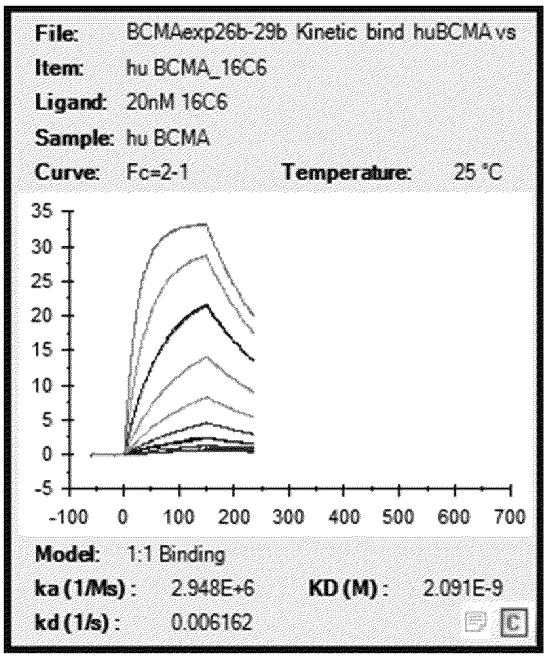
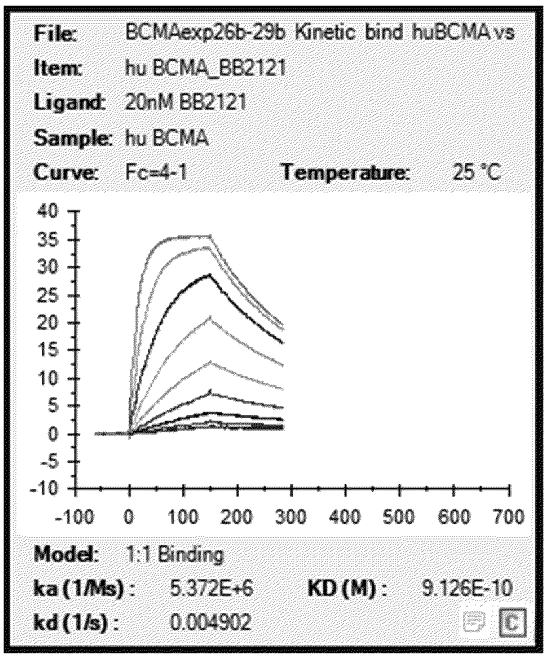
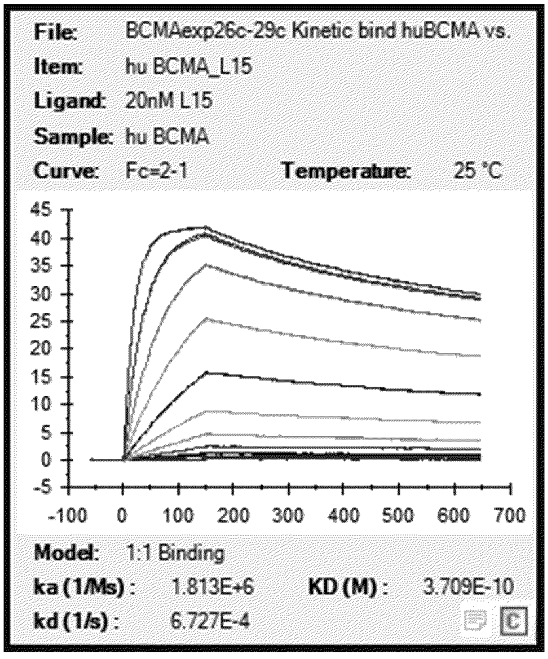
FIG. 1


File: BCMAexp26b-29b Kinetic bind huBCMA vs
Item: hu BCMA_16C6
Ligand: 20nM 16C6
Sample: hu BCMA
Curve: Fc=2-1 Temperature: 25 °C
Model: 1:1 Binding
ka (1/Ms) : 2.948E+6 KD (M) : 2.091E-9
kd (1/s) : 0.006162


File: BCMAexp26b-29b Kinetic bind huBCMA vs
Item: hu BCMA_BB2121
Ligand: 20nM BB2121
Sample: hu BCMA
Curve: Fc=4-1 Temperature: 25 °C
Model: 1:1 Binding
ka (1/Ms) : 5.372E+6 KD (M) : 9.126E-10
kd (1/s) : 0.004902


File: BCMAexp26c-29c Kinetic bind huBCMA vs.
Item: hu BCMA_L15
Ligand: 20nM L15
Sample: hu BCMA
Curve: Fc=2-1 Temperature: 25 °C
Model: 1:1 Binding
ka (1/Ms) : 1.813E+6 KD (M) : 3.709E-10
kd (1/s) : 6.727E-4

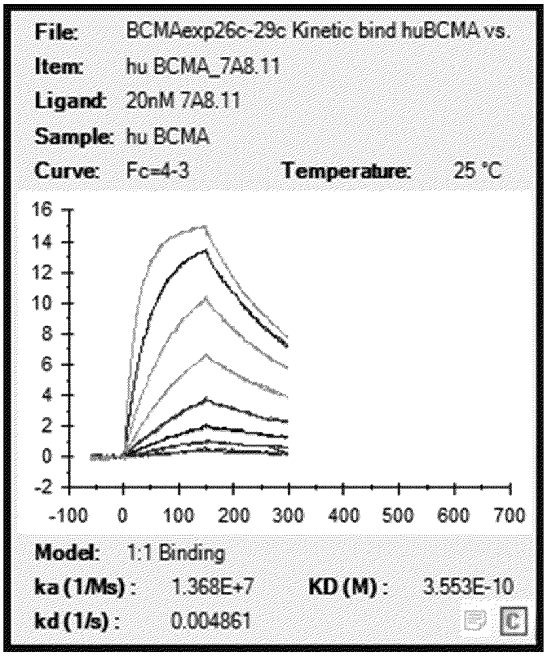

File: BCMAexp26c-29c Kinetic bind huBCMA vs.
Item: hu BCMA_7A8.11
Ligand: 20nM 7A8.11
Sample: hu BCMA
Curve: Fc=4-3 Temperature: 25 °C
Model: 1:1 Binding
ka (1/Ms) : 1.368E+7 KD (M) : 3.553E-10
kd (1/s) : 0.004861

FIG. 2

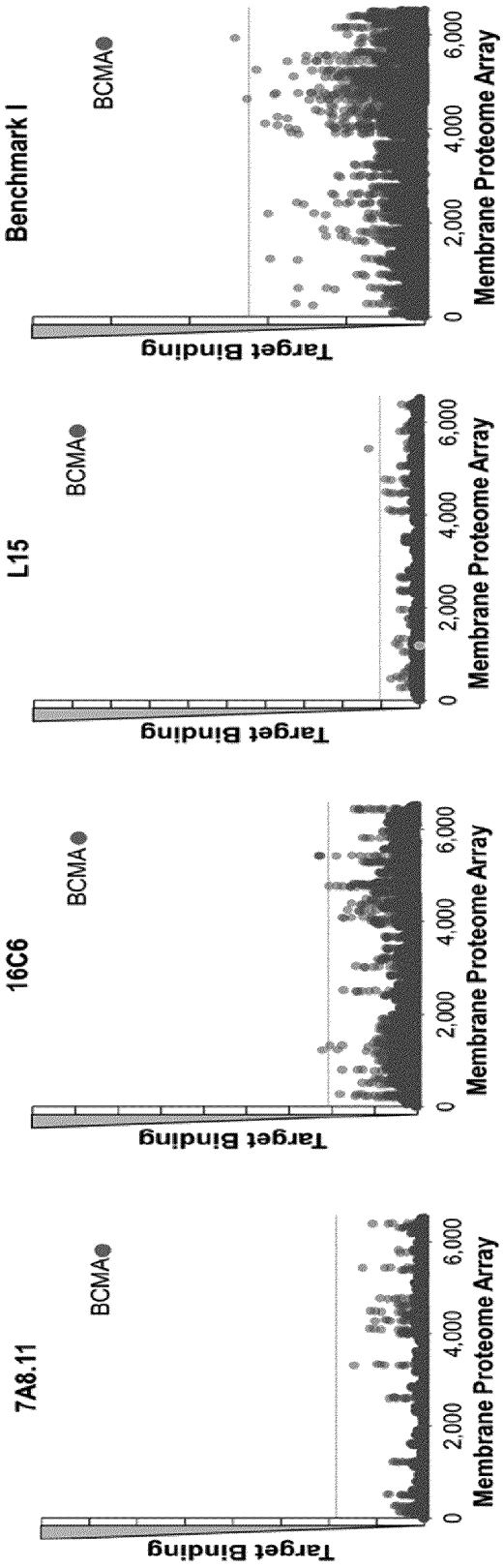

Benchmark I
BCMA
Target Binding
0
2,000
4,000
6,000
Membrane Proteome Array
L15
BCMA
Target Binding
0
2,000
4,000
6,000
Membrane Proteome Array
16C6
BCMA
Target Binding
0
2,000
4,000
6,000
Membrane Proteome Array
7A8.11
BCMA
Target Binding
0
2,000
4,000
6,000
Membrane Proteome Array

FIG. 3

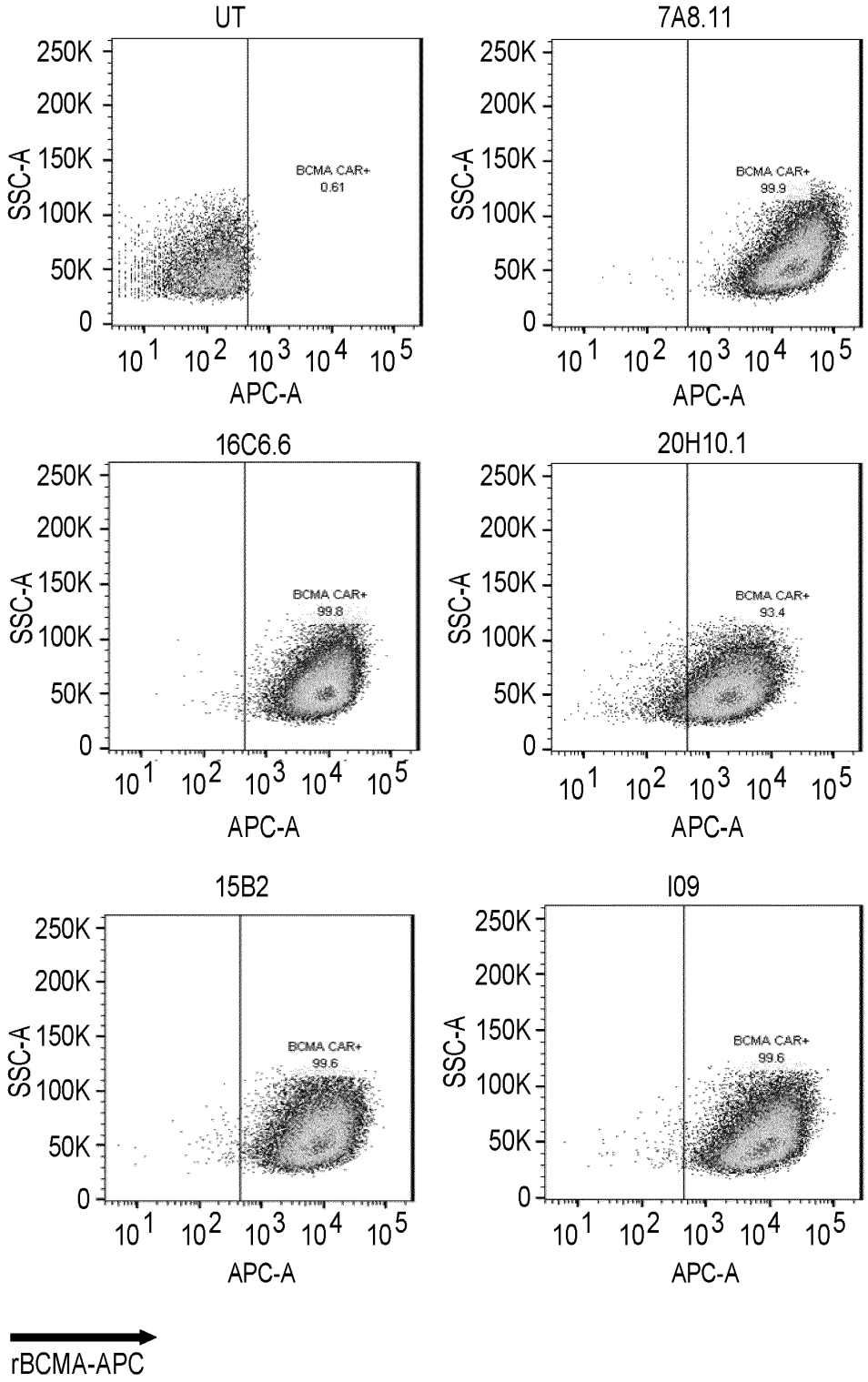

UT
BCMA CAR+
0.61
7A8.11
BCMA CAR+
99.9
16C6.6
BCMA CAR+
99.8
20H10.1
BCMA CAR+
93.4
15B2
BCMA CAR+
99.6
I09
BCMA CAR+
99.6
SSC-A
APC-A
250K
200K
150K
100K
50K
0
10^1 10^2 10^3 10^4 10^5
rBCMA-APC

FIG. 3 continued

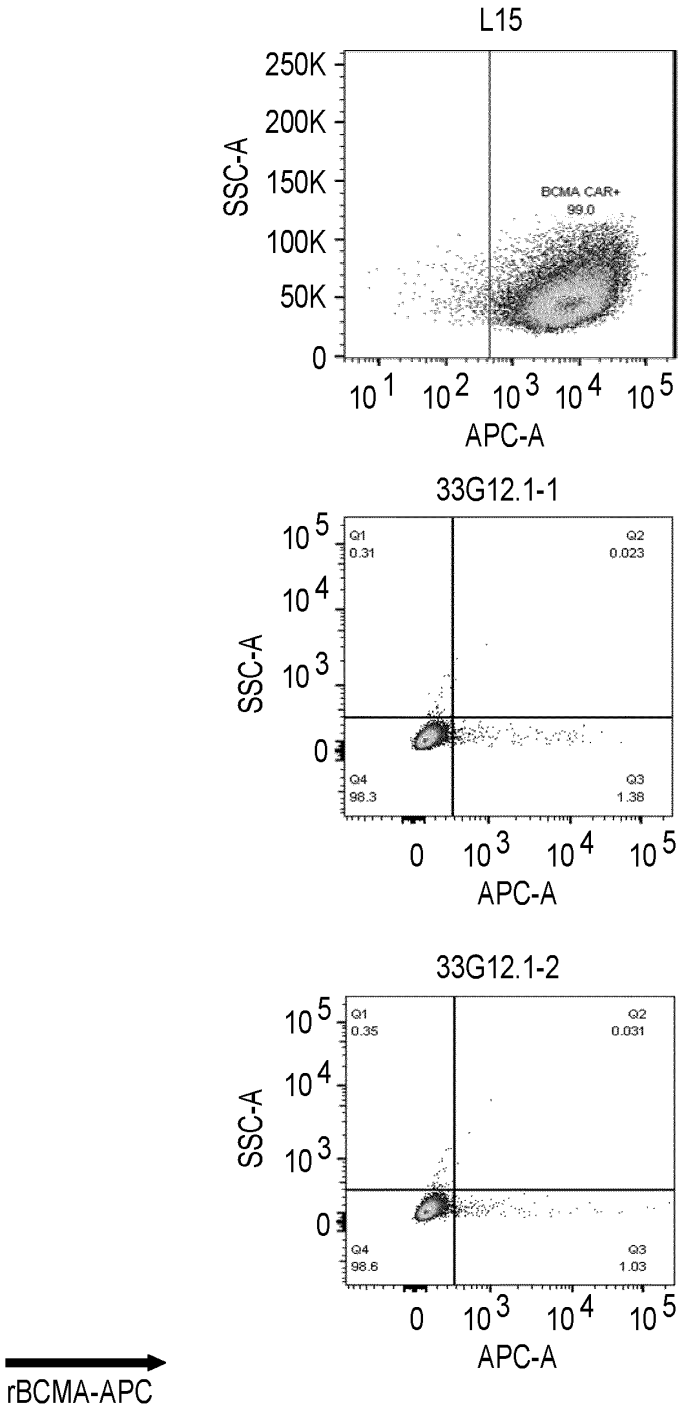


FIG. 3 continued

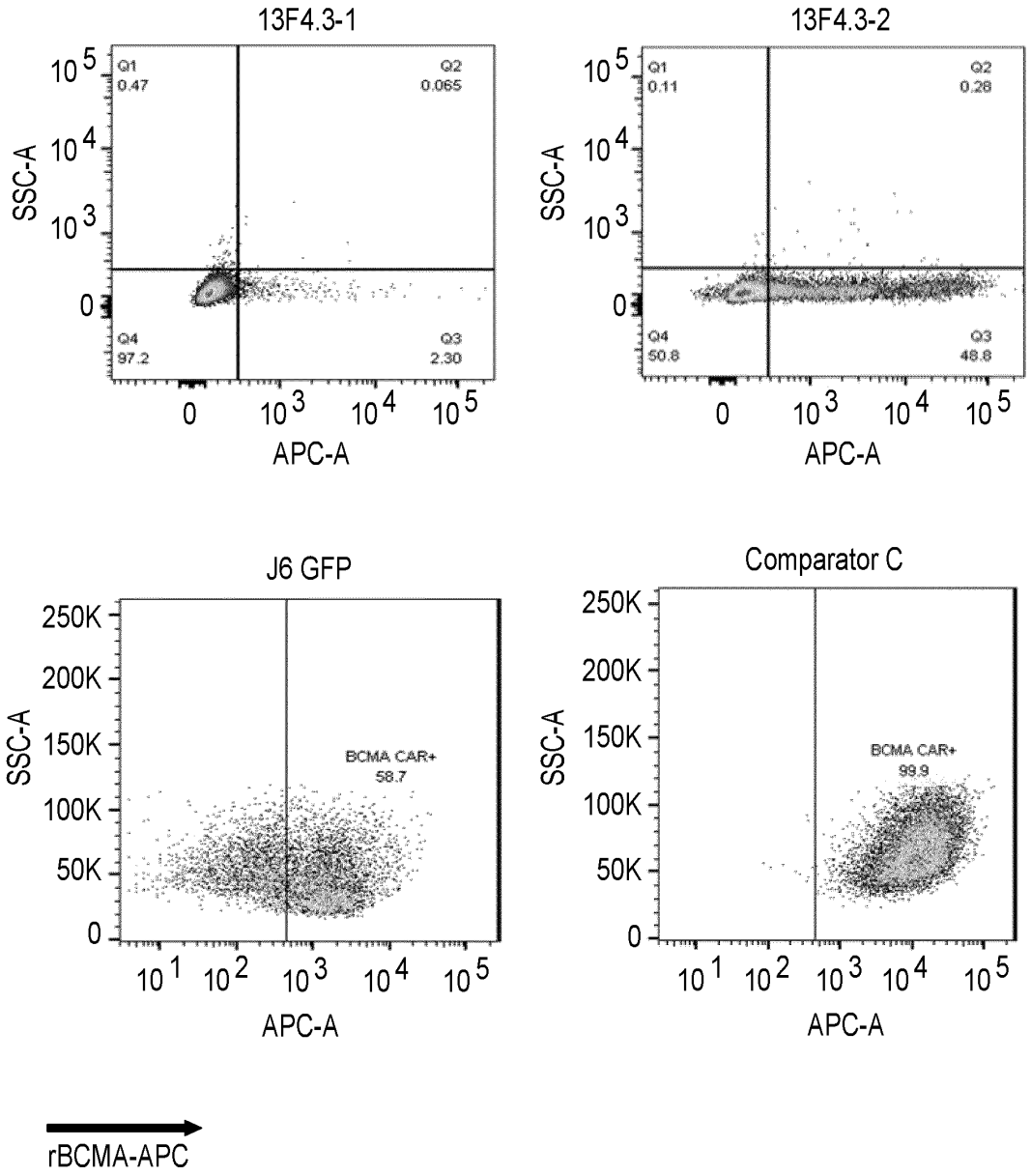


FIG. 4

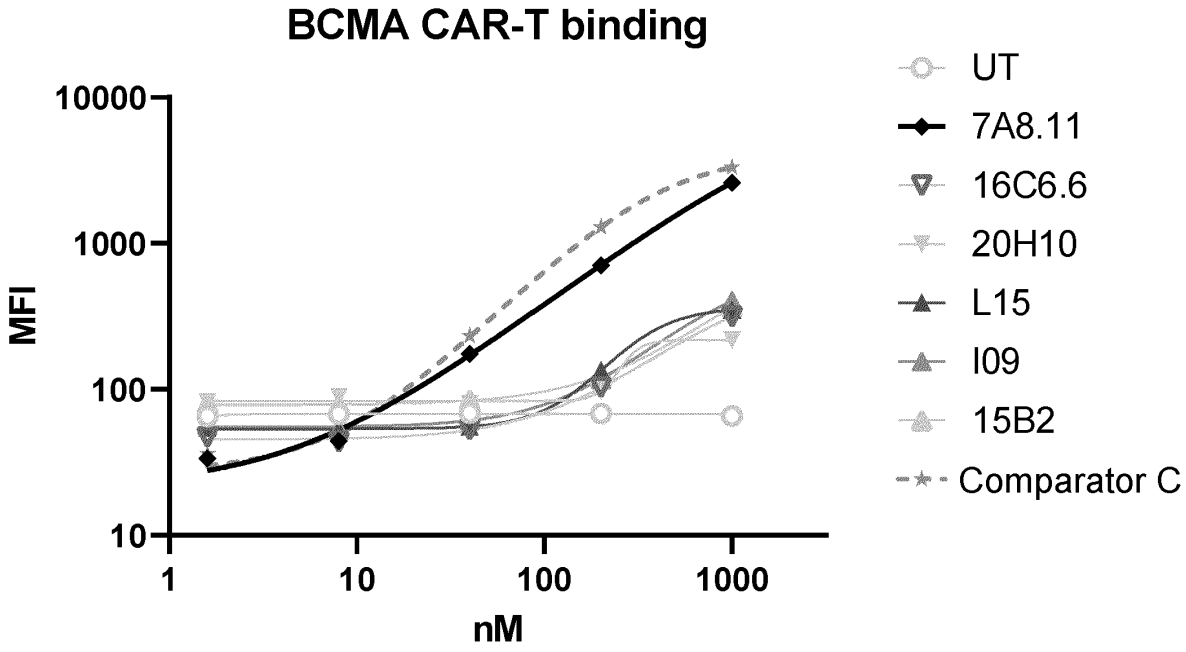

BCMA CAR-T binding
MFI
10000
1000
100
10
1
10
100
1000
nM
UT
7A8.11
16C6.6
20H10
L15
I09
15B2
Comparator C

FIG. 5

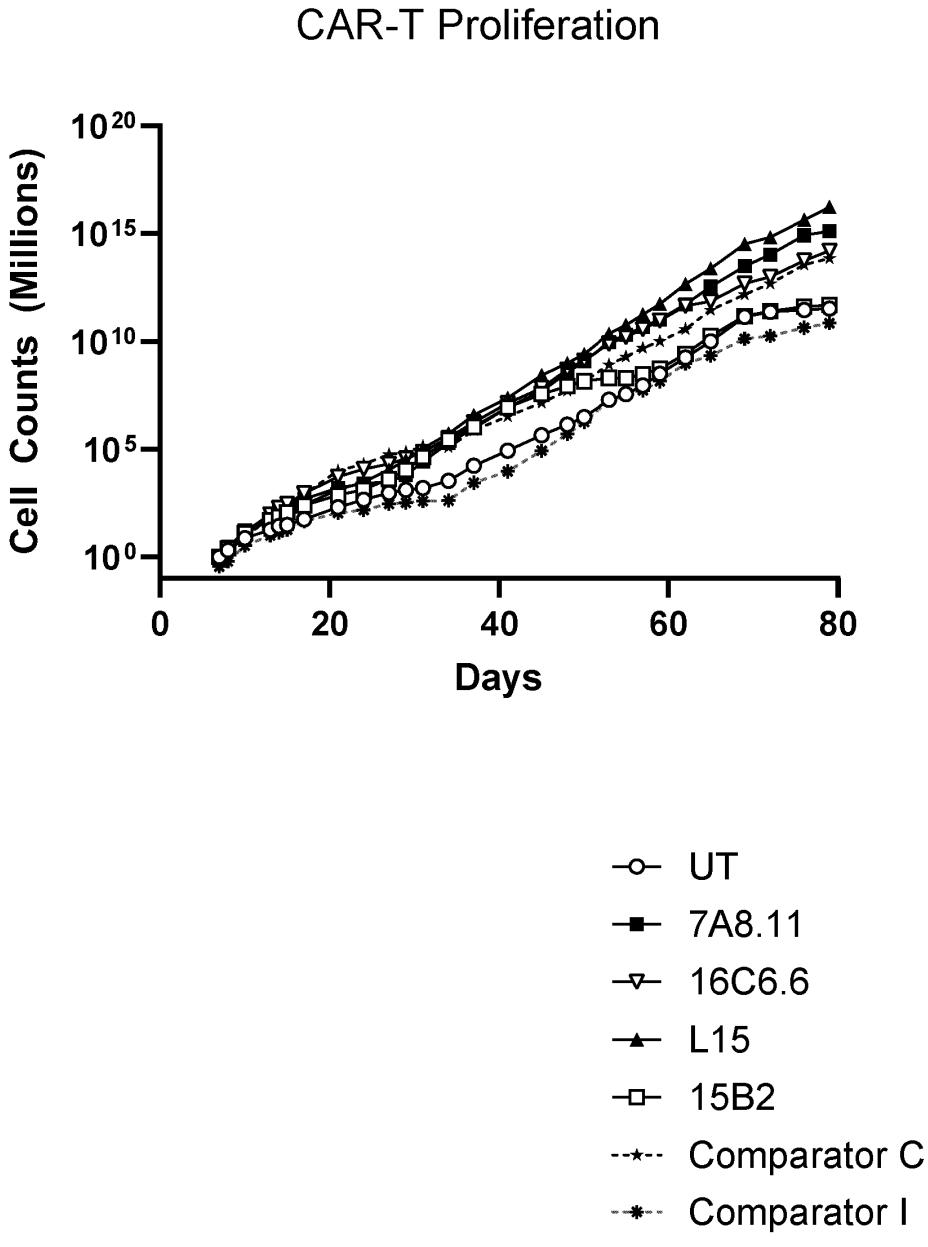

CAR-T Proliferation
Cell Counts (Millions)
10^20
10^15
10^10
10^5
10^0
0
20
40
60
80
Days
UT
7A8.11
16C6.6
L15
15B2
Comparator C
Comparator I

FIG. 6A

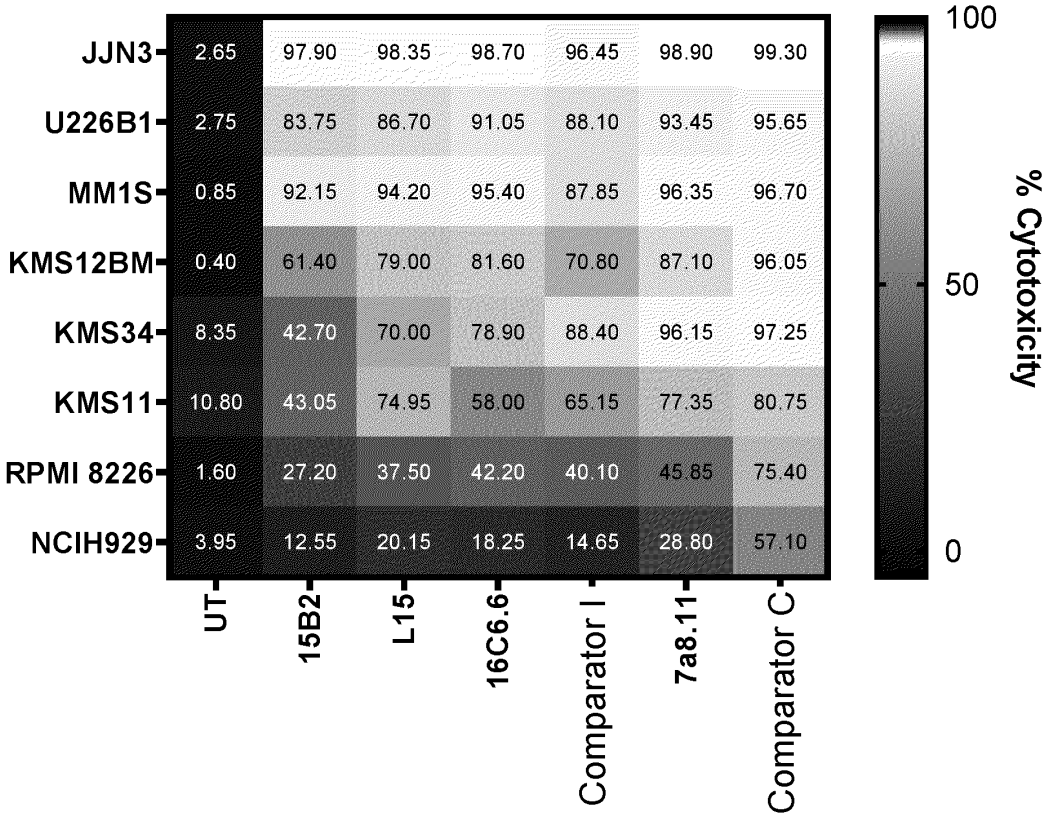

JJN3
U226B1
MM1S
KMS12BM
KMS34
KMS11
RPMI 8226
NCIH929
2.65 97.90 98.35 98.70 96.45 98.90 99.30
2.75 83.75 86.70 91.05 88.10 93.45 95.65
0.85 92.15 94.20 95.40 87.85 96.35 96.70
0.40 61.40 79.00 81.60 70.80 87.10 96.05
8.35 42.70 70.00 78.90 88.40 96.15 97.25
10.80 43.05 74.95 58.00 65.15 77.35 80.75
1.60 27.20 37.50 42.20 40.10 45.85 75.40
3.95 12.55 20.15 18.25 14.65 28.80 57.10
UT
15B2
L15
16C6.6
Comparator I
7a8.11
Comparator C
100
50
0
% Cytotoxicity

FIG. 6B

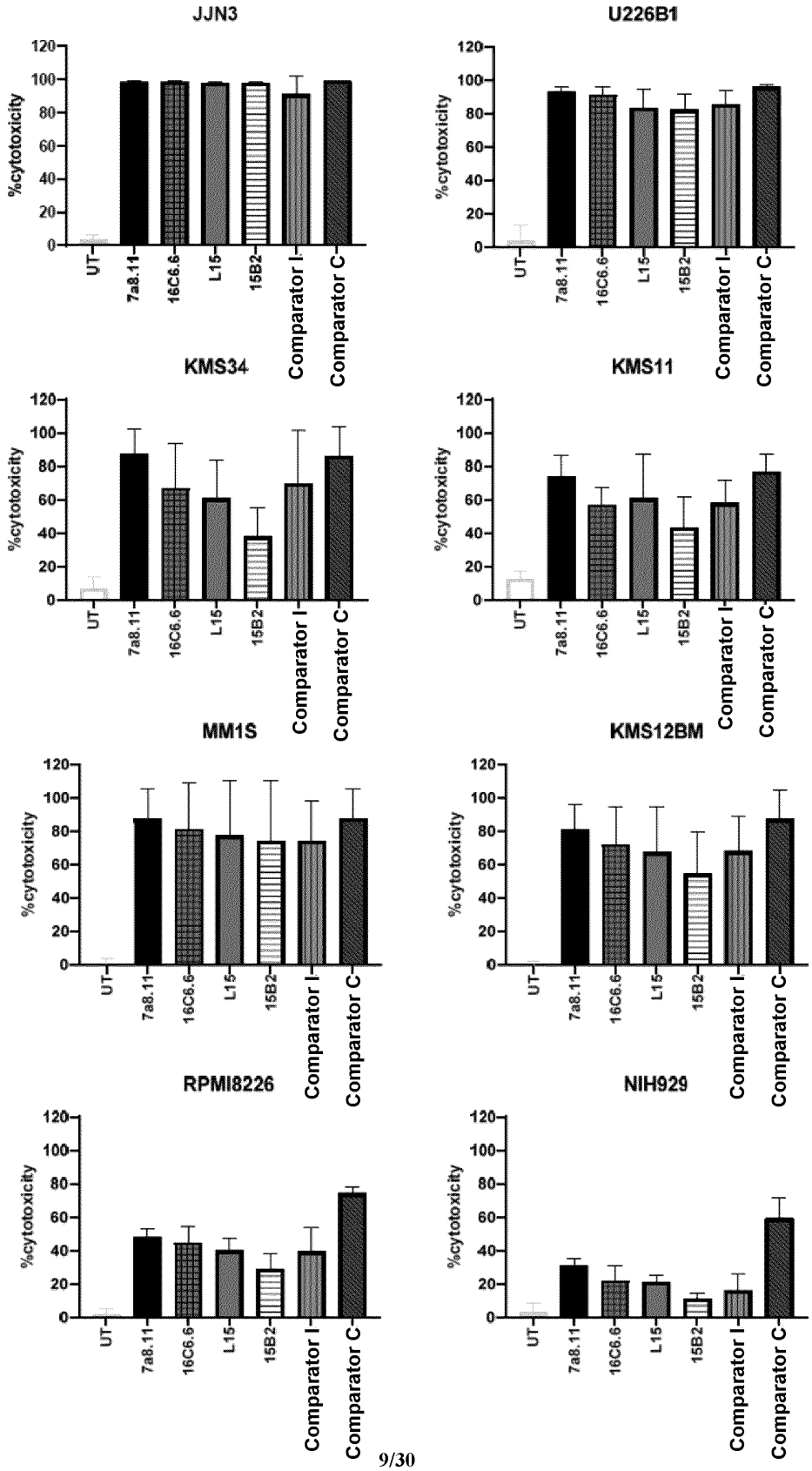

JJN3
U226B1
KMS34
KMS11
MM1S
KMS12BM
RPMI8226
NIH929
%cytotoxicity
0
20
40
60
80
100
120
UT
7a8.11
16C6.6
L15
15B2
Comparator I
Comparator C

FIG. 7

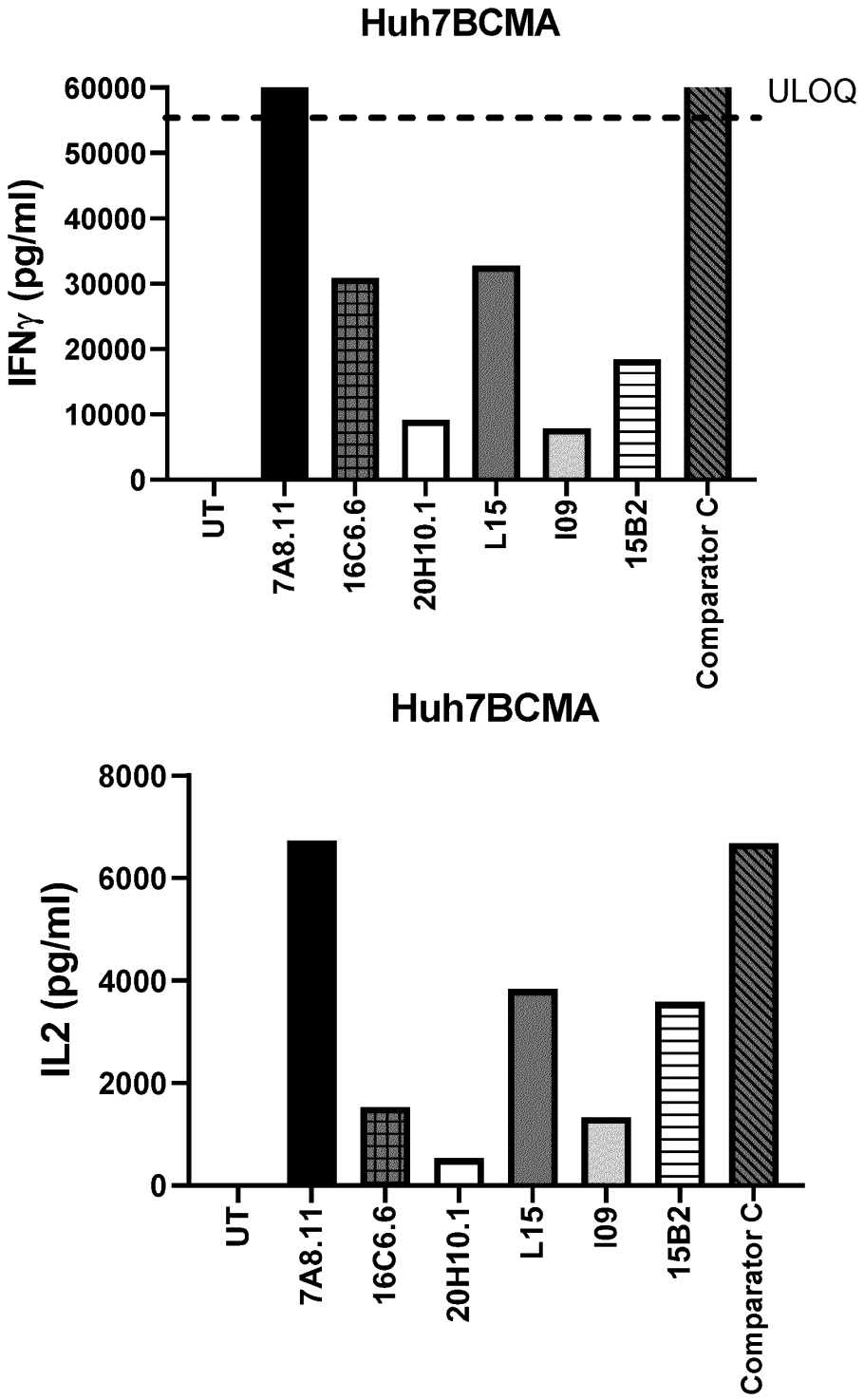

Huh7BCMA
IFNγ (pg/ml)
60000
50000
40000
30000
20000
10000
0
ULOQ
UT
7A8.11
16C6.6
20H10.1
L15
I09
15B2
Comparator C
Huh7BCMA
IL2 (pg/ml)
8000
6000
4000
2000
0
UT
7A8.11
16C6.6
20H10.1
L15
I09
15B2
Comparator C

FIG. 8

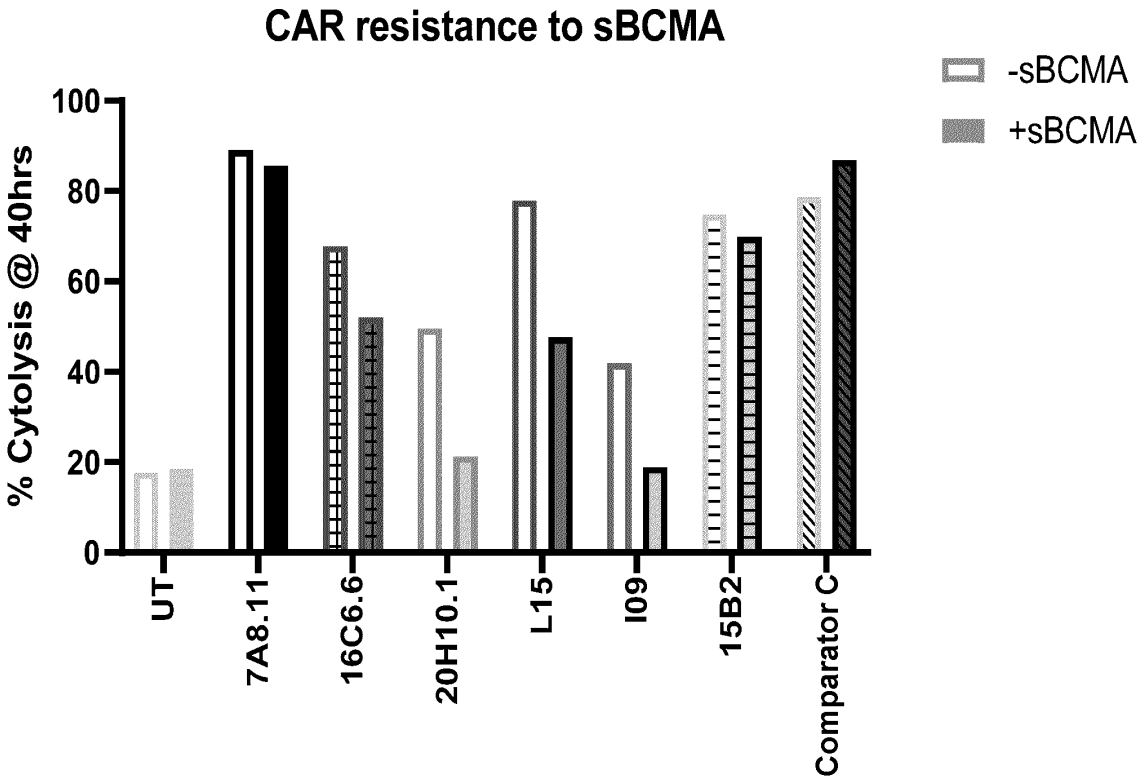

CAR resistance to sBCMA
-sBCMA
+sBCMA
% Cytolysis @ 40hrs
100
80
60
40
20
0
UT
7A8.11
16C6.6
20H10.1
L15
I09
15B2
Comparator C

FIG. 9

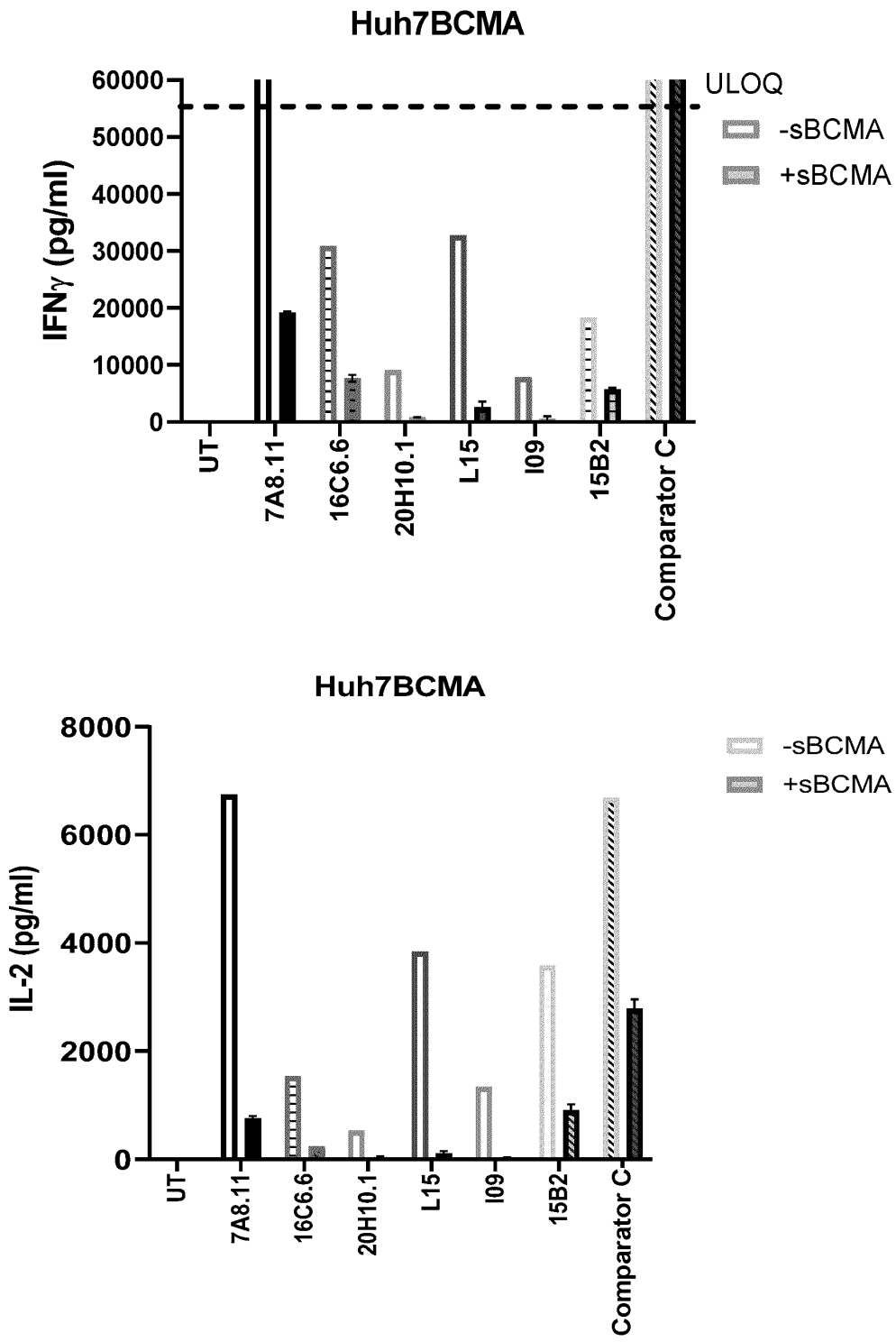

Huh7BCMA
IFNγ (pg/ml)
60000
50000
40000
30000
20000
10000
0
ULOQ
-sBCMA
+sBCMA
UT
7A8.11
16C6.6
20H10.1
L15
I09
15B2
Comparator C
Huh7BCMA
IL-2 (pg/ml)
8000
6000
4000
2000
0
-sBCMA
+sBCMA
UT
7A8.11
16C6.6
20H10.1
L15
I09
15B2
Comparator C

FIG. 10A

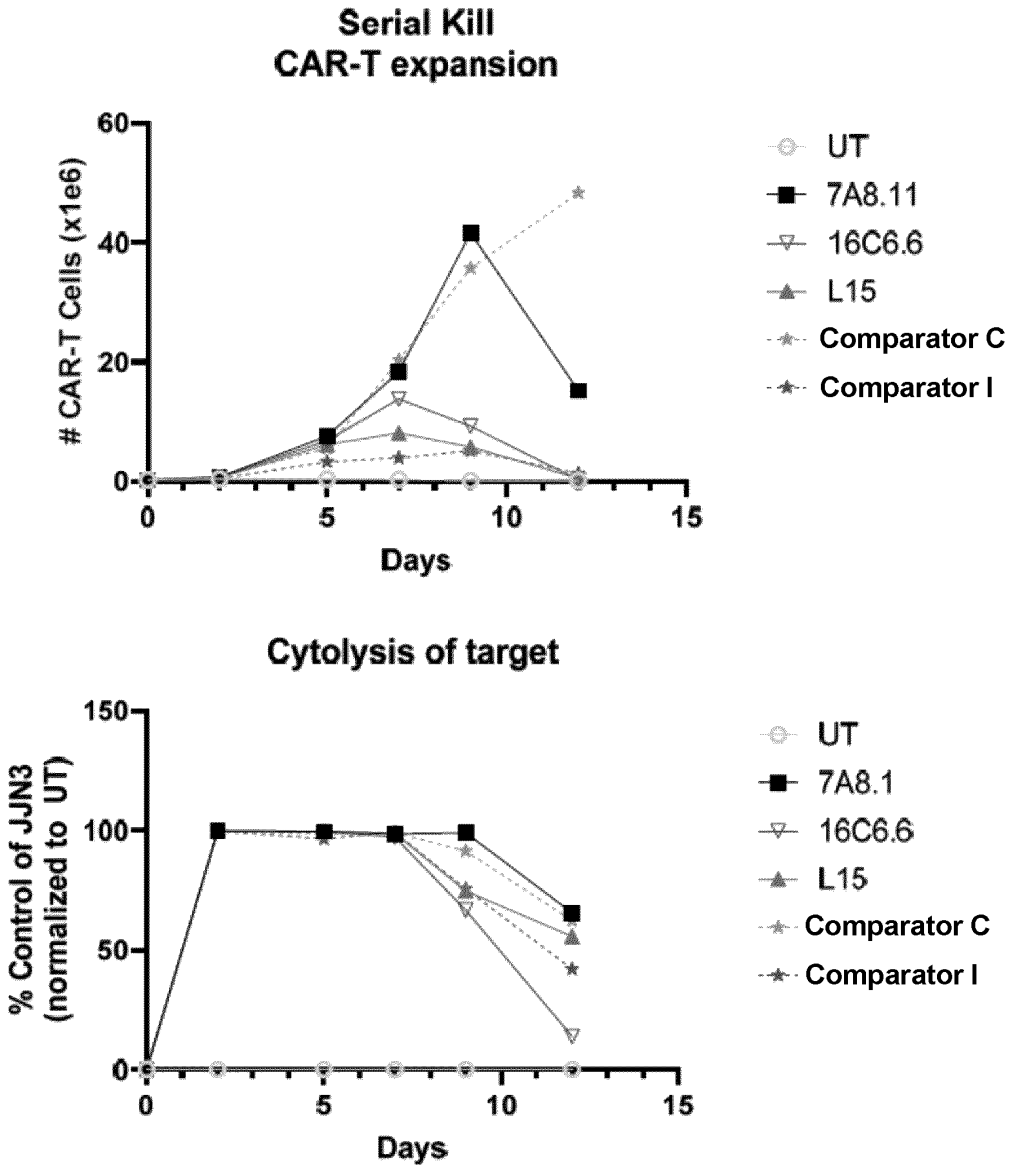

Serial Kill
CAR-T expansion
CAR-T Cells (x1e6)
60
40
20
0
0
5
10
15
Days
UT
7A8.11
16C6.6
L15
Comparator C
Comparator I
Cytolysis of target
% Control of JJN3 (normalized to UT)
150
100
50
0
0
5
10
15
Days
UT
7A8.1
16C6.6
L15
Comparator C
Comparator I

FIG. 10B

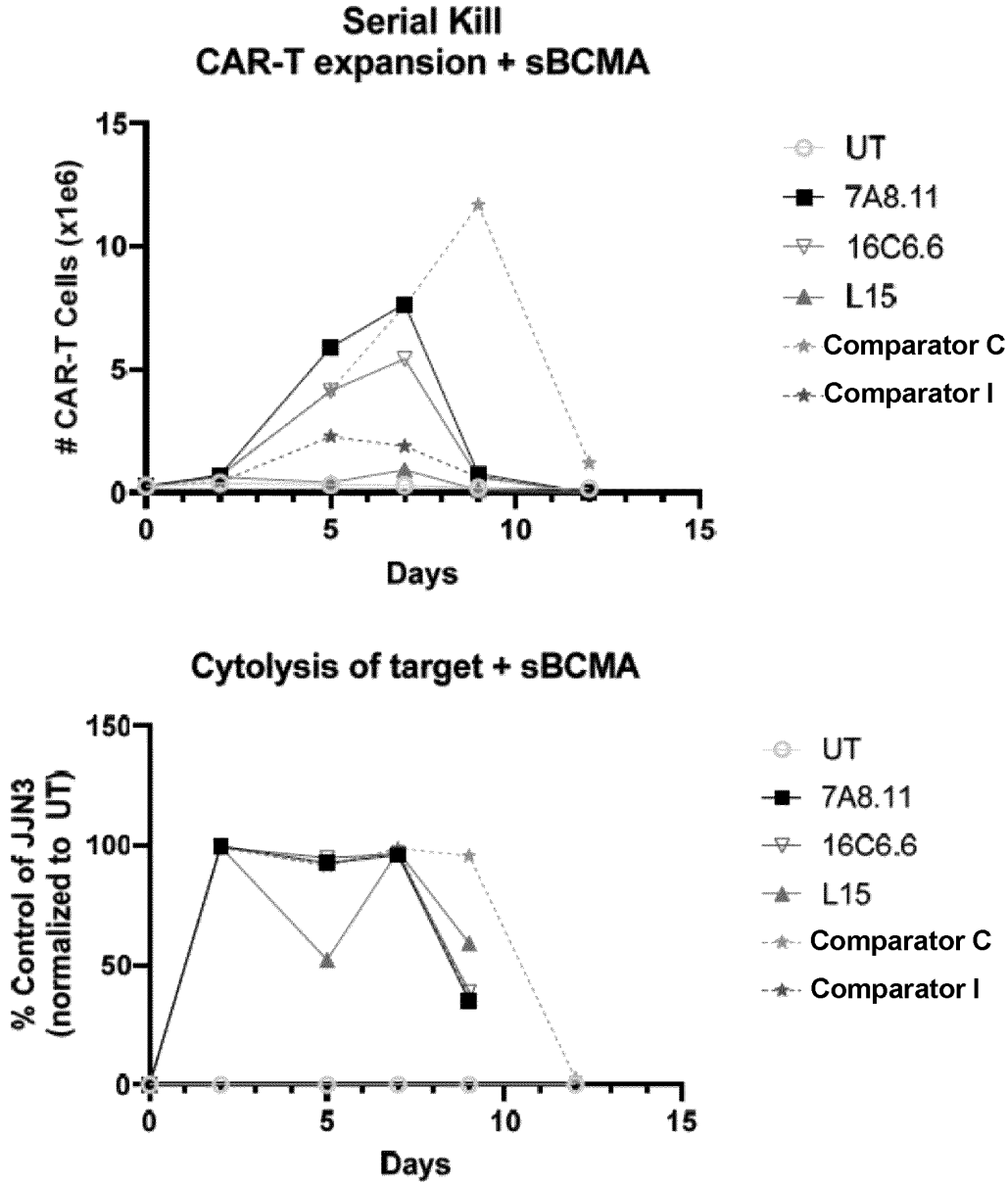

Serial Kill
CAR-T expansion + sBCMA
CAR-T Cells (x1e6)
15
10
5
0
0
5
10
15
Days
UT
7A8.11
16C6.6
L15
Comparator C
Comparator I
Cytolysis of target + sBCMA
% Control of JJN3 (normalized to UT)
150
100
50
0
0
5
10
15
Days
UT
7A8.11
16C6.6
L15
Comparator C
Comparator I

FIG. 11

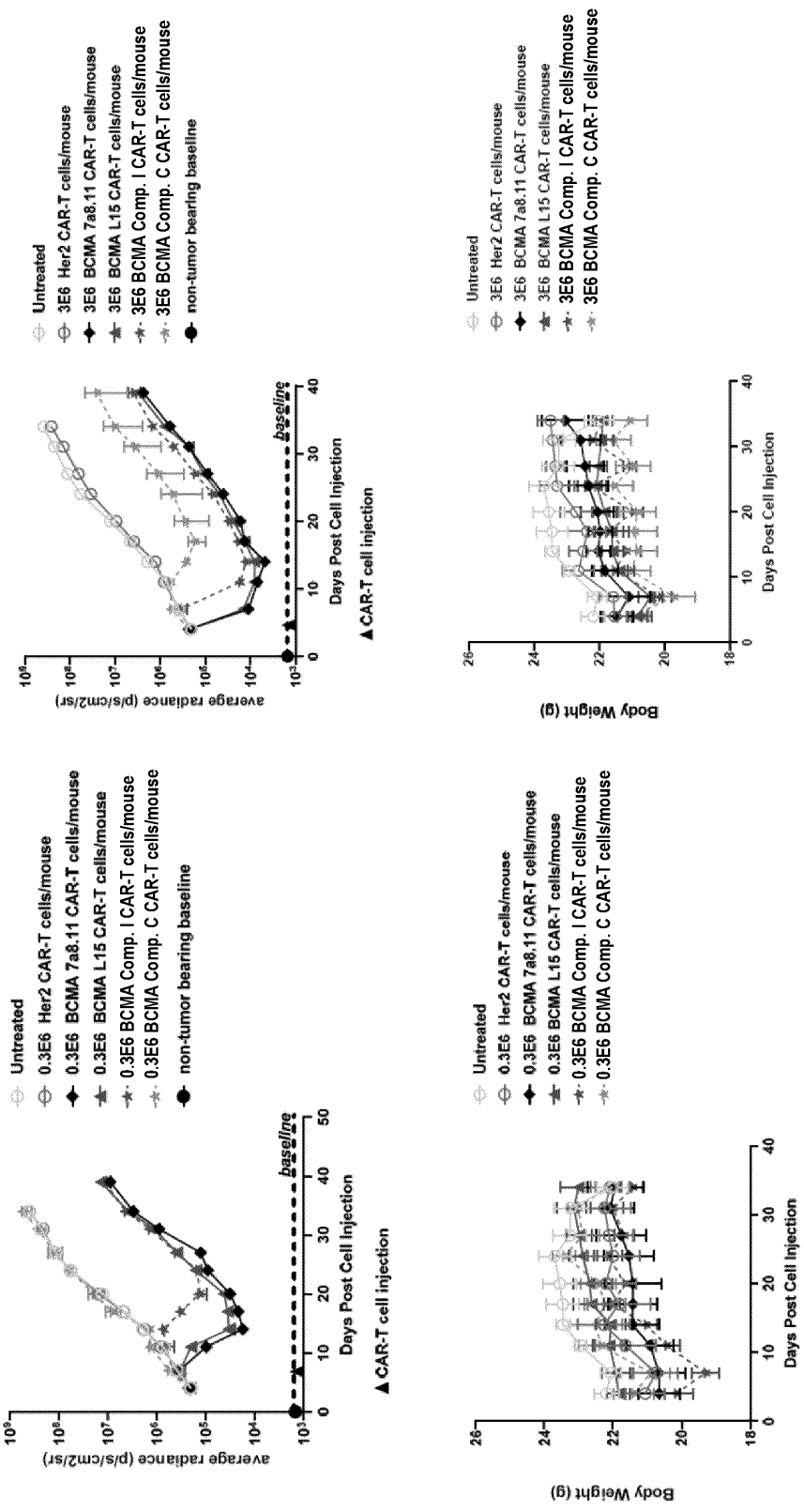

Untreated
0.3E6 Her2 CAR-T cells/mouse
0.3E6 BCMA 7a8.11 CAR-T cells/mouse
0.3E6 BCMA L15 CAR-T cells/mouse
0.3E6 BCMA Comp. I CAR-T cells/mouse
0.3E6 BCMA Comp. C CAR-T cells/mouse
non-tumor bearing baseline
average radiance (p/s/cm2/sr)
baseline
Days Post Cell Injection
▲CAR-T cell injection
Body Weight (g)

FIG. 12

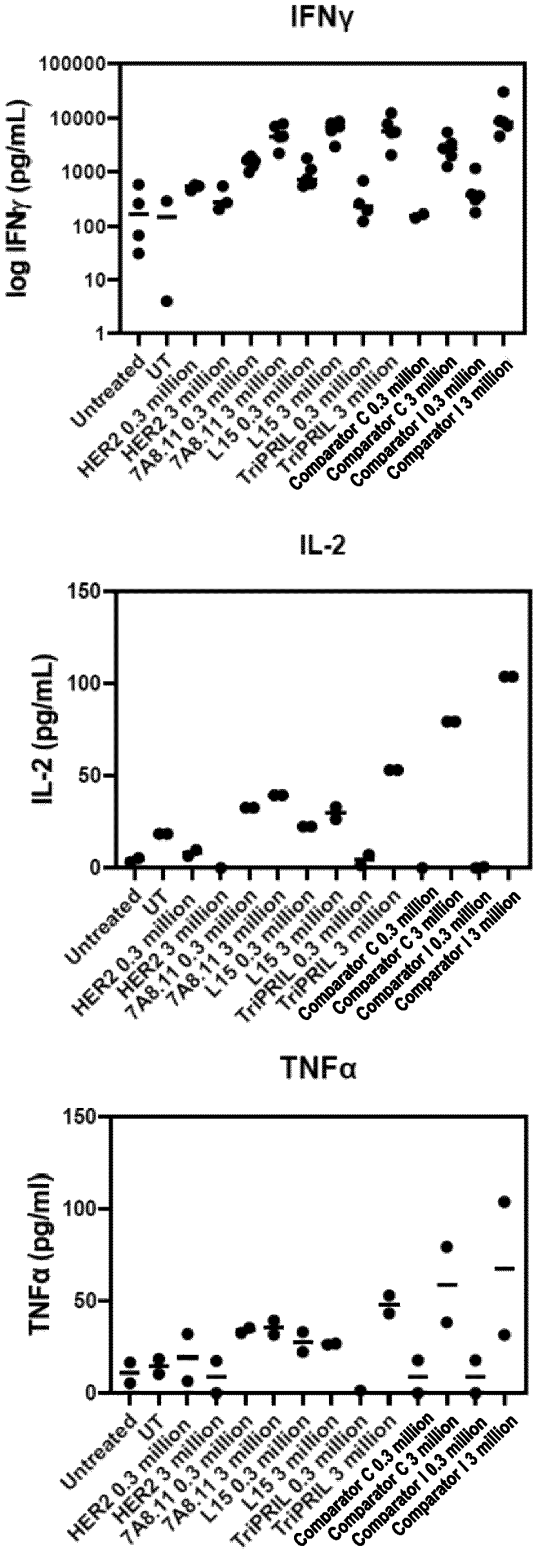
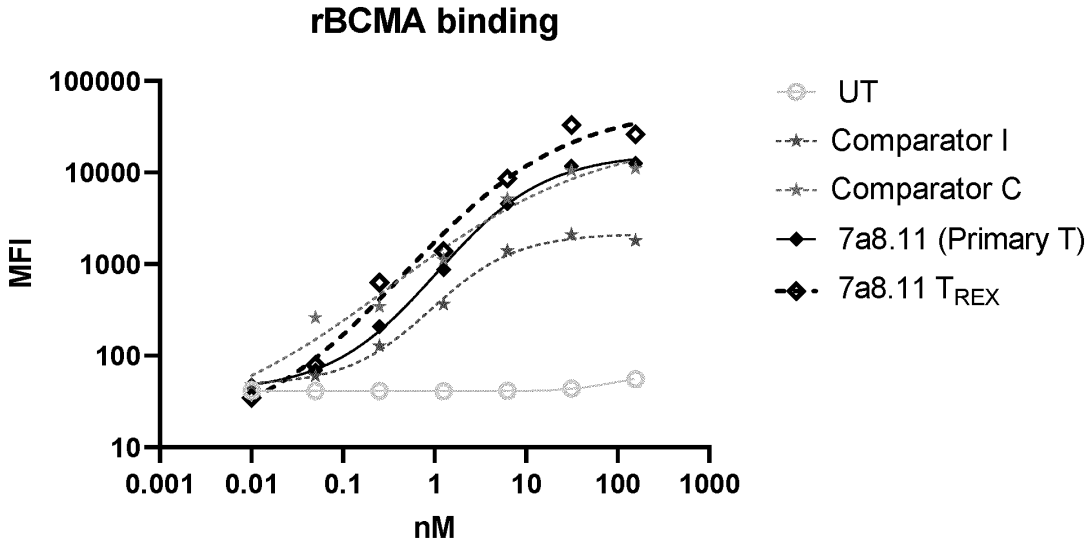

IFNγ
log IFNγ (pg/mL)
100000
10000
1000
100
10
1
IL-2
IL-2 (pg/mL)
150
100
50
0
TNFα
TNFα (pg/ml)
150
100
50
0
Untreated
UT
HER2 0.3 million
HER2 3 million
7A8.11 0.3 million
7A8.11 3 million
L15 0.3 million
L15 3 million
TriPRIL 0.3 million
TriPRIL 3 million
Comparator C 0.3 million
Comparator C 3 million
Comparator I 0.3 million
Comparator I 3 million

FIG. 13



Construct	EC50 of MFI (nM)
UT	87.1nM
7a8.11 primary T	1.06nM
Comparator I primary T	0.91nM
Comparator C primary T	0.34
7a8.11 TREX	0.46nM

FIG. 14

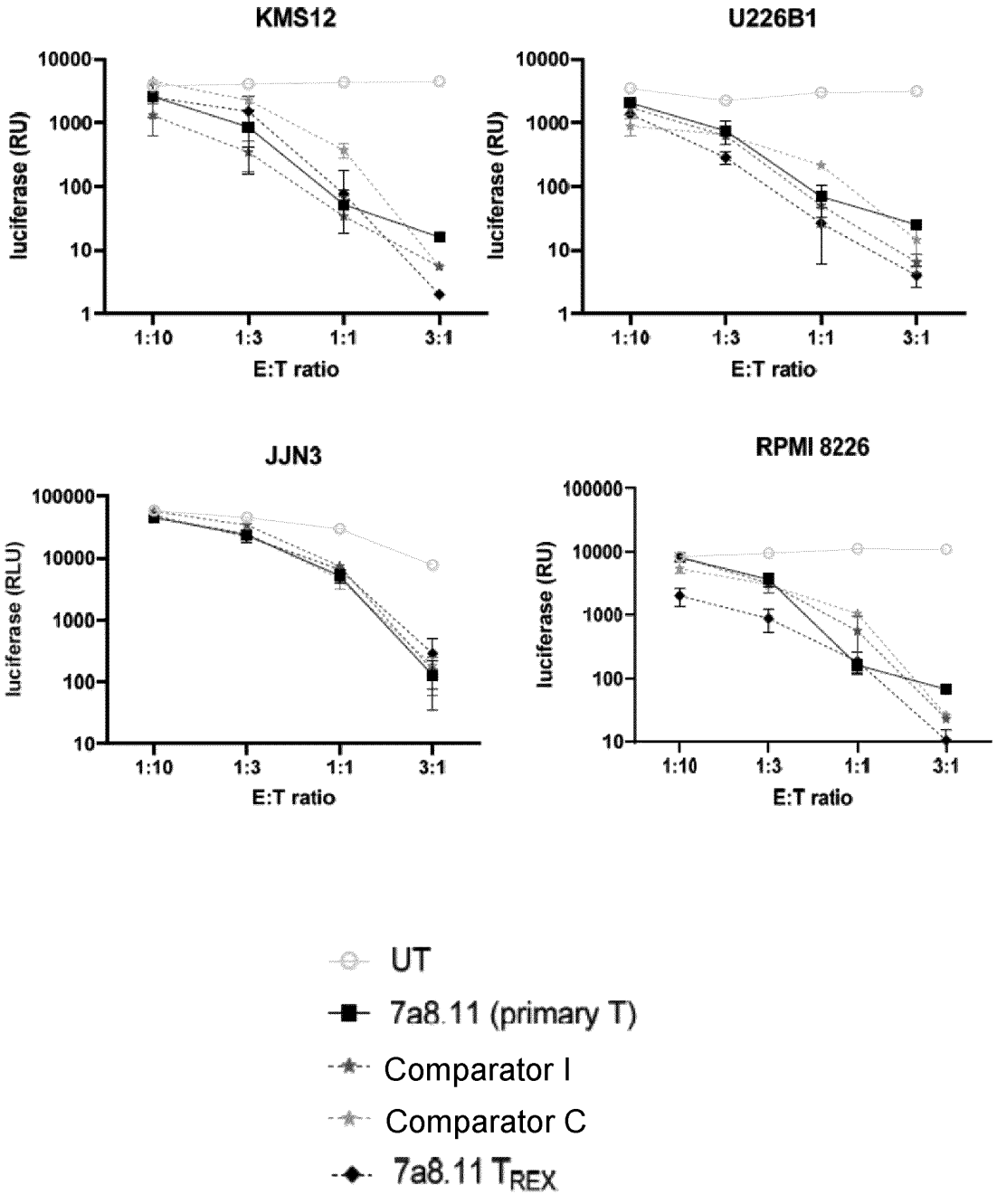

KMS12
U226B1
JJN3
RPMI 8226
luciferase (RU)
luciferase (RLU)
E:T ratio
1:10
1:3
1:1
3:1
10000
1000
100
10
1
100000
UT
7a8.11 (primary T)
Comparator I
Comparator C
7a8.11 TREX

FIG. 15

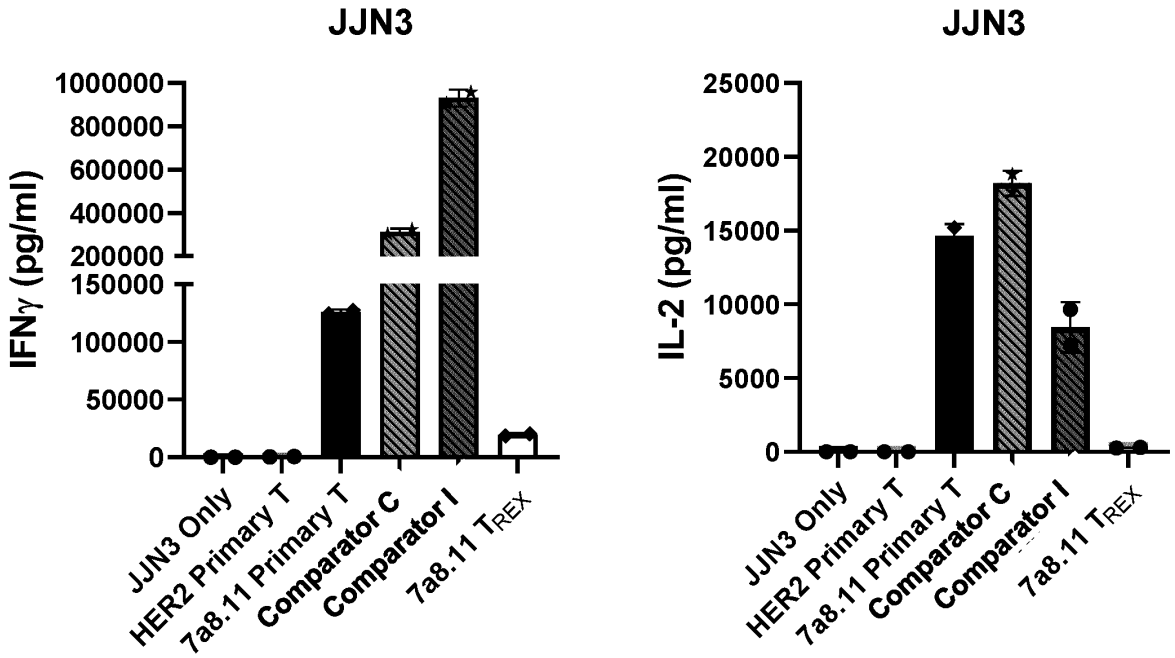

JJN3
IFNγ (pg/ml)
1000000
800000
600000
400000
200000
150000
100000
50000
0
JJN3 Only
HER2 Primary T
7a8.11 Primary T
Comparator C
Comparator I
7a8.11 TREX
JJN3
IL-2 (pg/ml)
25000
20000
15000
10000
5000
0
JJN3 Only
HER2 Primary T
7a8.11 Primary T
Comparator C
Comparator I
7a8.11 TREX

FIG. 16

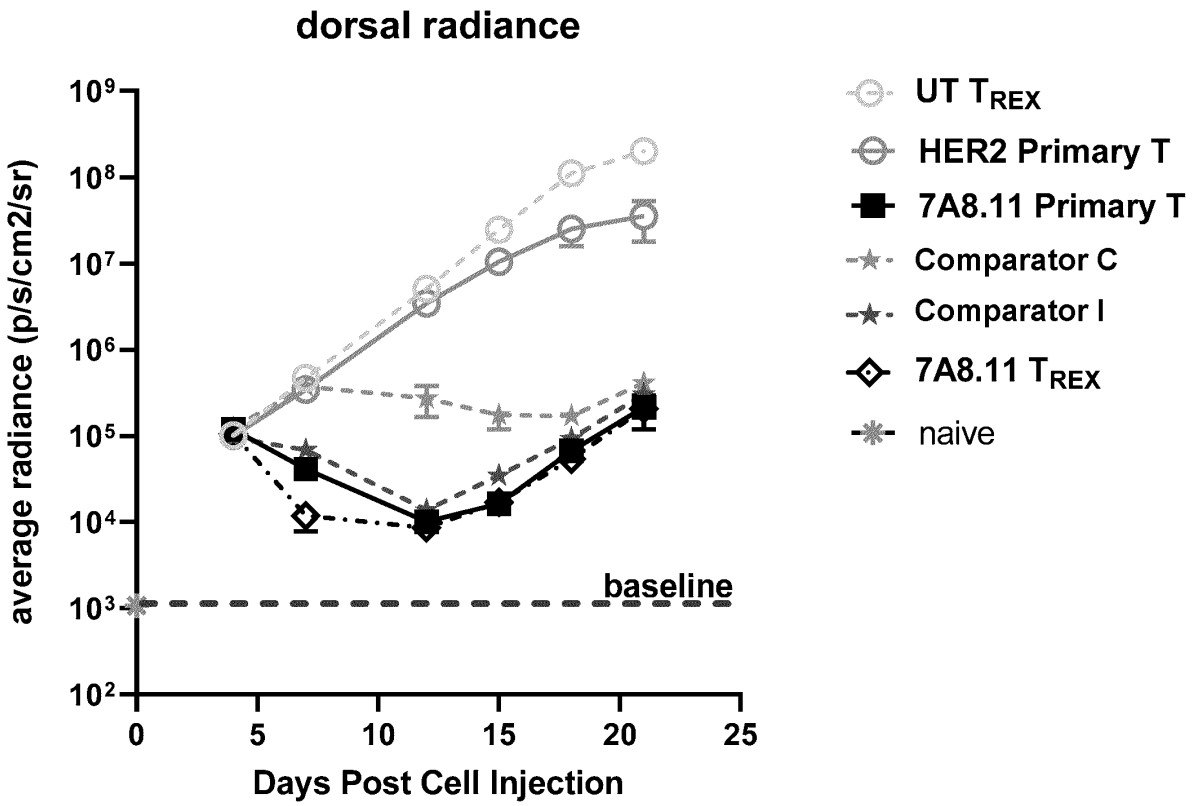

dorsal radiance
average radiance (p/s/cm2/sr)
10^9
10^8
10^7
10^6
10^5
10^4
10^3
10^2
baseline
0
5
10
15
20
25
Days Post Cell Injection
UT T_{REX}
HER2 Primary T
7A8.11 Primary T
Comparator C
Comparator I
7A8.11 T_{REX}
naive

FIG. 17A

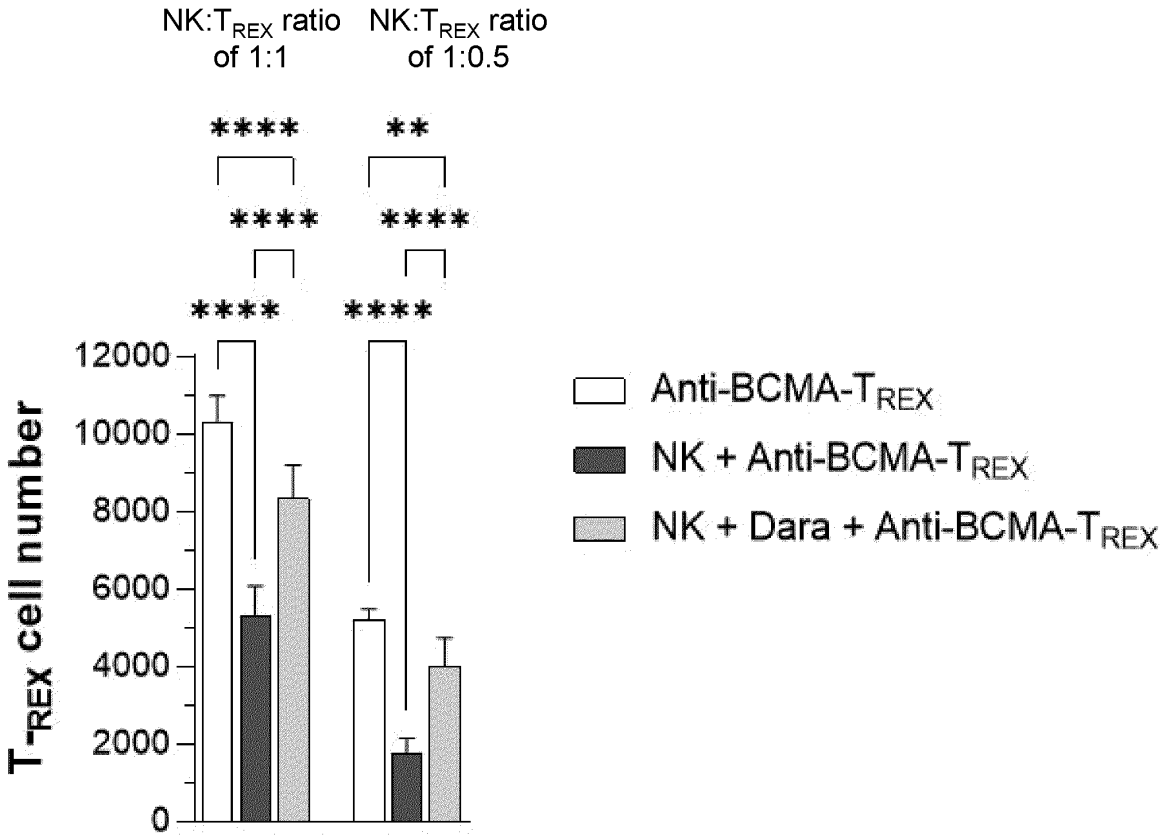

NK:T$_{REX}$ ratio of 1:1
NK:T$_{REX}$ ratio of 1:0.5
****
**
****
****
****
****
T$_{REX}$ cell number
12000
10000
8000
6000
4000
2000
0
Anti-BCMA-T$_{REX}$
NK + Anti-BCMA-T$_{REX}$
NK + Dara + Anti-BCMA-T$_{REX}$

FIG. 17B

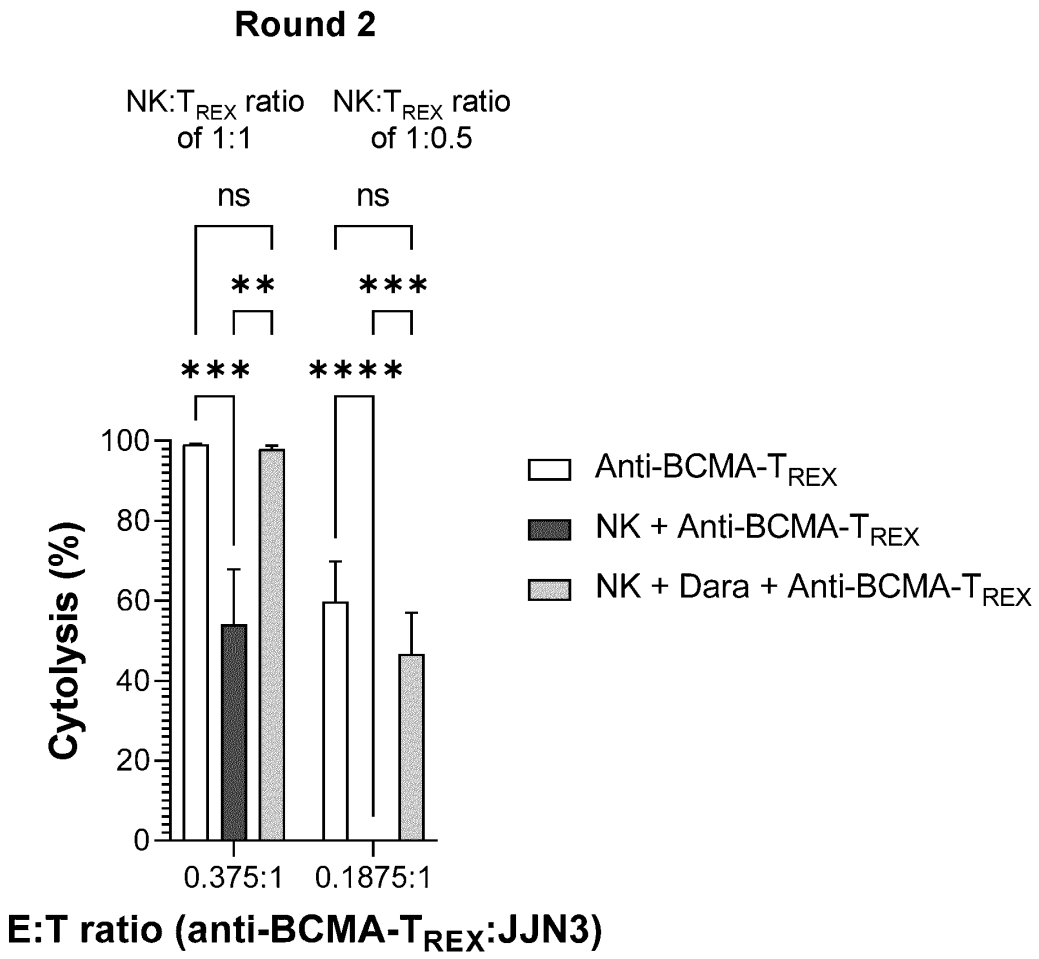

Round 2
NK:T$_{REX}$ ratio of 1:1
NK:T$_{REX}$ ratio of 1:0.5
ns
ns
**
***
***
****
Cytolysis (%)
100
80
60
40
20
0
0.375:1
0.1875:1
E:T ratio (anti-BCMA-T$_{REX}$:JJN3)
Anti-BCMA-T$_{REX}$
NK + Anti-BCMA-T$_{REX}$
NK + Dara + Anti-BCMA-T$_{REX}$

FIG. 17C

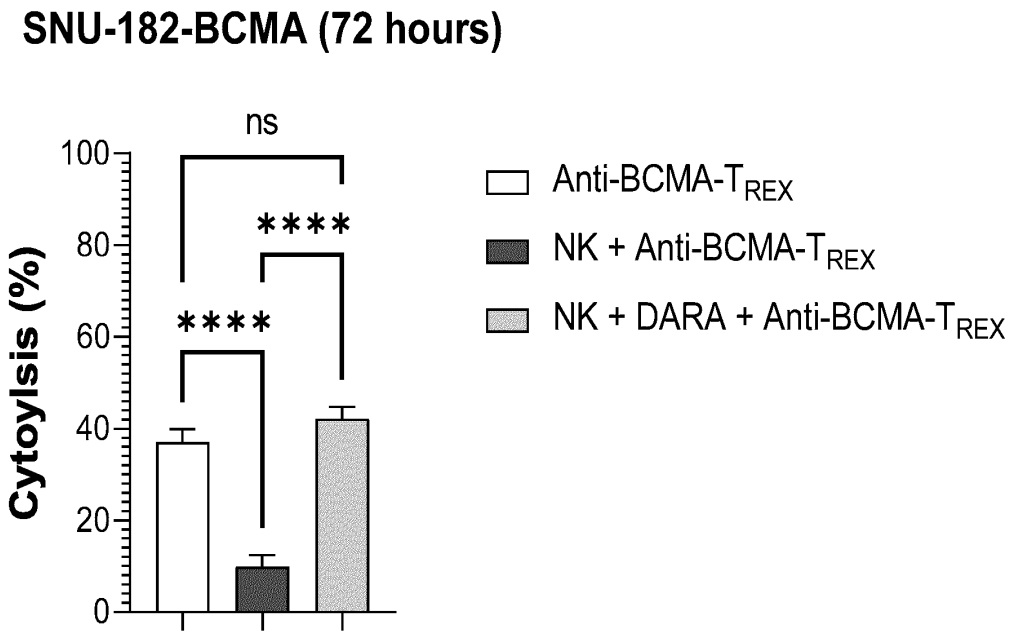

SNU-182-BCMA (72 hours)
ns
****
****
100
80
60
40
20
0
Cytoylsis (%)
Anti-BCMA-T$_{REX}$
NK + Anti-BCMA-T$_{REX}$
NK + DARA + Anti-BCMA-T$_{REX}$

FIG. 18

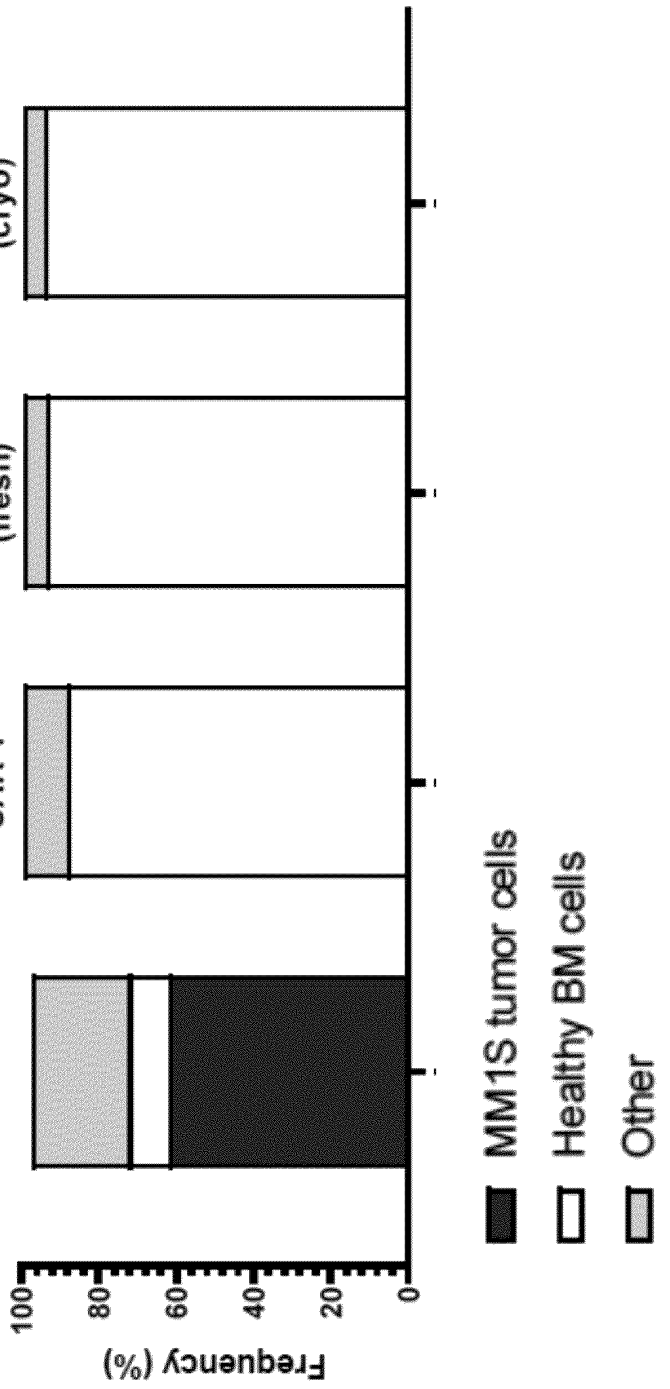

Frequency (%)
100
80
60
40
20
0
Untreated
Primary BCMA CAR-T
BCMA CAR-T REX (fresh)
BCMA CAR-T REX (cryo)
MM1S tumor cells
Healthy BM cells
Other

FIG. 19

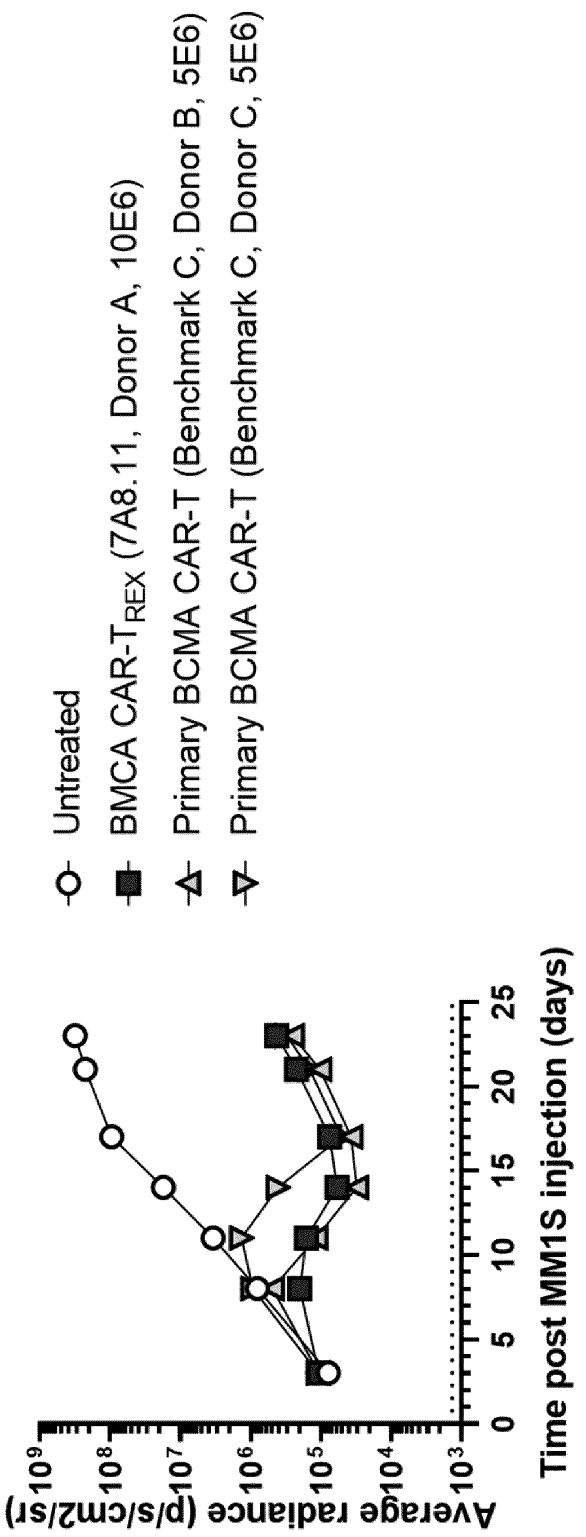
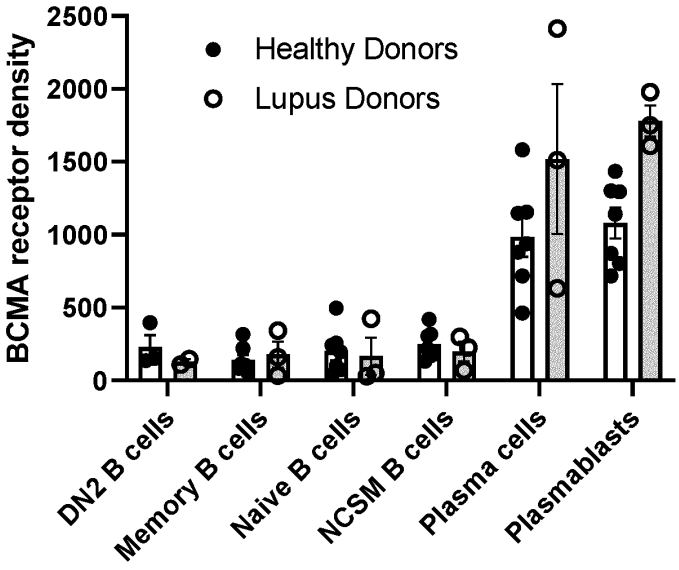
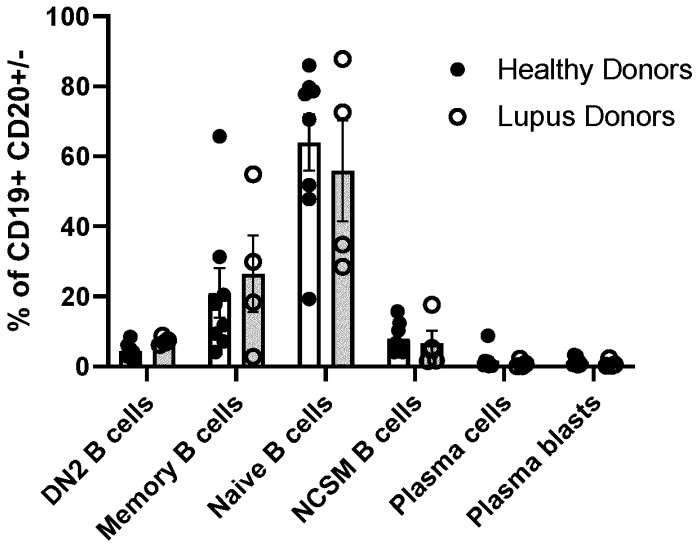

Untreated
BMCA CAR-T$_{REX}$ (7A8.11, Donor A, 10E6)
Primary BCMA CAR-T (Benchmark C, Donor B, 5E6)
Primary BCMA CAR-T (Benchmark C, Donor C, 5E6)
Average radiance (p/s/cm2/sr)
10^9
10^8
10^7
10^6
10^5
10^4
10^3
0
5
10
15
20
25
Time post MM1S injection (days)

FIG. 20



B-cell subsets in healthy and lupus donors



B-cell subsets in healthy and SLE donors

FIG. 21

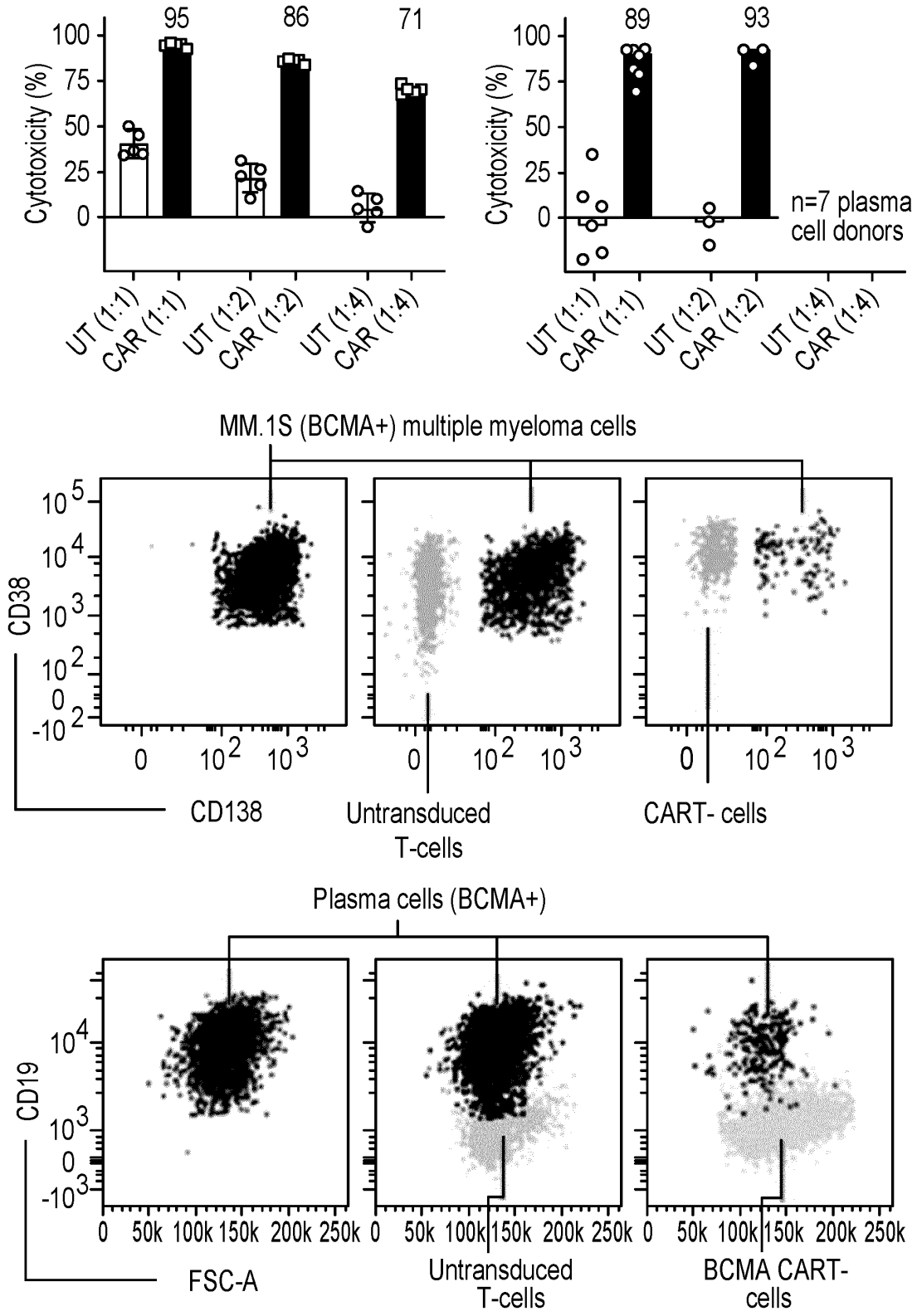
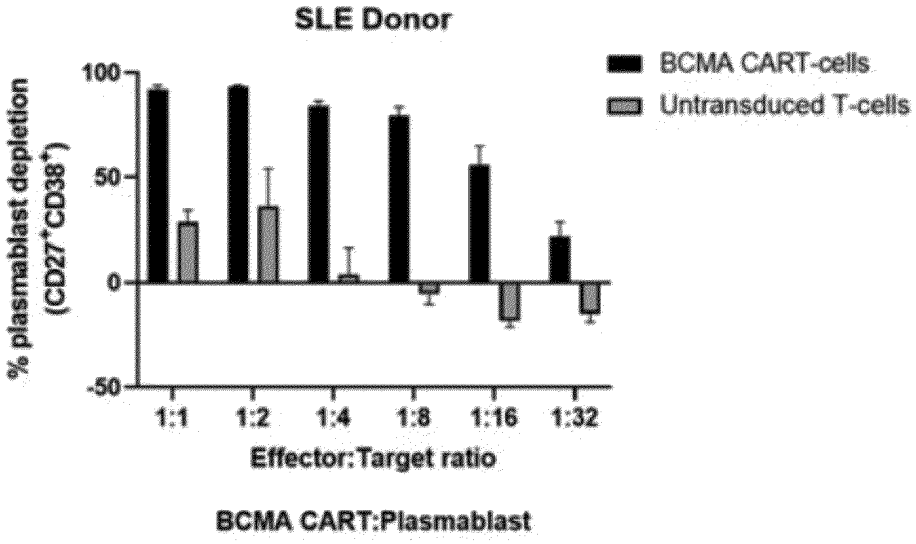

95
86
71
89
93
Cytotoxicity (%)
100
75
50
25
0
UT (1:1)
CAR (1:1)
UT (1:2)
CAR (1:2)
UT (1:4)
CAR (1:4)
n=7 plasma cell donors
MM.1S (BCMA+) multiple myeloma cells
CD38
CD138
Untransduced T-cells
CART- cells
Plasma cells (BCMA+)
CD19
FSC-A
BCMA CART-cells

FIG. 22


SLE Donor
BCMA CART-cells
Untransduced T-cells
% plasmablast depletion (CD27+CD38+)
100
50
0
-50
1:1
1:2
1:4
1:8
1:16
1:32
Effector:Target ratio
BCMA CART:Plasmablast

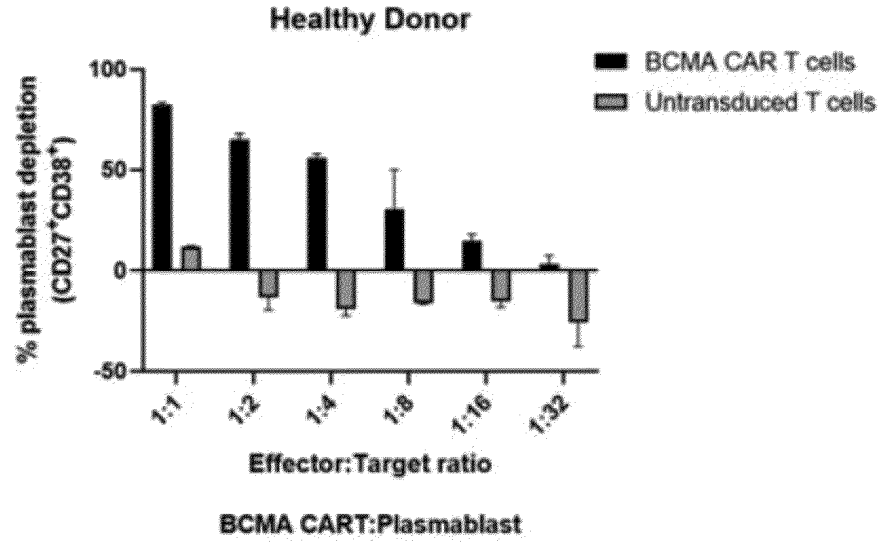

Healthy Donor
BCMA CAR T cells
Untransduced T cells
% plasmablast depletion (CD27+CD38+)
100
50
0
-50
1:1
1:2
1:4
1:8
1:16
1:32
Effector:Target ratio
BCMA CART:Plasmablast

FIG. 23

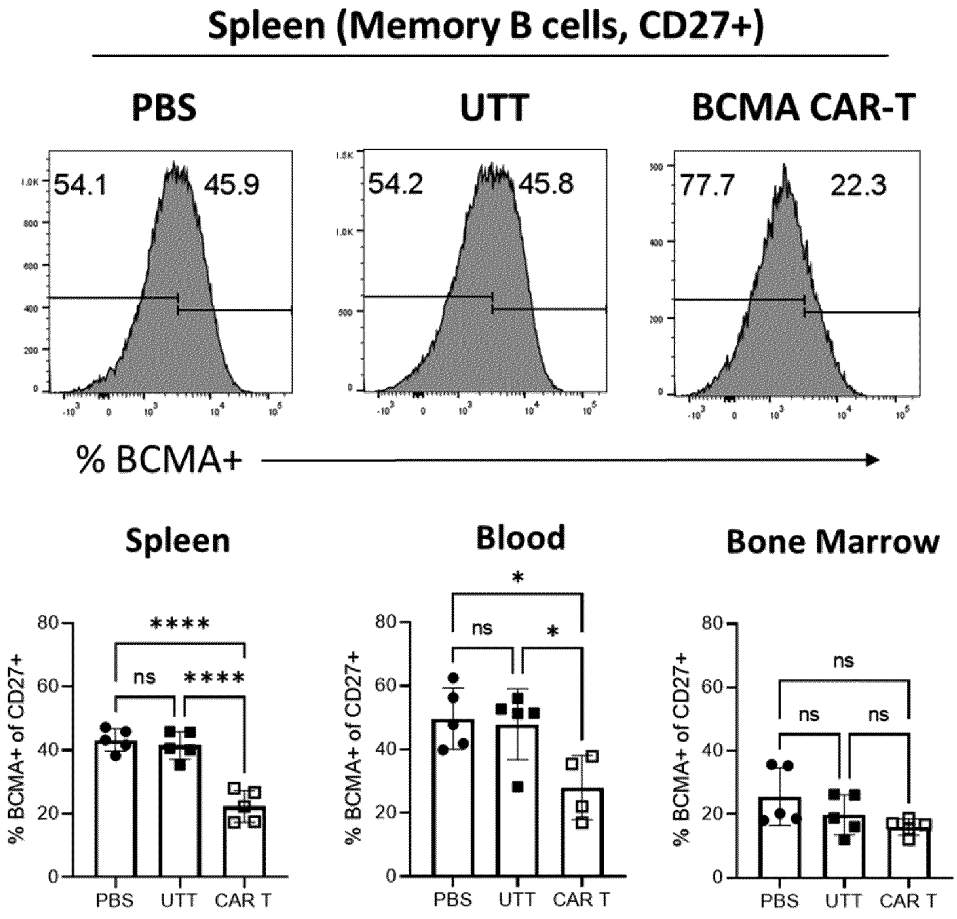
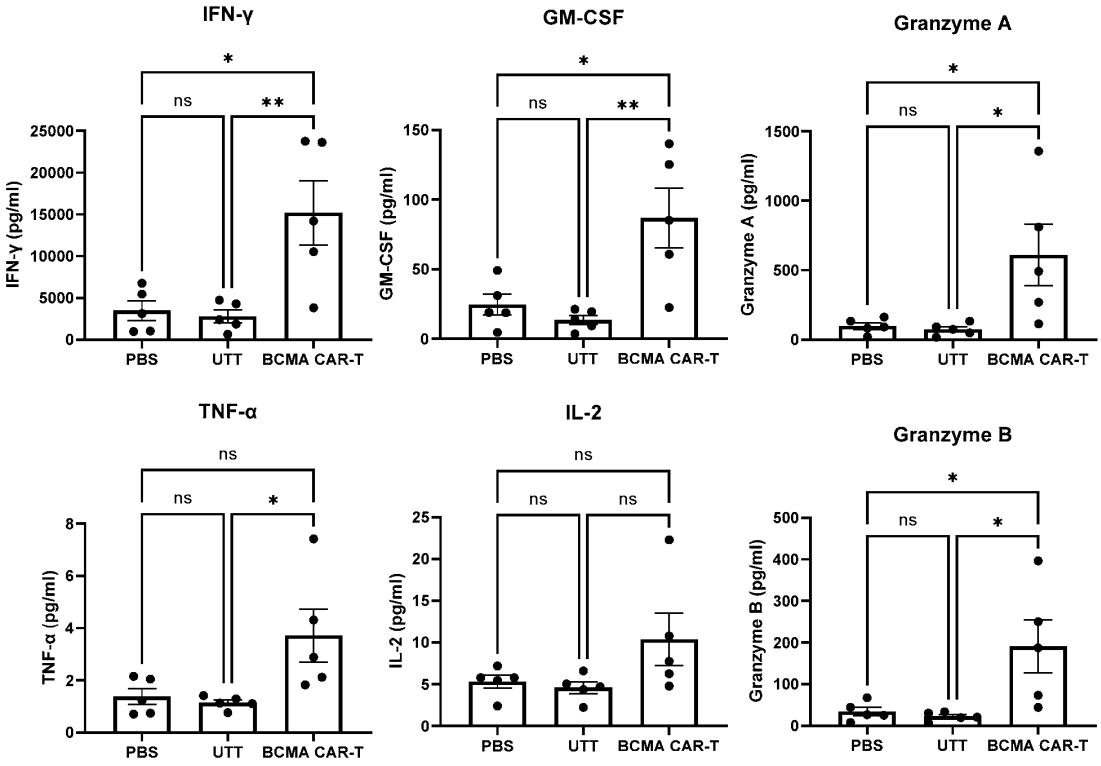

Spleen (Memory B cells, CD27+)
PBS
UTT
BCMA CAR-T
54.1
45.9
54.2
45.8
77.7
22.3
% BCMA+
Spleen
Blood
Bone Marrow
% BCMA+ of CD27+
****
ns
****
*
ns
*
ns
ns
ns
PBS
UTT
CAR T

FIG. 24


IFN-γ
IFN-γ (pg/ml)
25000
20000
15000
10000
5000
0
*
ns
**
PBS
UTT
BCMA CAR-T
GM-CSF
GM-CSF (pg/ml)
150
100
50
0
*
ns
**
PBS
UTT
BCMA CAR-T
Granzyme A
Granzyme A (pg/ml)
1500
1000
500
0
*
ns
*
PBS
UTT
BCMA CAR-T
TNF-α
TNF-α (pg/ml)
8
6
4
2
0
ns
ns
*
PBS
UTT
BCMA CAR-T
IL-2
IL-2 (pg/ml)
25
20
15
10
5
0
ns
ns
ns
PBS
UTT
BCMA CAR-T
Granzyme B
Granzyme B (pg/ml)
500
400
300
200
100
0
*
ns
*
PBS
UTT
BCMA CAR-T