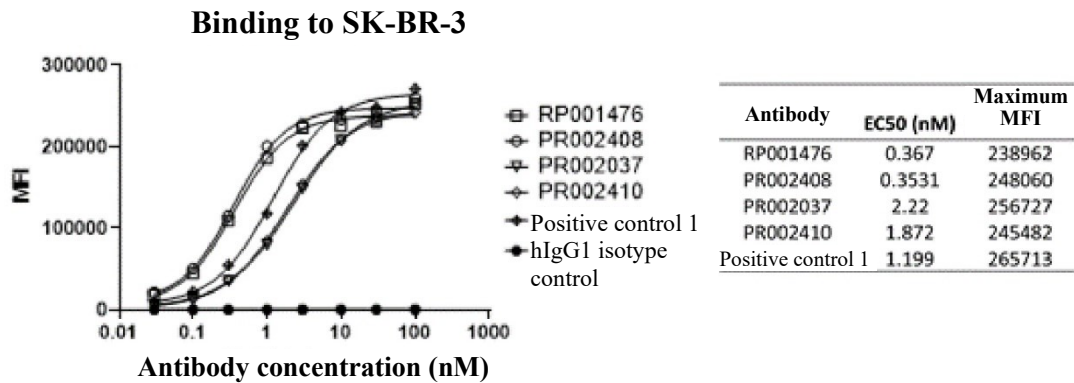
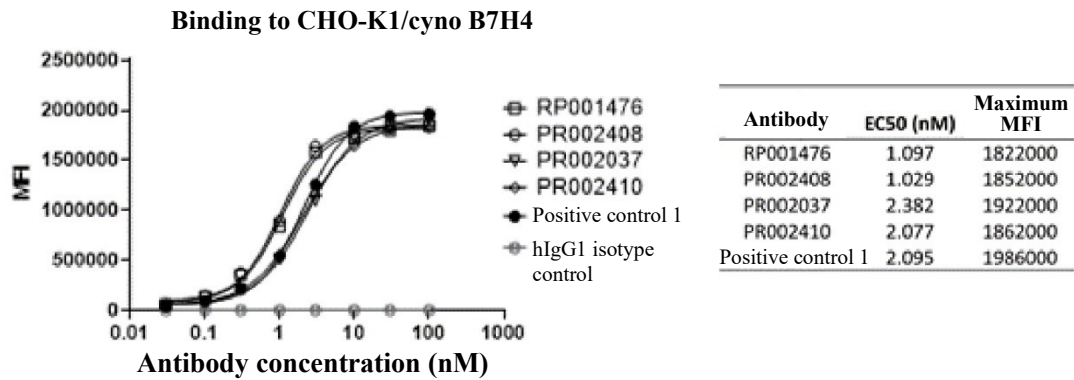


1-(A)



1-(B)



1-(C)

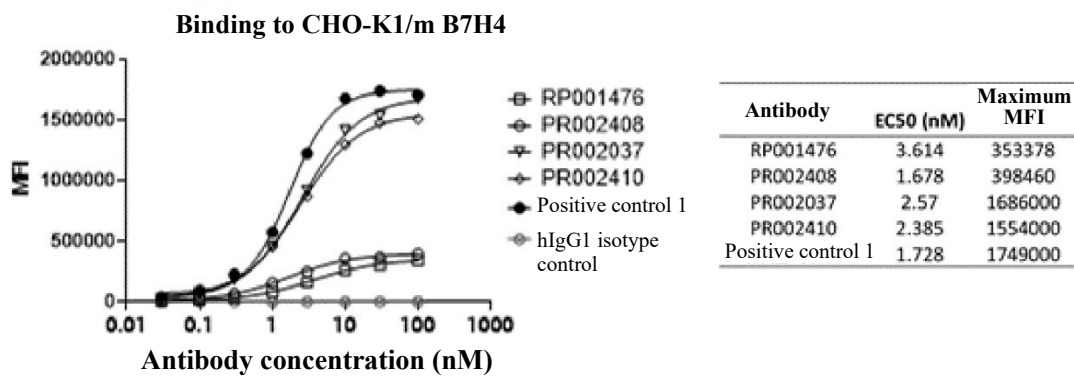
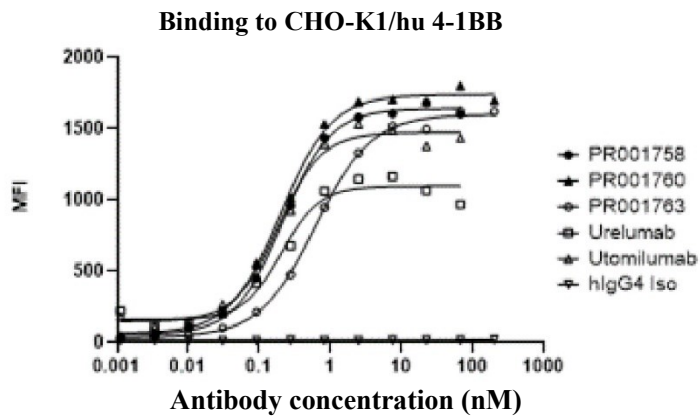


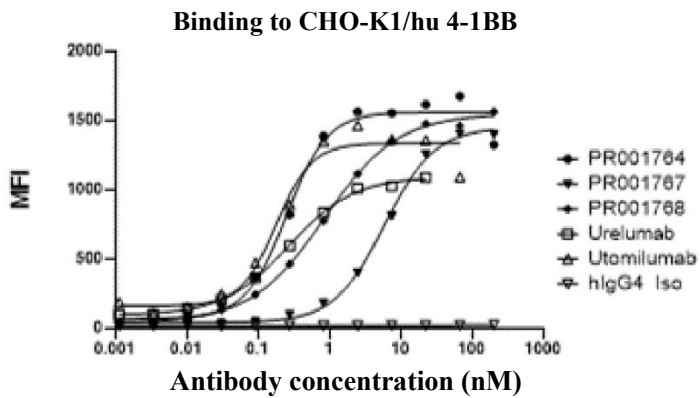
FIG. 1

2-(A)



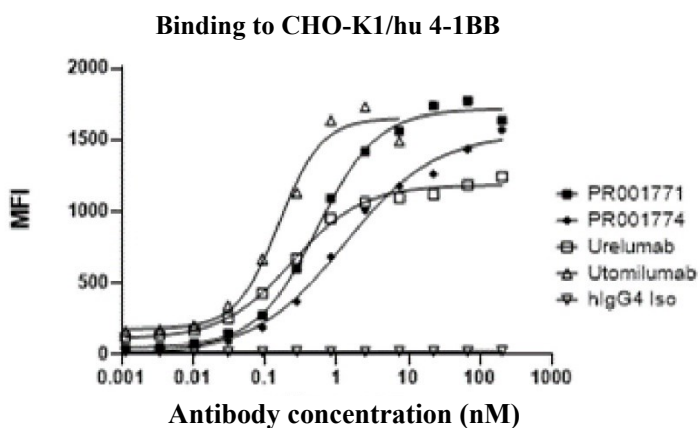
Antibody	EC50 (nM)	Maximum MFI
PR001758	0.2122	1644
PR001760	0.1981	1742
PR001763	0.616	1602
Urelumab	0.2223	1381
Utomilumab	0.1297	1584

2-(B)



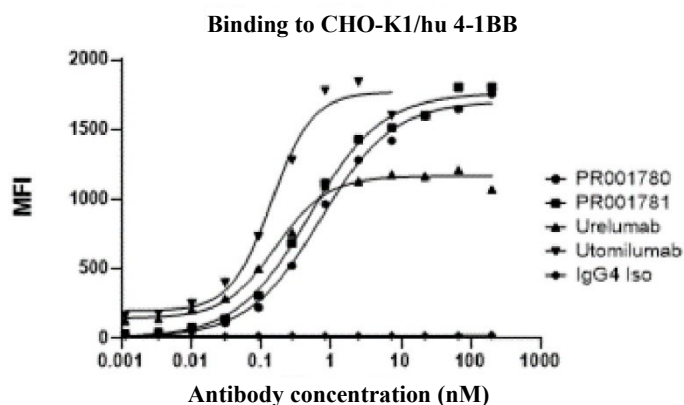
Antibody	EC50 (nM)	Maximum MFI
PR001764	0.2488	1562
PR001767	5.874	1453
PR001768	0.846	1552
Urelumab	0.2223	1381
Utomilumab	0.1297	1584

2-(C)



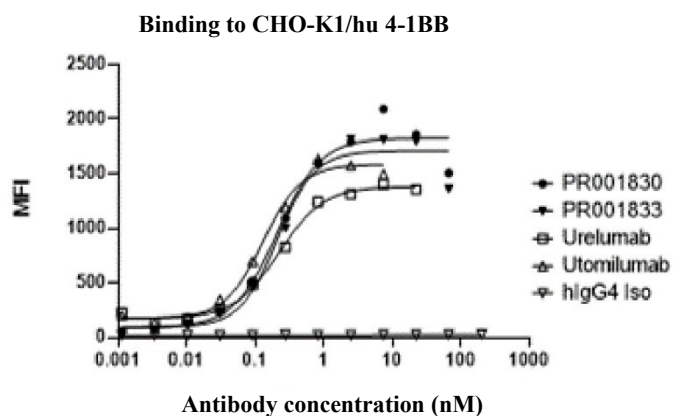
Antibody	EC50 (nM)	Maximum MFI
PR001771	0.5323	1716
PR001774	1.27	1544
Urelumab	0.2223	1381
Utomilumab	0.1297	1584

2-(D)



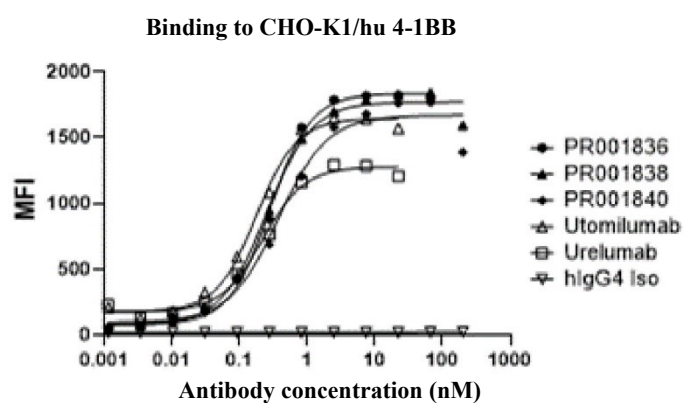
Antibody	EC50 (nM)	Maximum MFI
PR001780	0.7075	1703
PR001781	0.4917	1761
Urelumab	0.2223	1381
Utomilumab	0.1297	1584

2-(E)



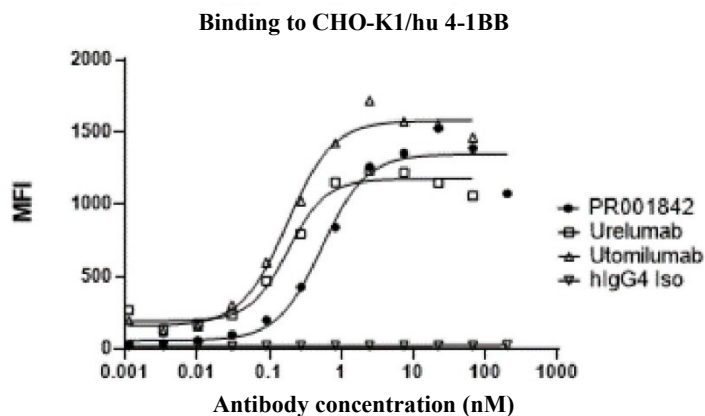
Antibody	EC50 (nM)	Maximum MFI
PR001830	0.2088	1826
PR001833	0.2099	1708
Urelumab	0.2223	1381
Utomilumab	0.1297	1584

2-(F)



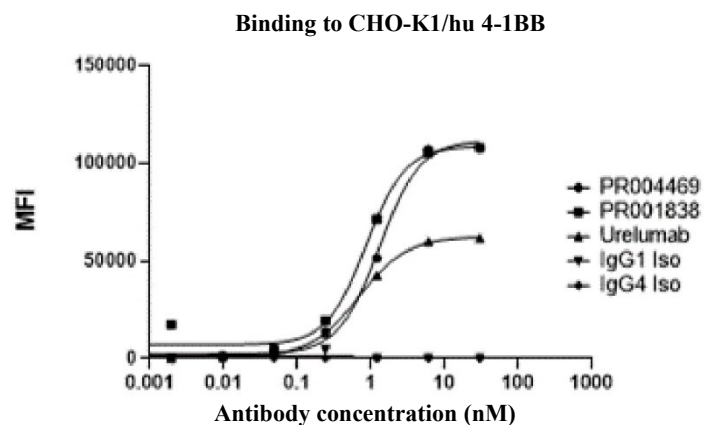
Antibody	EC50 (nM)	Maximum MFI
PR001836	0.2798	1833
PR001838	0.2482	1770
PR001840	0.3696	1669
Urelumab	0.2223	1381
Utomilumab	0.1297	1584

2-(G)



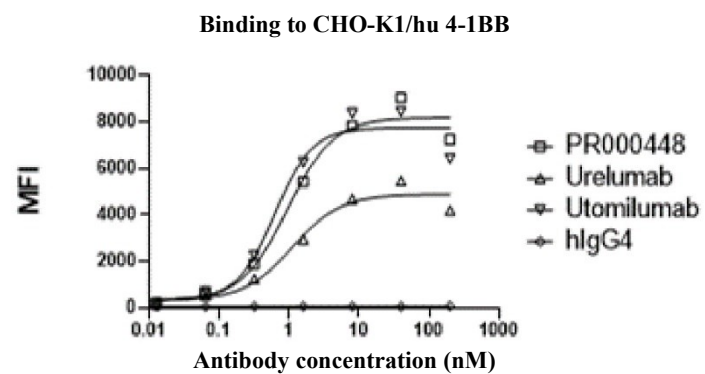
Antibody	EC50 (nM)	Maximum MFI
PR001842	0.5372	1346
Urelumab	0.2223	1381
Utomilumab	0.1297	1584

2-(H)



Antibody	EC50 (nM)	Maximum MFI
PR001838	0.8512	101674
PR004469	1.295	109216
Urelumab	0.6834	61805

2-(I)

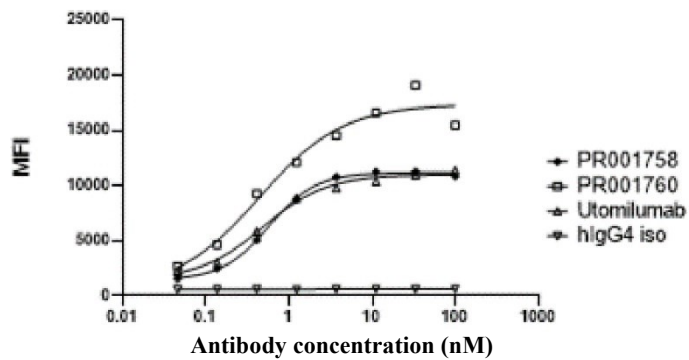


Antibody	EC50(nM)	Maximum MFI
PR000448	0.9473	8182
Urelumab	1.114	4898
Utomilumab	0.6271	7747

FIG. 2

3-(A)

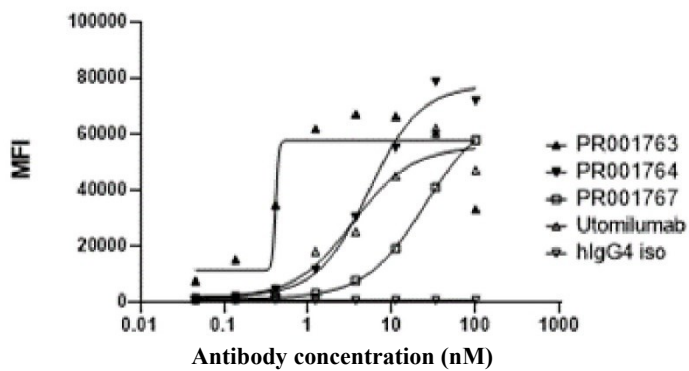
Binding to CHO-K1/cyno 4-1BB



Antibody	EC50 (nM)	Maximum MFI
PR001758	0.5747	11167
PR001760	0.4428	17361
Utomilumab	0.4848	10978
hlgG4 iso		

3-(B)

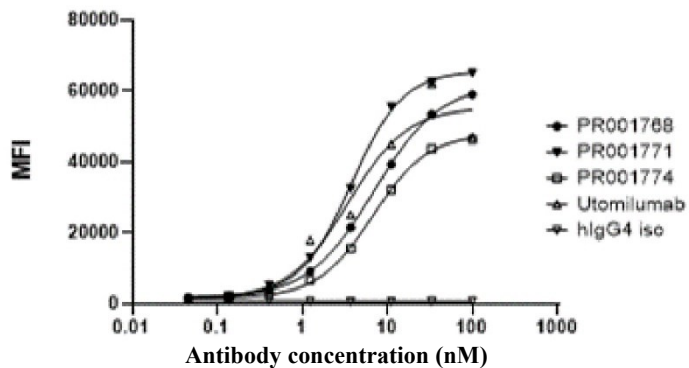
Binding to CHO-K1/cyno 4-1BB



Antibody	EC50 (nM)	Maximum MFI
PR001763	n.d.	57664
PR001764	5.325	77340
PR001767	25	68419
Utomilumab	3.459	55506
hlgG4 iso		

3-(C)

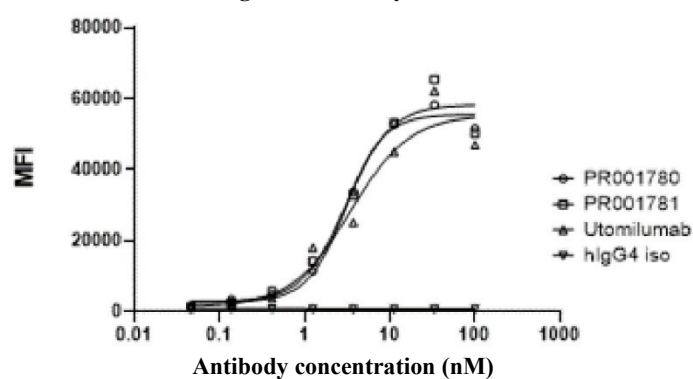
Binding to CHO-K1/cyno 4-1BB



Antibody	EC50 (nM)	Maximum MFI
PR001768	6.969	62154
PR001771	3.77	65713
PR001774	6.728	48008
Utomilumab	3.459	55506
hlgG4 iso		

3-(D)

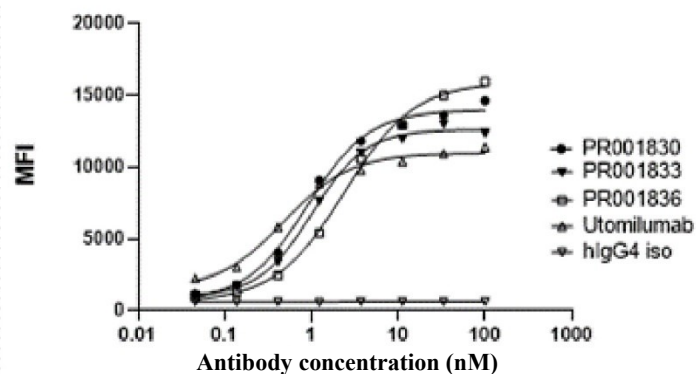
Binding to CHO-K1/cyno 4-1BB



Antibody	EC50 (nM)	Maximum MFI
PR001780	2.99	55516
PR001781	3.099	58329
Utomilumab	3.459	55506

3-(E)

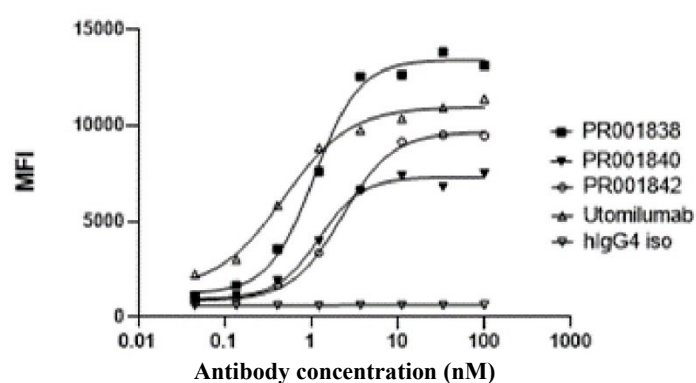
Binding to CHO-K1/cyno 4-1BB



Antibody	EC50 (nM)	Maximum MFI
PR001830	0.8991	13968
PR001833	1.018	12610
PR001836	2.410	15913
Utomilumab	0.4848	10978

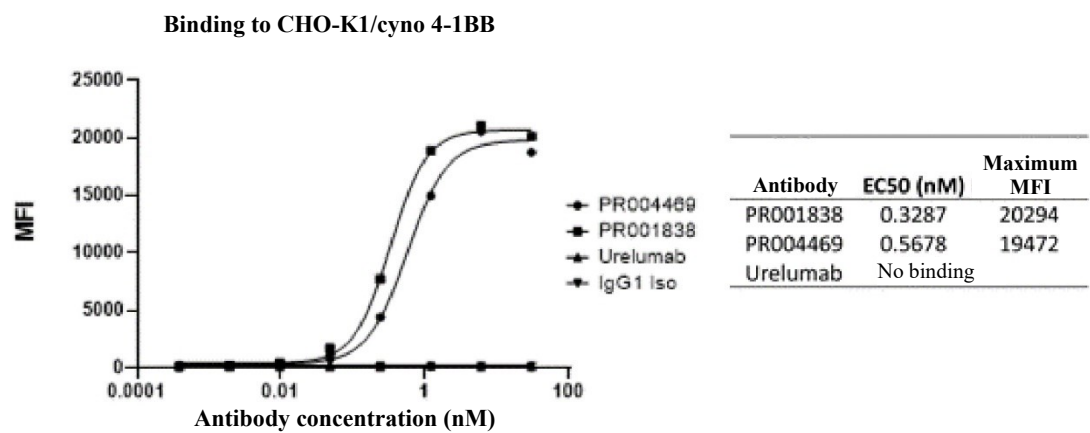
3-(F)

Binding to CHO-K1/cyno 4-1BB



Antibody	EC50 (nM)	Maximum MFI
PR001838	1.089	13431
PR001840	1.246	7303
PR001842	2.285	9660
Utomilumab	0.4848	10978

3-(G)



3-(H)

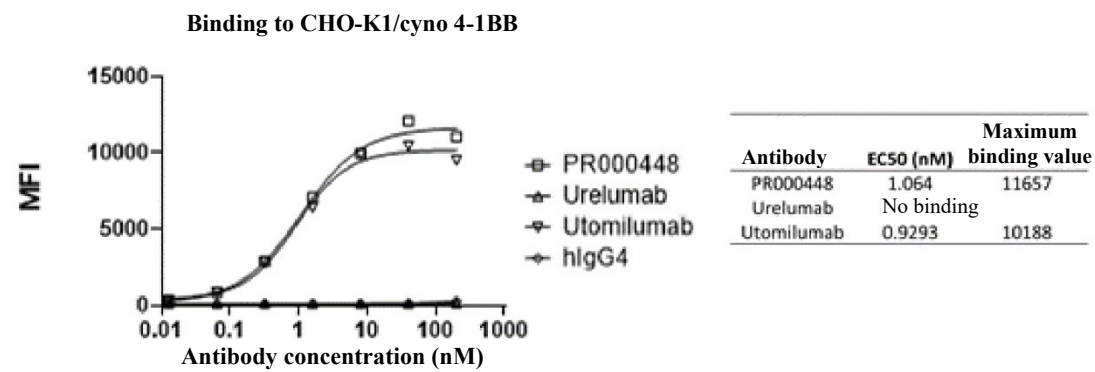
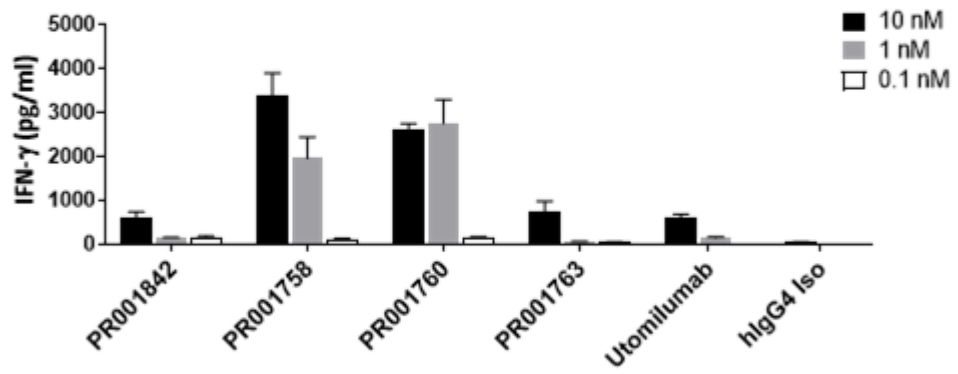
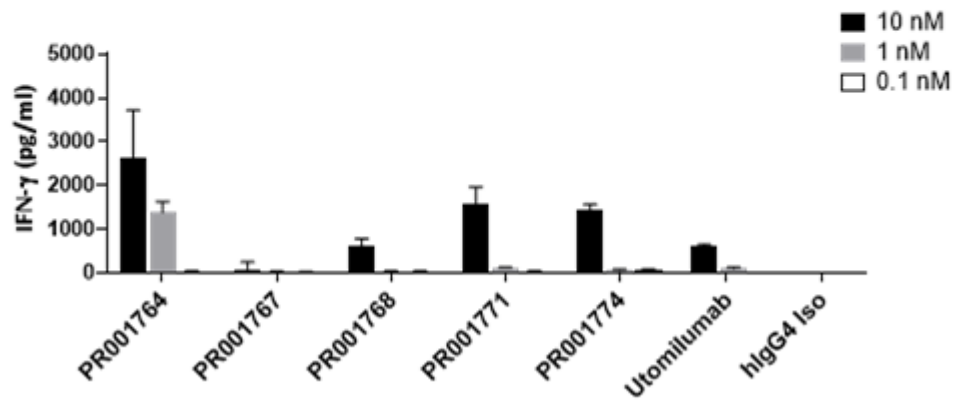


FIG. 3

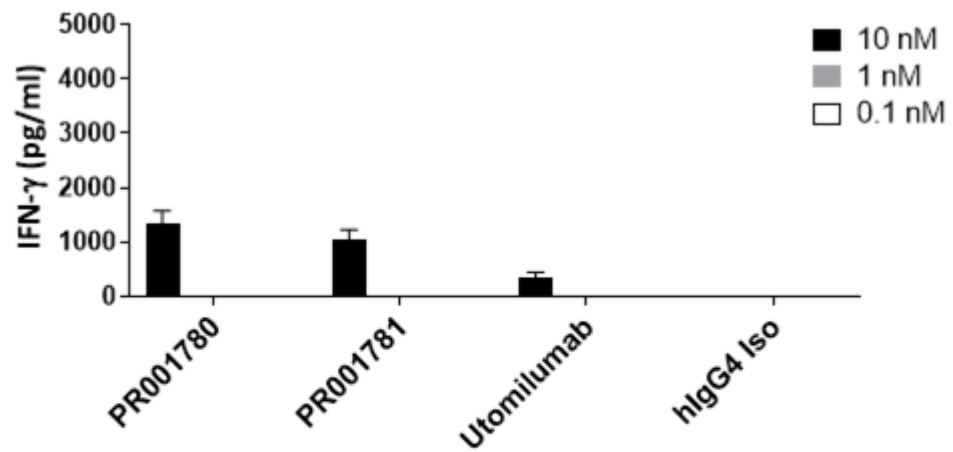
4-(A)



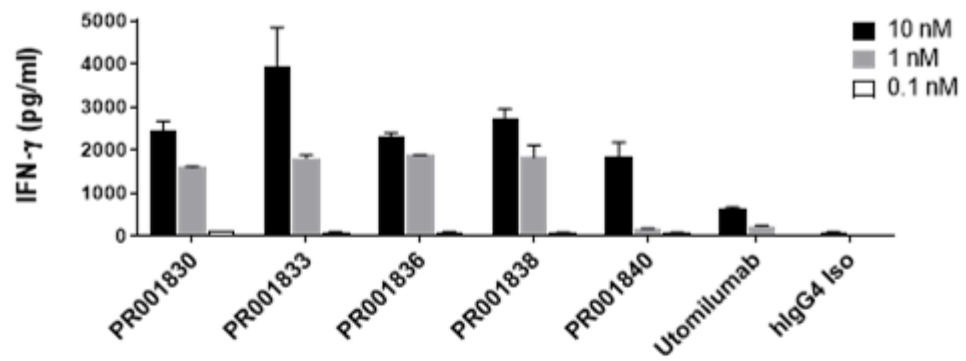
4-(B)



4-(C)



4-(D)



4-(E)

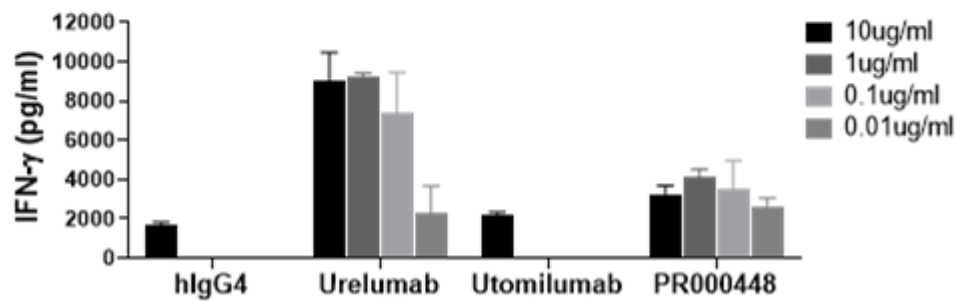
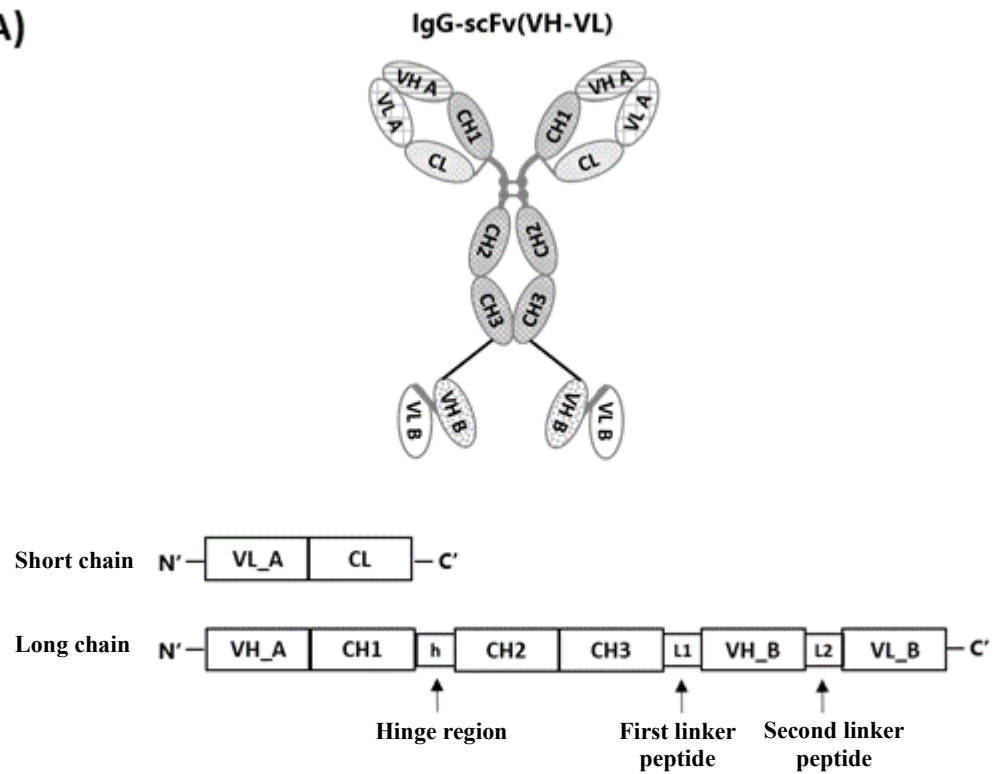
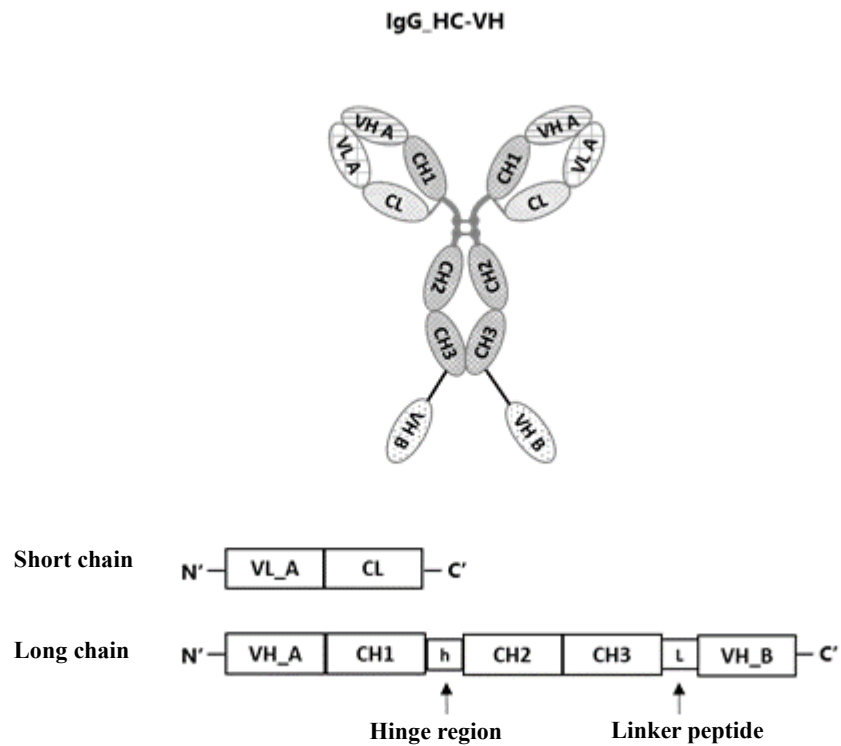


FIG. 4

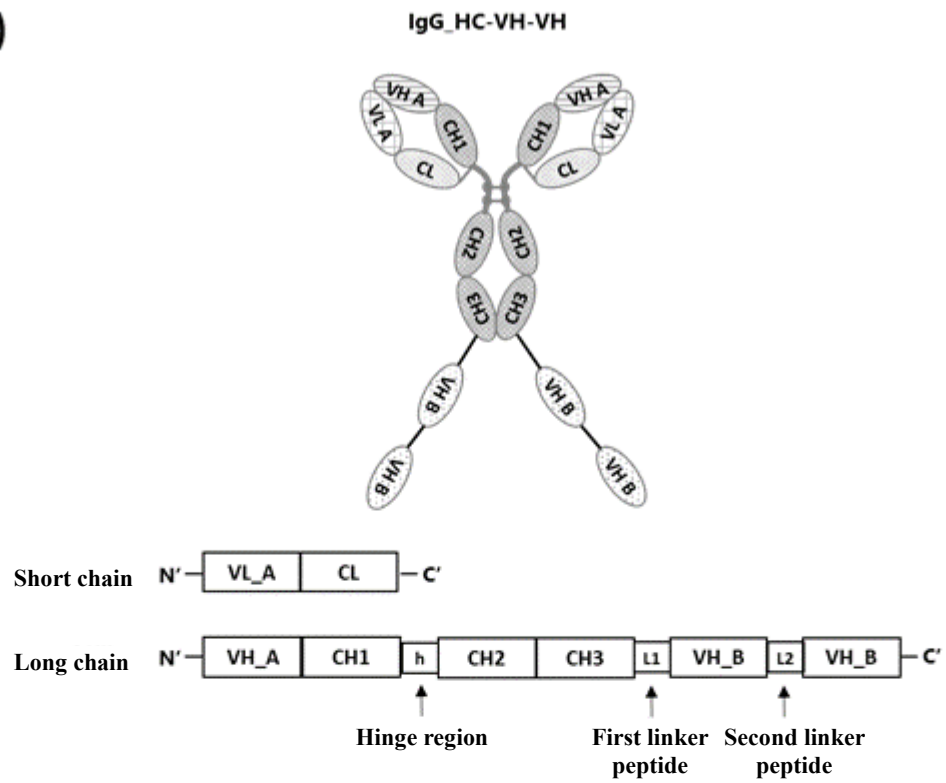
5-(A)



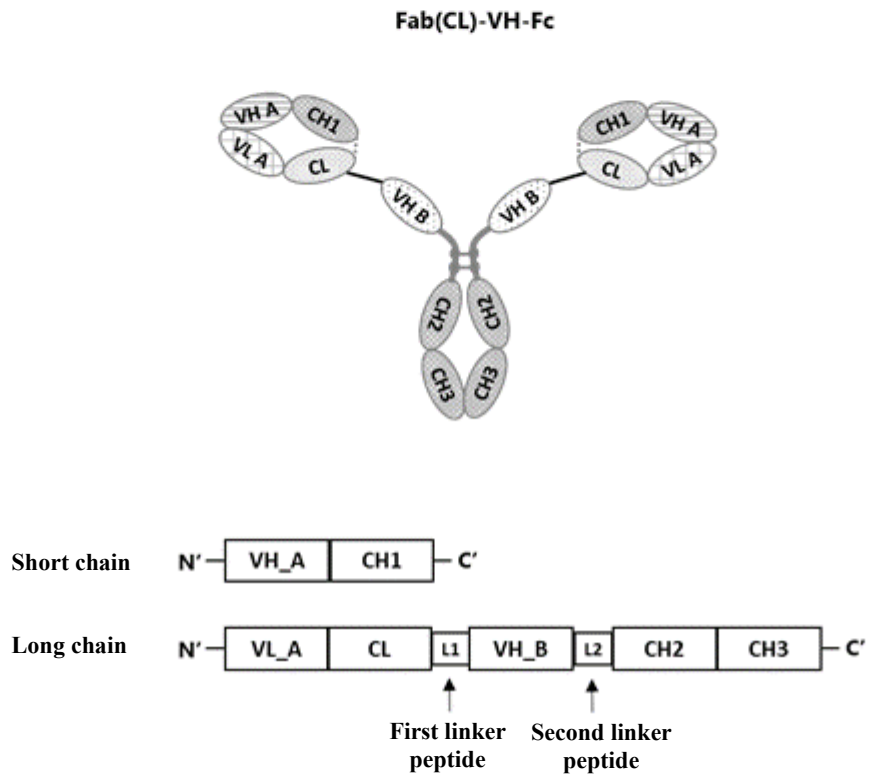
5-(B)



5-(C)



5-(D)



5-(E)

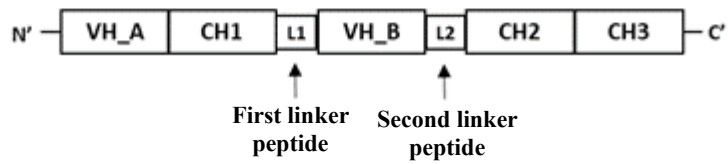
Fab(CH1)-VH-Fc



Short chain

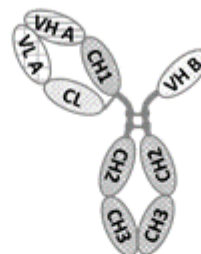


Long chain

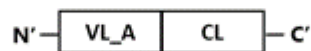


5-(F)

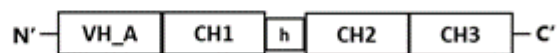
Fab-Fc-VH



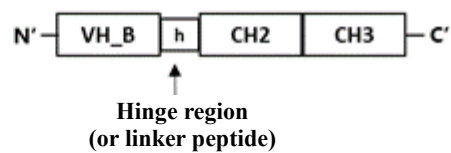
Polypeptide chain-1



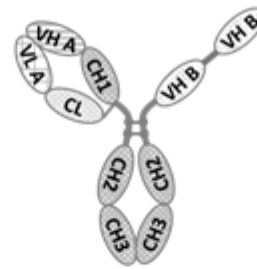
Polypeptide chain-2



Polypeptide chain-3



5-(G)



Polypeptide chain-1 N'—

VL_A	CL
------	----

—C'

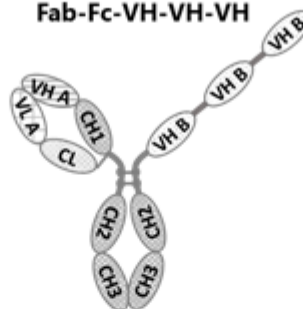
Polypeptide chain-2 N'—[VH_A][CH1][h][CH2][CH3]—C'

Polypeptide chain-3 N'—[VH_B][L][VH_B][h][CH2][CH3]—C'

↑ Linker peptide

↑ Hinge region (or linker peptide)

5-(H)



Polypeptide chain-1 N'—

VL_A

CL

—C'

Polypeptide chain-2 N'—

VH_A	CH1	h	CH2	CH3
------	-----	---	-----	-----

—C'

Polypeptide chain-3

N'—[VH_B]—[L1]—[VH_B]—[L2]—[VH_B]—[h]—[CH2]—[CH3]—C'

First linker peptide Second linker peptide Hinge region (or linker peptide)

5-(I)

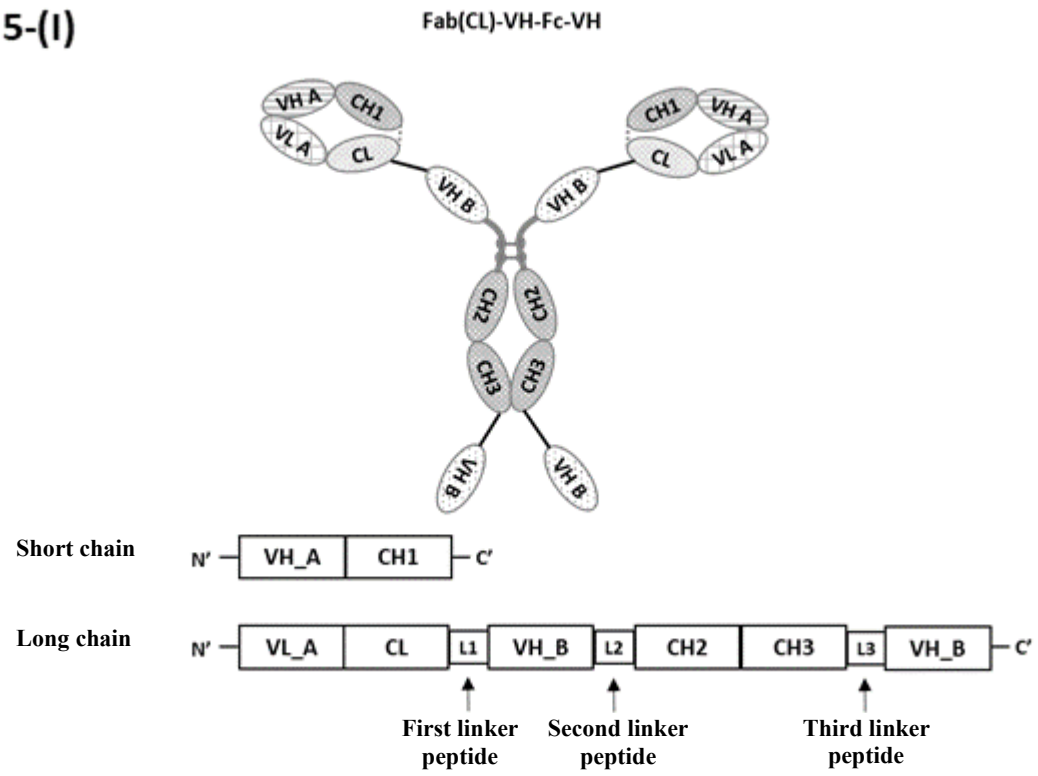
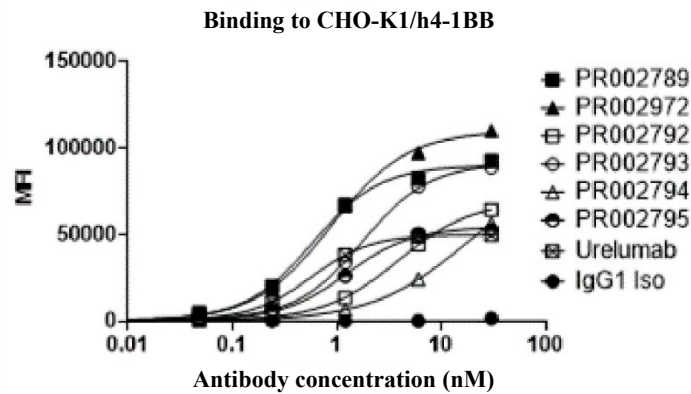


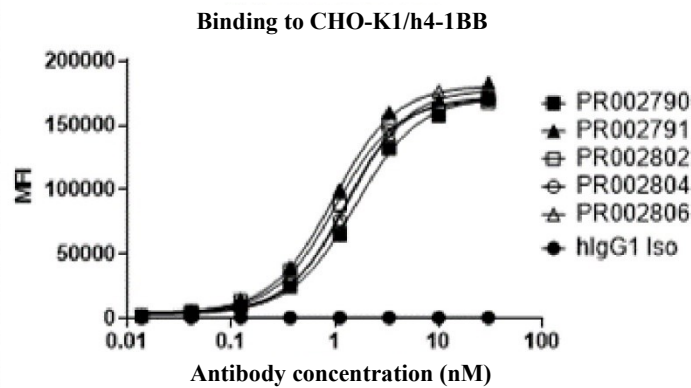
FIG. 5

6-(A)



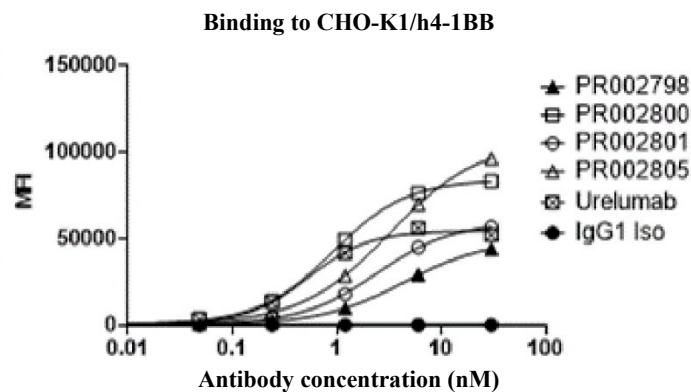
Antibody	EC50 (nM)	Maximum MFI
PR002789	0.5832	89905
PR002972	0.8787	109696
PR002792	3.867	69629
PR002793	1.757	91136
PR002794	17.26	89715
PR002795	1.242	54263
Urelumab	0.5638	50027

6-(B)



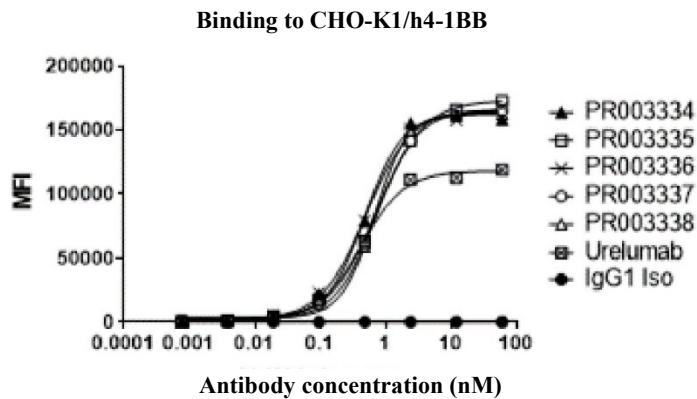
Antibody	EC50 (nM)	Maximum MFI
PR002790	1.569	172452
PR002791	0.964	181267
PR002802	1.011	169767
PR002804	1.248	171989
PR002806	1.346	178189

6-(C)



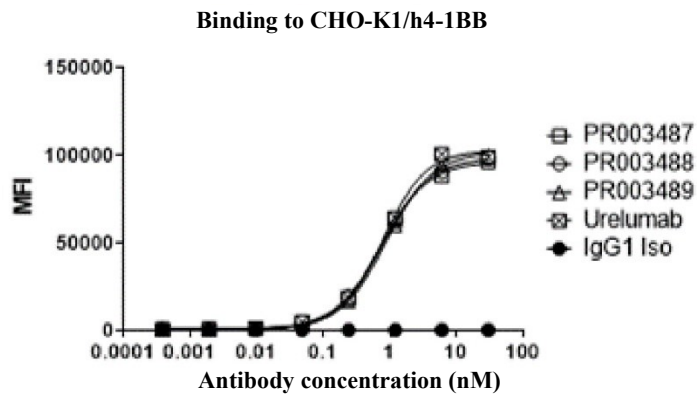
Antibody	EC50 (nM)	Maximum MFI
PR002798	4.383	49377
PR002800	0.909	84135
PR002801	2.412	59629
PR002805	3.204	106201
Urelumab	0.5328	54570

6-(D)



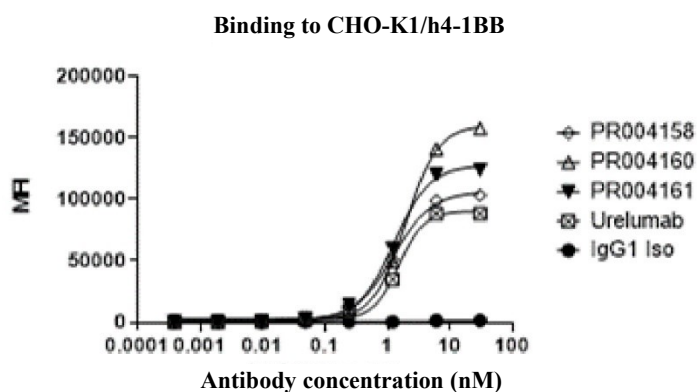
Antibody	EC50 (nM)	Maximum MFI
PR003334	0.4831	162519
PR003335	0.7395	173076
PR003336	0.5000	165948
PR003337	0.7215	165538
PR003338	0.6708	163354
Urelumab	0.4241	118060

6-(E)



Antibody	EC50 (nM)	Maximum MFI
PR003487	0.755	95740
PR003488	0.7735	98153
PR003489	0.8951	100804
urelumab	0.7945	101473

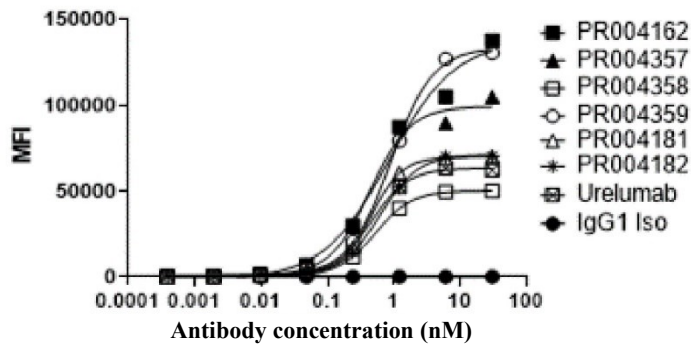
6-(F)



Antibody	EC50 (nM)	Maximum MFI
PR004158	1.23	104982
PR004160	1.943	158311
PR004161	1.266	126124
Urelumab	1.506	88235

6-(G)

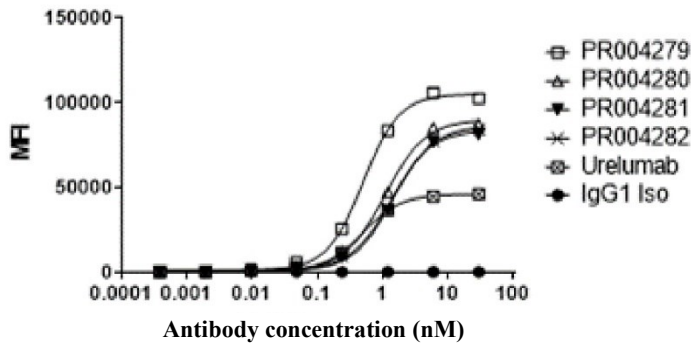
Binding to CHO-K1/h4-1BB



Antibody	EC50 (nM)	Maximum MFI
PR004162	0.8384	137301
PR004357	0.4317	99202
PR004358	0.5194	50246
PR004359	0.89	133337
PR004181	0.4487	69865
PR004182	0.6107	71139
Urelumab	0.4488	63326

6-(H)

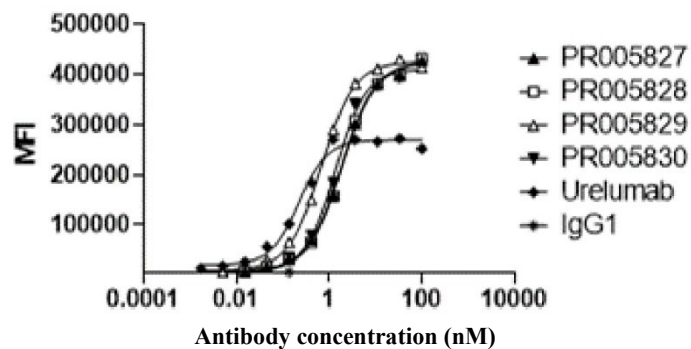
Binding to CHO-K1/h4-1BB



Antibody	EC50 (nM)	Maximum MFI
PR004279	0.5035	104957
PR004280	1.086	89959
PR004281	1.394	83574
PR004282	1.408	86442
Urelumab	0.4989	45925

6-(I)

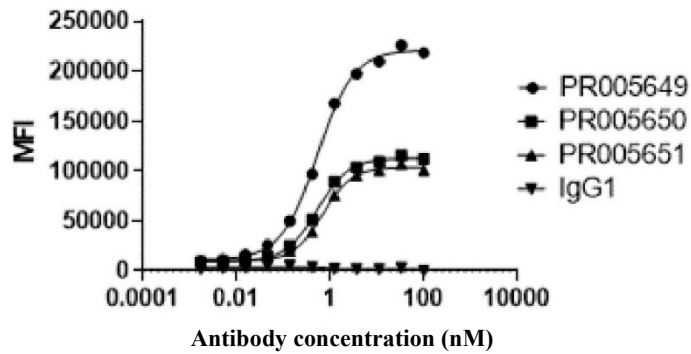
Binding to CHO-K1/h4-1BB cells



Antibody	EC50 (nM)	Maximum MFI
PR005827	1.853	424725
PR005828	1.844	423994
PR005829	0.6776	425447
PR005830	1.373	410829
Urelumab	0.2218	269486

6-(J)

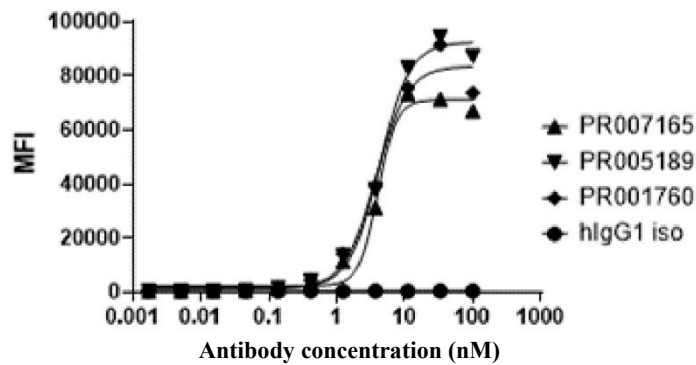
Binding to CHO-K1/h4-1BB cells



Antibody	EC50 (nM)	Maximum MFI
PR005649	0.5333	221290
PR005650	0.5313	112860
PR005651	0.6893	103596

6-(K)

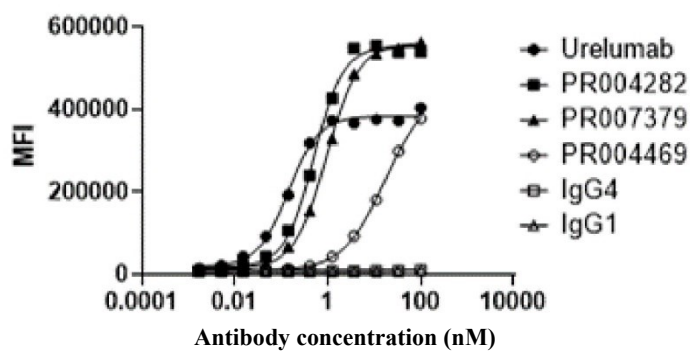
Binding to CHO-K1/h4-1BB



Antibody	EC50 (nM)	Maximum MFI
PR007165	3.996	71246
PR005189	4.255	92381
PR001760	3.761	83588

6-(L)

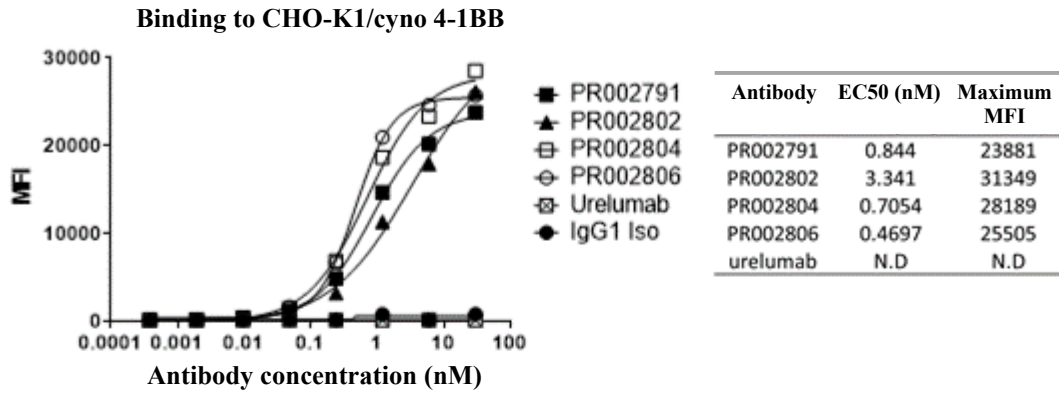
Binding to CHO-K1/h4-1BB cells



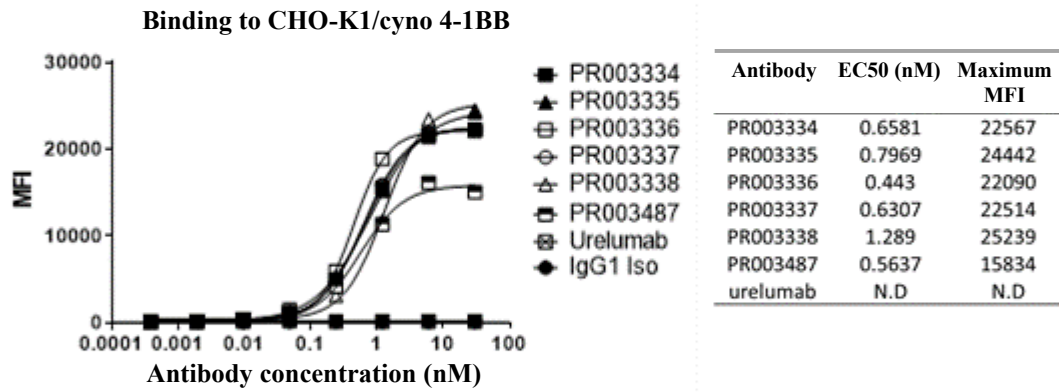
Antibody	EC50(nM)	Maximum MFI
Urelumab	0.1404	383660
PR004282	0.5024	552940
PR007379	0.9384	560073
PR004469	17.04	447078

FIG. 6

7-(A)



7-(B)



7-(C)

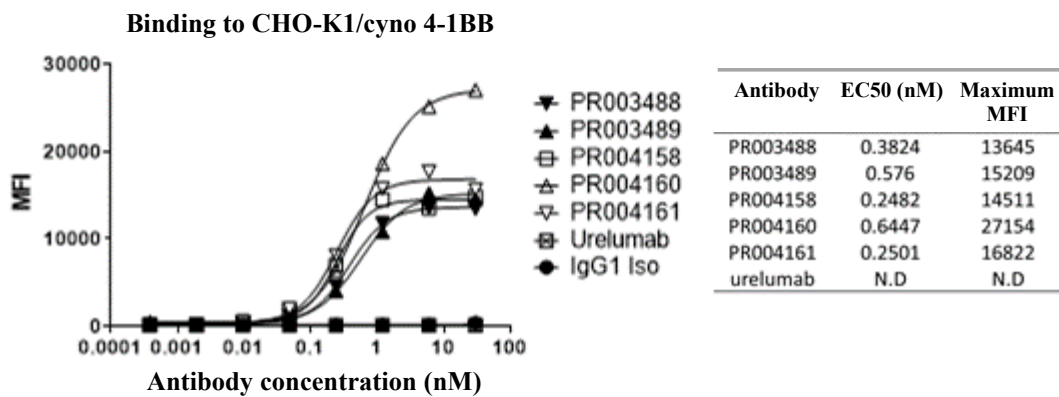
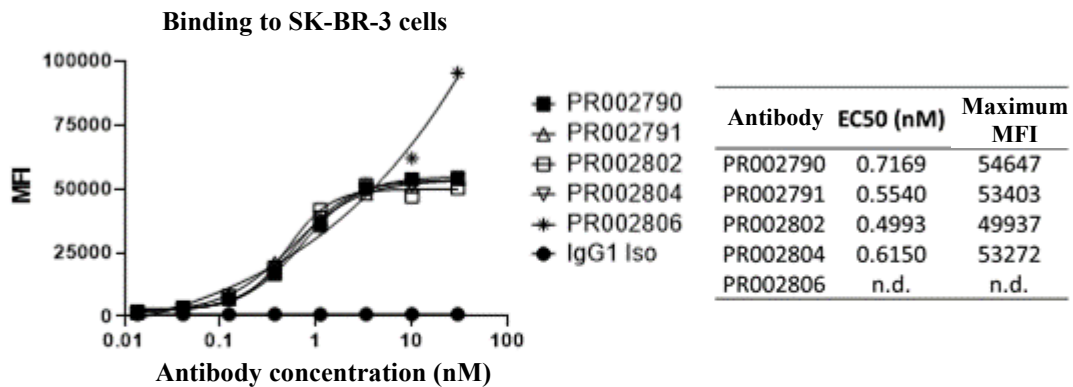
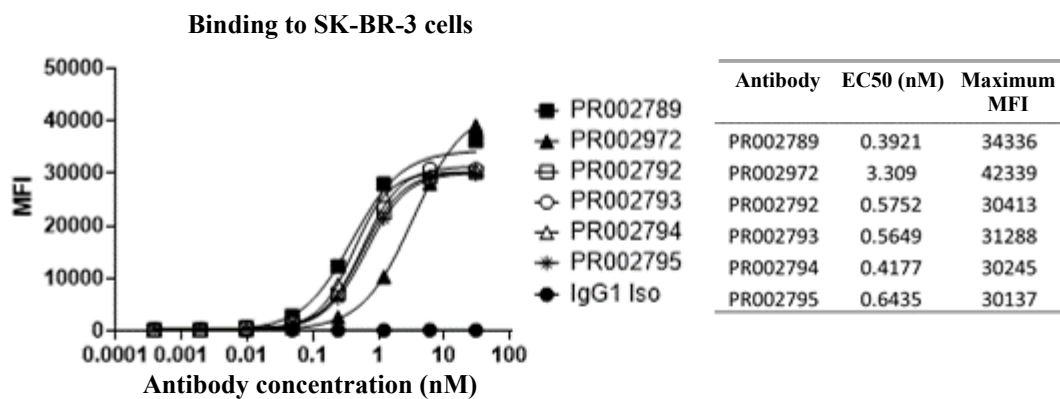


FIG. 7

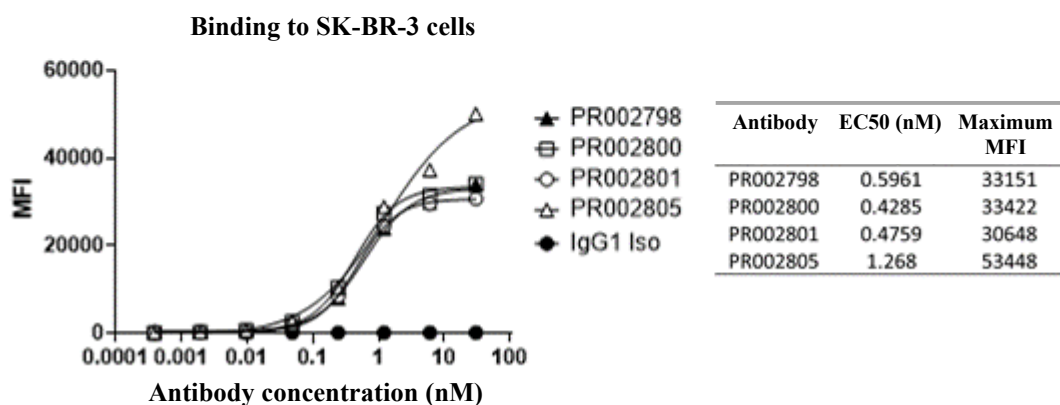
8-(A)



8-(B)

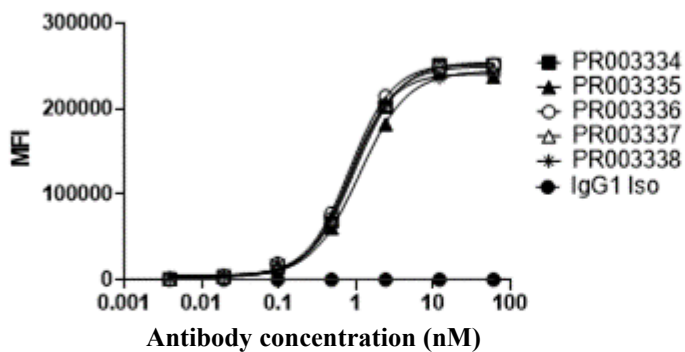


8-(C)



8-(D)

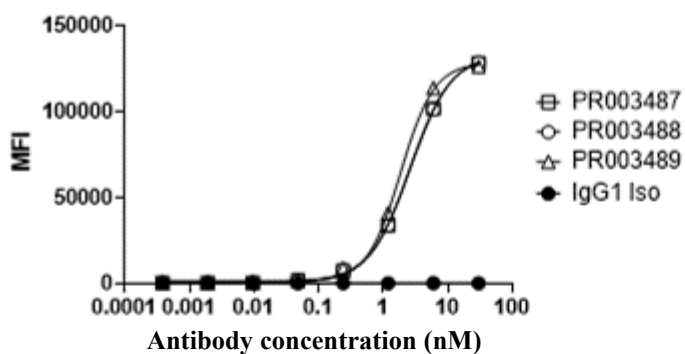
Binding to SK-BR-3 cells



Antibody	EC50 (nM)	Maximum MFI
PR003334	0.9685	254417
PR003335	1.102	244159
PR003336	0.8208	252359
PR003337	0.9001	249524
PR003338	0.8207	241092

8-(E)

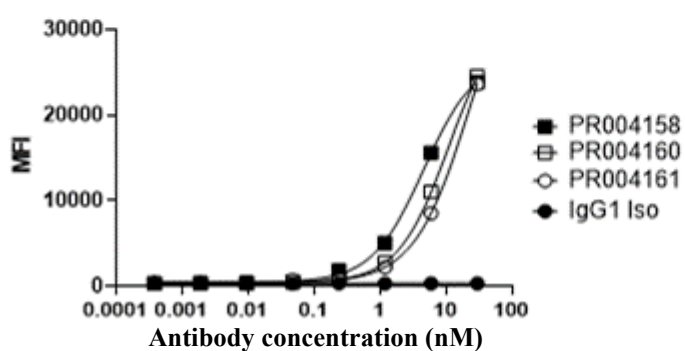
Binding to SK-BR-3 cells



Antibody	EC50 (nM)	Maximum MFI
PR003487	2.593	131617
PR003488	2.626	132285
PR003489	1.877	126775

8-(F)

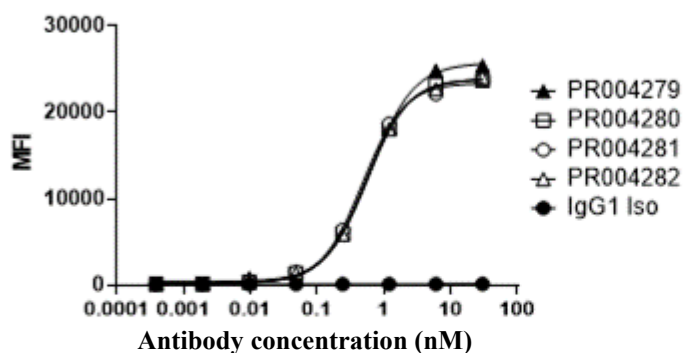
Binding to SK-BR-3 cells



Antibody	EC50 (nM)	Maximum MFI
PR004158	4.614	26398
PR004160	11.33	32312
PR004161	23.44	41230

8-(G)

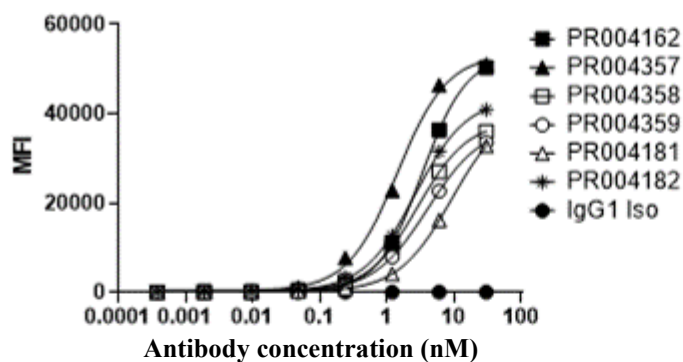
Binding to SK-BR-3 cells



Antibody	EC50 (nM)	Maximum MFI
PR004279	0.6201	25718
PR004280	0.5358	23858
PR004281	0.4801	23400
PR004282	0.5444	23879

8-(H)

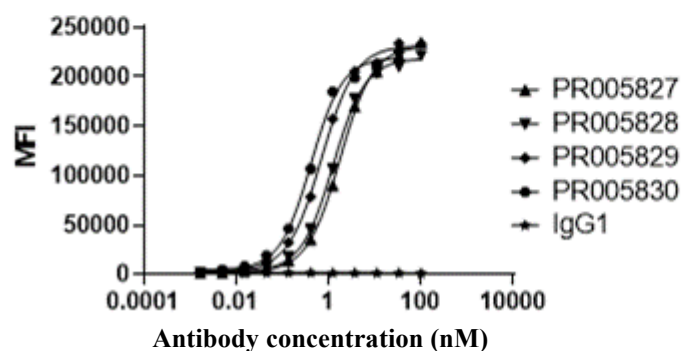
Binding to SK-BR-3 cells



Antibody	EC50 (nM)	Maximum MFI
PR004162	3.342	53207
PR004357	1.433	53334
PR004358	2.909	38512
PR004359	4.051	37469
PR004181	9.254	41920
PR004182	2.616	43637

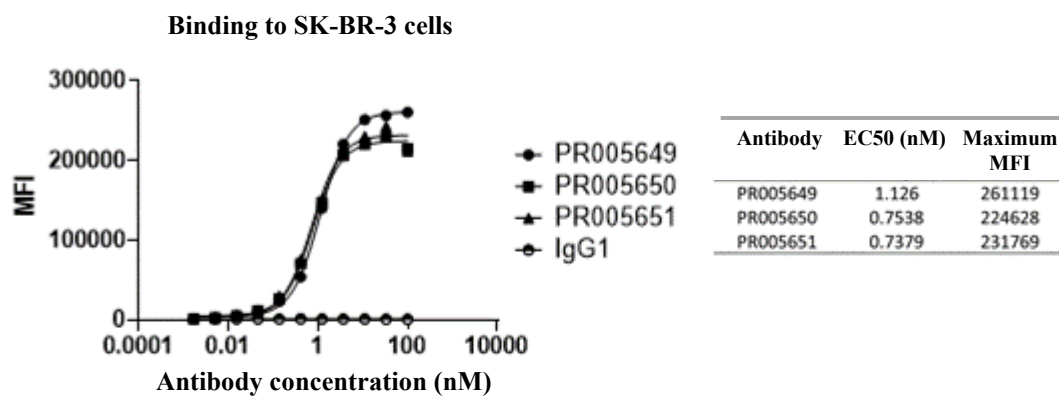
8-(I)

Binding to SK-BR-3 cells



Antibody	EC50 (nM)	Maximum MFI
PR005827	1.767	231310
PR005828	1.259	218403
PR005829	0.7033	231300
PR005830	0.4168	219262

8-(J)



8-(K)

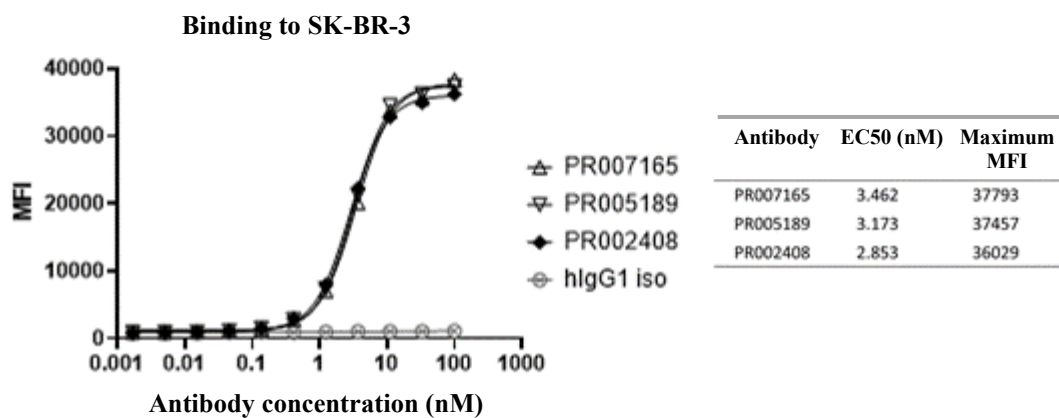
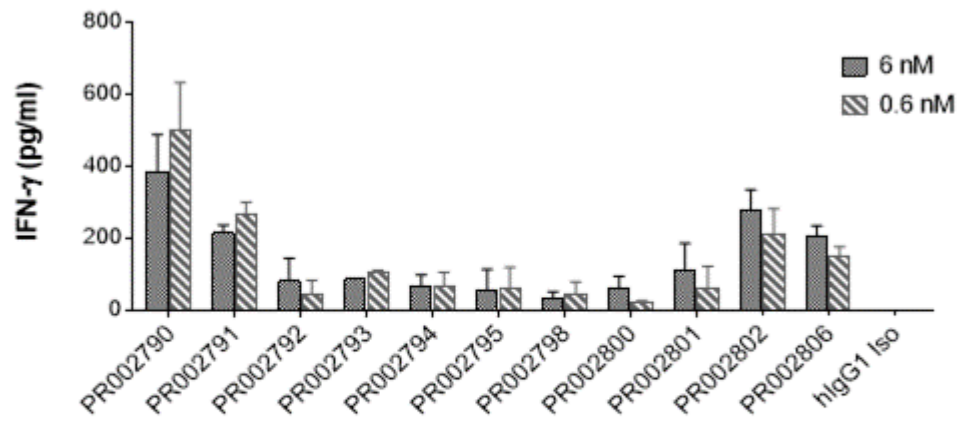


FIG. 8

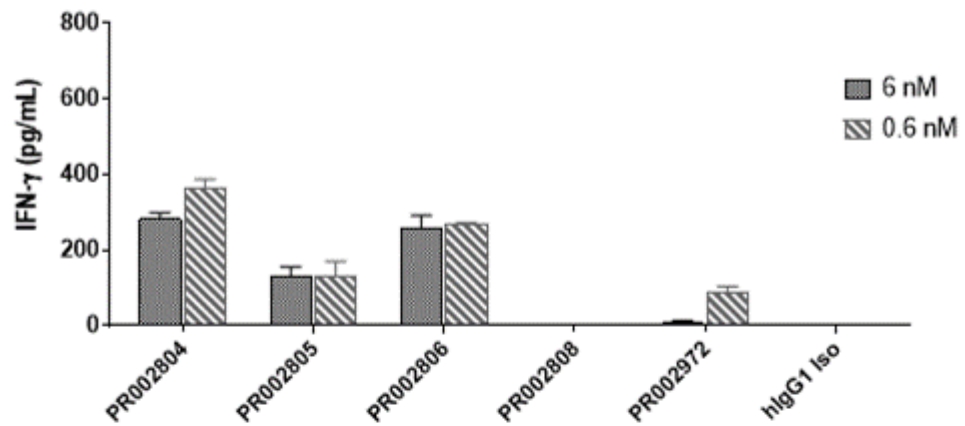
9-(A)

SK-BR-3 cell-mediated T cell activation



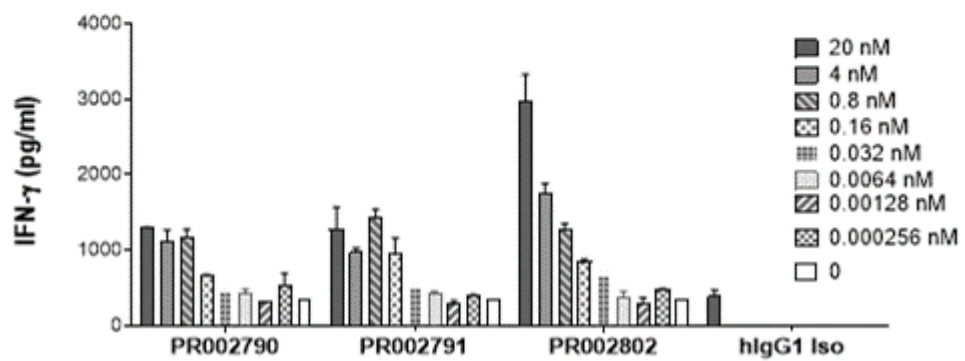
9-(B)

SK-BR-3 cell-mediated T cell activation



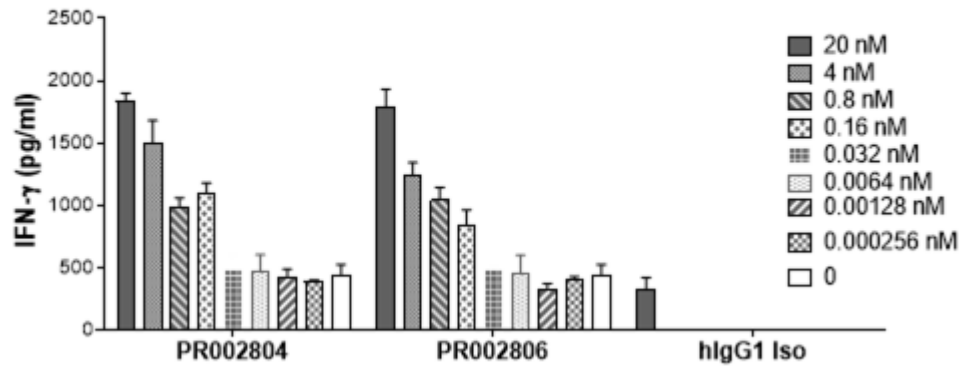
9-(C)

SK-BR-3 cell-mediated T cell activation



9-(D)

SK-BR-3 cell-mediated T cell activation



9-(E)

SK-BR-3 cell-mediated T cell activation

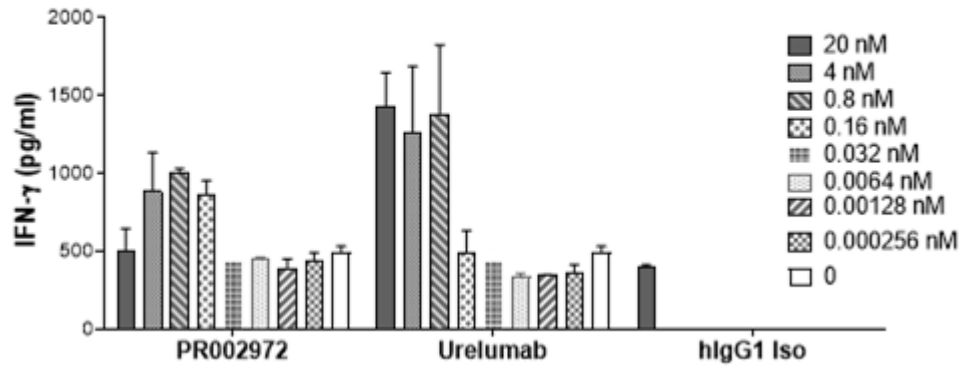
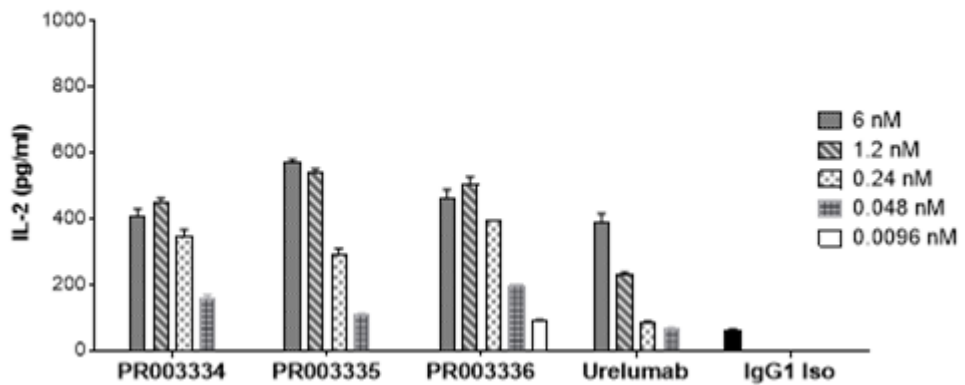


FIG. 9

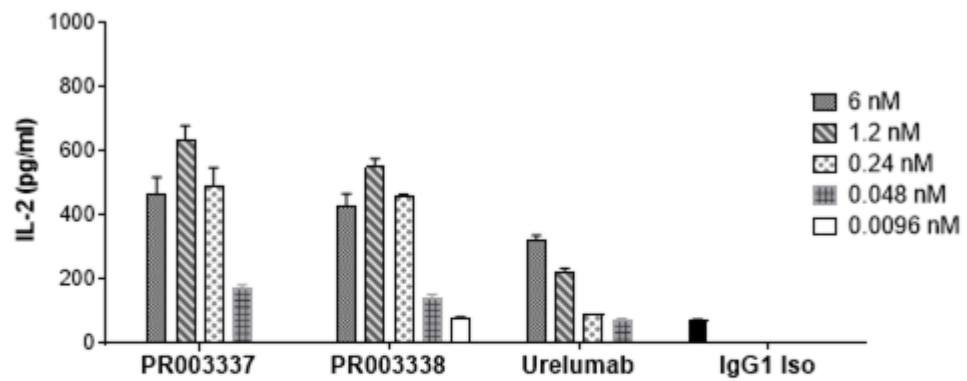
10-(A)

SK-BR-3 cell-mediated T cell activation



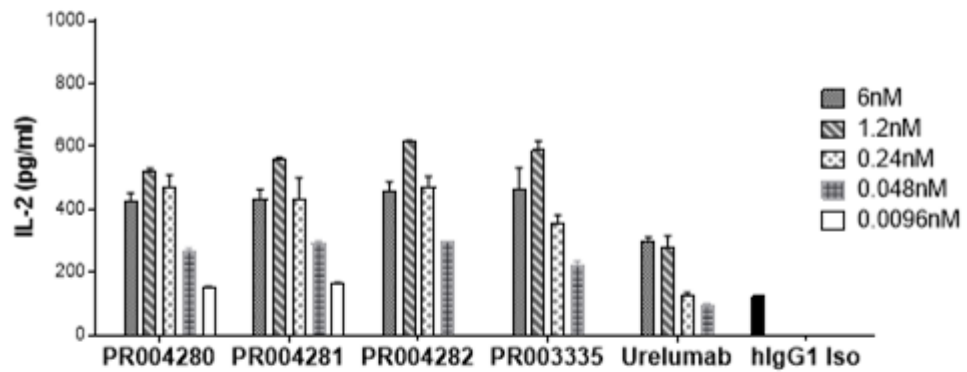
10-(B)

SK-BR-3 cell-mediated T cell activation



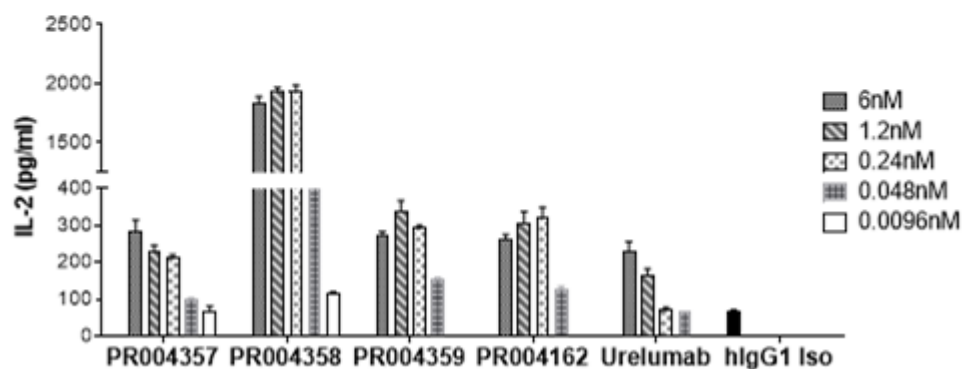
10-(C)

SK-BR-3 cell-mediated T cell activation



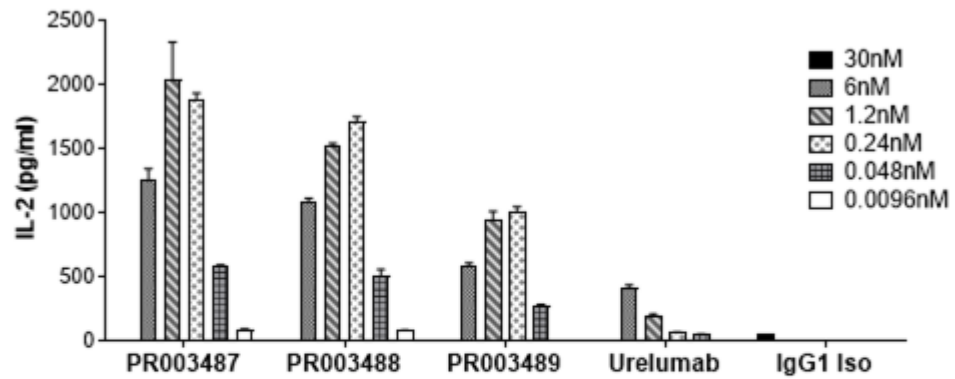
10-(D)

SK-BR-3 cell-mediated T cell activation



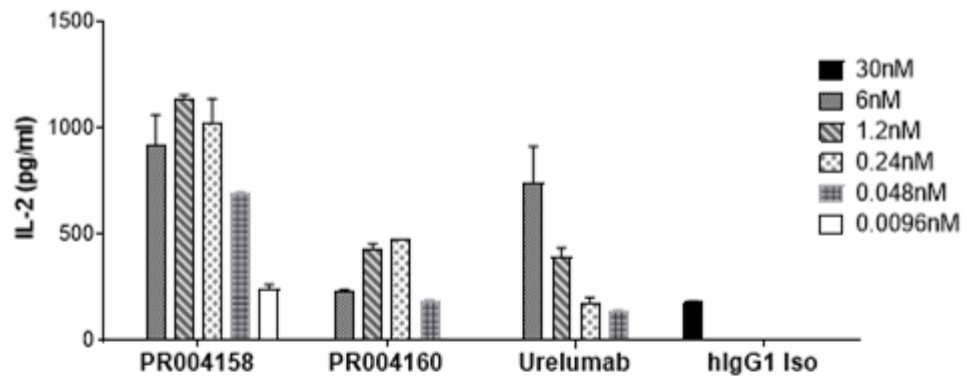
10-(E)

SK-BR-3 cell-mediated T cell activation



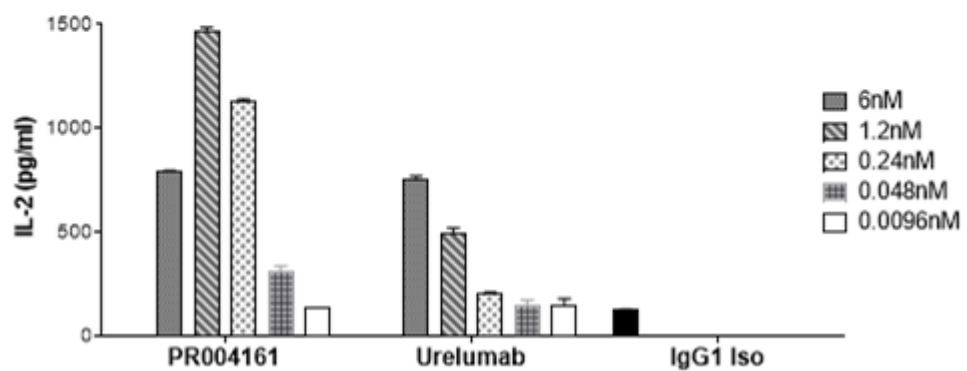
10-(F)

SK-BR-3 cell-mediated T cell activation



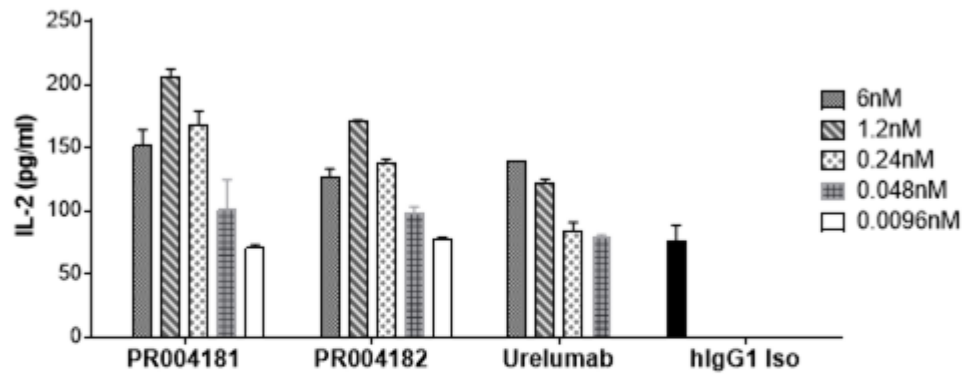
10-(G)

SK-BR-3 cell-mediated T cell activation



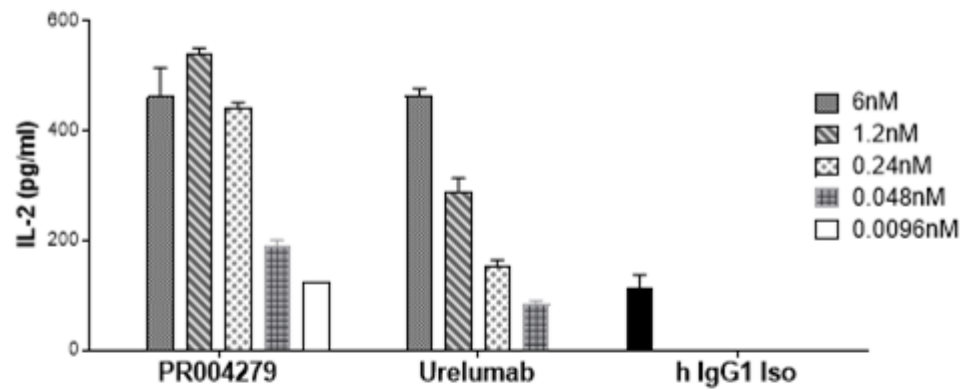
10-(H)

SK-BR-3 cell-mediated T cell activation



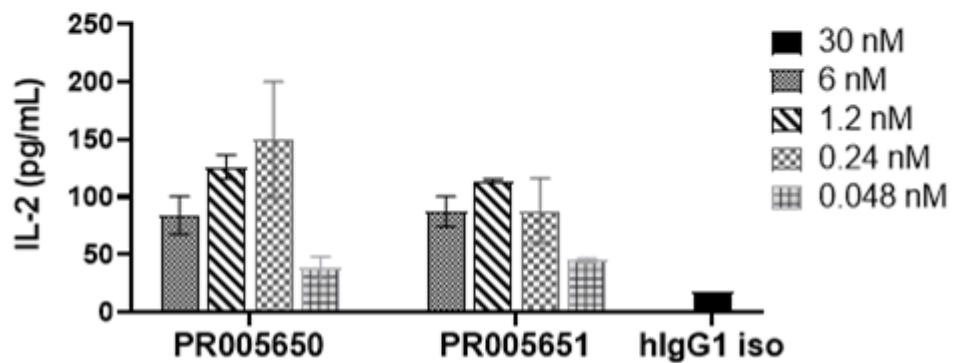
10-(I)

SK-BR-3 cell-mediated T cell activation



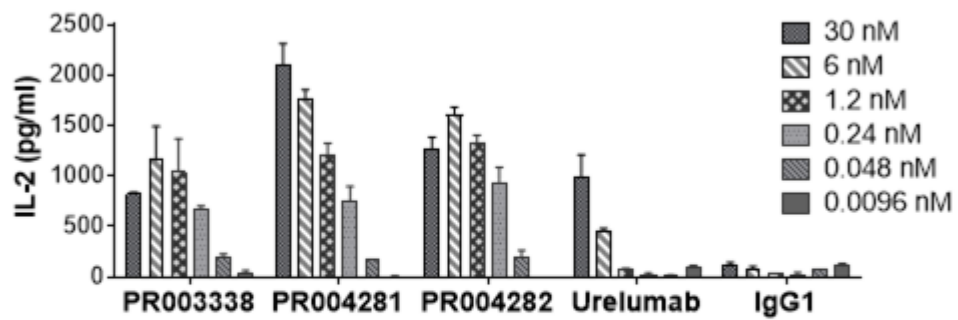
10-(J)

SK-BR-3 cell-mediated T cell activation



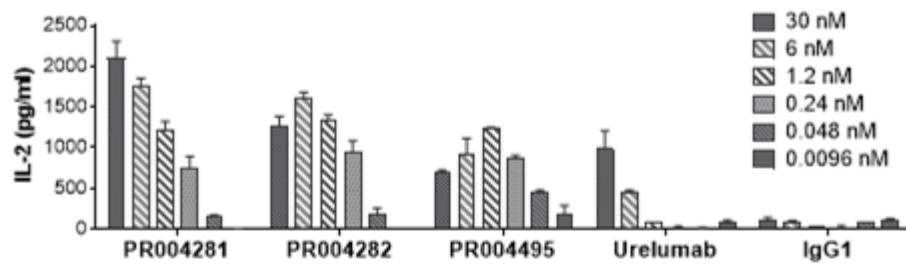
10-(K)

SK-BR-3 cell-mediated T cell activation



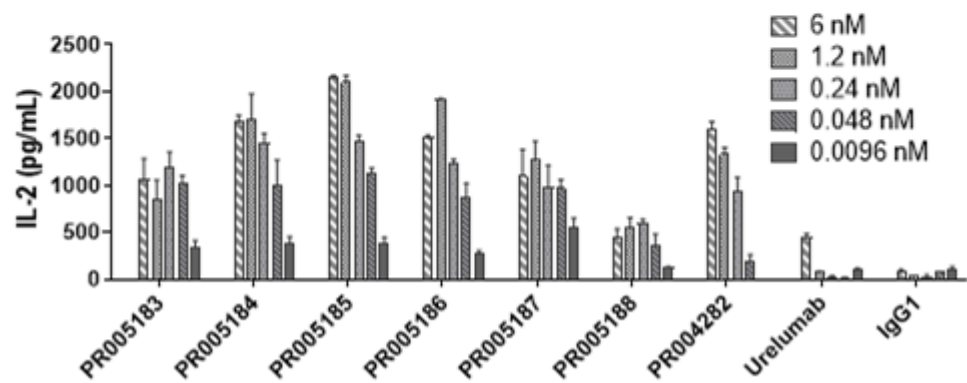
10-(L)

SK-BR-3 cell-mediated T cell activation



10-(M)

SK-BR-3-mediated T cell activation



10-(N)

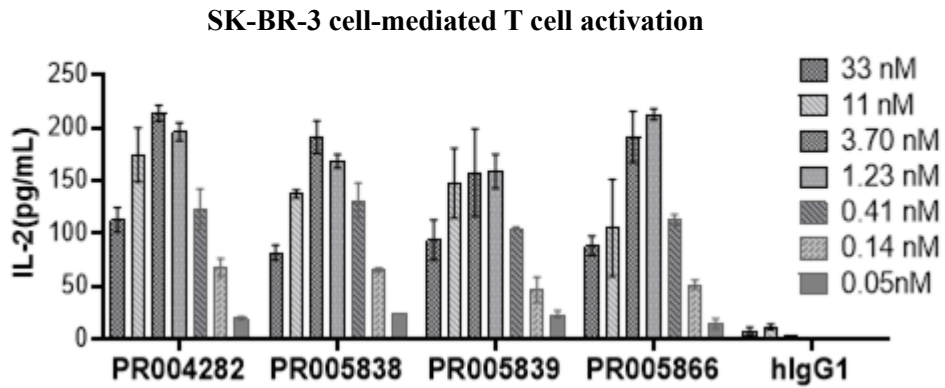
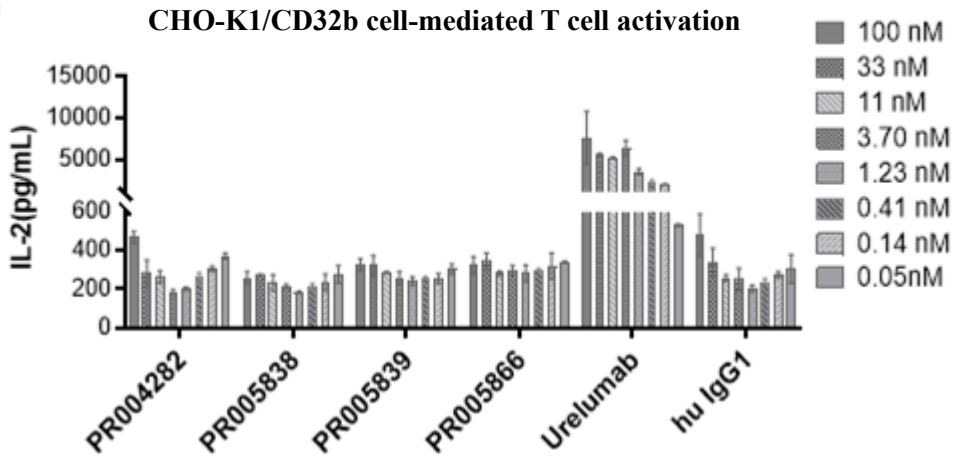


FIG. 10

11-(A)



11-(B)

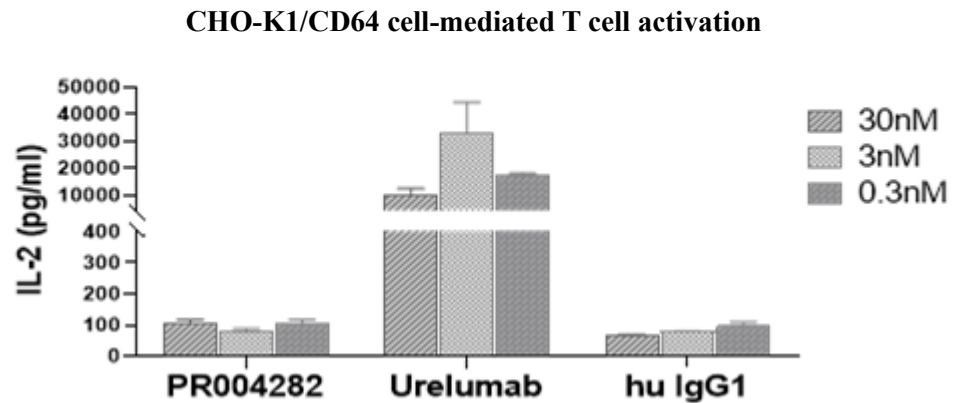
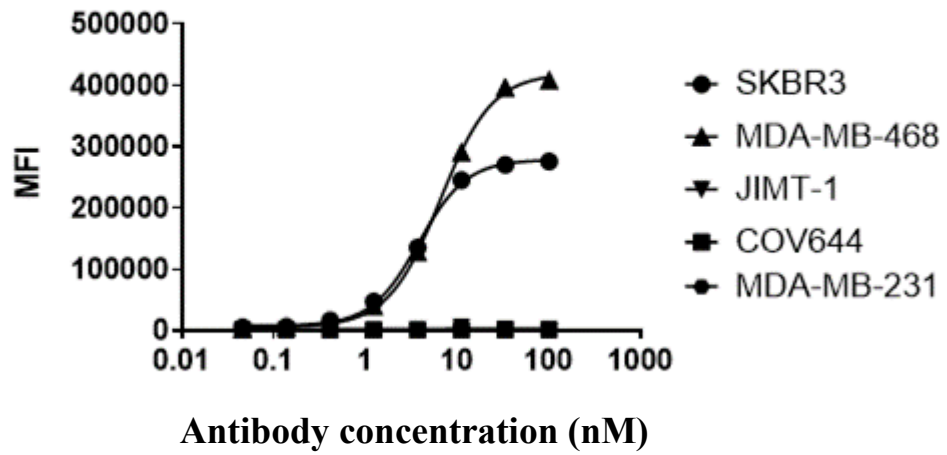


FIG. 11

12-(A)

Expression level of B7H4 on tumor cells determined using positive control antibody 1



12-(B)

Expression level of B7H4 on tumor cell surfaces determined using PR003334

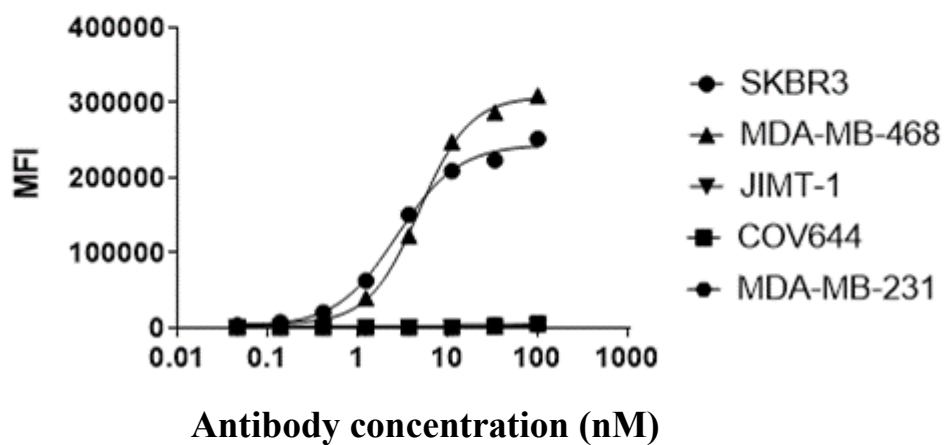
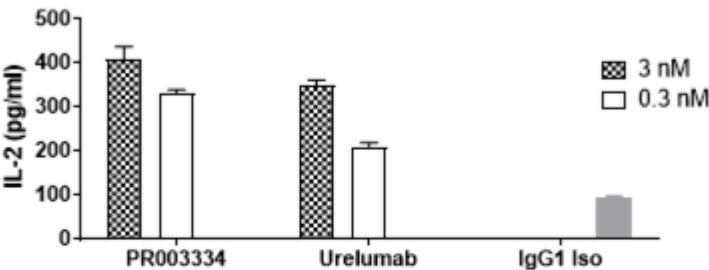


FIG. 12

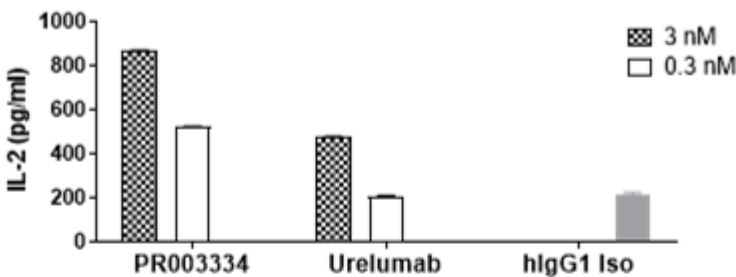
13-(A)

The bispecific antibody can specifically activate T cells in the presence of SK-BR-3 cells that highly express B7H4



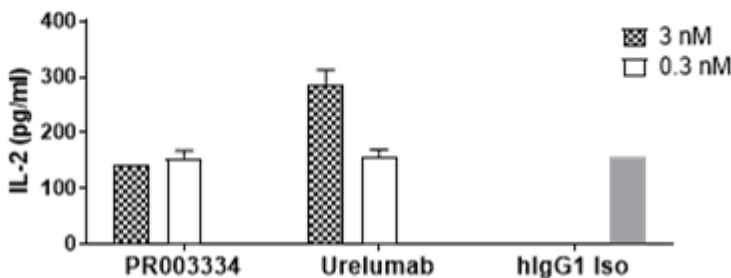
13-(B)

The bispecific antibody can specifically activate T cells in the presence of MAD-MB-468 cells that highly express B7H4



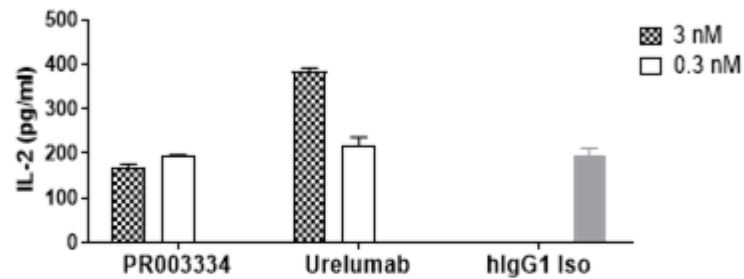
13-(C)

The bispecific antibody does not activate T cells in the presence of COV644 cells that do not express B7H4



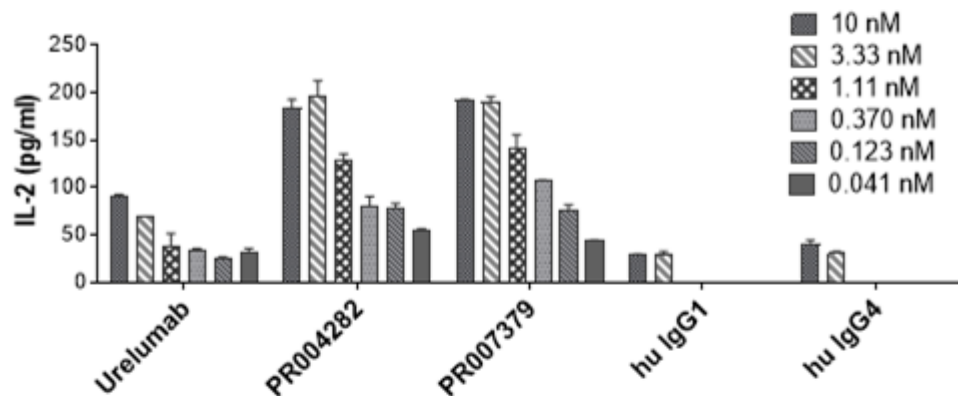
13-(D)

The bispecific antibody does not activate T cells in the presence of Jint-1 cells that do not express B7H4



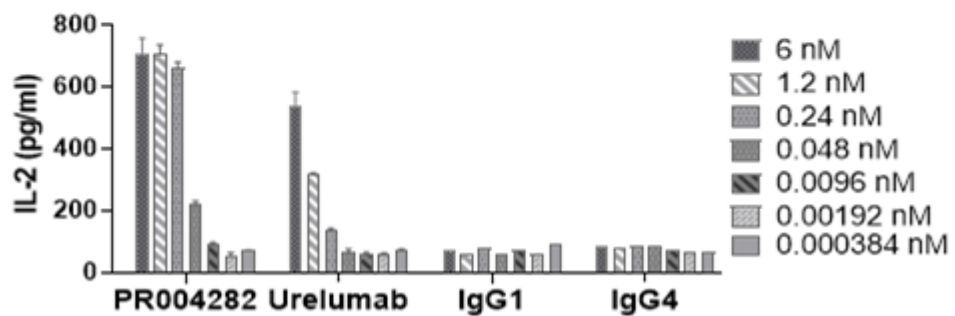
13-(E)

MDA-MB-468 cell-mediated T cell activation

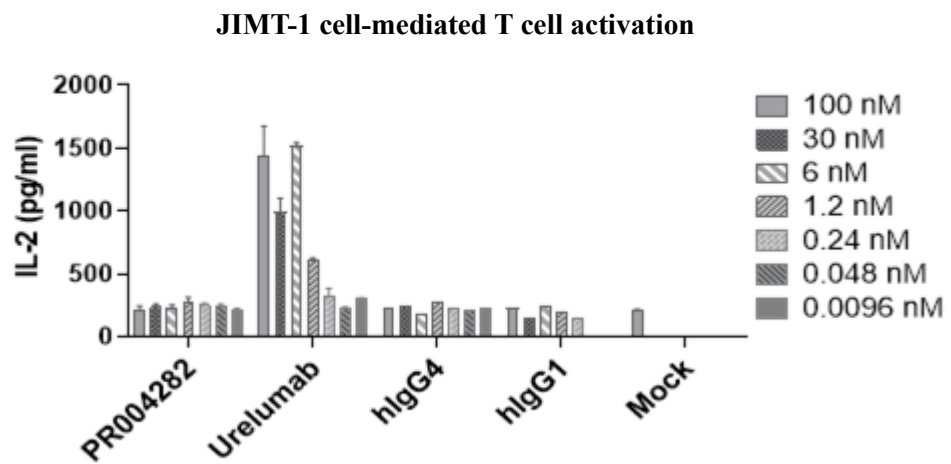


13-(F)

SK-BR-3 cell-mediated T cell activation



13-(G)



13-(H)

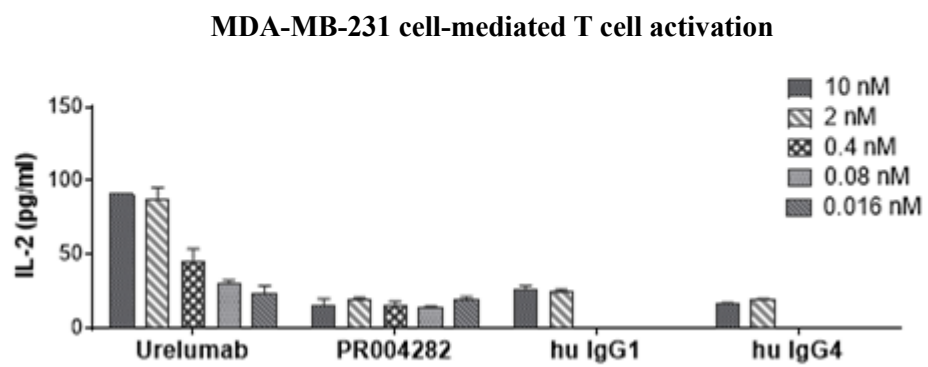
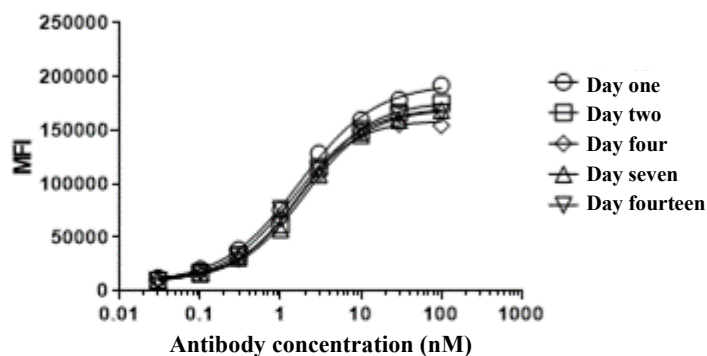


FIG. 13

14-(A)

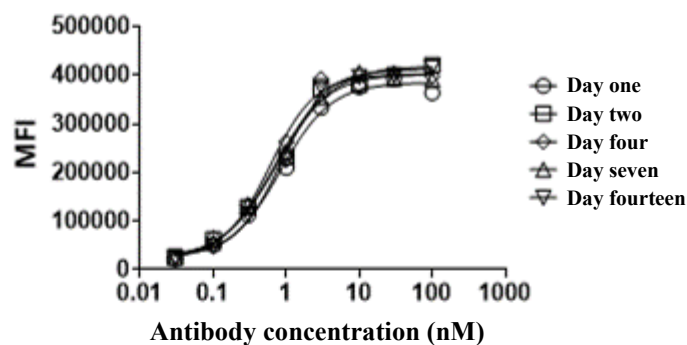
Binding of PR003334 to SK-BR-3 cells



Time point	EC50 (nM)	Maximum signal value
Day one	1.707	186430
Day two	1.912	168183
Day four	1.562	147497
Day seven	2.004	160471
Day fourteen	1.489	164959

14-(B)

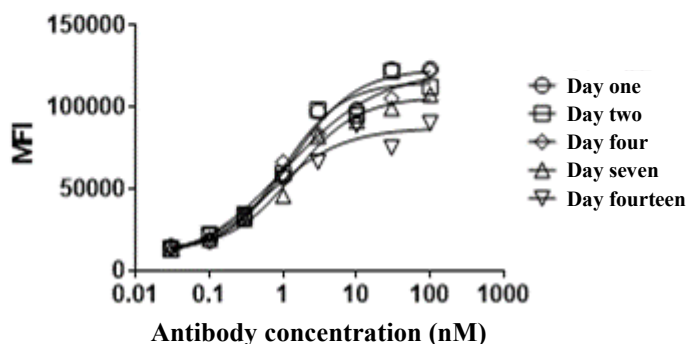
Binding of PR003334 to CHO-K1/hu 4-1BB cells



Time point	EC50 (nM)	Maximum signal value
Day one	0.841	360239
Day two	0.769	397943
Day four	0.607	374153
Day seven	0.680	381546
Day fourteen	0.851	383431

14-(C)

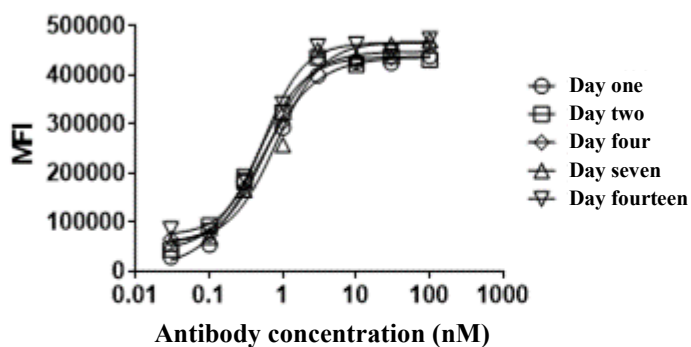
Binding of PR003335 to SK-BR-3 cells



Time point	EC50 (nM)	Maximum signal value
Day one	1.285	112575
Day two	1.039	102557
Day four	1.072	120474
Day seven	1.41	93520
Day fourteen	0.6645	78631

14-(D)

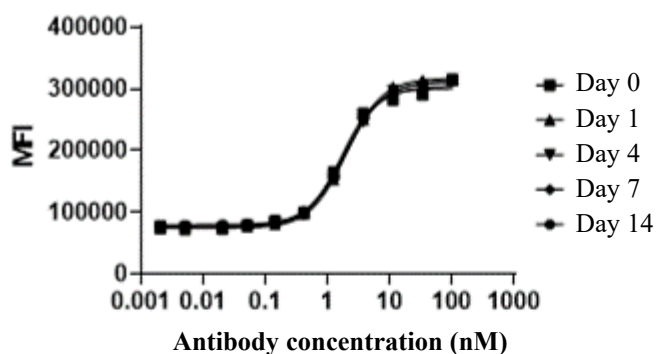
Binding of PR003335 to CHO-K1/hu 4-1BB cells



Time point	EC50 (nM)	Maximum signal value
Day one	0.4700	432153
Day two	0.4572	396669
Day four	0.6241	389379
Day seven	0.8201	410577
Day fourteen	0.5605	391641

14-(E)

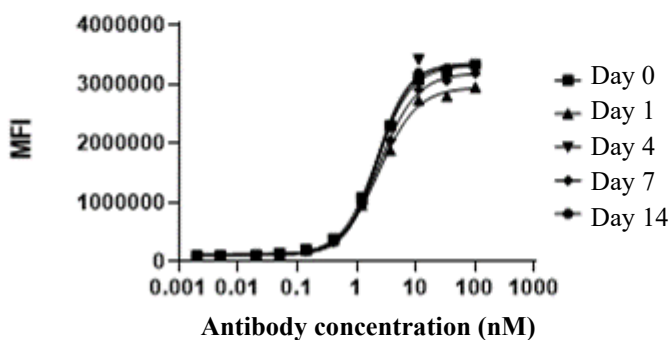
Binding of PR004282 to CHO-K1/human 4-1BB cells



Time point	EC50 (nM)	Maximum signal value
Day 0	1.613	300719
Day one	1.954	316913
Day four	1.813	312597
Day seven	1.766	304656
Day fourteen	1.953	311639

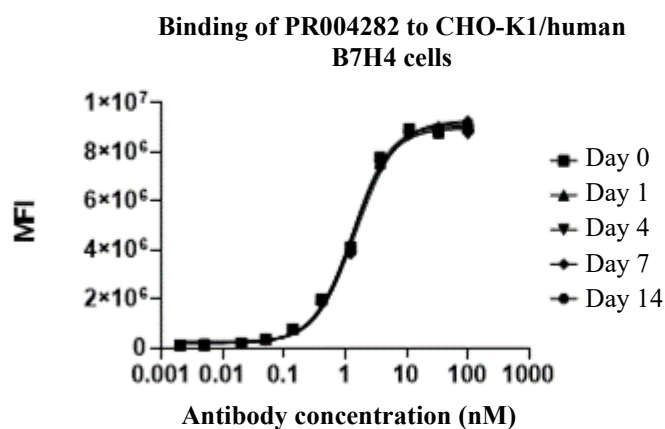
14-(F)

Binding of PR004282 to CHO-K1/monkey 4-1BB cells



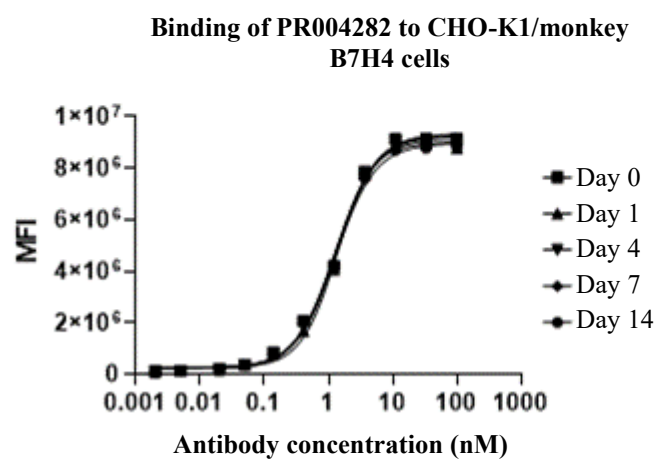
Time point	EC50 (nM)	Maximum signal value
Day 0	2.18	3314024
Day one	2.386	2942971
Day four	2.185	3320789
Day seven	2.416	3184374
Day fourteen	2.329	3344662

14-(G)



Time point	EC50 (nM)	Maximum signal value
Day 0	1.297	9300606
Day one	1.344	9028383
Day four	1.331	9334816
Day seven	1.294	9206150
Day fourteen	1.276	8974801

14-(H)

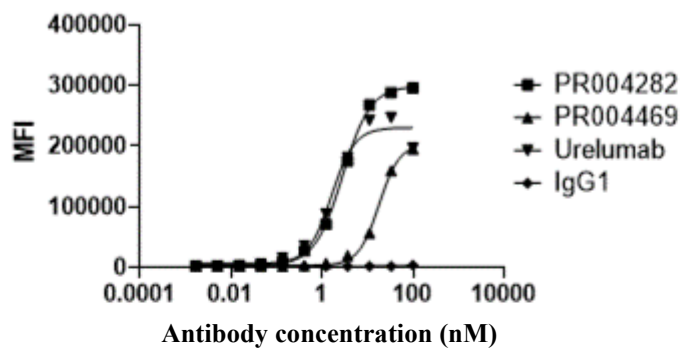


Time point	EC50 (nM)	Maximum signal value
Day 0	1.305	9090977
Day one	1.356	9217138
Day four	1.292	9000287
Day seven	1.496	9295882
Day fourteen	1.346	8990780

FIG. 14

15-(A)

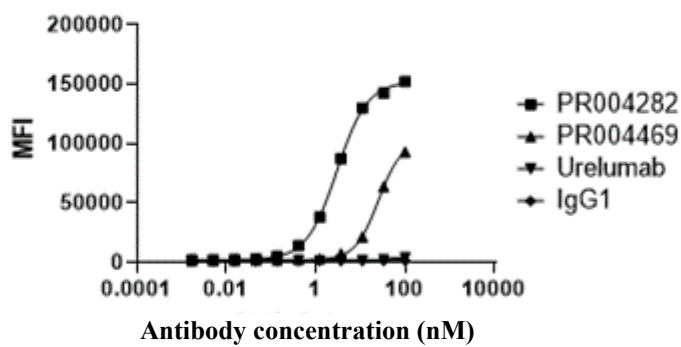
Binding of PR004282 to CHO-K1/h4-1BB cells



Antibody	EC50 (nM)	Maximum MFI
PR004282	2.851	299284
PR004469	18.01	203998
Urelumab	1.63	230882

15-(B)

Binding of PR004282 to CHO-K1/cyno-4-1BB cells



Antibody	EC50 (nM)	Maximum MFI
PR004282	2.99	151967
PR004469	25.38	102035
Urelumab	~ 39.92	3842

15-(C)

Binding of PR004282 to CHO-K1/m4-1BB

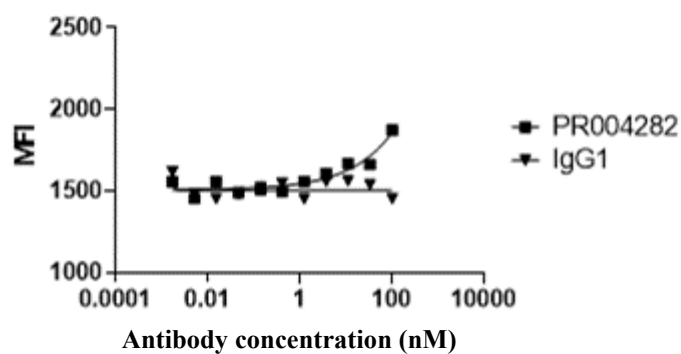
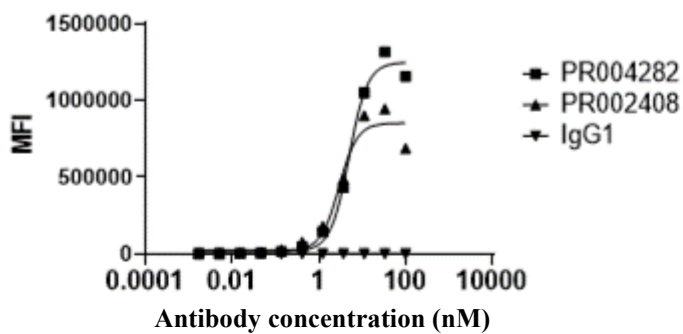


FIG. 15

16-(A)

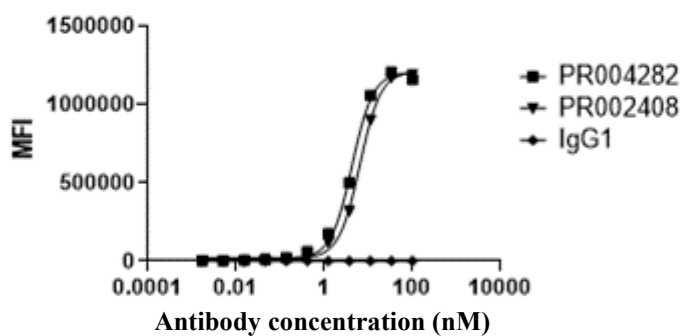
Binding to CHO-K1/human B7H4 cells



Antibody	EC50 (nM)	Maximum MFI
PR004282	4.961	1249032
PR002408	2.925	853508

16-(B)

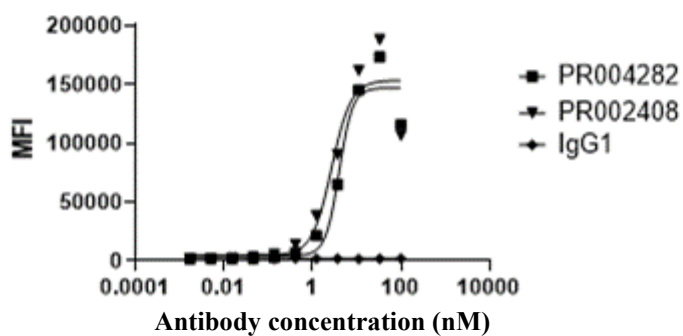
Binding to CHO-K1/monkey B7H4 cells



Antibody	EC50 (nM)	Maximum MFI
PR004282	4.272	1202740
PR002408	6.395	1208645

16-(C)

Binding to CHO-K1/mouse B7H4 cells



Antibody	EC50 (nM)	Maximum MFI
PR004282	3.997	146939
PR002408	2.714	153281

FIG. 16

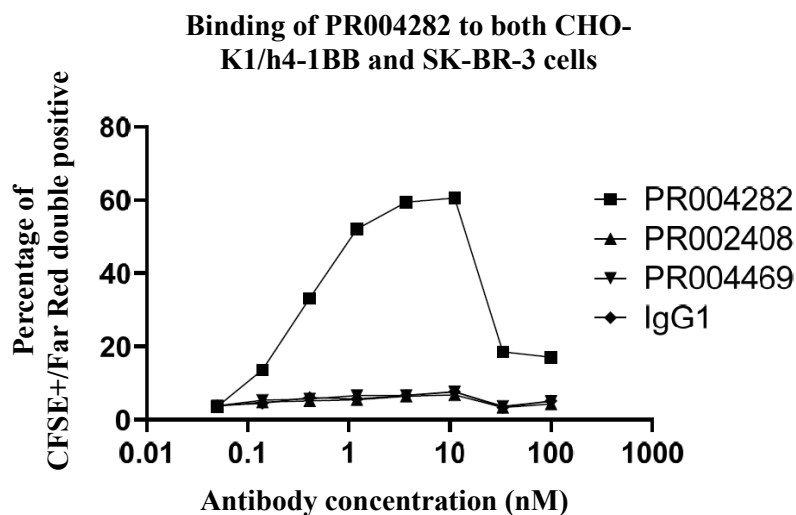
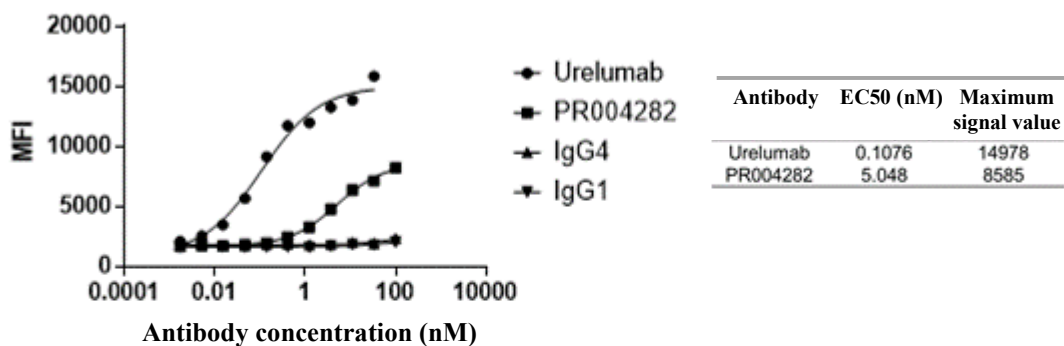


FIG. 17

18-(A)

Binding of PR004282 to activated human Pan T cells



18-(B)

Binding of PR004282 to activated monkey Pan T cells

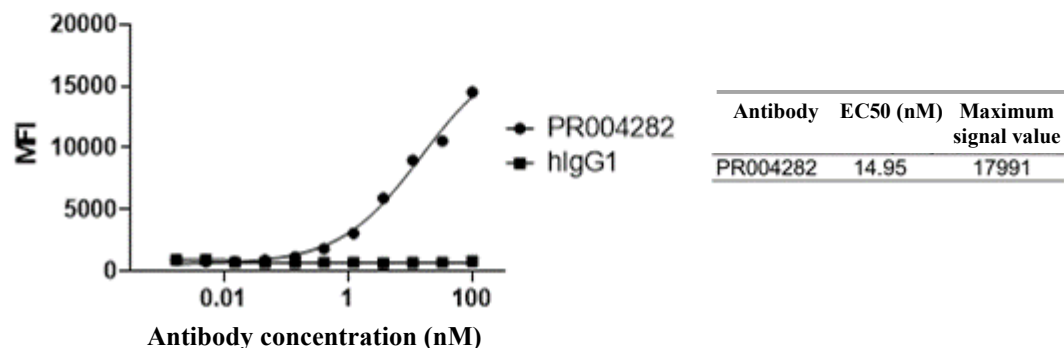
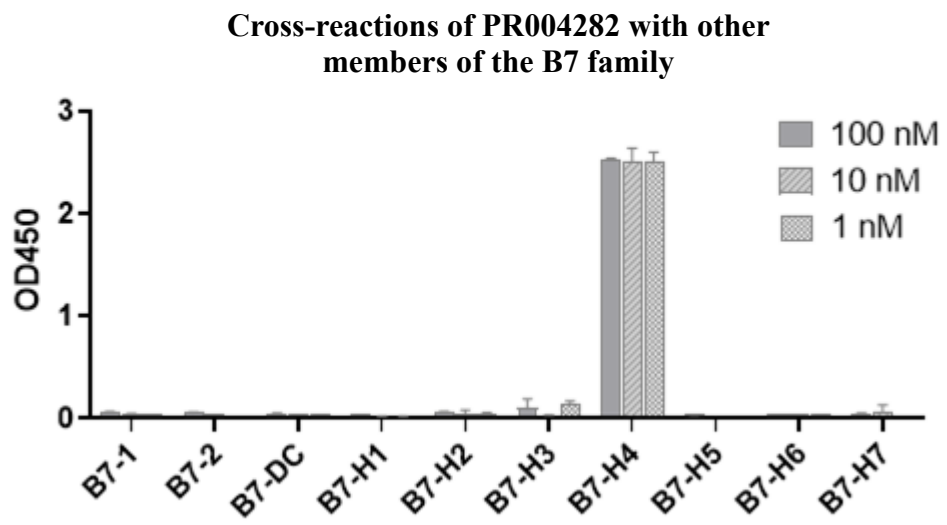


FIG. 18

19-(A)



19-(B)

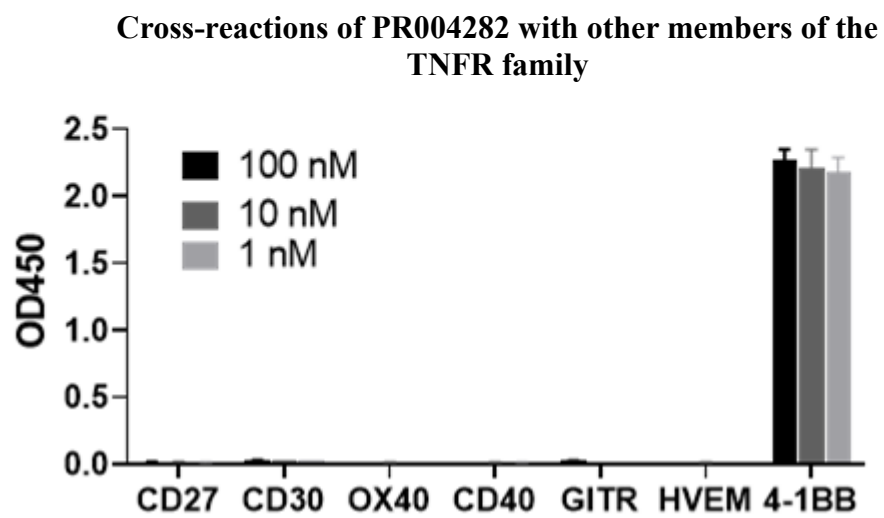
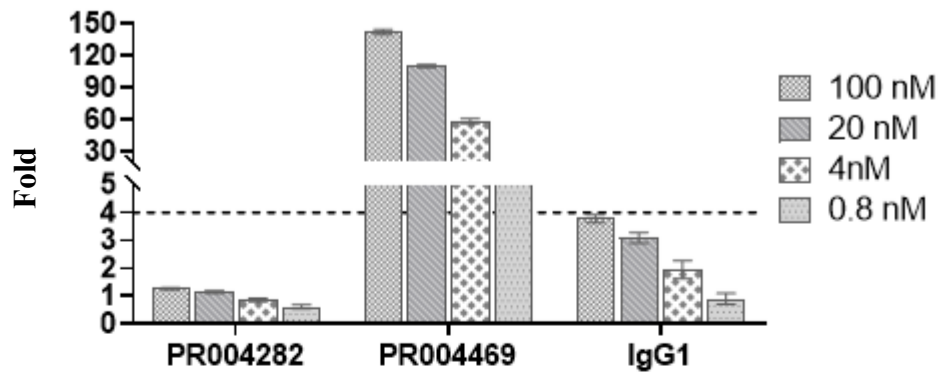


FIG. 19

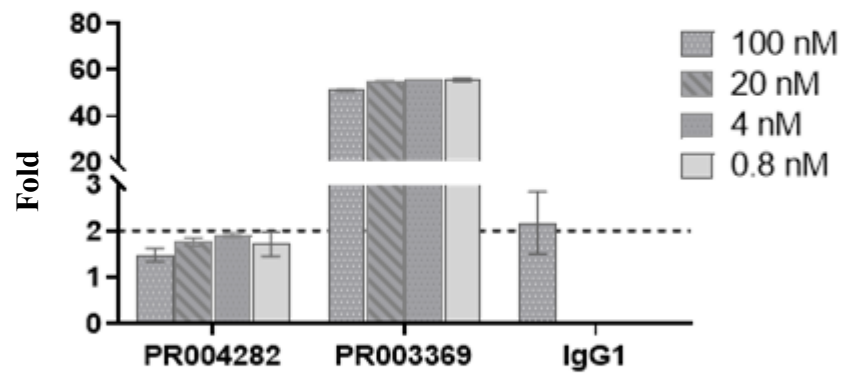
20-(A)

Jurkat-CD16a-NFAT: CHO-K1/4-1BB cells
effector-to-target ratio = 5:1



20-(B)

Jurkat-CD16a-NFAT: SK-BR-3
effector-to-target ratio E:T = 5:1



20-(C)

NK:SK-BR-3, effector-to-target ratio = 5:1

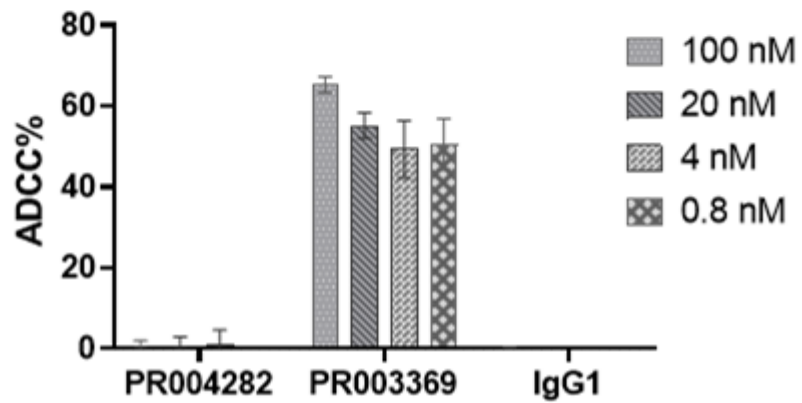
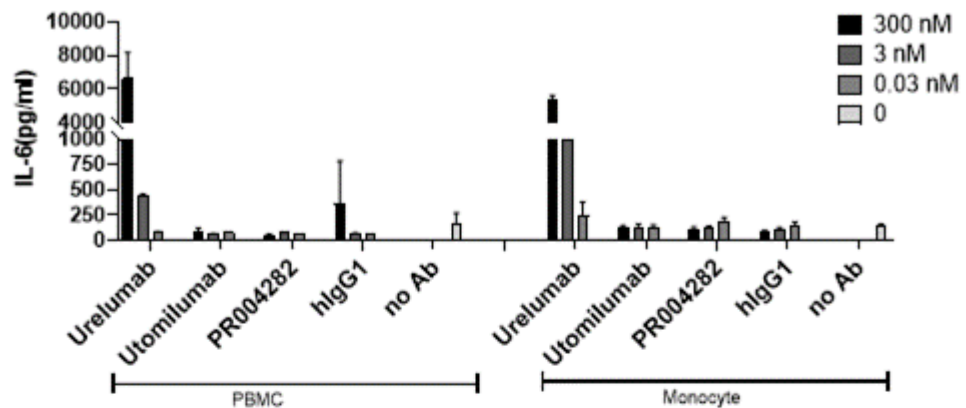


FIG. 20

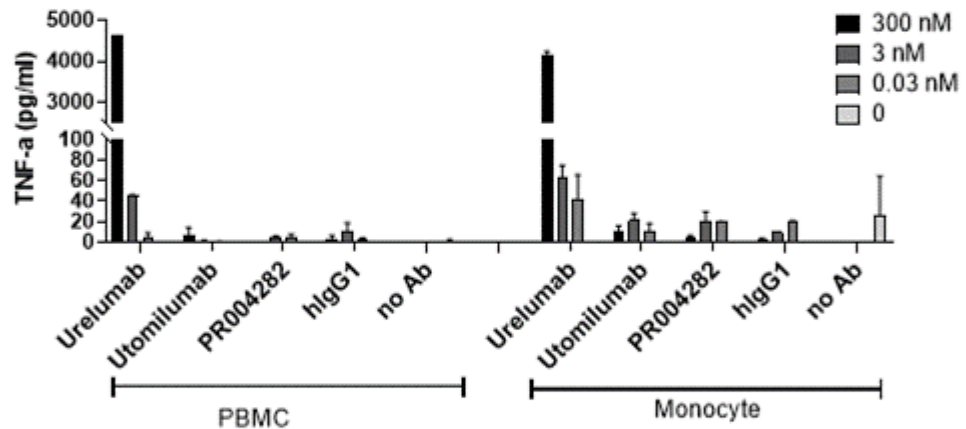
21-(A)

Release of IL-6 in the supernatant after 24-hour incubation of PR004282 with PBMCs or monocytes



21-(B)

Release of TNF- α in the supernatant after 24-hour incubation of PR004282 with PBMCs or monocytes



21-(C)

Release of IFN- γ in the supernatant after 72-hour incubation of PR004282 with PBMCs or monocytes

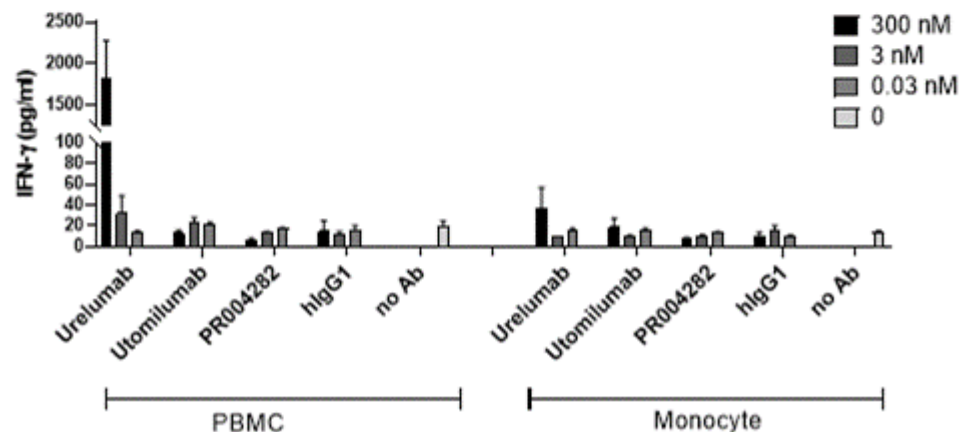
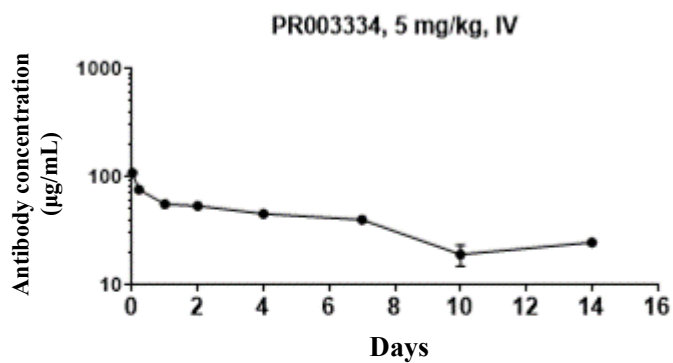


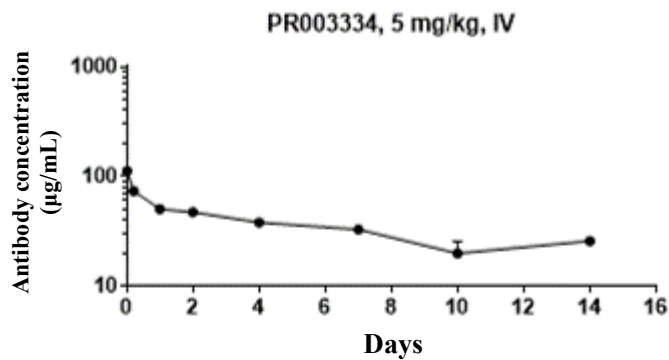
FIG. 21

22-(A)



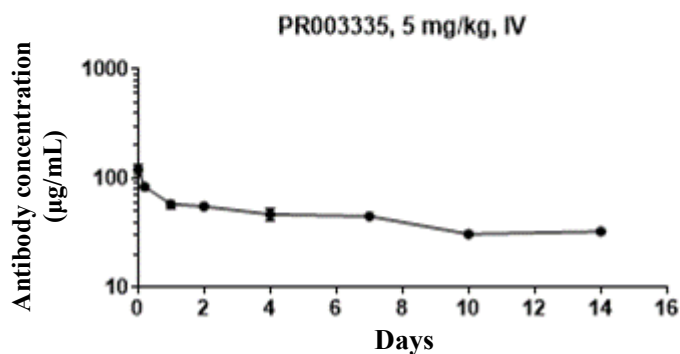
PK parameters	Unit	Average value
$T_{1/2}$	Hour	193
V_d	mL/kg	76
AUC_{0-14}	$\mu\text{g} \cdot \text{hour/mL}$	12,680
AUC *	%	100
CL	mL/hour/kg	0.28
C_0	$\mu\text{g/mL}$	111

22-(B)



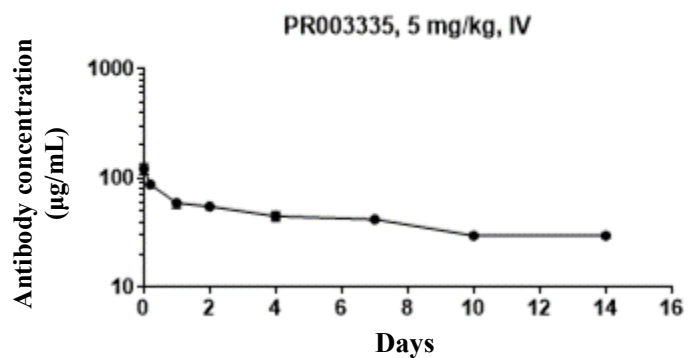
PK parameters	Unit	Average value
$T_{1/2}$	Hour	218
V_d	mL/kg	89
AUC_{0-14}	$\mu\text{g} \cdot \text{hour/mL}$	11,471
AUC *	%	90
CL	mL/hour/kg	0.28
C_0	$\mu\text{g/mL}$	114

22-(C)



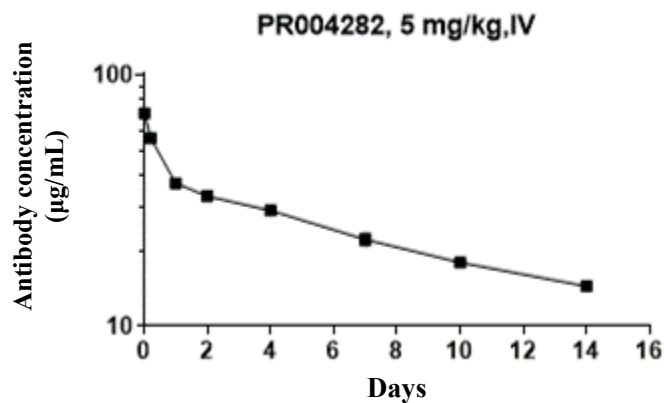
PK parameters	Unit	Average value
$T_{1/2}$	Hour	336
V_d	mL/kg	81
AUC_{0-14}	$\mu\text{g} \cdot \text{hour/mL}$	14,813
AUC *	%	100
CL	mL/hour/kg	0.17
C_0	$\mu\text{g/mL}$	123

22-(D)



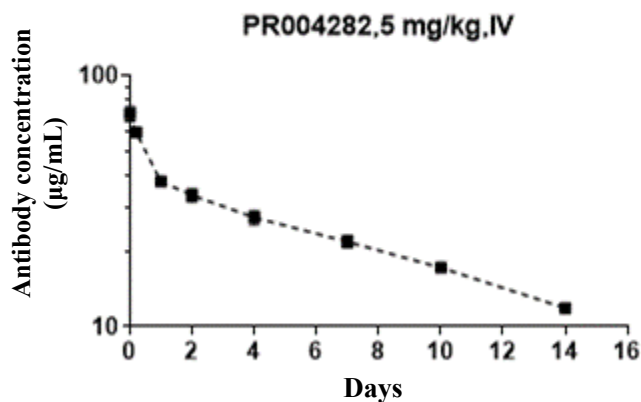
PK parameters	Unit	Average value
$T_{1/2}$	Hour	295
V_d	mL/kg	81
AUC_{0-14}	$\mu\text{g} \cdot \text{hour/mL}$	14,286
AUC *	%	96
CL	mL/hour/kg	0.19
C_0	$\mu\text{g/mL}$	124

22-(E)



PK parameters	Unit	Average value
$T_{1/2}$	Hour	274
V_d	mL/kg	133
AUC_{0-14}	$\mu\text{g} \cdot \text{hour/mL}$	8,363±102
AUC *	%	100
CL	mL/hour/kg	0.36
C_0	$\mu\text{g/mL}$	71

22-(F)



PK parameters	Unit	Average value
$T_{1/2}$	Hour	197
V_d	mL/kg	119
AUC_{0-14}	$\mu\text{g} \cdot \text{hour/mL}$	8,125±150
AUC *	%	97
CL	mL/hour/kg	0.43
C_0	$\mu\text{g/mL}$	71

FIG. 22

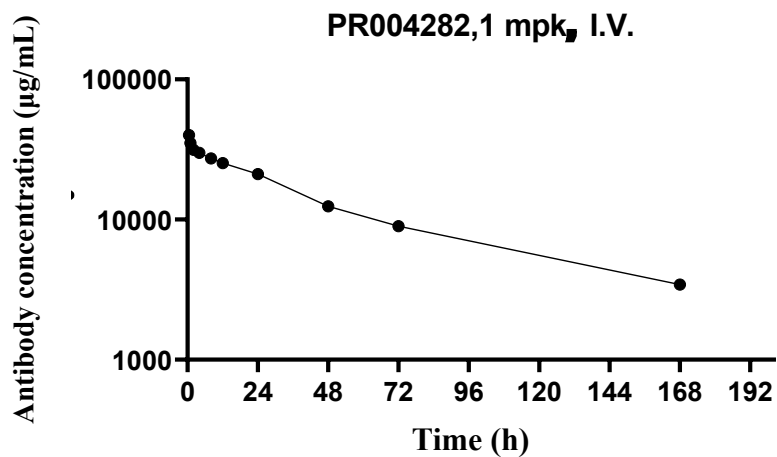
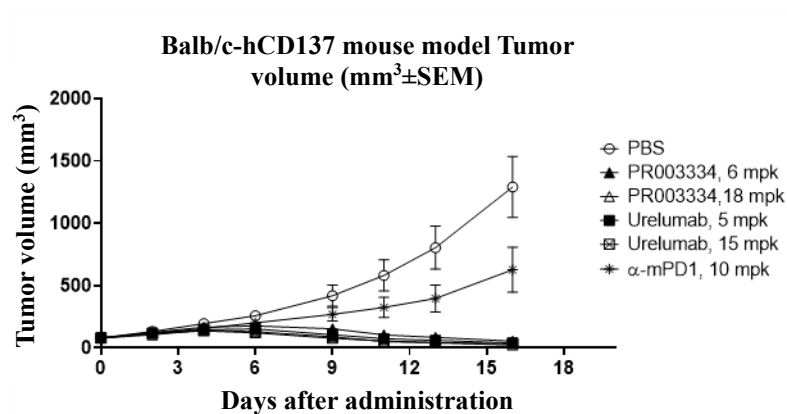


FIG. 23

24-(A)



24-(B)

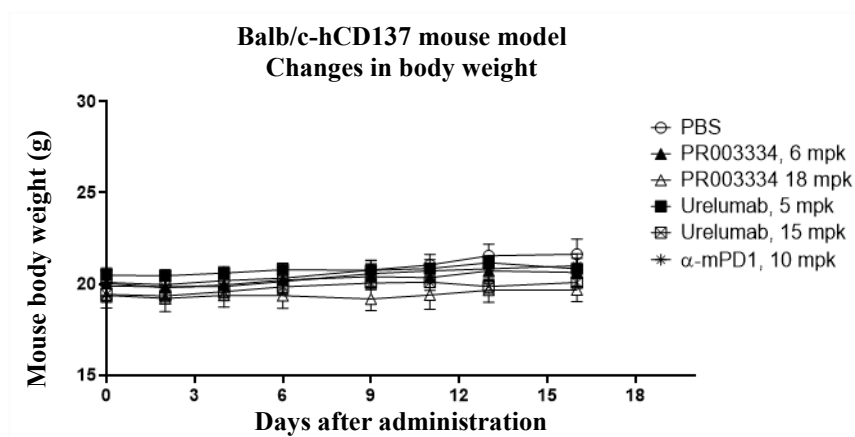
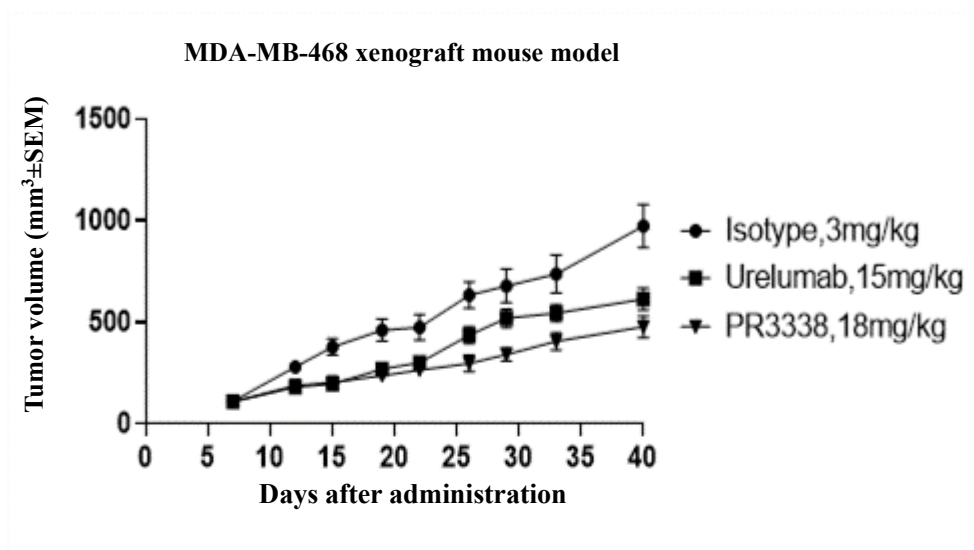


FIG. 24

25-(A)



25-(B)

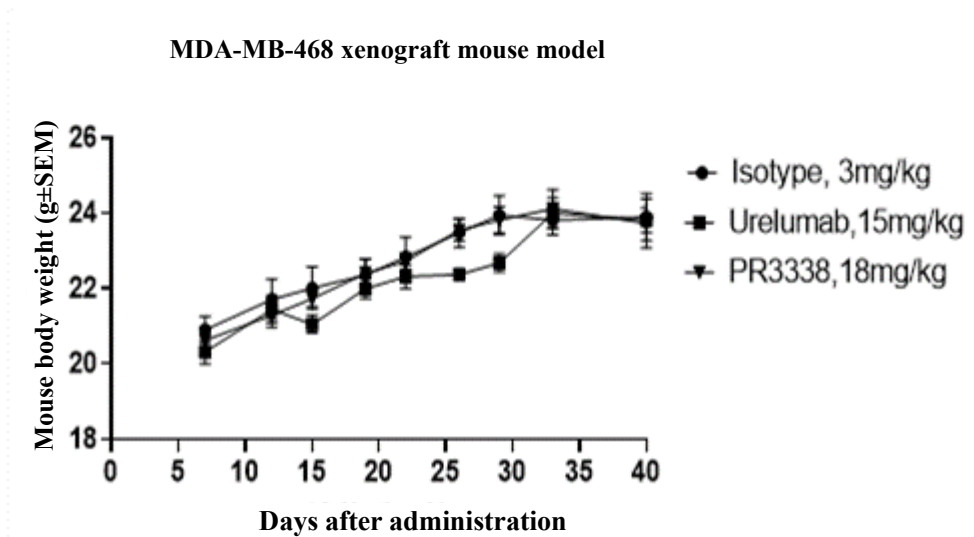
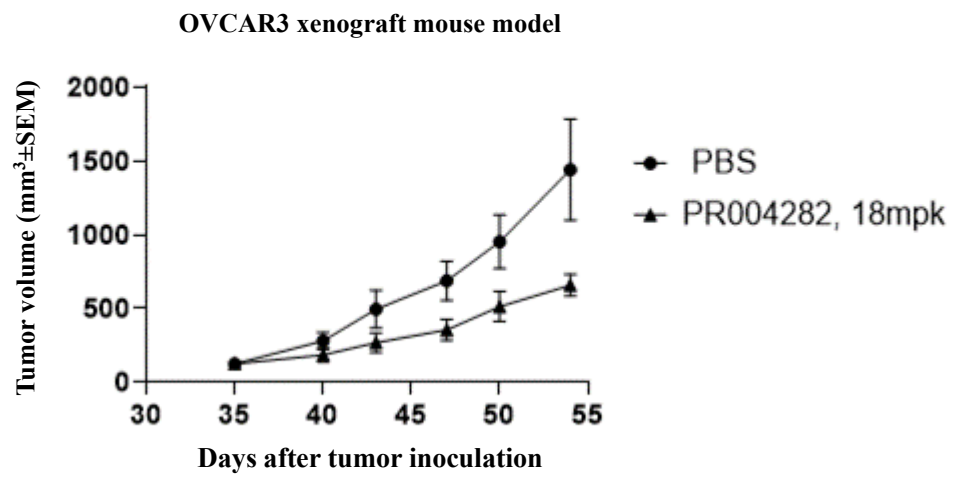


FIG. 25

26-(A)



26-(B)

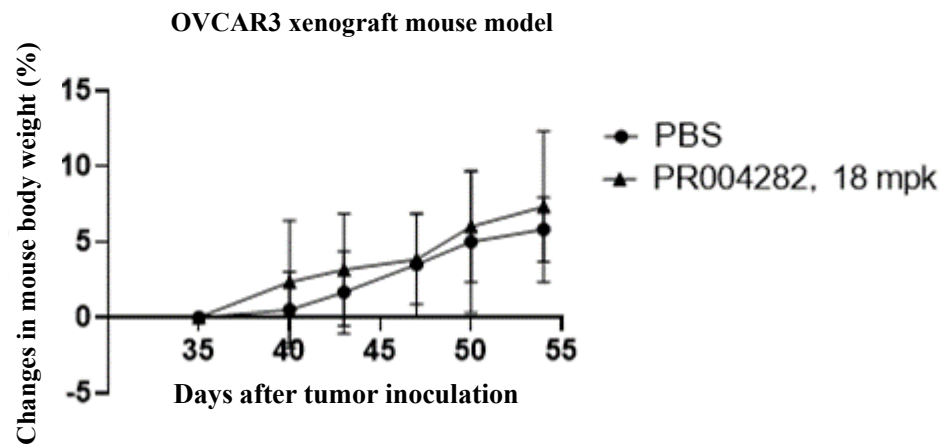
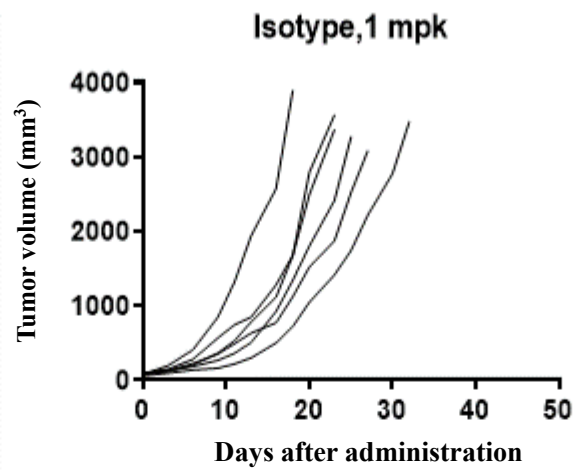
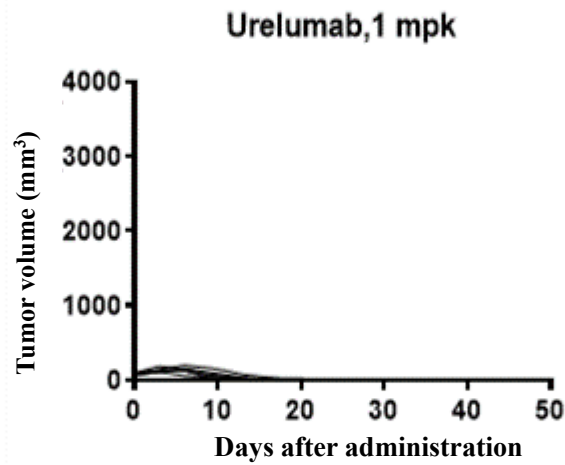


FIG. 26

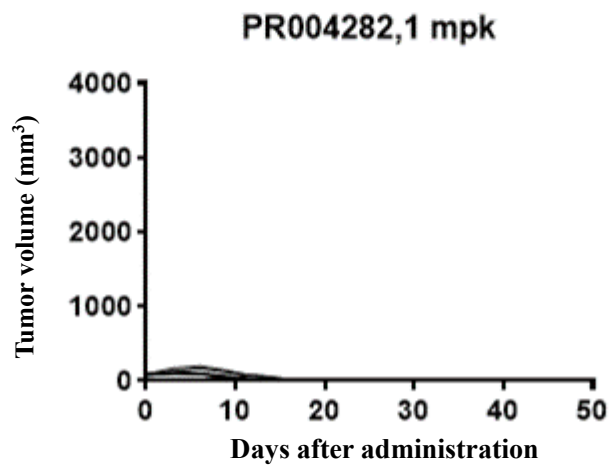
27-(A)



27-(B)

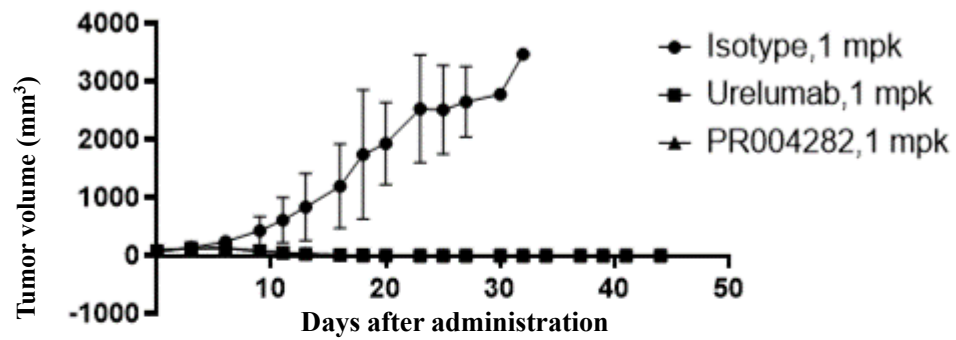


27-(C)



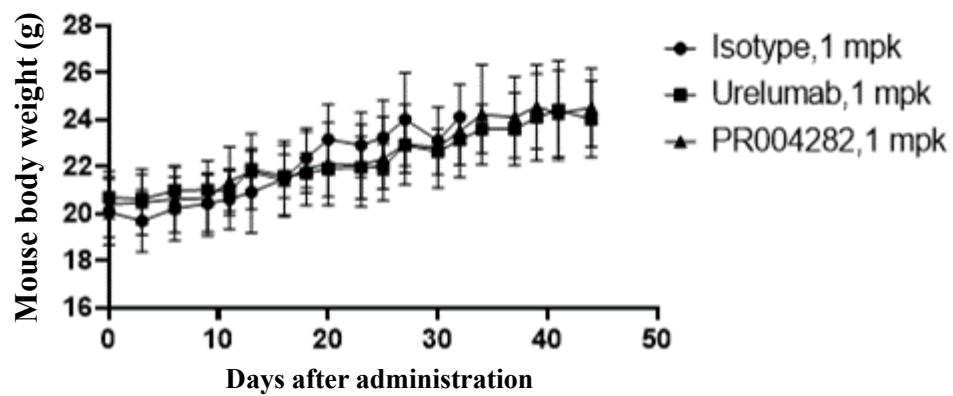
27-(D)

Balb/c-hCD137 mouse
model Tumor volume

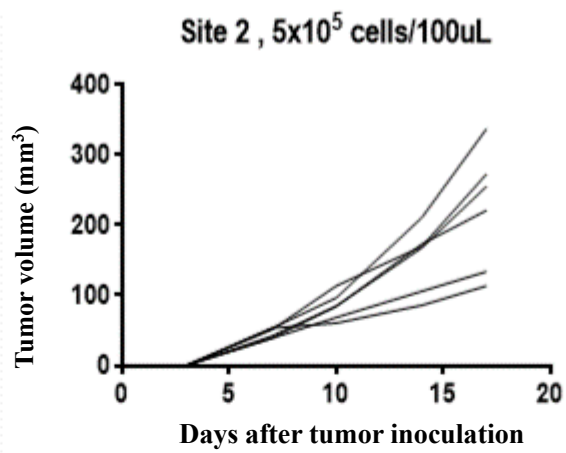


27-(E)

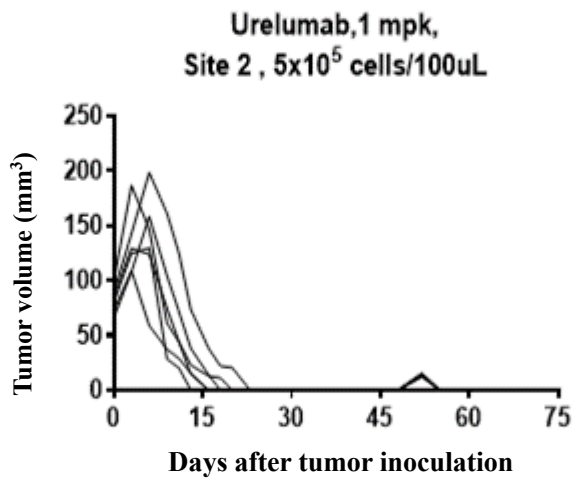
Balb/c-hCD137 mouse
model Mouse body weight



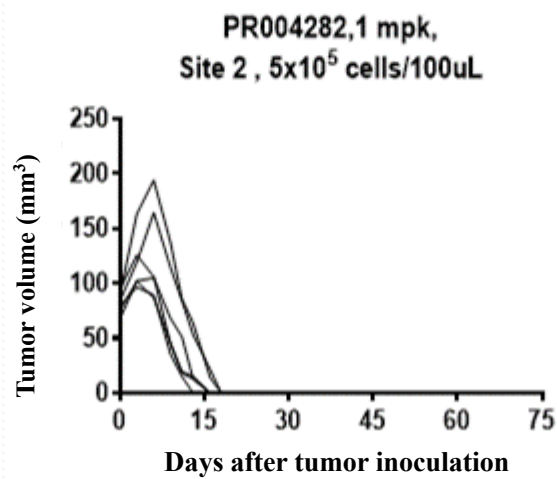
27-(F)



27-(G)



27-(H)



27-(I)

Balb/c-hCD137 mouse
model Tumor volume

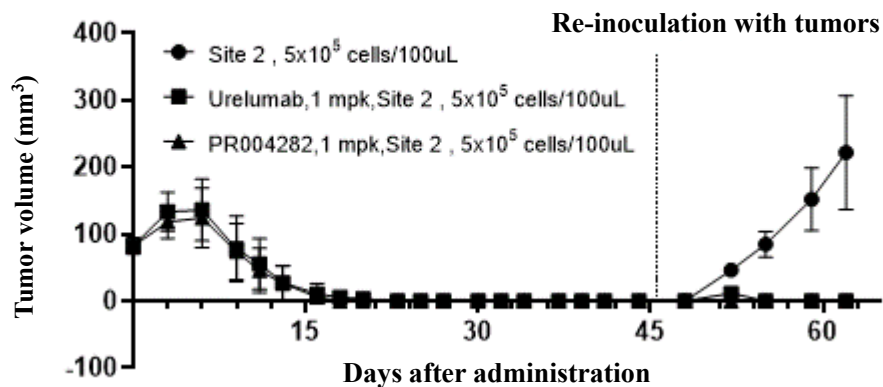
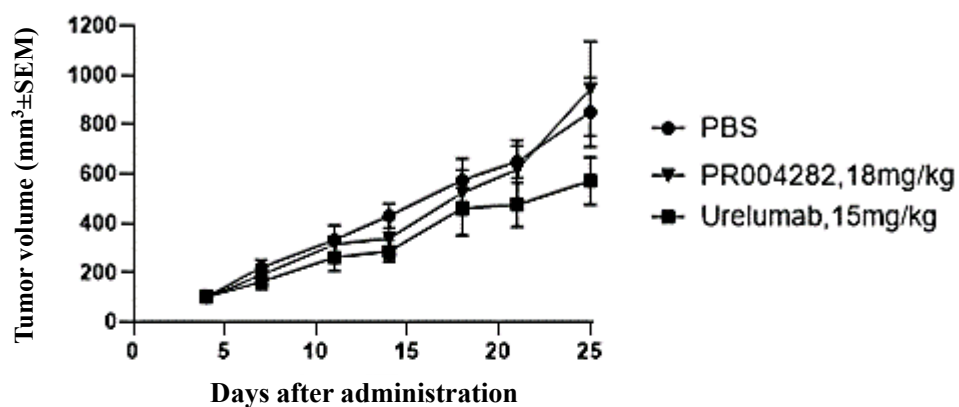


FIG. 27

28-(A)

JIMT-1 PBMC model



28-(B)

BALB/c-hCD137 mice bearing CT26 wild-
type tumors
Tumor volume

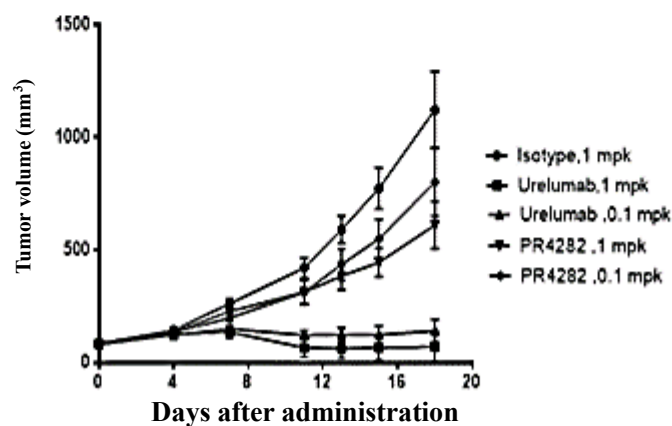


FIG. 28