

IL-2

IL-2

Peptide linker

Fc region
(CH2 and CH3 domains)

APTSSSTKKTQLQLEKLLLLDLQMLNGINN30

YKNPKLTRLRLTFRKFYMPKKATELKKHLQCLE60

EELKPLEEVLNLAQSKNFHLRPRDLISNIN90

VIVLELKGSETTFMCEYADETATIVEEFLNR120

WITFCQSIISTLTGS133

C125S- improve stability (present in all sequences)

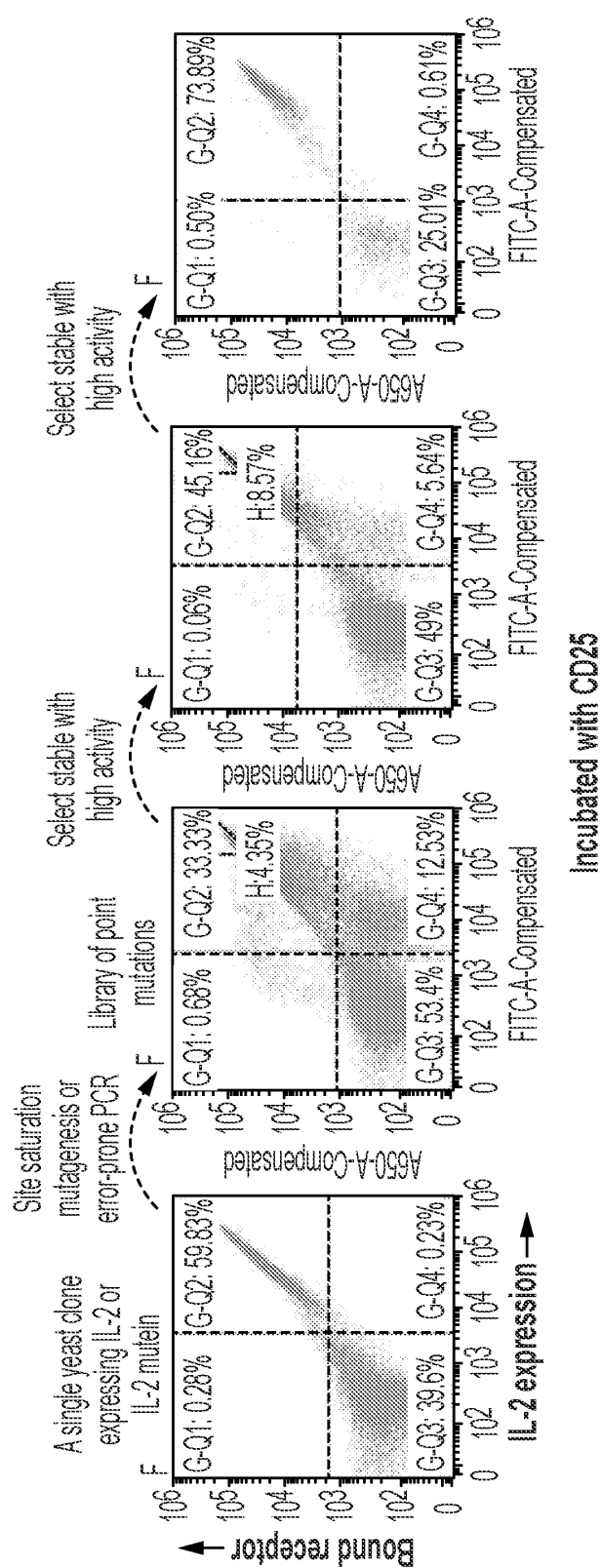
V69A/Q74P4- reduce aggregation

H16, D84, S87, N88, I92- sites mutated to affect affinity for CD122/CD132

K35, R38, F42- sites mutated to affect affinity for CD25

FIG. 1B

FIG. 1A

2. GL

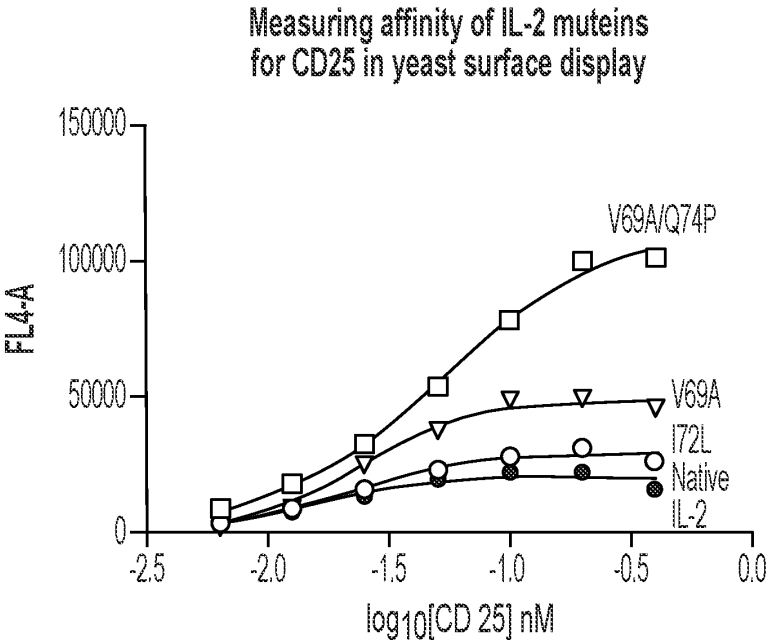


FIG. 3A

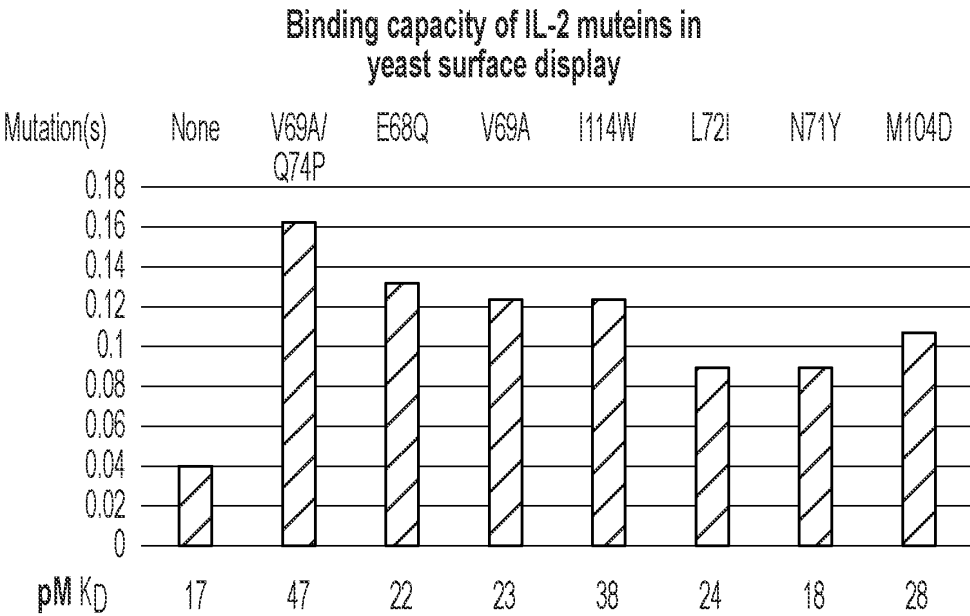


FIG. 3B

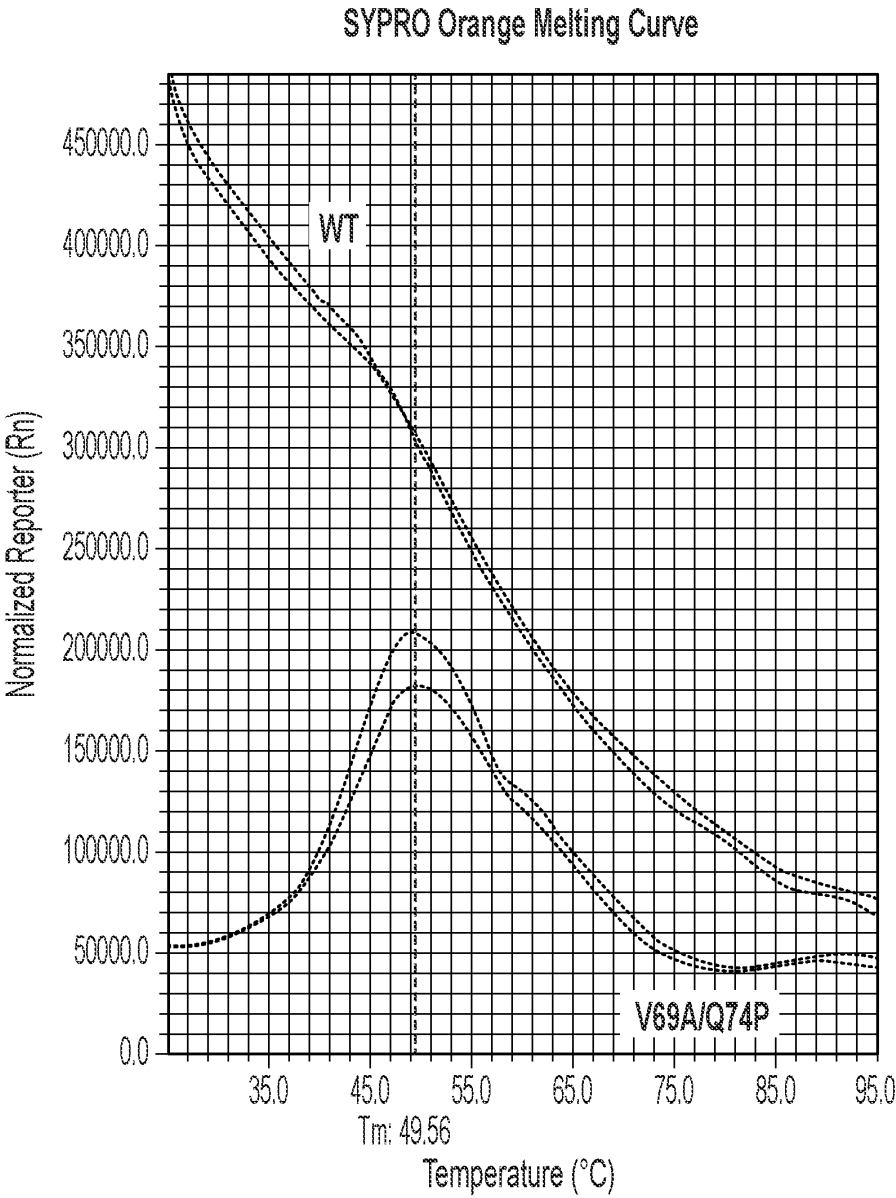


FIG. 4A

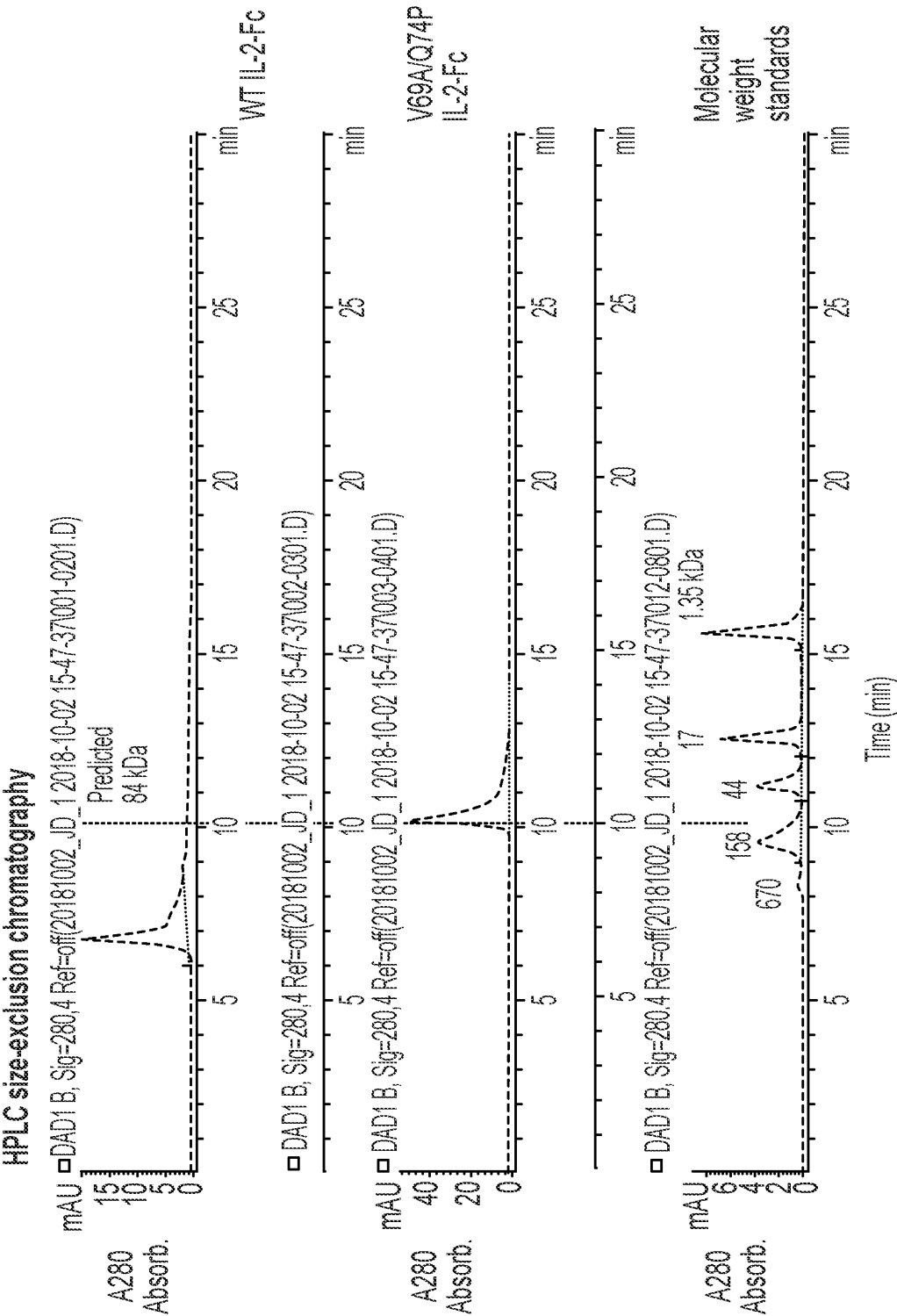


FIG. 4B

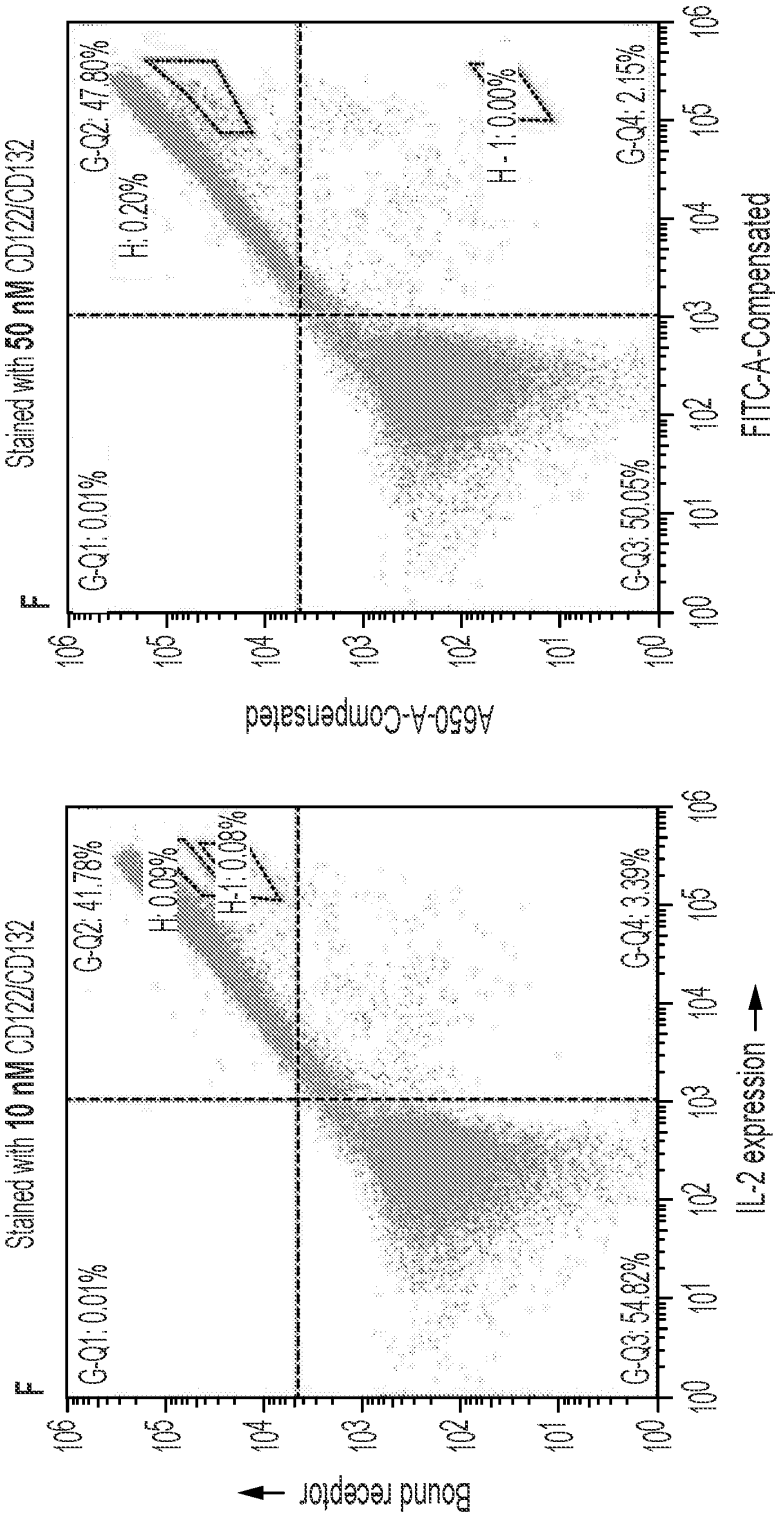
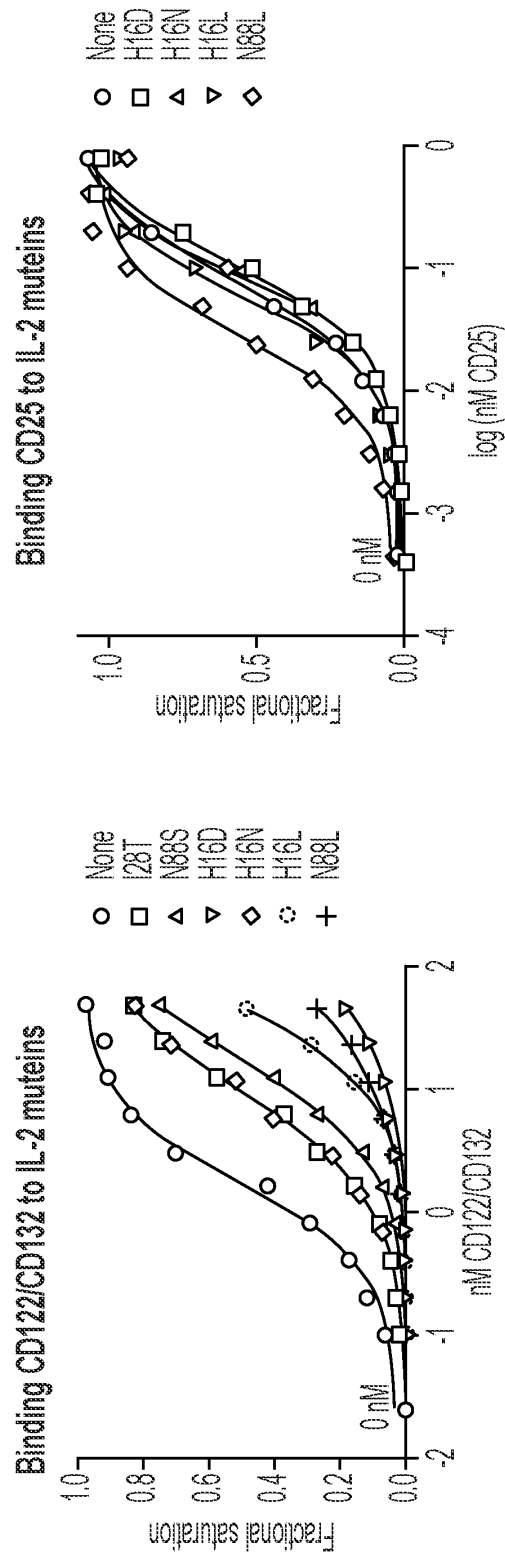


FIG. 5A

FIG. 5B



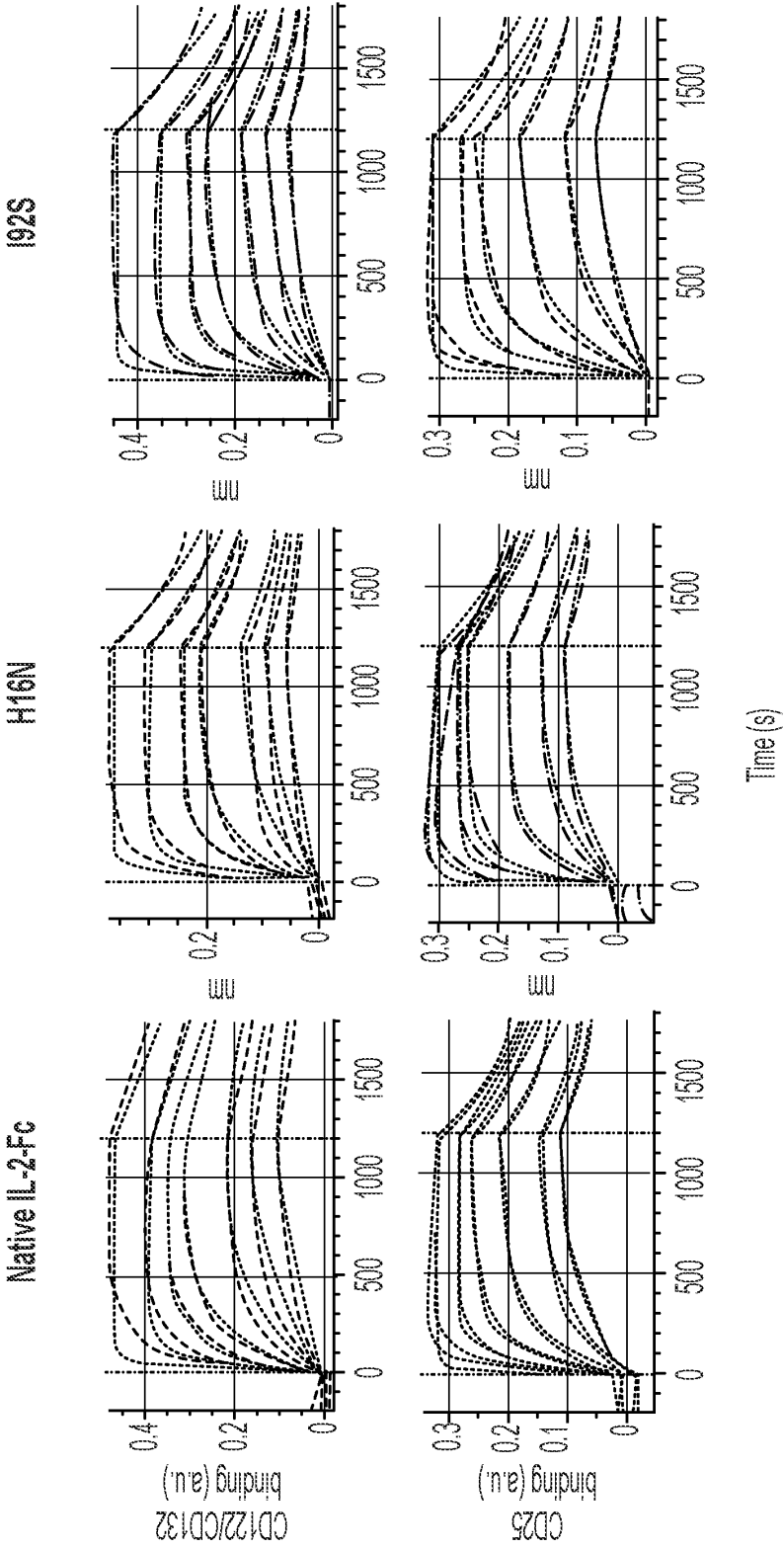


FIG. 7

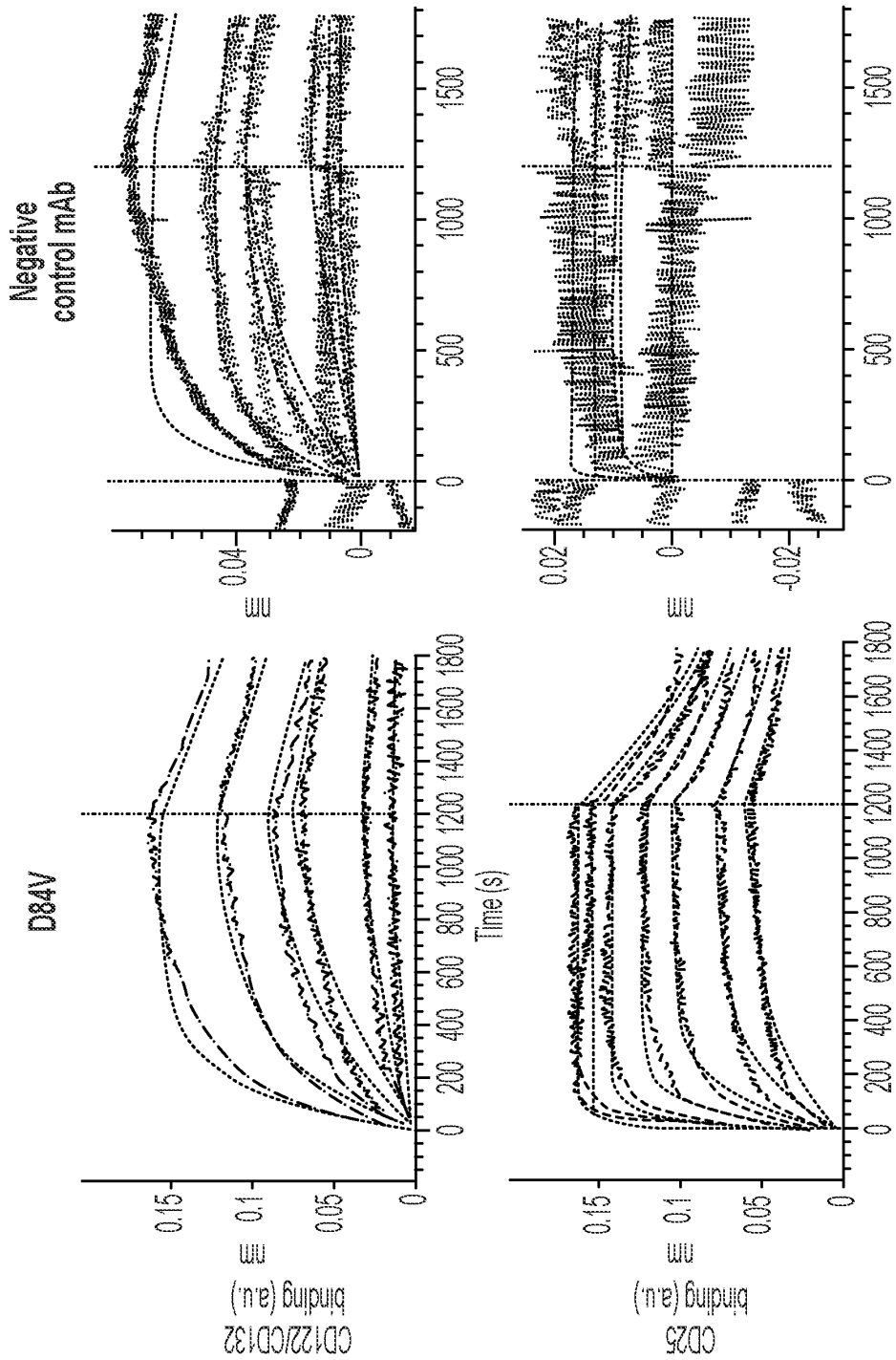


FIG. 7
continued

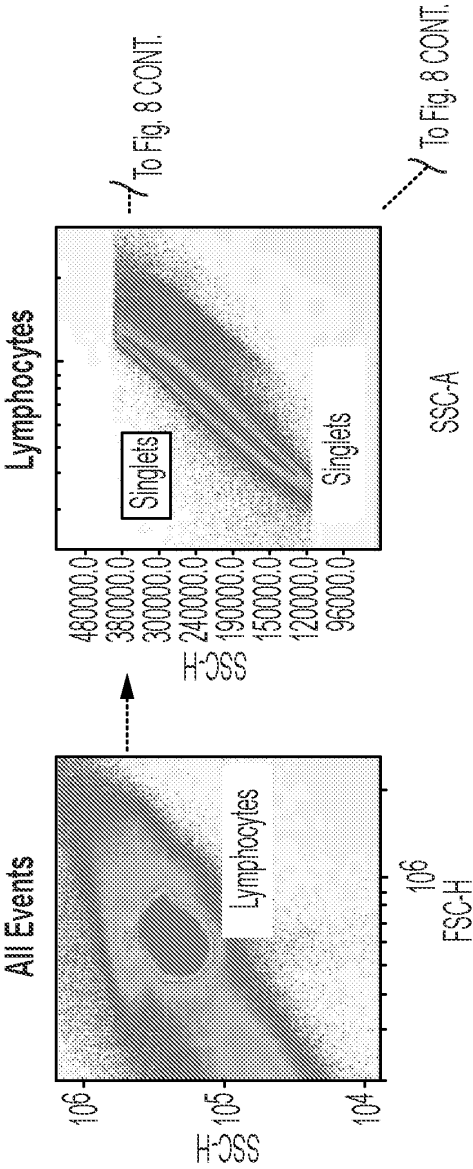


FIG. 8

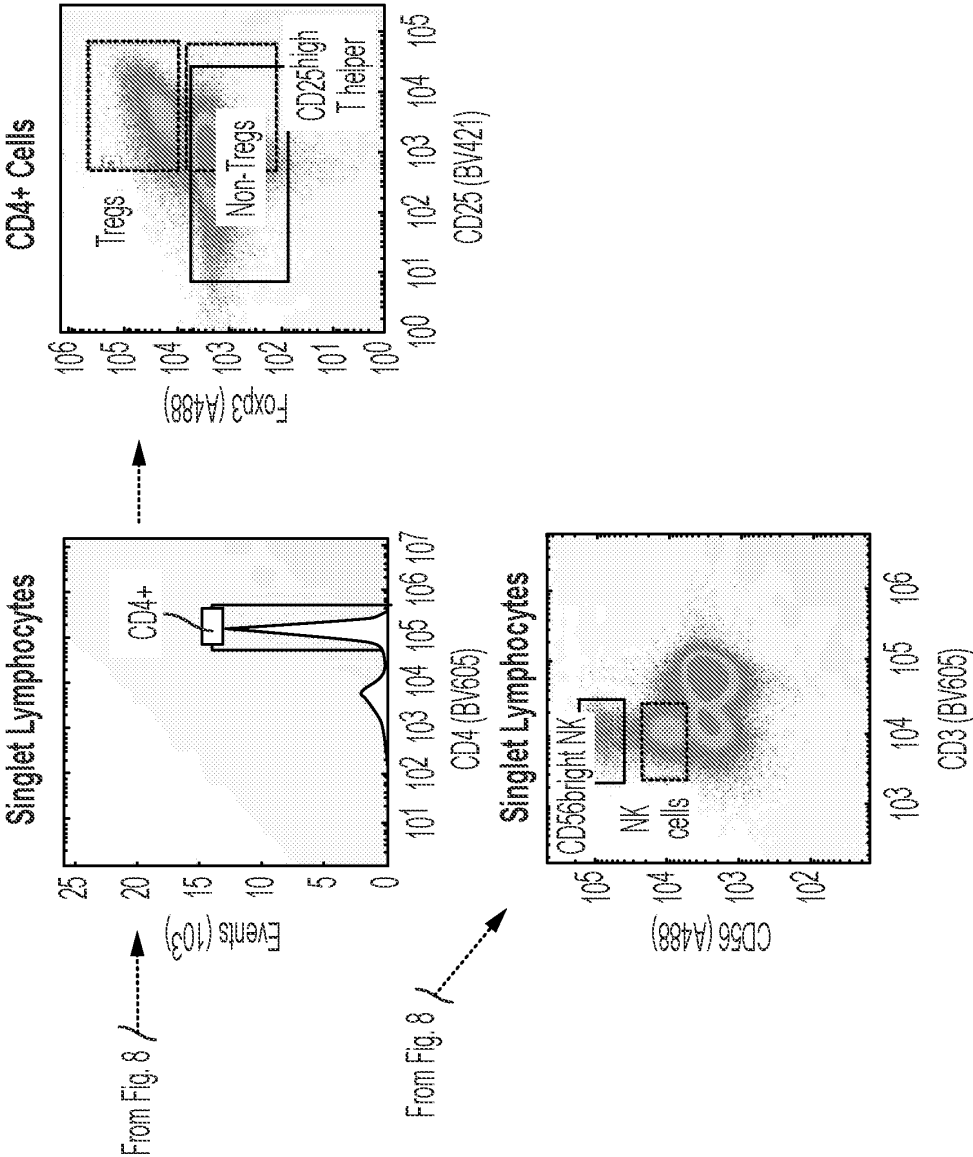


FIG. 8
continued

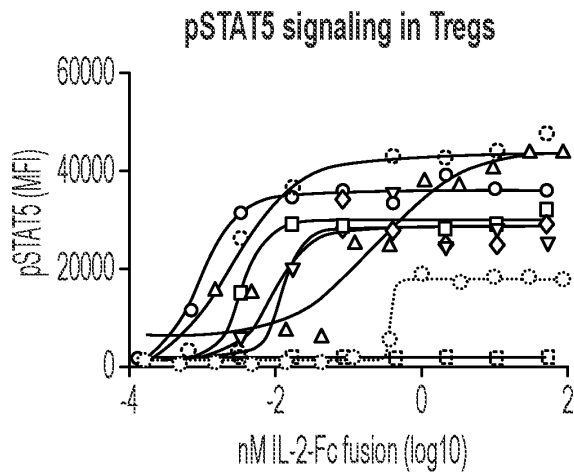


FIG. 9A

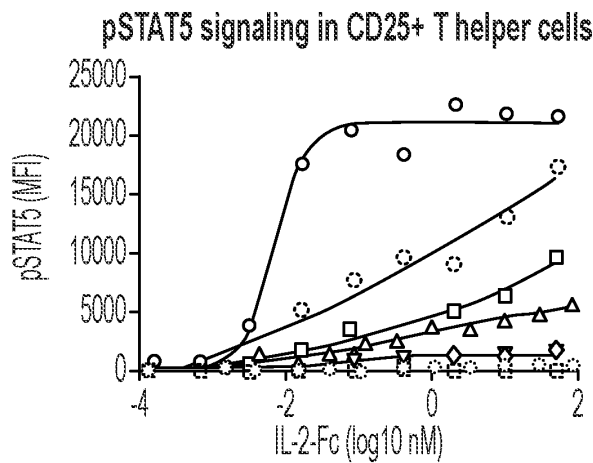


FIG. 9B

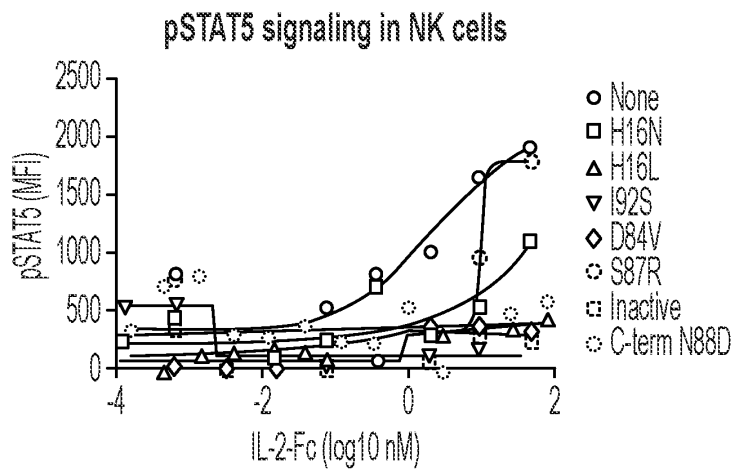


FIG. 9C

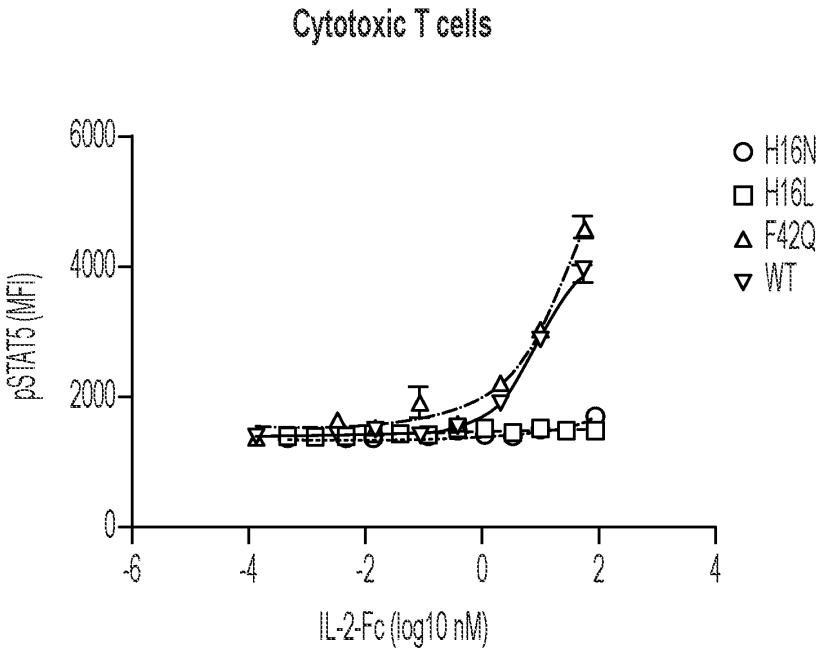


FIG. 9D

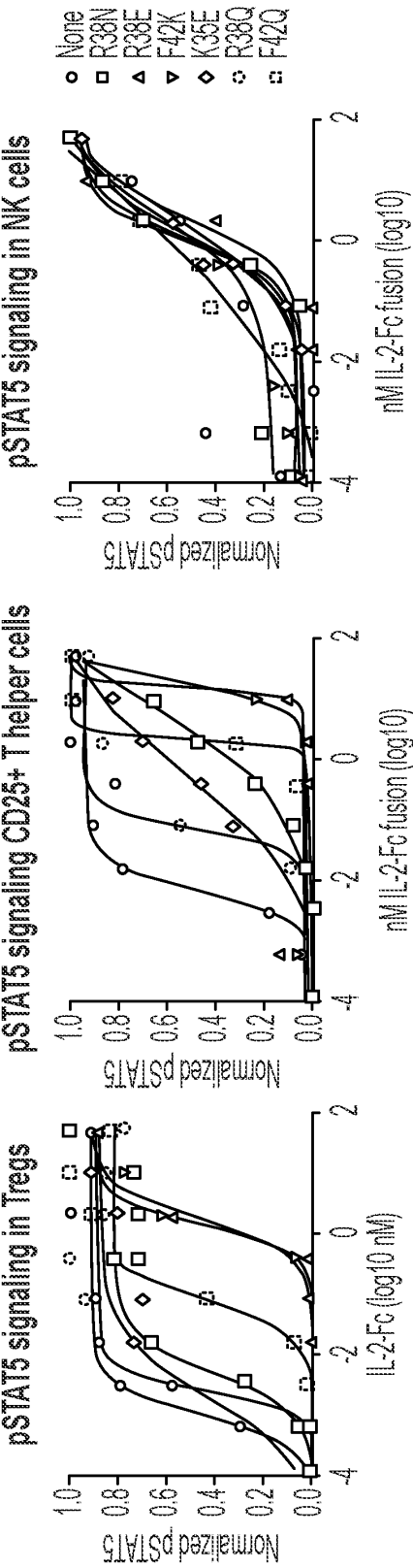


FIG. 10A

FIG. 10B

FIG. 10C

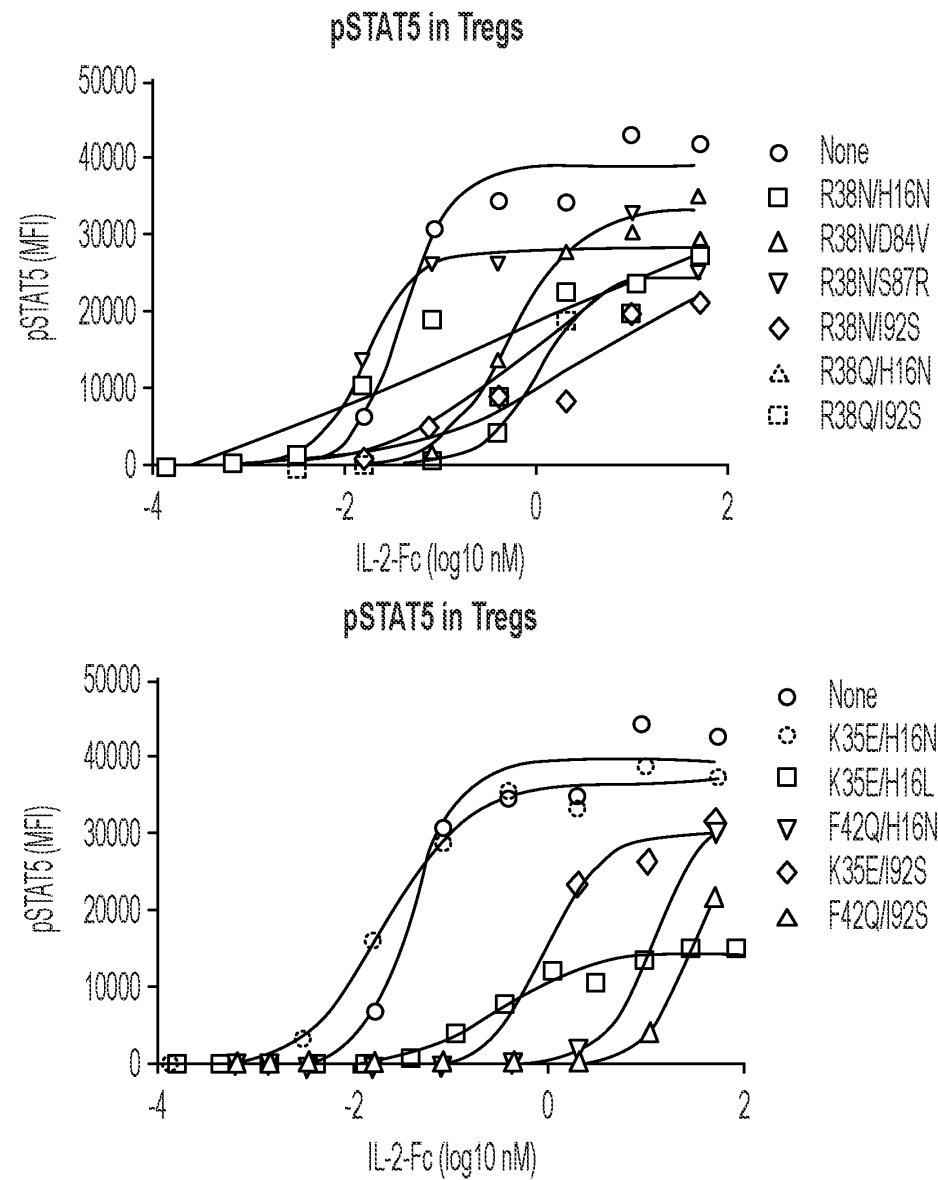


FIG. 11A

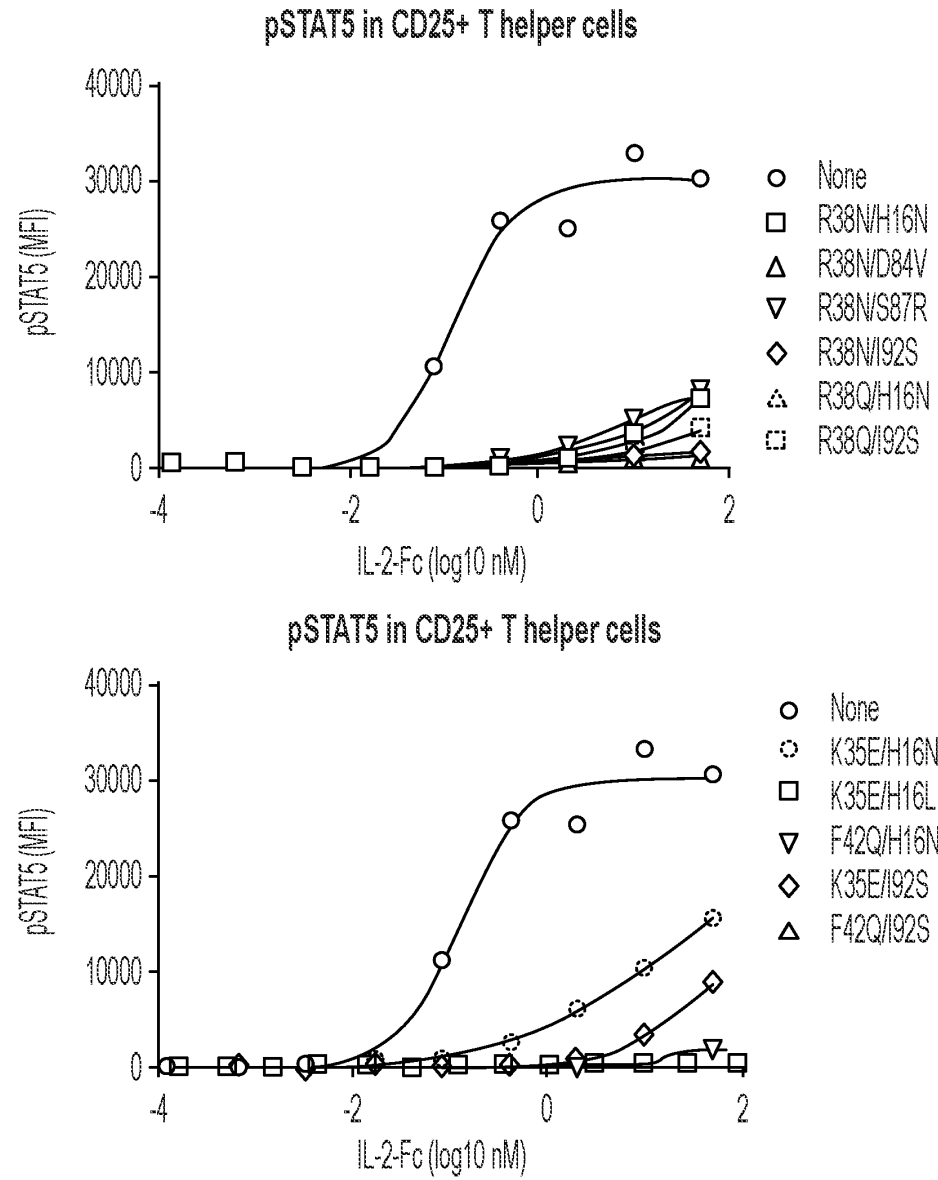


FIG. 11B

17/41

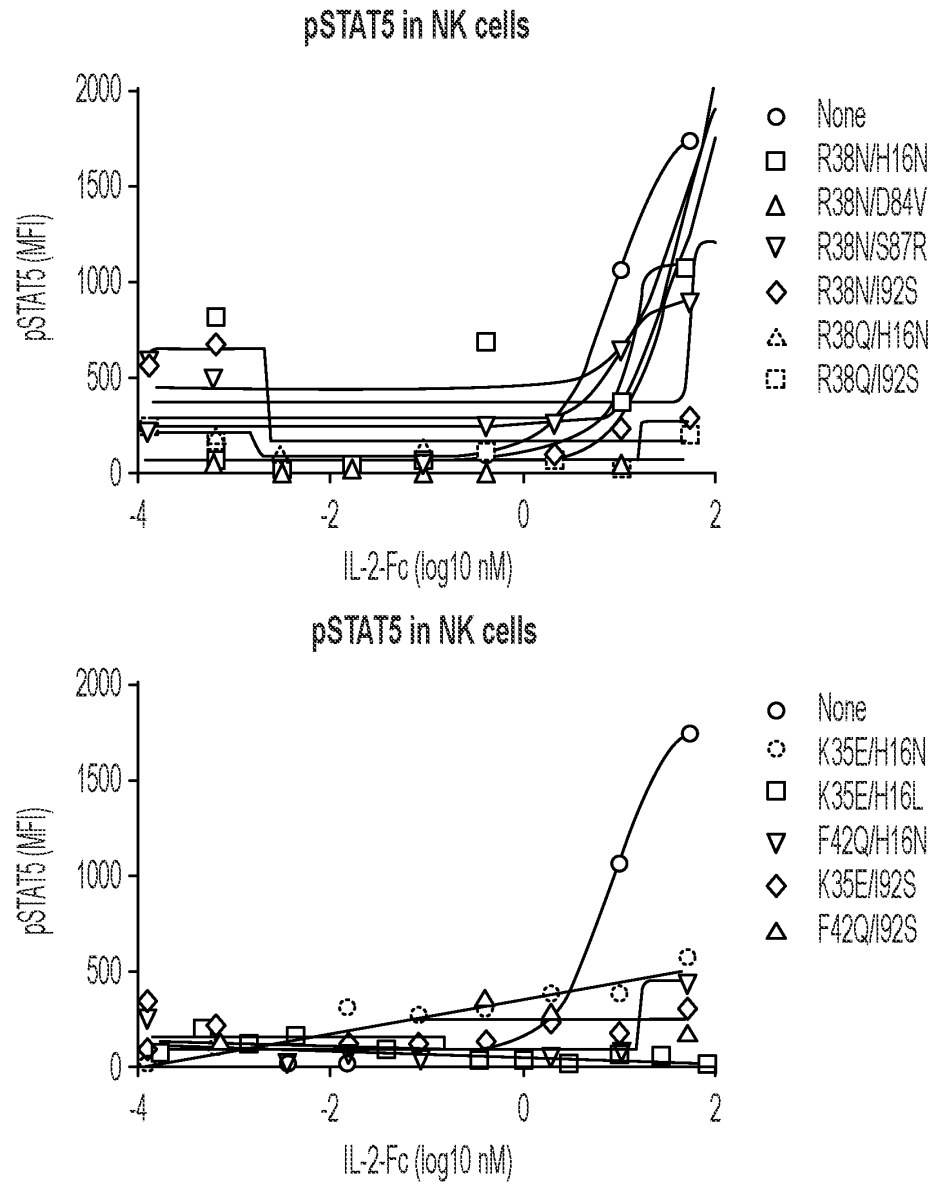


FIG. 11C

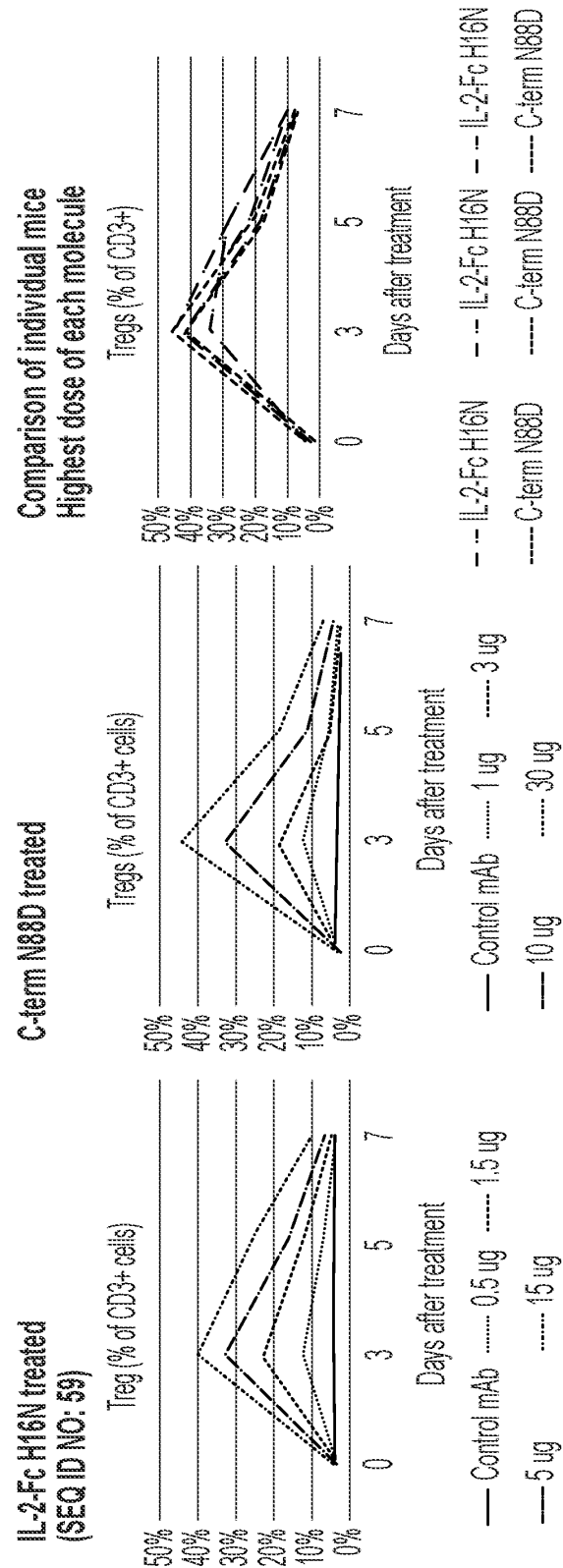
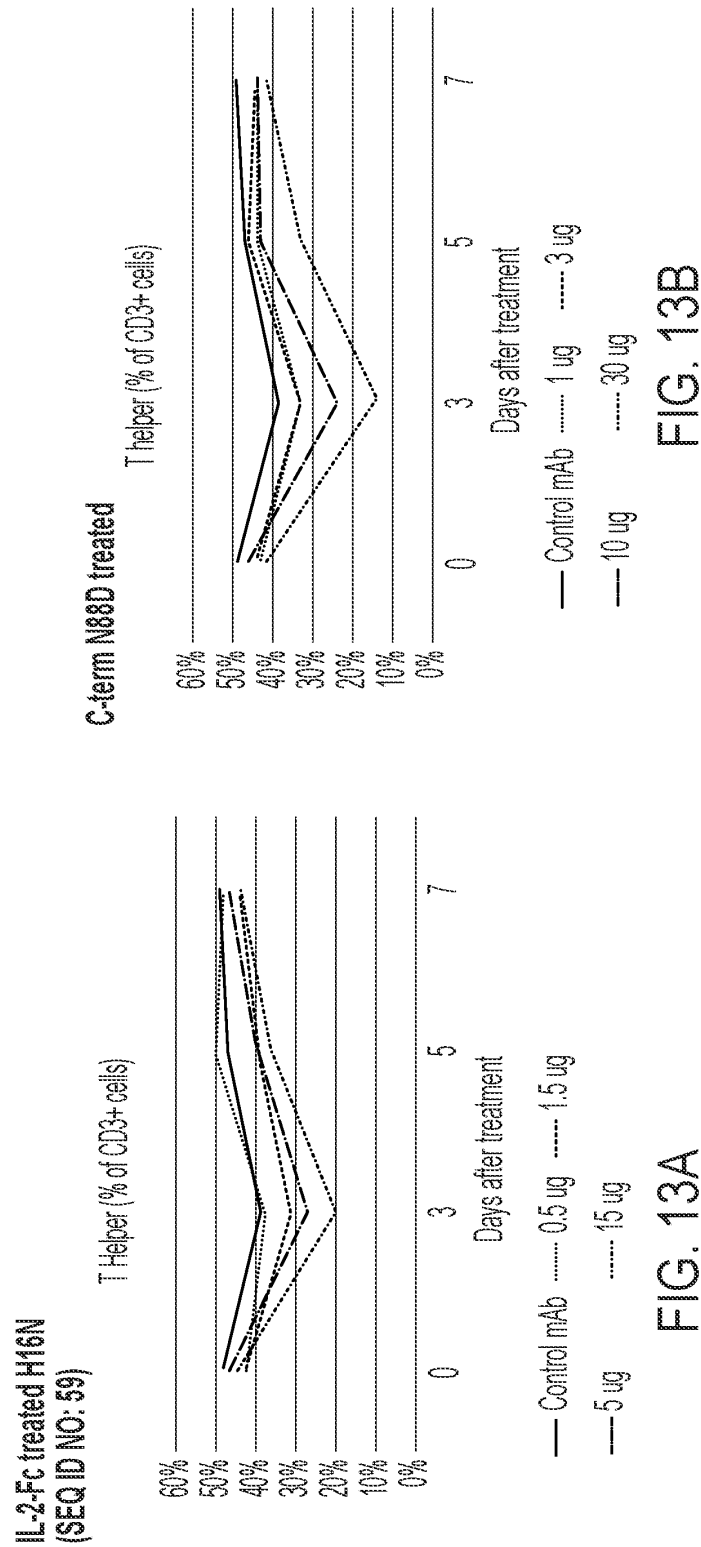


FIG. 12A

FIG. 12B

FIG. 12C



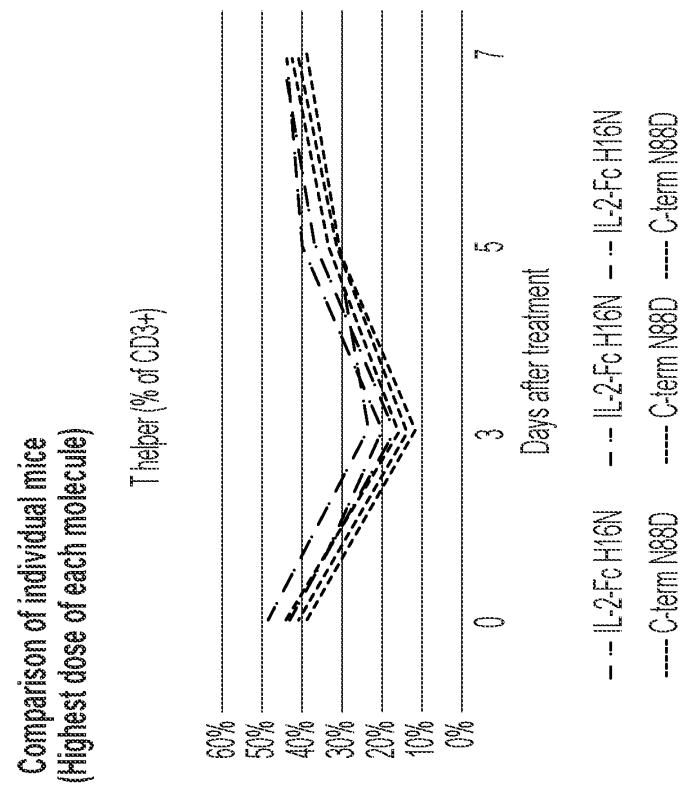


FIG. 13C

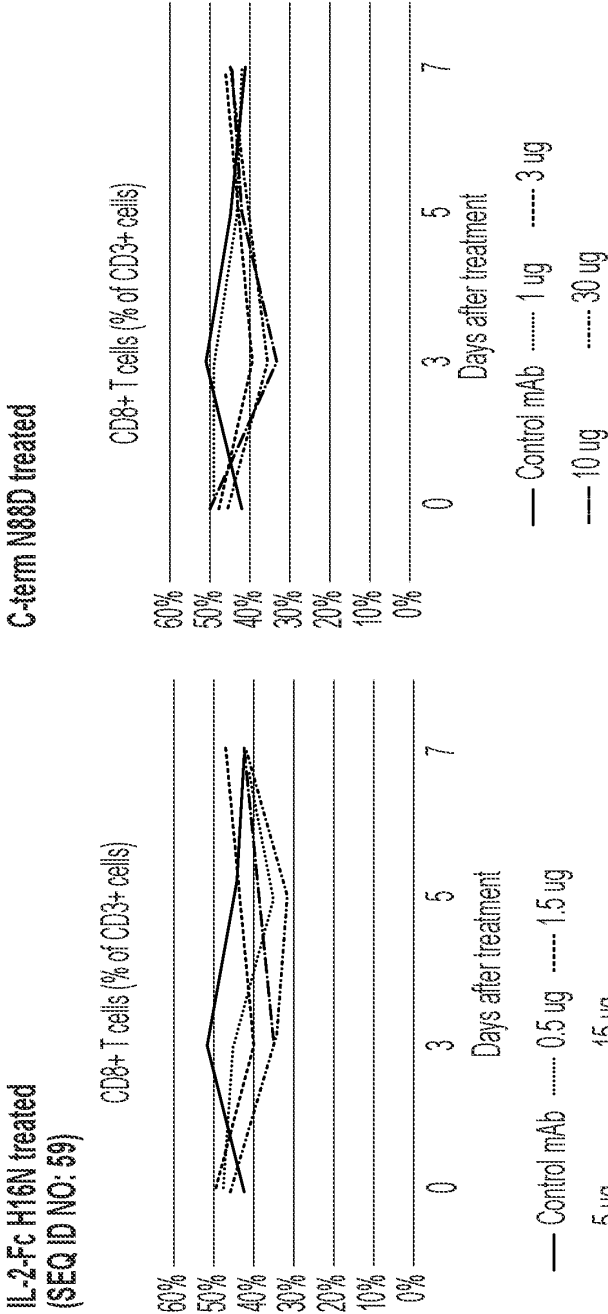


FIG. 14B

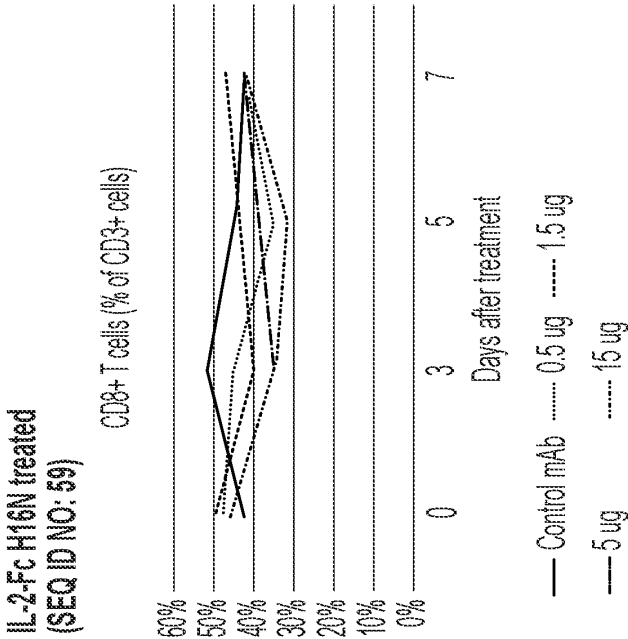


FIG. 14A

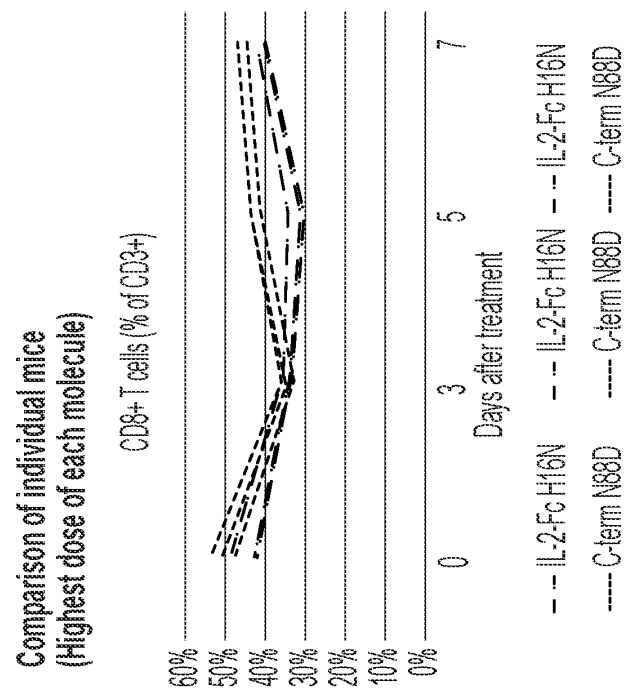


FIG. 14C

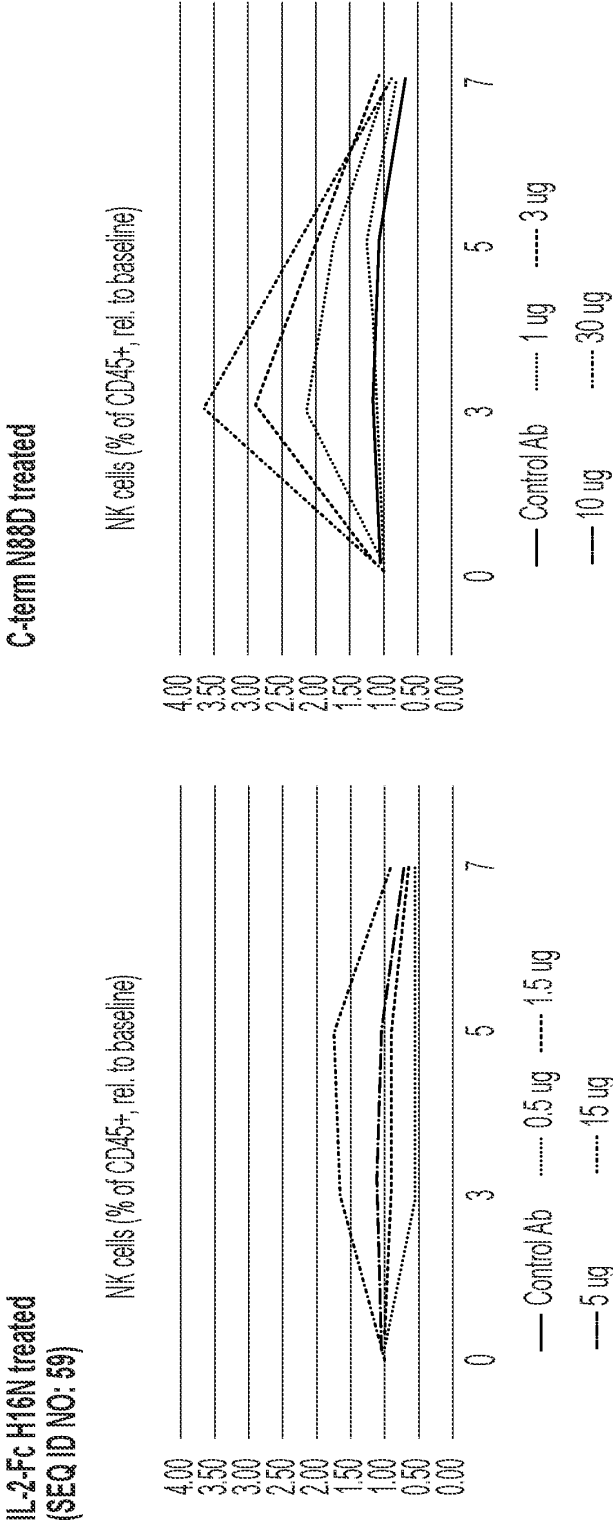


FIG. 15A

FIG. 15B

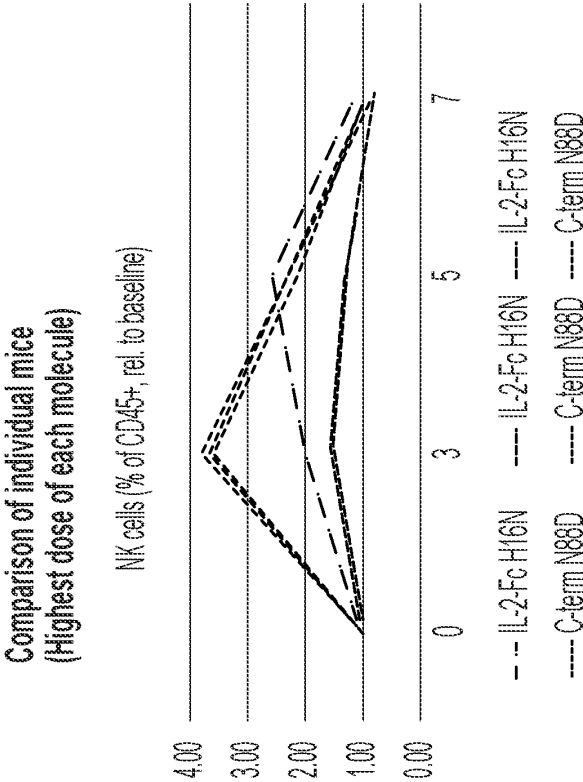


FIG. 15C

25/41

IL2-Fc Wild-type

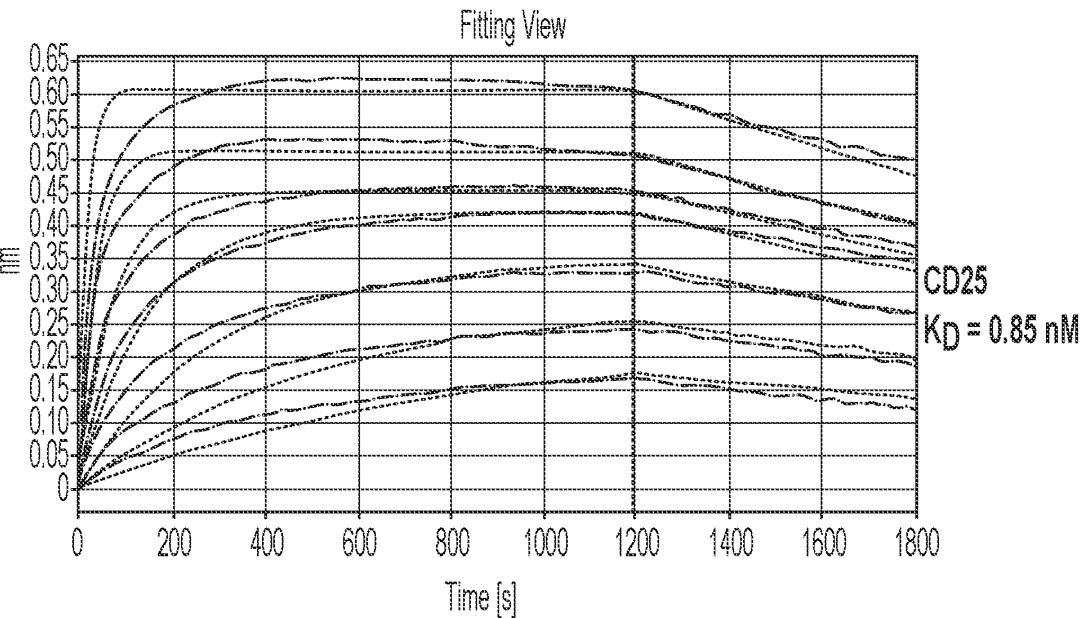
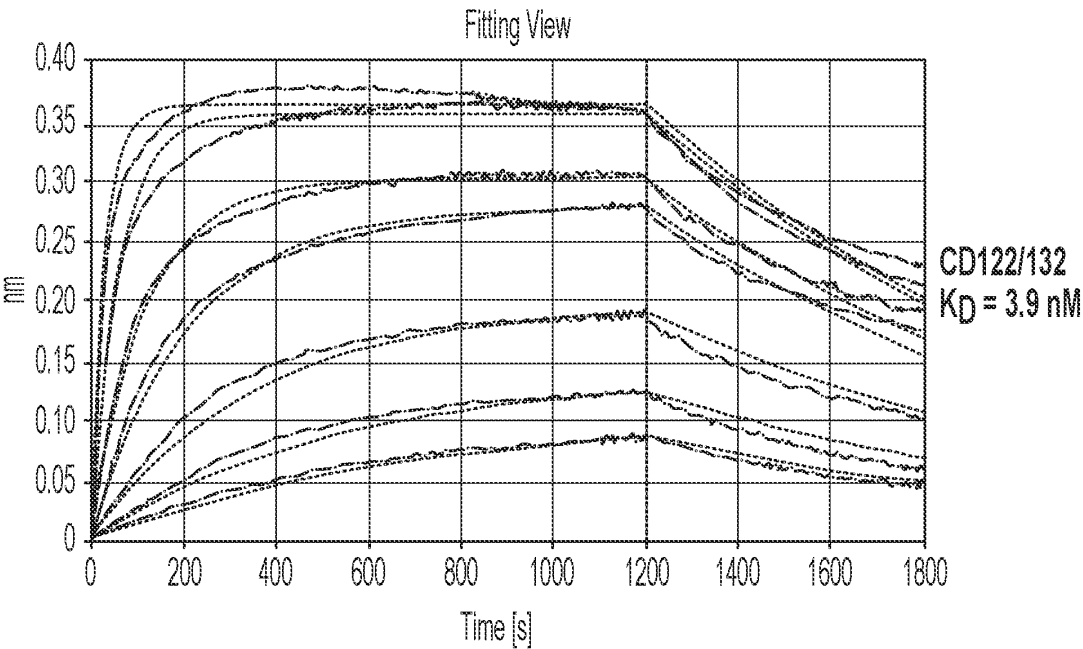
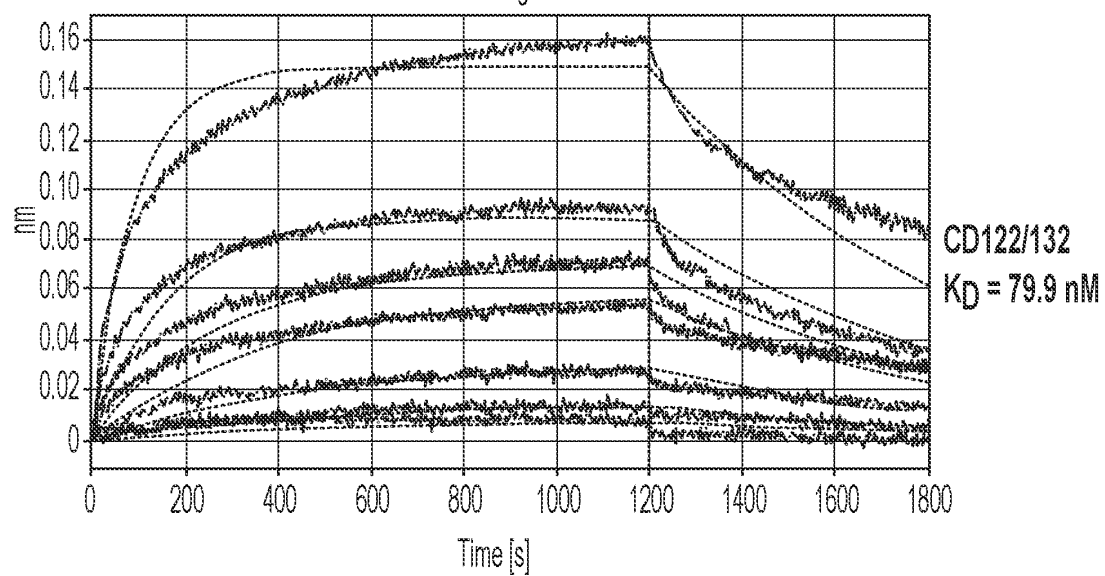


FIG. 16A

26/41

IL2-Fc Inactive

Fitting View



Fitting View

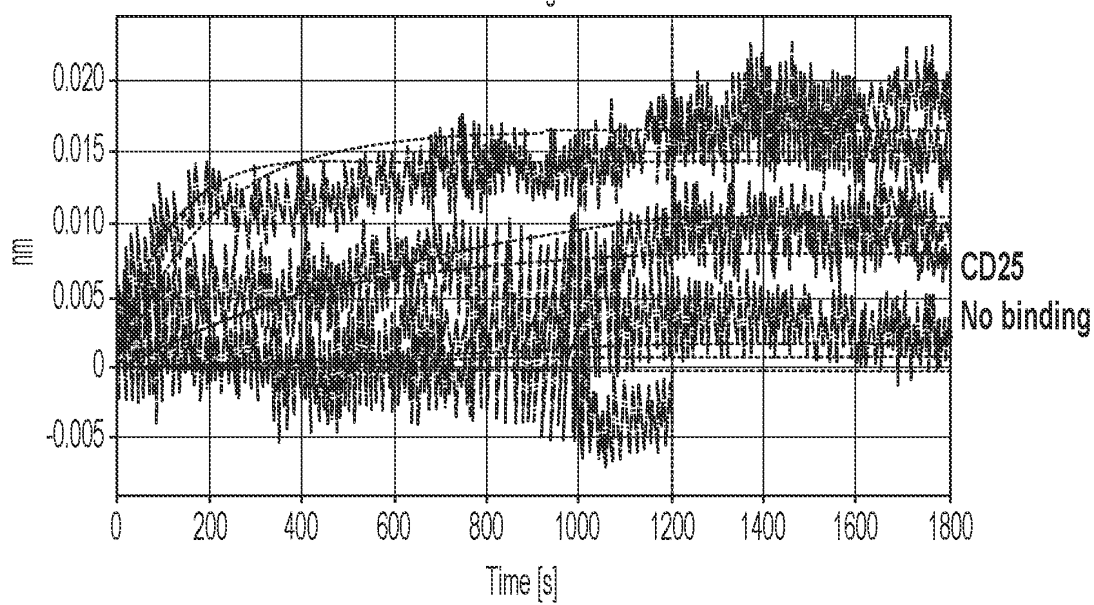


FIG. 16B

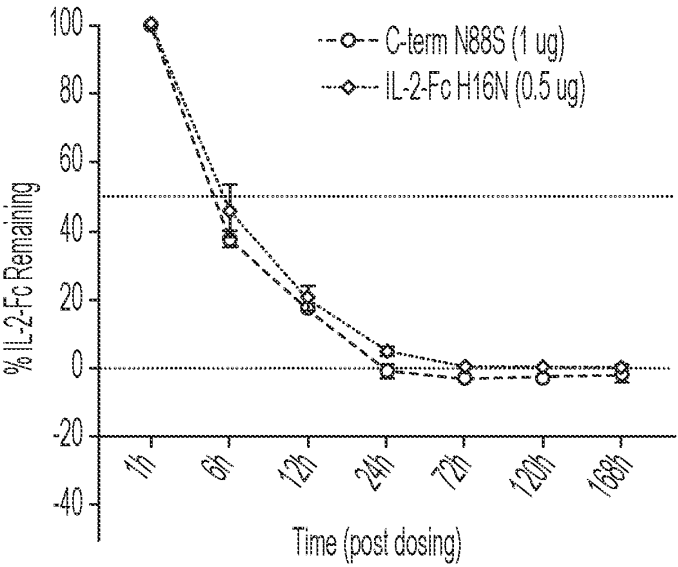


FIG. 17A

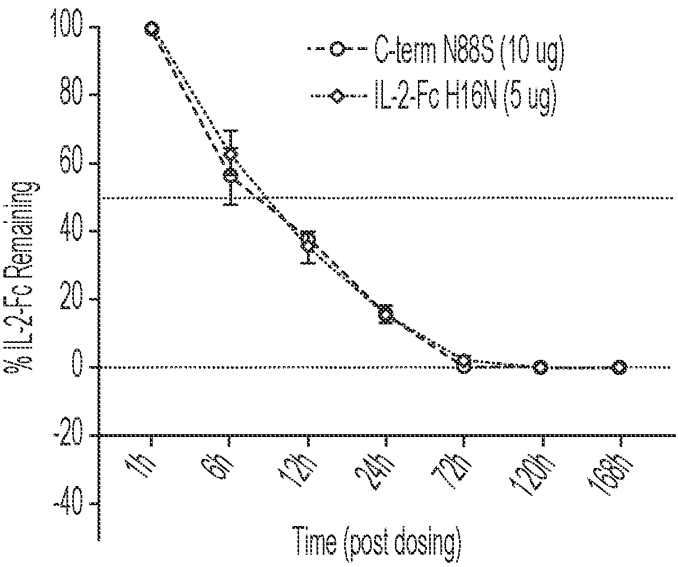


FIG. 17B

28/41

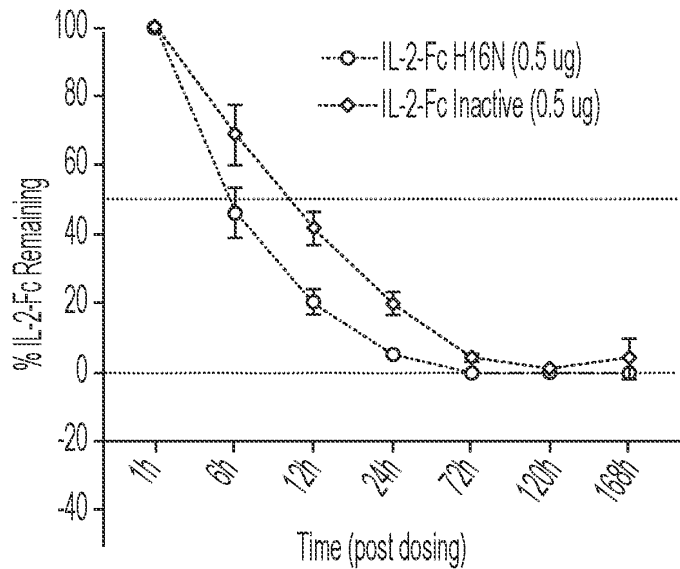


FIG. 17C

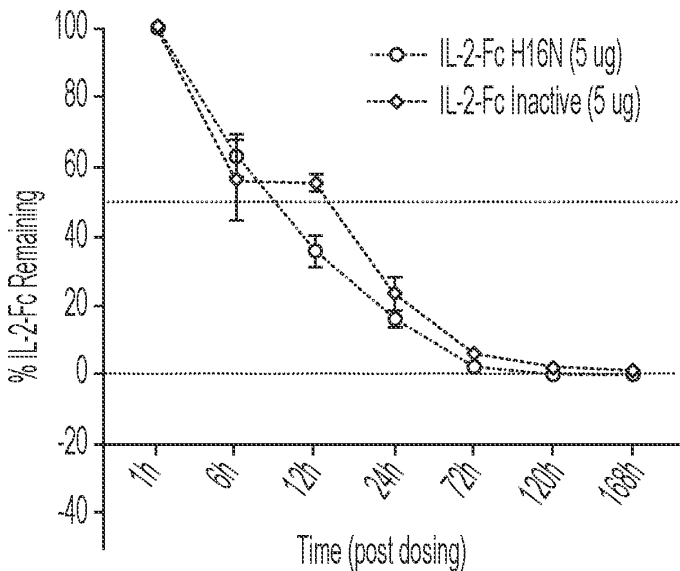


FIG. 17D

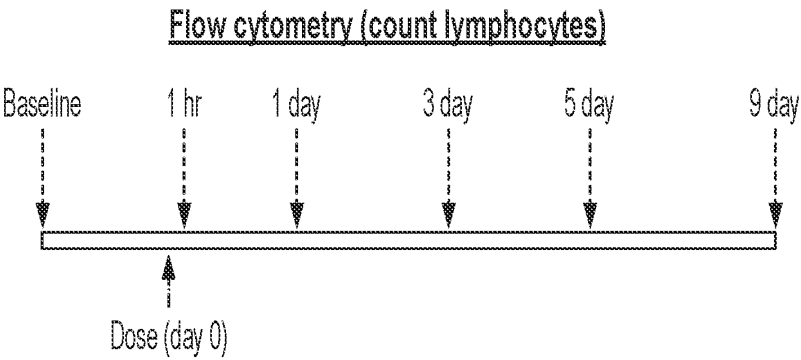


FIG. 18A

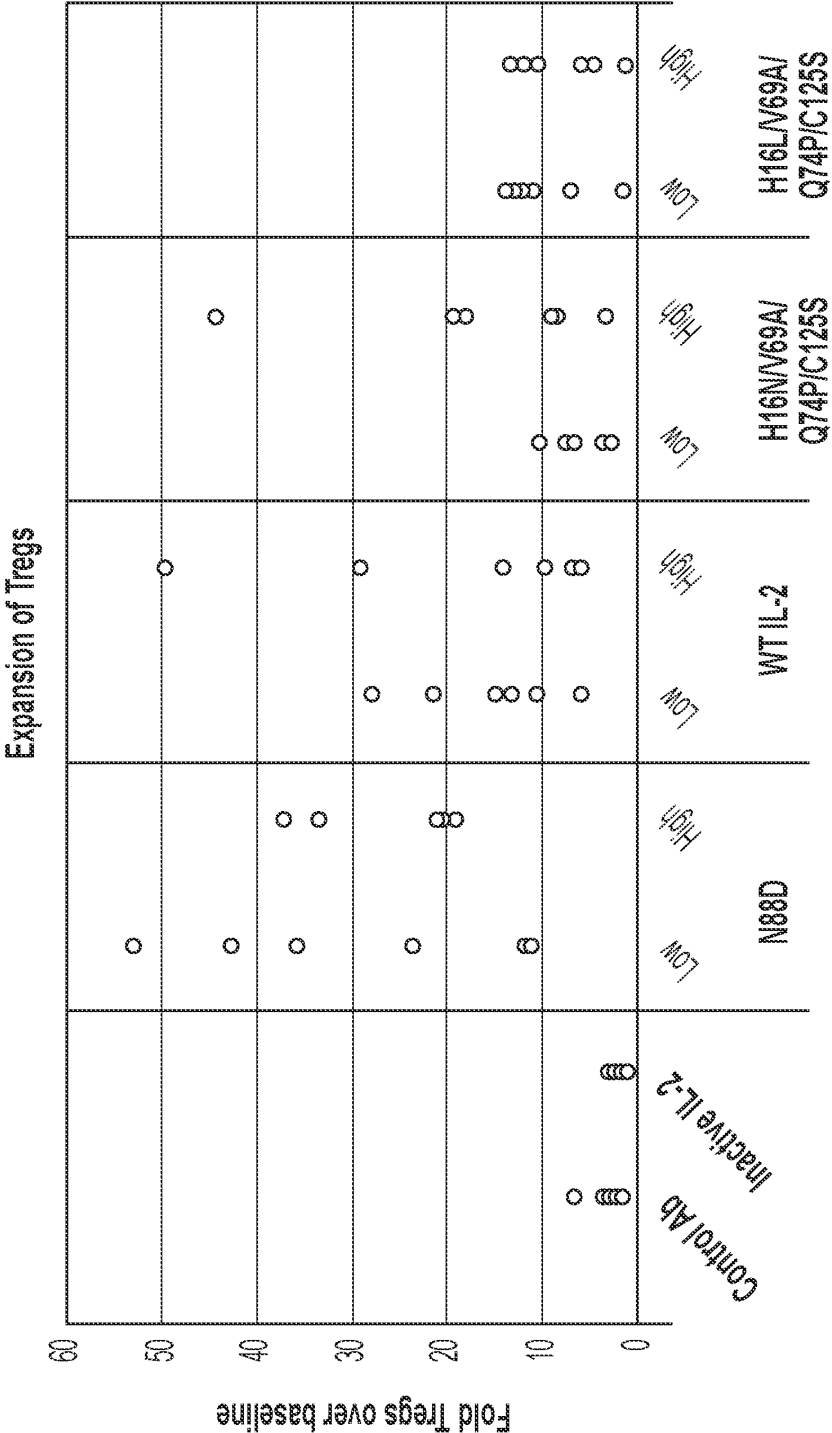
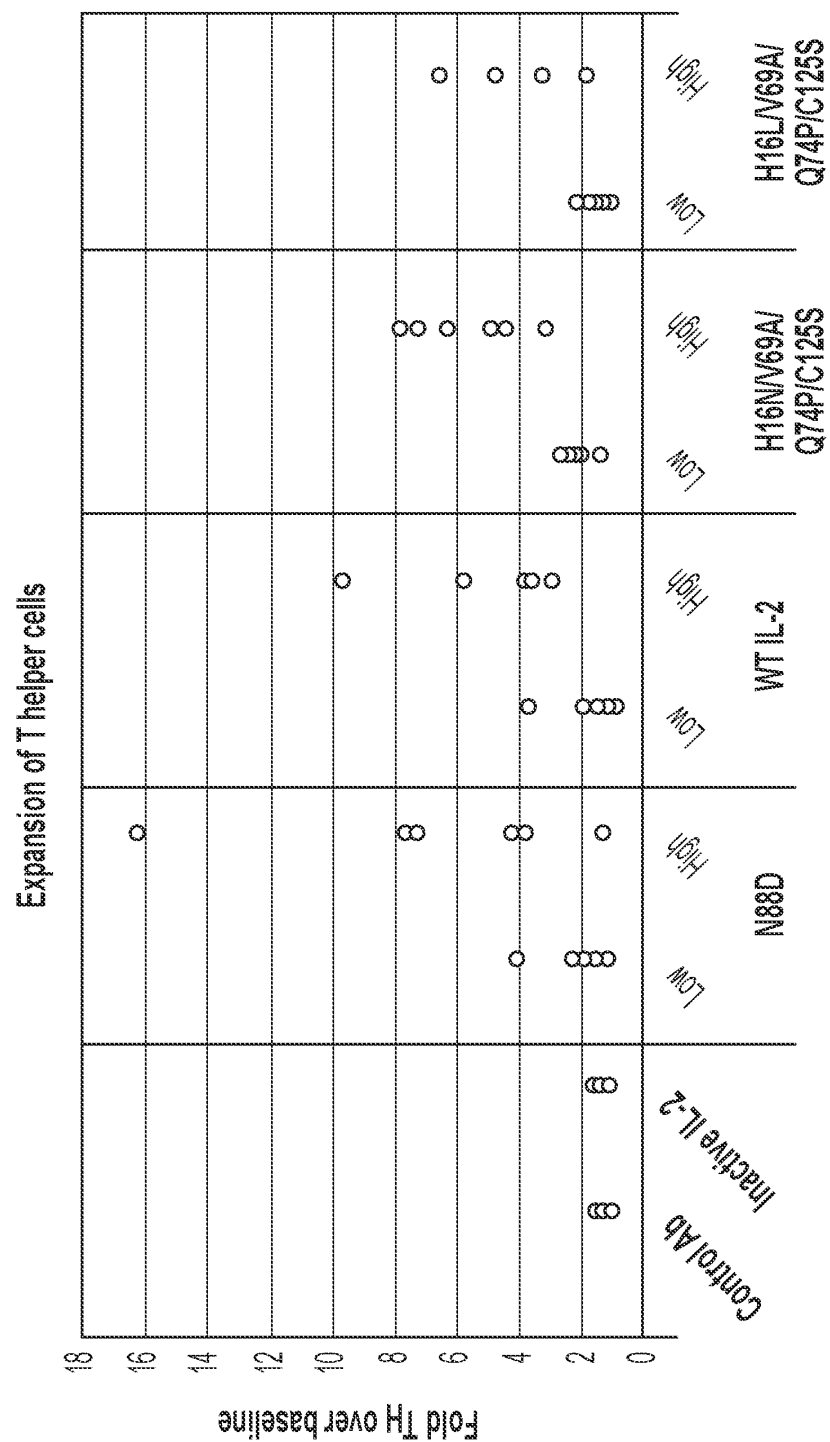


FIG. 18B



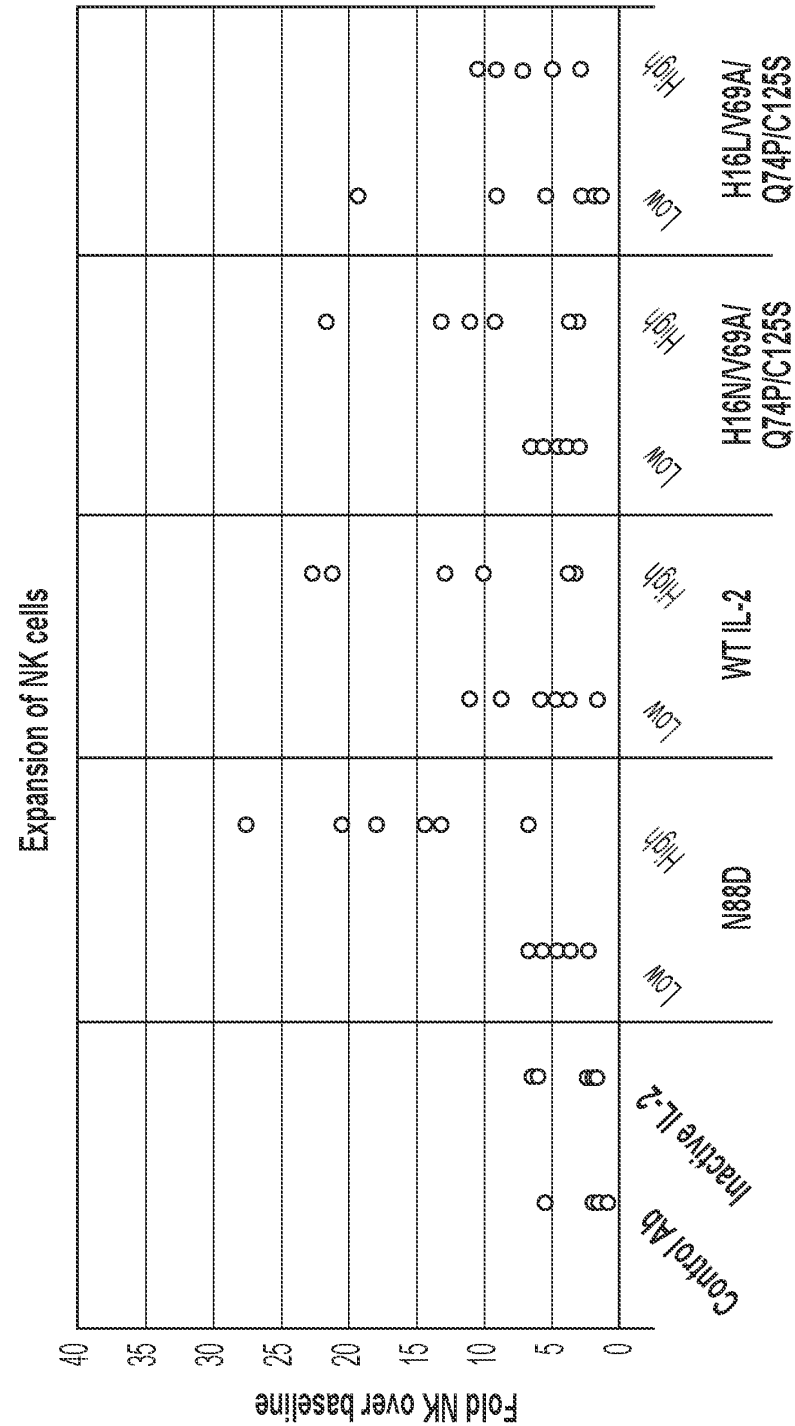


FIG. 18D

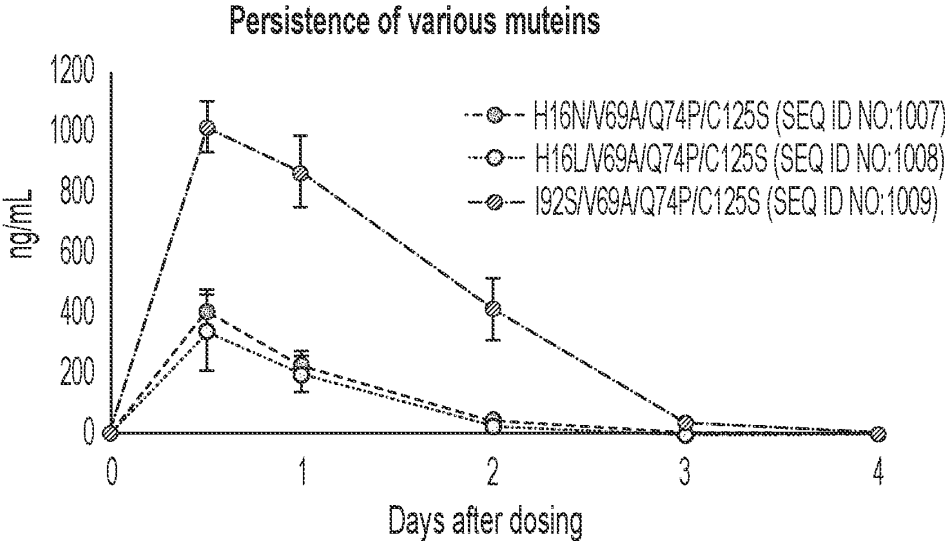


FIG. 19A

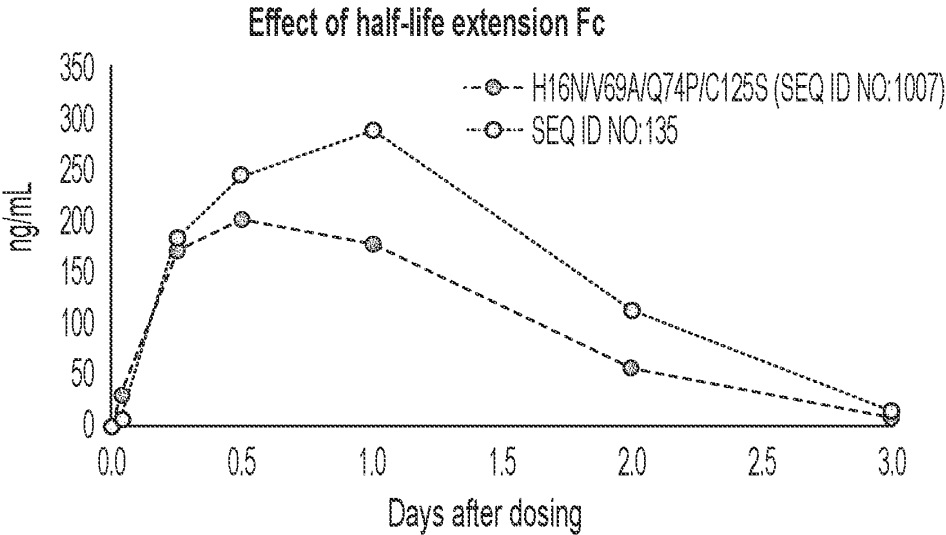


FIG. 19B

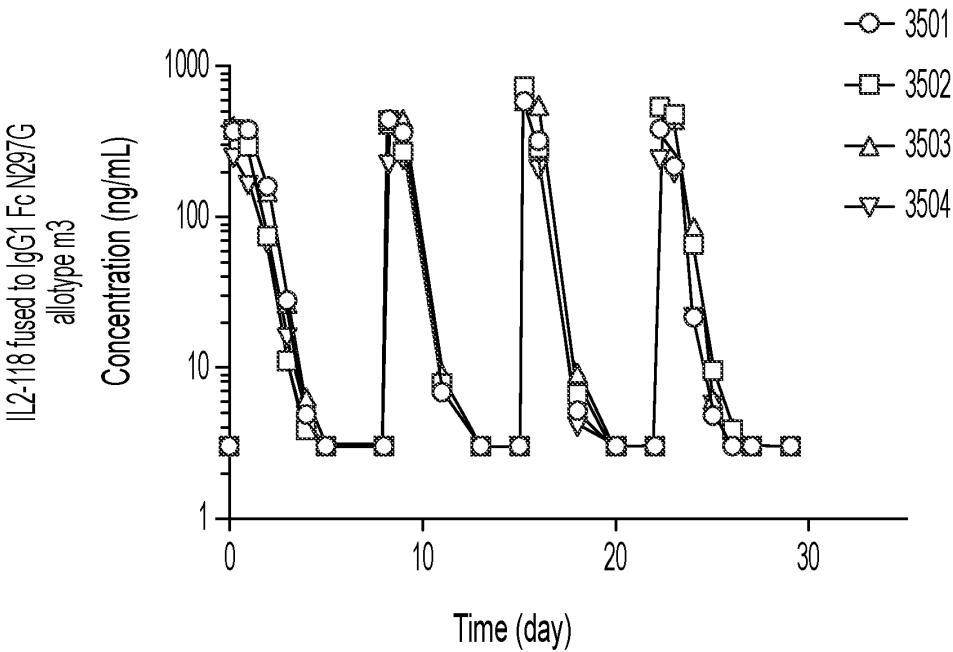


FIG. 20

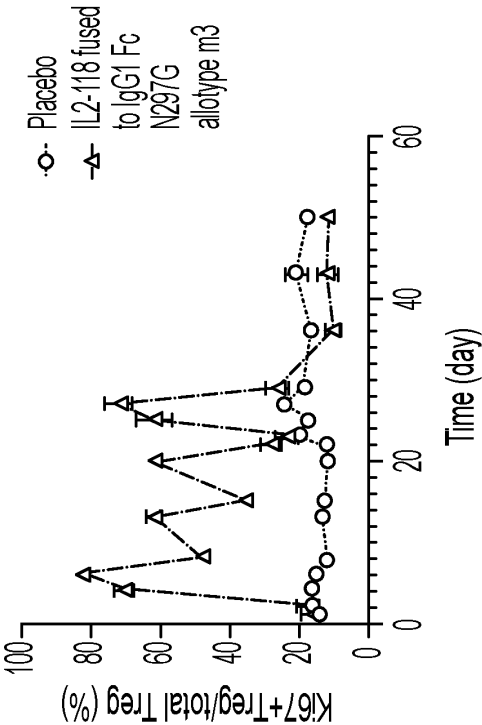


FIG. 21B

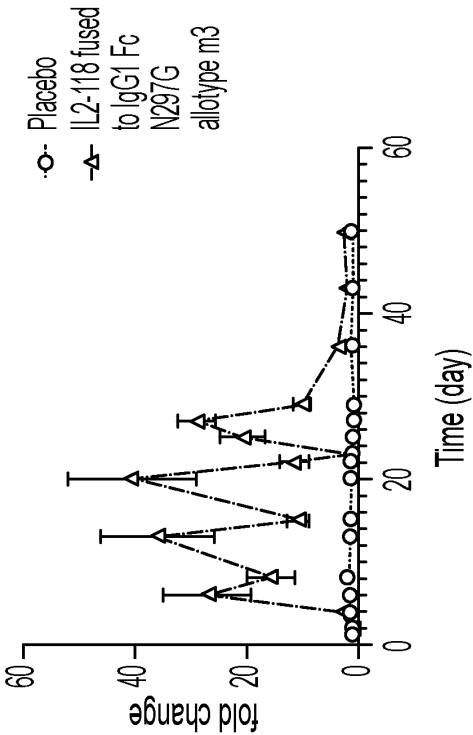


FIG. 21A

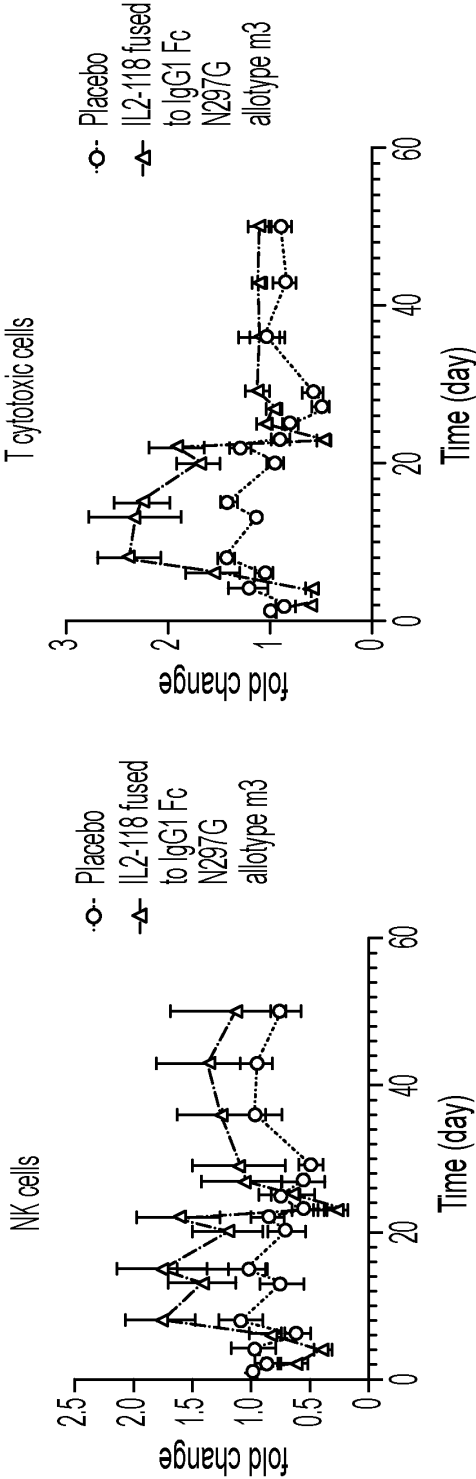


FIG. 22B

FIG. 22A

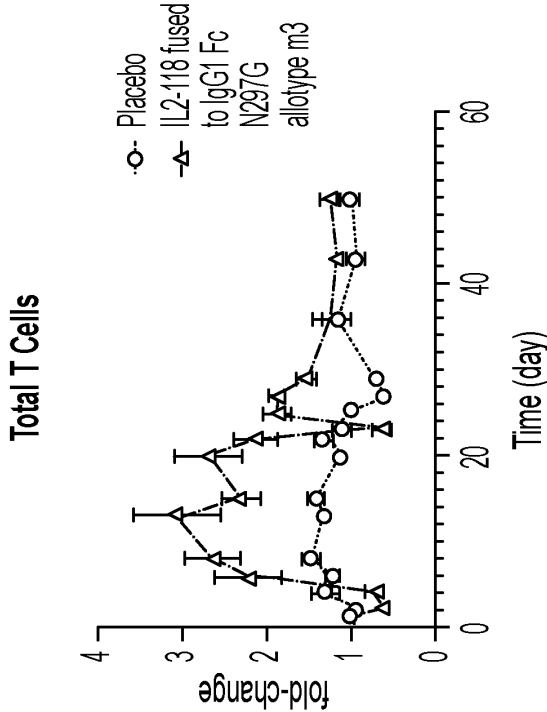


FIG. 22D

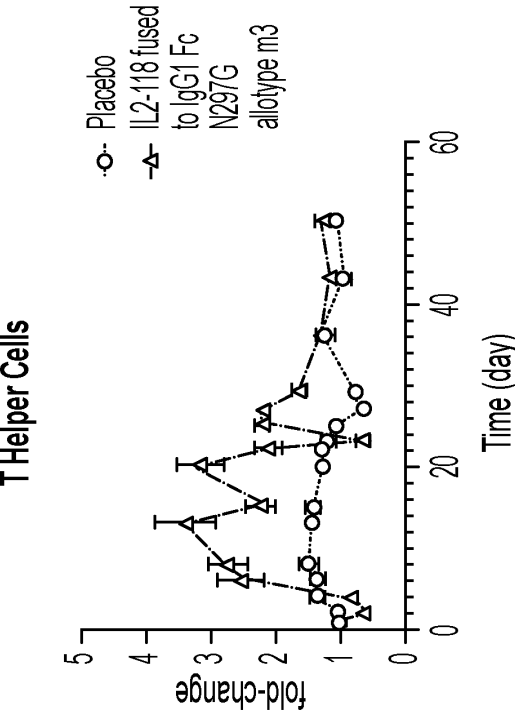


FIG. 22C

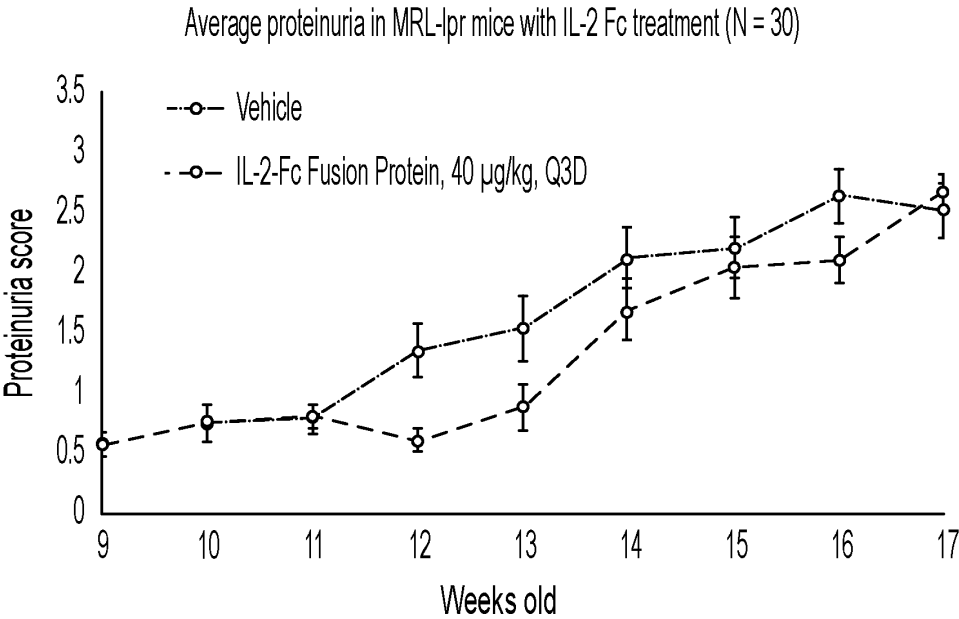


FIG. 23A

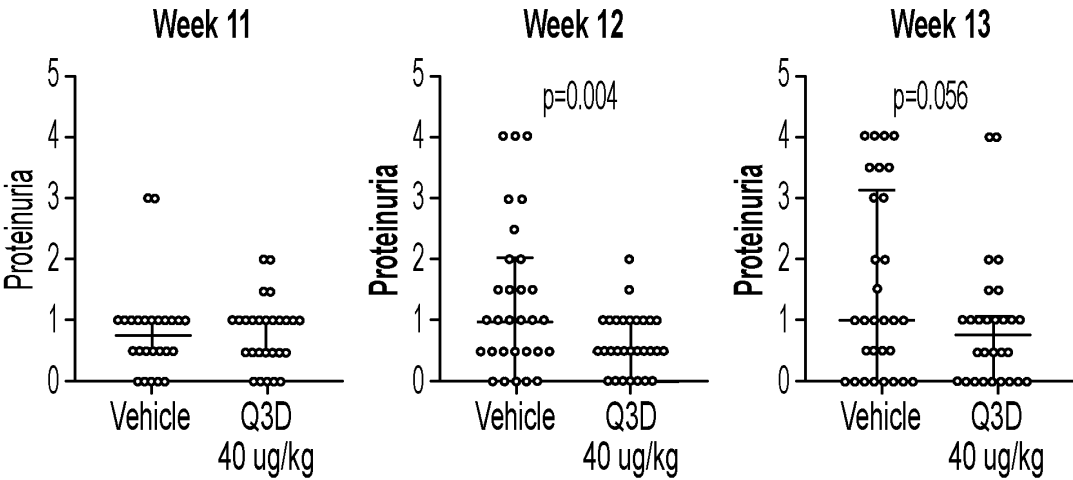


FIG. 23B

39/41

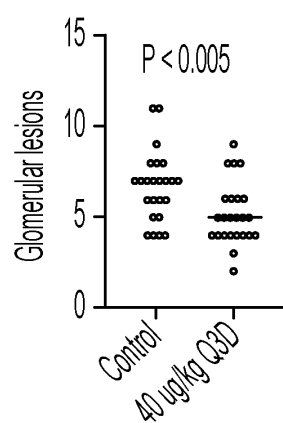


FIG. 23C

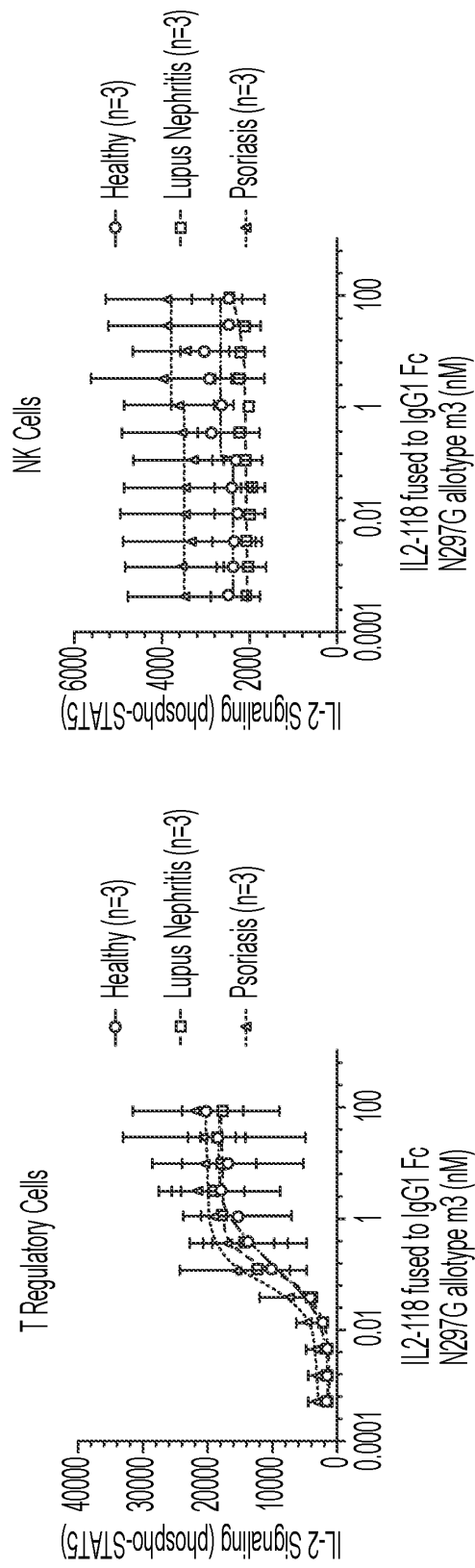


FIG. 24A

FIG. 24B

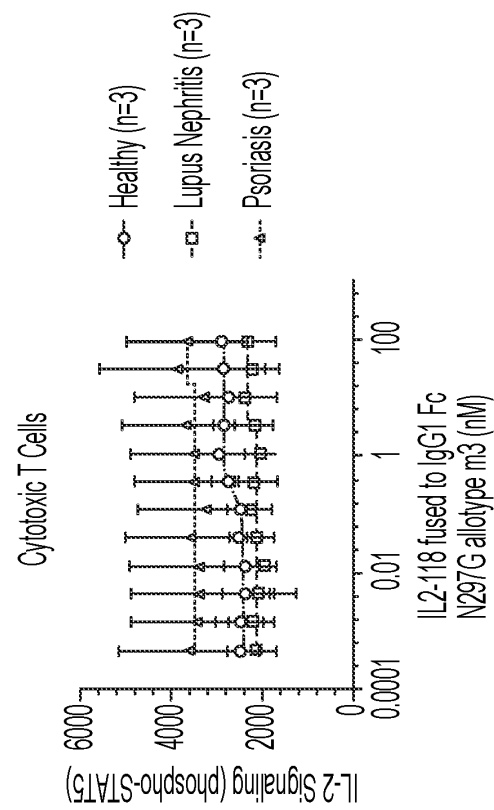


FIG. 24C