FIG. 1A

VH Alignment:

```
                 ----------FW1----------CDR1-----FW2----------CDR2--------

9F11             EVELVESGGGLVQPGGSMKLSCAASGFTFSDAWMDWVRQSPEKGLEWVAEIRSEADNHPTYYAESVKG
9F11-4           EVQLVESGGGLVQPGGSLRLSCAASGFTFSDAWMDWVRQAPGKGLEWVAEIRSEADNHPTYYAESVKG
9F11-6           EVQLVESGGGLVQPGGSLRLSCAASGFTFSDAWMDWVRQAPGKGLEWVAEIRSEADNHPTYYAESVKG
9F11-11          EVQLVESGGGLVQPGGSLRLSCAASGFTFSDAWMDWVRQAPGKGLEWVAEIRSEADNHPTYYAESVKG
```

VL Alignment:

```
                 ----------FW1----------CDR1----------FW2------CDR2---------

9F11             DIVLTQSPASLAVSLGQRATISCRASKSVSTYGYSYMHWYQQKPGQPPKLLIYLASNLESGVPARFSG
9F11-4           DIVMTQTPLSLSVTPGQPASISCRASKSVSTYGYSYMHWYLQKPGQPPQLLIYLASNLESGVPDRFSG
9F11-6           DIVMTQTPLSLSVTPGQPASISCRASKSVSTYGYSYMHWYLQKPGQPPQLLIYLASNLESGVPDRFSG
9F11-11          DIVLTQTPLSLSVTPGQPASISCRASKSVSTYGYSYMHWYLQKPGQPPQLLIYLASNLESGVPDRFSG
```

SUBSTITUTE SHEET (RULE 26)

FIG. 1A Contd.

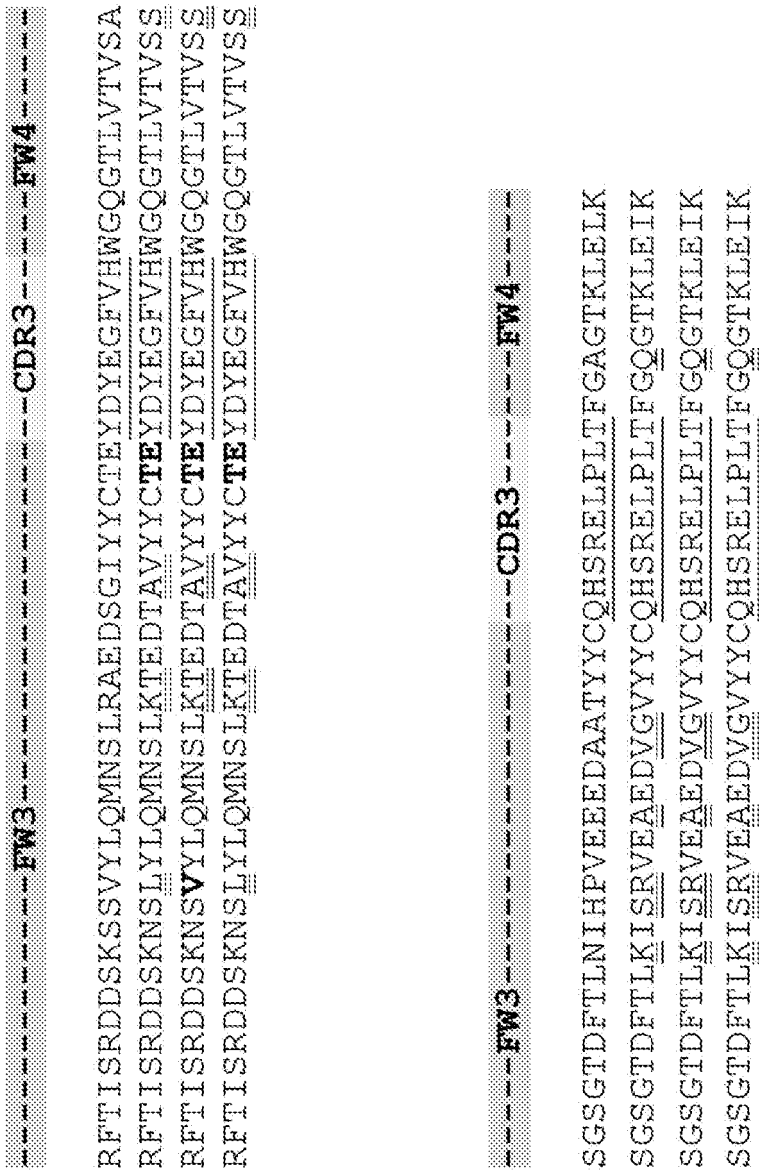

----------FW3----------CDR3----FW4----
RFTISRDDSKSSVYLQMNSLRAEDSGIYYCTEYDYEGFVHWGQGTLVTVSA
RFTISRDDSKNSLYLQMNSLKTEDTAVYYCTEYDYEGFVHWGQGTLVTVSS
RFTISRDDSKNSVYLQMNSLKTEDTAVYYCTEYDYEGFVHWGQGTLVTVSS
RFTISRDDSKNSLYLQMNSLKTEDTAVYYCTEYDYEGFVHWGQGTLVTVSS
----------FW3----------CDR3----FW4----
SGSGTDFTLNIHPVEEEDAATYYCQHSRELPLTFGAGTKLELK
SGSGTDFTLKISRVEAEDVGVYYCQHSRELPLTFGQGTKLEIK
SGSGTDFTLKISRVEAEDVGVYYCQHSRELPLTFGQGTKLEIK
SGSGTDFTLKISRVEAEDVGVYYCQHSRELPLTFGQGTKLEIK

FIG. 1B

VL Alignment:

```
                    ----------FW1----------CDR1---------FW2------CDR2----------

19E3VL-murine       DIQLTQTTSSLSASLGDRVTISCRASQDISNFLNWYQQTPDGTVKLLIYYTSRLHSGVPSRFSGSG
19E3VL-K1           DIQLTQSPSSLSASVGDRVTITCRASQDISNFLNWYQQKPGKAPKLLIYYTSRLHSGVPSRFSGSG
19E3VL-K2           DIQLTQSPSSLSASVGDRVTITCRASQDISNFLNWYQQKPGKAVKLLIYYTSRLHSGVPSRFSGSG
```

VH Alignment:

```
                    ----------FW1-----------------CDR1-----FW2-----------CDR2------

19E3VH-murine       QVQLQQPGSELVMPGASVKMSCKASGYIFTDYWMHWVKQRPGQGLEWIGTIDPSDNYTIYSQNFKG
19E3VH-Ha           QVQLVQSGAEVKKPGASVKVSCKASGYTFTDYWMHWVRQAPGQGLEWMGTIDPSDNYTIYSQNFKG
19E3VH-Hb           QVQLQQPGSELVMPGASVKMSCKASGYIFTDYWMHWVRQAPGQGLEWMGTIDPSDNYTIYSQNFKG
19E3VH-Hc           QVQLVQSGAEVKKPGASVKVSCKASGYTFTDYWMHWVRQAPGQGLEWMGTIDPSDNYTIYSQNFKG
```

SUBSTITUTE SHEET (RULE 26)

FIG. 1B Contd.

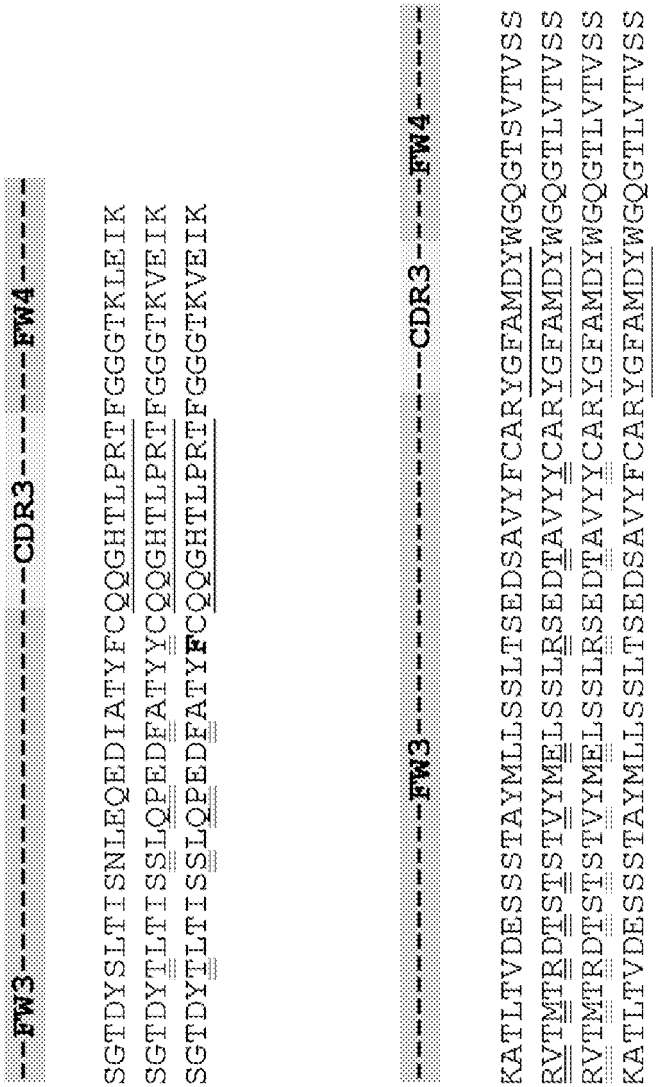

---FW3----------CDR3-----FW4-----
SGTDYSLTISNLEQEDIATYFCQQGHTLPRTFGGGTKLEIK
SGTDYTLTISSLQPEDFATYYCQQGHTLPRTFGGGTKVEIK
SGTDYTLTISSLQPEDFATYFCQQGHTLPRTFGGGTKVEIK
----------FW3----------CDR3-----FW4-----
KATLTVDESSSTAYMLLSSLTSEDSAVYFCARYGFAMDYWGQGTSVTVSS
RVTMTRDTSTSTVYMELSSLRSEDTAVYYCARYGFAMDYWGQGTLVTVSS
RVTMTRDTSTSTVYMELSSLRSEDTAVYYCARYGFAMDYWGQGTLVTVSS
KATLTVDESSSTAYMLLSSLTSEDSAVYFCARYGFAMDYWGQGTLVTVSS

FIG. 2A

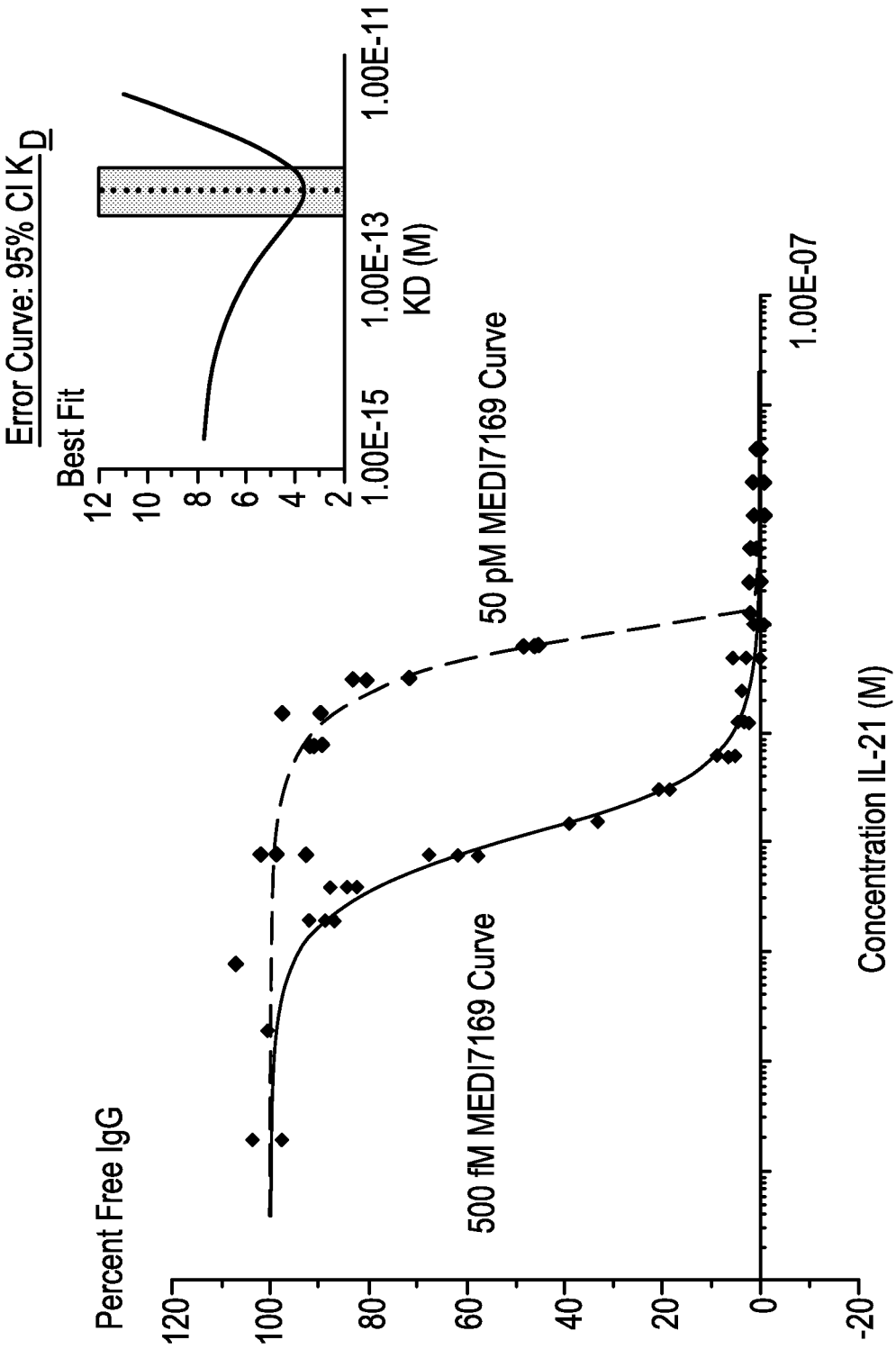

Error Curve: 95% CI K_D
Best Fit
12
10
8
6
4
2
1.00E-15
1.00E-13
1.00E-11
KD (M)
50 pM MEDI7169 Curve
500 fM MEDI7169 Curve
Percent Free IgG
120
100
80
60
40
20
0
-20
1.00E-07
Concentration IL-21 (M)

FIG. 2B

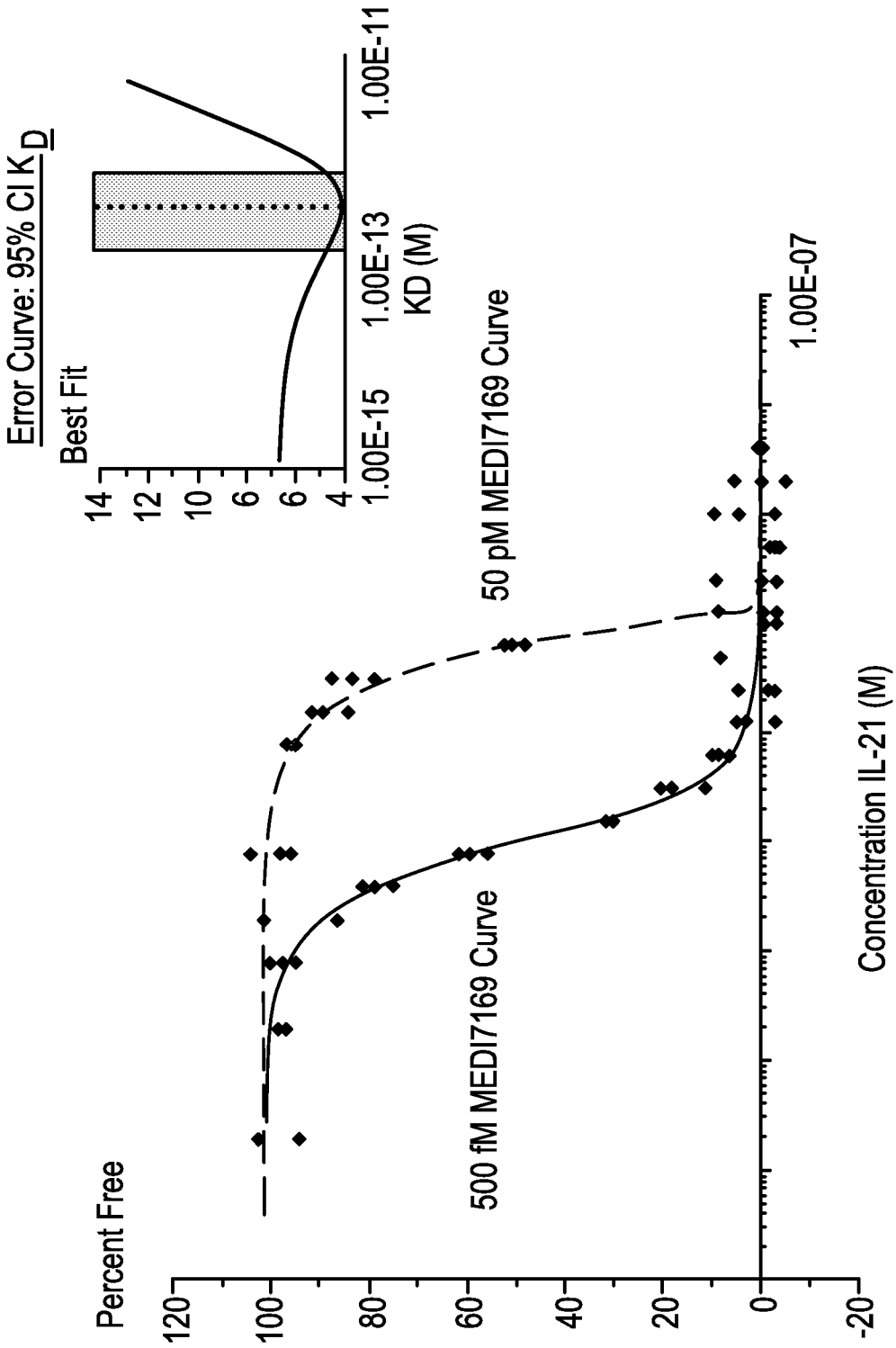

Error Curve: 95% CI K_D
Best Fit
14
12
10
6
6
4
1.00E-15
1.00E-13
1.00E-11
KD (M)
50 pM MEDI7169 Curve
500 fM MEDI7169 Curve
Percent Free
120
100
80
60
40
20
0
-20
1.00E-07
Concentration IL-21 (M)

FIG. 3A

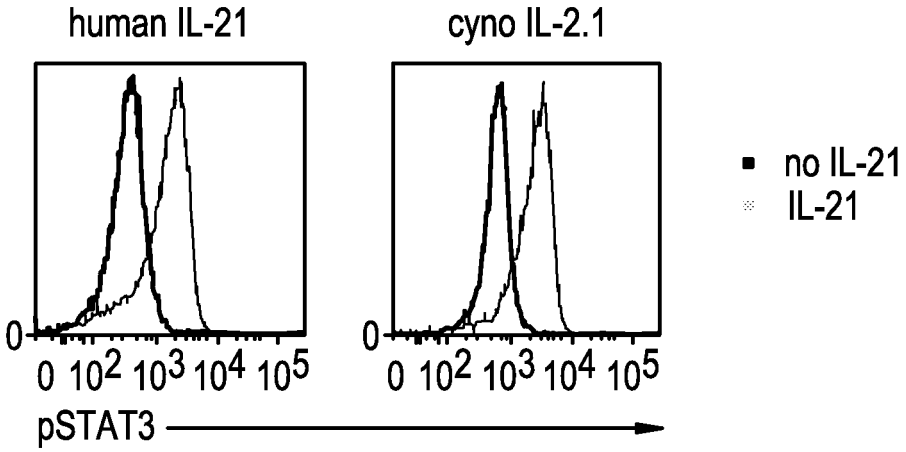

human IL-21
cyno IL-2.1
no IL-21
IL-21
0
0 10^2 10^3 10^4 10^5
pSTAT3

FIG. 3B

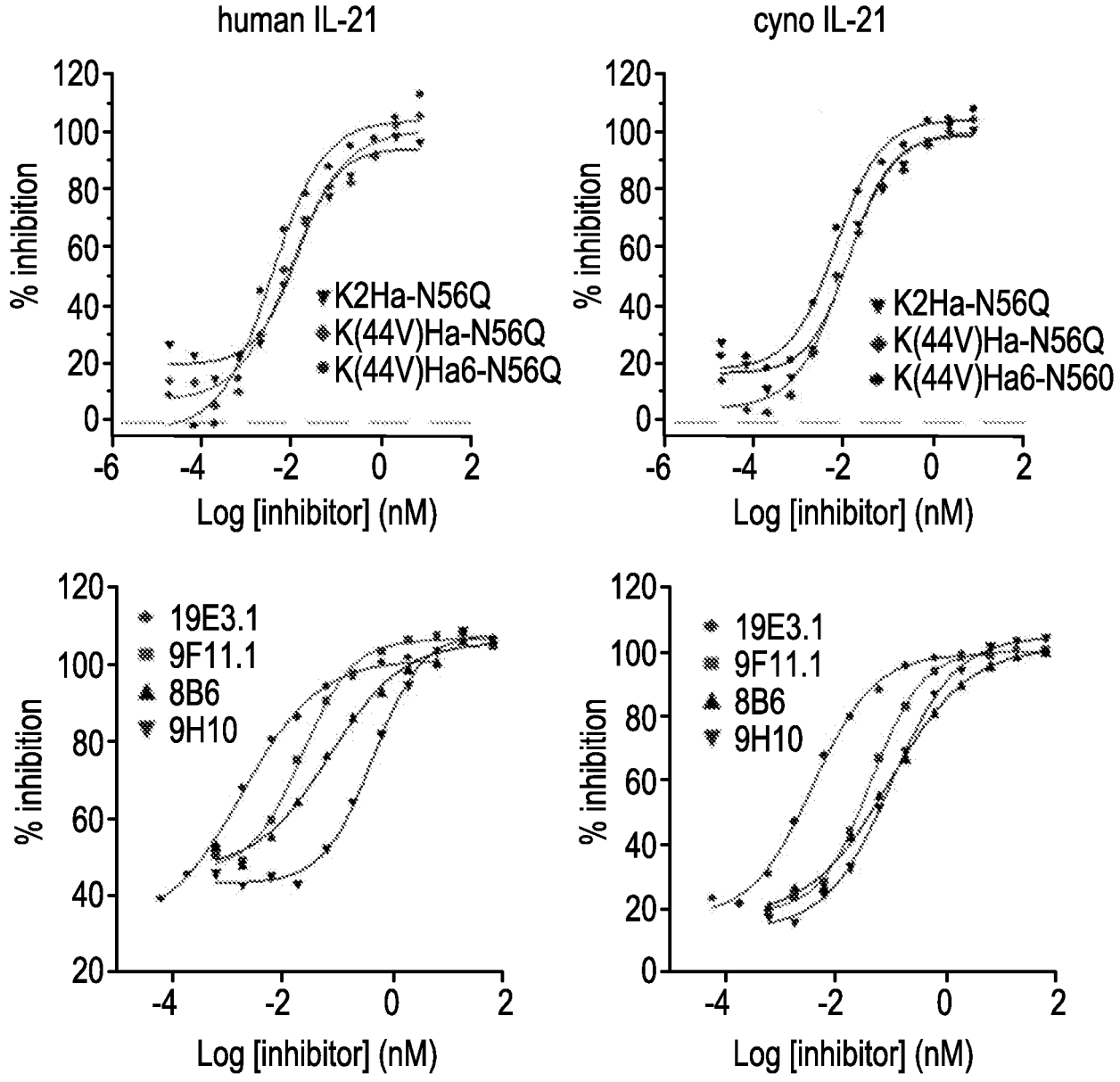

human IL-21
cyno IL-21
% inhibition
Log [inhibitor] (nM)
K2Ha-N56Q
K(44V)Ha-N56Q
K(44V)Ha6-N56Q
K(44V)Ha6-N560
19E3.1
9F11.1
8B6
9H10

FIG. 4A

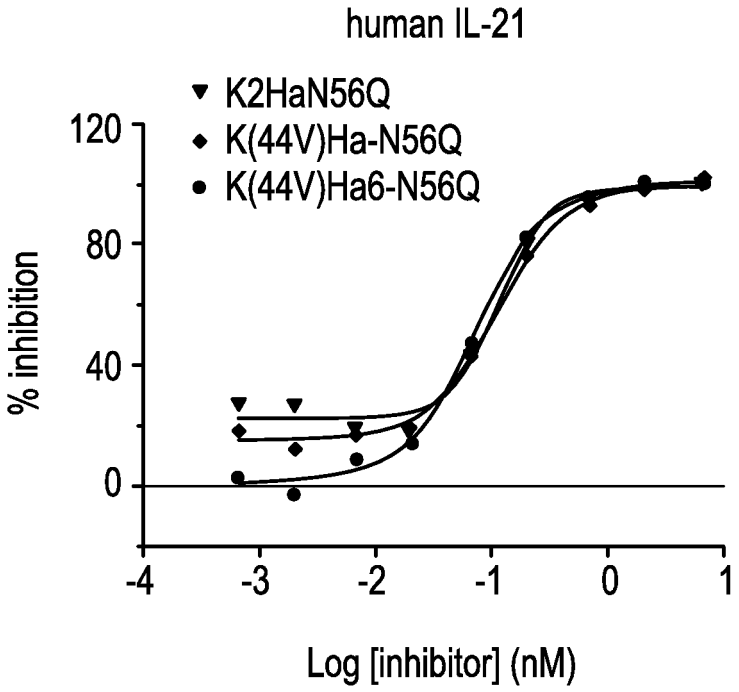

human IL-21
K2HaN56Q
K(44V)Ha-N56Q
K(44V)Ha6-N56Q
120
80
40
0
% inhibition
-4
-3
-2
-1
0
1
Log [inhibitor] (nM)

FIG. 4B

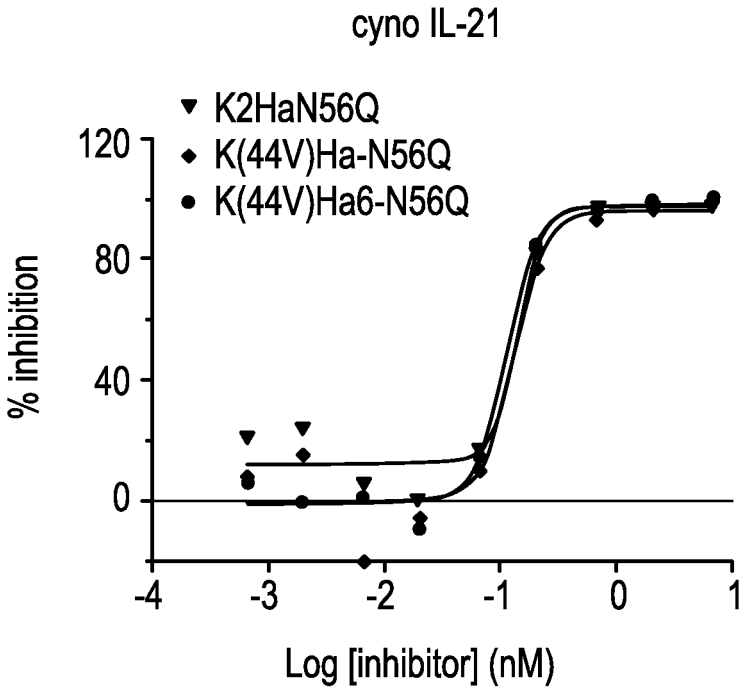

cyno IL-21
K2HaN56Q
K(44V)Ha-N56Q
K(44V)Ha6-N56Q
120
80
40
0
% inhibition
-4
-3
-2
-1
0
1
Log [inhibitor] (nM)

FIG. 5A

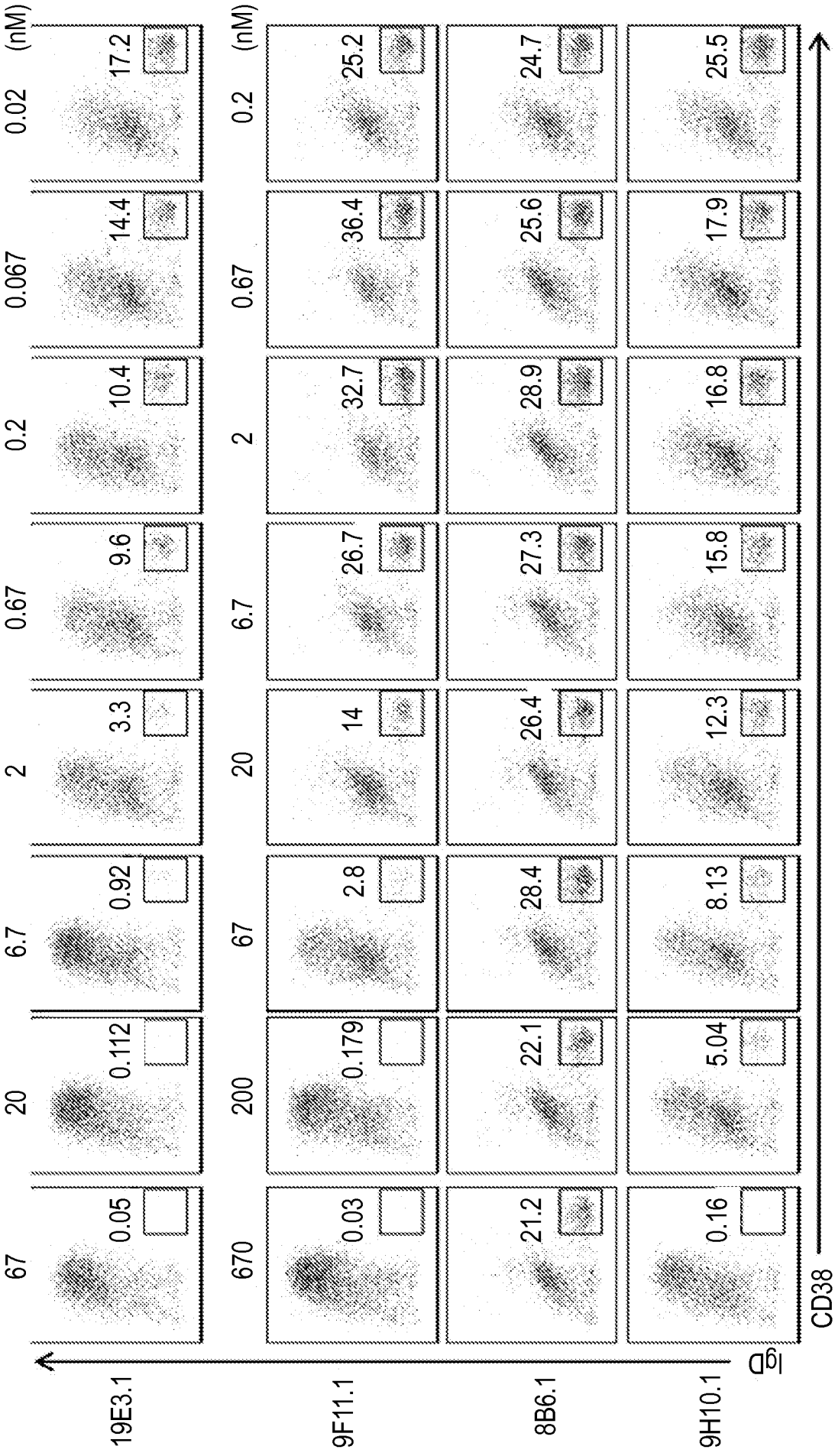

19E3.1
9F11.1
8B6.1
9H10.1
IgD
CD38
(nM)
0.02
0.067
0.2
0.67
2
6.7
20
67
200
670
0.05
0.112
0.92
3.3
9.6
10.4
14.4
17.2
0.03
0.179
2.8
14
26.7
32.7
36.4
25.2
21.2
22.1
28.4
26.4
27.3
28.9
25.6
24.7
0.16
5.04
8.13
12.3
15.8
16.8
17.9
25.5

FIG. 5B

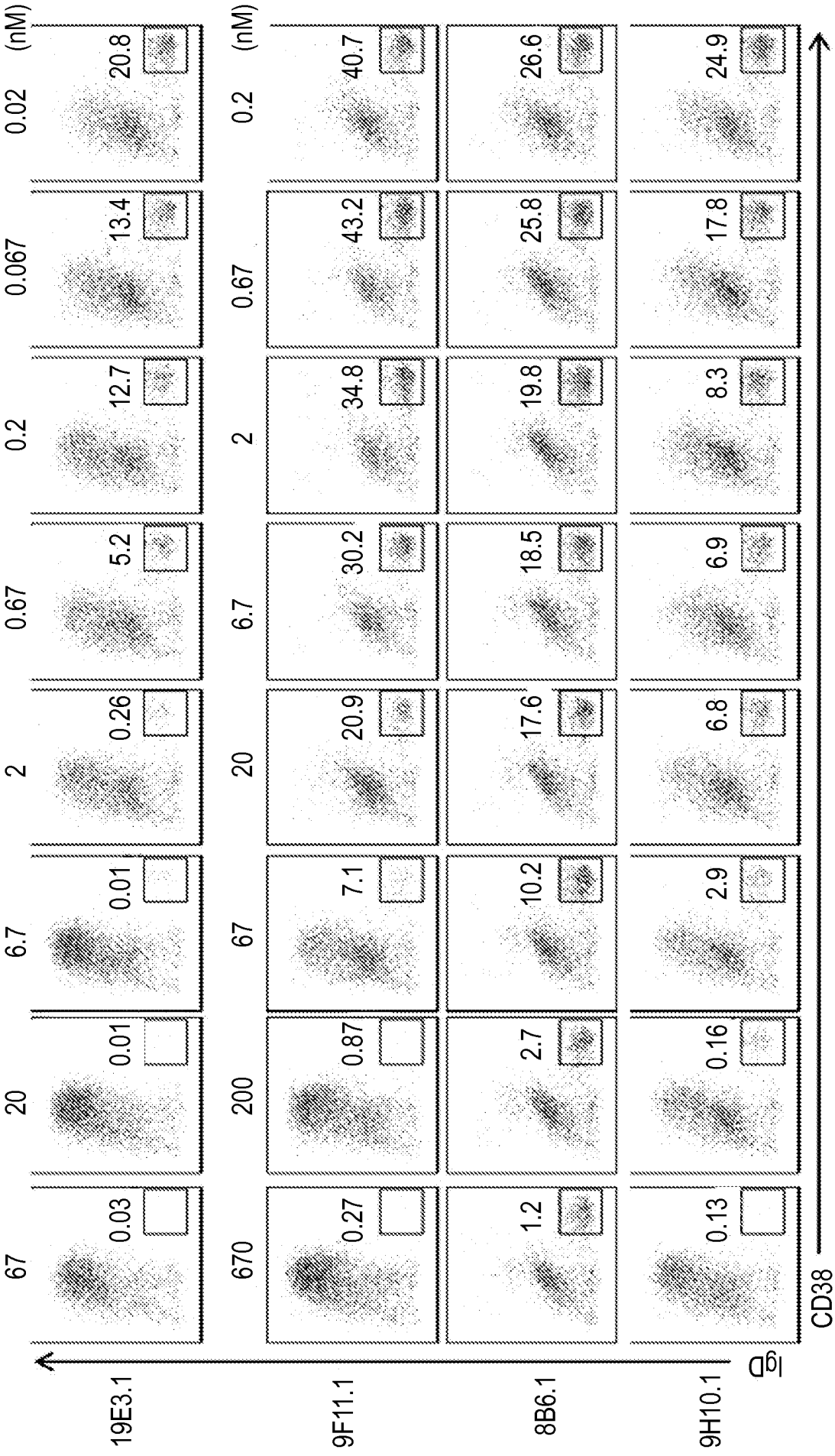

19E3.1
9F11.1
8B6.1
9H10.1
IgD
CD38
67
20
6.7
2
0.67
0.2
0.067
0.02 (nM)
670
200
67
20
6.7
2
0.67
0.2 (nM)
0.03
0.01
0.01
0.26
5.2
12.7
13.4
20.8
0.27
0.87
7.1
20.9
30.2
34.8
43.2
40.7
1.2
2.7
10.2
17.6
18.5
19.8
25.8
26.6
0.13
0.16
2.9
6.8
6.9
8.3
17.8
24.9

FIG. 5C

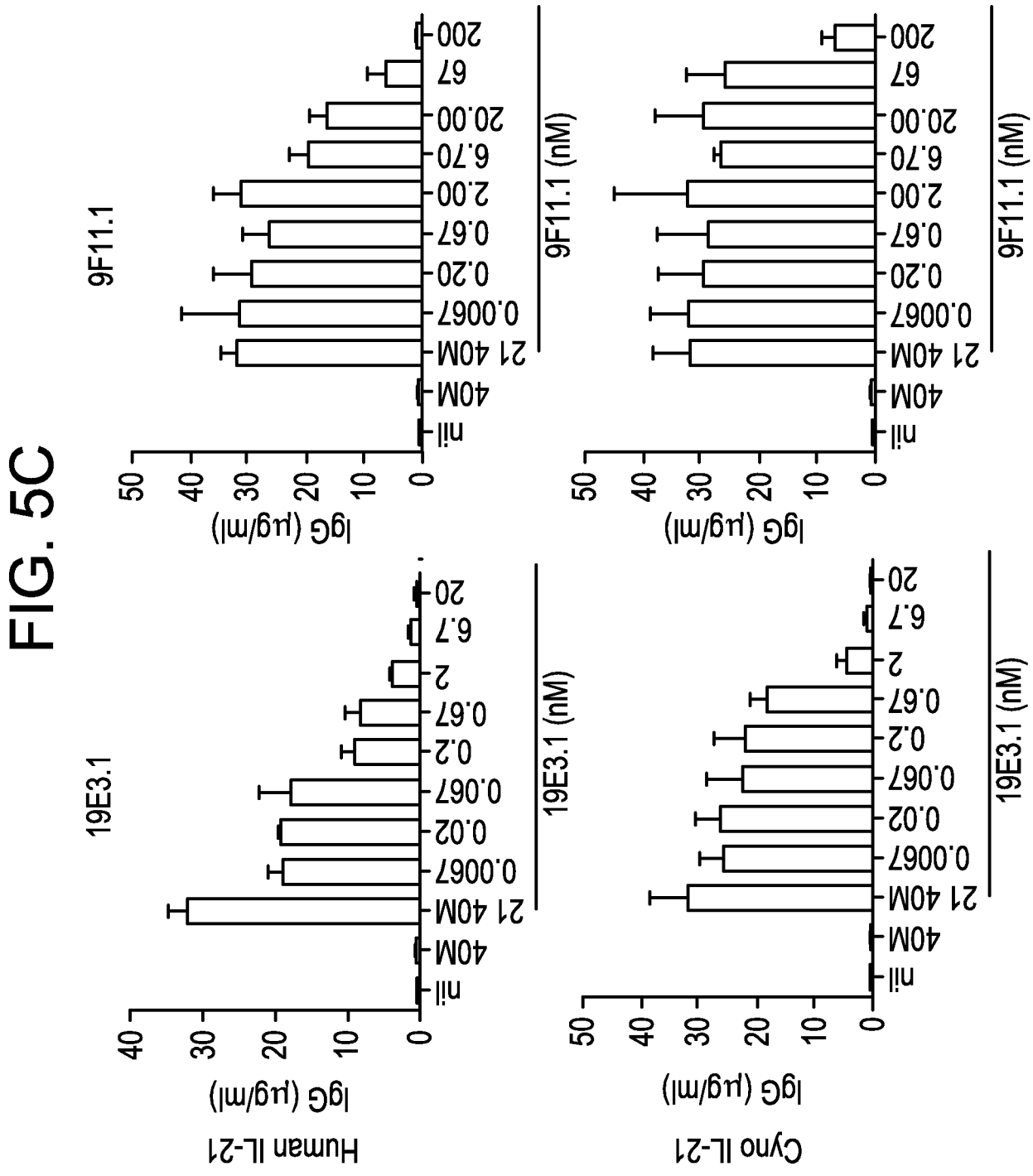

Human IL-21
Cyno IL-21
19E3.1
9F11.1
IgG (µg/ml)
19E3.1 (nM)
9F11.1 (nM)
nil
40M
21 40M
0.0067
0.02
0.067
0.2
0.67
2
6.7
20
0.20
2.00
6.70
20.00
67
200

FIG. 6A

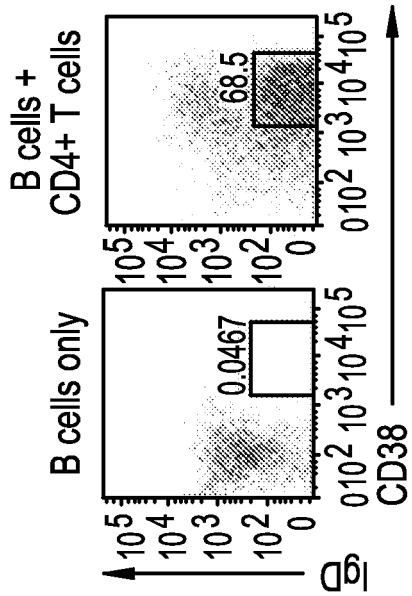

B cells only
B cells +
CD4+ T cells
0.0467
68.5
IgD
CD38
0
10^2
10^3
10^4
10^5

FIG. 6B

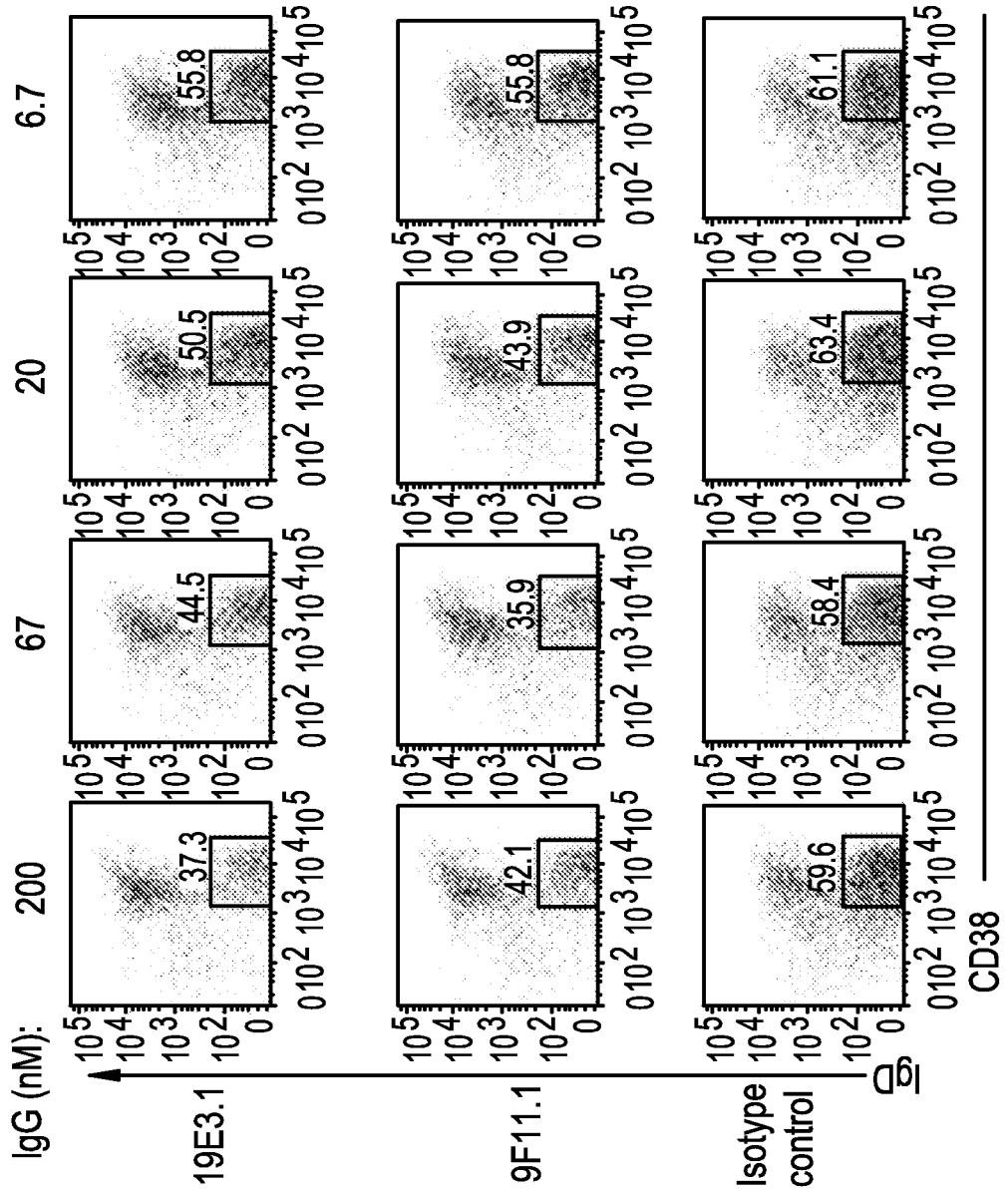

IgG (nM):
200
67
20
6.7
19E3.1
9F11.1
Isotype control
IgD
CD38
37.3
44.5
50.5
55.8
42.1
35.9
43.9
55.8
59.6
58.4
63.4
61.1

FIG. 6B Cont.

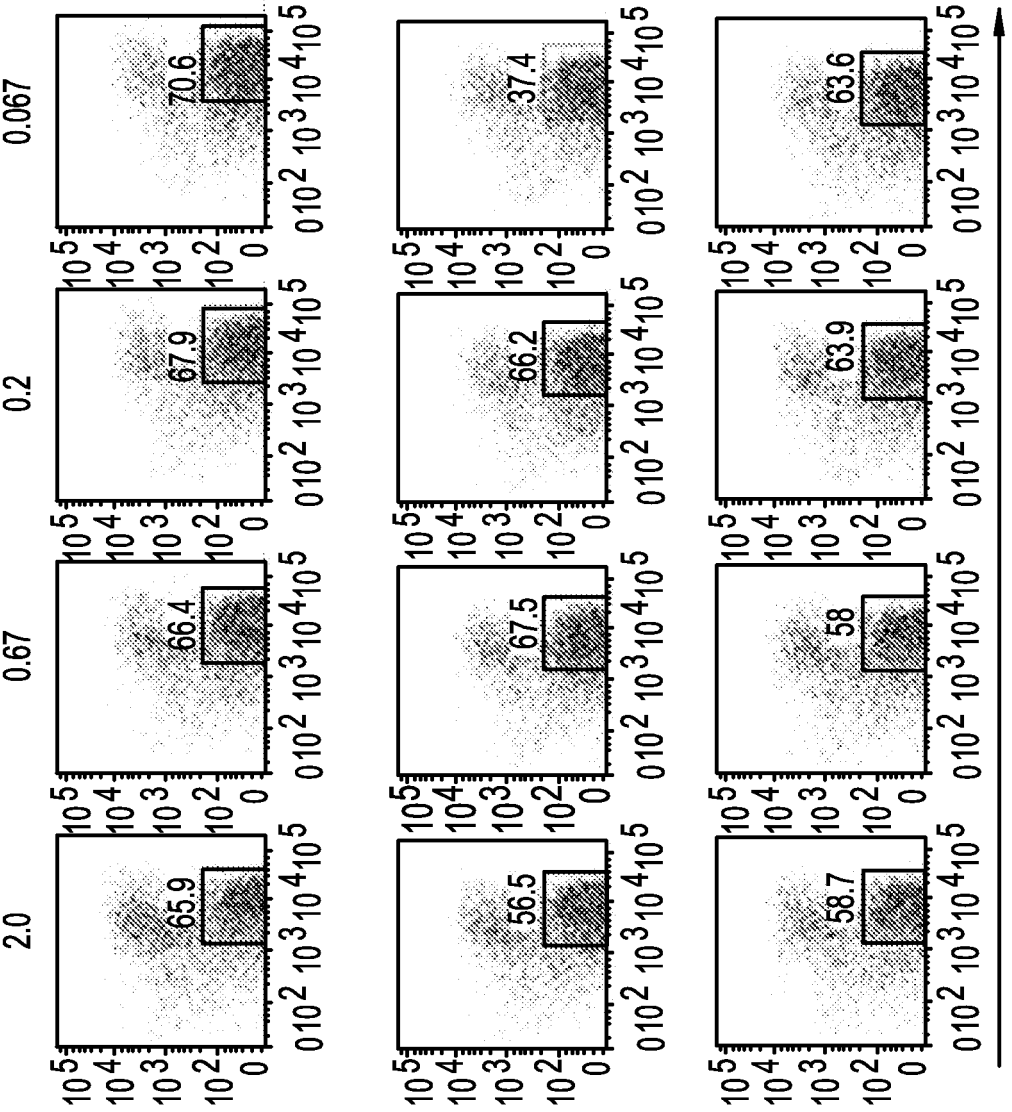


FIG. 6C

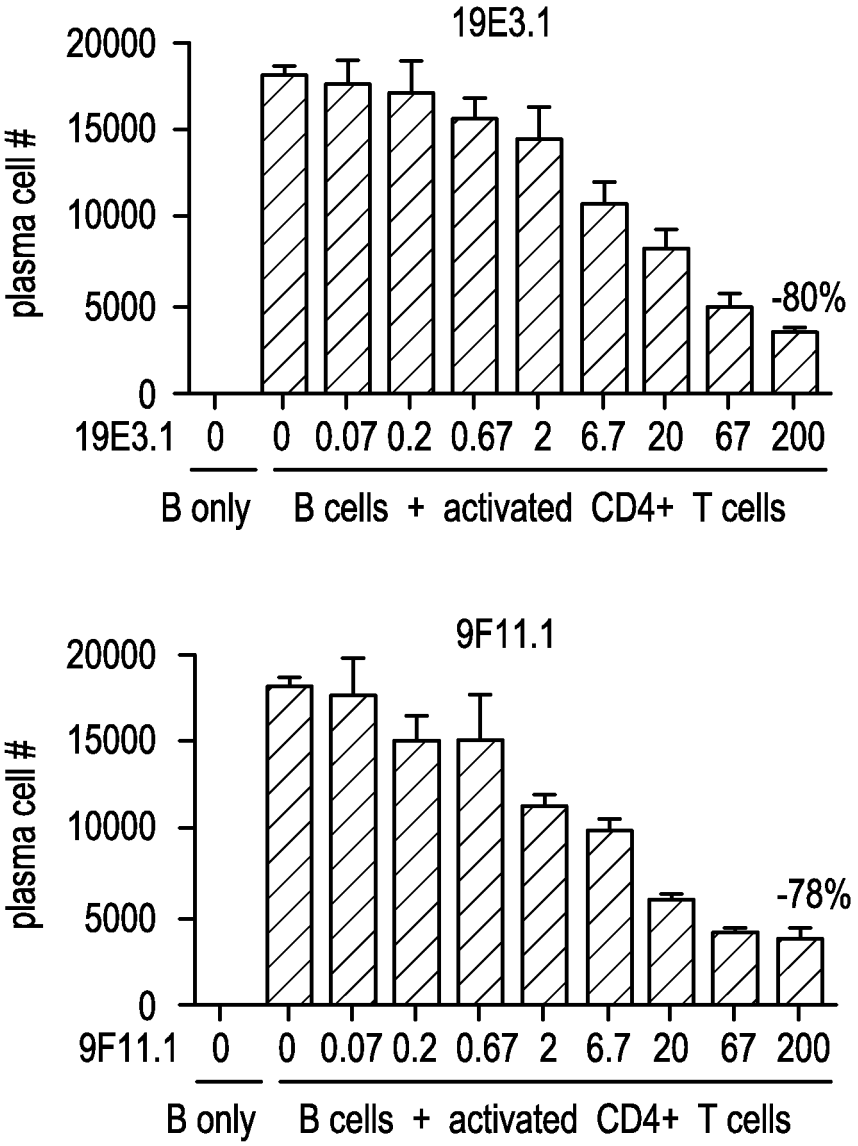
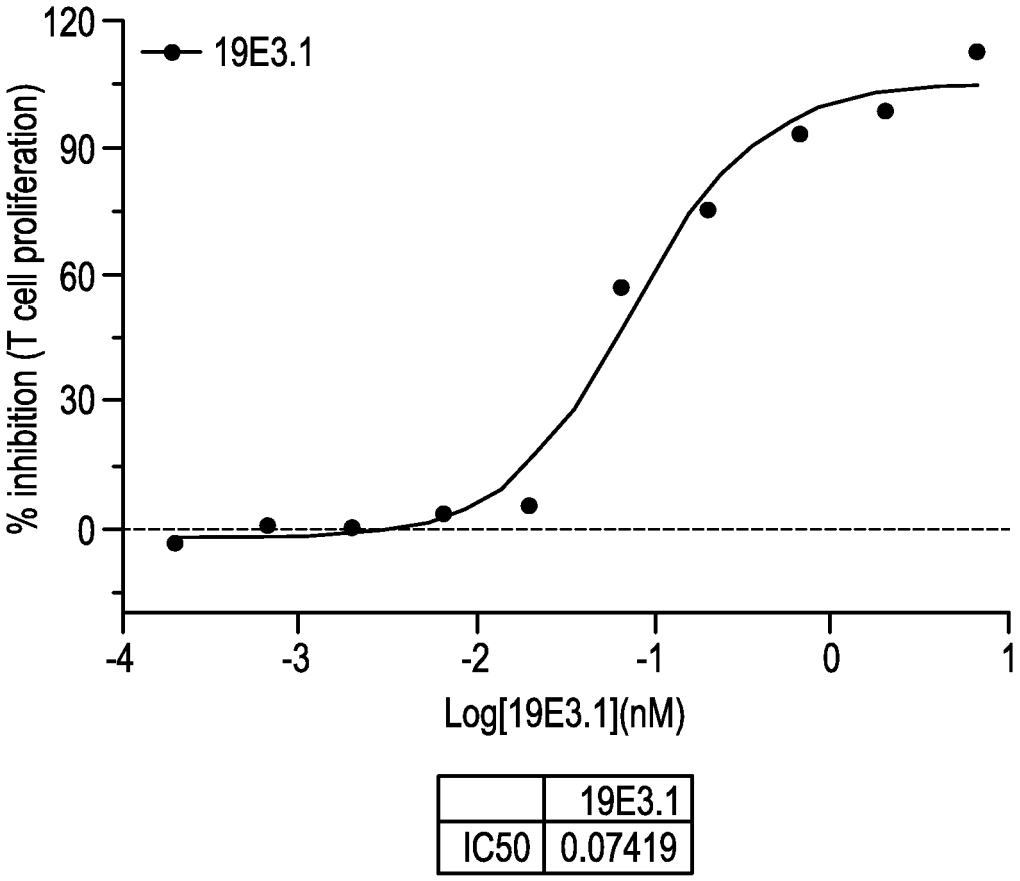

19E3.1
plasma cell #
20000
15000
10000
5000
0
-80%
19E3.1 0 0 0.07 0.2 0.67 2 6.7 20 67 200
B only
B cells + activated CD4+ T cells
9F11.1
plasma cell #
20000
15000
10000
5000
0
-78%
9F11.1 0 0 0.07 0.2 0.67 2 6.7 20 67 200
B only
B cells + activated CD4+ T cells

FIG. 7



	19E3.1
IC50	0.07419

FIG. 8A

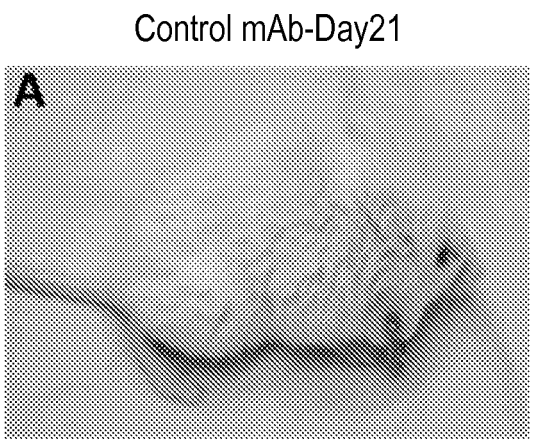


FIG. 8C

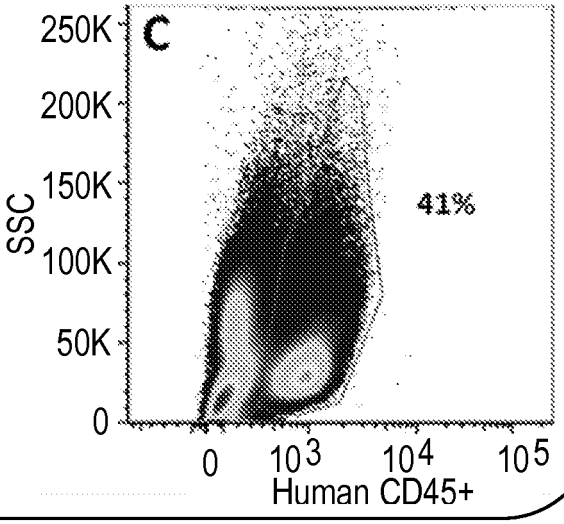


FIG. 8B

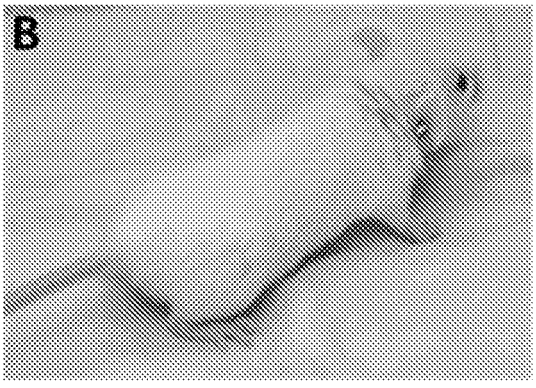


FIG. 8D

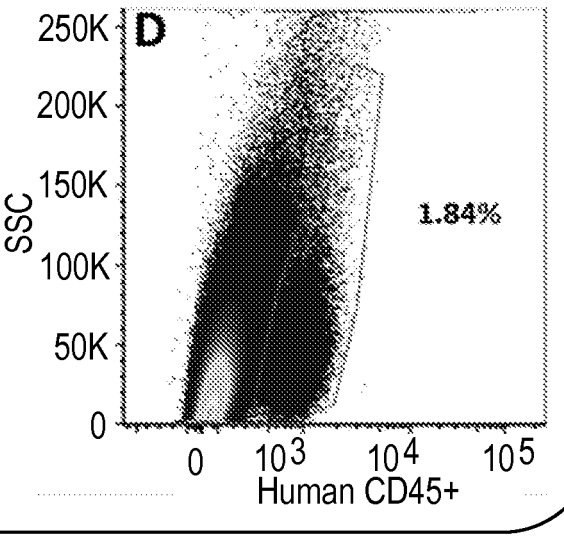


FIG. 8E

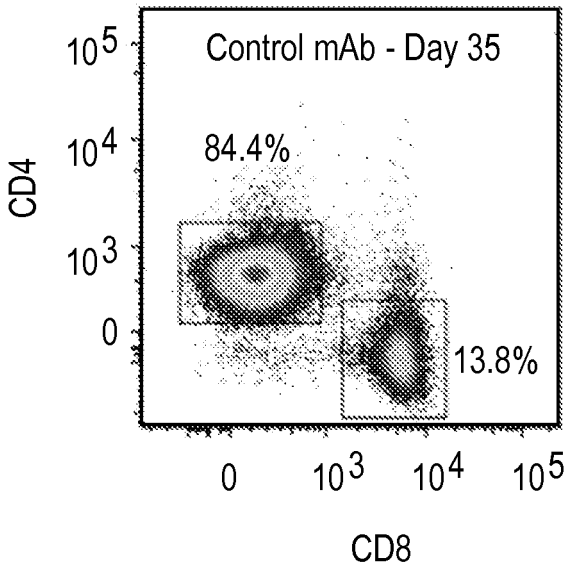

Control mAb - Day 35
84.4%
13.8%
CD4
CD8
10^5
10^4
10^3
0
0
10^3
10^4
10^5

FIG. 8F

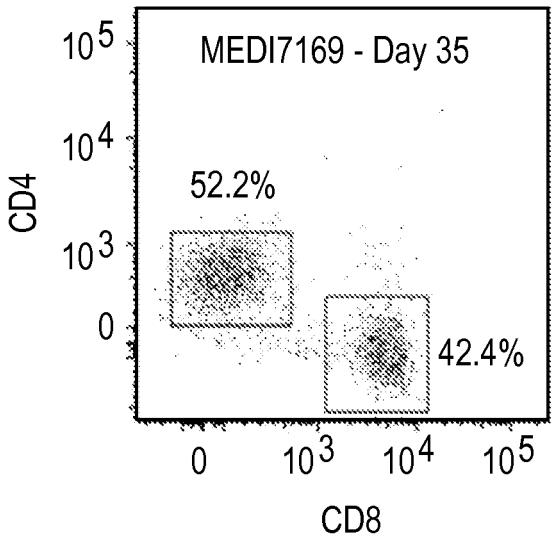

MEDI7169 - Day 35
52.2%
42.4%
CD4
CD8
10^5
10^4
10^3
0
0
10^3
10^4
10^5

FIG. 9

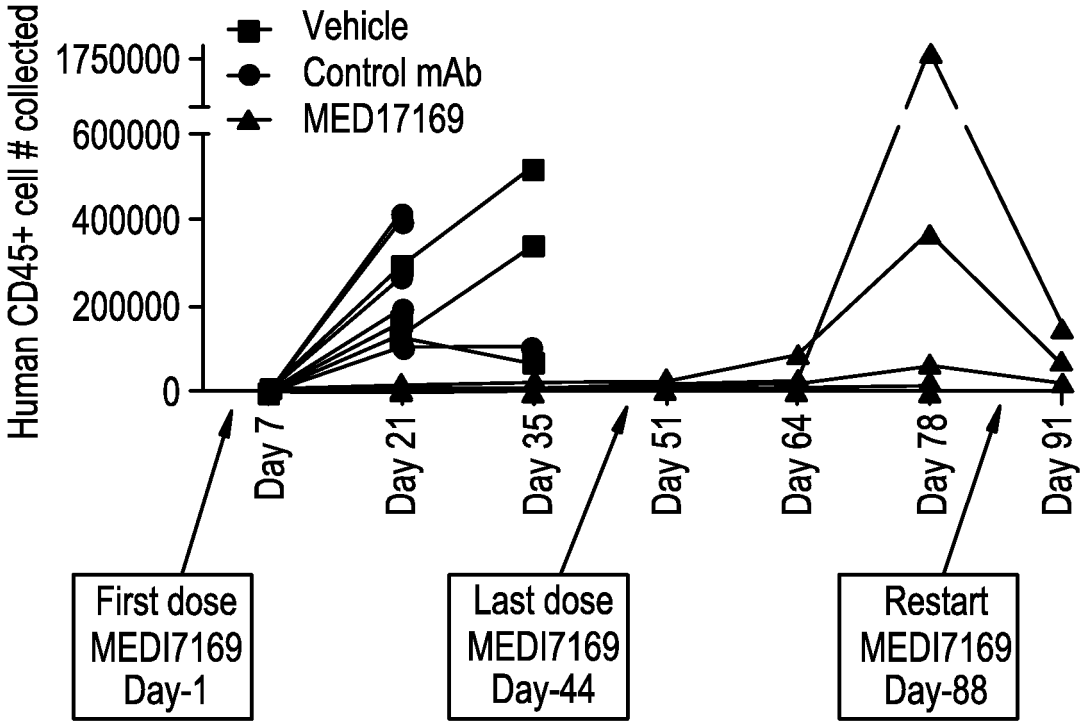

Human CD45+ cell # collected
1750000
600000
400000
200000
0
Vehicle
Control mAb
MED17169
Day 7
Day 21
Day 35
Day 51
Day 64
Day 78
Day 91
First dose MEDI7169 Day-1
Last dose MEDI7169 Day-44
Restart MEDI7169 Day-88

FIG. 10A

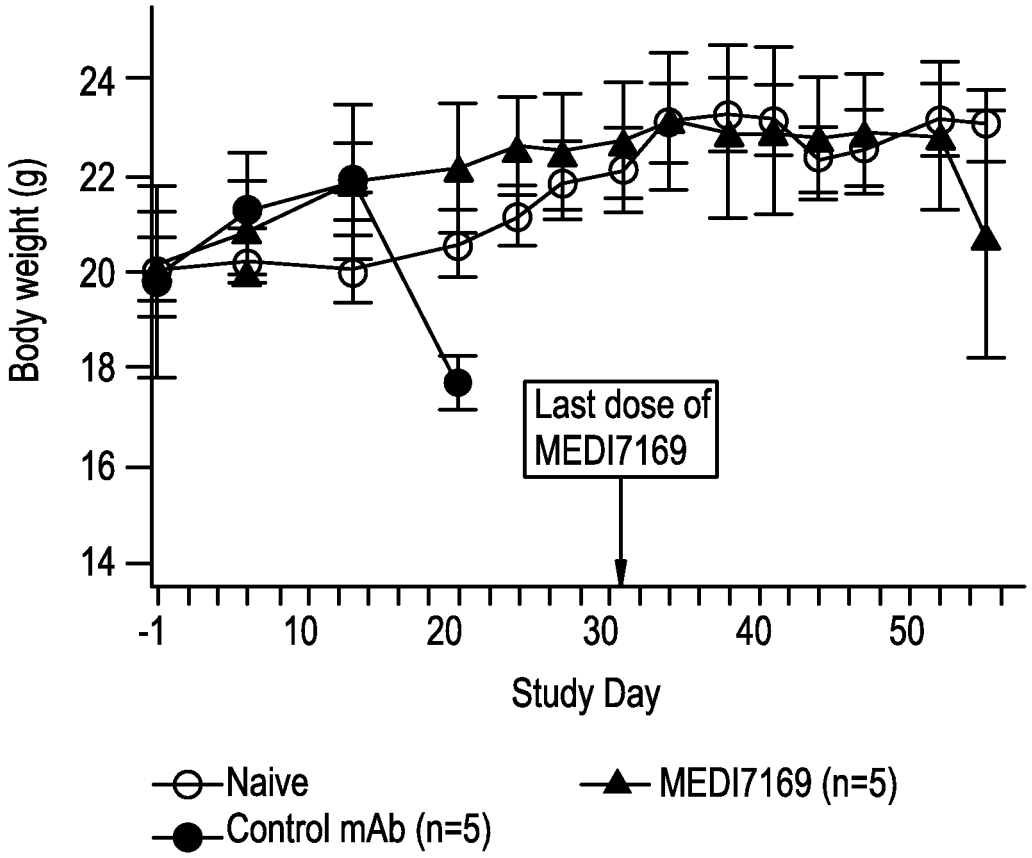


FIG. 10B

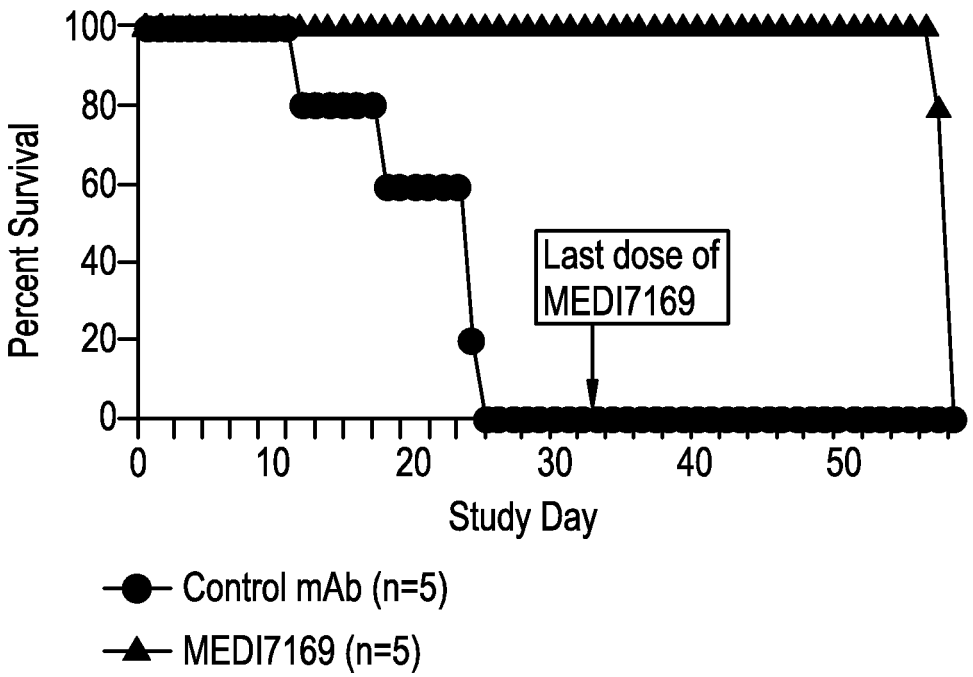


FIG. 11A

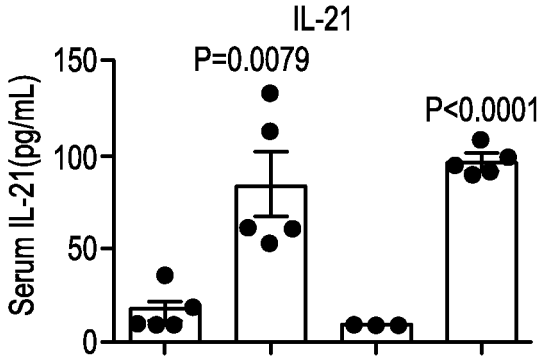


FIG. 11B

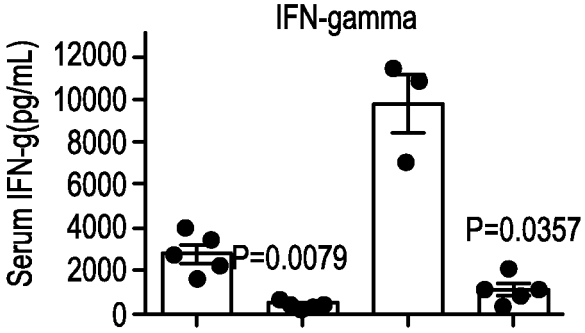


FIG. 11C

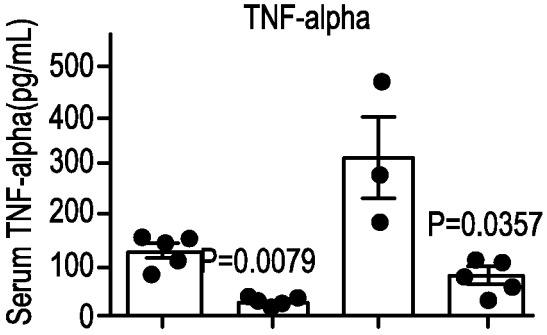


FIG. 11D

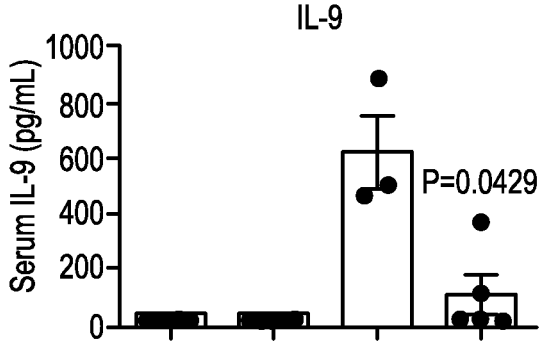


FIG. 11E

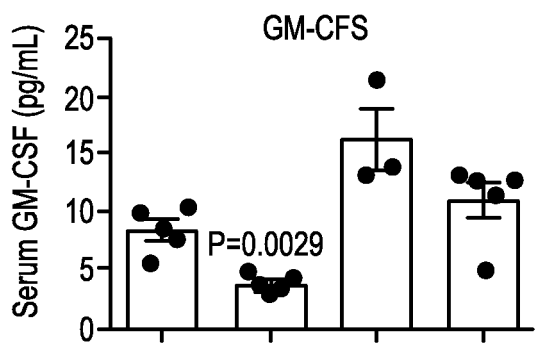


FIG. 11F

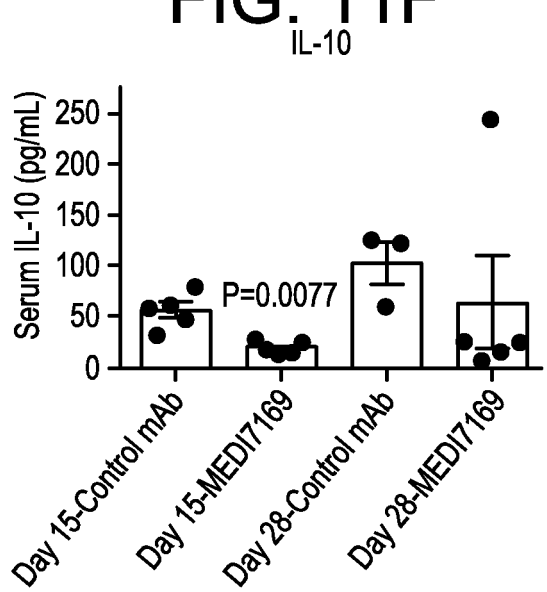
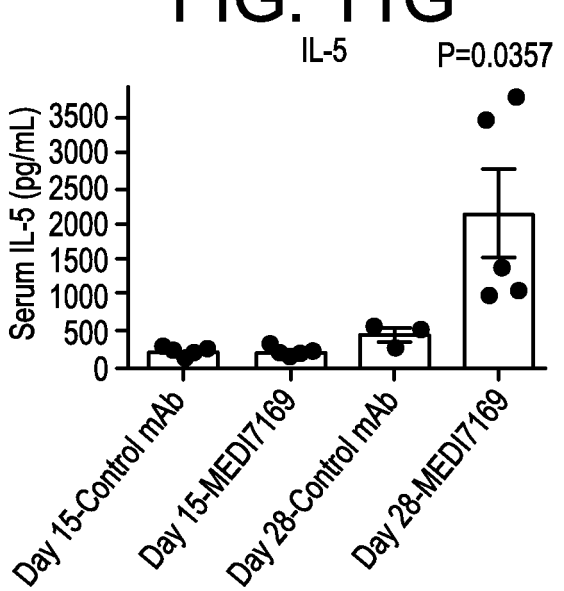


FIG. 11G



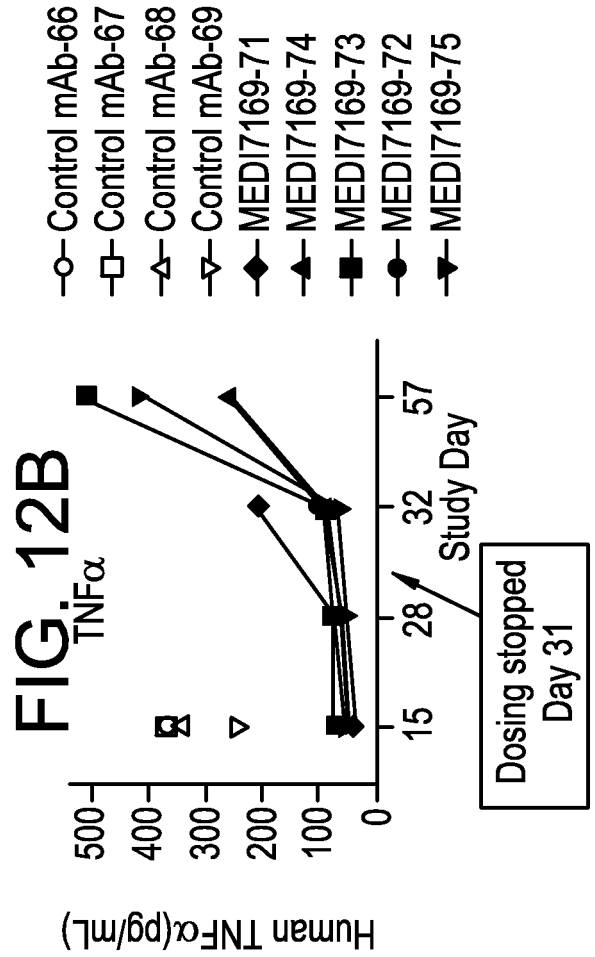

FIG. 12A
IFNγ
Human IFN γ(pg/mL)
12000
10000
8000
6000
4000
2000
0
15
28
43
57
Study Day
Dosing stopped
Day 31

FIG. 12B
TNFα
Human TNFα(pg/mL)
500
400
300
200
100
0
15
28
32
57
Study Day
Dosing stopped
Day 31
Control mAb-66
Control mAb-67
Control mAb-68
Control mAb-69
MEDI7169-71
MEDI7169-74
MEDI7169-73
MEDI7169-72
MEDI7169-75

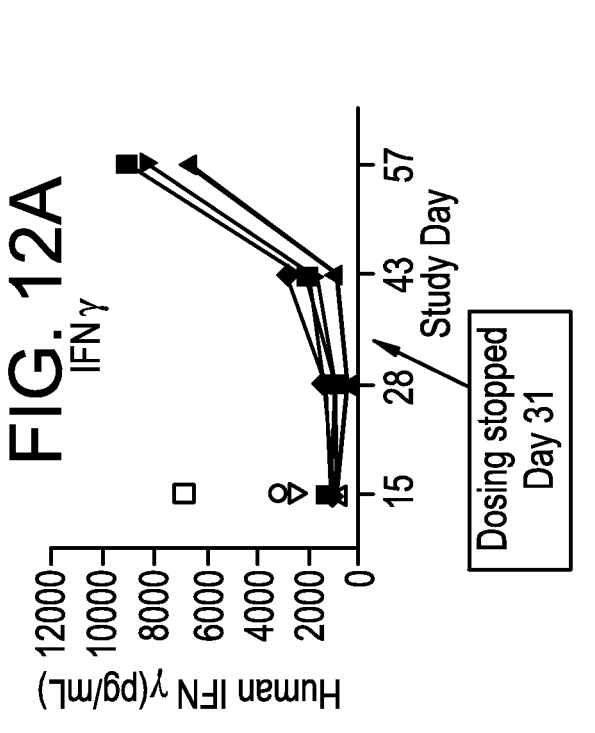

FIG. 12C
IL-10
Human IL-10 (pg/mL)
250
200
150
100
50
0
15
28
43
57
Study Day
Dosing stopped
Day 31

FIG. 12D
Cell Numbers
Human CD45+ Cells
1250000
1000000
750000
500000
250000
0
7
21
35
51
57
Study Day
Dosing stopped
Day 31
Control mAb-66
Control mAb-67
Control mAb-68
Control mAb-69
MEDI7169-71
MEDI7169-74
MEDI7169-73
MEDI7169-72
MEDI7169-75

FIG. 13

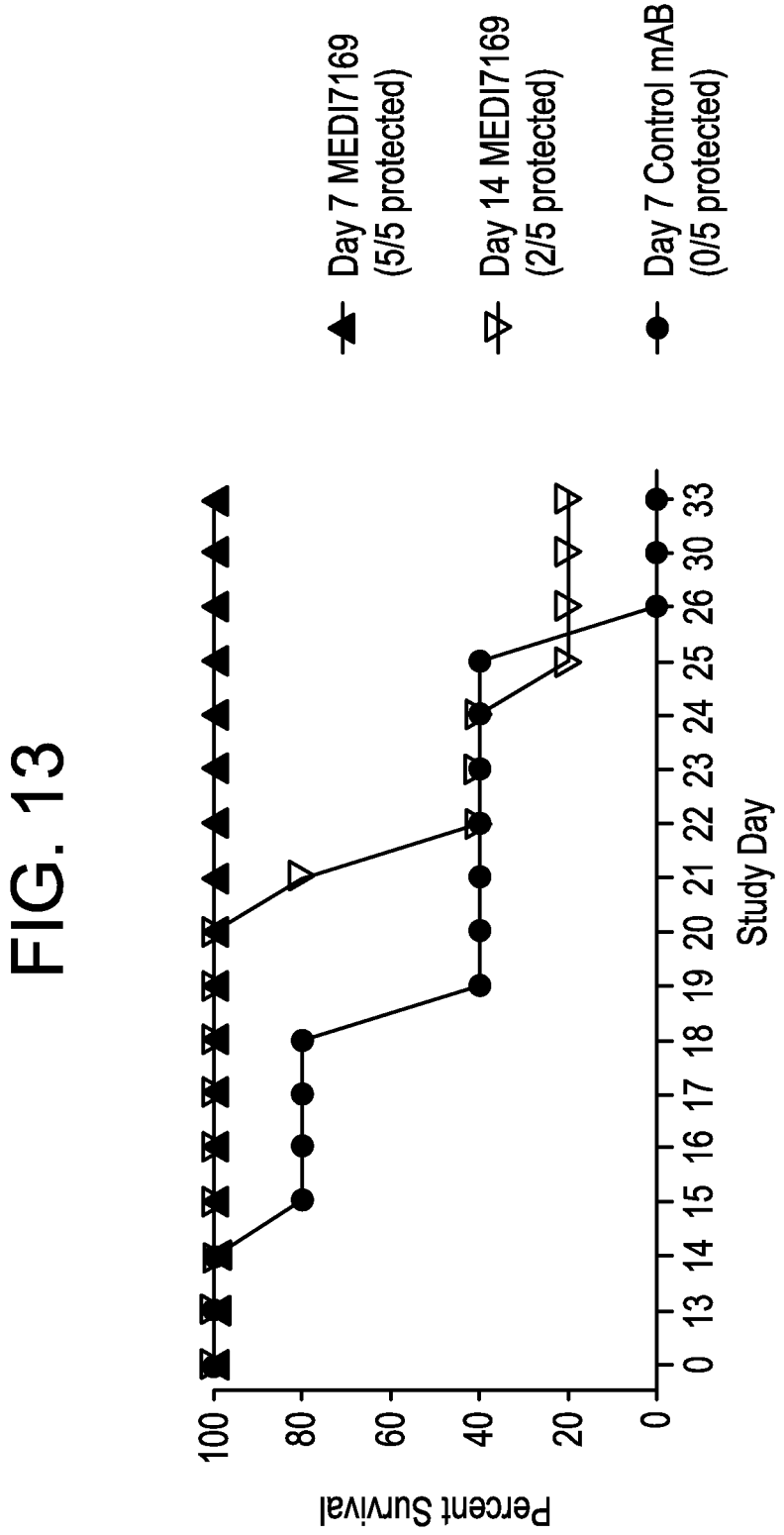

Day 7 MEDI7169
(5/5 protected)
Day 14 MEDI7169
(2/5 protected)
Day 7 Control mAB
(0/5 protected)
Percent Survival
100
80
60
40
20
0
0 13 14 15 16 17 18 19 20 21 22 23 24 25 26 30 33
Study Day

FIG. 14A

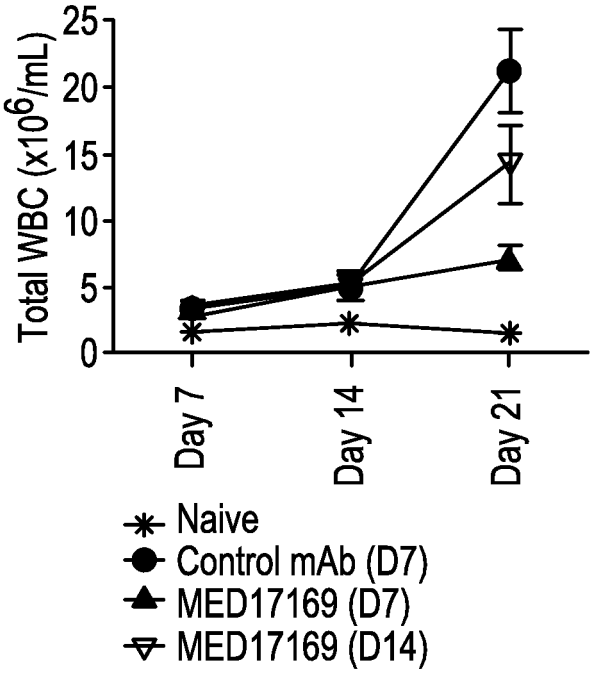


FIG. 14B

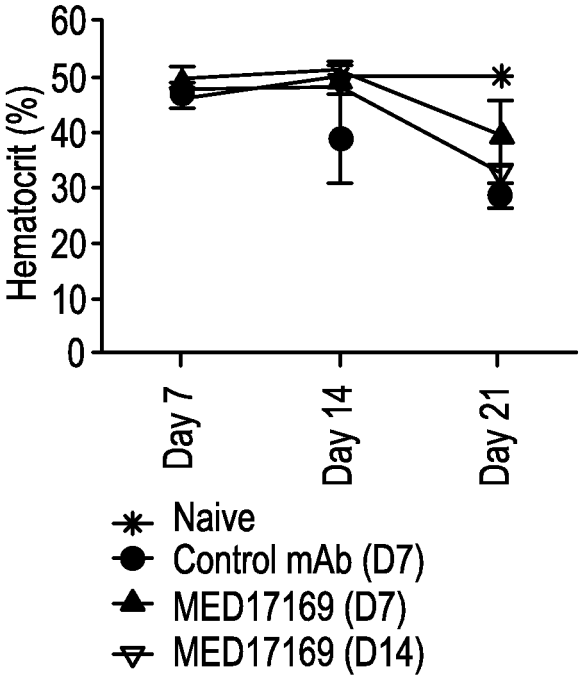


FIG. 14C

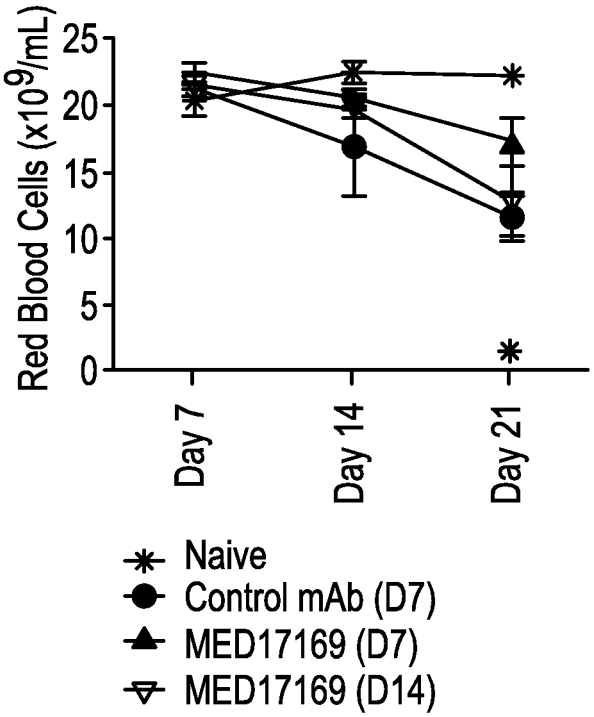


FIG. 14D

