

CD269-CD319 (BC1cCAR) lentiviral schematic

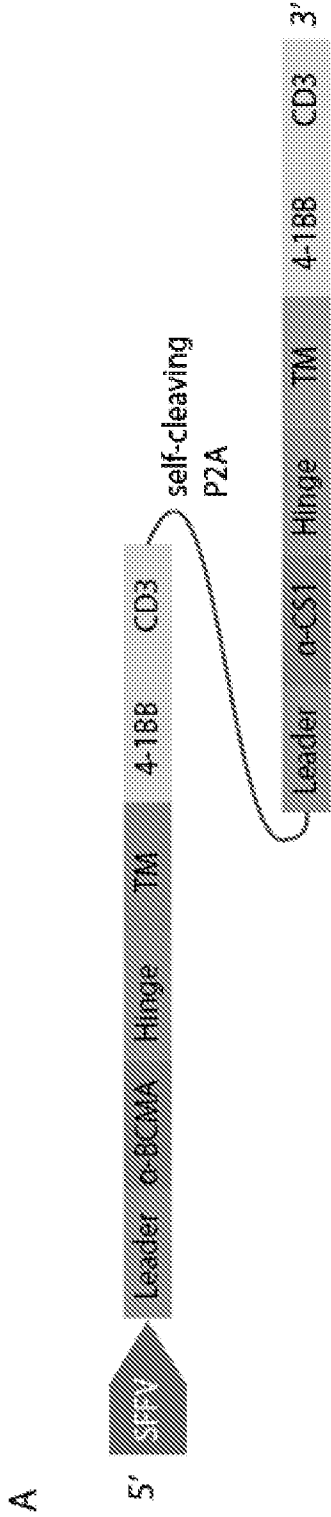


Figure 1A

BC1cCAR Surface Expression

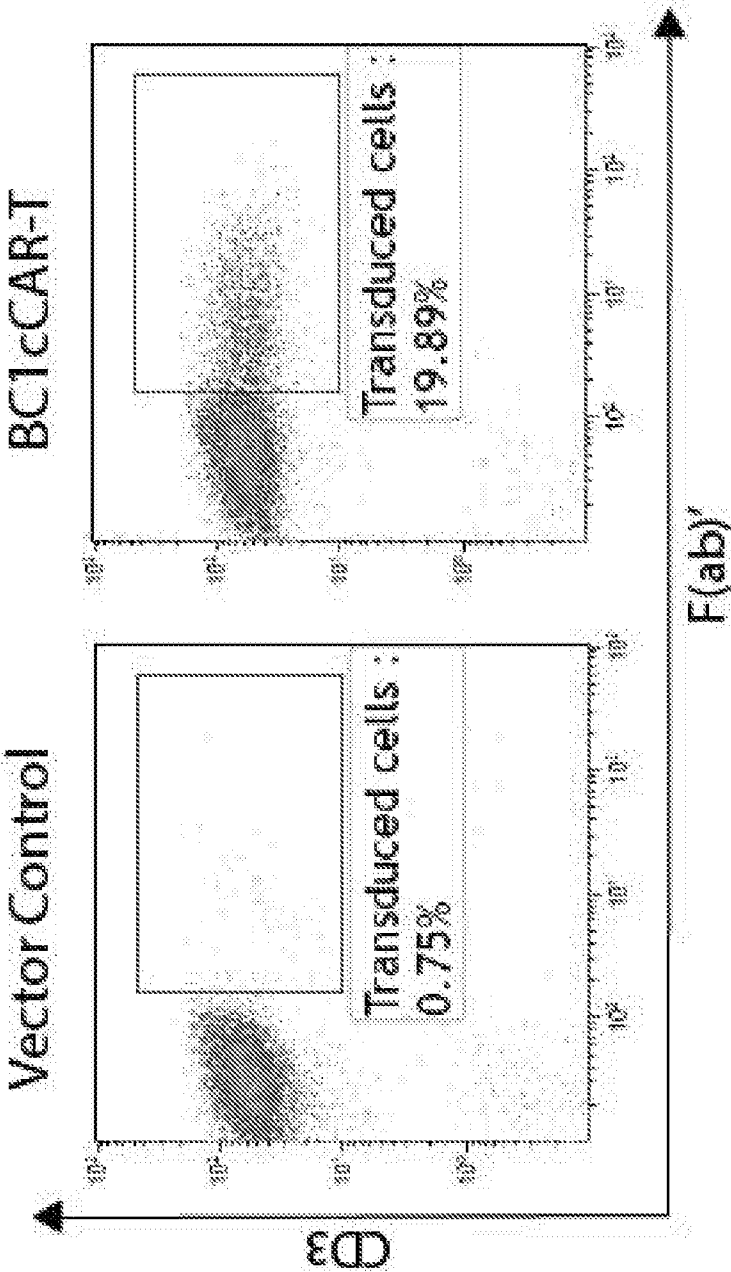


Figure 1B

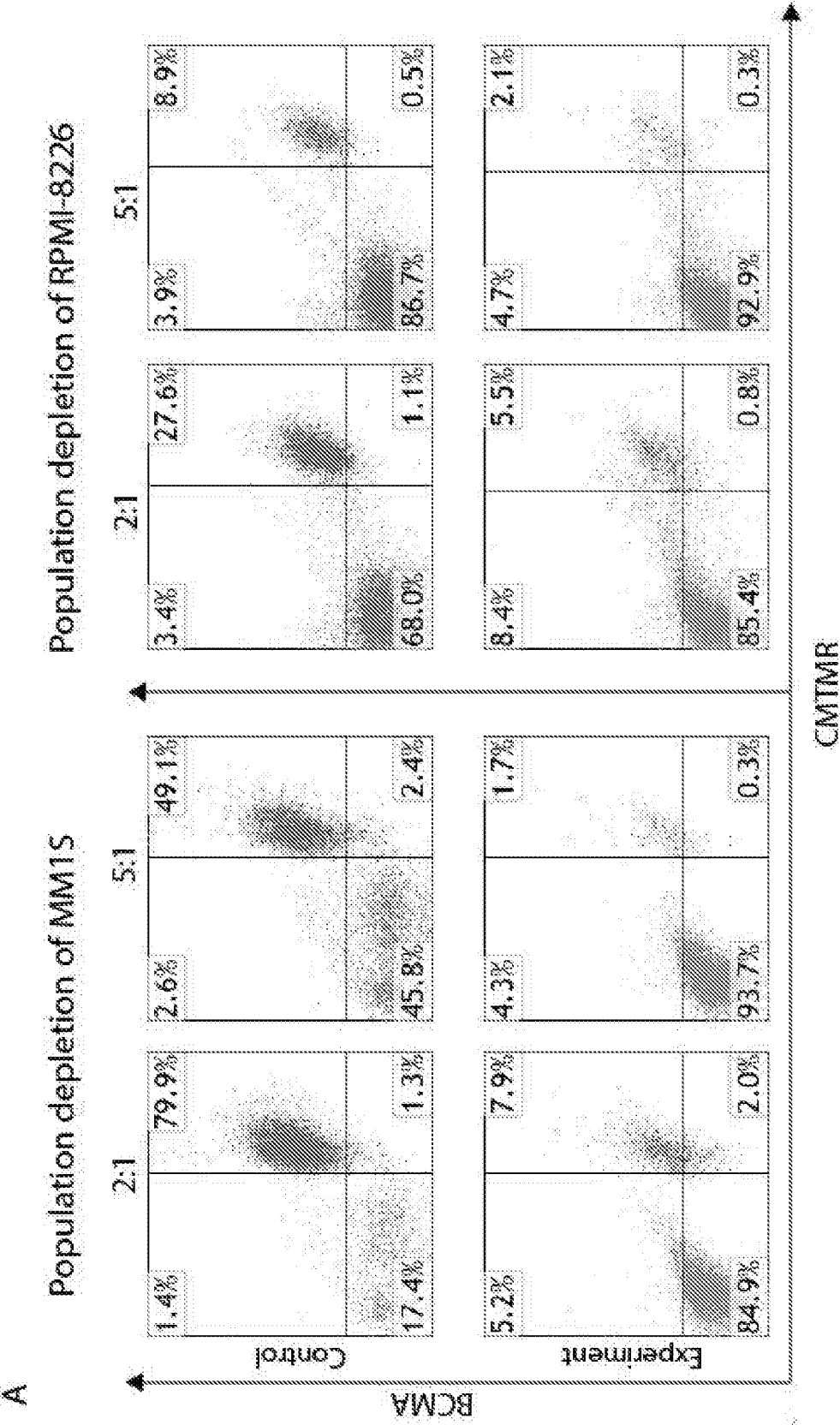


Figure 2A

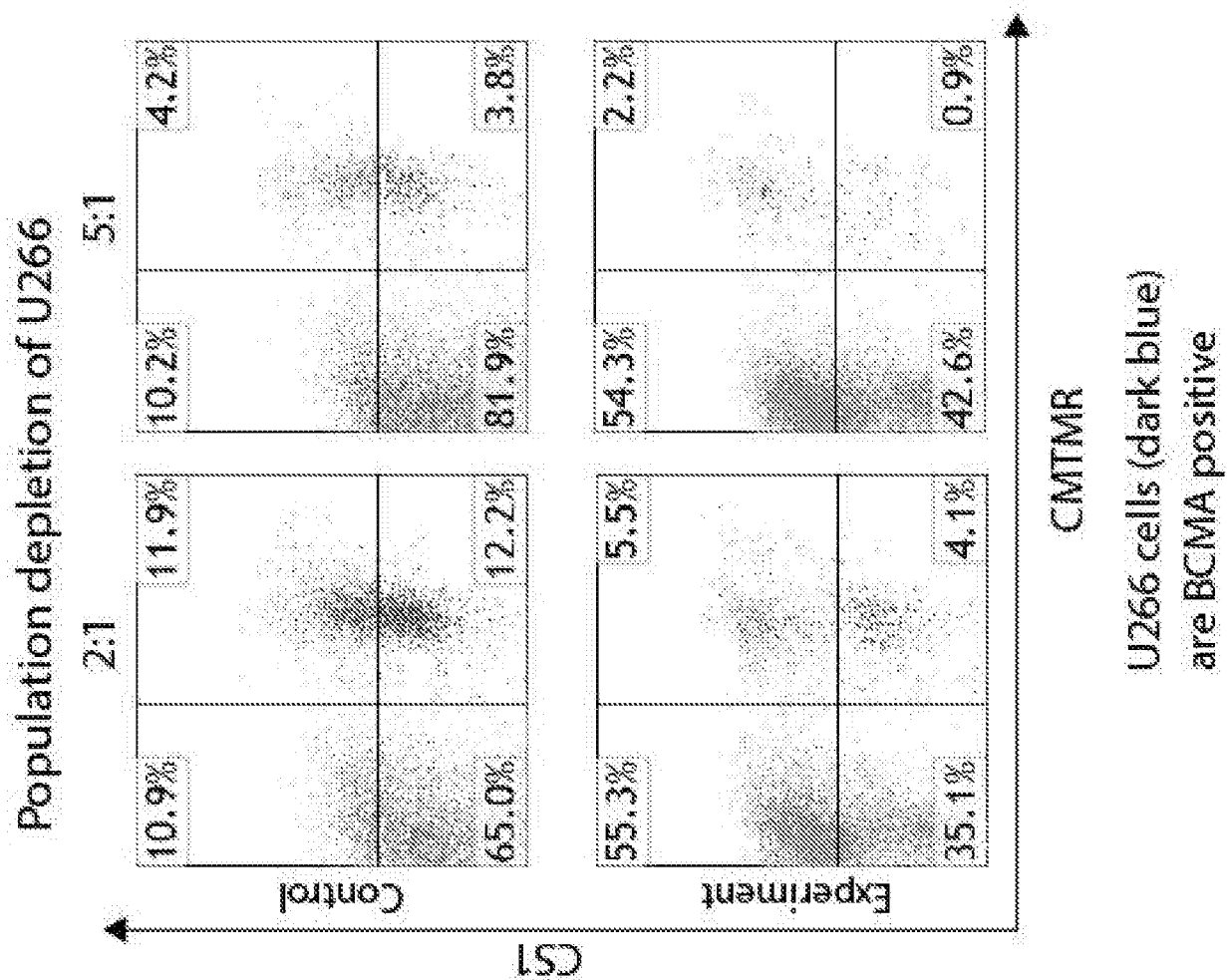


Figure 2B

In vitro summary of BC1cCAR T activity against human myeloma cell lines

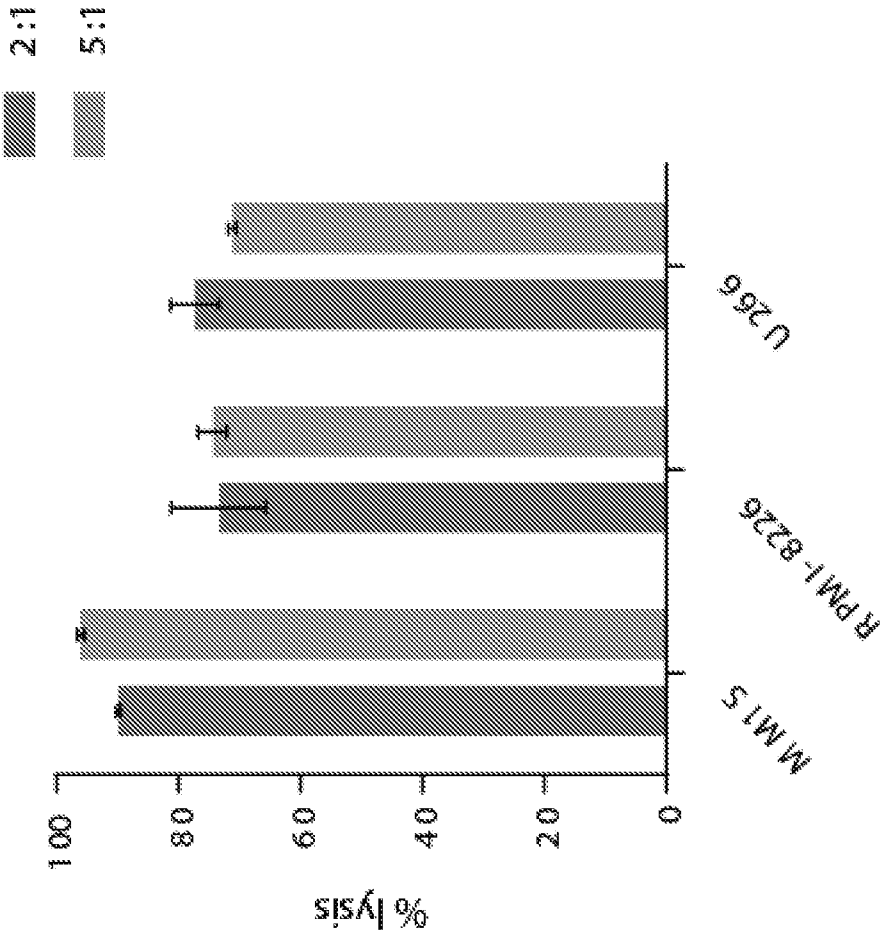


Figure 2C

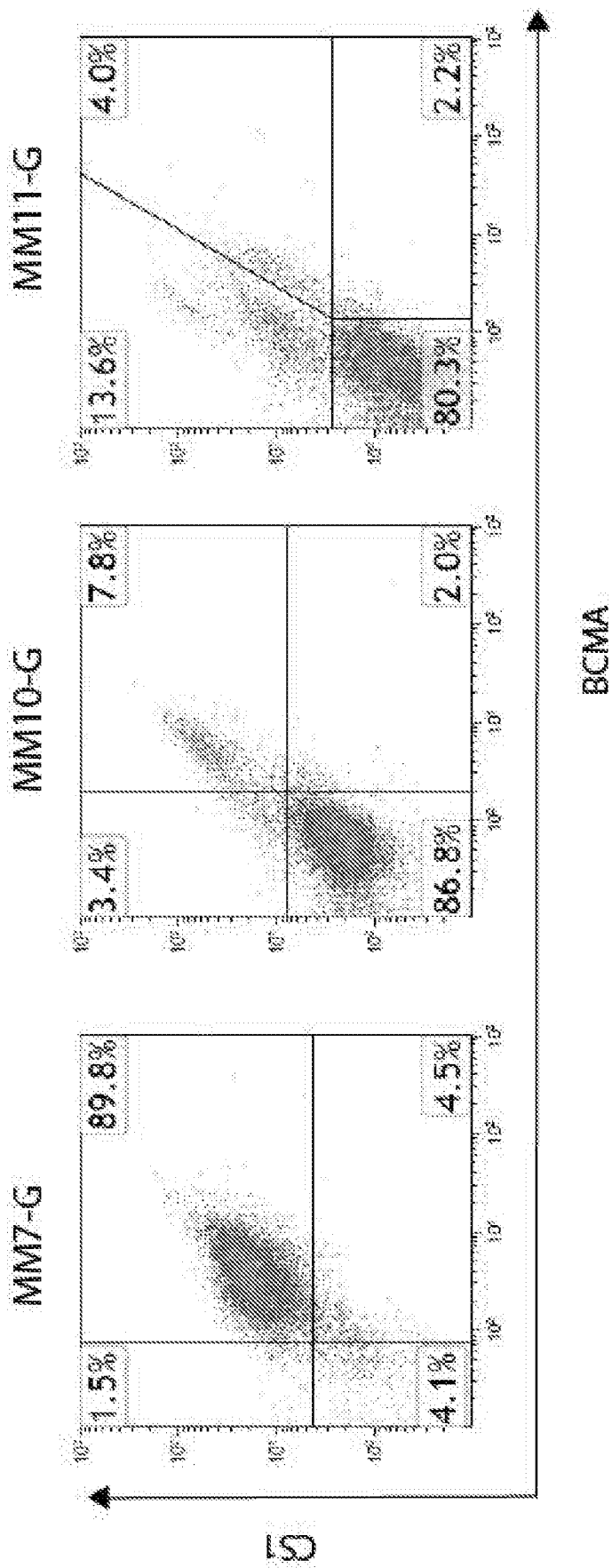


Figure 3

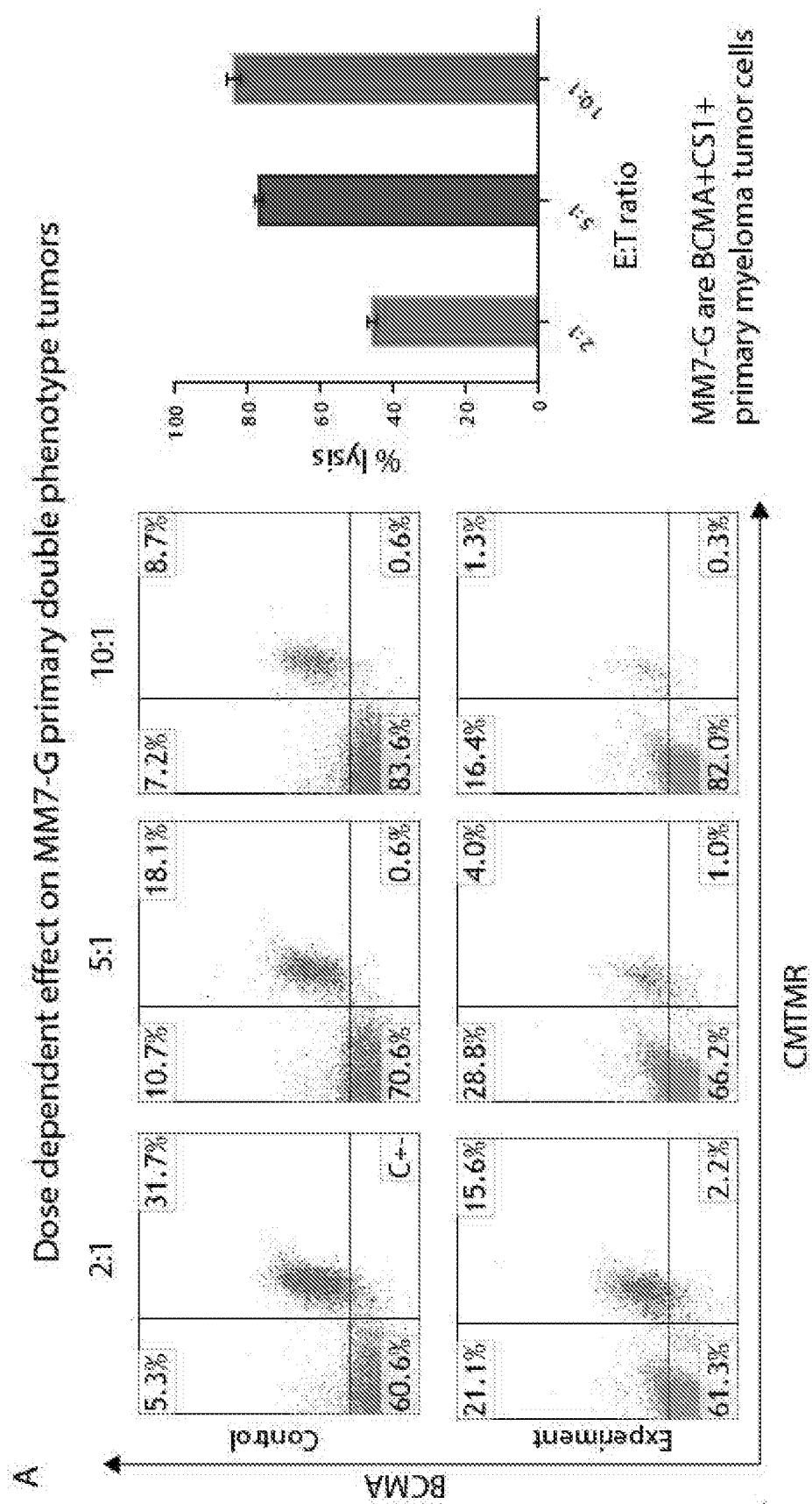


Figure 4A

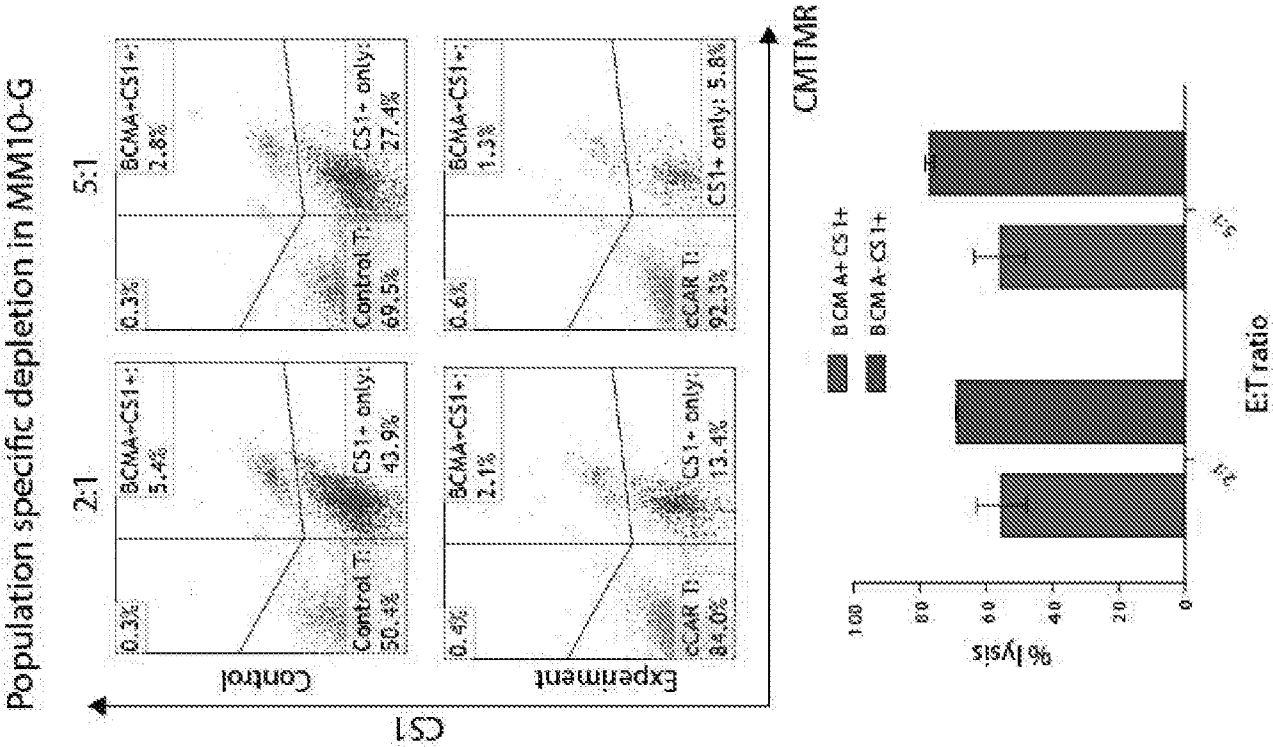


Figure 4B

Dose dependent effect on CS1dim BCMA-
MM11-G primary tumor

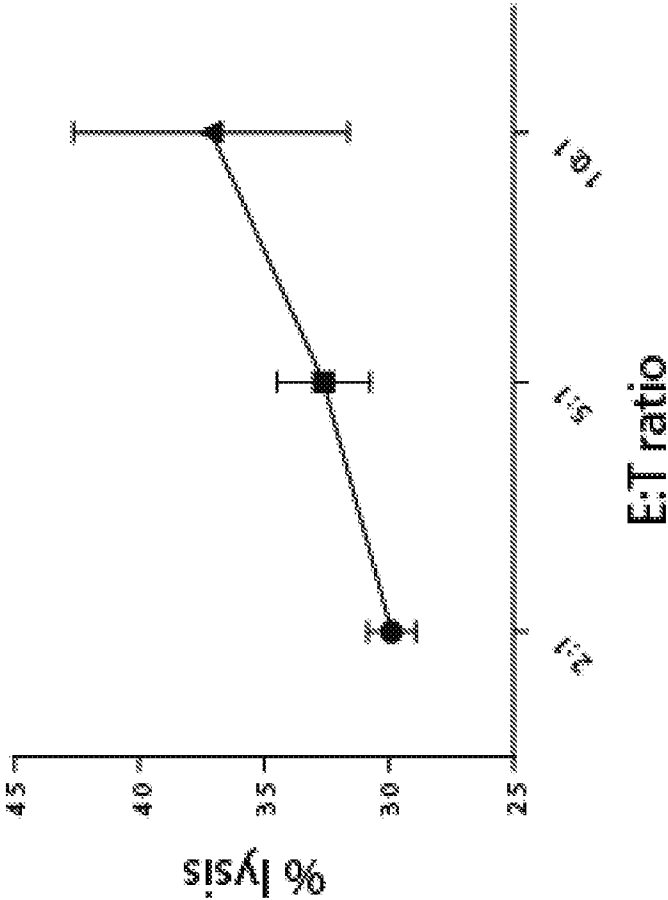


Figure 4C

In vitro summary of BC1cCART activity

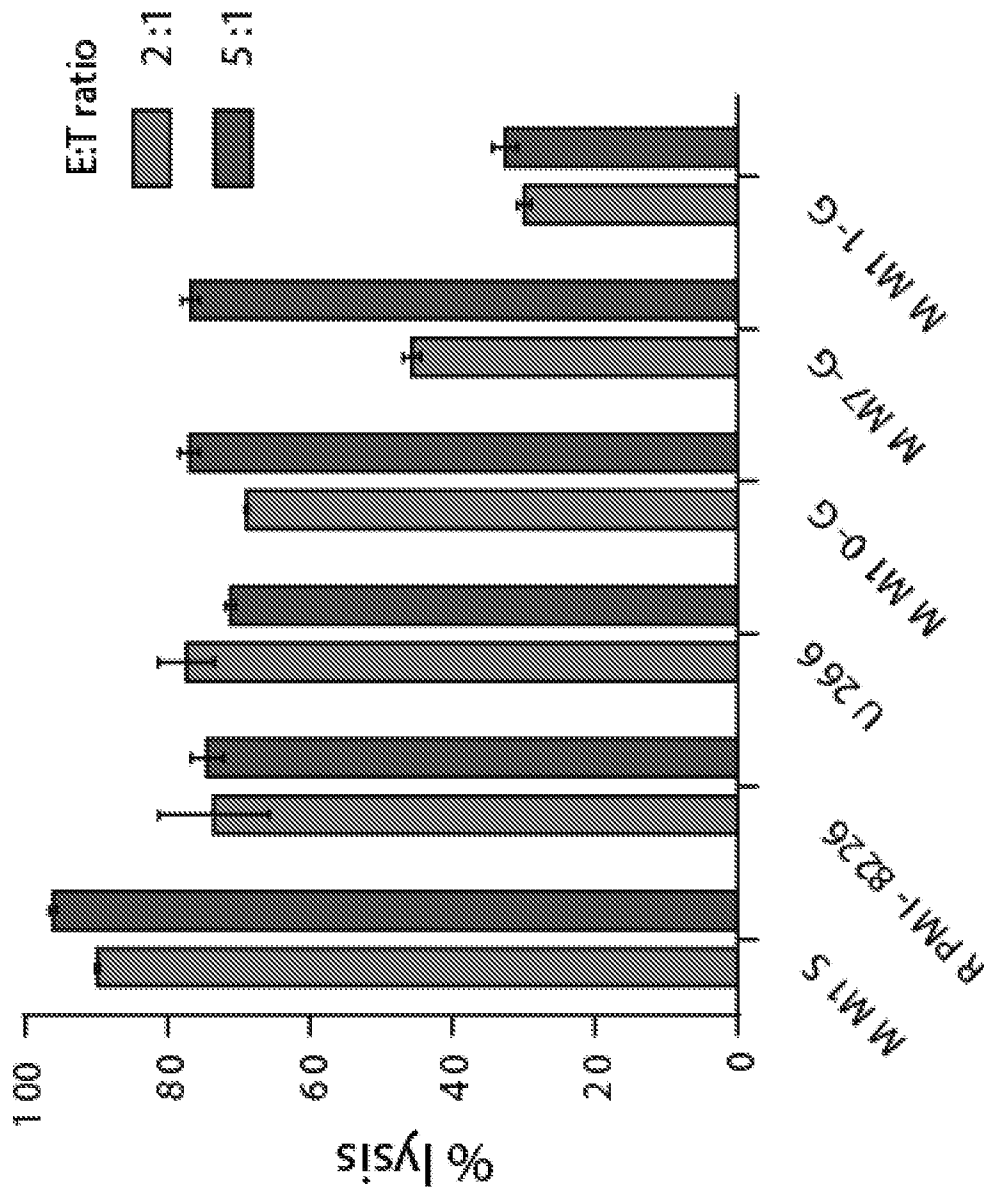


Figure 4D

Generation of antigen-specific
expressing K562

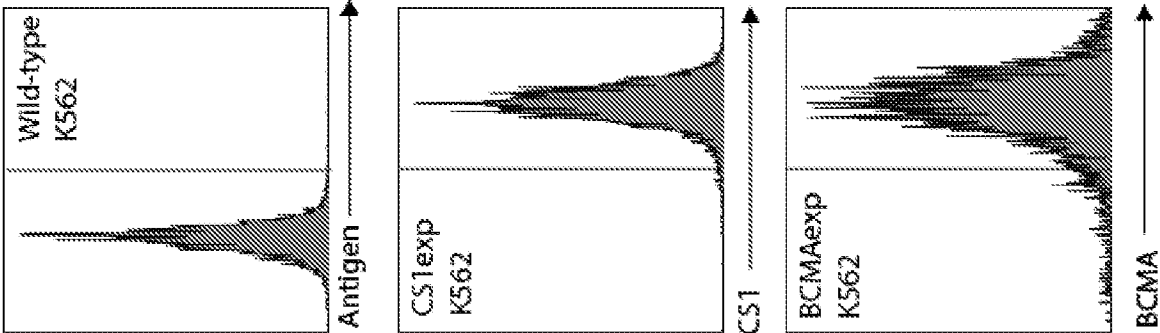
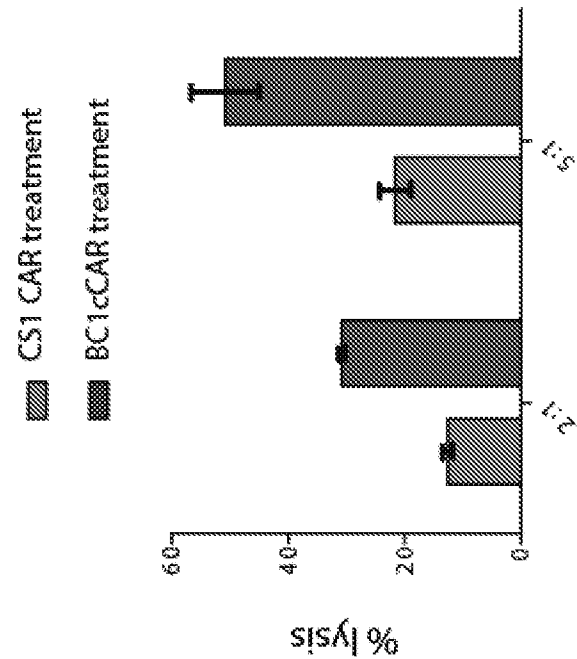


Figure 5A

Short-term CS1 depletion by BC1cCART vs. CS1 CART



BC1cCART T-cells do not exhibit off target cytotoxicity

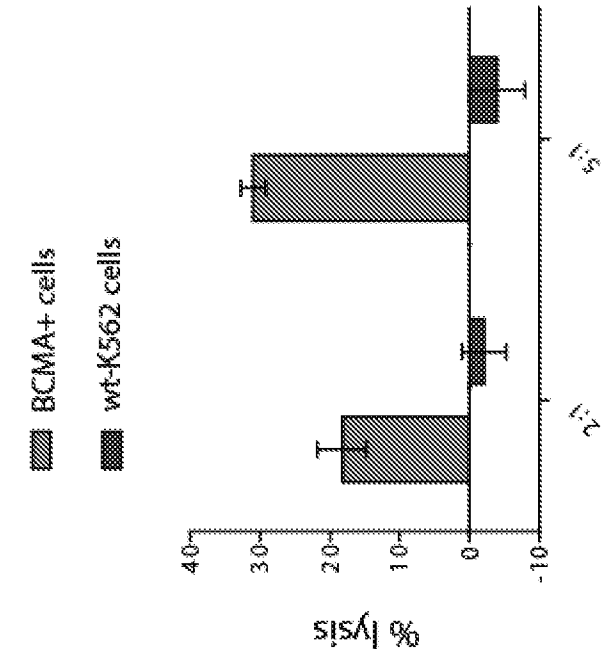


Figure 5B

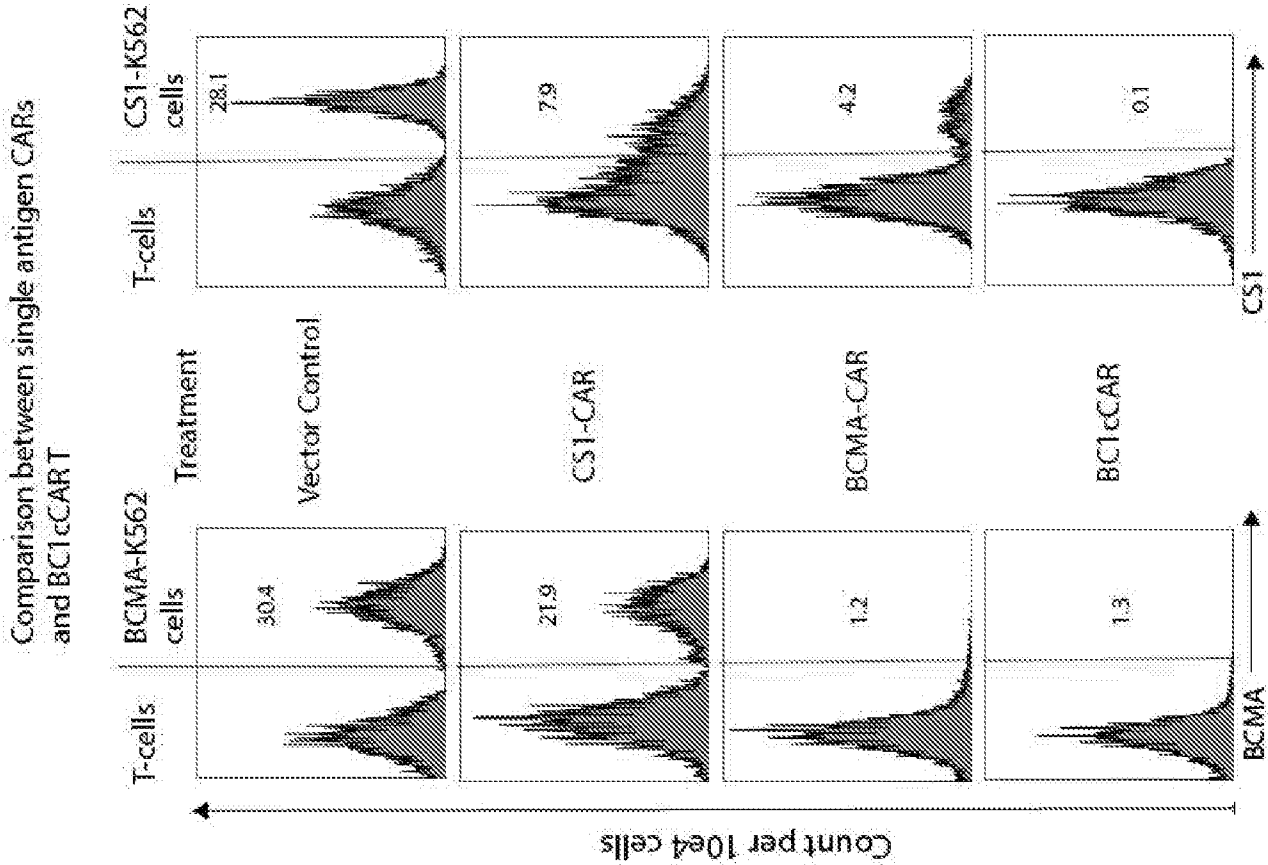


Figure 5C

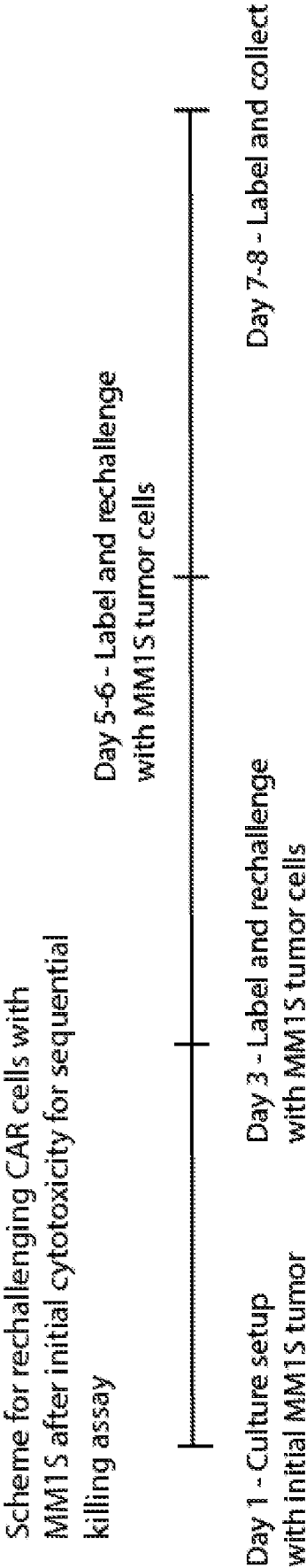


Figure 6A

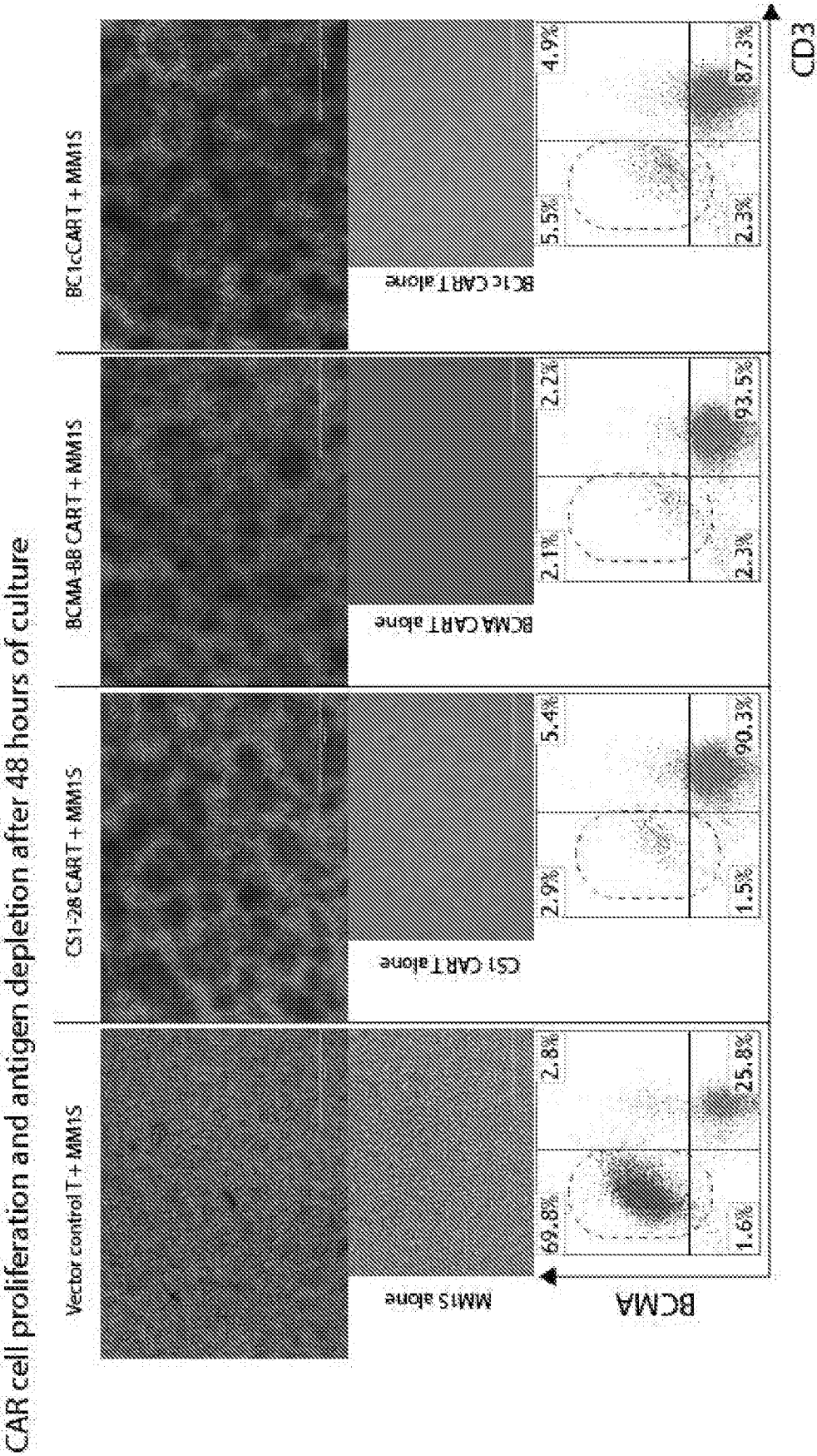


Figure 6B

CAR cell proliferation and antigen depletion after 108 hours of culture

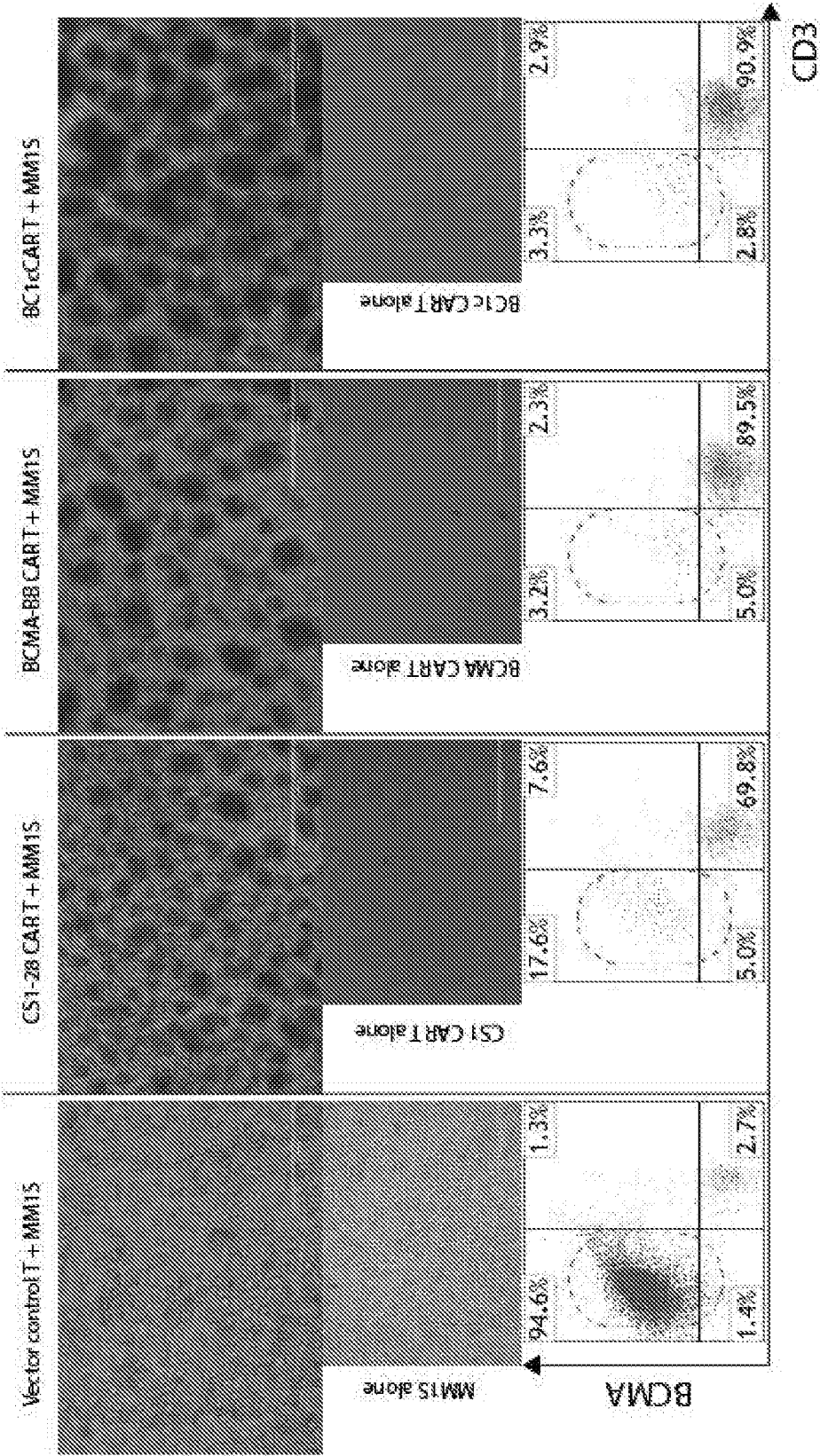


Figure 6C

BC1cCAR T-cells show superior tumor burden control in mixed cell model

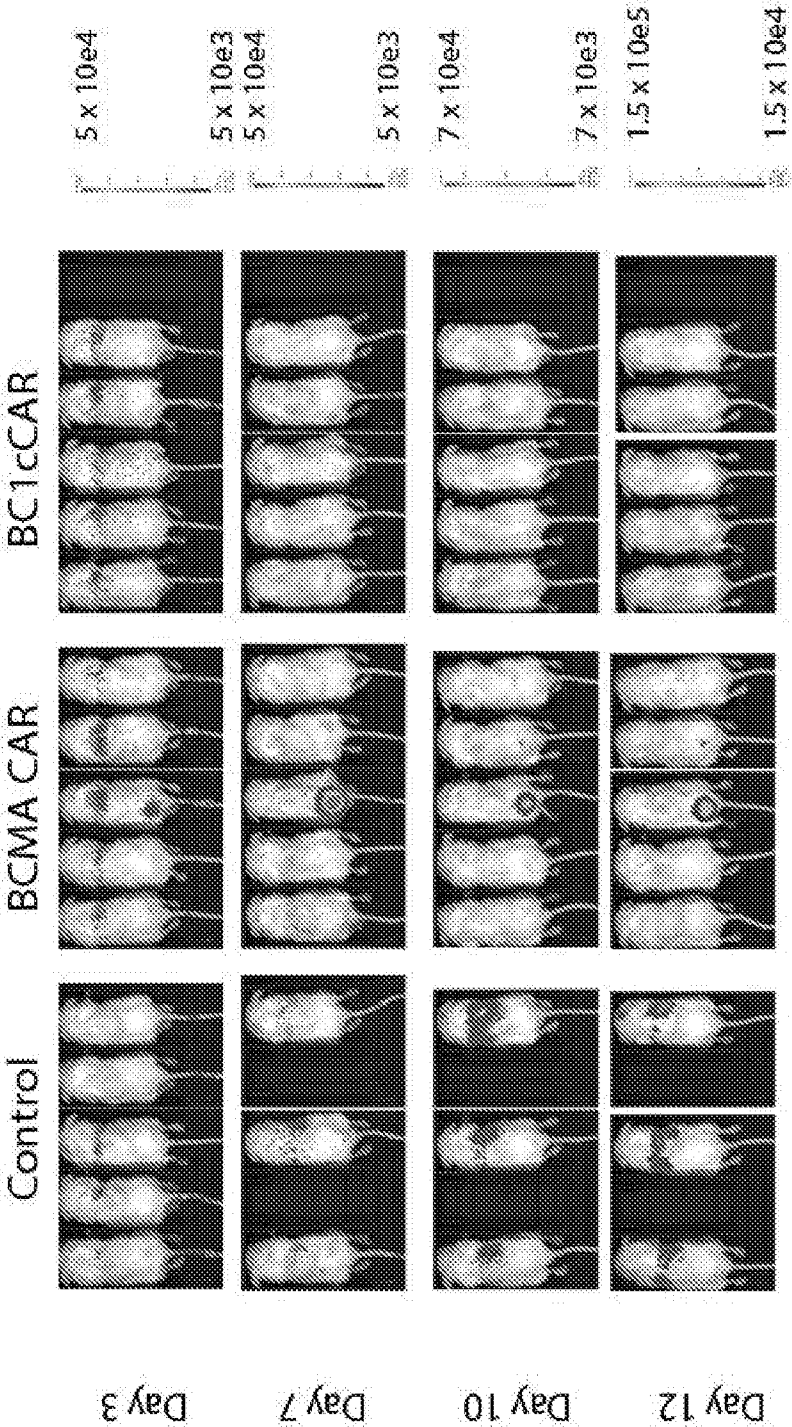


Figure 7A

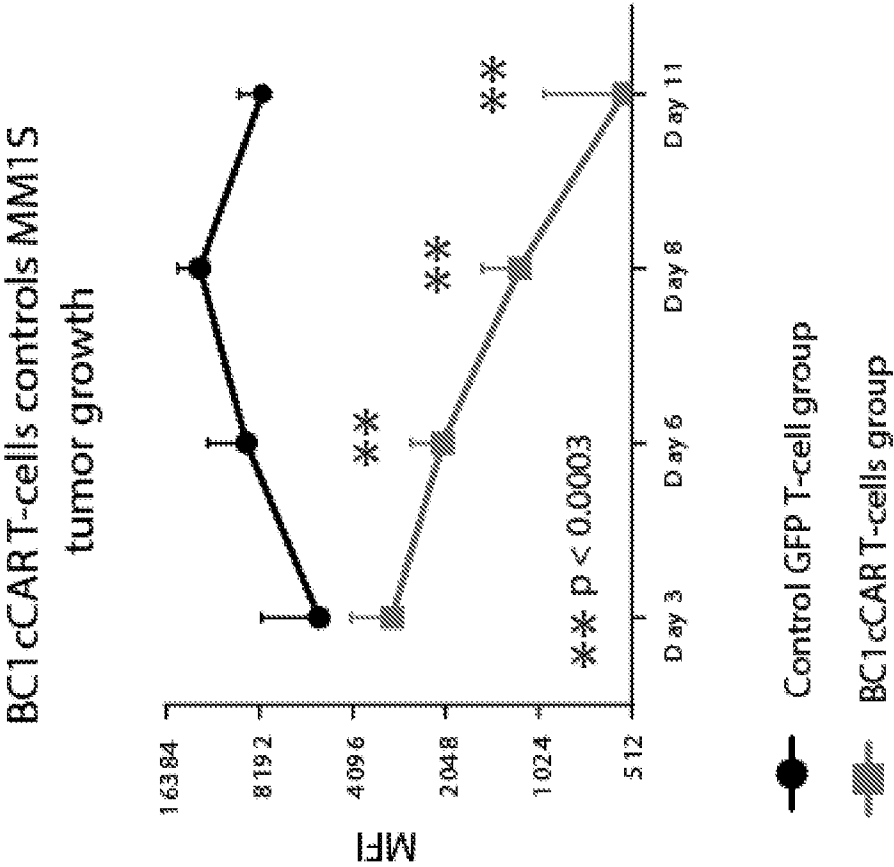


Figure 7B

BC1cCART-cell effects on murine survival outlook

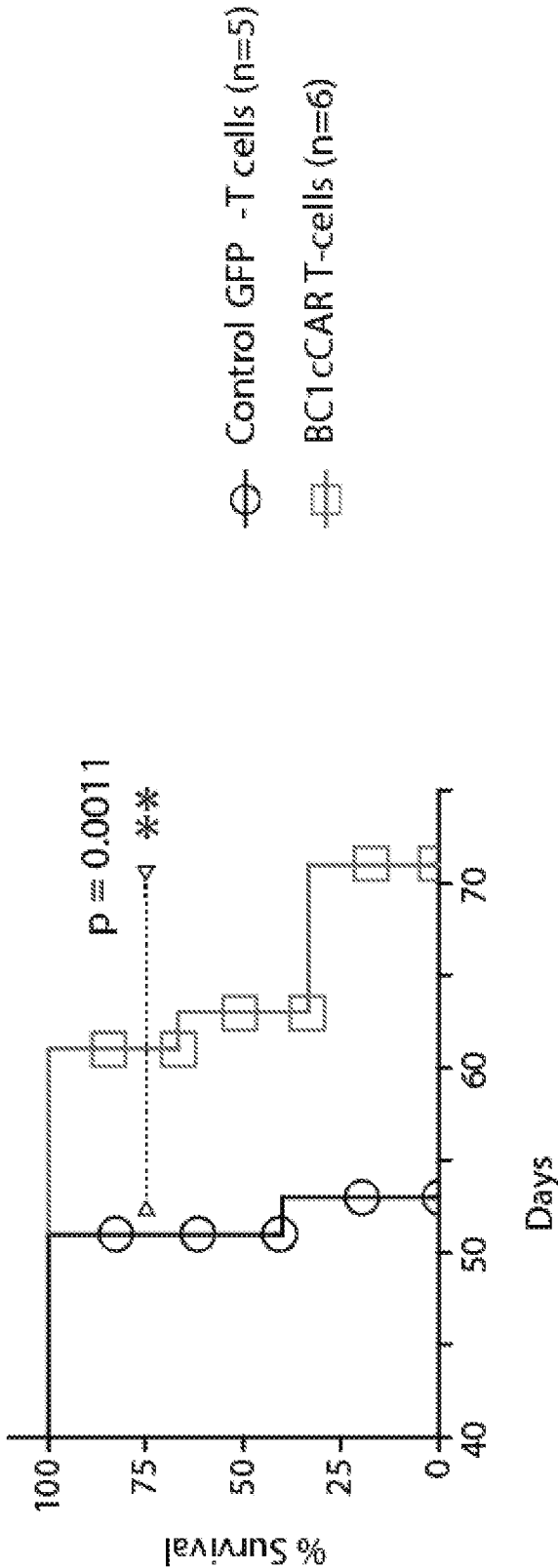


Figure 7C

BC1cCAR T-cells show superior tumor burden control in mixed cell model

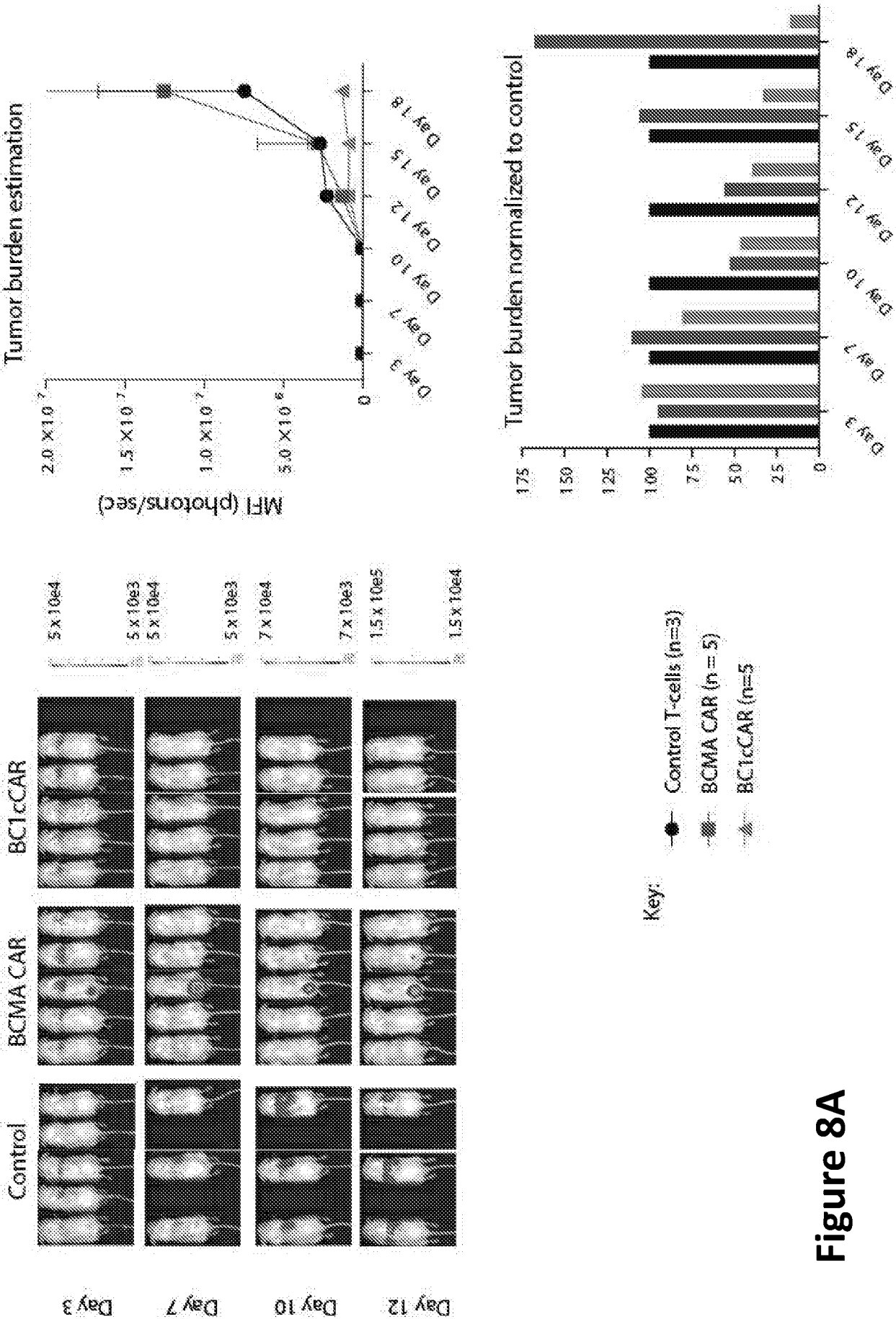


Figure 8A

BC1cCAR improves murine survival outcomes in mixed cell model

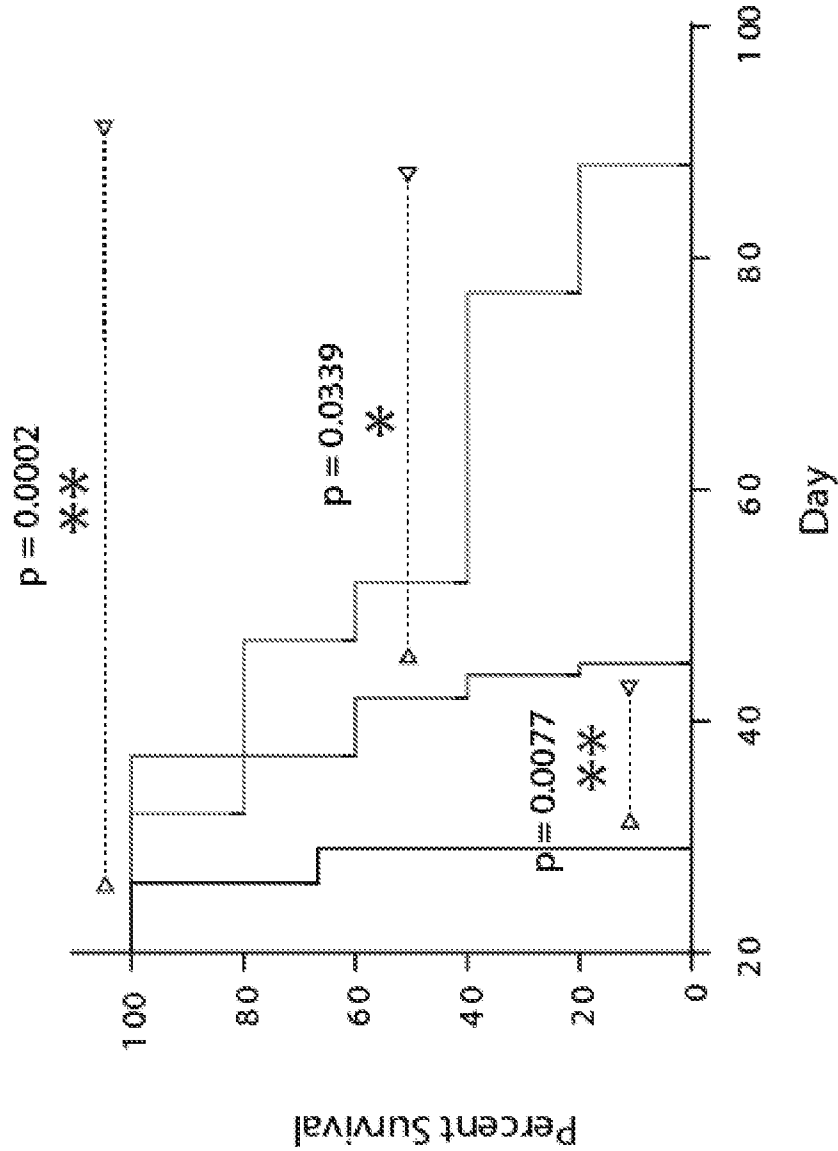


Figure 8B

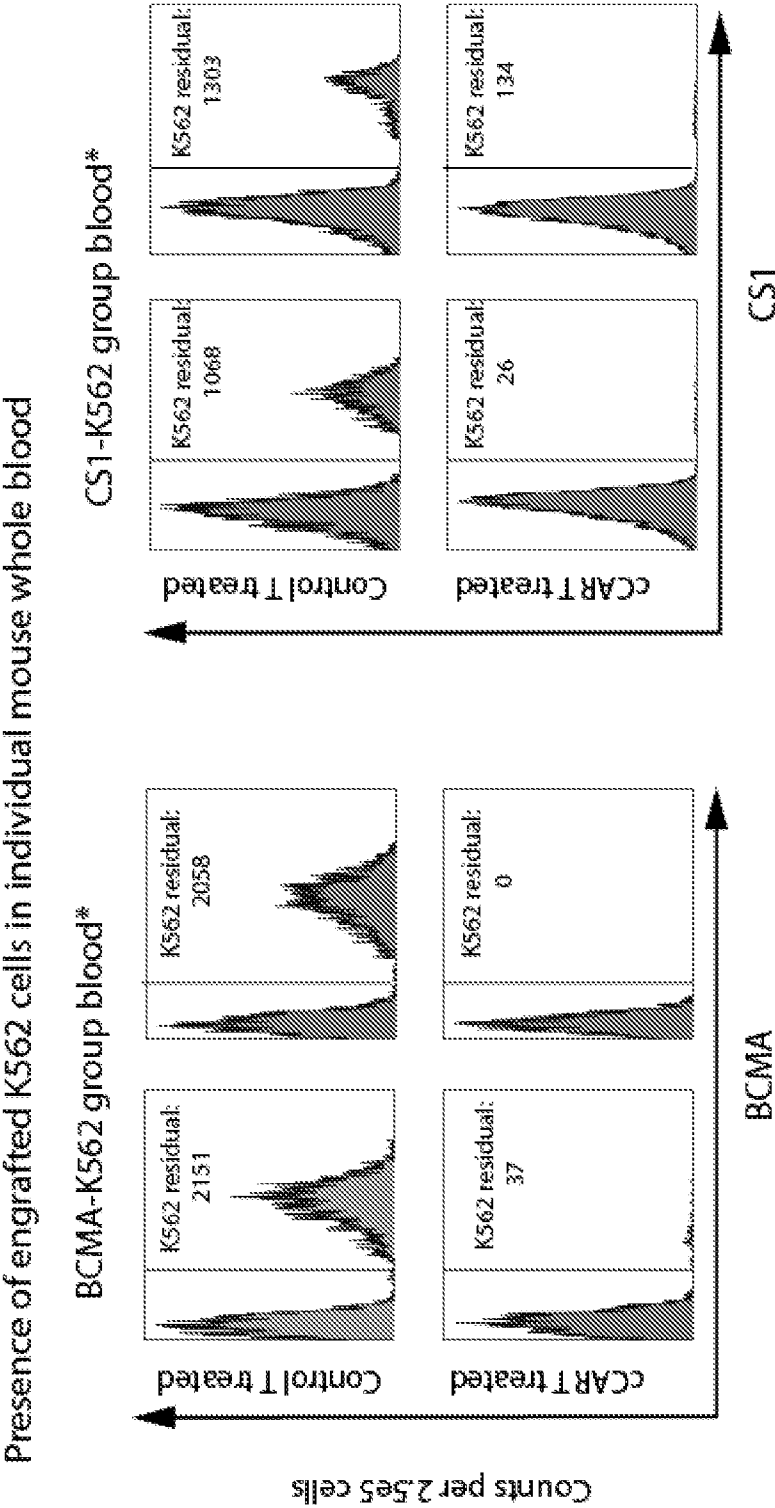


Figure 9A

Tumor persistency in aggregate mouse tissues

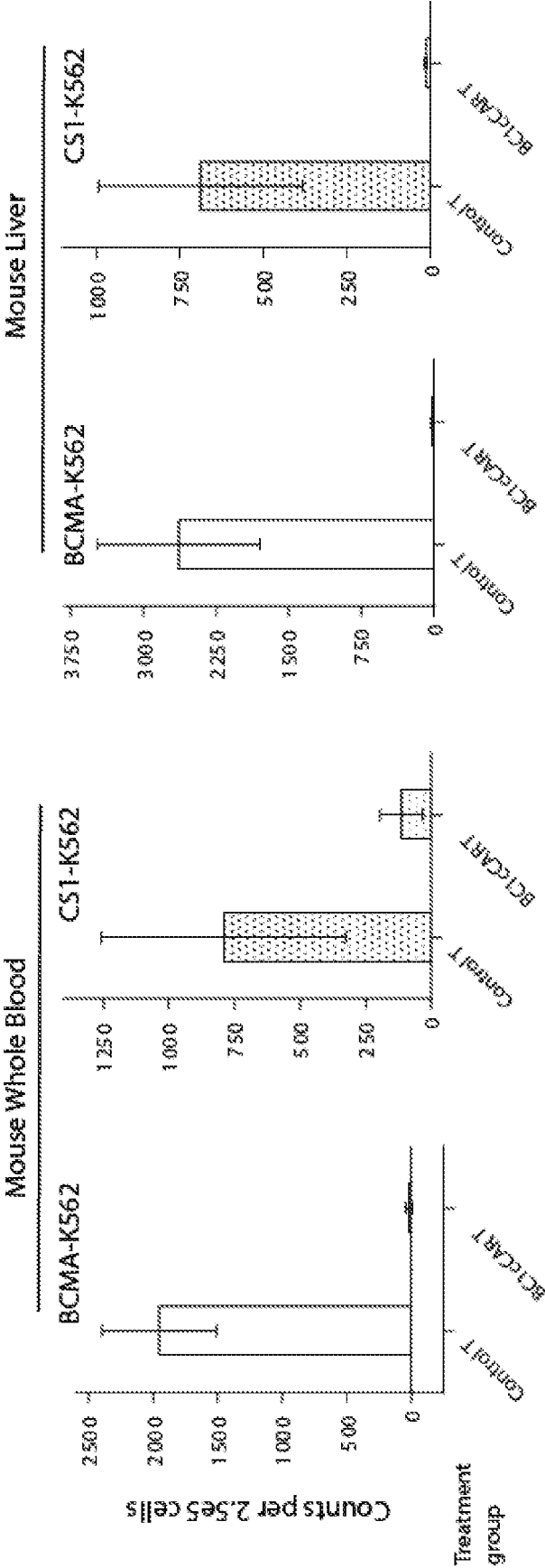


Figure 9B

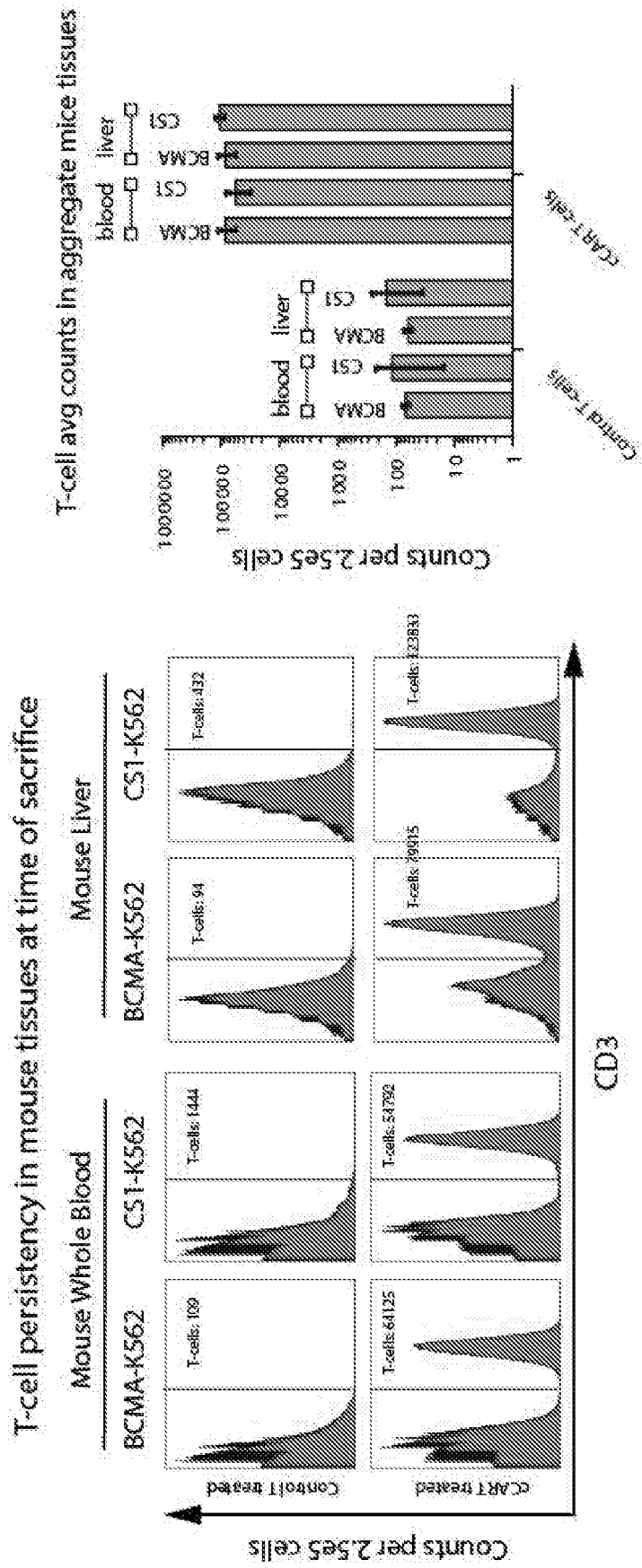


Figure 9C

Mice whole blood samples collected from BCMA and CS1 experimental groups

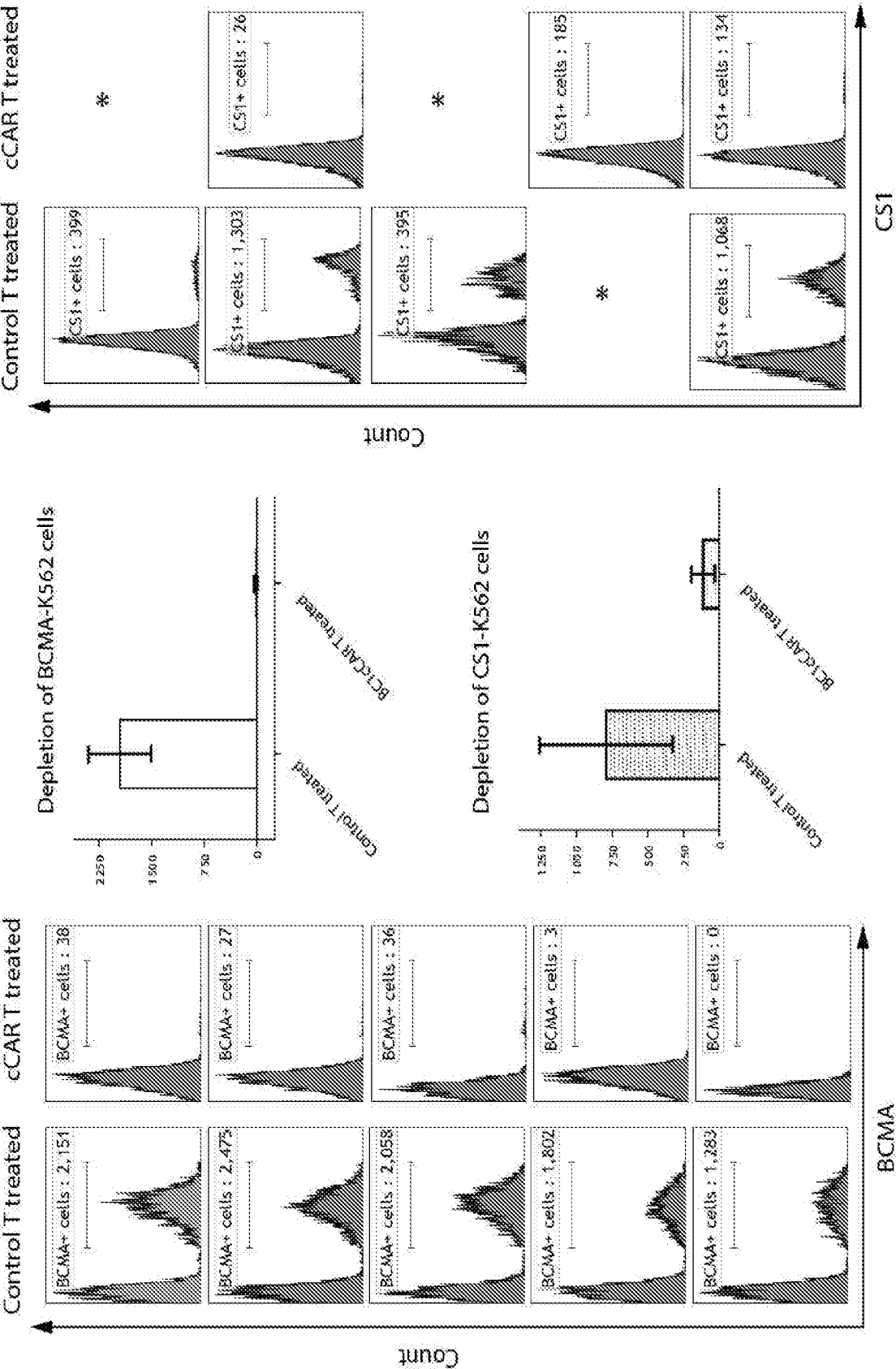


Figure 10A

*Samples were unable to be collected

Mice liver samples taken from BCMA and CS1 experimental groups

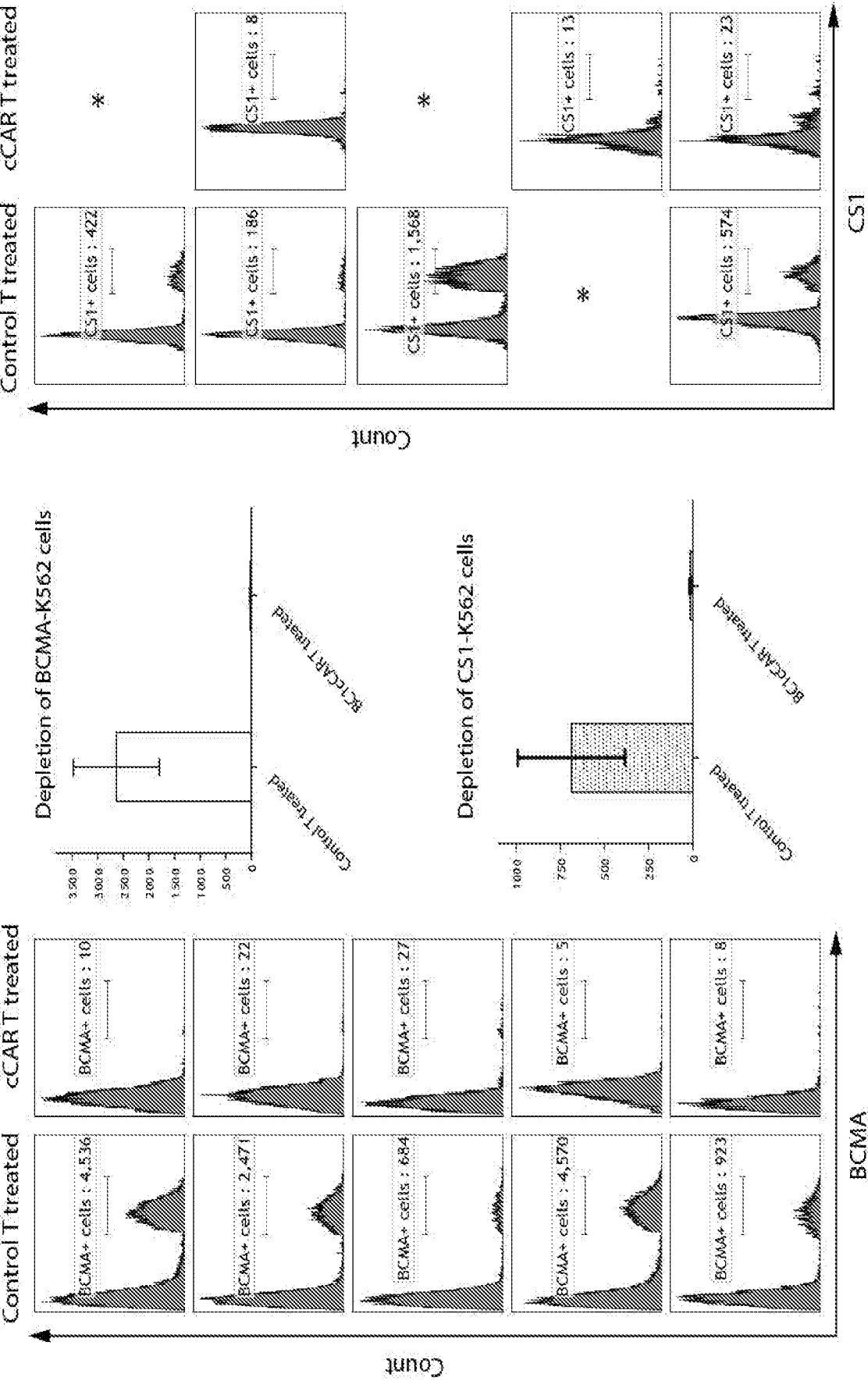


Figure 10B

*Samples were unable to be collected

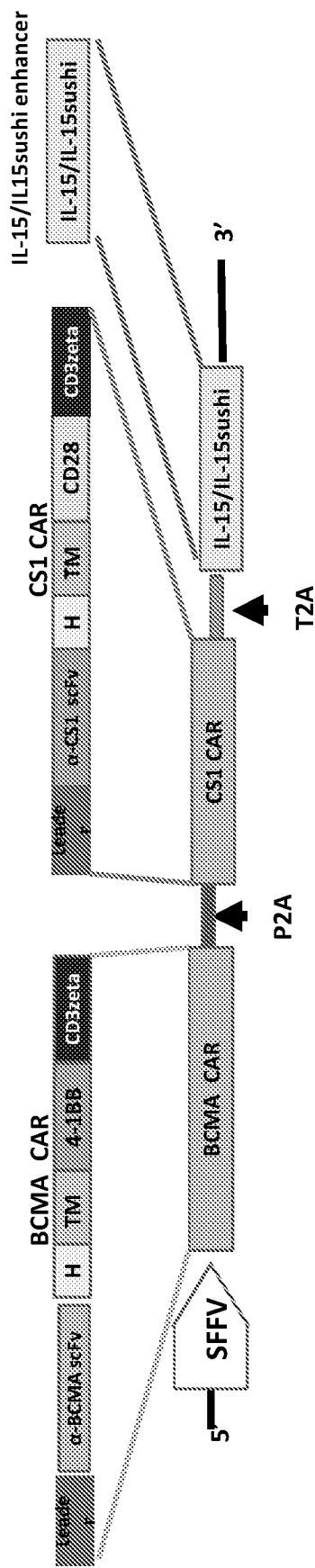


FIGURE 11A

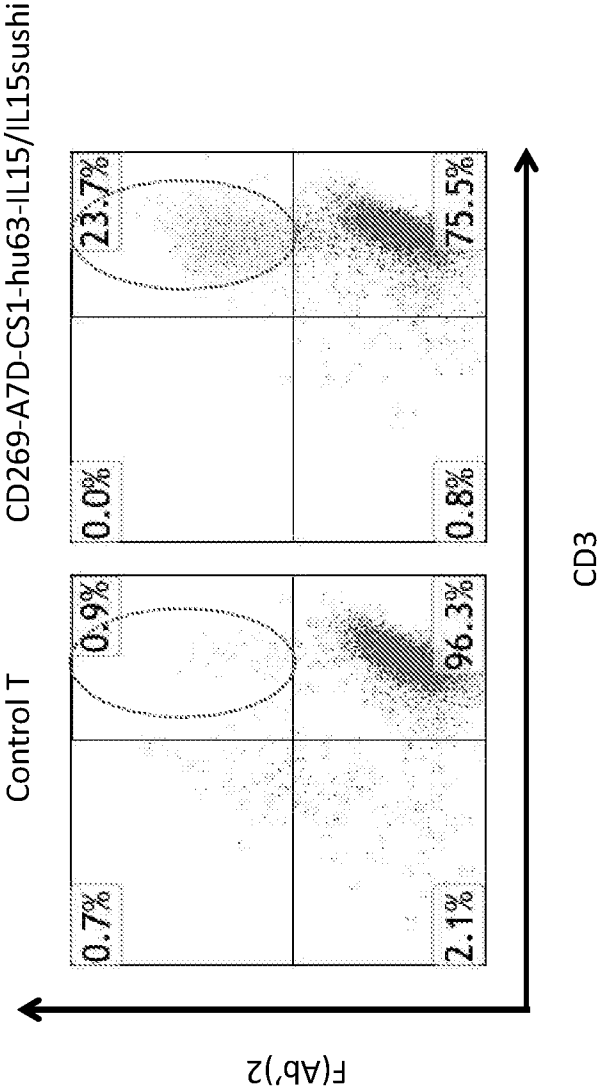


FIGURE 11B

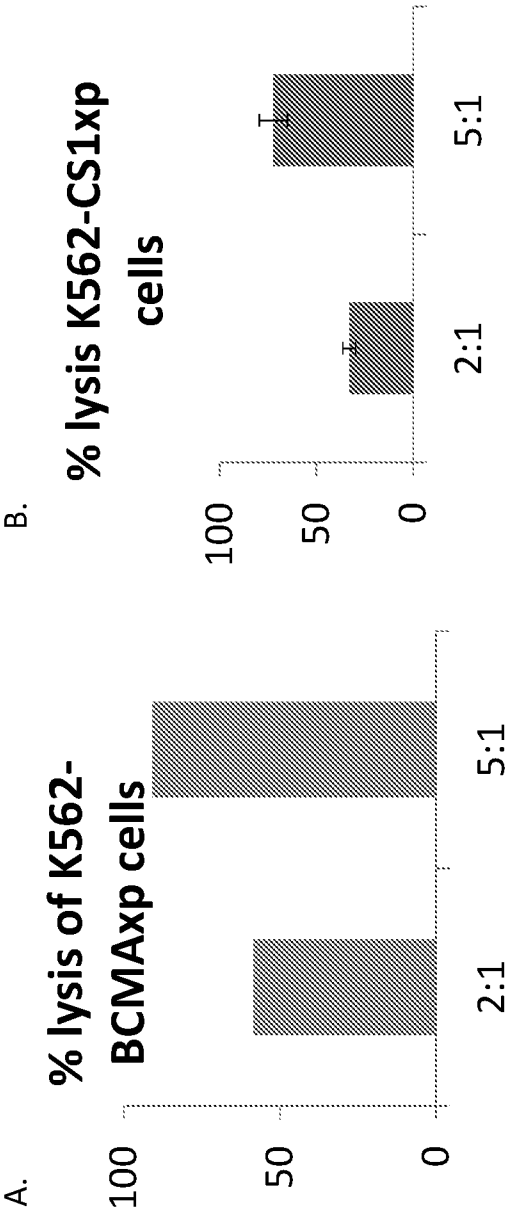


FIGURE 11C

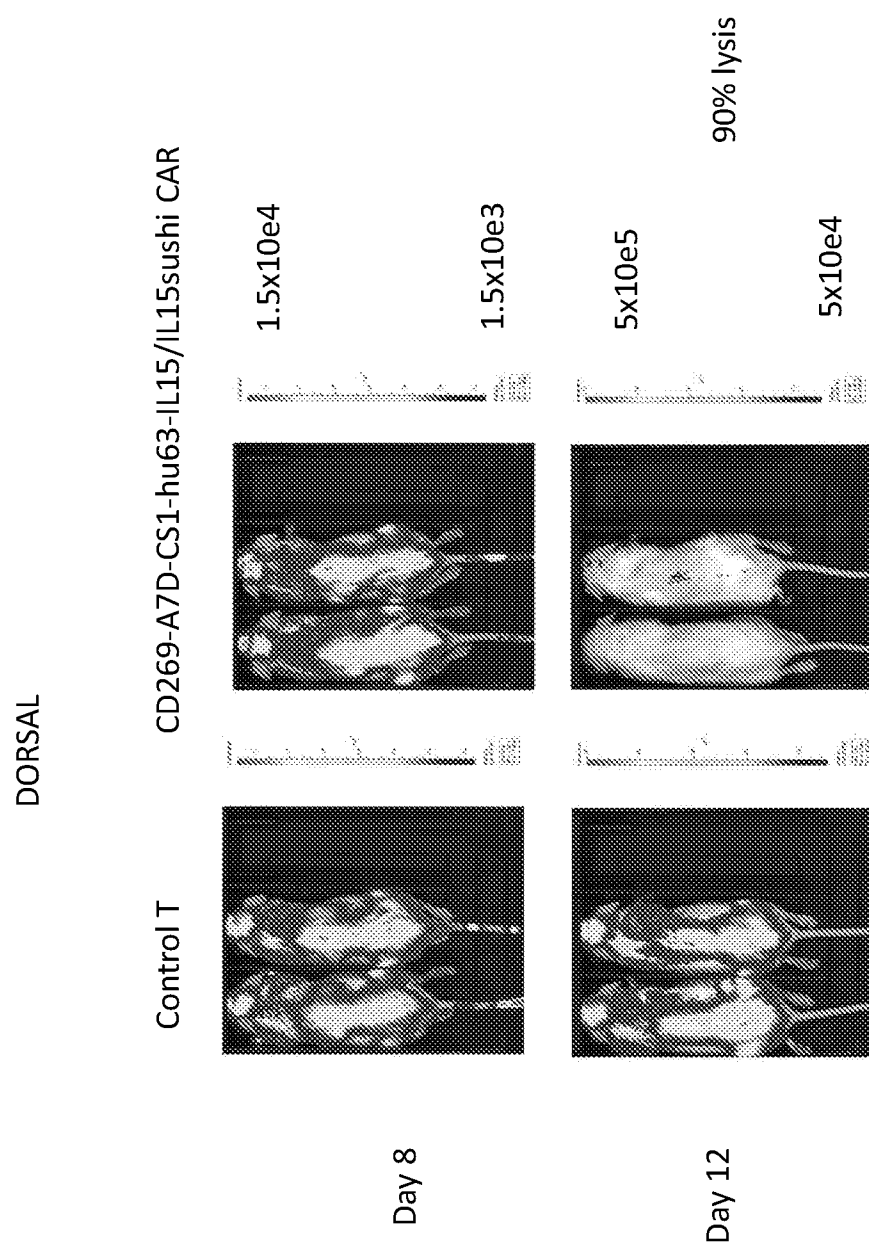


FIGURE 11D

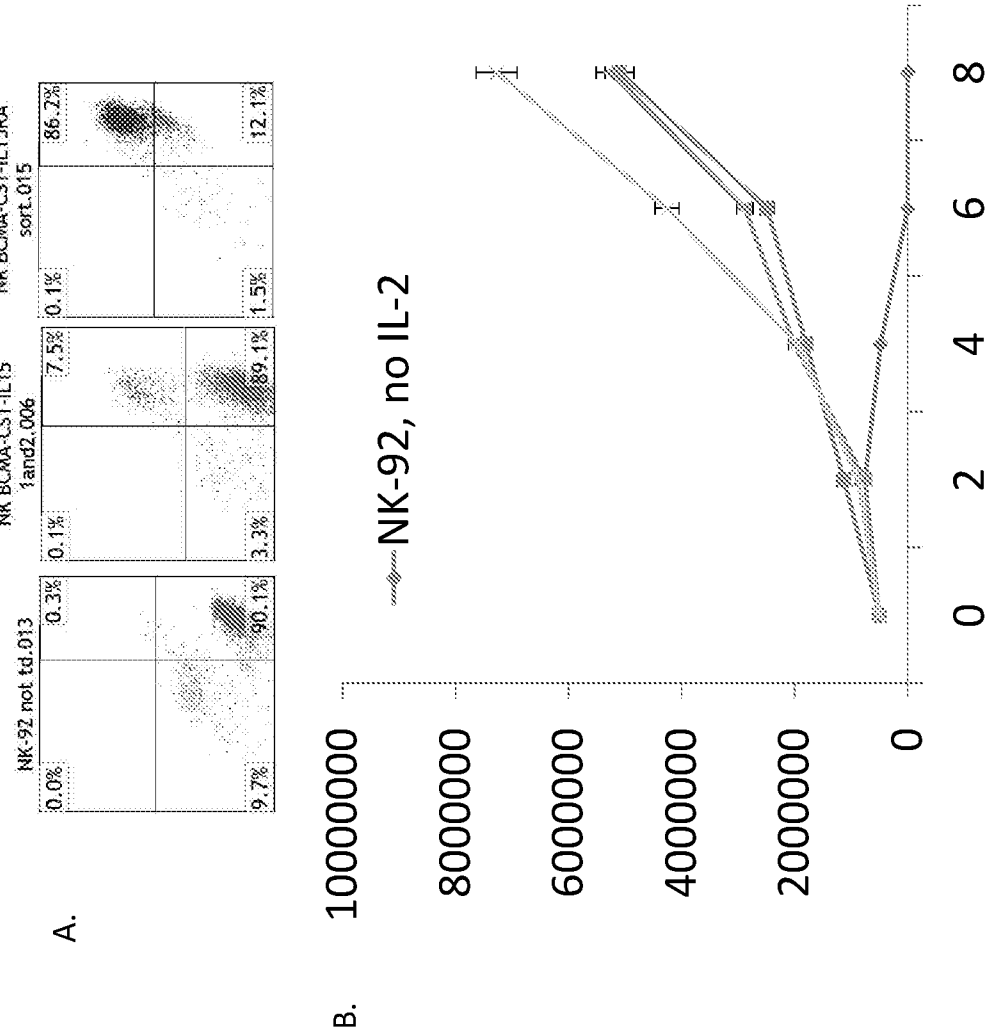


FIGURE 11E

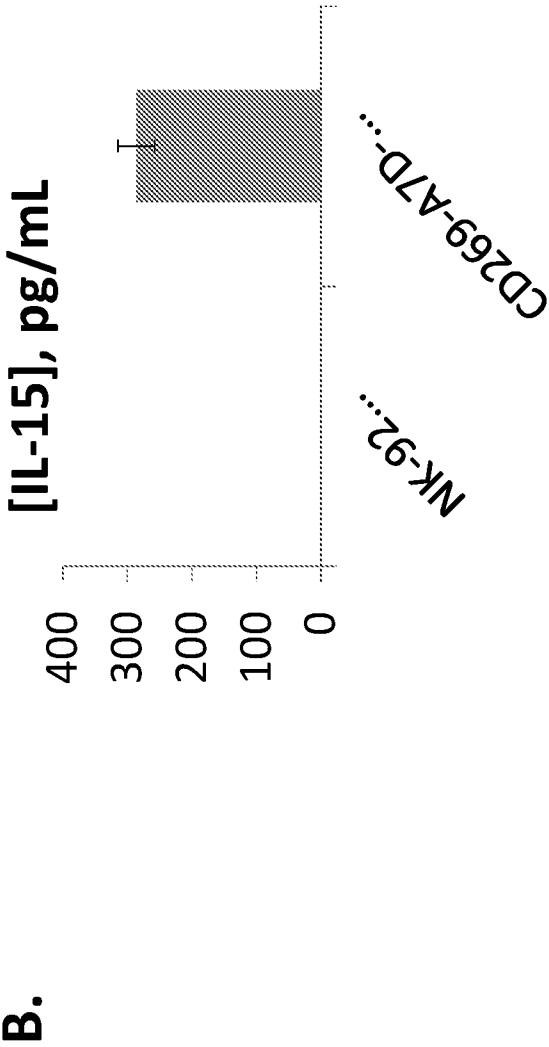
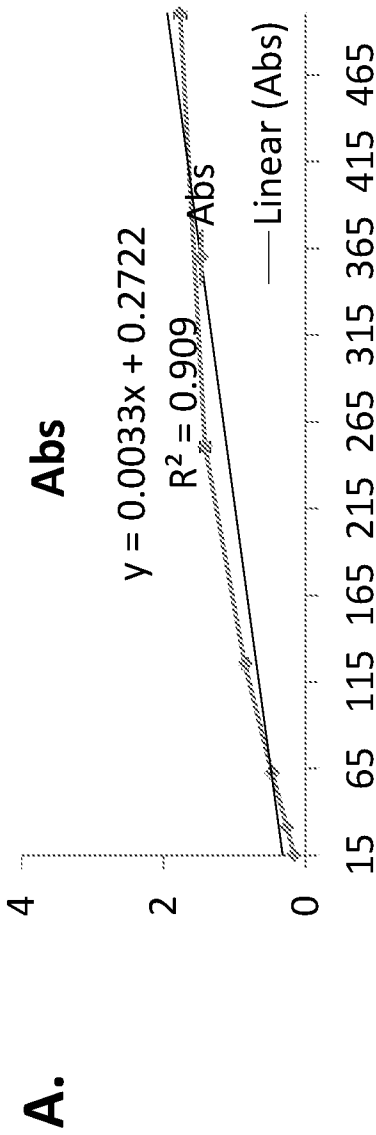


FIGURE 11F

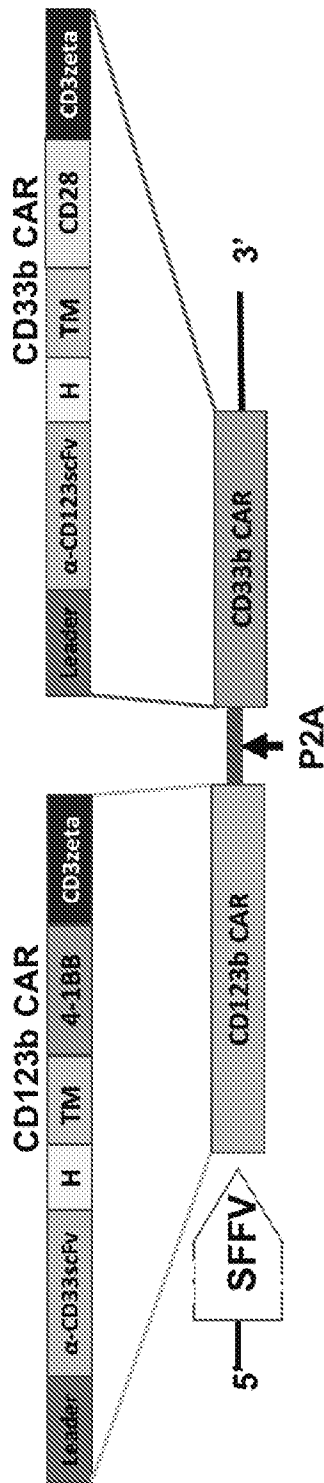


Figure 12A

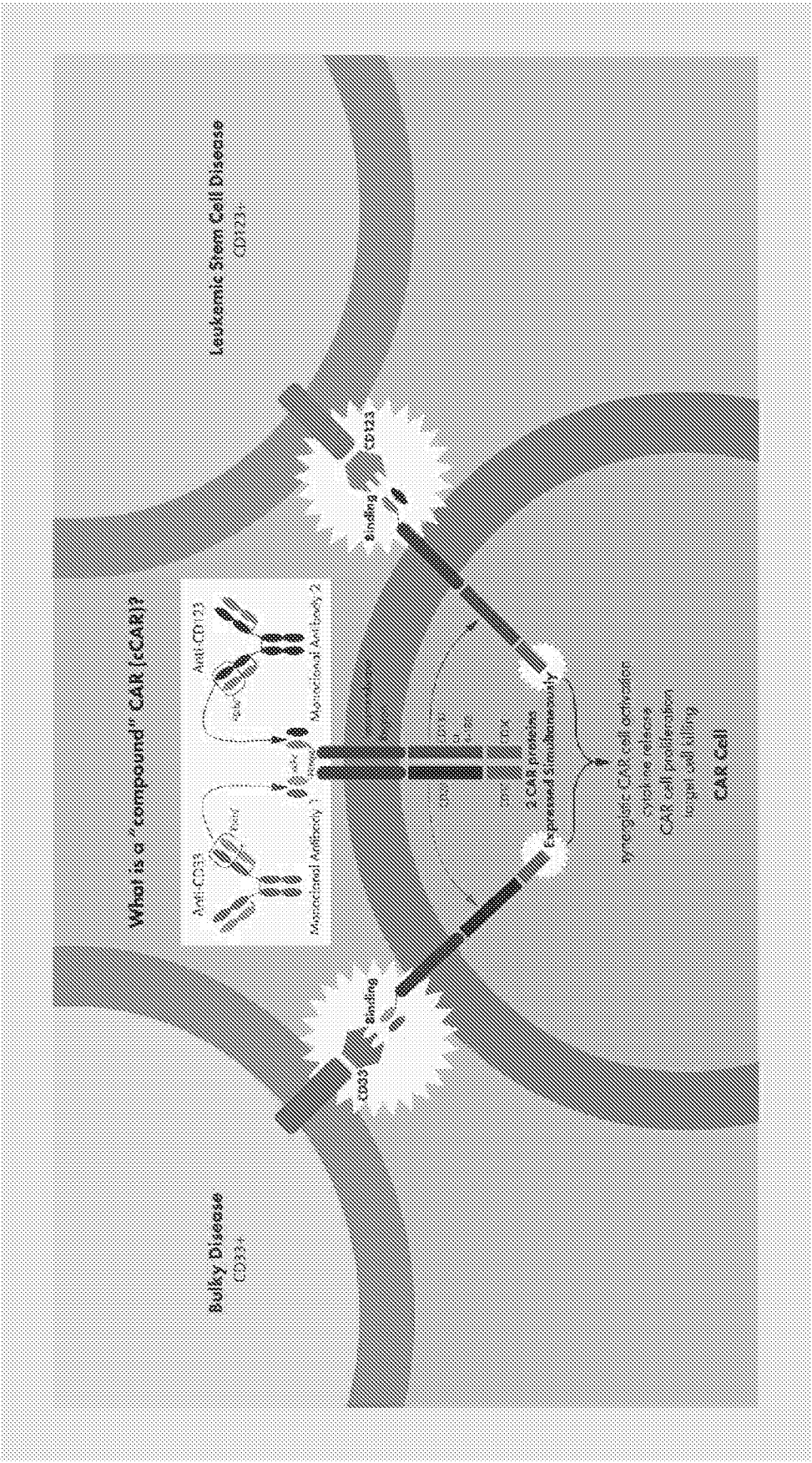


Figure 12B

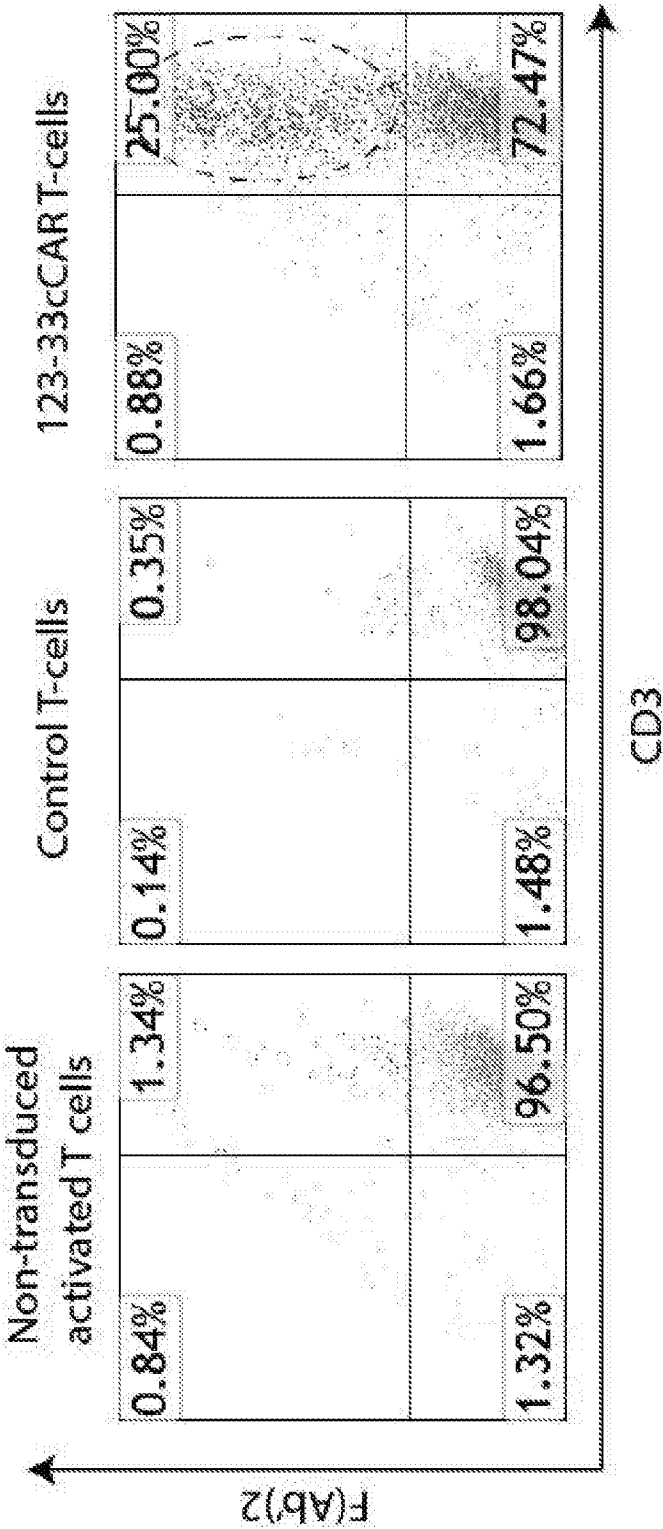


Figure 13

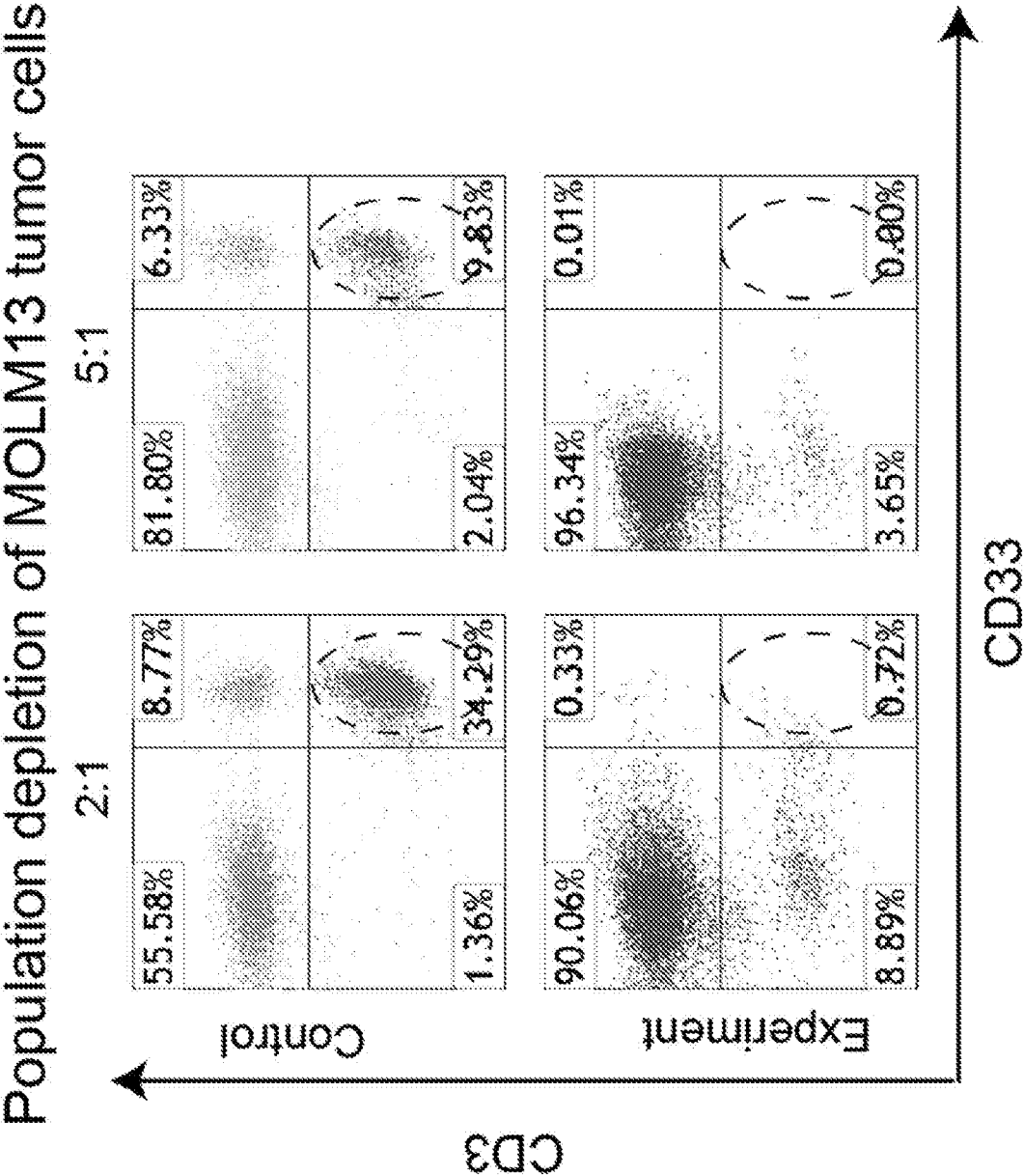


Figure 14A

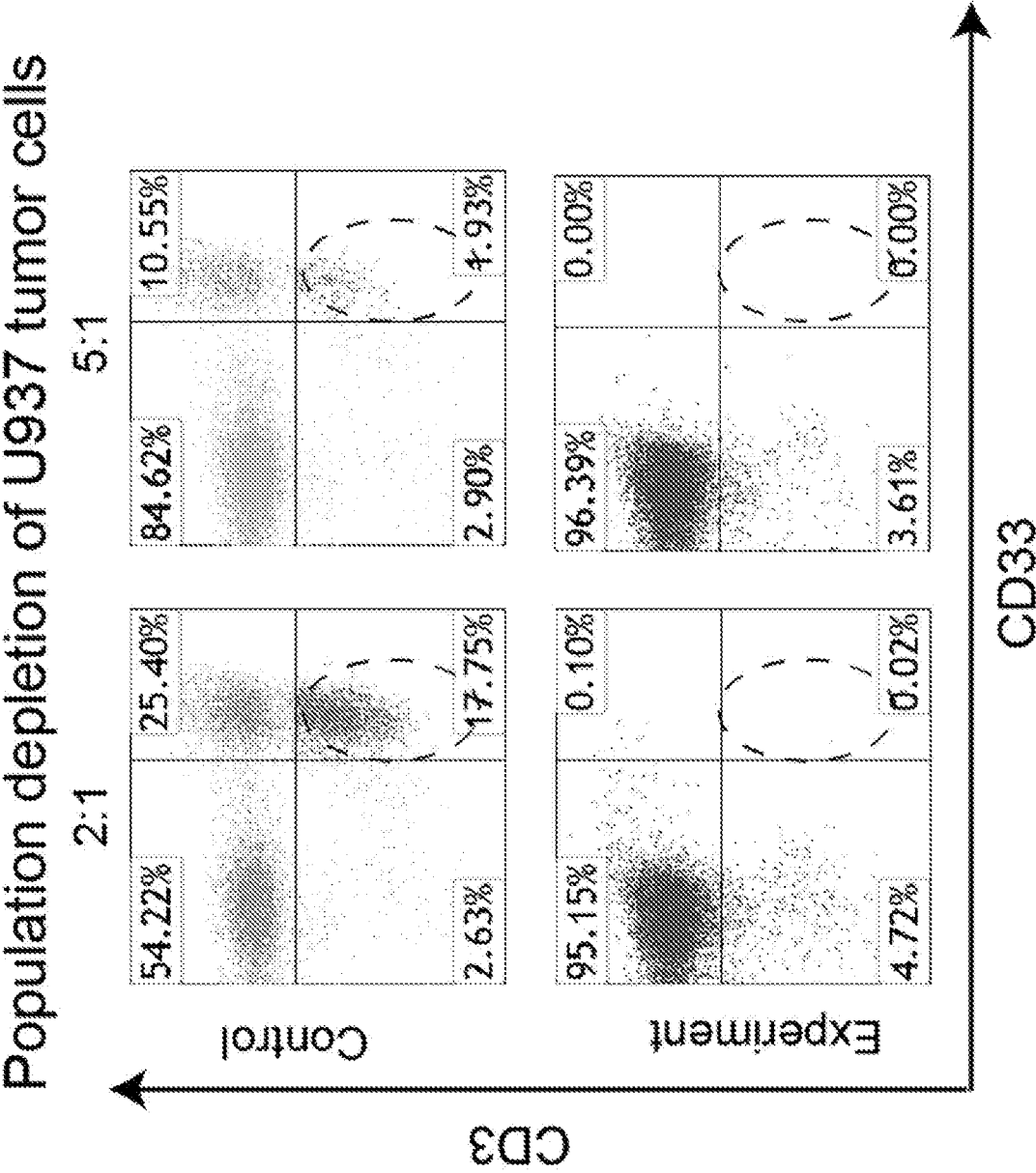


Figure 14B

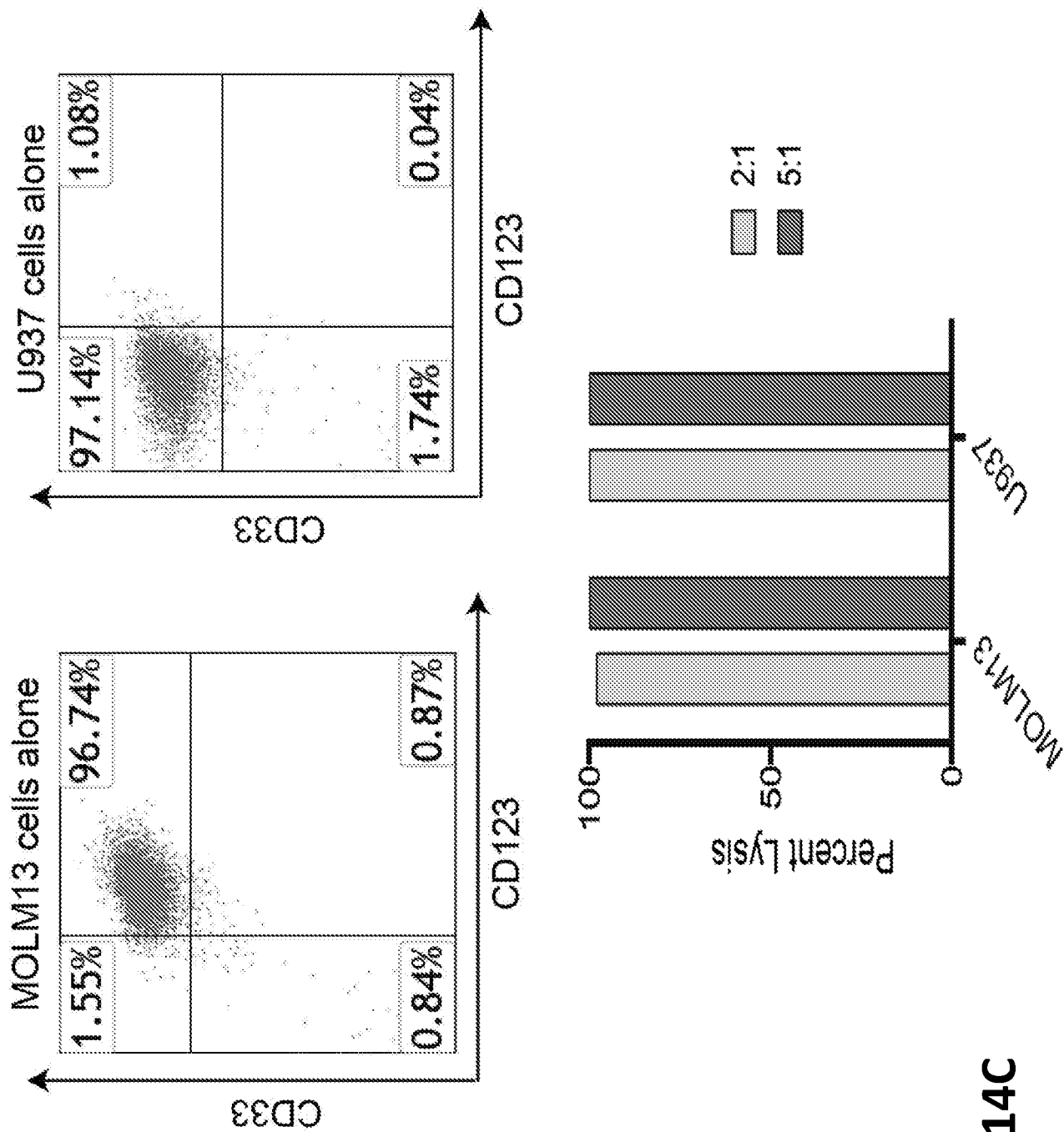


Figure 14C

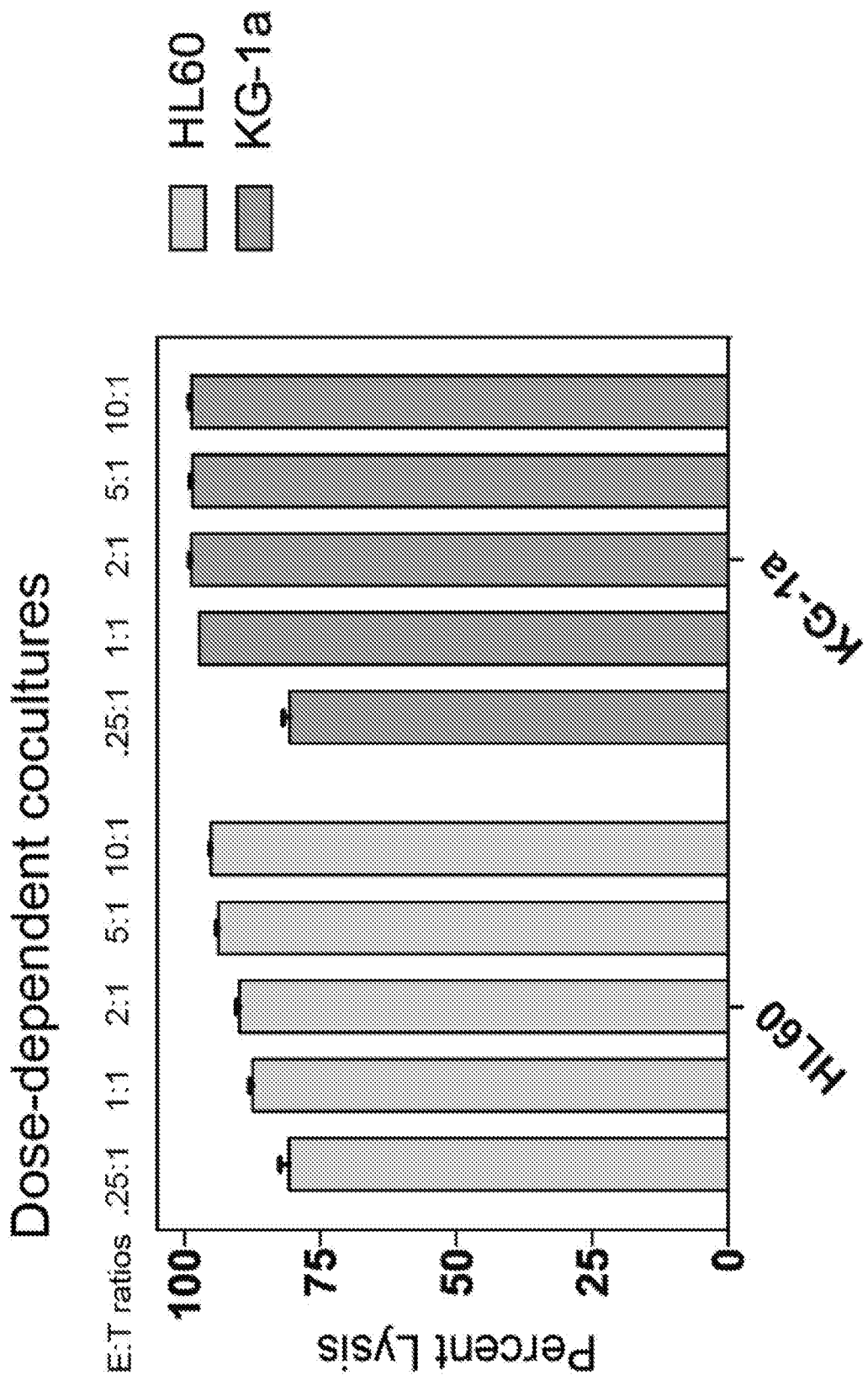


Figure 14D

Population depletion of PT1 (AML) tumor cells

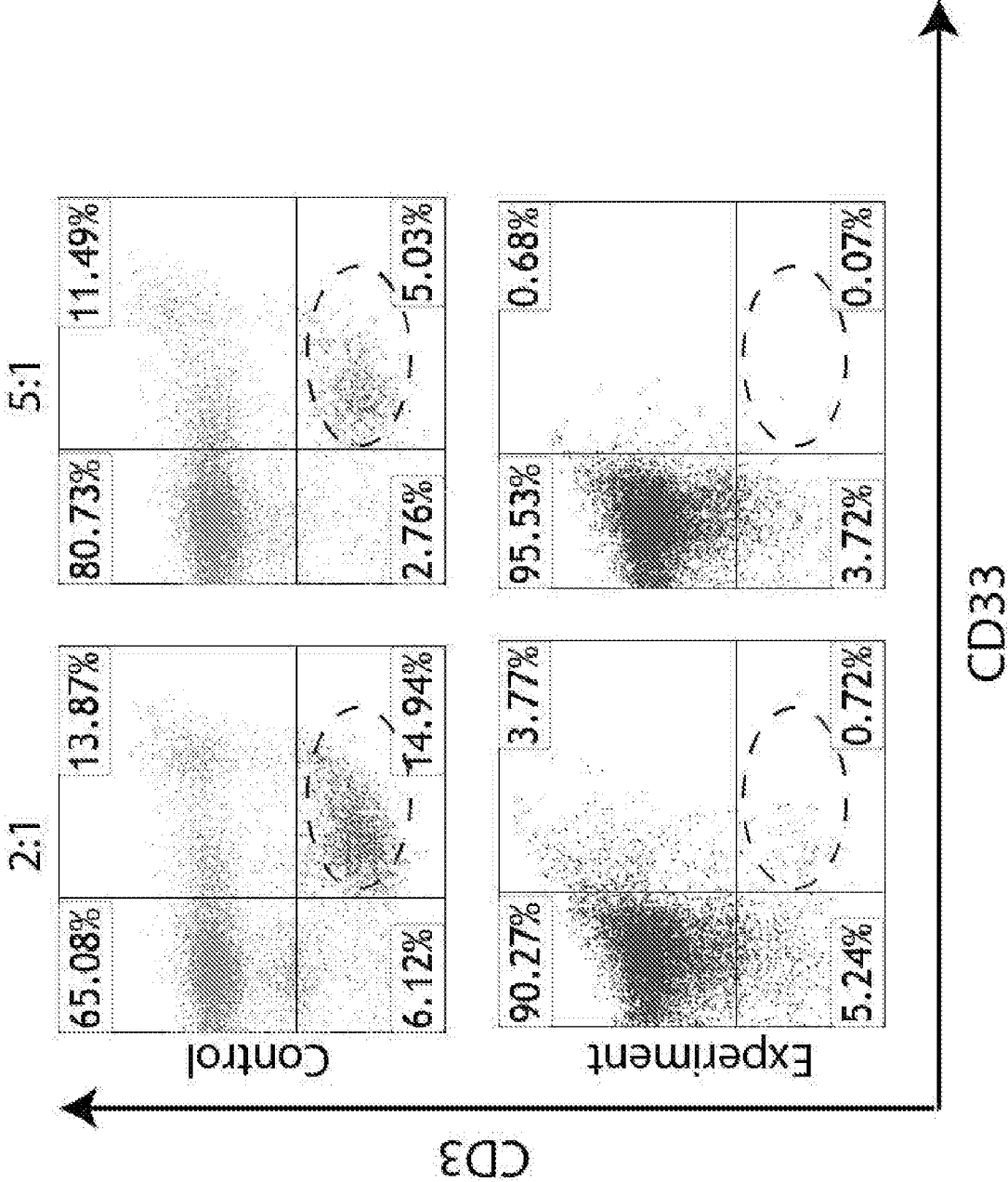


Figure 15A

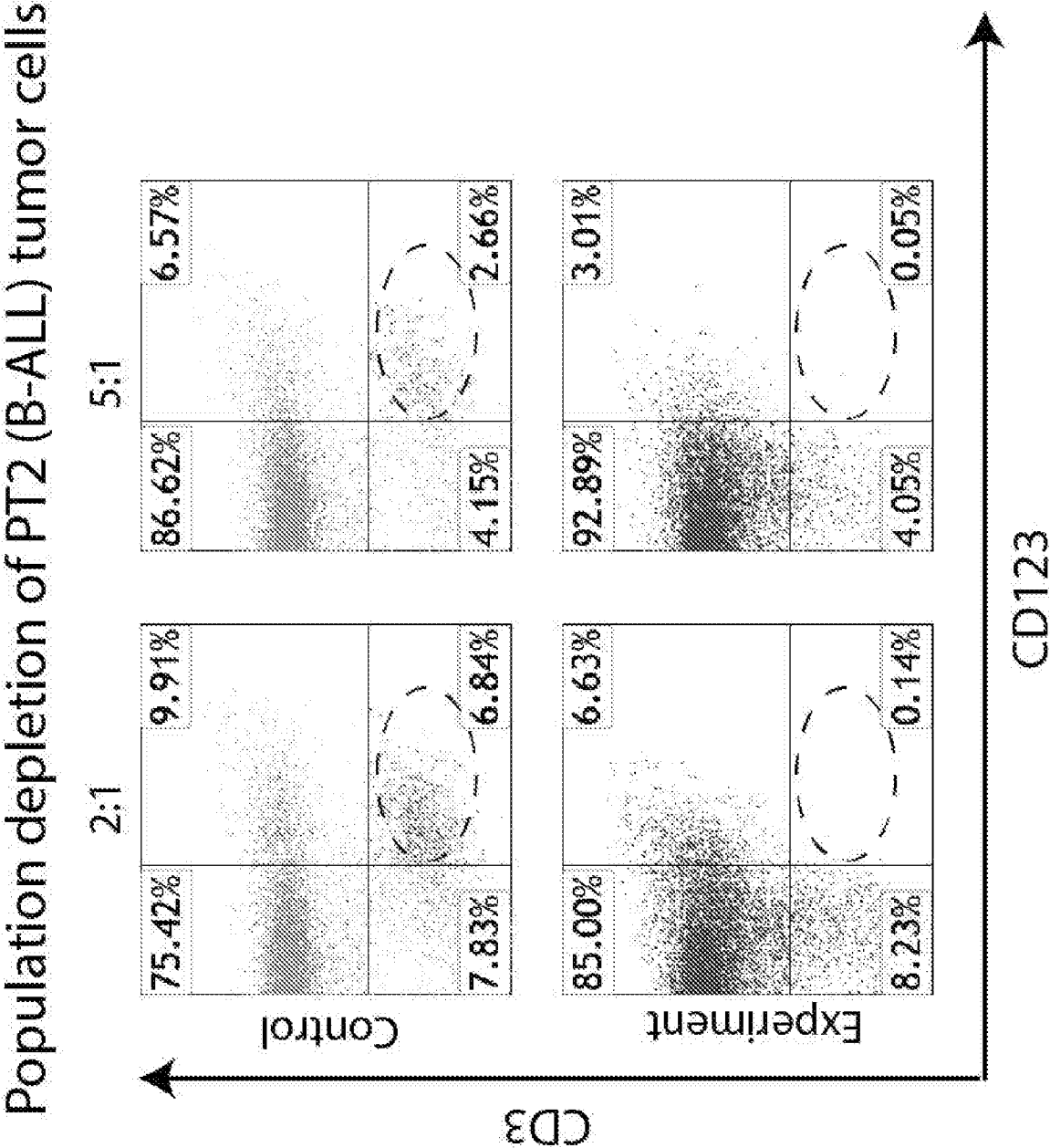


Figure 15B

C. Population depletion of PT3 leukemic stem cells

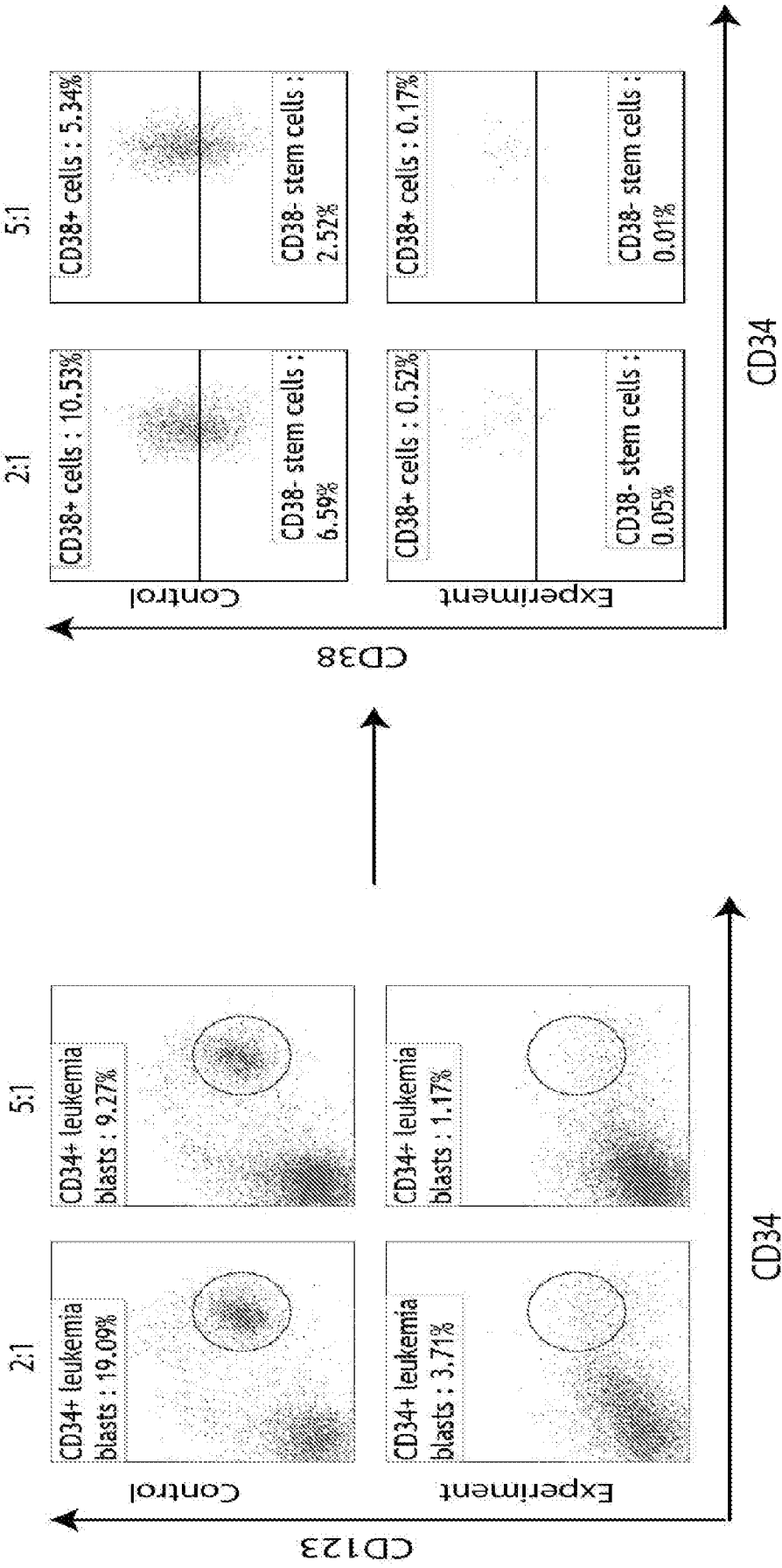


Figure 15C

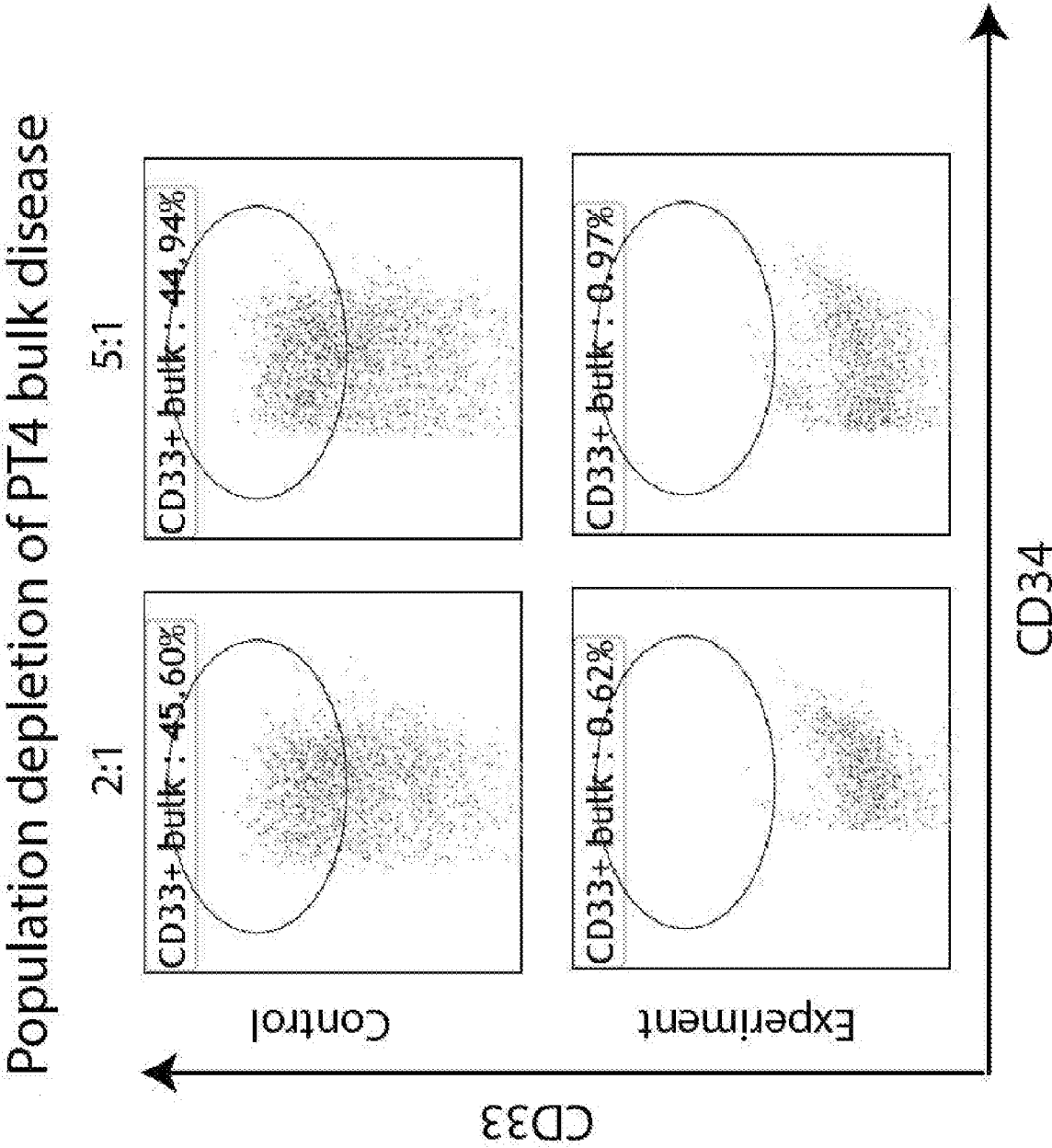


Figure 15D

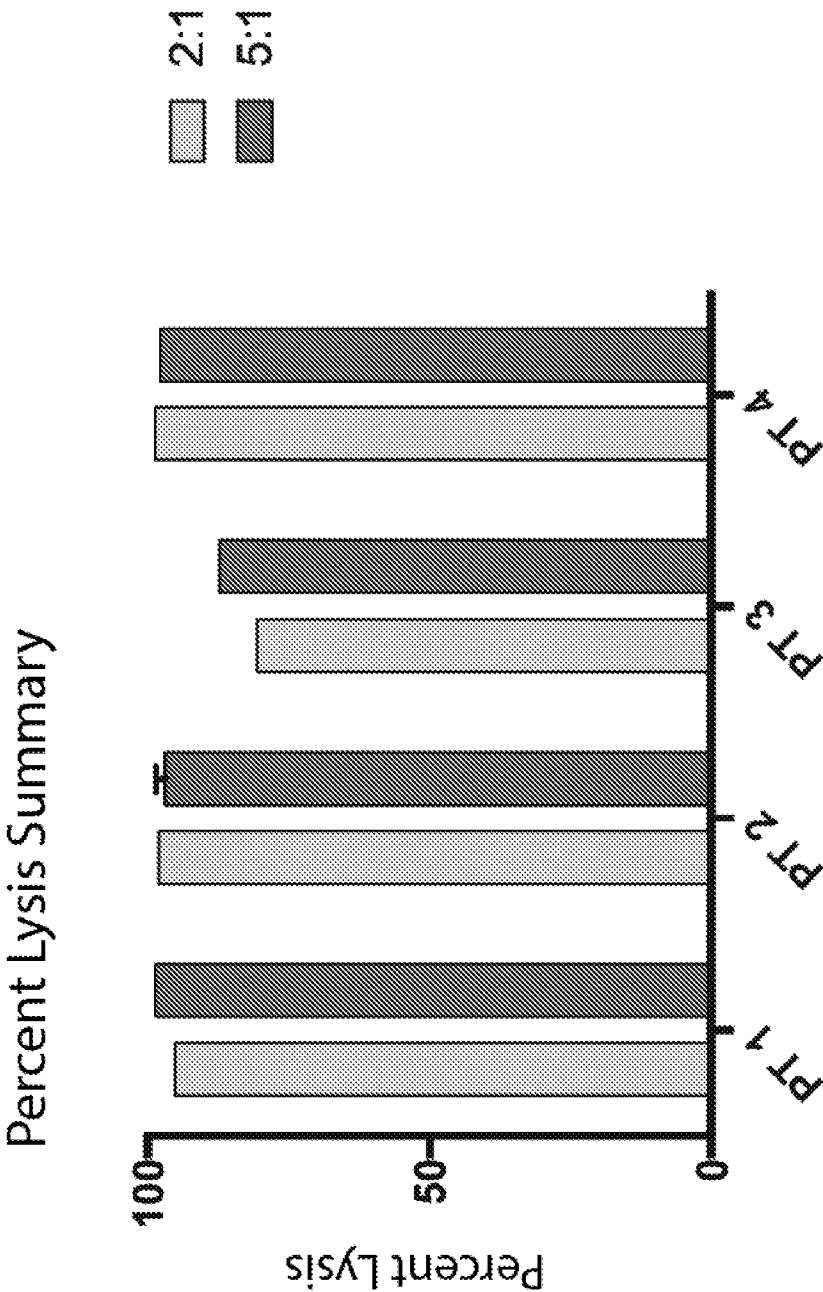


Figure 15E

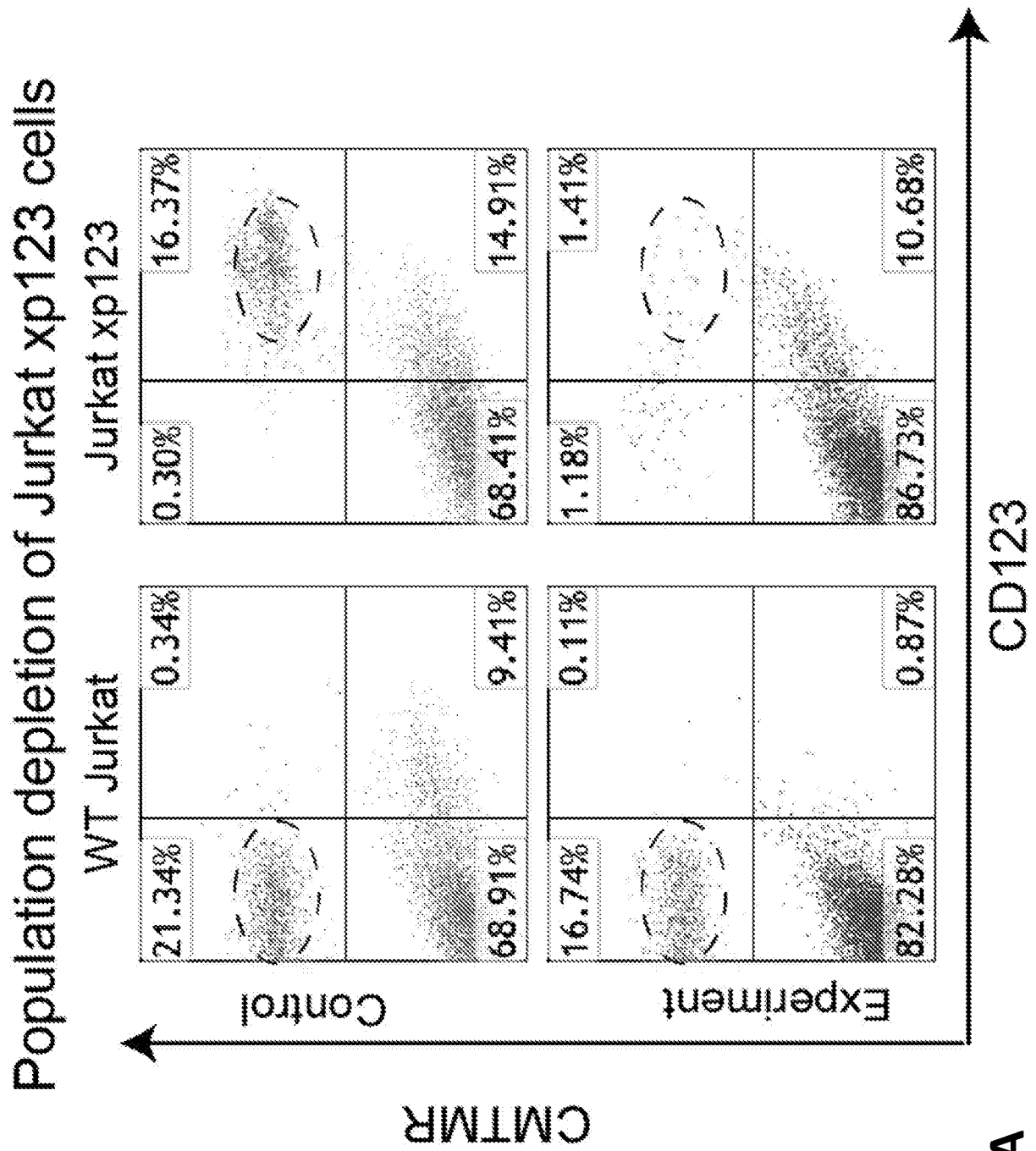


Figure 16A

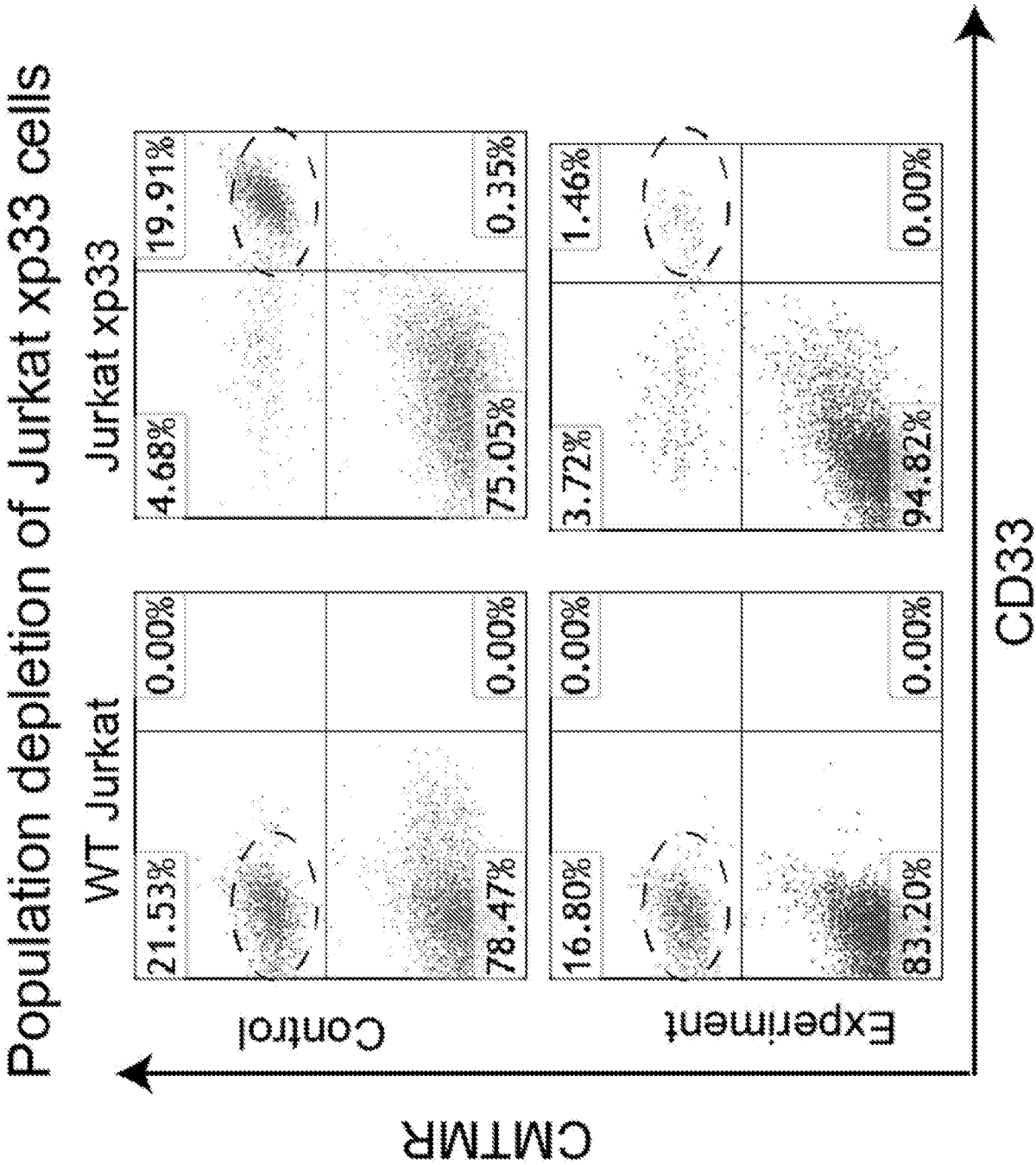


Figure 16B

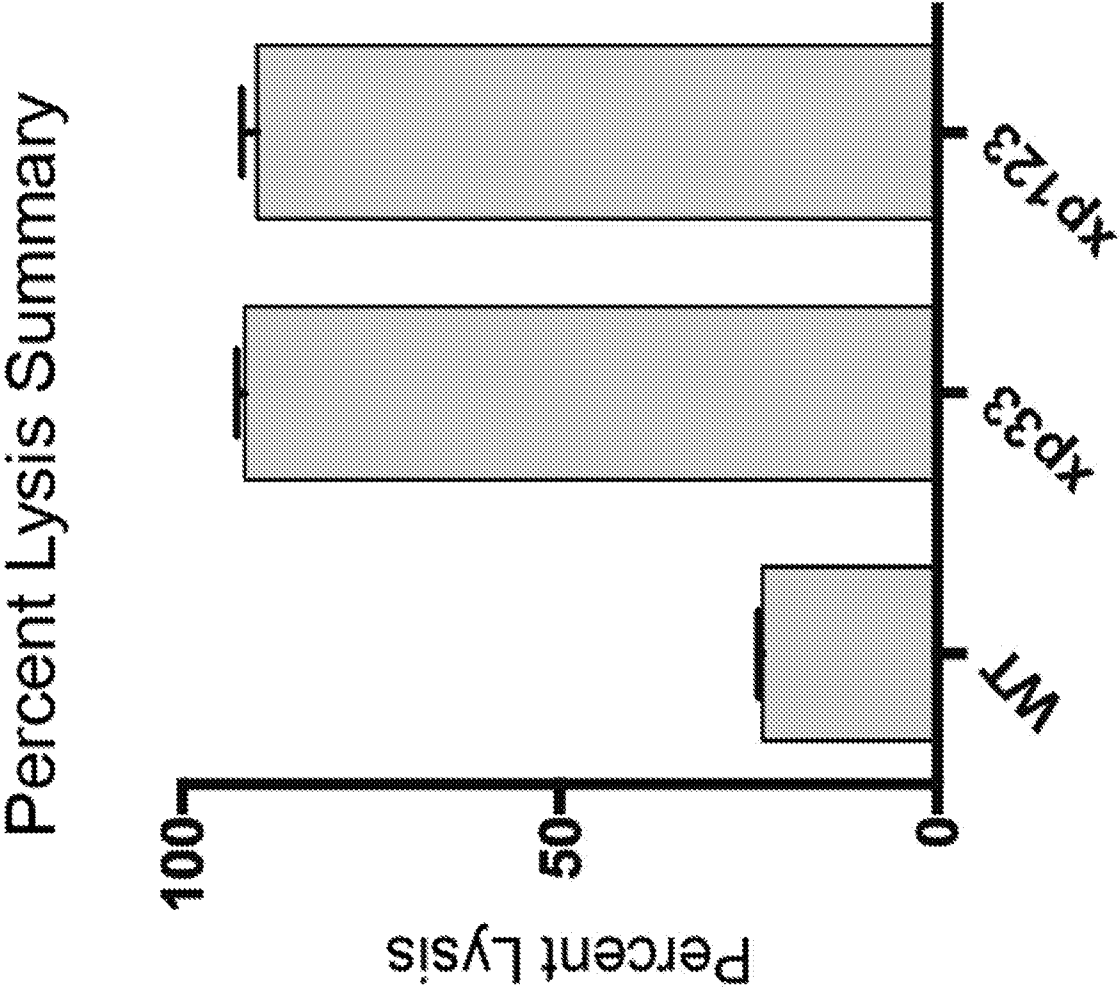


Figure 16C

CD123b-CD33b cCAR T-cells suppress MOLM tumor growth in vivo

IVIS imaging of MOLM13-Luc injected murine model

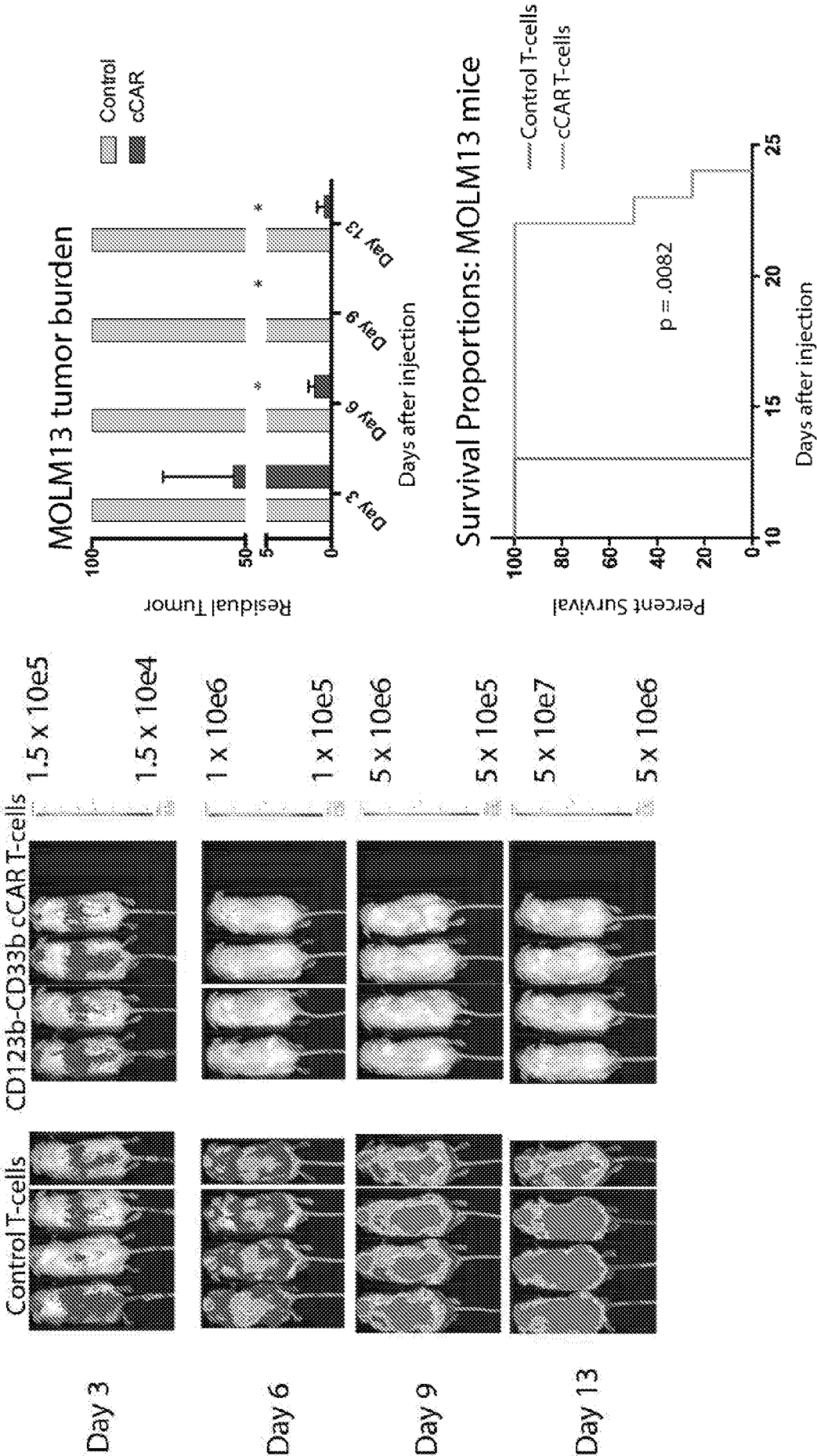


Figure 17A

CD123b-CD33b cCAR T-cells suppress U937 tumor growth in vivo

IVIS imaging of U937-Luc injected murine model

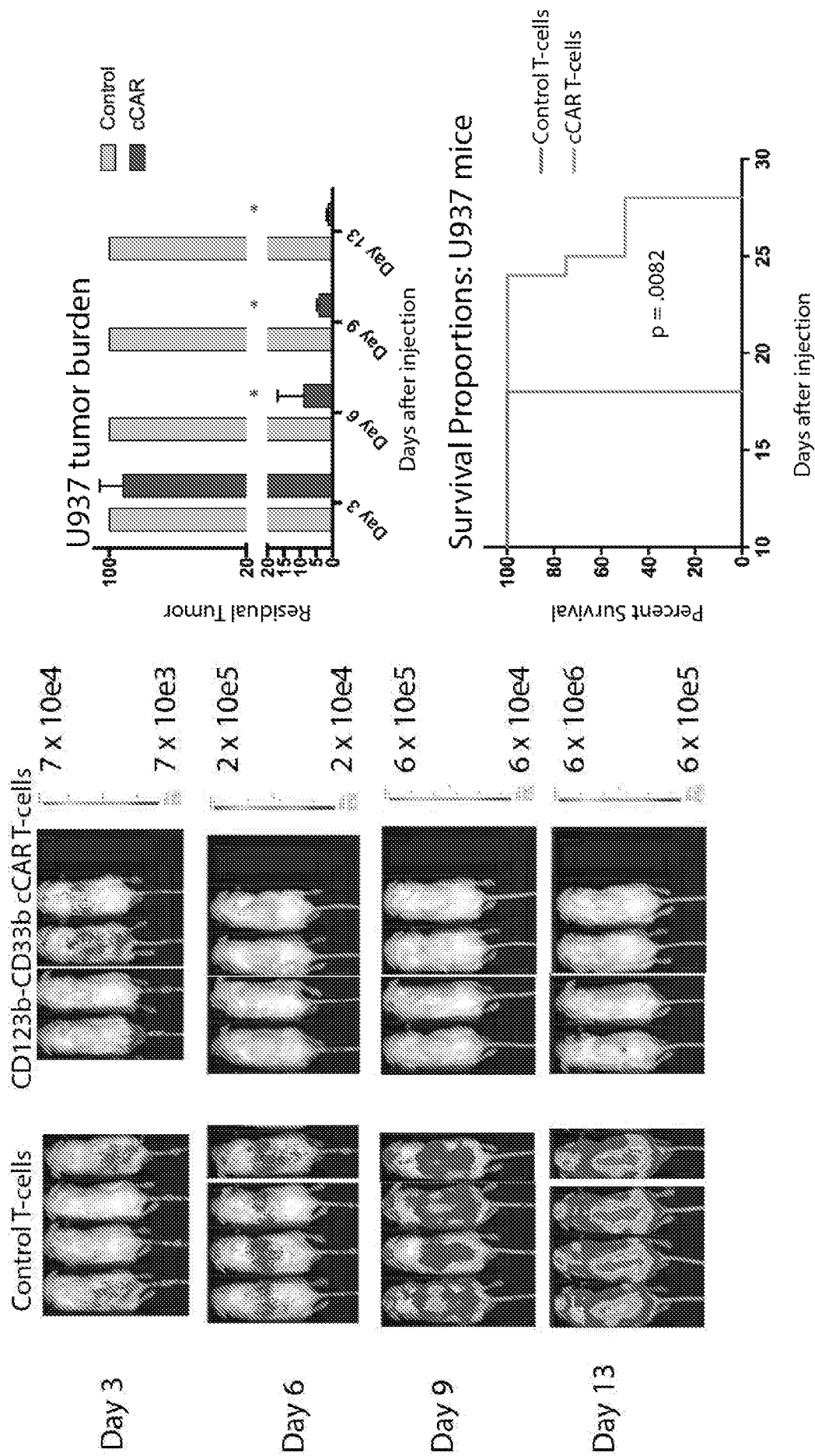


Figure 17B

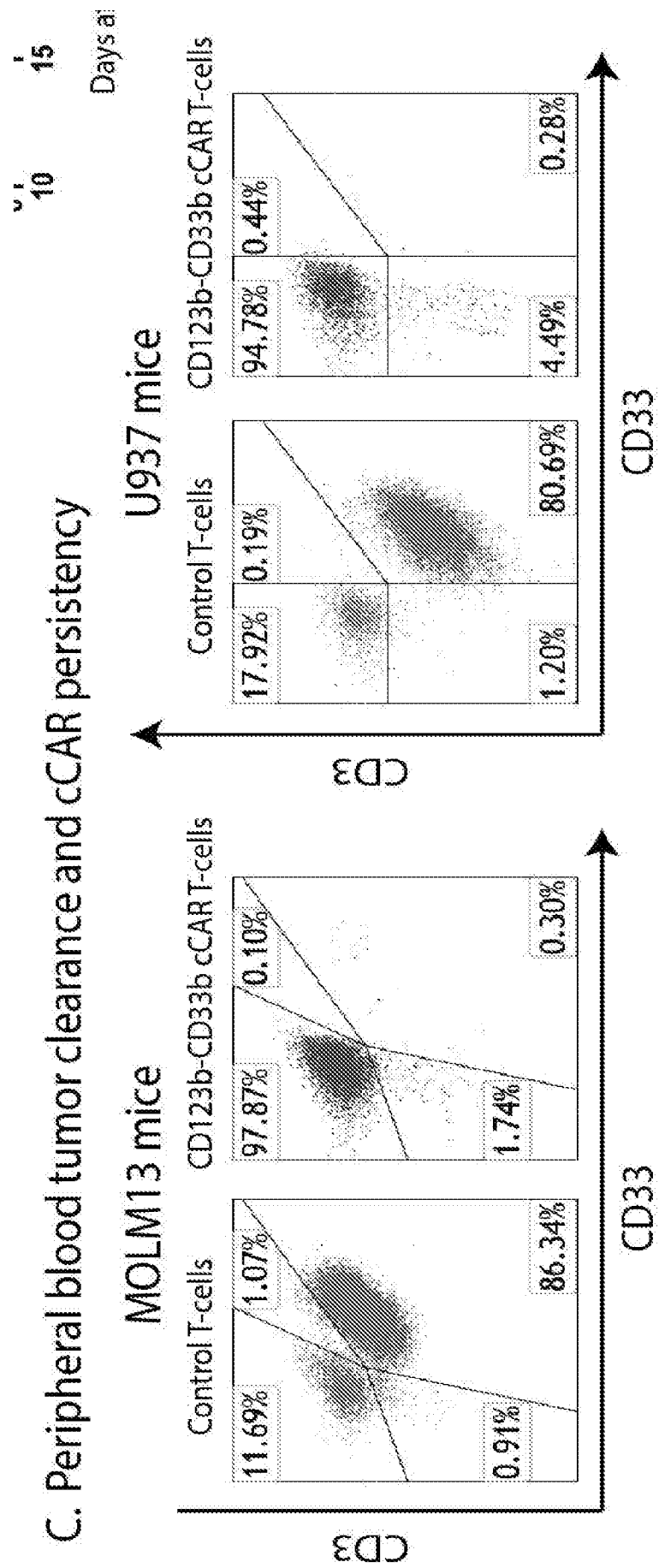


Figure 17C

CAMPATH protocol

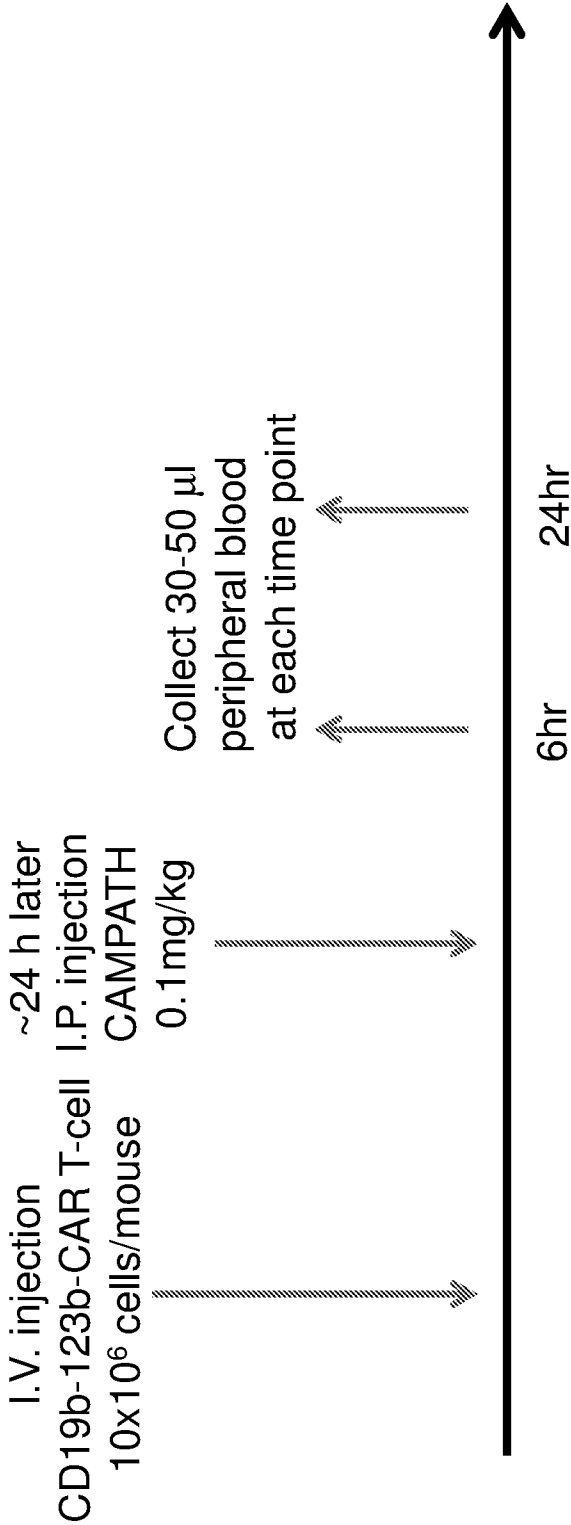


Figure 18A

Depletion of CAR T-cells in peripheral blood after 6 h

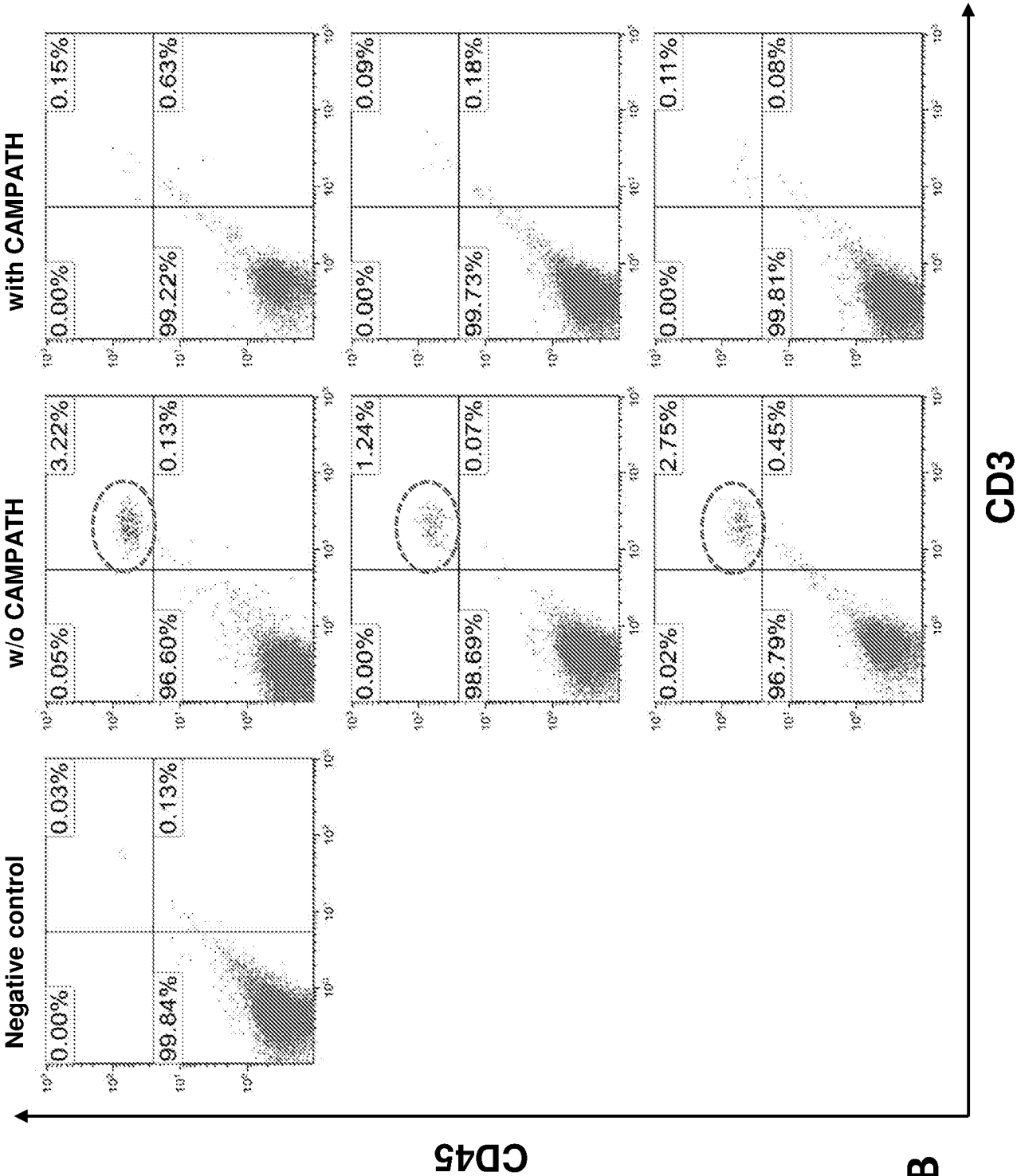


Figure 18B

Depletion of CAR T-cells in peripheral blood after 24

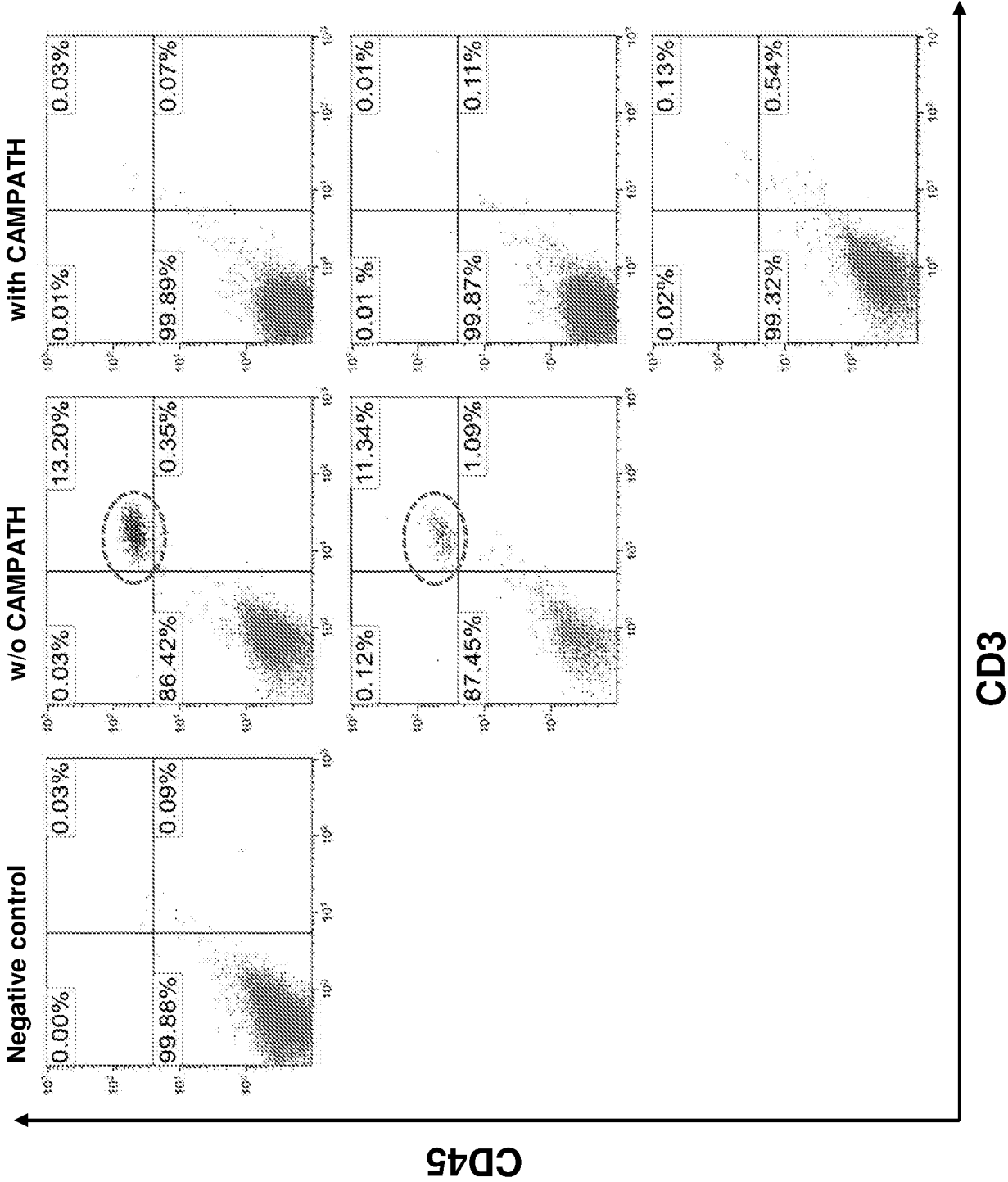


Figure 18C

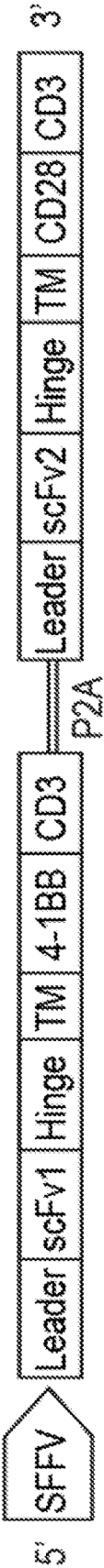


Figure 19

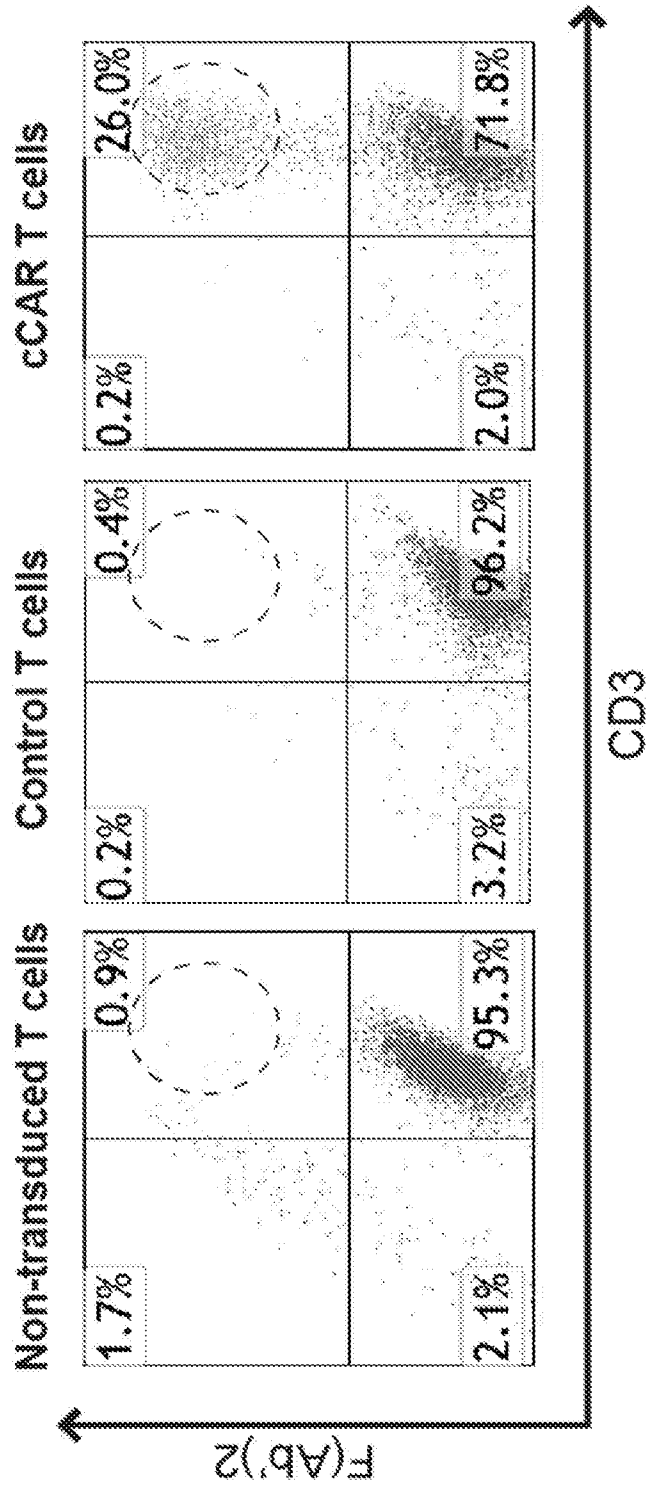


Figure 20

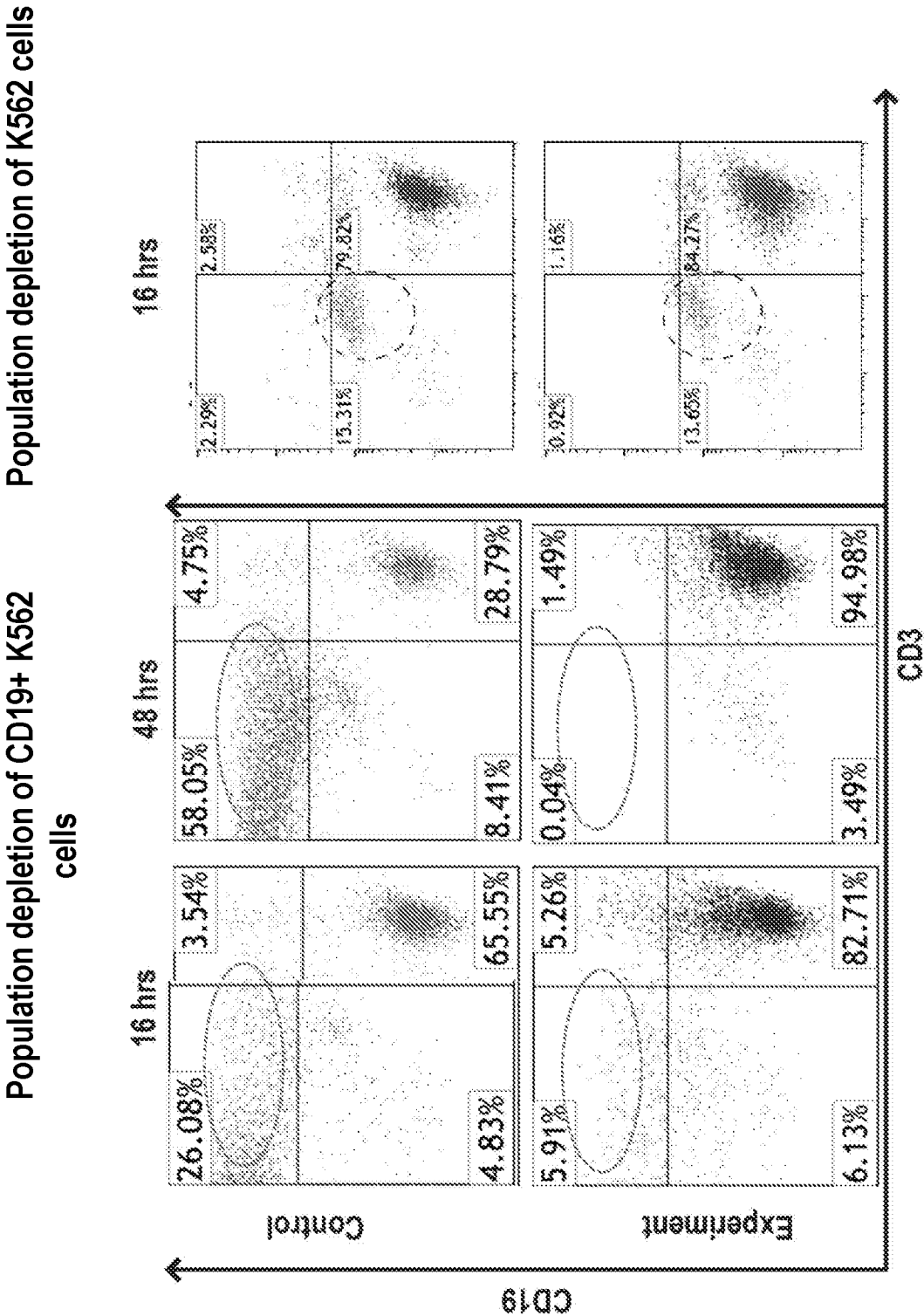


Figure 21A

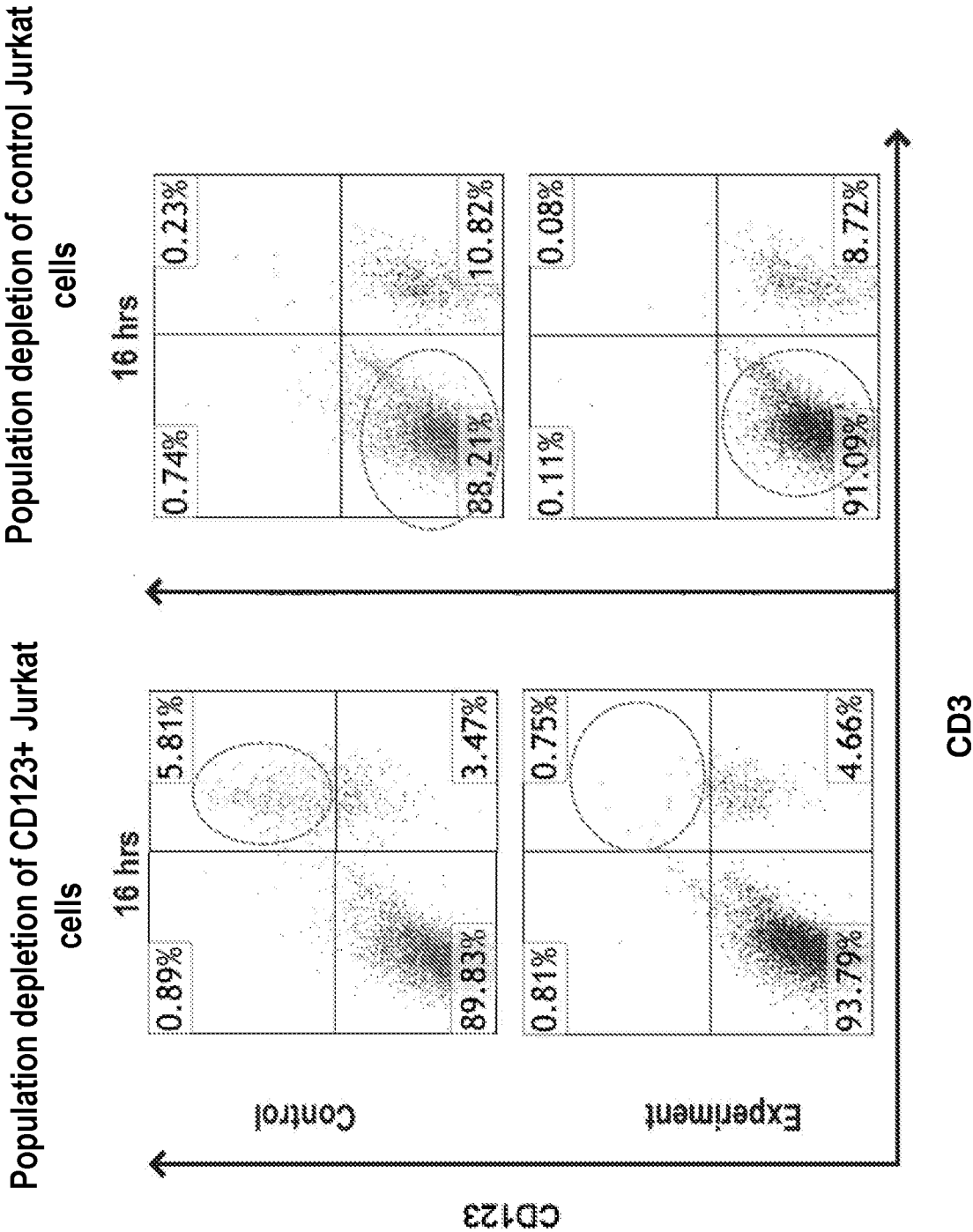


Figure 21B

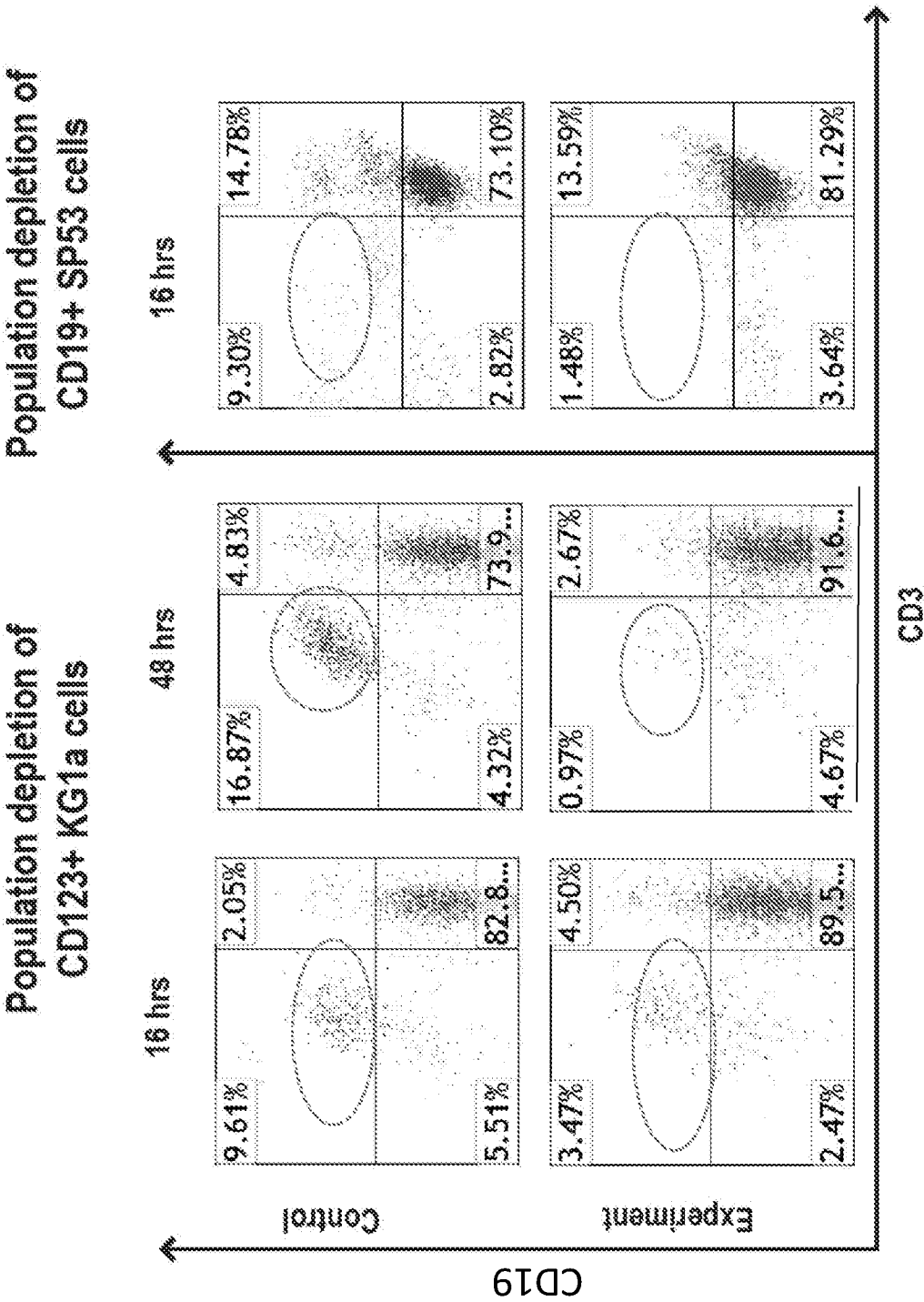


Figure 21C

In vitro summary of CAR T activity

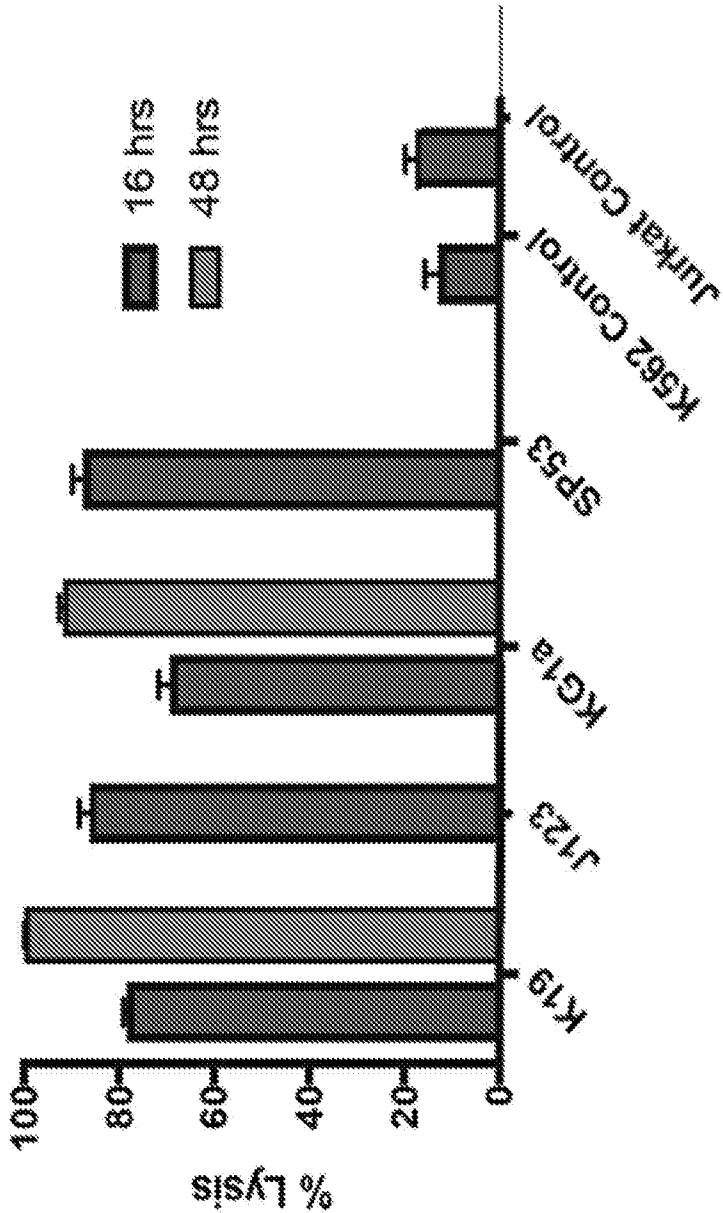


Figure 21D

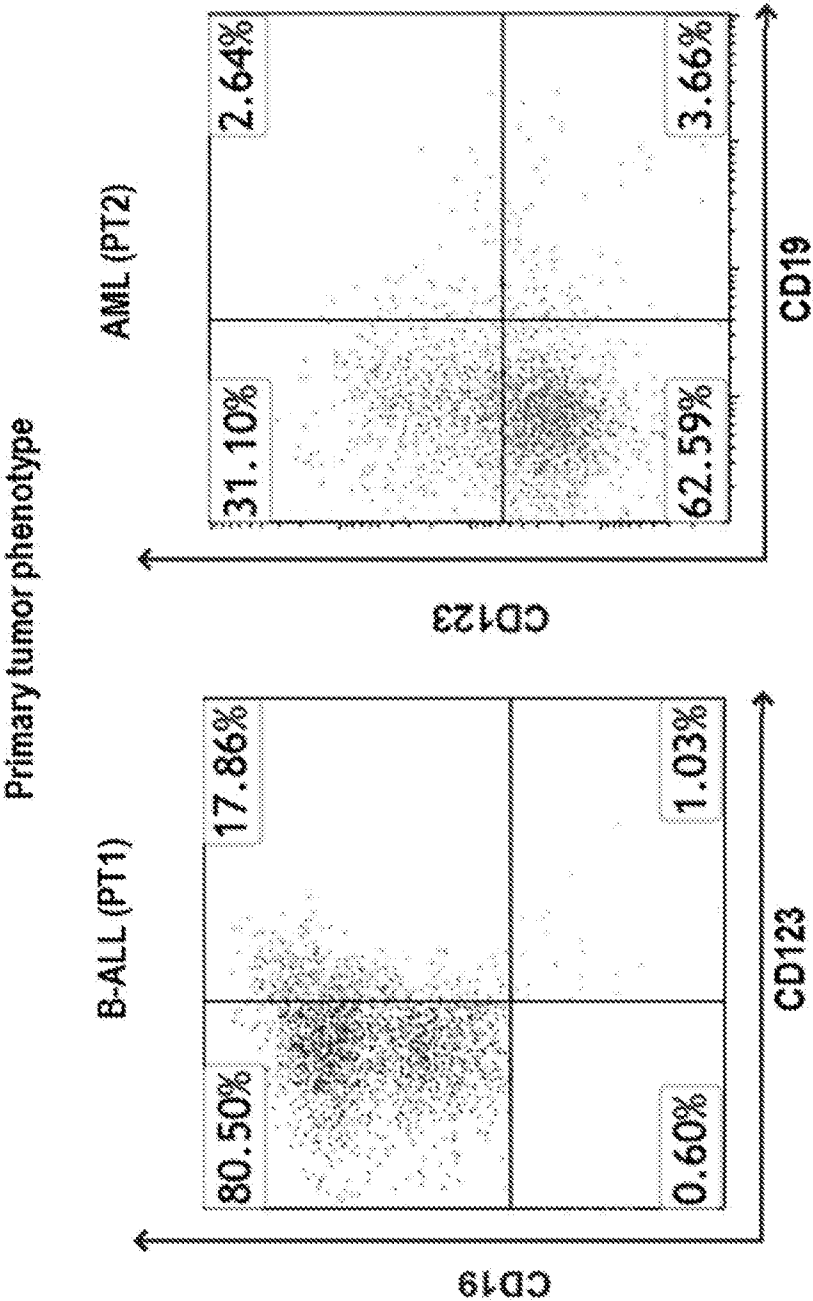


Figure 22A

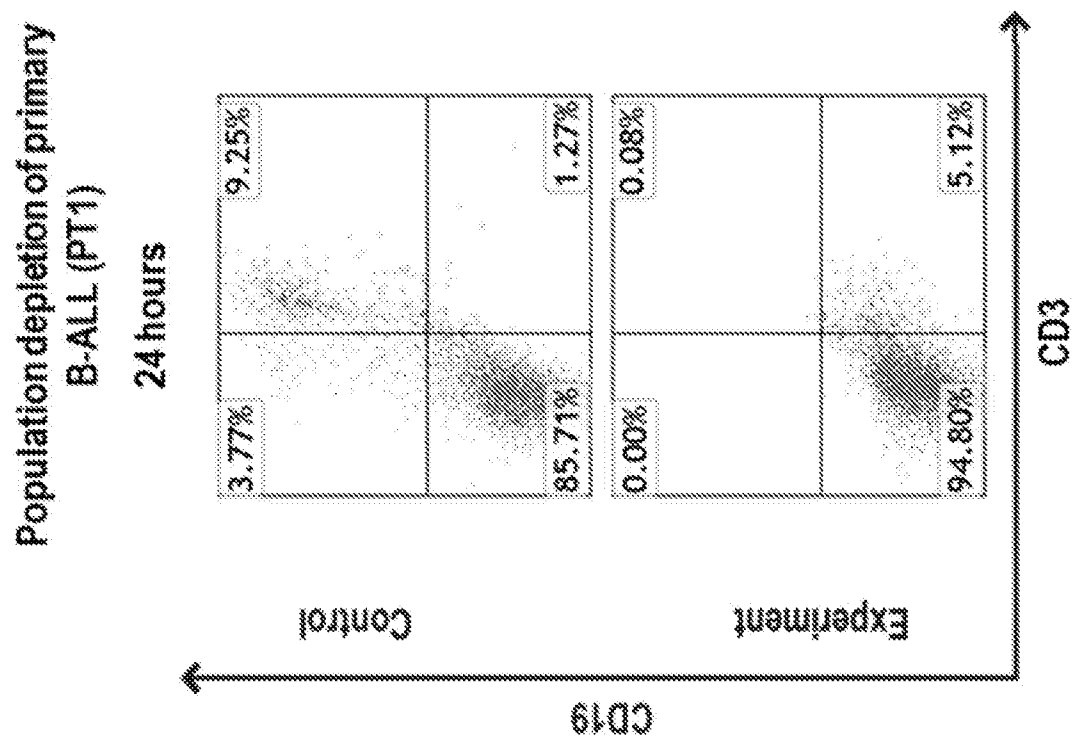


Figure 22B

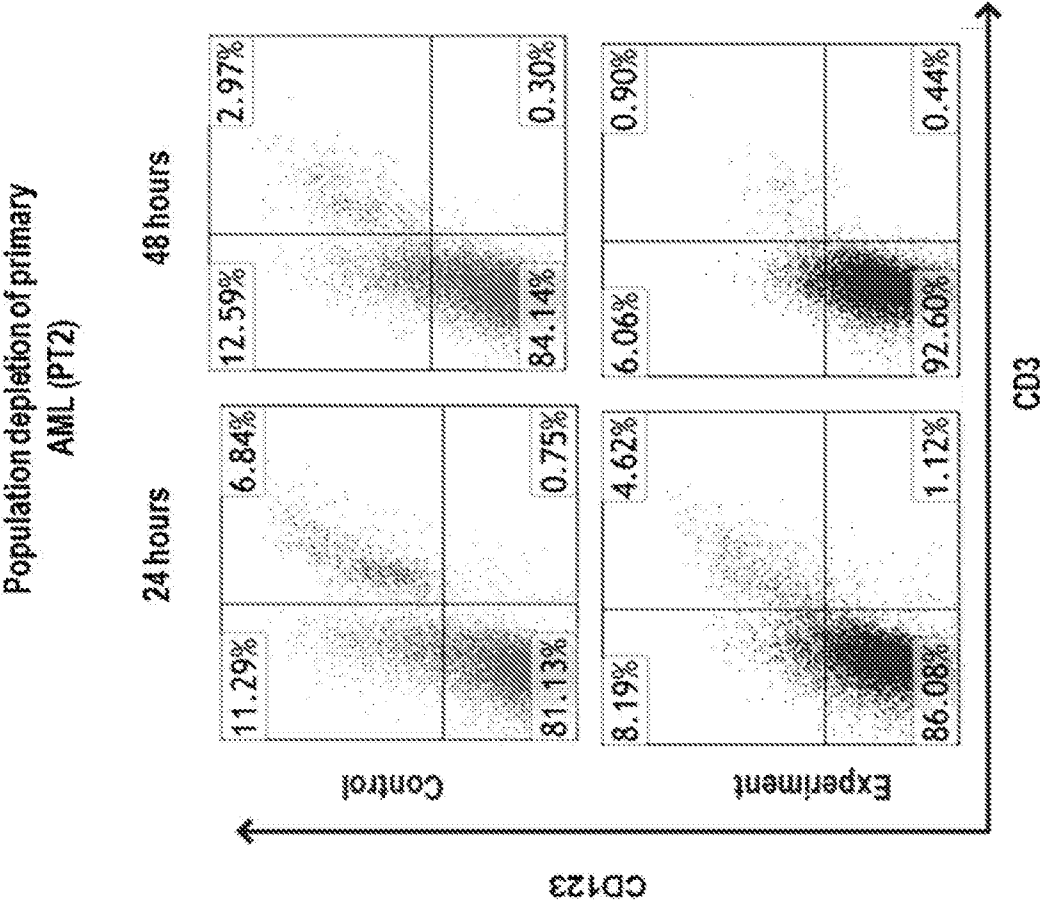


Figure 22C

In vitro summary of primary leukemic cell depletion

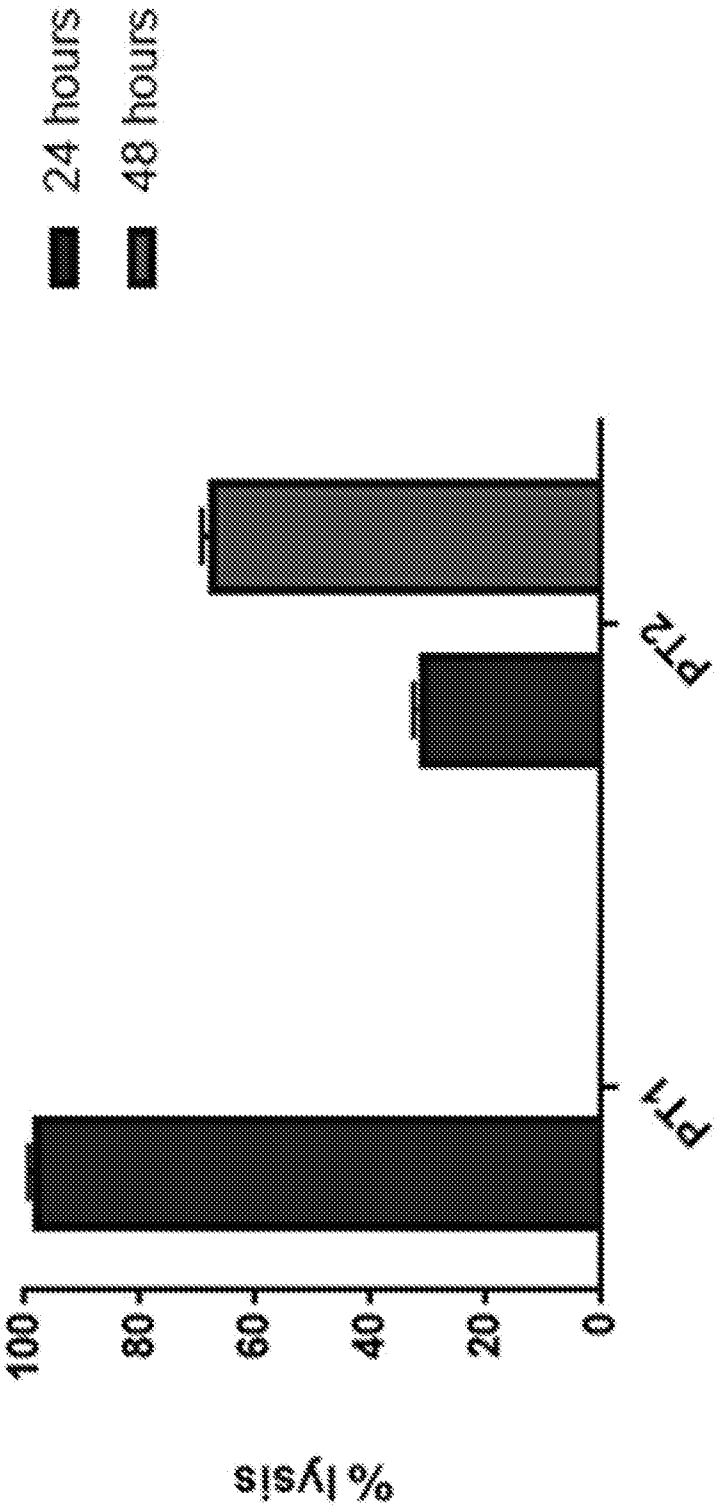


Figure 22D

IVIS imaging of MOLM13-Luc injected murine model

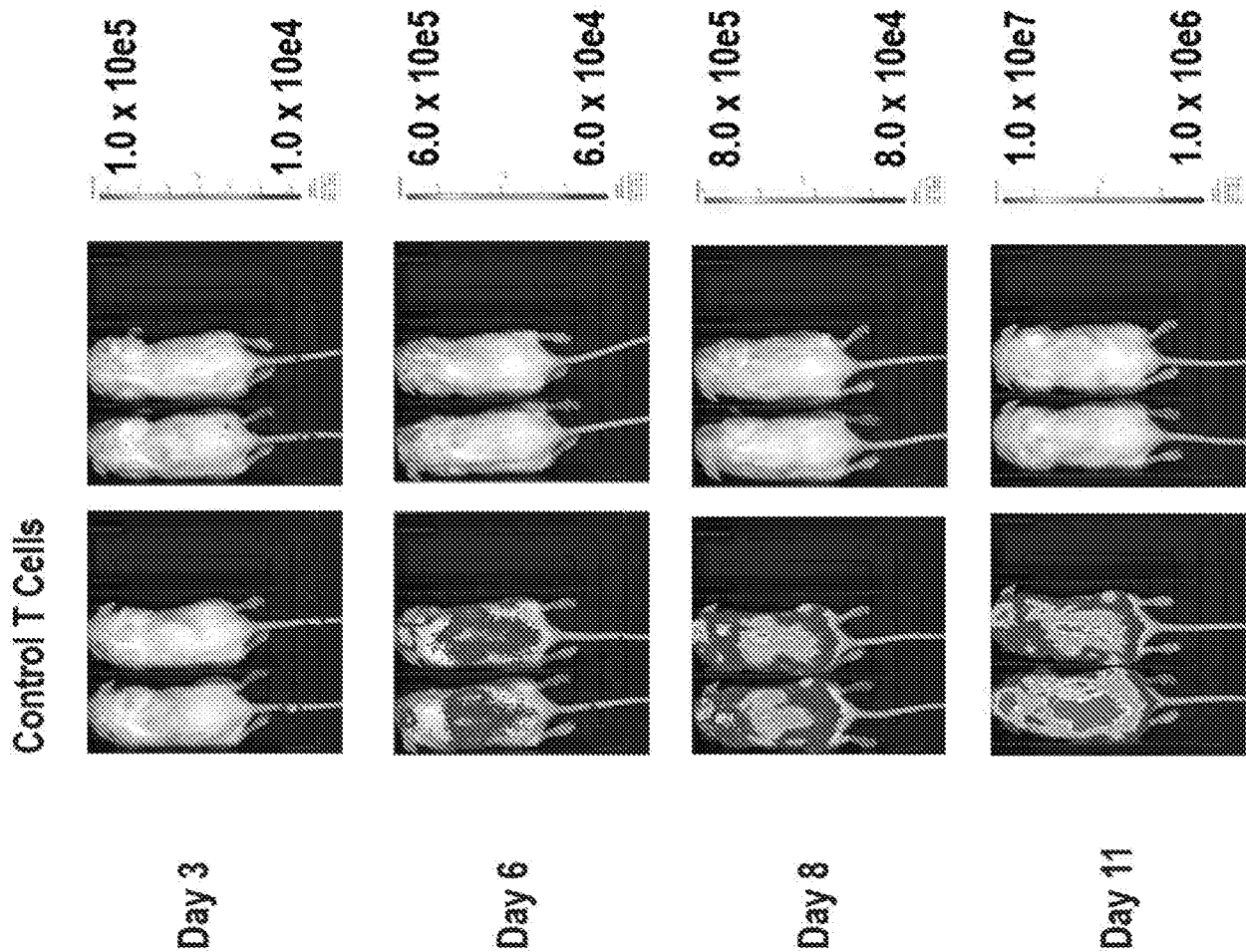


Figure 23A

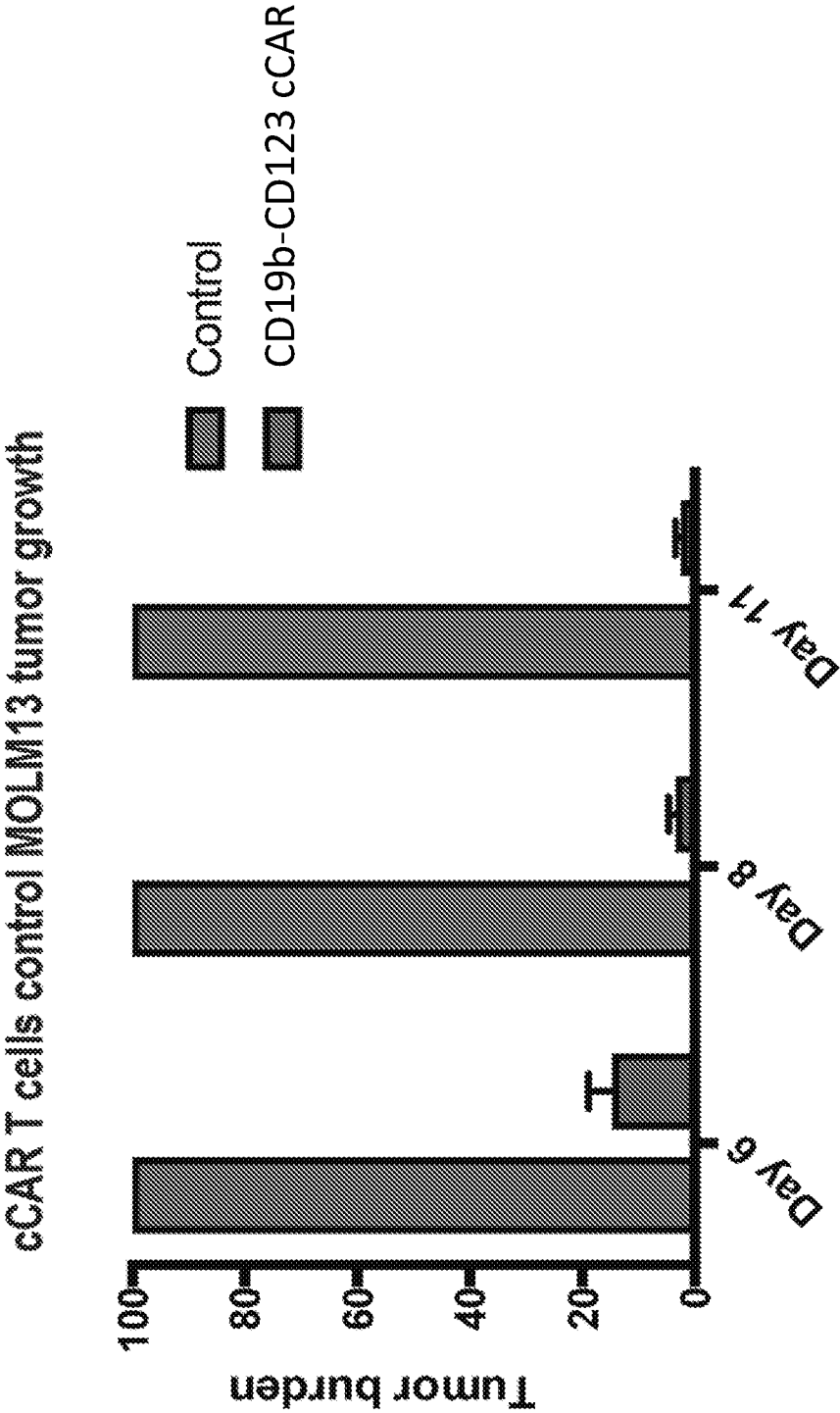


Figure 23B

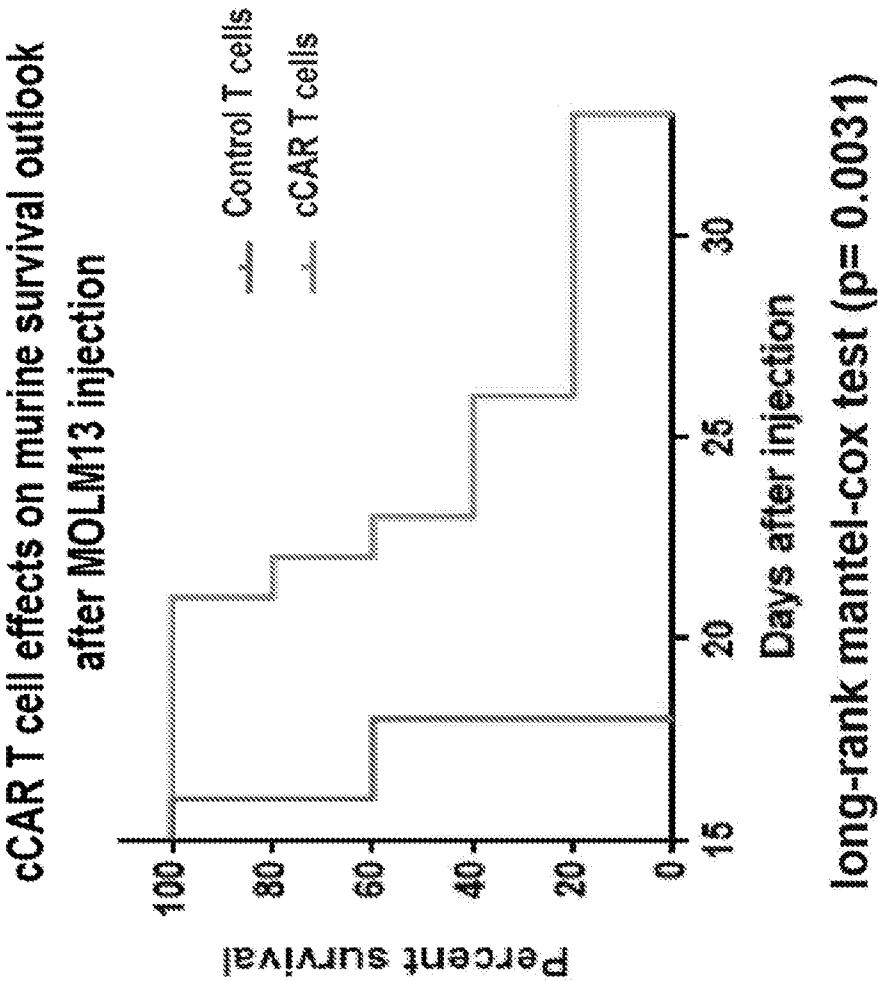


Figure 23C

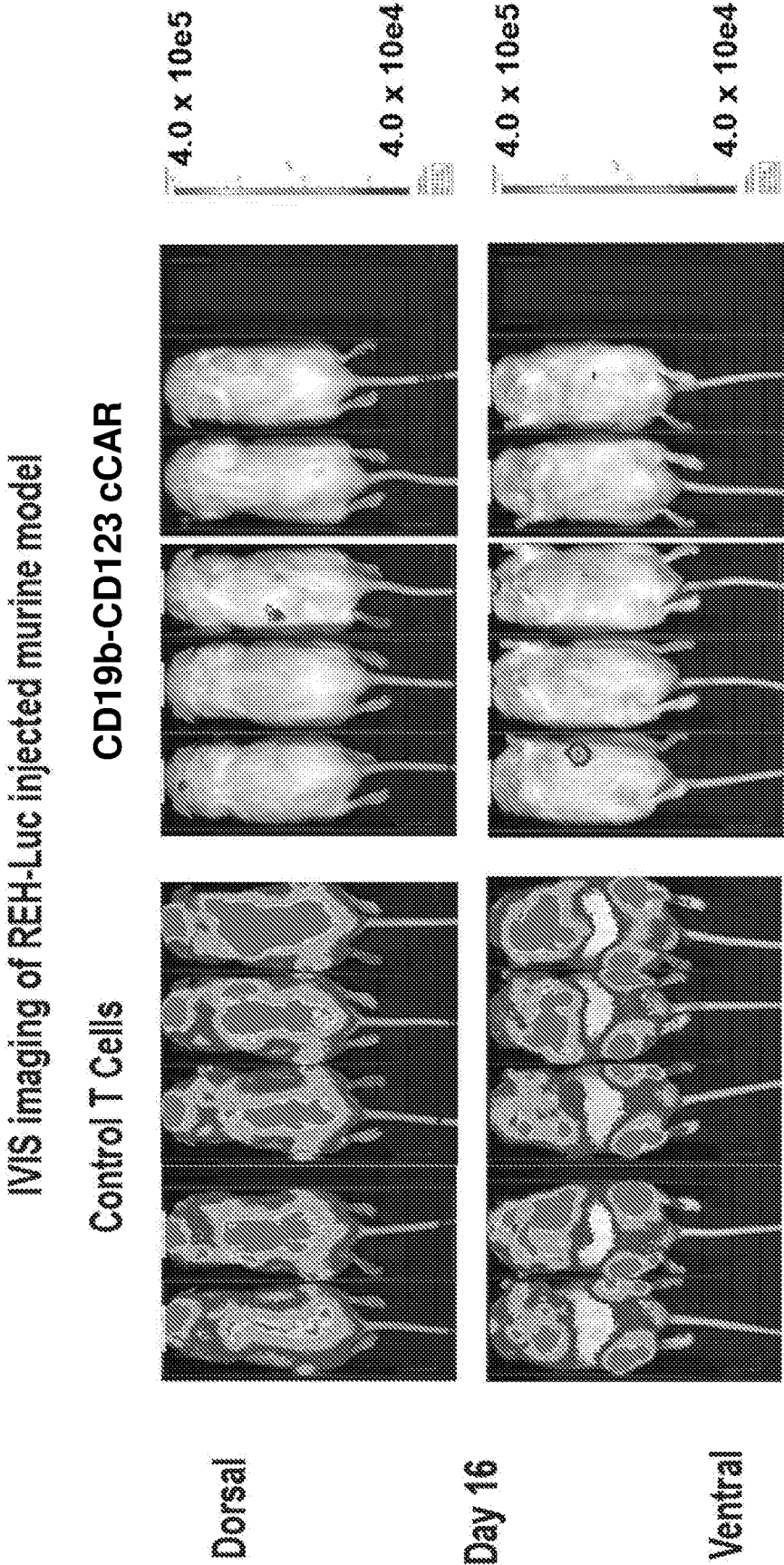


Figure 23D

cCAR T cells reduction of REH tumor at day 16

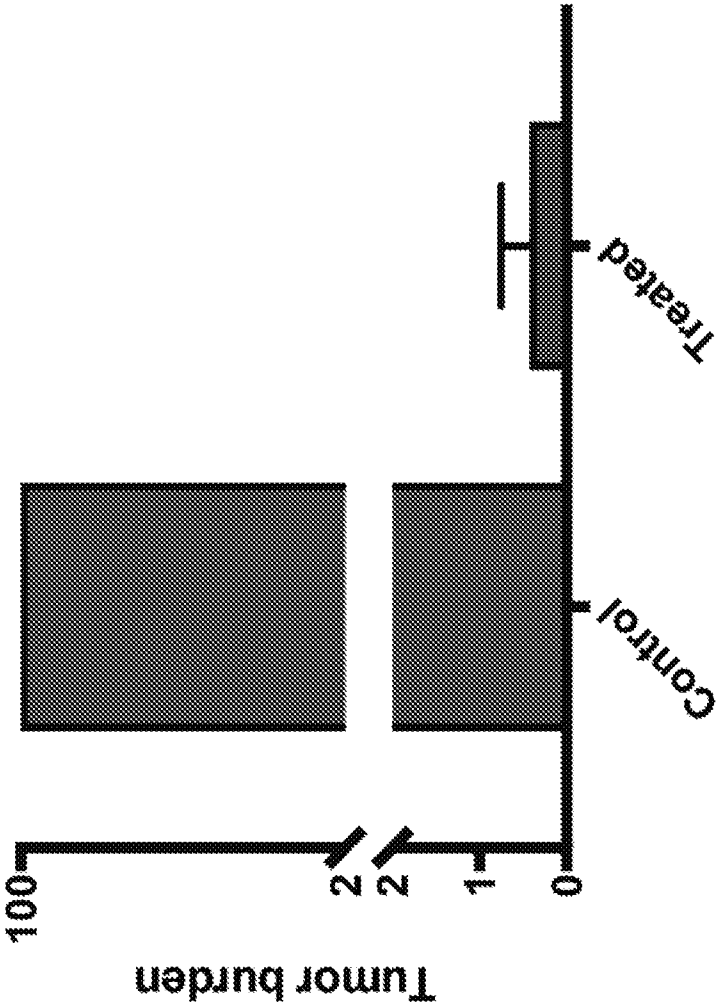


Figure 23E

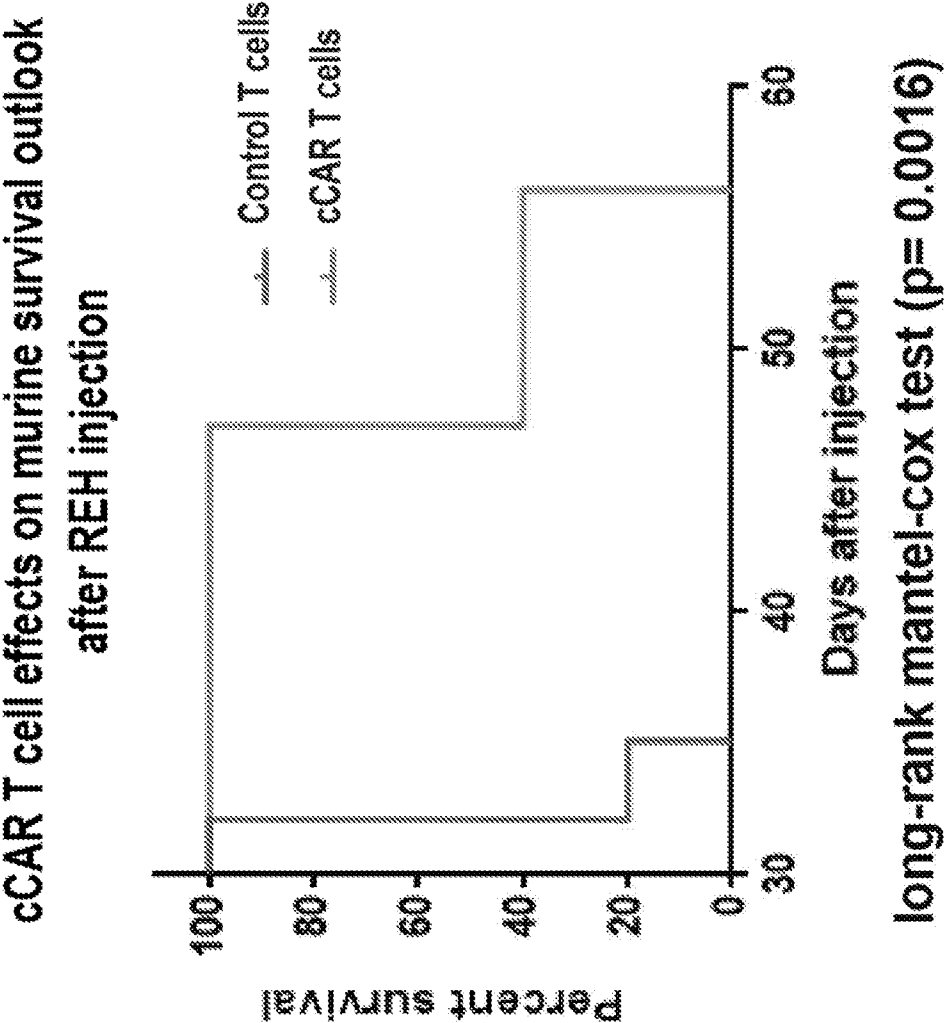


Figure 23F

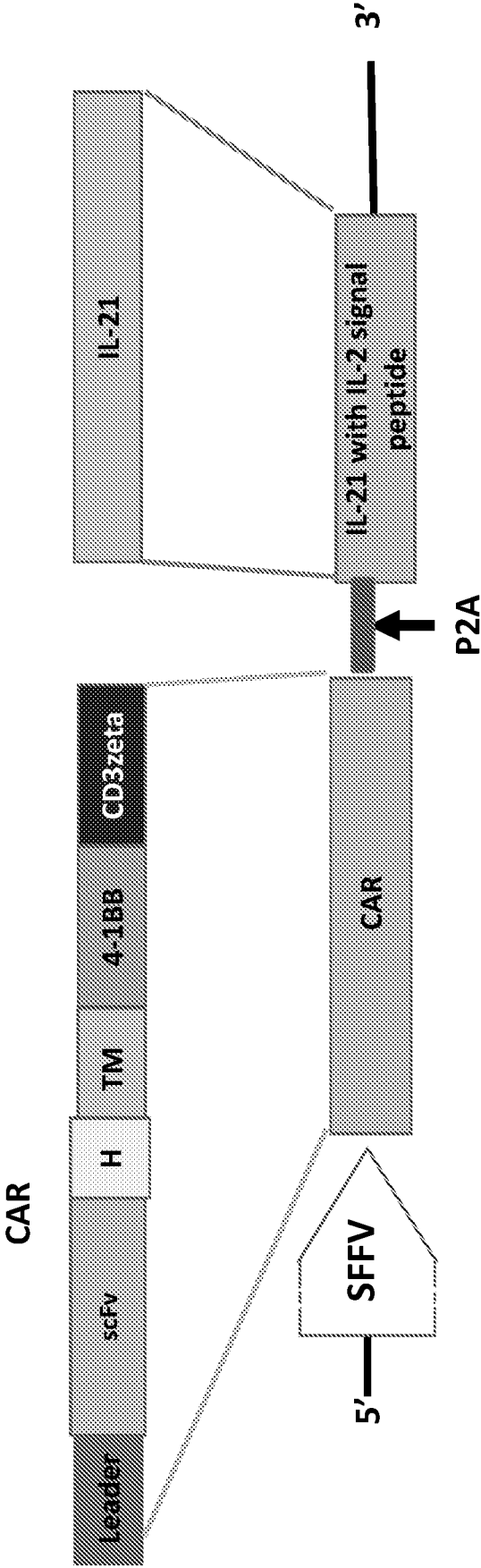


Figure 24

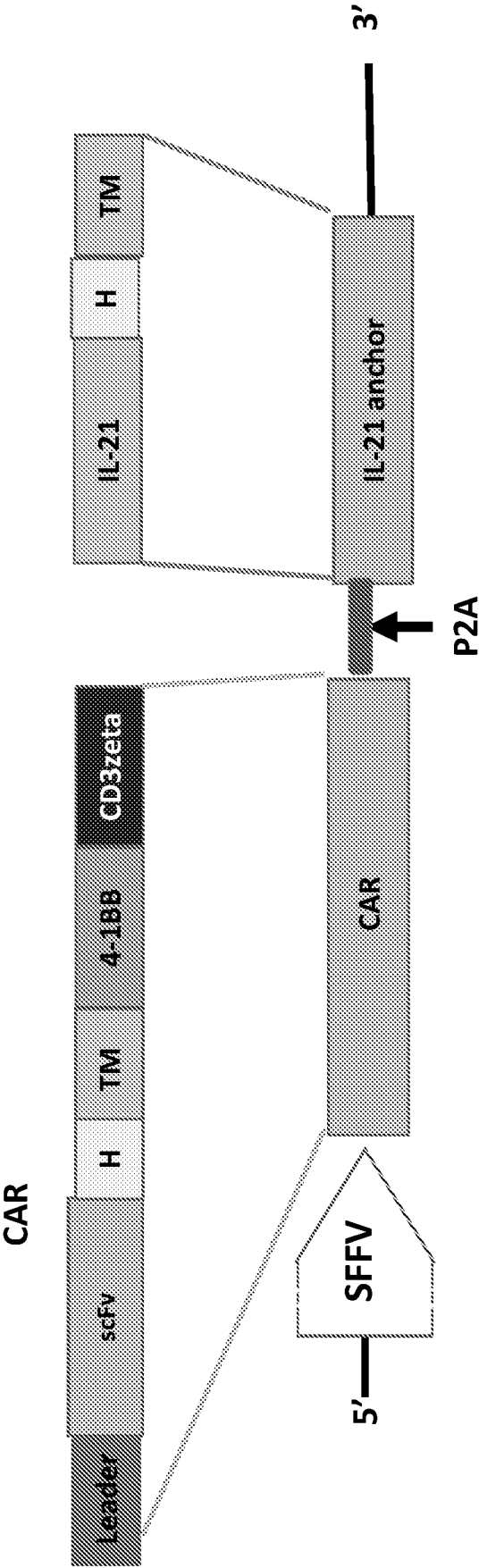


Figure 25

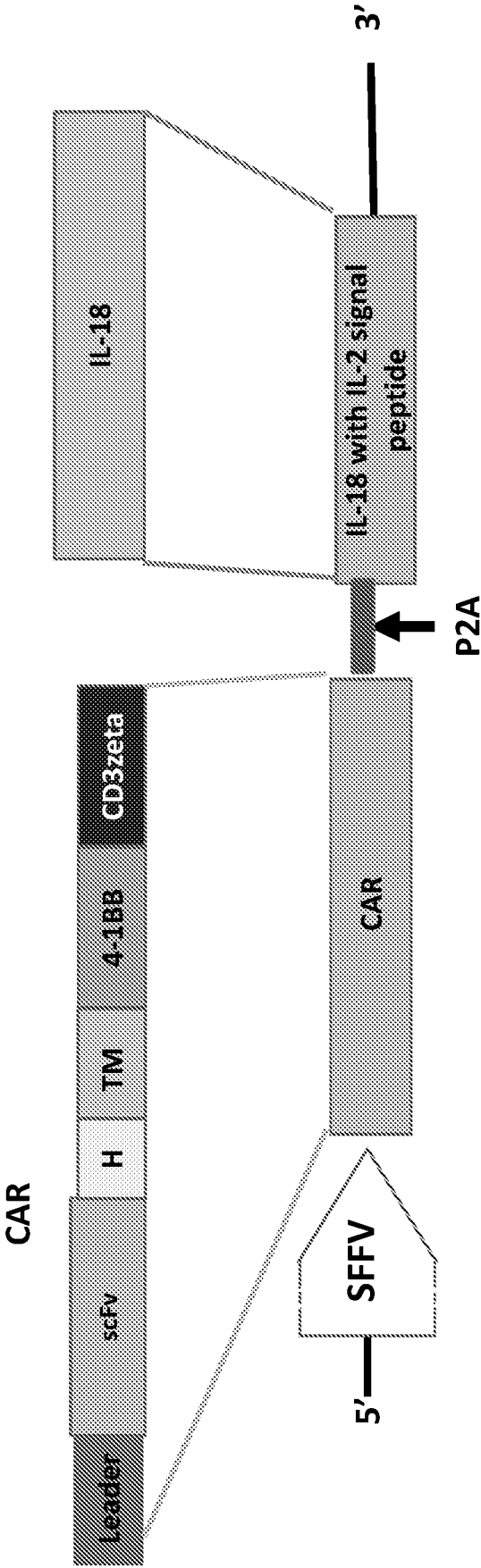


Figure 26

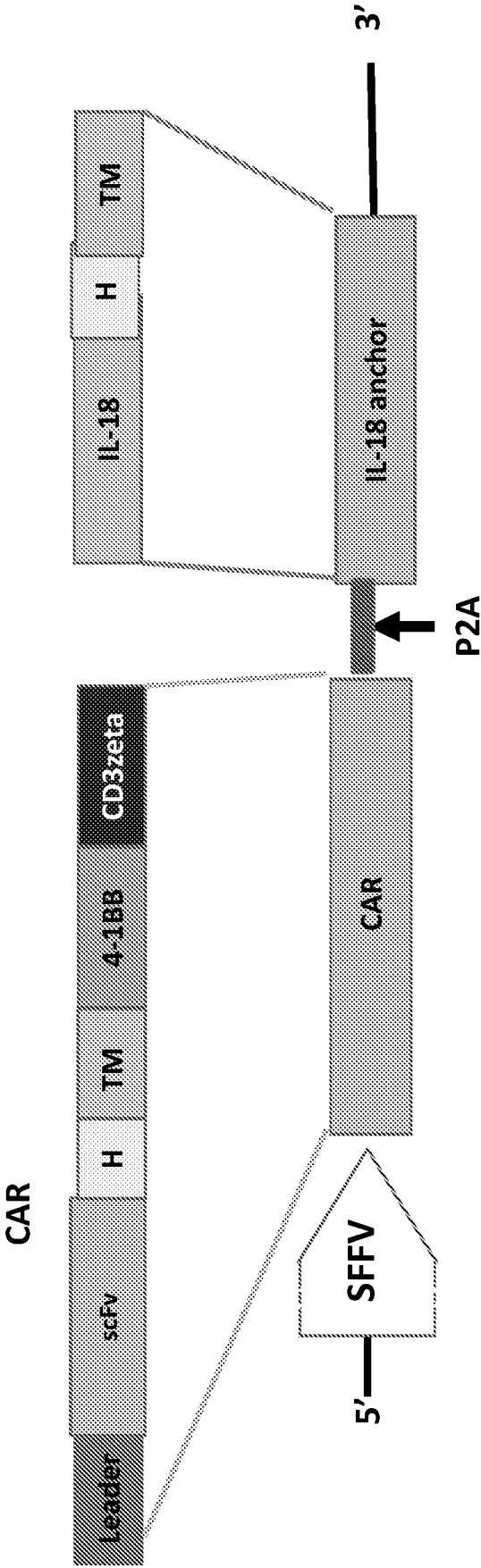


Figure 27

CAR expression in BCMA CARs

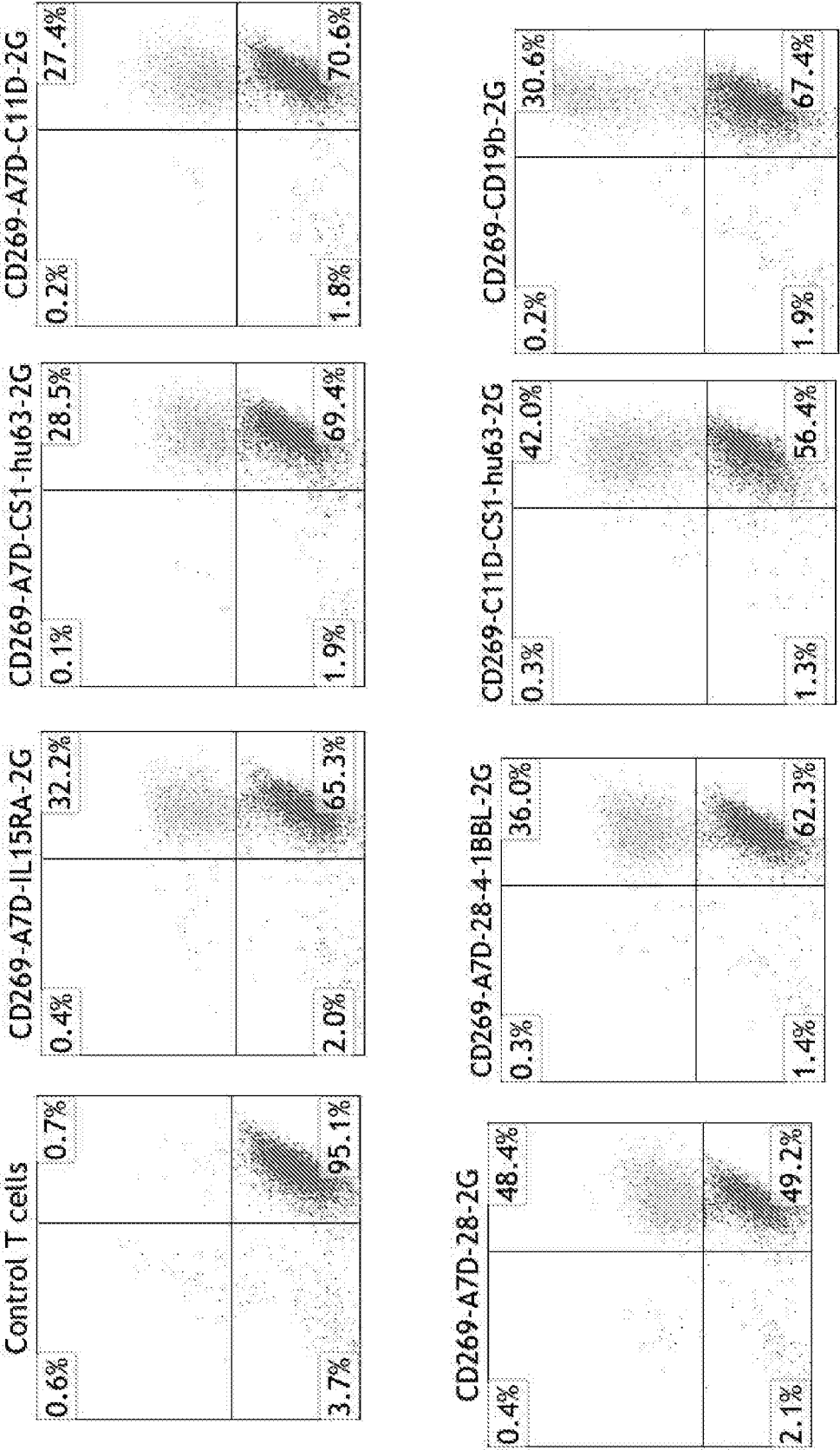


Figure 28A

CAR expression in compound CARs – BCMA-CS1

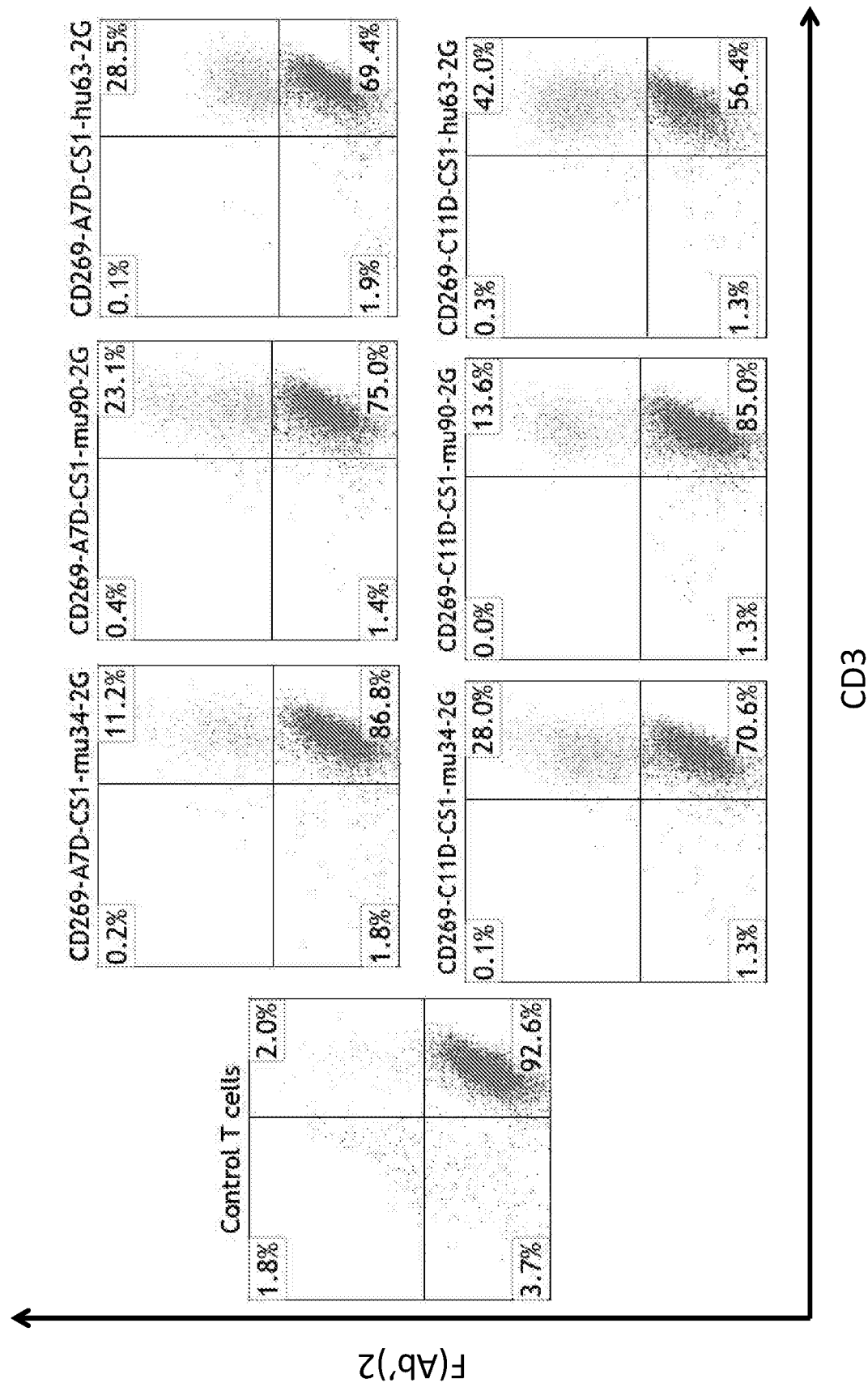


Figure 28B

CD269-A7D-CD19b-2G CAR T cells lyse CD19-expressing K562
tumor cells in overnight co-culture

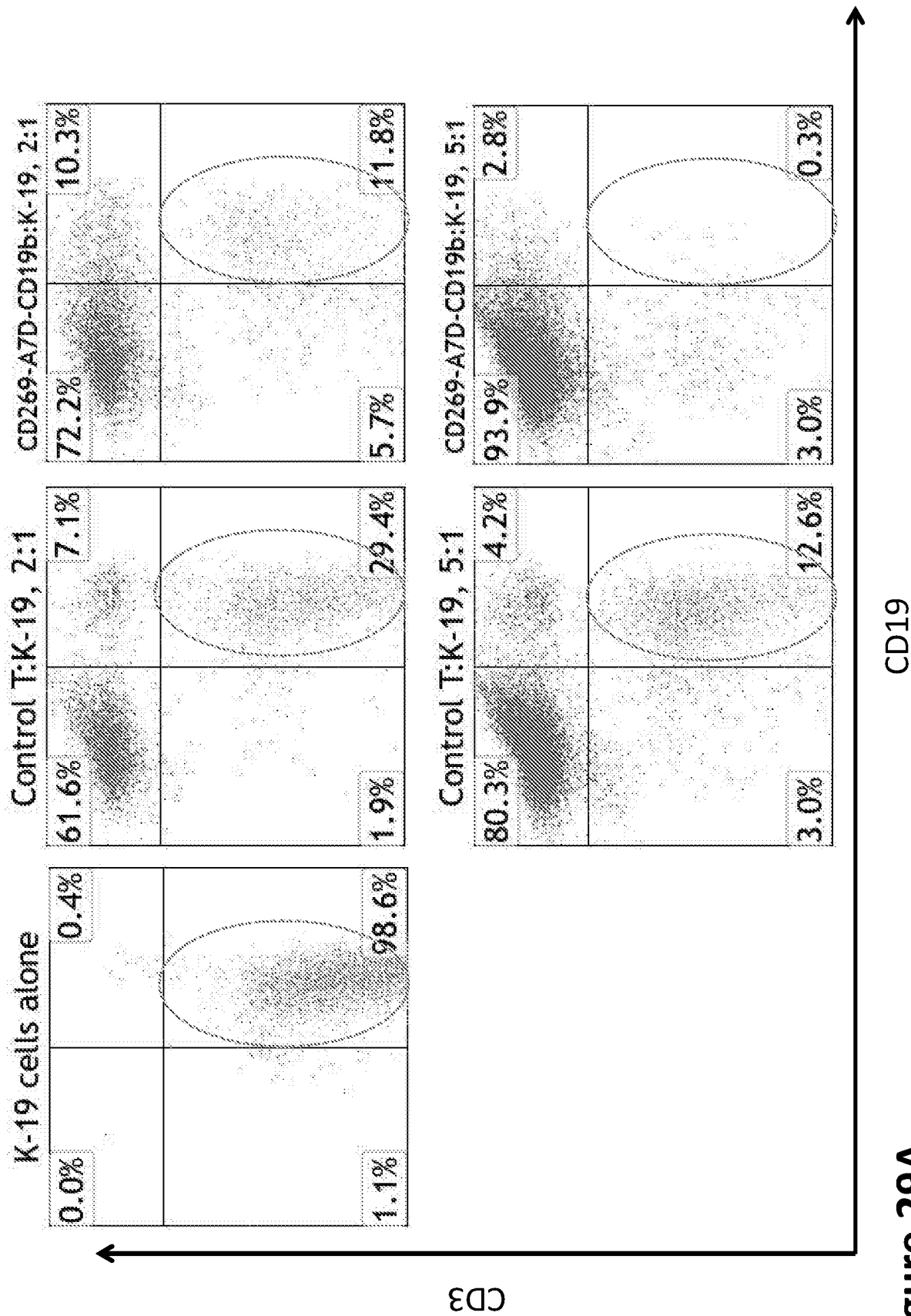


Figure 29A

CD269-A7D-CD19b-2G CAR T cells lyse BCMA-expressing K562
tumor cells in overnight co-culture

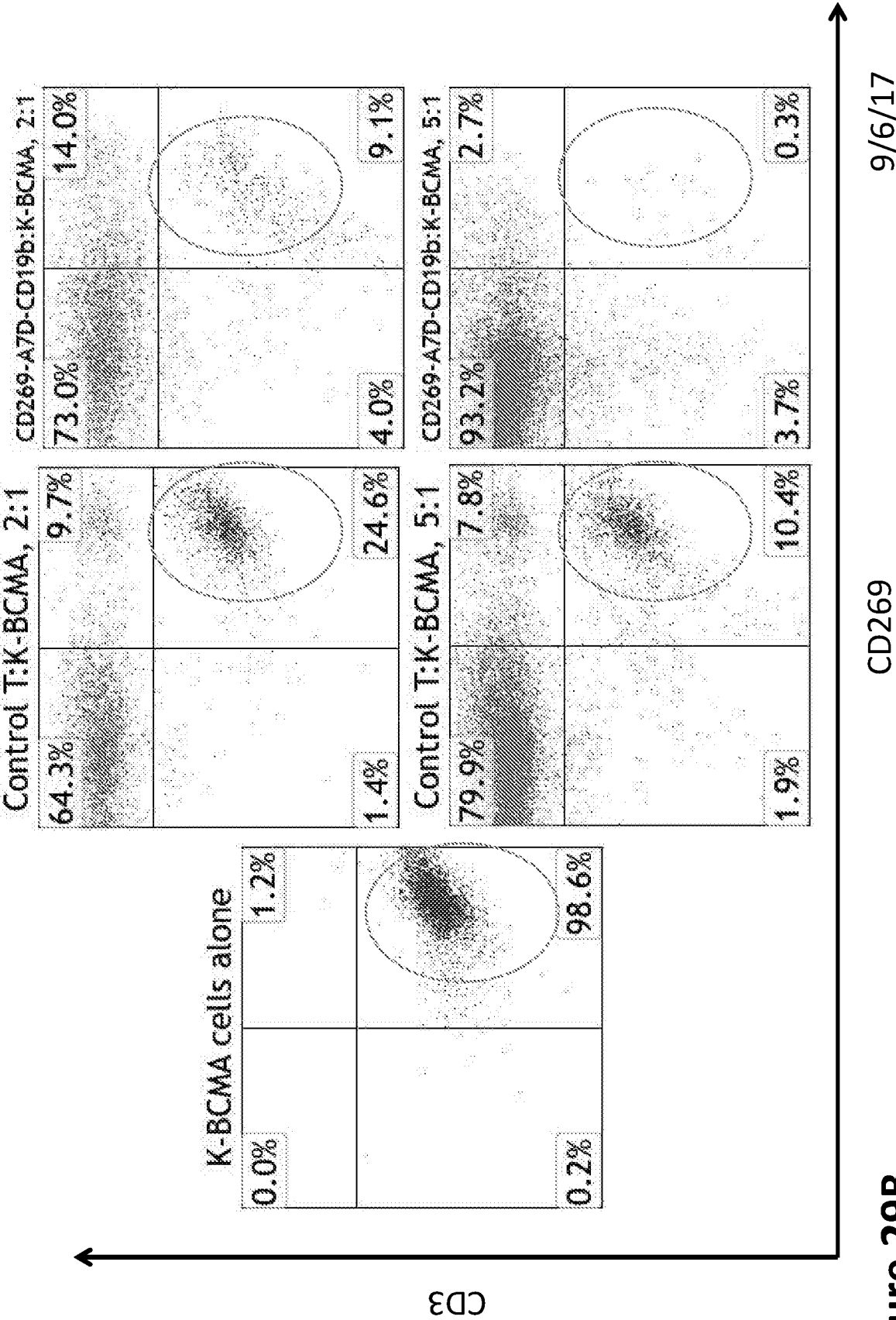


Figure 29B

CAR expression in compound CARs – BCMA-CS1

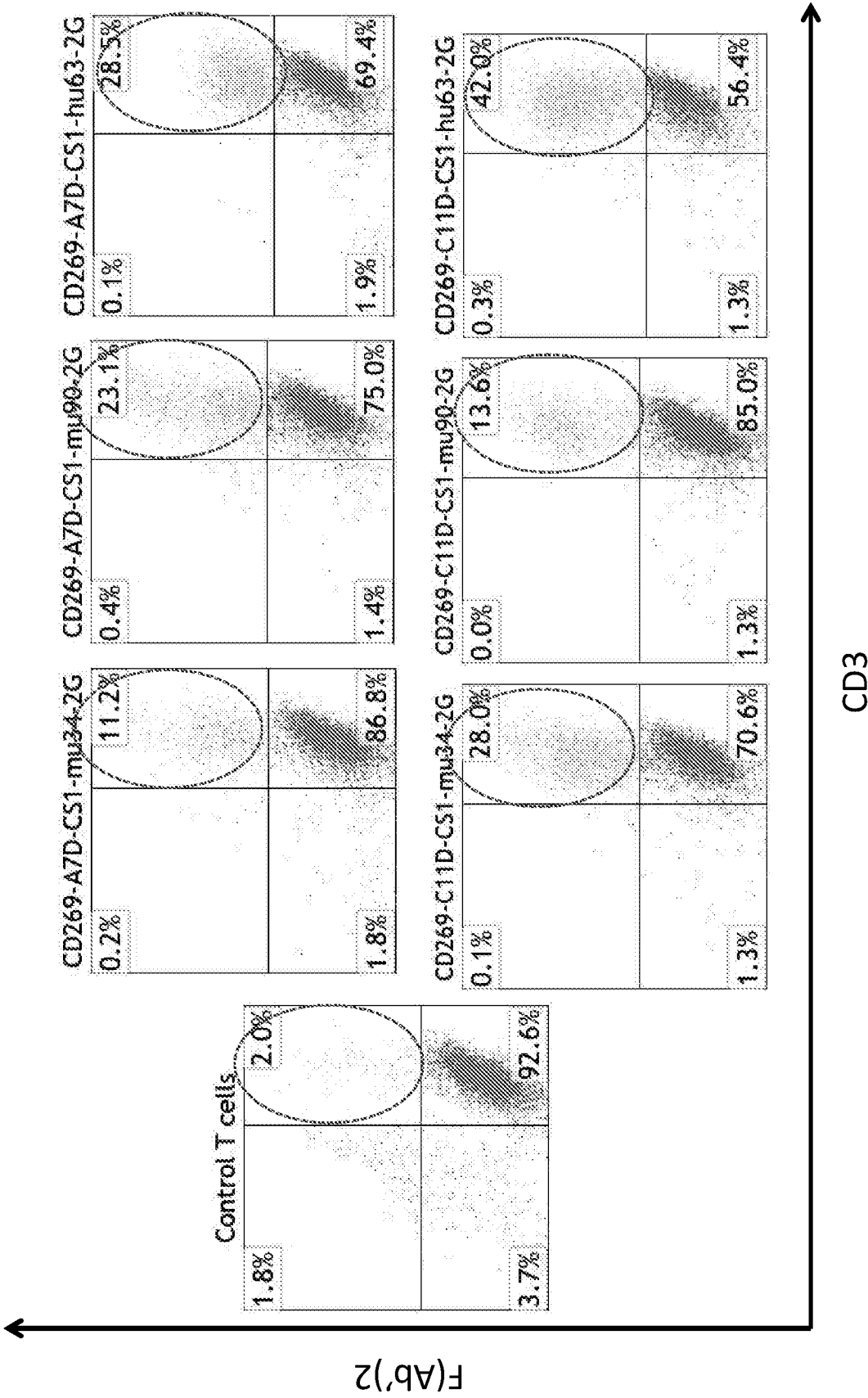


Figure 30A

CAR expression in BCMA CARs

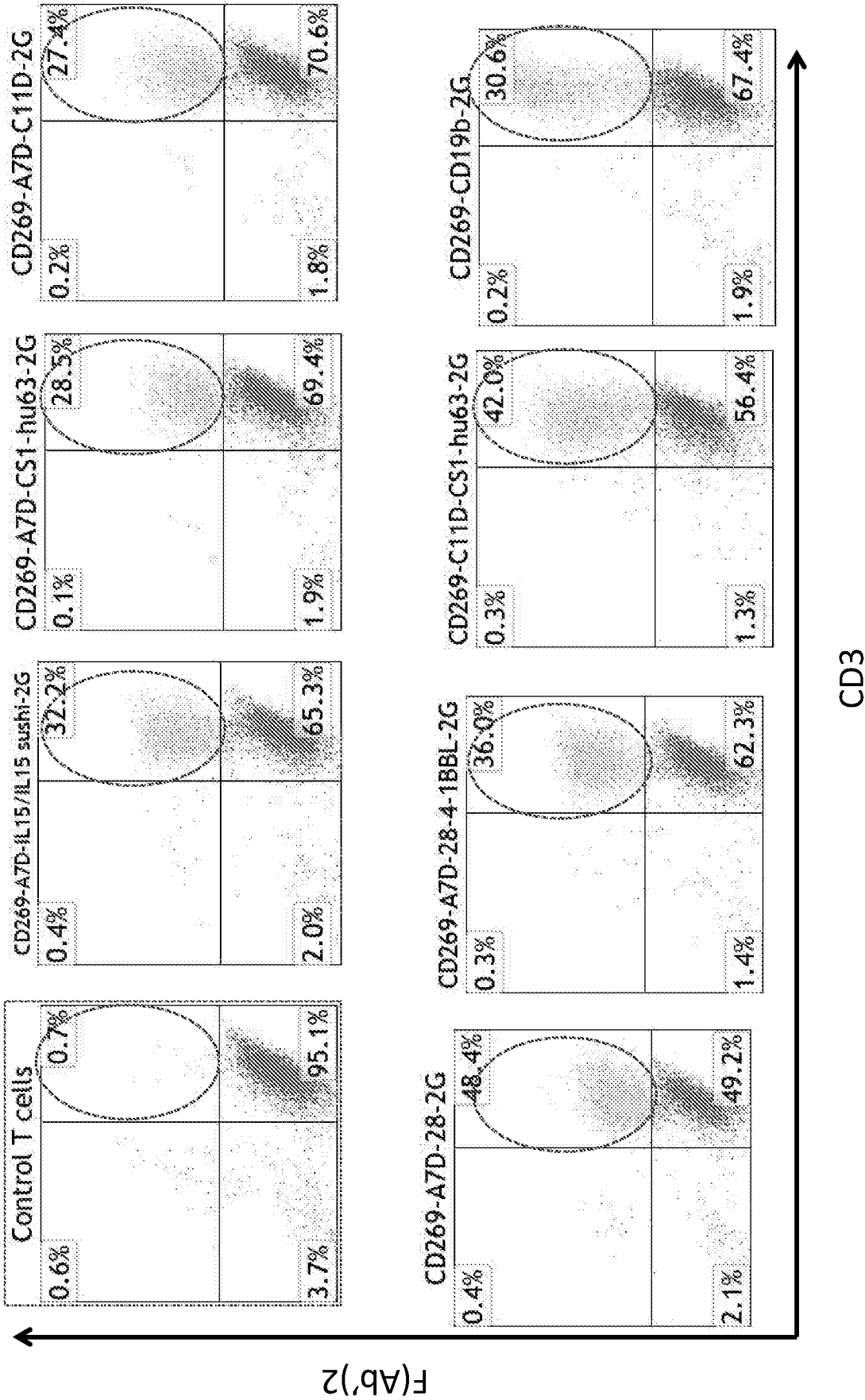


Figure 30B

CD269-A7D-CD19b-2G CAR T cells lyse BCMA-expressing K562
tumor cells in overnight co-culture

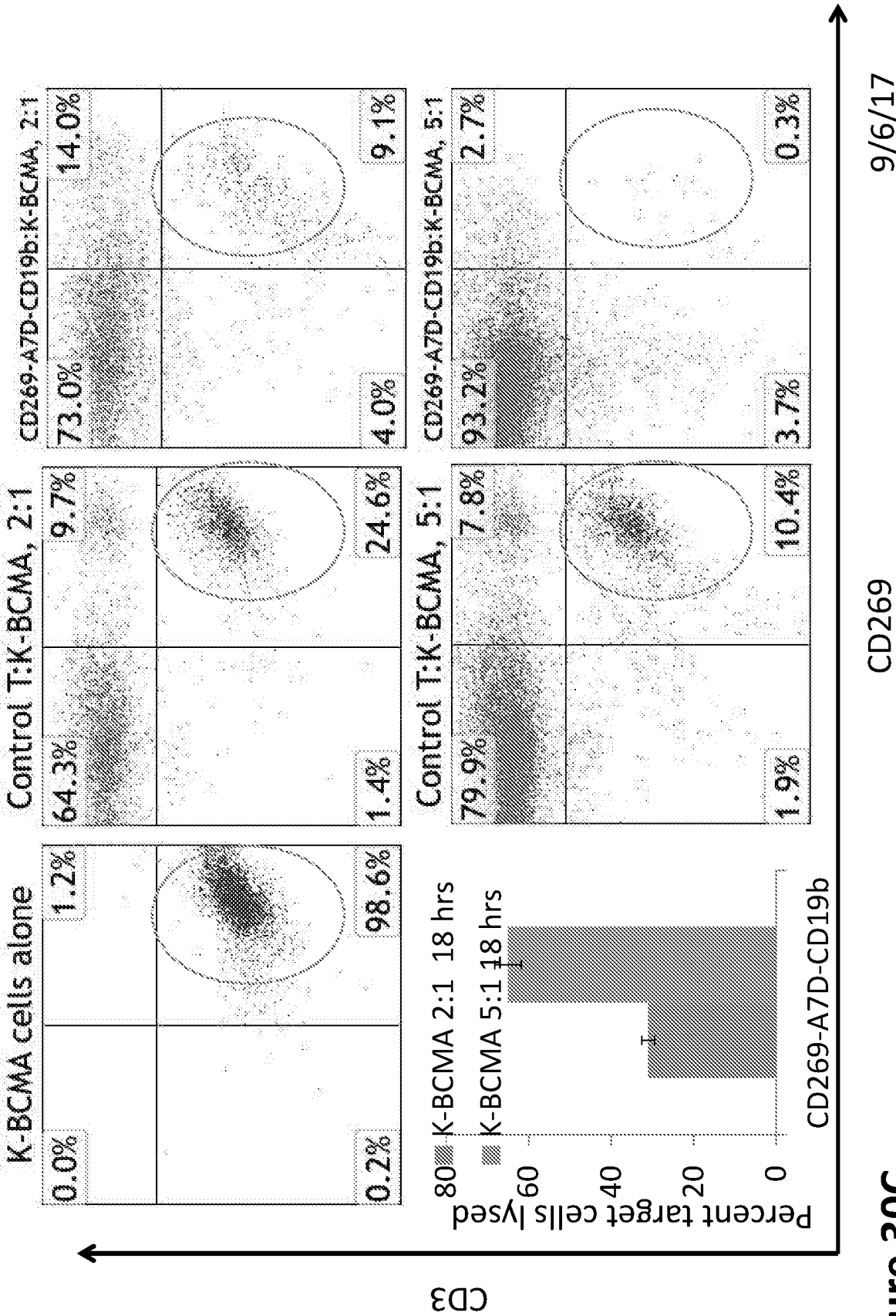


Figure 30C

CD269-A7D-CD19b-2G CAR T cells lyse CD19-expressing K562
tumor cells in overnight co-culture

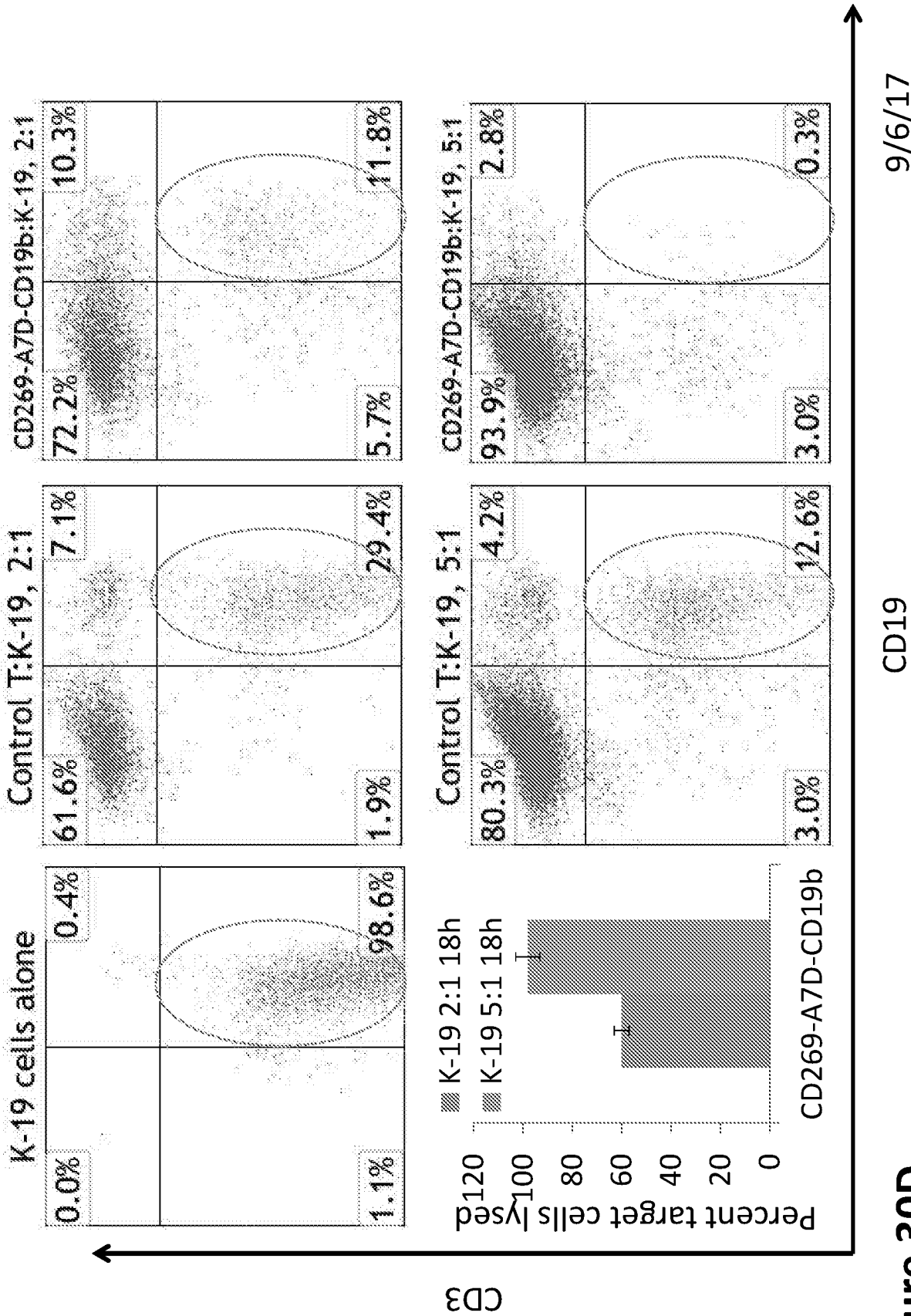


Figure 30D

Summary

Lysis of K562-BCMA and K562-CD19 cells

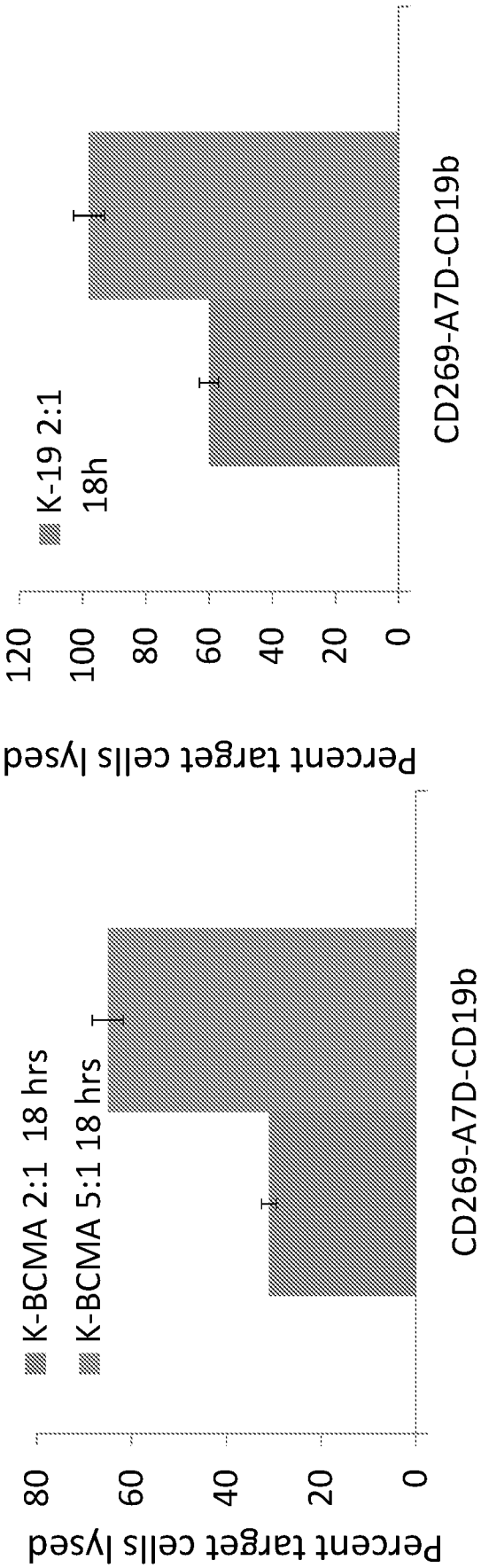


Figure 30E

Various BCMA CAR T cells lyse MM1S tumor cells in overnight co-

culture

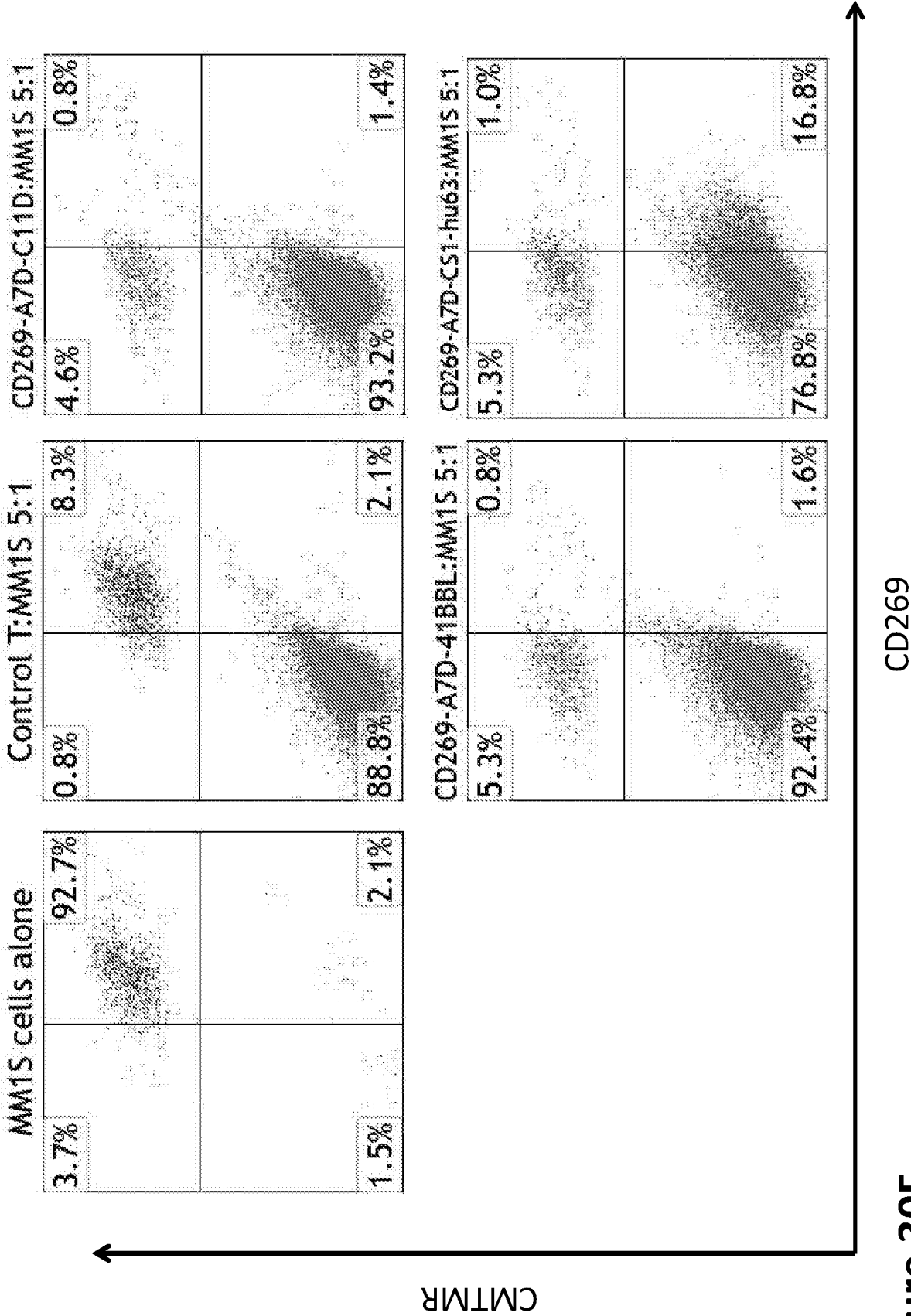


Figure 30F

Various BCMA CAR T cells lyse K562 tumor cells expressing BCMA in overnight co-culture

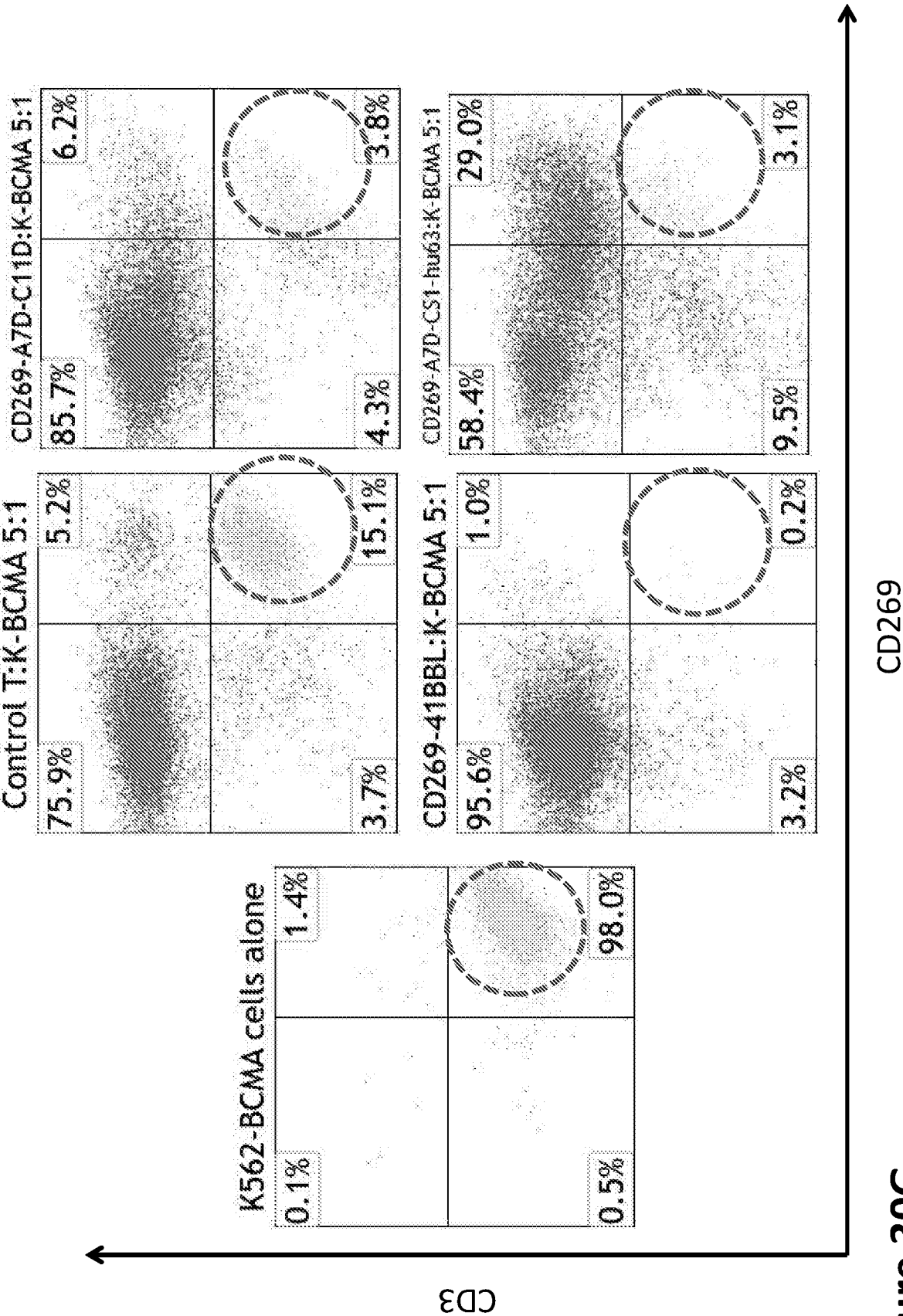


Figure 30G

Various BCMA CAR T cells lyse K562 tumor cells expressing CS1 in overnight co-culture

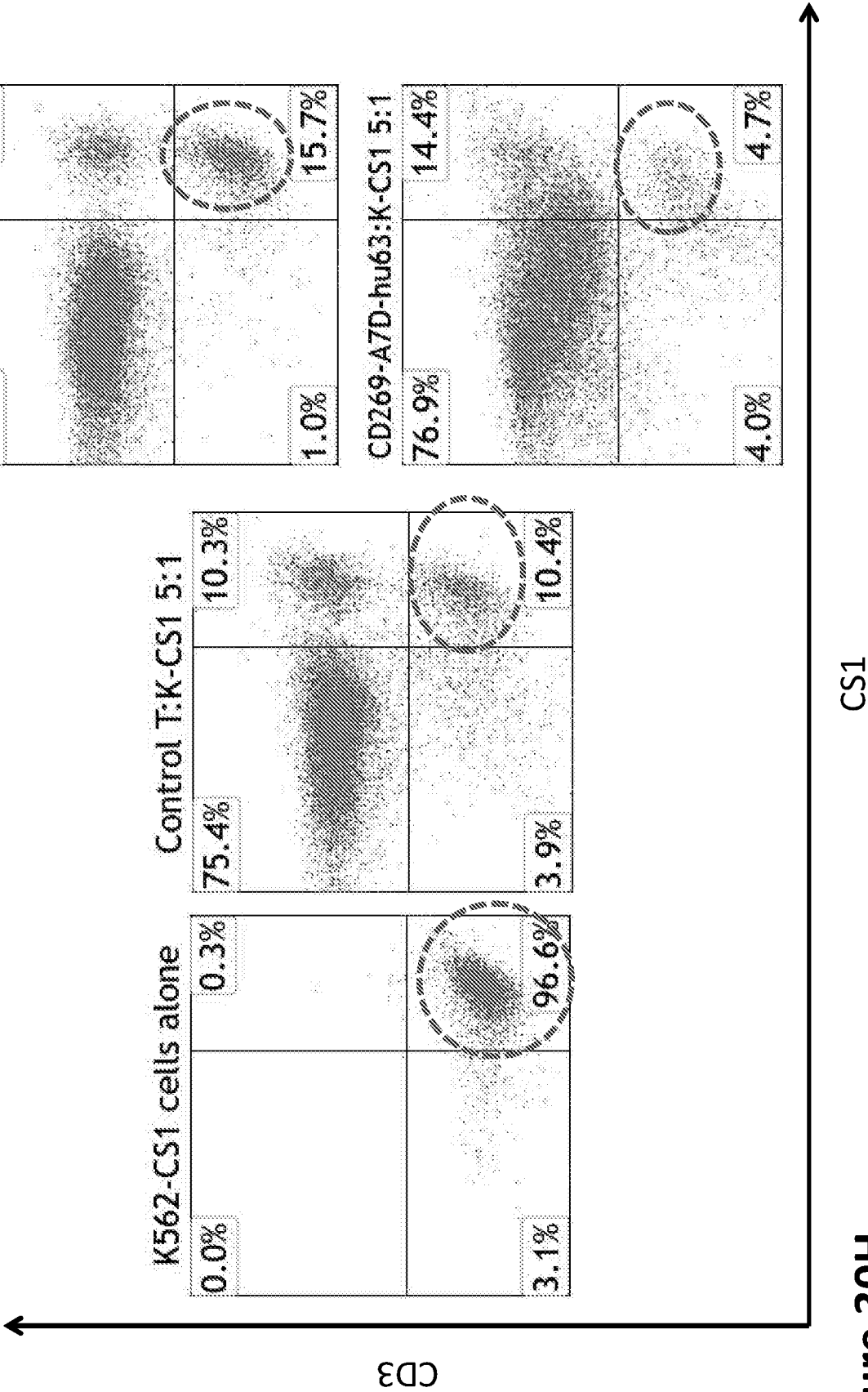


Figure 30H

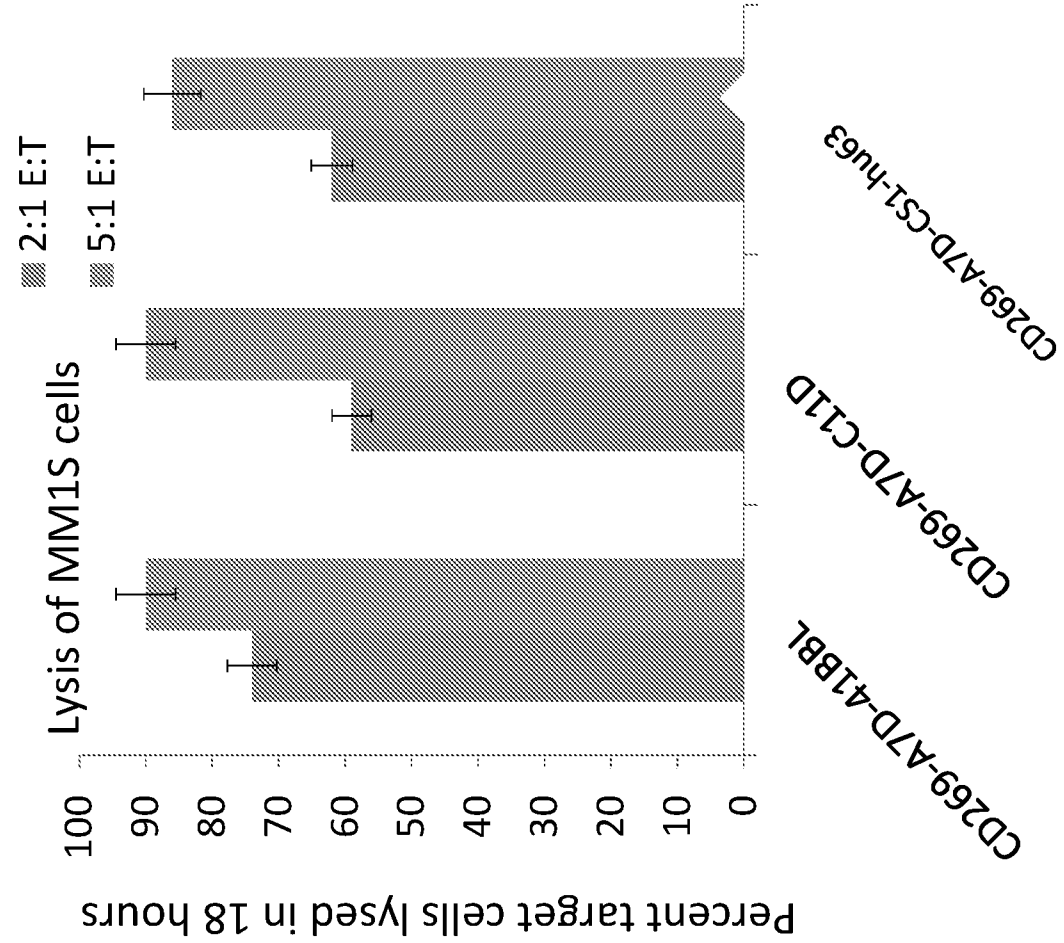


Figure 30I

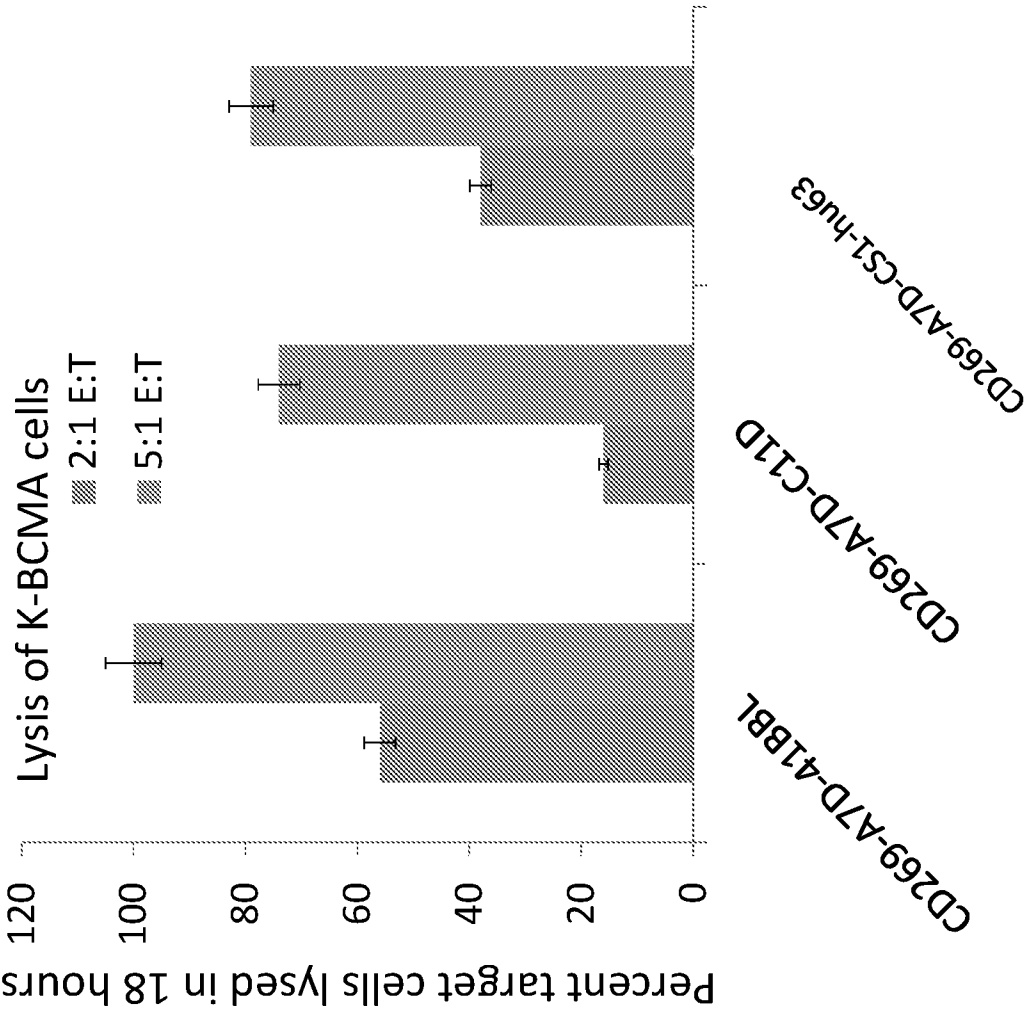


Figure 30J

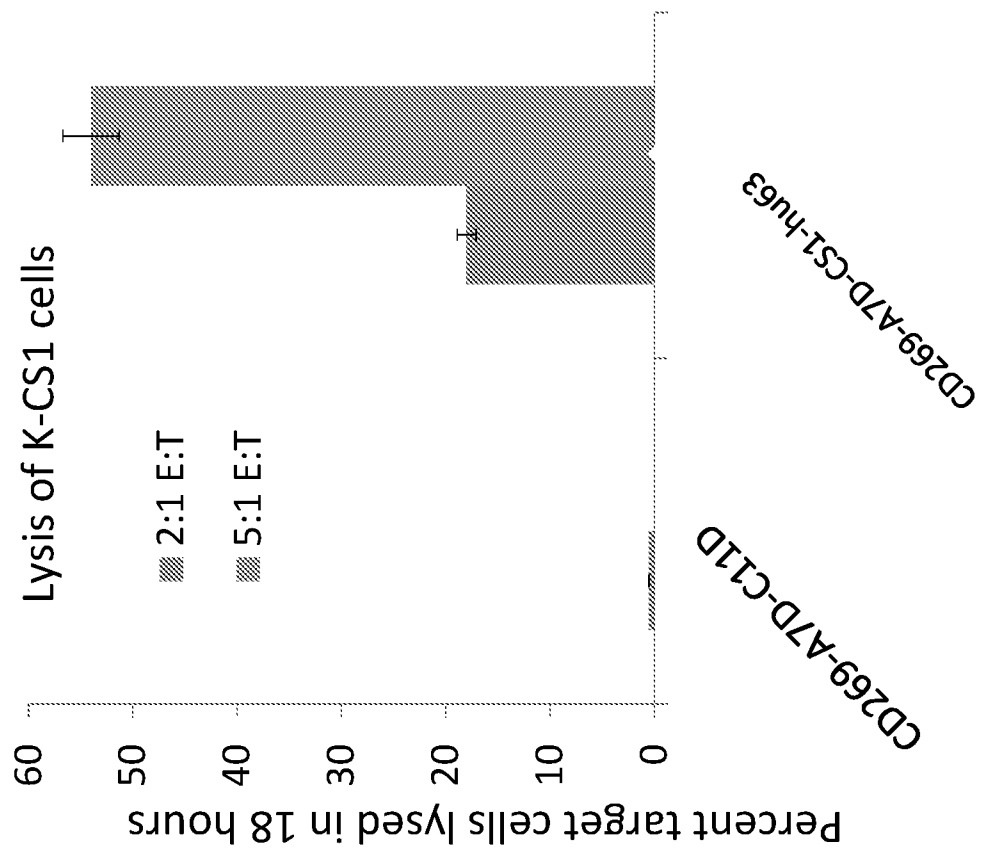


Figure 30K

CAR expression in transduced T cells

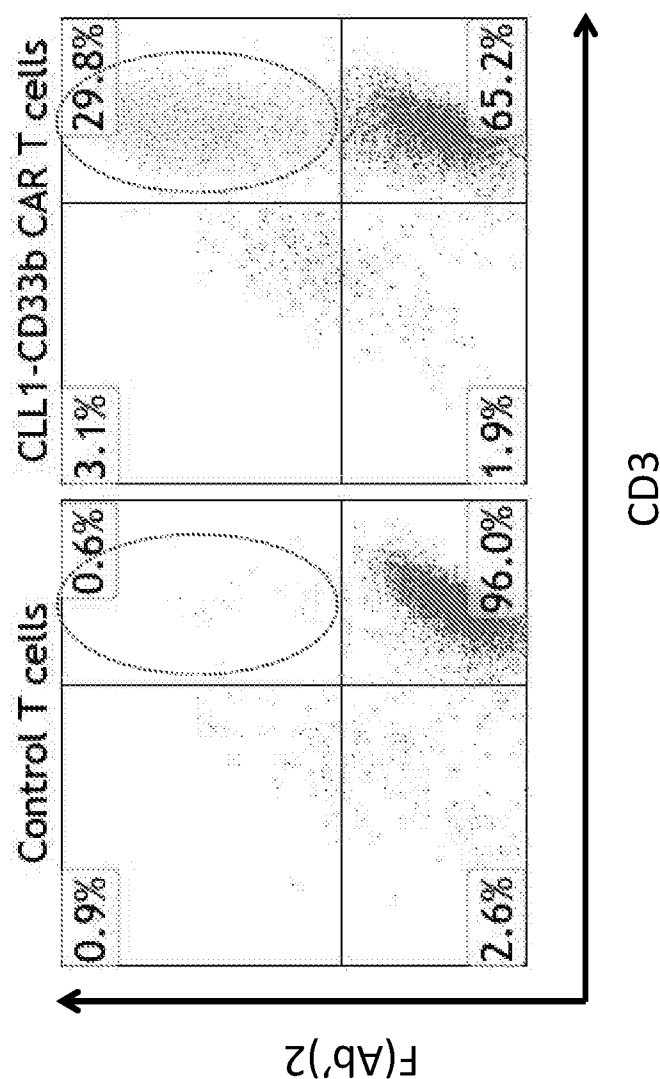


Figure 31

CLL1-CD33b cCAR T cells do not lyse REH cell line

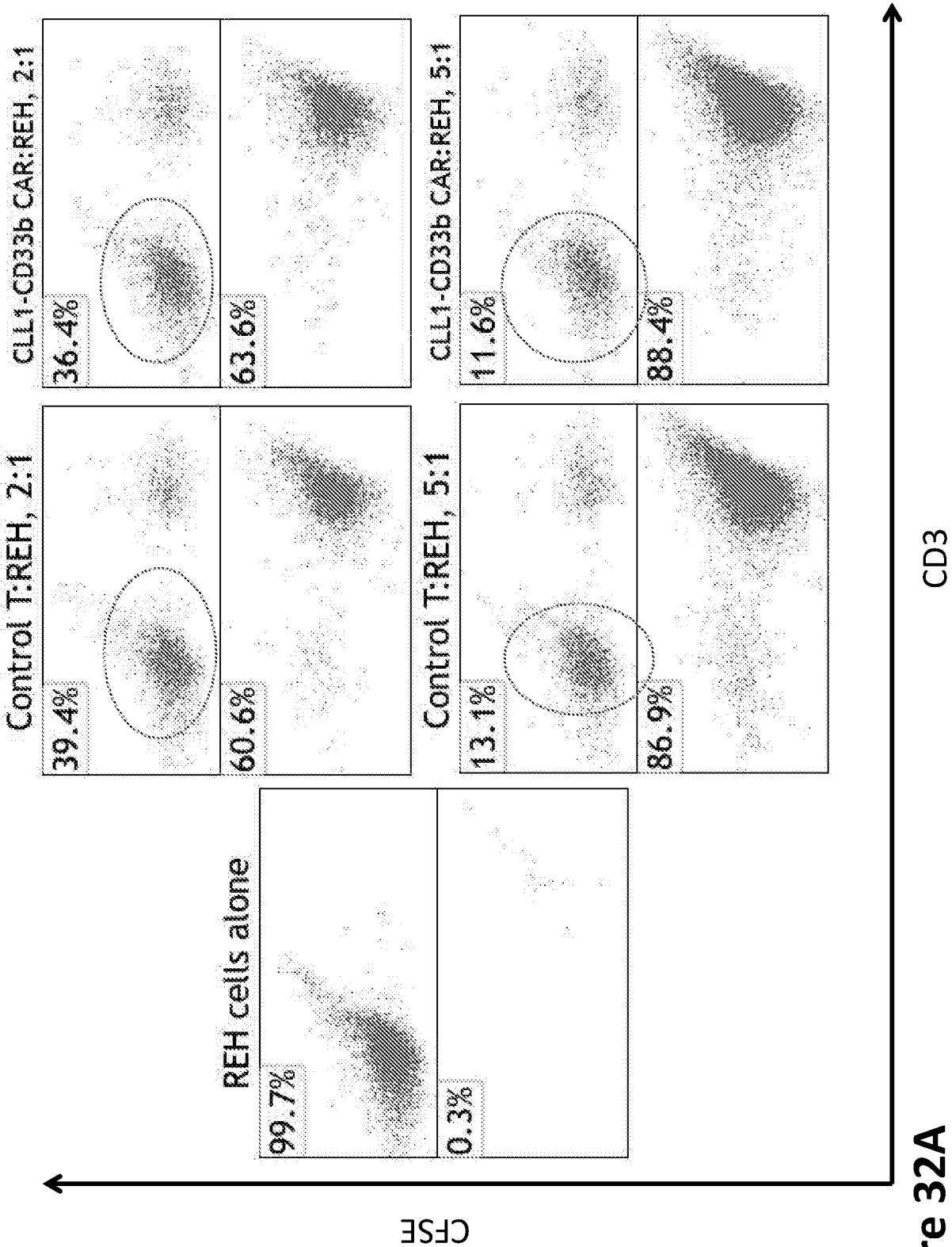


Figure 32A

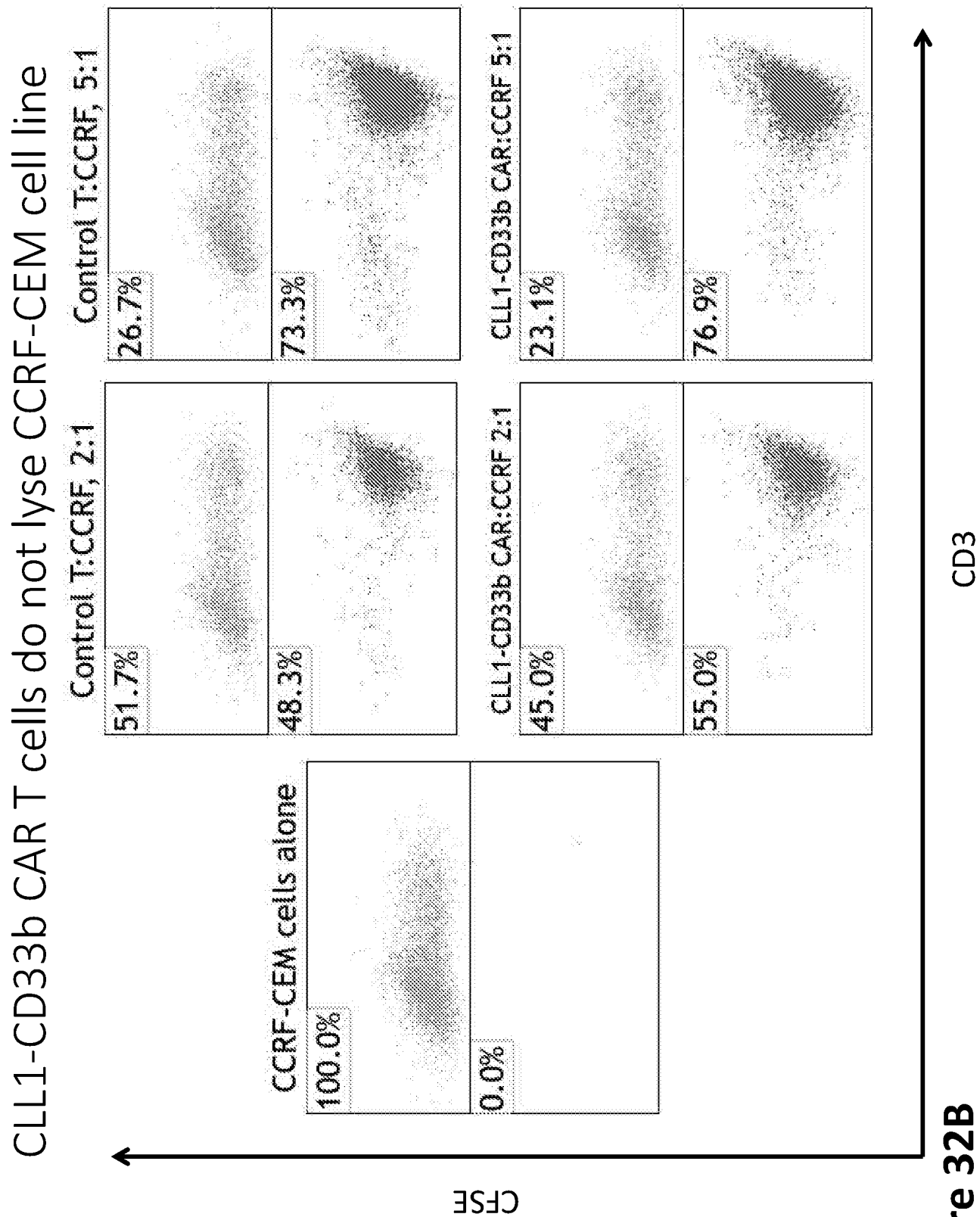


Figure 32B

CLL1-CD33b CAR T cells specifically lyse Jurkat cell line
expressing CLL-1

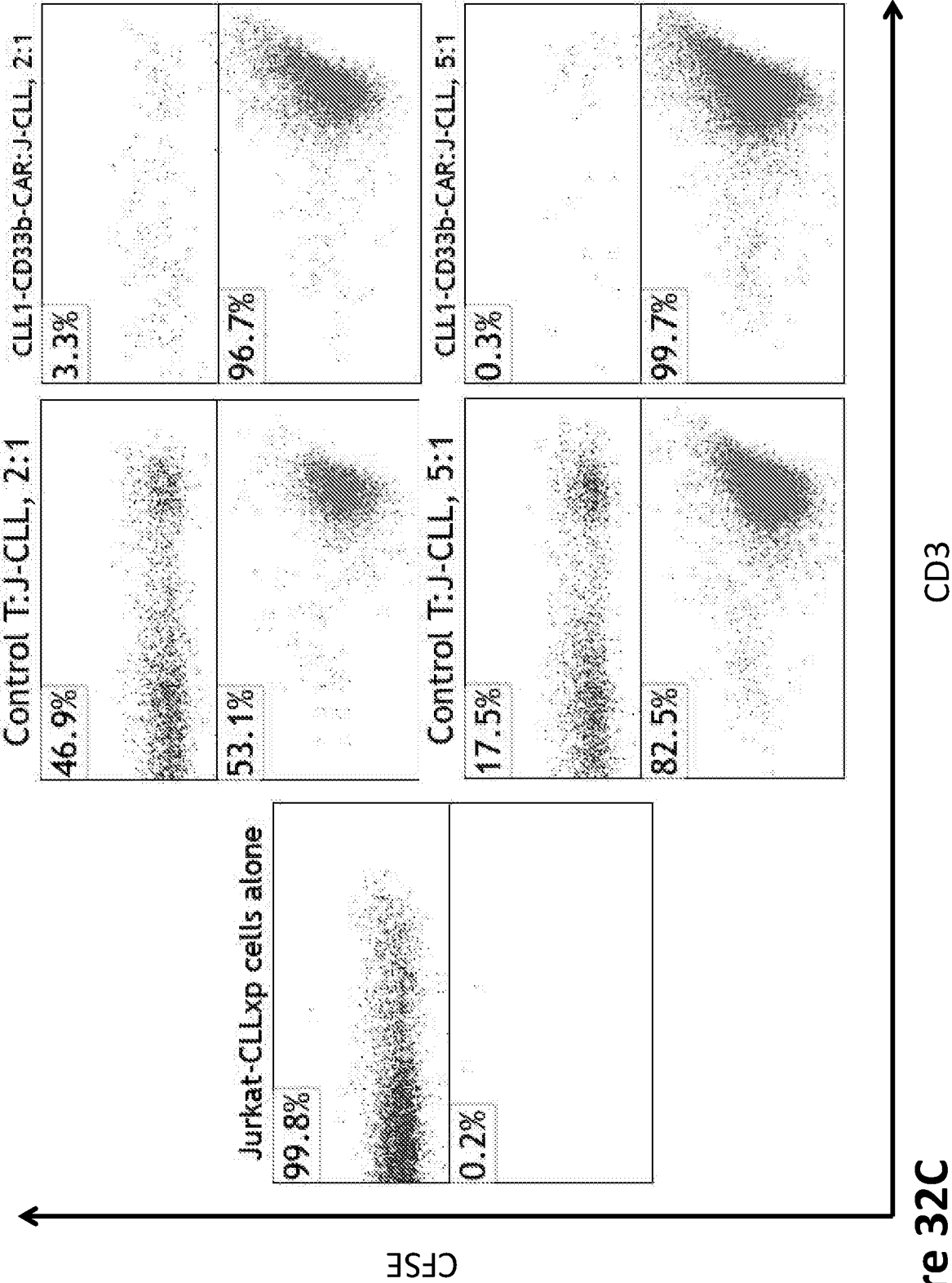


Figure 32C

CLL1-CD33b CAR T cells specifically lyse Jurkat cell line
expressing CD33 antigen

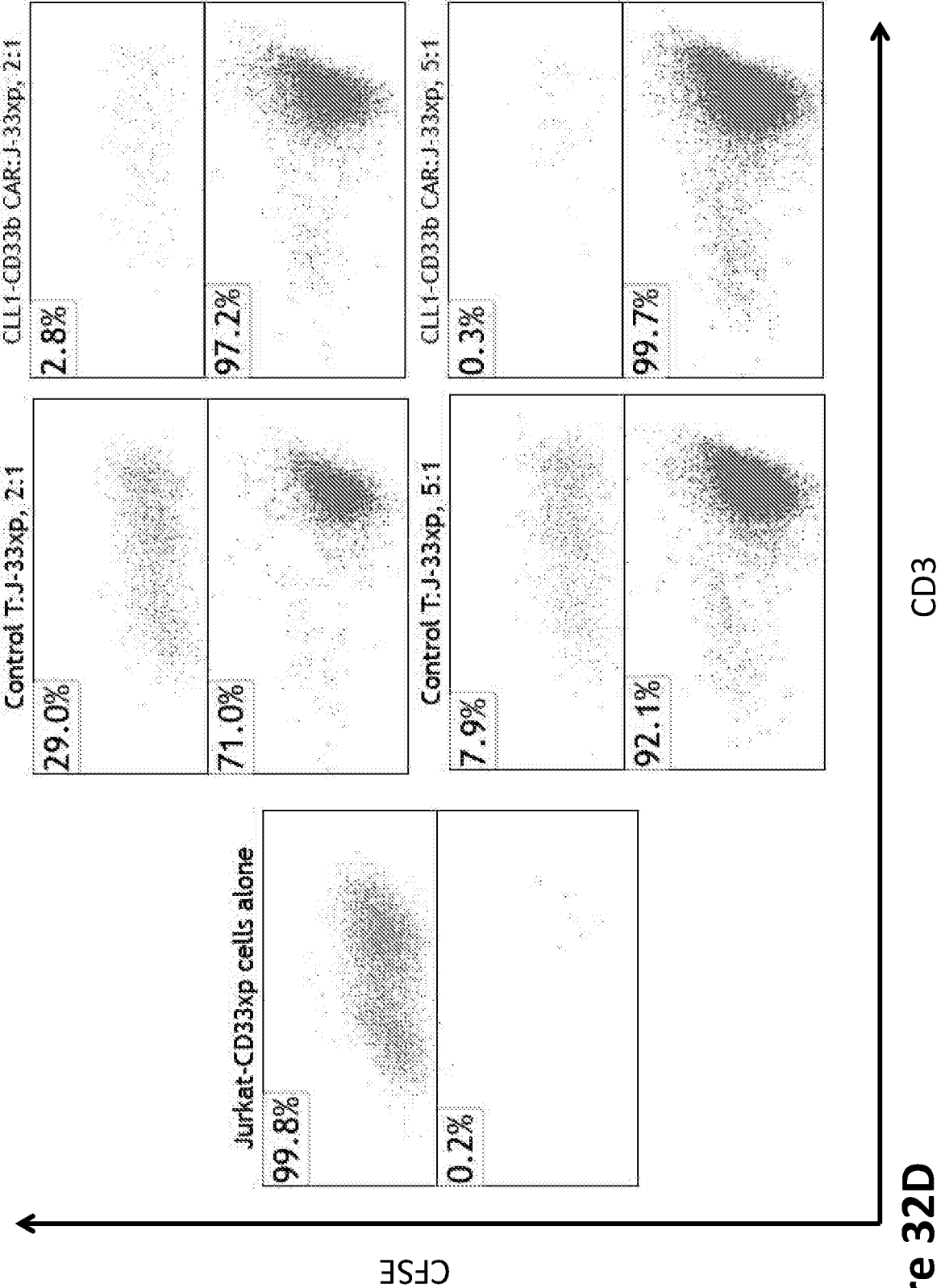
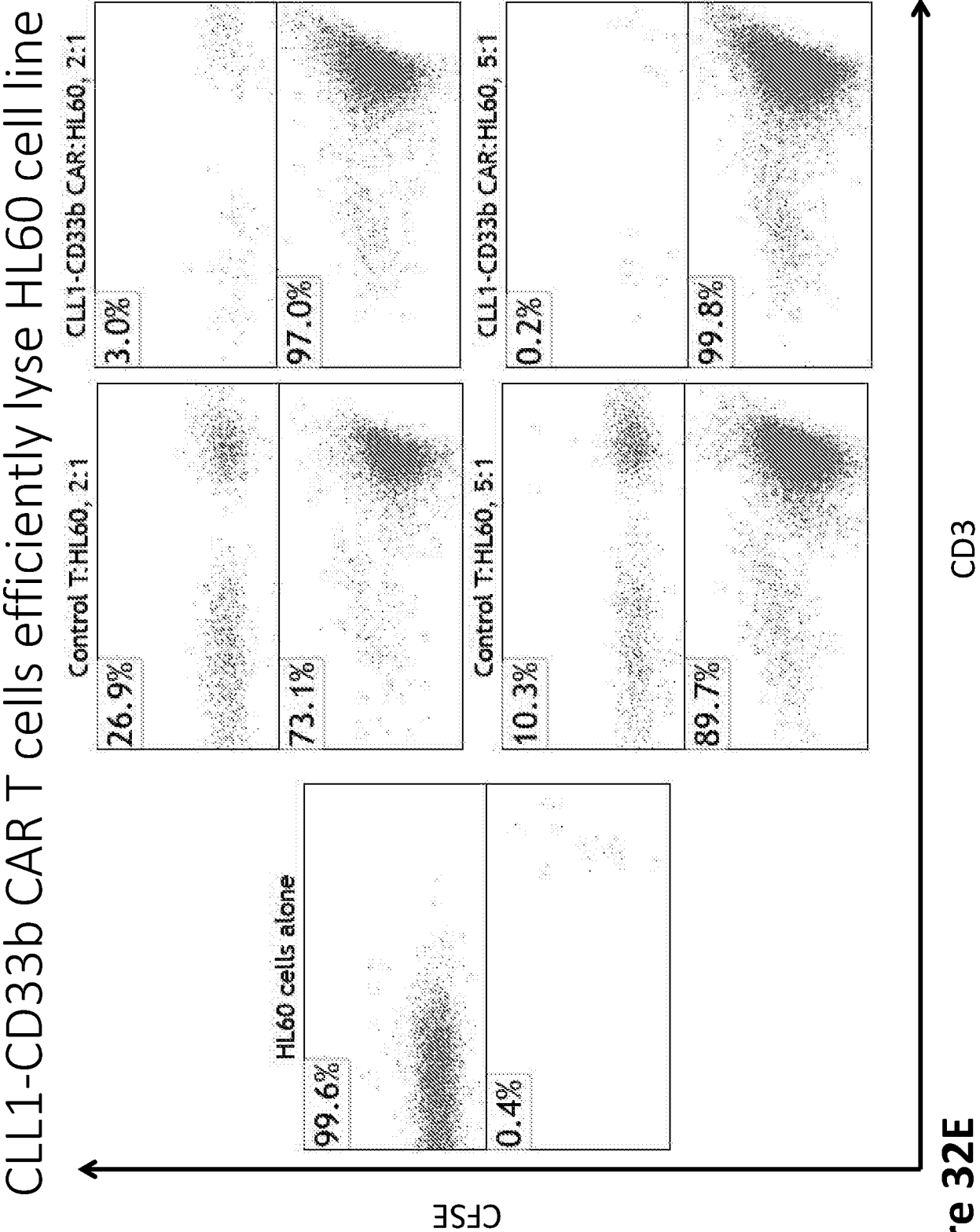
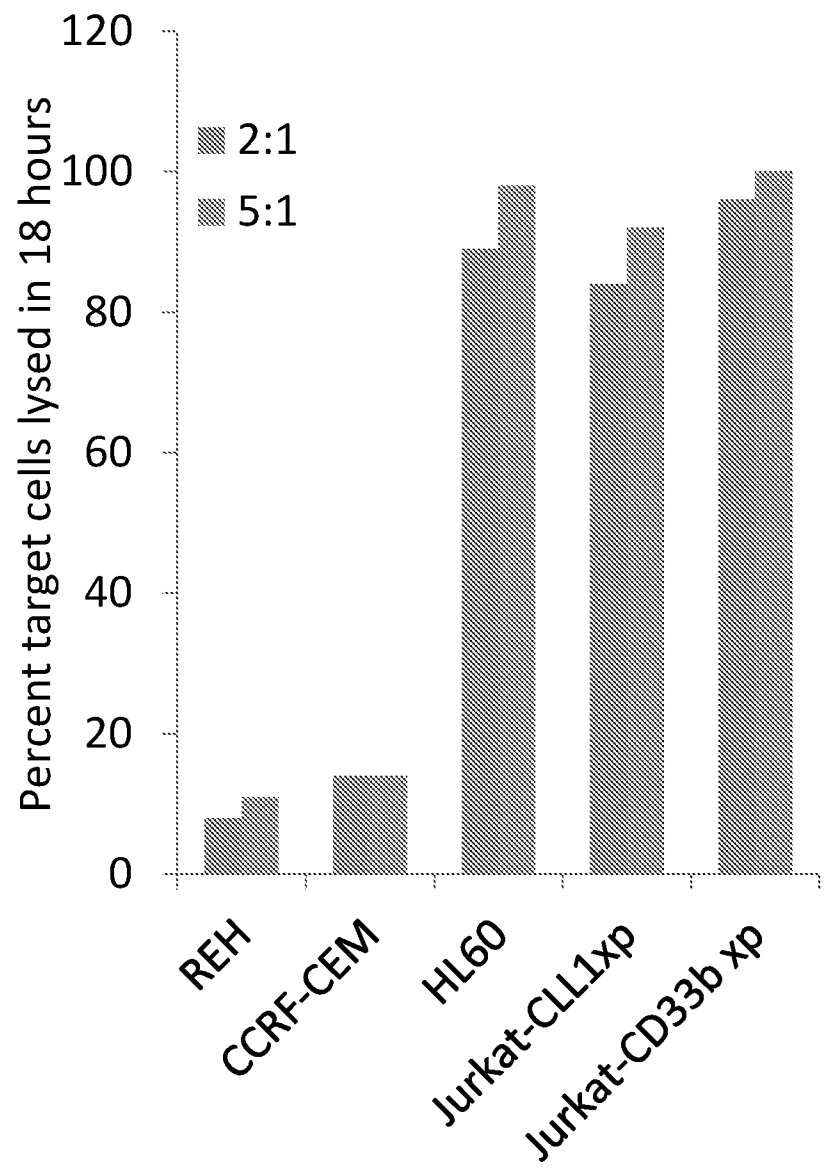


Figure 32D



**Figure 32F**

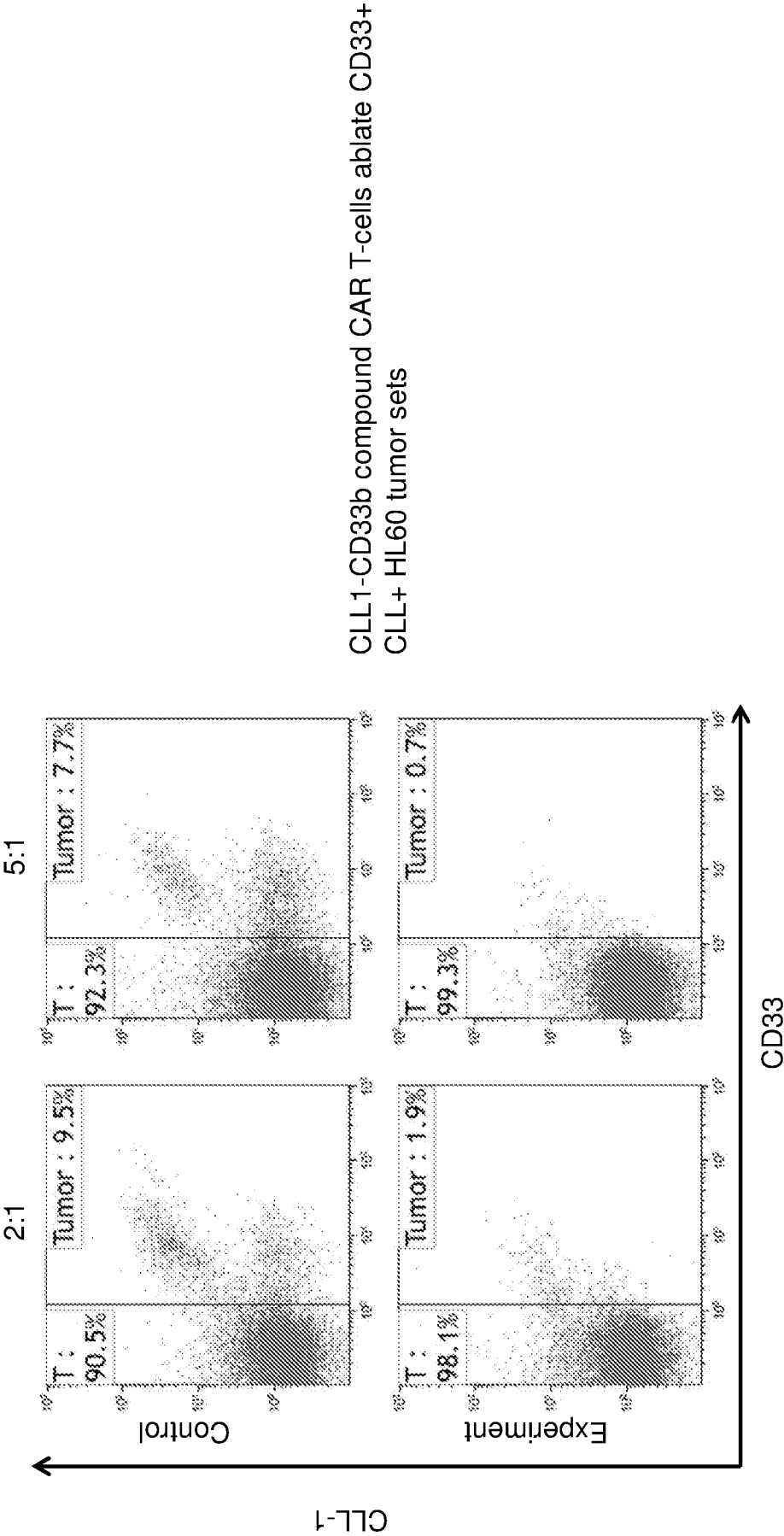


Figure 32G

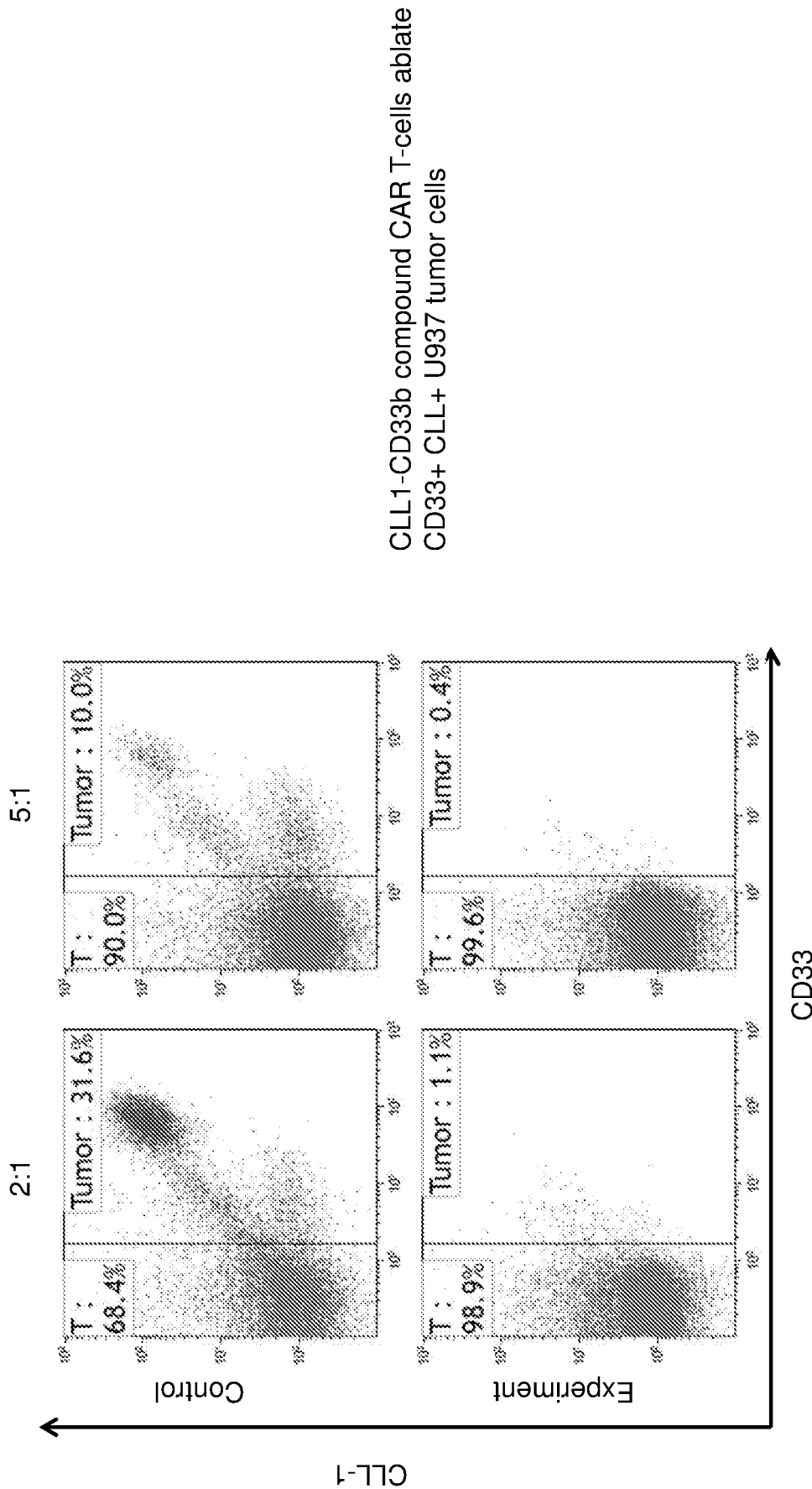


Figure 32H

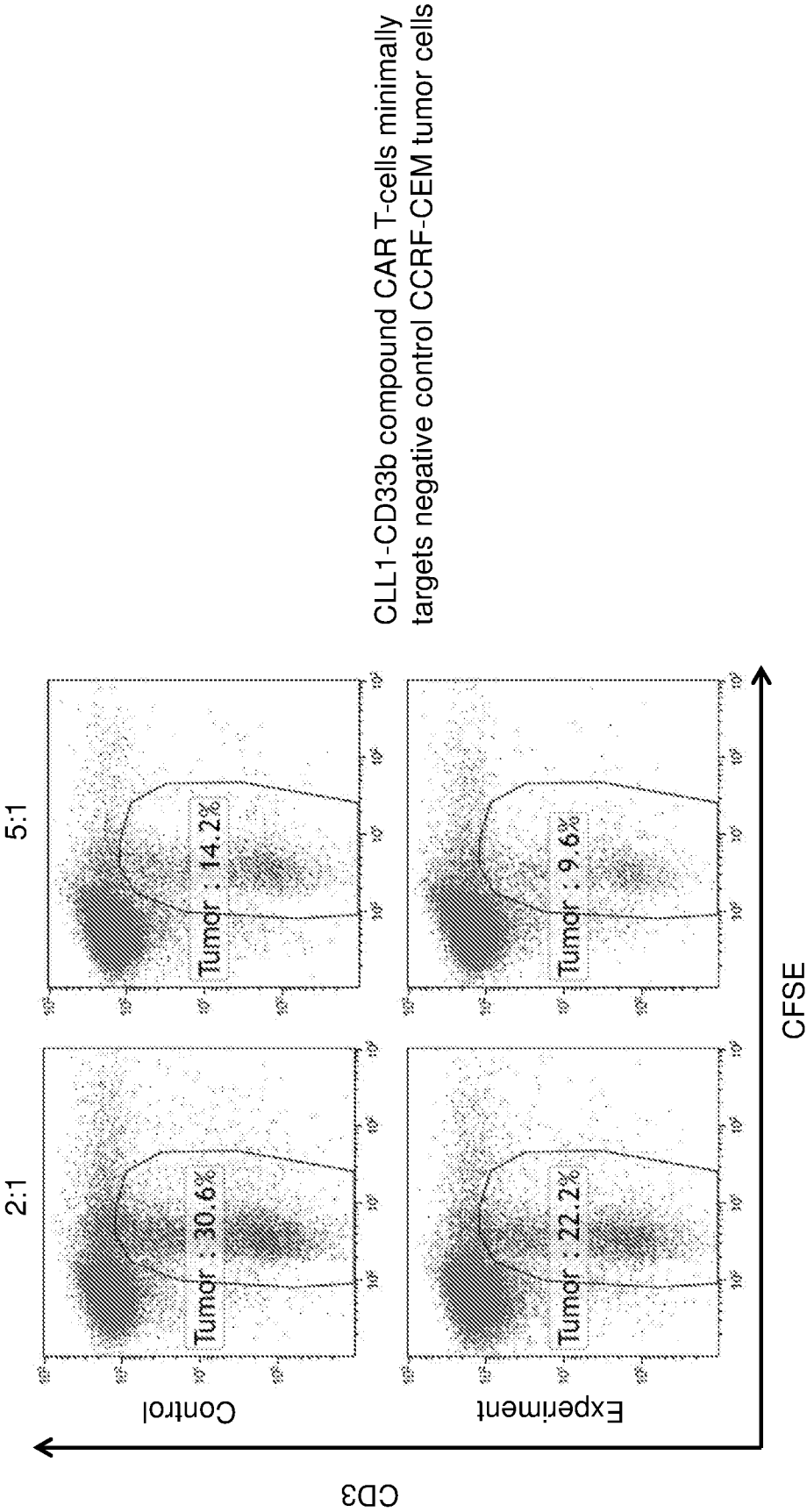
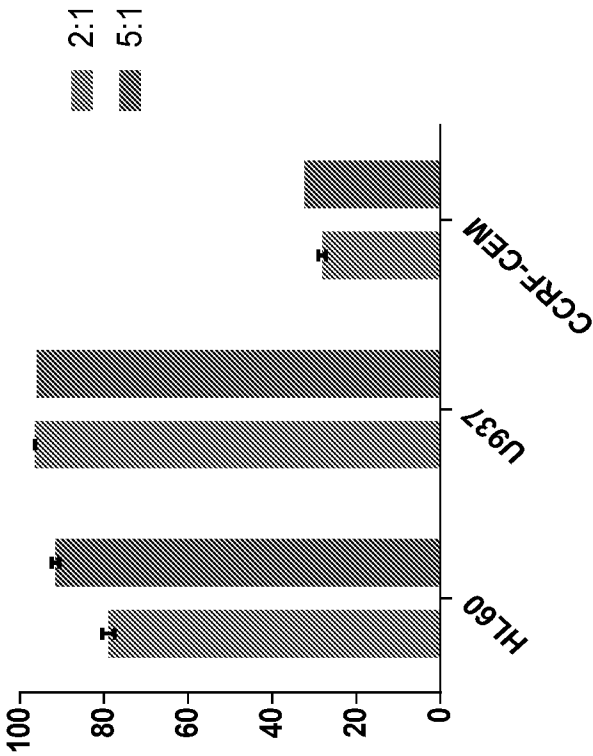


Figure 32I

Summary of CLL1-CD33b cCAR T cell in *vitro* activity



Dose-dependent effects of CLL1-CD33b cCAR T-cells on target HL60 tumor

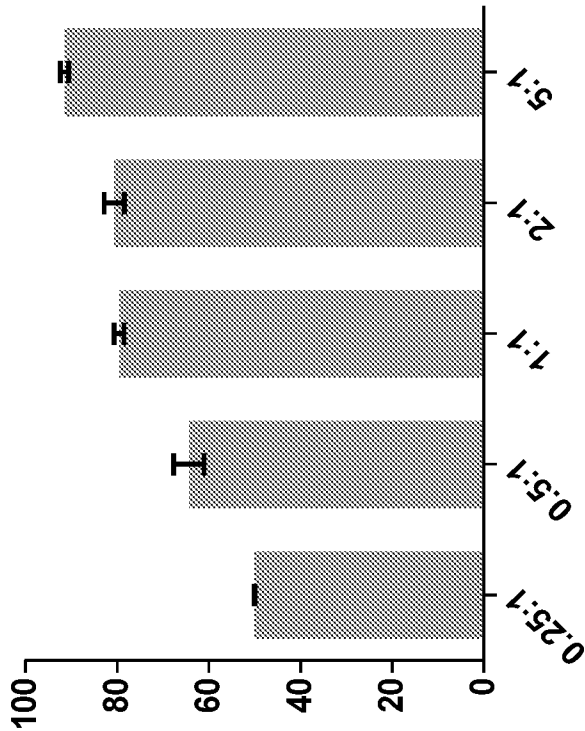


Figure 32J

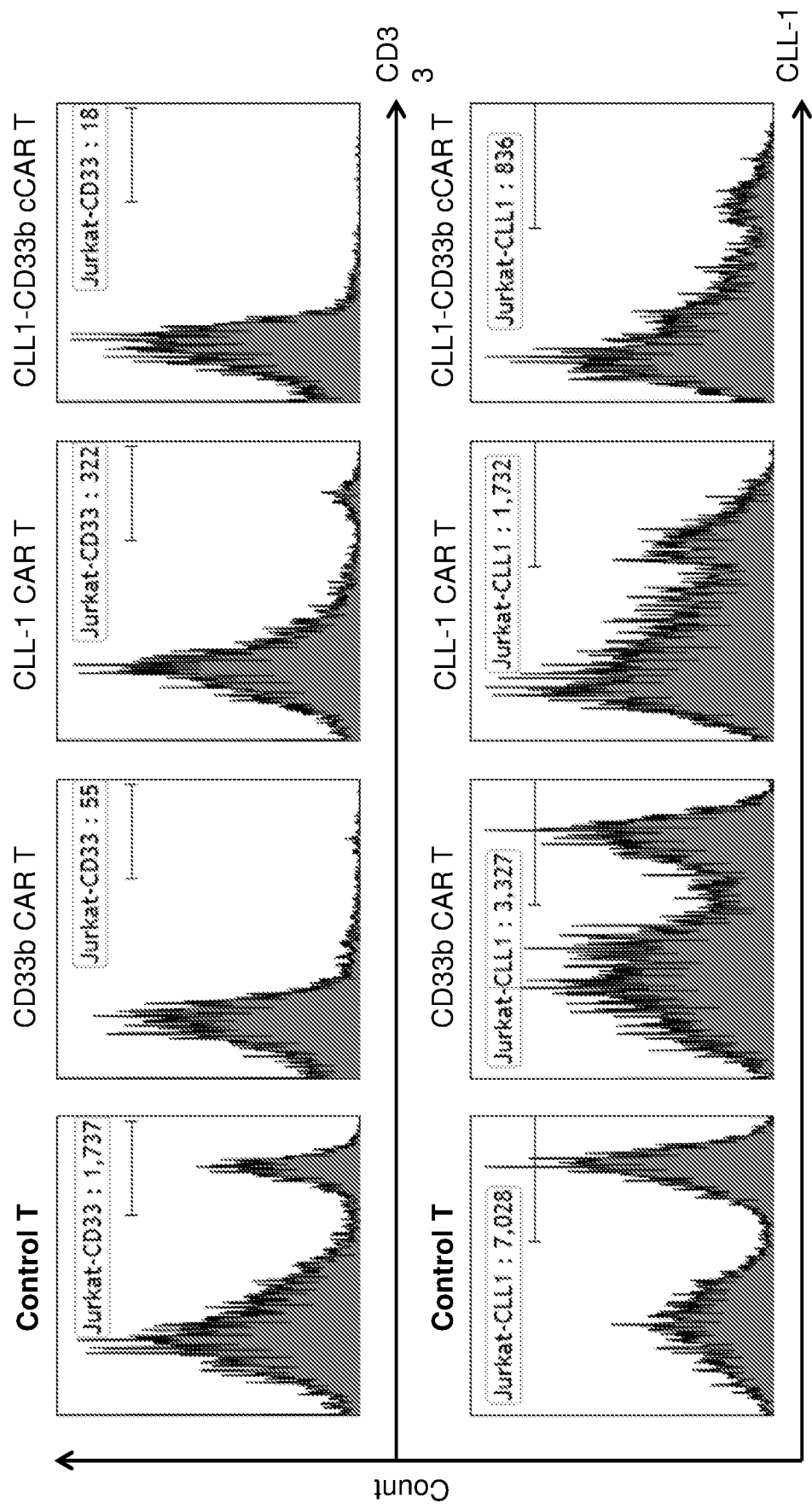


Figure 32K

CLL1-CD33b CAR T cells are able to target and destroy CD33 or CLL-1 expressing Jurkat cells in a mixed cell co-culture compared to control T cells

CLL1-CD33b CAR T cells exhibit increased cytotoxicity when compared to single target CARs against their respective target antigens

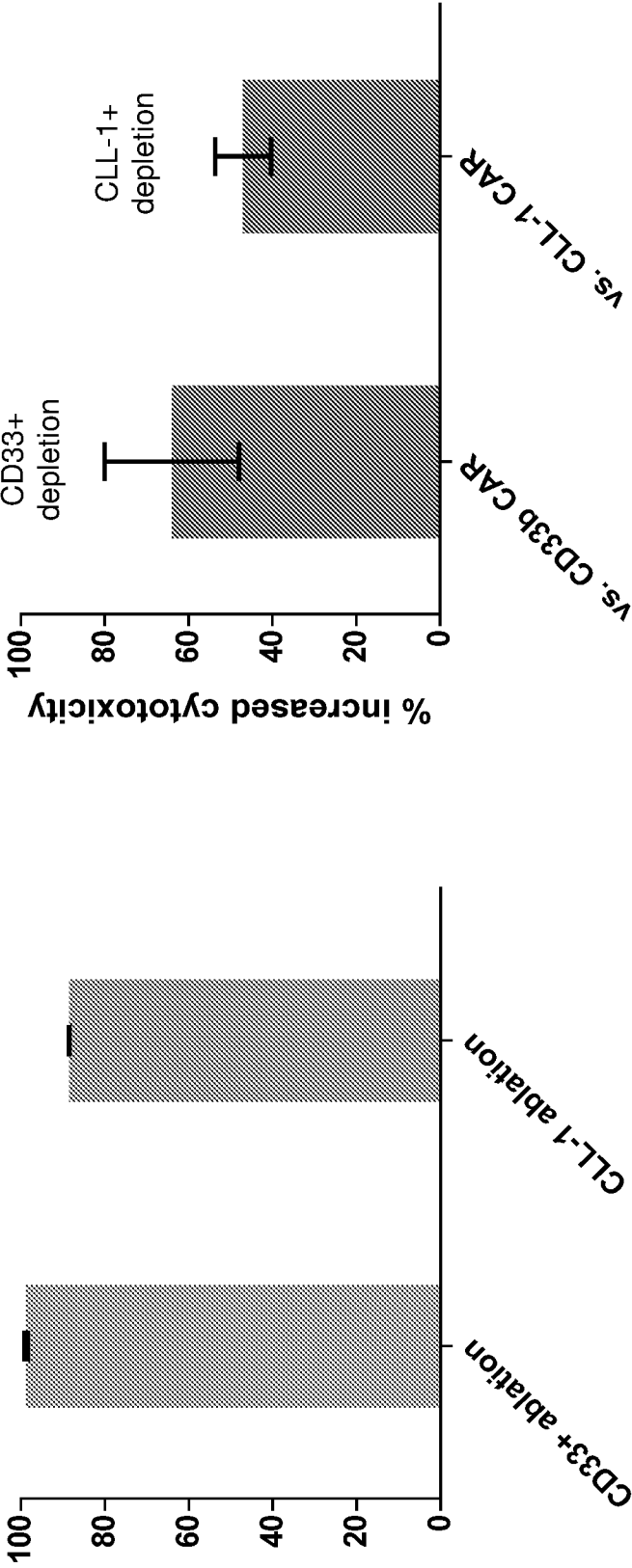


Figure 32L

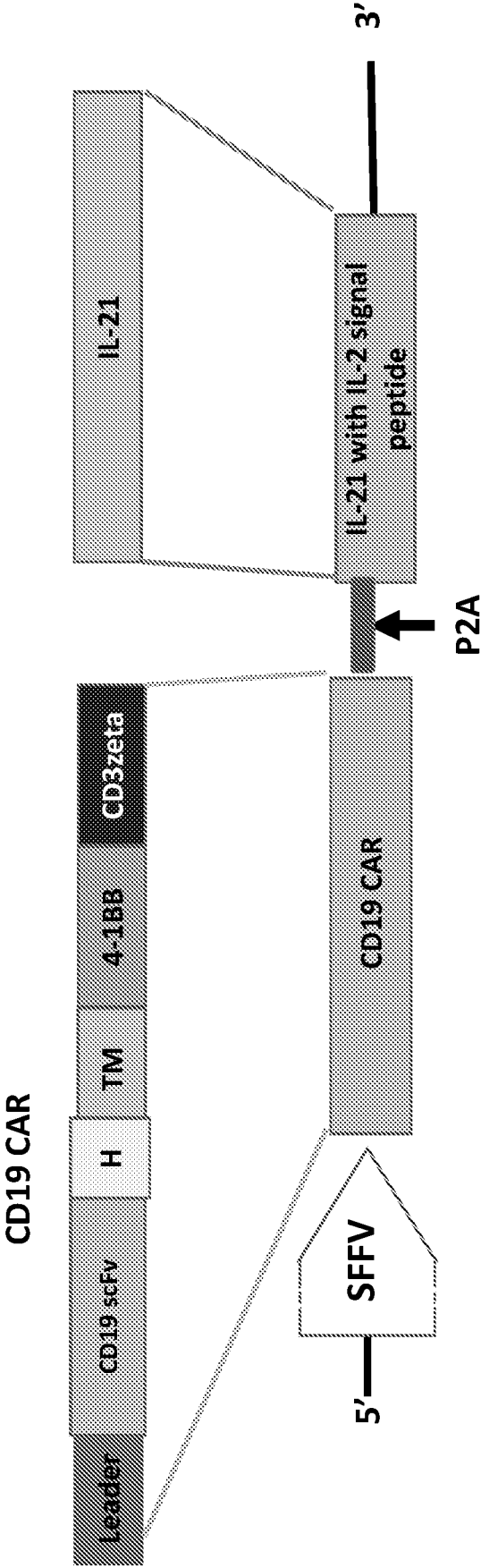


Figure 33A

CAR expression- CD19b-IL21 (CD19b-IL-21) or
CD19b-IL-21 anchor

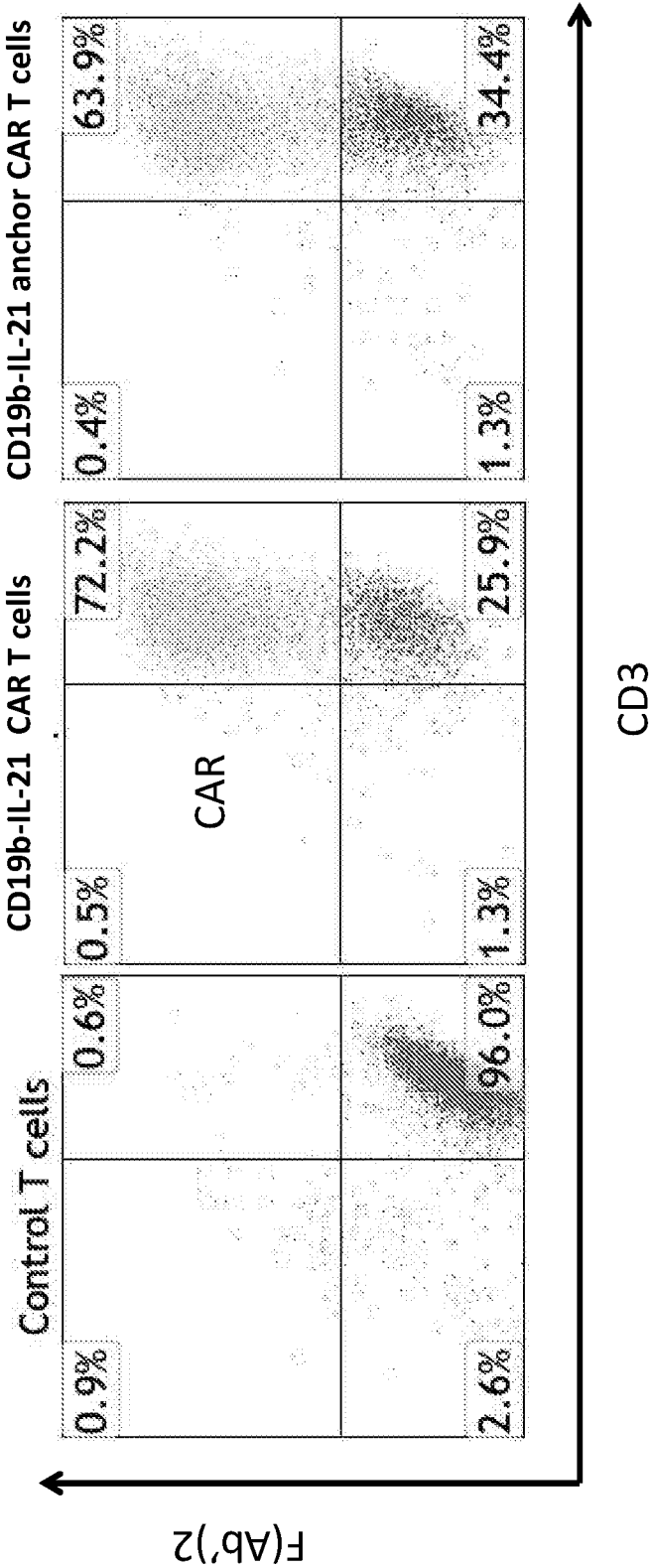


Figure 33B

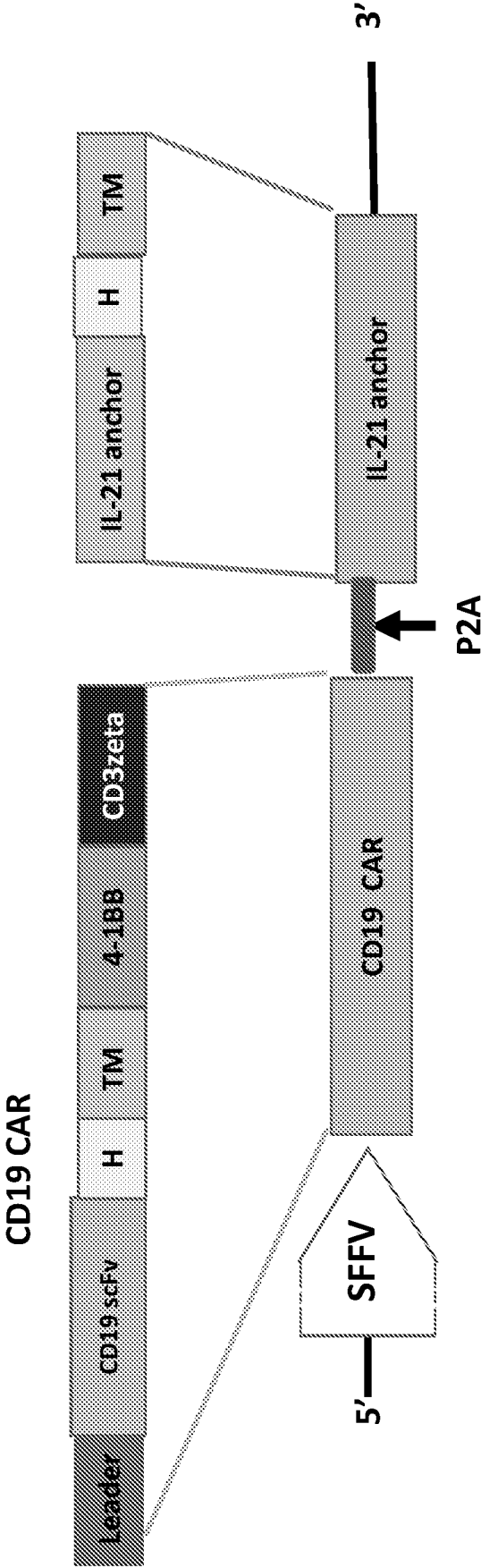


Figure 34

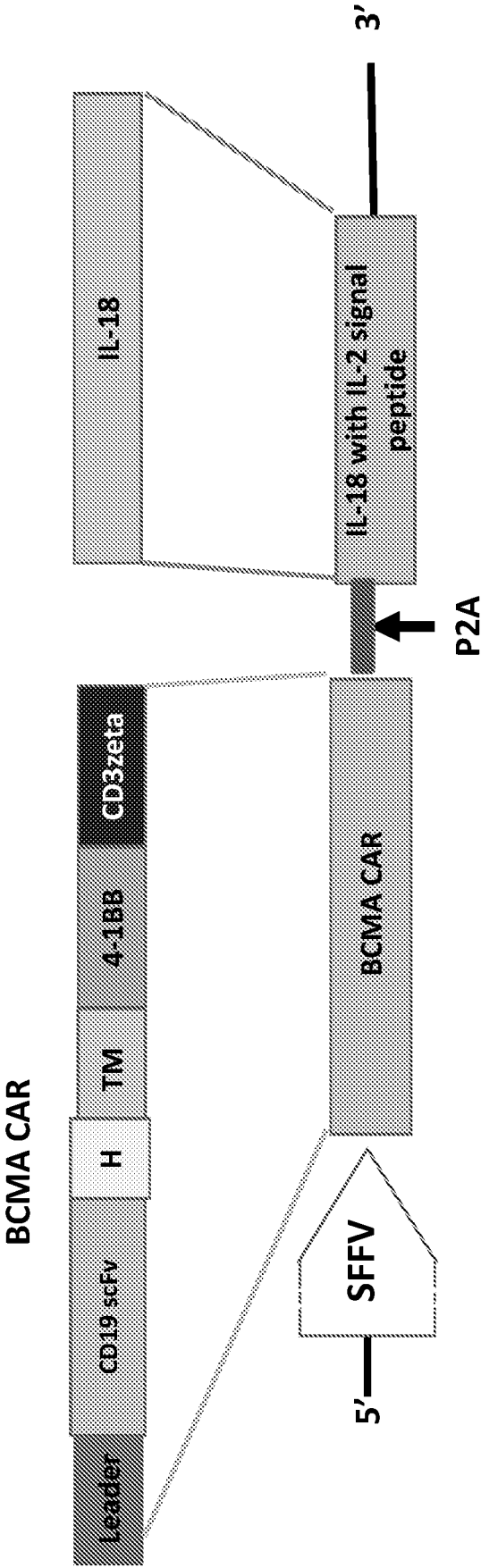


Figure 35

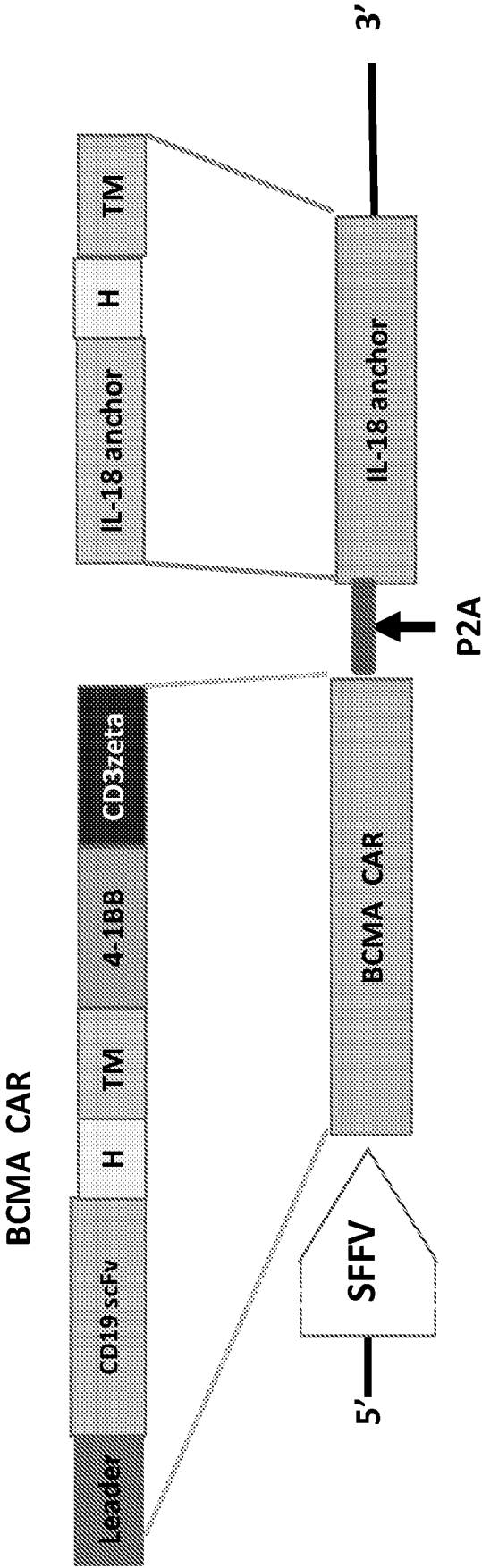


Figure 36

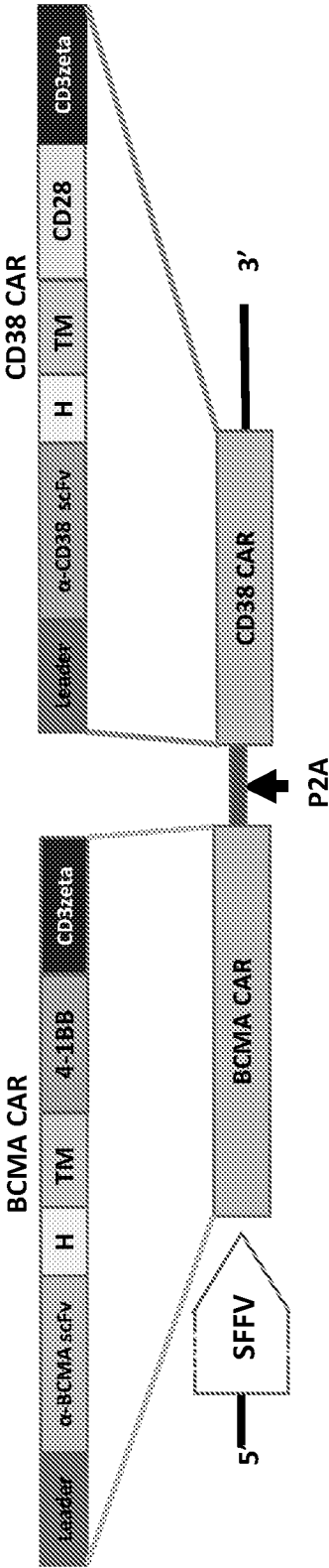


FIGURE 37

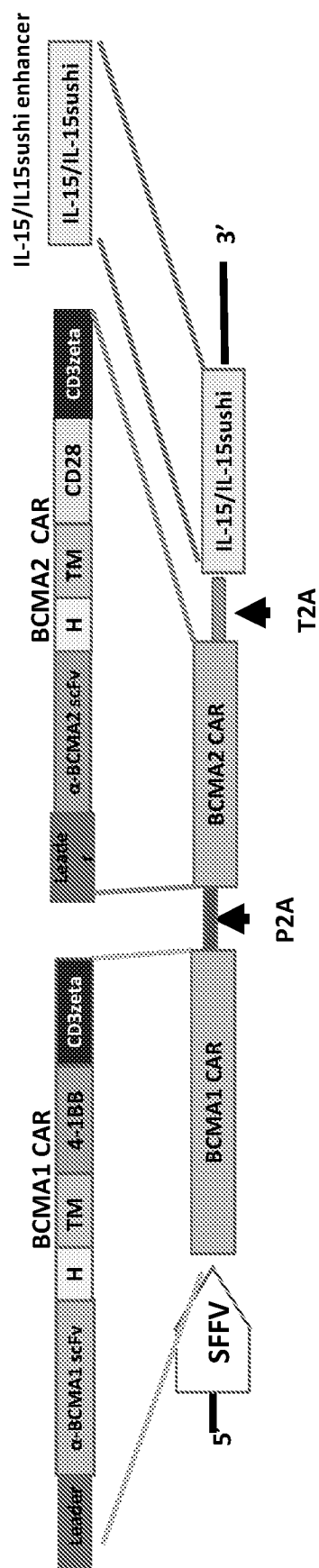


FIGURE 38

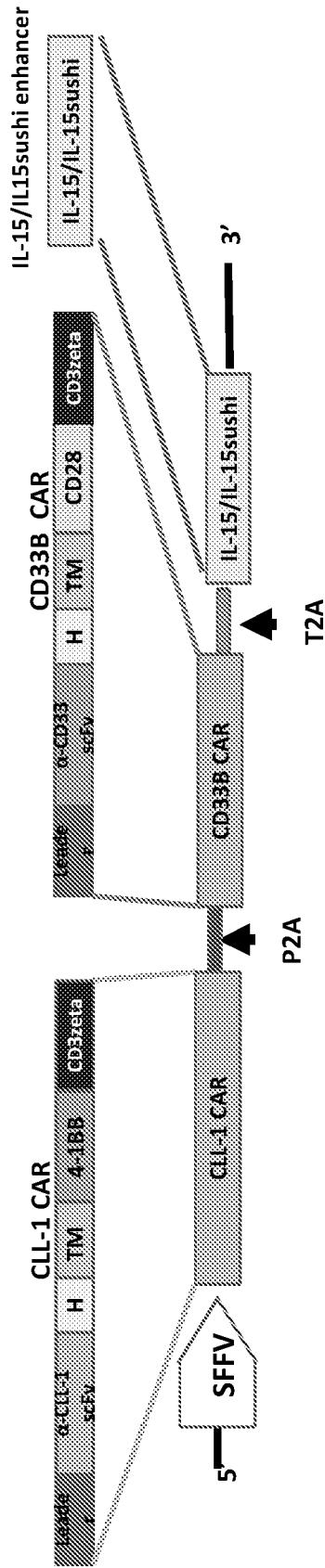


FIGURE 39A

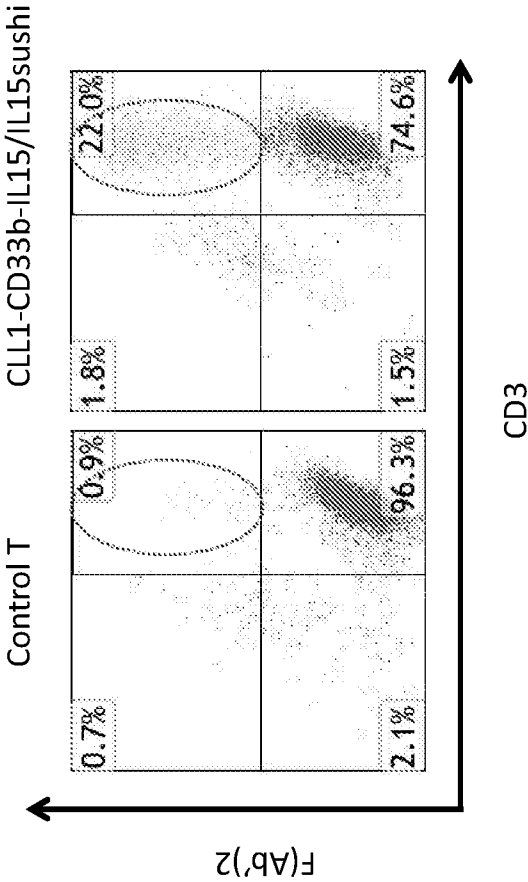


FIGURE 39B

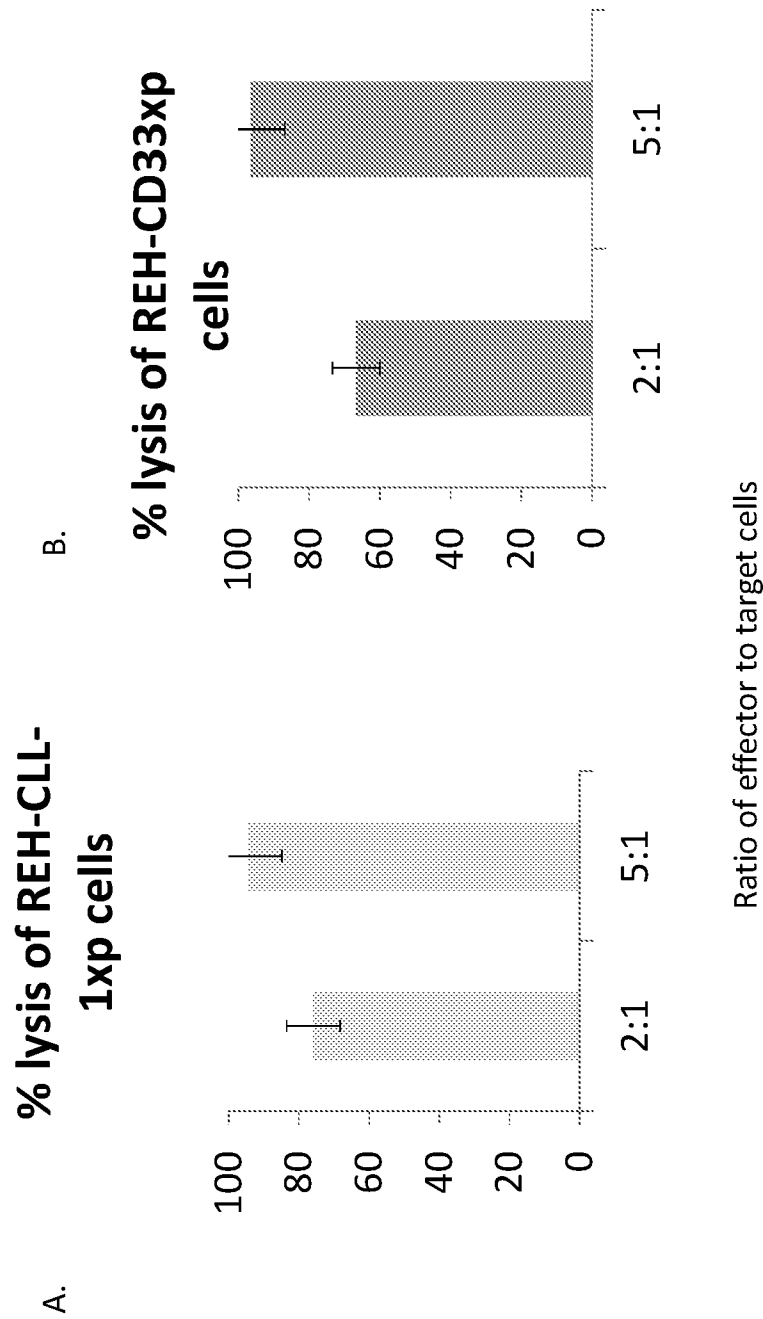


FIGURE 39C

MOLM13-luciferase cells; 1x10e6, Day 4 exposure

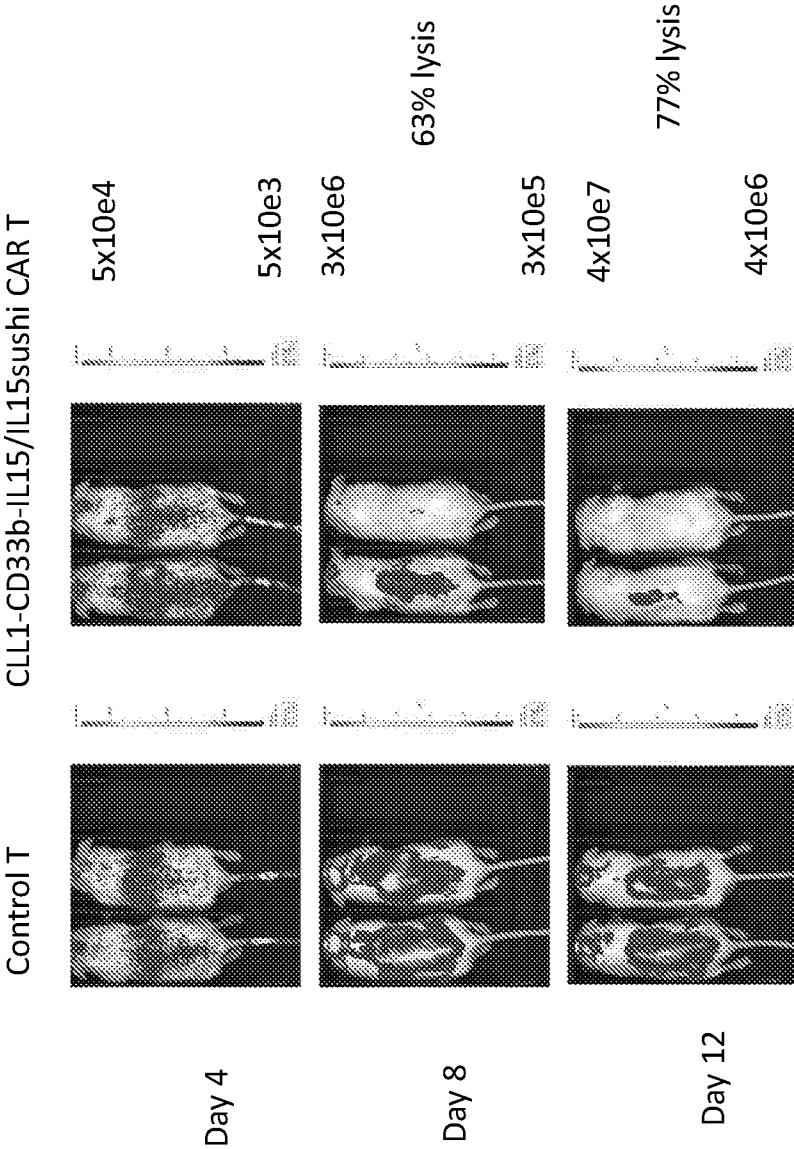


FIGURE 40A

MOLM13-luciferase cells; 1x10e6 , Day 4 exposure

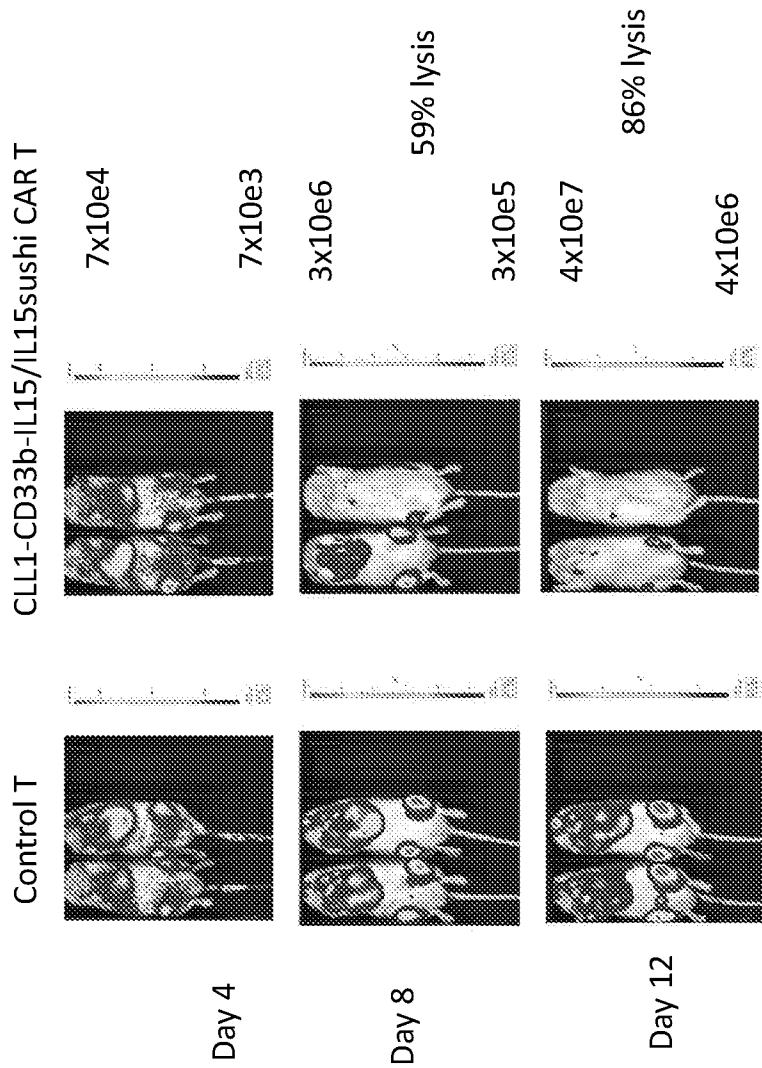


FIGURE 40B

Mouse peripheral blood

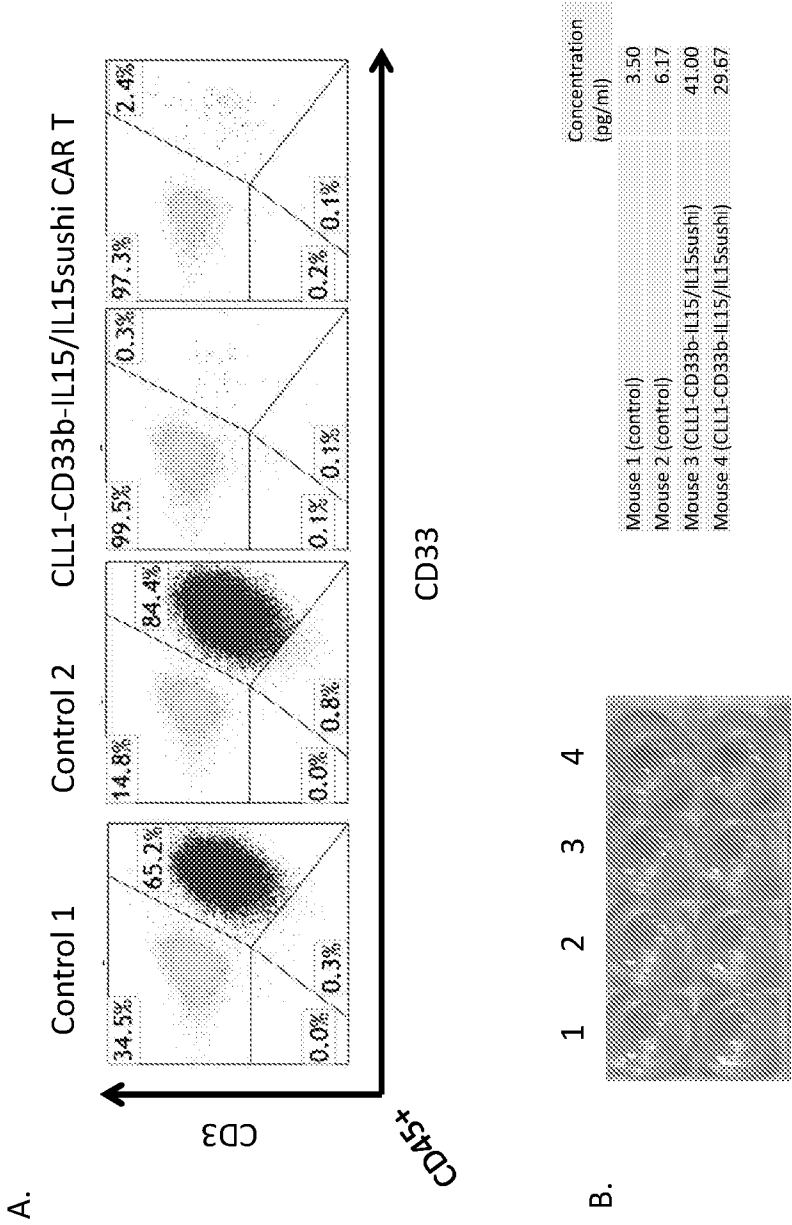


FIGURE 40C

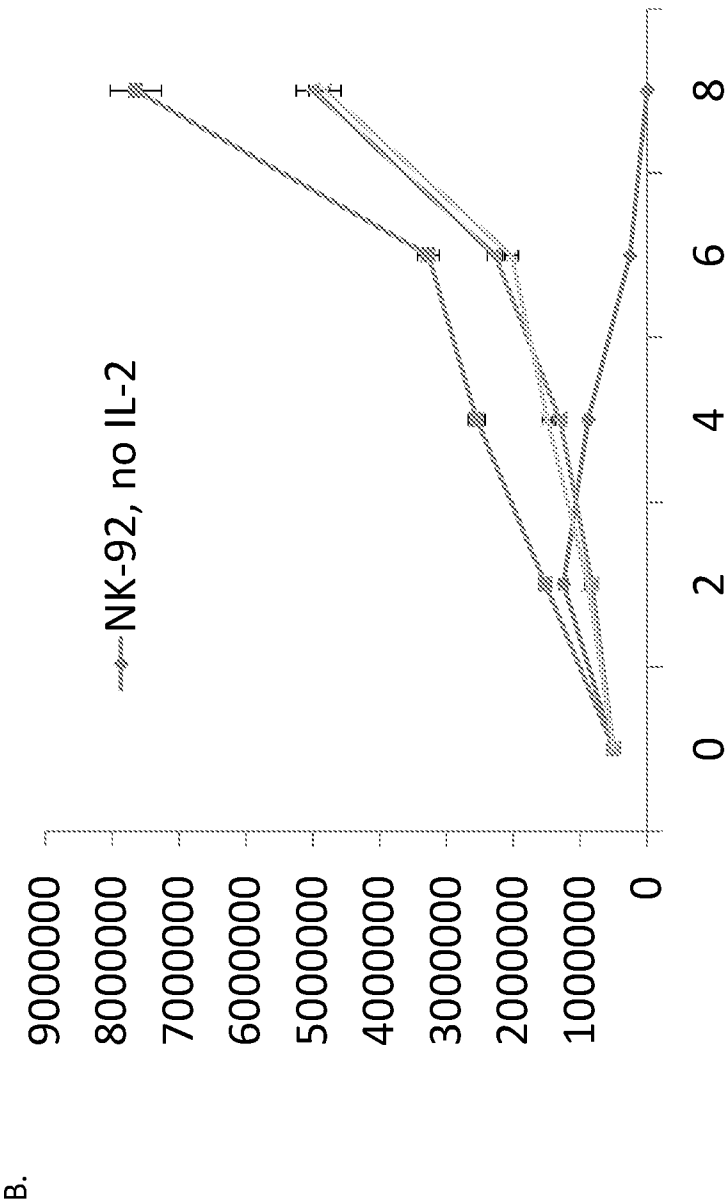
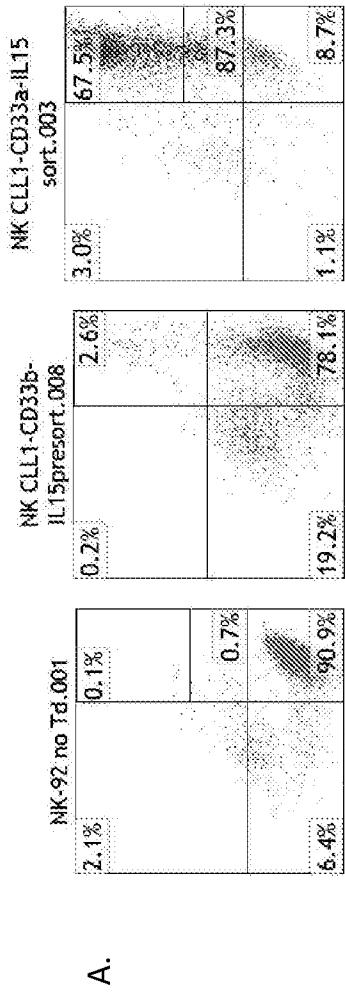


FIGURE 40D

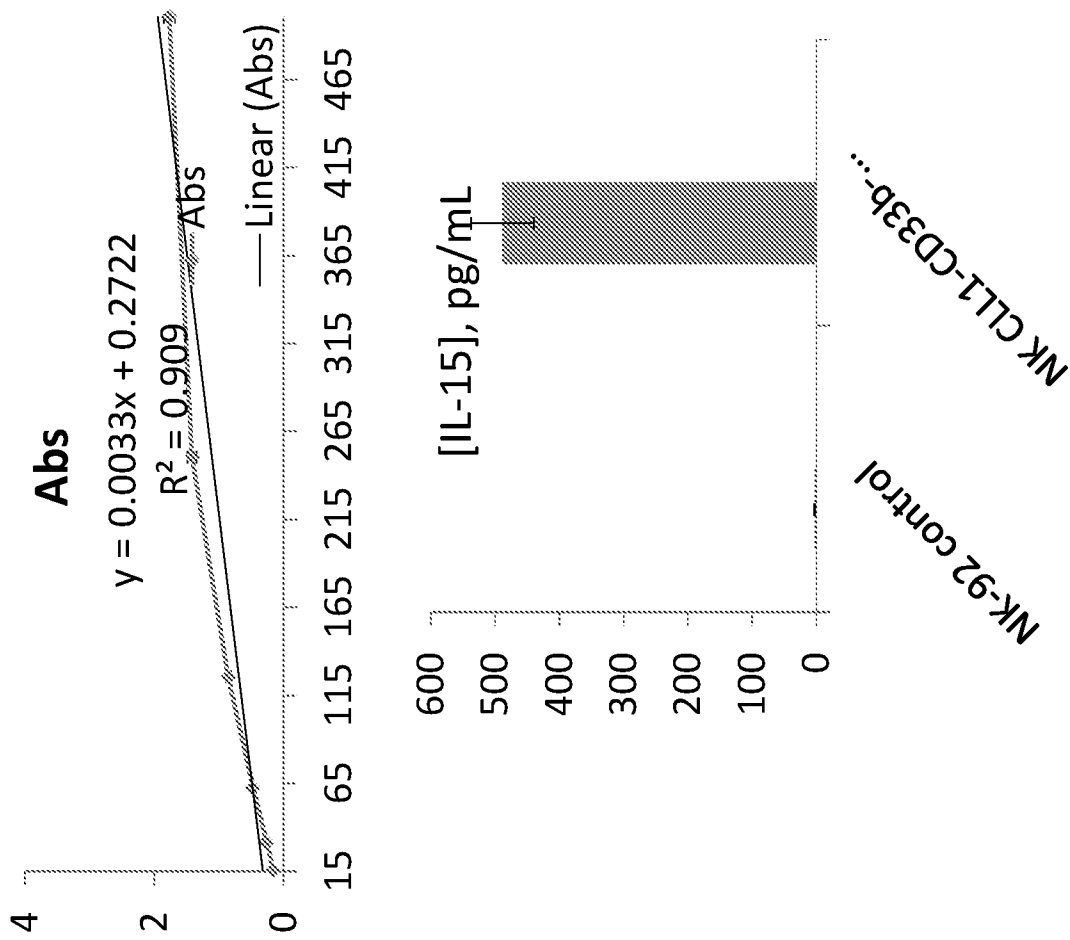


FIGURE 40E

CAR expression in transduced T cells

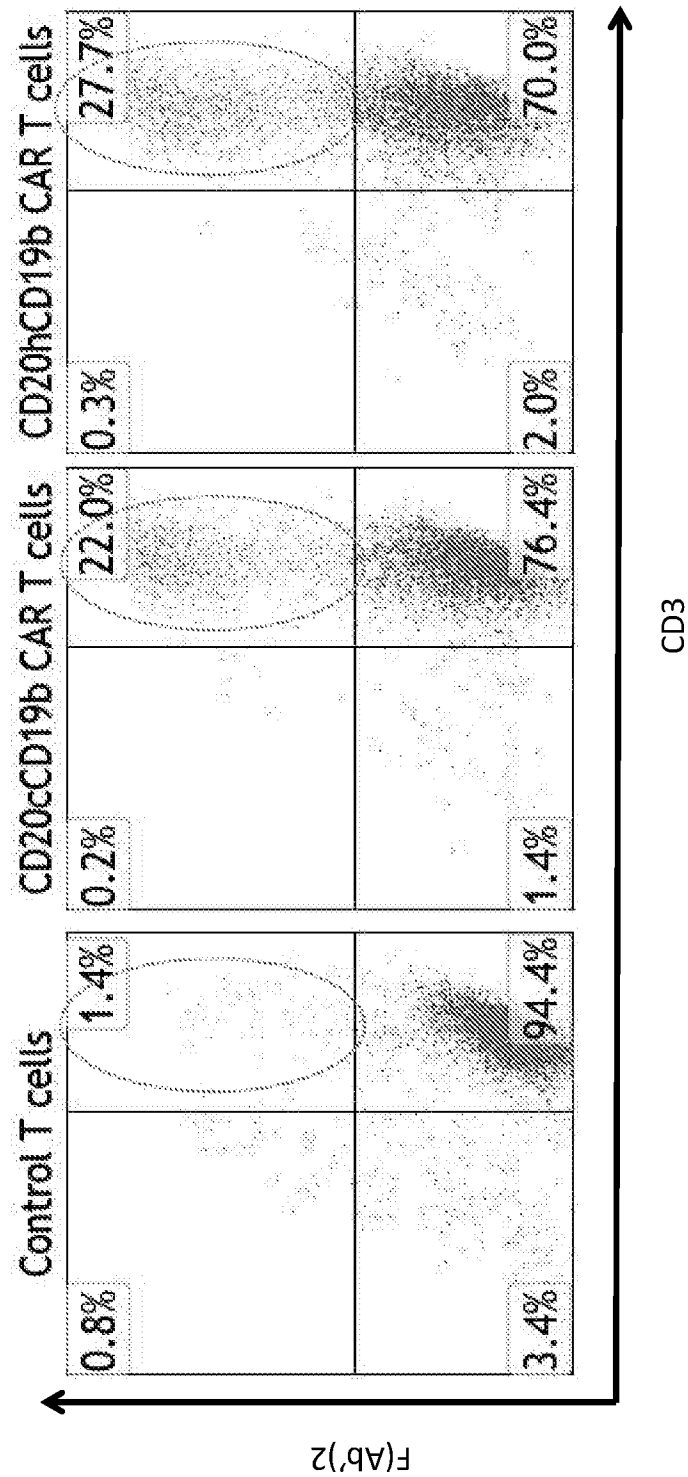


Figure 41A

CD20CD19b CAR T cells do not lyse wild type K562 cell line

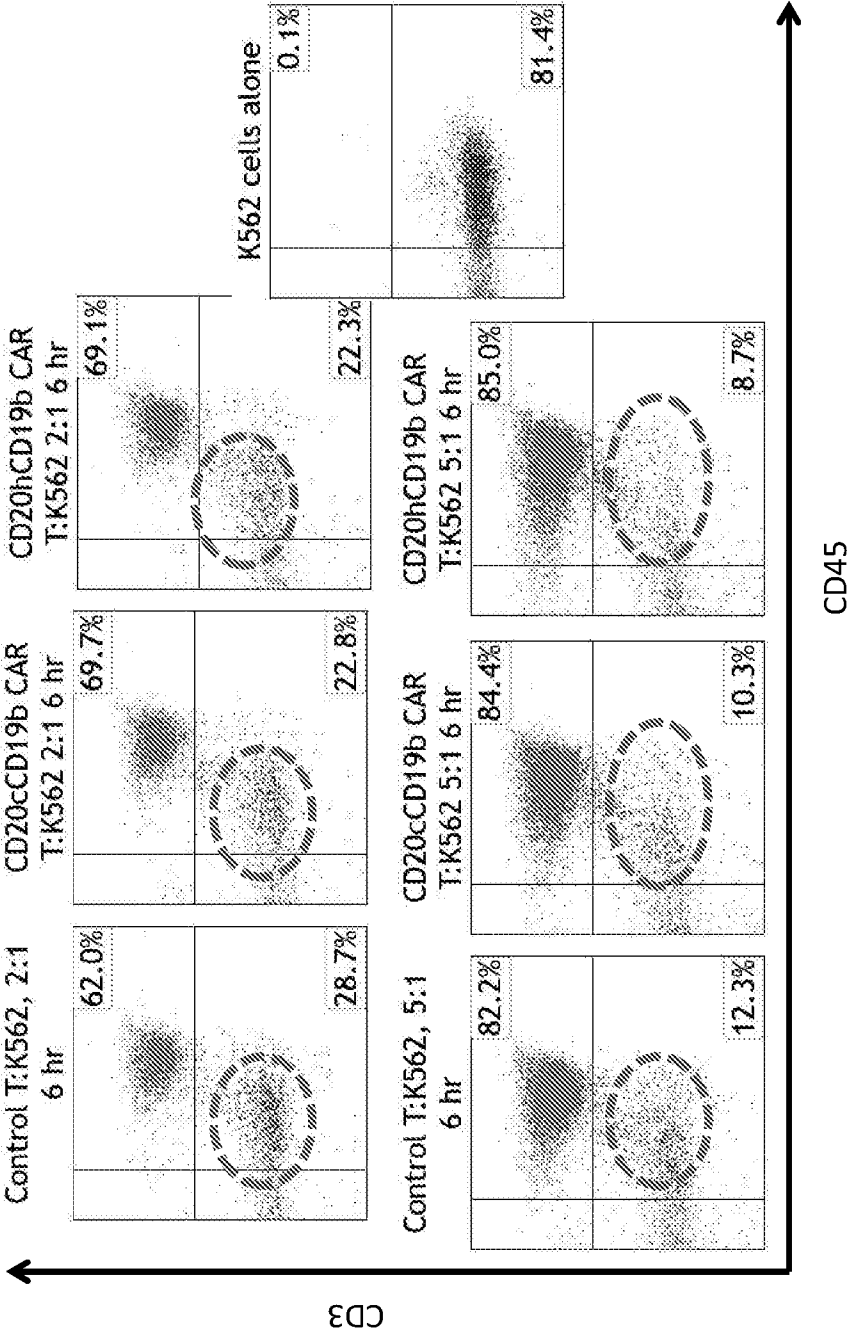


Figure 41B

CD20hCD19b CAR T cells completely lyse K562 cell line
synthetically expressing CD19 antigen

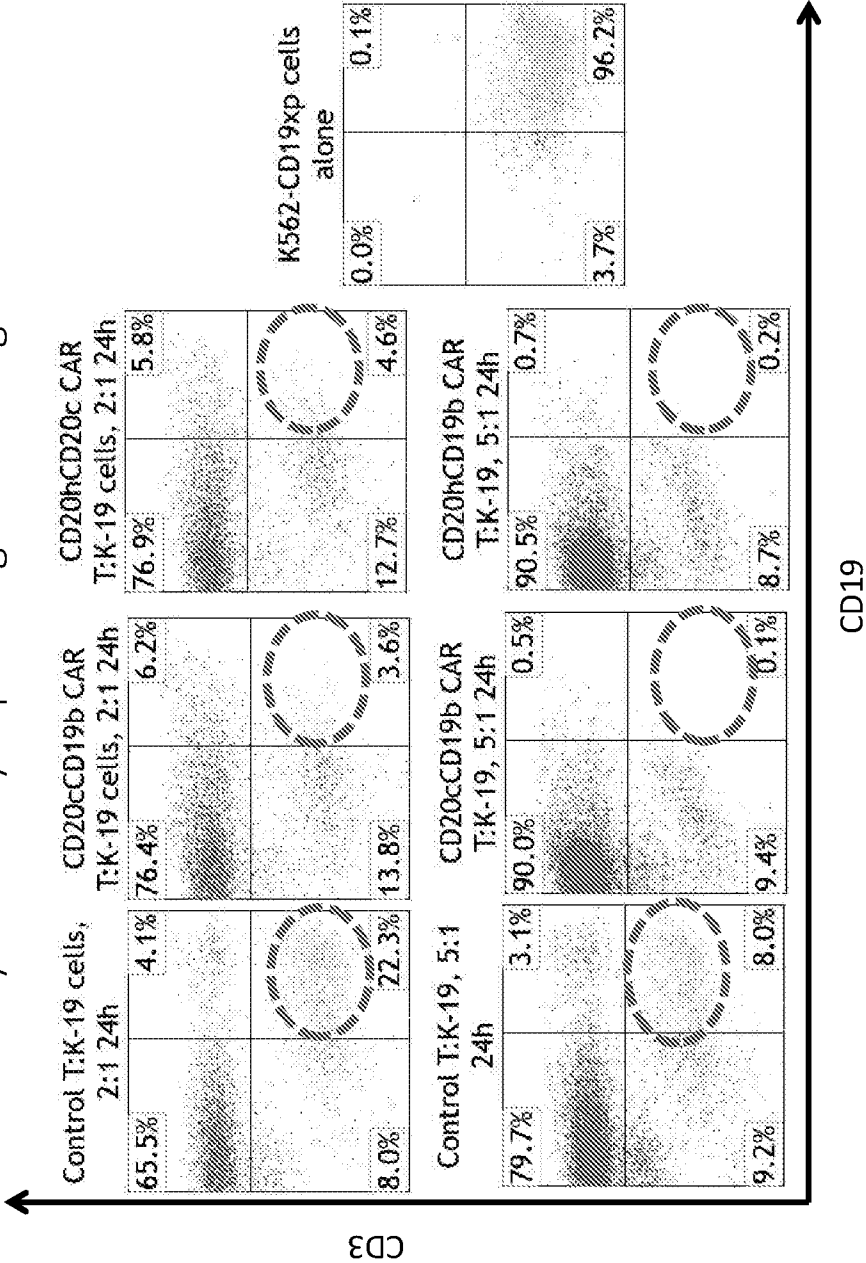


Figure 41C

CD20hCD19b CAR T cells completely lyse K562 cell line
synthetically expressing CD20 antigen

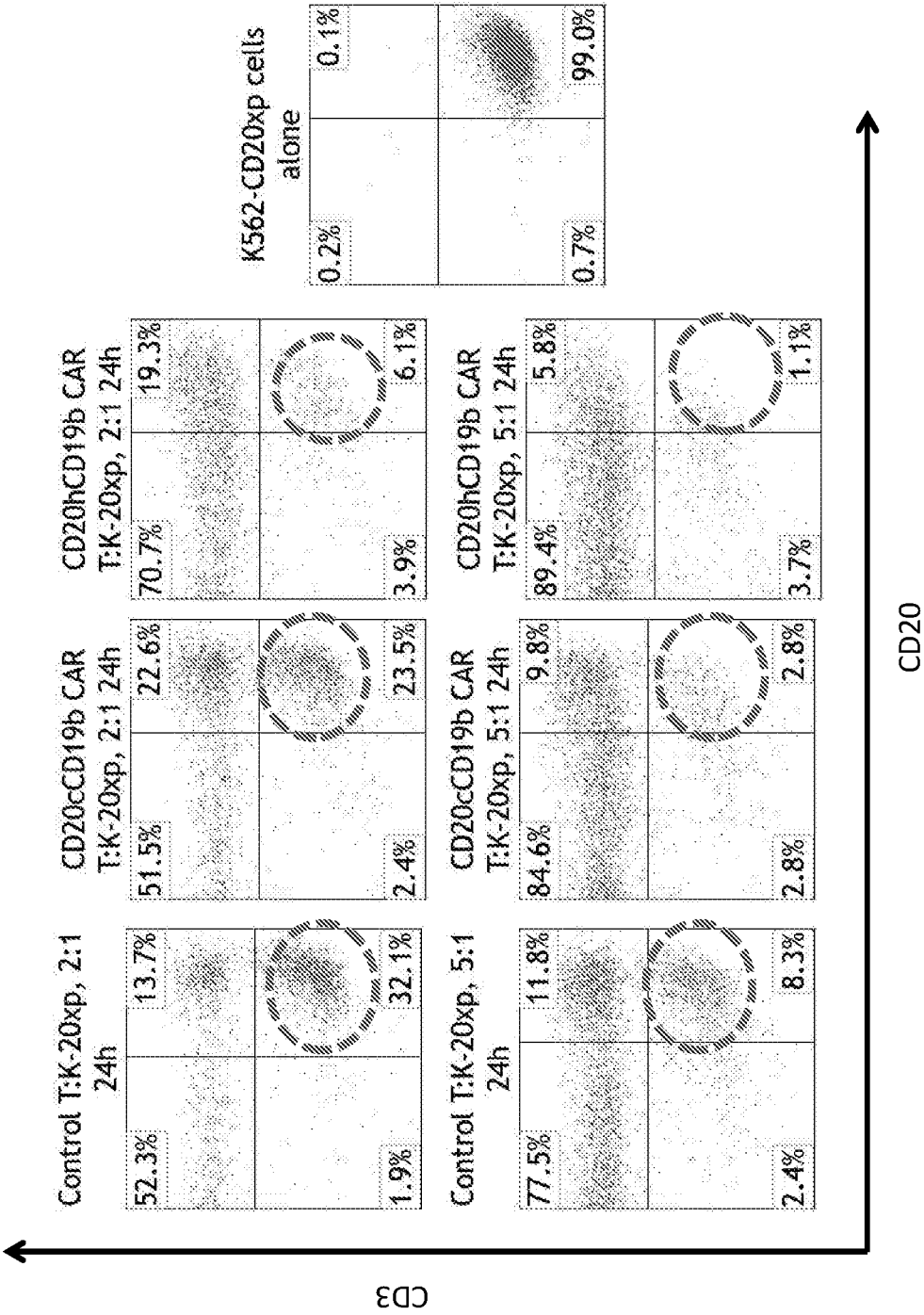


Figure 41D

CD20hCD19b CAR T cells completely lyse REH cell line

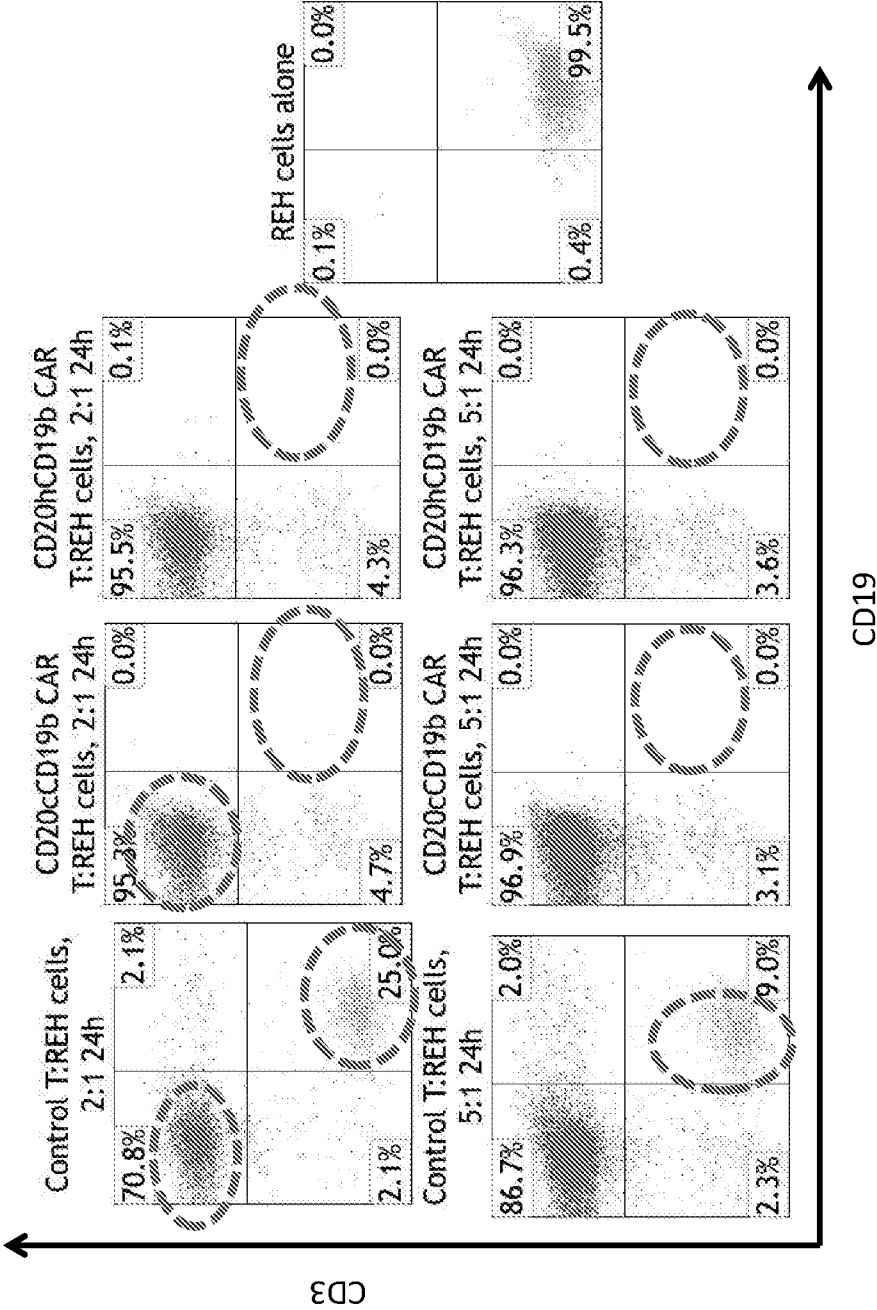


Figure 41E

CD20hCD19b CAR T cells completely lyse SP53 cell line

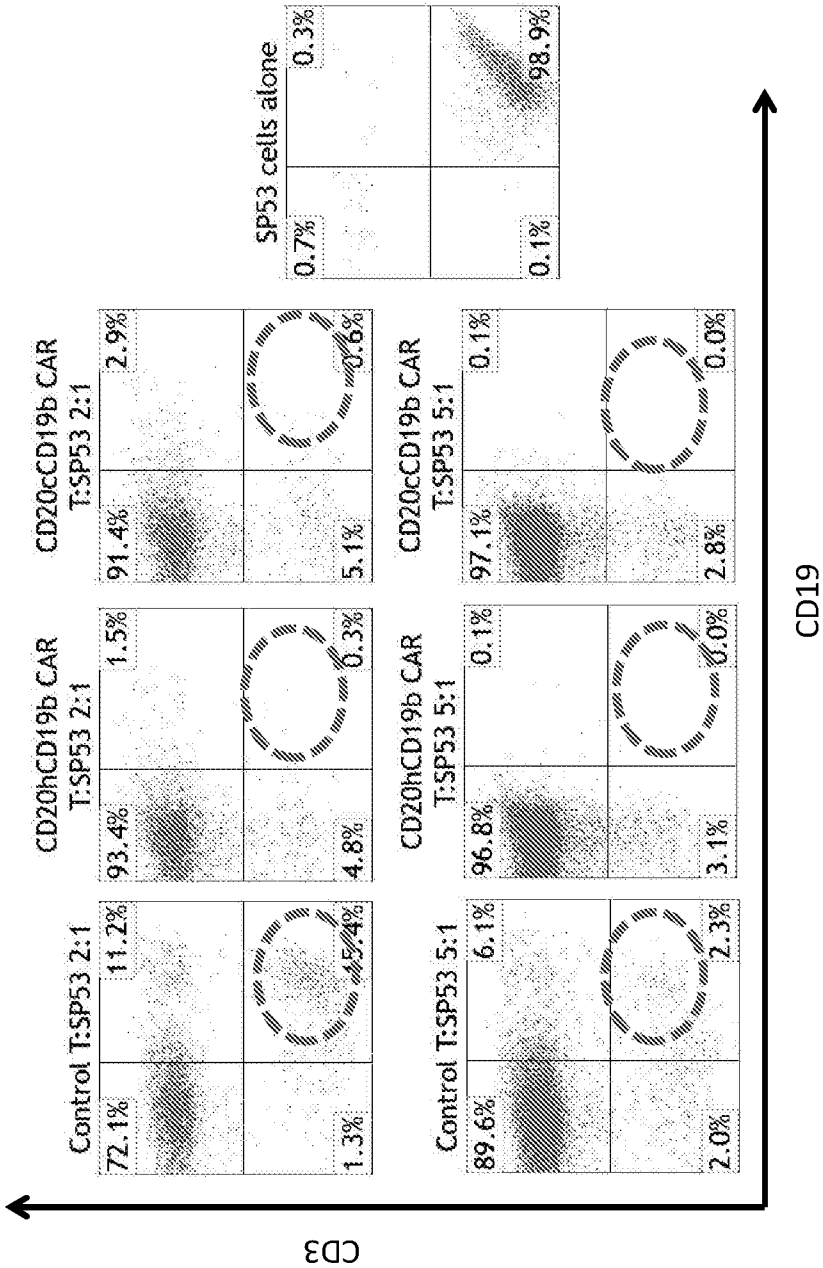


Figure 41F

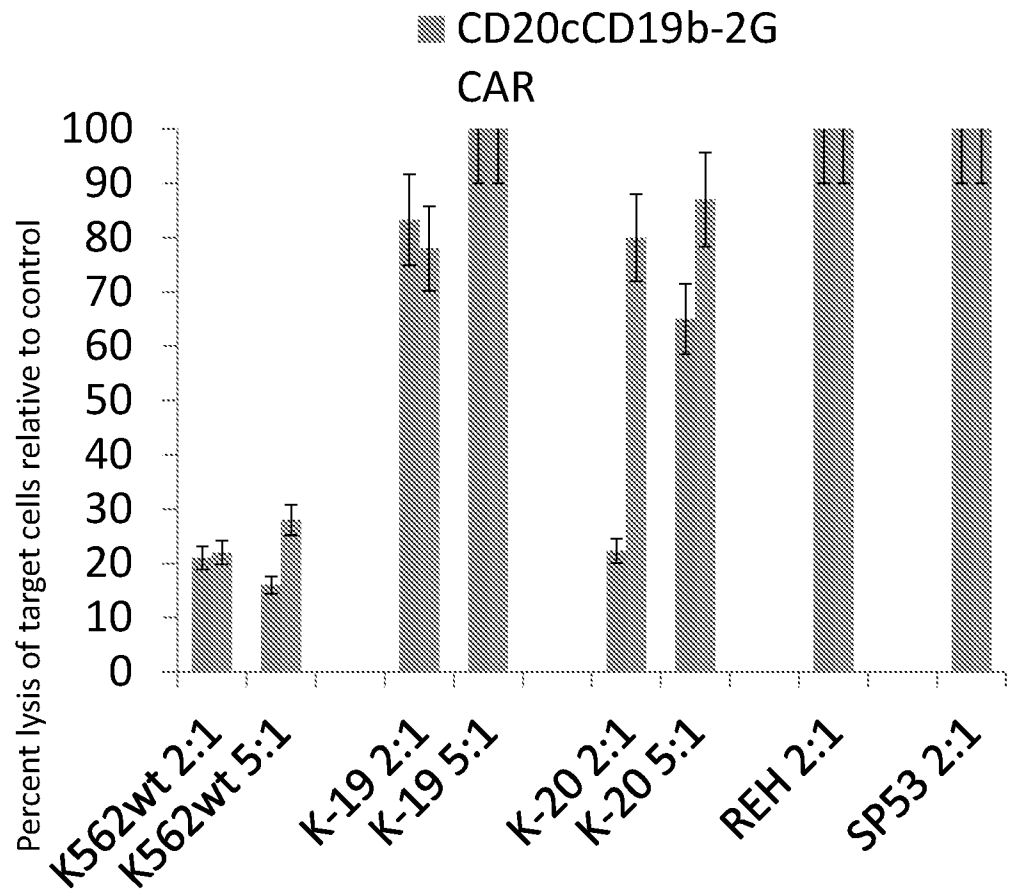
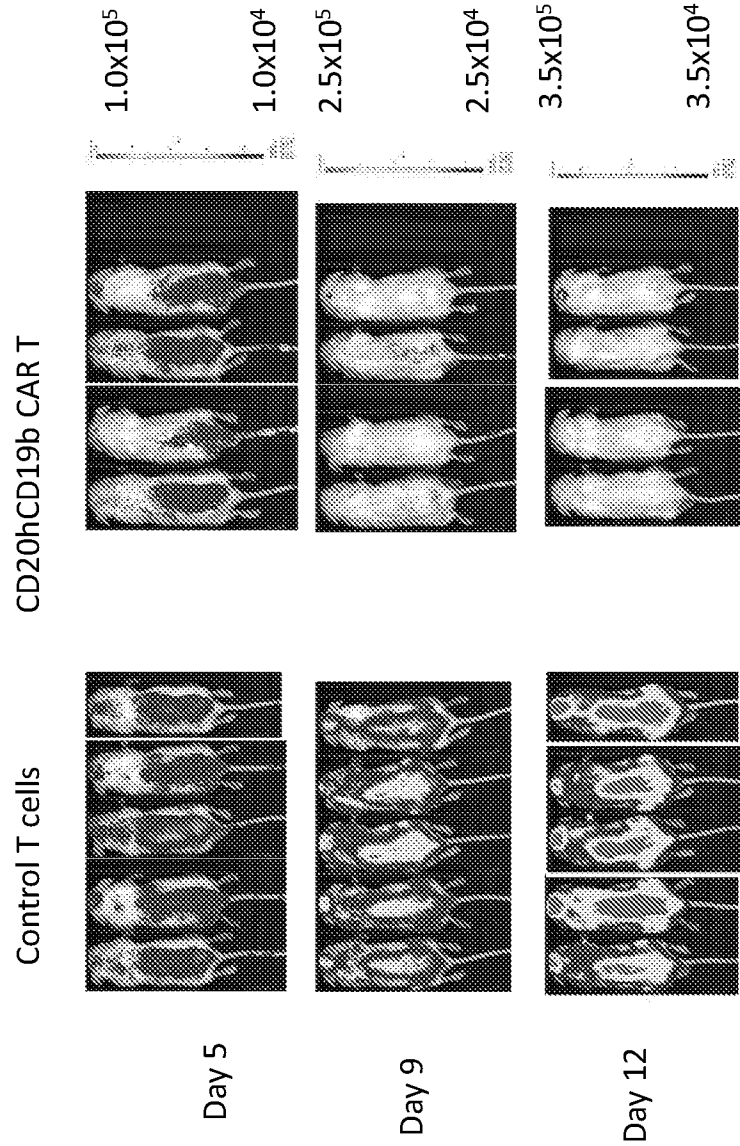


Figure 41G

In vivo – REH, CD20hCD19b cCAR T
DORSAL



Day 12 - 98% lysis, both dorsal and ventral

Figure 42A

In vivo – REH, CD20hCD19b cCAR T
VENTRAL

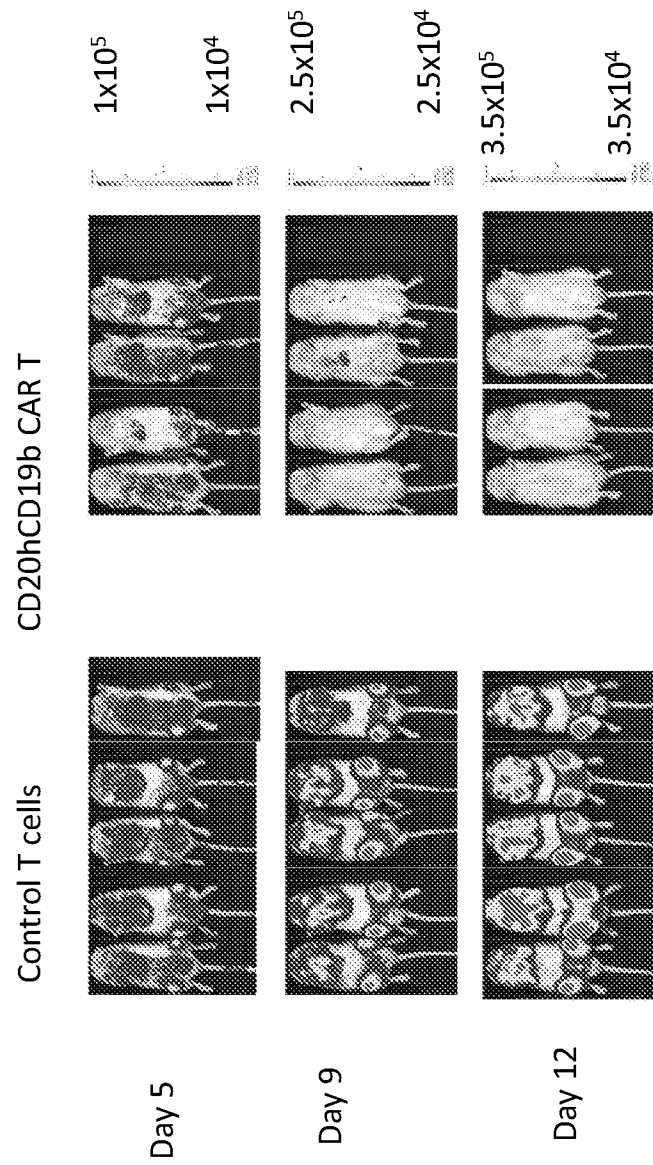


Figure 42B

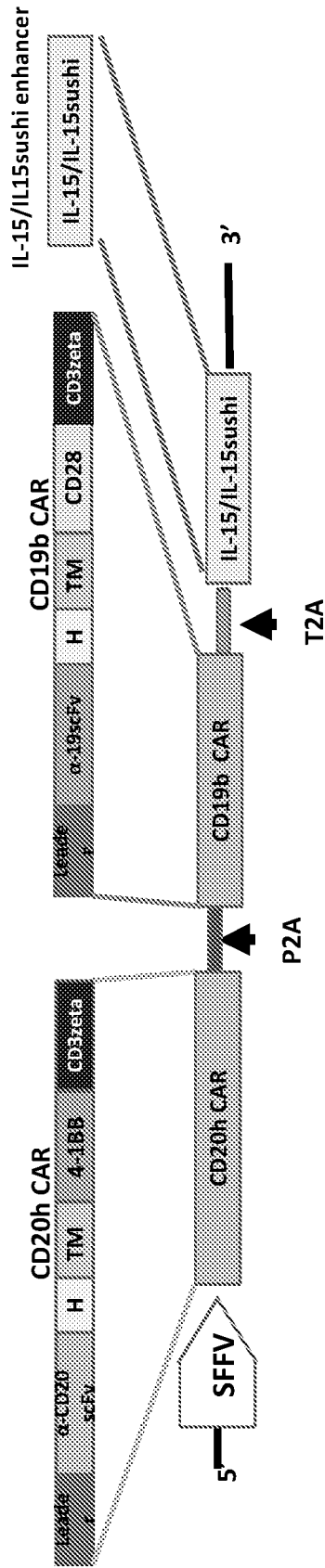


FIGURE 43A

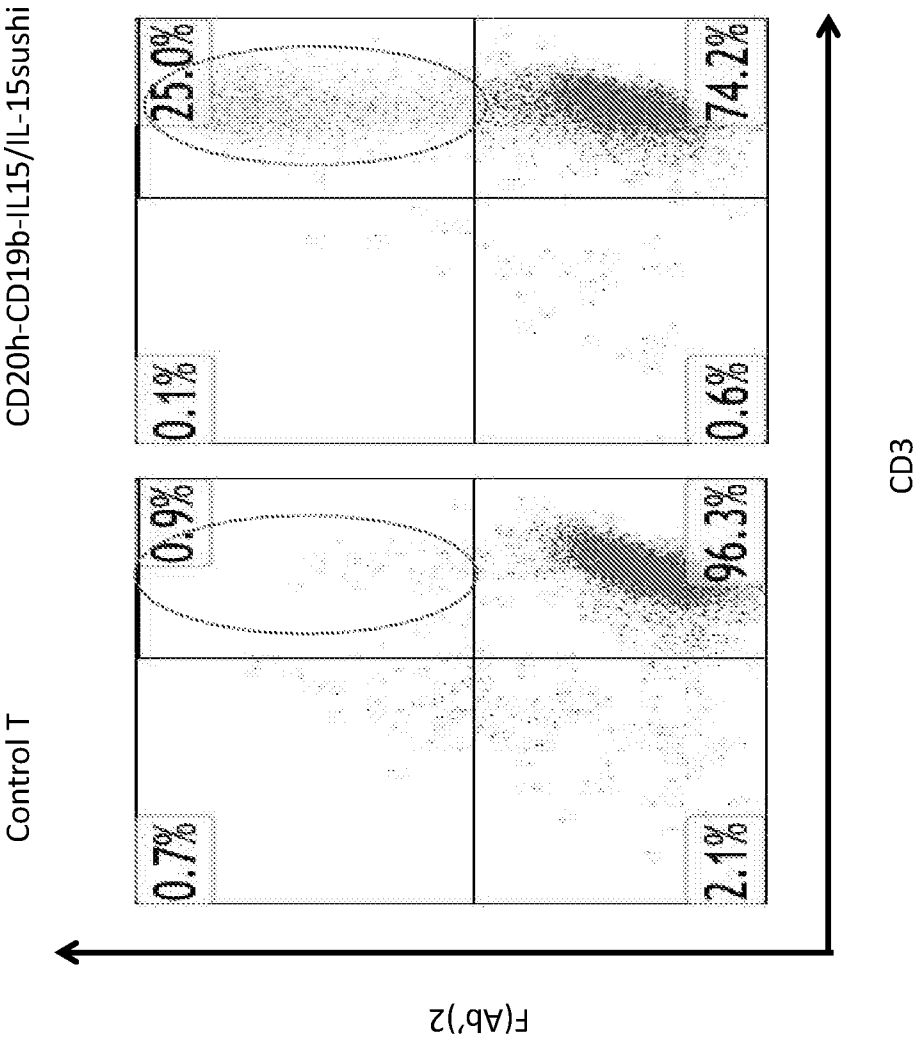


FIGURE 43B

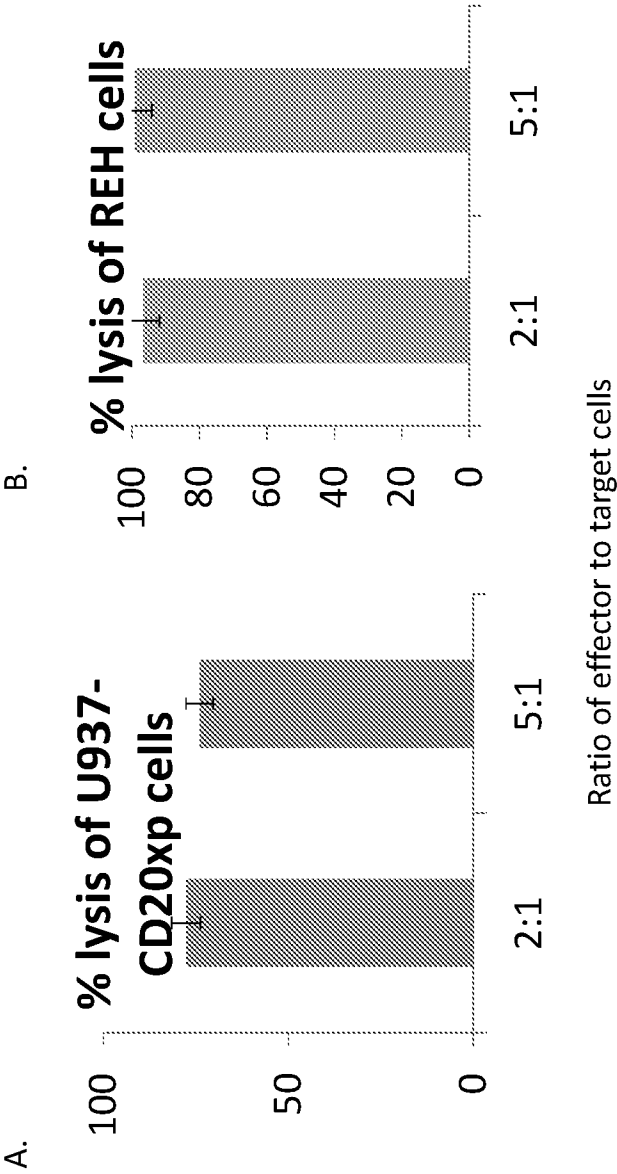


FIGURE 43C

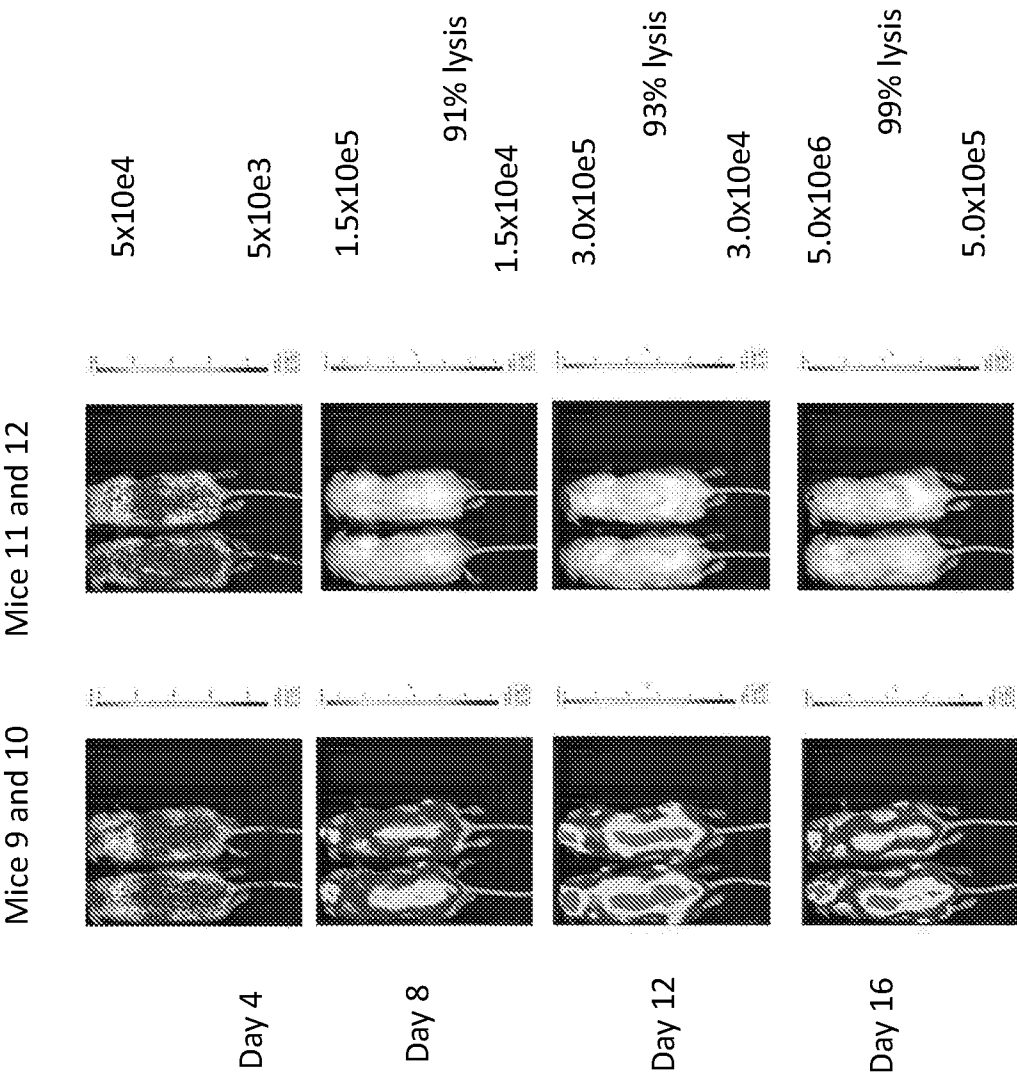


FIGURE 44A

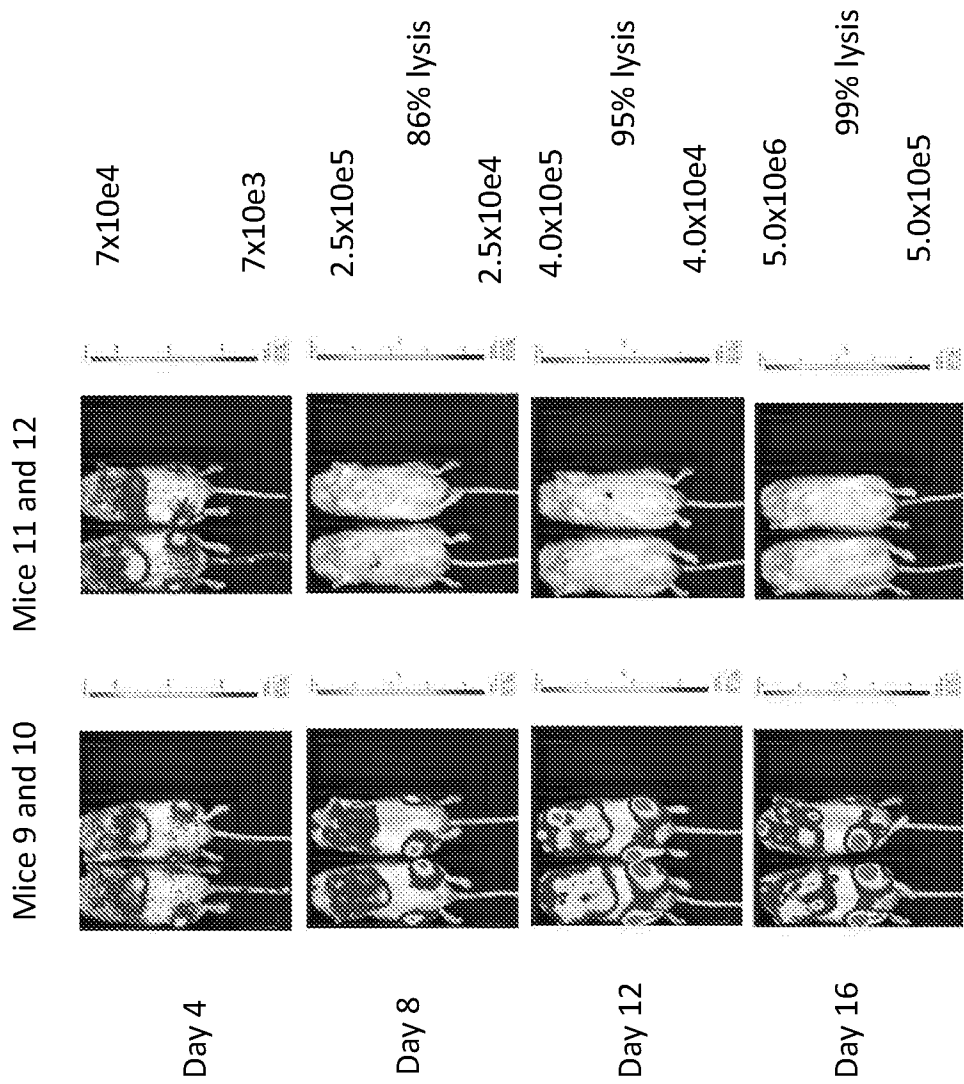


FIGURE 44B

Mouse peripheral blood

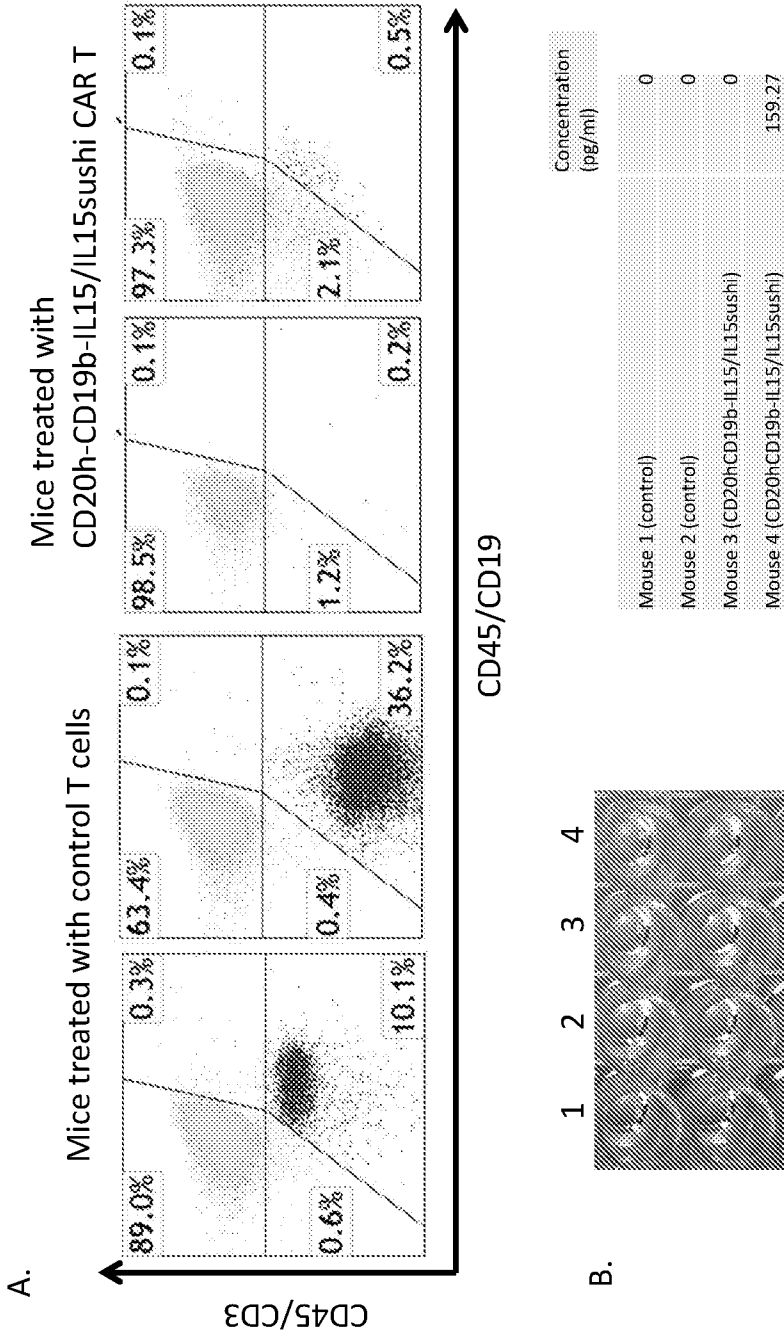


FIGURE 44C

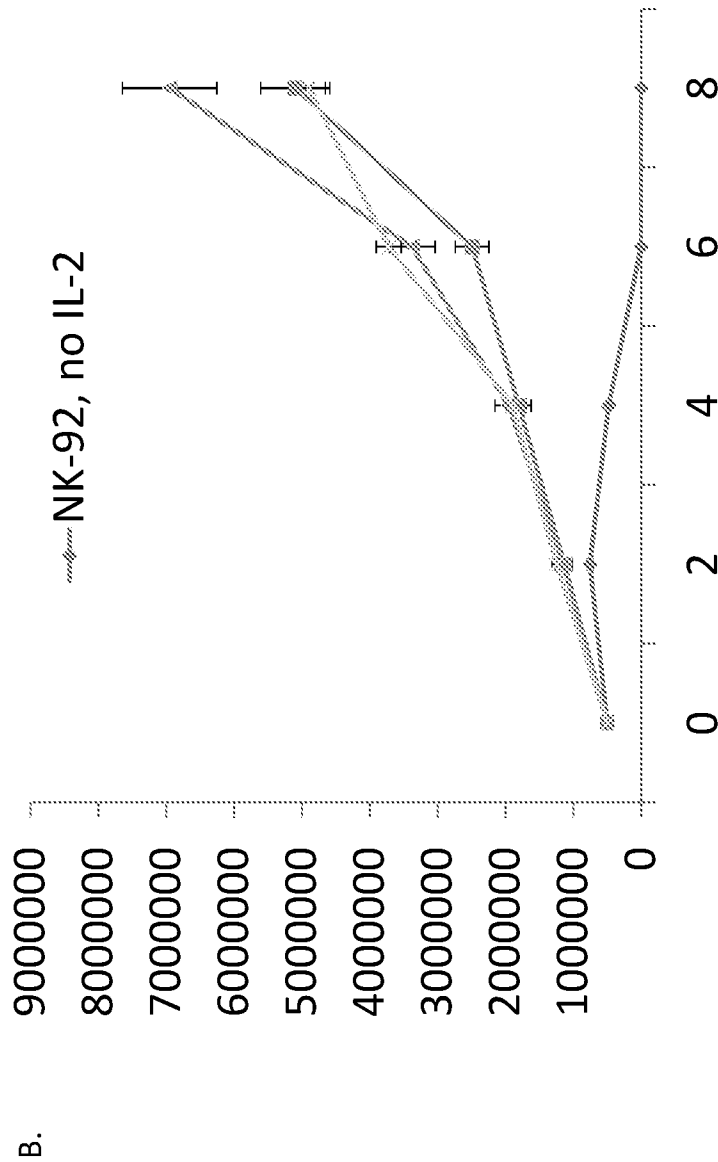
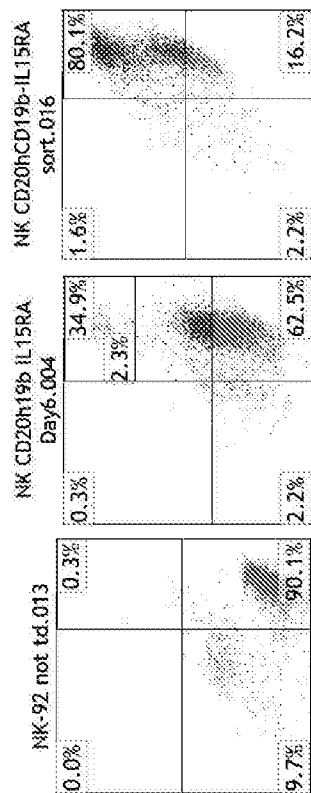


FIGURE 44D

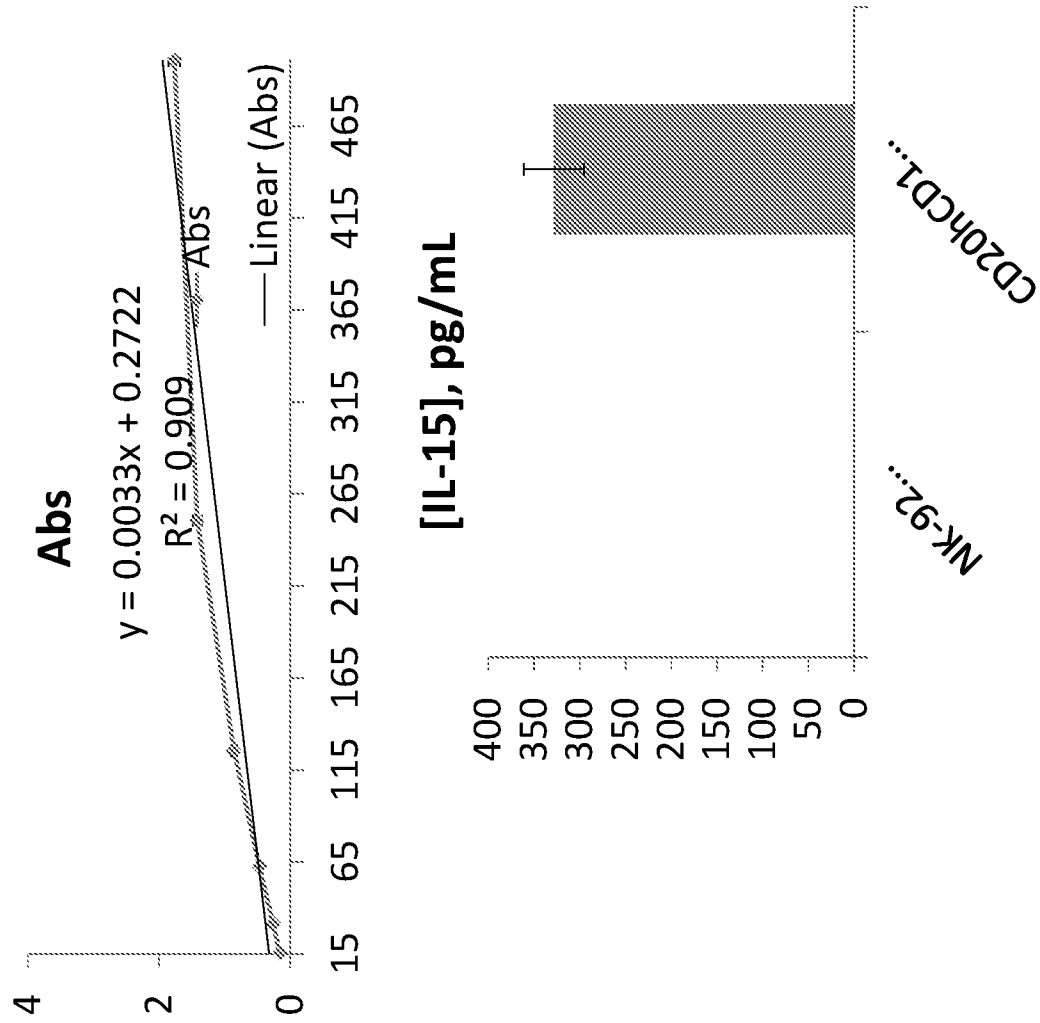


FIGURE 44E

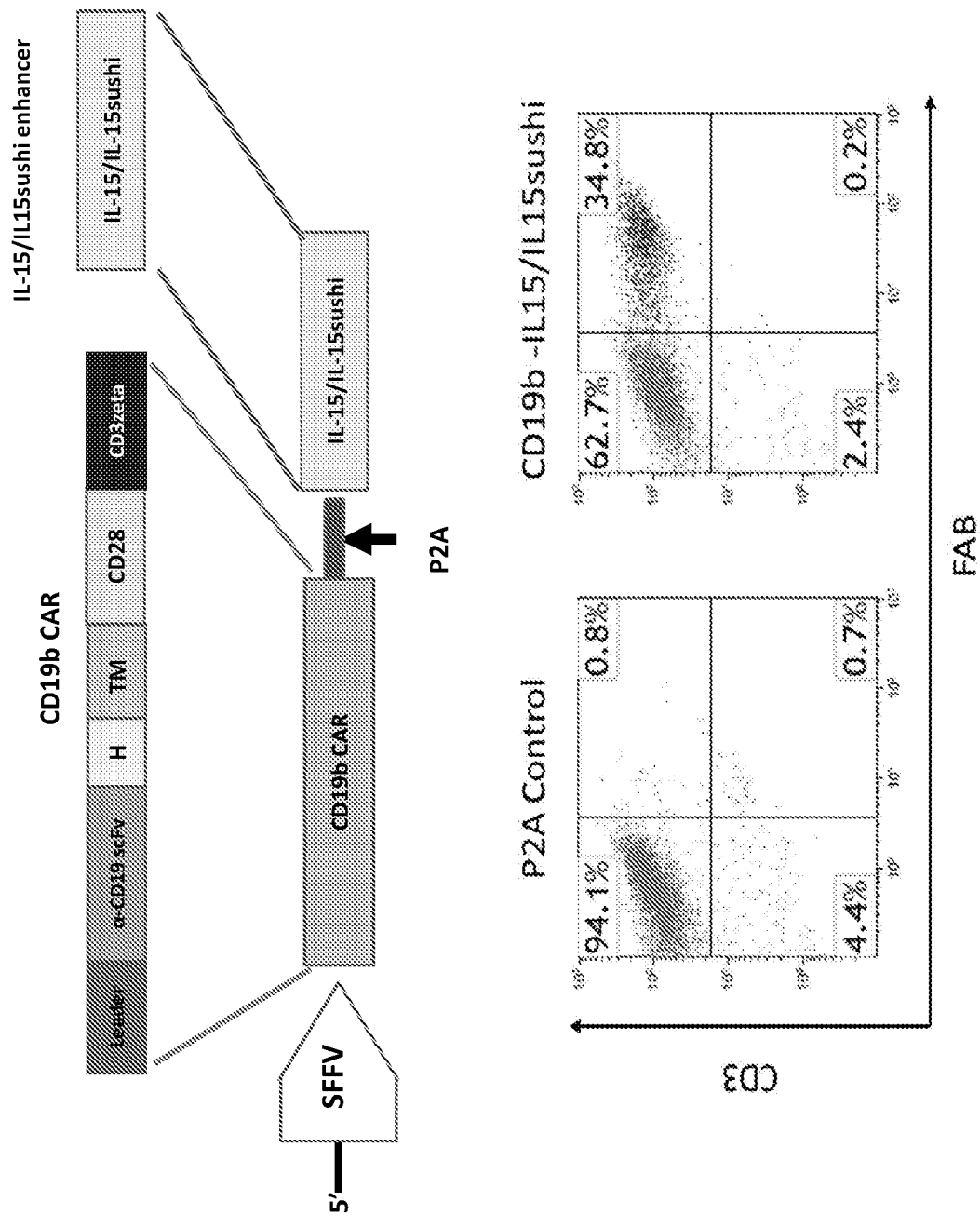


FIGURE 45A

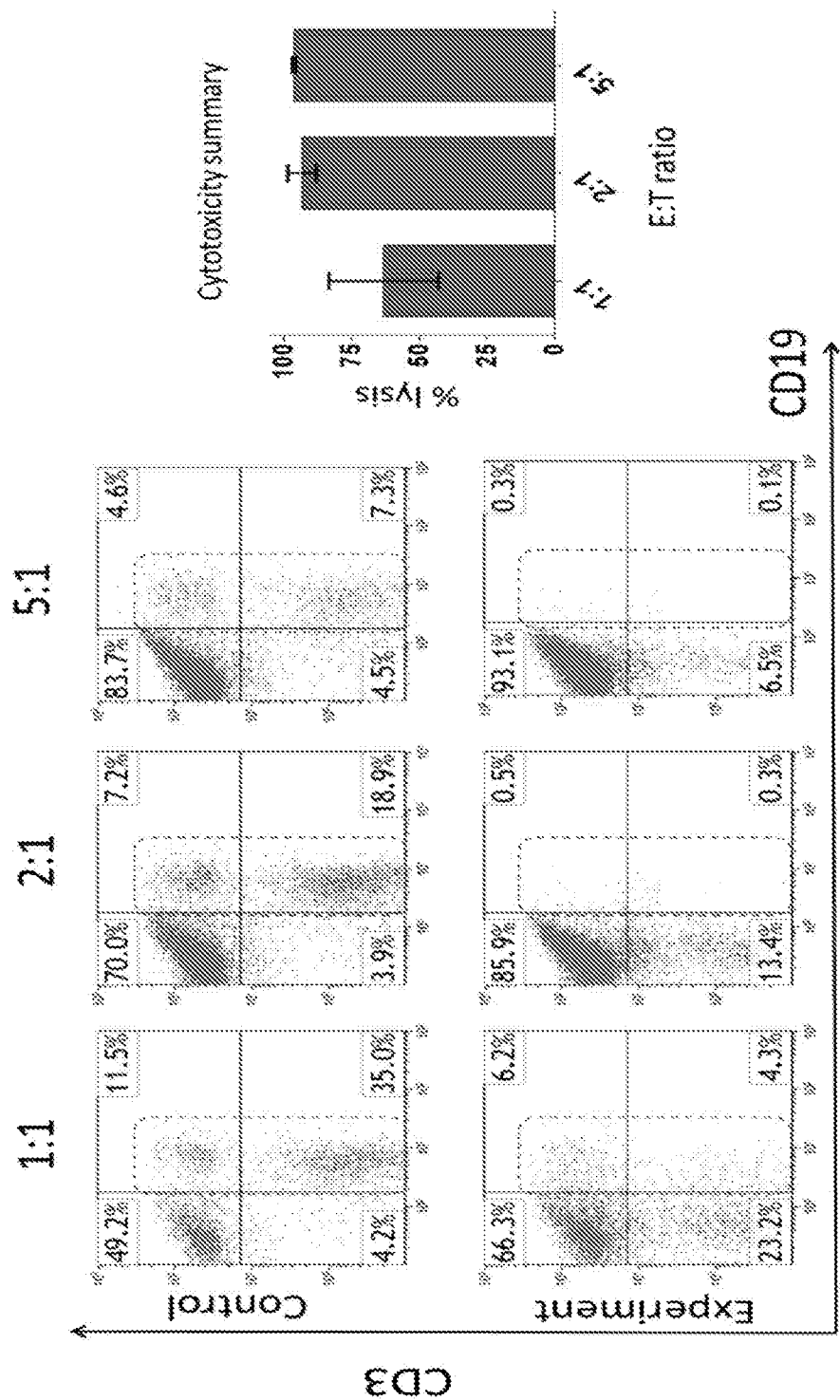


FIGURE 45B

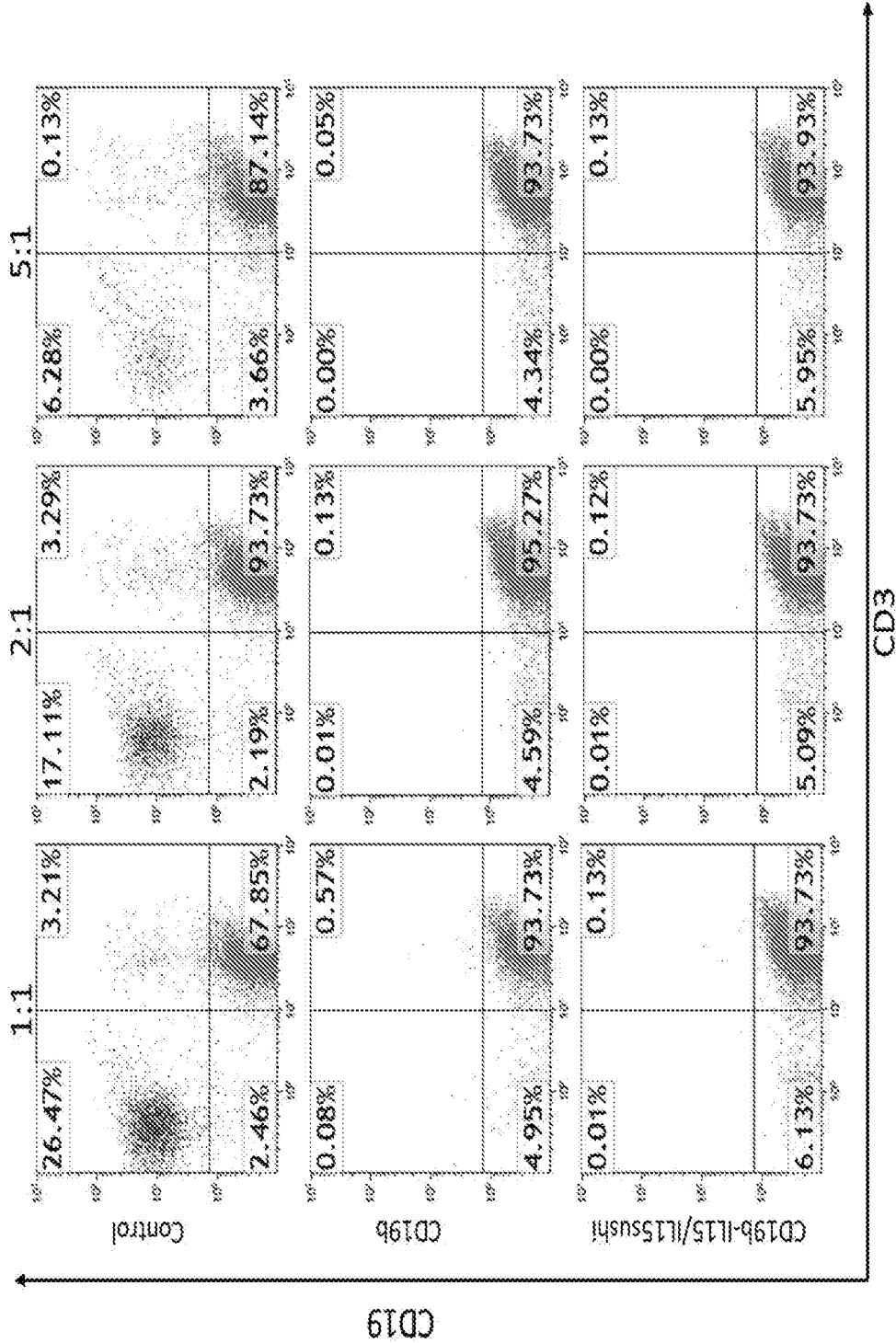


FIGURE 45C

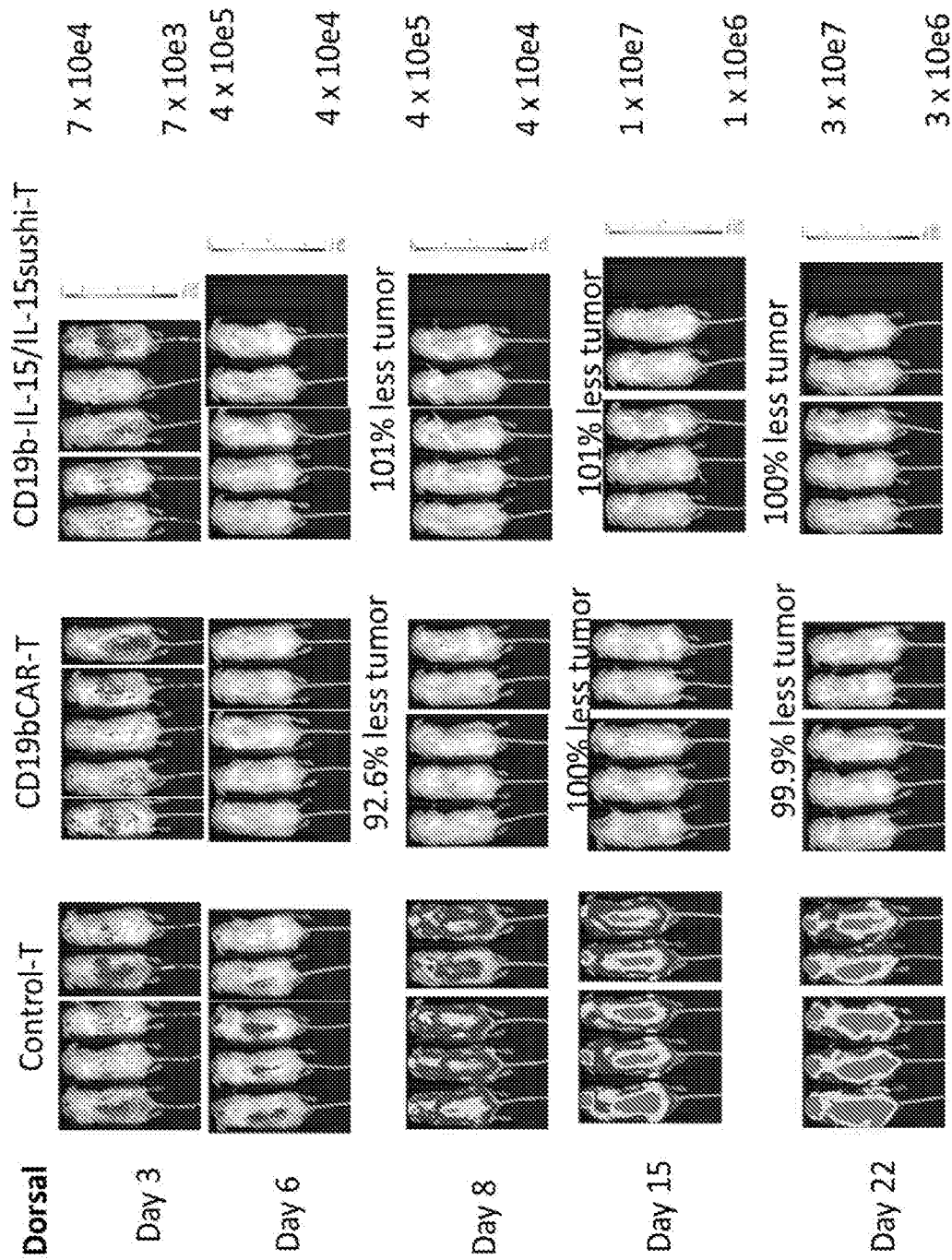


FIGURE 46A

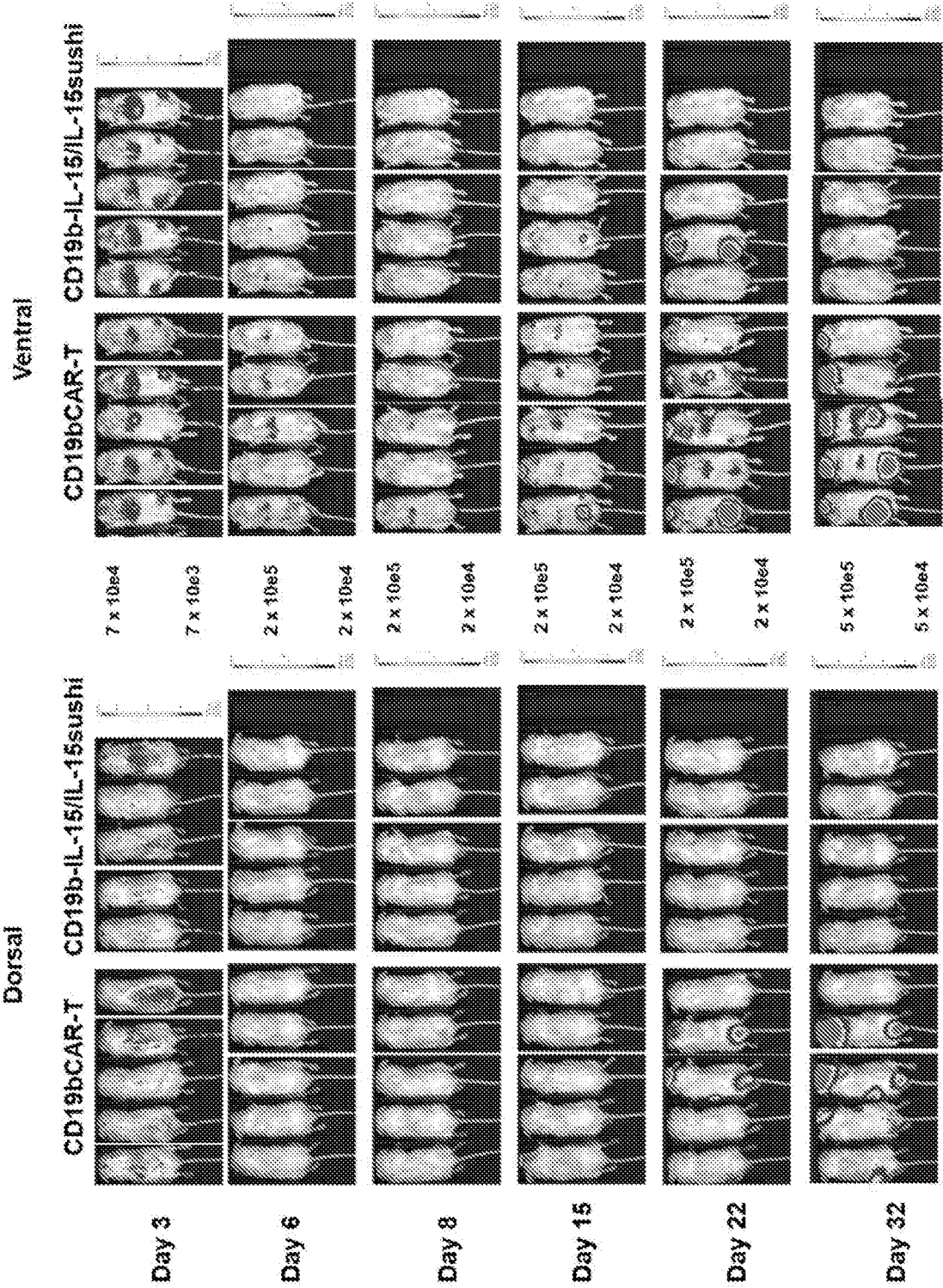


FIGURE 46B

IVIS data

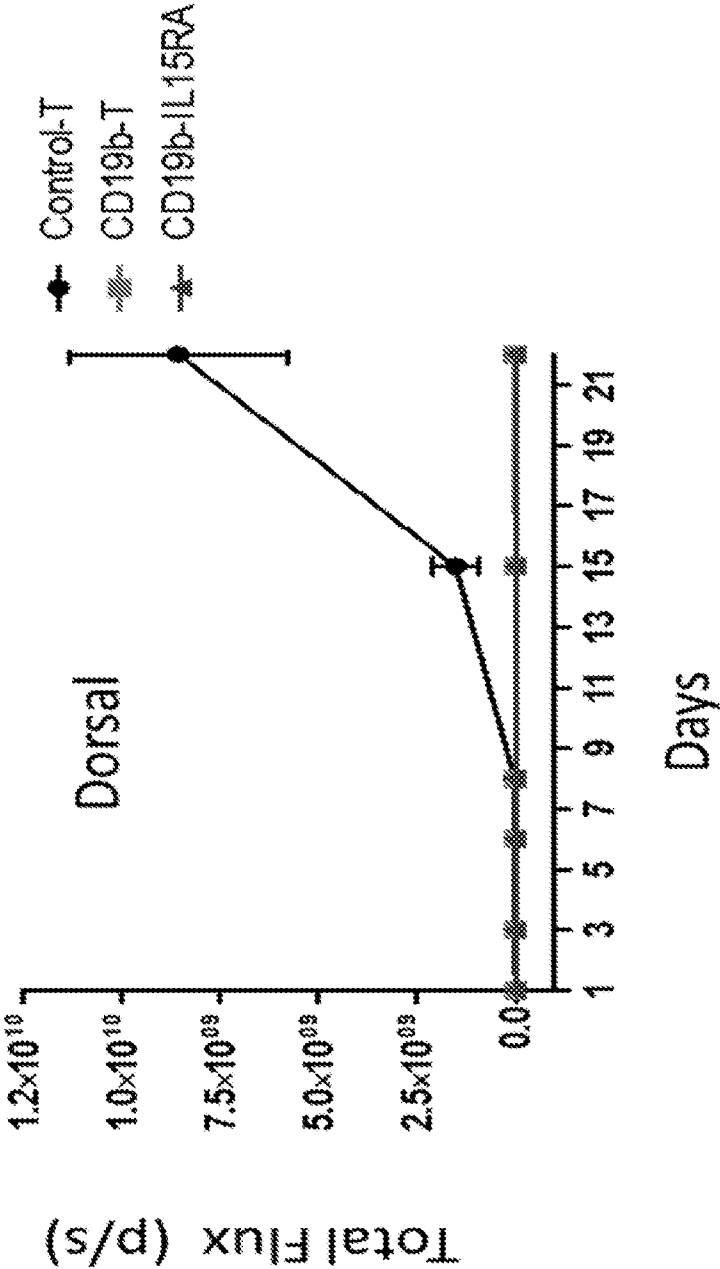


FIGURE 46C

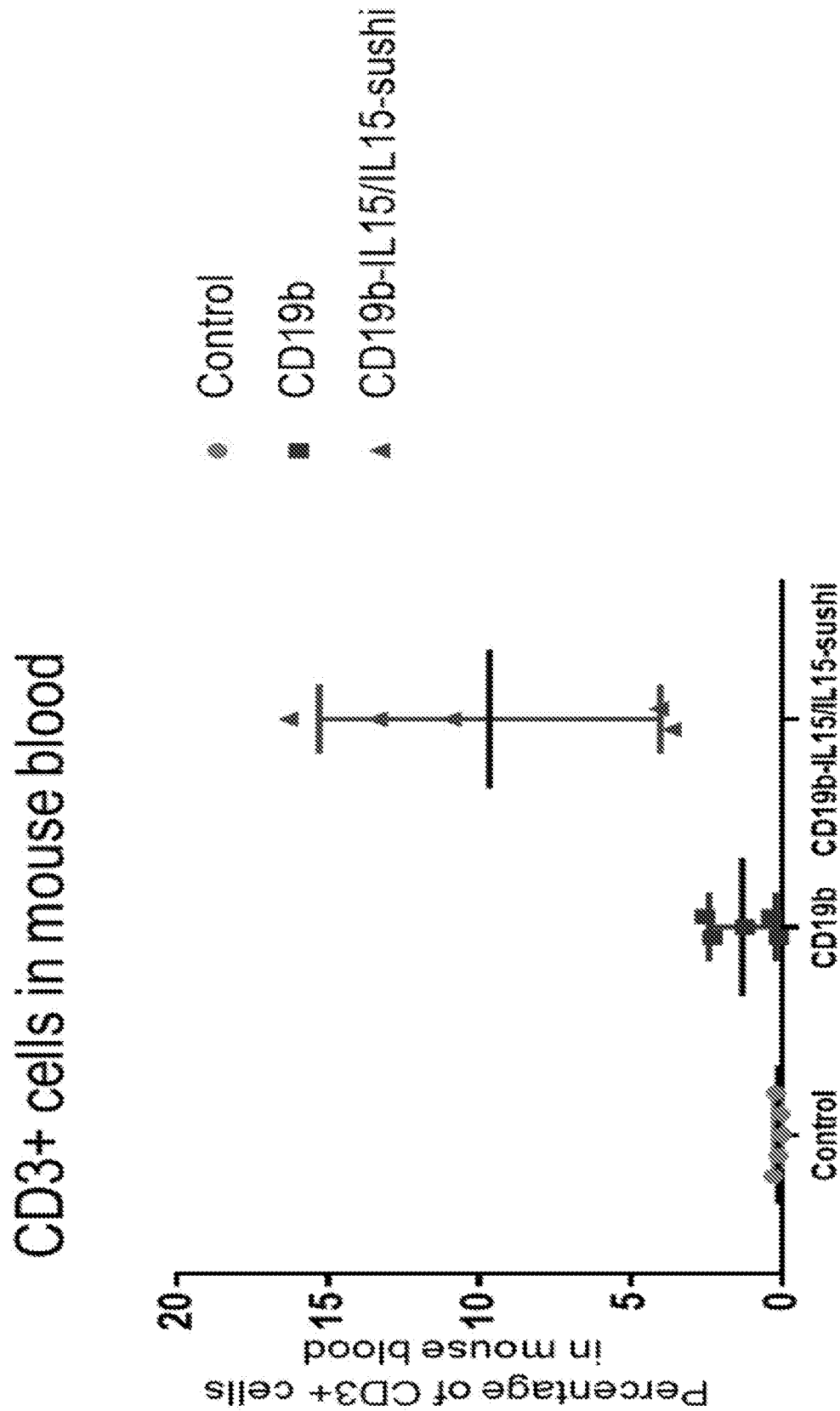


FIGURE 46D

Total mouse blood REH vs. CD19-IL15/IL15-sushi stain with CD19-APC and CD3-PE

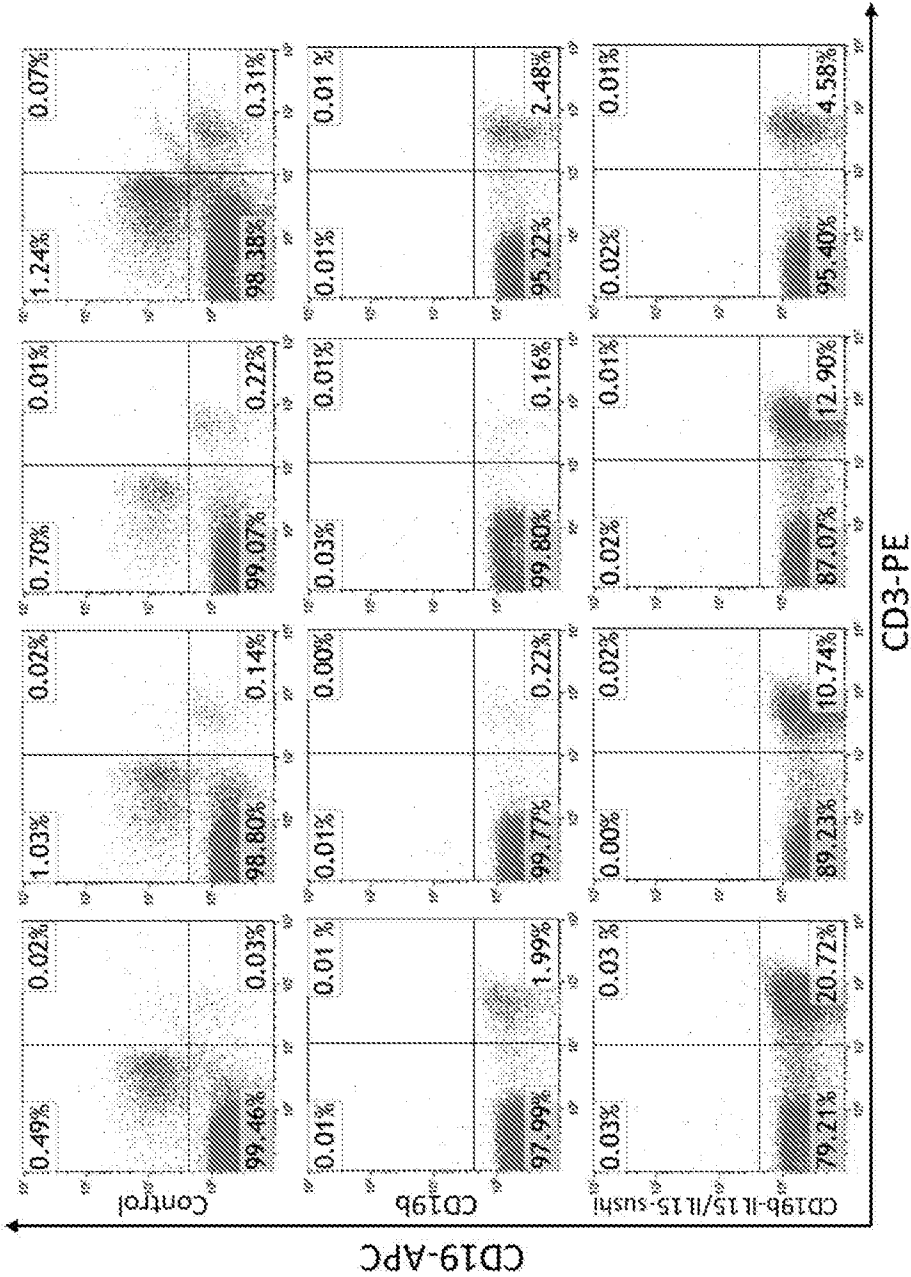


FIGURE 46E

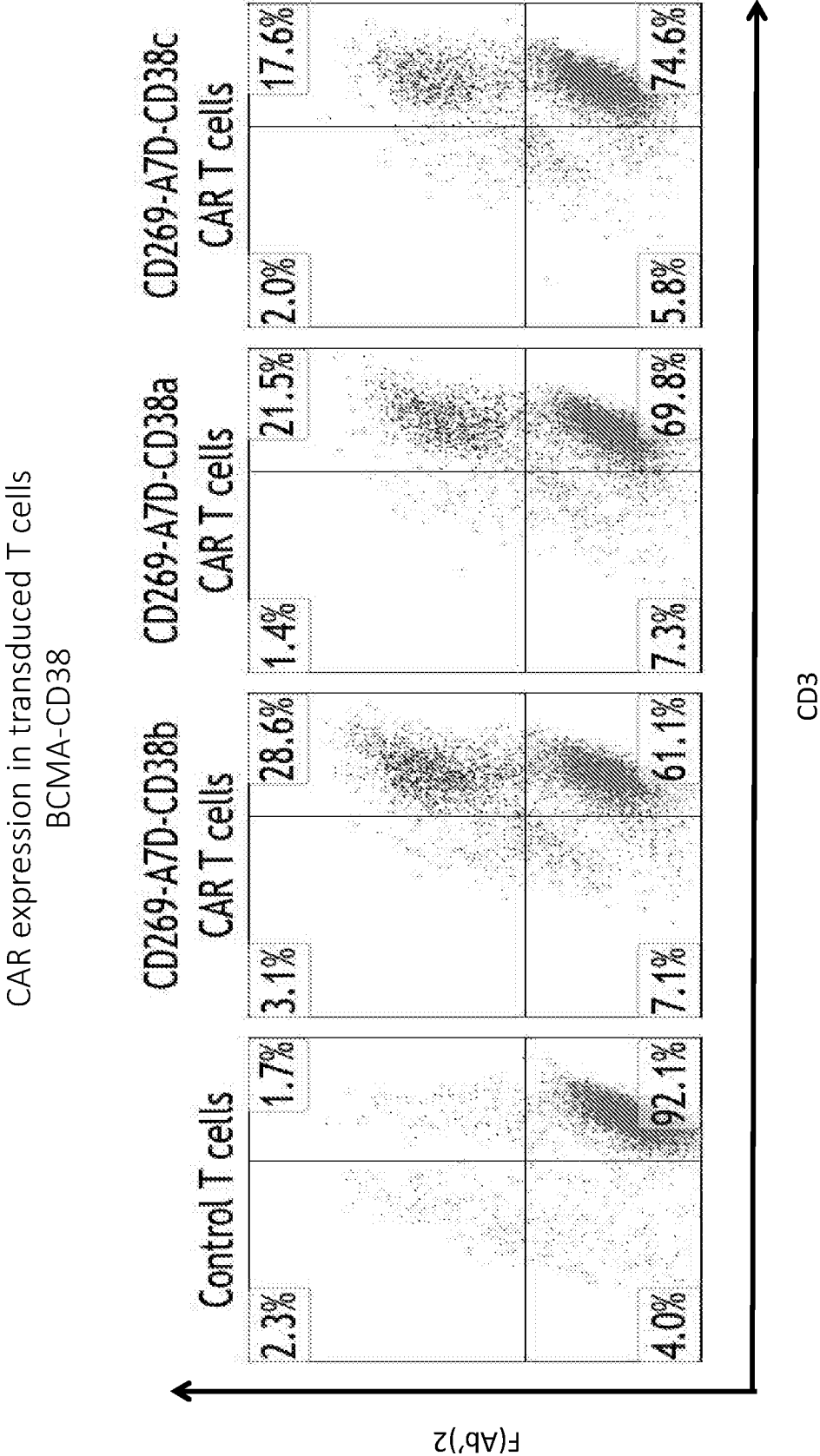


FIGURE 47A

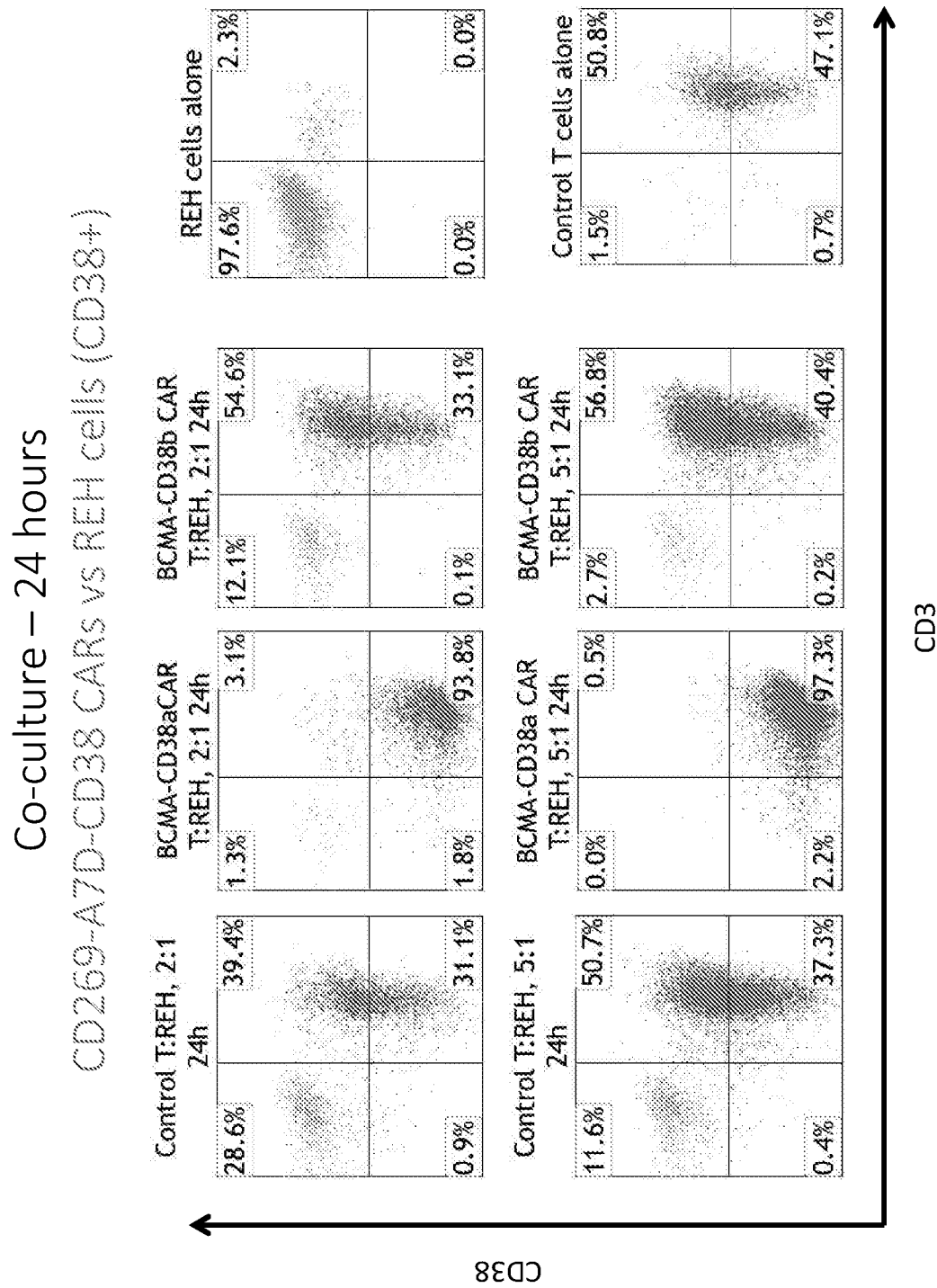


FIGURE 47B

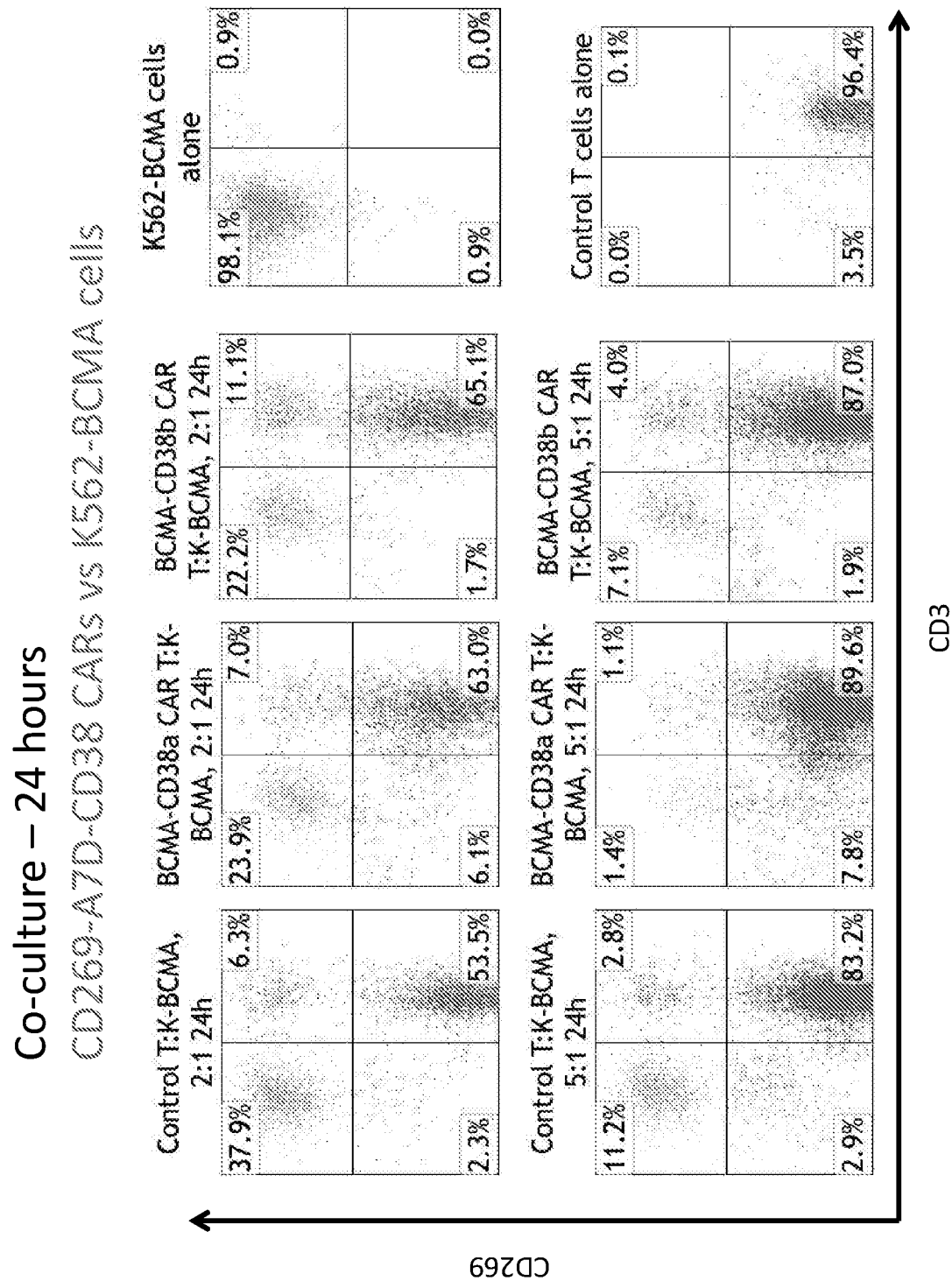


FIGURE 47C

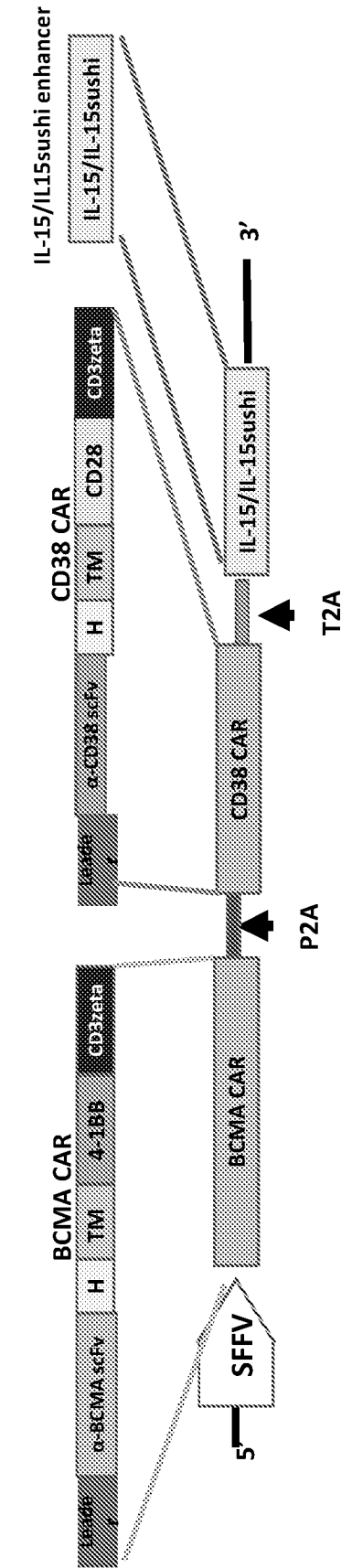


FIGURE 48A

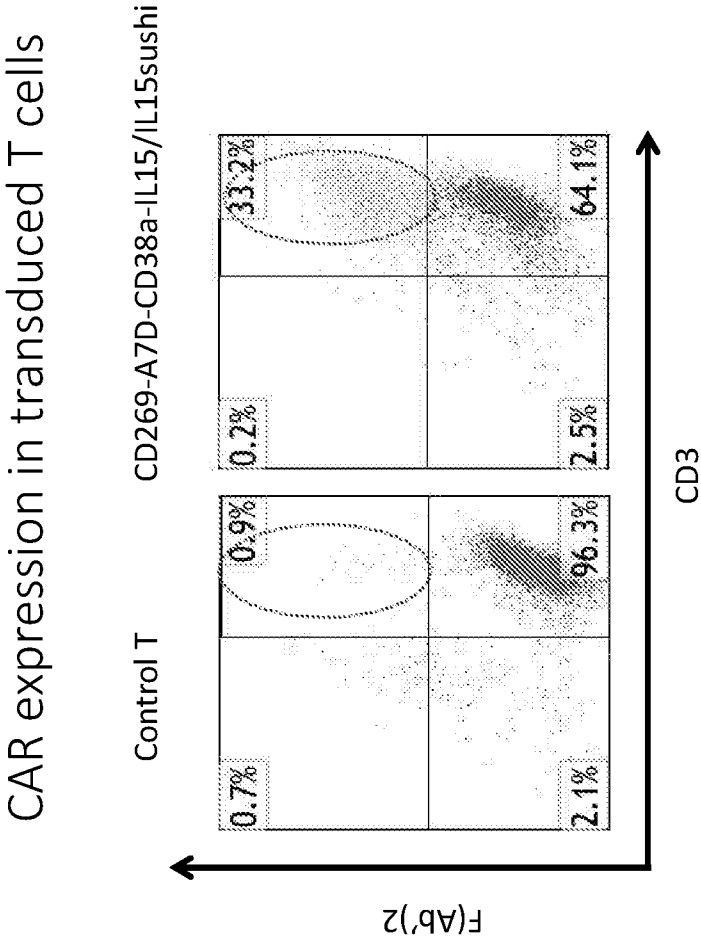


FIGURE 48B

Self-killing of CD269-A7D-CD38a-IL15/IL15sushi CAR T cells

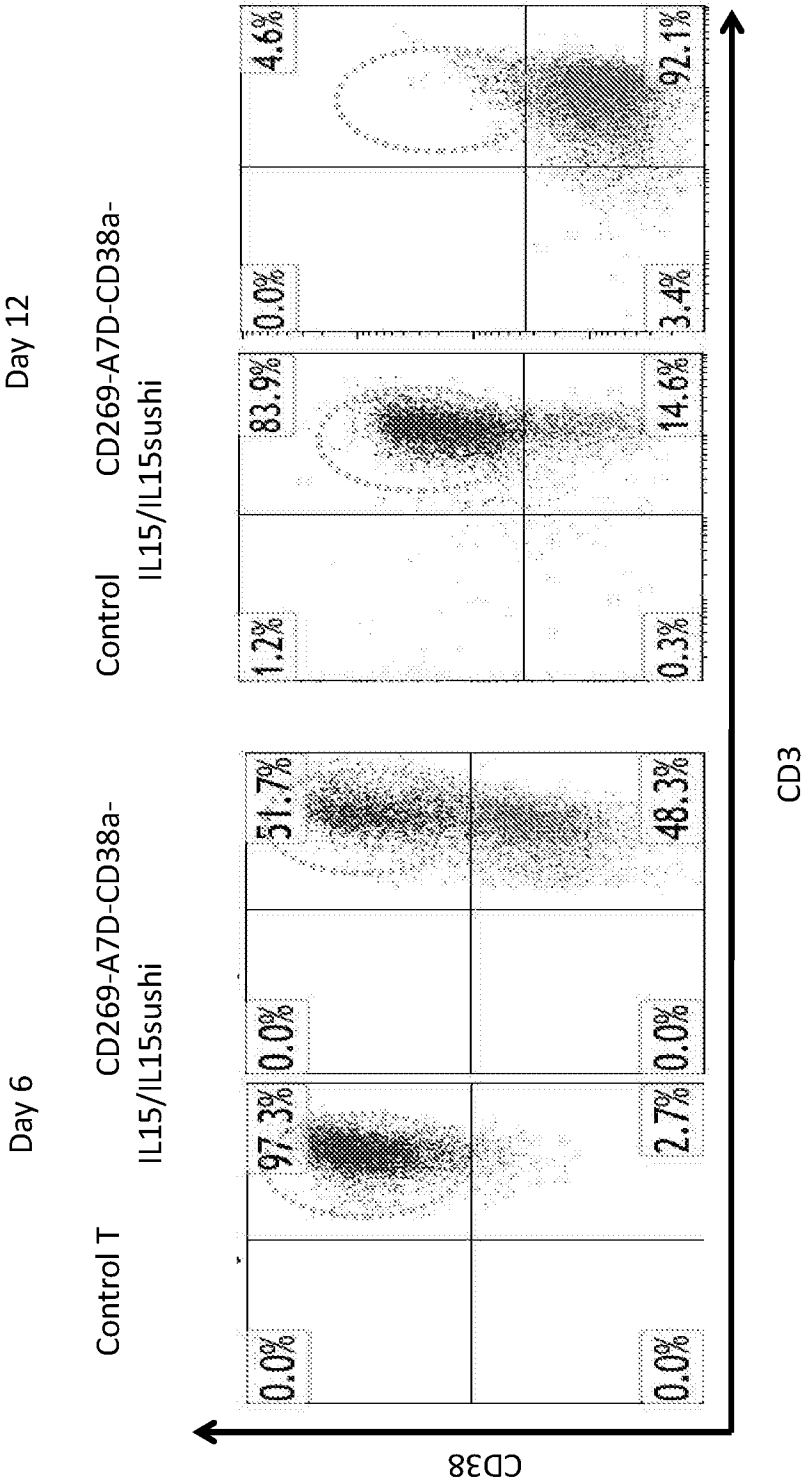


FIGURE 48C

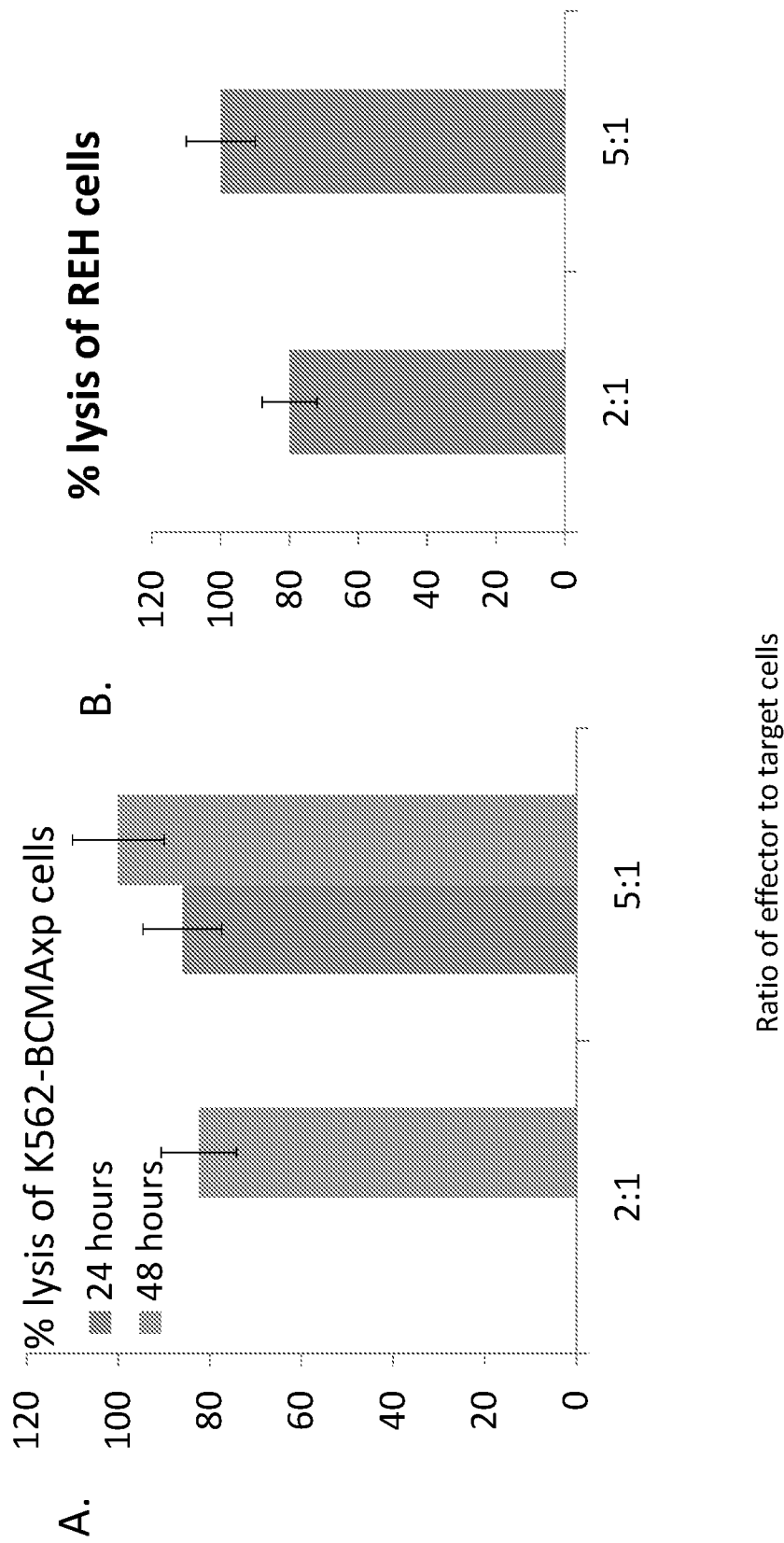


FIGURE 48D

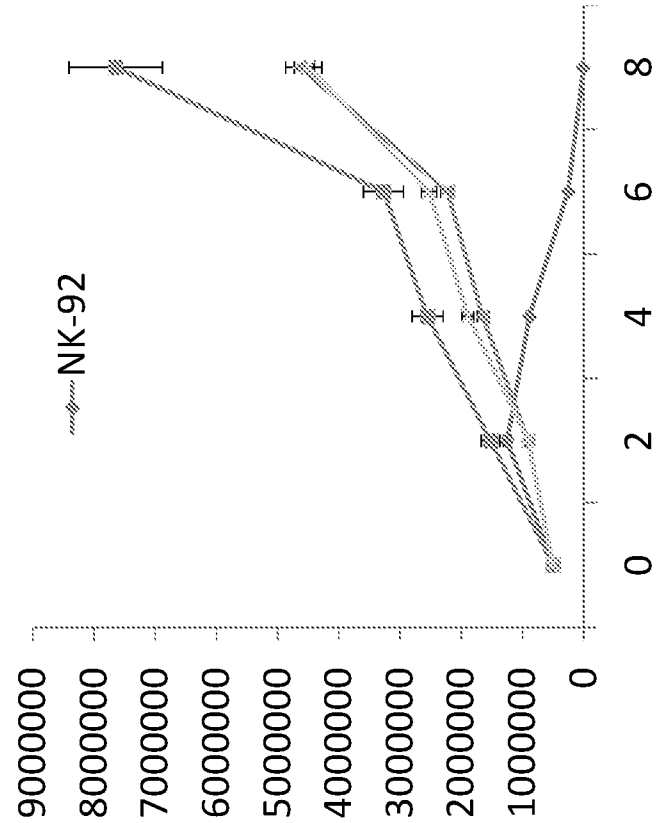
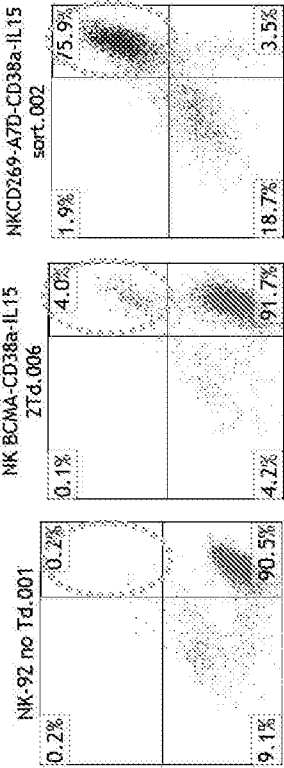


FIGURE 48E

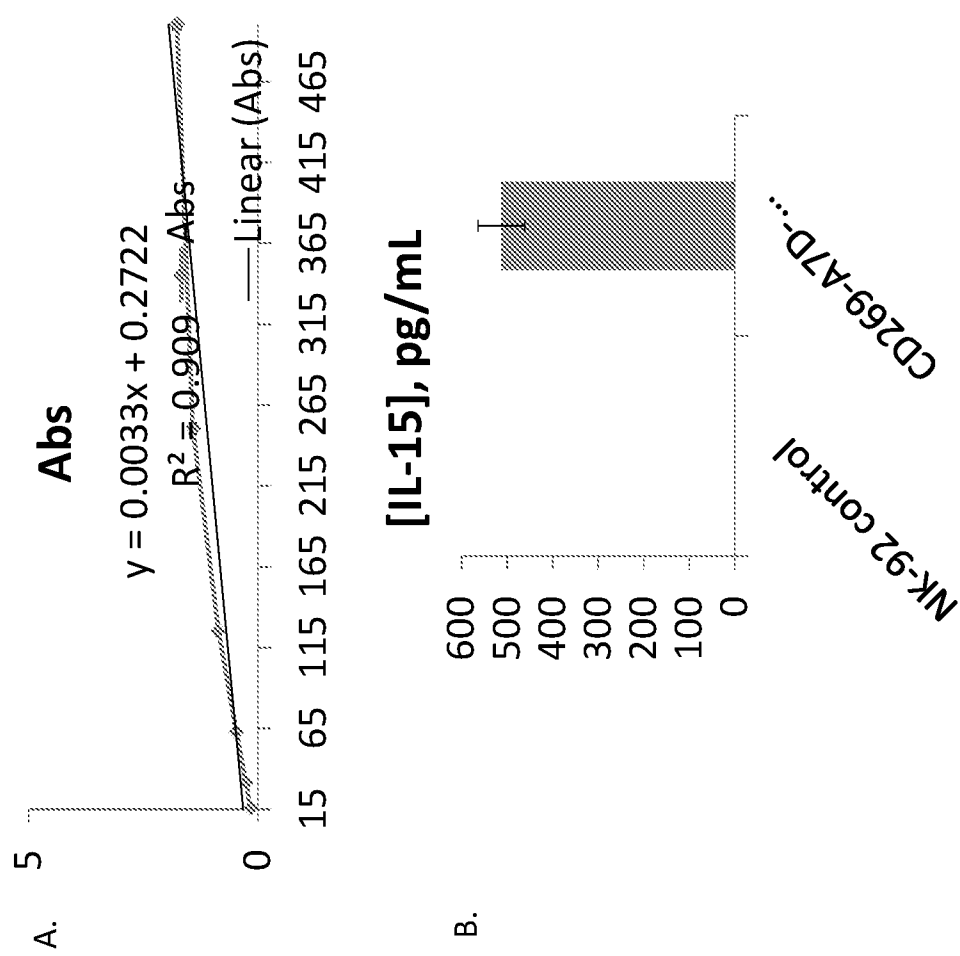


FIGURE 48F

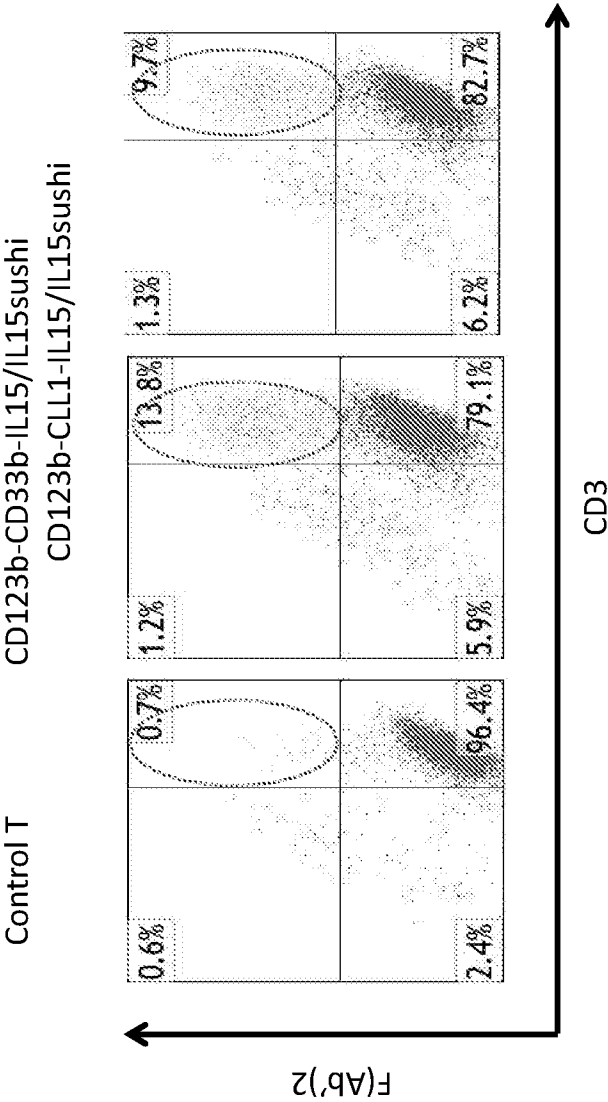


FIGURE 49A

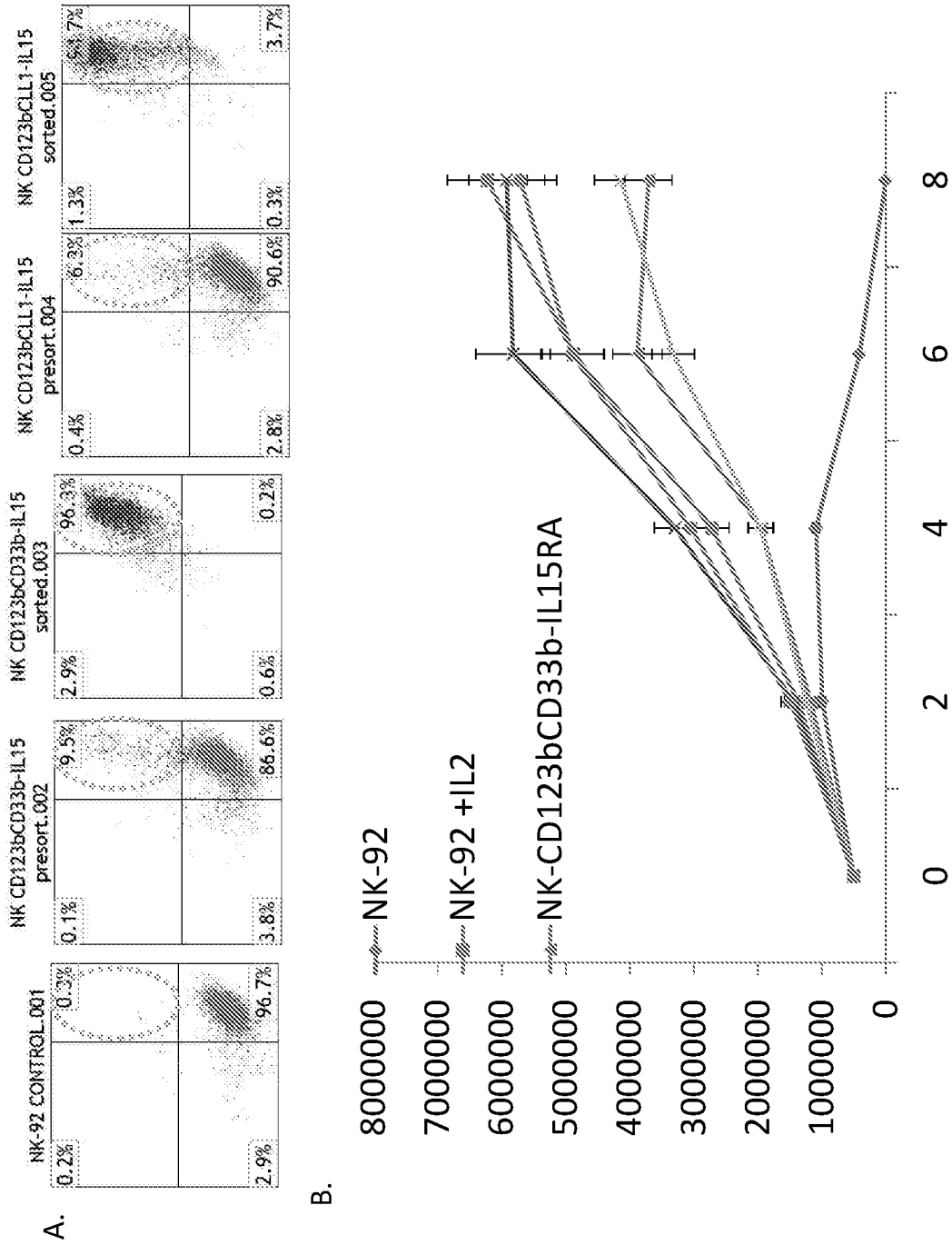


FIGURE 49B

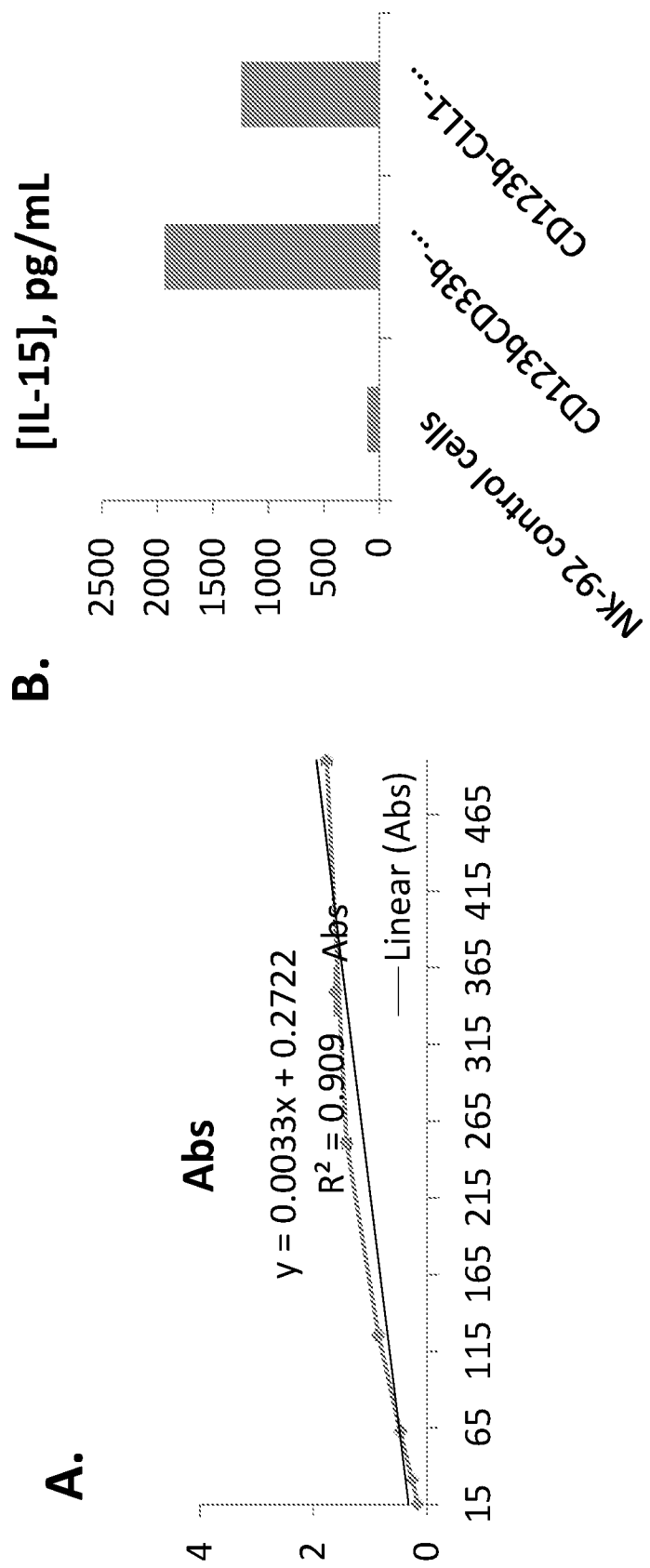


FIGURE 49C

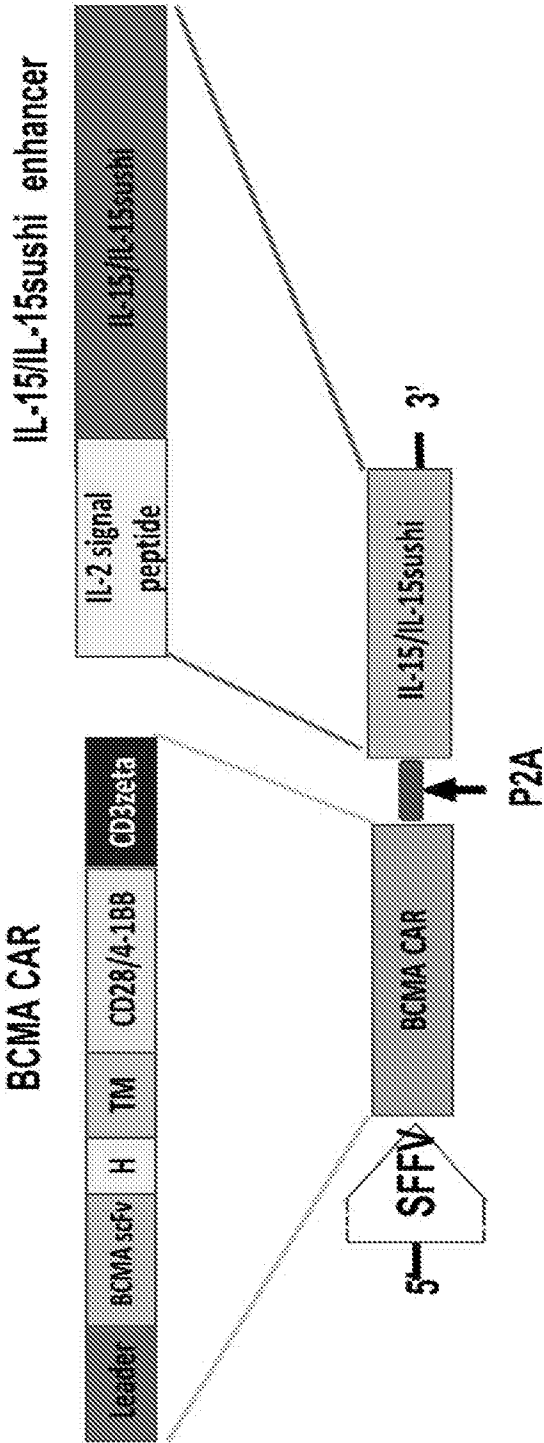


FIGURE 50A

Steps for generation and preparation of irradiated genetically modified K562 cells

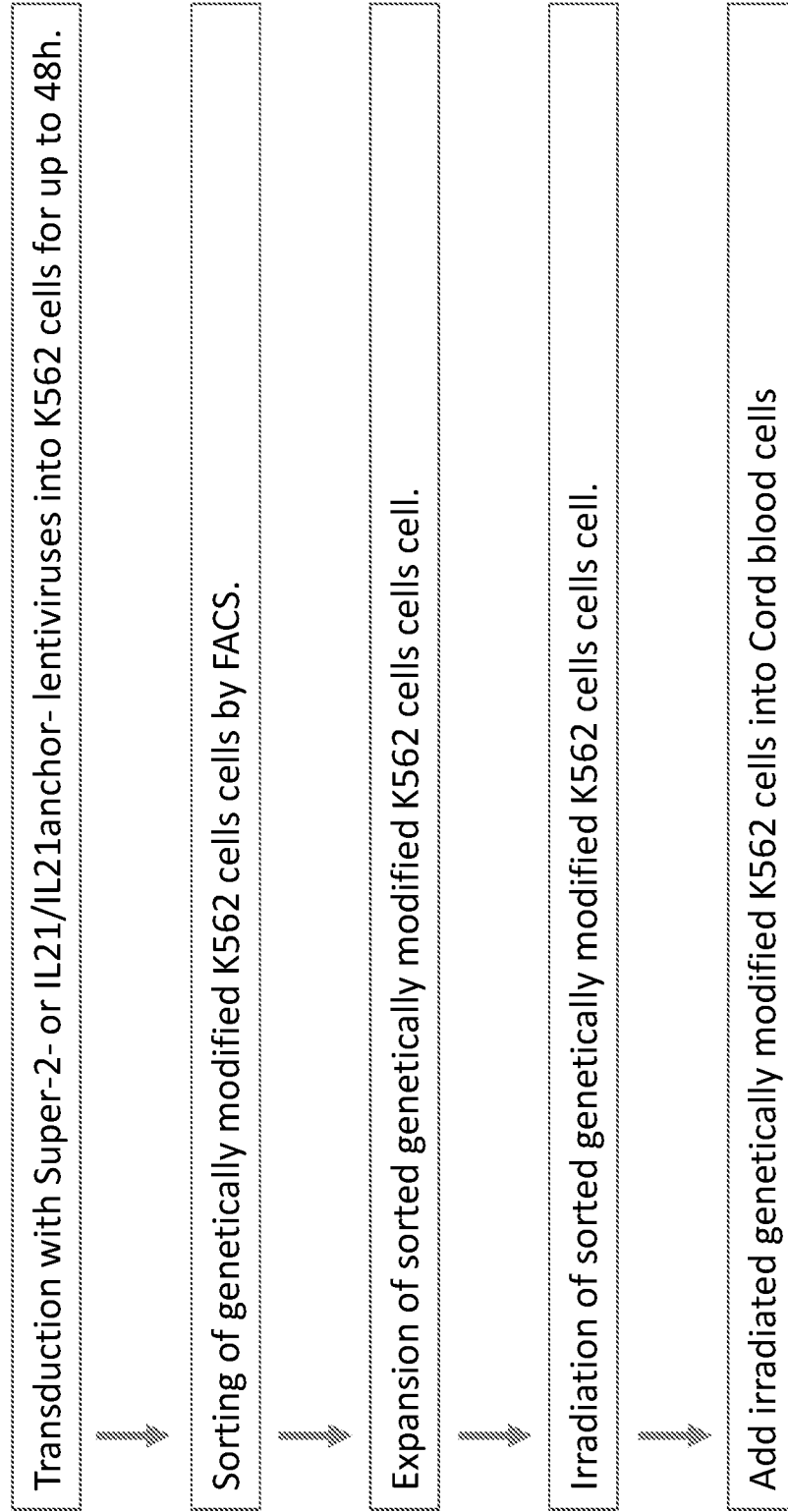


FIGURE 50B

Steps for generation and expansion of CAR-transduced natural killer (NK) cells from umbilical cord blood co-culture with irradiated genetically modified K562 cells



* All of cell culture medium including with exogenous IL-2

FIGURE 50C

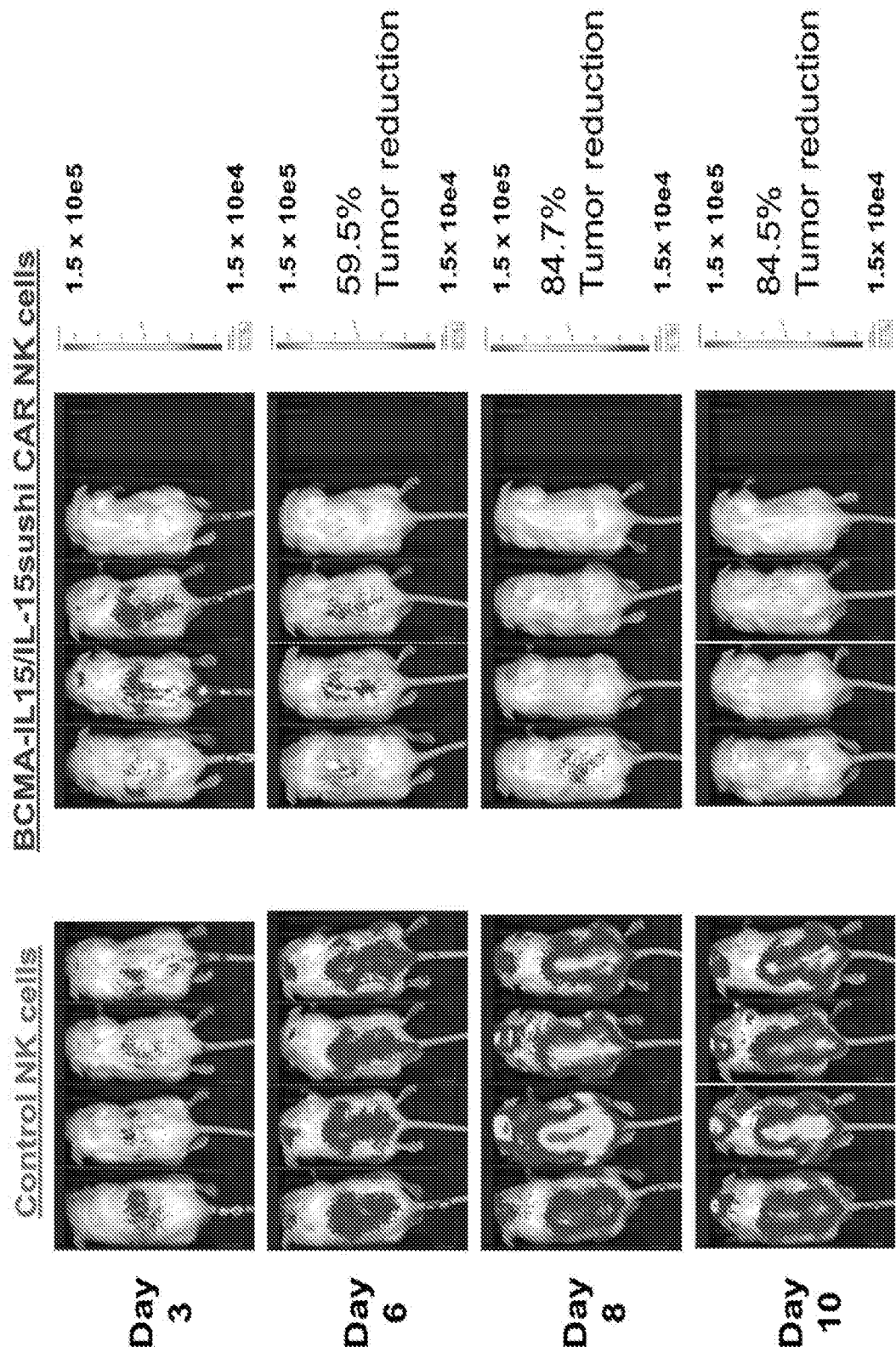


FIGURE 51A

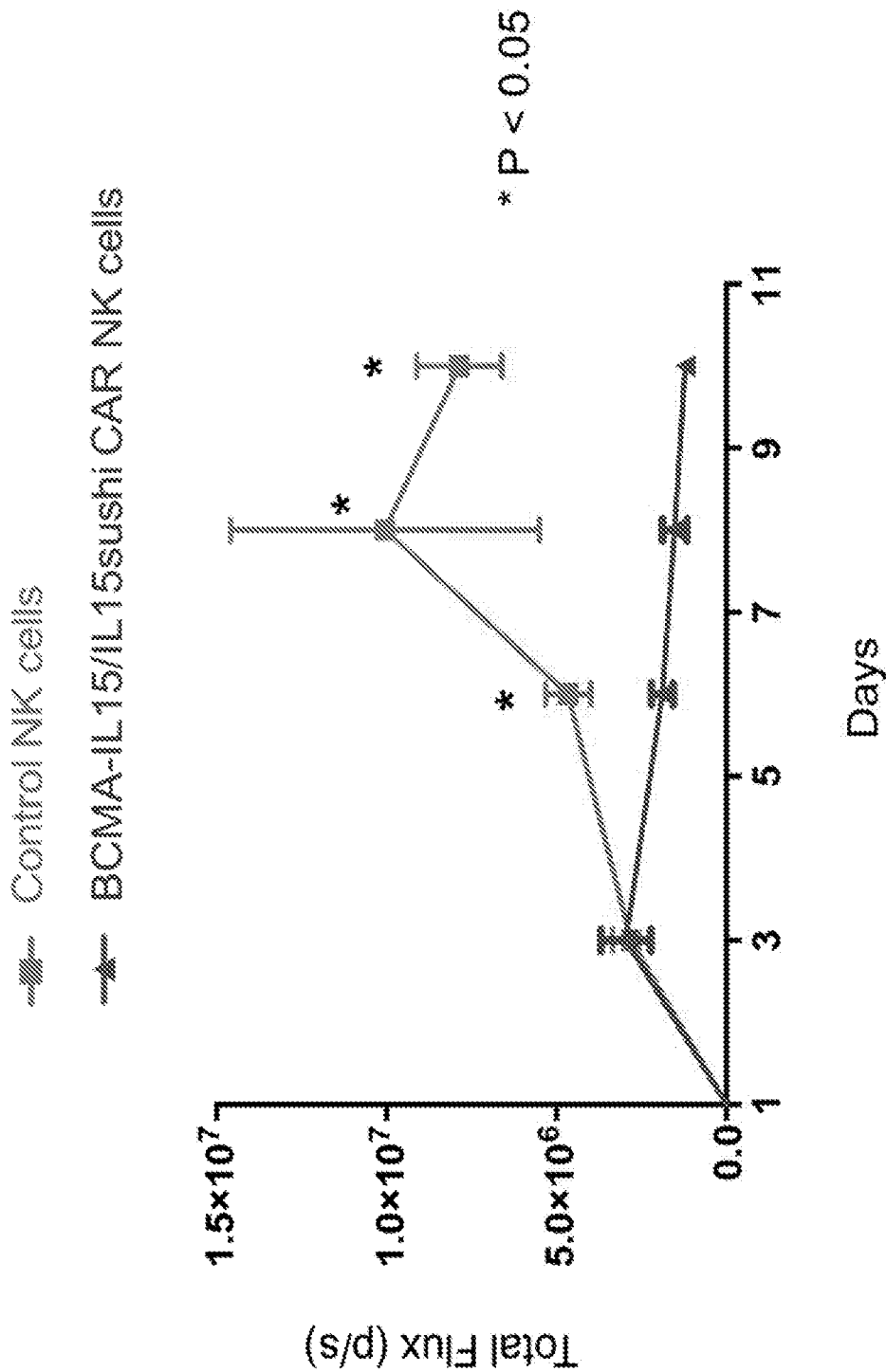


FIGURE 51B

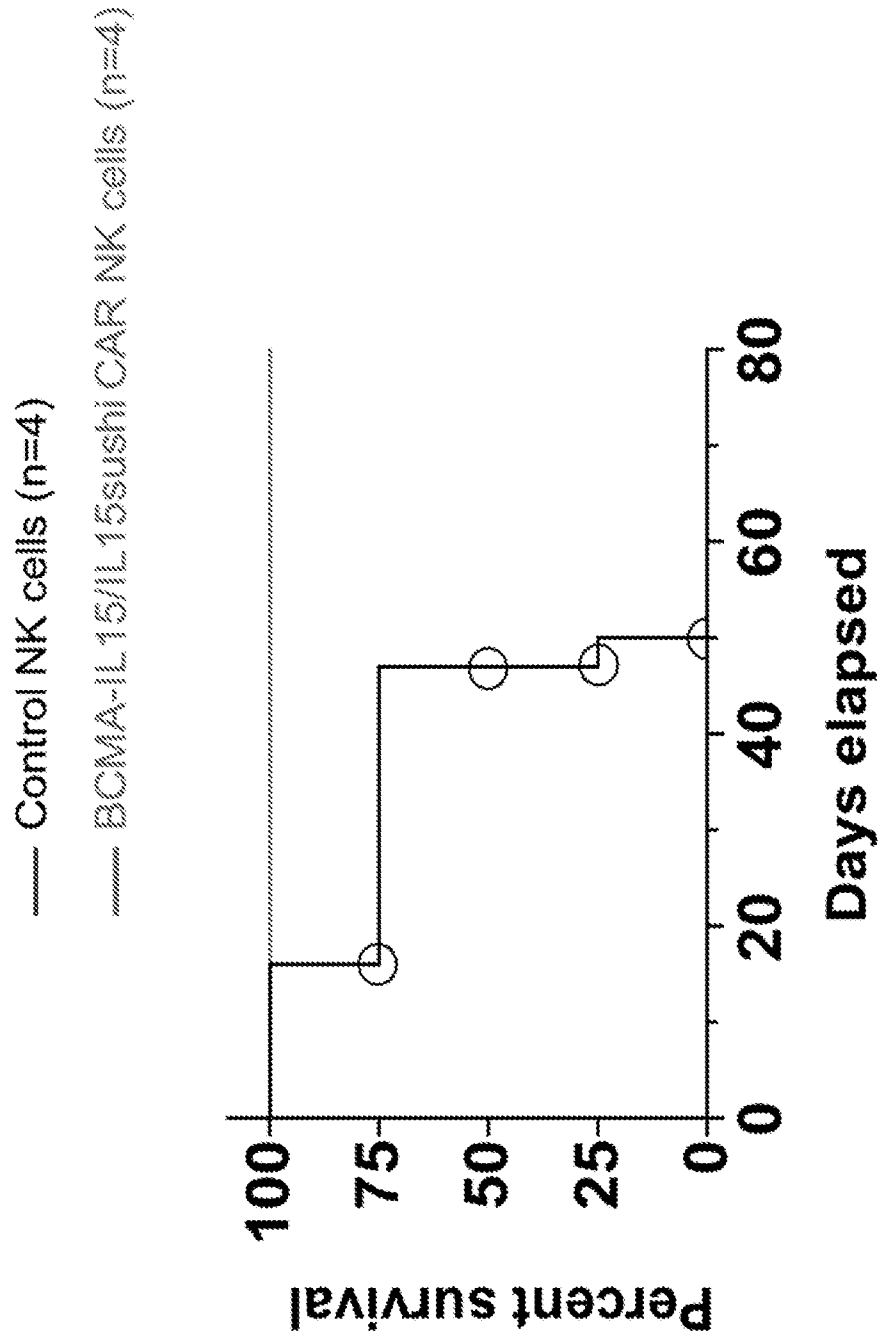


FIGURE 51C

Log-rank (Mantel-Cox) Test p=0.0069

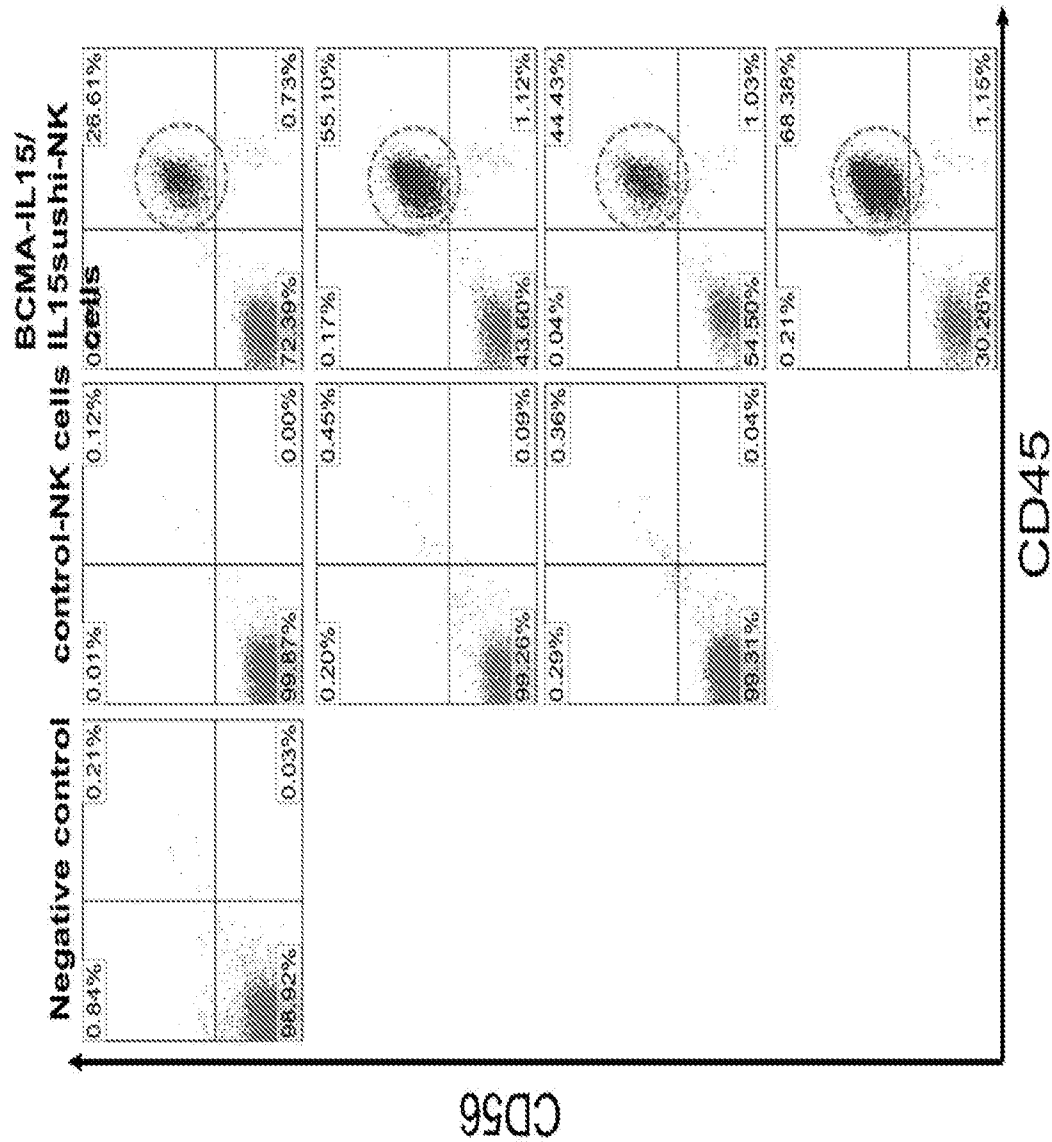


FIGURE 52A

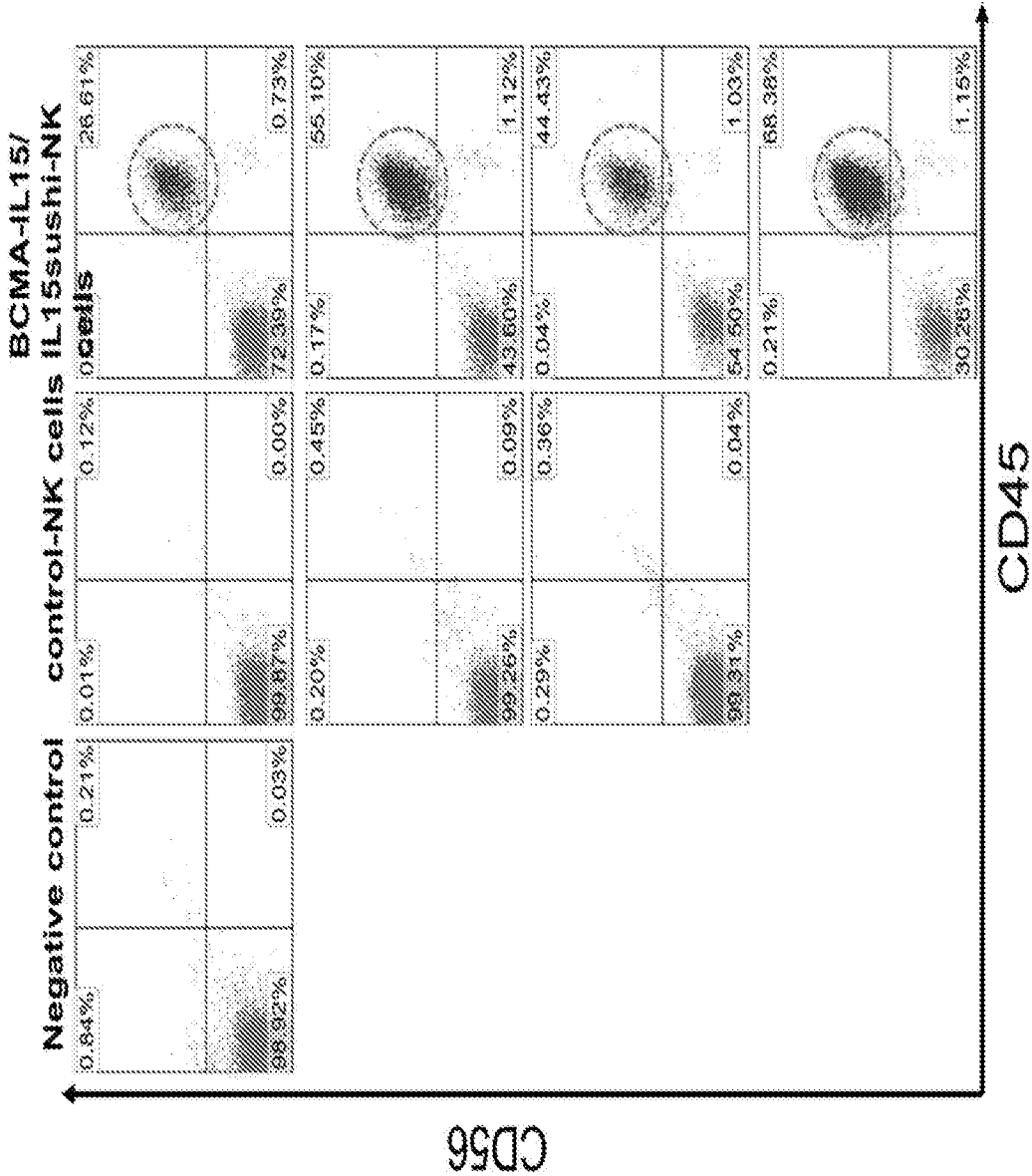


FIGURE 52B

FIGURE 53A

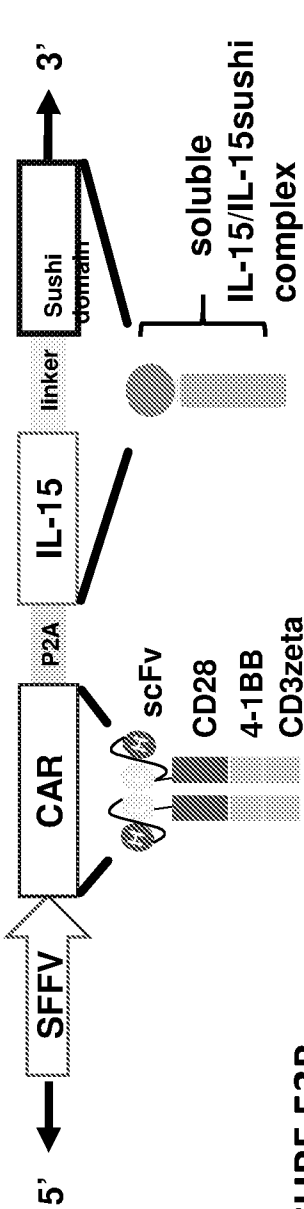


FIGURE 53B

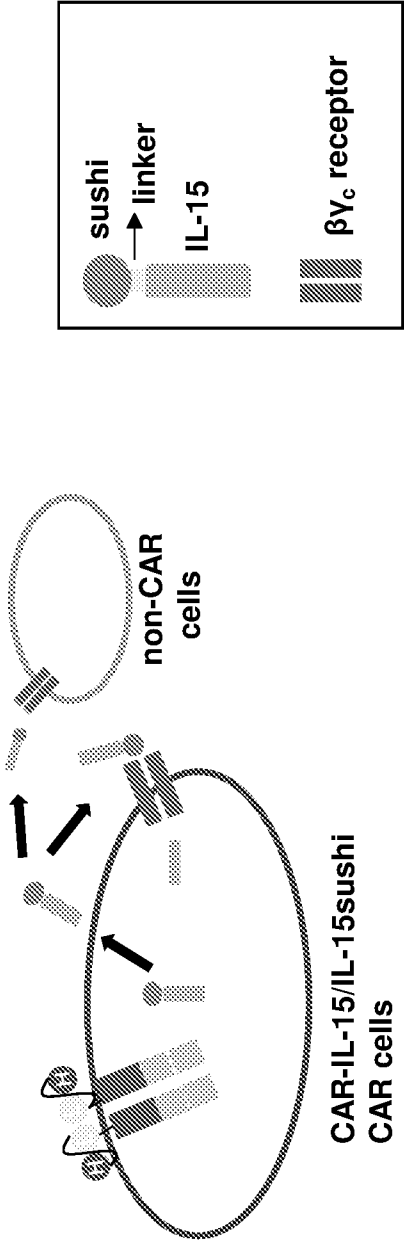


FIGURE 53

FIGURE 54A

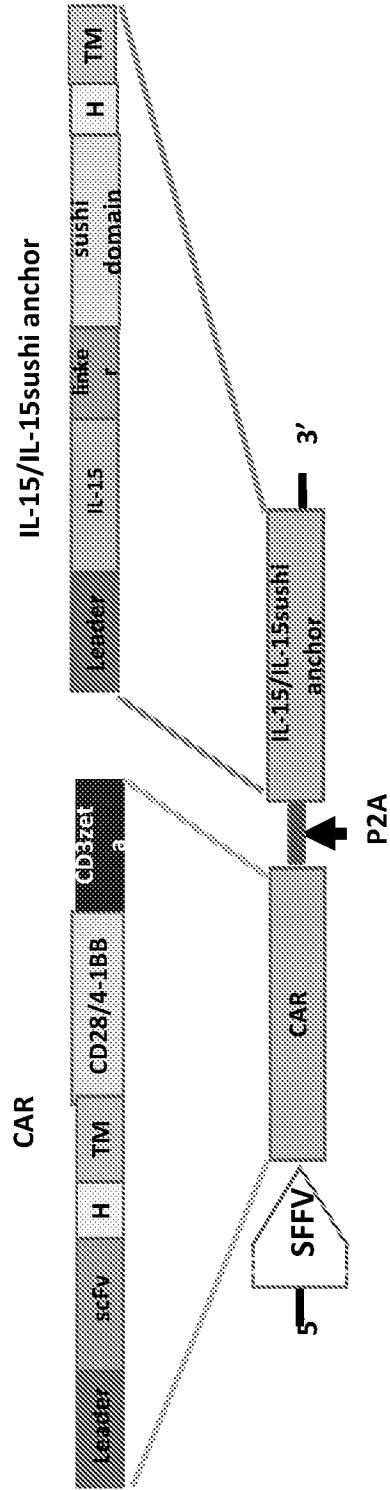
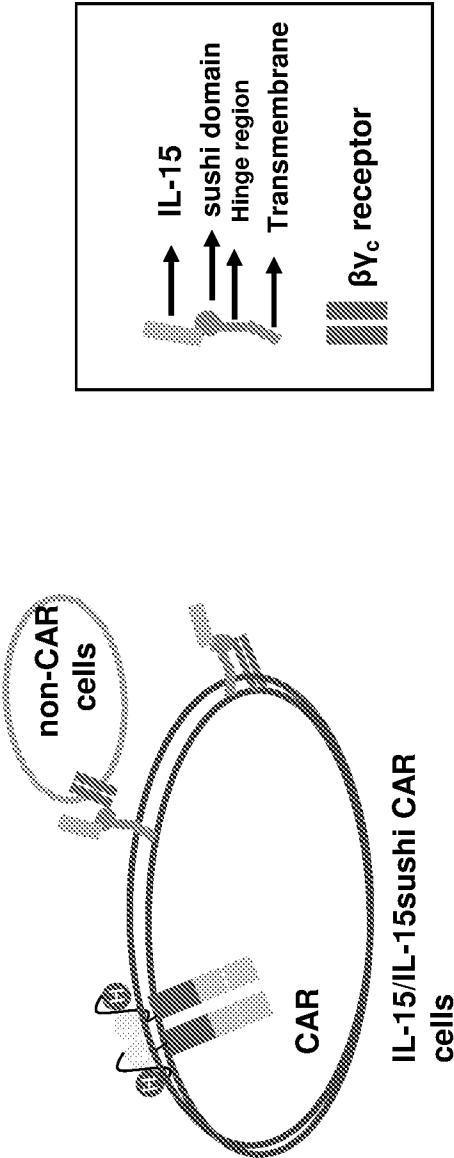


FIGURE 54B



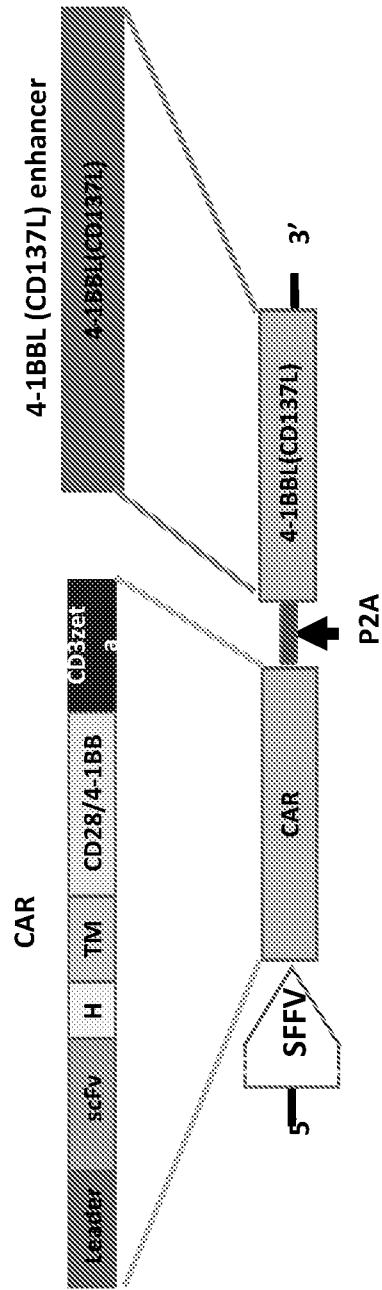


FIGURE 55

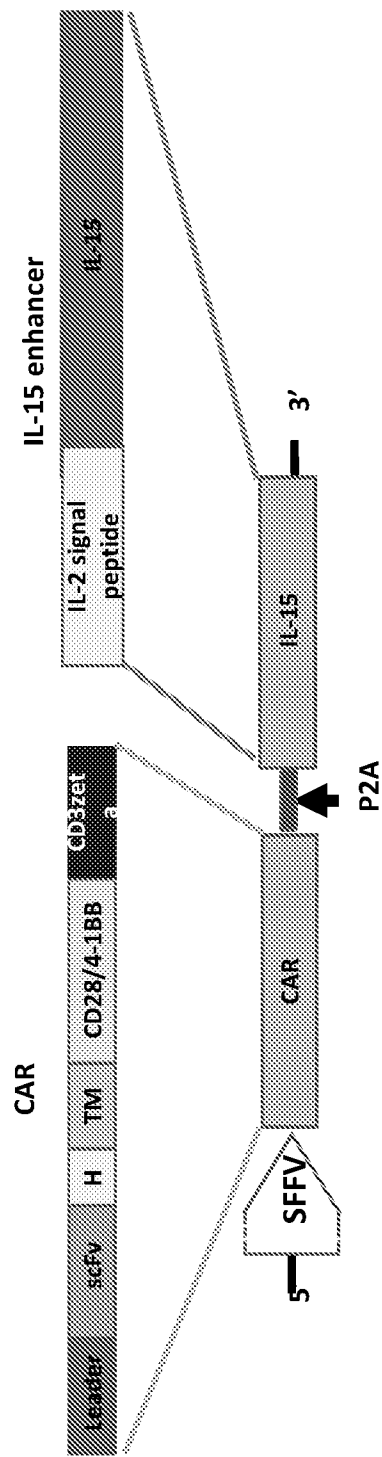


FIGURE 56

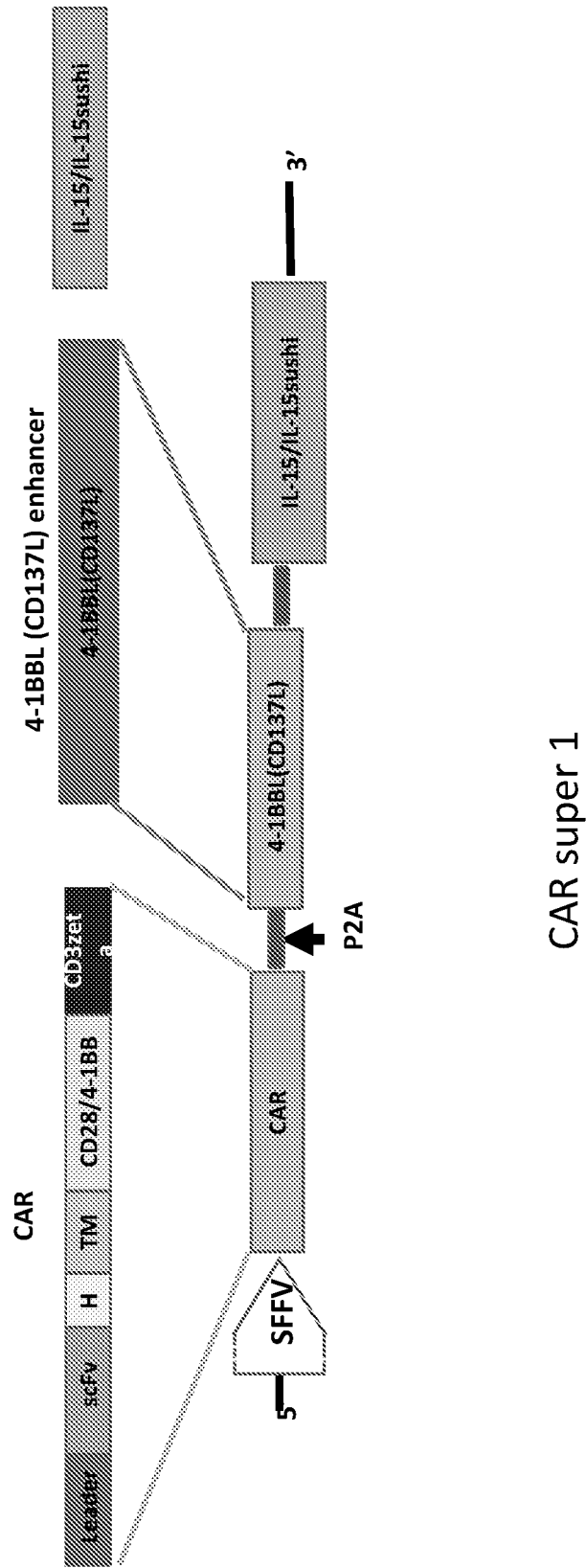


FIGURE 57

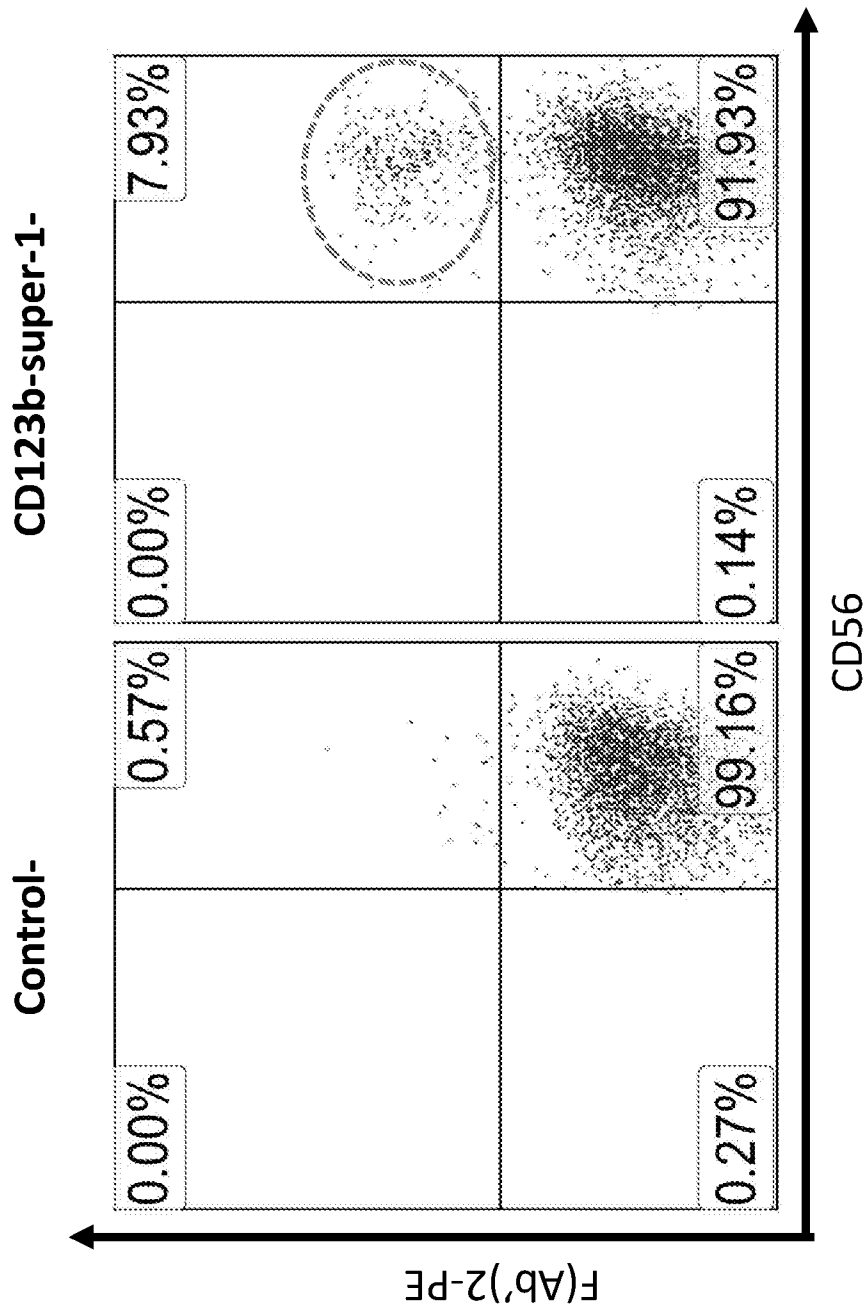


FIGURE 58

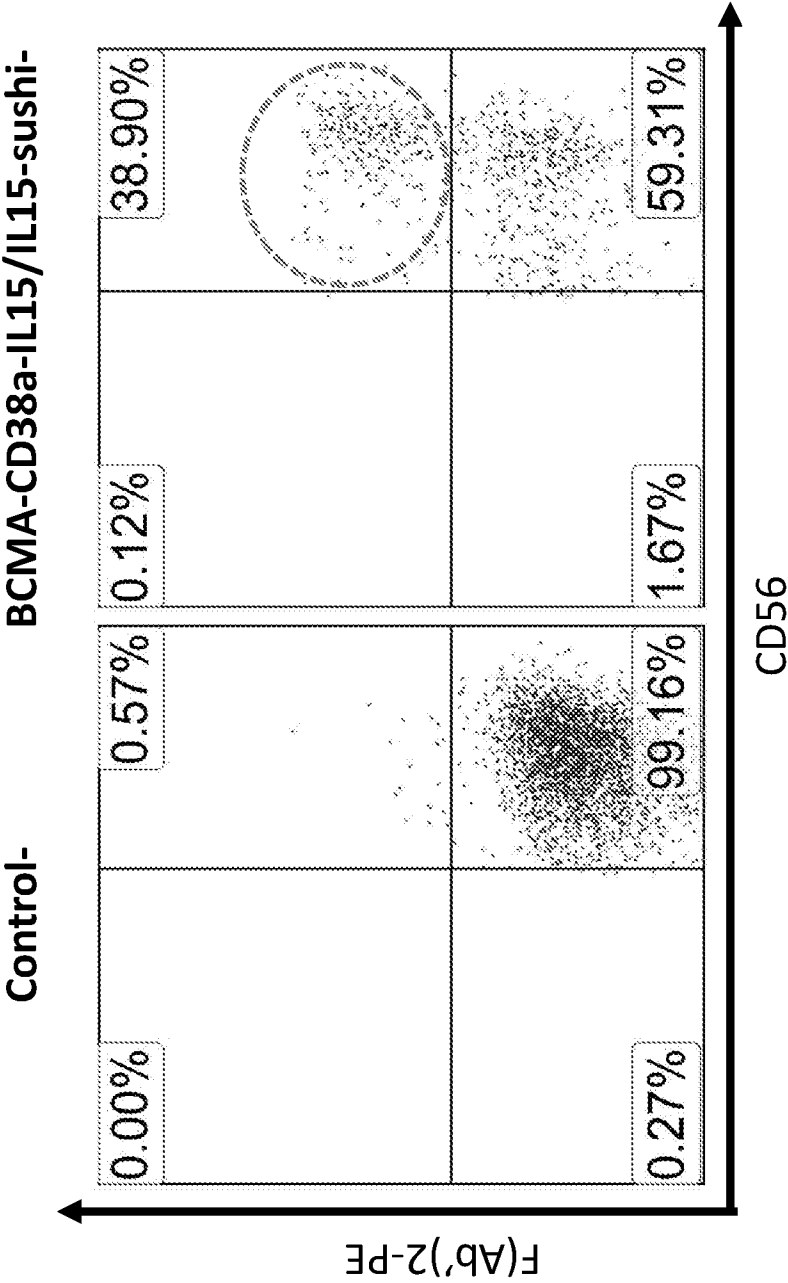


FIGURE 59

GD2-Super1-CAR T cells eliminate Y79 cells in mouse liver

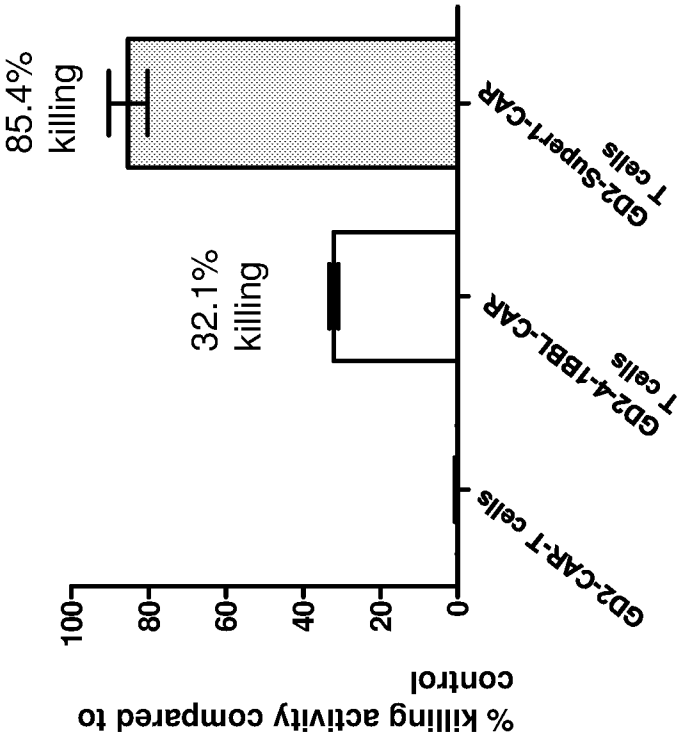
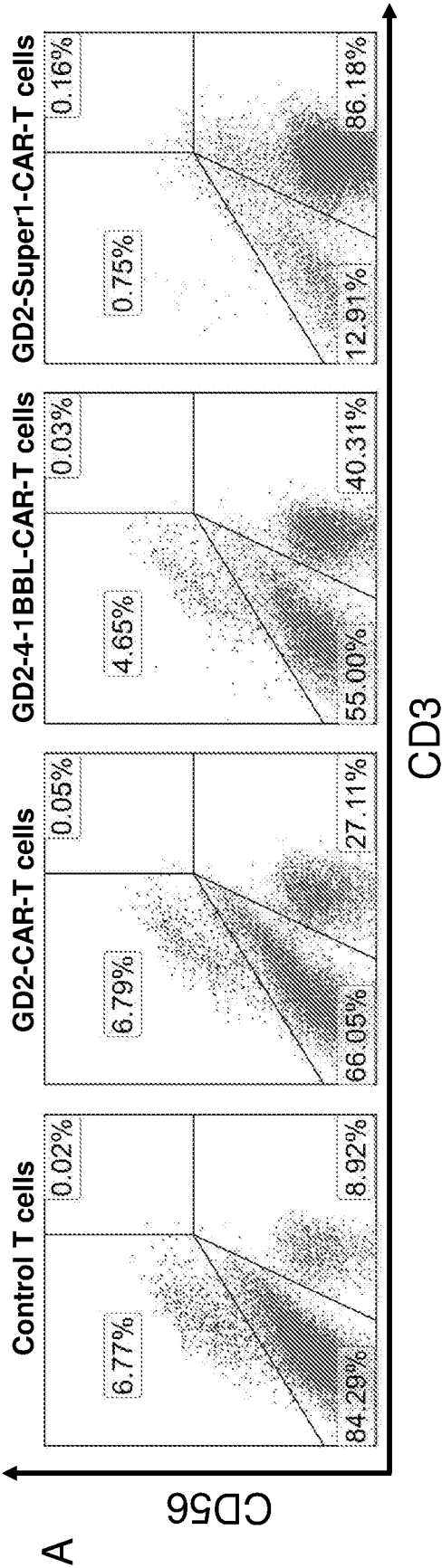


Figure 60B

GD2-Super1-CAR T cells show persistence in mouse spleen

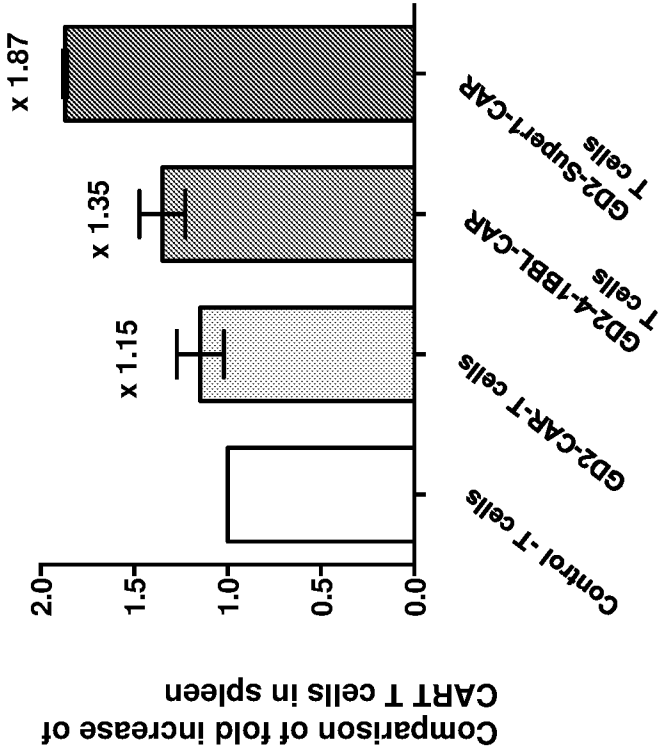
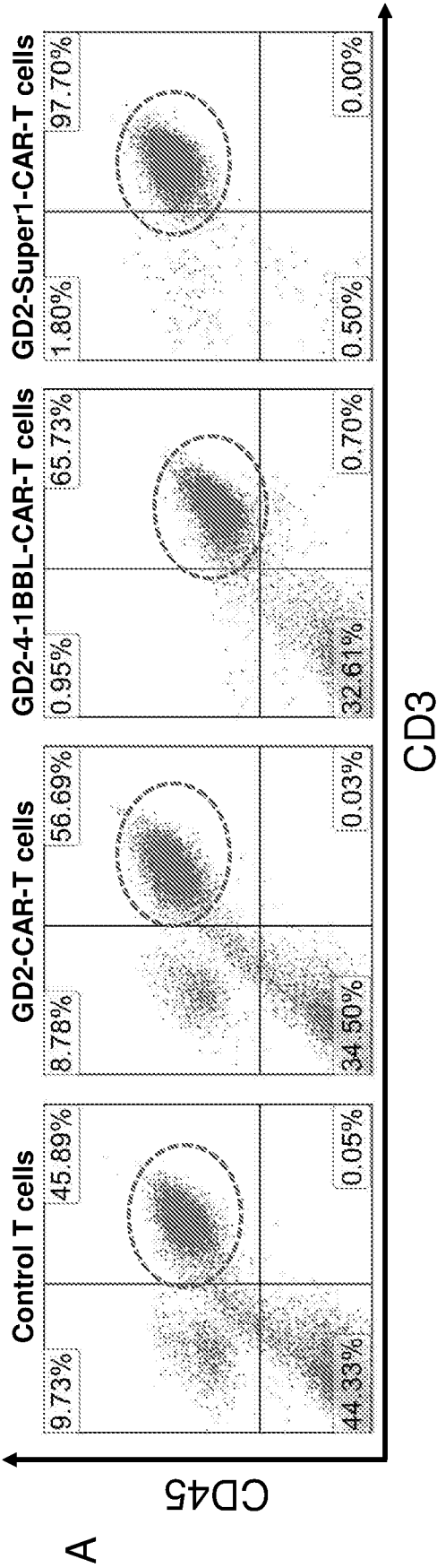


Figure 60C

Persistence of human T cells in mouse blood

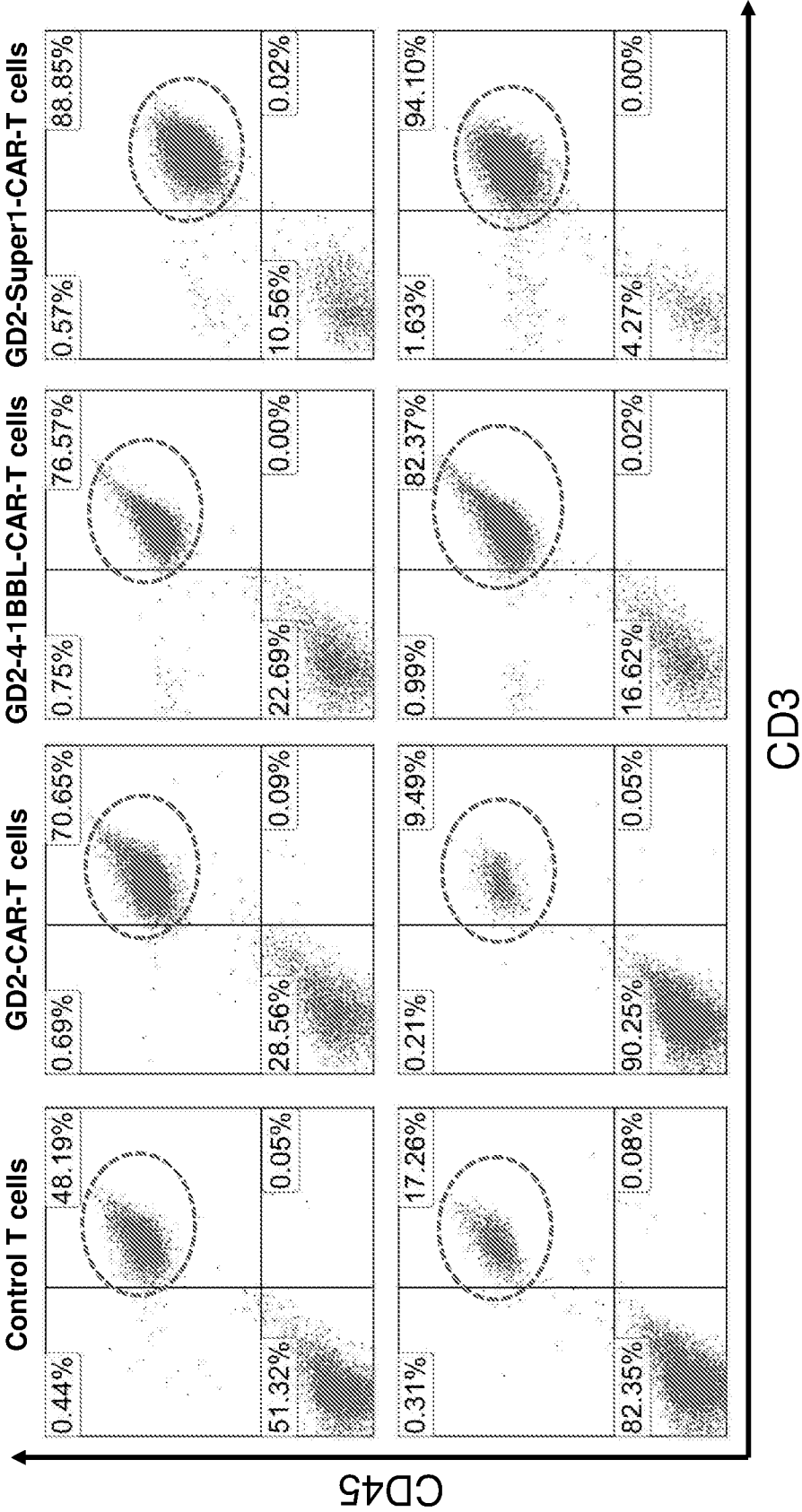


Figure 60D

Percent persistence of CAR T cells in mouse blood

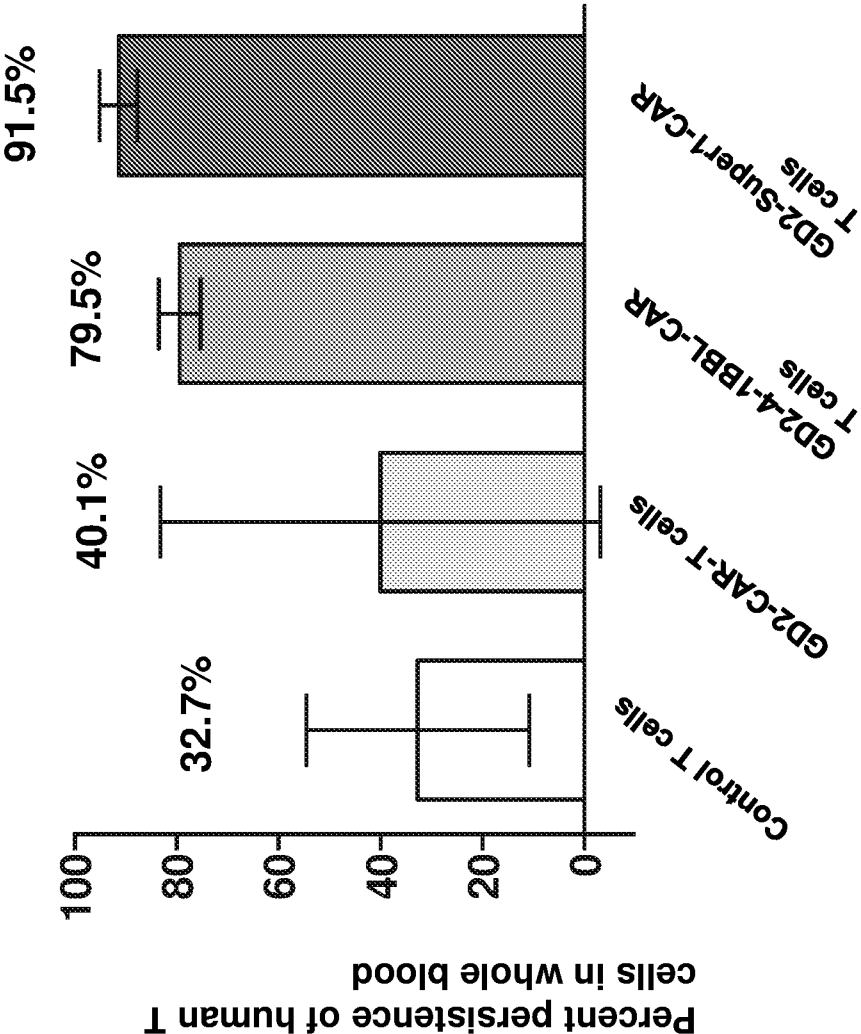


Figure 60E