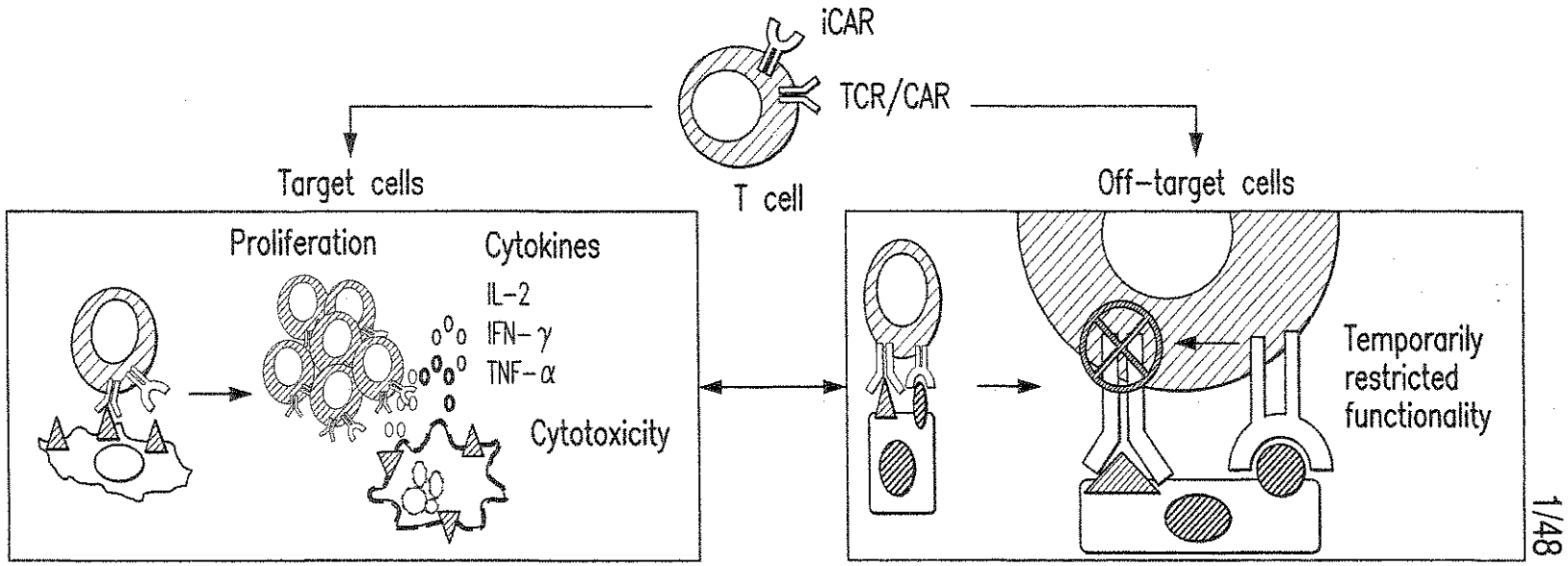

iCAR
TCR/CAR
T cell
Target cells
Off-target cells
Proliferation
Cytokines
IL-2
IFN-γ
TNF-α
Cytotoxicity
Temporarily
restricted
functionality

FIG. 1A

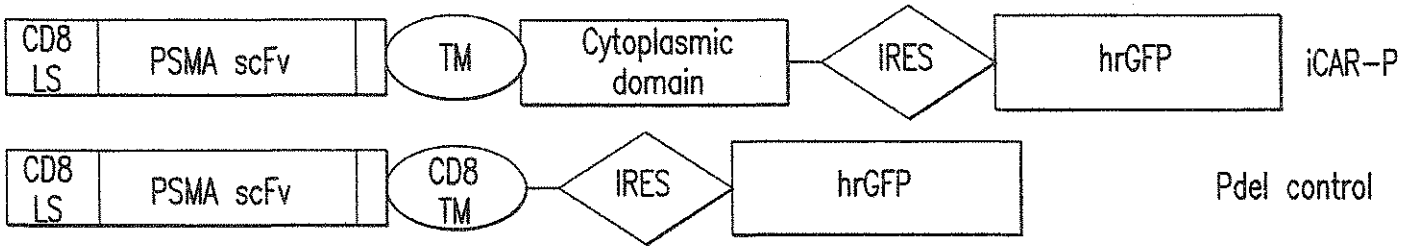

CD8
LS
PSMA scFv
TM
Cytoplasmic
domain
IRES
hrGFP
iCAR-P
CD8
LS
PSMA scFv
CD8
TM
IRES
hrGFP
Pdel control

FIG. 1B

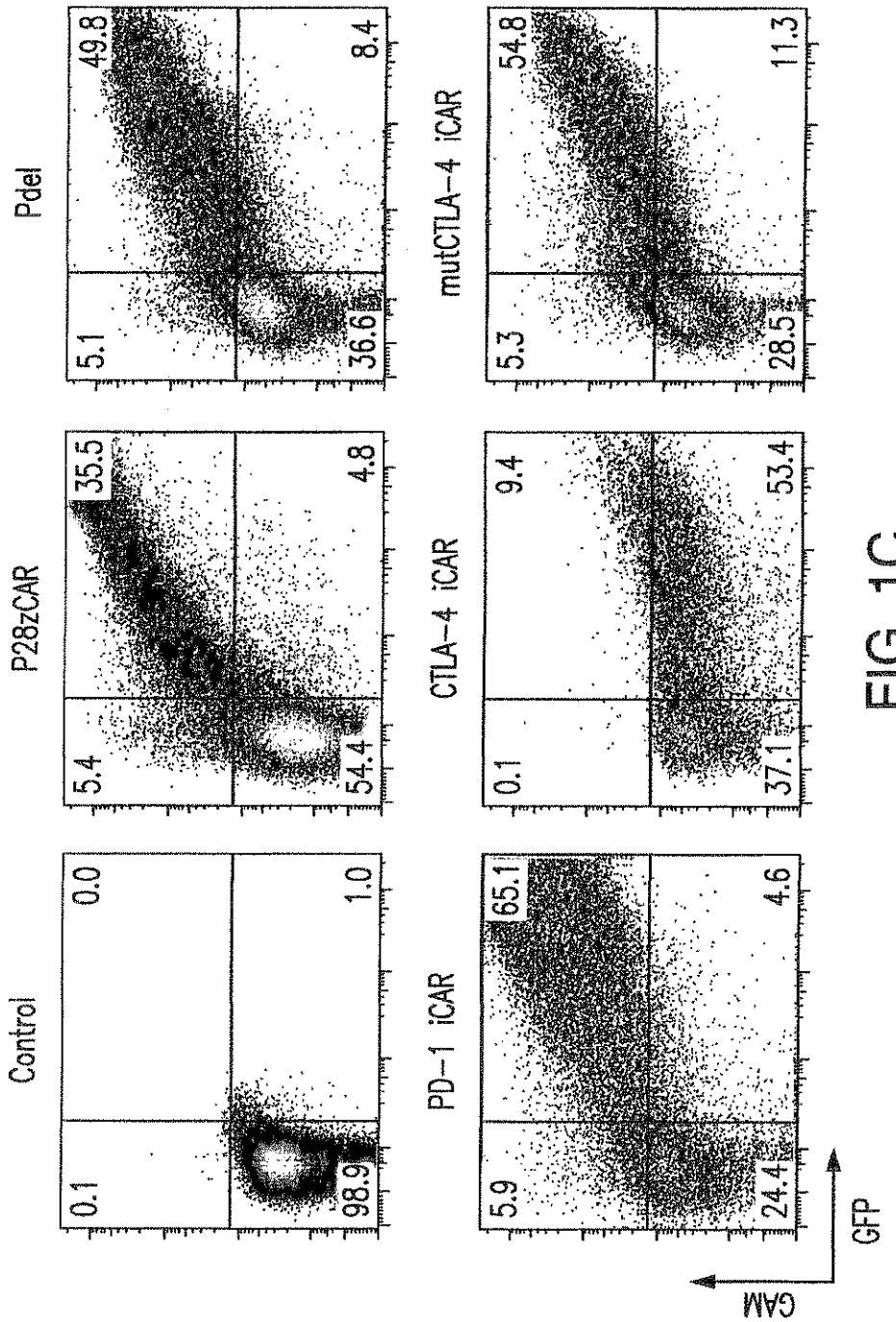

Control
P28zCAR
Pdel
PD-1 iCAR
CTLA-4 iCAR
mutCTLA-4 iCAR
0.1
0.0
98.9
1.0
5.4
35.5
54.4
4.8
5.1
49.8
36.6
8.4
5.9
65.1
24.4
4.6
0.1
9.4
37.1
53.4
5.3
54.8
28.5
11.3
GAM
GFP

FIG. 1C

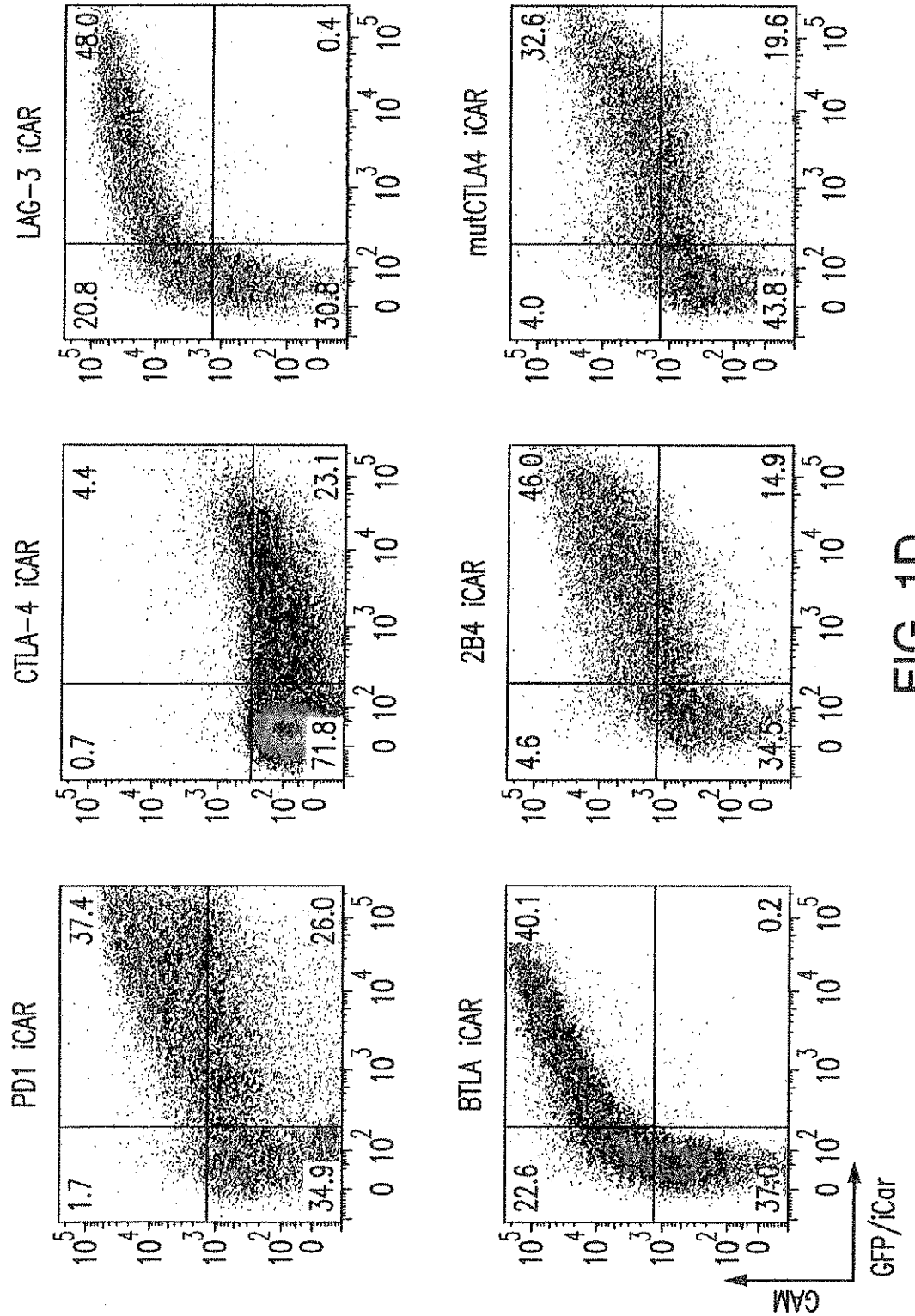

PD1 iCAR
CTLA-4 iCAR
LAG-3 iCAR
BTLA iCAR
2B4 iCAR
mutCTLA4 iCAR
1.7
37.4
34.9
26.0
0.7
4.4
71.8
23.1
20.8
48.0
30.8
0.4
22.6
40.1
37.0
0.2
4.6
46.0
34.5
14.9
4.0
32.6
43.8
19.6
CAM
GFP/iCar

FIG. 1D

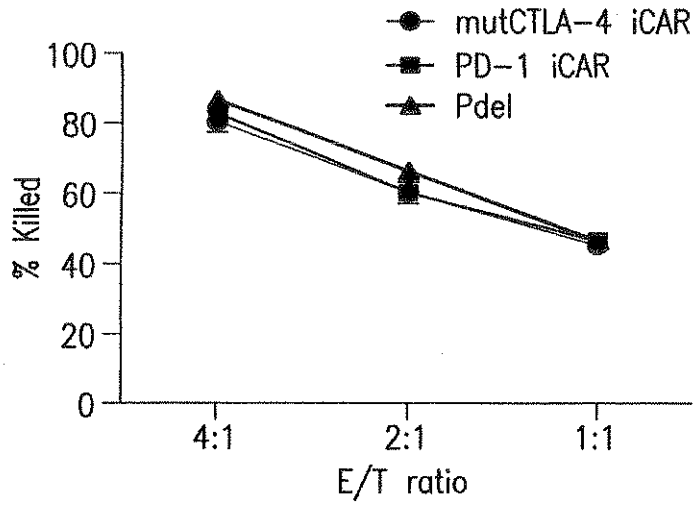

mutCTLA-4 iCAR
PD-1 iCAR
Pdel
100
80
60
40
20
0
% Killed
4:1
2:1
1:1
E/T ratio

FIG. 2A

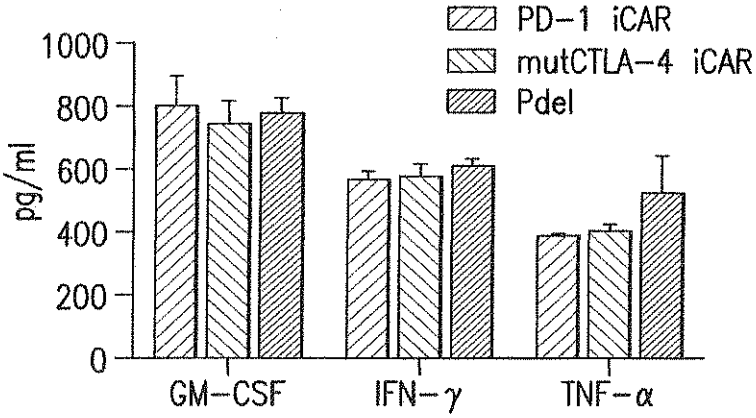

PD-1 iCAR
mutCTLA-4 iCAR
Pdel
1000
800
600
400
200
0
pg/ml
GM-CSF
IFN-γ
TNF-α

FIG. 2B

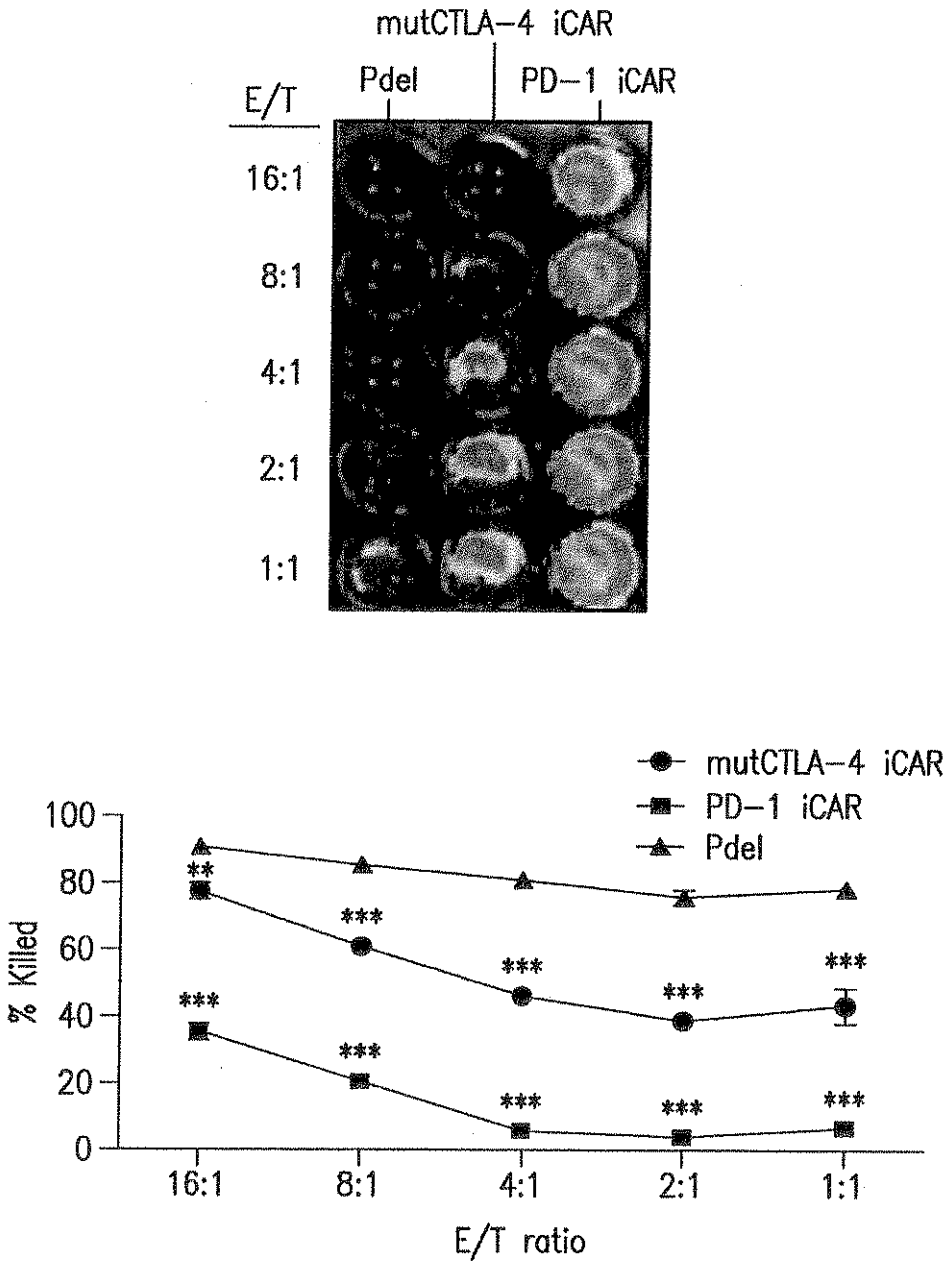

mutCTLA-4 iCAR
Pdel
PD-1 iCAR
E/T
16:1
8:1
4:1
2:1
1:1
mutCTLA-4 iCAR
PD-1 iCAR
Pdel
% Killed
100
80
60
40
20
0
**
***
***
***
***
***
***
***
***
16:1
8:1
4:1
2:1
1:1
E/T ratio

FIG. 2C

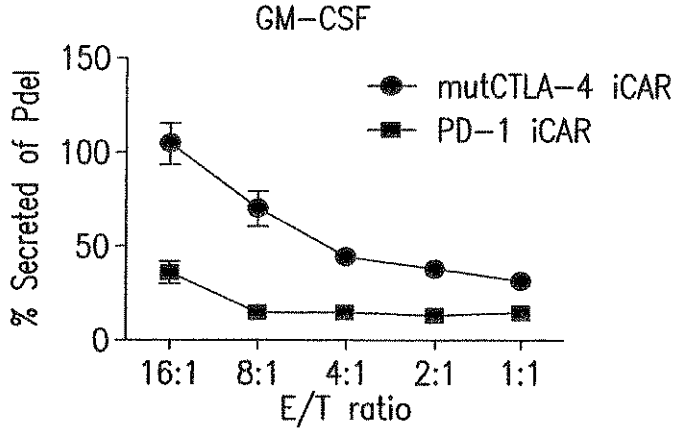


FIG. 2D

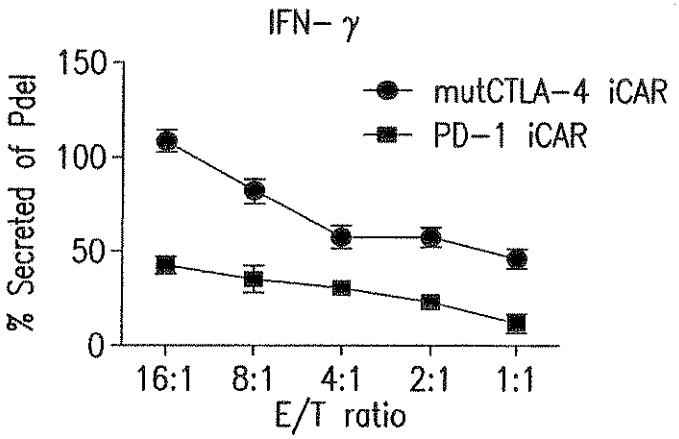


FIG. 2E

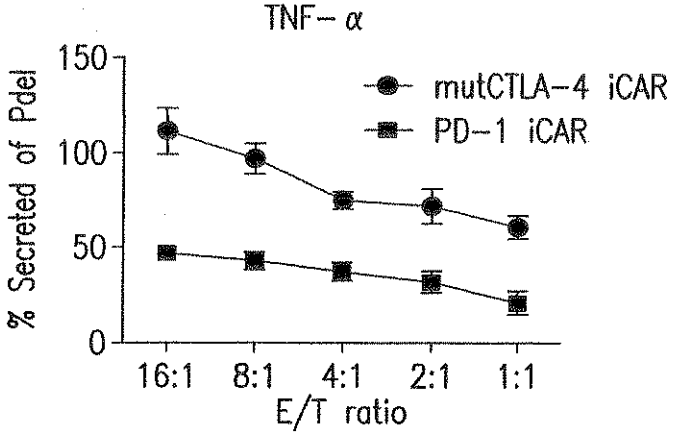


FIG. 2F

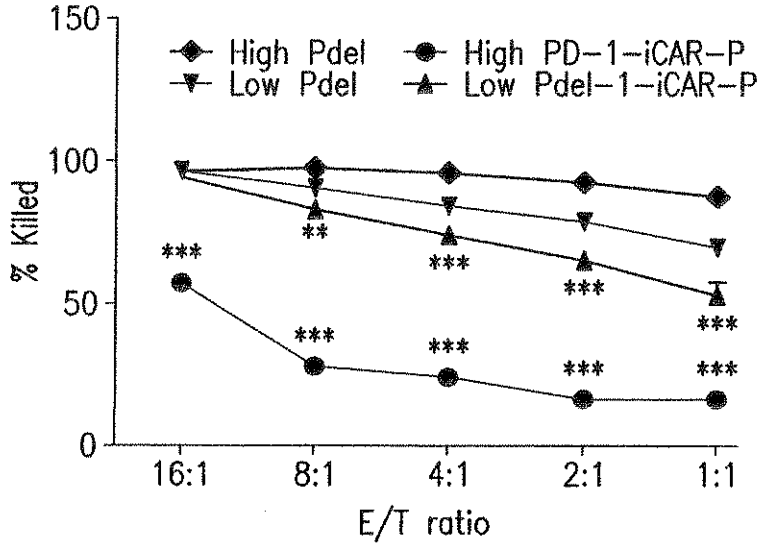

150
100
50
0
% Killed
High Pdel
Low Pdel
High PD-1-iCAR-P
Low Pdel-1-iCAR-P
***
**
***
***
***
***
***
***
***
16:1
8:1
4:1
2:1
1:1
E/T ratio

FIG. 3A

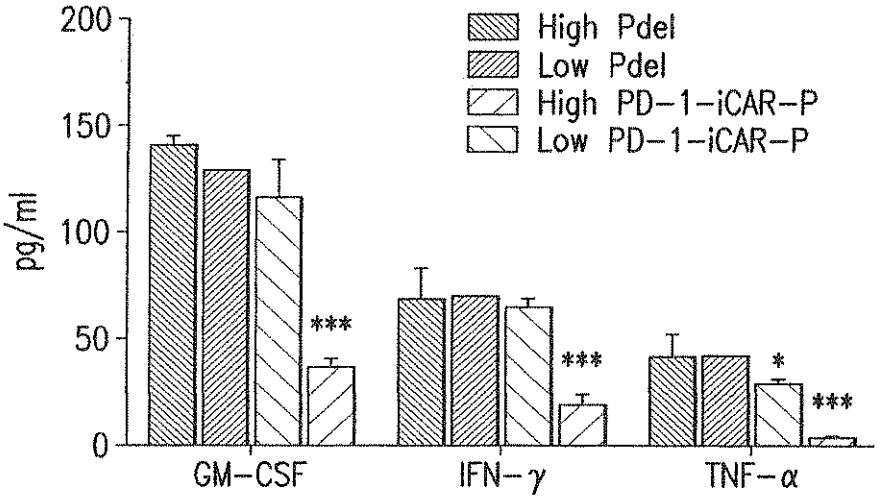

200
150
100
50
0
pg/ml
High Pdel
Low Pdel
High PD-1-iCAR-P
Low PD-1-iCAR-P
***
***
*
***
GM-CSF
IFN-γ
TNF-α

FIG. 3B

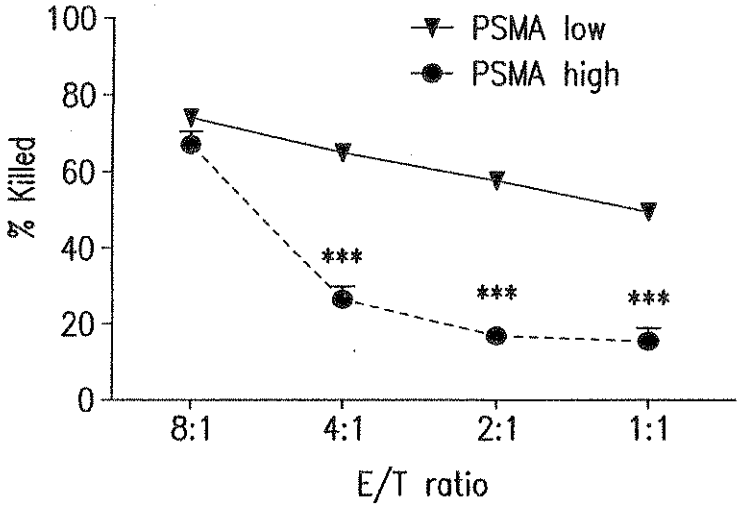

100
80
60
40
20
0
% Killed
PSMA low
PSMA high
***
***
***
8:1
4:1
2:1
1:1
E/T ratio

FIG. 3C

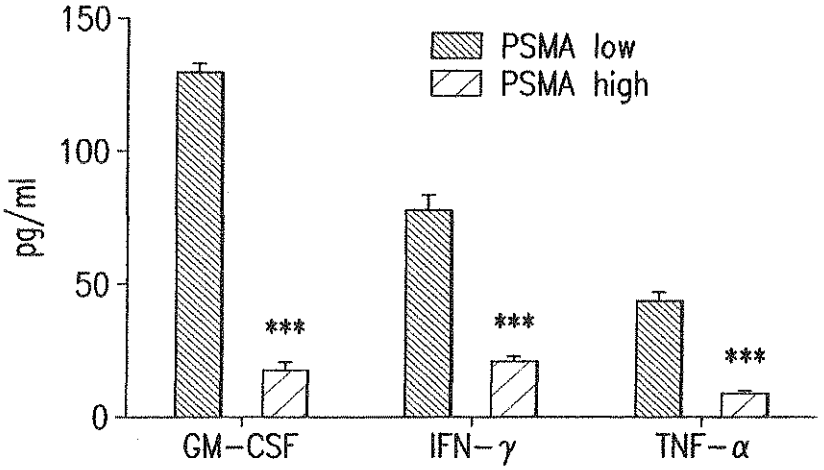

150
100
50
0
pg/ml
PSMA low
PSMA high
***
***
***
GM−CSF
IFN−γ
TNF−α

FIG. 3D


Pdel
PD-1 iCAR
No T cells
Pre T-cell
d3
d5
d8
d34
d48
10^7
9
8
7
6
5
4
3
2
1
10^6
10^5

FIG. 4A

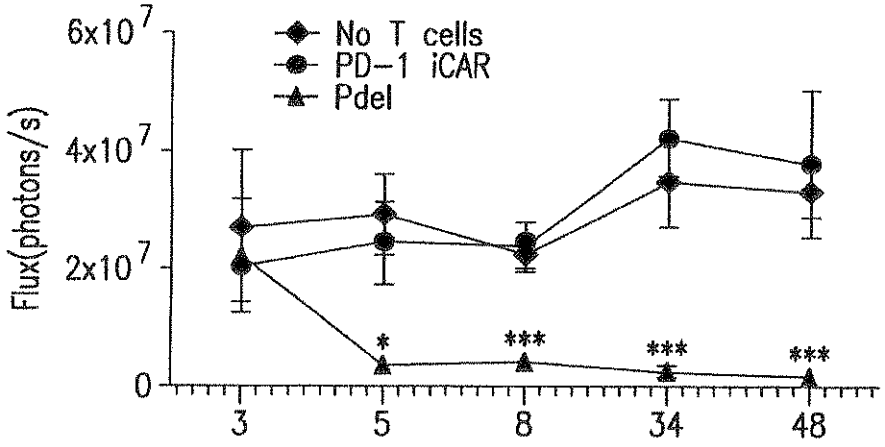

6x10^7
4x10^7
2x10^7
0
Flux(photons/s)
No T cells
PD-1 iCAR
Pdel
*
***
***
***
3
5
8
34
48

FIG. 4B

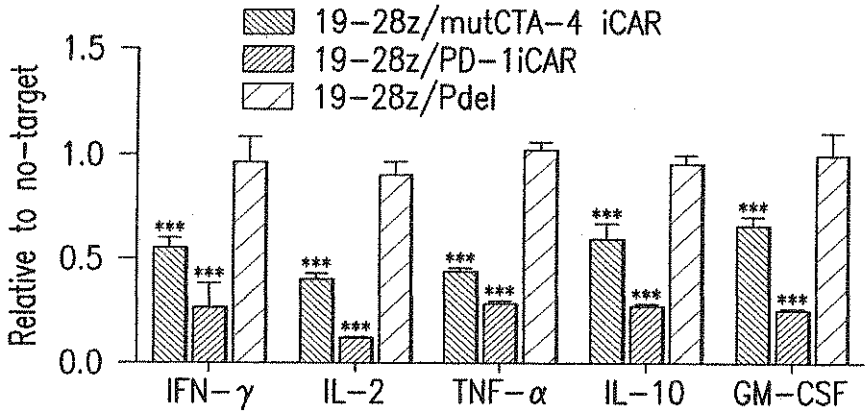


FIG. 5A

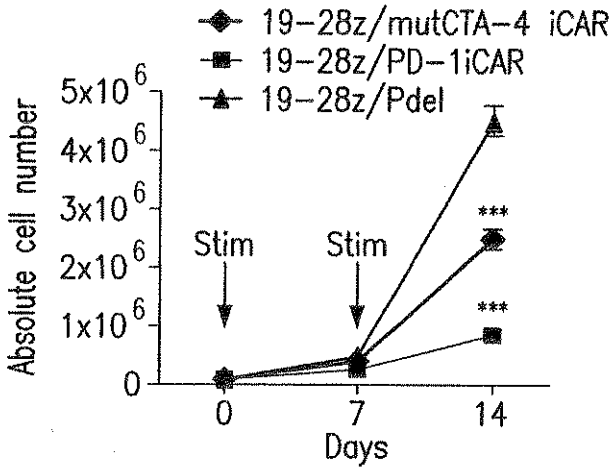


FIG. 5B

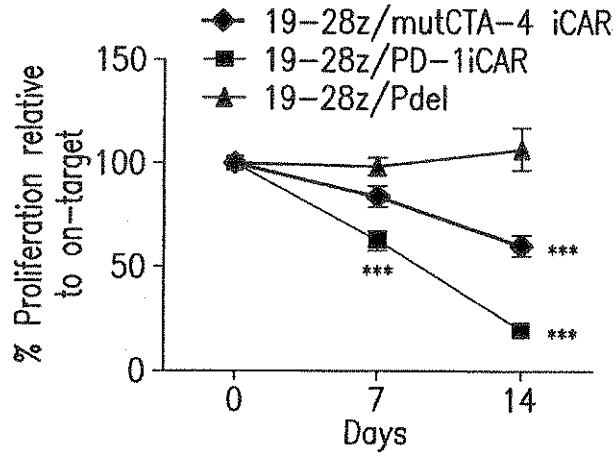


FIG. 5C

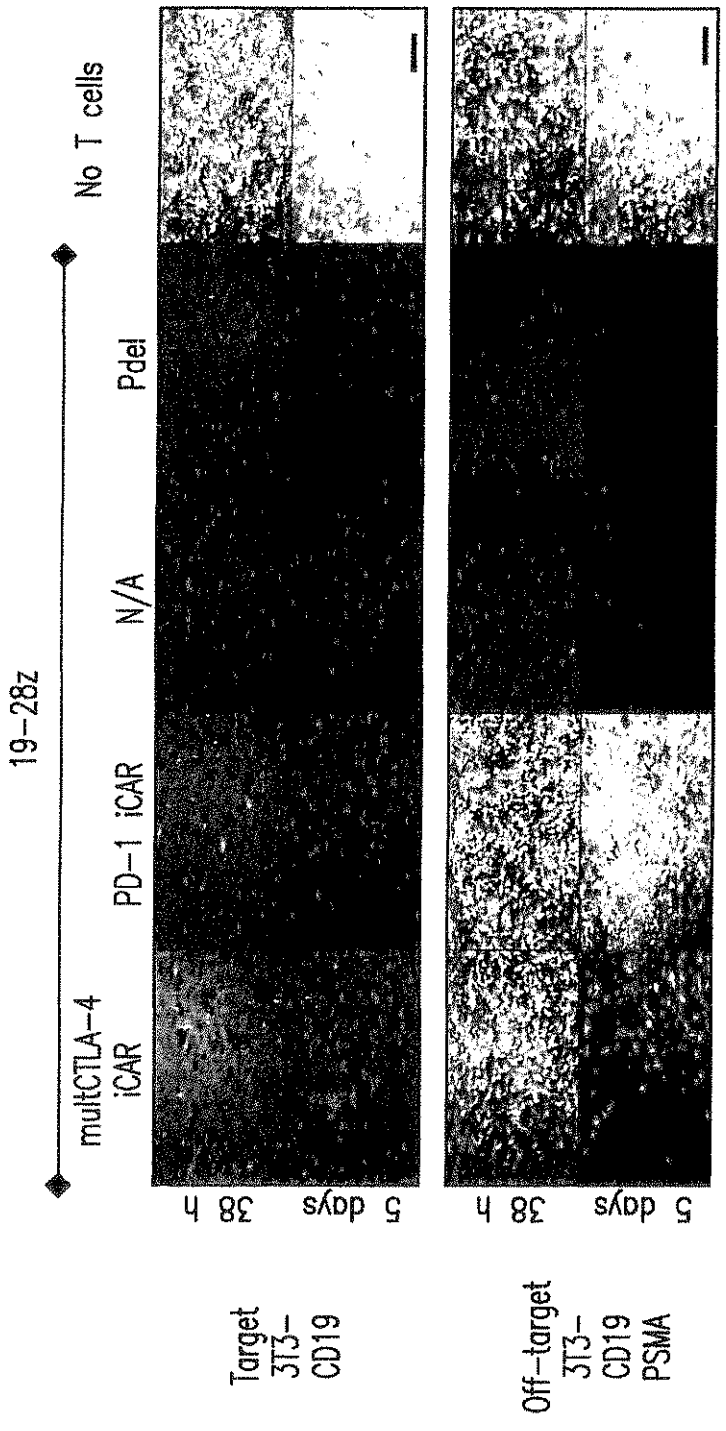

19-28z
multCTLA-4
iCAR
PD-1 iCAR
N/A
Pdel
No T cells
38 h
5 days
38 h
5 days
Target
3T3-
CD19
Off-target
3T3-
CD19
PSMA

FIG. 5D

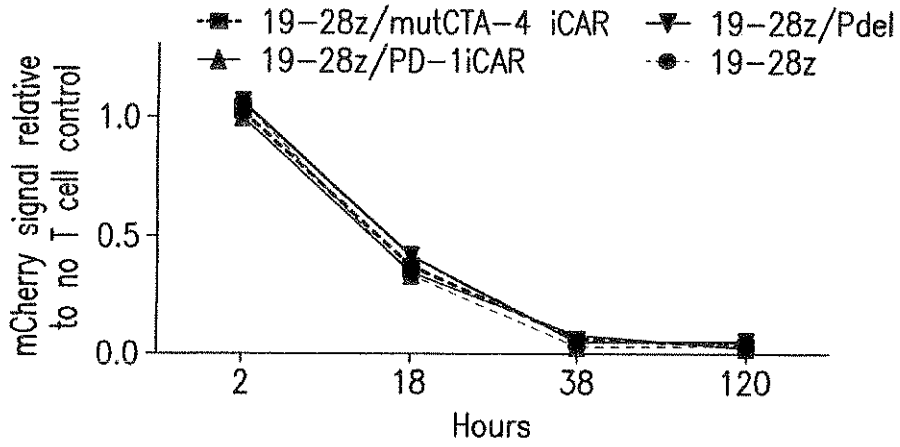

19-28z/mutCTA-4 iCAR
19-28z/Pdel
19-28z/PD-1iCAR
19-28z
mCherry signal relative to no T cell control
1.0
0.5
0.0
2
18
38
120
Hours

FIG. 5E

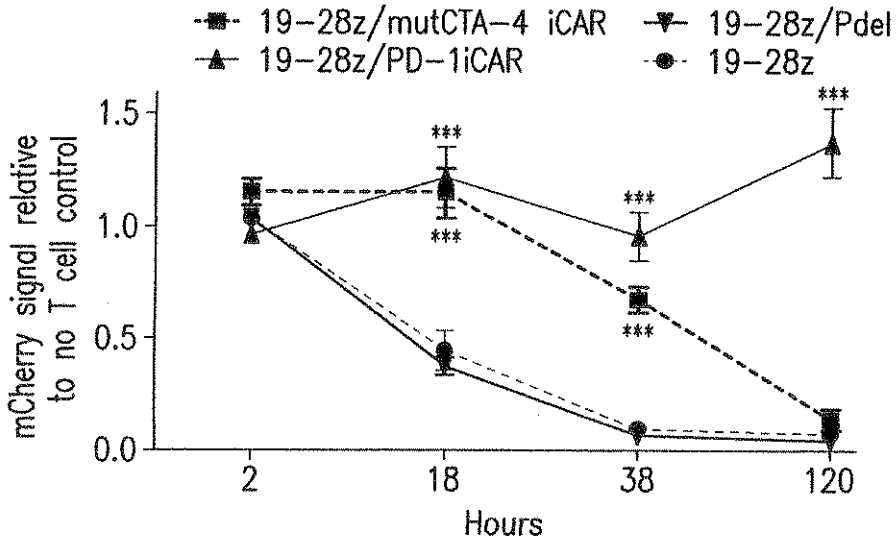

19-28z/mutCTA-4 iCAR
19-28z/Pdel
19-28z/PD-1iCAR
19-28z
mCherry signal relative to no T cell control
1.5
1.0
0.5
0.0
***
2
18
38
120
Hours

FIG. 5F

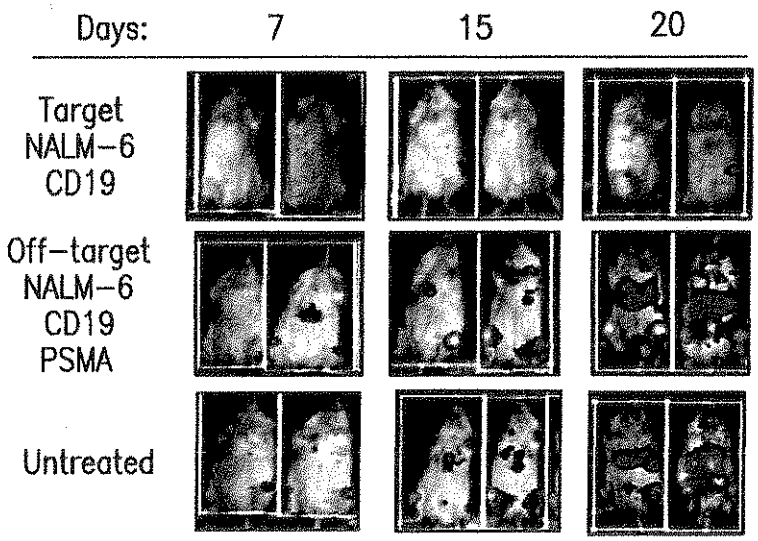

Days:
7
15
20
Target
NALM-6
CD19
Off-target
NALM-6
CD19
PSMA
Untreated

FIG. 6A

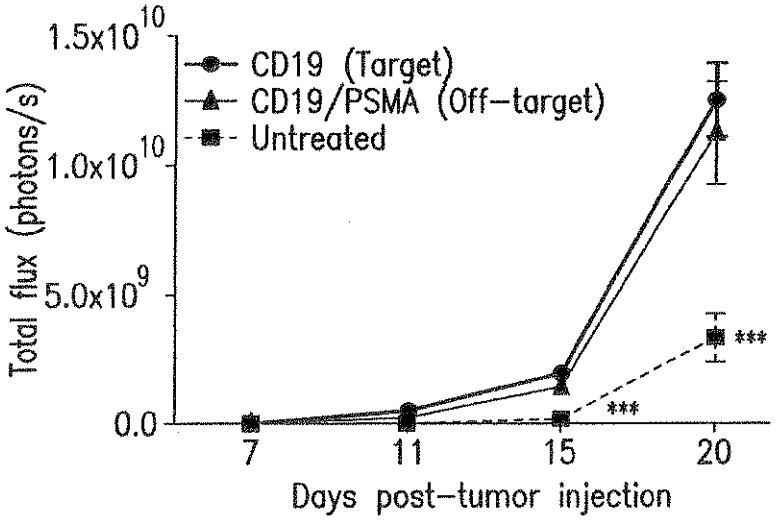

1.5x10^10
1.0x10^10
5.0x10^9
0.0
Total flux (photons/s)
CD19 (Target)
CD19/PSMA (Off-target)
Untreated
***
***
7
11
15
20
Days post-tumor injection

FIG. 6B

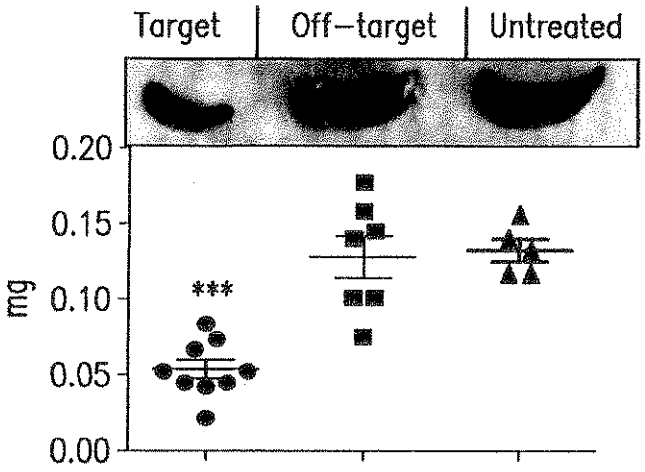

Target
Off-target
Untreated
0.20
0.15
0.10
0.05
0.00
mg
***

FIG. 6C

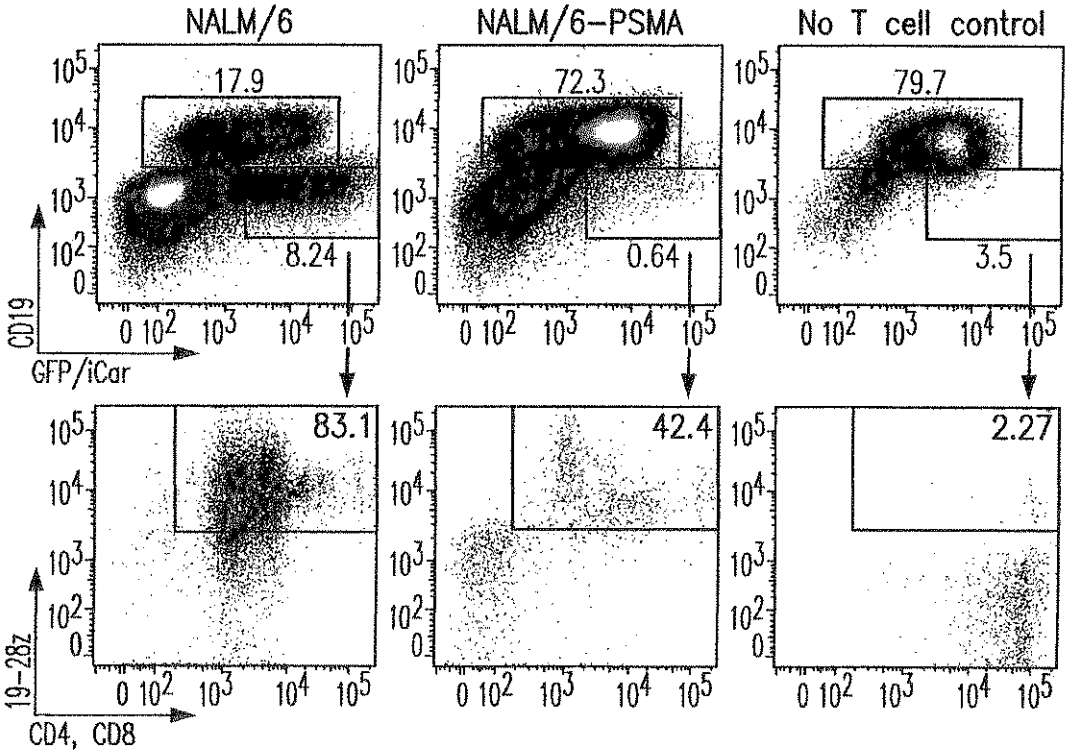

NALM/6
NALM/6-PSMA
No T cell control
17.9
8.24
72.3
0.64
79.7
3.5
CD19
GFP/iCar
83.1
42.4
2.27
19-28z
CD4, CD8

FIG. 6D

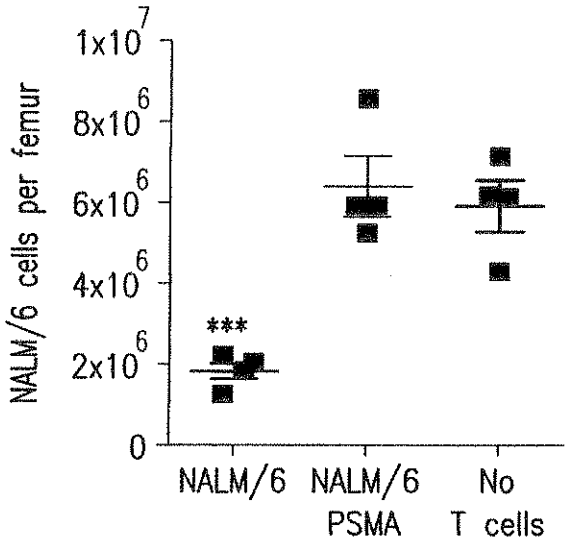

1x10^7
8x10^6
6x10^6
4x10^6
2x10^6
0
NALM/6 cells per femur
***
NALM/6
NALM/6 PSMA
No T cells

FIG. 6E

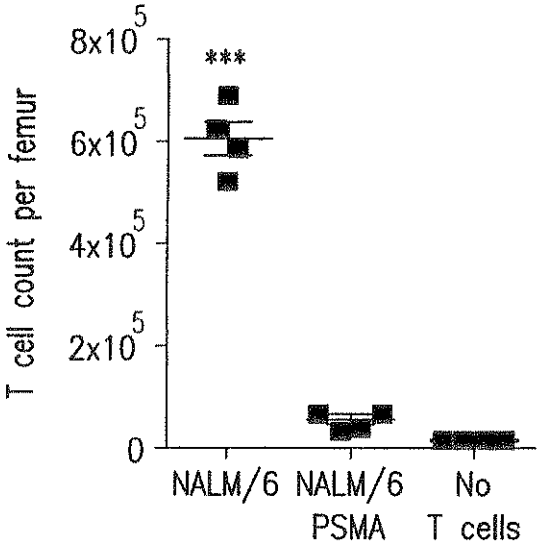

8x10^5
6x10^5
4x10^5
2x10^5
0
T cell count per femur
***
NALM/6
NALM/6 PSMA
No T cells

FIG. 6F

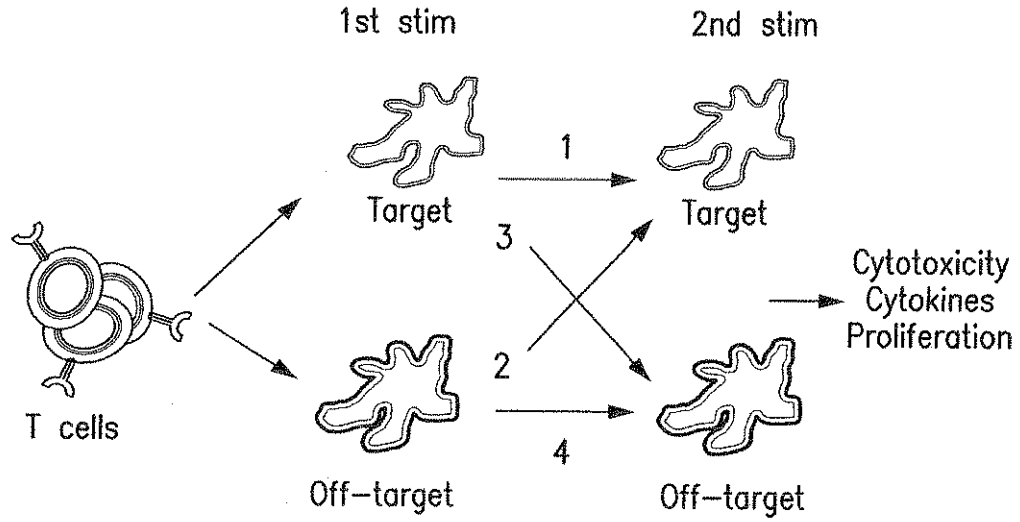

1st stim
2nd stim
Target
Target
1
3
2
4
T cells
Off-target
Off-target
Cytotoxicity
Cytokines
Proliferation

FIG. 7A

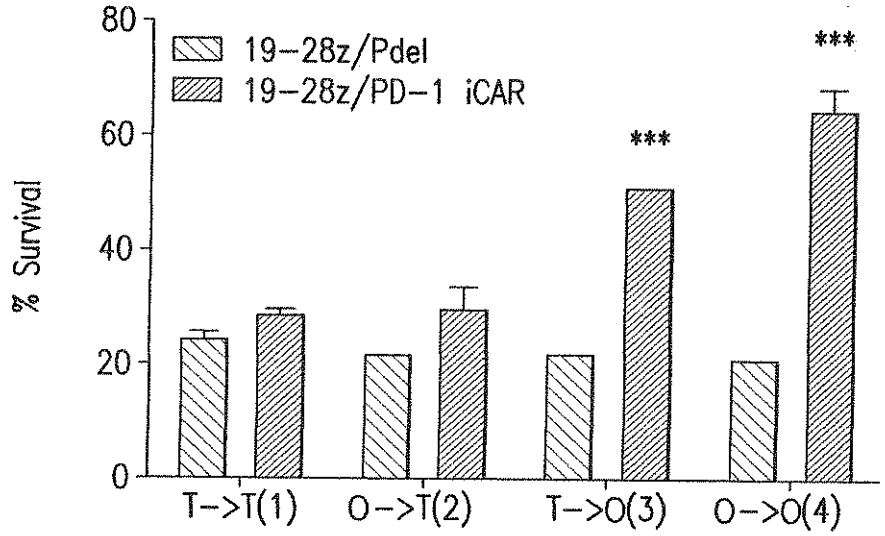

80
60
40
20
0
% Survival
19-28z/Pdel
19-28z/PD-1 iCAR
***
***
T->T(1)
O->T(2)
T->O(3)
O->O(4)

FIG. 7B

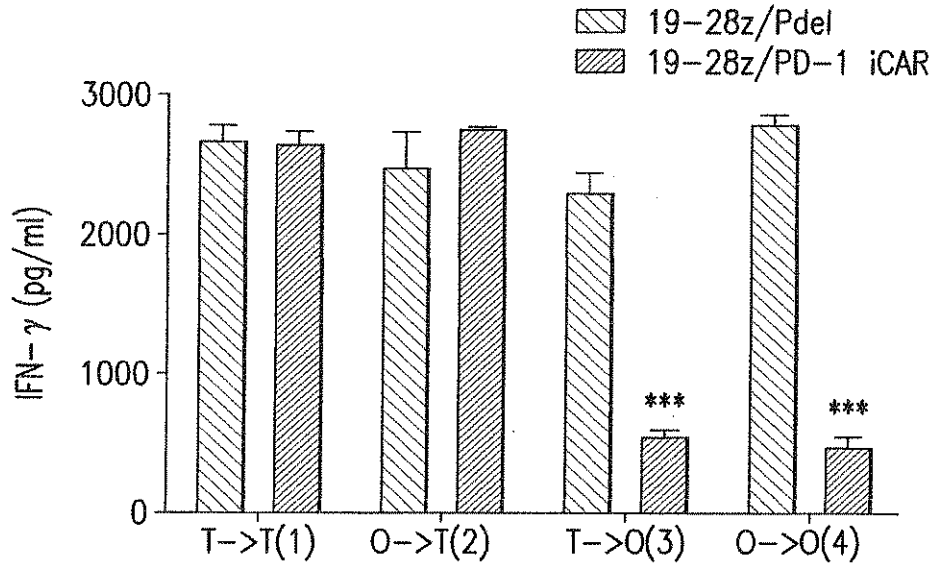

19-28z/Pdel
19-28z/PD-1 iCAR
IFN-γ (pg/ml)
3000
2000
1000
0
***
***
T->T(1)
O->T(2)
T->O(3)
O->O(4)

FIG. 7C

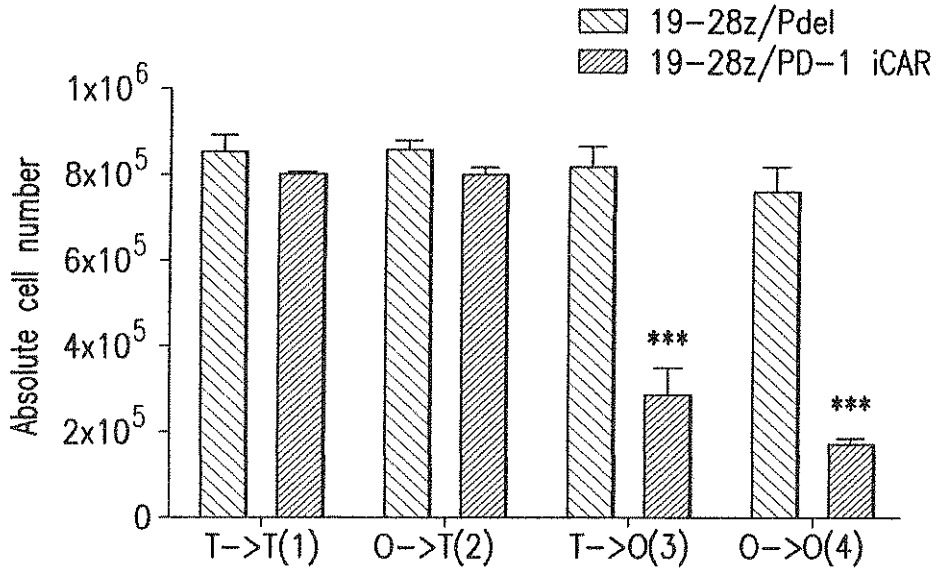

19-28z/Pdel
19-28z/PD-1 iCAR
Absolute cell number
1x10^6
8x10^5
6x10^5
4x10^5
2x10^5
0
***
***
T->T(1)
O->T(2)
T->O(3)
O->O(4)

FIG. 7D

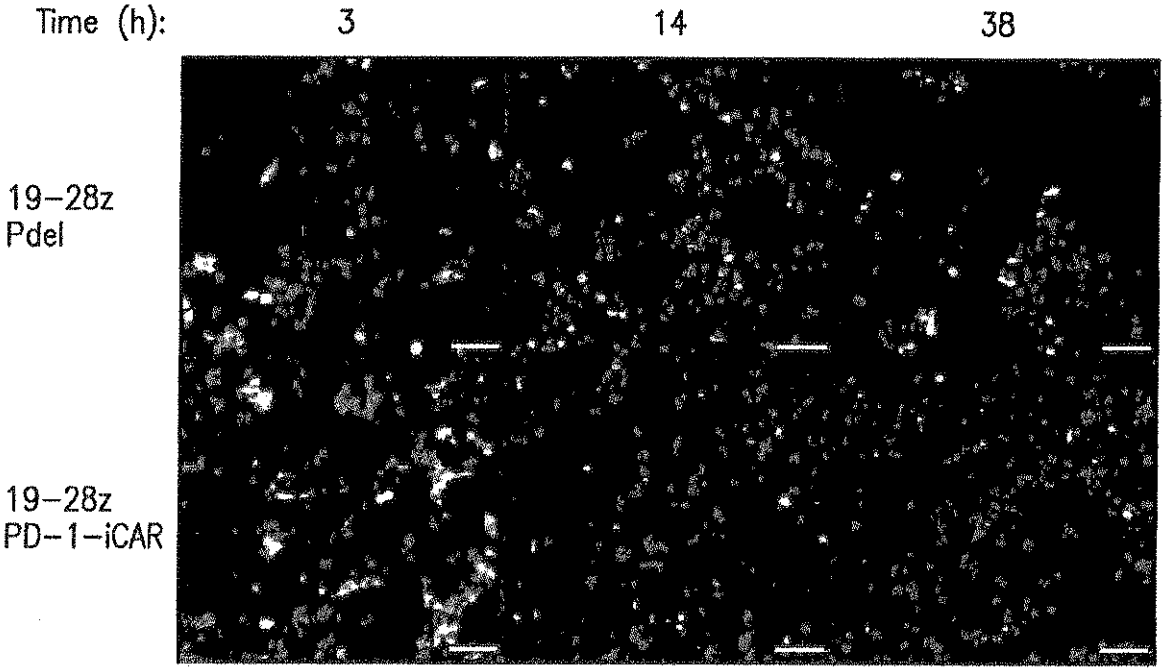

Time (h):
3
14
38
19−28z
Pdel
19−28z
PD−1−iCAR

FIG. 8A

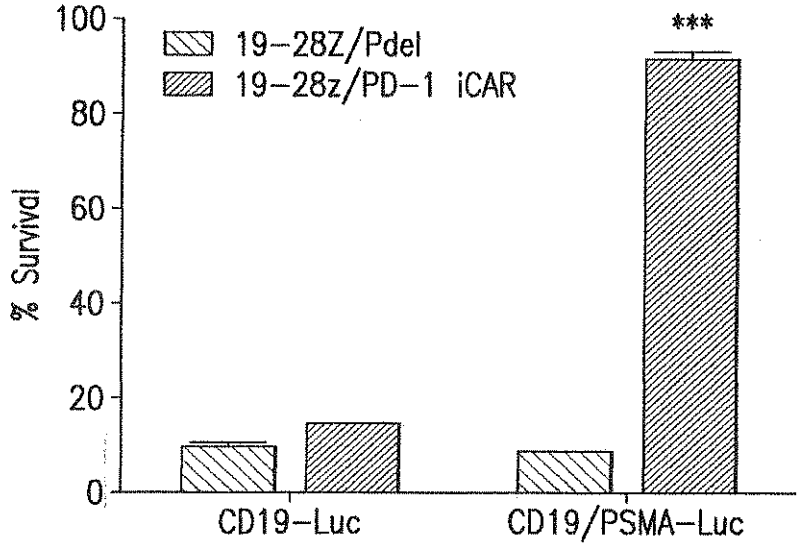

100
80
60
40
20
0
% Survival
19−28Z/Pdel
19−28z/PD−1 iCAR
***
CD19−Luc
CD19/PSMA−Luc

FIG. 8B

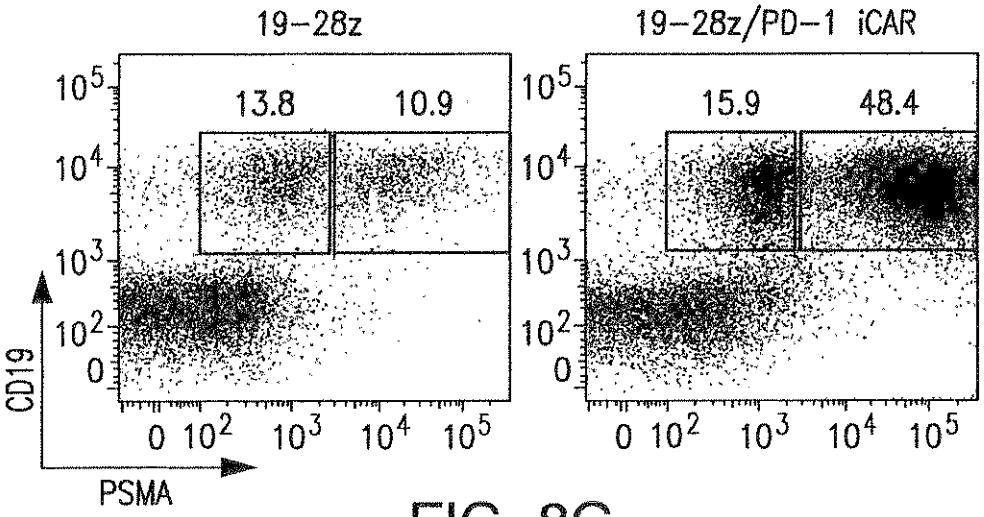


FIG. 8C

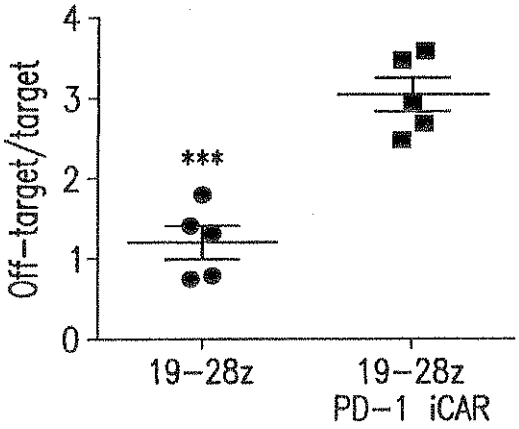


FIG. 8D

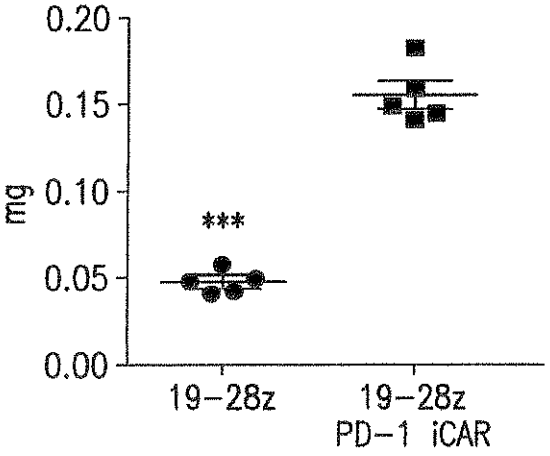


FIG. 8E

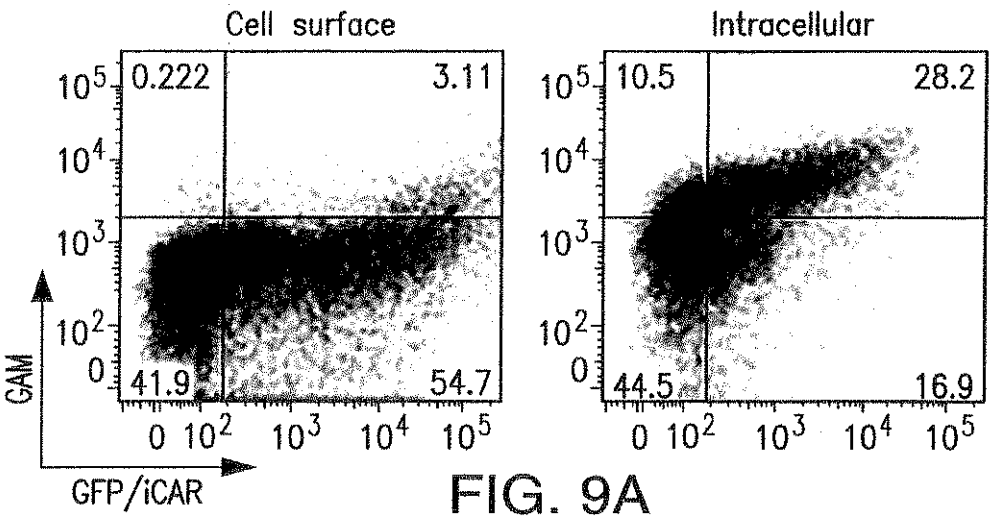
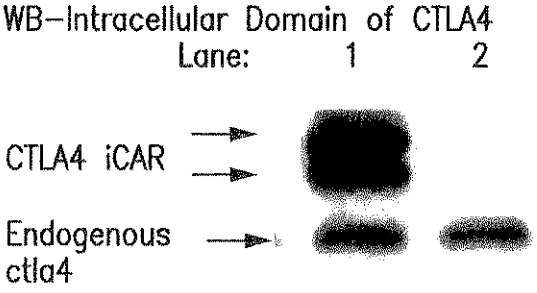


FIG. 9A



1. CTLA4 iCAR Transduced T–cells
2. Untransduced T–cells
3. EL4

FIG. 9B

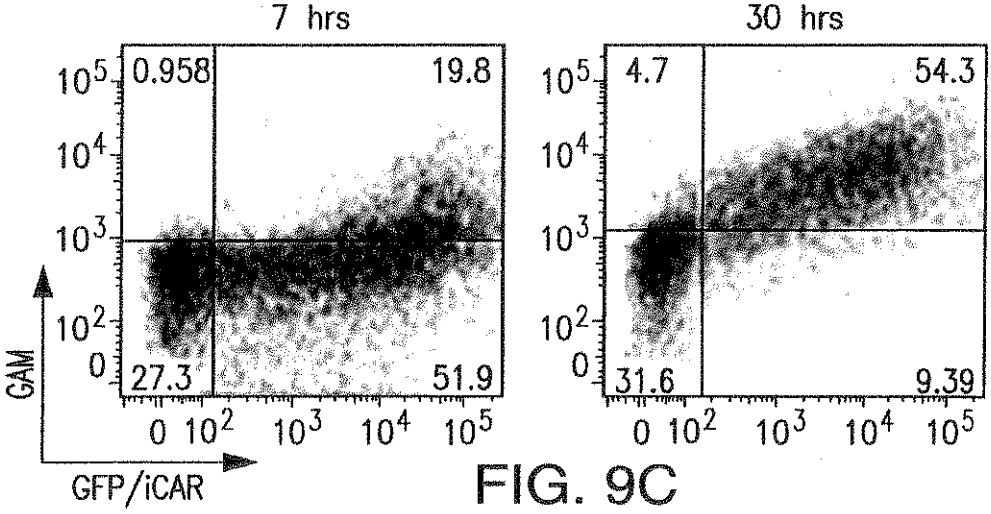


FIG. 9C

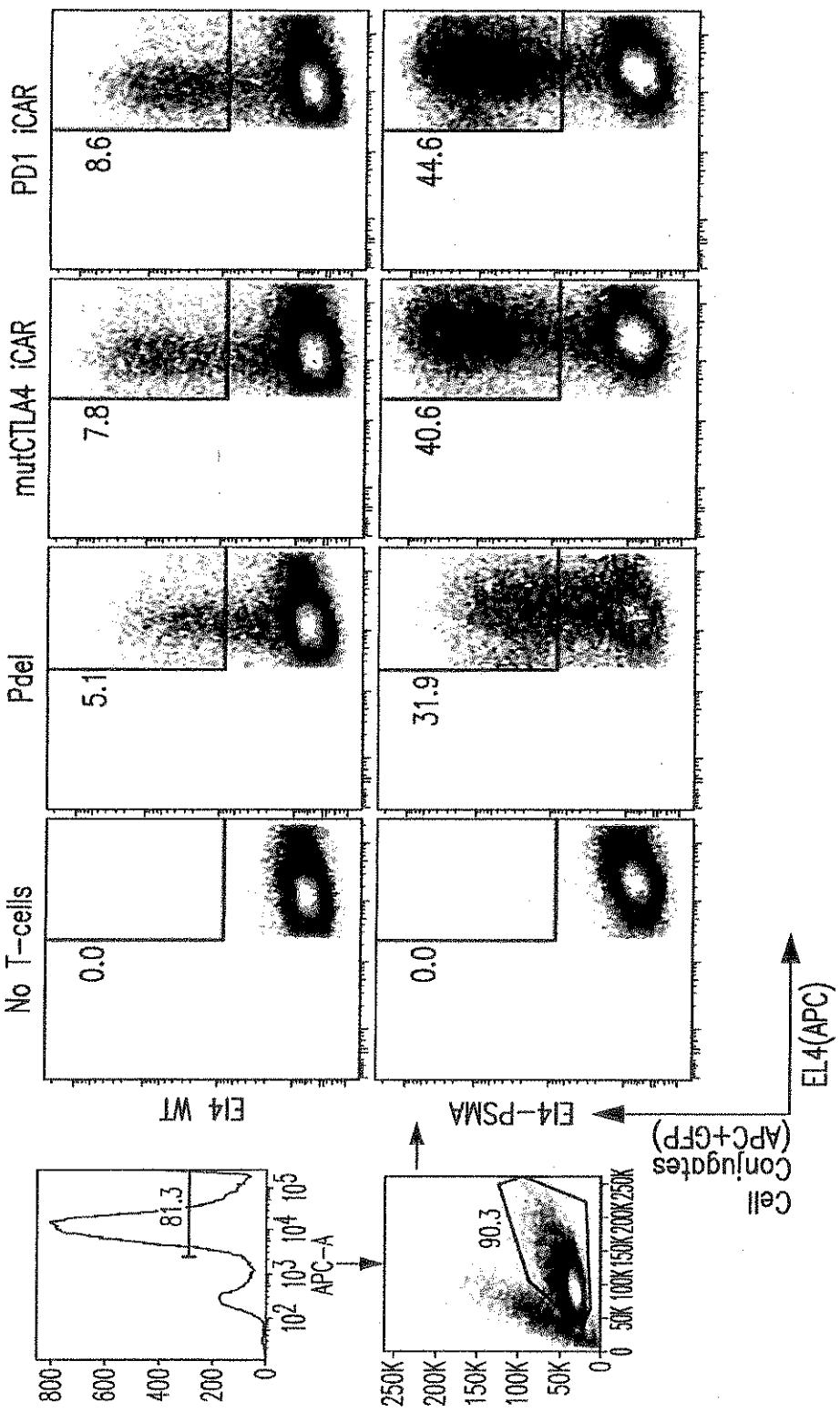

No T-cells
Pdel
mutCTLA4 iCAR
PD1 iCAR
0.0
5.1
7.8
8.6
0.0
31.9
40.6
44.6
EL4 WT
EL4-PSMA
EL4(APC)
Cell Conjugates (APC+GFP)
81.3
90.3
APC-A
800
600
400
200
0
250K
200K
150K
100K
50K
0
50K 100K 150K 200K 250K

FIG. 10

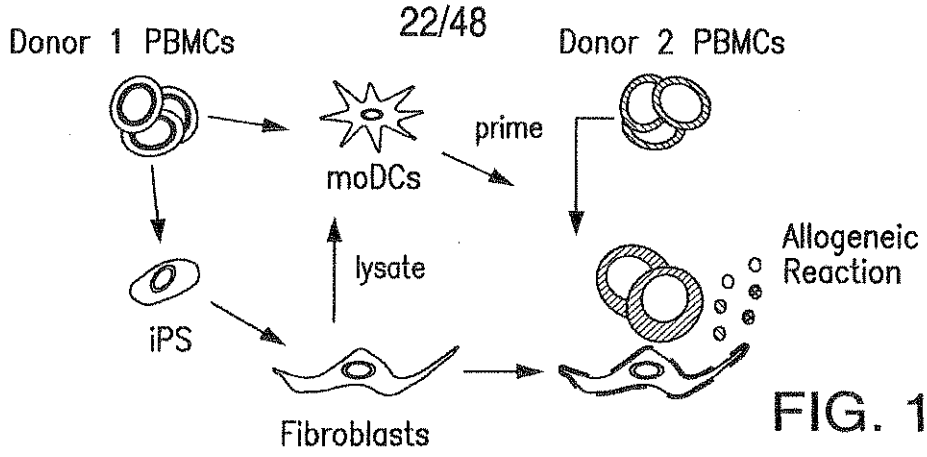


FIG. 11A

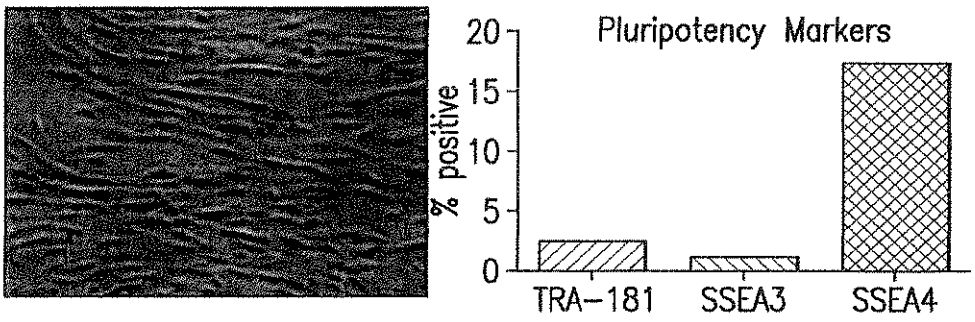


FIG. 11B

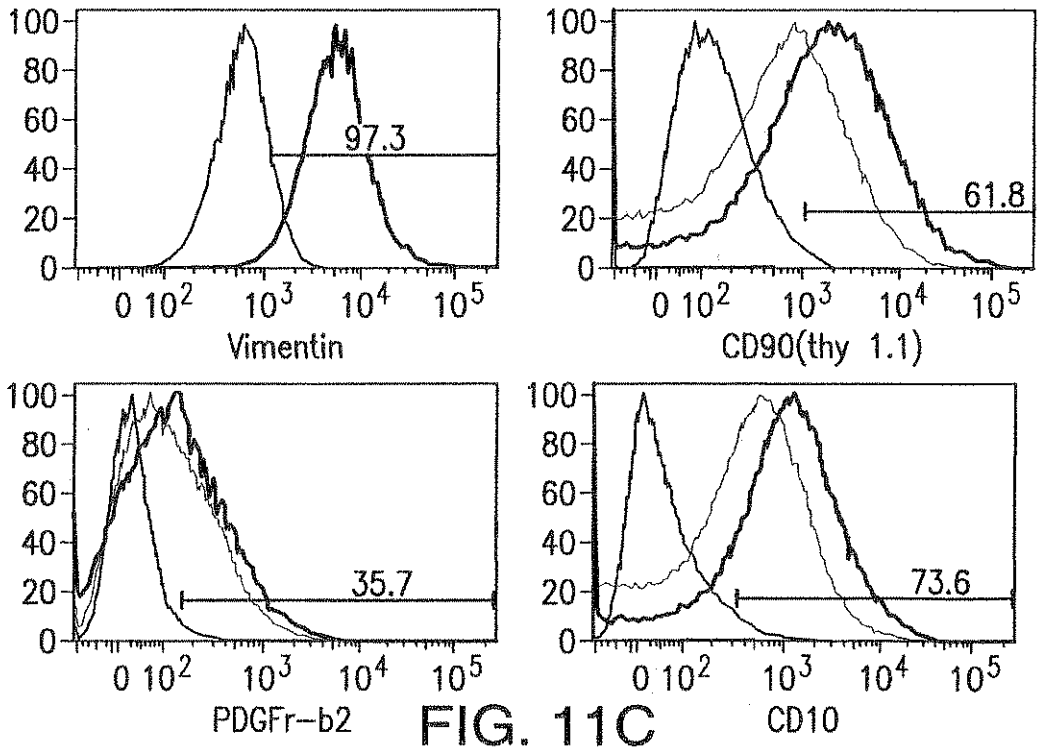


FIG. 11C

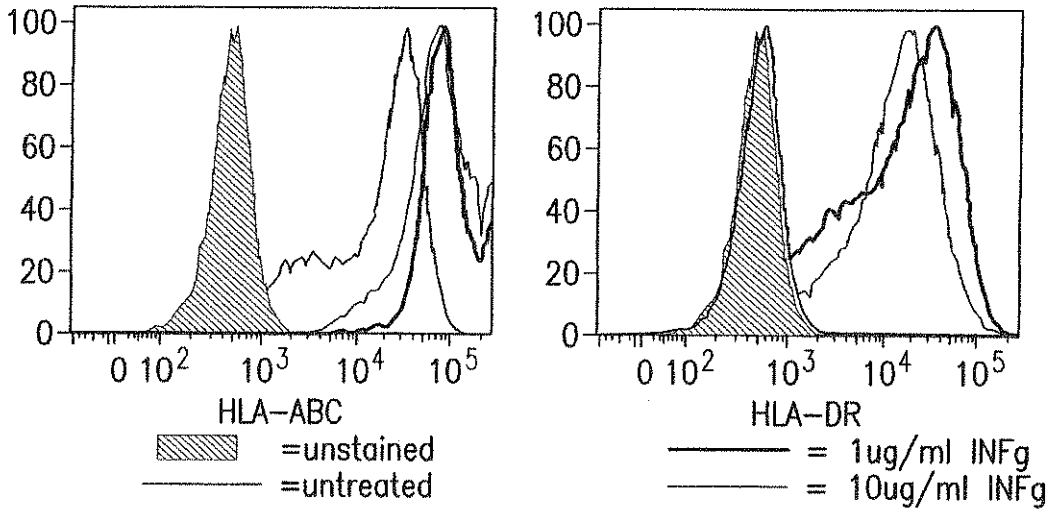

100
80
60
40
20
0
0 10^2
10^3
10^4
10^5
HLA-ABC
=unstained
=untreated
HLA-DR
= 1ug/ml INFg
= 10ug/ml INFg

FIG. 11D

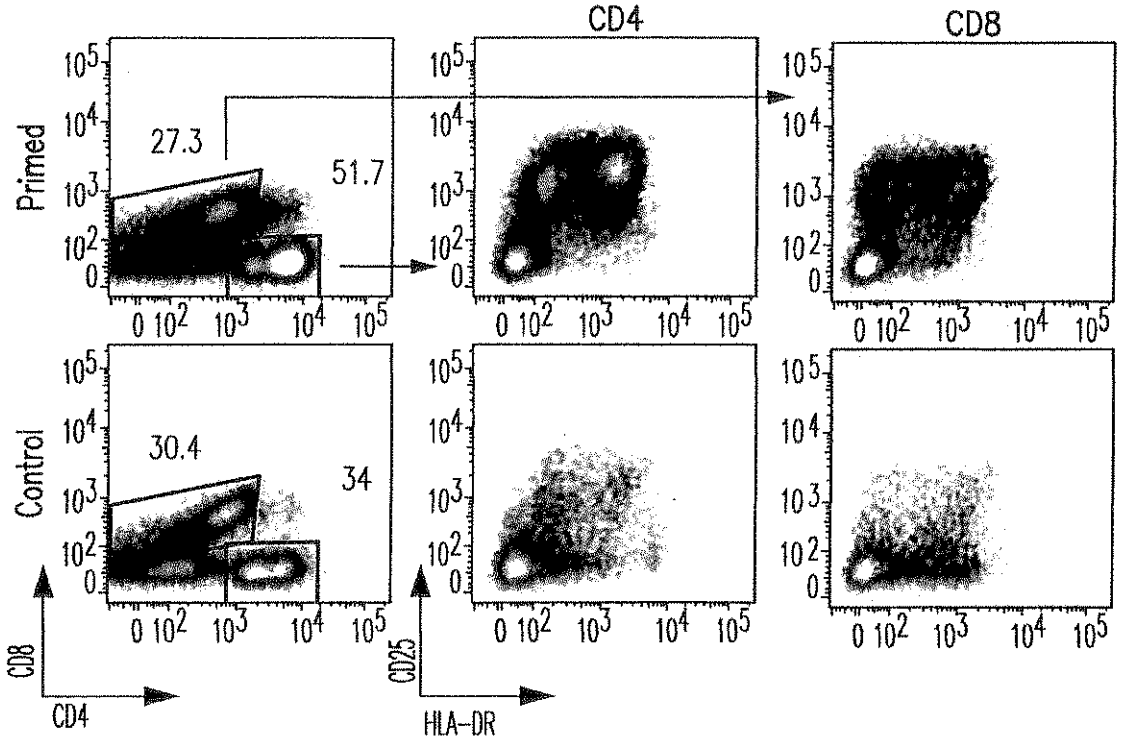


FIG. 12A

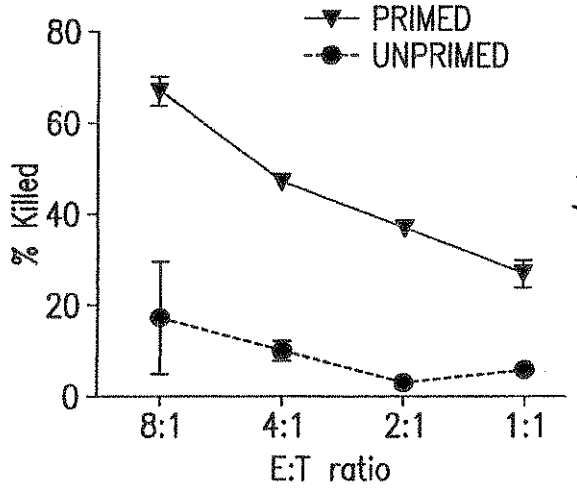


FIG. 12B

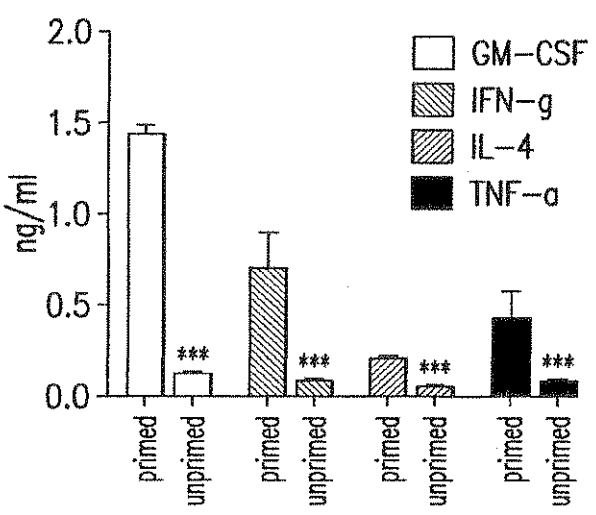


FIG. 12C

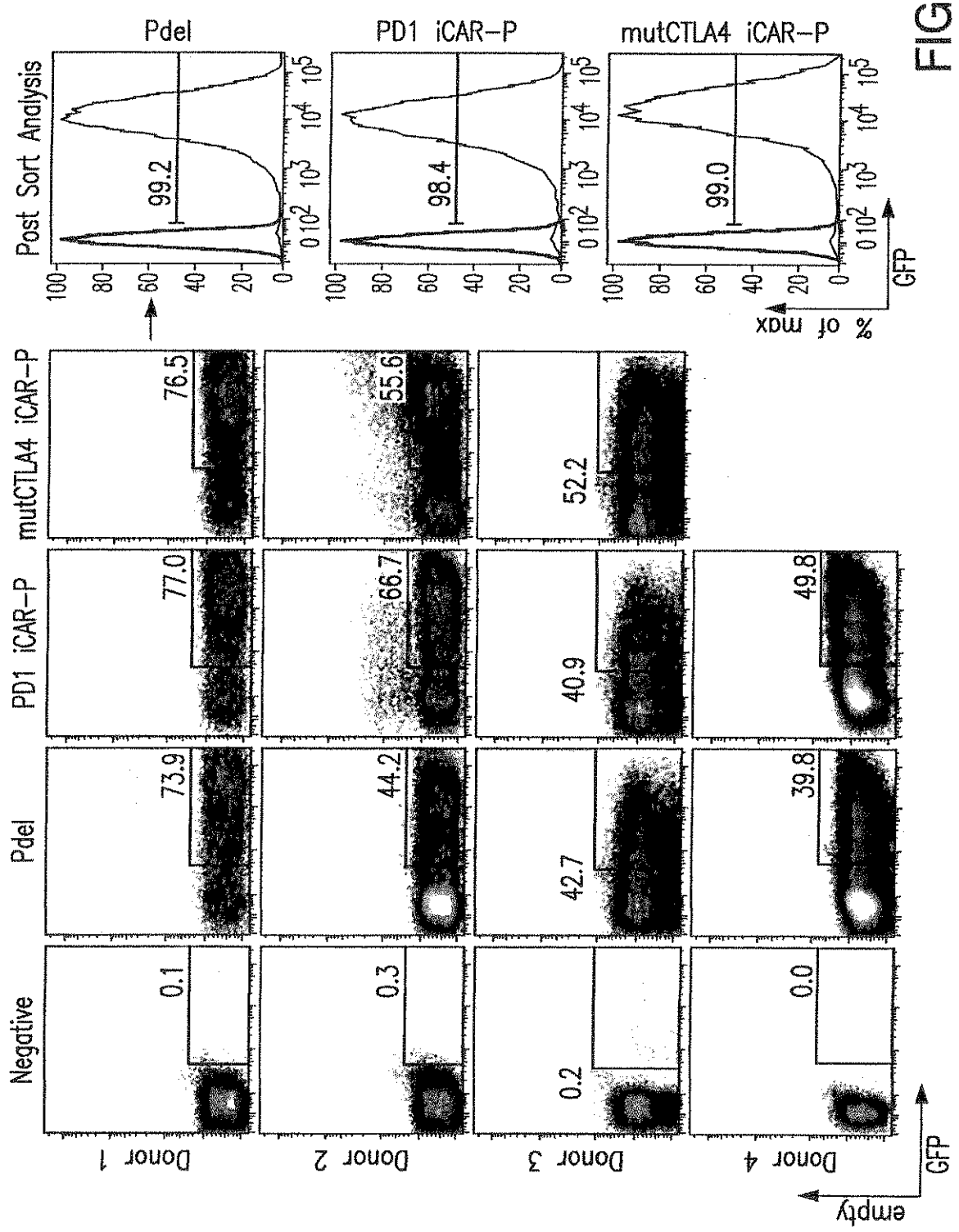

Negative
Pdel
PD1 iCAR-P
mutCTLA4 iCAR-P
Donor 1
Donor 2
Donor 3
Donor 4
0.1
73.9
77.0
76.5
0.3
44.2
66.7
55.6
0.2
42.7
40.9
52.2
0.0
39.8
49.8
empty
GFP
Post Sort Analysis
Pdel
PD1 iCAR-P
mutCTLA4 iCAR-P
99.2
98.4
99.0
% of max
GFP

FIG. 13A

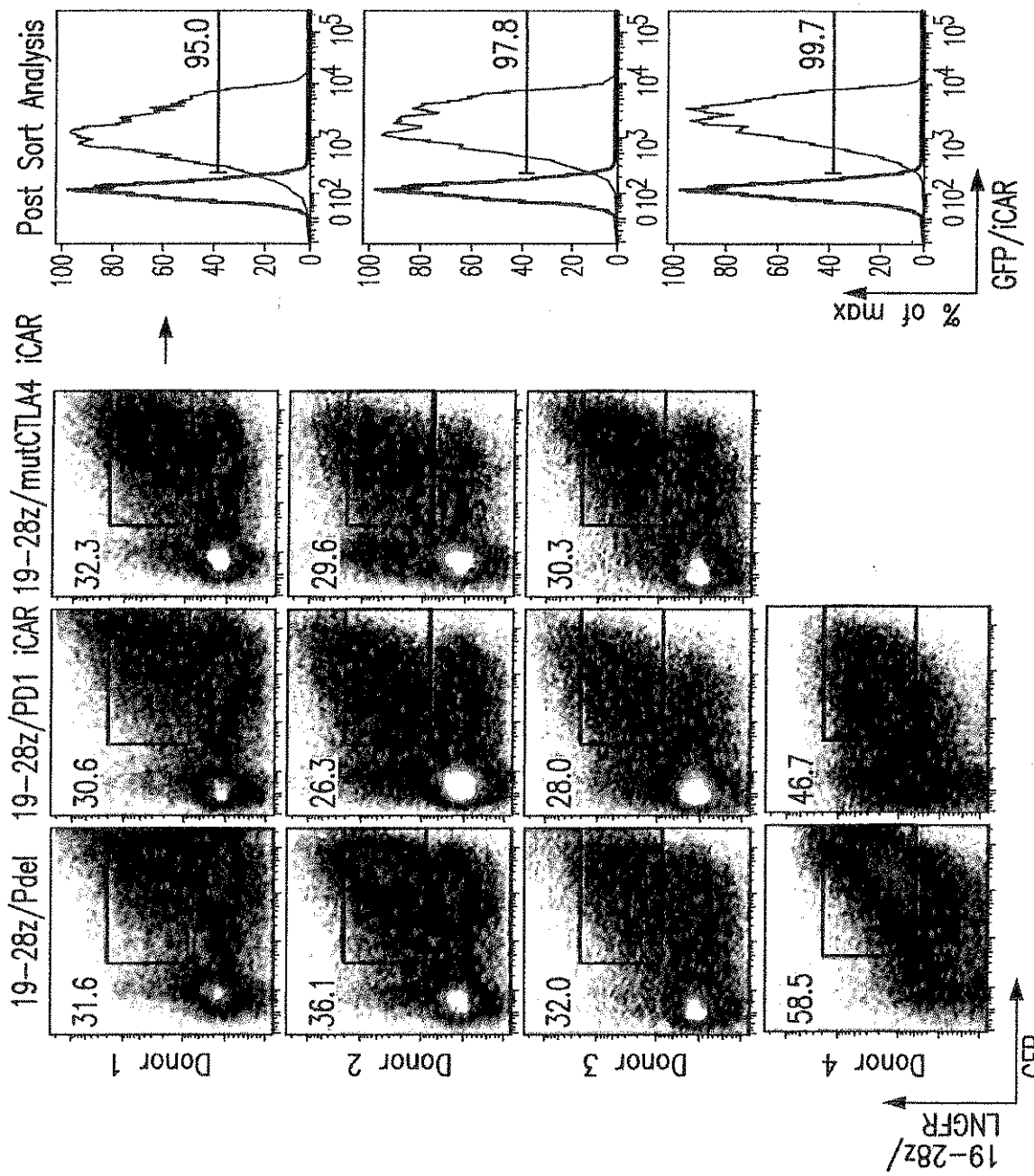
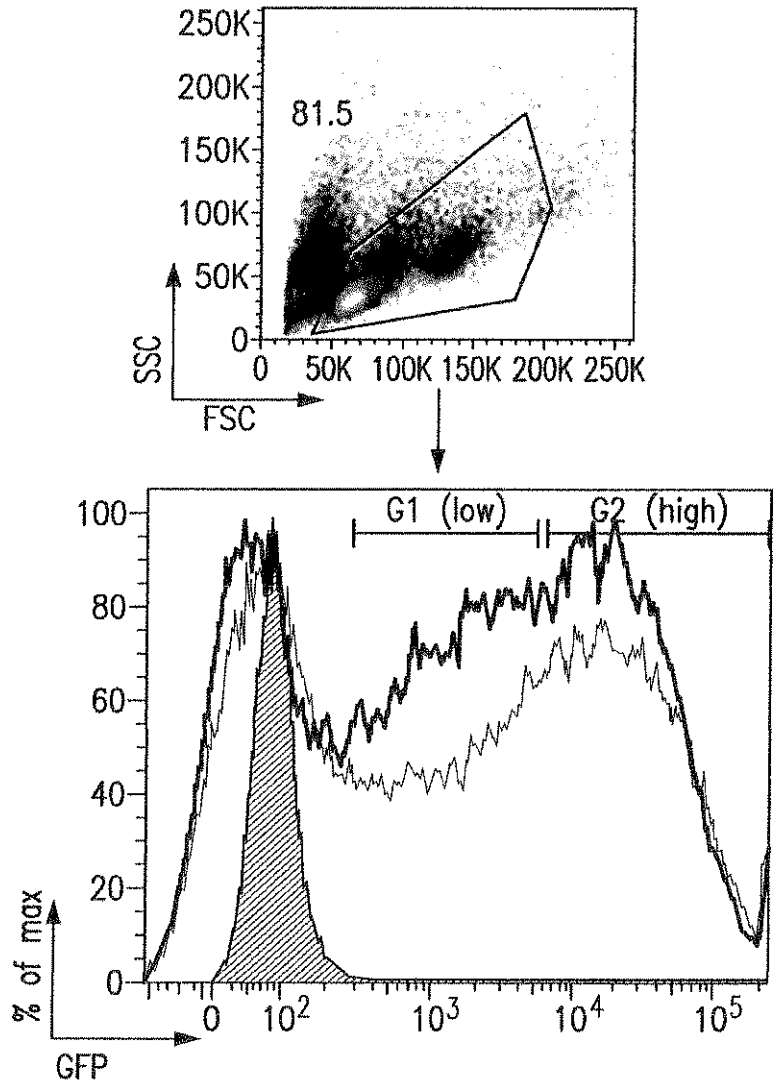
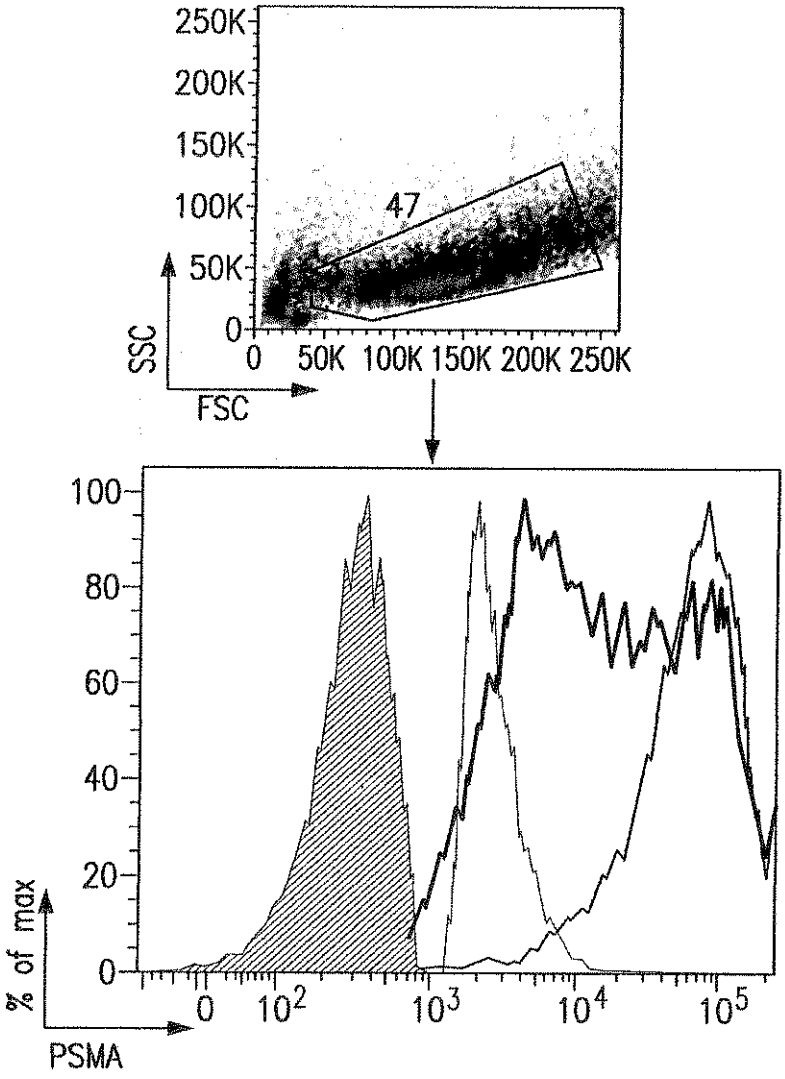

19-28z/Pdel
19-28z/PD1 iCAR
19-28z/mutCTLA4 iCAR
Post Sort Analysis
Donor 1
Donor 2
Donor 3
Donor 4
31.6
30.6
32.3
36.1
26.3
29.6
32.0
28.0
30.3
58.5
46.7
95.0
97.8
99.7
19-28z/ LNGFR
GFP
% of max
GFP/iCAR

FIG. 13B



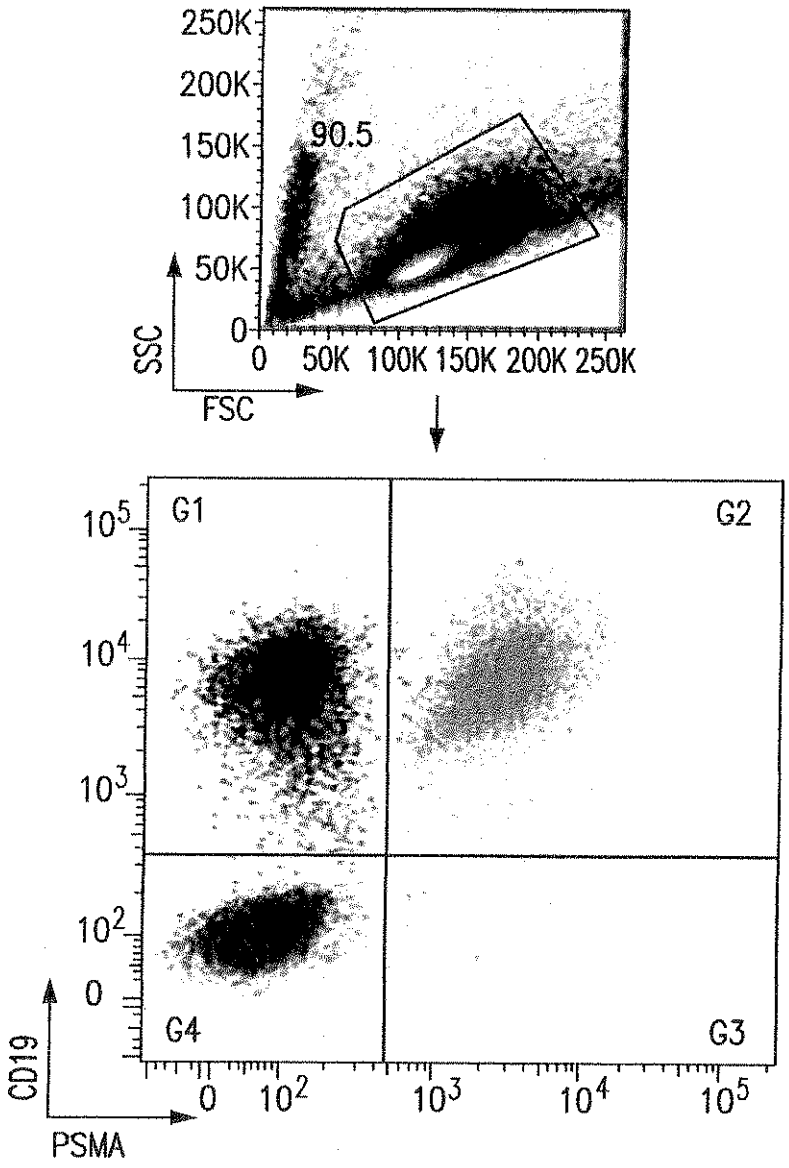
	G1 (frequency)	G1 (MFI)	G2 (frequency)	G2 (MFI)
PD-1-iCAR-P	33.7	1403	34.8	25881
Pdel	27.8	1406	36.7	28487

FIG. 14A



Sample	PSMA (MFI)
iPS-fib PSMA (high level)	53404
iPS-fib PSMA (low level)	2627
iPS-fib PSMA (sort bulk+)	14622
iPS-fib wt	291

FIG. 14B



Sample	CD19 (MFI)	PSMA (MFI)
3T3 CD19 PSMA	6225	2747
3T3 CD19	5891	111
3T3 WT	102	72.9

FIG. 15A

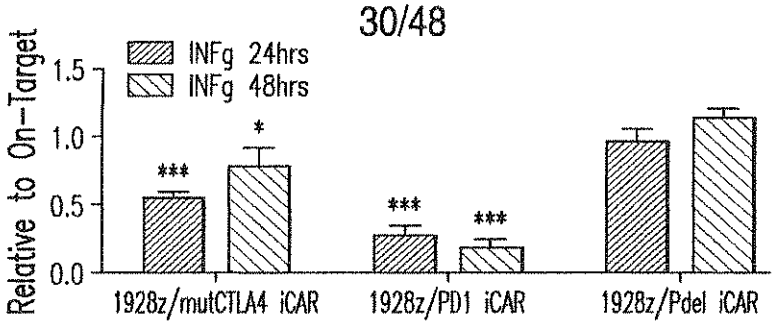


FIG. 15B

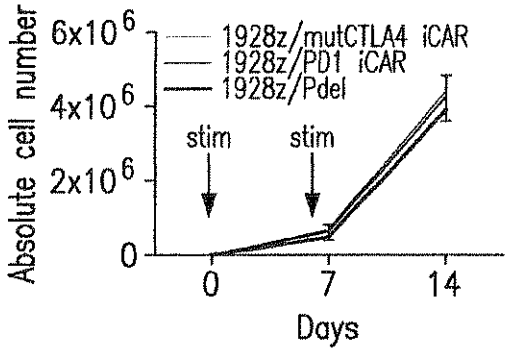
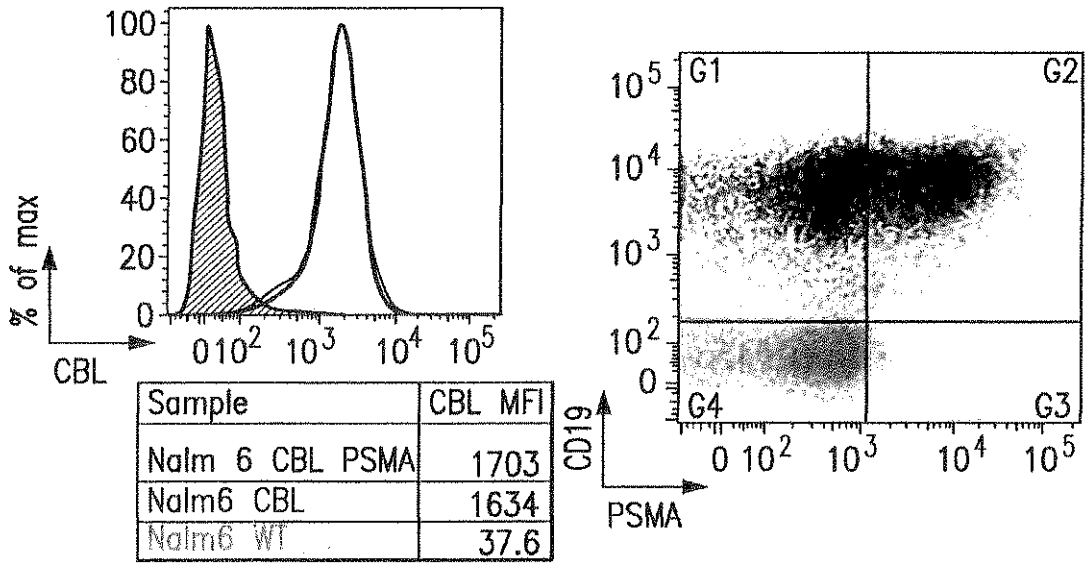


FIG. 15C



Sample	CBL MFI
Nalm 6 CBL PSMA	1703
Nalm6 CBL	1634
Nalm6 WT	37.6

FIG. 15D

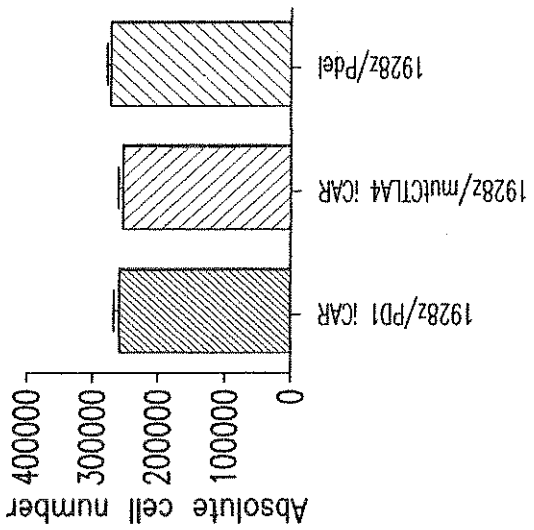


FIG. 16C

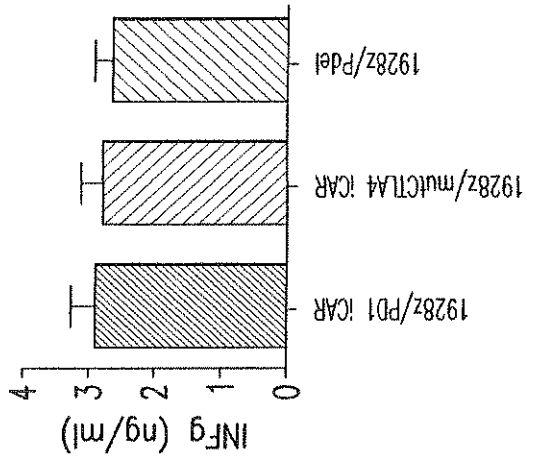


FIG. 16B

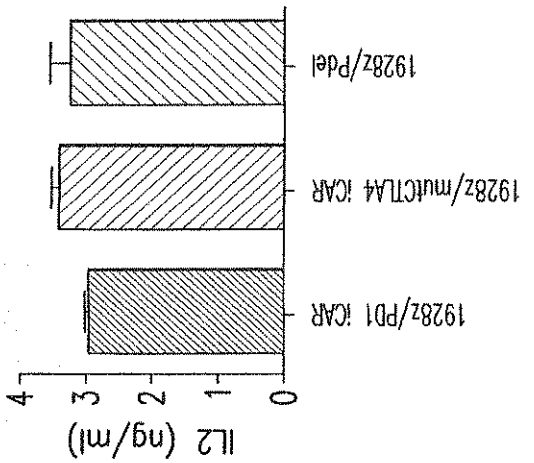


FIG. 16A

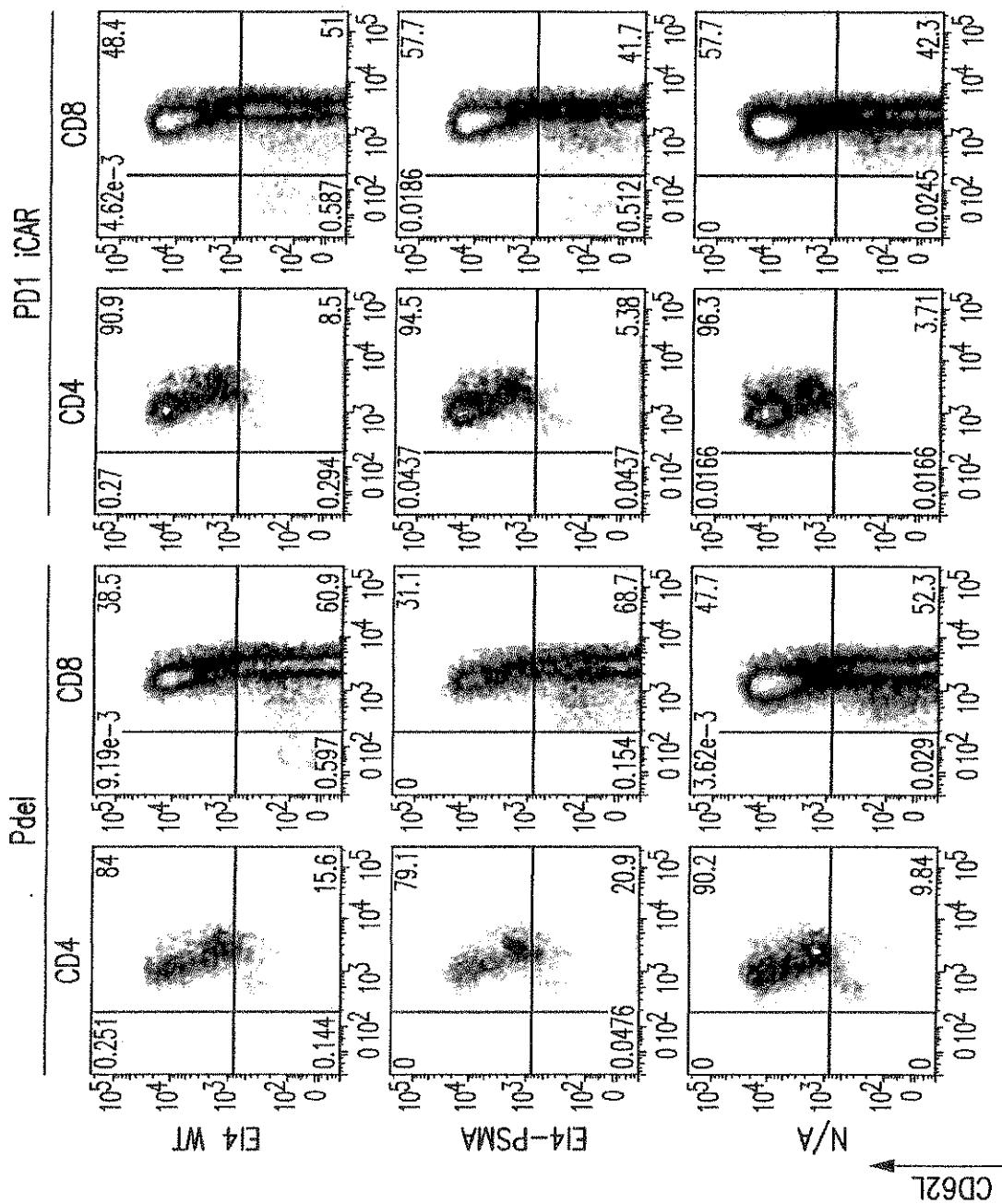

Pdel
PD1 iCAR
CD4
CD8
CD4
CD8
E14 WT
E14-PSMA
N/A
CD62L
CD45RA
0.251
84
15.6
0.144
9.19e-3
38.5
60.9
0.597
0.27
90.9
8.5
0.294
4.62e-3
48.4
51
0.587
0
79.1
20.9
0.0476
0
31.1
68.7
0.154
0.0437
94.5
5.38
0.0437
0.0186
57.7
41.7
0.512
0
90.2
9.84
0
3.62e-3
47.7
52.3
0.029
0.0166
96.3
3.71
0.0166
0
57.7
42.3
0.0245

FIG. 16D

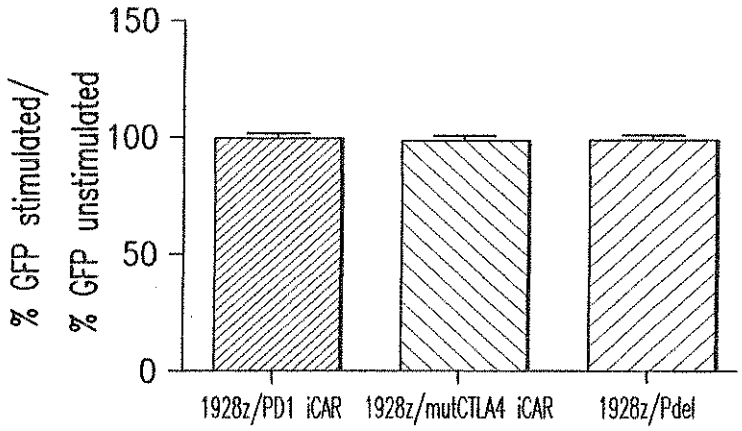

150
100
50
0
% GFP stimulated/
% GFP unstimulated
1928z/PD1 iCAR
1928z/mutCTLA4 iCAR
1928z/Pdel

FIG. 16E

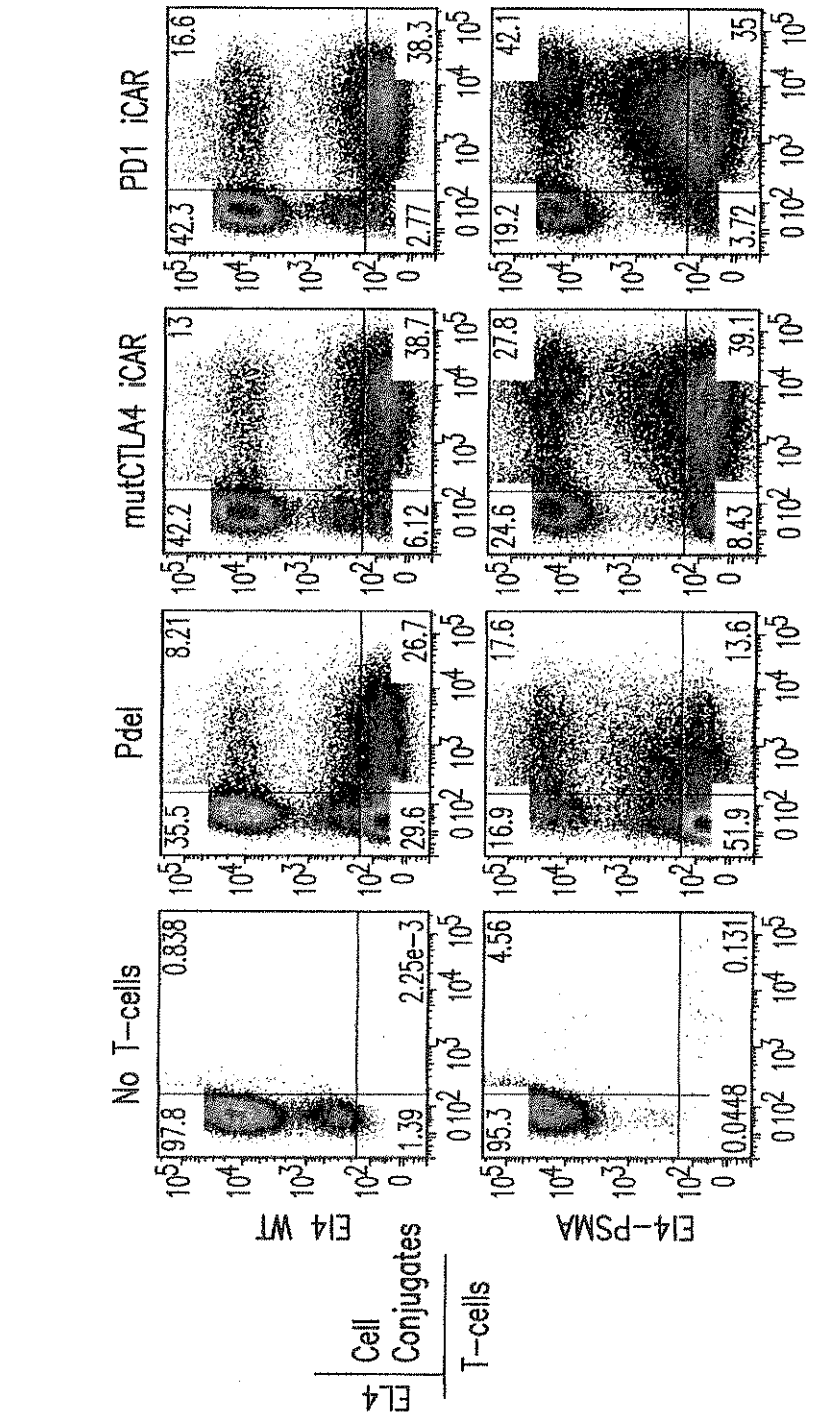

No T-cells
Pdel
mutCTLA4 iCAR
PD1 iCAR
EL4 Cell Conjugates
T-cells
E14 WT
E14-PSMA
97.8
0.838
1.39
2.25e-3
95.3
4.56
0.0448
0.131
35.5
8.21
29.6
26.7
16.9
17.6
51.9
13.6
42.2
13
6.12
38.7
24.6
27.8
8.43
39.1
42.3
16.6
2.77
38.3
19.2
42.1
3.72
35

FIG. 16F

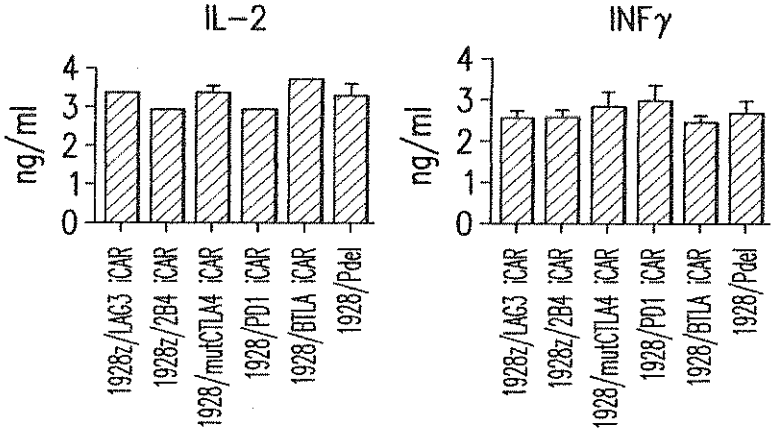


FIG. 16G

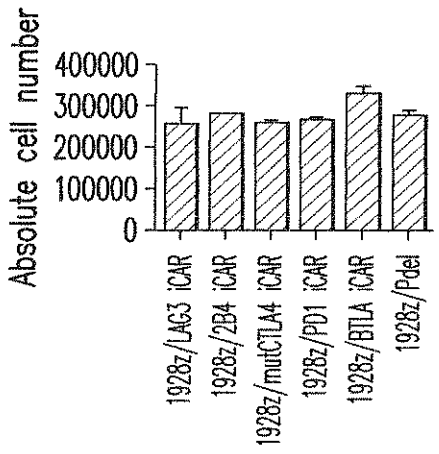


FIG. 16H

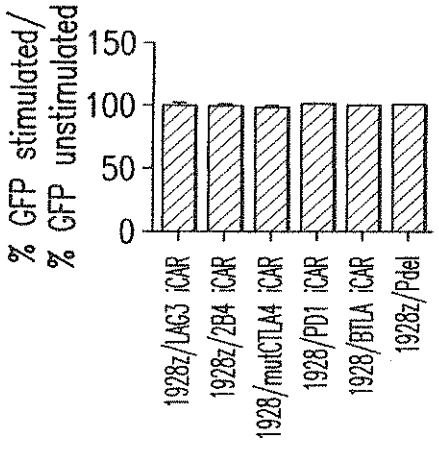


FIG. 16I

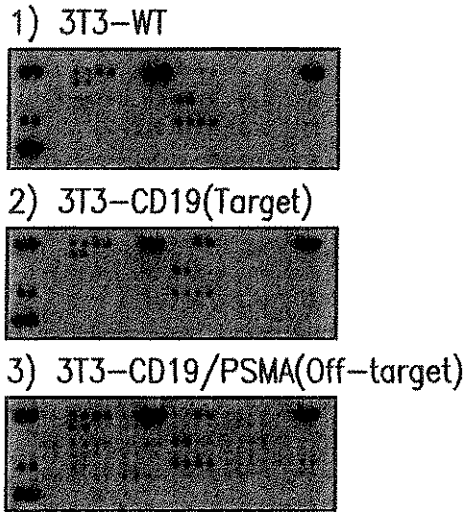


FIG. 17A

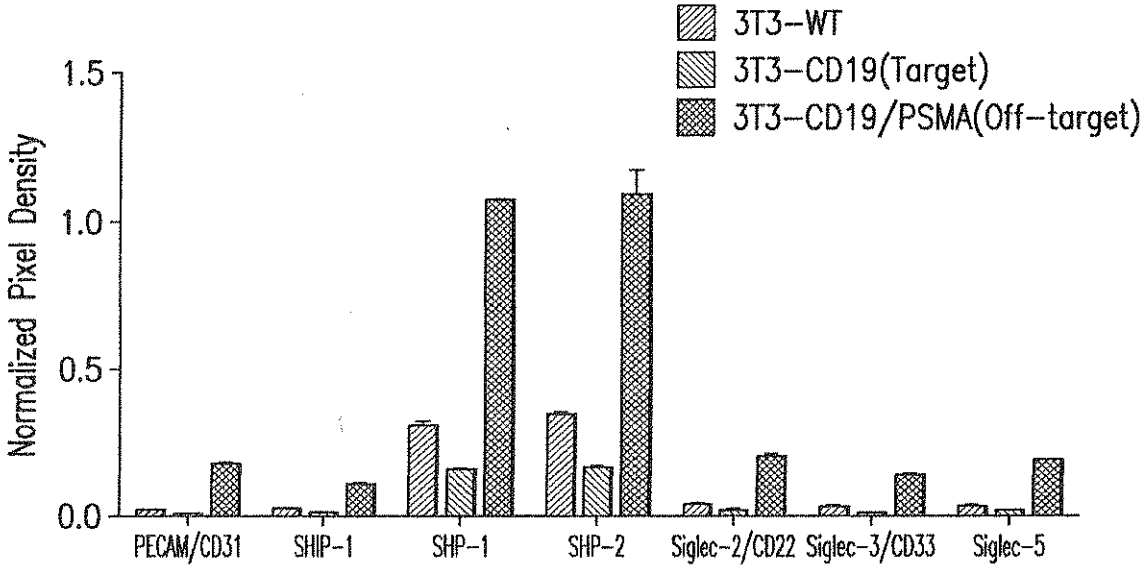


FIG. 17B

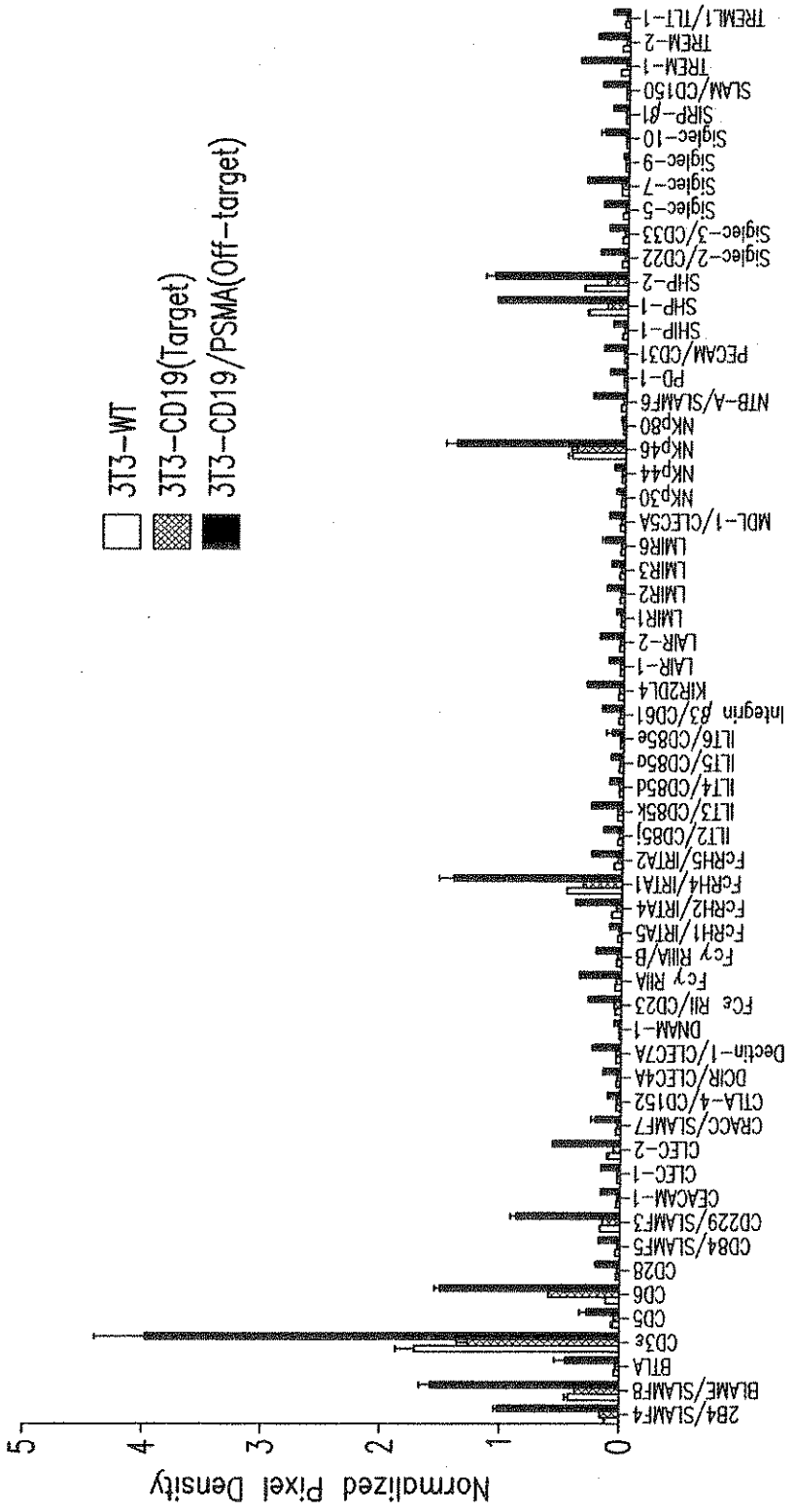

3T3-WT
3T3-CD19(Target)
3T3-CD19/PSMA(Off-target)
Normalized Pixel Density
0
1
2
3
4
5
2B4/SLAMF4
BLAME/SLAMFB
BTLA
CD3ε
CD5
CD6
CD28
CD84/SLAMF5
CD229/SLAMF3
CEACAM-1
CLEC-1
CLEC-2
CRACC/SLAMF7
CTLA-4/CD152
DCIR/CLEC4A
Dectin-1/CLEC7A
DNAM-1
FCε RII/CD23
Fcγ RIIA
Fcγ RIIA/B
FcRH1/IRTA5
FcRH2/IRTA4
FcRH4/IRTA1
FcRH5/IRTA2
ILT2/CD85j
ILT3/CD85k
ILT4/CD85d
ILT5/CD85a
ILT6/CD85e
Integrin β3/CD61
KIR2DL4
LAIR-1
LAIR-2
LMIR1
LMIR2
LMIR3
LMIR6
MDL-1/CLEC5A
NKp30
NKp44
NKp46
NKp80
NTB-A/SLAMF6
PD-1
PECAM/CD31
SHIP-1
SHP-1
SHP-2
Siglec-2/CD22
Siglec-3/CD33
Siglec-5
Siglec-7
Siglec-9
Siglec-10
SIRP-β1
SLAM/CD150
TREM-1
TREM-2
TREML1/TLT-1

FIG. 17C

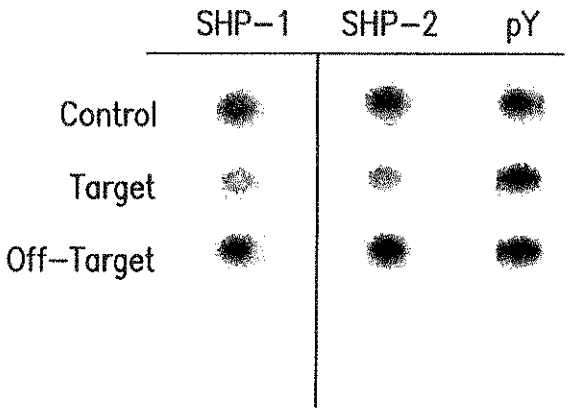


FIG. 18

Raw BLI (Flux-photons)	mutCTLA4 iCAR			PD1 iCAR			Pdel		
4:1	1.5E+07	1.4E+07	1.4E+07	1.5E+07	1.5E+07	1.5E+07	1.6E+07	1.6E+07	1.6E+07
2:1	1.2E+07	9.9E+06	1.1E+07	1.2E+07	1.0E+07	1.1E+07	1.2E+07	1.2E+07	1.2E+07
1:1	8.2E+06	8.2E+06	8.2E+06	8.3E+06	8.5E+06	8.4E+06	7.9E+06	9.0E+06	8.4E+06
No T cells	2.4E+07	1.2E+07	1.9E+07						

FIG. 19A

pg/mL	mutCTLA4 iCAR			PD1 iCAR			Pdel		
GM-CSF	647.2	801.3	765.5	703.8	897.3	783.4	714.8	818.8	774.9
INF γ	621.2	552.2	534.4	533	595	533.2	581	622	618.8
TNF-α	379	422	400.1	388	379	375.5	394	643	523.2

FIG. 19B

Raw BLI (Flux-photons)	mutCTLA4 iCAR			PD1 iCAR			Pdel		
16:1	3.87E+01	4.28E+01	4.07E+01	1.67E+01	2.09E+01	1.85E+01	4.88E+01	4.74E+01	4.70E+01
8:1	3.09E+01	3.30E+01	3.23E+01	9.96E+00	1.19E+01	1.10E+01	4.56E+01	4.45E+01	4.50E+01
4:1	2.30E+01	2.62E+01	2.40E+01	3.27E+00	3.06E+00	3.21E+00	4.24E+01	4.28E+01	4.25E+01
2:1	2.11E+01	1.98E+01	2.02E+01	5.27E+01	3.48E+00	1.90E+00	3.80E+01	4.21E+01	3.99E+01
1:1	2.78E+01	1.81E+01	2.25E+01	5.01E+00	2.00E+00	3.53E+00	4.11E+01	4.15E+01	4.12E+01
No T cells	3.92E+07	3.85E+07	3.76E+07						

FIG. 19C

SUBSTITUTE SHEET (RULE 26)

PD1 vs Pdel	Significant?	P value	PDI	Pdel	Difference	SE of difference	t ratio	df
16:1	*	2.72372E-05	35.47	90.58	-55.12	2.55	21.59	4
8:1	*	7.47524E-07	20.80	85.47	-64.67	1.22	53.20	4
4:1	*	9.99669E-10	6.03	80.83	-74.80	0.27	278.33	4
2:1	*	1.2563E-05	3.73	75.87	-72.13	2.75	26.23	4
1:1	*	1.74306E-06	6.67	78.23	-71.57	1.66	43.03	4

CTLA4 vs Pdel	Significant?	P value	CTLA4	Pdel	Difference	SE of difference	t ratio	df
16:1	*	0.00581413	77.33	90.58	-13.25	2.47	5.37	4
8:1	*	5.02912E-05	60.86	85.47	-24.61	1.33	18.50	4
4:1	*	4.23971E-05	46.33	80.83	-34.50	1.79	19.31	4
2:1	*	9.05225E-05	38.67	75.87	-37.20	2.33	15.94	4
1:1	*	0.0027265	43.27	78.23	-34.97	5.30	6.60	4

FIG. 19D

SUBSTITUTE SHEET (RULE 26)

GM-CSF
RAW
(pg/ml)

	Pdel			Avg Pdel	mutCTLA4 iCAR			PD1 iCAR		
16:1	564.94	573.44	591.49	576.62	549.74	670.09	596.70	181.79	245.95	209.53
8:1	339.22	378.48	320.44	346.05	277.03	217.73	243.96	58.42	42.98	48.67
4:1	179.60	136.10	190.34	168.68	74.20	75.28	75.93	26.04	25.31	25.69
2:1	63.26	71.91	73.08	69.42	26.72	26.80	26.34	9.54	8.97	9.06
1:1	20.49	23.10	16.49	20.03	6.15	6.92	6.59	2.49	3.38	2.91

%PDEL

	mutCTLA4 iCAR			PD1 iCAR		
16:1	95.34	116.21	103.48	31.53	42.65	36.34
8:1	80.05	62.92	70.50	16.88	12.42	14.06
4:1	43.99	44.63	45.02	15.44	15.00	15.23
2:1	38.49	38.61	37.94	13.74	12.92	13.06
1:1	30.72	34.57	32.89	12.42	16.88	14.55

FIG. 19E

SUBSTITUTE SHEET (RULE 26)

Normalized flux	Low Pdel			High Pdel			High P-PDI			Low P-PDI		
16:1	96.76	96.88	96.99	97.41	96.9	97.2	54.7	59.9	57.8	96.65	93.5	95
8:1	87.3	92.68	89.71	97.66	97.02	97.03	24.7	30.7	27.3	83.6	82.4	83.8
4:1	83.2	84.2	83.81	96.65	95.1	95.44	21.5	25.8	23.48	74.3	74.2	74.8
2:1	77.6	80.1	78	91.4	92.68	92.87	18.3	15.3	16.2	64.3	66.8	65.1
1:1	71.1	68	69.1	89.4	85.7	87.37	13.7	17.5	15.1	48.6	57.5	53.4

Low PD1 vs Low Pdel								
	Significant?	P value	Low PDI	Low Pdel	Difference	SE of difference	t ratio	df
16:1		0.12	95.05	96.88	-1.83	0.91	2.00	4.00
8:1	*	0.01	83.27	89.90	-6.63	1.62	4.10	4.00
4:1	*	0.00	74.43	83.74	-9.30	0.35	26.96	4.00
2:1	*	0.00	65.40	78.57	-13.17	1.07	12.31	4.00
1:1	*	0.00	53.17	69.40	-16.23	2.73	5.95	4.00
High PD1 vs High Pdel								
	Significant?	P value	High PDI	High Pdel	Difference	SE of difference	t ratio	df
16:1	*	0.00	57.47	97.17	-39.70	1.52	26.16	4.00
8:1	*	0.00	27.57	97.24	-69.67	1.75	39.81	4.00
4:1	*	0.00	23.59	95.73	-72.14	1.33	54.29	4.00
2:1	*	0.00	16.60	92.32	-75.72	1.00	75.60	4.00
1:1	*	0.00	15.43	87.49	-72.06	1.54	46.75	4.00

FIG. 20A

SUBSTITUTE SHEET (RULE 26)

Normalized flux	PSMA low			PSMA high		
8:1	74.3	73	73.8	61.3	68.6	70.7
4:1	64.3	64.1	64.7	21.5	31.6	25.54
2:1	57.5	57	57.6	13.8	19.9	16.1
1:1	48.6	49.4	49.3	20.7	9.7	15.9

PSAM low vs PSMA High								
	Significant?	P value	PSMA Low	PSMA high	Difference	SE of difference	t ratio	df
8:1		0.08	73.70	66.87	6.83	2.87	2.38	4.00
4:1	*	0.00	64.37	26.21	38.15	2.94	12.98	4.00
2:1	*	0.00	57.37	16.60	40.77	1.79	22.80	4.00
1:1	*	0.00	49.10	15.43	33.67	3.19	10.54	4.00

FIG. 20B

SUBSTITUTE SHEET (RULE 26)

Raw BLI (Flux-photons)															
Days	No T Cells					PD1 iCAR					Pdel				
3.00	7.78E+07	1.43E+07	1.40E+07	1.48E+07	1.44E+07	1.46E+07	1.69E+07	1.42E+07	4.44E+07	1.15E+07	2.74E+07	8.59E+05	5.46E+07	5.81E+06	2.32E+07
5.00	4.09E+07	1.91E+07	1.04E+07	4.73E+07	2.78E+07	8.26E+06	9.87E+06	3.95E+07	3.93E+07	2.58E+07	6.17E+06	4.41E+06	2.09E+06	2.05E+06	4.09E+06
8.00	2.22E+07	2.01E+07	1.50E+07	2.82E+07	2.60E+07	3.28E+07	1.47E+07	1.66E+07	3.29E+07	2.17E+07	5.28E+06	4.76E+06	5.43E+06	2.59E+06	3.19E+06
34.00	4.62E+07	2.55E+07	1.34E+07	5.53E+07	3.36E+07	5.63E+07	3.42E+07	2.84E+07	5.85E+07	3.31E+07	2.01E+06	6.37E+06	1.32E+06	1.25E+06	2.19E+06
48.00	4.39E+07	1.96E+07	3.81E+07	3.65E+07	2.70E+07	7.50E+07	2.56E+07	3.94E+06	5.23E+07	3.17E+07	2.83E+06	7.10E+05	1.44E+06	1.86E+06	2.06E+06

FIG. 21A

No T cells vs Pdel								
	Significant?	P value	No Tcells	Pdel	Difference	SE of difference	t ratio	df
3.00E+00		7.75E-01	2.71E+07	2.24E+07	4.69E+06	1.58E+07	2.96E-01	8.00E+00
5.00E+00	*	5.97E-03	2.91E+07	3.76E+06	2.53E+07	6.83E+06	3.71E+00	8.00E+00
8.00E+00	*	6.39E-05	2.23E+07	4.25E+06	1.81E+07	2.38E+06	7.59E+00	8.00E+00
3.40E+01	*	2.58E-03	3.48E+07	2.63E+06	3.22E+07	7.46E+06	4.31E+00	8.00E+00
4.80E+01	*	9.12E-05	3.30E+07	1.78E+06	3.12E+07	4.33E+06	7.21E+00	8.00E+00

No T cells vs PD1								
	Significant?	P value	No Tcells	PD1	Difference	SE of difference	t ratio	df
3.00E+00		6.45E-01	2.71E+07	2.03E+07	6.74E+06	1.41E+07	4.79E-01	8.00E+00
5.00E+00		6.48E-01	2.91E+07	2.45E+07	4.55E+06	9.61E+06	4.74E-01	8.00E+00
8.00E+00		7.58E-01	2.23E+07	2.37E+07	-1.44E+06	4.52E+06	3.18E-01	8.00E+00
3.40E+01		4.75E-01	3.48E+07	4.21E+07	-7.30E+06	9.74E+06	7.49E-01	8.00E+00
4.80E+01		7.25E-01	3.30E+07	3.77E+07	-4.69E+06	1.28E+07	3.65E-01	8.00E+00

FIG. 21B

SUBSTITUTE SHEET (RULE 26)

Relative to On-Target	1928z/Pdel			1928z/PD1 iCAR			1928z/mutCTLA4 iCAR		
INFg	1.05	0.93	0.87	0.26	0.35	0.18	0.58	0.51	0.54
IL2	0.85	0.94	0.89	0.14	0.10	0.11	0.40	0.38	0.42
TNFa	1.05	1.02	1.00	0.24	0.29	0.28	0.44	0.45	0.43
IL10	0.92	0.98	0.97	0.31	0.27	0.27	0.59	0.54	0.65
GMCSF	0.95	1.04	1.01	0.26	0.23	0.26	0.63	0.62	0.69

	Significant?	P value	1928z/pdel	1928z/pd1	Difference	SE of difference	t ratio	df
INFg	*	0.00	0.95	0.26	0.69	0.07	9.51	4.00
IL2	*	0.00	0.89	0.12	0.78	0.03	27.09	4.00
TNFa	*	0.00	1.02	0.27	0.75	0.02	35.73	4.00
IL10	*	0.00	0.96	0.28	0.67	0.02	29.46	4.00
GMCSF	*	0.00	1.00	0.25	0.75	0.03	26.52	4.00

	Significant?	P value	1928z/pdel	1928z/mutCTLA4	Difference	SE of difference	t ratio	df
INFg	*	0.00	0.95	0.54	0.41	0.06	7.18	4.00
IL2	*	0.00	0.89	0.40	0.49	0.03	17.32	4.00
TNFa	*	0.00	1.02	0.44	0.58	0.02	37.31	4.00
IL10	*	0.00	0.96	0.59	0.36	0.04	9.87	4.00
GMCSF	*	0.00	1.00	0.65	0.35	0.03	10.30	4.00

FIG. 22A

SUBSTITUTE SHEET (RULE 26)

Cell Counts	Significant?	P value	1928z/pdel	1928z/pd1	Difference	SE of difference	t ratio	df
0								
7	*	0.00226118	464667	246000	218667	31497.8	6.94229	4
14	*	0.000187776	4490000	840333	3649667	275554	13.2448	4

FIG. 22B

Normalized mCherry signal	1928z/mutCTLA4 iCAR				1928z/PD1 iCAR				1928z/Pdel				1928z			
2.00	0.98	1.23	1.19	1.21	0.96	0.98	0.90	1.02	1.00	1.02	1.02	1.06	1.03	1.11	1.02	0.98
18.00	0.88	1.43	1.09	1.21	1.27	1.58	1.00	1.02	0.38	0.42	0.41	0.27	0.43	0.69	0.40	0.26
38.00	0.73	0.54	0.62	0.78	0.79	1.09	0.75	1.20	0.08	0.08	0.06	0.06	0.09	0.09	0.09	0.10
120.00	0.12	0.27	0.11	0.06	1.66	1.58	1.00	1.26	0.04	0.05	0.05	0.03	0.07	0.09	0.07	0.07

	Significant?	P value	1928z/pdel	1928z/pd1	Difference	SE of difference	t ratio	df
2.00		1.06E-01	1.02	0.97	-0.06	0.03	1.90	6.00
18.00	*	9.54E-04	0.37	1.22	0.85	0.14	6.01	6.00
38.00	*	2.11E-04	0.07	0.96	0.89	0.11	7.95	6.00
120.00	*	1.32E-04	0.04	1.38	1.33	0.15	8.64	6.00

	Significant?	P value	1928z/pdel	1928z/mutCTLA4	Difference	SE of difference	t ratio	df
2.00		7.44E-02	1.02	1.15	-0.13	0.06	2.16	6.00
18.00	*	6.04E-04	0.37	1.15	-0.78	0.12	6.55	6.00
38.00	*	3.79E-05	0.07	0.67	-0.60	0.06	10.77	6.00
120.00		8.37E-02	0.04	0.14	-0.10	0.05	2.07	6.00

FIG. 22C

SUBSTITUTE SHEET (RULE 26)

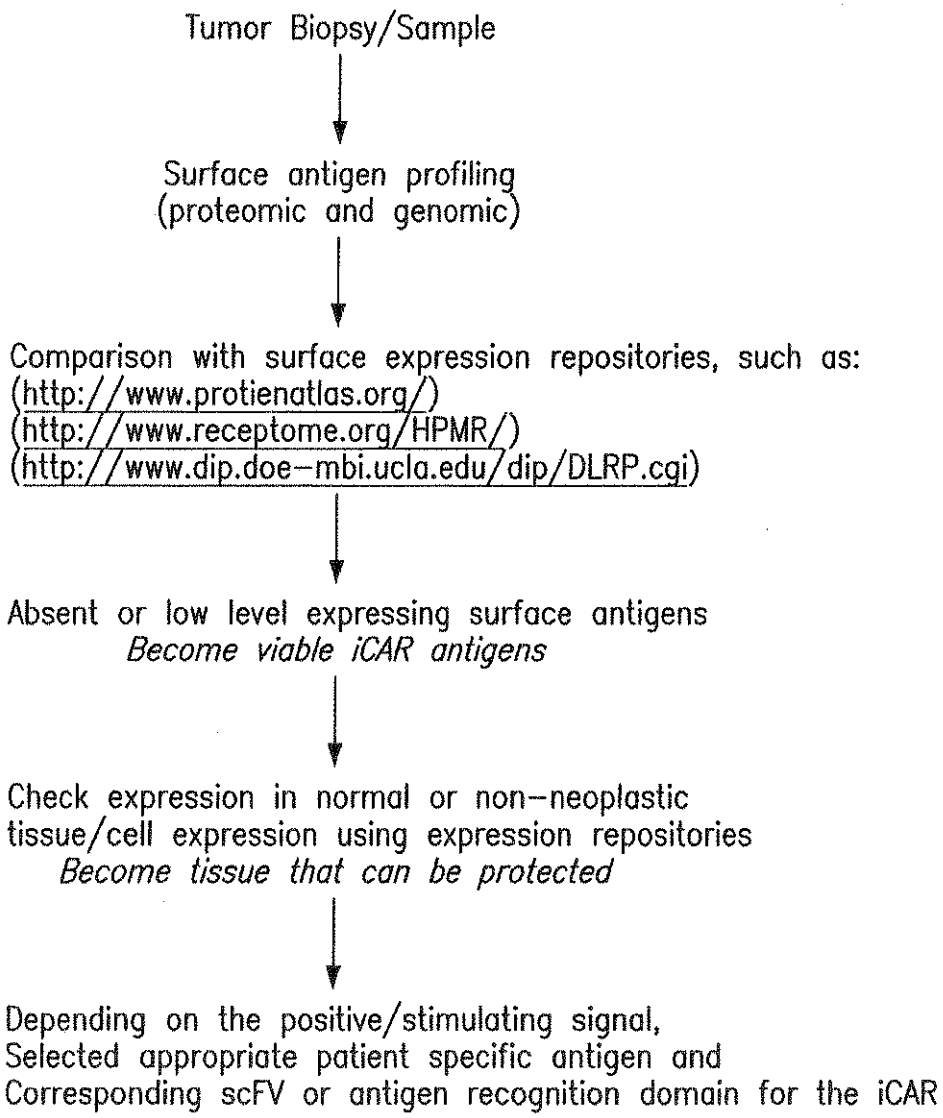

Tumor Biopsy/Sample
Surface antigen profiling
(proteomic and genomic)
Comparison with surface expression repositories, such as:
(http://www.protienatlas.org/)
(http://www.receptome.org/HPMR/)
(http://www.dip.doe-mbi.ucla.edu/dip/DLRP.cgi)
Absent or low level expressing surface antigens
Become viable iCAR antigens
Check expression in normal or non-neoplastic
tissue/cell expression using expression repositories
Become tissue that can be protected
Depending on the positive/stimulating signal,
Selected appropriate patient specific antigen and
Corresponding scFV or antigen recognition domain for the iCAR

FIG. 23