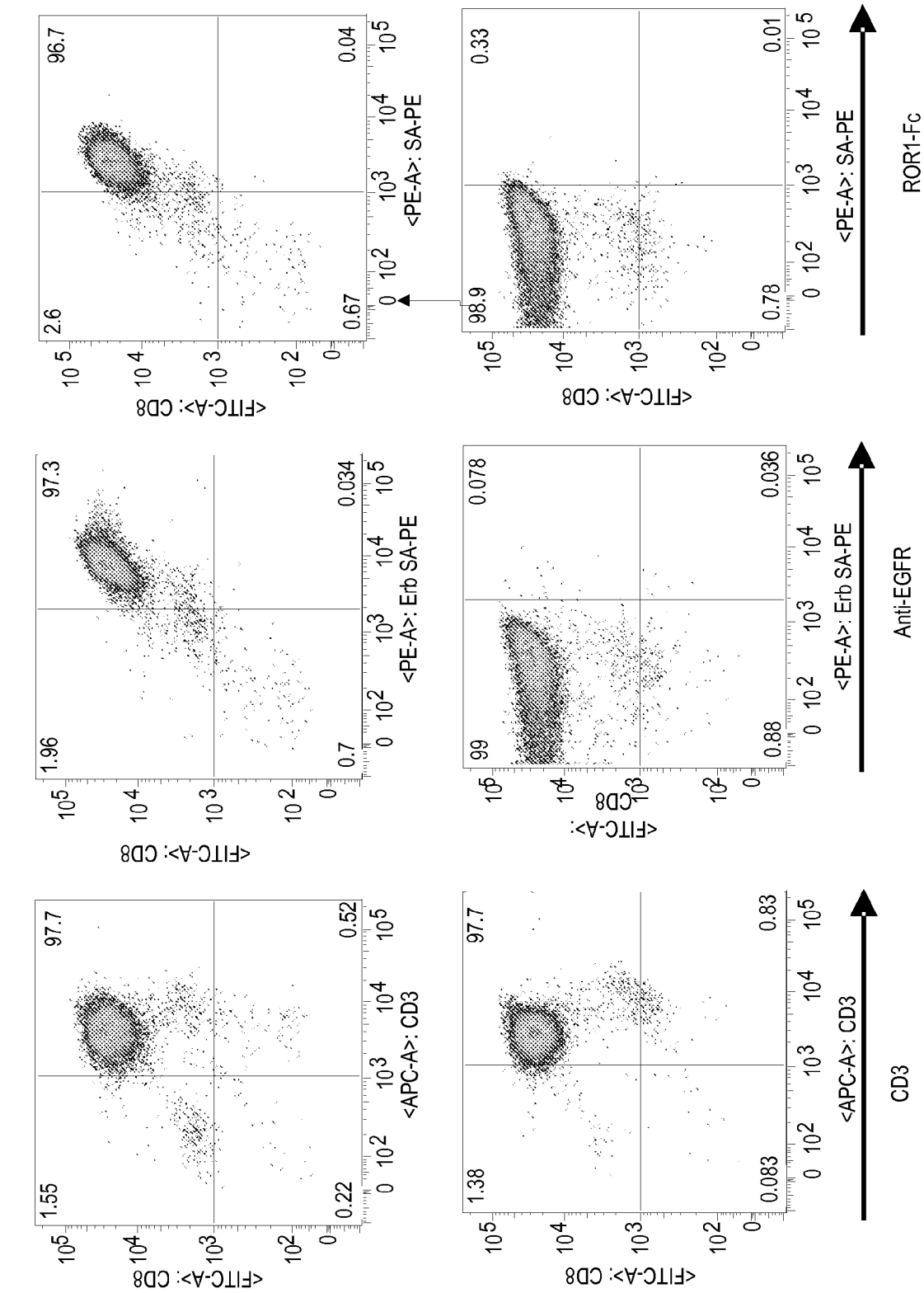
FIG. 1


CD8
untransduced control CTL
<FITC-A>: CD8
<APC-A>: CD3
CD3
<PE-A>: Erb SA-PE
Anti-EGFR
<PE-A>: SA-PE
ROR1-Fc
1.55
97.7
0.22
0.52
1.96
97.3
0.7
0.034
99
0.078
0.88
0.036
1.38
97.7
0.083
0.83
2.6
96.7
0.67
0.04
98.9
0.33
0.78
0.01

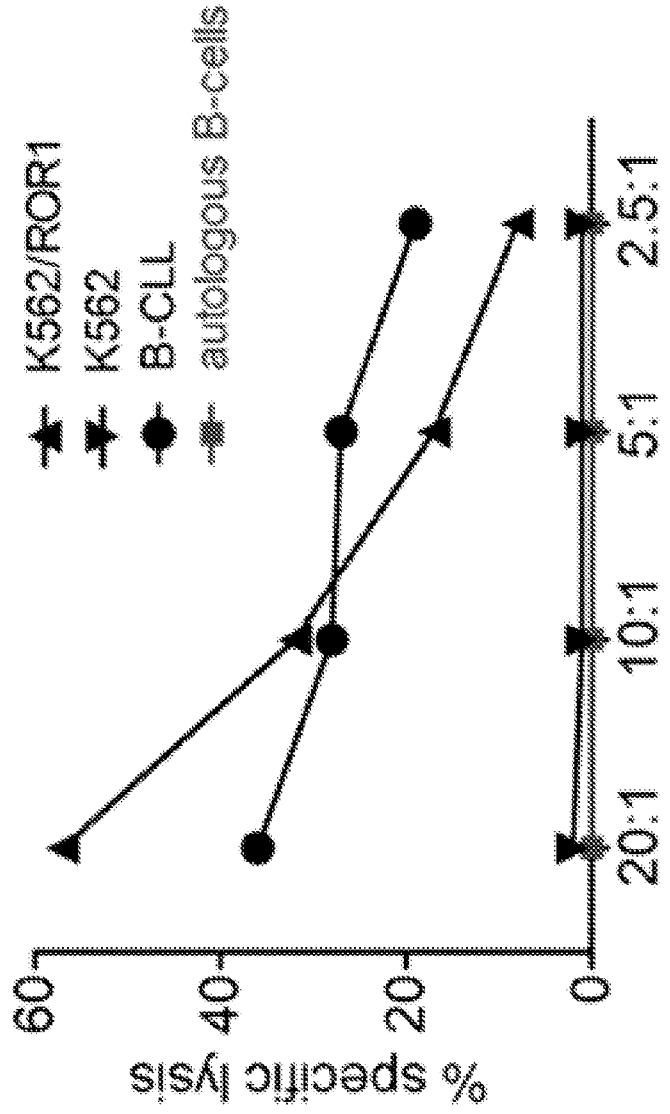

ROR1-CAR CD8+ CTL
K562/ROR1
K562
B-CLL
autologous B-cells
% specific lysis
60
40
20
0
20:1
10:1
5:1
2.5:1

FIG. 2

FIG. 3

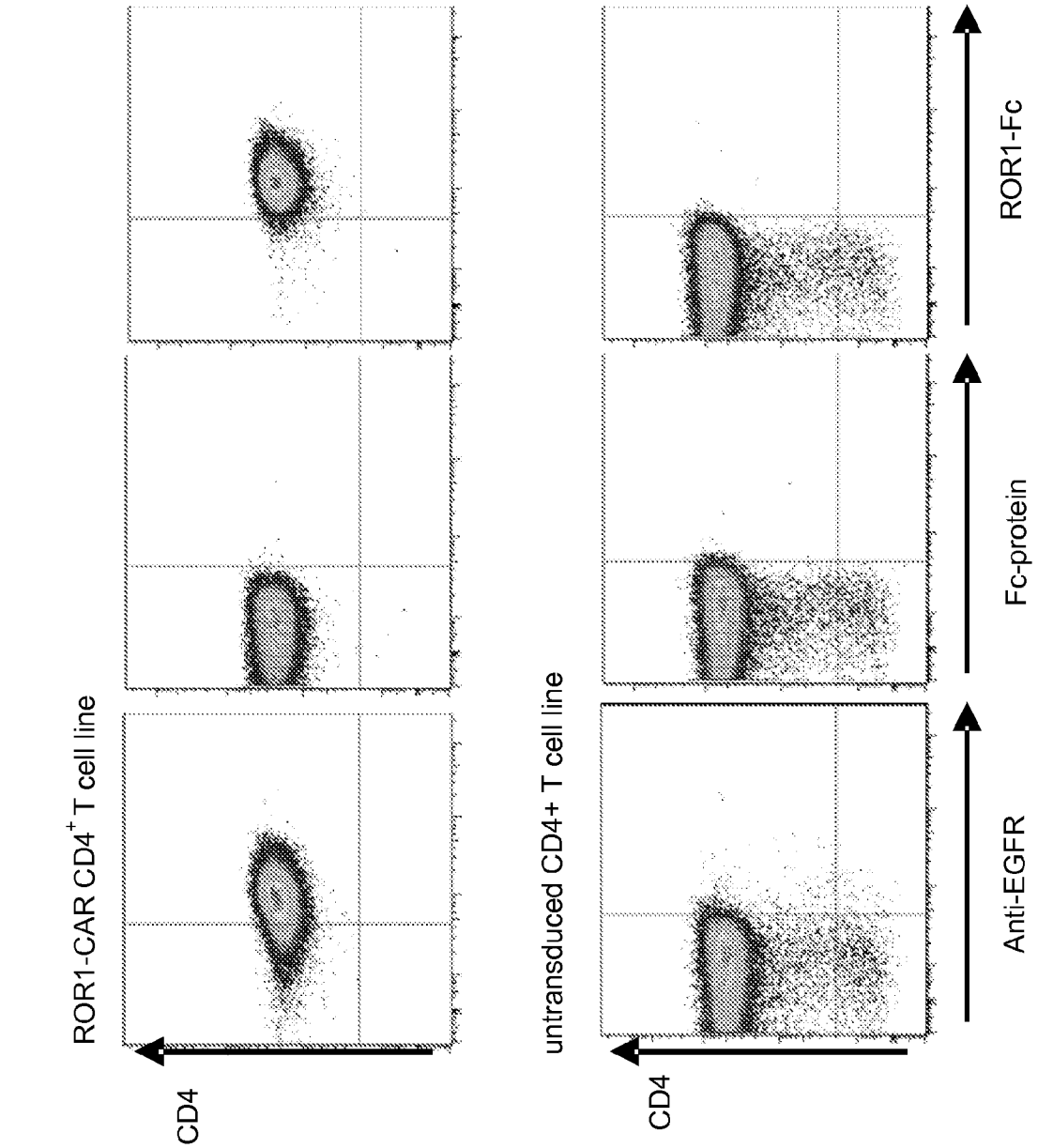

ROR1-CAR CD4+ T cell line
CD4
untransduced CD4+ T cell line
CD4
Anti-EGFR
Fc-protein
ROR1-Fc

FIG. 4A

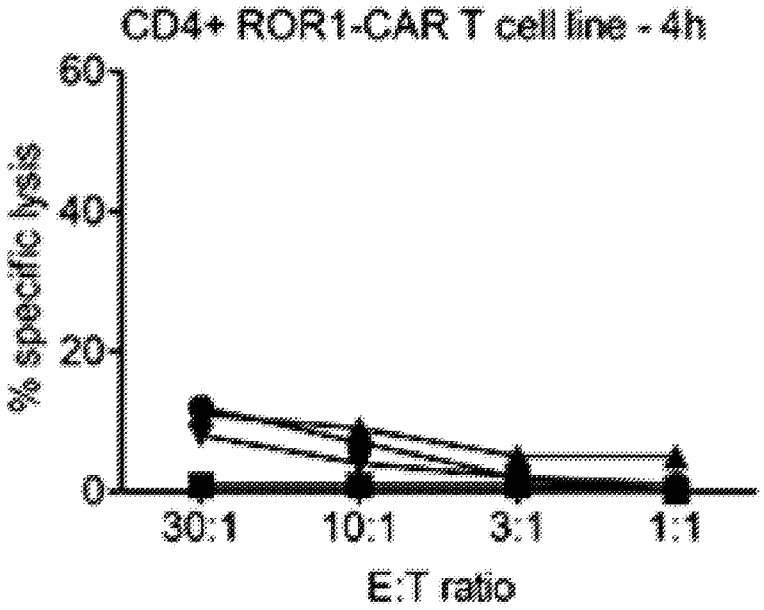
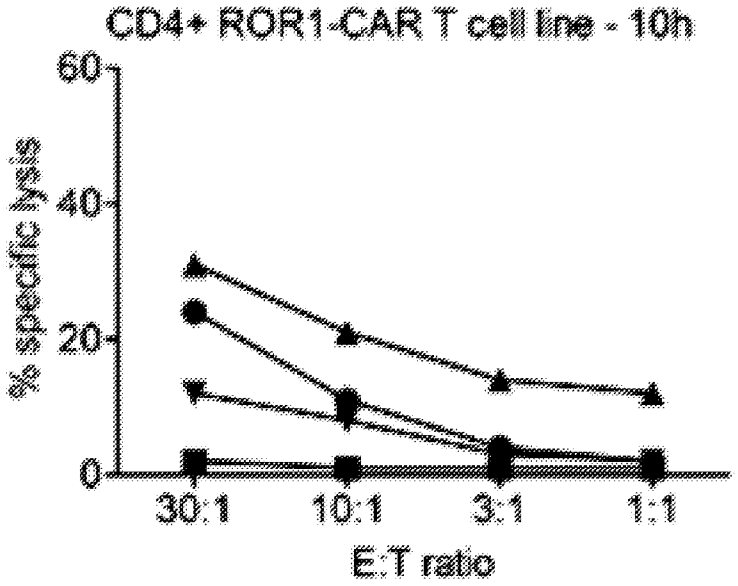


FIG. 4B



Triangle (up) – Jeko-1 (mantle cell lymphoma)
Circles – K562/ROR1
Triangle (down) – primary CLL
Squares – K562

FIG. 5A

IFNg ELISA

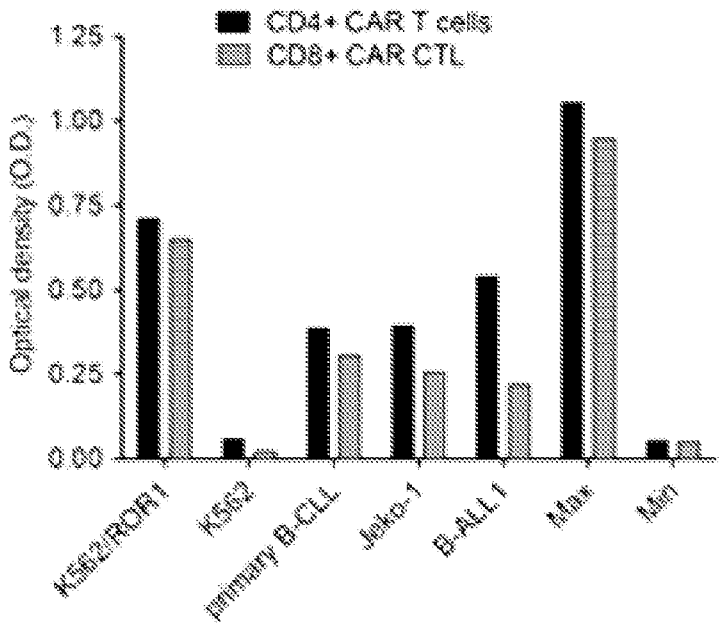


FIG. 5B

Multiplex cytokine assay (Luminex)

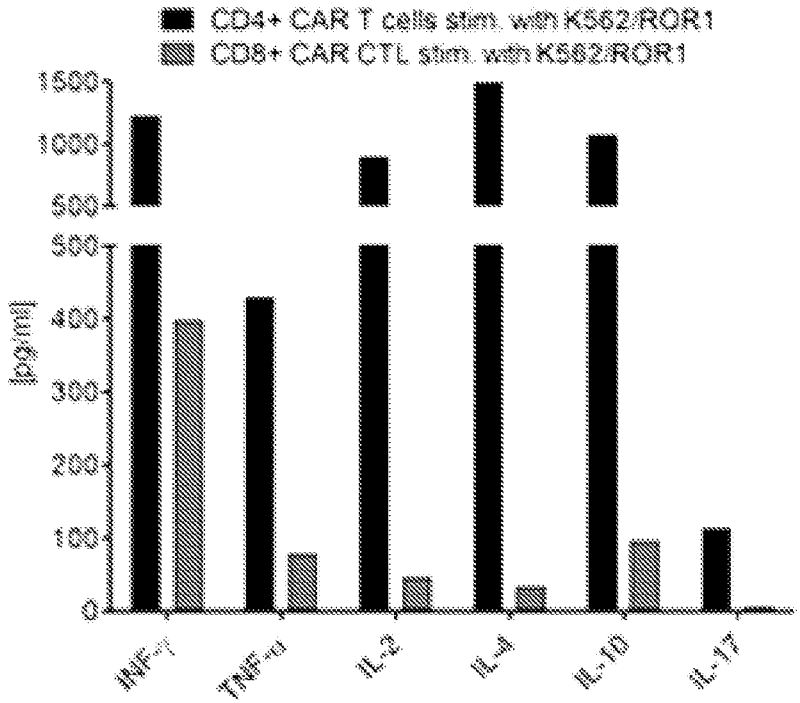


FIG. 6

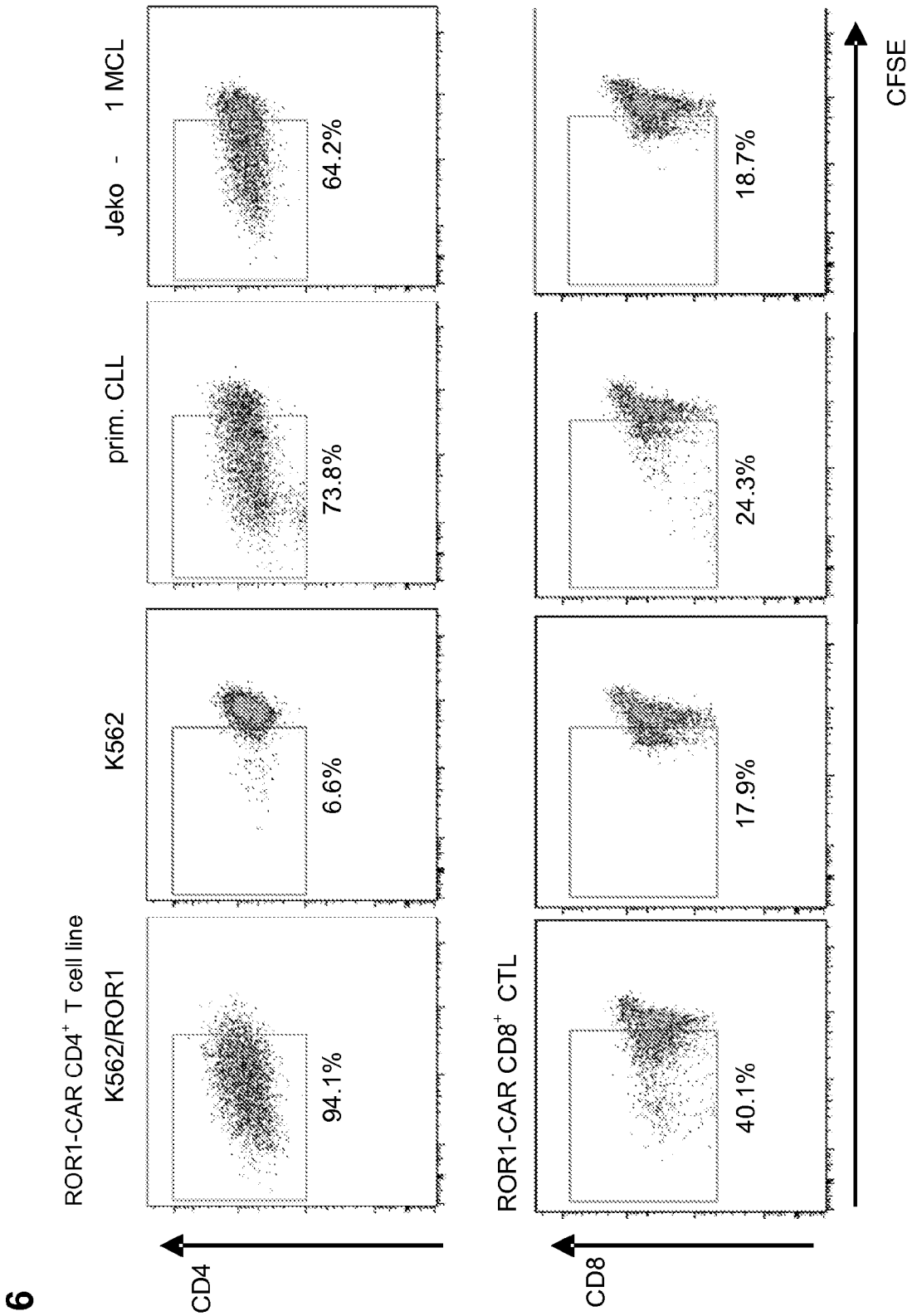

ROR1-CAR CD4+ T cell line
K562/ROR1
K562
prim. CLL
Jeko - 1 MCL
CD4
94.1%
6.6%
73.8%
64.2%
ROR1-CAR CD8+ CTL
CD8
40.1%
17.9%
24.3%
18.7%
CFSE

FIG. 7

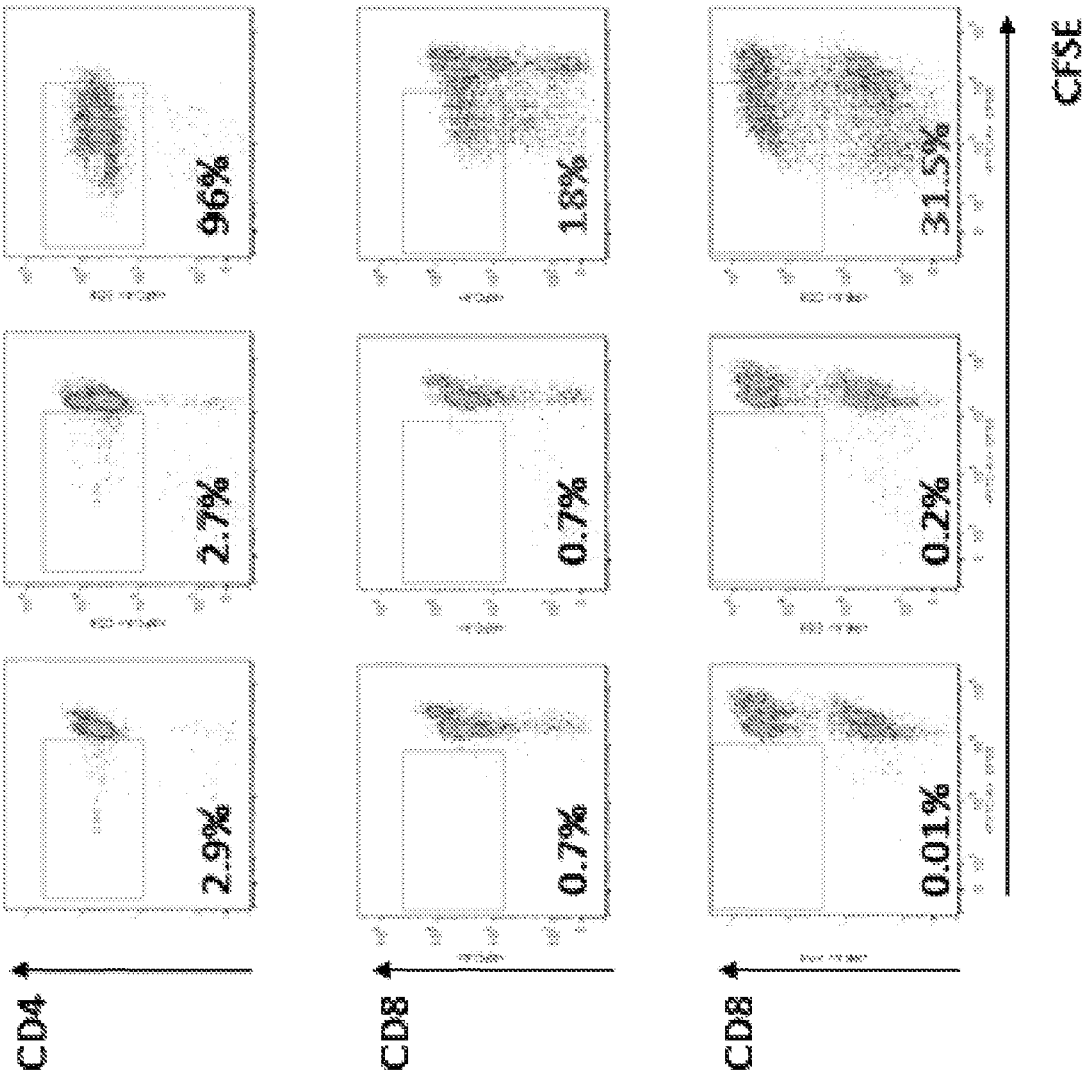

Medium
K562
K562/ROR1
CD4
CD8
CD8
2.9%
2.7%
96%
0.7%
0.7%
1.8%
0.01%
0.2%
31.5%
CD4+ ROR1-CAR CTL individual culture
CD8+ ROR1-CAR CTL individual culture
CD4+ / CD8+ ROR1-CAR CTL co-culture - gated on CD8+
CFSE

FIG. 8A

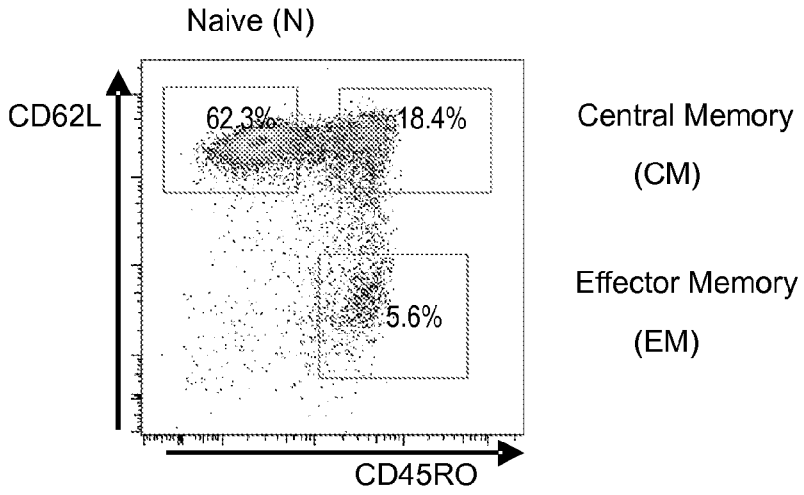

Naive (N)
CD62L
62.3%
18.4%
5.6%
CD45RO
Central Memory
(CM)
Effector Memory
(EM)

FIG. 8B

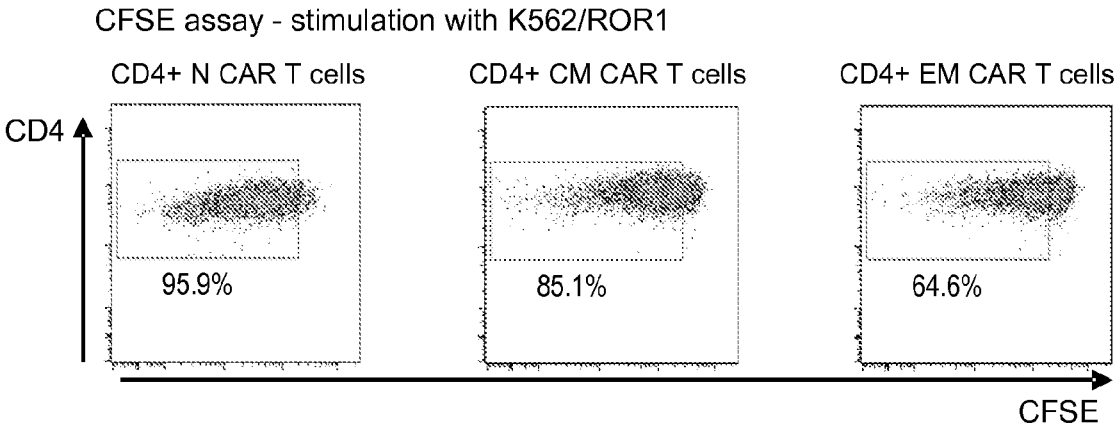

CFSE assay - stimulation with K562/ROR1
CD4+ N CAR T cells
CD4+ CM CAR T cells
CD4+ EM CAR T cells
CD4
95.9%
85.1%
64.6%
CFSE

FIG. 8C

Luminex assay - stimulation with K562/CD19

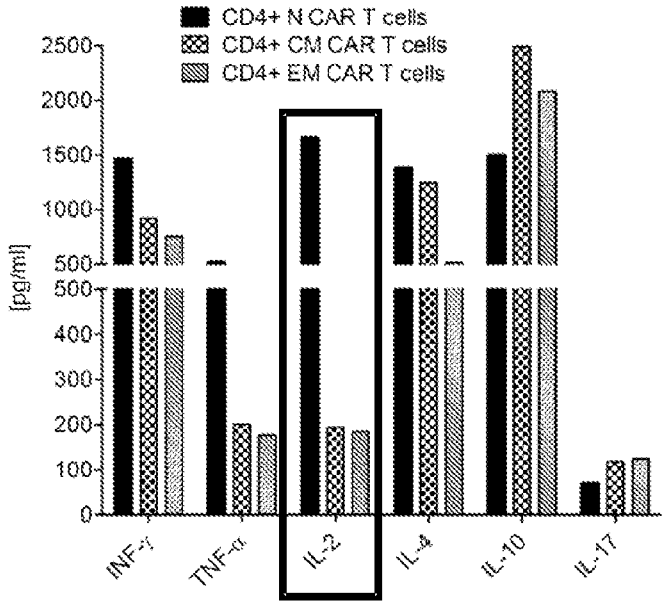


FIG. 8D

Luminex assay - stimulation with K562/CD19

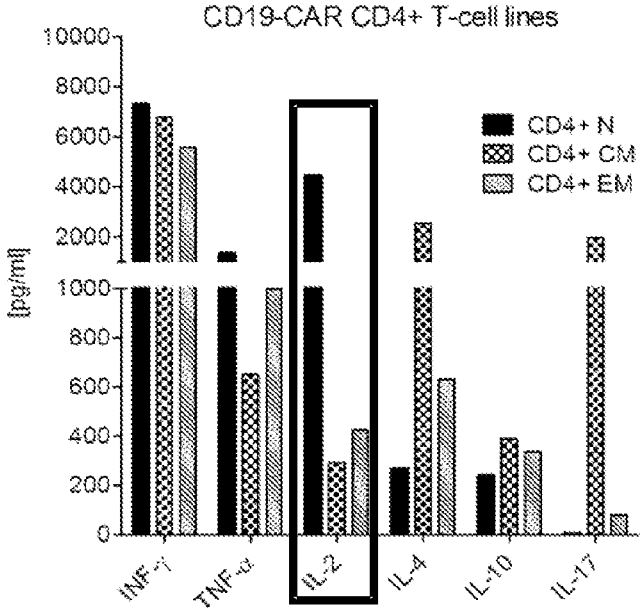


FIG. 9

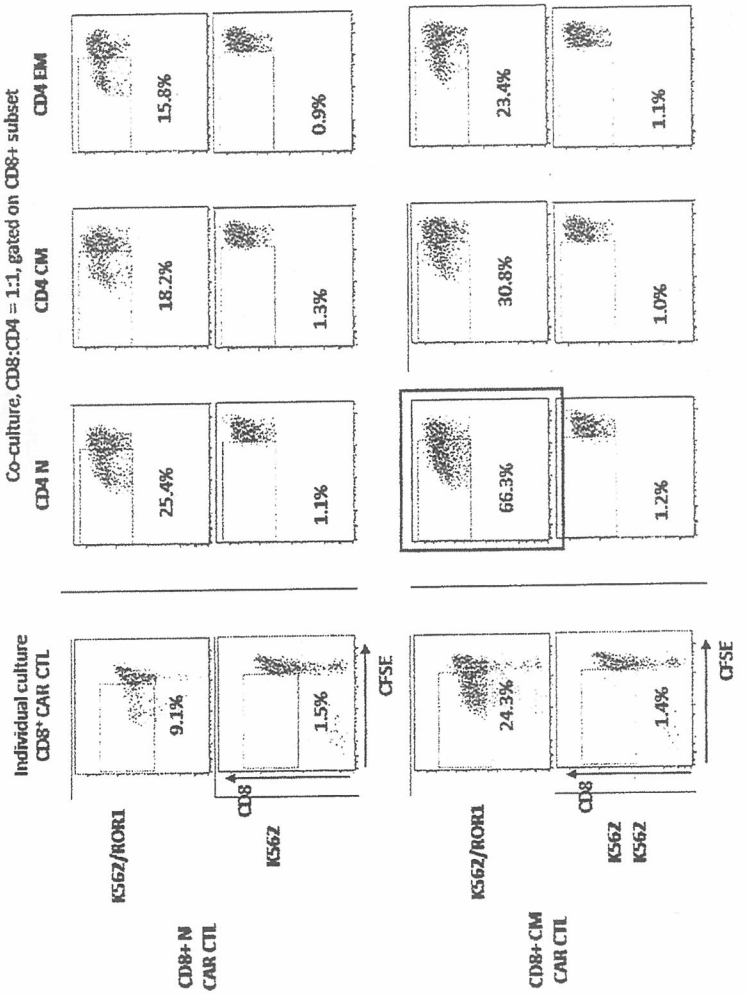

Co-culture, CD8:CD4 = 1:1, gated on CD8+ subset
CD4 N
CD4 CM
CD4 EM
Individual culture
CD8+ CAR CTL
CD8+ N CAR CTL
CD8+ CM CAR CTL
K562/ROR1
CD8
K562
CFSE
9.1%
1.5%
25.4%
1.1%
18.2%
1.3%
15.8%
0.9%
24.3%
1.4%
66.3%
1.2%
30.8%
1.0%
23.4%
1.1%

FIG. 10

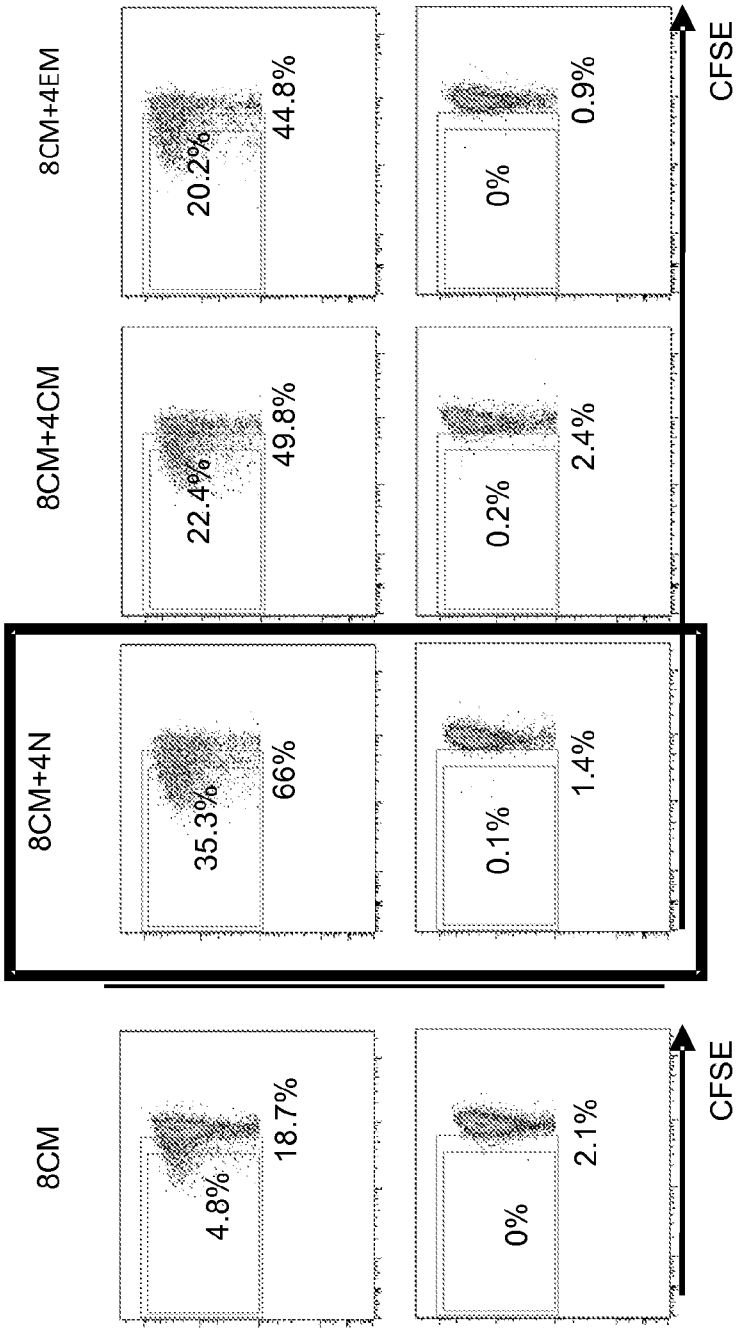
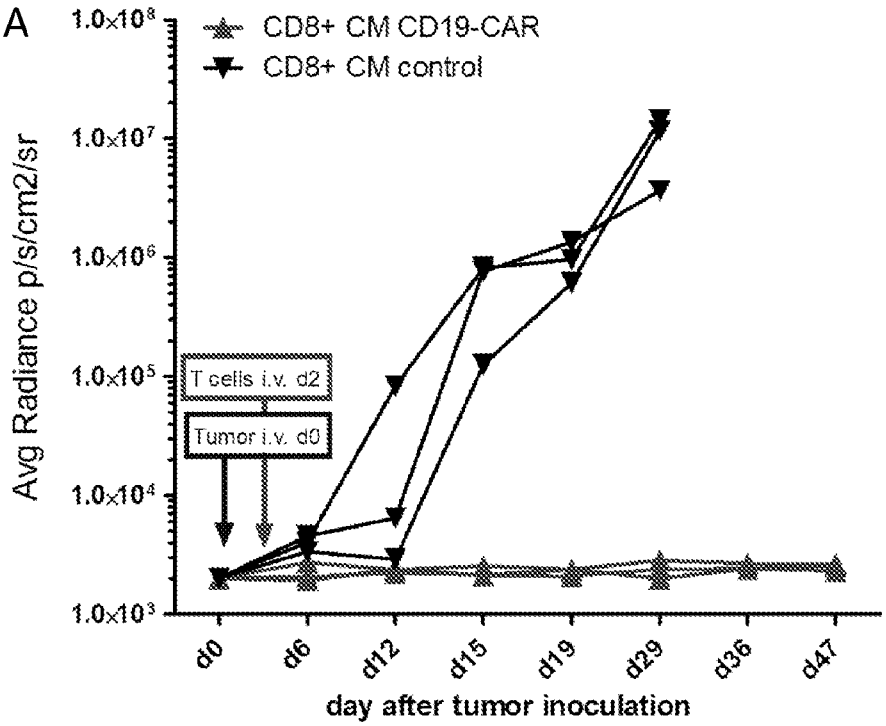
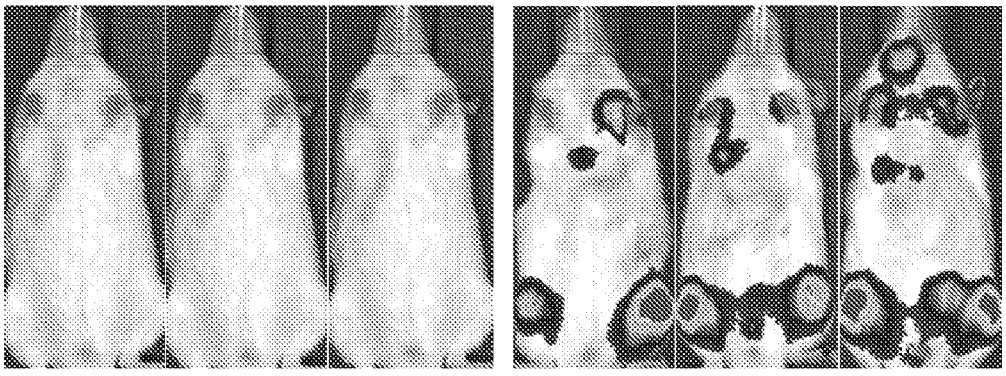

8CM
8CM+4N
8CM+4CM
8CM+4EM
CD19 – CAR
T-cell lines
Jeko-1
medium
4.8%
18.7%
35.3%
66%
22.4%
49.8%
20.2%
44.8%
0%
2.1%
0.1%
1.4%
0.2%
2.4%
0%
0.9%
CFSE
CFSE

FIG. 11A



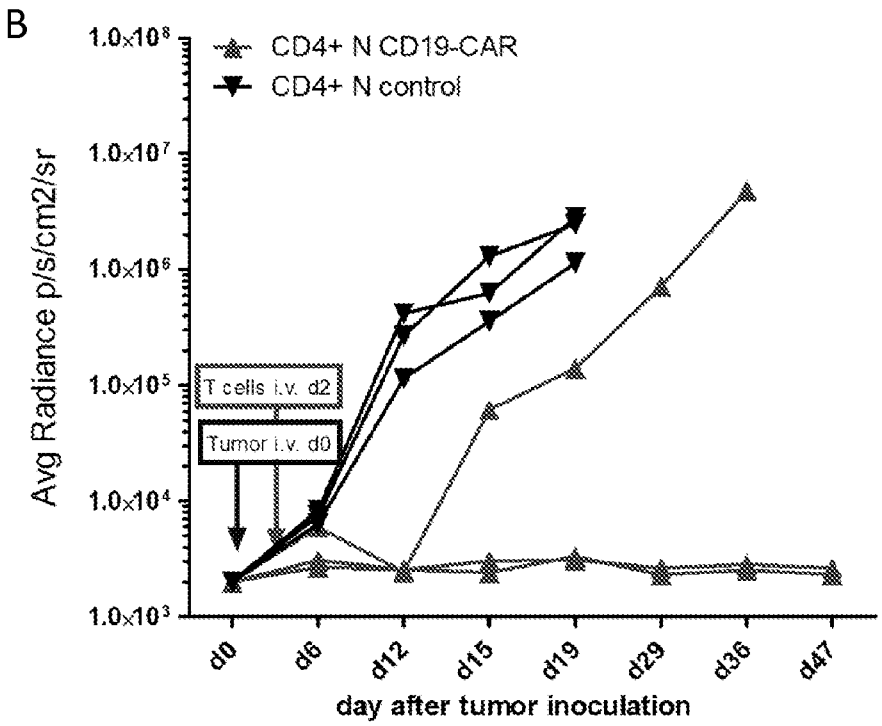


CD8+ CM CD19 -

CD8+ C

d19 after T - cell infusion

FIG. 11B





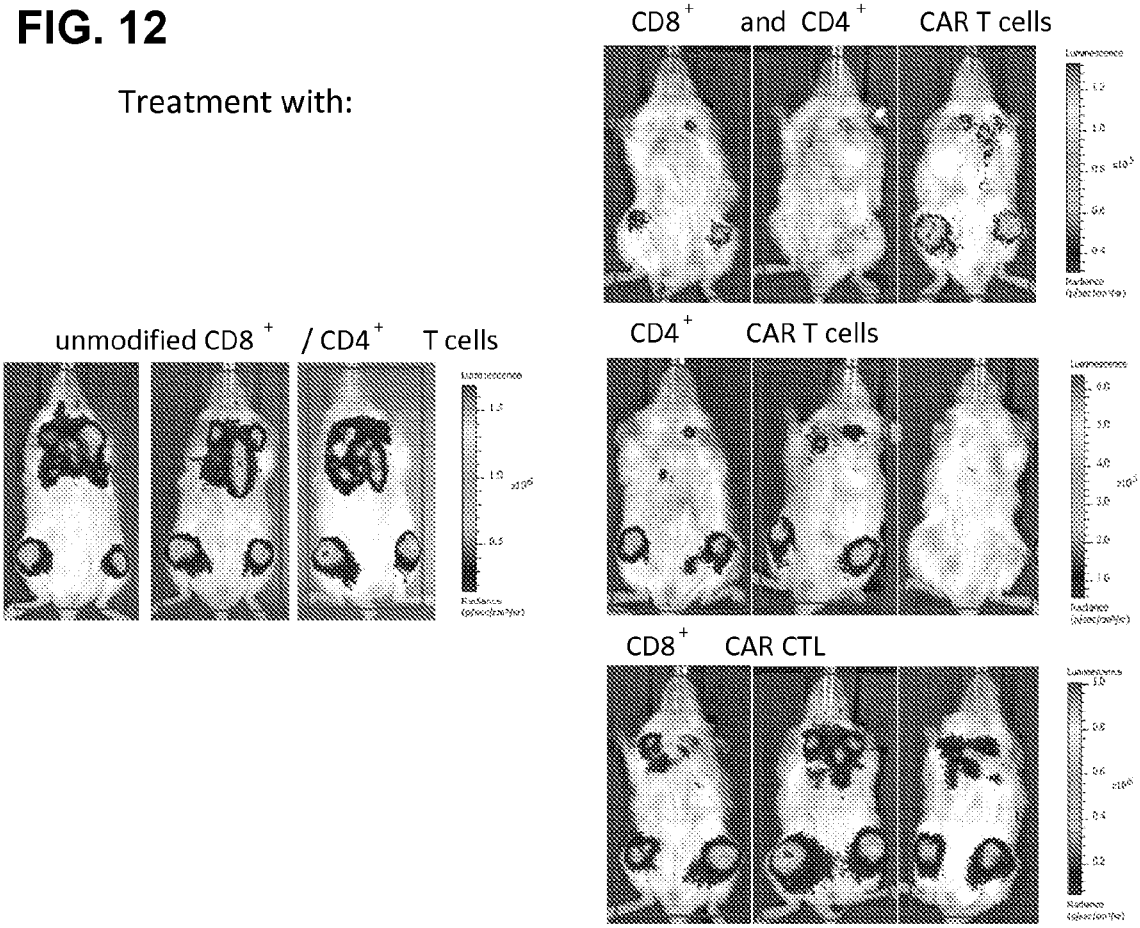
CD4+ N CD19 - CAR

CD4+ N control

d19 after T - cell infusion

FIG. 12

Treatment with:



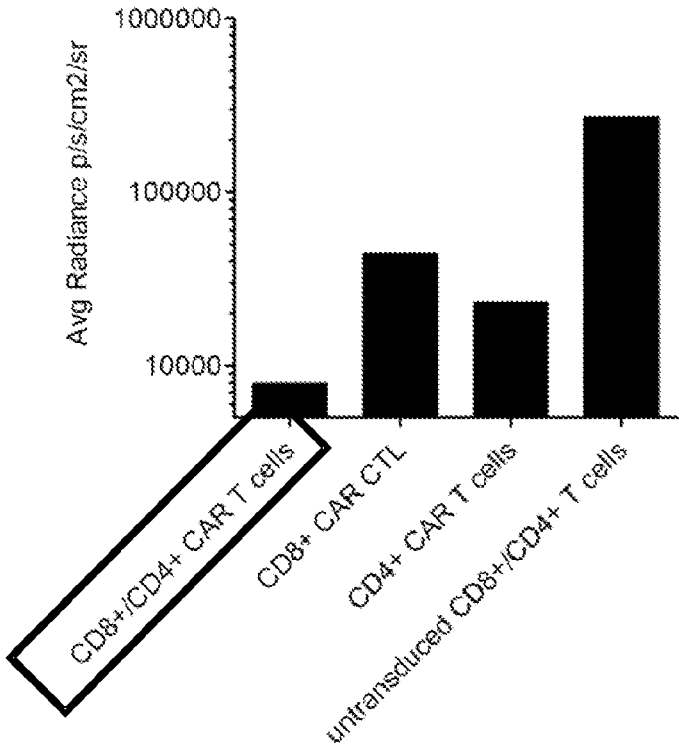
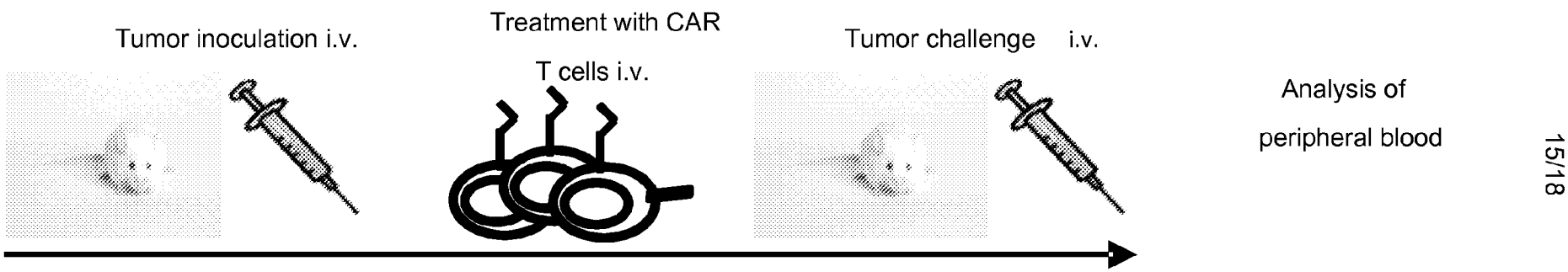


FIG. 13A


Tumor inoculation i.v.
Treatment with CAR
T cells i.v.
Tumor challenge i.v.
Analysis of
peripheral blood

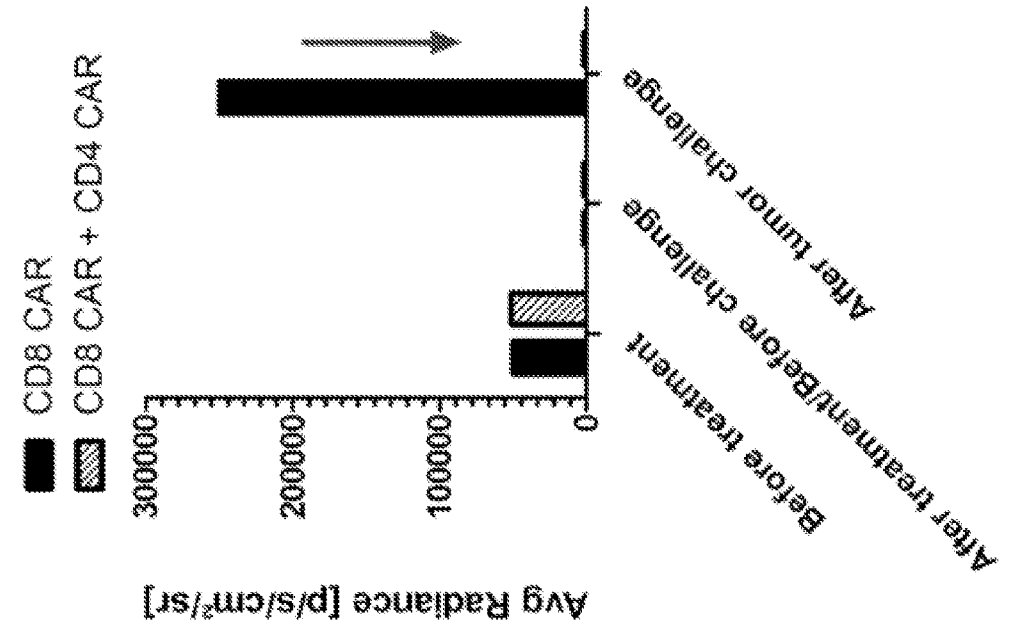

CD8 CAR
CD8 CAR + CD4 CAR
300000
200000
100000
0
Avg Radiance [p/s/cm²/sr]
Before treatment
After treatment/Before challenge
After tumor challenge

FIG. 13B

FIG. 13C

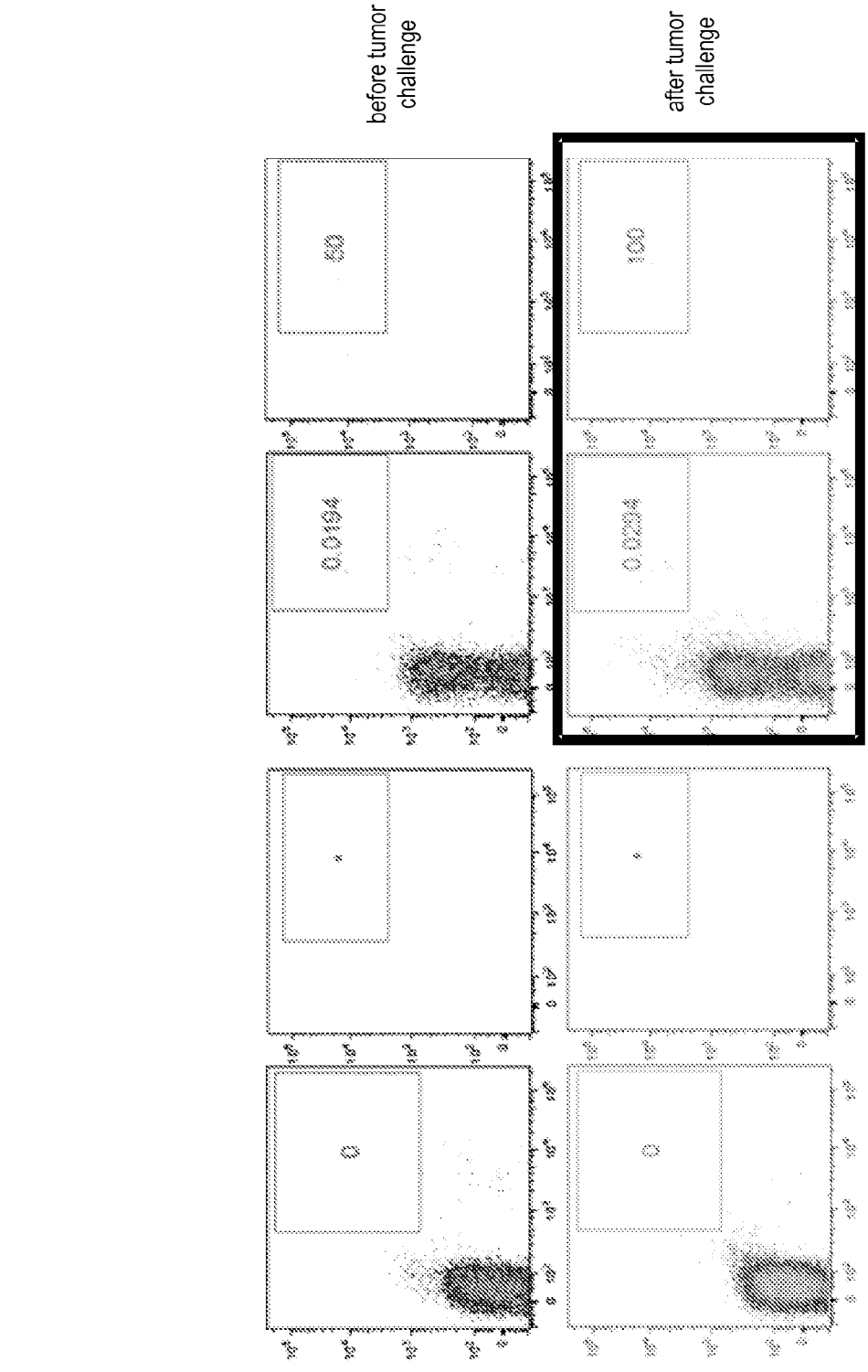

Mouse treated with CD8+ CAR T cells alone
before tumor challenge
after tumor challenge
0
0.0194
60
0.0204
100

FIG. 13D

Mouse treated with combined CD8+ and CD4+ CAR T cells

