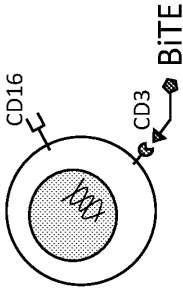


BiTEs- Bispecific T cell Engagers

- Two FDA approved and many in development

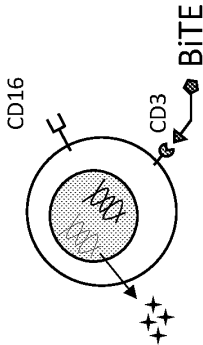


First generation

NK cells engineered with a viral vector to express CD3-activated by a dual engager BiTE

Second generation

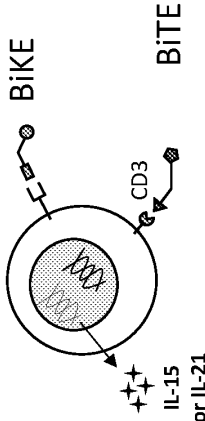
- NK cells engineered with a viral vector to secrete cytokines “armored NK cells”.
- Increased efficacy, potency-mandatory for solid tumors



BiKEs- Bispecific NK cell Engagers

Third generation

- NK cells respond to both NK engagers and T cell engagers
- Opens the way to combine with BiKEs “dual BiTE/BiKE NK cells”



Fourth generation

- Any of the previous generation plus CAR

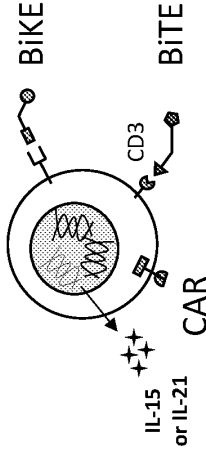


FIG. 1A

NK adapted CD3 and TCR for best cancer immunotherapy

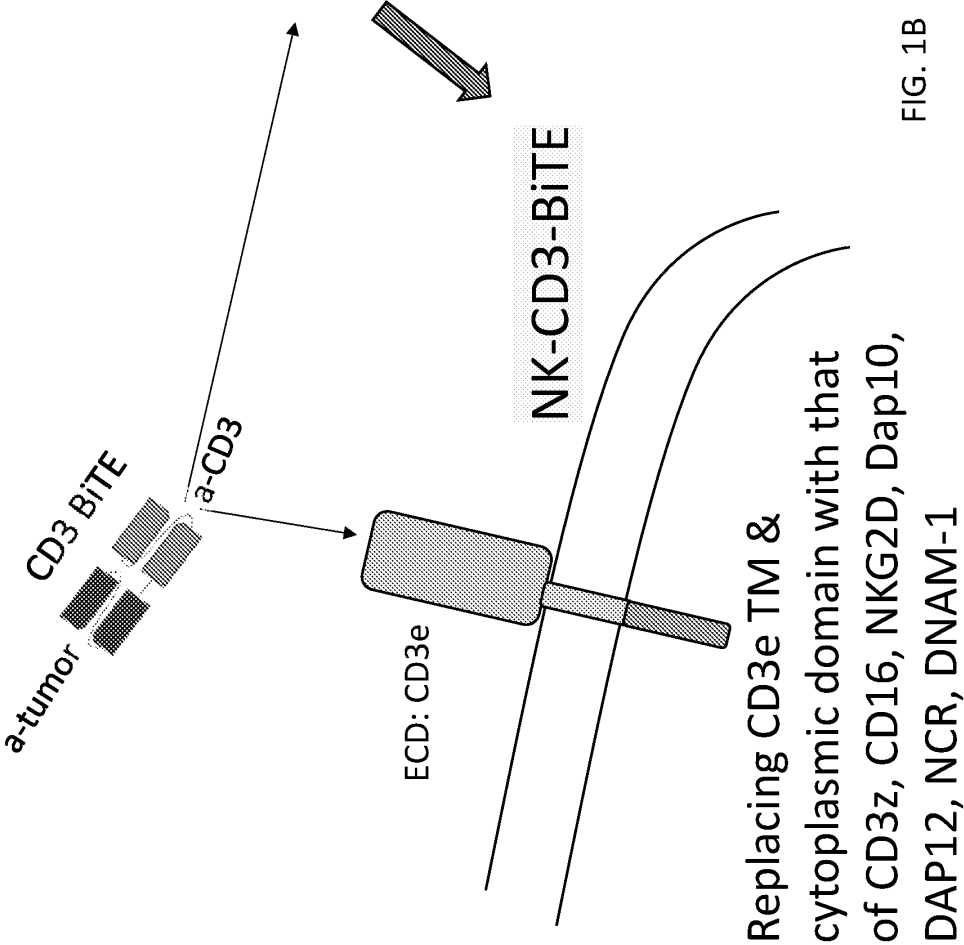
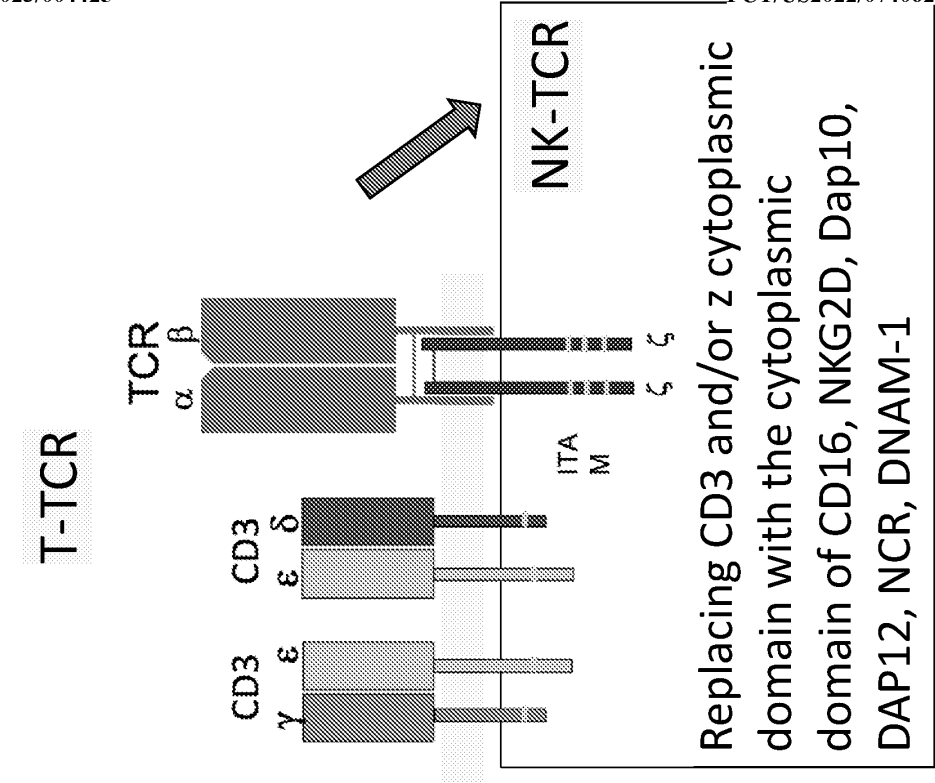


FIG. 1B

CD3-BiTE using a single chimeric CD3e

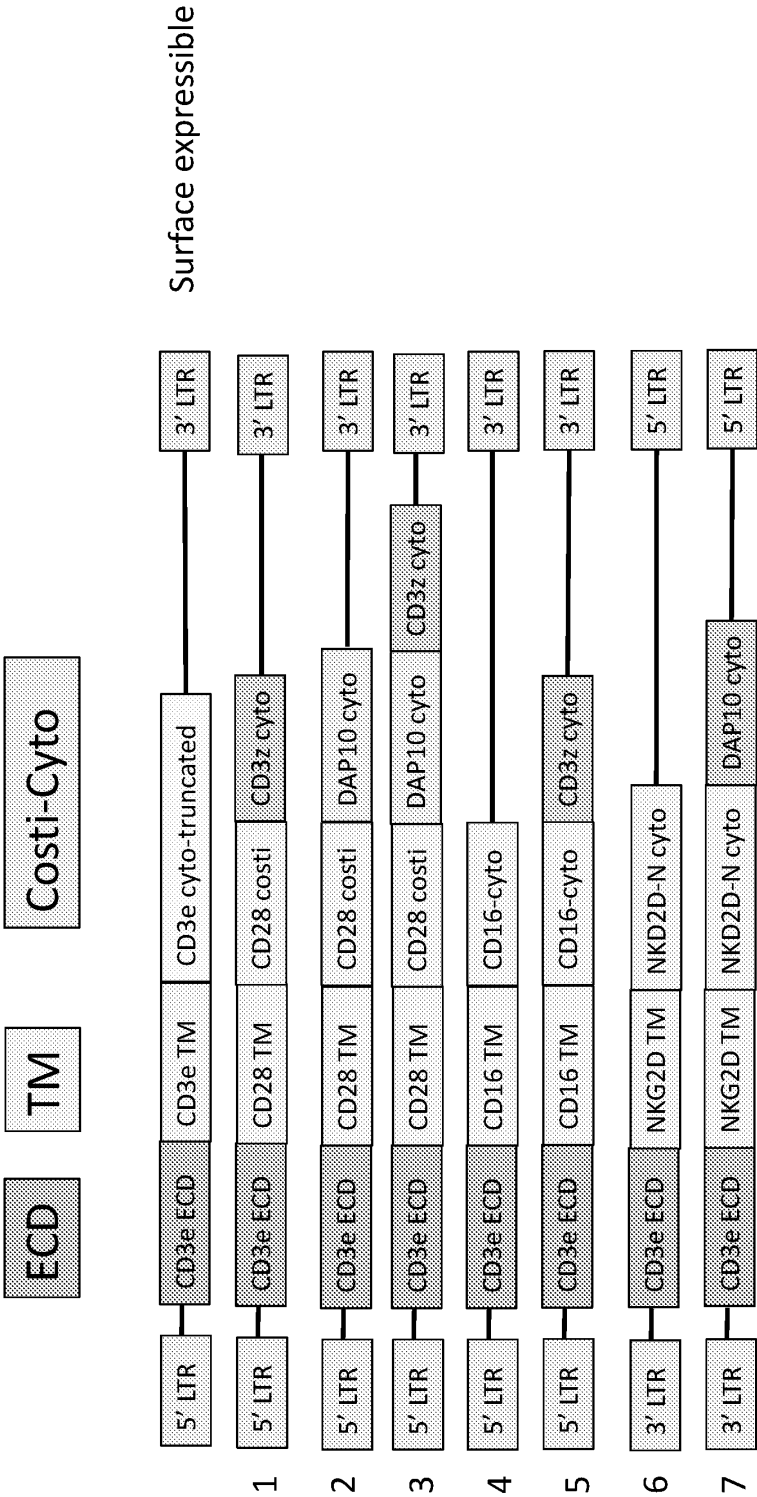
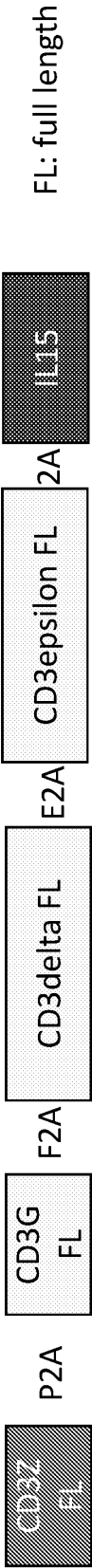


FIG. 1C



CD3ZFLGDEFL15

FIG. 2A

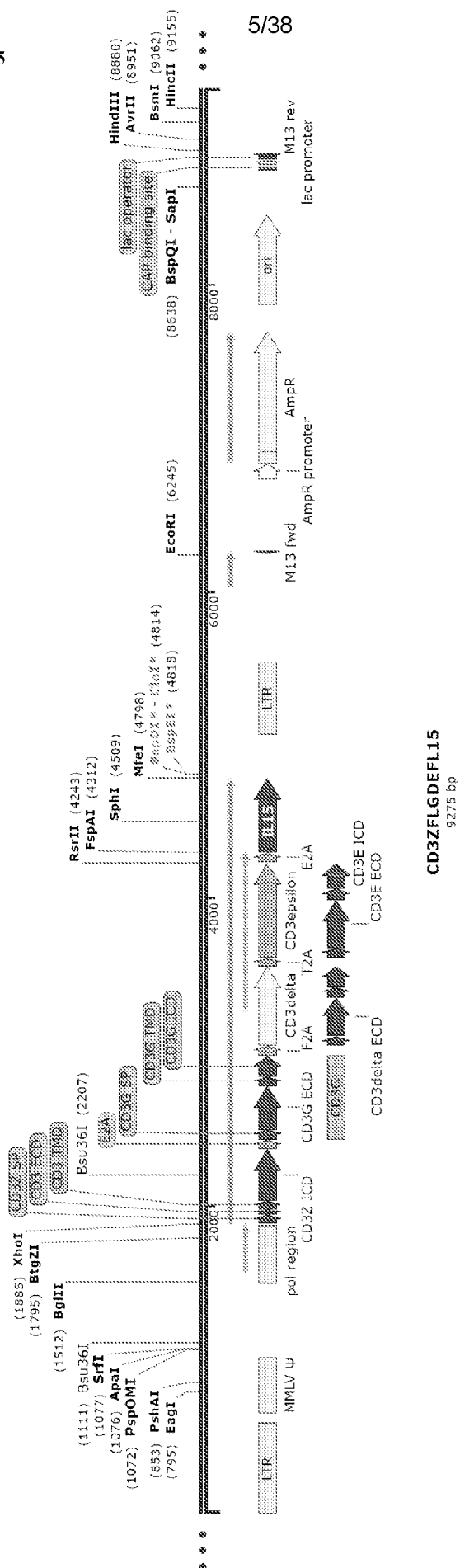


FIG. 2B

TCRpp65ZicdGDEFL	TCR1
TCRpp65ZFLGDEFL	TCR2
TCRpp65Zicd15	TCR3
TCRpp65betaalpha	TCR4
CD3ZFLGDEFL15	Z1
CD3ZGDEFL8SP21CD8	Z2
3ZGDEFLSP82121CD28	Z3

FIG. 3

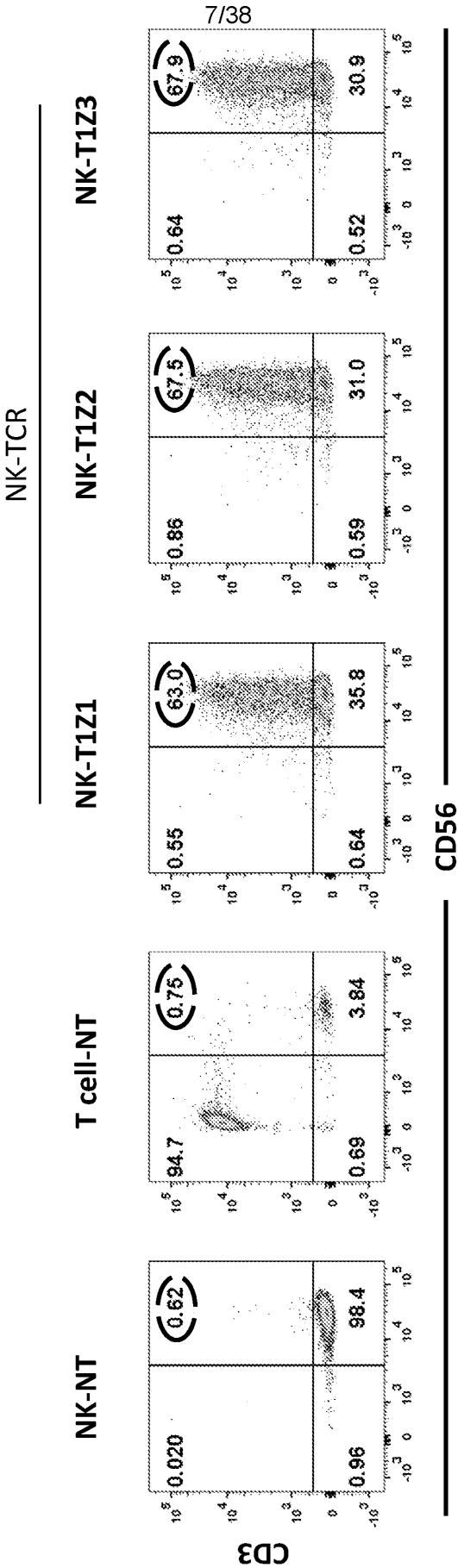


FIG. 4

NK-TCR

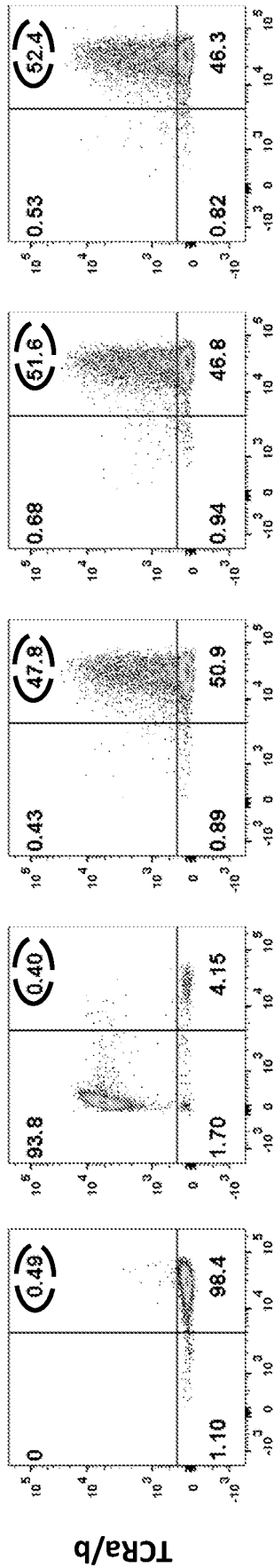
NK-T1Z3

NK-T1Z2

NK-T1Z1

T cell-NT

NK-NT



CD56

FIG. 5

NK-TCR

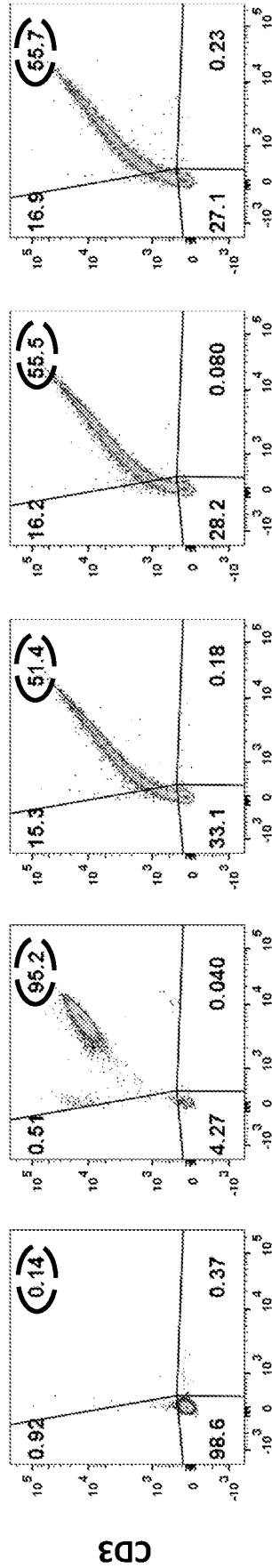
NK-NT

T cell-NT

NK-T1Z1

NK-T1Z2

NK-T1Z3



TCRa/b

FIG. 6

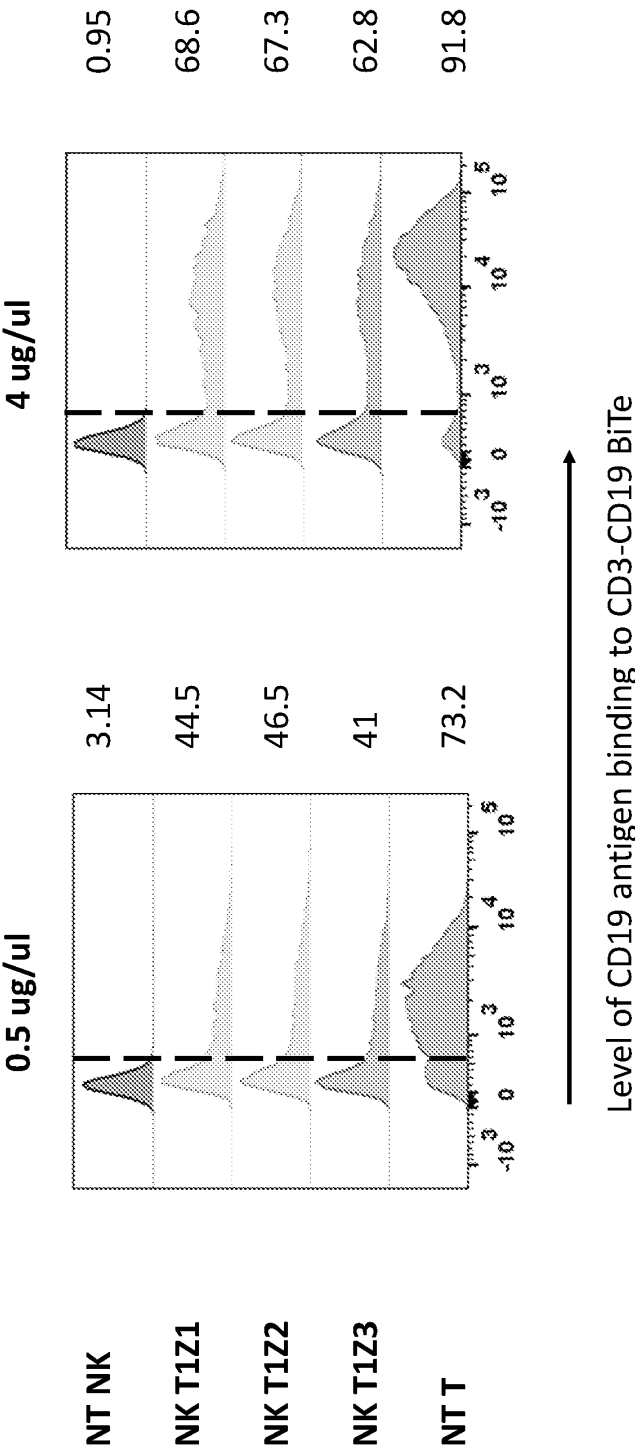


FIG. 7

NK-TCR

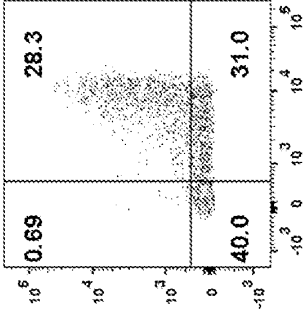
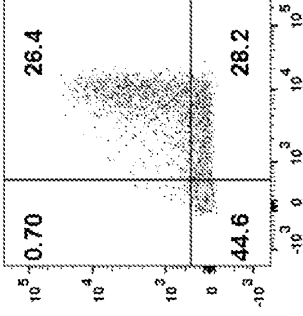
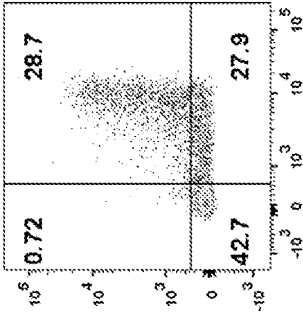
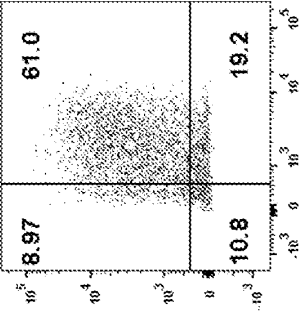
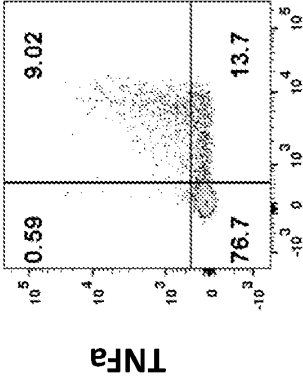
NK-NT

T cell-NT

NK-T1Z1

NK-T1Z2

NK-T1Z3



CD107a

FIG. 8

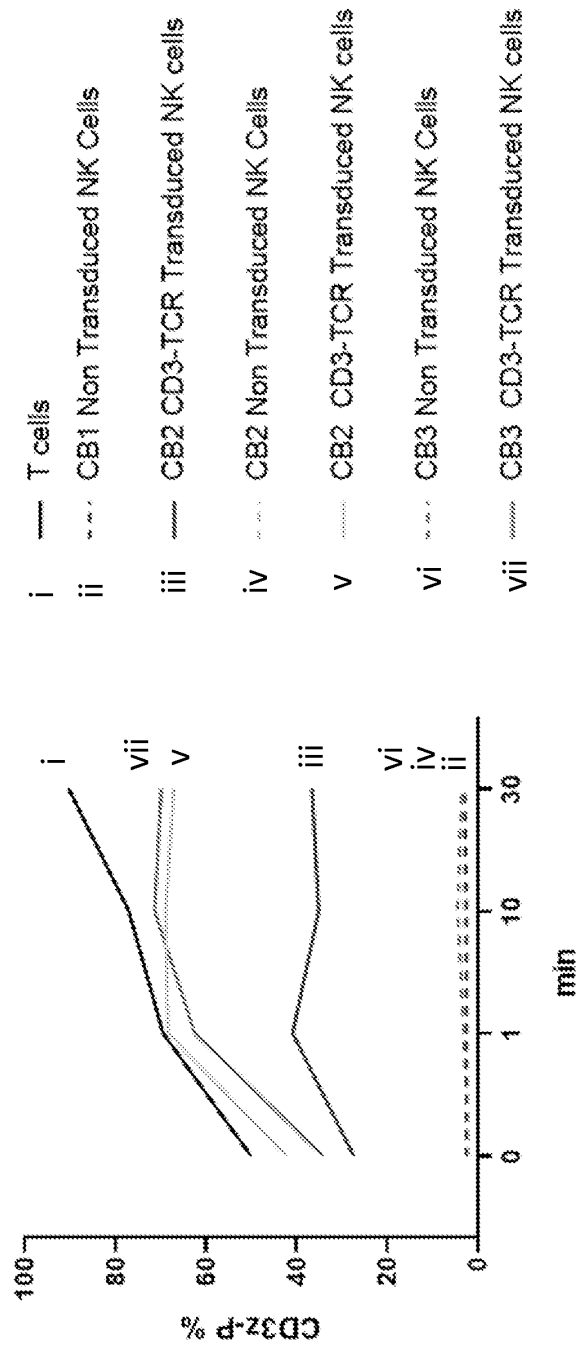


FIG. 9

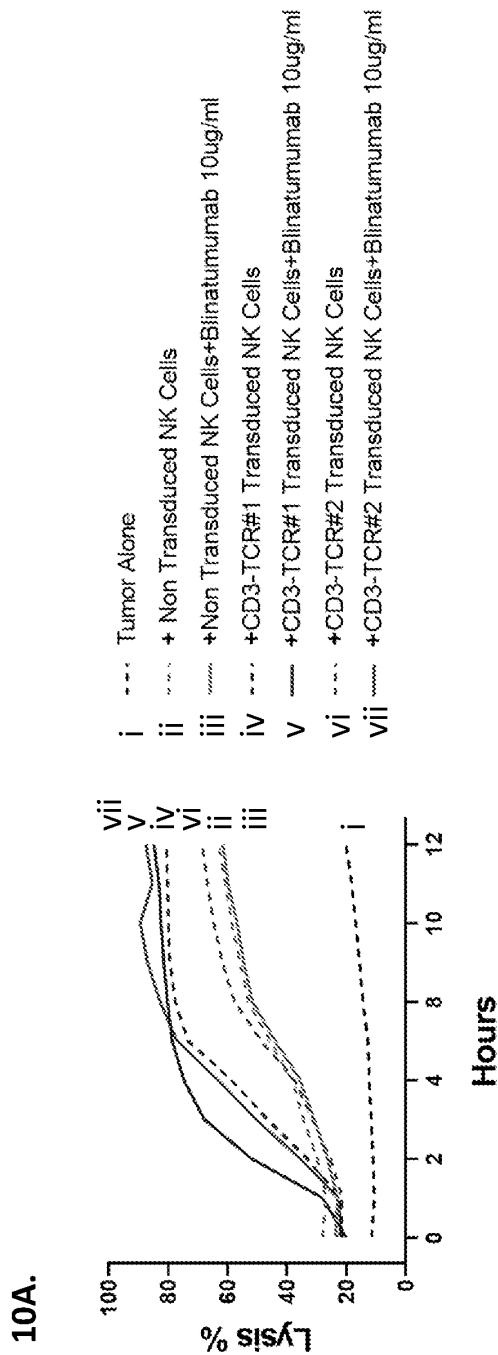


FIG. 10A

10B.

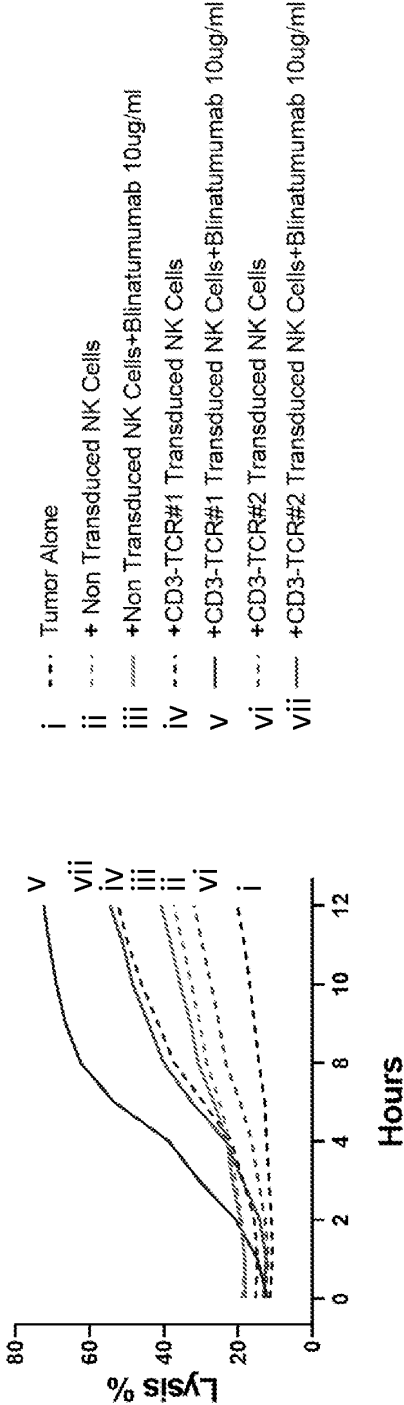


FIG. 10B

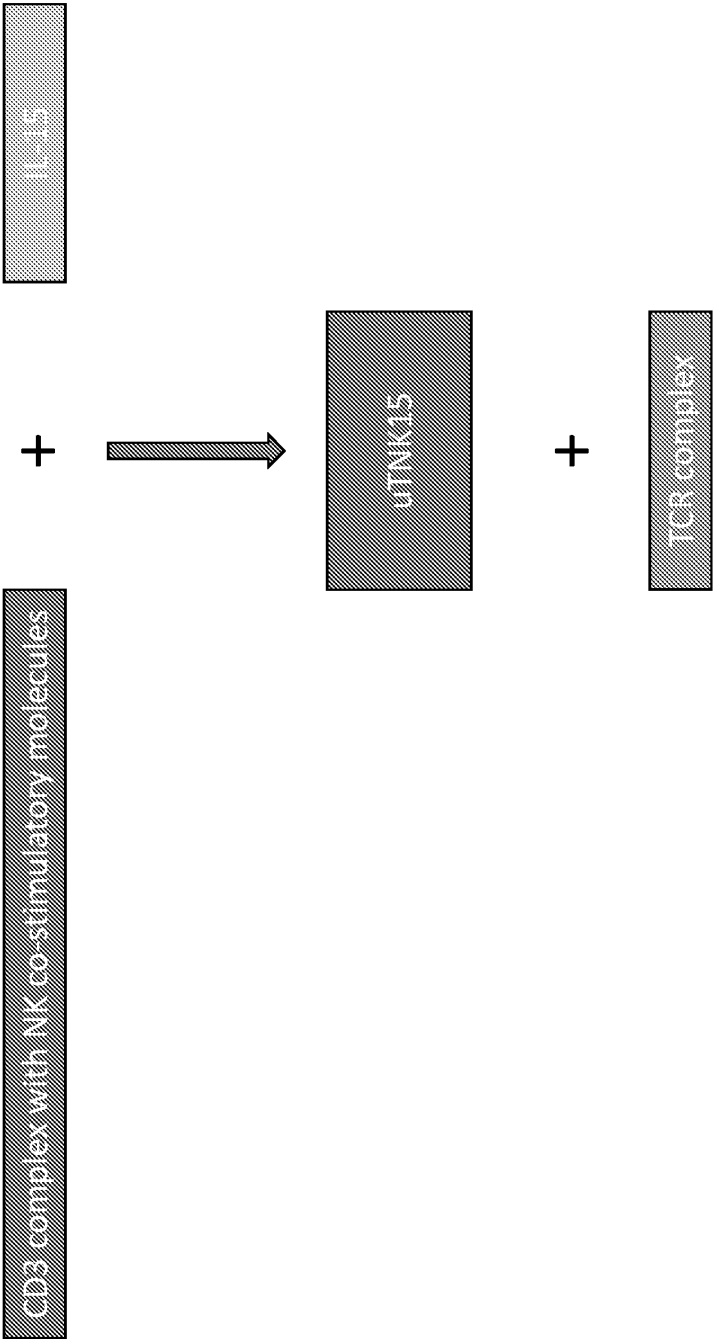


FIG. 11

Expression of NY-ESO TCR on NK cells transduced with uTNK15

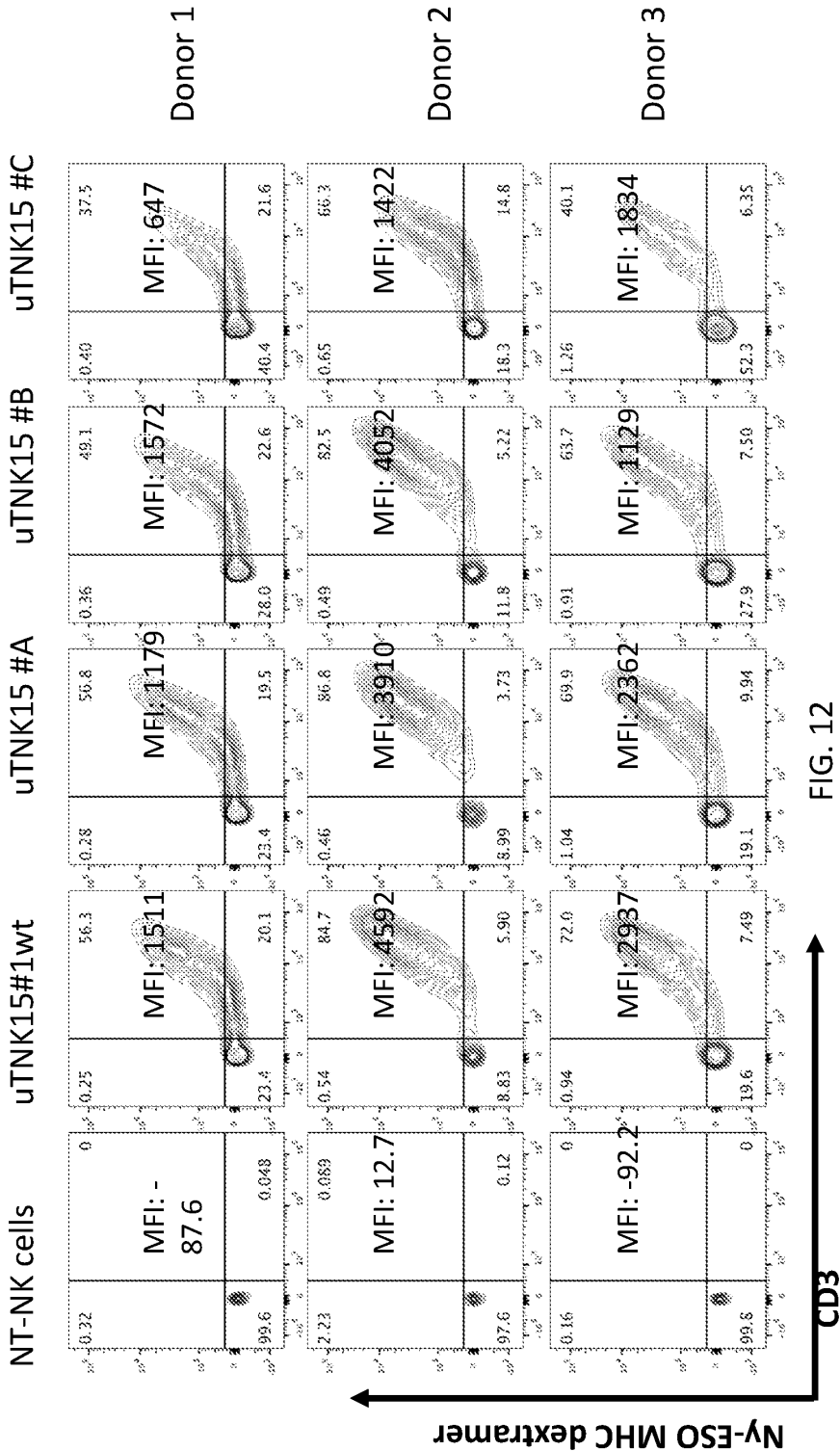


FIG. 12

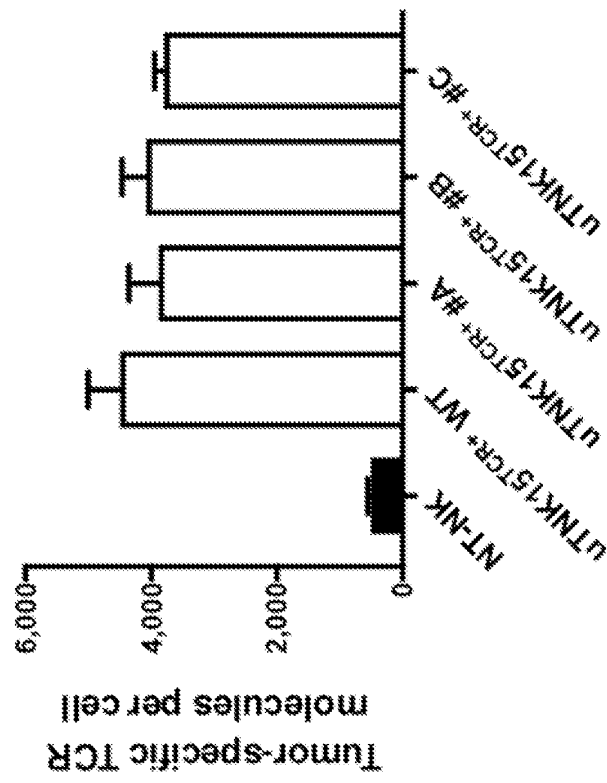


FIG. 13

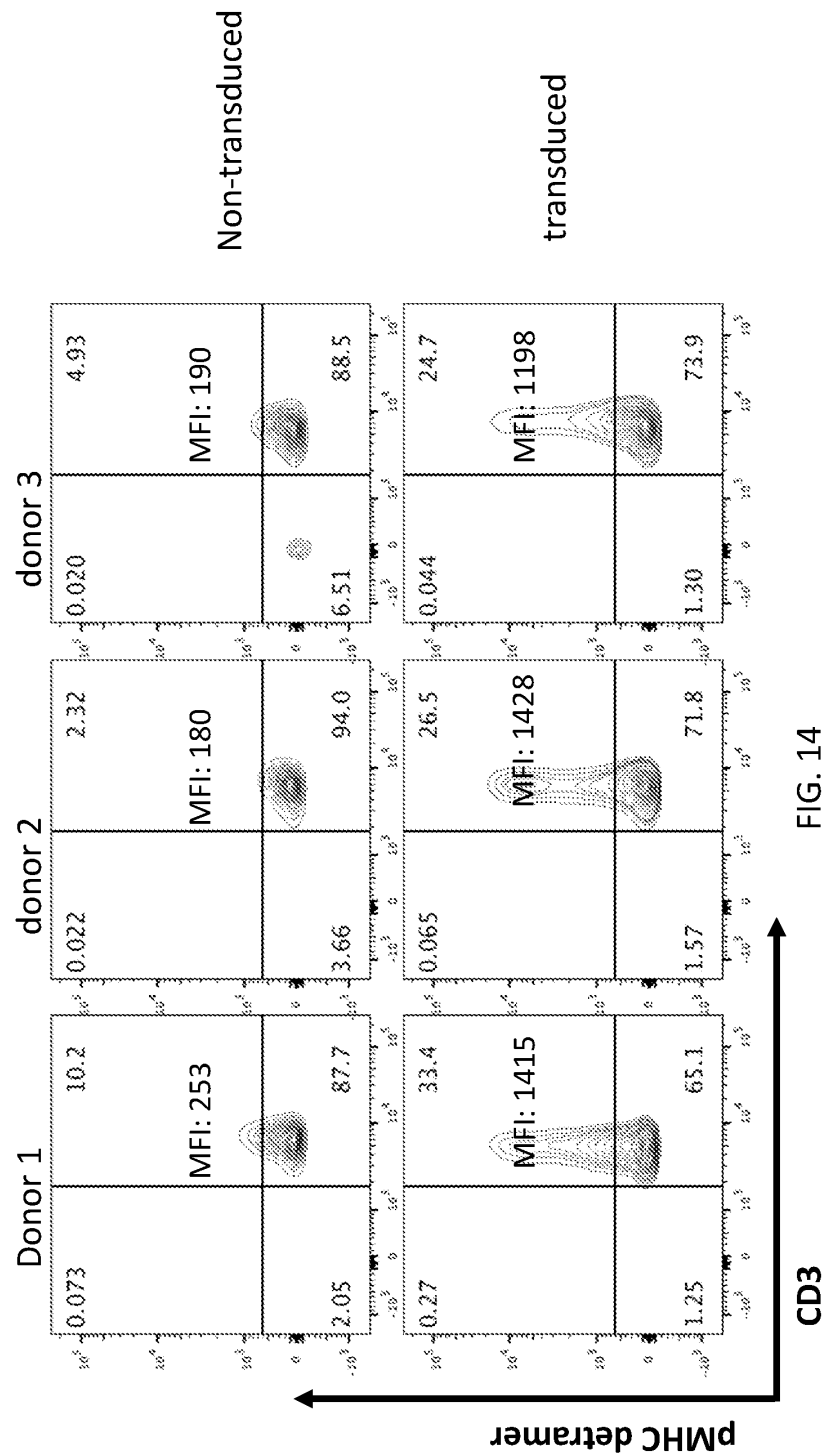


FIG. 14

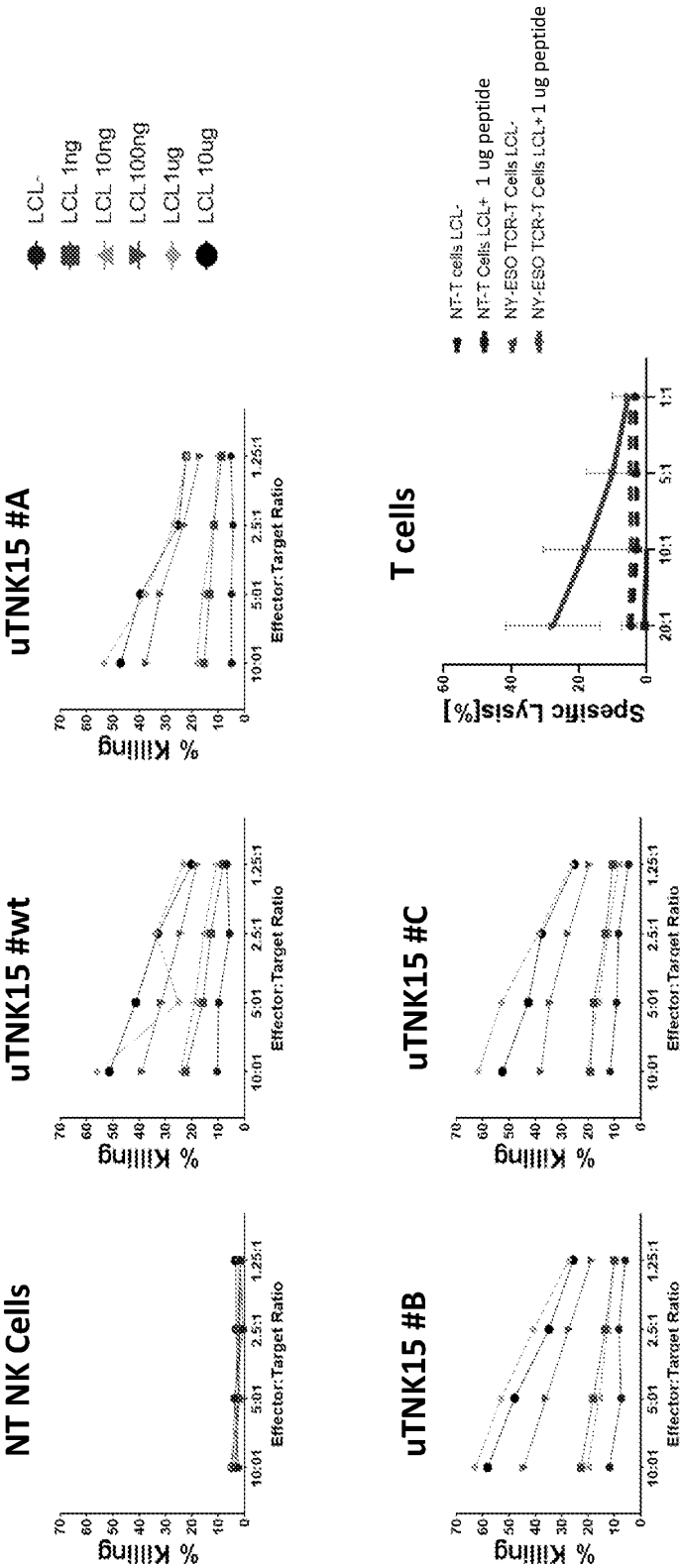


FIG. 15

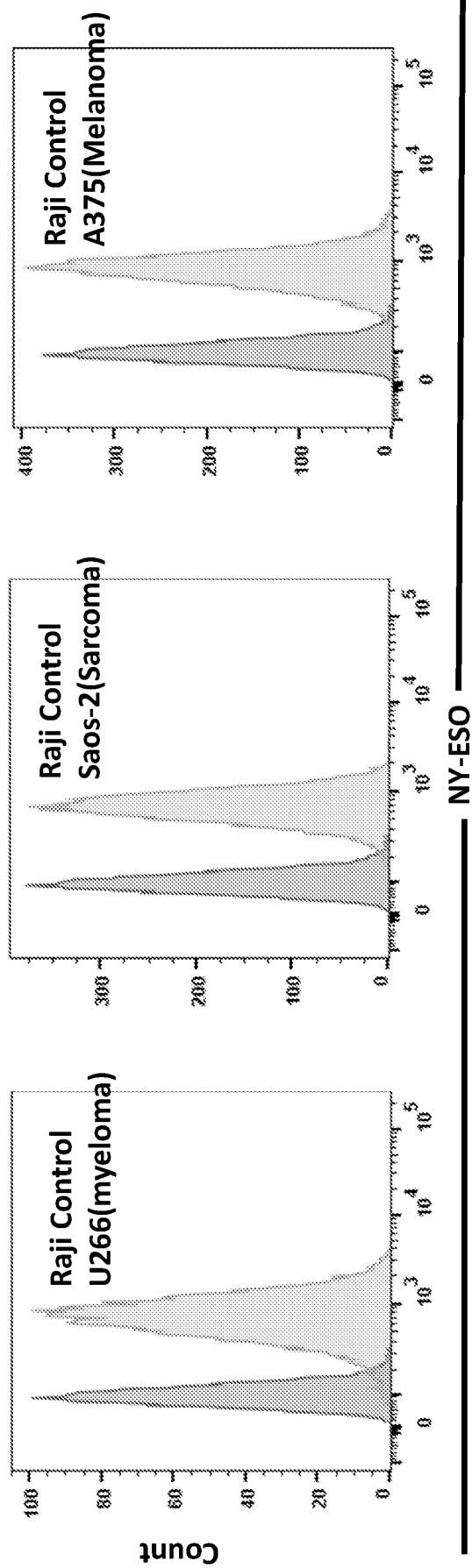
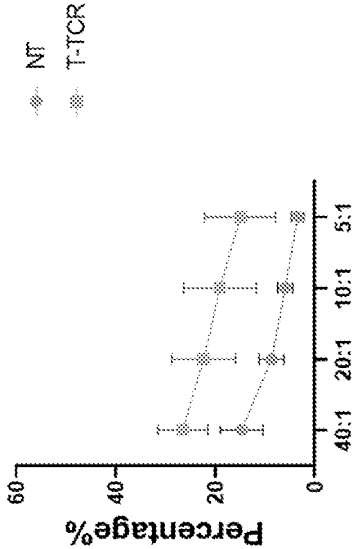
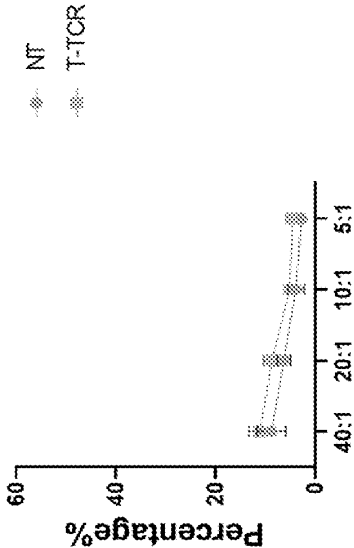


FIG. 16

A375(Melanoma)



Saos-2(Osteosarcoma))



U266(M.Myeloma)

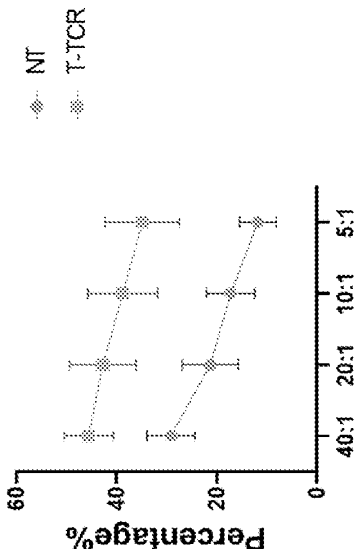
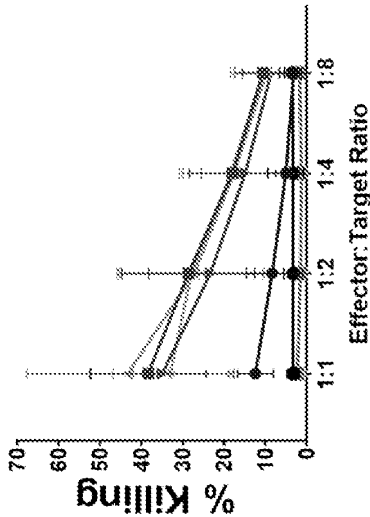
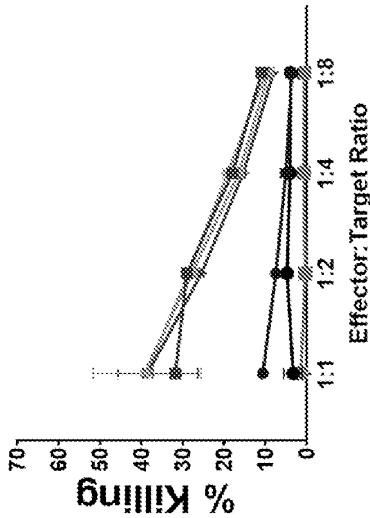


FIG. 17

A375(Melanoma)



Saos-2(Osteosarcoma))



U266(M.Myeloma)

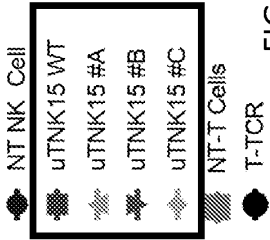
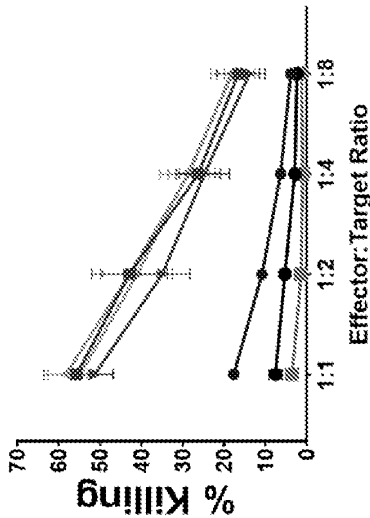
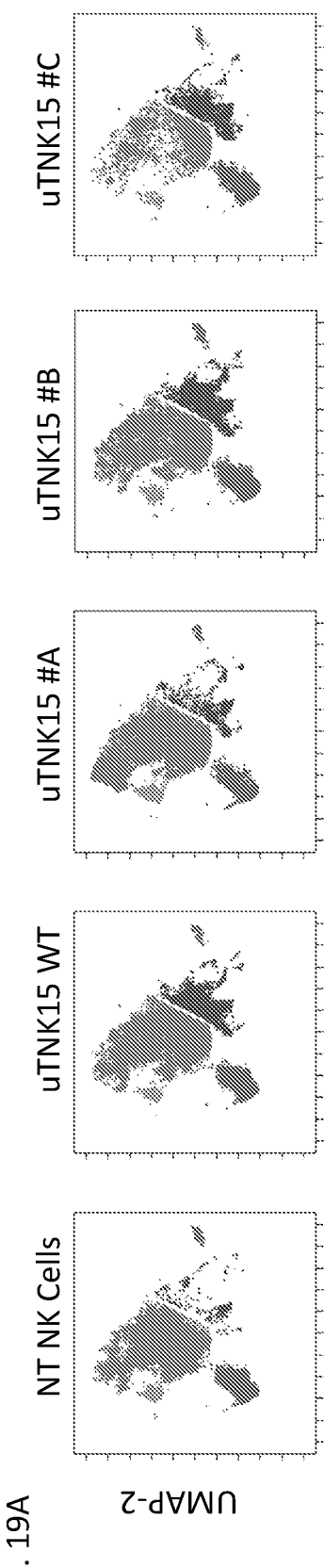
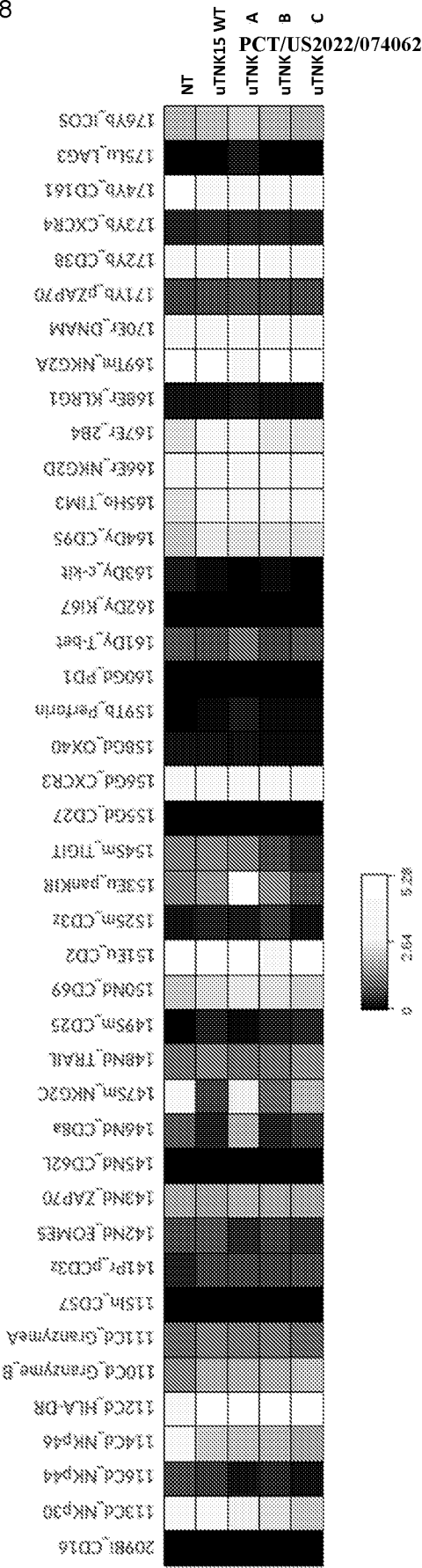


FIG. 18



UMAP-1

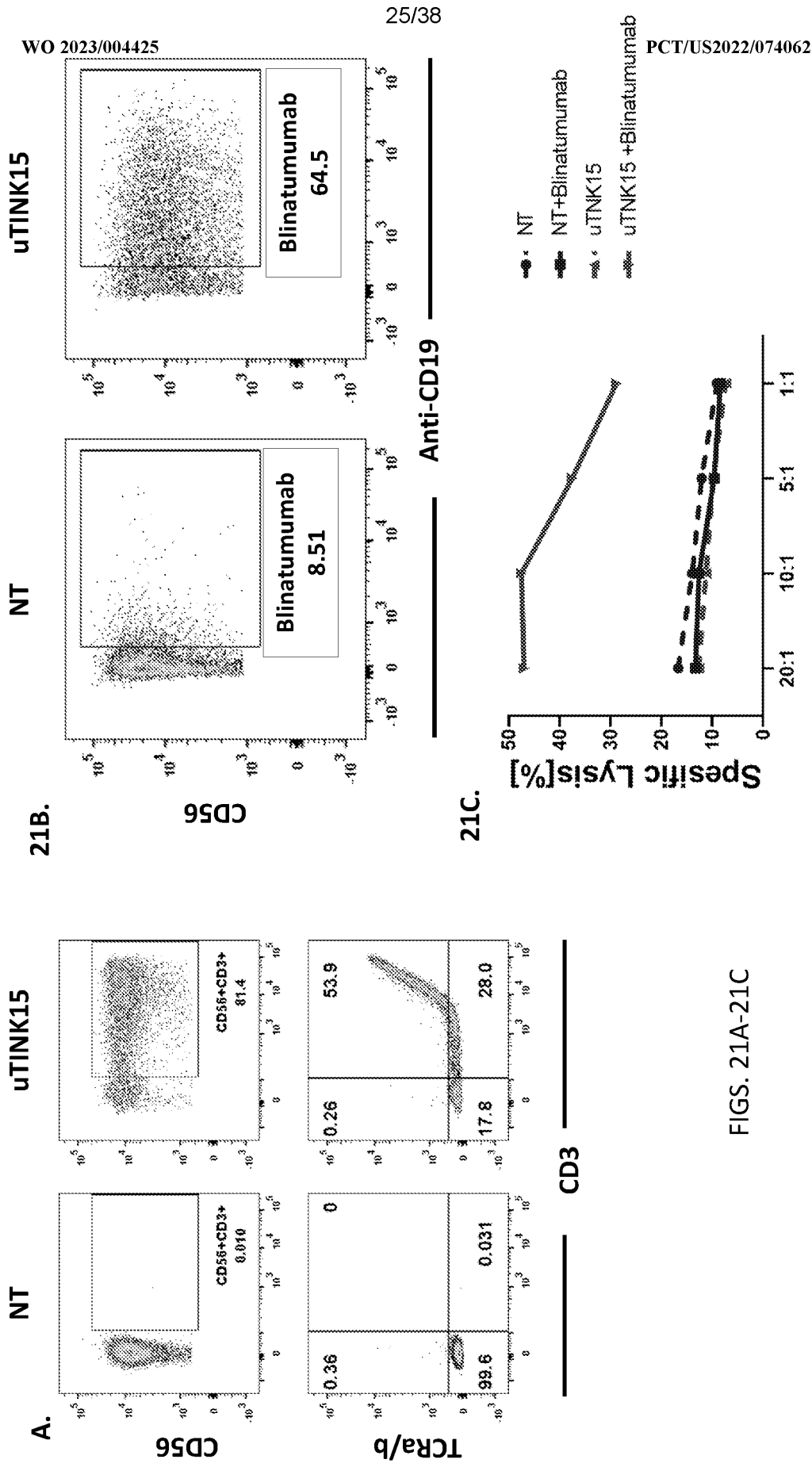
FIG. 19B



Cellular composition of the expanded uTNK15 product

	Gated on CD56+ NK cells	Gated on CD56+ NK cells
	CD3+	CD3+TCR+
NT	0.091	0.18
uTNK15 WT	81.1	42.2
uTNK15 #A	77.1	41.1
uTNK15 #B	80.9	43.8
uTNK15 #C	66	25.6

FIG. 20



FIGS. 21A-21C

22A.

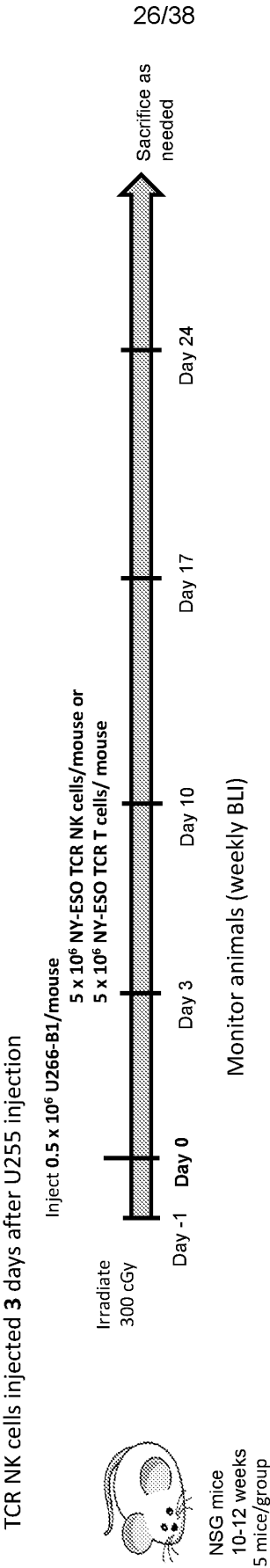


FIG. 22A

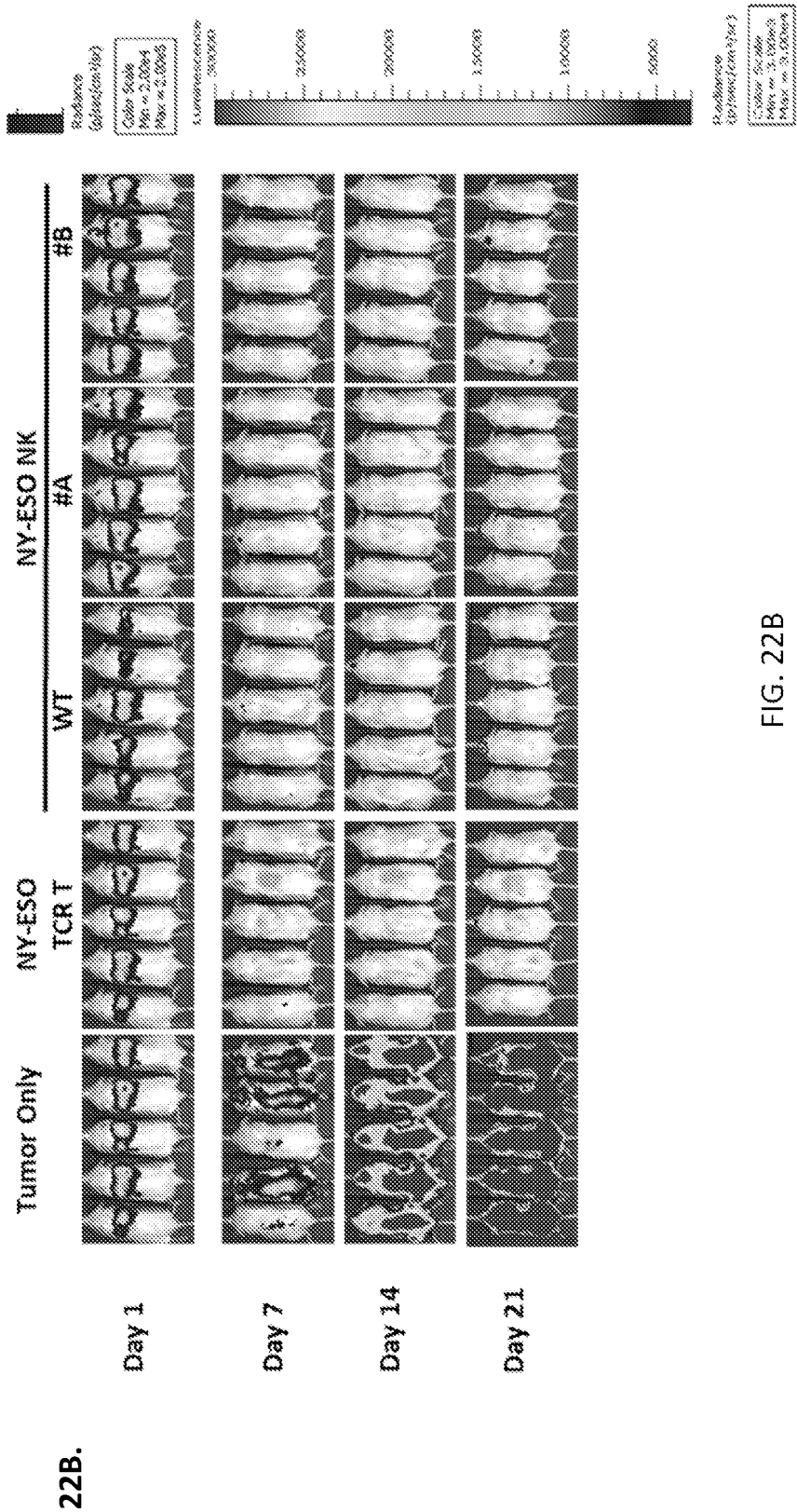


FIG. 22B

22C.

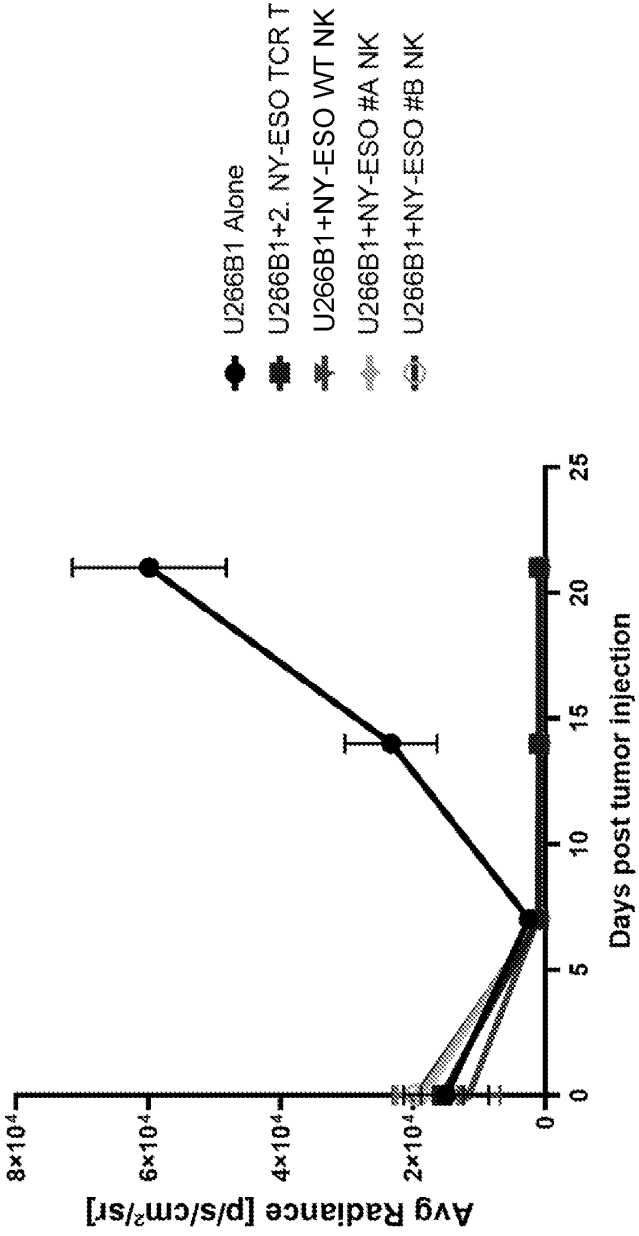
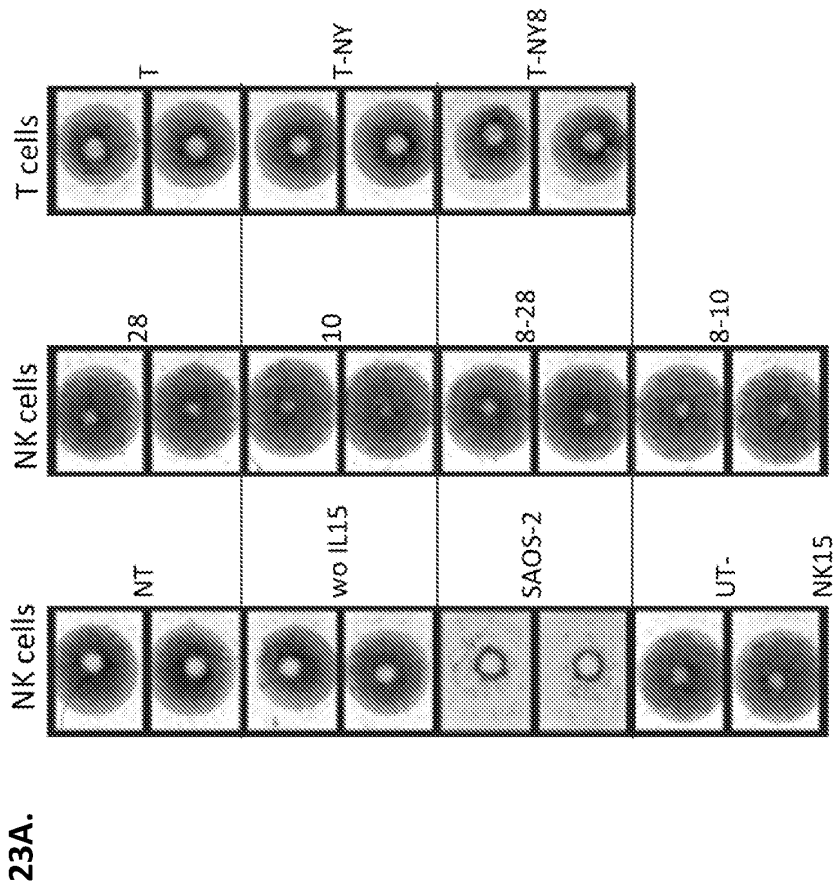


FIG. 22C



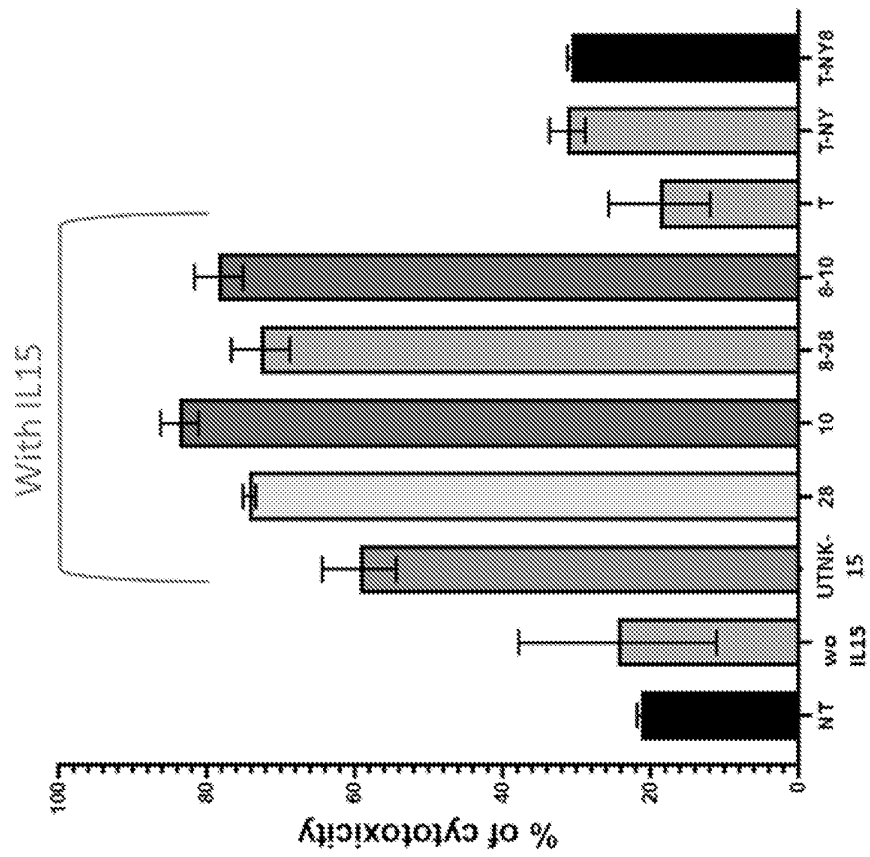


FIG. 23B

24A.

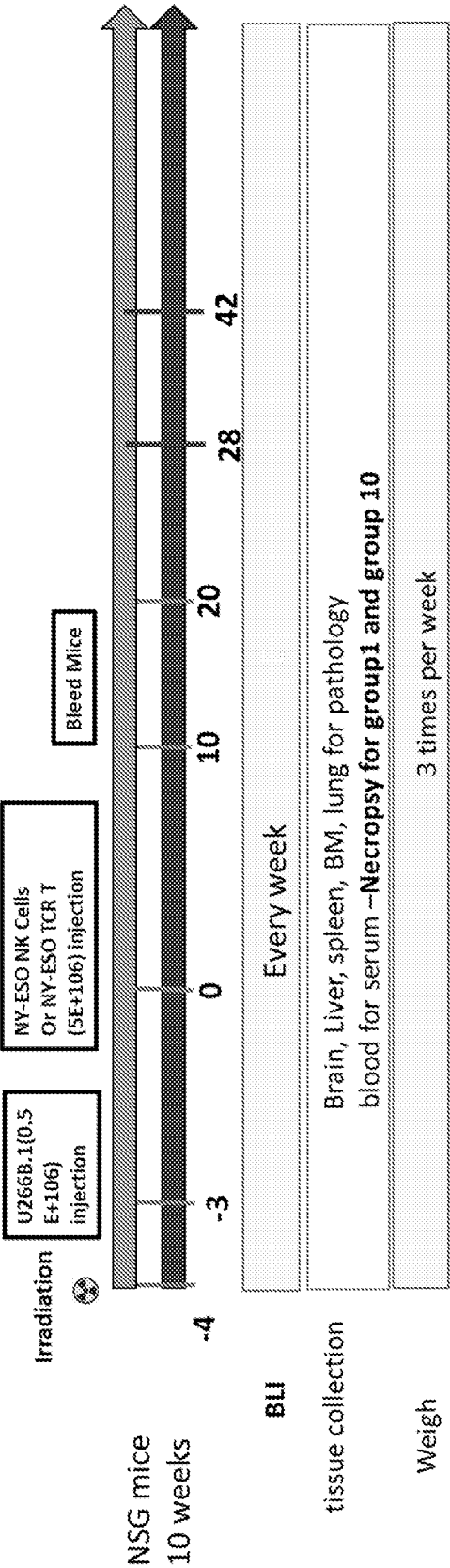
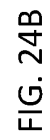


FIG. 24A



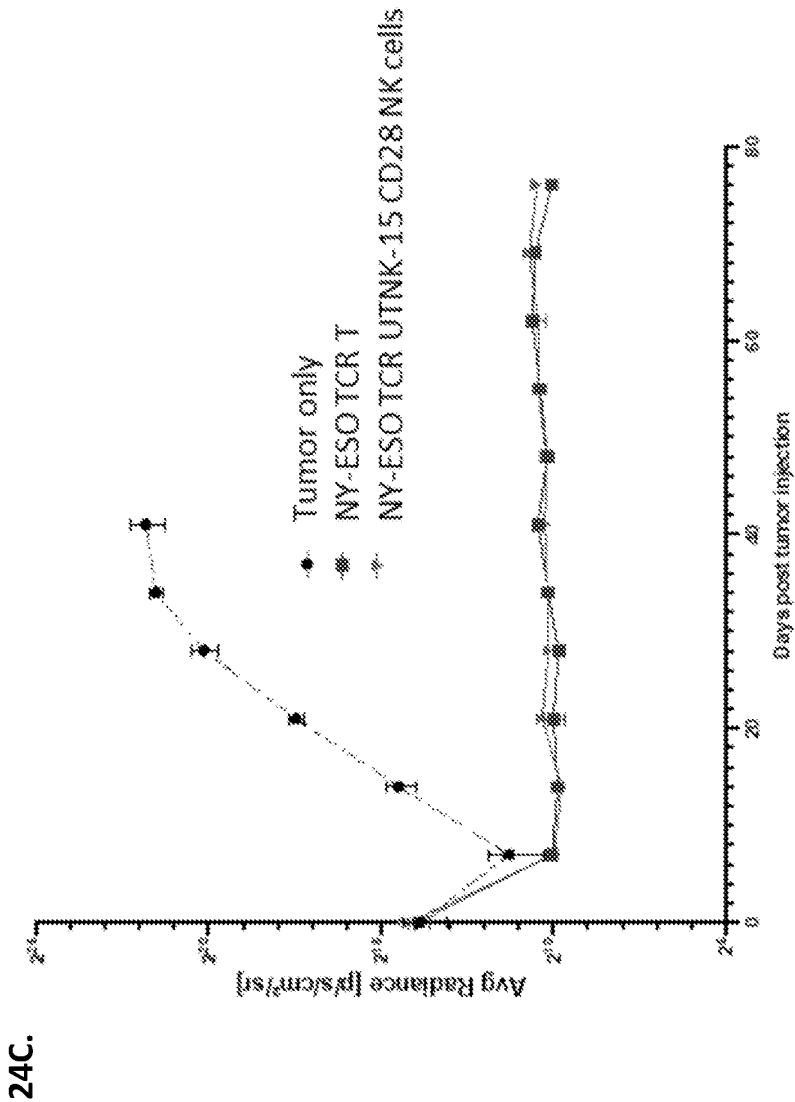


FIG. 24C

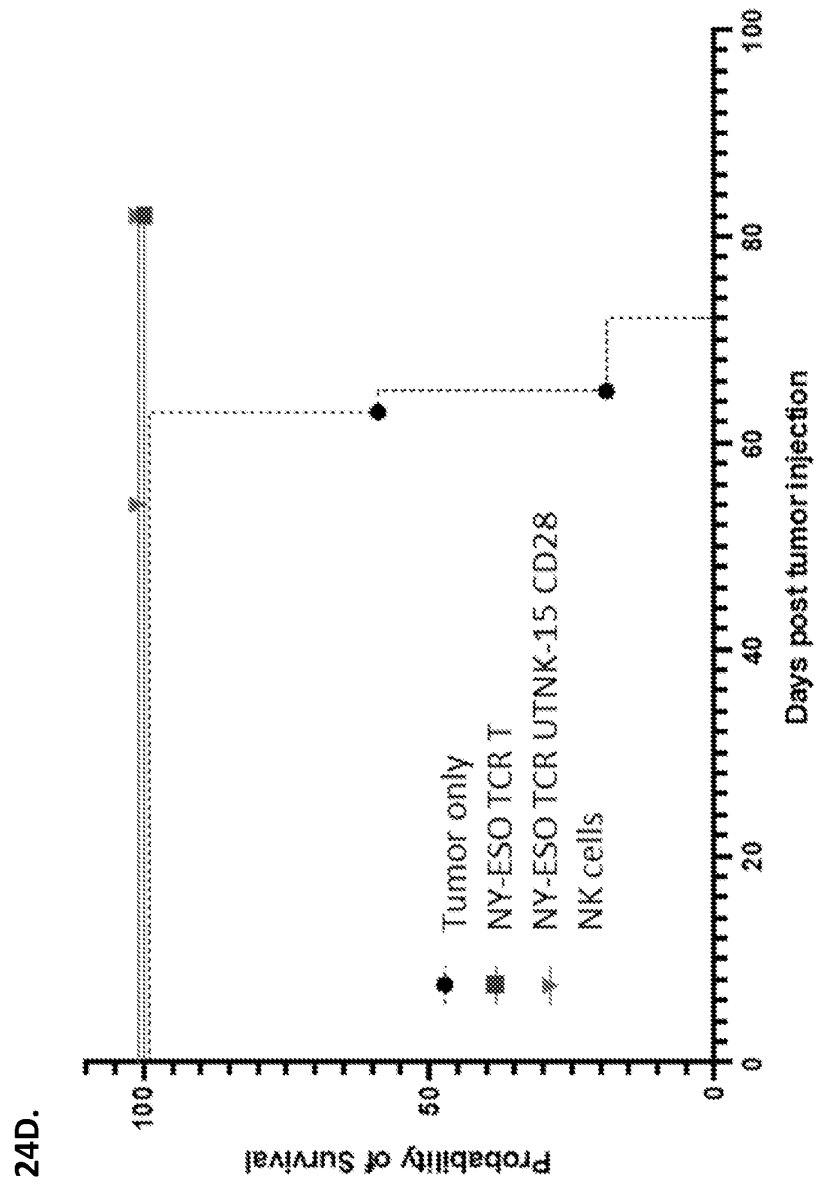


FIG. 24D

25.

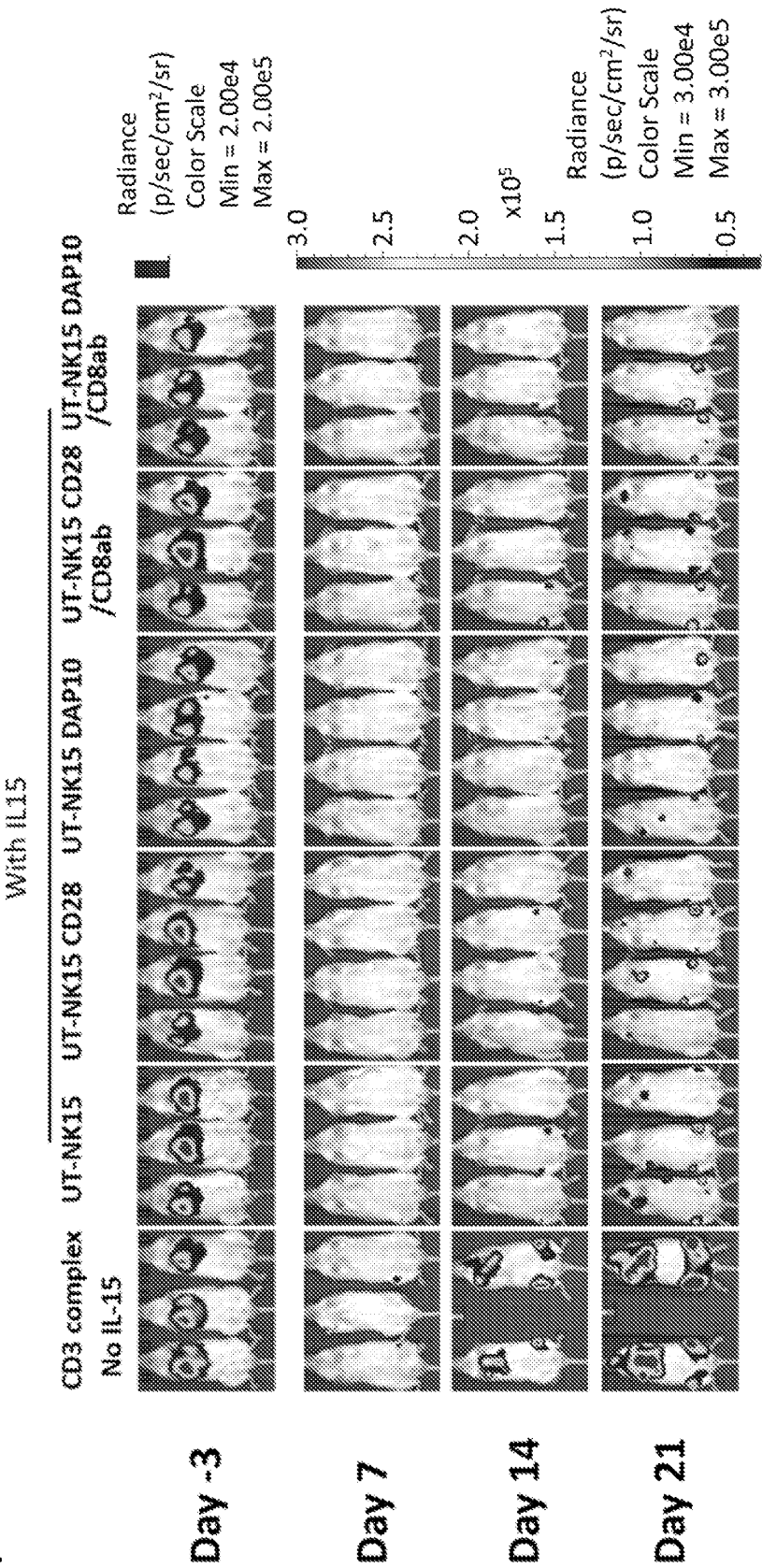


FIG. 25

26A.

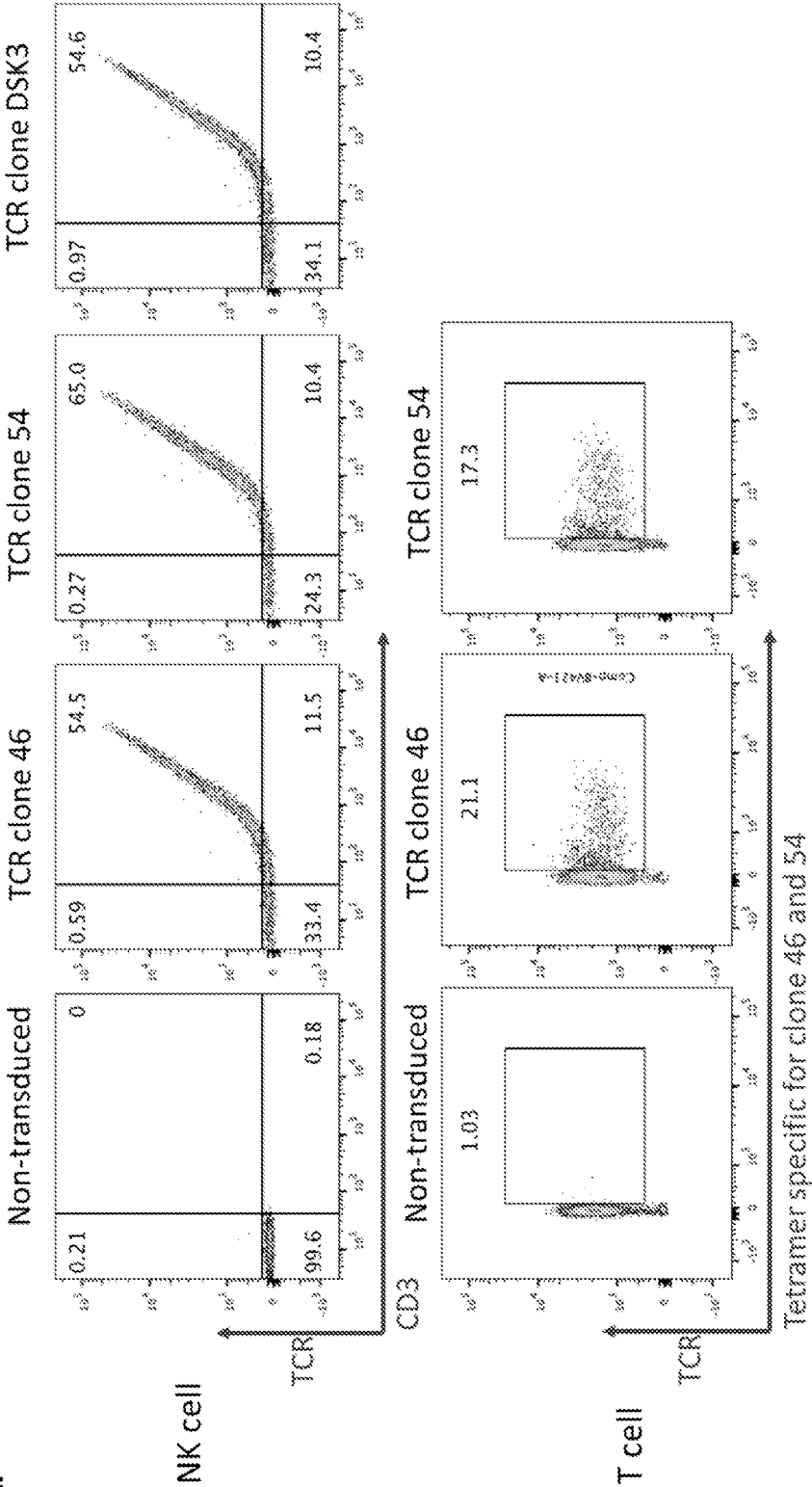


FIG. 26A

26B.

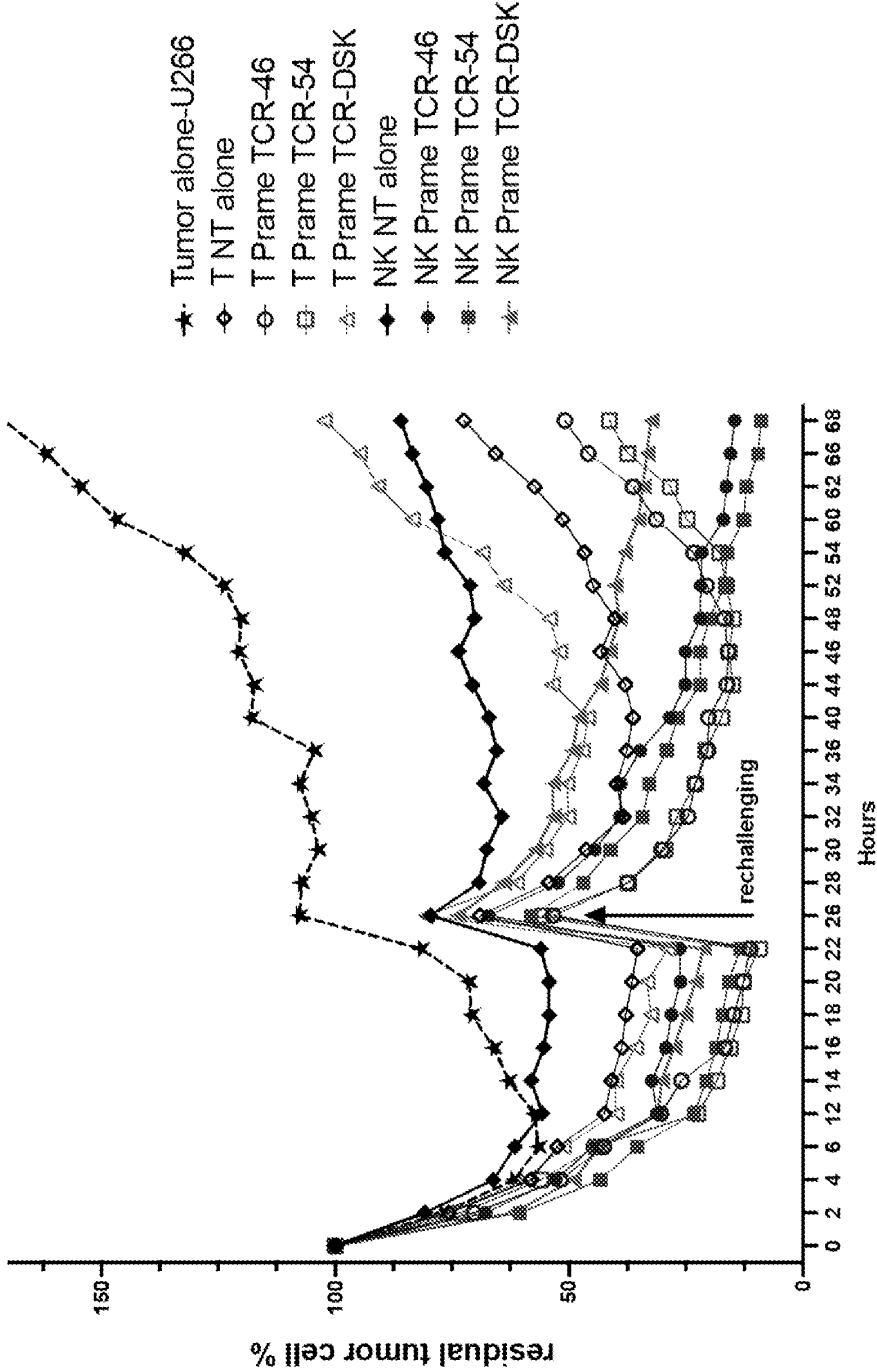


FIG. 26B

26C.

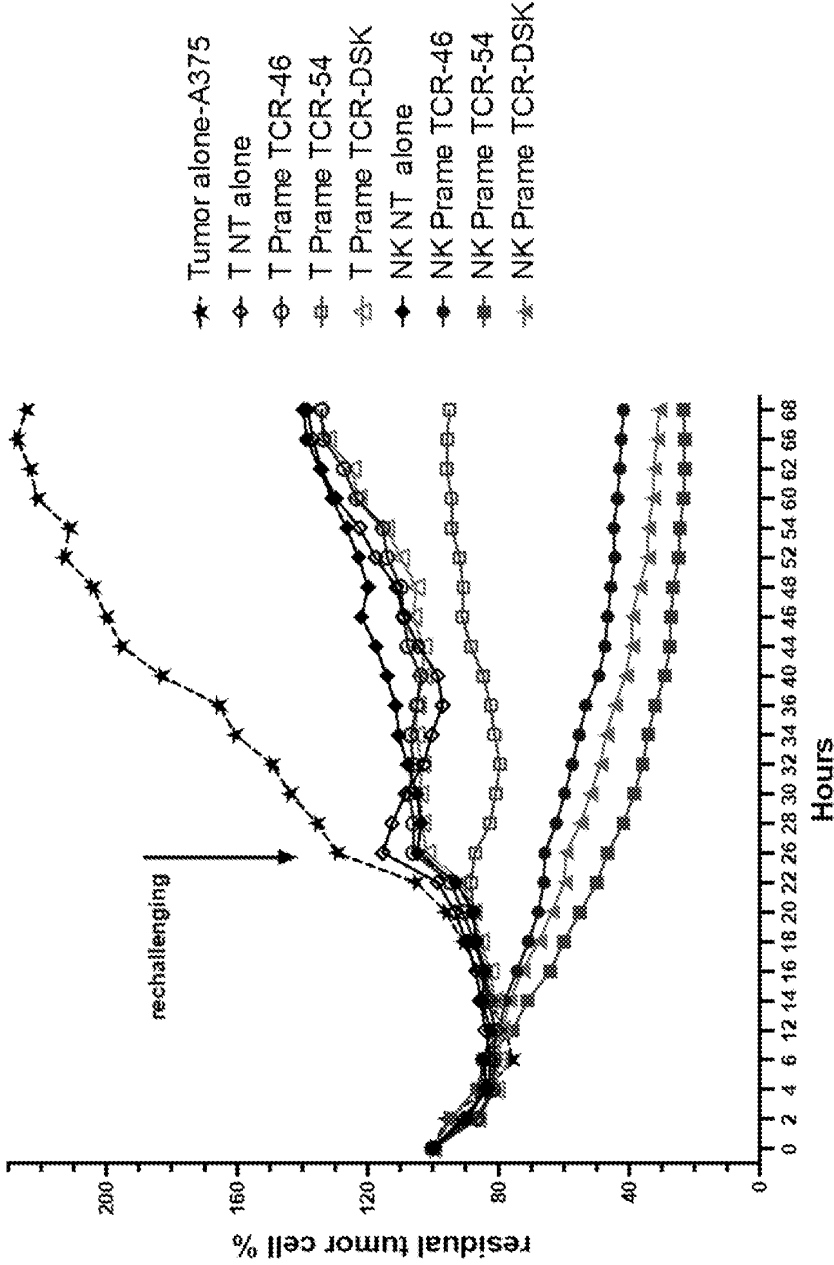


FIG. 26C