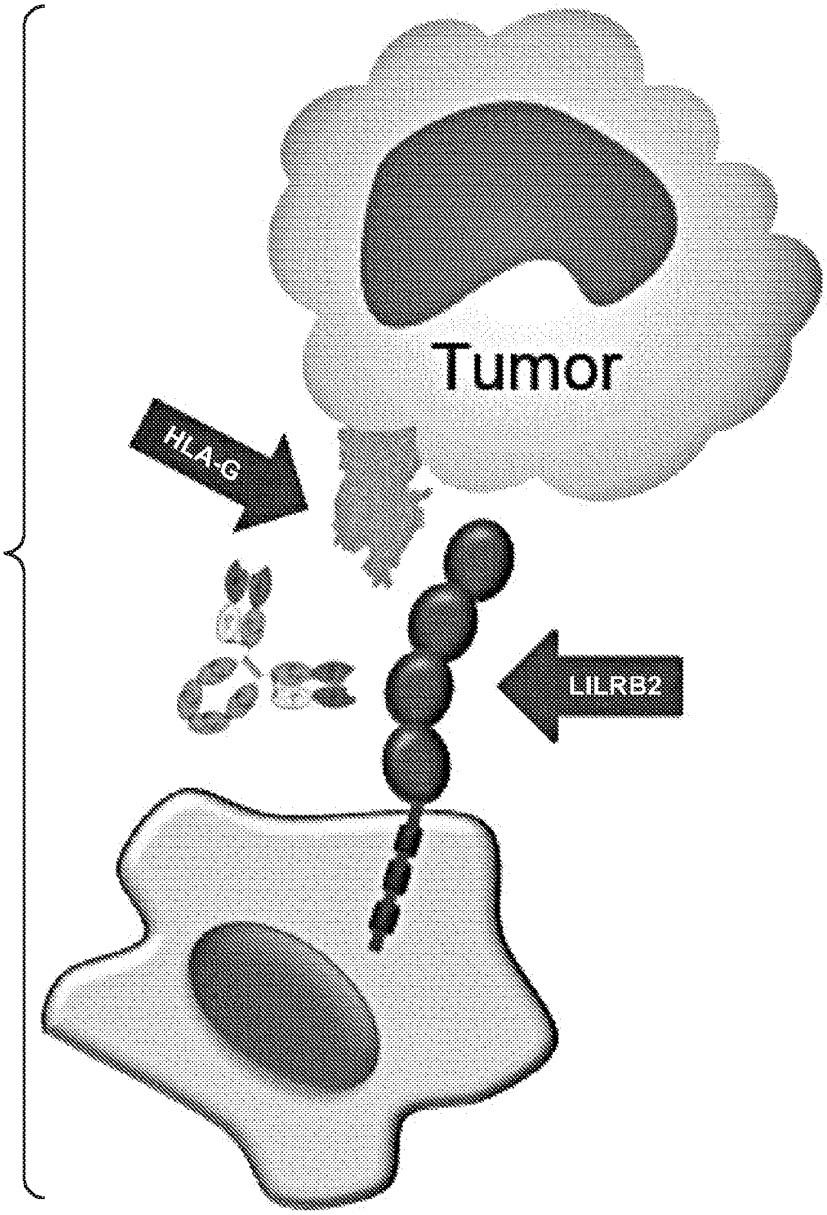
FIG. 1



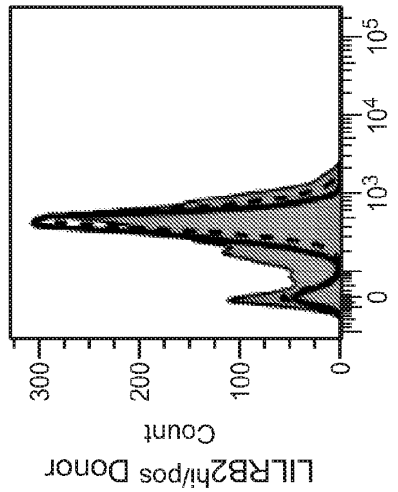


FIG. 2C

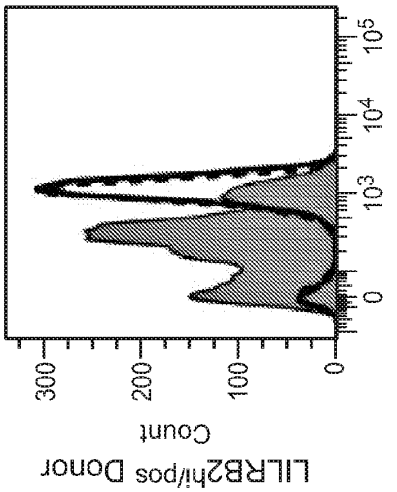


FIG. 2F

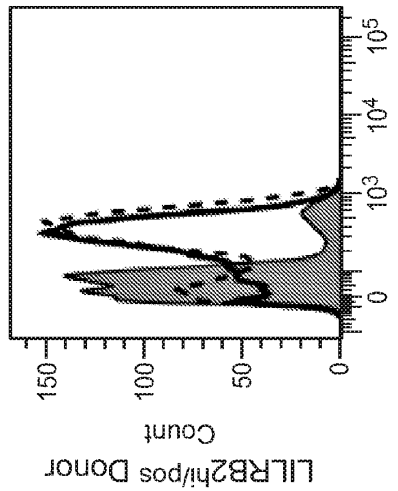


FIG. 2B

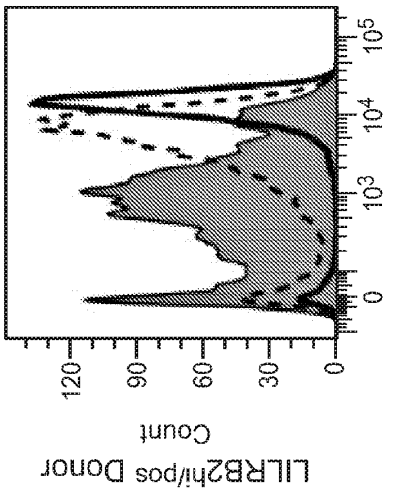


FIG. 2E

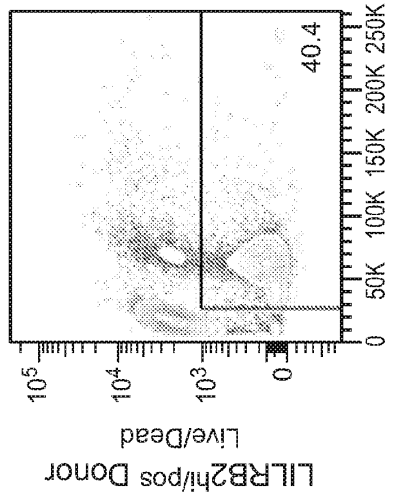


FIG. 2A

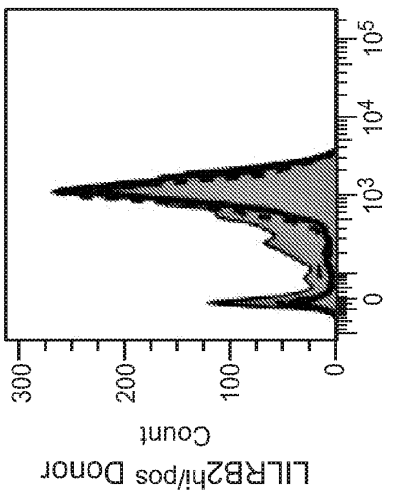


FIG. 2D

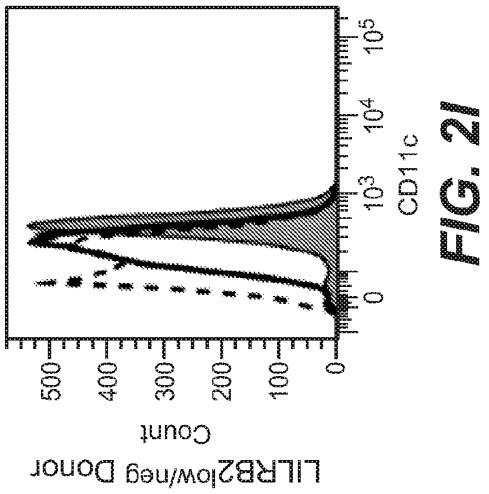


FIG. 2I

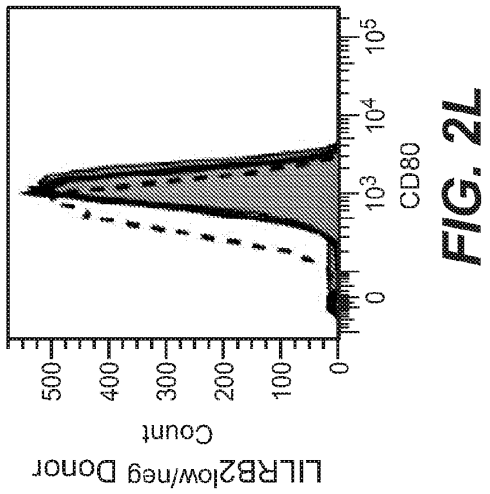


FIG. 2L

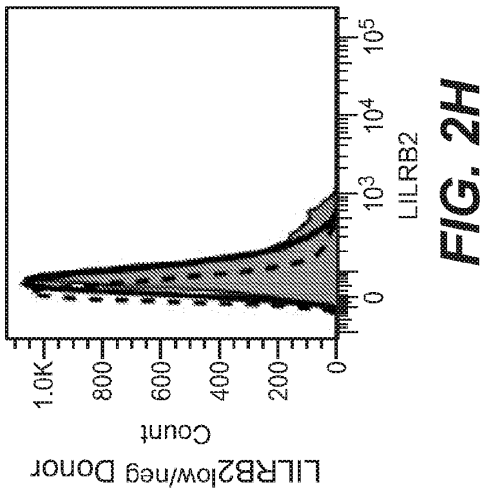


FIG. 2H

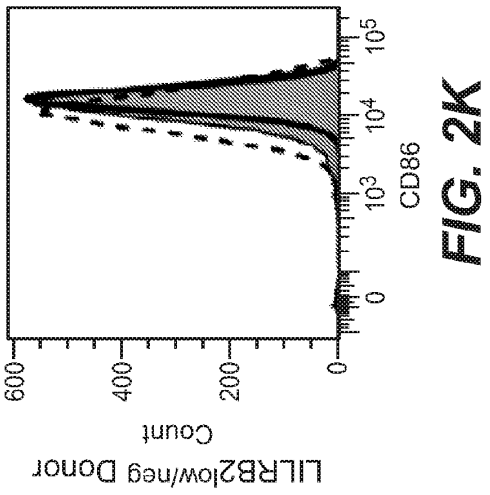


FIG. 2K

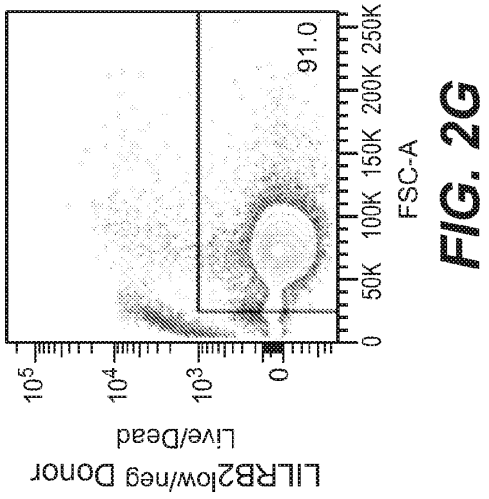


FIG. 2G

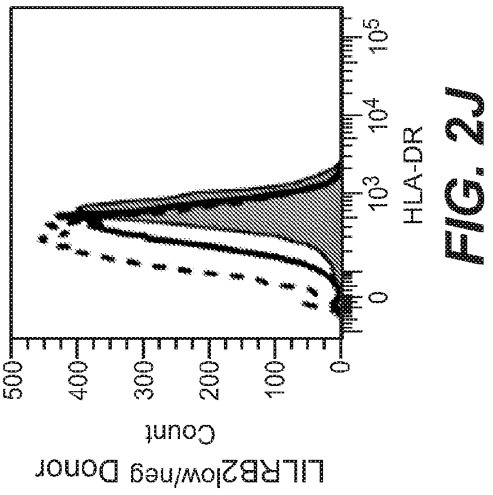


FIG. 2J

FIG. 3A

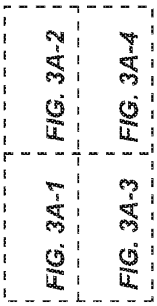


FIG. 3A-1

Reference	Hybridoma clone isotype	LILRB1 CHOs binding (fold over iso)	LILRB2 CHOs binding (fold over iso)	LILRB3 CHOs binding (fold over iso)	LILRB4 CHOs binding (fold over iso)	LILRB5 CHOs binding (fold over iso)	LILRA1 CHOs binding (fold over iso)
J-01	mG1	0.96	19.95	2.49	0.87	1.23	0.90
J-02	mG1	1.03	12.18	1.00	1.00	1.09	0.98
J-03	mG2b	0.94	30.14	0.97	1.02	1.00	0.89
J-04	mG2b	0.95	33.80	0.90	0.83	1.08	0.88
J-05	mG2b	0.95	25.09	0.91	0.76	1.03	0.87
J-06	mG1	0.83	9.58	0.89	0.83	1.00	1.42
J-07	mG2b	0.97	38.66	0.93	0.91	1.29	0.96
J-08	mG1	1.00	25.19	1.03	0.98	1.40	1.01
J-09	mG1	0.96	13.19	1.01	0.90	1.18	1.06
J-10	mG1	1.04	19.03	1.22	0.94	1.36	1.13
J-11	mG2b	1.07	3.49	1.09	1.03	1.22	-1.63
J-12	mG2a	0.99	1.25	0.99	0.99	0.98	1.28
J-13	mG1	0.86	14.40	0.90	0.84	1.01	0.89
J-14	mG1	0.92	25.97	0.92	1.01	1.03	0.94
J-15	mG2b	1.00	28.06	1.02	0.95	1.24	1.17
J-16	rG1	1.03	3.75	1.11	1.01	1.10	611.88
J-17	mG1	1.05	3.68	0.99	1.00	1.03	7.31

FIG. 3A-2

LILRA2 CHOs binding (fold over iso)	LILRA3 CHOs binding (fold over iso)	LILRA4 CHOs binding (fold over iso)	LILRA5 CHOs binding (fold over iso)	LILRA6 CHOs binding (fold over iso)
1.34	1.06	1.90	0.77	1.23
1.34	1.08	1.63	1.03	1.14
1.58	1.05	2.01	0.96	1.23
1.62	0.93	2.07	0.74	1.30
1.34	0.90	1.69	0.82	1.23
1.09	1.04	1.85	0.73	1.28
1.57	1.02	1.39	0.98	1.09
1.64	1.03	0.28	1.06	1.08
1.28	1.03	1.32	0.91	0.90
1.49	1.10	1.00	0.99	0.19
-2.52	1.02	-1.27	1.34	1.00
1.24	1.23	0.20	1.12	0.41
1.08	0.99	1.93	0.76	1.19
1.42	1.01	1.46	0.99	1.17
1.86	1.17	0.43	1.19	0.92
-31.56	182.92	-35.47	3.09	0.62
-1.05	1.35	-36.53	0.82	0.94

J-18	rG1	0.98	1.23	0.81	0.96	0.97	-12.44
J-19	rG1	1.05	3.78	1.09	1.03	1.19	-3.31
J-20	rG1	1.02	3.43	1.00	0.99	1.03	375.00
J-21	mG2a	1.08	2.50	1.22	1.10	1.06	13.94
J-22	mG1	1.05	1.46	1.01	0.97	1.00	-19.25
J-23	mG2b	0.99	1.15	1.36	0.99	0.94	11.00
J-24	mG1	1.06	1.01	1.00	0.99	0.95	22.44
J-25	mG1	0.98	1.57	1.06	0.99	0.96	-6.31
Isotype		1.00	1.00	1.00	1.00	1.00	1.00
Total screened		25	25	25	25	25	25
Hit cut-off		2	2	2	2	2	2
Total hits		0	18	1	0	0	6
% hit		0.0	72.0	4.0	0.0	0.0	24.0

FIG. 3A-3

1.91	0.45	2.67	-1.93	-0.64
-0.51	0.97	-26.80	-0.62	1.07
3.12	0.18	19.73	-3.65	-0.08
-1.26	1.46	-26.33	1.63	1.21
3.03	0.51	16.00	-1.05	-0.20
0.34	1.33	-16.13	1.33	0.70
0.04	1.36	-17.67	0.59	1.19
1.85	0.51	29.73	-1.33	0.26
1.00	1.00	1.00	1.00	1.00
25	25	25	25	25
2	2	2	2	2
2	1	6	1	0
8.0	4.0	24.0	4.0	0.0

FIG. 3A-4

FIG. 3B

FIG. 3B-1 FIG. 3B-2

FIG. 3B-3 FIG. 3B-4

FIG. 3B-1

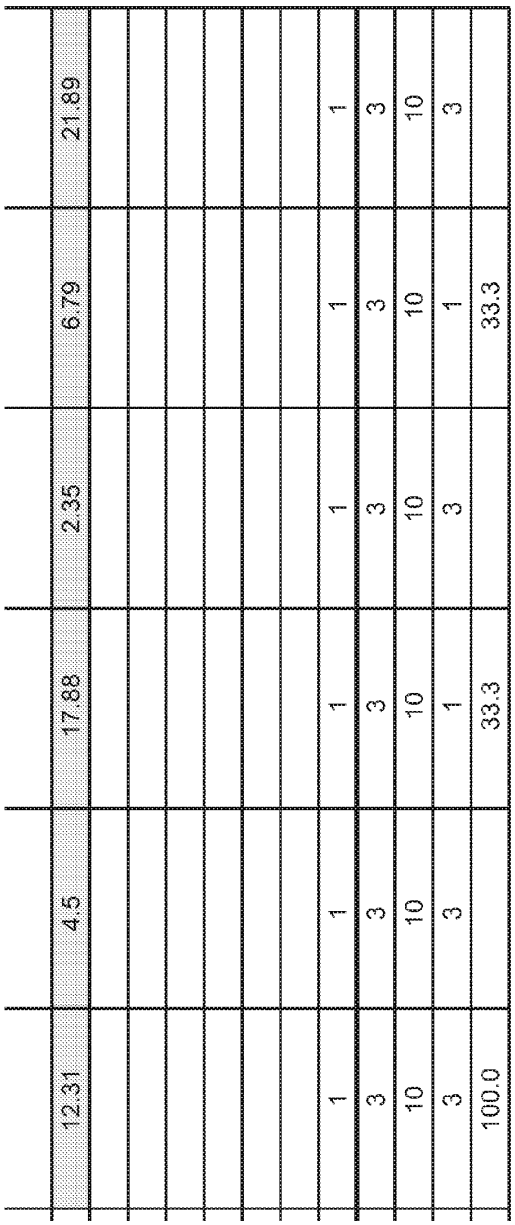
Reference	Hybridoma clone isotype	HLA-G:LILRB2 CHOs blocking (% blocked)	HLA-A2:LILRB2 CHOs blocking (% blocked)	TNFa production (fold over LPS alone)	IL-6 production (fold over LPS alone)	IL-10 production (fold over LPS alone)	CCL2 production (fold over LPS alone)
J-01	mG1	-40.25	15.12	3.86	2.55	0.78	0.88
J-02	mG1	50.41	43.21	1.58	1.38	0.79	0.79
J-03	mG2b	-156.17	-208.49	1.27	1.10	0.97	0.95
J-04	mG2b	-255.13	-319.42	1.18	1.36	0.95	1.00
J-05	mG2b	-21.97	15.16	1.16	1.00	1.01	1.02
J-06	mG1	-62.70	-59.10	0.56	1.10	0.92	0.84
J-07	mG2b	44.29	70.93	2.66	1.58	0.91	0.95
J-08	mG1	-186.51	-177.77	3.63	2.64	0.75	0.89
J-09	mG1	-13.66	2.46	3.32	1.68	0.90	0.92
J-10	mG1	-73.72	-34.77	2.44	1.97	1.01	1.01
J-11	mG2b	99.86	94.44	7.61	3.06	0.81	0.96
J-12	mG2a	-7.16	-10.40	0.31	0.87	0.89	0.94
J-13	mG1	-61.85	-61.85	n/a	n/a	n/a	n/a
J-14	mG1	-160.30	-204.08	0.91	2.97	0.75	0.84
J-15	mG2b	-243.96	-288.39	1.07	1.29	0.92	0.93
J-16	rG1	96.77	94.80	2.49	1.41	1.09	1.31
J-17	mG1	96.56	93.44	8.12	2.57	0.89	1.85

FIG. 3B-2

Human Monocytes binding (fold over iso)	Human Neutrophils binding (fold over iso)	Cyno Monocytes binding (fold over iso)	Cyno Neutrophils binding (fold over iso)	Rhesus Monocytes binding (fold over iso)	Rhesus Neutrophils binding (fold over iso)
8.54	2.89	0.71	0.94	0.88	0.64
11.35	4.55	0.92	0.87	1.41	1.44

J-18	rG1	-15.14	16.04	0.92	1.08	0.99	1.00
J-19	rG1	97.01	95.32	8.90	2.72	0.80	1.69
J-20	rG1	-188.75	11.03	9.02	2.58	0.67	1.64
J-21	mG2a	95.61	56.57	5.46	2.23	1.00	1.48
J-22	mG1	-24.90	21.76	2.62	1.39	1.10	1.24
J-23	mG2b	58.97	16.27	2.07	1.14	1.03	1.12
J-24	mG1	0.08	6.30	1.16	0.84	0.83	0.87
J-25	mG1	-139.70	7.12	1.82	1.57	1.20	1.29
Isotype		-8.00	-12.49	0.82	1.08	0.96	1.02
Total screened		25	25	24	24	24	24
Hit cut-off		50	50	1.5	1.5	0.85	0.85
Total hits		7	6	15	12	8	3
% hit		28.0	24.0	62.5	50.0	33.3	12.5

FIG. 3B-3



12.31	4.5	17.88	2.35	6.79	21.89
1	1	1	1	1	1
3	3	3	3	3	3
10	10	10	10	10	10
3	3	1	3	1	3
100.0		33.3		33.3	

FIG. 3B-4

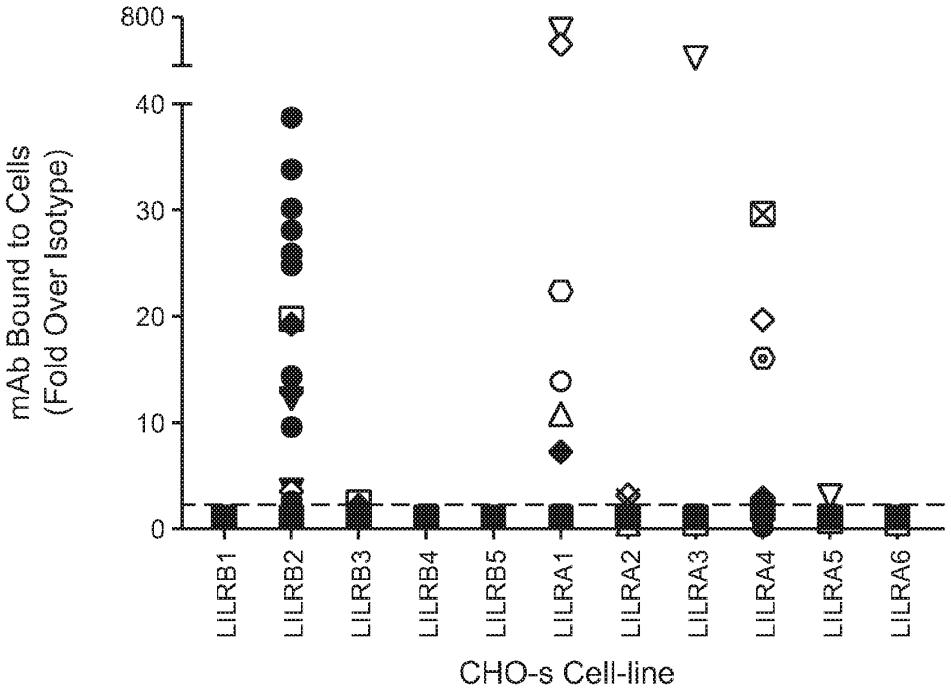

800
40
30
20
10
0
mAb Bound to Cells
(Fold Over Isotype)
LILRB1
LILRB2
LILRB3
LILRB4
LILRB5
LILRA1
LILRA2
LILRA3
LILRA4
LILRA5
LILRA6
CHO-s Cell-line

FIG. 4

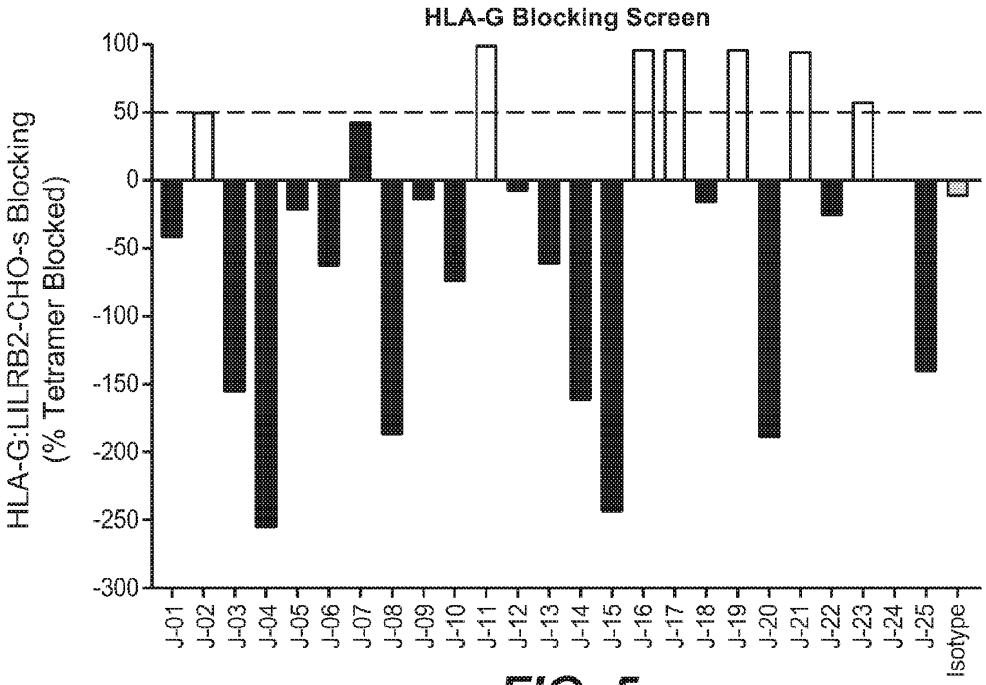

HLA-G Blocking Screen
HLA-G:LILRB2-CHO-s Blocking
(% Tetramer Blocked)
100
50
0
-50
-100
-150
-200
-250
-300
J-01
J-02
J-03
J-04
J-05
J-06
J-07
J-08
J-09
J-10
J-11
J-12
J-13
J-14
J-15
J-16
J-17
J-18
J-19
J-20
J-21
J-22
J-23
J-24
J-25
Isotype

FIG. 5

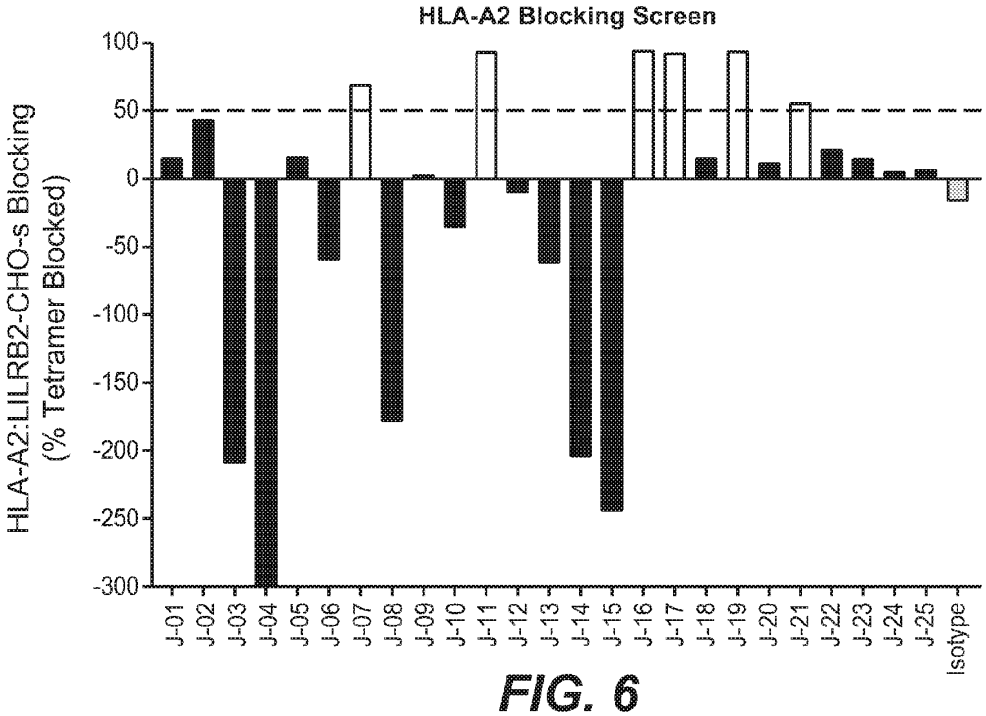

HLA-A2 Blocking Screen
HLA-A2:LILRB2-CHO-s Blocking
(% Tetramer Blocked)
100
50
0
-50
-100
-150
-200
-250
-300
J-01
J-02
J-03
J-04
J-05
J-06
J-07
J-08
J-09
J-10
J-11
J-12
J-13
J-14
J-15
J-16
J-17
J-18
J-19
J-20
J-21
J-22
J-23
J-24
J-25
Isotype

FIG. 6

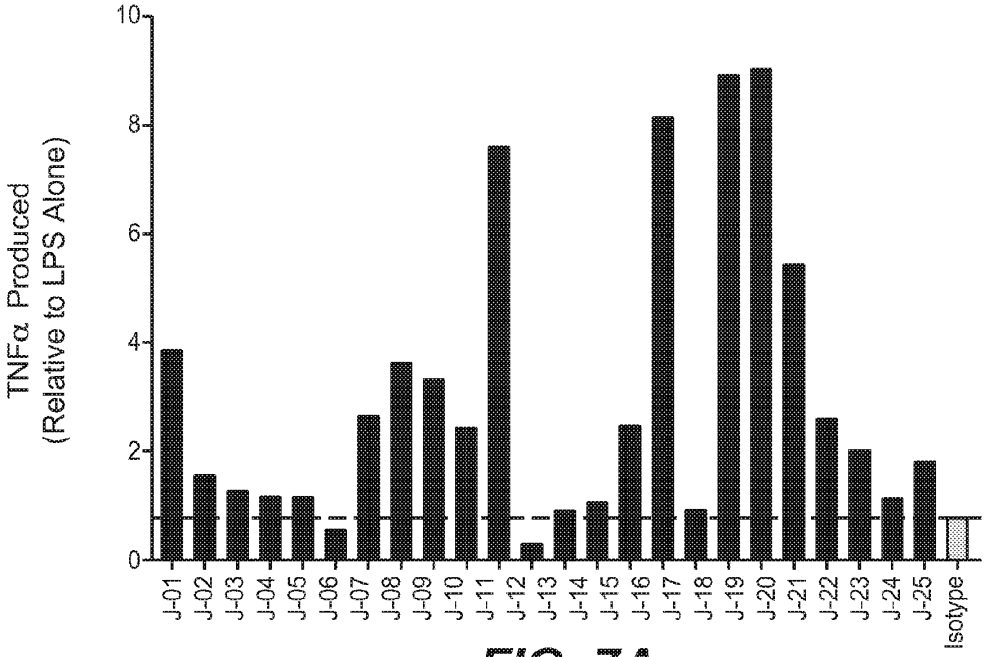

TNFα Produced
(Relative to LPS Alone)
0
2
4
6
8
10
J-01
J-02
J-03
J-04
J-05
J-06
J-07
J-08
J-09
J-10
J-11
J-12
J-13
J-14
J-15
J-16
J-17
J-18
J-19
J-20
J-21
J-22
J-23
J-24
J-25
Isotype

FIG. 7A

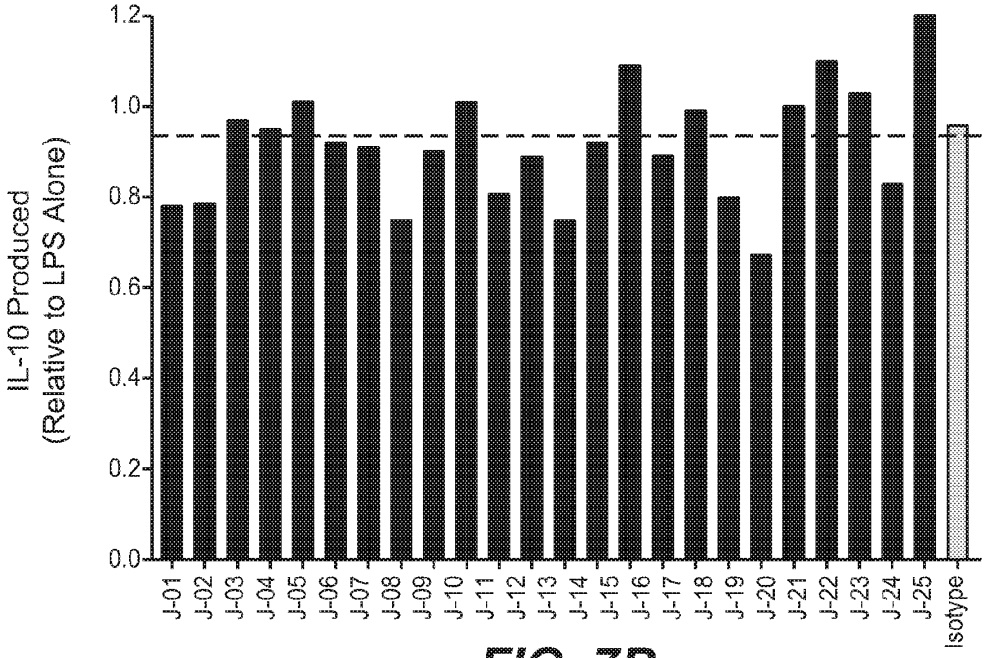

IL-10 Produced
(Relative to LPS Alone)
0.0
0.2
0.4
0.6
0.8
1.0
1.2
J-01
J-02
J-03
J-04
J-05
J-06
J-07
J-08
J-09
J-10
J-11
J-12
J-13
J-14
J-15
J-16
J-17
J-18
J-19
J-20
J-21
J-22
J-23
J-24
J-25
Isotype

FIG. 7B

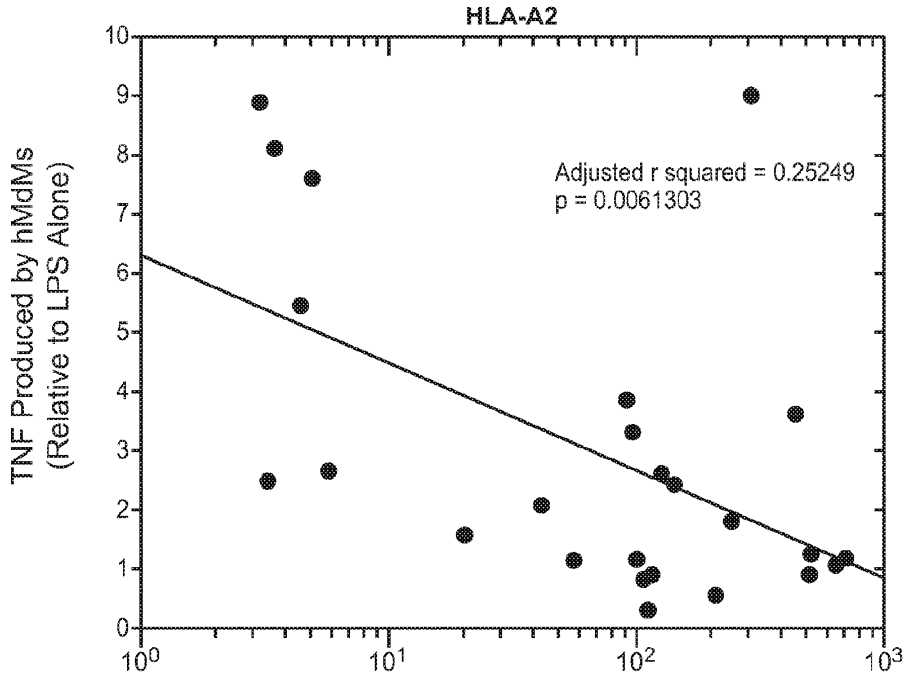

HLA-A2
TNF Produced by hMdMs
(Relative to LPS Alone)
Adjusted r squared = 0.25249
p = 0.0061303
HLA-A2 Bound to hLILRB2 (%)

FIG. 8A

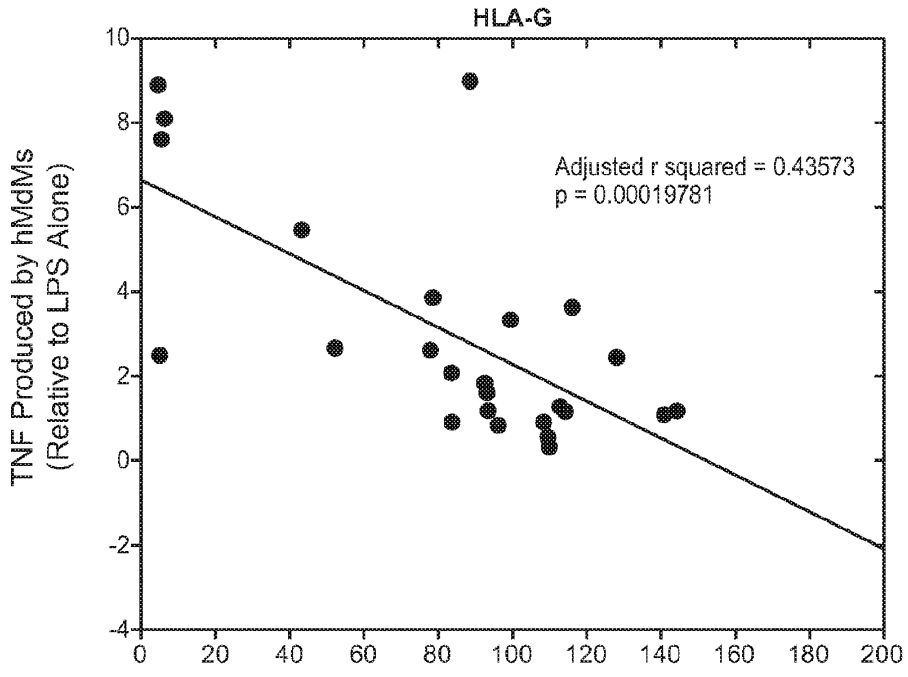

HLA-G
TNF Produced by hMdMs
(Relative to LPS Alone)
Adjusted r squared = 0.43573
p = 0.00019781
HLA-G Bound to hLILRB2 (%)

FIG. 8B

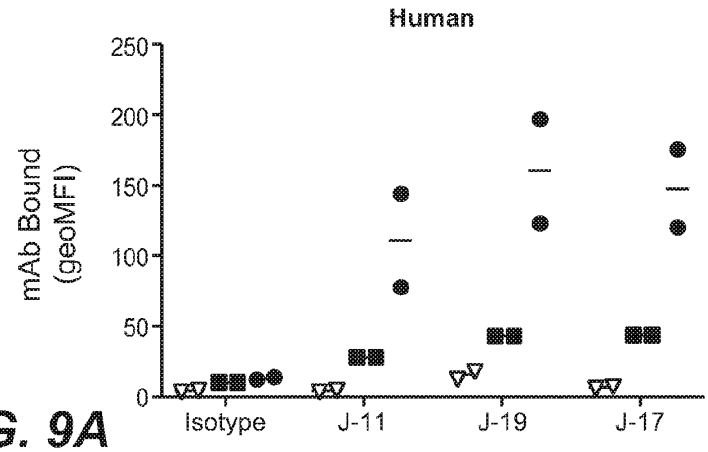


FIG. 9A

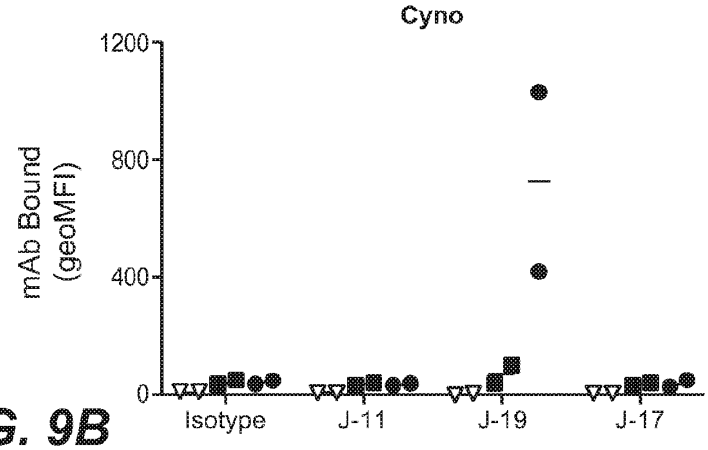


FIG. 9B

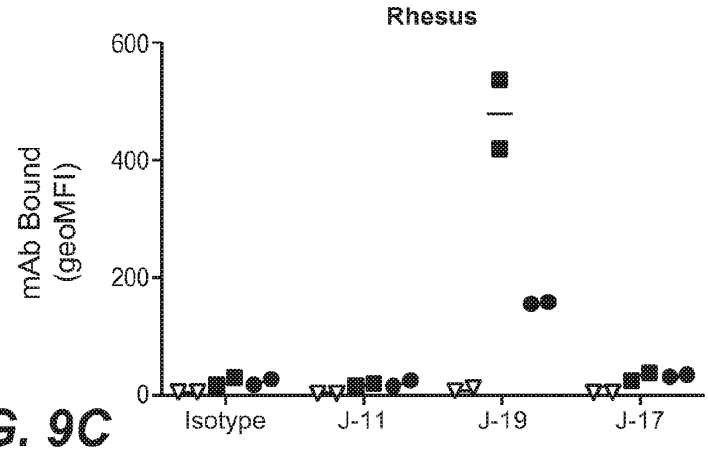


FIG. 9C

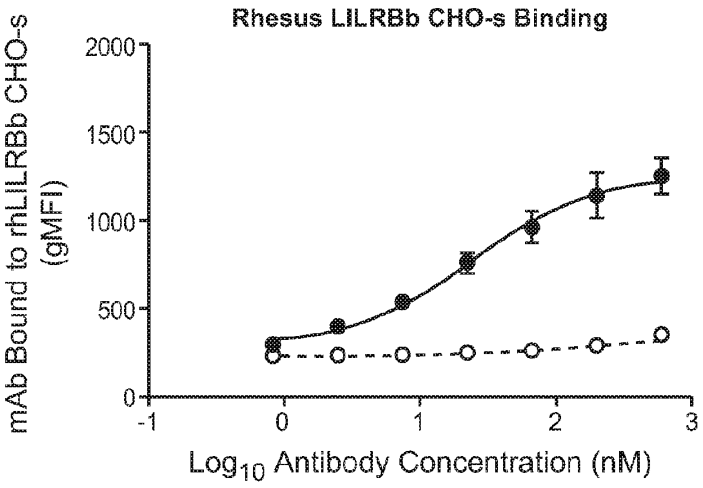


FIG. 10A

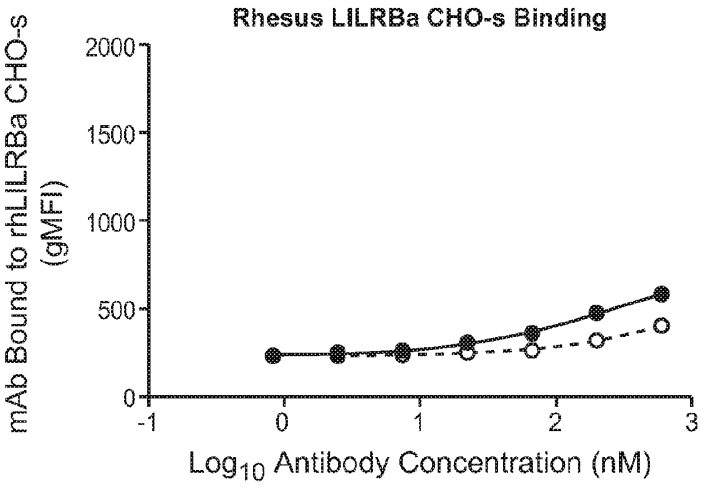


FIG. 10B

mAb	LILRB1 CHOs binding (fold over iso)	LILRB2 CHOs binding (fold over iso)	LILRB3 CHOs binding (fold over iso)	LILRB4 CHOs binding (fold over iso)	LILRB5 CHOs binding (fold over iso)	LILRA1 CHOs binding (fold over iso)	LILRA2 CHOs binding (fold over iso)	LILRA3 CHOs binding (fold over iso)	LILRA4 CHOs binding (fold over iso)	LILRA5 CHOs binding (fold over iso)	LILRA6 CHOs binding (fold over iso)
J-19.h1	0.79	73.25	1.00	1.22	1.01	0.95	0.88	0.97	0.95	1.34	0.98
J-19.h2	0.73	74.45	0.81	0.90	0.76	0.89	0.66	0.83	0.84	0.86	0.74
J-19.h3	0.84	79.40	0.97	1.16	0.95	1.00	0.83	0.92	0.99	1.22	1.03
J-19.h4	0.87	76.50	1.24	2.02	1.27	0.99	0.96	0.99	1.09	2.14	1.27
Isotype	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00

FIG. 11A

mAb	EC50 (nM) hLILRB2 CHOs binding	EC50 (nM) HLA-G: LILRB2 blocking	EC50 (nM) HLA-A2: LILRB2 blocking	EC50 (nM) TNFa production	EC50 (nM) IL-6 production	IC50 (nM) IL-10 production	IC50 (nM) CCL2 production
J-19.h1	0.03204	0.162	0.083	0.076	0.085	0.450	0.005
J-19.h2	0.4467	0.122	0.087	0.120	0.186	0.702	0.011
J-19.h3	0.03248	0.113	0.103	0.087	0.083	0.270	5.902
J-19.h4	0.001749	0.131	0.106	0.084	0.091	0.190	0.010
Isotype	N/A	N/A	N/A	N/A	N/A	N/A	N/A

FIG. 11B

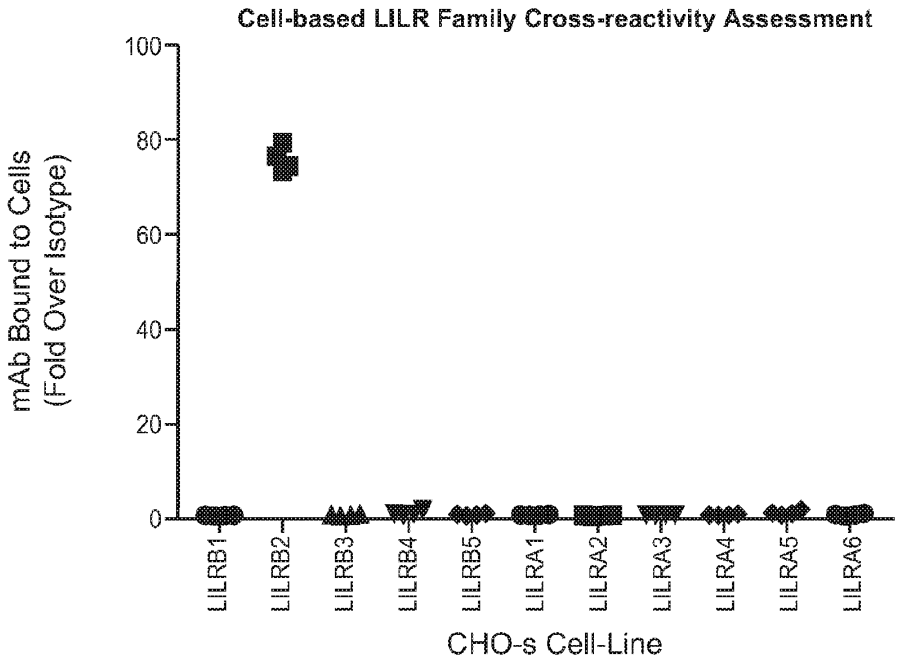

Cell-based LILR Family Cross-reactivity Assessment
mAb Bound to Cells
(Fold Over Isotype)
100
80
60
40
20
0
LILRB1
LILRB2
LILRB3
LILRB4
LILRB5
LILRA1
LILRA2
LILRA3
LILRA4
LILRA5
LILRA6
CHO-s Cell-Line

FIG. 12

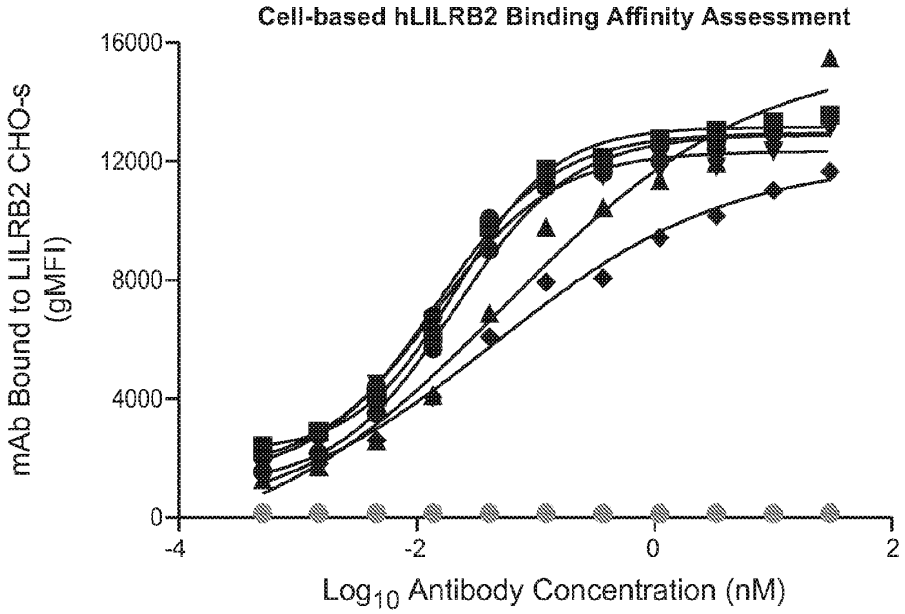

Cell-based hLILRB2 Binding Affinity Assessment
mAb Bound to LILRB2 CHO-s
(gMFI)
16000
12000
8000
4000
0
-4
-2
0
2
Log10 Antibody Concentration (nM)

FIG. 13

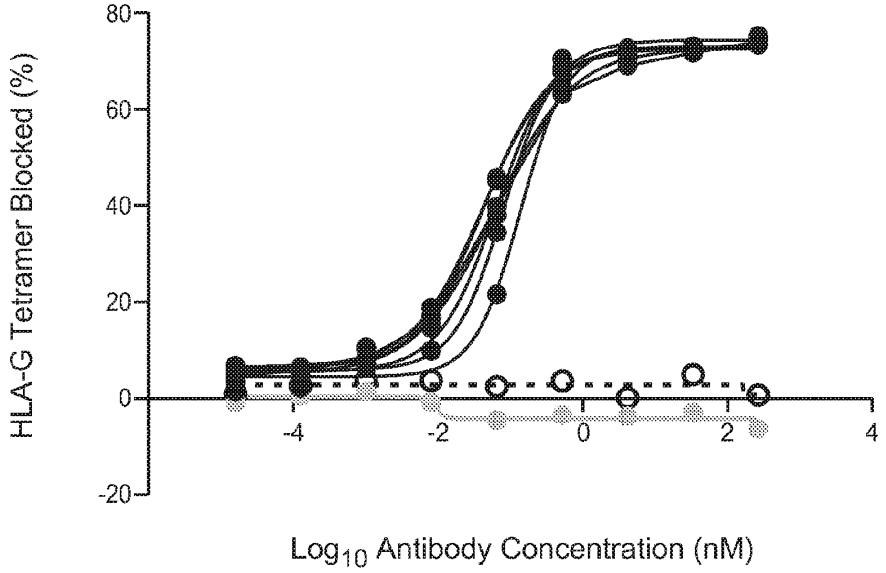

HLA-G Tetramer Blocked (%)
80
60
40
20
0
-20
-4
-2
0
2
4
Log10 Antibody Concentration (nM)

FIG. 14

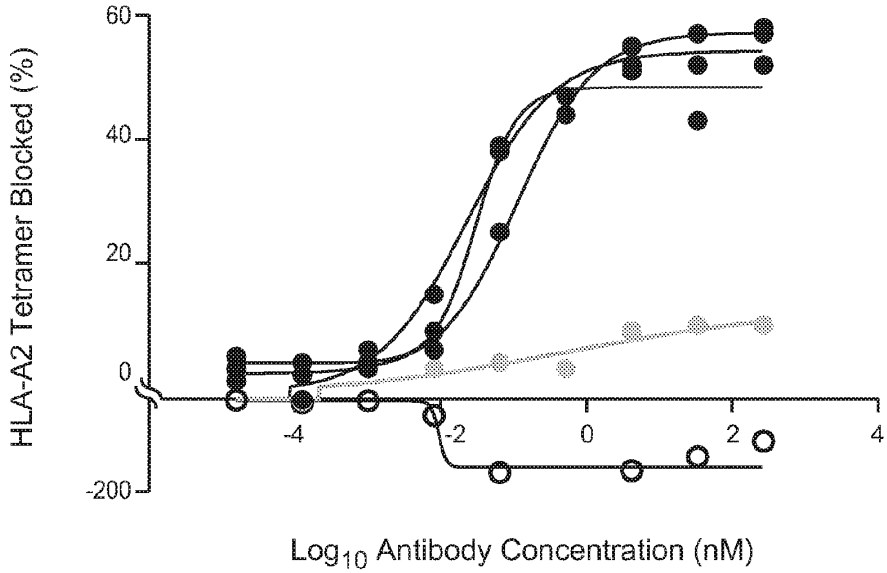

HLA-A2 Tetramer Blocked (%)
60
40
20
0
-200
-4
-2
0
2
4
Log10 Antibody Concentration (nM)

FIG. 15

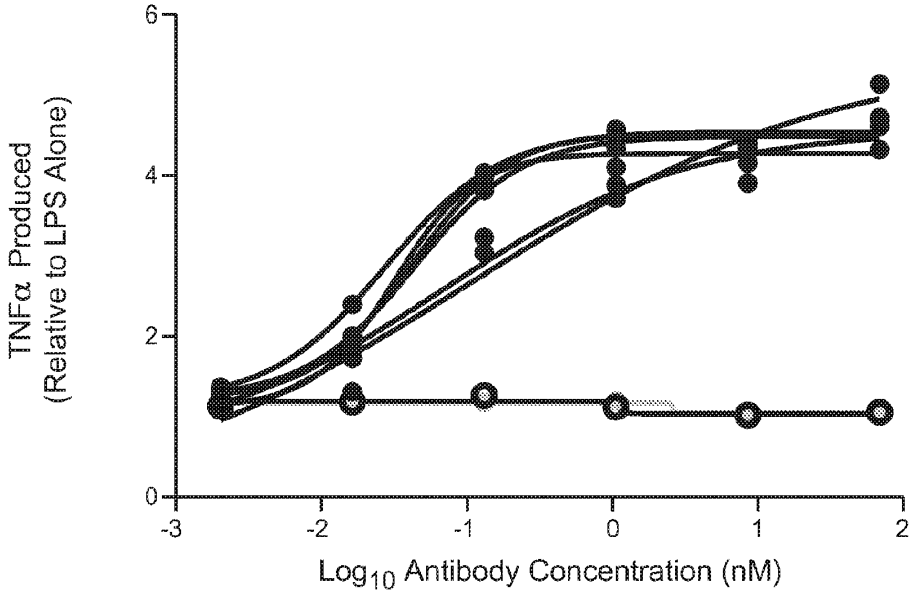


FIG. 16A

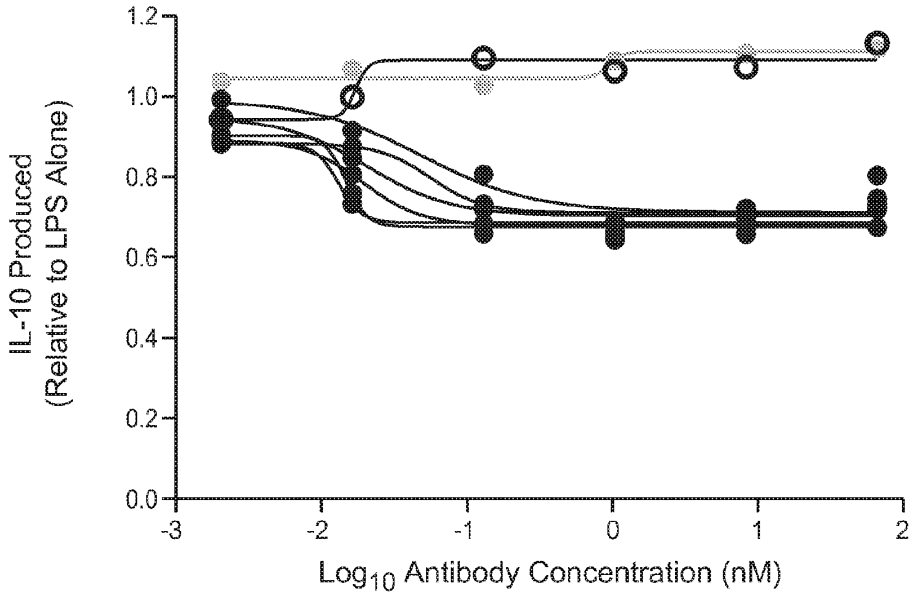


FIG. 16B

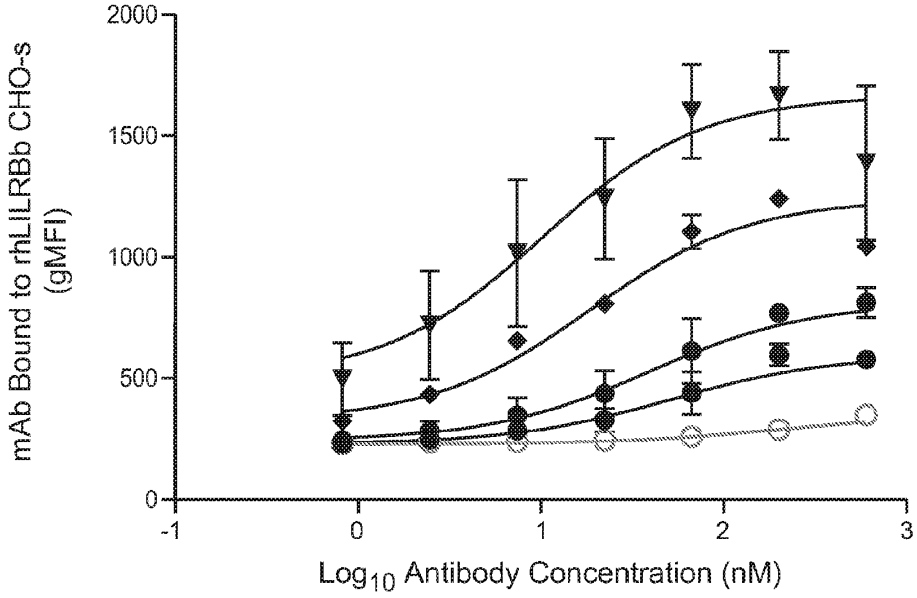


FIG. 17A

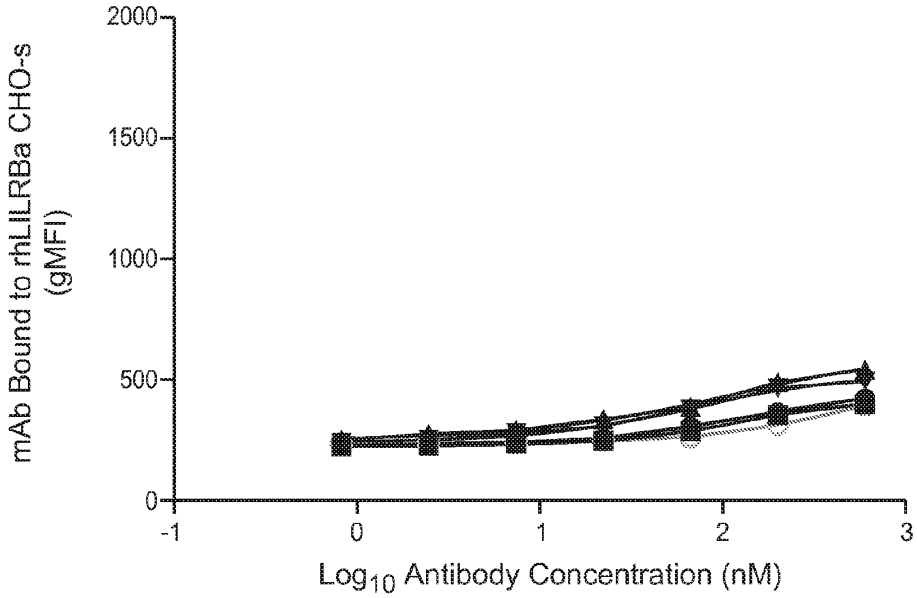


FIG. 17B

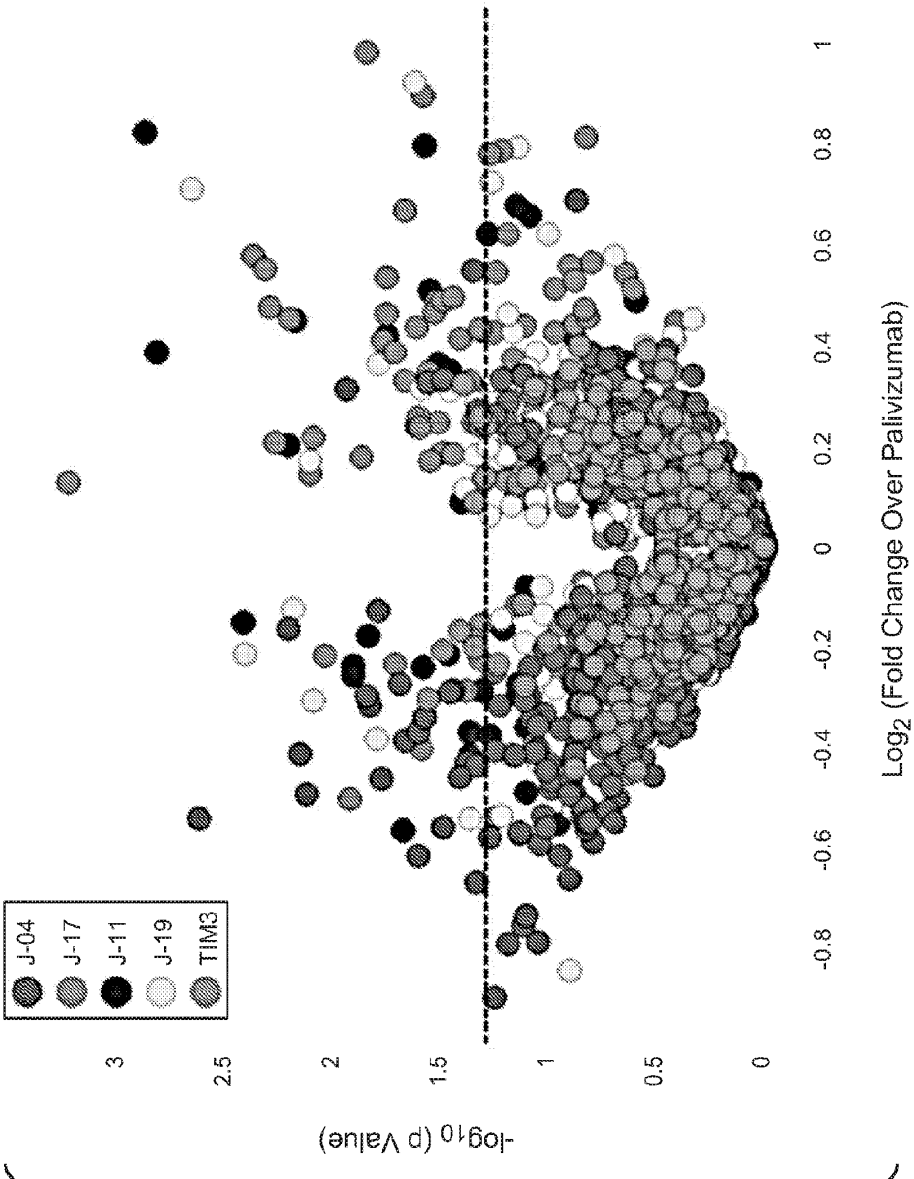

J-04
J-17
J-11
J-19
TIM3
3
2.5
2
1.5
1
0.5
0
-log10 (p Value)
1
0.8
0.6
0.4
0.2
0
-0.2
-0.4
-0.6
-0.8
Log2 (Fold Change Over Palivizumab)

FIG. 18

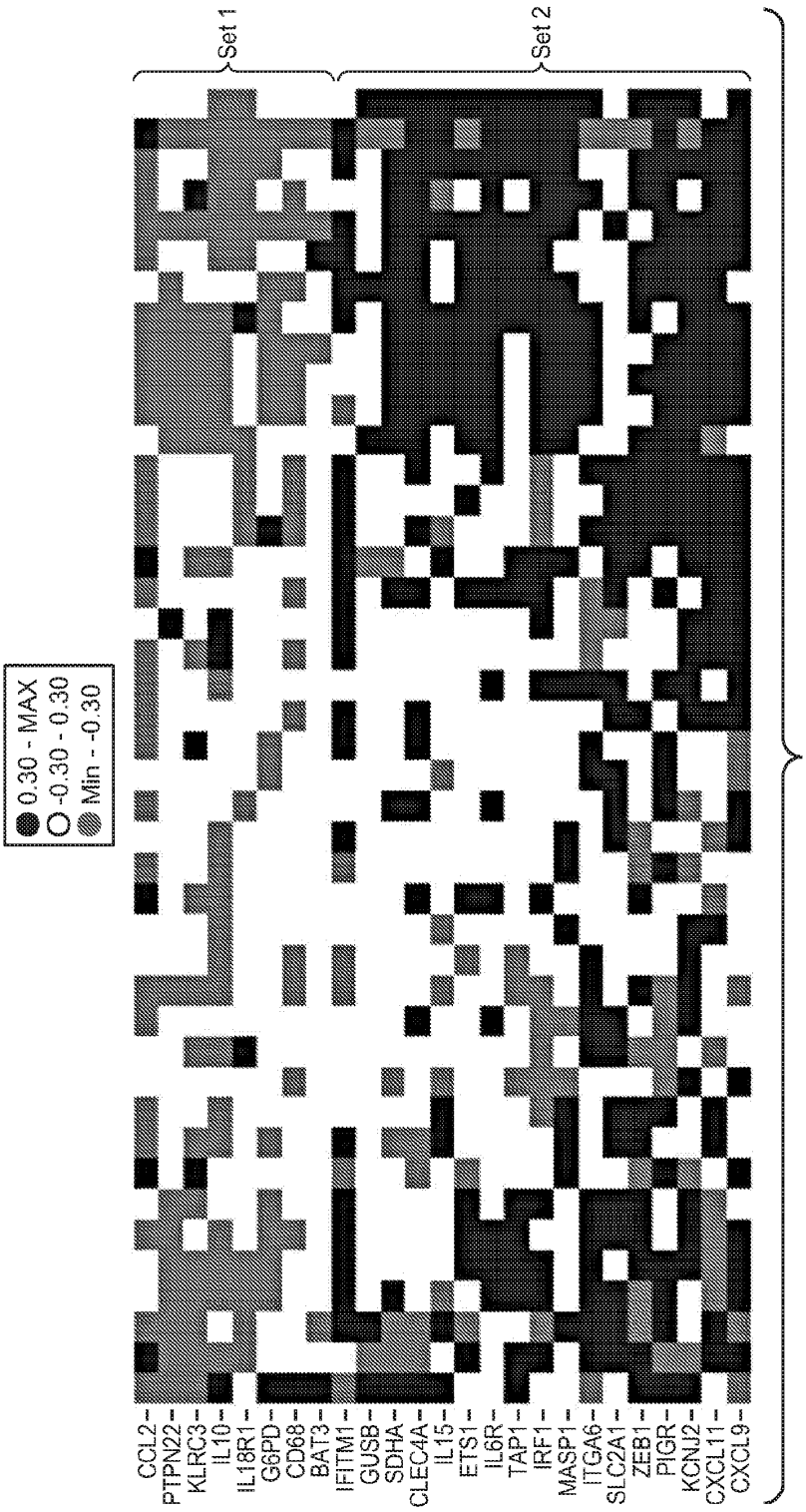

Set 1
Set 2
0.30 - MAX
-0.30 - 0.30
Min - -0.30
CCL2
PTPN22
KLRC3
IL10
IL18R1
G6PD
CD68
BAT3
IFITM1
GUSB
SDHA
CLEC4A
IL15
ETS1
IL6R
TAP1
IRF1
MASP1
ITGA6
SLC2A1
ZEB1
PIGR
KCNJ2
CXCL11
CXCL9

FIG. 19

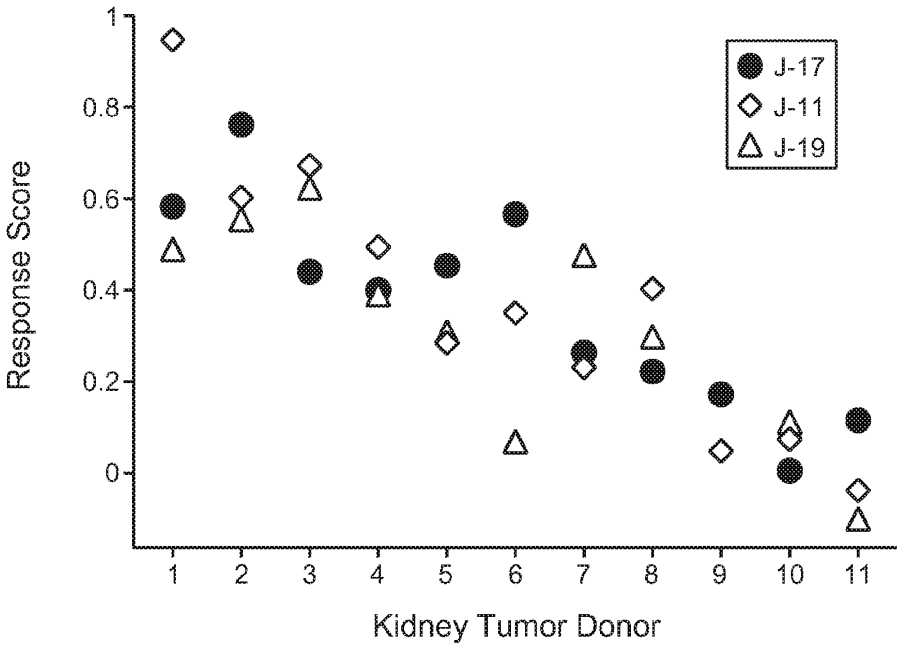

Response Score
1
0.8
0.6
0.4
0.2
0
1
2
3
4
5
6
7
8
9
10
11
Kidney Tumor Donor
J-17
J-11
J-19

FIG. 20

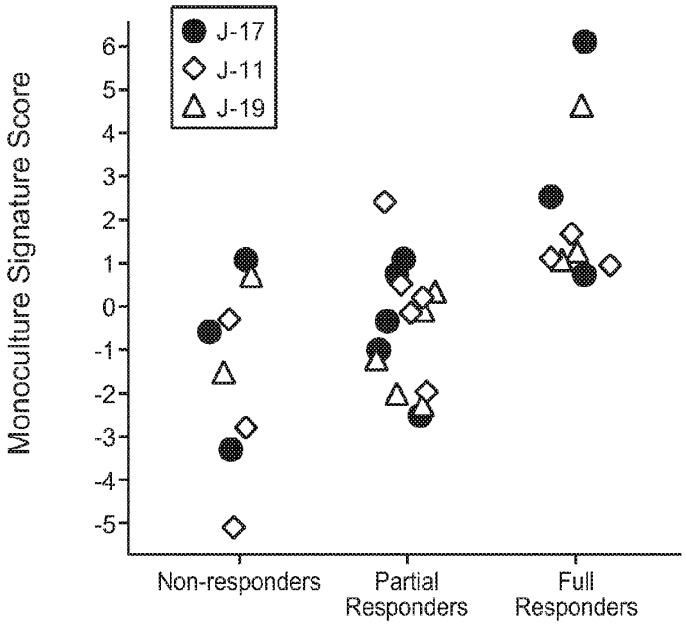


FIG. 21A

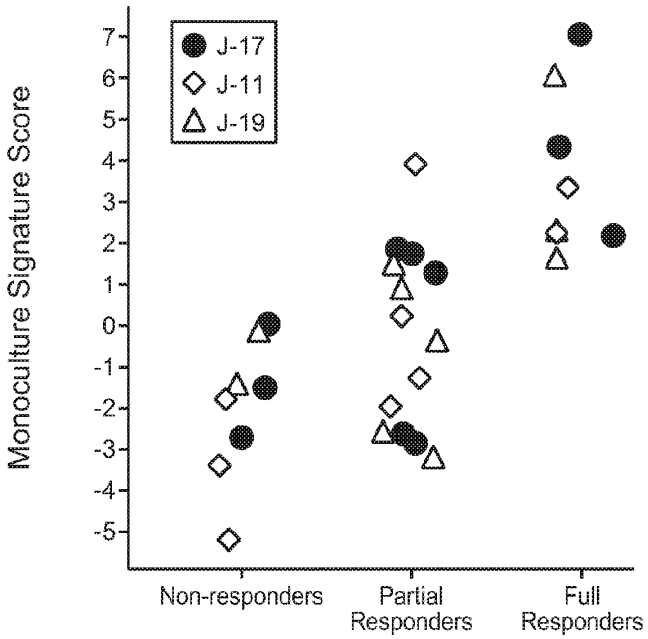


FIG. 21B

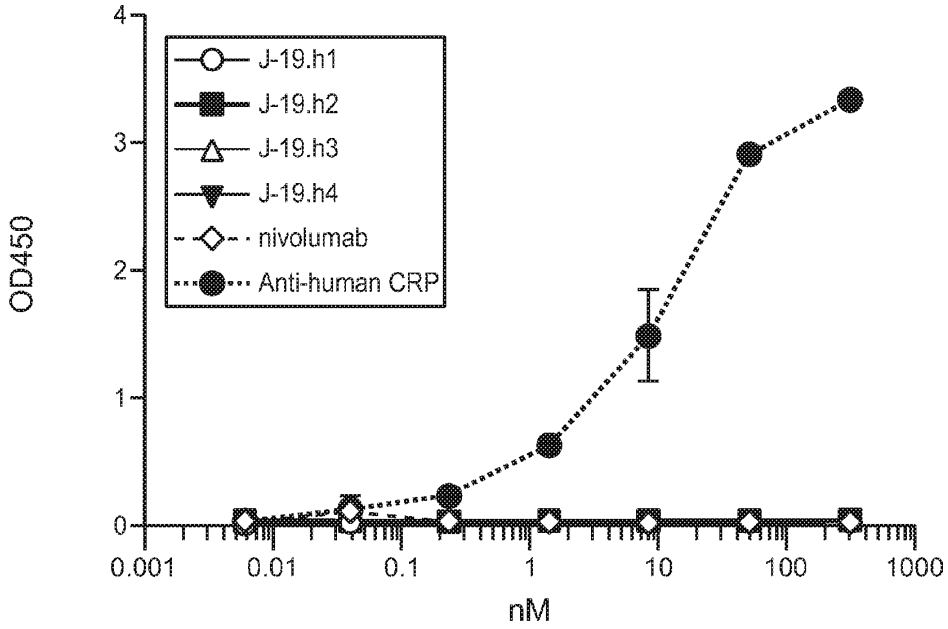

OD450
4
3
2
1
0
J-19.h1
J-19.h2
J-19.h3
J-19.h4
nivolumab
Anti-human CRP
0.001
0.01
0.1
1
10
100
1000
nM

FIG. 22

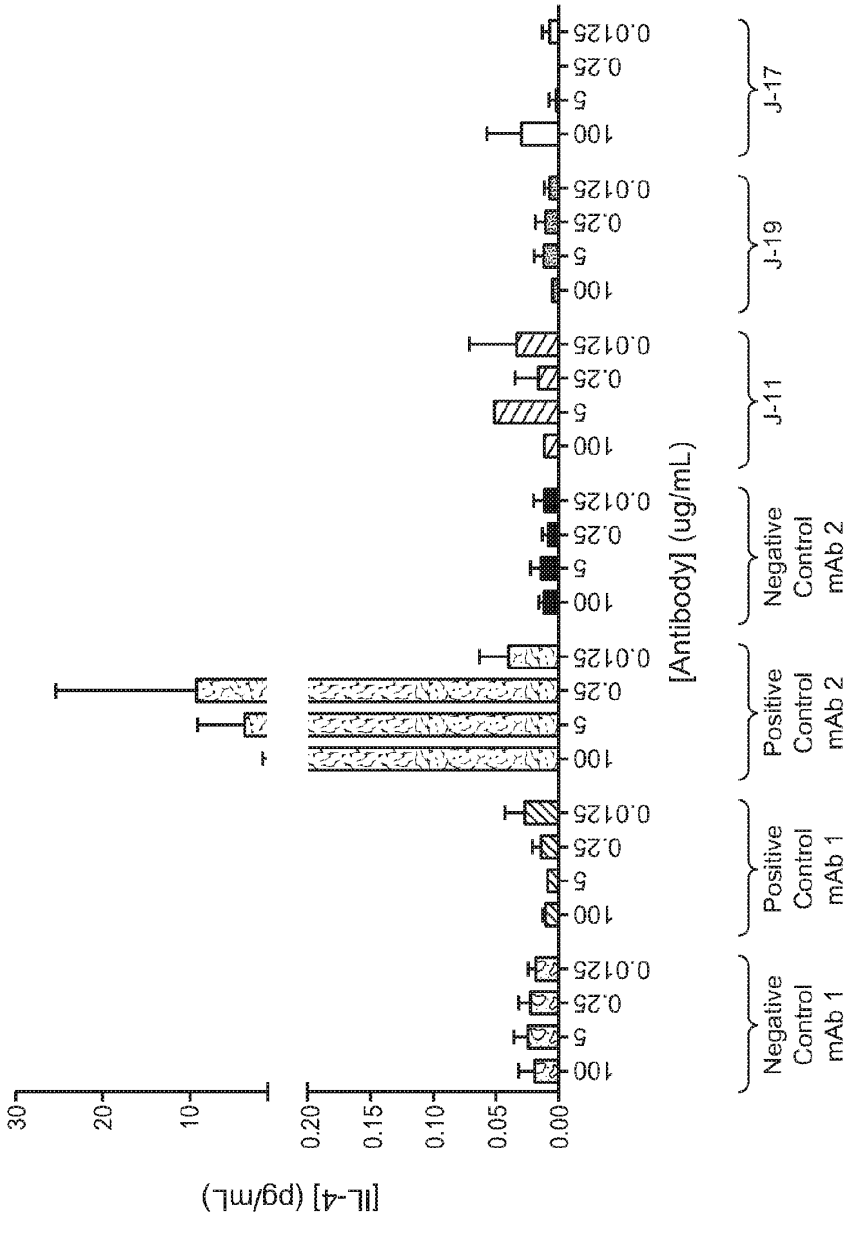

[IL-4] (pg/mL)
30
20
10
0.20
0.15
0.10
0.05
0.00
[Antibody] (ug/mL)
100
5
0.25
0.0125
Negative Control mAb 1
Positive Control mAb 1
Positive Control mAb 2
Negative Control mAb 2
J-11
J-19
J-17

FIG. 23A

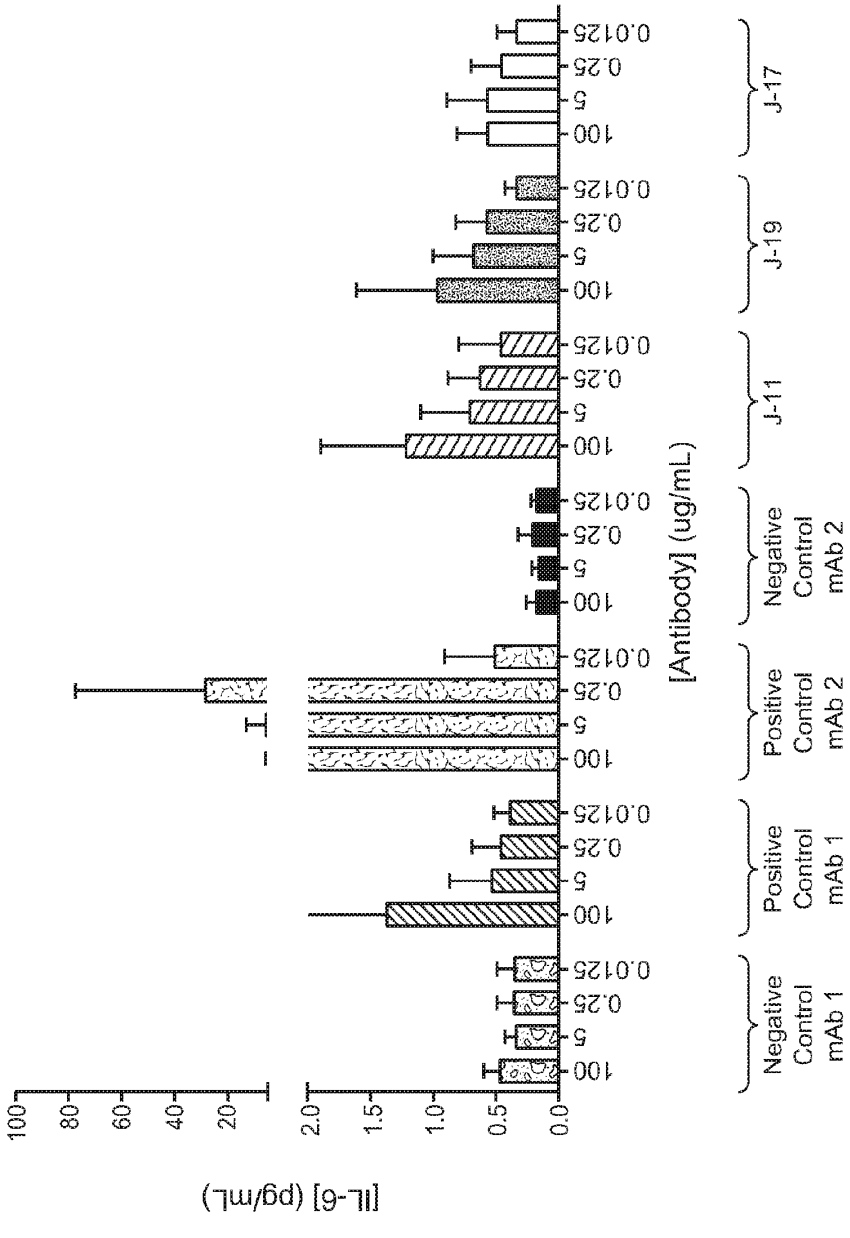

[IL-6] (pg/mL)
100
80
60
40
20
2.0
1.5
1.0
0.5
0.0
[Antibody] (ug/mL)
100
5
0.25
0.0125
Negative Control mAb 1
Positive Control mAb 1
Positive Control mAb 2
Negative Control mAb 2
J-11
J-19
J-17

FIG. 23B

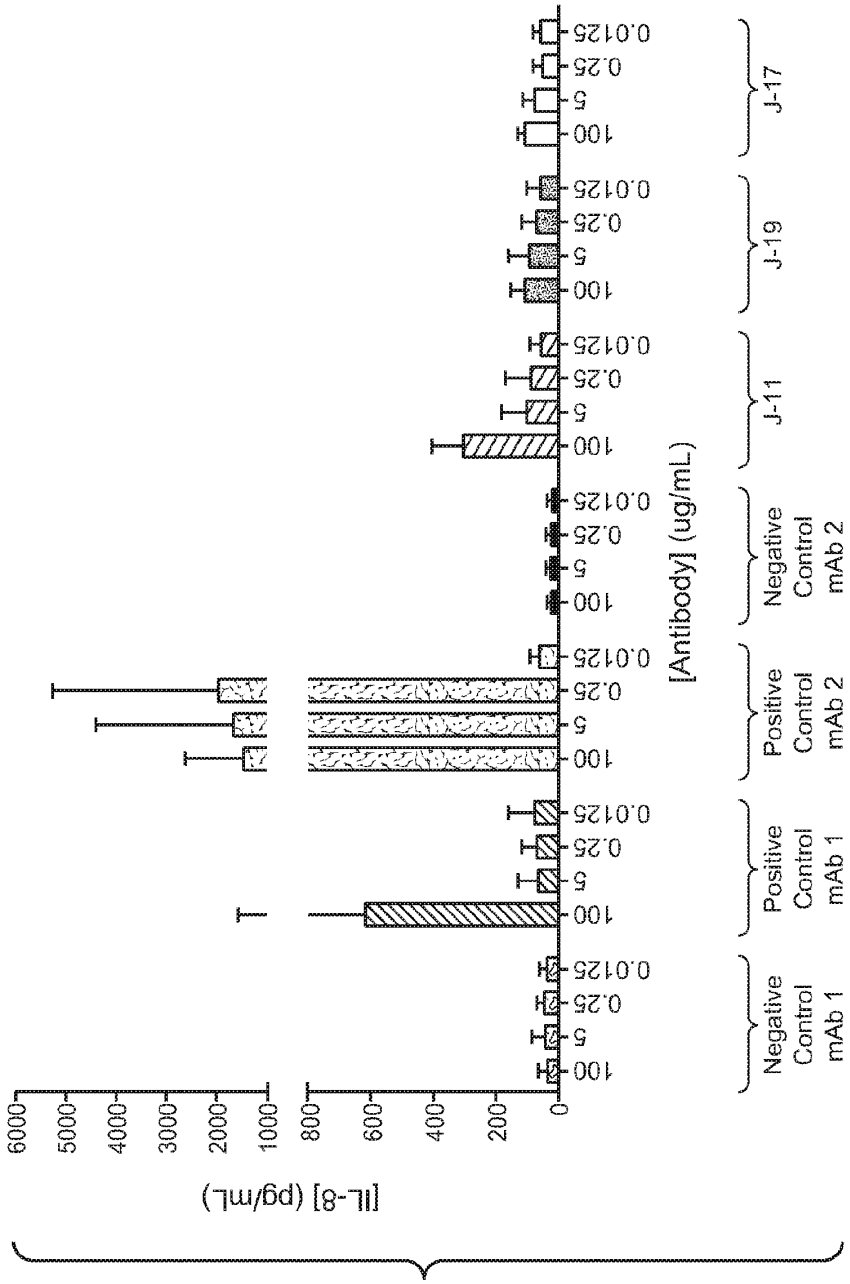

[IL-8] (pg/mL)
6000
5000
4000
3000
2000
1000
800
600
400
200
0
[Antibody] (ug/mL)
100
5
0.25
0.0125
Negative Control mAb 1
Positive Control mAb 1
Positive Control mAb 2
Negative Control mAb 2
J-11
J-19
J-17

FIG. 23C

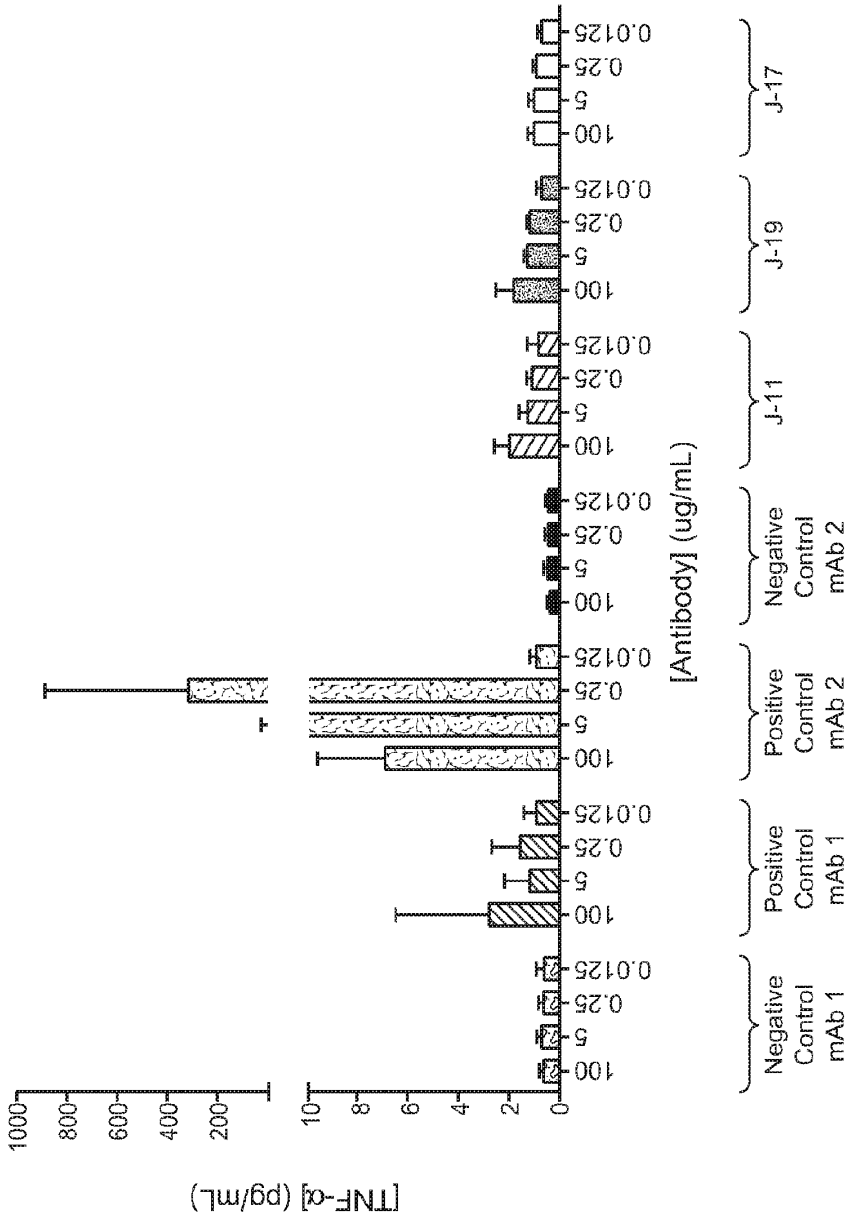

[TNF-α] (pg/mL)
1000
800
600
400
200
10
8
6
4
2
0
[Antibody] (ug/mL)
100
5
0.25
0.0125
Negative Control mAb 1
Positive Control mAb 1
Positive Control mAb 2
Negative Control mAb 2
J-11
J-19
J-17

FIG. 23D

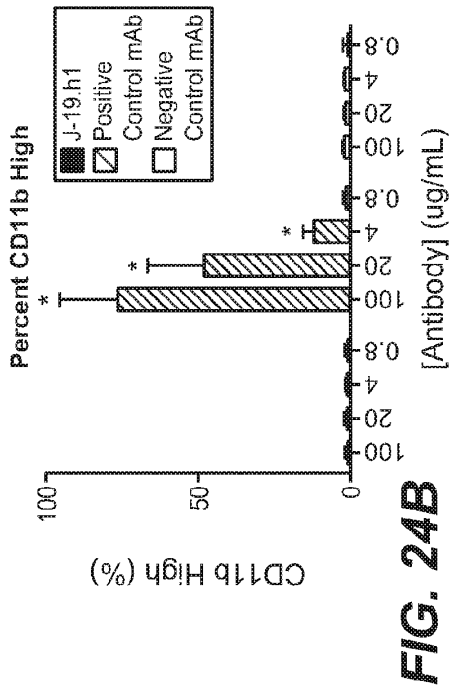


FIG. 24B

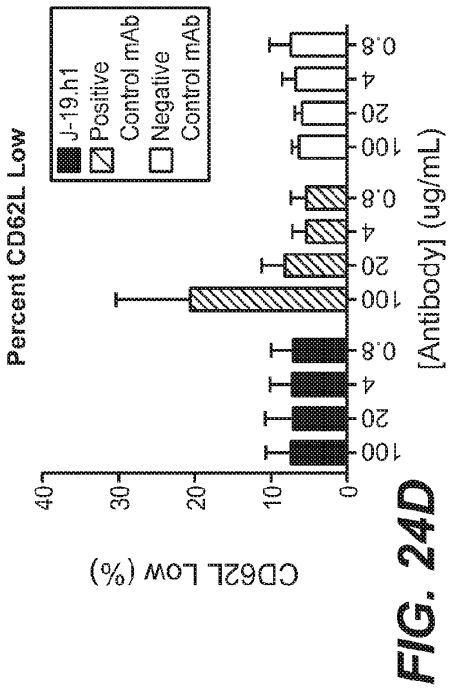


FIG. 24D

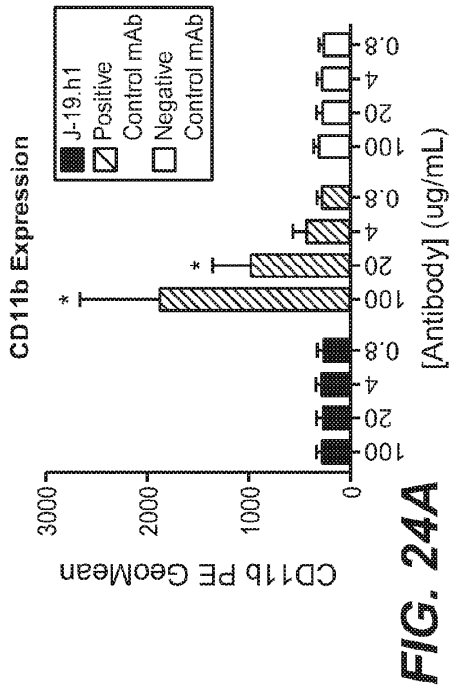


FIG. 24A

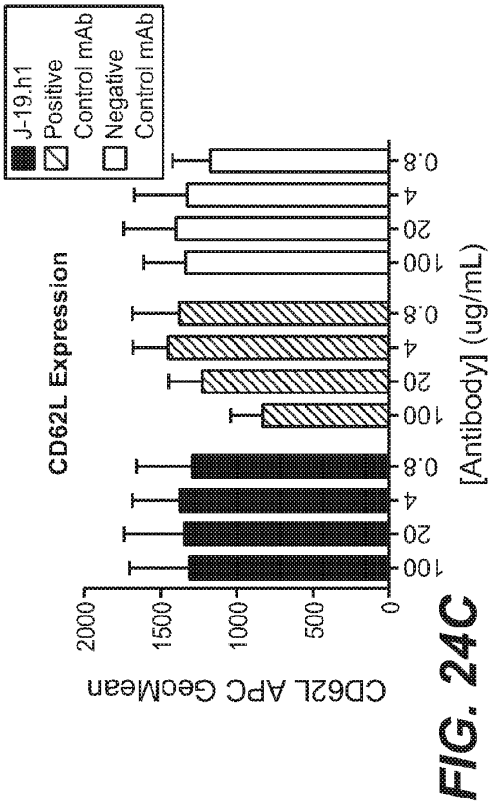


FIG. 24C

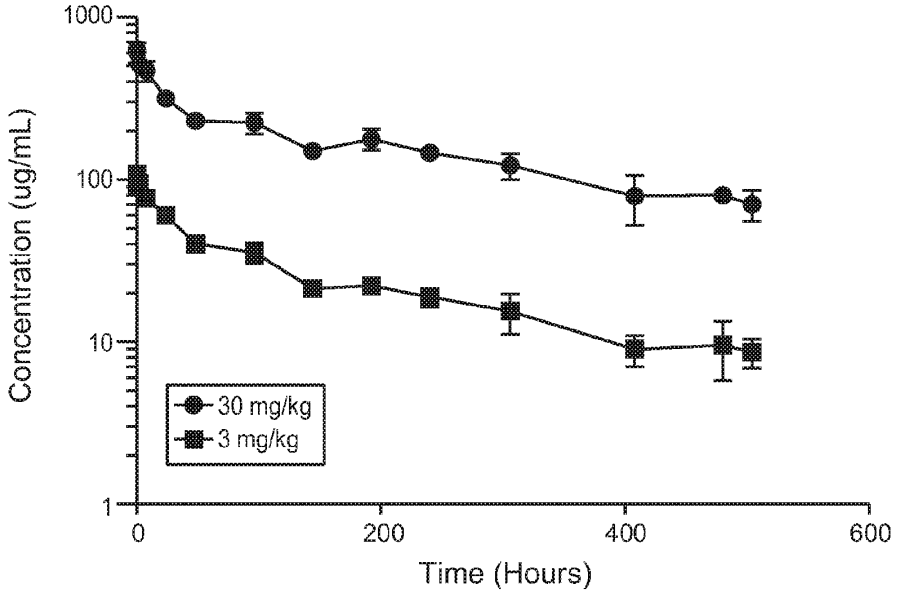

1000
100
10
1
Concentration (ug/mL)
30 mg/kg
3 mg/kg
0
200
400
600
Time (Hours)

FIG. 25

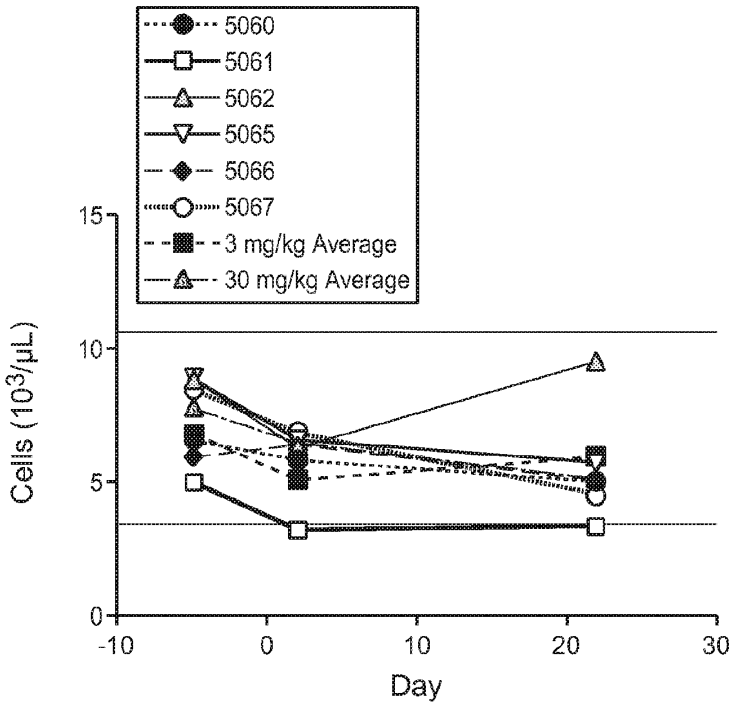


FIG. 26A

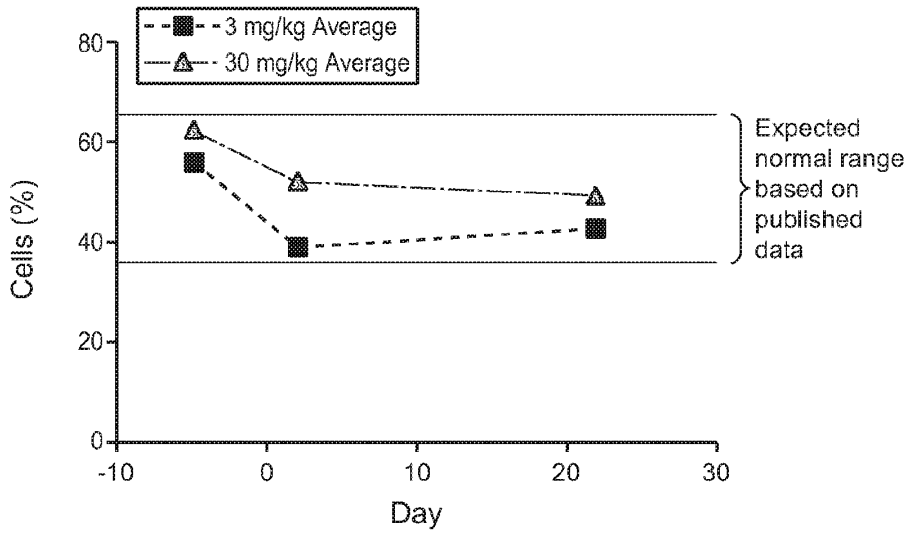


FIG. 26B

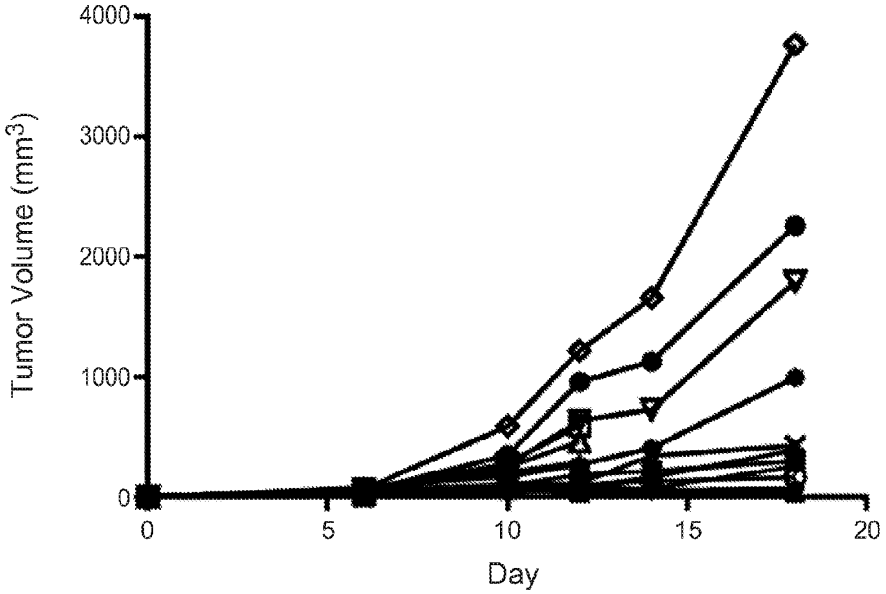


FIG. 27A

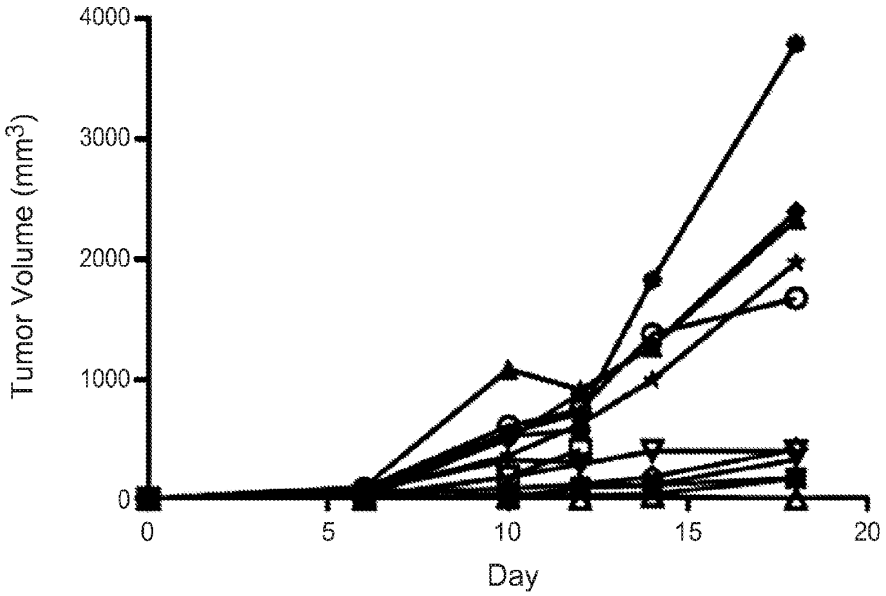


FIG. 27B

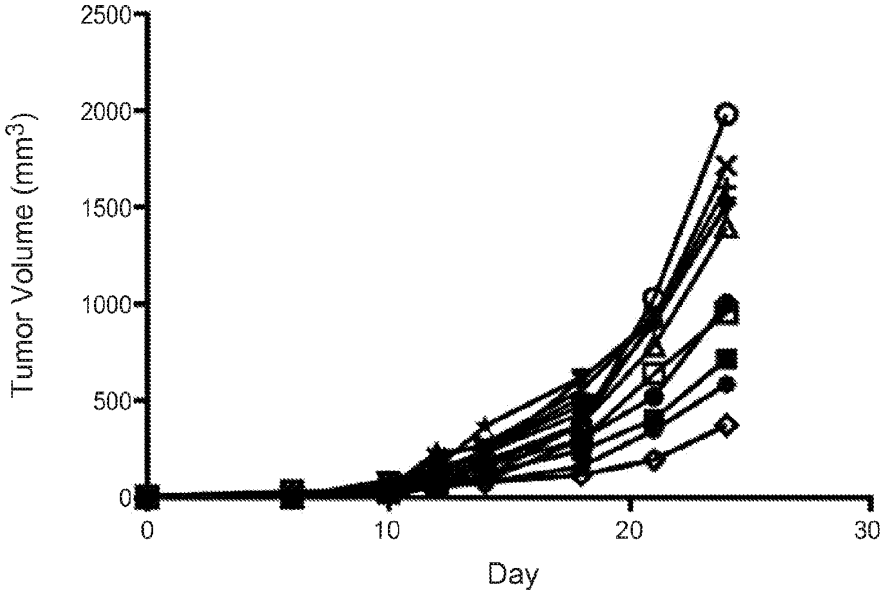


FIG. 28A

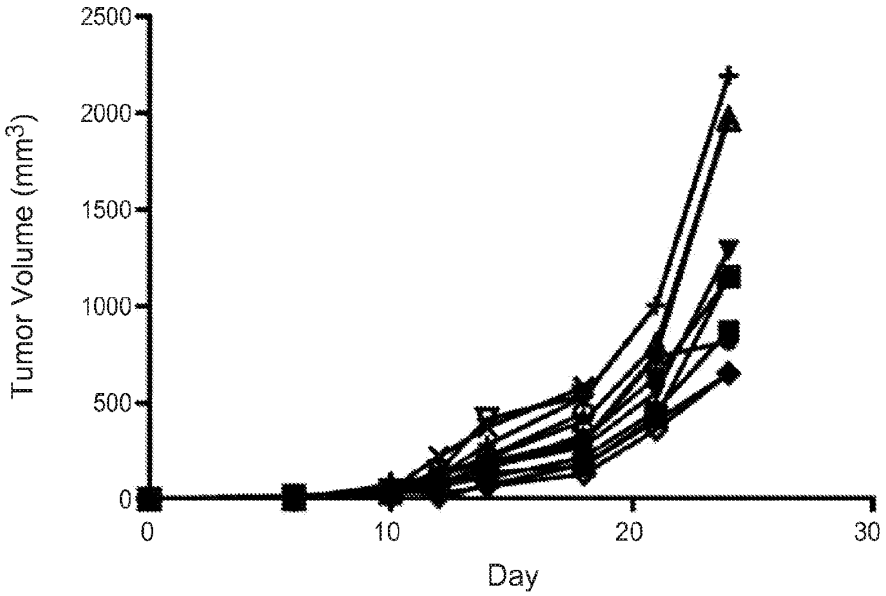


FIG. 28B

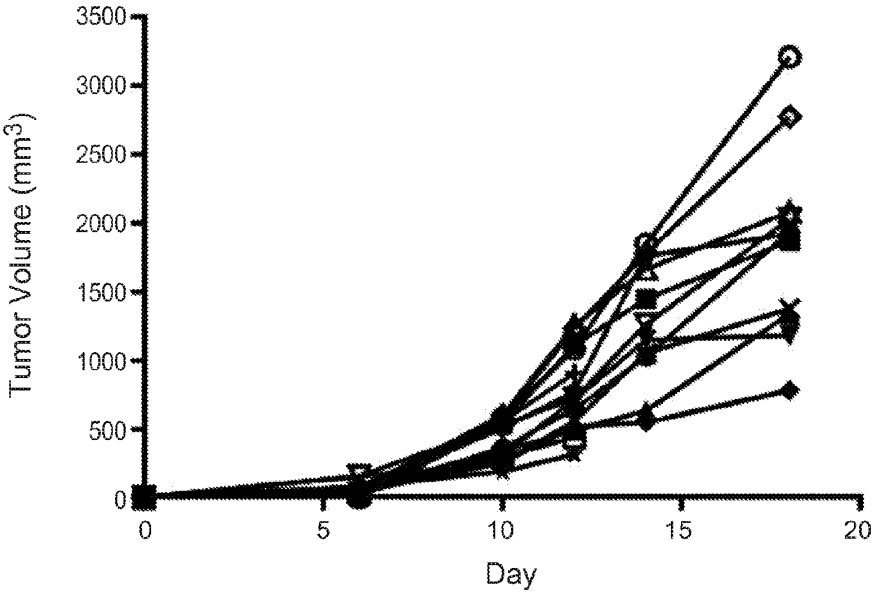


FIG. 29A

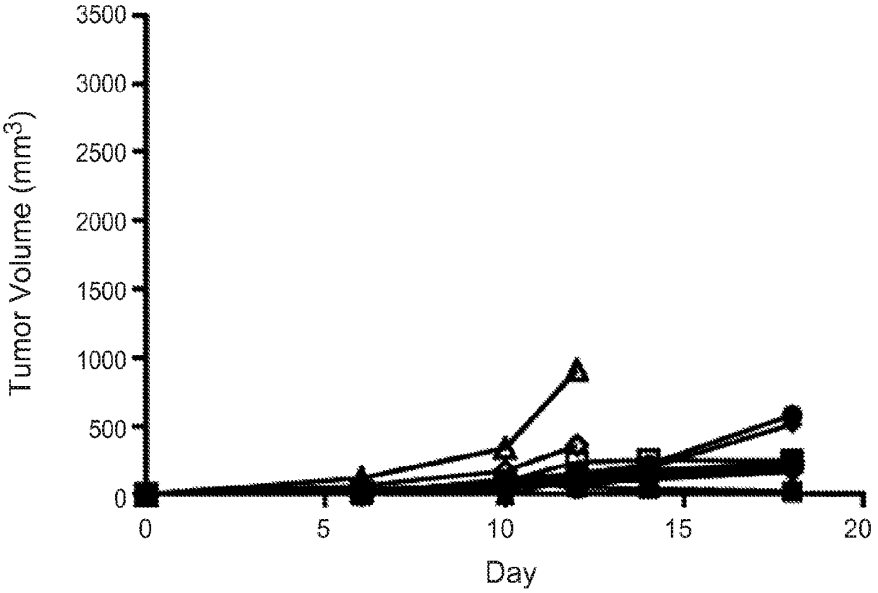


FIG. 29B

J-19.h1 Heavy Chain Variable Region

QITLKESGPTLVKPTQTLTLTCTFSGFSLNTYAMGVSW IRQPPGKALEWLASIWWNGNKYNNPSLKSRLTVTKDT SKNQVVLTMTNMDPVDTATYYCAHSRIIR* FTDYVMDA WGQGTLVTVSS (SEQ ID NO: 53)

J-19.h1 Light Chain Variable Region

DIQMTQSPSSLSTSVGDRVTITCRASEDIYNDLAWYQ QKPGKAPKLLIYNANSLHTGVASRFSGSGSGTDFTFTI SSLQPEDVATYFCQQYYDYPLTFGQGTKLEIK (SEQ ID NO: 54)

FIG. 30

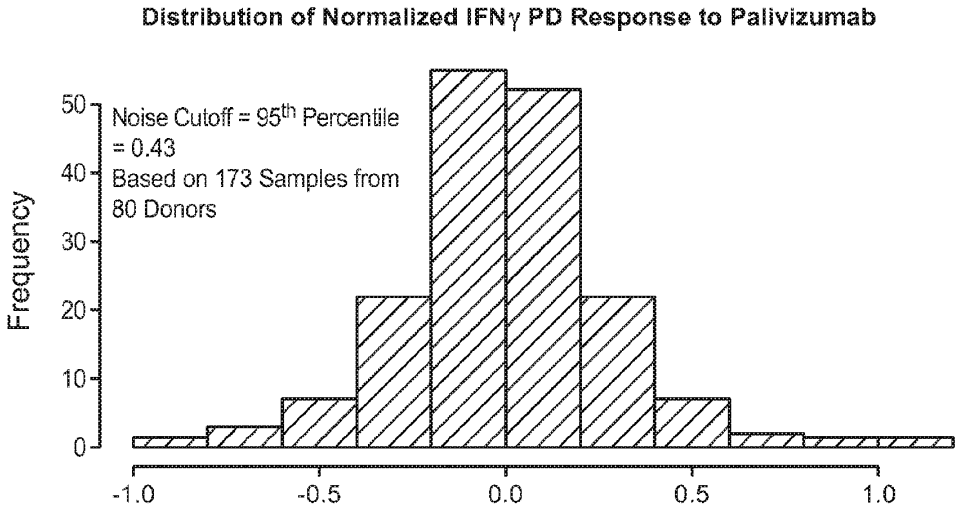
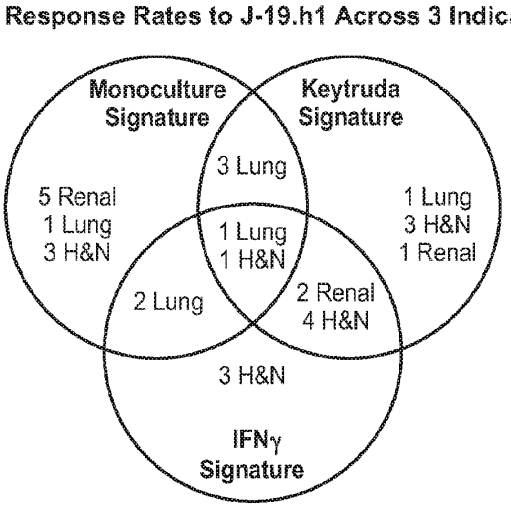


FIG. 31



Indication	Monoculture Signature	Keytruda Signature	IFNγ Signature
Renal Cell Carcinoma	5/44 = 11%	3/44 = 7%	2/44 = 5%
Head and Neck Cancer	4/42 = 10%	8/42 = 19%	8/42 = 19%
Lung Cancer	7/28 = 25%	5/28 = 18%	3/28 = 11%

FIG. 32

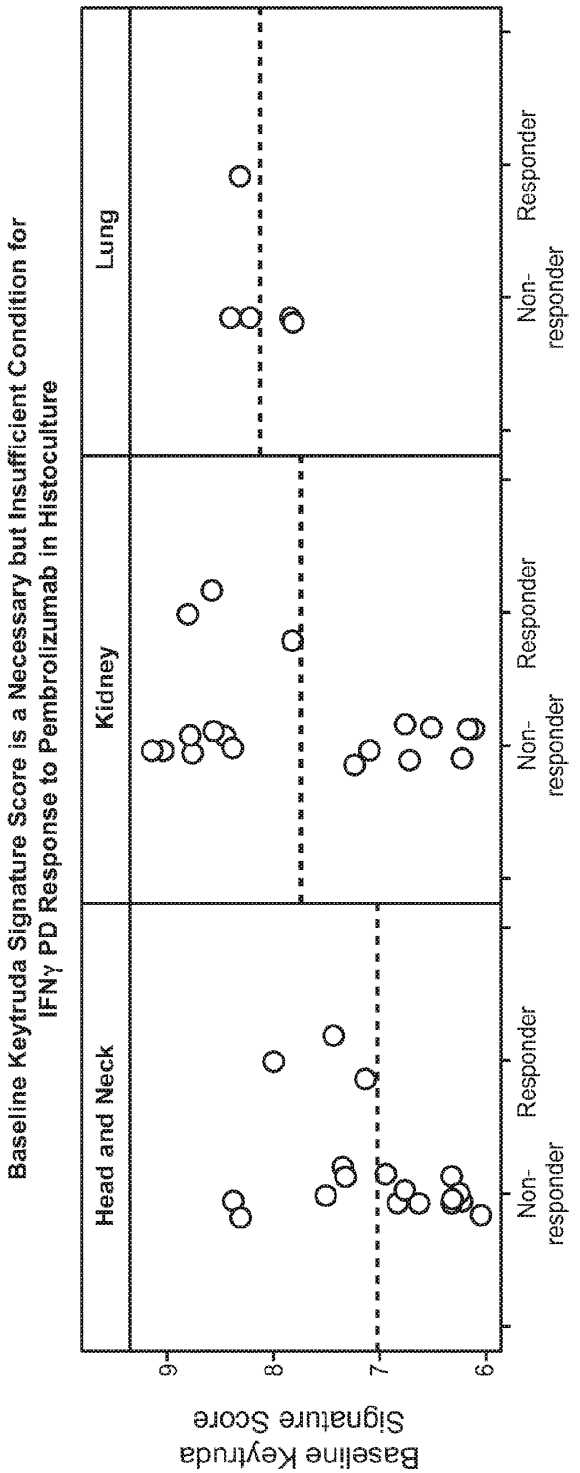

Baseline Keytruda Signature Score is a Necessary but Insufficient Condition for IFNγ PD Response to Pembrolizumab in Histoculture
Head and Neck
Kidney
Lung
Baseline Keytruda Signature Score
9
8
7
6
Non-responder
Responder

FIG. 33

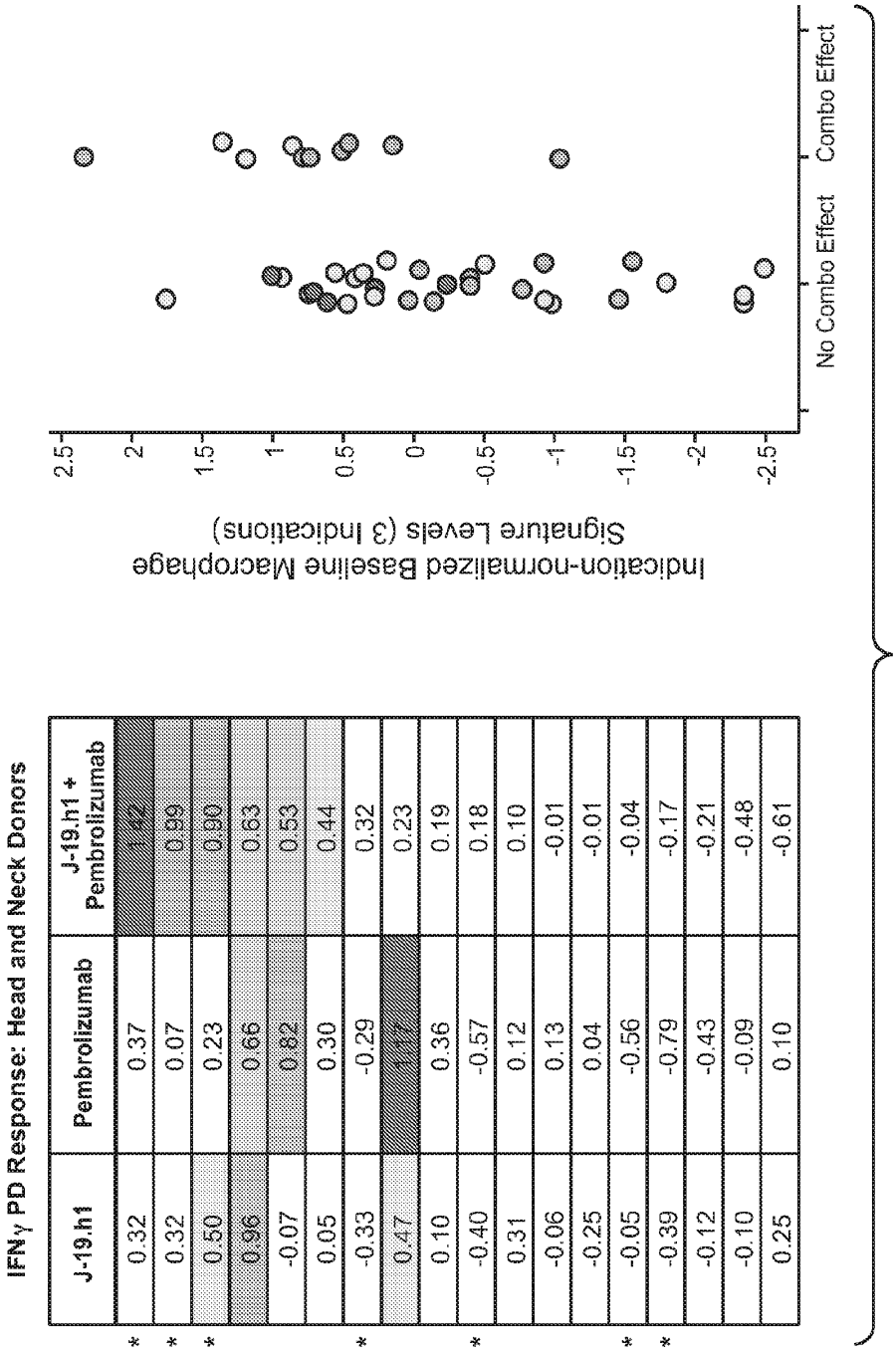

IFNγ PD Response: Head and Neck Donors
J-19.h1
Pembrolizumab
J-19.h1 + Pembrolizumab
0.32 0.37 1.42 *
0.32 0.07 0.99 *
0.50 0.23 0.90 *
0.96 0.66 0.63
-0.07 0.82 0.53
0.05 0.30 0.44
-0.33 -0.29 0.32 *
0.47 1.17 0.23
0.10 0.36 0.19
-0.40 -0.57 0.18 *
0.31 0.12 0.10
-0.06 0.13 -0.01
-0.25 0.04 -0.01
-0.05 -0.56 -0.04 *
-0.39 -0.79 -0.17 *
-0.12 -0.43 -0.21
-0.10 -0.09 -0.48
0.25 0.10 -0.61
Indication-normalized Baseline Macrophage Signature Levels (3 Indications)
2.5
2
1.5
1
0.5
0
-0.5
-1
-1.5
-2
-2.5
No Combo Effect
Combo Effect

FIG. 34