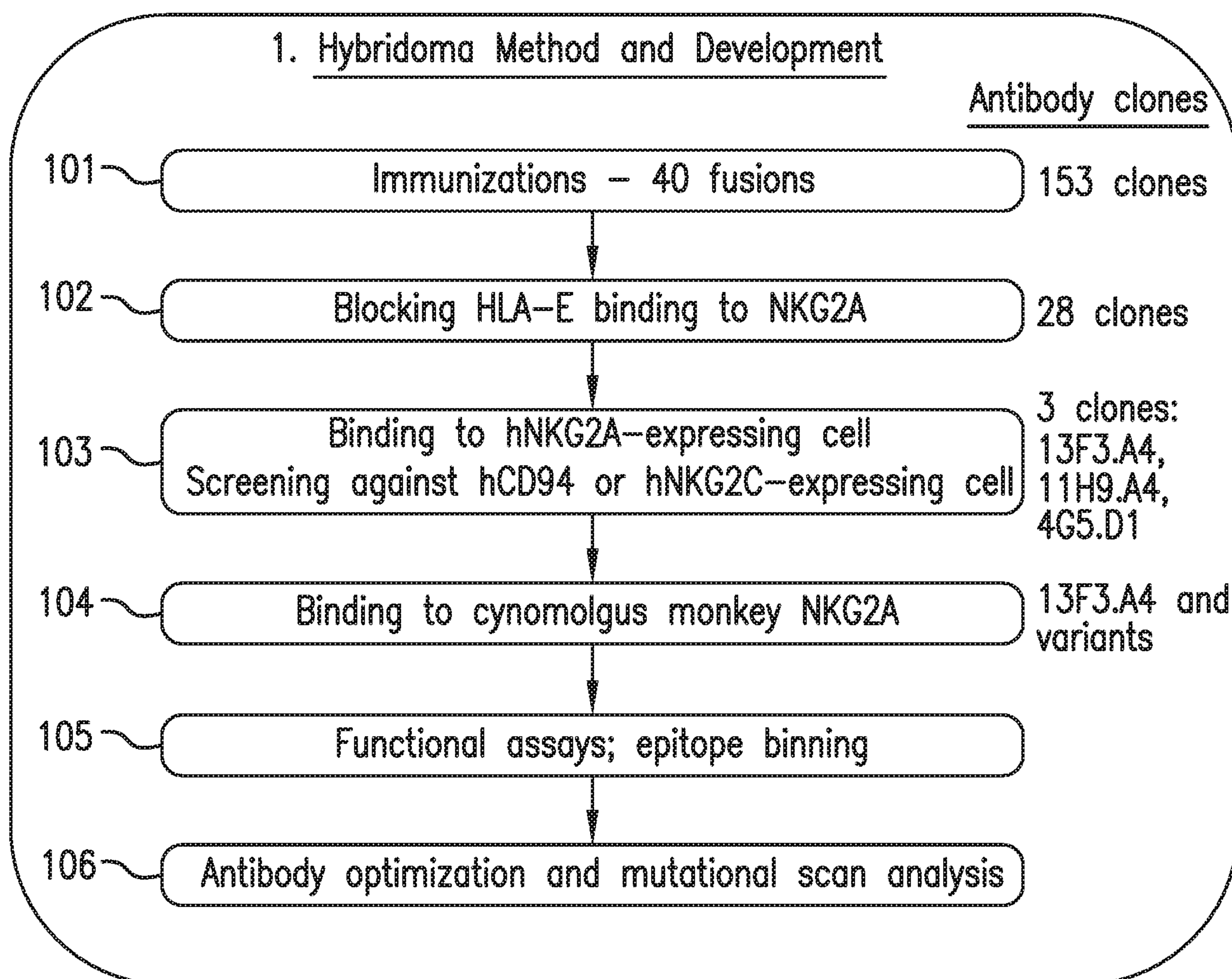
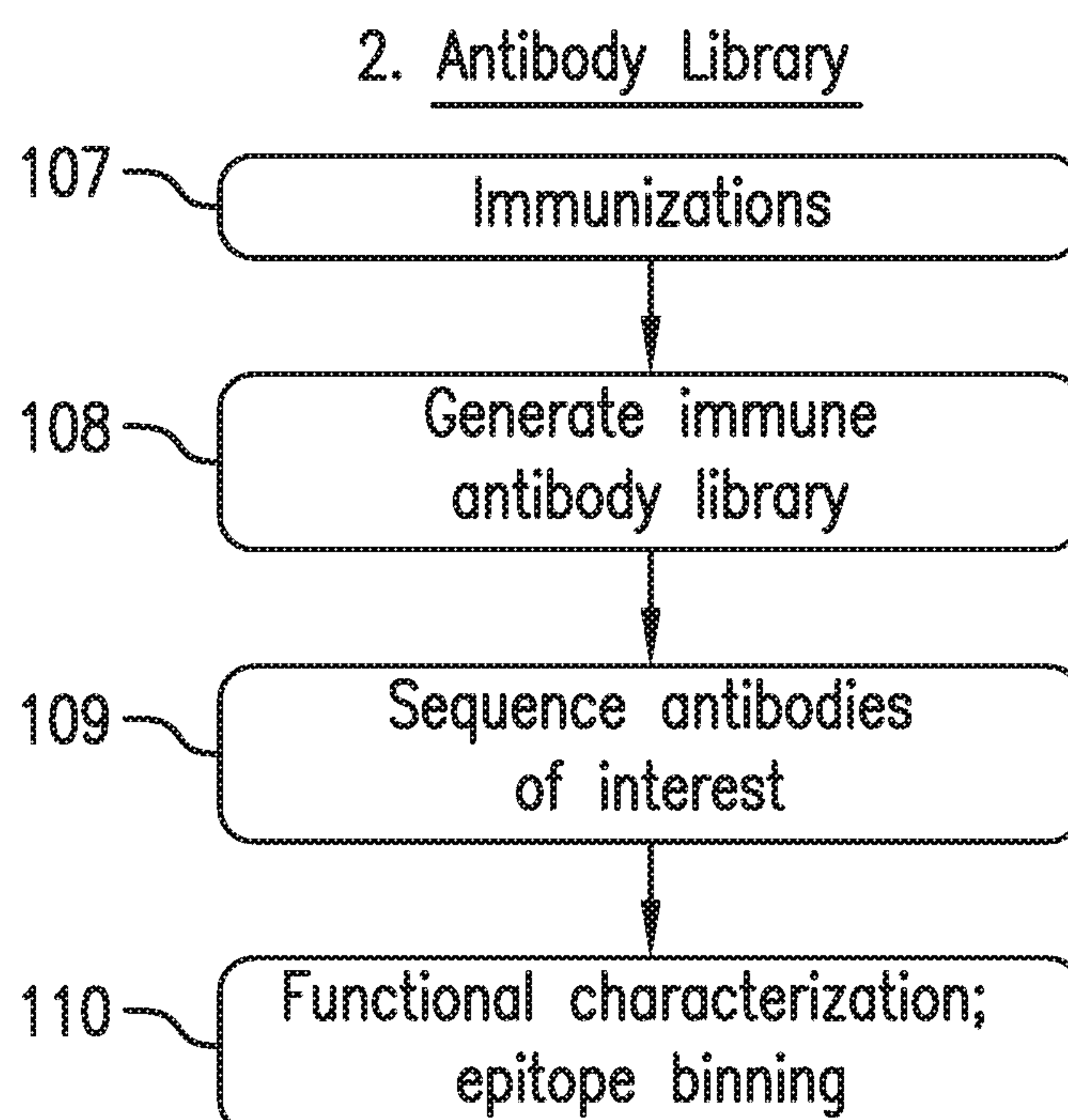


**FIG. 1A****FIG. 1B**

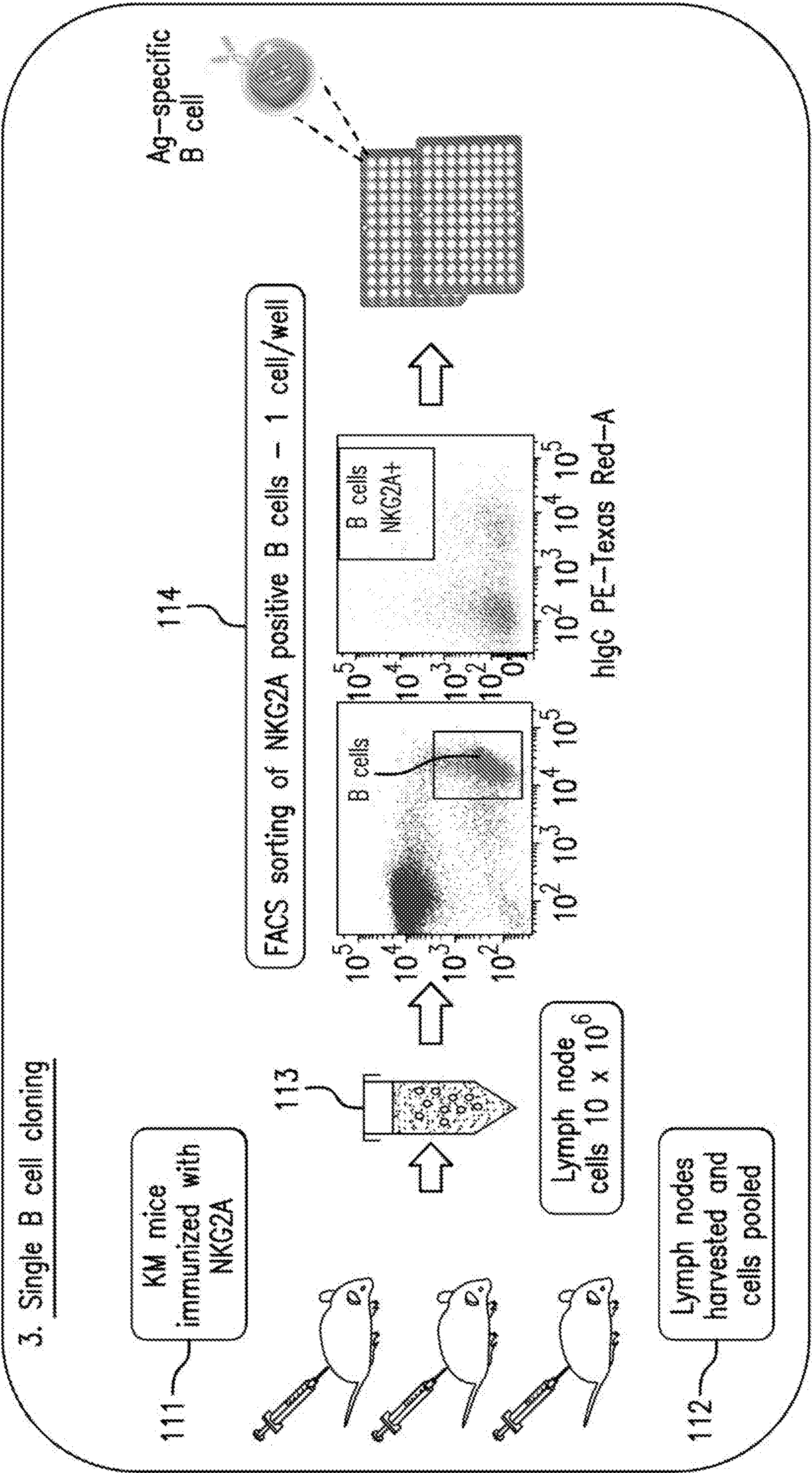


FIG.1C

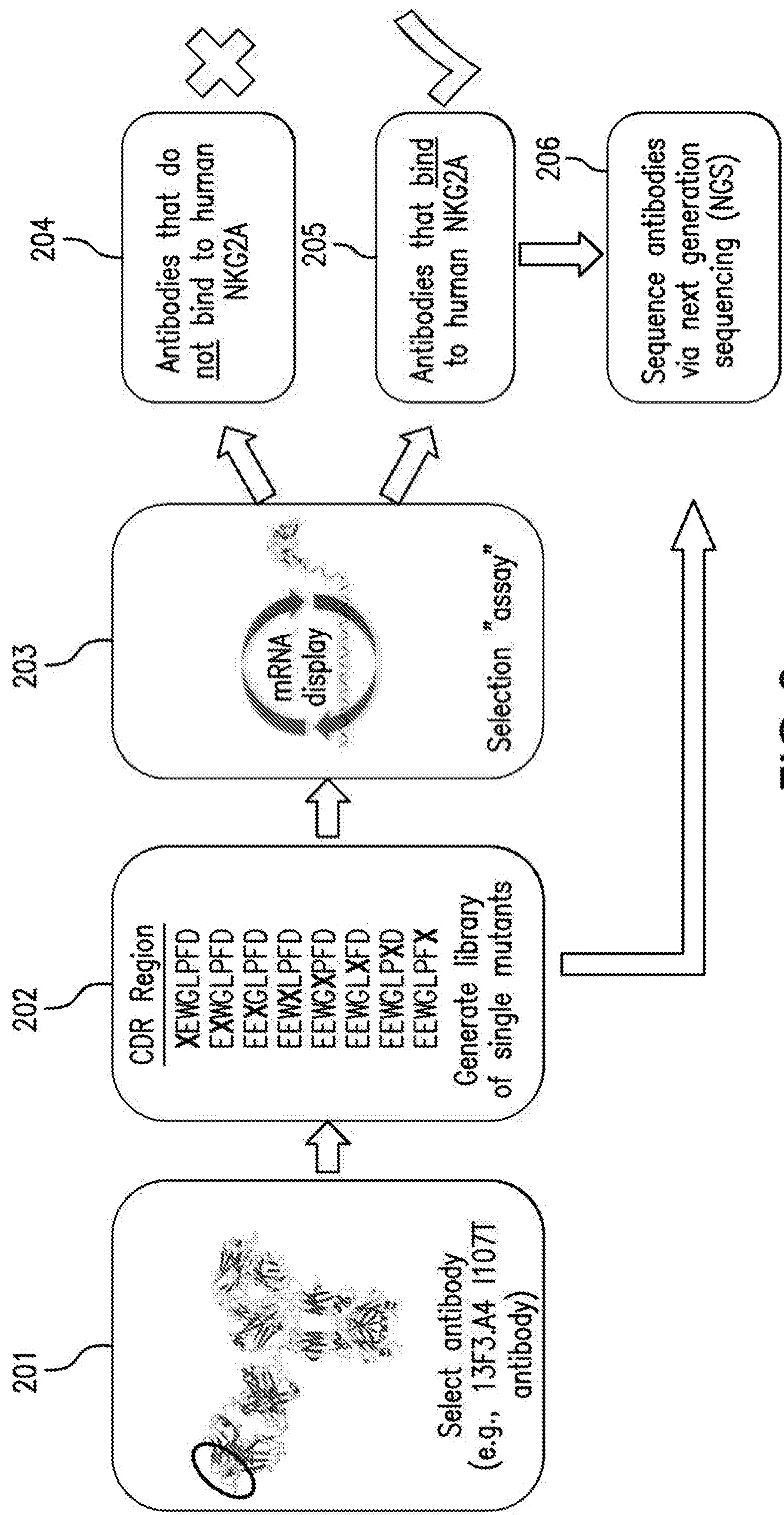
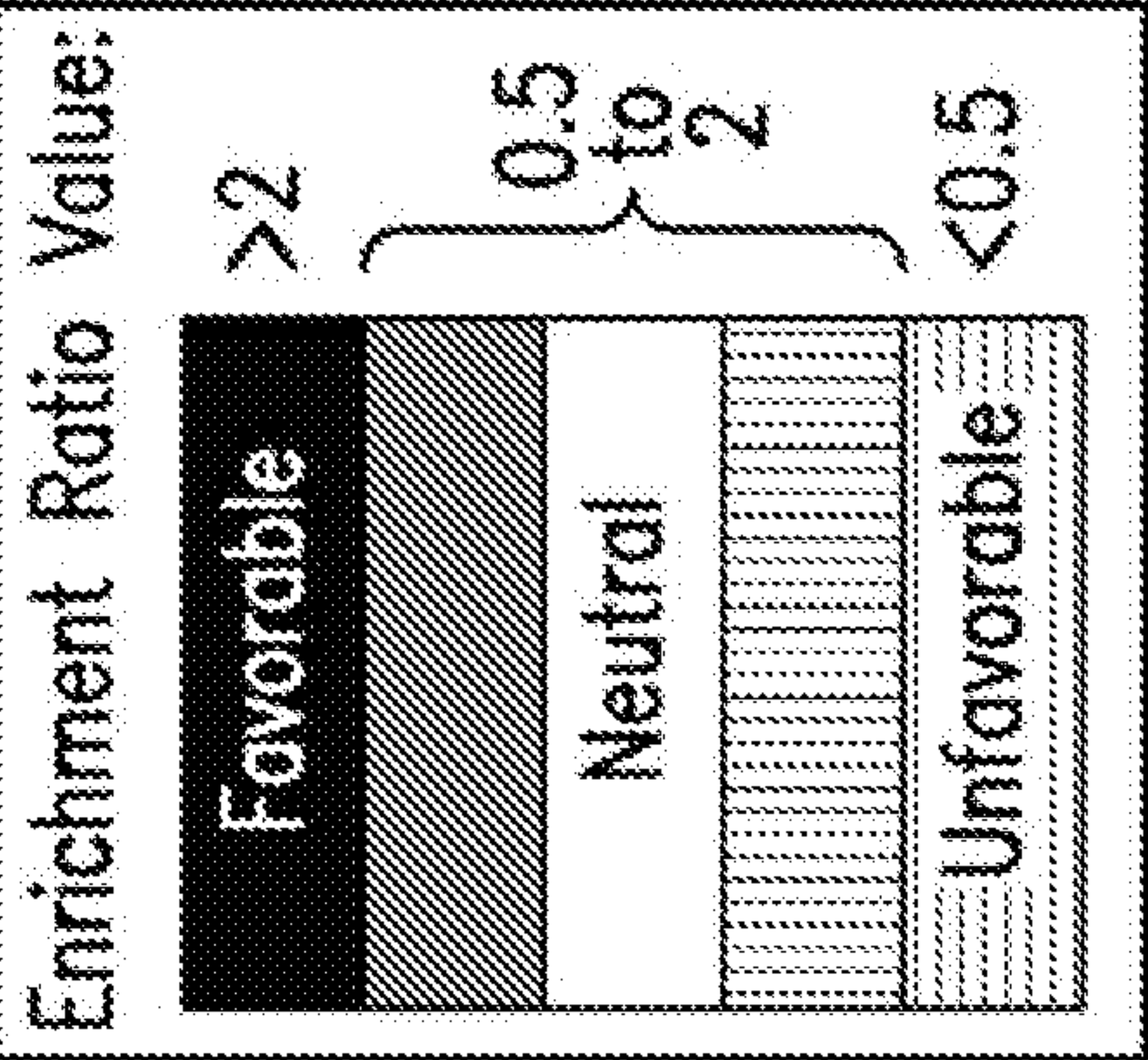


FIG. 2

Mutational Scan Data Analysis Generates
Sequence-Activity Relationship -- Example



All possible
amino acid
substitutions

Sequence of
parent clone
501

Position in
sequence
502

Example of
favorable
substitution

Germline	26	27	28	29	30	31	32	33	34	35
Parental	G	F	T	F	S	S	H	S	M	N
Normalized Enrichment Ratio										
*	0.00	0.00	0.00	0.00	0.00	0.29	0.00	0.00	0.00	0.07
P	0.00	0.00	0.26	0.00	0.77	0.03	0.18	0.00	0.05	0.08
G	1.03	0.02	1.13	0.01	3.01	3.02	0.01	0.11	0.02	3.22
A	0.08	0.00	1.45	0.01	1.05	4.21	0.01	1.52	0.03	3.85
C	0.22	0.02	1.06	0.02	0.62	0.05	0.12	3.11	0.22	0.04
S	0.07	0.02	1.20	0.02	1.03	1.03	0.01	1.03	0.02	5.16
T	0.02	0.00	1.03	0.02	0.16	0.99	0.01	0.33	0.21	1.60
V	0.04	0.03	2.24	0.02	0.06	5.08	0.01	0.03	0.33	1.15
L	0.18	0.07	0.94	0.04	0.29	0.02	0.07	0.30	0.29	0.04
I	0.03	0.15	1.97	0.02	0.14	0.25	0.02	0.27	0.33	0.09
M	0.11	0.02	0.87	0.04	1.04	0.02	0.02	1.31	1.03	0.07
K	0.08	0.00	0.81	0.00	1.34	0.10	0.00	0.67	0.16	0.11
R	0.10	0.03	0.73	0.00	1.91	0.02	0.06	1.45	0.14	0.06
H	0.18	0.00	0.54	0.00	0.79	0.06	1.03	0.00	0.04	0.46
F	0.06	1.03	0.64	1.03	0.17	0.06	0.02	0.02	0.03	0.01
Y	0.08	0.41	0.53	0.47	0.23	0.03	0.16	0.00	0.02	0.03
W	0.10	0.09	0.44	0.02	0.20	0.07	0.03	0.04	0.04	0.04
N	0.25	0.02	0.62	0.02	2.03	0.00	0.22	0.18	0.00	1.03
D	0.07	0.00	1.16	0.01	1.82	0.01	0.03	0.04	0.03	1.20
E	0.18	0.00	1.86	0.02	0.98	1.14	0.02	0.10	0.03	0.16
Q	0.15	0.00	0.85	0.00	1.06	0.74	0.19	0.28	0.02	0.22

FIG. 3

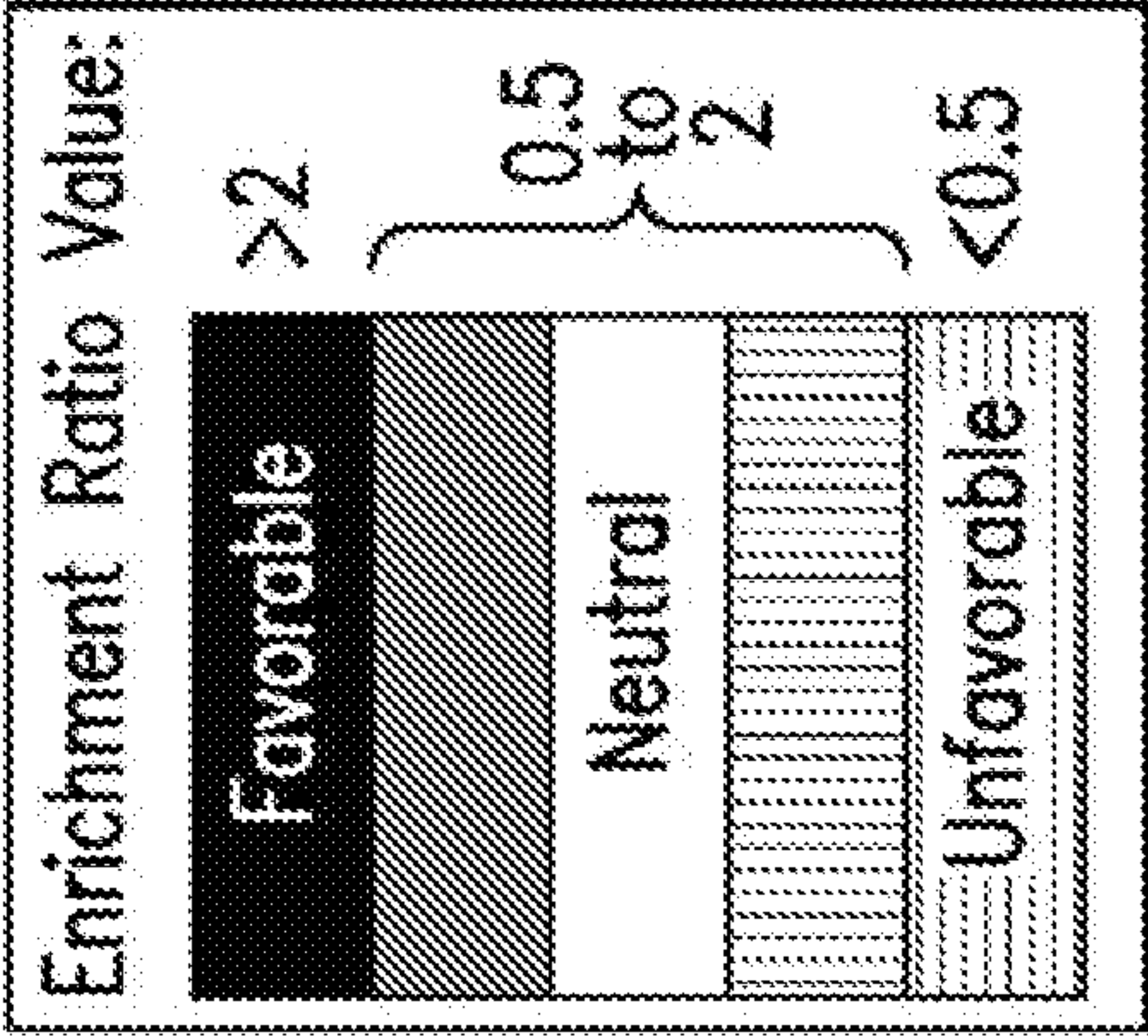
13F3 I107T Anti-NKG2A Antibody Mutational Scan -
CDR Positions Analyzed

Light Chain	
LCDR1	24 R 25 A 26 S 27 Q 28 G 29 I 30 N 31 S 32 A 33 L 34 A
LCDR2	None
LCDR3	89 Q 90 Q 91 F 92 N 93 S 94 Y 95 P 96 L 97 T
Heavy Chain	
HCDR1*	26 G 27 F 28 T 29 F 30 S 31 S 32 H 33 S 34 M 35 N
HCDR2	50 A 51 I 52 S 53 S 54 S 55 S 56 Y 57 I 58 Y 59 Y 60 A 61 D 62 S 63 V 64 K 65 G
HCDR3	95 E 96 E 97 W 98 G 99 L 100 P 100a F 101 D

*Kabat definition was used for all CDRs except HCDR1, where the AbM definition was used

FIG.4

13F3 I107T Antibody – LCDR1 Substitutions



Germline	R	A	S	Q	G	I	S	N	S	A	L	A
Parental	R	A	S	Q	G	I	S	N	S	A	L	A
Normalized Enrichment Ratio												
*	0.26	0.00	0.00	0.90	0.33	0.00	0.10	0.09	0.00	0.00	0.00	0.11
P	0.43	1.72	1.37	0.70	1.26	1.88	2.22	2.30	0.12	0.03	0.08	0.18
G	0.89	1.10	0.93	2.02	1.00	1.84	0.65	4.66	0.82	0.40	0.18	1.00
A	0.99	1.00	1.33	1.46	1.04	0.80	0.78	1.20	1.00	0.54	1.00	0.09
C	1.23	2.69	1.02	1.26	1.13	3.43	1.23	2.83	1.53	0.59	0.09	0.11
S	1.38	0.95	1.00	1.20	0.90	1.29	0.80	1.00	0.65	0.40	0.11	0.51
T	1.14	2.61	1.23	1.15	1.22	1.99	0.77	0.62	1.42	0.82	0.51	0.68
V	0.84	2.12	1.00	0.97	1.38	0.94	0.53	0.49	4.72	1.13	0.68	0.01
L	0.86	1.92	0.98	0.92	2.16	0.87	0.62	0.81	1.59	1.00	0.01	0.02
I	0.61	1.70	0.77	0.92	1.18	1.00	0.54	0.67	5.26	1.08	0.02	0.02
M	0.97	2.45	0.95	1.20	1.08	1.49	0.65	1.44	1.04	0.45	0.02	0.04
K	1.12	0.31	1.20	0.71	1.07	1.36	0.59	0.18	0.02	0.04	0.04	0.02
R	1.00	0.18	1.08	0.65	0.86	0.98	0.39	0.28	0.03	0.03	0.02	0.37
H	0.94	0.43	0.99	1.06	1.04	2.09	0.73	0.76	0.54	0.08	0.02	0.02
F	0.94	0.86	1.08	0.98	1.23	2.97	0.62	1.00	2.45	0.25	0.05	0.05
Y	1.23	0.65	1.03	0.99	1.12	1.57	0.55	1.08	2.12	0.07	0.05	0.05
W	0.92	0.43	0.78	0.83	0.84	0.96	0.55	0.86	1.91	0.03	0.05	0.02
N	0.99	0.69	1.16	1.36	0.62	2.04	1.00	1.99	1.10	0.16	0.02	0.08
D	0.64	0.44	1.02	1.82	1.28	3.41	1.45	4.49	2.74	0.09	0.08	2.66
E	0.81	0.81	1.32	1.48	1.75	2.67	1.45	3.06	5.98	0.10	0.01	0.01
Q	0.93	1.50	1.47	1.00	1.44	1.52	0.88	1.04	0.20	0.10	0.01	0.01

Preferred
(favorable)
substitution
of N30P was
selected

FIG. 5A

13F3 I107T Antibody – LCDR3 Substitutions

Germline	Q	Q	F	N	N	Y	P	L	T
Parental	Q	Q	F	N	S	Y	P	L	T
Normalized Enrichment Ratio									
	89	90	91	92	93	94	95	96	97
*	0.00	0.81	0.00	0.09	0.13	0.38	0.00	0.00	0.00
P	0.07	0.17	0.02	1.58	0.20	0.27	1.00	0.06	0.04
G	0.02	0.37	0.21	0.47	0.60	0.08	1.11	0.06	0.71
A	0.02	0.56	0.68	0.63	1.25	0.11	0.76	0.05	0.71
C	0.01	0.14	2.01	1.76	1.80	0.21	0.15	0.59	0.70
S	0.02	0.86	0.26	0.56	1.00	0.10	0.64	0.04	1.01
T	0.02	0.73	0.62	0.49	1.52	0.11	0.49	0.09	1.00
V	0.03	0.30	0.28	0.37	2.39	0.27	0.19	0.10	0.74
L	0.02	0.46	0.65	0.35	1.38	0.34	0.18	1.00	0.49
I	0.07	0.15	0.19	0.52	1.65	0.36	0.17	0.26	0.55
M	0.02	0.14	3.26	0.40	1.18	0.73	0.56	0.30	0.85
K	0.06	0.94	0.11	0.30	0.58	0.08	0.31	0.03	0.60
R	0.03	0.17	0.05	0.23	0.59	0.11	0.16	0.02	0.41
H	0.36	0.33	2.04	0.99	1.06	0.74	0.28	0.12	0.62
F	0.02	0.09	1.00	0.95	1.51	0.95	0.11	1.66	0.55
Y	0.02	0.16	0.10	0.90	1.63	1.00	0.07	0.11	0.61
W	0.03	0.11	2.53	1.08	1.50	0.51	0.10	0.76	0.55
N	0.02	1.75	2.14	1.00	0.99	0.15	0.31	0.19	0.98
D	0.03	11.50	0.32	1.85	2.36	0.05	1.69	0.04	1.67
E	0.39	1.15	0.36	1.99	2.95	0.05	1.04	0.02	0.90
Q	1.00	1.00	0.42	0.62	1.53	0.21	0.61	0.12	0.83

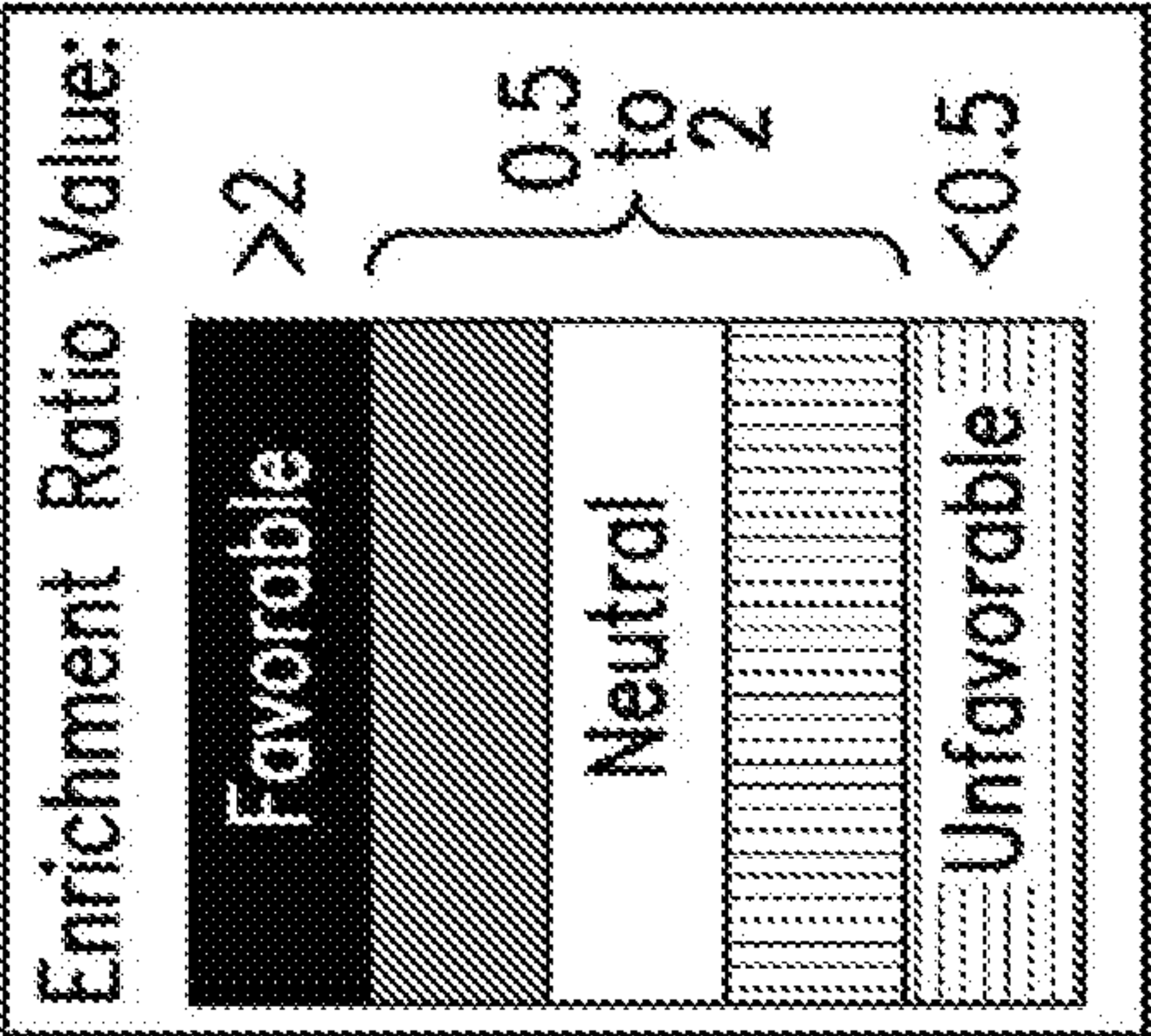


FIG.5B

13F3 I107T Antibody – HCDR1 Substitutions

Germline	26	27	28	29	30	31	32	33	34	35
Parental	G	F	T	F	S	S	H	S	M	N
Normalized Enrichment Ratio										
*	0.00	0.00	0.00	0.00	0.00	0.29	0.00	0.00	0.00	0.07
P	0.00	0.00	0.26	0.00	0.77	0.03	0.18	0.00	0.05	0.08
G	1.03	0.02	1.13	0.01	3.01	3.02	0.01	0.11	0.02	3.22
A	0.08	0.00	1.45	0.01	1.05	4.21	0.01	1.52	0.03	3.85
C	0.22	0.02	1.06	0.02	0.62	0.05	0.12	3.11	0.22	0.04
S	0.07	0.02	1.20	0.02	1.03	1.03	0.01	1.03	0.02	5.16
T	0.02	0.00	1.03	0.02	0.16	0.99	0.01	0.33	0.21	1.60
V	0.04	0.03	2.24	0.02	0.06	5.08	0.01	0.03	0.33	1.15
L	0.18	0.07	0.94	0.04	0.29	0.02	0.07	0.30	0.29	0.04
I	0.03	0.15	1.97	0.02	0.14	0.25	0.02	0.27	0.33	0.09
M	0.11	0.02	0.87	0.04	1.04	0.02	0.02	1.31	1.03	0.07
K	0.08	0.00	0.81	0.00	1.34	0.10	0.00	0.67	0.16	0.11
R	0.10	0.03	0.73	0.00	1.91	0.02	0.06	1.45	0.14	0.06
H	0.18	0.00	0.54	0.00	0.79	0.06	1.03	0.00	0.04	0.46
F	0.06	1.03	0.64	1.03	0.17	0.06	0.02	0.02	0.03	0.01
Y	0.08	0.41	0.53	0.47	0.23	0.03	0.16	0.00	0.02	0.03
W	0.10	0.09	0.44	0.02	0.20	0.07	0.03	0.04	0.04	0.04
N	0.25	0.02	0.62	0.02	2.03	0.00	0.22	0.18	0.00	1.03
D	0.07	0.00	1.16	0.01	1.82	0.01	0.03	0.04	0.03	1.20
E	0.18	0.00	1.86	0.02	0.98	1.14	0.02	0.10	0.03	0.16
Q	0.15	0.00	0.85	0.00	1.06	0.74	0.19	0.28	0.02	0.22

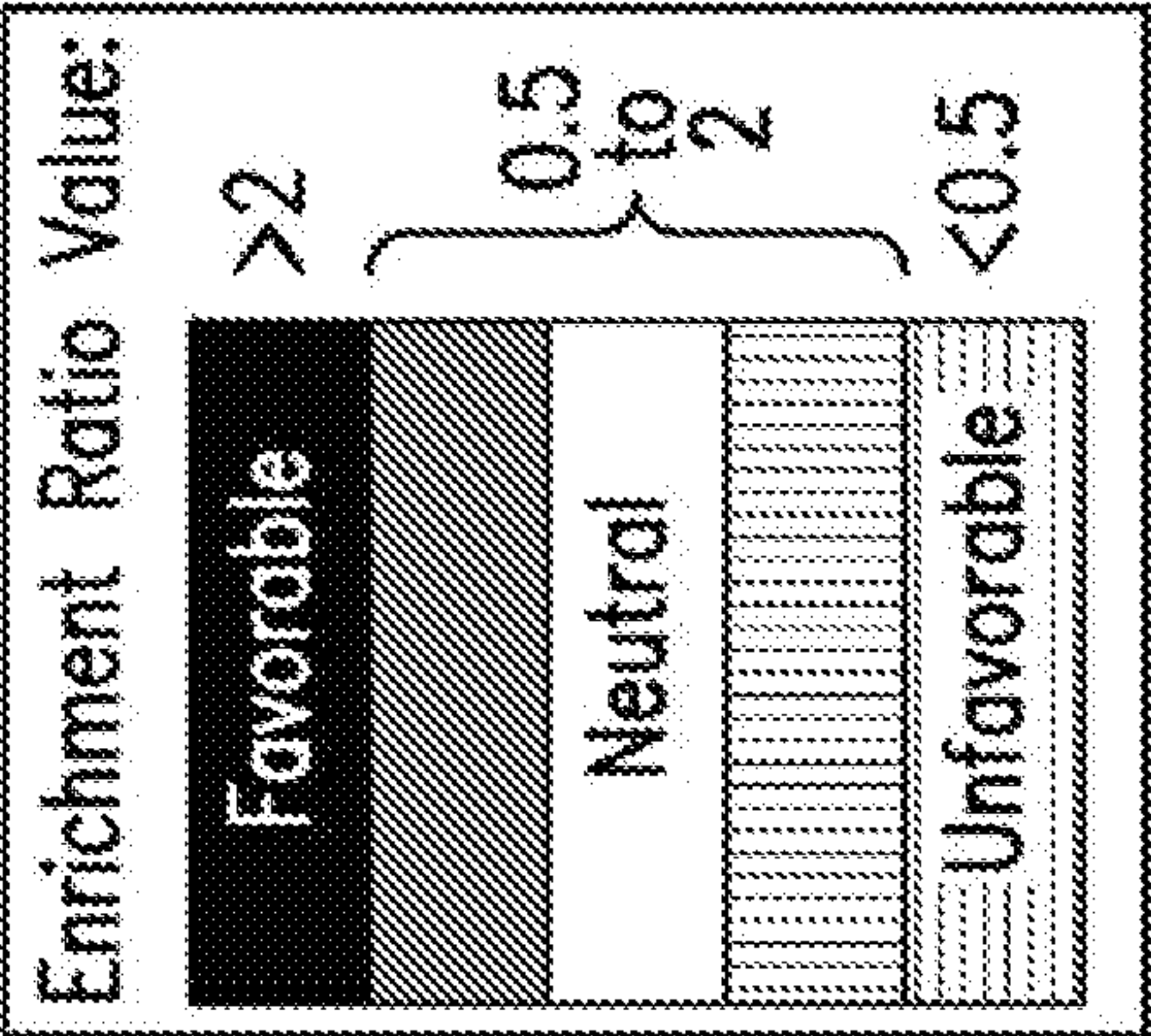


FIG.5C

Enrichment Ratio Value:

Favorable

Neutral

Unfavorable

>2

0.5 to 2

<0.5

FIG. 5D

13F3 I107T Antibody – HCDR3 Substitutions

Germline	E	E	W	G	L	P	F	D
Parental	E	E	W	G	L	P	F	D
Normalized Enrichment Ratio								
	95	96	97	98	99	100	100a	101
*	0.00	0.70	0.28	0.00	0.00	0.00	0.00	0.00
P	0.03	0.01	0.00	0.01	0.02	1.36	0.00	0.03
G	0.01	0.27	0.05	1.36	0.03	0.01	0.02	0.04
A	0.03	0.03	0.01	0.03	0.18	0.02	0.01	0.02
C	0.04	0.05	0.13	0.30	0.17	0.02	0.47	0.03
S	0.02	0.03	0.01	0.02	0.50	0.01	0.15	0.02
T	0.04	0.02	0.00	0.02	0.03	0.04	0.03	0.03
V	0.04	0.09	0.01	0.07	0.02	0.02	0.16	0.03
L	0.06	0.03	0.14	0.04	1.36	0.04	0.37	0.02
I	0.04	0.02	0.02	0.04	0.02	0.03	0.13	0.01
M	0.03	0.93	0.02	0.03	0.11	0.01	0.09	0.02
K	0.14	0.10	0.02	0.02	0.02	0.00	0.03	0.03
R	0.02	0.01	0.07	0.04	0.02	0.01	0.02	0.03
H	0.03	0.03	0.02	0.02	1.19	0.02	0.02	0.03
F	0.03	0.06	0.02	0.04	0.21	0.01	1.36	0.03
Y	0.05	0.03	0.02	0.03	0.11	0.01	0.33	0.02
W	0.05	0.05	1.36	0.14	0.05	0.03	0.04	0.04
N	0.01	0.03	0.00	0.02	0.15	0.03	0.05	0.04
D	0.14	0.28	0.01	0.02	0.05	0.02	0.00	1.36
E	1.36	1.36	0.01	0.06	0.01	0.02	0.01	0.04
Q	0.01	0.03	0.00	0.01	0.14	0.00	0.00	0.03

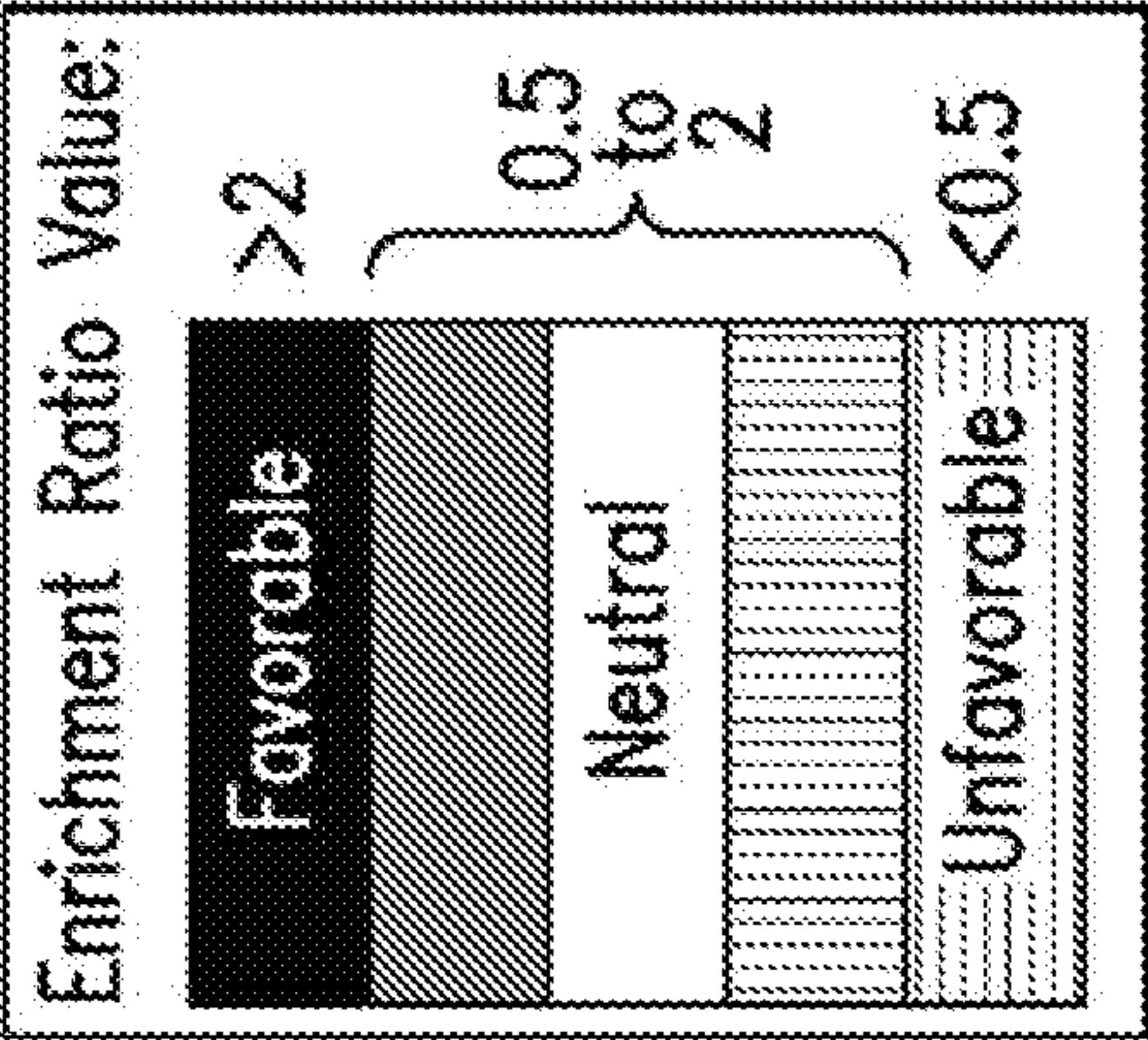


FIG. 5E

Alignment of Full Length Human NKG2C and Human NKG2C Amino Acid Sequences

hNKG2C	MSKQ	R	G	T	E	V	S	L	A	Q	D	F	K	R	Q	Q	R	K	P	K	G	N	K	S	I	S	G	T	E	Q	E	I	F	Q	V	E	L	N	L	Q	N	P	S	L	50				
hNKG2A	MDNQ	G	V	I	Y	S	D	L	N	L	P	P	N	F	K	R	Q	Q	R	K	P	K	G	N	K	S	I	L	A	T	E	Q	E	I	T	Y	A	E	L	N	L	Q	K	A	S	Q	50		
hNKG2C	NHQI	D	K	I	Y	D	C	Q	C	I	L	P	P	P	E	K	L	T	A	E	V	L	G	I	I	C	I	V	L	M	A	T	V	L	K	T	I	V	L	I	P	E	E	Q	-	100			
hNKG2A	DFOG	N	D	K	T	Y	H	C	K	D	L	P	S	A	P	E	K	L	I	V	G	I	L	G	I	I	C	L	I	L	M	A	S	V	T	I	V	I	P	S	T	L	I	Q	R	100			
hNKG2C	-NNSS	P	N	T	R	T	Q	K	A	R	H	C	G	H	C	P	E	E	N	I	T	Y	S	N	S	C	Y	Y	I	G	K	E	R	R	T	W	E	E	S	L	L	A	C	T	S	K	150		
hNKG2A	HNSS	L	N	T	R	T	Q	K	A	R	H	C	G	H	C	P	E	E	N	I	T	Y	S	N	S	C	Y	Y	I	G	K	E	R	R	T	W	E	E	S	L	L	A	C	T	S	K	150		
hNKG2C	NSSLL	S	I	D	N	E	E	E	M	K	F	L	A	S	I	L	P	S	S	W	I	G	V	F	R	N	S	S	H	H	P	N	V	T	I	N	G	L	A	F	K	H	K	I	K	D	200		
hNKG2A	NSSLL	S	I	D	N	E	E	E	M	K	F	L	S	I	L	S	I	L	P	S	S	W	I	G	V	F	R	N	S	S	H	H	P	N	V	T	I	N	G	L	A	F	K	H	E	I	K	D	200
hNKG2C	SDNAE	L	N	C	A	V	L	Q	V	N	R	L	K	S	A	Q	C	G	S	S	I	I	Y	H	C	K	H	L																				233	
hNKG2A	SDNAE	L	N	C	A	V	L	Q	V	N	R	L	K	S	A	Q	C	G	S	S	I	I	Y	H	C	K	H	L																				233	

Conserved (identical) amino acid residues: 177 of 233 (76%)

Similar amino acid residues: 14 of 233 (6%)

Different amino acid residues: 42 of 233 (18%)

FIG.6

Anti-NKG2A Antibody 13F3.A4 Heavy Chain Variable Region

1	E	V	Q	L	V	E	S	G	G	L	V	K	P	G	G	S																																																		
	GAG	GTG	CAG	CTG	GTG	GAG	TCT	GGG	GGA	GGC	CTG	GTC	AAG	CCG	GGG	GGG	TCC																																																	
	<table><tr><td colspan="16">CDR1</td></tr><tr><td>S</td><td>H</td><td>S</td><td>M</td><td colspan="12"></td></tr><tr><td>TCC</td><td>CAT</td><td>AGT</td><td>ATG</td><td colspan="12"></td></tr></table>																CDR1																S	H	S	M													TCC	CAT	AGT	ATG														
CDR1																																																																		
S	H	S	M																																																															
TCC	CAT	AGT	ATG																																																															
52	L	R	L	S	C	A	A	S	G	F	T	F	S																																																					
	CTG	AGA	CTC	TCC	TGT	GCA	GCC	TCT	GGA	TTC	ACC	TTC	AGT																																																					
	<table><tr><td colspan="16">CDR1, cont'd</td></tr><tr><td>N</td><td>W</td><td>V</td><td>R</td><td>Q</td><td>A</td><td>P</td><td>G</td><td>K</td><td>G</td><td>L</td><td>E</td><td>W</td><td>V</td><td>S</td><td>A</td><td>I</td></tr><tr><td>AAC</td><td>TGG</td><td>GTC</td><td>CGC</td><td>CAG</td><td>GCT</td><td>CCA</td><td>GGG</td><td>AAG</td><td>GGG</td><td>CTG</td><td>GAG</td><td>TGG</td><td>GTC</td><td>TCA</td><td>GCC</td><td>ATA</td></tr></table>																CDR1, cont'd																N	W	V	R	Q	A	P	G	K	G	L	E	W	V	S	A	I	AAC	TGG	GTC	CGC	CAG	GCT	CCA	GGG	AAG	GGG	CTG	GAG	TGG	GTC	TCA	GCC	ATA
CDR1, cont'd																																																																		
N	W	V	R	Q	A	P	G	K	G	L	E	W	V	S	A	I																																																		
AAC	TGG	GTC	CGC	CAG	GCT	CCA	GGG	AAG	GGG	CTG	GAG	TGG	GTC	TCA	GCC	ATA																																																		
103	<table><tr><td colspan="16">CDR2, cont'd</td></tr><tr><td>S</td><td>S</td><td>S</td><td>S</td><td>Y</td><td>I</td><td>Y</td><td>Y</td><td>A</td><td>D</td><td>S</td><td>V</td><td>K</td><td>G</td><td>R</td><td>F</td><td></td></tr><tr><td>AGT</td><td>AGT</td><td>AGT</td><td>AGT</td><td>TAC</td><td>ATA</td><td>TAC</td><td>TAC</td><td>GCA</td><td>GAC</td><td>TCA</td><td>GTG</td><td>AAG</td><td>GGC</td><td>CGA</td><td>TTC</td><td></td></tr></table>																CDR2, cont'd																S	S	S	S	Y	I	Y	Y	A	D	S	V	K	G	R	F		AGT	AGT	AGT	AGT	TAC	ATA	TAC	TAC	GCA	GAC	TCA	GTG	AAG	GGC	CGA	TTC	
CDR2, cont'd																																																																		
S	S	S	S	Y	I	Y	Y	A	D	S	V	K	G	R	F																																																			
AGT	AGT	AGT	AGT	TAC	ATA	TAC	TAC	GCA	GAC	TCA	GTG	AAG	GGC	CGA	TTC																																																			
154																																																																		
205	T	I	S	R	D	N	A	K	N	S	L	Y	L	Q	M	N	S																																																	
	ACC	ATC	TCC	AGA	GAC	AAC	GCC	AAG	AAC	TCA	CTG	TAT	CTG	CAA	ATG	AAC	AGC																																																	
	<table><tr><td colspan="16">CDR3</td></tr><tr><td>E</td><td>E</td><td>W</td><td>G</td><td colspan="12"></td></tr><tr><td>GAA</td><td>GAG</td><td>TGG</td><td>GGG</td><td colspan="12"></td></tr></table>																CDR3																E	E	W	G													GAA	GAG	TGG	GGG														
CDR3																																																																		
E	E	W	G																																																															
GAA	GAG	TGG	GGG																																																															
256	L	R	A	E	D	T	A	V	Y	Y	C	A	R																																																					
	CTG	AGA	GCC	GAG	GAC	ACG	GCT	GTG	TAT	TAC	TGT	GCG	AGA																																																					
	<table><tr><td colspan="16">CDR3, cont'd</td></tr><tr><td>L</td><td>P</td><td>F</td><td>D</td><td>Y</td><td>W</td><td>G</td><td>Q</td><td>G</td><td>I</td><td>L</td><td>V</td><td>T</td><td>V</td><td>S</td><td>S</td><td></td></tr><tr><td>CTA</td><td>CCC</td><td>TTT</td><td>GAC</td><td>TAC</td><td>TGG</td><td>GGC</td><td>CAG</td><td>GGA</td><td>ATC</td><td>CTG</td><td>GTC</td><td>ACC</td><td>GTC</td><td>TCC</td><td>TCA</td><td></td></tr></table>																CDR3, cont'd																L	P	F	D	Y	W	G	Q	G	I	L	V	T	V	S	S		CTA	CCC	TTT	GAC	TAC	TGG	GGC	CAG	GGA	ATC	CTG	GTC	ACC	GTC	TCC	TCA	
CDR3, cont'd																																																																		
L	P	F	D	Y	W	G	Q	G	I	L	V	T	V	S	S																																																			
CTA	CCC	TTT	GAC	TAC	TGG	GGC	CAG	GGA	ATC	CTG	GTC	ACC	GTC	TCC	TCA																																																			
307																																																																		

FIG.7A

Anti-NKG2A Antibody 13F3.A4 Light Chain Variable Region

1	A	I	Q	L	T	Q	S	P	S	S	L	S	A	S	V	G	D
	GCC	ATC	CAG	TTG	ACC	CAG	TCT	CCA	TCC	TCC	CTG	TCT	GCA	TCT	GTA	GGA	GAC
	CDR1																
	R	V	T	I	T	C	R	A	S	Q	G	I	N	S	A	L	A
52	AGA	GTC	ACC	ATC	ACT	TGC	CGG	GCA	AGT	CAG	GGC	ATT	AAC	AGT	GCT	TTA	GCC
	CDR2																
	W	Y	Q	Q	K	P	G	K	A	P	K	L	L	I	Y	D	A
103	TGG	TAT	CAG	CAG	AAA	CCA	GGG	AAA	GCT	CCT	AAG	CTC	CTG	ATC	TAT	GAT	GCC
	CDR2, cont'd																
	S	S	L	K	S	G	V	P	S	R	F	S	G	S	G	S	G
154	TCC	AGT	TTG	AAA	AGT	GGG	GTC	CCA	TCA	AGG	TTC	AGC	GGC	AGT	GGA	TCT	GGG
	CDR3																
	T	D	F	T	L	T	I	S	S	L	Q	P	E	D	F	A	T
205	ACA	GAT	TTC	ACT	CTC	ACC	ATC	AGC	AGC	CTG	CAG	CCT	GAA	GAT	TTT	GCA	ACT
	Y	Y	C	Q	Q	F	N	S	Y	P	L	T	F	G	Q	G	T
256	TAT	TAC	TGT	CAA	CAG	TTT	AAT	AGT	TAC	CCT	CTC	ACC	TTC	GGC	CAA	GGG	ACA
	R	L	E	I	K												
307	CGA	CTG	GAG	ATT	AAA												

FIG.7B

Anti-NKG2A Antibody 2G6.C2 Heavy Chain Variable Region

	-1--2--3--4--5--6--7--8--9--10--11--12--13--14--15--16--17-
	E V Q L V E S G G G L V Q R G G S
1	GAG GTG CAA CTG GTG GAG TCT GGG GGA GGC TTG GTA CAG CGG GGG GGG TCC
	-18--19--20--21--22--23--24--25--26--27--28--29--30--31--32--33--34-
	L R L S C A A S G F T F S
52	CTG AGA CTC TCC TGT GCA GCC TCT GGA TTC ACC TTC AGT
	-35--36--37--38--39--40--41--42--43--44--45--46--47--48--49--50--51-
	CDR1, cont'd
	N W I R Q A P G K G L E W V A
103	AAC TGG ATC CGC CAG GCT CCA GGG AAG GGG CTG GAG TGG GTT GCA
	-52-52A--53--54--55--56--57--58--59--60--61--62--63--64--65--66--67-
	CDR2, cont'd
	S S G S S F I Y Y A D S V K G
154	AGT AGT GGT AGC AGT TTC ATA TAC TAC GCA GAC TCT GTG AAG GGC
	-68--69--70--71--72--73--74--75--76--77--78--79--80--81--82-82A-82B-
	T I S R D N A K N S L S L Q M N S
205	ACC ATC TCC AGA GAC AAT GCC AAG AAC TCT CTG TCT CTG CAA ATG AAC AGC
	-82C-83--84--85--86--87--88--89--90--91--92--93--94--95--96--97--98-
	L R D E D T A V Y Y C A R
256	CTG AGA GAC GAA GAC ACG GCT GTG TAT TAC TGT GCG AGA
	-99-100-100A-100B-101-102-103-104-105-106-107-108-109-110-111-112-113-
	CDR3, cont'd
	I D A F N I
307	ATT GAT GCT TTT AAT ATC

FIG.8A

Anti-NKG2A Antibody 2G6.C2 Light Chain Variable Region

```

-1---2---3---4---5---6---7---8---9---10---11---12---13---14---15---16---17-
E   I   V   L   T   Q   S   F   A   T   L   S   L   S   P   G   E
1  GAA ATT GTG TTG ACA CAG TCT CCA GCC ACC CTG TCT TTG TCT CCA GGG GAA

-18---19---20---21---22---23---24---25---26---27---28---29---30---31---32---33---34-
                                     CDR1
R   A   T   L   S   C   R   A   S   Q   S   V   S   S   S   L   A
52 AGA GCC ACC CTC TCC TGC AGG GCC AGT CAG AGT GTT AGC AGC TCC TTA GCC

-35---36---37---38---39---40---41---42---43---44---45---46---47---48---49---50---51-
                                     CDR2
W   Y   Q   Q   K   P   G   Q   A   P   R   L   L   I   Y   D   A
103 TGG TAC CAA CAG AAA CCT GGC CAG GCT CCC AGG CTC CTC ATC TAT GAT GCA

-52---53---54---55---56---57---58---59---60---61---62---63---64---65---66---67---68-
CDR2, cont'd
S   N   R   A   T   G   I   P   A   R   F   S   G   S   G   S   G
154 TCC AAC AGG GCC ACT GGC ATC CCA GCC AGG TTC AGT GGC AGT GGG TCT GGG

-69---70---71---72---73---74---75---76---77---78---79---80---81---82---83---84---85-
T   D   F   T   L   T   I   S   S   L   E   P   E   D   F   A   V
205 ACA GAC TTC ACT CTC ACC ATC AGC AGC CTA GAG CCT GAA GAT TTT GCA GTT

-86---87---88---89---90---91---92---93---94---95---96---97---98---99-100-101-102-
                                     CDR3
Y   Y   C   Q   Q   R   S   N   W   I   F   T   F   G   P   G   T
256 TAT TAC TGT CAG CAG CGT AGC AAC TGG ATA TTC ACT TTC GGC CCT GGG ACC

103-104-105-106-107-

K   V   D   I   K
307 AAA GTG GAT ATC AAA

```

FIG.8B

Anti-NKG2A Antibody 11H9.A1 Heavy Chain Variable Region

1	E	V	Q	L	V	E	S	G	G	L	V	K	P	G	G	S
	GAG	GTG	CAG	TTG	GTG	GAG	TCT	GGG	GGA	GGC	CTG	GTC	AAG	CCT	GGG	TCC
	CDR1															
	L	R	L	S	C	A	A	S	G	F	T	F	S	S	Y	S
52	CTG	AGA	CTC	TCC	TGT	GCA	GCC	TCT	GGA	TTC	ACC	TTC	AGT	AGC	TAT	AGC
	CDR1, cont'd															
	N	W	V	R	Q	A	P	G	K	G	L	E	W	V	S	I
103	AAC	TGG	GTC	CGC	CAG	GCT	CCA	GGG	AAG	GGG	CTG	GAG	TGG	GTC	TCA	TCC
	CDR2, cont'd															
	S	S	S	S	Y	I	Y	Y	A	D	S	V	K	G	R	F
154	AGT	AGT	AGT	AGT	TAC	ATA	TAC	TAC	GCA	GAC	TCA	GTG	AAG	GGC	CGA	TTC
	CDR3															
205	T	I	S	R	D	N	A	K	N	S	L	Y	L	Q	M	N
	ACC	ATC	TCC	AGA	GAC	AAC	GCC	AAG	AAC	TCA	CTG	TAT	CTG	CAA	ATG	AAC
	CDR3, cont'd															
256	L	R	A	E	D	T	A	V	Y	Y	C	A	R	L	L	N
	CTG	AGA	GCC	GAG	GAC	ACG	GCT	GTG	TAT	TAC	TGT	GCG	AGA	CTA	CTA	TGG
	CDR3, cont'd															
307	G	E	I	F	D	Y	W	G	Q	G	T	L	V	T	V	S
	GGG	GAG	ATT	TTT	GAC	TAC	TGG	GGC	CAG	GGA	ACC	CTG	GTC	ACC	GTC	TCC

FIG.9A

Anti-NKG2A Antibody 11H9.A1 Light Chain Variable Region

1	A	I	Q	L	T	Q	S	P	S	S	L	S	A	S	V	G	D
	GCC	ATC	CAG	TTG	ACC	CAG	TCT	CCA	TCC	TCC	CTG	TCT	GCA	TCT	GTA	GGA	GAC
	CDR1																
	R	V	T	I	T	C	R	A	S	Q	G	I	S	S	A	L	A
52	AGA	GTC	ACC	ATC	ACT	TGC	CGG	GCA	AGT	CAG	GGC	ATT	AGC	AGT	GCT	TTA	GCC
	CDR2																
	W	Y	Q	Q	K	P	G	K	A	P	K	L	L	I	Y	D	A
103	TGG	TAT	CAG	CAG	AAA	CCA	GGG	AAA	GCT	CCT	AAG	CTC	CTG	ATC	TAT	GAT	GCC
	CDR2, cont'd																
	S	S	L	K	S	G	V	P	S	R	F	S	G	S	G	S	G
154	TCC	AGT	TTG	AAA	AGT	GGG	GTC	CCA	TCA	AGG	TTC	AGC	GGC	AGT	GGA	TCT	GGG
	CDR3																
	Y	Y	C	Q	Q	F	N	S	Y	P	I	T	F	G	Q	G	T
205	ACA	GAT	TTC	ACT	CTC	ACC	ATC	AGC	AGC	CTG	CAG	CCT	GAA	GAT	TTT	GCA	ACT
	CDR3																
256	TAT	TAC	TGT	CAA	CAG	TTT	AAT	AGT	TAC	CCG	ATC	ACC	TTC	GGC	CAA	GGG	ACA
	CDR3																
	R	L	E	I	K												
307	CGA	CTG	GAG	ATT	AAA												

FIG.9B

Anti-NKG2A Antibody 4G5.D1 Heavy Chain Variable Region

1	Q	M	Q	L	Q	E	S	G	P	G	L	V	K	P	S	E	T
	CAG	ATG	CAG	CTG	GAG	GAG	TCG	GGC	CCA	GGA	CTG	GTG	AAG	CCT	TCG	GAG	ACC
	CDR1																
	L	S	L	T	C	T	V	S	G	G	S	V	S	S	G	R	Y
52	CTG	TCC	CTC	ACC	TGC	ACT	GTC	TCT	GGT	GGC	TCC	GTC	AGC	AGT	GGT	CGT	TAC
	CDR1, cont'd																
	Y	W	S														
103	TAC	TGG	AGT	TGG	ATC	CGG	CAG	CCC	CCC	GGG	AAG	GGA	CTG	GAG	TGG	ATT	GGG
	CDR2																
	Y	I	Y	Y	S	G	S	T	N	Y	N	P	S	L	K	S	R
154	TAT	ATC	TAT	TAC	AGT	GGG	AGC	ACC	AAC	TAC	AAC	CCC	TCC	CTC	AAG	AGT	CGA
	CDR3																
	V	T	I	S	V	D	T	S	K	N	Q	F	S	L	K	L	T
205	GTC	ACC	ATA	TCA	GTA	GAC	ACG	TCC	AAG	AAC	CAG	TTC	TCC	CTG	AAG	CTG	ACC
	S	V	T	A	A	D	T	A	V	Y	Y	C	A	R	E	G	G
256	TCT	GTG	ACC	GCT	GCG	GAC	ACG	GCC	GTG	TAT	TAC	TGT	GCG	AGA	GAG	GGT	GGA
	CDR3, cont'd																
	D	Y	Y	Y	Y	N	M	D	V	W	G	P	G	T	T	V	T
307	GAC	TAC	TAC	TAC	TAC	AAT	ATG	GAC	GTC	TGG	GGC	CCA	GGG	ACC	ACG	GTC	ACC
	V	S	S														
358	GTC	TCC	TCA														

FIC 10A

FIG.10A

Anti-NKG2A Antibody 4G5.D1 Light Chain Variable Region

1	E	I	V	L	T	Q	S	P	G	T	L	S	L	S	P	G	E						
	GAA	ATT	GTG	TTG	ACG	CAG	TCT	CCA	GGC	ACC	CTG	TCT	TTG	TCT	CCA	GGG	GAA						
52	R	A	T	L	S	C	CDR1																
	AGA	GCC	ACC	CTC	TCC	TGC	R	A	S	Q	S	V	S	S	S	Y	L						
							AGG GCC AGT CAG AGT GTT AGC AGC AGC TAC TTA																
103	CDR1, cont'd						A	W	Y	Q	Q	K	P	G	Q	A	P	R	L	L	I	Y	G
	GCC	TGG	TAC	CAG	CAG	AAA	CCT	GGC	CAG	GCT	CCC	AGG	CTC	CTC	ATC	TAT	GGT	CDR2					
154	CDR2, cont'd						A	S	S	R	A	T	G	I	P	D	R	F	S	G	S	G	S
	GCA	TCC	AGC	AGG	GCC	ACT	GGC	ATC	CCA	GAC	AGG	TTC	AGT	GGC	AGT	GGG	TCT						
205	G	T	D	F	T	L	T	I	S	R	L	E	P	E	D	F	A						
	GGG	ACA	GAC	TTC	ACT	CTC	ACC	ATC	AGC	AGA	CTG	GAG	CCT	GAA	GAT	TTT	GCA						
256	V	Y	Y	C	Q	Q	Y	G	S	S	P	Y	T	F	G	Q	G	CDR3					
	GTG	TAT	TAC	TGT	CAG	CAG	TAT	GGT	AGC	TCA	CCG	TAC	ACT	TTT	GGC	CAG	GGG						
307	T	K	L	E	I	K																	
	ACC	AAG	CTG	GAC	ATC	AAA																	

FIG.10B

Anti-NKG2A Antibody 1G5.B2 Heavy Chain Variable Region

1	Q	V	Q	L	V	E	S	G	G	V	V	Q	P	G	R	S	
	CAG	GTG	CAG	CTG	GTG	GAG	TCT	GGG	GGA	GGC	GTG	GTC	CAG	CCT	GGG	AGG	TCC
	CDR1																
	L	R	L	S	C	A	A	S	G	F	T	F	S	D	Y	A	M
52	CTG	AGA	CTC	TCC	TGT	GCA	GCC	TCT	GGA	TTC	ACC	TTC	AGT	GAC TAT GCT ATG			
	CDR1, cont'd												CDR2				
	H	W	V	R	Q	T	P	G	R	G	L	E	W	L	T	F	I
103	CAC	TGG	GTC	CGC	CAG	ACT	CCA	GGC	AGG	GGG	CTG	CAG	TGG	CTG	ACA	TTT ATA	
	CDR2, cont'd																
	S	Y	D	G	S	N	K	Y	H	A	D	S	V	K	G	R	F
154	TCA	TAT	GAT	GGA	AGC	AAT	AAA	TAC	CAC	GCA	GAC	TCC	GTG	AAG	GGC	CGA	TTC
205	T	I	S	R	D	N	S	K	N	T	L	F	L	Q	M	N	S
	ACC	ATC	TCC	AGA	GAC	AAT	TCC	AAG	AAC	ACG	CTG	TTT	CTG	CAA	ATG	AAC	AGT
	CDR3																
	L	R	A	E	D	T	A	V	Y	C	A	R	D	S	W	D	
256	CTG	AGA	GCT	GAG	GAC	ACG	GCT	GTT	TAT	TAC	TGT	GCG	AGA	GAT TCC TGG GAT			
	CDR3, cont'd																
	R	G	Y	F	D	L	W	G	R	G	T	L	V	T	V	S	S
307	CGG	GGG	TAC	TTC	GAT	CTC	TGG	GGC	CGT	GGC	ACC	CTG	GTC	ACT	GTC	TCC	TCA

FIG.11A

Anti-NKG2A Antibody 1G5.B2 Light Chain Variable Region

1	E	I	V	L	T	Q	S	P	A	T	L	S	P	G	E
	GAA	ATT	GTG	TTG	ACA	CAG	TCT	CCA	GCC	ACC	CTG	TCT	TTG	TCT	CCA
	GGG	GAA													
52	R	A	T	L	S	C									
	AGA	GCC	ACC	CTC	TCC	TGC									
	CDR1														
	R	A	S	Q	S	V	S	S	Y	L	A				
	AGG	GCC	AGT	CAG	AGT	GTT	AGC	AGC	TAC	TTA	GCC				
103	W	Y	Q	Q	K	P	G	Q	A	P	R	L	I	Y	
	TGG	TAC	CAA	CAG	AAA	CCT	GGC	CAG	GCT	CCC	AGG	CTC	ATC	TAT	
	CDR2, cont'd														
	S	N	R	A	T										
	TCC	AAC	AGG	GCC	ACT										
154	GGC	ATC	CCA	GCC	AGG	TTC	AGT	GGC	AGT	GGG	TCT	GGG			
	CDR2														
205	T	D	F	T	L	T	I	S	S	L	E	P	E	D	F
	ACA	GAC	TTC	ACT	CTC	ACC	ATC	AGC	AGC	CTA	GAG	CCT	GAA	GAT	TTT
	GCA	GTT													
	CDR3														
	Y	Y	C	Q	Q	R	S	N	W	W	T	F	G	Q	G
	TAT	TAC	TGT	CAG	CAG	CGT	AGC	AAC	TGG	TGG	ACG	TTC	GGC	CAA	GGG
256															
307	V	E	I	K											
	GTC	GAA	ATC	AAA											

FIG.11B

Anti-NKG2A Antibody 13F3.A4 - Sequence Liabilities Assessed

V-SEGMENT	FAMILY	LOCUS	RF	TGL	VBASEENTRY	V-SEGMENT	FAMILY	LOCUS	TGL	VBASEENTRY
D-SEGMENT	VH3	3-21		Y10	TGL-Y10		VK1	L18		Va''+
J-SEGMENT	UNDETERMINED									
J-SEGMENT	JH4	4			JH4b	J-SEGMENT	JK5	5		JK5
INPUT	13F3.A4-VH1					INPUT	13F3.A4-VK1			
3-21	E V Q L V E S G G G L V K P G G S L R L S C A	L18	A I Q L T Q S P S S L S A S V G D R V T I T C			INPUT				
INPUT										
3-21	A S G F T F S S S Y S (M) N W V R Q A P G K G L E	L18	R A S Q G I S S A L A W Y Q Q K P G K A P K L			INPUT				
INPUT										
3-21	W V S S I S S S S S Y I Y Y A D S V K G R F T	L18	L I Y D A S S L E S G V P S R F S G S G T			INPUT				
INPUT										
3-21	I S R D N A K N S L Y L Q M N S L R A E D T A	L18	D F T L T I S S L Q P E D F A T Y Y C Q Q F N			INPUT				
INPUT										
3-21	V Y Y C A R		N Y			L18				
JH4						JK5				
INPUT						INPUT				
JH4										
INPUT										

VK-N30S mutation to decrease deamidation

VH-I107T framework mutation

M34 potential risk of oxidation: de-risked

NKG2A.9 Antibody Amino Acid Sequence

Light Chain Sequence	
CDR1	CDR2
AIQLTQSPSSLASVGDRTITCRASQGISSALAWYQQKPGKAPKLLIYDASSLKSGVPSRFSGSGSGDTFTLTISLQPEDFATYYCQQFN SYPLTF FGQGT RL EIK	CDR3
RTVAAPSVFIFPPSDEQLKSGTASVVCCLNNFYPREAKVQWVKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC	CL

Heavy Chain Sequence	
CDR1	CDR2
EVQLVESGGGLVPGGSLRLSCAASGETFSSHSMNWVRQAPGKGLEWVSAISSSSSYIYADSVKGRFTISRDNAKNSLYIQMNSLRAEDTAVYYCAREEWGLPFDY	CDR3
WGQGGLVTVSS	VH
ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVPSSSLGTQTYICNVNHKPSNTKVDKRVKPSCKDTHTCPPC	CH
PAPEAGGAPSVFLFPPKPKDTLMISRTPEVTCVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQVNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKA	
KGPQPREPQVYITLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTTPPVLDSGDSFFLYSKLTVDKSRWQQGNVFCSCVMHEALHNHYTQKSLSLSPG (K)	

Legend	
Bold underline	CDR regions
<u> </u>	Two mutations made to 13F3 hybridoma VL sequence (N30S) and VH sequence (I107T)
<u>(NST)</u>	N-glycosylation motif
(K)	K was removed from the mature sequence
<i>Bold italics</i>	Three G1.3f mutations (L234A, L235E and G237A) made to g1f Fc region

FIG.13

NKG2A.9 Antibody Amino Acid Sequence

Light Chain

AIQLTQSPSS LSASVGDRVT ITCRASQGIS SALAWYQQKP GKAPKLLIYD ASSLKSGVPS
RFSGSGSGTD FTLTISSLQP EDFATYYCQQ FNSYPLTFGQ GTRLEIKRTV AAPSVFIFPP
SDEQLKSGTA SVVCLLNIFY PREAKVQWKV DNALQSGNSQ ESVTEQDSKD STYSLSTLT
LSKADYEKHK VYACEVTHQG LSSPVTKSFN RGEN

Heavy Chain

EVQLVESGGG LVKPGGSLRL SCAASGFTFS SHSMNWVRQA PGKGLEWVSA ISSSSYIYY
ADSVKGRFTI SRDNAKNSLY LQMNSLRAED TAVYYCAREE WGLPFDYWGQ GTLVTVSSAS
TKGPSVFPLA PSSKSTSGGT AALGCLVKDY FPEPVTVSWN SGALTSGVHT FPAVLQSSGL
YSLSSVVTVP SSSLGTQTYI CNVNHKPSNT KVDKRVEPKS CDKTHTCPPC PAPEAEGAPS
VFLEPPKPKD TLMISRTPEV TCVVVDVSHE DPEVKFNWYV DGVEVHNAKT KPREEQYNST
YRVVSVLTVL HQDWLNGKEY KCKVSNKALP APIEKTISKA KGQPREPQVY TLPPSREEMT
KNQVSLTCLV KGFYPSDIAV EWESNGQPEN NYKTTPPVLD SDGSFFLYSK LTVDKSRWQQ
GNVFSCSVMH EALHNHYTQK SLSLSPG

FIG.14

NKG2A.11 Antibody Amino Acid Sequence

Light Chain

AIQLTQSPSS LSASVGDRVT ITCRASQGIP SALAWYQQKP GKAPKLLIYD ASSLKSGVPS
RFSGSGSGTD FTLTISSLQP EDFATYYCQQ FNSYPLTFGQ GTRLEIKRTV AAPSVFIFPP
SDEQLKSGTA SVVCLLNIFY PREAKVQWKV DNALQSGNSQ ESVTEQDSKD STYSLSTLT
LSKADYEKHK VYACEVTHQG LSSPVTKSFN RGEC

Heavy Chain

EVQLVESGGG LVKPGGSLRL SCAASGFTFS SHSMNWVRQA PGKGLEWVSA ISSSSYIYY
ADSVKGRFTI SRDNAKNSLY LQMNSLRAED TAVYYCAREE WGLPFDYWGQ GTLVTVSSAS
TKGPSVFPLA PSSKSTSGGT AALGCLVKDY FPEPVTVSWN SGALTSGVHT FPAVLQSSGL
YSLSSVVTVP SSSLGTQTYI CNVNHKPSNT KVDKRVEPKS CDKTHTCPPC PAPEAEGAPS
VFLFPPKPKD TLMISRTPEV TCVVVDVSHE DPEVKFNWYV DGVEVHNAKT KPREEQYNST
YRVVSVLTVL HQDWLNGKEY KCKVSNKALP APIEKTISKA KGQPREPQVY TLPPTSREEMT
KNQVSLTCLV KGFYPSDIAV EWESNGQPEN NYKTTPPVLD SDGSFFLYSK LTVDKSRWQQ
GNVFSCSVMH EALHNHYTQK SLSLSPG

FIG.15

Epitope Binning of Antibodies Generated by Single B Cell Cloning Against Control Antibodies

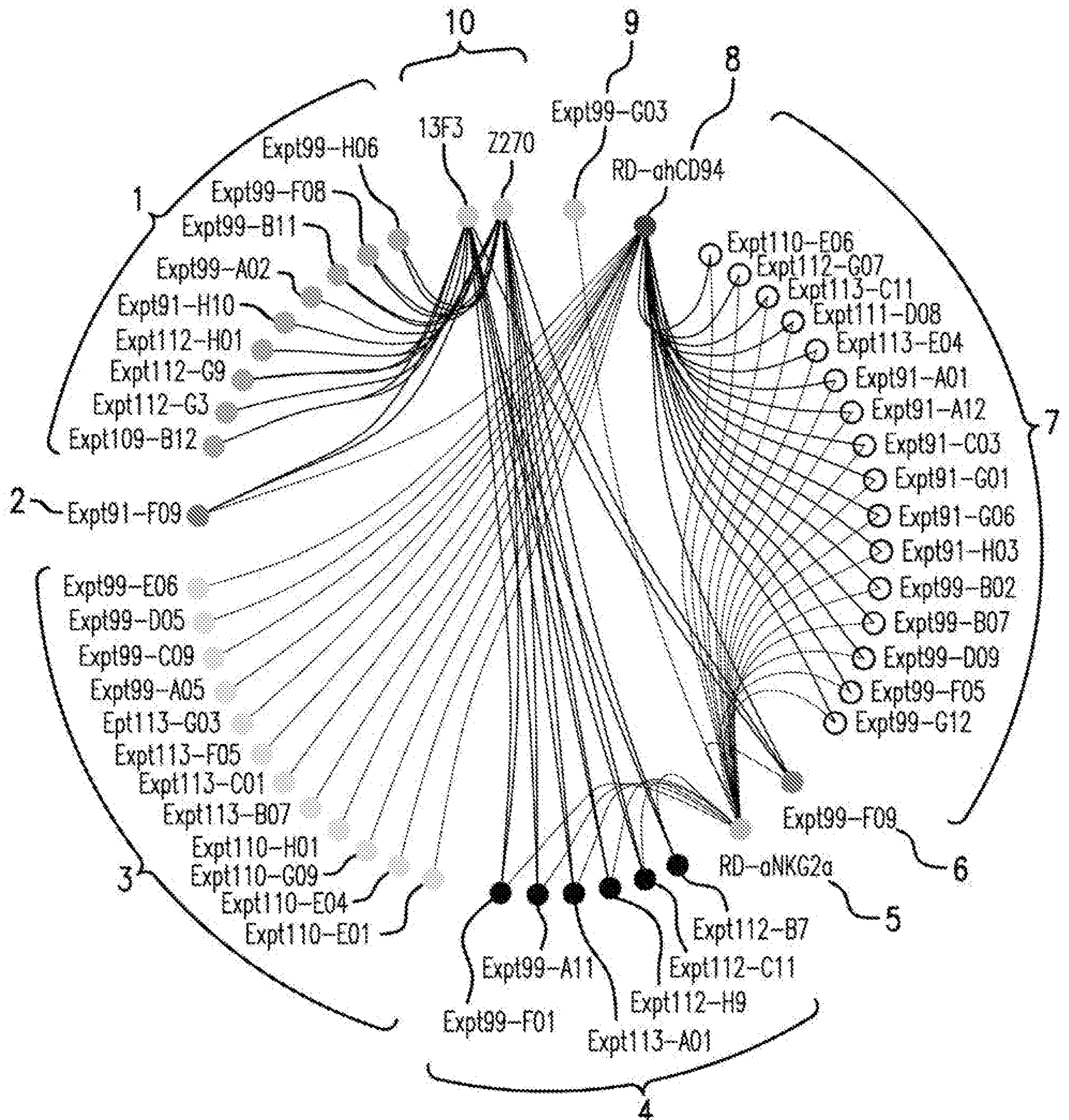


FIG. 16

CHO--Human NKG2A/HLA--E Blocking
By Antibodies Generated Using the Single B Cell Cloning Method

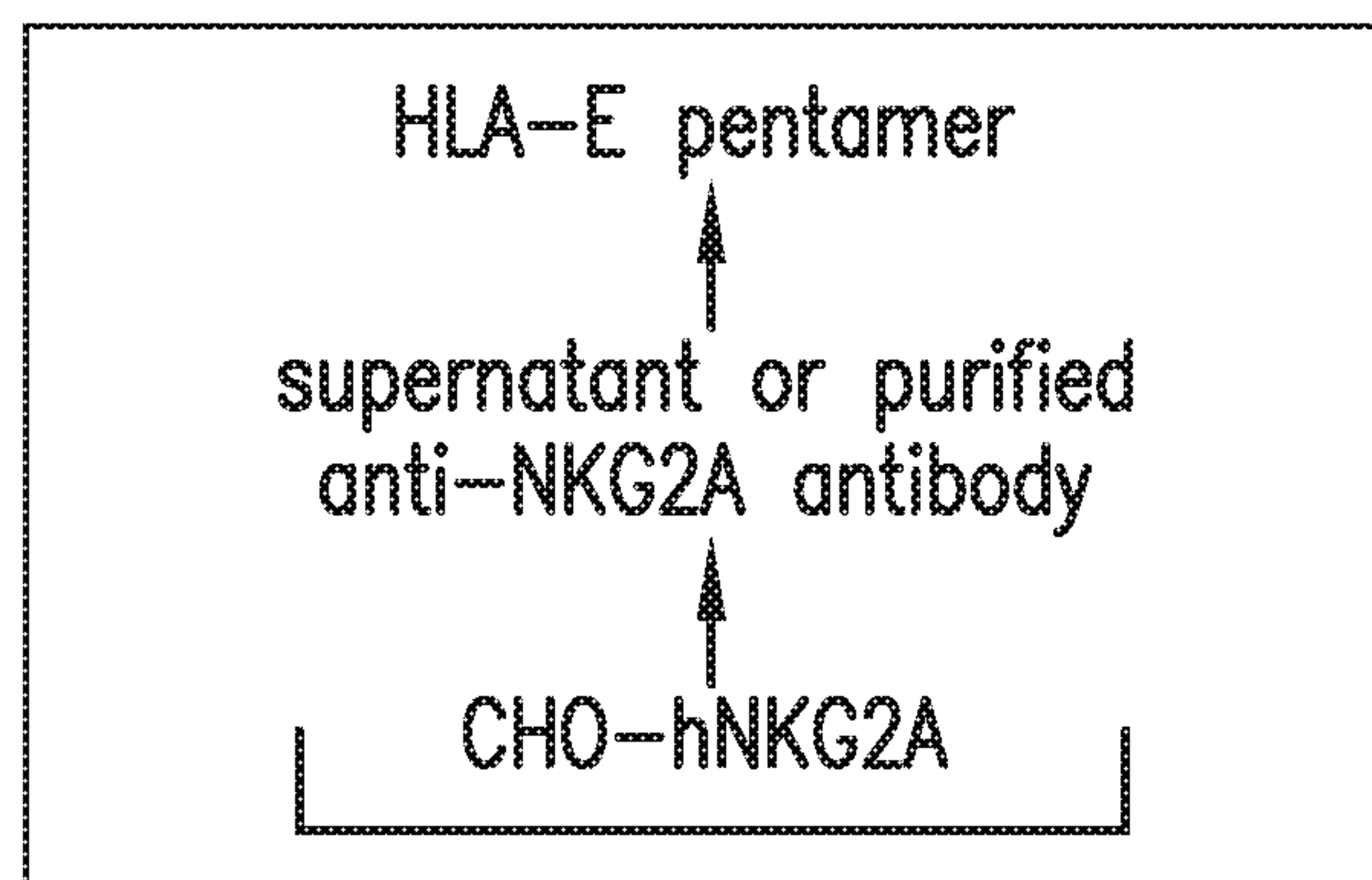


FIG. 17A

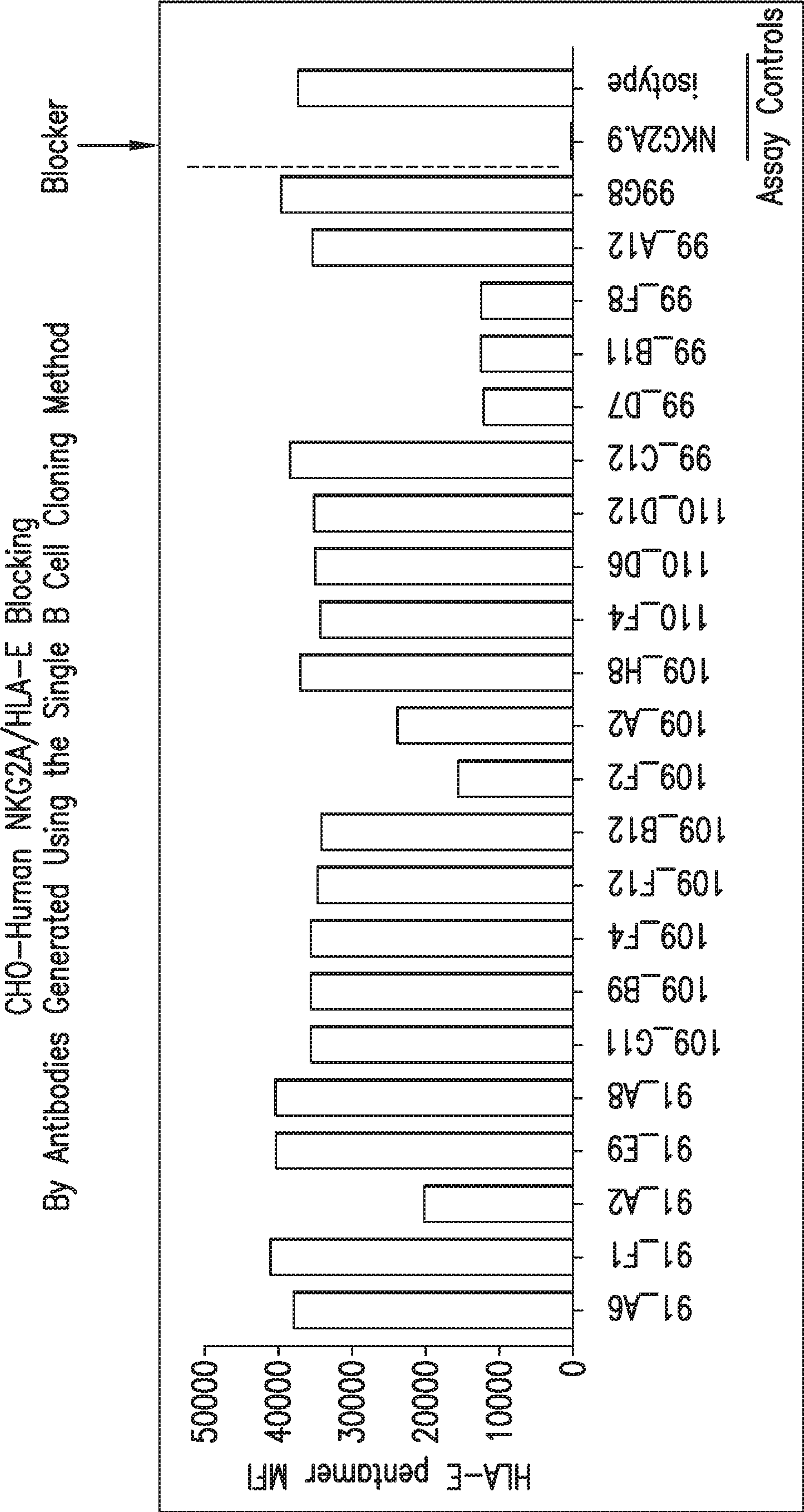


FIG.17B

Anti-NKG2A Antibodies: Binding and Blocking Human CHO Transfectants

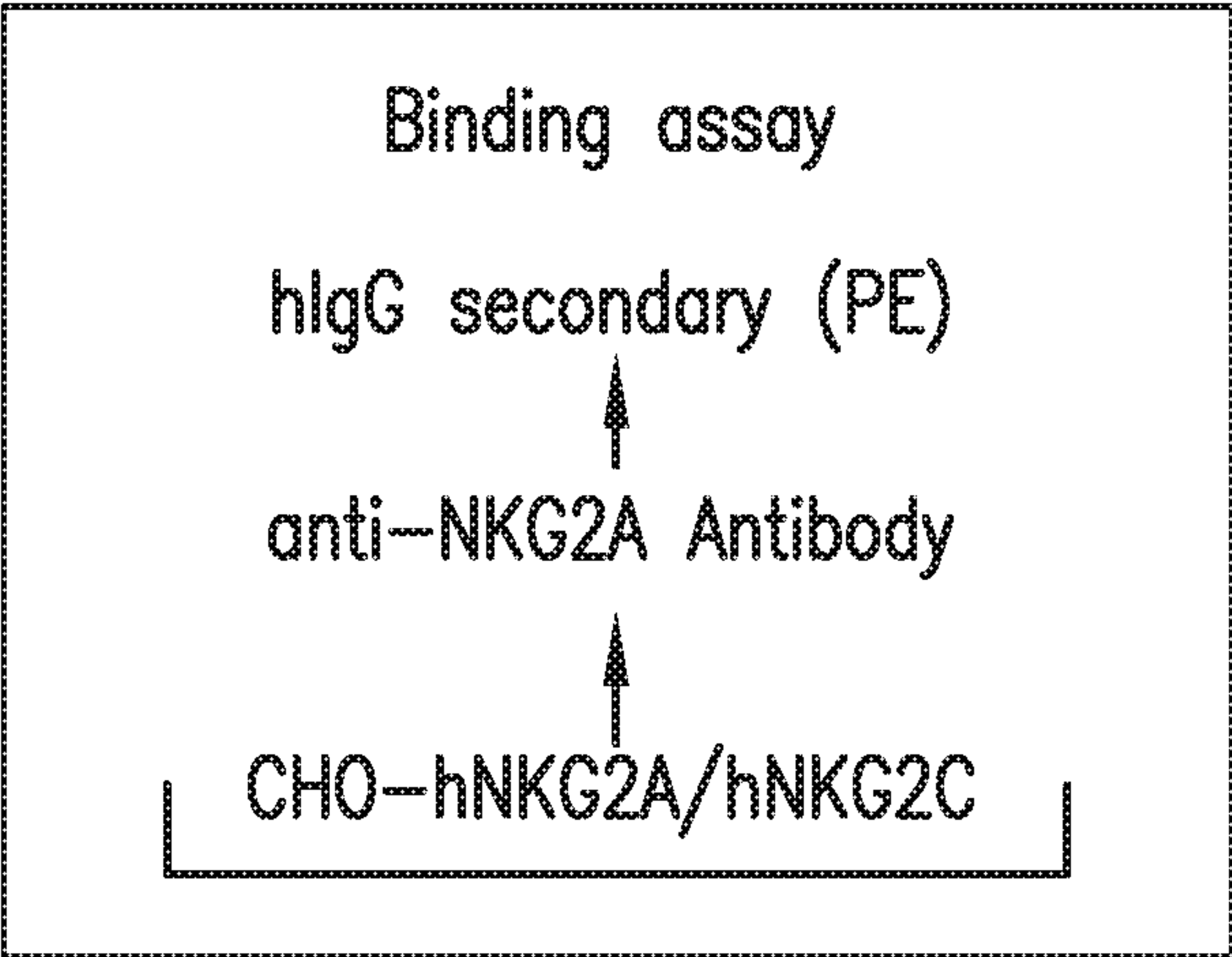


FIG. 18A

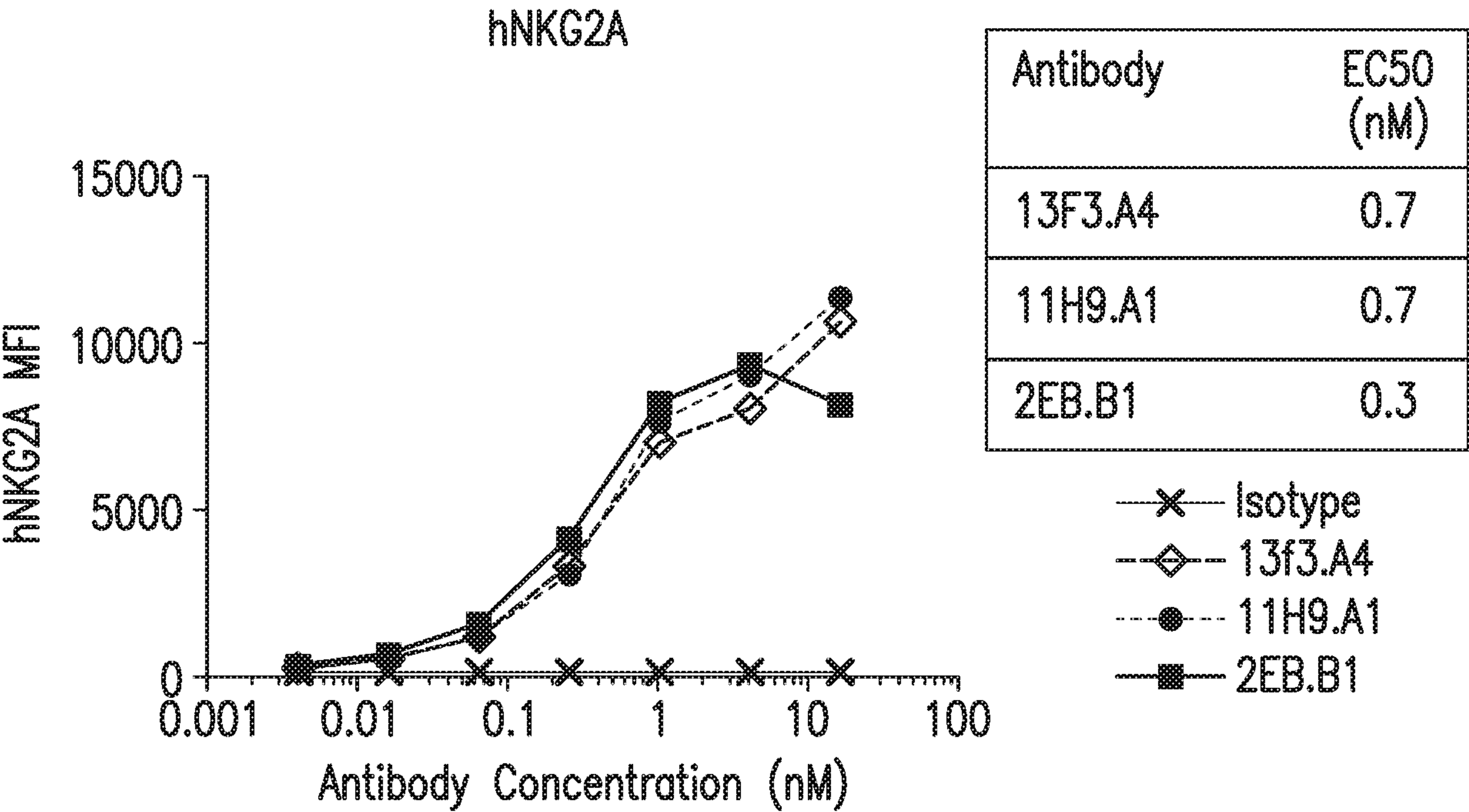


FIG. 18B

Anti-NKG2A Antibodies: Binding and Blocking Human CHO Transfectants

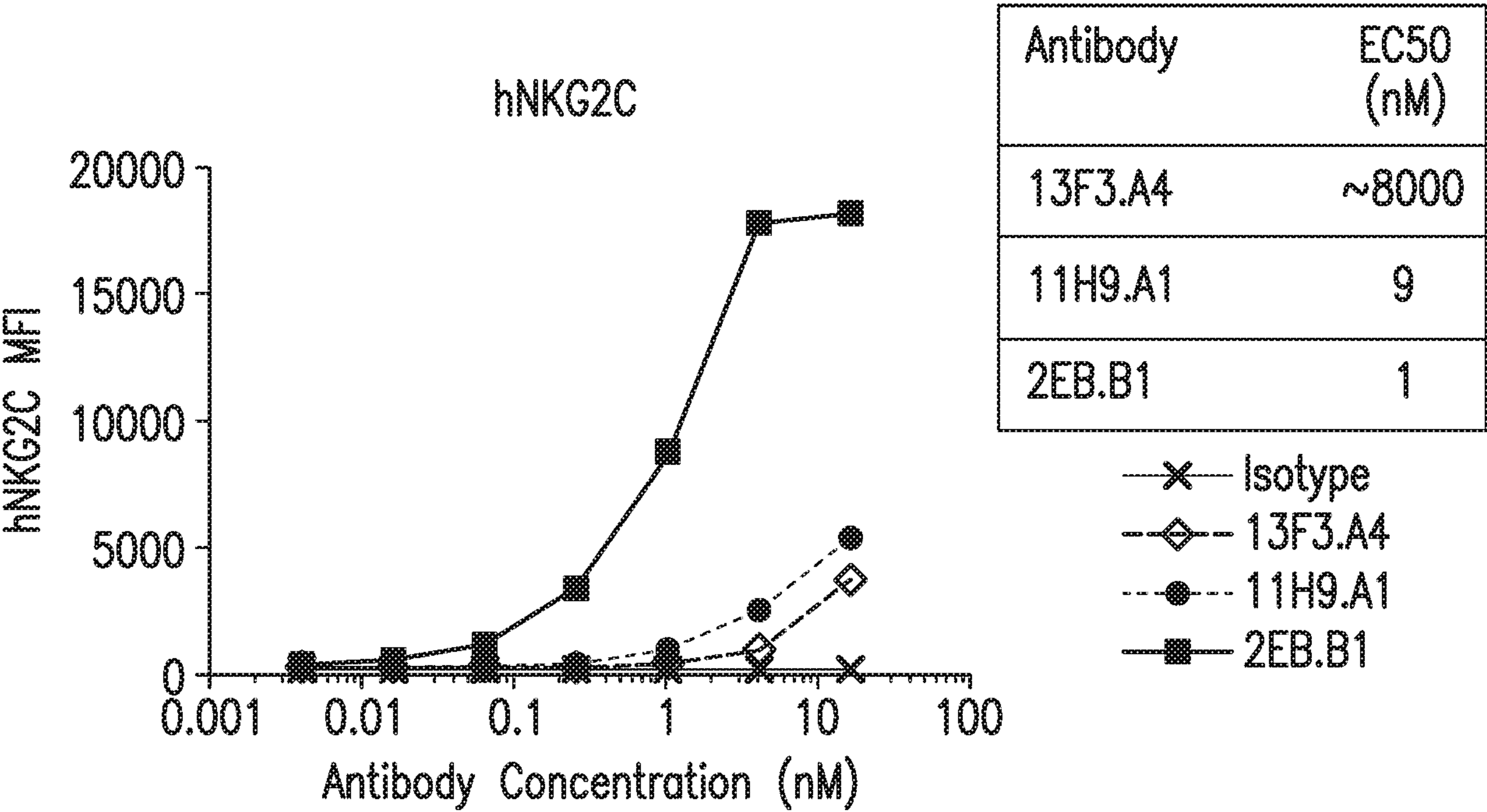


FIG. 18C

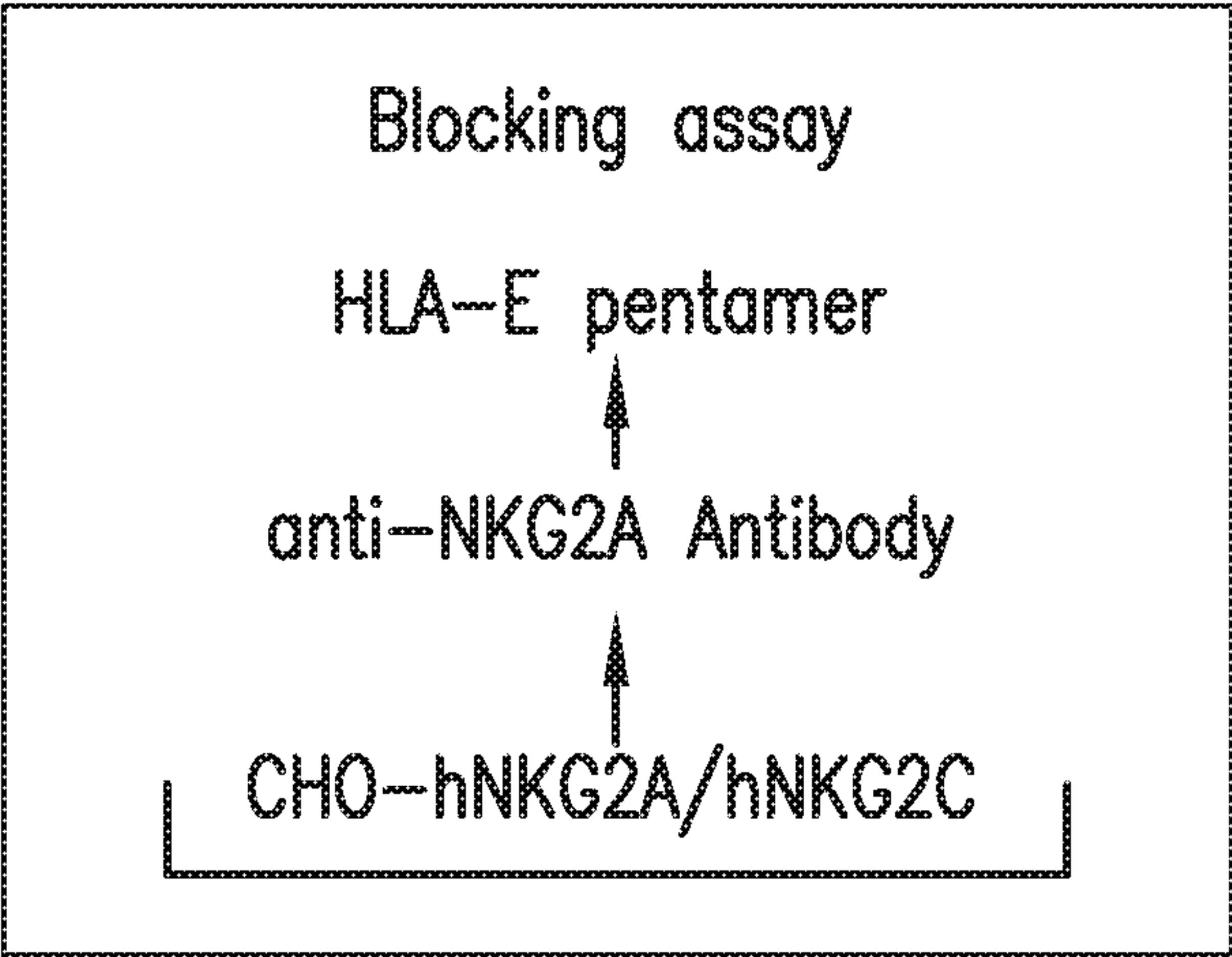


FIG. 18D

Anti-NKG2A Antibodies: Binding and Blocking Human CHO Transfectants

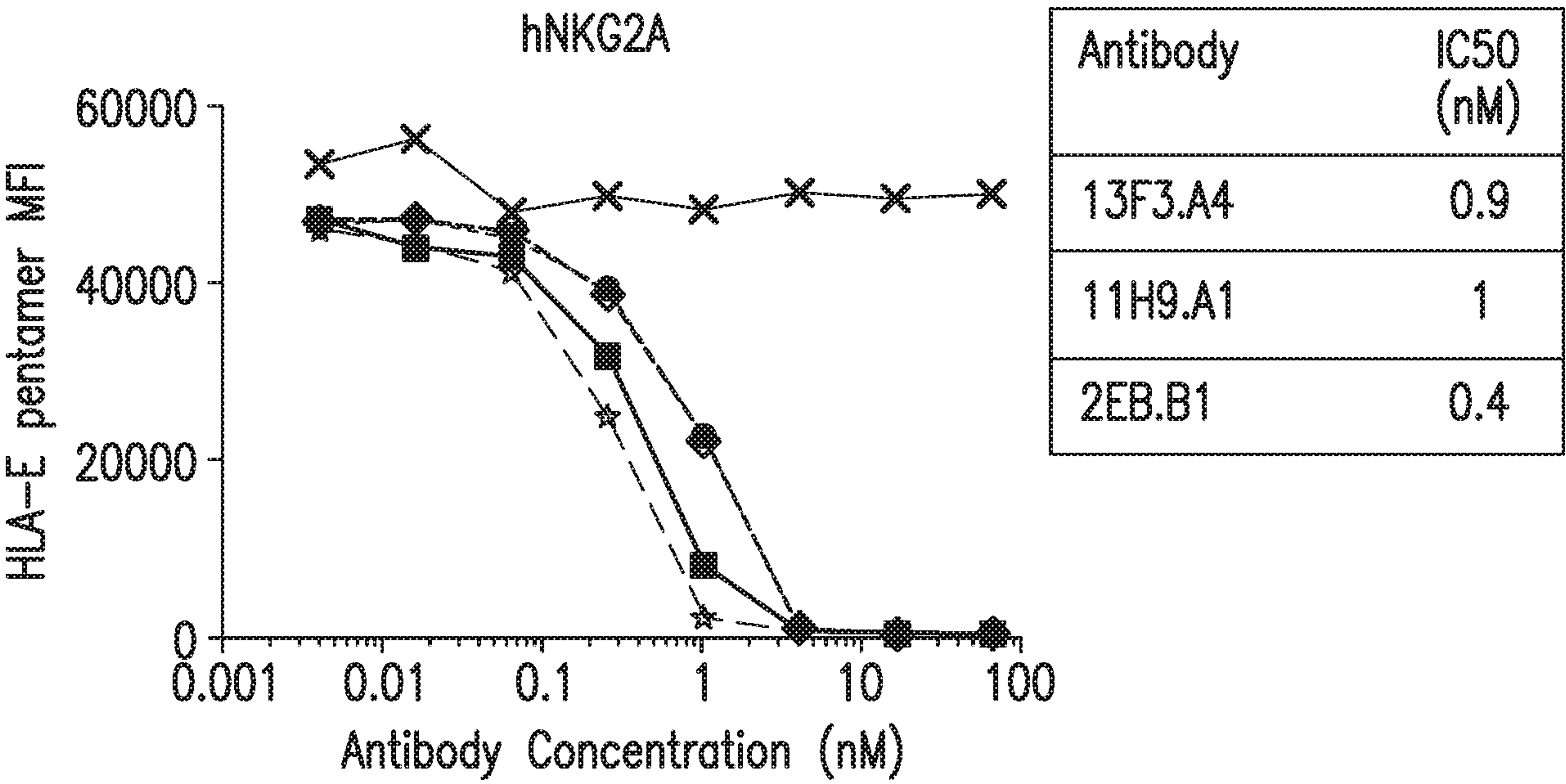


FIG.18E

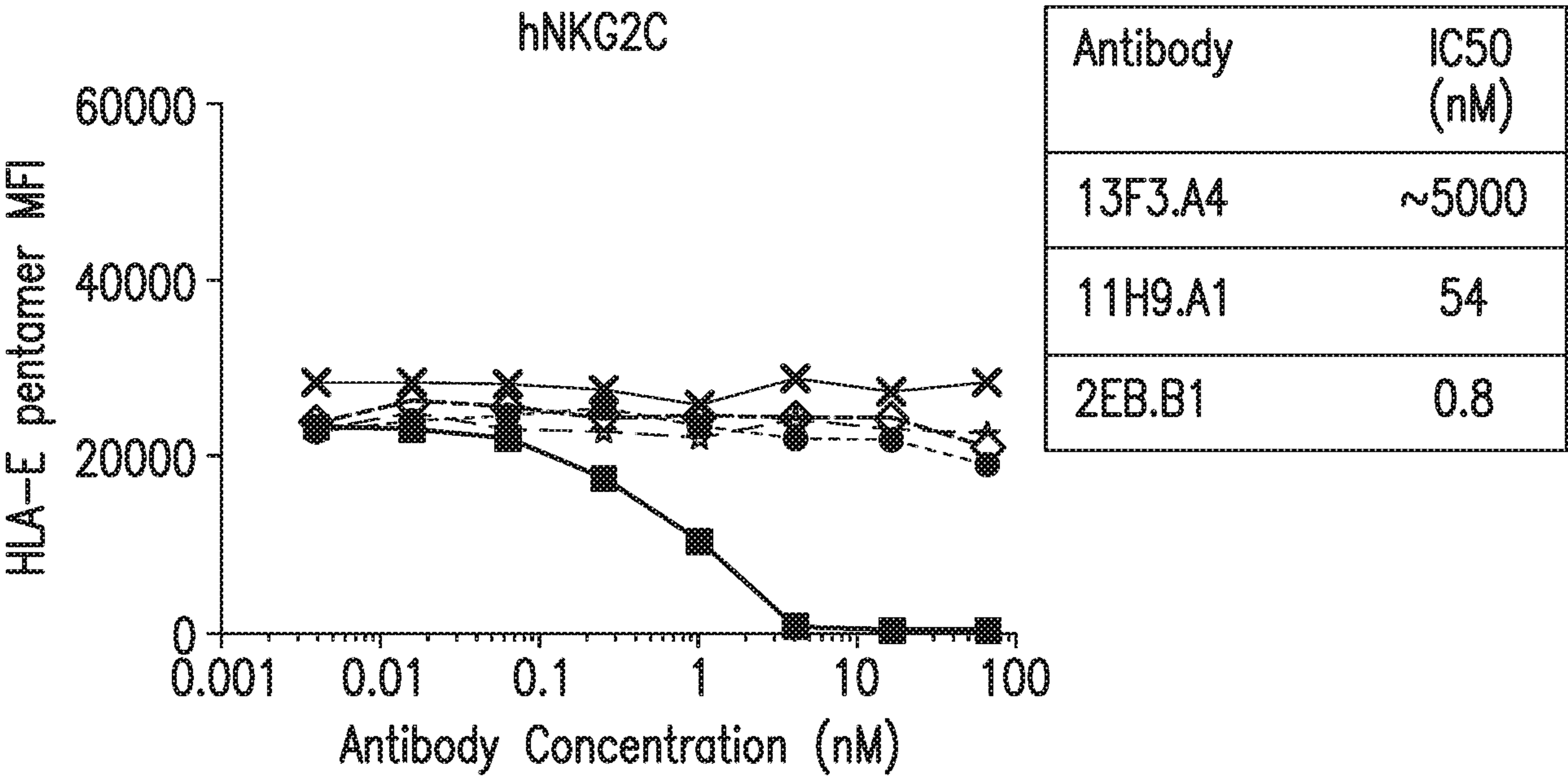


FIG.18F

Anti-NKG2A Antibodies: Binding and Blocking Human NKG2A⁺ Natural Killer Cell Line (NKL)

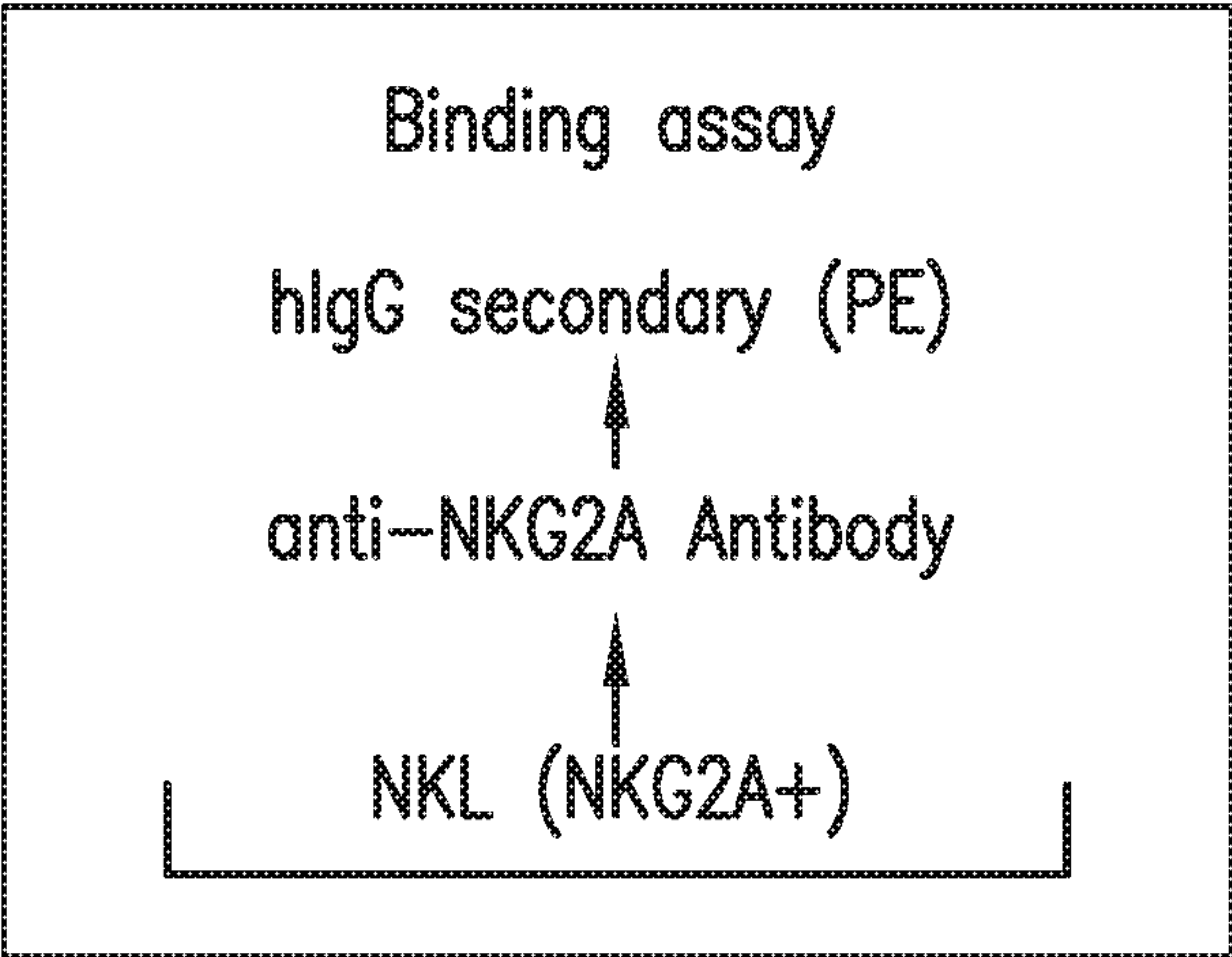


FIG.19A

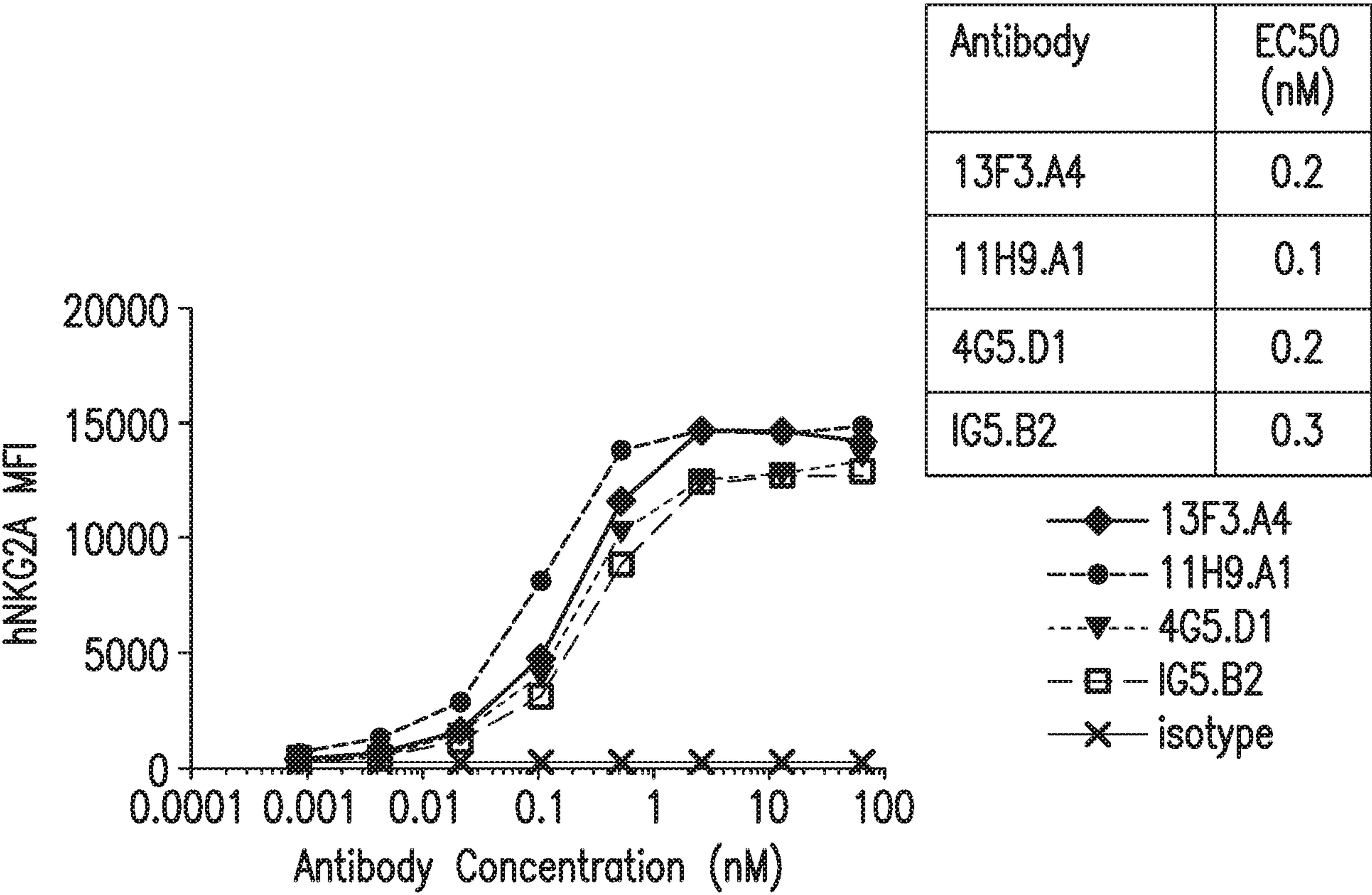


FIG.19B

Anti-NKG2A Antibodies: Binding and Blocking Human NKG2A⁺ Natural Killer Cell Line (NKL)

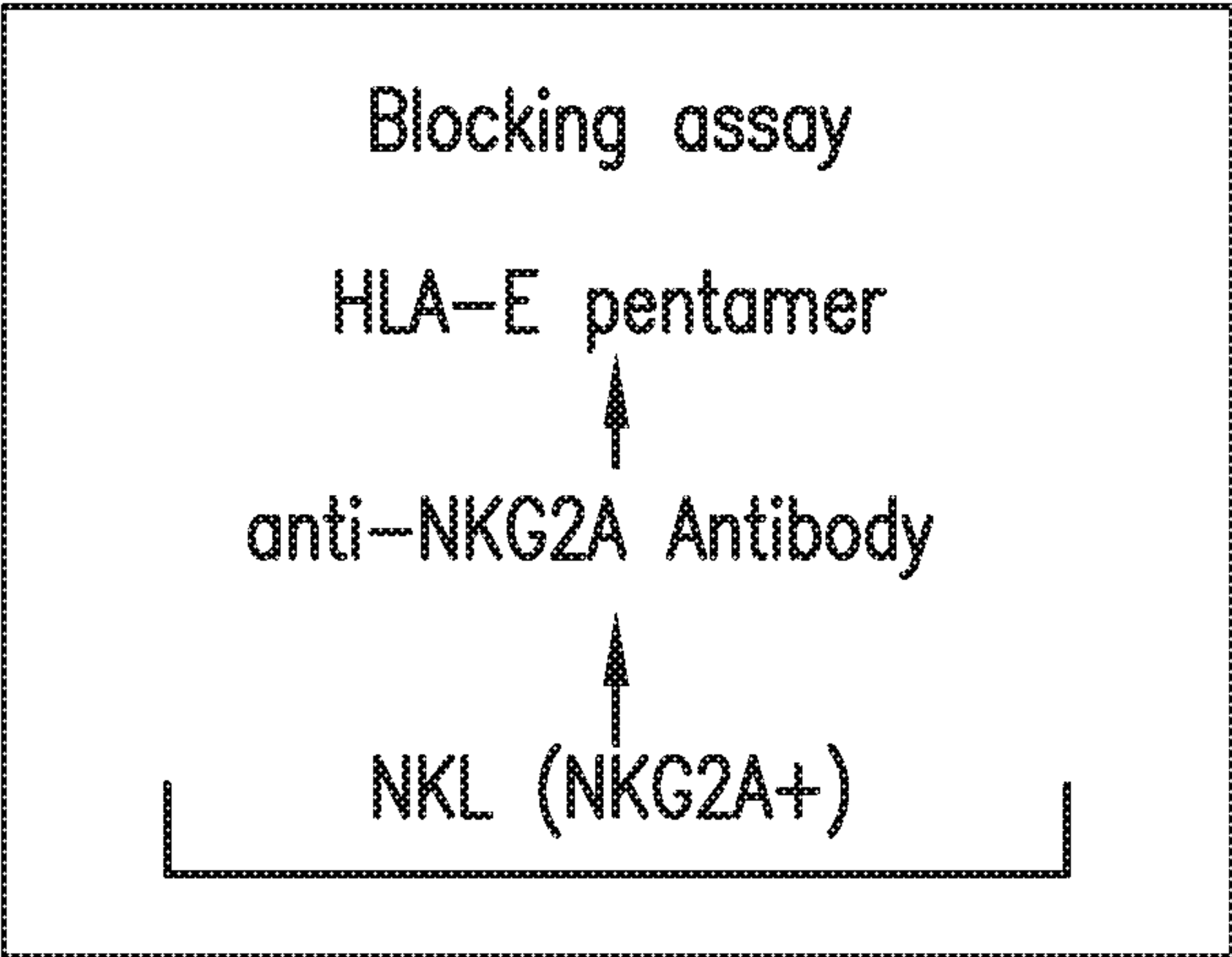


FIG. 19C

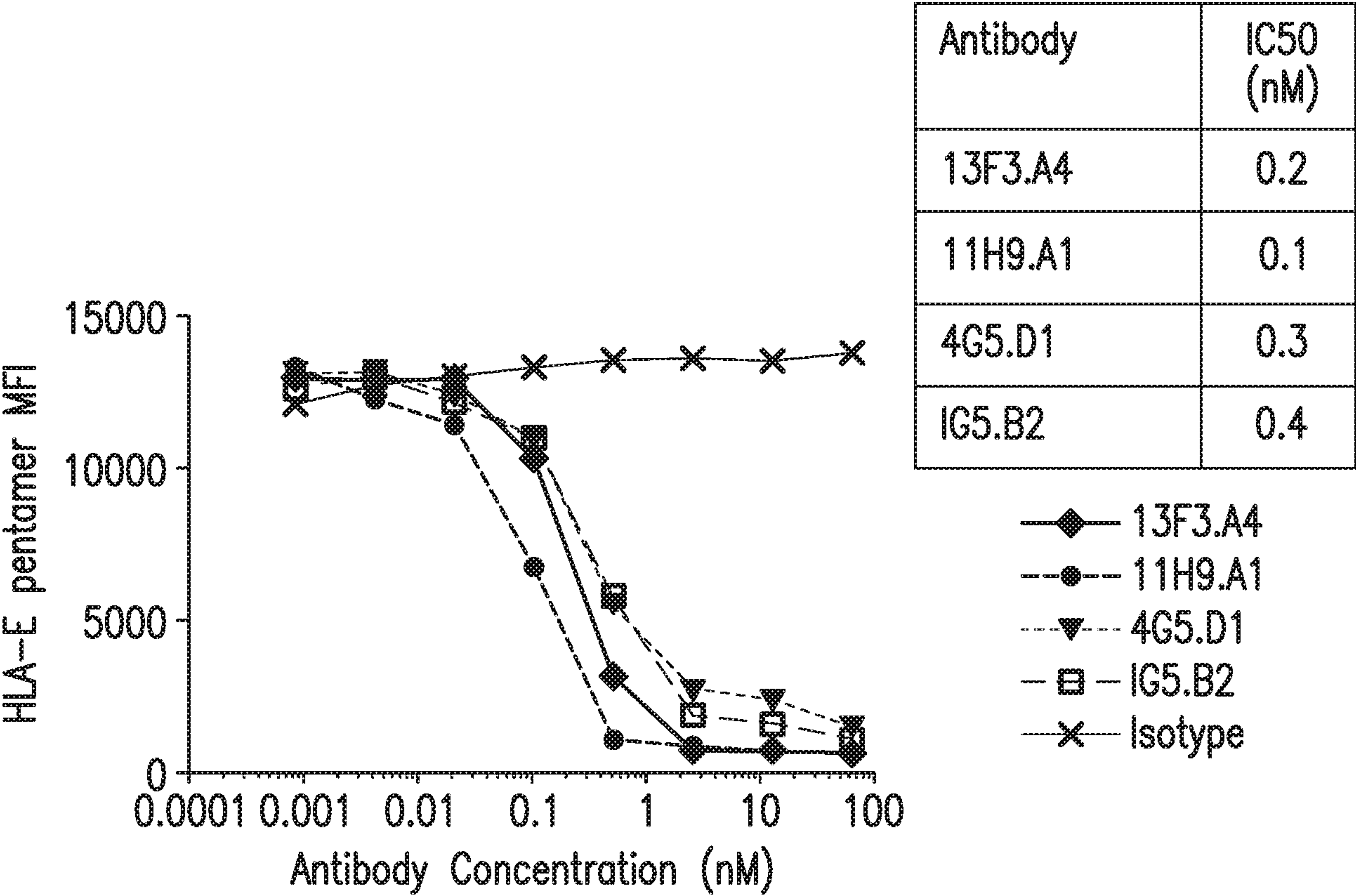


FIG. 19D

Ability of Anti-NKG2A Antibodies to Block NKG2A/HLA-E Interaction in hNKG2A-expressing CHO Cells

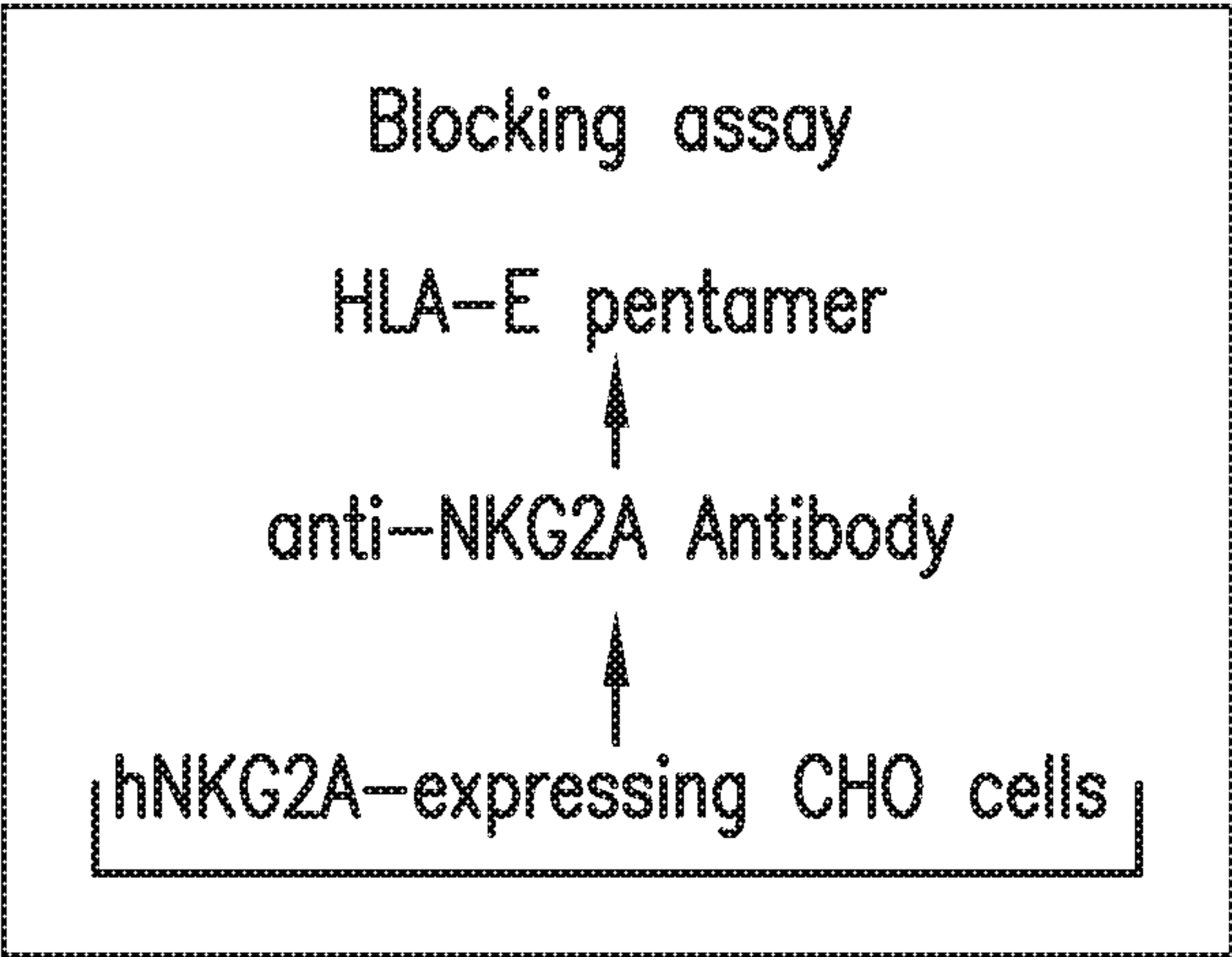


FIG.20A

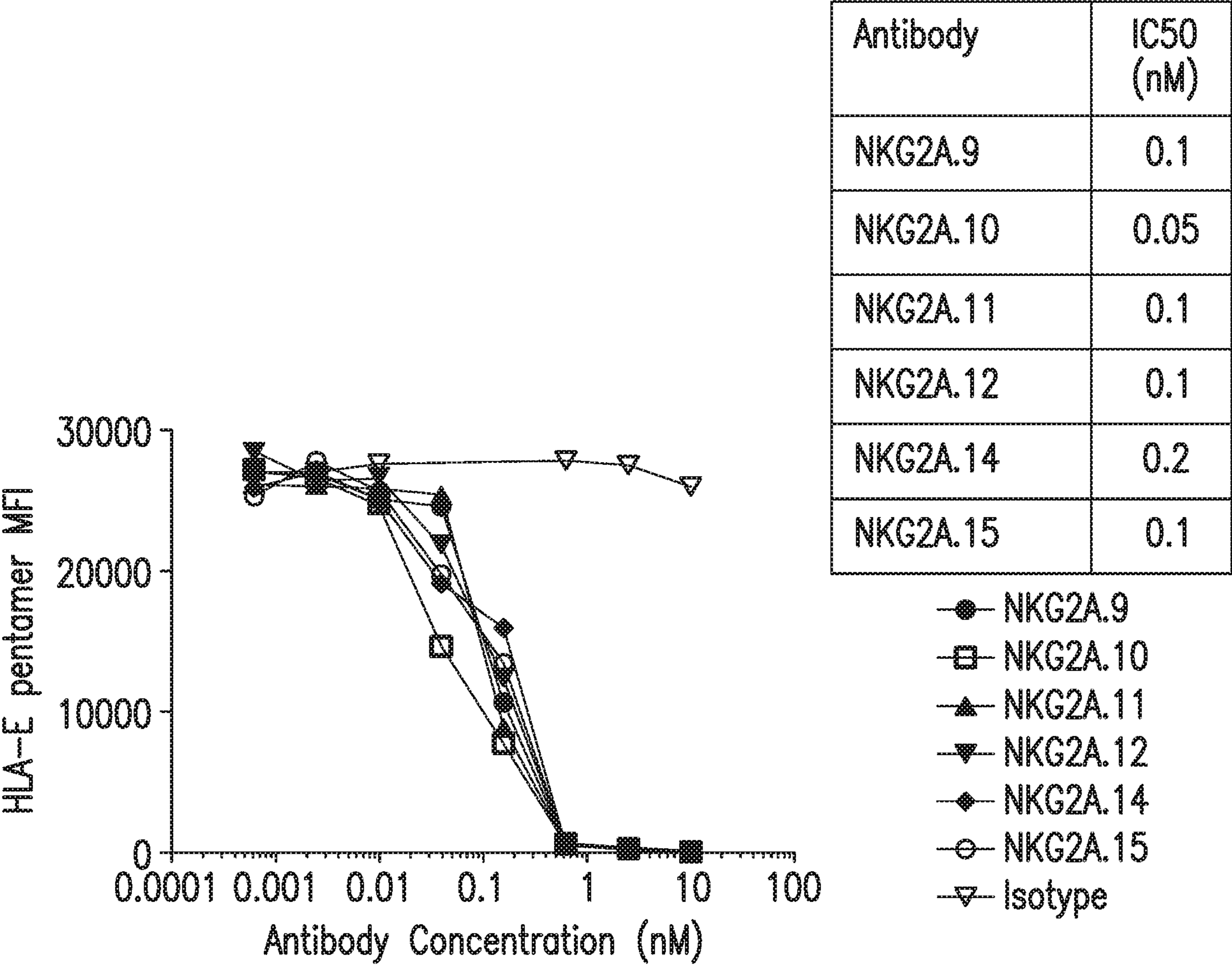


FIG.20B

Ability of Anti-NKG2A Antibodies to Block NKG2A/HLA-E Interaction in hNKG2A-expressing CHO Cells

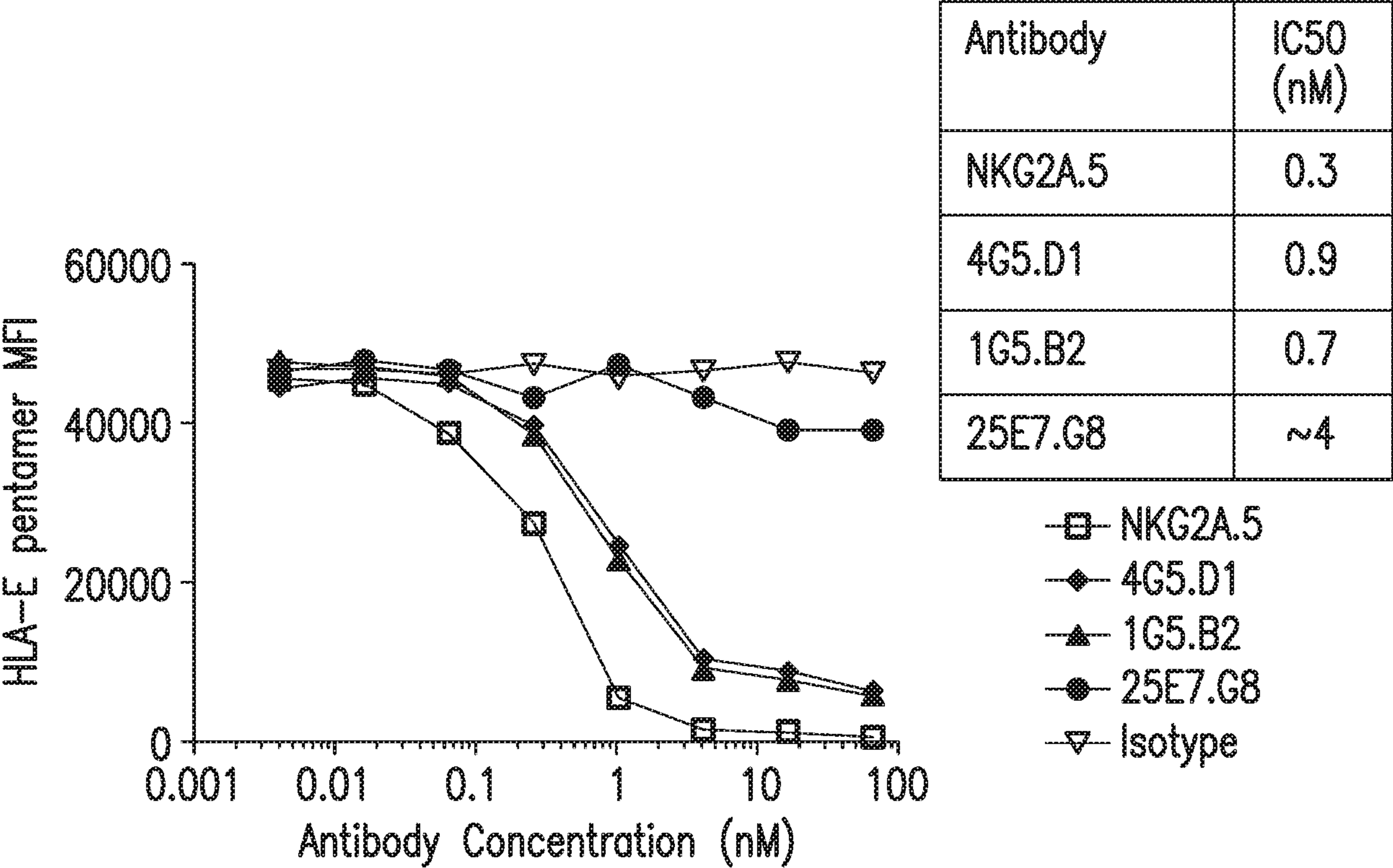


FIG.20C

Anti-NKG2A Antibodies Binding to hNKG2A-expressing CHO Cells

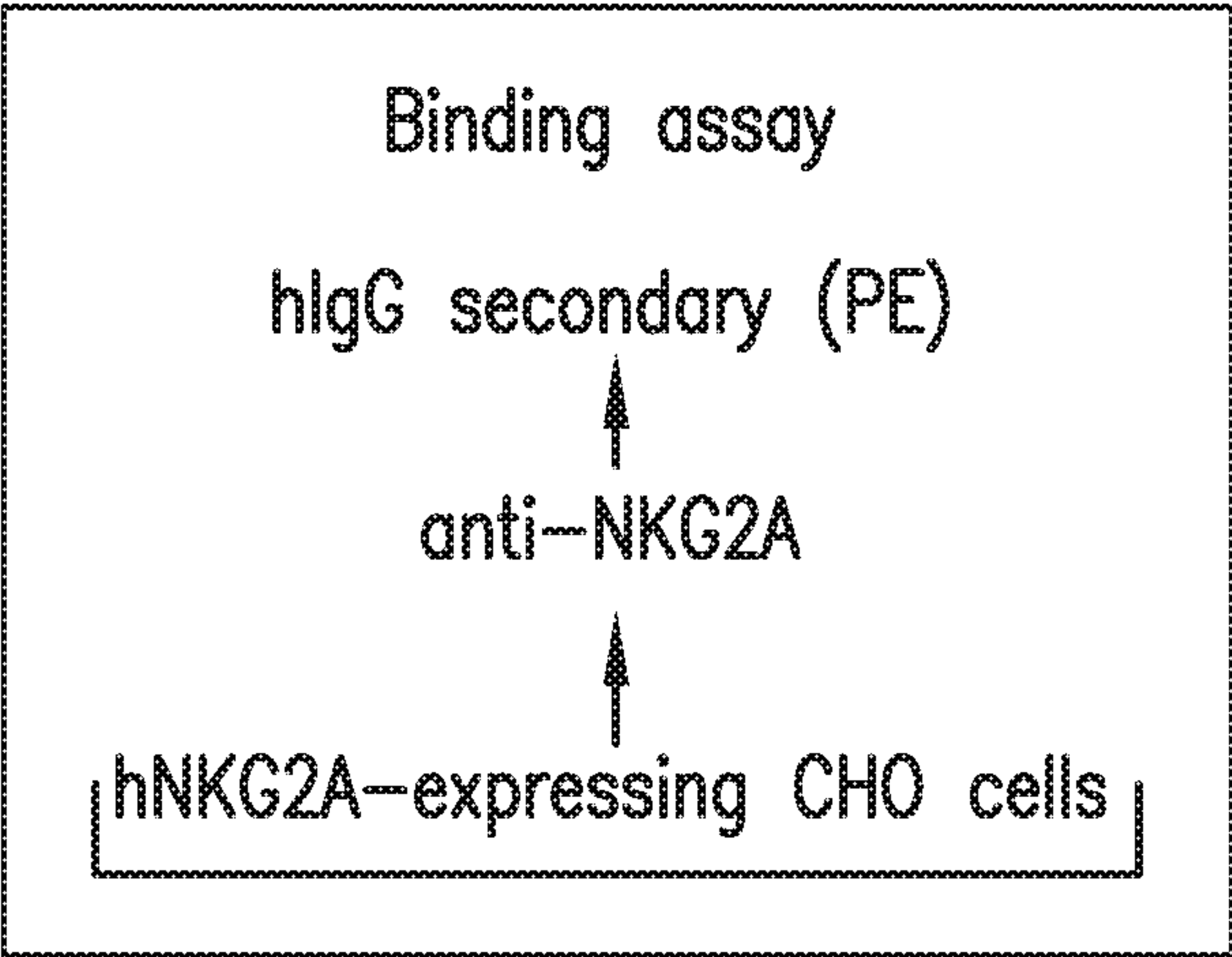
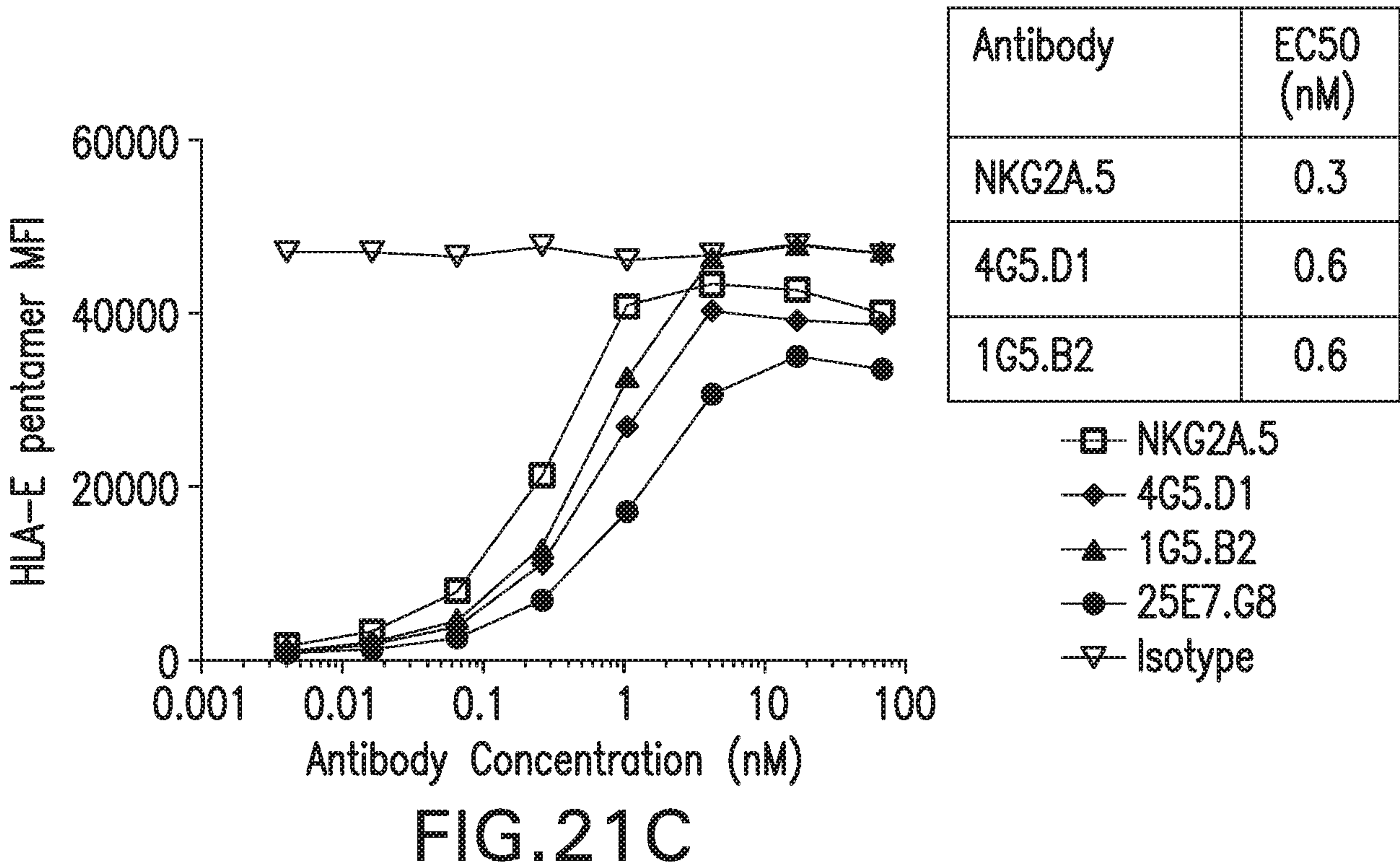
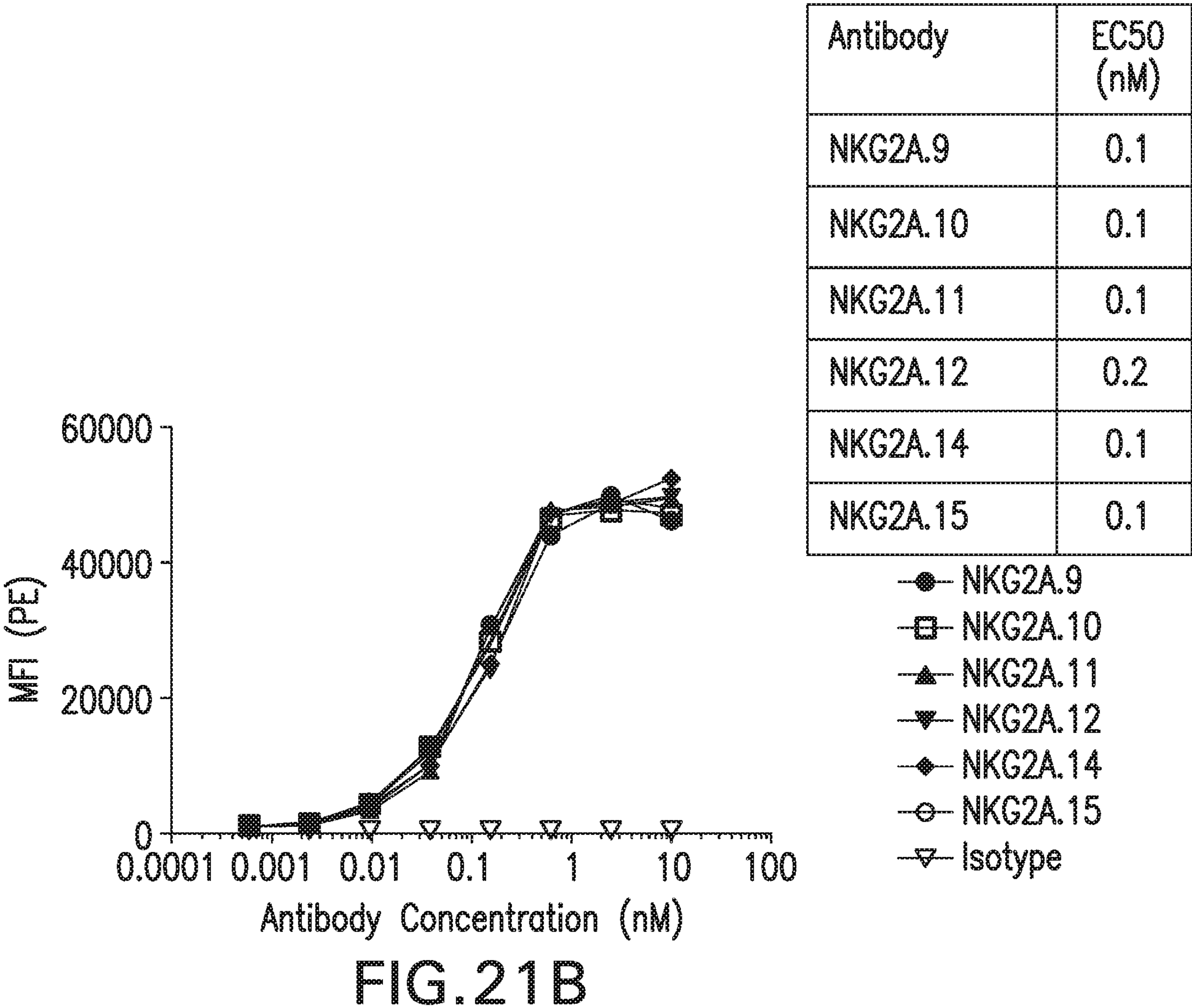


FIG.21A

Anti-NKG2A Antibodies Binding to hNKG2A-expressing CHO Cells



Anti-NKG2A Antibodies Binding to Cynomolgus NKG2A-expressing CHO Cells

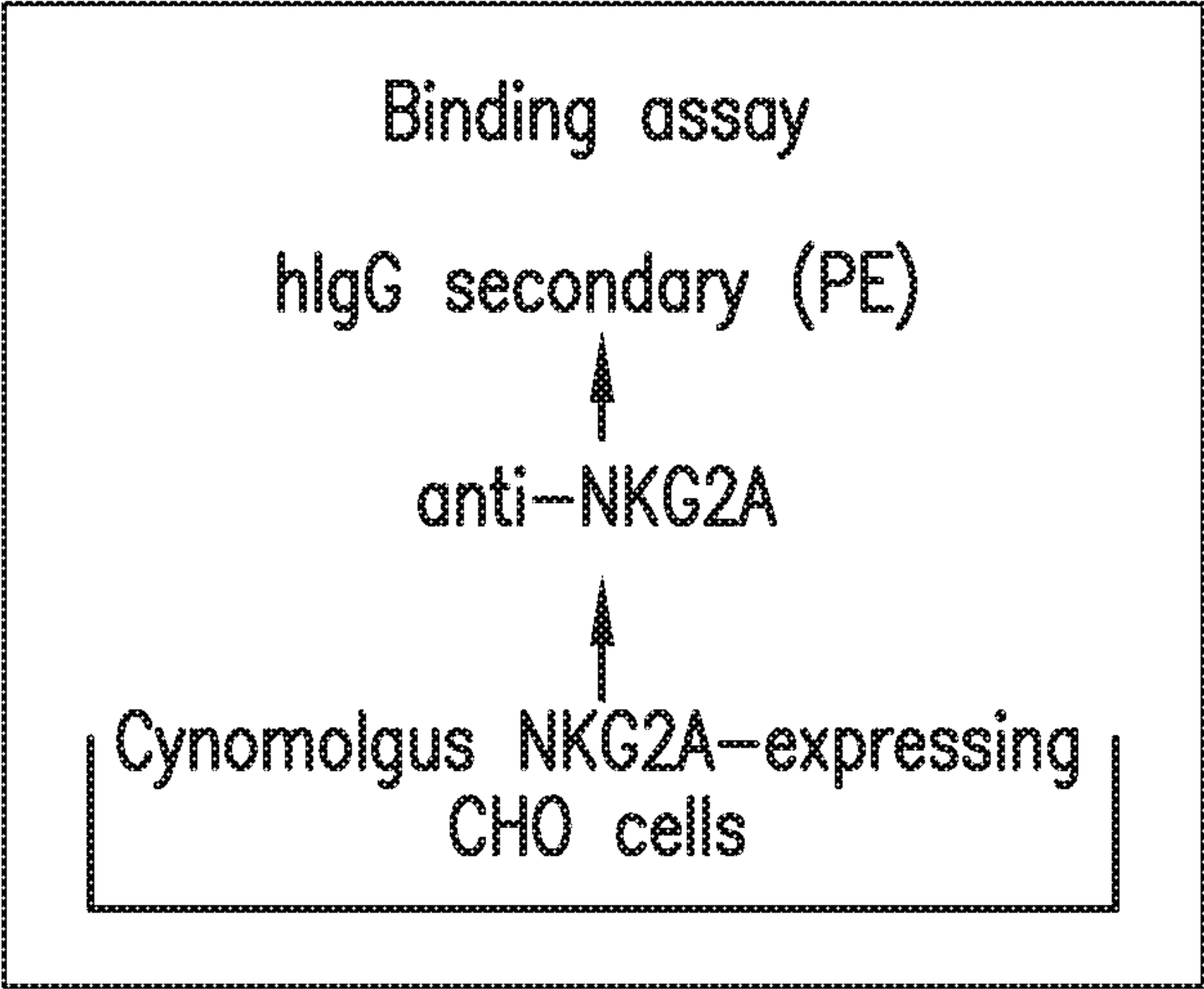


FIG.22A

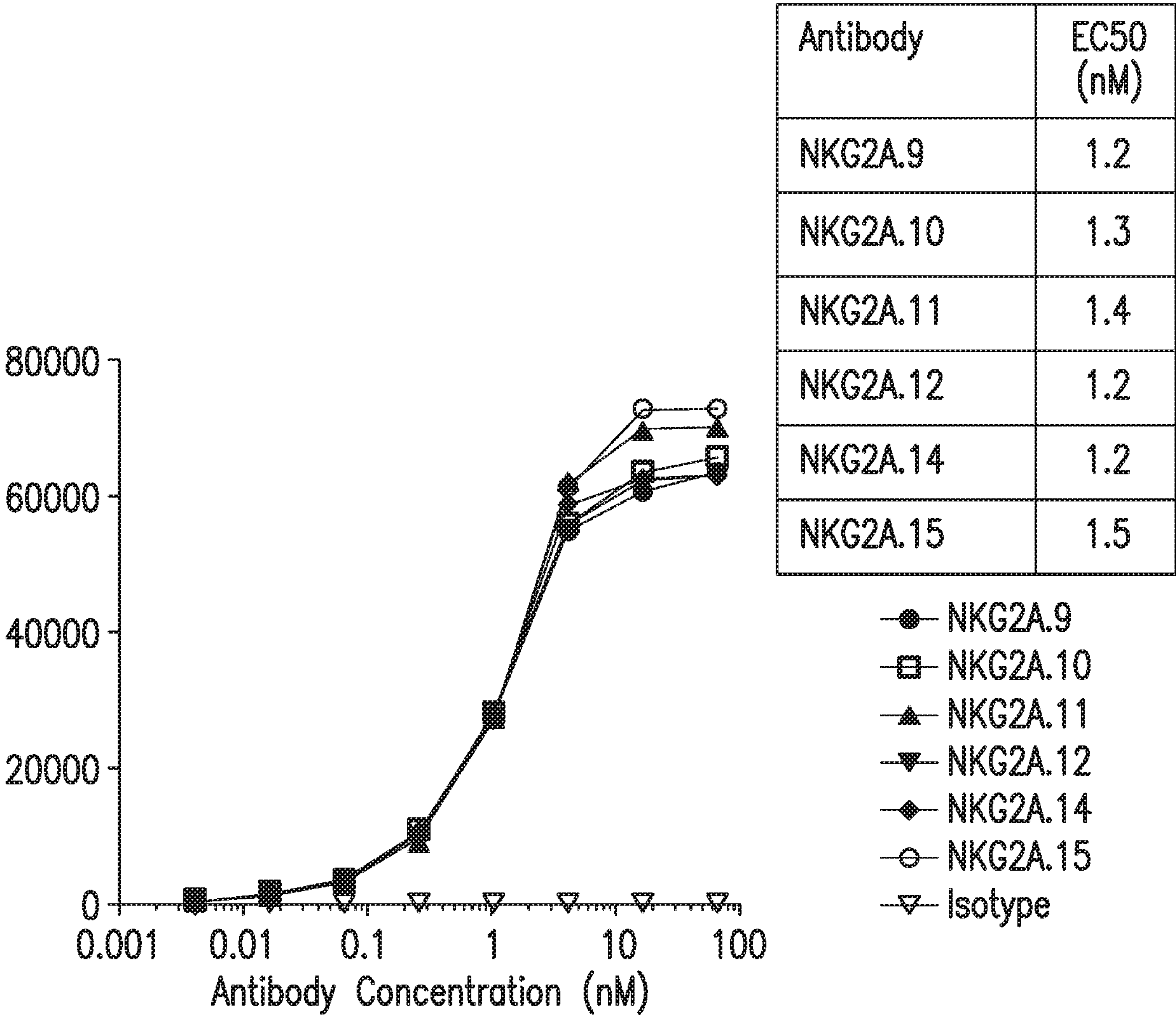


FIG.22B

Anti-NKG2A Antibodies Binding to Cynomolgus NKG2A-expressing CHO Cells

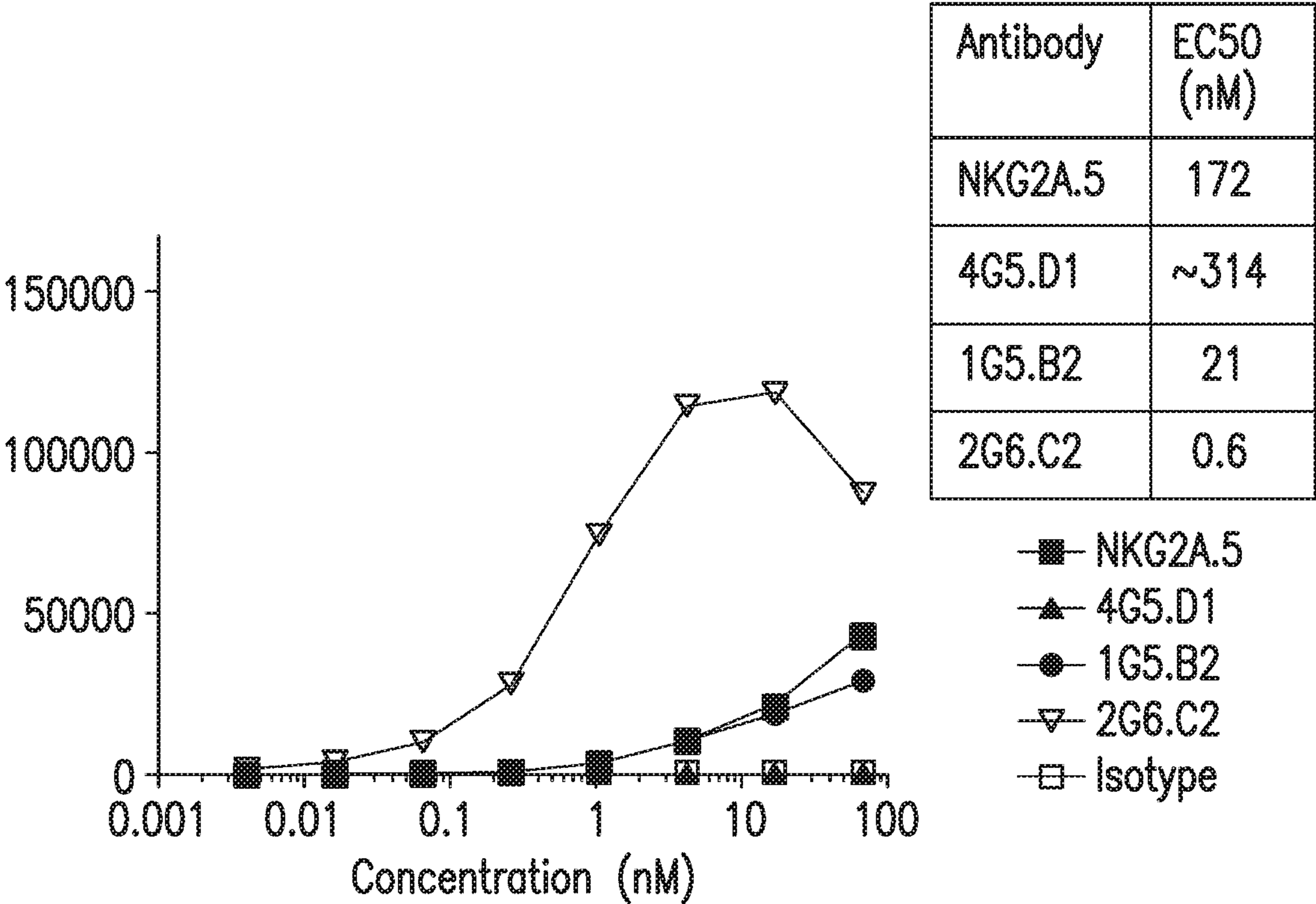


FIG.22C

Ability of 2G6.C2 Antibody to Bind Human NKG2A expressing CHO Cells and Block NKG2A/HLA-E Interaction

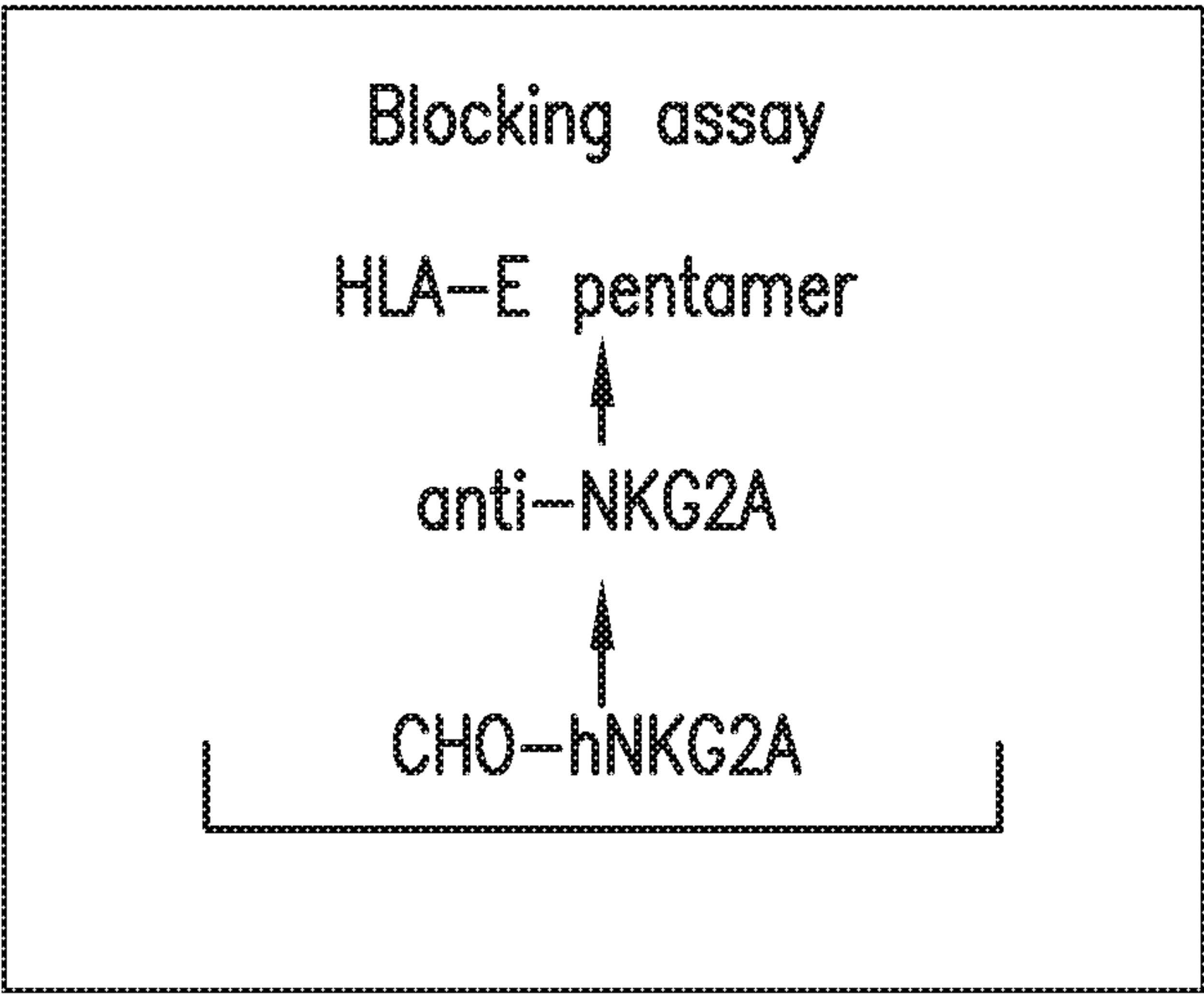


FIG.23A

Ability of 2G6.C2 Antibody to Bind Human NKG2A expressing CHO Cells and Block NKG2A/HLA-E Interaction

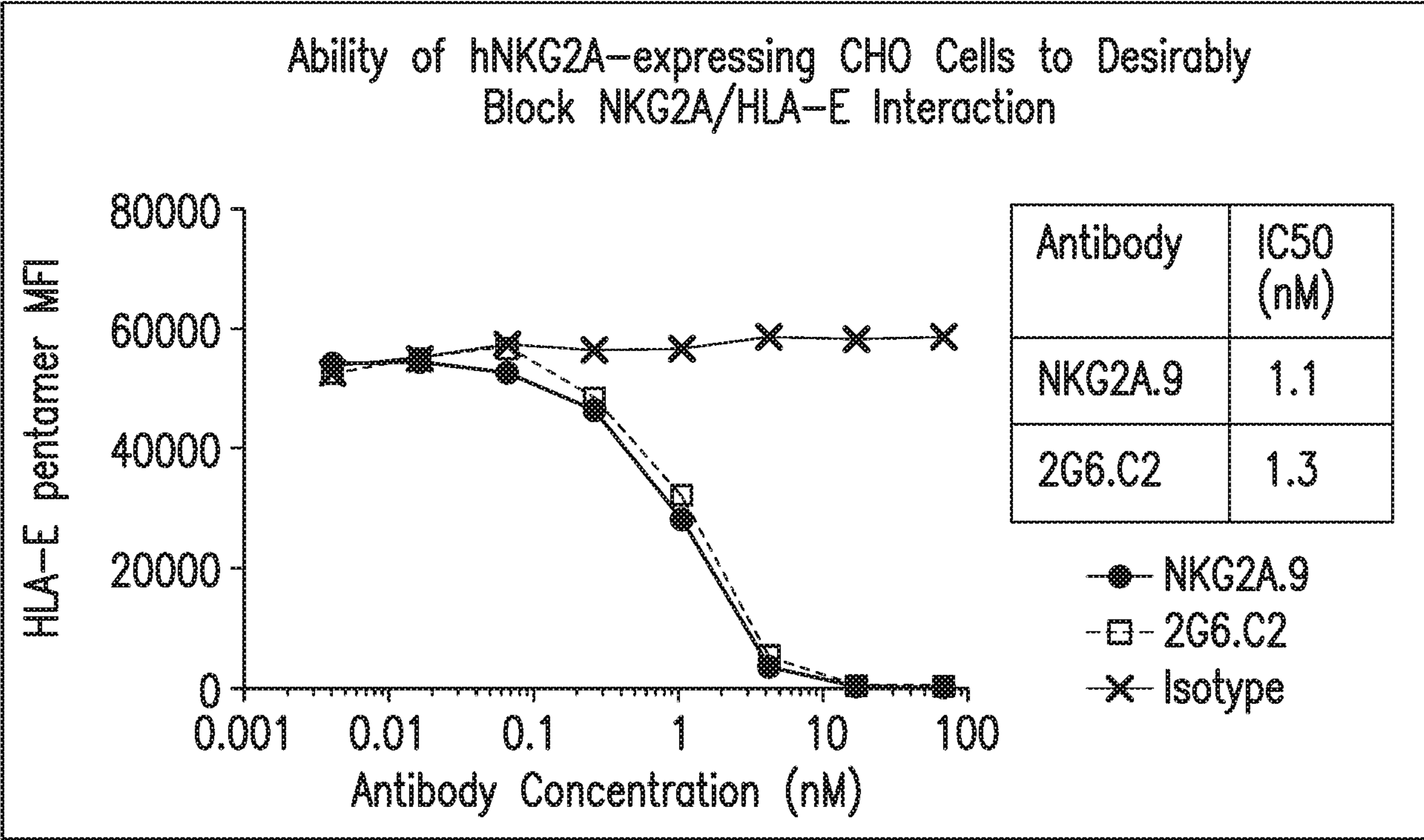


FIG.23B

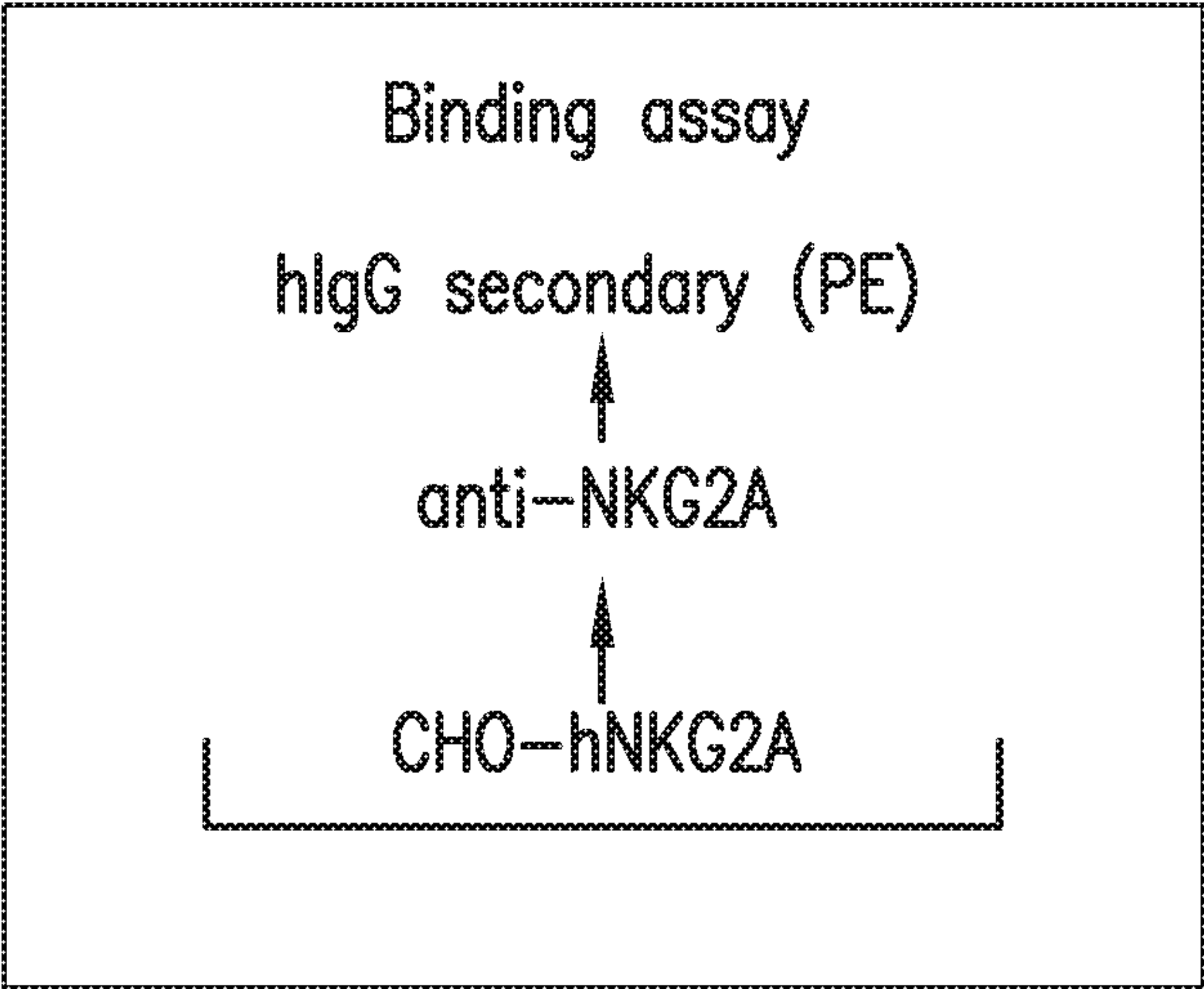


FIG.23C

Ability of 2G6.C2 Antibody to Bind Human NKG2A expressing CHO Cells
and Block NKG2A/HLA-E Interaction

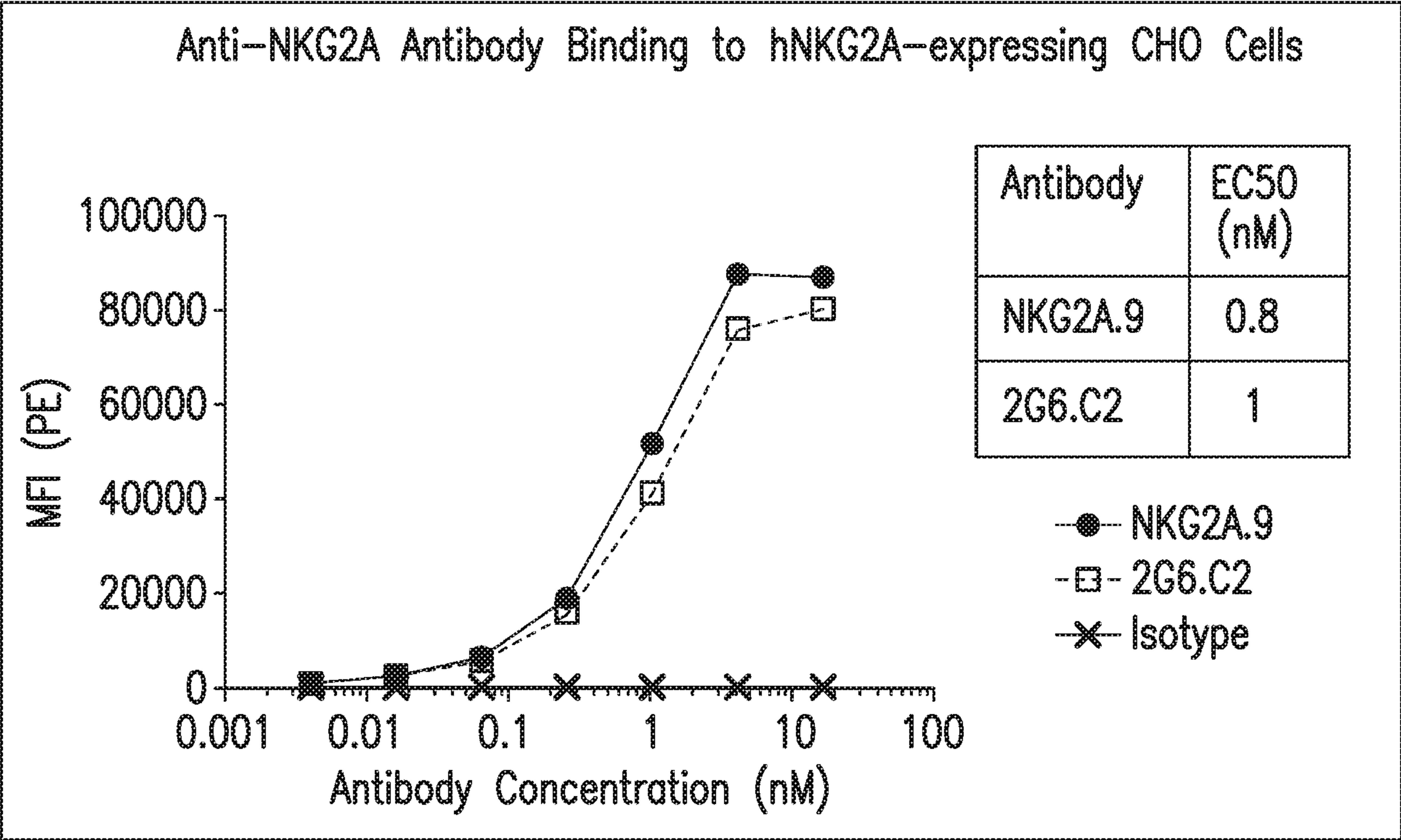


FIG.23D

Anti-NKG2A Antibodies Bound to Cynomolgus Monkey NK cells

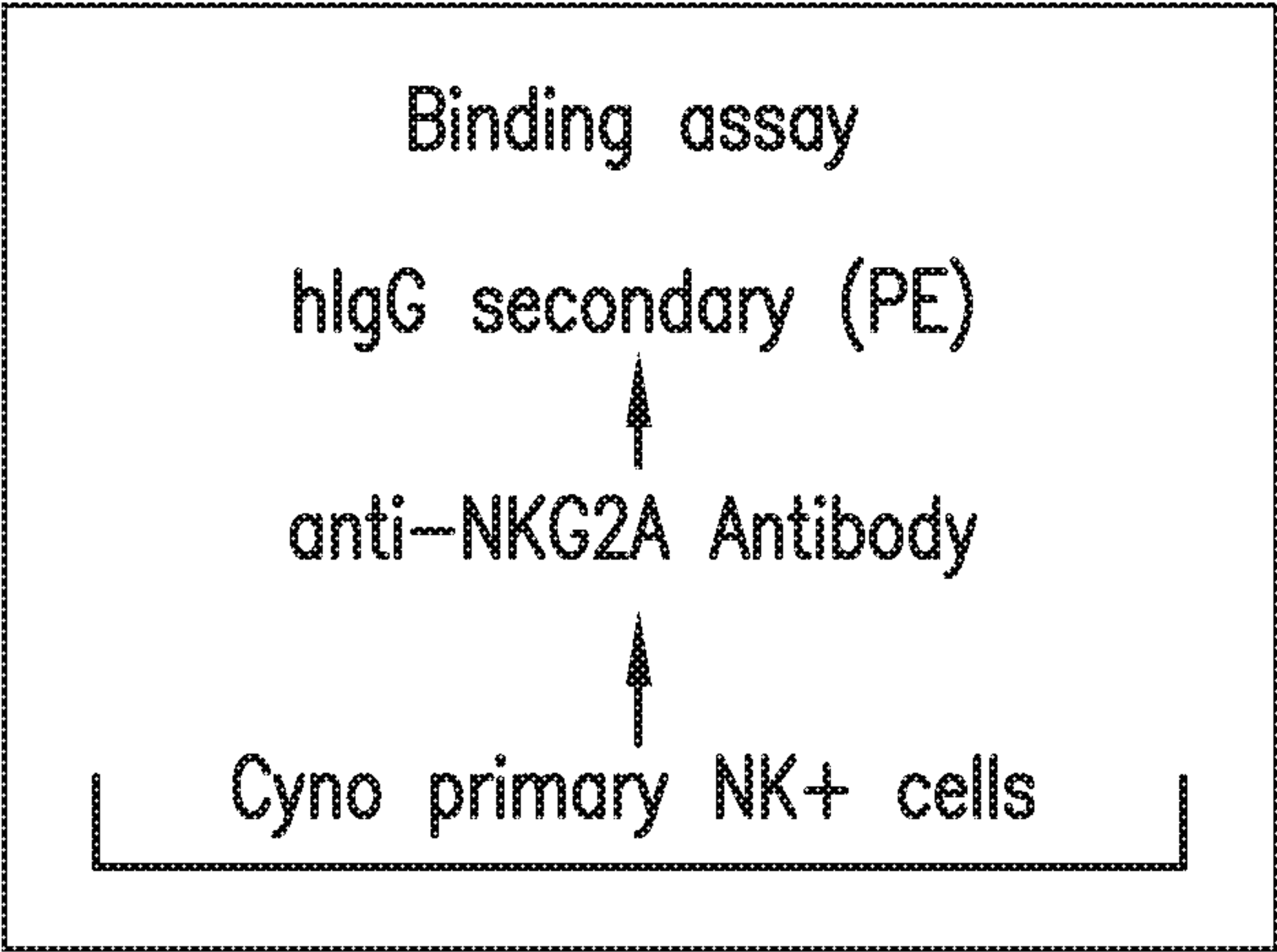


FIG.24A

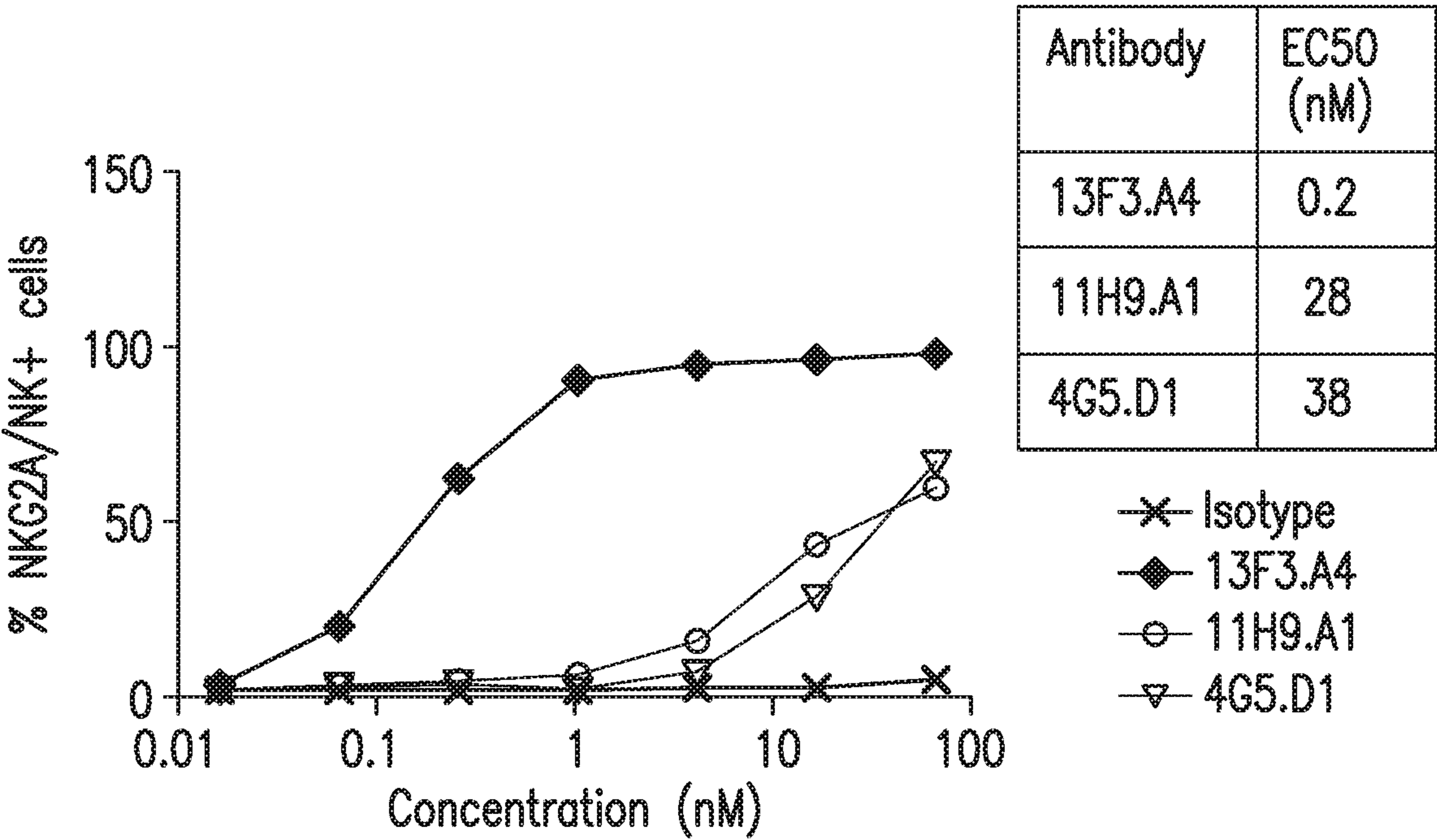
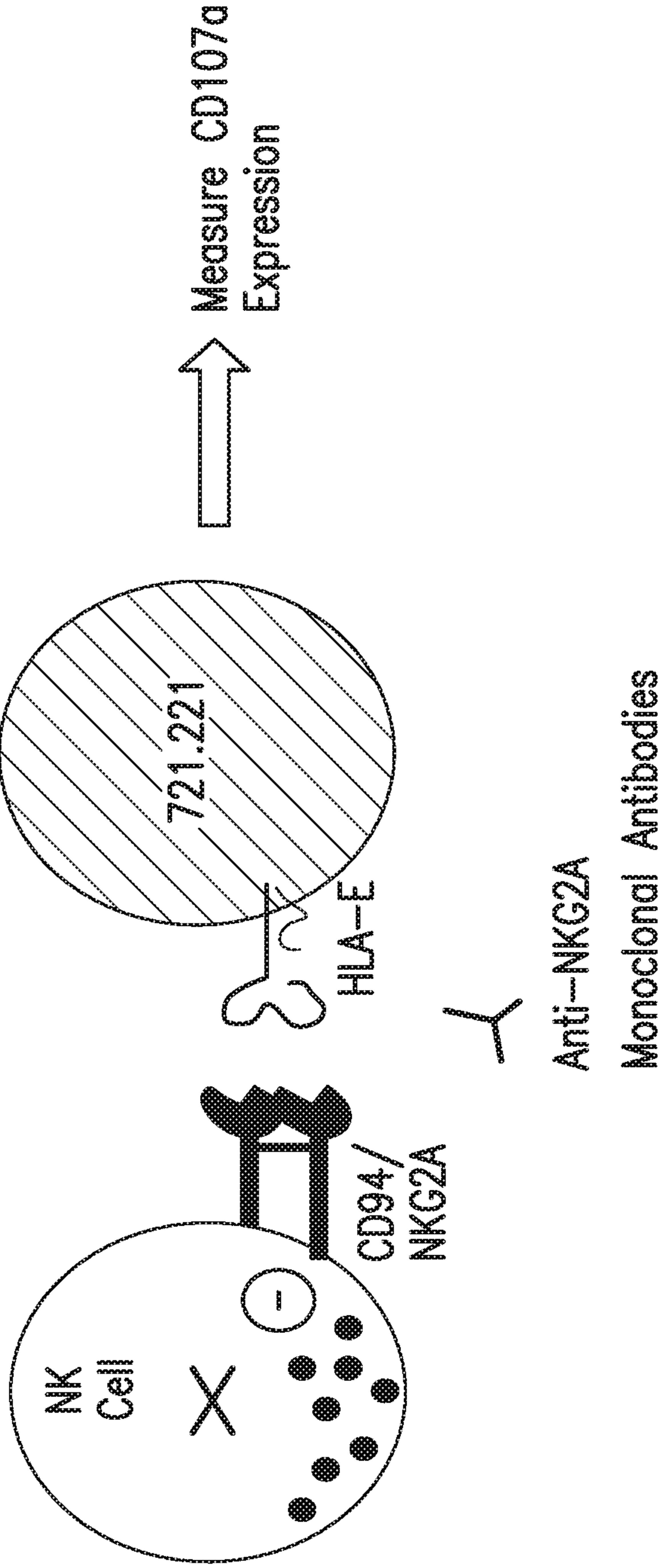


FIG.24B

Anti-NKG2A Antibodies Enhanced NK Cell Degranulation



Effectors: Primary NK cells

Targets: Human B-lymphoblastoid target cell line 721.221 expressing HLA-E

FIG. 25A

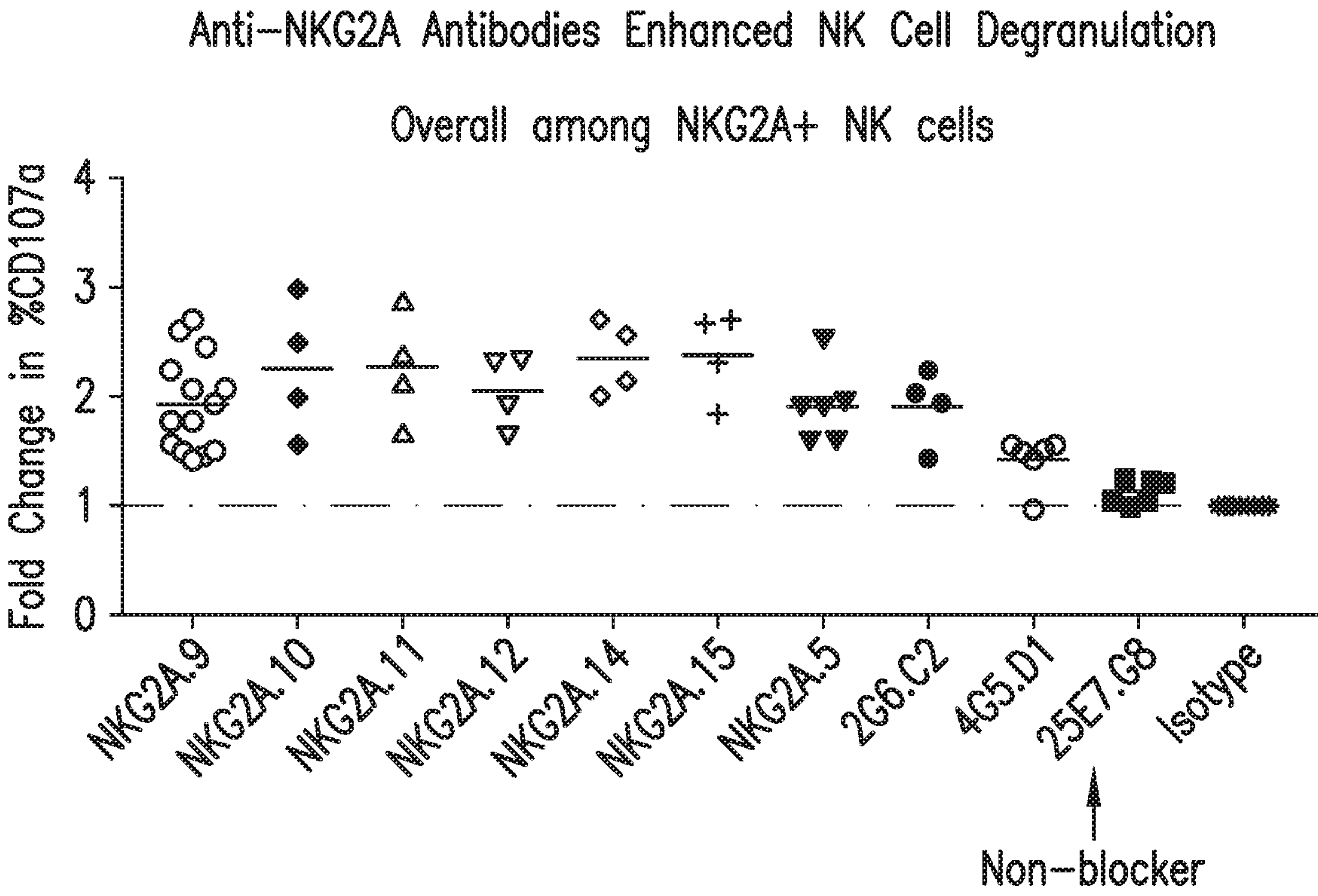


FIG. 25B

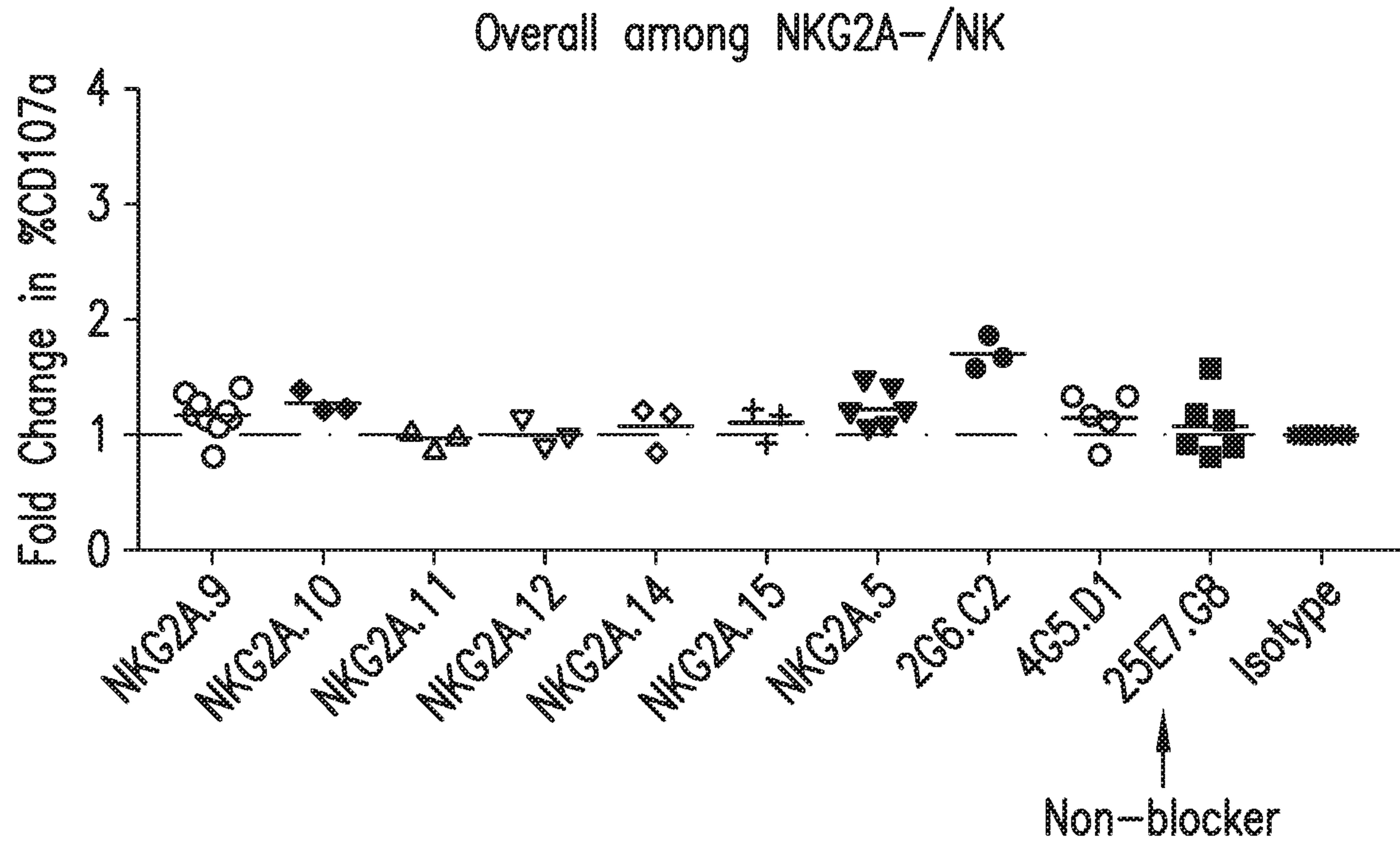


FIG. 25C

Anti-NKG2A Antibodies Enhanced NK Cell Responses
of Interferon-gamma (IFN γ) Production

IFN γ production

Effectors: NKL

Targets: CHO/MICA/HLA-E

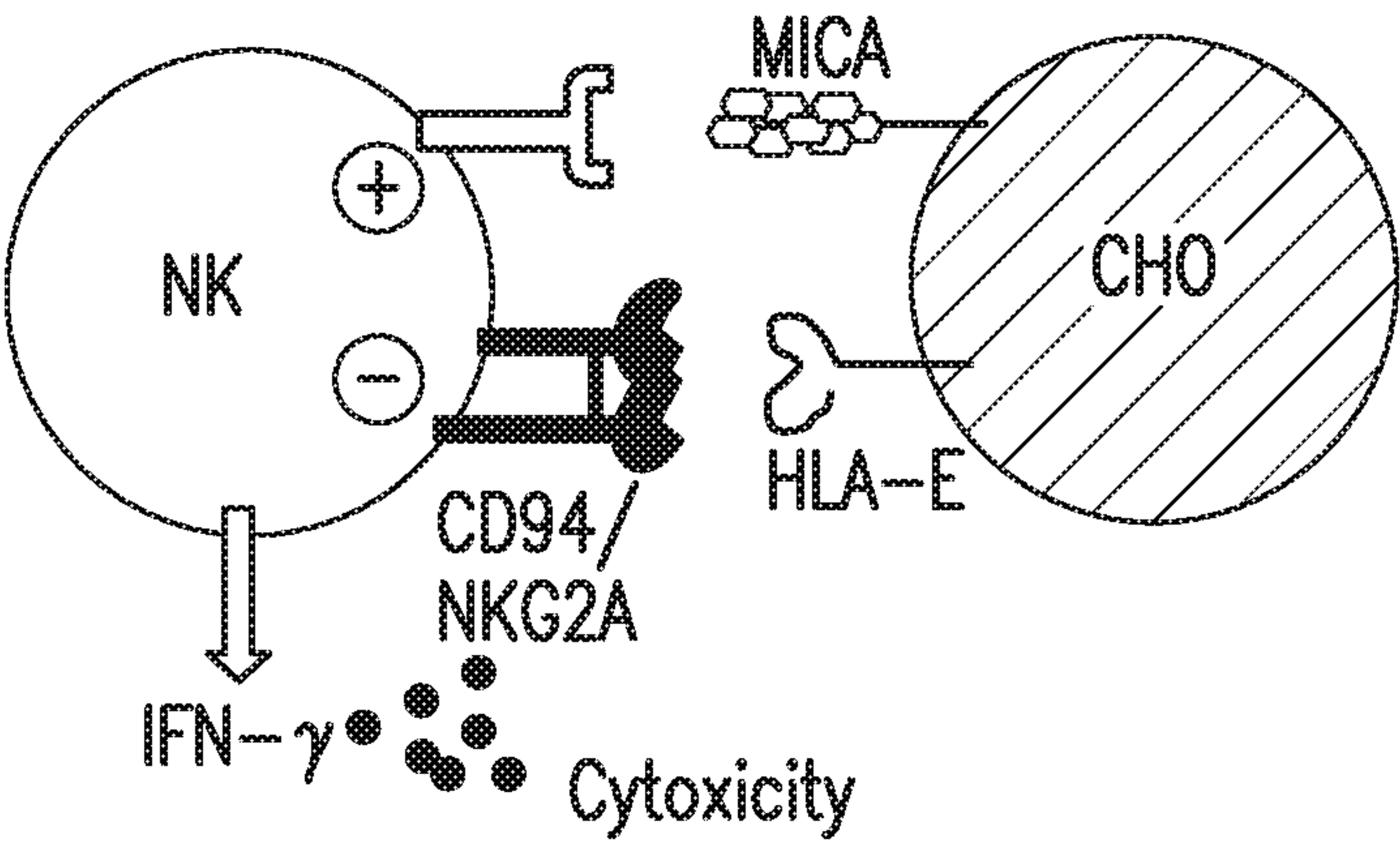


FIG.26A

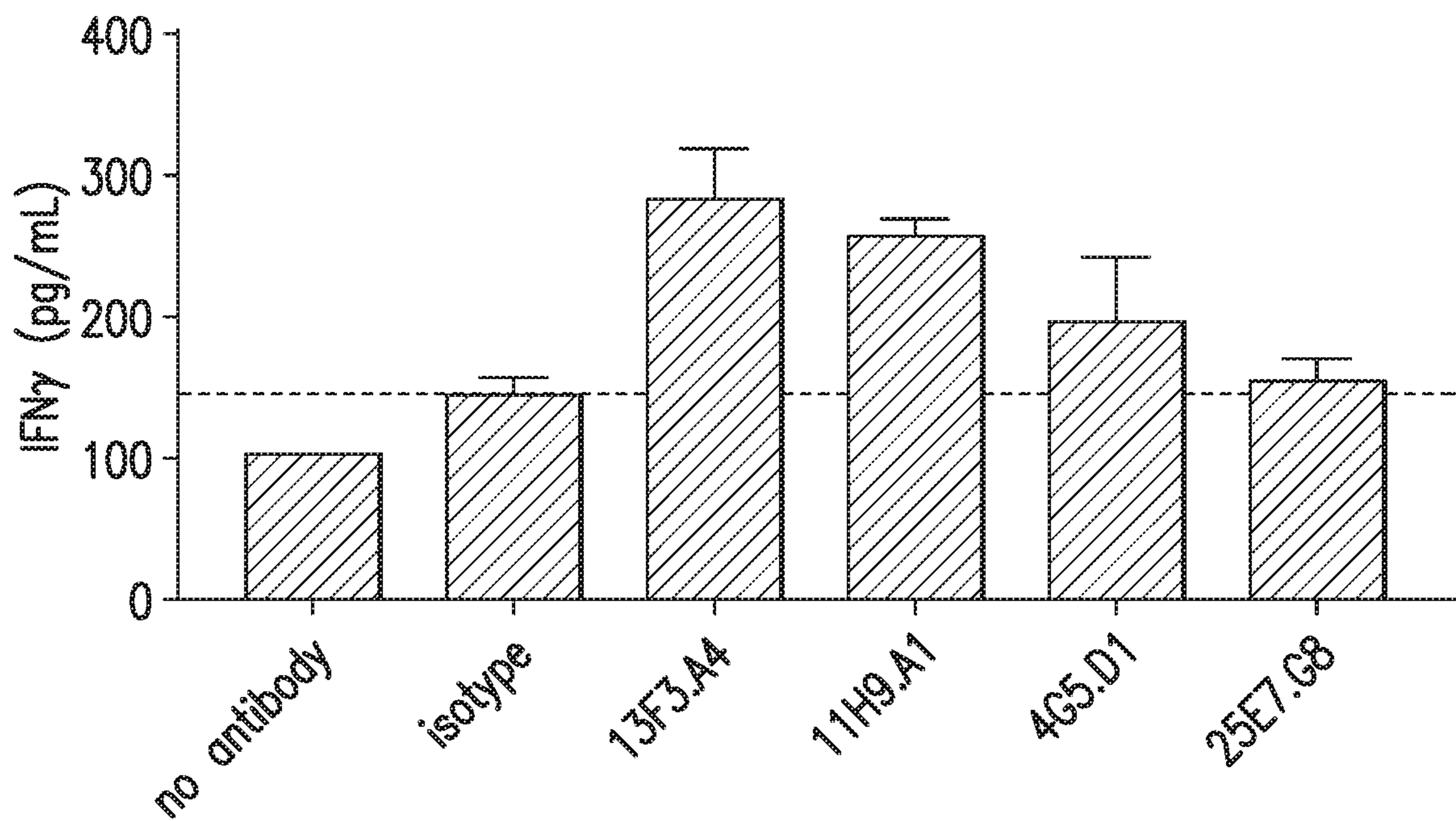
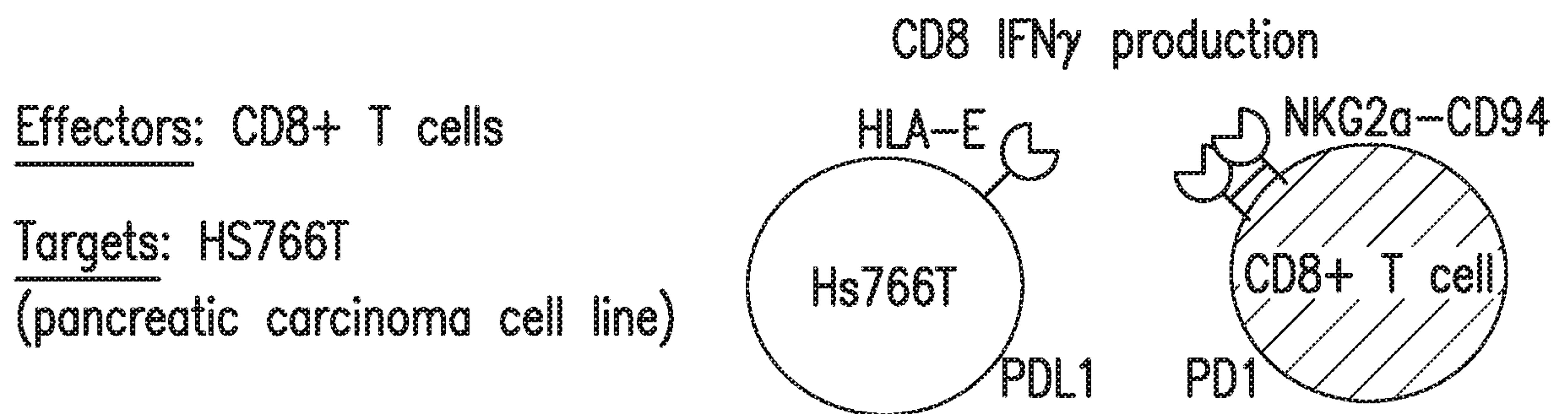
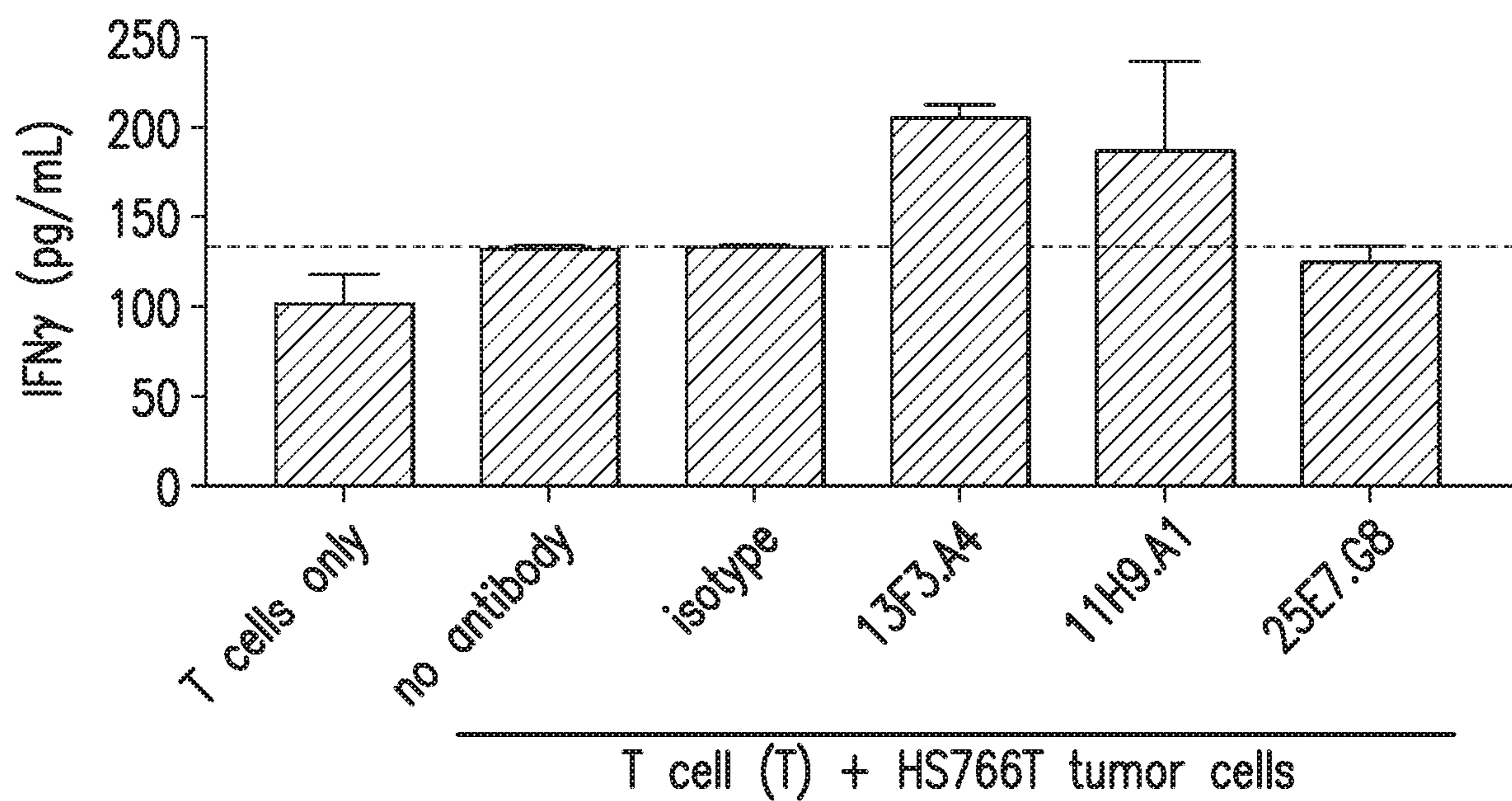


FIG.26B

Anti-NKG2A Antibodies Enhanced CD8+ T Cell Response of Increased IFN γ Production

**FIG.27A**

Anti-NKG2A Antibodies Enhanced CD8+ T Cell Response of Increased IFN γ Production

**FIG.27B**

Differential Hydrogen/Deuterium Exchange--Mass Spectrometry (HDX--MS) Analysis of
mFc--hNKG2A--hCD94 upon interaction with NKG2A.9 Antibody

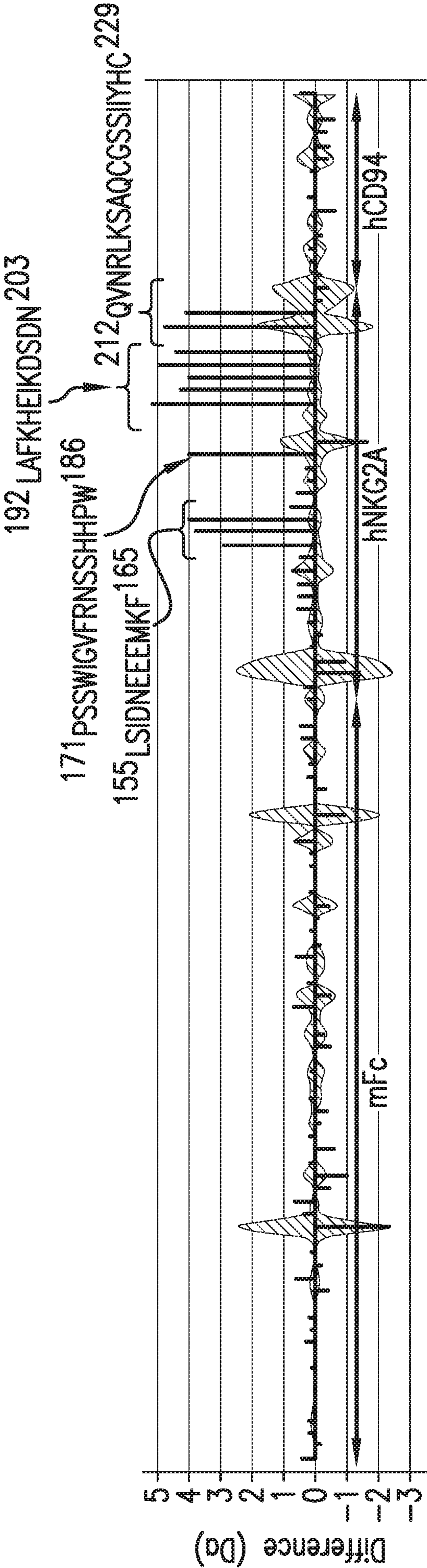


FIG. 28A

Differential HDX-MS Analysis of mFc-NKG2A-CD94 upon interaction with 13F3.A4 Antibody

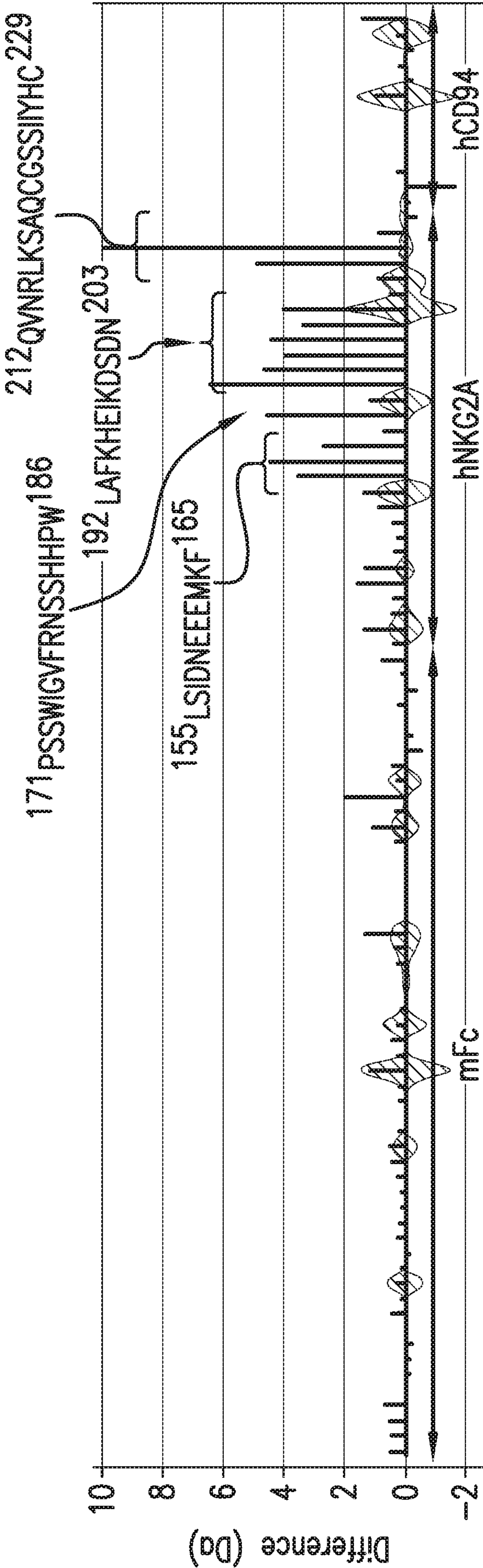


FIG. 28B

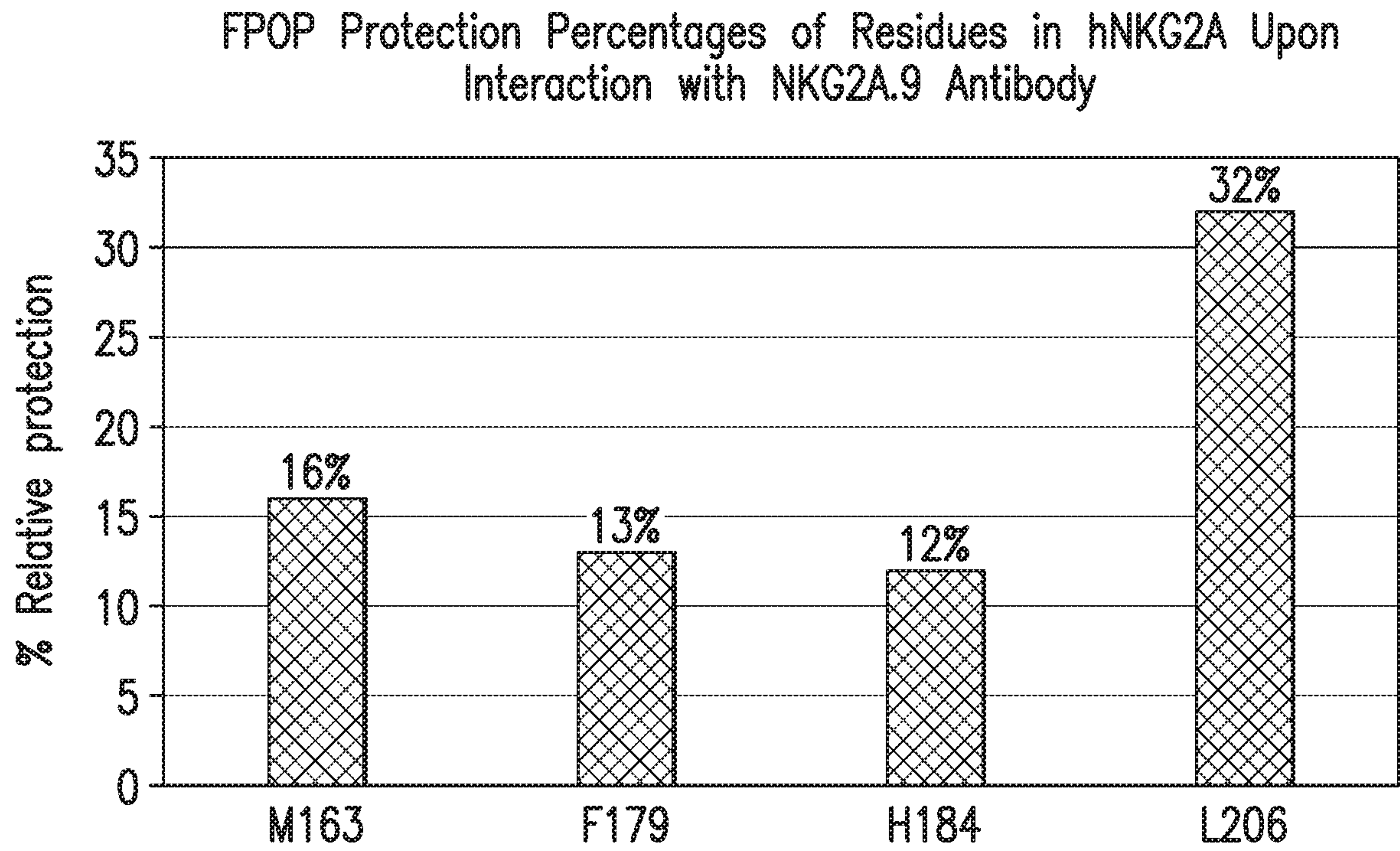


FIG.29A

FP0P Protection Percentages of Residues in hNKG2A Upon
Interaction with 13F3.A4 Antibody

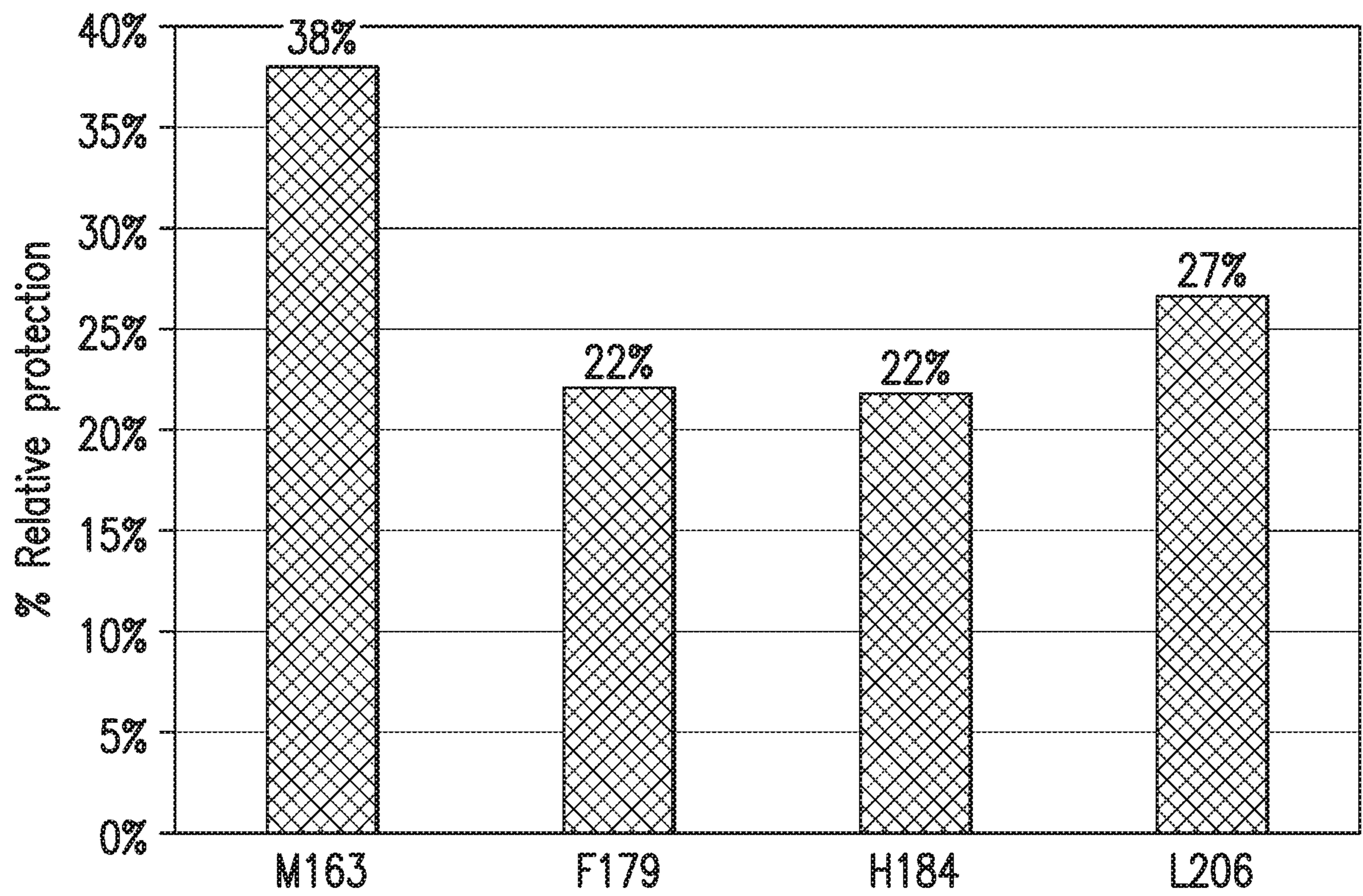


FIG.29B

Epitope of 13F3.A4 and NKG2A.9	HDX	EPOP
	BOLD	

Linker amino acid sequence

VPRDSGSKPSISTVPEVSSVFIFPPKPKDVLITITLTPKVTCTVVDISKDDPEVQFSW

FVDDVEVHTAQTPREEQENSTFRSVSELPIMHQDWLNGKEFKCRVNSAAFPAPI

EKTISKTKGRPKAPQVYTIPPPKEQMAKDQVSLTCMITDFFPEDITVEWQWNGQ

PAENYKNTQIMDTDGSYFVYSKLNQKSNWEAGNTFTCSVLHEGLHNNHHTK

SLSHSPGKASIEGRCGHCPEEWITYSNSCYIIGKERRTWEESLLACTSKNSSLLSI

DNEEFKFLSIISPSWIGVGRNSSHPWVTMNGLAFKHEIKDSDNAEINCAVLQ

VNRLKSAQCGSSIYHCKHKLGGSGSCCSCQEKWVG YRCNCYFISSEQKTWNE

SRHLCASQKSSLLQLQNTDELDEMSSSQQFYWIGLSYSEHTAWLWENGSA LSQ

YLFPSFETNTKNCIAYNPNGNALDESCEDKNRYICKQQLI

mFc

hNKG2A

hCD94

FIG.30

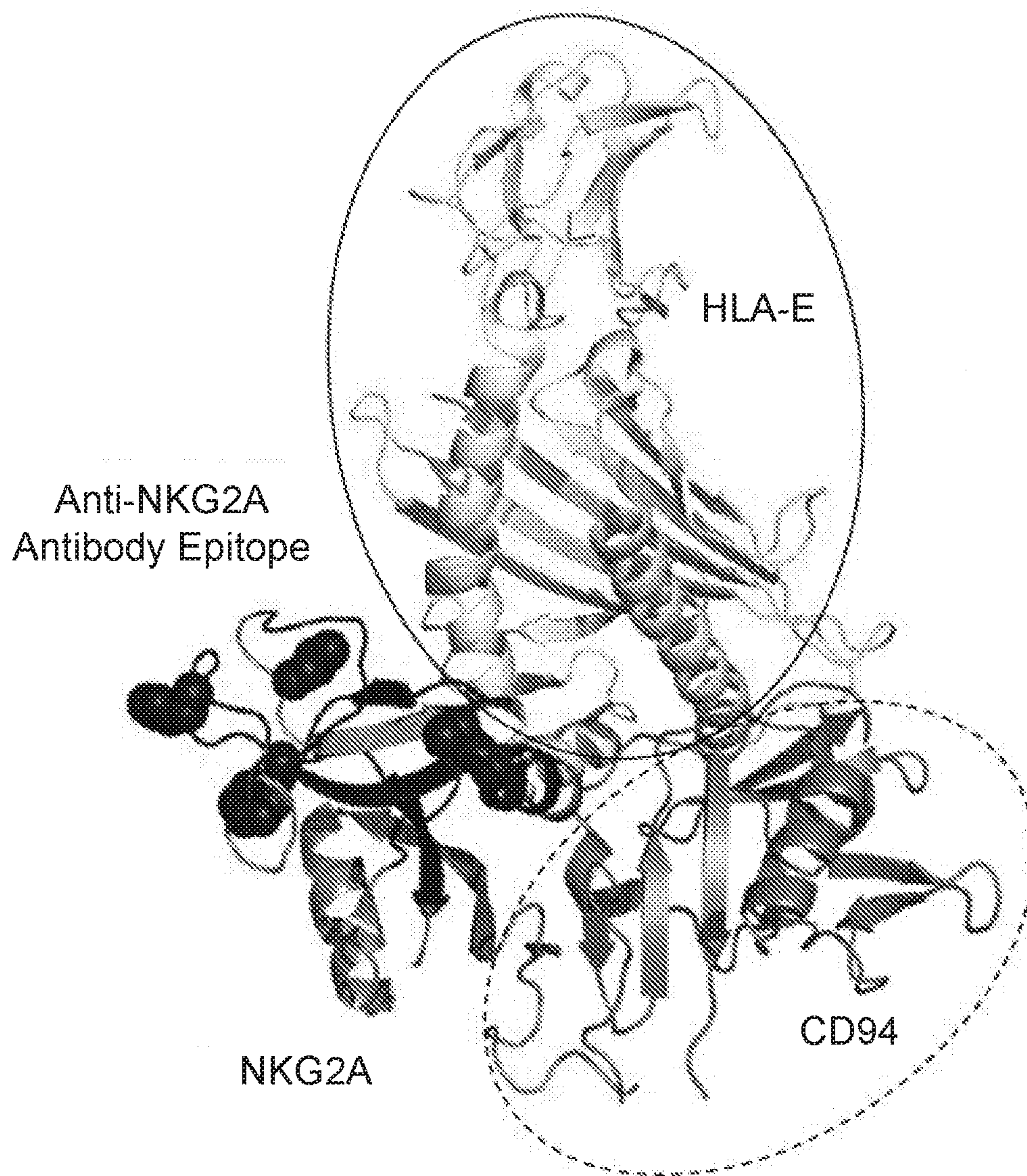


FIG.31

Heavy Chain Variable Region Clustal 2.1 Alignment of Anti-NKG2A Antibodies

	FR1	CDR1	FR2	CDR2	
13F3	EVQLVESGGGLVKPGGSLRLSCAASGFTFS	SHSMNWVRQAPGKLEWVSA	ISSSSYIYYADSVKG	66	
NKG2a.9	EVQLVESGGGLVKPGGSLRLSCAASGFTFS	SHSMNWVRQAPGKLEWVSA	ISSSSYIYYADSVKG	66	
NKG2a.11	EVQLVESGGGLVKPGGSLRLSCAASGFTFS	SHSMNWVRQAPGKLEWVSA	ISSSSYIYYADSVKG	66	
	*****	*****	*****	*****	
	FR3	CDR3	FR4		
13F3	RFTISRDNAKNSLYLQMNSLRAEDTAVYYCAREEWGLPFDYW	QGILTVSS	118		
NKG2a.9	RFTISRDNAKNSLYLQMNSLRAEDTAVYYCAREEWGLPFDYW	QGILTVSS	118		
NKG2a.11	RFTISRDNAKNSLYLQMNSLRAEDTAVYYCAREEWGLPFDYW	QGILTVSS	118		
	*****	*****	*****	*****	

FIG.32A

NKG2A.9 Reversed the Inhibition of NK-KB Signaling in NKG2A-Expressing Jurkat Cells Stimulated by CHO/scOKT3/HLA-E

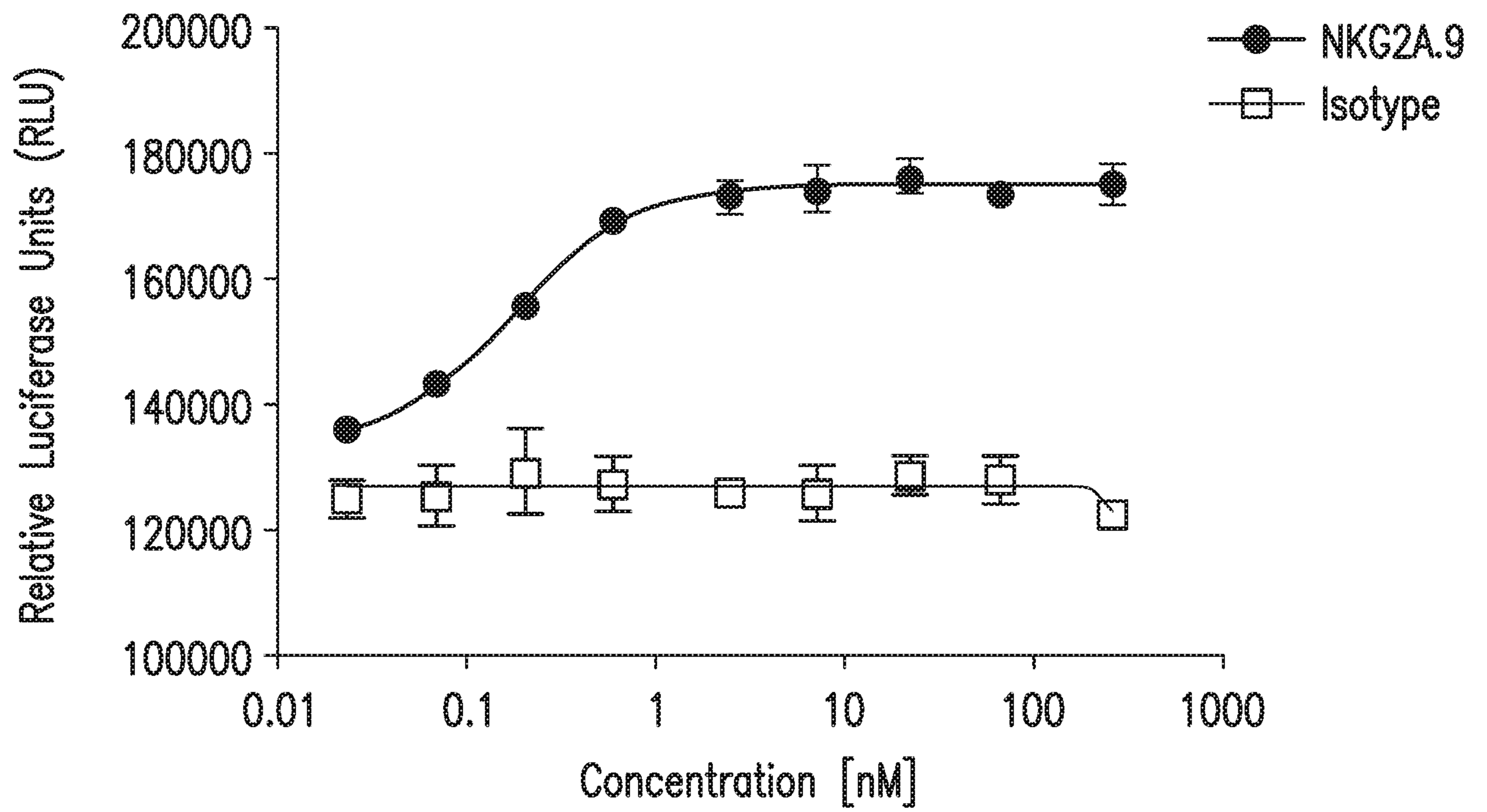


FIG.33

NKG2A.9 and Anti-PD-L1 Antibodies Enhanced IFN- γ Induction by NKG2A⁺ CD8 T Cells Co-cultured with CHO/scOKT3/HLA-E/PD-L1

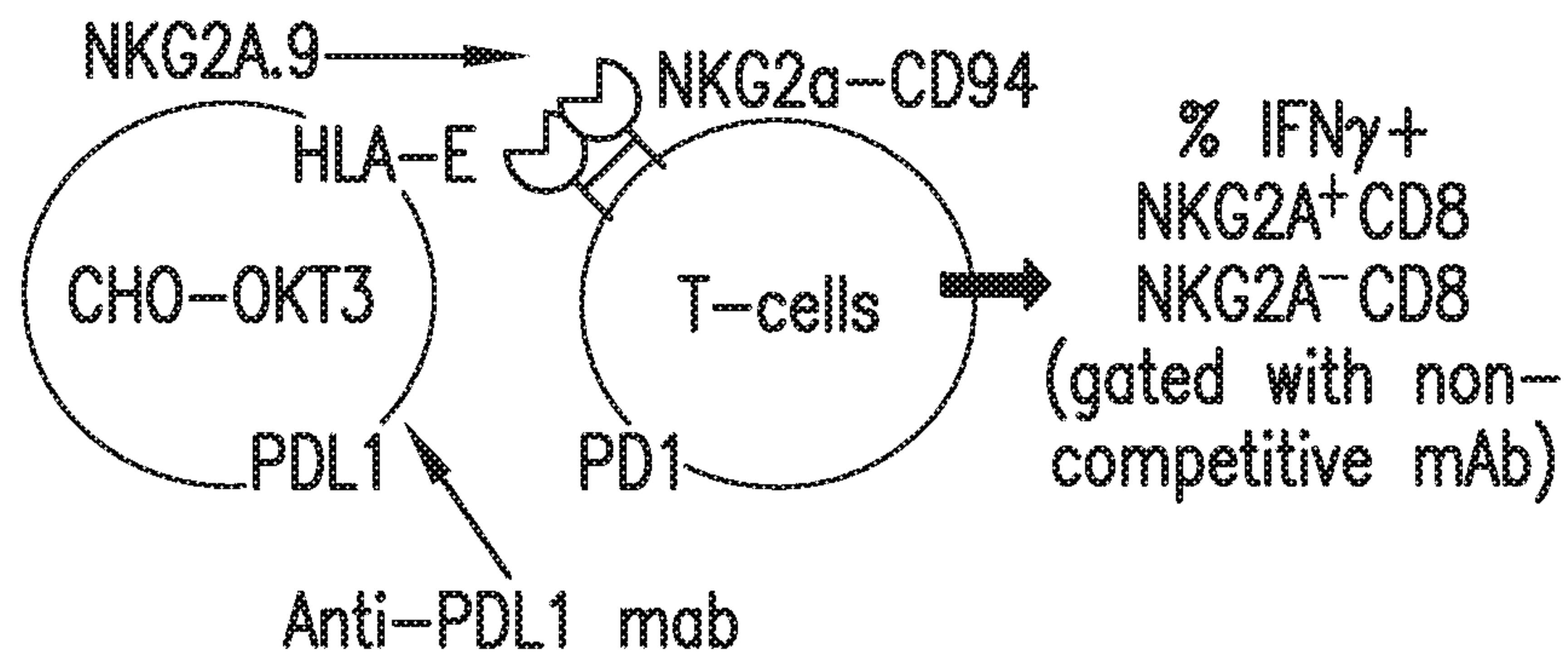


FIG.34A

NKG2A.9 and Anti-PD-L1 Antibodies Enhanced IFN- γ Induction by NKG2A⁺ CD8 T Cells Co-cultured with CHO/scOKT3/HLA-E/PD-L1

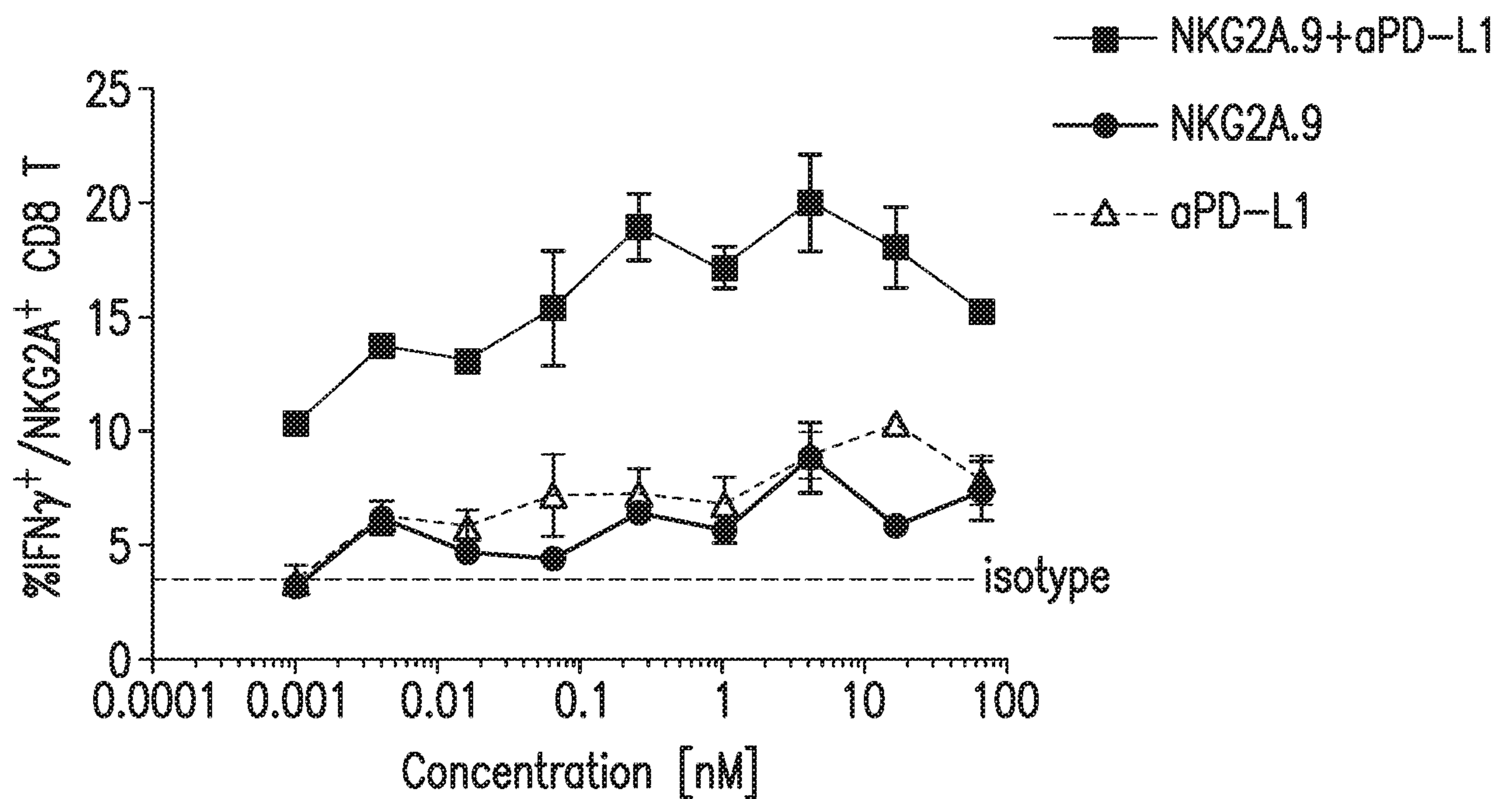


FIG.34B

NKG2A.9 and anti-PD-L1 Antibodies Enhanced IFN- γ
Production by Tumor Infiltrating NKG2A⁺ CD8⁺ T Cells
Co-cultured with CHO/scOKT3/HLA-E/PD-L1

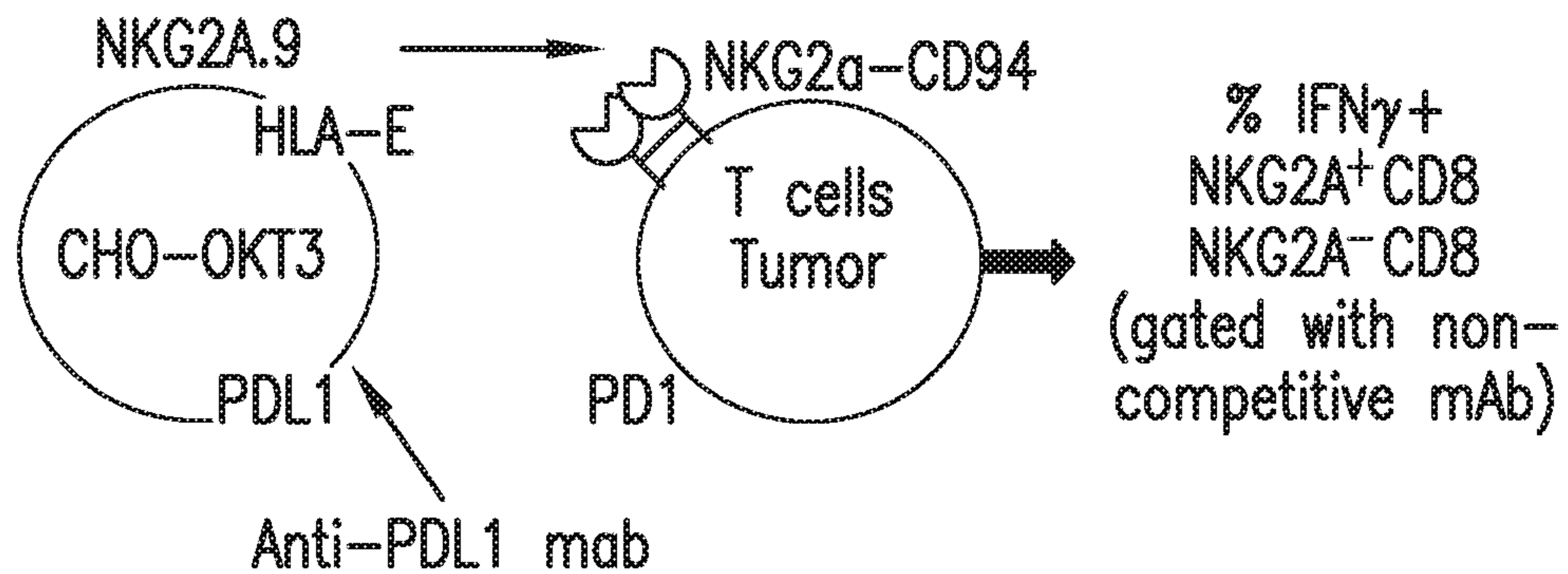
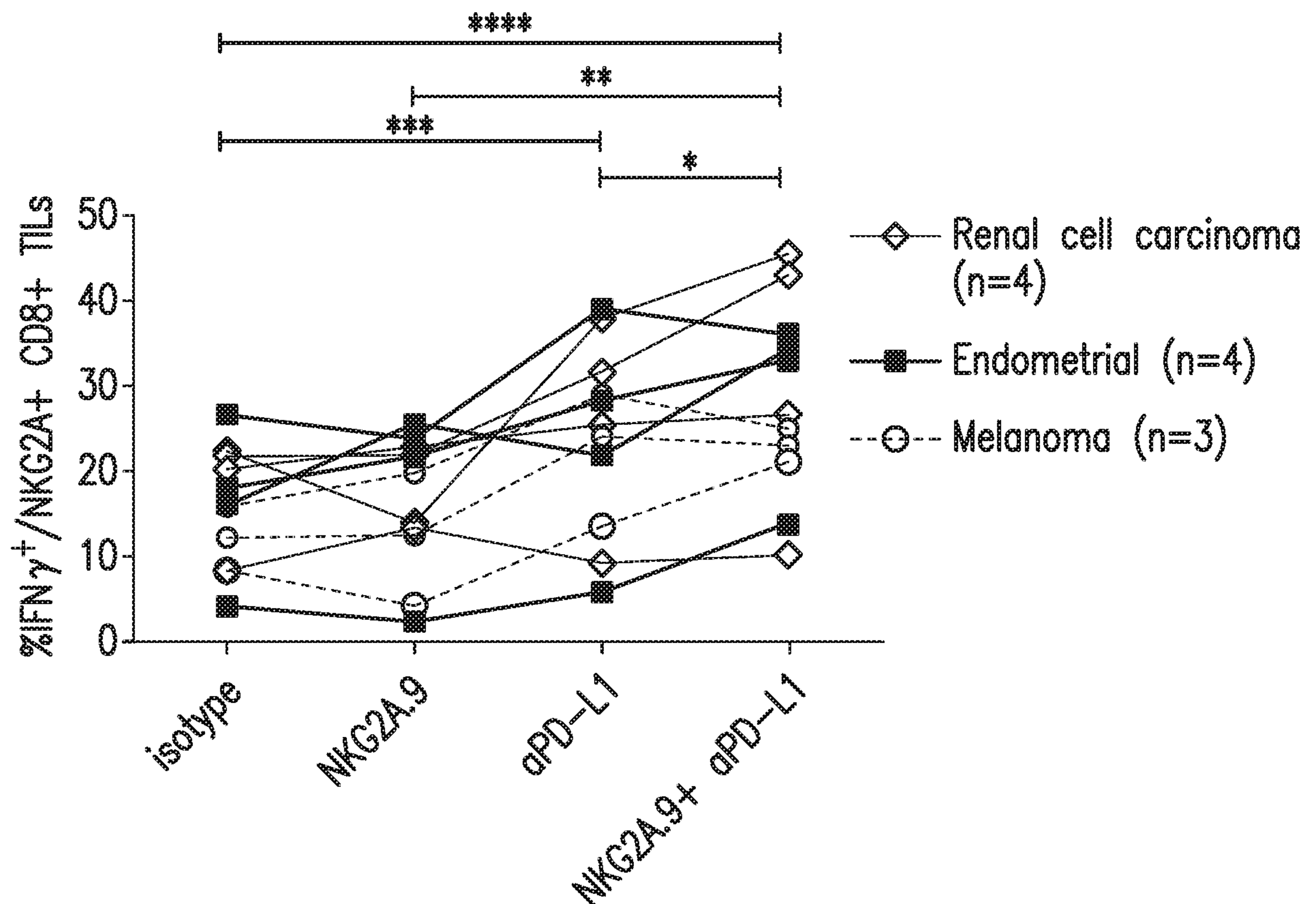


FIG.35A



Paired t test ****p<0.0001, ***p<0.0005, **p<0.005, *p<0.05

— Represents comparison of groups

FIG.35B

NKG2A.9 Antibody Was Internalized After Binding to NKG2A-expressing Cells

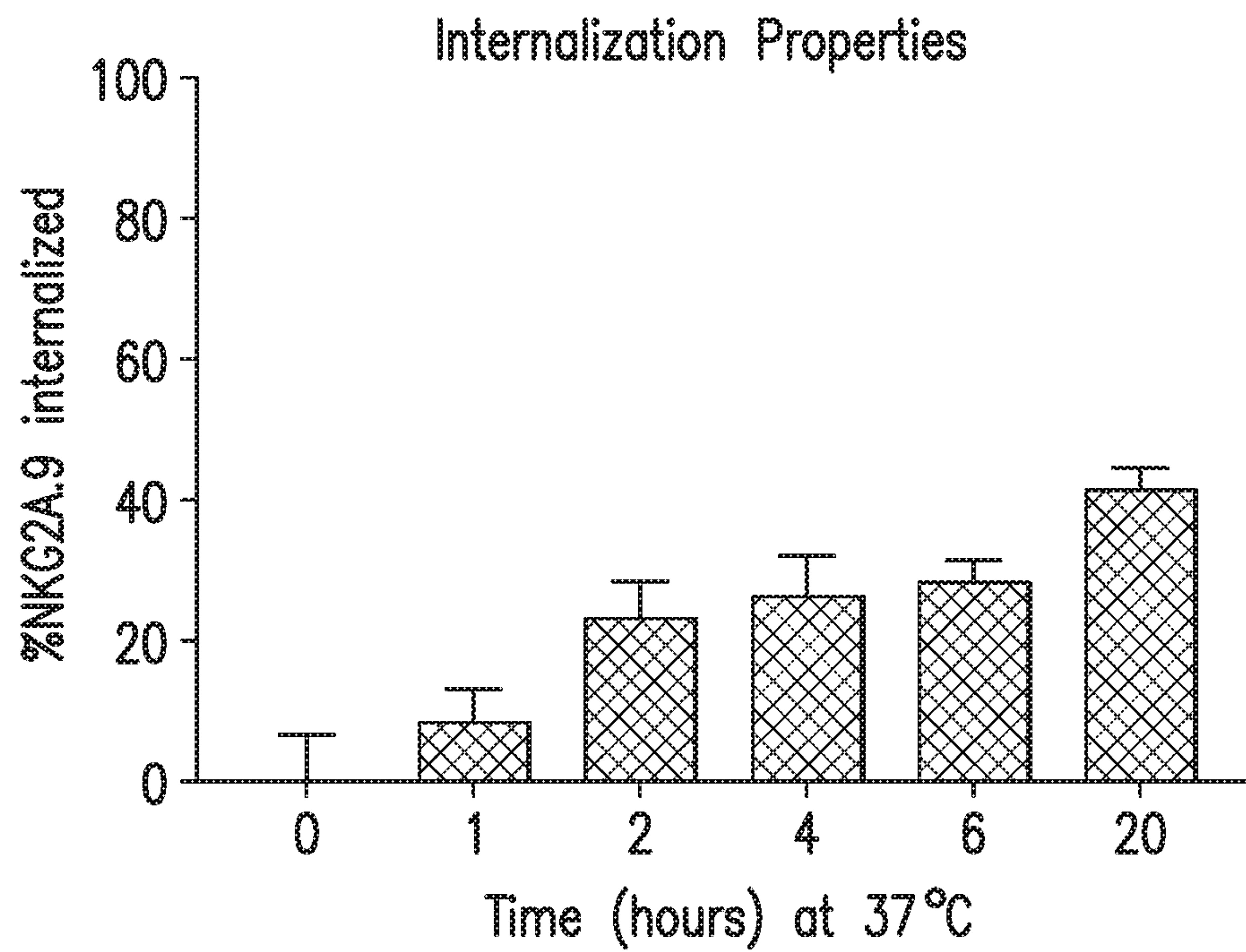


FIG.36A

NKG2A.9 Antibody Was Internalized After Binding to NKG2A-expressing Cells

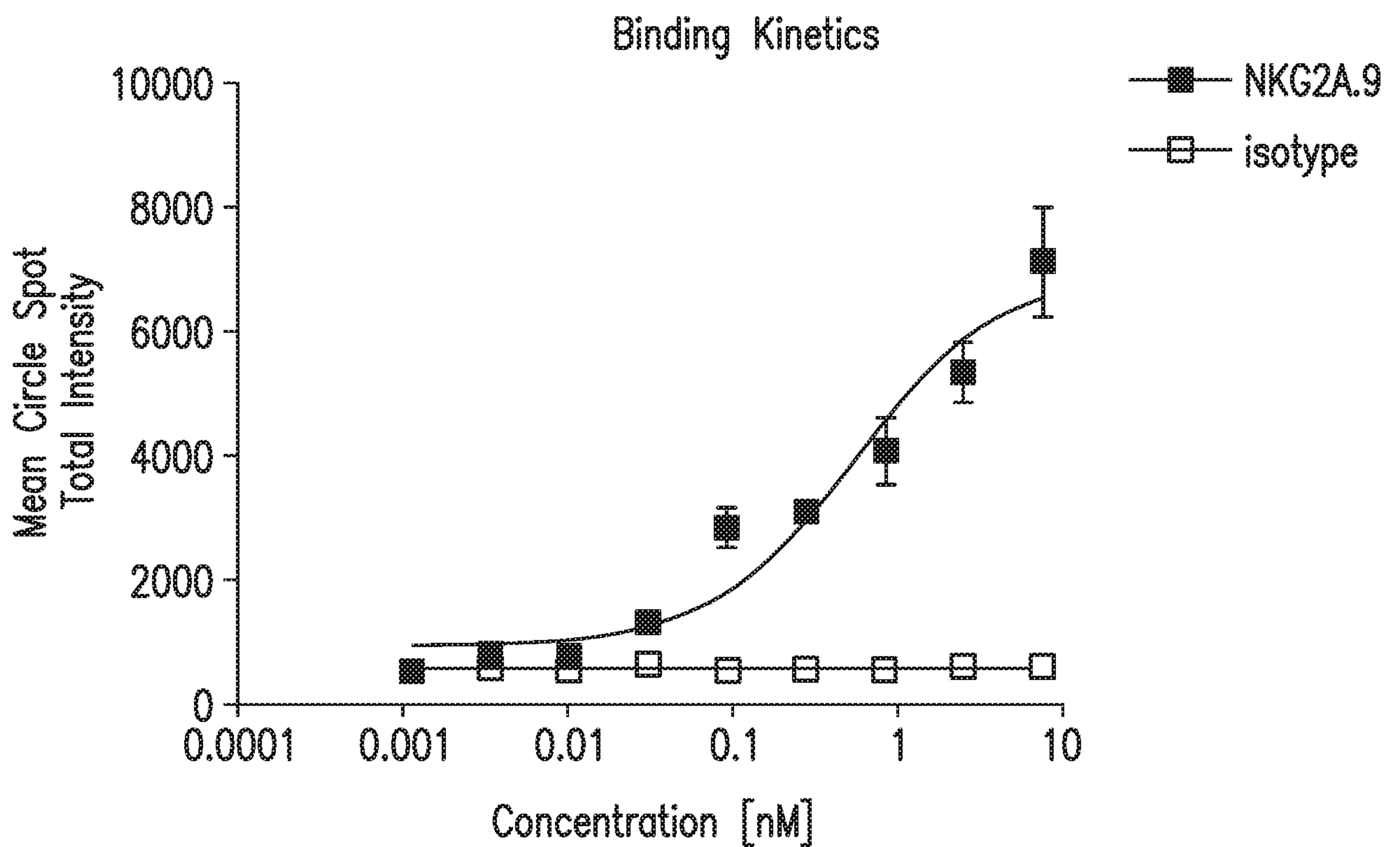


FIG.36B

NKG2A.9 Antibody Enhanced NK Cell Degranulation and Lysis of HLA-E Expressing Head and Neck Tumor Cells

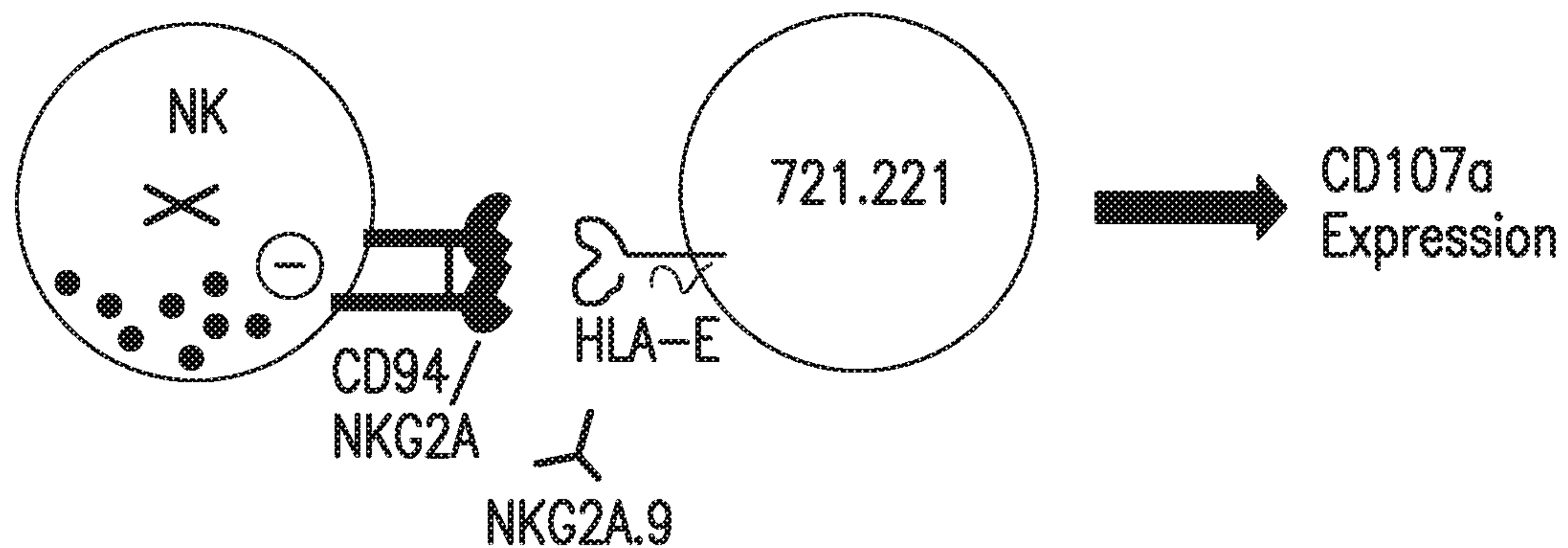


FIG.37A

NKG2A.9 Antibody Enhanced NK Cell Degranulation and Lysis of HLA-E Expressing Head and Neck Tumor Cells

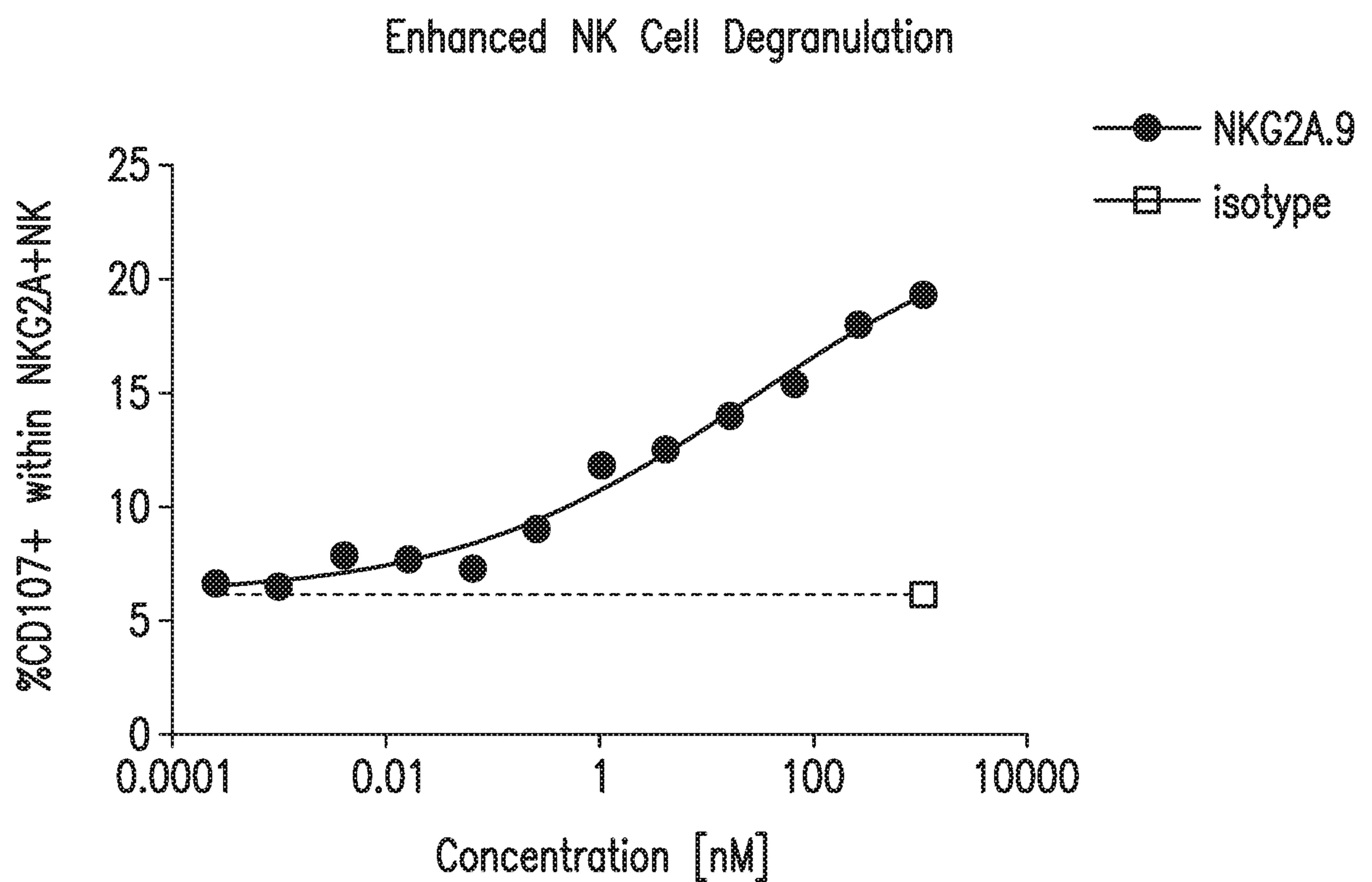


FIG.37B

NKG2A.9 Antibody Enhanced NK Cell Degranulation and Lysis of HLA-E Expressing Head and Neck Tumor Cells

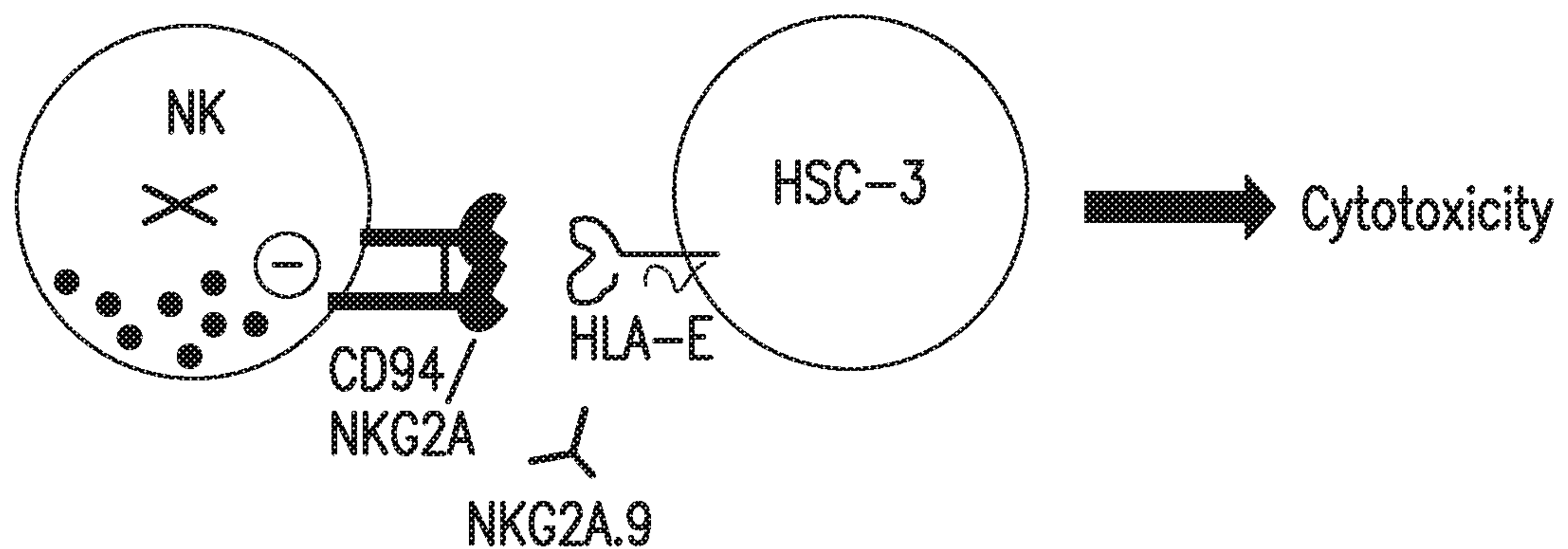


FIG.37C

NKG2A.9 Antibody Enhanced NK Cell Degranulation and Lysis of HLA-E Expressing Head and Neck Tumor Cells

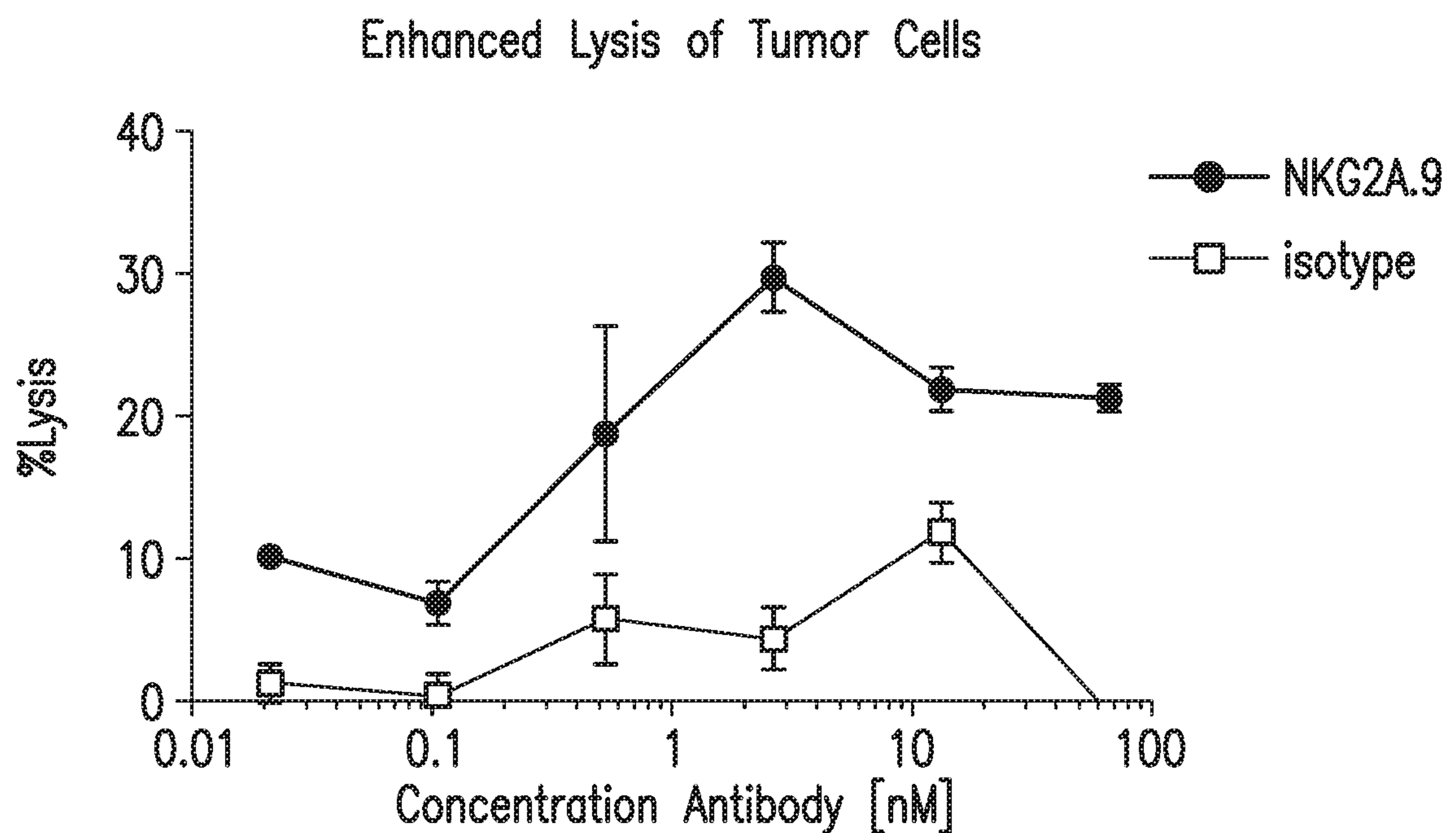


FIG.37D

13F3.A4 Antibody Enhanced the Functional Activity of Natural Killer Cells

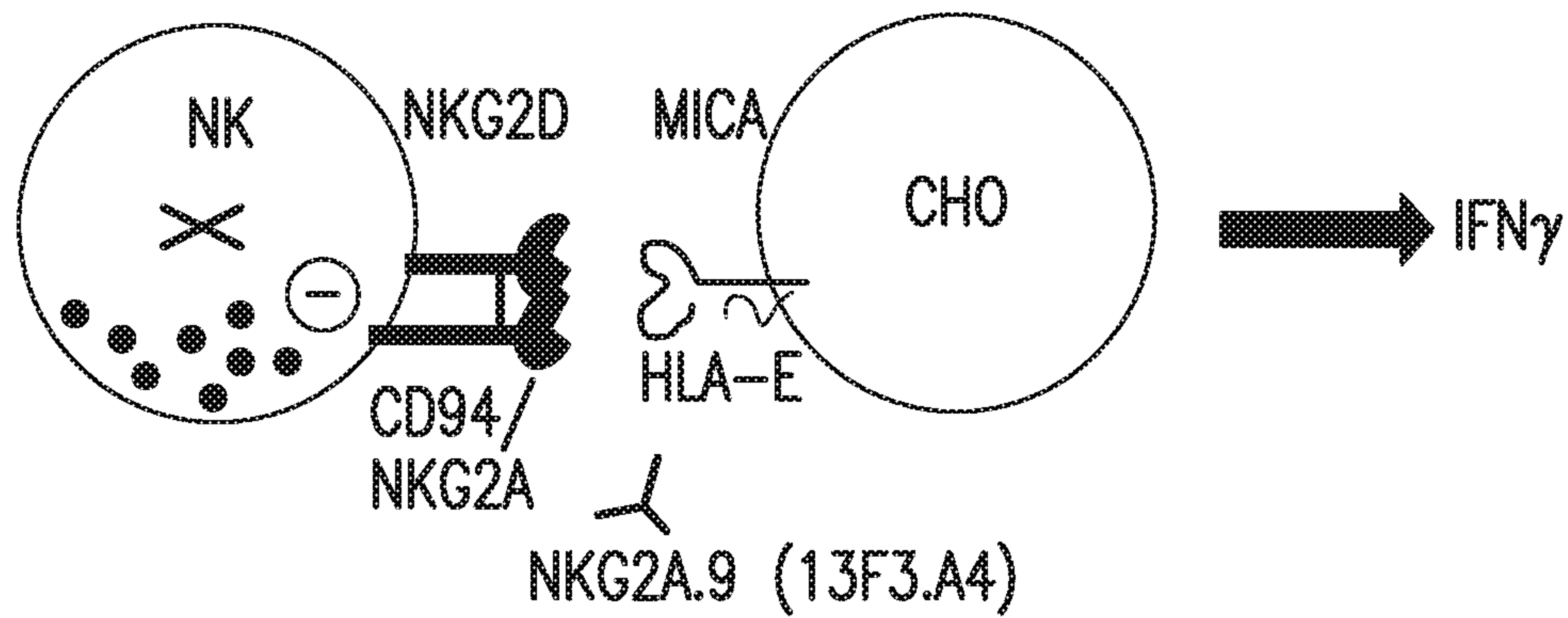


FIG.38A

13F3.A4 Antibody Enhanced the Functional Activity of Natural Killer Cells

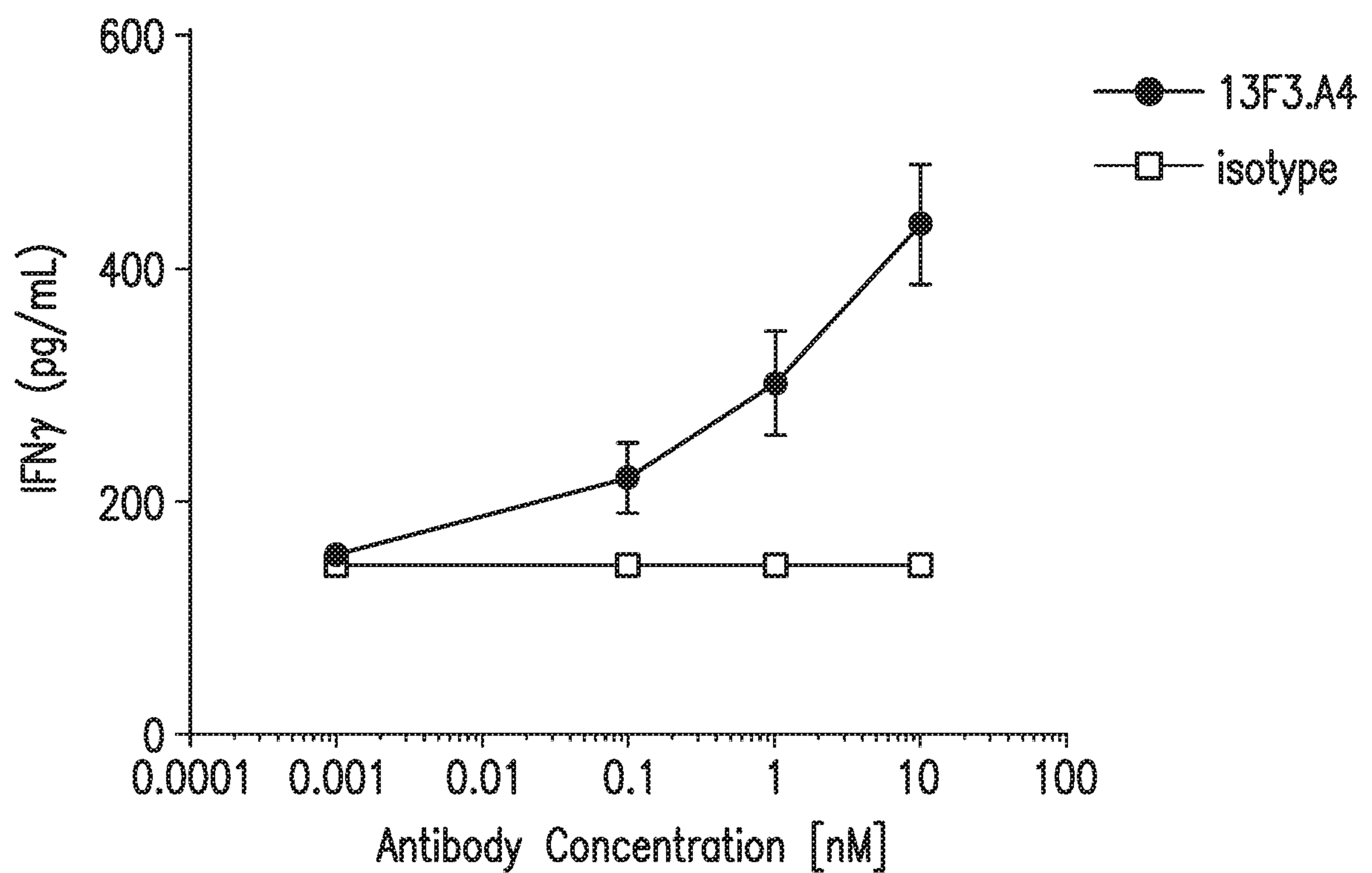


FIG.38B

Anti-mNKG2A Antibody Monotherapy Inhibited Tumor Growth
in the CT26 Colon Carcinoma Tumor Model

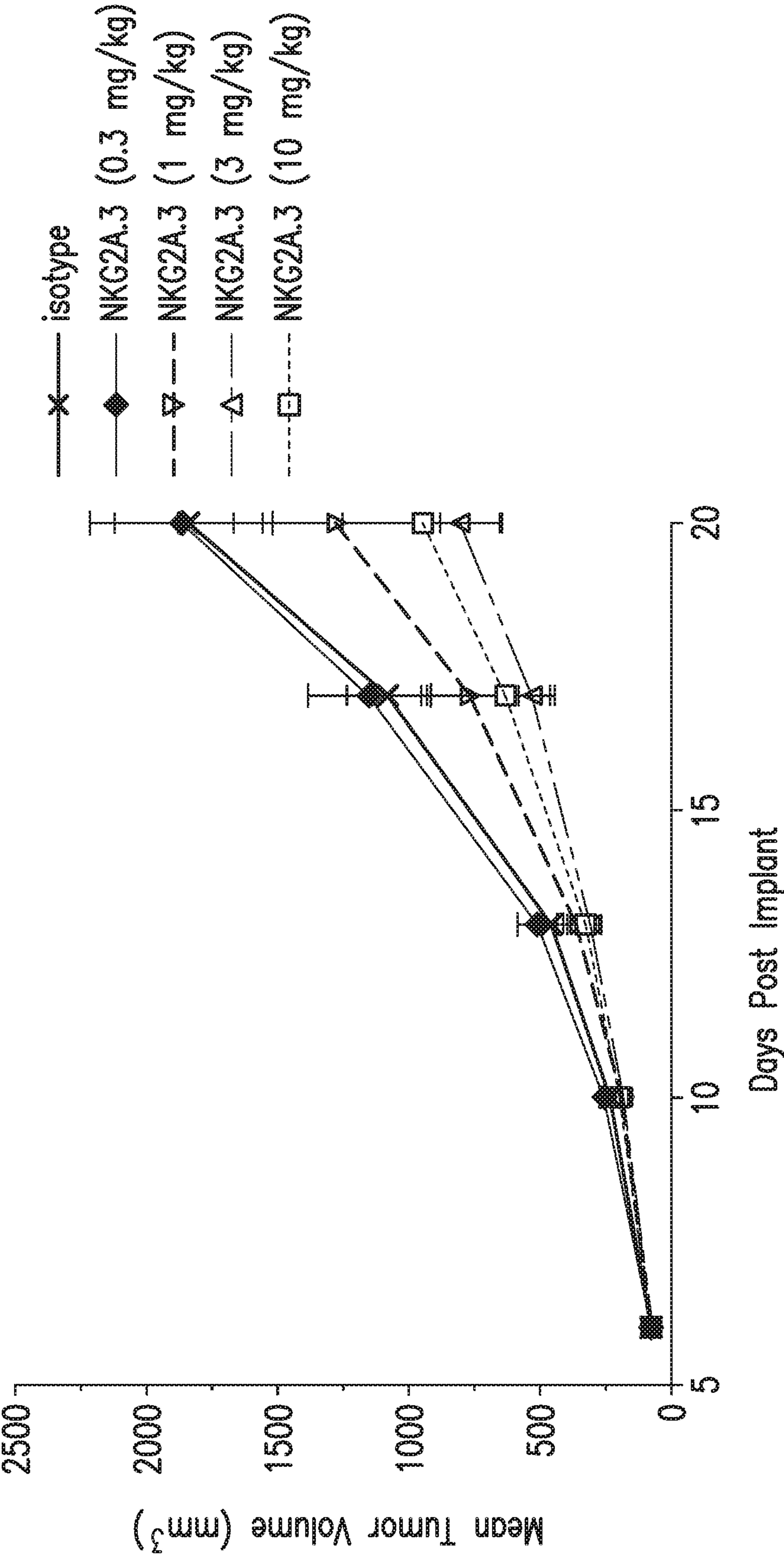


FIG. 39

Combination of Anti-mNKG2A and Anti-mPD-1 Antibodies
Reduced Tumor Growth in the CT26 Mouse Model

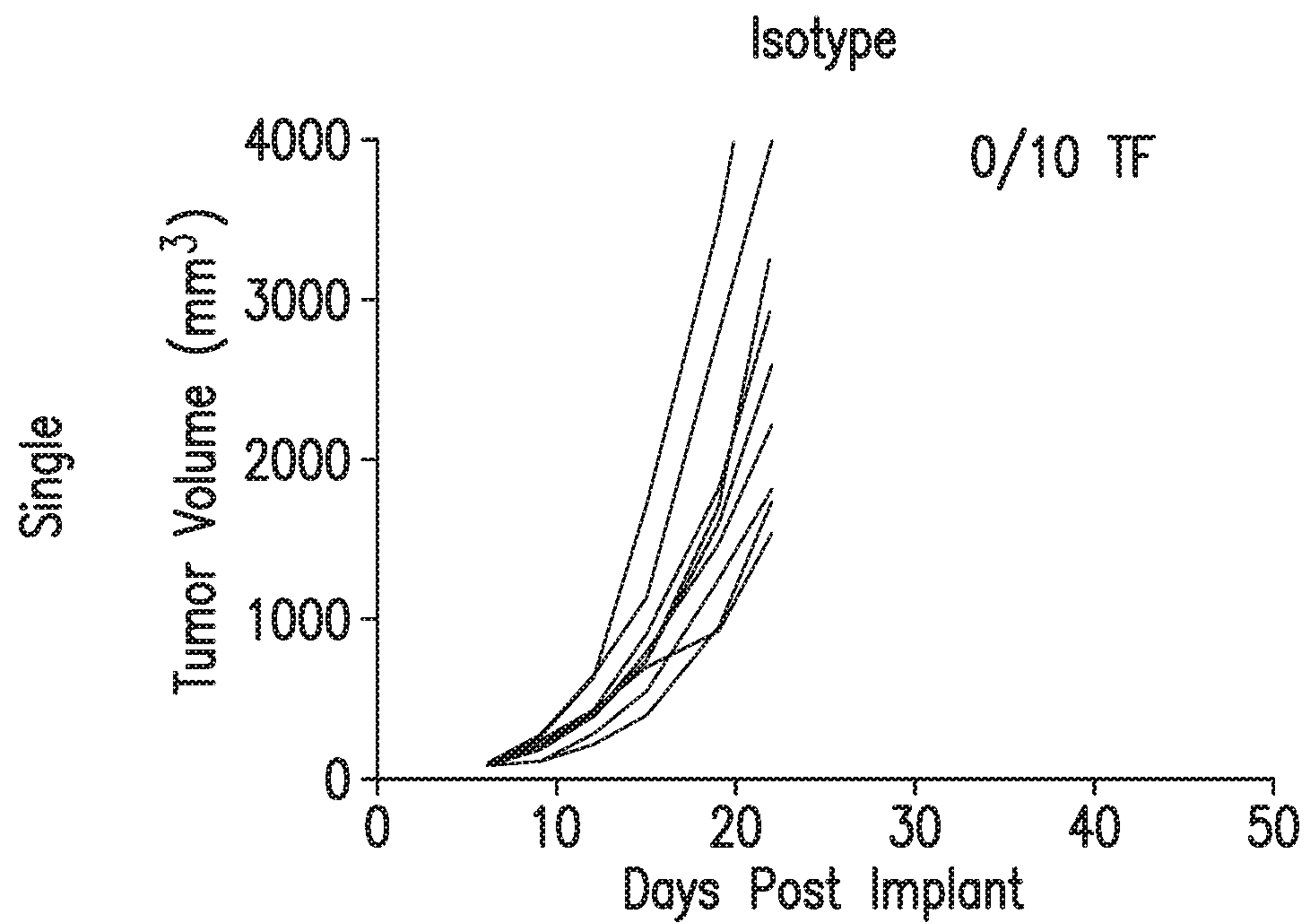


FIG.40A

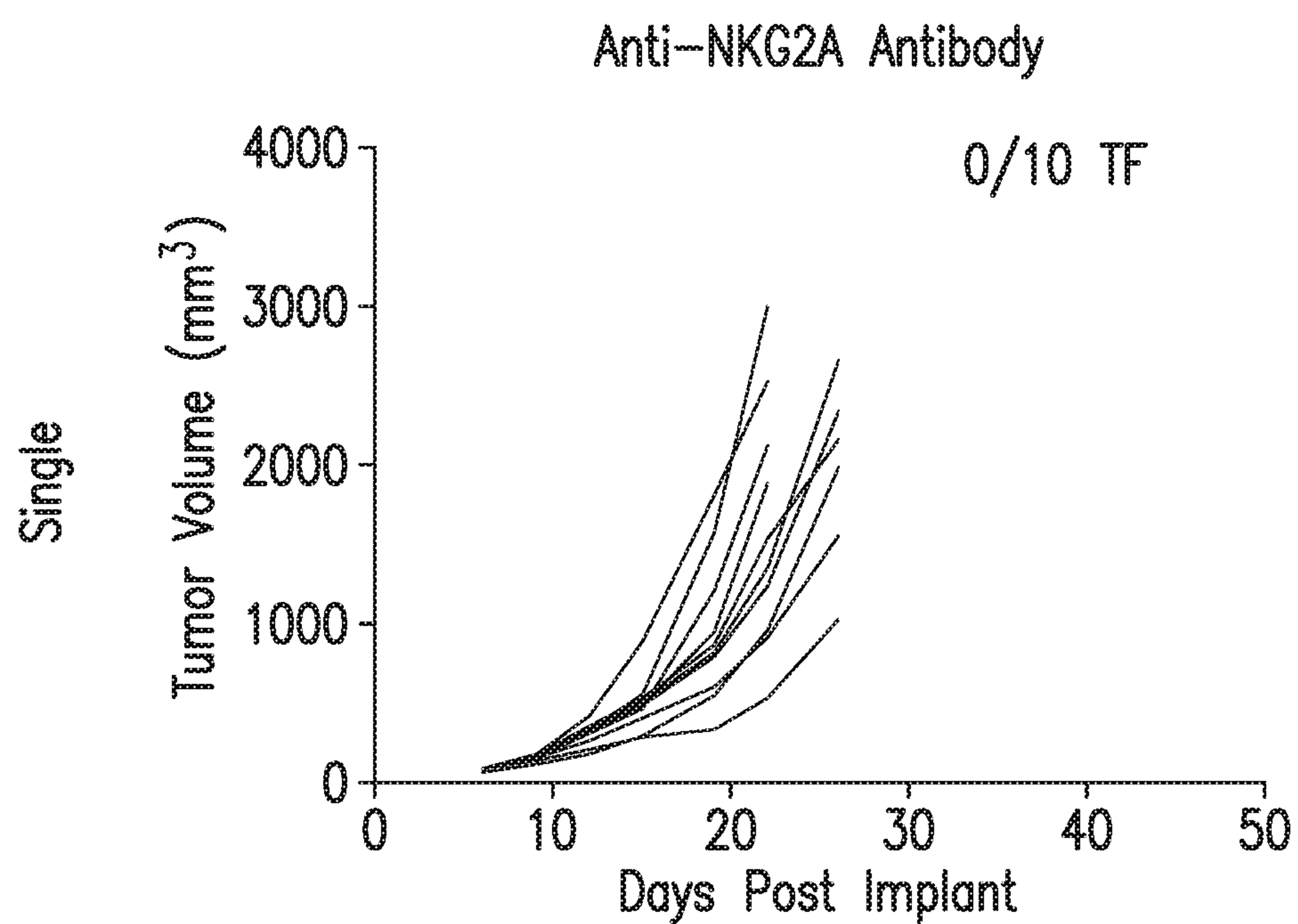


FIG.40B

Combination of Anti-mNKG2A and Anti-mPD-1 Antibodies
Reduced Tumor Growth in the CT26 Mouse Model

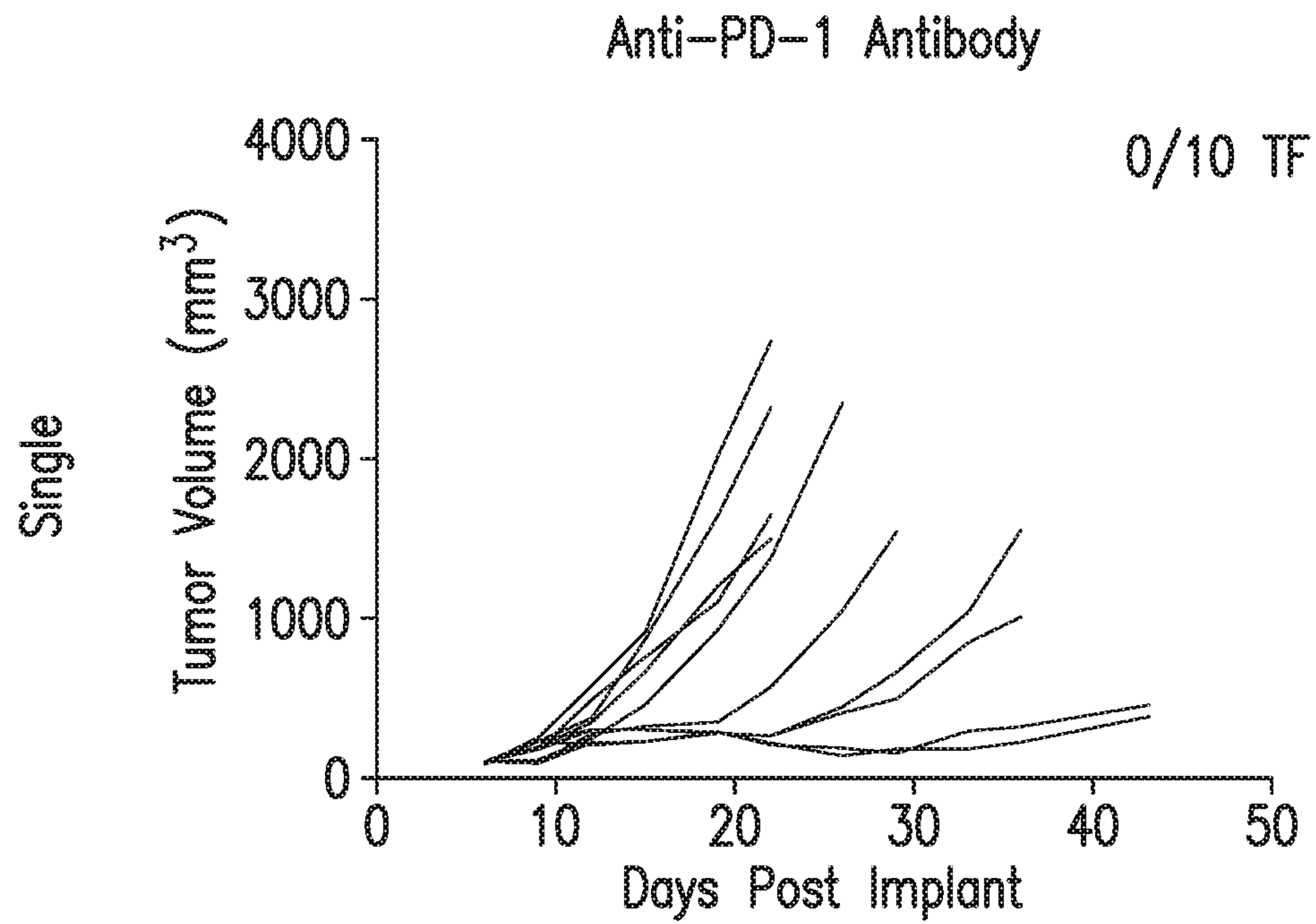


FIG. 40C

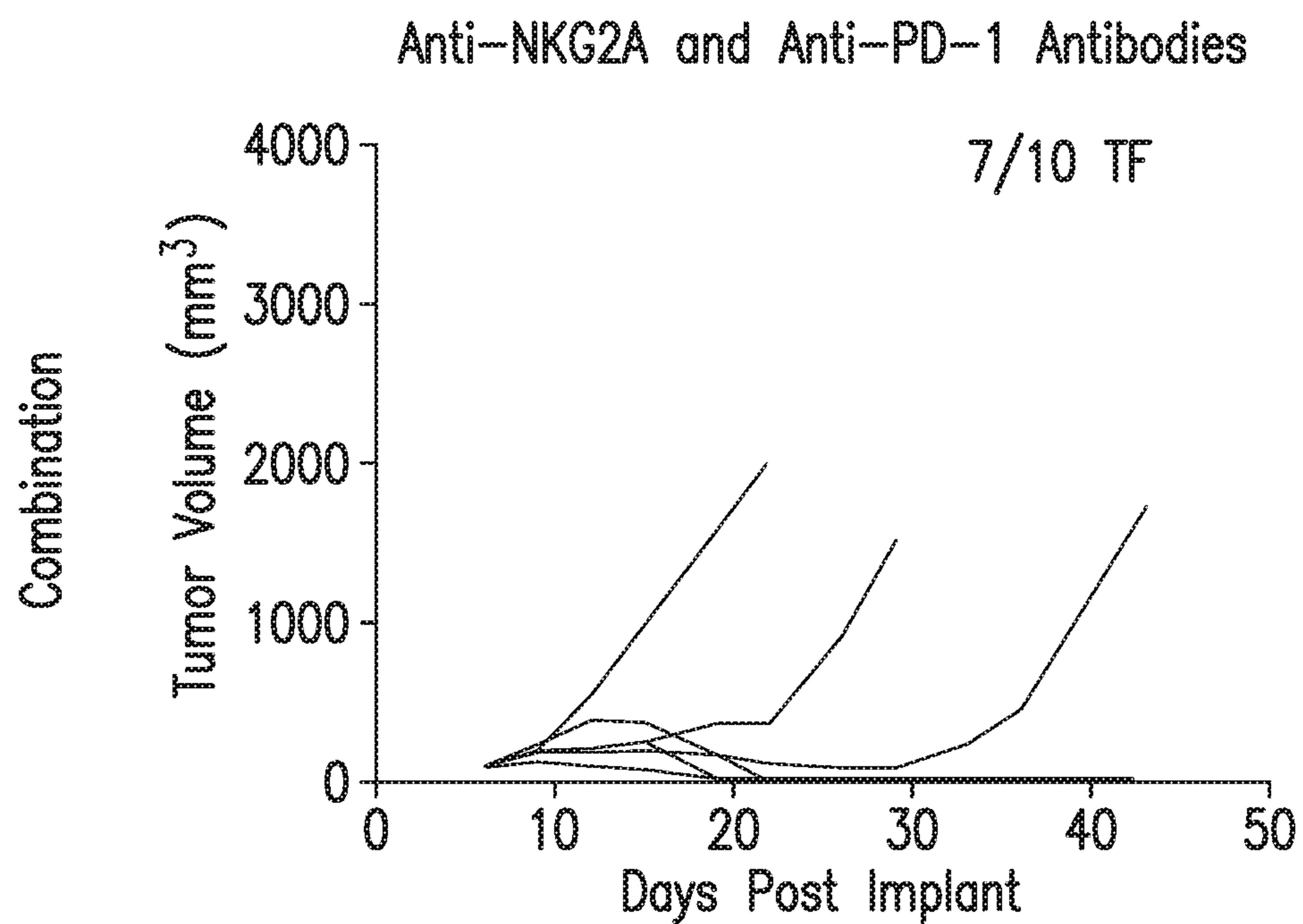


FIG. 40D

Combination of Anti-mNKG2A and Anti-mPD-1 Antibodies
Reduced Tumor Growth in the CT26 Mouse Model

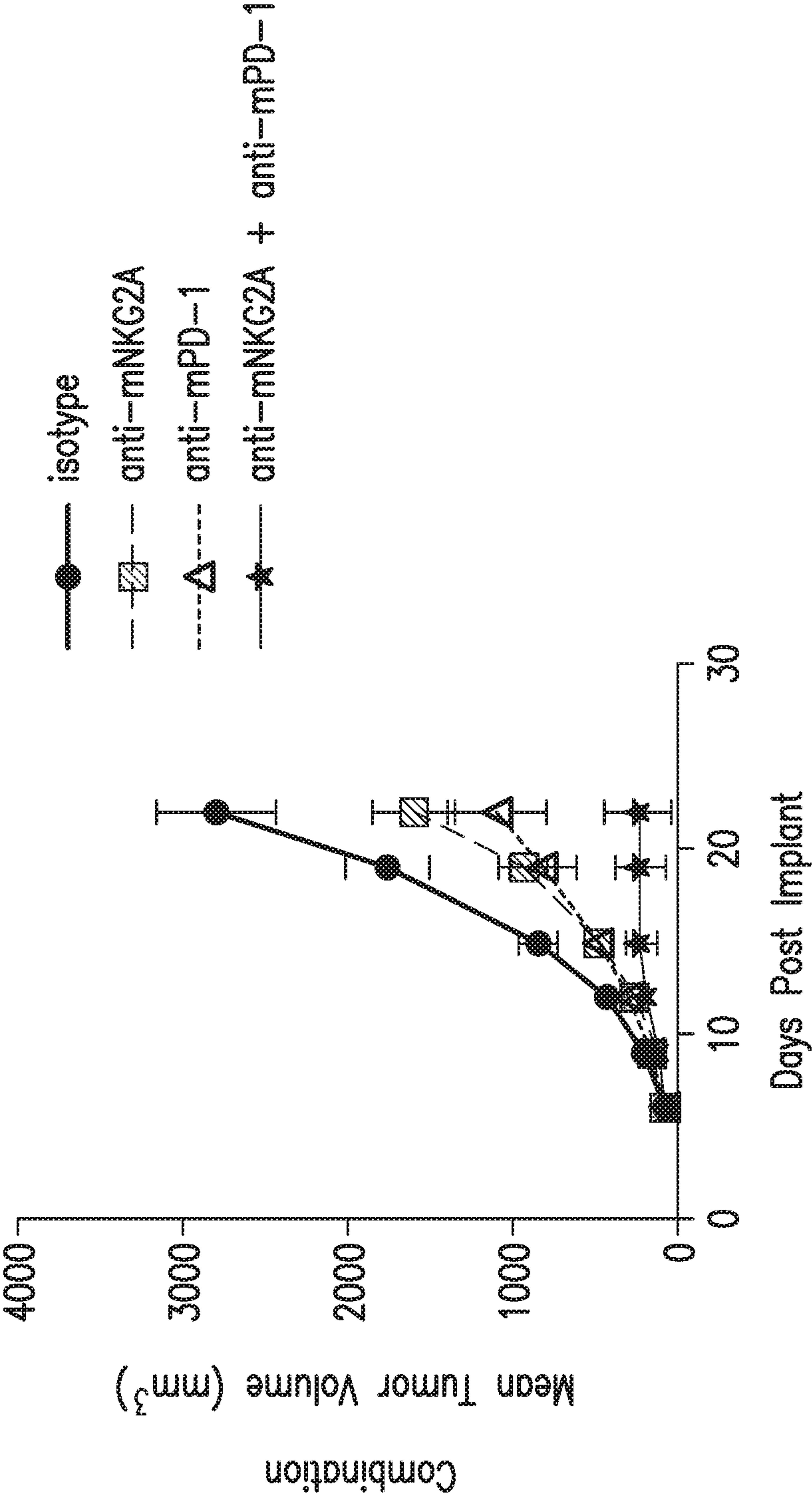


FIG.40E

Anti-mNKG2A and Anti-mPD-1 Antibodies Increased NK and Tumor-specific CD8 T cell Cytotoxicity and IFN- γ in the CT26 Murine Colon Carcinoma

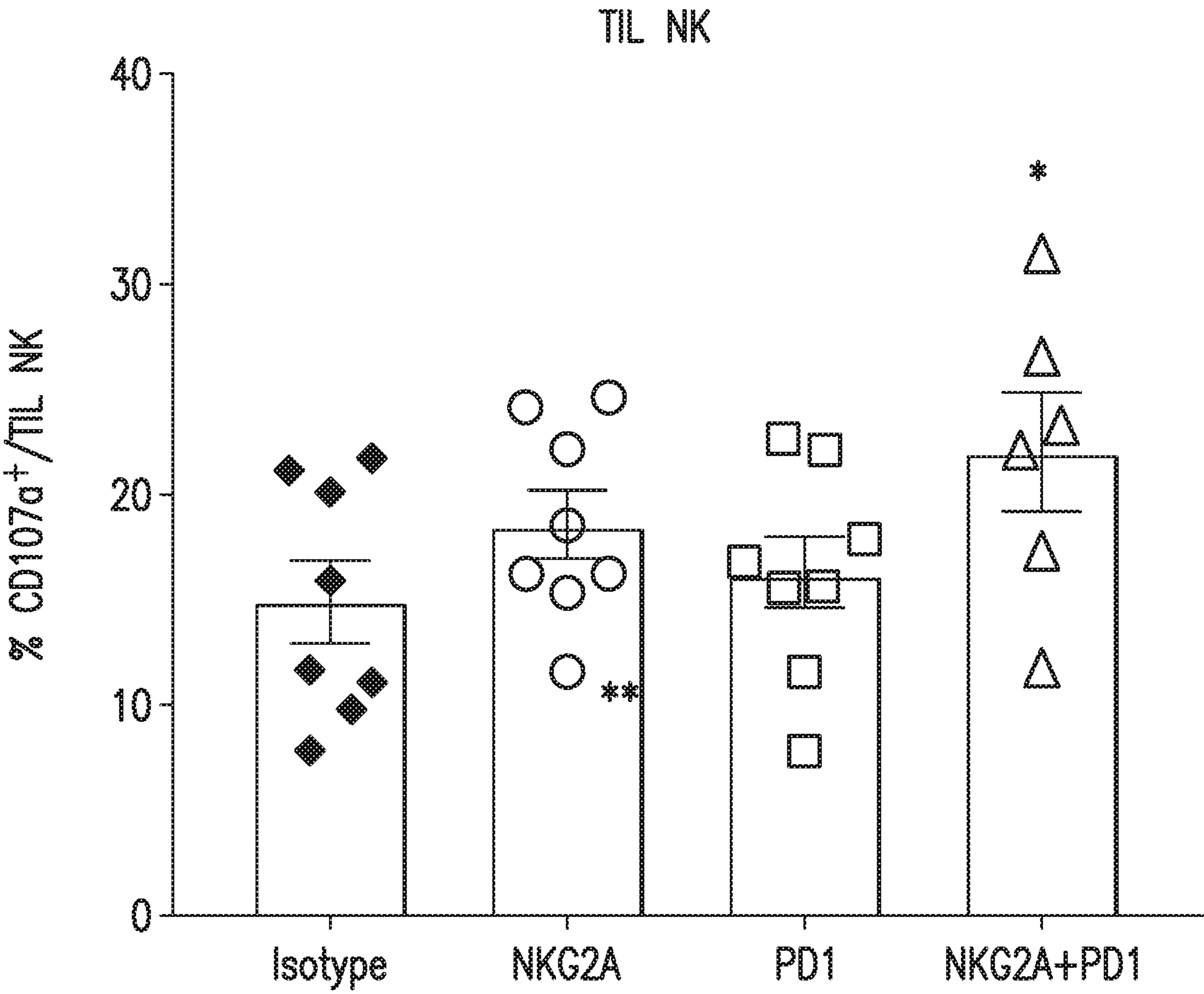


FIG.41A

Anti-mNKG2A and Anti-mPD-1 Antibodies Increased NK and Tumor-specific CD8 T cell Cytotoxicity and IFN- γ in the CT26 Murine Colon Carcinoma

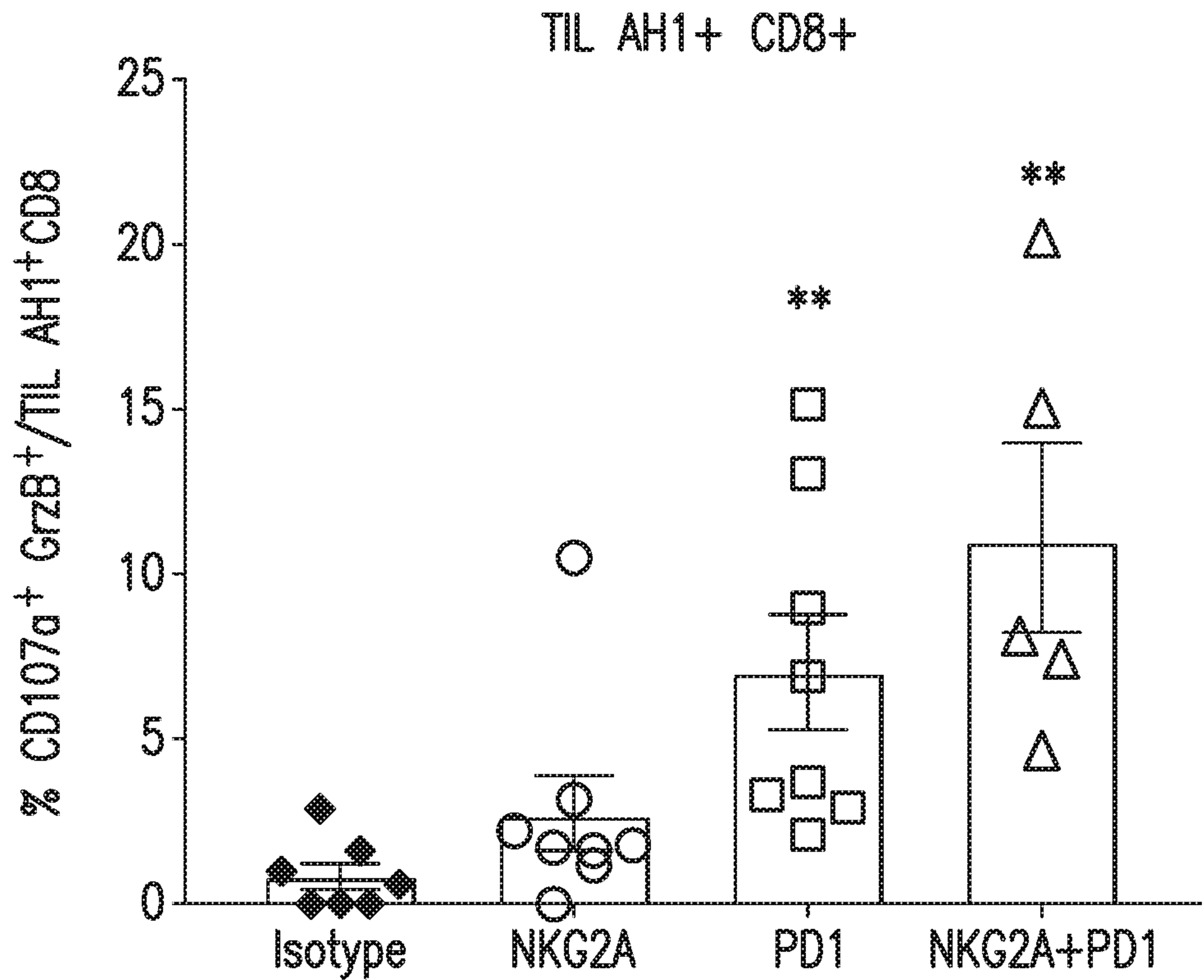


FIG.41B

Anti-mNKG2A and Anti-mPD-1 Antibodies Increased NK and Tumor-specific CD8 T cell Cytotoxicity and IFN- γ in the CT26 Murine Colon Carcinoma

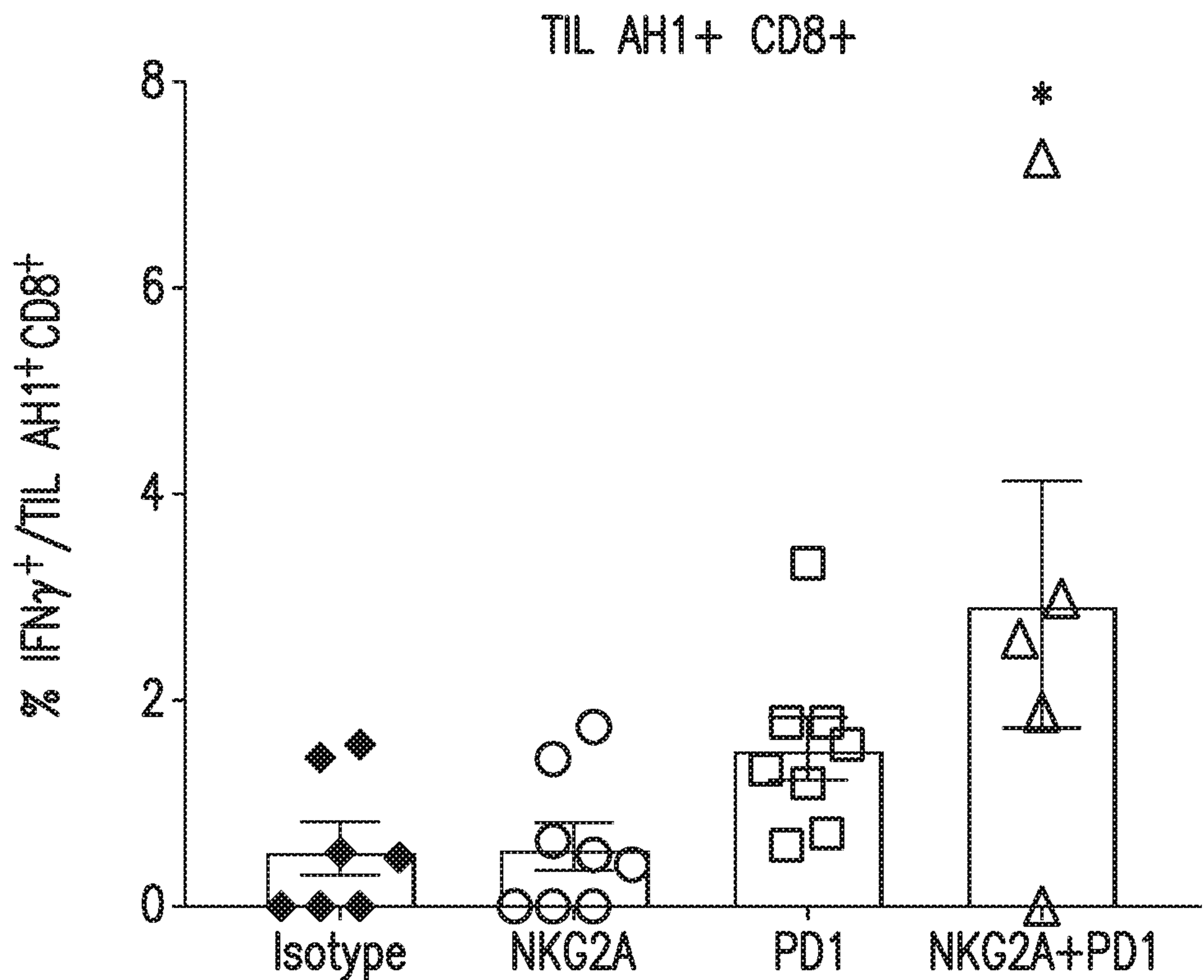


FIG.41C

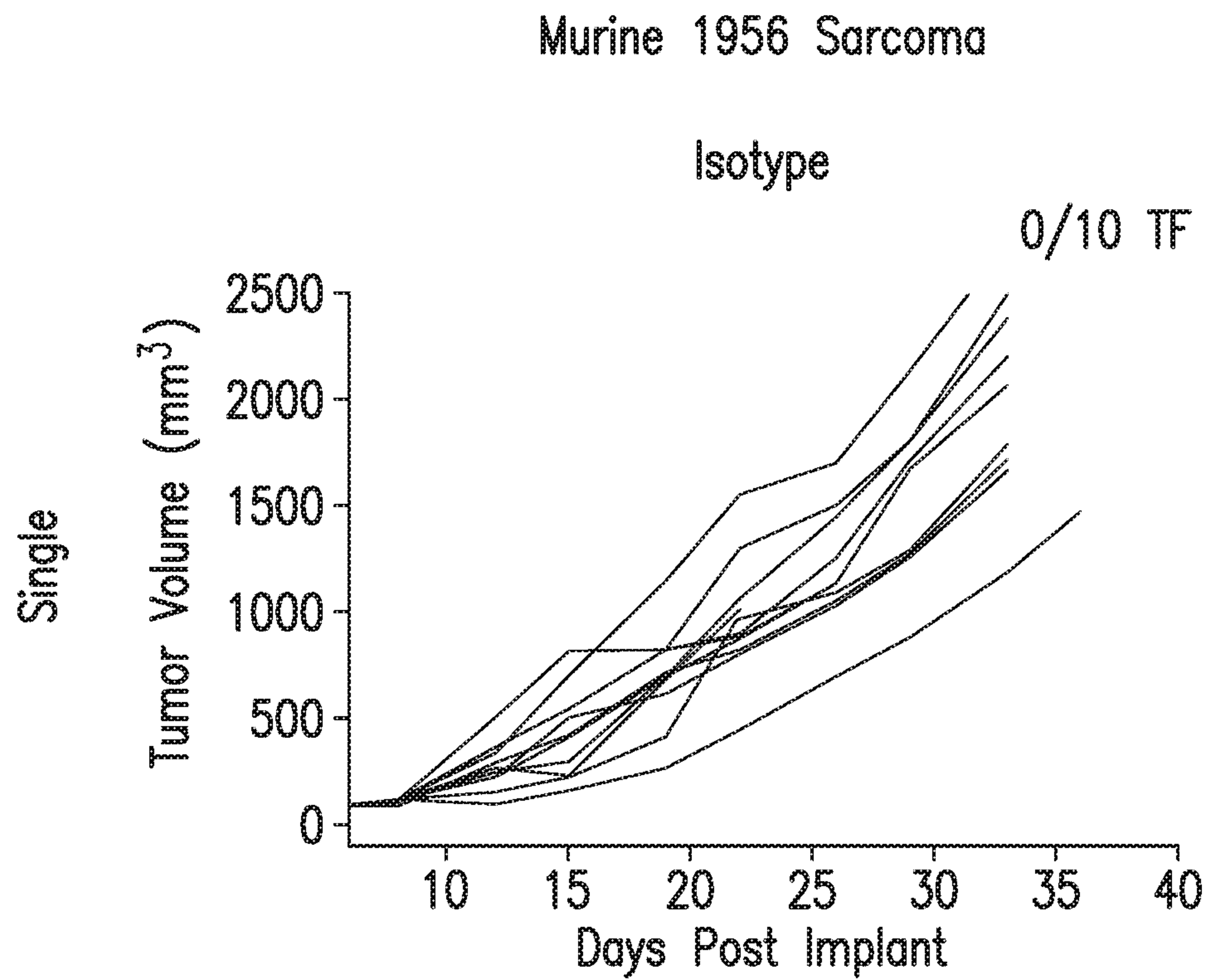


FIG.42A

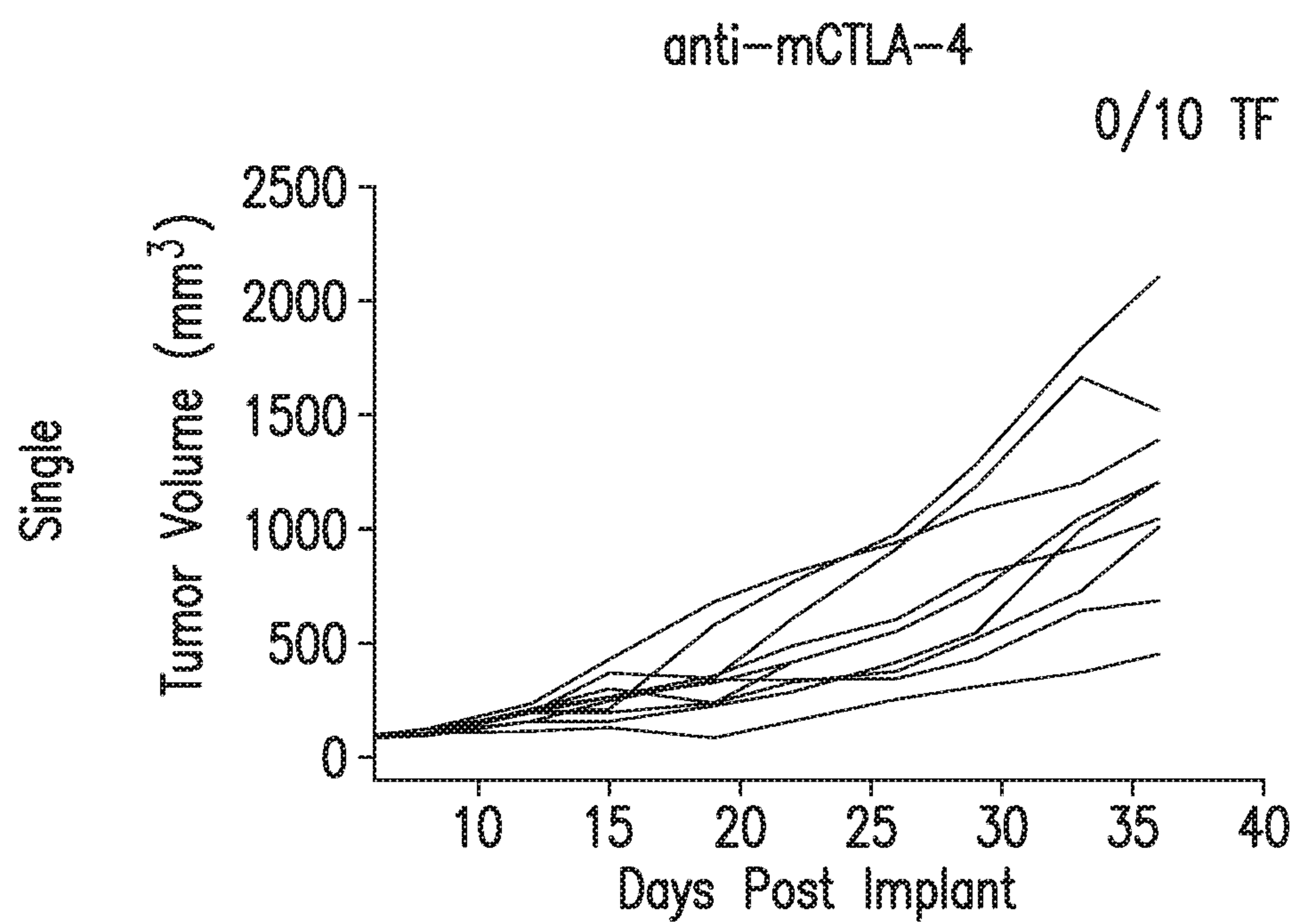


FIG.42B

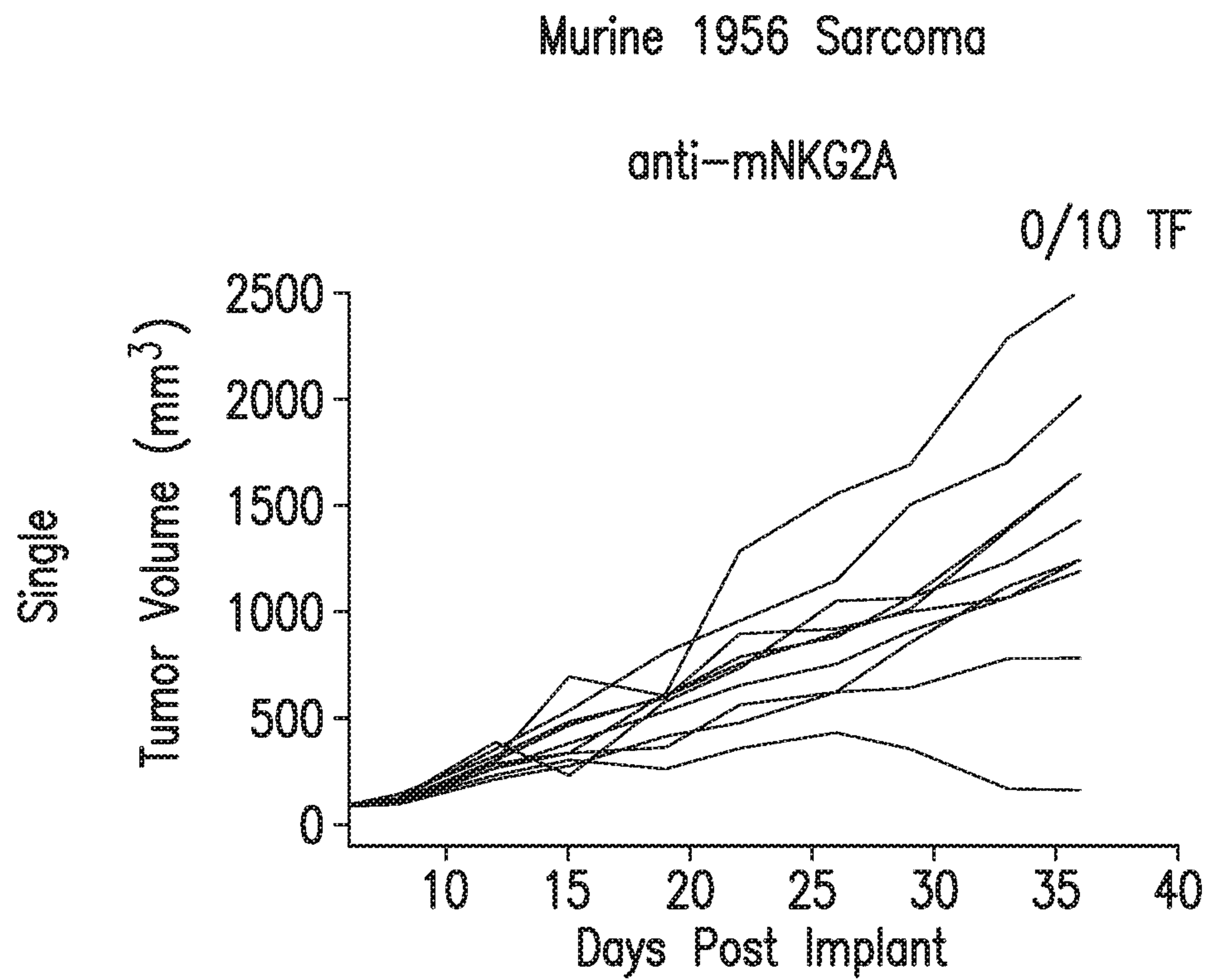


FIG.42C

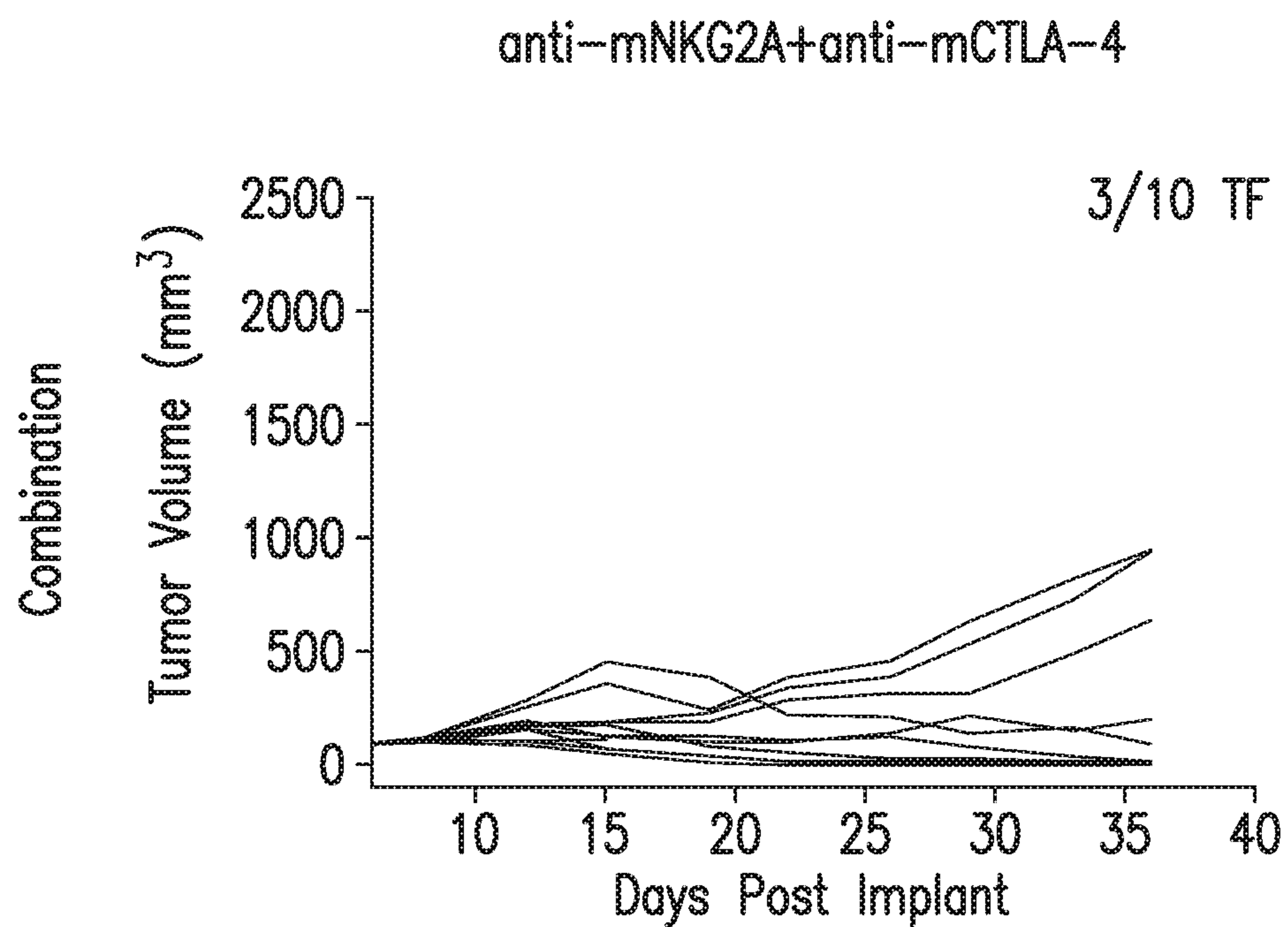


FIG.42D

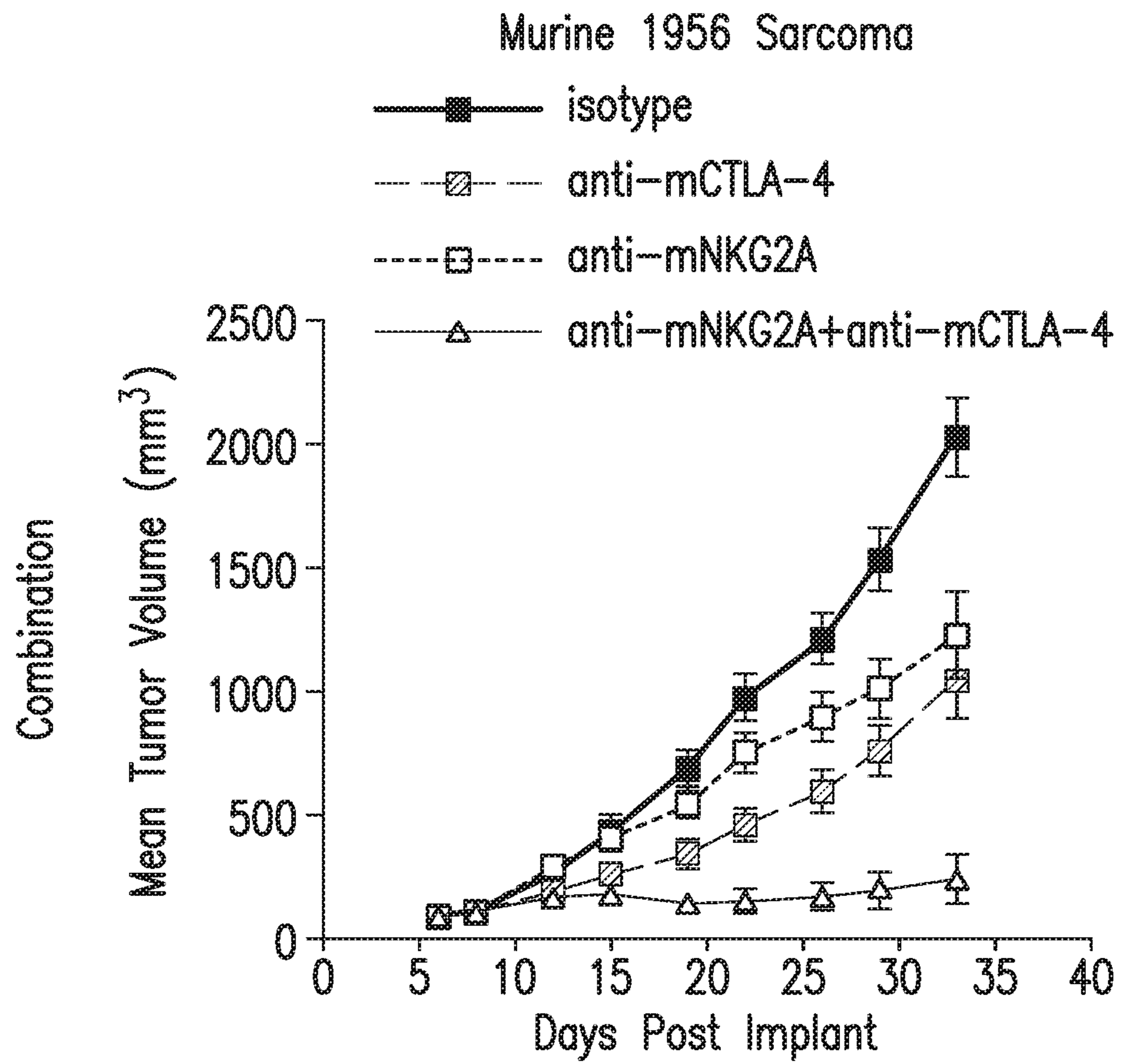


FIG.42E

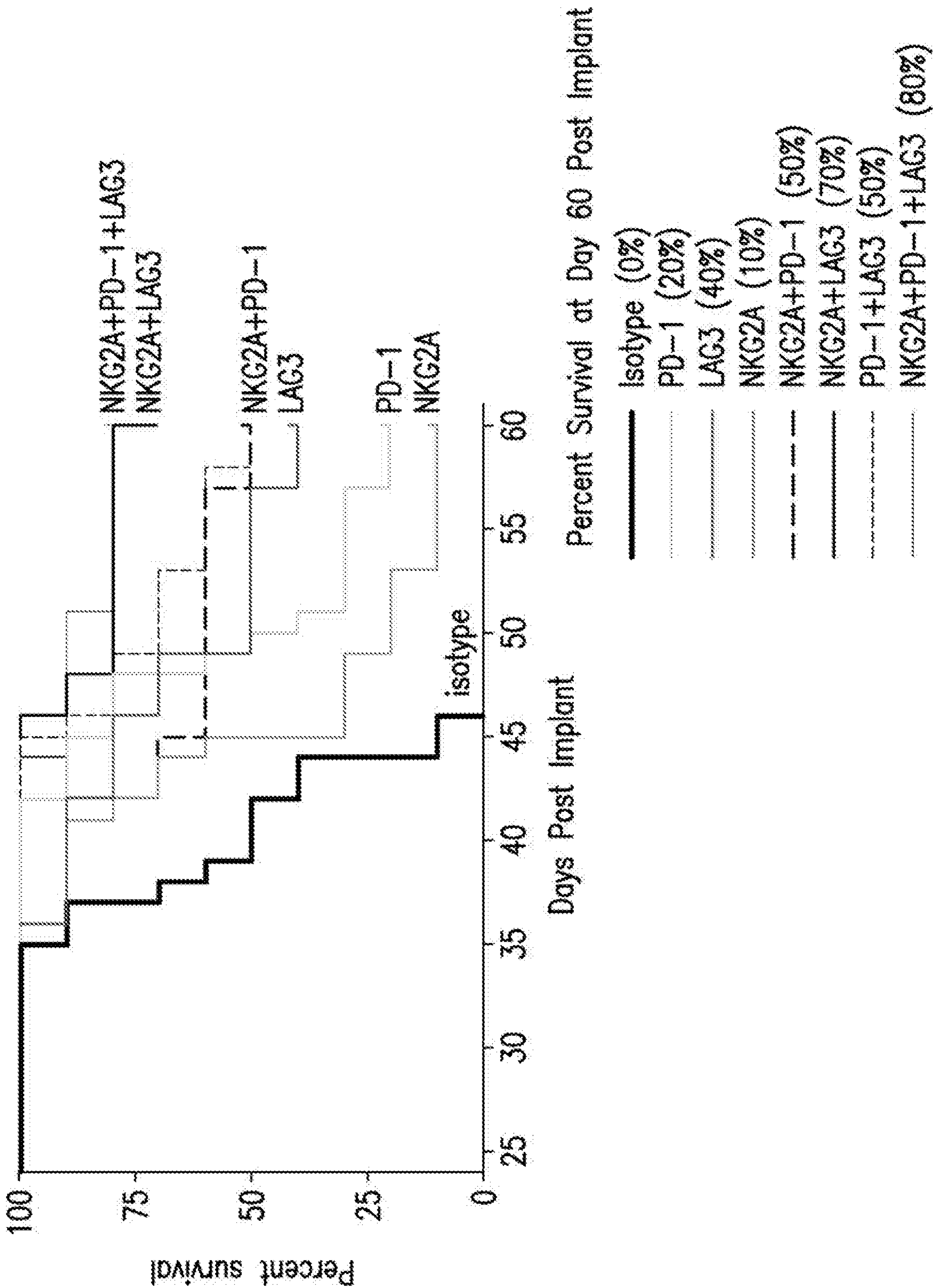


FIG. 43

Surface NKG2A Changes After Treatment with anti-mNKG2A Antibody

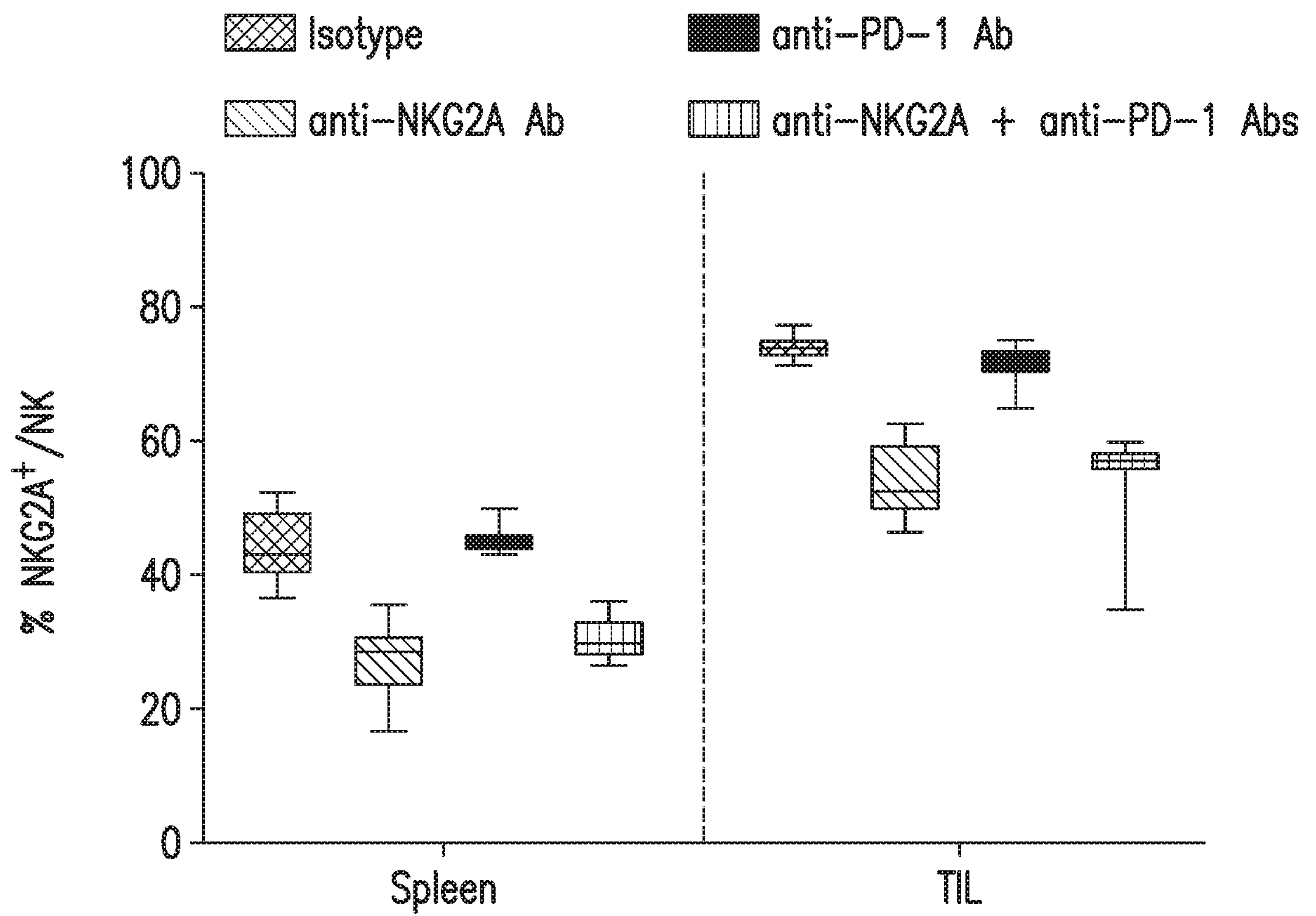


FIG.44

NKG2A Expression in Human Tumors by Immunohistochemistry

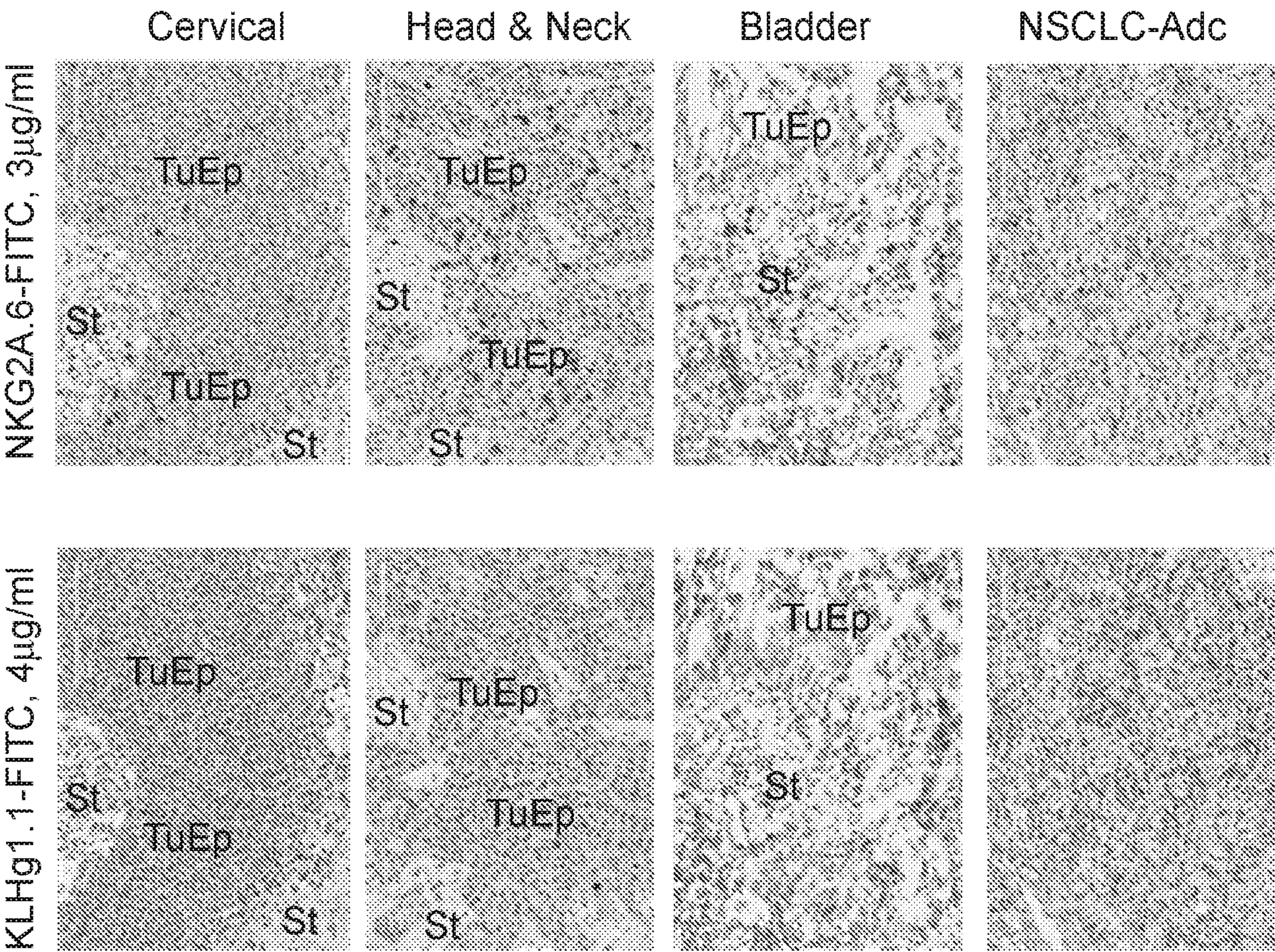


FIG.45

NKG2A.6-FITC binding profile in multiple tumors
(‘Hot spot’ analysis using HALO on frozen sections; 3 spots/sample)

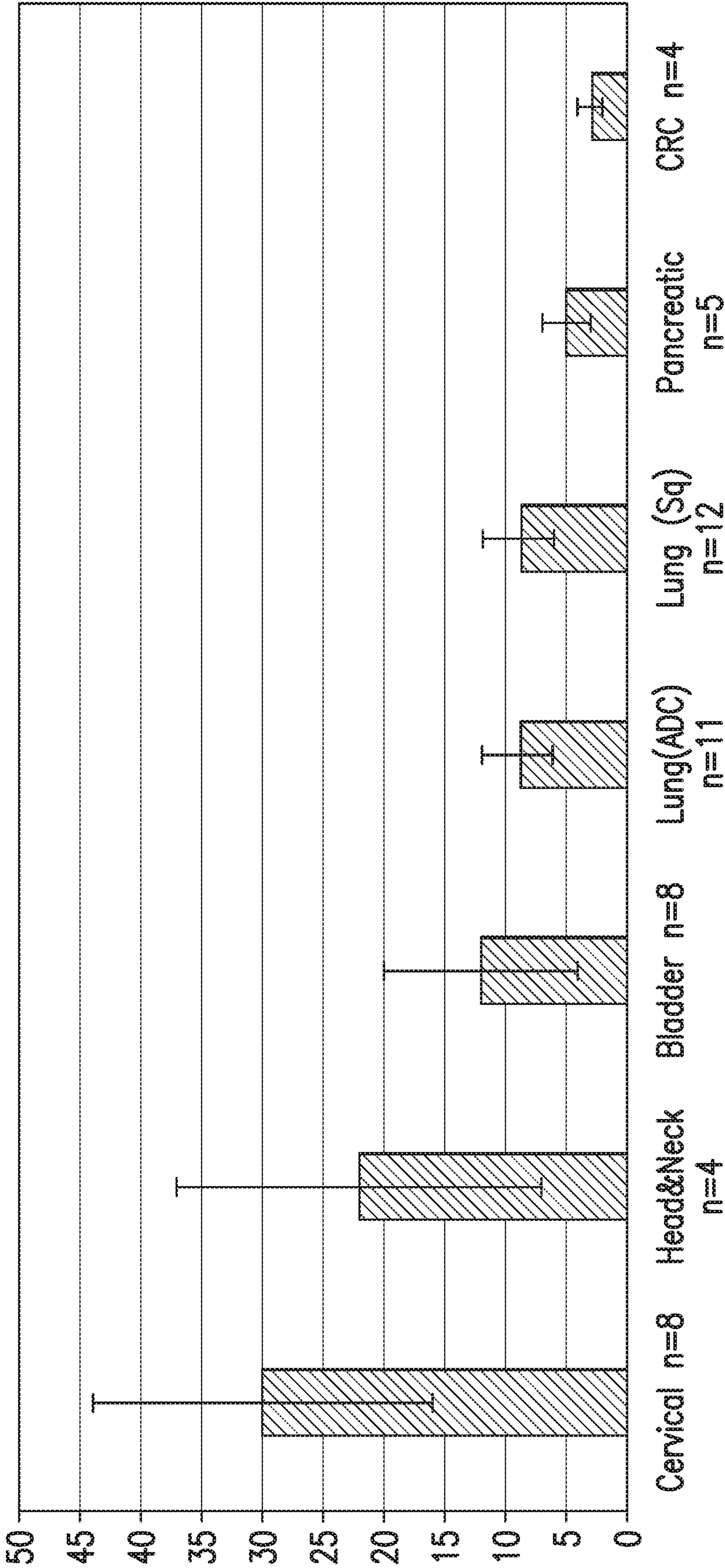


FIG. 46

HLA-E Levels Across Tumor Types
Measured By Immunohistochemistry

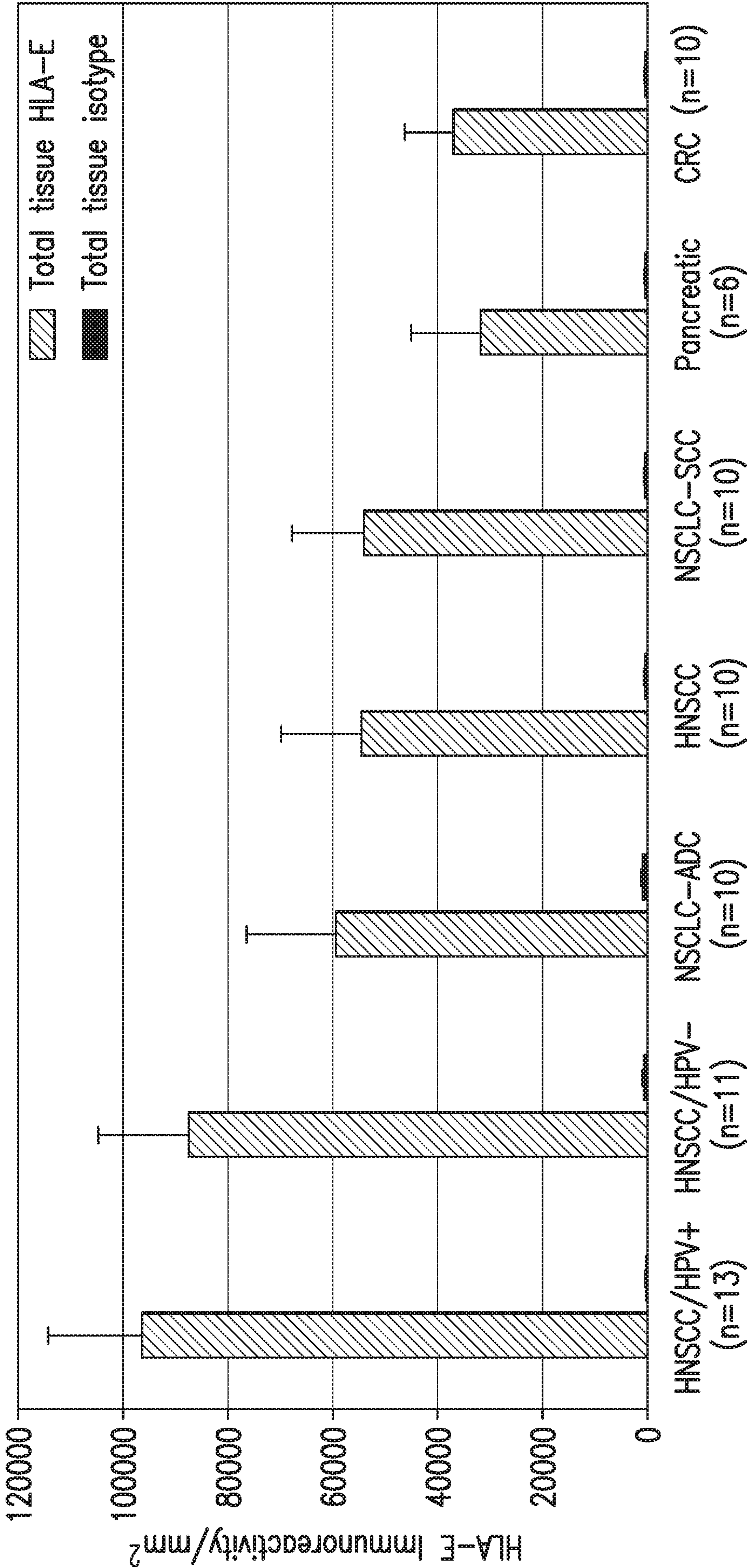


FIG.47

HLA-E Expression in Multiple Tumor Types by Immunohistochemistry

HNSCC/HPV+ NSCLC-ADC NSCLC-SCC CRC

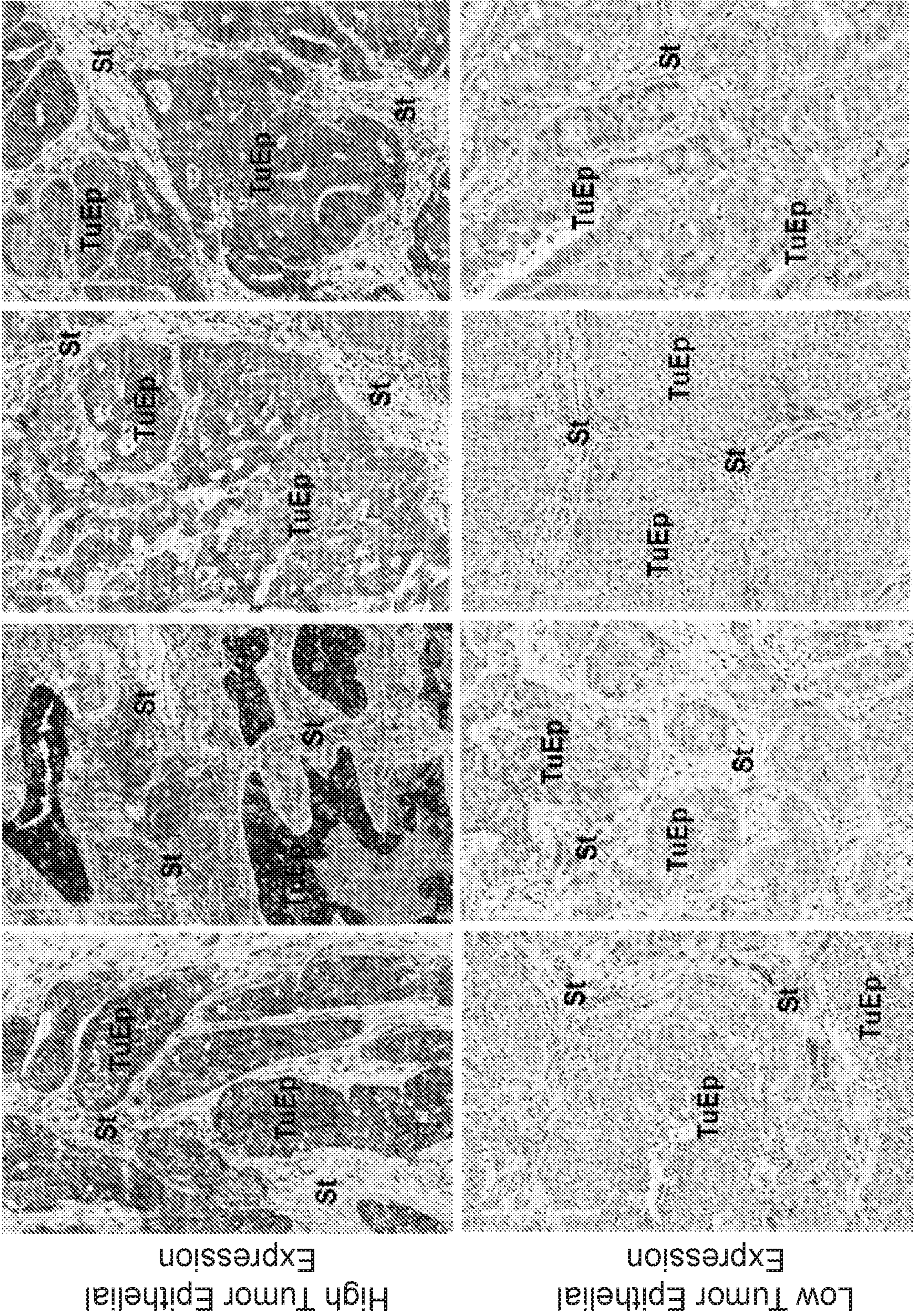


FIG.48

Levels of soluble HLA-E across Healthy Controls and Cancer Patients

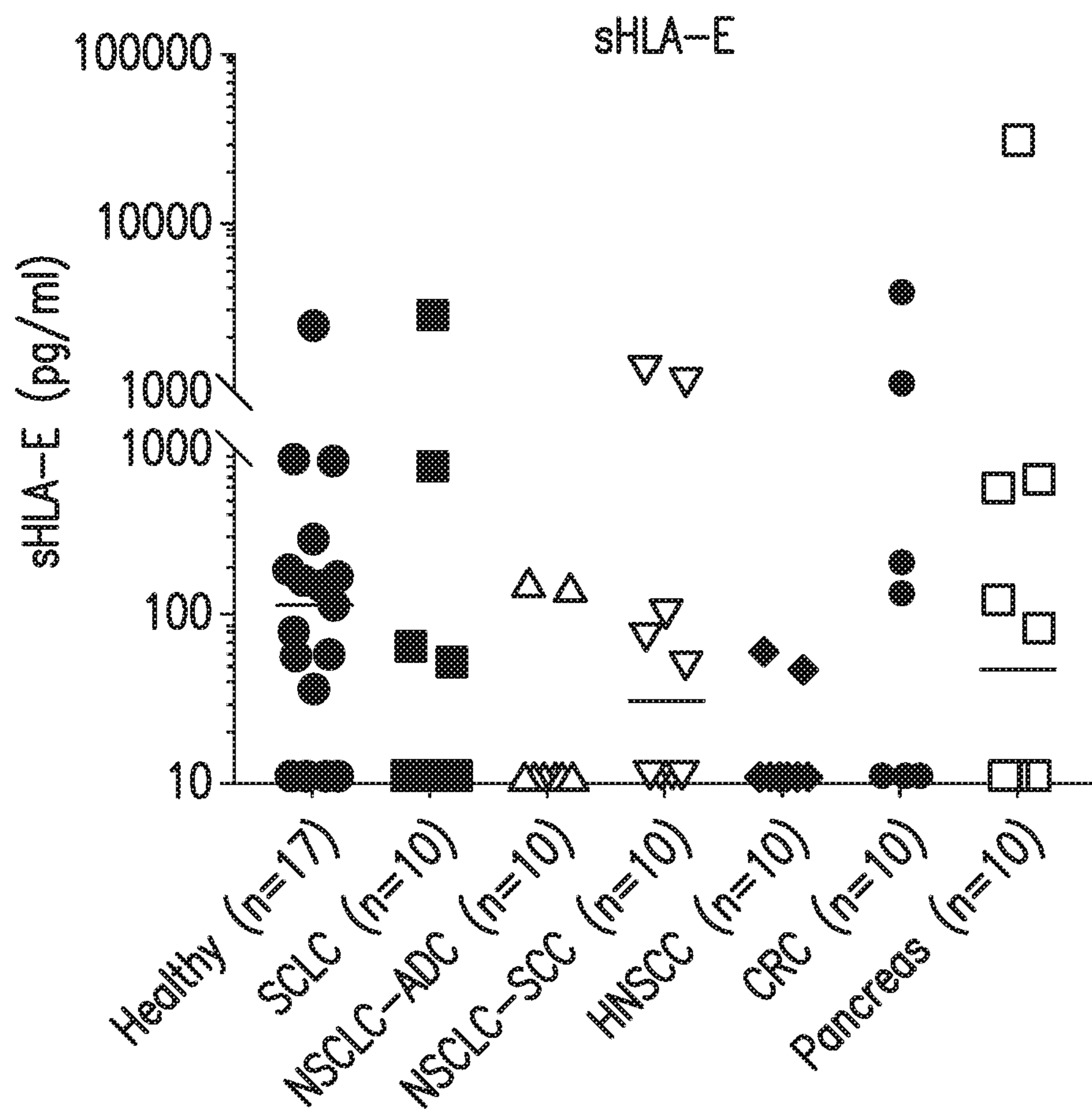


FIG.49A

Levels of soluble HLA-E across Healthy Controls and Cancer Patients

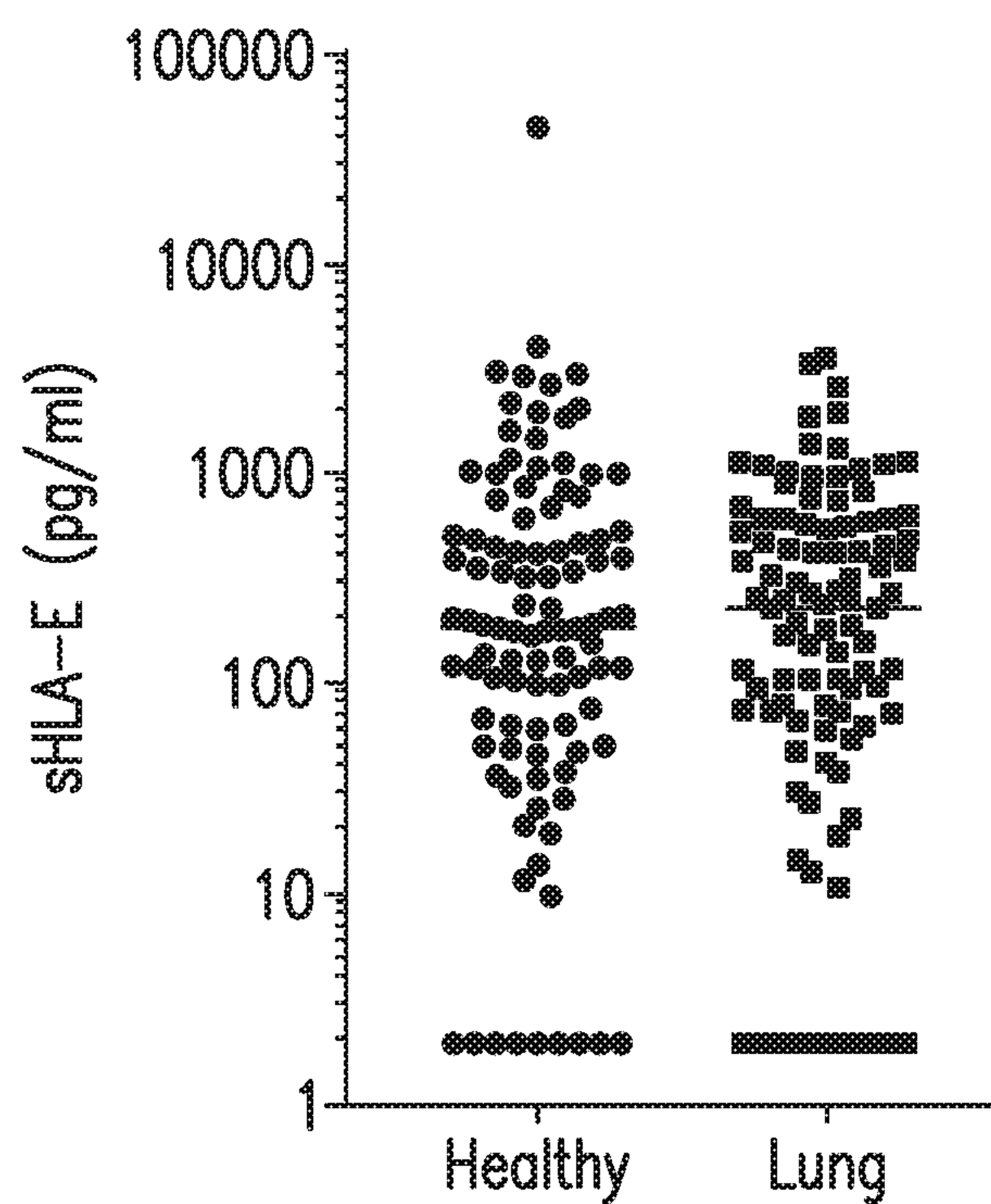


FIG.49B

Anti-NKG2A Antibody Clinical Development

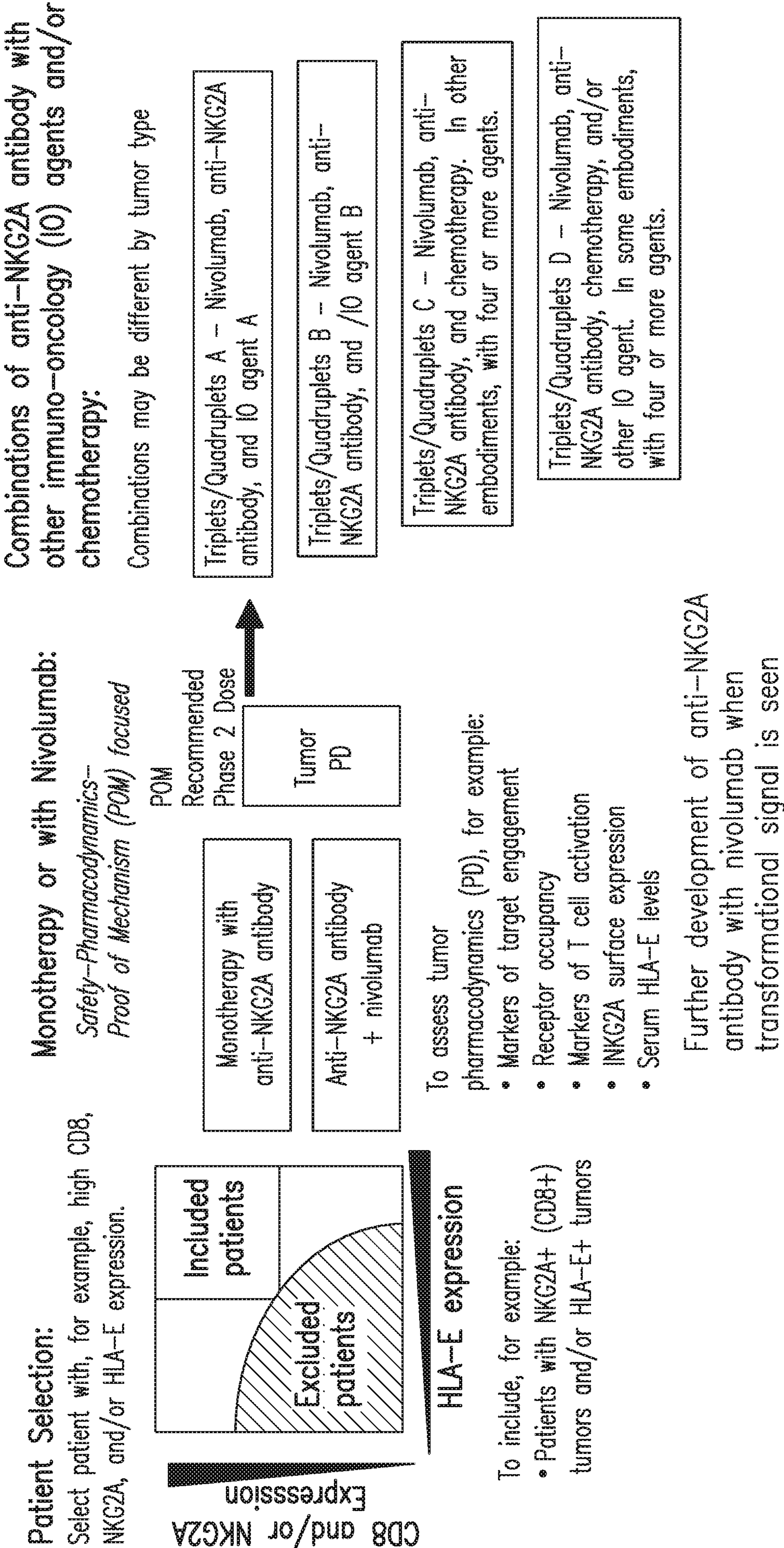


FIG.50

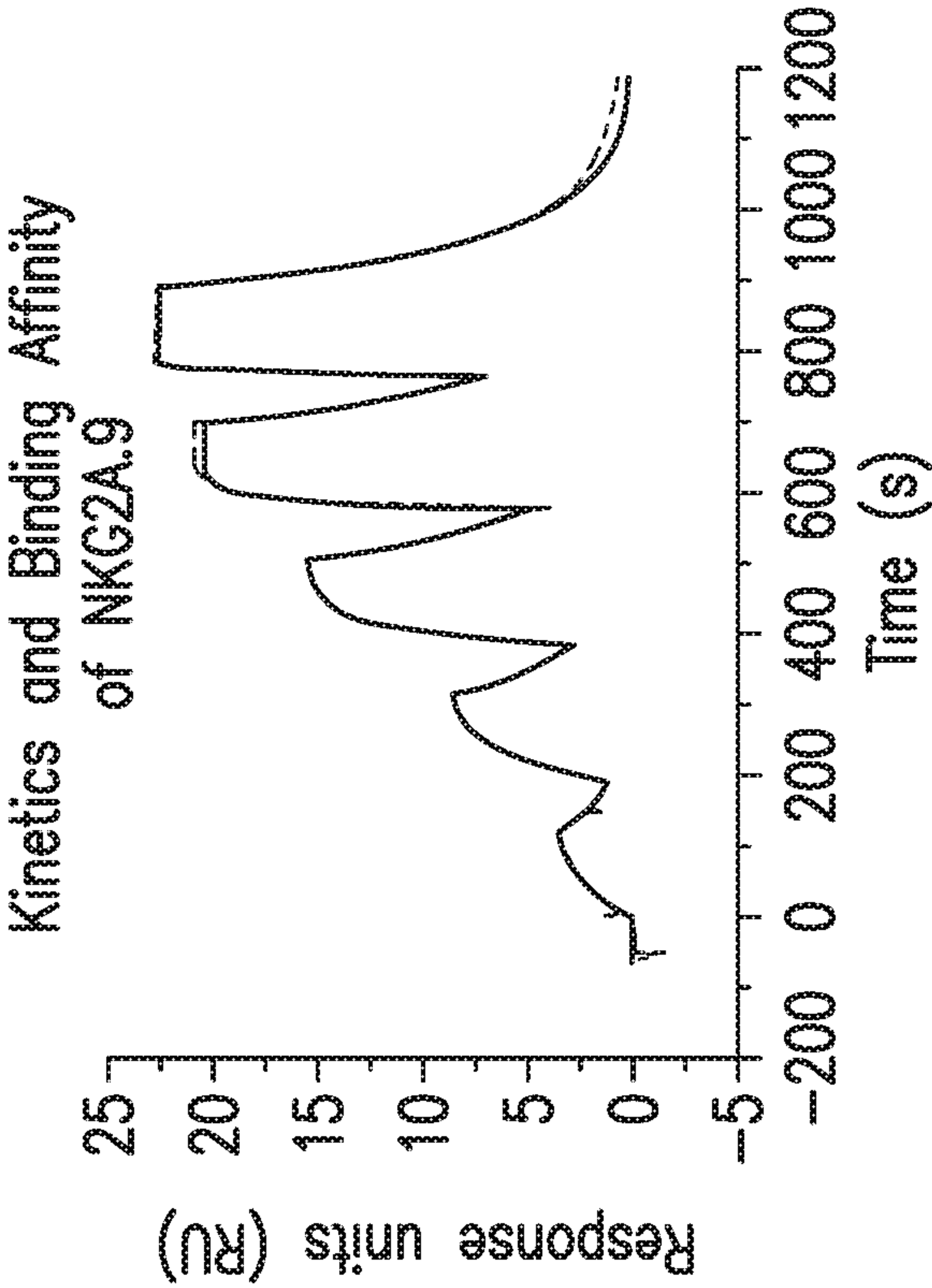


FIG. 51A

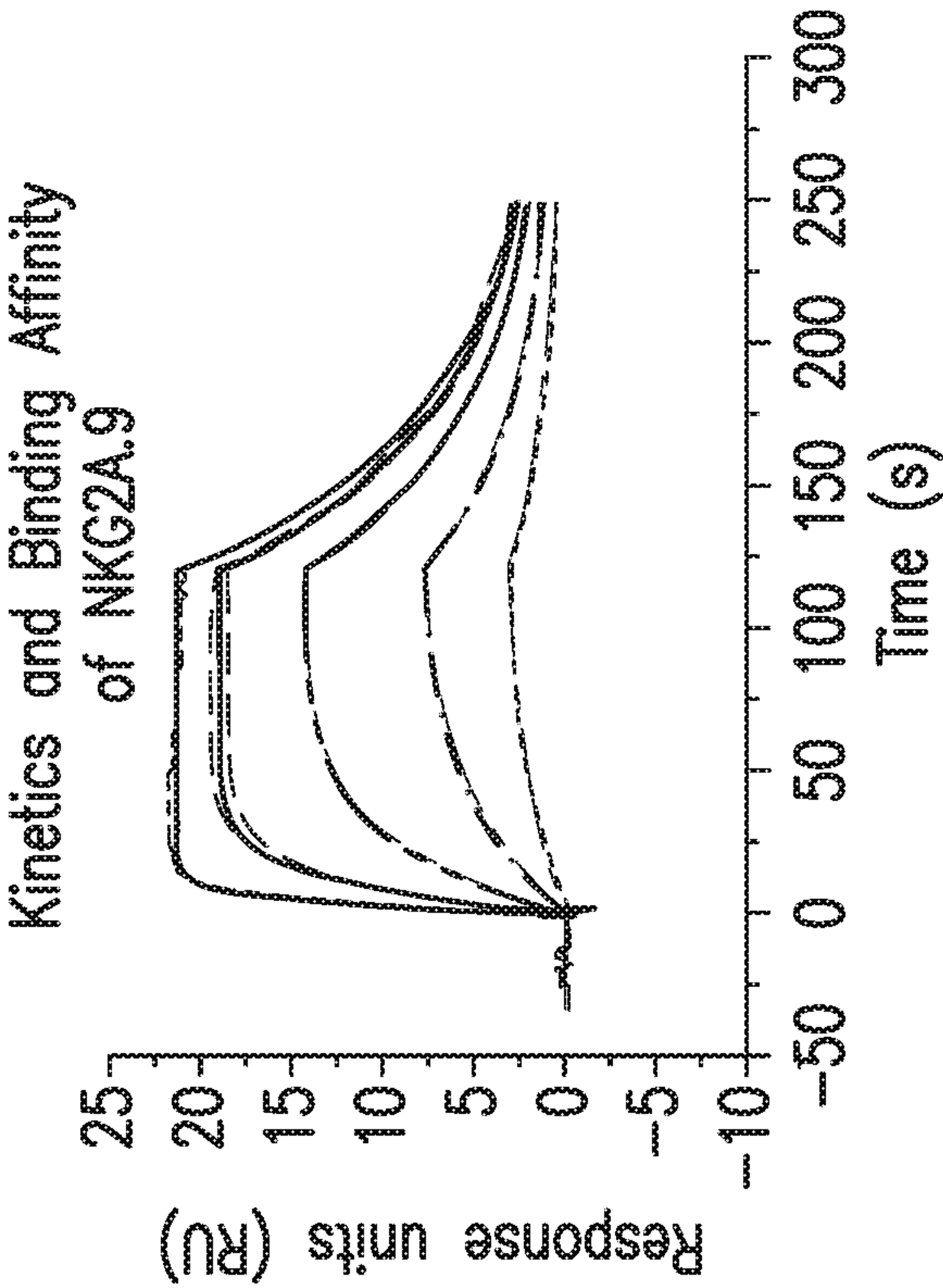


FIG. 51B

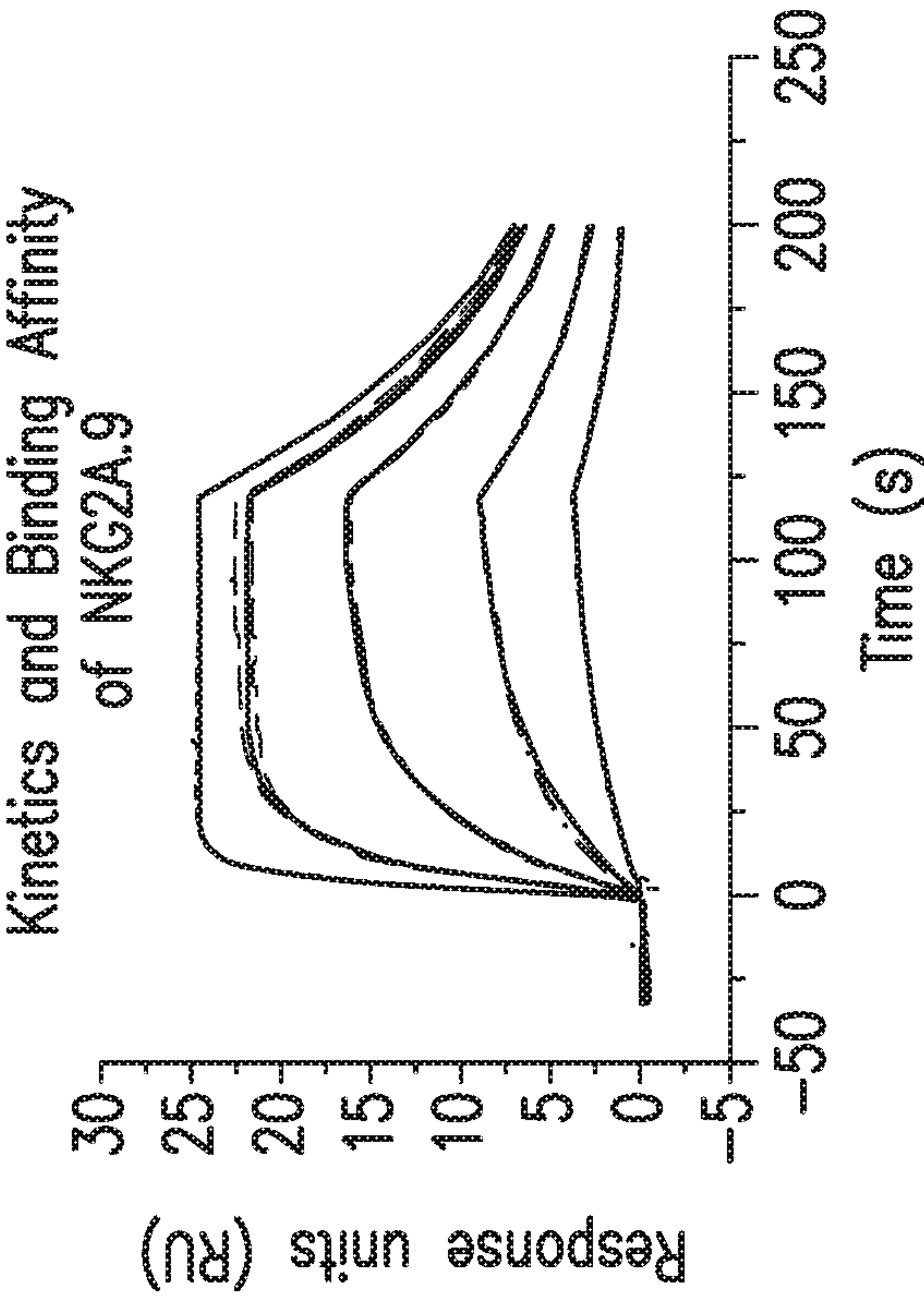


FIG. 51C

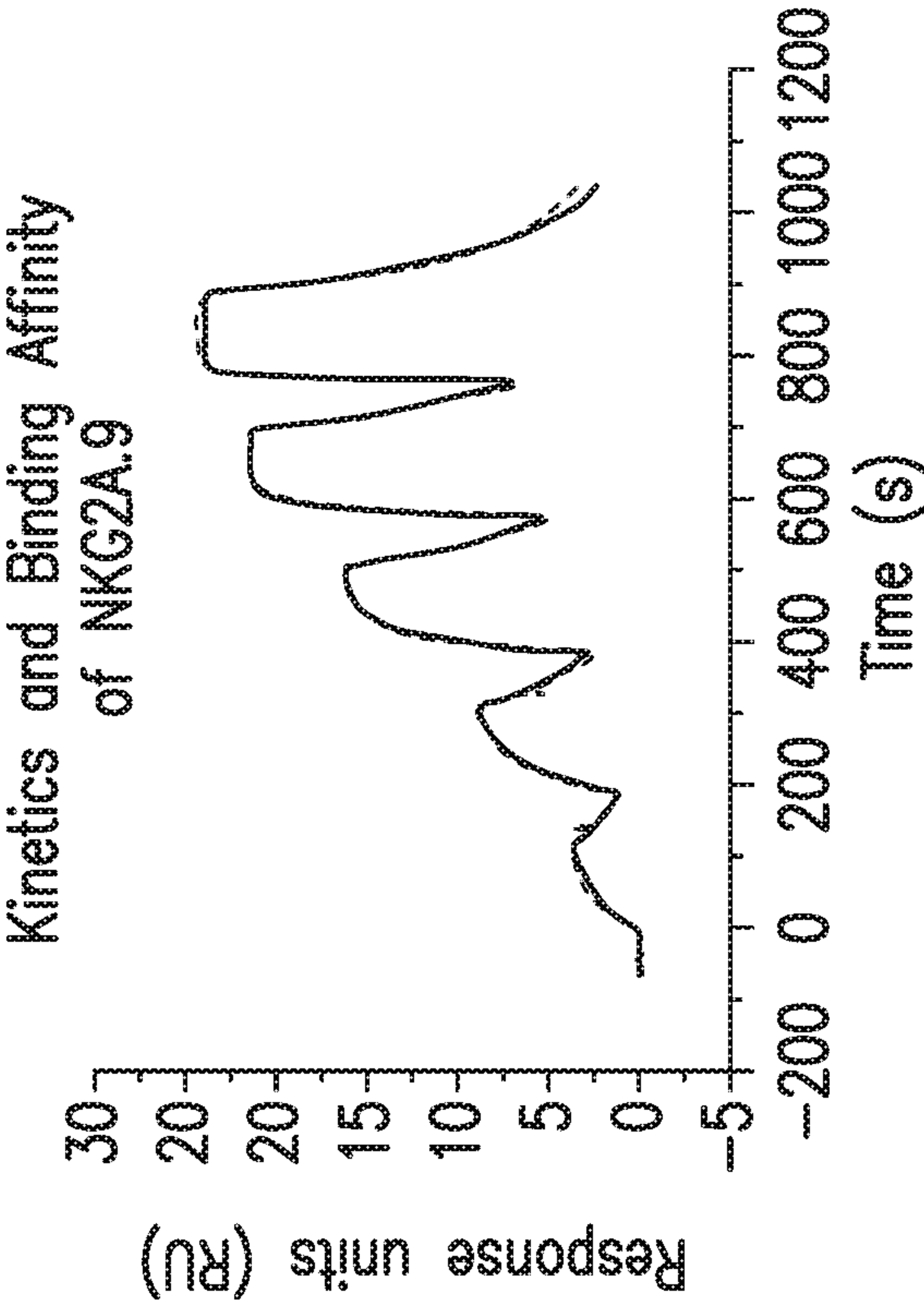
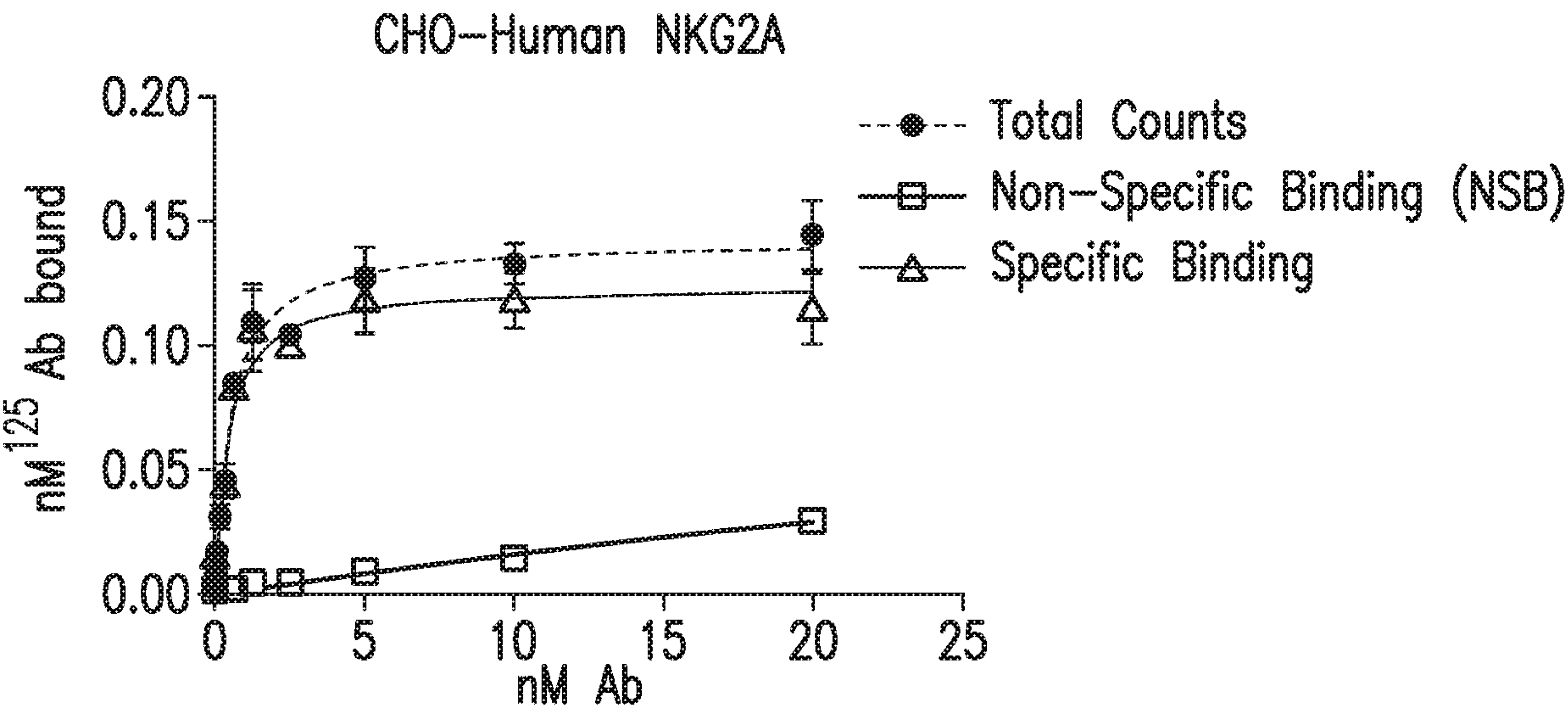


FIG. 51D

Binding Affinity of NKG2A.9 to Human and Cynomolgus
NKG2A-expressing CHO Cells By Scatchard Analysis

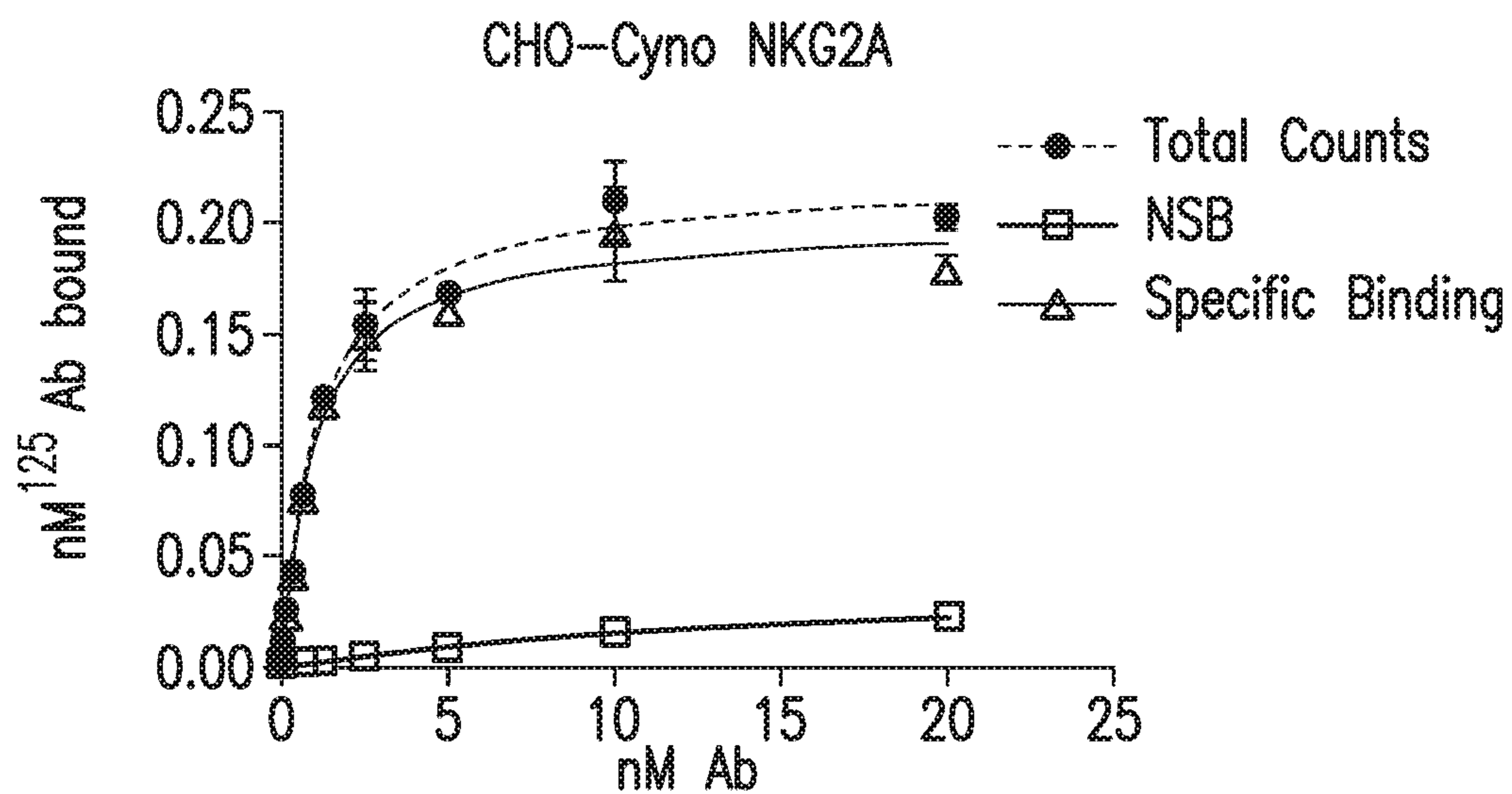


	Total Counts	NSB	Specific Binding
Bmax (nM)	0.1	0.2	0.1
Kd (nM)	0.5	79	0.4

Receptors per cell = Bmax* 6x10¹⁰/50,000
= 148,680 receptors per cell

FIG.52A

Binding Affinity of NKG2A.9 to Human and Cynomolgus NKG2A-expressing CHO Cells By Scatchard Analysis



	Total Counts	NSB	Specific Binding
Bmax (nM)	0.2	0.05	0.2
Kd (nM)	1.1	19.6	1

$$\begin{aligned} \text{Receptors per cell} &= \text{Bmax} * 6 \times 10^{10} / 50,000 \\ &= 240,360 \text{ Receptors/Cell} \end{aligned}$$

FIG.52B

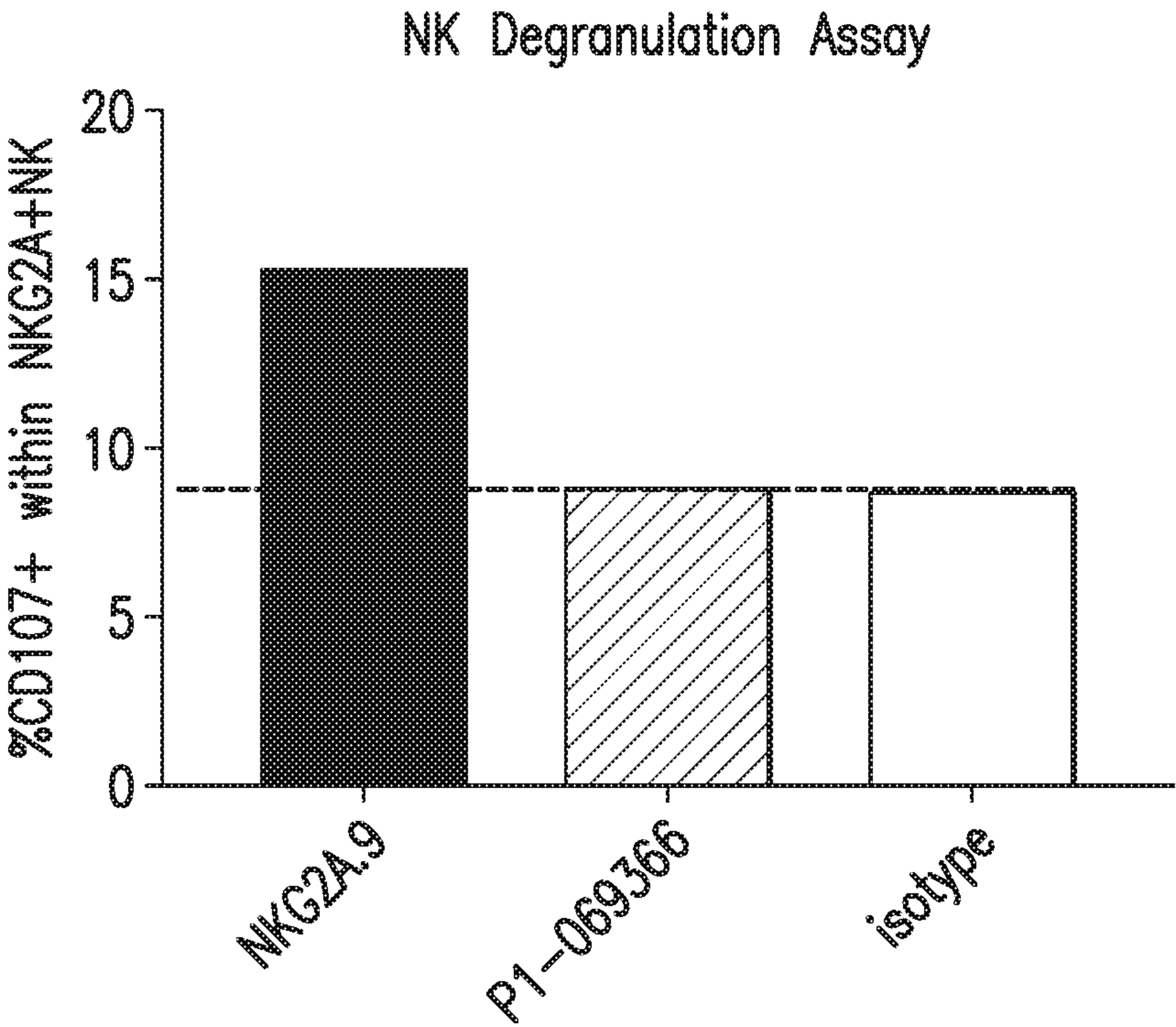
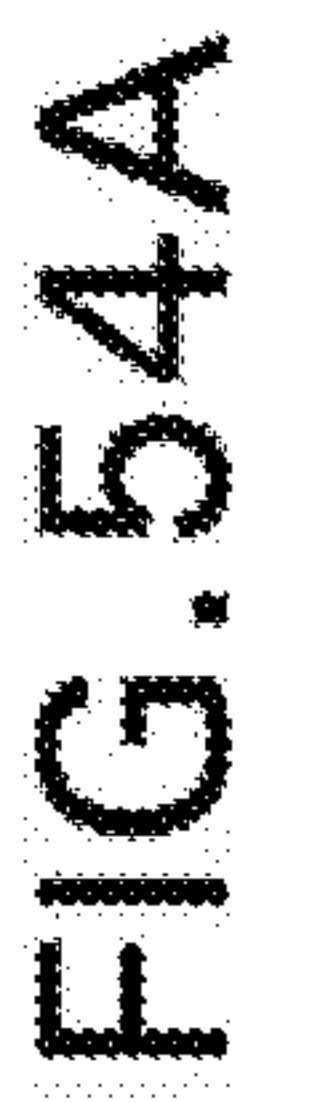
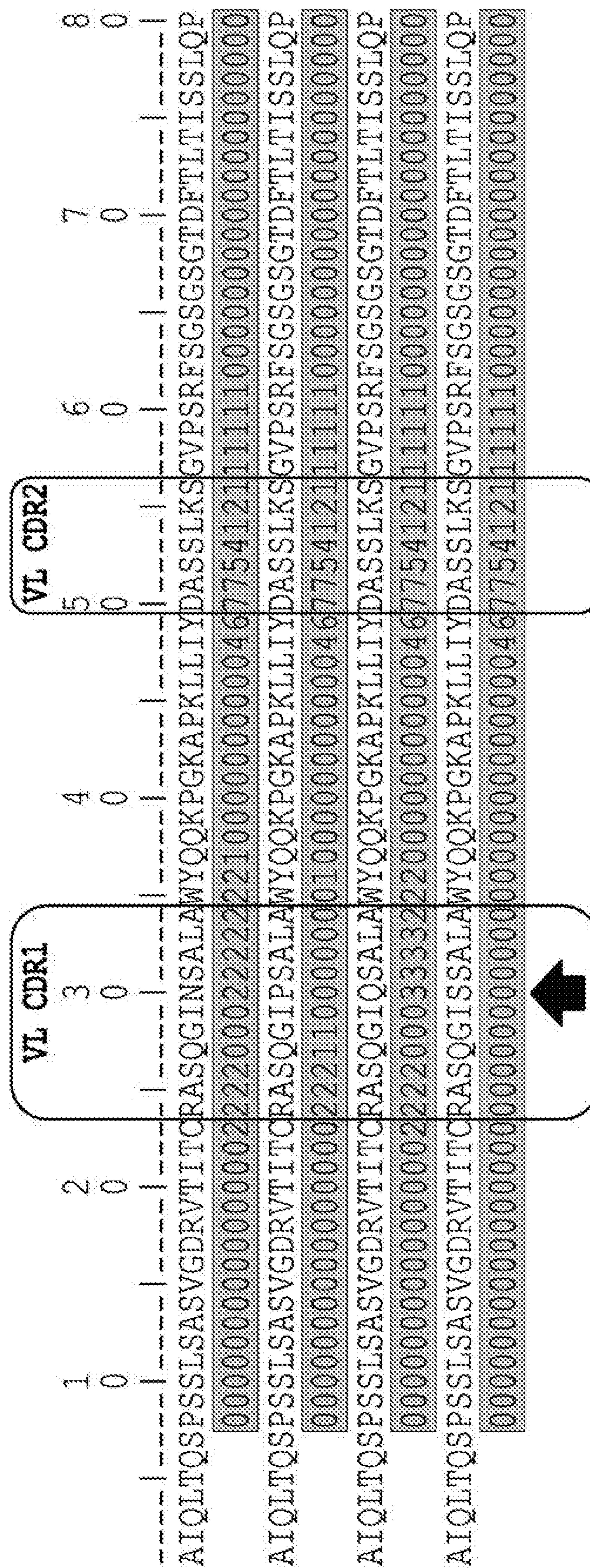
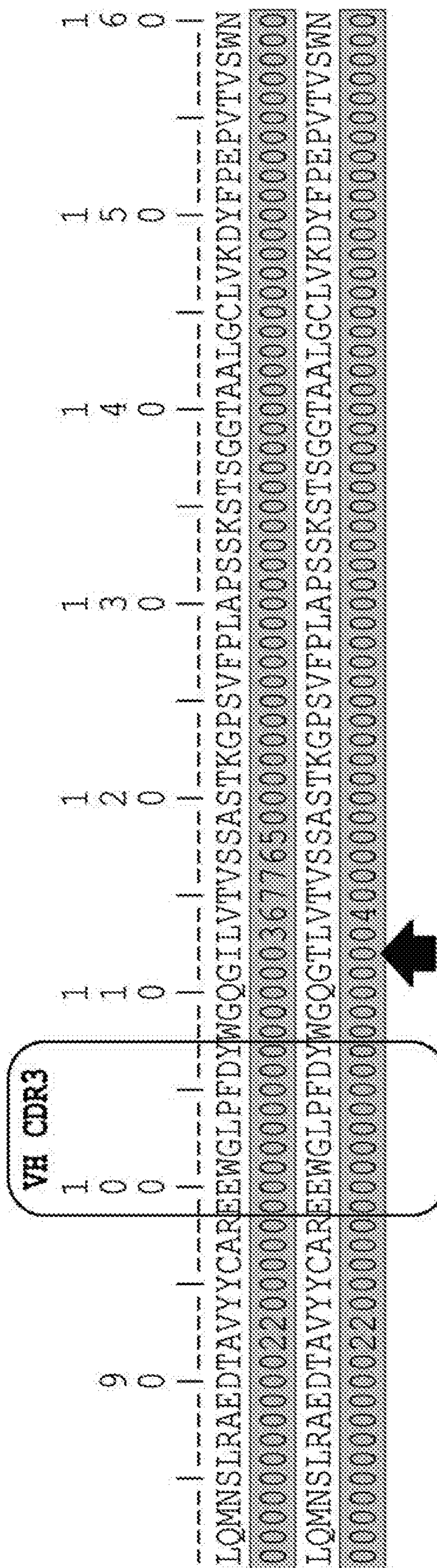


FIG.53





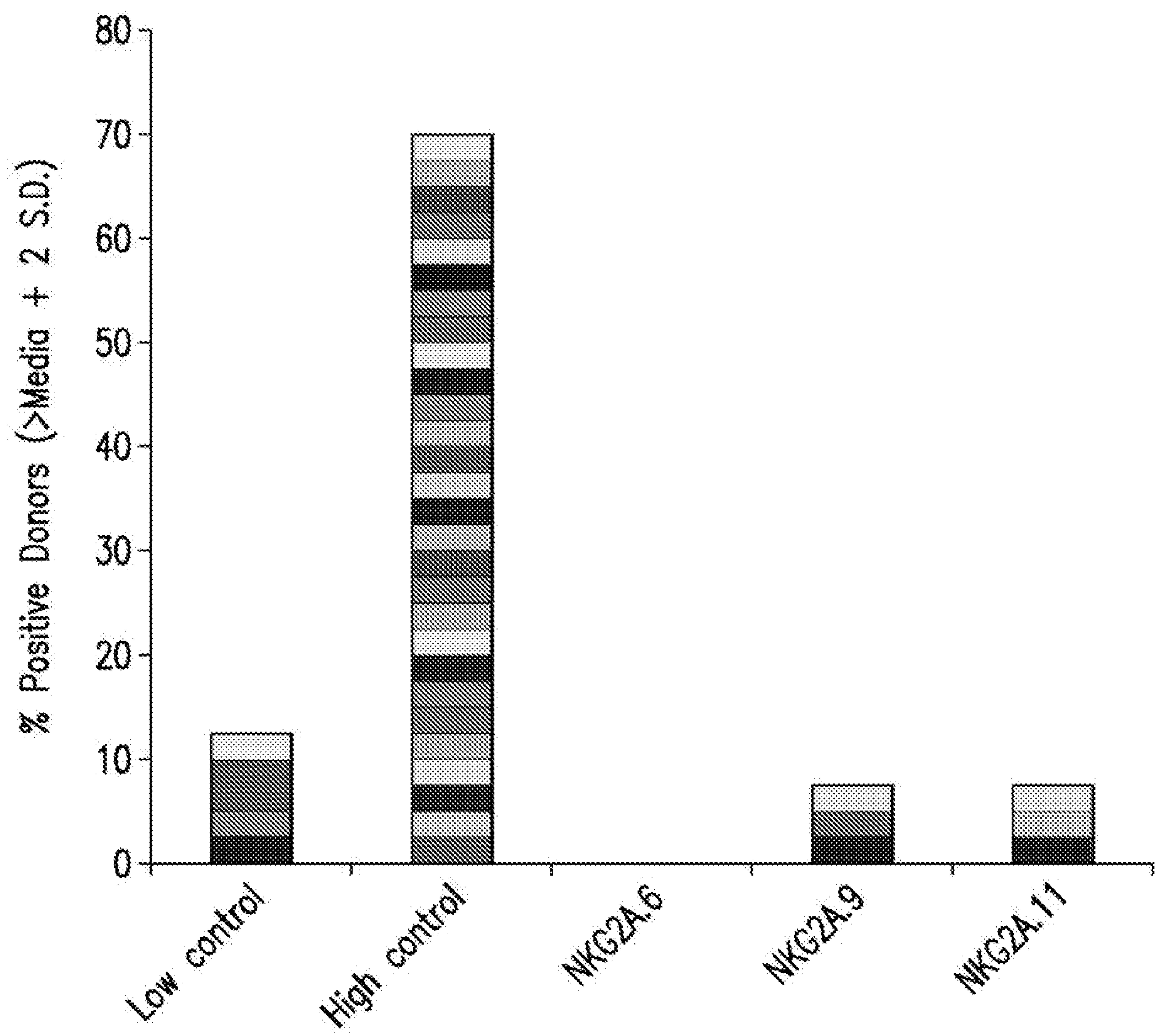


FIG.55

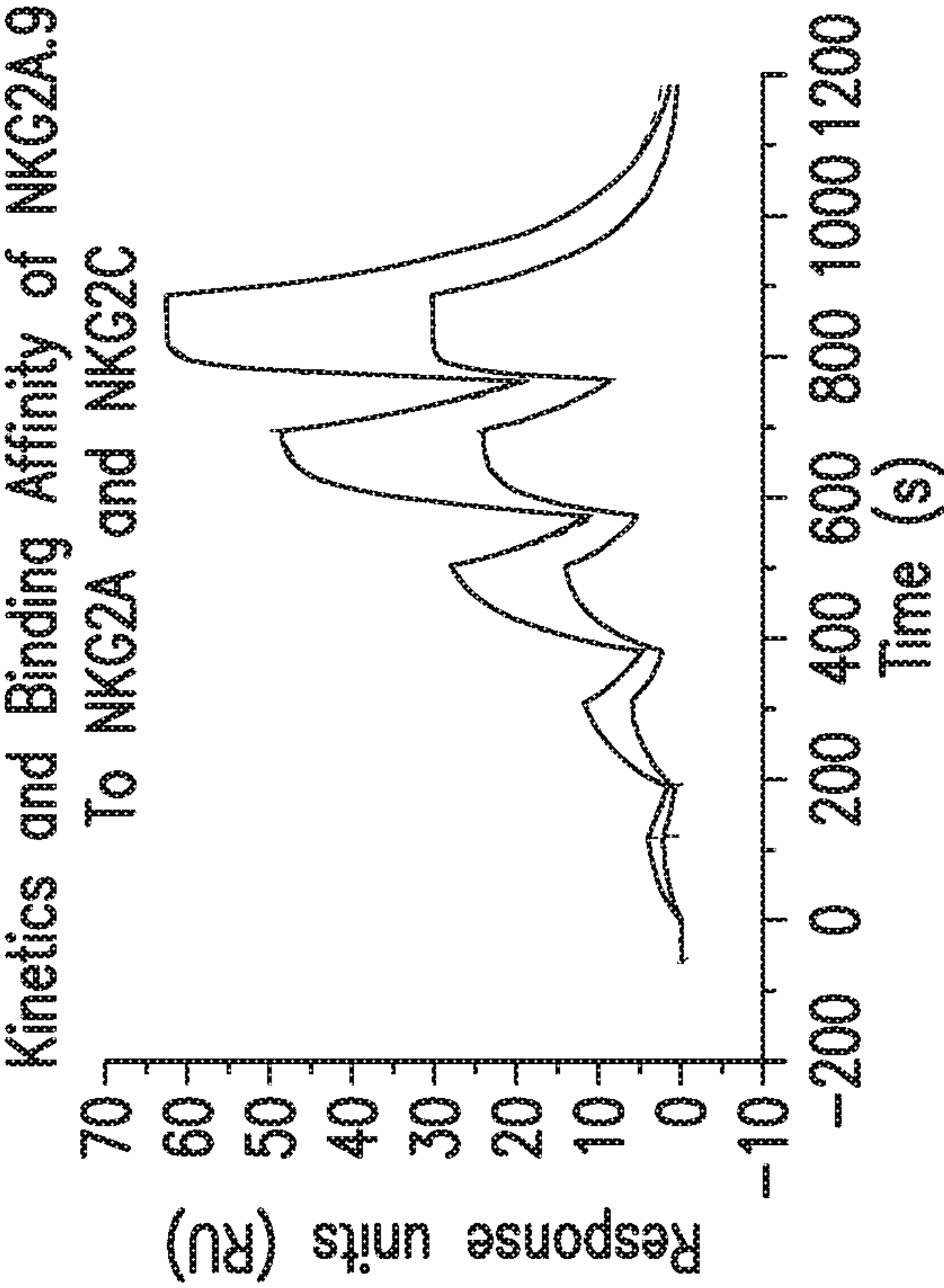


FIG. 56A

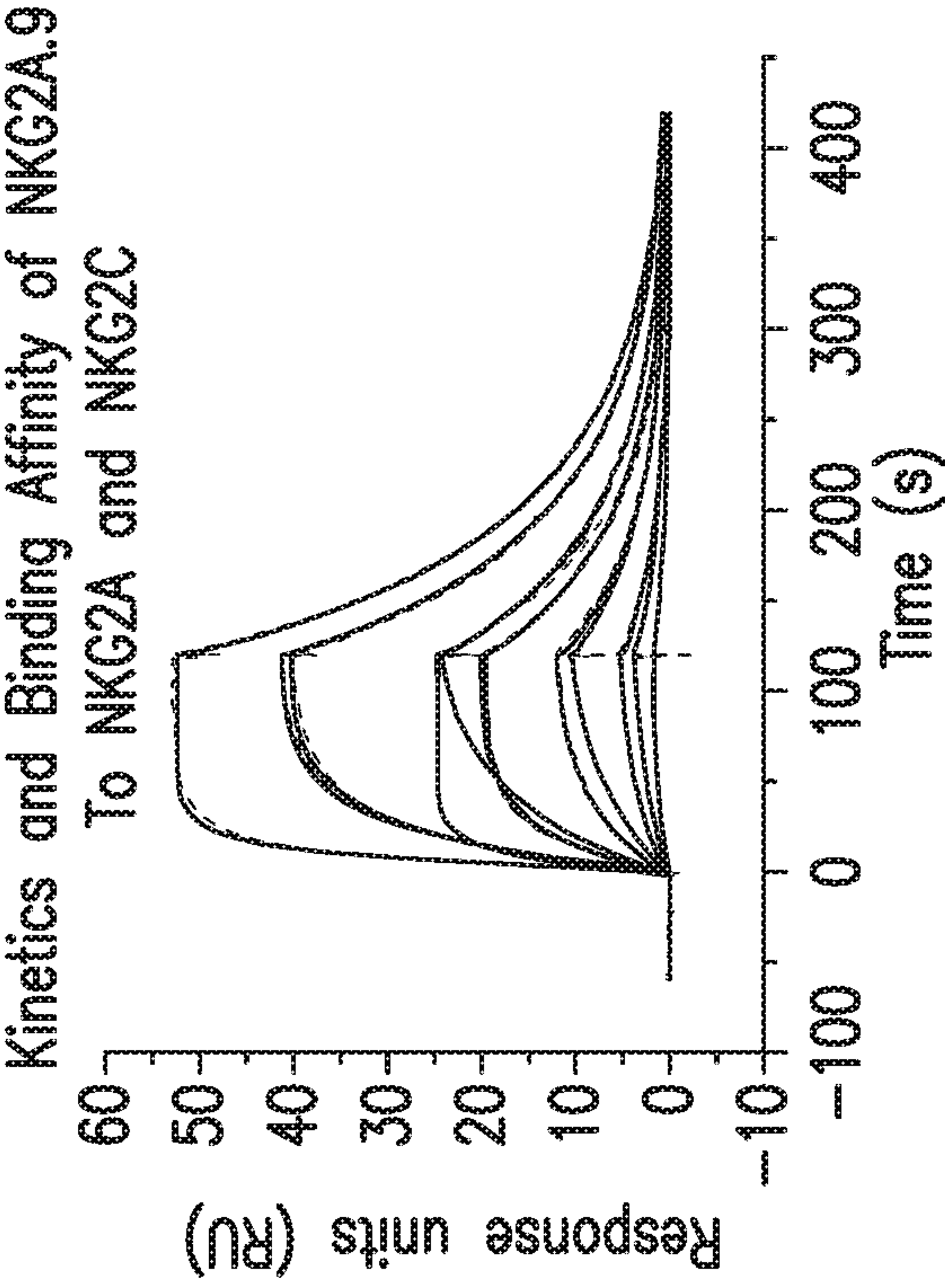


FIG. 56B

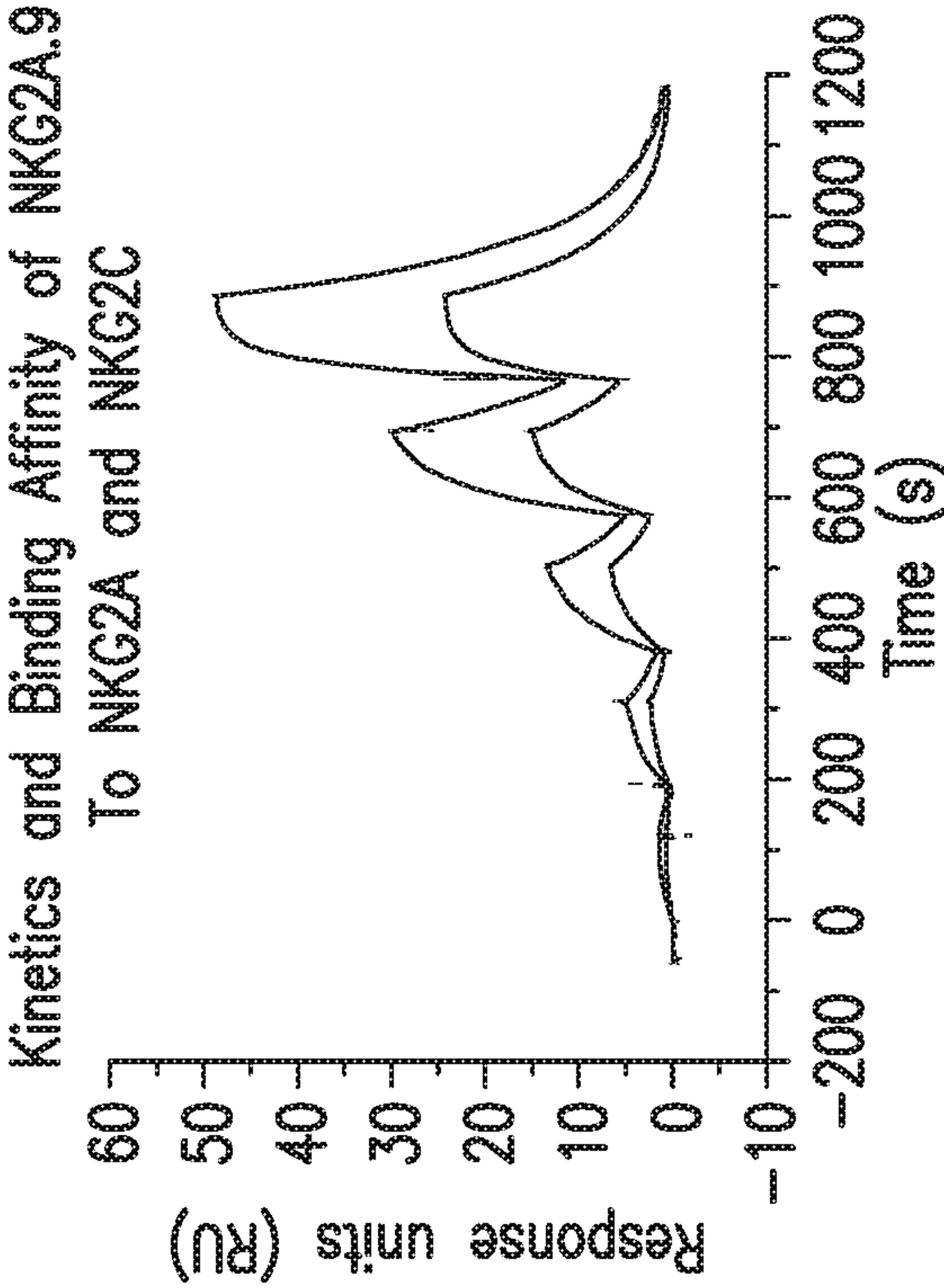


FIG. 56C

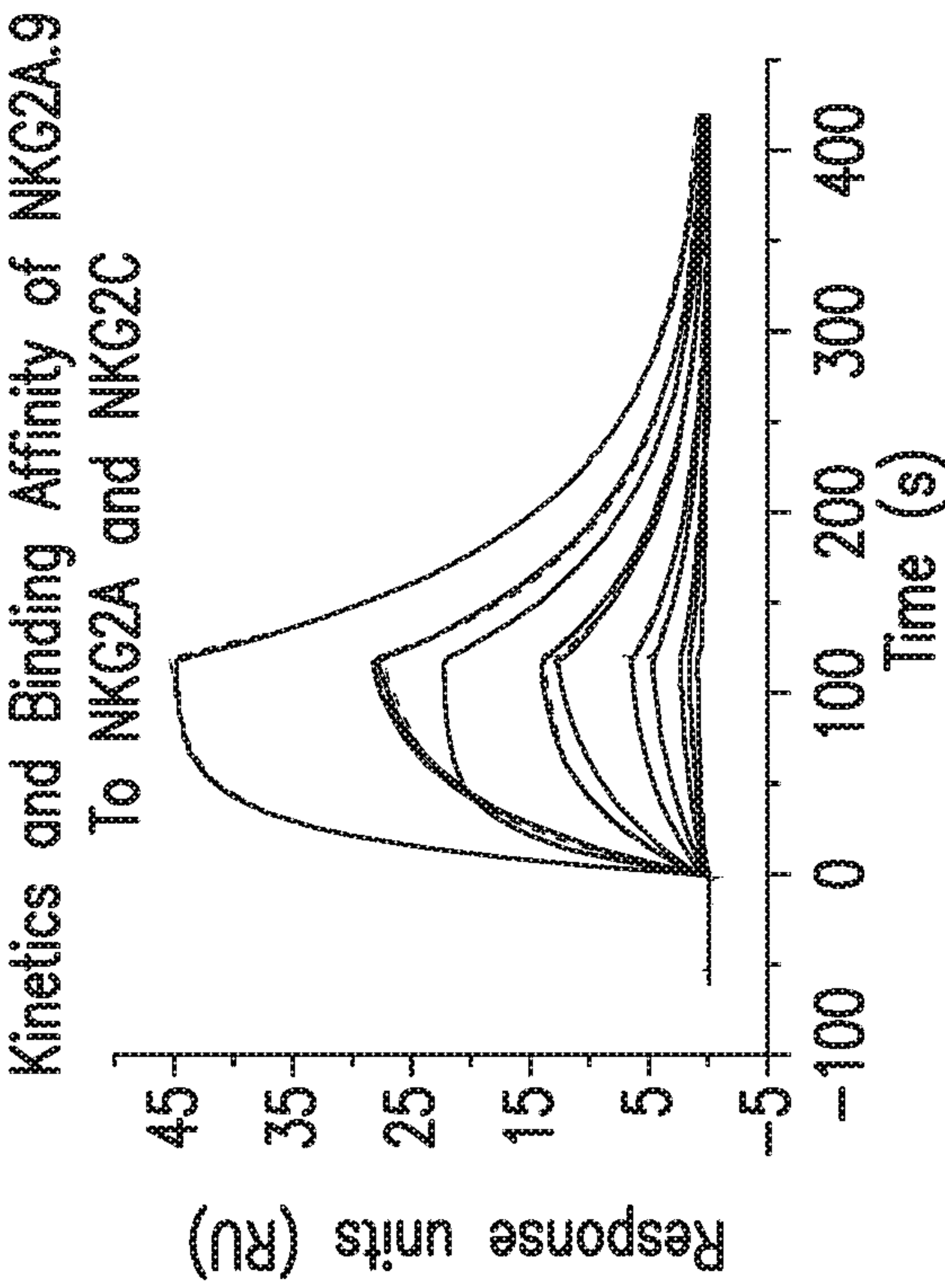


FIG. 56D

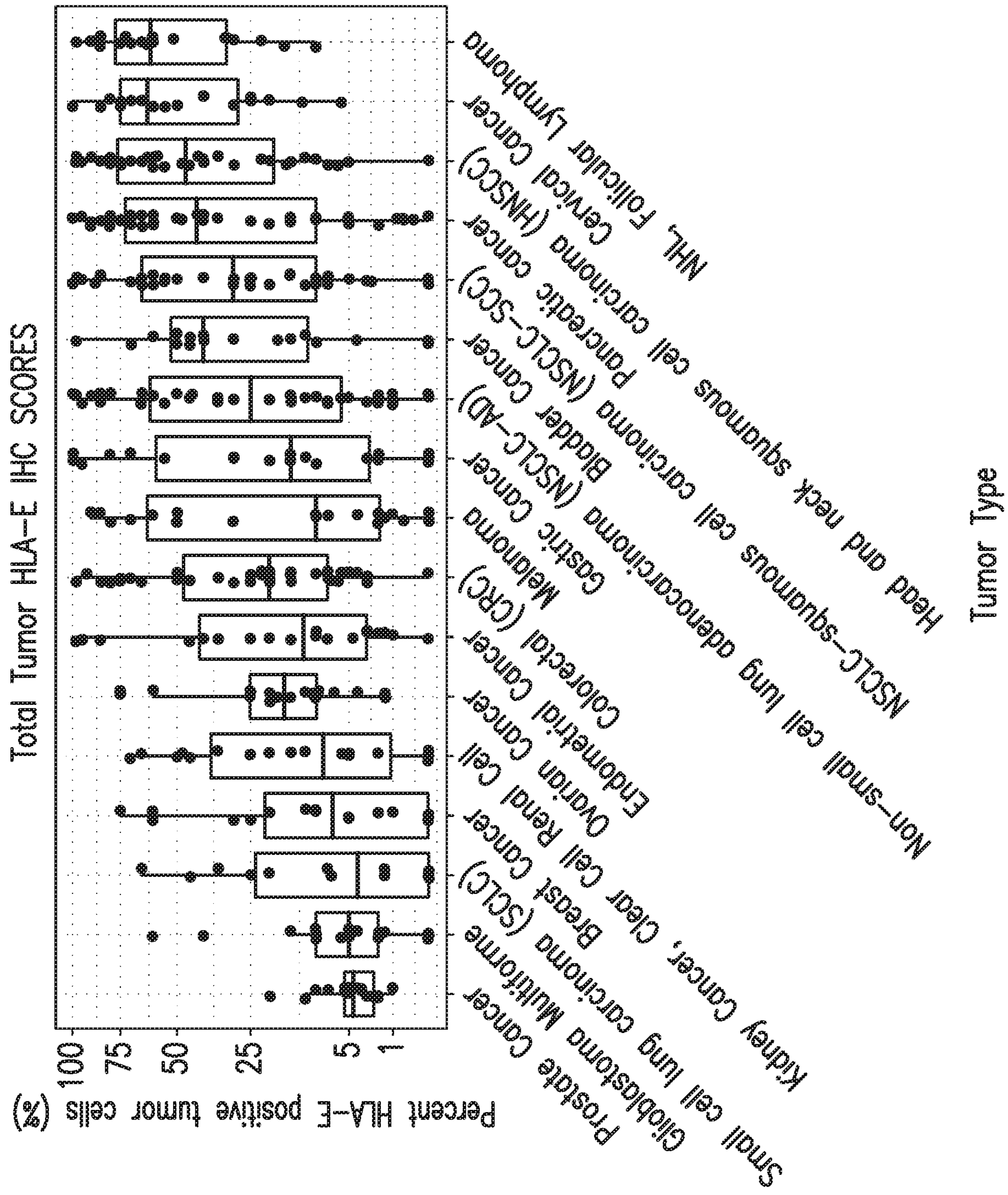


FIG.57