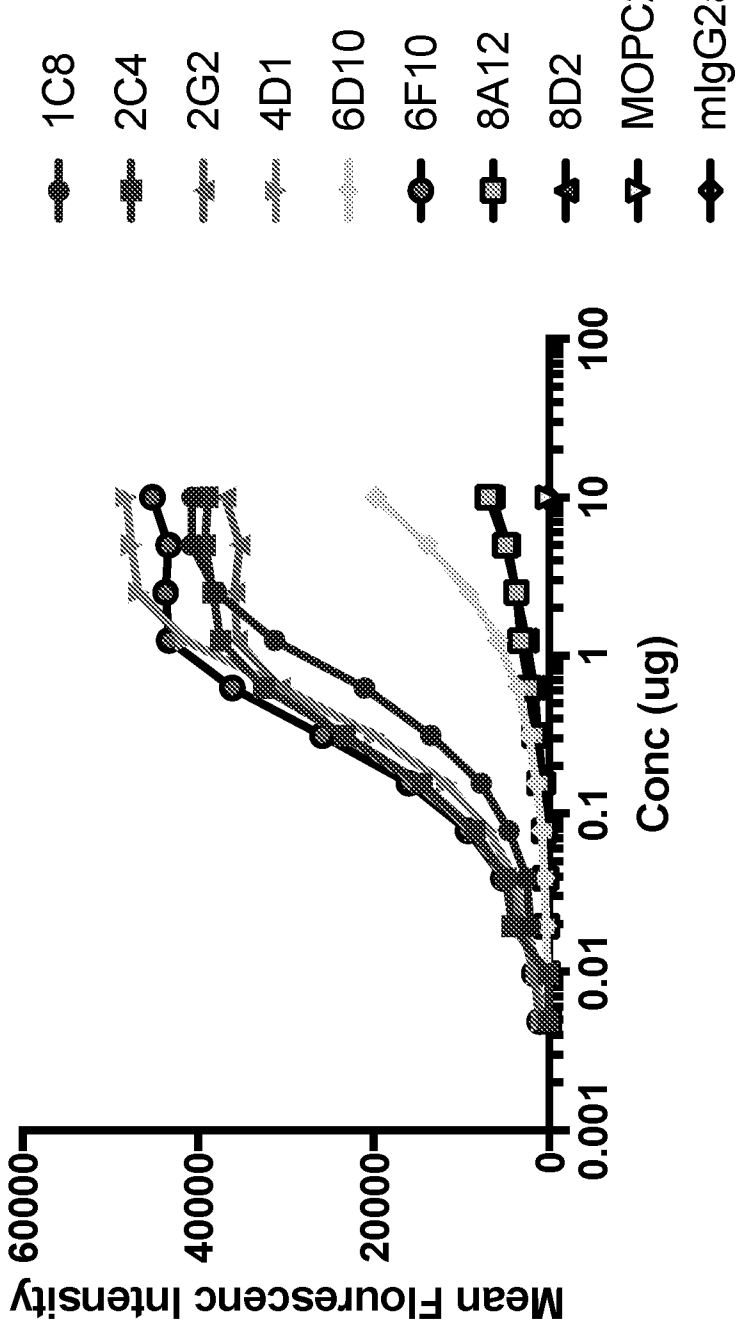
Figure 1A



	1C8	2C4	2G2	4D1	6D10	6F10	8A12	8D2
EC-50	0.63	0.24	0.21	0.44	22.49	0.25		
Function	Non blocker	Augments	Weak Blocker	Blocker	Non Blocker	Blocker	IHC WB	IHC WB

Figure 1B

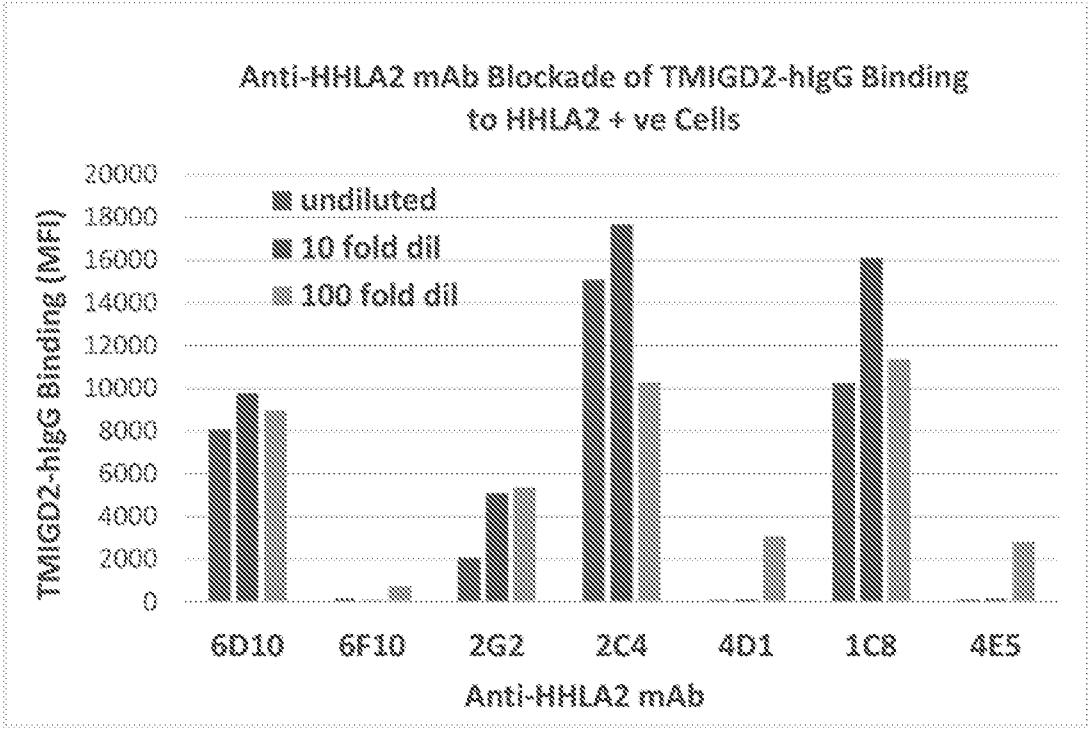

Anti-HHLA2 mAb Blockade of TMIGD2-hIgG Binding to HHLA2 + ve Cells
TMIGD2-hIgG Binding (MFI)
20000
18000
16000
14000
12000
10000
8000
6000
4000
2000
0
undiluted
10 fold dil
100 fold dil
6D10
6F10
2G2
2C4
4D1
1C8
4E5
Anti-HHLA2 mAb

Figure 2

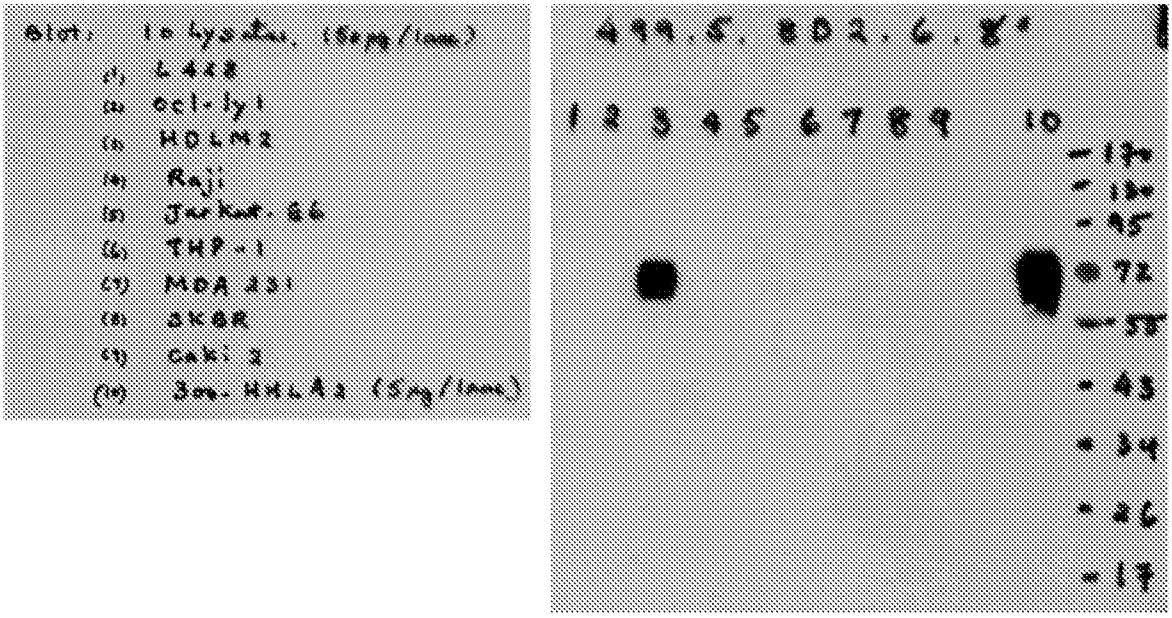
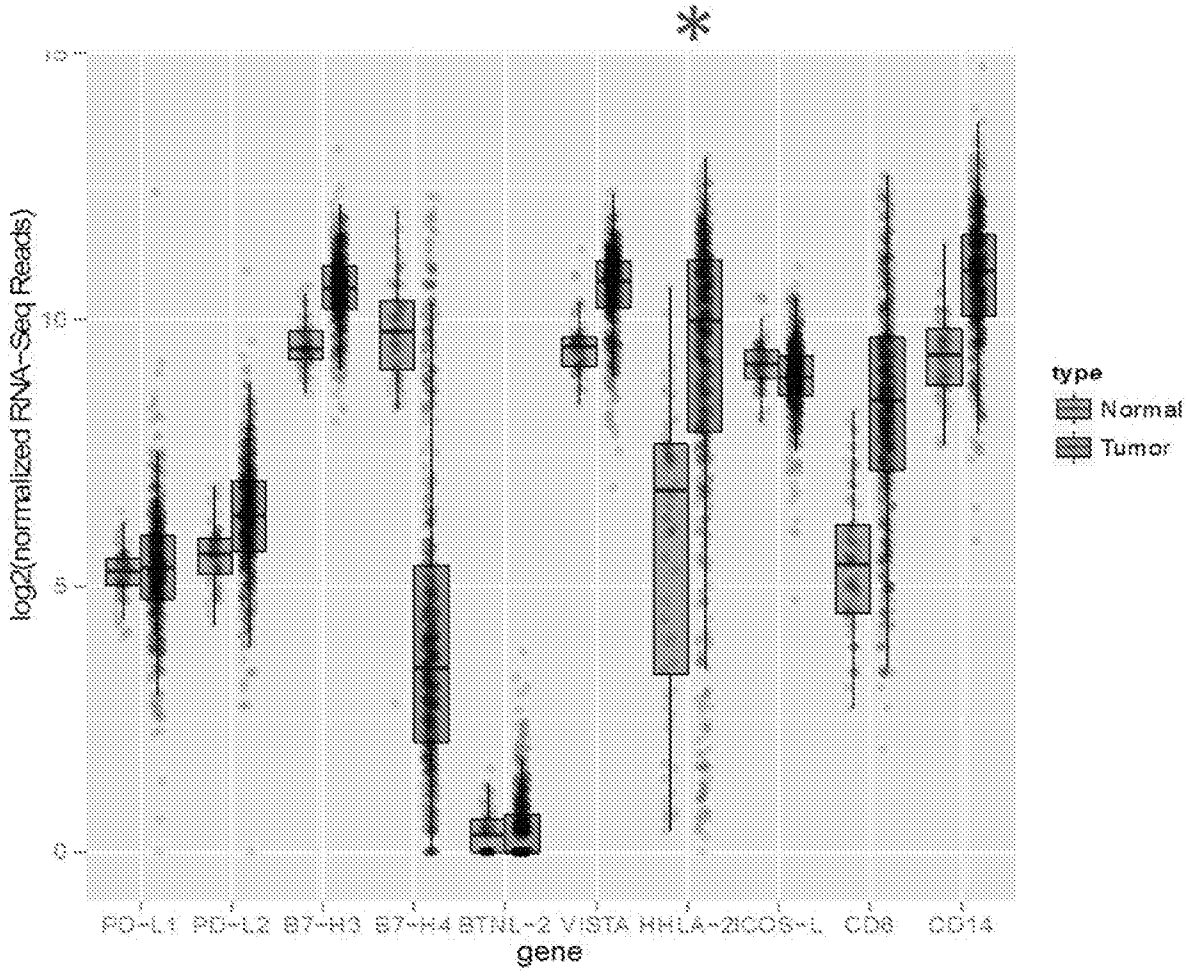


Figure 3



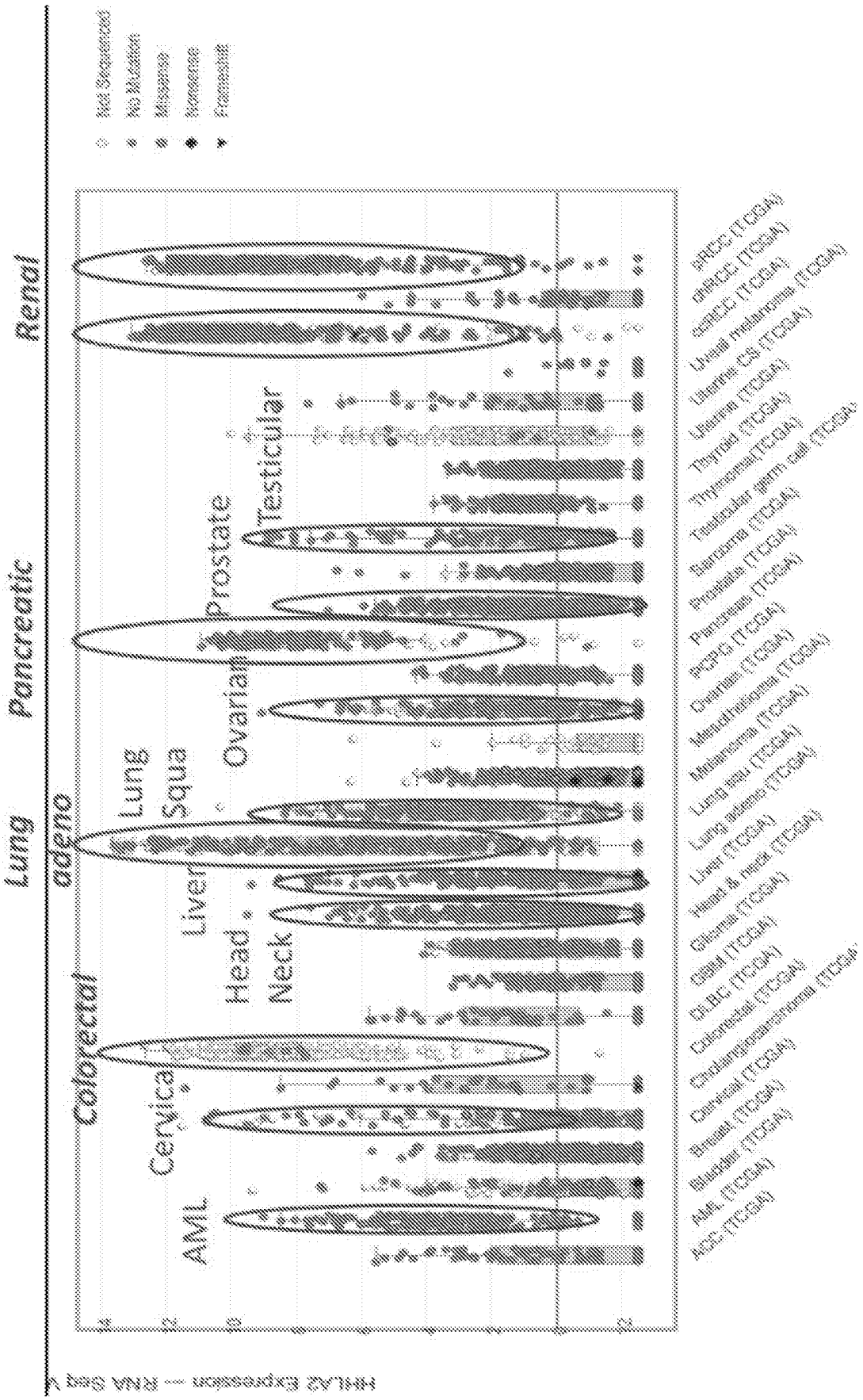

Lung adeno
Pancreatic
Renal
Colorectal
Cervical
AML
Head & Neck
Liver
Lung Squa
Ovarian
Prostate
Testicular
Not Sequenced
No Mutation
Missense
Nonsense
Frameshift
HHLA2 Expression — RNA Seq V2
ccRCC (TCGA)
pRCC (TCGA)
chRCC (TCGA)
ccRCC (TCGA)
Uveal melanoma (TCGA)
Uterine CS (TCGA)
Uterine (TCGA)
Thymoma (TCGA)
Thyroid (TCGA)
Testicular germ cell (TCGA)
Sarcoma (TCGA)
Prostate (TCGA)
Pancreas (TCGA)
PCPG (TCGA)
Ovarian (TCGA)
Mesothelioma (TCGA)
Melanoma (TCGA)
Lung squ (TCGA)
Lung adeno (TCGA)
Liver (TCGA)
Head & neck (TCGA)
Glioma (TCGA)
GBM (TCGA)
GI.BC (TCGA)
Colorectal (TCGA)
Cholangiocarcinoma (TCGA)
Cervical (TCGA)
Breast (TCGA)
Bladder (TCGA)
AML (TCGA)
ACC (TCGA)

Figure 4

Figure 5A

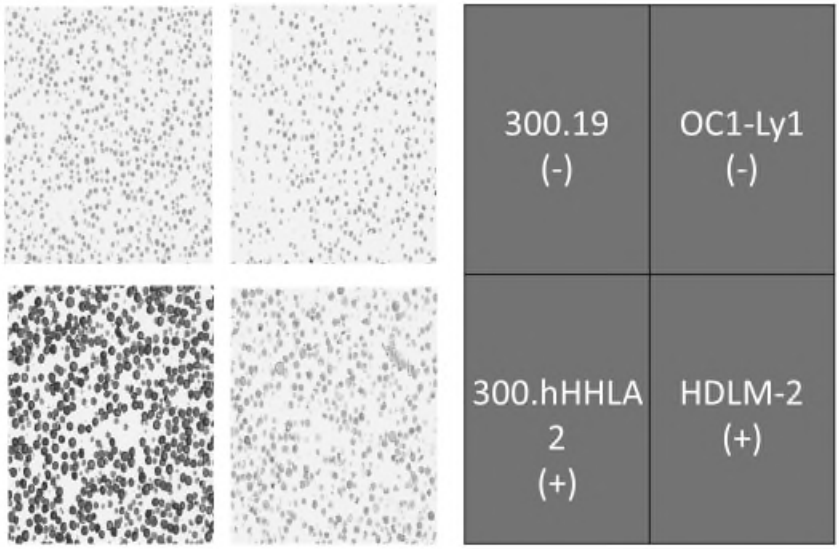


Figure 5B

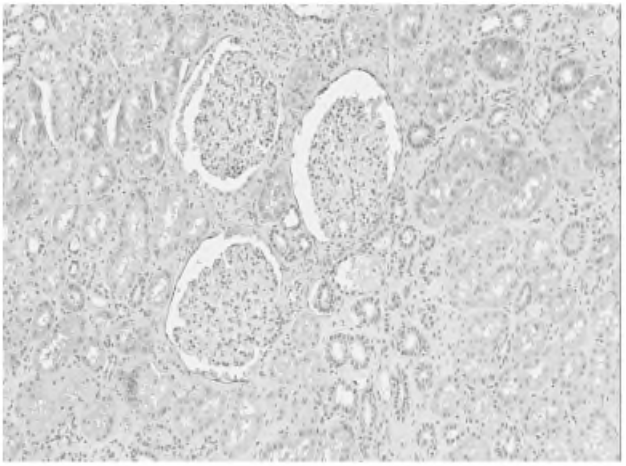


Figure 5C



Figure 5D

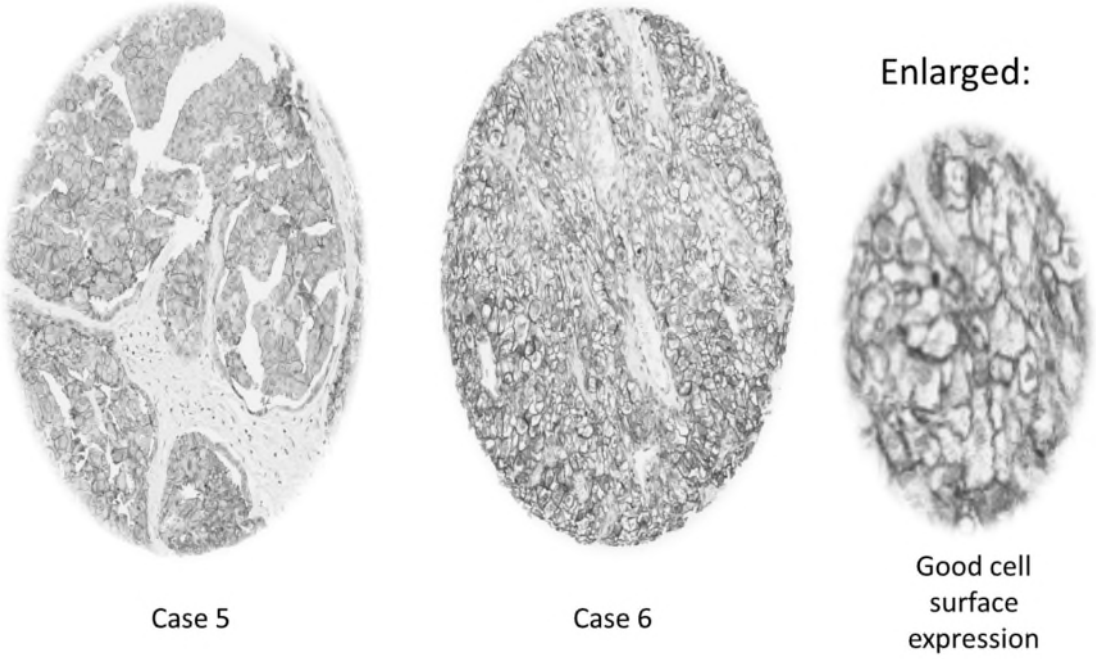
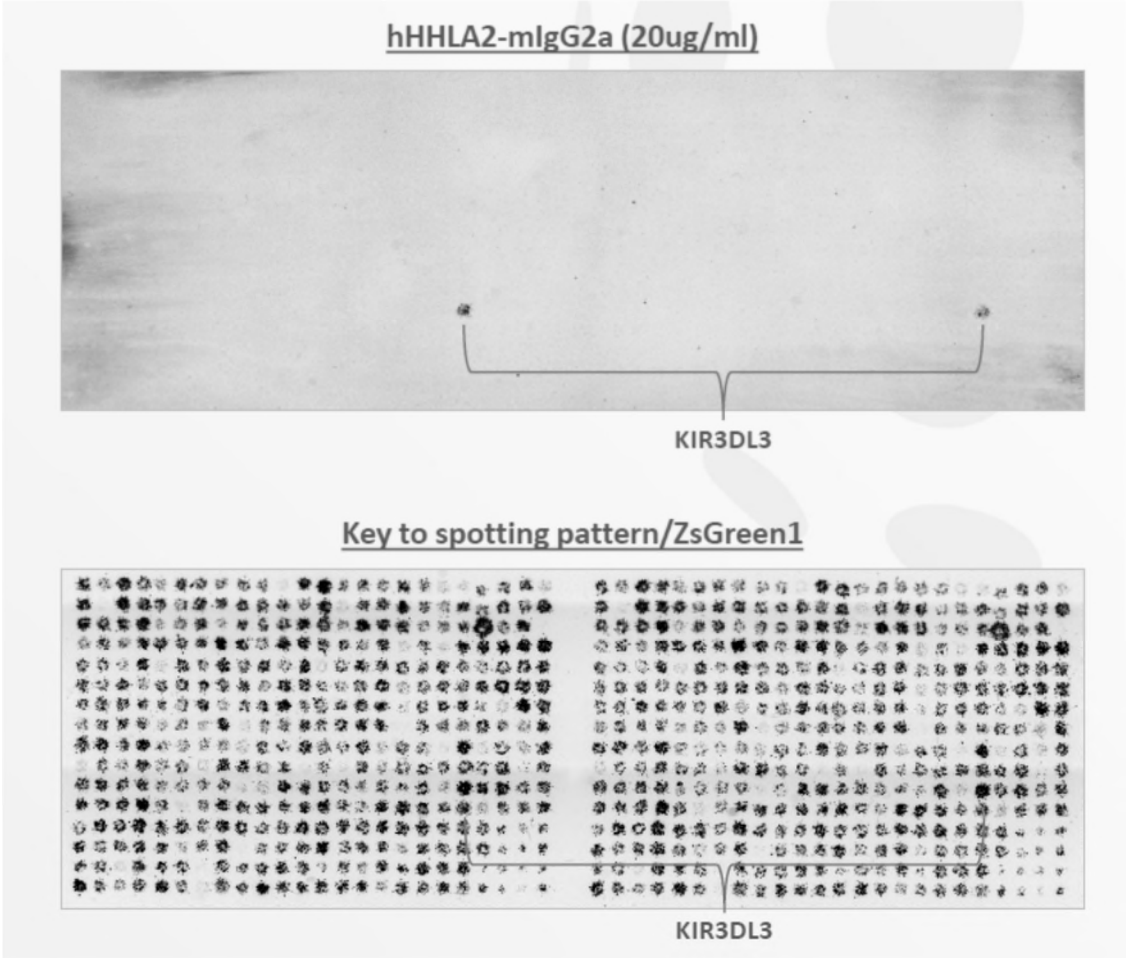


Figure 6A



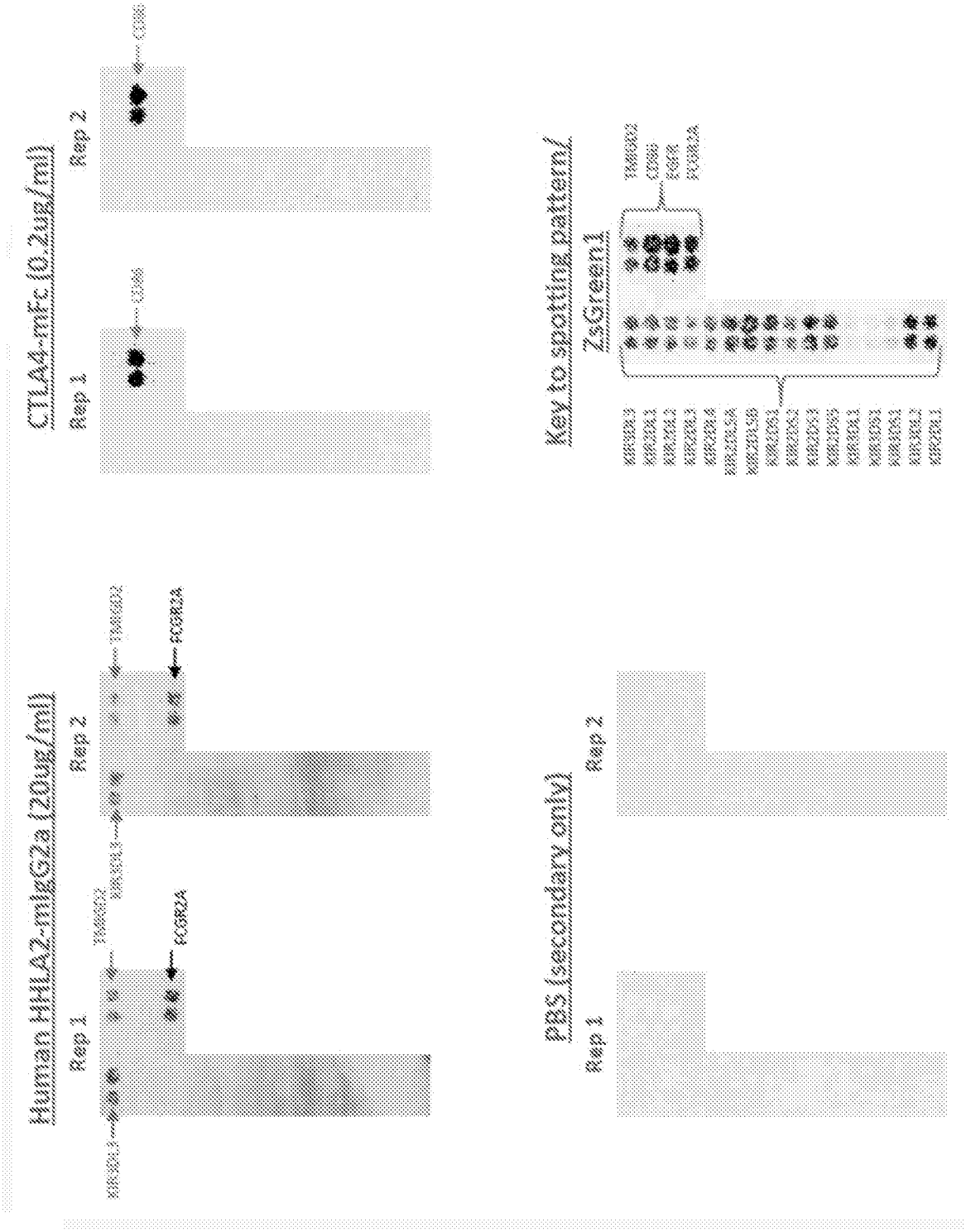

CTLA4-mFc (0.2ug/ml)
Rep 1
Rep 2
CD86
Human HHLA2-mIgG2a (20ug/ml)
Rep 1
Rep 2
TMIGD2
KIR3DL3
FCGR2A
PBS (secondary only)
Rep 1
Rep 2
Key to spotting pattern/
ZsGreen1
TMIGD2
CD86
FCGR
FCGR2A
KIR3DL3
KIR2DL1
KIR2DL3
KIR2DL2
KIR2DL4
KIR2DL5A
KIR2DL5B
KIR3DL1
KIR3DS1
KIR2DS2
KIR2DS3
KIR2DS5
KIR3DL2
KIR3DP1
KIR2DL2
KIR2DL1

Figure 6B

Figure 6C

Position	Gene ID	Accession	Position	Gene ID	Accession
1	KIR3DL3	BC143802	17	TMIGD2	NM_1444615.1
2	KIR2DL1	BC069344	18	CD86	
3	KIR2DL2	NM_014219	19	EGFR	
4	KIR2DL3	BC032422	20	FCGR2A	
5	KIR2DL4	BC041611			
6	KIR2DL5A	NM_020535			
7	KIR2DL5B	NM_001018081			
8	KIR2DS1	NM_014512			
9	KIR2DS2	BC108917			
10	KIR2DS3	NM_012313			
11	KIR2DS5	NM_014513			
12	KIR3DL1	BC028206			
13	KIR3DS1	NM_001083539			
14	KIR3DS1	BC098107			
15	KIR3DL2	NM_006737			
16	KIR2DL1	NM_014218			

Figure 7

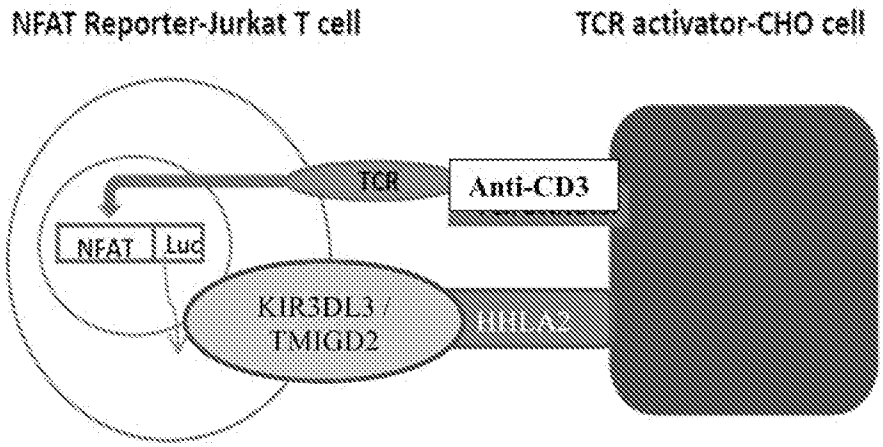


Figure 8

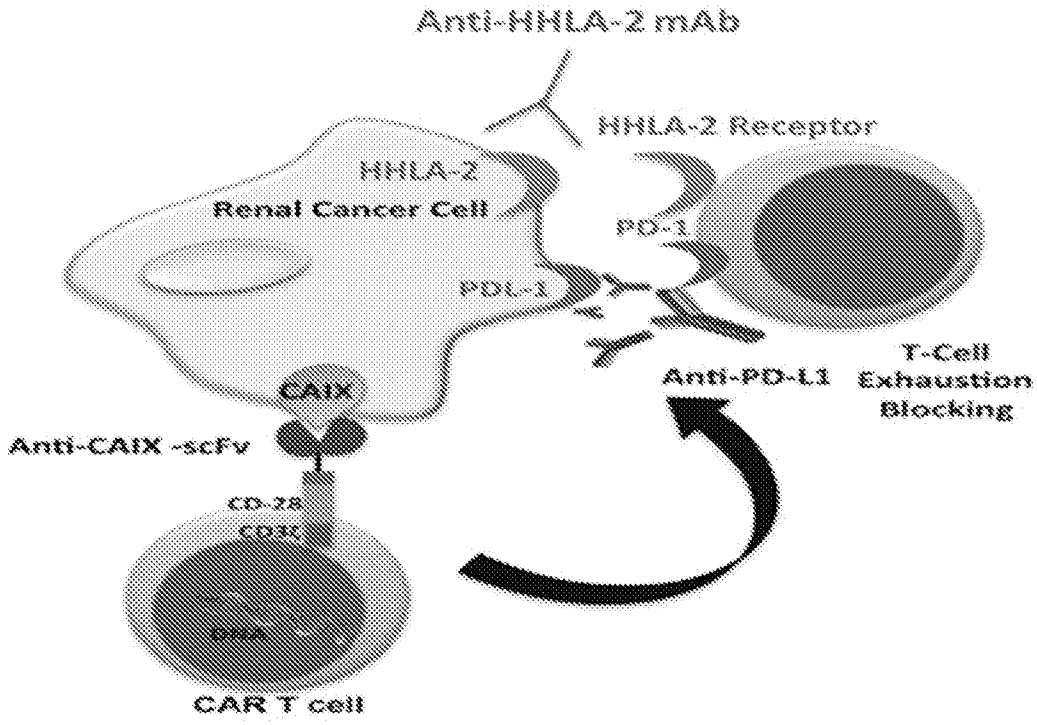
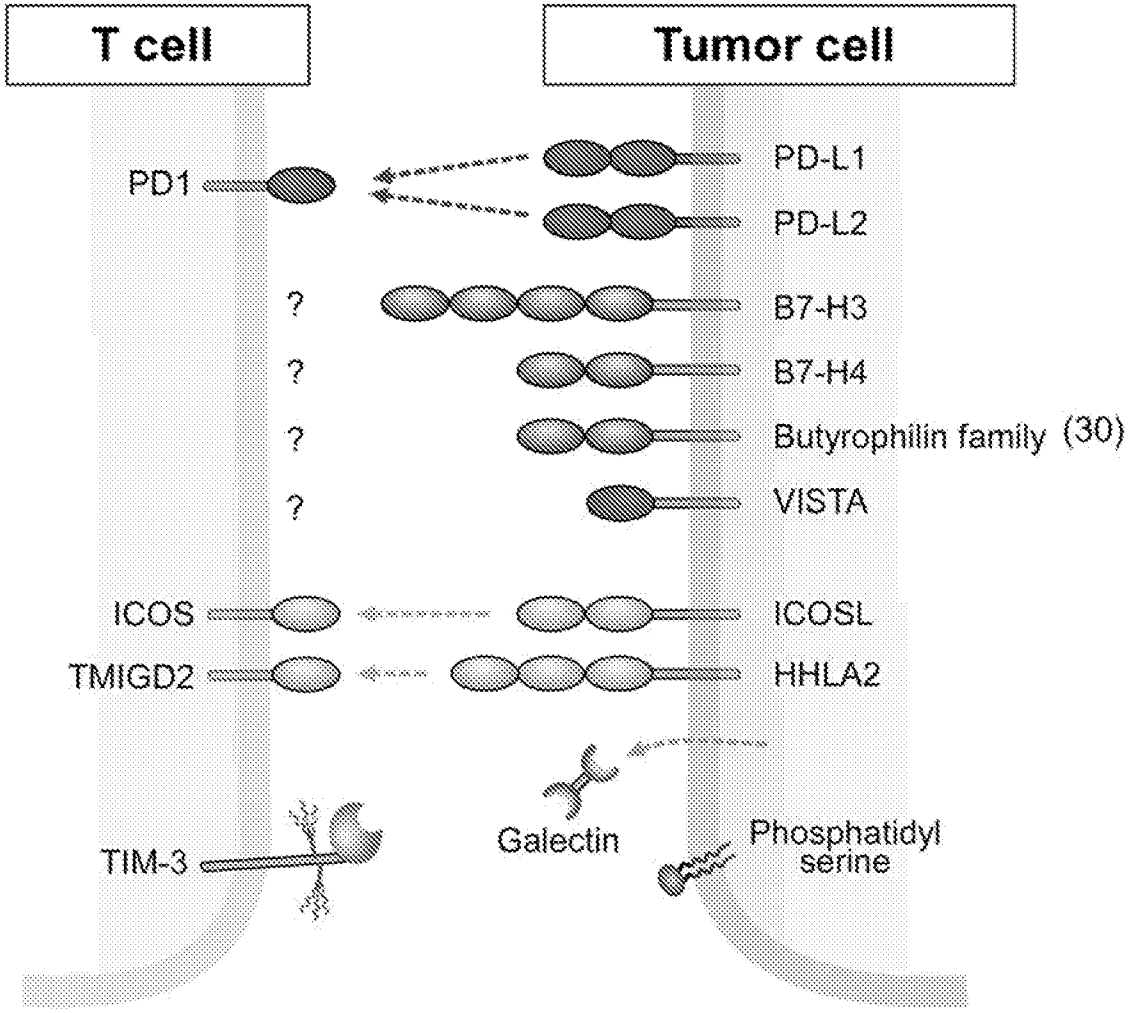


Figure 9


T cell
Tumor cell
PD1
PD-L1
PD-L2
?
B7-H3
?
B7-H4
?
Butyrophilin family (30)
?
VISTA
ICOS
ICOSL
TMIGD2
HHLA2
Galectin
TIM-3
Phosphatidyl serine

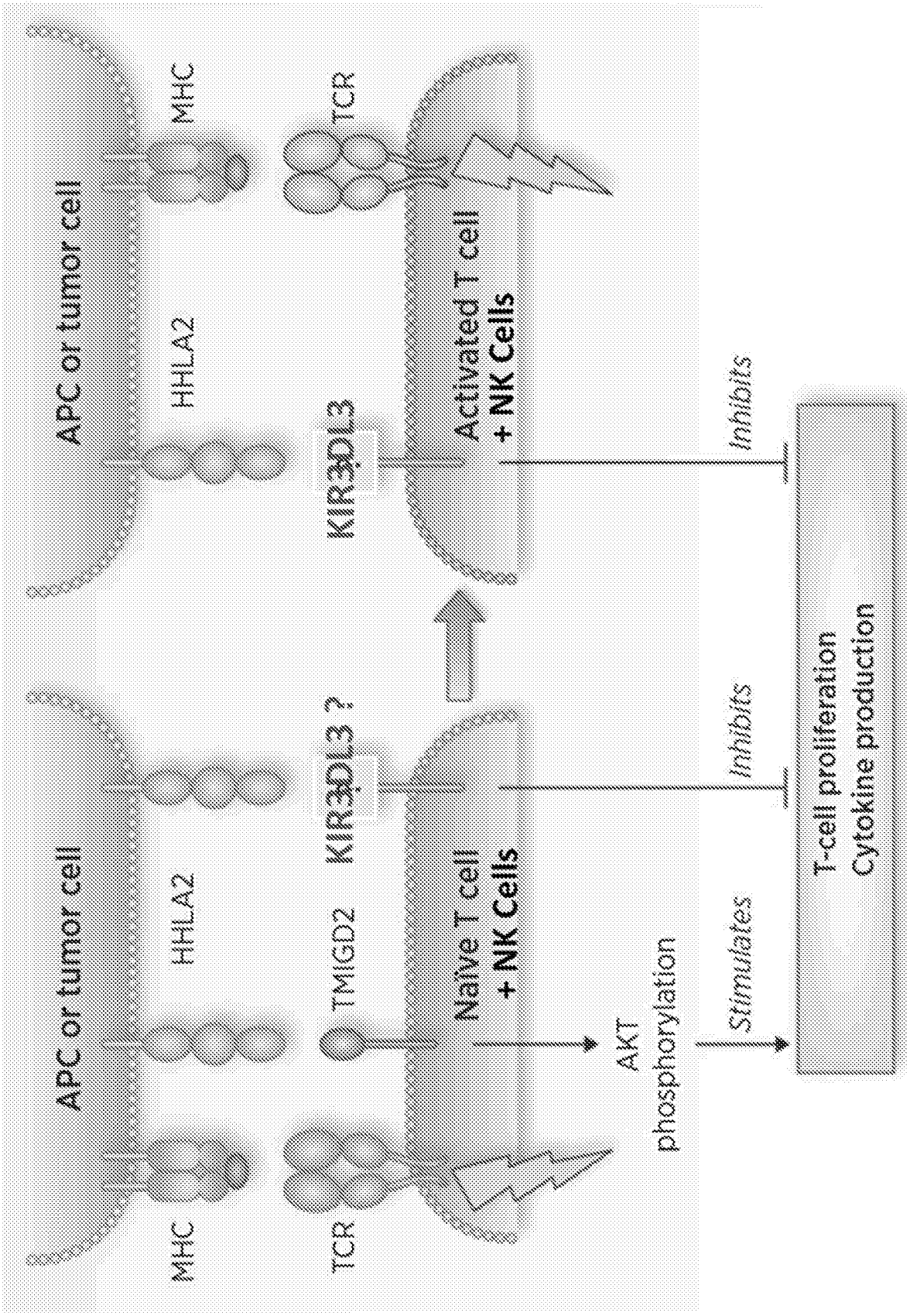

APC or tumor cell
MHC
HHLA2
TCR
KIR3DL3
Activated T cell
+ NK Cells
Inhibits
APC or tumor cell
HHLA2
TMIGD2
KIR3DL3 ?
Naive T cell
+ NK Cells
AKT
phosphorylation
Inhibits
Stimulates
T-cell proliferation
Cytokine production
MHC
TCR

Figure 10

Figure 11

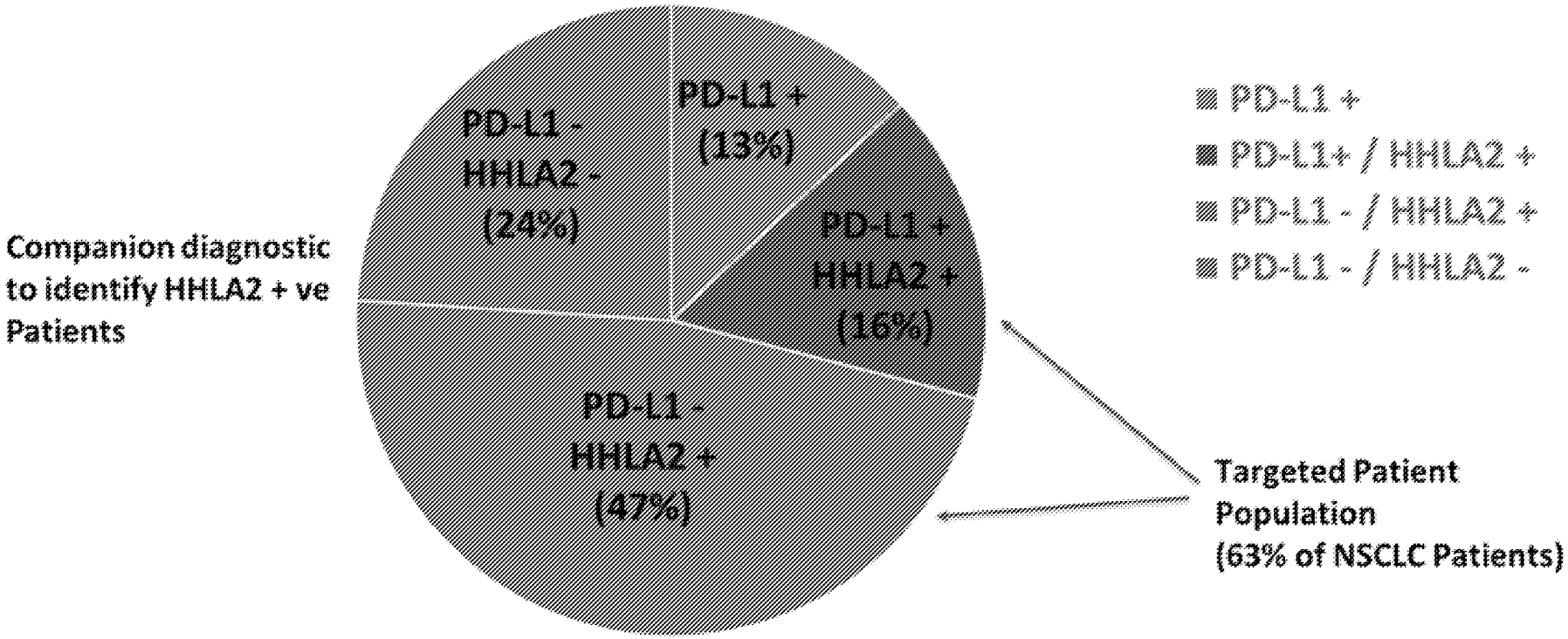
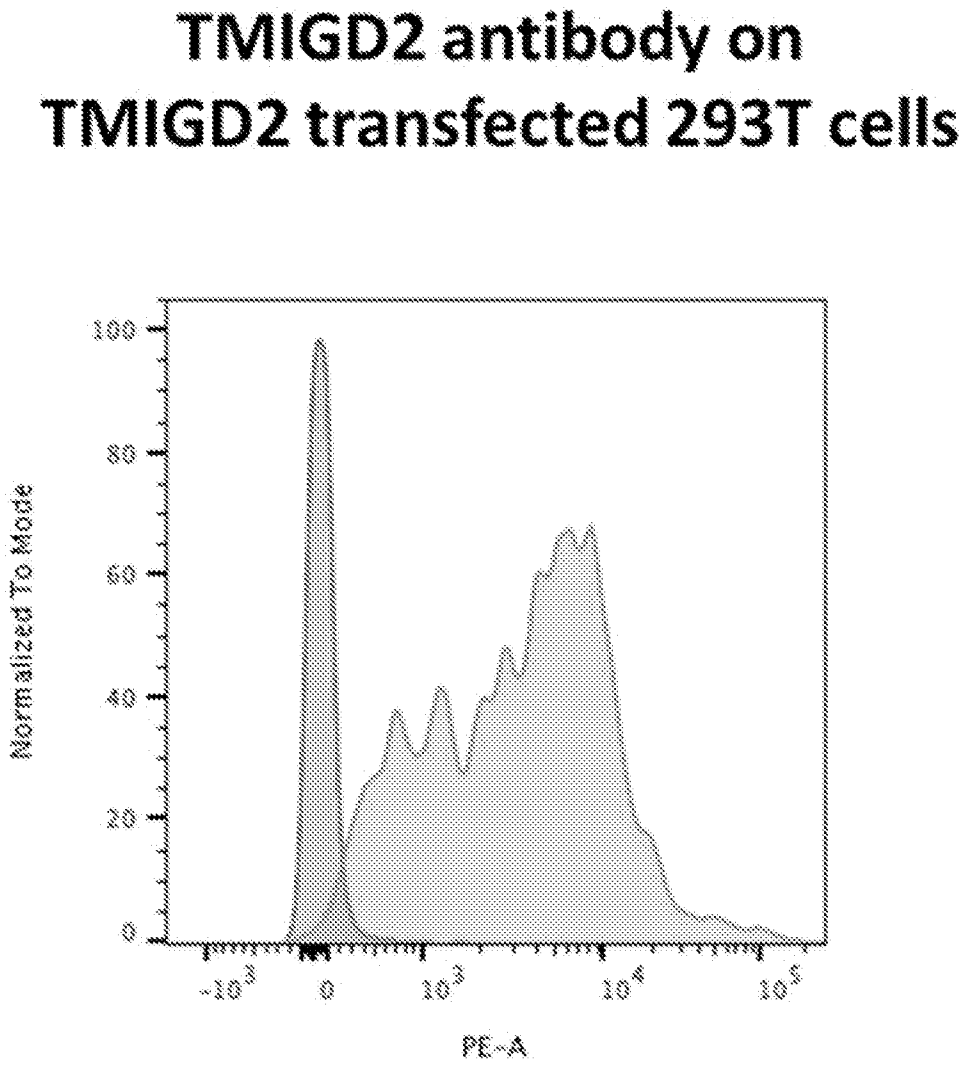
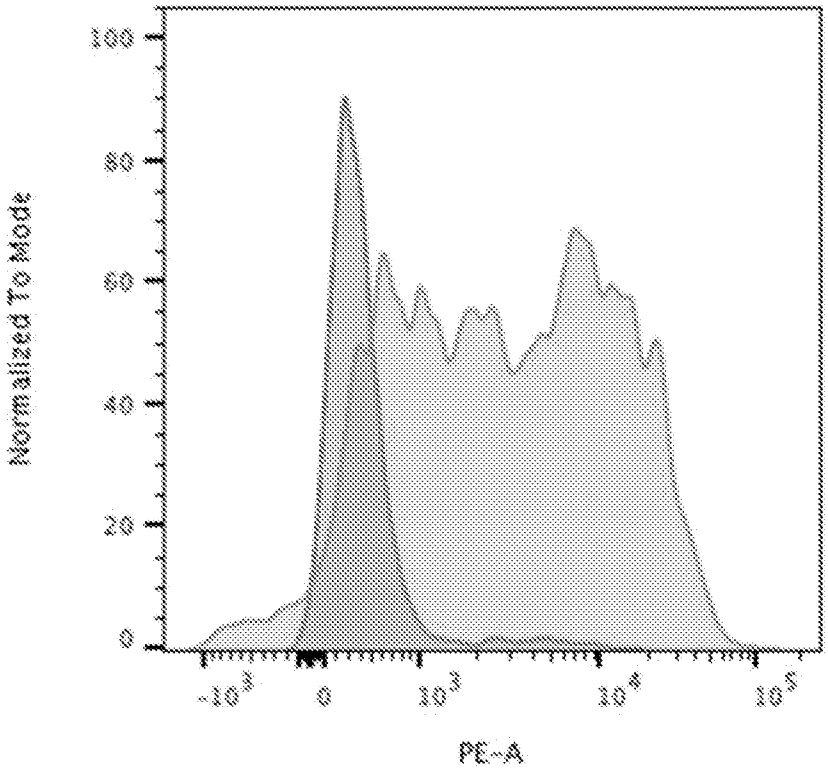

Companion diagnostic to identify HHLA2 + ve Patients
PD-L1 - HHLA2 - (24%)
PD-L1 + (13%)
PD-L1 + HHLA2 + (16%)
PD-L1 - HHLA2 + (47%)
PD-L1 +
PD-L1+ / HHLA2 +
PD-L1 - / HHLA2 +
PD-L1 - / HHLA2 -
Targeted Patient Population (63% of NSCLC Patients)

Figure 12A



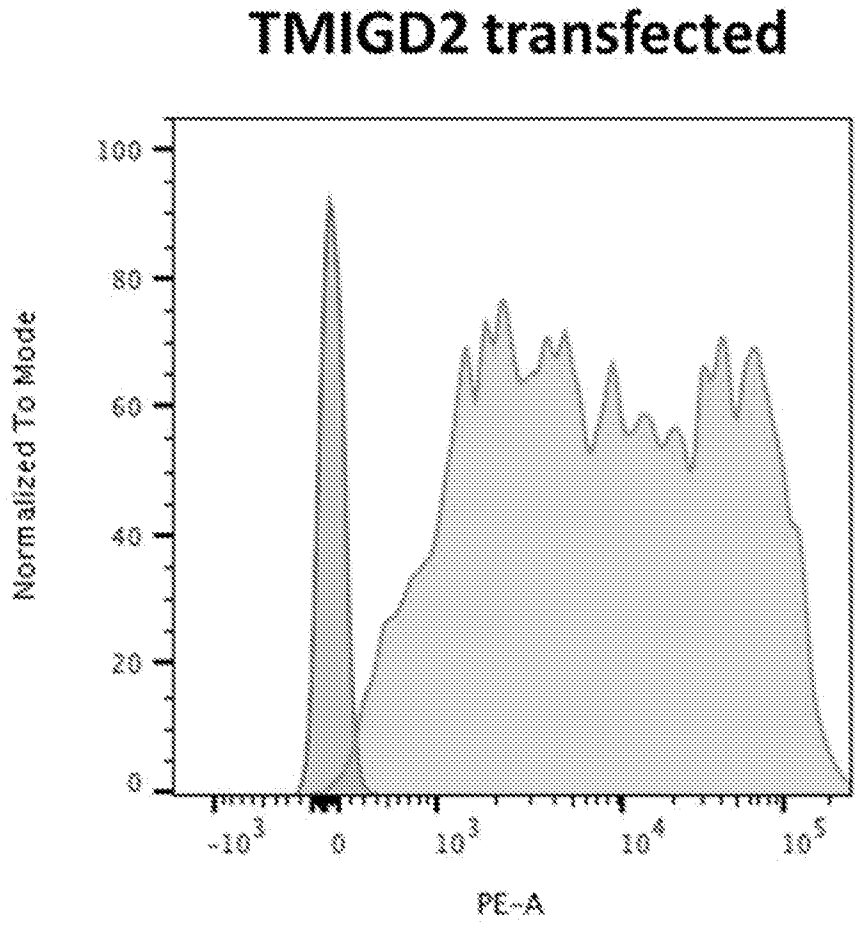
	Sample Name	Subset Name	Count	Mean : PE-A
	293T cells Assay 6-25-18_Specimen_001_B2_B02_005.fc	293T cells	1320	6923
	293T cells Assay 6-25-18_Specimen_001_D2_D02_011.fc	293T cells	2332	583

Figure 12B



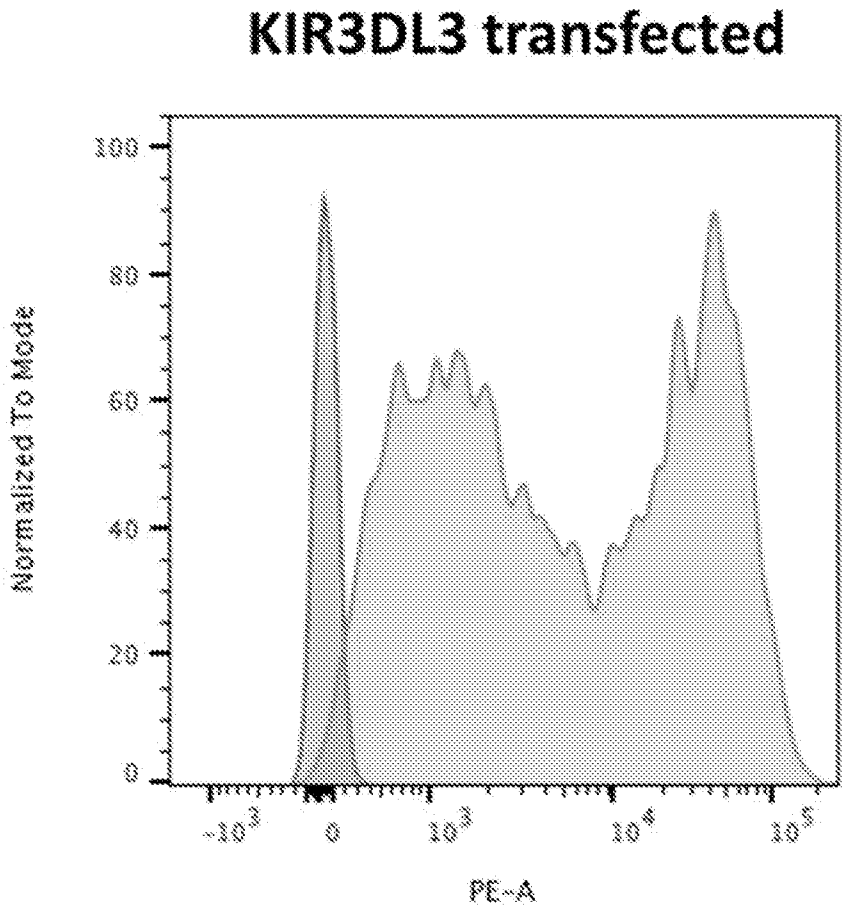
	Sample Name	Subset Name	Count	Mean : PE-A
	293T cells Assay 6-25-18_Specimen_001_C1_C01_003.fc	293T cells	1863	6885
	293T cells Assay 6-25-18_Specimen_001_D1_D01_004.fc	293T cells	2730	749

Figure 12C



	Sample Name	Subset Name	Count	Mean : PE-A
	293T cells Assay 6-25-18_Specimen_001_C3_C03_011.fc	293T cell	5477	23536
	293T cells Assay 6-25-18_Specimen_001_F3_F03_023.fc	293T cell	4405	58.4

Figure 12D



	Sample Name	Subset Name	Count	Mean : PE-A
	293T cells Assay 6-25-18_Specimen_001_E3_E03_019.fc	293T cell	4536	18525
	293T cells Assay 6-25-18_Specimen_001_F3_F03_023.fc	293T cell	4405	58.4

Figure 13A

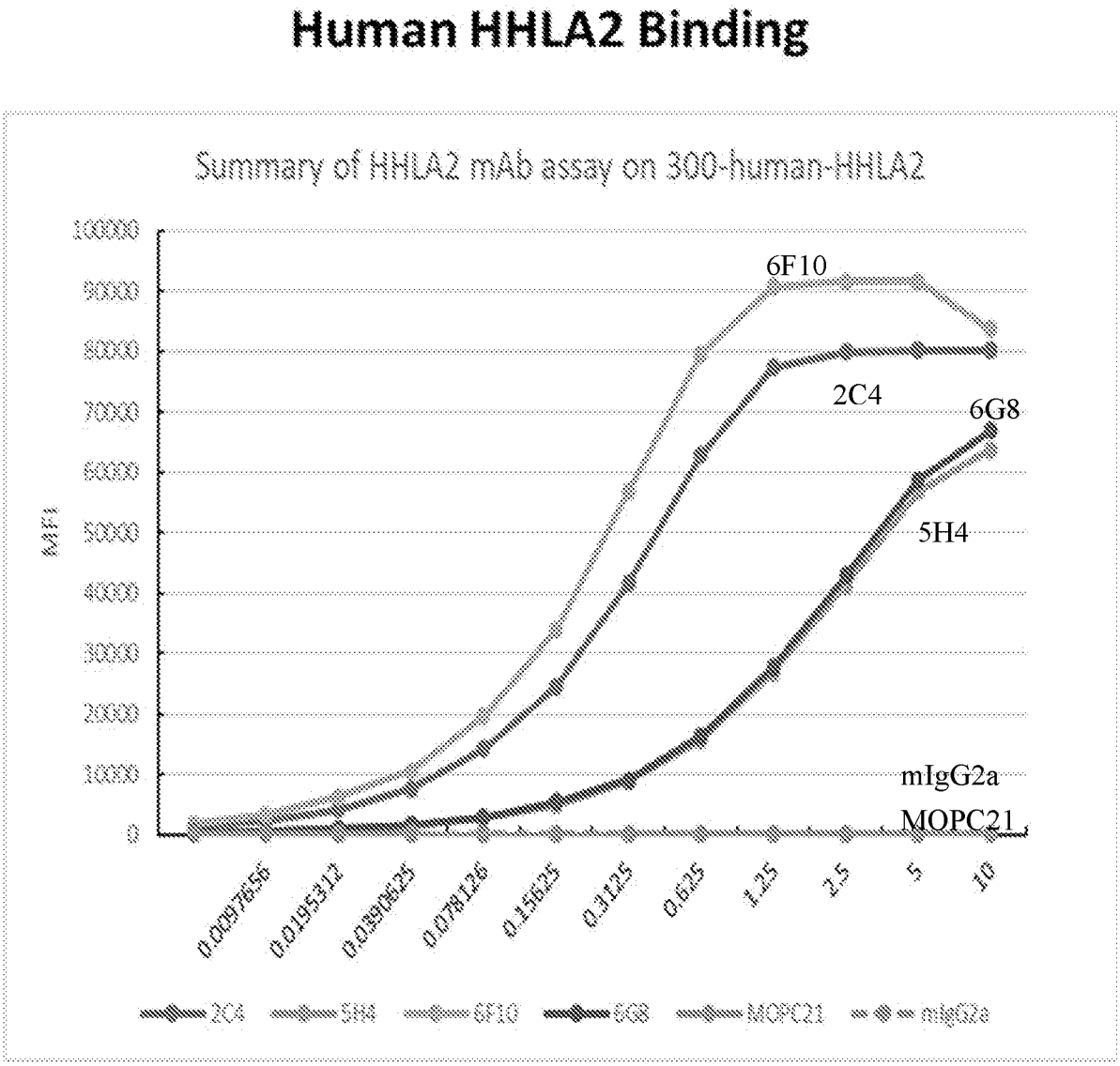
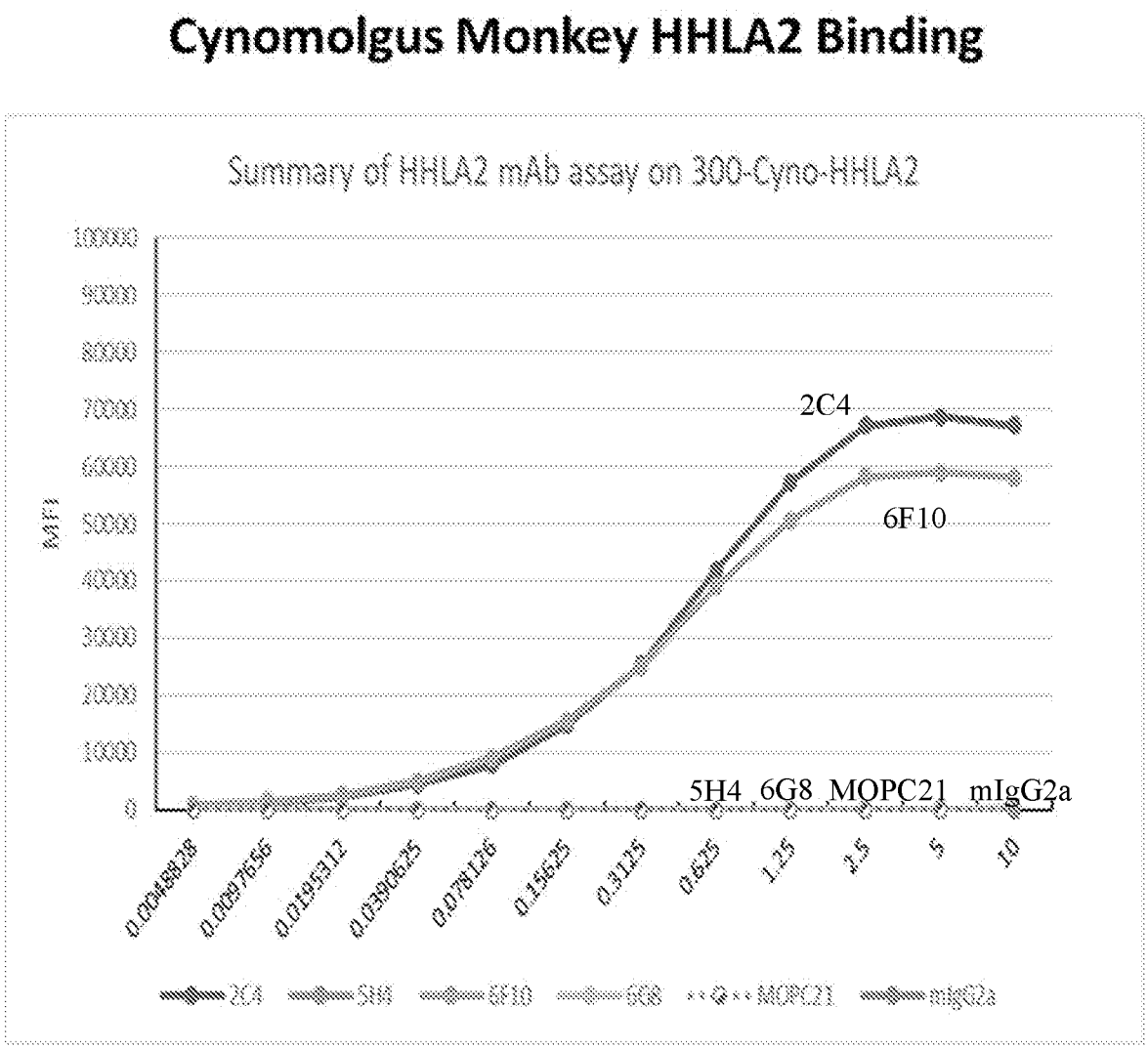

Human HHLA2 Binding
Summary of HHLA2 mAb assay on 300-human-HHLA2
MFI
100000
90000
80000
70000
60000
50000
40000
30000
20000
10000
0
6F10
2C4
6G8
5H4
mIgG2a
MOPC21
0.009765625
0.019531250
0.039062500
0.078125000
0.156250000
0.312500000
0.625
1.25
2.5
5
10
2C4
5H4
6F10
6G8
MOPC21
mIgG2a

Figure 13B


Cynomolgus Monkey HHLA2 Binding
Summary of HHLA2 mAb assay on 300-Cyno-HHLA2
MFI
10000
9000
8000
7000
6000
5000
4000
3000
2000
1000
0
2C4
6F10
5H4 6G8 MOPC21 mIgG2a
0.00468638
0.00937656
0.01875312
0.03906625
0.078126
0.15625
0.3125
0.625
1.25
2.5
5
10
2C4
5H4
6F10
6G8
MOPC21
mIgG2a

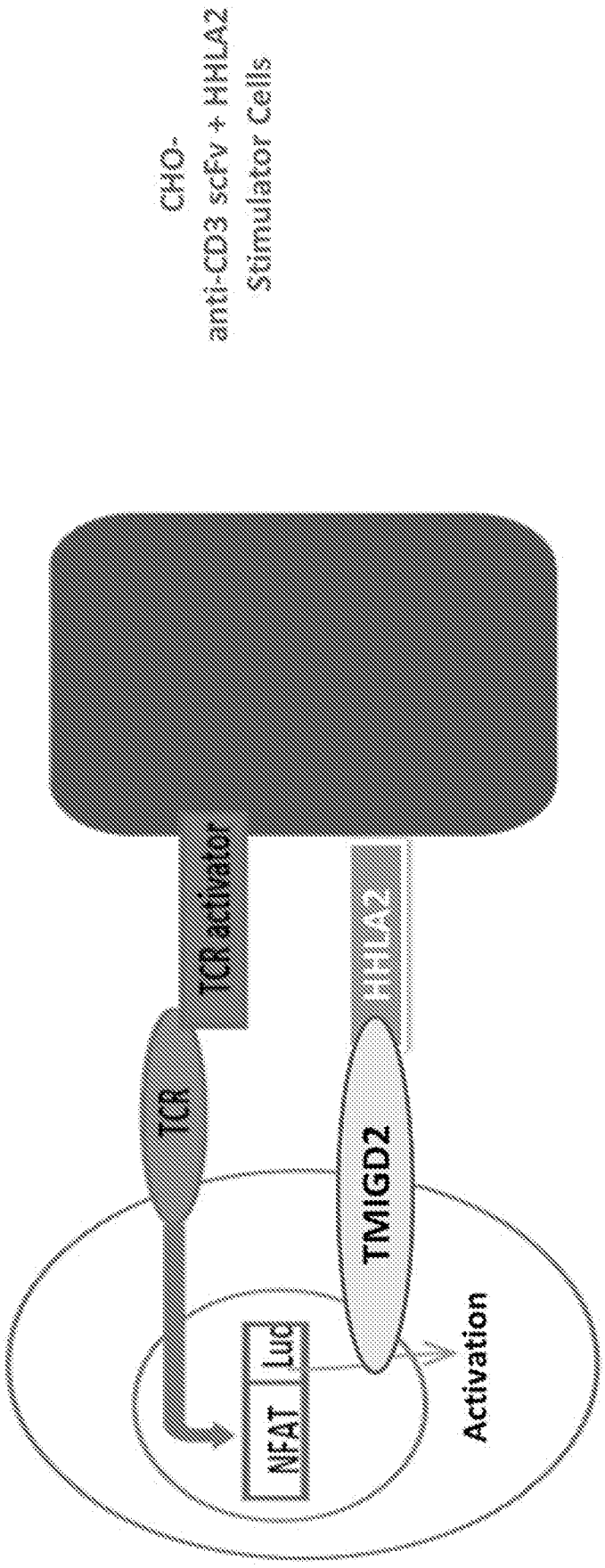
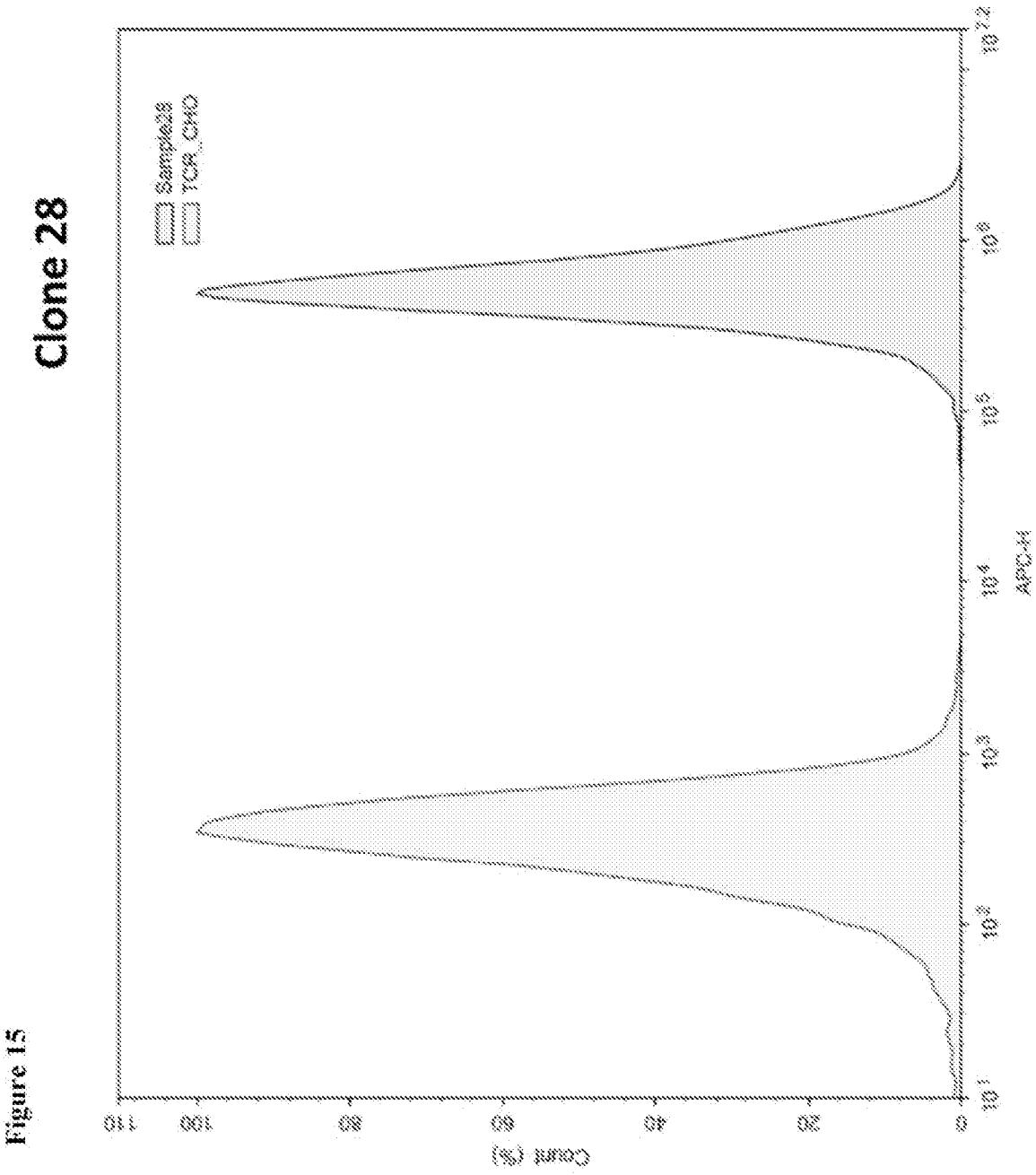

CHO-
anti-CD3 scFv + HHLA2
Stimulator Cells
TCR activator
HHLA2
TCR
TMIGD2
NFAT
Luc
Activation

Figure 14

Figure 15


Clone 28
Sample28
TCR_CHO
Count (%)
APC-H
0
20
40
60
80
100
110
10^{-1}
10^{0}
10^{1}
10^{2}
10^{3}
10^{4}
10^{5}
10^{6}
$10^{7.2}$

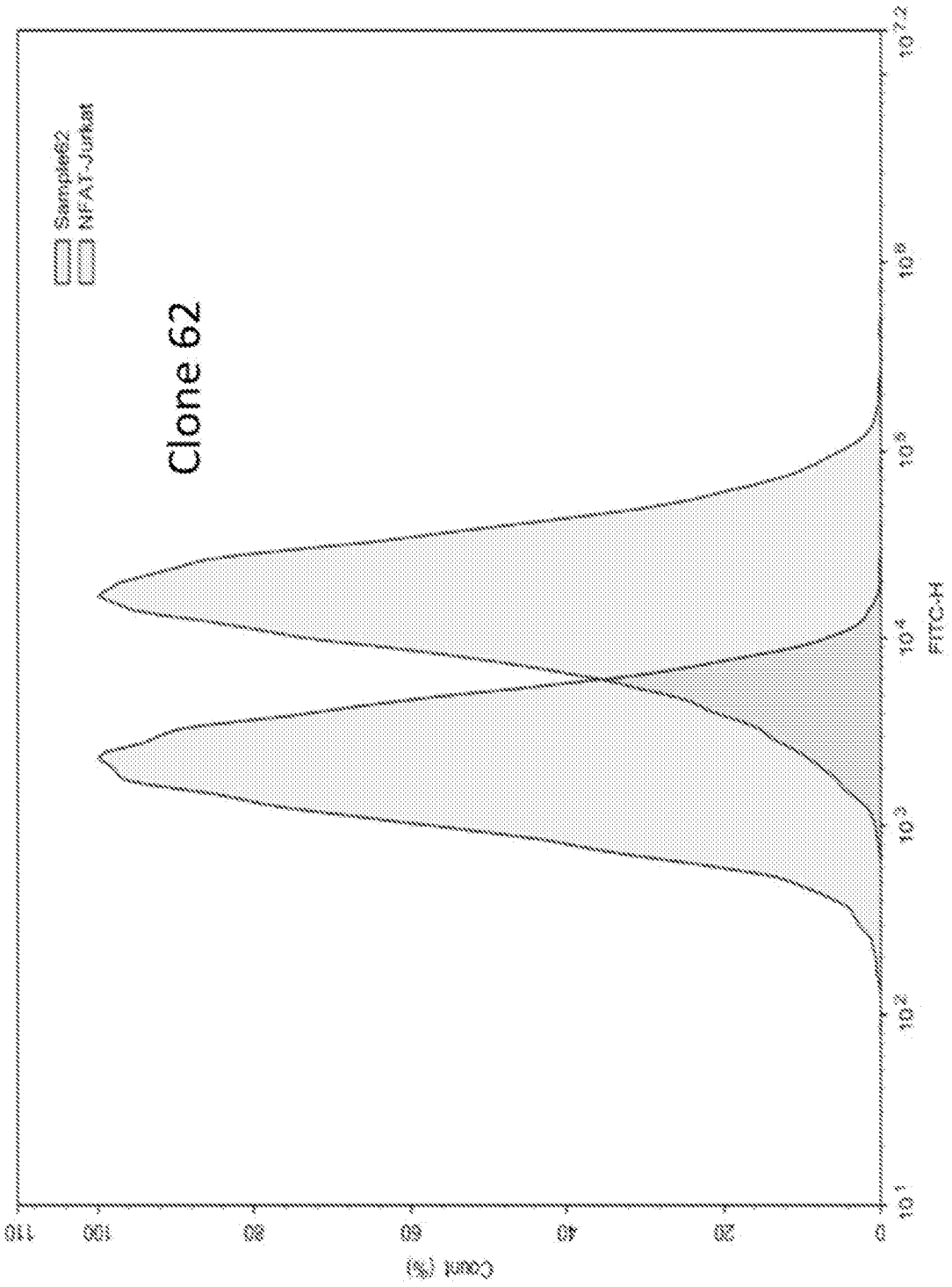

Clone 62
Sample62
NFAT-Jurkat
Count (%)
FITC-H
0
20
40
60
80
100
110
10^1
10^2
10^3
10^4
10^5
10^6
10^7

Figure 16

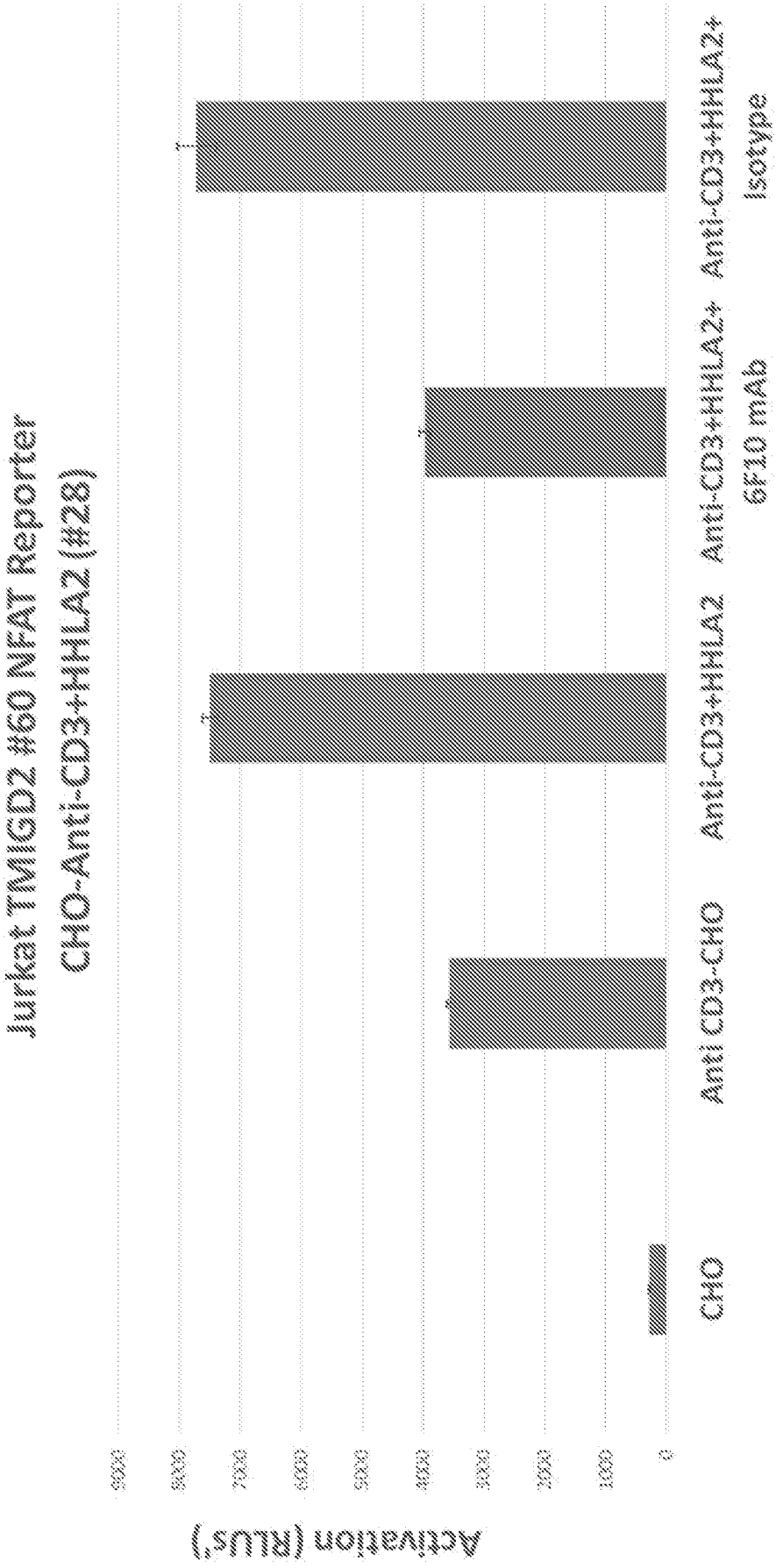
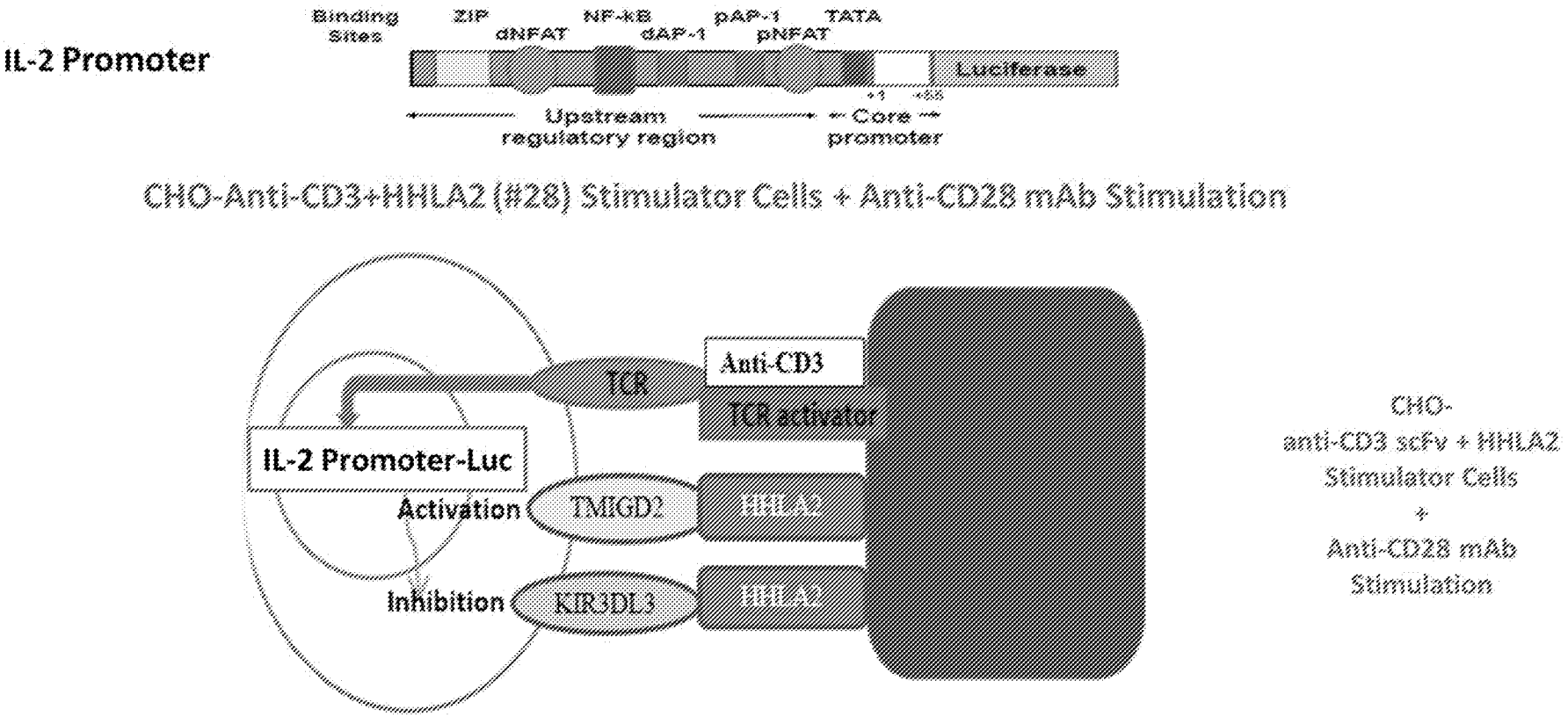

Jurkat TMIGD2 #60 NFAT Reporter
CHO-Anti-CD3+HHLA2 (#28)
Activation (RLUs')
9000
8000
7000
6000
5000
4000
3000
2000
1000
0
CHO
Anti CD3-CHO
Anti-CD3+HHLA2
Anti-CD3+HHLA2+ 6F10 mAb
Anti-CD3+HHLA2+ Isotype

Figure 17

Figure 18


IL-2 Promoter
Binding Sites
ZIP
dNFAT
NF-κB
dAP-1
pAP-1
pNFAT
TATA
Luciferase
+1
-48
Upstream regulatory region
Core promoter
CHO-Anti-CD3+HHLA2 (#28) Stimulator Cells + Anti-CD28 mAb Stimulation
IL-2 Promoter-Luc
Activation
Inhibition
TCR
Anti-CD3
TCR activator
TMIGD2
KIR3DL3
HHLA2
HHLA2
CHO-
anti-CD3 scFv + HHLA2
Stimulator Cells
+
Anti-CD28 mAb
Stimulation

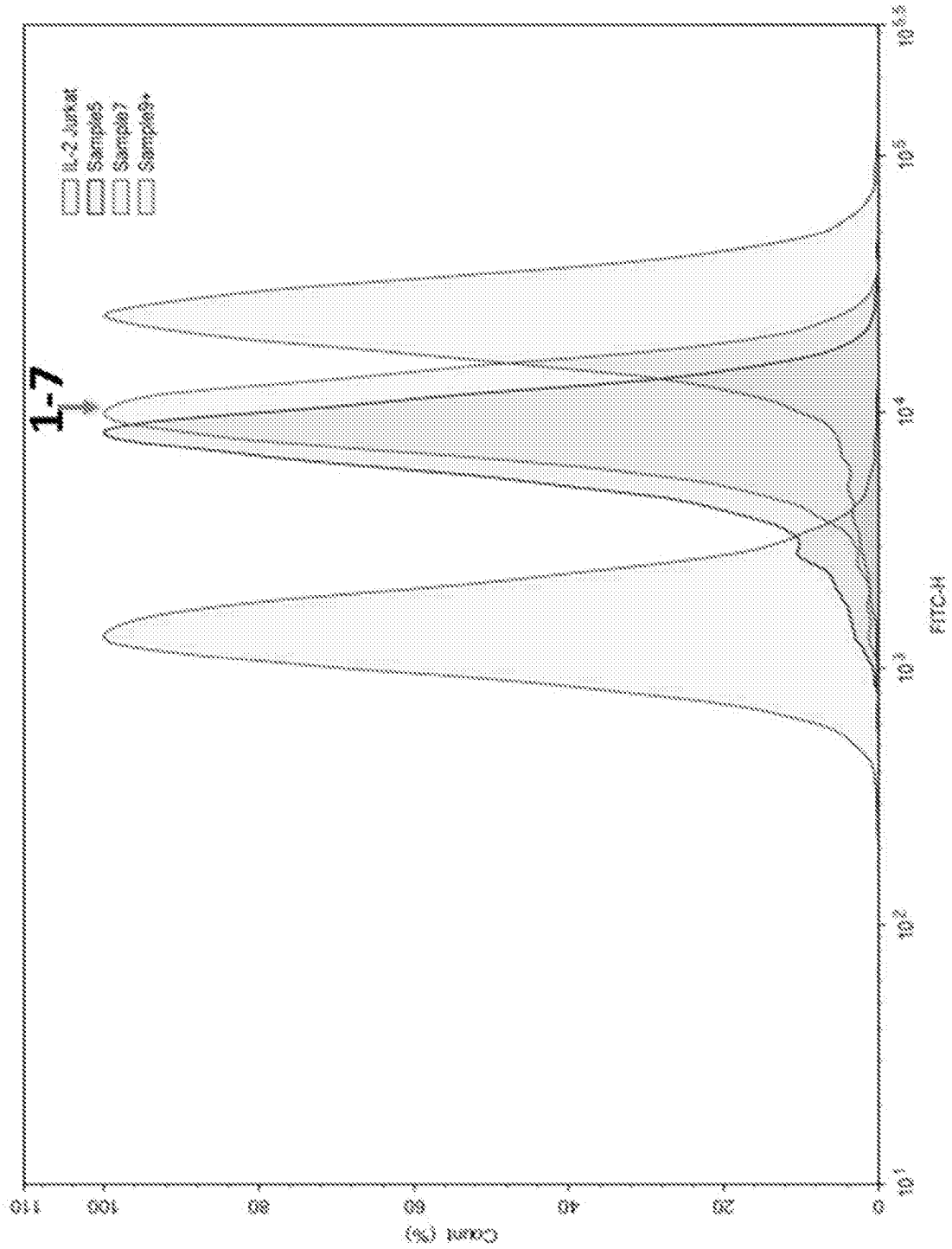


Figure 19A

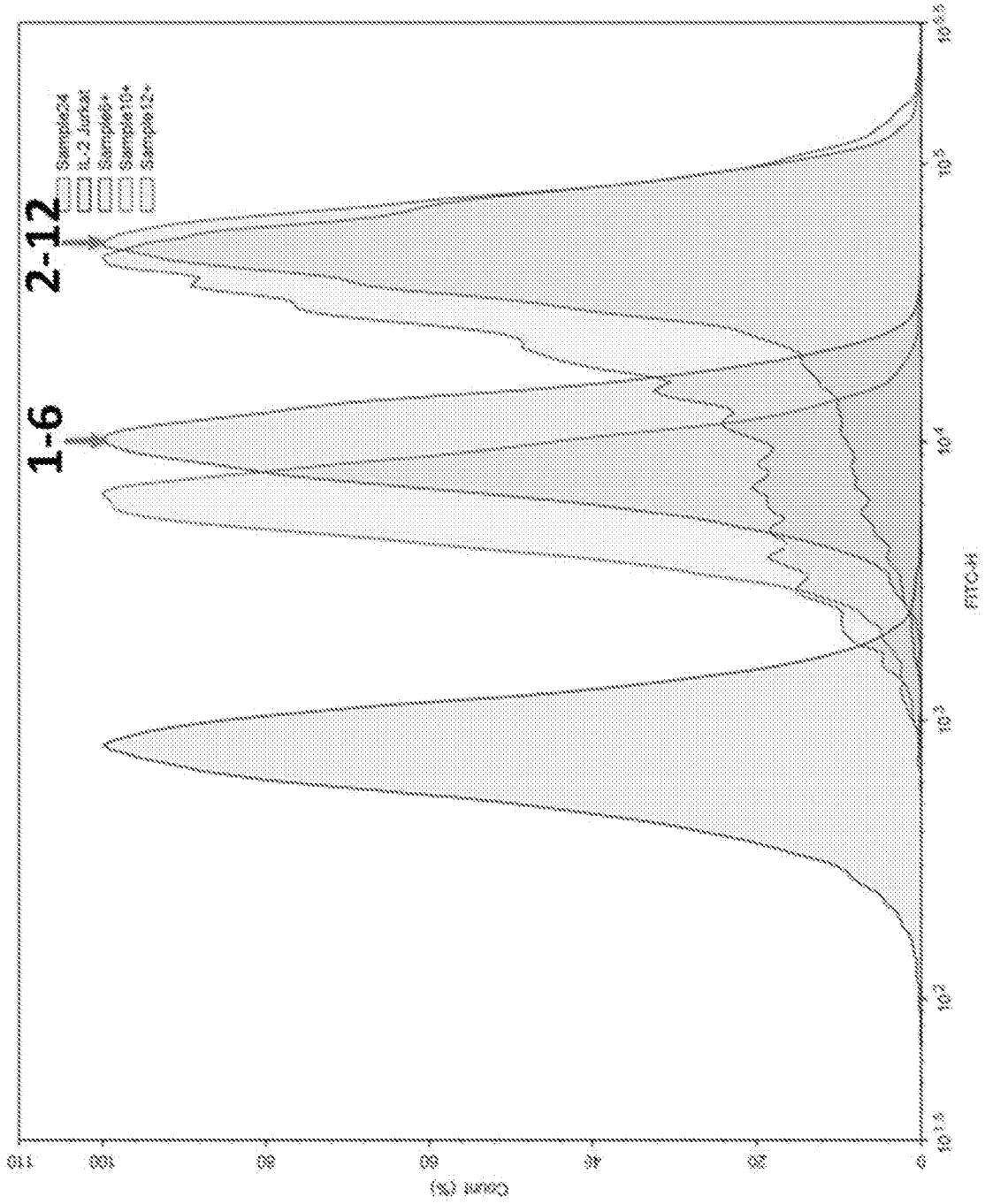

2-12
1-6
Sample24
IL-2 Jurkat
Sample+
Sample10+
Sample12+
Count (%)
FITC-A

Figure 19B

Figure 20A

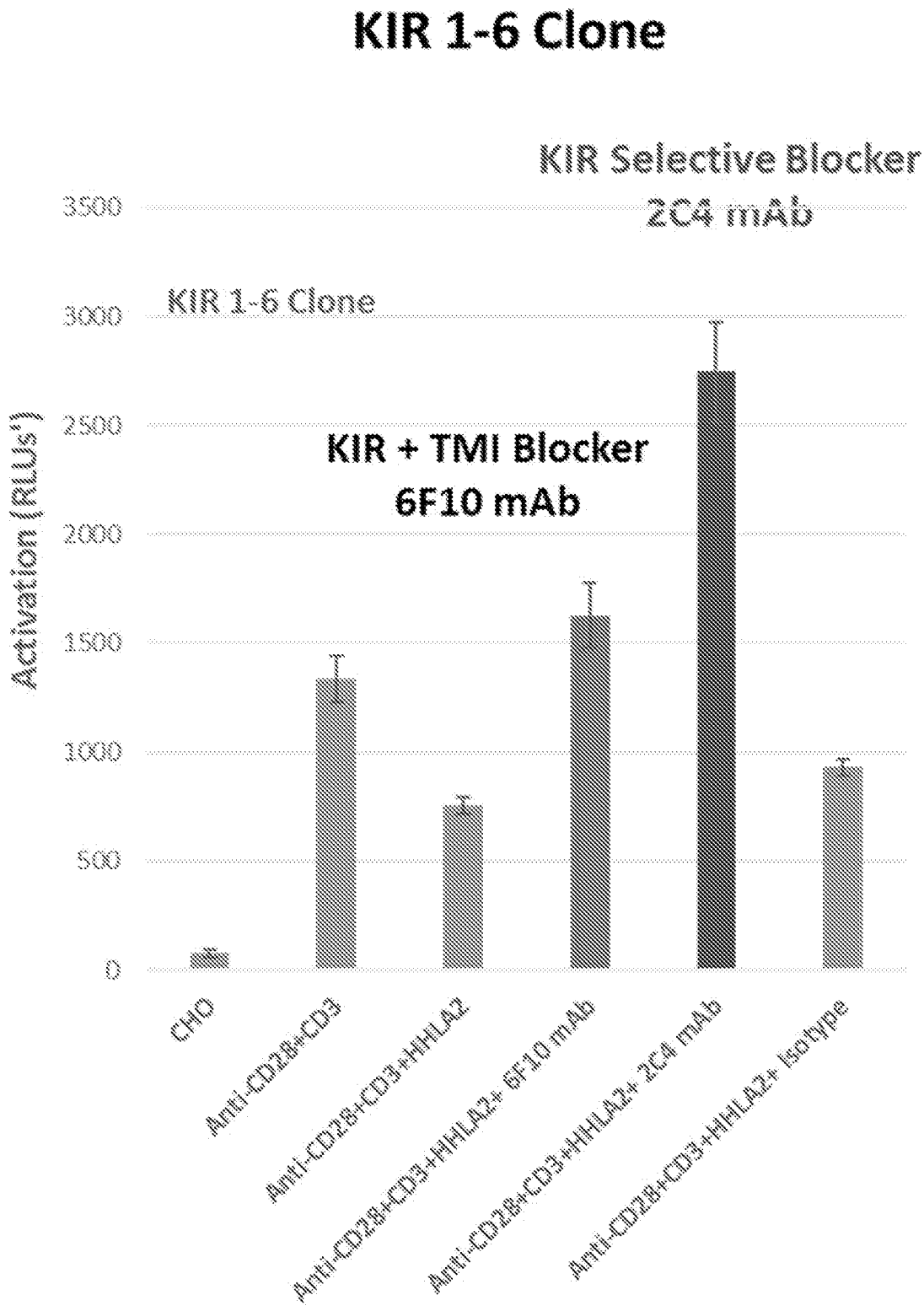

KIR 1-6 Clone
KIR Selective Blocker
2C4 mAb
KIR 1-6 Clone
KIR + TMI Blocker
6F10 mAb
Activation (RLUs')
3500
3000
2500
2000
1500
1000
500
0
CHO
Anti-CD28+CD3
Anti-CD28+CD3+HHLA2
Anti-CD28+CD3+HHLA2+ 6F10 mAb
Anti-CD28+CD3+HHLA2+ 2C4 mAb
Anti-CD28+CD3+HHLA2+ isotype

Figure 20B

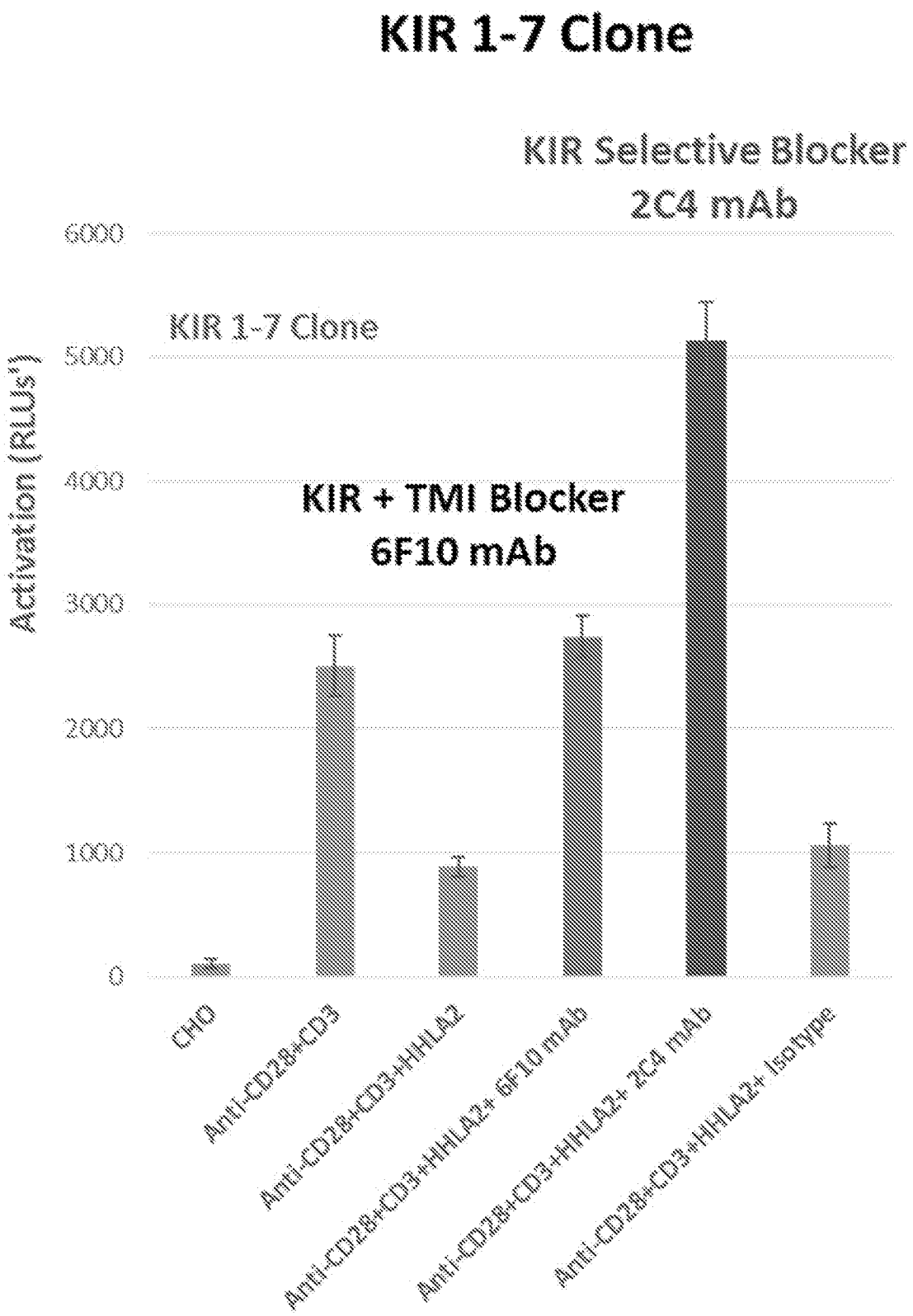

KIR 1-7 Clone
KIR Selective Blocker
2C4 mAb
KIR 1-7 Clone
KIR + TMI Blocker
6F10 mAb
Activation (RLUs')
6000
5000
4000
3000
2000
1000
0
CHO
Anti-CD28+CD3
Anti-CD28+CD3+HHLA2
Anti-CD28+CD3+HHLA2+ 6F10 mAb
Anti-CD28+CD3+HHLA2+ 2C4 mAb
Anti-CD28+CD3+HHLA2+ Isotype

Figure 20C

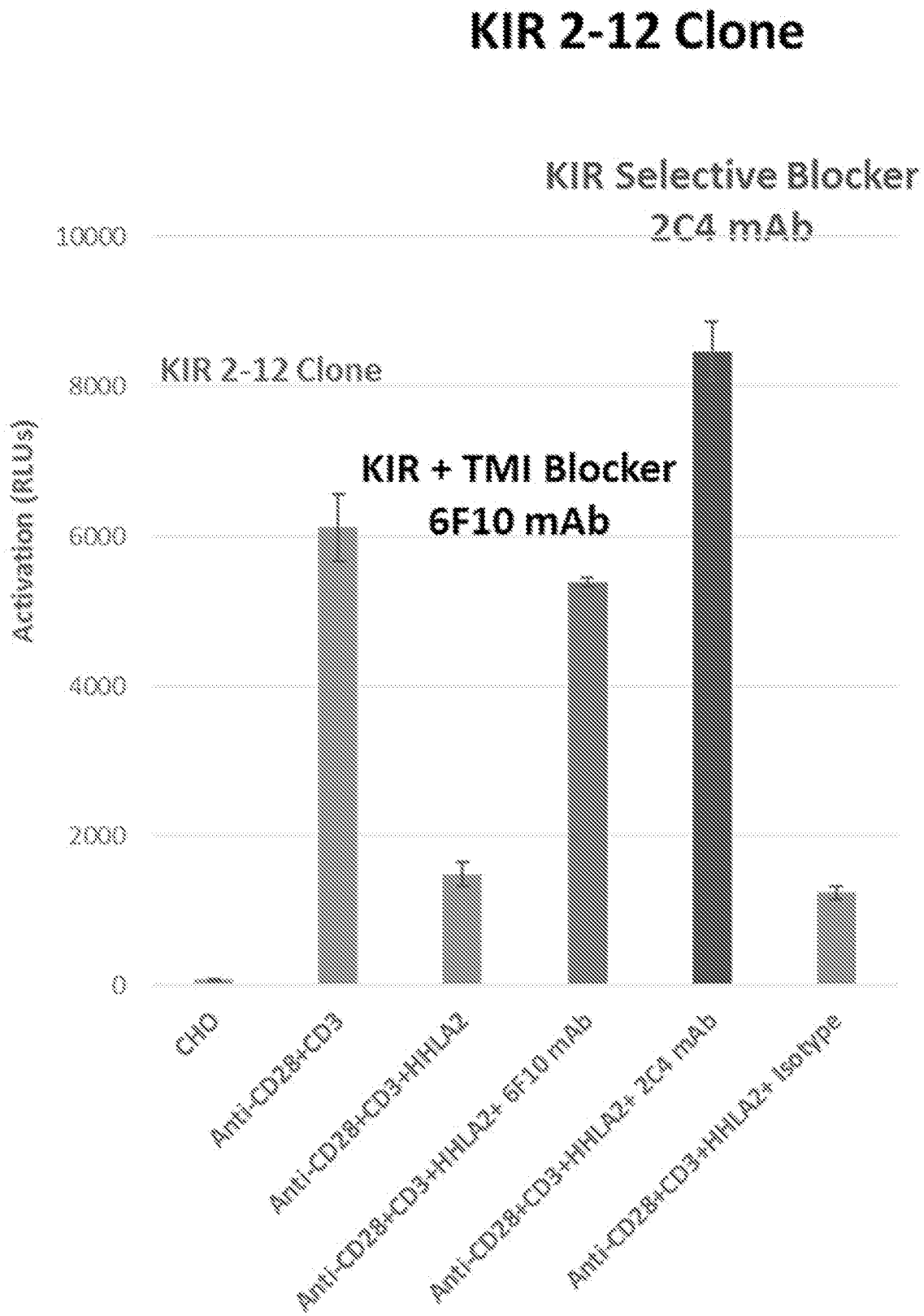

KIR 2-12 Clone
KIR Selective Blocker
2C4 mAb
KIR 2-12 Clone
KIR + TMI Blocker
6F10 mAb
Activation (RLUs)
10000
8000
6000
4000
2000
0
CHO
Anti-CD28+CD3
Anti-CD28+CD3+HHLA2
Anti-CD28+CD3+HHLA2+ 6F10 mAb
Anti-CD28+CD3+HHLA2+ 2C4 mAb
Anti-CD28+CD3+HHLA2+ Isotype

Figure 21A

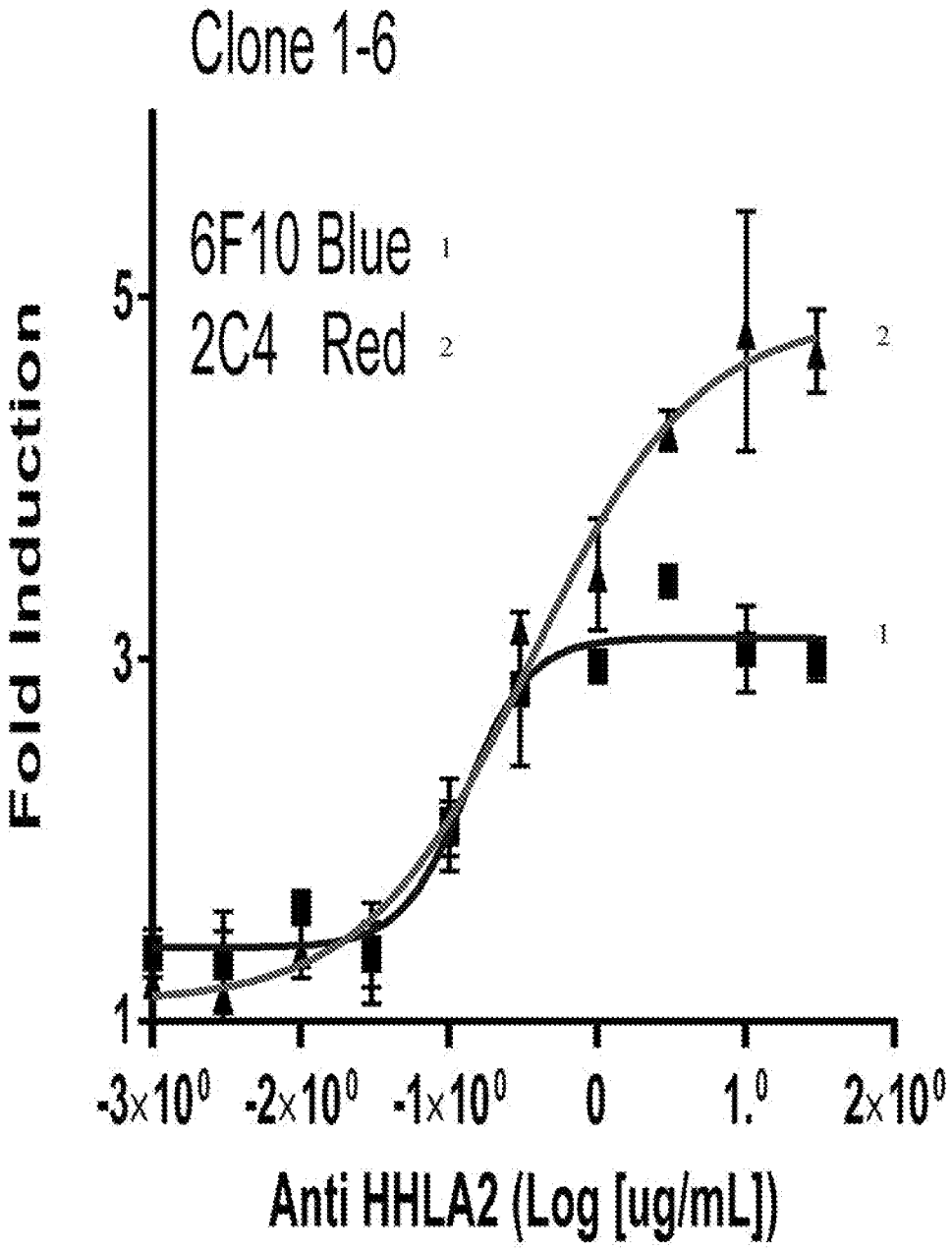

Clone 1-6
6F10 Blue 1
2C4 Red 2
Fold Induction
5
3
1
2
1
-3x10^0
-2x10^0
-1x10^0
0
1.^0
2x10^0
Anti HHLA2 (Log [ug/mL])

Figure 21B

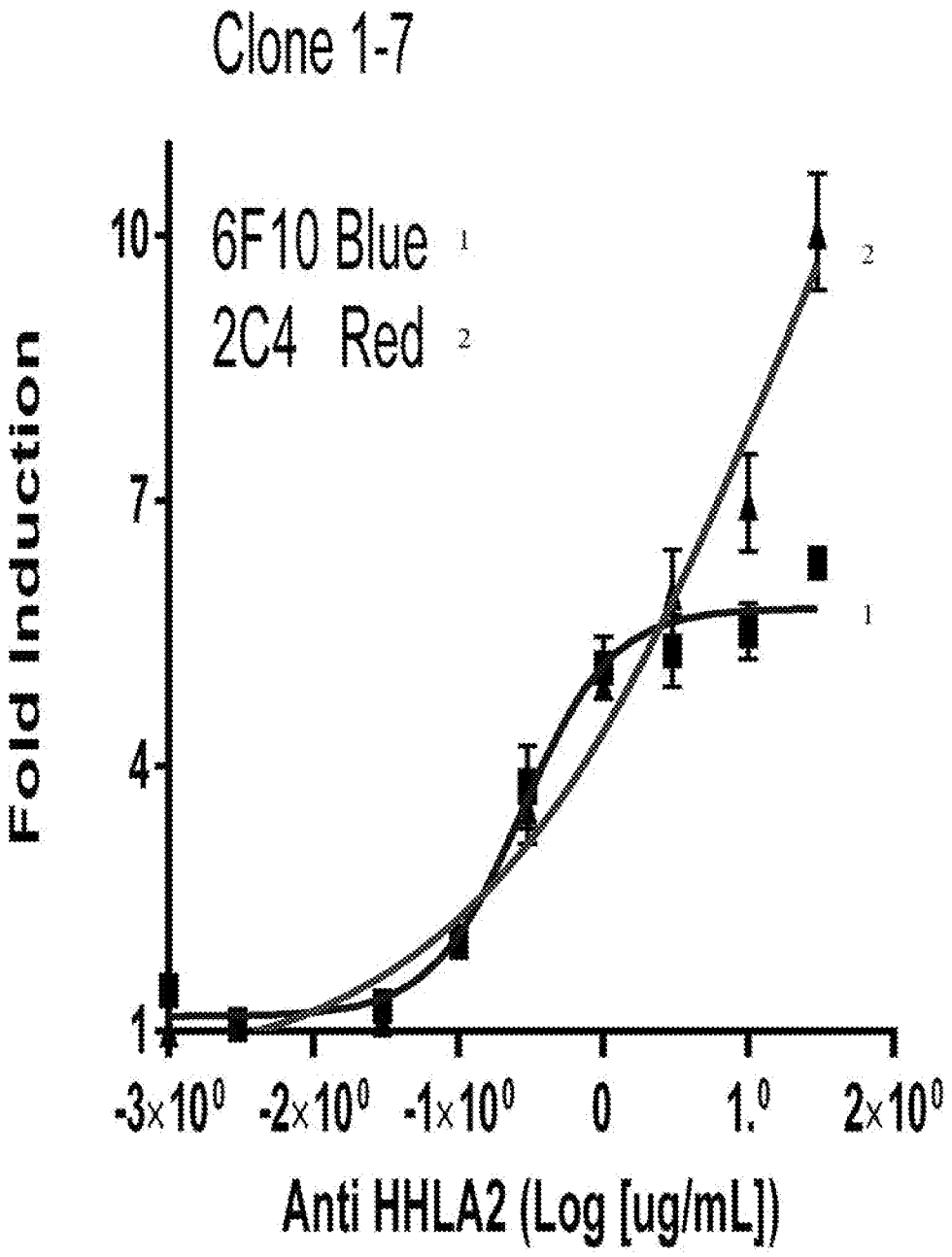

Clone 1-7
6F10 Blue 1
2C4 Red 2
Fold Induction
10
7
4
1
-3x10^0
-2x10^0
-1x10^0
0
1.^0
2x10^0
Anti HHLA2 (Log [ug/mL])
1
2

Figure 21C

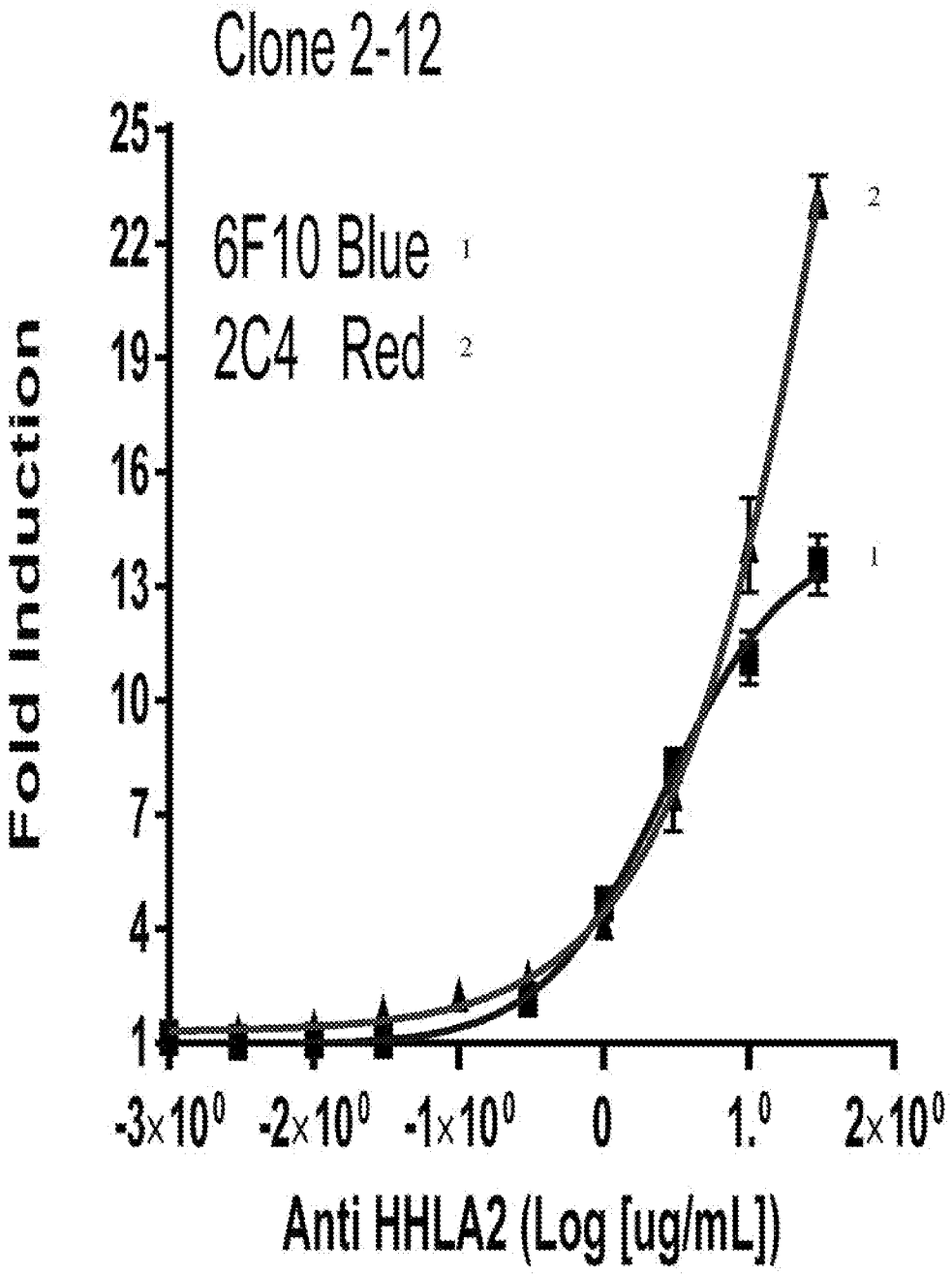

Clone 2-12
6F10 Blue 1
2C4 Red 2
Fold Induction
25
22
19
16
13
10
7
4
1
-3x10^0
-2x10^0
-1x10^0
0
1.^0
2x10^0
Anti HHLA2 (Log [ug/mL])
1
2

Figure 22

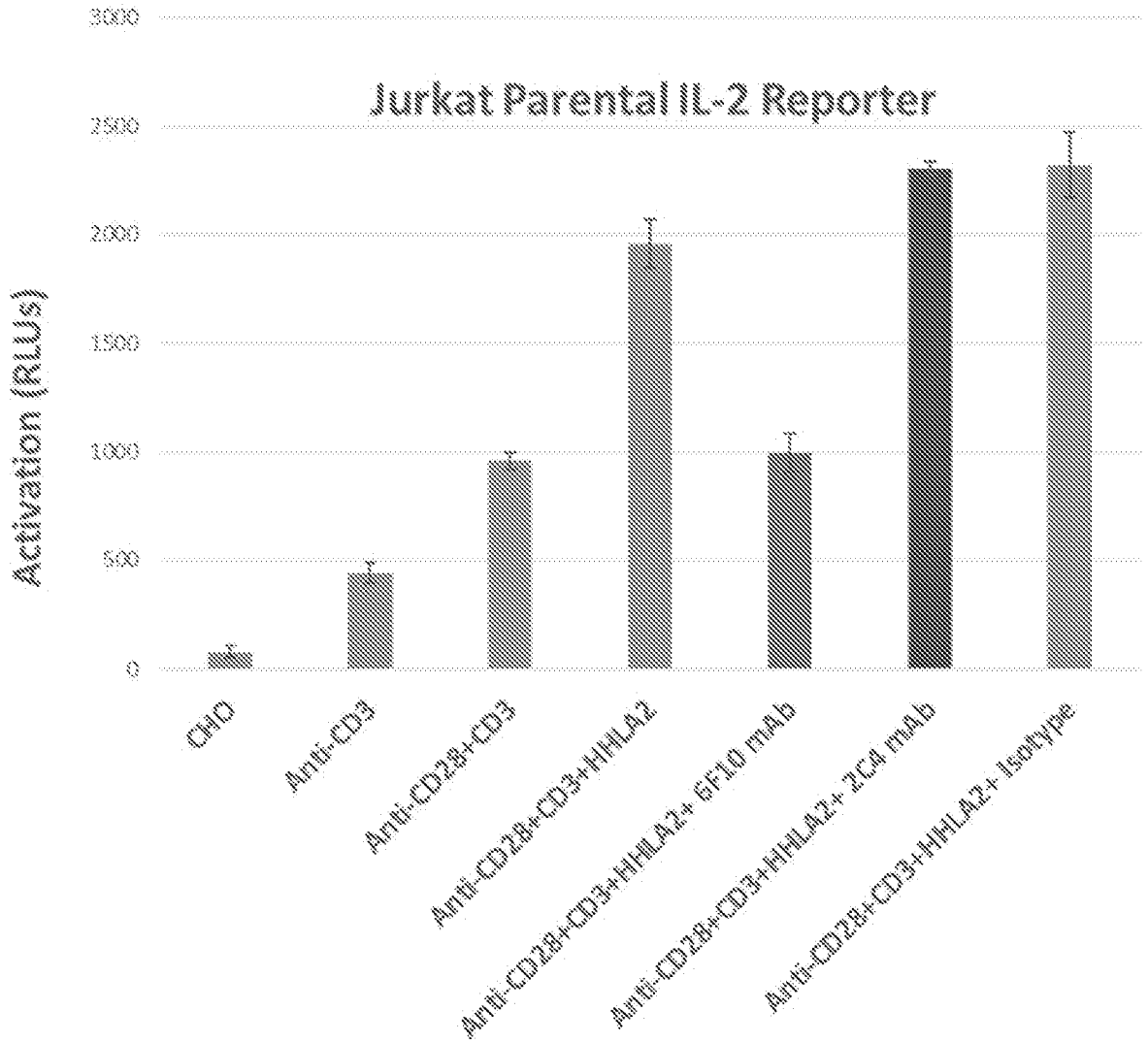

Jurkat Parental IL-2 Reporter
Activation (RLUs)
3000
2500
2000
1500
1000
500
0
CHO
Anti-CD3
Anti-CD28+CD3
Anti-CD28+CD3+HHLA2
Anti-CD28+CD3+HHLA2+ 6F10 mAb
Anti-CD28+CD3+HHLA2+ 2C4 mAb
Anti-CD28+CD3+HHLA2+ Isotype

Figure 23A

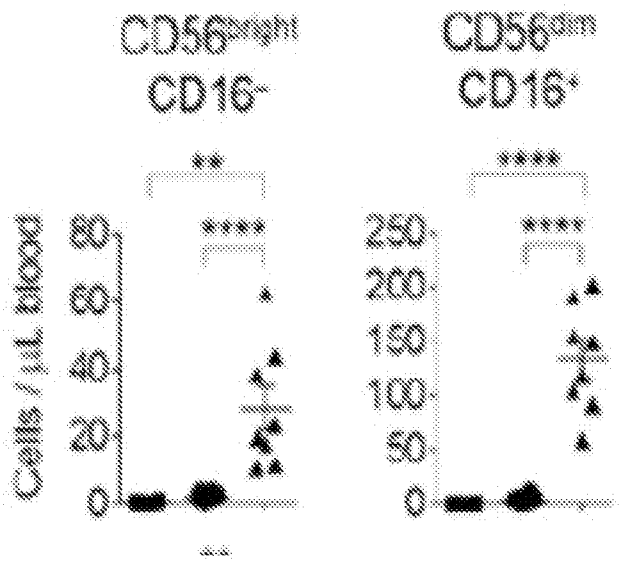


Figure 23B

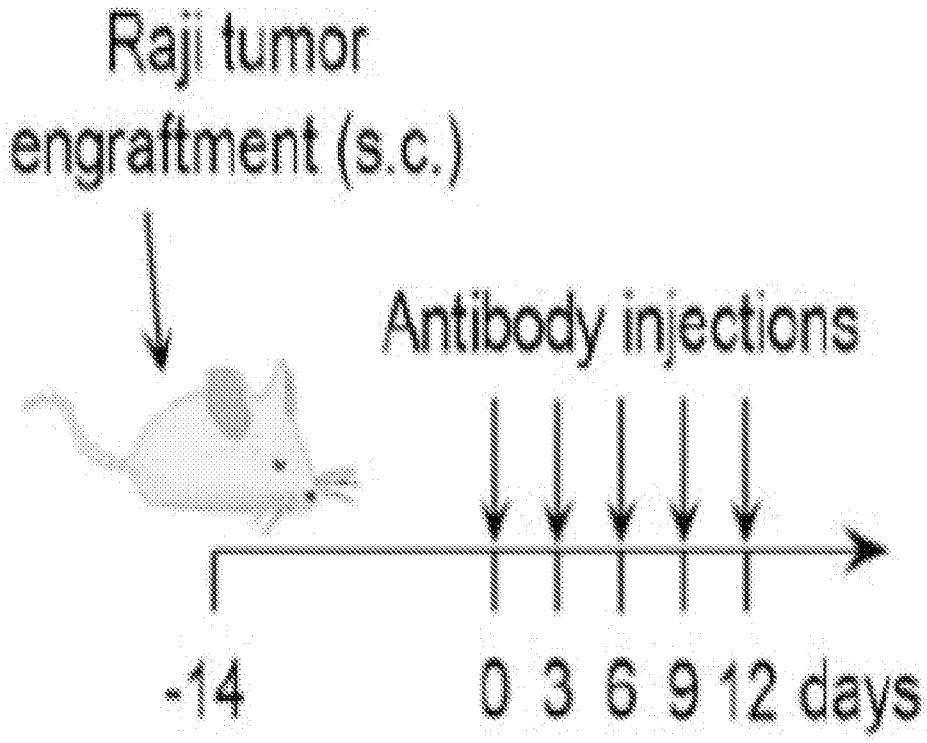


Figure 23C

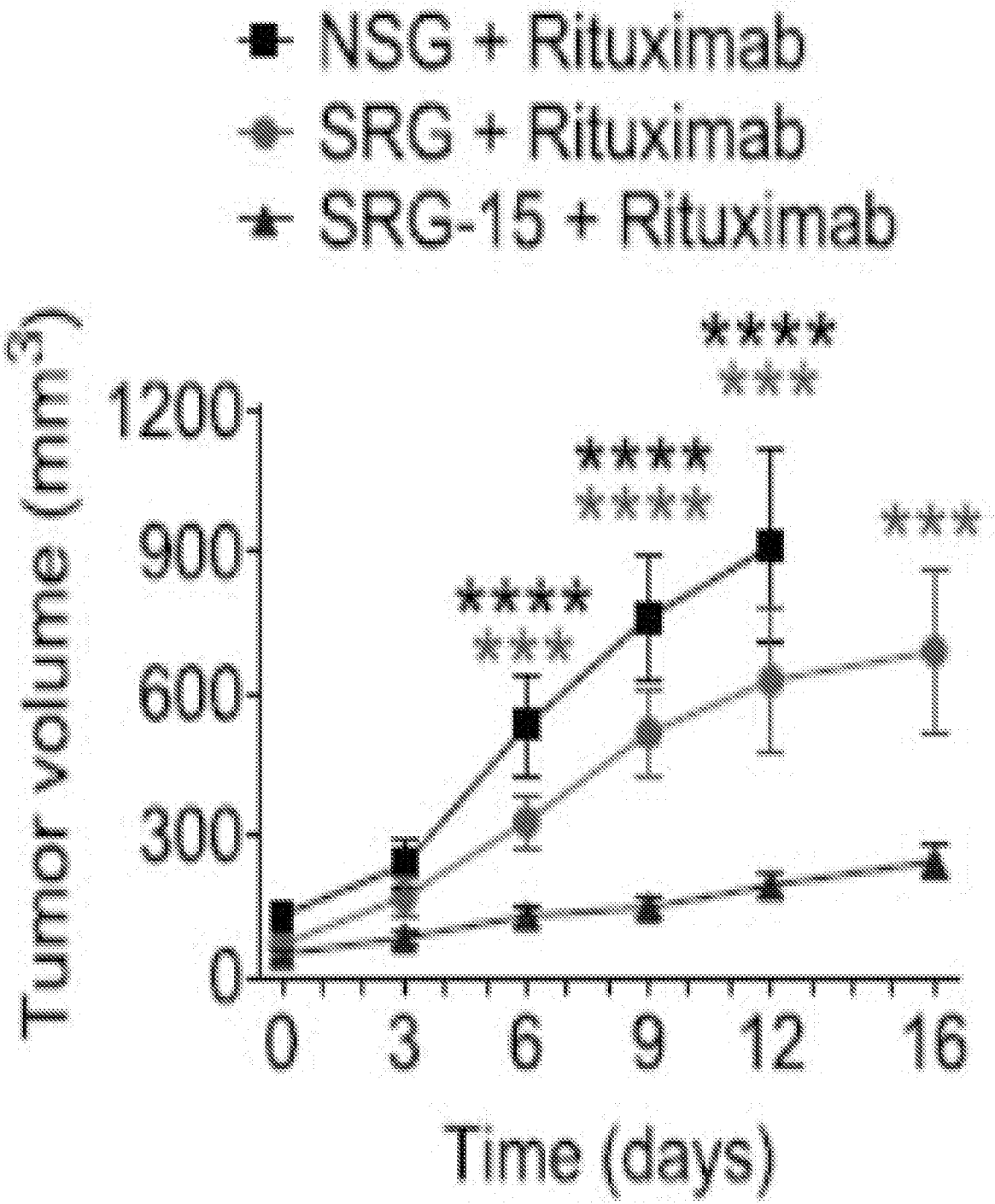

NSG + Rituximab
SRG + Rituximab
SRG-15 + Rituximab
Tumor volume (mm3)
1200
900
600
300
0
0
3
6
9
12
16
Time (days)
****
***
****
****
****
***
***

Figure 24A

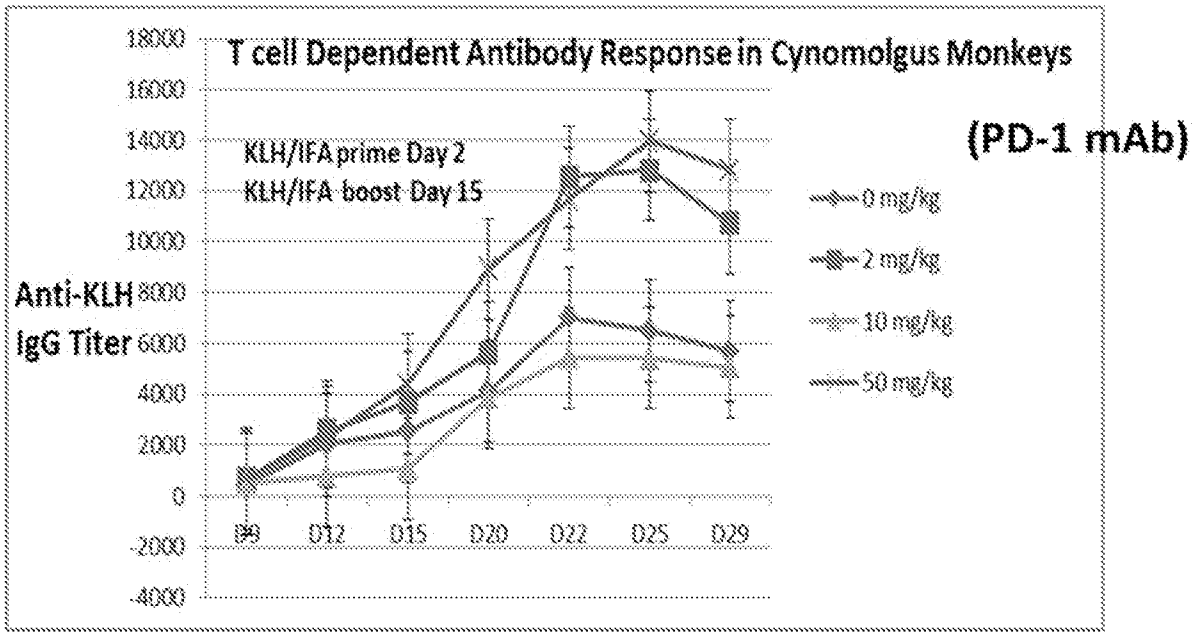


Figure 24B

