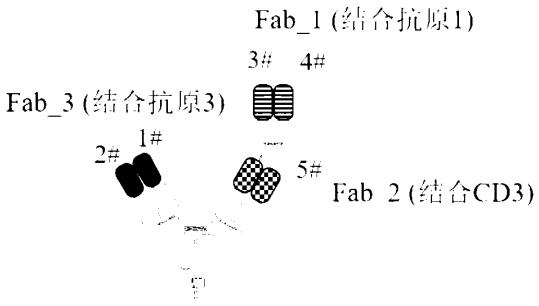
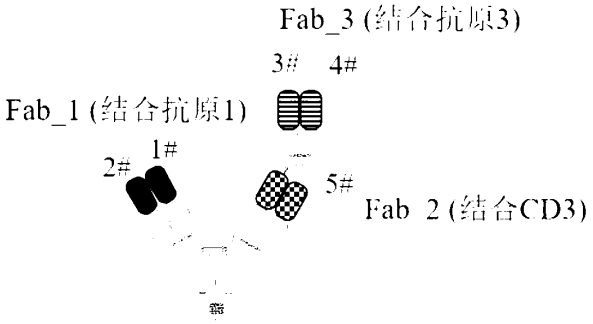
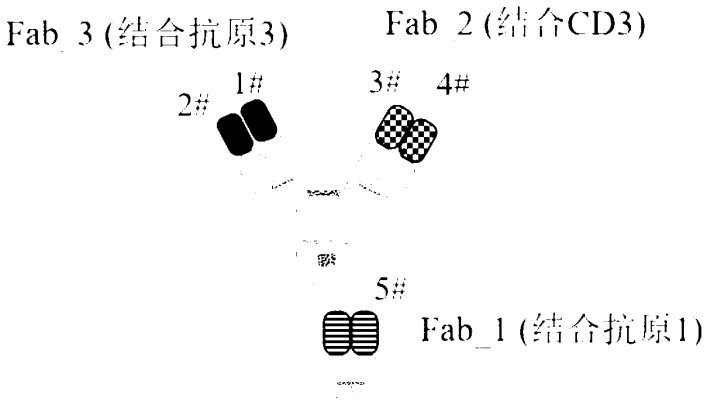


Chain 1#	重链1（H1），VH-CH1-Fc
Chain 2#	轻链1（L1），VL-CL
Chain 3#	重链2（H2），VH-CH1-VH-CH1-Fc
Chain 4#	轻链2（L2），VL-CL
Chain 5#	轻链3（L3），VL-CL
Fc	CH2-CH3，非对称 IgG1. LALA, knob-in-hole
Format	B3



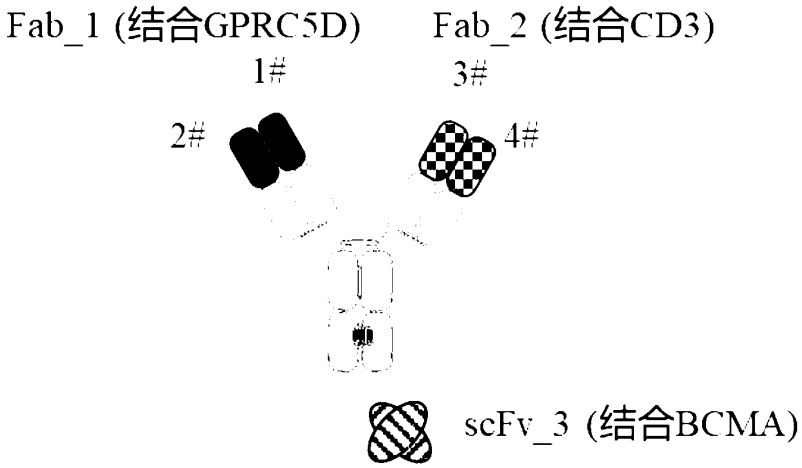
Chain 1#	重链1（H1），VH-CH1-Fc
Chain 2#	轻链1（L1），VL-CL
Chain 3#	重链2（H2），VH-CH1-VH-CH1-Fc
Chain 4#	轻链2（L2），VL-CL
Chain 5#	轻链3（L3），VL-CL
Fc	CH2-CH3，非对称 IgG1. LALA, knob-in-hole
Format	B3b

图 1A



Chain 1#	重链1（H1），VH-CH1-Fc
Chain 2#	轻链1（L1），VL-CL
Chain 3#	重链2（H2），VH-CH1-Fc-VH-CH1
Chain 4#	轻链2（L2），VL-CL
Chain 5#	轻链3（L3），VL-CL
Fc	CH2-CH3，非对称 IgG1、LALA、knob-in-hole
Format	B5

图 1B



Chain 1#	重链1（H1），VH-CH1-Fc
Chain 2#	轻链1（L1），VL-CL
Chain 3#	重链2（H2），VH-CH1-Fc-scFv
Chain 4#	轻链2（L2），VL-CL
Fc	CH2-CH3， 非对称 IgG1、LALA、knob-in-hole
Format	F2

图 1C

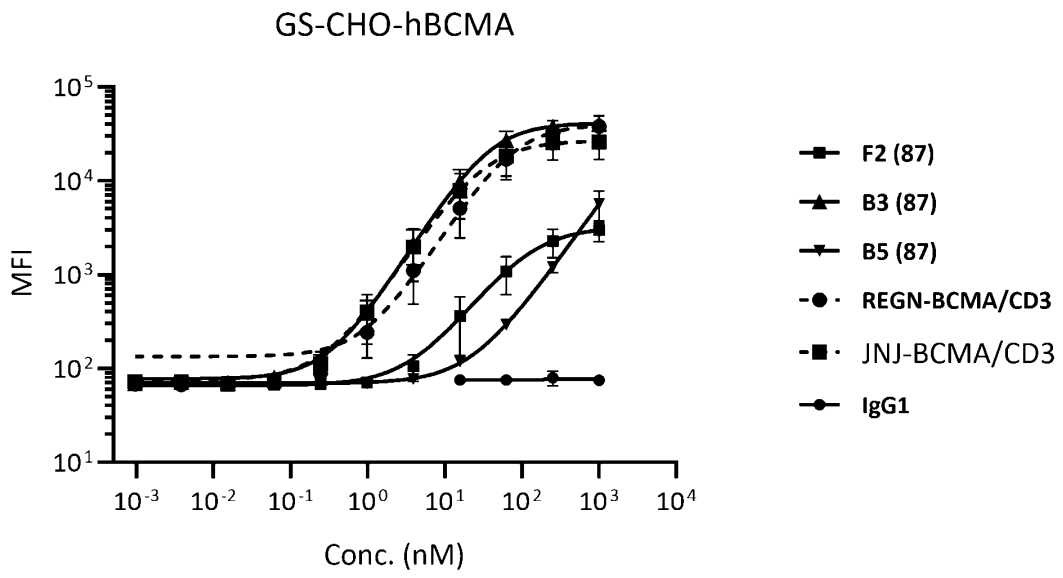

GS-CHO-hBCMA
MFI
Conc. (nM)
F2 (87)
B3 (87)
B5 (87)
REGN-BCMA/CD3
JNJ-BCMA/CD3
IgG1

图 2A

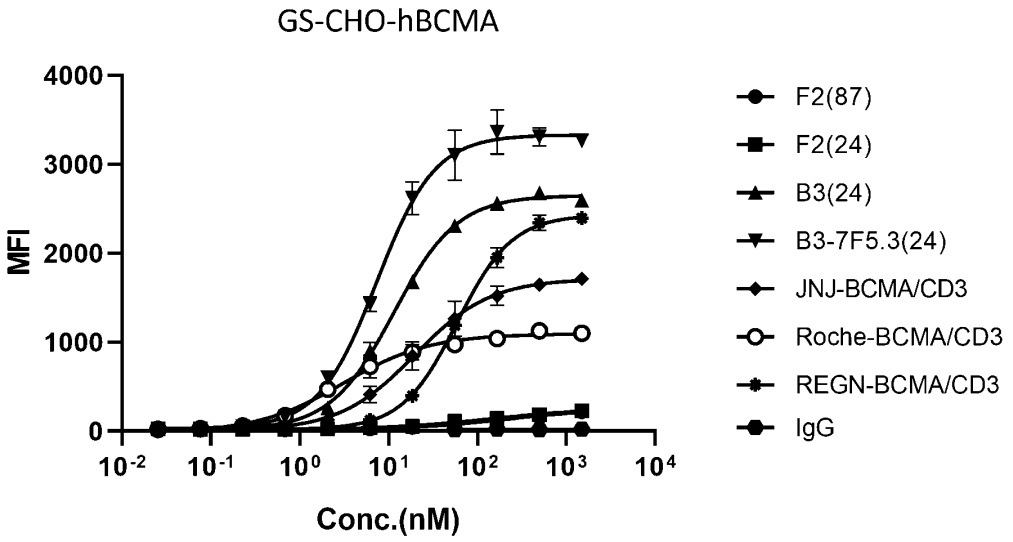

GS-CHO-hBCMA
MFI
Conc.(nM)
F2(87)
F2(24)
B3(24)
B3-7F5.3(24)
JNJ-BCMA/CD3
Roche-BCMA/CD3
REGN-BCMA/CD3
IgG

图 2B

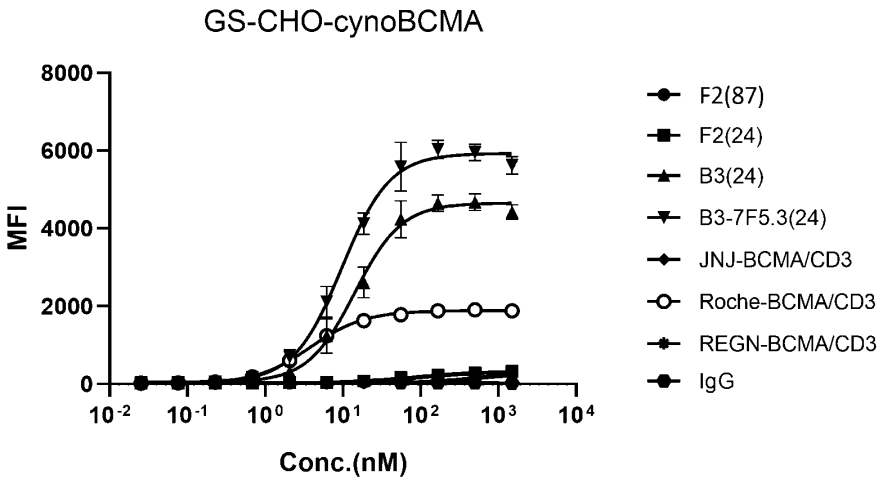

GS-CHO-cynoBCMA
MFI
8000
6000
4000
2000
0
10-2
10-1
100
101
102
103
104
Conc.(nM)
F2(87)
F2(24)
B3(24)
B3-7F5.3(24)
JNJ-BCMA/CD3
Roche-BCMA/CD3
REGN-BCMA/CD3
IgG

图 2C

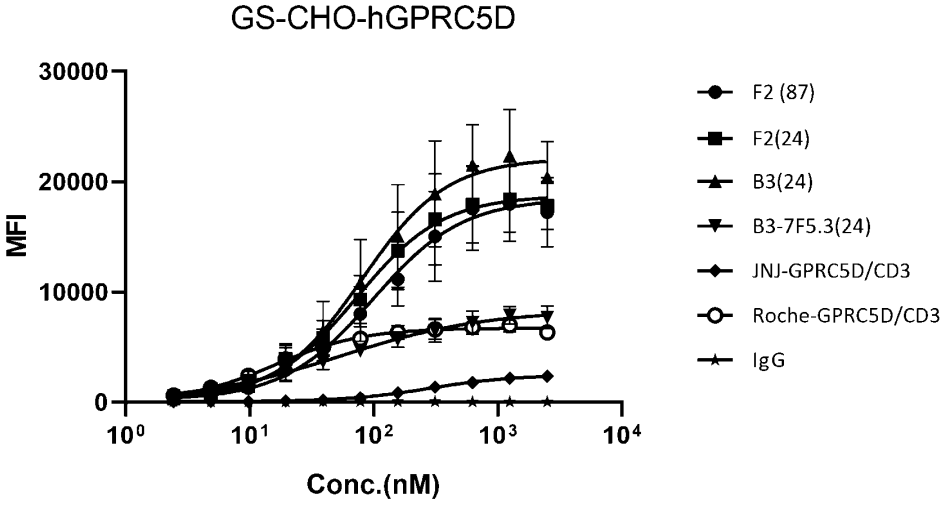

GS-CHO-hGPRC5D
MFI
30000
20000
10000
0
100
101
102
103
104
Conc.(nM)
F2 (87)
F2(24)
B3(24)
B3-7F5.3(24)
JNJ-GPRC5D/CD3
Roche-GPRC5D/CD3
IgG

图 2D

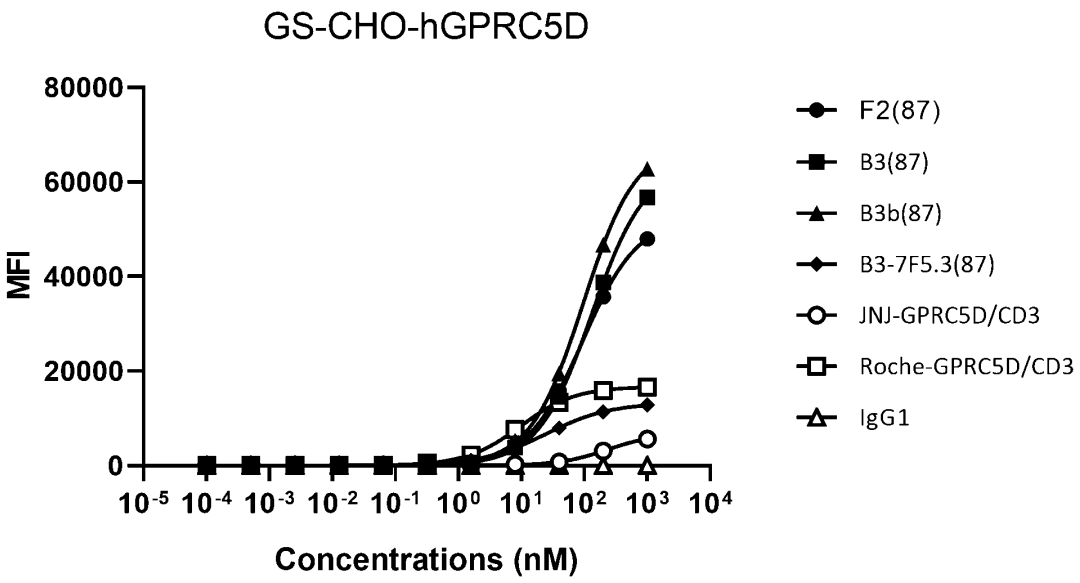

GS-CHO-hGPRC5D
MFI
80000
60000
40000
20000
0
10-5 10-4 10-3 10-2 10-1 100 101 102 103 104
Concentrations (nM)
F2(87)
B3(87)
B3b(87)
B3-7F5.3(87)
JNJ-GPRC5D/CD3
Roche-GPRC5D/CD3
IgG1

图 2E

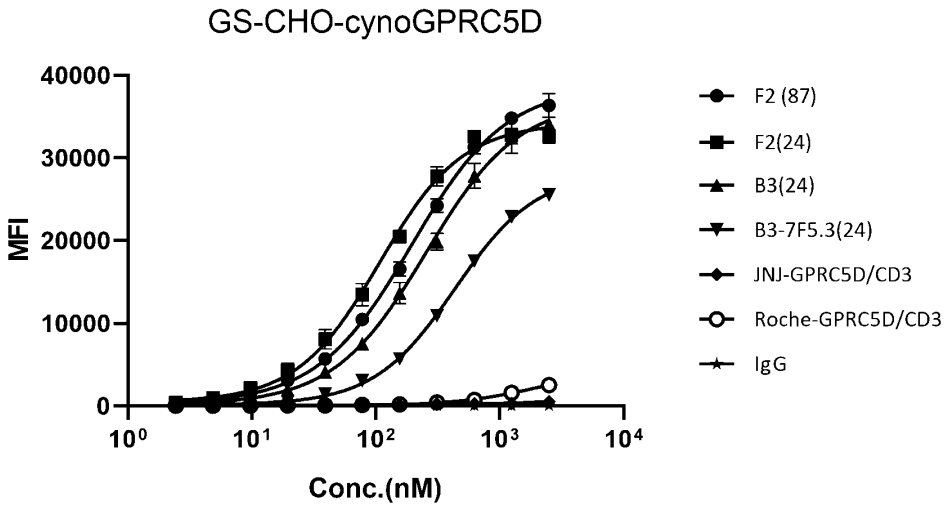

GS-CHO-cynoGPRC5D
MFI
40000
30000
20000
10000
0
100 101 102 103 104
Conc.(nM)
F2 (87)
F2(24)
B3(24)
B3-7F5.3(24)
JNJ-GPRC5D/CD3
Roche-GPRC5D/CD3
IgG

图 2F

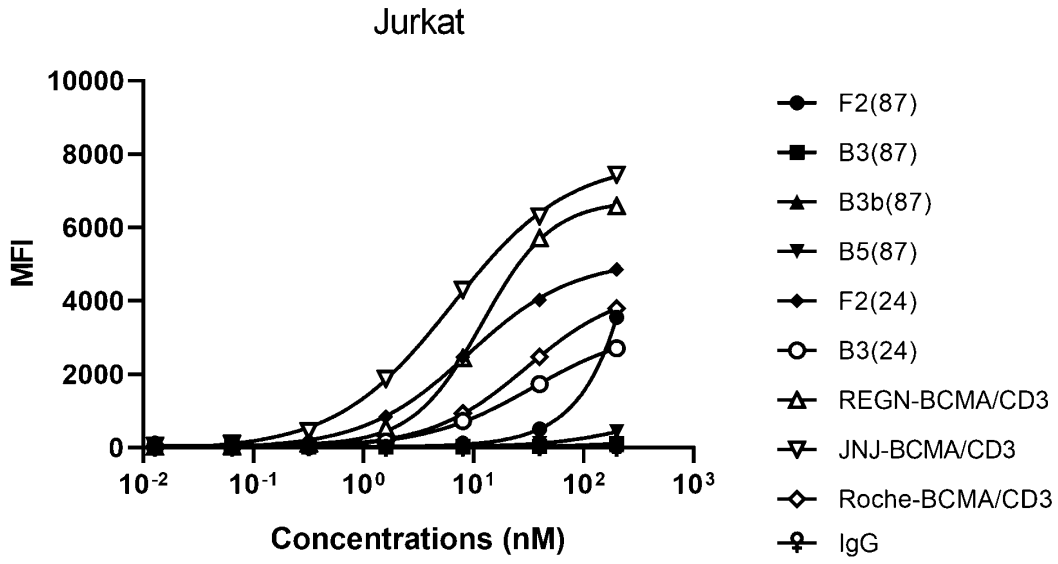

Jurkat
MFI
10000
8000
6000
4000
2000
0
10-2
10-1
100
101
102
103
Concentrations (nM)
F2(87)
B3(87)
B3b(87)
B5(87)
F2(24)
B3(24)
REGN-BCMA/CD3
JNJ-BCMA/CD3
Roche-BCMA/CD3
IgG

图 2G

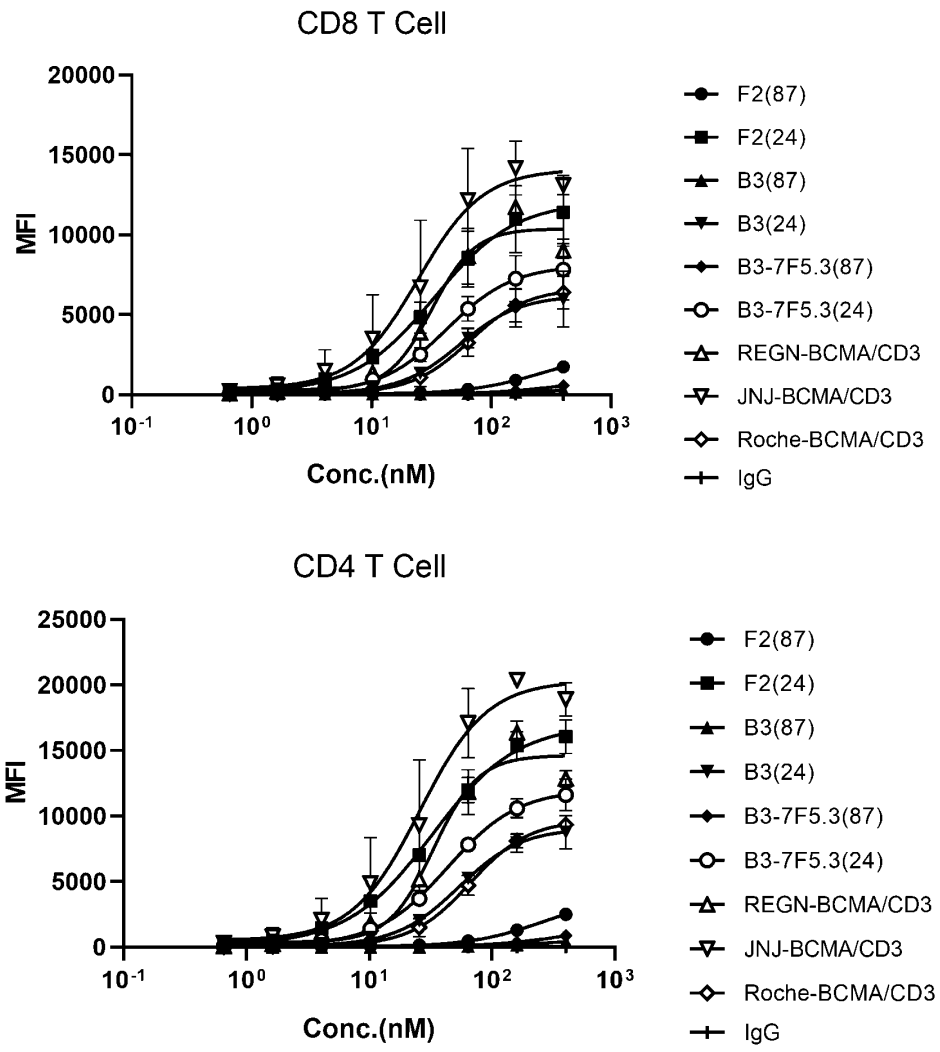
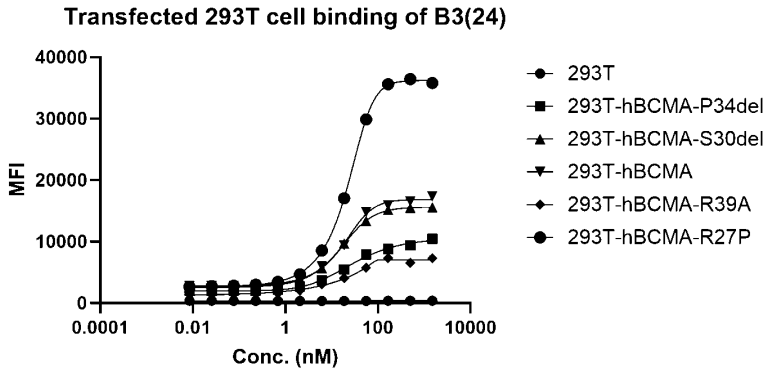
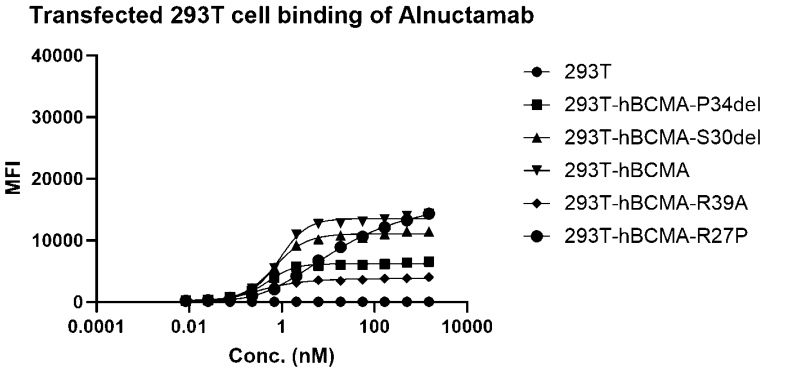

CD8 T Cell
MFI
20000
15000
10000
5000
0
10-1
100
101
102
103
Conc.(nM)
F2(87)
F2(24)
B3(87)
B3(24)
B3-7F5.3(87)
B3-7F5.3(24)
REGN-BCMA/CD3
JNJ-BCMA/CD3
Roche-BCMA/CD3
IgG
CD4 T Cell
MFI
25000
20000
15000
10000
5000
0
10-1
100
101
102
103
Conc.(nM)
F2(87)
F2(24)
B3(87)
B3(24)
B3-7F5.3(87)
B3-7F5.3(24)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

图 2H

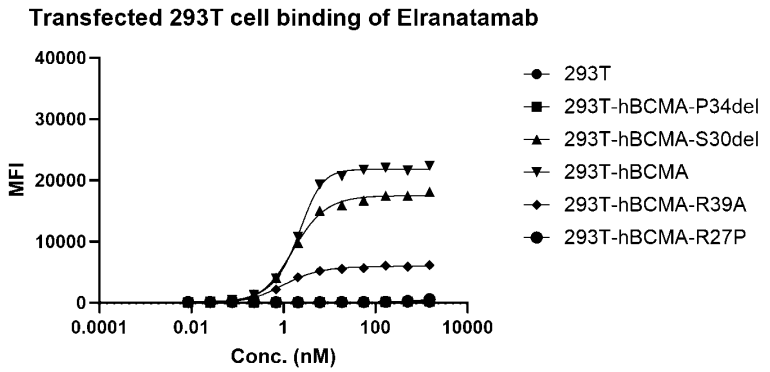


	293T	293T-hBCMA-P34del	293T-hBCMA-S30del	293T-hBCMA	293T-hBCMA-R39A	293T-hBCMA-R27P
EC50	316.9	26.90	16.26	18.95	21.36	22.86

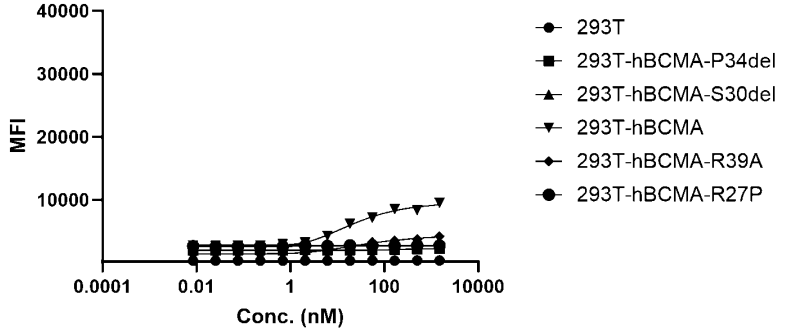


	293T	293T-hBCMA-P34del	293T-hBCMA-S30del	293T-hBCMA	293T-hBCMA-R39A	293T-hBCMA-R27P
EC50	0.000	0.4737	0.6858	0.8747	0.3973	12.88

图 21

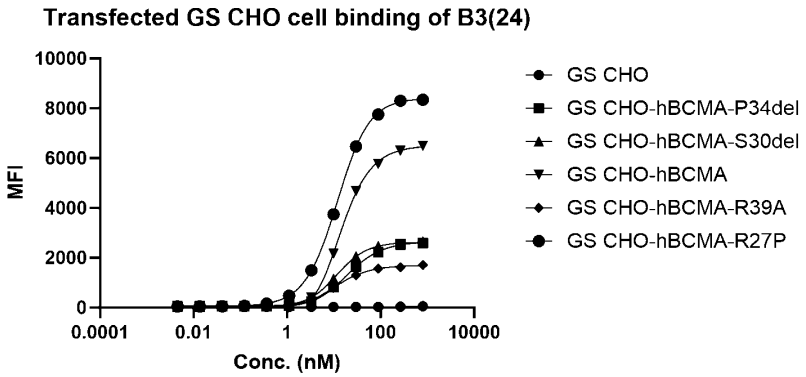


	293T	293T-hBCMA-P34del	293T-hBCMA-S30del	293T-hBCMA	293T-hBCMA-R39A	293T-hBCMA-R27P
EC50	164.1	363.7	1.690	2.059	1.095	145051090

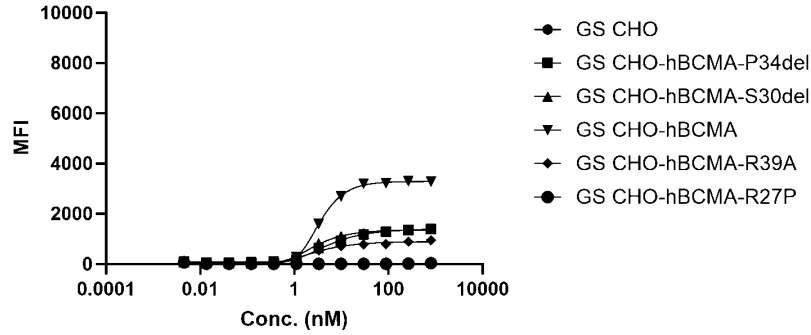


	293T	293T-hBCMA-P34del	293T-hBCMA-S30del	293T-hBCMA	293T-hBCMA-R39A	293T-hBCMA-R27P
EC50	3606	228.6	0.000	21.87	37.24	1.815

图 21（续）

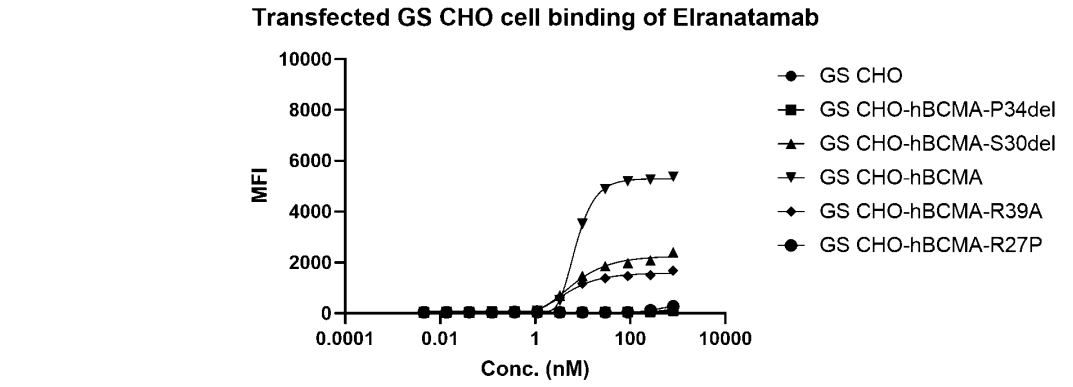


	GS CHO	GS CHO-hBCMA-P34del	GS CHO-hBCMA-S30del	GS CHO-hBCMA	GS CHO-hBCMA-R39A	GS CHO-hBCMA-R27P
EC50	350.1	20.18	11.91	15.66	11.28	11.74

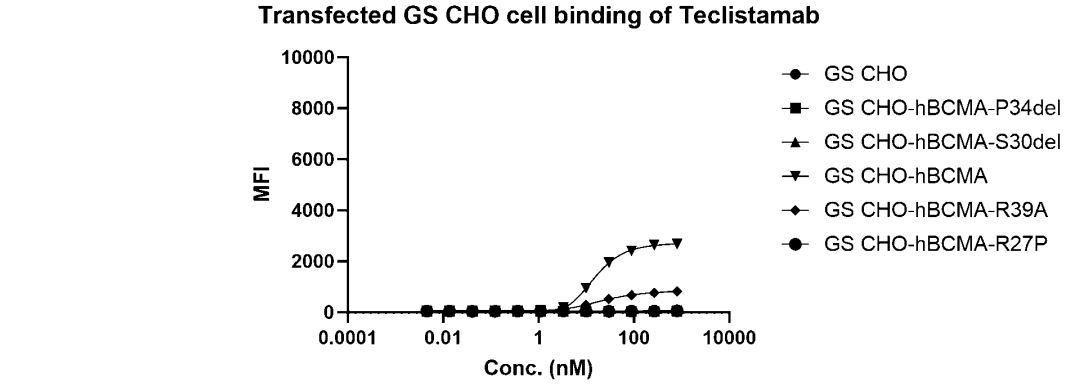


	GS CHO	GS CHO-hBCMA-P34del	GS CHO-hBCMA-S30del	GS CHO-hBCMA	GS CHO-hBCMA-R39A	GS CHO-hBCMA-R27P
EC50	0.004658	4.810	2.691	3.542	2.728	+infinity

图 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

图 2J(续)

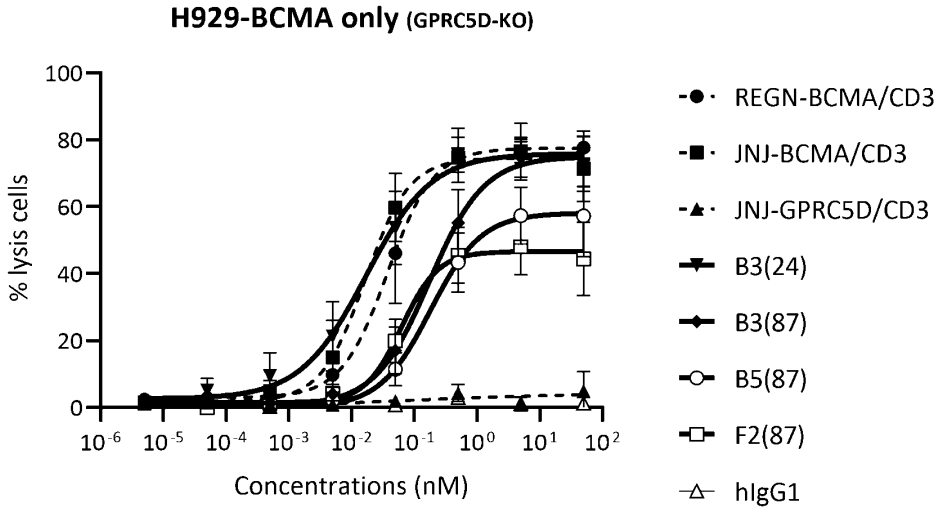

H929-BCMA only (GPRC5D-KO)
% lysis cells
100
80
60
40
20
0
10^{-6} 10^{-5} 10^{-4} 10^{-3} 10^{-2} 10^{-1} 10^{0} 10^{1} 10^{2}
Concentrations (nM)
REGN-BCMA/CD3
JNJ-BCMA/CD3
JNJ-GPRC5D/CD3
B3(24)
B3(87)
B5(87)
F2(87)
hIgG1

图 3A

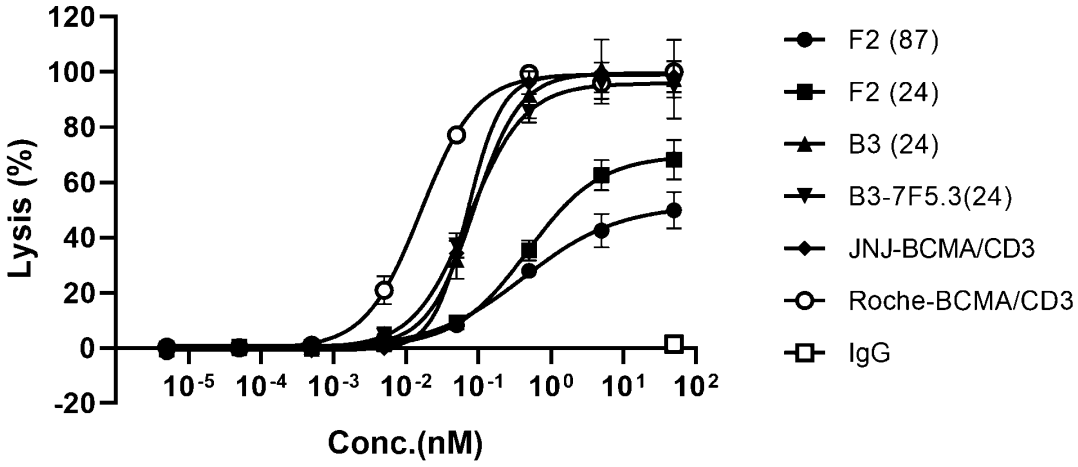

Lysis (%)
120
100
80
60
40
20
0
-20
10^{-5} 10^{-4} 10^{-3} 10^{-2} 10^{-1} 10^{0} 10^{1} 10^{2}
Conc.(nM)
F2 (87)
F2 (24)
B3 (24)
B3-7F5.3(24)
JNJ-BCMA/CD3
Roche-BCMA/CD3
IgG

图 3B

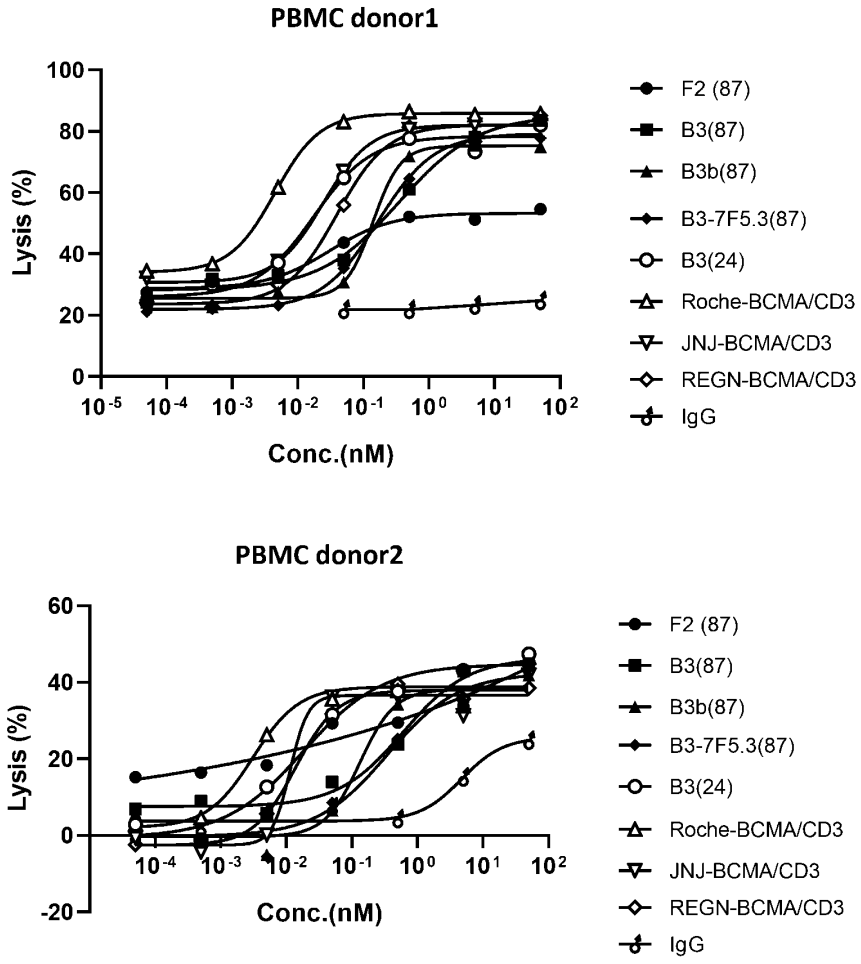

PBMC donor1
Lysis (%)
100
80
60
40
20
0
10-5 10-4 10-3 10-2 10-1 100 101 102
Conc.(nM)
F2 (87)
B3(87)
B3b(87)
B3-7F5.3(87)
B3(24)
Roche-BCMA/CD3
JNJ-BCMA/CD3
REGN-BCMA/CD3
IgG
PBMC donor2
Lysis (%)
60
40
20
0
-20
10-4 10-3 10-2 10-1 100 101 102
Conc.(nM)
F2 (87)
B3(87)
B3b(87)
B3-7F5.3(87)
B3(24)
Roche-BCMA/CD3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

图 3C

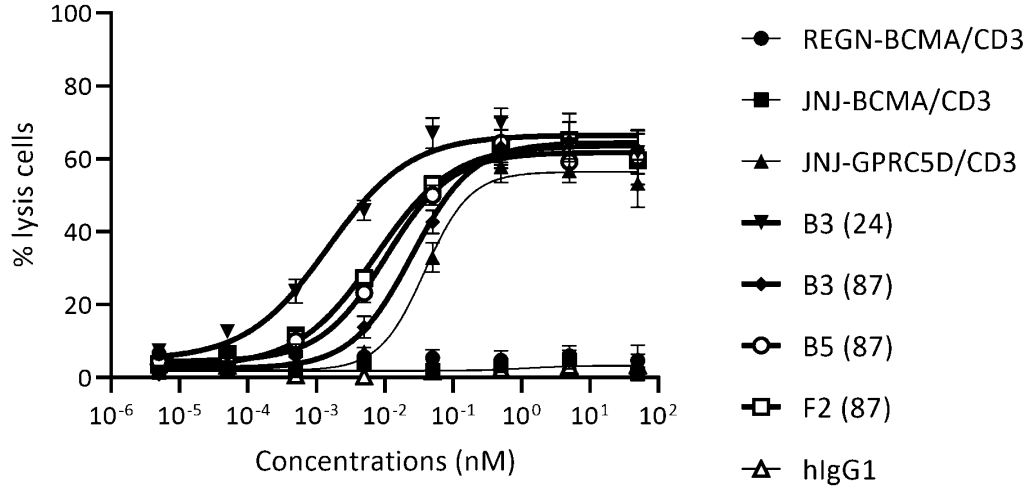

100
80
60
40
20
0
% lysis cells
10-6 10-5 10-4 10-3 10-2 10-1 100 101 102
Concentrations (nM)
REGN-BCMA/CD3
JNJ-BCMA/CD3
JNJ-GPRC5D/CD3
B3 (24)
B3 (87)
B5 (87)
F2 (87)
hIgG1

图 3D

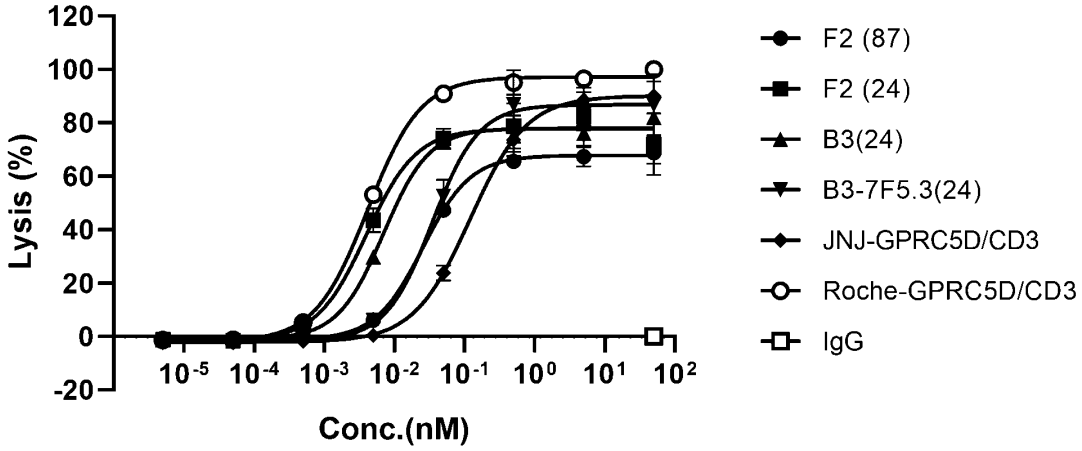

120
100
80
60
40
20
0
-20
Lysis (%)
10-5 10-4 10-3 10-2 10-1 100 101 102
Conc.(nM)
F2 (87)
F2 (24)
B3(24)
B3-7F5.3(24)
JNJ-GPRC5D/CD3
Roche-GPRC5D/CD3
IgG

图 3E

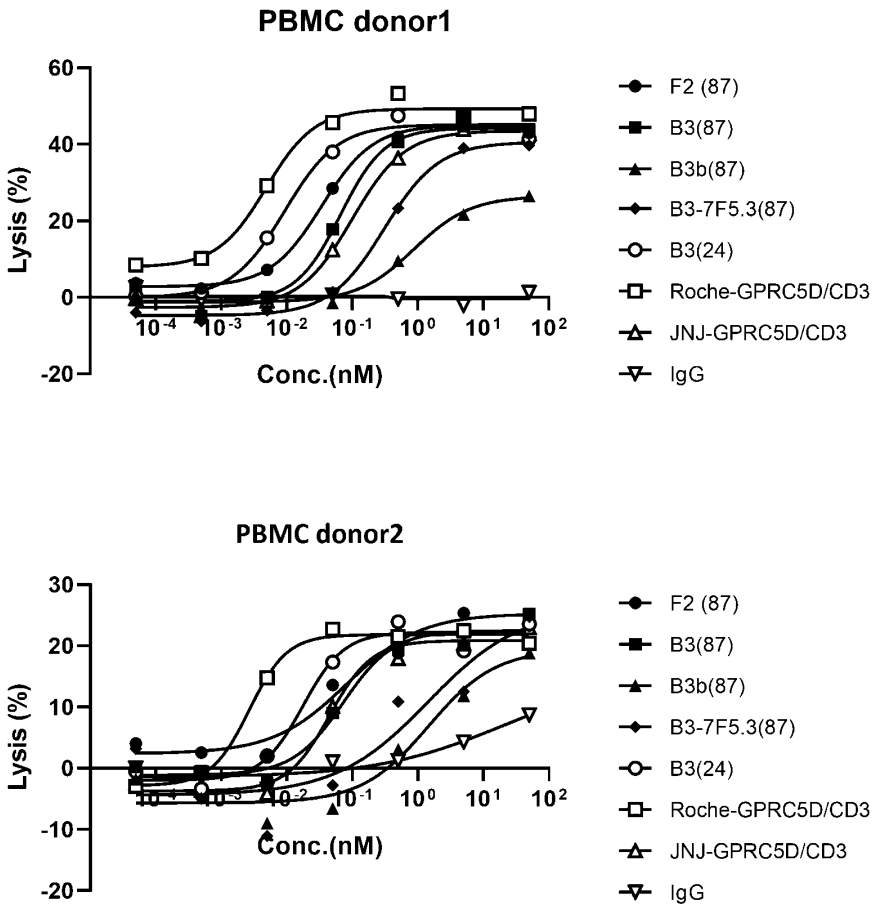

PBMC donor1
Lysis (%)
60
40
20
0
-20
10-4 10-3 10-2 10-1 100 101 102
Conc.(nM)
F2 (87)
B3(87)
B3b(87)
B3-7F5.3(87)
B3(24)
Roche-GPRC5D/CD3
JNJ-GPRC5D/CD3
IgG
PBMC donor2
Lysis (%)
30
20
10
0
-10
-20
Conc.(nM)
F2 (87)
B3(87)
B3b(87)
B3-7F5.3(87)
B3(24)
Roche-GPRC5D/CD3
JNJ-GPRC5D/CD3
IgG

图 3F

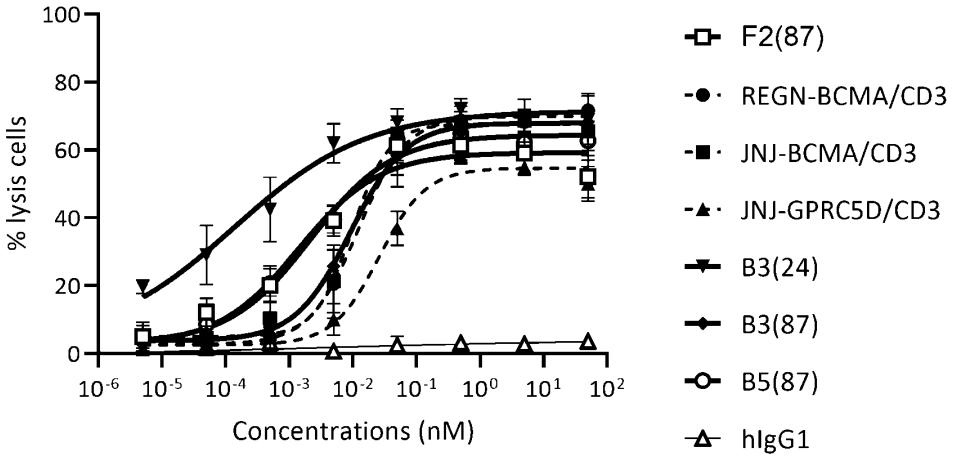

100
80
60
40
20
0
% lysis cells
10-6 10-5 10-4 10-3 10-2 10-1 100 101 102
Concentrations (nM)
F2(87)
REGN-BCMA/CD3
JNJ-BCMA/CD3
JNJ-GPRC5D/CD3
B3(24)
B3(87)
B5(87)
hIgG1

图 3G

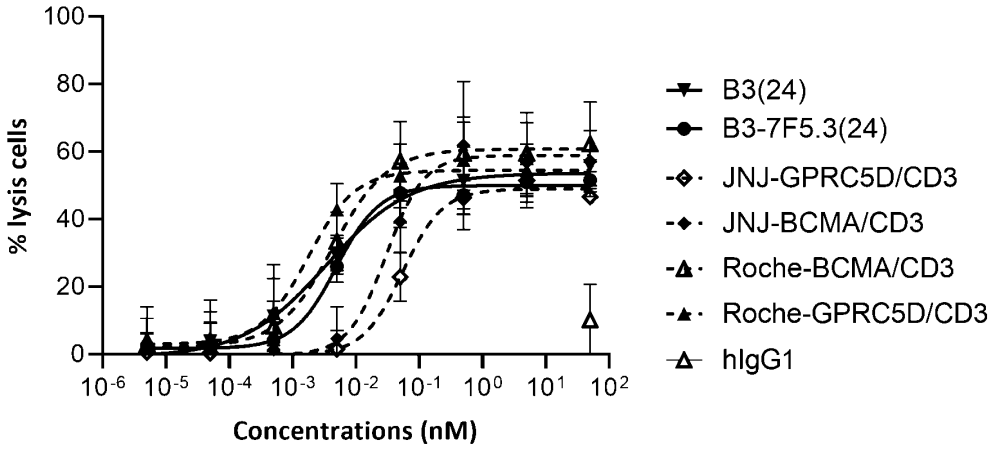

100
80
60
40
20
0
% lysis cells
10-6 10-5 10-4 10-3 10-2 10-1 100 101 102
Concentrations (nM)
B3(24)
B3-7F5.3(24)
JNJ-GPRC5D/CD3
JNJ-BCMA/CD3
Roche-BCMA/CD3
Roche-GPRC5D/CD3
hIgG1

图 3H

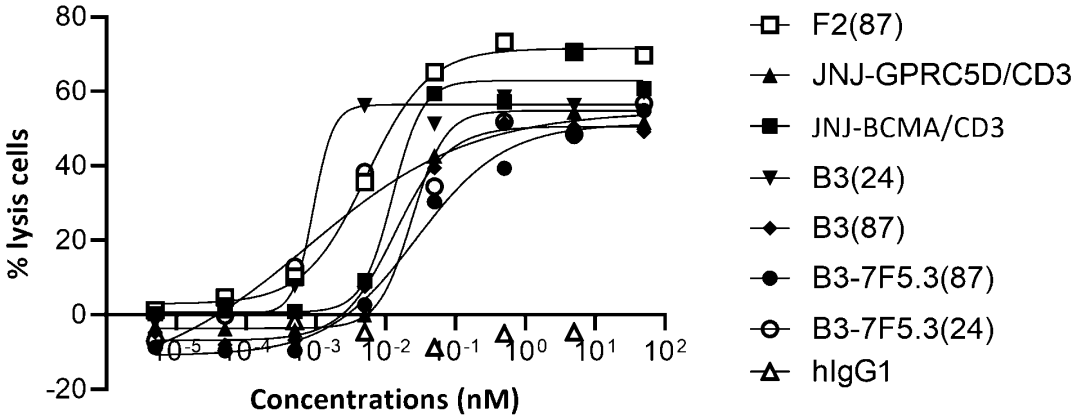

80
60
40
20
0
-20
% lysis cells
10-5 10-4 10-3 10-2 10-1 100 101 102
Concentrations (nM)
F2(87)
JNJ-GPRC5D/CD3
JNJ-BCMA/CD3
B3(24)
B3(87)
B3-7F5.3(87)
B3-7F5.3(24)
hIgG1

图 3I

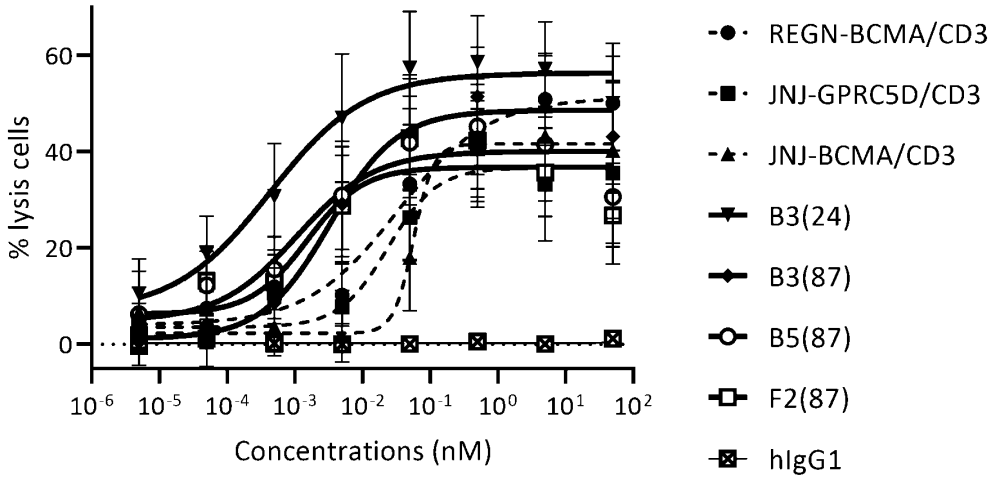

60
40
20
0
% lysis cells
10-6 10-5 10-4 10-3 10-2 10-1 100 101 102
Concentrations (nM)
REGN-BCMA/CD3
JNJ-GPRC5D/CD3
JNJ-BCMA/CD3
B3(24)
B3(87)
B5(87)
F2(87)
hIgG1

图 3J

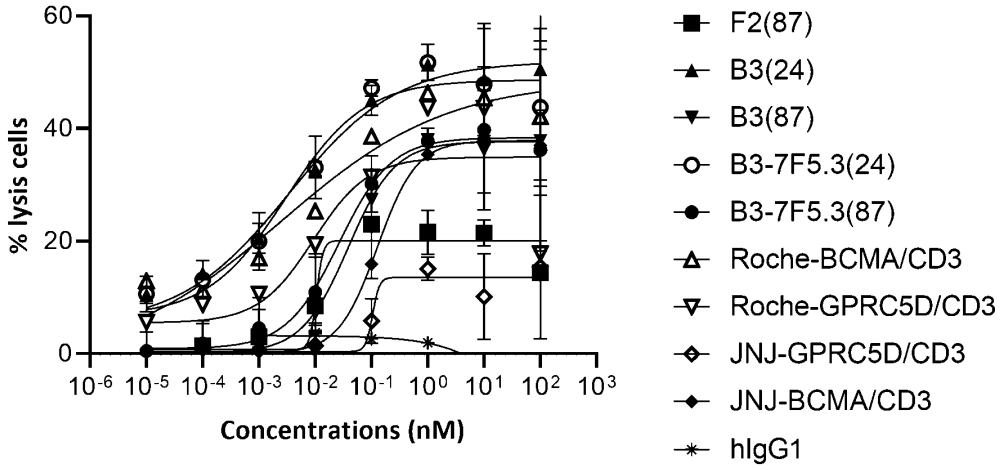

% lysis cells
60
40
20
0
10-6 10-5 10-4 10-3 10-2 10-1 100 101 102 103
Concentrations (nM)
F2(87)
B3(24)
B3(87)
B3-7F5.3(24)
B3-7F5.3(87)
Roche-BCMA/CD3
Roche-GPRC5D/CD3
JNJ-GPRC5D/CD3
JNJ-BCMA/CD3
hIgG1

图 3K

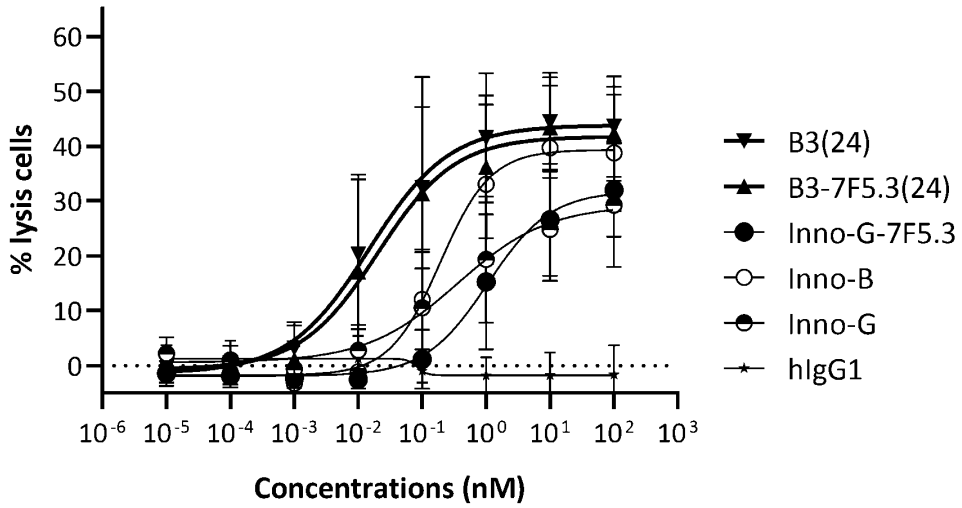

% lysis cells
60
50
40
30
20
10
0
10-6 10-5 10-4 10-3 10-2 10-1 100 101 102 103
Concentrations (nM)
B3(24)
B3-7F5.3(24)
Inno-G-7F5.3
Inno-B
Inno-G
hIgG1

图 3L

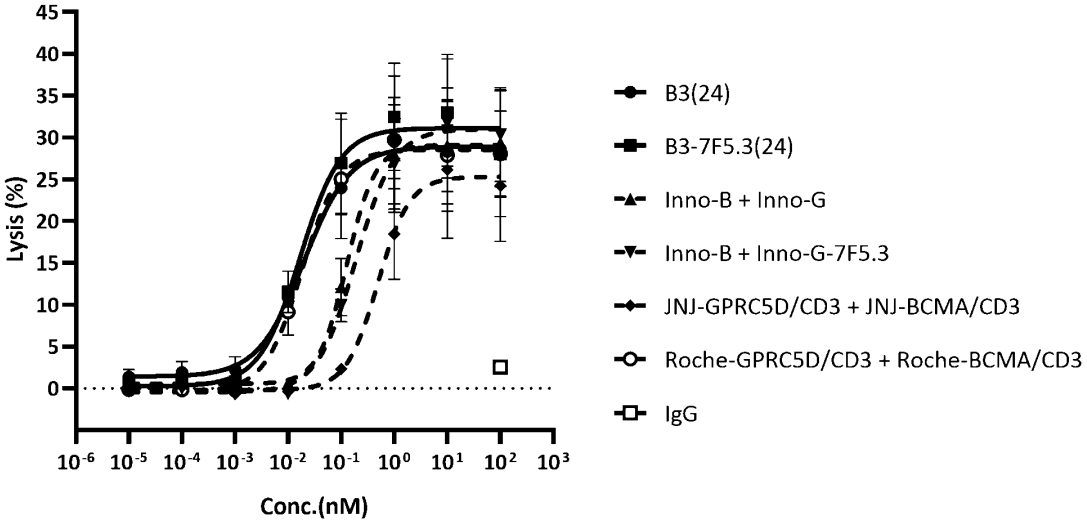

Lysis (%)
45
40
35
30
25
20
15
10
5
0
10^{-6} 10^{-5} 10^{-4} 10^{-3} 10^{-2} 10^{-1} 10^{0} 10^{1} 10^{2} 10^{3}
Conc.(nM)
B3(24)
B3-7F5.3(24)
Inno-B + Inno-G
Inno-B + Inno-G-7F5.3
JNJ-GPRC5D/CD3 + JNJ-BCMA/CD3
Roche-GPRC5D/CD3 + Roche-BCMA/CD3
IgG

图 3M

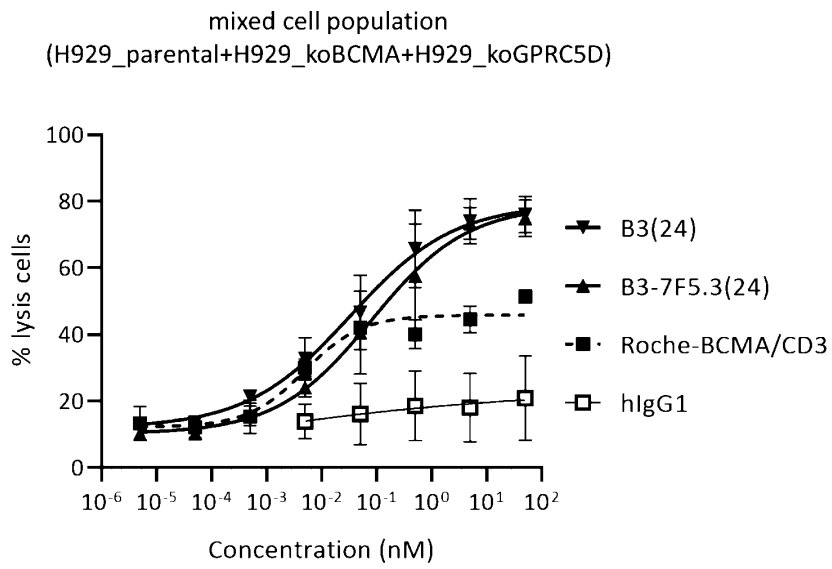

mixed cell population
(H929_parental+H929_koBCMA+H929_koGPRC5D)
% lysis cells
100
80
60
40
20
0
10^{-6} 10^{-5} 10^{-4} 10^{-3} 10^{-2} 10^{-1} 10^{0} 10^{1} 10^{2}
Concentration (nM)
B3(24)
B3-7F5.3(24)
Roche-BCMA/CD3
hIgG1

图 3N

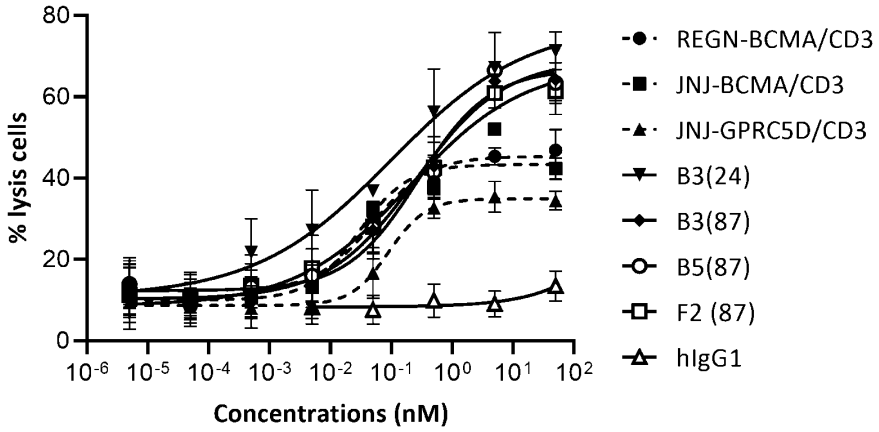

% lysis cells
Concentrations (nM)
REGN-BCMA/CD3
JNJ-BCMA/CD3
JNJ-GPRC5D/CD3
B3(24)
B3(87)
B5(87)
F2 (87)
hIgG1

图 30

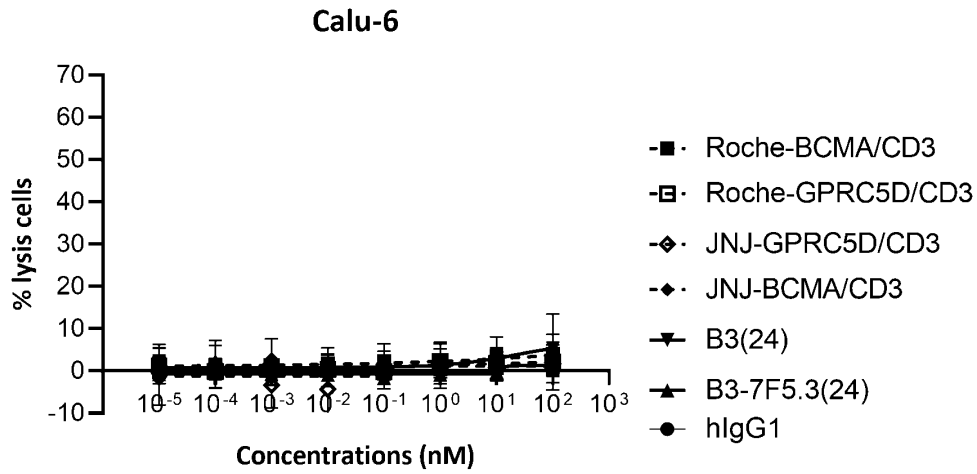

Calu-6
% lysis cells
Concentrations (nM)
Roche-BCMA/CD3
Roche-GPRC5D/CD3
JNJ-GPRC5D/CD3
JNJ-BCMA/CD3
B3(24)
B3-7F5.3(24)
hIgG1

图 3P

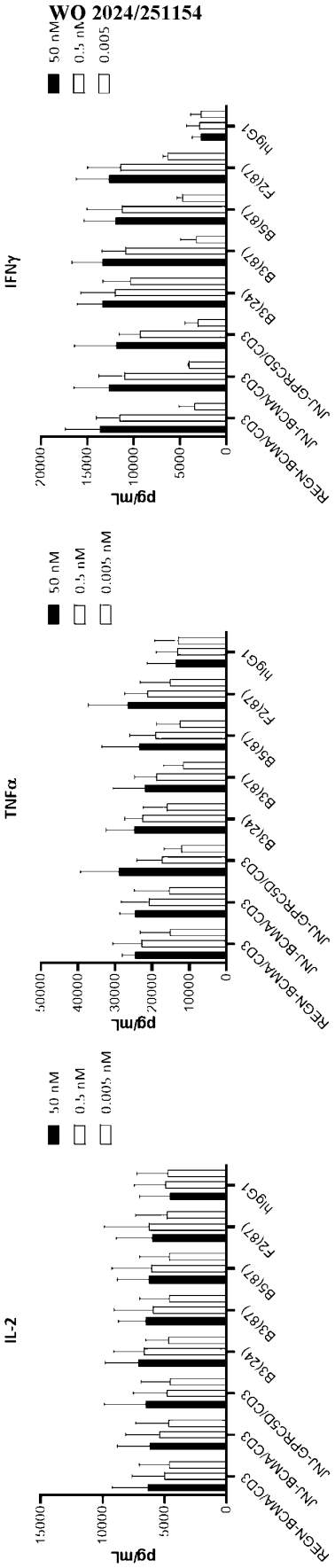

IL-2
TNFα
IFNγ
pg/mL
50 nM
0.5 nM
0.005 nM
REGN-BCMA/CD3
JNJ-BCMA/CD3
JNJ-GPRC5D/CD3
B3(24)
B3(87)
B5(87)
F2(87)
hIgG1

图 3Q

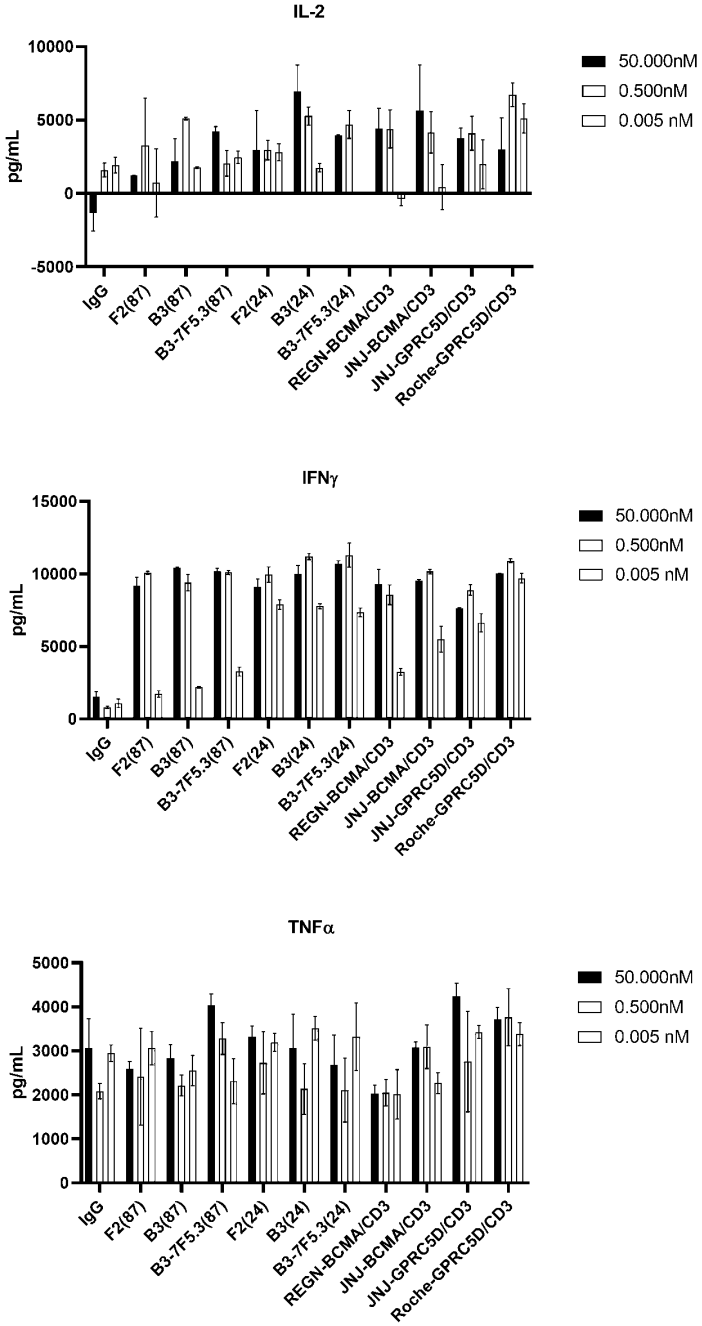

IL-2
10000
5000
0
-5000
pg/mL
50.000nM
0.500nM
0.005 nM
IgG
F2(87)
B3(87)
B3-7F5.3(87)
F2(24)
B3(24)
B3-7F5.3(24)
REGN-BCMA/CD3
JNJ-BCMA/CD3
JNJ-GPRC5D/CD3
Roche-GPRC5D/CD3
IFNγ
15000
10000
5000
0
pg/mL
50.000nM
0.500nM
0.005 nM
IgG
F2(87)
B3(87)
B3-7F5.3(87)
F2(24)
B3(24)
B3-7F5.3(24)
REGN-BCMA/CD3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

图 3R

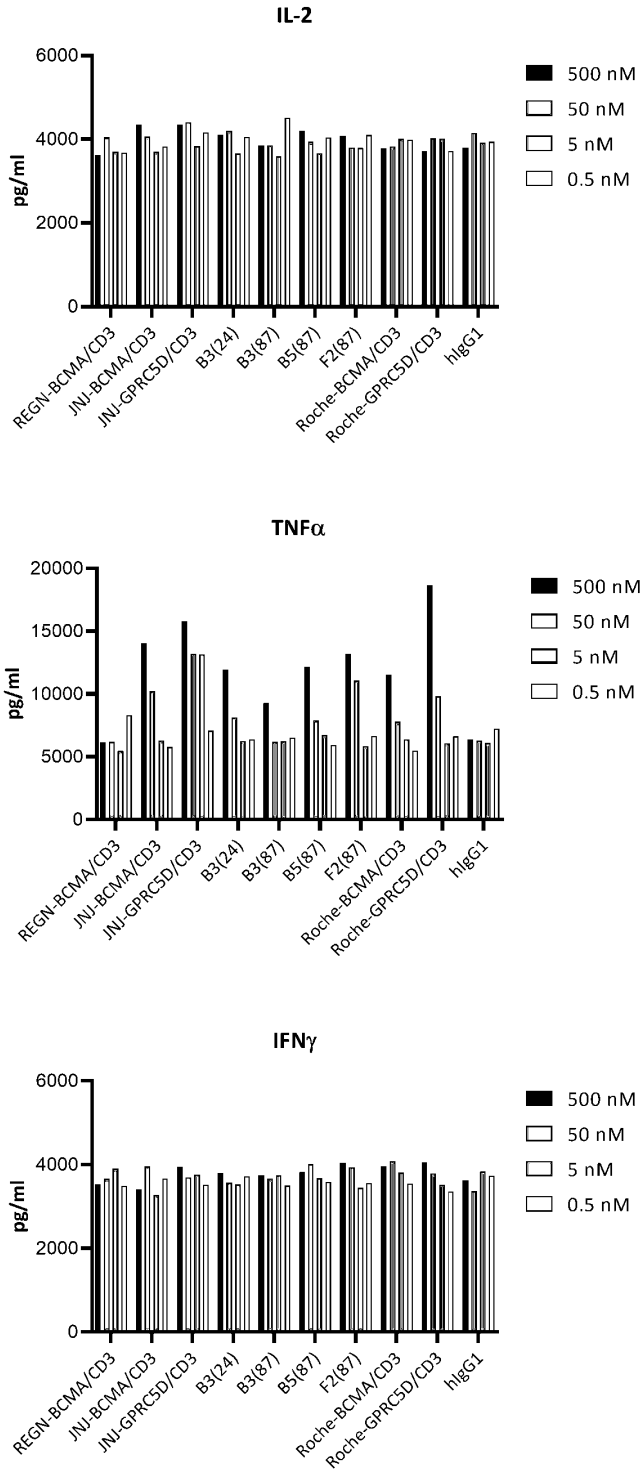

IL-2
6000
4000
2000
0
pg/ml
500 nM
50 nM
5 nM
0.5 nM
REGN-BCMA/CD3
JNJ-BCMA/CD3
JNJ-GPRC5D/CD3
B3(24)
B3(87)
B5(87)
F2(87)
Roche-BCMA/CD3
Roche-GPRC5D/CD3
hIgG1
TNFα
20000
15000
10000
5000
0
pg/ml
500 nM
50 nM
5 nM
0.5 nM
REGN-BCMA/CD3
JNJ-BCMA/CD3
JNJ-GPRC5D/CD3
B3(24)
B3(87)
B5(87)
F2(87)
Roche-BCMA/CD3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

图 3S

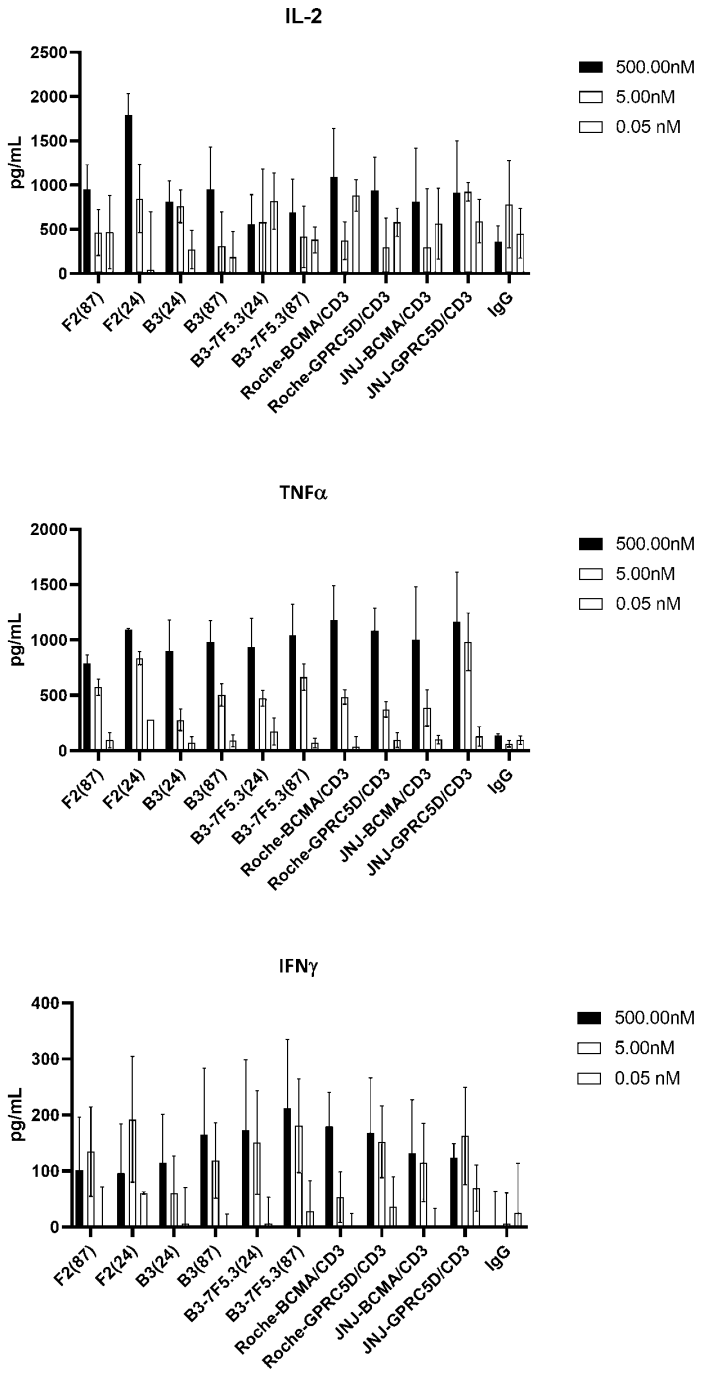
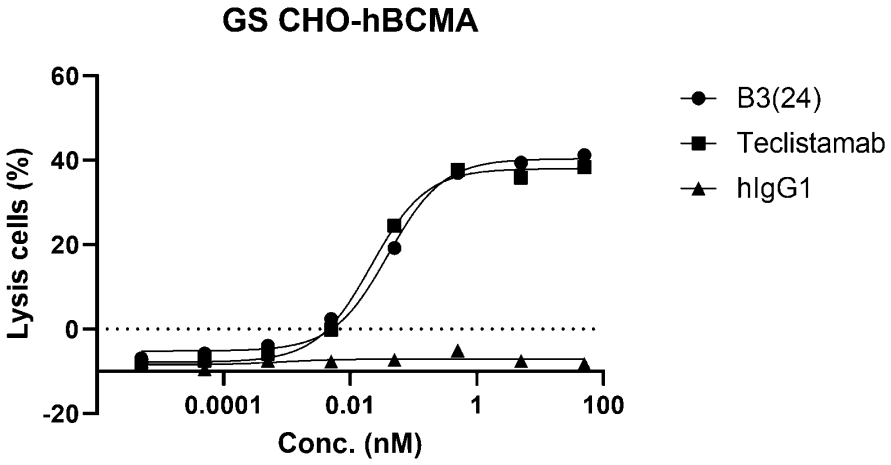
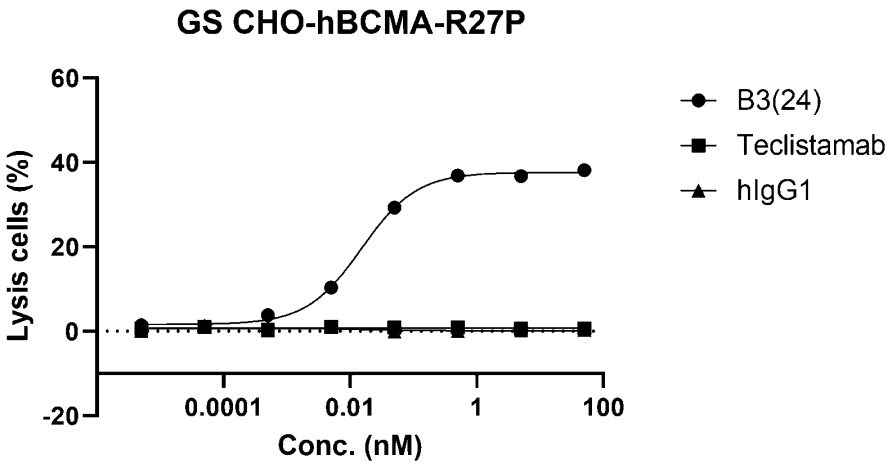

IL-2
pg/mL
2500
2000
1500
1000
500
0
500.00nM
5.00nM
0.05 nM
F2(87)
F2(24)
B3(24)
B3(87)
B3-7F5.3(24)
B3-7F5.3(87)
Roche-BCMA/CD3
Roche-GPRC5D/CD3
JNJ-BCMA/CD3
JNJ-GPRC5D/CD3
IgG
TNFα
pg/mL
2000
1500
1000
500
0
500.00nM
5.00nM
0.05 nM
F2(87)
F2(24)
B3(24)
B3(87)
B3-7F5.3(24)
B3-7F5.3(87)
Roche-BCMA/CD3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

图 3T

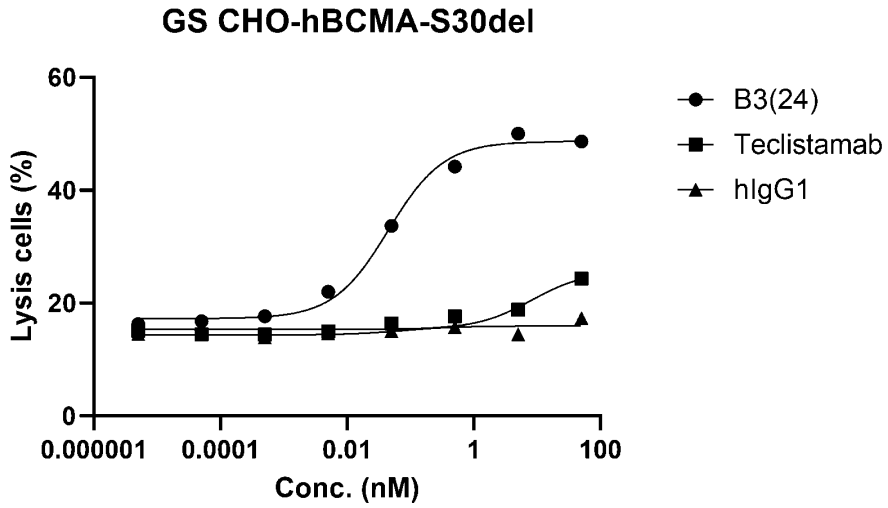


	B3(24)	Teclistamab
EC50	0.03971	0.02157

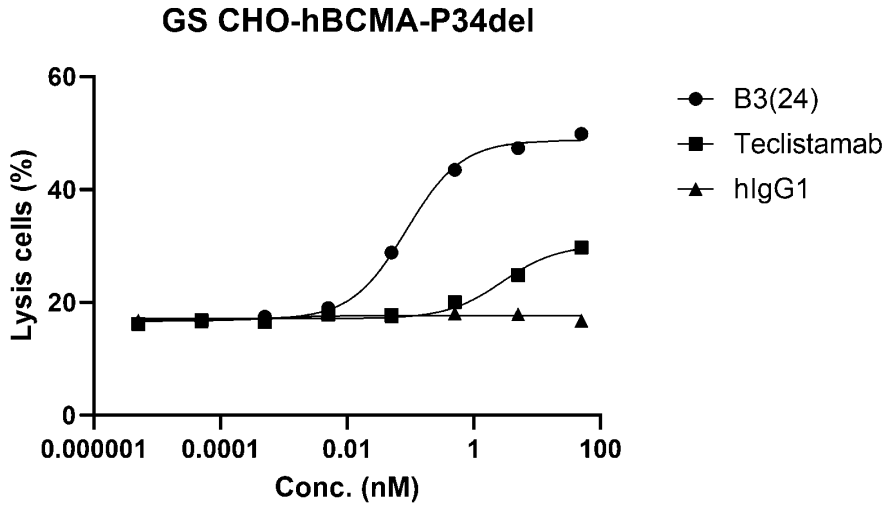


	B3(24)	Teclistamab
EC50	0.01519	0.001808

图 3U

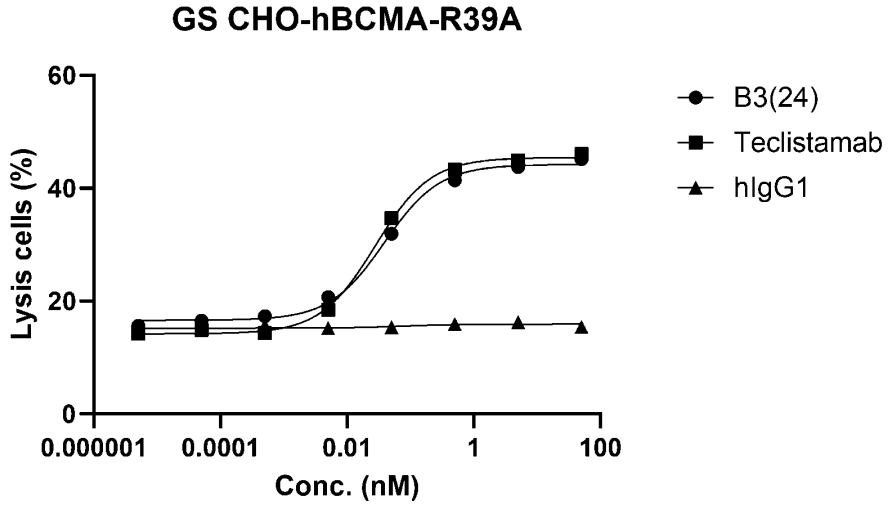


	B3(24)	Teclistamab
EC50	0.04496	8.156



	B3(24)	Teclistamab
EC50	0.08652	2.809

图 3U（续）



	B3(24)	Teclistamab
EC50	0.03884	0.02782

图 3U（续）

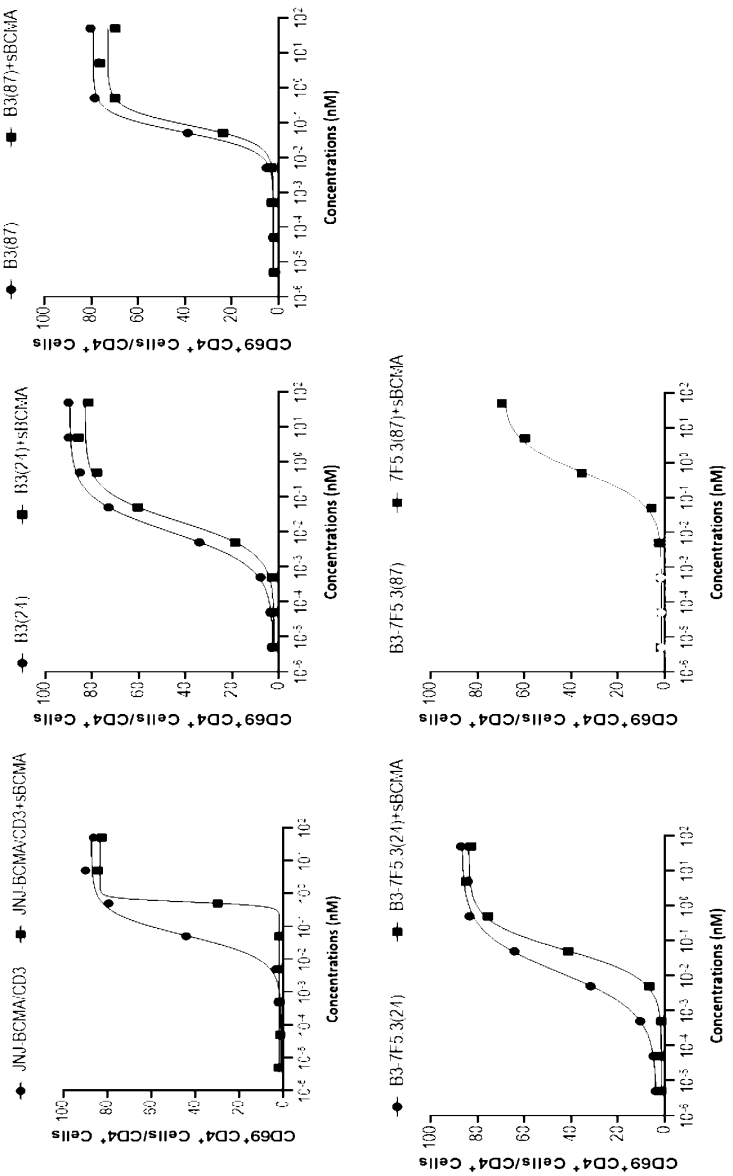

JNJ-BCMA/CD3
JNJ-BCMA/CD3+sBCMA
B3(24)
B3(24)+sBCMA
B3(87)
B3(87)+sBCMA
B3-7F5 3(24)
B3-7F5 3(24)+sBCMA
B3-7F5 3(87)
B3-7F5 3(87)+sBCMA
CD69+CD4+ cells/CD4+ cells
Concentrations (nM)

图 4A

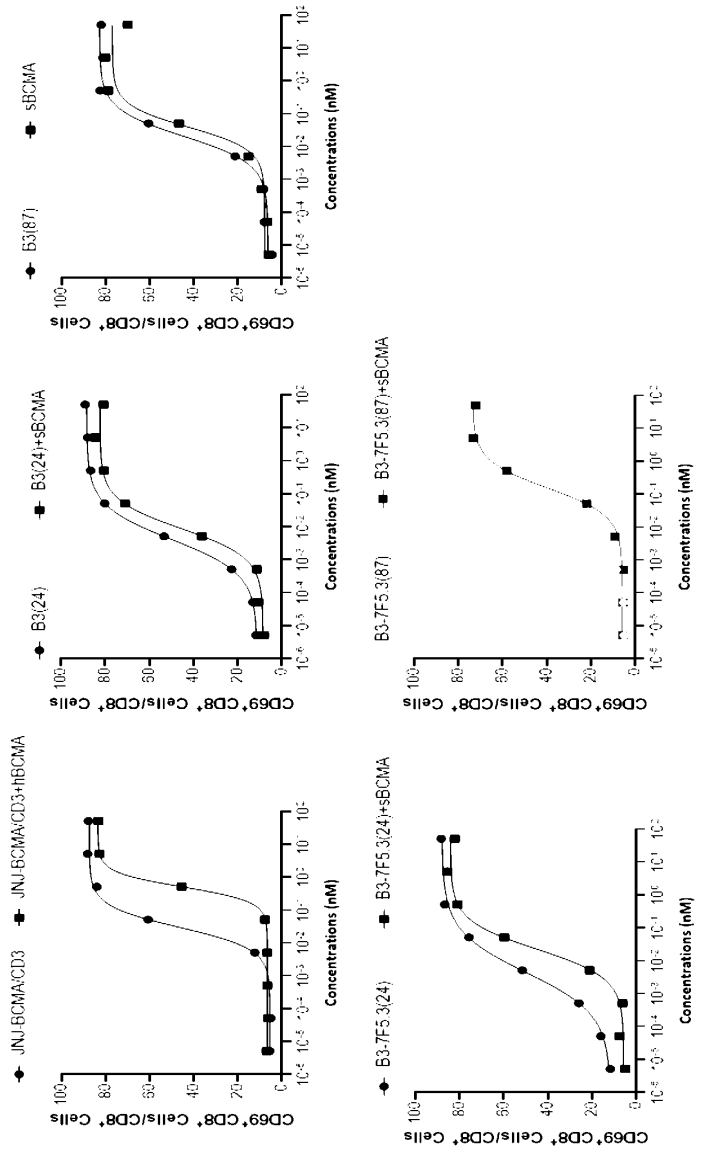

JNJ-BCMA/CD3
JNJ-BCMA/CD3+hBCMA
B3(87)
sBCMA
B3(24)
B3(24)+sBCMA
B3-7F5 3(87)
B3-7F5 3(87)+sBCMA
B3-7F5 3(24)
B3-7F5 3(24)+sBCMA
CD69+CD8+ cells/CD8+ cells
Concentrations (nM)

图 4B

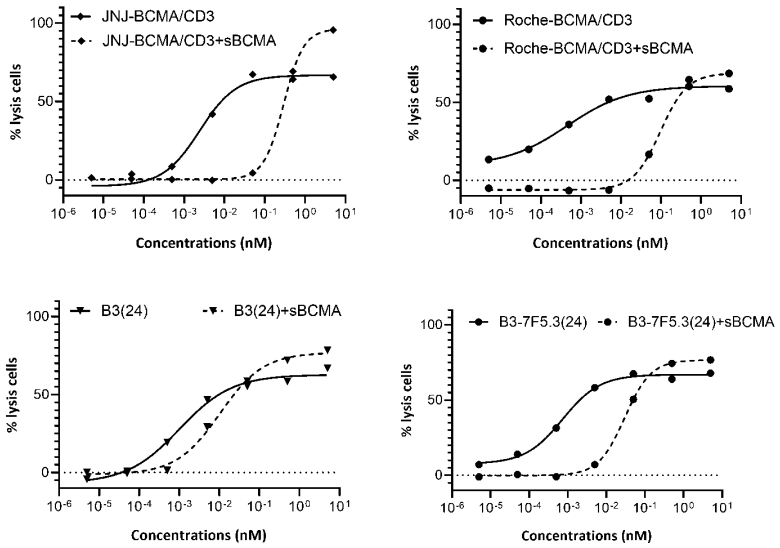

JNJ-BCMA/CD3
JNJ-BCMA/CD3+sBCMA
Roche-BCMA/CD3
Roche-BCMA/CD3+sBCMA
B3(24)
B3(24)+sBCMA
B3-7F5.3(24)
B3-7F5.3(24)+sBCMA
% lysis cells
Concentrations (nM)

图 4C

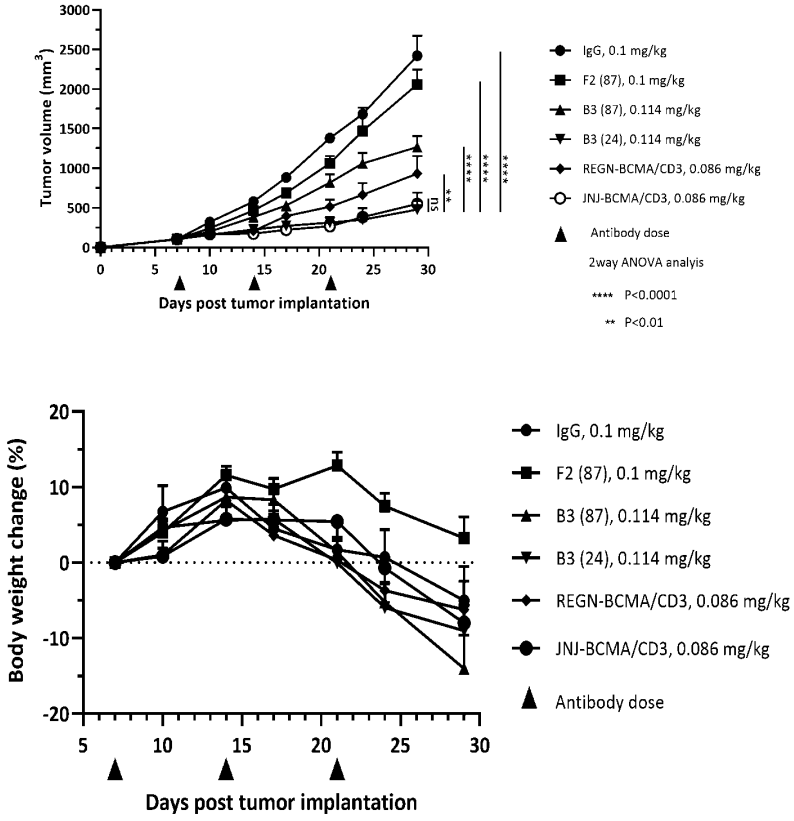

Tumor volume (mm3)
Days post tumor implantation
IgG, 0.1 mg/kg
F2 (87), 0.1 mg/kg
B3 (87), 0.114 mg/kg
B3 (24), 0.114 mg/kg
REGN-BCMA/CD3, 0.086 mg/kg
JNJ-BCMA/CD3, 0.086 mg/kg
Antibody dose
2way ANOVA analyis
**** P<0.0001
** P<0.01
Body weight change (%)
Days post tumor implantation

图 5A

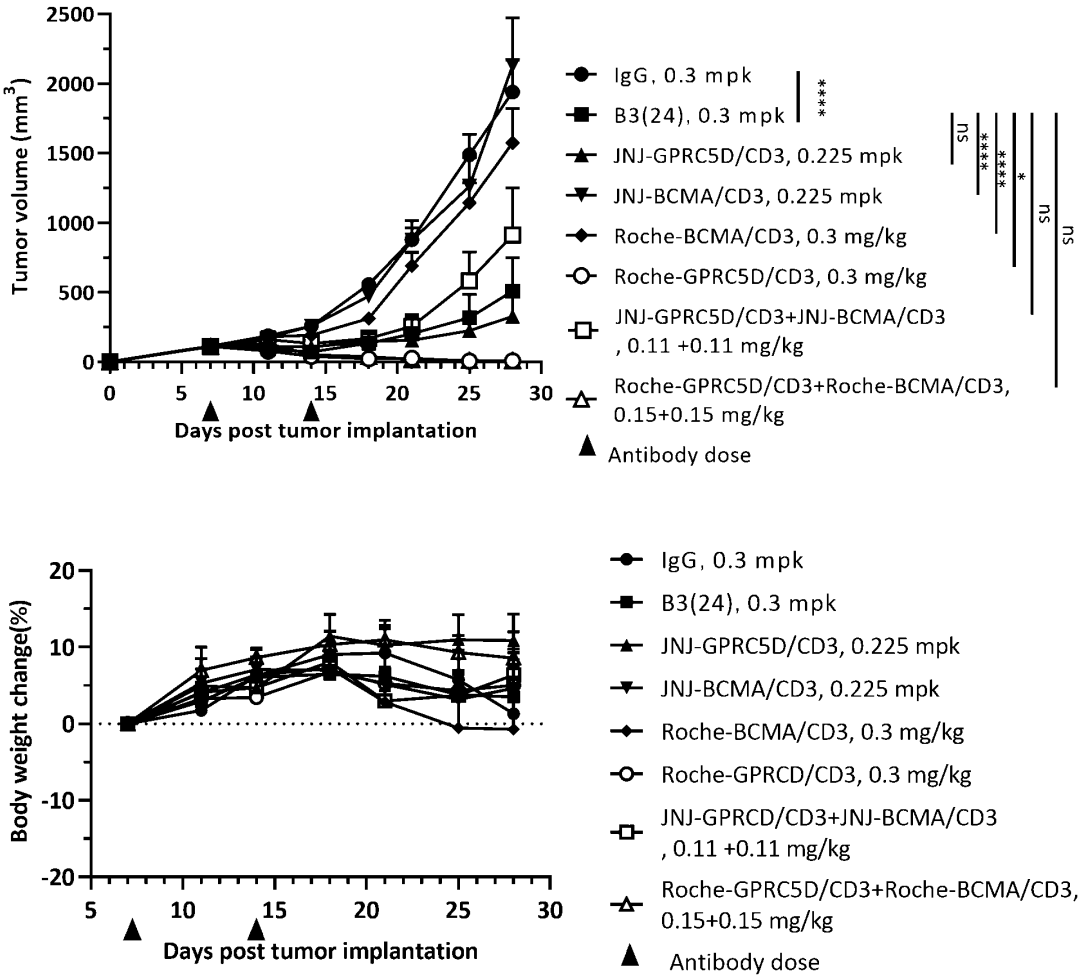

Tumor volume (mm3)
2500
2000
1500
1000
500
0
0 5 10 15 20 25 30
Days post tumor implantation
IgG, 0.3 mpk
B3(24), 0.3 mpk
JNJ-GPRC5D/CD3, 0.225 mpk
JNJ-BCMA/CD3, 0.225 mpk
Roche-BCMA/CD3, 0.3 mg/kg
Roche-GPRC5D/CD3, 0.3 mg/kg
JNJ-GPRC5D/CD3+JNJ-BCMA/CD3 , 0.11 +0.11 mg/kg
Roche-GPRC5D/CD3+Roche-BCMA/CD3, 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

图 5B

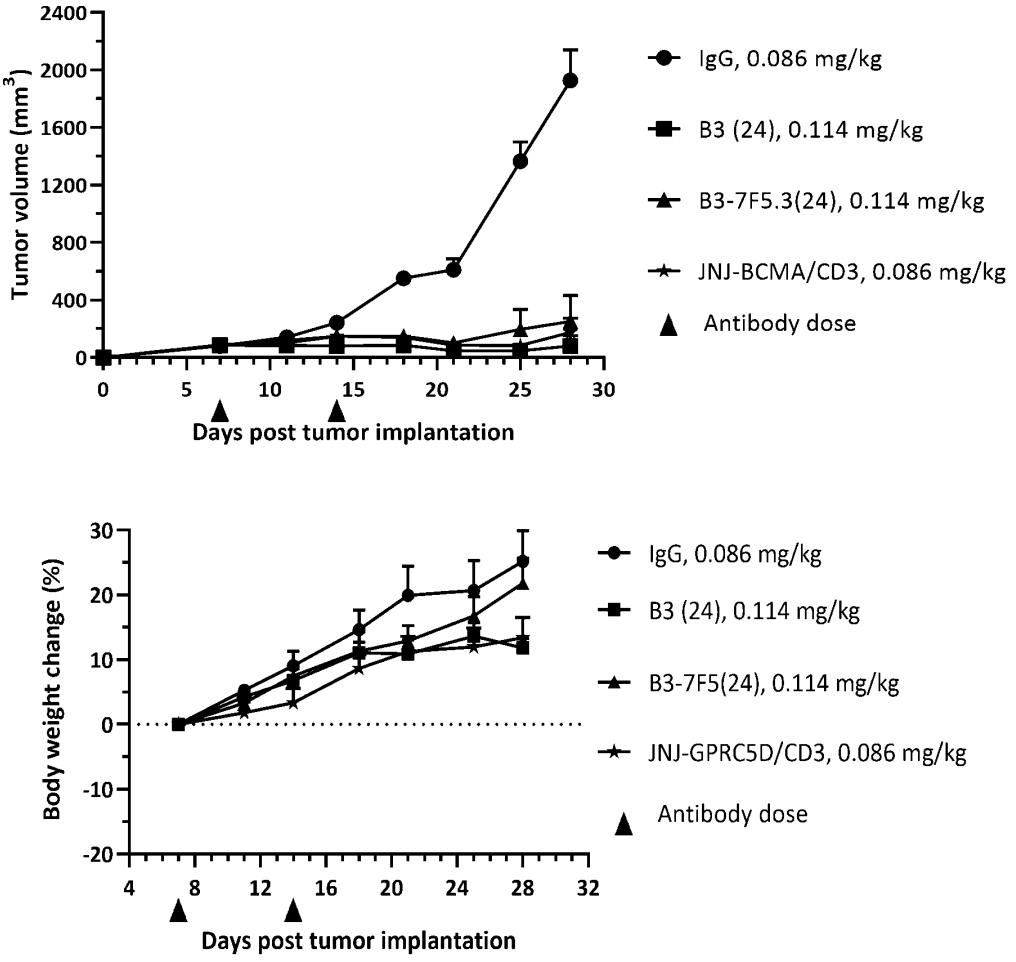

Tumor volume (mm3)
2400
2000
1600
1200
800
400
0
0
5
10
15
20
25
30
Days post tumor implantation
IgG, 0.086 mg/kg
B3 (24), 0.114 mg/kg
B3-7F5.3(24), 0.114 mg/kg
JNJ-BCMA/CD3, 0.086 mg/kg
Antibody dose
Body weight change (%)
30
20
10
0
-10
-20
4
8
12
16
20
24
28
32
Days post tumor implantation
IgG, 0.086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

图 5C

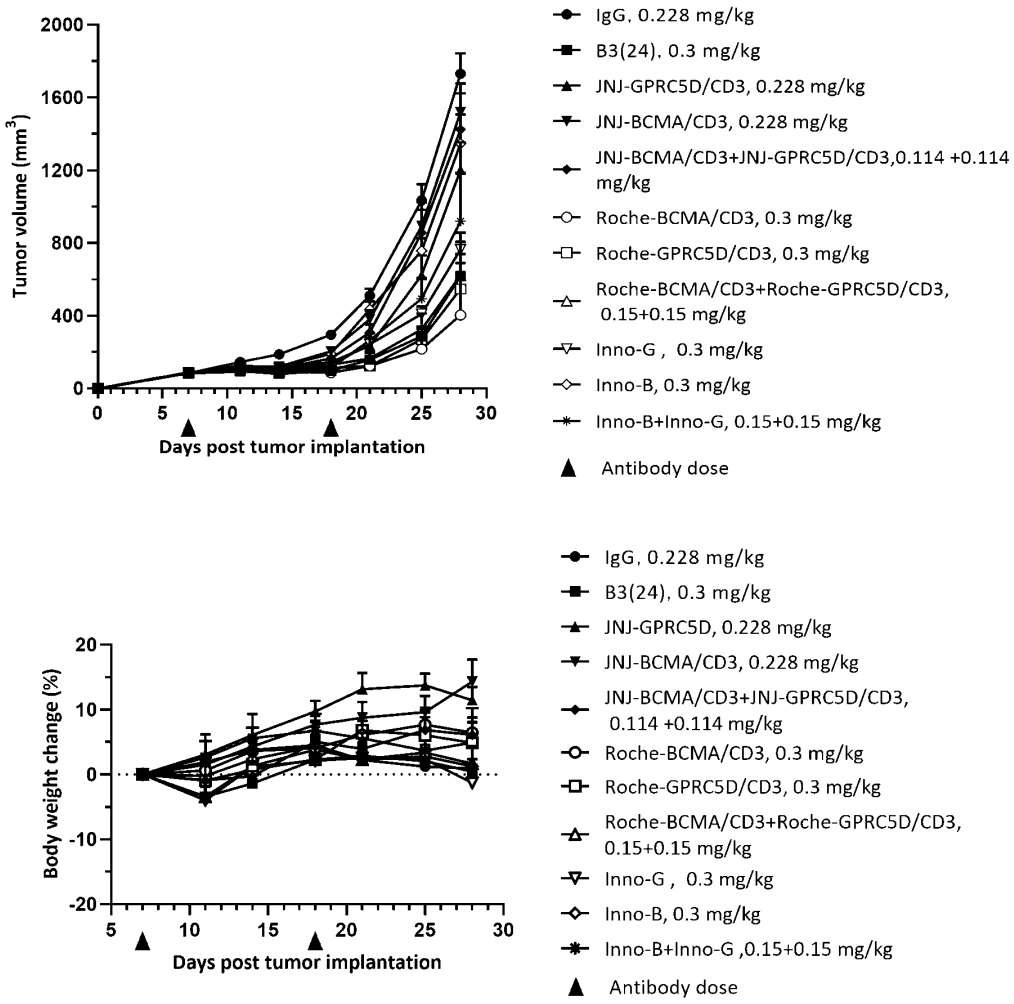

Tumor volume (mm3)
2000
1600
1200
800
400
0
0 5 10 15 20 25 30
Days post tumor implantation
IgG, 0.228 mg/kg
B3(24), 0.3 mg/kg
JNJ-GPRC5D/CD3, 0.228 mg/kg
JNJ-BCMA/CD3, 0.228 mg/kg
JNJ-BCMA/CD3+JNJ-GPRC5D/CD3,0.114 +0.114 mg/kg
Roche-BCMA/CD3, 0.3 mg/kg
Roche-GPRC5D/CD3, 0.3 mg/kg
Roche-BCMA/CD3+Roche-GPRC5D/CD3, 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

图 5D

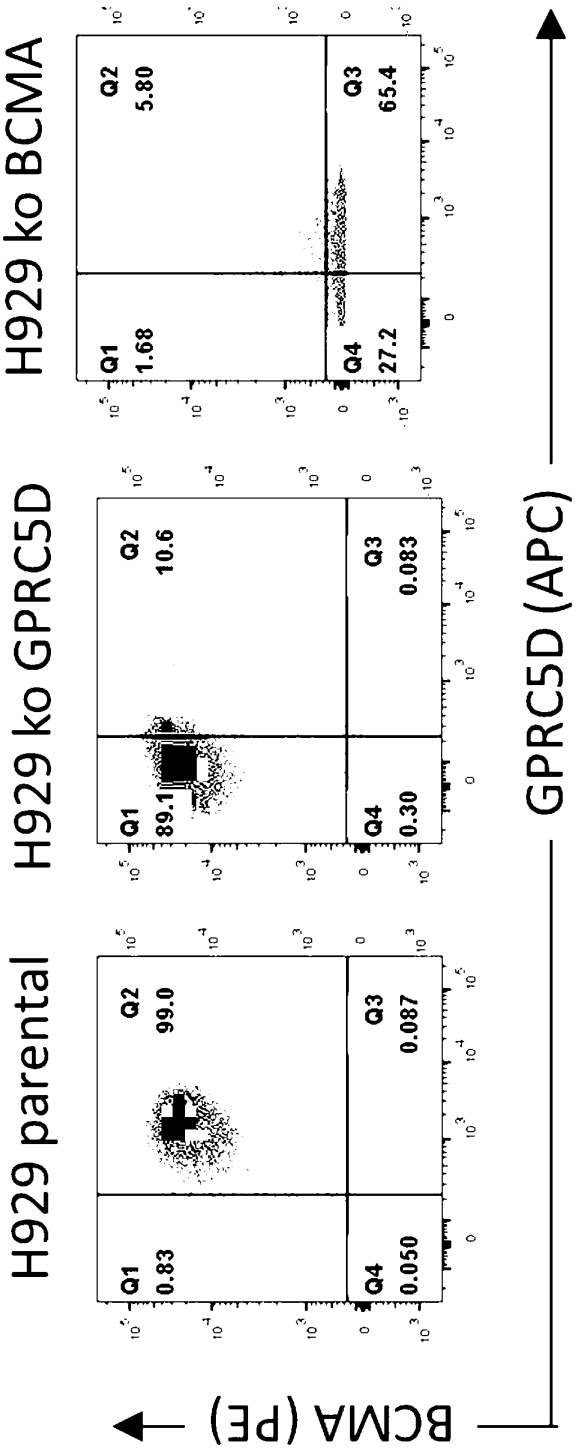

H929 parental
H929 ko GPRC5D
H929 ko BCMA
Q1 0.83
Q2 99.0
Q3 0.087
Q4 0.050
Q1 89.1
Q2 10.6
Q3 0.083
Q4 0.30
Q1 1.68
Q2 5.80
Q3 65.4
Q4 27.2
BCMA (PE)
GPRC5D (APC)

图 6

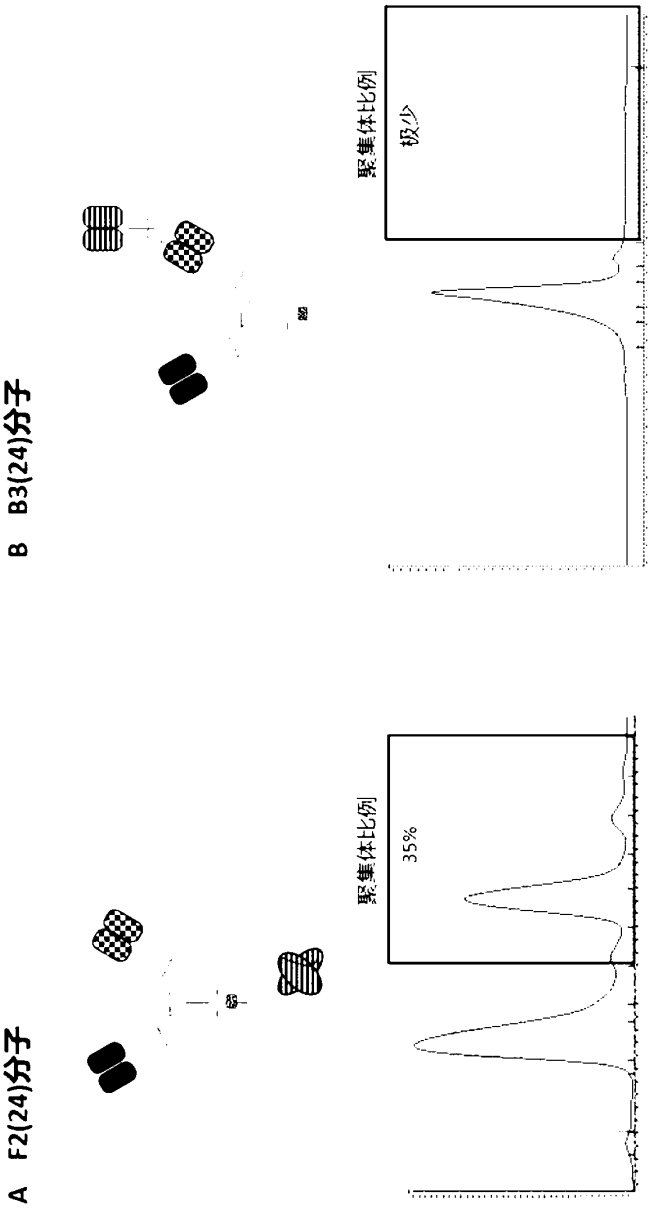


图 7