FIG. 1A

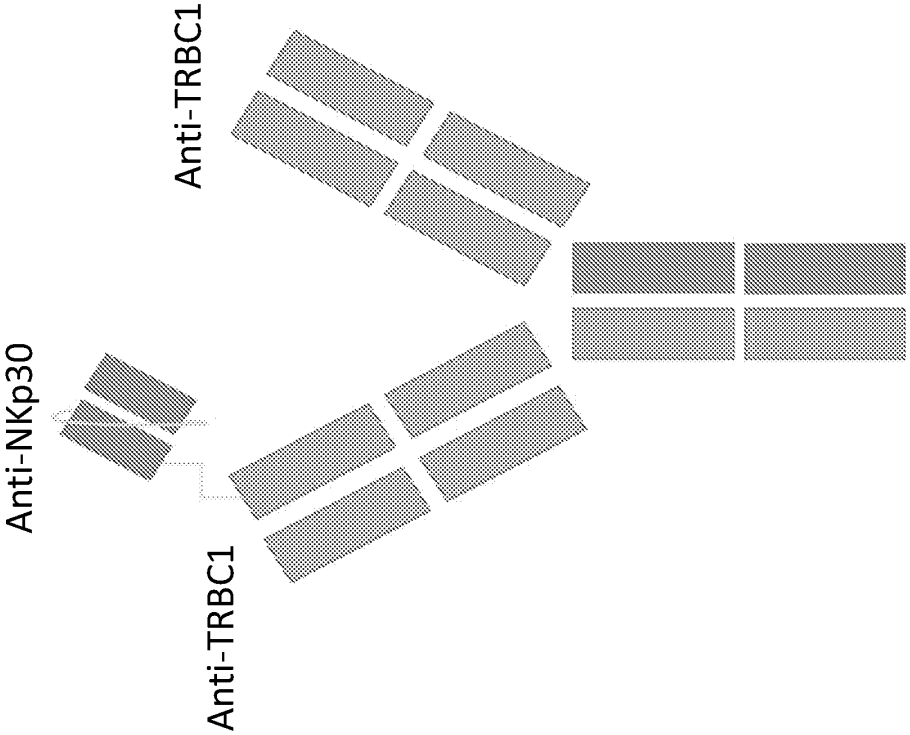


FIG. 1B

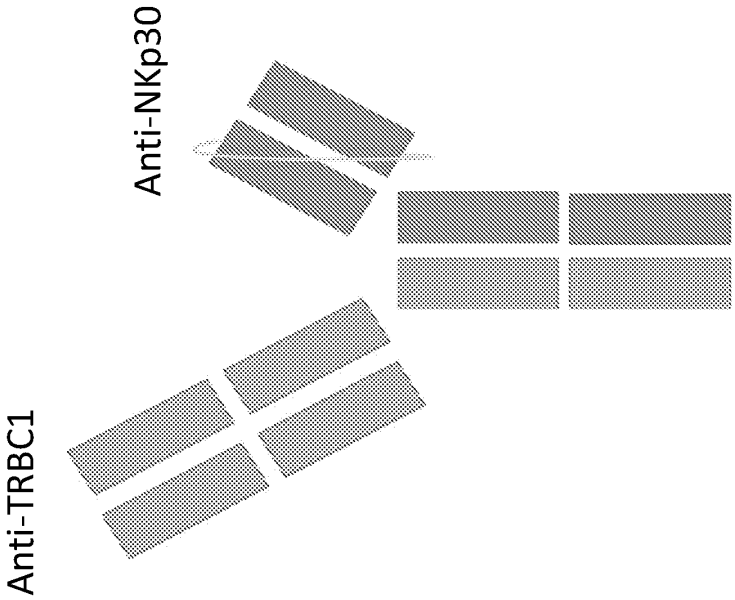


FIG. 1C

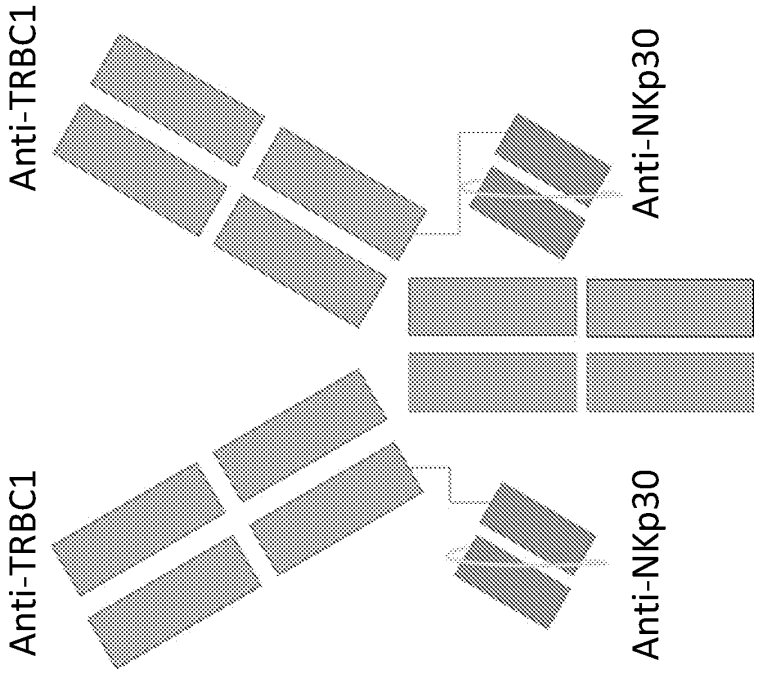

Anti-TRBC1
Anti-NKp30

FIG. 1D

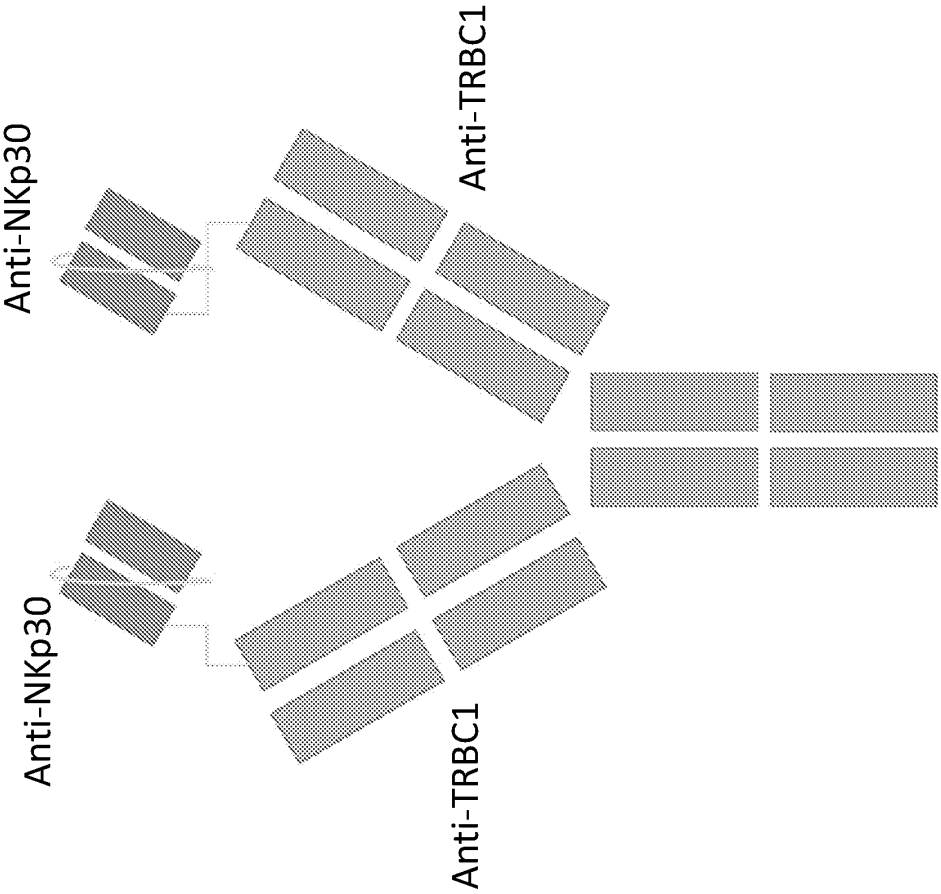

Anti-NKp30
Anti-TRBC1
Anti-NKp30
Anti-TRBC1

FIG. 2B

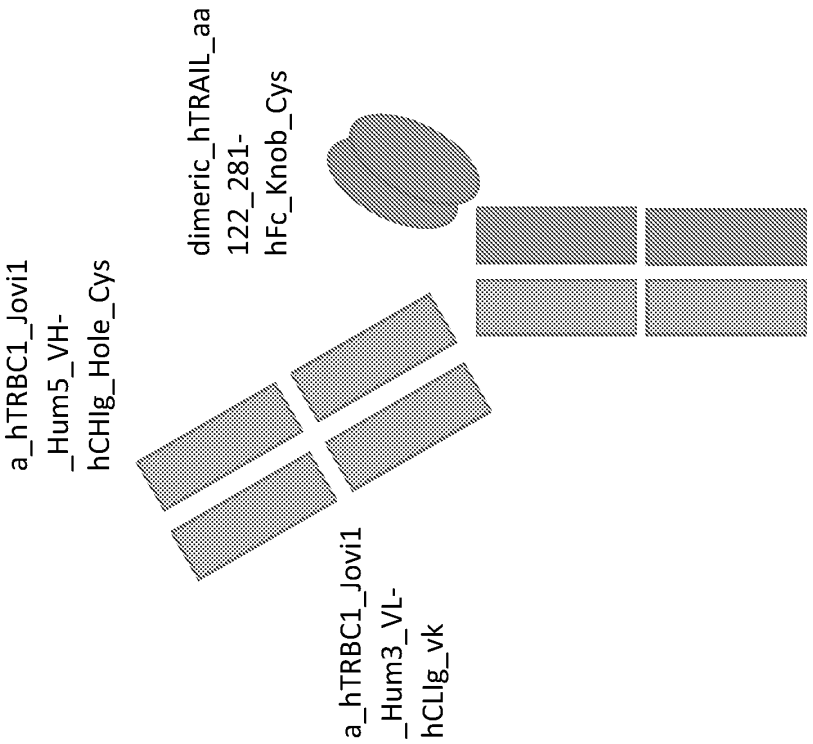

a_hTRBC1_Jovi1
_Hum5_VH-
hCHIg_Hole_Cys
dimeric_hTRAIL_aa
122_281-
hFc_Knob_Cys
a_hTRBC1_Jovi1
_Hum3_VL-
hCLIg_vk

FIG. 2A

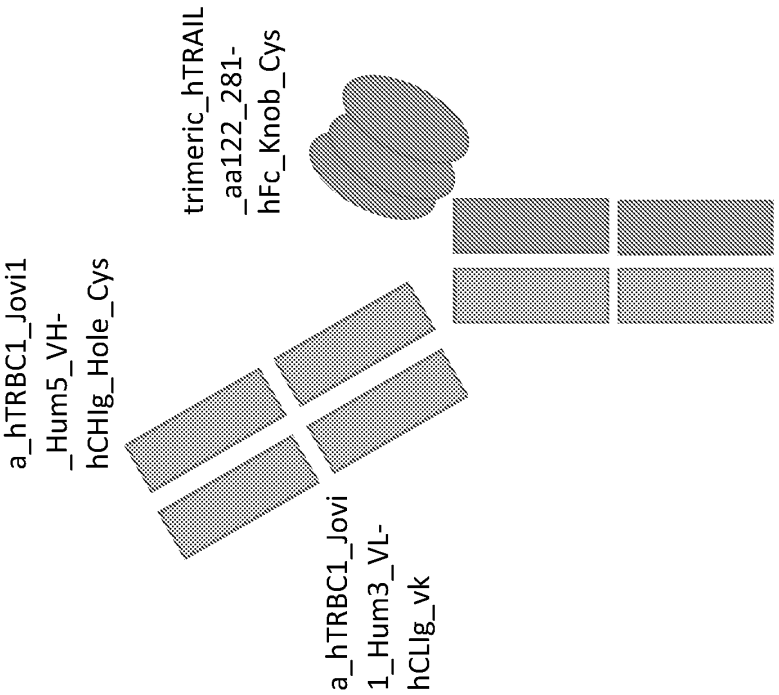

a_hTRBC1_Jovi1
_Hum5_VH-
hCHIg_Hole_Cys
trimeric_hTRAIL
_aa122_281-
hFc_Knob_Cys
a_hTRBC1_Jovi
1_Hum3_VL-
hCLIg_vk

FIG. 2C

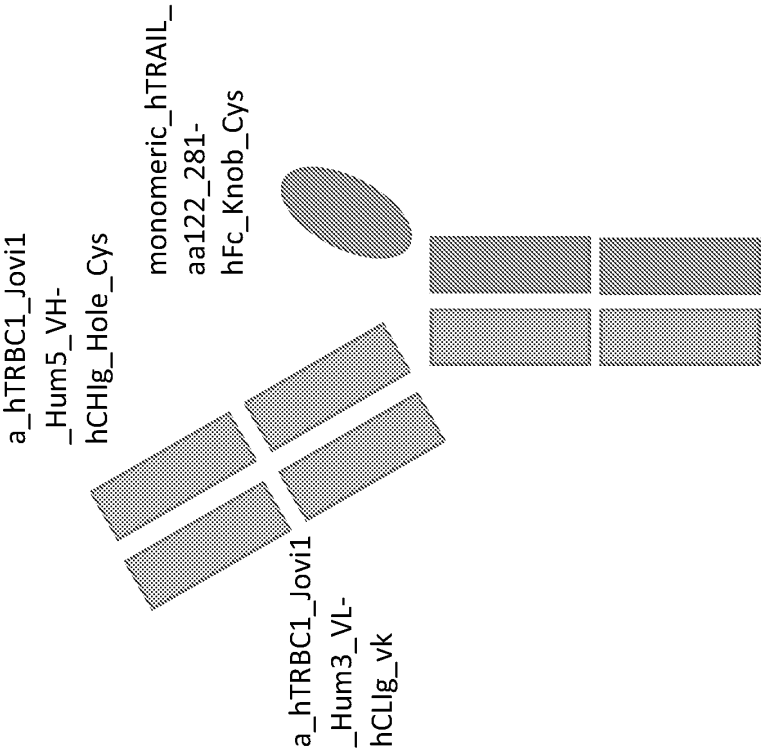

a_hTRBC1_Jovi1
_Hum5_VH-
hCHIg_Hole_Cys
monomeric_hTRAIL_
aa122_281-
hFc_Knob_Cys
a_hTRBC1_Jovi1
_Hum3_VL-
hCLIg_vk

FIG. 2D

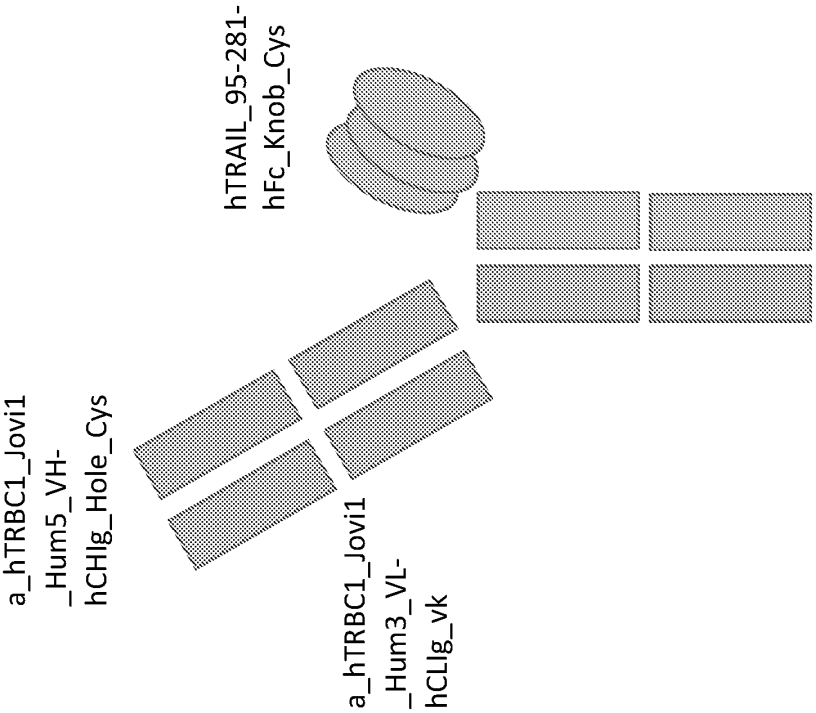

a_hTRBC1_Jovi1
_Hum5_VH-
hCHIg_Hole_Cys
hTRAIL_95-281-
hFc_Knob_Cys
a_hTRBC1_Jovi1
_Hum3_VL-
hCLIg_vk

FIG. 2F

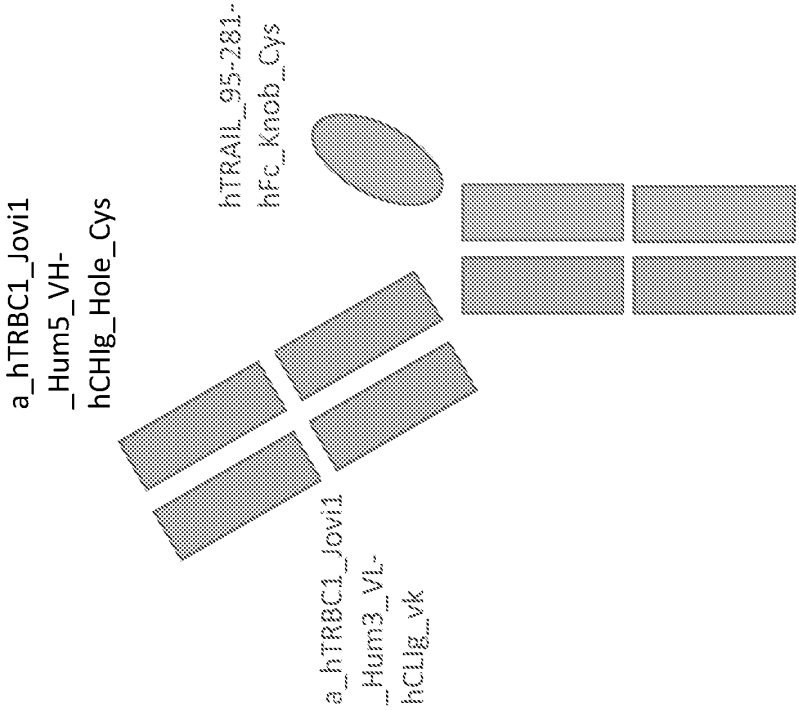

a_hTRBC1_Jovi1
_Hum5_VH-
hCHIg_Hole_Cys
hTRAIL_95-281-
hFc_Knob_Cys
a_hTRBC1_Jovi1
_Hum3_VL-
hCLIg_vk

FIG. 2E

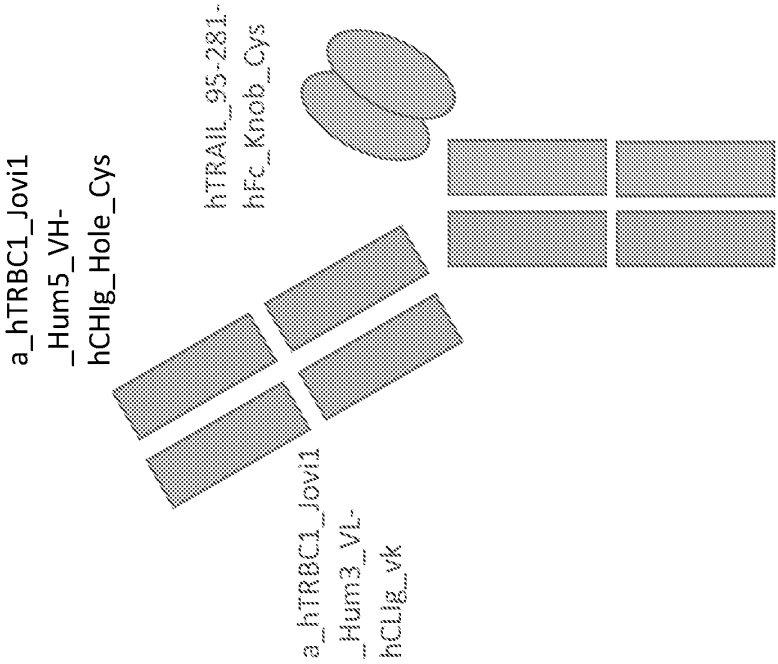

a_hTRBC1_Jovi1
_Hum5_VH-
hCHIg_Hole_Cys
hTRAIL_95-281-
hFc_Knob_Cys
a_hTRBC1_Jovi1
_Hum3_VL-
hCLIg_vk

FIG. 3A

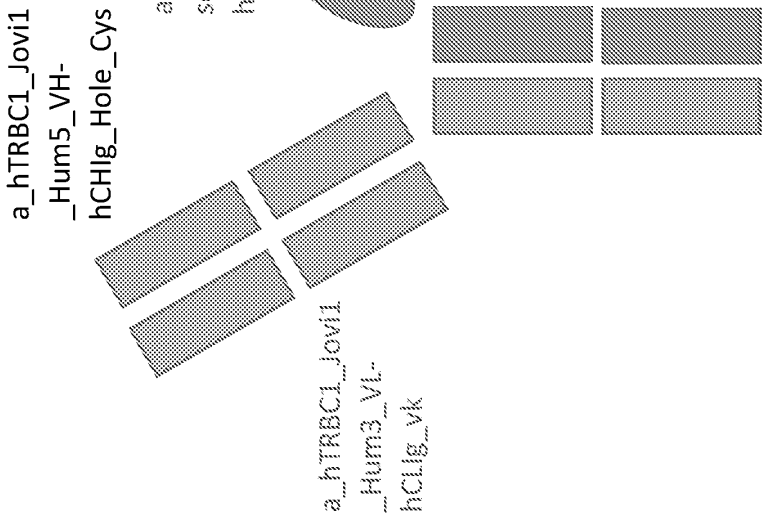
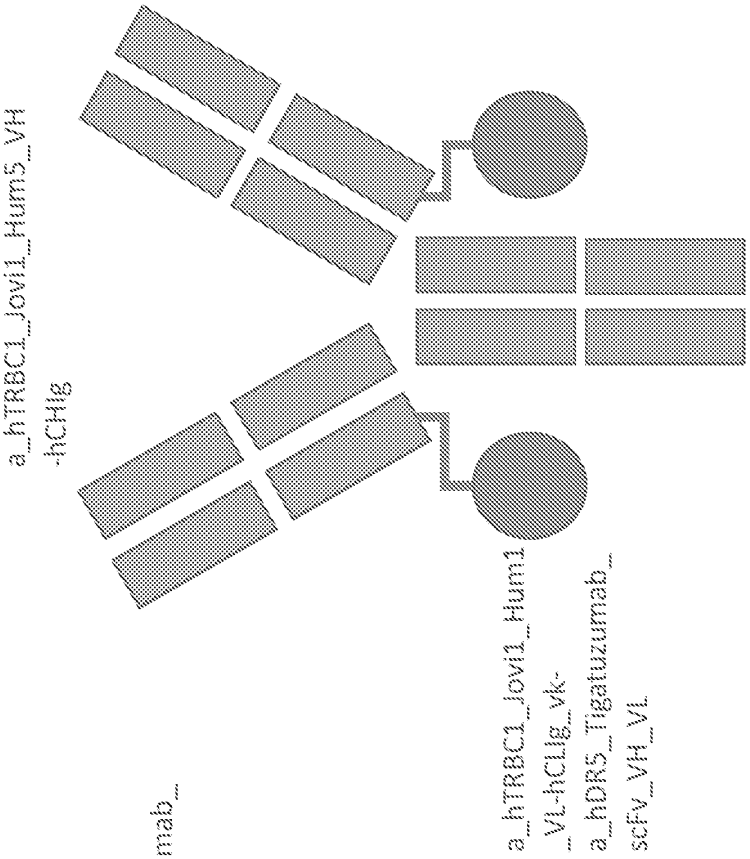

a_hTRBC1_Jovi1
_Hum5_VH-
hCHIg_Hole_Cys
a_hTRBC1_Jovi1
_Hum3_VL-
hCLIg_vk
a_hDR5_Tigatuzumab_
scFv_VH_VL-
hFc_Knob_Cys

FIG. 3B


a_hTRBC1_Jovi1_Hum5_VH
-hCHIg
a_hTRBC1_Jovi1_Hum1
_VL-hCLIg_vk-
a_hDR5_Tigatuzumab_
scFv_VH_VL

VH

	Framework 1																									CDR 1									
	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28	29	30	31	32	33	34	35
SEQ ID NO: 1	Q	V	Q	L	Q	Q	S	G	P	E	L	V	K	P	G	T	S	V	K	I	S	C	K	A	S	*G*	*Y*	*S*	*F*	*T*	***T***	***Y***	**Y**	**I**	**H**
SEQ ID NO: 9	Q	V	Q	L	V	Q	S	G	A	E	V	K	K	P	G	S	S	V	K	V	S	C	K	A	S	*G*	*Y*	*S*	*F*	*T*	***T***	***Y***	**Y**	**I**	**H**

	Framework 2														CDR 2																	
	36	37	38	39	40	41	42	43	44	45	46	47	48	49	50	51	52	52a	53	54	55	56	57	58	59	60	61	62	63	64	65
SEQ ID NO: 1	W	V	K	Q	R	P	G	Q	G	L	E	W	I	G	**W**	**F**	***F***	***P***	***G***	***S***	***G***	***N***	**I**	**K**	**Y**	**N**	**E**	**K**	**F**	**K**	**G**
SEQ ID NO: 9	W	V	R	Q	A	P	G	Q	G	L	E	W	M	G	**W**	**F**	***F***	***P***	***G***	***S***	***G***	***N***	**I**	**K**	**Y**	**N**	**E**	**K**	**F**	**K**	**G**

	66	67	68	69	70	71	72	73	74	75	76	77	78	79	80	81	82	82a	82b	82c	83	84	85	86	87	88	89	90	91	92	93	94
SEQ ID NO: 1	K	A	T	L	T	A	D	T	S	S	S	T	A	Y	M	Q	L	S	S	L	T	S	E	E	S	A	V	Y	F	C	A	G
SEQ ID NO: 9	R	V	T	I	T	A	D	T	S	T	S	T	A	Y	M	E	L	S	S	L	R	S	E	D	T	A	V	Y	Y	C	A	G

	CDR 3										Framework 4										
	95	96	97	98	99	100	100a	100b	101	102	103	104	105	106	107	108	109	110	111	112	113
SEQ ID NO: 1	***S***	***Y***	***Y***	***S***	***Y***	***D***	***V***	***L***	***D***	***Y***	W	G	H	G	T	T	L	T	V	S	S
SEQ ID NO: 9	***S***	***Y***	***Y***	***S***	***Y***	***D***	***V***	***L***	***D***	***Y***	W	G	Q	G	T	T	V	T	V	S	S

FIG. 4A

VL

Framework 1 | CDR 1

	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28	29	30	31	32	33	34
SEQ ID NO: 2	D	I	L	M	T	Q	S	Q	K	F	M	S	T	S	L	G	D	R	V	S	V	S	C	*K*	*A*	*S*	*Q*	*N*	*V*	*G*	*I*	*N*	*V*	*V*
SEQ ID NO: 10	D	I	Q	M	T	Q	S	P	S	F	L	S	A	S	V	G	D	R	V	T	I	T	C	*K*	*A*	*S*	*Q*	*N*	*V*	*G*	*I*	*N*	*V*	*V*
SEQ ID NO: 11	D	I	Q	M	T	Q	S	P	S	S	L	S	A	S	V	G	D	R	V	T	I	T	C	*K*	*A*	*S*	*Q*	*N*	*V*	*G*	*I*	*N*	*V*	*V*

Framework 2 | CDR 2

	35	36	37	38	39	40	41	42	43	44	45	46	47	48	49	50	51	52	53	54	55	56
SEQ ID NO: 2	W	H	Q	Q	K	P	G	Q	S	P	K	A	L	I	Y	*S*	*S*	*S*	*H*	*R*	*Y*	*S*
SEQ ID NO: 10	W	H	Q	Q	K	P	G	K	A	P	K	A	L	I	Y	*S*	*S*	*S*	*H*	*R*	*Y*	*S*
SEQ ID NO: 11	W	H	Q	Q	K	P	G	K	V	P	K	A	L	I	Y	*S*	*S*	*S*	*H*	*R*	*Y*	*S*

Framework 3

	57	58	59	60	61	62	63	64	65	66	67	68	69	70	71	72	73	74	75	76	77	78	79	80	81	82	83	84	85	86	87	88
SEQ ID NO: 2	G	V	P	D	R	F	T	G	S	G	S	G	T	D	F	T	L	T	I	N	N	V	Q	S	E	D	L	A	E	Y	F	C
SEQ ID NO: 10	G	V	P	S	R	F	S	G	S	G	S	G	T	E	F	T	L	T	I	S	S	L	Q	P	E	D	F	A	T	Y	F	C
SEQ ID NO: 11	G	V	P	S	R	F	S	G	S	G	S	G	T	D	F	T	L	T	I	S	S	L	Q	P	E	D	V	A	T	Y	F	C

CDR 3 | Framework 4

	89	90	91	92	93	94	95	96	97	98	99	100	101	102	103	104	105	106	107
SEQ ID NO: 2	*Q*	*Q*	*F*	*K*	*S*	*Y*	*P*	*L*	*T*	F	G	A	G	T	K	L	E	L	K
SEQ ID NO: 10	*Q*	*Q*	*F*	*K*	*S*	*Y*	*P*	*L*	*T*	F	G	Q	G	T	K	L	E	I	K
SEQ ID NO: 11	*Q*	*Q*	*F*	*K*	*S*	*Y*	*P*	*L*	*T*	F	G	Q	G	T	K	L	E	I	K

FIG. 4B

VH

	Framework 1																									CDR 1									
	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28	29	30	31	32	33	34	35
SEQ ID NO: 15	D	V	Q	L	V	E	S	G	G	G	L	V	Q	P	G	G	S	R	K	L	S	C	A	A	S	G	F	T	F	S	N	F	G	M	H
SEQ ID NO: 25	Q	V	Q	L	V	E	S	G	G	G	V	V	Q	P	G	R	S	L	R	L	S	C	A	A	S	G	F	T	F	S	N	F	G	M	H
SEQ ID NO: 23	E	V	Q	L	V	E	S	G	G	G	L	V	Q	P	G	G	S	L	R	L	S	C	A	A	S	G	F	T	F	S	N	F	G	M	H
SEQ ID NO: 24	E	V	Q	L	V	E	S	G	G	G	L	V	Q	P	G	G	S	L	R	L	S	C	A	A	S	G	F	T	F	S	N	F	G	M	H

	Framework 2														CDR 2															
	36	37	38	39	40	41	42	43	44	45	46	47	48	49	50	51	52	52a	53	54	55	56	57	58	59	60	61	62	63	64	65
SEQ ID NO: 15	W	V	R	Q	A	P	D	K	G	L	E	W	V	A	Y	I	S	S	G	S	S	T	I	Y	Y	A	D	T	L	K	G
SEQ ID NO: 25	W	V	R	Q	A	P	G	K	G	L	E	W	V	A	Y	I	S	S	G	S	S	T	I	Y	Y	A	D	T	L	K	G
SEQ ID NO: 23	W	V	R	Q	A	P	G	K	G	L	E	W	V	S	Y	I	S	S	G	S	S	T	I	Y	Y	A	D	T	L	K	G
SEQ ID NO: 24	W	V	R	Q	A	P	G	K	G	L	E	W	V	S	Y	I	S	S	G	S	S	T	I	Y	Y	A	D	T	L	K	G

	Framework 3																															
	66	67	68	69	70	71	72	73	74	75	76	77	78	79	80	81	82	82a	82b	82c	83	84	85	86	87	88	89	90	91	92	93	94
SEQ ID NO: 15	R	F	T	I	S	R	D	N	P	K	N	T	L	F	L	Q	M	T	S	L	R	S	E	D	T	A	M	Y	Y	C	A	R
SEQ ID NO: 25	R	F	T	I	S	R	D	N	S	K	N	T	L	Y	L	Q	M	N	S	L	R	A	E	D	T	A	V	Y	Y	C	A	R
SEQ ID NO: 23	R	F	T	I	S	R	D	N	A	K	N	S	L	Y	L	Q	M	N	S	L	R	A	E	D	T	A	V	Y	Y	C	A	R
SEQ ID NO: 24	R	F	T	I	S	R	D	N	S	K	N	T	L	Y	L	Q	M	N	S	L	R	A	E	D	T	A	V	Y	Y	C	A	R

	CDR 3								Framework 4										
	95	96	97	98	99	100	101	102	103	104	105	106	107	108	109	110	111	112	113
SEQ ID NO: 15	R	G	E	G	A	M	D	Y	W	G	Q	G	T	S	V	T	V	S	S
SEQ ID NO: 25	R	G	E	G	A	M	D	Y	W	G	Q	G	T	T	V	T	V	S	S
SEQ ID NO: 23	R	G	E	G	A	M	D	Y	W	G	Q	G	T	T	V	T	V	S	S
SEQ ID NO: 24	R	G	E	G	A	M	D	Y	W	G	Q	G	T	T	V	T	V	S	S

FIG. 5A

VL

	Framework 1																							CDR 1										
	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28	29	30	31	32	33	34
SEQ ID NO: 16	E	N	V	L	T	Q	S	P	A	I	M	S	A	S	L	G	E	K	V	T	M	S	C	***R***	***A***	***S***	***S***	***S***	***V***	***-***	***N***	***Y***	***I***	***Y***
SEQ ID NO: 26	D	N	Q	L	T	Q	S	P	S	F	L	S	A	S	V	G	D	R	V	T	I	T	C	***R***	***A***	***S***	***S***	***S***	***V***	***-***	***N***	***Y***	***I***	***Y***
SEQ ID NO: 27	D	N	Q	L	T	Q	S	P	S	S	L	S	A	S	V	G	D	R	V	T	I	T	C	***R***	***A***	***S***	***S***	***S***	***V***	***-***	***N***	***Y***	***I***	***Y***
SEQ ID NO: 28	E	N	V	L	T	Q	S	P	A	T	L	S	V	S	P	G	E	R	A	T	L	S	C	***R***	***A***	***S***	***S***	***S***	***V***	***-***	***N***	***Y***	***I***	***Y***
SEQ ID NO: 29	Q	N	V	L	T	Q	P	P	S	-	A	S	G	T	P	G	Q	R	V	T	I	S	C	***R***	***A***	***S***	***S***	***S***	***V***	***-***	***N***	***Y***	***I***	***Y***
SEQ ID NO: 30	S	N	E	L	T	Q	P	P	S	-	V	S	V	S	P	G	Q	T	A	R	I	T	C	***R***	***A***	***S***	***S***	***S***	***V***	***-***	***N***	***Y***	***I***	***Y***

	Framework 2															CDR 2						
	35	36	37	38	39	40	41	42	43	44	45	46	47	48	49	50	51	52	53	54	55	56
SEQ ID NO: 16	W	Y	Q	Q	K	S	D	A	S	P	K	L	W	I	Y	***Y***	***T***	***S***	***N***	***L***	***A***	***P***
SEQ ID NO: 26	W	Y	Q	Q	K	P	G	K	A	P	K	L	L	I	Y	***Y***	***T***	***S***	***N***	***L***	***A***	***P***
SEQ ID NO: 27	W	Y	Q	Q	K	P	G	K	A	P	K	L	L	I	Y	***Y***	***T***	***S***	***N***	***L***	***A***	***P***
SEQ ID NO: 28	W	Y	Q	Q	K	P	G	Q	A	P	R	L	L	I	Y	***Y***	***T***	***S***	***N***	***L***	***A***	***P***
SEQ ID NO: 29	W	Y	Q	Q	L	P	G	T	A	P	K	L	L	I	Y	***Y***	***T***	***S***	***N***	***L***	***A***	***P***
SEQ ID NO: 30	W	Y	Q	Q	K	S	G	Q	A	P	V	L	V	I	Y	***Y***	***T***	***S***	***N***	***L***	***A***	***P***

	Framework 3																																	
	57	58	59	60	61	62	63	64	65	66	67	68	69	70	71	72	73	74	75	76	77	78	79	80	81	82	83	84	85	86	87	88
SEQ ID NO: 16	G	V	P	T	R	F	S	G	S	G	S	G	N	S	Y	S	L	T	I	S	S	M	E	G	E	D	A	A	T	Y	Y	C
SEQ ID NO: 26	G	V	P	S	R	F	S	G	S	G	S	G	N	E	Y	T	L	T	I	S	S	L	Q	P	E	D	F	A	T	Y	Y	C
SEQ ID NO: 27	G	V	P	S	R	F	S	G	S	G	S	G	N	D	Y	T	L	T	I	S	S	L	Q	P	E	D	F	A	T	Y	Y	C
SEQ ID NO: 28	G	I	P	A	R	F	S	G	S	G	S	G	N	E	Y	T	L	T	I	S	S	L	Q	S	E	D	F	A	V	Y	Y	C
SEQ ID NO: 29	G	V	P	D	R	F	S	G	S	G	S	G	N	S	Y	S	L	A	I	S	G	L	R	S	E	D	E	A	D	Y	Y	C
SEQ ID NO: 30	G	I	P	E	R	F	S	G	S	G	S	G	N	M	Y	T	L	T	I	S	G	A	Q	V	E	D	E	A	D	Y	Y	C

	CDR 3									Framework 4									
	89	90	91	92	93	94	95	96	97	98	99	100	101	102	103	104	105	106	107
SEQ ID NO: 16	***Q***	***Q***	***F***	***T***	***S***	***S***	***P***	***F***	***T***	F	G	S	G	T	K	L	E	I	K
SEQ ID NO: 26	***Q***	***Q***	***F***	***T***	***S***	***S***	***P***	***F***	***T***	F	G	Q	G	T	K	L	E	I	K
SEQ ID NO: 27	***Q***	***Q***	***F***	***T***	***S***	***S***	***P***	***F***	***T***	F	G	Q	G	T	K	L	E	I	K
SEQ ID NO: 28	***Q***	***Q***	***F***	***T***	***S***	***S***	***P***	***F***	***T***	F	G	Q	G	T	K	L	E	I	K
SEQ ID NO: 29	***Q***	***Q***	***F***	***T***	***S***	***S***	***P***	***F***	***T***	F	G	T	G	T	K	V	T	V	L
SEQ ID NO: 30	***Q***	***Q***	***F***	***T***	***S***	***S***	***P***	***F***	***T***	F	G	T	G	T	K	V	T	V	L

FIG. 5B

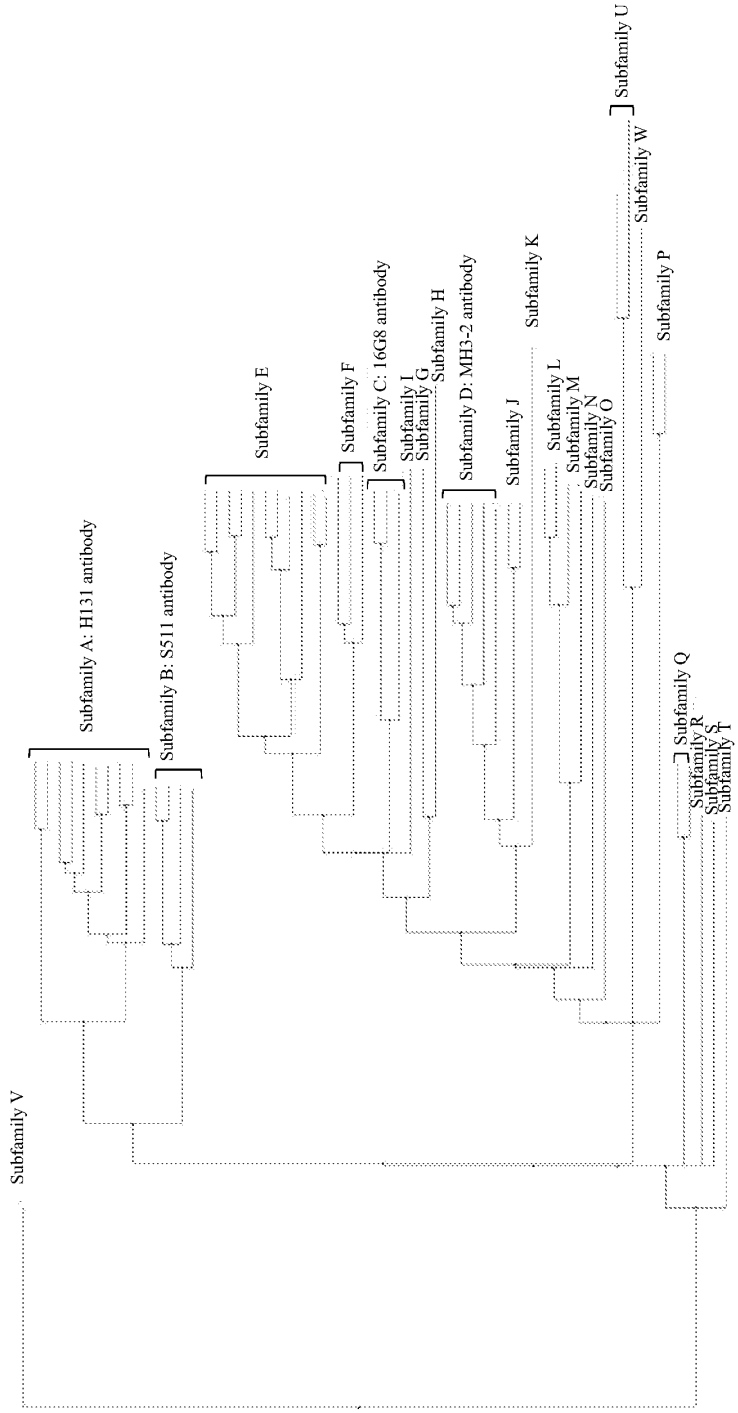
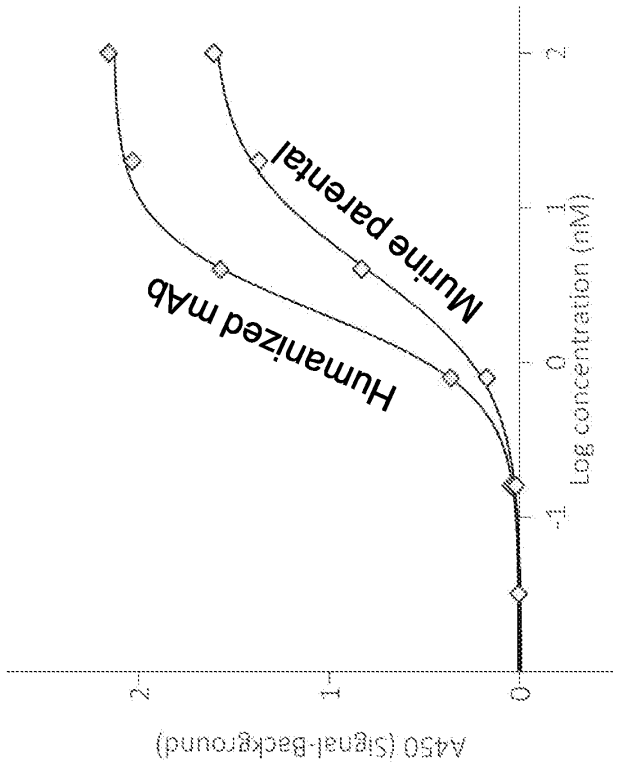
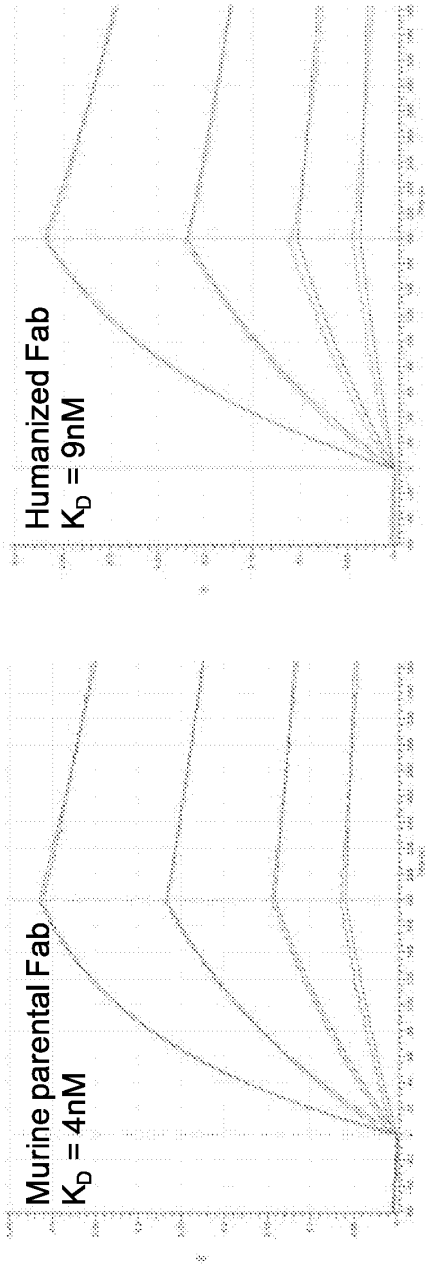

Subfamily V
Subfamily A: H131 antibody
Subfamily B: S511 antibody
Subfamily E
Subfamily F
Subfamily C: 16G8 antibody
Subfamily I
Subfamily G
Subfamily H
Subfamily D: MH3-2 antibody
Subfamily J
Subfamily K
Subfamily L
Subfamily M
Subfamily N
Subfamily O
Subfamily U
Subfamily W
Subfamily P
Subfamily Q
Subfamily R
Subfamily S
Subfamily T

FIG. 6



ELISA data showing direct binding of anti-TRBC1 mAbs (bivalent) to hTRBC1 coated on the plate

FIG. 7



Octet data showing binding of anti-TRBC1 Fabs to hTRBC1. hTRBC1 was captured on the sensor tip and dipped in solution containing different concentrations of monovalent Fabs

FIG. 8

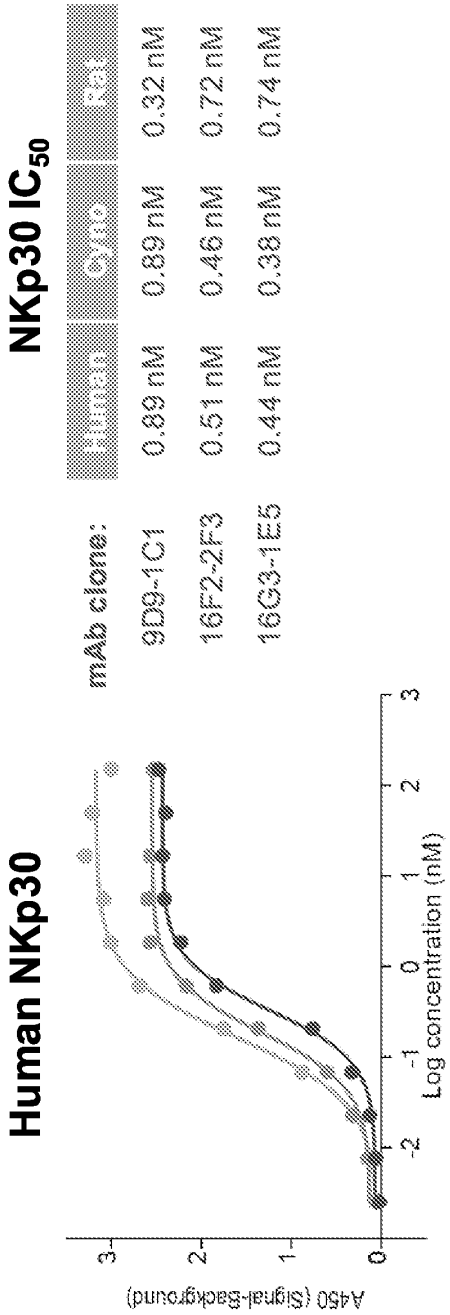

Human NKp30
A450 (Signal-Background)
3
2
1
0
-2
-1
0
1
2
3
Log concentration (nM)
mAb clone:
9D9-1C1
16F2-2F3
16G3-1E5
NKp30 IC50
Human
Cyno
Rat
0.89 nM
0.51 nM
0.44 nM
0.89 nM
0.46 nM
0.38 nM
0.32 nM
0.72 nM
0.74 nM

FIG. 9

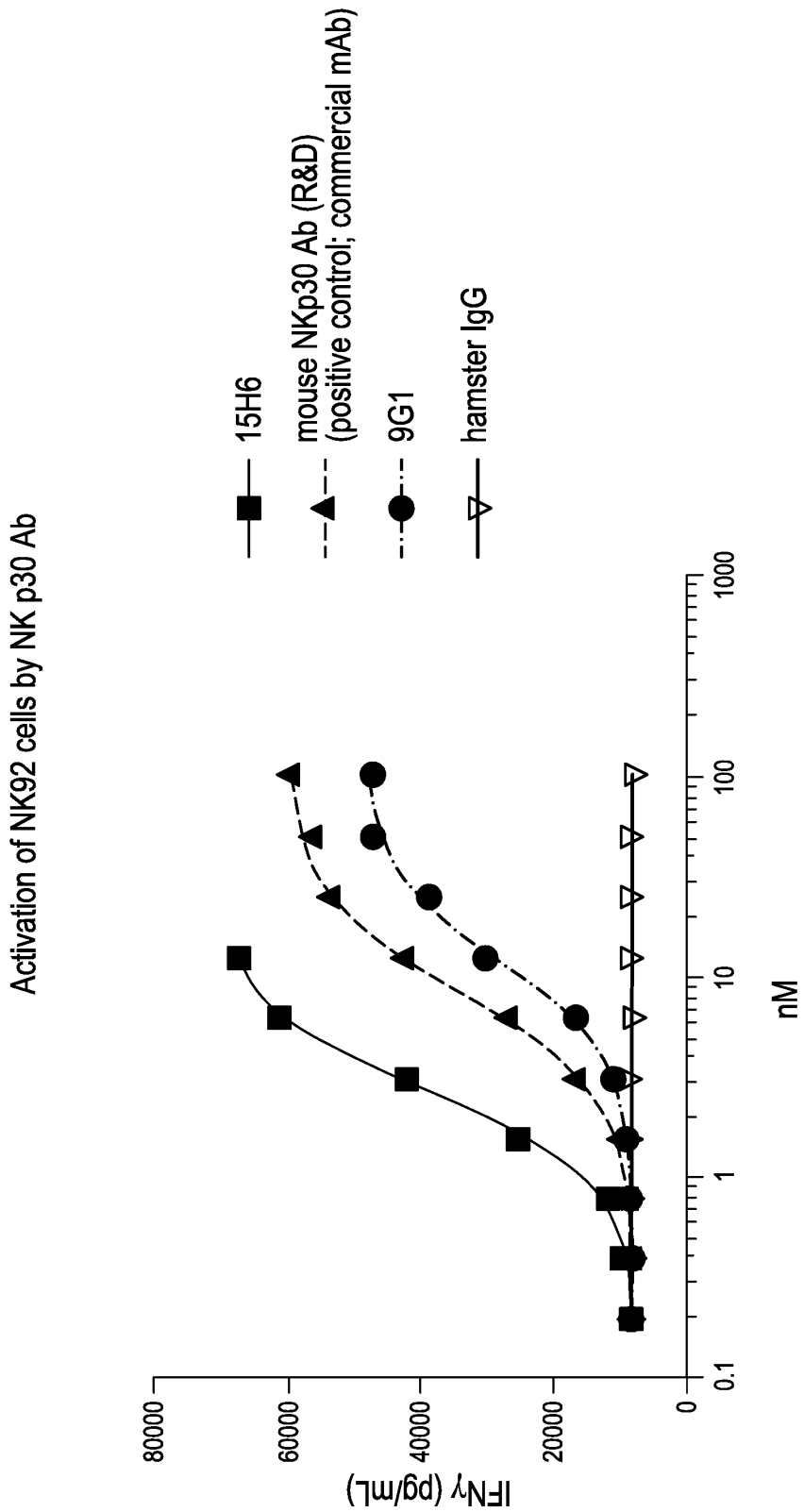

Activation of NK92 cells by NK p30 Ab
15H6
mouse NKp30 Ab (R&D)
(positive control; commercial mAb)
9G1
hamster IgG
IFNγ (pg/mL)
80000
60000
40000
20000
0
0.1
1
10
100
1000
nM

FIG. 10

FIG. 11A

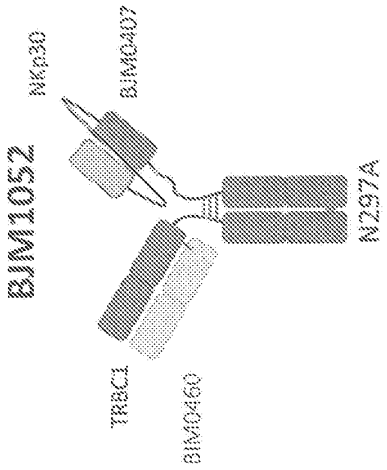


FIG. 11B

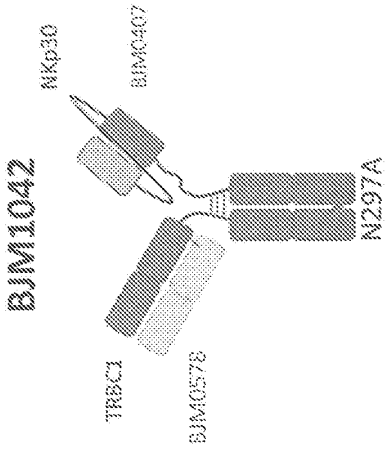


FIG. 11C

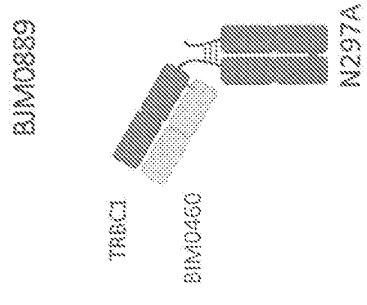


FIG. 11D

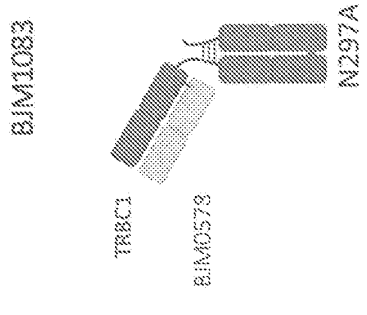
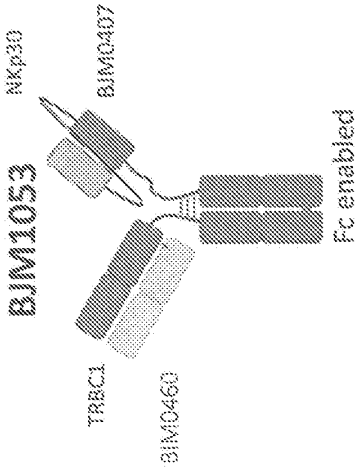


FIG. 11E



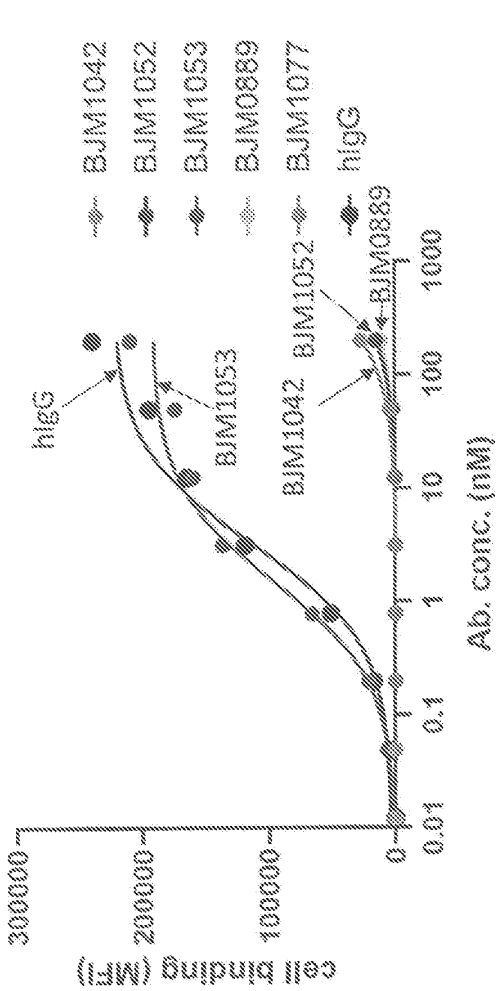


FIG. 12A

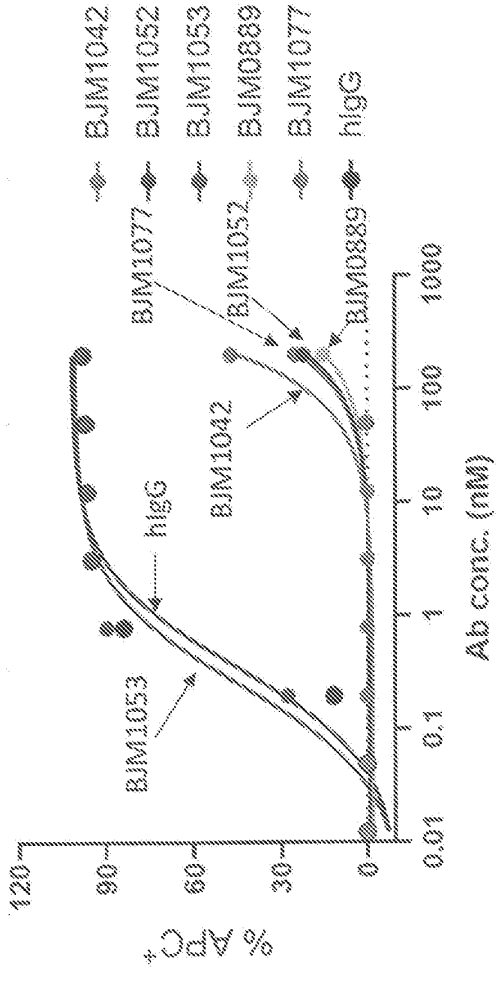


FIG. 12B

FIG. 13A

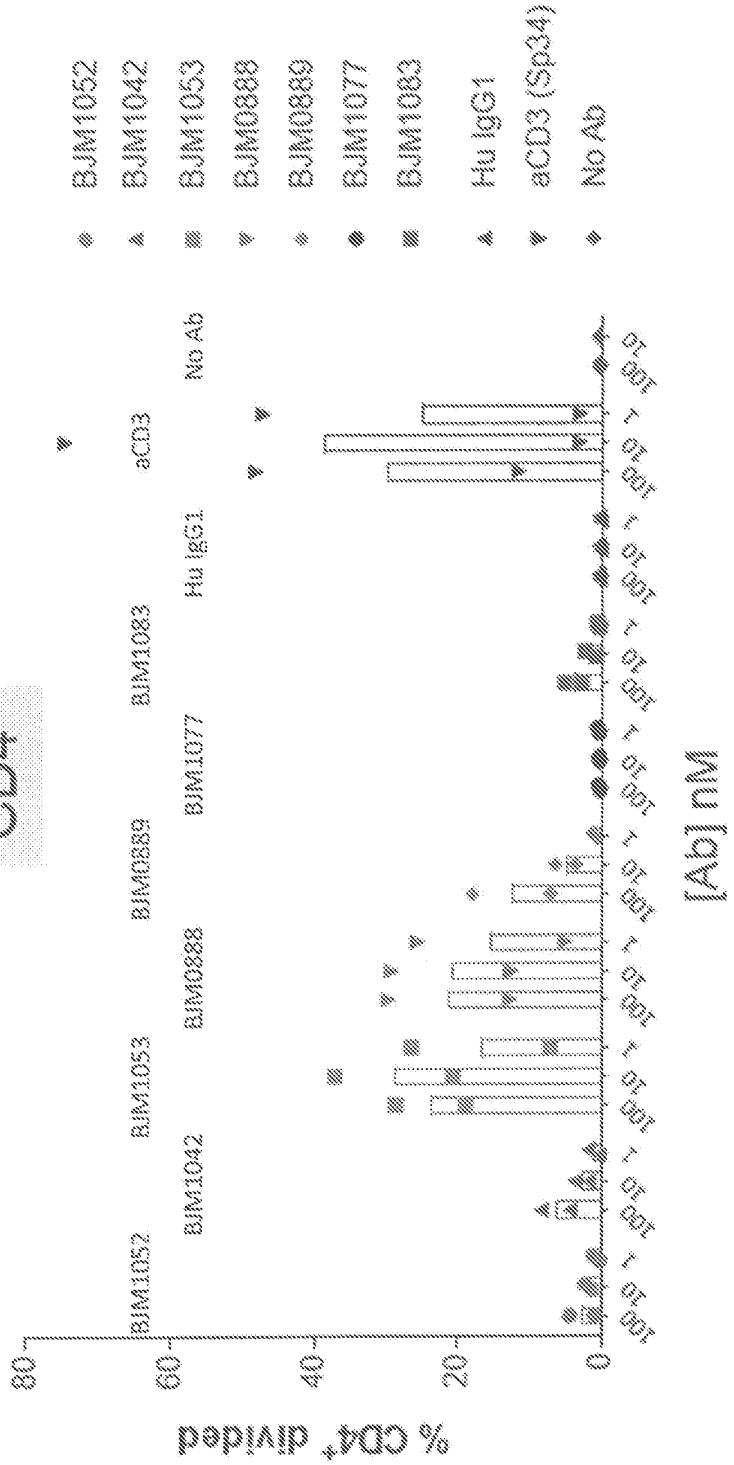

CD4
% CD4+ divided
80
60
40
20
0
BJM1052
BJM1042
BJM1053
BJM0888
BJM0889
BJM1077
BJM1083
Hu IgG1
aCD3
No Ab
[Ab] nM
100
10
1
0.1
0.01
0.001
BJM1052
BJM1042
BJM1053
BJM0888
BJM0889
BJM1077
BJM1083
Hu IgG1
aCD3 (Sp34)
No Ab

FIG. 13B

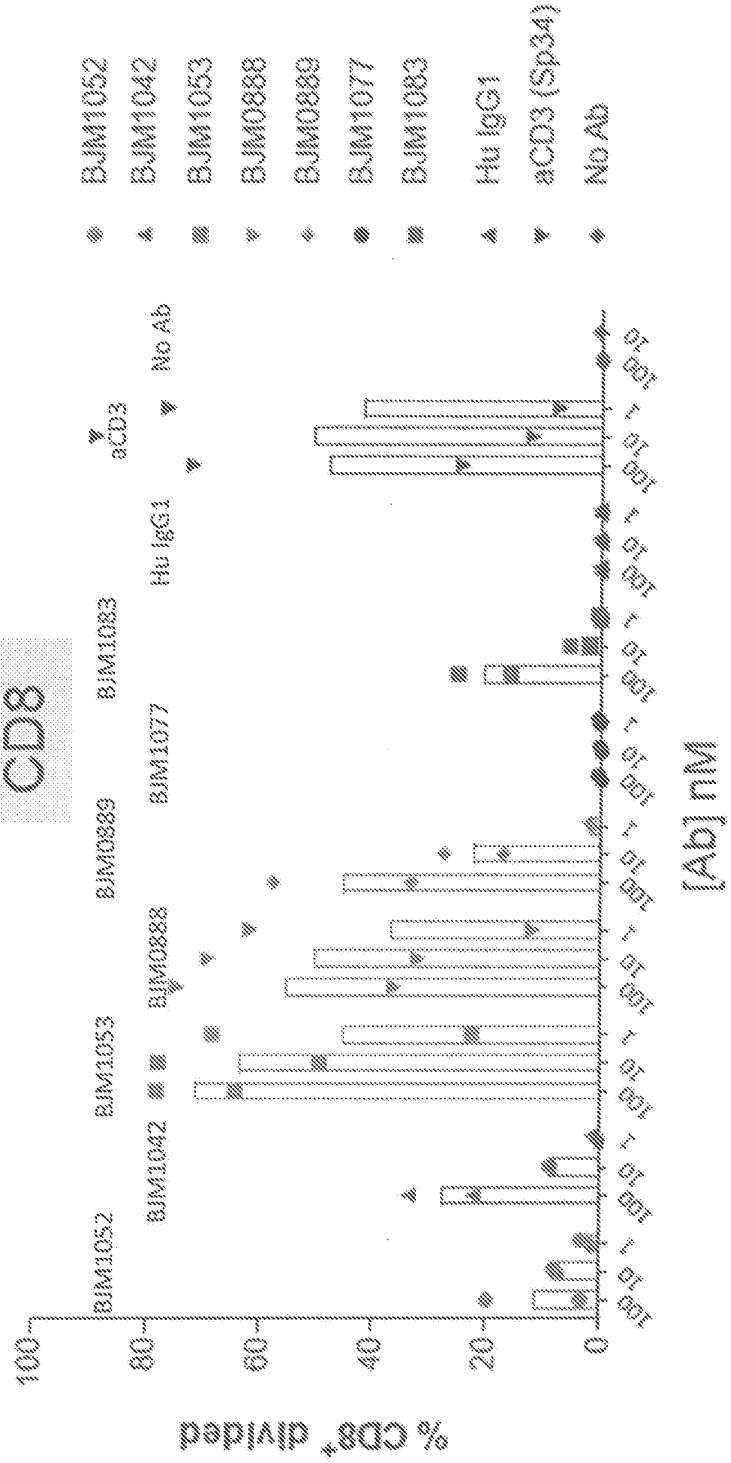

CD8
BJM1052
BJM1042
BJM1053
BJM0888
BJM0889
BJM1077
BJM1083
Hu IgG1
aCD3
No Ab
% CD8+ divided
100
80
60
40
20
0
[Ab] nM
100
10
1
0.1
0.01

FIG. 13C

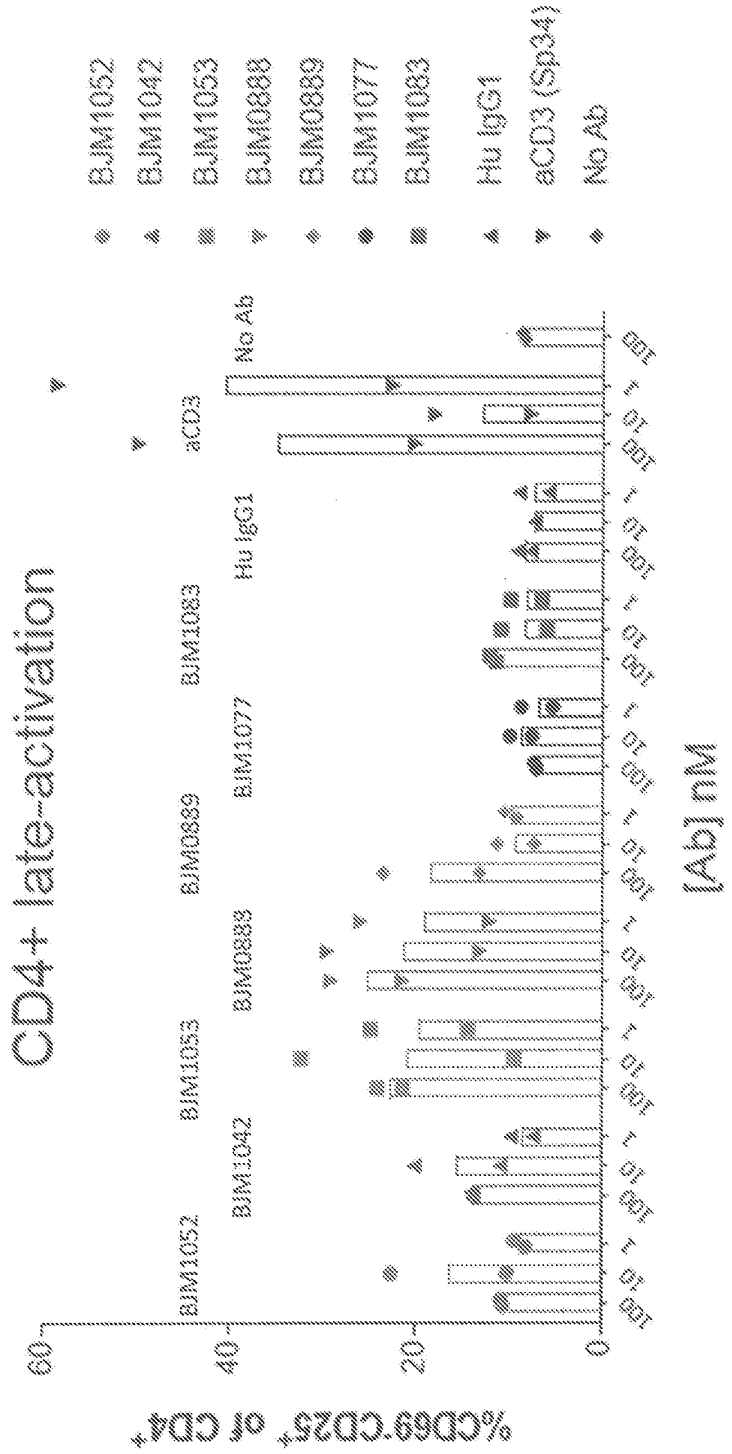

CD4+ late-activation
%CD69.CD25+ of CD4+
60
40
20
0
BJM1052
BJM1042
BJM1053
BJM0888
BJM0889
BJM1077
BJM1083
Hu IgG1
aCD3
No Ab
100
10
1
0.1
0.01
[Ab] nM
BJM1052
BJM1042
BJM1053
BJM0888
BJM0889
BJM1077
BJM1083
Hu IgG1
aCD3 (Sp34)
No Ab

FIG. 13D

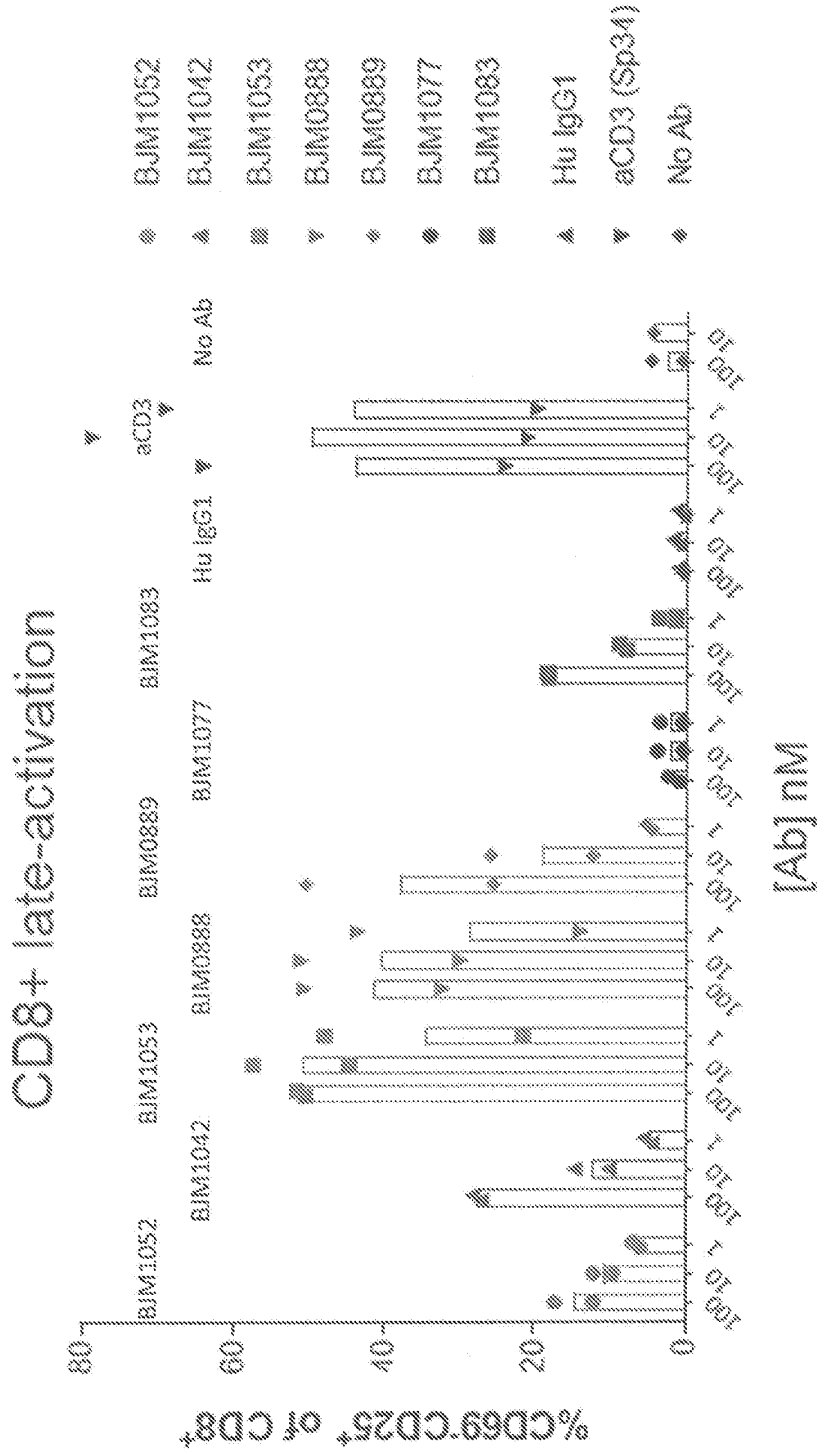

CD8+ late-activation
BJM1052
BJM1042
BJM1053
BJM0888
BJM0889
BJM1077
BJM1083
Hu IgG1
aCD3
No Ab
%CD69.CD25+ of CD8+
80
60
40
20
0
[Ab] nM
100
10
1
0.1
0.01
BJM1052
BJM1042
BJM1053
BJM0888
BJM0889
BJM1077
BJM1083
Hu IgG1
aCD3 (Sp34)
No Ab

FIG. 14A

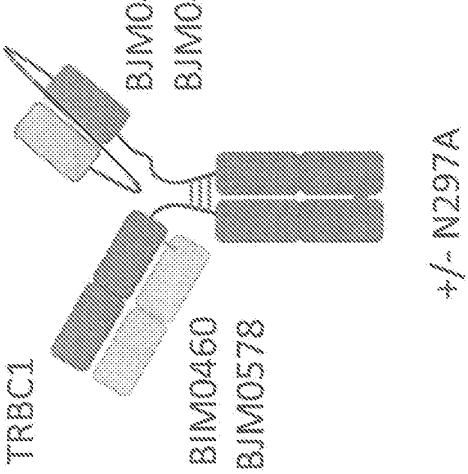


FIG. 14B

BJM1048 460/407 N297A	BJM1032 578/407
BJM1051 460/407	BJM1034 578/411
BJM1052 460/411 N297A	BJM1038 578/407 N297A
BJM1053 460/411	BJM1042 578/411 N297A

FIG. 14C

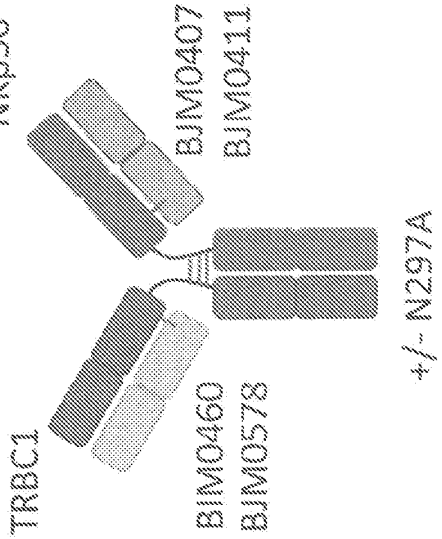
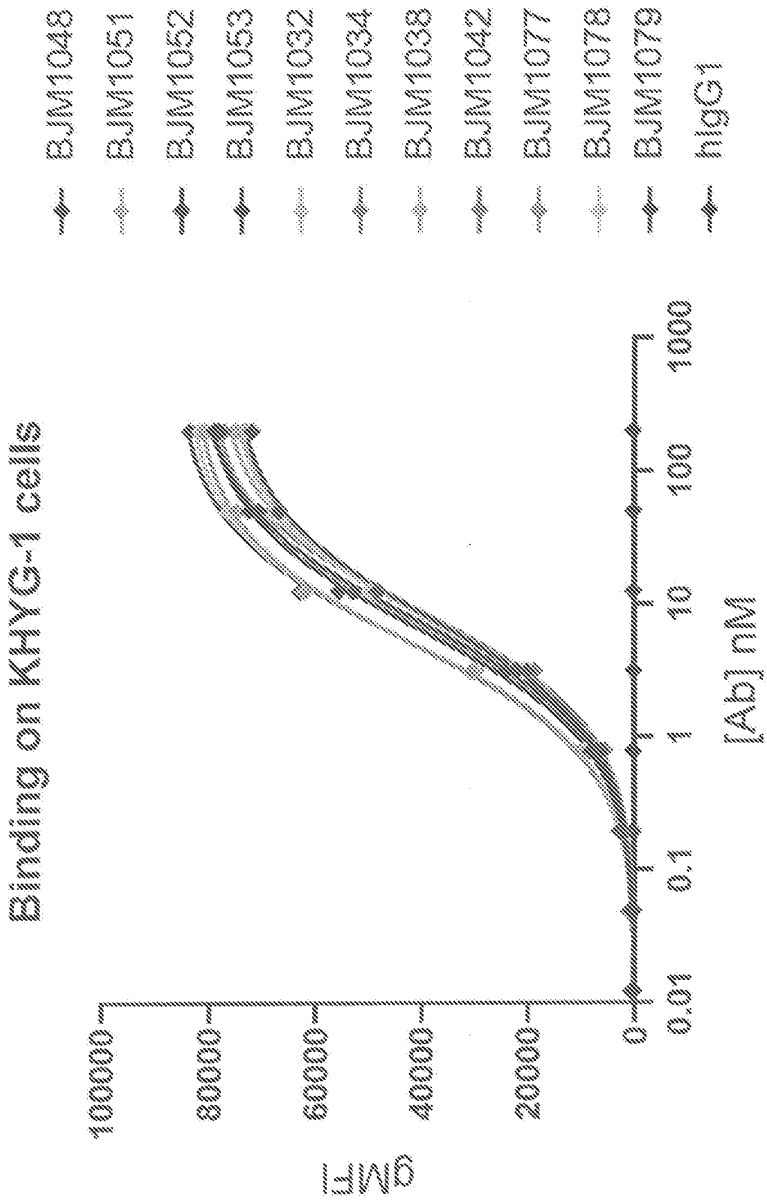


FIG. 14D

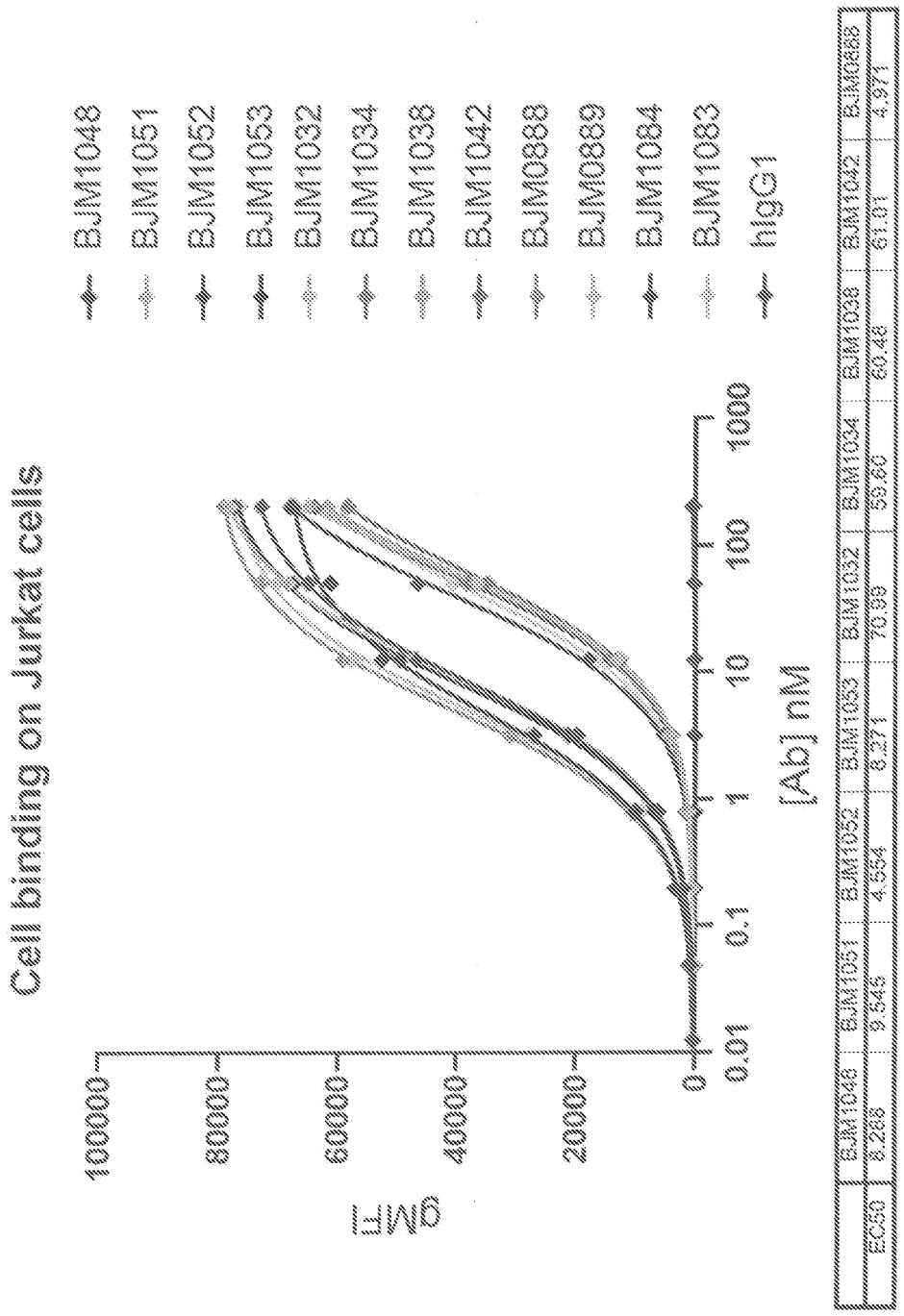
BJM0862 460/407
BJM0863 460/411
BJM1028 578/407 N297A
BJM1046 578/411 N297A

FIG. 15A



	BJM1048	BJM1051	BJM1052	BJM1053	BJM1032	BJM1034	BJM1038	BJM1042	BJM1077
EC50	7.656	8.051	6.608	7.664	7.494	7.064	7.988	9.484	4.947

FIG. 15B



	BJM1048	BJM1051	BJM1052	BJM1053	BJM1032	BJM1034	BJM1038	BJM1042	BJM0888
EC50	8.288	9.545	4.554	8.271	70.99	59.60	60.48	61.01	4.971

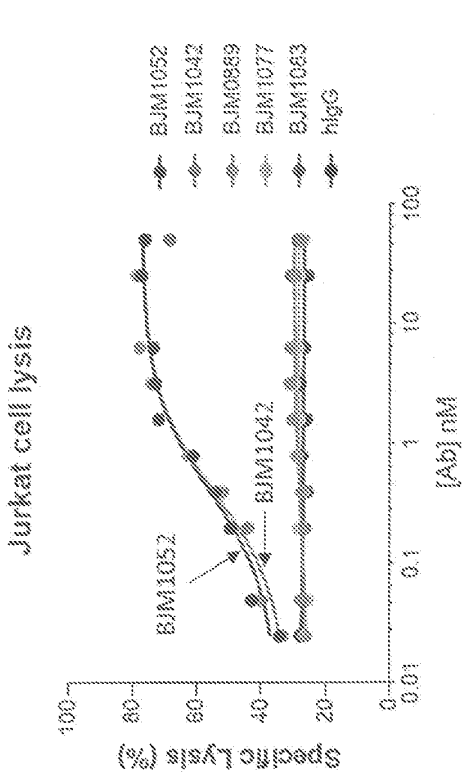
FIG. 15C

BJM1048	Nkp30/TRBC1 bispecific 407/460_N297A
BJM1051	Nkp30/TRBC1 bispecific 407/460_WT
BJM1052	Nkp30/TRBC1 bispecific 411/460_N297A
BJM1053	Nkp30/TRBC1 bispecific 411/460_WT
BJM1032	Nkp30/TRBC1 bispecific 407/578_WT
BJM1034	Nkp30/TRBC1 bispecific 411/578_WT
BJM1038	Nkp30/TRBC1 bispecific 407/578_N297A
BJM1042	Nkp30/TRBC1 bispecific 411/578_N297A
BJM1077	Nkp30 single arm control 411 N297A
BJM1078	Nkp30 single arm control 407 WT
BJM1079	Nkp30 single arm control 411 WT
BJM0888	TRBC1 single arm WT 460
BJM0889	TRBC1 single arm N297A 460
BJM1084	TRBC1 578 Single arm control WT
BJM1083	TRBC1 578 Single arm control N297A knob

FIG. 15D

	gMFI	
Sample	EC50 KHYG-1 (NKp30) [nM]	EC50 Jurkat (TRBC1) [nM]
BJM1048	7.656	8.288
BJM1051	8.051	9.545
BJM1052	6.608	4.554
BJM1053	7.664	8.271
BJM1032	7.494	70.99
BJM1034	7.064	59.6
BJM1038	7.989	60.48
BJM1042	9.484	61.01
BJM1077	4.947	
BJM1078	5.2	
BJM1079	5.357	
BJM0888		4.971
BJM0889		5.261
BJM1084		40.33
BJM1083		44.16

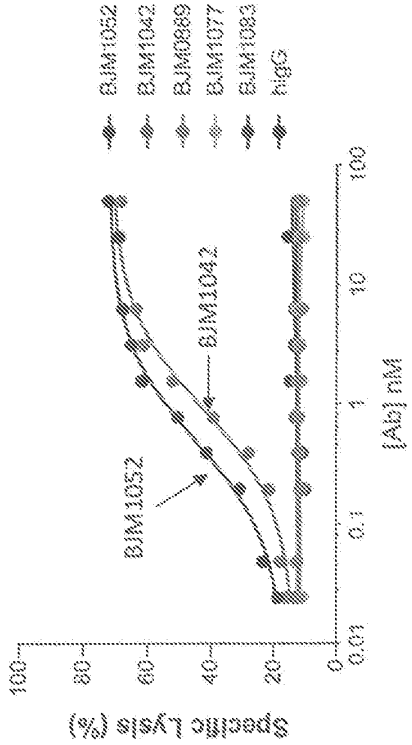
FIG. 16A



Jurkat	BJM1052	BJM1042
EC_{50}	0.2976	0.3836

BJM1052: NKp30xTRBC1(460)
BJM1042: NKp30xTRBC1(578)
BJM0889: TRBC1 (460, N297A)
BJM1077: NKp30 (N297A)
BJM1083:TRBC1 (578, N297A)

FIG. 16B



H9	BJM1052	BJM1042
EC_{50}	0.4775	0.9382

FIG. 16C

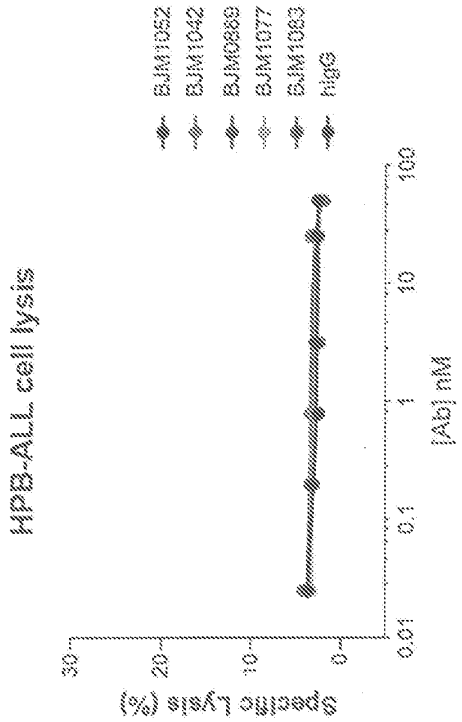
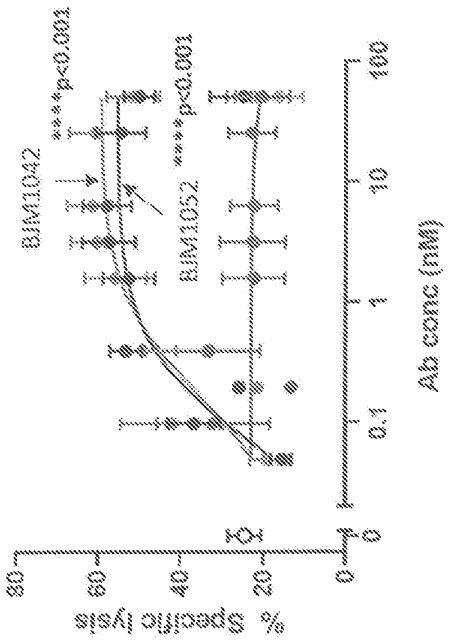

HPB-ALL cell lysis
Specific Lysis (%)
30
20
10
0
0.01
0.1
1
10
100
[Ab] nM
BJM1052
BJM1042
BJM0989
BJM1077
BJM1083
HuIgG

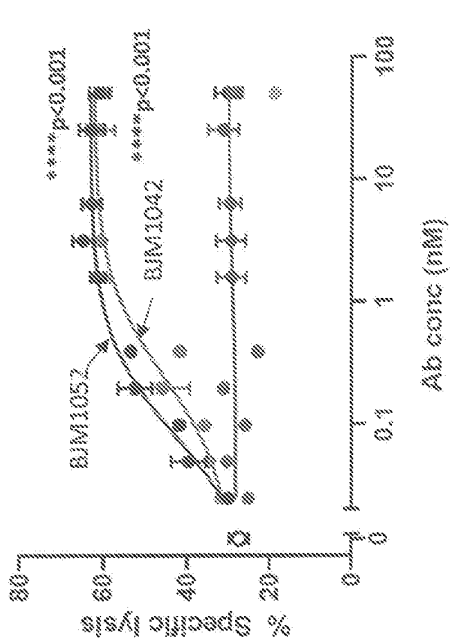
FIG. 17A



	BJM1052	BJM1042
EC50	0.064	0.1778

BJM1052: NKp30xTRBC1(460)
BJM1042: NKp30xTRBC1(578)
BJM0889: TRBC1 (460, N297A)
BJM1077: NKp30 (N297A)
BJM1083:TRBC1 (578, N297A)

FIG. 17B



	BJM1052	BJM1042
EC50	0.075	0.238

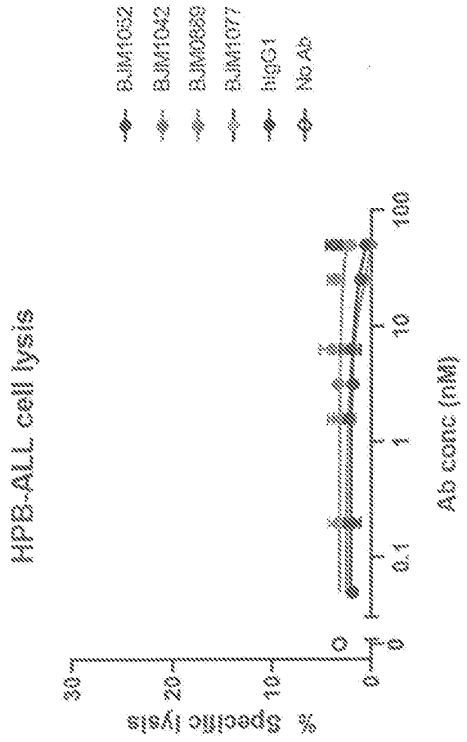

HPB-ALL cell lysis
% Specific lysis
30
20
10
0
0
0.1
1
10
100
Ab conc (nM)
BJM1052
BJM1042
BJM0969
BJM1077
IgG1
No Ab

FIG. 17C

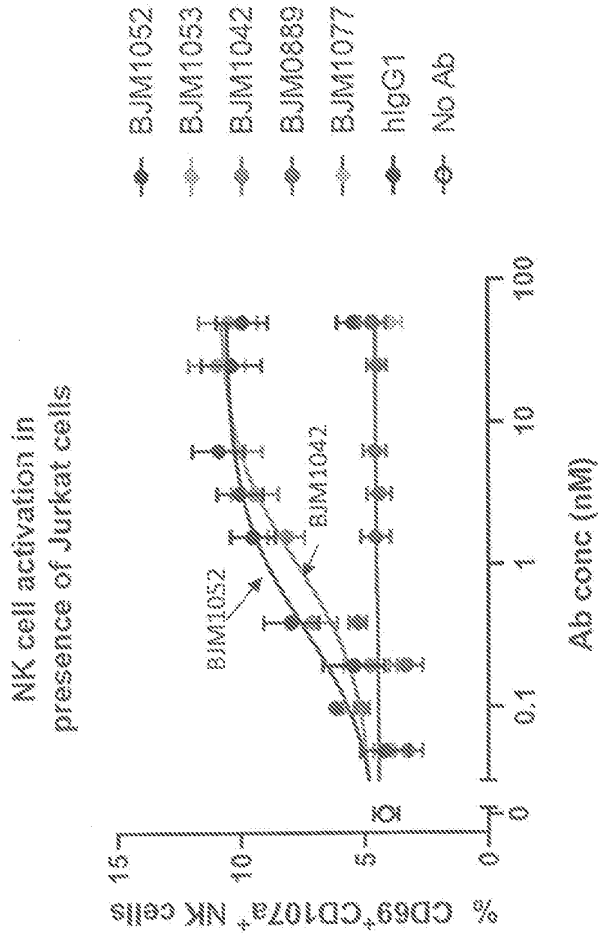


FIG. 18A

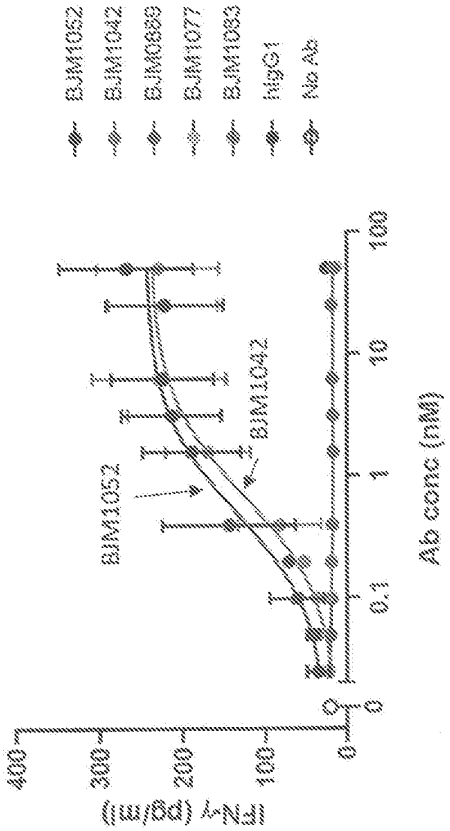


FIG. 18B

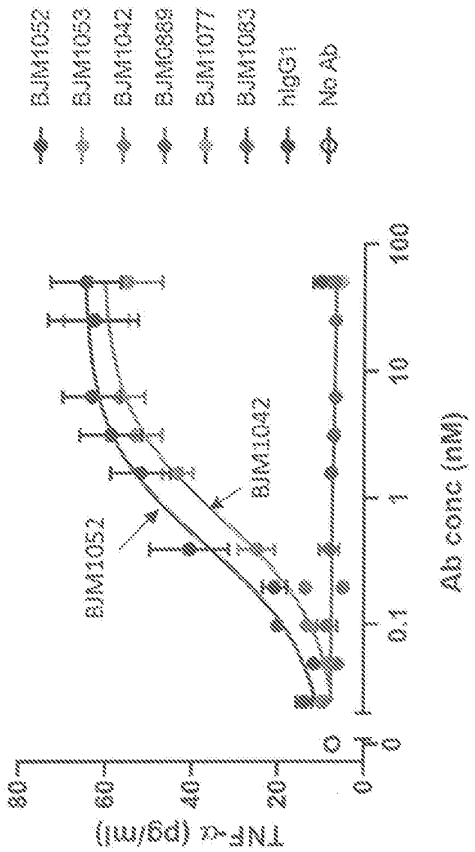

TNFα
TNF-α (pg/ml)
80
60
40
20
0
0
0.1
1
10
100
Ab conc (nM)
BJM1052
BJM1042
BJM1052
BJM1053
BJM1042
BJM0869
BJM1077
BJM1083
hIgG1
No Ab

FIG. 18C

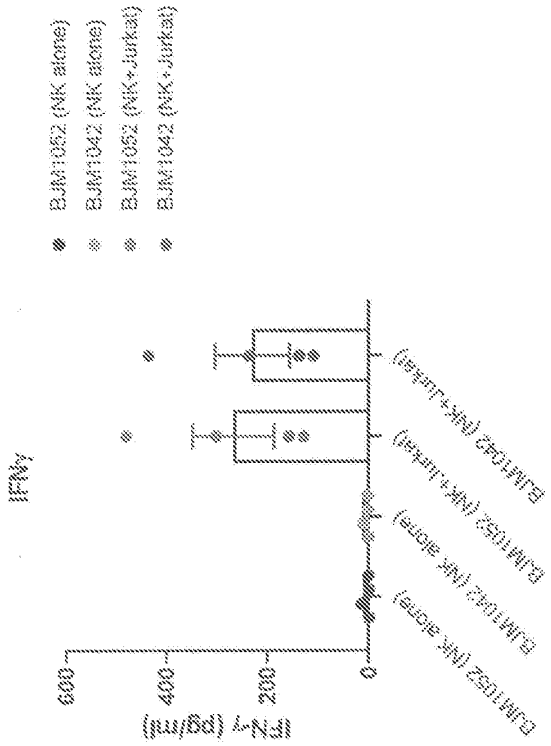


FIG. 19A

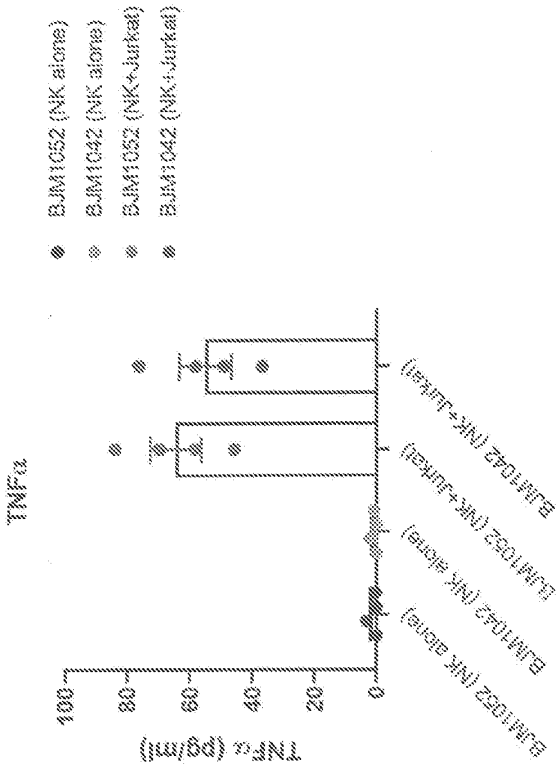


FIG. 19B

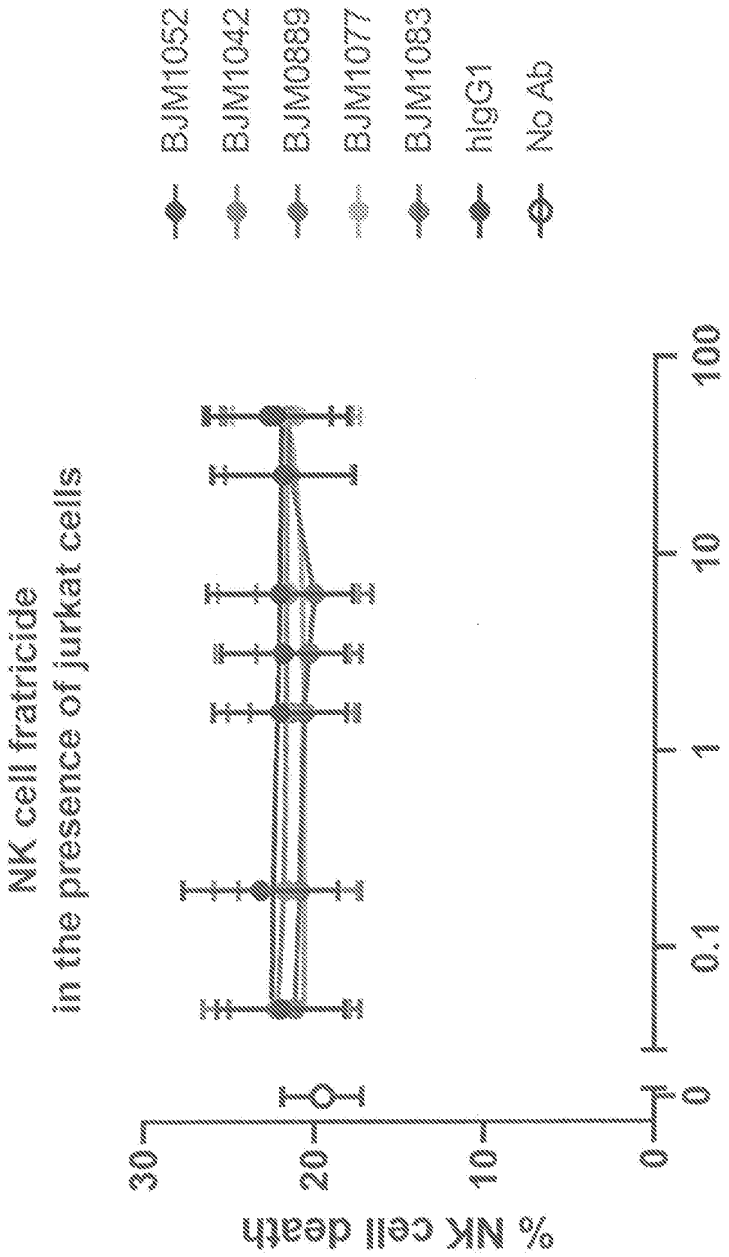

NK cell fratricide
in the presence of jurkat cells
% NK cell death
30
20
10
0
0
0.1
1
10
100
BJM1052
BJM1042
BJM0889
BJM1077
BJM1083
hIgG1
No Ab

FIG. 20

FIG. 21B

BJM0773

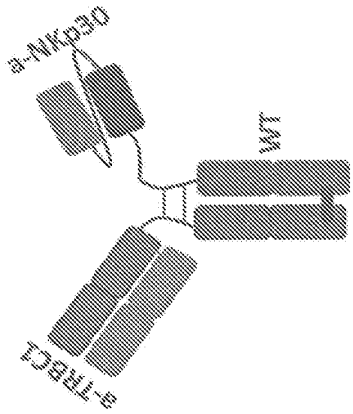


FIG. 21A

BJM0145

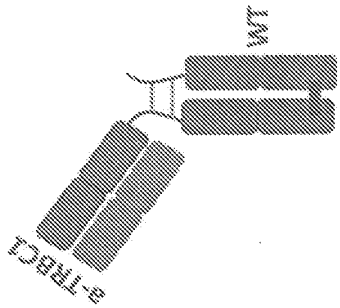


FIG. 22A

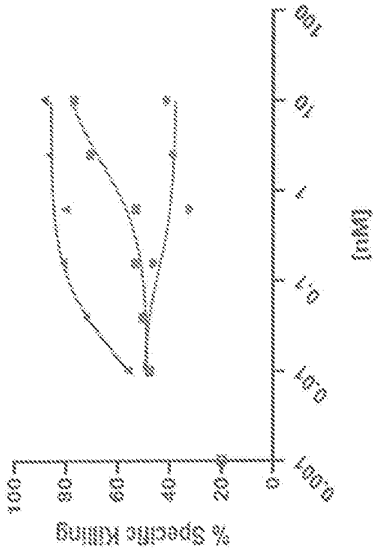
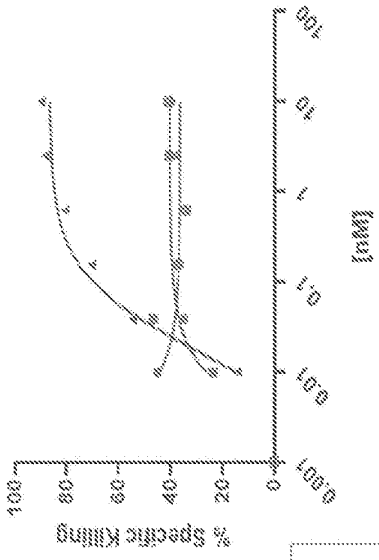


FIG. 22B



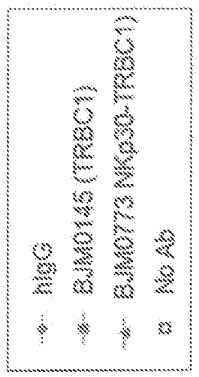


FIG. 22C

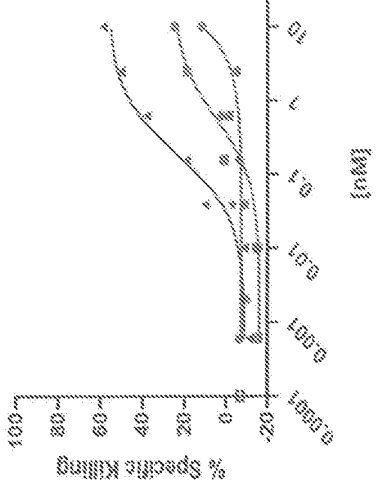


FIG. 22D

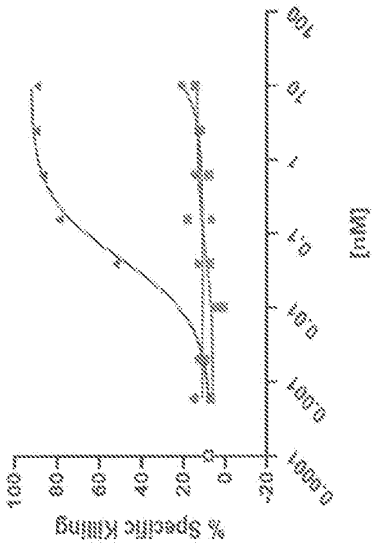
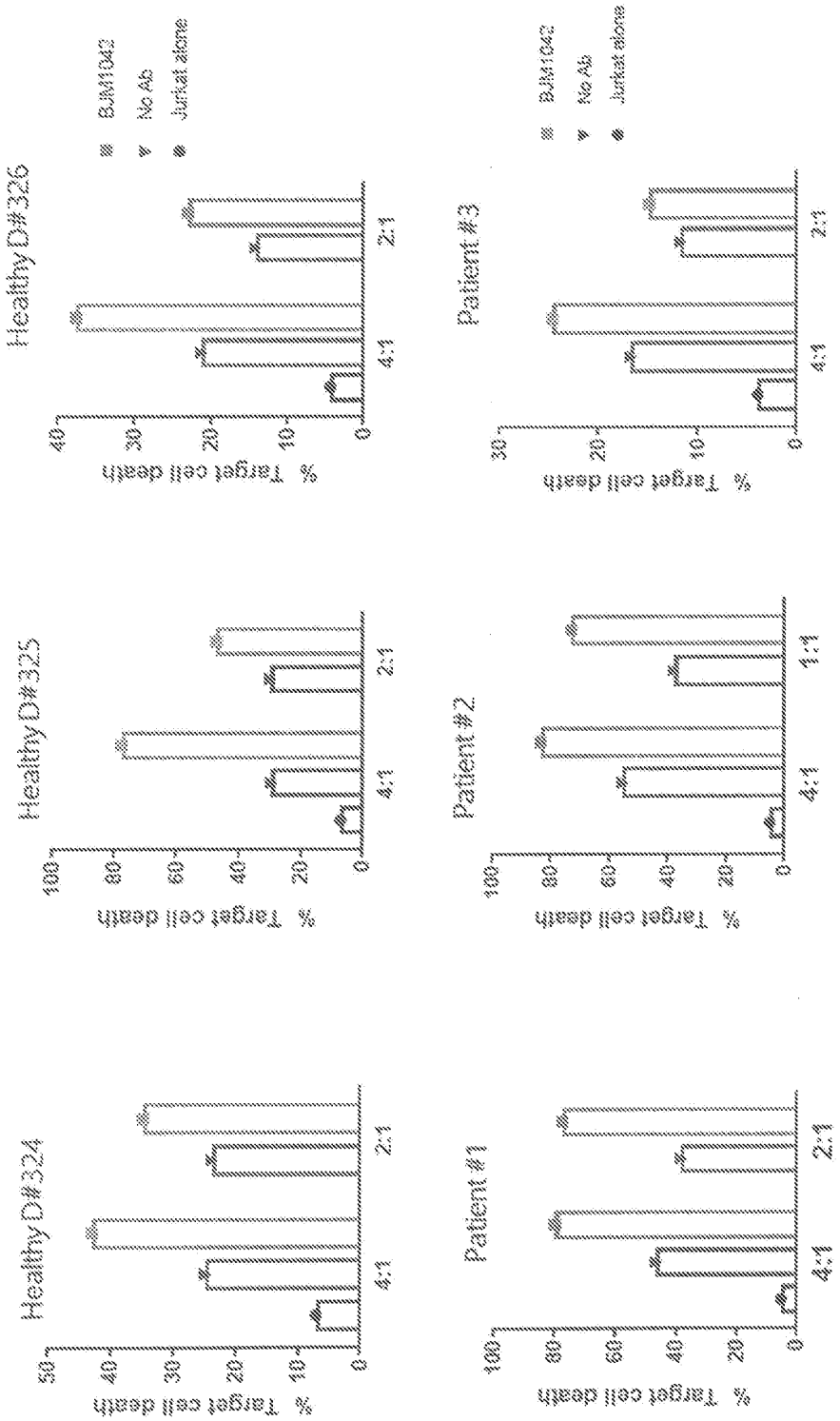


FIG. 23


Healthy D#324
Healthy D#325
Healthy D#326
Patient #1
Patient #2
Patient #3
% Target cell death
4:1
2:1
1:1
BJM1042
No Ab
Jurkat alone

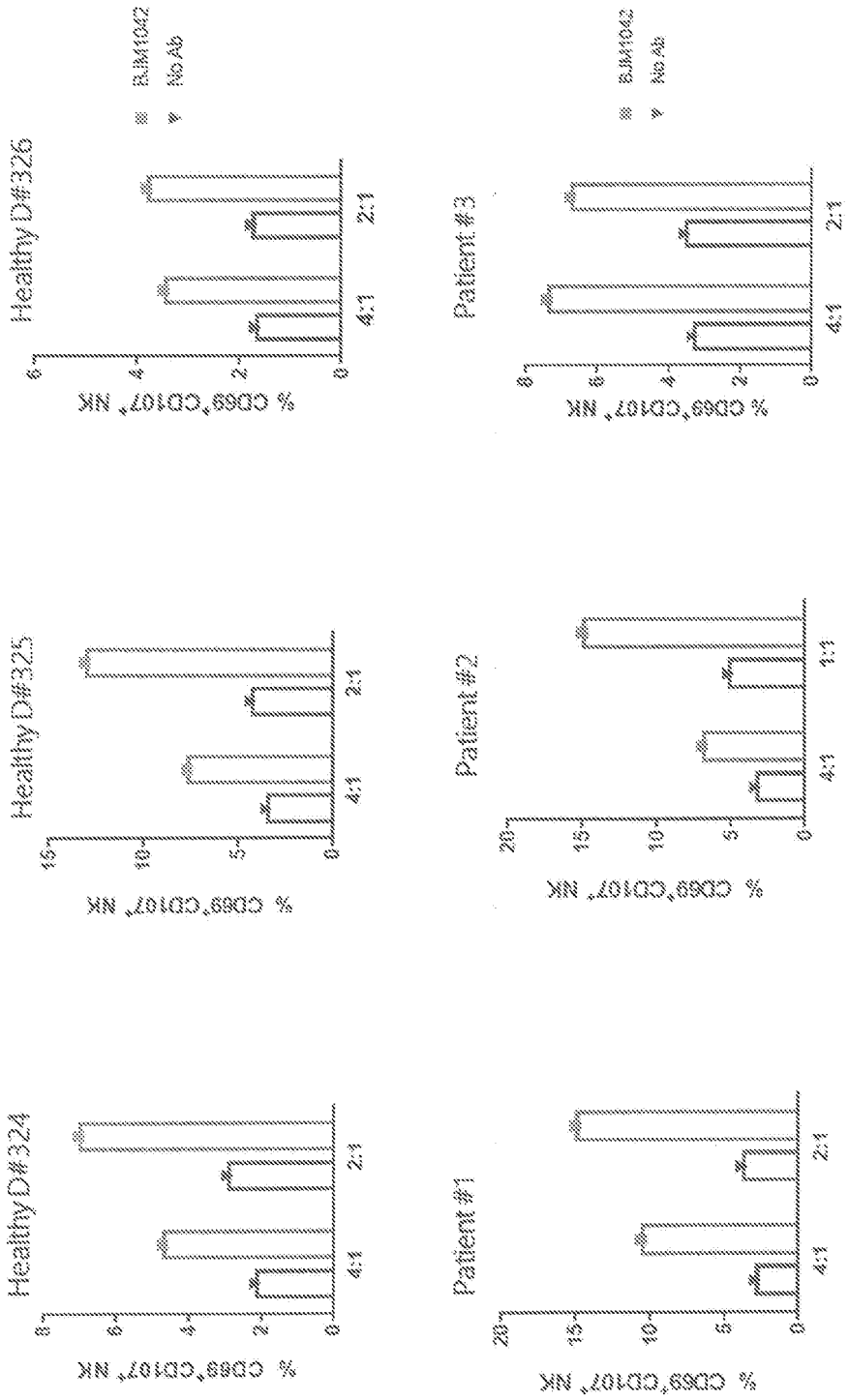

Healthy D#324
Healthy D#325
Healthy D#326
Patient #1
Patient #2
Patient #3
% CD69+CD107+ NK
BJM1042
No Ab
4:1
2:1
1:1

FIG. 24

FIG. 25A

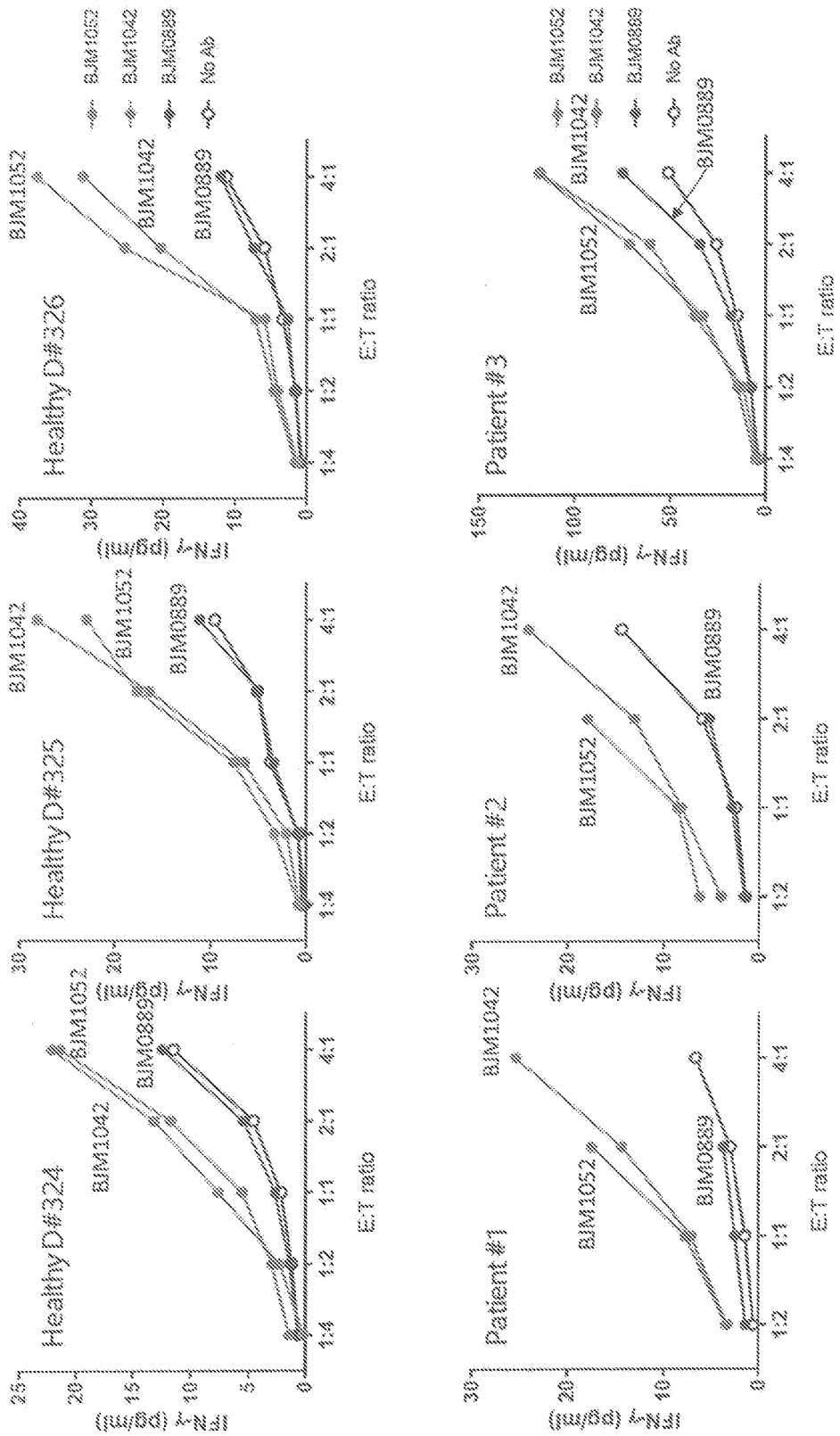

Healthy D#324
Healthy D#325
Healthy D#326
Patient #1
Patient #2
Patient #3
IFN-γ (pg/ml)
E:T ratio
1:4
1:2
1:1
2:1
4:1
BJM1052
BJM1042
BJM0889
No Ab

FIG. 25B

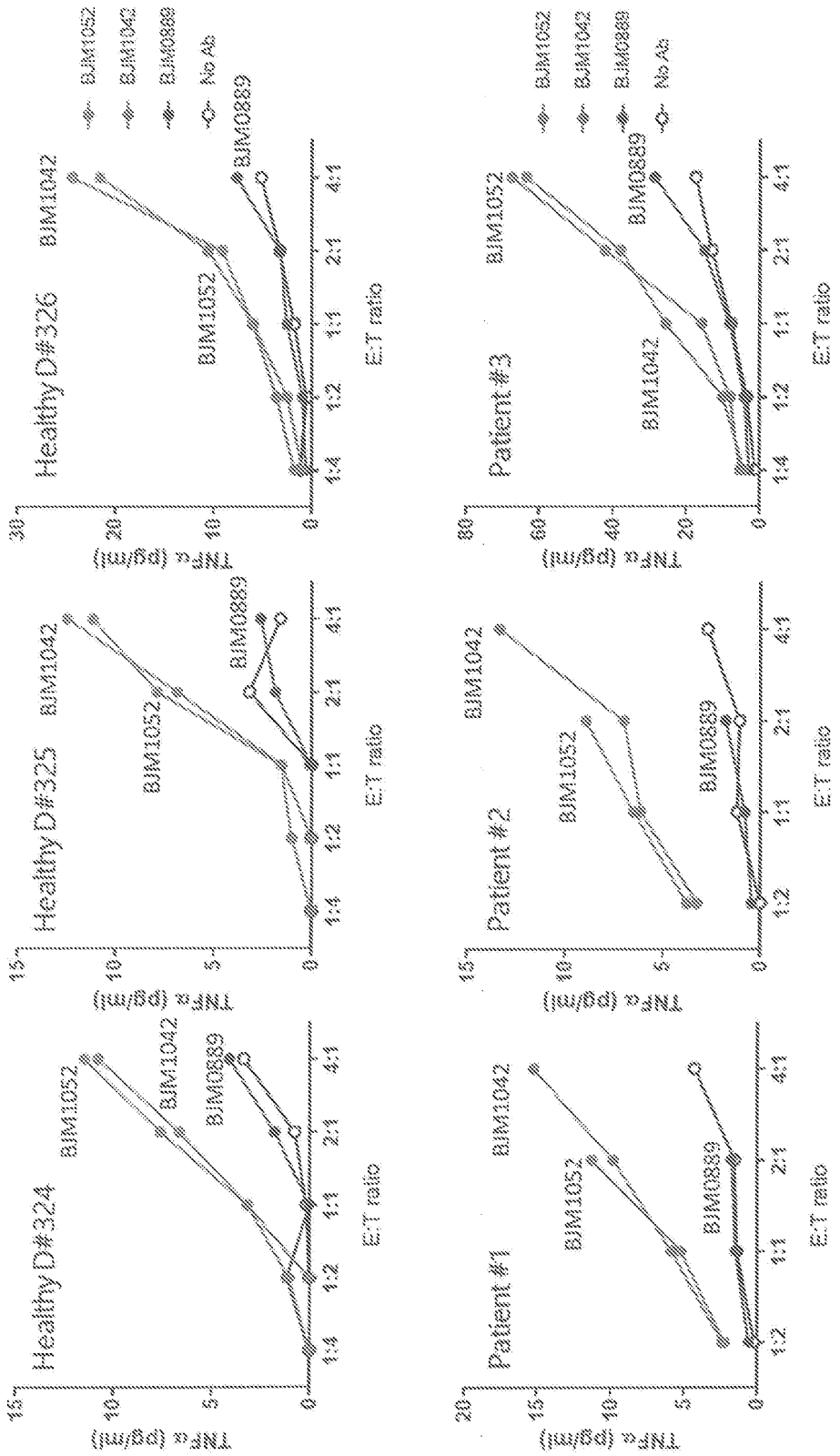
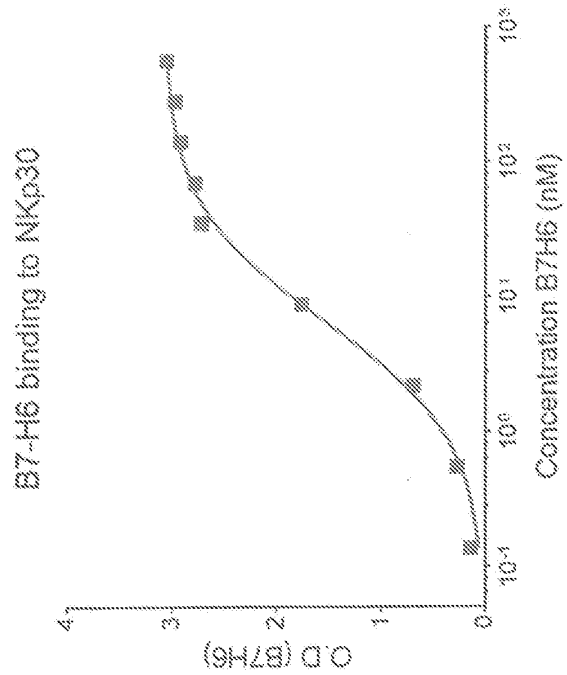
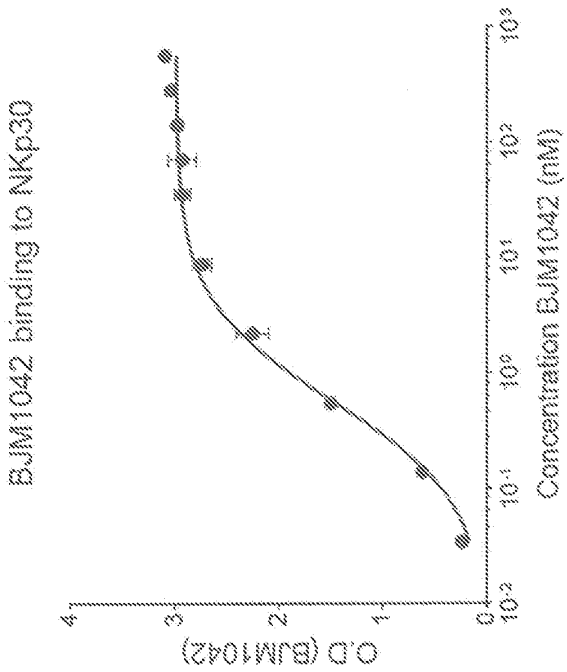

Healthy D#324
Healthy D#325
Healthy D#326
Patient #1
Patient #2
Patient #3
BJM1052
BJM1042
BJM0889
No Ab
TNFα (pg/ml)
E:T ratio
1:4
1:2
1:1
2:1
4:1

FIG. 26A



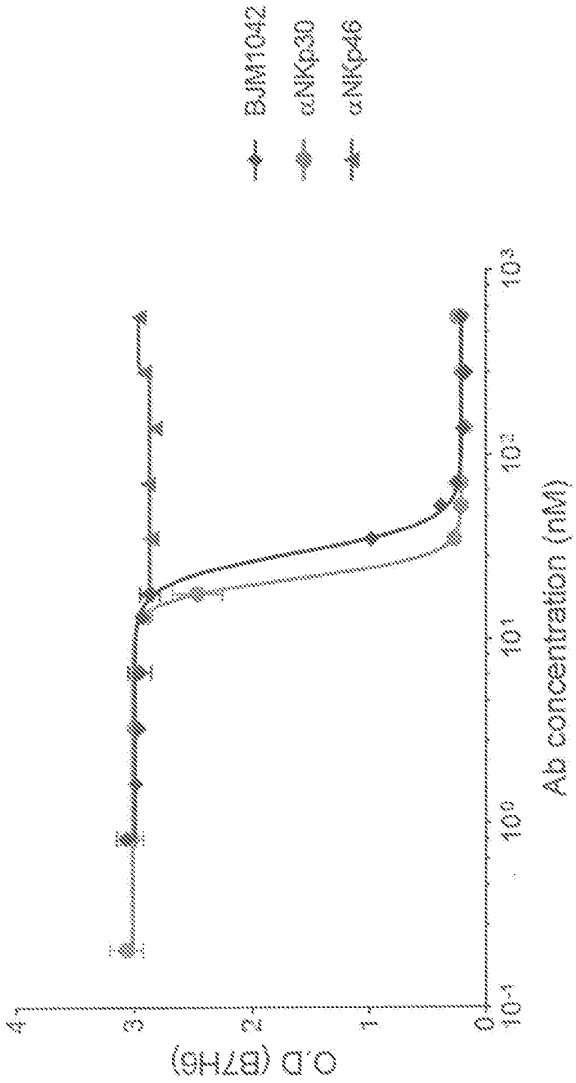
	B7H6
Kd	8.558

FIG. 26B



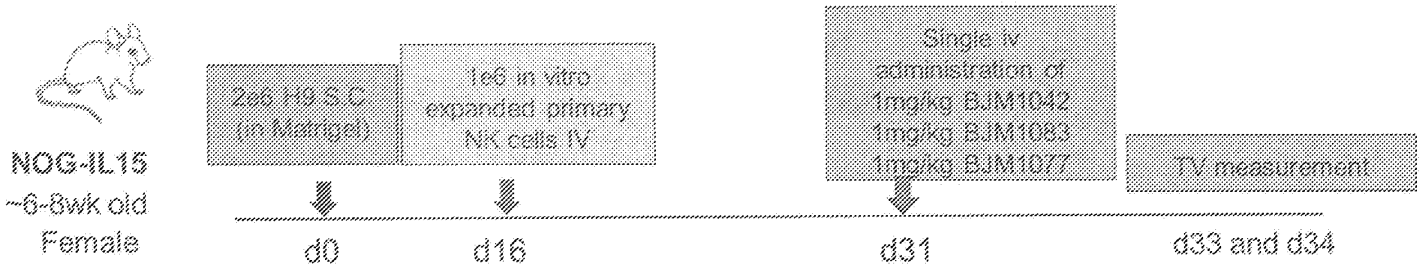
	BJM1042
Kd	0.5781

FIG. 26C



	αNKp30	αNKp46	BJM1042
IC50	21.24	~ 278.7	29.41

FIG. 27A



SN	Molecule	N	Dose (mg/kg)	Schedule	1e6 primary NK cells
1	Vehicle	5	NA	qd	-
2	**BJM1042** (NKp30/TRBC1 411/578_N297A)	5	1	qd	-
3	Vehicle	5	NA	qd	+
4	**BJM1042** (NKp30/TRBC1 411/578_N297A)	5	1	qd	+
5	**BJM1083** (TRBC1 single arm 578 N297A)	5	1	qd	+
6	**BJM1077** (NKp30 single arm 411 N297A)	5	1	qd	+

FIG. 27B

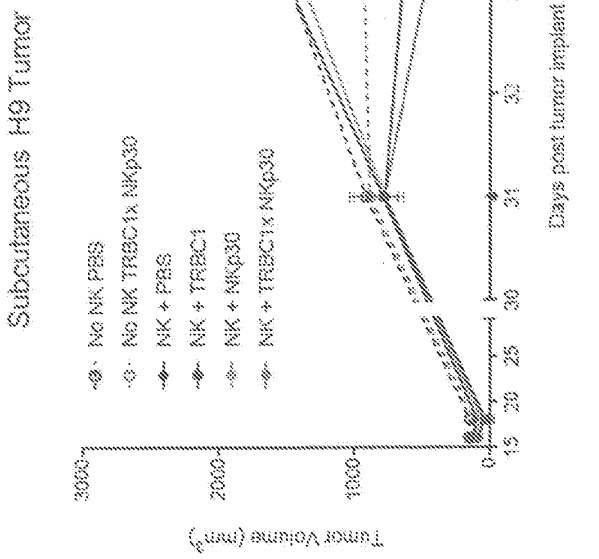


FIG. 27C

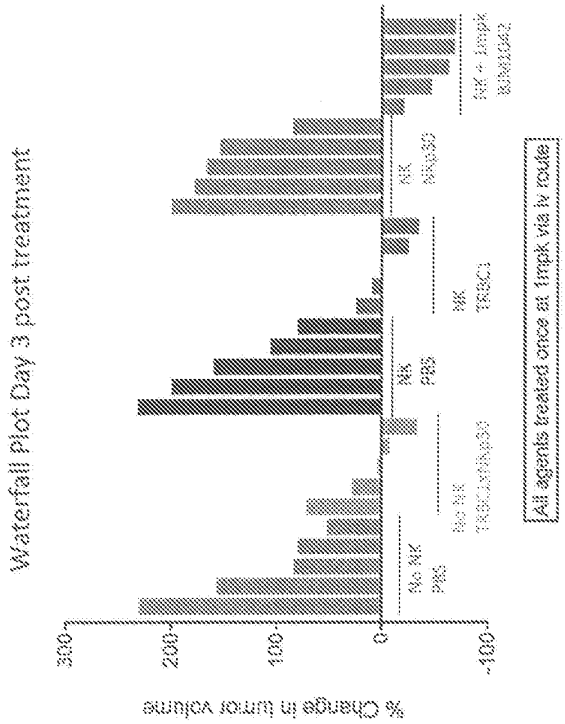
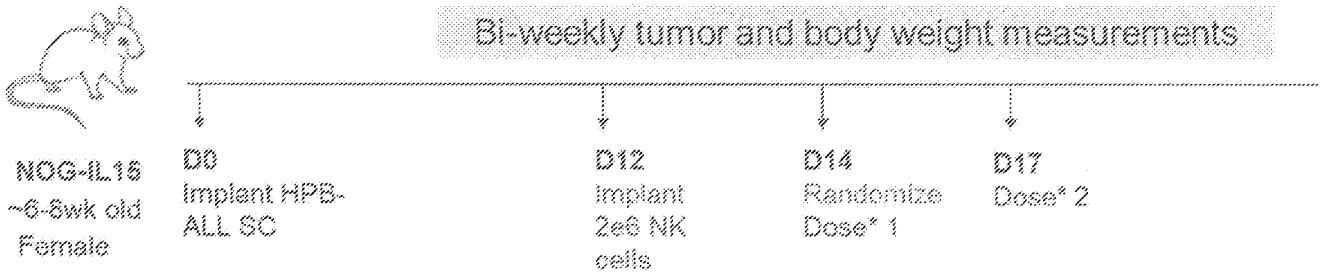


FIG. 28A



SN	Cell line	NK cells	n	Strain	Treatment	Schedule	Dose
1	5e6 HPB-ALL SC	2e6 IV	4	NOG-IL-15	PBS	Q3D x 2	NA
2	5e6 HPB-ALL SC	2e6 IV	5	NOG-IL-15	BJM1042	Q3D x 2	0.5mg/kg
3	5e6 HPB-ALL SC	2e6 IV	4	NOG-IL-15	BJM1083	Q3D x 2	0.5mg/kg
4	5e6 HPB-ALL SC	2e6 IV	4	NOG-IL-15	BJM1077	Q3D x 2	0.5mg/kg

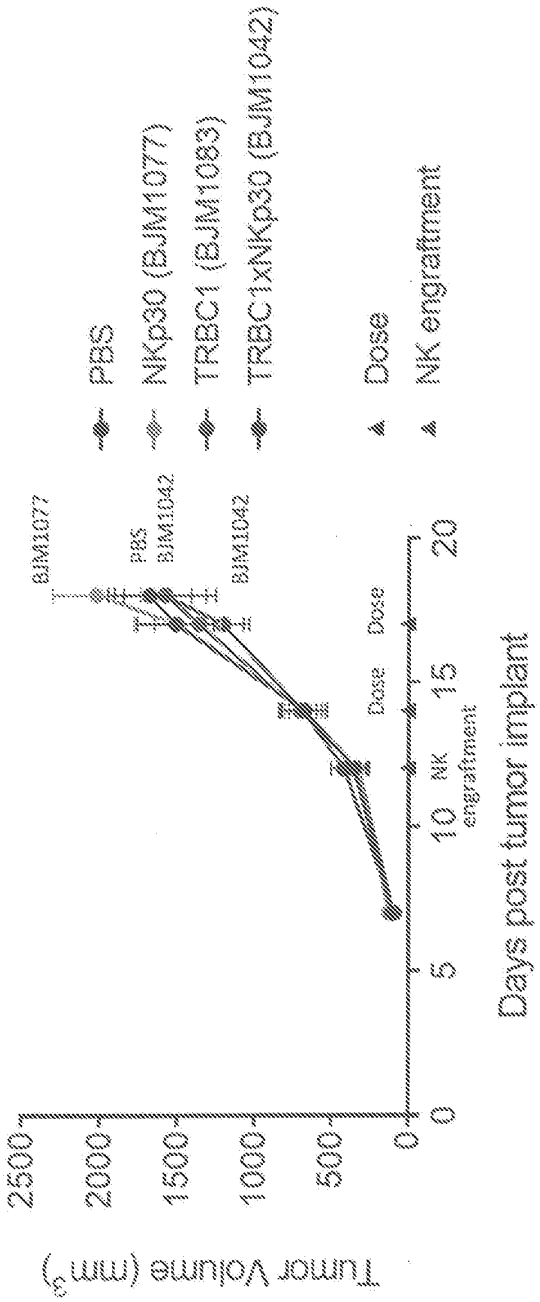

Tumor Volume (mm³)
2500
2000
1500
1000
500
0
0
5
10
15
20
Days post tumor implant
NK engraftment
Dose
Dose
BJM1077
PBS
BJM1042
BJM1042
PBS
NKp30 (BJM1077)
TRBC1 (BJM1083)
TRBC1xNKp30 (BJM1042)
Dose
NK engraftment

FIG. 28B

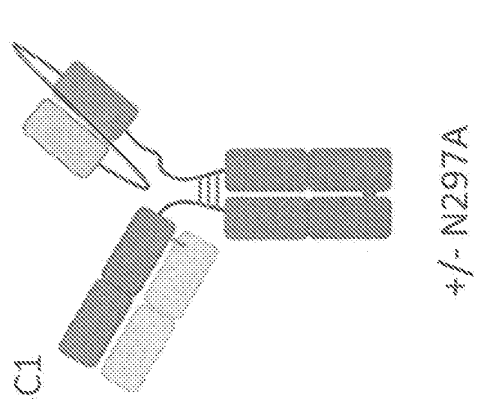


FIG. 29A

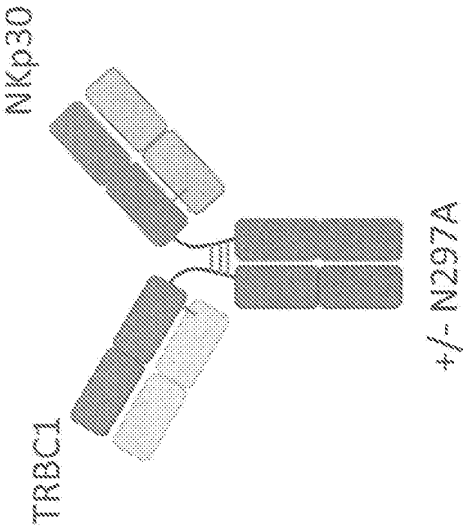


FIG. 29B

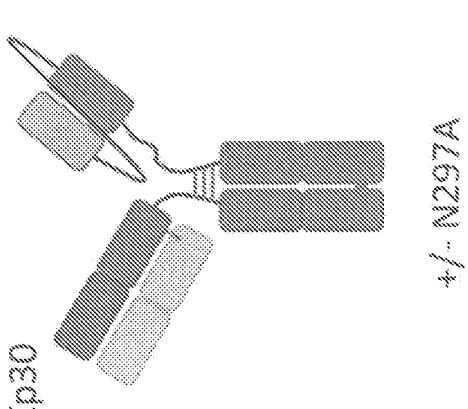


FIG. 29C

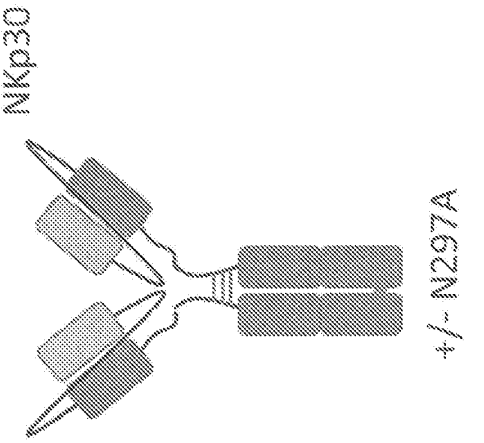


FIG. 29D

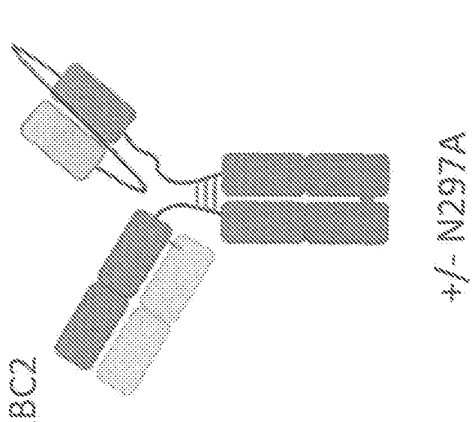


FIG. 30A

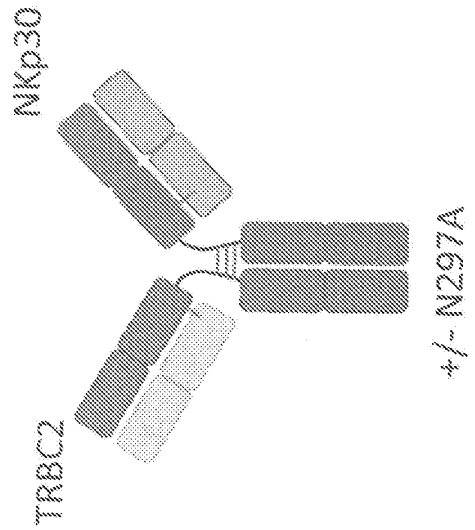


FIG. 30B

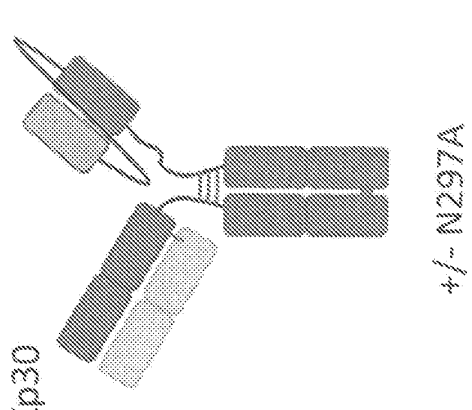


FIG. 30C

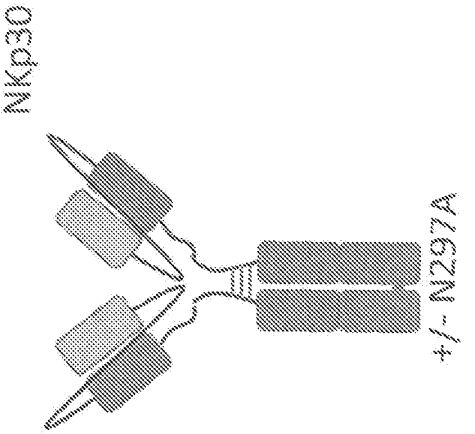


FIG. 30D

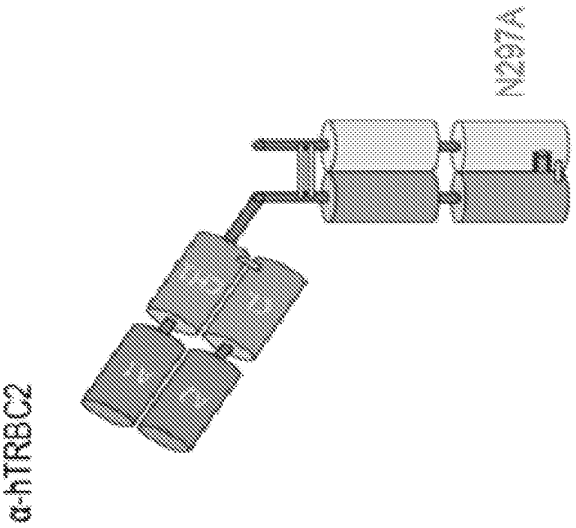


FIG. 31B

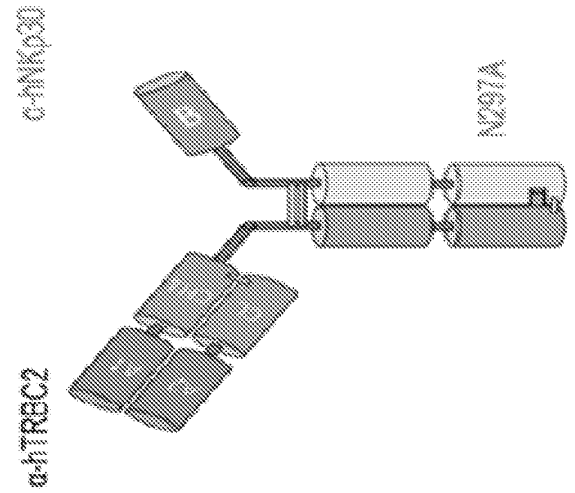


FIG. 31A

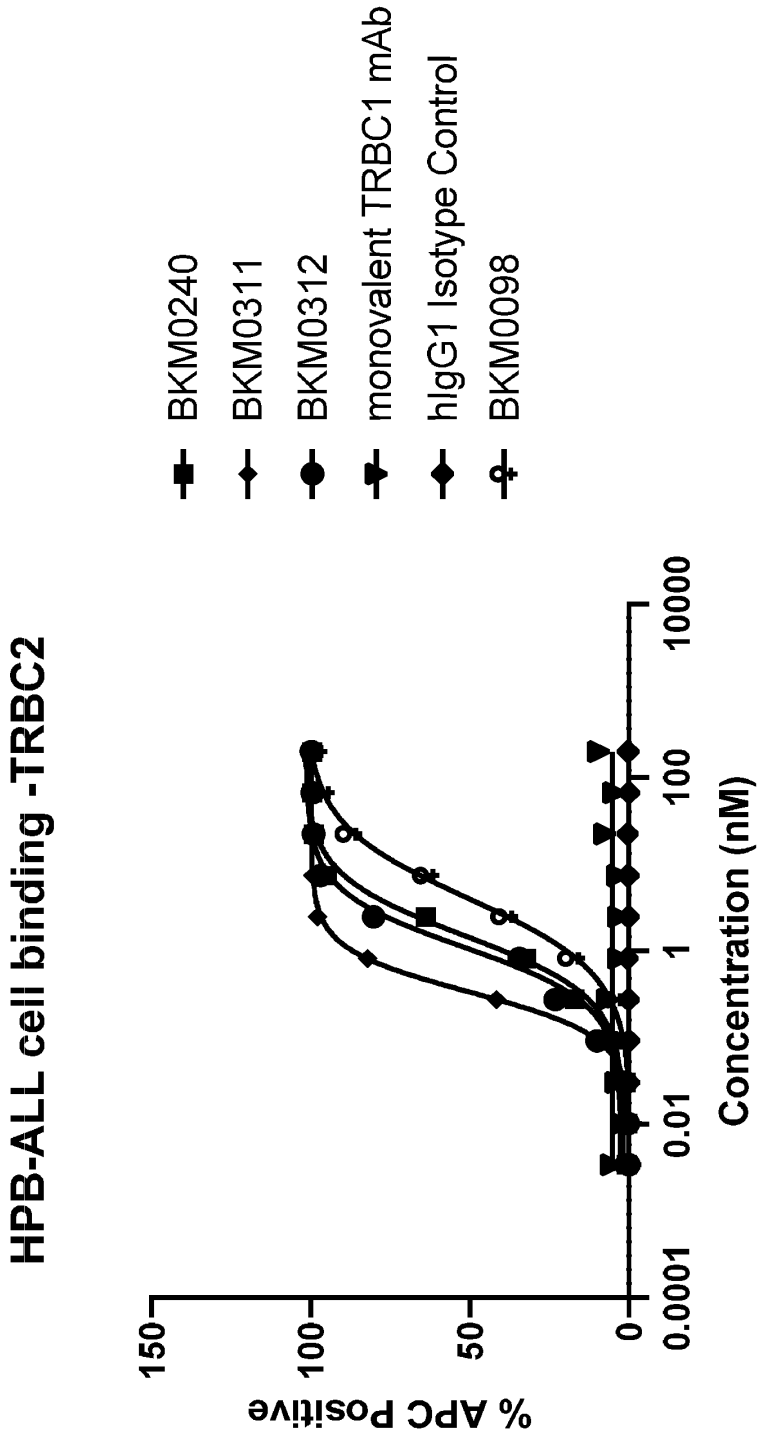

HPB-ALL cell binding -TRBC2
% APC Positive
150
100
50
0
0.0001
0.01
1
100
10000
Concentration (nM)
BKM0240
BKM0311
BKM0312
monovalent TRBC1 mAb
hIgG1 Isotype Control
BKM0098

FIG. 32A

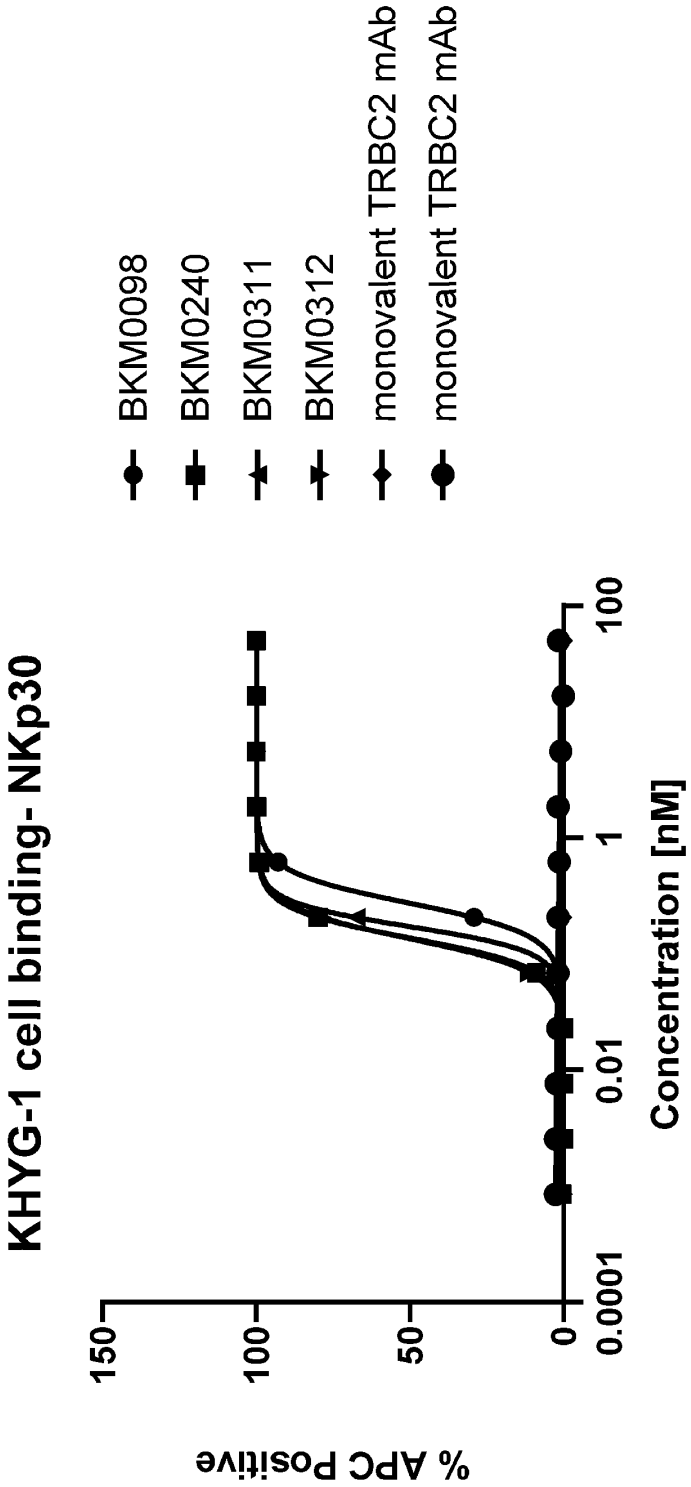

KHYG-1 cell binding- NKp30
% APC Positive
150
100
50
0
0.0001
0.01
1
100
Concentration [nM]
BKM0098
BKM0240
BKM0311
BKM0312
monovalent TRBC2 mAb
monovalent TRBC2 mAb

FIG. 32B

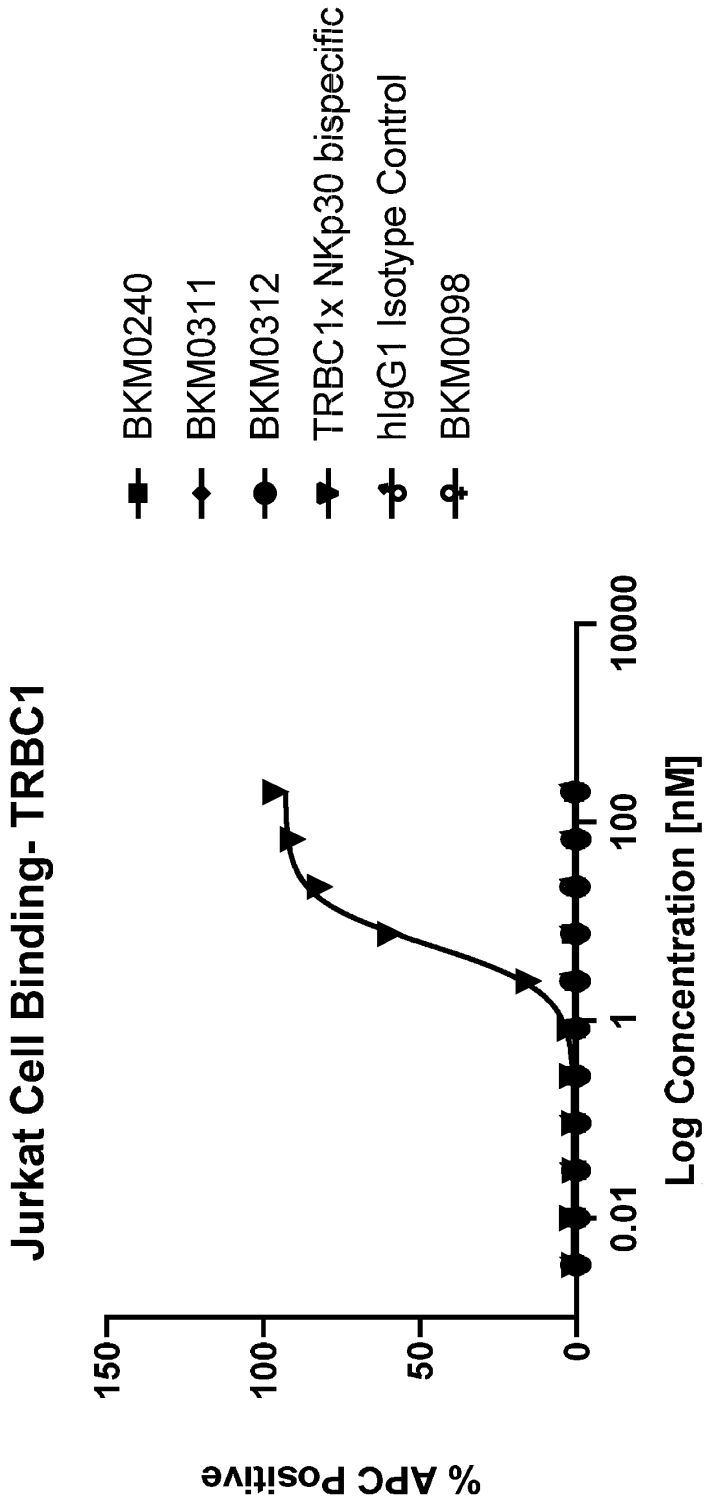
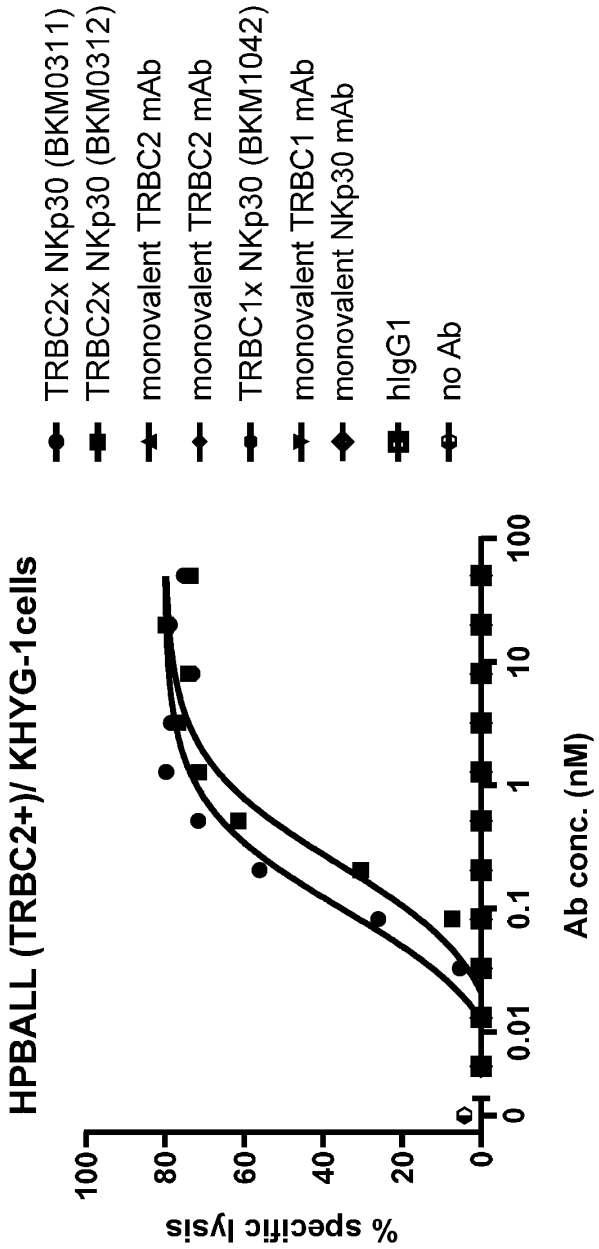

Jurkat Cell Binding- TRBC1
% APC Positive
150
100
50
0
0.01
1
100
10000
Log Concentration [nM]
BKM0240
BKM0311
BKM0312
TRBC1x NKp30 bispecific
hIgG1 Isotype Control
BKM0098

FIG. 32C



	aNKp30xTRBC2 (0311)	aNKp30xTRBC2 (0312)
EC50	0.09821	0.2324

FIG. 33A

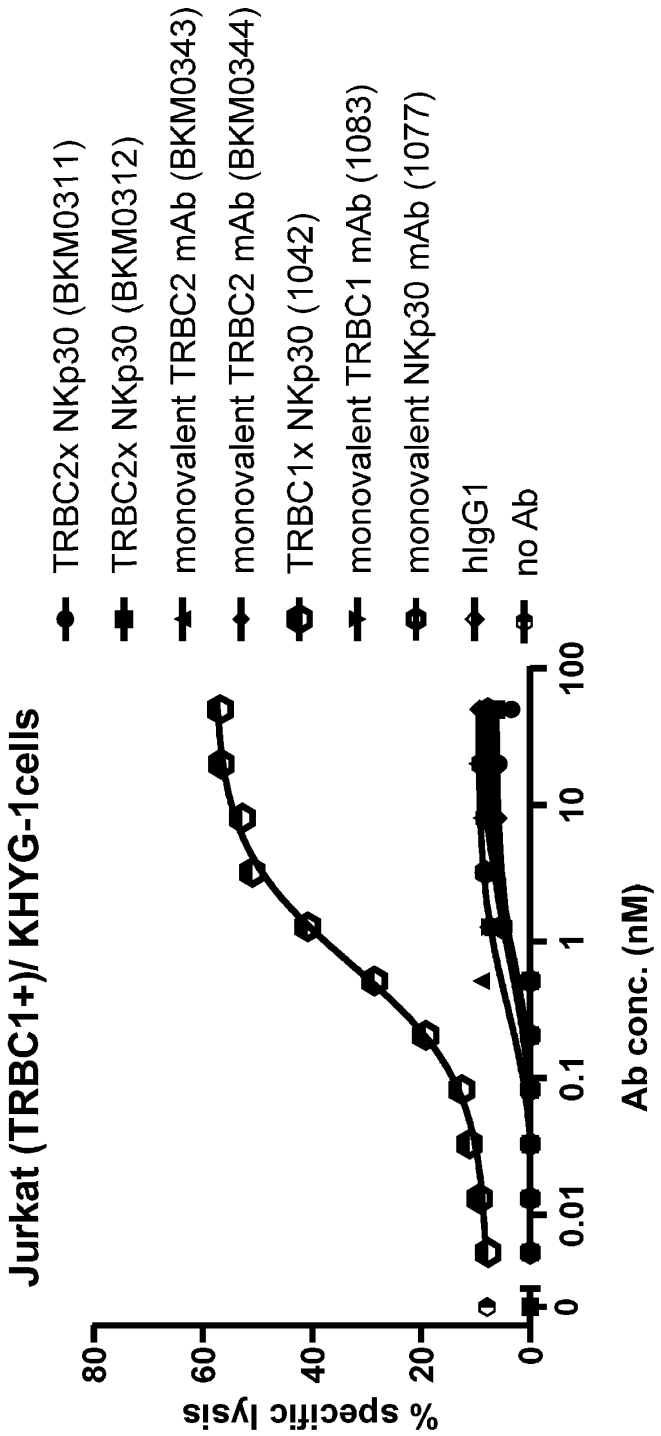
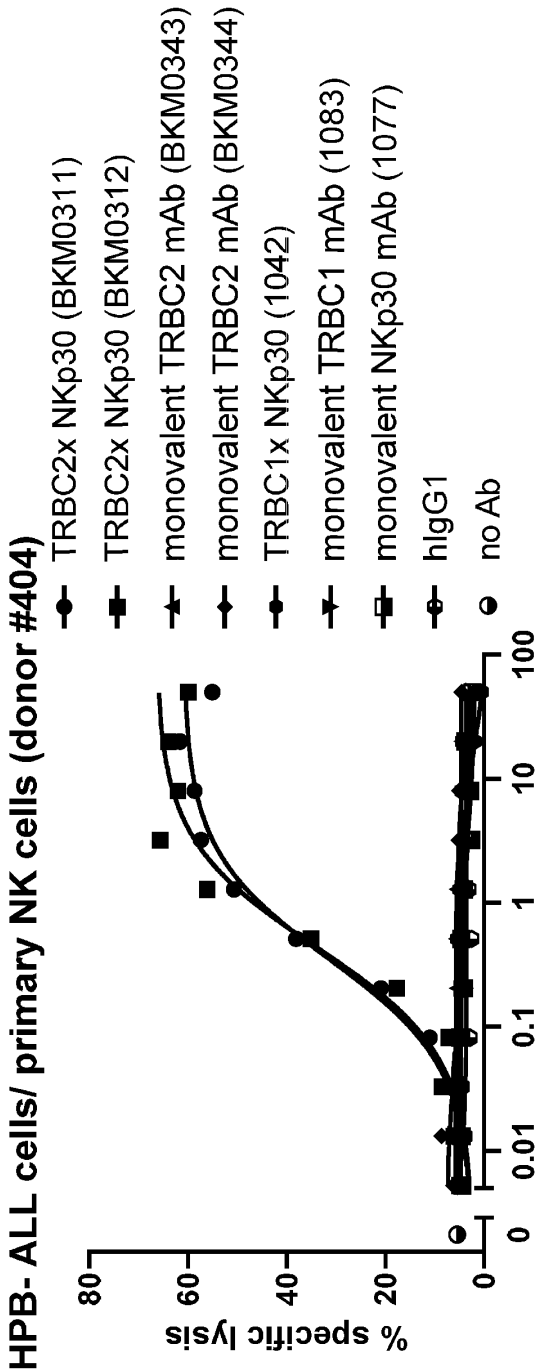

Jurkat (TRBC1+)/ KHYG-1cells
% specific lysis
80
60
40
20
0
0
0.01
0.1
1
10
100
Ab conc. (nM)
TRBC2x NKp30 (BKM0311)
TRBC2x NKp30 (BKM0312)
monovalent TRBC2 mAb (BKM0343)
monovalent TRBC2 mAb (BKM0344)
TRBC1x NKp30 (1042)
monovalent TRBC1 mAb (1083)
monovalent NKp30 mAb (1077)
hIgG1
no Ab

FIG. 33B



	aNKp30xTRBC2 (0311)	aNKp30xTRBC2 (0312)
EC50	0.3570	0.4469

FIG. 33C

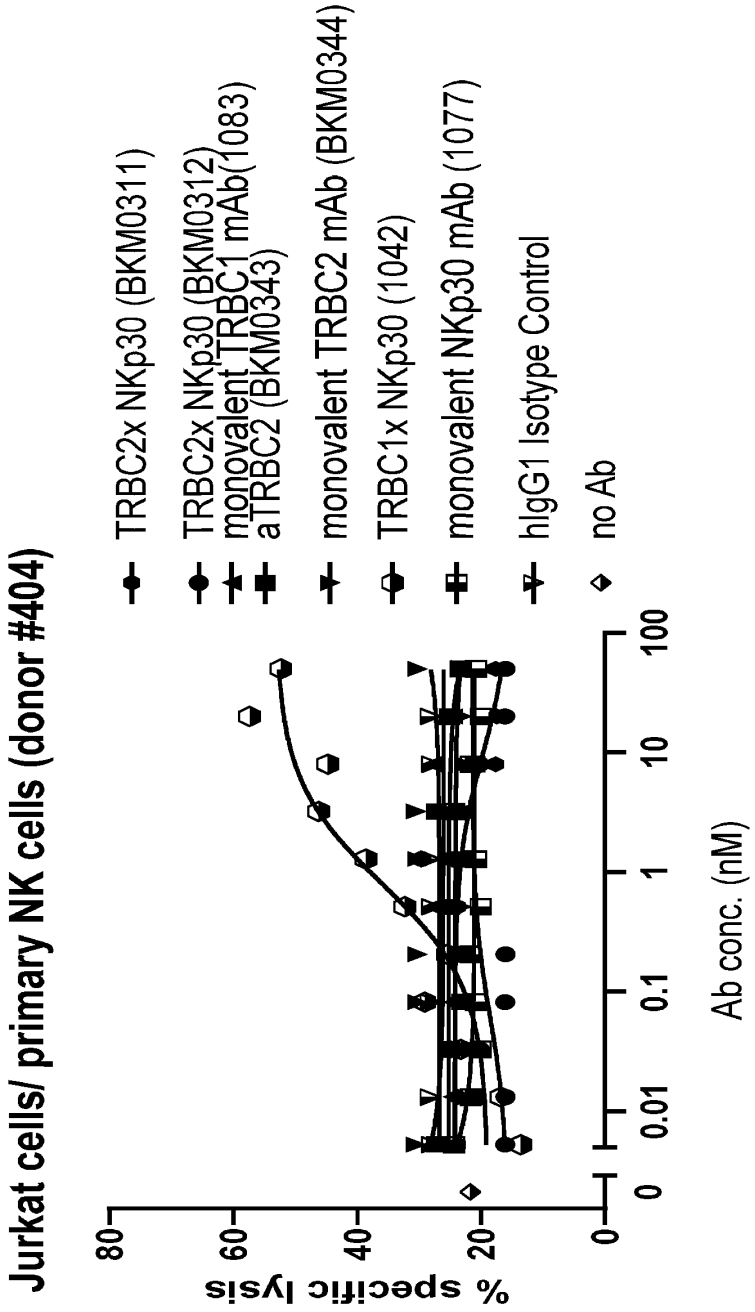
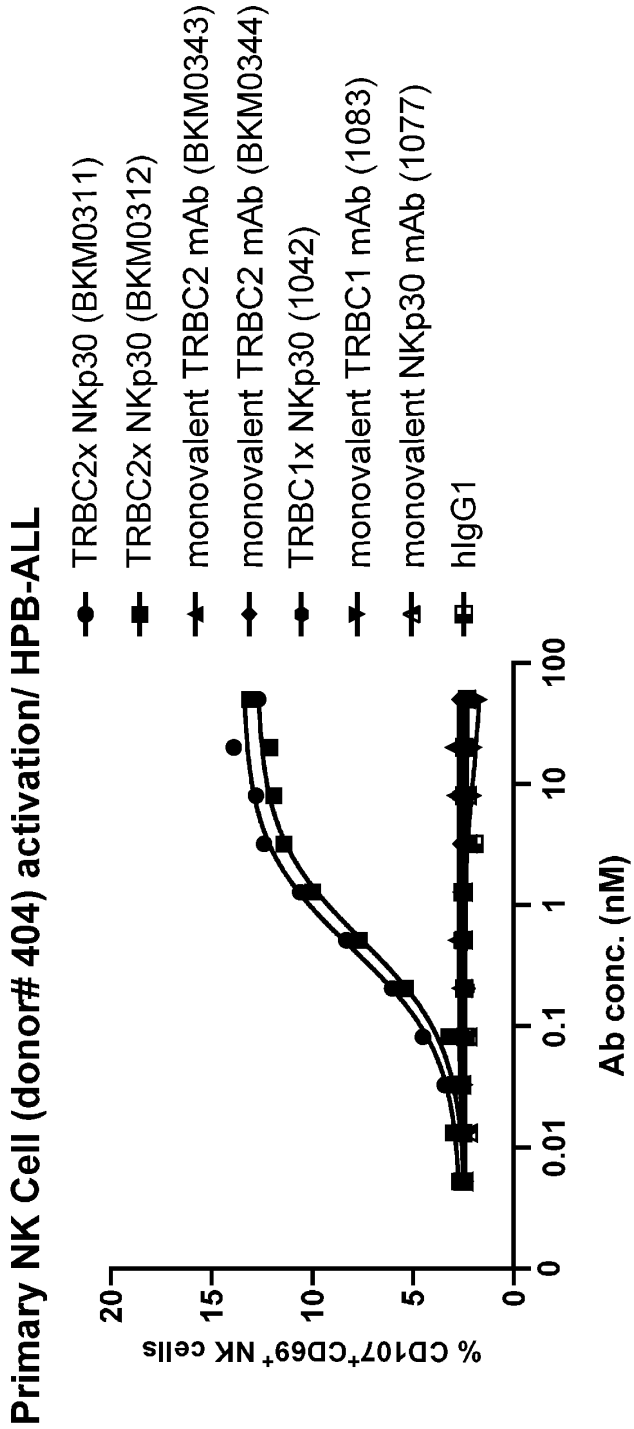

Jurkat cells/ primary NK cells (donor #404)
% specific lysis
80
60
40
20
0
0
0.01
0.1
1
10
100
Ab conc. (nM)
TRBC2x NKp30 (BKM0311)
TRBC2x NKp30 (BKM0312)
monovalent TRBC1 mAb(1083)
aTRBC2 (BKM0343)
monovalent TRBC2 mAb (BKM0344)
TRBC1x NKp30 (1042)
monovalent NKp30 mAb (1077)
hIgG1 Isotype Control
no Ab

FIG. 33D



	aNKp30xTRBC2 (0311)	aNKp30xTRBC2 (0312)
EC50	0.4397	0.5176

FIG. 34A

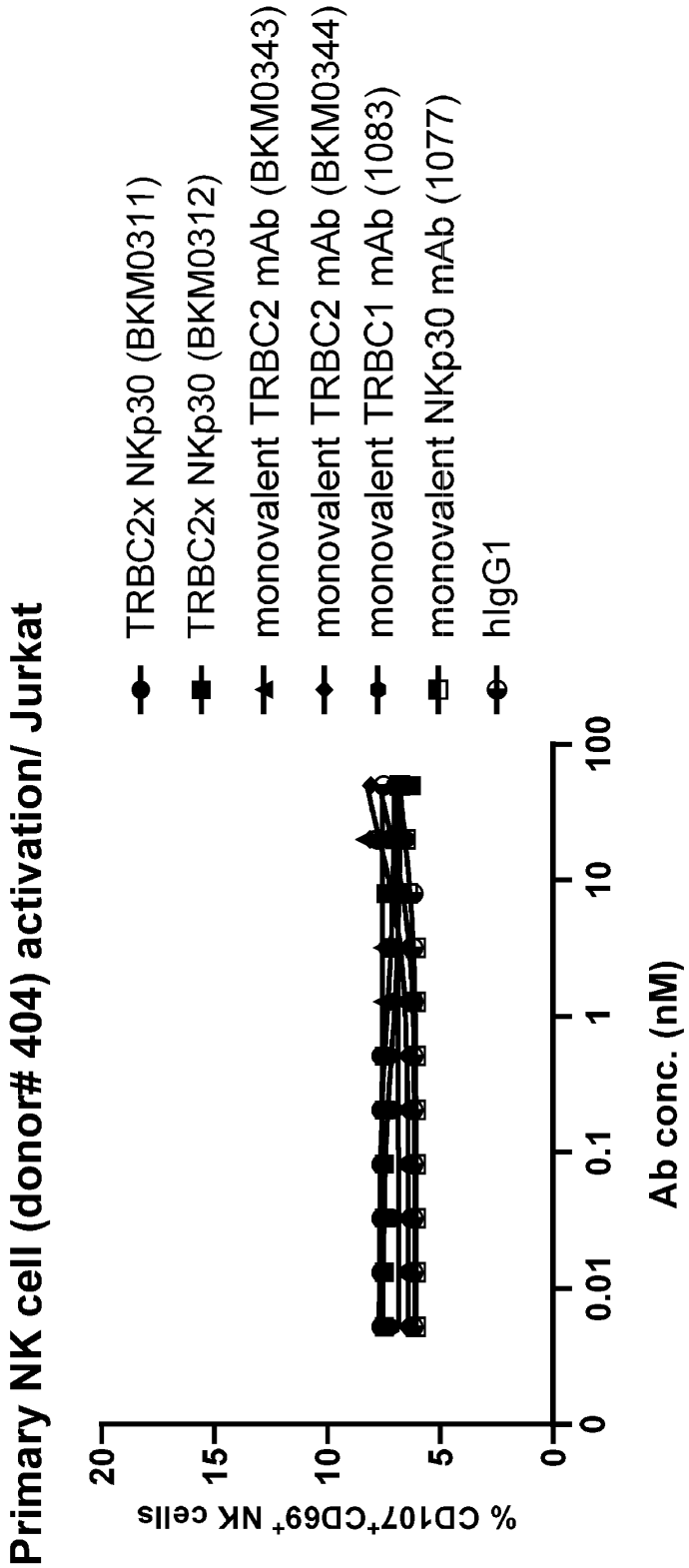

Primary NK cell (donor# 404) activation/ Jurkat
% CD107+CD69+ NK cells
20
15
10
5
0
0
0.01
0.1
1
10
100
Ab conc. (nM)
TRBC2x NKp30 (BKM0311)
TRBC2x NKp30 (BKM0312)
monovalent TRBC2 mAb (BKM0343)
monovalent TRBC2 mAb (BKM0344)
monovalent TRBC1 mAb (1083)
monovalent NKp30 mAb (1077)
hIgG1

FIG. 34B

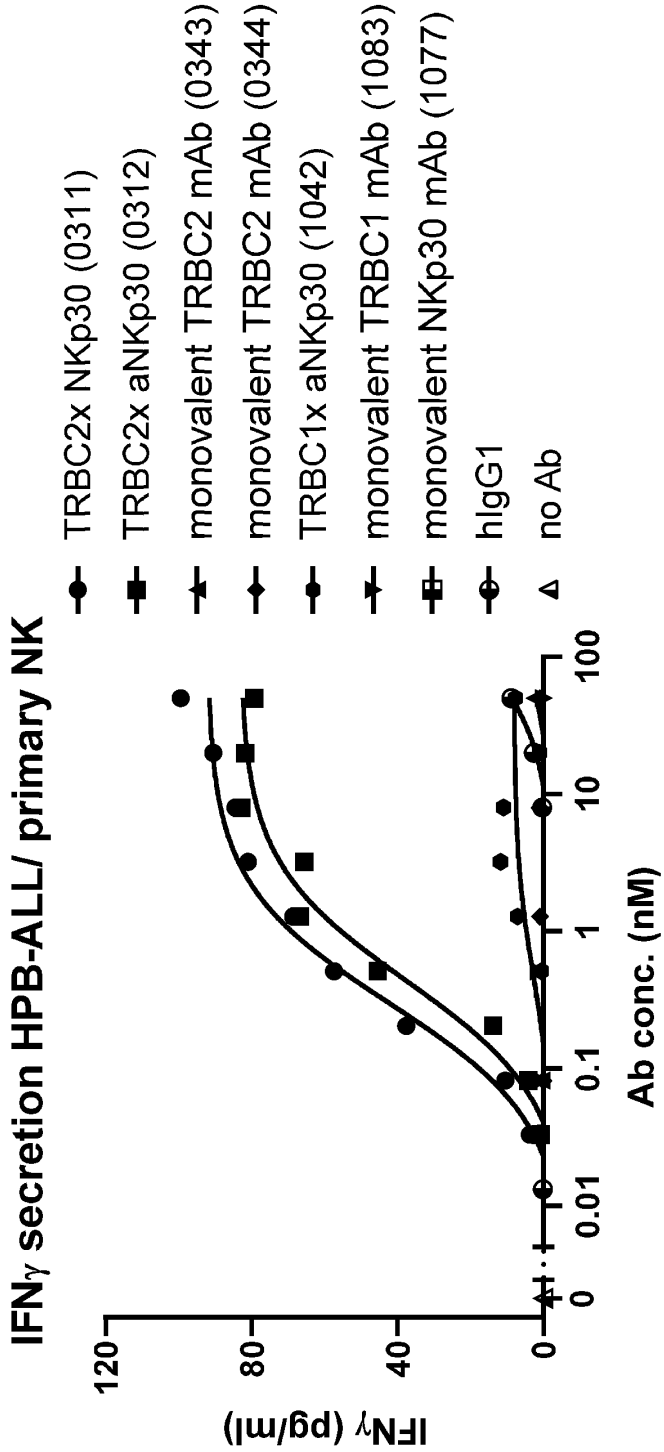

IFNγ secretion HPB-ALL/ primary NK
IFNγ (pg/ml)
120
80
40
0
0
0.01
0.1
1
10
100
Ab conc. (nM)
TRBC2x NKp30 (0311)
TRBC2x aNKp30 (0312)
monovalent TRBC2 mAb (0343)
monovalent TRBC2 mAb (0344)
TRBC1x aNKp30 (1042)
monovalent TRBC1 mAb (1083)
monovalent NKp30 mAb (1077)
hIgG1
no Ab

FIG. 35A

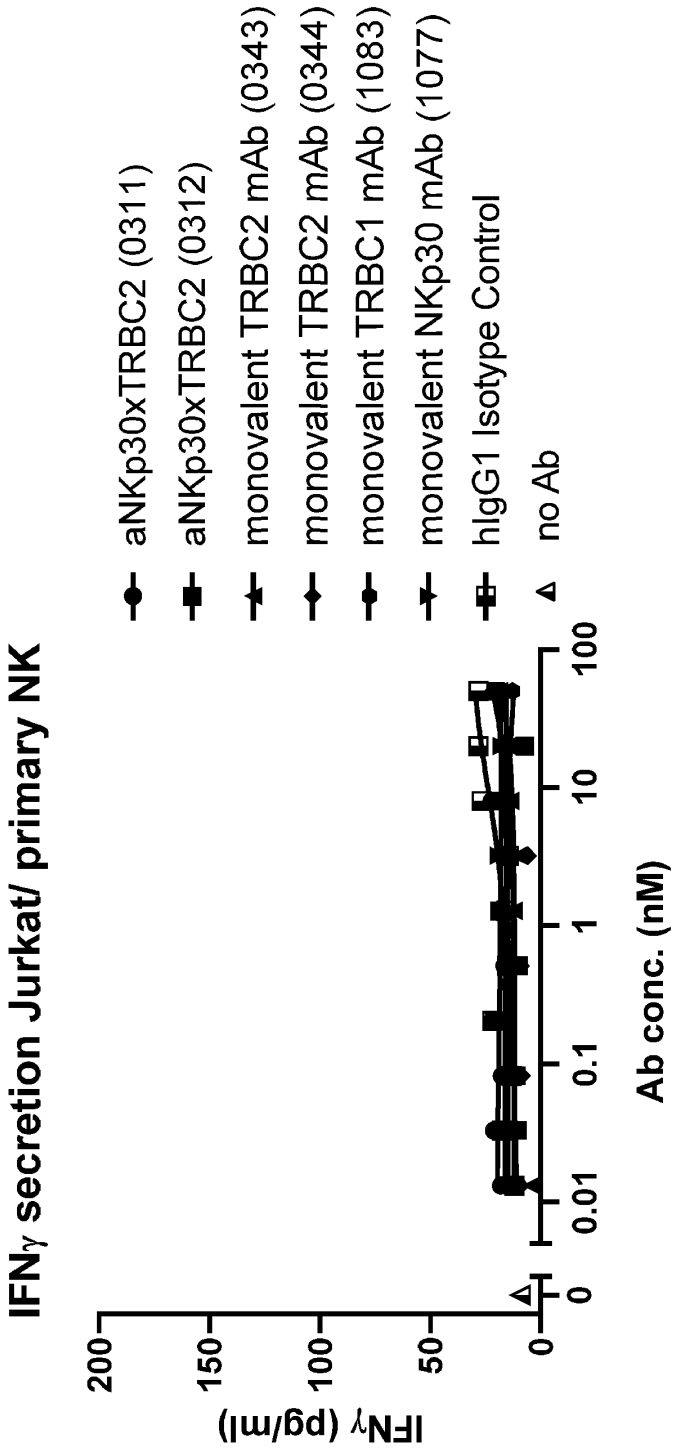

IFNγ secretion Jurkat/ primary NK
IFNγ (pg/ml)
200
150
100
50
0
0
0.01
0.1
1
10
100
Ab conc. (nM)
aNKp30xTRBC2 (0311)
aNKp30xTRBC2 (0312)
monovalent TRBC2 mAb (0343)
monovalent TRBC2 mAb (0344)
monovalent TRBC1 mAb (1083)
monovalent NKp30 mAb (1077)
hIgG1 Isotype Control
no Ab

FIG. 35B

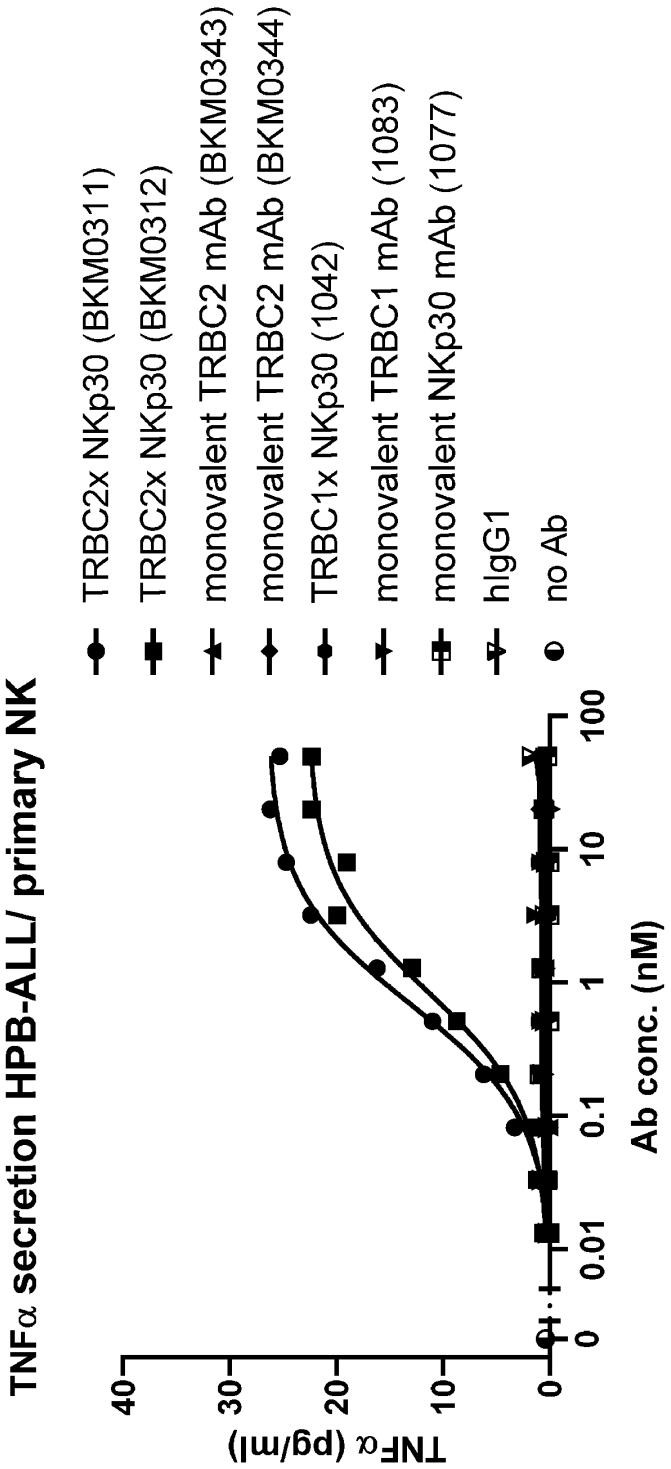

TNFα secretion HPB-ALL/ primary NK
TNFα (pg/ml)
40
30
20
10
0
0
0.01
0.1
1
10
100
Ab conc. (nM)
TRBC2x NKp30 (BKM0311)
TRBC2x NKp30 (BKM0312)
monovalent TRBC2 mAb (BKM0343)
monovalent TRBC2 mAb (BKM0344)
TRBC1x NKp30 (1042)
monovalent TRBC1 mAb (1083)
monovalent NKp30 mAb (1077)
hIgG1
no Ab

FIG. 35C

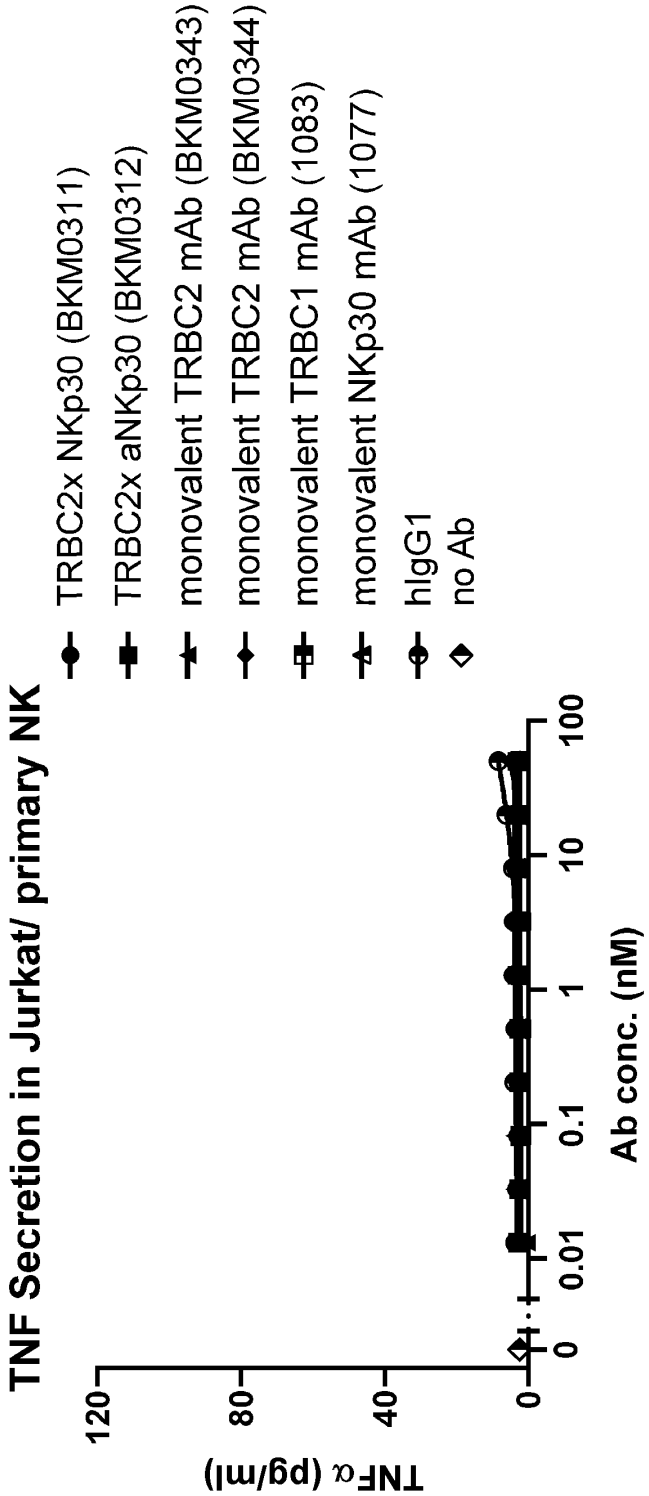
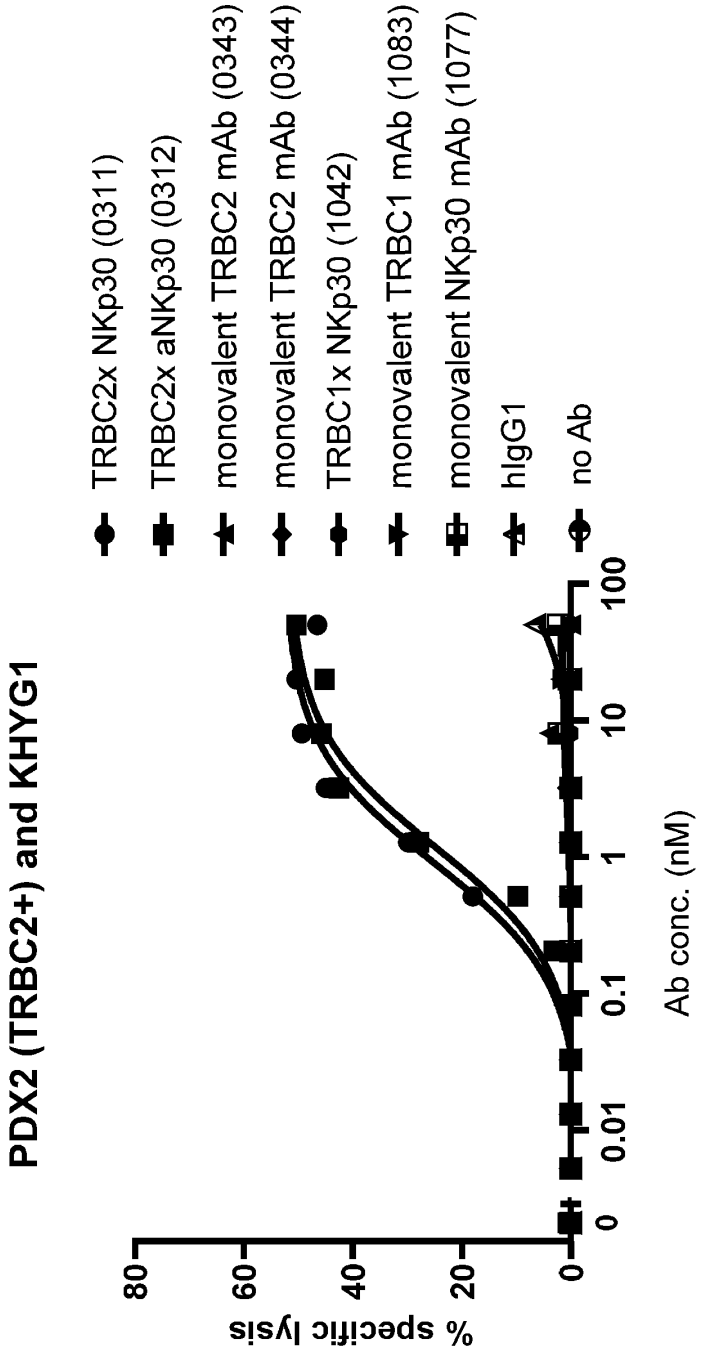
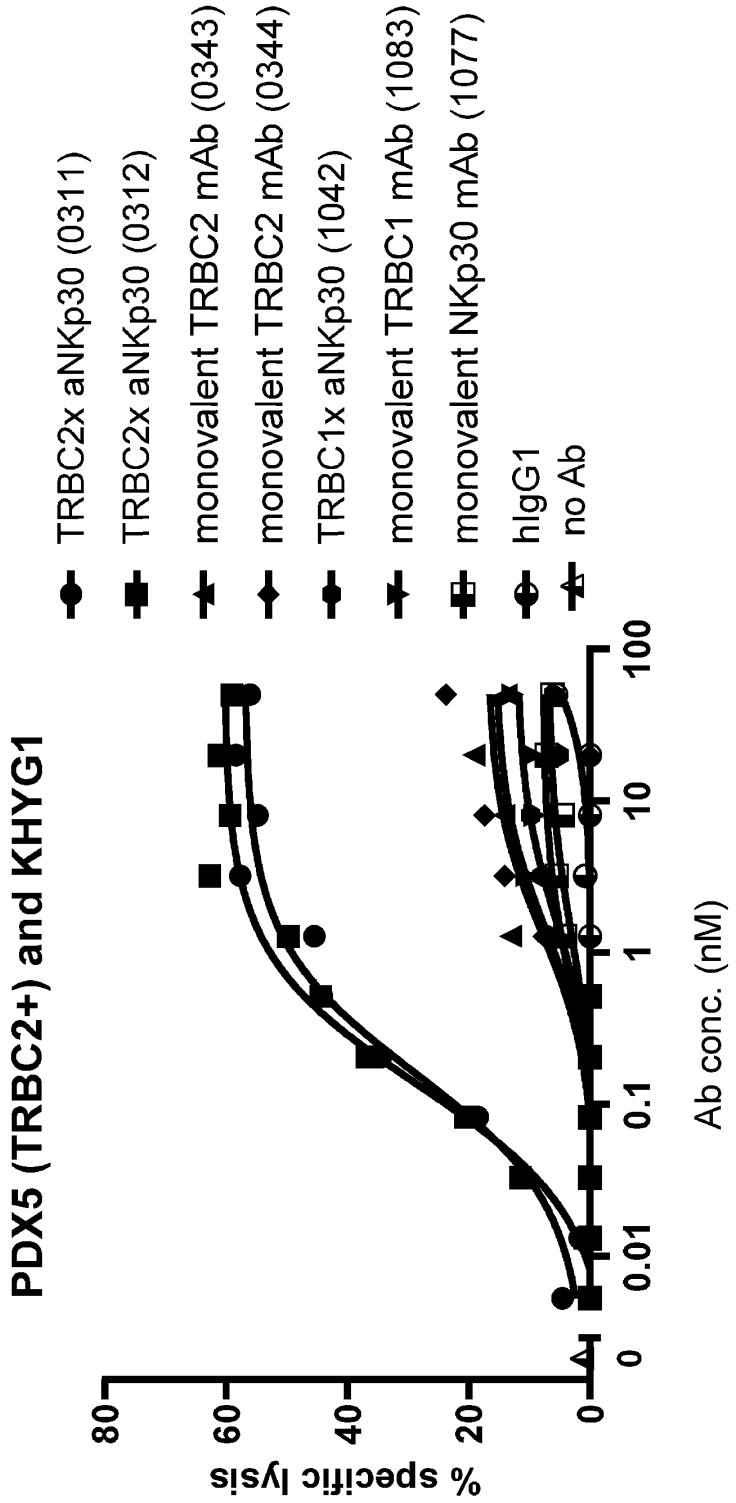

TNF Secretion in Jurkat/ primary NK
TNFα (pg/ml)
120
80
40
0
0
0.01
0.1
1
10
100
Ab conc. (nM)
TRBC2x NKp30 (BKM0311)
TRBC2x aNKp30 (BKM0312)
monovalent TRBC2 mAb (BKM0343)
monovalent TRBC2 mAb (BKM0344)
monovalent TRBC1 mAb (1083)
monovalent NKp30 mAb (1077)
hIgG1
no Ab

FIG. 35D



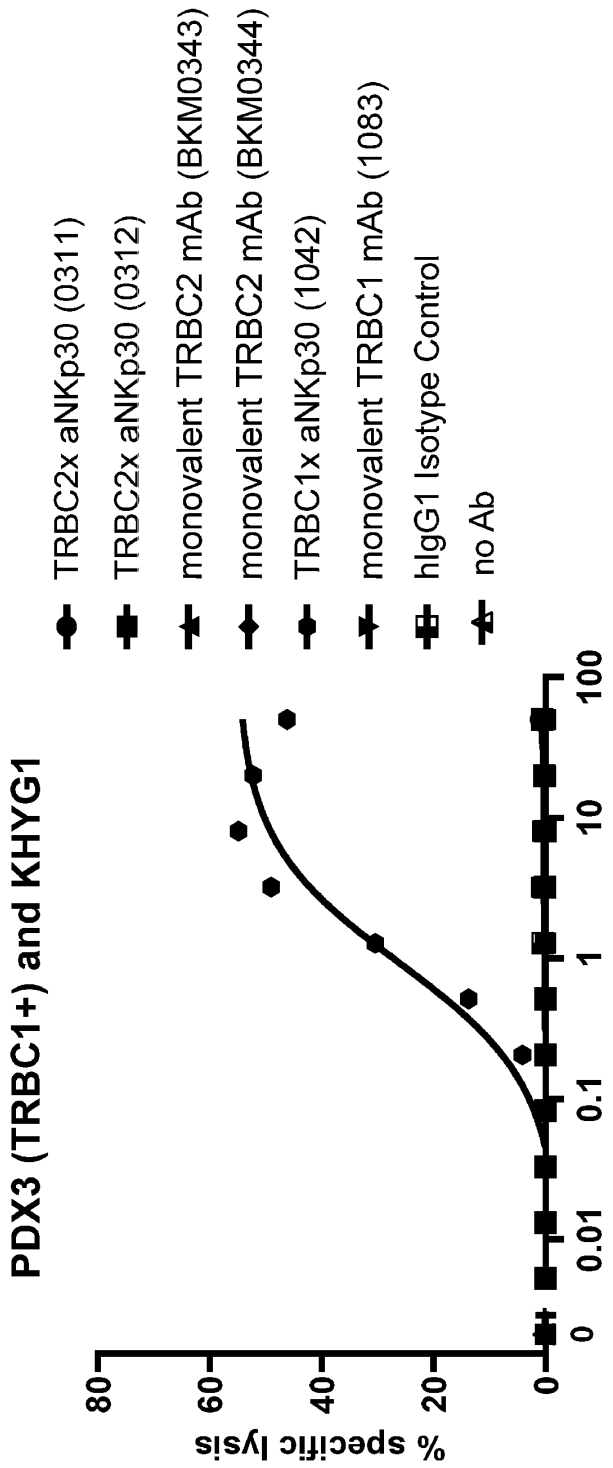
	aNKp30xTRBC2 (0311)	aNKp30xTRBC2 (0312)
EC50	0.9083	1.196

FIG. 36A



	aNKp30xTRBC2 (0311)	aNKp30xTRBC2 (0312)
EC50	0.1592	0.1335

FIG. 36B



	aNKp30xTRBC1(1042)
EC50	0.9346

FIG. 36C

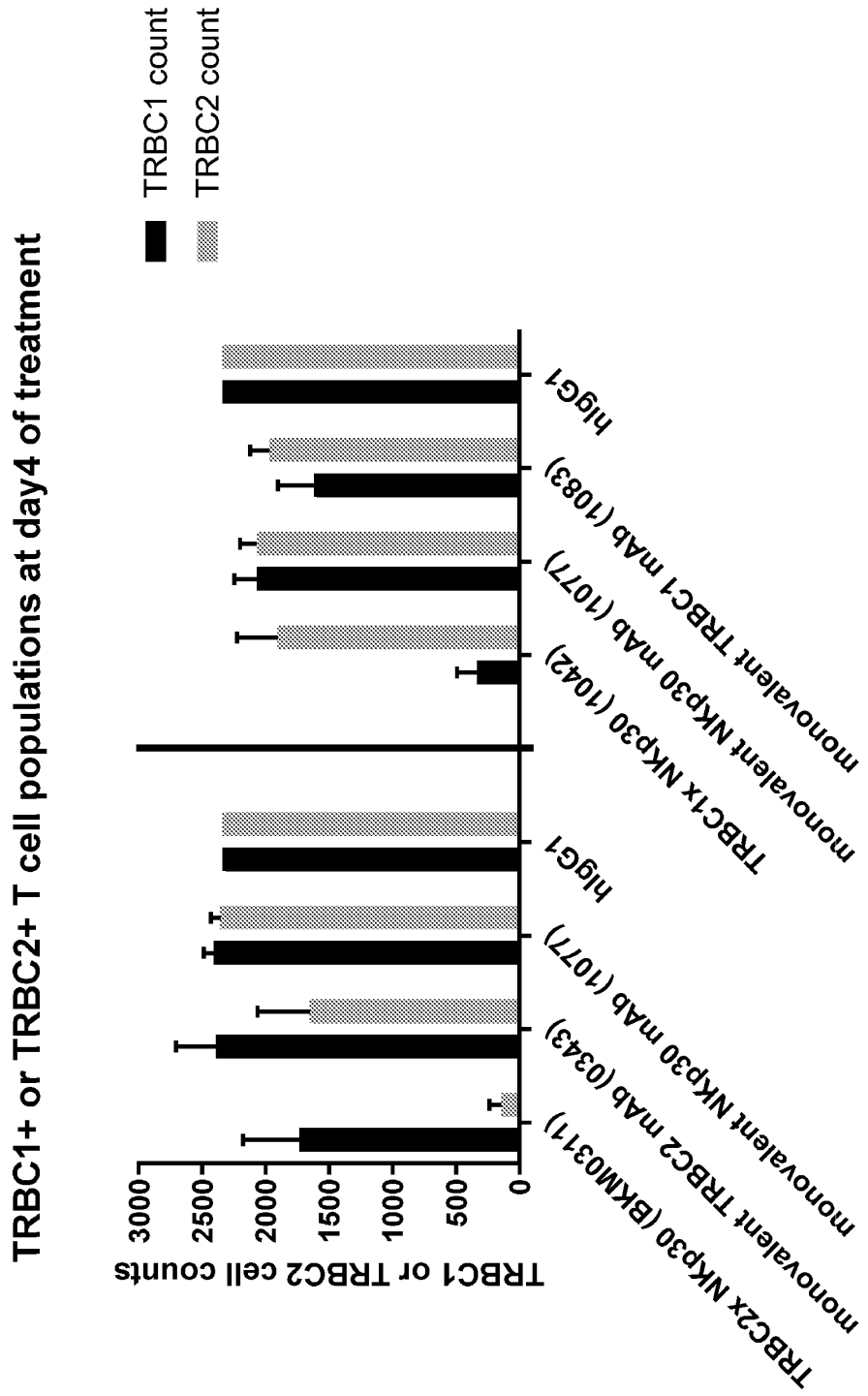

TRBC1+ or TRBC2+ T cell populations at day4 of treatment
TRBC1 count
TRBC2 count
TRBC1 or TRBC2 cell counts
3000
2500
2000
1500
1000
500
0
TRBC2x NKp30 (BKM0311)
monovalent TRBC2 mAb (0343)
monovalent NKp30 mAb (1077)
hIgG1
TRBC1x NKp30 (1042)
monovalent NKp30 mAb (1077)
monovalent TRBC1 mAb (1083)
hIgG1

FIG. 37

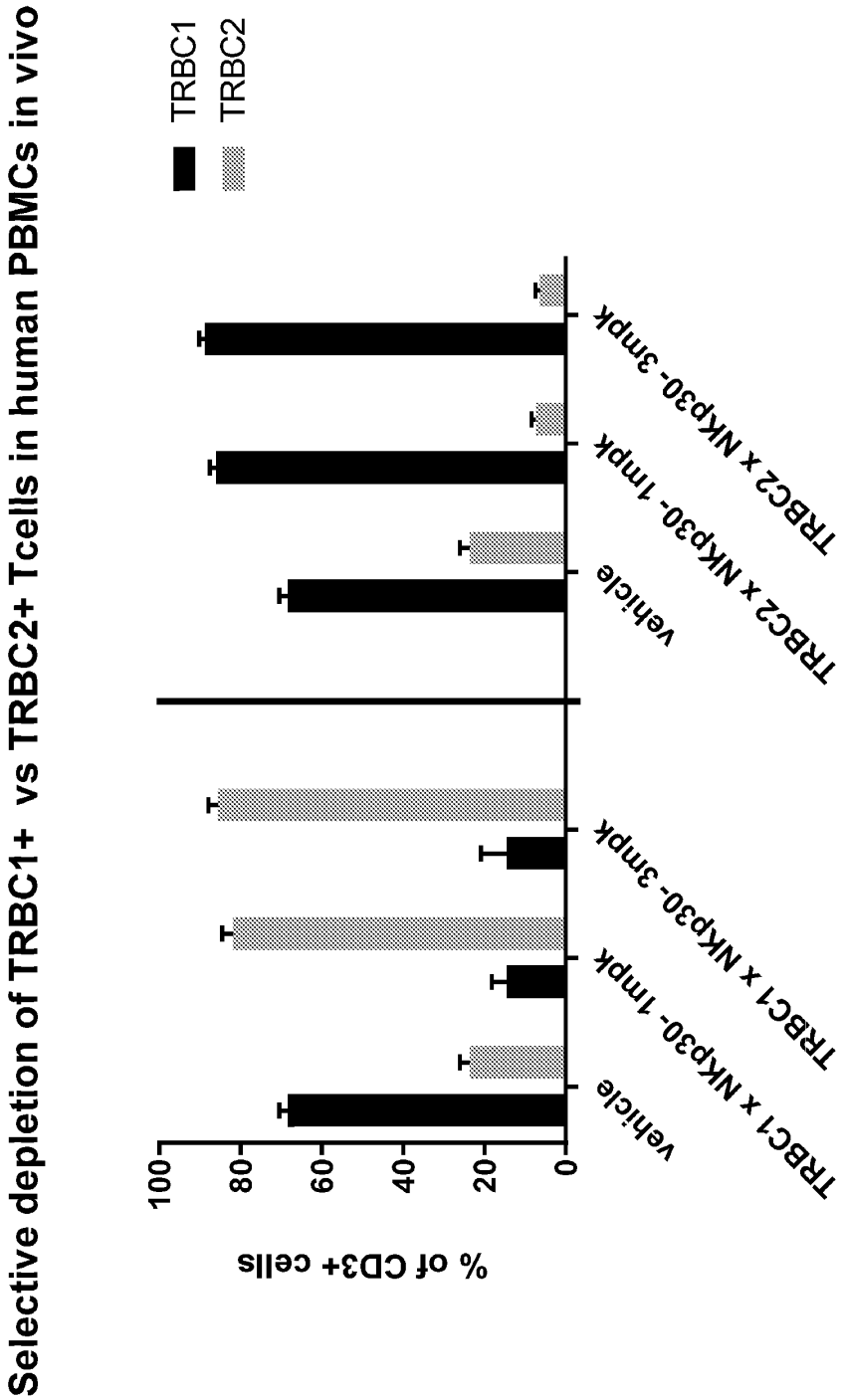

Selective depletion of TRBC1+ vs TRBC2+ Tcells in human PBMCs in vivo
TRBC1
TRBC2
% of CD3+ cells
100
80
60
40
20
0
vehicle
TRBC1 x NKp30- 1mpk
TRBC1 x NKp30- 3mpk
vehicle
TRBC2 x NKp30- 1mpk
TRBC2 x NKp30- 3mpk

FIG. 38

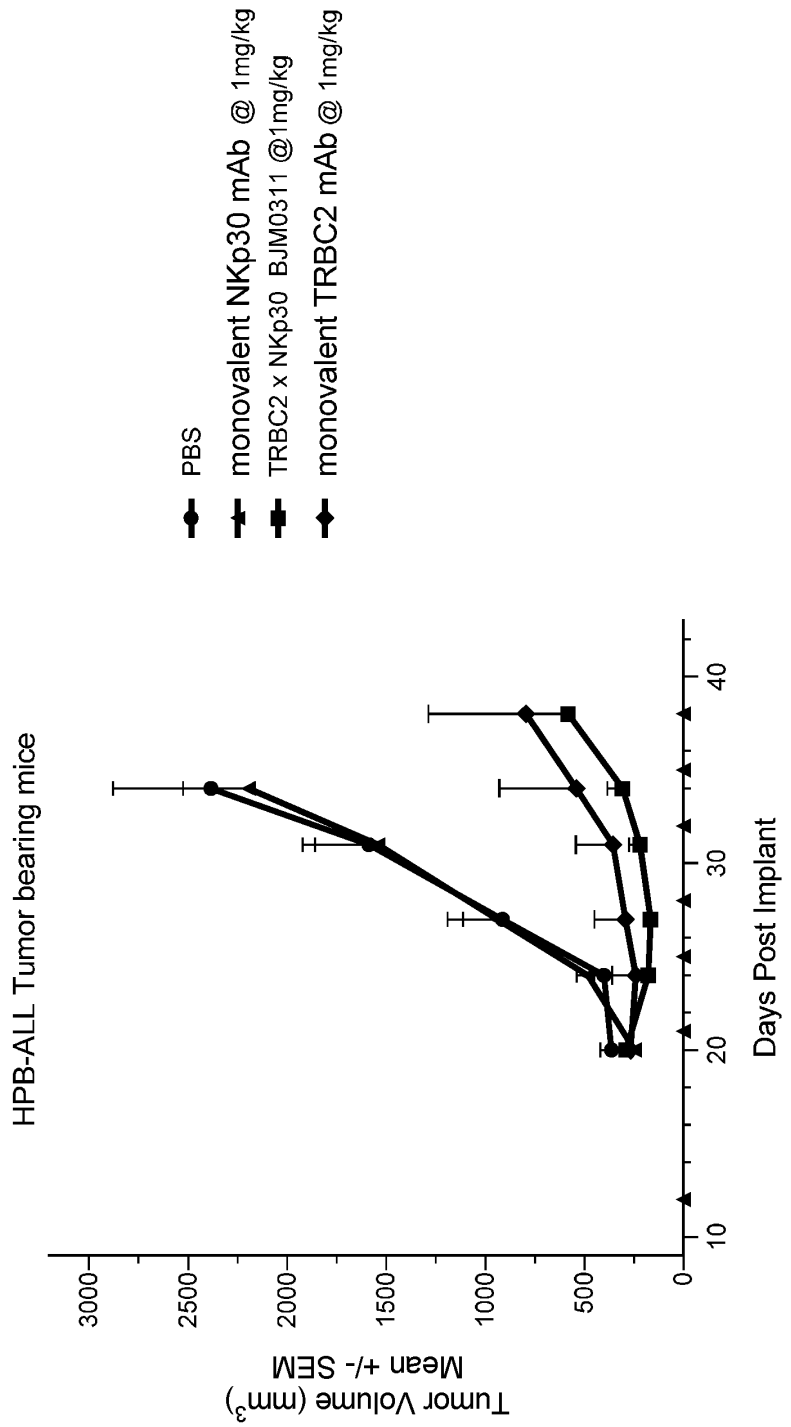

HPB-ALL Tumor bearing mice
Tumor Volume (mm3)
Mean +/- SEM
3000
2500
2000
1500
1000
500
0
10
20
30
40
Days Post Implant
PBS
monovalent NKp30 mAb @ 1mg/kg
TRBC2 x NKp30 BJM0311 @1mg/kg
monovalent TRBC2 mAb @ 1mg/kg

FIG. 39