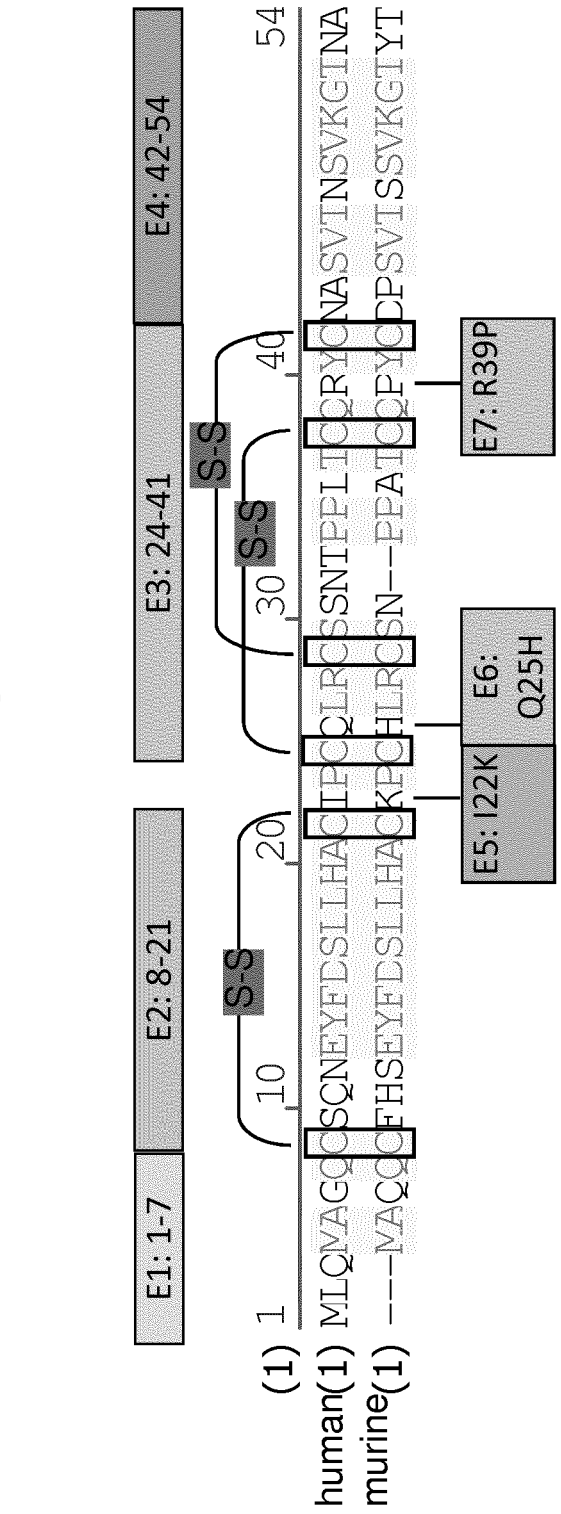
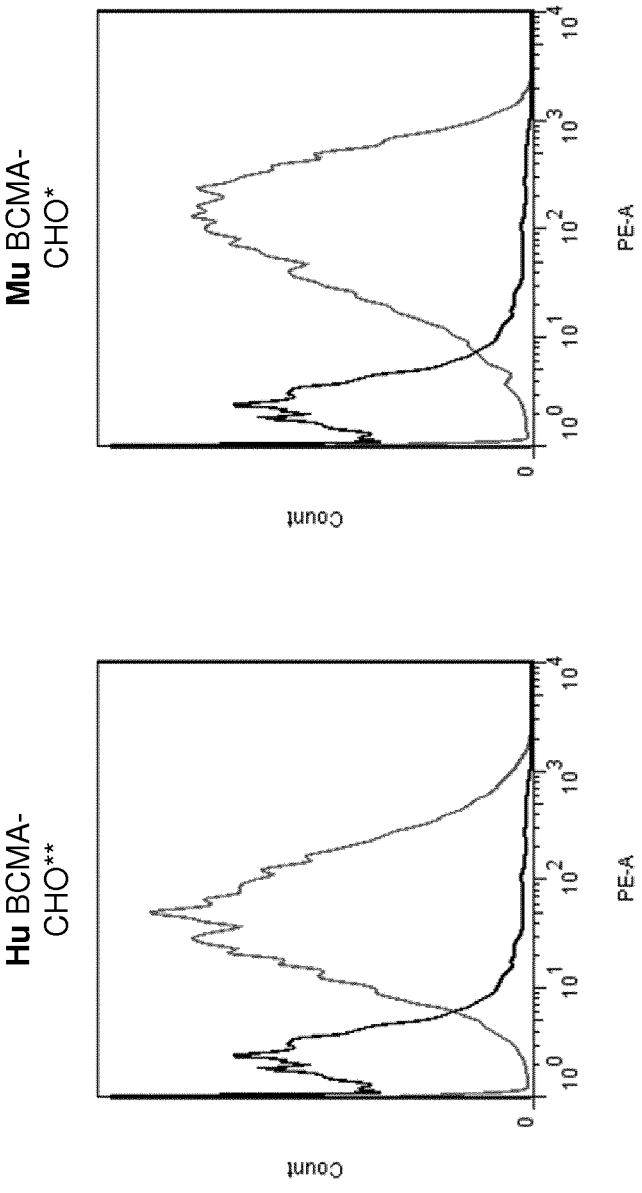
Figure 1



E1: N-terminal domain
E2: First disulfide bound defined domain
E3: Second (double) disulfide bound defined domain
E4: C-terminal extracellular domain
E5: Inter-E2/E3 point mutation
E6+E7: E3 point mutations

Figure 2a



* Extracellular BCMA fused to transmembrane plus cytoplasmatic human EpCAM

** unmodified transmembrane BCMA

Figure 2b

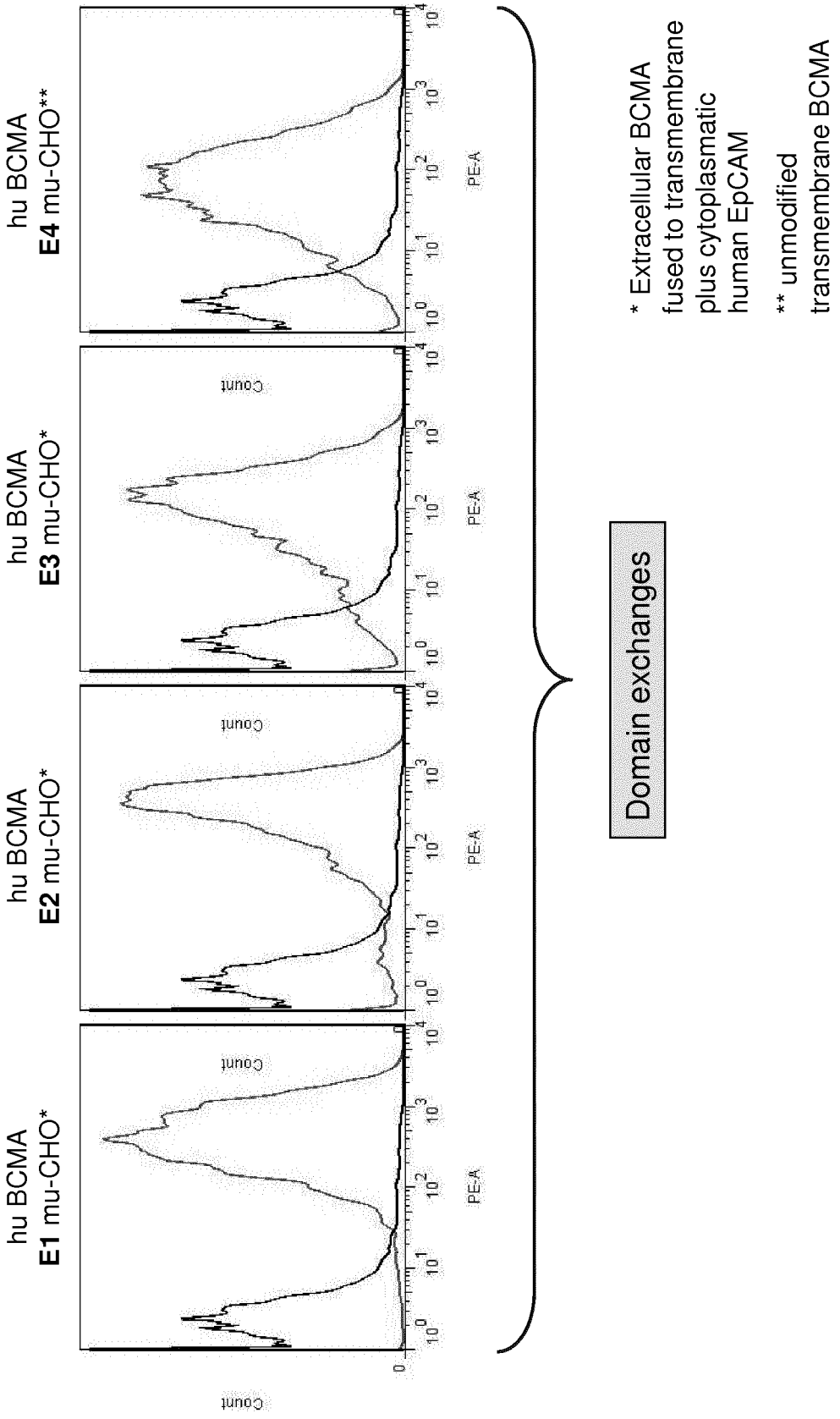

hu BCMA
E1 mu-CHO*
hu BCMA
E2 mu-CHO*
hu BCMA
E3 mu-CHO*
hu BCMA
E4 mu-CHO**
Count
PE-A
Domain exchanges
* Extracellular BCMA fused to transmembrane plus cytoplasmatic human EpCAM
** unmodified transmembrane BCMA

Figure 2b (continued)

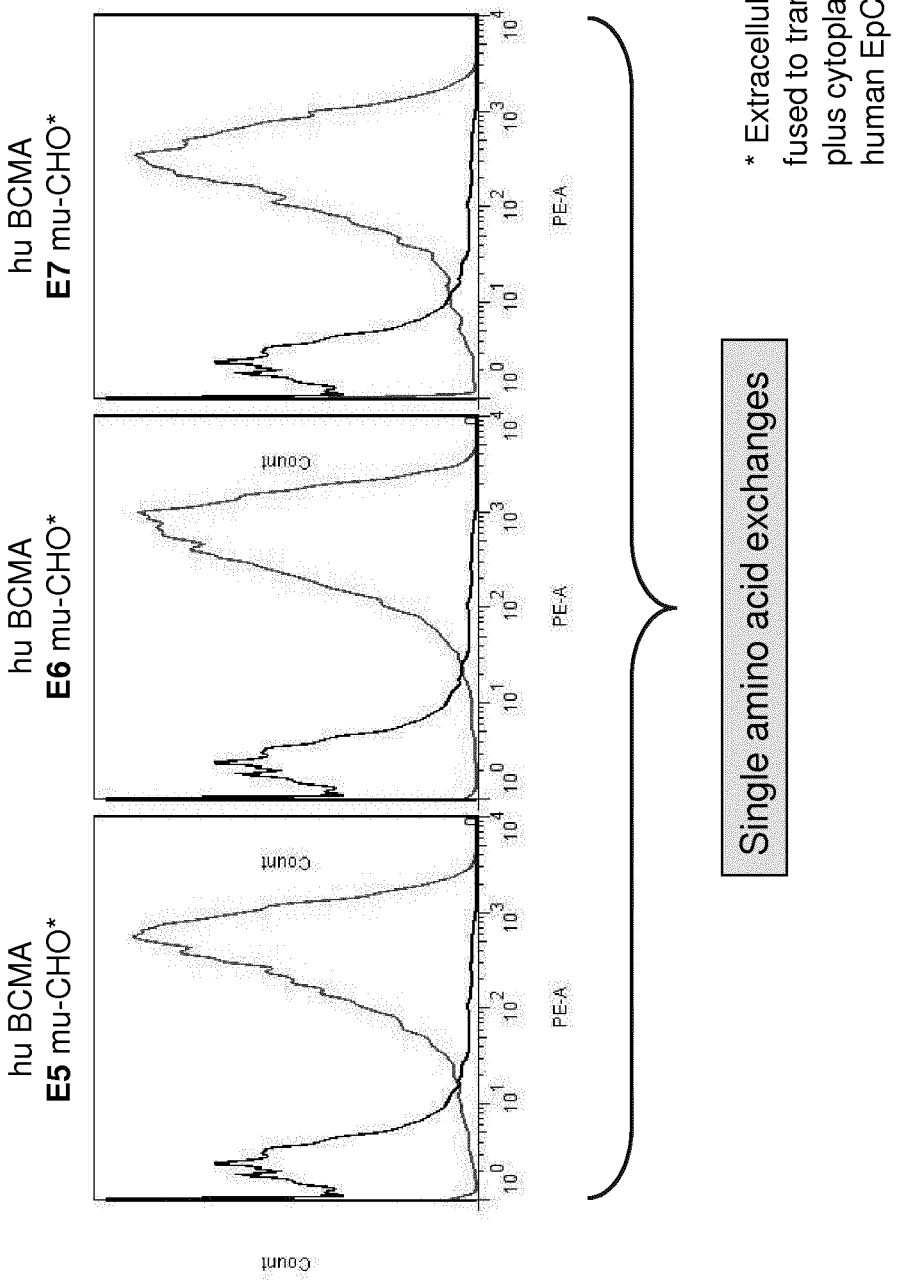


Figure A3

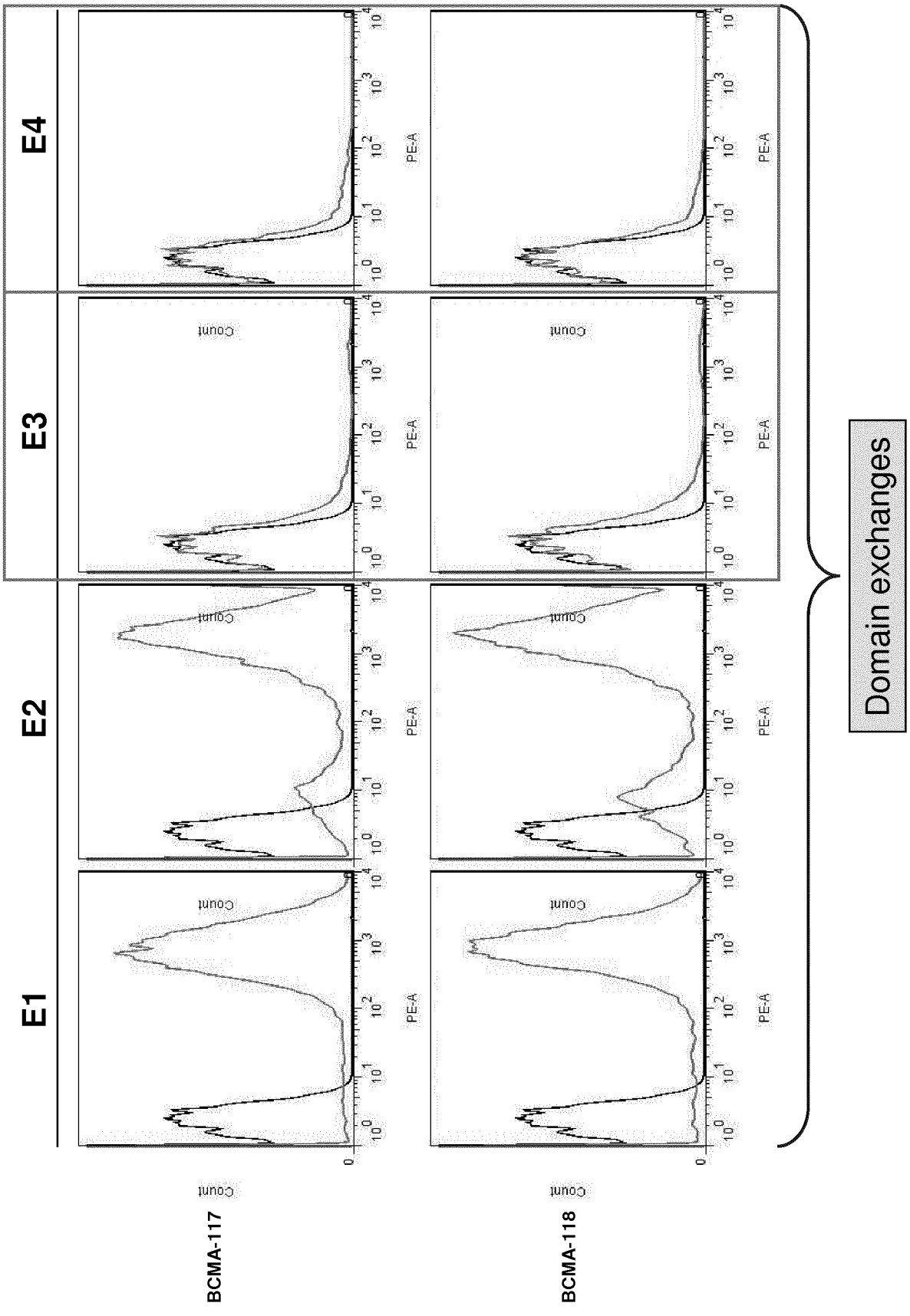


Figure A3 (continued)

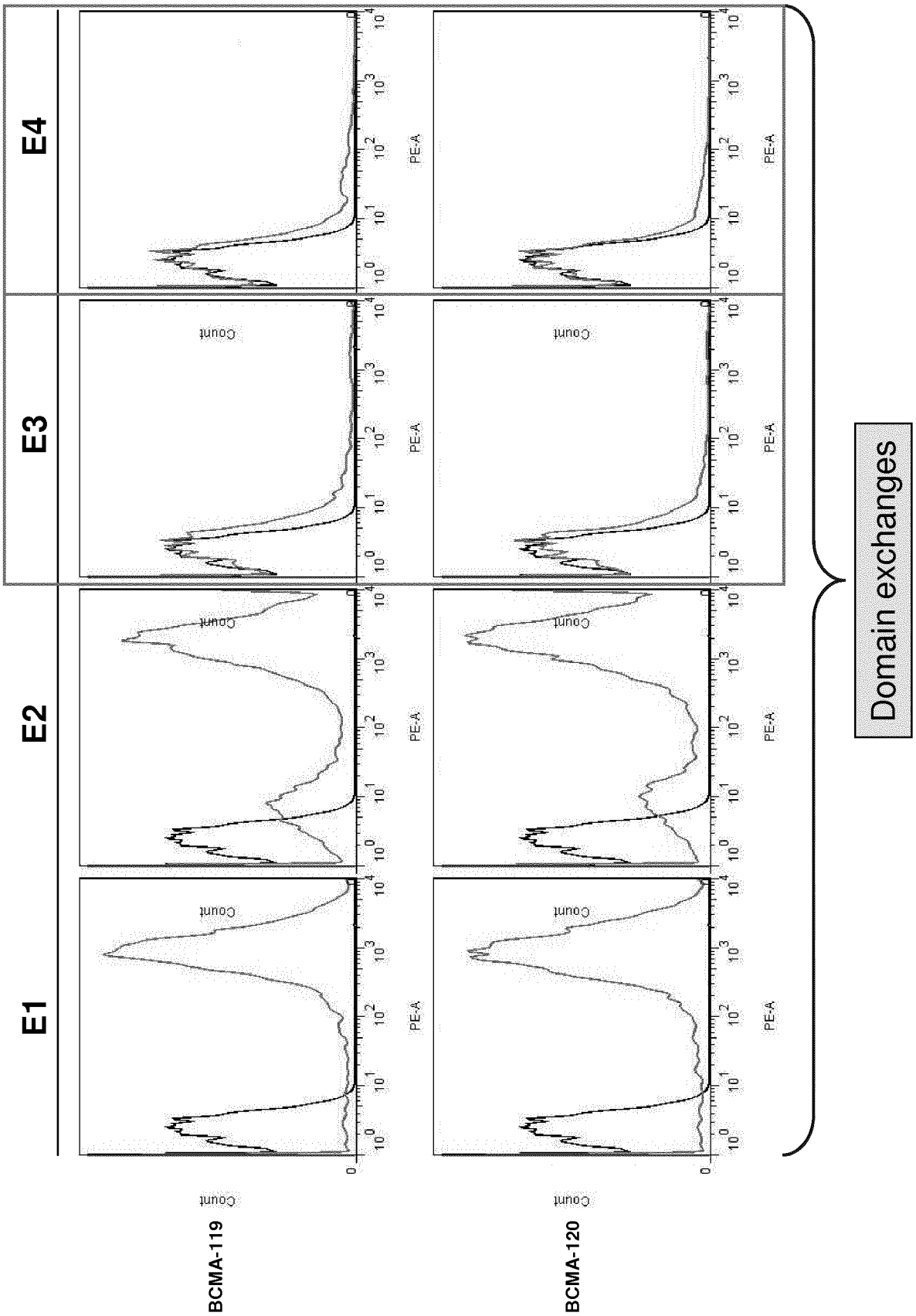


Figure A3 (continued)

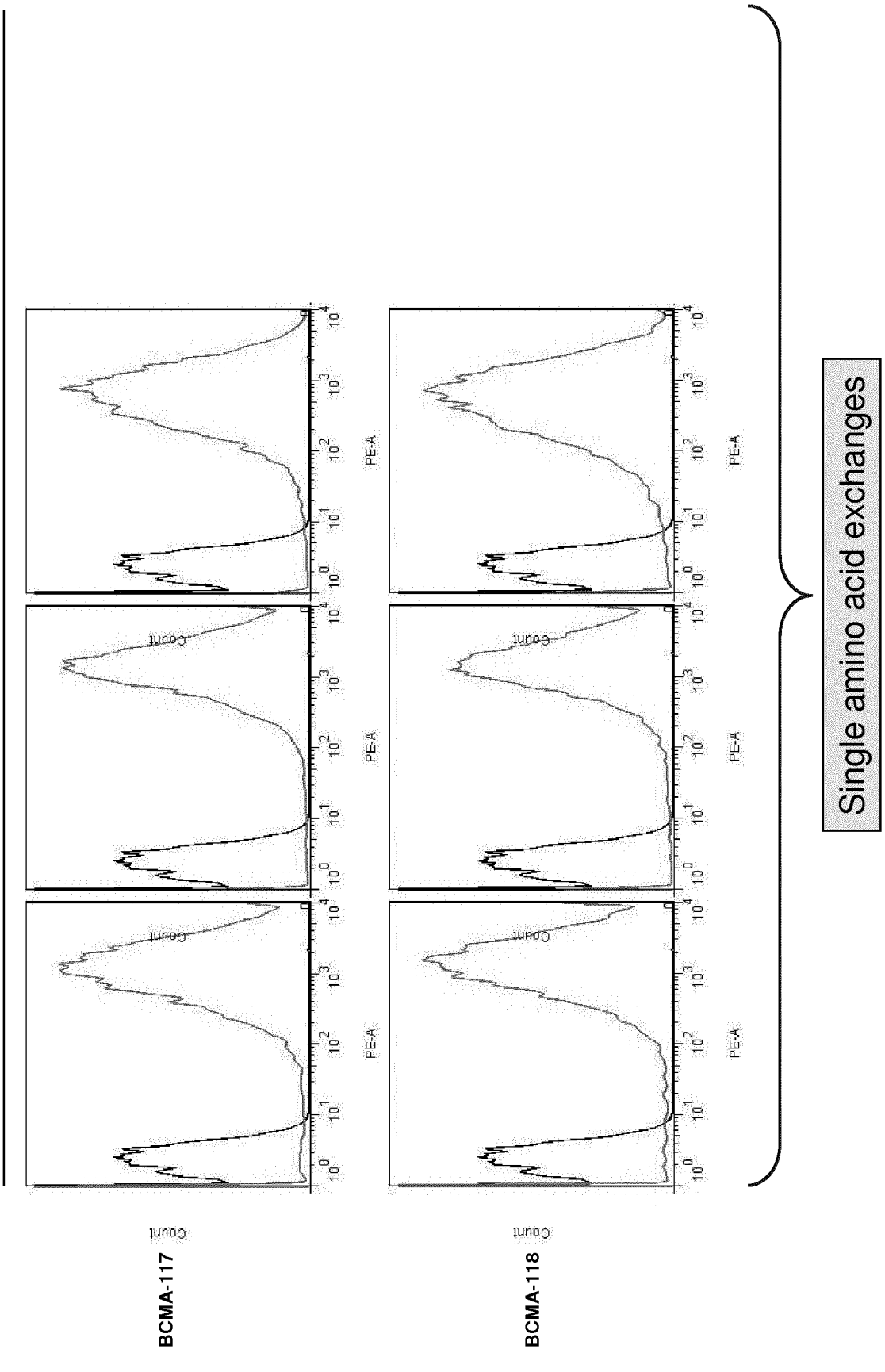


Figure A3 (continued)

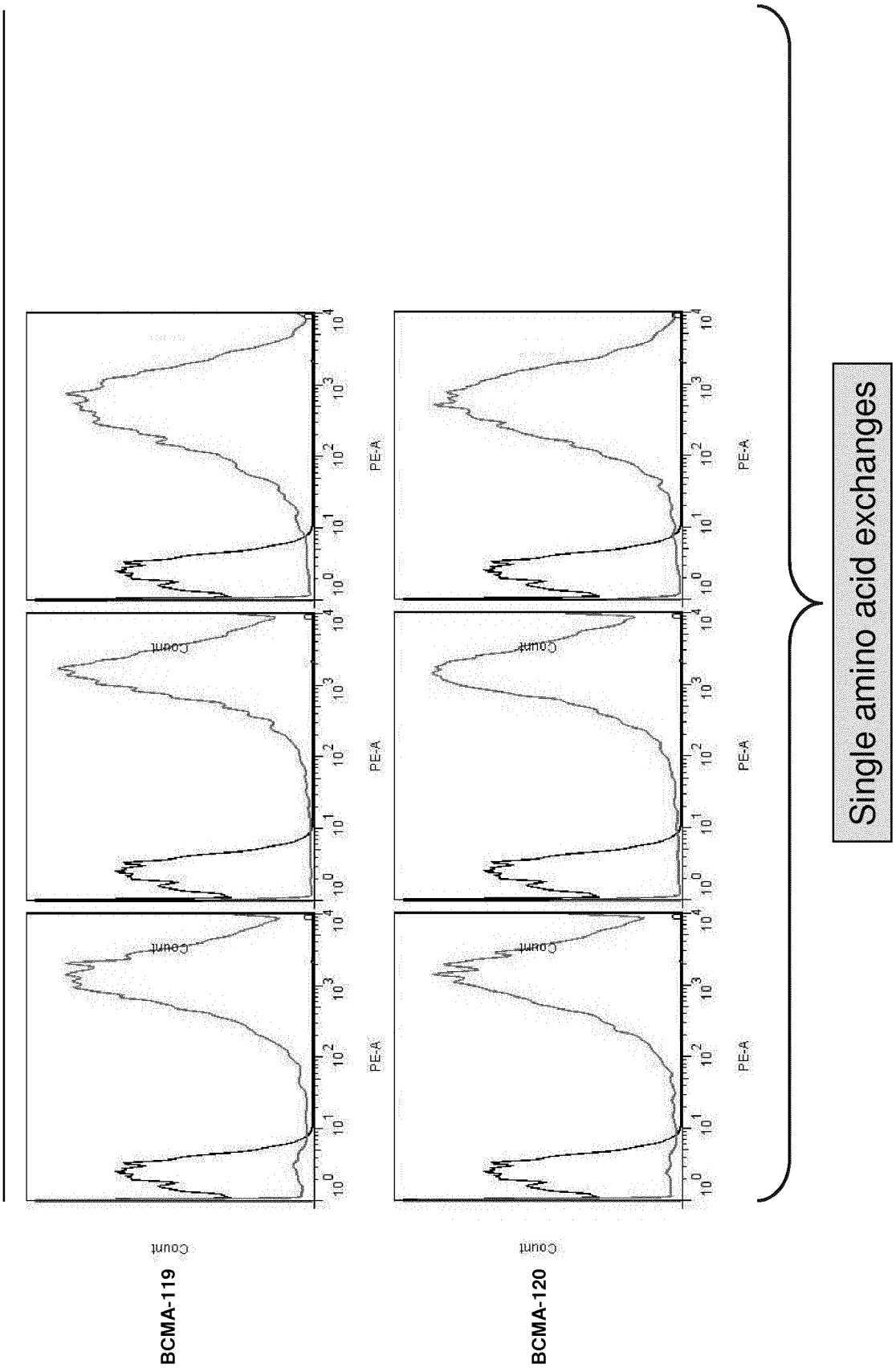


Figure A3 (continued)

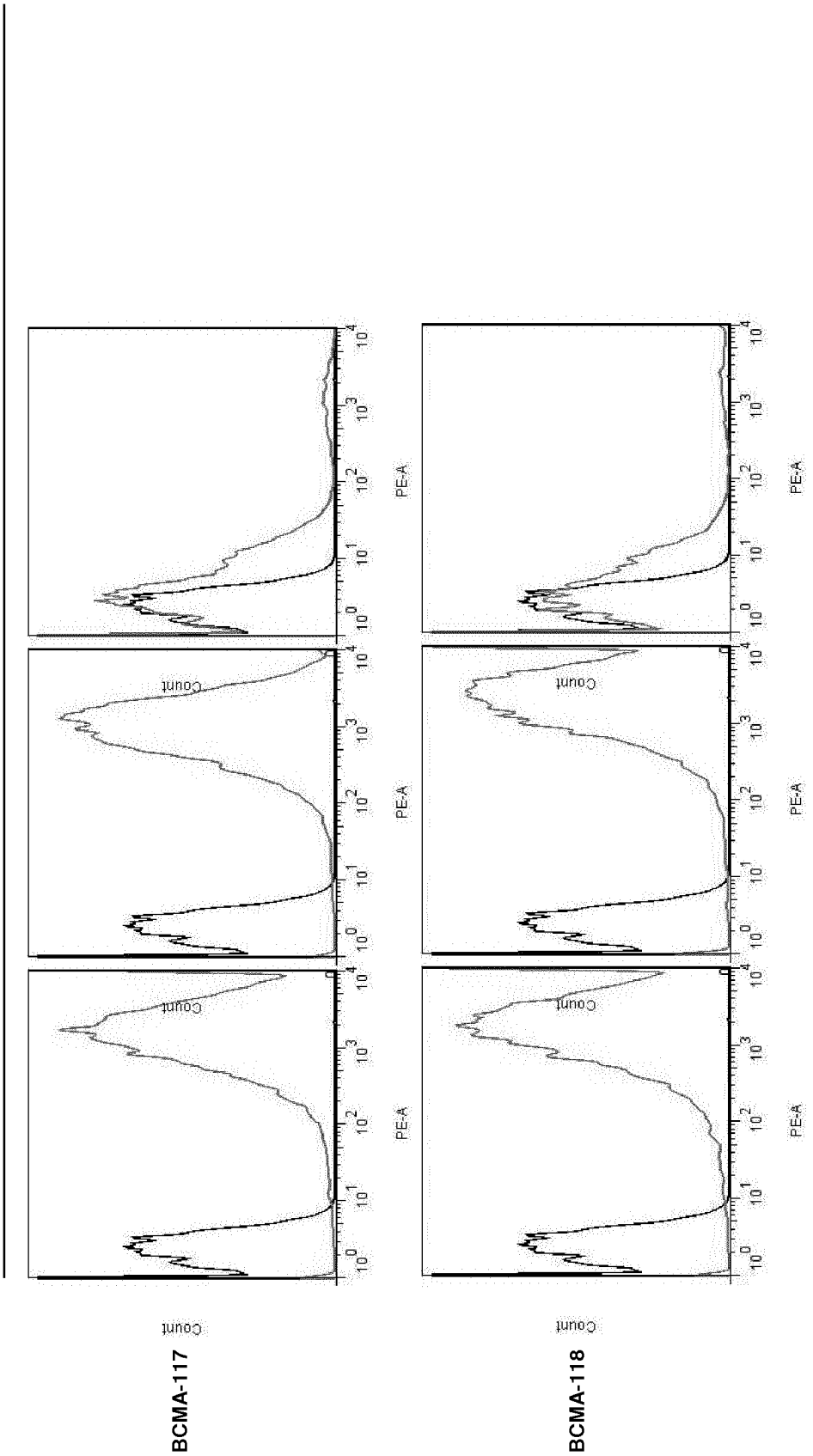


Figure A3 (continued)

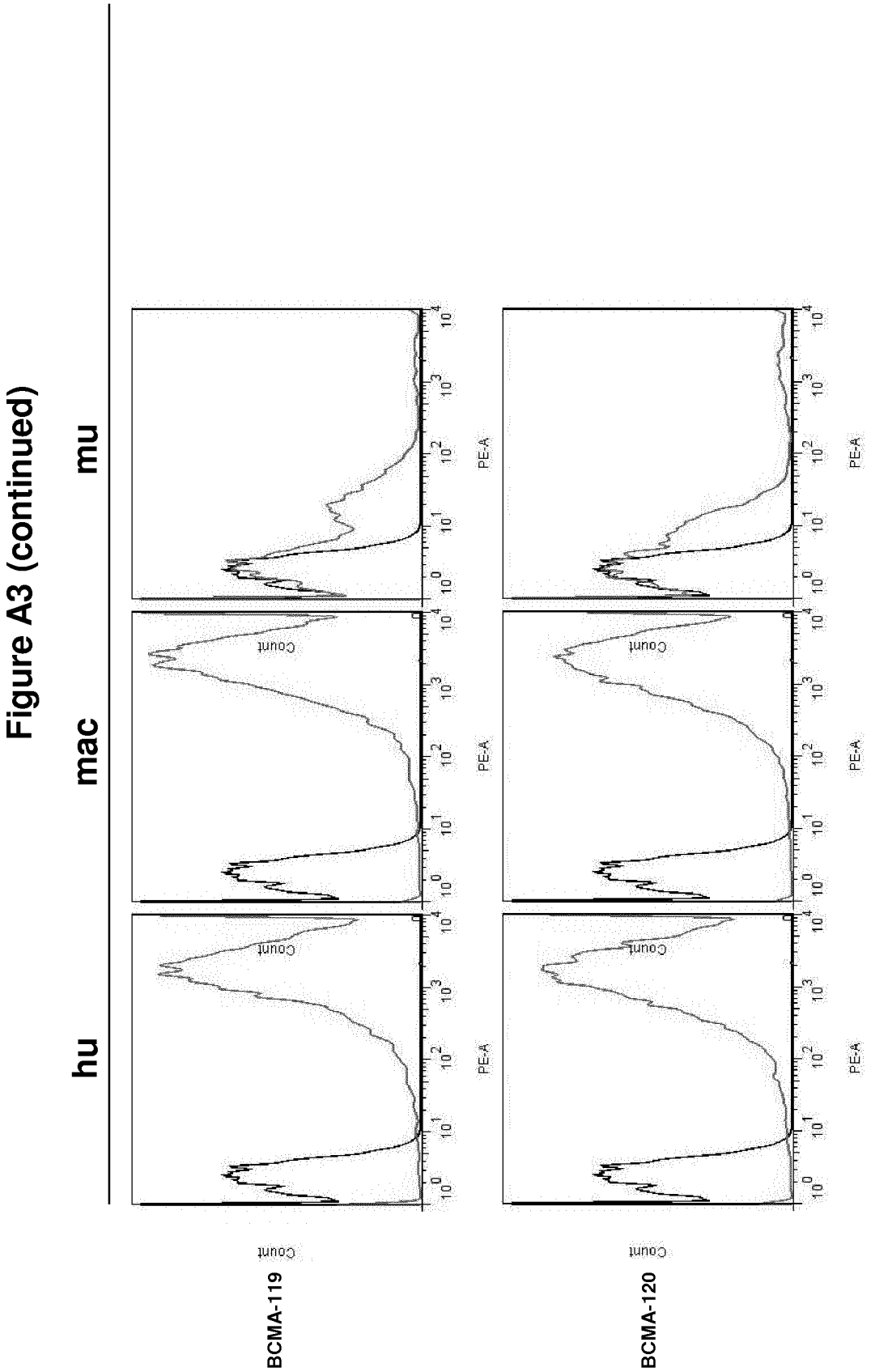


Figure A3 (continued)

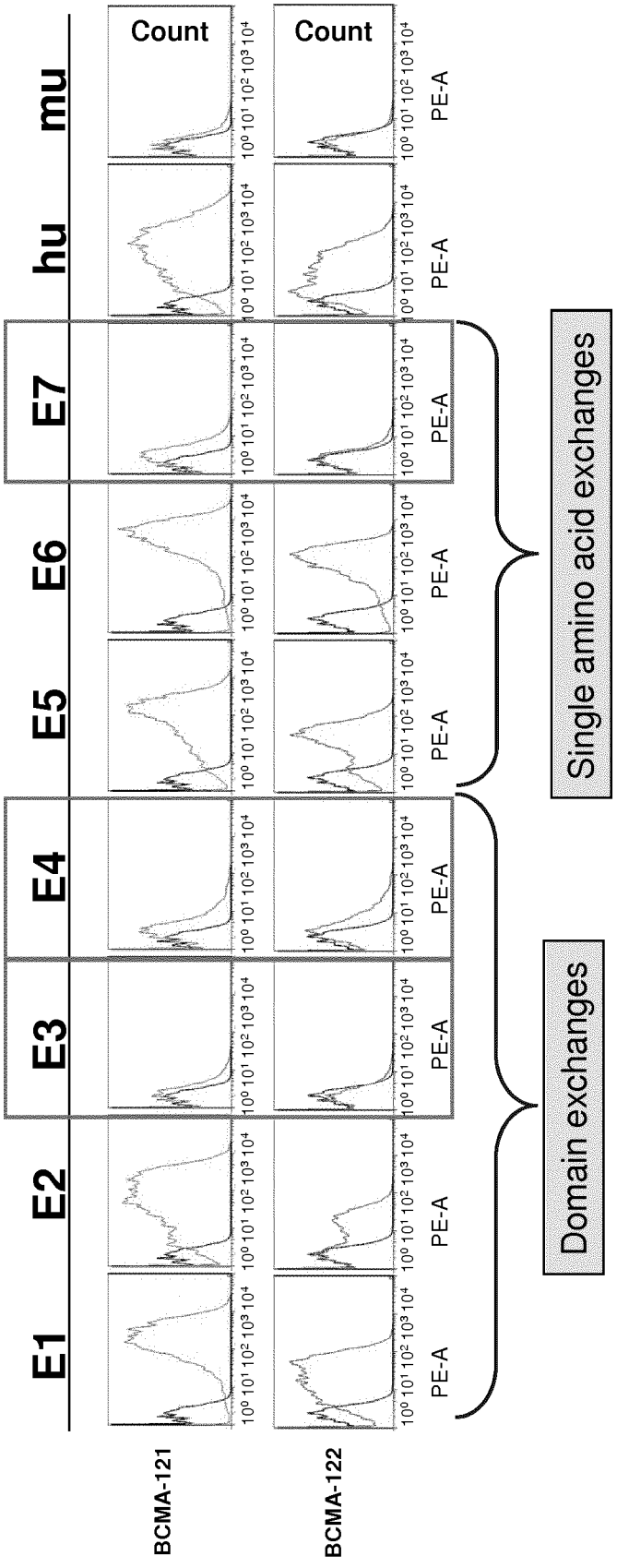


Figure B3

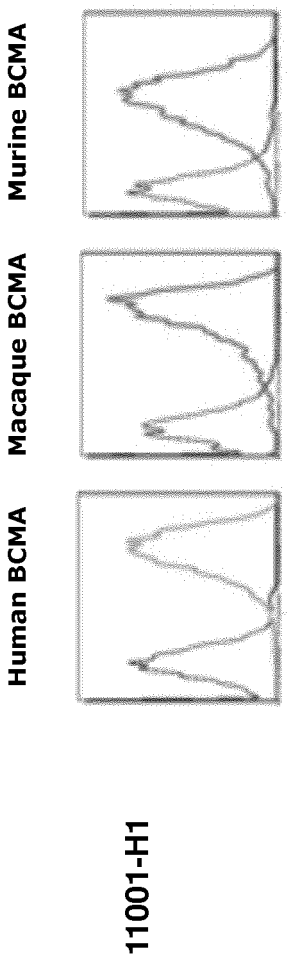


Figure C3

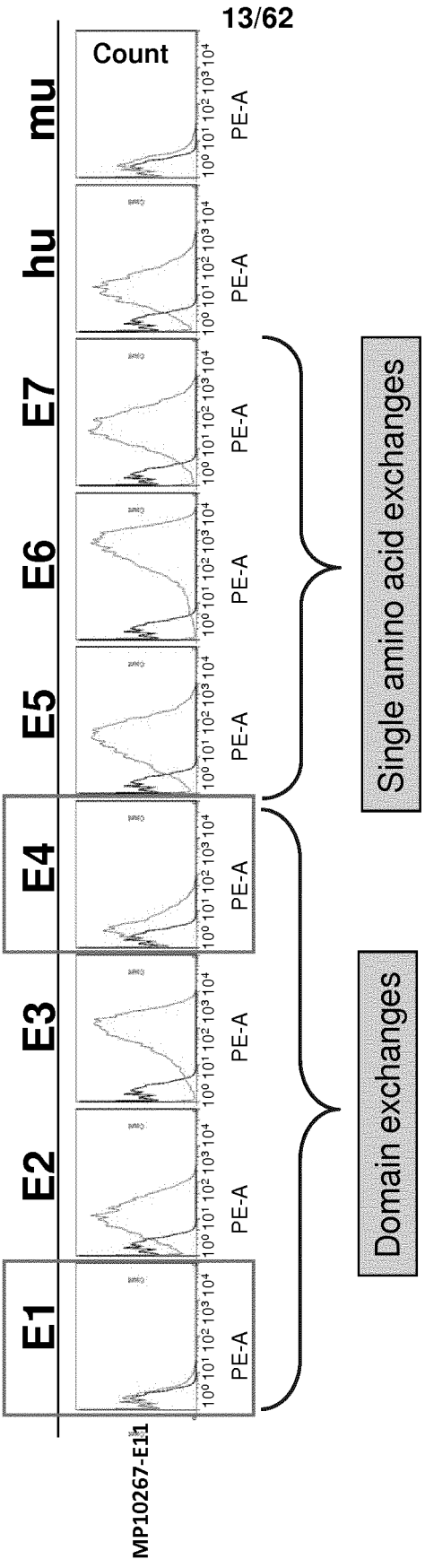

Count
E1
E2
E3
E4
E5
E6
E7
hu
mu
PE-A
MP10267-E11
Domain exchanges
Single amino acid exchanges

Figure D3

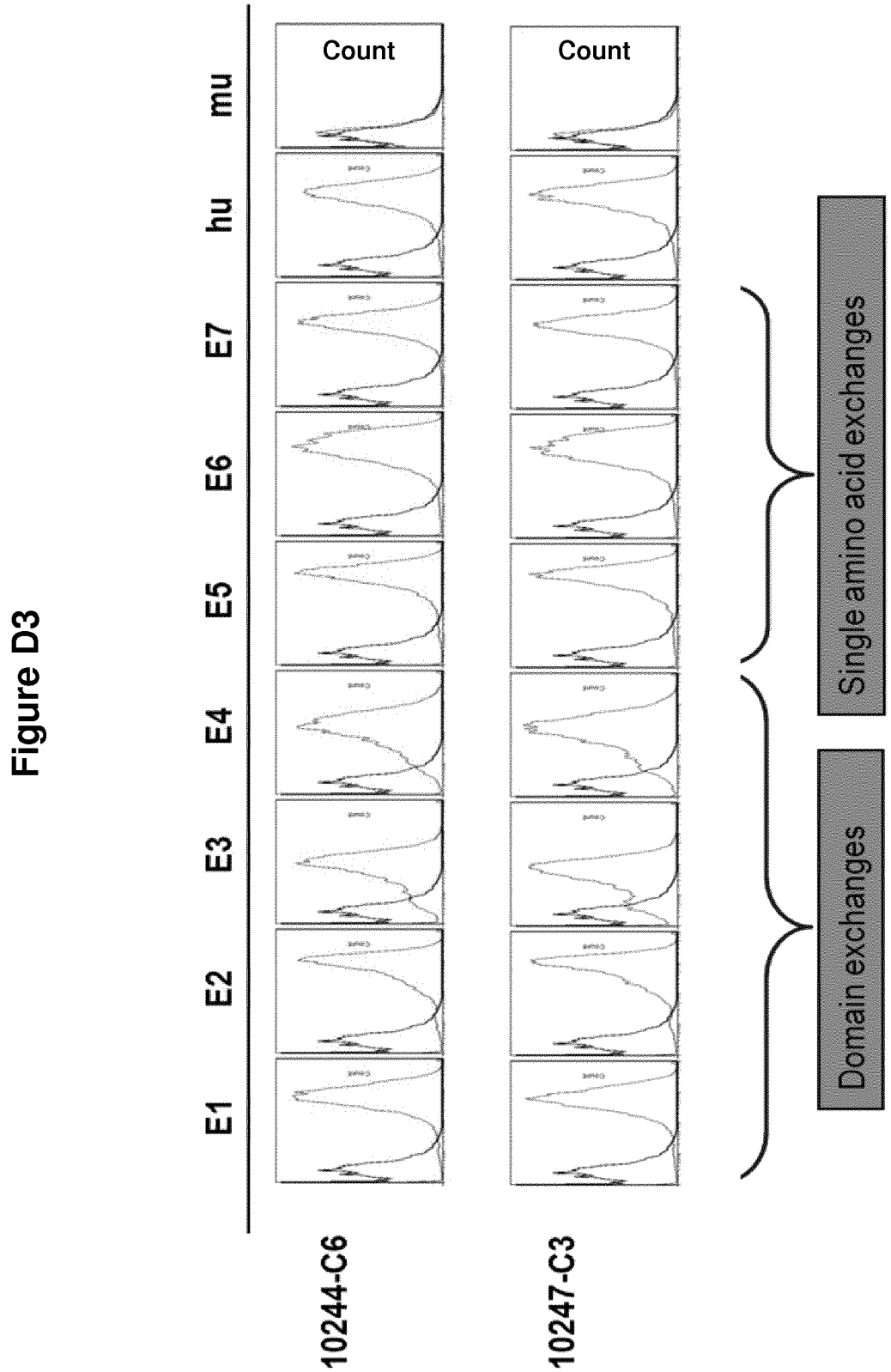
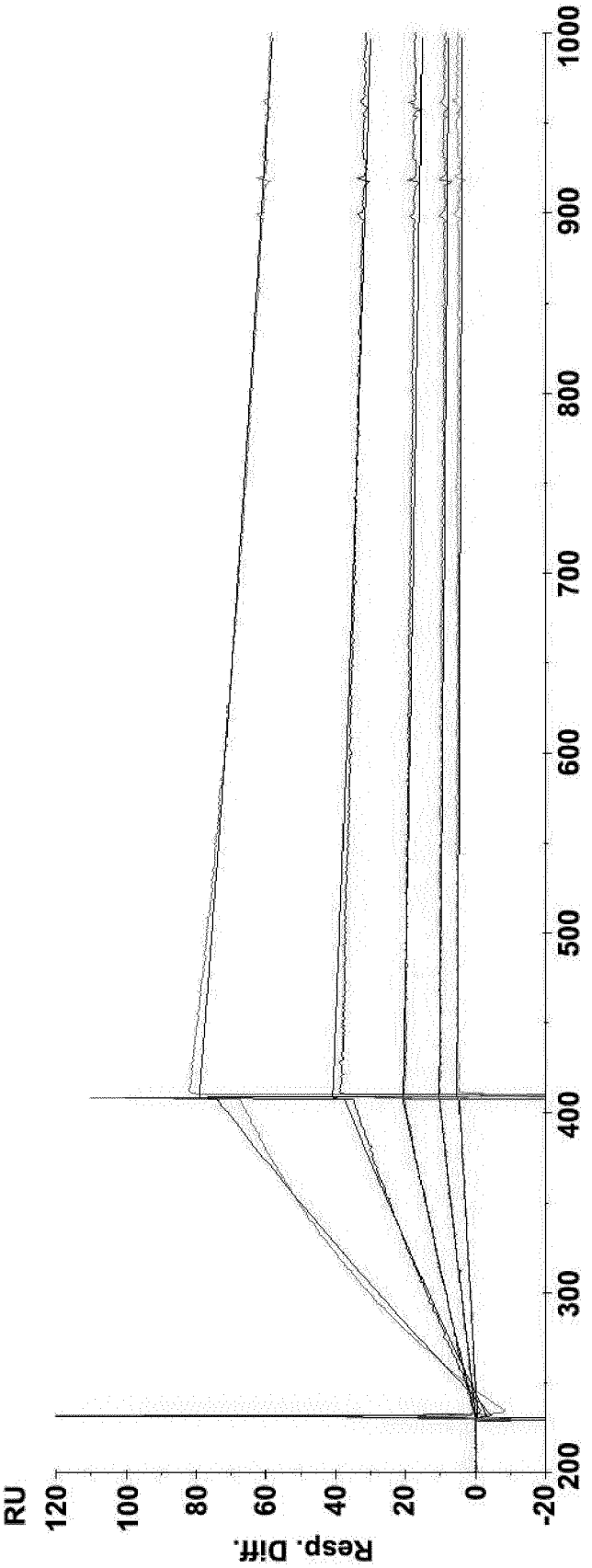

Count
Count
mu
hu
E7
E6
E5
E4
E3
E2
E1
10244-C6
10247-C3
Single amino acid exchanges
Domain exchanges

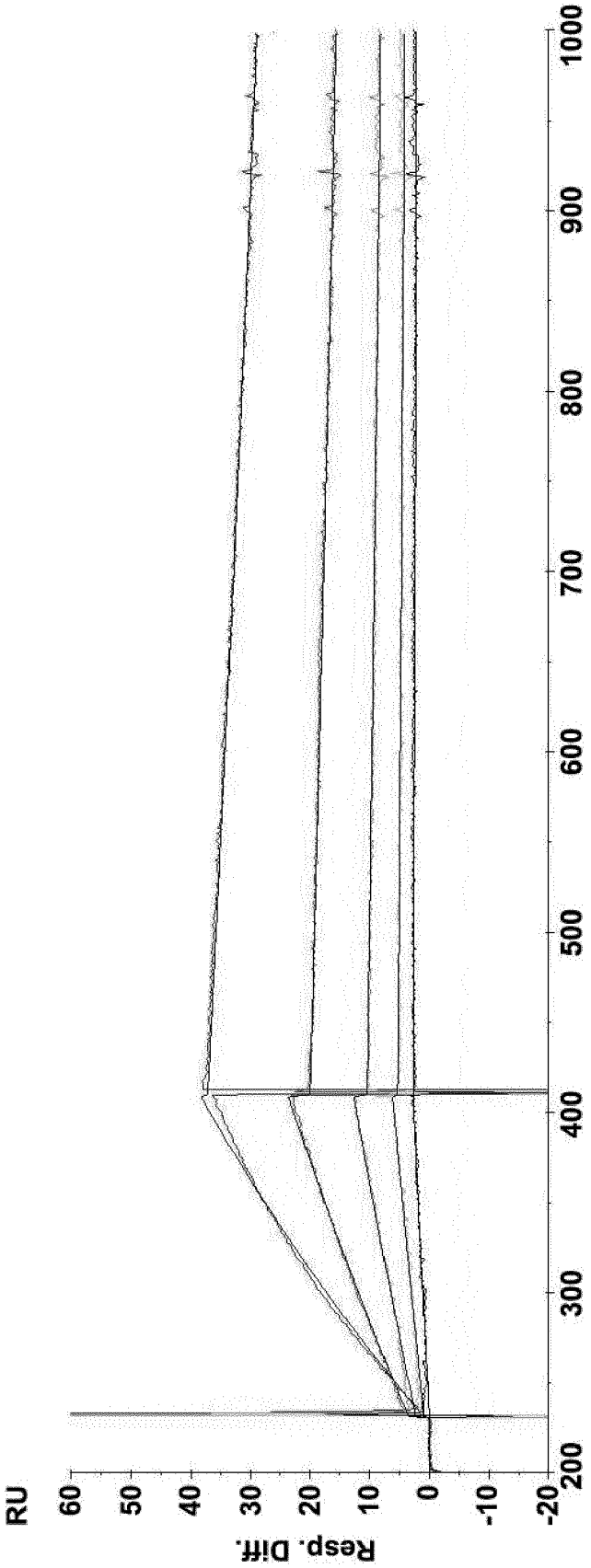
Figure A4



KD = 34.2 nM

k off = 5.2 x 10^{-4} x s^{-1}

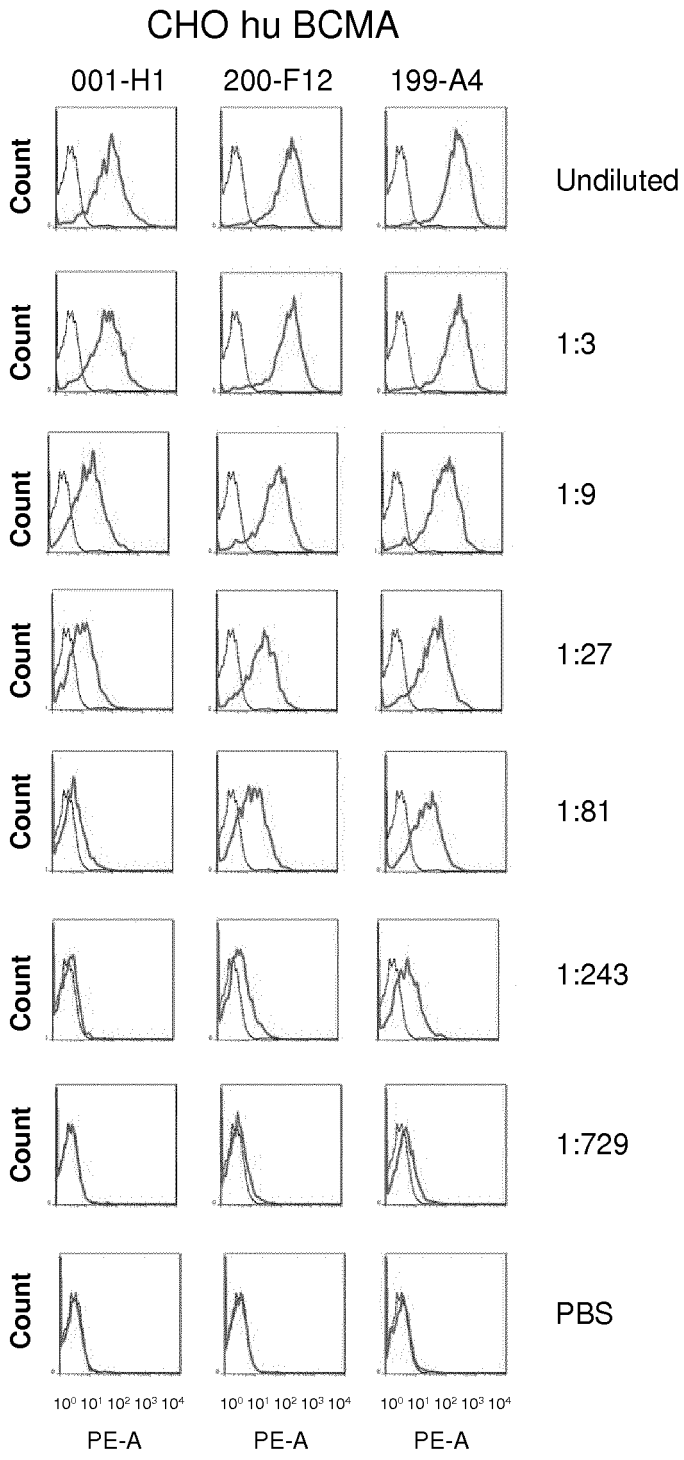
Figure A4 (continued)



KD = 11.7 nM

k off = 4.2 x 10^{-4} x s^{-1}

Figure B4


CHO hu BCMA
001-H1
200-F12
199-A4
Count
Undiluted
1:3
1:9
1:27
1:81
1:243
1:729
PBS
10⁰ 10¹ 10² 10³ 10⁴
PE-A

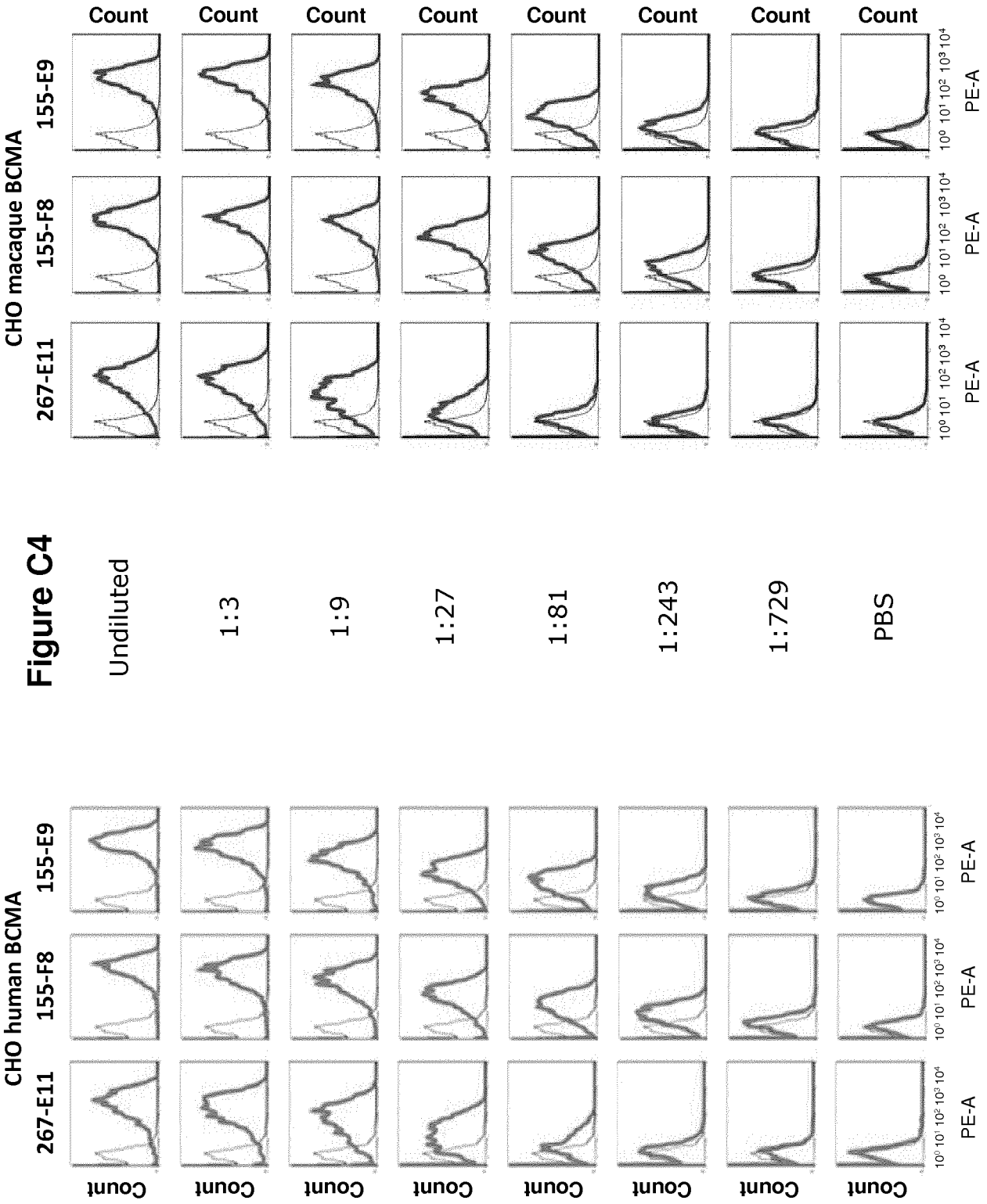
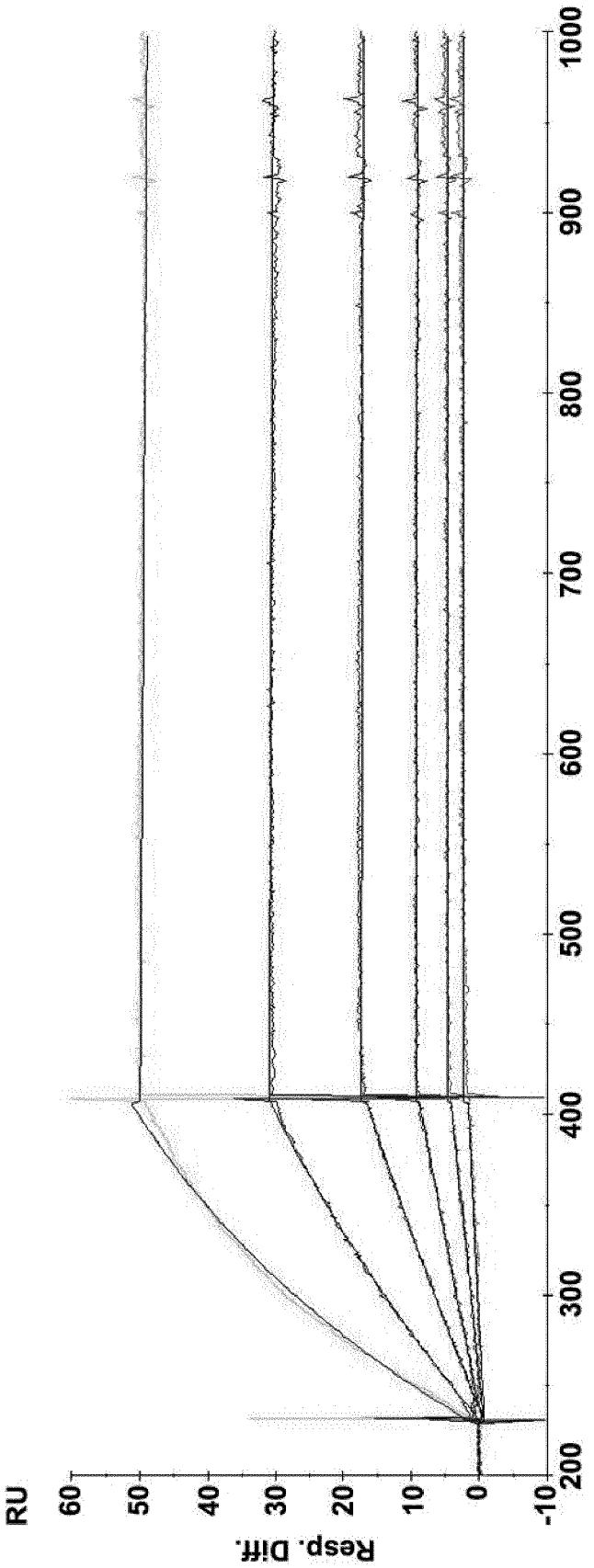

CHO human BCMA
267-E11
155-F8
155-E9
CHO macaque BCMA
267-E11
155-F8
155-E9
Count
PE-A
Undiluted
1:3
1:9
1:27
1:81
1:243
1:729
PBS

Figure C4

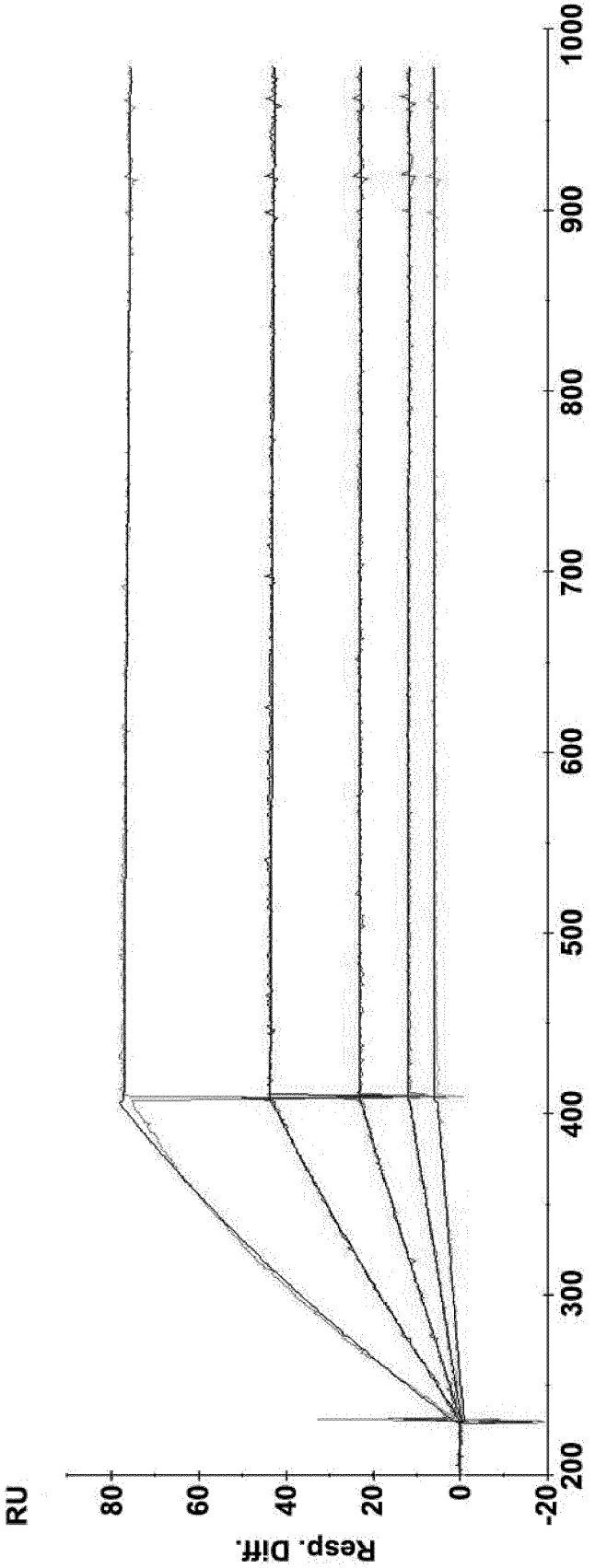
Figure D4



KD = 0.3 nM

k off = 0.34 x 10^{-4} x s^{-1}

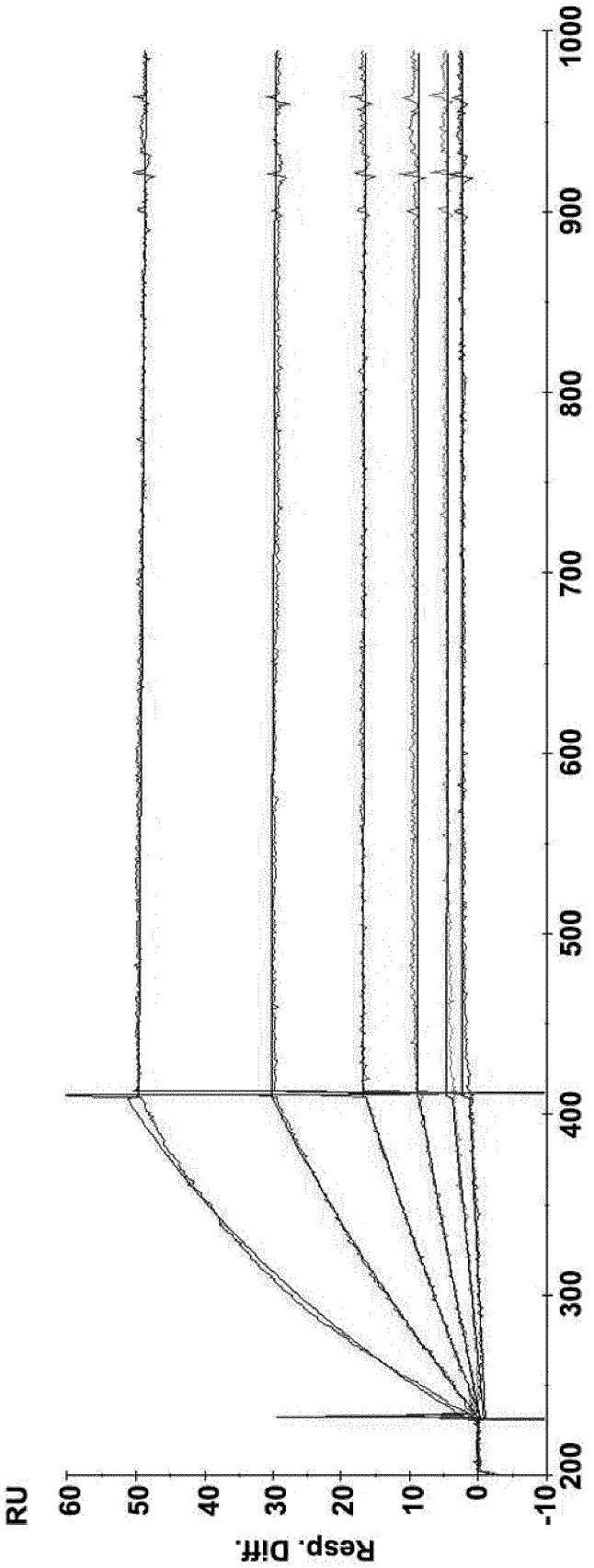
Figure D4 (continued)



KD = 0.6 nM

k off = 0.38 x 10^{-4} x s^{-1}

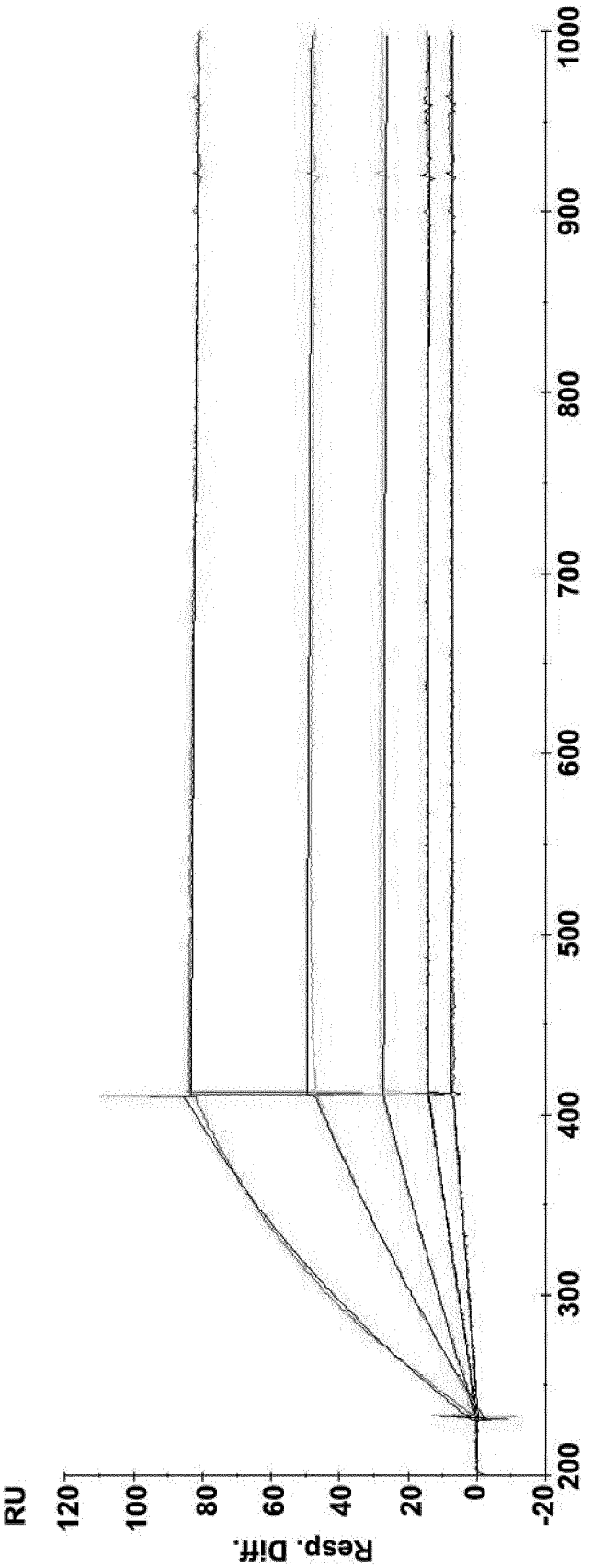
Figure D4 (continued)



KD = 0.4 nM

k off = 0.34 x 10^{-4} x s^{-1}

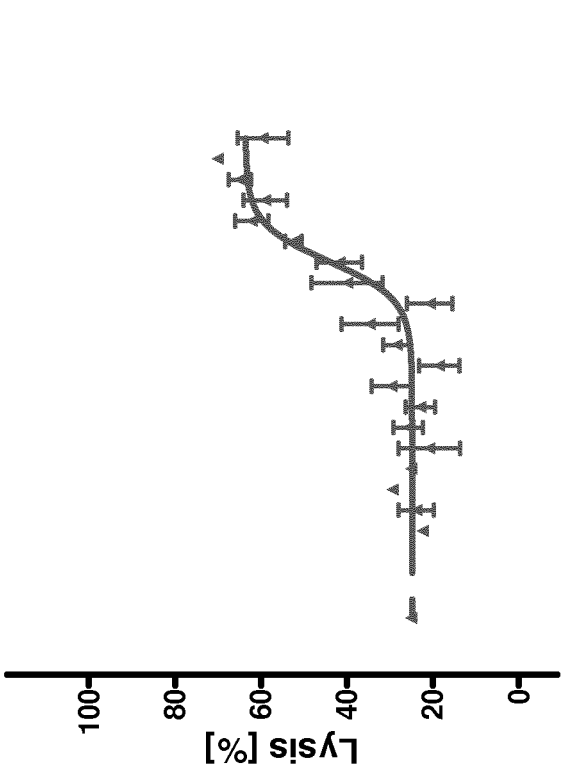
Figure D4 (continued)



KD = 0.6 nM

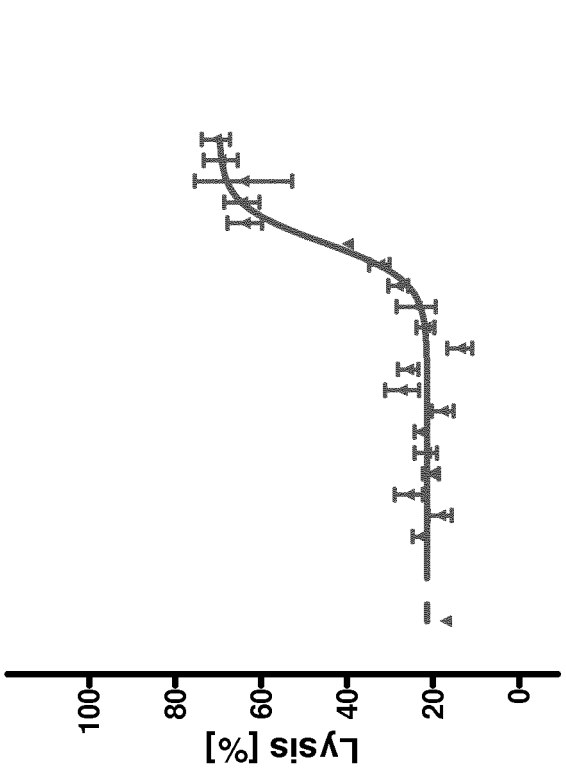
k off = 0.52 x 10^{-4} x s^{-1}

Figure A5



Target: human BCMA-transfected CHO cells

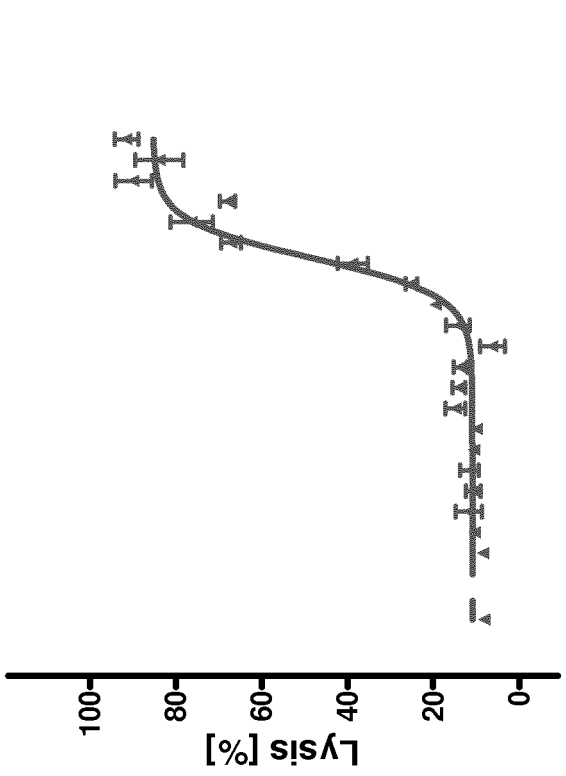
EC_{50} = 96.5 pg/ml



Target: macaque BCMA-transfected CHO cells

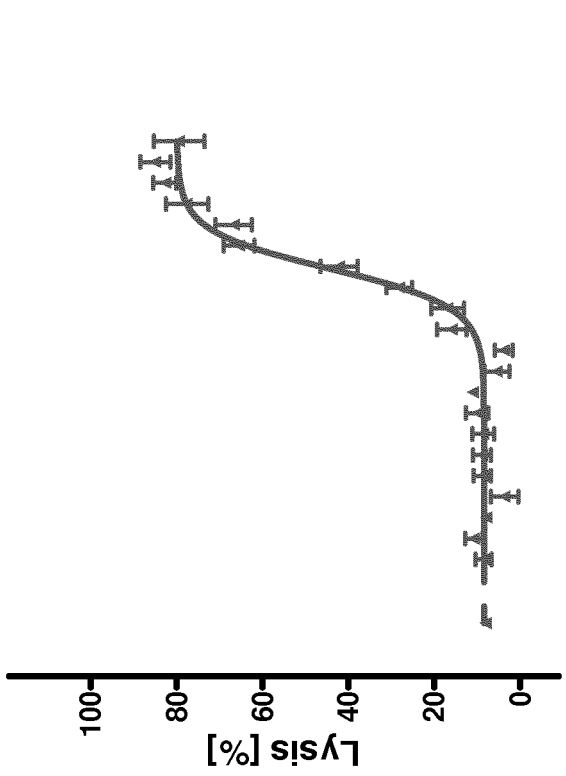
EC_{50} = 16.0 pg/ml

Figure D5



Target: human BCMA-transfected CHO cells

EC_{50} = 12 pg/ml



Target: macaque BCMA-transfected CHO cells

EC_{50} = 18 pg/ml

Figure A6

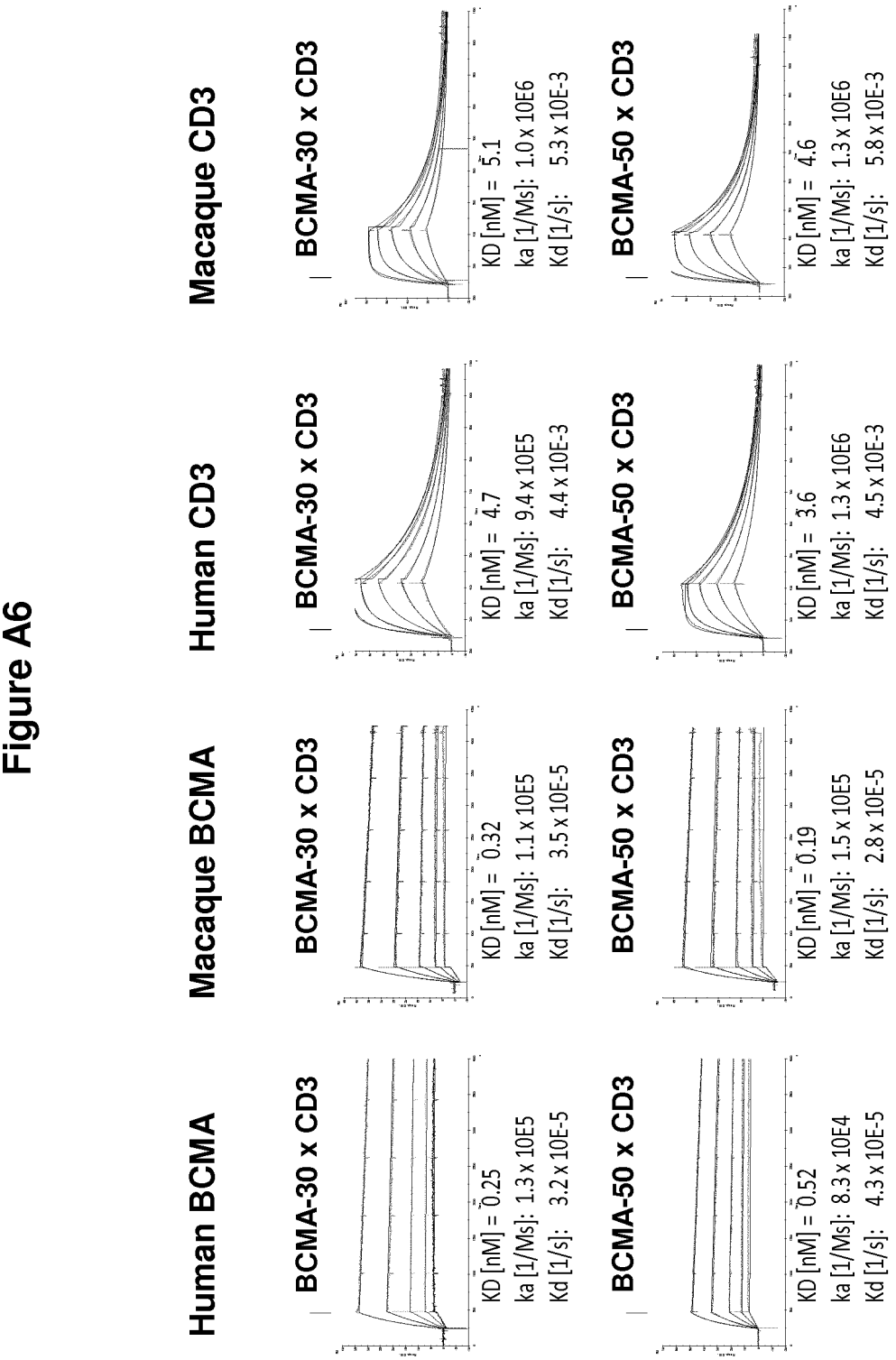

Human BCMA
Macaque BCMA
Human CD3
Macaque CD3
BCMA-30 x CD3
KD [nM] = 0.25
ka [1/Ms]: 1.3 x 10E5
Kd [1/s]: 3.2 x 10E-5
BCMA-30 x CD3
KD [nM] = 0.32
ka [1/Ms]: 1.1 x 10E5
Kd [1/s]: 3.5 x 10E-5
BCMA-30 x CD3
KD [nM] = 4.7
ka [1/Ms]: 9.4 x 10E5
Kd [1/s]: 4.4 x 10E-3
BCMA-30 x CD3
KD [nM] = 5.1
ka [1/Ms]: 1.0 x 10E6
Kd [1/s]: 5.3 x 10E-3
BCMA-50 x CD3
KD [nM] = 0.52
ka [1/Ms]: 8.3 x 10E4
Kd [1/s]: 4.3 x 10E-5
BCMA-50 x CD3
KD [nM] = 0.19
ka [1/Ms]: 1.5 x 10E5
Kd [1/s]: 2.8 x 10E-5
BCMA-50 x CD3
KD [nM] = 3.6
ka [1/Ms]: 1.3 x 10E6
Kd [1/s]: 4.5 x 10E-3
BCMA-50 x CD3
KD [nM] = 4.6
ka [1/Ms]: 1.3 x 10E6
Kd [1/s]: 5.8 x 10E-3

Figure A7

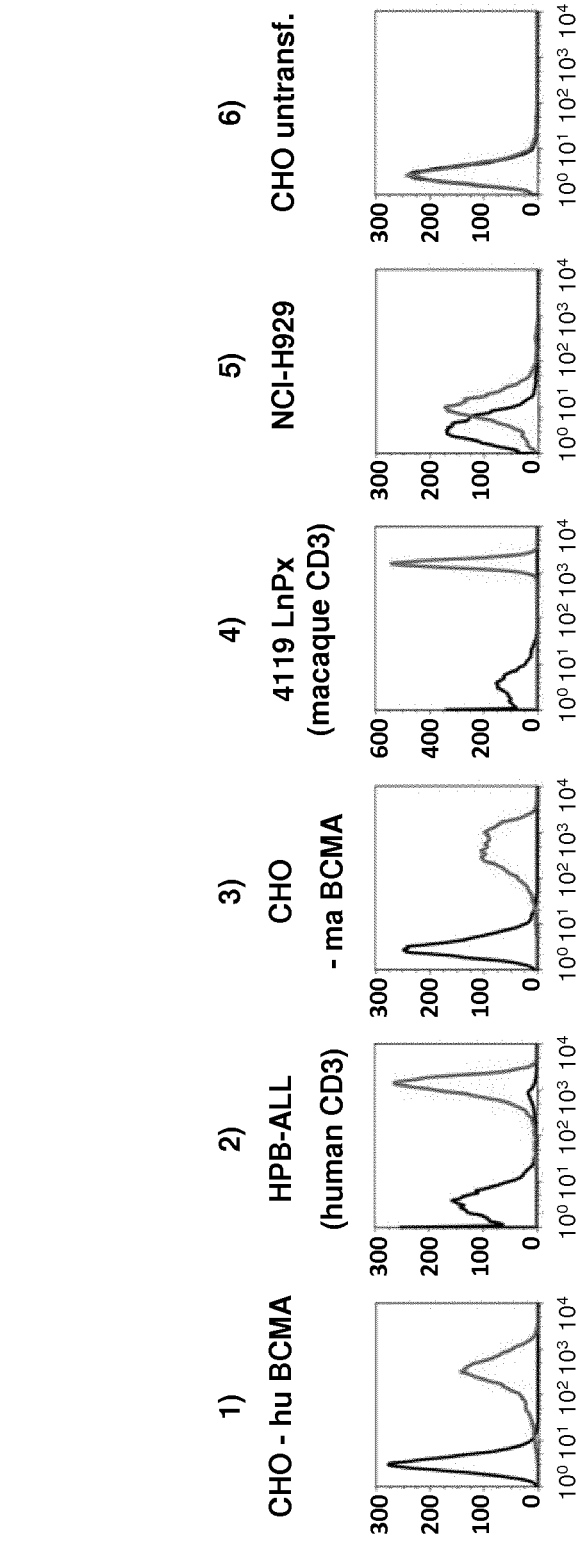

1)
CHO - hu BCMA
2)
HPB-ALL
(human CD3)
3)
CHO
- ma BCMA
4)
4119 LnPx
(macaque CD3)
5)
NCI-H929
6)
CHO untransf.
BCMA-50 x CD3

Figure A8

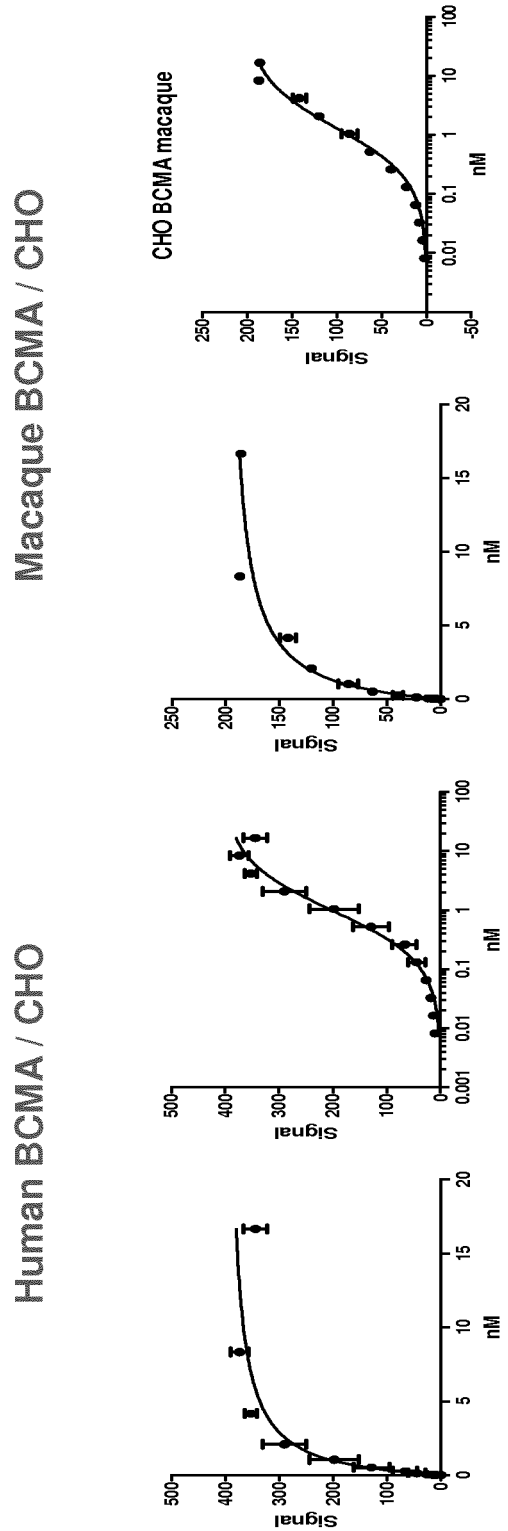

Human BCMA / CHO
Macaque BCMA / CHO
CHO BCMA macaque
Signal
nM
BCMA-50 x CD3

Figure A9

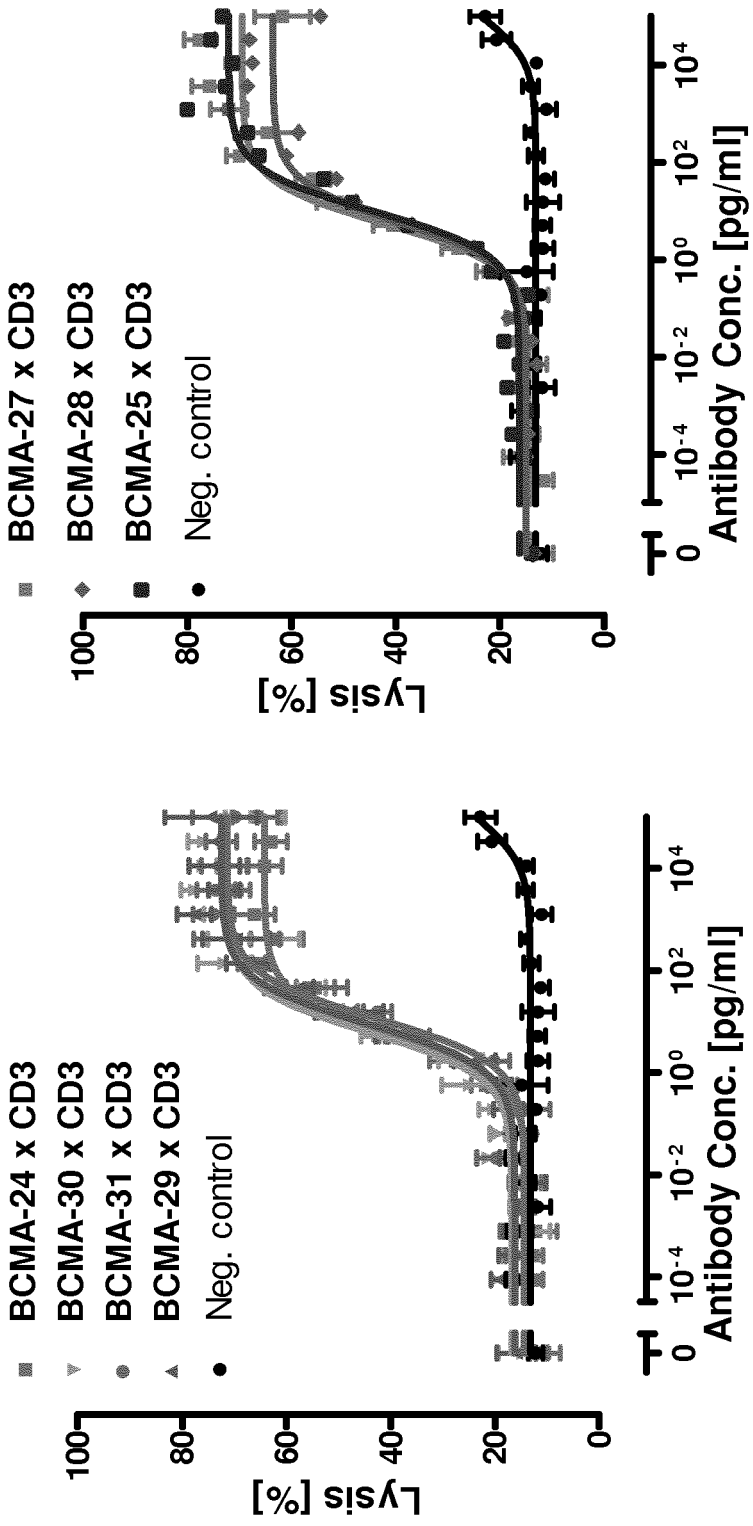

BCMA-24 x CD3
BCMA-30 x CD3
BCMA-31 x CD3
BCMA-29 x CD3
Neg. control
Lysis [%]
100
80
60
40
20
0
0
10-4
10-2
100
102
104
Antibody Conc. [pg/ml]
BCMA-27 x CD3
BCMA-28 x CD3
BCMA-25 x CD3
Neg. control
Lysis [%]
100
80
60
40
20
0
0
10-4
10-2
100
102
104
Antibody Conc. [pg/ml]

Figure A9 (continued)

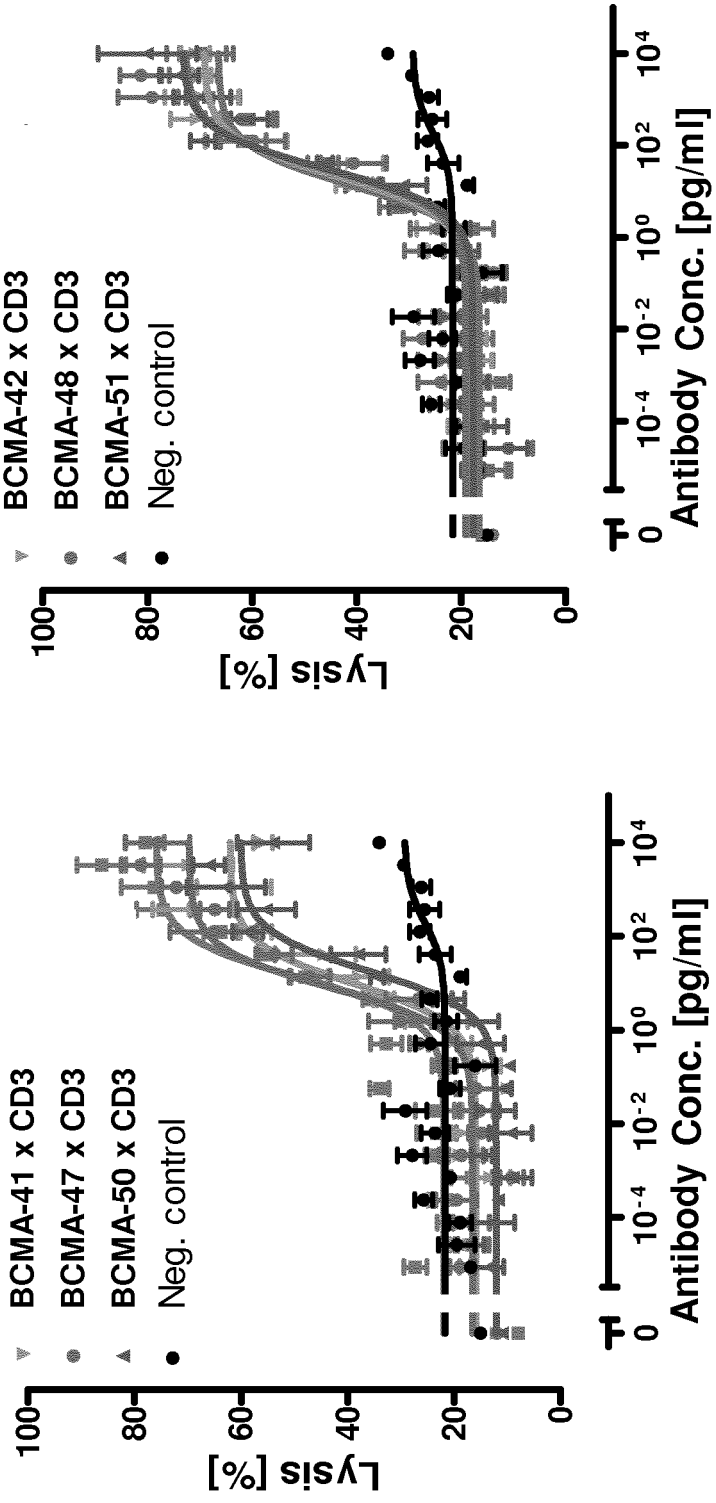


Figure A10

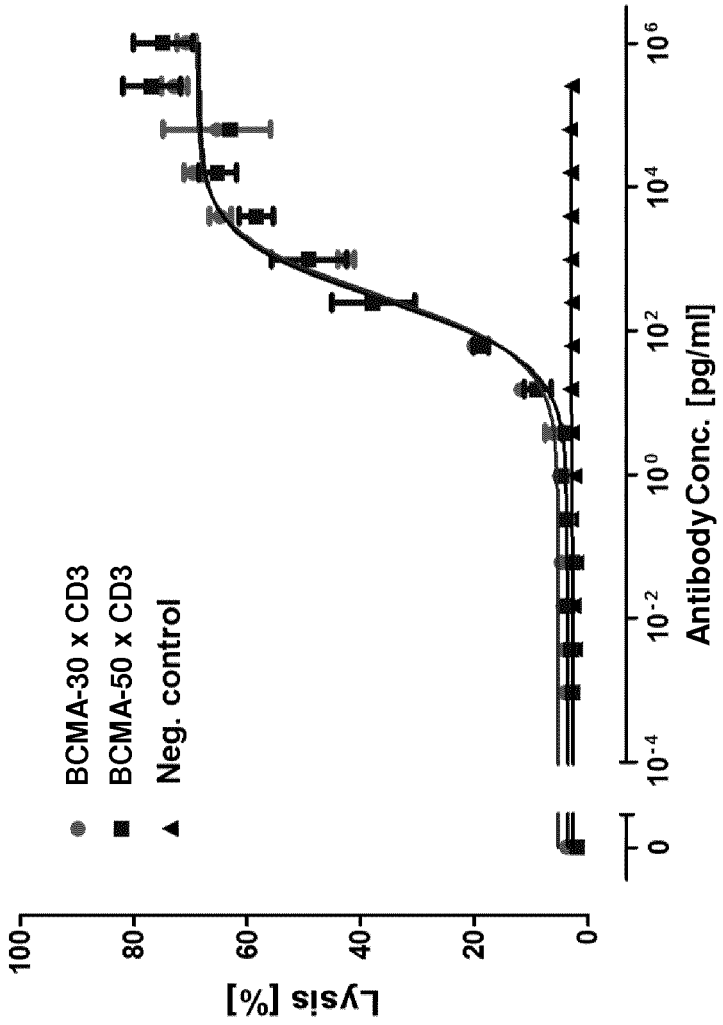

BCMA-30 x CD3
BCMA-50 x CD3
Neg. control
Lysis [%]
100
80
60
40
20
0
0
10-4
10-2
100
102
104
106
Antibody Conc. [pg/ml]

Figure A11

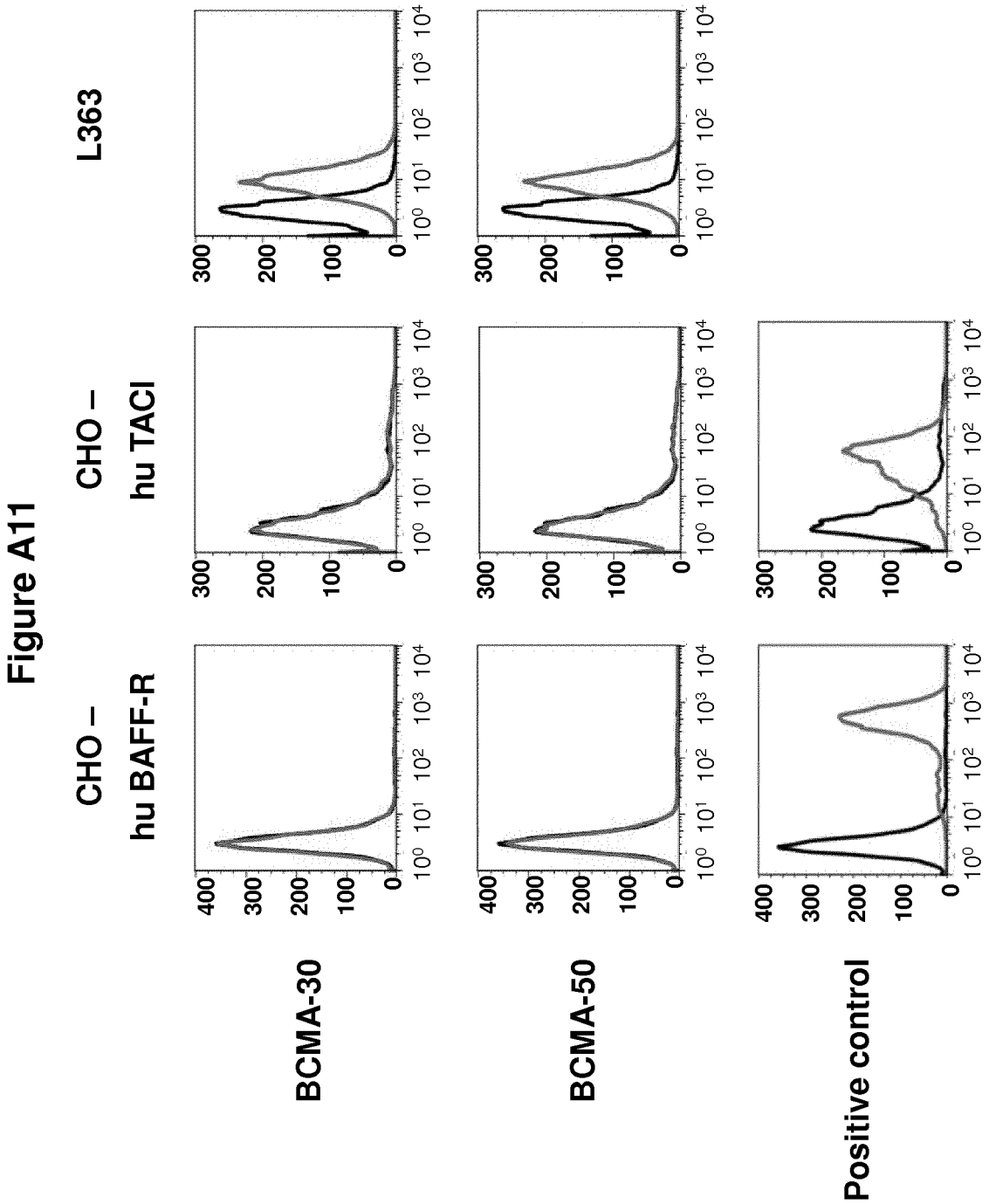

CHO – hu BAFF-R
CHO – hu TACI
L363
BCMA-30
BCMA-50
Positive control

Figure A12

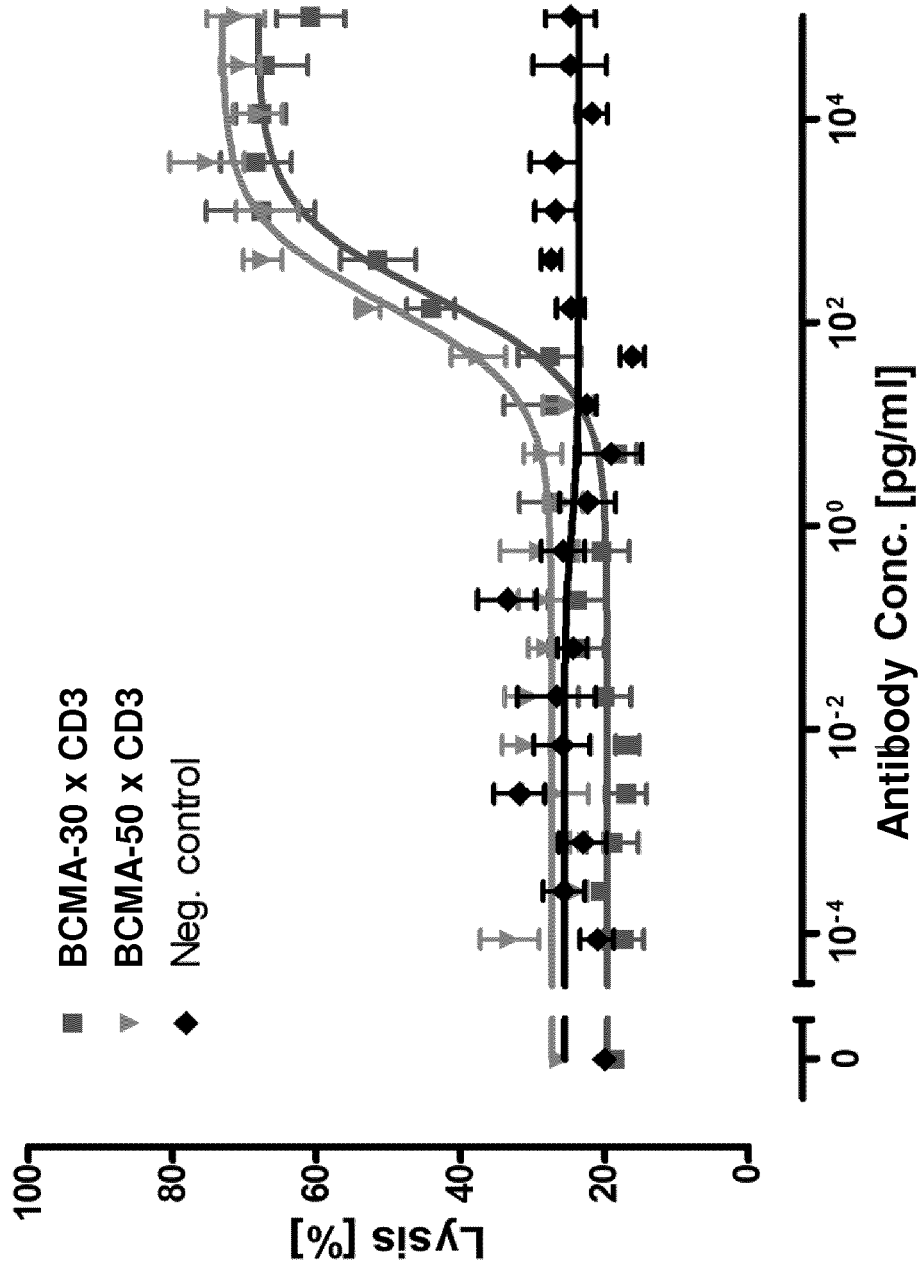

BCMA-30 x CD3
BCMA-50 x CD3
Neg. control
Lysis [%]
100
80
60
40
20
0
0
10-4
10-2
100
102
104
Antibody Conc. [pg/ml]

Figure A13

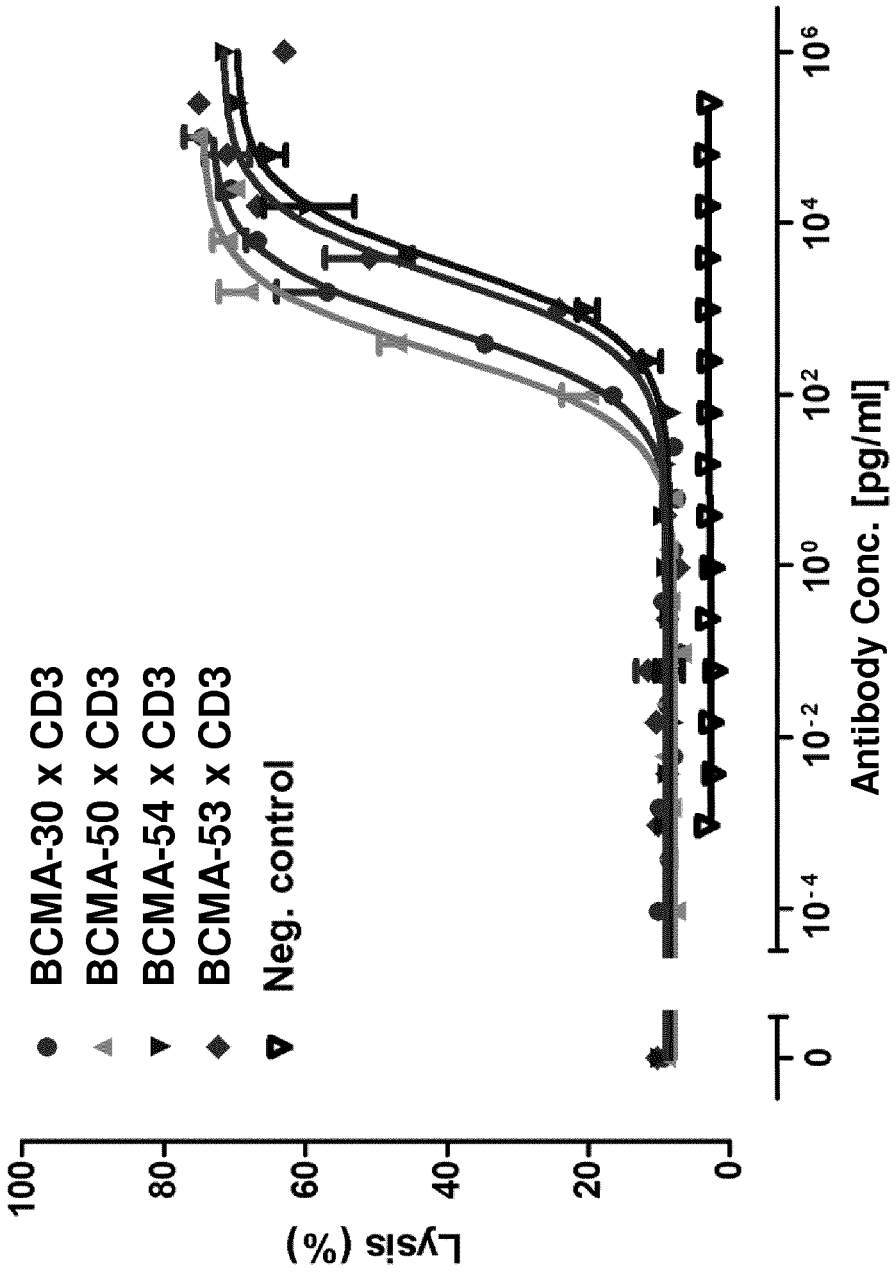

BCMA-30 x CD3
BCMA-50 x CD3
BCMA-54 x CD3
BCMA-53 x CD3
Neg. control
Lysis (%)
100
80
60
40
20
0
0
10-4
10-2
100
102
104
106
Antibody Conc. [pg/ml]

Figure A14

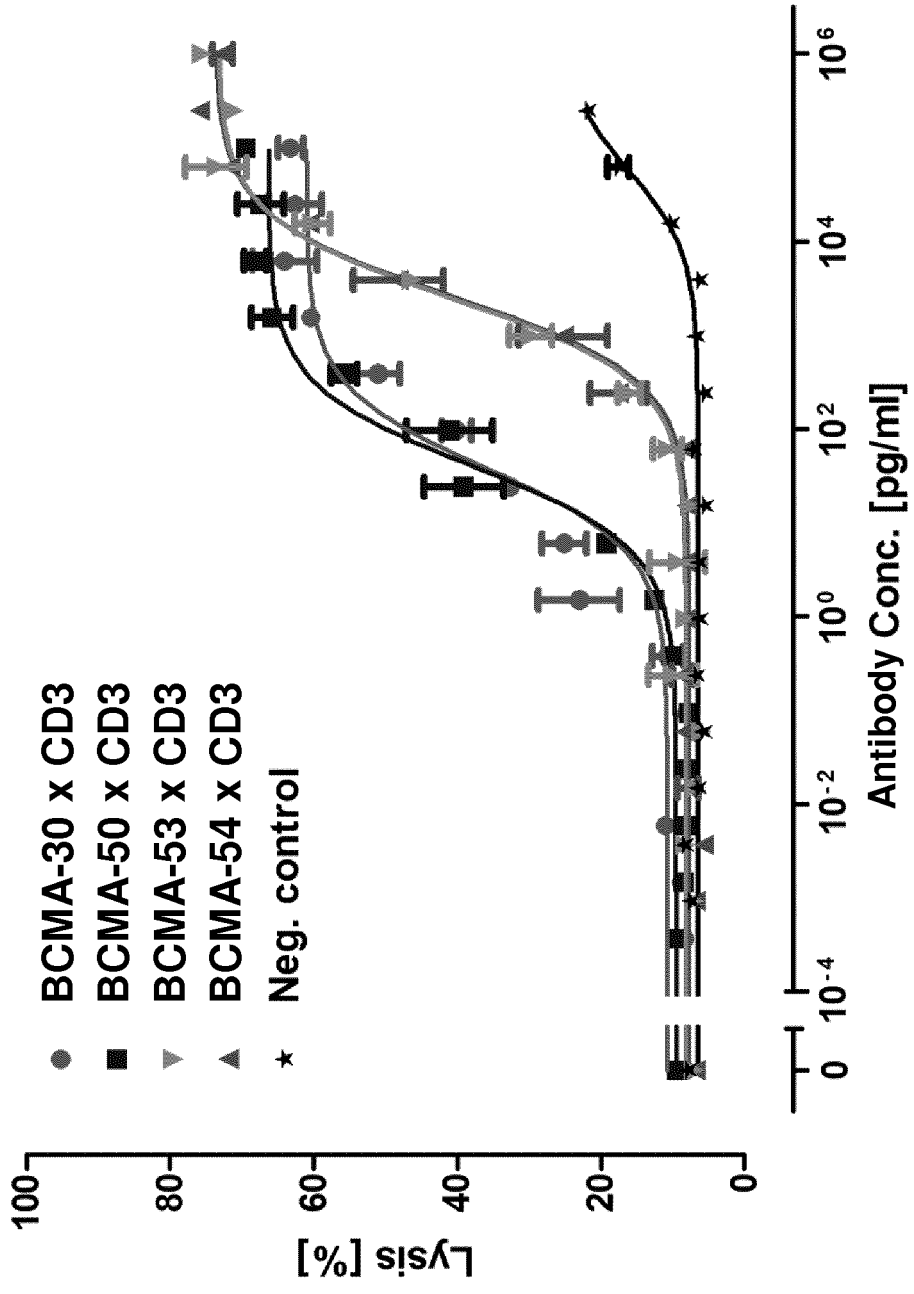

BCMA-30 x CD3
BCMA-50 x CD3
BCMA-53 x CD3
BCMA-54 x CD3
Neg. control
Lysis [%]
100
80
60
40
20
0
0
10-4
10-2
100
102
104
106
Antibody Conc. [pg/ml]

Figure A15

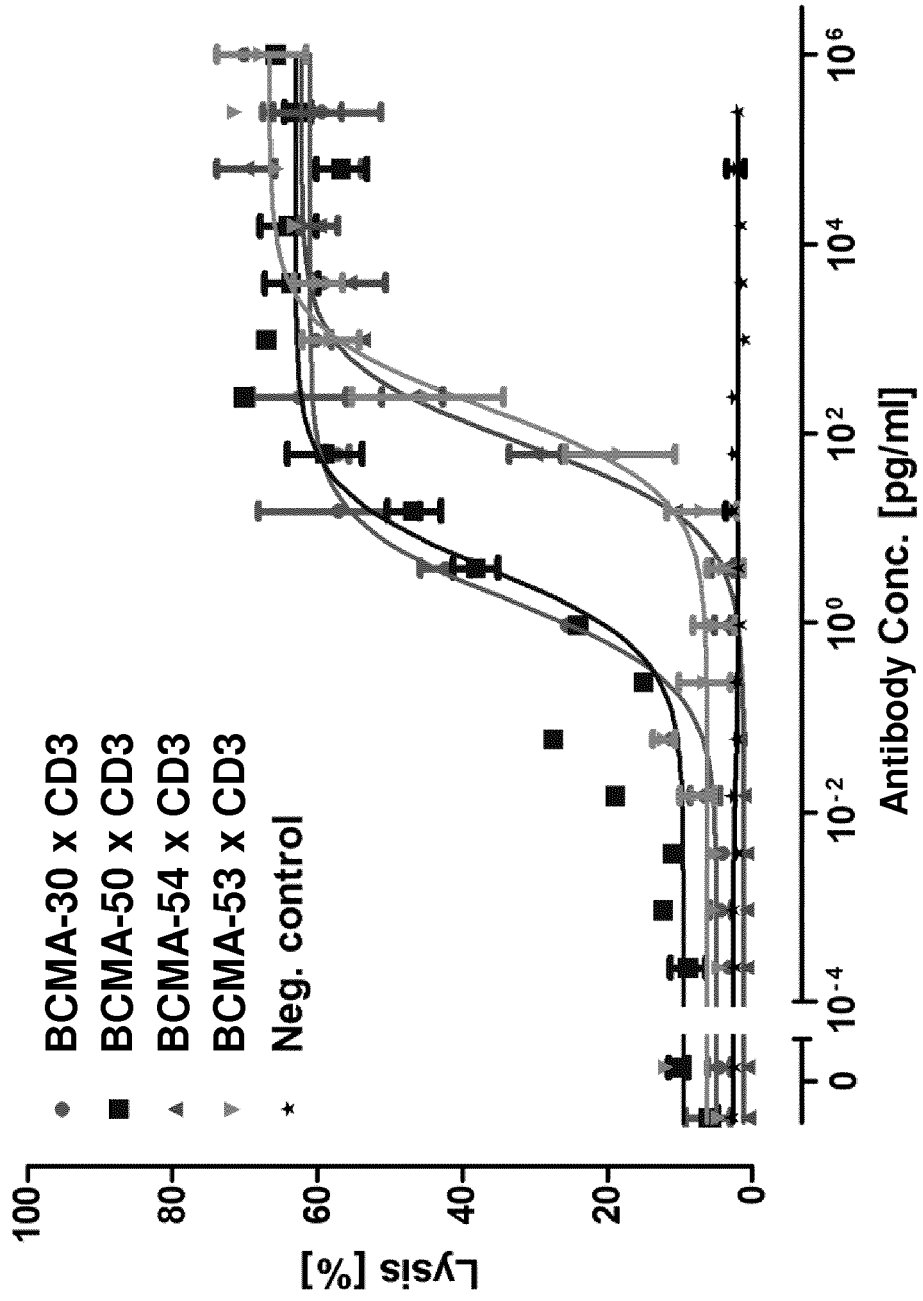

BCMA-30 x CD3
BCMA-50 x CD3
BCMA-54 x CD3
BCMA-53 x CD3
Neg. control
Lysis [%]
100
80
60
40
20
0
0
10-4
10-2
100
102
104
106
Antibody Conc. [pg/ml]

Figure A16

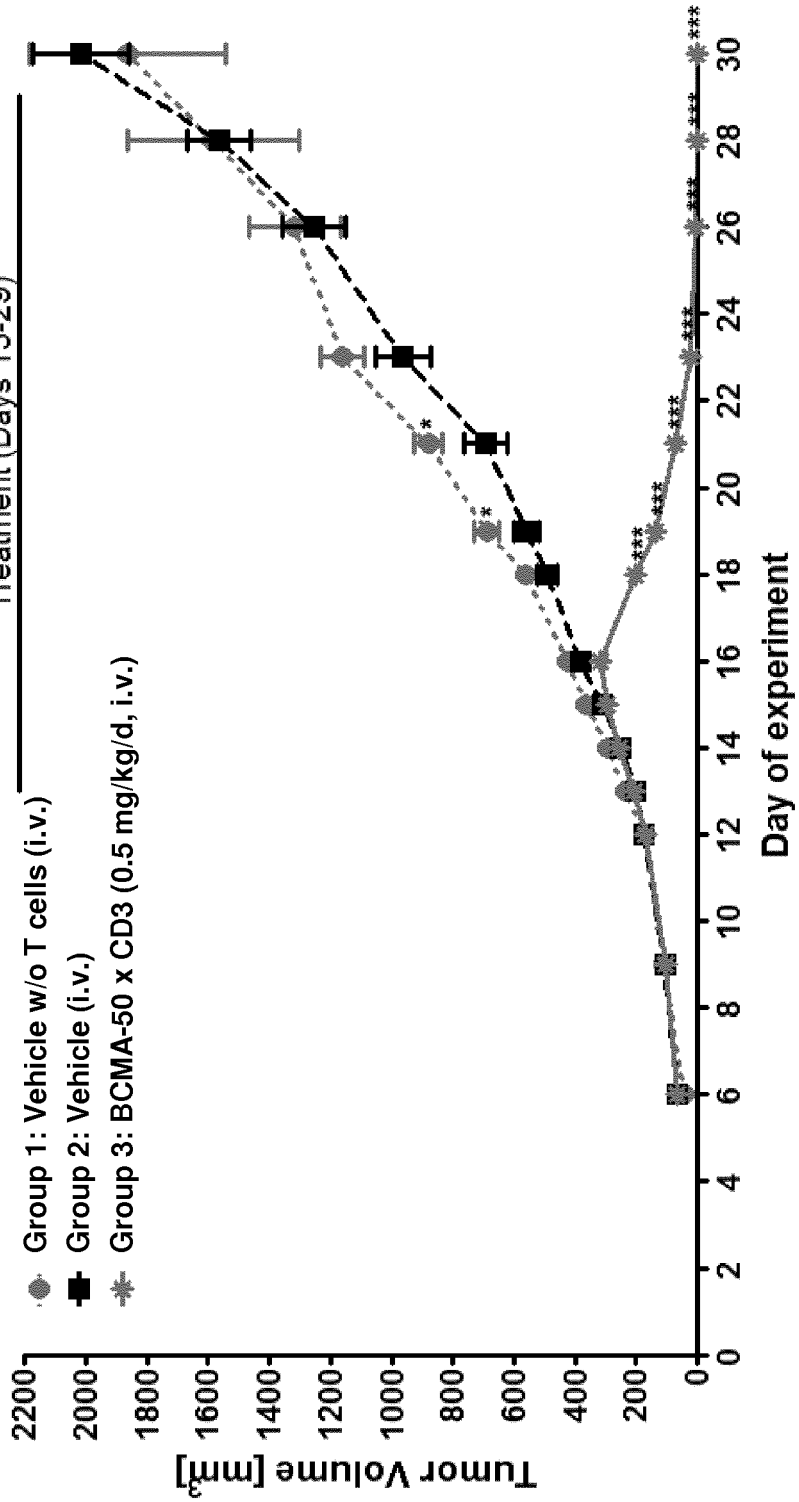

Treatment (Days 13-29)
Group 1: Vehicle w/o T cells (i.v.)
Group 2: Vehicle (i.v.)
Group 3: BCMA-50 x CD3 (0.5 mg/kg/d, i.v.)
Tumor Volume [mm³]
Day of experiment
0
200
400
600
800
1000
1200
1400
1600
1800
2000
2200
0
2
4
6
8
10
12
14
16
18
20
22
24
26
28
30
*
***

Figure A17

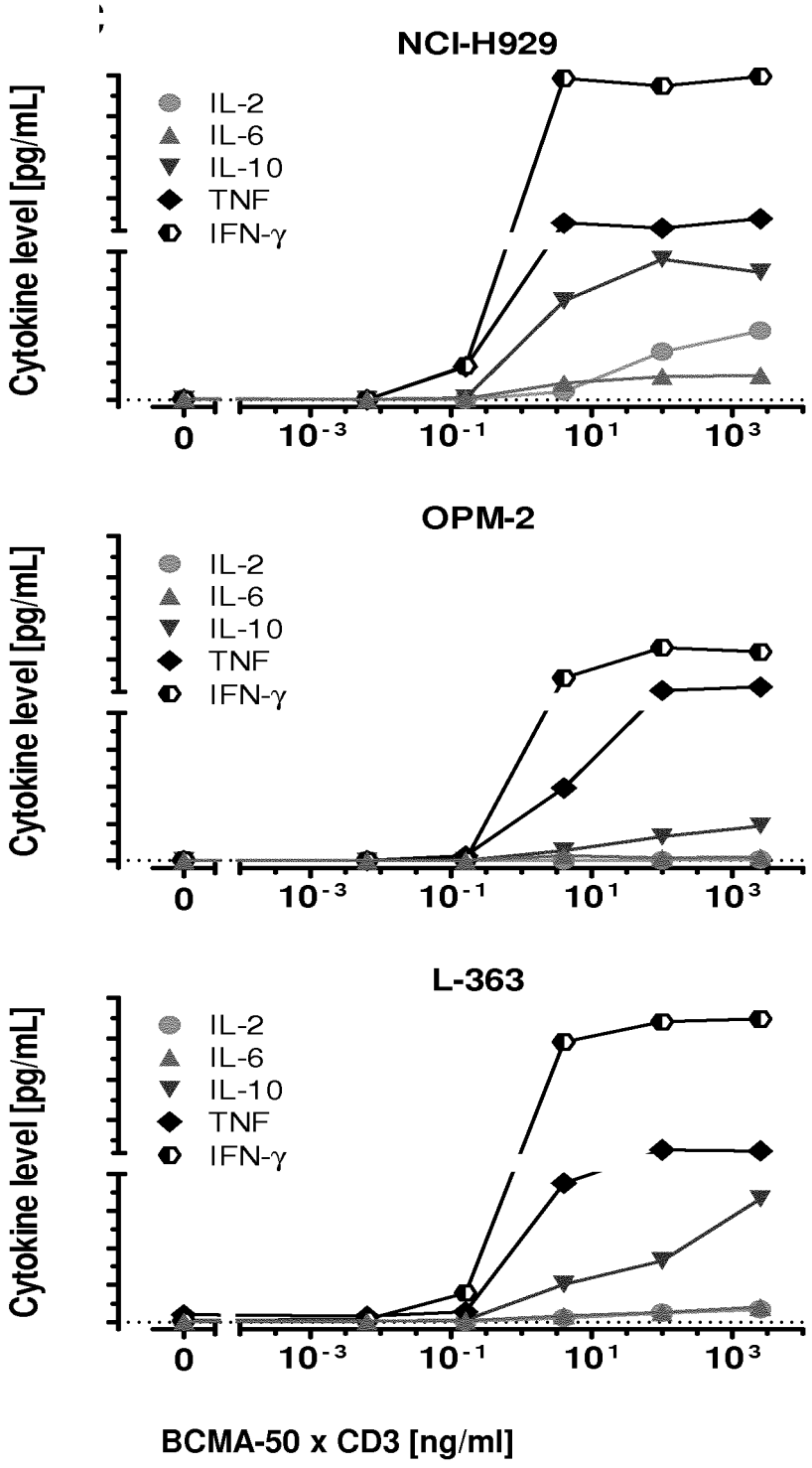

NCI-H929
OPM-2
L-363
IL-2
IL-6
IL-10
TNF
IFN-γ
Cytokine level [pg/mL]
0
10-3
10-1
101
103
BCMA-50 x CD3 [ng/ml]

Figure A18

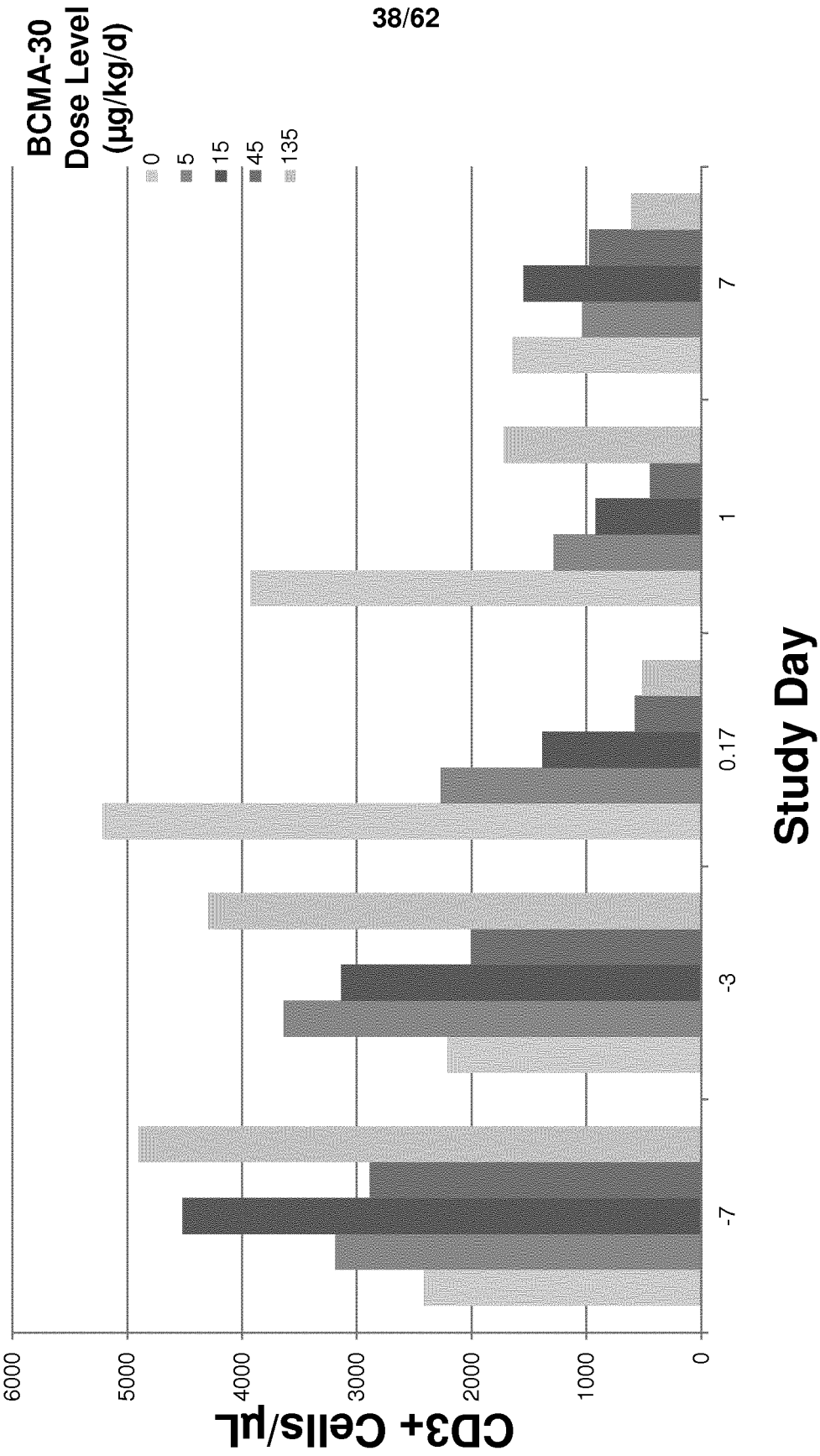

BCMA-30
Dose Level
(µg/kg/d)
0
5
15
45
135
CD3+ Cells/µL
6000
5000
4000
3000
2000
1000
0
-7
-3
0.17
1
7
Study Day

Figure A19

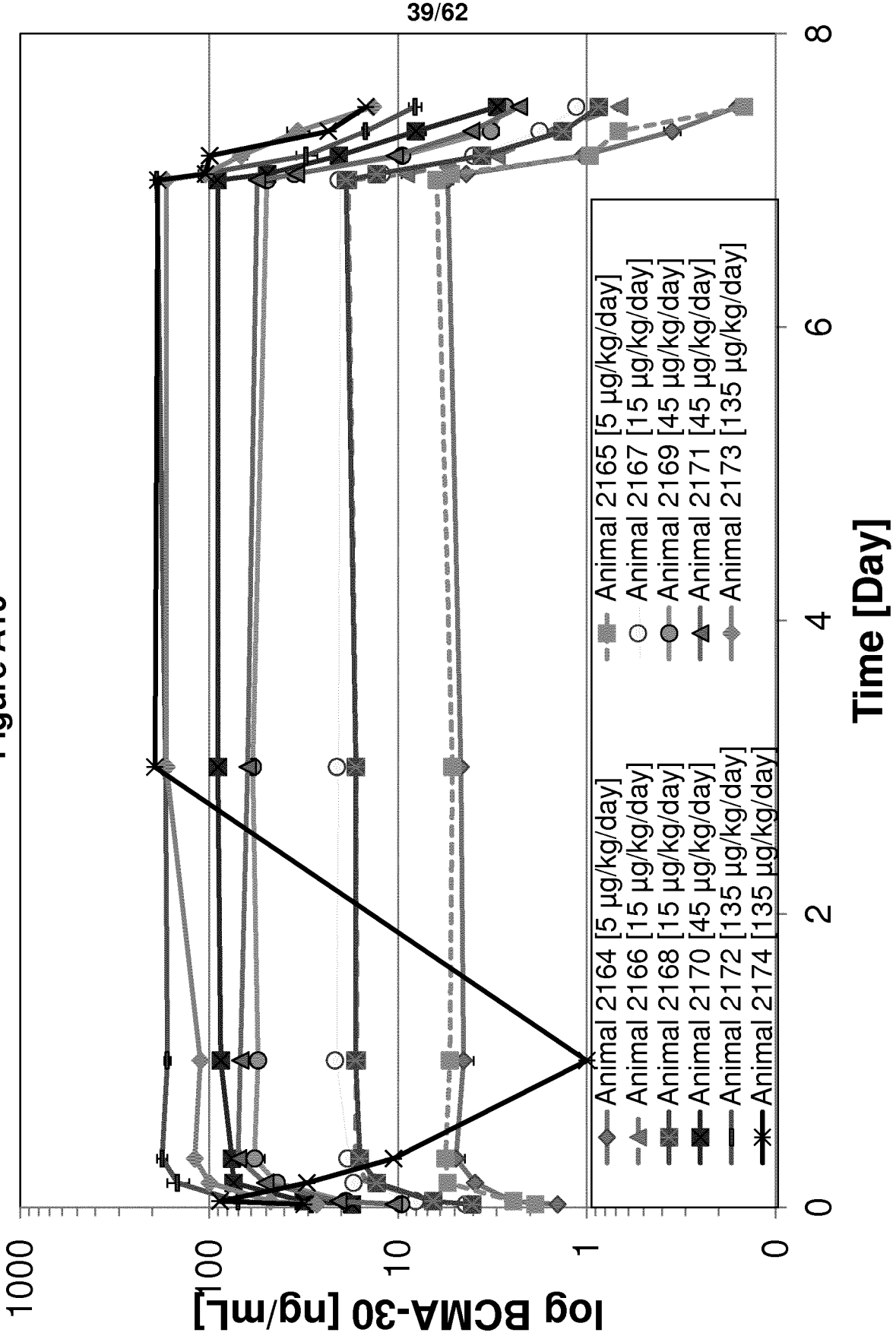

log BCMA-30 [ng/mL]
1000
100
10
1
0
0
2
4
6
8
Time [Day]
Animal 2164 [5 µg/kg/day]
Animal 2165 [5 µg/kg/day]
Animal 2166 [15 µg/kg/day]
Animal 2167 [15 µg/kg/day]
Animal 2168 [15 µg/kg/day]
Animal 2169 [45 µg/kg/day]
Animal 2170 [45 µg/kg/day]
Animal 2171 [45 µg/kg/day]
Animal 2172 [135 µg/kg/day]
Animal 2173 [135 µg/kg/day]
Animal 2174 [135 µg/kg/day]

Figure A20

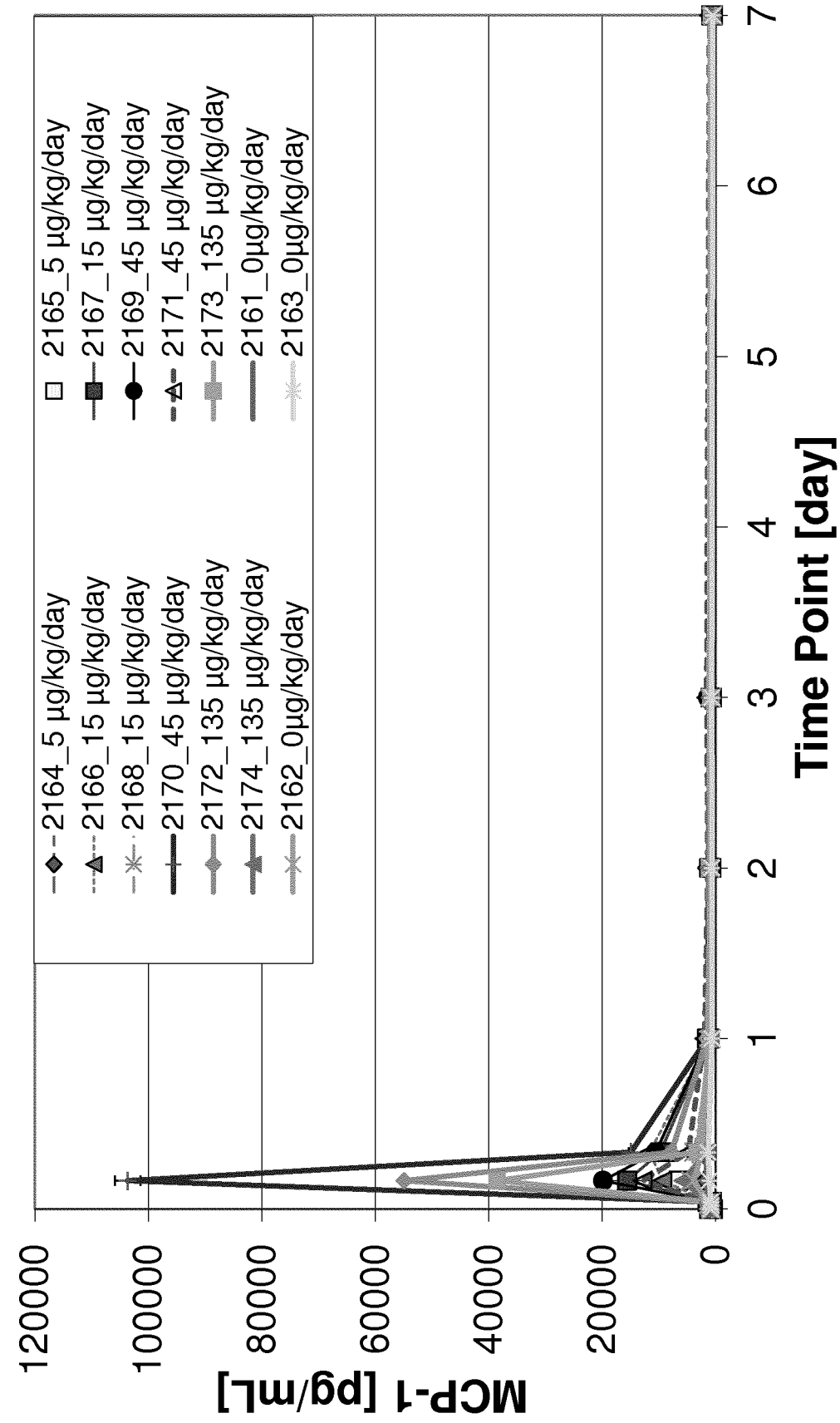

MCP-1 [pg/mL]
120000
100000
80000
60000
40000
20000
0
Time Point [day]
0
1
2
3
4
5
6
7
2164_5 µg/kg/day
2166_15 µg/kg/day
2168_15 µg/kg/day
2170_45 µg/kg/day
2172_135 µg/kg/day
2174_135 µg/kg/day
2162_0µg/kg/day
2165_5 µg/kg/day
2167_15 µg/kg/day
2169_45 µg/kg/day
2171_45 µg/kg/day
2173_135 µg/kg/day
2161_0µg/kg/day
2163_0µg/kg/day

Figure A21

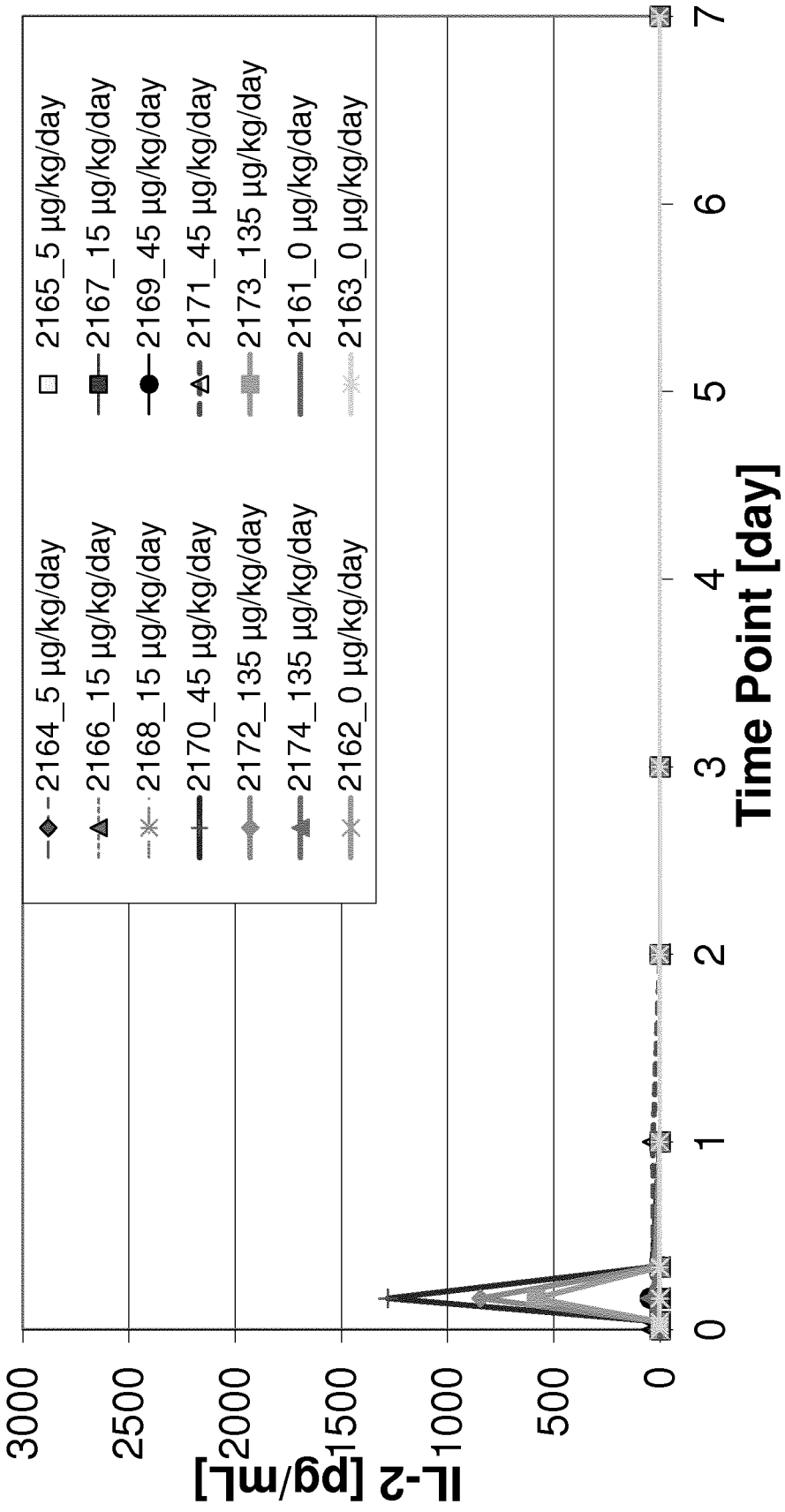

IL-2 [pg/mL]
3000
2500
2000
1500
1000
500
0
0
1
2
3
4
5
6
7
Time Point [day]
2164_5 µg/kg/day
2166_15 µg/kg/day
2168_15 µg/kg/day
2170_45 µg/kg/day
2172_135 µg/kg/day
2174_135 µg/kg/day
2162_0 µg/kg/day
2165_5 µg/kg/day
2167_15 µg/kg/day
2169_45 µg/kg/day
2171_45 µg/kg/day
2173_135 µg/kg/day
2161_0 µg/kg/day
2163_0 µg/kg/day

Figure A22

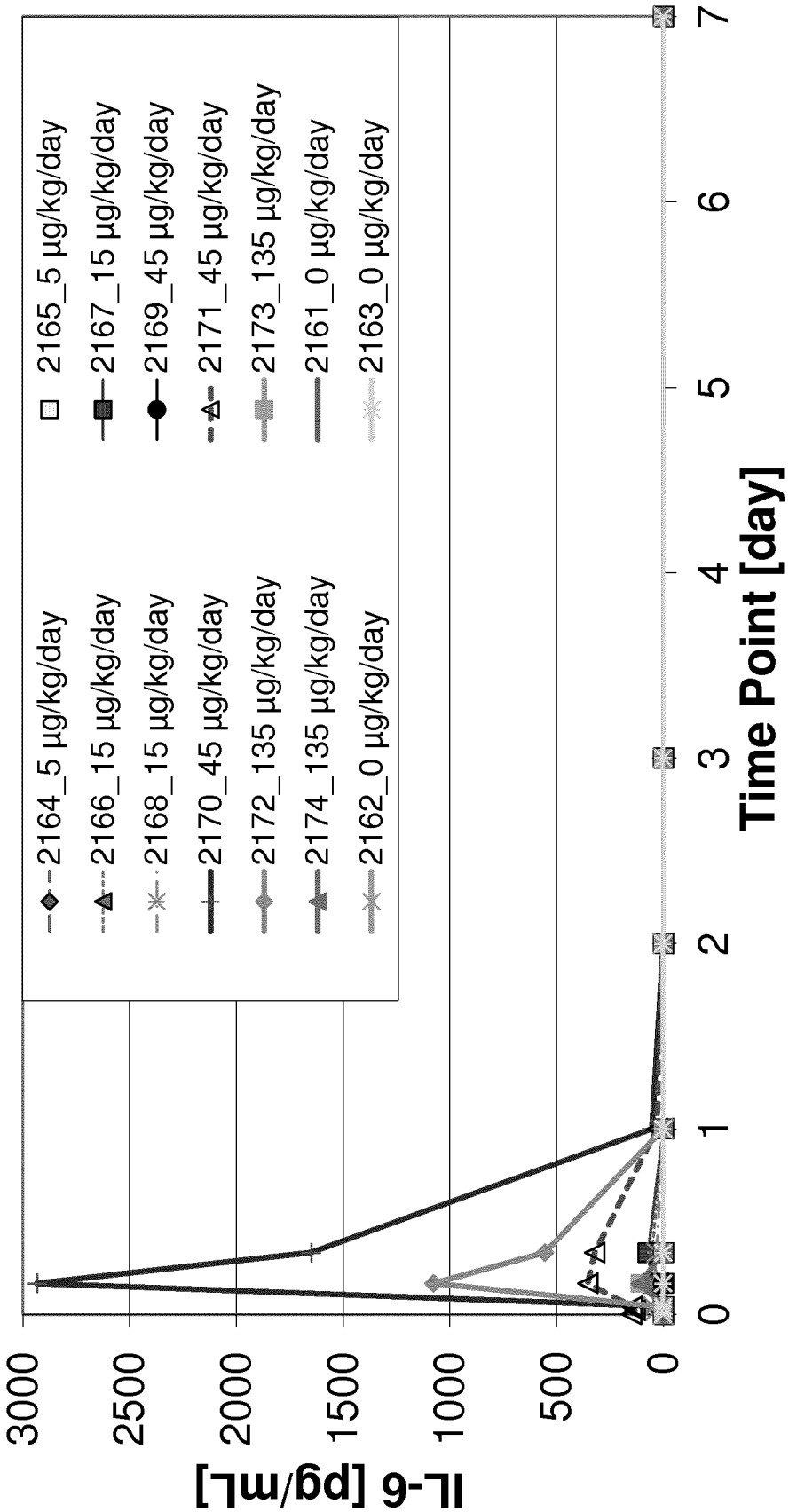

IL-6 [pg/mL]
3000
2500
2000
1500
1000
500
0
Time Point [day]
0
1
2
3
4
5
6
7
2164_5 µg/kg/day
2166_15 µg/kg/day
2168_15 µg/kg/day
2170_45 µg/kg/day
2172_135 µg/kg/day
2174_135 µg/kg/day
2162_0 µg/kg/day
2165_5 µg/kg/day
2167_15 µg/kg/day
2169_45 µg/kg/day
2171_45 µg/kg/day
2173_135 µg/kg/day
2161_0 µg/kg/day
2163_0 µg/kg/day

Figure E3

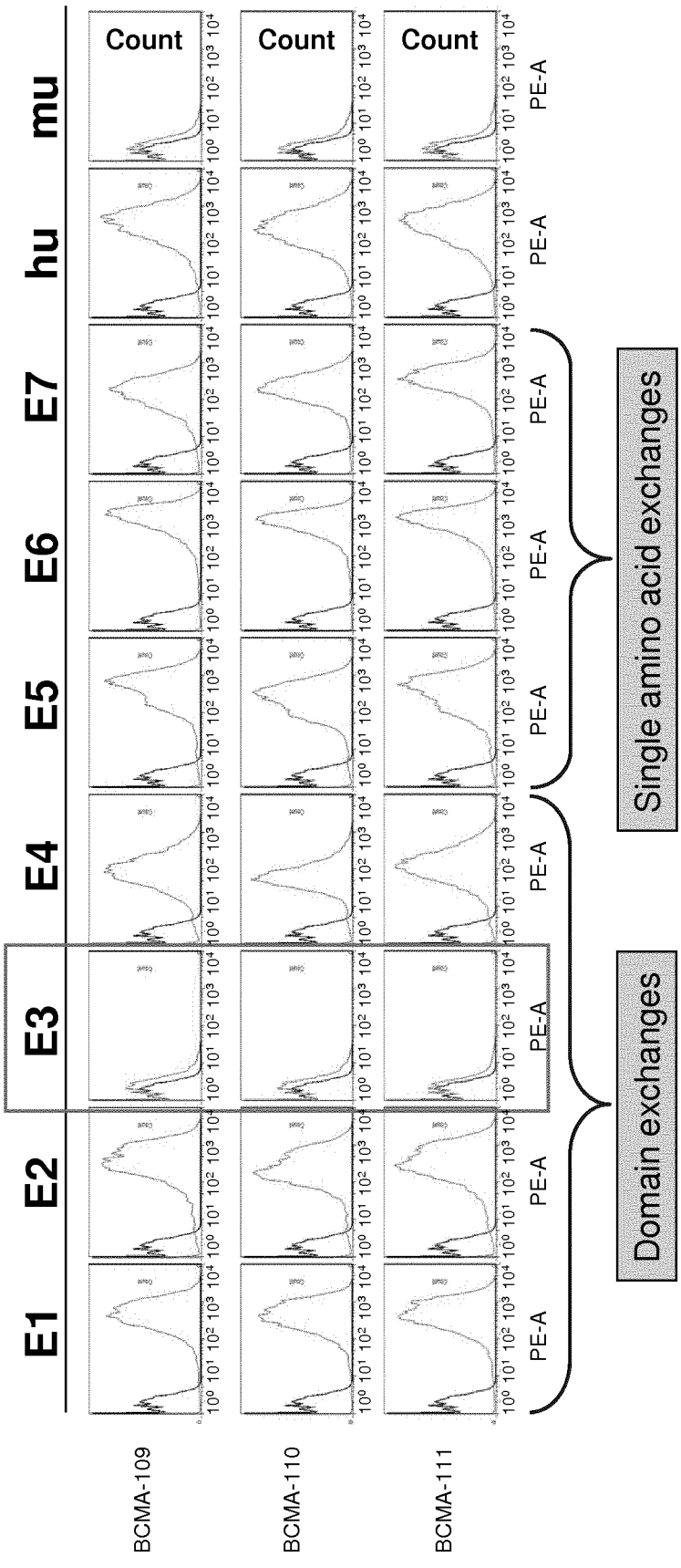

E1
E2
E3
E4
E5
E6
E7
hu
mu
Count
PE-A
BCMA-109
BCMA-110
BCMA-111
Domain exchanges
Single amino acid exchanges

Figure E3 (continued)

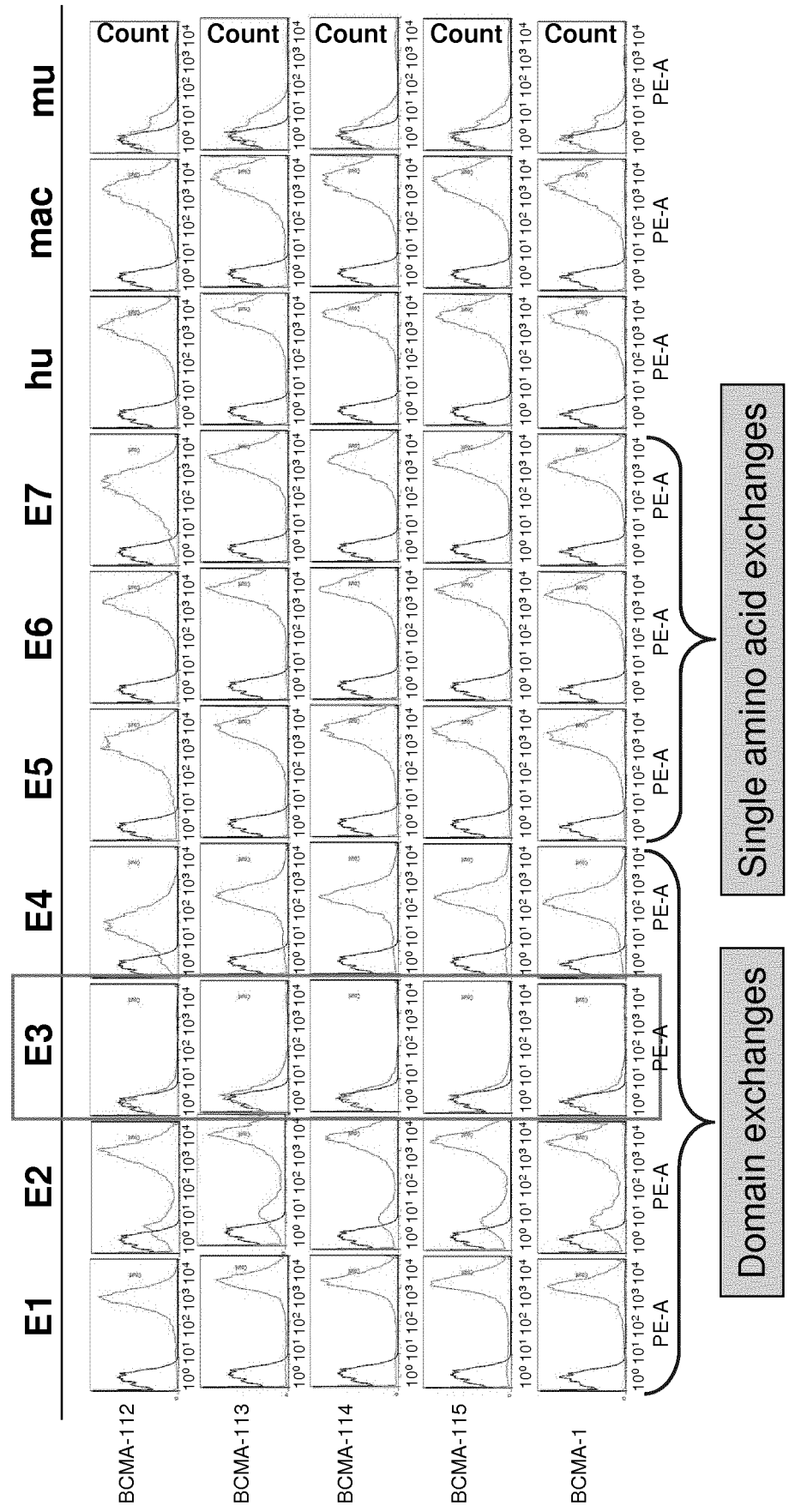
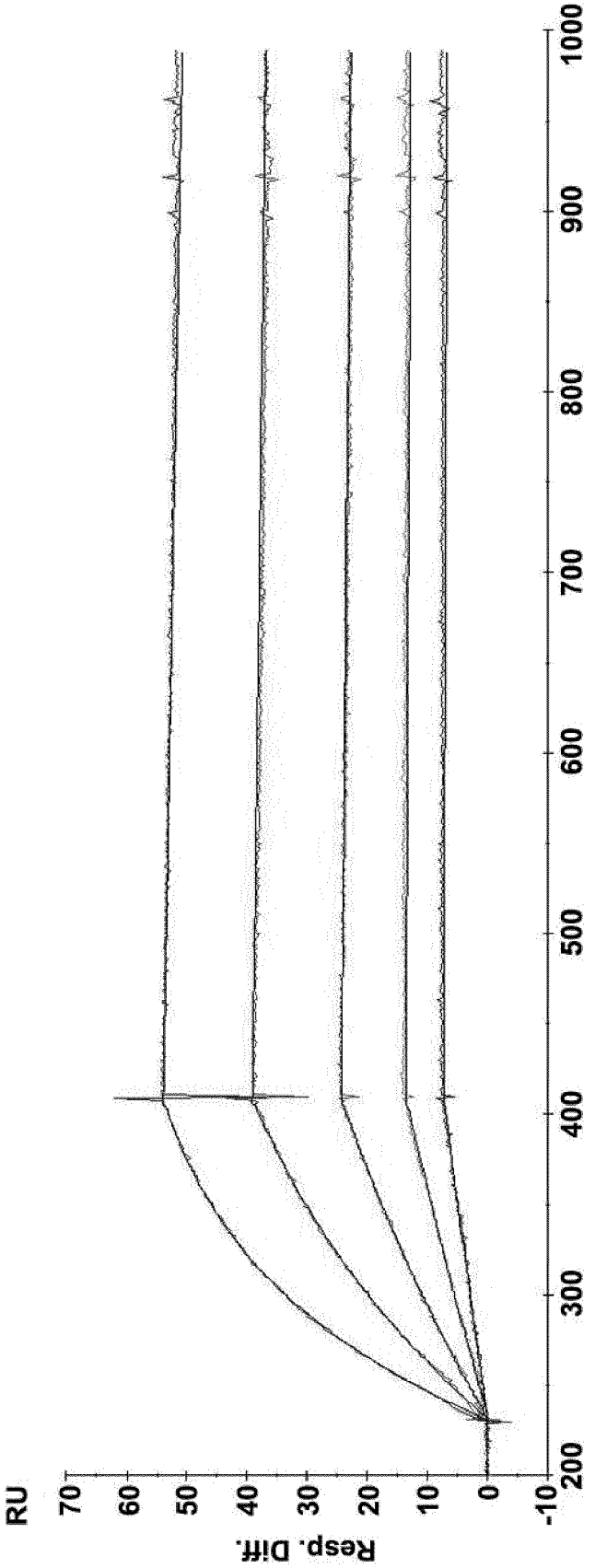


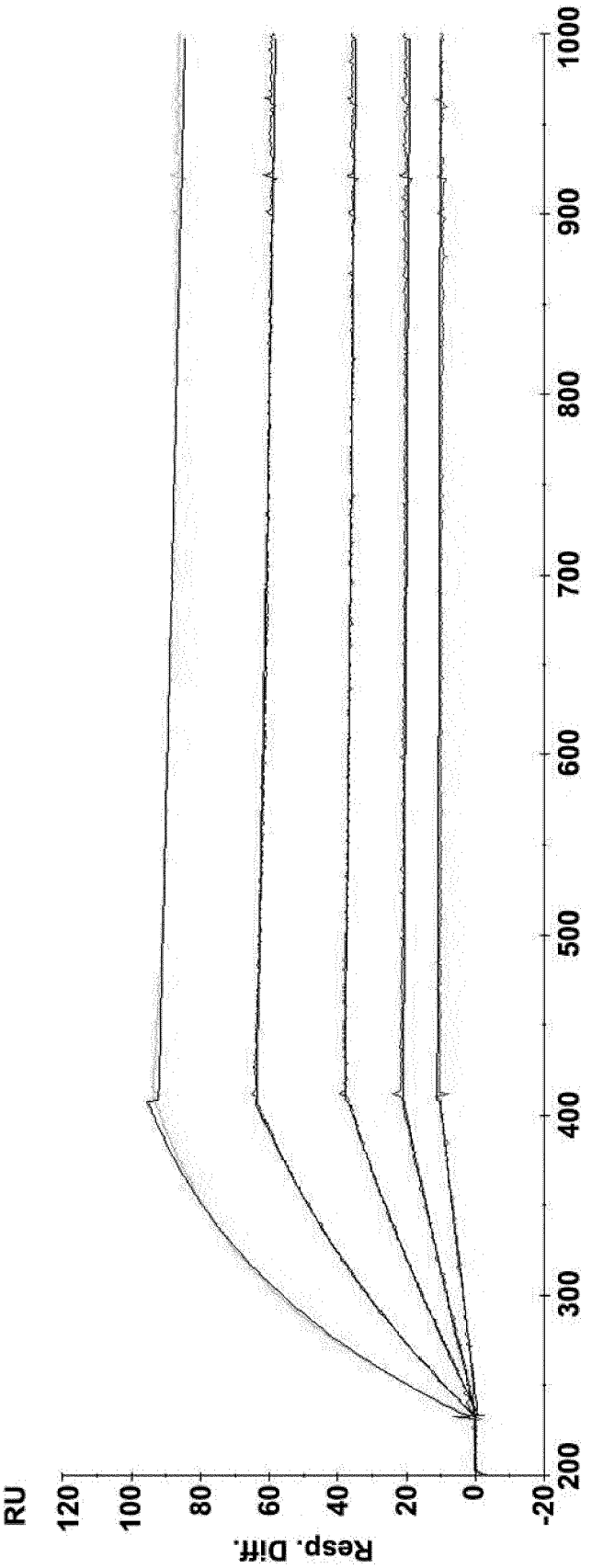
Figure E4



KD = 0.5 nM

k off = 1.1 x 10^{-4} x s^{-1}

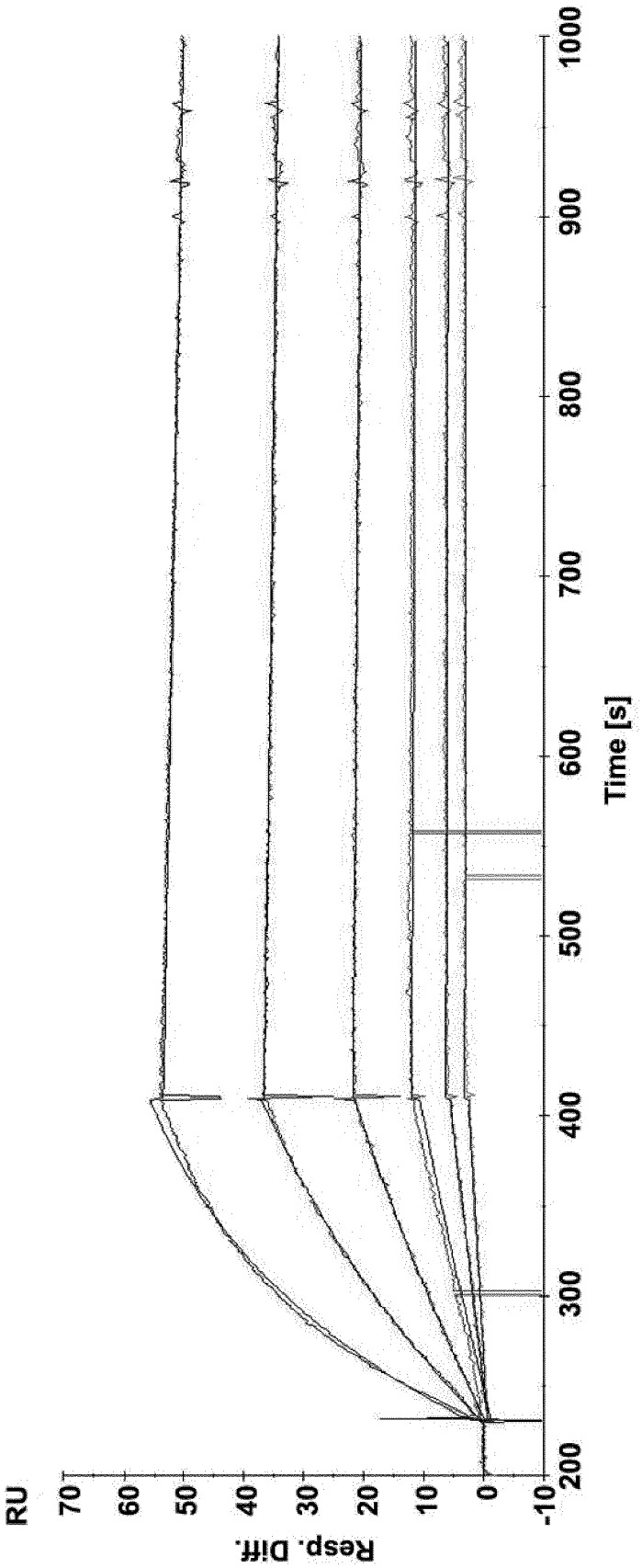
Figure E4 (continued)



KD = 0.8 nM

k off = 1.5 x 10^{-4} x s^{-1}

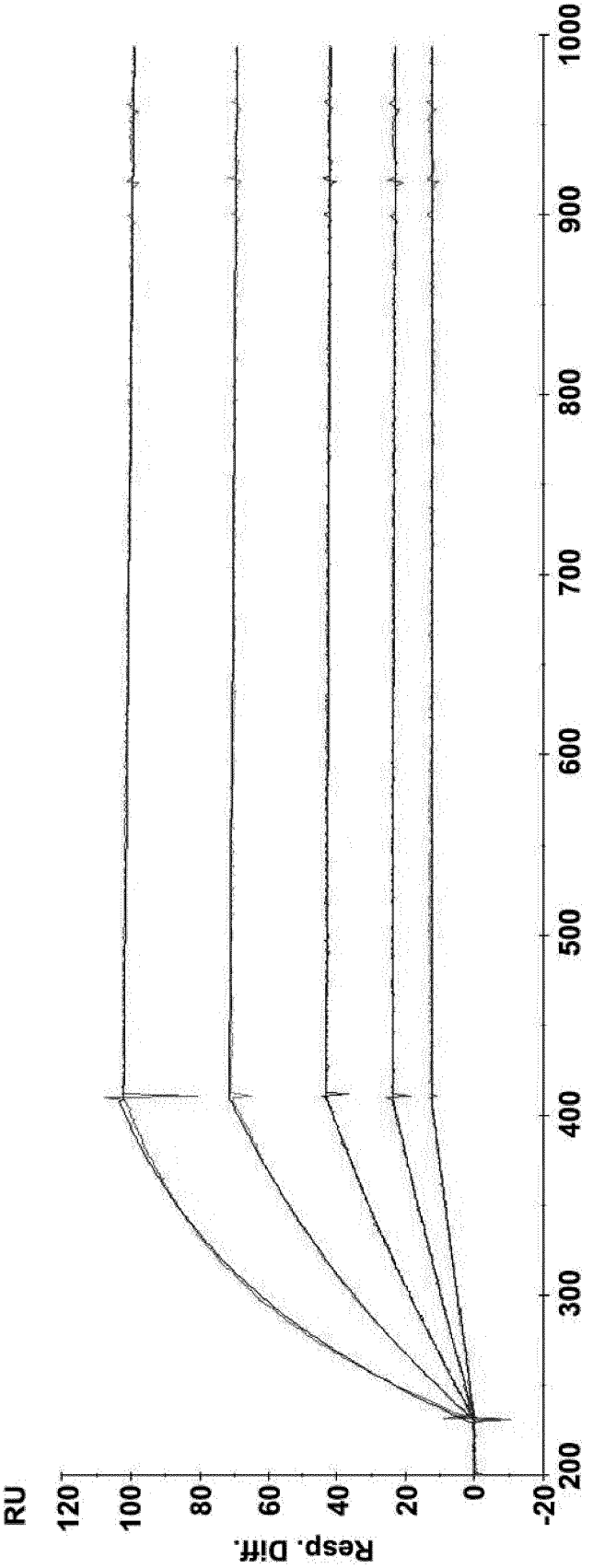
Figure E4 (continued)



KD = 0.6 nM

k off = 1.1 x 10^{-4} x s^{-1}

Figure E4 (continued)



KD = 0.3 nM

k off = 0.54 x 10^{-4} x s^{-1}

Figure E5

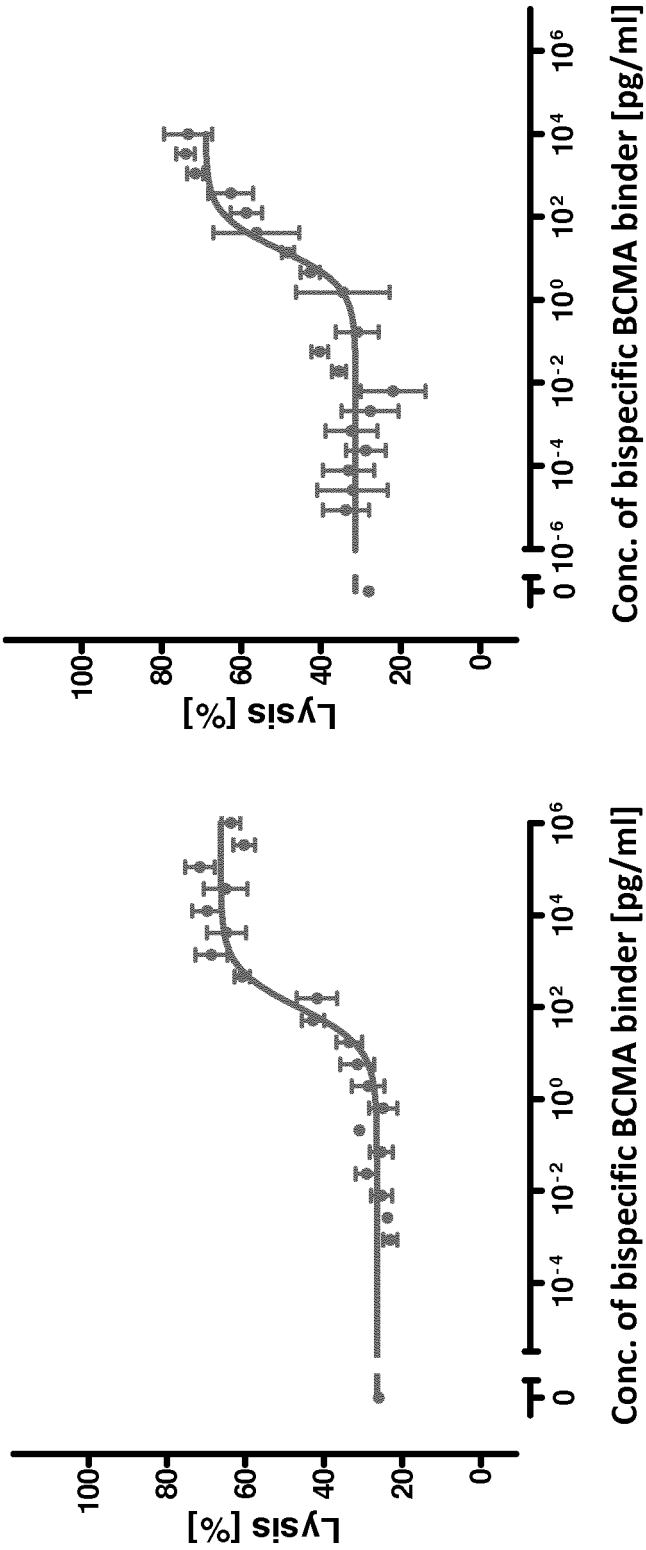

Lysis [%]
100
80
60
40
20
0
0
10-4
10-2
100
102
104
106
Conc. of bispecific BCMA binder [pg/ml]
Target: human BCMA-transfected CHO cells
EC50 = 44.4 pg/ml
Lysis [%]
100
80
60
40
20
0
0
10-6
10-4
10-2
100
102
104
106
Conc. of bispecific BCMA binder [pg/ml]
Target: macaque BCMA-transfected CHO cells
EC50 = 14.2 pg/ml

Figure E6

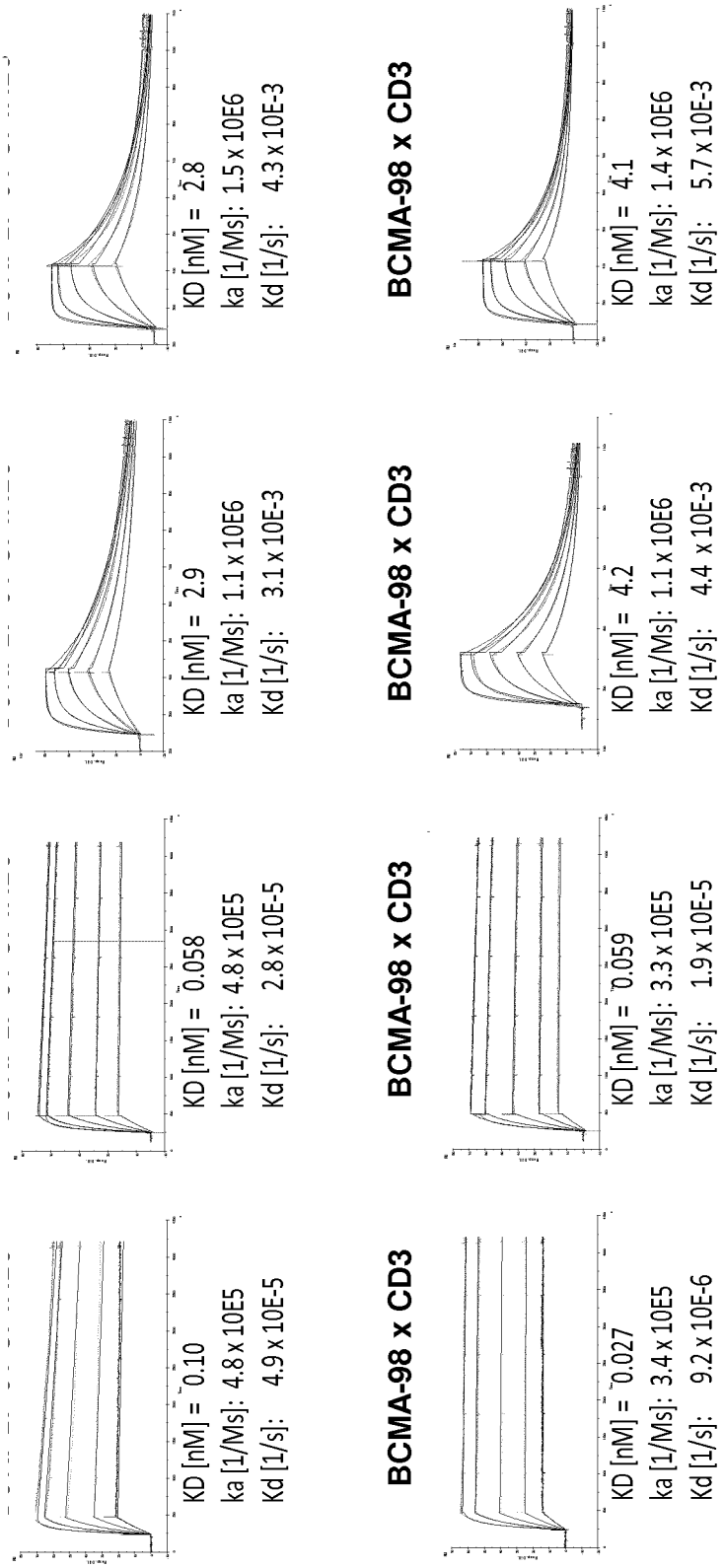

Human BCMA
Macaque BCMA
Human CD3
Macaque CD3
BCMA-34 x CD3
KD [nM] = 0.10
ka [1/Ms]: 4.8 x 10E5
Kd [1/s]: 4.9 x 10E-5
BCMA-34 x CD3
KD [nM] = 0.058
ka [1/Ms]: 4.8 x 10E5
Kd [1/s]: 2.8 x 10E-5
BCMA-34 x CD3
KD [nM] = 2.9
ka [1/Ms]: 1.1 x 10E6
Kd [1/s]: 3.1 x 10E-3
BCMA-34 x CD3
KD [nM] = 2.8
ka [1/Ms]: 1.5 x 10E6
Kd [1/s]: 4.3 x 10E-3
BCMA-98 x CD3
KD [nM] = 0.027
ka [1/Ms]: 3.4 x 10E5
Kd [1/s]: 9.2 x 10E-6
BCMA-98 x CD3
KD [nM] = 0.059
ka [1/Ms]: 3.3 x 10E5
Kd [1/s]: 1.9 x 10E-5
BCMA-98 x CD3
KD [nM] = 4.2
ka [1/Ms]: 1.1 x 10E6
Kd [1/s]: 4.4 x 10E-3
BCMA-98 x CD3
KD [nM] = 4.1
ka [1/Ms]: 1.4 x 10E6
Kd [1/s]: 5.7 x 10E-3

Figure E7

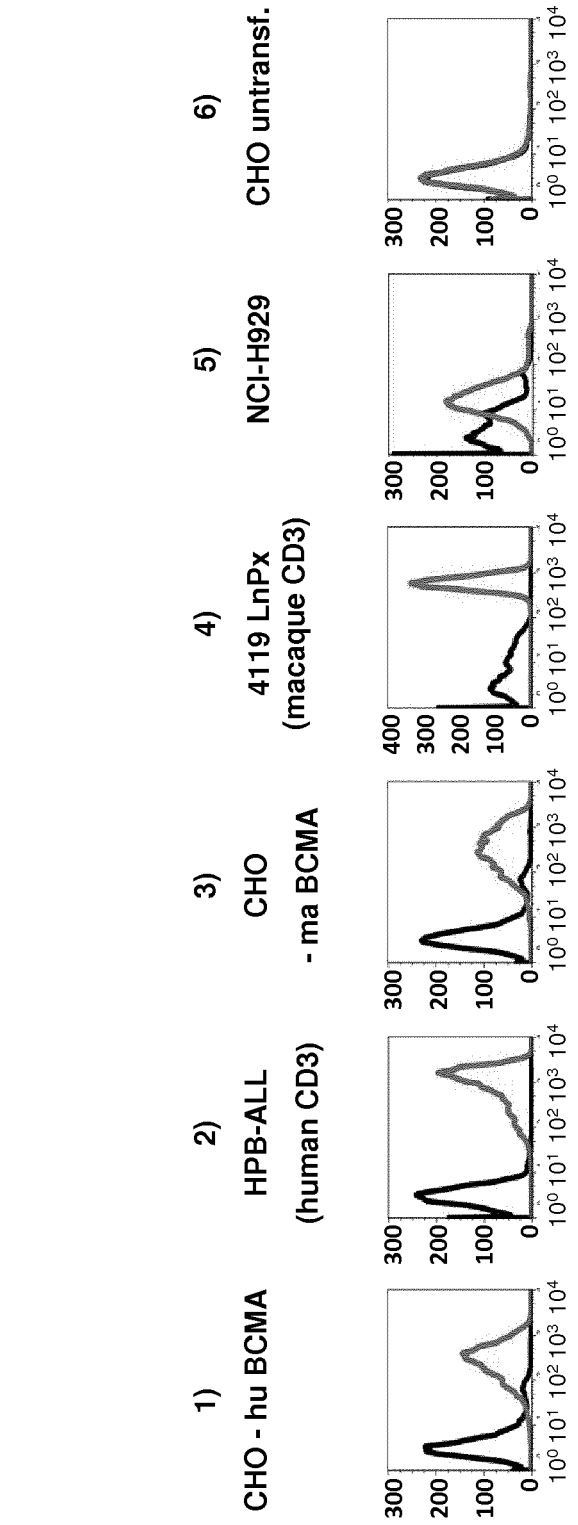

1)
CHO - hu BCMA
2)
HPB-ALL
(human CD3)
3)
CHO
- ma BCMA
4)
4119 LnPx
(macaque CD3)
5)
NCI-H929
6)
CHO untransf.
BCMA-98 x CD3

Figure E8

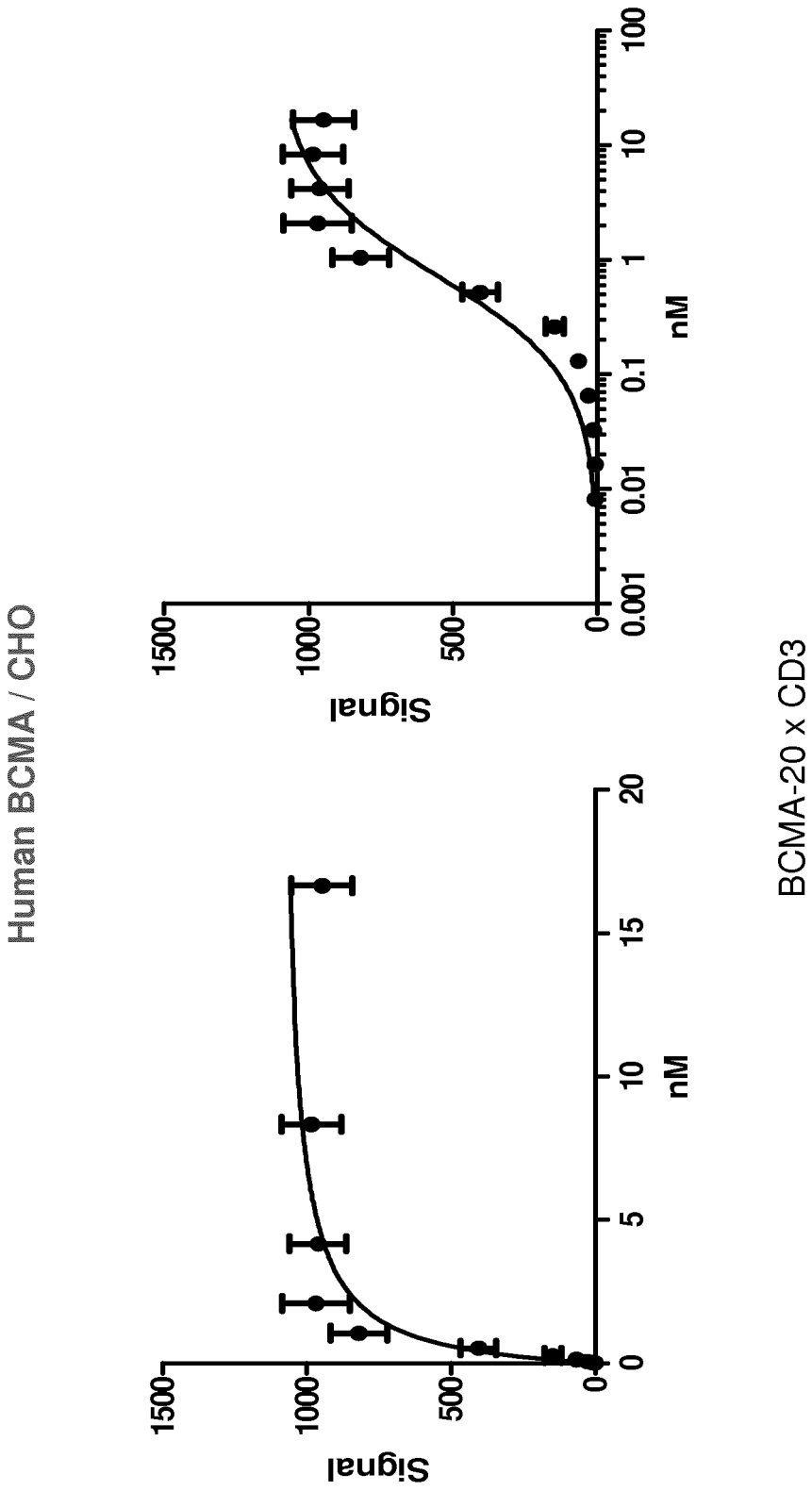

Human BCMA / CHO
Signal
1500
1000
500
0
0.001
0.01
0.1
1
10
100
nM
Signal
1500
1000
500
0
0
5
10
15
20
nM
BCMA-20 x CD3

Figure E8 (continued)

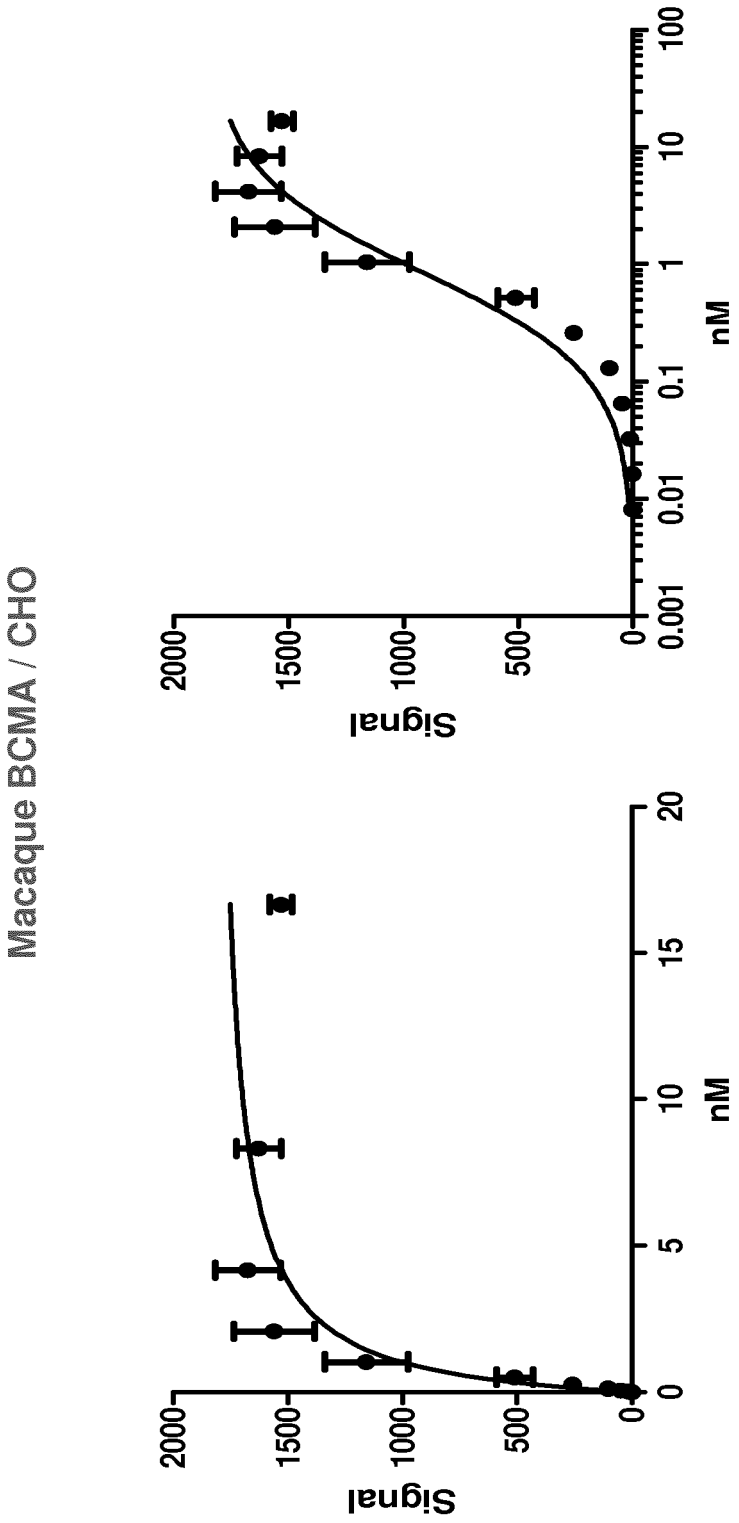


Figure E9

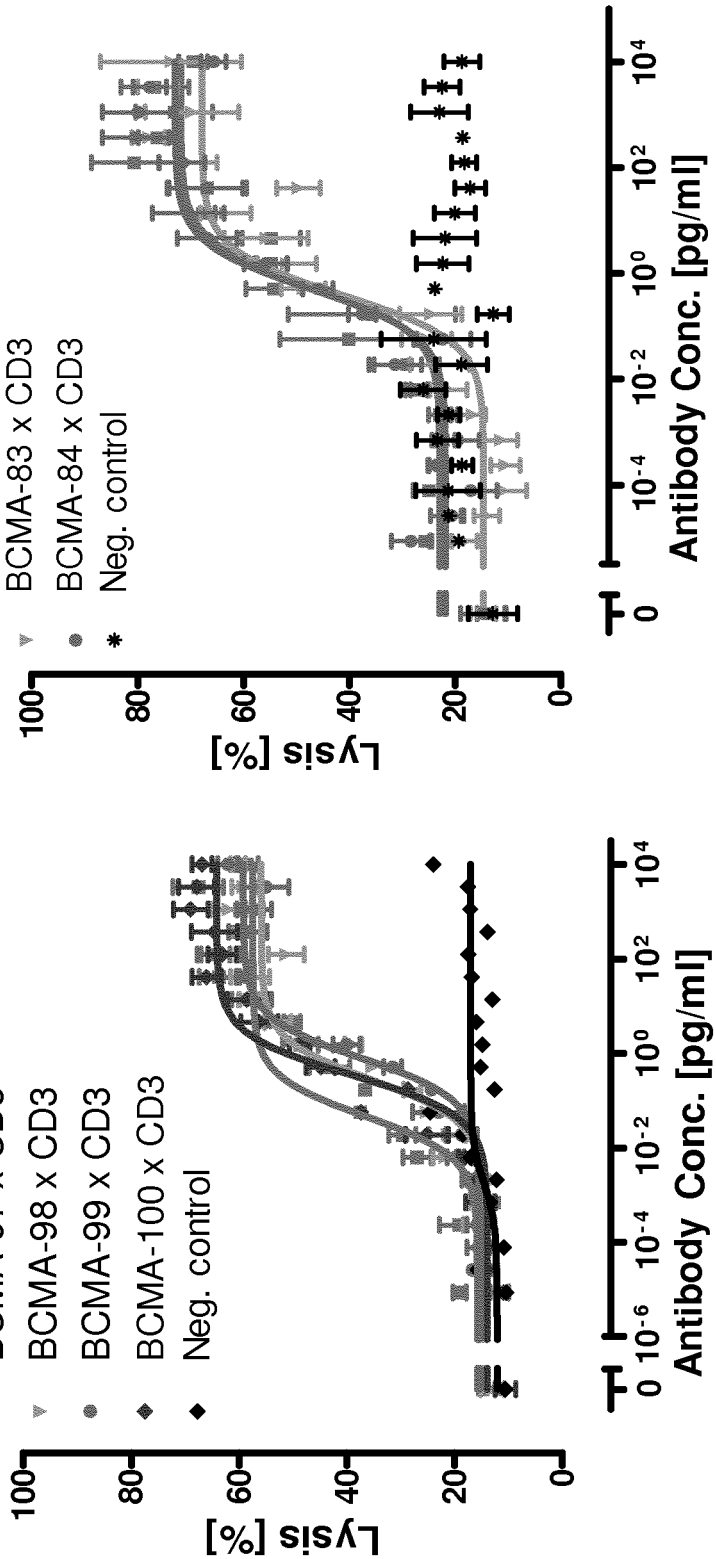

BCMA-82 x CD3
BCMA-83 x CD3
BCMA-84 x CD3
Neg. control
Lysis [%]
Antibody Conc. [pg/ml]
BCMA-97 x CD3
BCMA-98 x CD3
BCMA-99 x CD3
BCMA-100 x CD3
Neg. control
Lysis [%]
Antibody Conc. [pg/ml]

Figure E10

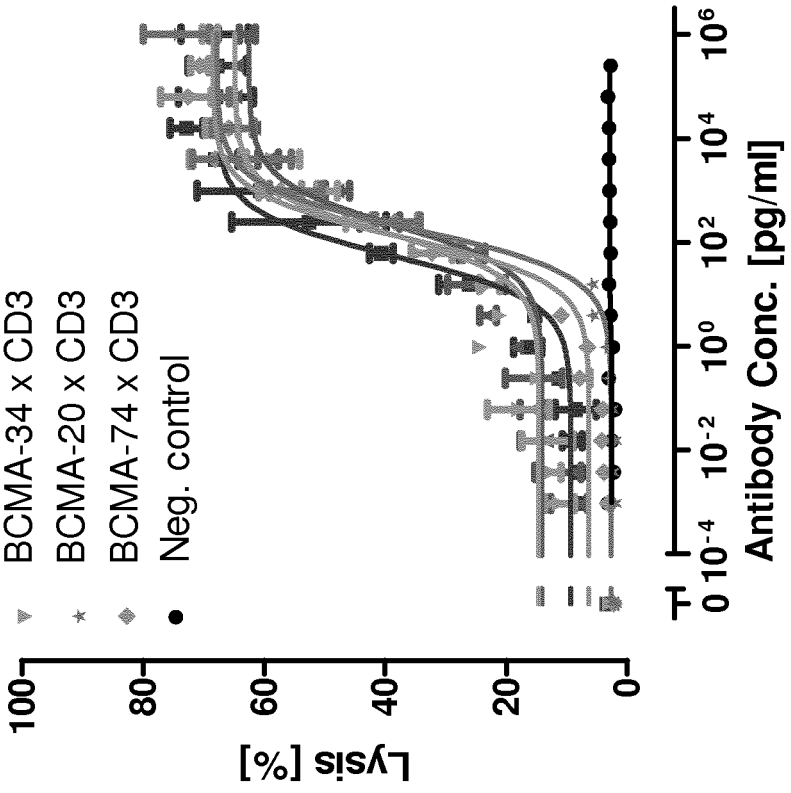

BCMA-98 x CD3
BCMA-71 x CD3
BCMA-34 x CD3
BCMA-20 x CD3
BCMA-74 x CD3
Neg. control
Lysis [%]
100
80
60
40
20
0
0
10-4
10-2
100
102
104
106
Antibody Conc. [pg/ml]

Figure E11

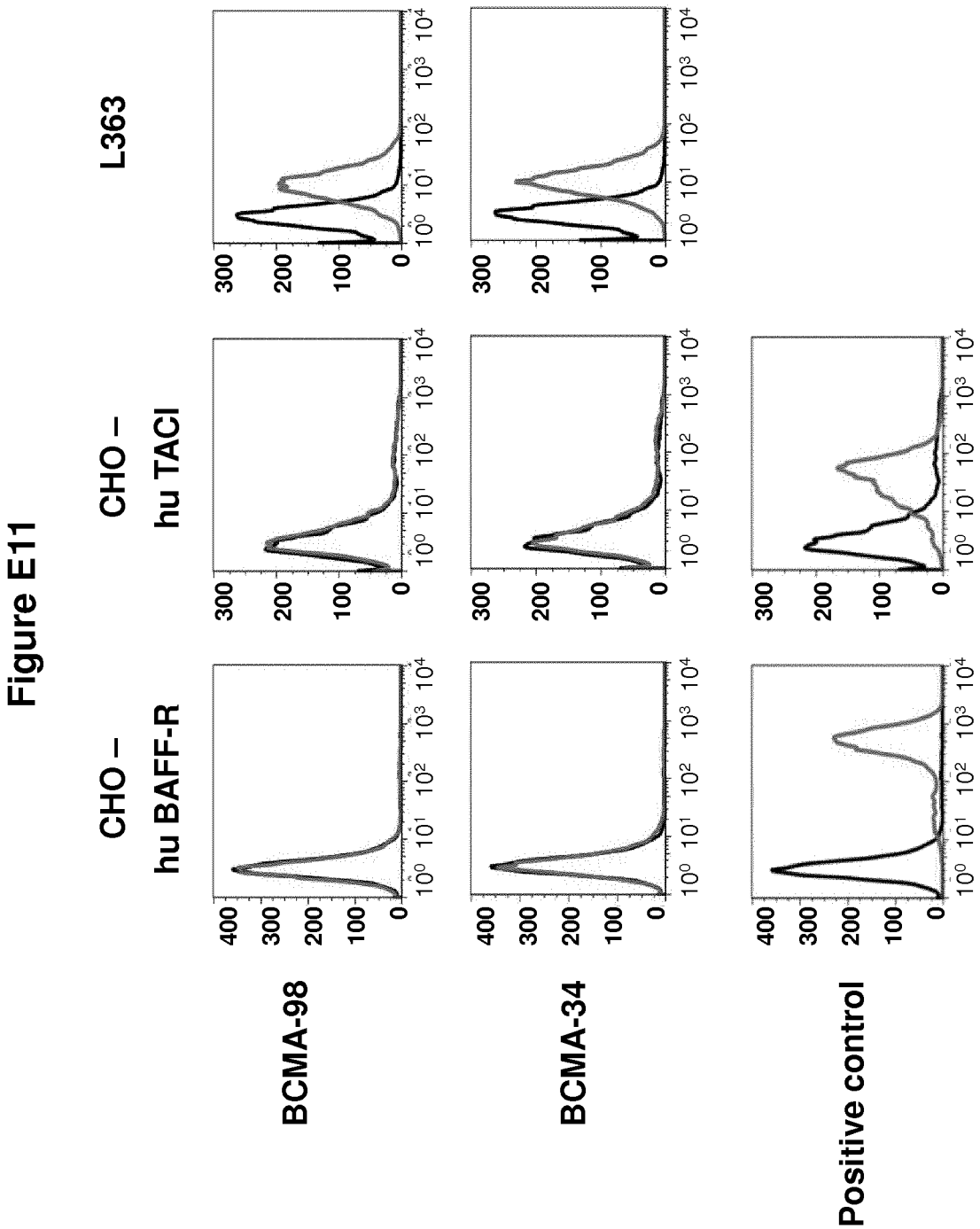

CHO – hu BAFF-R
CHO – hu TACI
L363
BCMA-98
BCMA-34
Positive control

Figure E12

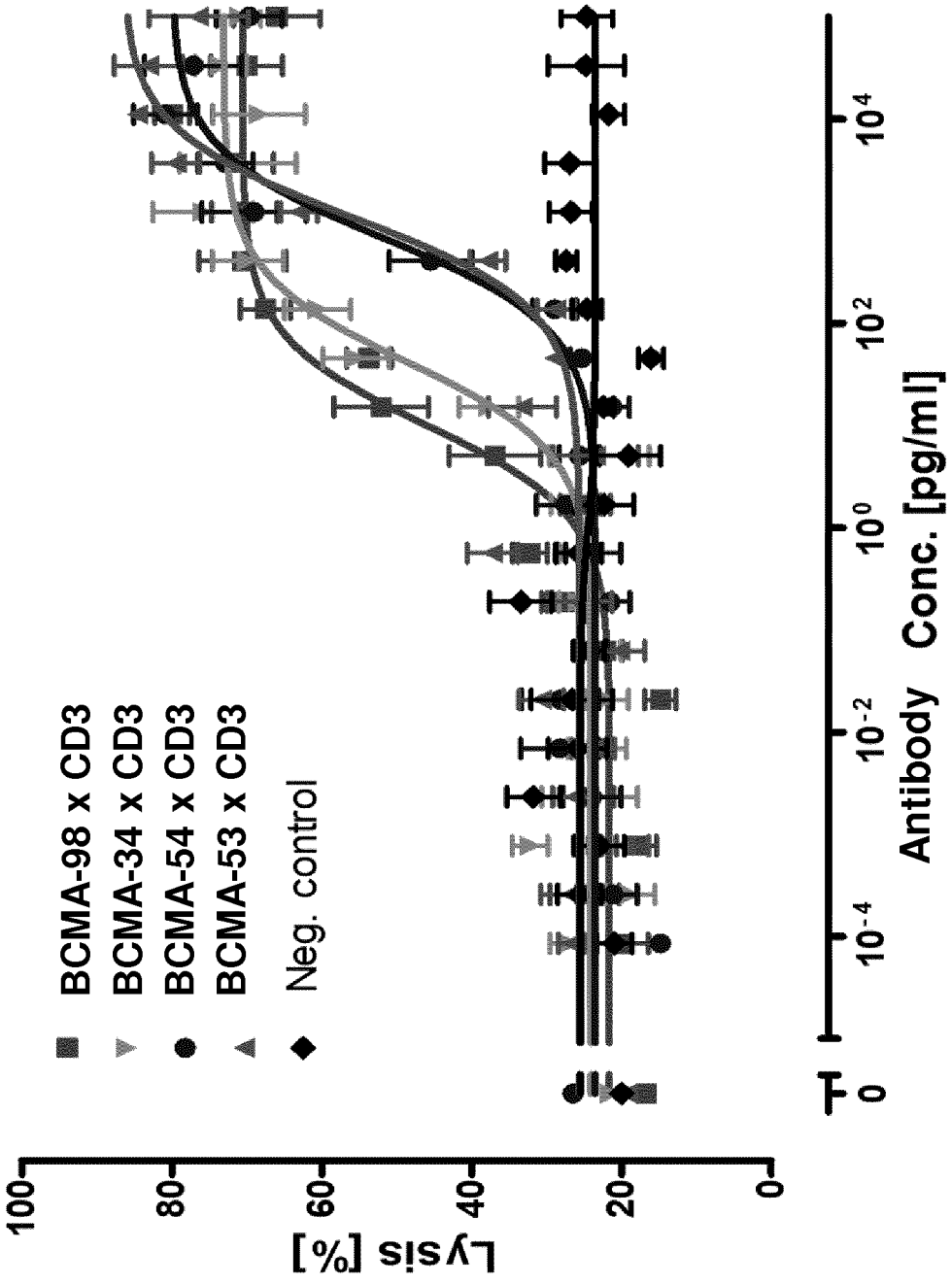

BCMA-98 x CD3
BCMA-34 x CD3
BCMA-54 x CD3
BCMA-53 x CD3
Neg. control
Lysis [%]
100
80
60
40
20
0
0
10-4
10-2
100
102
104
Antibody Conc. [pg/ml]

Figure E13

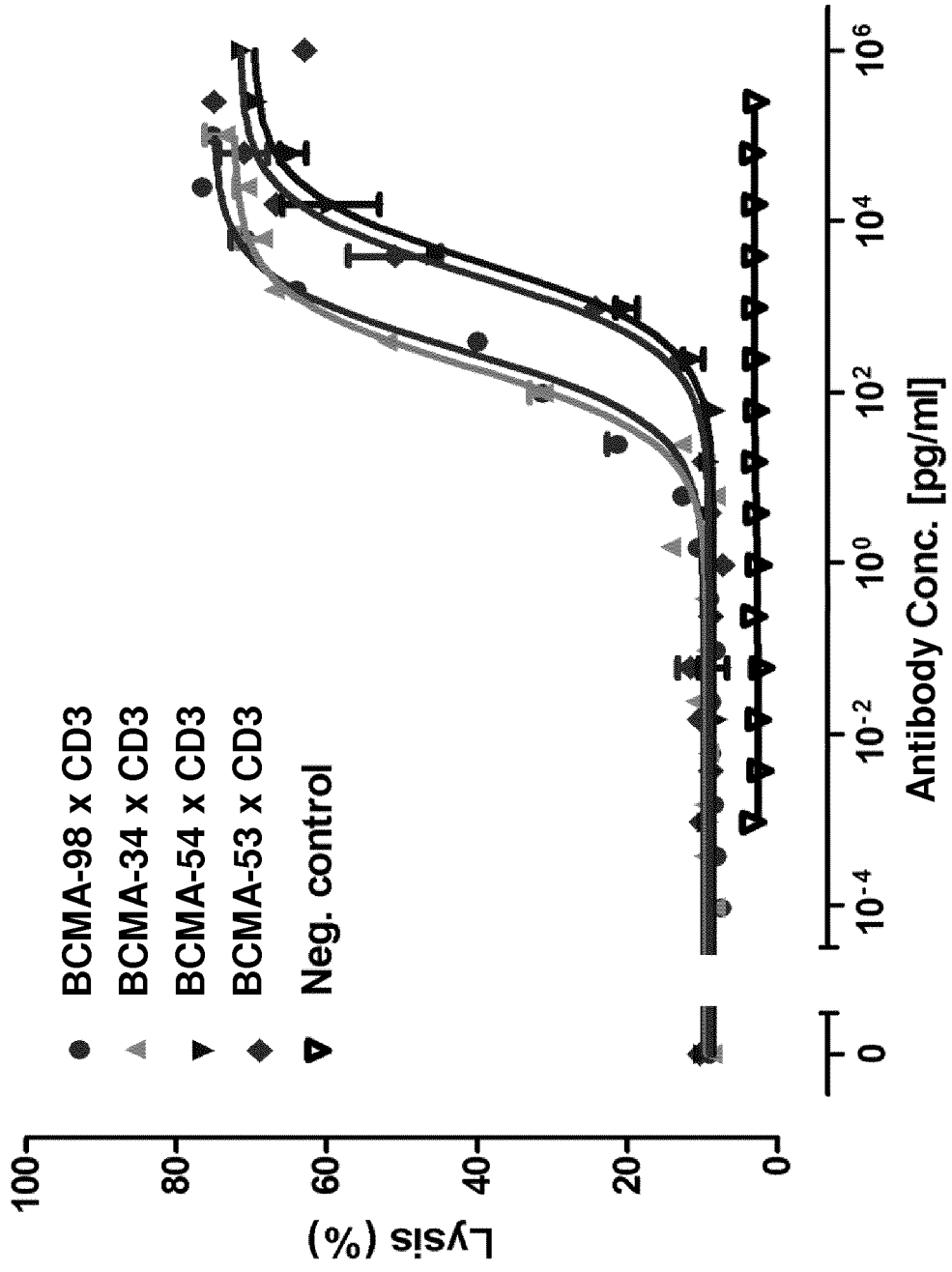

BCMA-98 x CD3
BCMA-34 x CD3
BCMA-54 x CD3
BCMA-53 x CD3
Neg. control
Lysis (%)
100
80
60
40
20
0
0
10^{-4}
10^{-2}
10^{0}
10^{2}
10^{4}
10^{6}
Antibody Conc. [pg/ml]

Figure E14

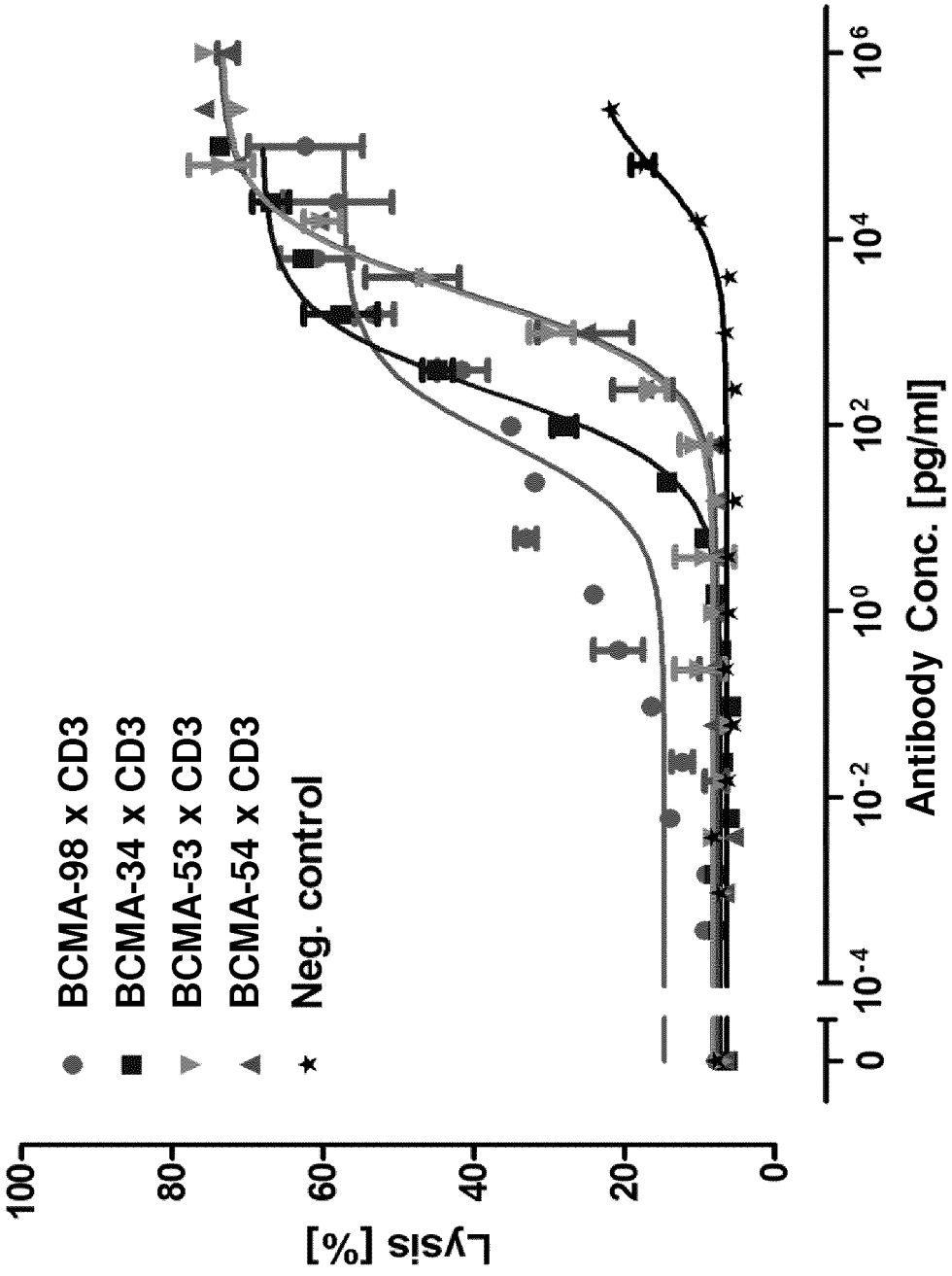

BCMA-98 x CD3
BCMA-34 x CD3
BCMA-53 x CD3
BCMA-54 x CD3
Neg. control
Lysis [%]
0
20
40
60
80
100
0
10-4
10-2
100
102
104
106
Antibody Conc. [pg/ml]

Figure E15

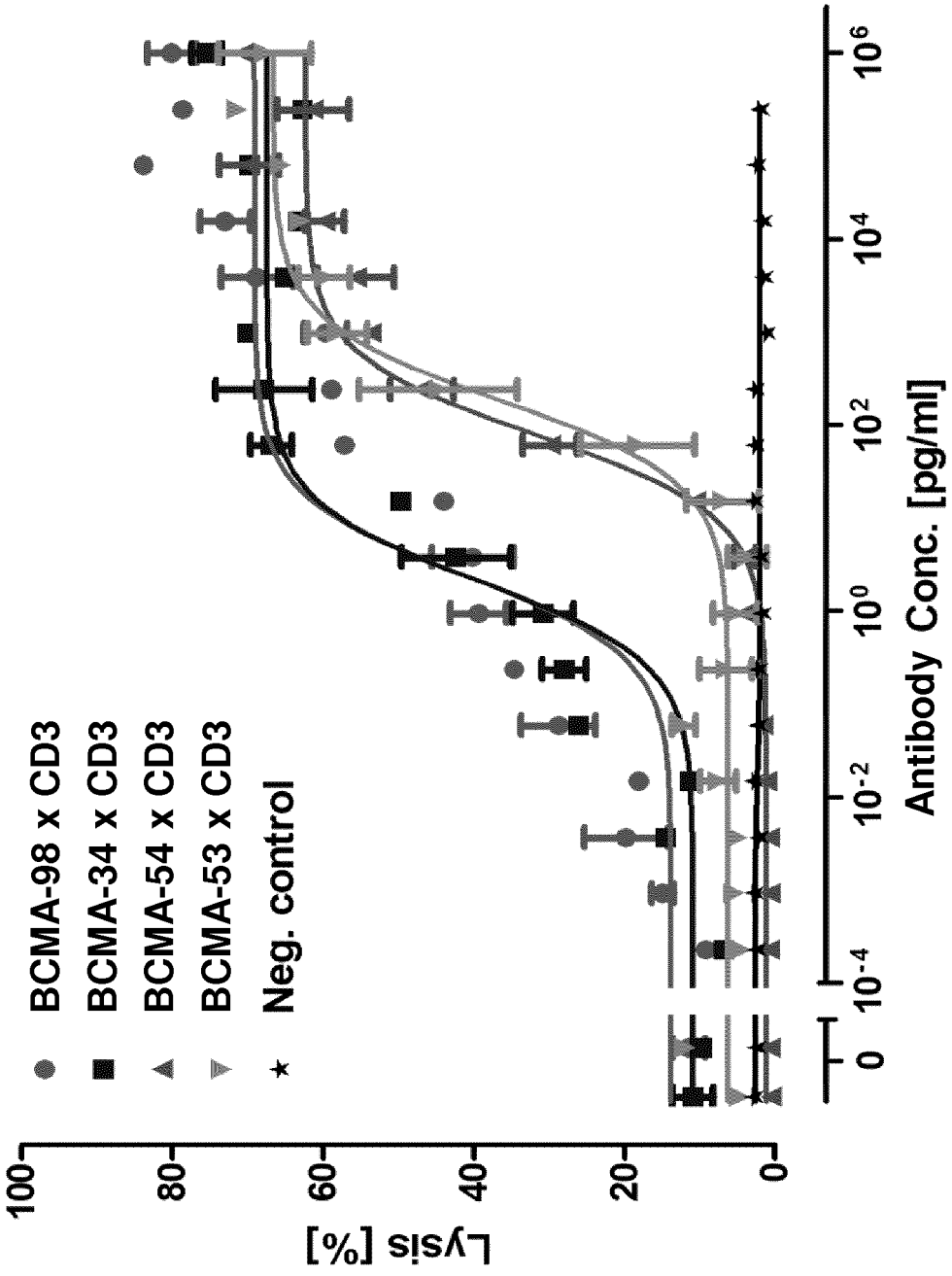

BCMA-98 x CD3
BCMA-34 x CD3
BCMA-54 x CD3
BCMA-53 x CD3
Neg. control
Lysis [%]
100
80
60
40
20
0
0
10-4
10-2
100
102
104
106
Antibody Conc. [pg/ml]

Figure E16

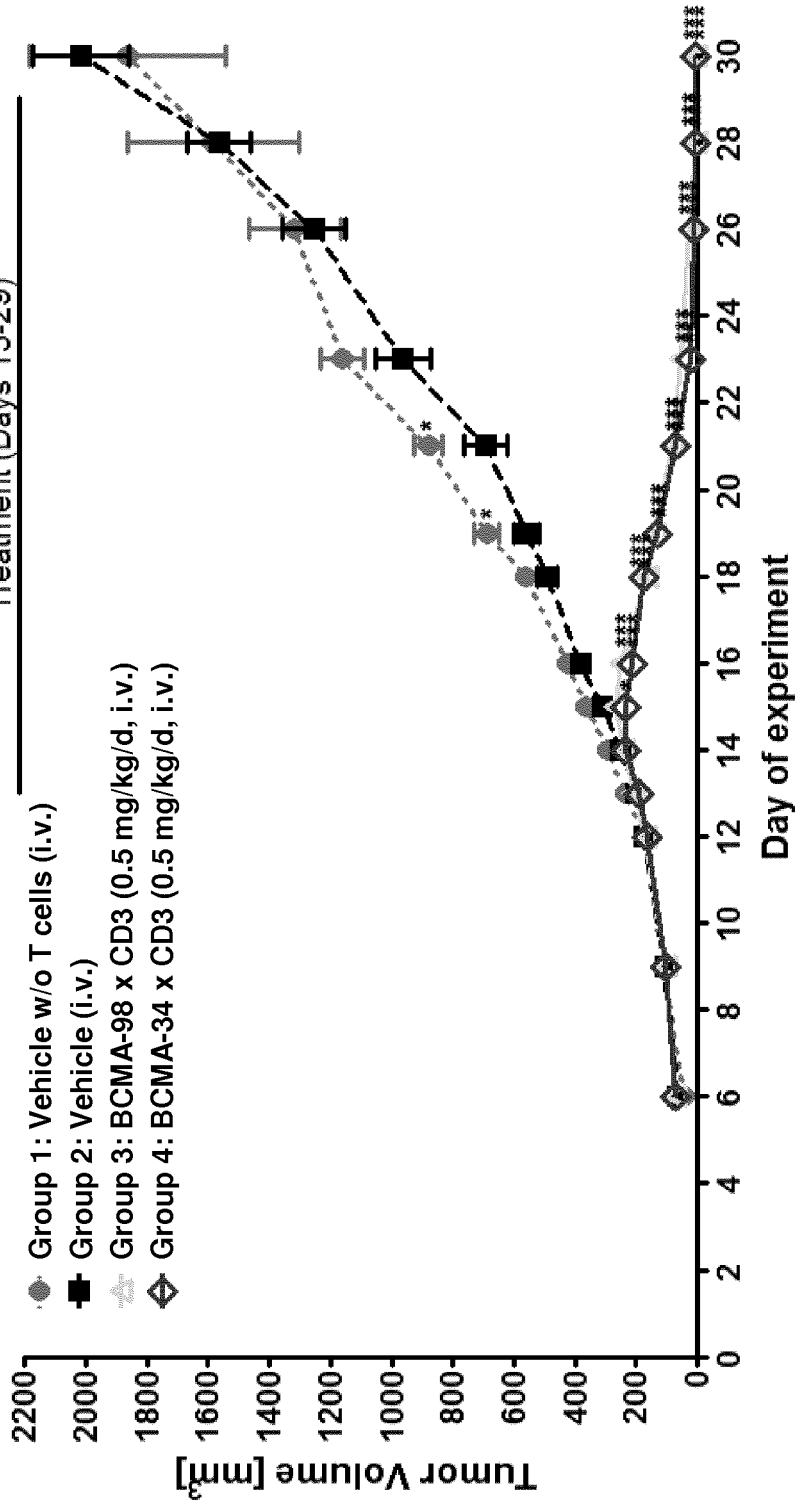
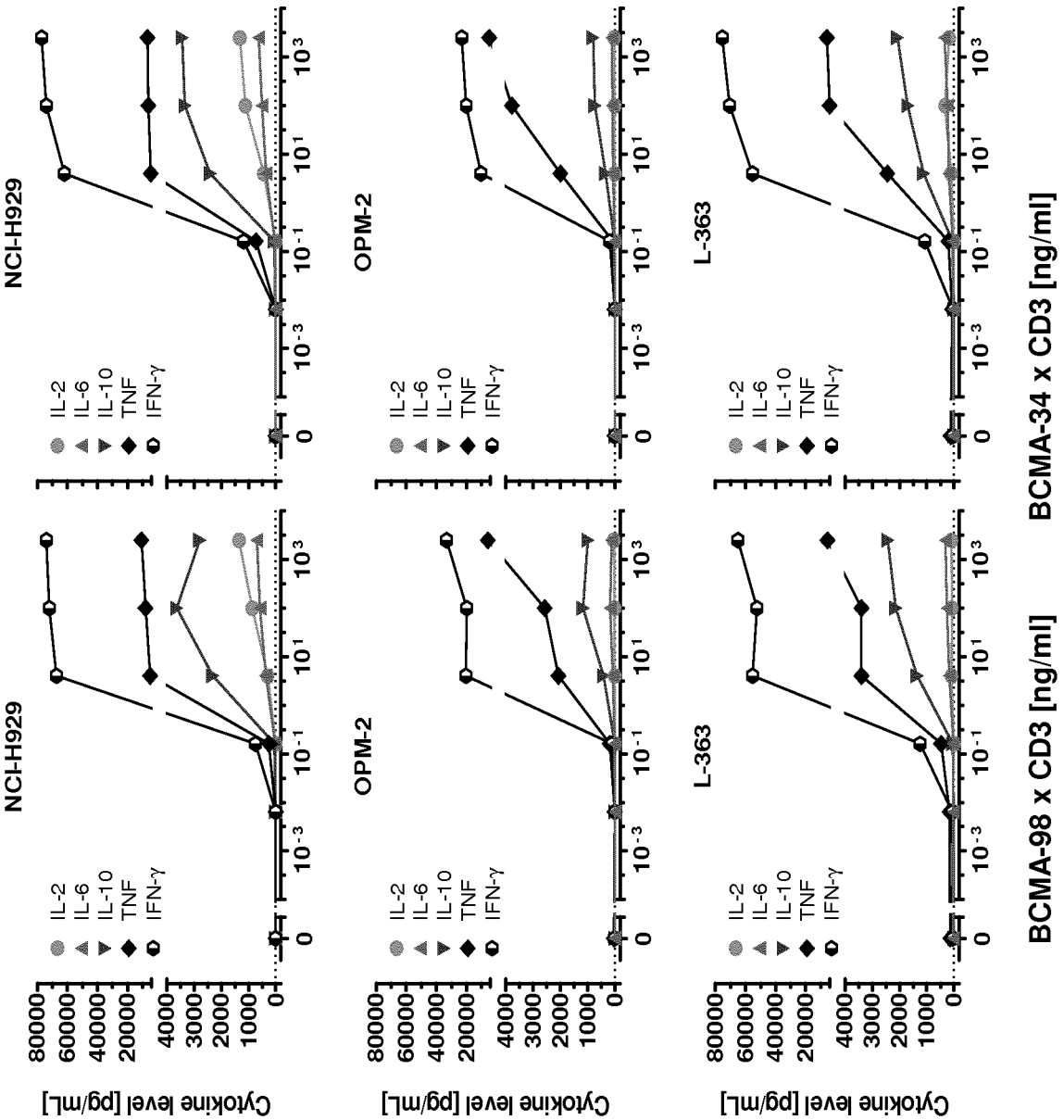

Treatment (Days 13-29)
Group 1: Vehicle w/o T cells (i.v.)
Group 2: Vehicle (i.v.)
Group 3: BCMA-98 x CD3 (0.5 mg/kg/d, i.v.)
Group 4: BCMA-34 x CD3 (0.5 mg/kg/d, i.v.)
Tumor Volume [mm³]
Day of experiment
0
200
400
600
800
1000
1200
1400
1600
1800
2000
2200
0
2
4
6
8
10
12
14
16
18
20
22
24
26
28
30
*
###

Figure E17


NCI-H929
NCI-H929
OPM-2
OPM-2
L-363
L-363
IL-2
IL-6
IL-10
TNF
IFN-γ
Cytokine level [pg/mL]
BCMA-98 x CD3 [ng/ml]
BCMA-34 x CD3 [ng/ml]