FIG. 1A

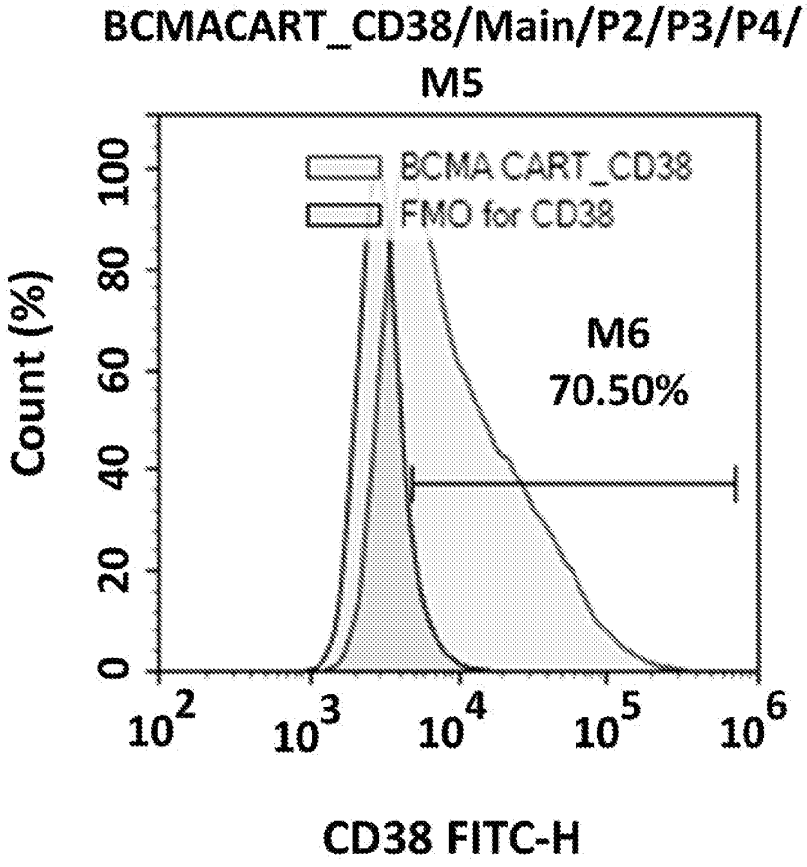

BCMACART_CD38/Main/P2/P3/P4/
M5
BCMA CART_CD38
FMO for CD38
M6
70.50%
Count (%)
0
20
40
60
80
100
10^2
10^3
10^4
10^5
10^6
CD38 FITC-H

FIG. 1B

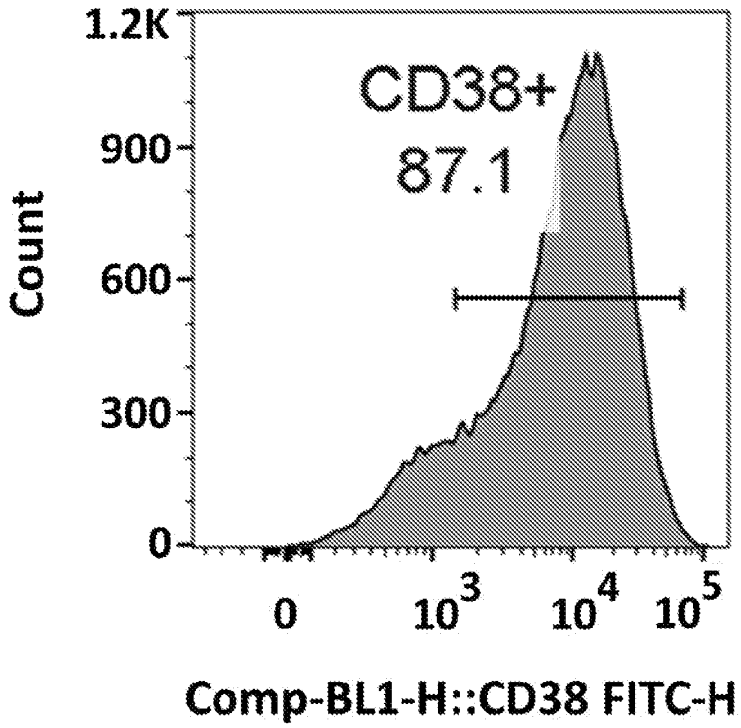

1.2K
900
600
300
0
Count
CD38+
87.1
0
10^3
10^4
10^5
Comp-BL1-H::CD38 FITC-H

FIG. 1C

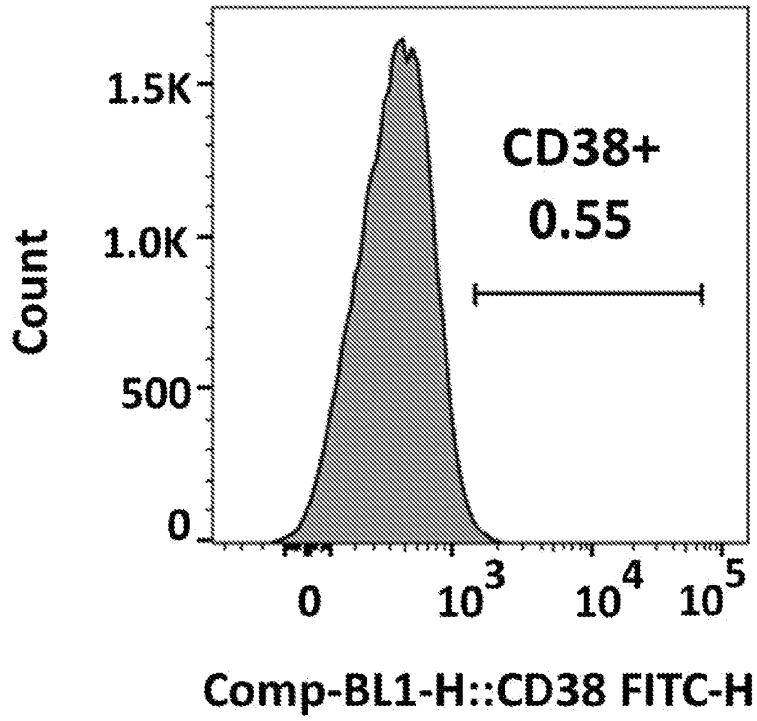


FIG. 2B

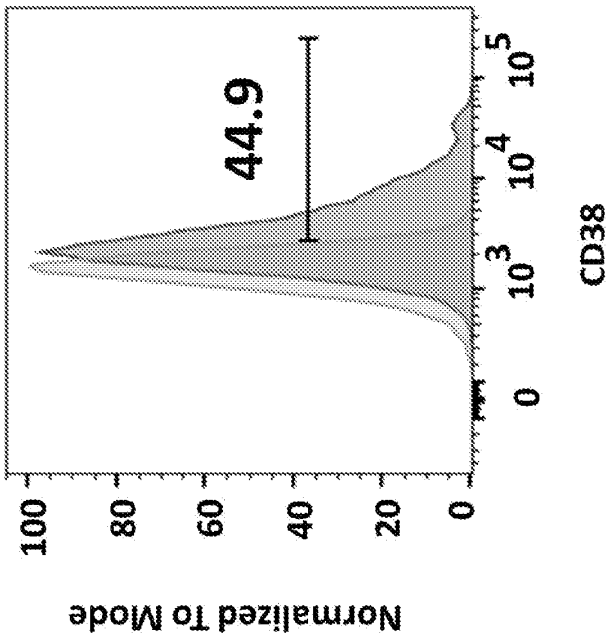

10% Comp
44.9
Normalized To Mode
CD38
0
20
40
60
80
100
0
10^3
10^4
10^5

FIG. 2A

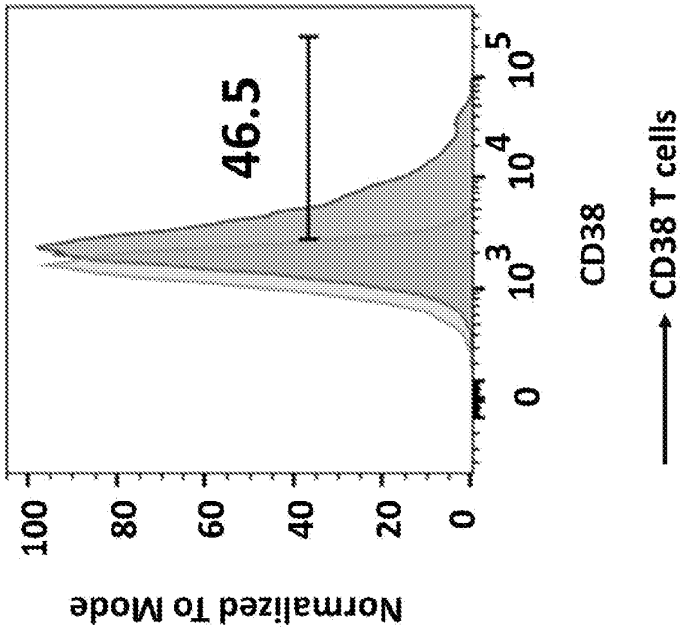

46.5
Normalized To Mode
CD38
CD38 T cells
0
20
40
60
80
100
0
10^3
10^4
10^5

FIG. 2C

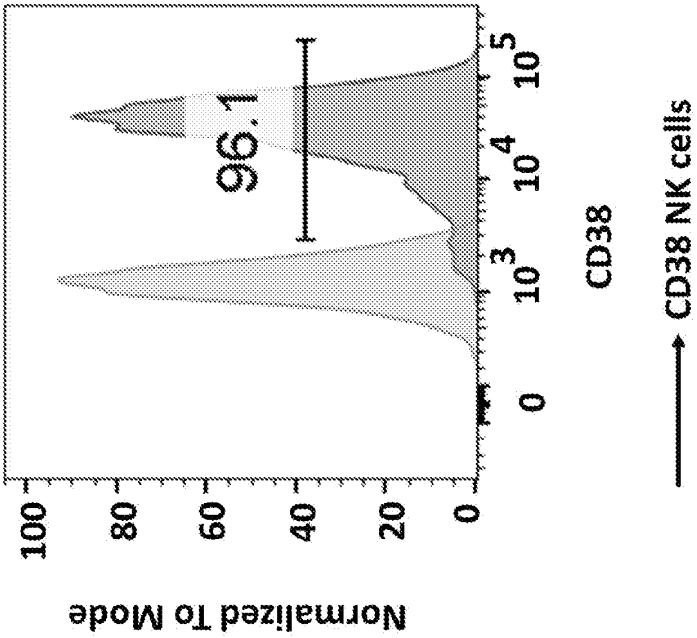

96.1
Normalized To Mode
100
80
60
40
20
0
0
10^3
10^4
10^5
CD38
CD38 NK cells

FIG. 2D

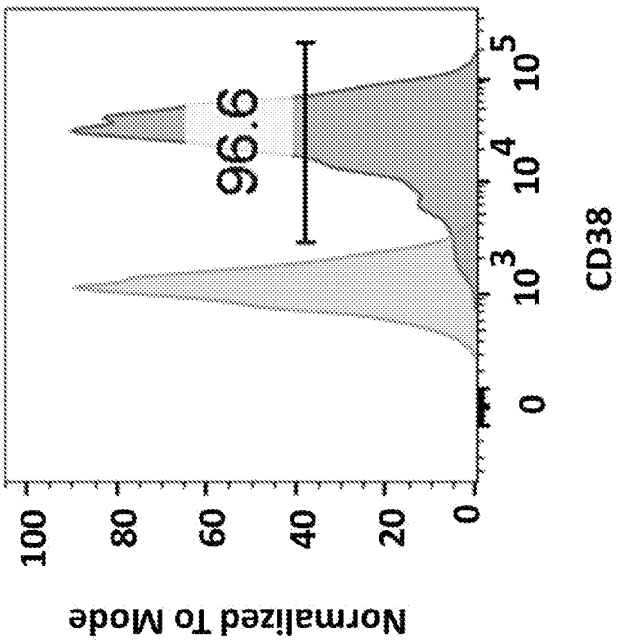

10% Comp
96.6
Normalized To Mode
100
80
60
40
20
0
0
10^3
10^4
10^5
CD38

FIG. 3B

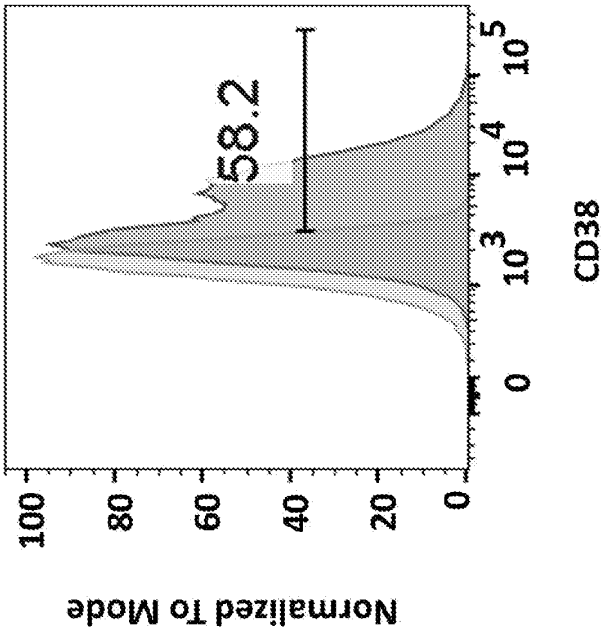

10% Comp
58.2
Normalized To Mode
100
80
60
40
20
0
0
10^3
10^4
10^5
CD38

FIG. 3A

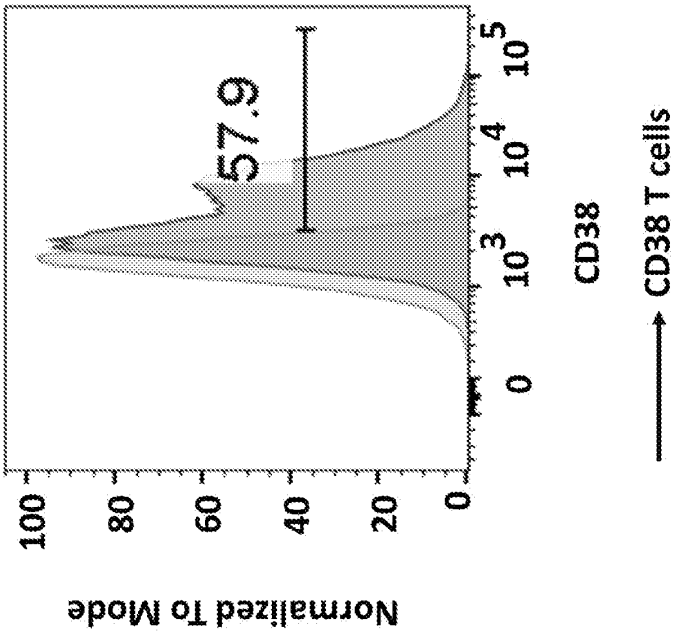

57.9
Normalized To Mode
100
80
60
40
20
0
0
10^3
10^4
10^5
CD38
CD38 T cells

FIG. 3D

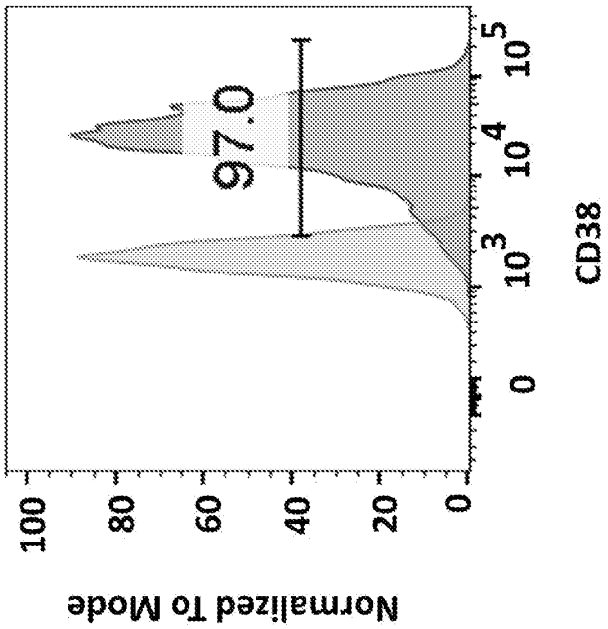

10% Comp
97.0
Normalized To Mode
CD38
0
20
40
60
80
100
0
10^3
10^4
10^5

FIG. 3C

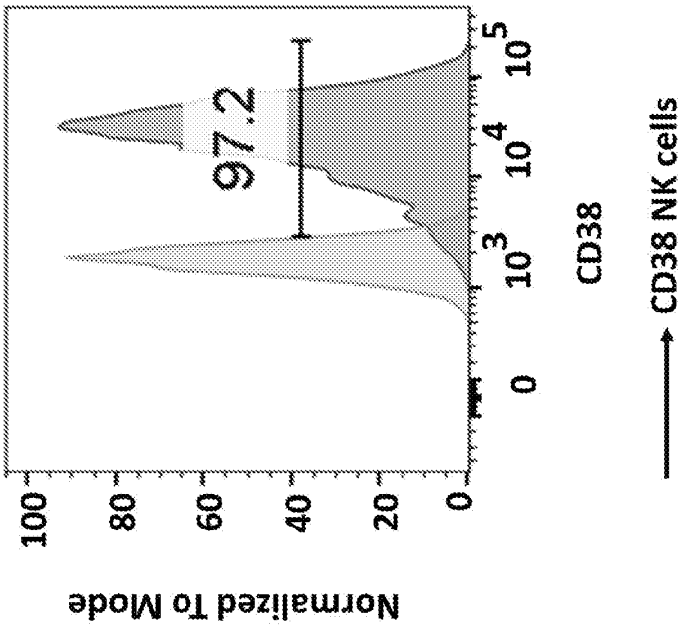

97.2
Normalized To Mode
CD38
CD38 NK cells
0
20
40
60
80
100
0
10^3
10^4
10^5

FIG. 4B

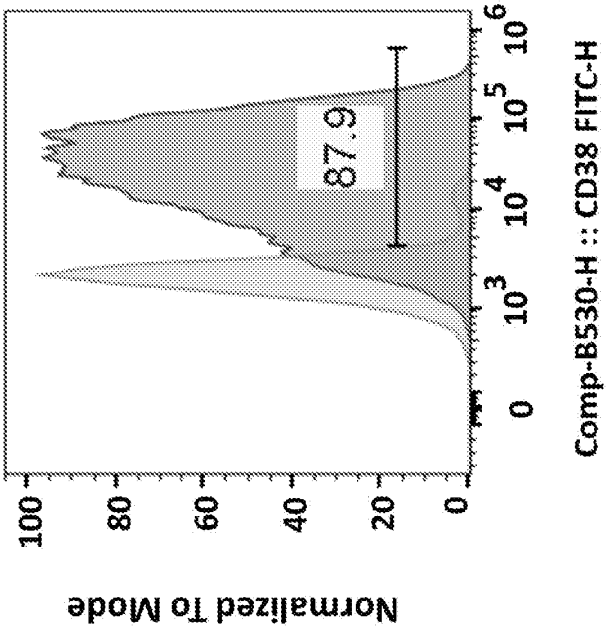

10% Comp
87.9
Normalized To Mode
Comp-B530-H :: CD38 FITC-H

FIG. 4A

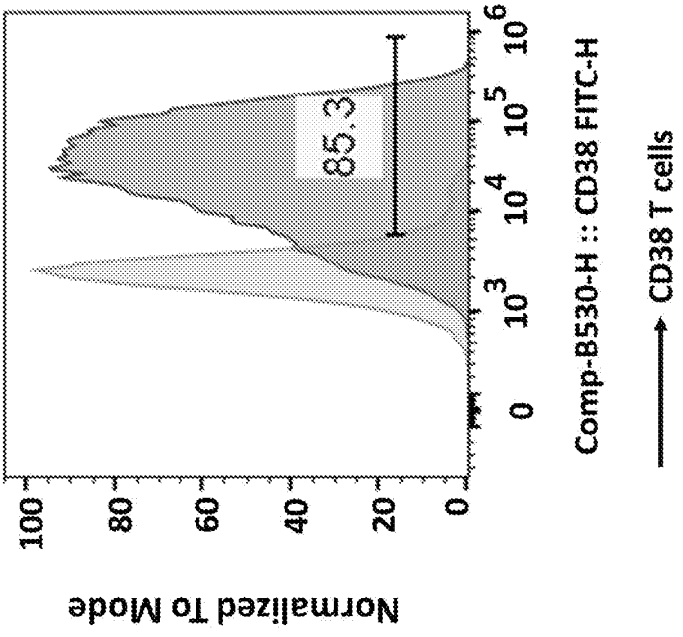

85.3
Normalized To Mode
Comp-B530-H :: CD38 FITC-H
CD38 T cells

FIG. 4D

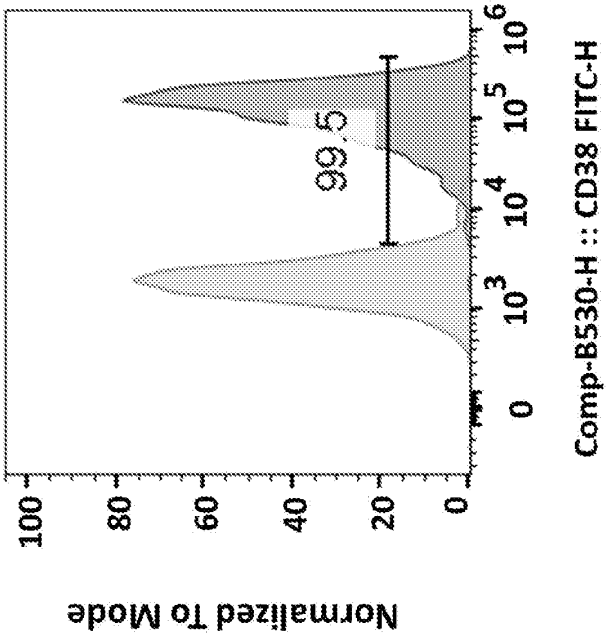

10% Comp
99.5
Normalized To Mode
Comp-B530-H :: CD38 FITC-H
0
20
40
60
80
100
0
10^3
10^4
10^5
10^6

FIG. 4C

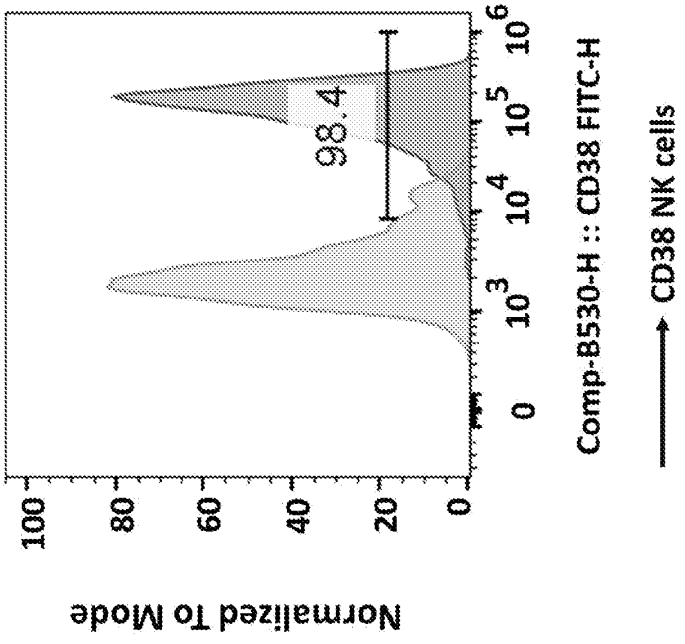

98.4
Normalized To Mode
Comp-B530-H :: CD38 FITC-H
CD38 NK cells
0
20
40
60
80
100
0
10^3
10^4
10^5
10^6

FIG. 5A

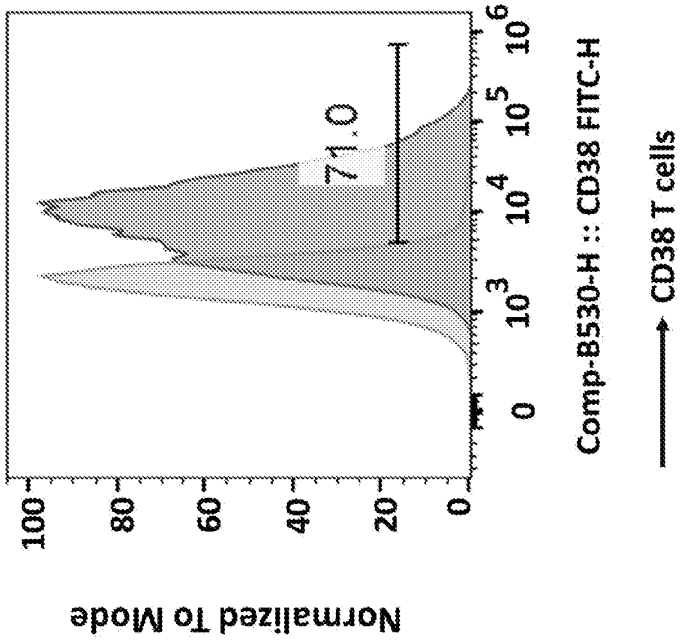


FIG. 5B

10% Comp

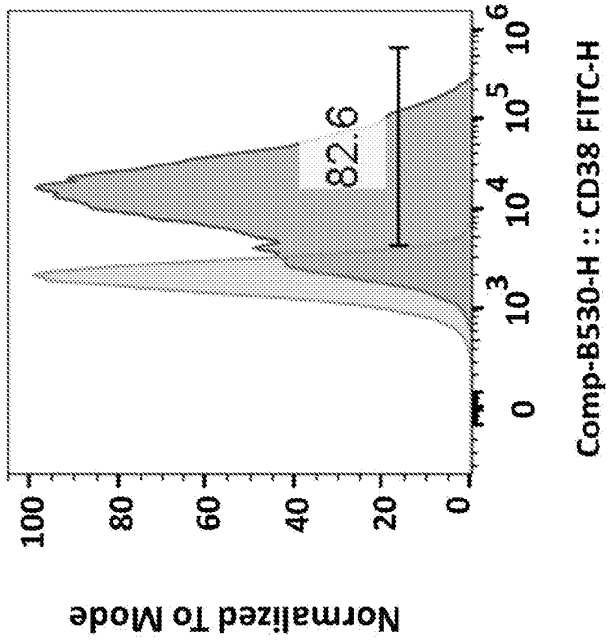


FIG. 5D

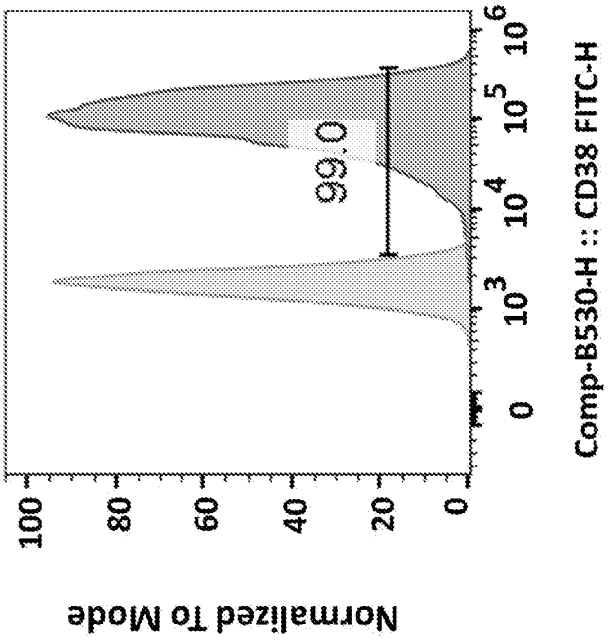

10% Comp
99.0
Normalized To Mode
Comp-B530-H :: CD38 FITC-H

FIG. 5C

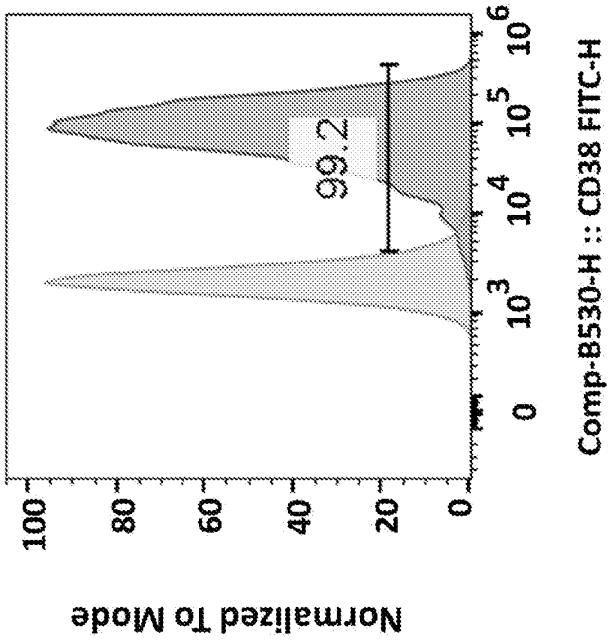
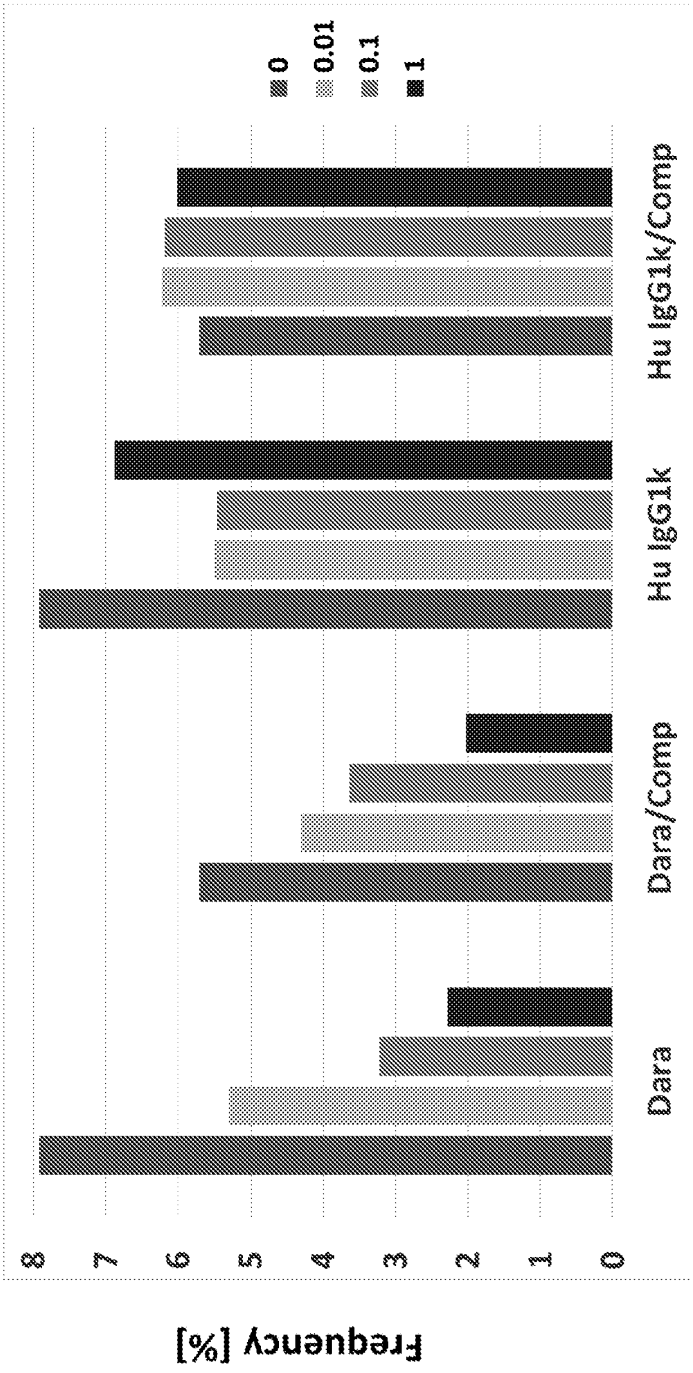

99.2
Normalized To Mode
Comp-B530-H :: CD38 FITC-H
CD38 NK cells

FIG. 6A
NK cells



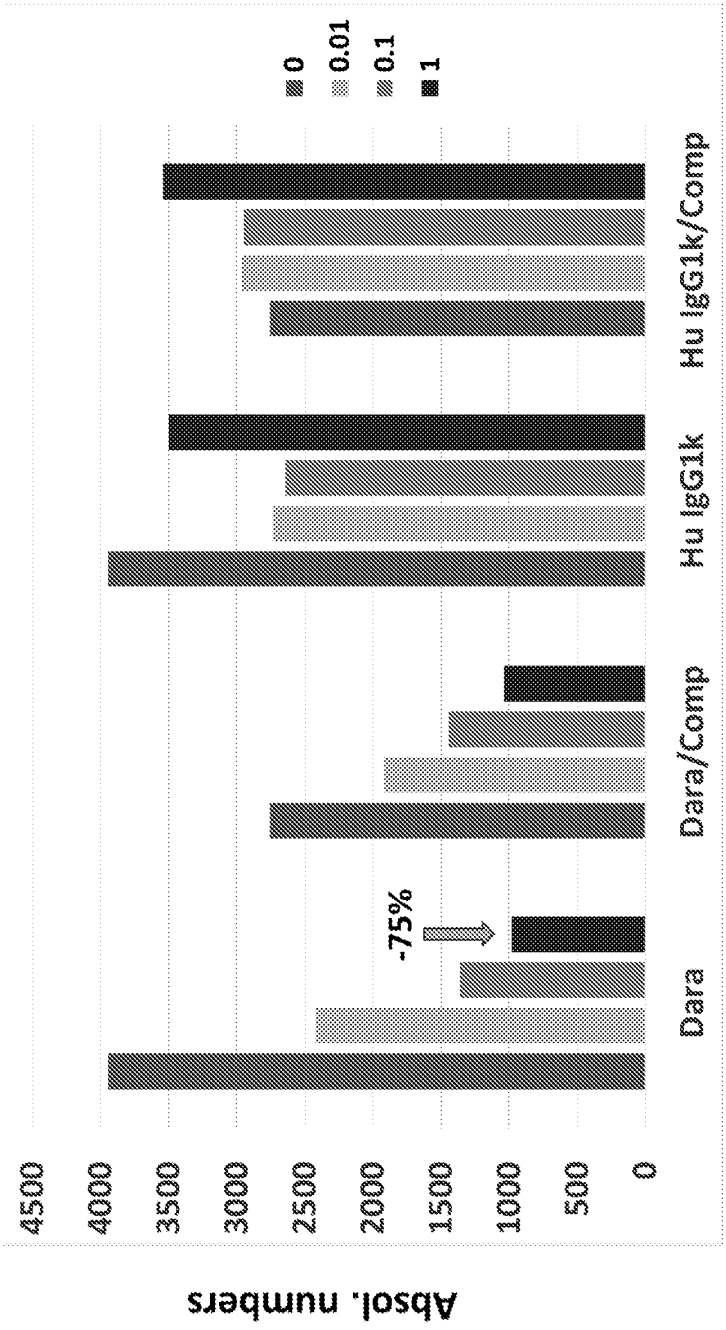

0
0.01
0.1
1
Hu IgG1k/Comp
Hu IgG1k
Dara/Comp
Dara
-75%
4500
4000
3500
3000
2500
2000
1500
1000
500
0
Absol. numbers

FIG. 6B

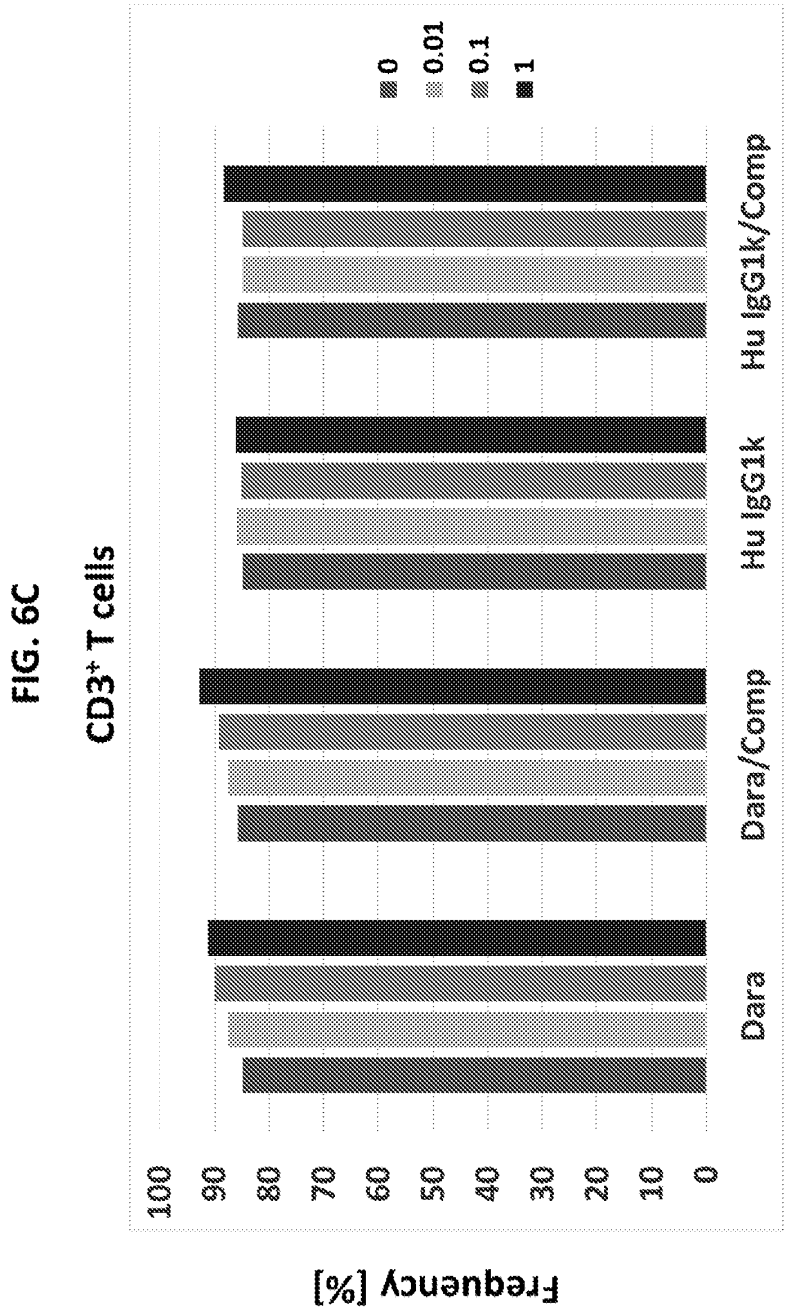
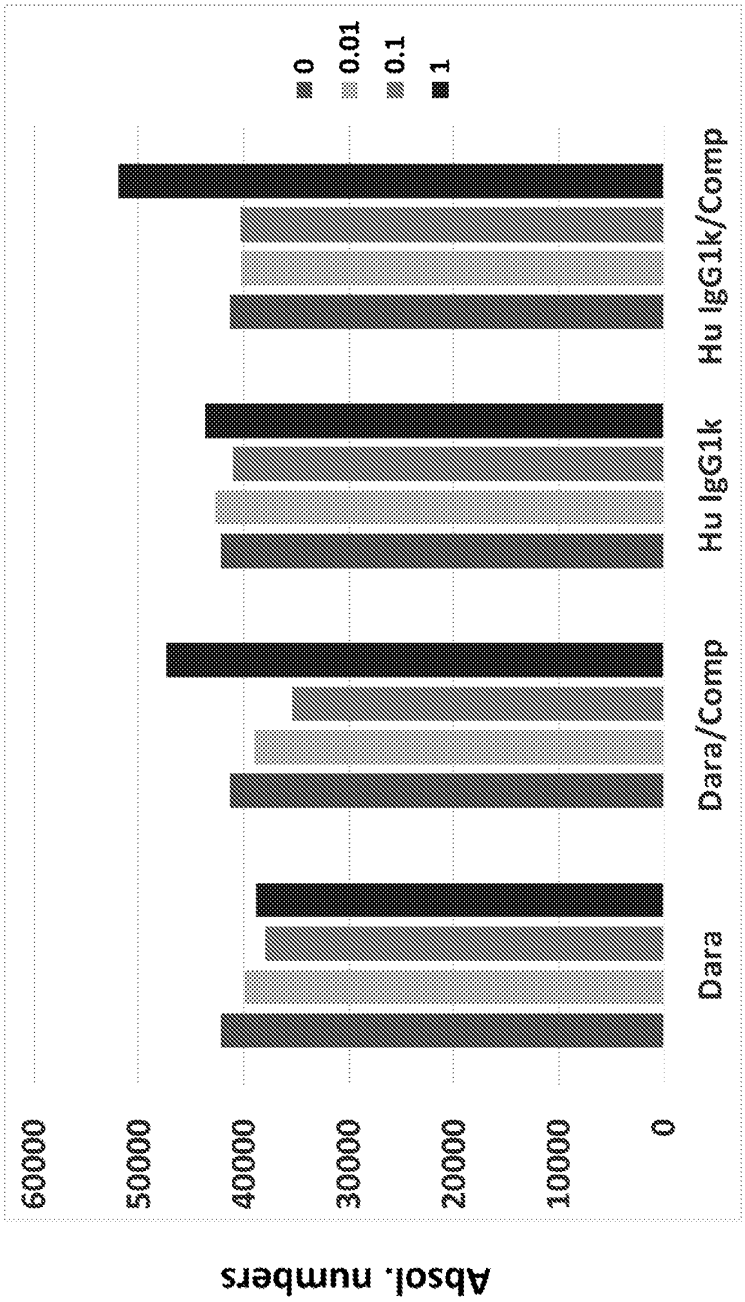


FIG. 6C
CD3+ T cells
0
0.01
0.1
1
Hu IgG1k/Comp
Hu IgG1k
Dara/Comp
Dara
100
90
80
70
60
50
40
30
20
10
0
Frequency [%]

FIG. 6D


0
0.01
0.1
1
60000
50000
40000
30000
20000
10000
0
Absol. numbers
Dara
Dara/Comp
Hu IgG1k
Hu IgG1k/Comp

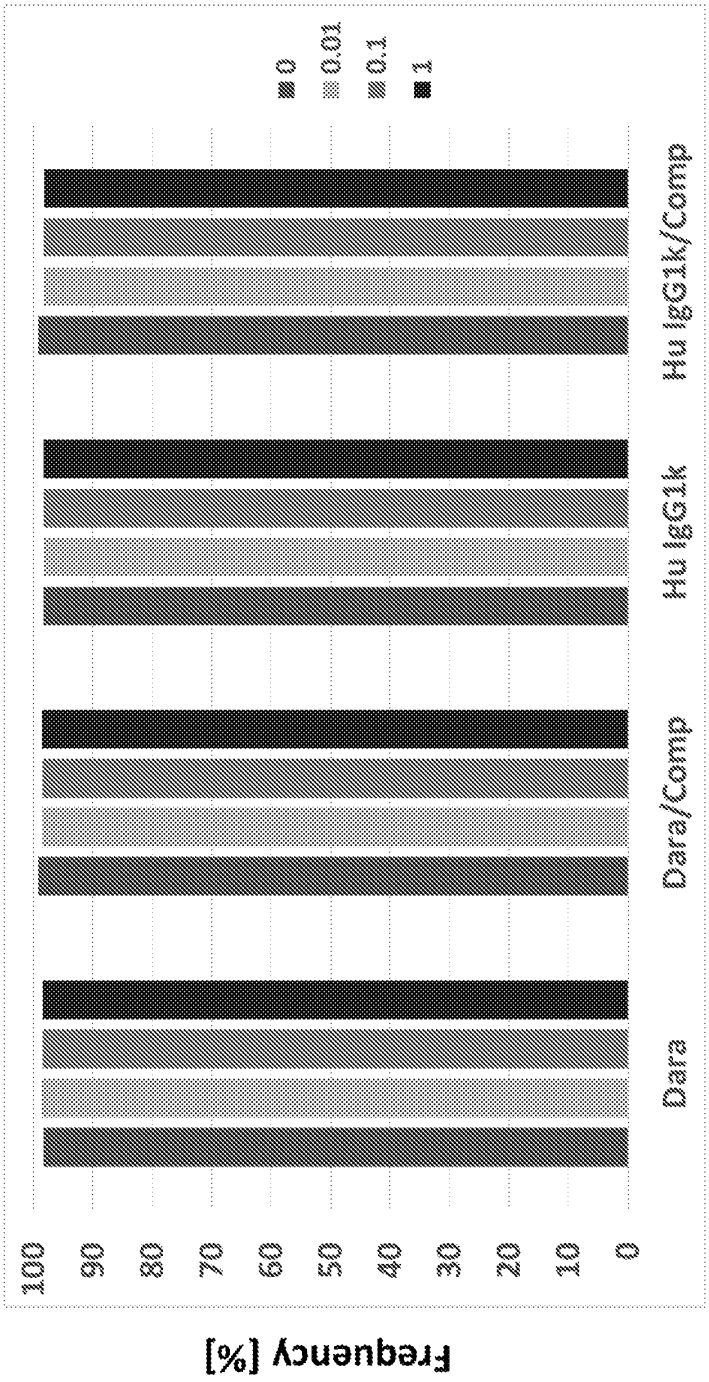

0
0.01
0.1
1
Hu IgG1k/Comp
Hu IgG1k
Dara/Comp
Dara
100
90
80
70
60
50
40
30
20
10
0
Frequency [%]

FIG. 7A

FIG. 7B

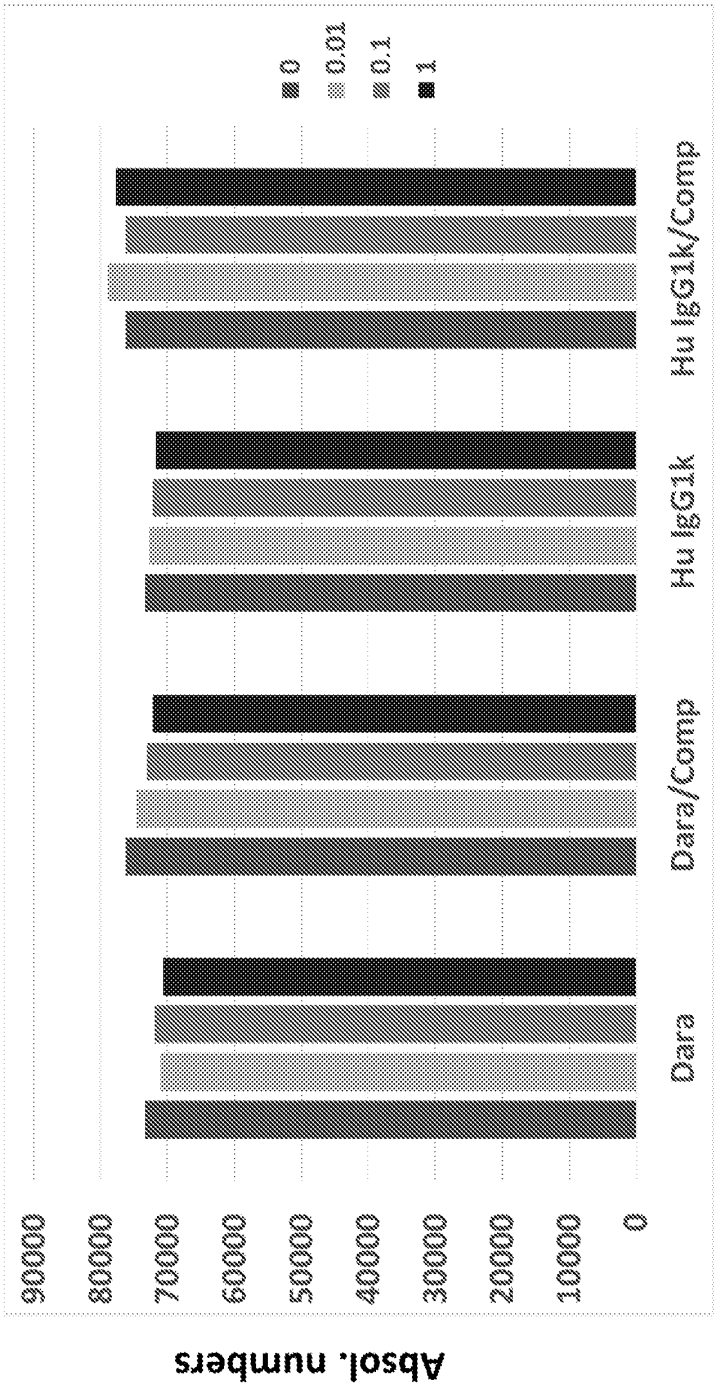

0
0.01
0.1
1
Hu IgG1k/Comp
Hu IgG1k
Dara/Comp
Dara
90000
80000
70000
60000
50000
40000
30000
20000
10000
0
Absol. numbers

FIG. 8A

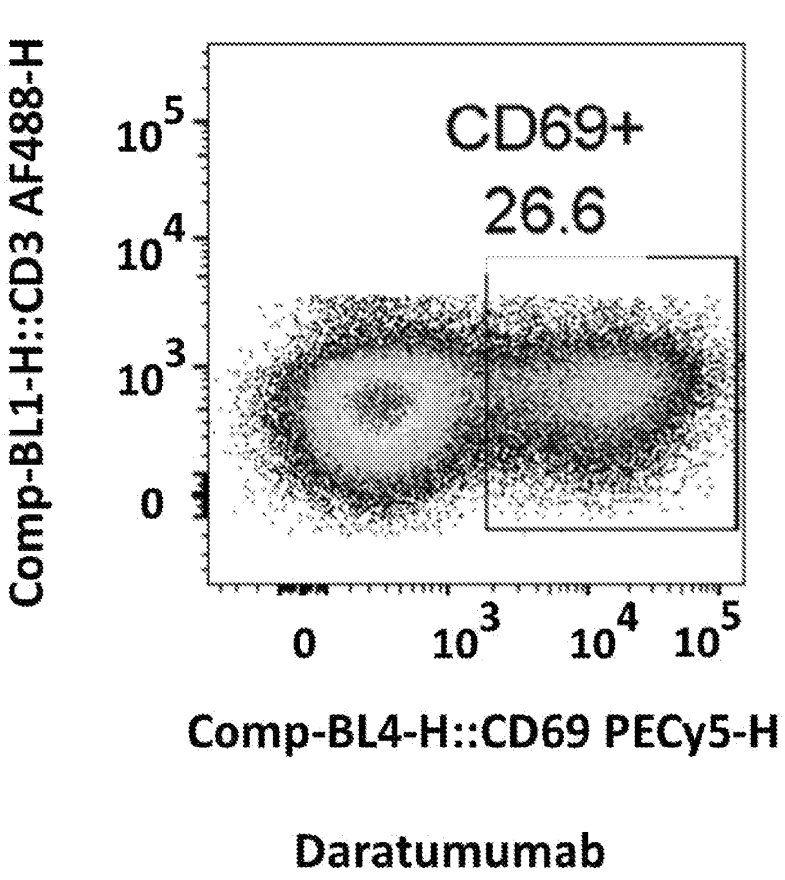

0
CD69+
26.6
Comp-BL1-H::CD3 AF488-H
10^5
10^4
10^3
0
0
10^3
10^4
10^5
Comp-BL4-H::CD69 PECy5-H
Daratumumab

FIG. 8B

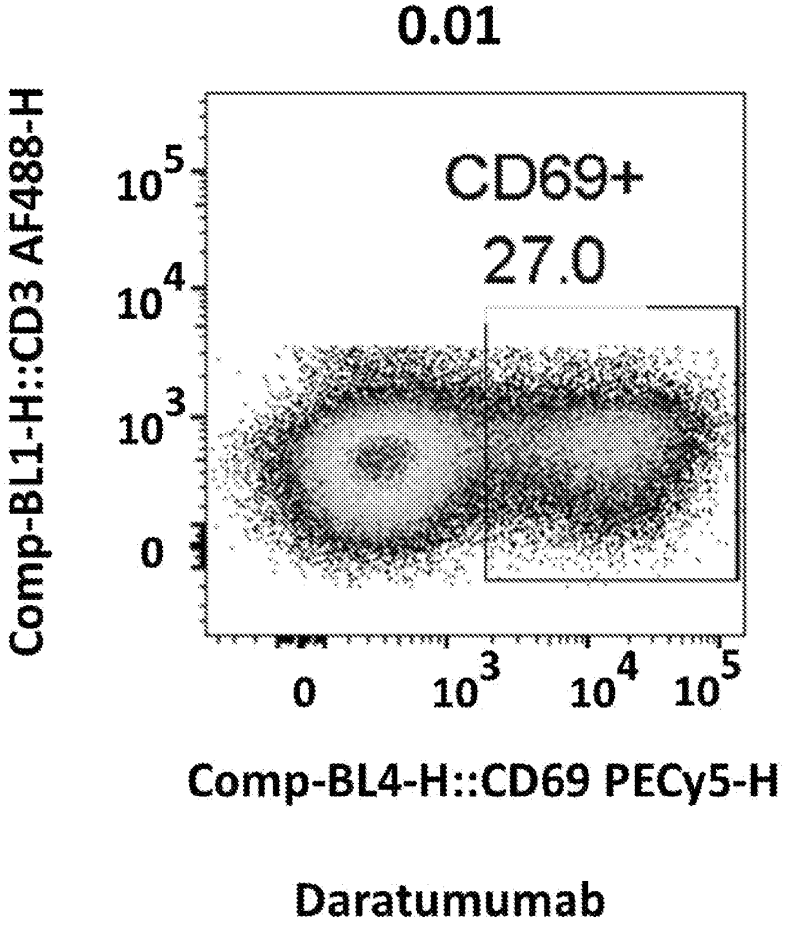

0.01
CD69+
27.0
Comp-BL1-H::CD3 AF488-H
10^5
10^4
10^3
0
0
10^3
10^4
10^5
Comp-BL4-H::CD69 PECy5-H
Daratumumab

FIG. 8C

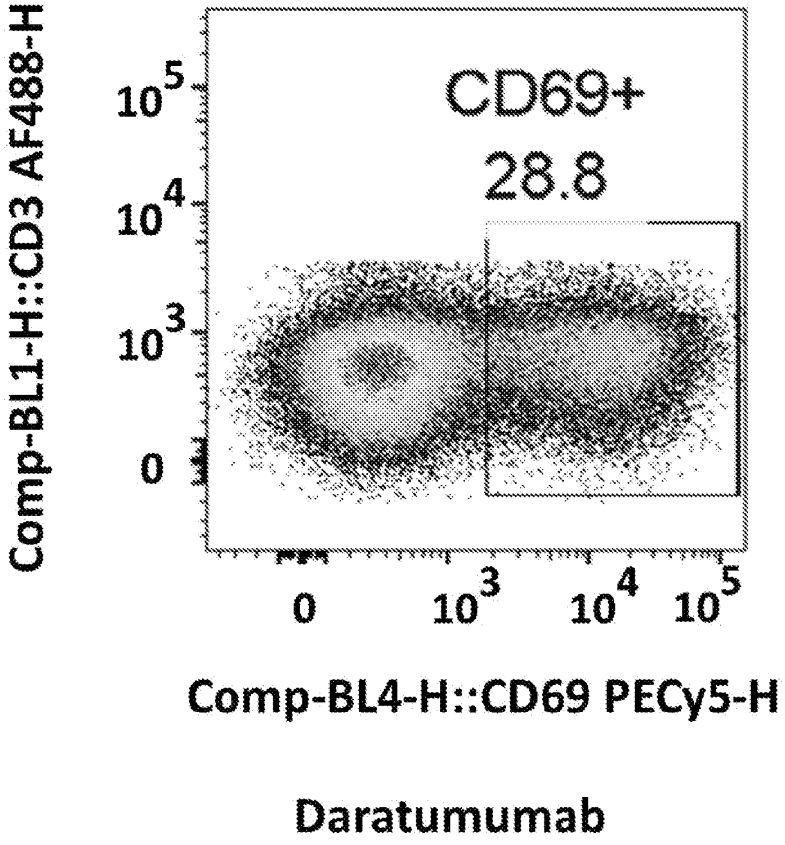

0.1
CD69+
28.8
Comp-BL1-H::CD3 AF488-H
10^5
10^4
10^3
0
0
10^3
10^4
10^5
Comp-BL4-H::CD69 PECy5-H
Daratumumab

FIG. 8D

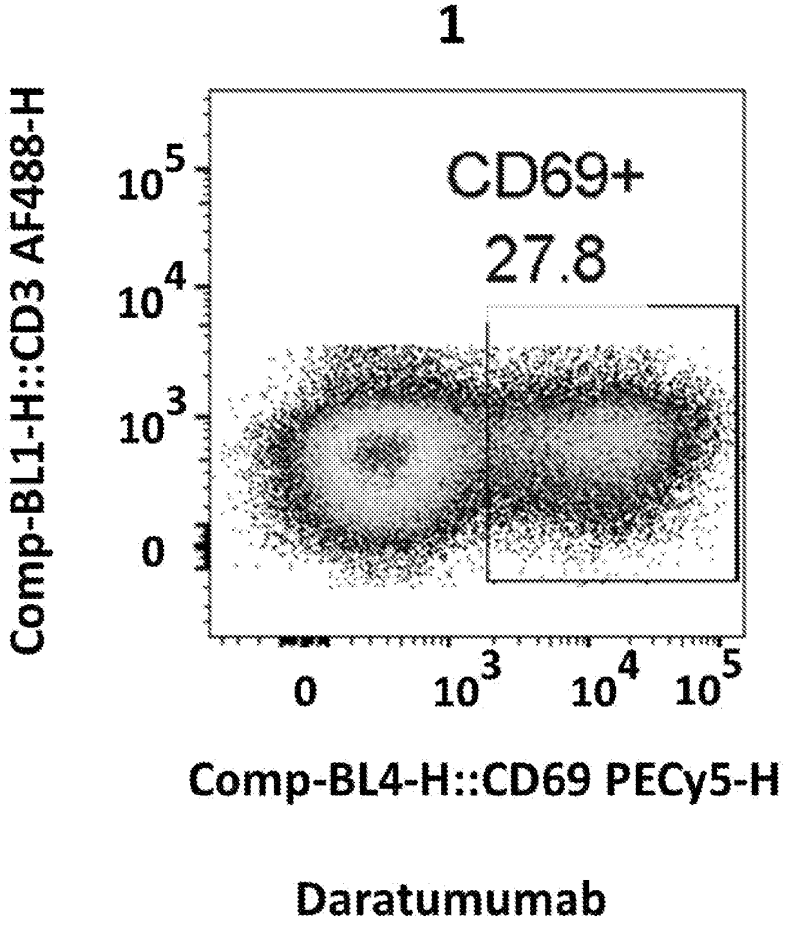

1
CD69+
27.8
Comp-BL1-H::CD3 AF488-H
10^5
10^4
10^3
0
0
10^3
10^4
10^5
Comp-BL4-H::CD69 PECy5-H
Daratumumab

FIG. 8E

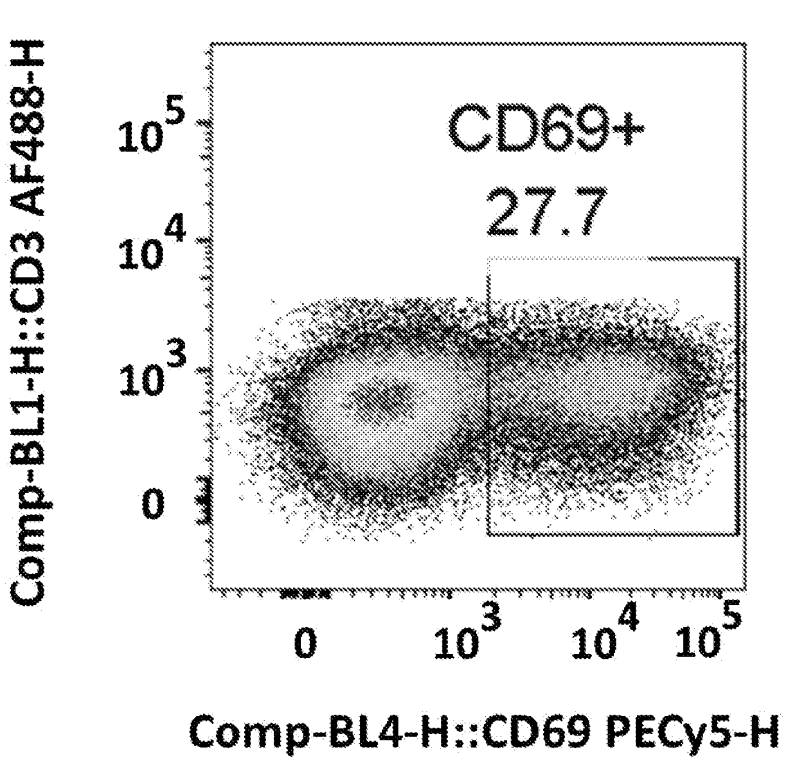

0
CD69+
27.7
Comp-BL1-H::CD3 AF488-H
10^5
10^4
10^3
0
0
10^3
10^4
10^5
Comp-BL4-H::CD69 PECy5-H
Daratumumab
+ Goat anti-human

FIG. 8F

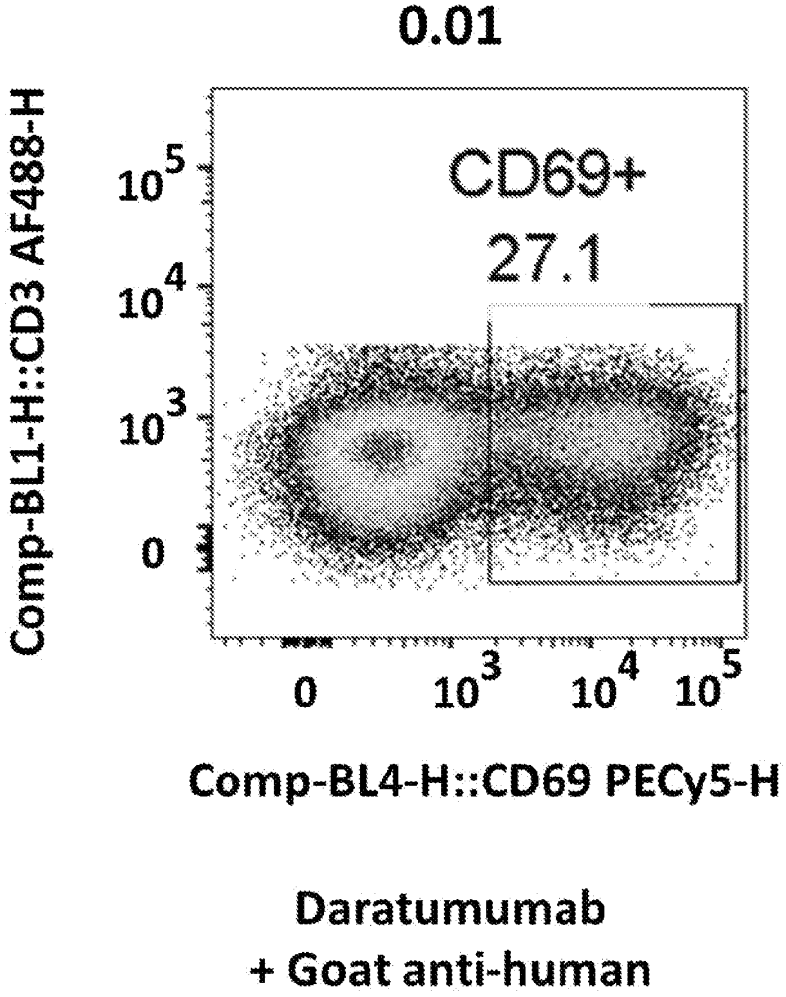

0.01
CD69+
27.1
Comp-BL1-H::CD3 AF488-H
10^5
10^4
10^3
0
0
10^3
10^4
10^5
Comp-BL4-H::CD69 PECy5-H
Daratumumab
+ Goat anti-human

FIG. 8G

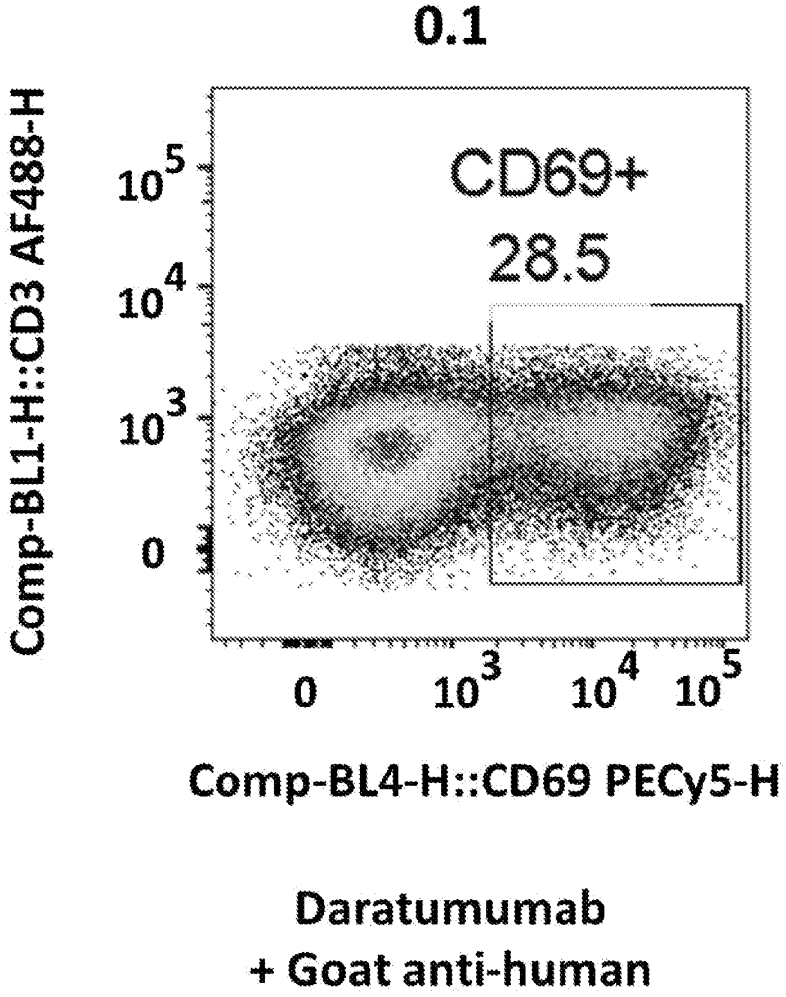
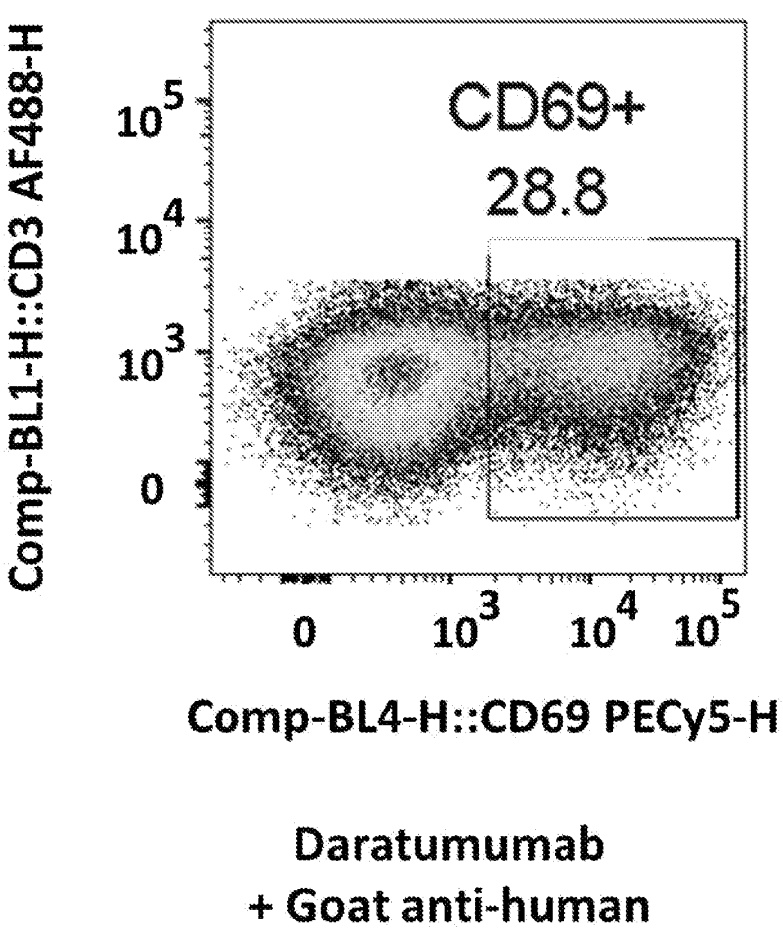

0.1
CD69+
28.5
Comp-BL1-H::CD3 AF488-H
10^5
10^4
10^3
0
0
10^3
10^4
10^5
Comp-BL4-H::CD69 PECy5-H
Daratumumab
+ Goat anti-human

FIG. 8H



Daratumumab
+ Goat anti-human

FIG. 8I

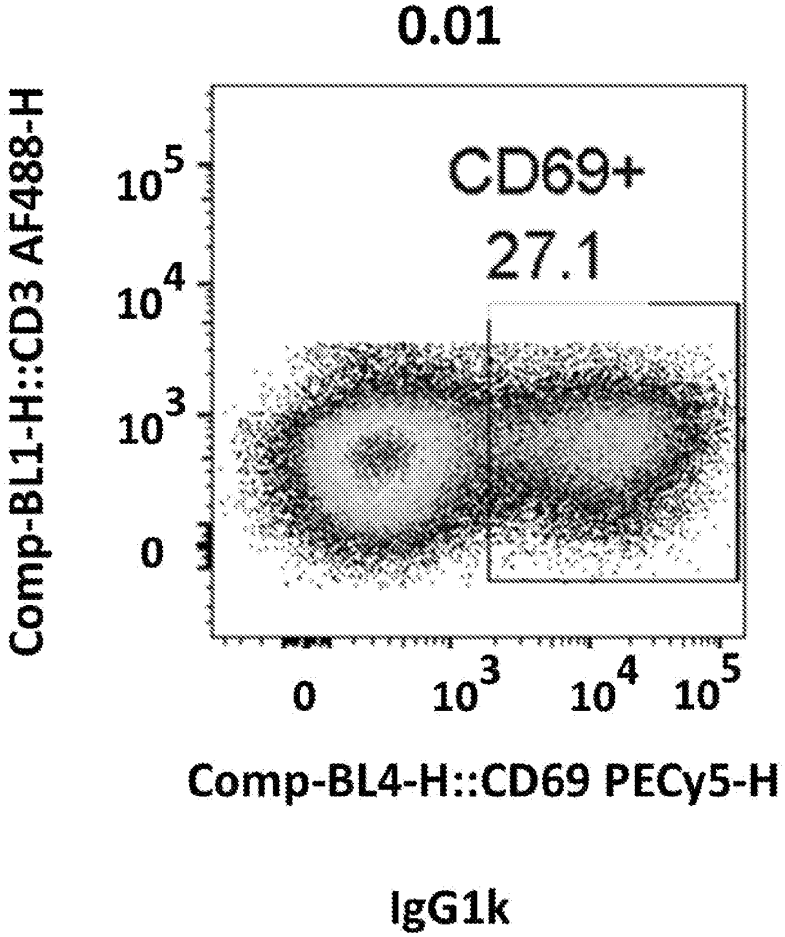

0.01
CD69+
27.1
Comp-BL1-H::CD3 AF488-H
10^5
10^4
10^3
0
0
10^3
10^4
10^5
Comp-BL4-H::CD69 PECy5-H
IgG1k

FIG. 8J

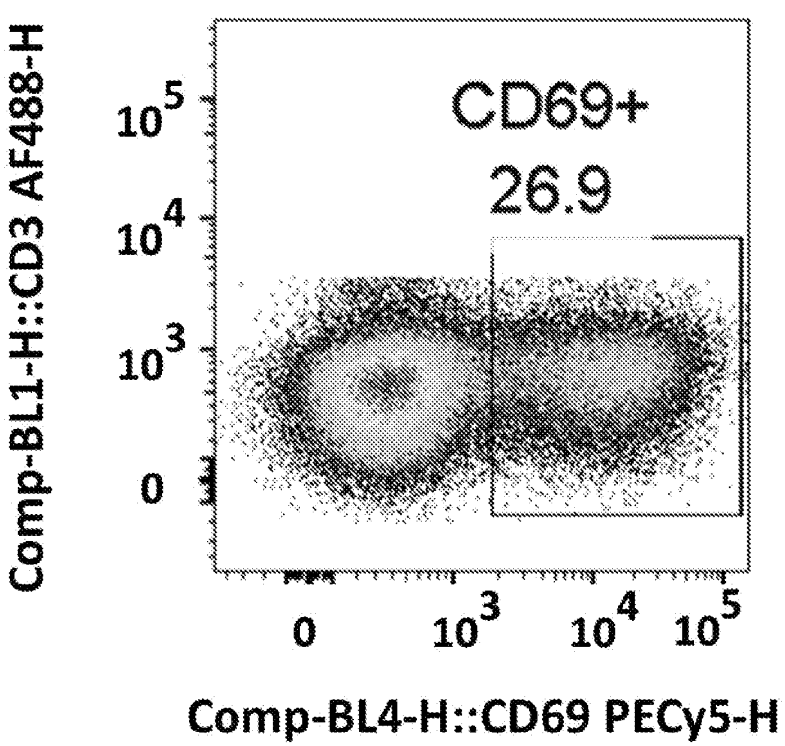

0.1
CD69+
26.9
Comp-BL1-H::CD3 AF488-H
10^5
10^4
10^3
0
0
10^3
10^4
10^5
Comp-BL4-H::CD69 PECy5-H
IgG1k

FIG. 8K

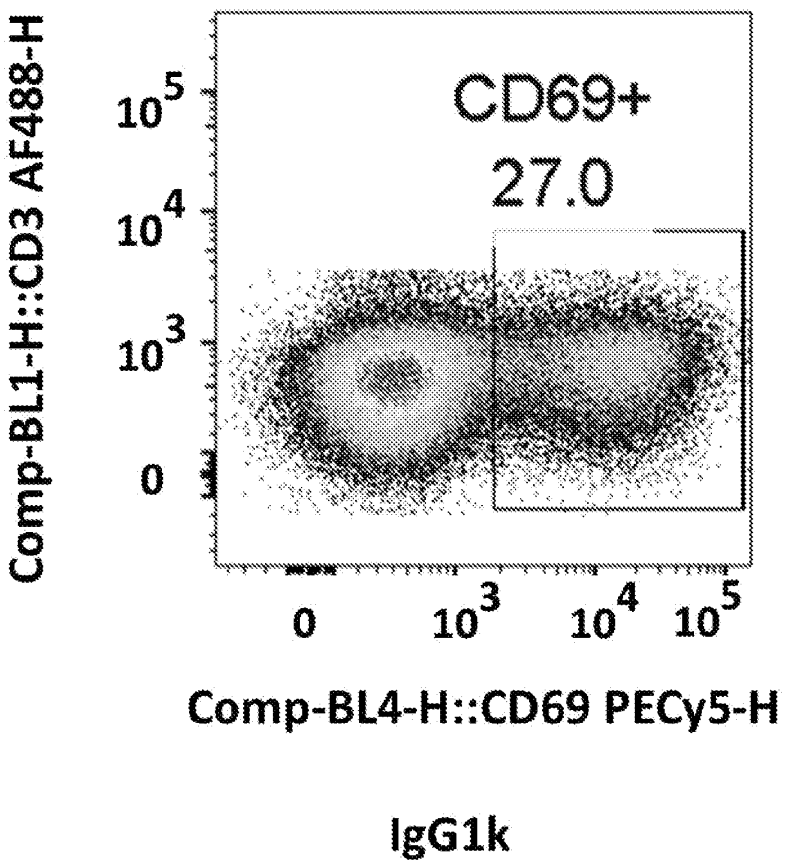

1
CD69+
27.0
Comp-BL1-H::CD3 AF488-H
10^5
10^4
10^3
0
0
10^3
10^4
10^5
Comp-BL4-H::CD69 PECy5-H
IgG1k

FIG. 8L

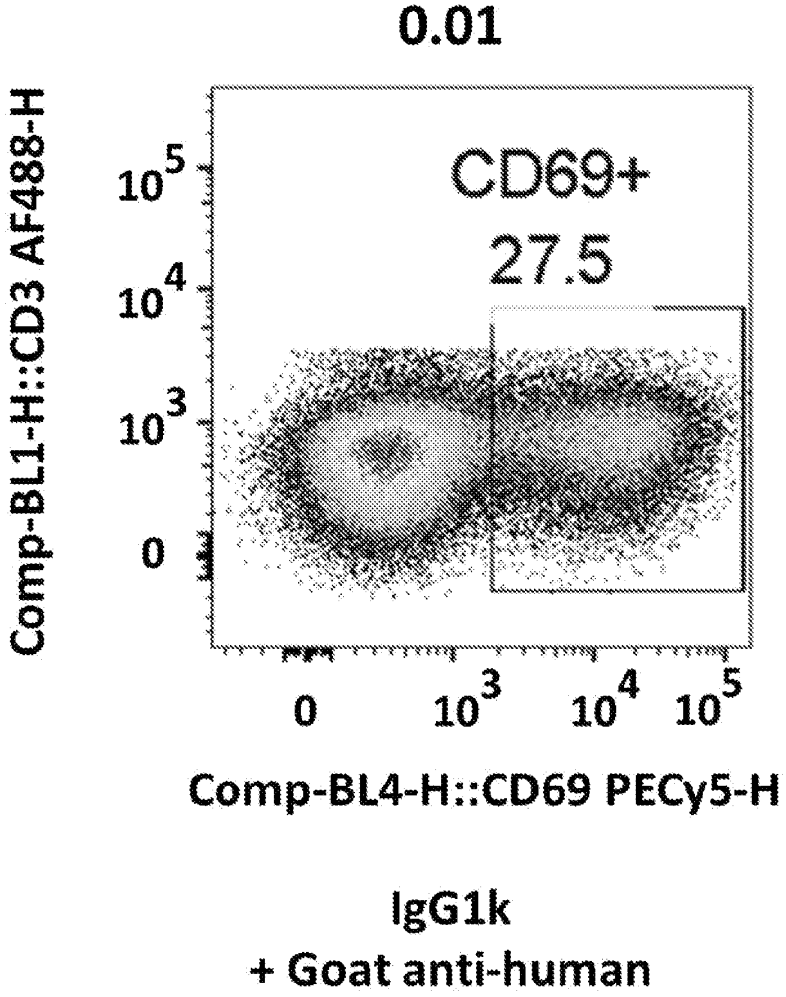

0.01
CD69+
27.5
Comp-BL1-H::CD3 AF488-H
10^5
10^4
10^3
0
0
10^3
10^4
10^5
Comp-BL4-H::CD69 PECy5-H
IgG1k
+ Goat anti-human

FIG. 8M

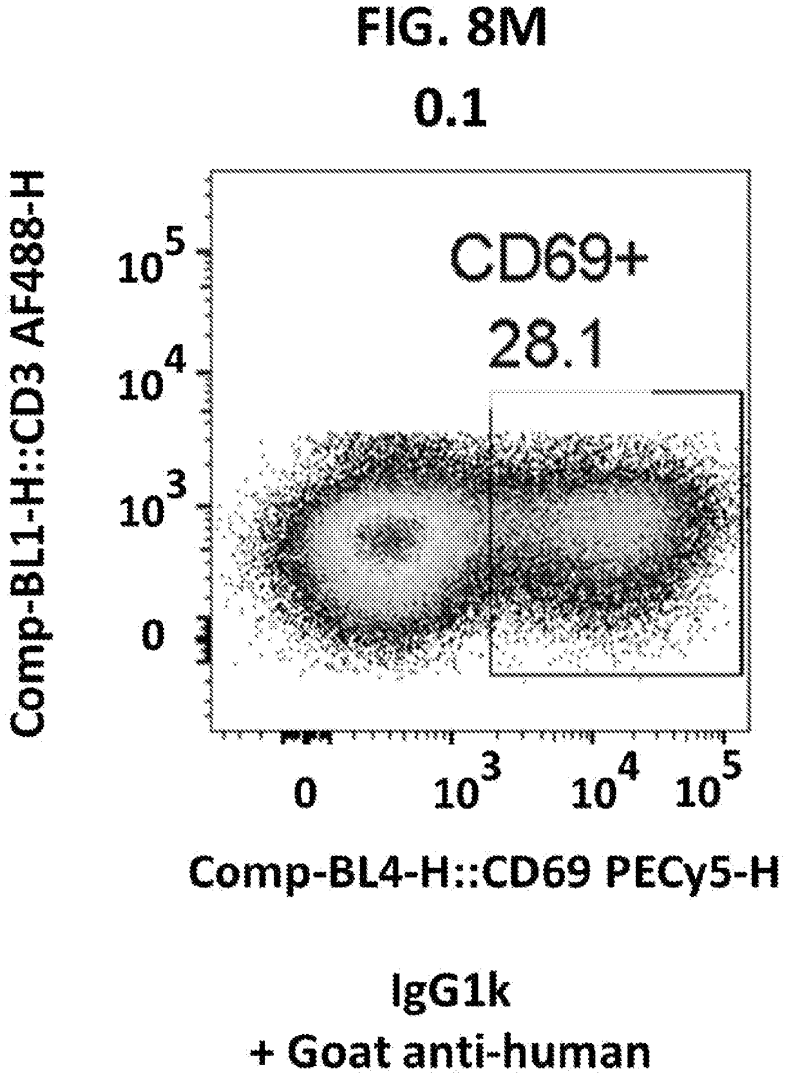

0.1
CD69+
28.1
Comp-BL1-H::CD3 AF488-H
10^5
10^4
10^3
0
0
10^3
10^4
10^5
Comp-BL4-H::CD69 PECy5-H
IgG1k
+ Goat anti-human

FIG. 8N

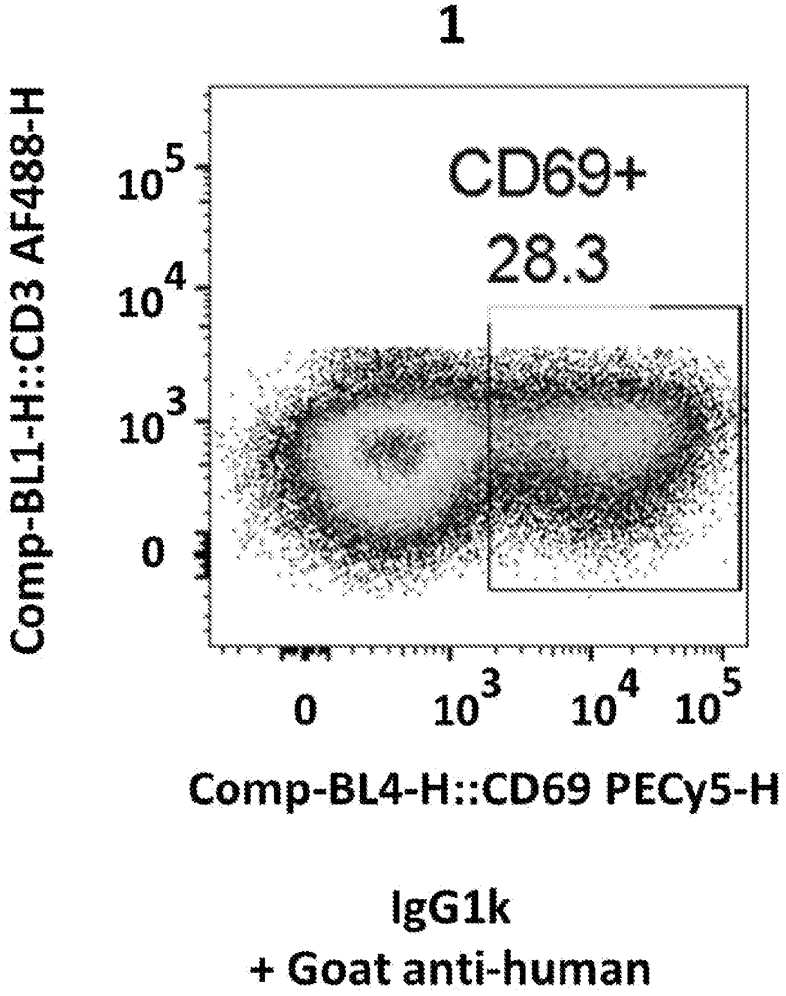

1
CD69+
28.3
Comp-BL1-H::CD3 AF488-H
10^5
10^4
10^3
0
0
10^3
10^4
10^5
Comp-BL4-H::CD69 PECy5-H
IgG1k
+ Goat anti-human

FIG. 9A

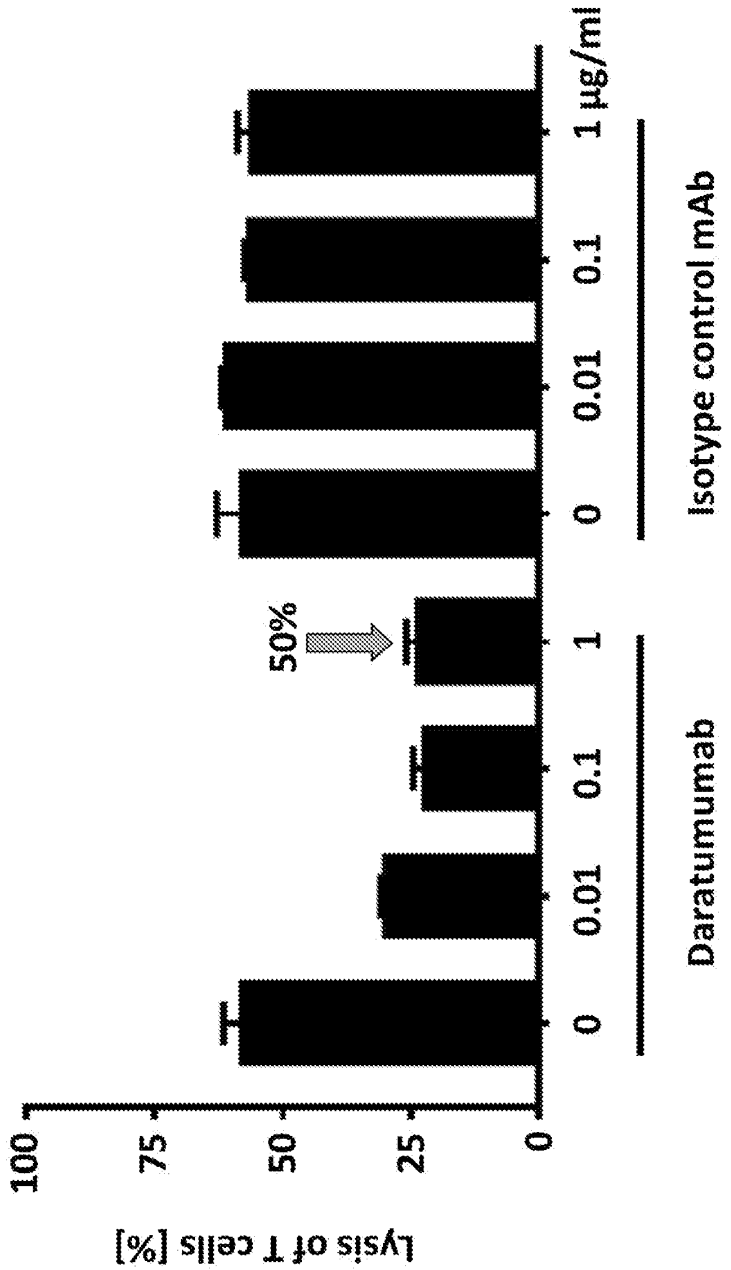

Lysis of T cells [%]
100
75
50
25
0
50%
0
0.01
0.1
1
0
0.01
0.1
1 µg/ml
Daratumumab
Isotype control mAb

FIG. 9B

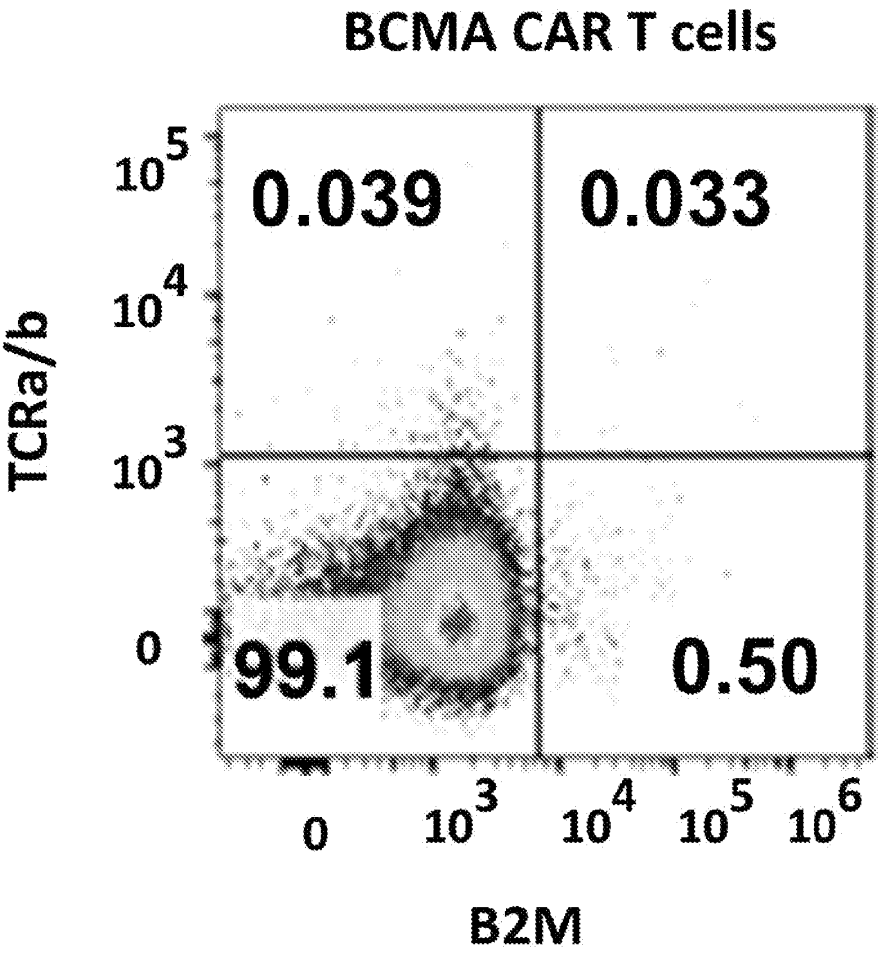


FIG. 10A

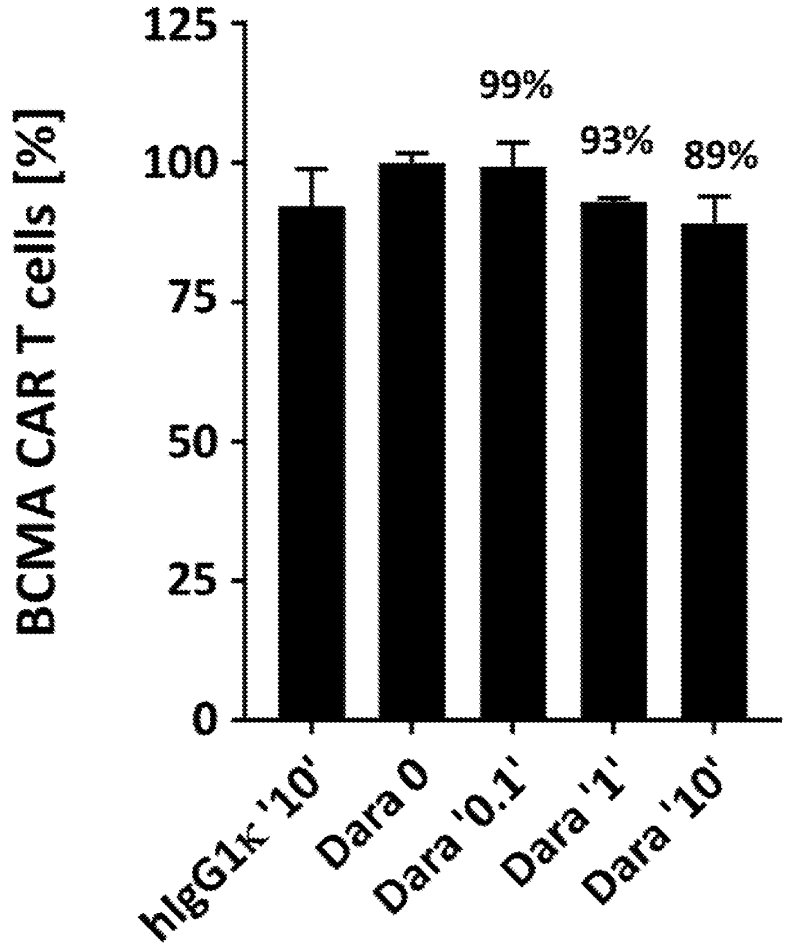

BCMA CAR T cells [%]
125
100
75
50
25
0
99%
93%
89%
hIgG1κ '10'
Dara 0
Dara '0.1'
Dara '1'
Dara '10'

FIG. 10B

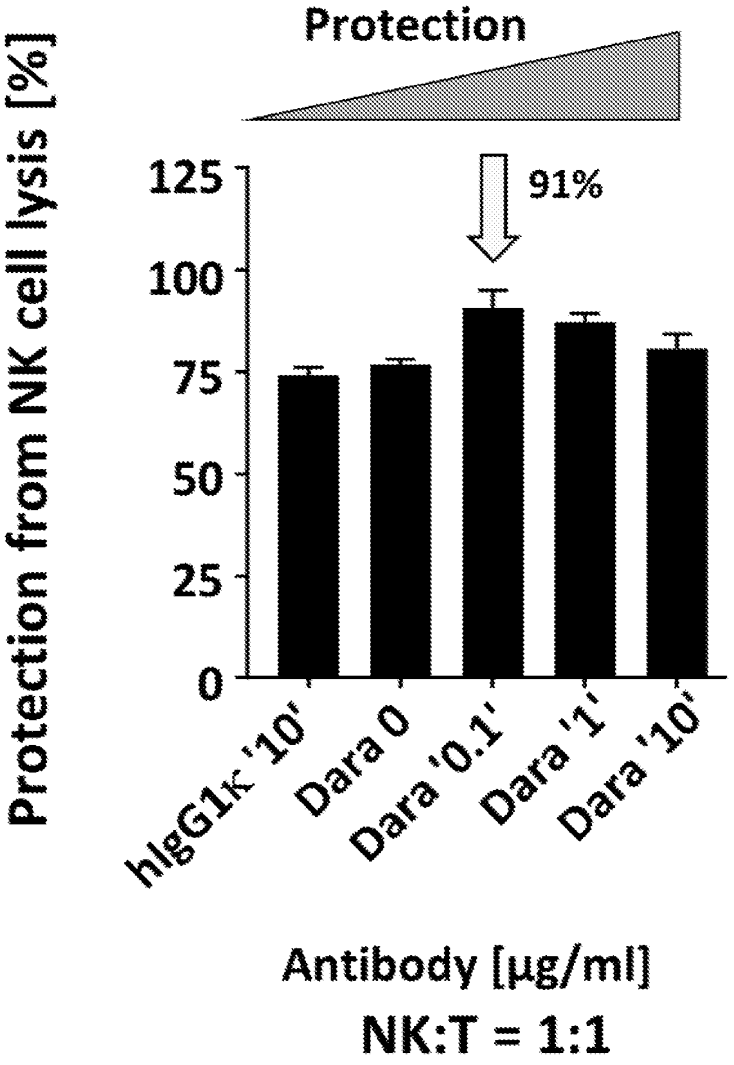

Protection
91%
125
100
75
50
25
0
Protection from NK cell lysis [%]
hIgG1κ '10'
Dara 0
Dara '0.1'
Dara '1'
Dara '10'
Antibody [µg/ml]
NK:T = 1:1

FIG. 10C

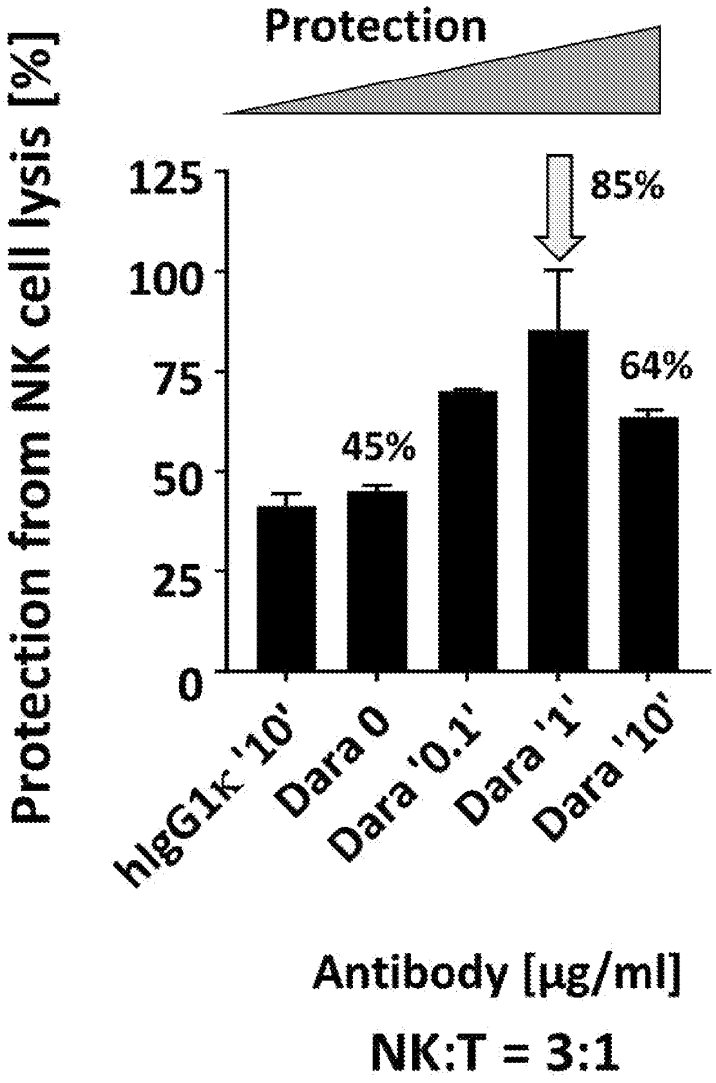

Protection
Protection from NK cell lysis [%]
125
100
75
50
25
0
85%
64%
45%
hIgG1κ '10'
Dara 0
Dara '0.1'
Dara '1'
Dara '10'
Antibody [µg/ml]
NK:T = 3:1

FIG. 11A

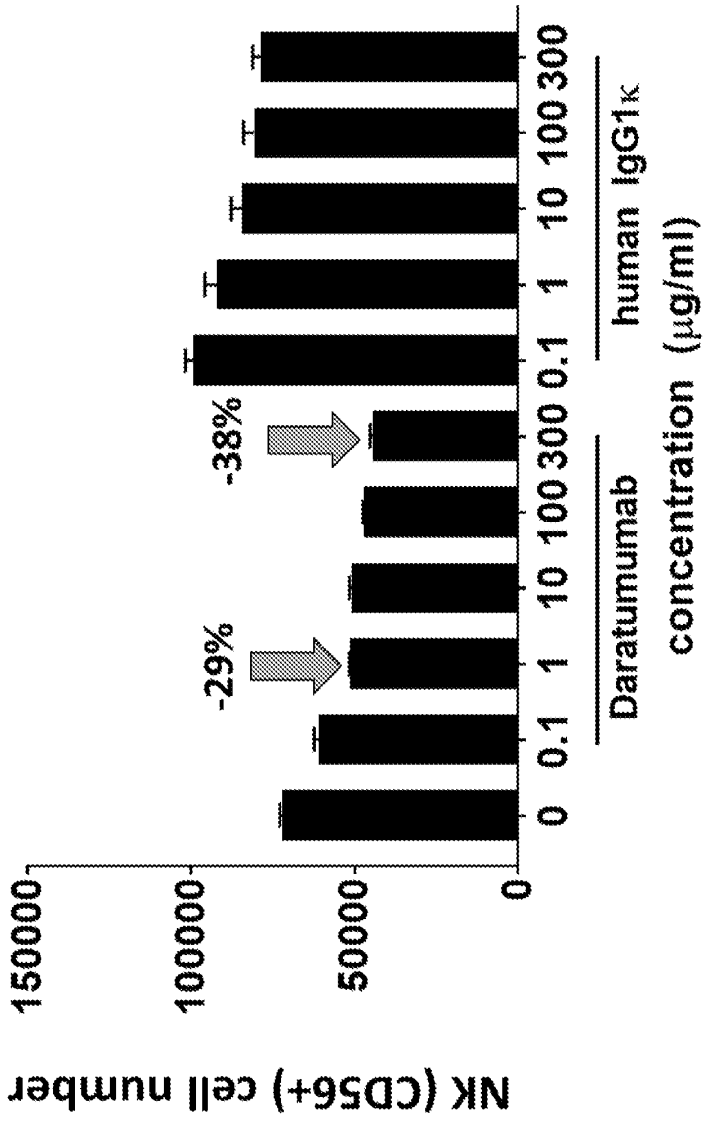

NK cell count: 72 hr post Dara
NK (CD56+) cell number
150000
100000
50000
0
-29%
-38%
0
0.1
1
10
100
300
0.1
1
10
100
300
Daratumumab
human IgG1κ
concentration (μg/ml)

FIG. 11B

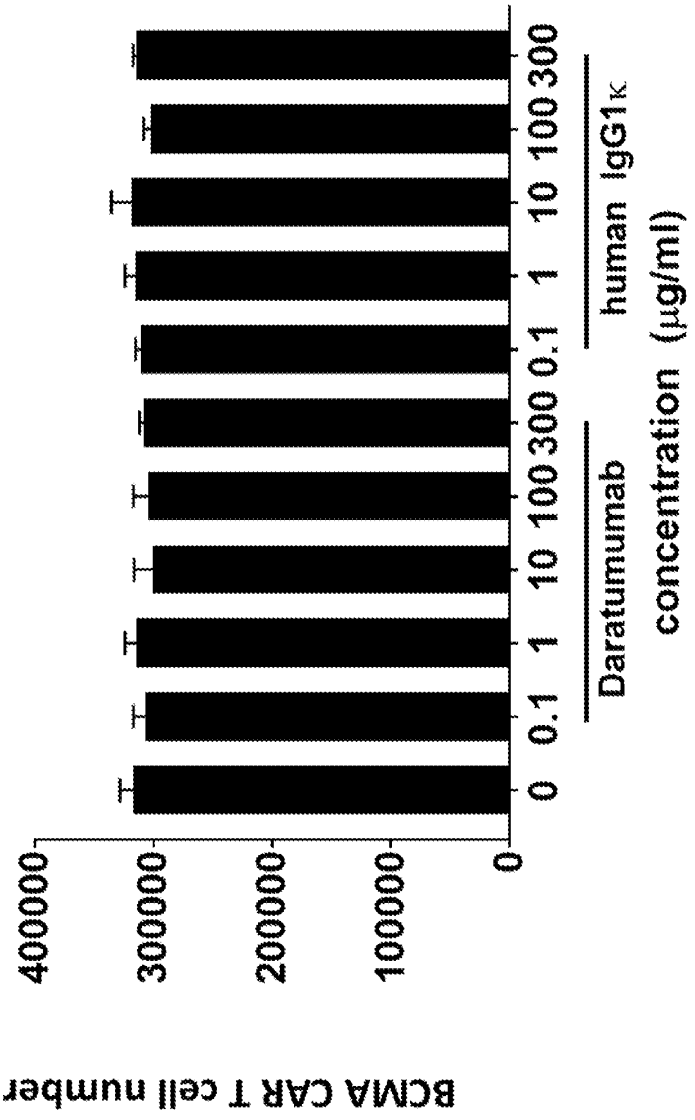

CAR T cell count: 72 hr post Dara
BCMA CAR T cell number
400000
300000
200000
100000
0
0 0.1 1 10 100 300 0.1 1 10 100 300
Daratumumab
human IgG1κ
concentration (μg/ml)

FIG. 12

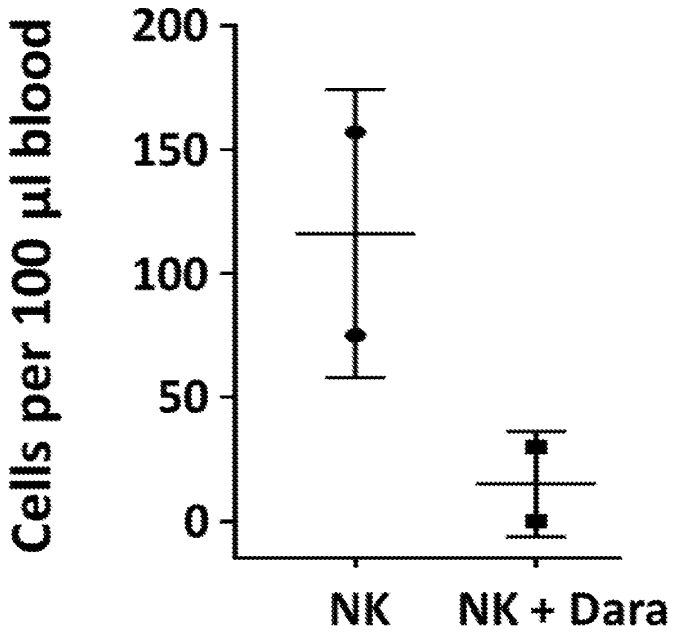


FIG. 13

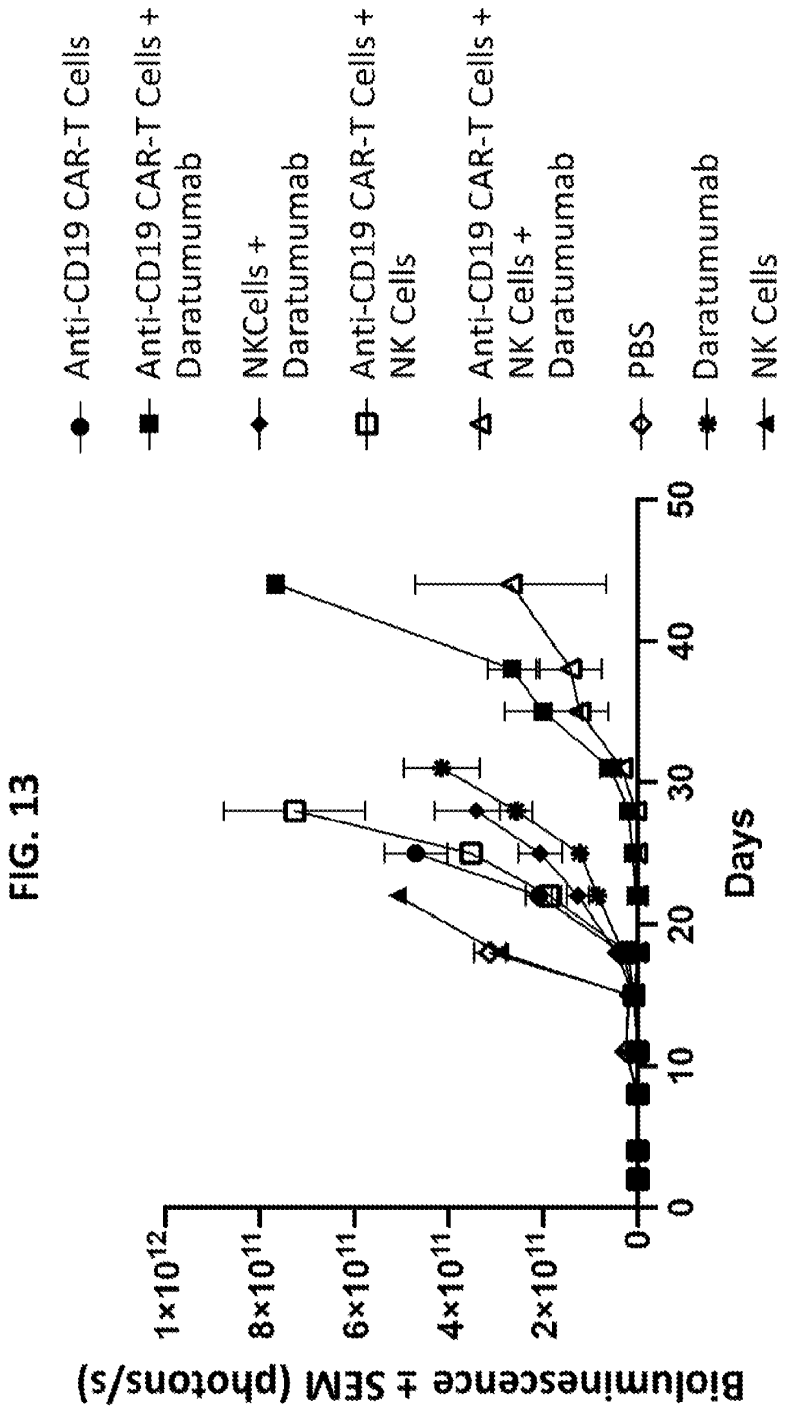

Anti-CD19 CAR-T Cells
Anti-CD19 CAR-T Cells + Daratumumab
NKCells + Daratumumab
Anti-CD19 CAR-T Cells + NK Cells
Anti-CD19 CAR-T Cells + NK Cells + Daratumumab
PBS
Daratumumab
NK Cells
Bioluminescence ± SEM (photons/s)
1×10^12
8×10^11
6×10^11
4×10^11
2×10^11
0
0
10
20
30
40
50
Days

FIG. 14A

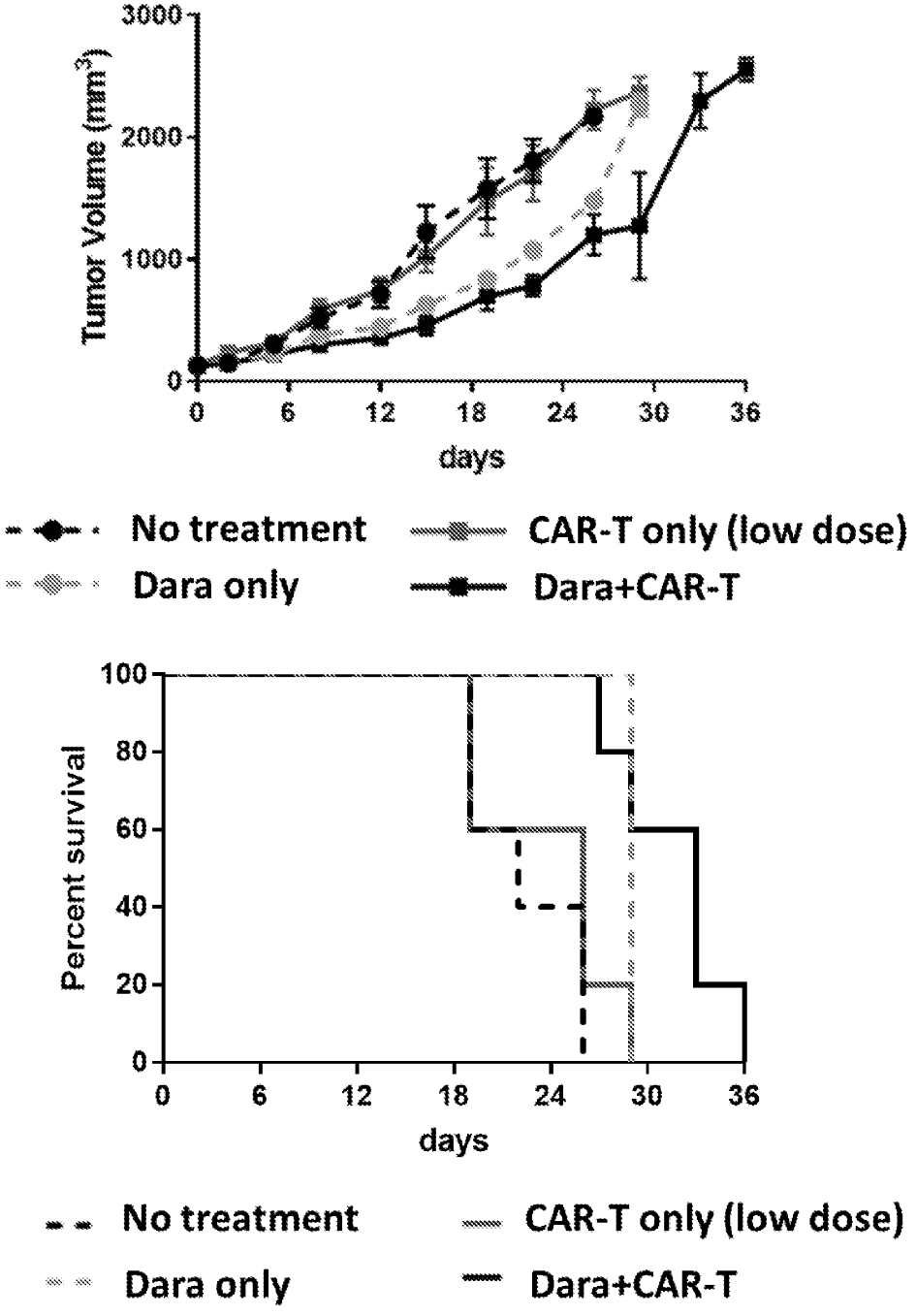

Tumor Volume (mm3)
3000
2000
1000
0
0
6
12
18
24
30
36
days
No treatment
CAR-T only (low dose)
Dara only
Dara+CAR-T
Percent survival
100
80
60
40
20
0
0
6
12
18
24
30
36
days
No treatment
CAR-T only (low dose)
Dara only
Dara+CAR-T

FIG. 14B

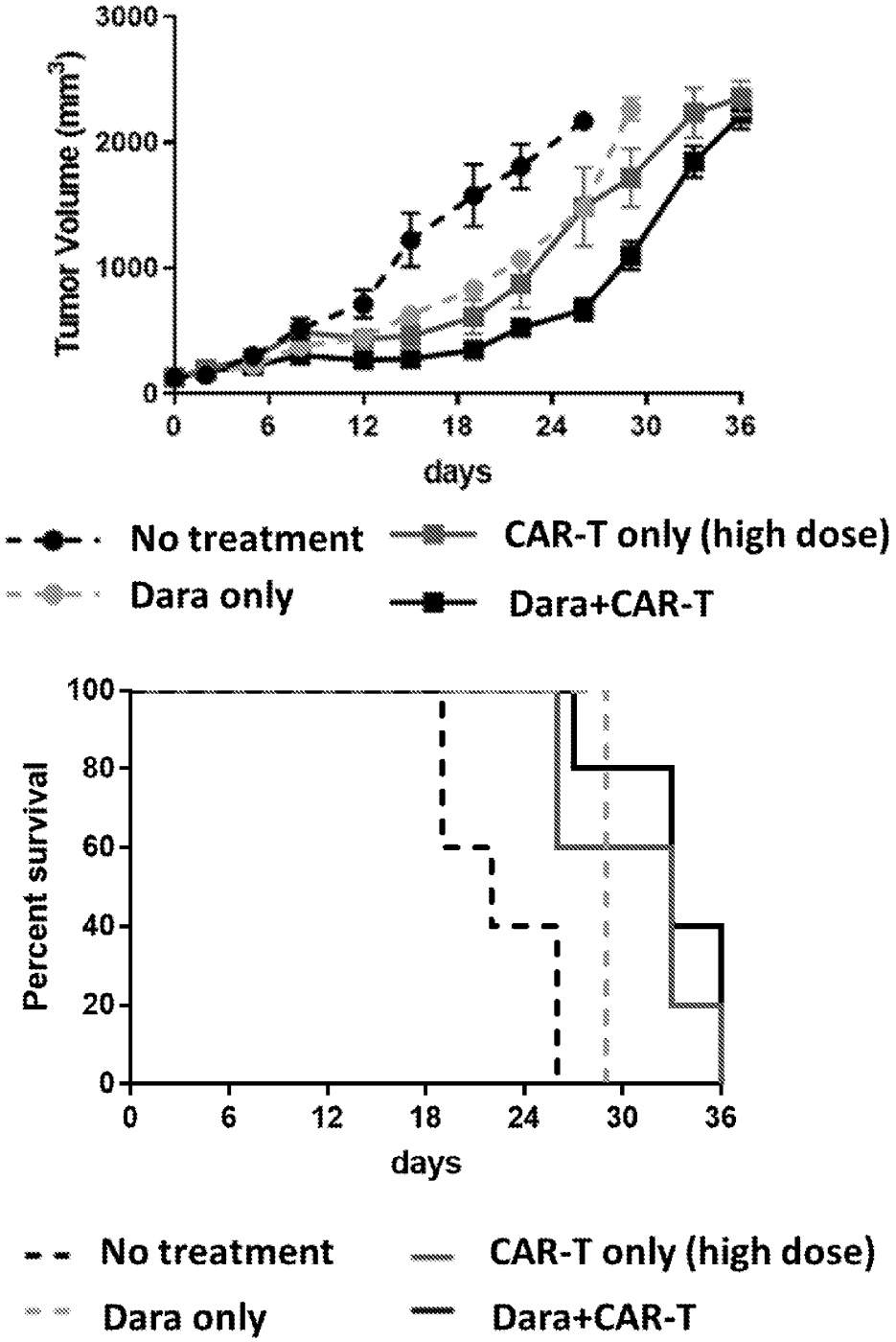
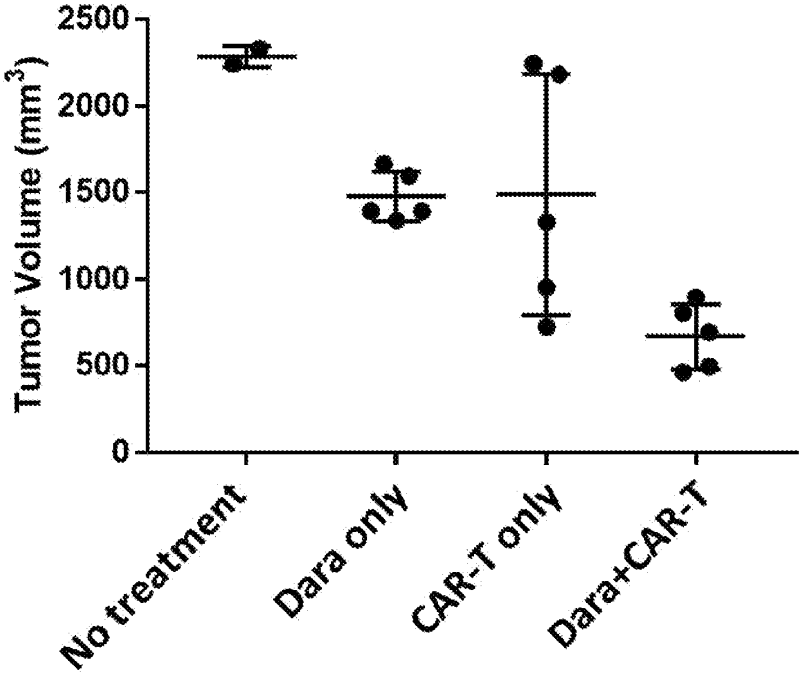

Tumor Volume (mm3)
3000
2000
1000
0
0
6
12
18
24
30
36
days
No treatment
CAR-T only (high dose)
Dara only
Dara+CAR-T
Percent survival
100
80
60
40
20
0
0
6
12
18
24
30
36
days
No treatment
CAR-T only (high dose)
Dara only
Dara+CAR-T

FIG. 14C


Tumor Volume (mm3)
2500
2000
1500
1000
500
0
No treatment
Dara only
CAR-T only
Dara+CAR-T