

FIG. 1B

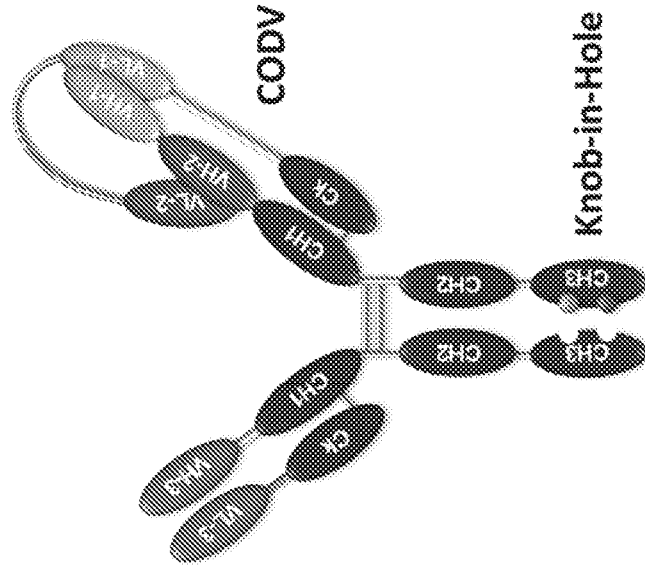


FIG. 1A

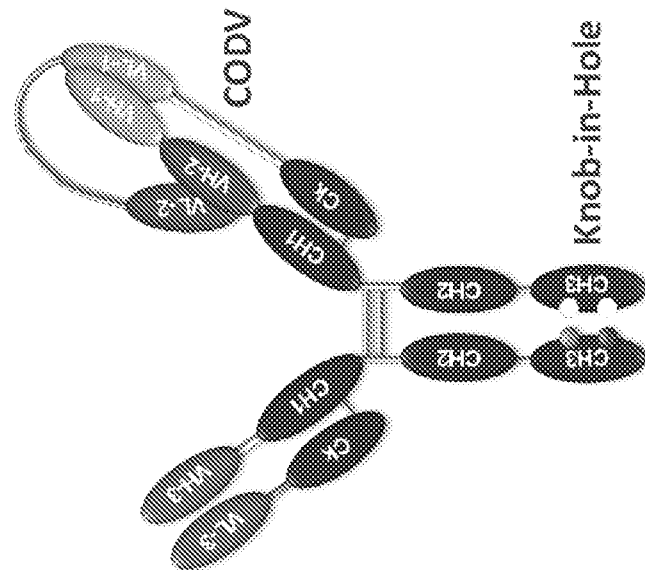


FIG. 1C

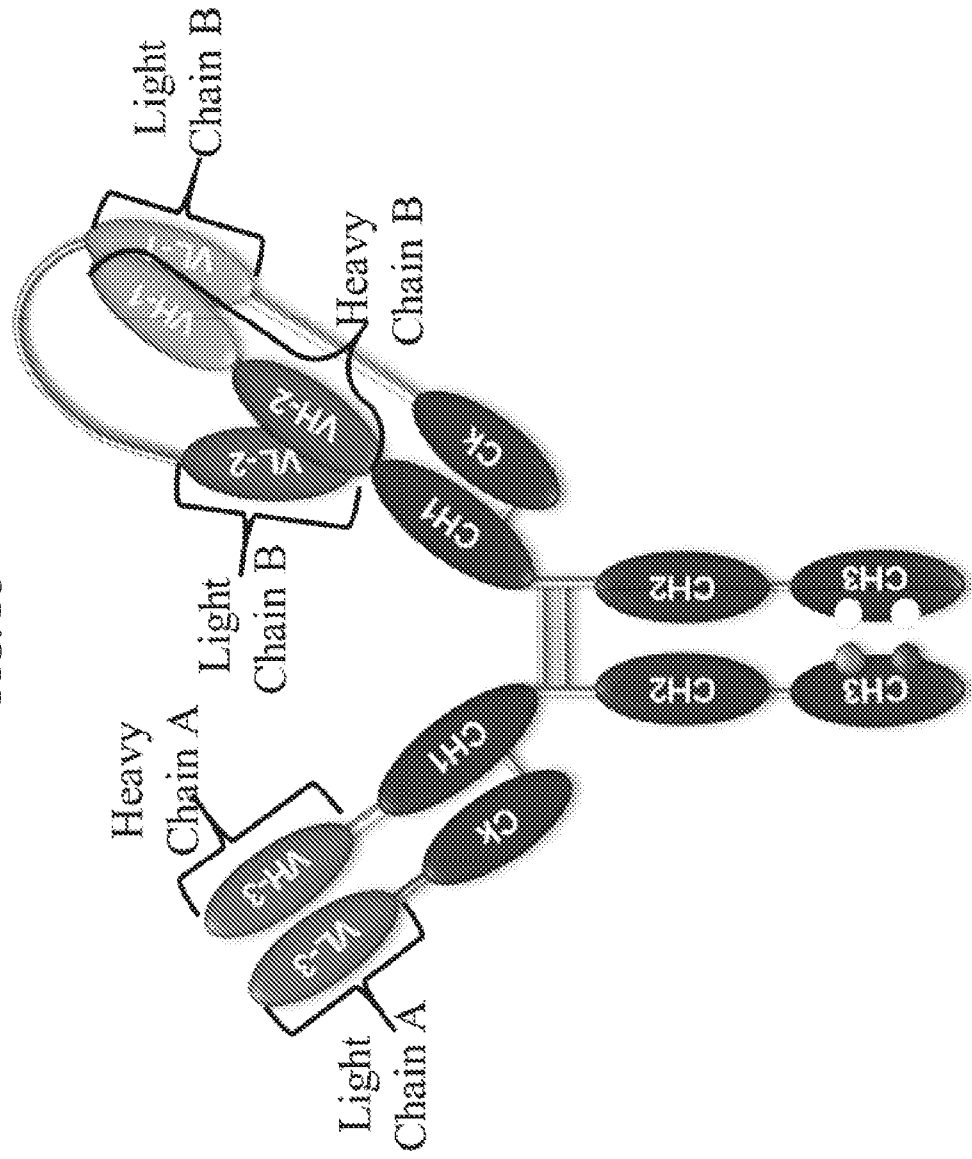
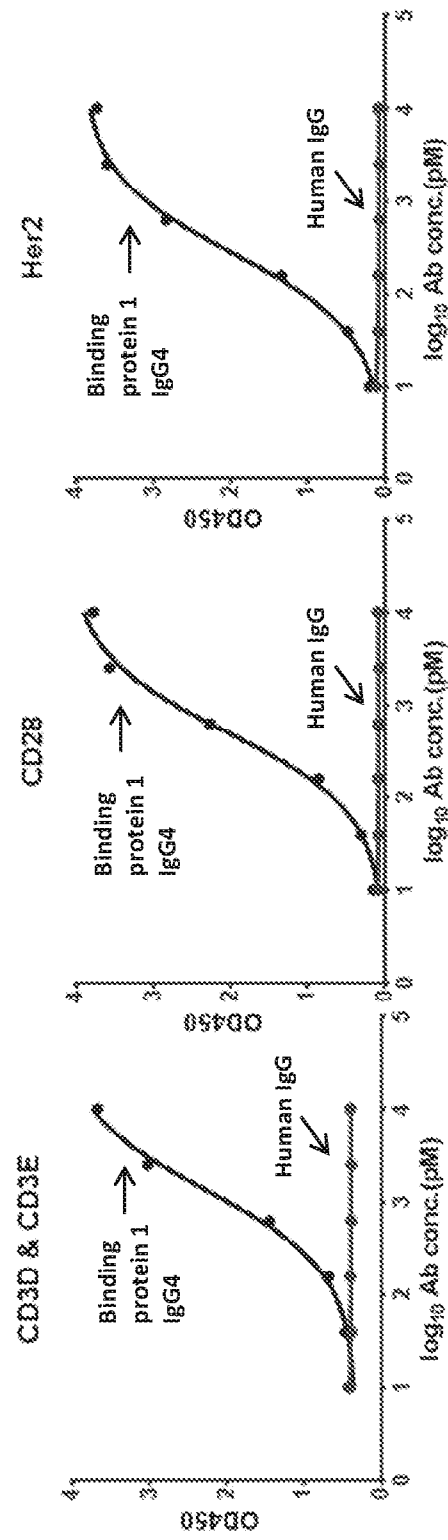


FIG. 2



◆ Human IgG

◆ Binding Protein 1 IgG4

FIG. 3B

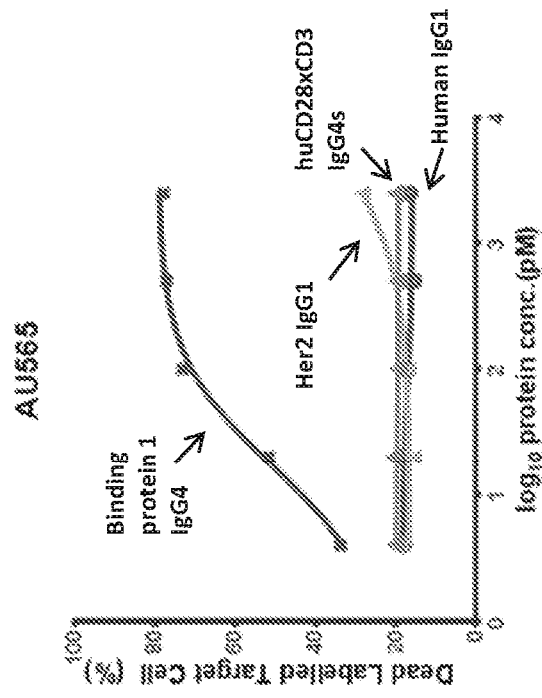
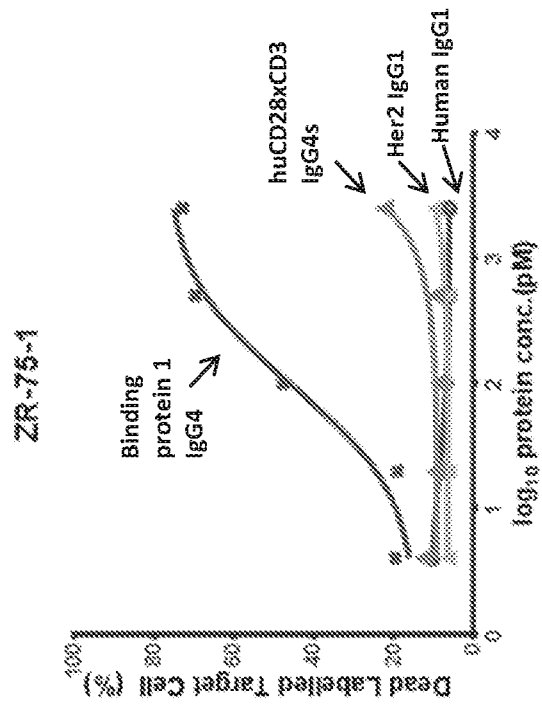


FIG. 3A



- huCD28 x CD3 IgG4s
- Binding Protein 1 IgG4
- Her2 IgG1
- human IgG1

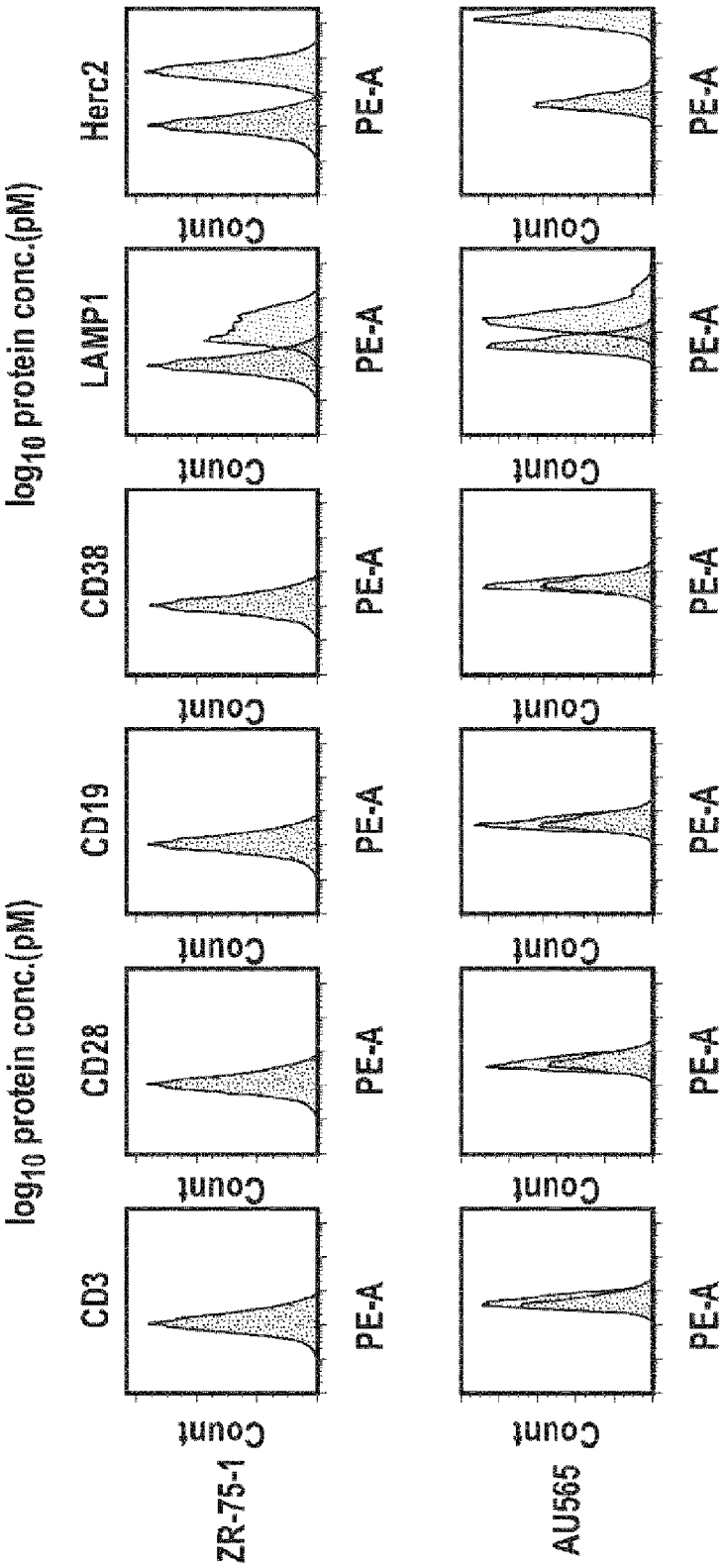
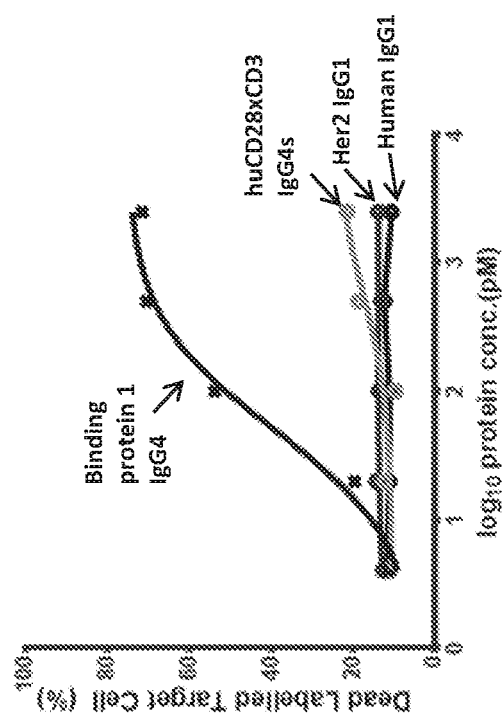
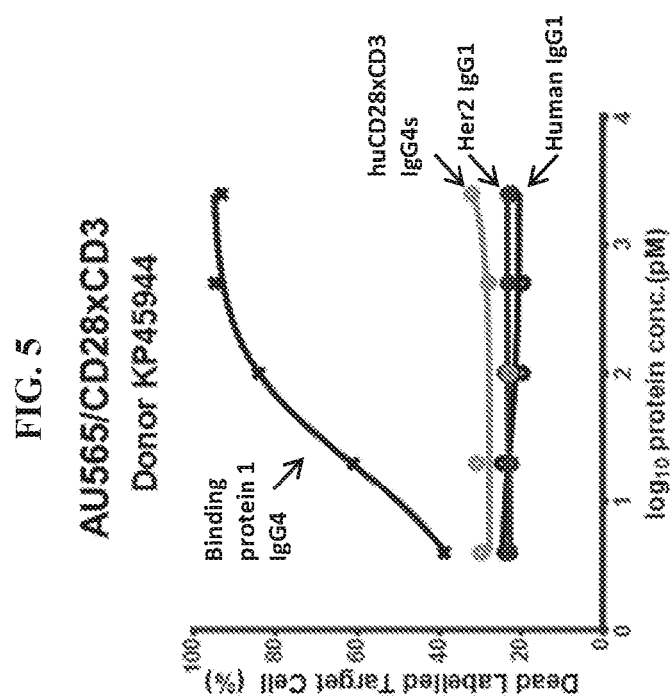


FIG. 3C

FIG. 4
ZR-75-1/CD28xCD3
 Donor KP45926



- huCD28 x CD3 IgG4s
- Binding Protein 1 IgG4
- Her2 IgG1
- human IgG1

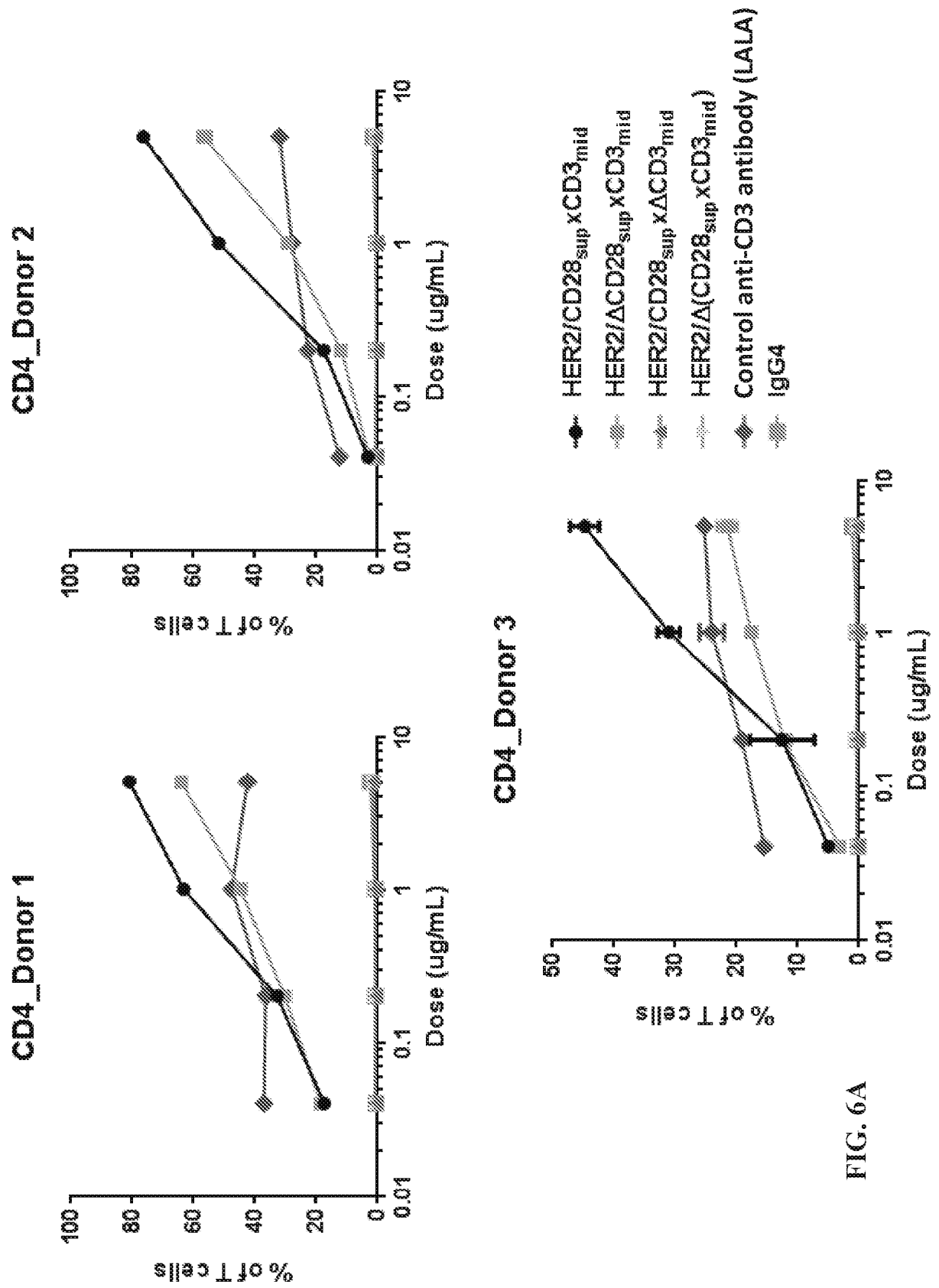


FIG. 6A

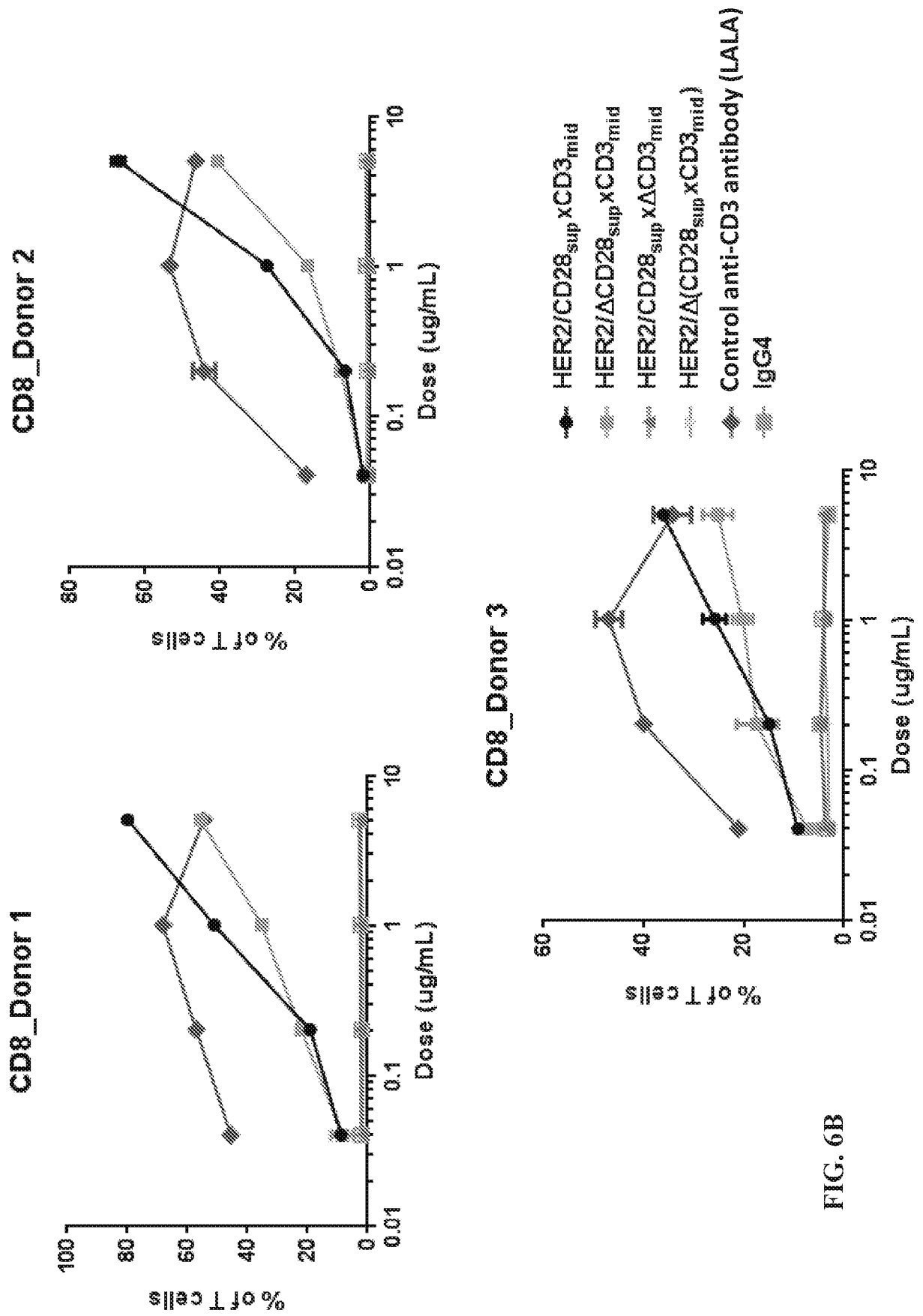


FIG. 6B

FIG. 7A

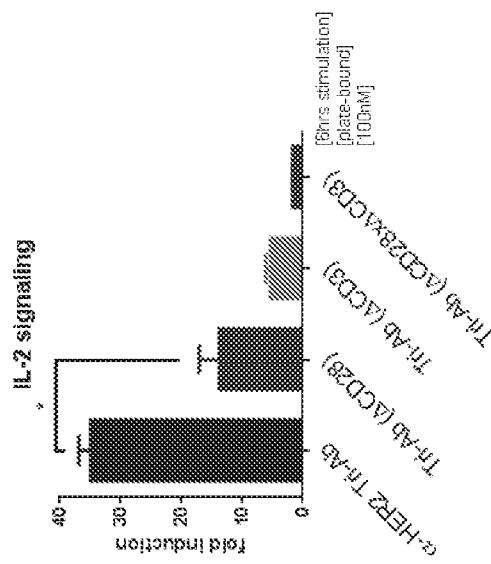


FIG. 7B

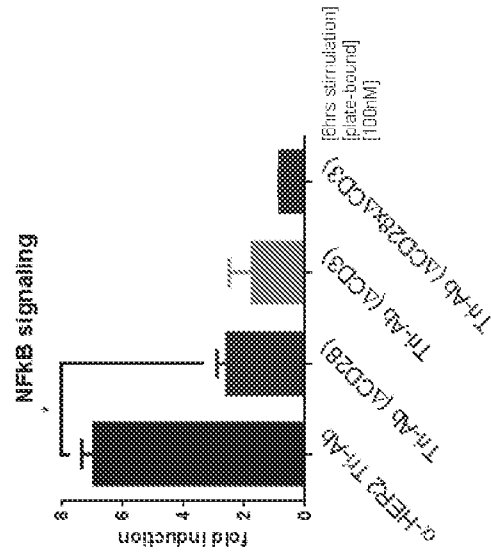


FIG. 7C

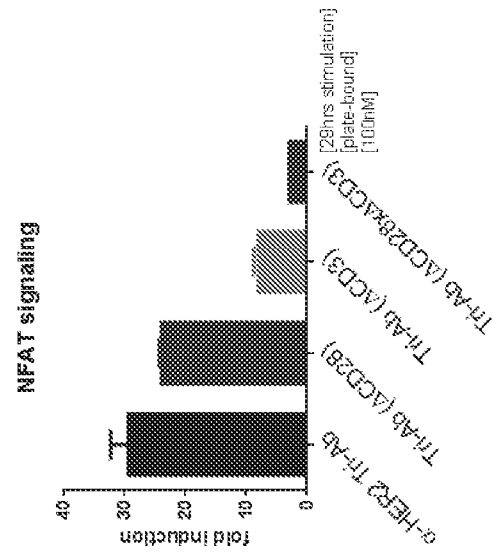
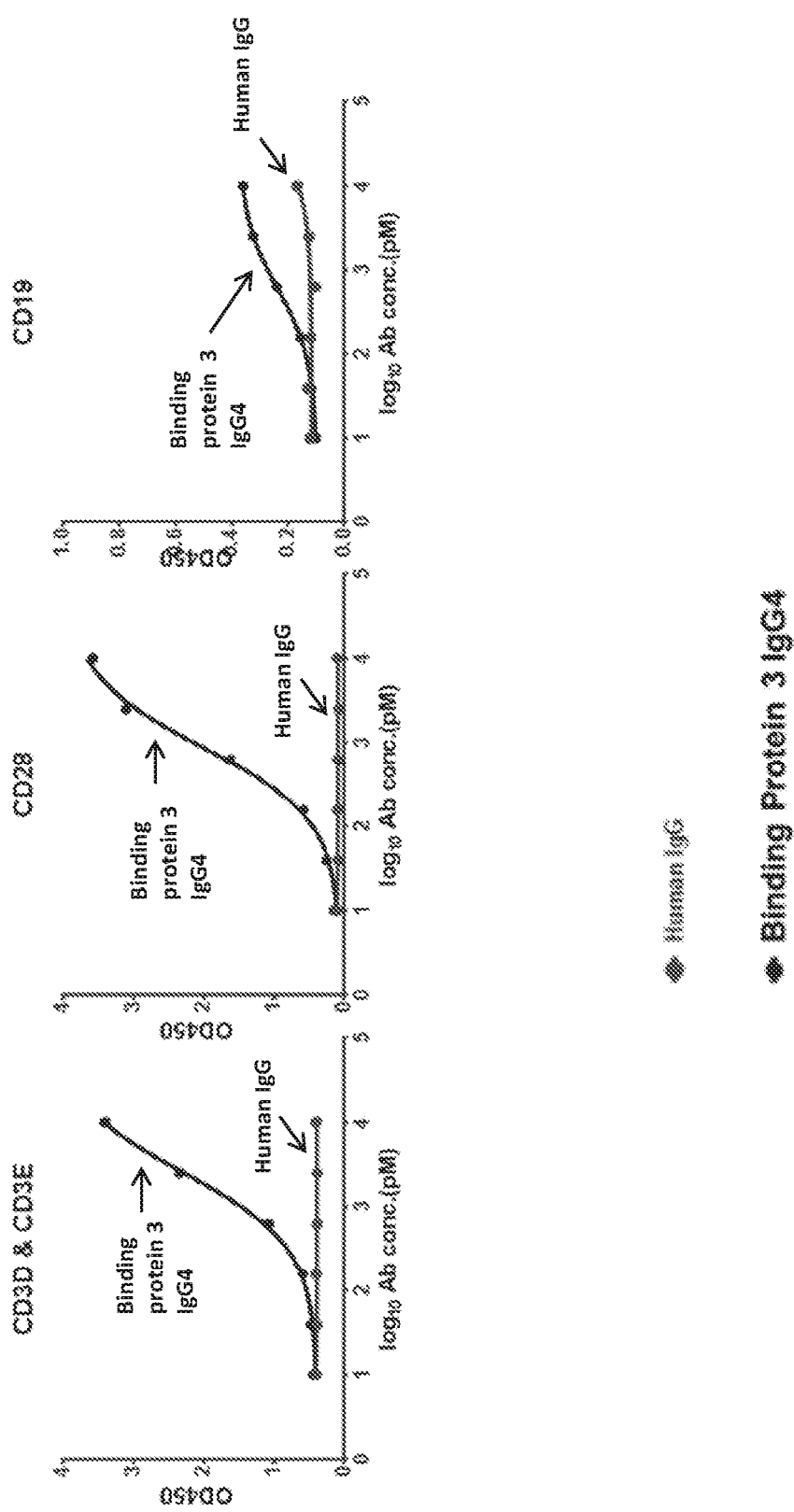


FIG. 8



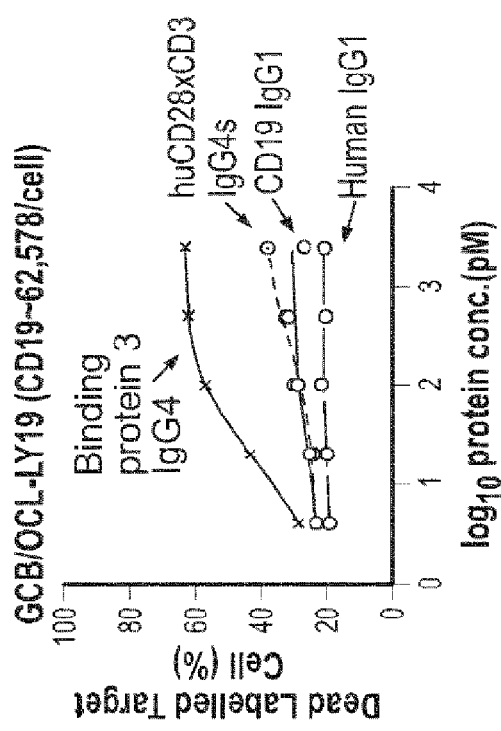
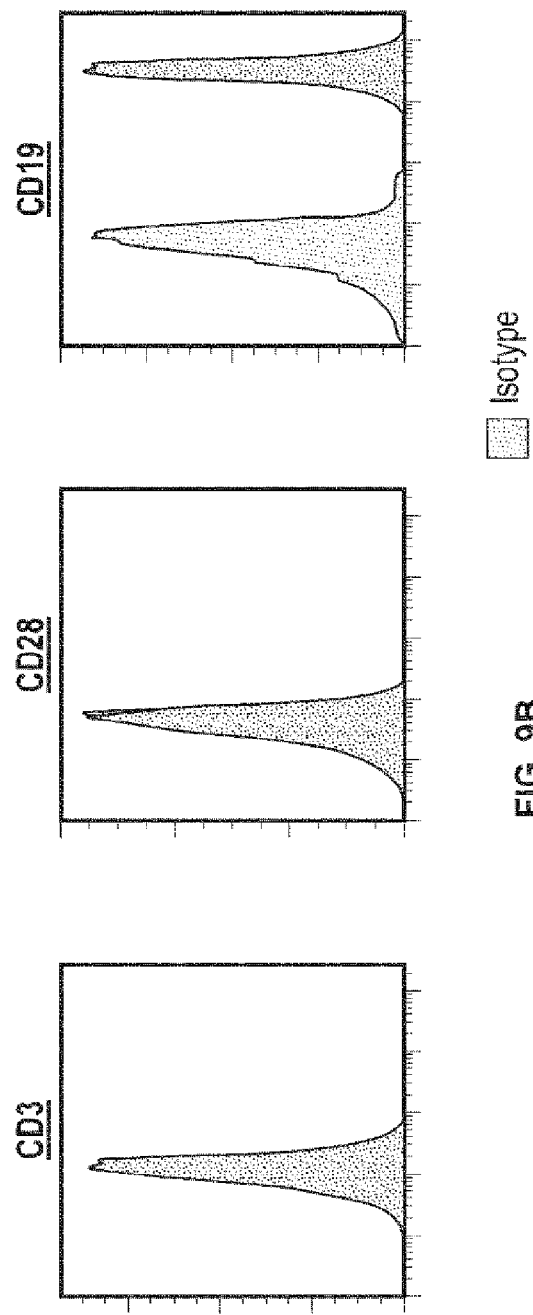


FIG. 9C

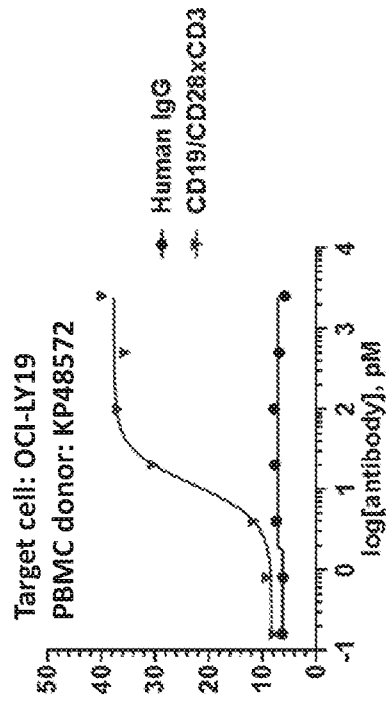


FIG. 9D

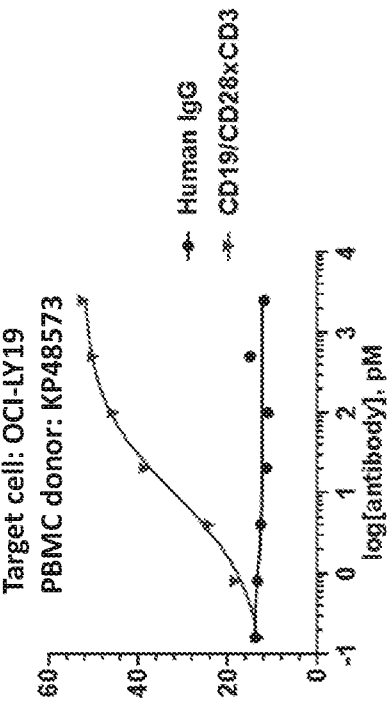


FIG. 9E

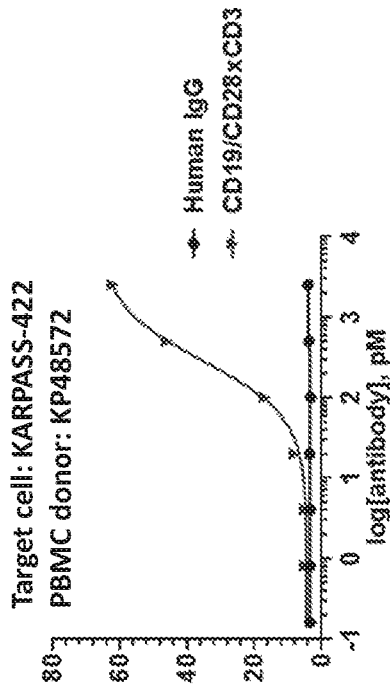


FIG. 9F

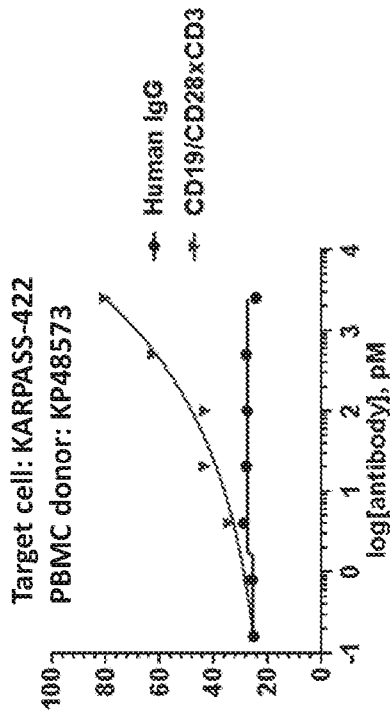


FIG. 9G

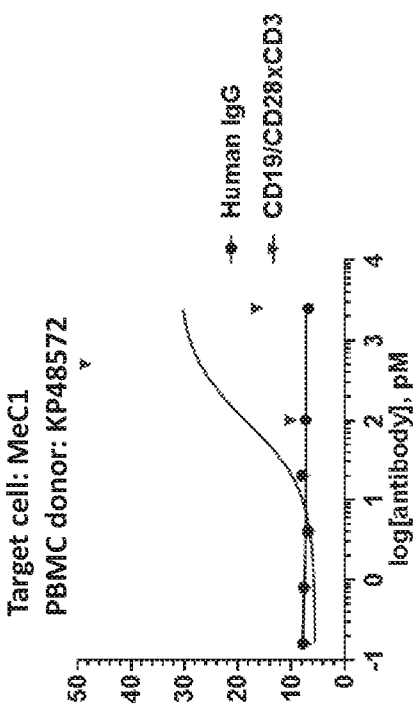


FIG. 9I

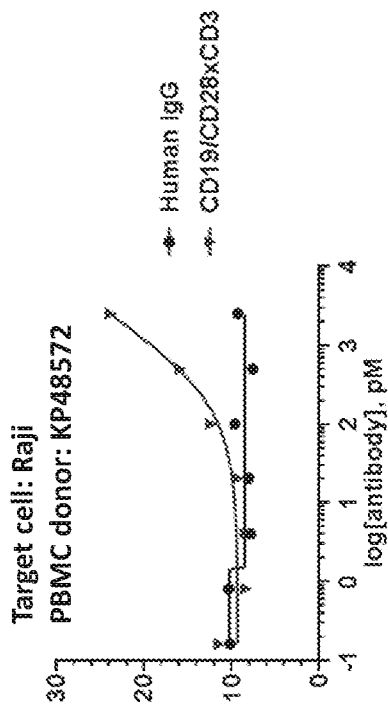


FIG. 9H

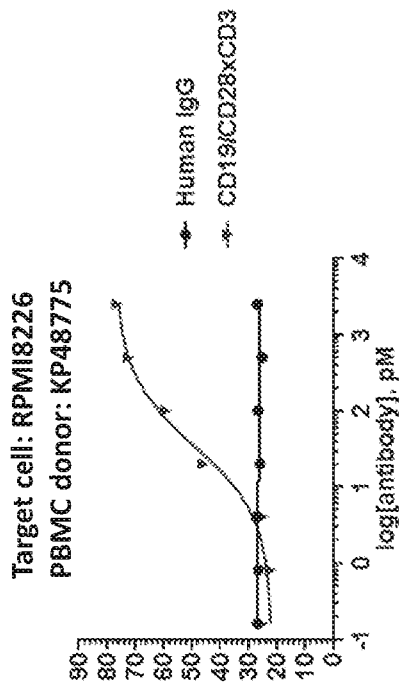


FIG. 9J

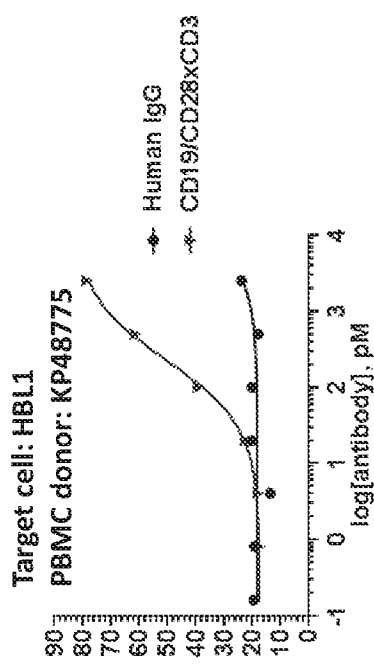


FIG. 9K

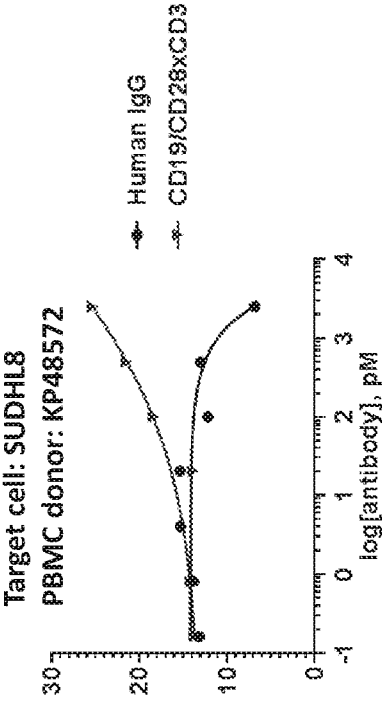


FIG. 9L

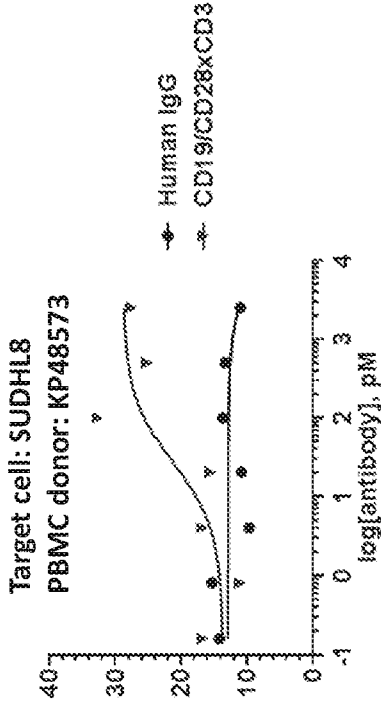


FIG. 9M

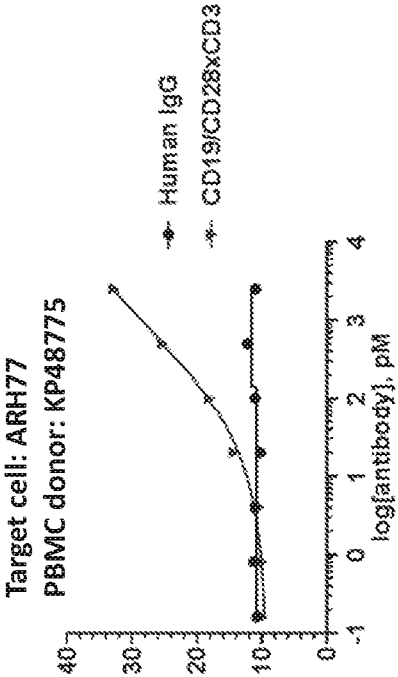


FIG. 9N

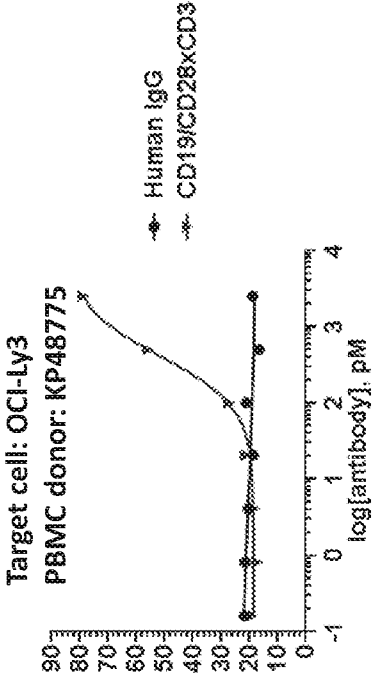


FIG. 10

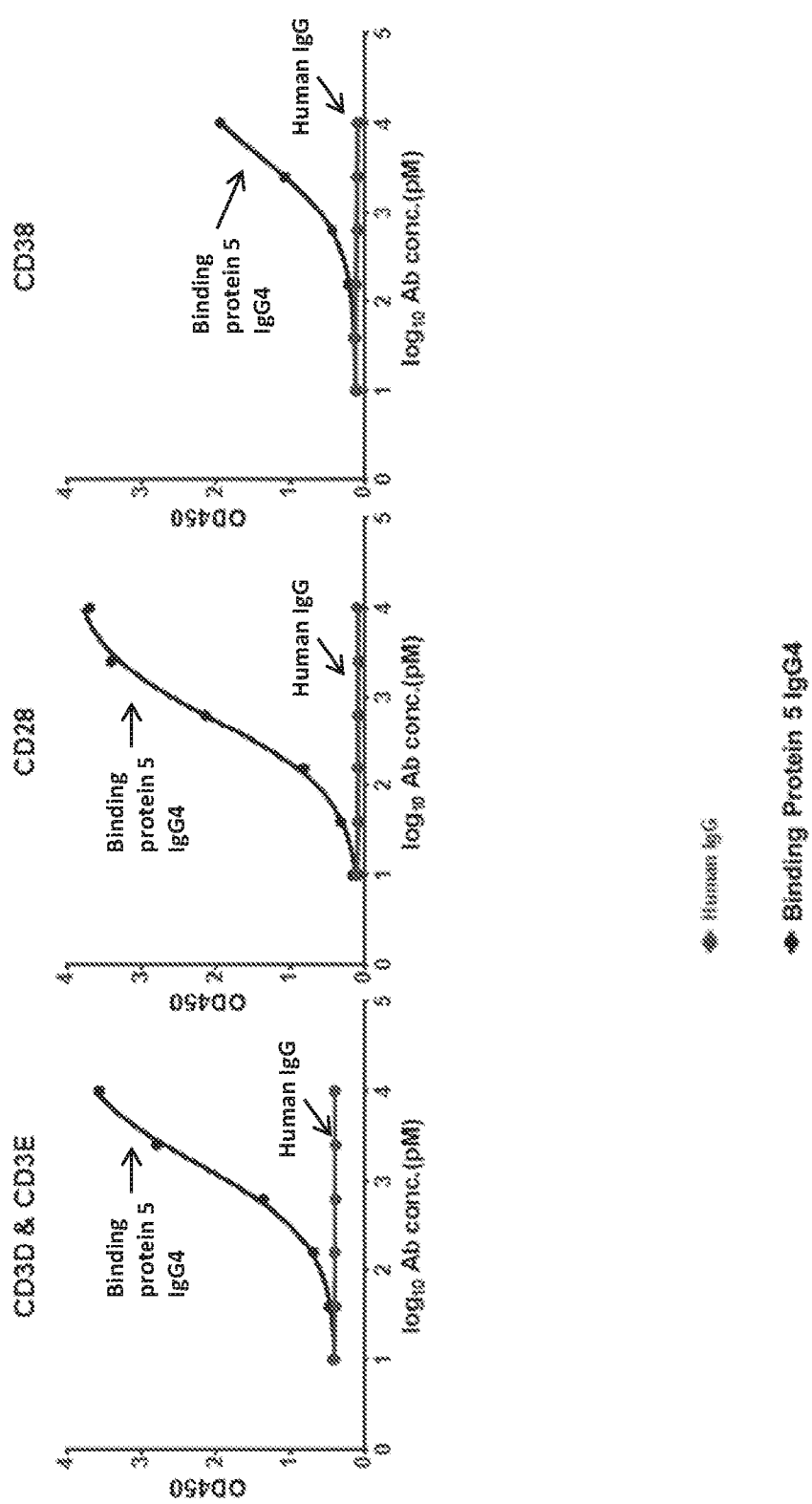


FIG. 11A

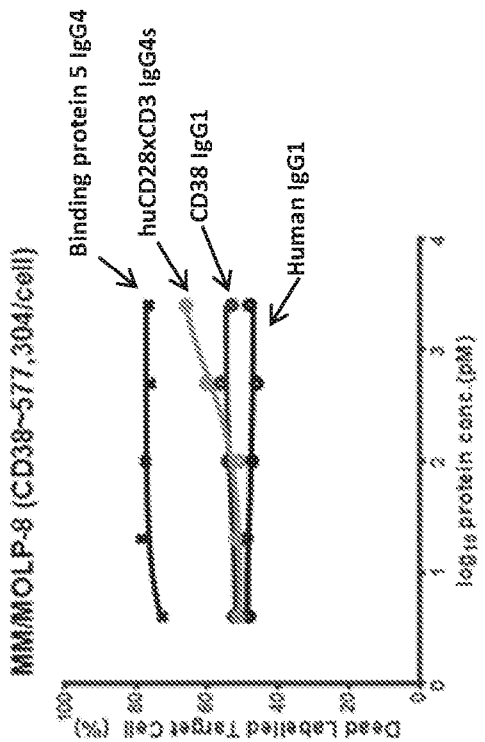


FIG. 11B

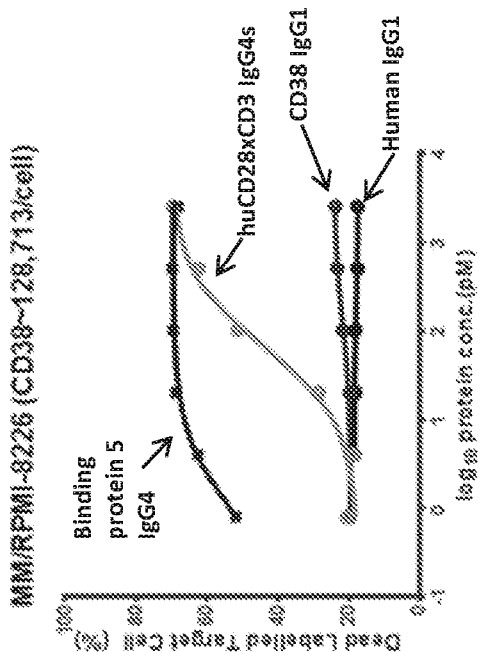
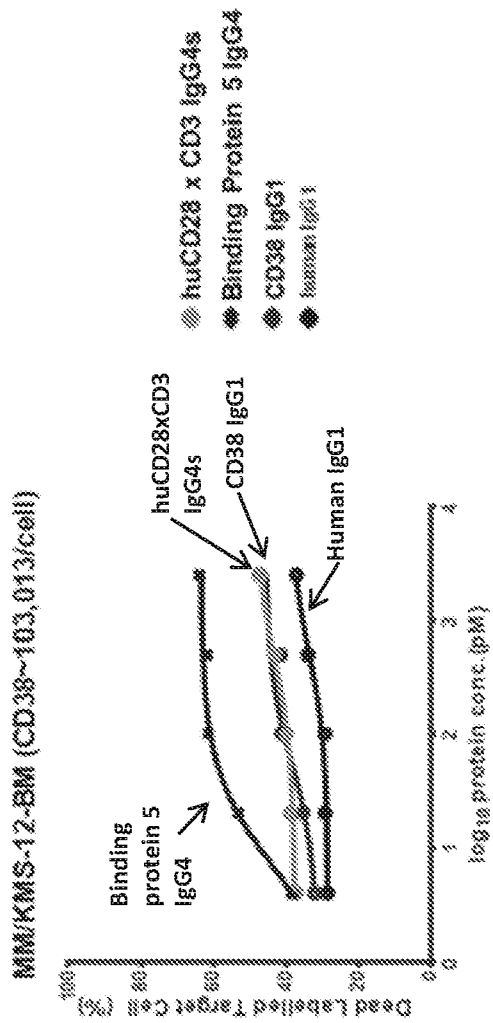


FIG. 11C



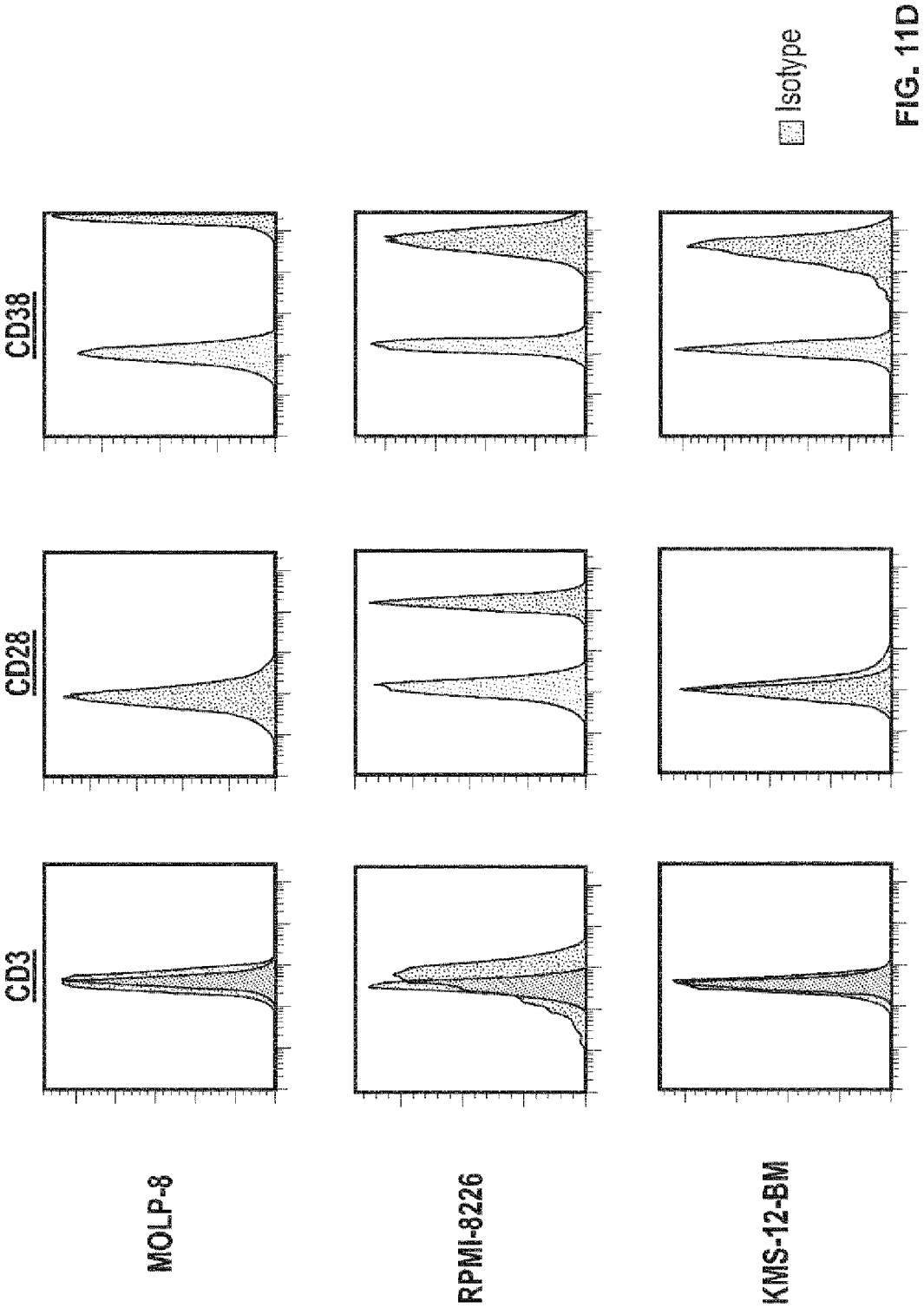


FIG. 11D

FIG. 12A

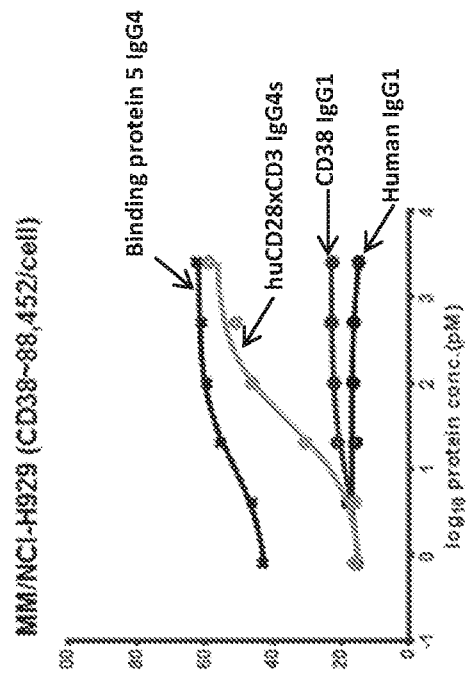


FIG. 12B

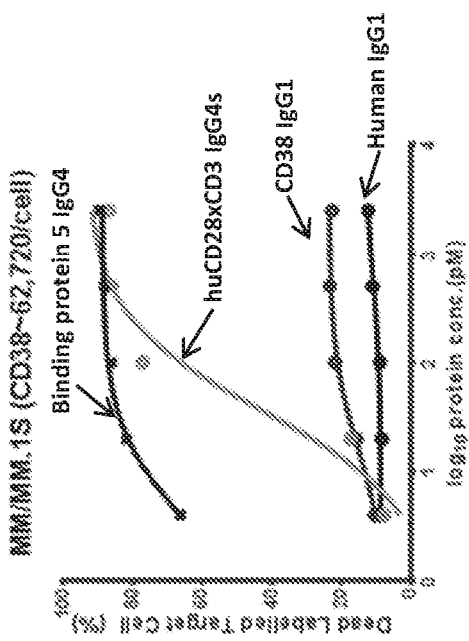
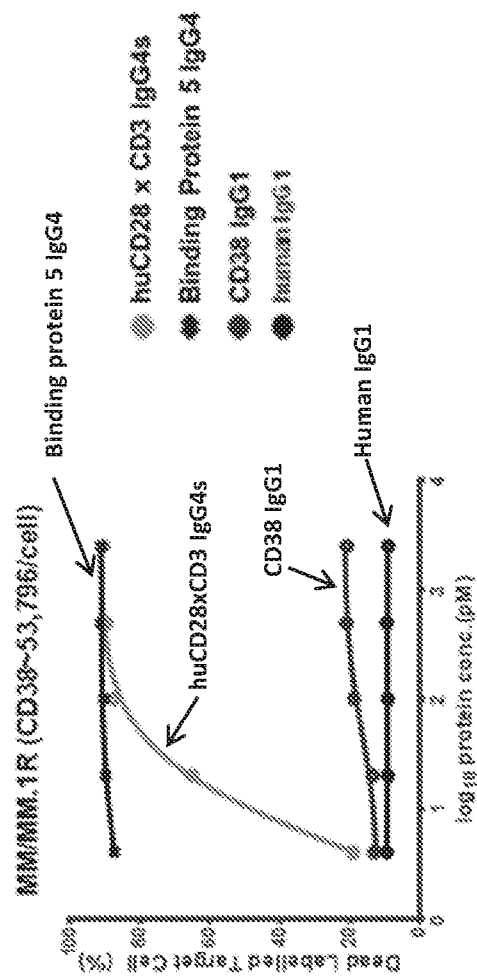


FIG. 12C



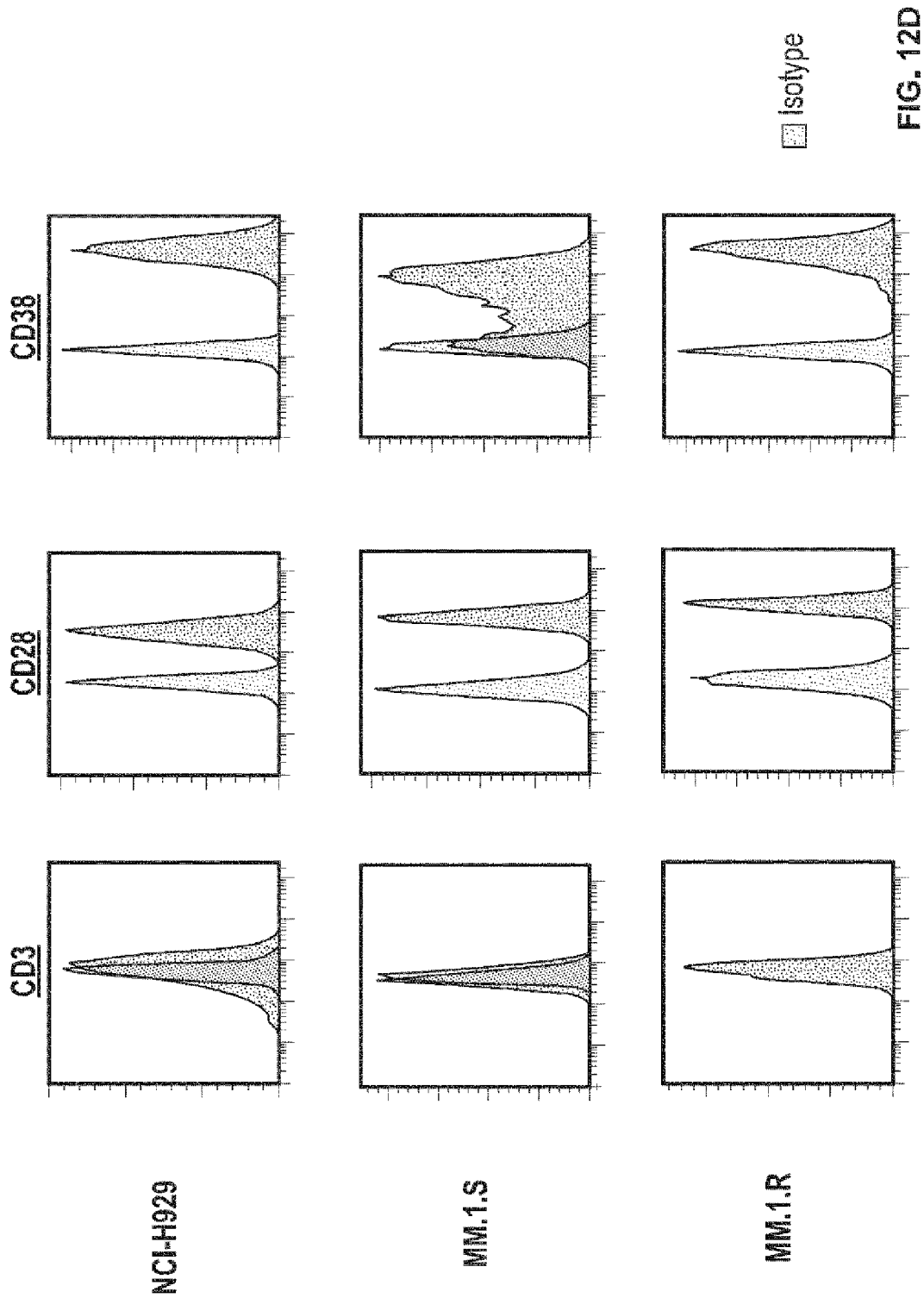


FIG. 13B

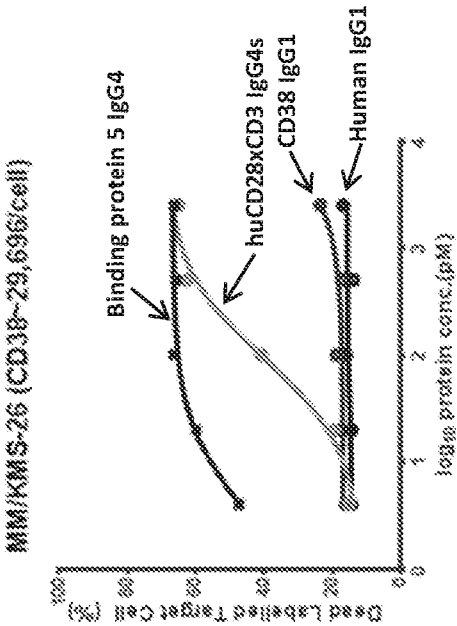


FIG. 13A

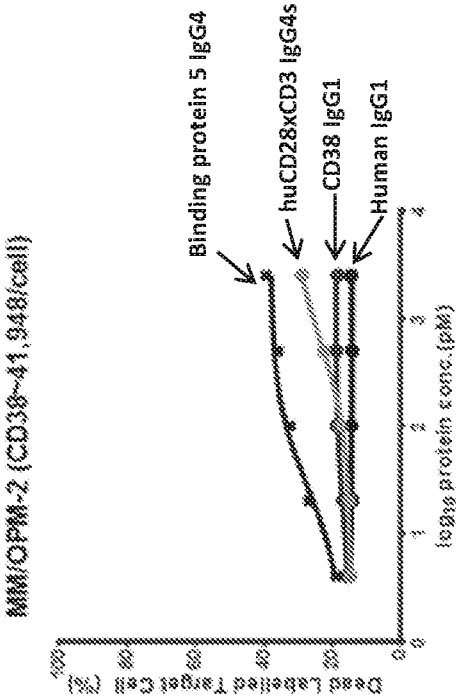
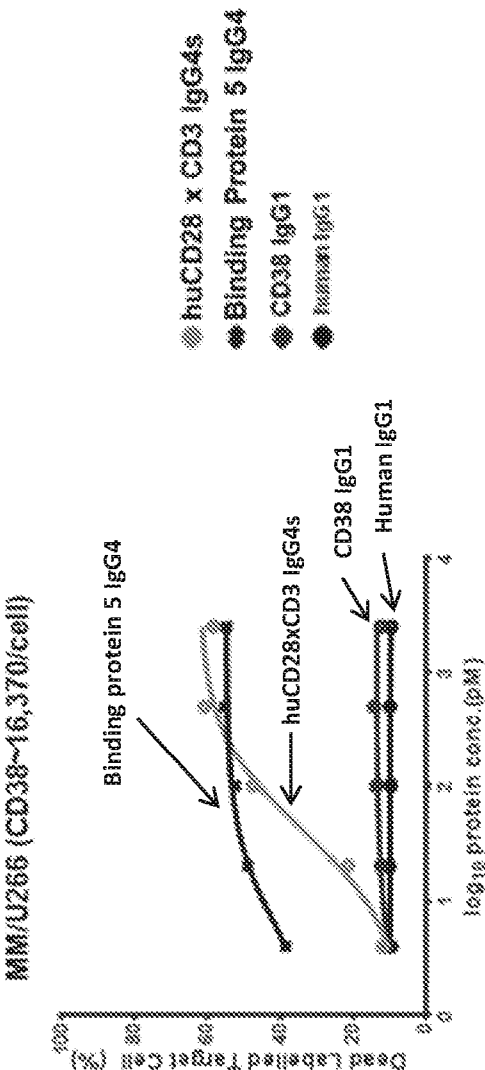


FIG. 13C



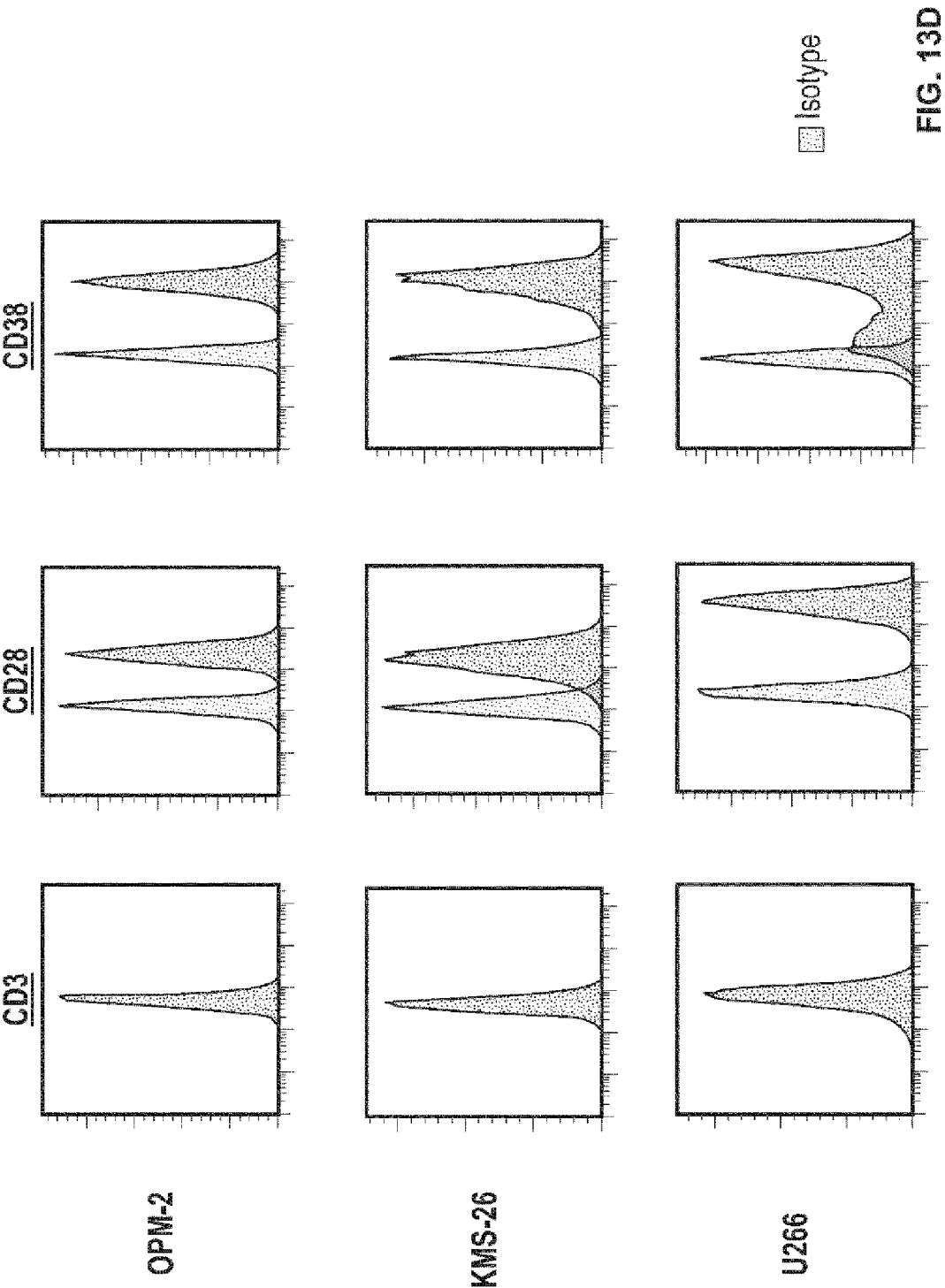
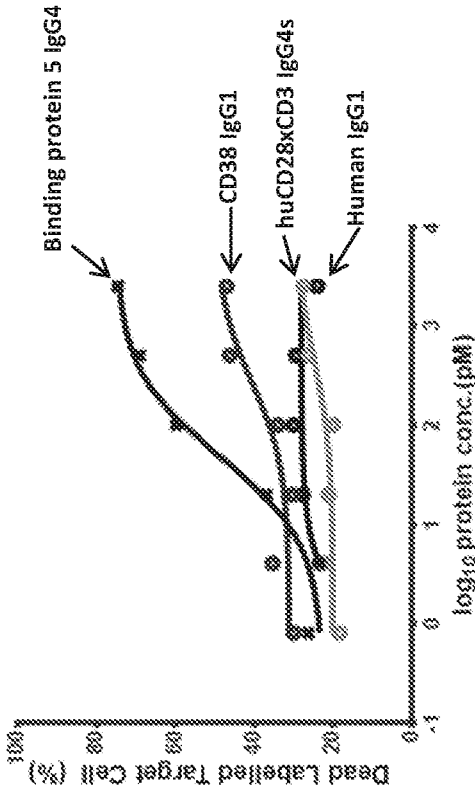


FIG. 13D

FIG. 14A

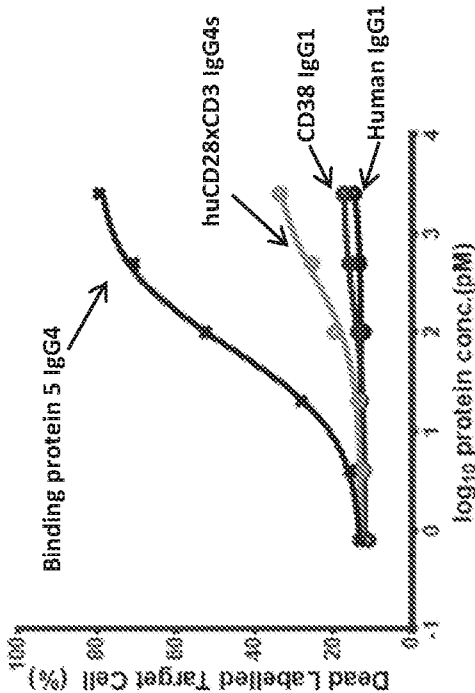
GCB/SUDHL-8 (CD38~327,209/cell)



- huCD28 x CD3 IgG4s
- Binding Protein 5 IgG4
- CD38 IgG1
- human IgG1

FIG. 14B

GCB/OCL-LY19 (CD38~33,504/cell)



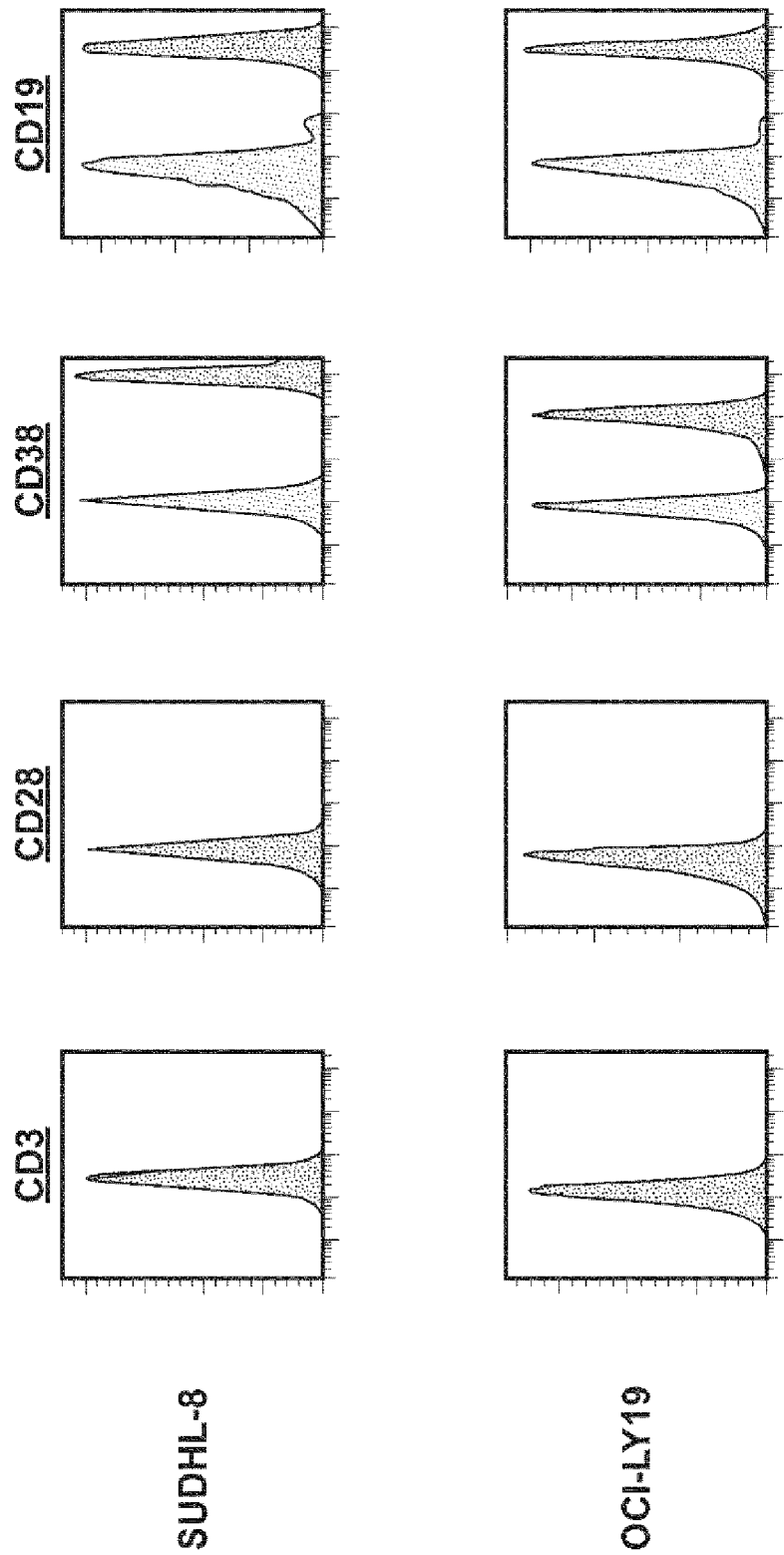


FIG. 14C

FIG. 15A

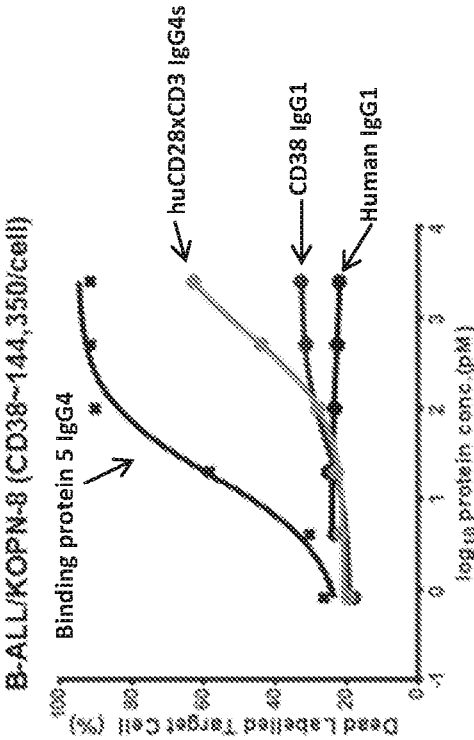


FIG. 15B

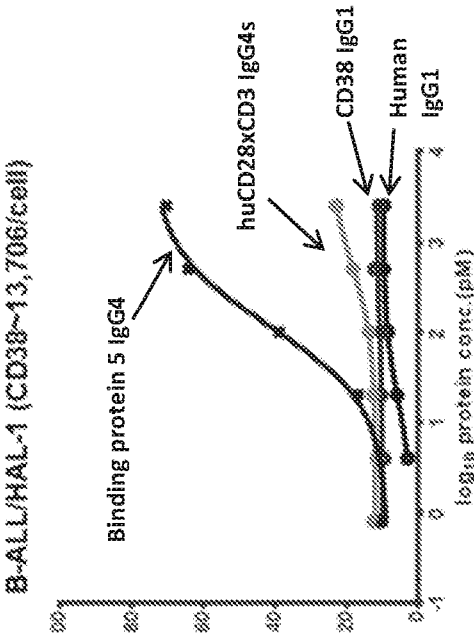
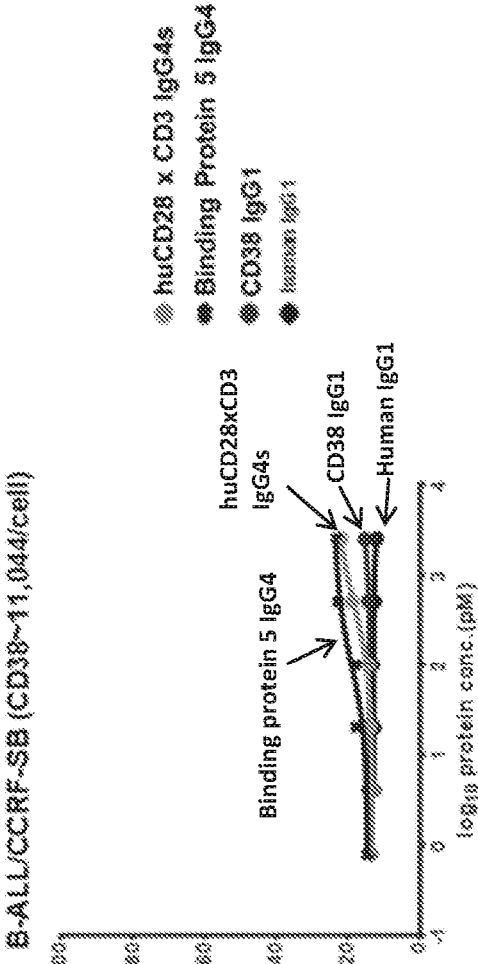


FIG. 15C



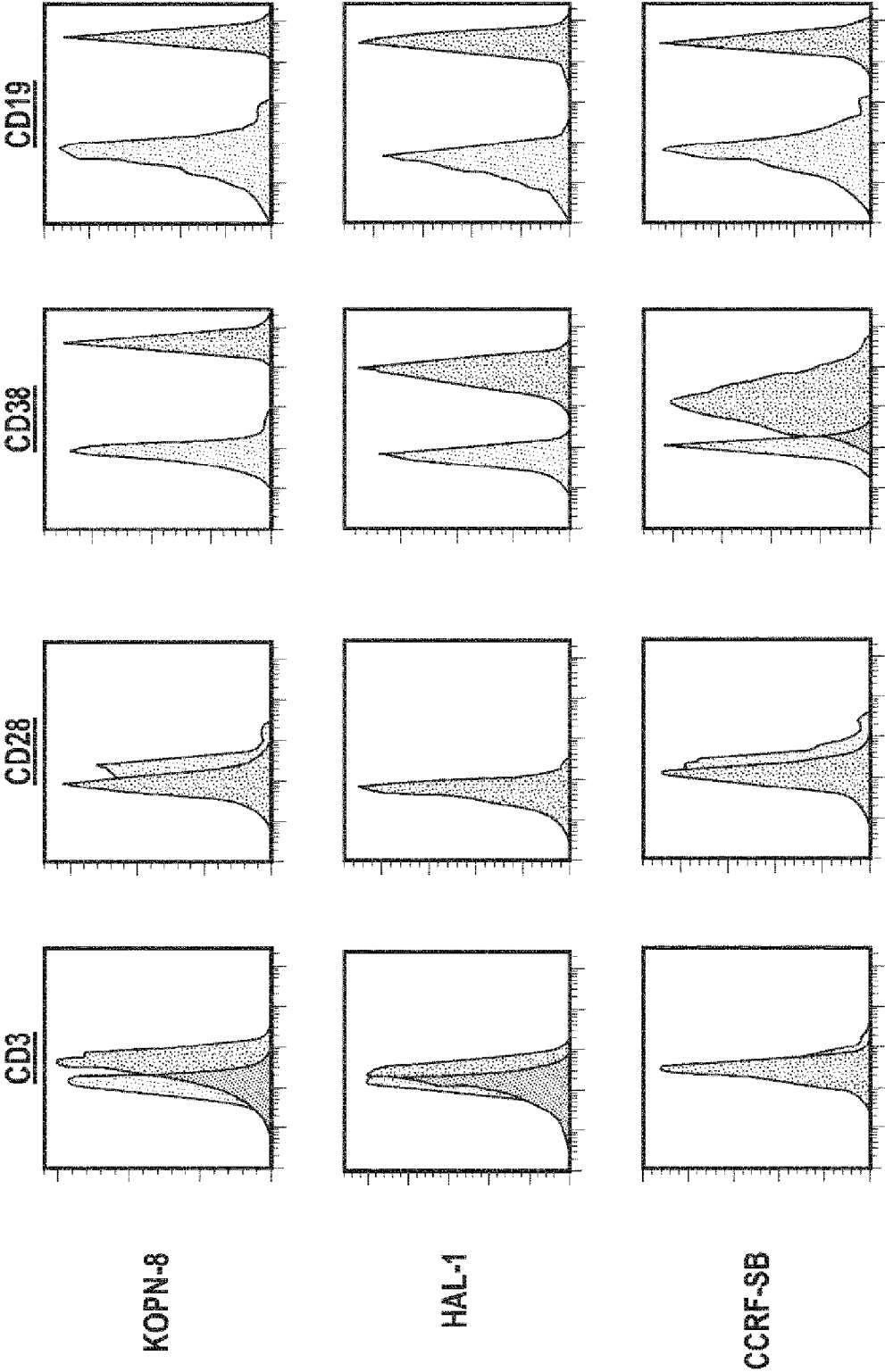


FIG. 15D

FIG. 16

MM/RPMI (CD38~128,713/cell)

Donor PK45926

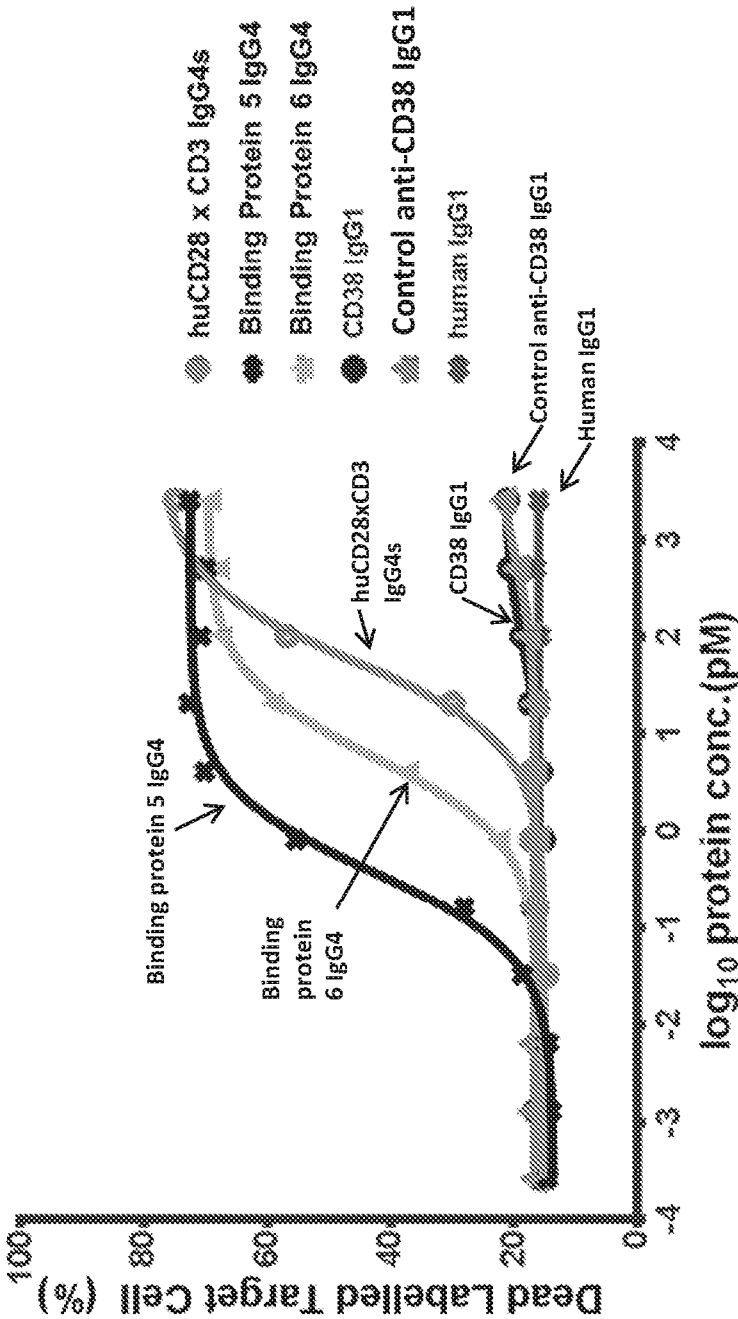


FIG. 17A

IL-2 signaling

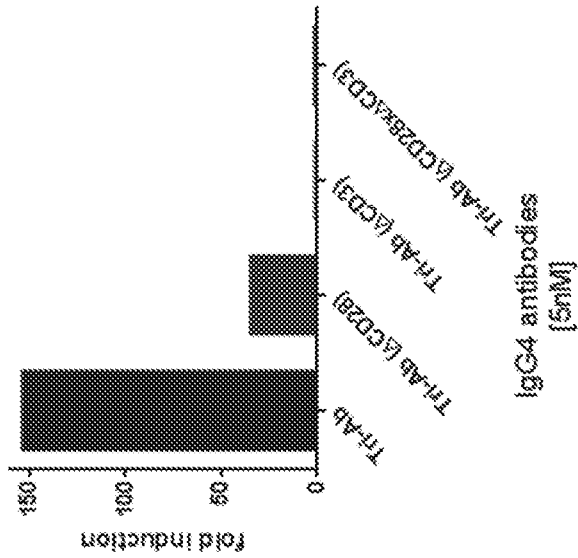
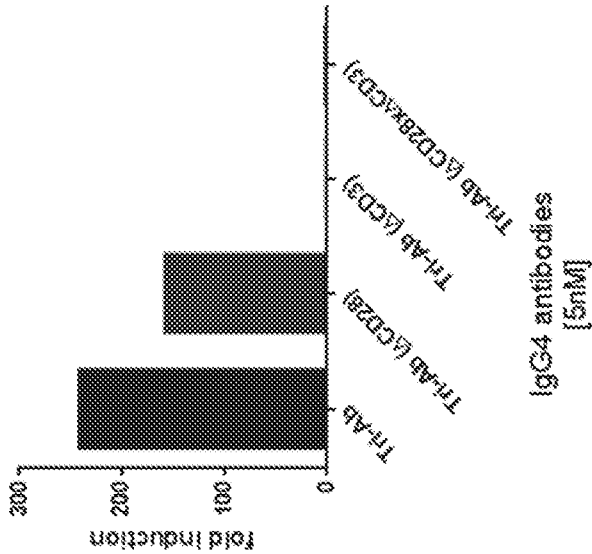


FIG. 17B

NFAT signaling



5 hr stimulation

FIG. 18A

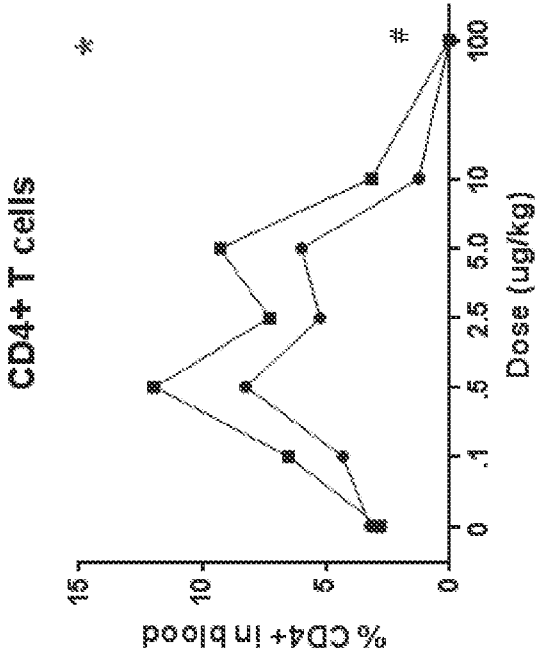
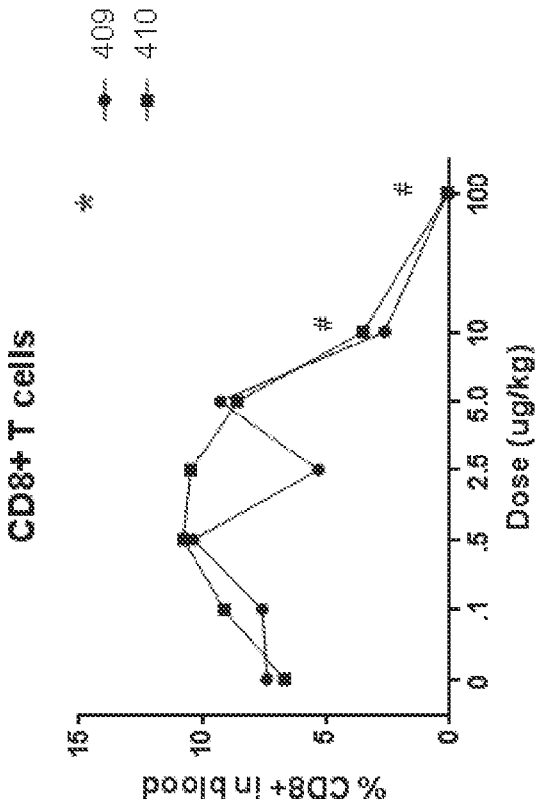


FIG. 18B



* severe vomiting
p<0.05 vs. Dose 0
5 hours post dosing

FIG. 18C

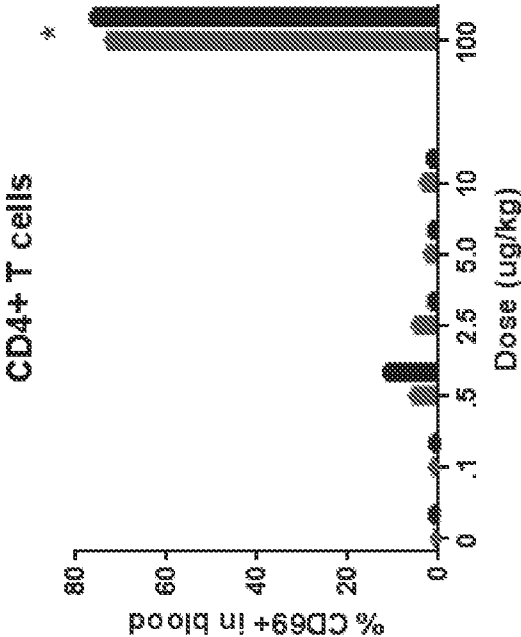
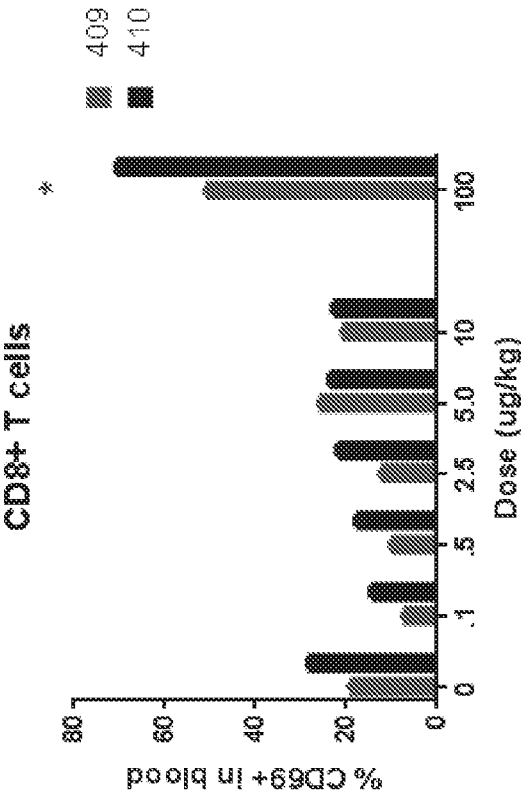


FIG. 18D



* severe vomitus
p<0.05 vs. Dose 0

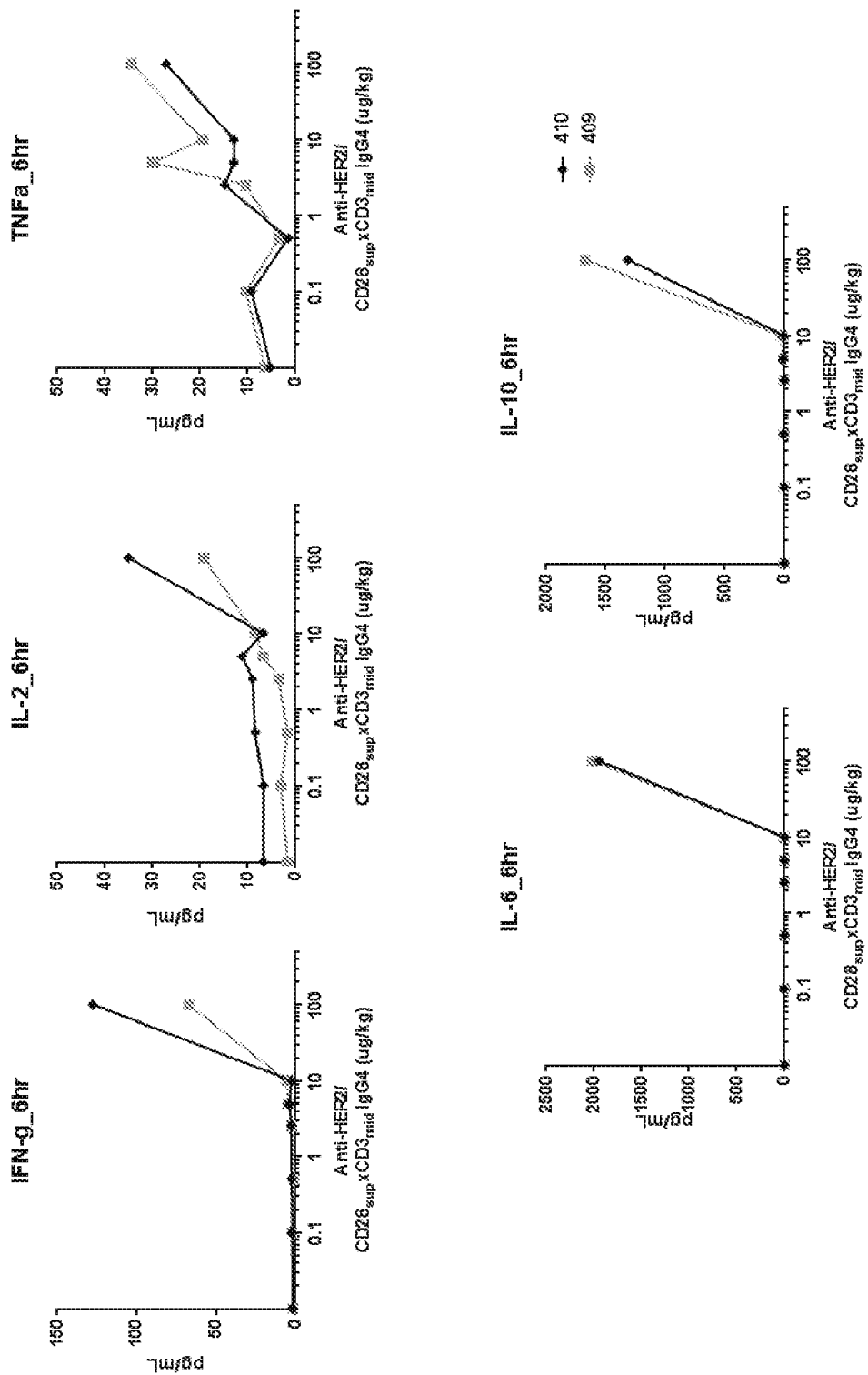


FIG. 18E

FIG. 19A

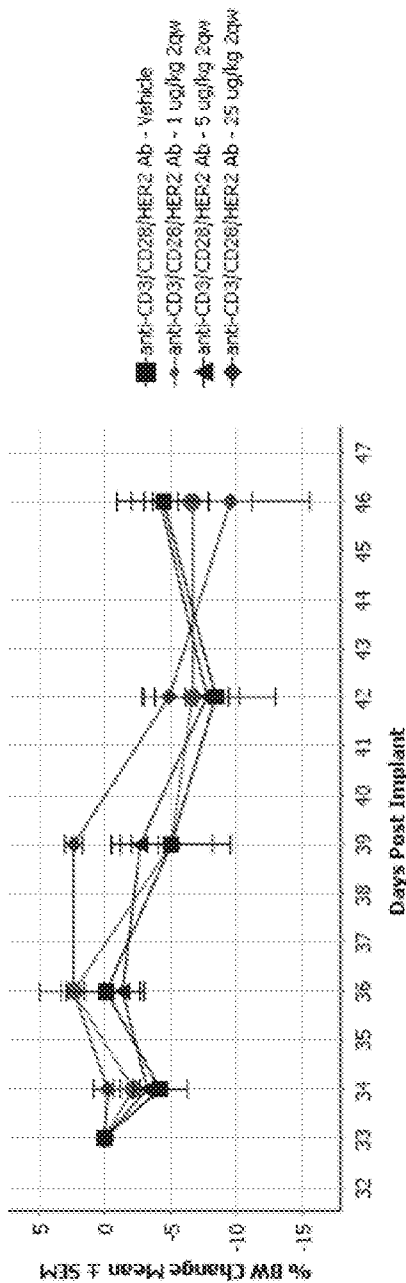
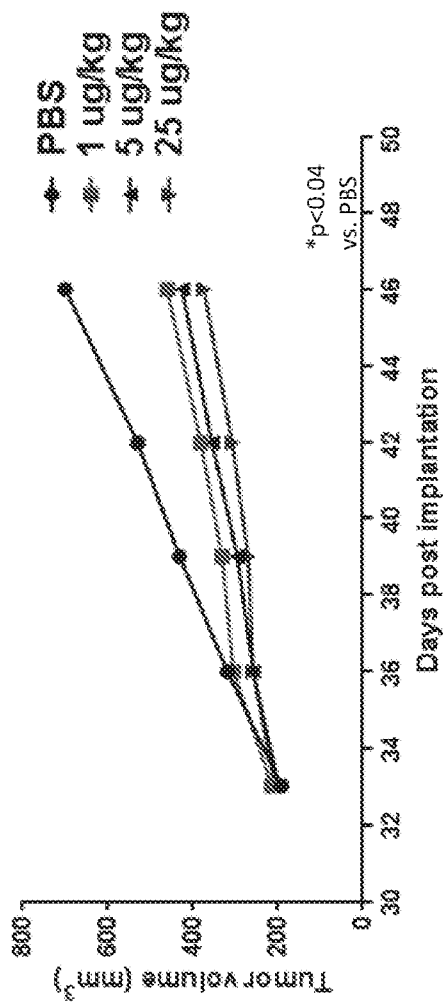


FIG. 19B



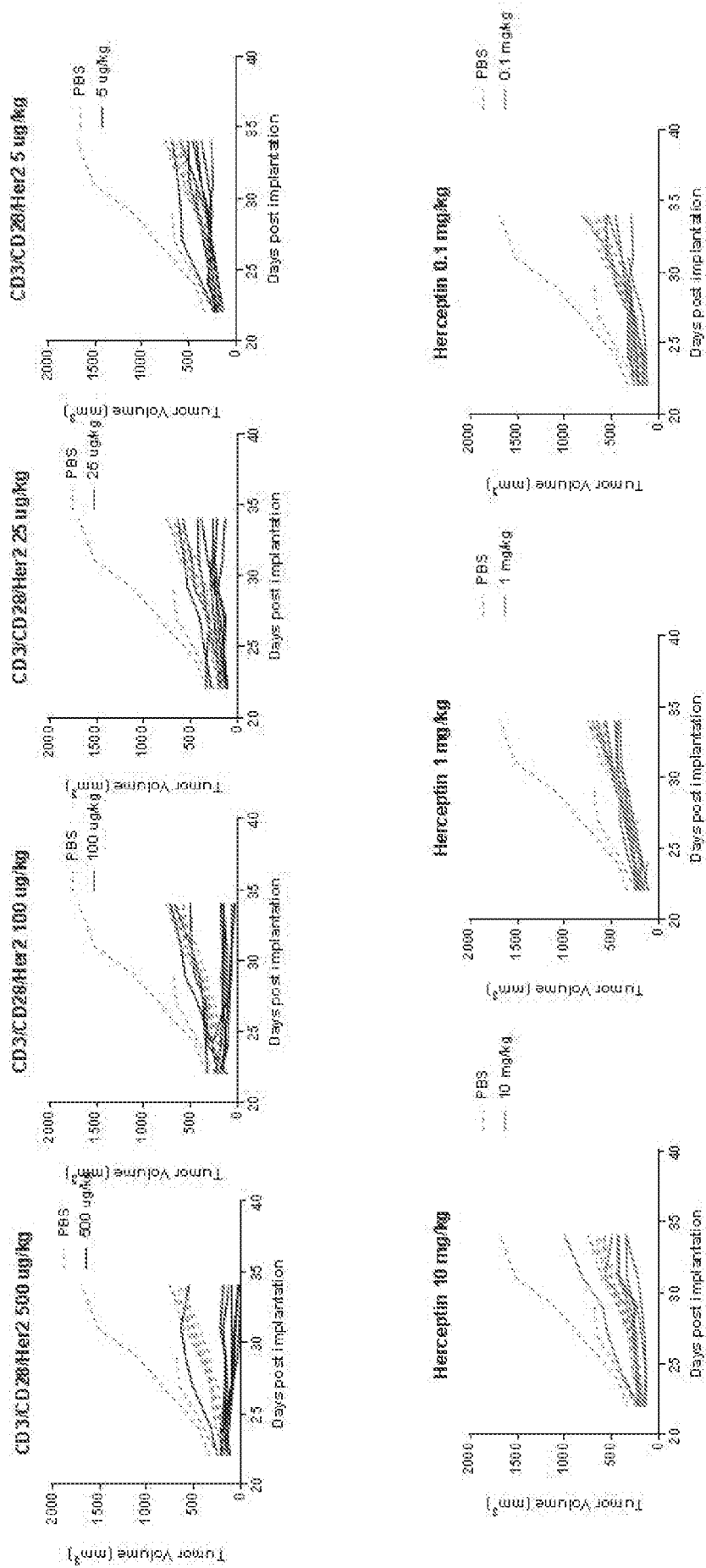


FIG. 20B

FIG. 20C

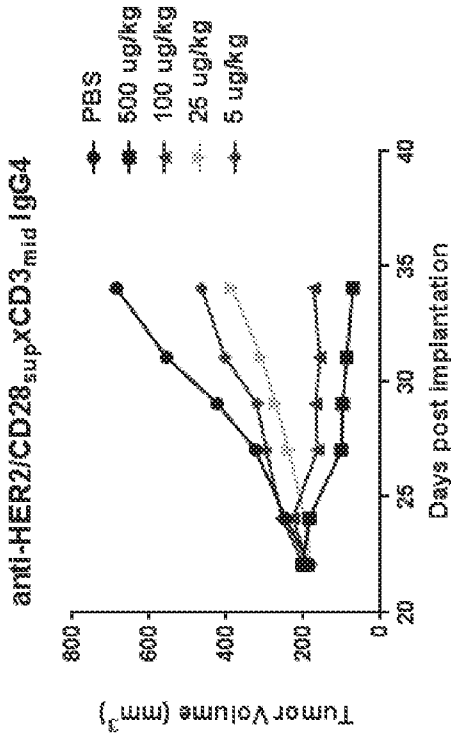


FIG. 20D

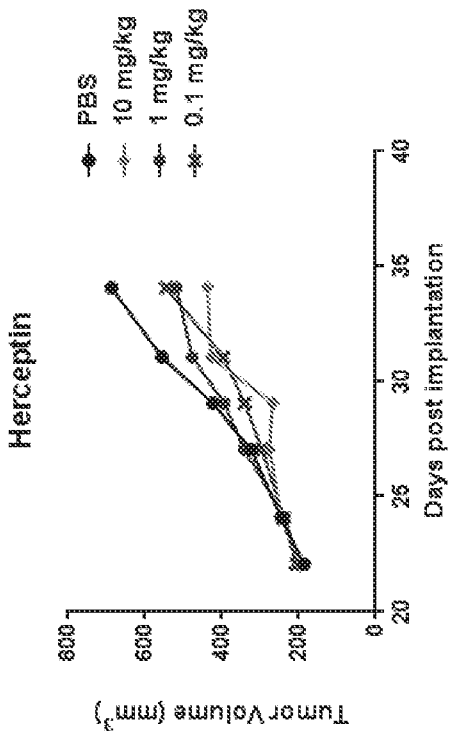


FIG. 20E

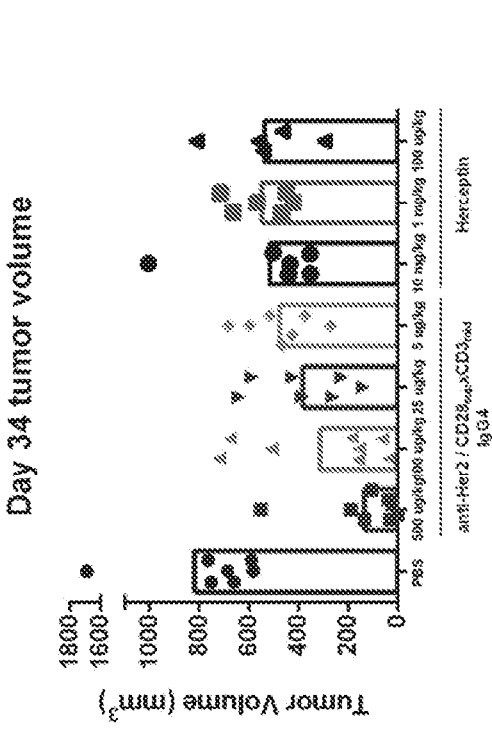
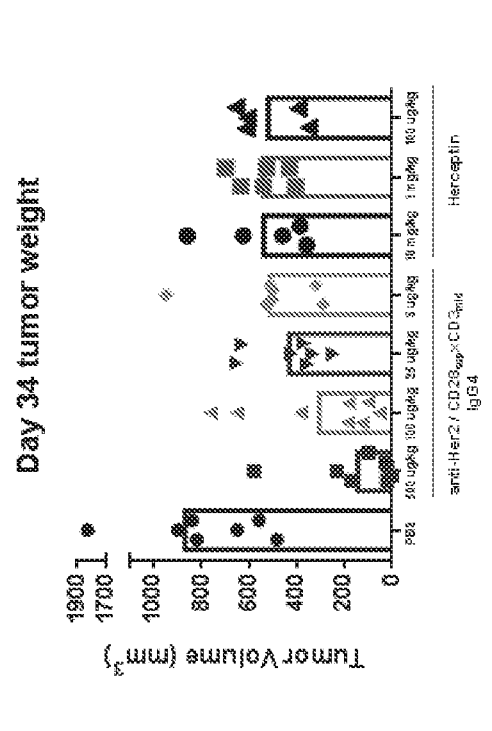


FIG. 20F



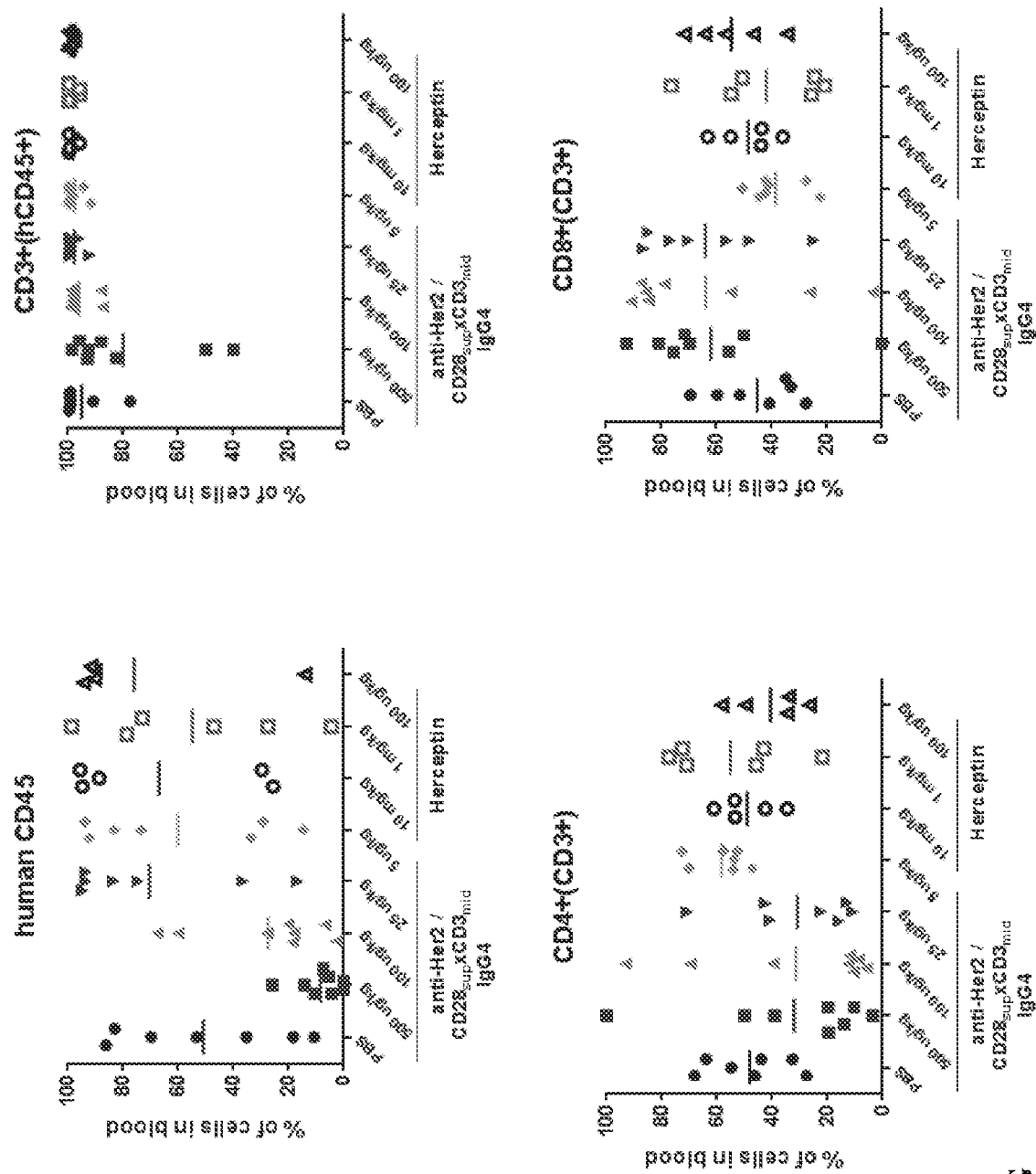


FIG. 20G

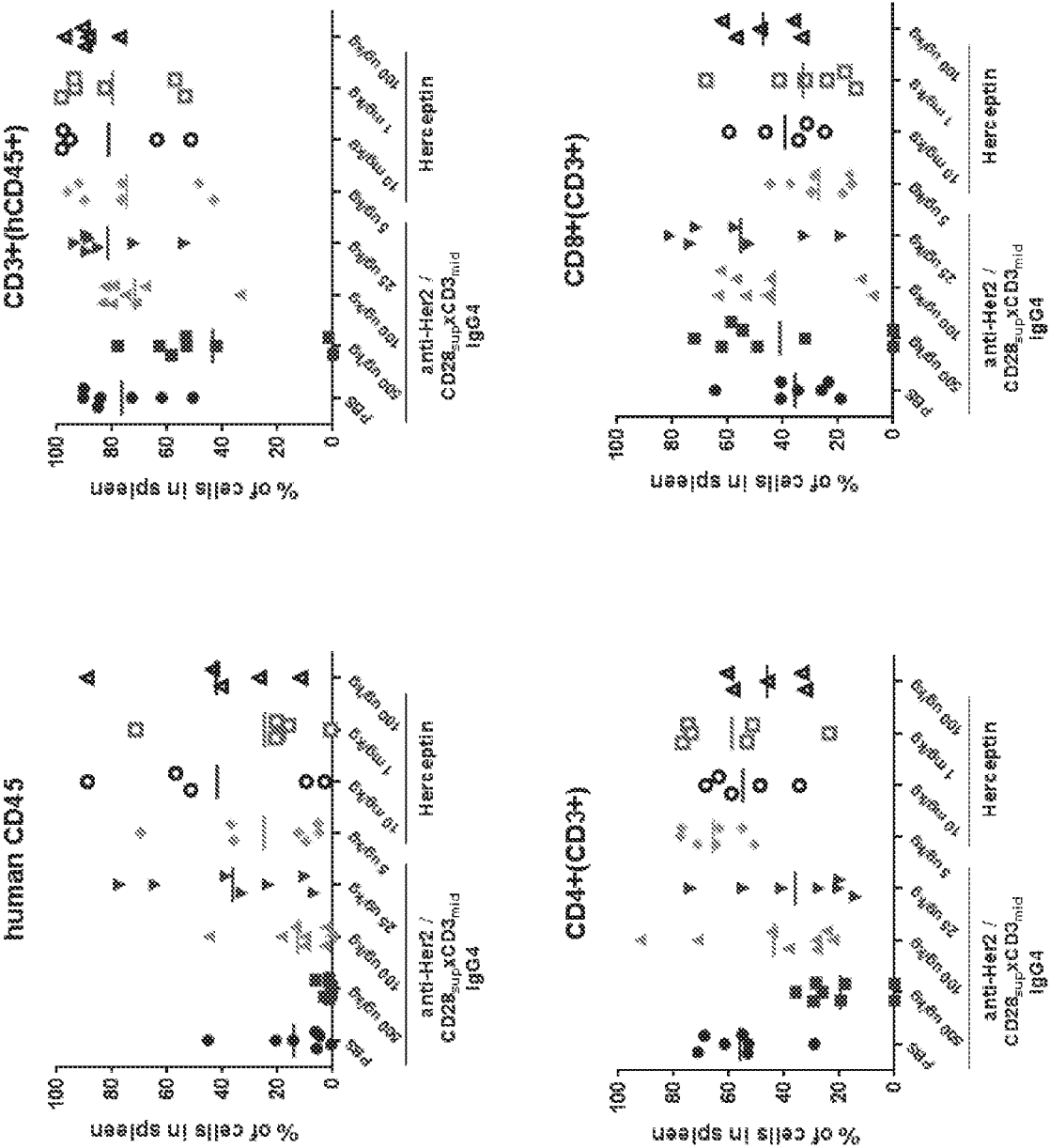


FIG. 20H

FIG. 21A

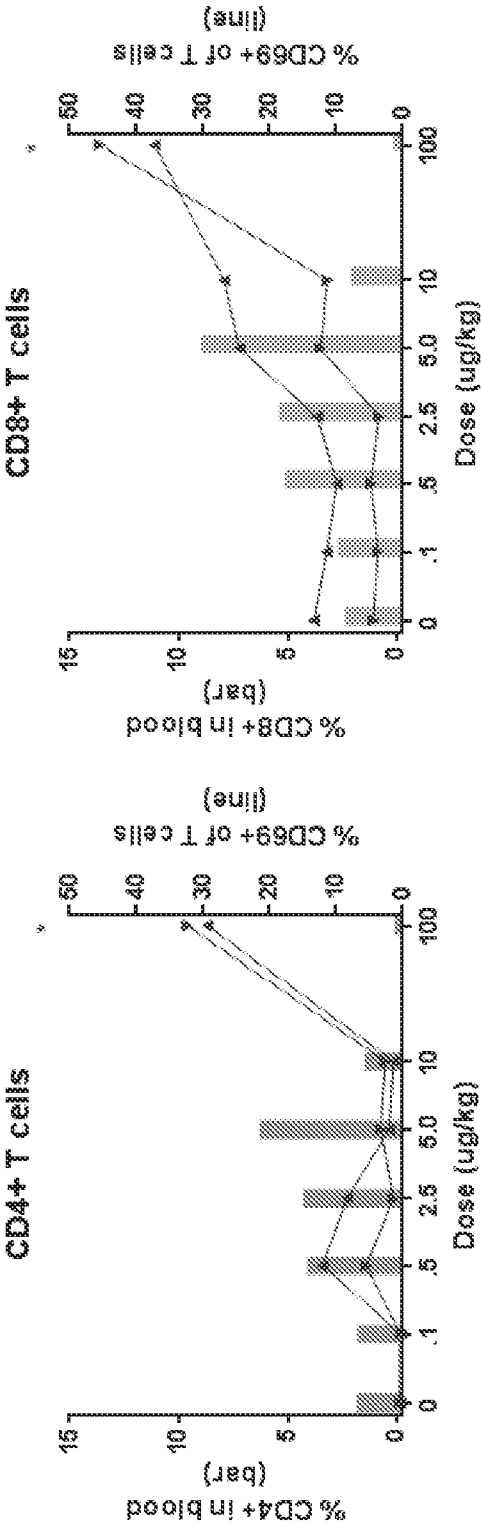
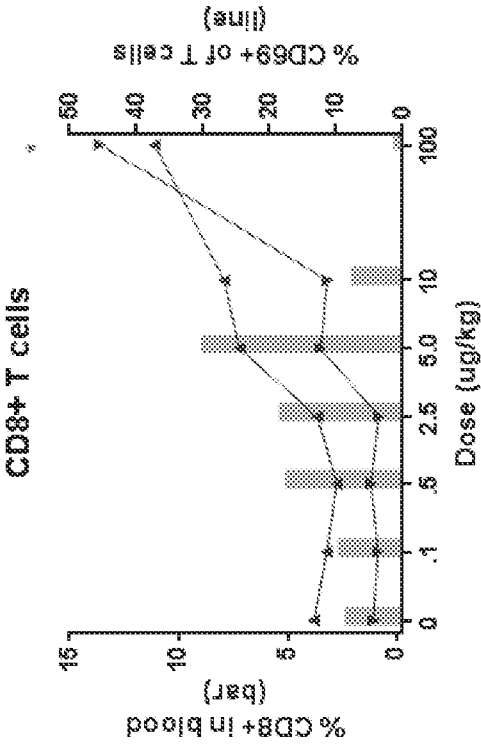


FIG. 21B



*Serious adverse event (vomiting). Animals recovered 24 hrs later.

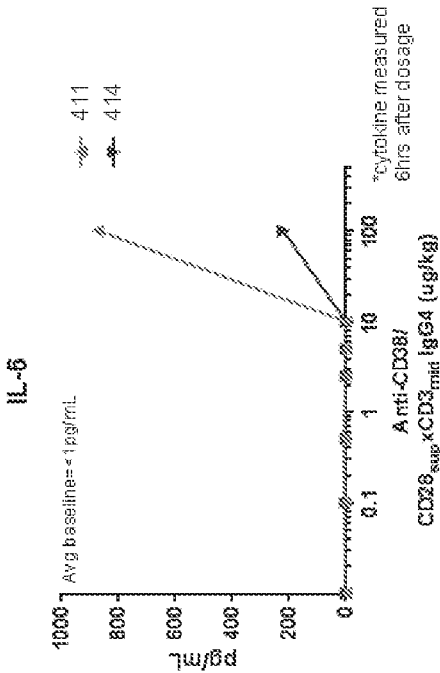


FIG. 21C

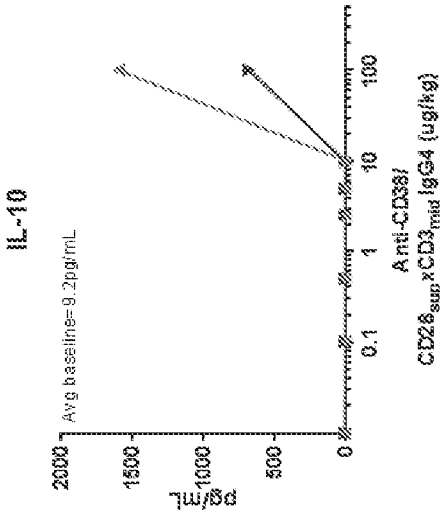


FIG. 21D

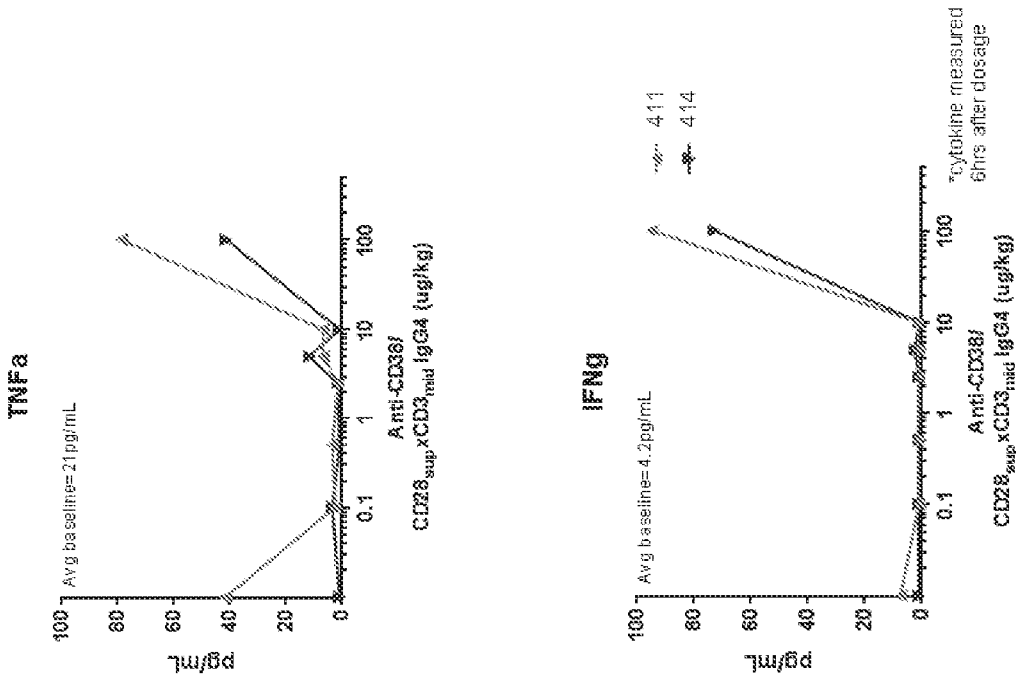


FIG. 21E

FIG. 21F

FIG. 22A

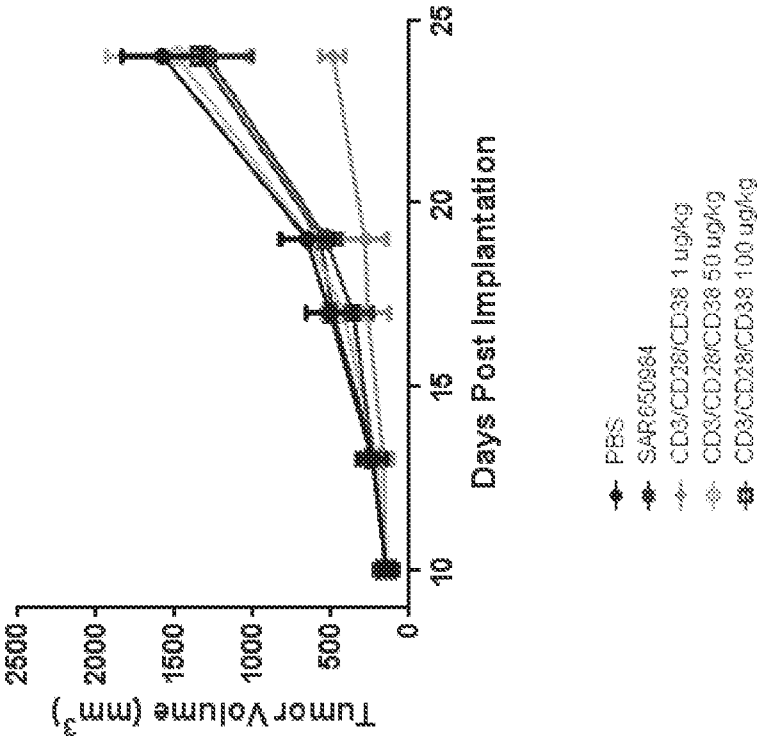
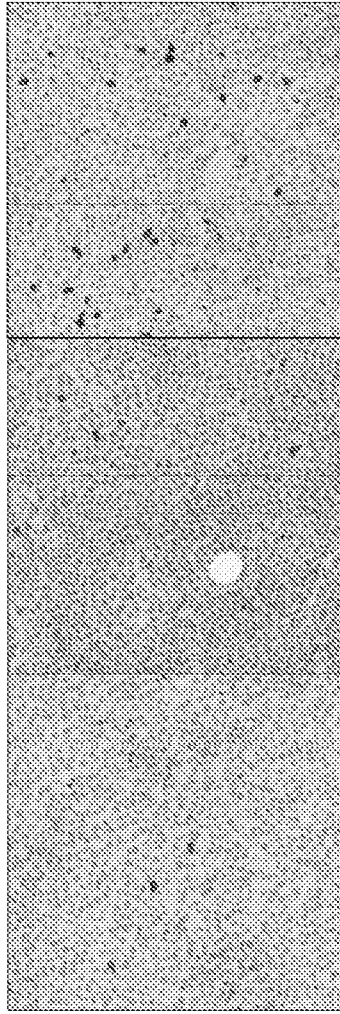
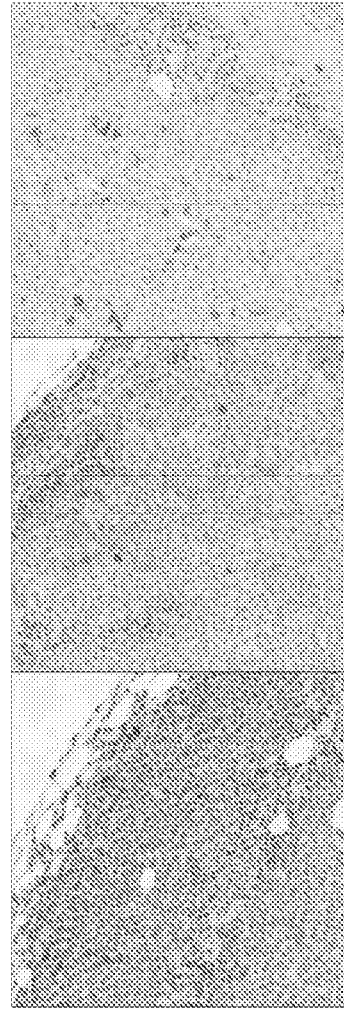


FIG. 22B



Anti-hCD8

FIG. 22C



Anti-hCD4

FIG. 23A

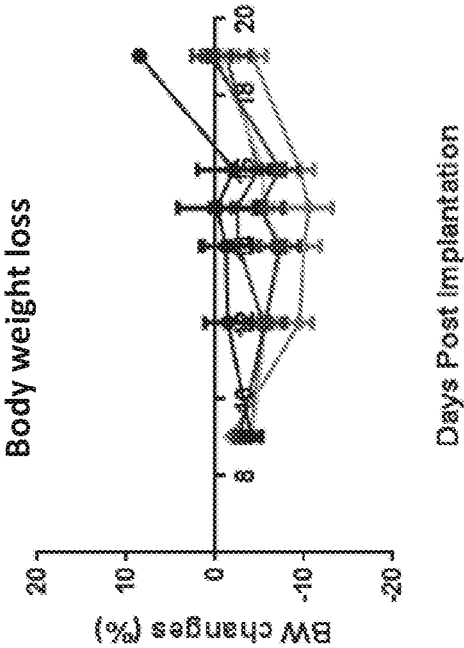
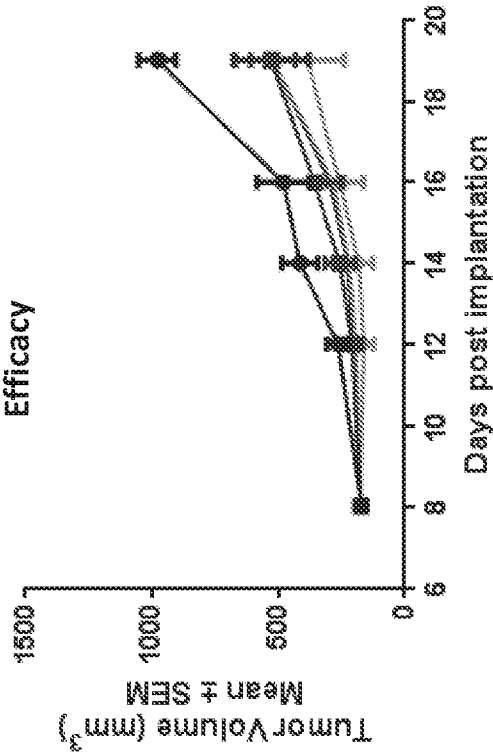


FIG. 23B



- ◆ PBS
- CD3/CD28/CD38 0.04 ug/kg
- CD3/CD28/CD38 0.2 ug/kg
- ▲ CD3/CD28/CD38 1 ug/kg
- ▼ CD3/CD28/CD38 5 ug/kg

FIG. 23C

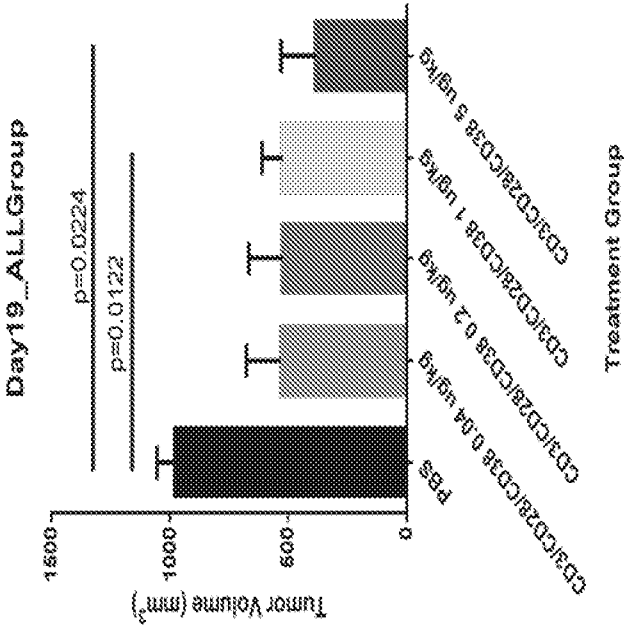


FIG. 23D

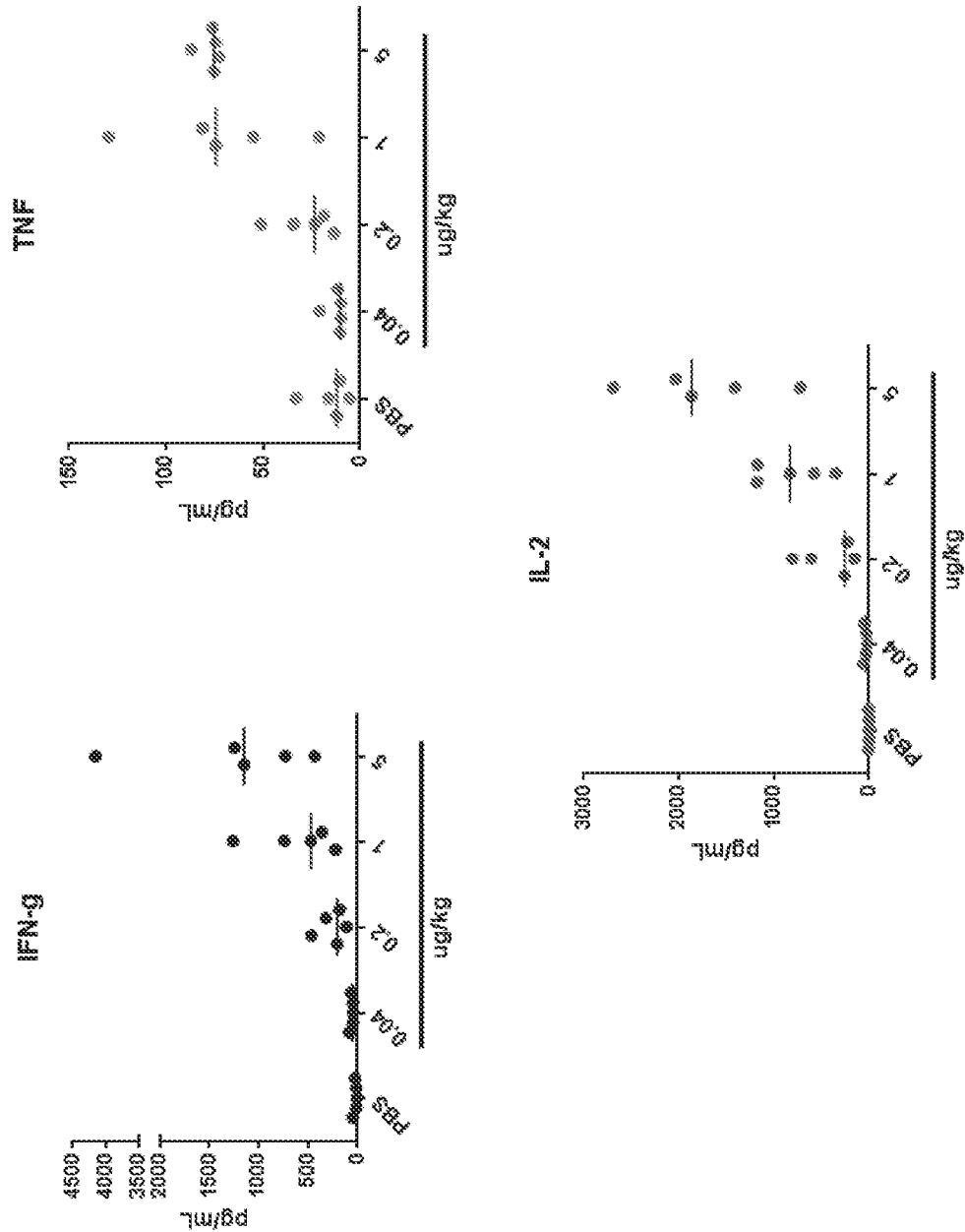


FIG. 24

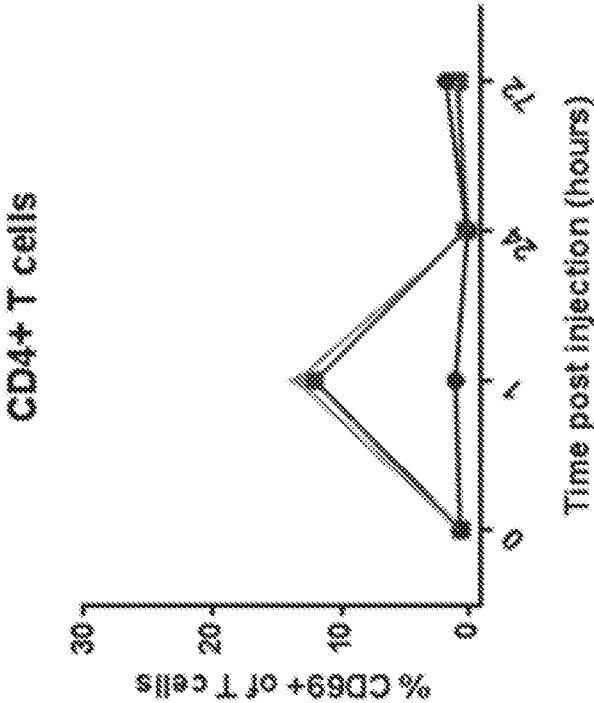
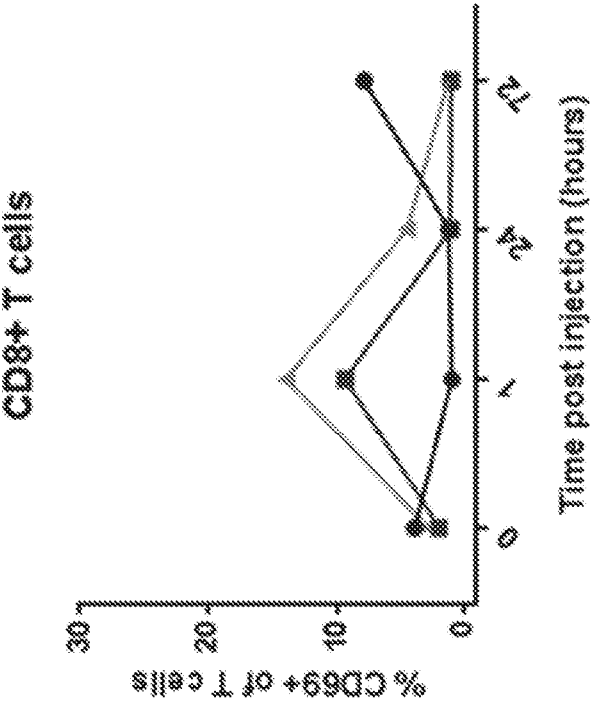


FIG. 25



- CD38_{SB}19 x CD28_{sup} x CD3_{mid} IgG4
- CD28_{sup} x CD3_{mid} IgG4
- CD28_{sup} IgG4

FIG. 26A

IL-2

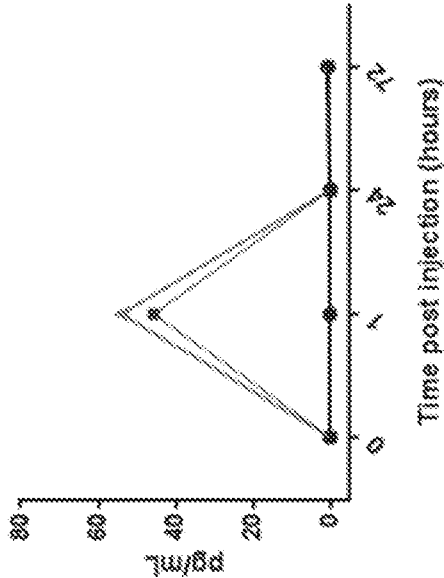


FIG. 26B

TNF

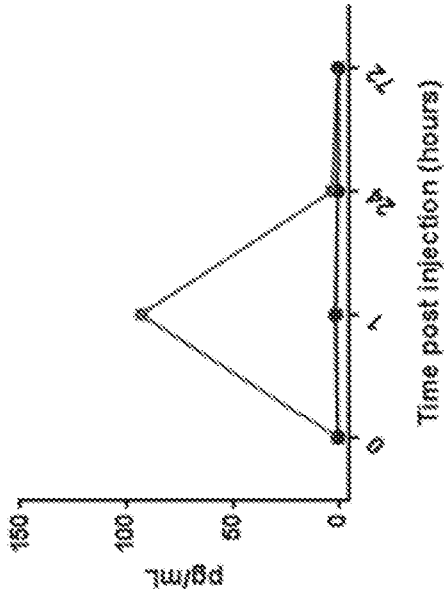
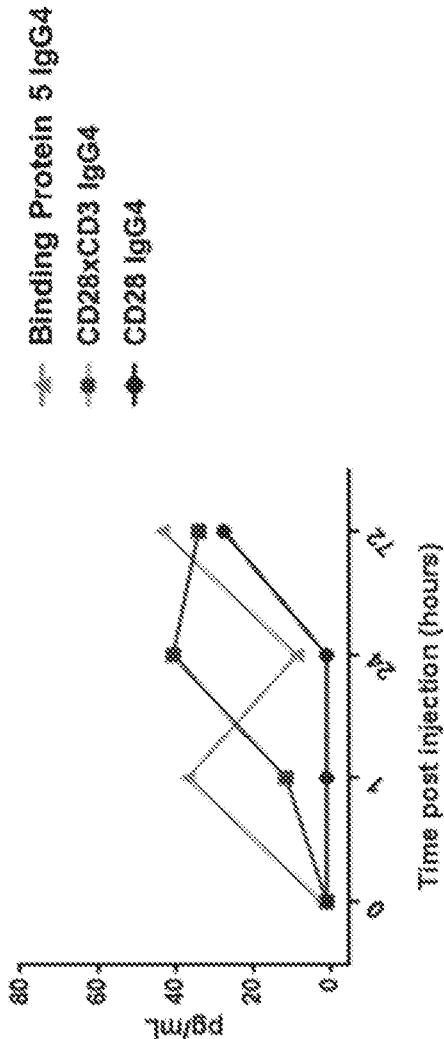


FIG. 26C

IFN- γ



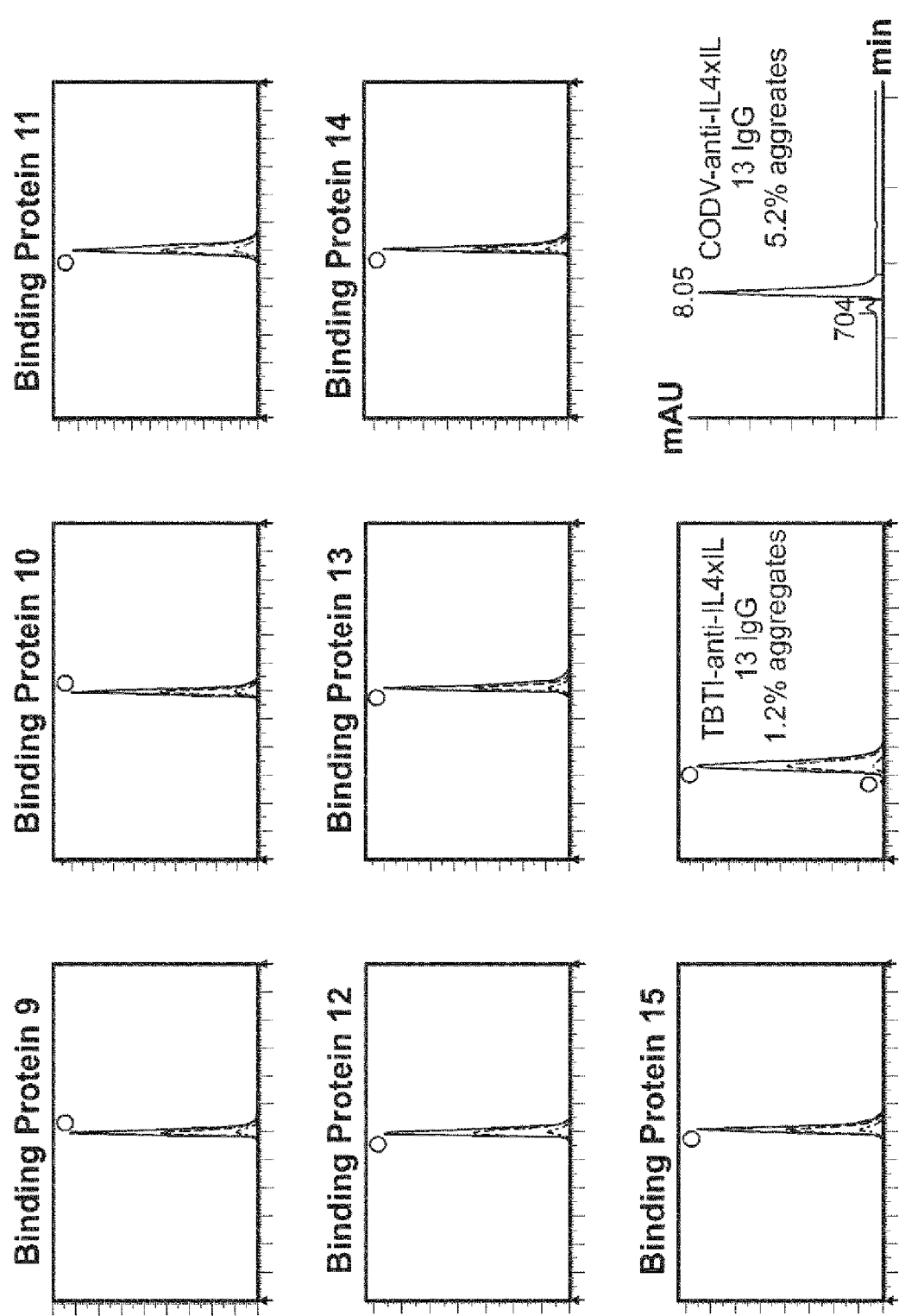


FIG. 27A

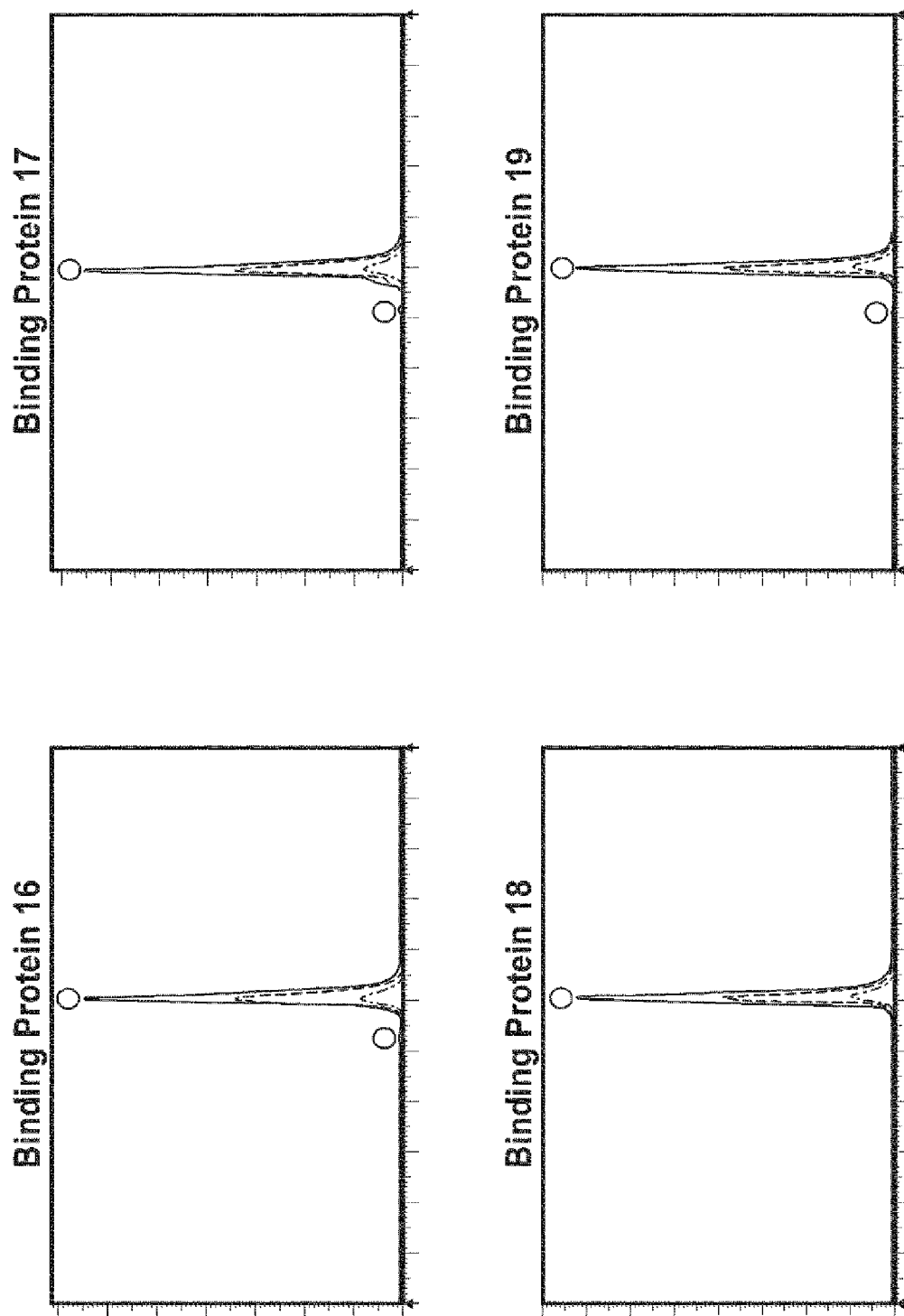


FIG. 27B

FIG. 28A

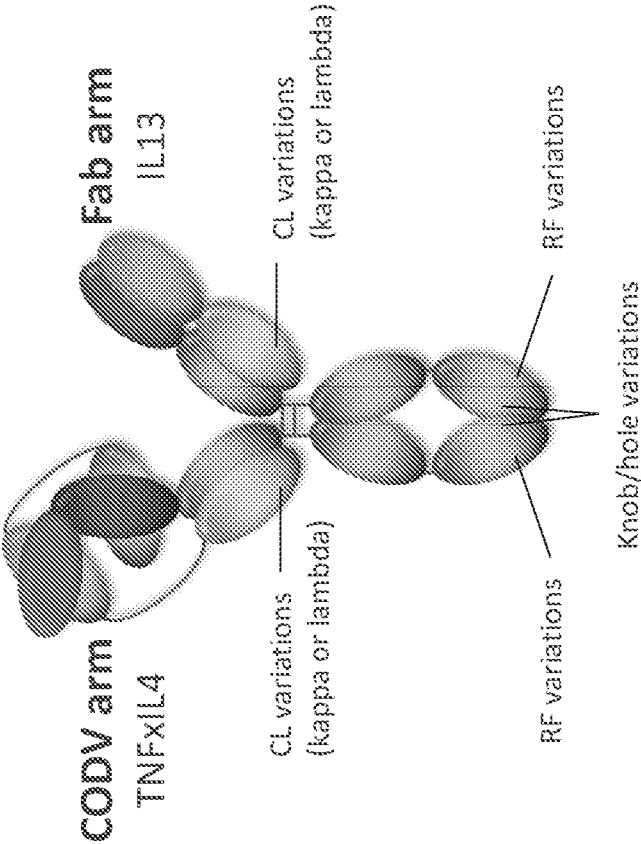


FIG. 28B

CODV- arm	Fab- arm	CODV- arm	Fab- arm	RF mutation
Kappa	Kappa	Hole	Knob	no RF
Kappa	Kappa	Hole	Knob	Hole
Kappa	Kappa	Hole	Knob	Knob
Kappa	lambda	Knob	Hole	no RF
Kappa	lambda	Knob	Hole	Hole
Kappa	lambda	Knob	Hole	Knob
lambda	Kappa	Knob	Hole	no RF
lambda	Kappa	Knob	Hole	Hole
lambda	Kappa	Knob	Hole	Knob
Kappa	Kappa	Knob	Hole	no RF
Kappa	Kappa	Knob	Hole	Hole
Kappa	Kappa	Knob	Hole	Knob
Kappa	lambda	Hole	Knob	no RF
Kappa	lambda	Hole	Knob	Hole
Kappa	lambda	Hole	Knob	Knob
lambda	Kappa	Hole	Knob	no RF
lambda	Kappa	Hole	Knob	Hole
lambda	Kappa	Hole	Knob	Knob

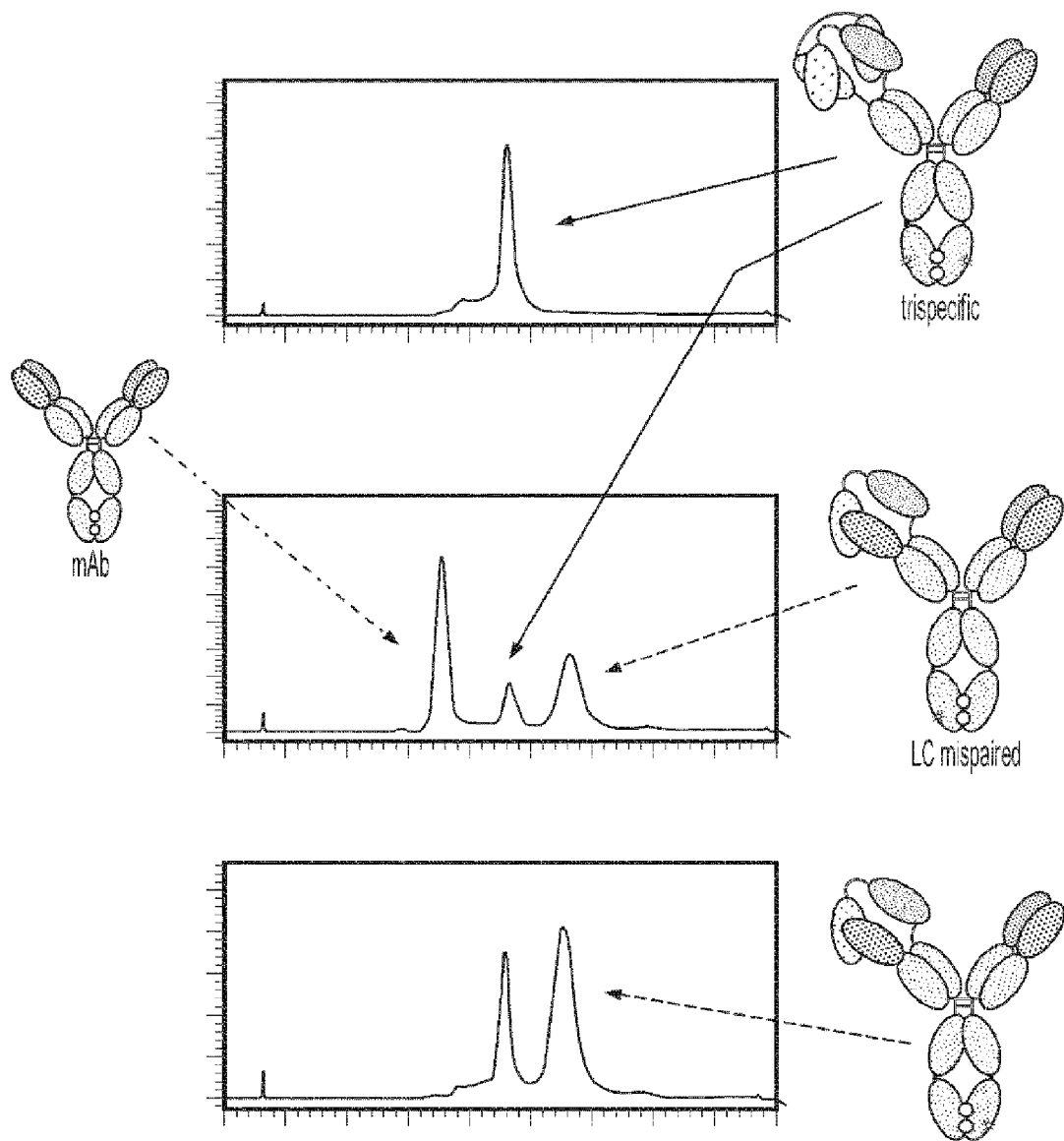


FIG. 29

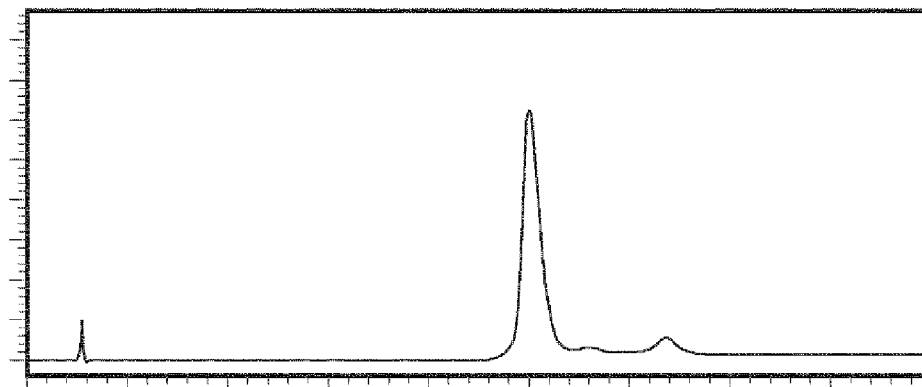


FIG. 30A

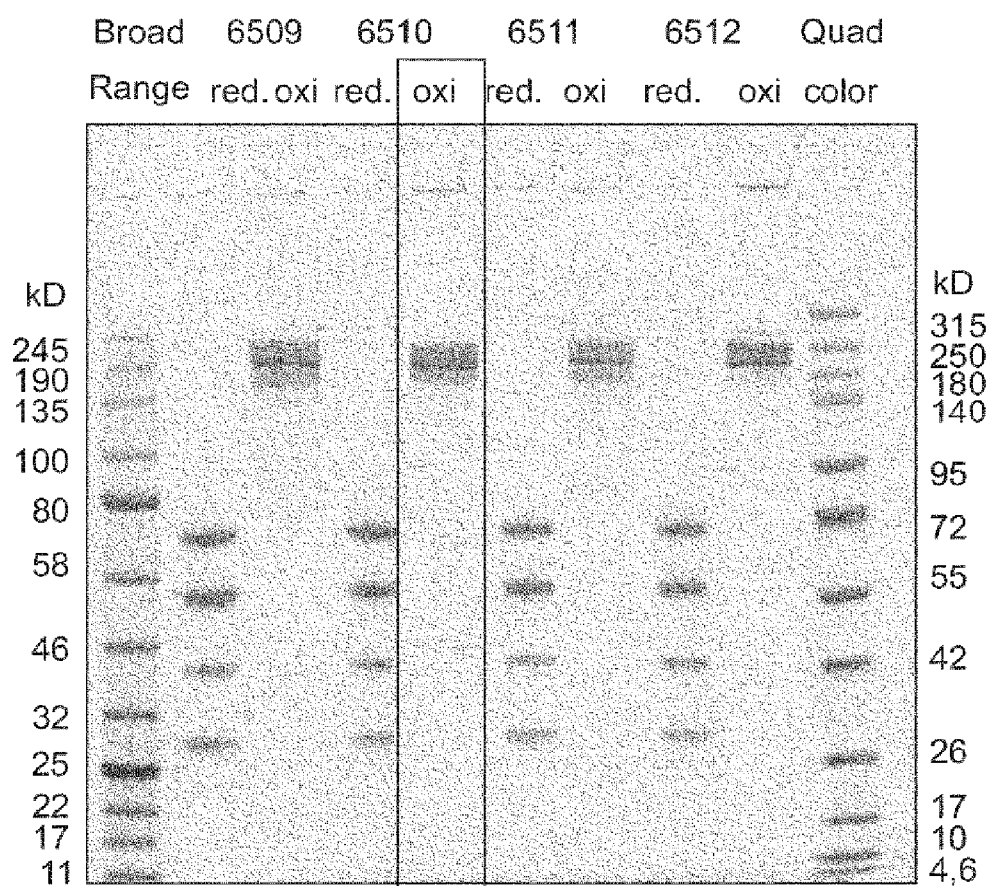


FIG. 30B