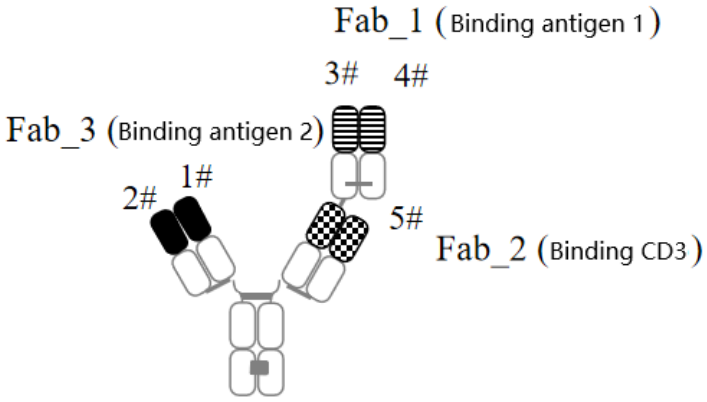
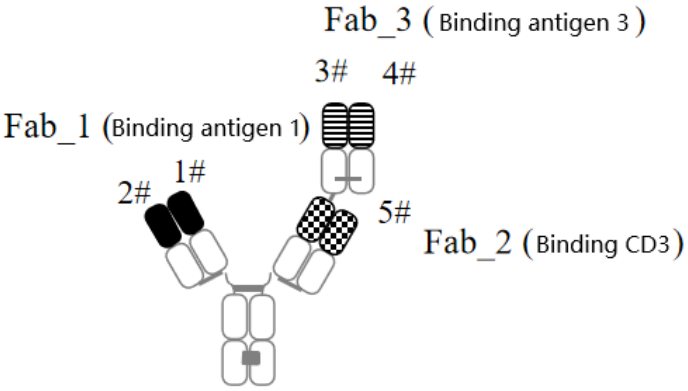
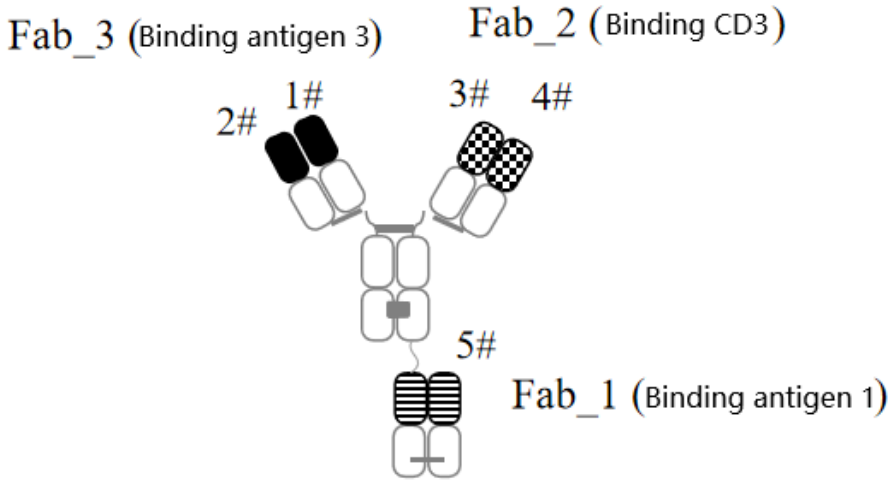


Chain 1#	Heavy chain 1(H1), VH-CH1-Fc
Chain 2#	Light chain 1(L1), VL-CL
Chain 3#	Heavy chain 2(H2), VH-CH1-VH-CH1-Fc
Chain 4#	Light chain 2(L2), VL-CL
Chain 5#	Light chain 3(L3), VL-CL
Fc	CH2-CH3, asymmetric IgG1, LALA, knob-in-hole
Format	B3



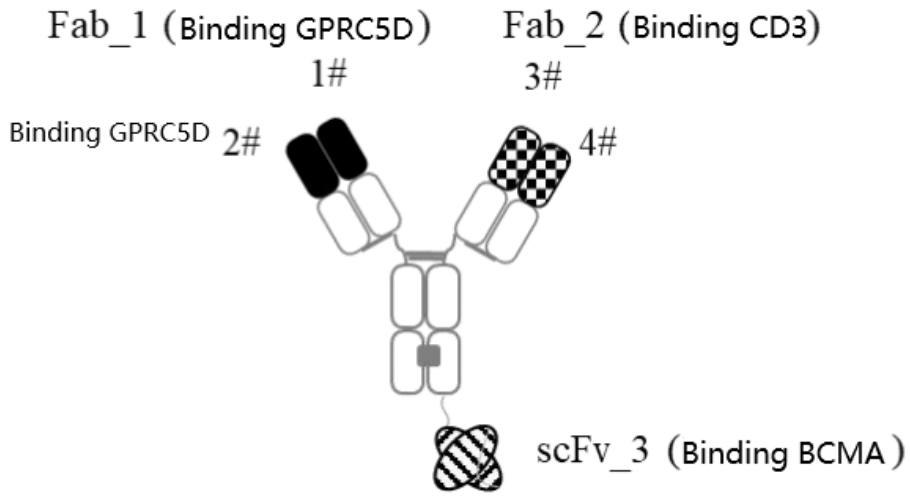
Chain 1#	Heavy chain 1(H1), VH-CH1-Fc
Chain 2#	Light chain 1(L1), VL-CL
Chain 3#	Heavy chain 2(H2), VH-CH1-VH-CH1-Fc
Chain 4#	Light chain 2(L2), VL-CL
Chain 5#	Light chain 3(L3), VL-CL
Fc	CH2-CH3, asymmetric IgG1, LALA, knob-in-hole
Format	B3b

FIG. 1A



Chain 1#	Heavy chain 1(H1), VH-CH1-Fc
Chain 2#	Light chain 1(L1), VL-CL
Chain 3#	Heavy chain 2(H2), VH-CH1-Fc-VH-CH1
Chain 4#	Light chain 2(L2), VL-CL
Chain 5#	Light chain 3(L3), VL-CL
Fc	CH2-CH3, asymmetric IgG1, LALA, knob-in-hole
Format	B5

FIG. 1B



Chain 1#	Heavy chain 1(H1), VH-CH1-Fc
Chain 2#	Light chain 2(L1), VL-CL
Chain 3#	Heavy chain 2(H2), VH-CH1-Fc-scFv
Chain 4#	Light chain 2 (L2), VL-CL
Fc	CH2-CH3, asymmetric IgG1 , LALA, knob-in-hole
Format	F2

FIG. 1C

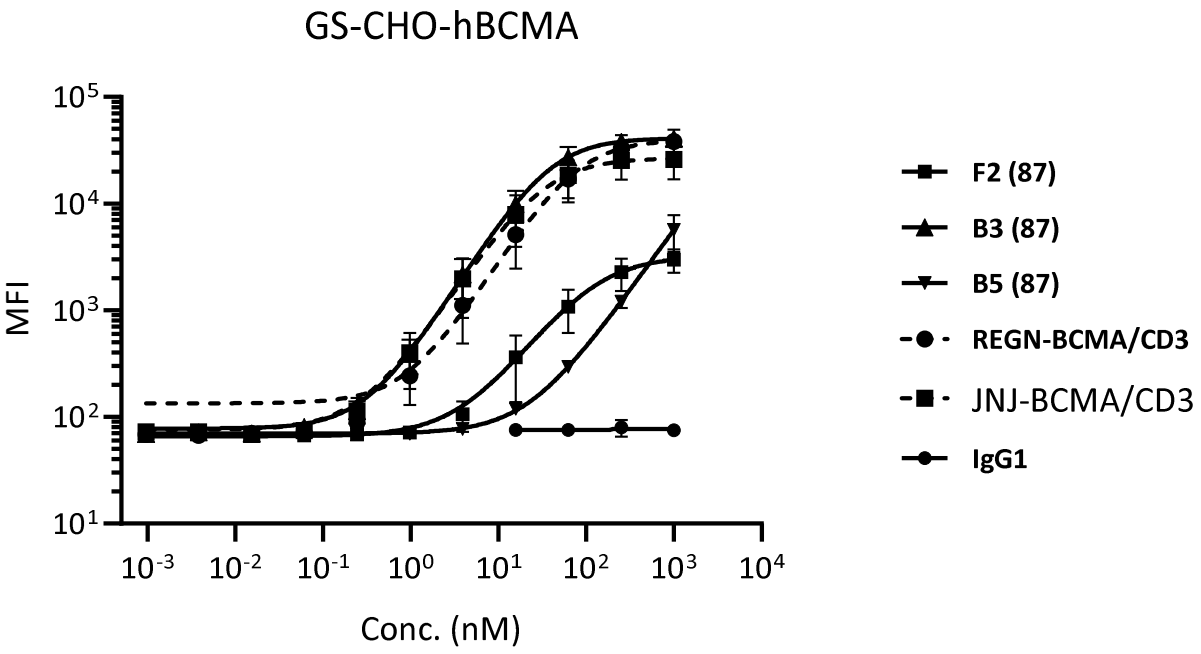

GS-CHO-hBCMA
MFI
Conc. (nM)
F2 (87)
B3 (87)
B5 (87)
REGN-BCMA/CD3
JNJ-BCMA/CD3
IgG1

FIG. 2A

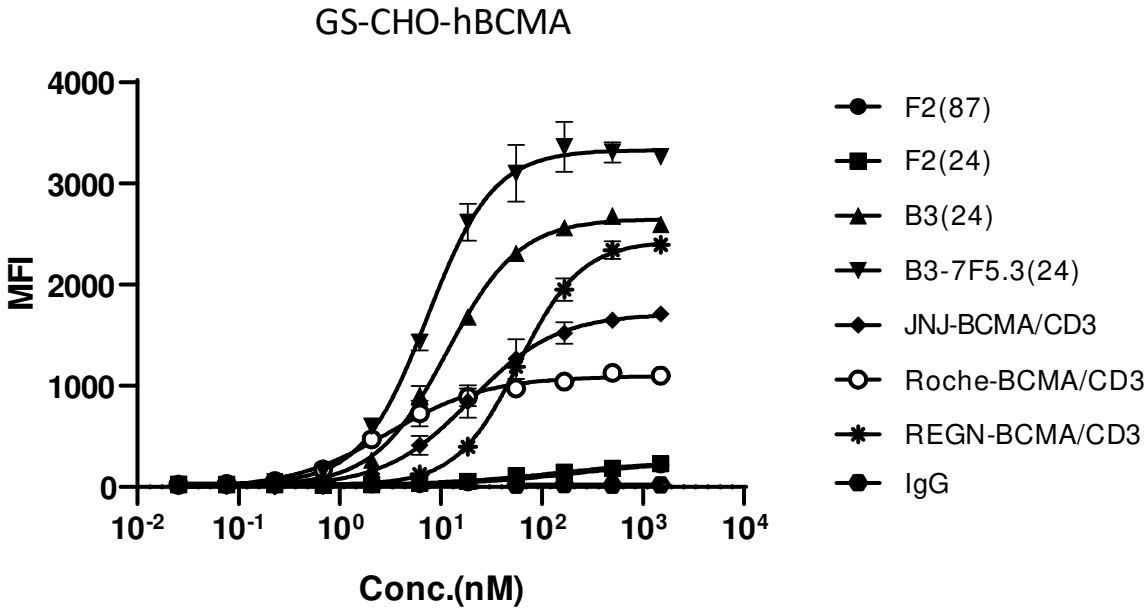

GS-CHO-hBCMA
MFI
Conc.(nM)
F2(87)
F2(24)
B3(24)
B3-7F5.3(24)
JNJ-BCMA/CD3
Roche-BCMA/CD3
REGN-BCMA/CD3
IgG

FIG. 2B

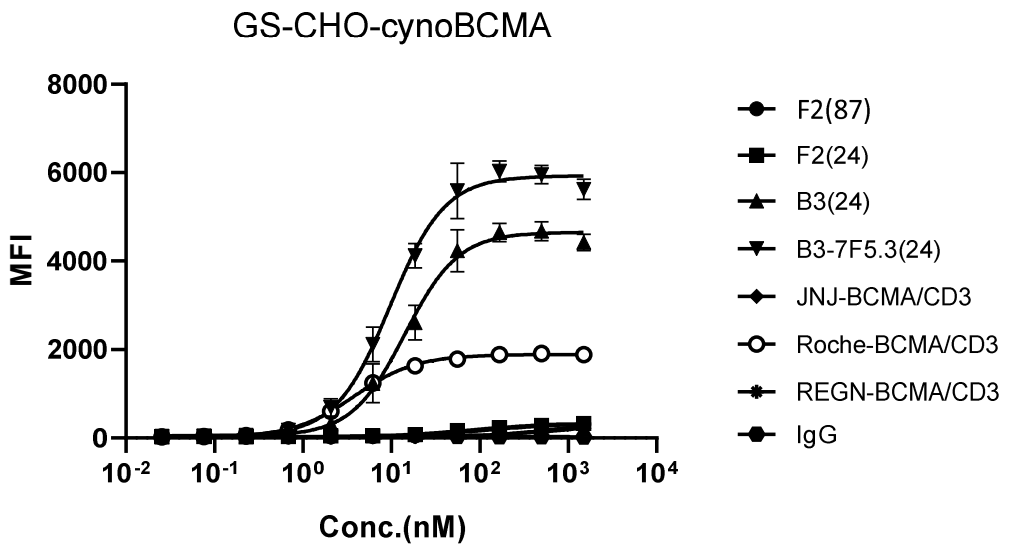

GS-CHO-cynoBCMA
8000
6000
4000
2000
0
MFI
10-2
10-1
100
101
102
103
104
Conc.(nM)
F2(87)
F2(24)
B3(24)
B3-7F5.3(24)
JNJ-BCMA/CD3
Roche-BCMA/CD3
REGN-BCMA/CD3
IgG

FIG. 2C

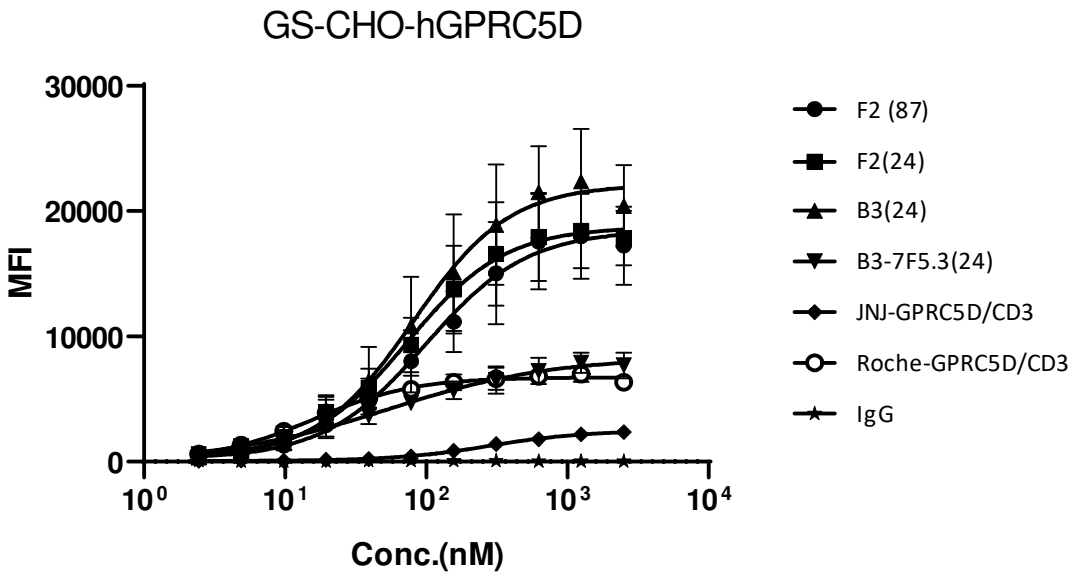

GS-CHO-hGPRC5D
30000
20000
10000
0
MFI
100
101
102
103
104
Conc.(nM)
F2 (87)
F2(24)
B3(24)
B3-7F5.3(24)
JNJ-GPRC5D/CD3
Roche-GPRC5D/CD3
IgG

FIG. 2D

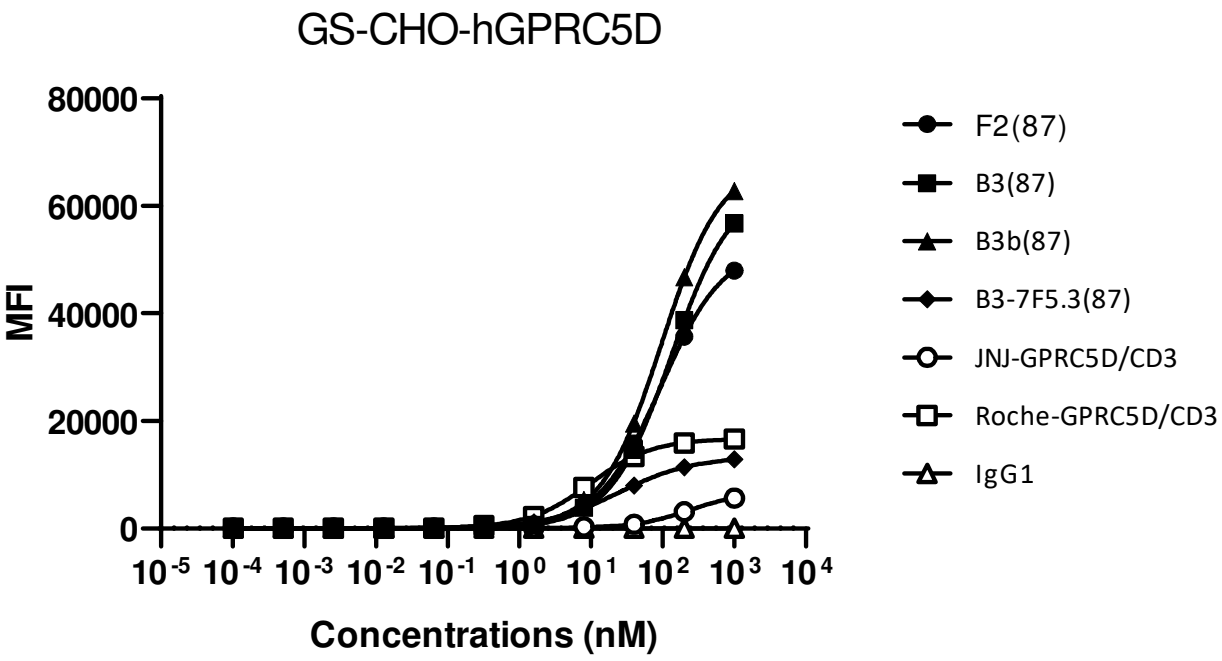

GS-CHO-hGPRC5D
80000
60000
40000
20000
0
MFI
10-5 10-4 10-3 10-2 10-1 100 101 102 103 104
Concentrations (nM)
F2(87)
B3(87)
B3b(87)
B3-7F5.3(87)
JNJ-GPRC5D/CD3
Roche-GPRC5D/CD3
IgG1

FIG. 2E

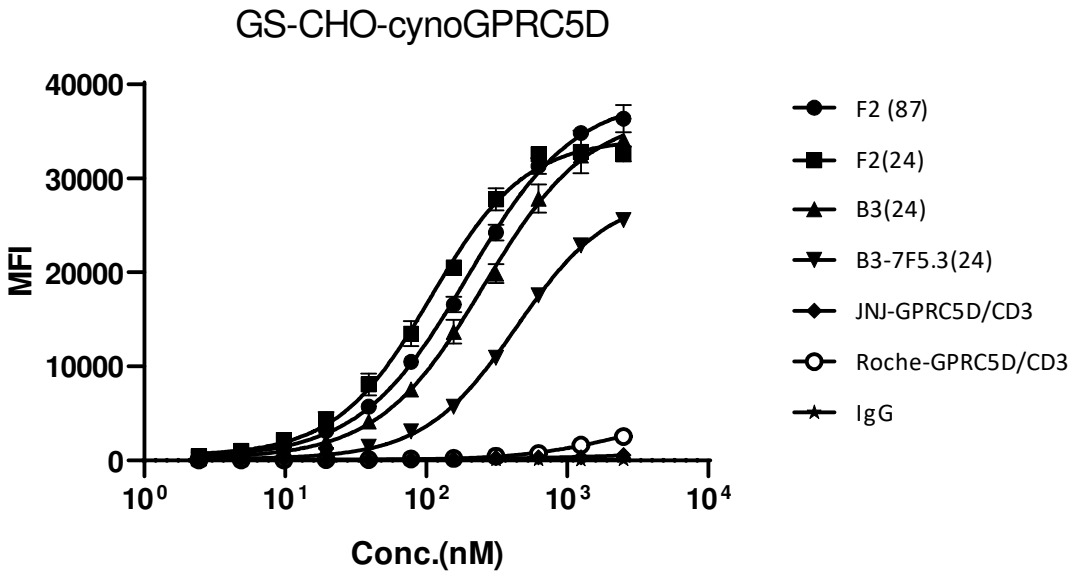

GS-CHO-cynoGPRC5D
40000
30000
20000
10000
0
MFI
100 101 102 103 104
Conc.(nM)
F2 (87)
F2(24)
B3(24)
B3-7F5.3(24)
JNJ-GPRC5D/CD3
Roche-GPRC5D/CD3
IgG

FIG. 2F

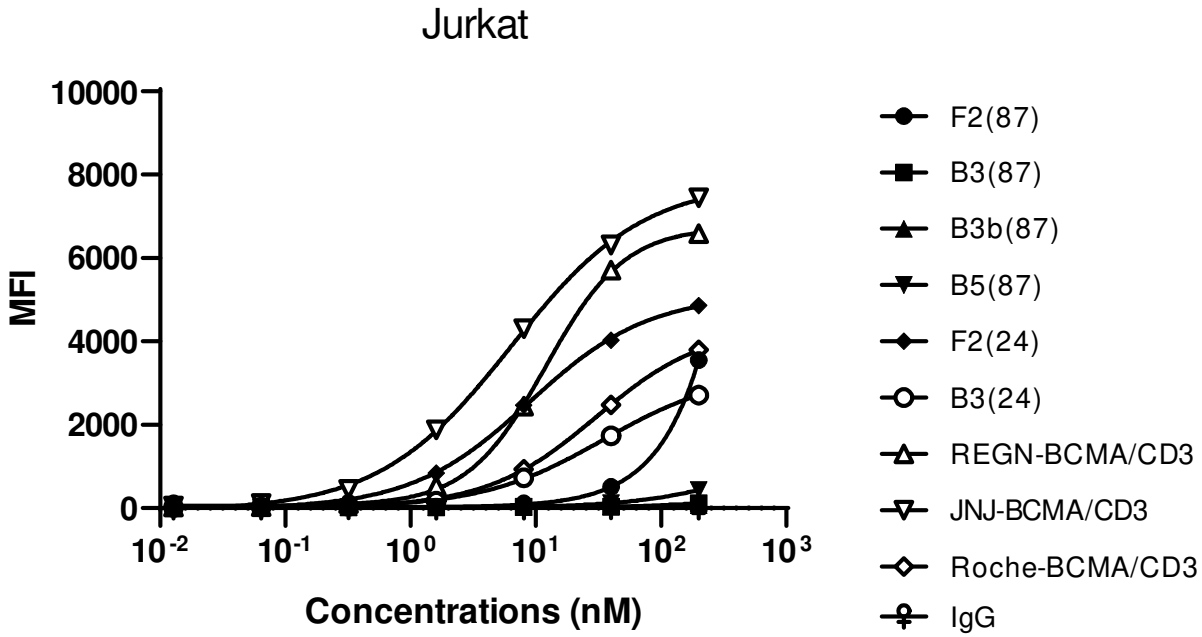

Jurkat
10000
8000
6000
4000
2000
0
MFI
10-2
10-1
100
101
102
103
Concentrations (nM)
F2(87)
B3(87)
B3b(87)
B5(87)
F2(24)
B3(24)
REGN-BCMA/CD3
JNJ-BCMA/CD3
Roche-BCMA/CD3
IgG

FIG. 2G

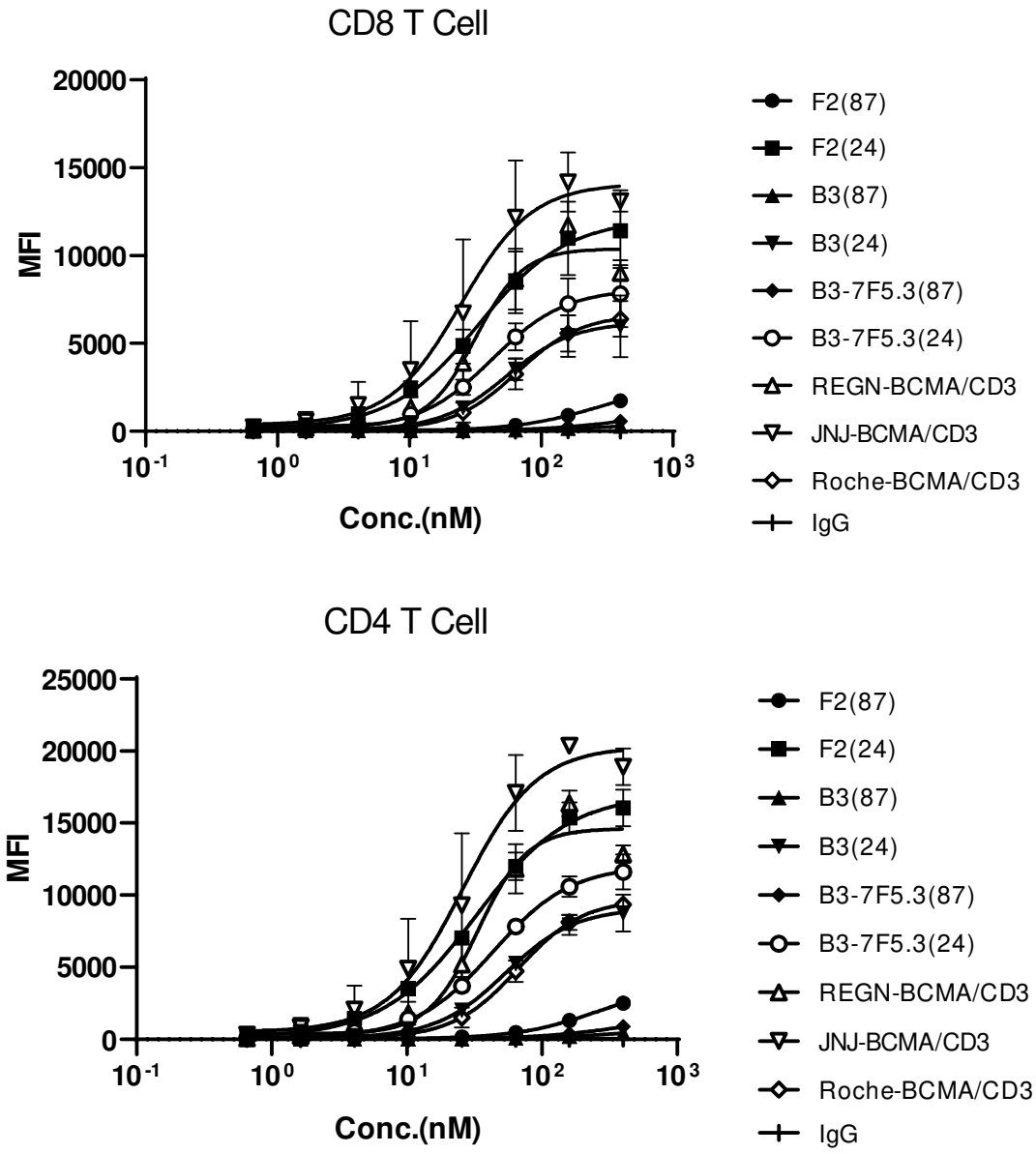
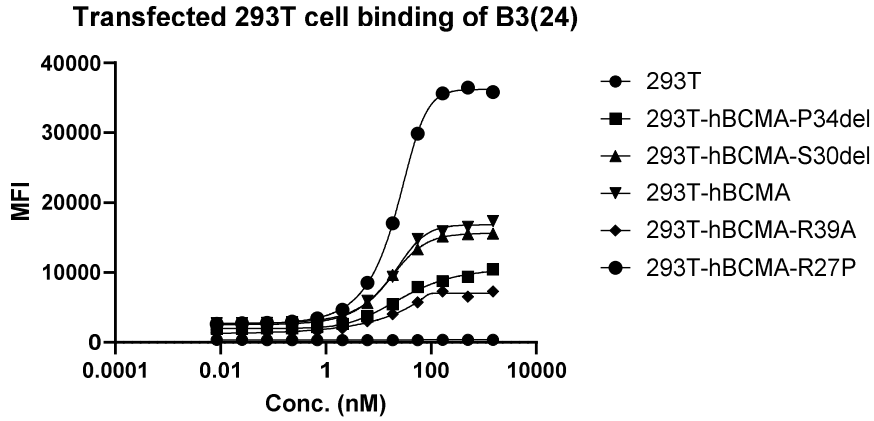
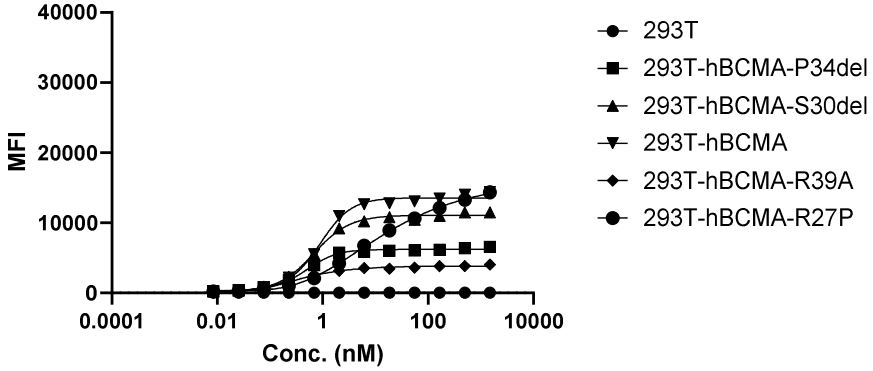

CD8 T Cell
MFI
20000
15000
10000
5000
0
10-1
100
101
102
103
Conc.(nM)
F2(87)
F2(24)
B3(87)
B3(24)
B3-7F5.3(87)
B3-7F5.3(24)
REGN-BCMA/CD3
JNJ-BCMA/CD3
Roche-BCMA/CD3
IgG
CD4 T Cell
MFI
25000
20000
15000
10000
5000
0
10-1
100
101
102
103
Conc.(nM)
F2(87)
F2(24)
B3(87)
B3(24)
B3-7F5.3(87)
B3-7F5.3(24)
REGN-BCMA/CD3
JNJ-BCMA/CD3
Roche-BCMA/CD3
IgG

FIG. 2H

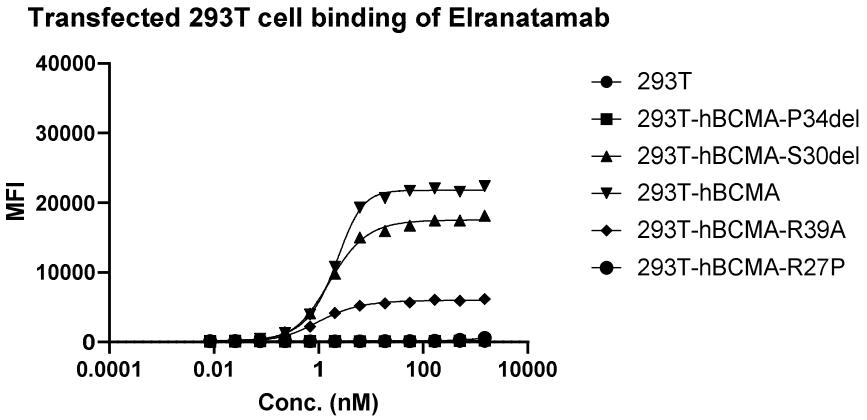


	293T	293T-hBCMA-P34del	293T-hBCMA-S30del	293T-hBCMA	293T-hBCMA-R39A	293T-hBCMA-R27P
EC50	316.9	26.90	16.26	18.95	21.36	22.86

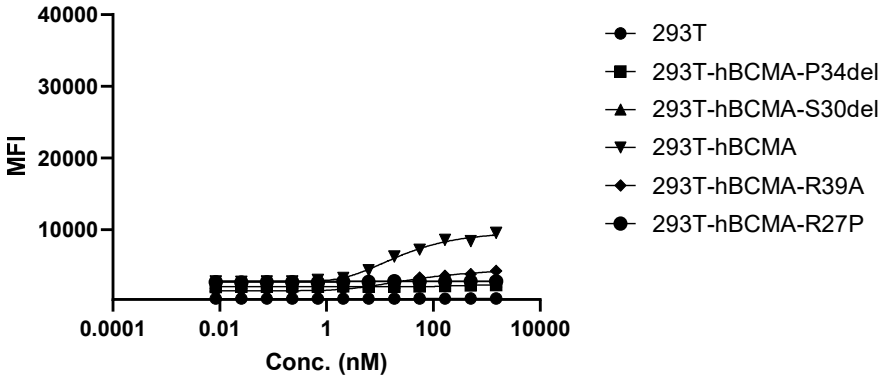


	293T	293T-hBCMA-P34del	293T-hBCMA-S30del	293T-hBCMA	293T-hBCMA-R39A	293T-hBCMA-R27P
EC50	0.000	0.4737	0.6858	0.8747	0.3973	12.88

FIG. 2I

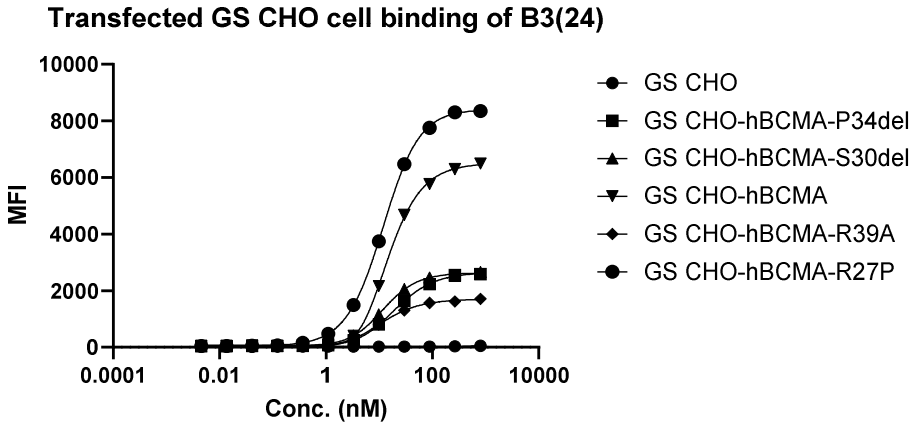


	293T	293T-hBCMA-P34del	293T-hBCMA-S30del	293T-hBCMA	293T-hBCMA-R39A	293T-hBCMA-R27P
EC50	164.1	363.7	1.690	2.059	1.095	145051090

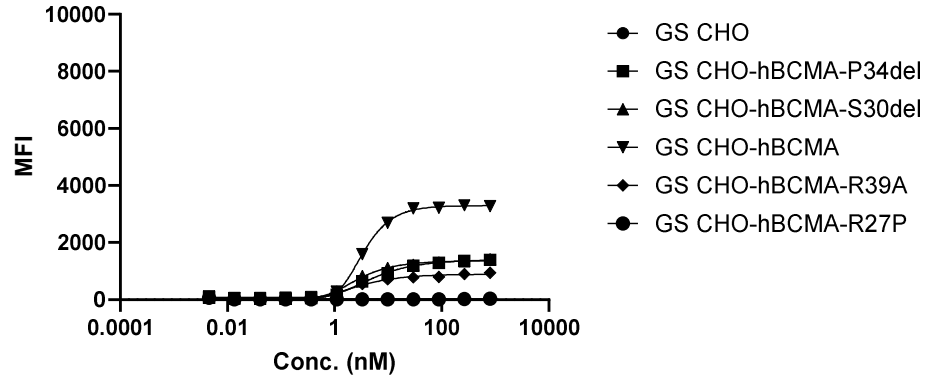


	293T	293T-hBCMA-P34del	293T-hBCMA-S30del	293T-hBCMA	293T-hBCMA-R39A	293T-hBCMA-R27P
EC50	3606	228.6	0.000	21.87	37.24	1.815

FIG. 2I(Continued)

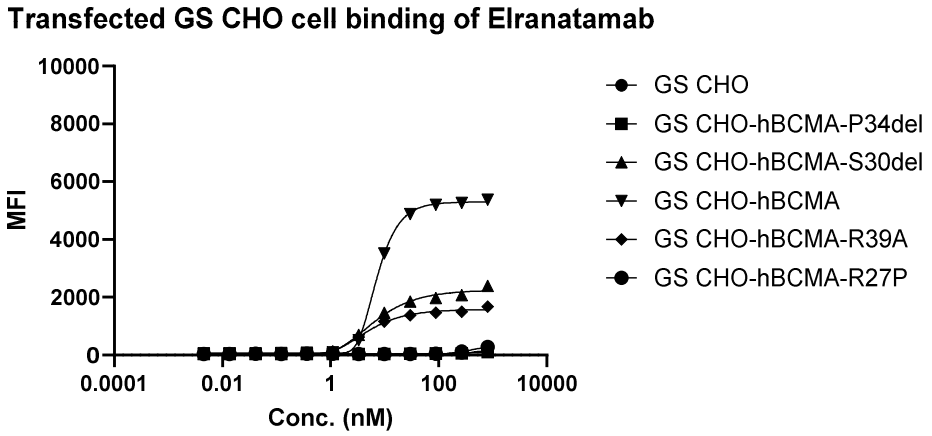


	GS CHO	GS CHO-hBCMA-P34del	GS CHO-hBCMA-S30del	GS CHO-hBCMA	GS CHO-hBCMA-R39A	GS CHO-hBCMA-R27P
EC50	350.1	20.18	11.91	15.66	11.28	11.74

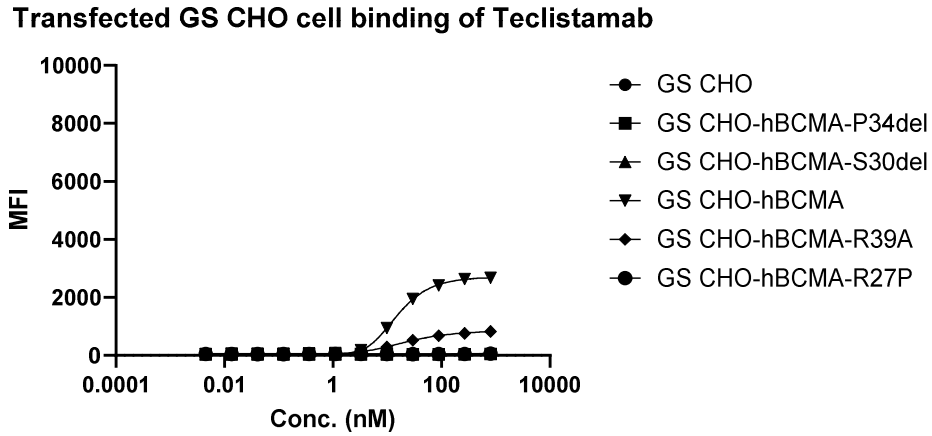


	GS CHO	GS CHO-hBCMA-P34del	GS CHO-hBCMA-S30del	GS CHO-hBCMA	GS CHO-hBCMA-R39A	GS CHO-hBCMA-R27P
EC50	0.004658	4.810	2.691	3.542	2.728	+infinity

FIG. 2J



	GS CHO	GS CHO-hBCMA-P34del	GS CHO-hBCMA-S30del	GS CHO-hBCMA	GS CHO-hBCMA-R39A	GS CHO-hBCMA-R27P
EC50	24902	883.3	6.405	7.235	4.729	562.3



	GS CHO	GS CHO-hBCMA-P34del	GS CHO-hBCMA-S30del	GS CHO-hBCMA	GS CHO-hBCMA-R39A	GS CHO-hBCMA-R27P
EC50	759.3	409.8	852.0	15.33	21.00	211446

FIG. 2J(Continued)

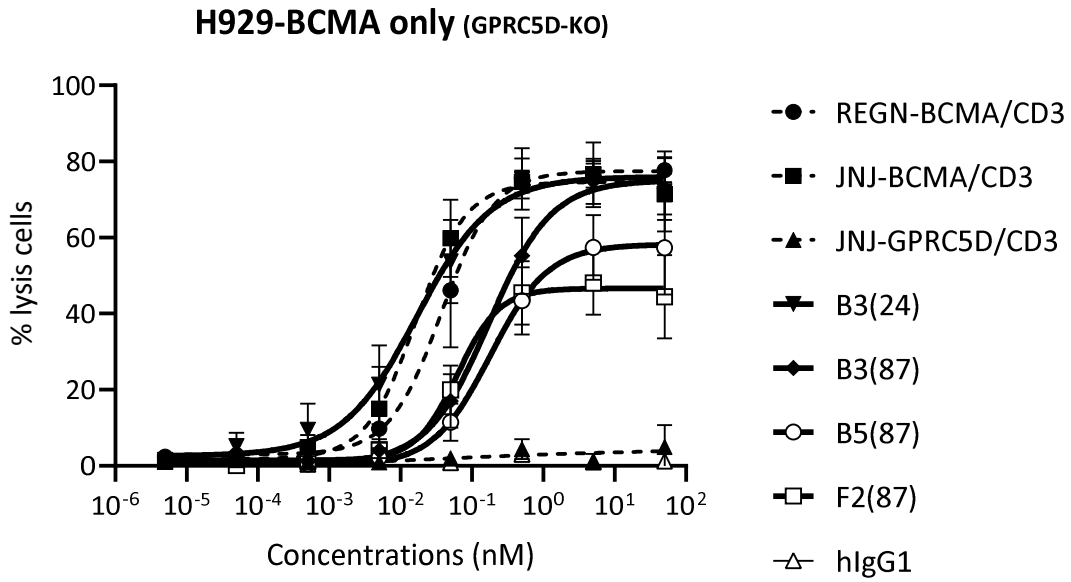

H929-BCMA only (GPRC5D-KO)
% lysis cells
100
80
60
40
20
0
10^{-6} 10^{-5} 10^{-4} 10^{-3} 10^{-2} 10^{-1} 10^{0} 10^{1} 10^{2}
Concentrations (nM)
REGN-BCMA/CD3
JNJ-BCMA/CD3
JNJ-GPRC5D/CD3
B3(24)
B3(87)
B5(87)
F2(87)
hIgG1

FIG. 3A

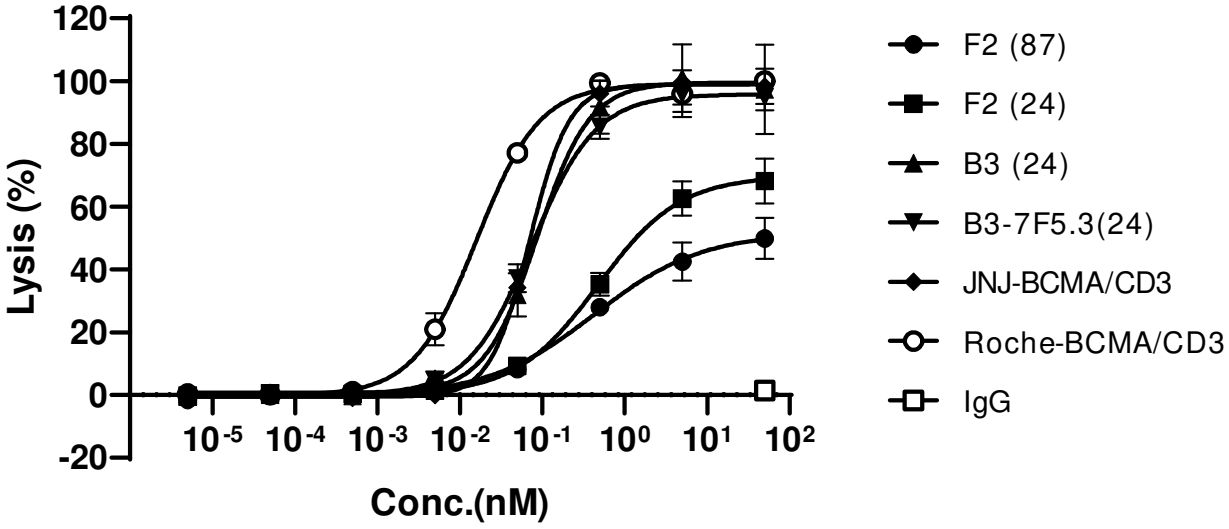

Lysis (%)
120
100
80
60
40
20
0
-20
10^{-5} 10^{-4} 10^{-3} 10^{-2} 10^{-1} 10^{0} 10^{1} 10^{2}
Conc.(nM)
F2 (87)
F2 (24)
B3 (24)
B3-7F5.3(24)
JNJ-BCMA/CD3
Roche-BCMA/CD3
IgG

FIG. 3B

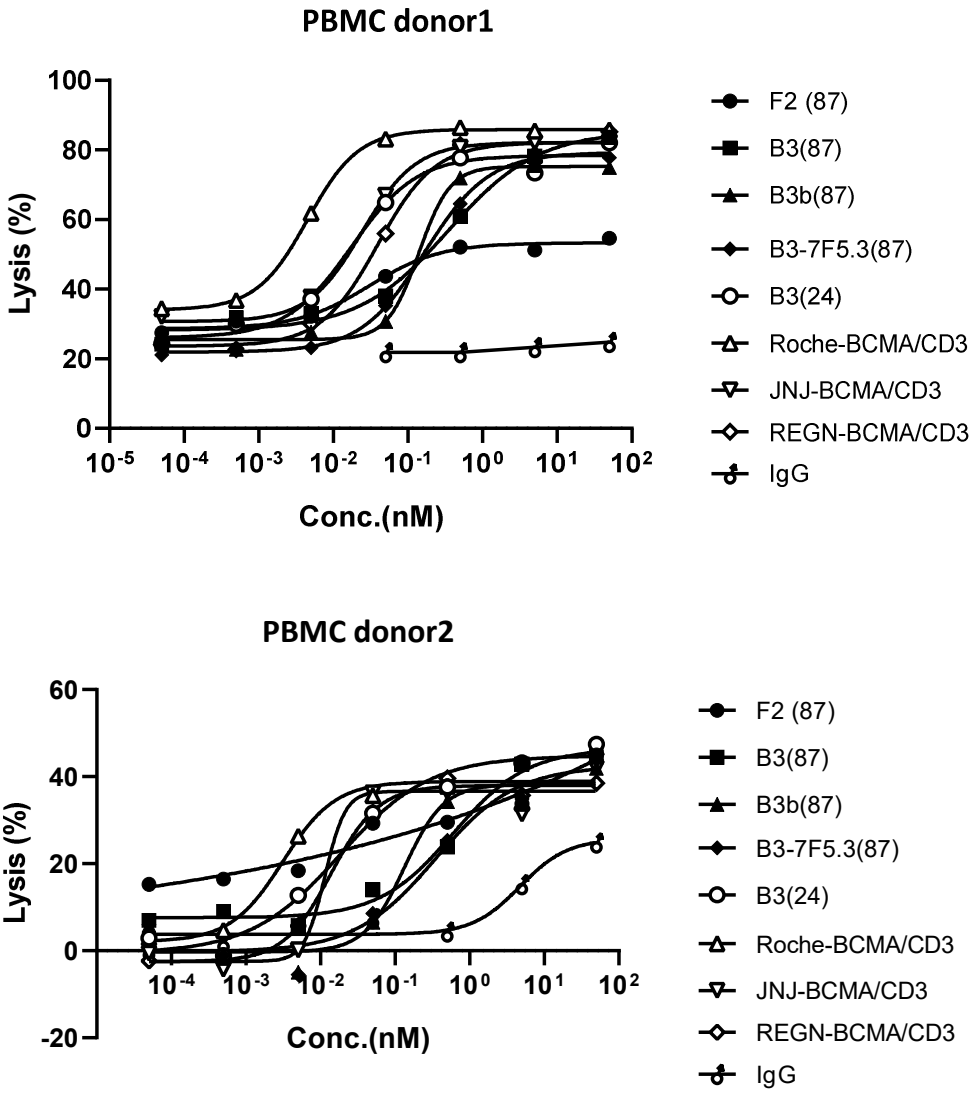

PBMC donor1
Lysis (%)
100
80
60
40
20
0
10-5 10-4 10-3 10-2 10-1 100 101 102
Conc.(nM)
F2 (87)
B3(87)
B3b(87)
B3-7F5.3(87)
B3(24)
Roche-BCMA/CD3
JNJ-BCMA/CD3
REGN-BCMA/CD3
IgG
PBMC donor2
Lysis (%)
60
40
20
0
-20
10-4 10-3 10-2 10-1 100 101 102
Conc.(nM)
F2 (87)
B3(87)
B3b(87)
B3-7F5.3(87)
B3(24)
Roche-BCMA/CD3
JNJ-BCMA/CD3
REGN-BCMA/CD3
IgG

FIG. 3C

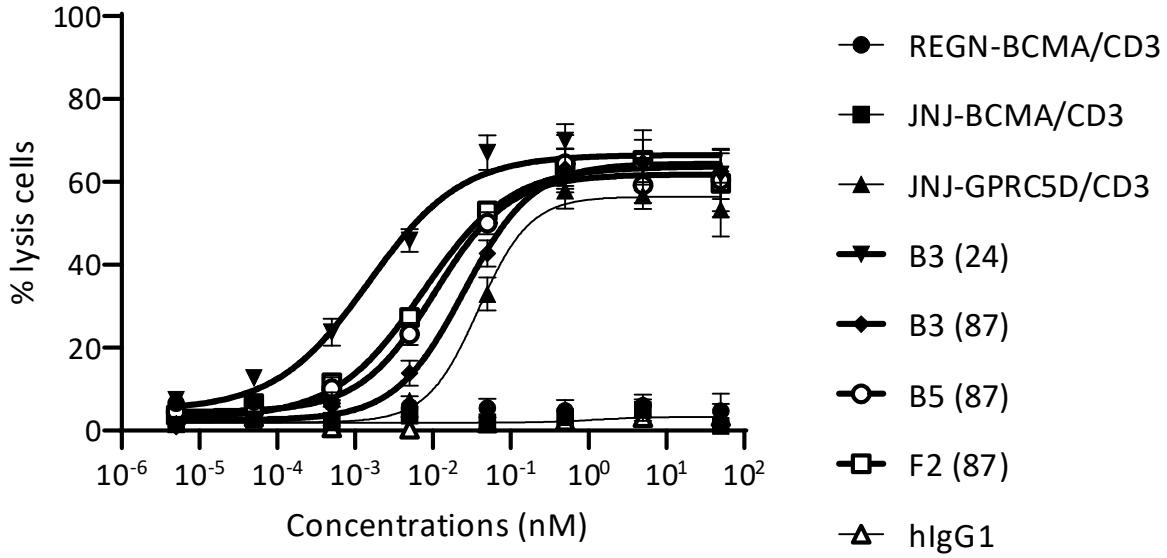

100
80
60
40
20
0
% lysis cells
10^{-6} 10^{-5} 10^{-4} 10^{-3} 10^{-2} 10^{-1} 10^{0} 10^{1} 10^{2}
Concentrations (nM)
REGN-BCMA/CD3
JNJ-BCMA/CD3
JNJ-GPRC5D/CD3
B3 (24)
B3 (87)
B5 (87)
F2 (87)
hIgG1

FIG. 3D

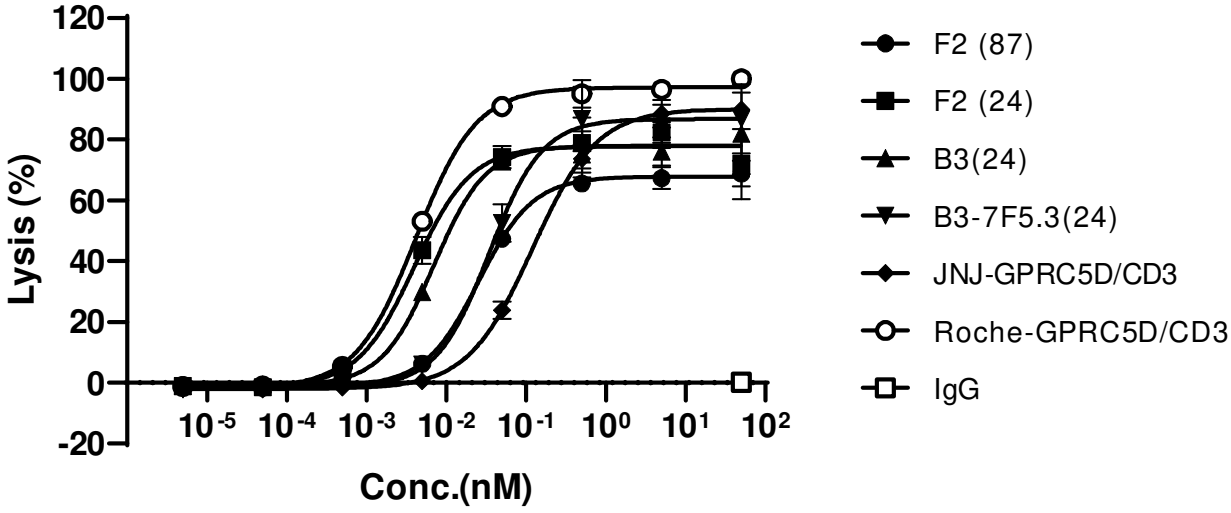

120
100
80
60
40
20
0
-20
Lysis (%)
10^{-5} 10^{-4} 10^{-3} 10^{-2} 10^{-1} 10^{0} 10^{1} 10^{2}
Conc.(nM)
F2 (87)
F2 (24)
B3(24)
B3-7F5.3(24)
JNJ-GPRC5D/CD3
Roche-GPRC5D/CD3
IgG

FIG. 3E

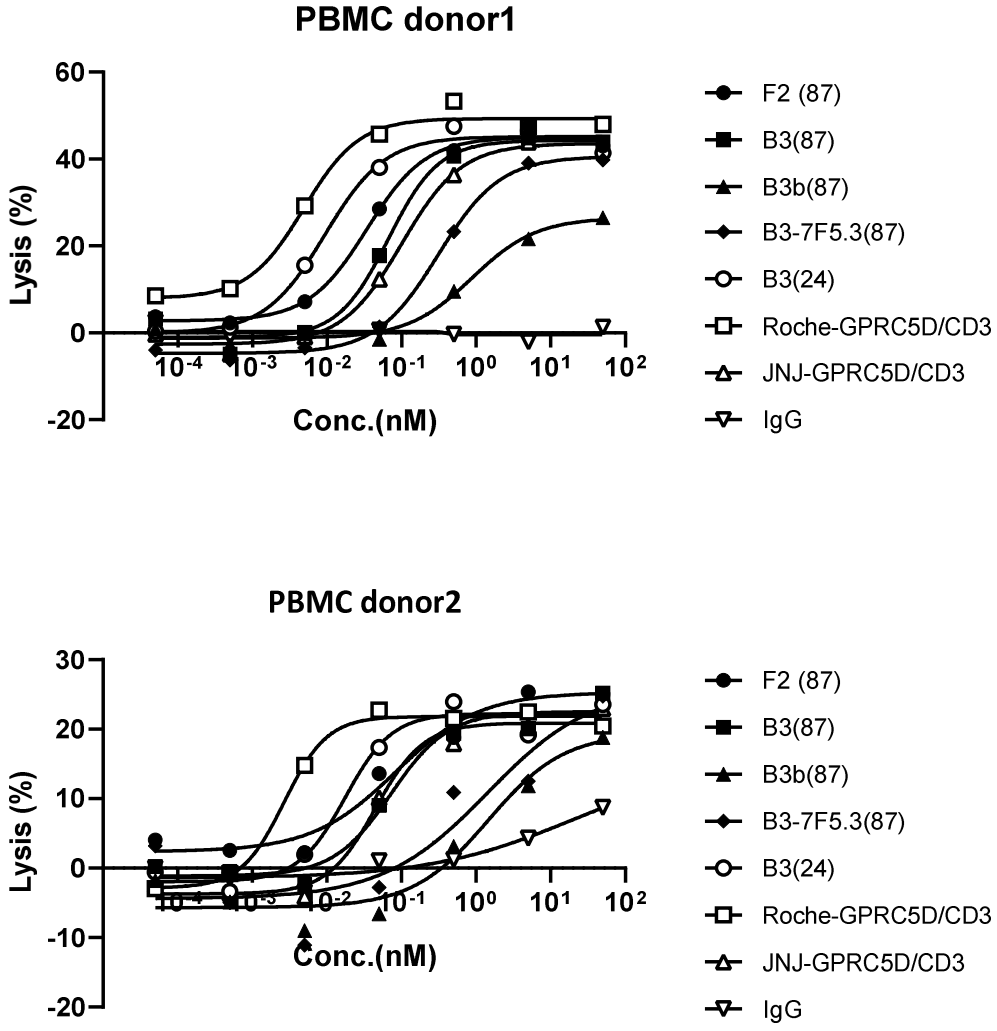

PBMC donor1
Lysis (%)
60
40
20
0
-20
10-4
10-3
10-2
10-1
100
101
102
Conc.(nM)
F2 (87)
B3(87)
B3b(87)
B3-7F5.3(87)
B3(24)
Roche-GPRC5D/CD3
JNJ-GPRC5D/CD3
IgG
PBMC donor2
Lysis (%)
30
20
10
0
-10
-20
Conc.(nM)
F2 (87)
B3(87)
B3b(87)
B3-7F5.3(87)
B3(24)
Roche-GPRC5D/CD3
JNJ-GPRC5D/CD3
IgG

FIG. 3F

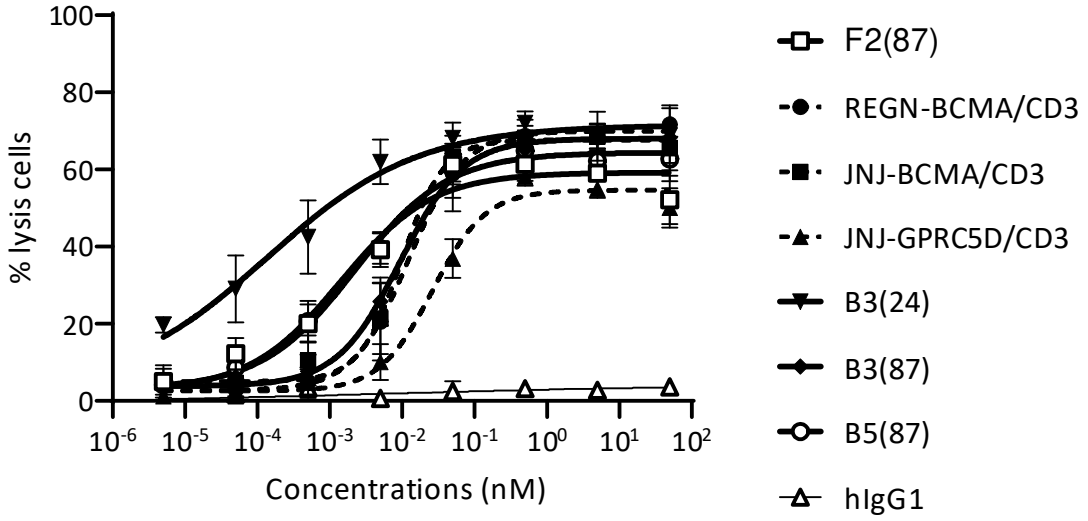

100
80
60
40
20
0
% lysis cells
10-6 10-5 10-4 10-3 10-2 10-1 100 101 102
Concentrations (nM)
F2(87)
REGN-BCMA/CD3
JNJ-BCMA/CD3
JNJ-GPRC5D/CD3
B3(24)
B3(87)
B5(87)
hIgG1

FIG. 3G

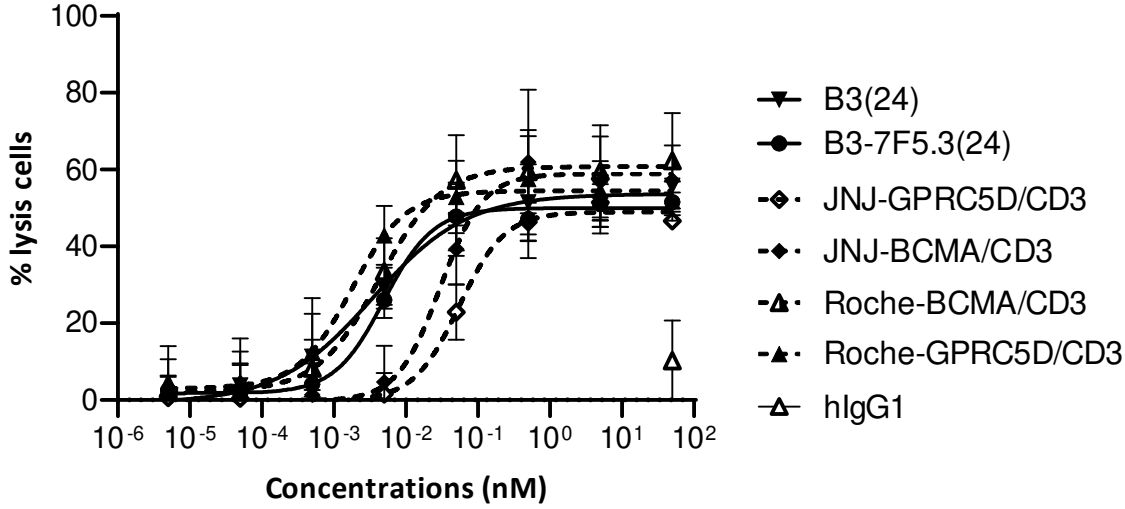

100
80
60
40
20
0
% lysis cells
10-6 10-5 10-4 10-3 10-2 10-1 100 101 102
Concentrations (nM)
B3(24)
B3-7F5.3(24)
JNJ-GPRC5D/CD3
JNJ-BCMA/CD3
Roche-BCMA/CD3
Roche-GPRC5D/CD3
hIgG1

FIG. 3H

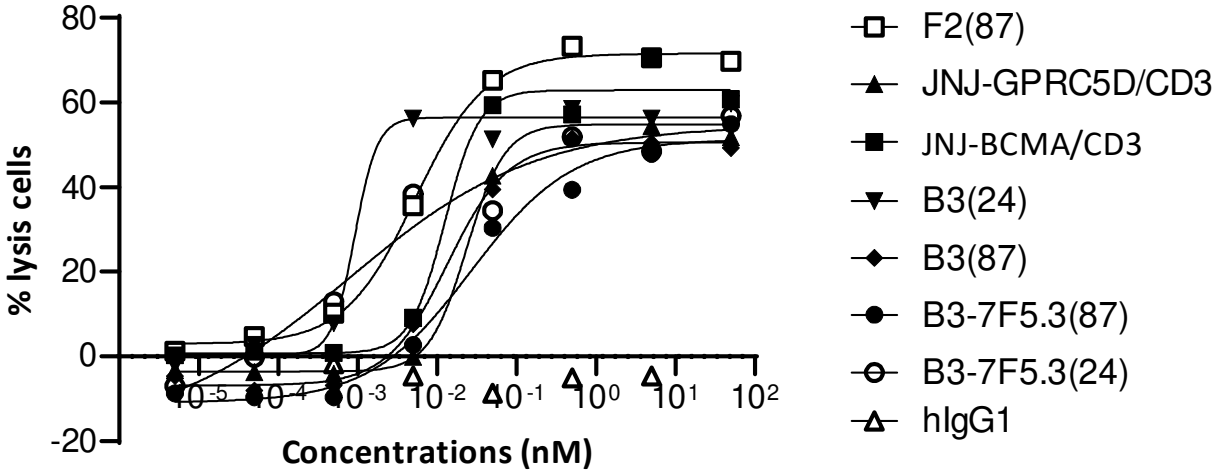

80
60
40
20
0
-20
% lysis cells
Concentrations (nM)
F2(87)
JNJ-GPRC5D/CD3
JNJ-BCMA/CD3
B3(24)
B3(87)
B3-7F5.3(87)
B3-7F5.3(24)
hIgG1

FIG. 3I

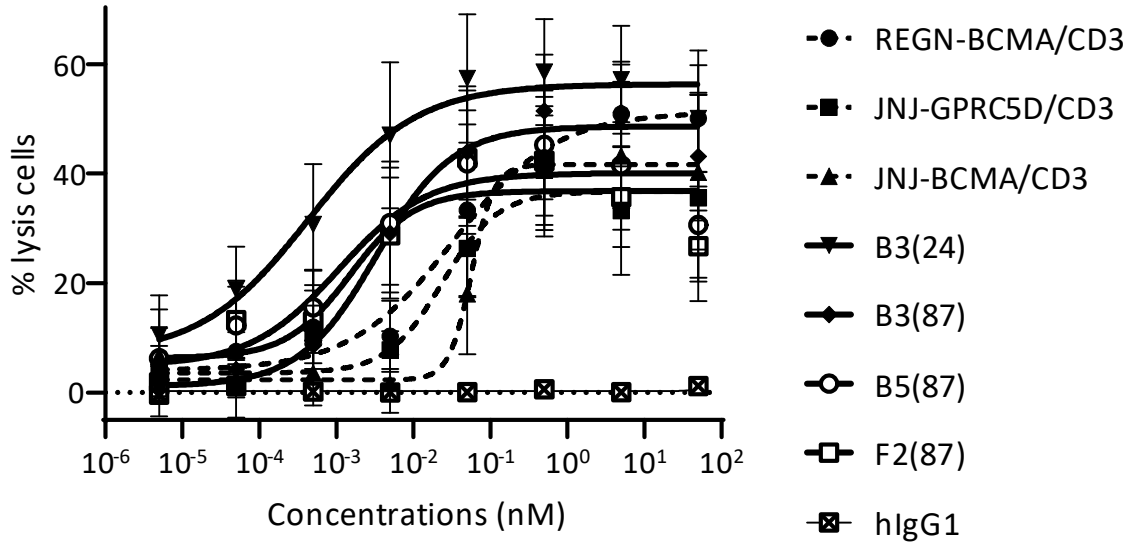

60
40
20
0
% lysis cells
Concentrations (nM)
REGN-BCMA/CD3
JNJ-GPRC5D/CD3
JNJ-BCMA/CD3
B3(24)
B3(87)
B5(87)
F2(87)
hIgG1

FIG. 3J

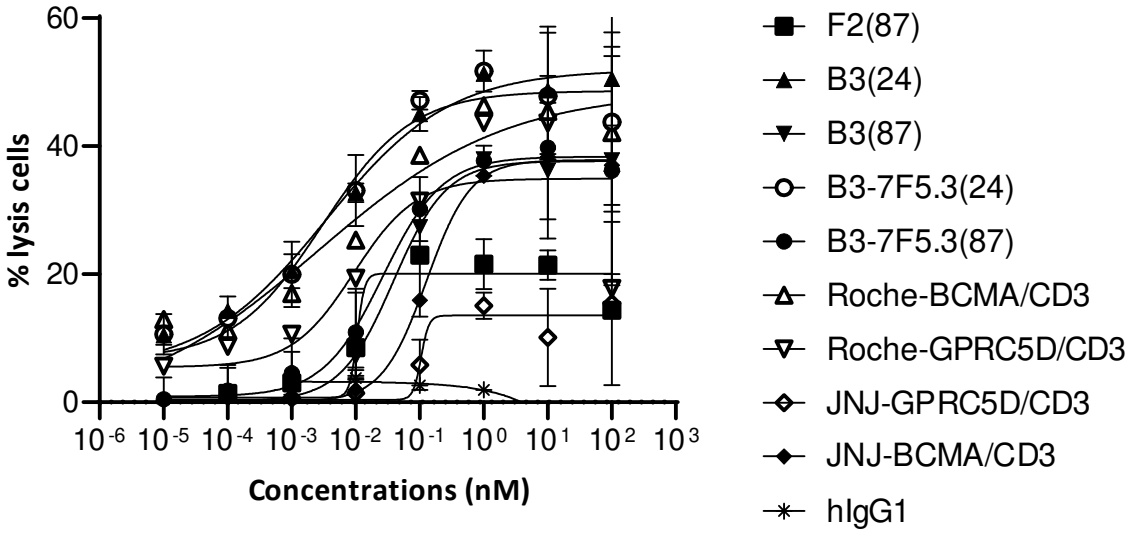

% lysis cells
60
40
20
0
10-6 10-5 10-4 10-3 10-2 10-1 100 101 102 103
Concentrations (nM)
F2(87)
B3(24)
B3(87)
B3-7F5.3(24)
B3-7F5.3(87)
Roche-BCMA/CD3
Roche-GPRC5D/CD3
JNJ-GPRC5D/CD3
JNJ-BCMA/CD3
hIgG1

FIG. 3K

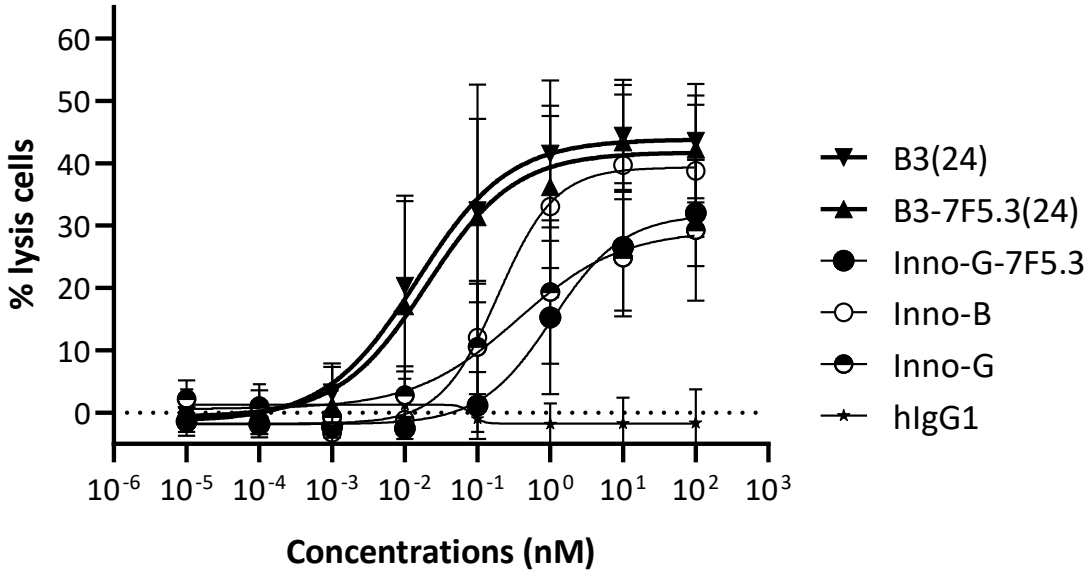

% lysis cells
60
50
40
30
20
10
0
10-6 10-5 10-4 10-3 10-2 10-1 100 101 102 103
Concentrations (nM)
B3(24)
B3-7F5.3(24)
Inno-G-7F5.3
Inno-B
Inno-G
hIgG1

FIG. 3L

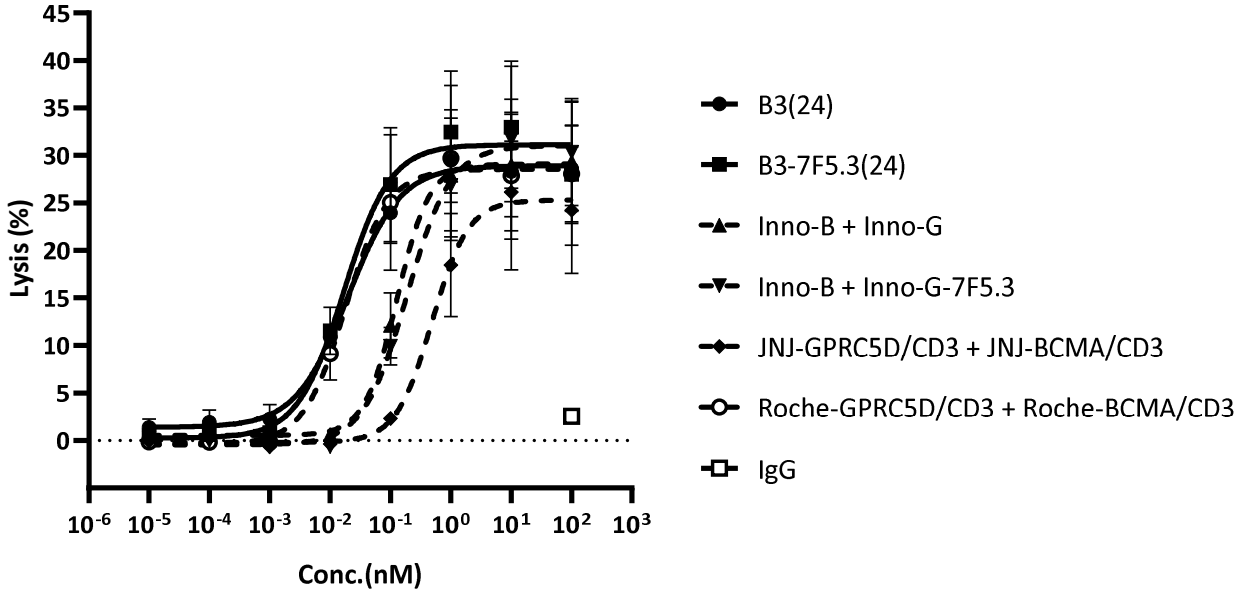


FIG. 3M

mixed cell population
(H929_parental+H929_koBCMA+H929_koGPRC5D)

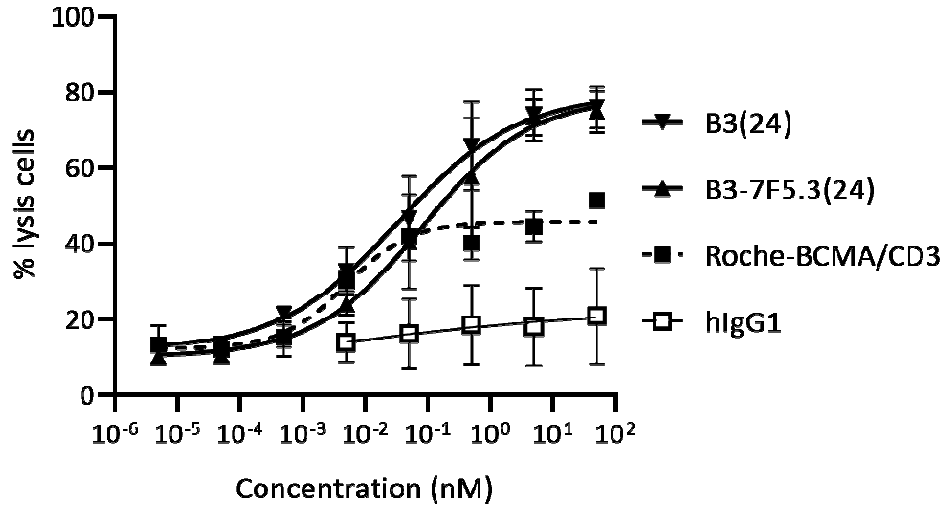


FIG. 3N

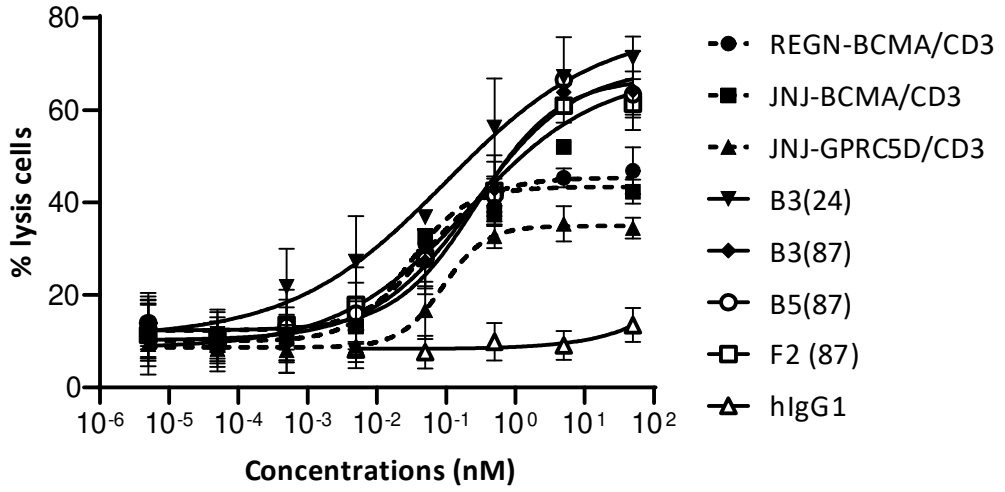

% lysis cells
80
60
40
20
0
10-6 10-5 10-4 10-3 10-2 10-1 100 101 102
Concentrations (nM)
REGN-BCMA/CD3
JNJ-BCMA/CD3
JNJ-GPRC5D/CD3
B3(24)
B3(87)
B5(87)
F2 (87)
hIgG1

FIG. 3O

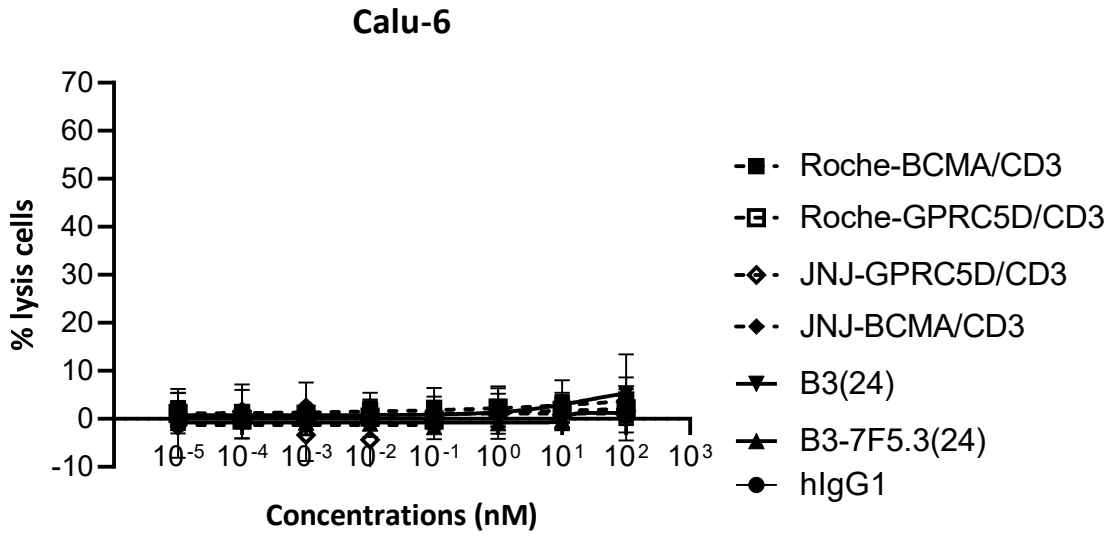

Calu-6
% lysis cells
70
60
50
40
30
20
10
0
-10
10-5 10-4 10-3 10-2 10-1 100 101 102 103
Concentrations (nM)
Roche-BCMA/CD3
Roche-GPRC5D/CD3
JNJ-GPRC5D/CD3
JNJ-BCMA/CD3
B3(24)
B3-7F5.3(24)
hIgG1

FIG. 3P

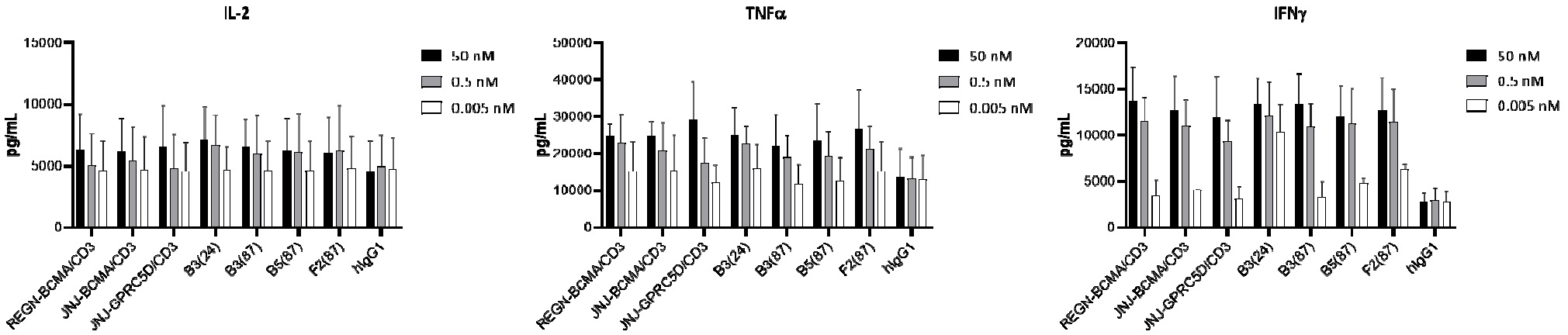

IL-2
pg/mL
15000
10000
5000
0
50 nM
0.5 nM
0.005 nM
REGN-BCMA/CD3
JNJ-BCMA/CD3
JNJ-GPRC5D/CD3
B3(24)
B3(87)
B5(87)
F2(87)
hIgG1
TNFα
pg/mL
50000
40000
30000
20000
10000
0
50 nM
0.5 nM
0.005 nM
REGN-BCMA/CD3
JNJ-BCMA/CD3
JNJ-GPRC5D/CD3
B3(24)
B3(87)
B5(87)
F2(87)
hIgG1
IFNγ
pg/mL
20000
15000
10000
5000
0
50 nM
0.5 nM
0.005 nM
REGN-BCMA/CD3
JNJ-BCMA/CD3
JNJ-GPRC5D/CD3
B3(24)
B3(87)
B5(87)
F2(87)
hIgG1

FIG. 3Q

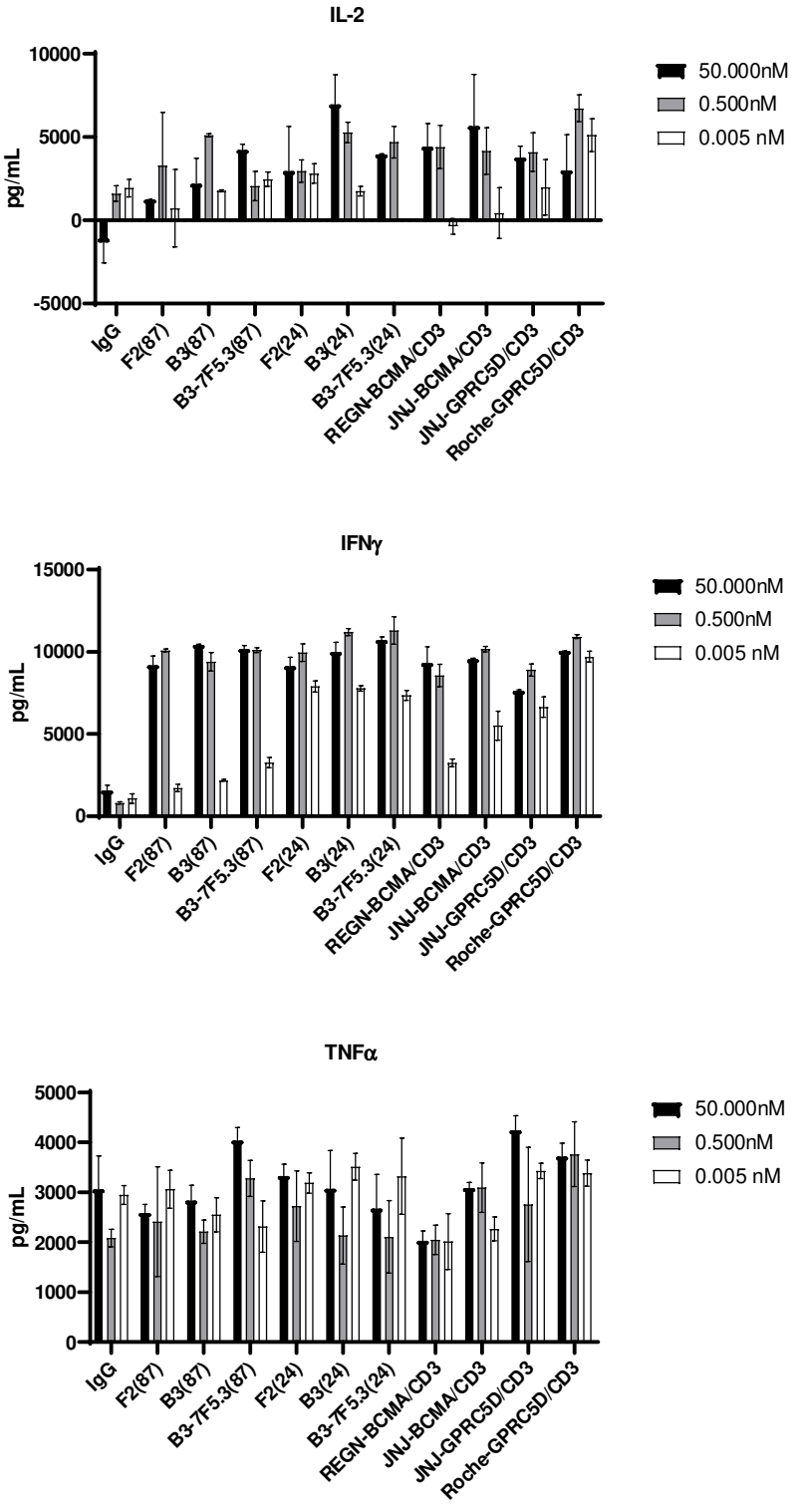

IL-2
10000
5000
0
-5000
pg/mL
50.000nM
0.500nM
0.005 nM
IgG
F2(87)
B3(87)
B3-7F5.3(87)
F2(24)
B3(24)
B3-7F5.3(24)
REGN-BCMA/CD3
JNJ-BCMA/CD3
JNJ-GPRC5D/CD3
Roche-GPRC5D/CD3
IFNγ
15000
10000
5000
0
pg/mL
50.000nM
0.500nM
0.005 nM
IgG
F2(87)
B3(87)
B3-7F5.3(87)
F2(24)
B3(24)
B3-7F5.3(24)
REGN-BCMA/CD3
JNJ-BCMA/CD3
JNJ-GPRC5D/CD3
Roche-GPRC5D/CD3
TNFα
5000
4000
3000
2000
1000
0
pg/mL
50.000nM
0.500nM
0.005 nM
IgG
F2(87)
B3(87)
B3-7F5.3(87)
F2(24)
B3(24)
B3-7F5.3(24)
REGN-BCMA/CD3
JNJ-BCMA/CD3
JNJ-GPRC5D/CD3
Roche-GPRC5D/CD3

FIG. 3R

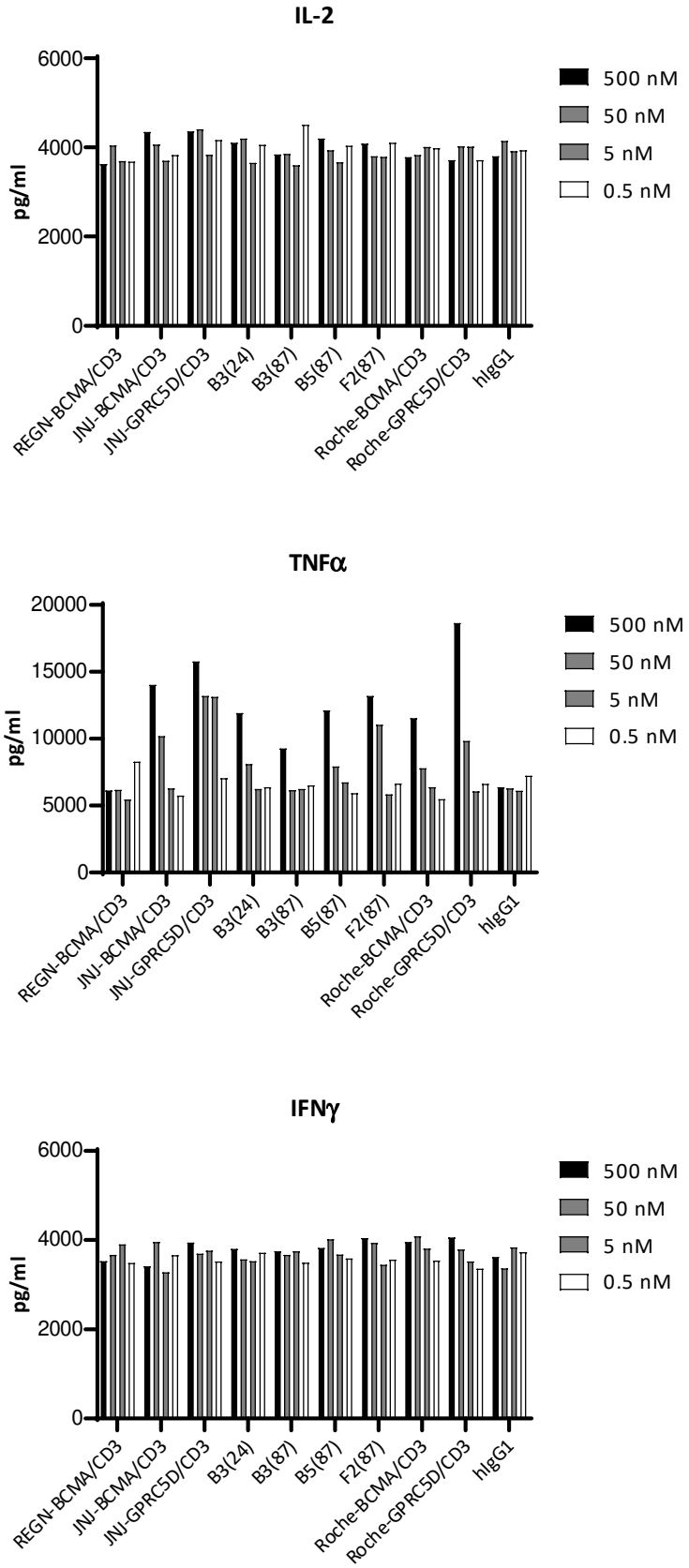

IL-2
6000
4000
2000
0
pg/ml
500 nM
50 nM
5 nM
0.5 nM
REGN-BCMA/CD3
JNJ-BCMA/CD3
JNJ-GPRC5D/CD3
B3(24)
B3(87)
B5(87)
F2(87)
Roche-BCMA/CD3
Roche-GPRC5D/CD3
hIgG1
TNFα
20000
15000
10000
5000
0
pg/ml
500 nM
50 nM
5 nM
0.5 nM
REGN-BCMA/CD3
JNJ-BCMA/CD3
JNJ-GPRC5D/CD3
B3(24)
B3(87)
B5(87)
F2(87)
Roche-BCMA/CD3
Roche-GPRC5D/CD3
hIgG1
IFNγ
6000
4000
2000
0
pg/ml
500 nM
50 nM
5 nM
0.5 nM
REGN-BCMA/CD3
JNJ-BCMA/CD3
JNJ-GPRC5D/CD3
B3(24)
B3(87)
B5(87)
F2(87)
Roche-BCMA/CD3
Roche-GPRC5D/CD3
hIgG1

FIG. 3S

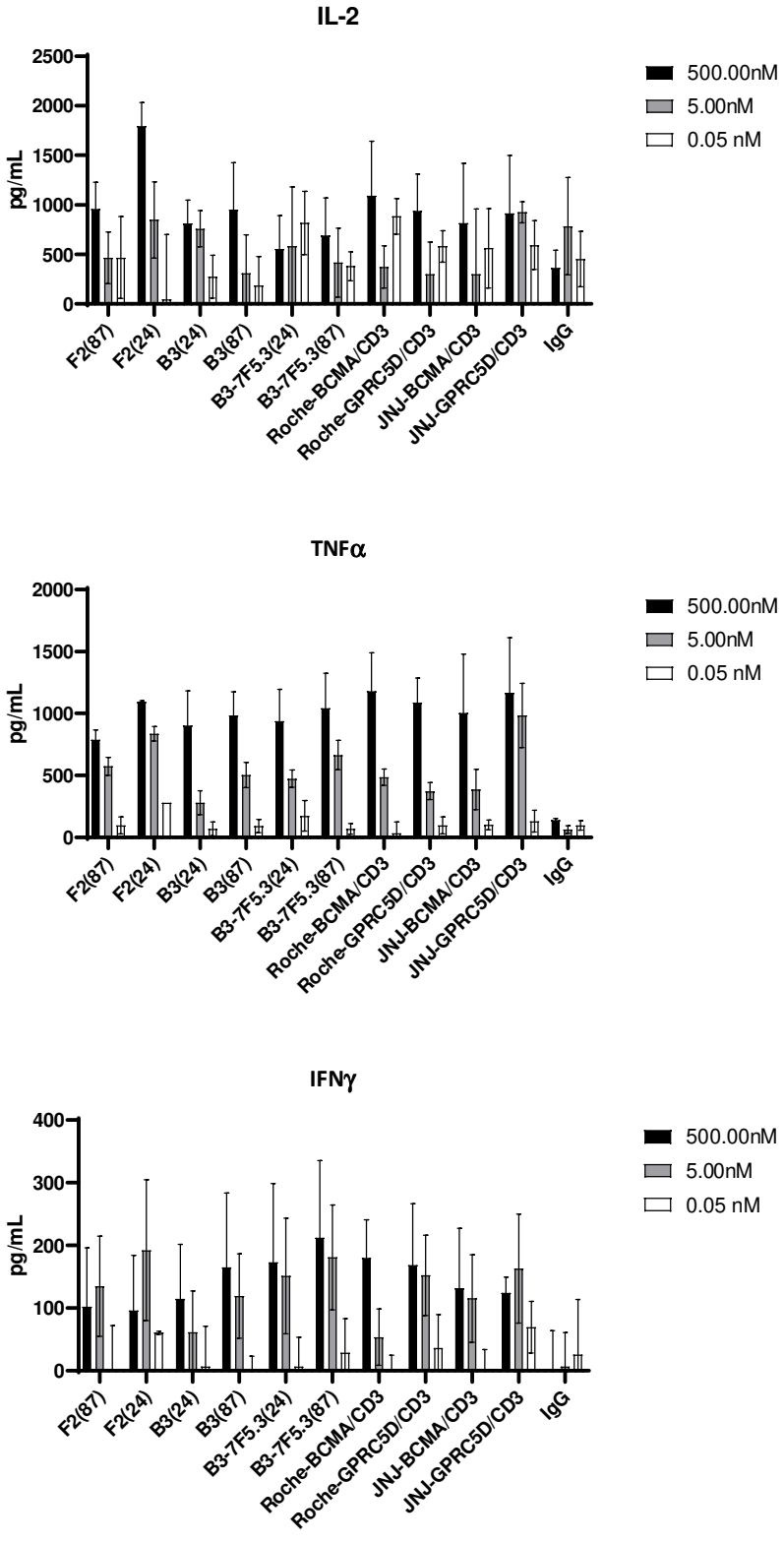
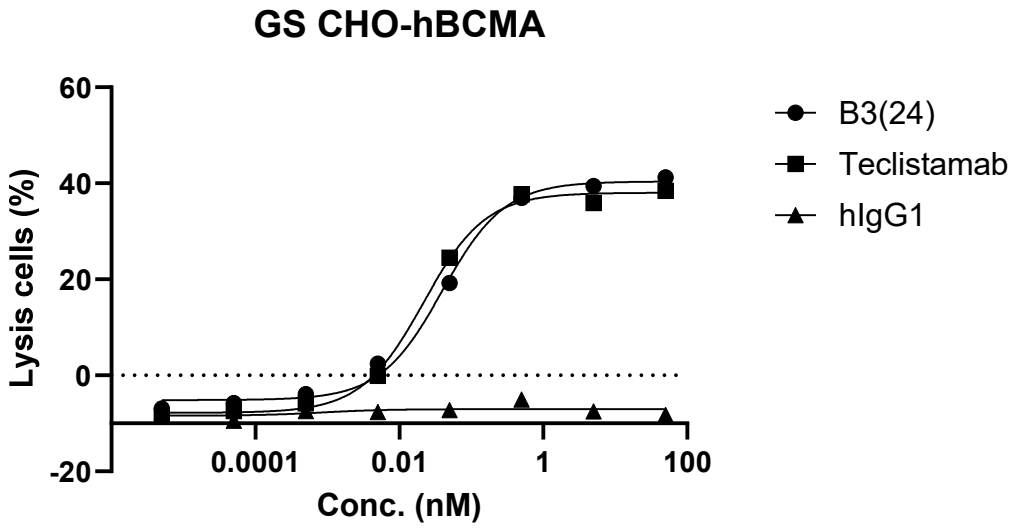
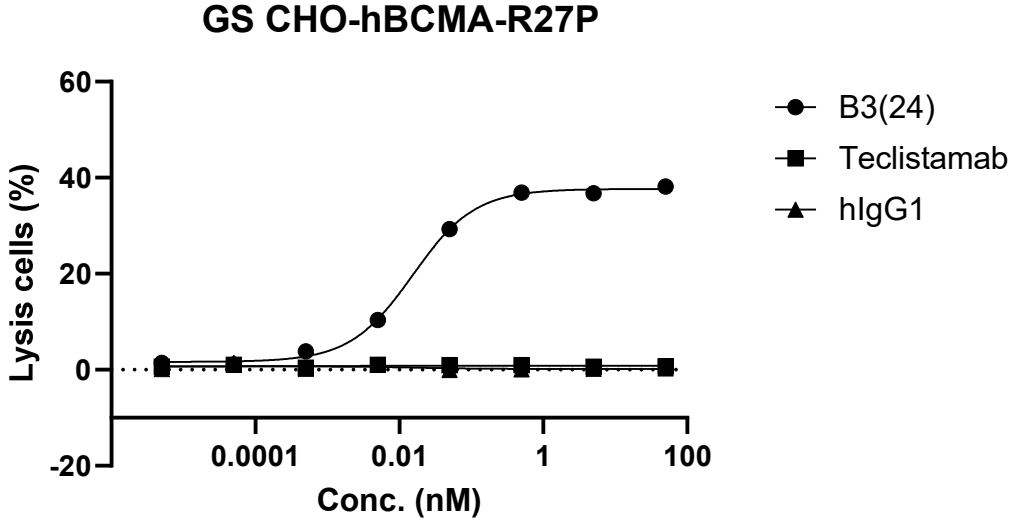

IL-2
pg/mL
2500
2000
1500
1000
500
0
500.00nM
5.00nM
0.05 nM
F2(87)
F2(24)
B3(24)
B3(87)
B3-7F5.3(24)
B3-7F5.3(87)
Roche-BCMA/CD3
Roche-GPRC5D/CD3
JNJ-BCMA/CD3
JNJ-GPRC5D/CD3
IgG
TNFα
pg/mL
2000
1500
1000
500
0
500.00nM
5.00nM
0.05 nM
F2(87)
F2(24)
B3(24)
B3(87)
B3-7F5.3(24)
B3-7F5.3(87)
Roche-BCMA/CD3
Roche-GPRC5D/CD3
JNJ-BCMA/CD3
JNJ-GPRC5D/CD3
IgG
IFNγ
pg/mL
400
300
200
100
0
500.00nM
5.00nM
0.05 nM
F2(87)
F2(24)
B3(24)
B3(87)
B3-7F5.3(24)
B3-7F5.3(87)
Roche-BCMA/CD3
Roche-GPRC5D/CD3
JNJ-BCMA/CD3
JNJ-GPRC5D/CD3
IgG

FIG. 3T

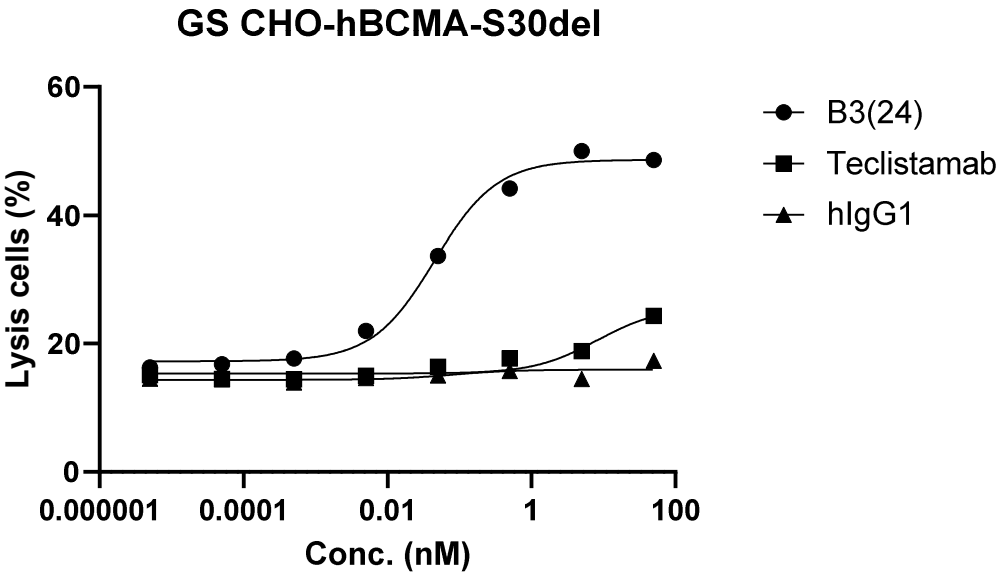


	B3(24)	Teclistamab
EC50	0.03971	0.02157

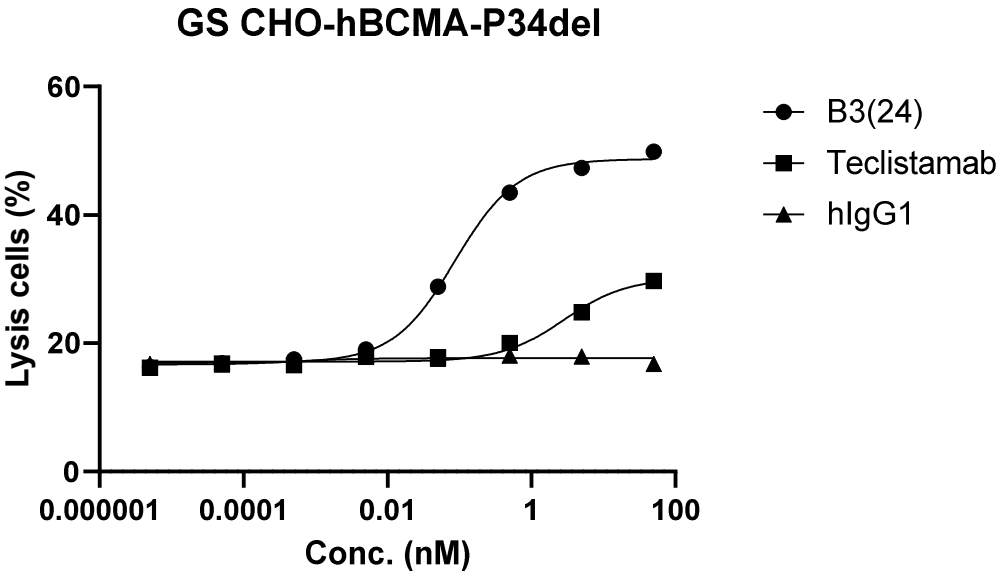


	B3(24)	Teclistamab
EC50	0.01519	0.001808

FIG. 3U

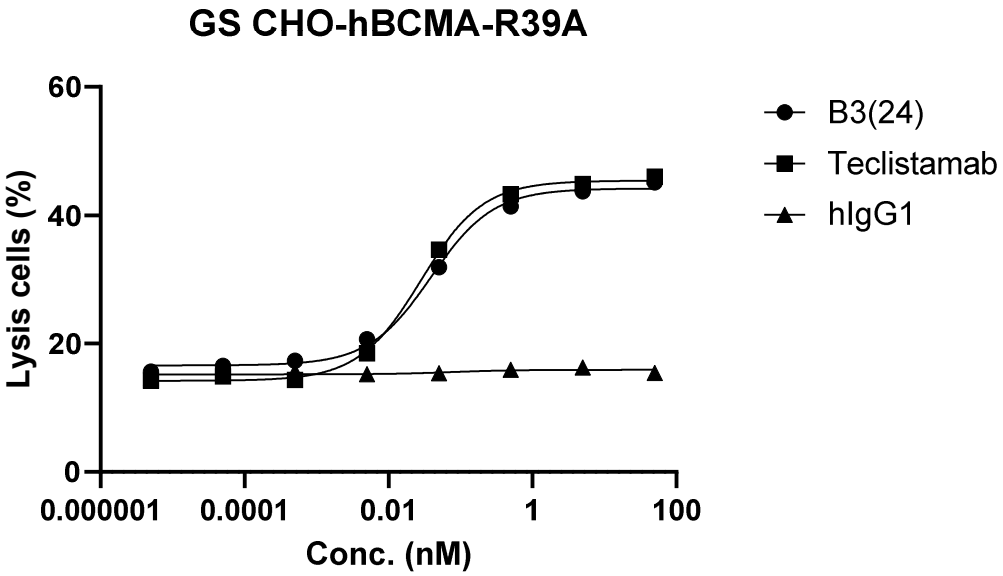


	B3(24)	Teclistamab
EC50	0.04496	8.156



	B3(24)	Teclistamab
EC50	0.08652	2.809

FIG. 3U(Continued)



	B3(24)	Teclistamab
EC50	0.03884	0.02782

FIG. 3U(Continued)

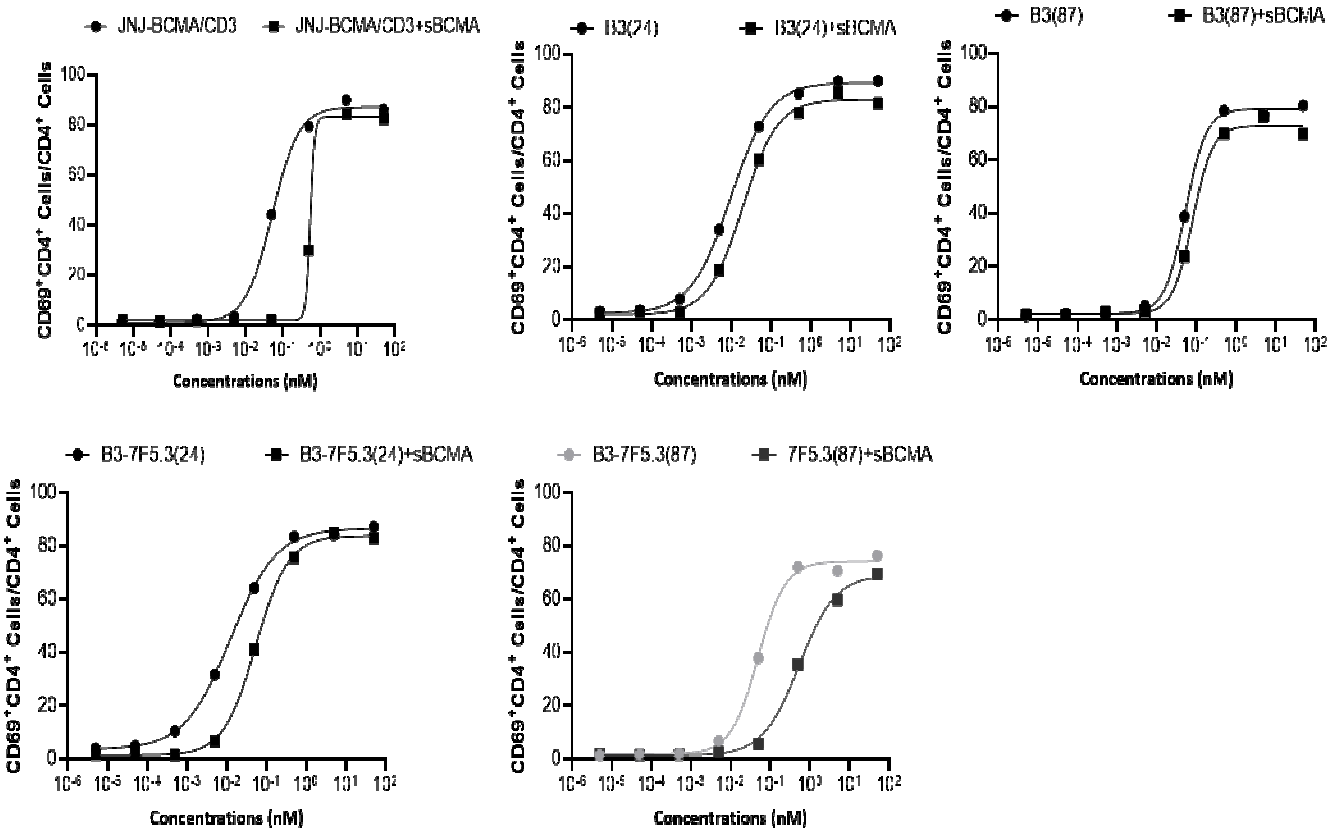

JNJ-BCMA/CD3
JNJ-BCMA/CD3+sBCMA
B3(24)
B3(24)+sBCMA
B3(87)
B3(87)+sBCMA
B3-7F5.3(24)
B3-7F5.3(24)+sBCMA
B3-7F5.3(87)
7F5.3(87)+sBCMA
CD69+CD4+ Cells/CD4+ Cells
Concentrations (nM)

FIG. 4A

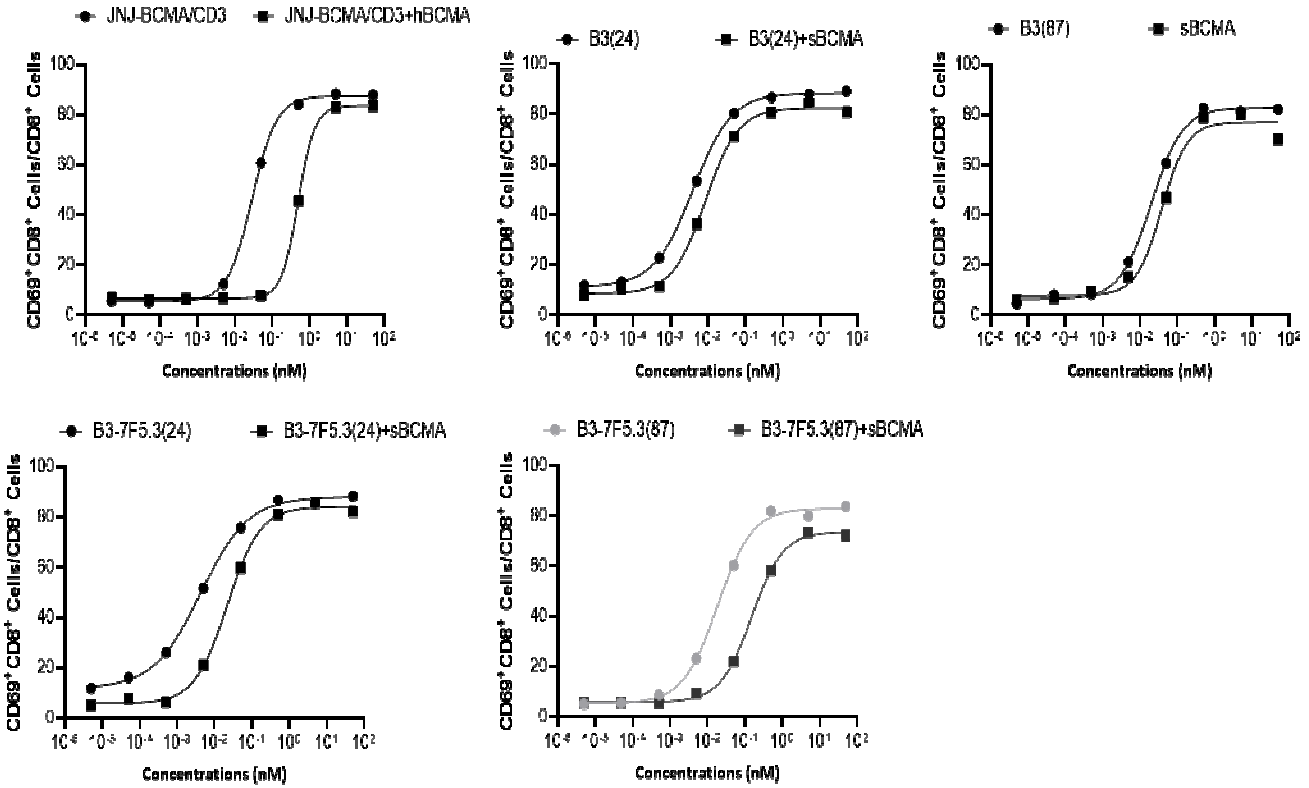

JNJ-BCMA/CD3
JNJ-BCMA/CD3+hBCMA
B3(24)
B3(24)+sBCMA
B3(87)
sBCMA
B3-7F5.3(24)
B3-7F5.3(24)+sBCMA
B3-7F5.3(87)
B3-7F5.3(87)+sBCMA
CD69+CD8+ Cells/CD8+ Cells
Concentrations (nM)

FIG. 4B

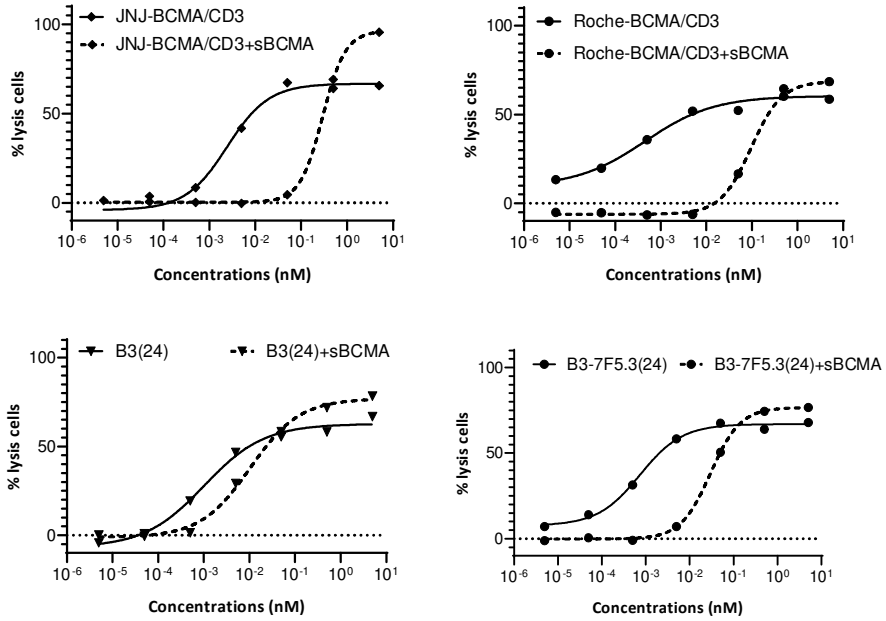

JNJ-BCMA/CD3
JNJ-BCMA/CD3+sBCMA
% lysis cells
Concentrations (nM)
Roche-BCMA/CD3
Roche-BCMA/CD3+sBCMA
% lysis cells
Concentrations (nM)
B3(24)
B3(24)+sBCMA
% lysis cells
Concentrations (nM)
B3-7F5.3(24)
B3-7F5.3(24)+sBCMA
% lysis cells
Concentrations (nM)

FIG. 4C

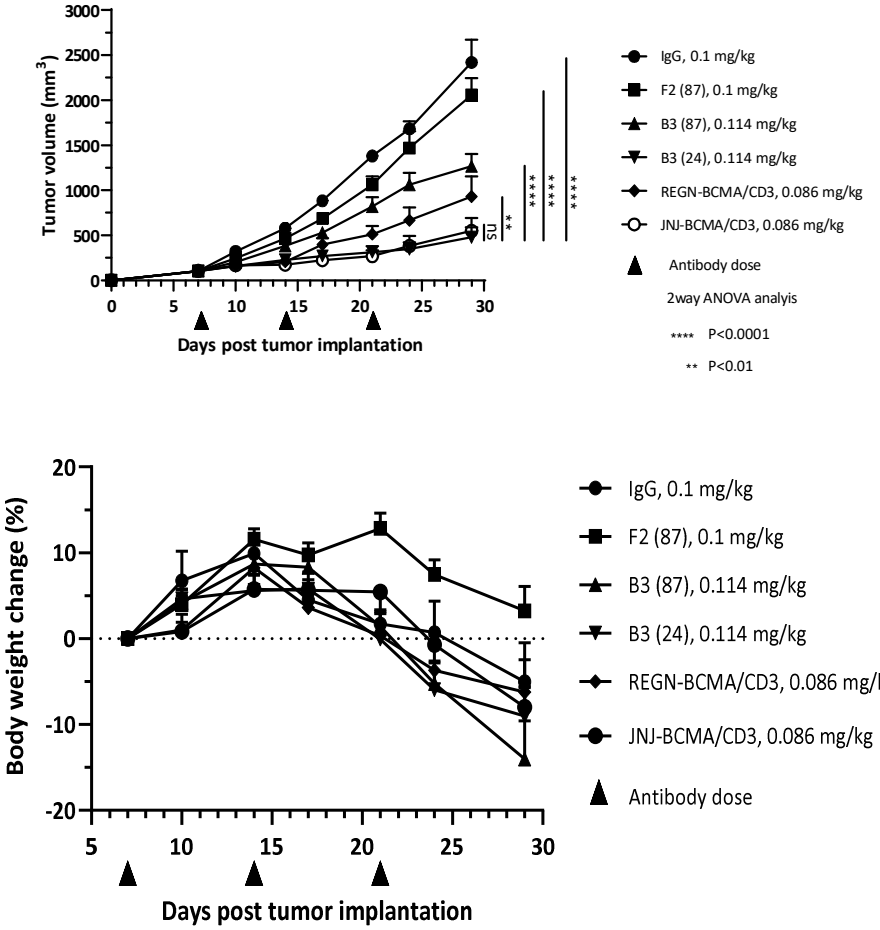

Tumor volume (mm3)
Days post tumor implantation
IgG, 0.1 mg/kg
F2 (87), 0.1 mg/kg
B3 (87), 0.114 mg/kg
B3 (24), 0.114 mg/kg
REGN-BCMA/CD3, 0.086 mg/kg
JNJ-BCMA/CD3, 0.086 mg/kg
Antibody dose
2way ANOVA analyis
**** P<0.0001
** P<0.01
Body weight change (%)
Days post tumor implantation
IgG, 0.1 mg/kg
F2 (87), 0.1 mg/kg
B3 (87), 0.114 mg/kg
B3 (24), 0.114 mg/kg
REGN-BCMA/CD3, 0.086 mg/kg
JNJ-BCMA/CD3, 0.086 mg/kg
Antibody dose

FIG. 5A

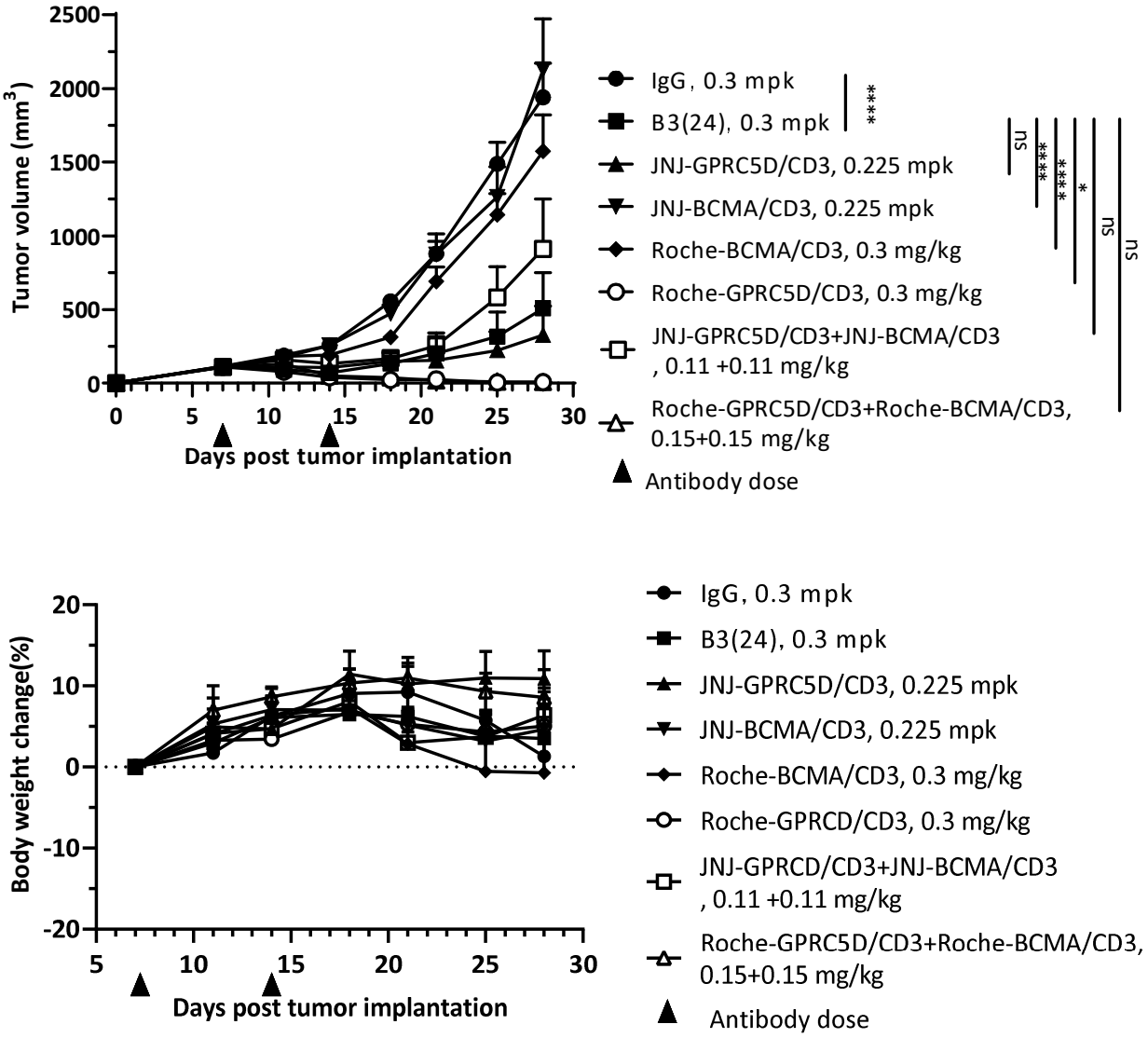

Tumor volume (mm3)
2500
2000
1500
1000
500
0
0
5
10
15
20
25
30
Days post tumor implantation
IgG, 0.3 mpk
B3(24), 0.3 mpk
JNJ-GPRC5D/CD3, 0.225 mpk
JNJ-BCMA/CD3, 0.225 mpk
Roche-BCMA/CD3, 0.3 mg/kg
Roche-GPRC5D/CD3, 0.3 mg/kg
JNJ-GPRC5D/CD3+JNJ-BCMA/CD3
, 0.11 +0.11 mg/kg
Roche-GPRC5D/CD3+Roche-BCMA/CD3,
0.15+0.15 mg/kg
Antibody dose
****
ns
****
****
*
ns
ns
Body weight change(%)
20
10
0
-10
-20
5
10
15
20
25
30
Days post tumor implantation
IgG, 0.3 mpk
B3(24), 0.3 mpk
JNJ-GPRC5D/CD3, 0.225 mpk
JNJ-BCMA/CD3, 0.225 mpk
Roche-BCMA/CD3, 0.3 mg/kg
Roche-GPRCD/CD3, 0.3 mg/kg
JNJ-GPRCD/CD3+JNJ-BCMA/CD3
, 0.11 +0.11 mg/kg
Roche-GPRC5D/CD3+Roche-BCMA/CD3,
0.15+0.15 mg/kg
Antibody dose

FIG. 5B

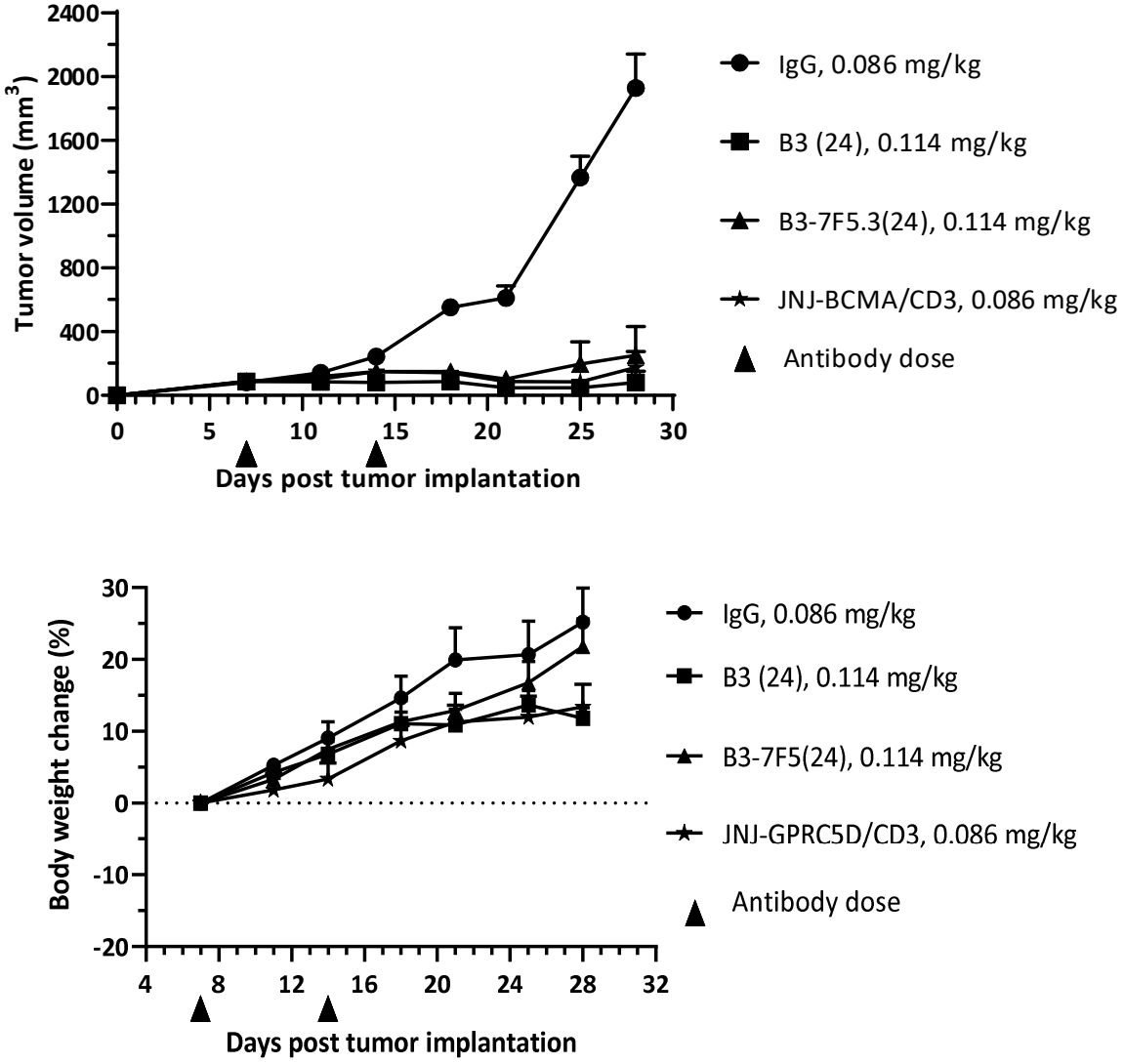

Tumor volume (mm3)
2400
2000
1600
1200
800
400
0
0
5
10
15
20
25
30
Days post tumor implantation
IgG, 0.086 mg/kg
B3 (24), 0.114 mg/kg
B3-7F5.3(24), 0.114 mg/kg
JNJ-BCMA/CD3, 0.086 mg/kg
Antibody dose
Body weight change (%)
30
20
10
0
-10
-20
4
8
12
16
20
24
28
32
Days post tumor implantation
IgG, 0.086 mg/kg
B3 (24), 0.114 mg/kg
B3-7F5(24), 0.114 mg/kg
JNJ-GPRC5D/CD3, 0.086 mg/kg
Antibody dose

FIG. 5C

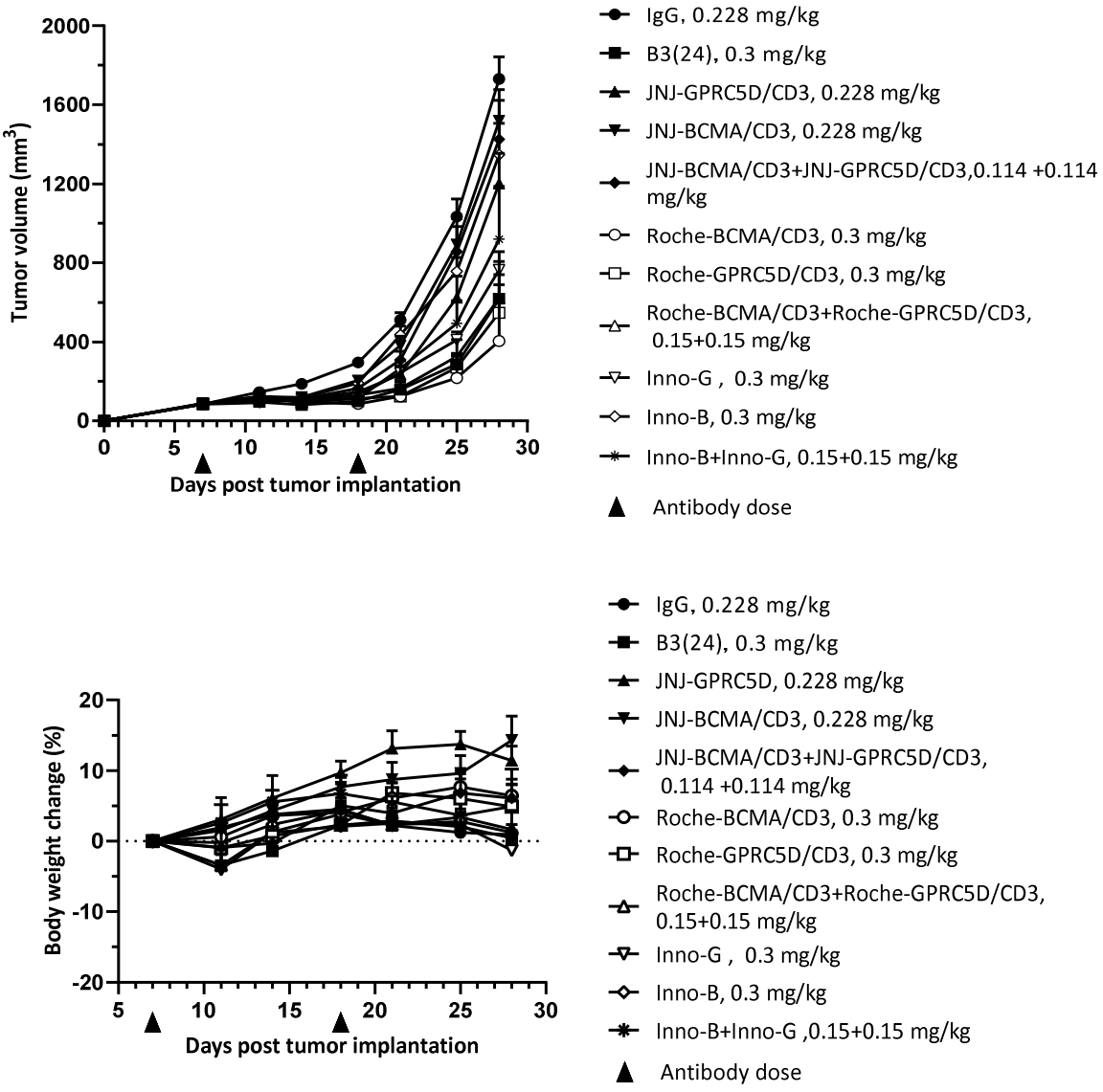

Tumor volume (mm3)
2000
1600
1200
800
400
0
0
5
10
15
20
25
30
Days post tumor implantation
IgG, 0.228 mg/kg
B3(24), 0.3 mg/kg
JNJ-GPRC5D/CD3, 0.228 mg/kg
JNJ-BCMA/CD3, 0.228 mg/kg
JNJ-BCMA/CD3+JNJ-GPRC5D/CD3,0.114 +0.114 mg/kg
Roche-BCMA/CD3, 0.3 mg/kg
Roche-GPRC5D/CD3, 0.3 mg/kg
Roche-BCMA/CD3+Roche-GPRC5D/CD3, 0.15+0.15 mg/kg
Inno-G , 0.3 mg/kg
Inno-B, 0.3 mg/kg
Inno-B+Inno-G, 0.15+0.15 mg/kg
Antibody dose
Body weight change (%)
20
10
0
-10
-20
5
10
15
20
25
30
Days post tumor implantation
IgG, 0.228 mg/kg
B3(24), 0.3 mg/kg
JNJ-GPRC5D, 0.228 mg/kg
JNJ-BCMA/CD3, 0.228 mg/kg
JNJ-BCMA/CD3+JNJ-GPRC5D/CD3, 0.114 +0.114 mg/kg
Roche-BCMA/CD3, 0.3 mg/kg
Roche-GPRC5D/CD3, 0.3 mg/kg
Roche-BCMA/CD3+Roche-GPRC5D/CD3, 0.15+0.15 mg/kg
Inno-G , 0.3 mg/kg
Inno-B, 0.3 mg/kg
Inno-B+Inno-G ,0.15+0.15 mg/kg
Antibody dose

FIG. 5D

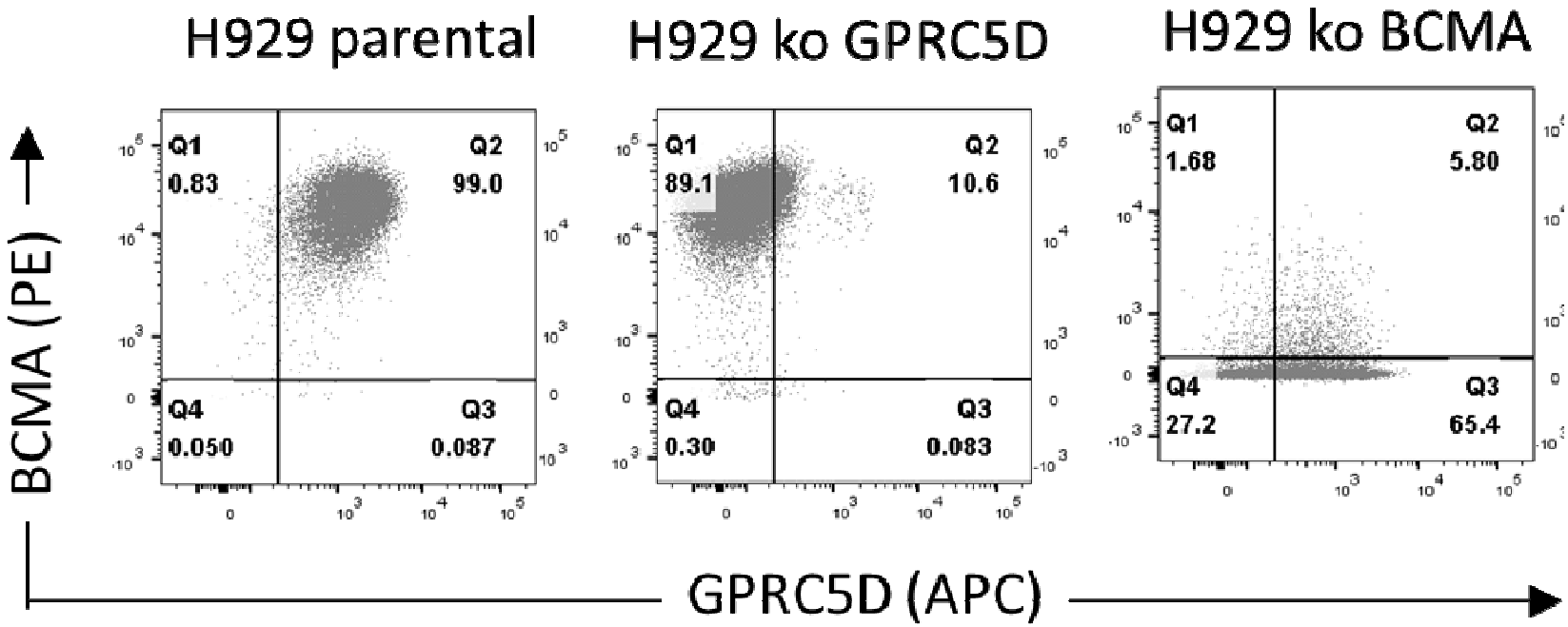

H929 parental
H929 ko GPRC5D
H929 ko BCMA
BCMA (PE)
GPRC5D (APC)
Q1
0.83
Q2
99.0
Q4
0.050
Q3
0.087
Q1
89.1
Q2
10.6
Q4
0.30
Q3
0.083
Q1
1.68
Q2
5.80
Q4
27.2
Q3
65.4

FIG. 6

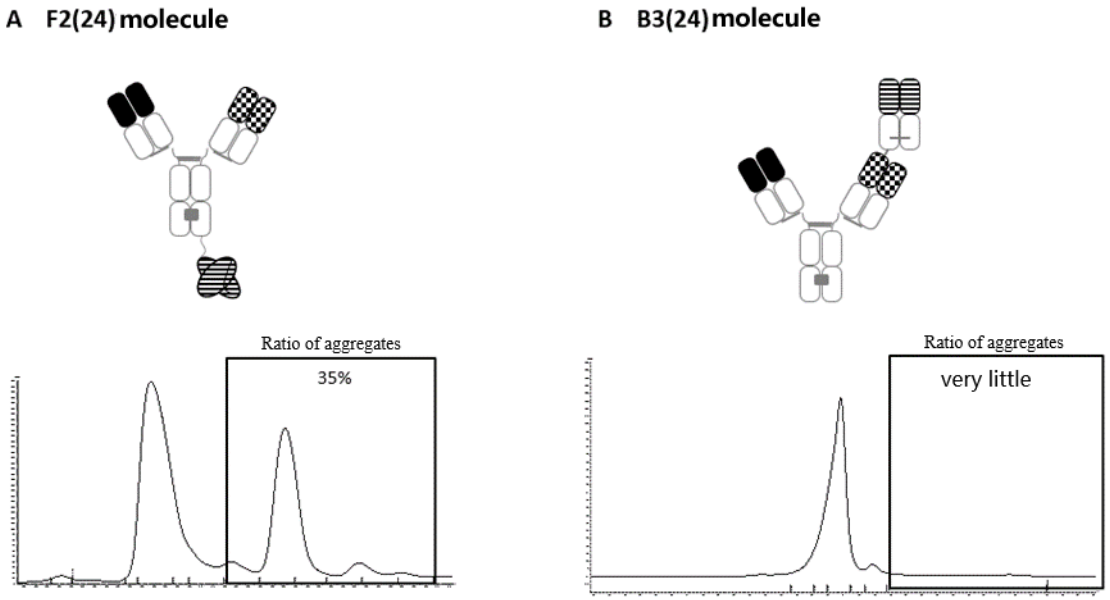

A F2(24) molecule
B B3(24) molecule
Ratio of aggregates
35%
Ratio of aggregates
very little

FIG. 7