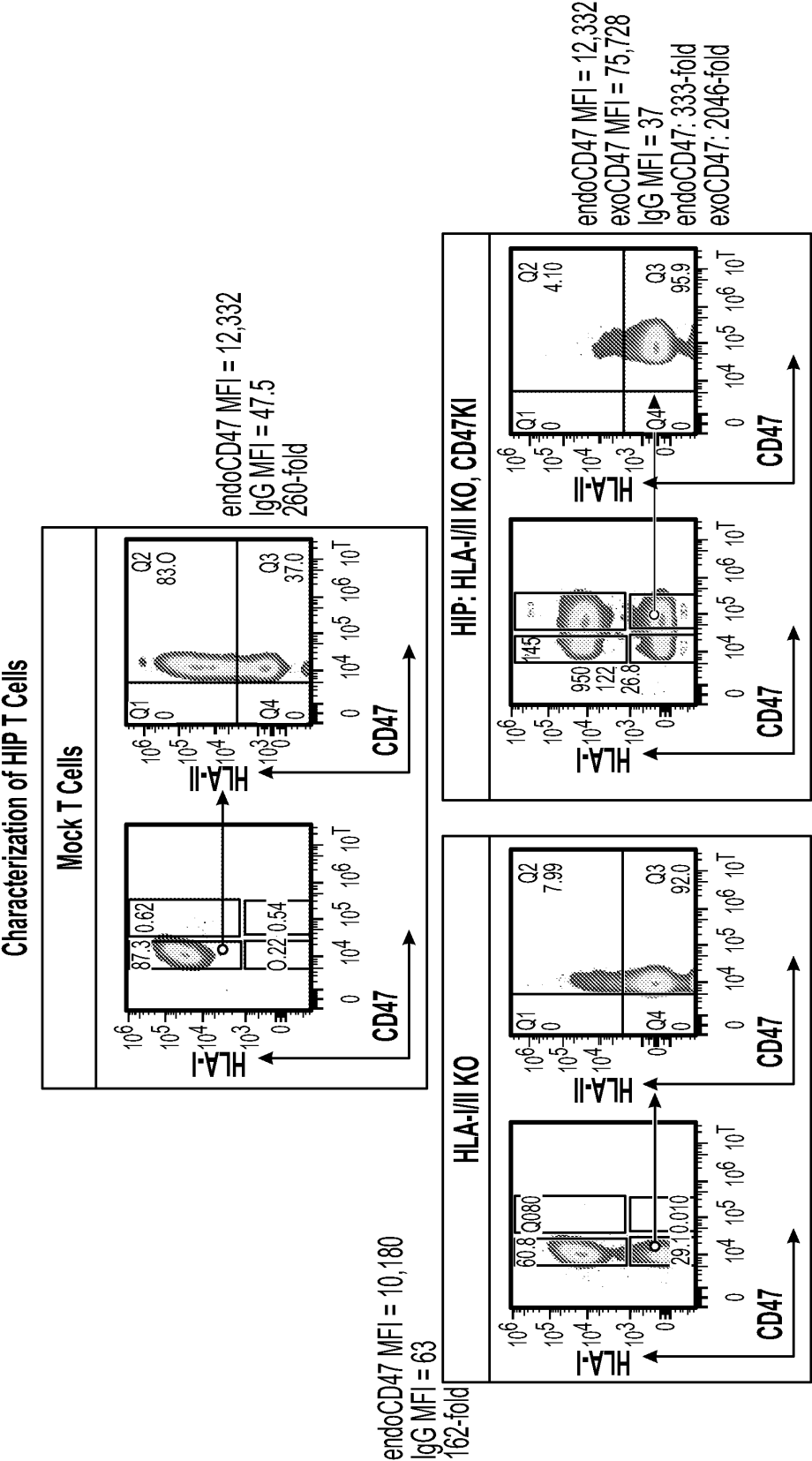




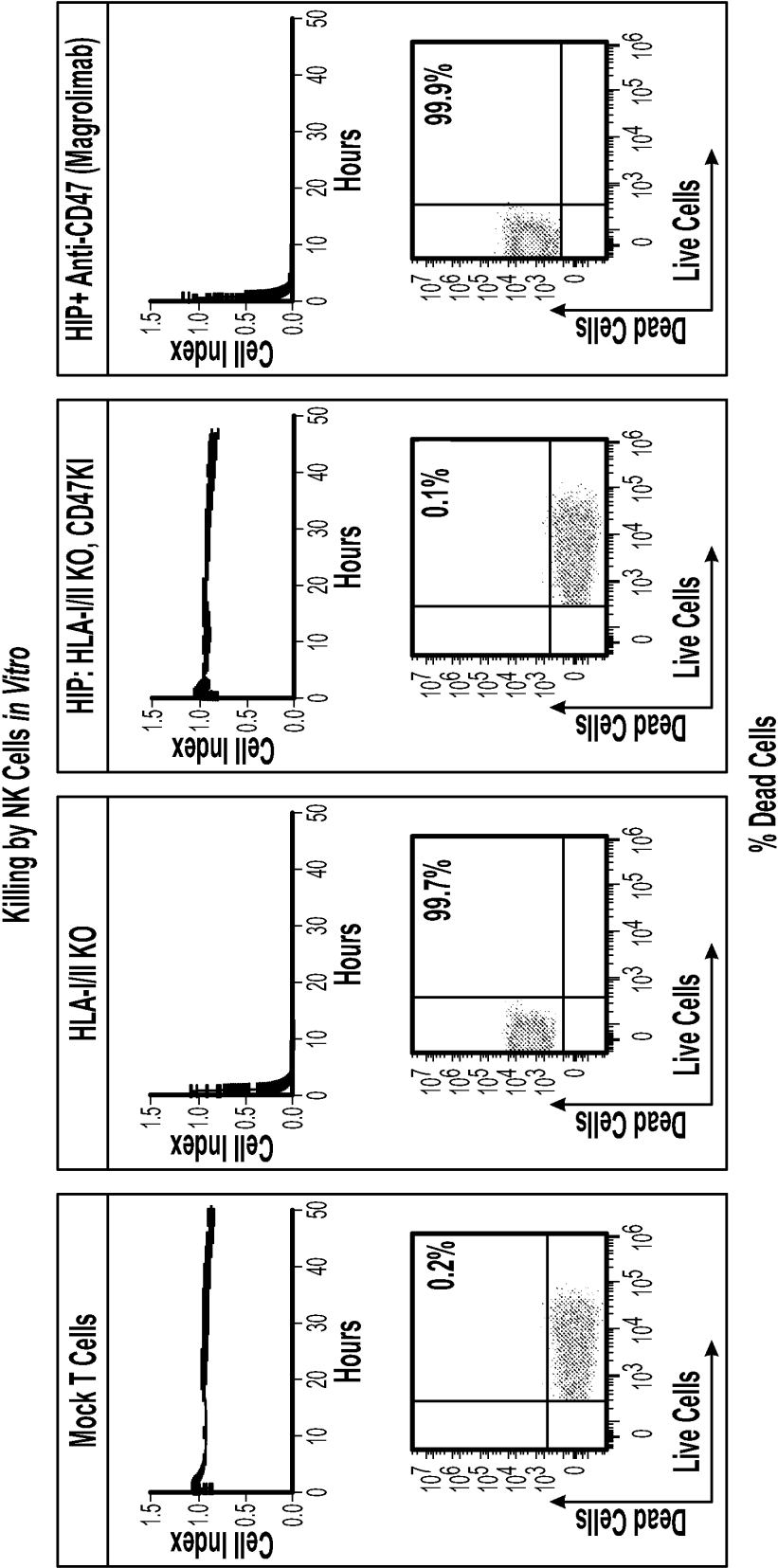


FIG. 2

3/62

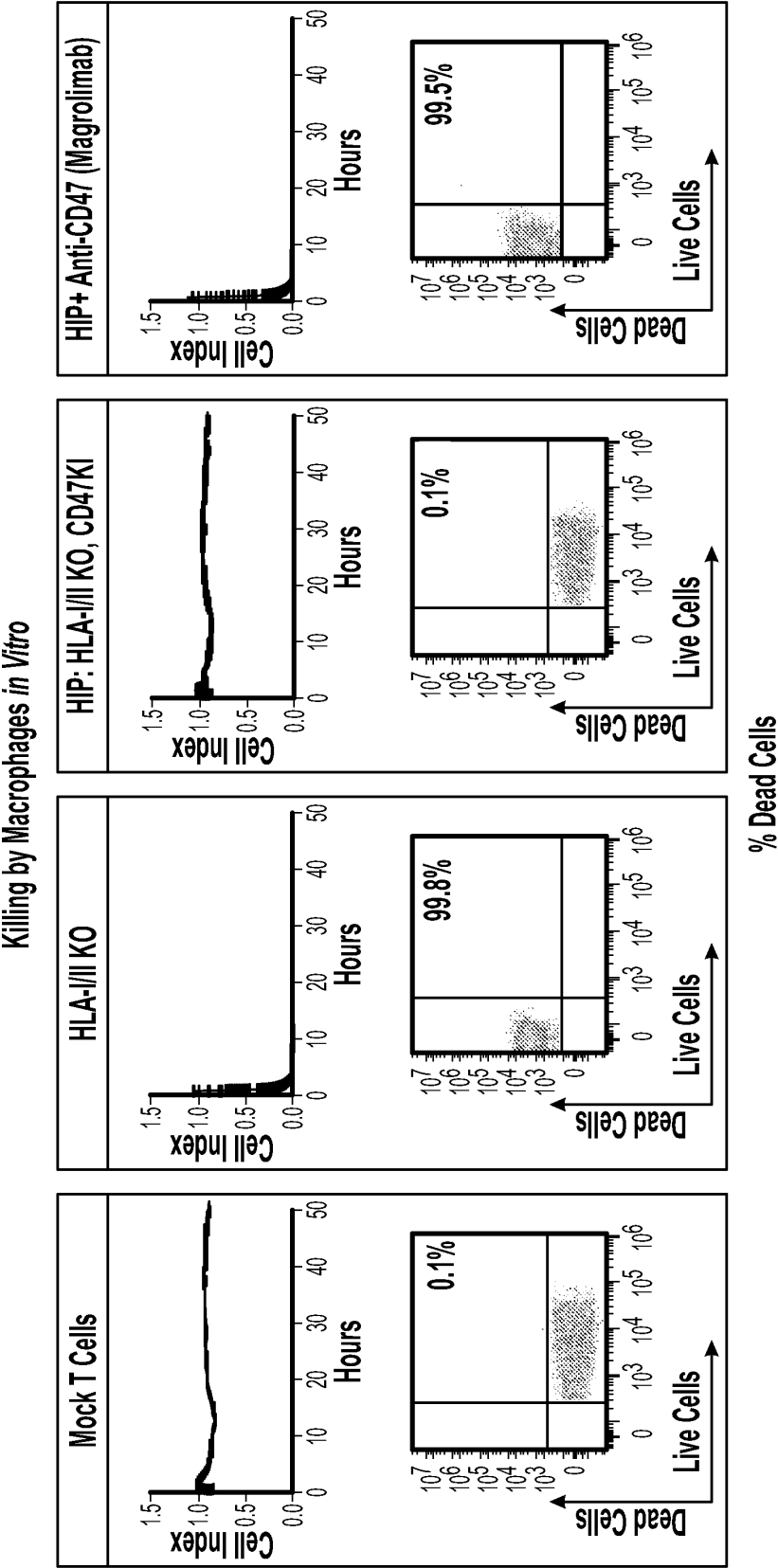


FIG. 3

Expression of CD19 CAR and CAR-CD47 Constructs in T Cells

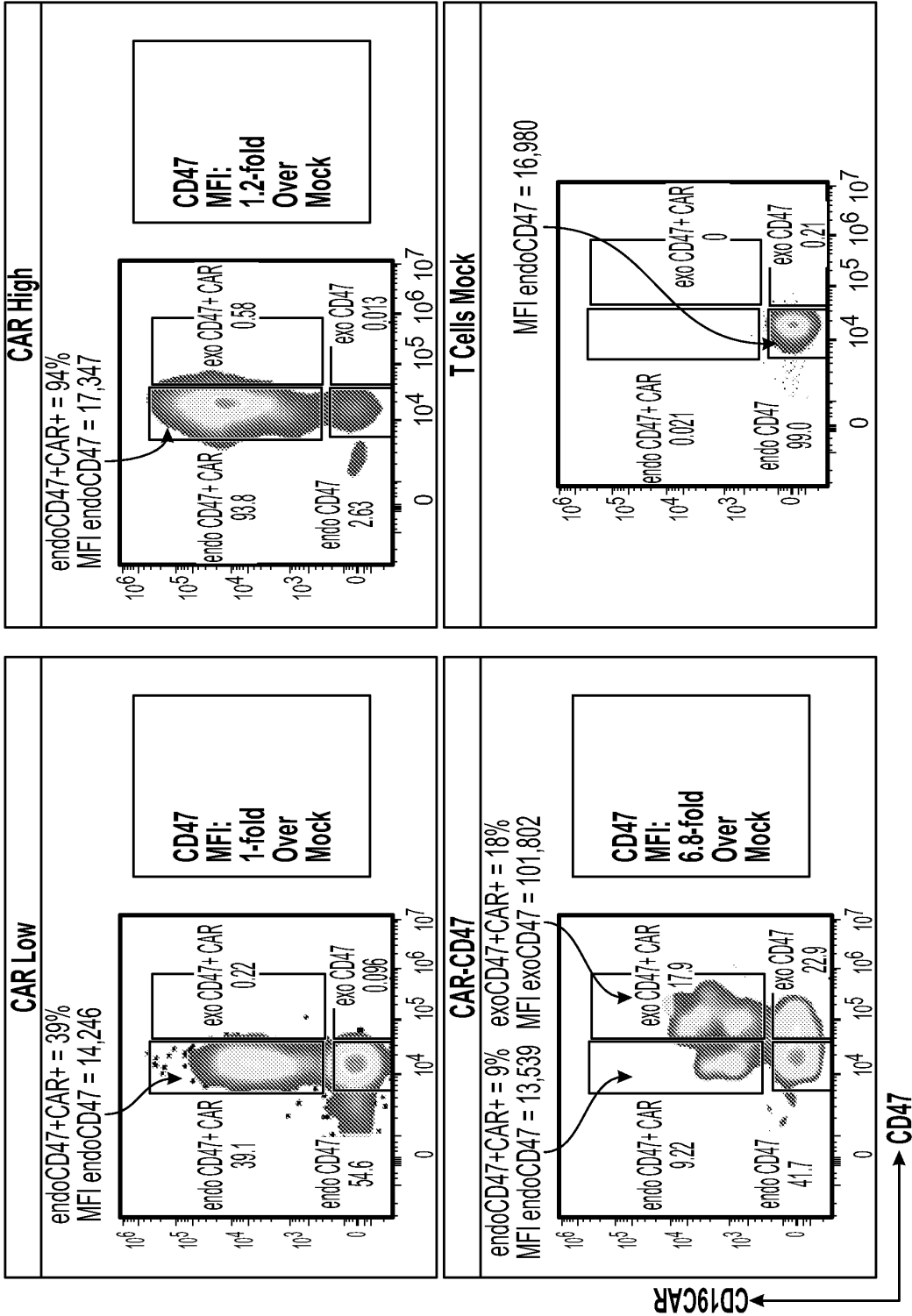


FIG. 4

Killing of CD19+ Tumor Cells by CAR-T Cells and CAR-CD47 T Cells in Vitro

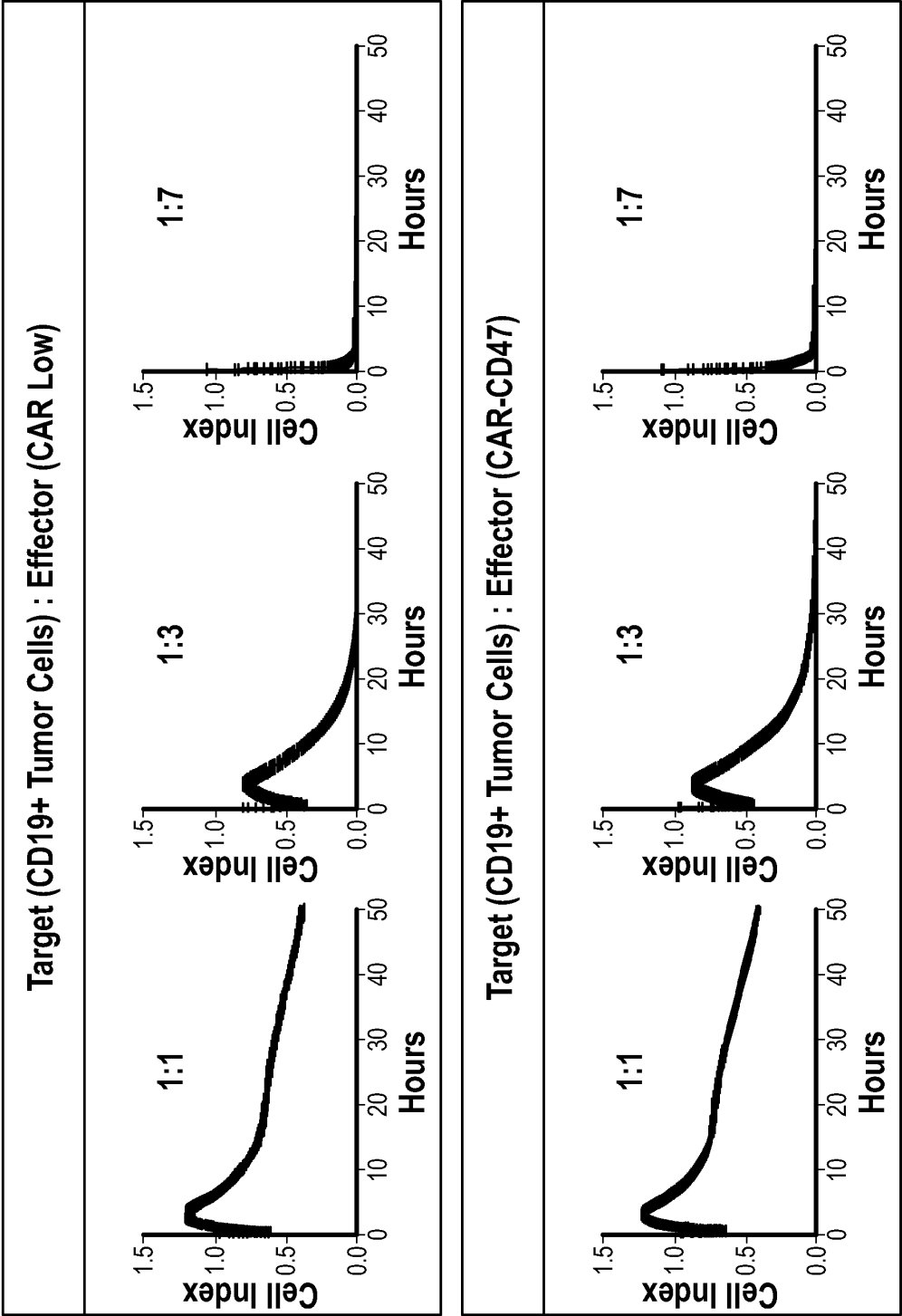


FIG. 5A

Killing of CD19+ Tumor Cells by CAR-T Cells and CAR-CD47 T Cells in Vitro

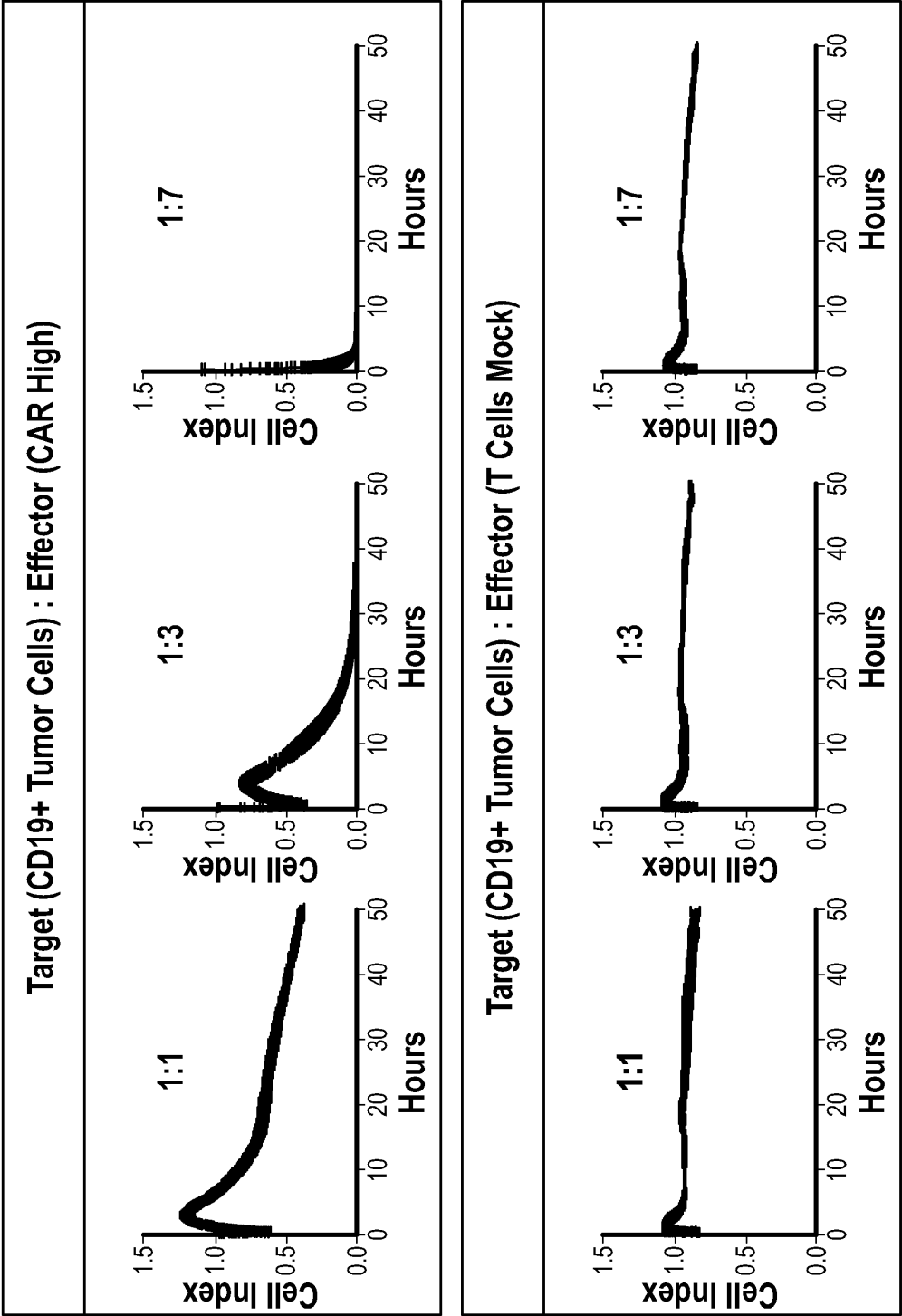


FIG. 5B

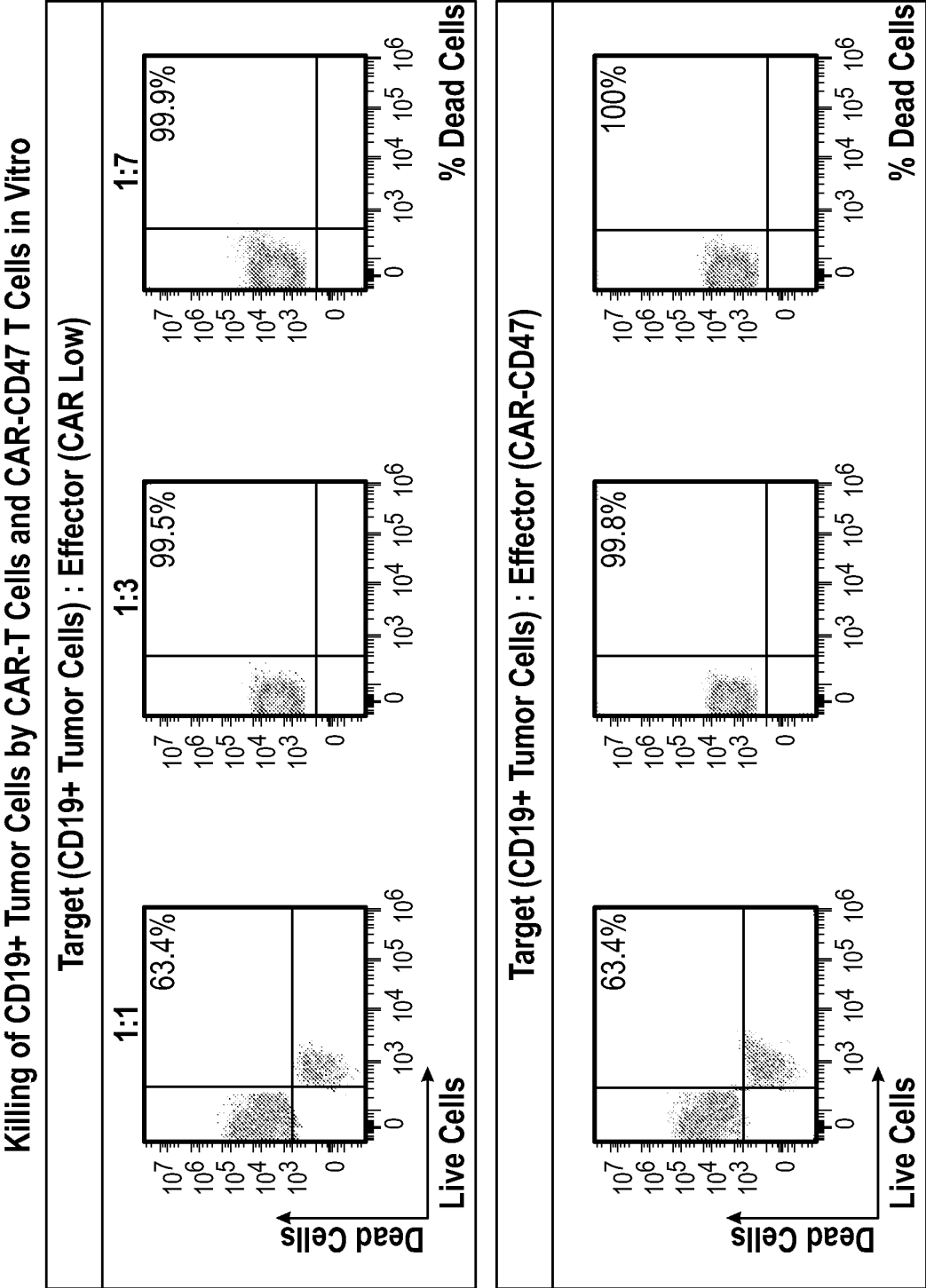


FIG. 6A

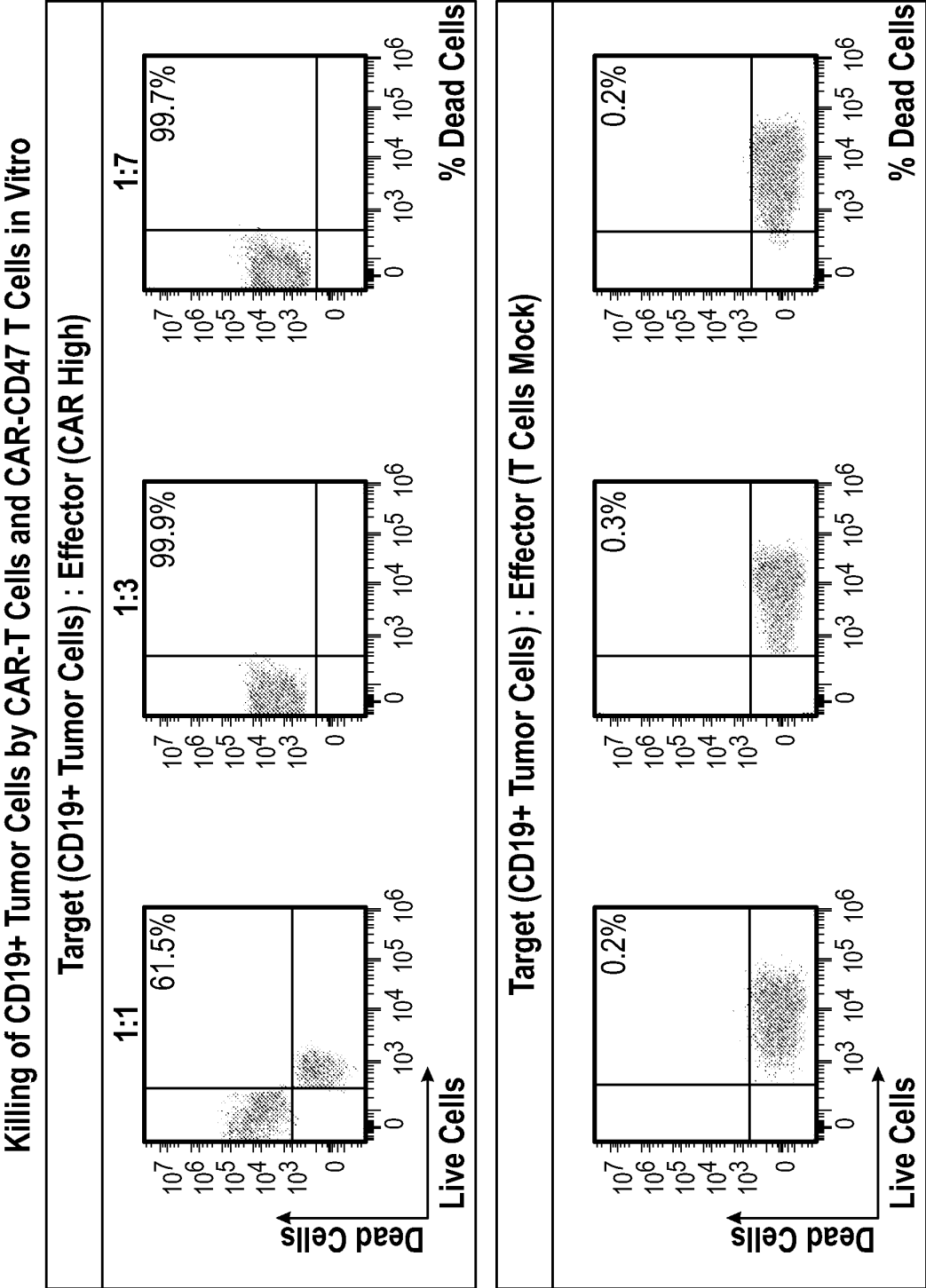


FIG. 6B

Killing of CD19+ Tumor Cells by Sorted CAR-T Cells in Vitro

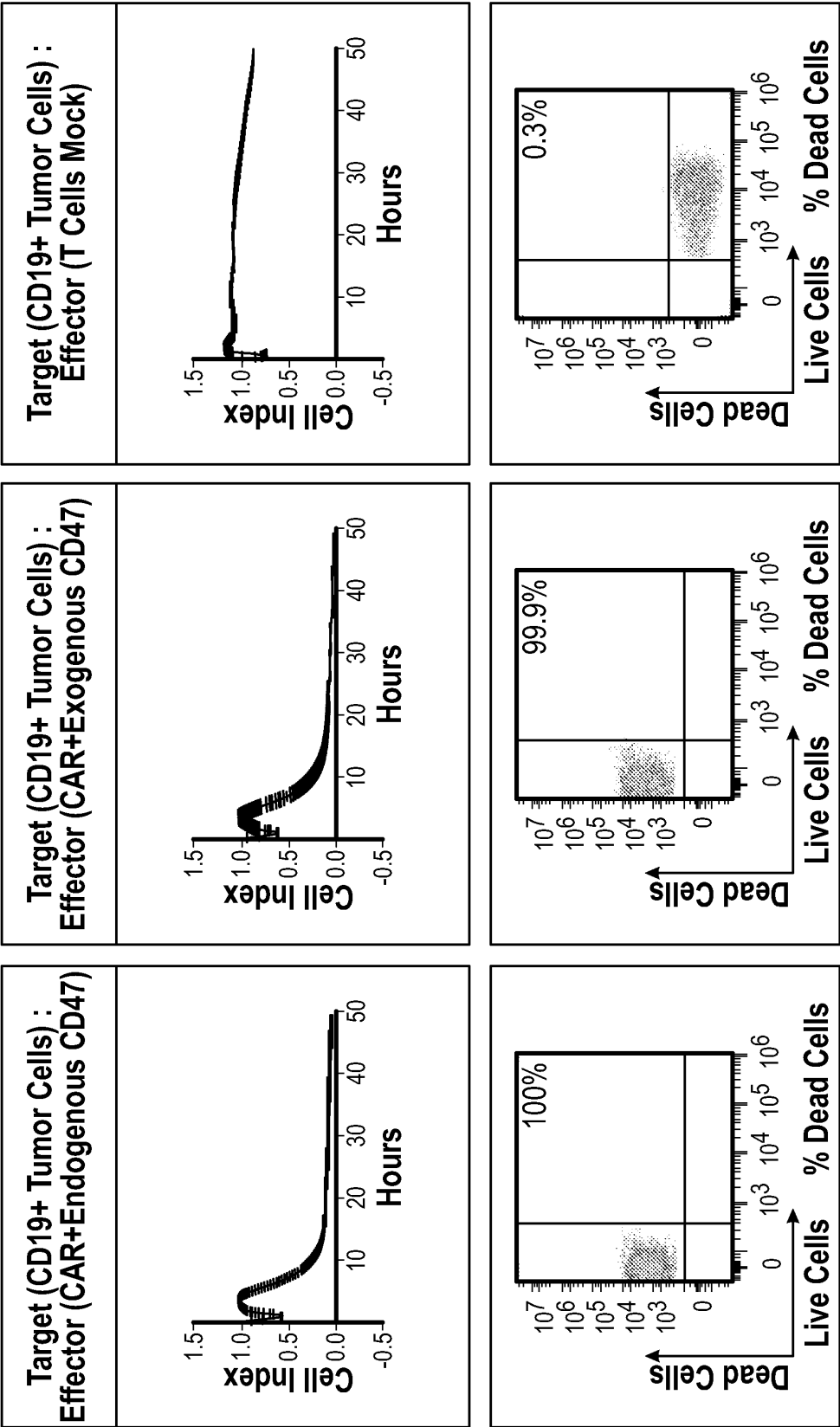


FIG. 7

10/62

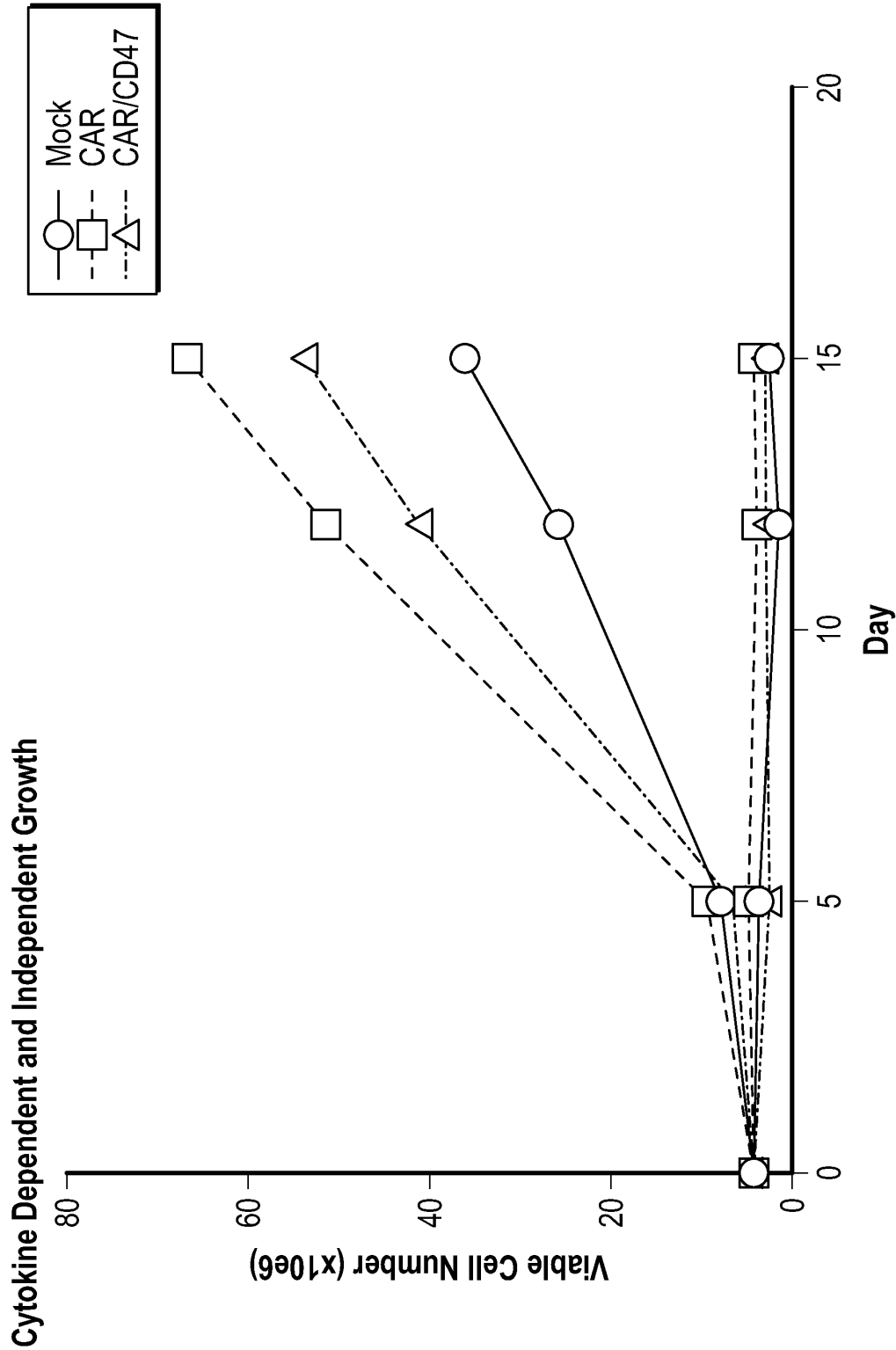


FIG. 8

Efficacy of CAR-T Cells in CD19+ Tumor Model

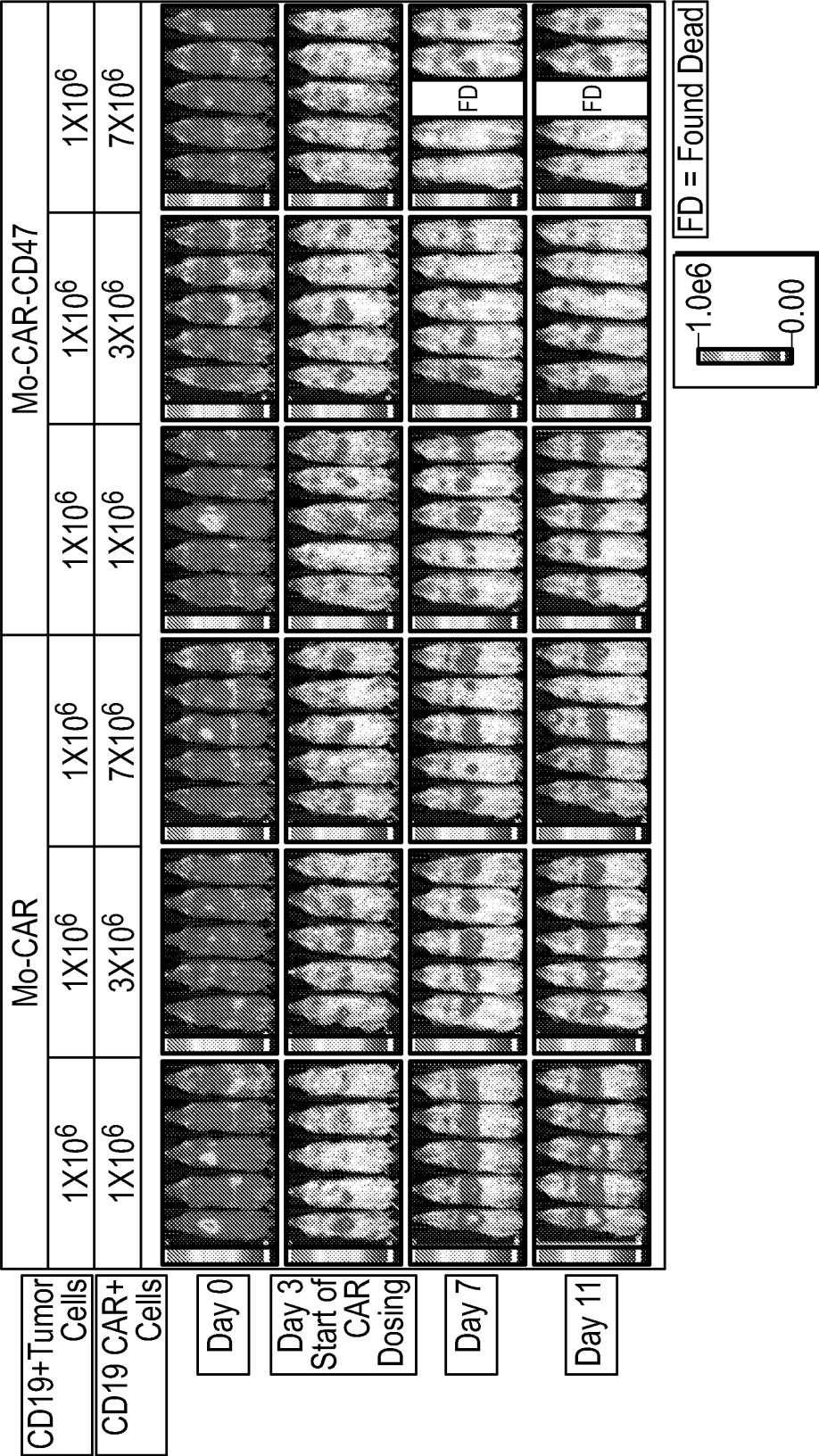


FIG. 9A

Efficacy of CAR-T Cells in a CD19+ Tumor Model

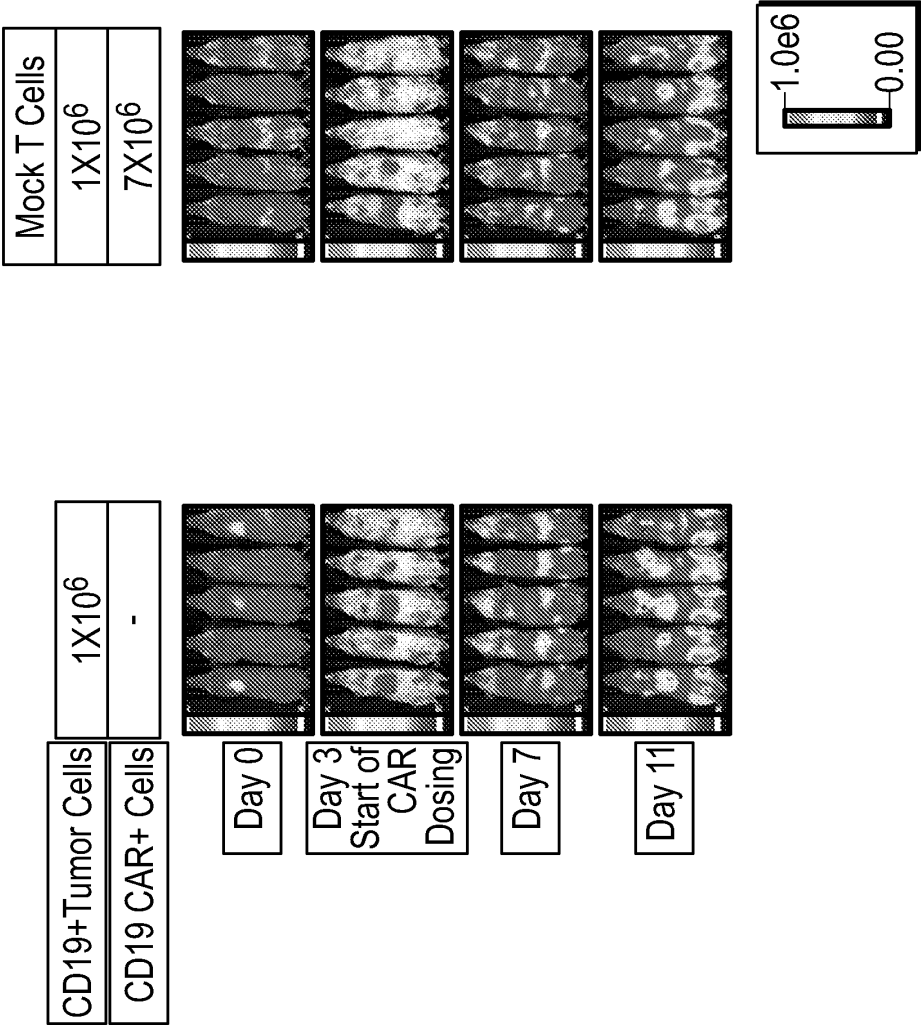


FIG. 9B

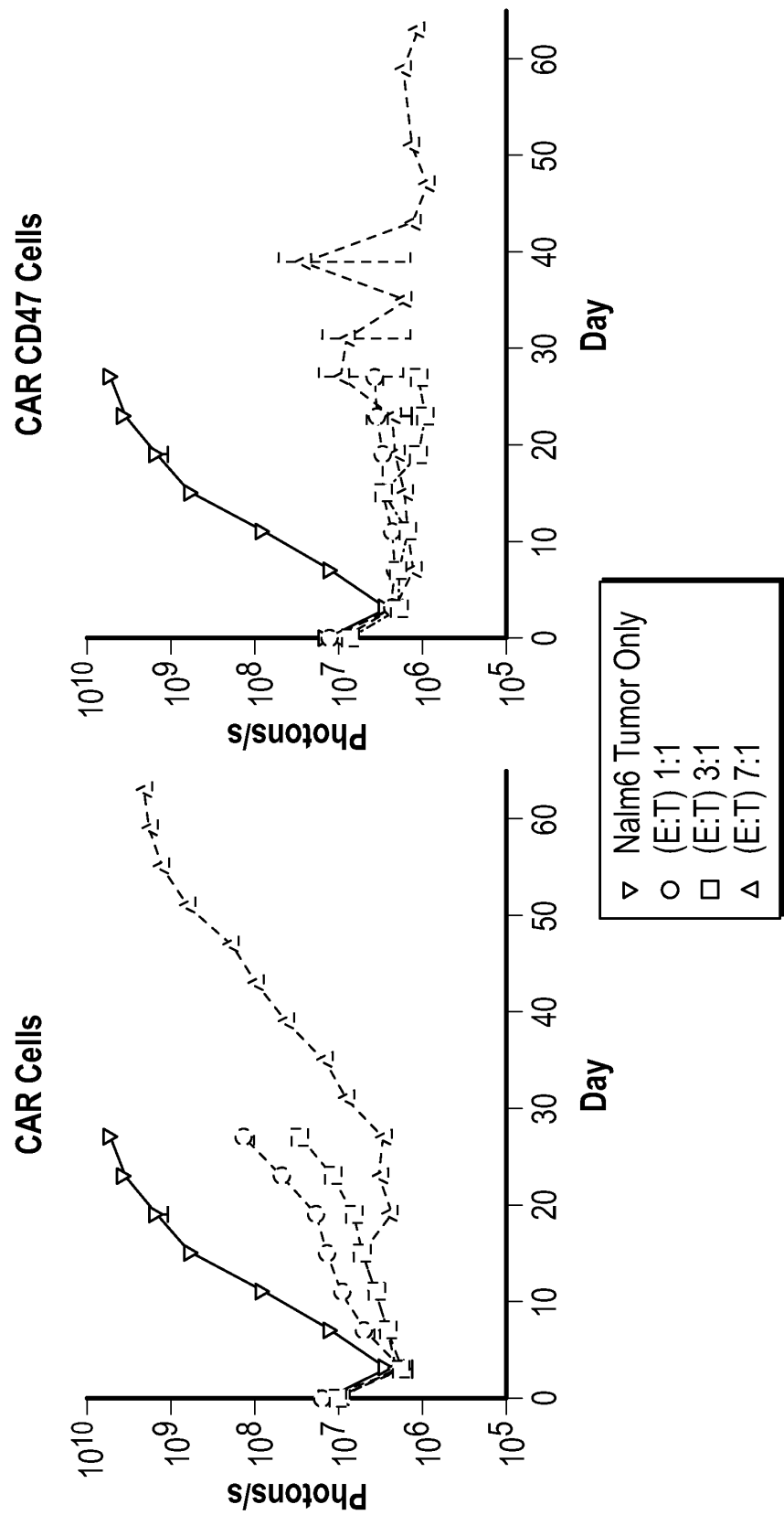
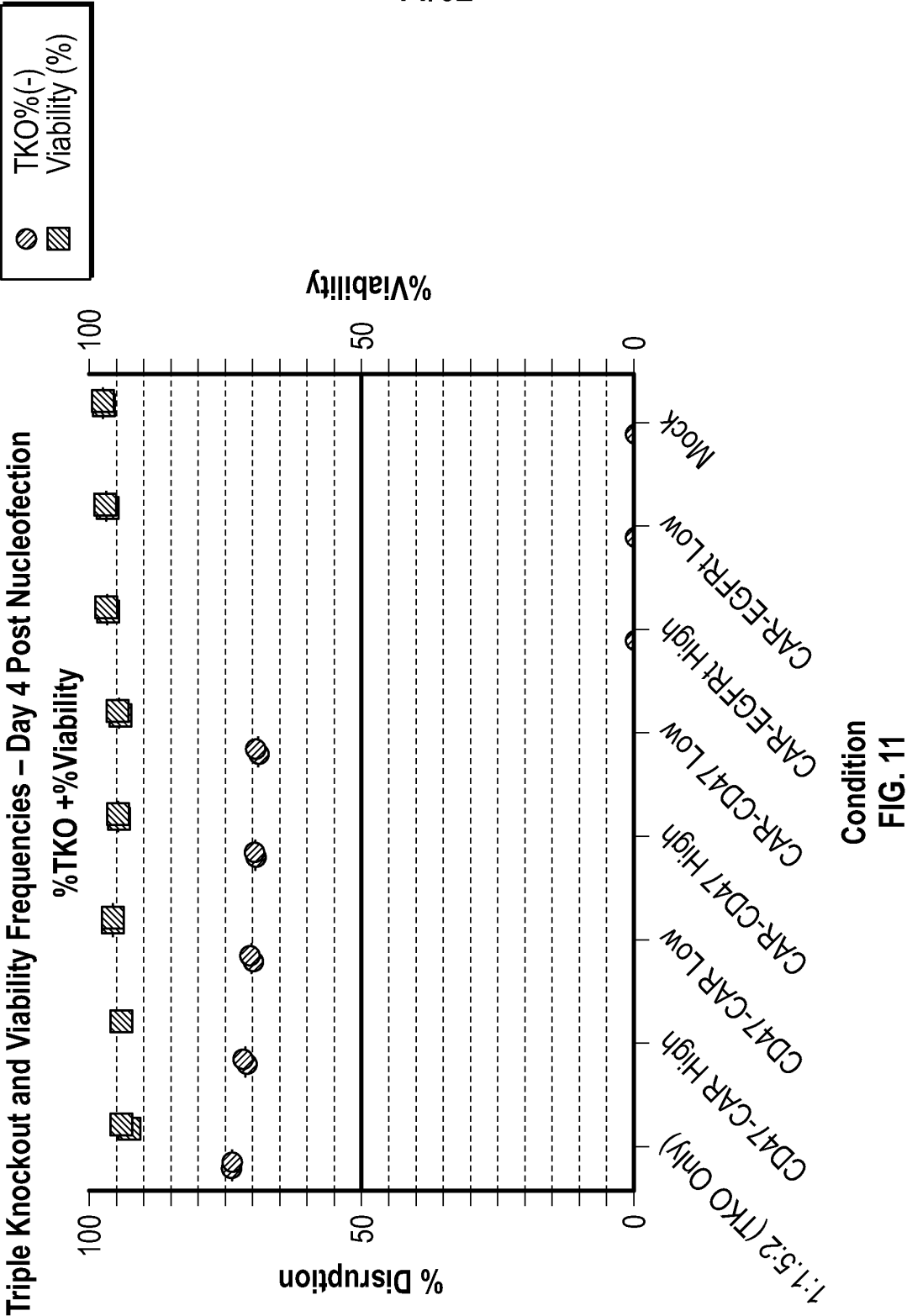
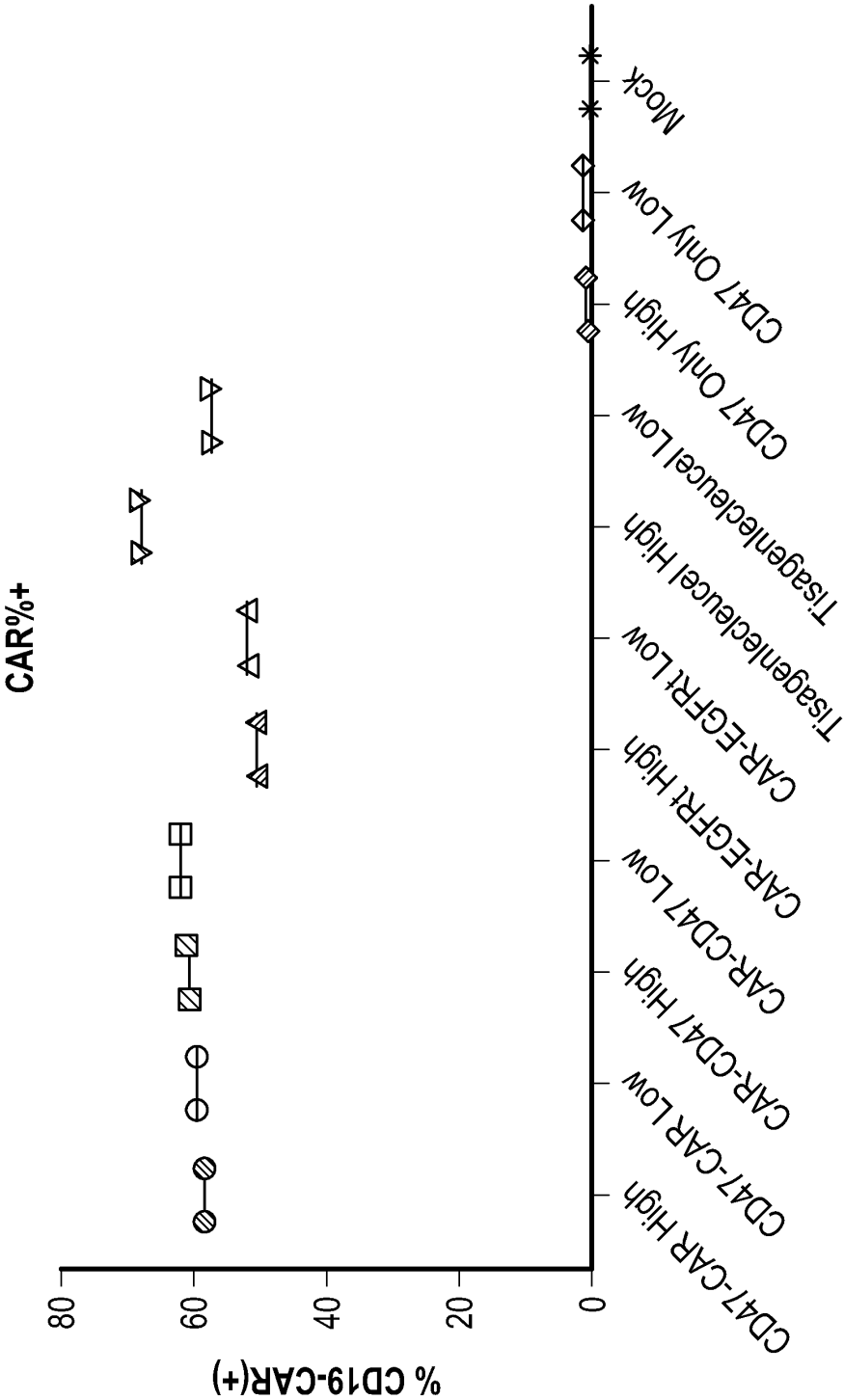


FIG. 10

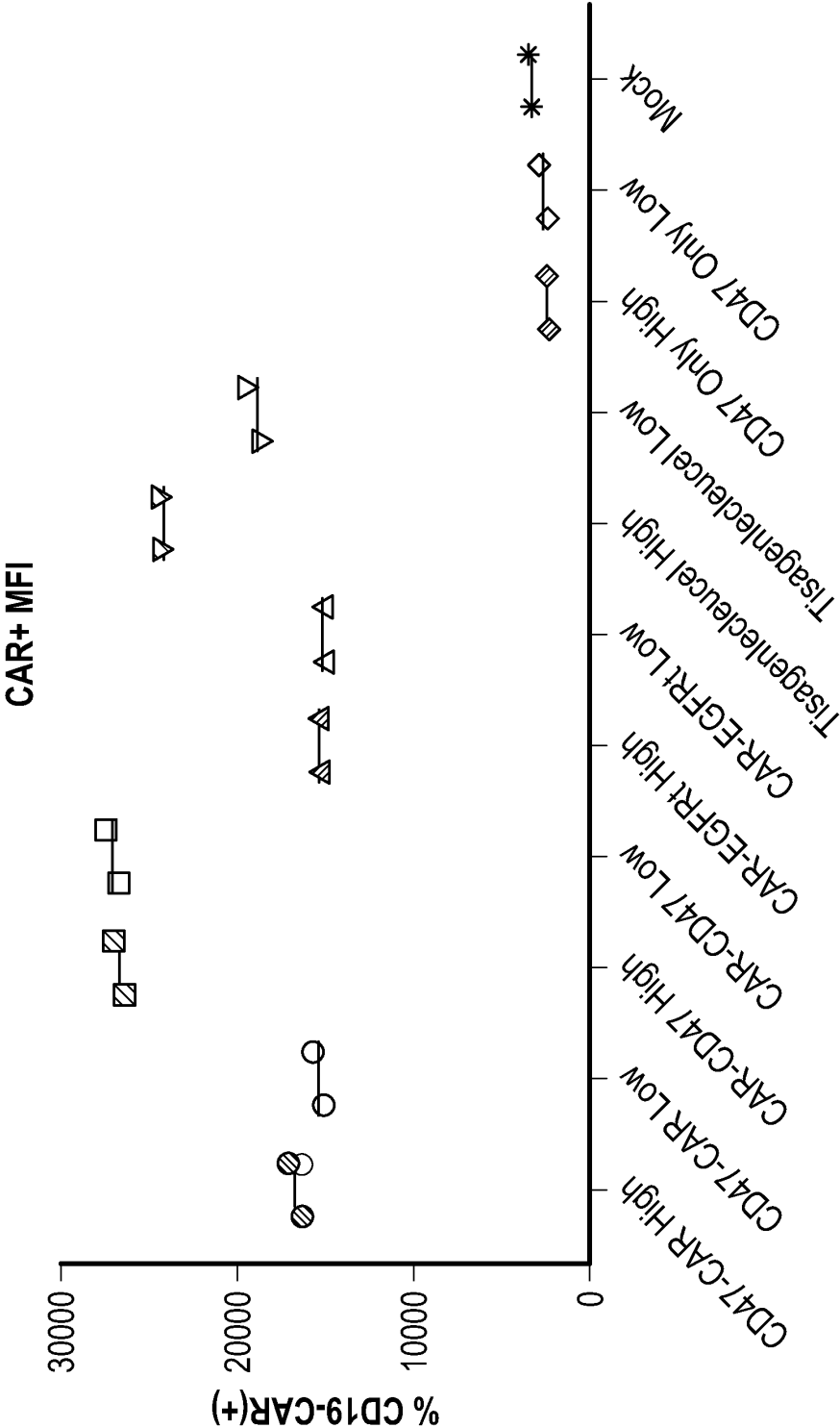


CAR Positive Frequencies and CAR MFIs



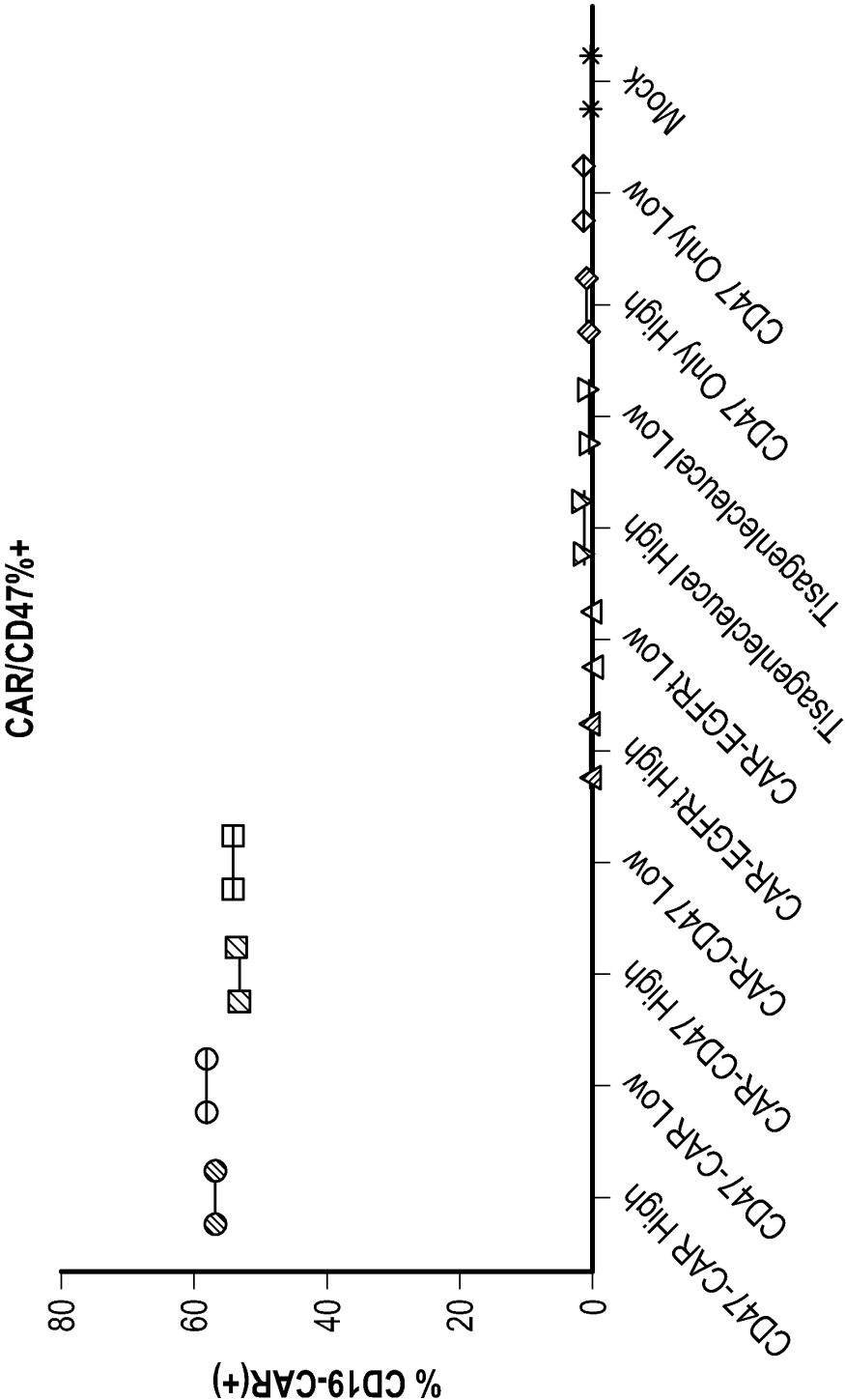
Conditions
FIG. 12A

CAR Positive Frequencies and CAR MFIs



Conditions
FIG. 12B

CAR and CD47 Double Positive Frequencies



Conditions
FIG. 13

Vector Copy Number Measurements: Day 8 Post-Activation

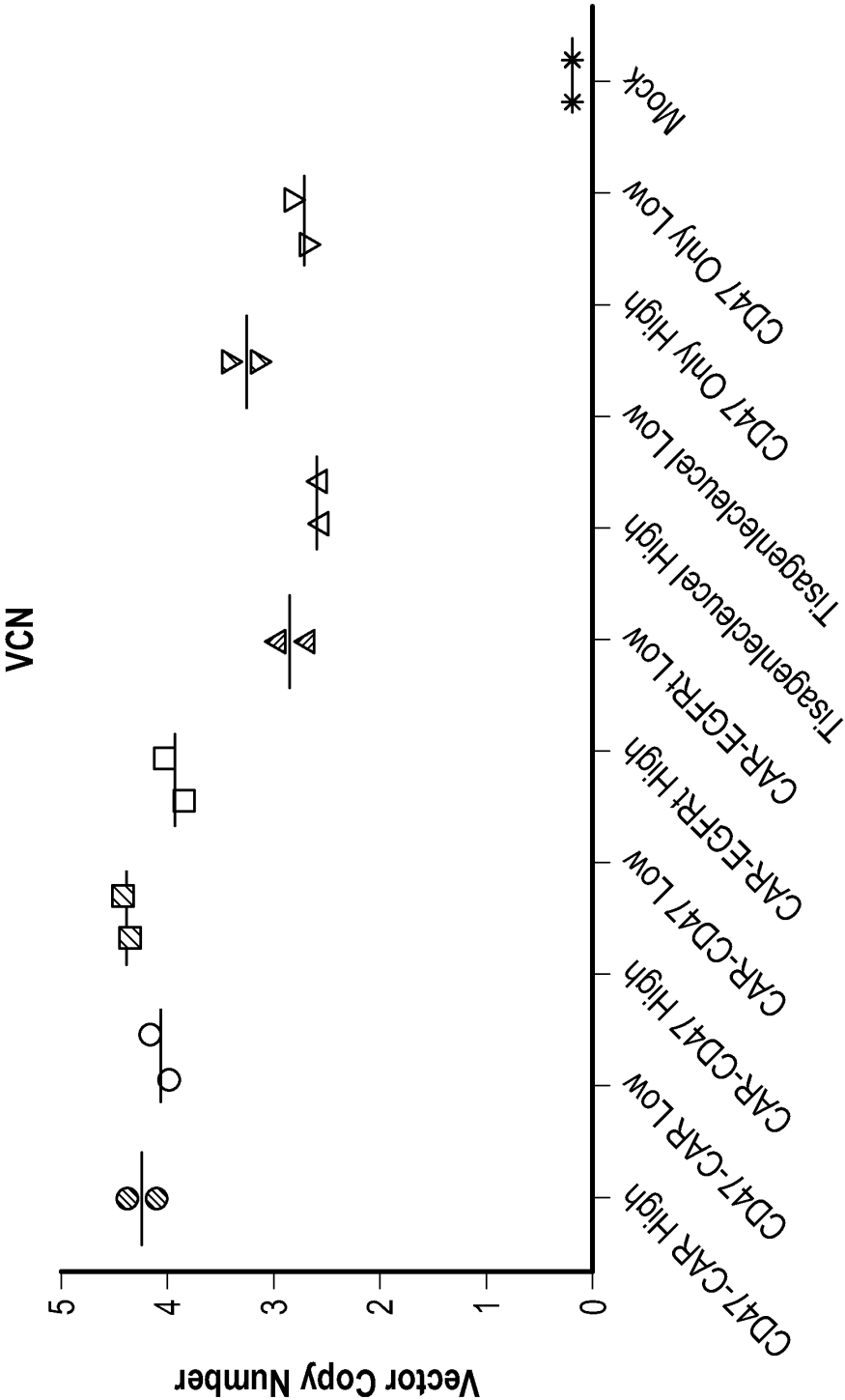


FIG. 14

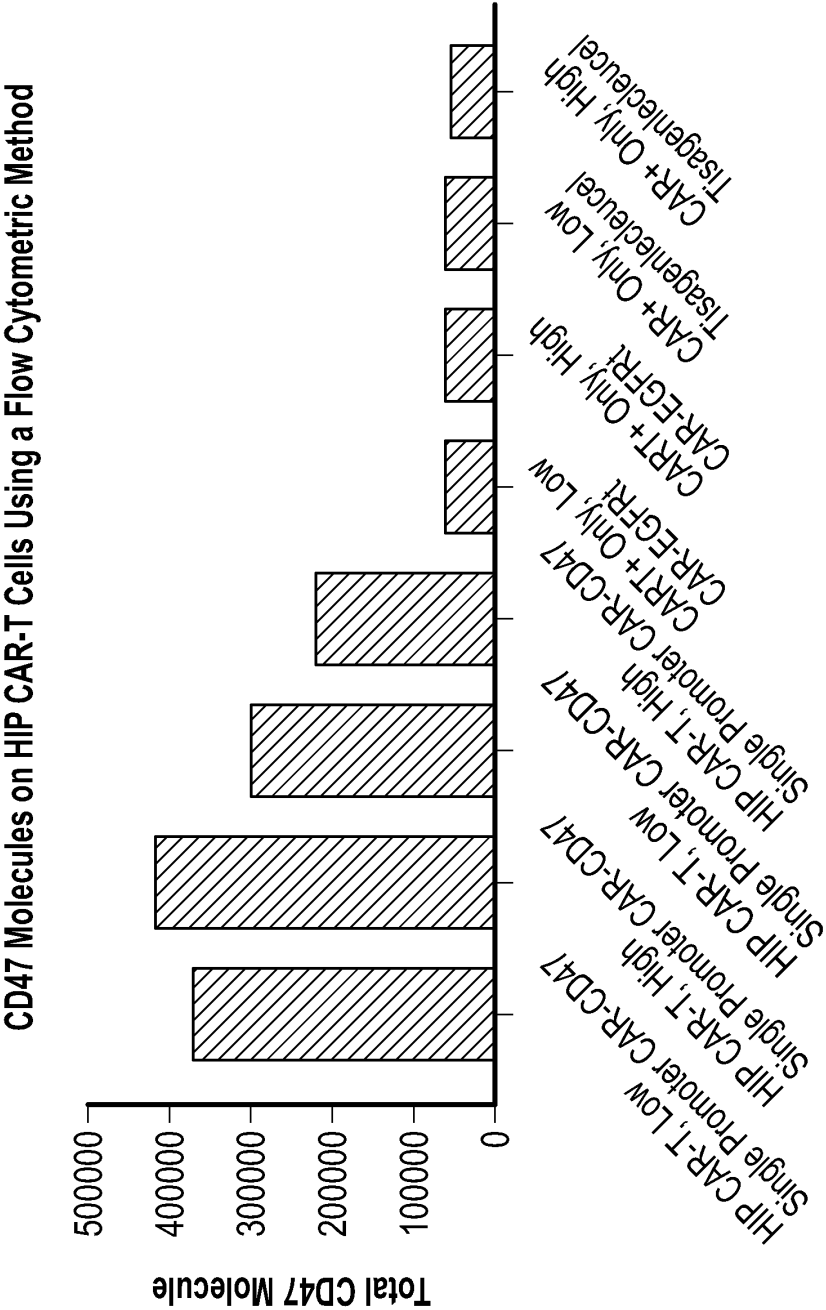


FIG. 15

HIP CAR-T, Low Single Promoter CAR-CD47

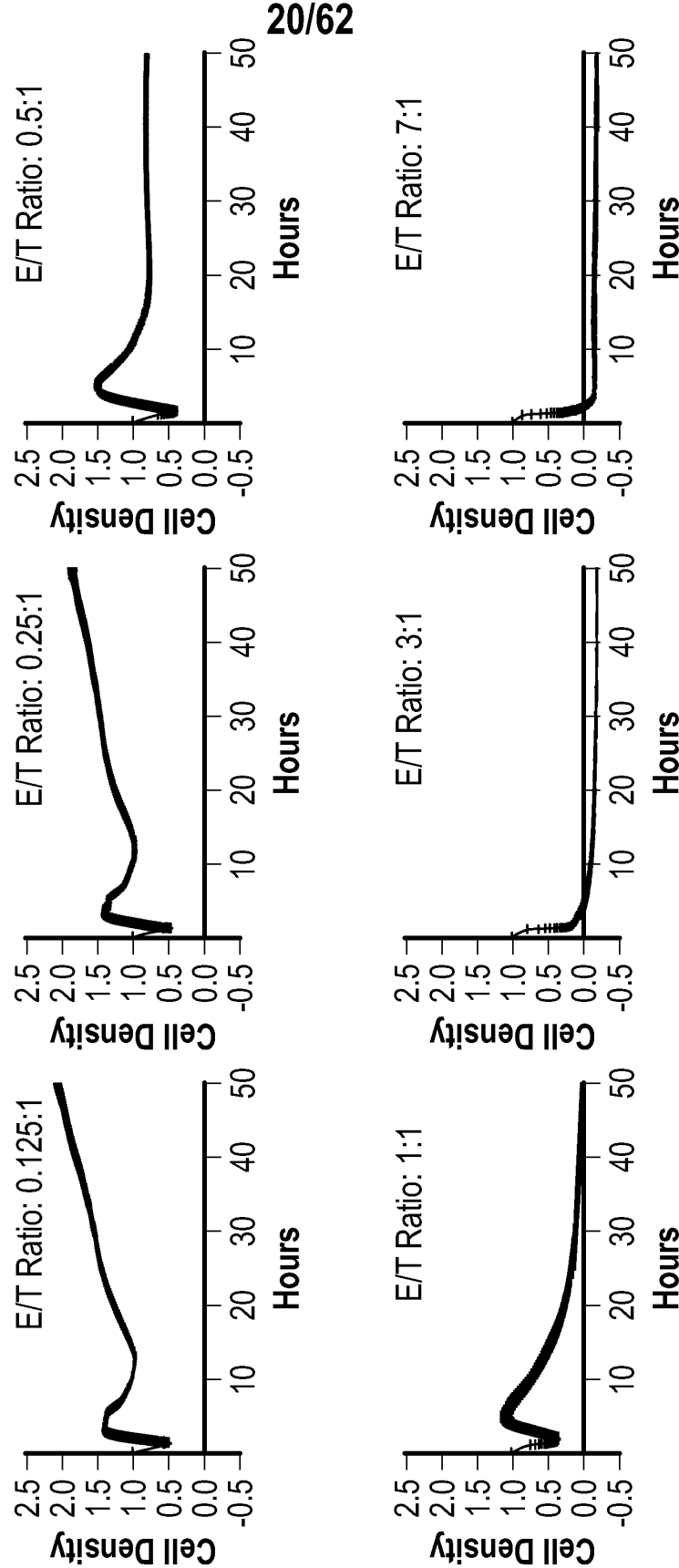


FIG. 16A

HIP CAR-T, High Single Promoter CAR-CD47

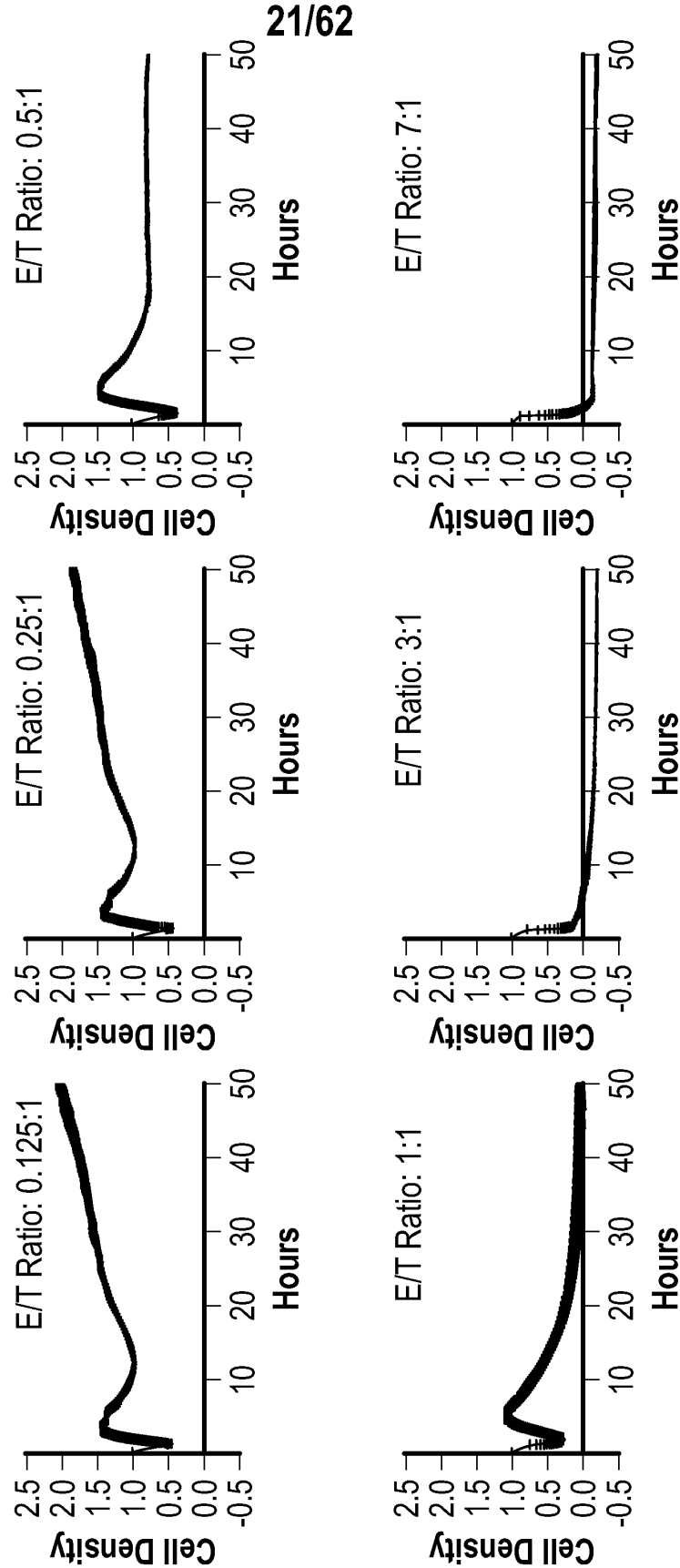


FIG. 16B

HIP CAR-T, Low Single Promoter CAR-CD47

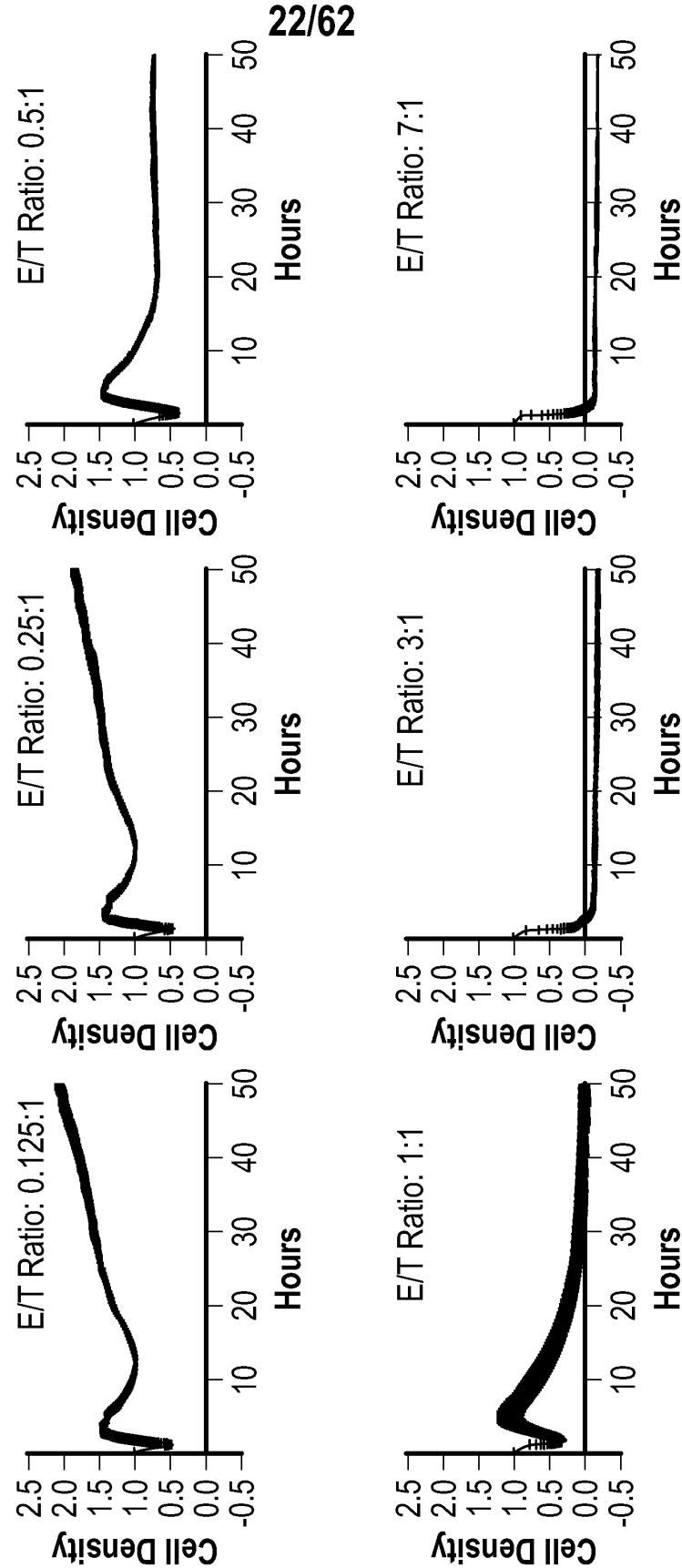


FIG. 16C

HIP CAR-T, High Single Promoter CAR-CD47

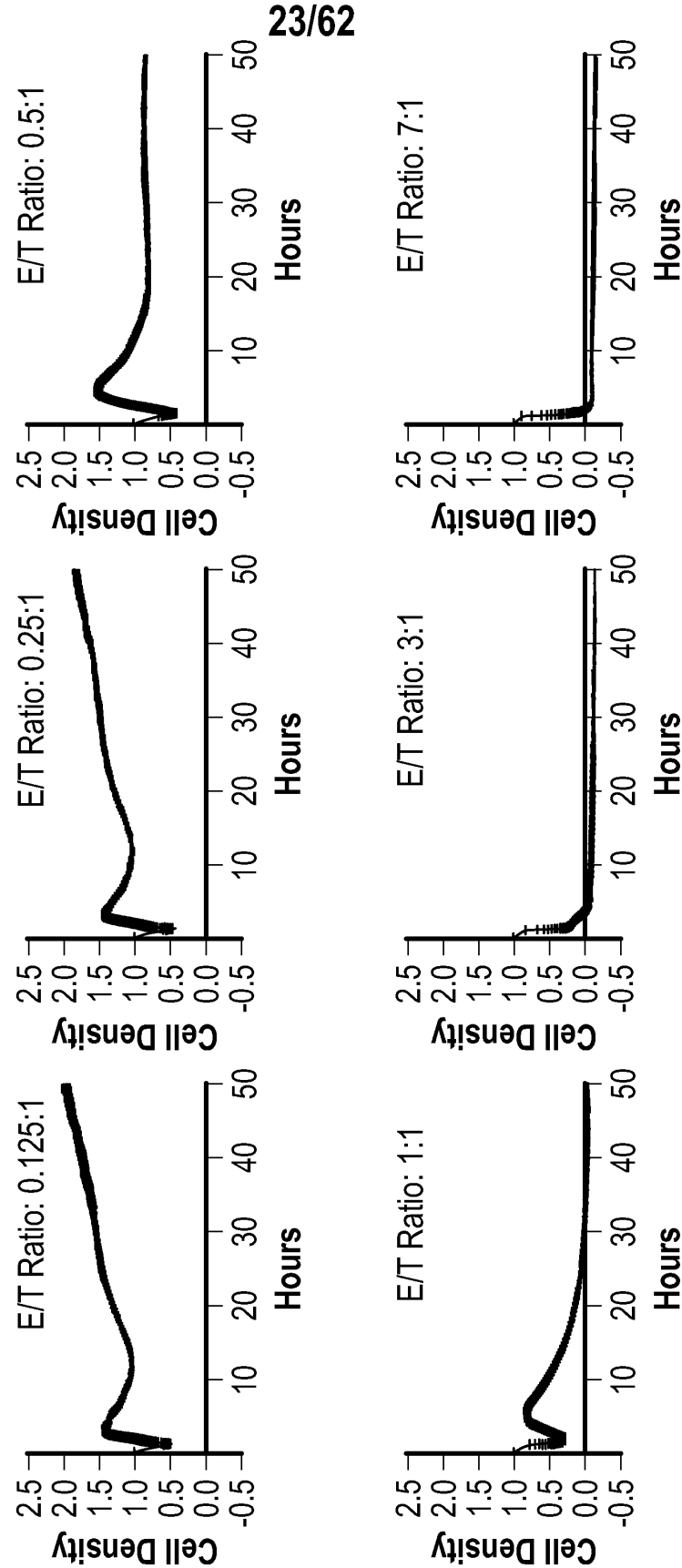


FIG. 16D

HIP CAR-T, High Single Promoter CAR-CD47, Dilution 1

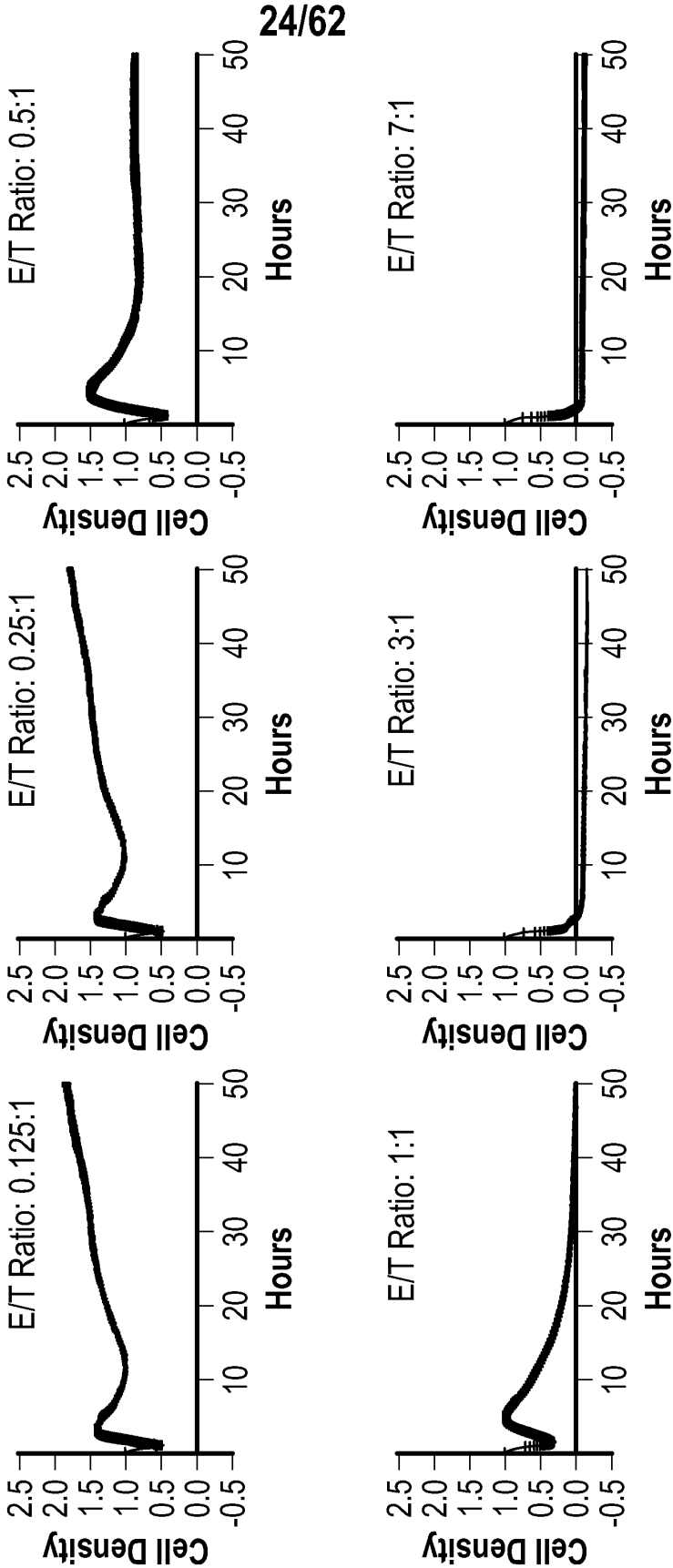


FIG. 17A

HIP CAR-T, High Single Promoter CAR-CD47, Dilution 4

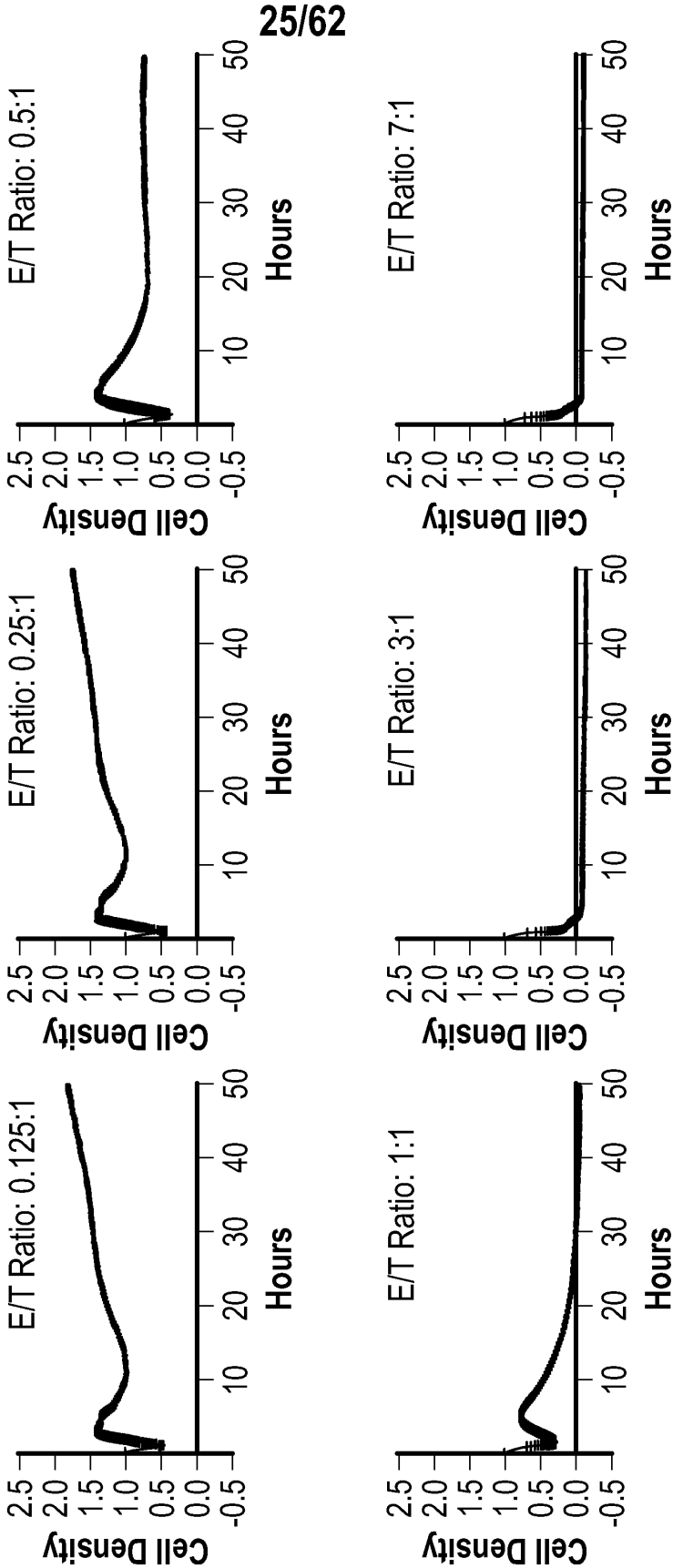


FIG. 17B

CAR+ Only, Low CAR-EGFRt

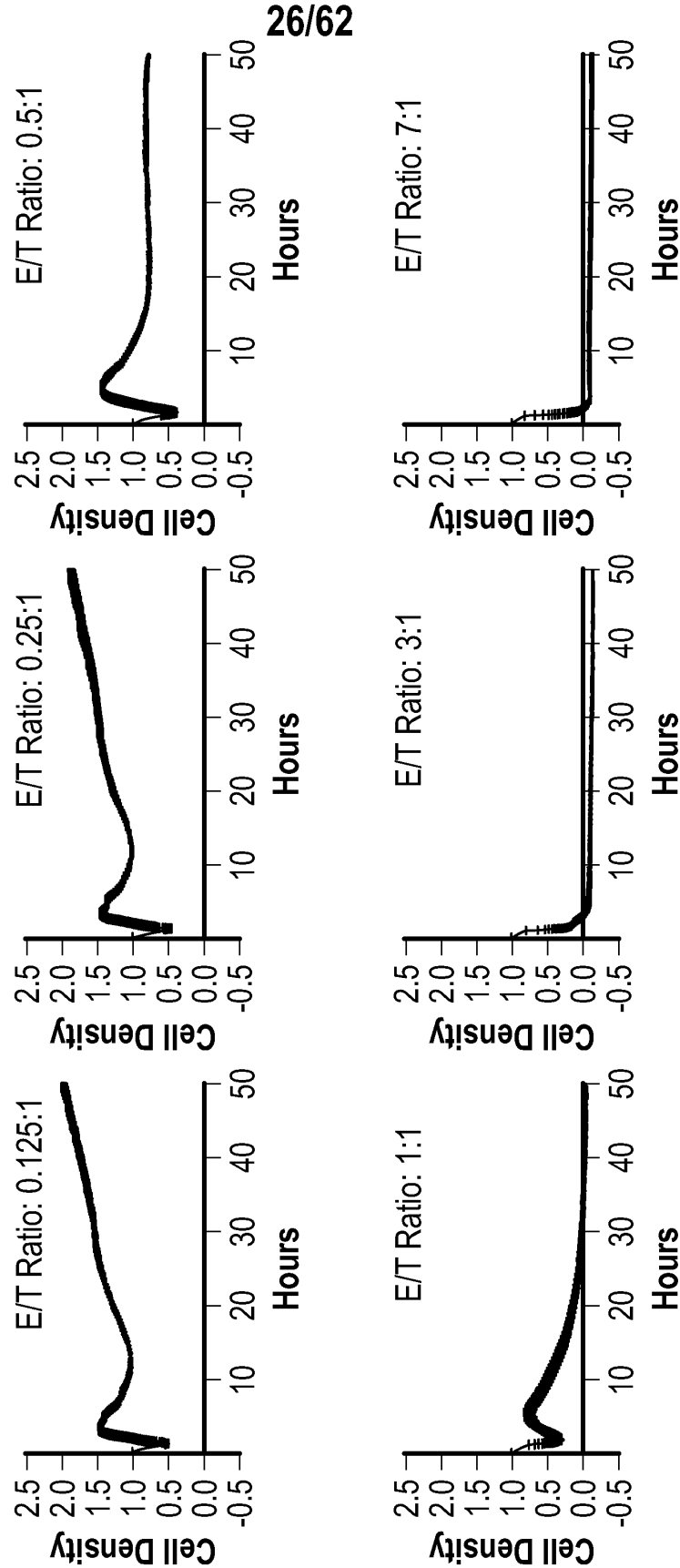


FIG. 17C

CAR+ Only, High CAR-EGFRt

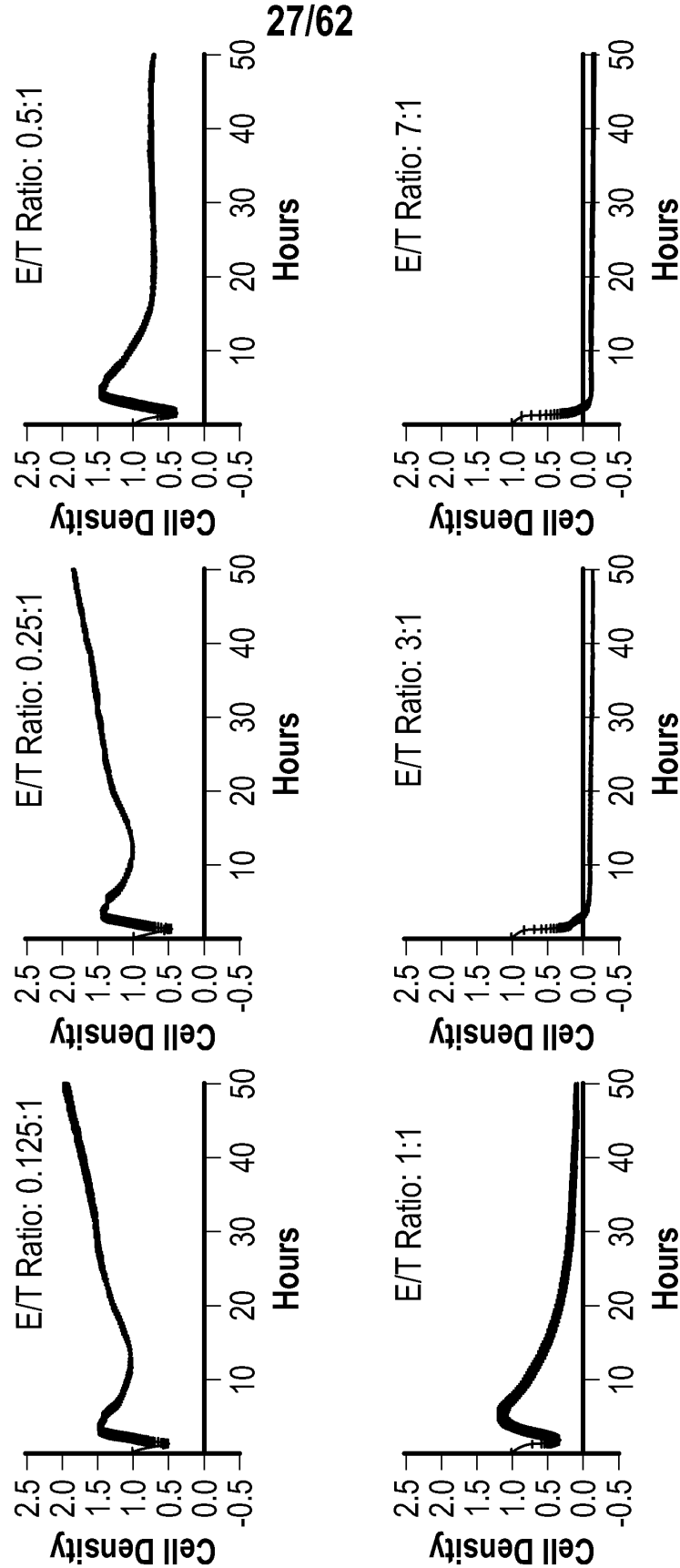


FIG. 17D

CAR+ Only, Low Tisagenlecleucel

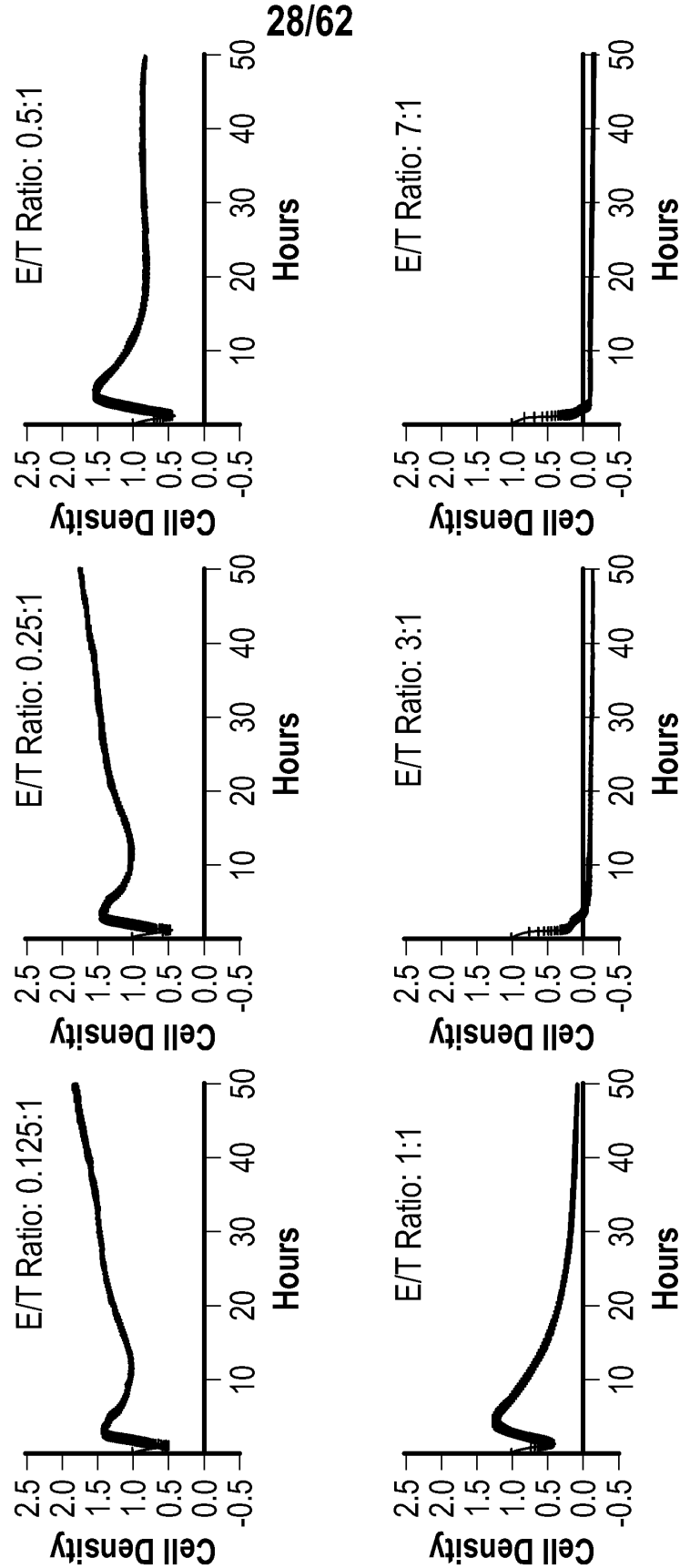


FIG. 18A

CAR+ Only, High Tisagenlecleucel

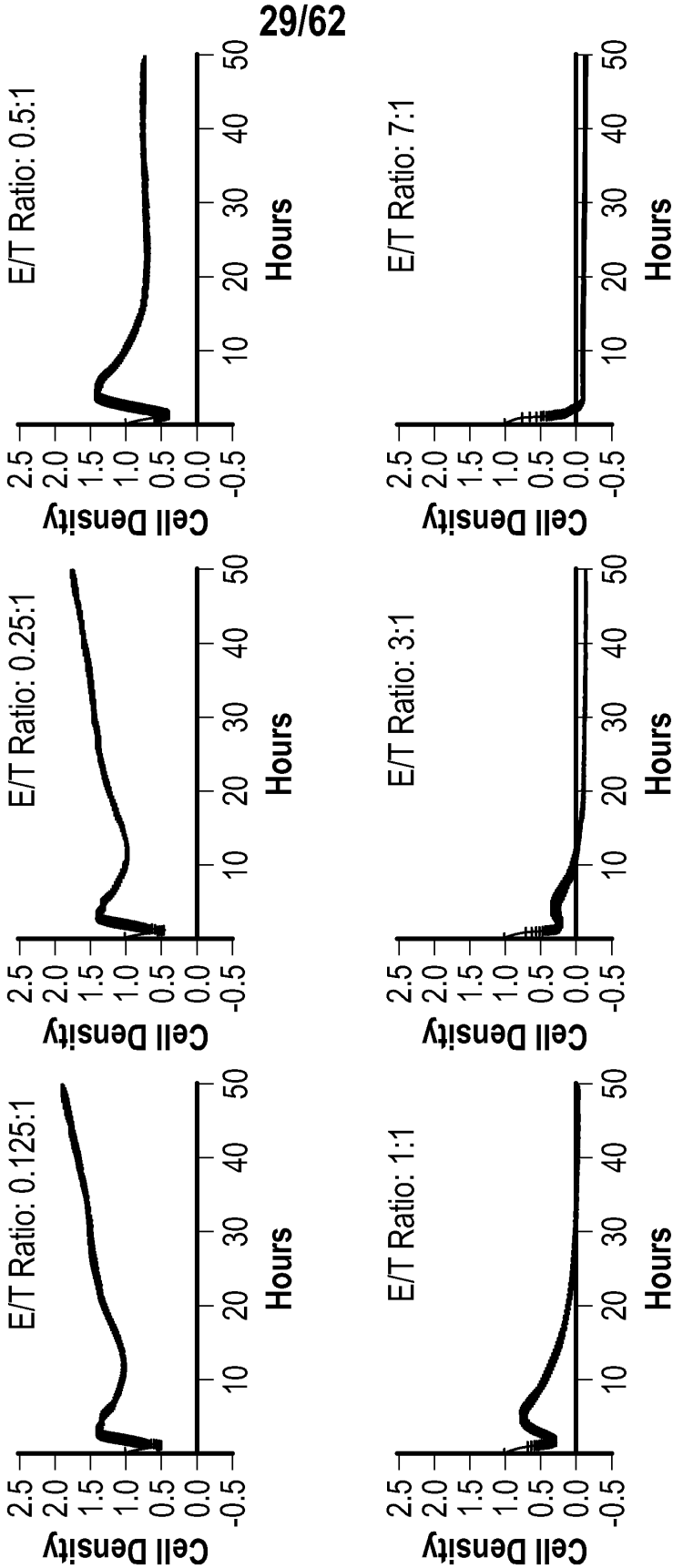


FIG. 18B

Mock T-Cells

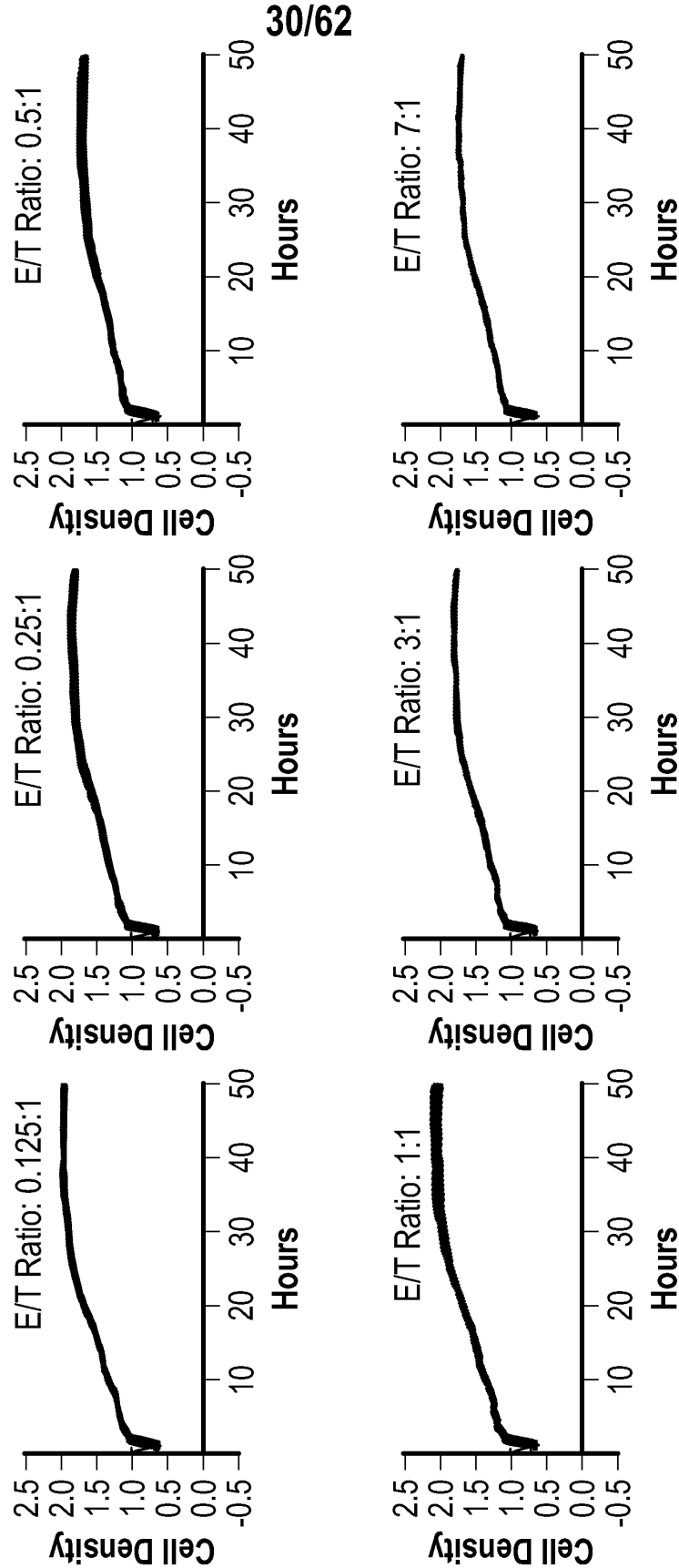


FIG. 18C

Efficacy of HIP CAR-T Cells in Mouse Model of CD19+ Cancer

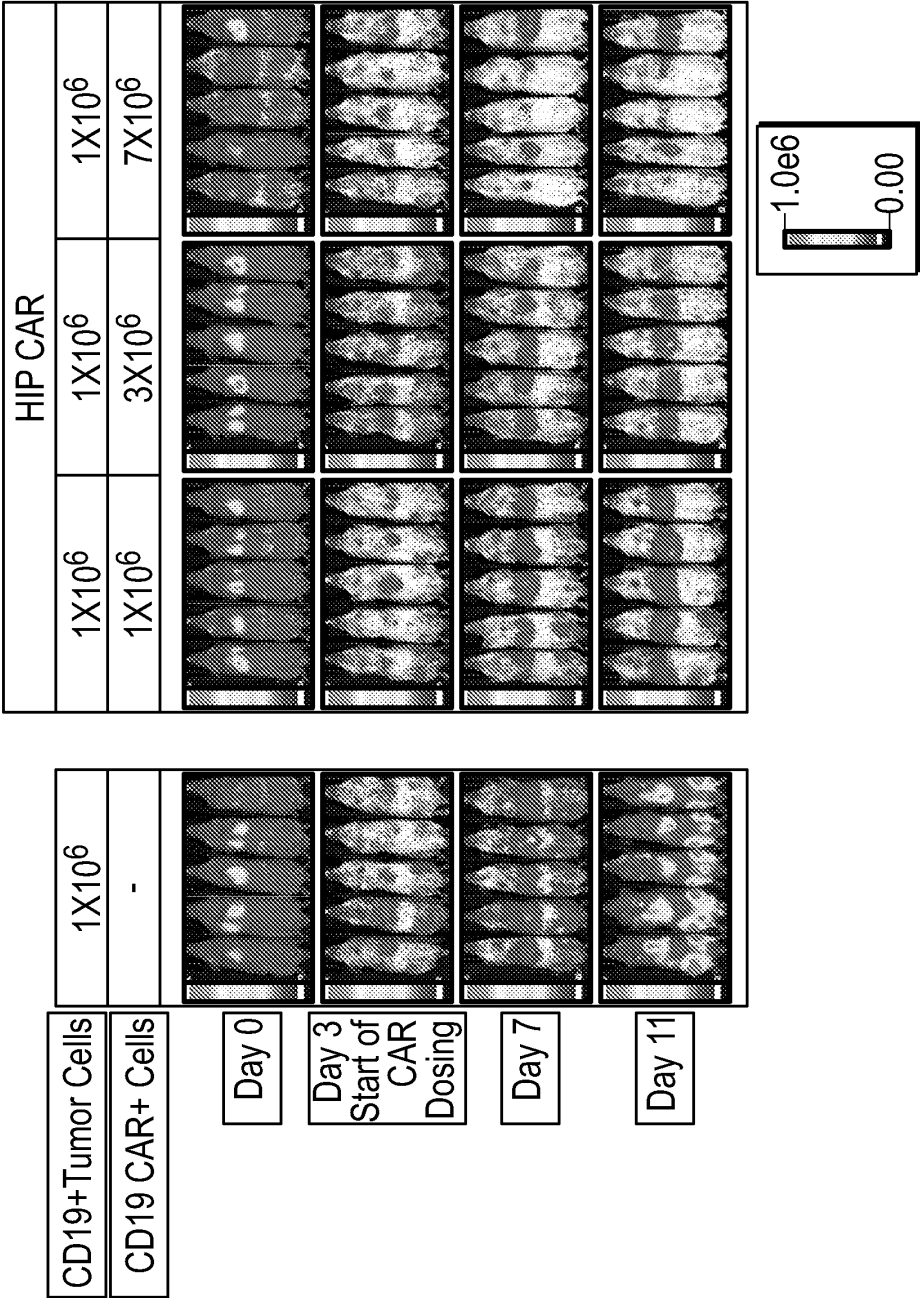


FIG. 19

Efficacy of HIP CAR-T Cells in Mouse Model of CD19+ Cancer

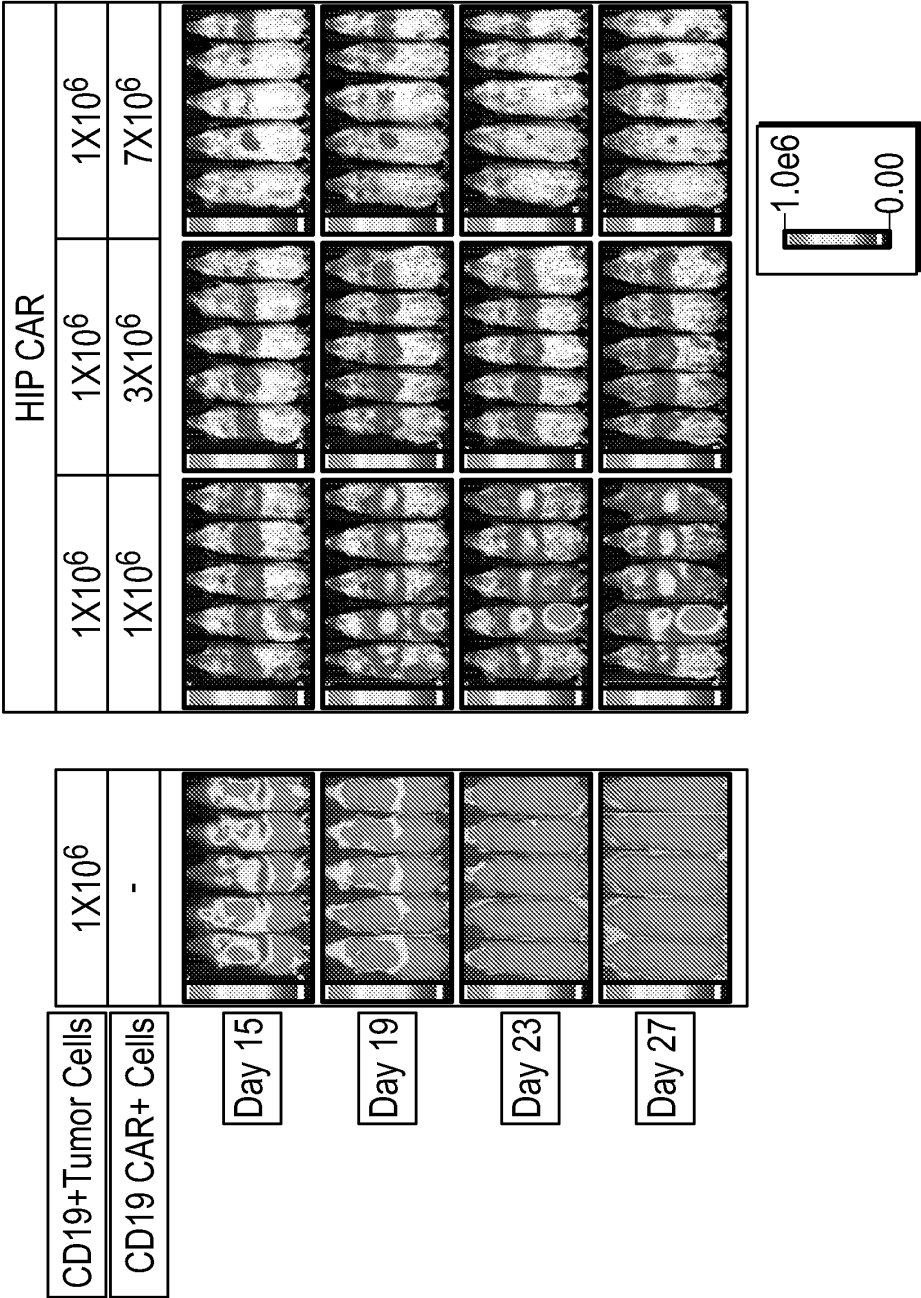


FIG. 20

Efficacy of CAR-T Cells in Mouse Model of CD19+ Cancer

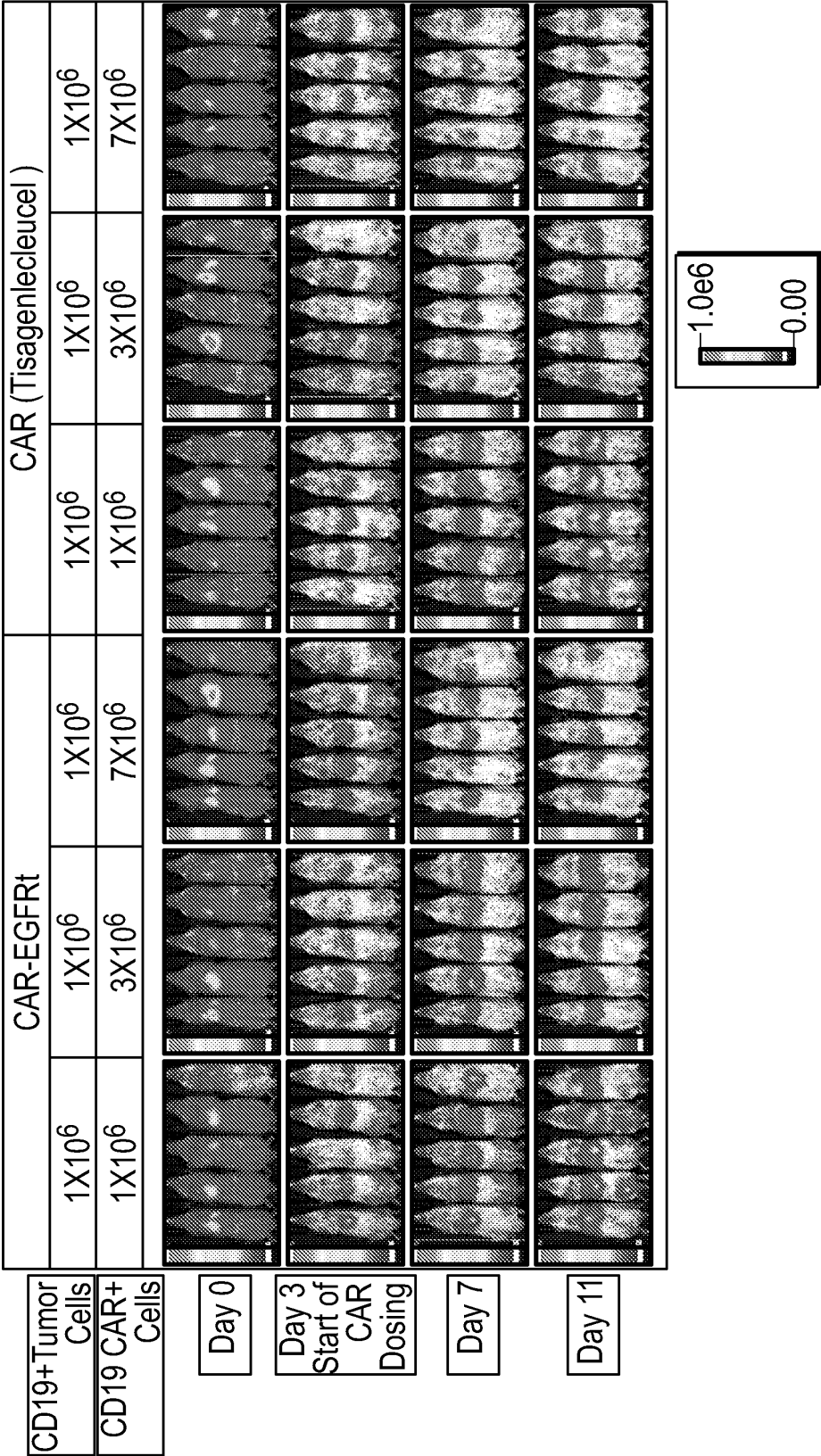


FIG. 21

Efficacy of CAR-T Cells in Mouse Model of CD19+ Cancer

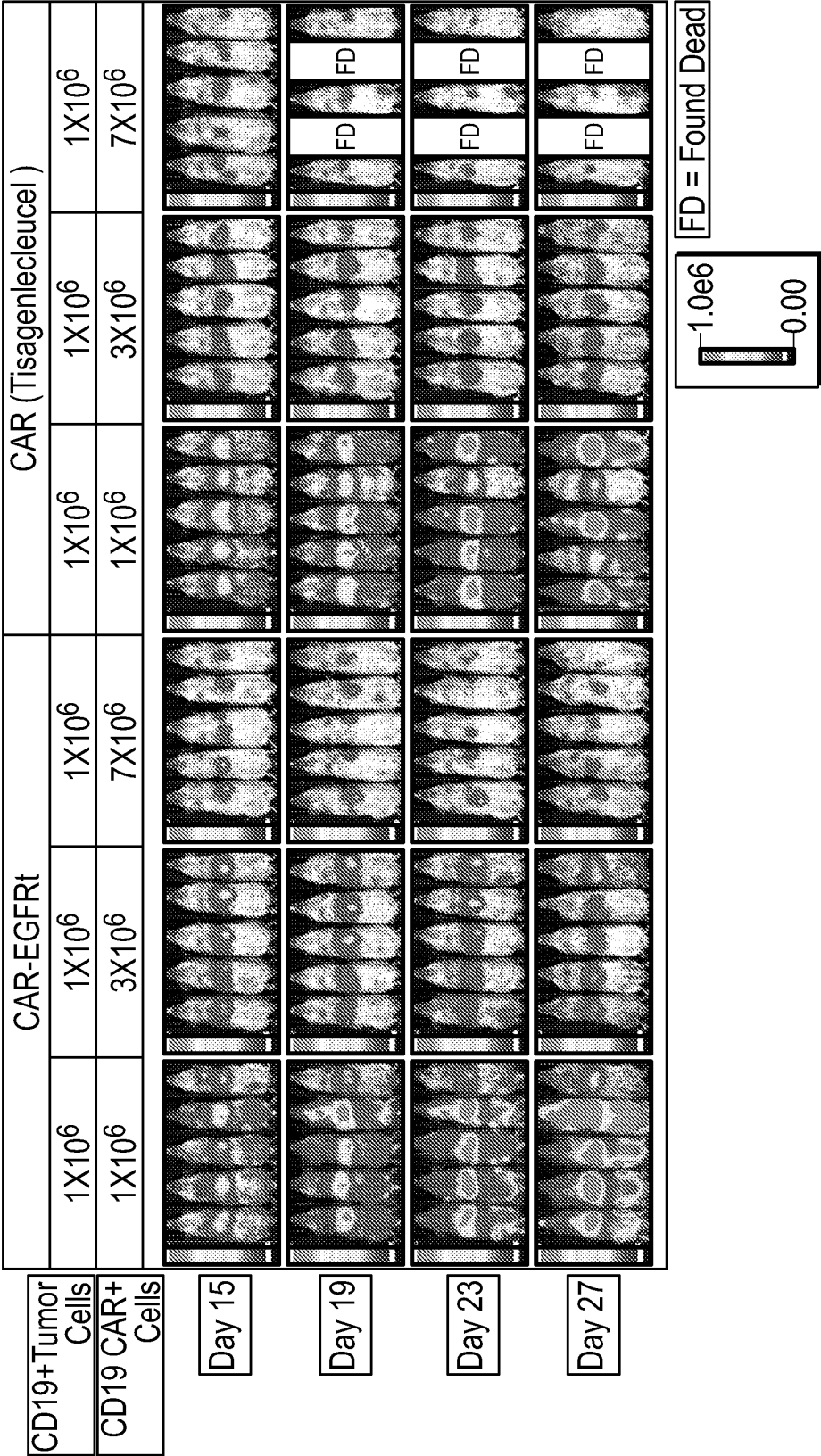


FIG. 22

Efficacy of CAR-T Cells in CD19+ Tumor Model in Vitro

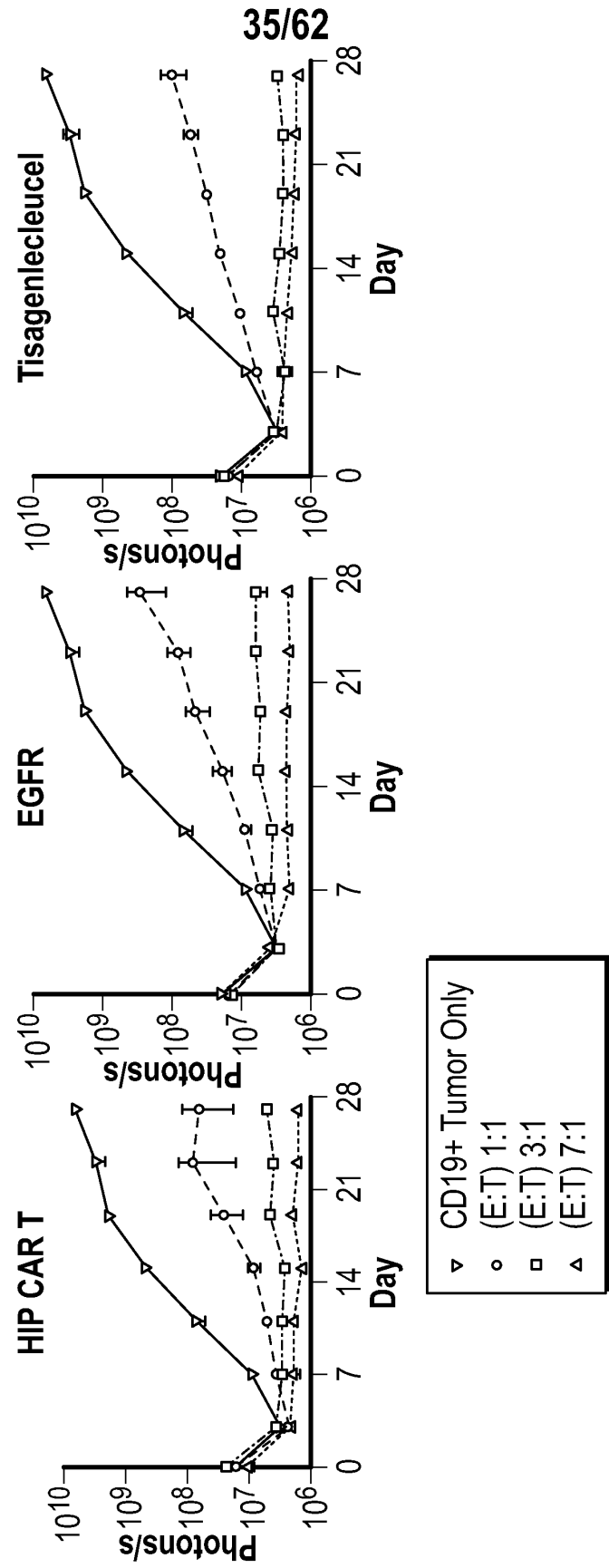


FIG. 23

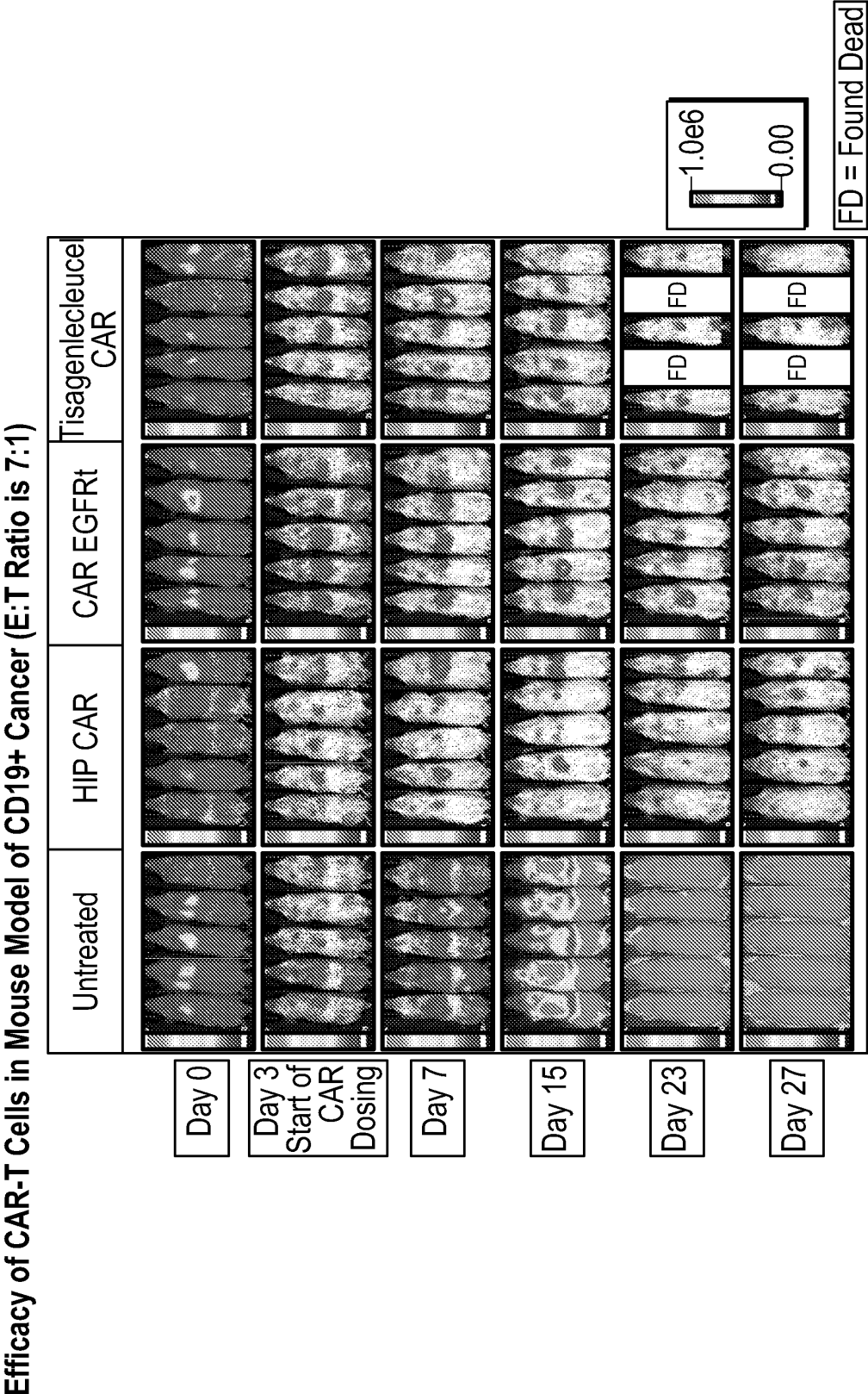


FIG. 24

Tested Cell Lines

Cell Line	Transgene (Via Lentiviral Transduction)	Genome Edits	% Triple Knockout	% CAR+ Cells	% CD47+	% CAR+CD47+ (Double Positive)
HIP CAR- T	CD19-Specific CAR-CD47	B2M, CIITA, TRAC	69.3	61.7	55.8	53.9
CAR+ Only	CD47-EGFRt	None	NA	51.3	NA	NA
CAR+ Only	Tisagenlecleucel Biosimilar/ Surrogate	None	NA	68.9	NA	NA

FIG. 25

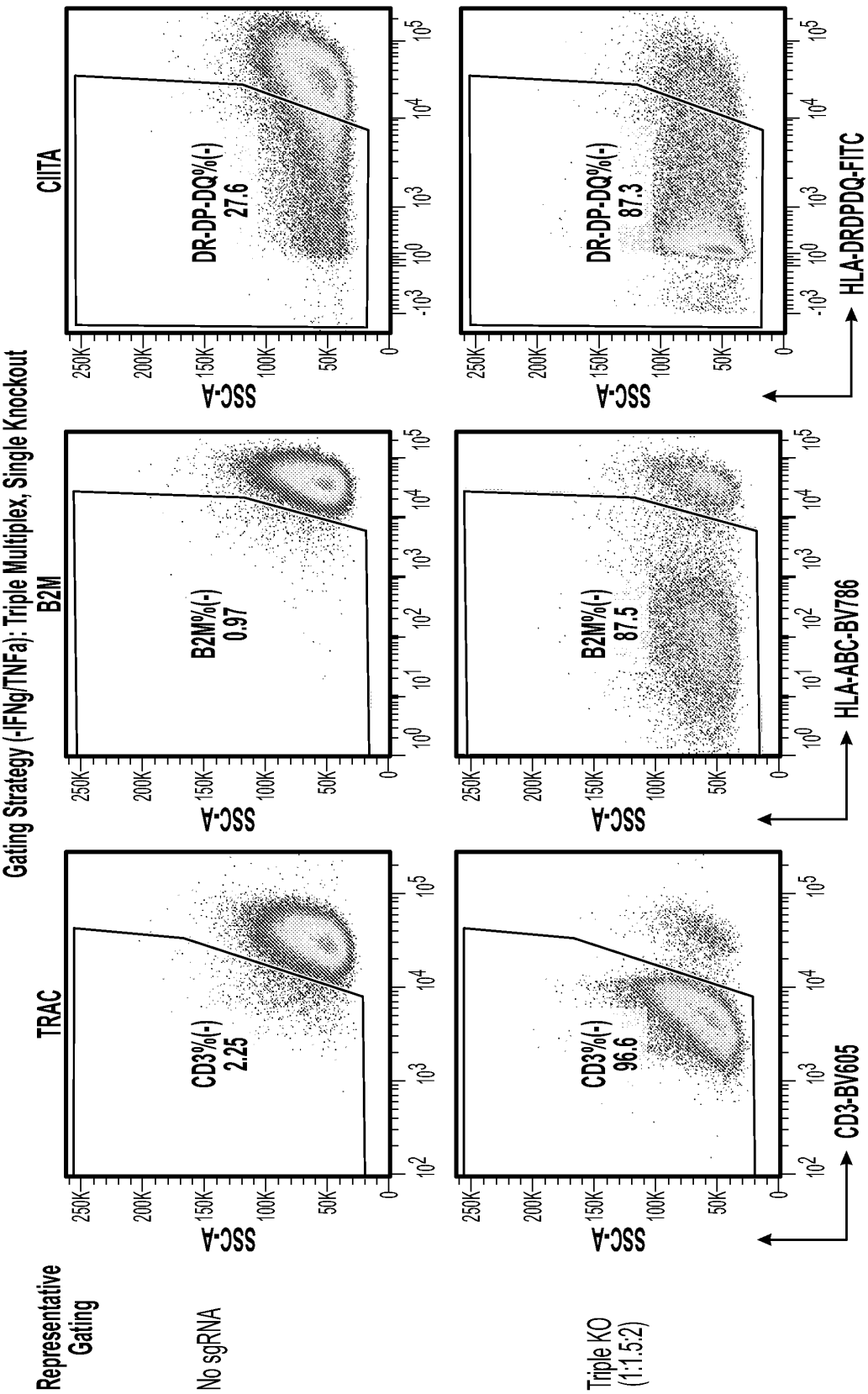


FIG. 26

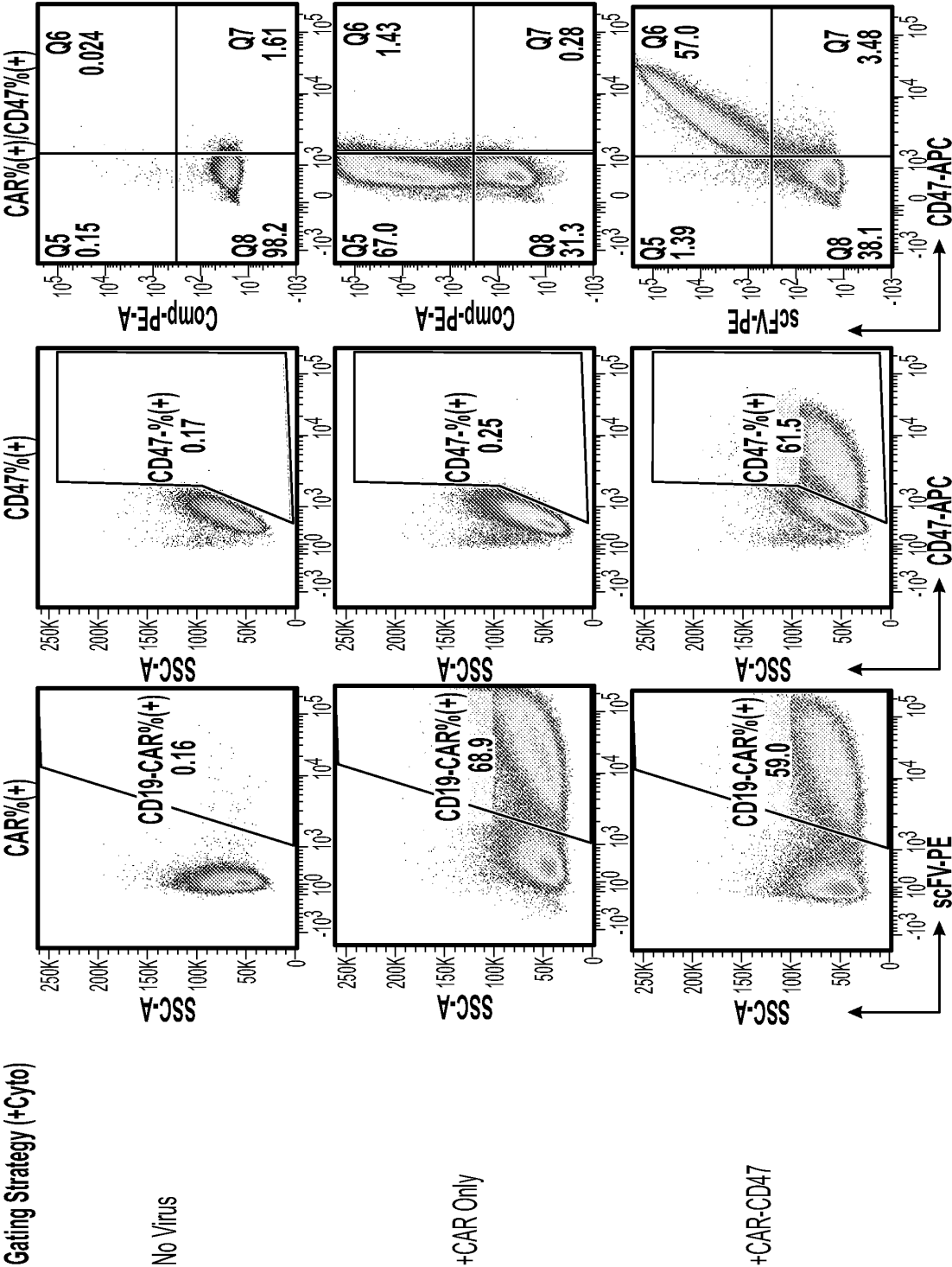


FIG. 28

41/62

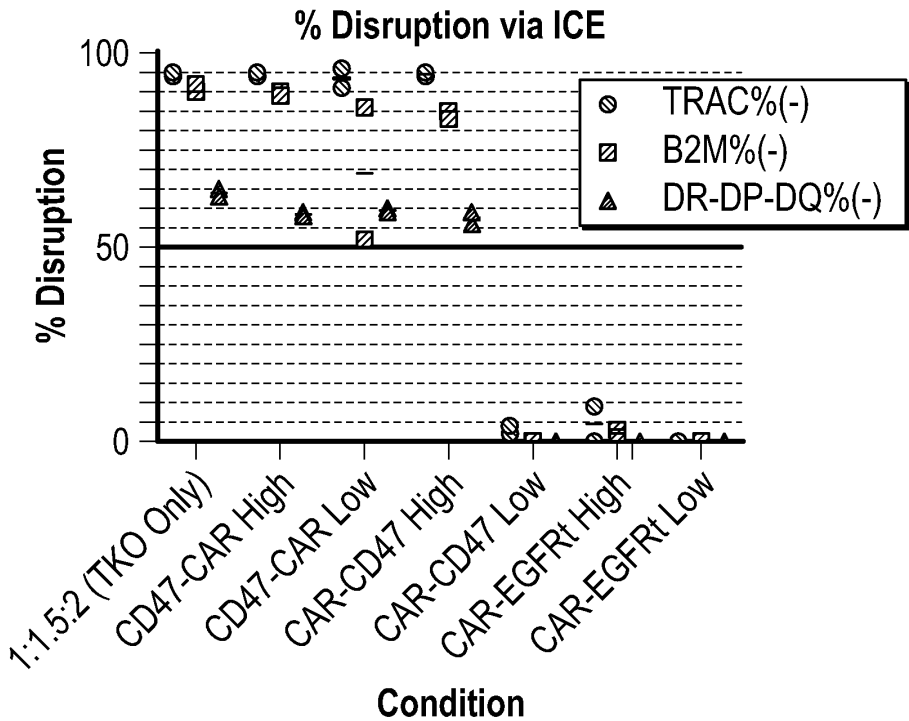
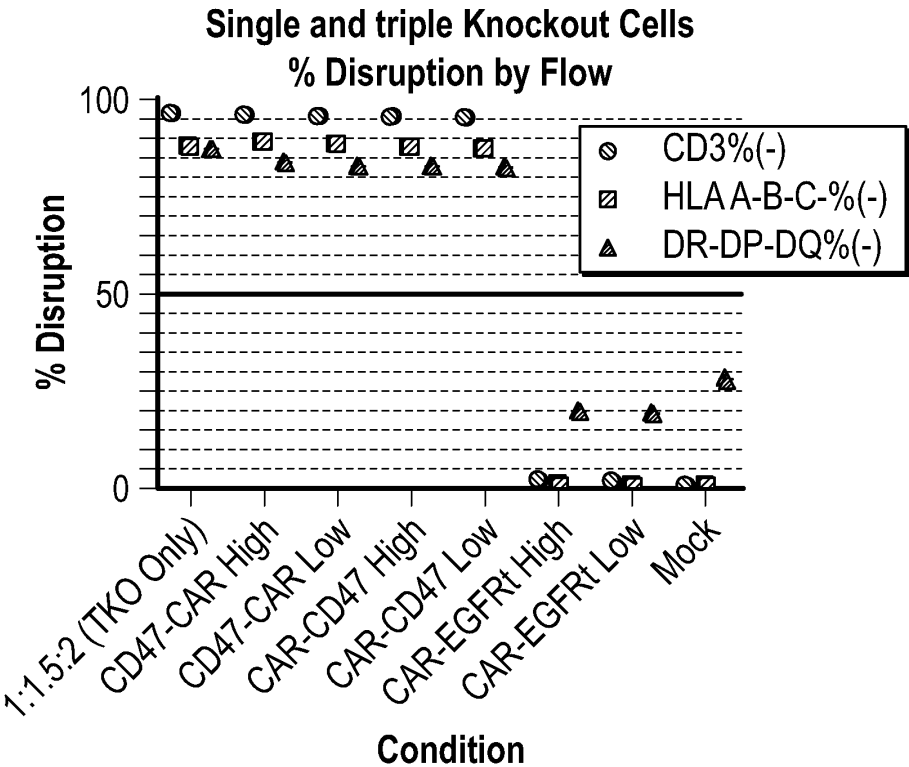


FIG. 29

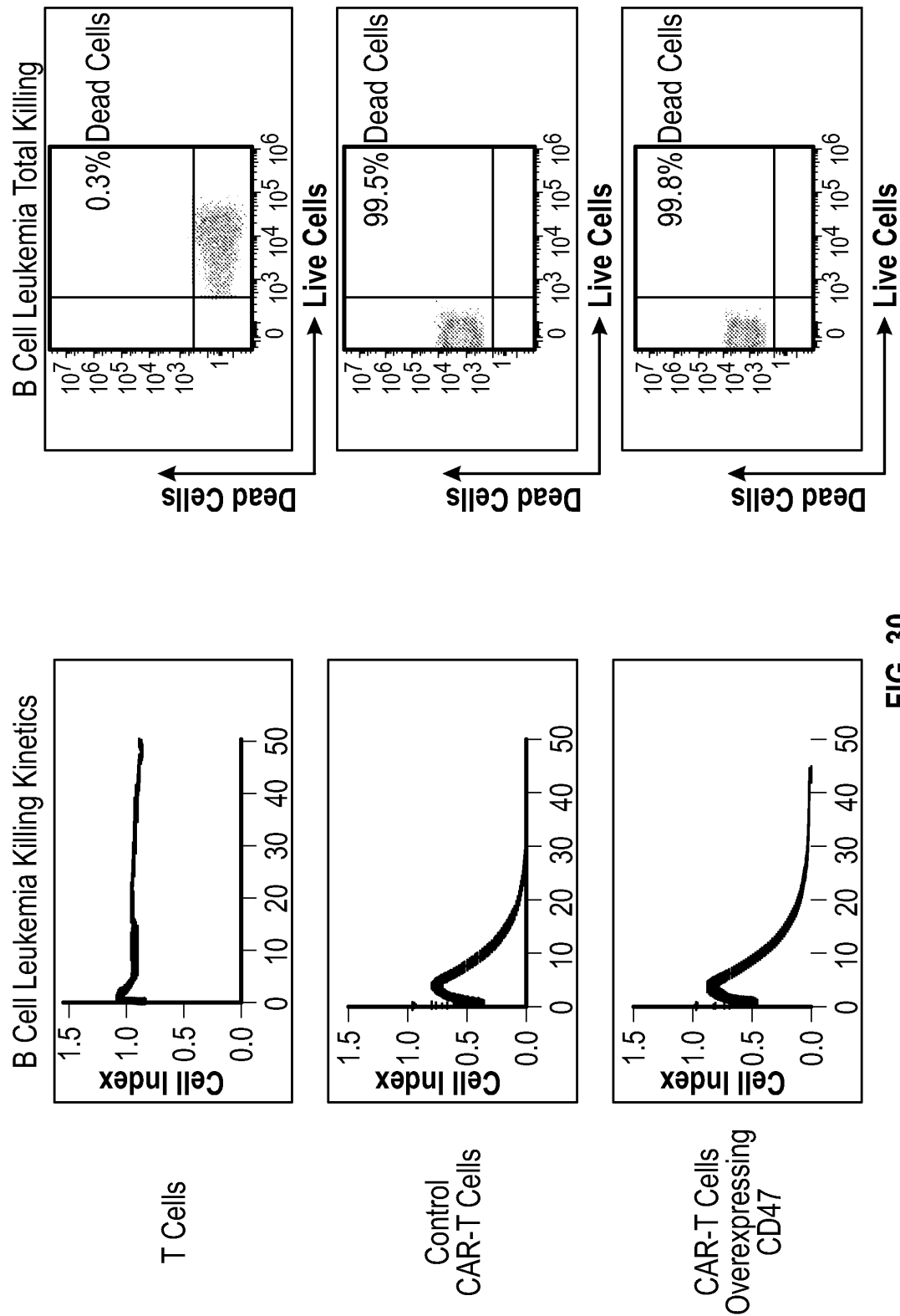
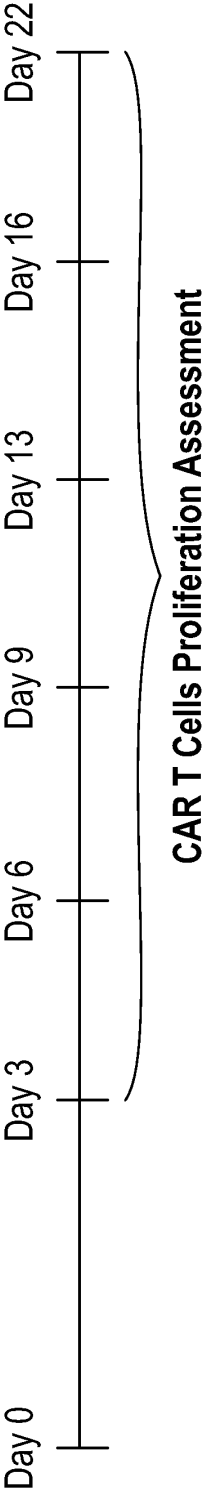


FIG. 30

Experimental Approach



- HLA-/-, TCR-/-, CD47tg CAR-T Cells Cultured +/- IL-2
- Cell Culture Media Replaced Every 3 Days

FIG. 31

44/62

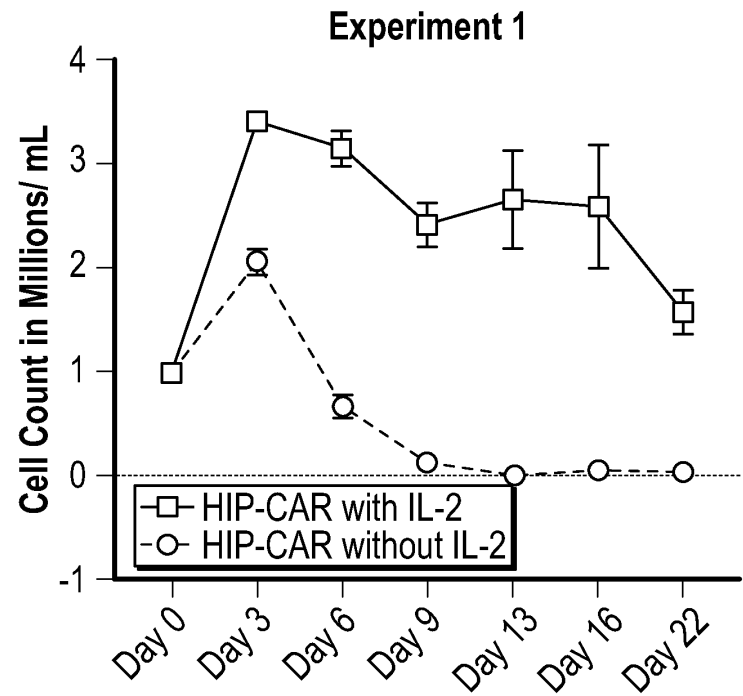


FIG. 32A

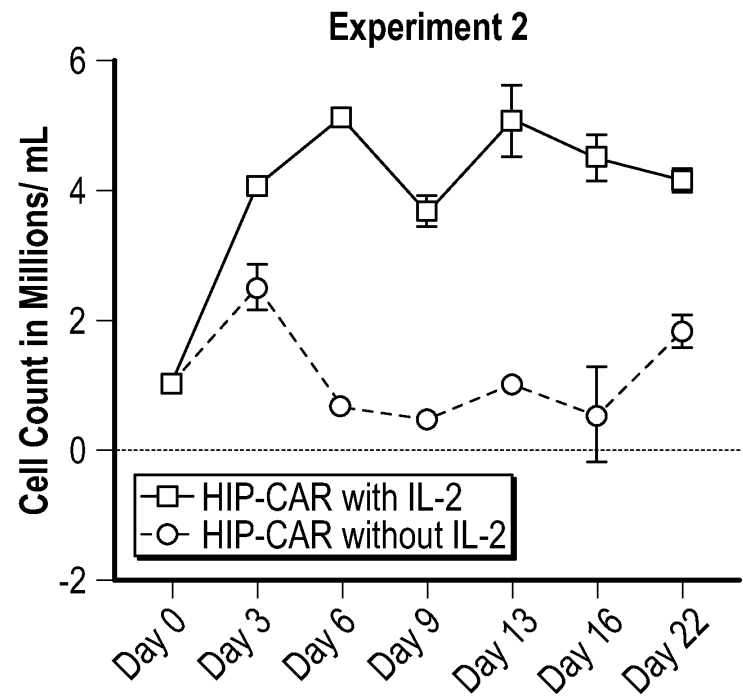


FIG. 32B

Experimental Approach

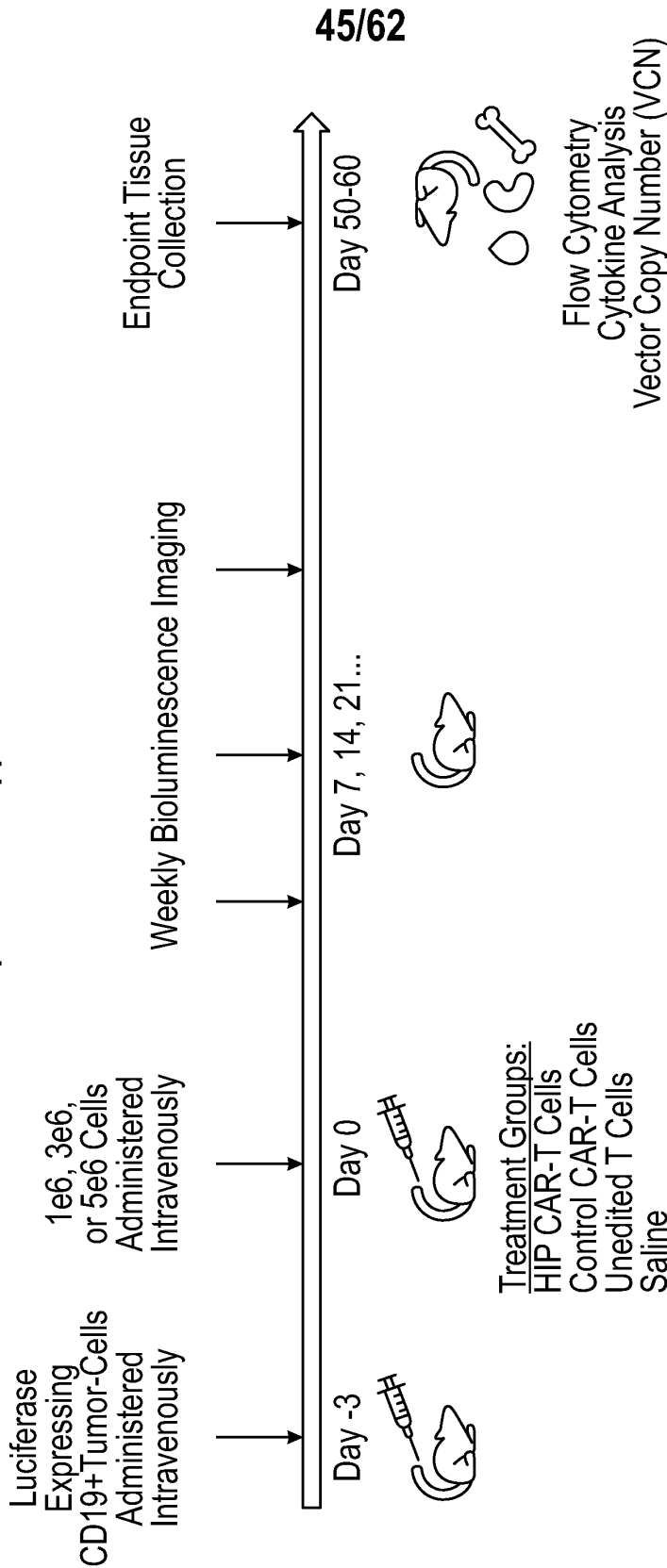


FIG. 33

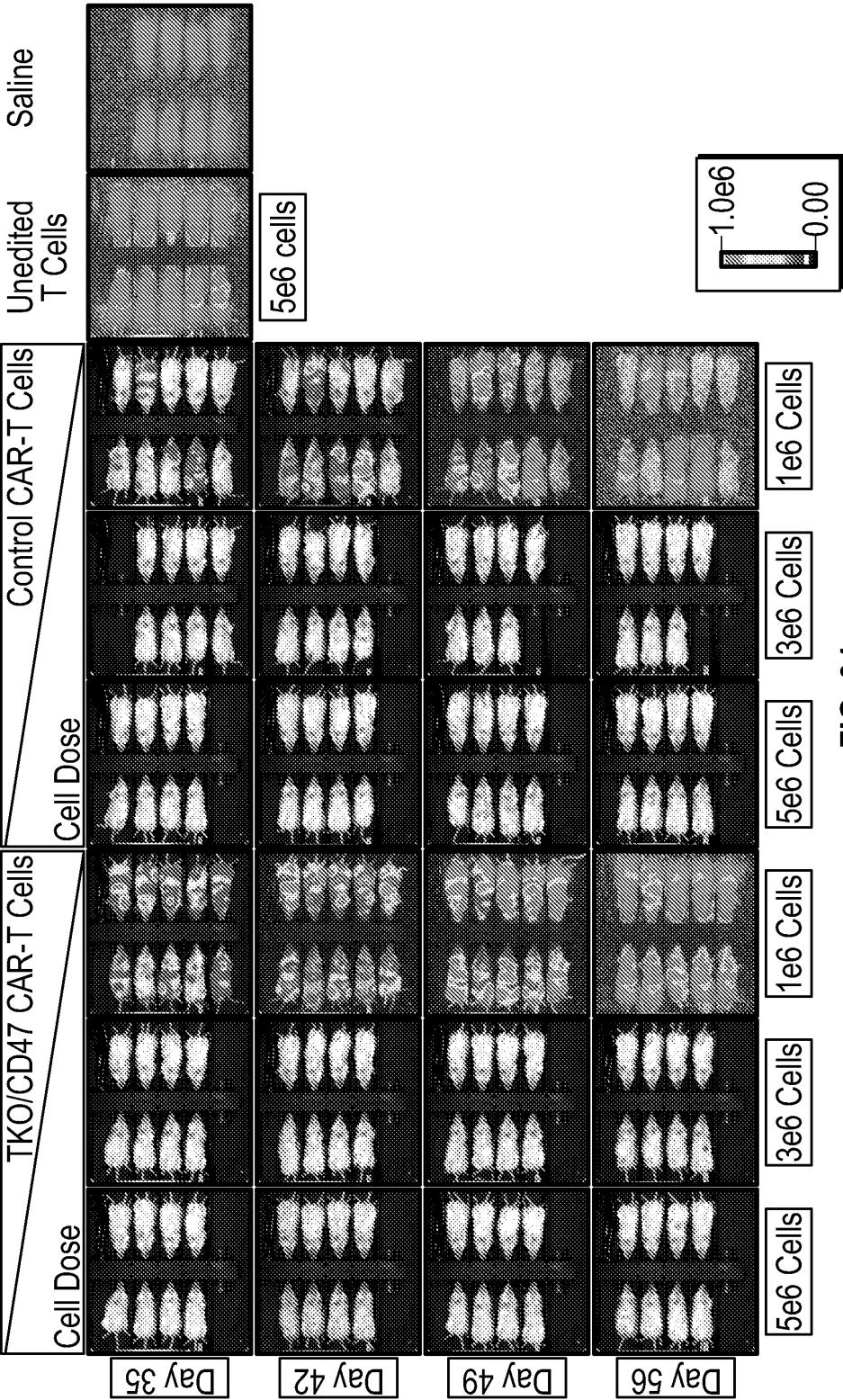


FIG. 34

47/62

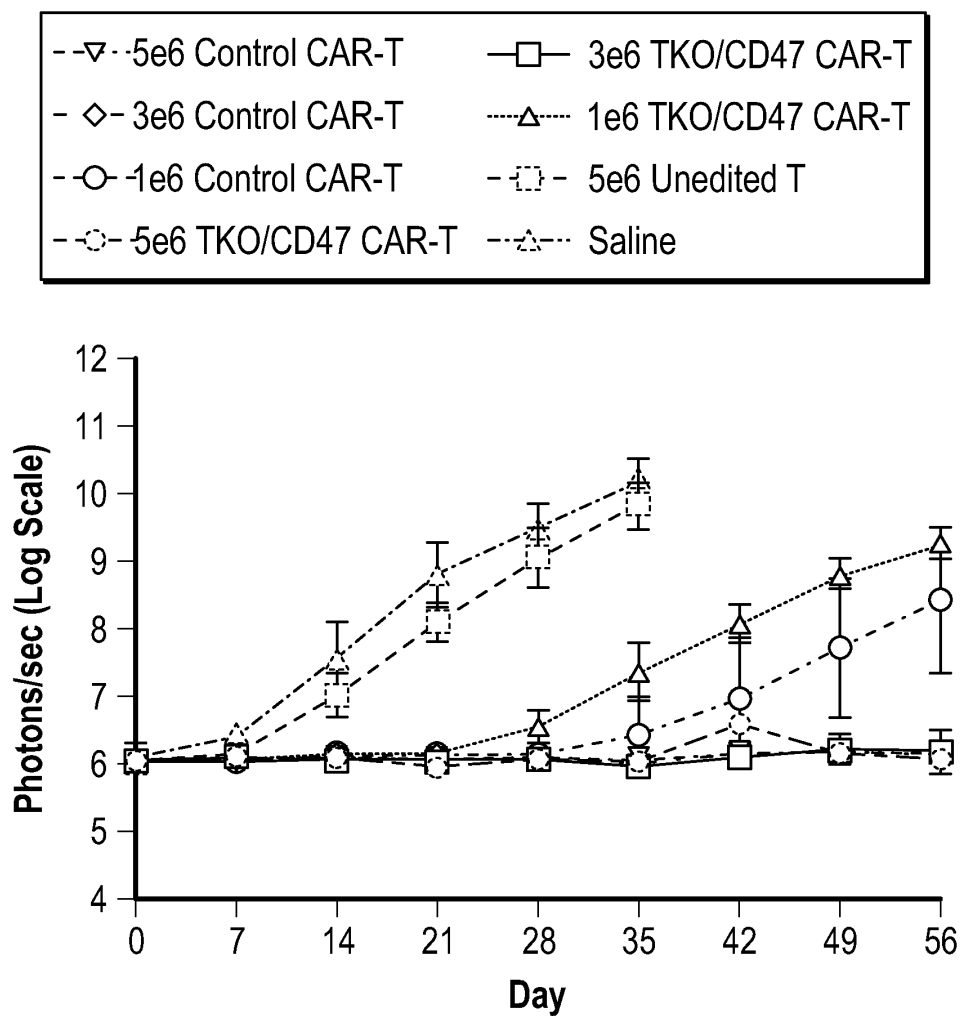


FIG. 35

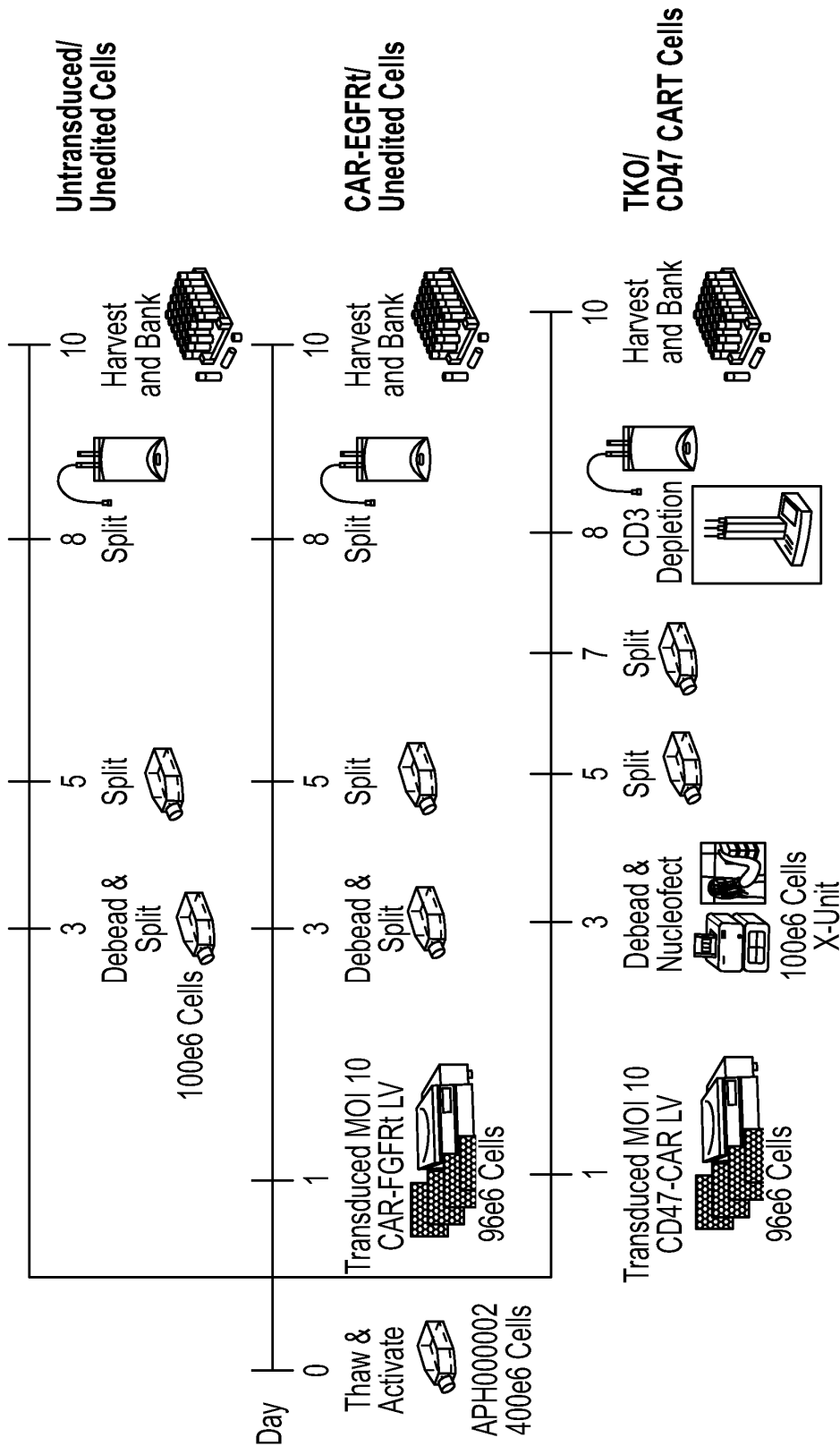


FIG. 36

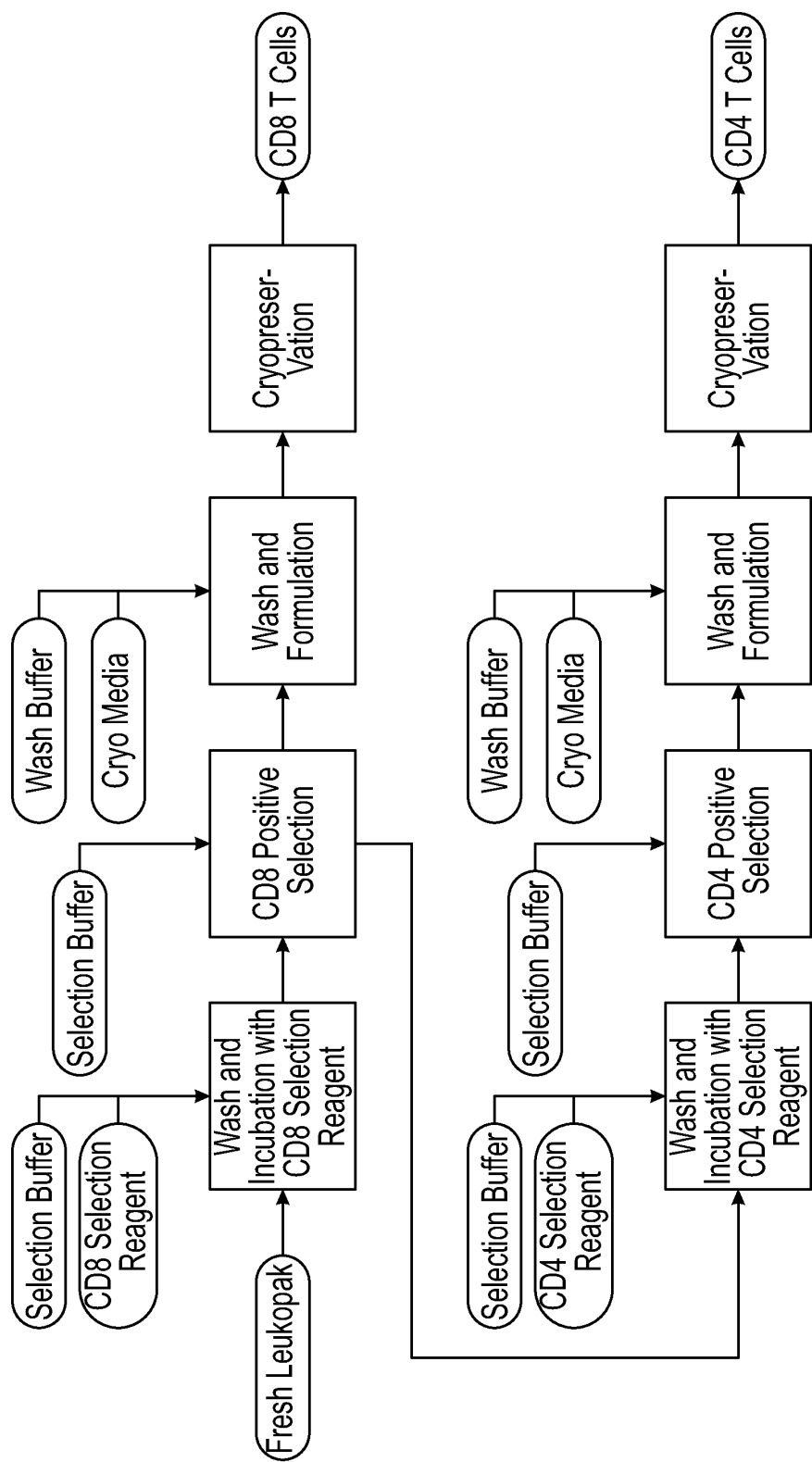


FIG. 37

T Cell Line	%CD19 CAR+ Cells	%CD47+	Fold-Change CD47+ MFI Over Unedited T Cells	%CAR+ CD47+	%CD3- neg	%HLA- ABC-neg	%HLA- DR-DP- DQ-neg	%TKO	%CD8+	%CD4+
Unedited T Cells	0.2	0.2	N/A	0.02	0.30	0.36	58.4	0.0	70.4	28.3
Control CAR-T Cells	74.7	0.1	N/A	0.51	0.25	0.35	41.0	0.0	69.2	29.4
TKO/CD47 CAR-T Cells	70.1	74.0	4.4	68.40	99.9	88.4	83.7	73.5	46.0	52.0

FIG. 38

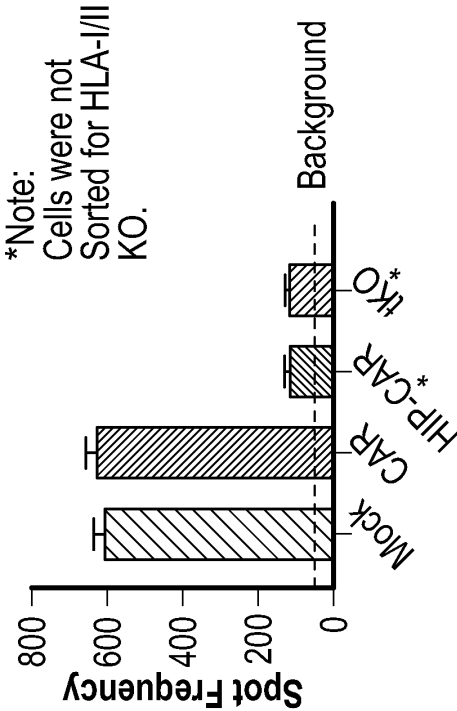


FIG. 39A

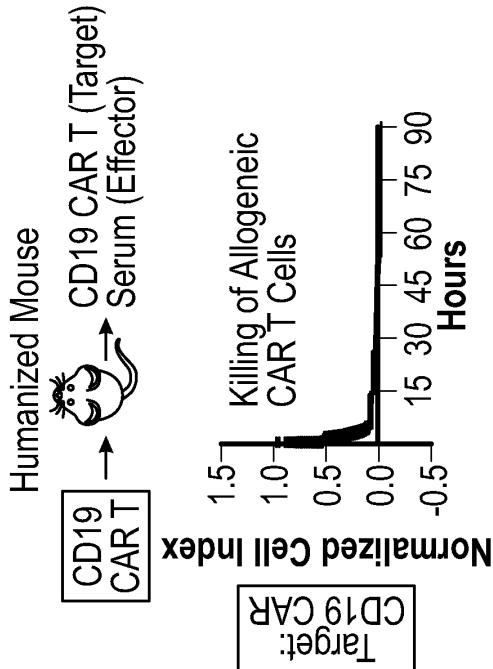


FIG. 39C

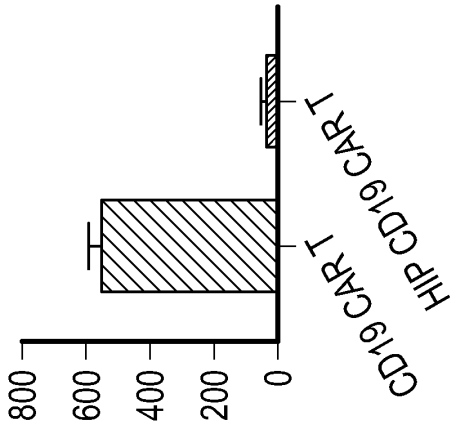


FIG. 39B

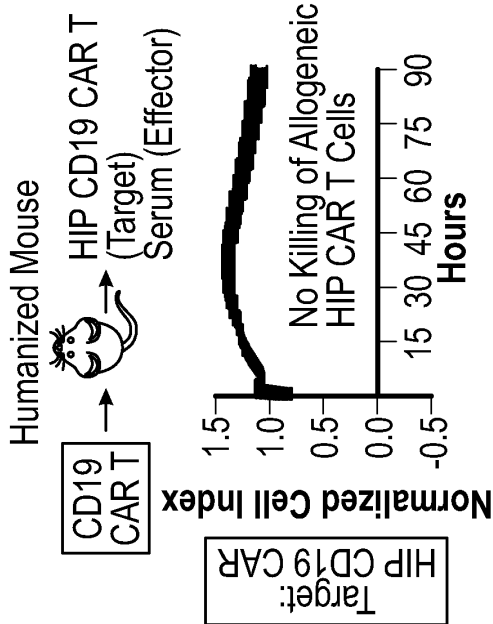


FIG. 39D

52/62

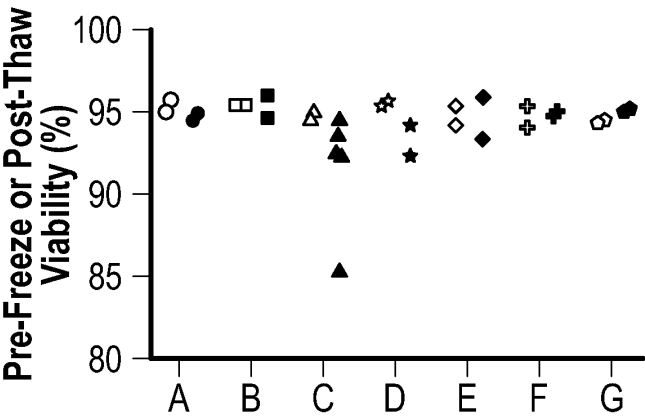


FIG. 40A

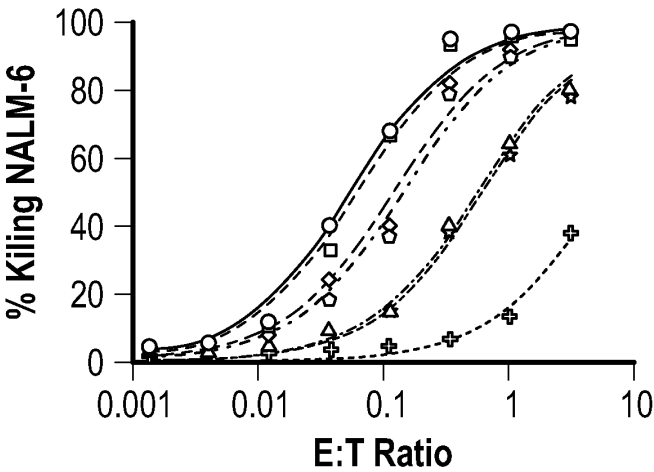
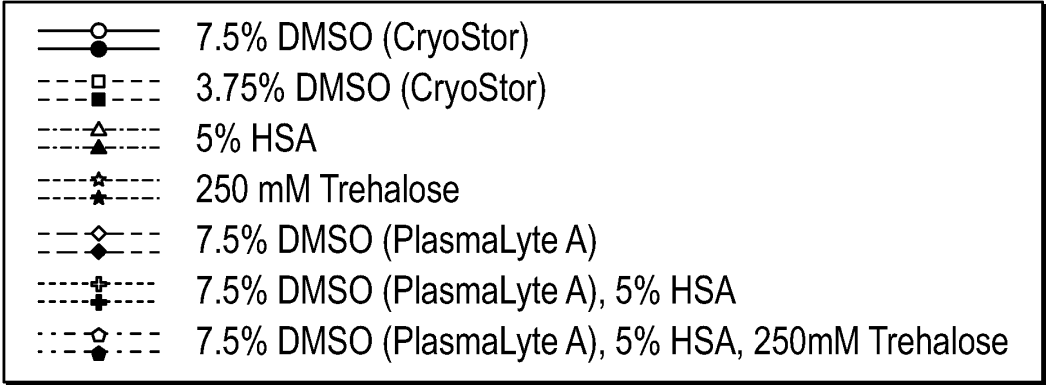


FIG. 40B

HIP-CAR-= Sorted for CAR-Negative HIP
HIP-CAR = HLA-I/IIKO, CD47KI, TCRKO, CD19CARKI
HIP-/-CAR = HIP-CAR Sorted for HLA-I/IIKO
CAR = CD19CARKI
Mock = T Cells

Elispot: Th1 (IFNg) Response

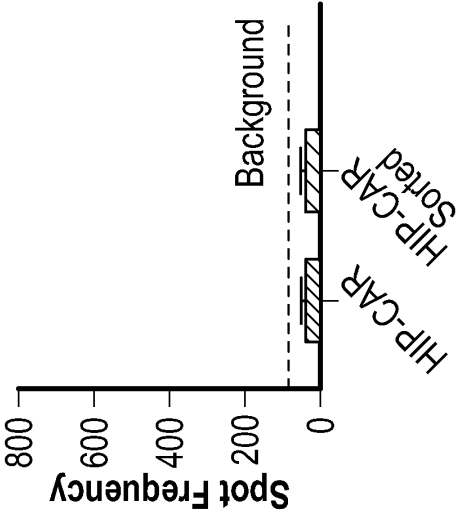


FIG. 41A

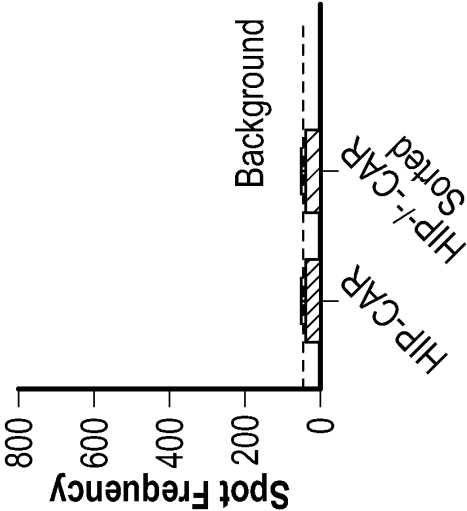
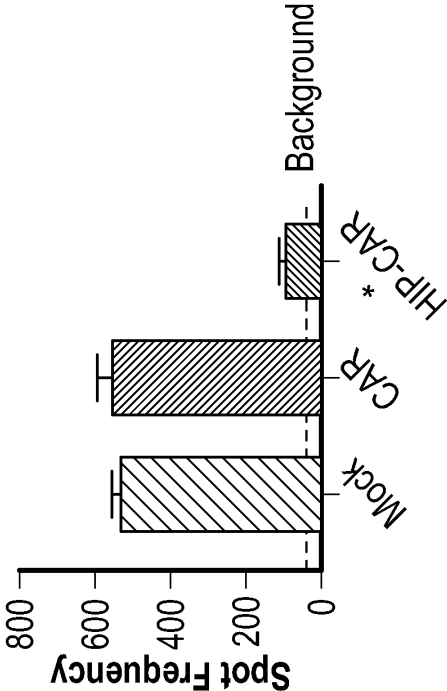


FIG. 41B

HIP-CAR⁺= Sorted for CAR-Positive HIP
HIP-CAR⁻= Sorted for CAR-Negative HIP
HIP-CAR = HLA-I/IIKO, CD47KI, TCRKO, CD19CARKI
CAR = CD19CARKI
Mock = T Cells

Elispot: Th1 (IFNg) Response



* Same Graph.
HIP-CAR: 88.4% are HLA-I KO and 83.7% are HLA-II KO

FIG. 41C

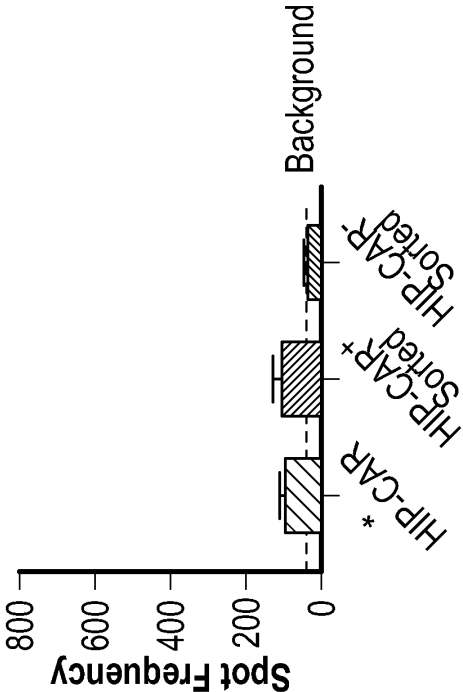


FIG. 41D

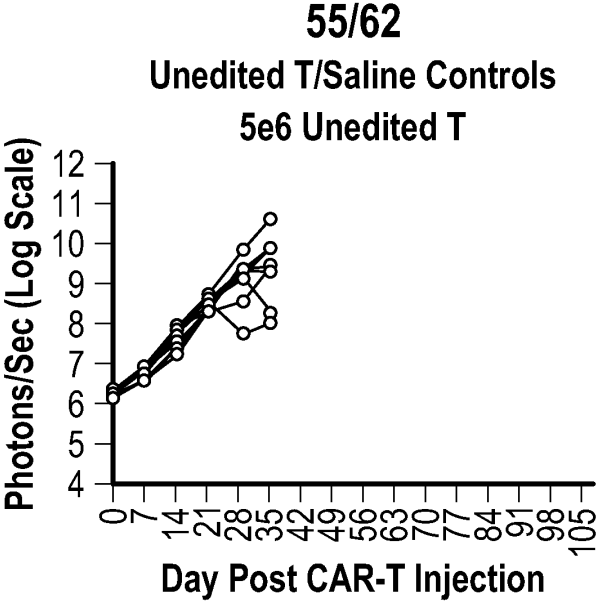


FIG. 42A

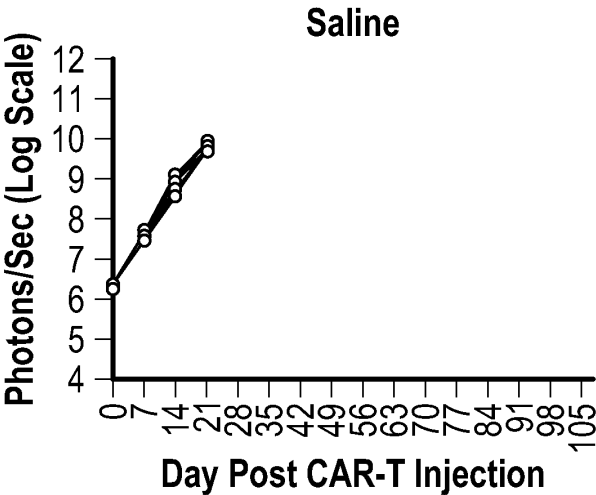


FIG. 42B

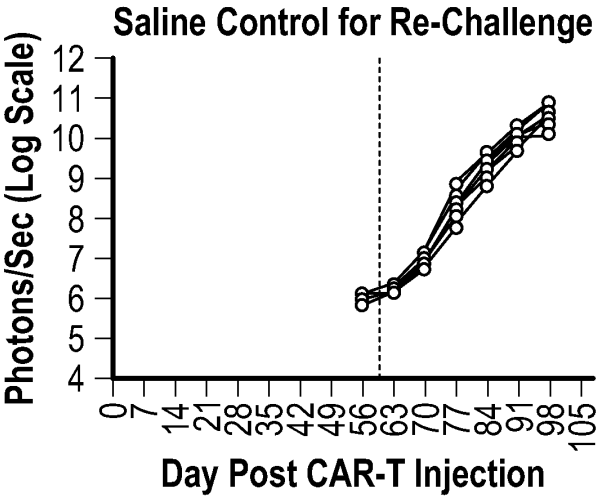


FIG. 42C

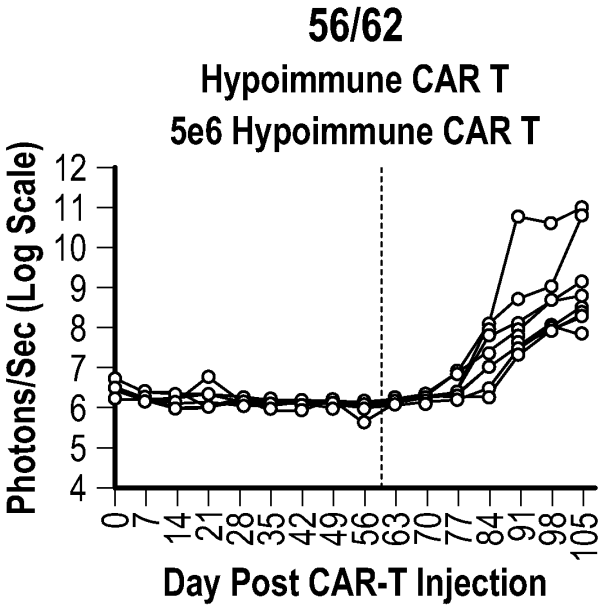


FIG. 42D

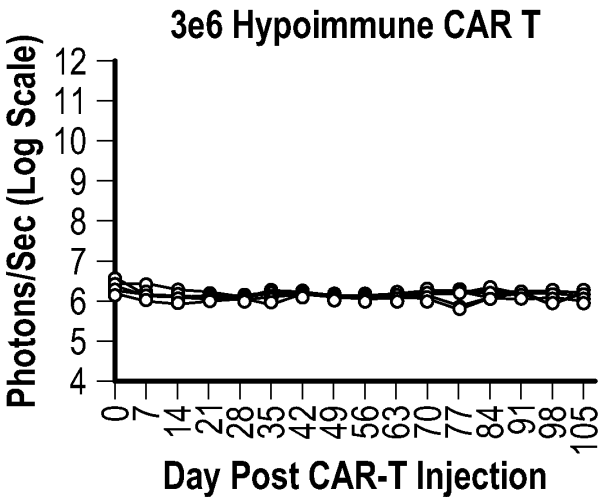


FIG. 42E

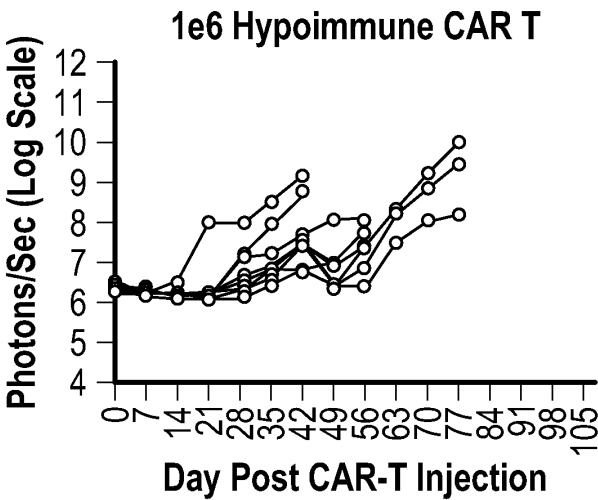


FIG. 42F

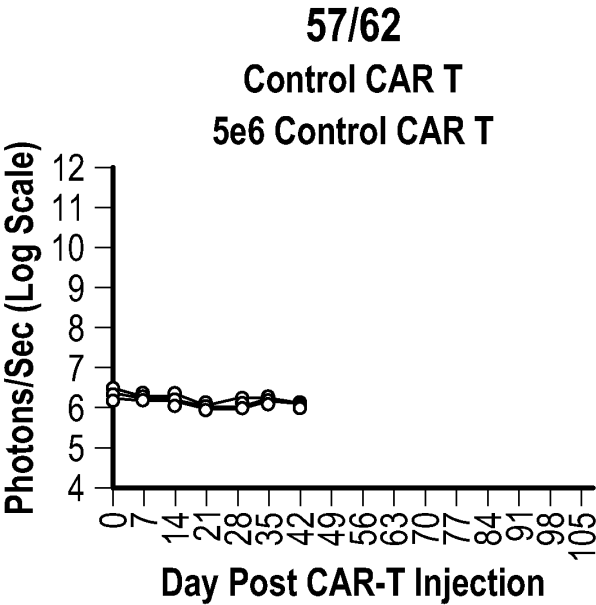


FIG. 42G

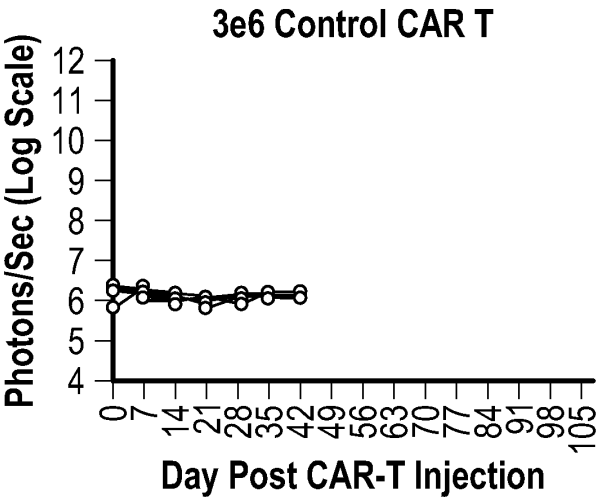


FIG. 42H

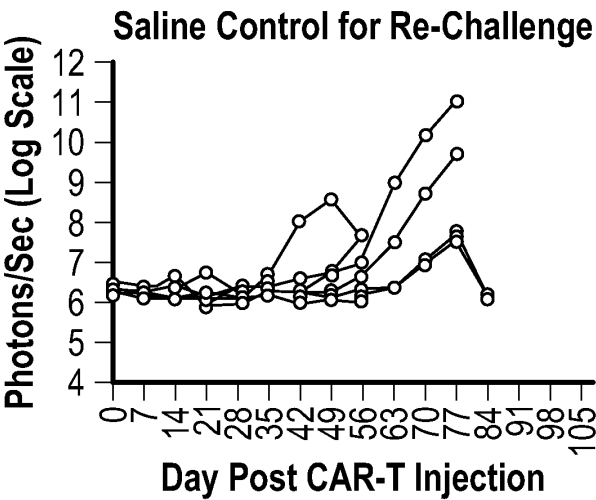


FIG. 42I

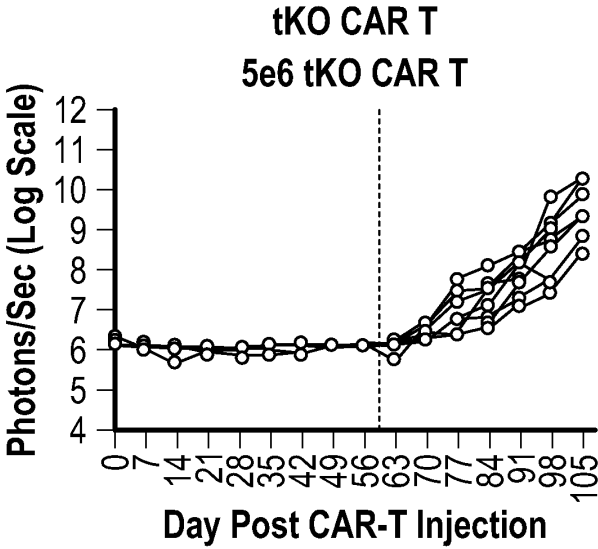


FIG. 42J

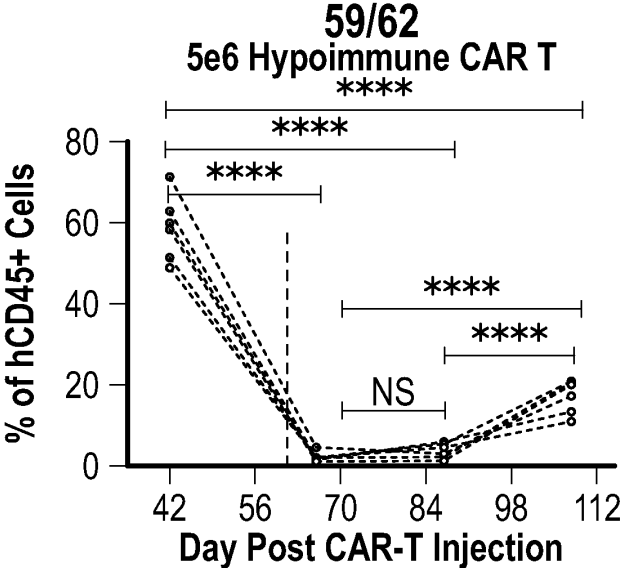


FIG. 43A

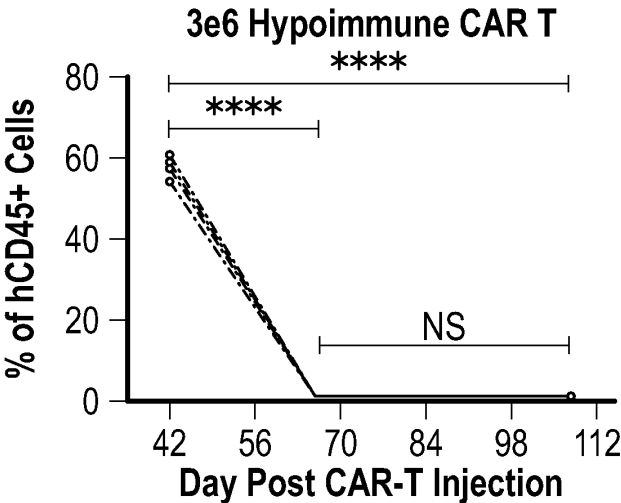


FIG. 43B

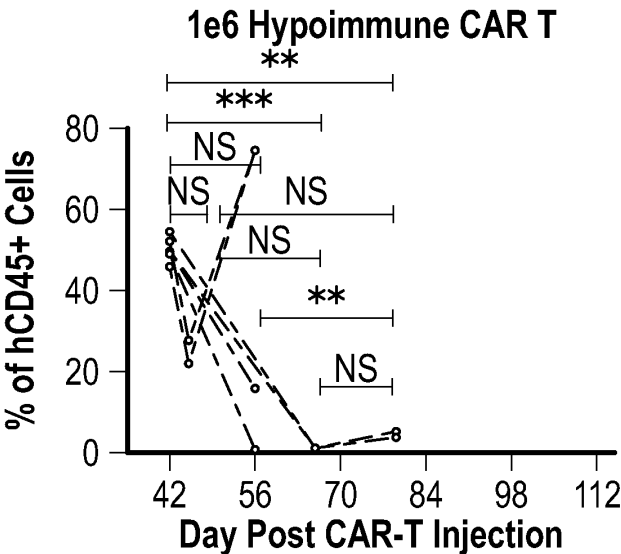


FIG. 43C

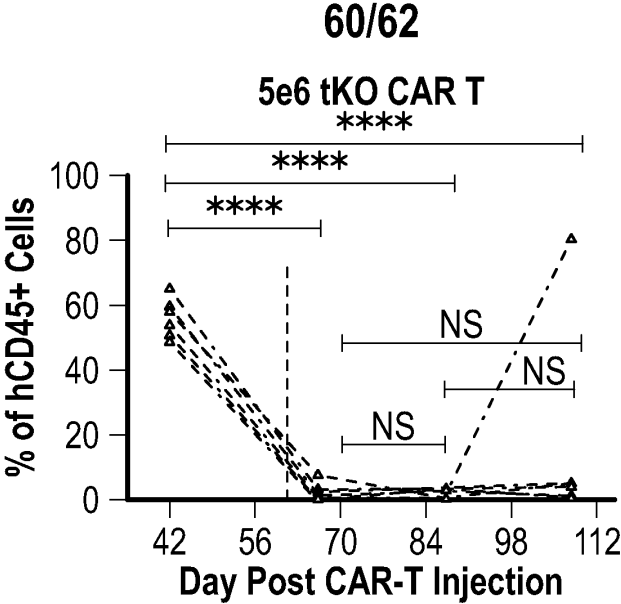


FIG. 43D

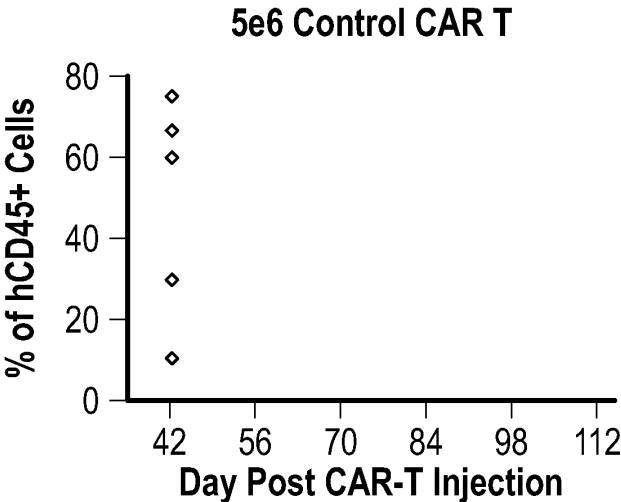


FIG. 43E

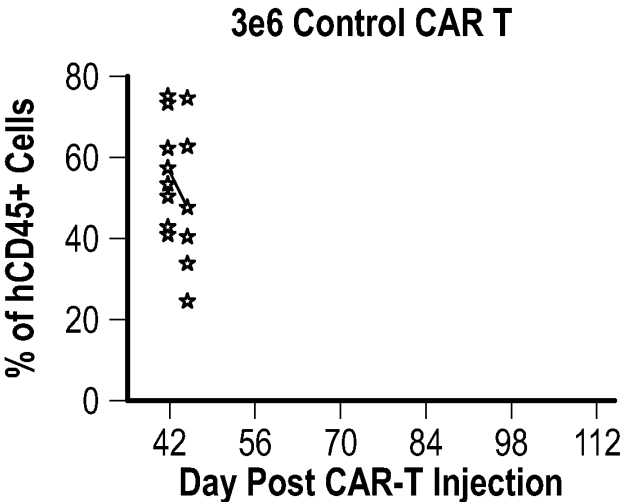


FIG. 43F

61/62

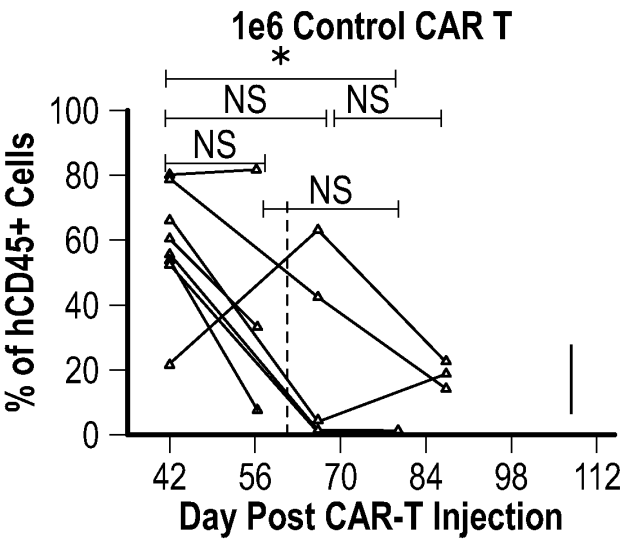


FIG. 43G

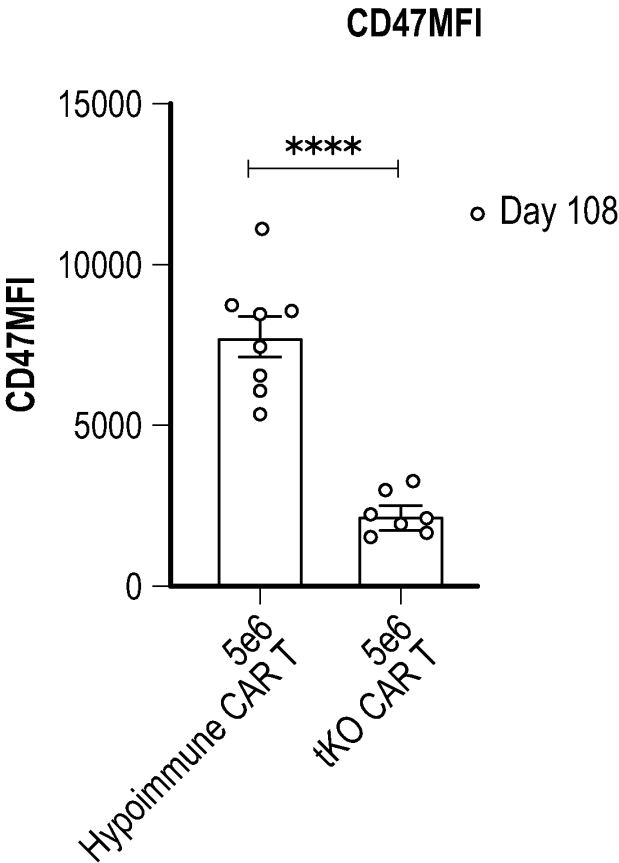


FIG. 43H

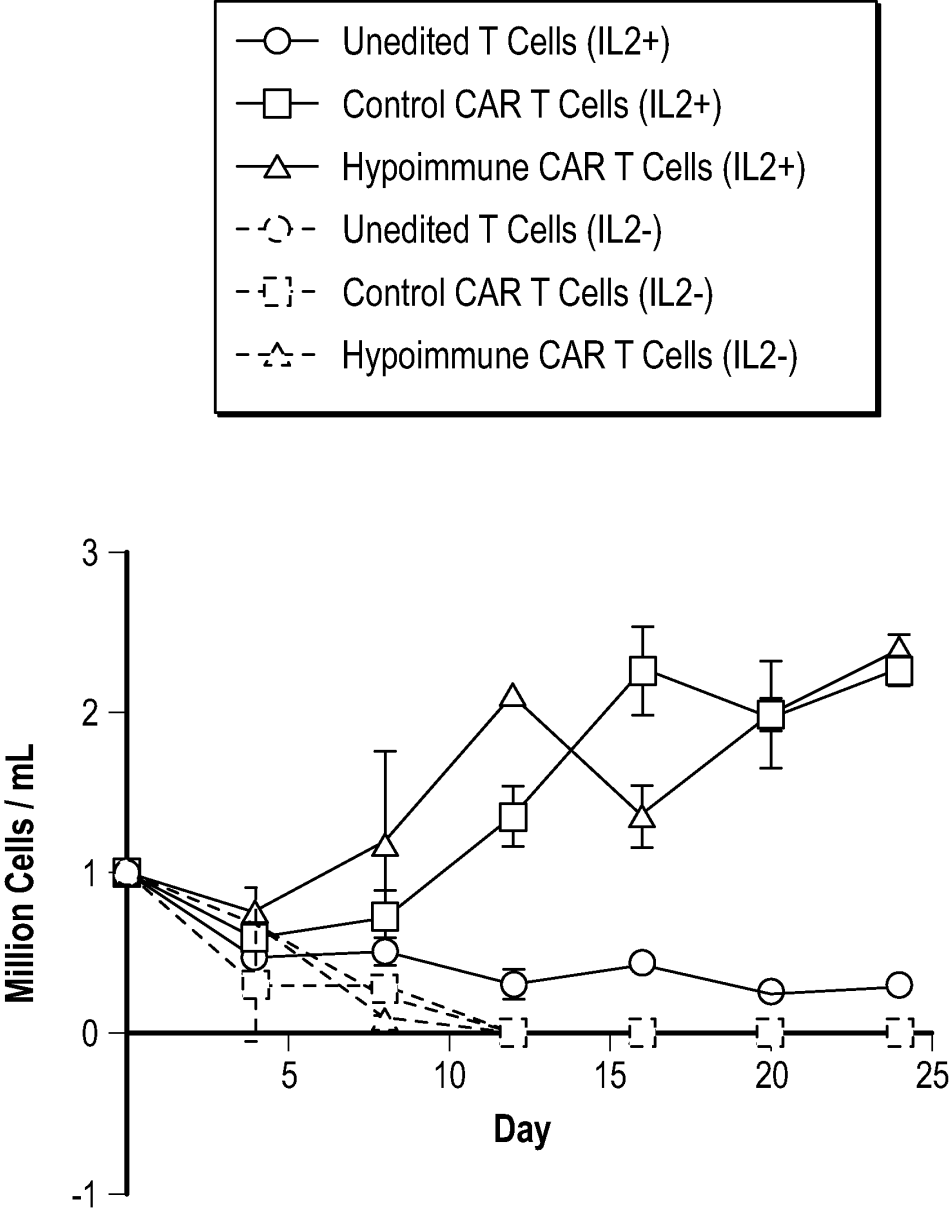


FIG. 44