

IL-2

IL-2

Peptide linker

Fc region
(CH2 and CH3 domains)

APTSSSTKKTQLQLLEHLLLDLQMLNGINN30

YKNPKLTRLTLTKFYMPKKATELKHLCLE60

EELKPLEEFVLNLAQSKNFHLRPRDLISNIN90

VIVLELKGSETTFMCEYADETATIVVEFLNR120

WITFCIQSIISTLTGS133

C125S- improve stability (present in all sequences)

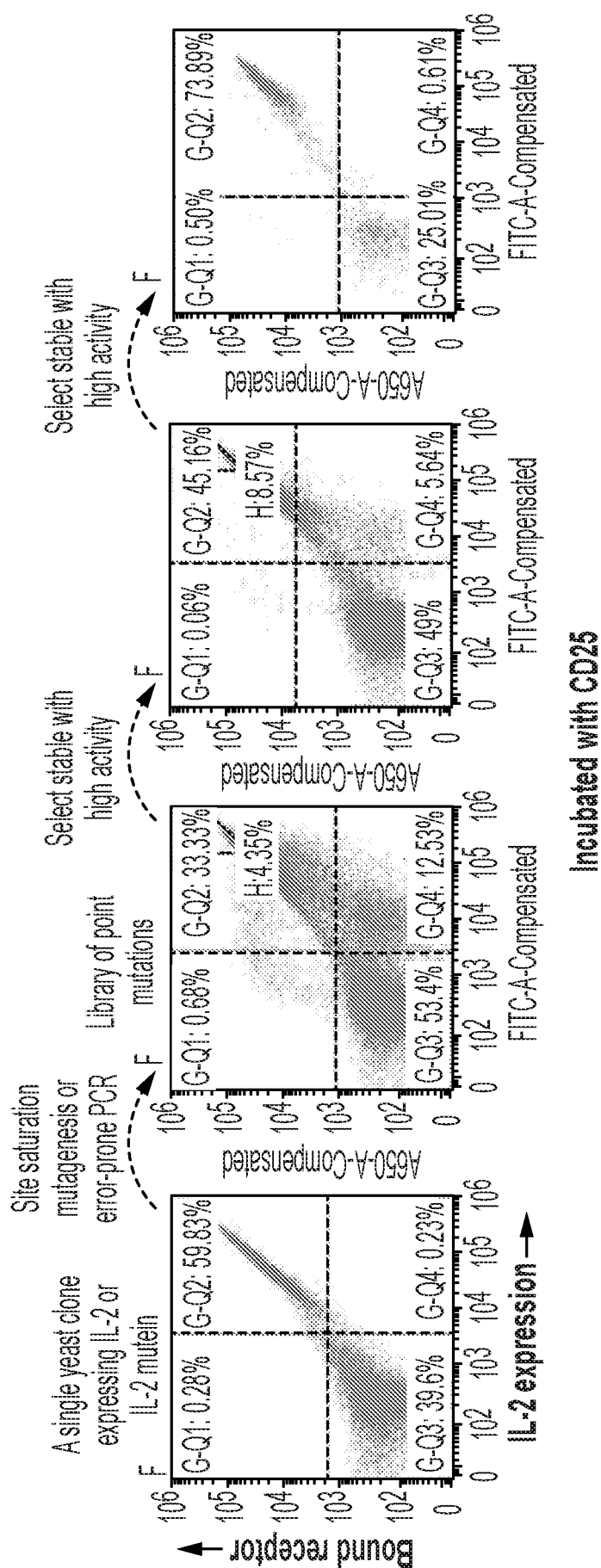
V69A/Q74P- reduce aggregation

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
5
G
L

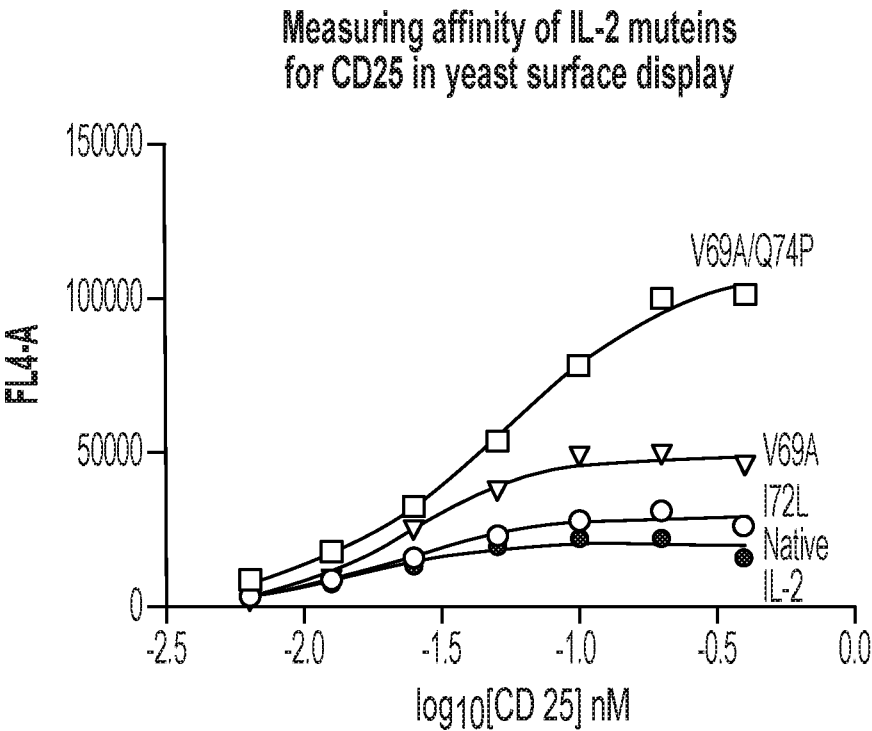


FIG. 3A

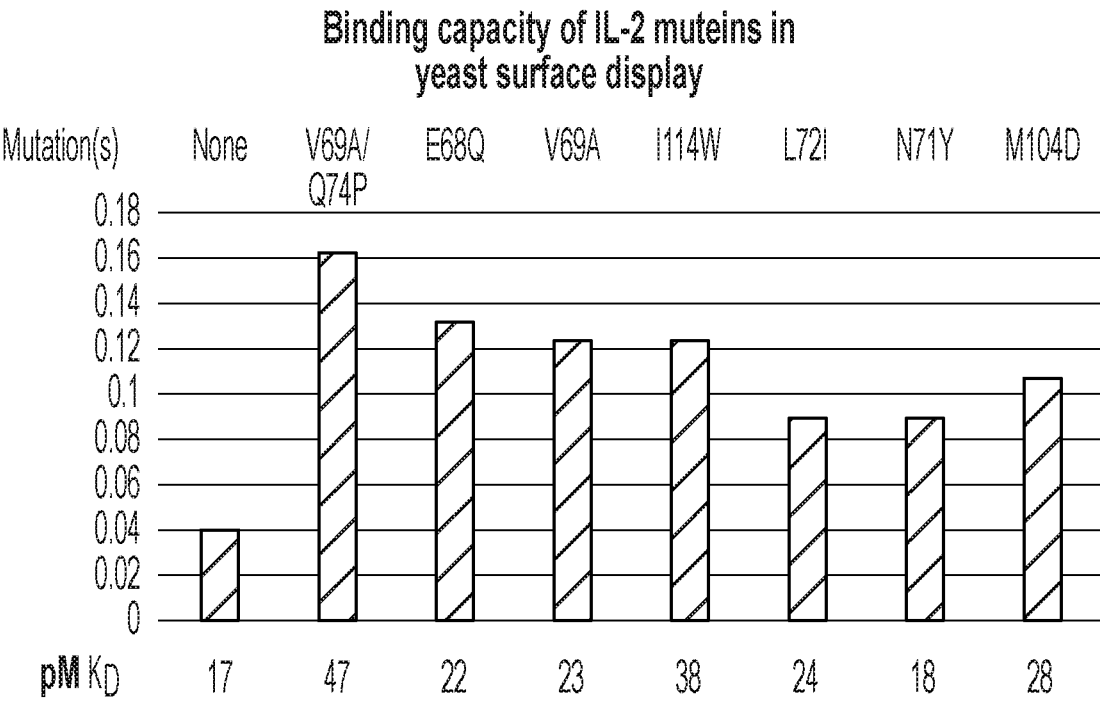


FIG. 3B

4/39

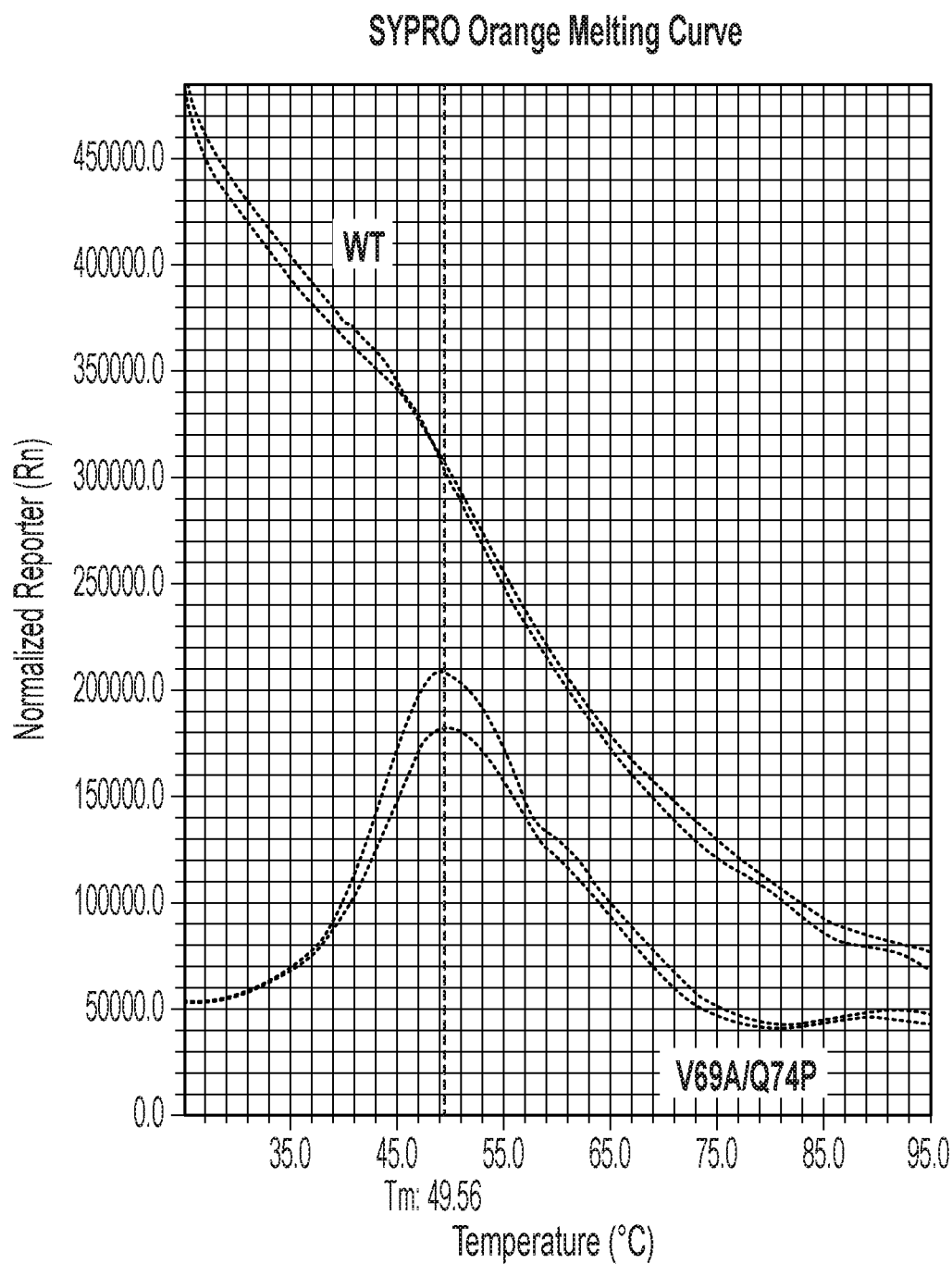


FIG. 4A

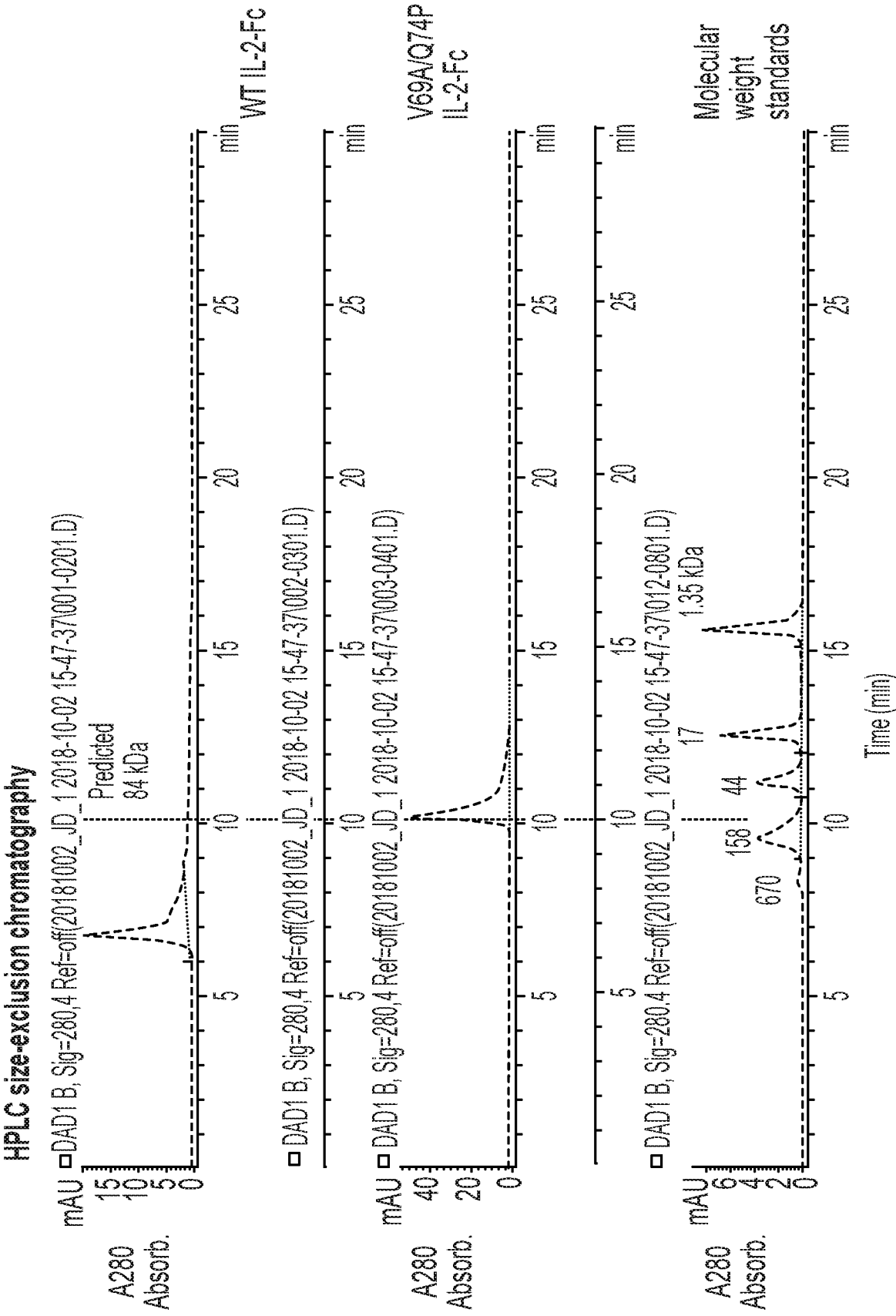


FIG. 4B

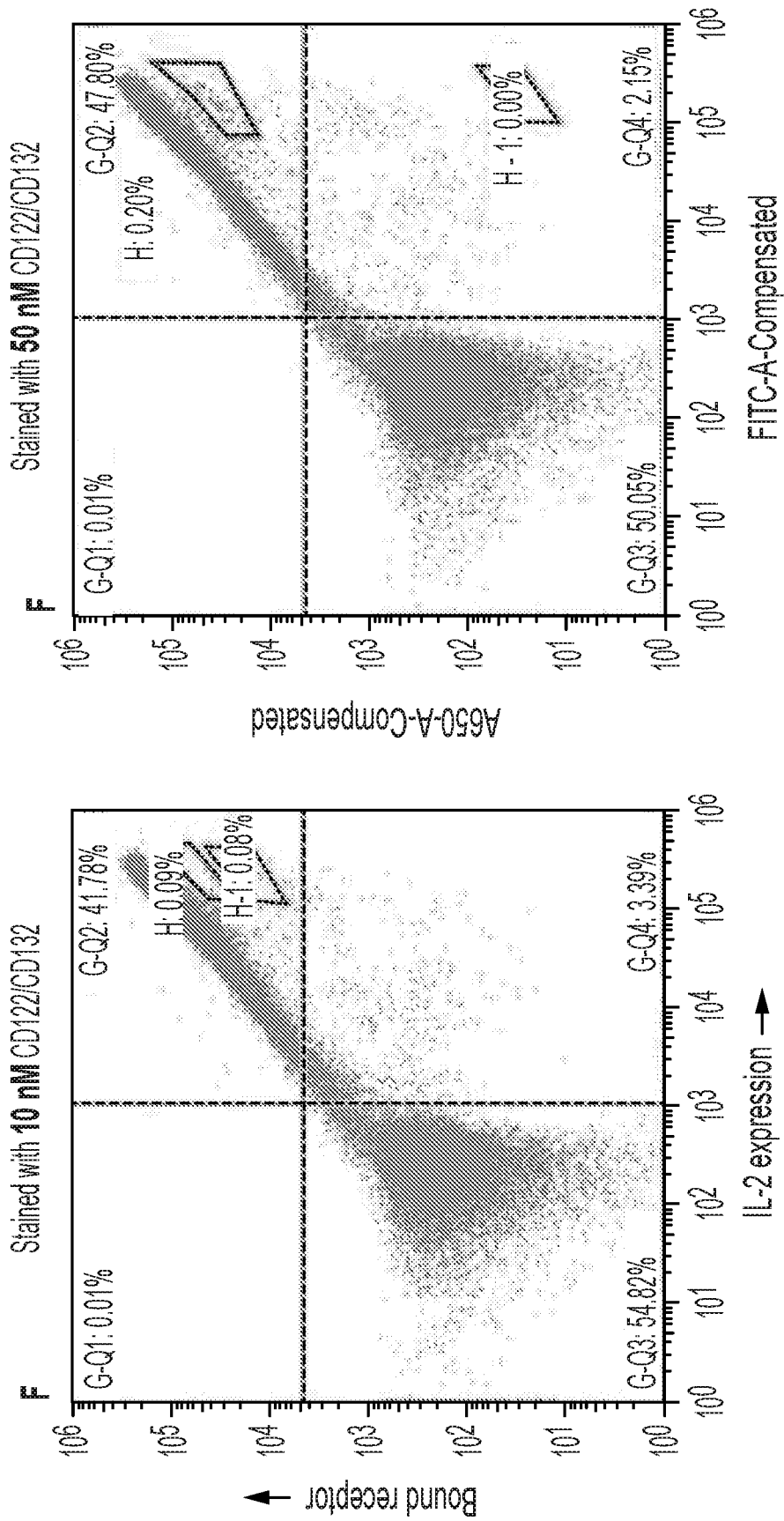


FIG. 5A

FIG. 5B

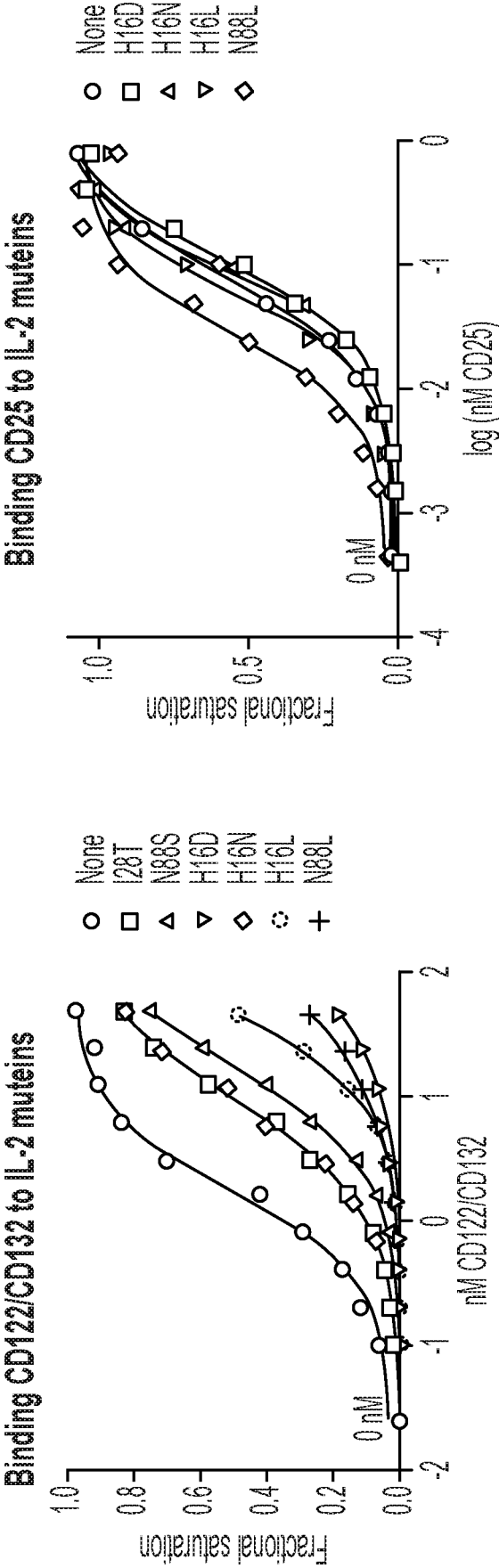


FIG. 6B

FIG. 6A

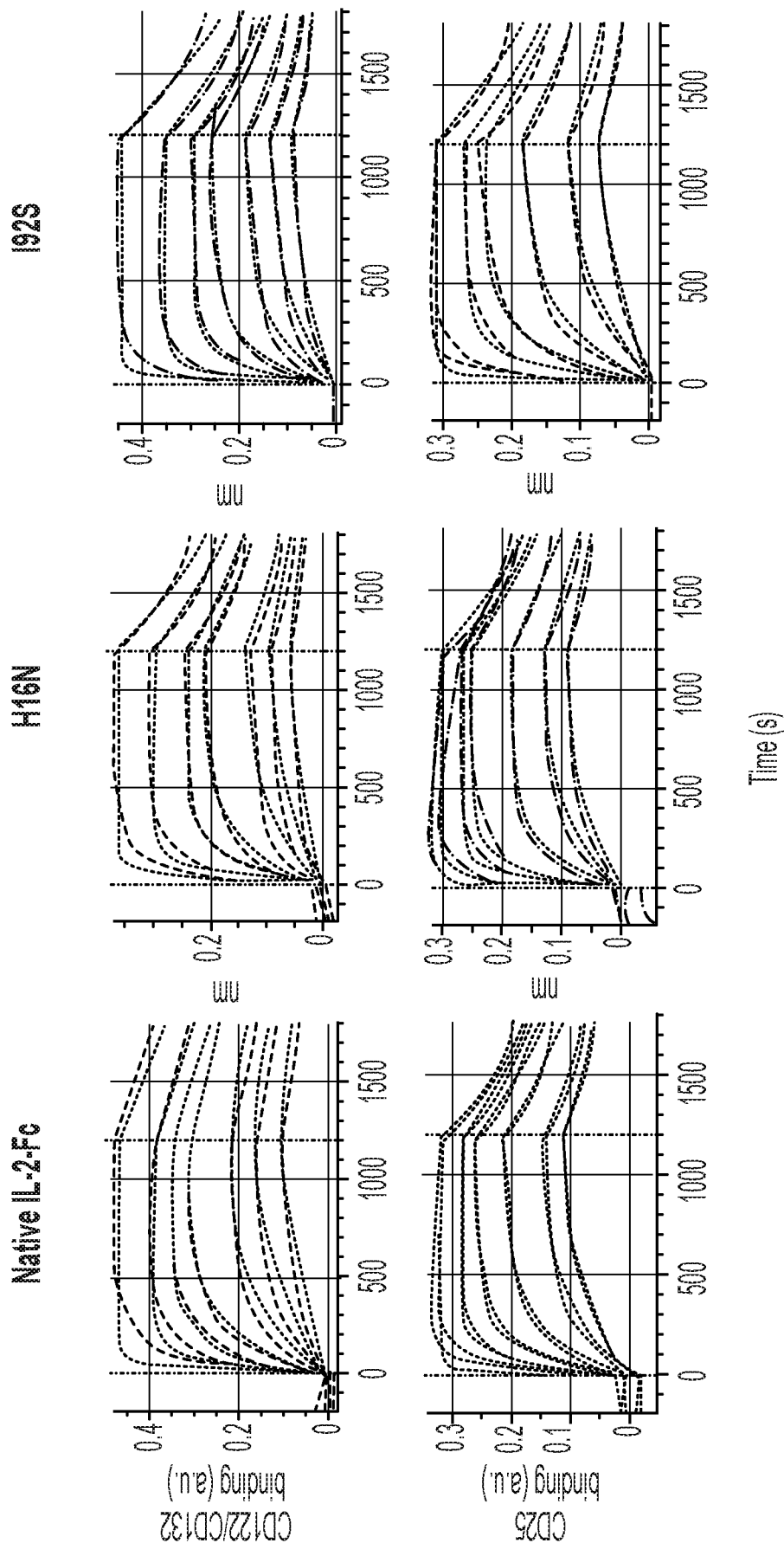


FIG. 7

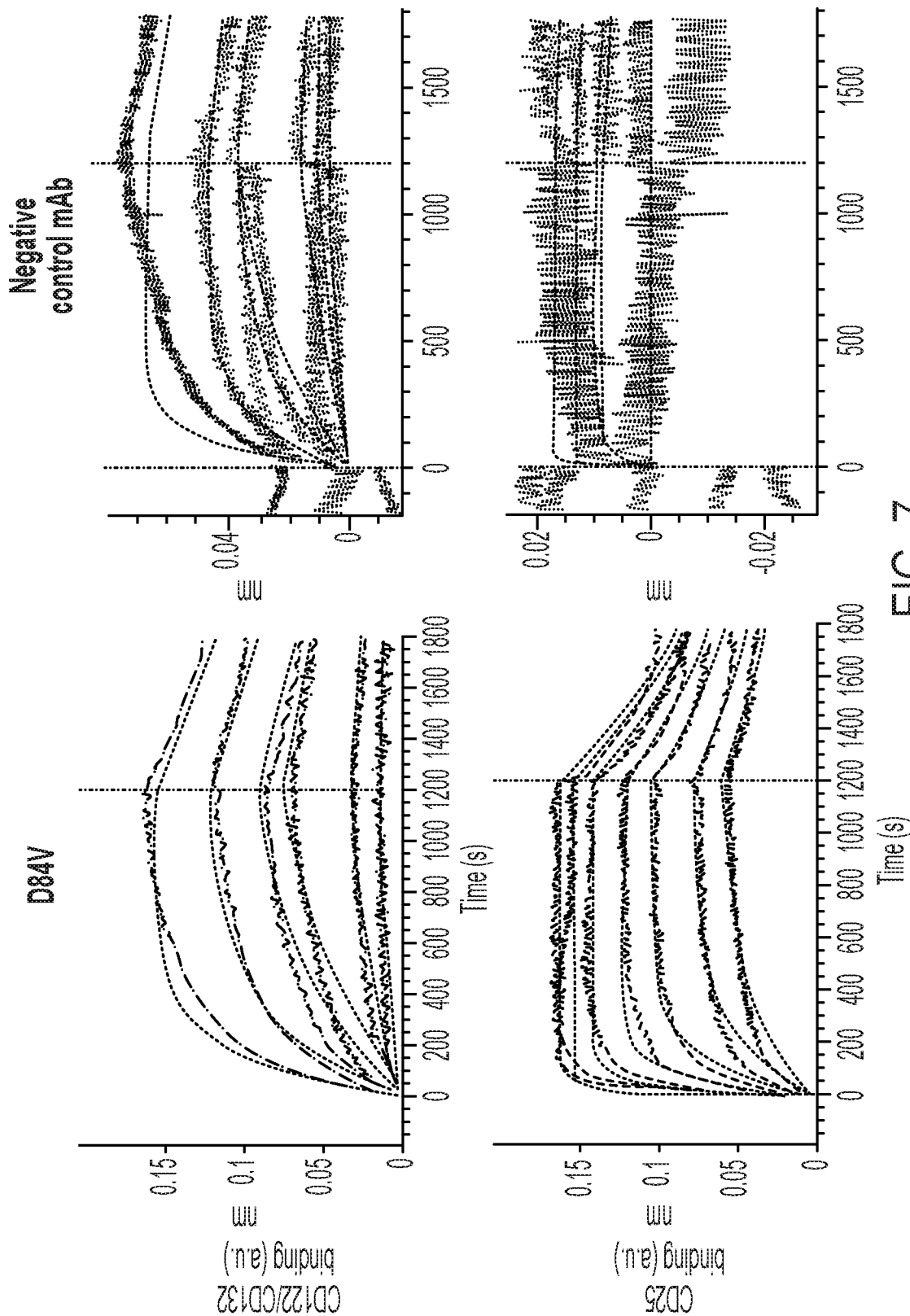


FIG. 7
continued

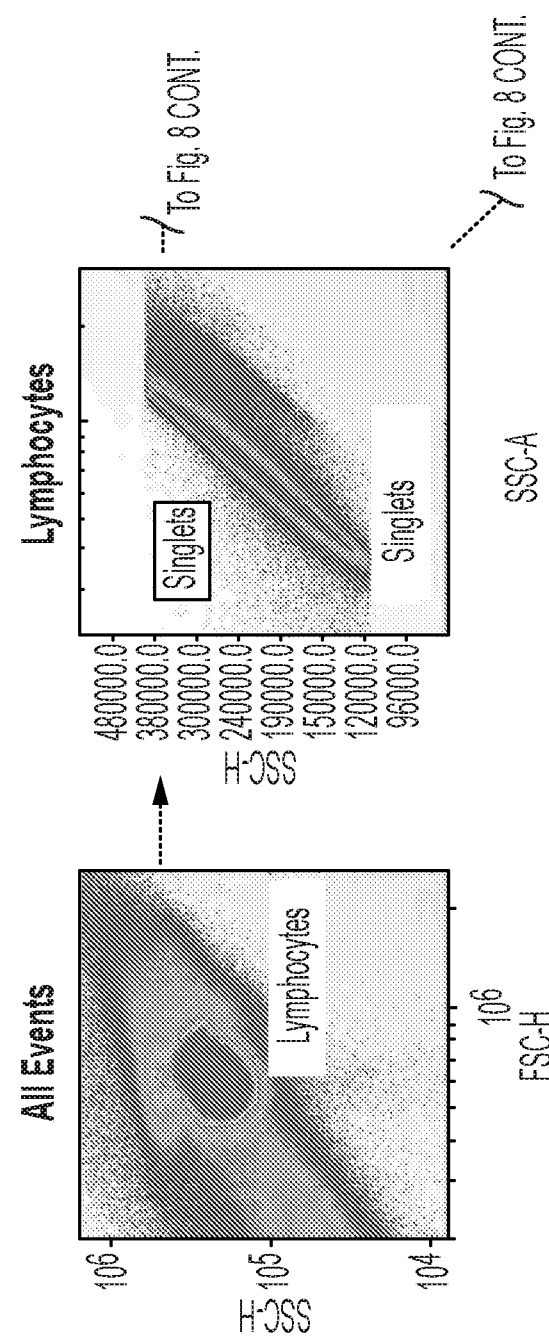


FIG. 8

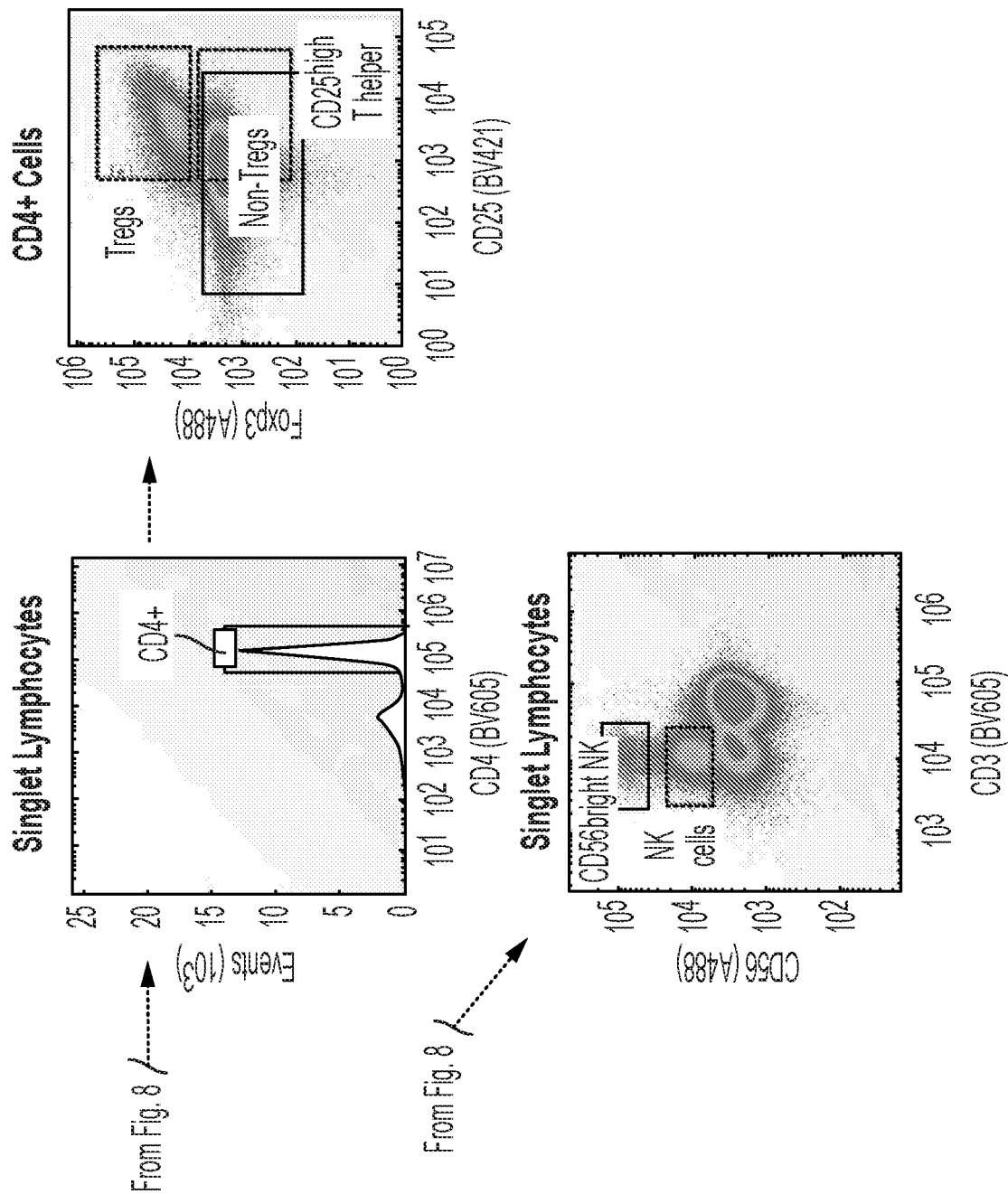


FIG. 8
continued

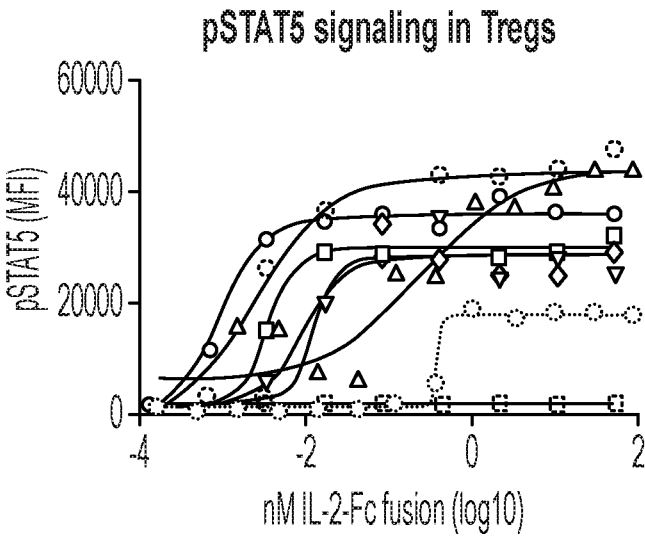


FIG. 9A

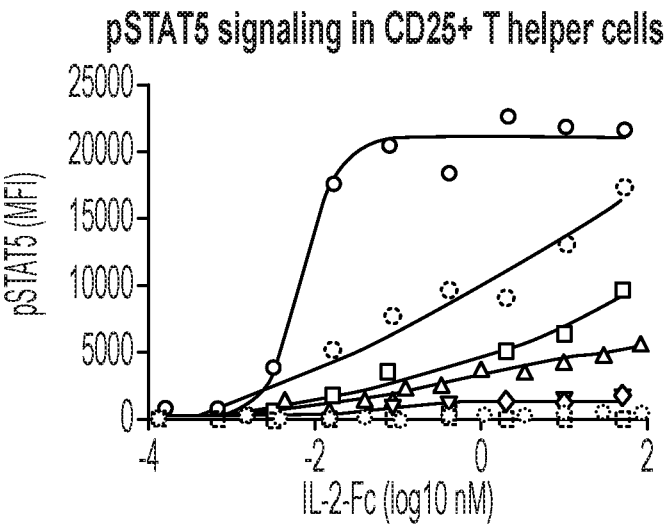


FIG. 9B

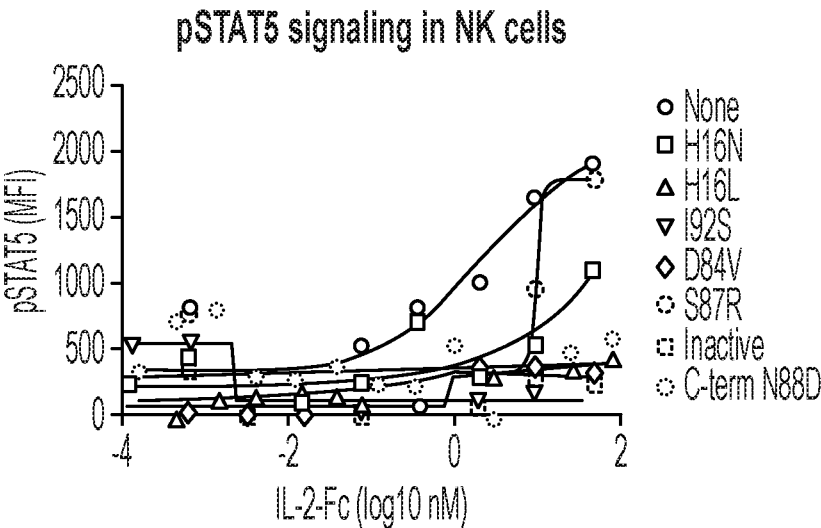


FIG. 9C

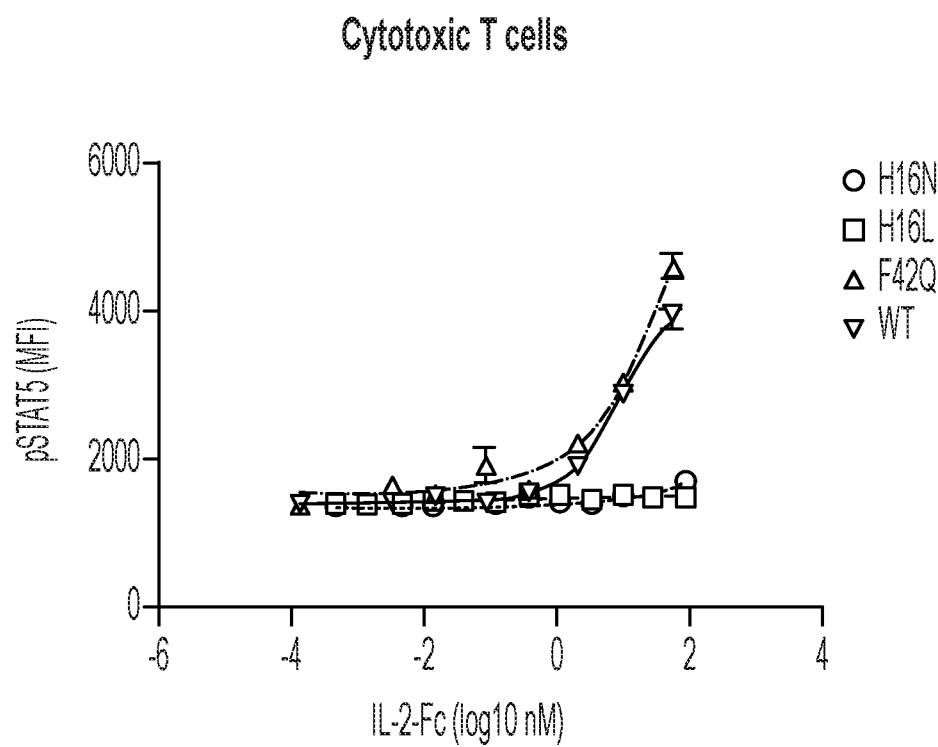


FIG. 9D

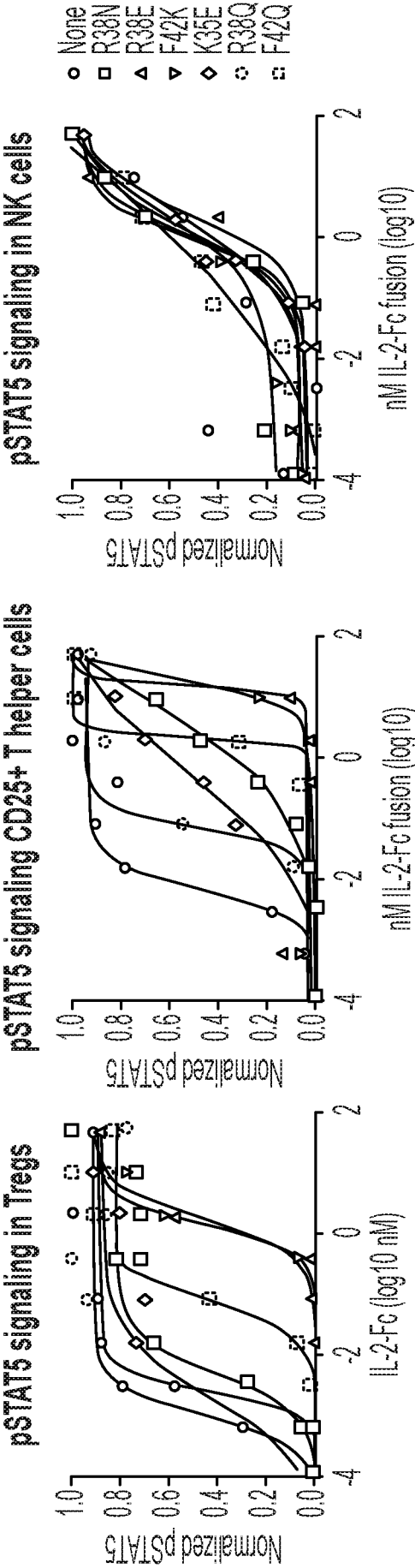


FIG. 10A

FIG. 10B

FIG. 10C

15/39

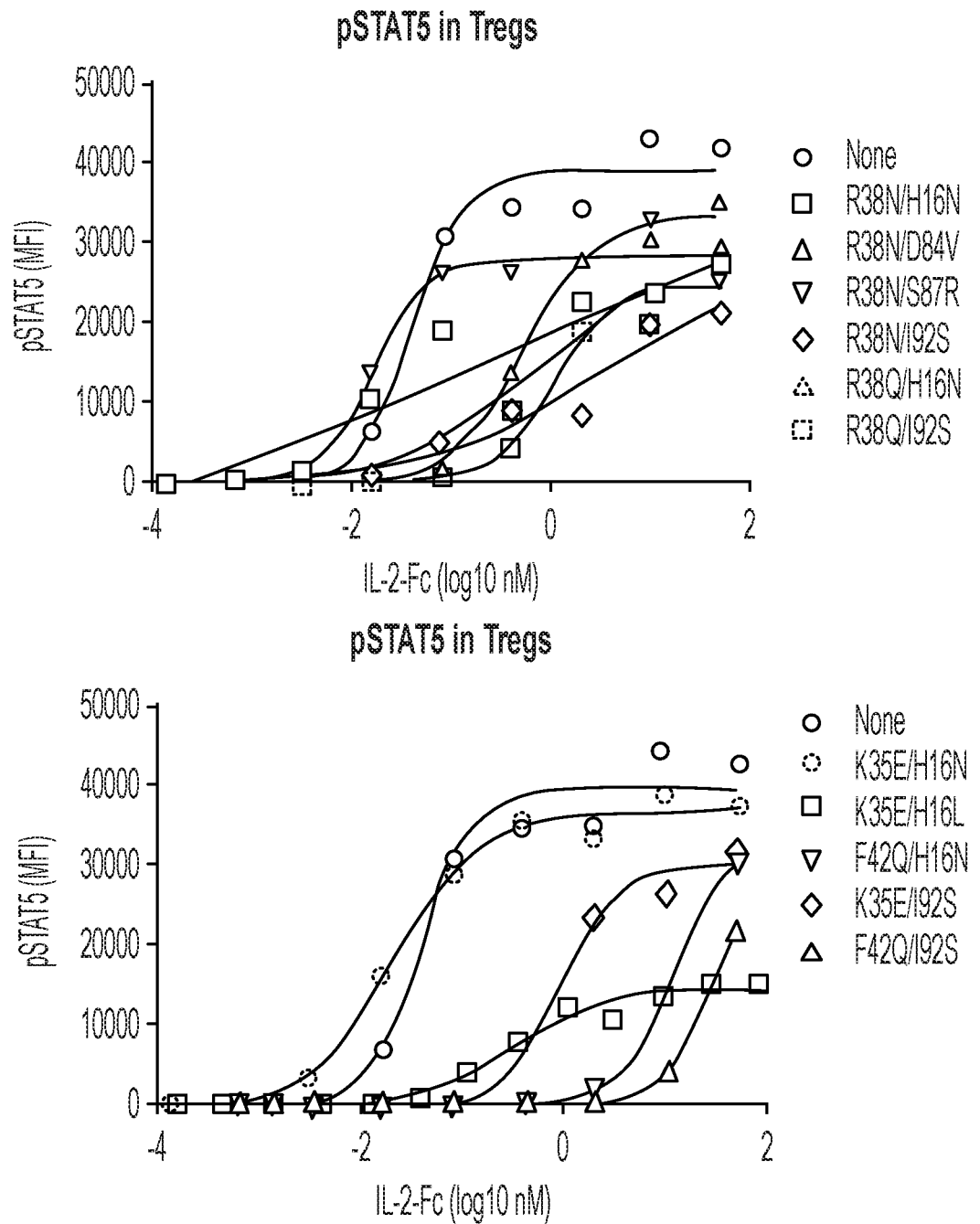


FIG. 11A

16/39

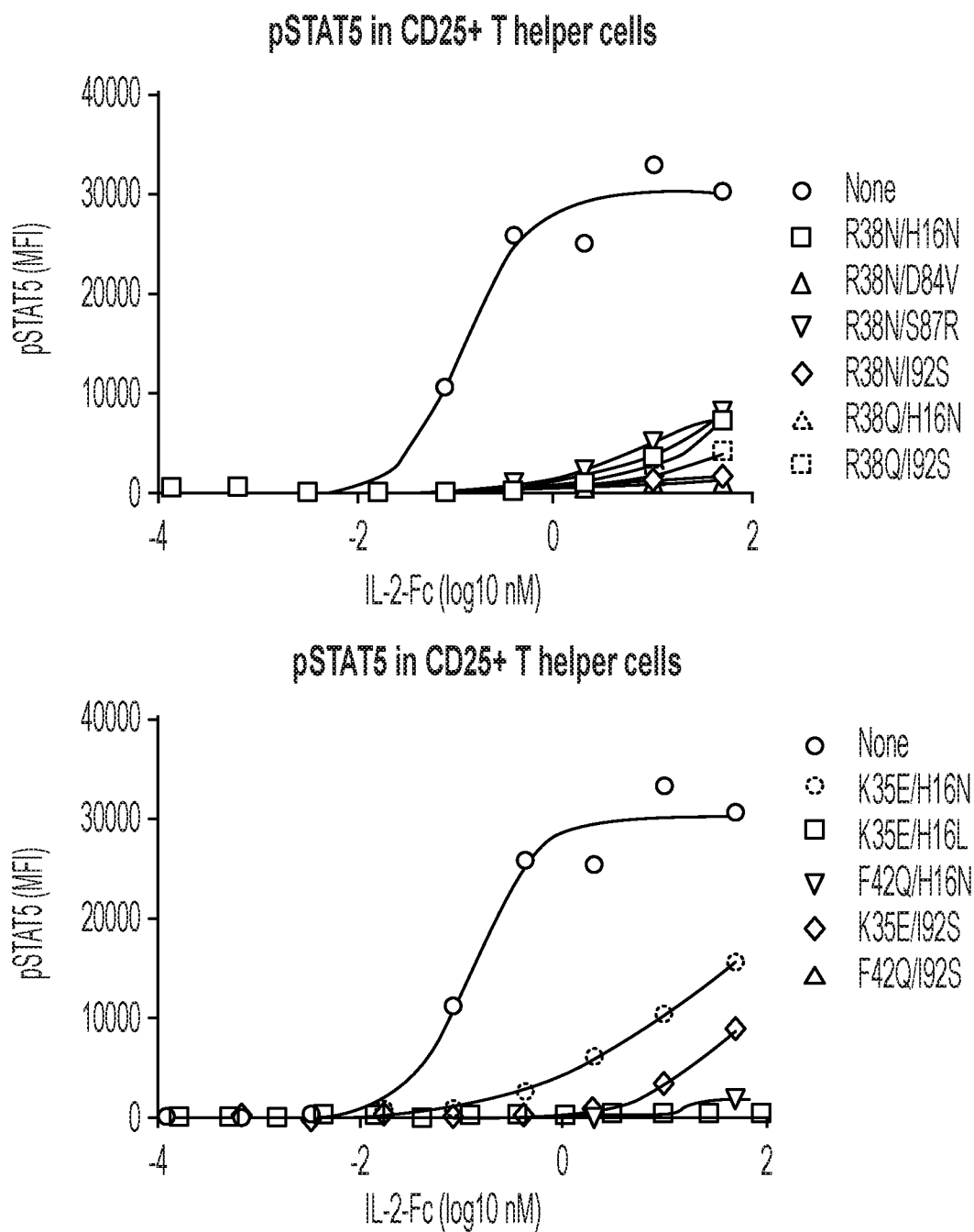


FIG. 11B

17/39

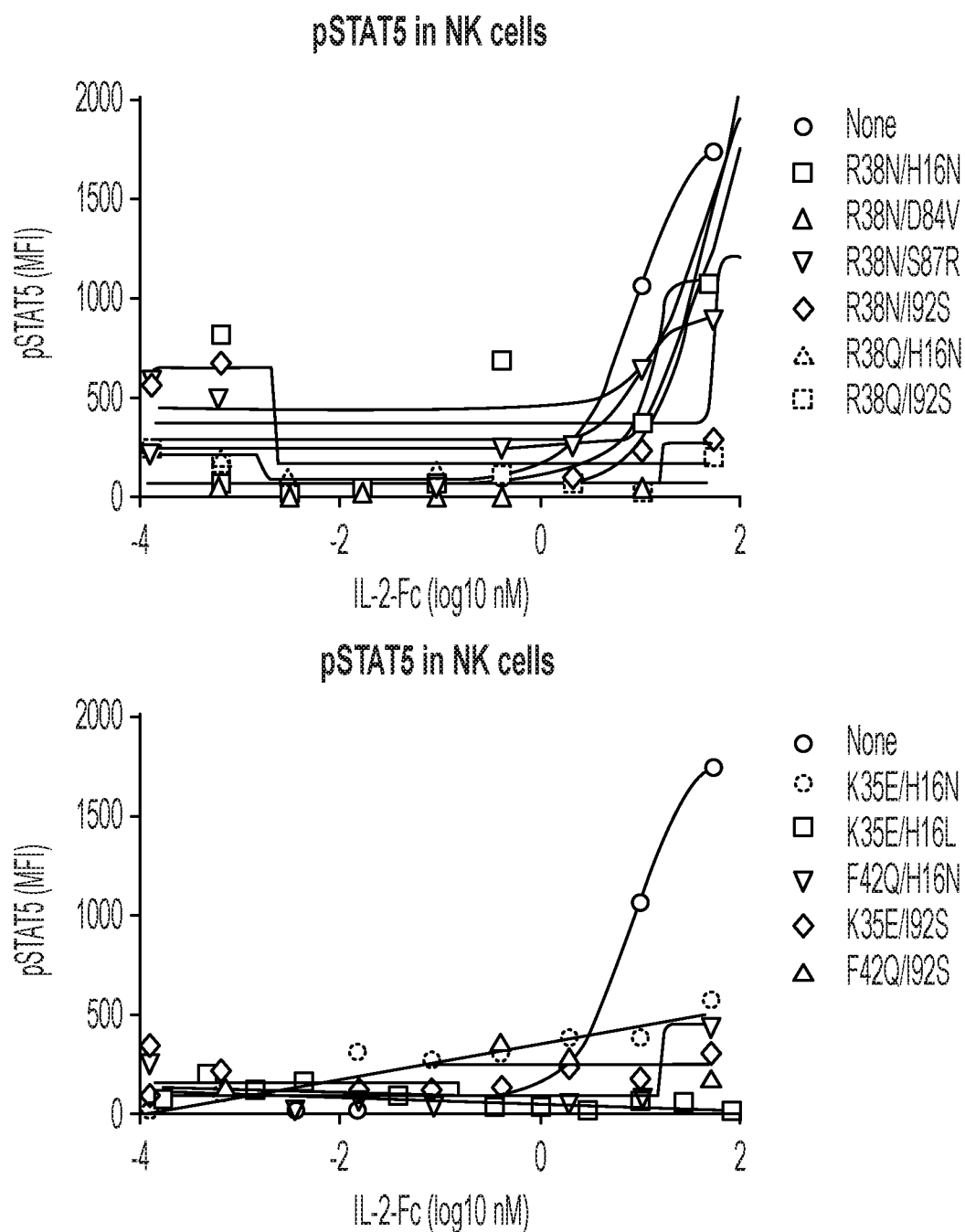


FIG. 11C

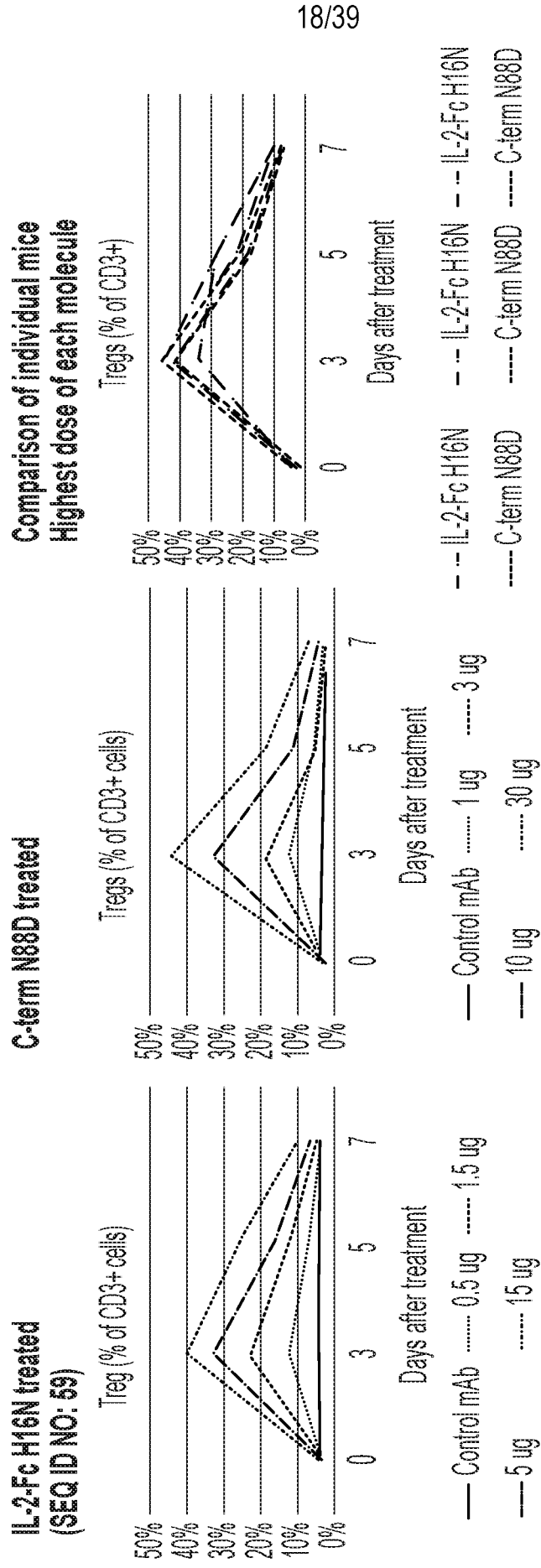
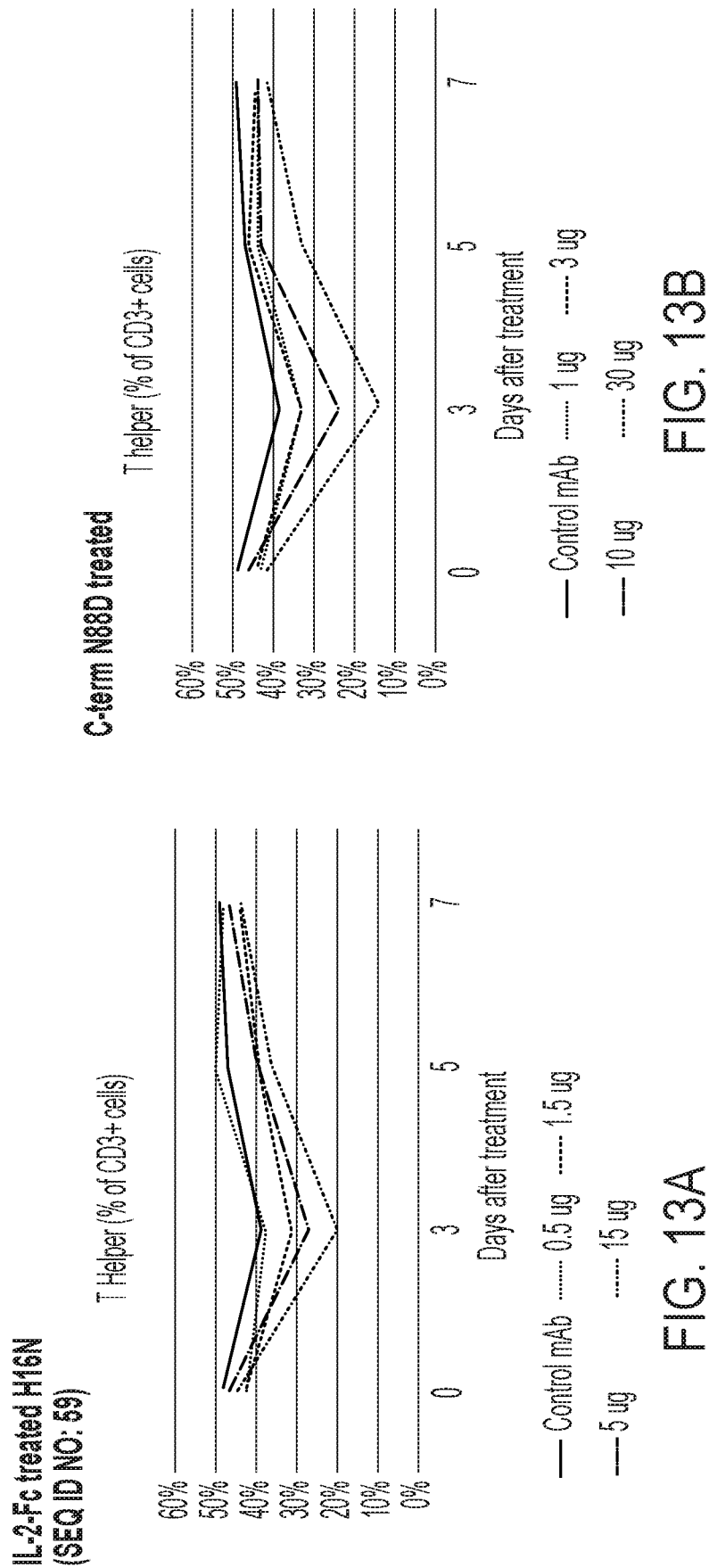


FIG. 12A

FIG. 12B

FIG. 12C



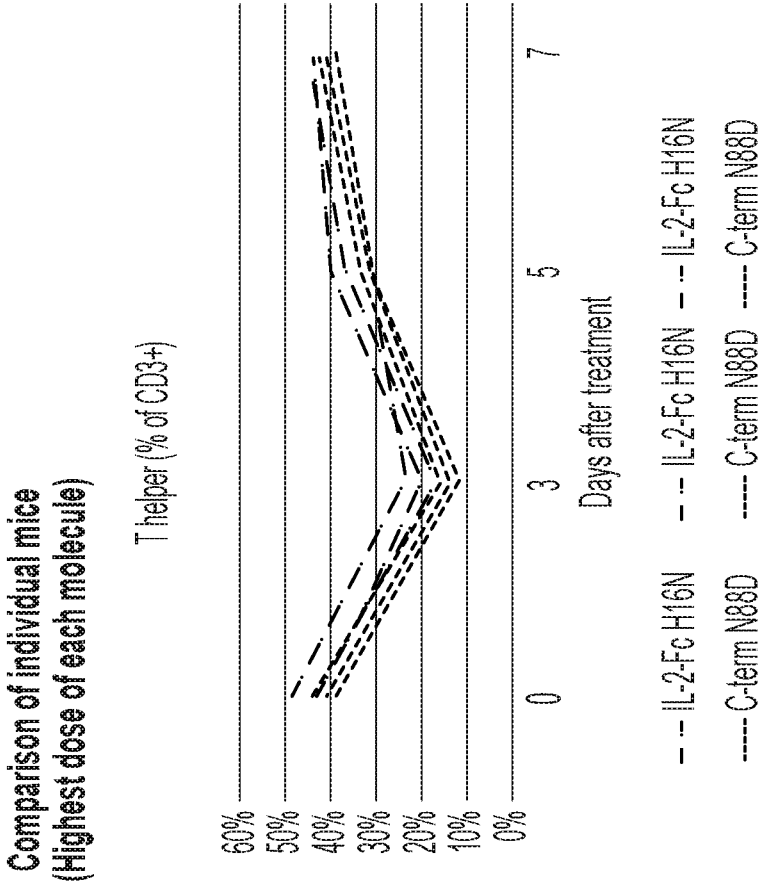


FIG. 13C

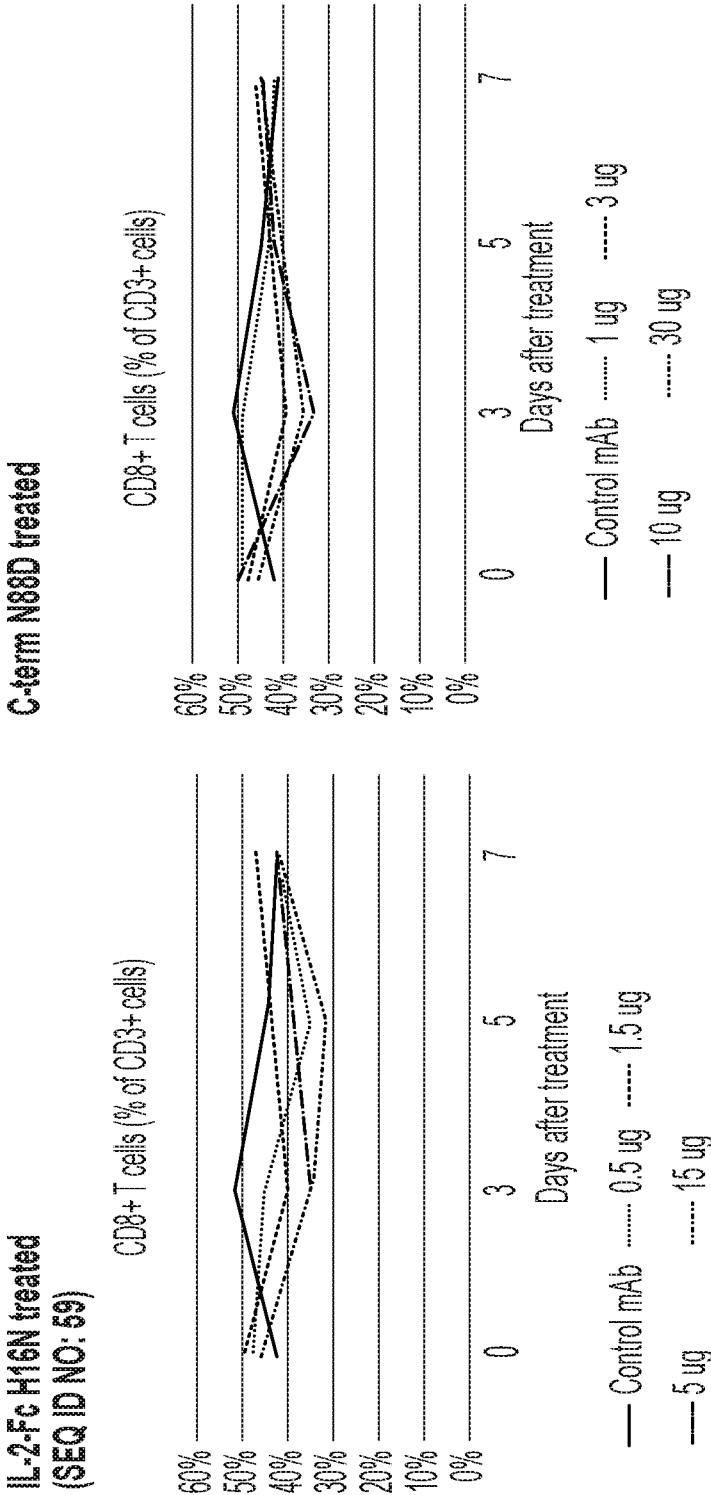


FIG. 14A

FIG. 14B

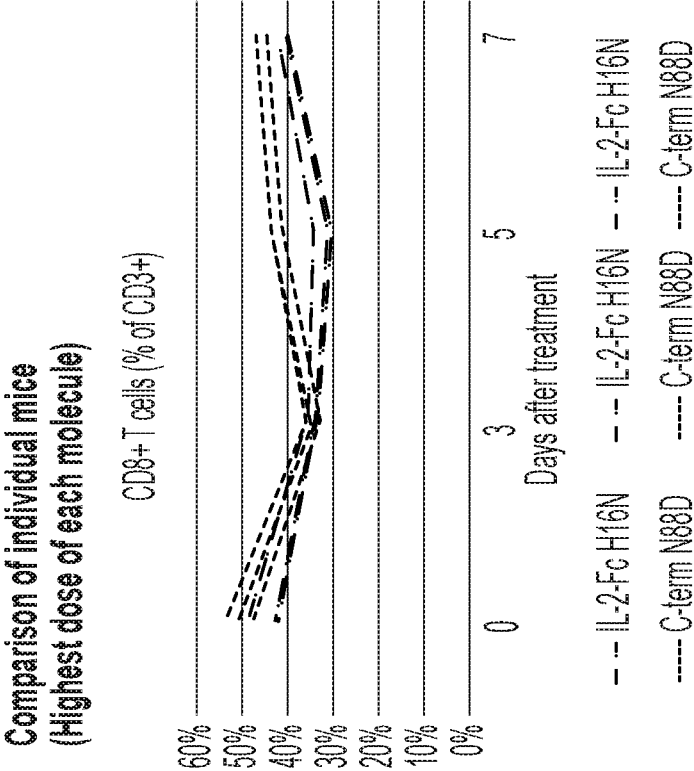
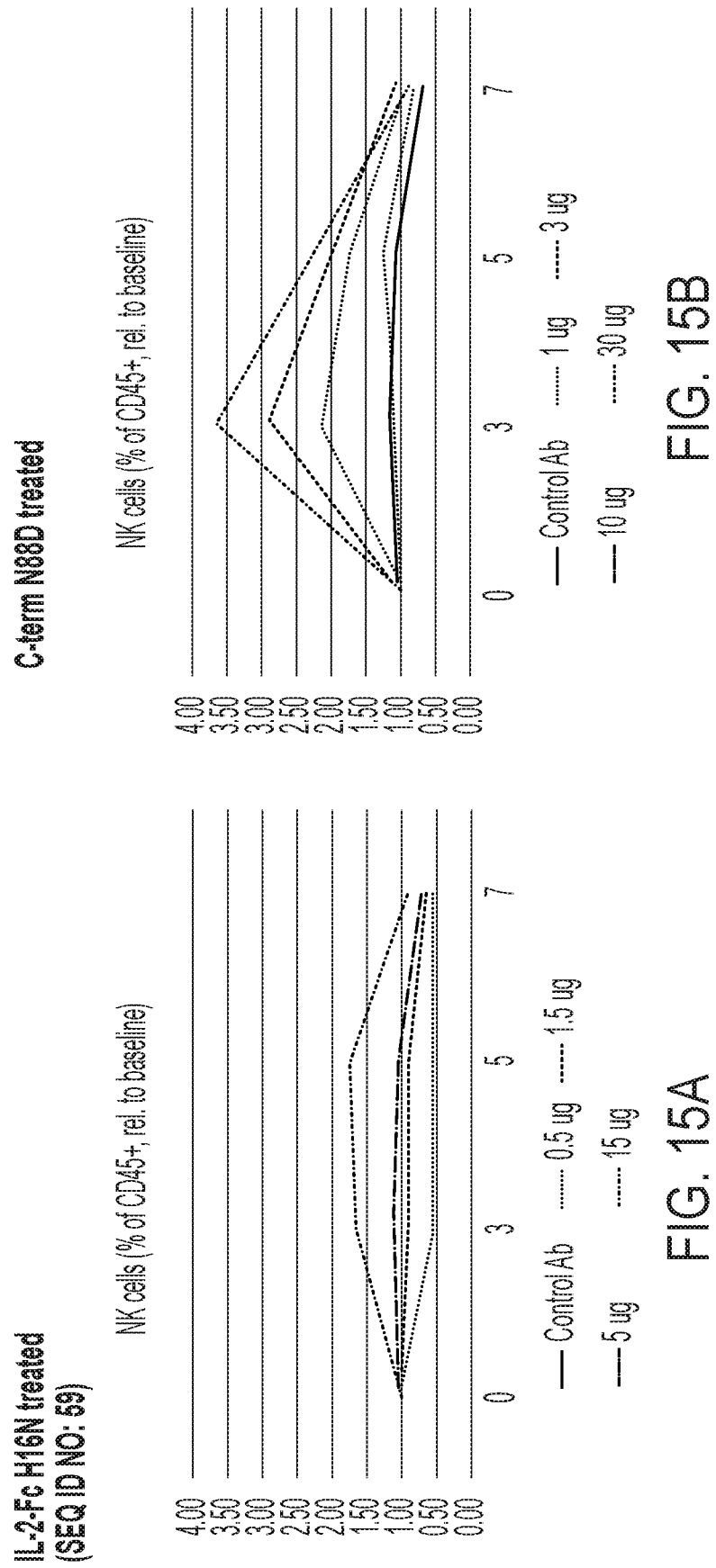


FIG. 14C



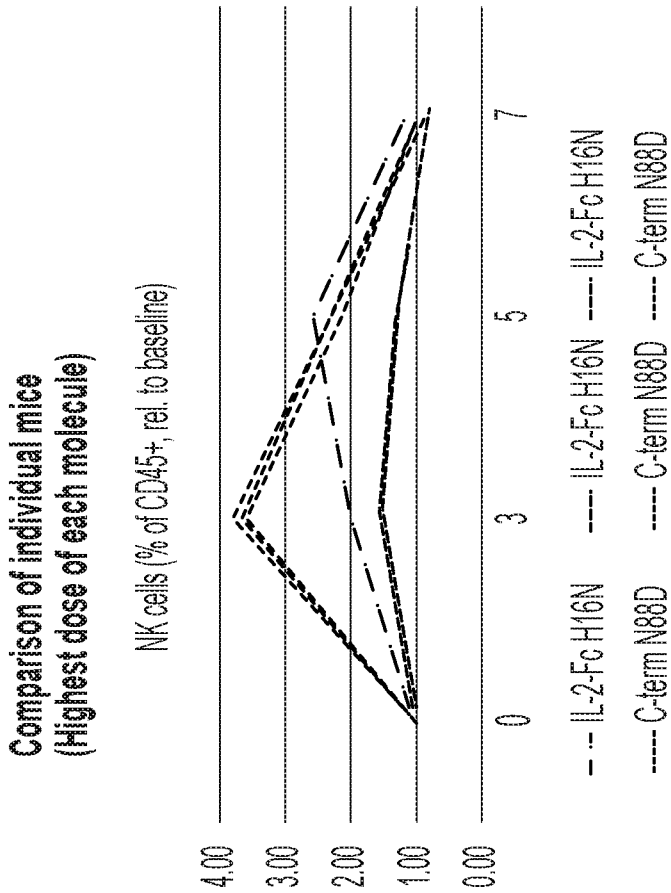


FIG. 15C

25/39

IL2-Fc Wild-type

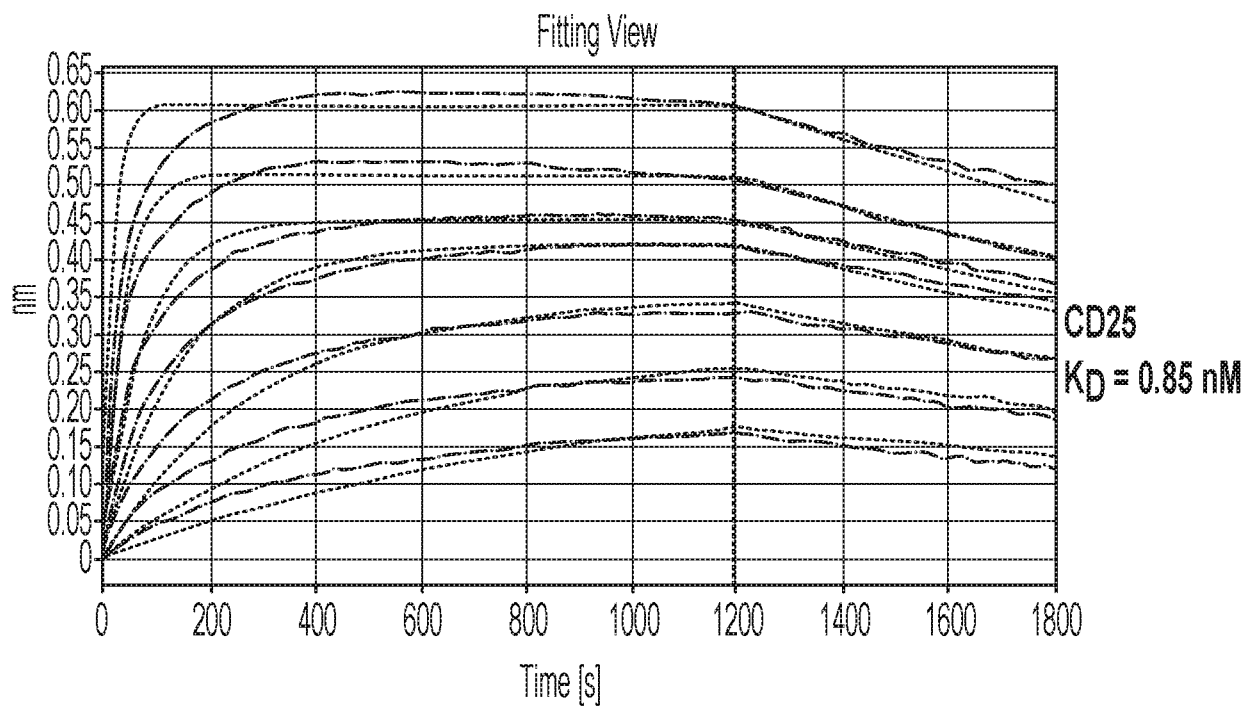
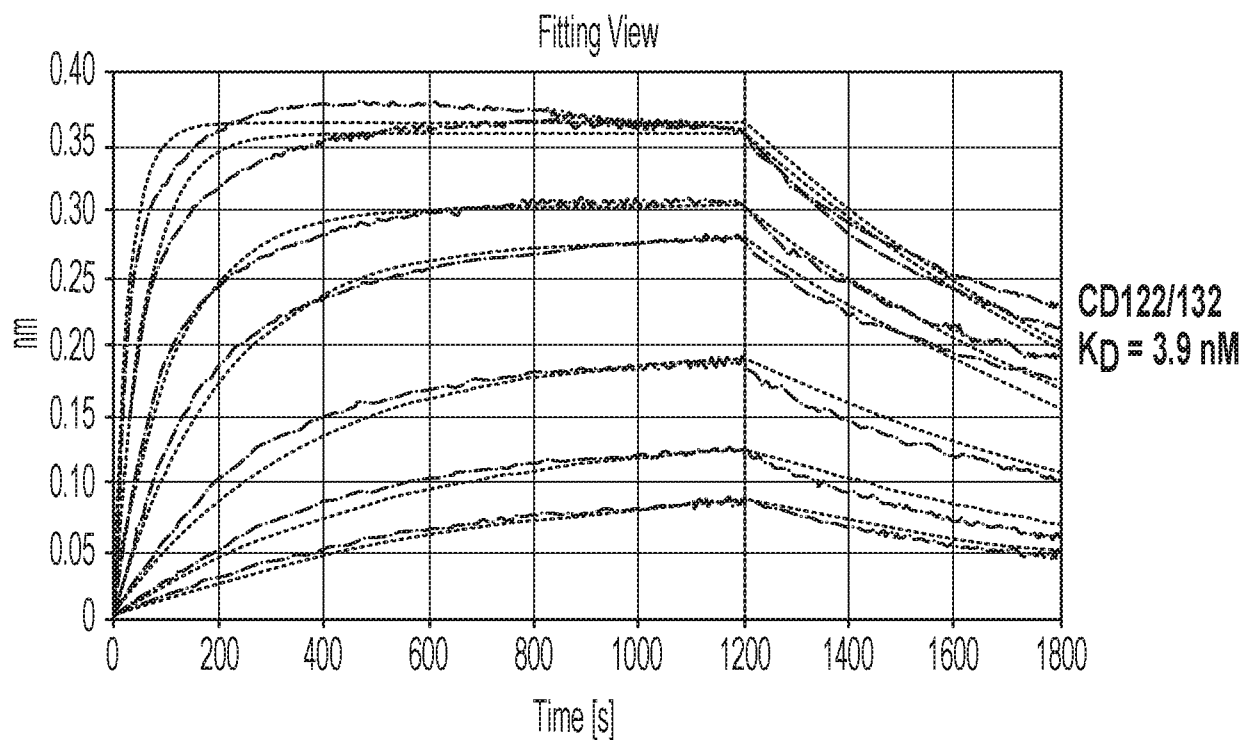
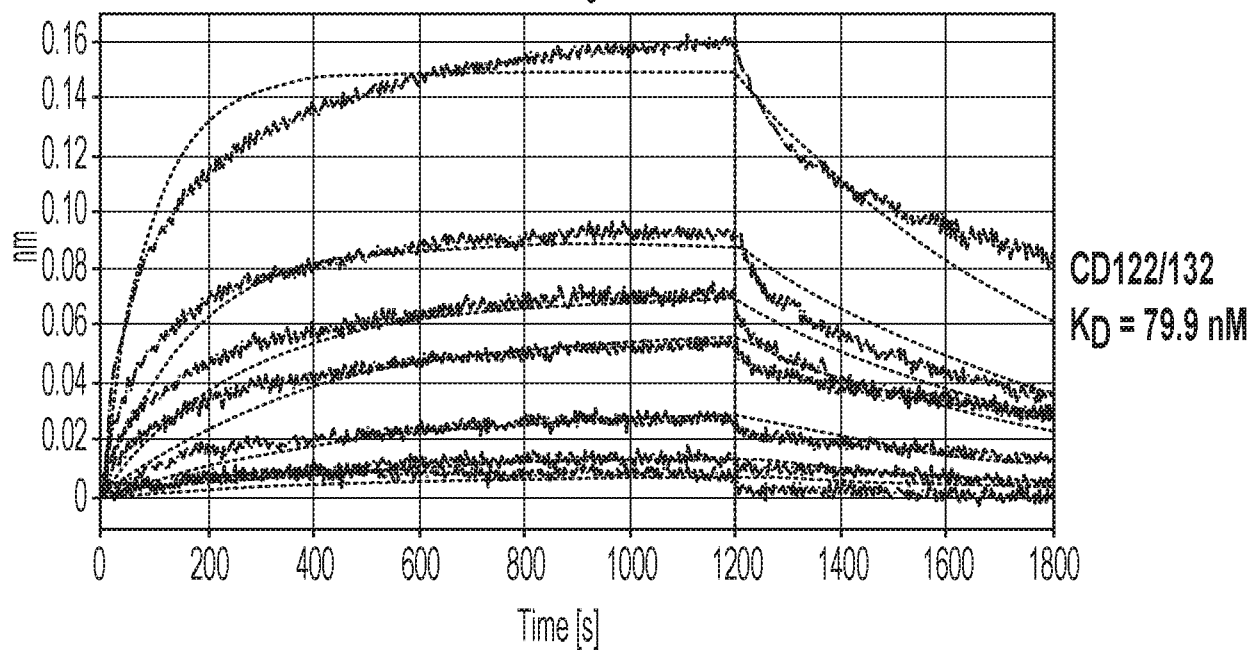


FIG. 16A

26/39

IL2-Fc Inactive

Fitting View



Fitting View

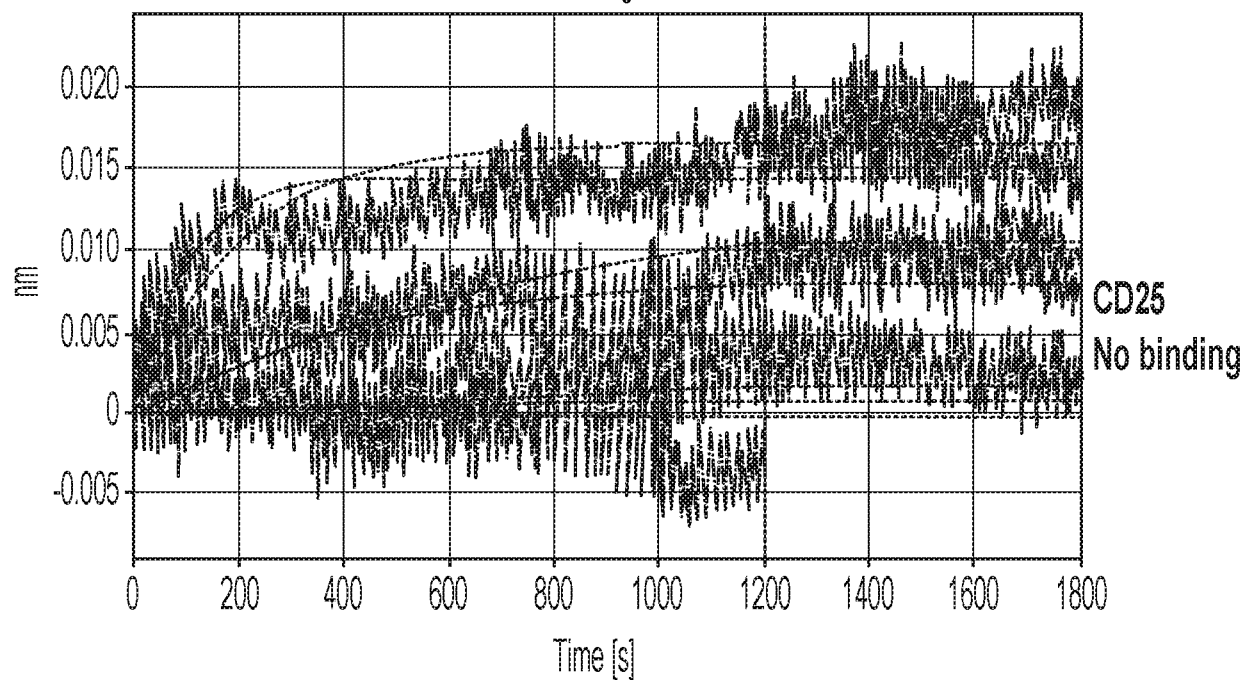


FIG. 16B

27/39

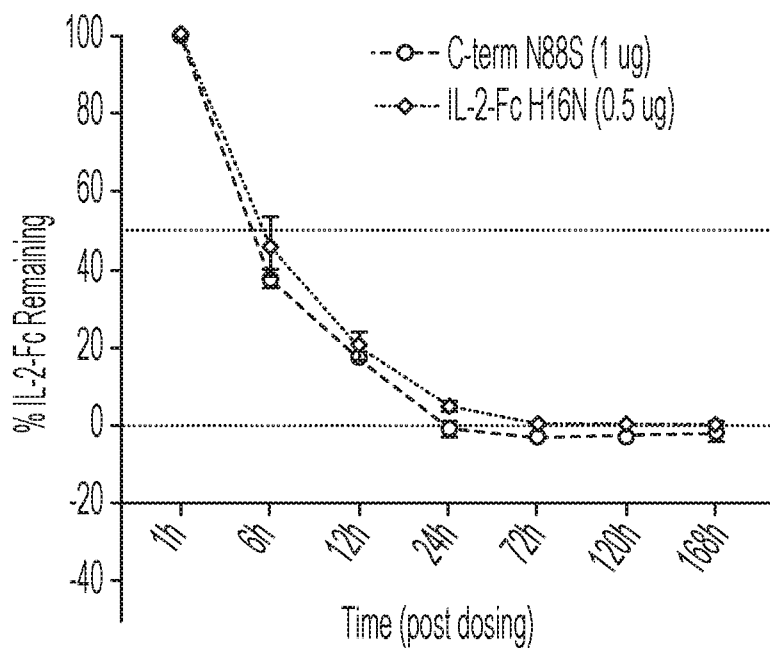


FIG. 17A

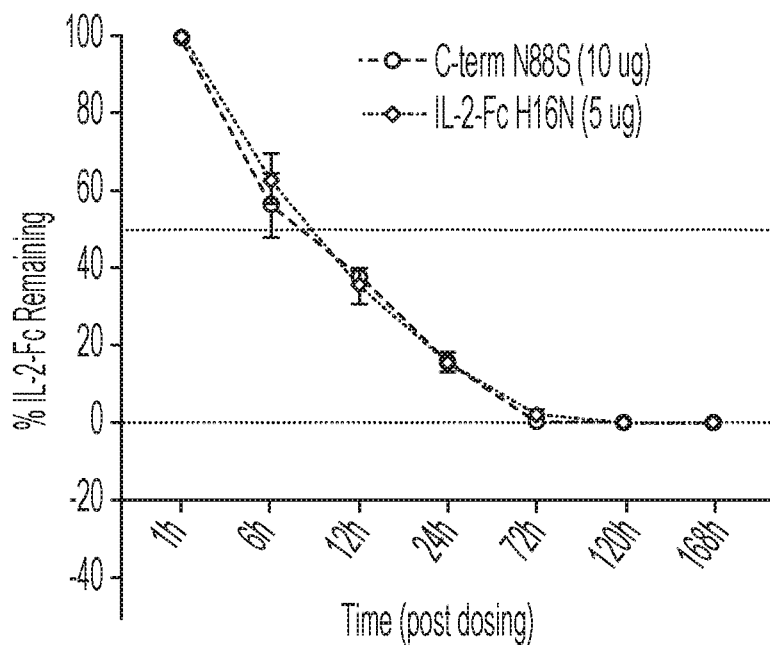


FIG. 17B

28/39

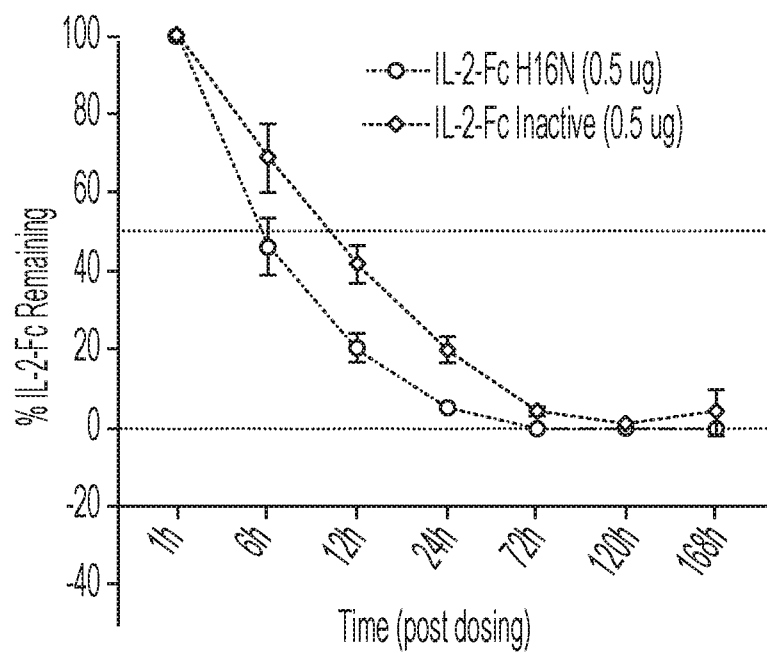


FIG. 17C

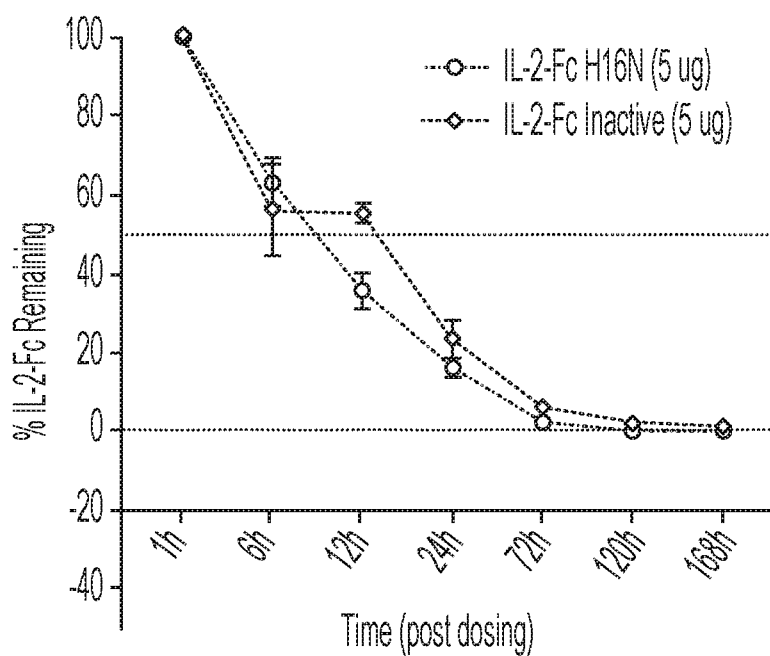


FIG. 17D

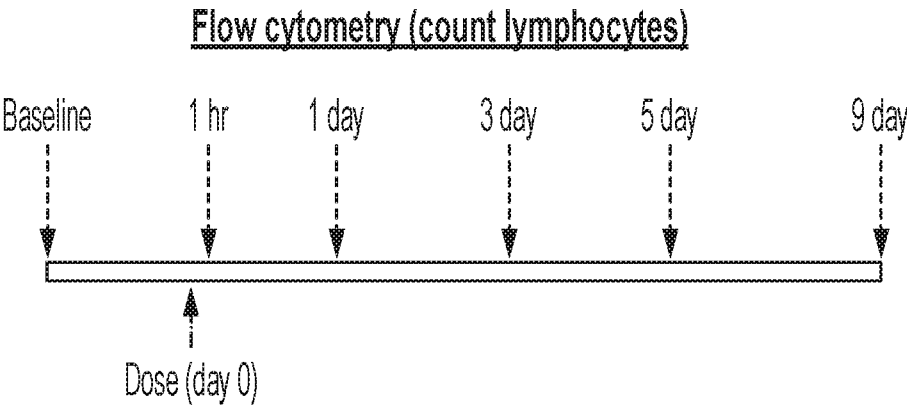


FIG. 18A

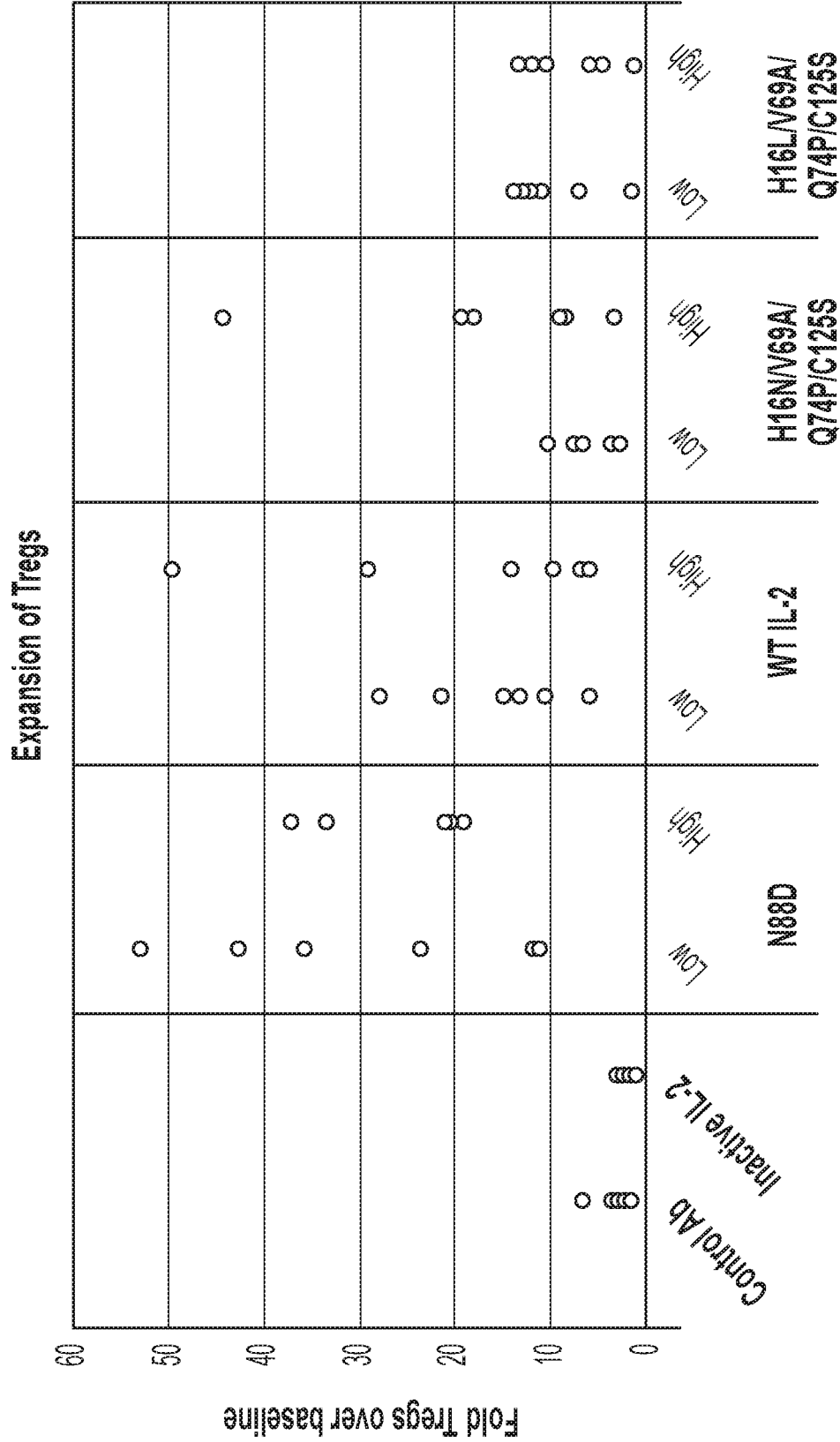
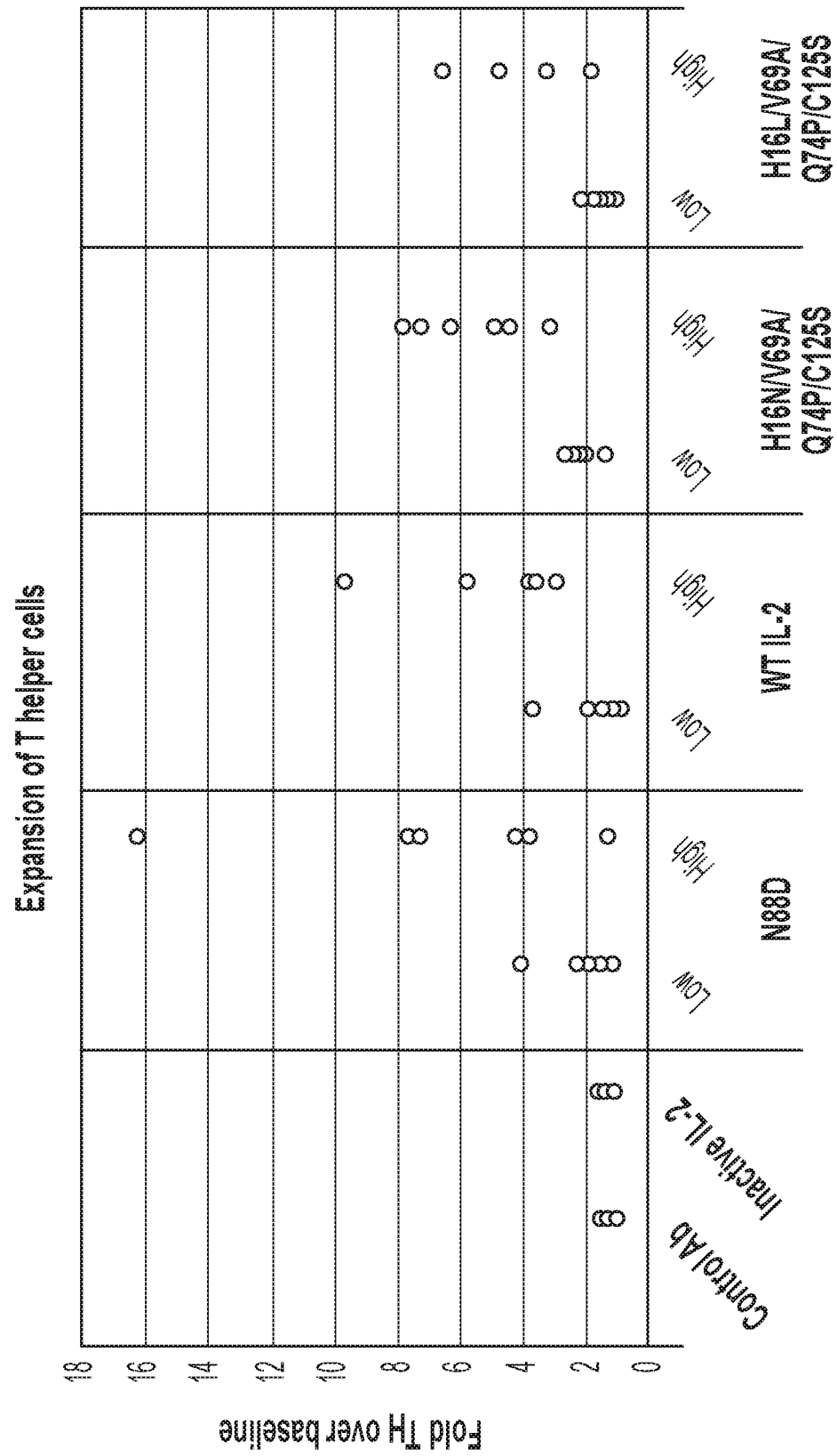


FIG. 18B



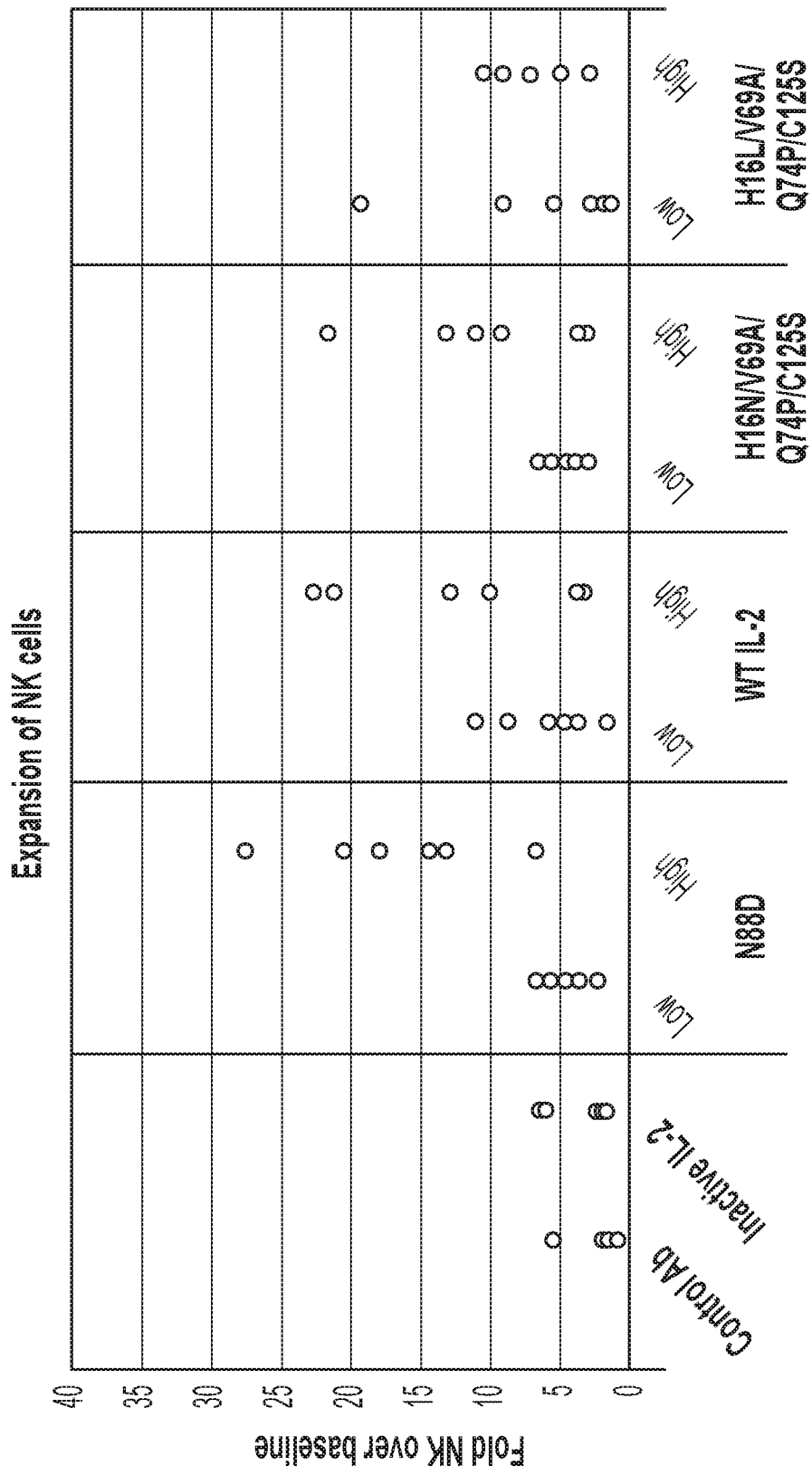


FIG. 18D

33/39

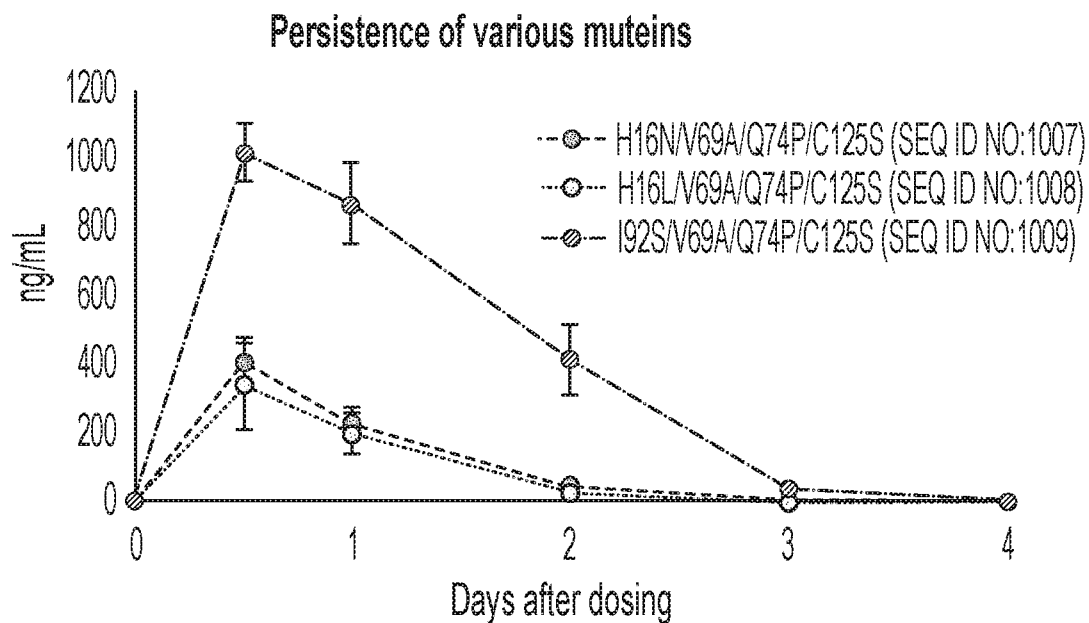


FIG. 19A

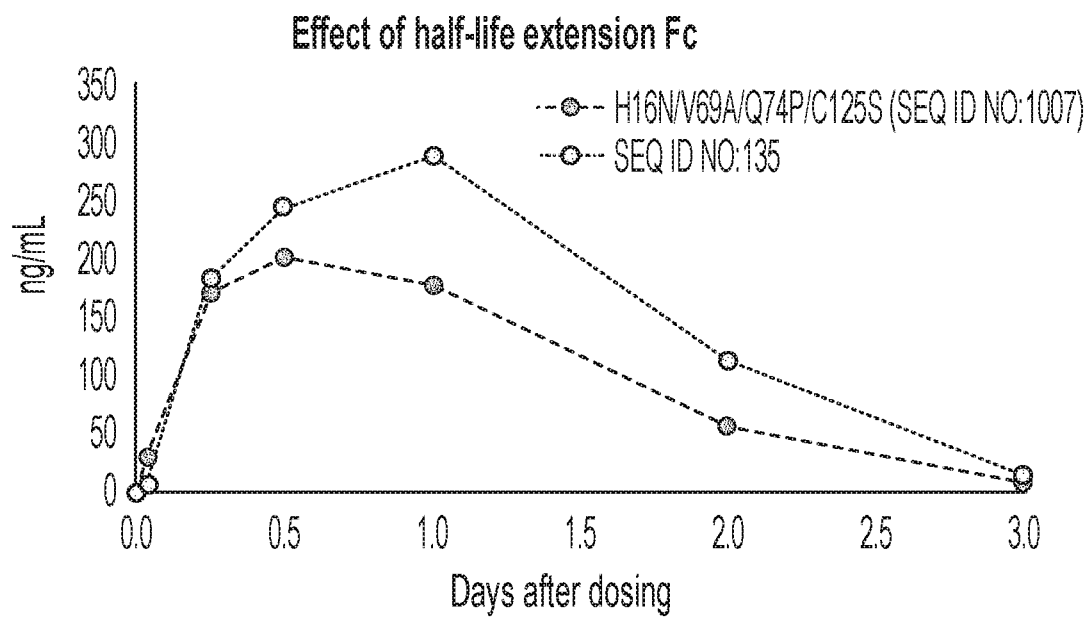


FIG. 19B

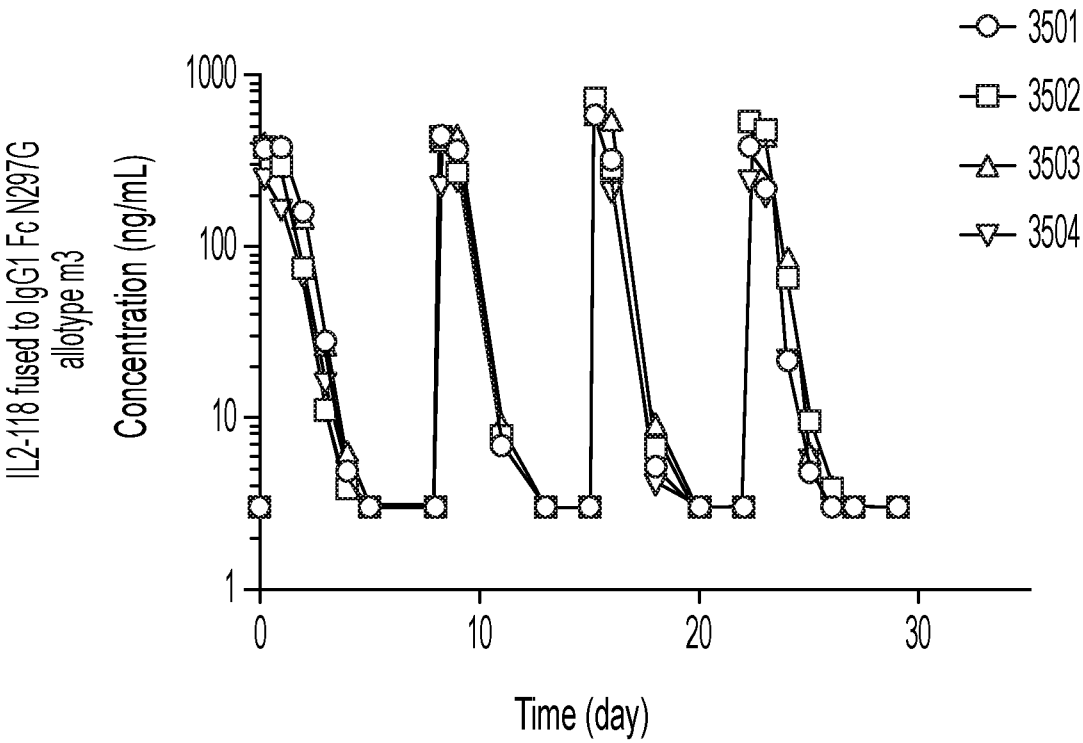


FIG. 20

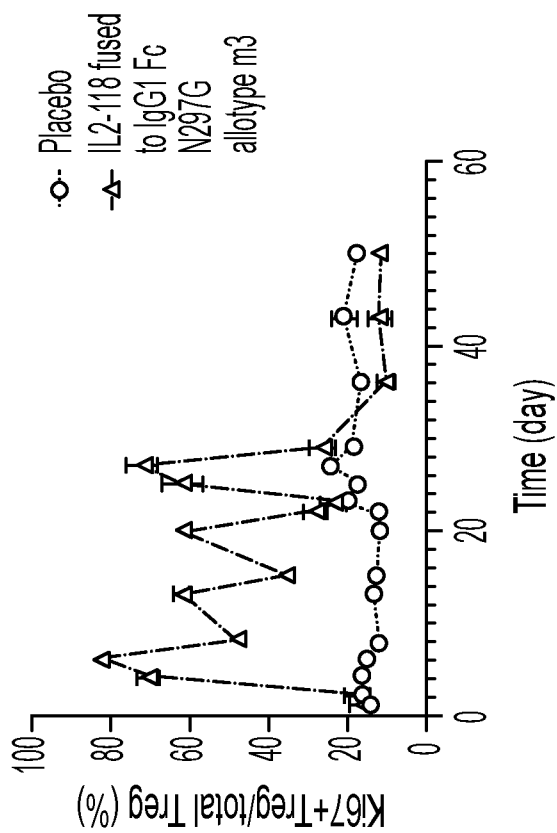


FIG. 21B

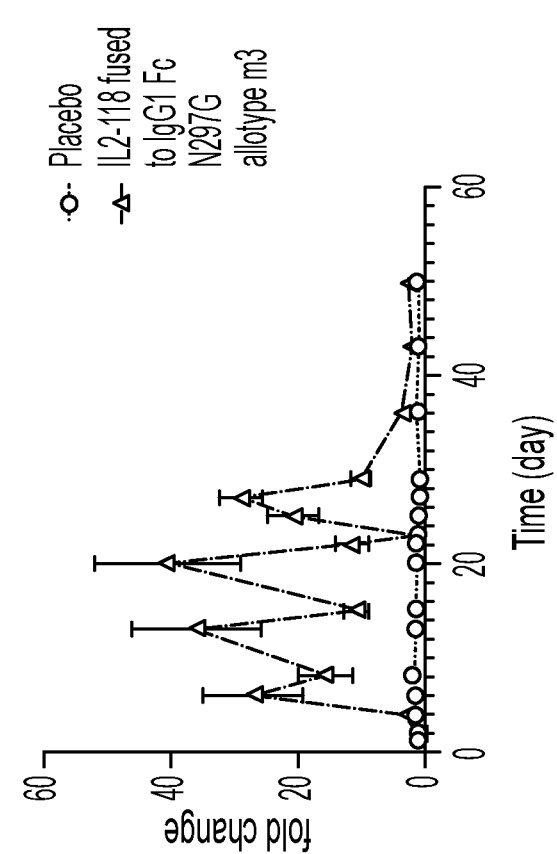


FIG. 21A

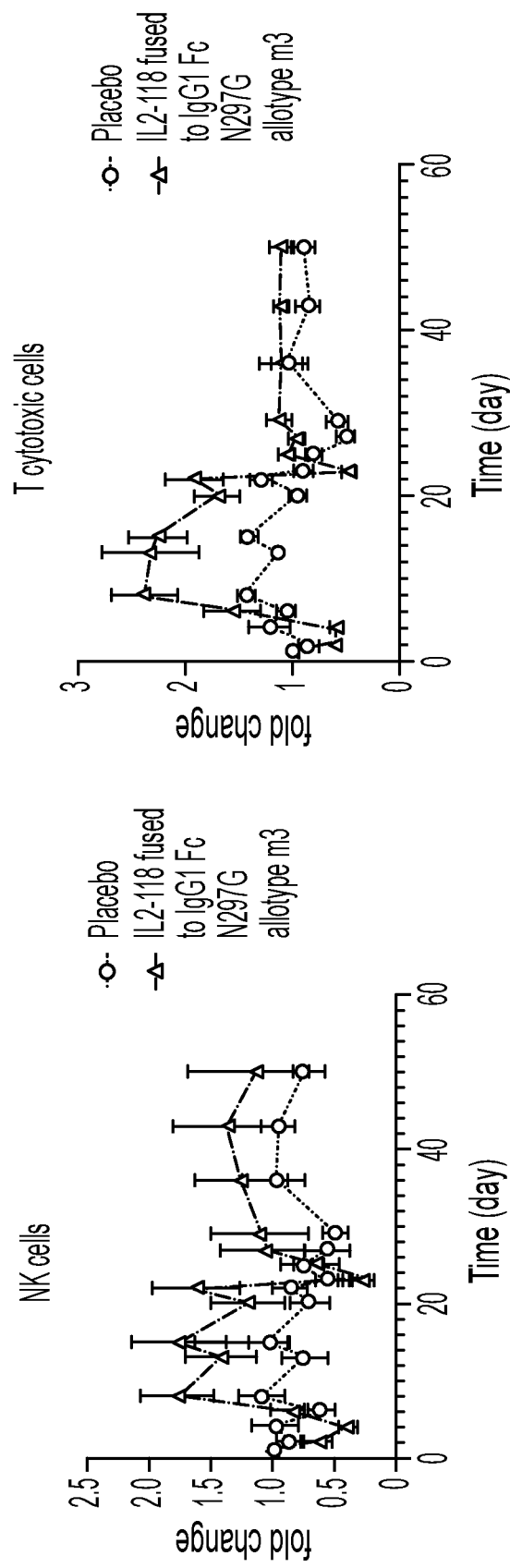


FIG. 22A

FIG. 22B

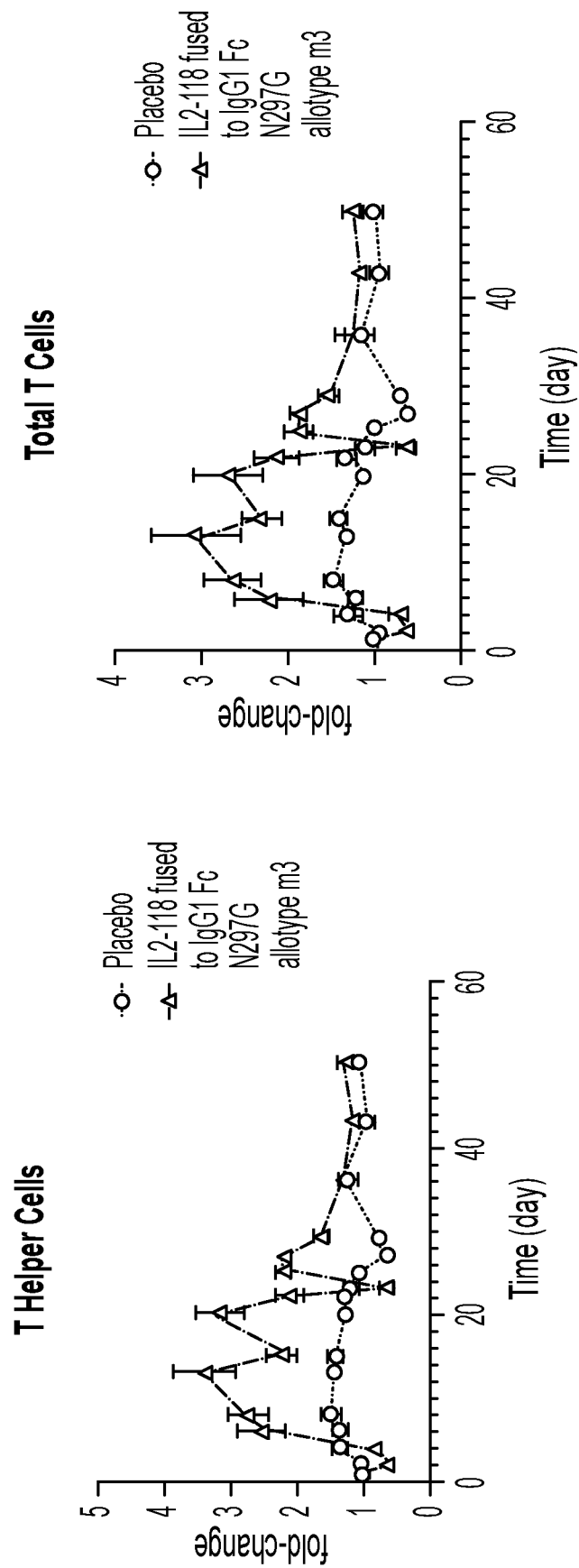


FIG. 22C

FIG. 22D

38/39

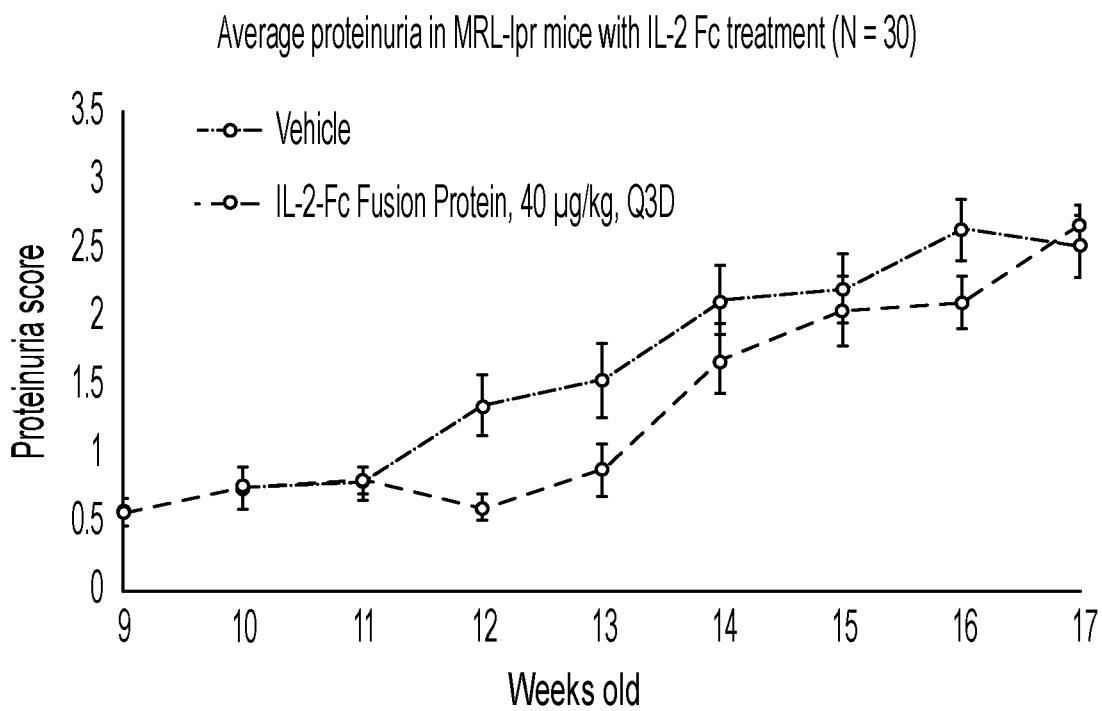


FIG. 23A

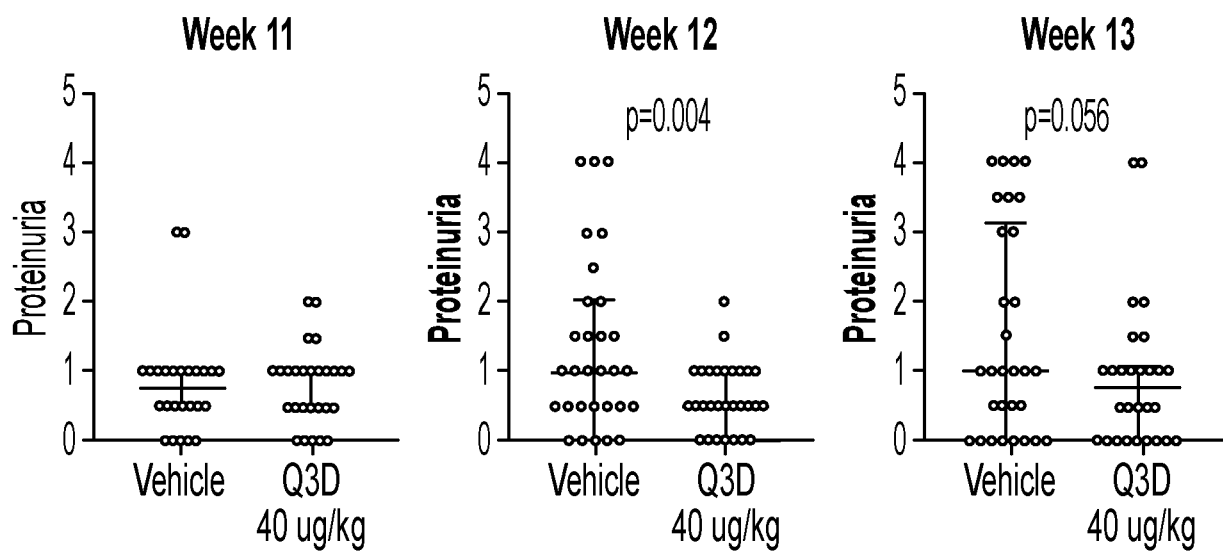


FIG. 23B

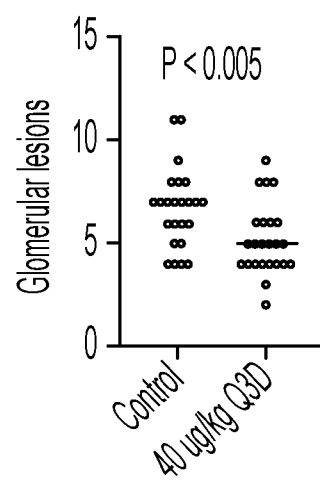


FIG. 23C