

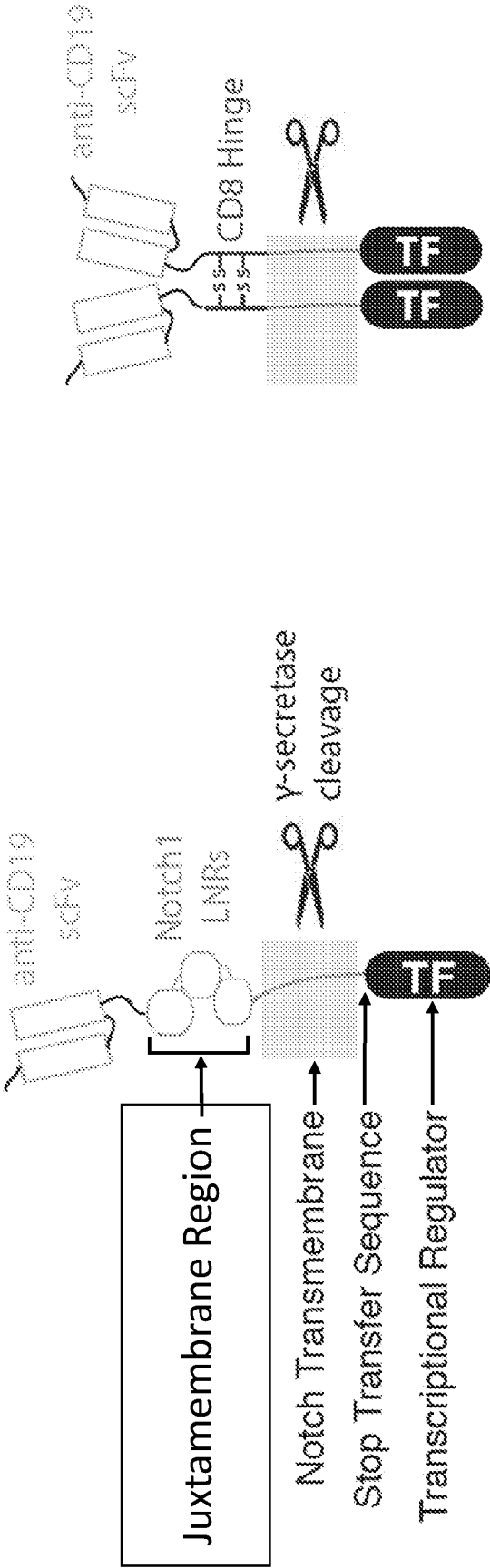


FIG. 1A

FIG. 1B

Primary Human CD4 T cells: anti-CD19 CD8hinge SynNotch Activation

SynNotch1 CD8 HingeNotch1 truncCD8 HingeNotch1

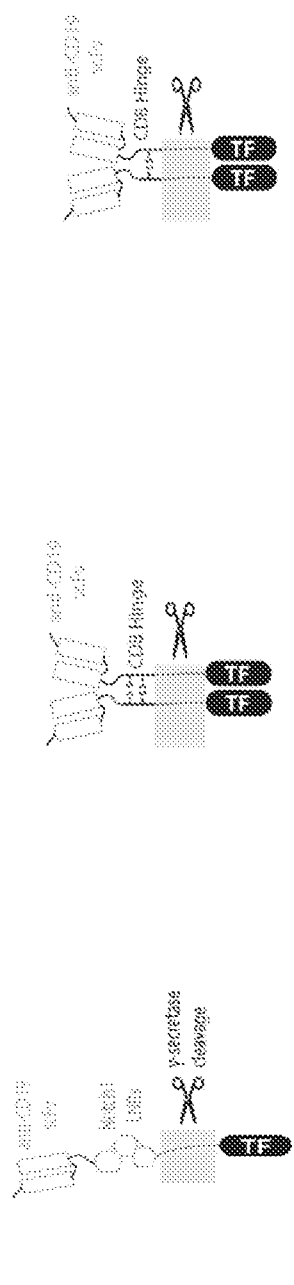


FIG. 2A

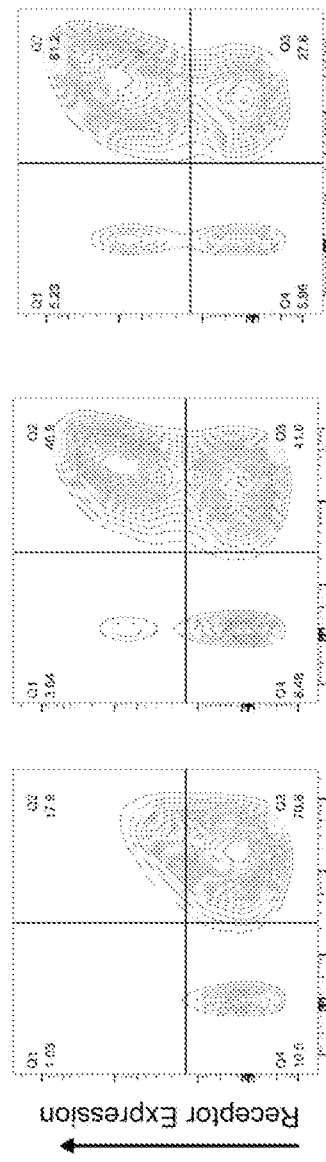


FIG. 2B

Reporter Expression

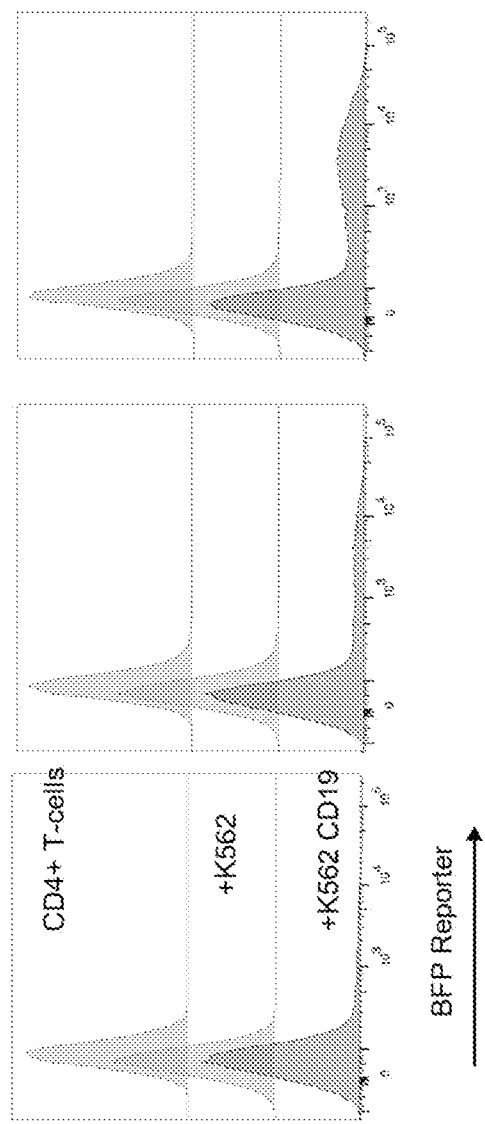


FIG. 2C

Primary Human CD4 T cells: anti-CD19 CD8hinge SynNotch Activation

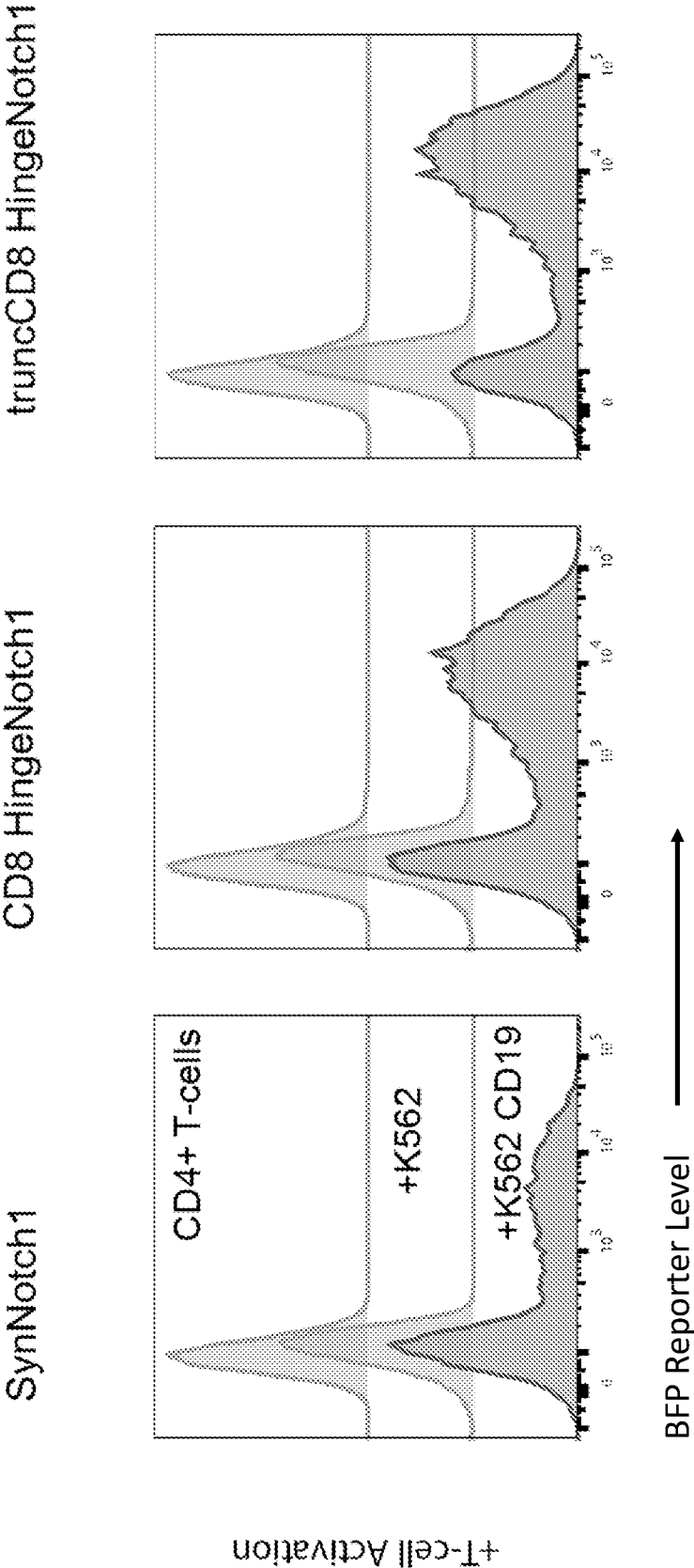


FIG. 3

CD8 Hinge SynNotch Optimization

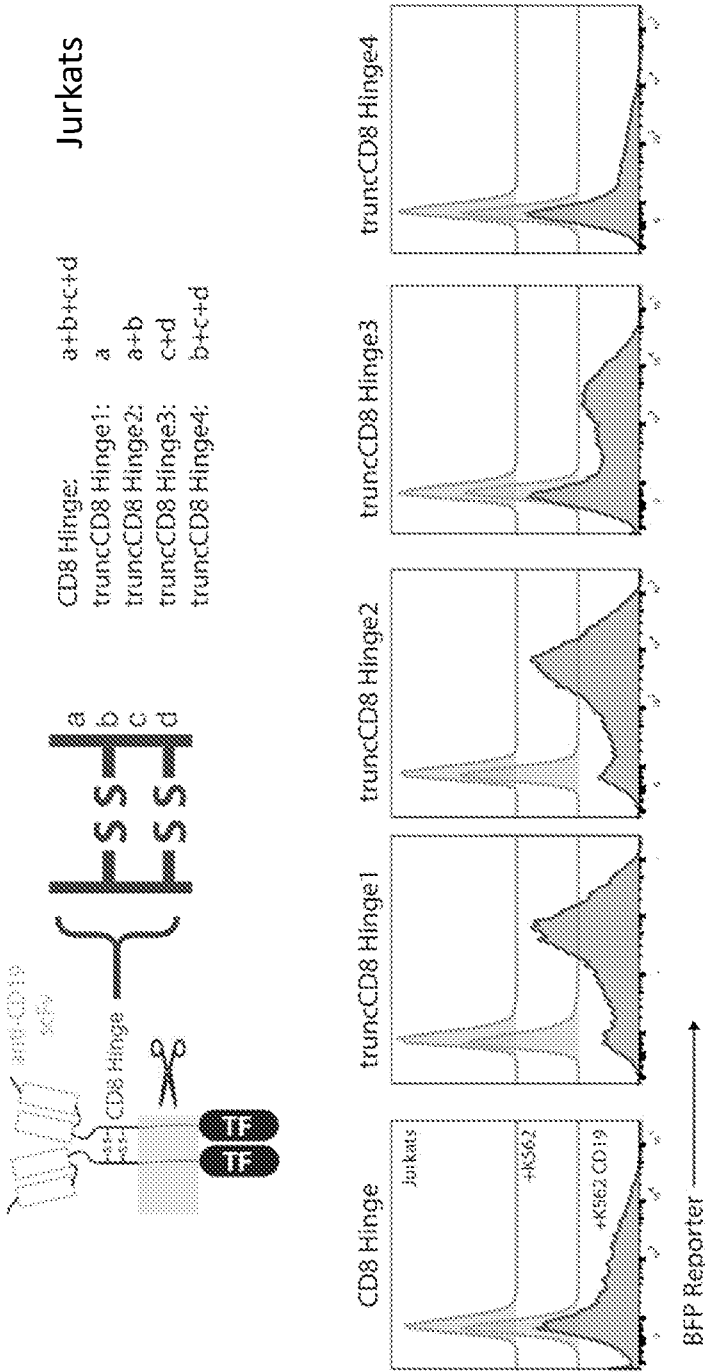
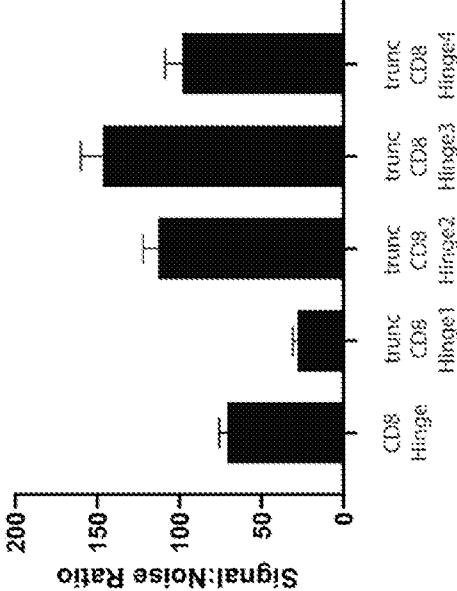
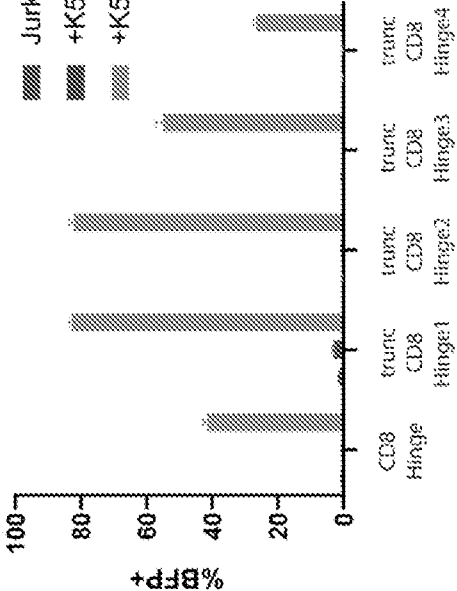


FIG. 4C CD8 HingeNotch, %BFP Activation



TruncCD8Hinge2 SynNotch1 Optimization
Regulation by PKC signaling

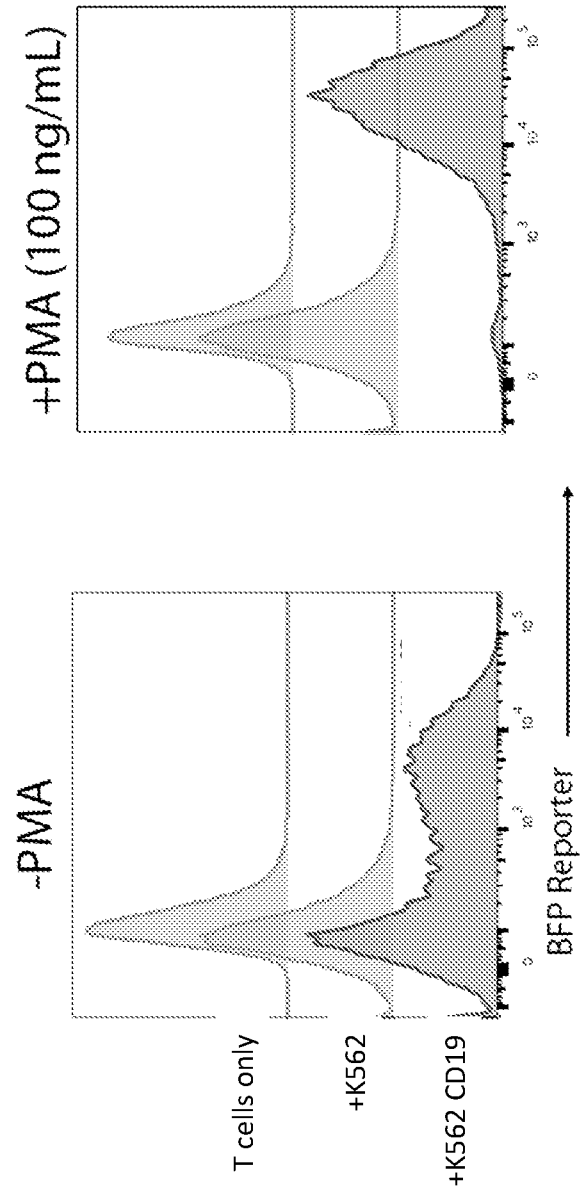


FIG. 5

Hinge SynNotch1 Variant
Jurkat T cells

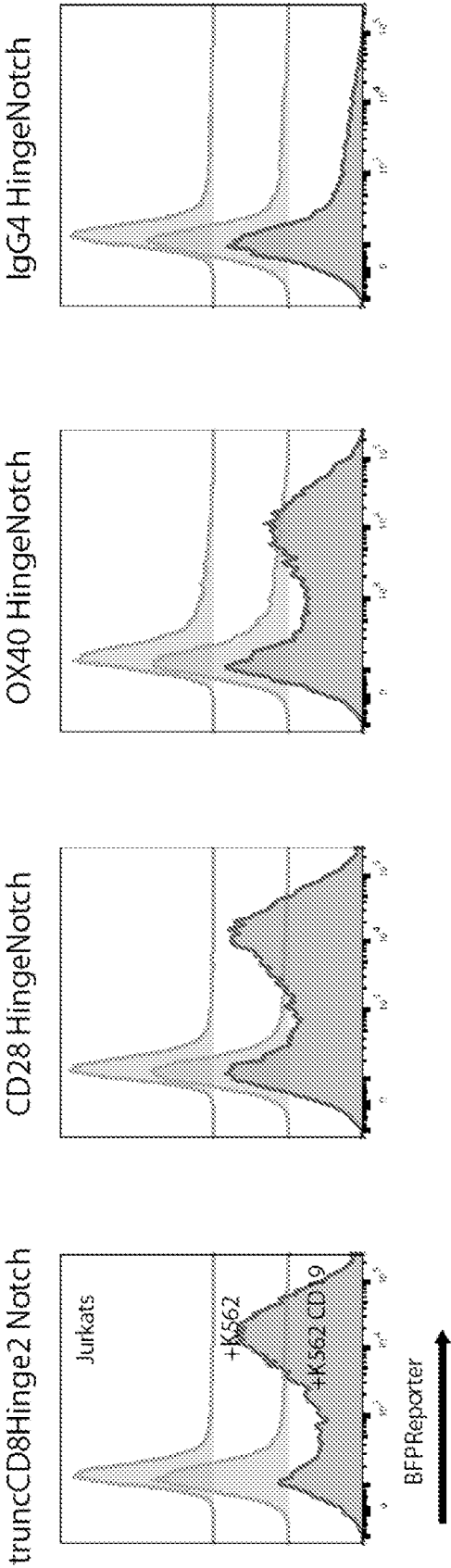


FIG. 6A

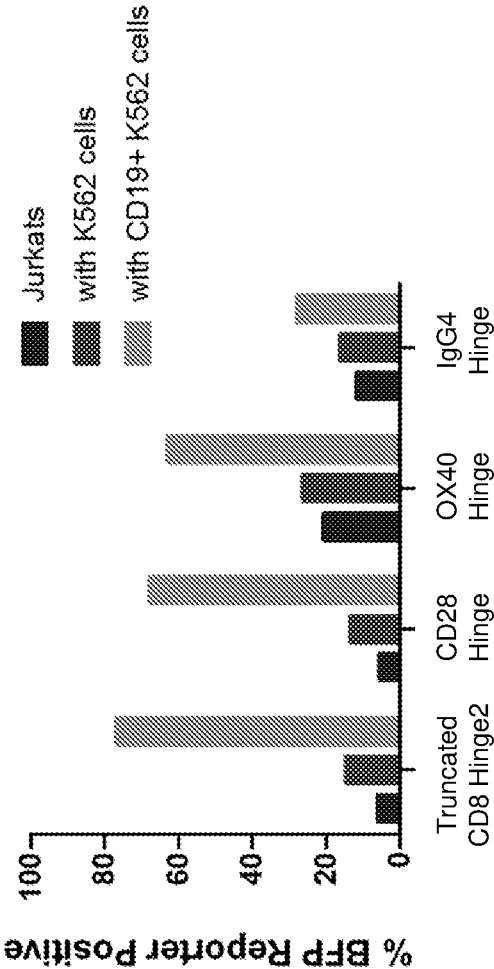


FIG. 6B

TruncCD8Hinge2 SynNotch1
Swapping the Ligand-binding Domain

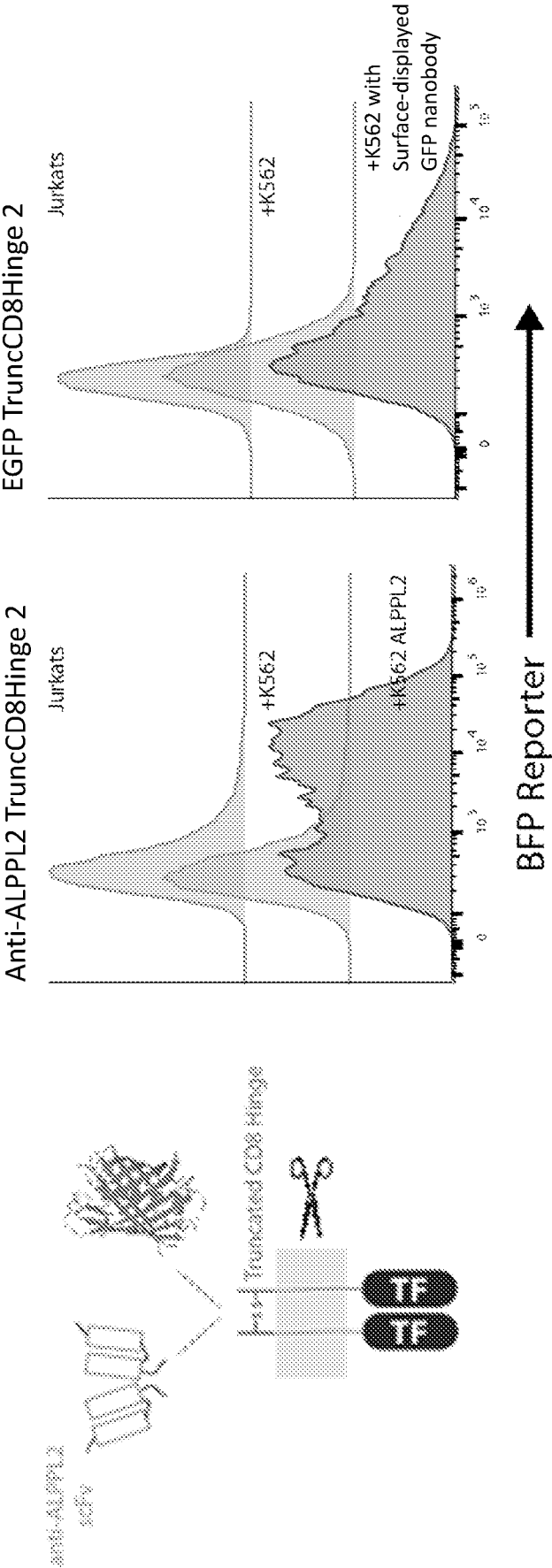


FIG. 7A

FIG. 7B

TruncCD8Hinge2 SynNotch1 Stop Transfer Variant

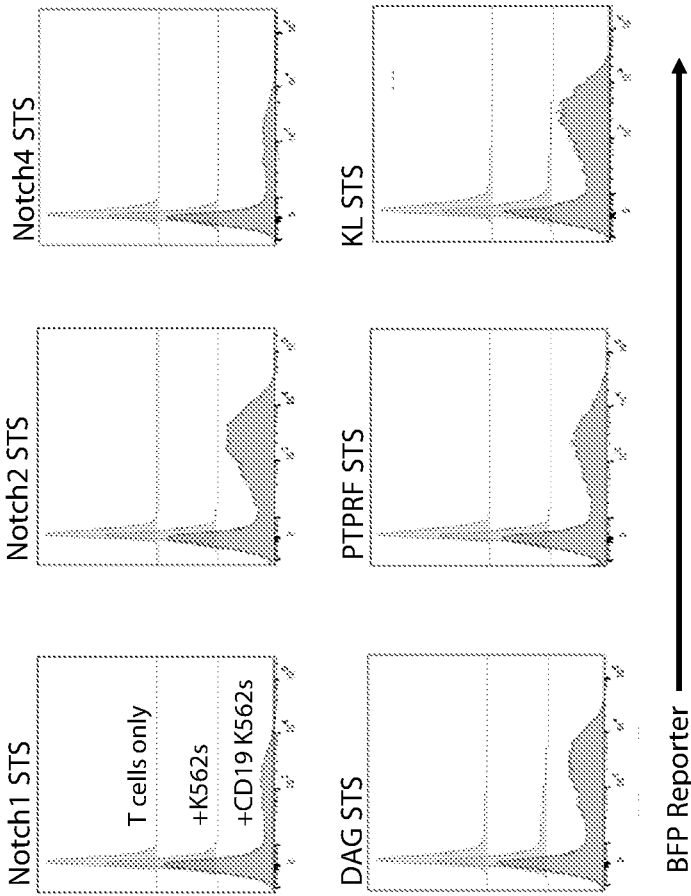


FIG. 8A

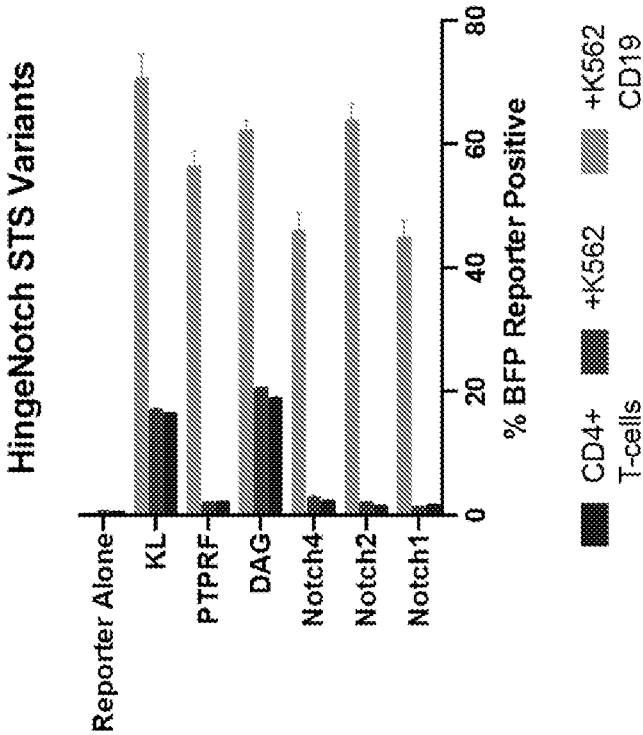


FIG. 8B

CD8Hinge SynNotch1 Optimization with co-expressed CAR Confirmation in CD45+ T cells



FIG. 9A

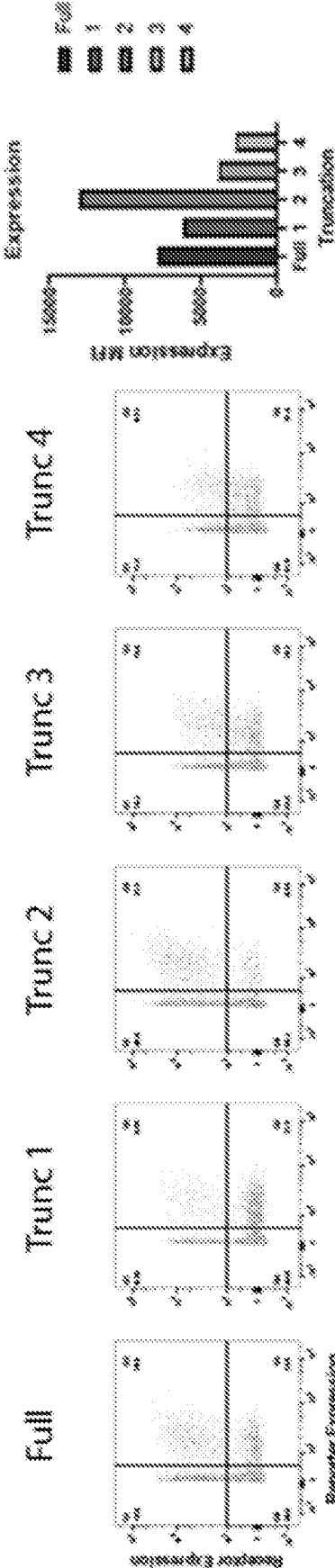


FIG. 9B

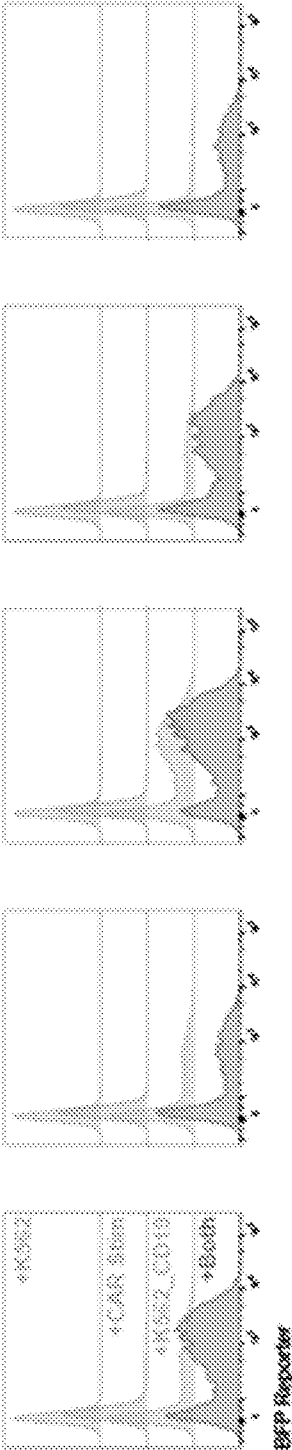


FIG. 9C

Activation with other binding domains and dependence on proteolytic activity

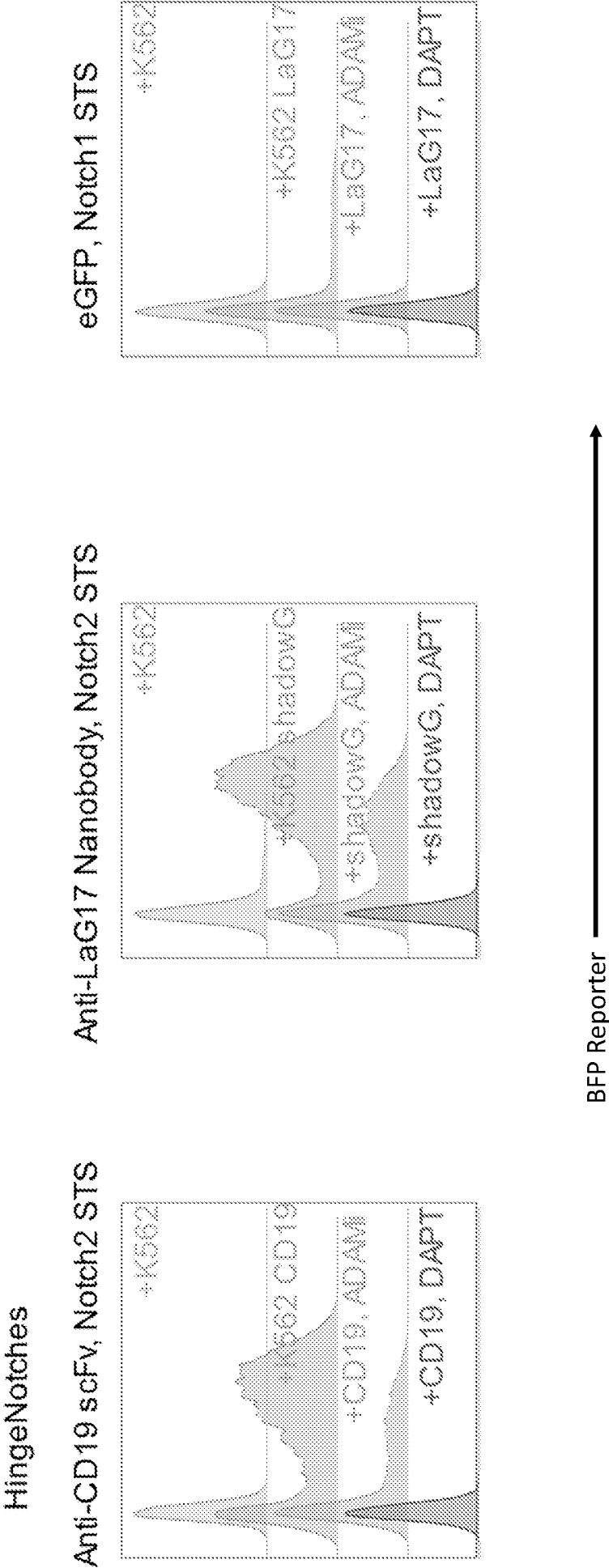


FIG. 10

HingeNotch with Notch2 STS receptor activation with other binding domains

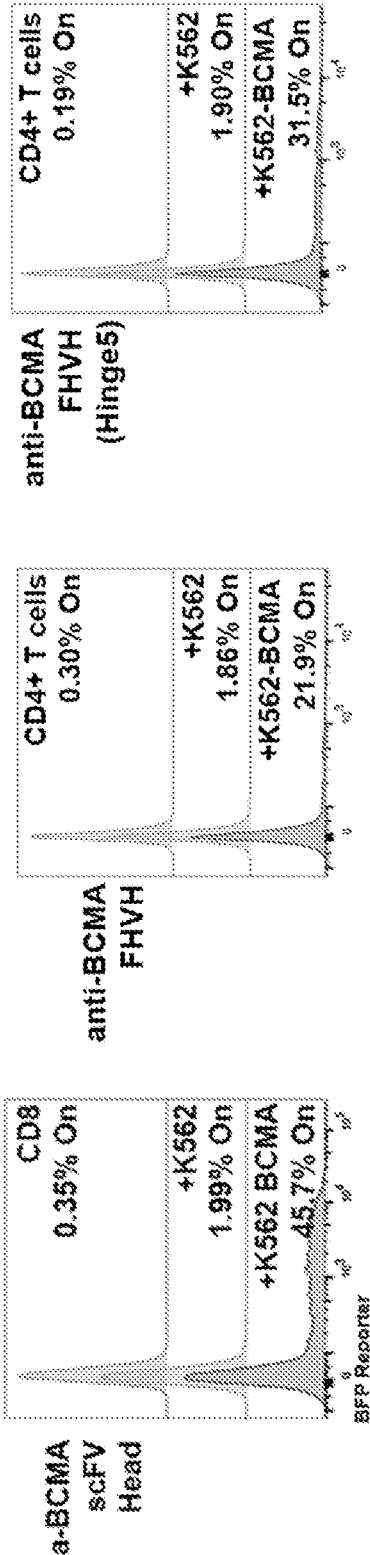


FIG. 11A

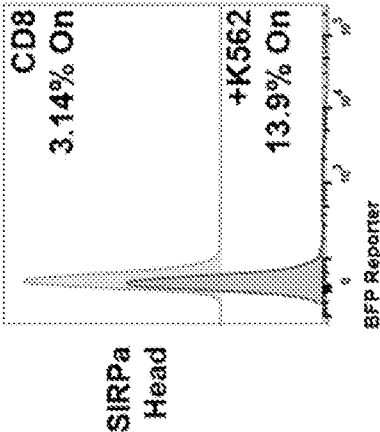


FIG. 11B

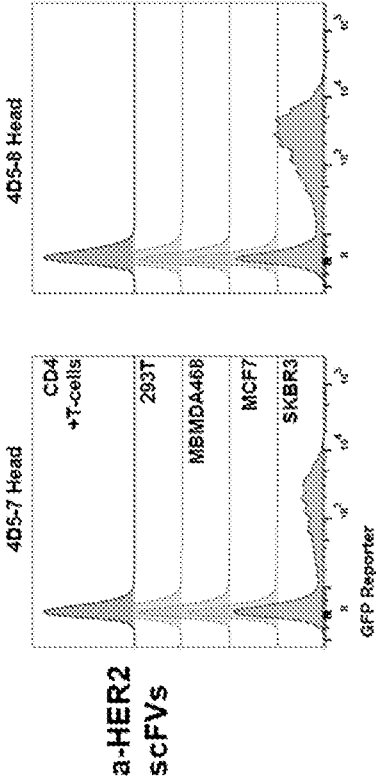


FIG. 11C

HingeNotch activation with different STS and promoters

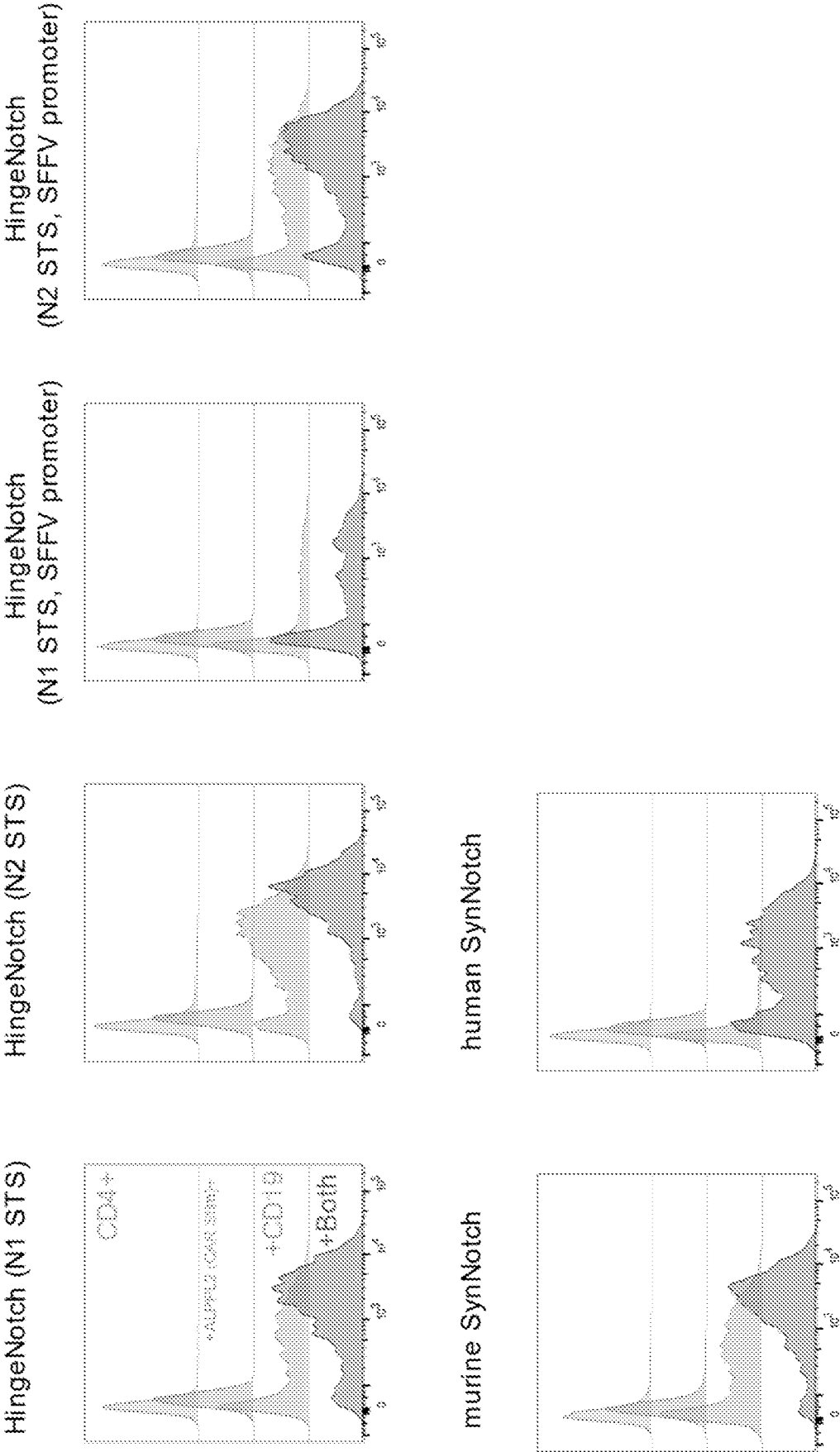
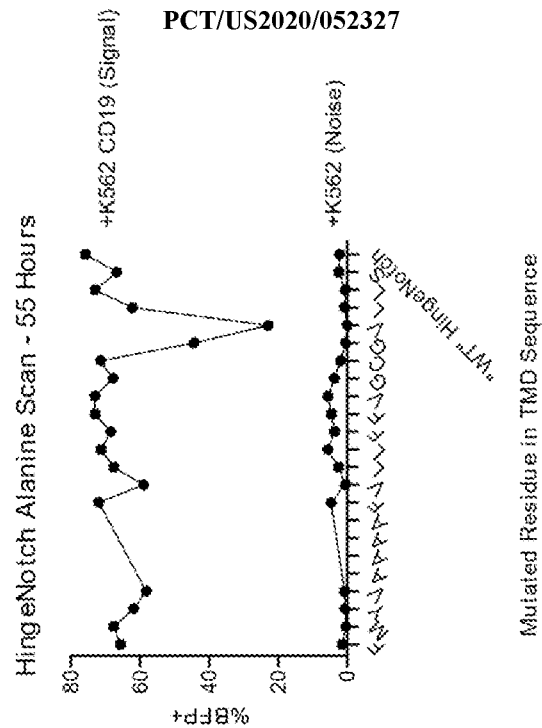


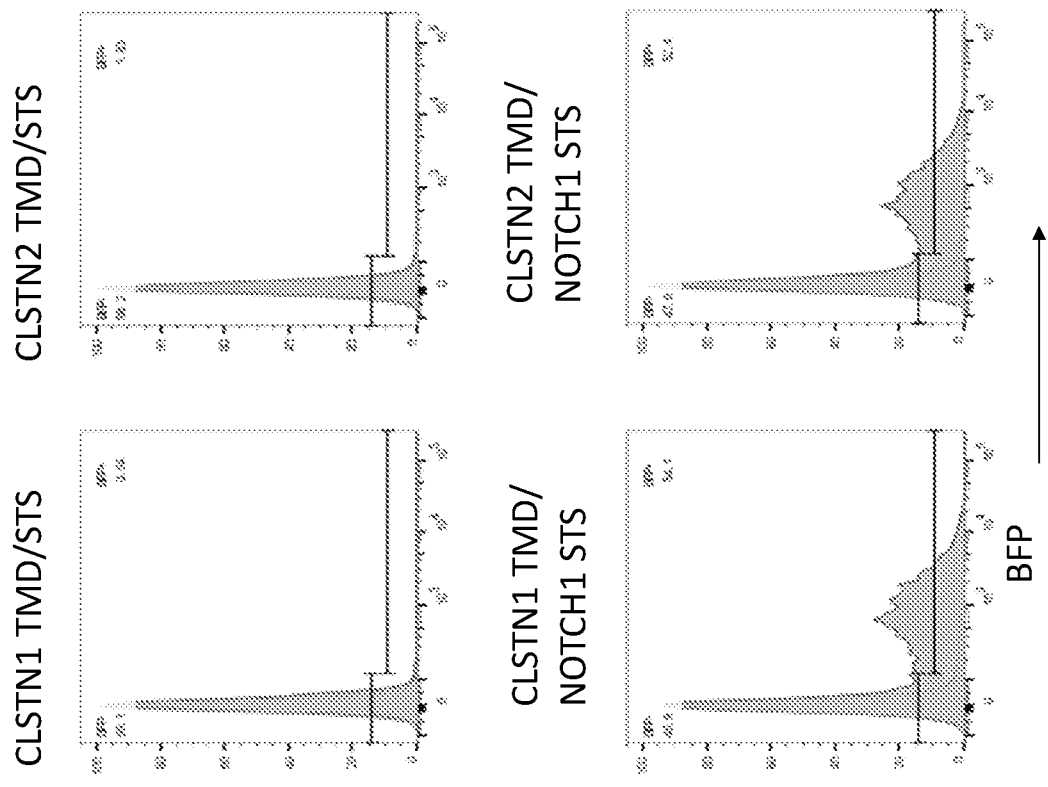
FIG. 12

FIG. 13A



SynCLSTN1/2 Receptors

-CAR
Activity



+CAR
Activity

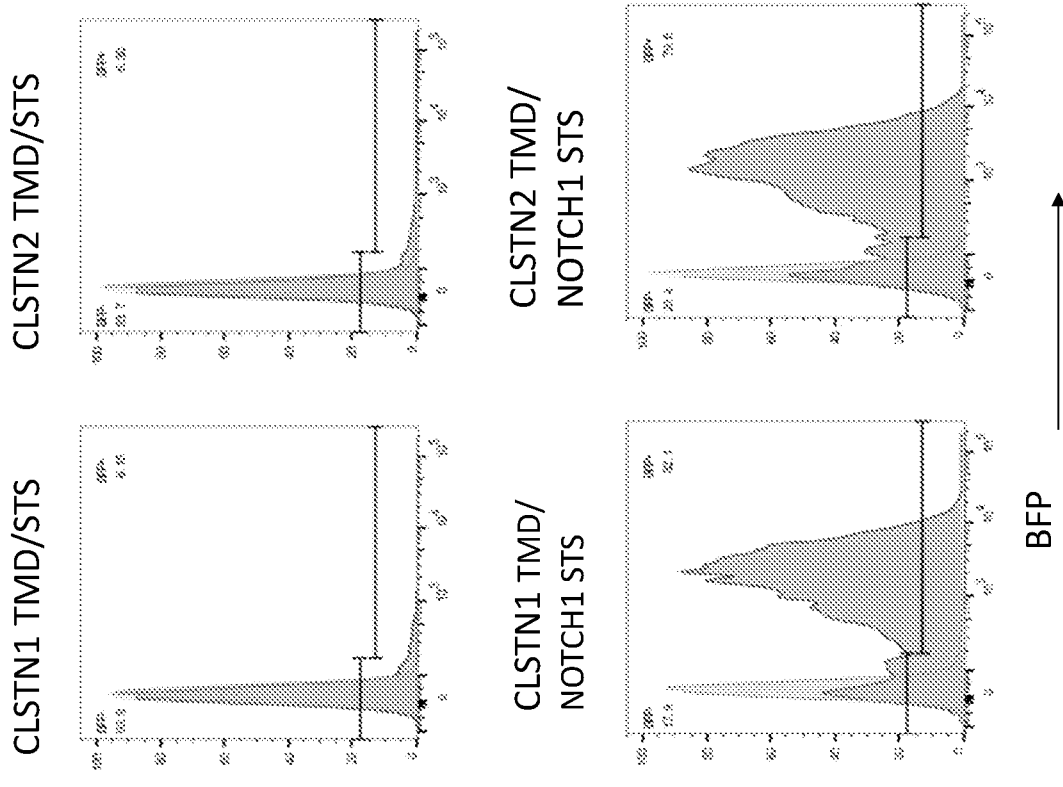


FIG. 14

Tunable, ligand-dependent expansion of T cells using HingeNotch-controlled expression of an engineered cytokine

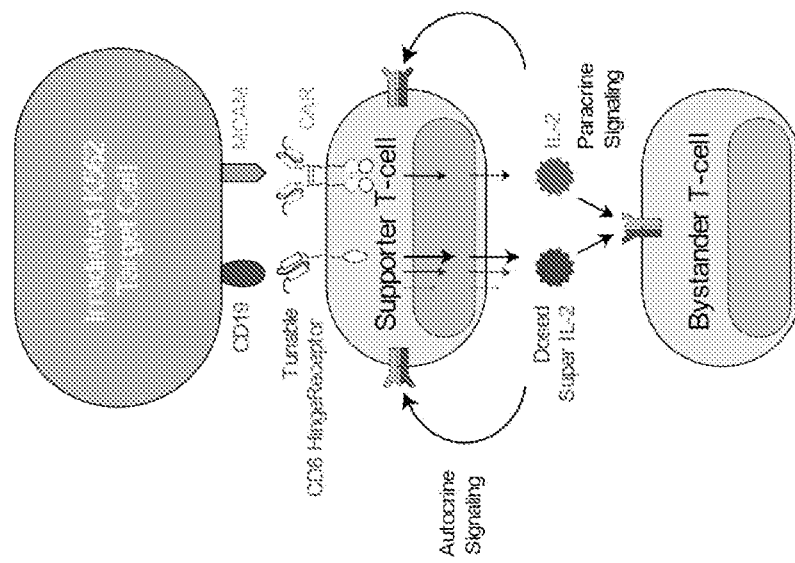


FIG. 15A

Receptor Expression of HingeNotch STS variants

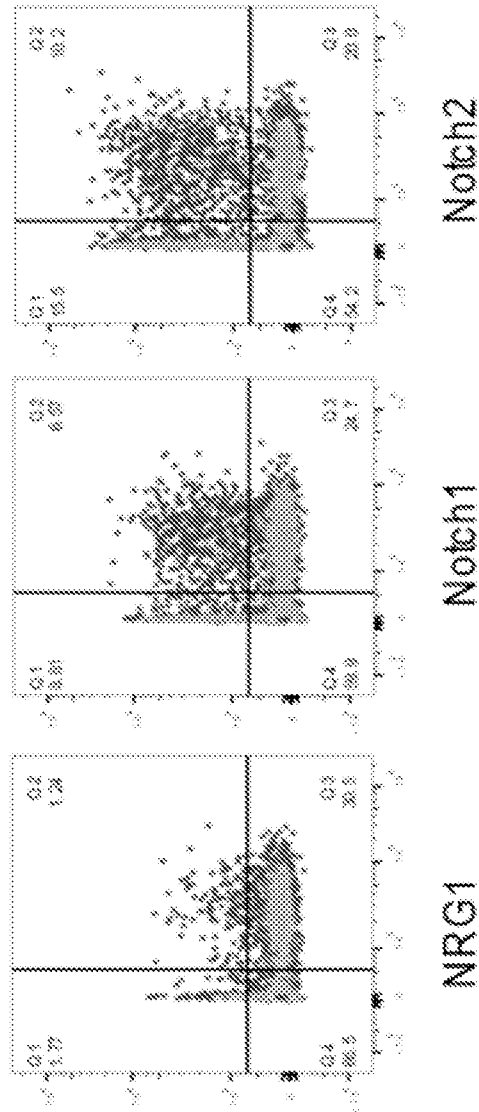


FIG. 15B

Tunable, ligand-dependent expansion of T cells using
HingeNotch-controlled expression of an engineered cytokine

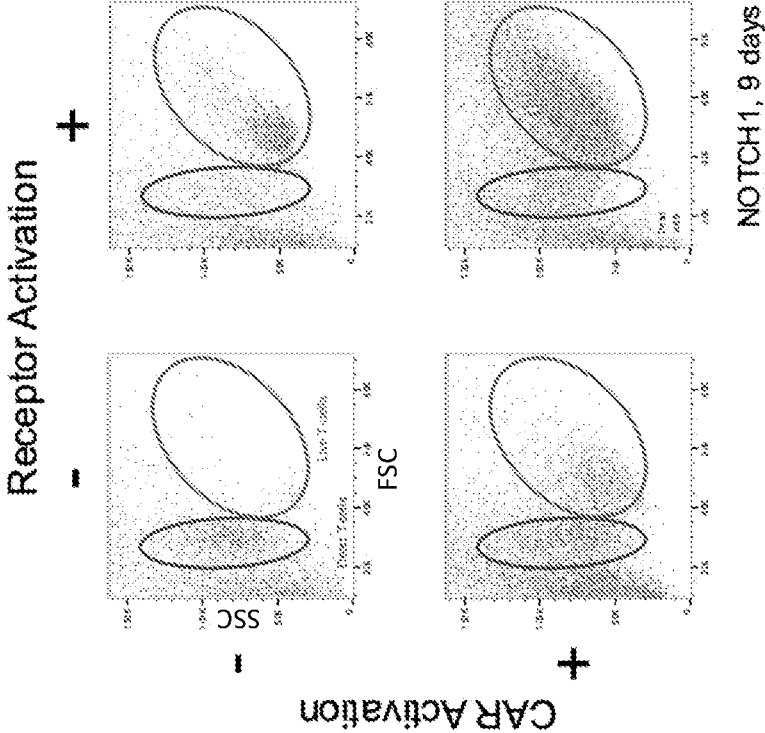


FIG. 16

Tunable, ligand-dependent expansion of T cells using
HingeNotch-controlled expression of an engineered cytokine

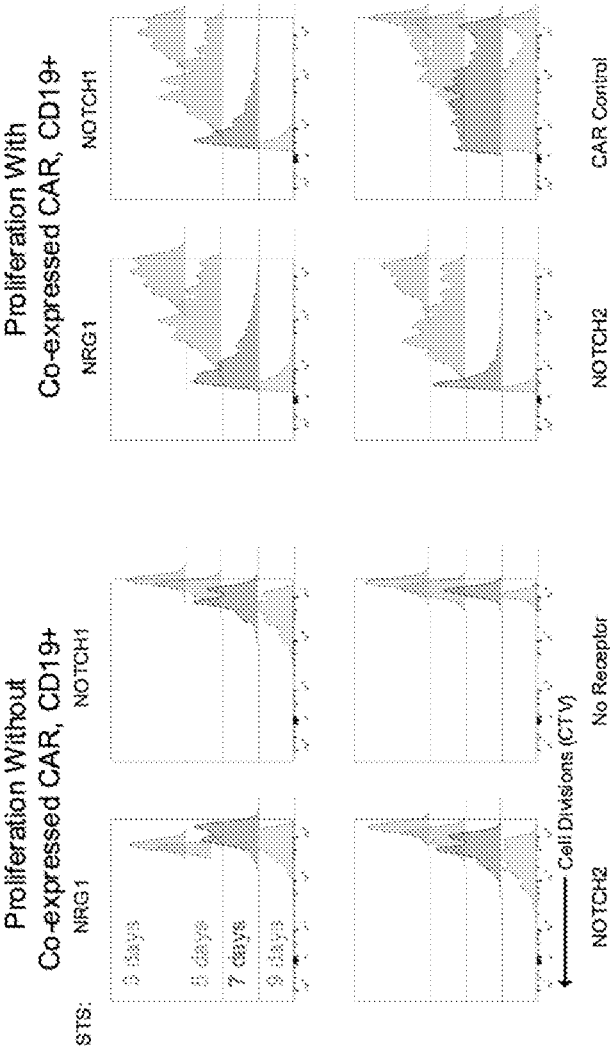


FIG. 17

Tunable, ligand-dependent expansion of T cells using
HingeNotch-controlled expression of an engineered cytokine

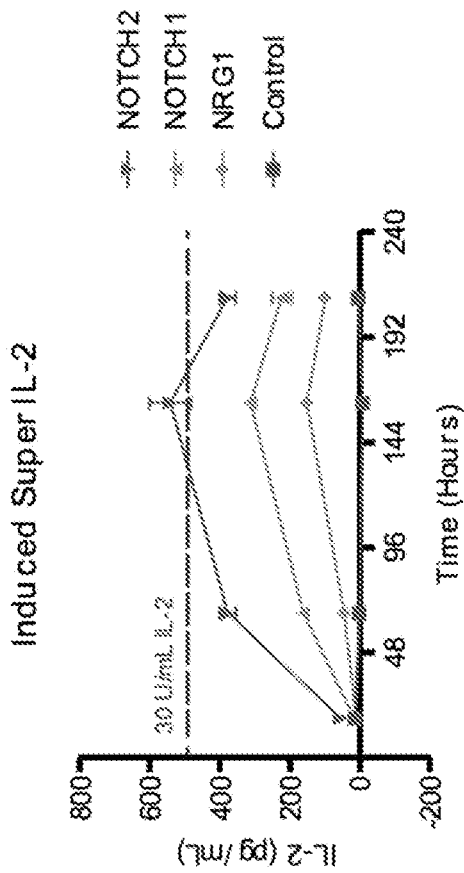


FIG. 18A

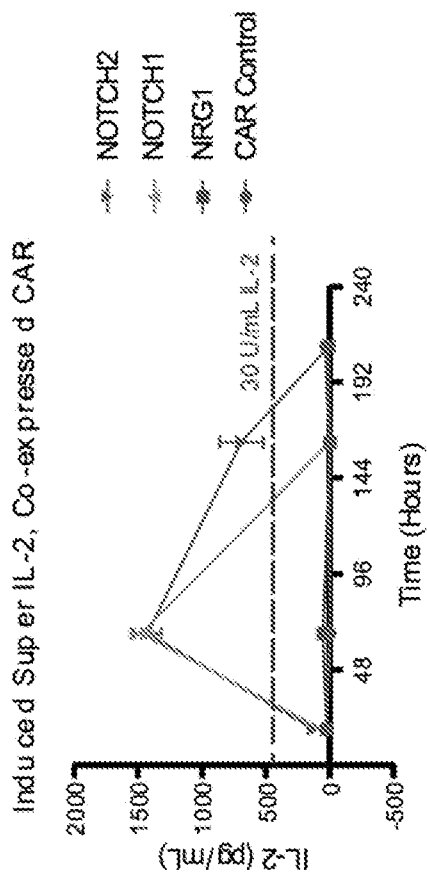


FIG. 18B

Tunable, ligand-dependent expansion of T cells using
HingeNotch-controlled expression of an engineered cytokine

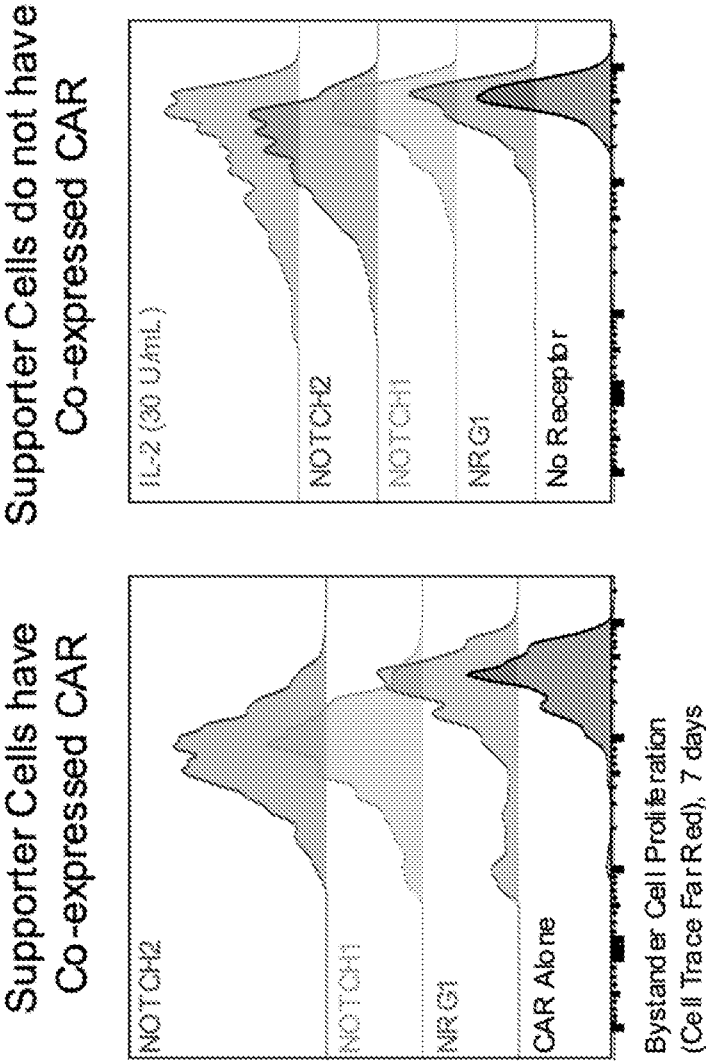


FIG. 19

HingeNotch receptor circuits can function on a single lentiviral vector

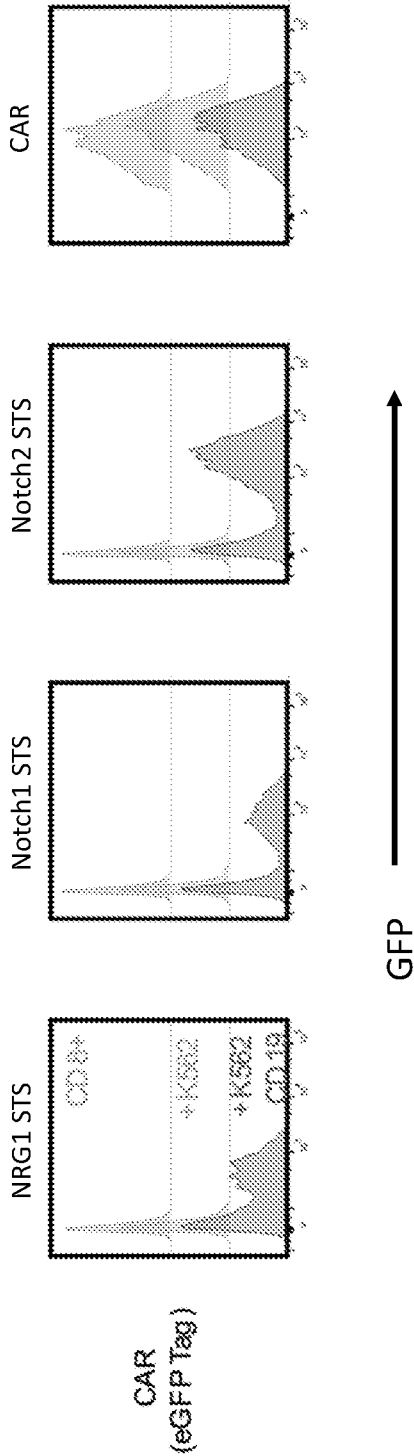


FIG. 20

CAR induction from HingeNotch single vector constructs can specifically eliminate dual-antigen target cells

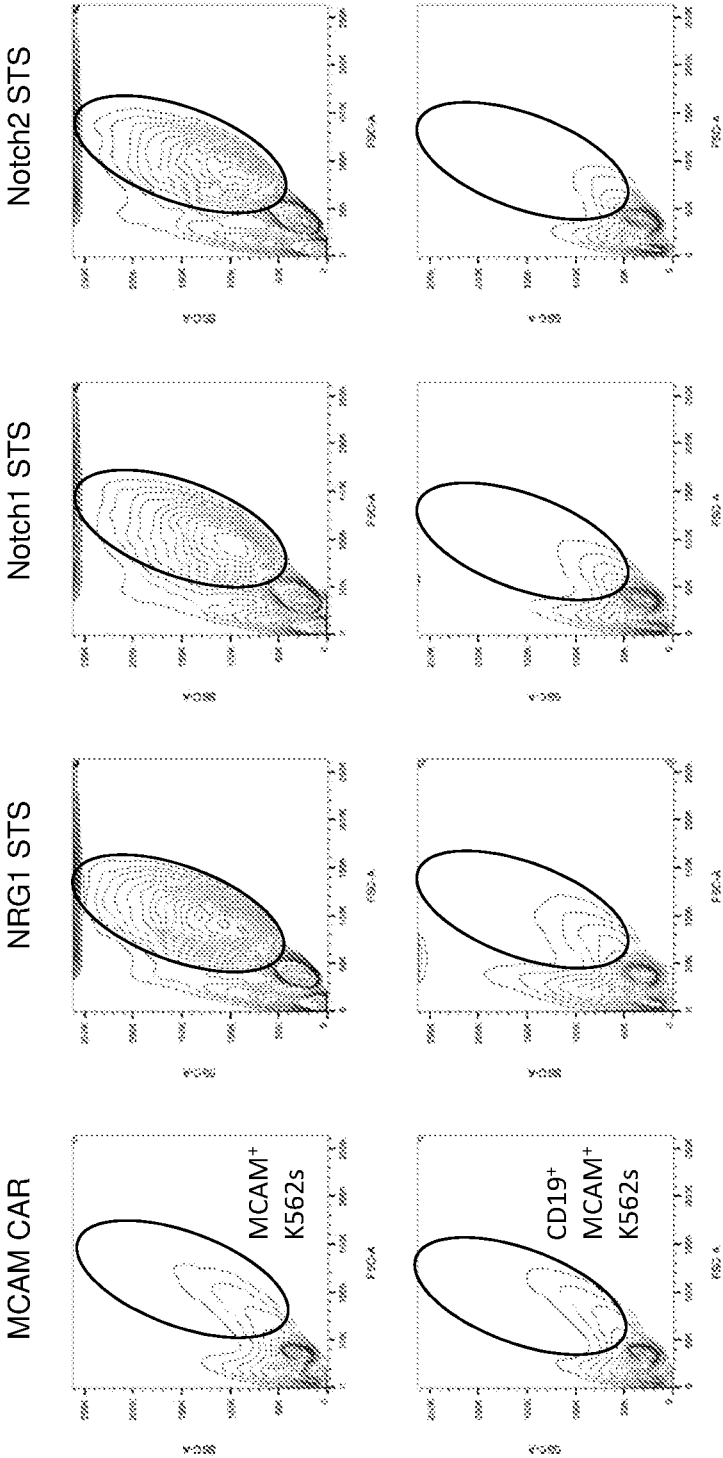


FIG. 21

CAR induction from HingeNotch single vector constructs can specifically eliminate dual-antigen target cells

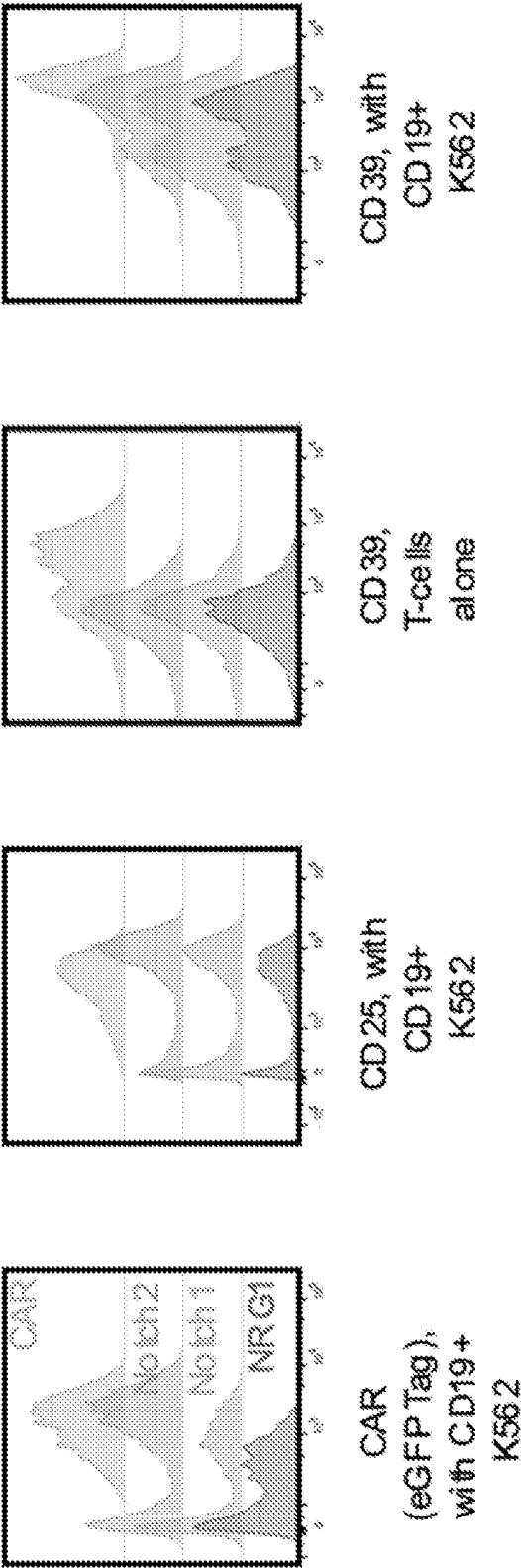


FIG. 22

Selective Dual Antigen Tumor Clearance with a HingeNotch CAR Circuit

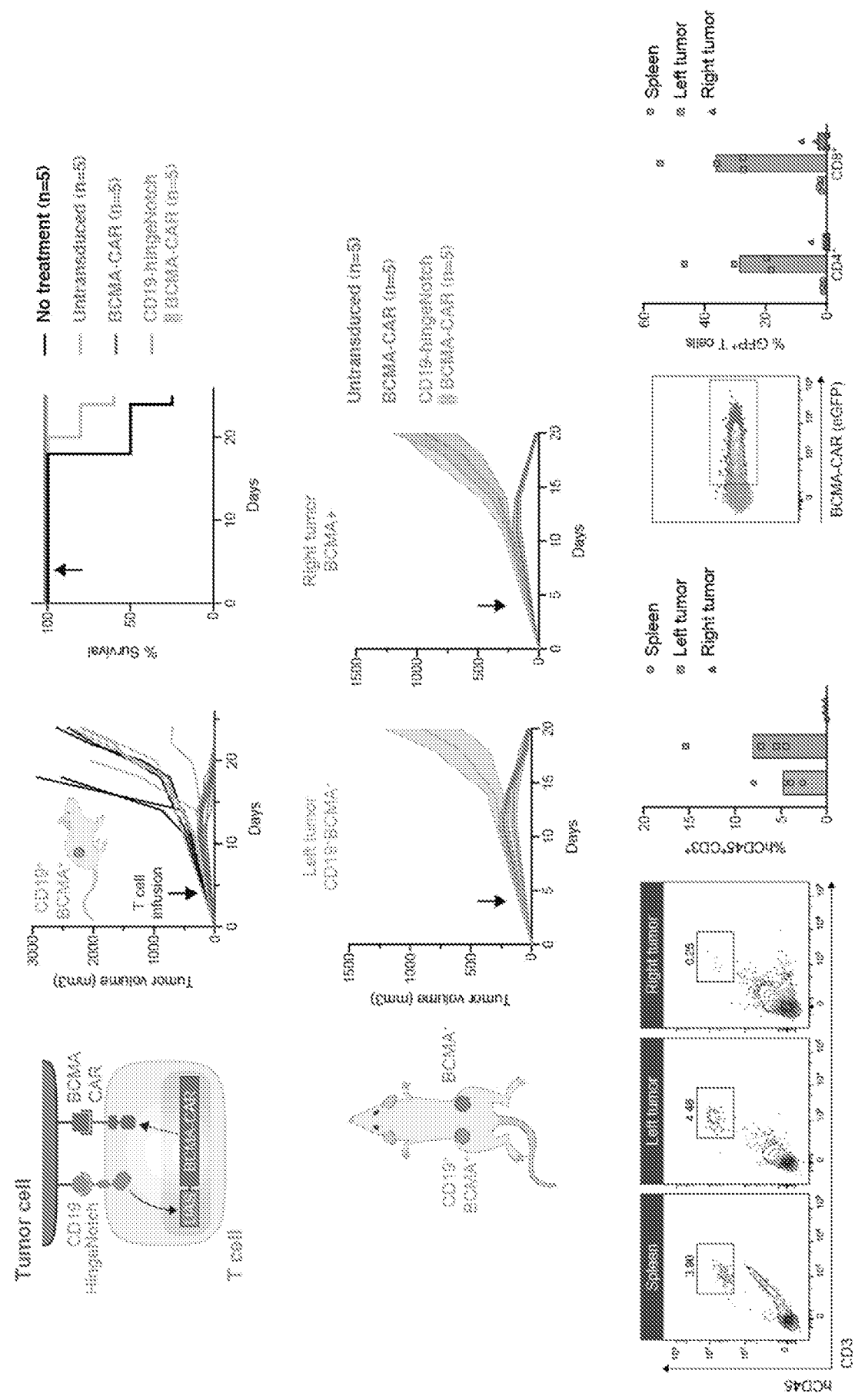


FIG. 23