

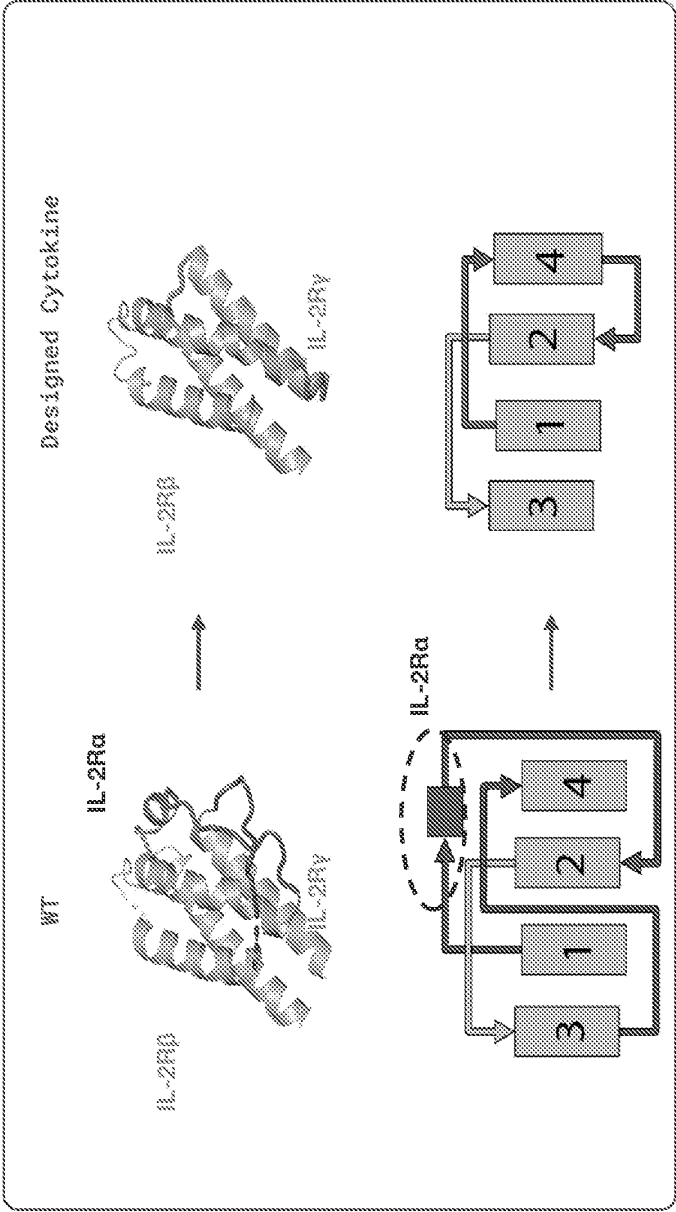


FIG. 1A

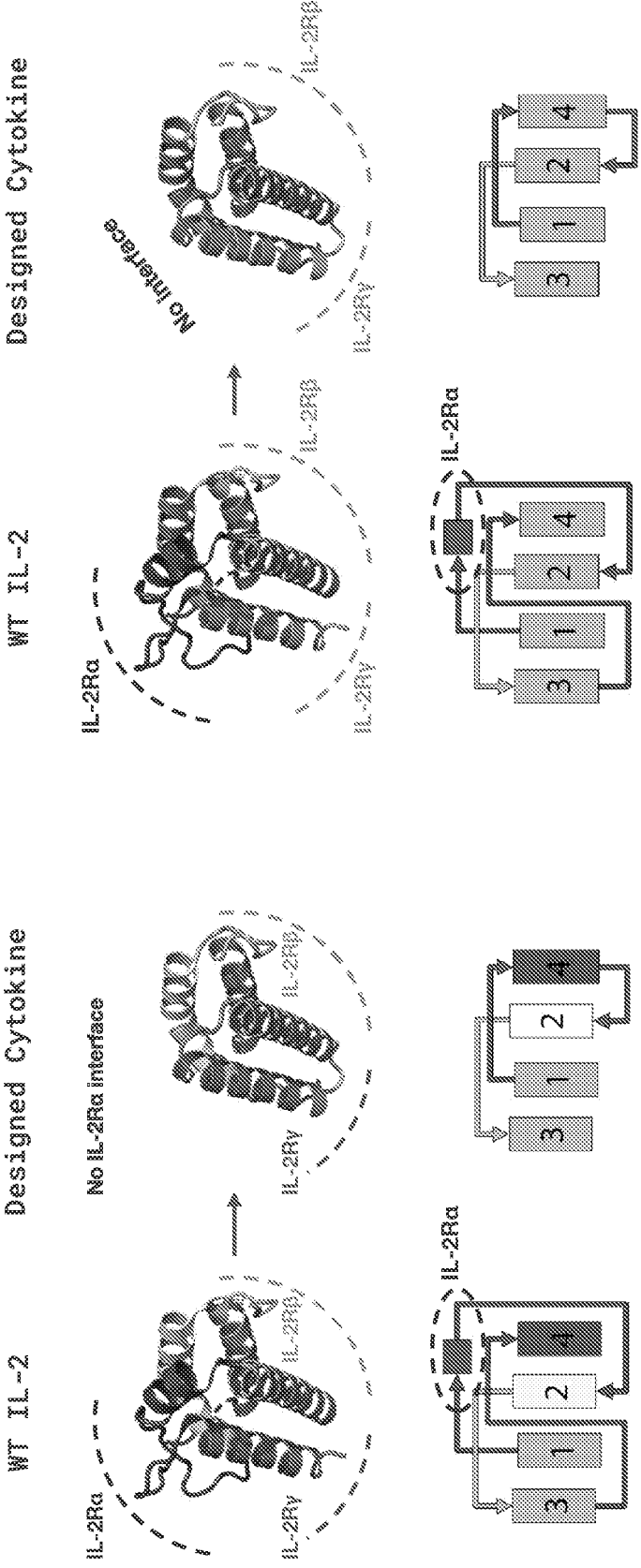


FIG. 1B

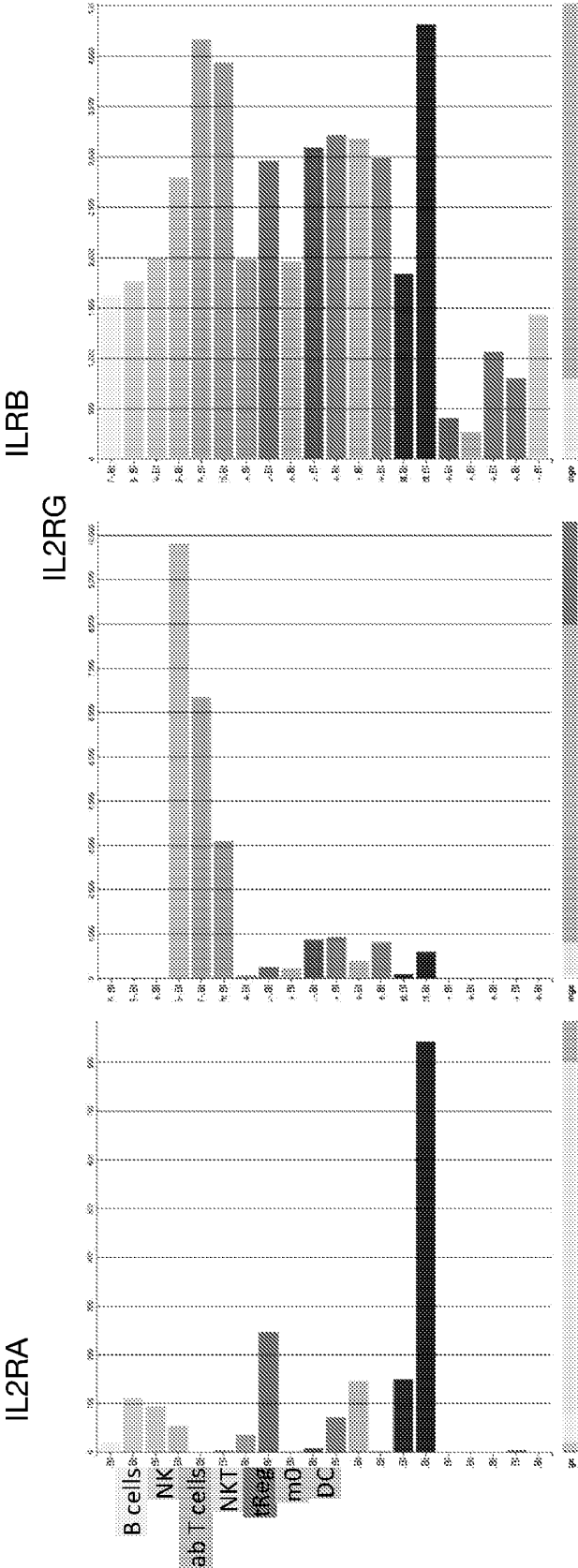


FIG. 2

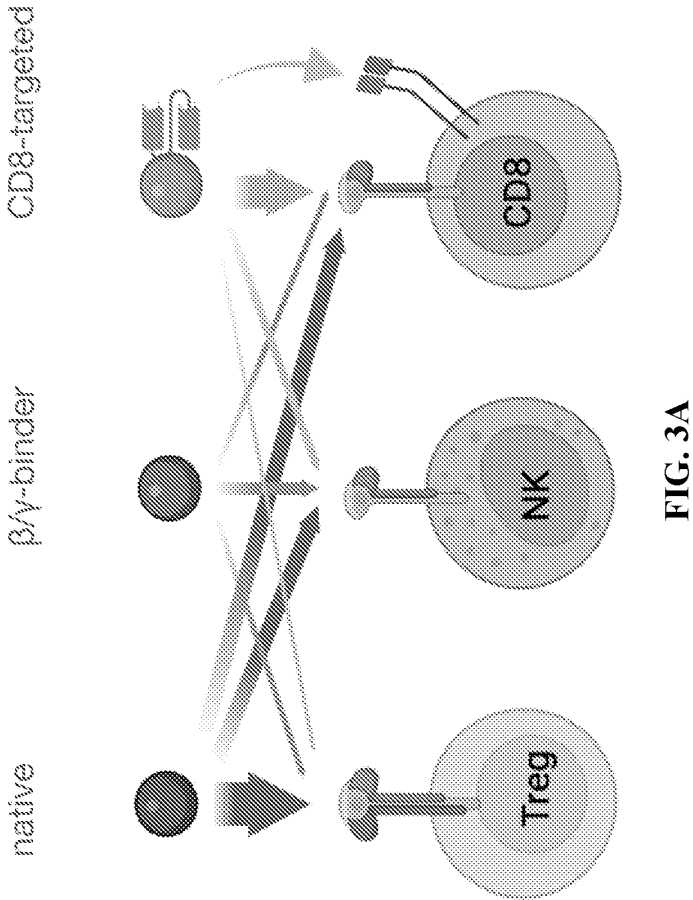


FIG. 3A

Use of Designed Cytokine in a variety of cell types and for different applications

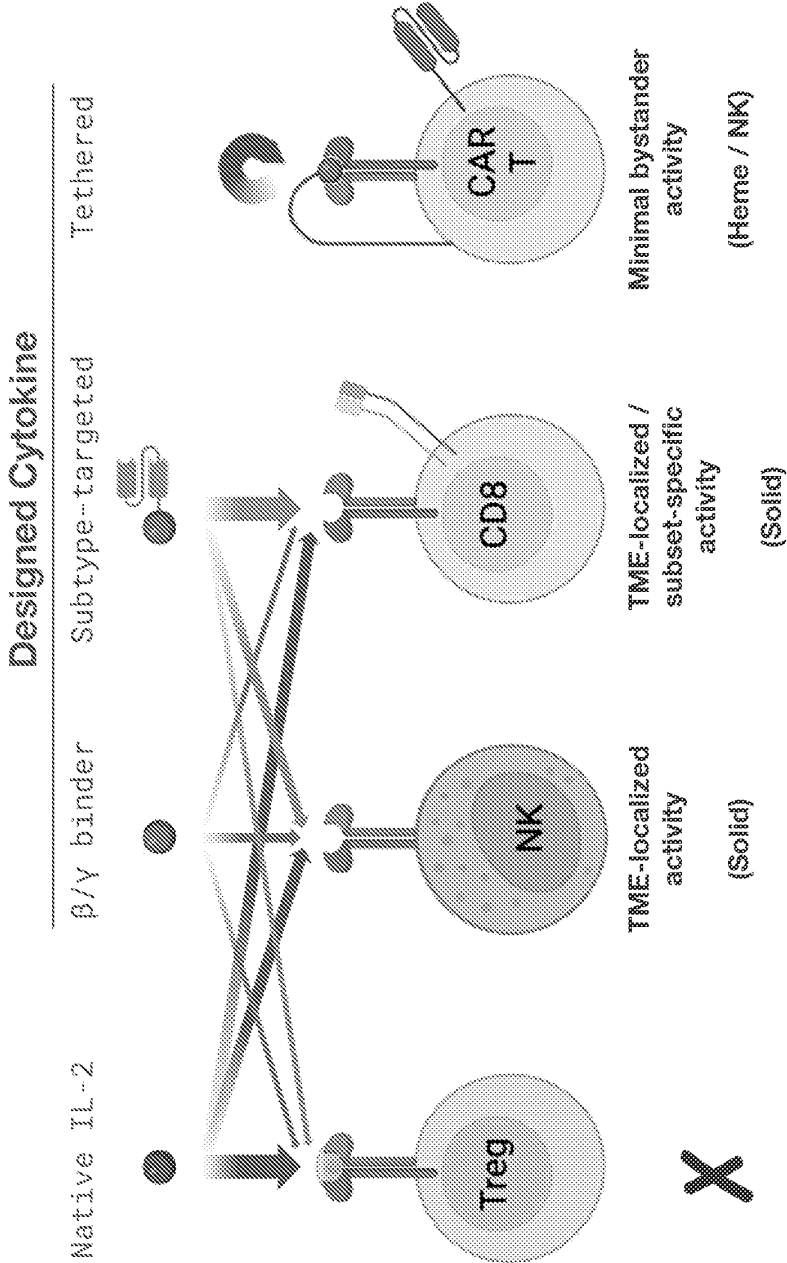


FIG. 3B

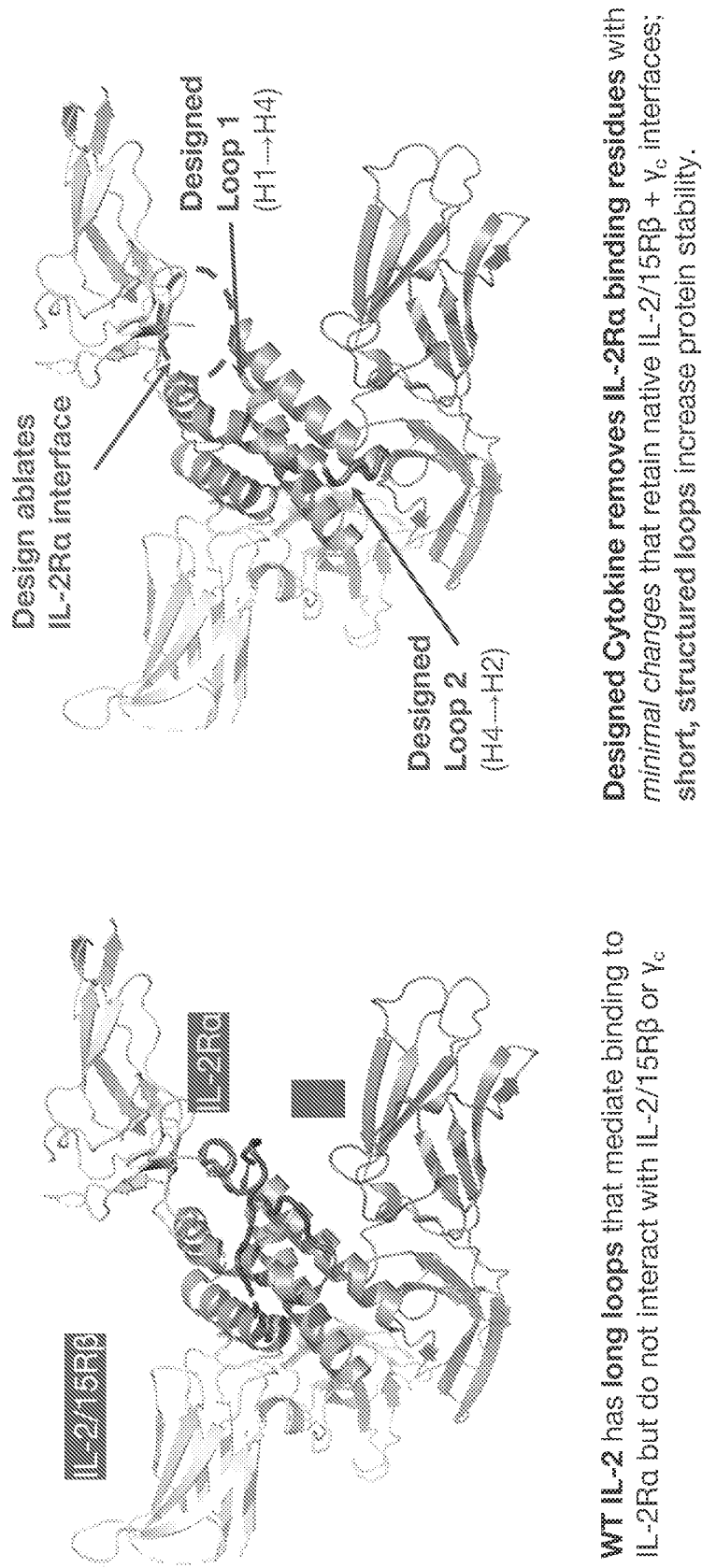
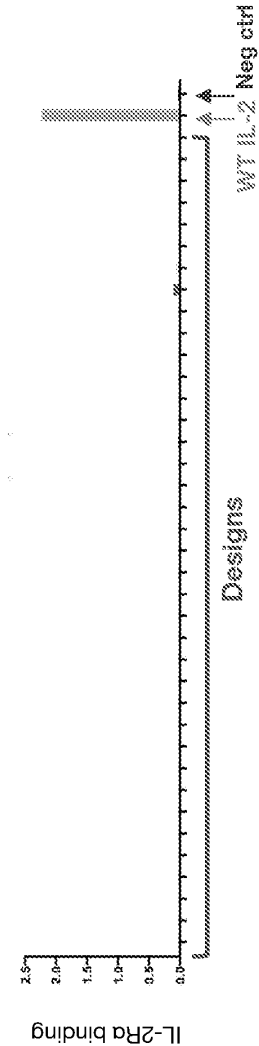


FIG. 4

38/38 Designed Cytokines ablate IL-2Ra binding



33/38 Designed Cytokines retain IL-2/15R β signaling

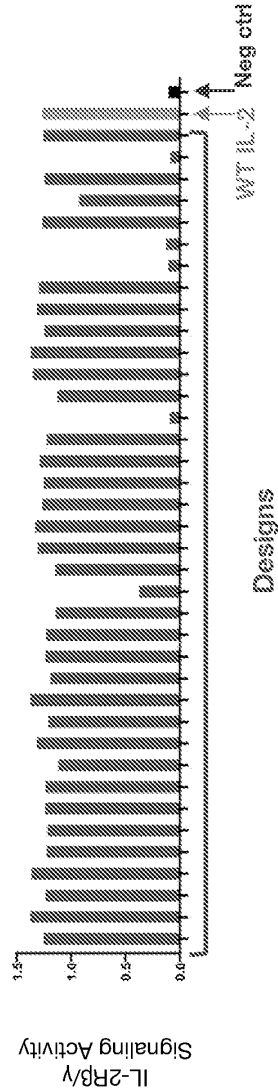
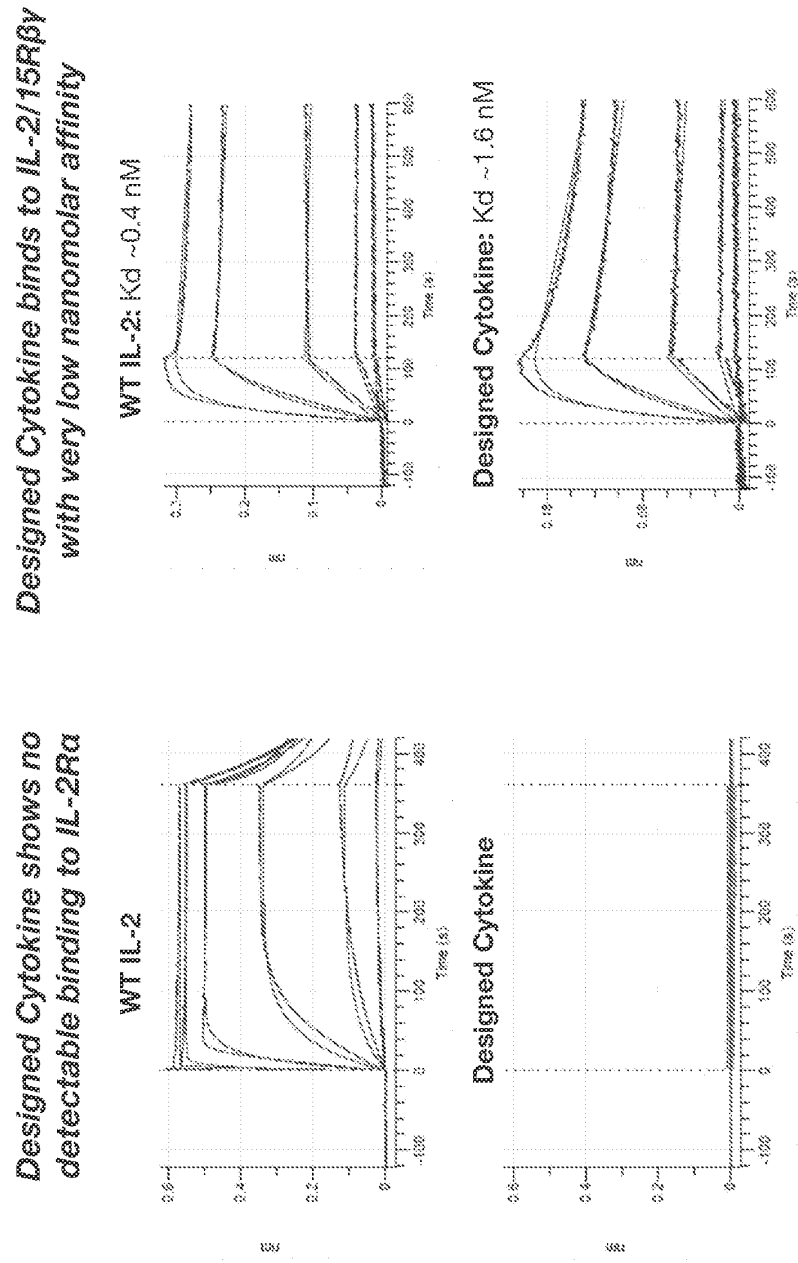


FIG. 5A



0.9 nM to 3000 nM cytokine tested

FIG. 5B

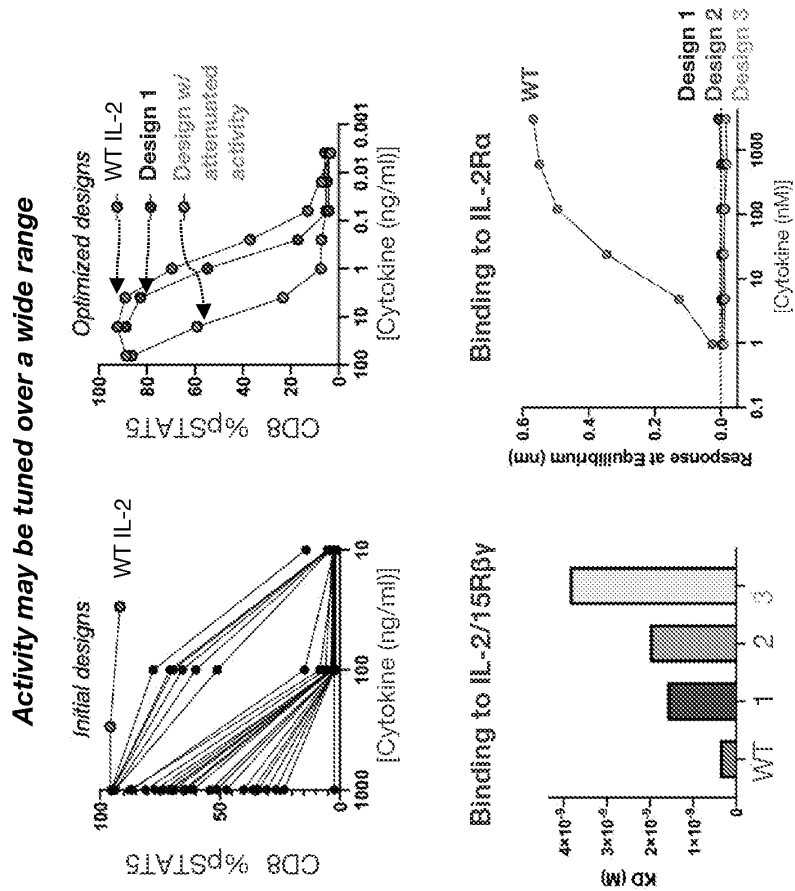
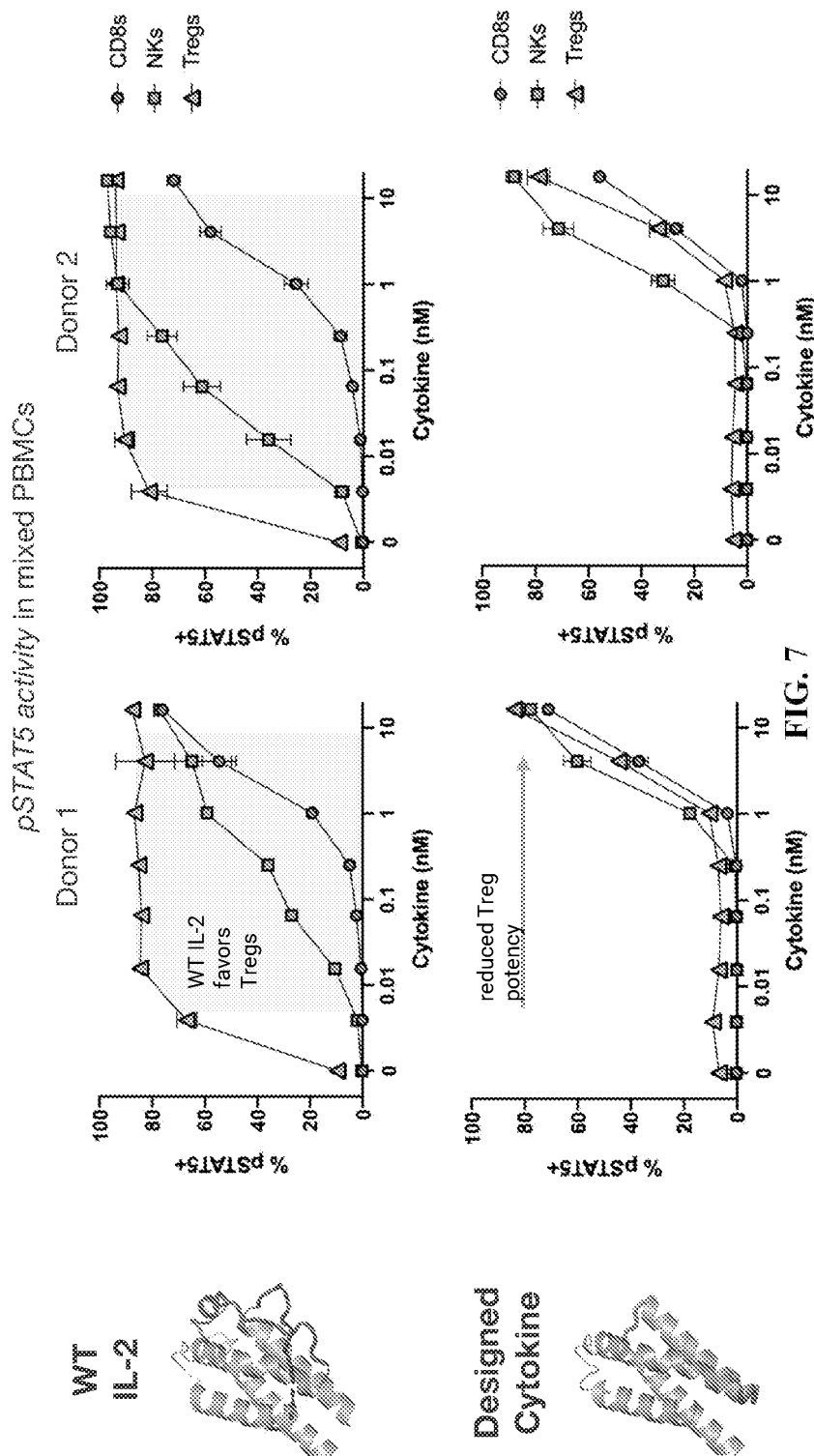


FIG. 6

Designed Cytokine eliminates Treg preference, preserving NK and CD8 activity



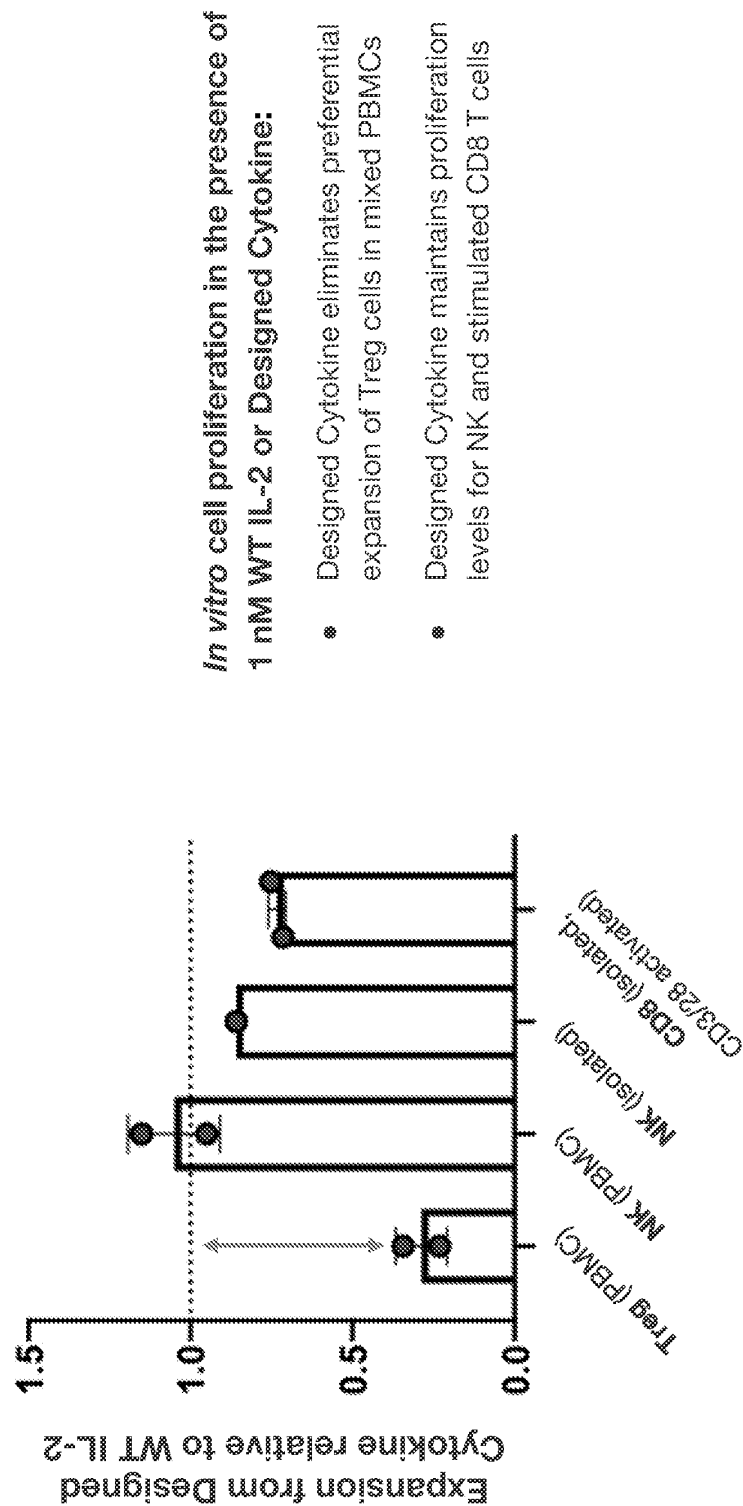
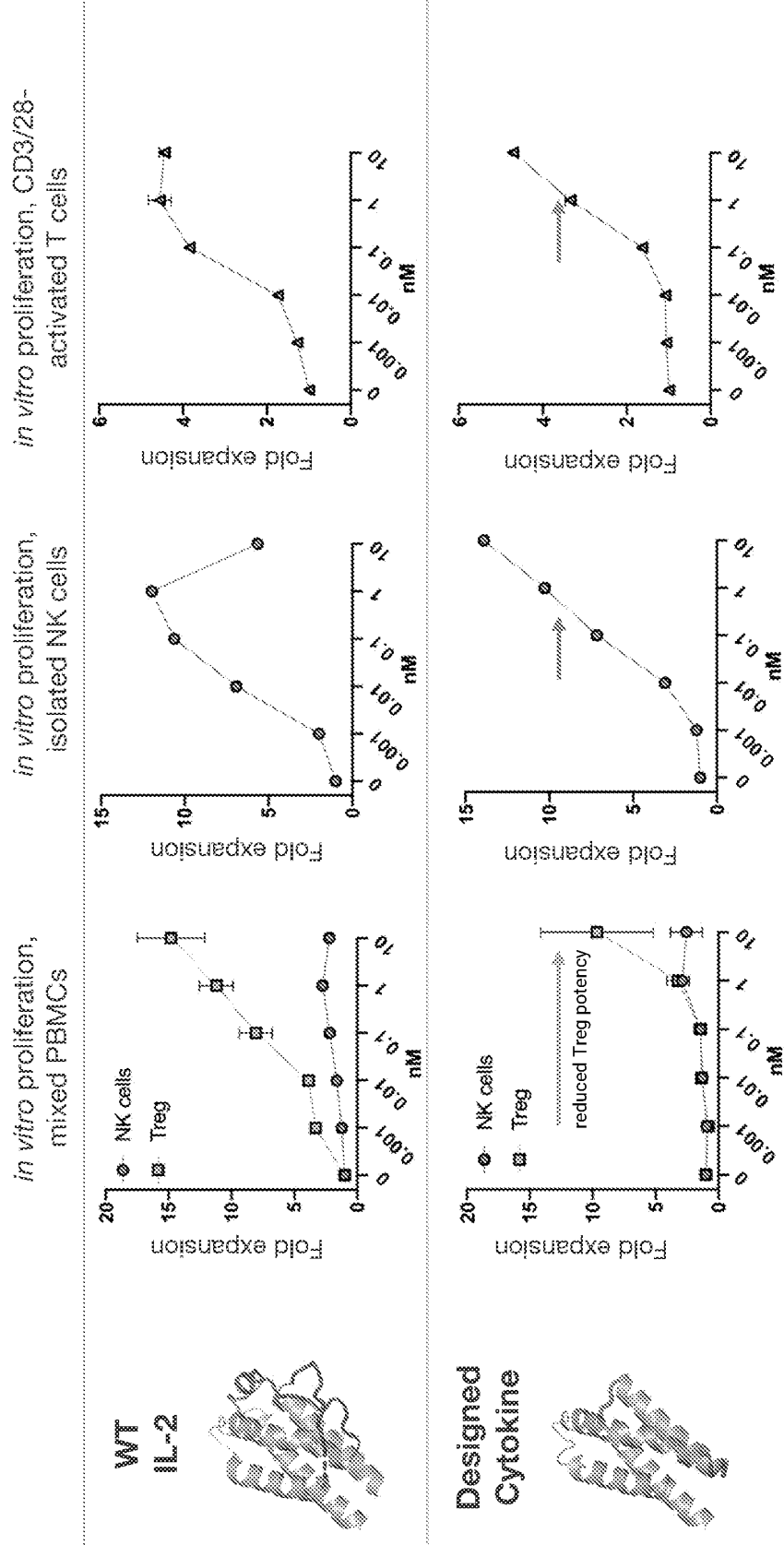


FIG. 8



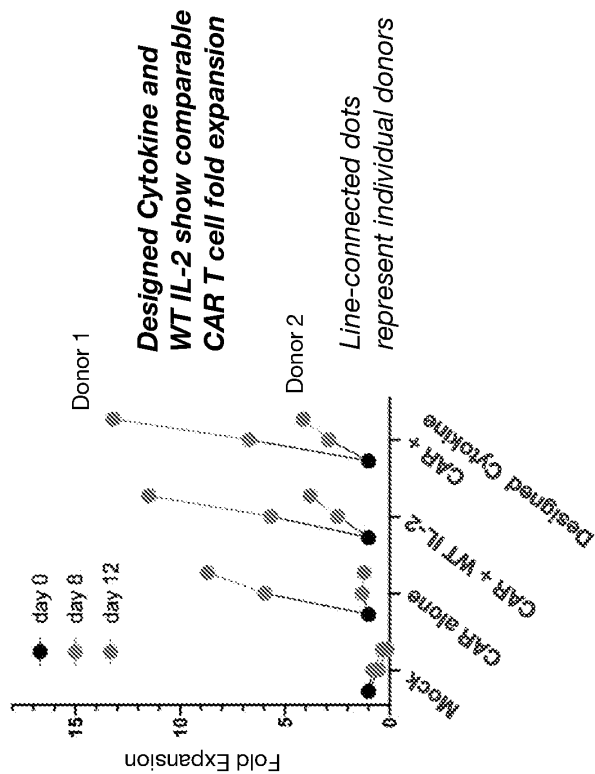
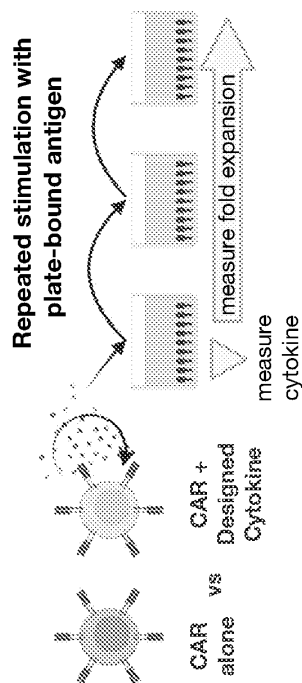


FIG. 10



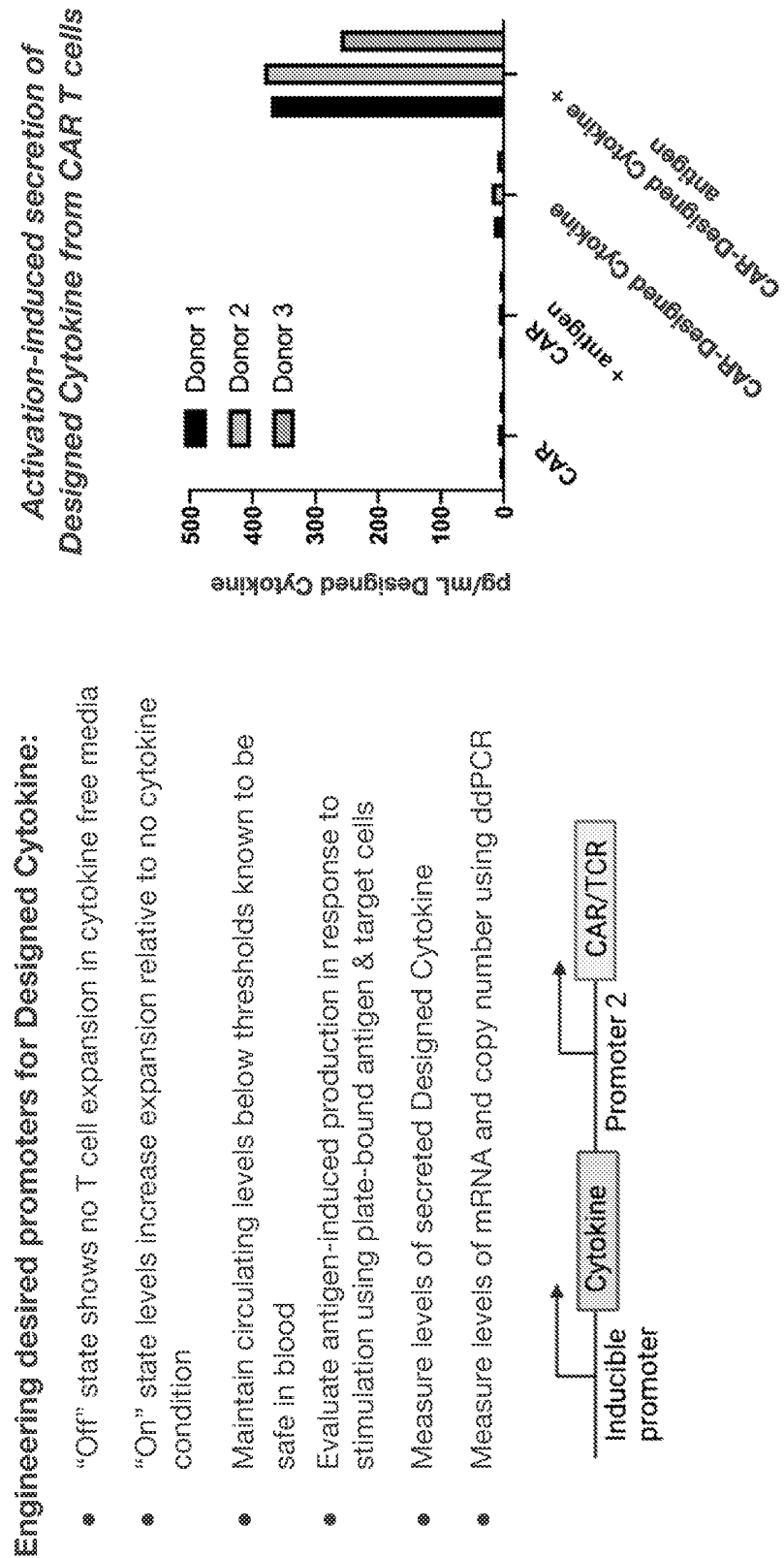


FIG. 11

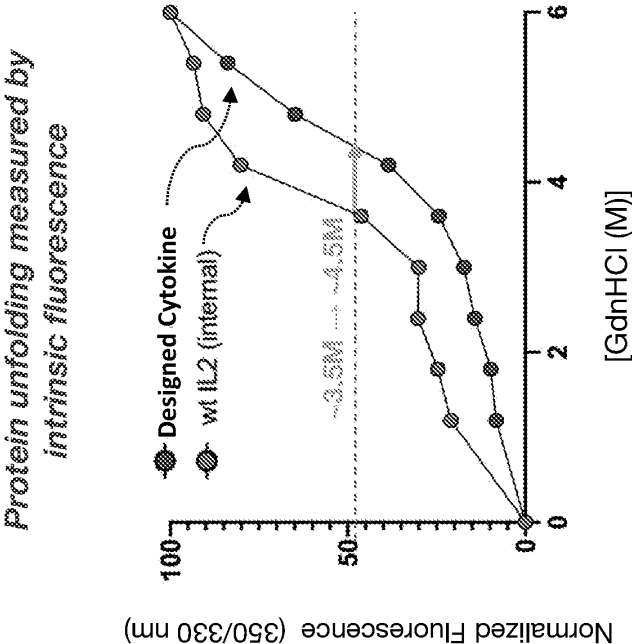
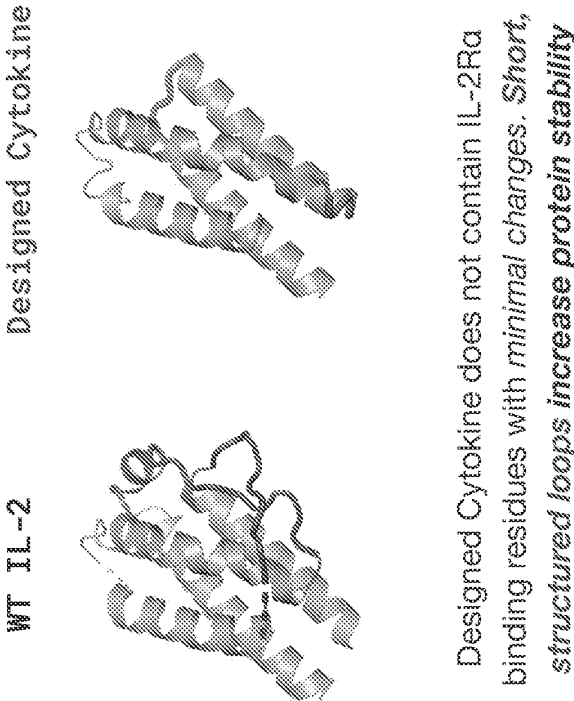


FIG. 12



Designed Cytokine demonstrates IL15-like effects on NK cells in vitro

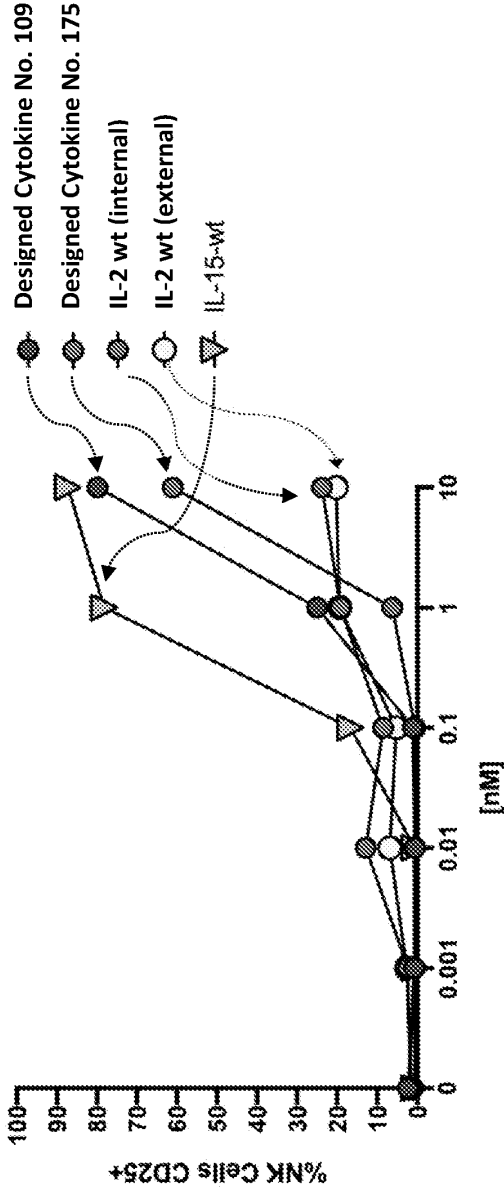


FIG. 13

TME-targeting of Designed Cytokines having Targeting Moieties

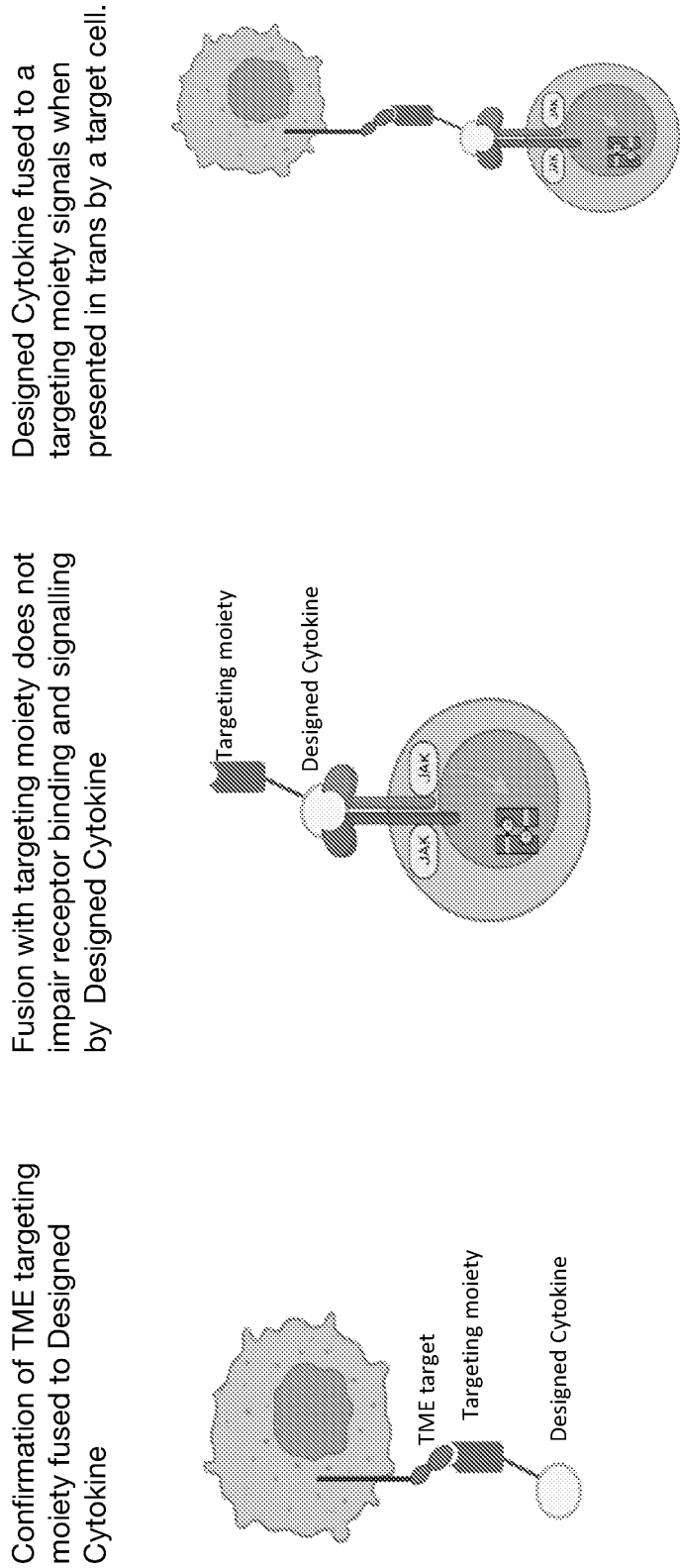


FIG. 14A

TME-targeting of Designed Cytokines

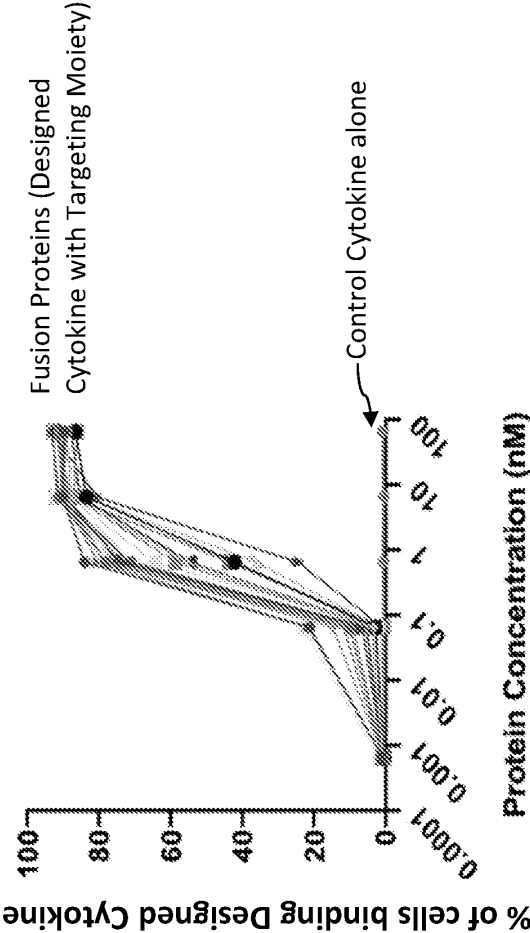


FIG. 14B

TME-targeting of Designed Cytokines

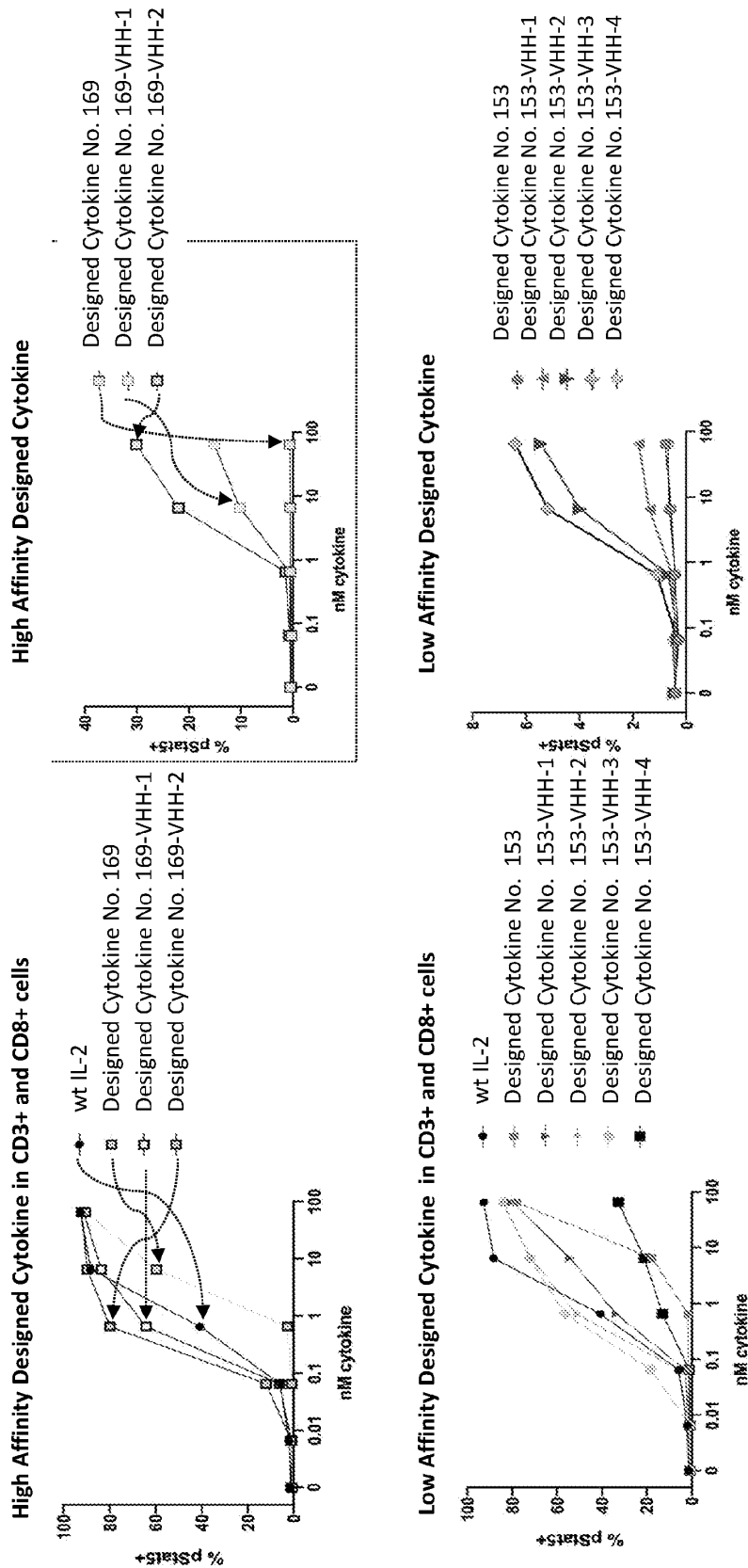


FIG. 14C

Designed Cytokine No. 201 shows no detectable binding to IL2Ra
WT IL-2 binds with nanomolar affinity

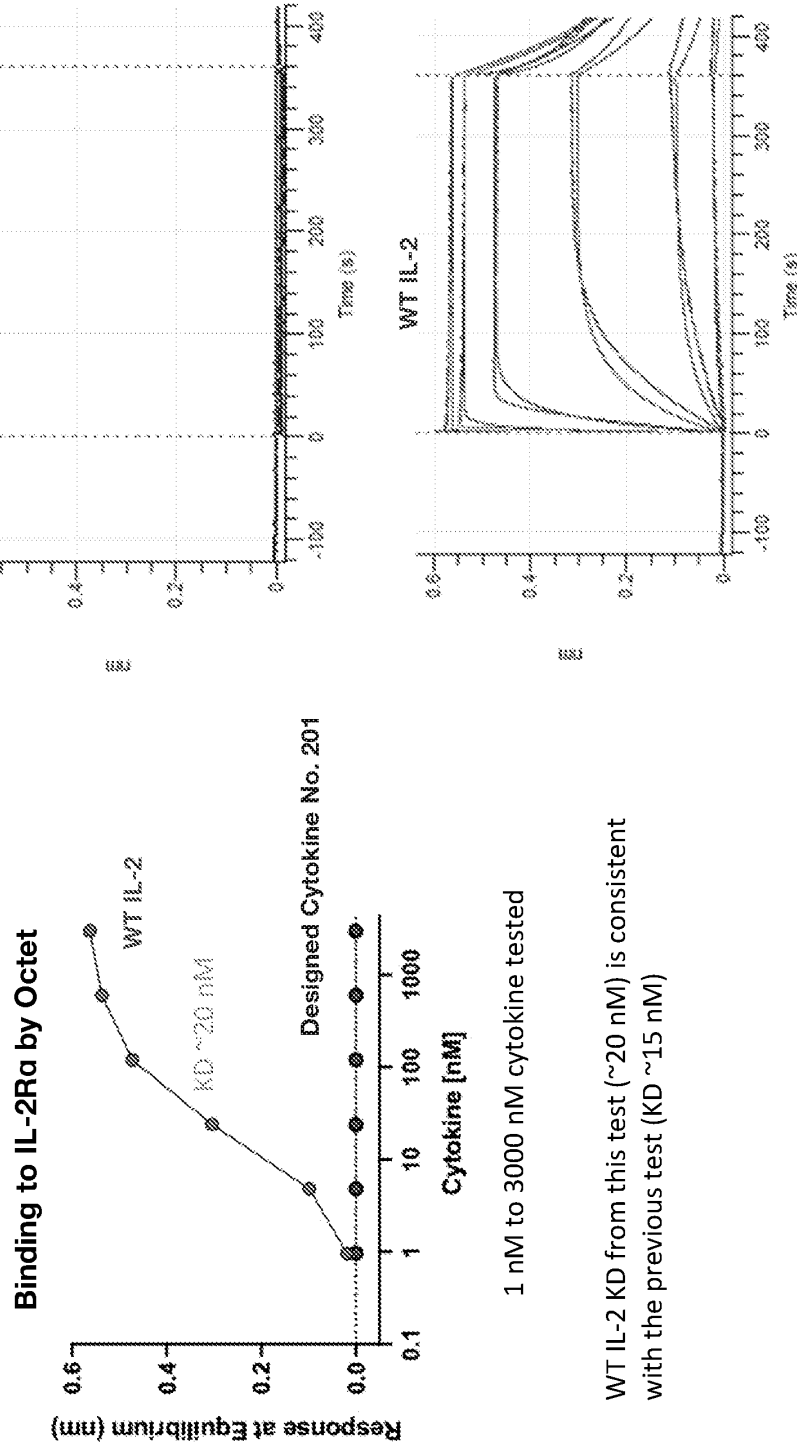


FIG. 16

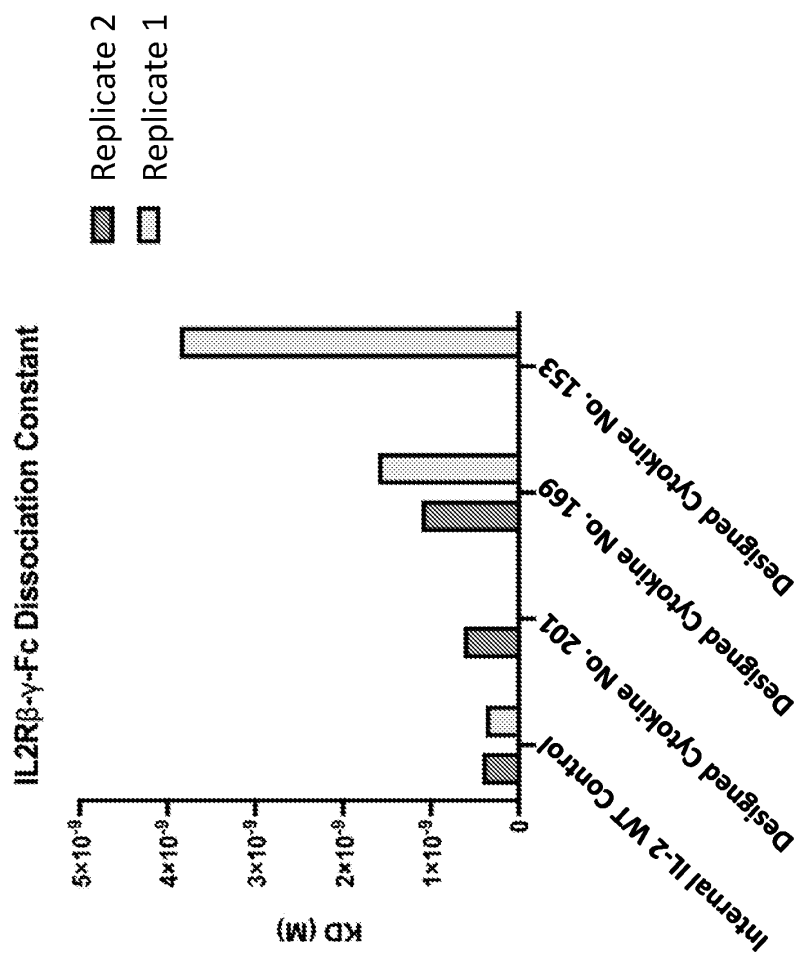


FIG. 17A

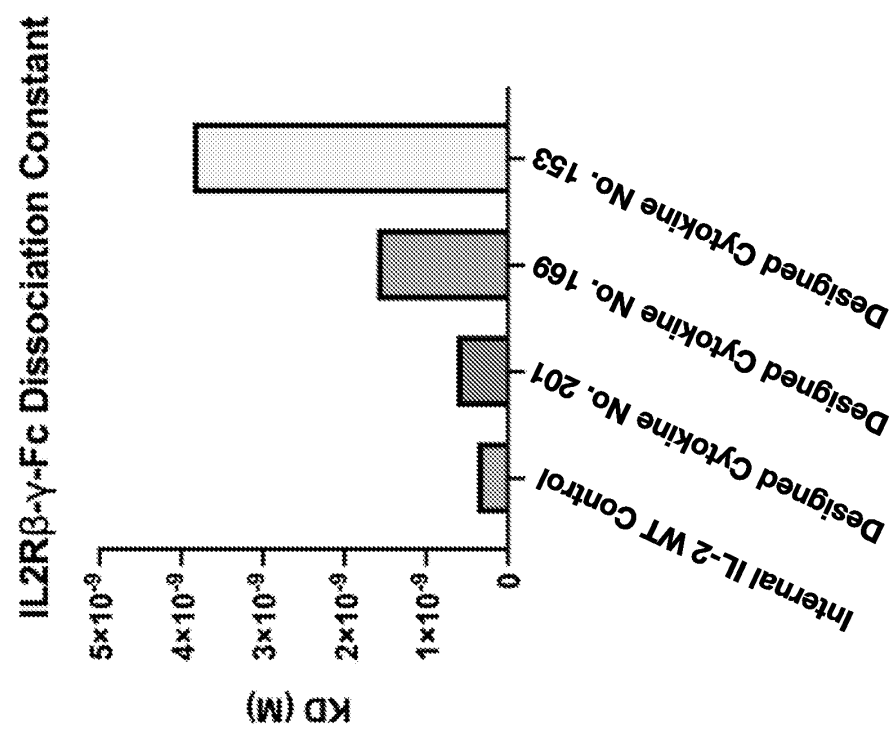


FIG. 17B

Binding affinity (by Octet) to IL-2Rβγ

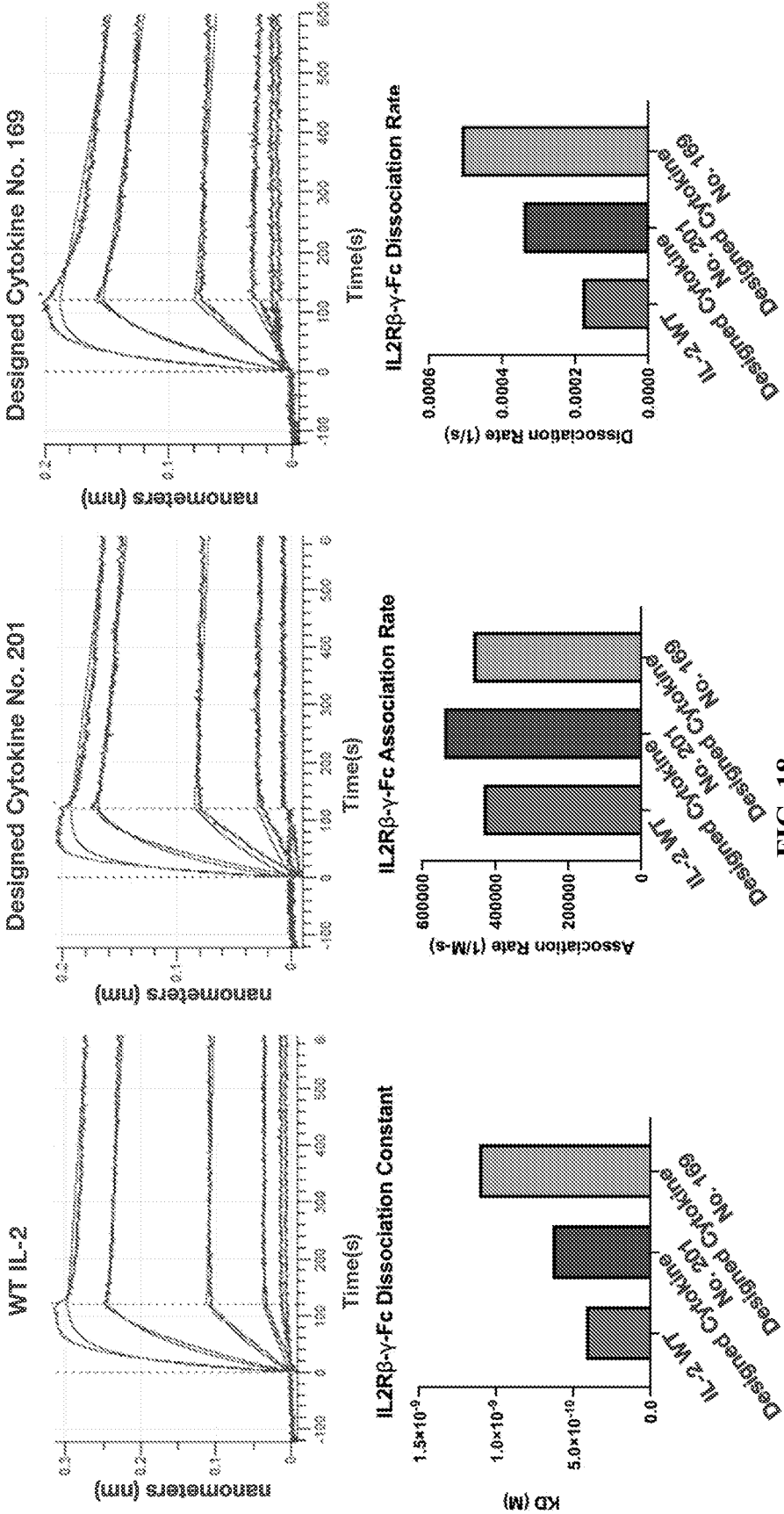


FIG. 18

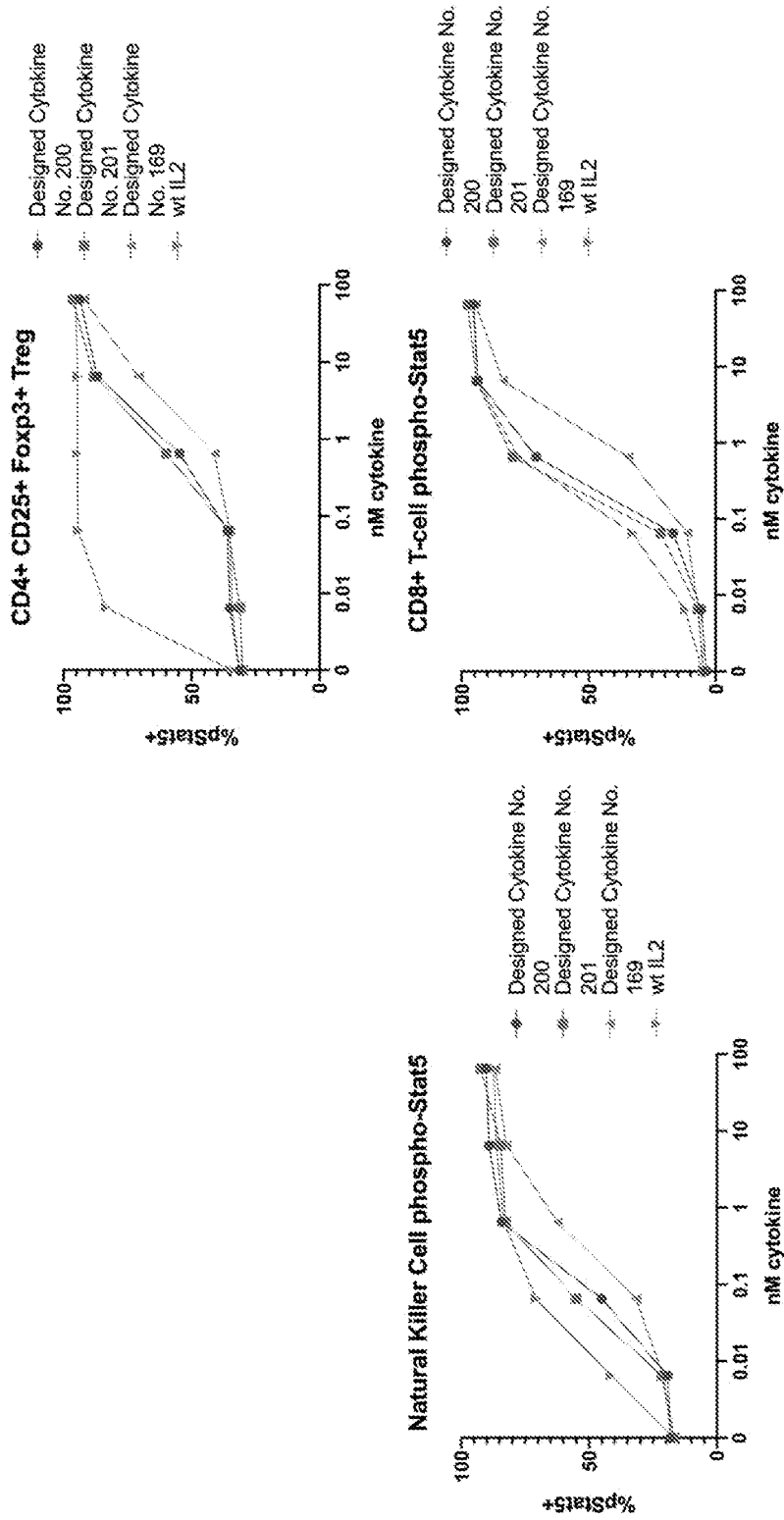


FIG. 19

Targeting of Designed Cytokine

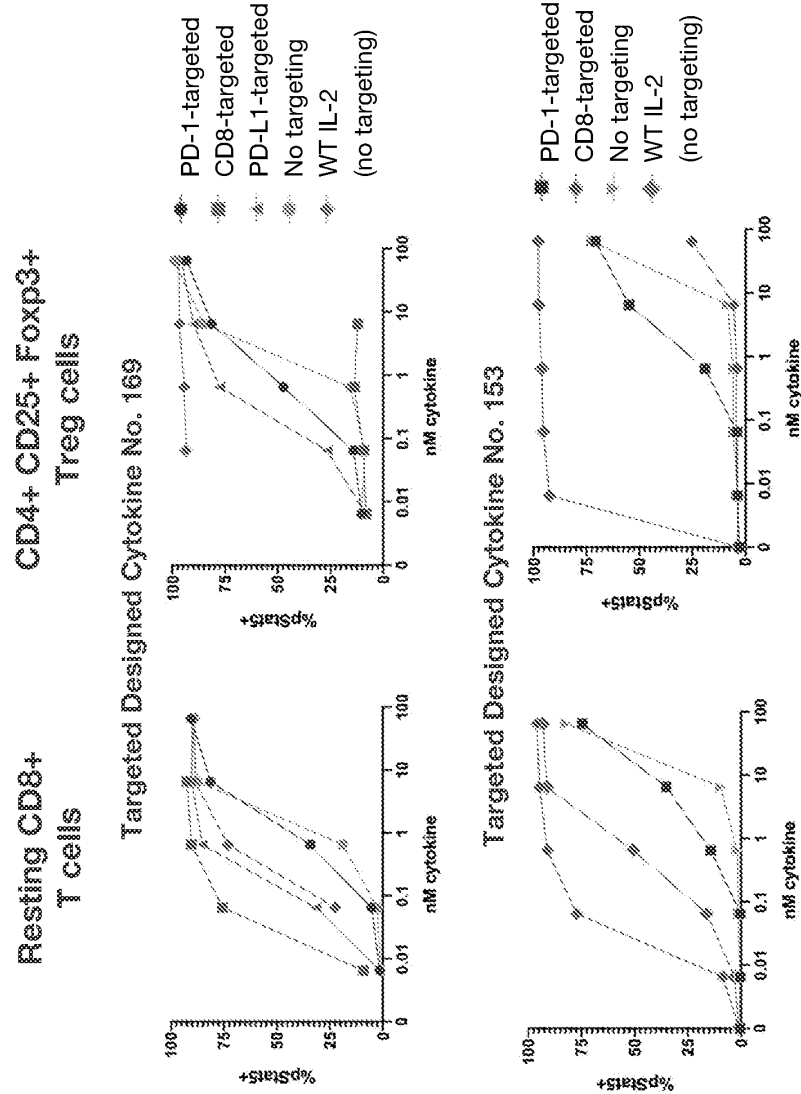
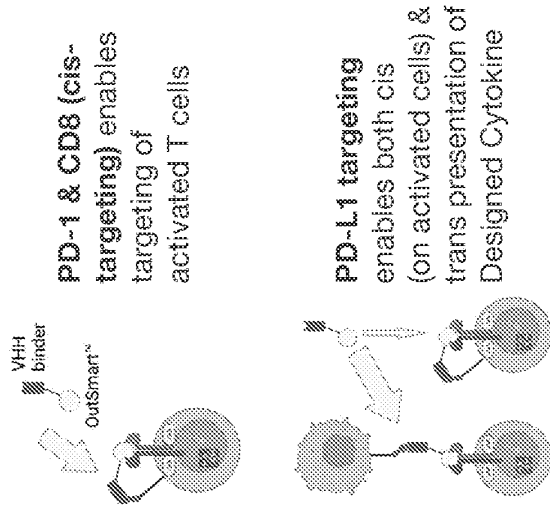


FIG. 20



Targeting of Designed Cytokine

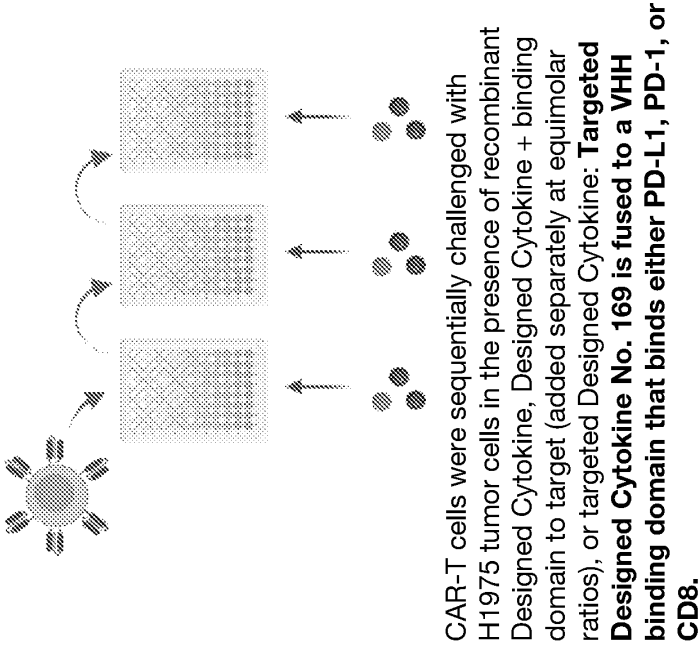


FIG. 21A

**Killing activity
(AUC, lower is more killing)**

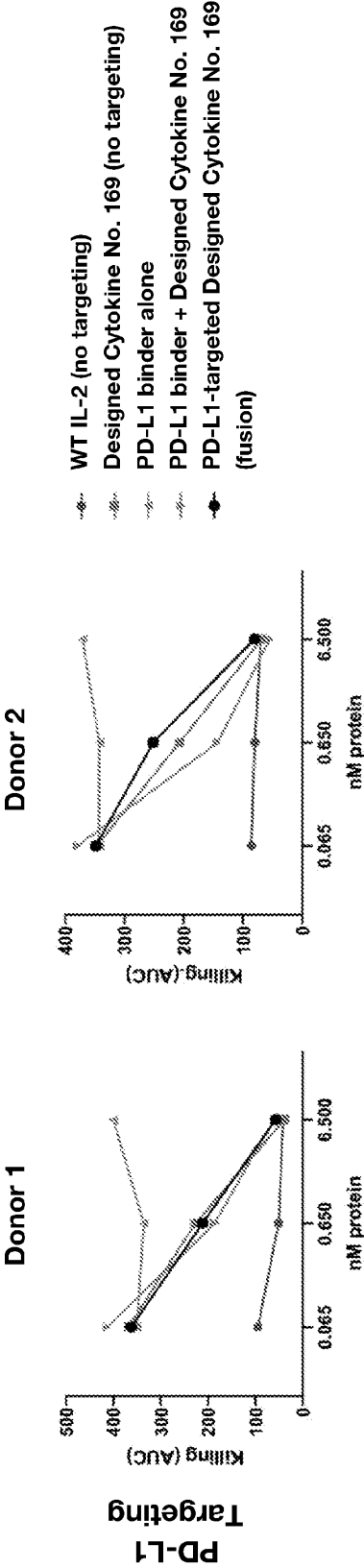


FIG. 21B

Killing activity
(AUC, lower is more killing)

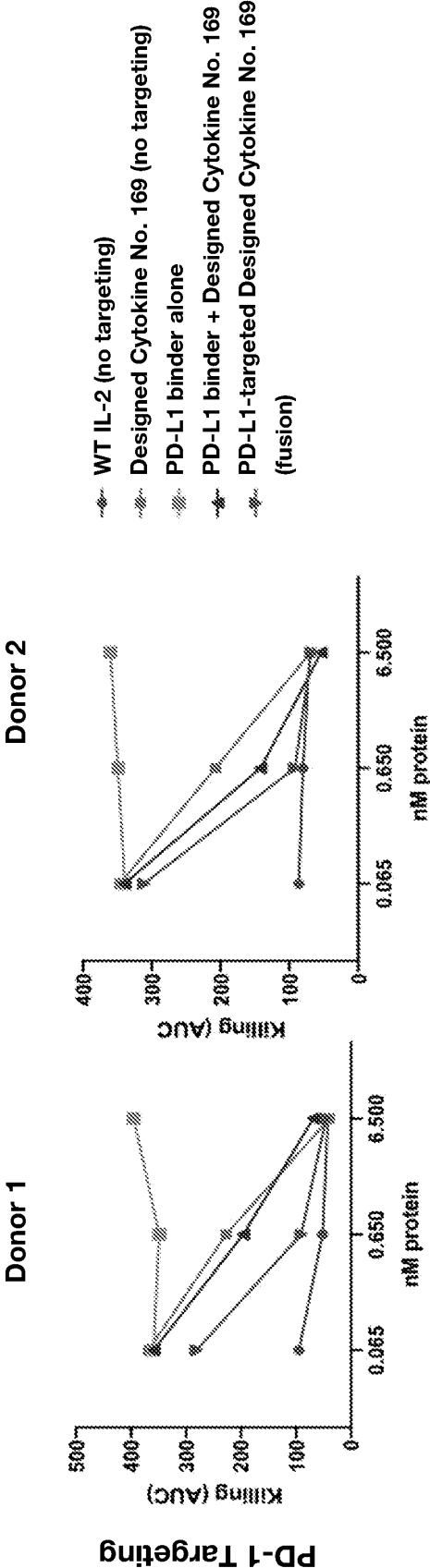


FIG. 21C

**Killing activity
(AUC, lower is more killing)**

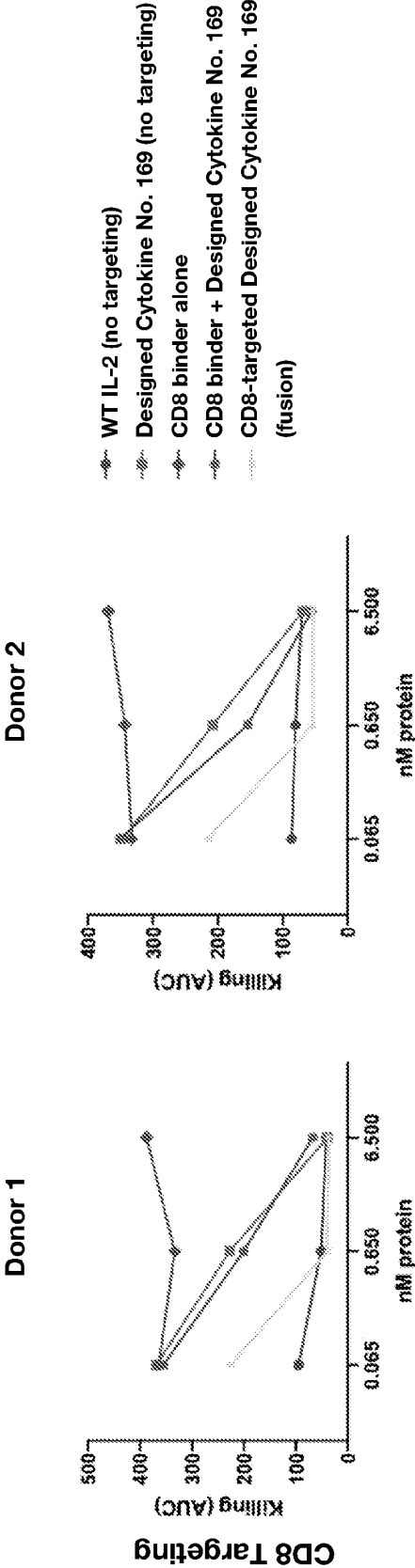


FIG. 21D

Phospho-STAT5 Activity of Designed Cytokines Derived from
Designed Cytokine No. 153

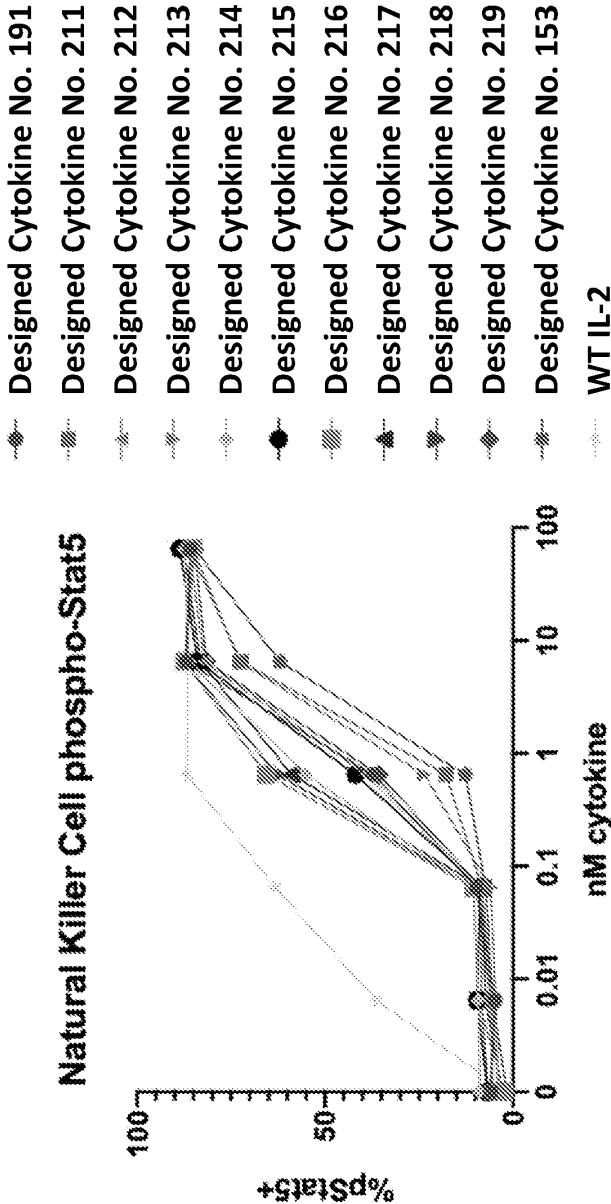


FIG. 22A

Phospho-STAT5 Activity of Designed Cytokines Derived from Designed Cytokine No. 153

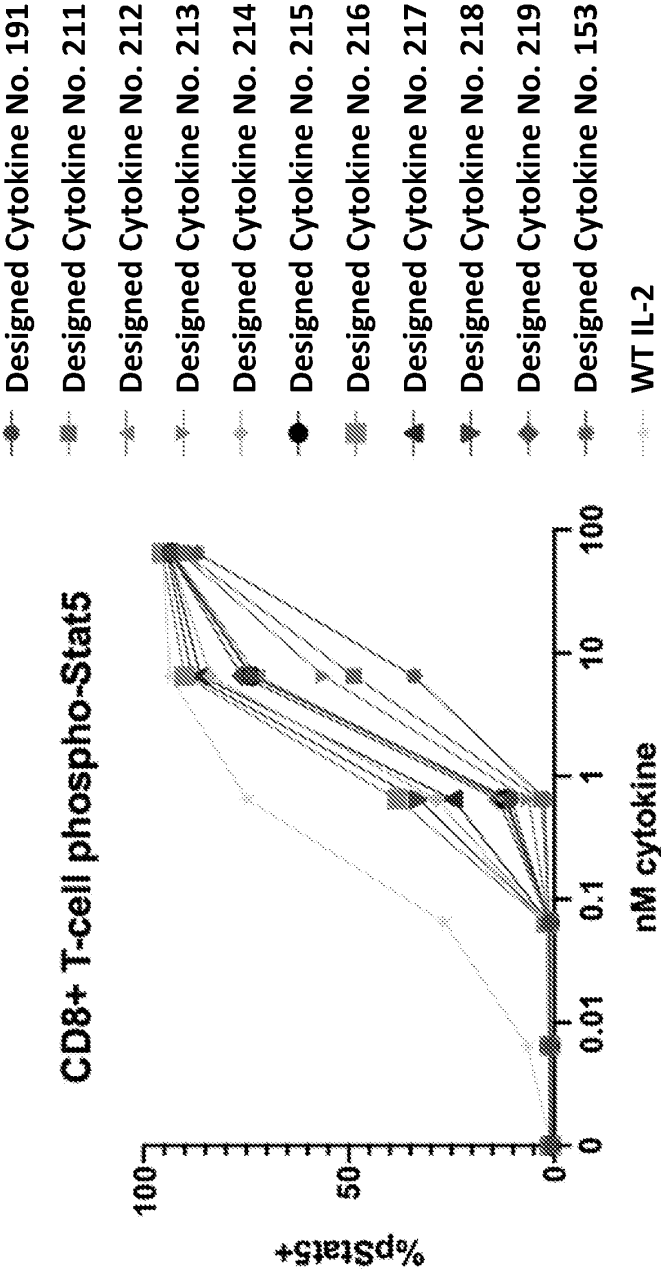


FIG. 22B

Inducible Designed Cytokines (DCs), Vectors and Circuits

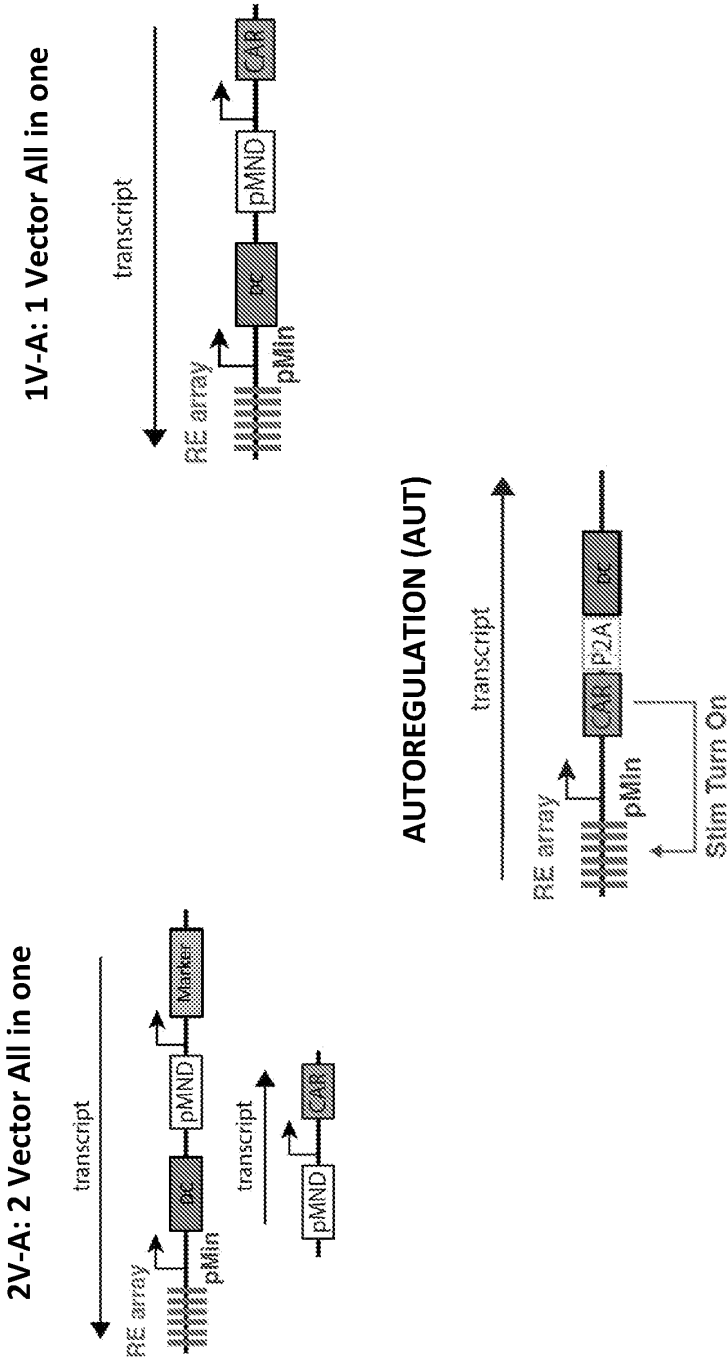


FIG. 23A

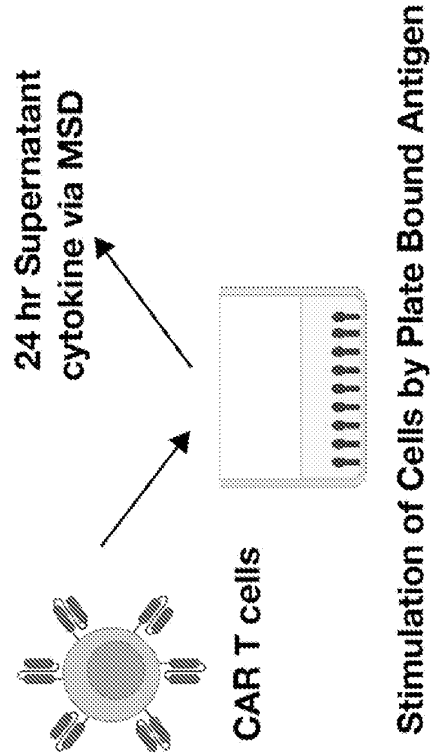


FIG. 23B

Inducible Designed Cytokines (DCs) show increased expression relative to Control

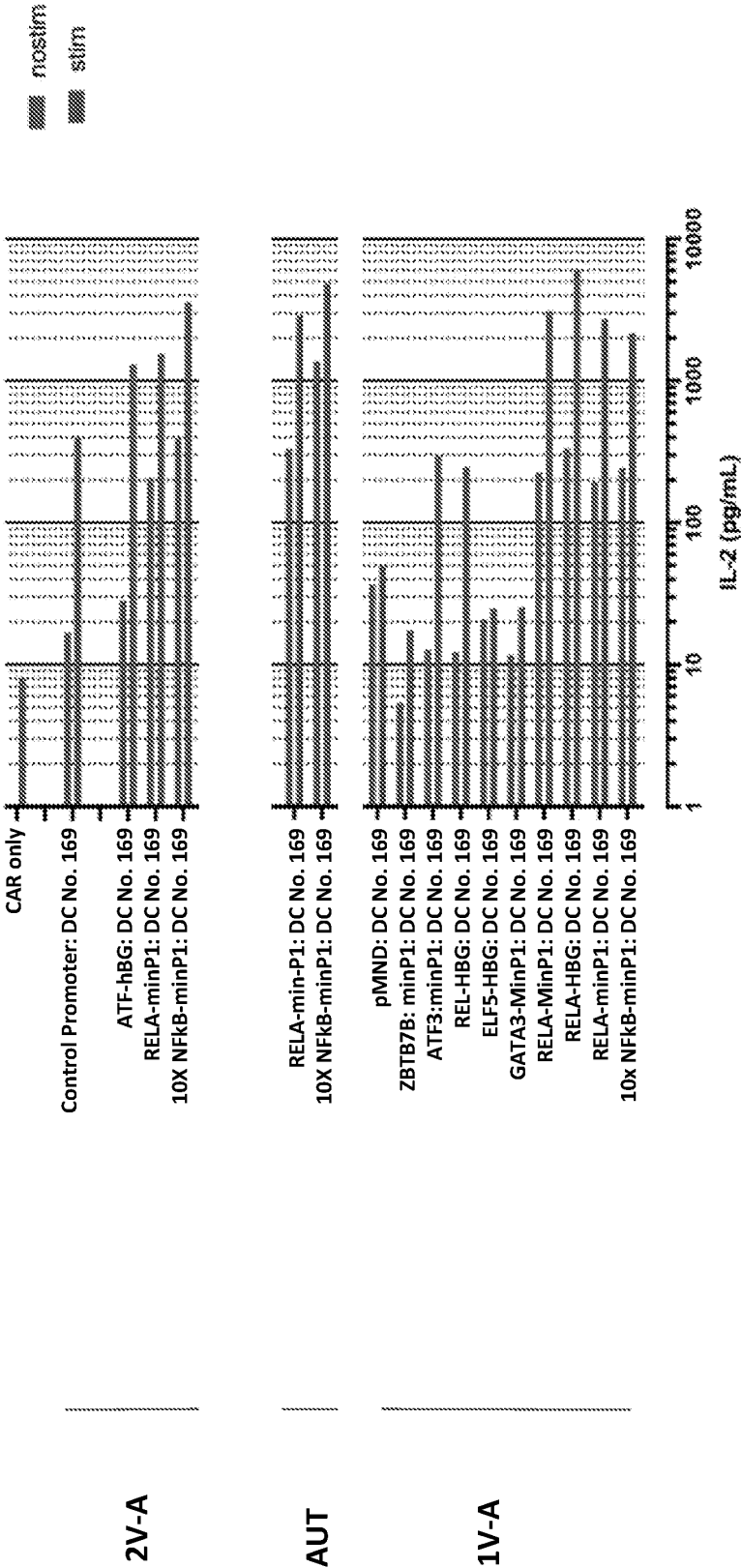
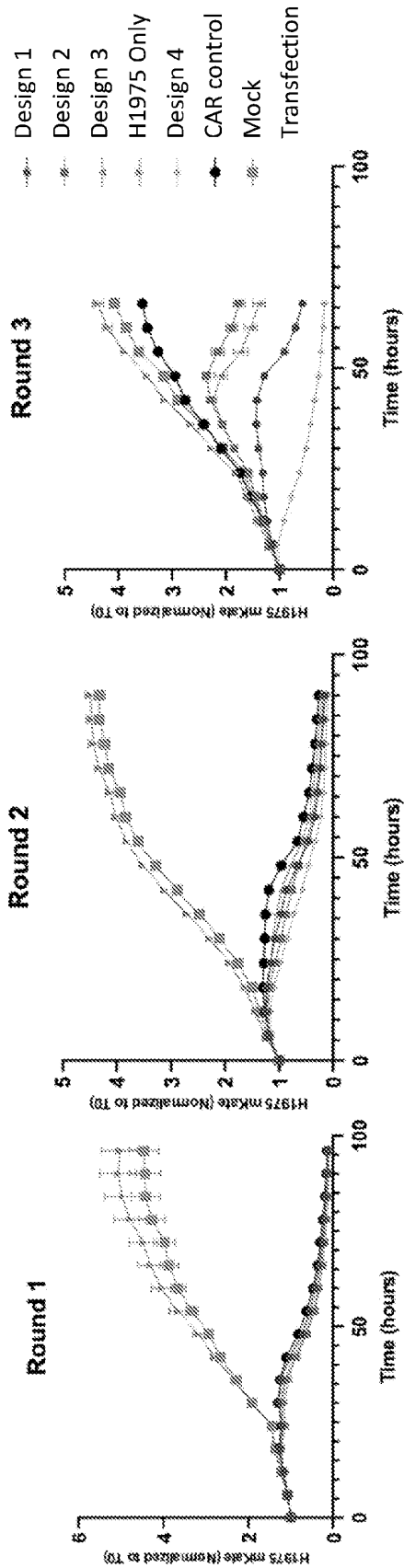


FIG. 23C

Sequential Killing with Inducible Designed Cytokines



- These constructs continued to kill at the end of round 3
 - Design 1: V1-a, RELA-HBG; DC No. 169
 - Design 2: V1-a, RELA-minP1; DC No. 169
 - Design 3: V1-a, GATA3-MinP1; DC No. 169
 - Design 4: Autoregulated, RELA-minP1; DC No. 169
 - CAR only control

FIG. 24