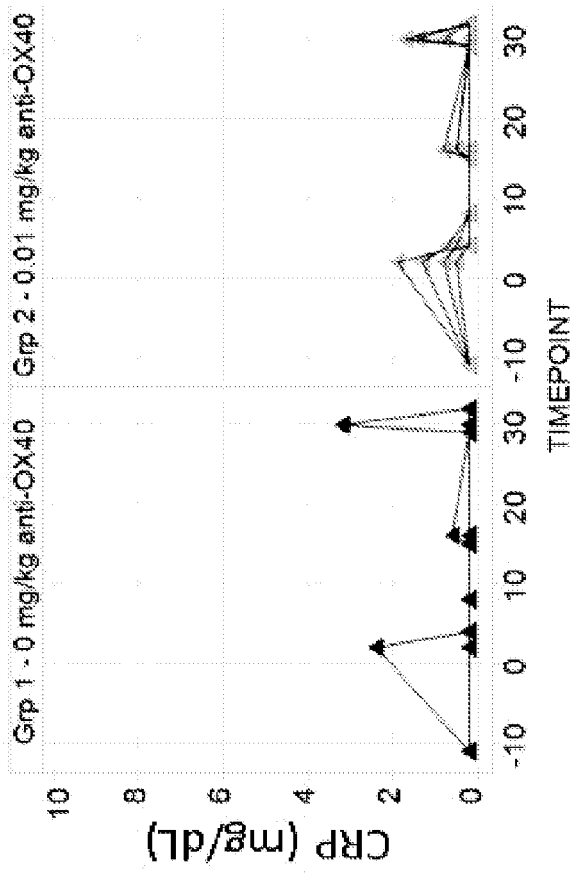

Grp 1 - 0 mg/kg anti-OX40
Grp 2 - 0.01 mg/kg anti-OX40
CRP (mg/dL)
0
2
4
6
8
10
-10
0
10
20
30
-10
0
10
20
30
TIMEPOINT

FIG. 14A

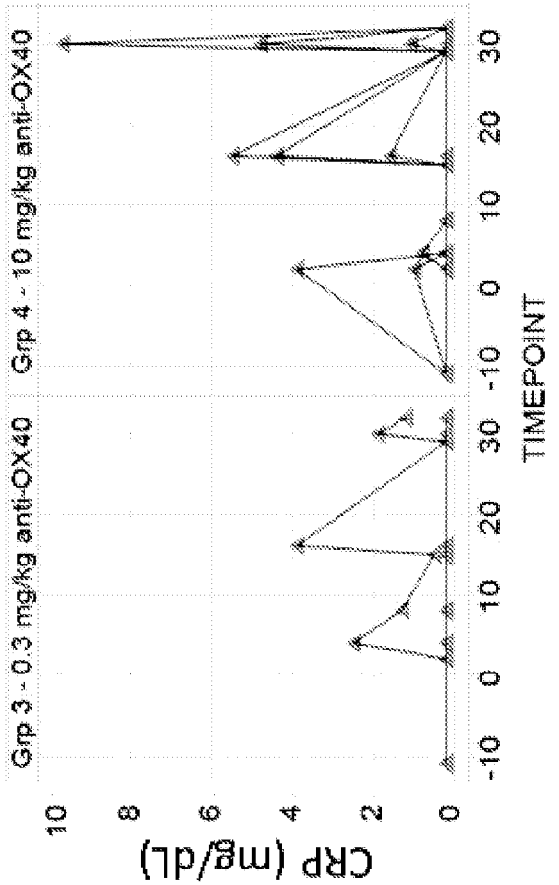

Grp 3 - 0.3 mg/kg anti-OX40
Grp 4 - 10 mg/kg anti-OX40
CRP (mg/dL)
0
2
4
6
8
10
-10
0
10
20
30
-10
0
10
20
30
TIMEPOINT

FIG. 14B

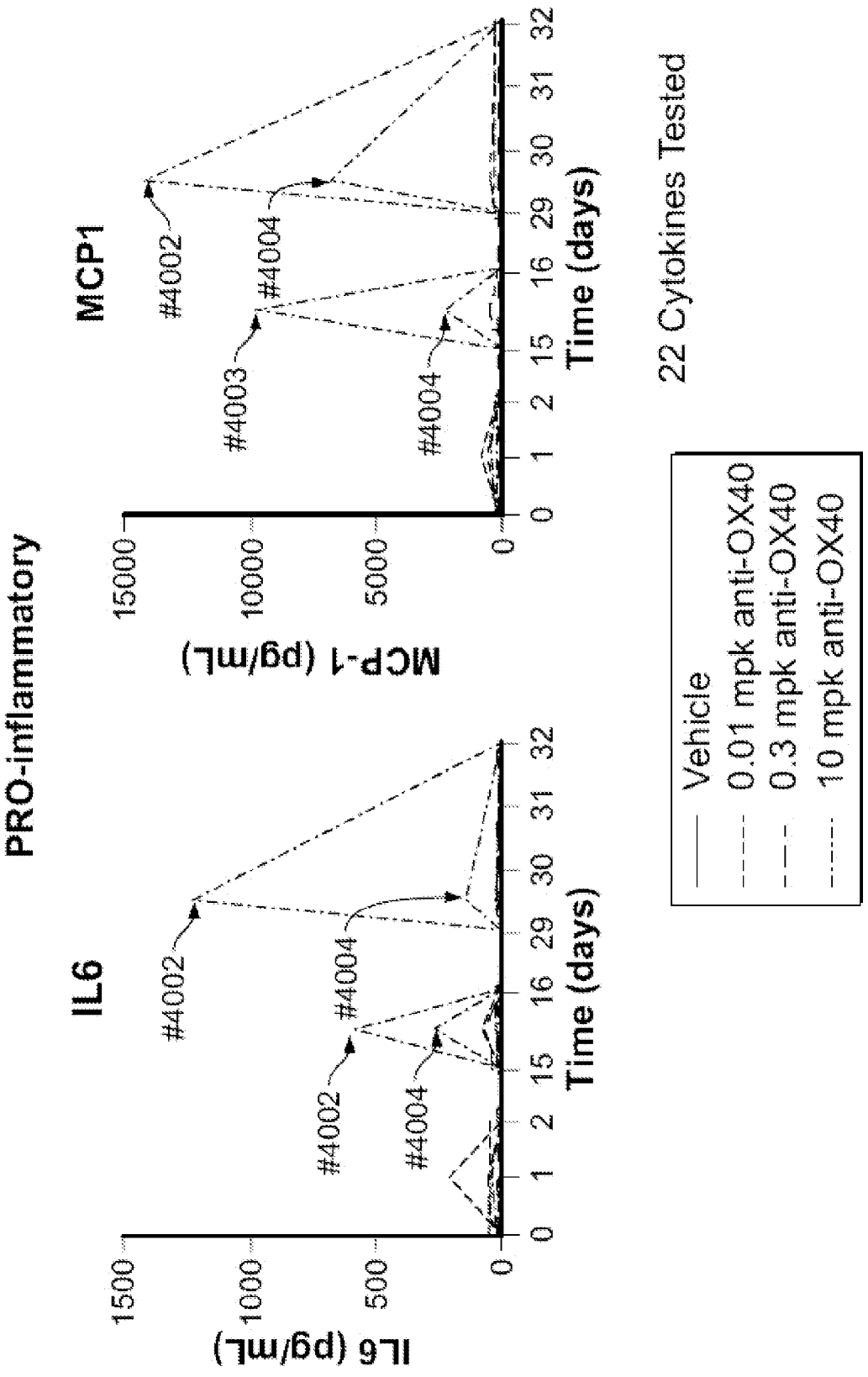

PRO-inflammatory
IL6
IL6 (pg/mL)
1500
1000
500
0
0 1 2 15 16 29 30 31 32
Time (days)
#4002
#4004
#4002
#4004
MCP1
MCP-1 (pg/mL)
15000
10000
5000
0
0 1 2 15 16 29 30 31 32
Time (days)
#4002
#4003
#4004
#4004
22 Cytokines Tested
Vehicle
0.01 mpk anti-OX40
0.3 mpk anti-OX40
10 mpk anti-OX40

FIG. 15A

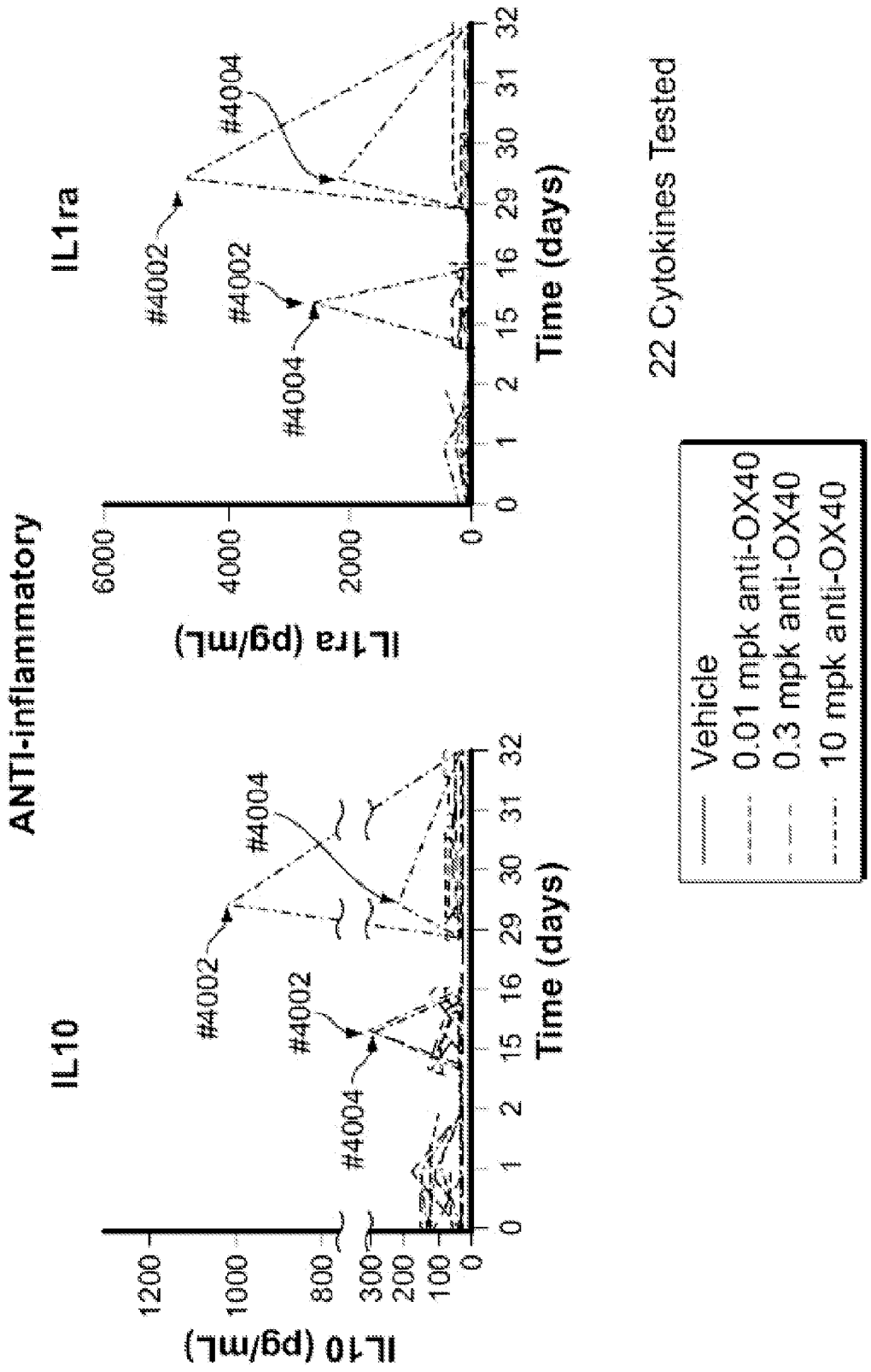

ANTI-inflammatory
IL10
IL-10 (pg/mL)
1200
1000
800
300
200
100
0
#4002
#4004
#4002
#4004
0 1 2 15 16 29 30 31 32
Time (days)
IL1ra
IL1ra (pg/mL)
6000
4000
2000
0
#4002
#4004
#4002
#4004
0 1 2 15 16 29 30 31 32
Time (days)
22 Cytokines Tested
Vehicle
0.01 mpk anti-OX40
0.3 mpk anti-OX40
10 mpk anti-OX40

FIG. 15B

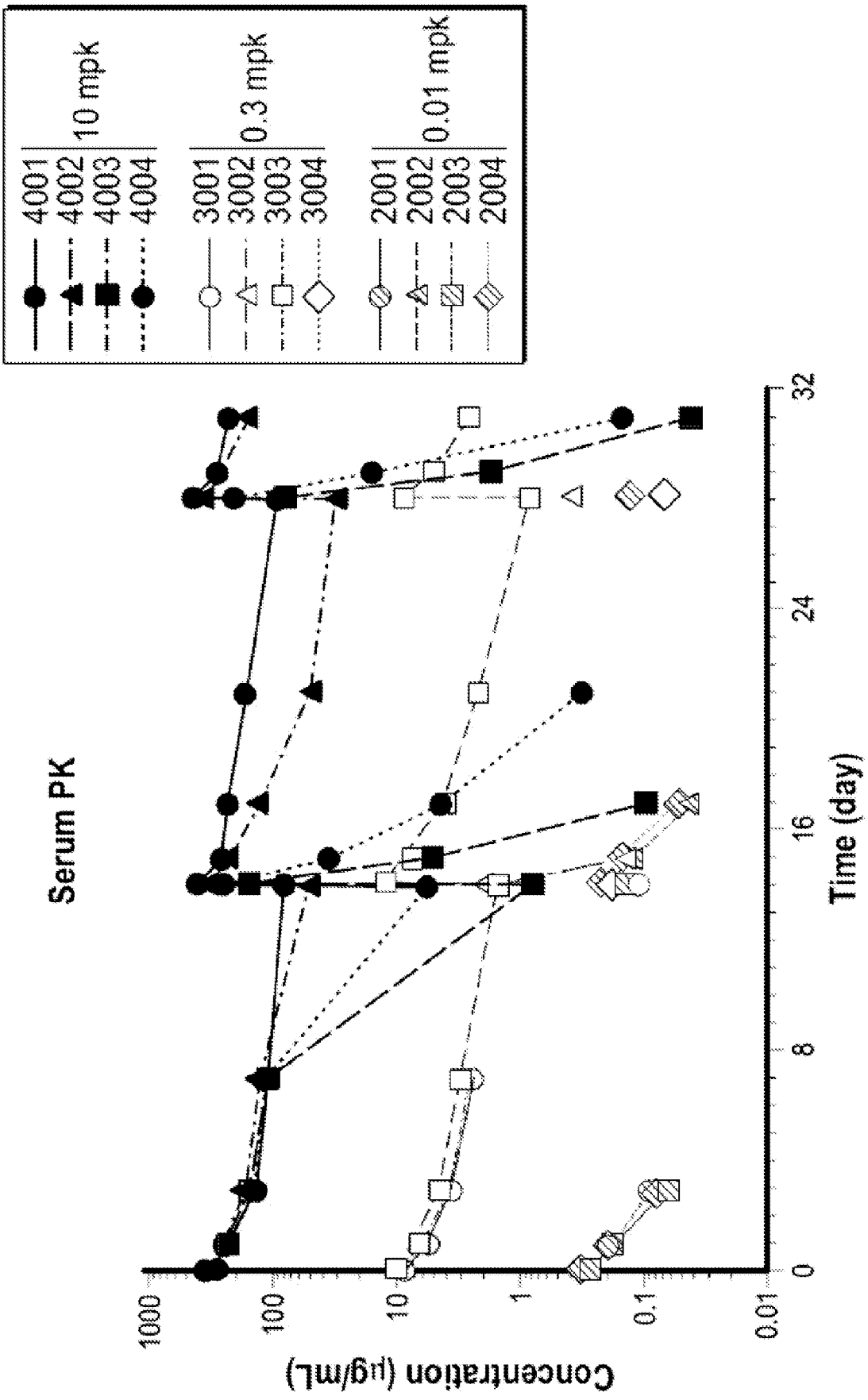

4001
4002
4003
4004
10 mpk
3001
3002
3003
3004
0.3 mpk
2001
2002
2003
2004
0.01 mpk
Serum PK
Concentration (μg/mL)
1000
100
10
1
0.1
0.01
0
8
16
24
32
Time (day)

FIG. 16A

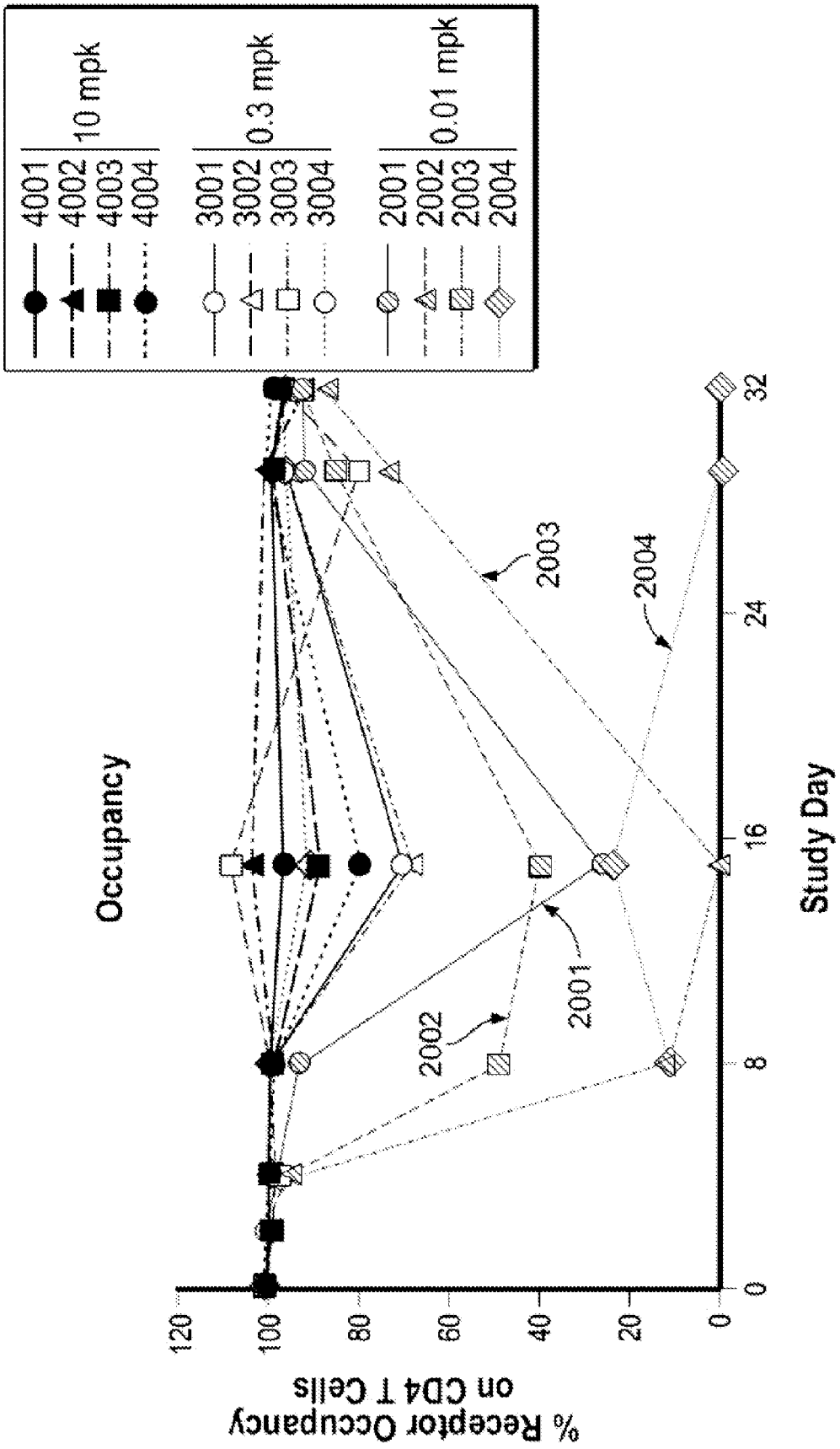

10 mpk
4001
4002
4003
4004
0.3 mpk
3001
3002
3003
3004
0.01 mpk
2001
2002
2003
2004
Occupancy
% Receptor Occupancy on CD4 T Cells
120
100
80
60
40
20
0
0
8
16
24
32
Study Day
2003
2004
2001
2002

FIG. 16B

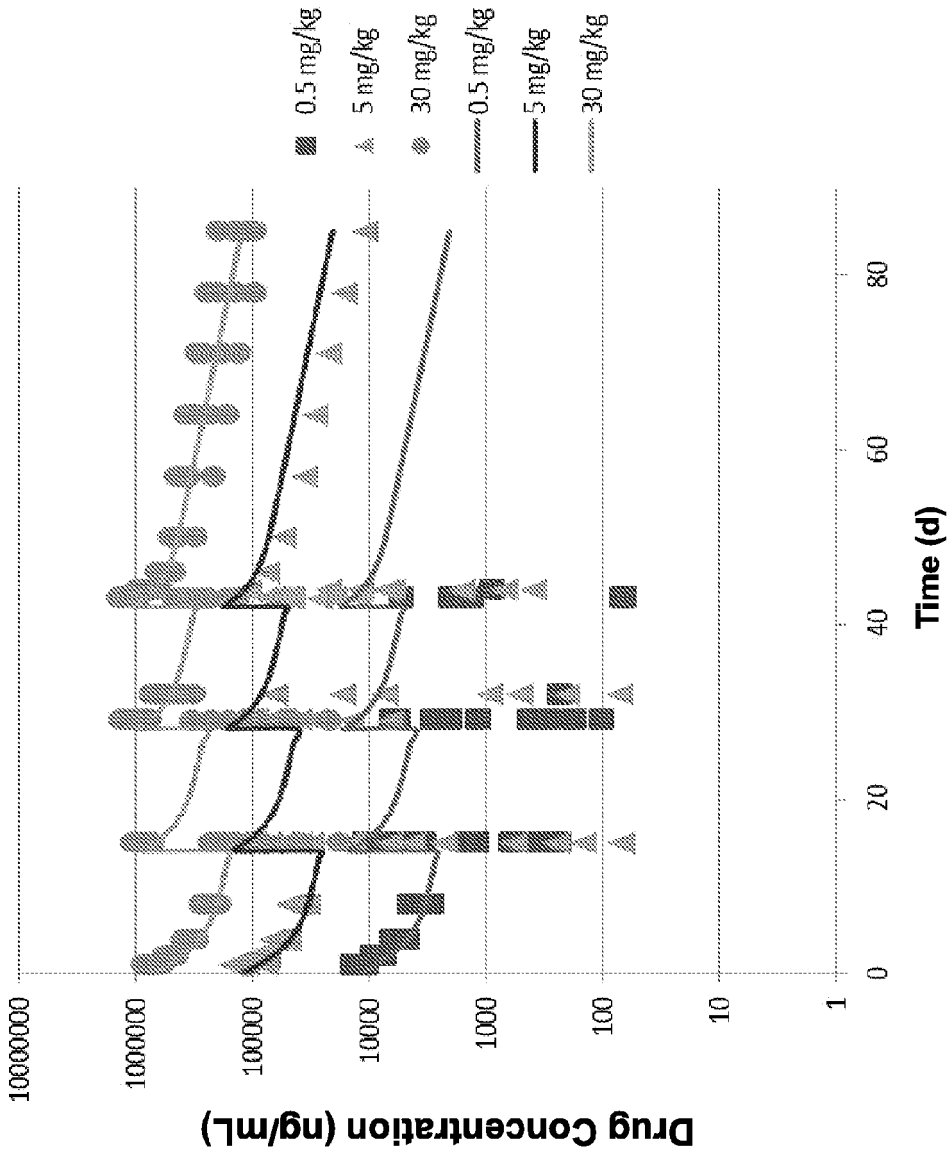

Drug Concentration (ng/mL)
10000000
1000000
100000
10000
1000
100
10
1
0
20
40
60
80
Time (d)
0.5 mg/kg
5 mg/kg
30 mg/kg
0.5 mg/kg
5 mg/kg
30 mg/kg

FIG. 17

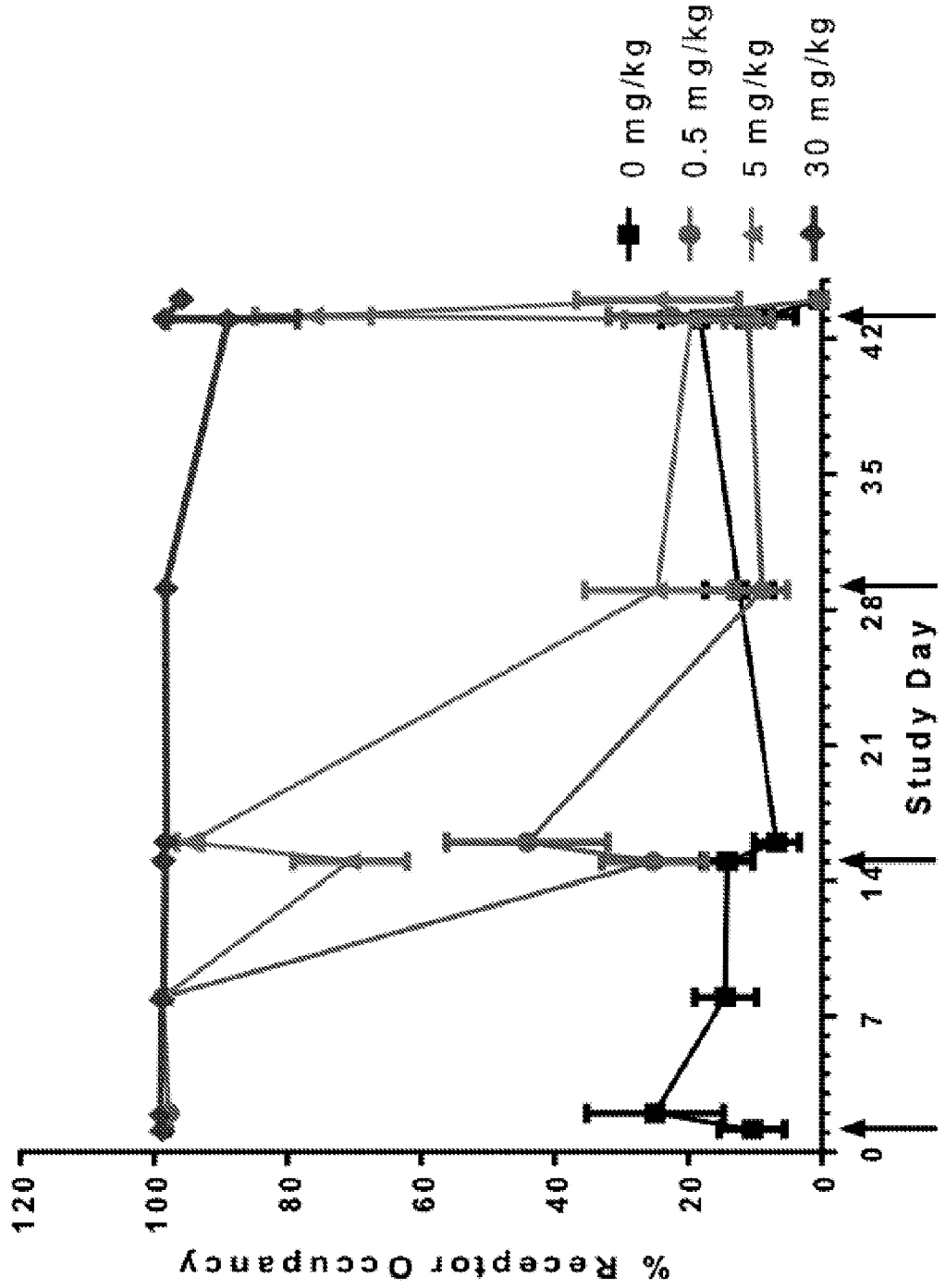

0 mg/kg
0.5 mg/kg
5 mg/kg
30 mg/kg
% Receptor Occupancy
120
100
80
60
40
20
0
0
7
14
21
28
35
42
Study Day

FIG. 18

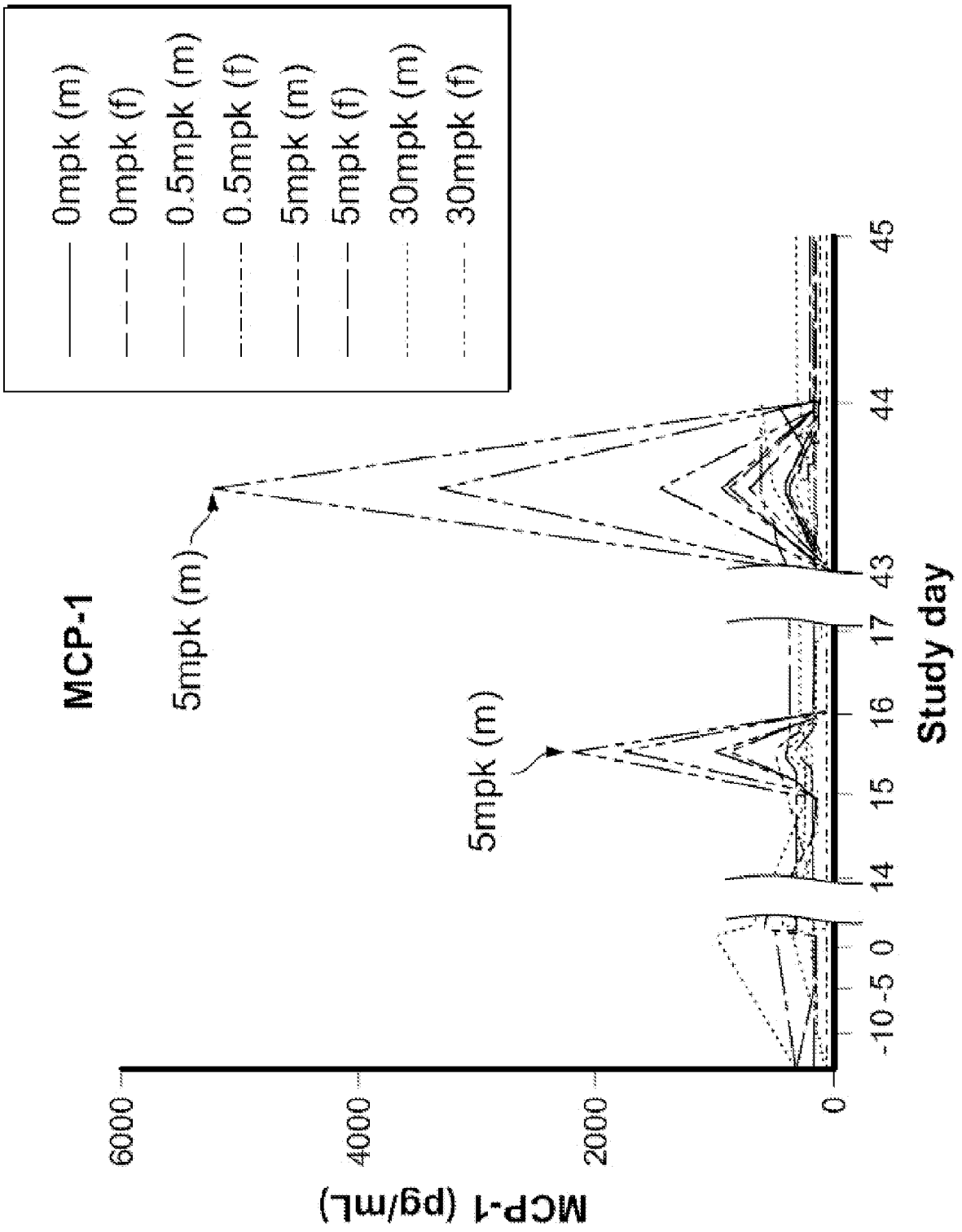

MCP-1
0mpk (m)
0mpk (f)
0.5mpk (m)
0.5mpk (f)
5mpk (m)
5mpk (f)
30mpk (m)
30mpk (f)
5mpk (m)
5mpk (m)
MCP-1 (pg/mL)
6000
4000
2000
0
-10 -5 0
14 15 16 17
43 44 45
Study day

FIG. 19

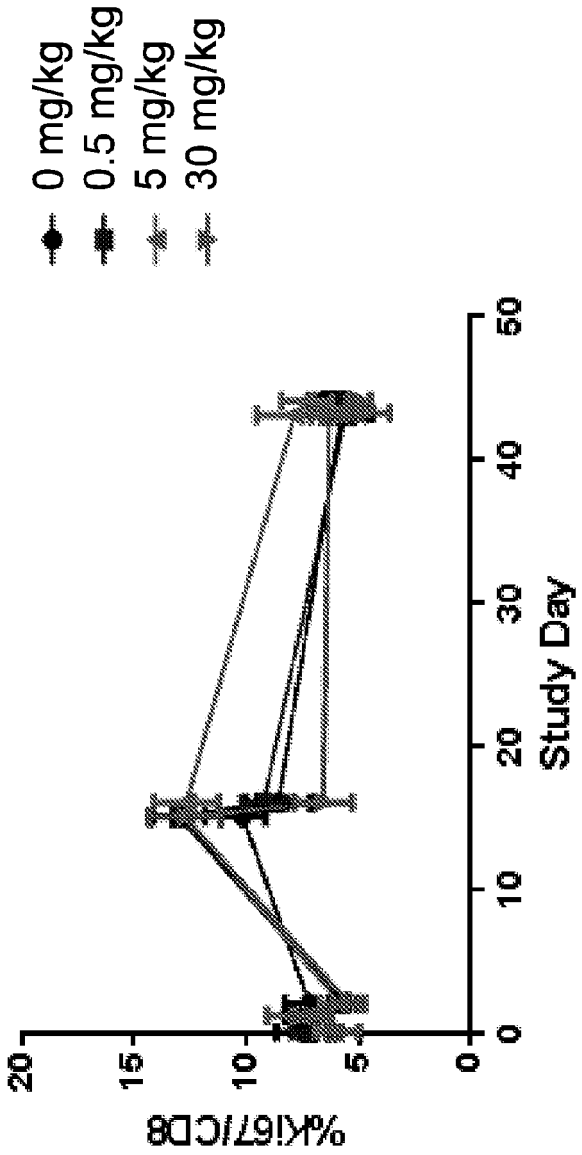

0 mg/kg
0.5 mg/kg
5 mg/kg
30 mg/kg
%Ki67/CD8
0
5
10
15
20
0
10
20
30
40
50
Study Day

FIG. 20