

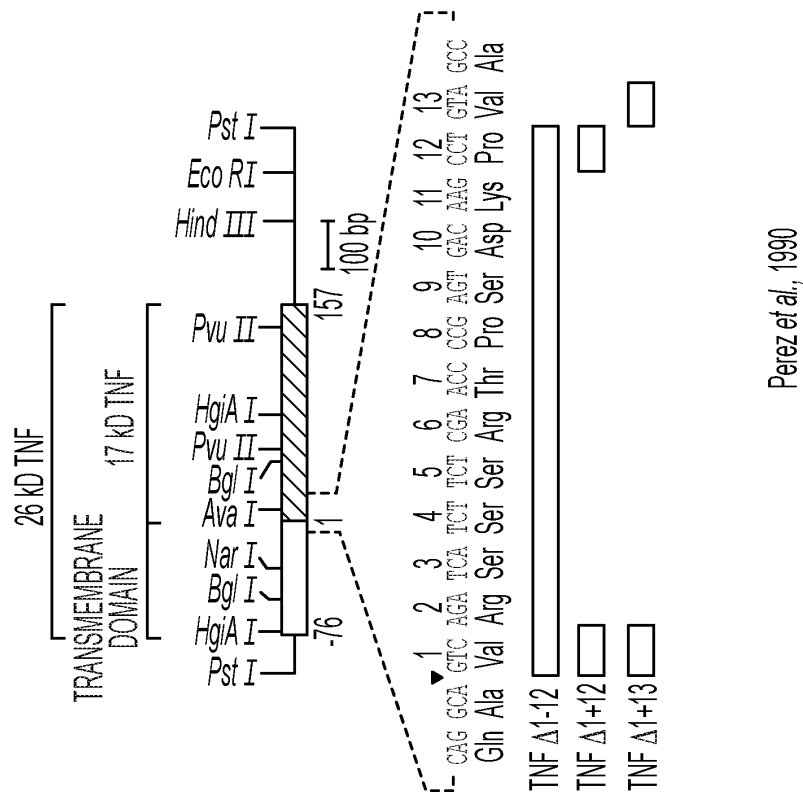


FIG. 1

TNFa mutant- delVal1 and delPro12

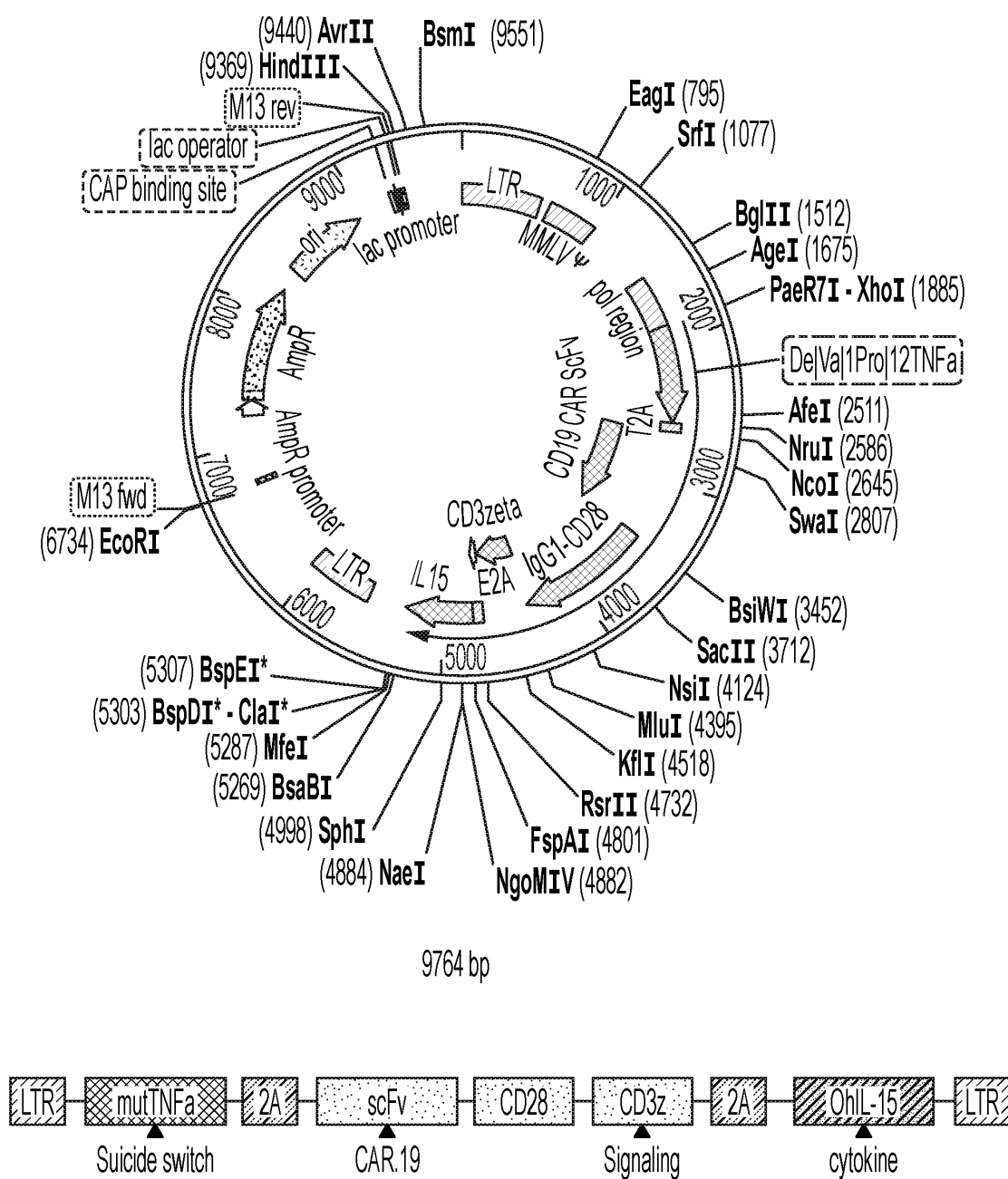


FIG. 2A

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TNFa mutant- delVal13

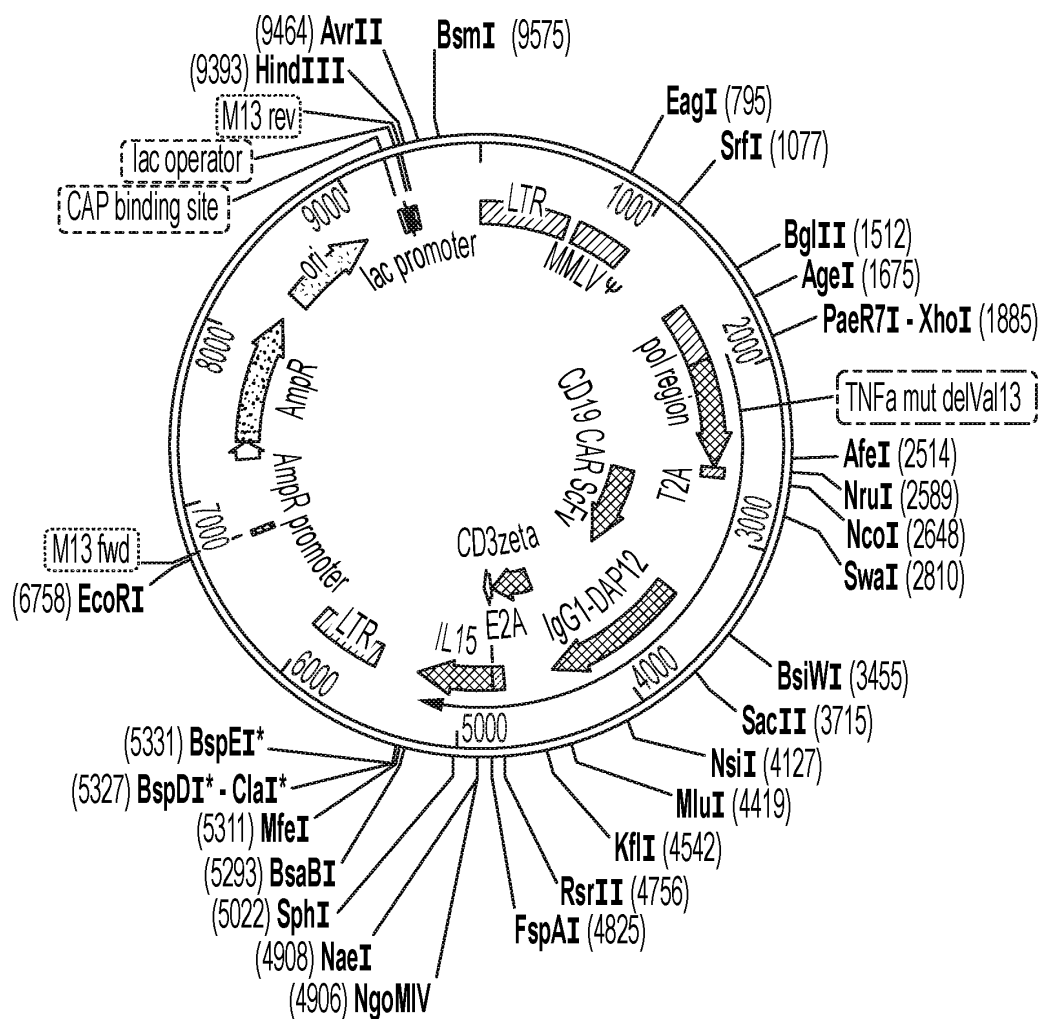


FIG. 2B

TNF α mutant- delVal1 and delVal13

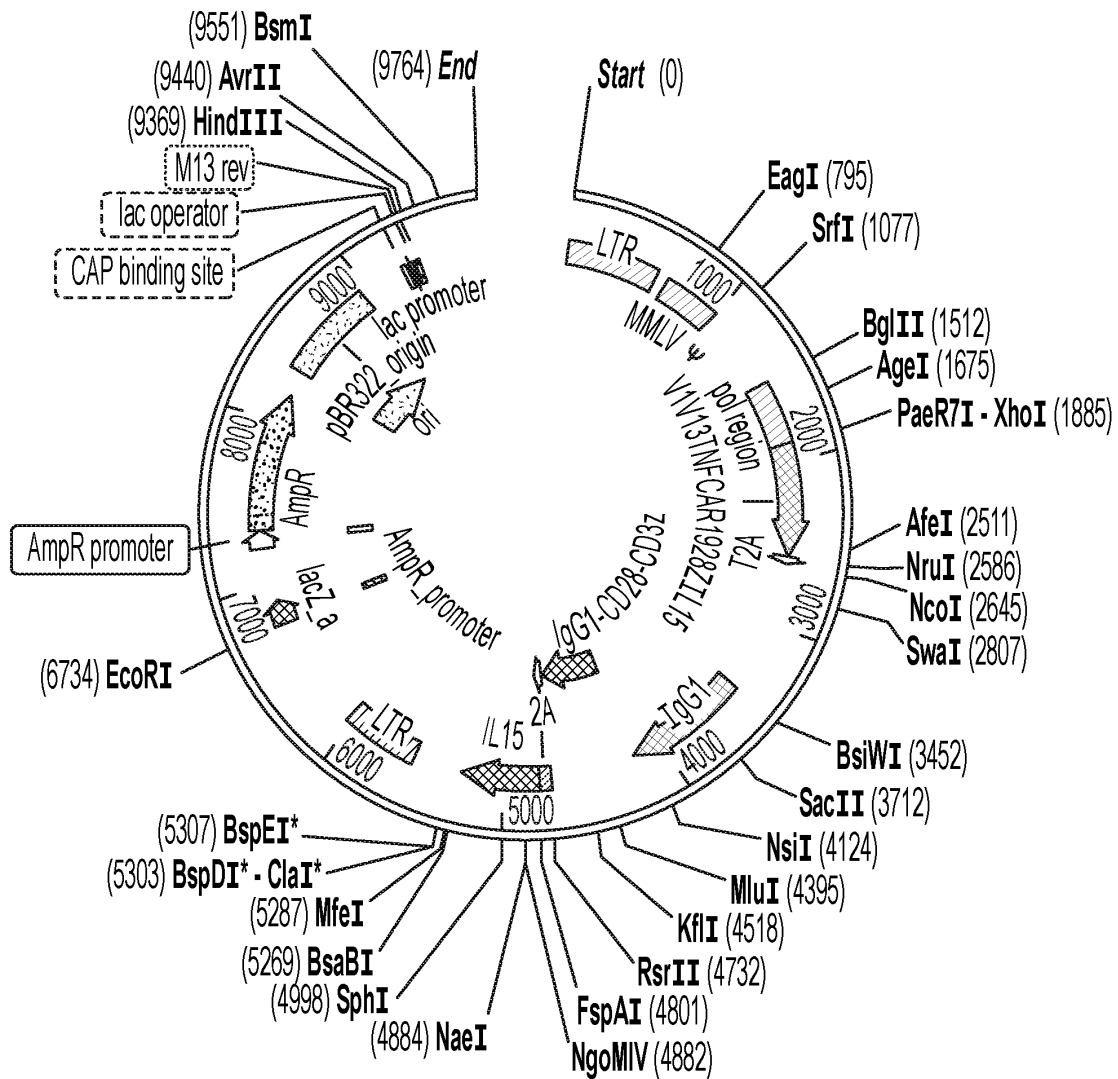


FIG. 2C

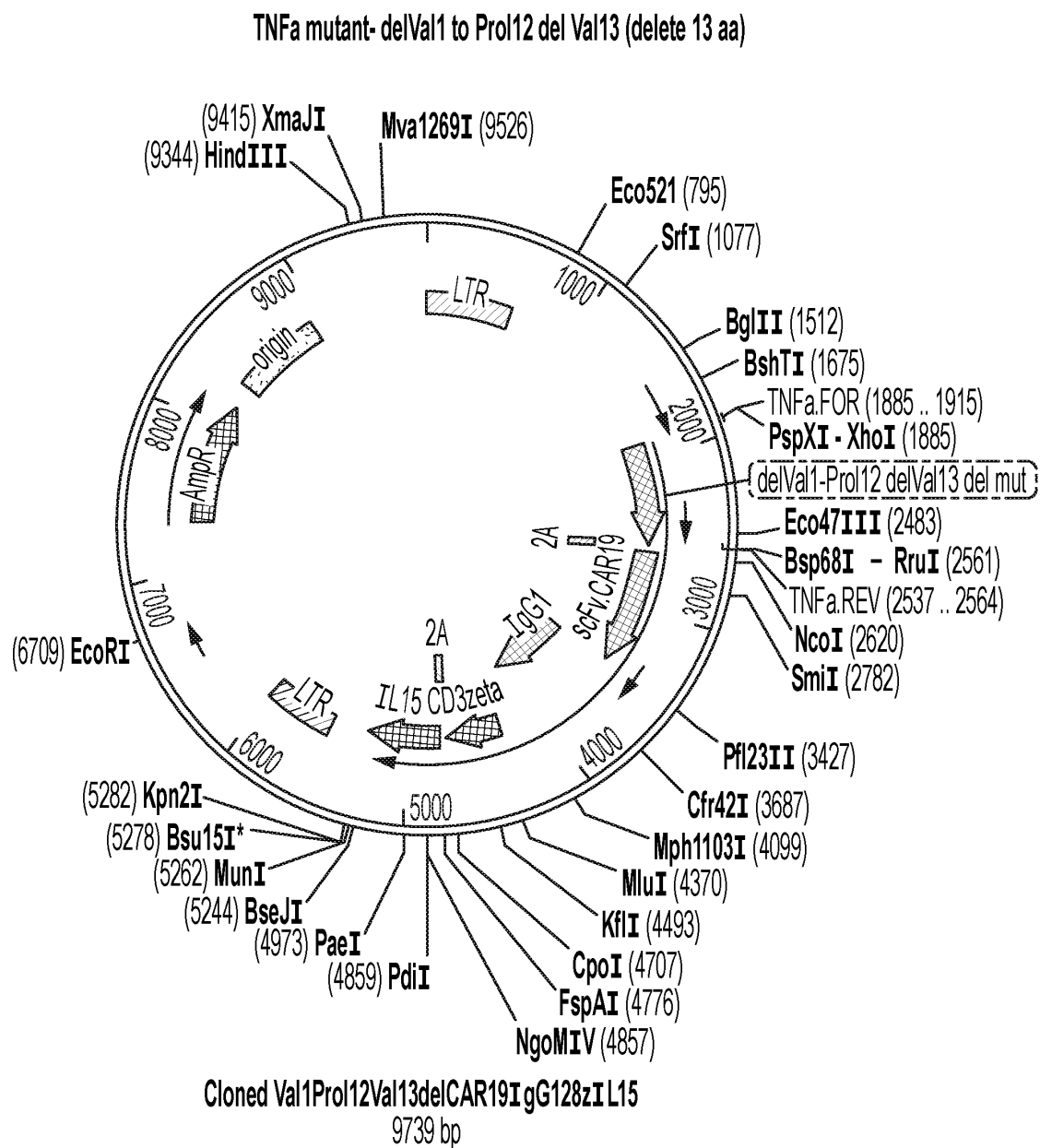


FIG. 2D

TNFa mutant- delAla-1 to Val13 (delete 14aa)

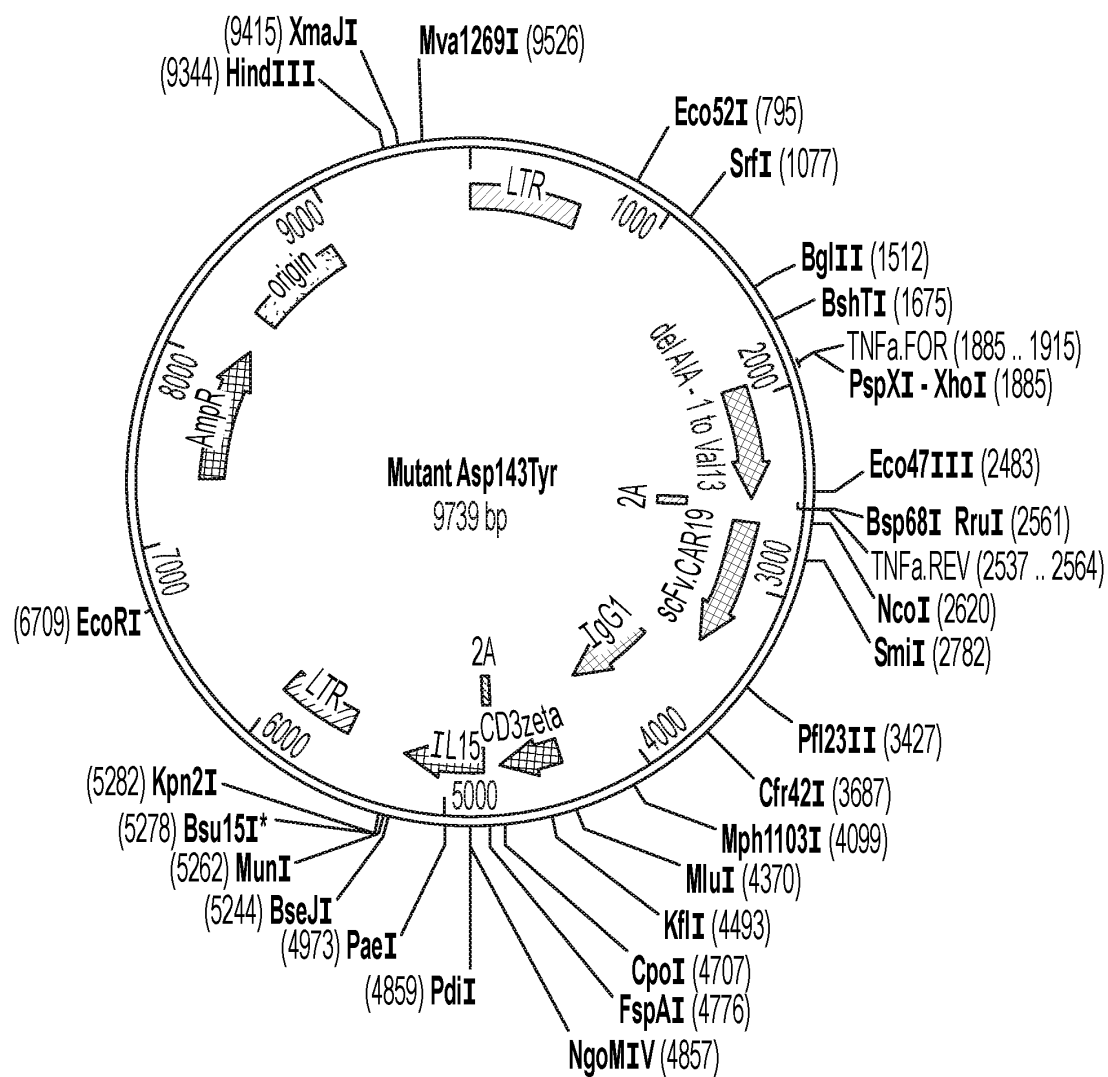


FIG. 2E

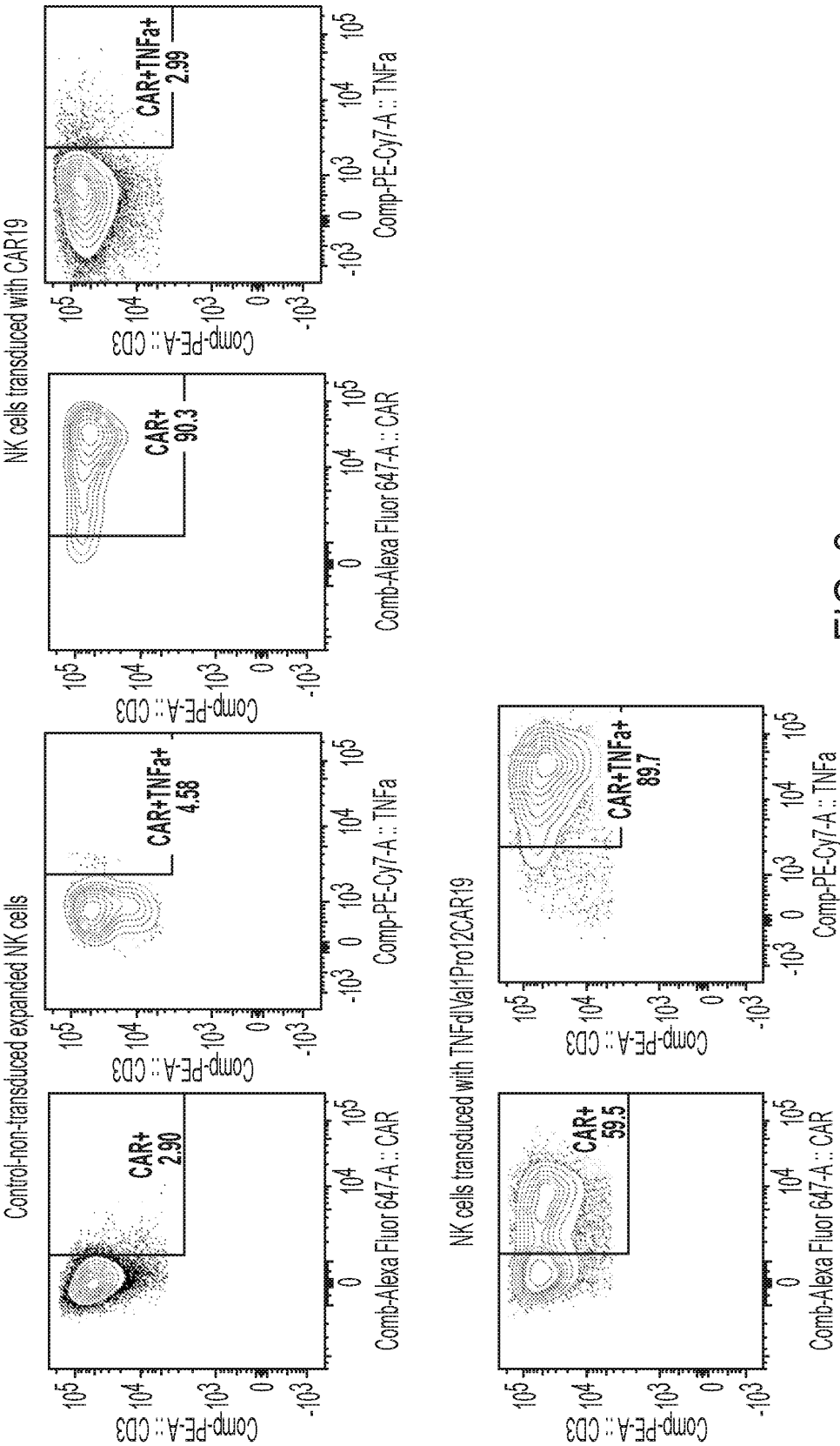
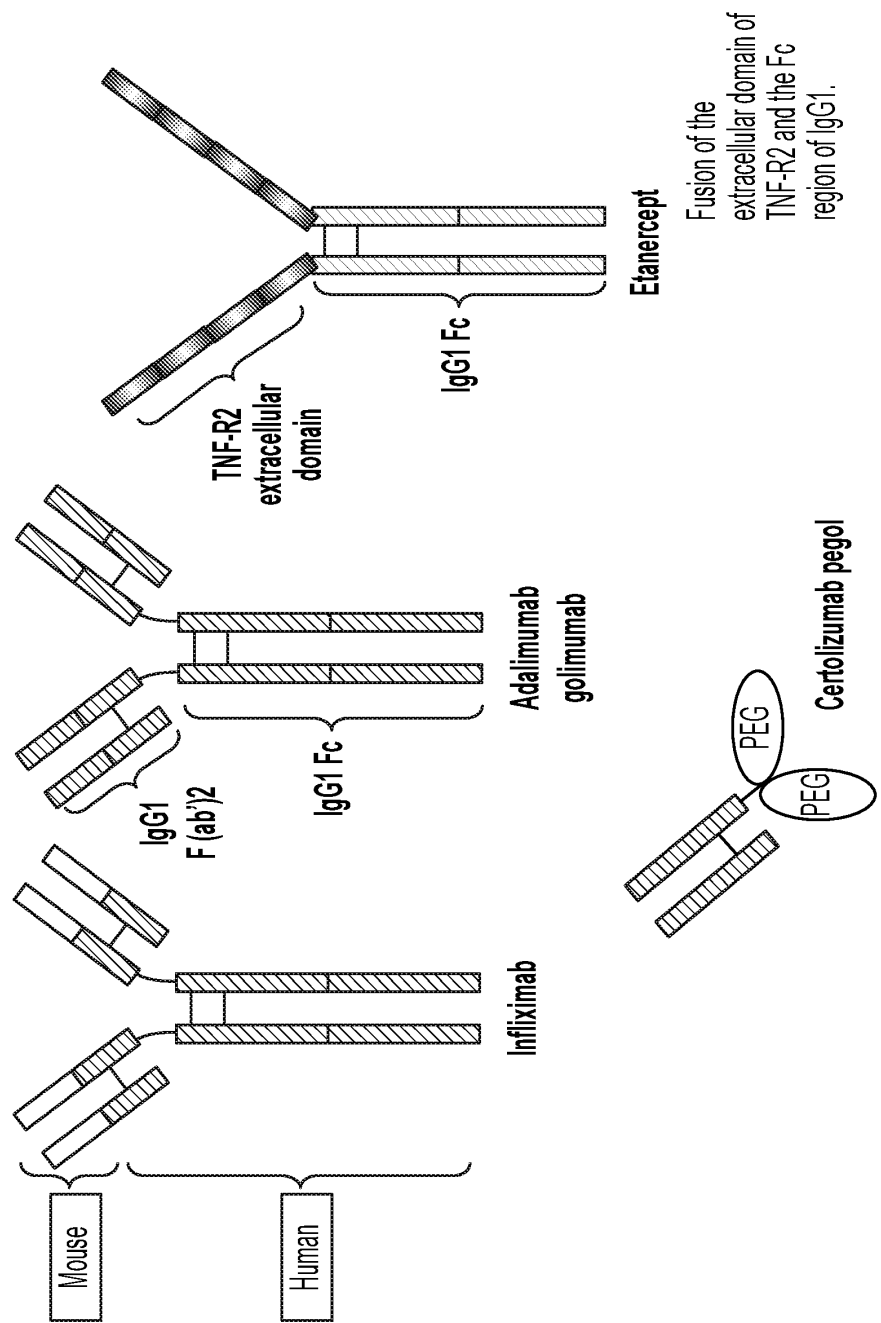


FIG. 3



PEGylated Fab' fragment of humanized monoclonal anti-TNF antibody.

FIG. 4A

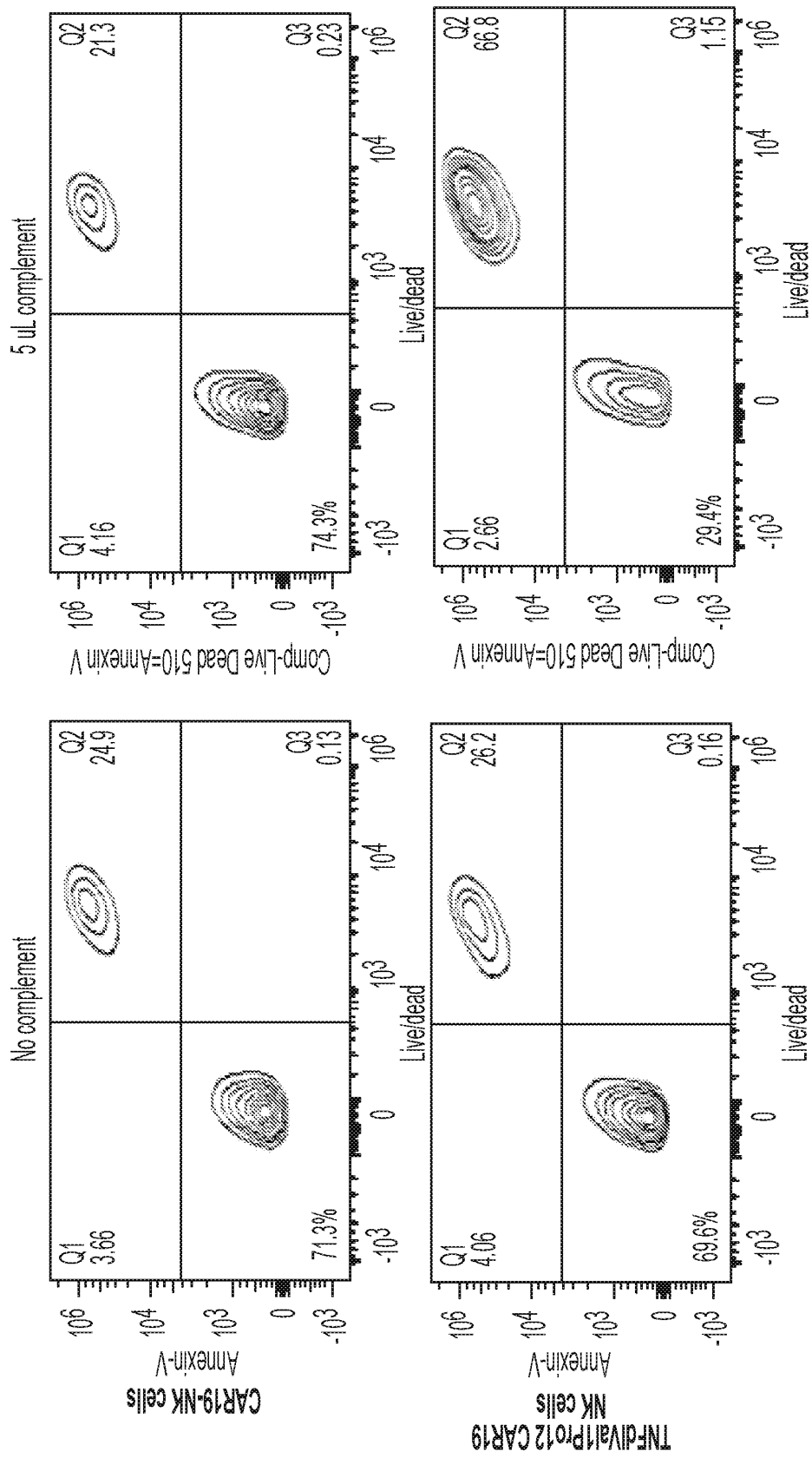


FIG. 4B

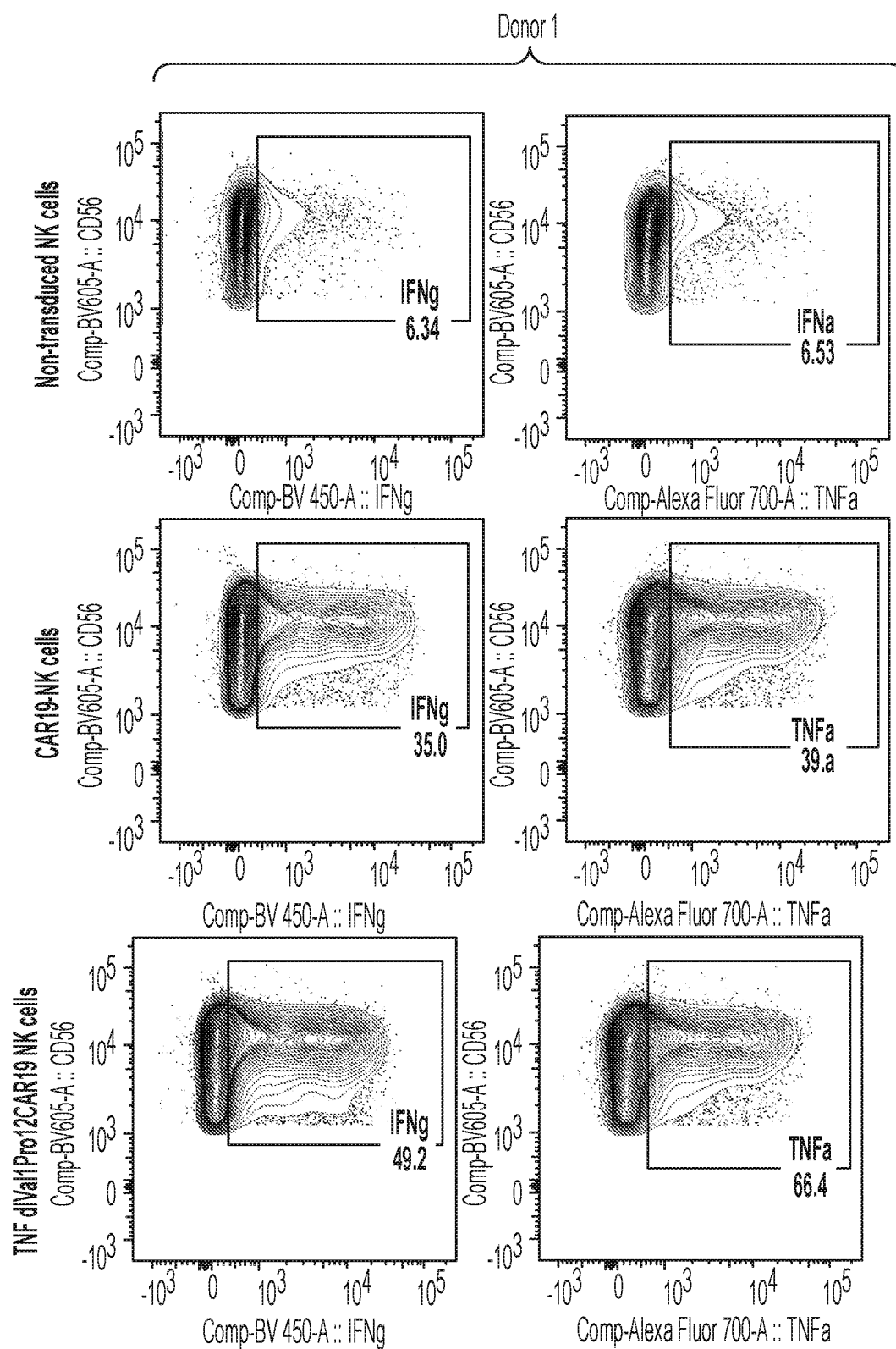


FIG. 5A

SUBSTITUTE SHEET (RULE 26)

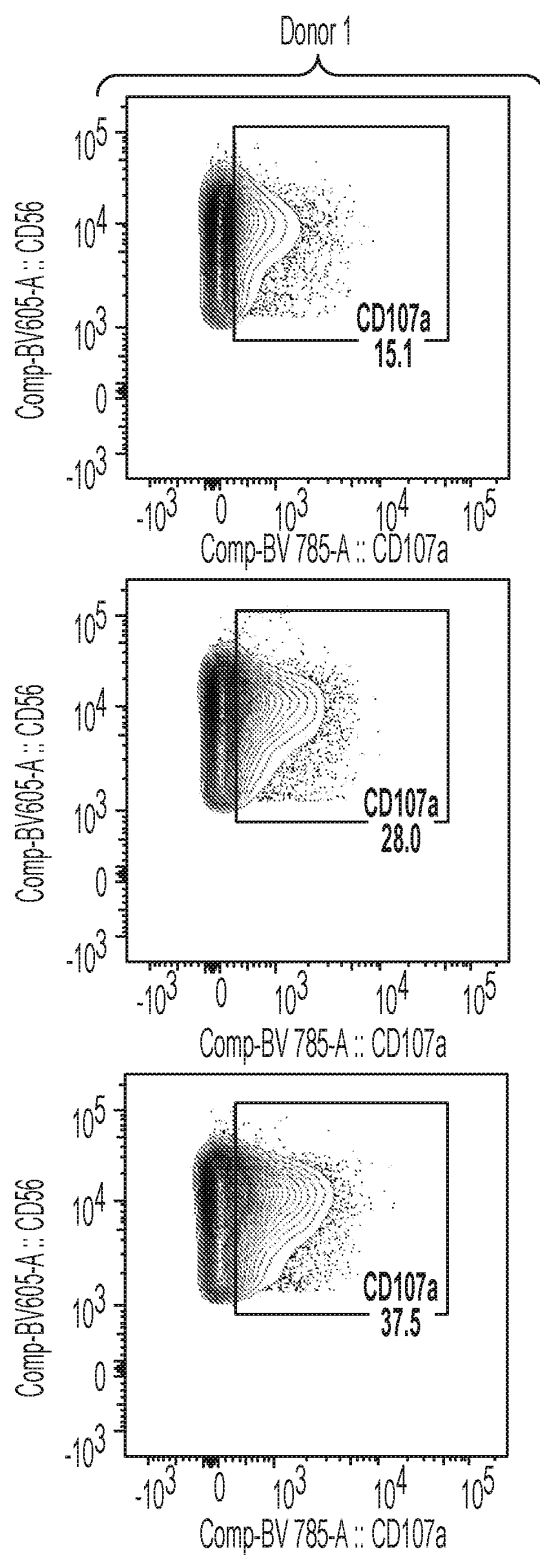


FIG. 5A
CONTINUED

SUBSTITUTE SHEET (RULE 26)

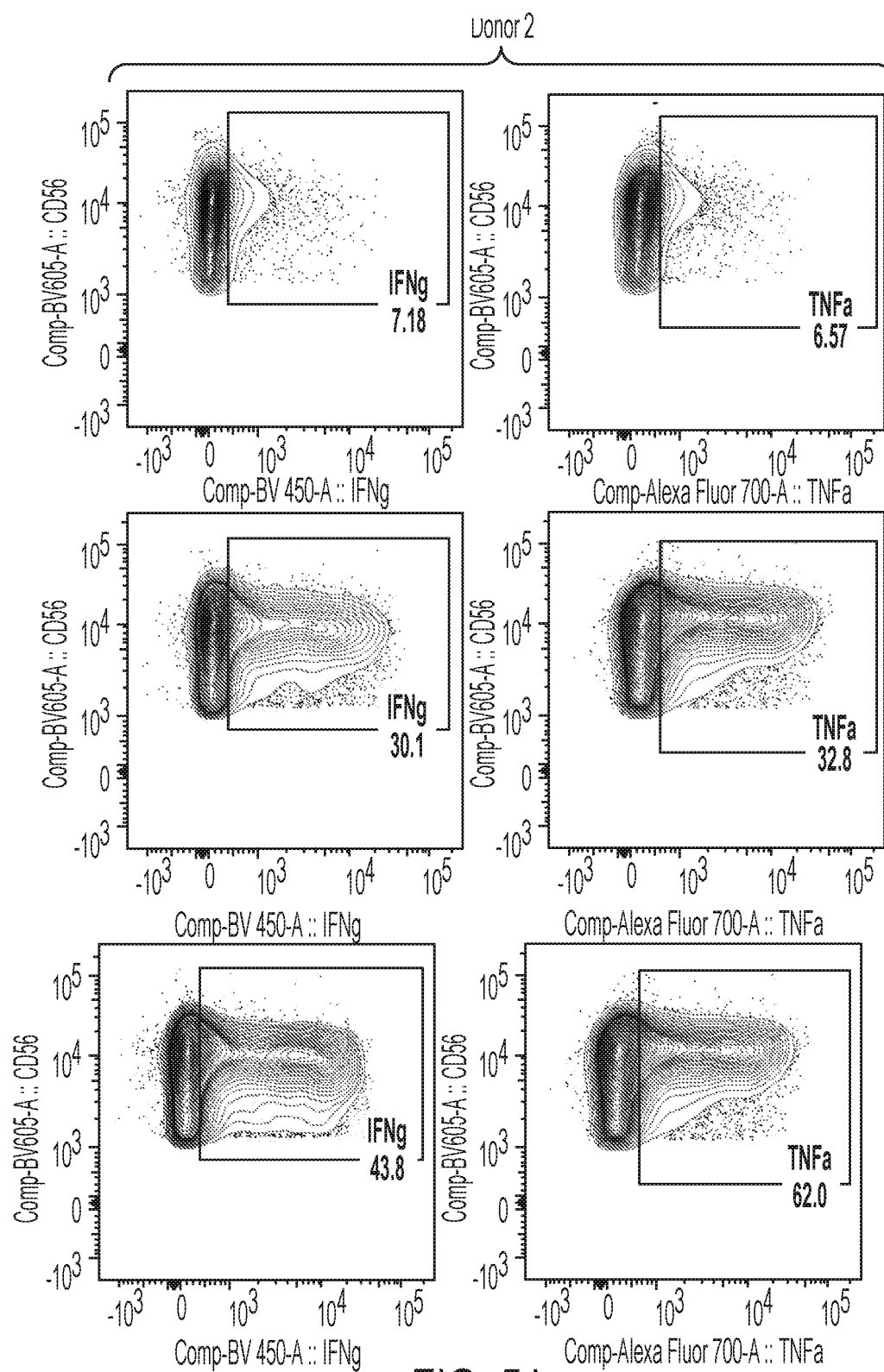


FIG. 5A
CONTINUED

SUBSTITUTE SHEET (RULE 26)

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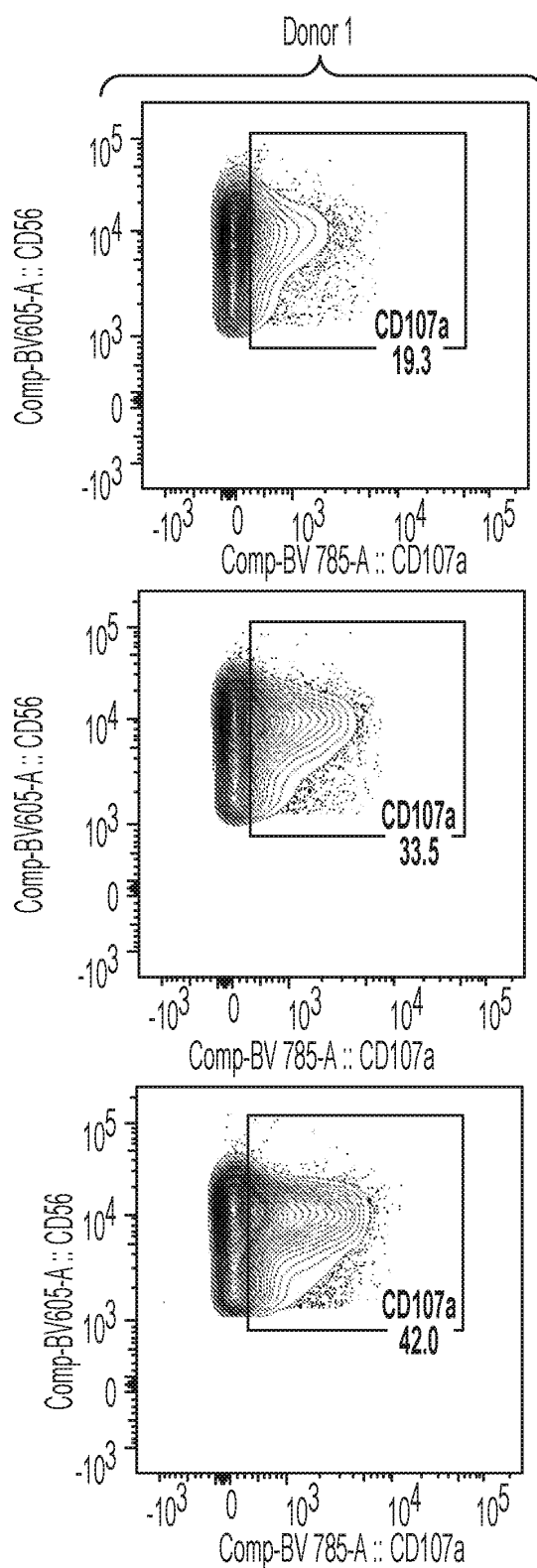


FIG. 5A
CONTINUED

SUBSTITUTE SHEET (RULE 26)

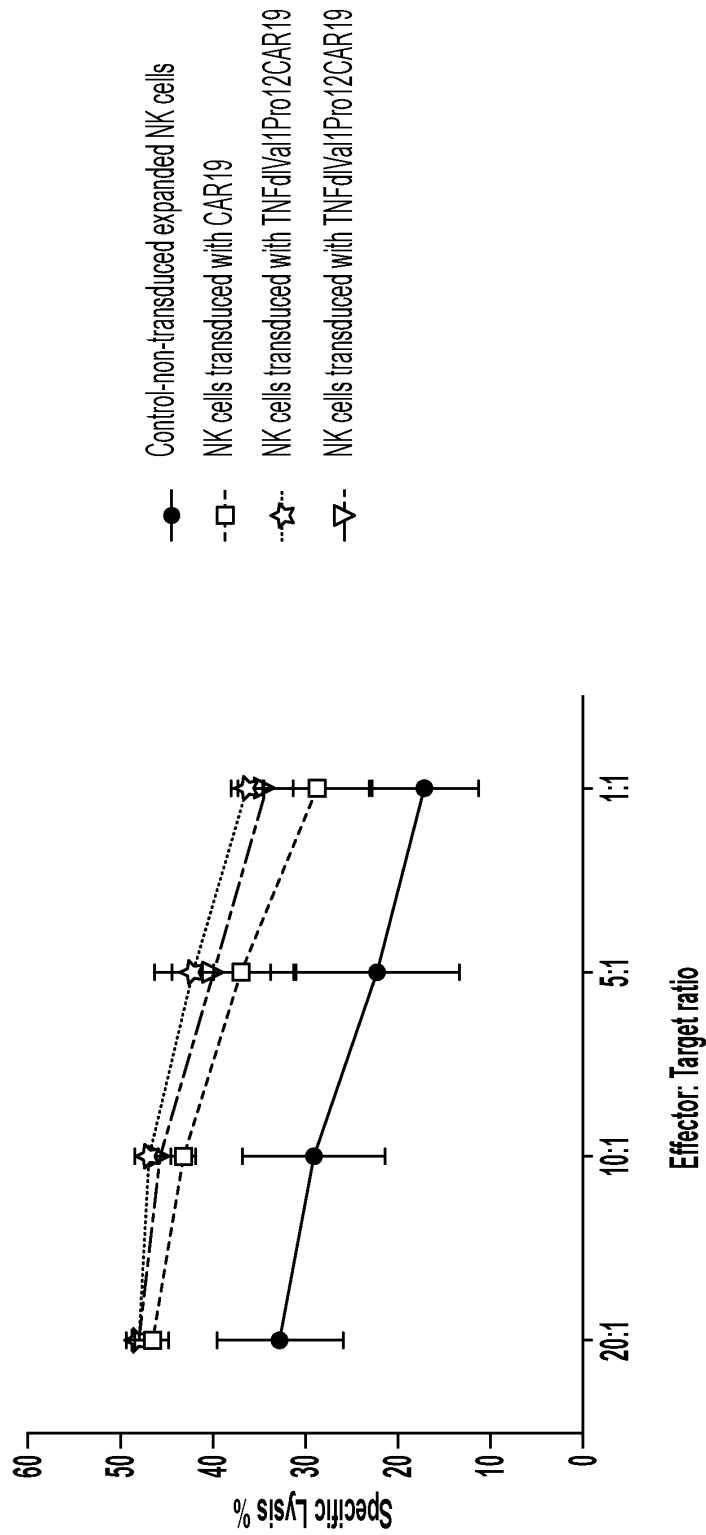


FIG. 5B

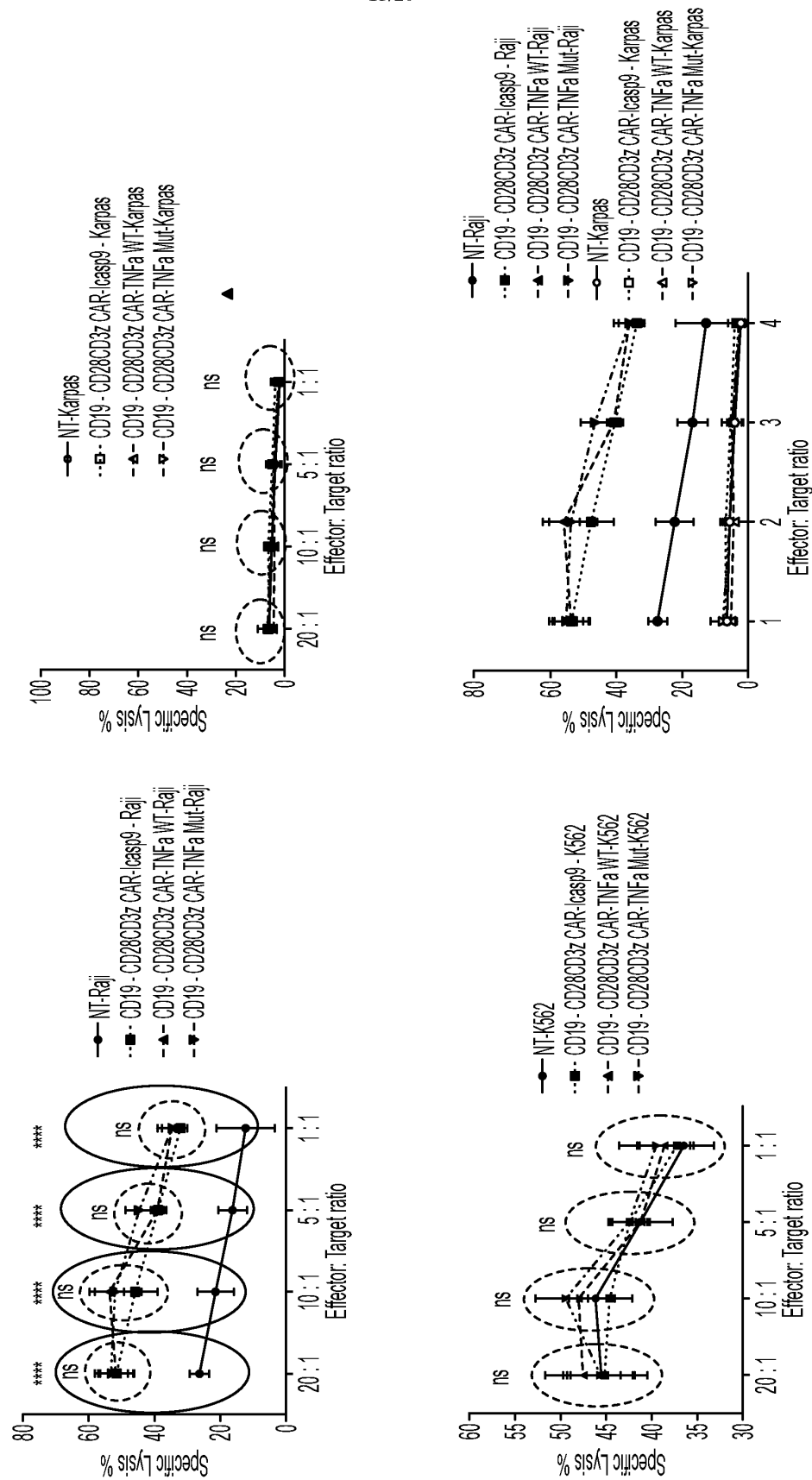


FIG. 6

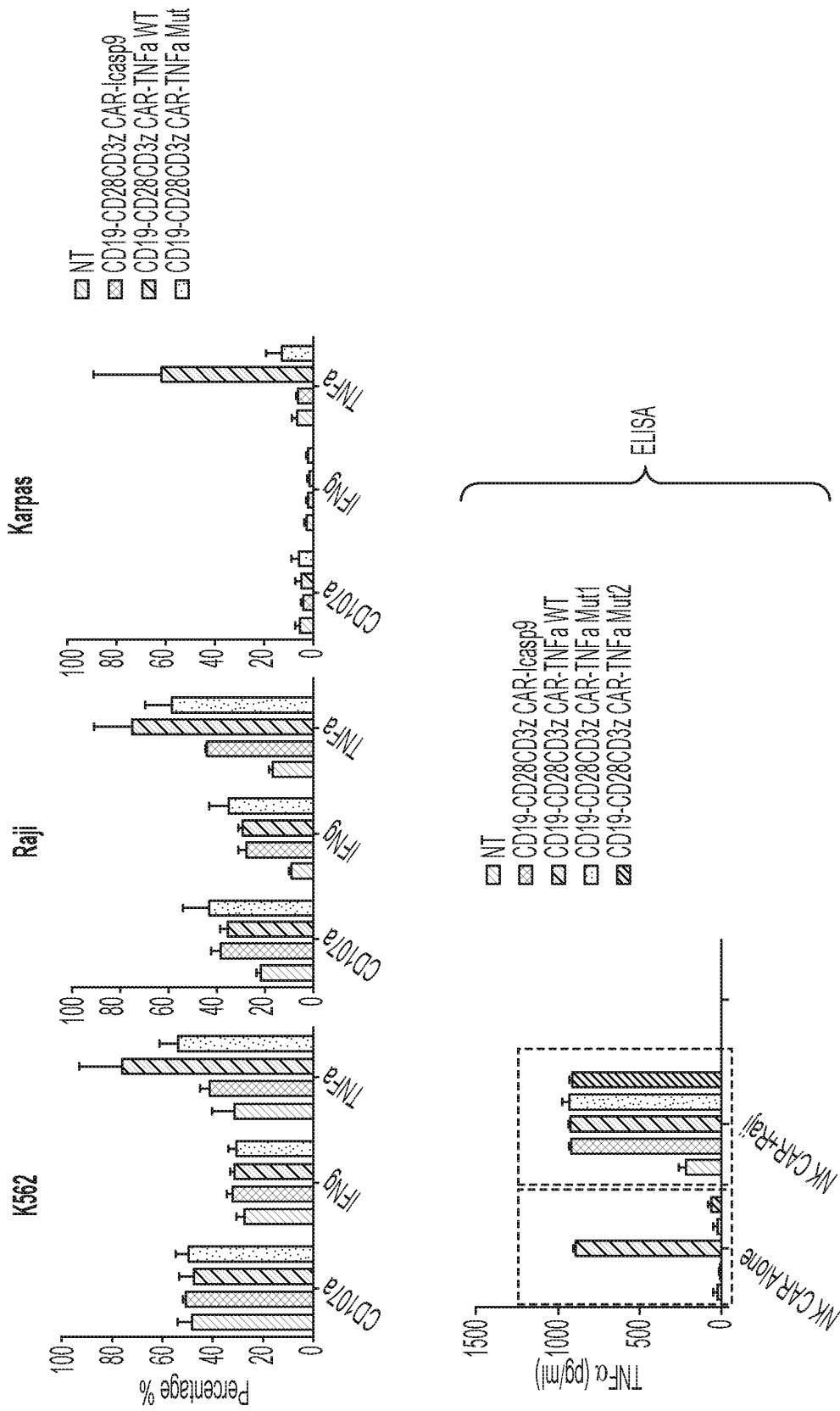


FIG. 7

MSTESMIRDVELAEALPKKTGGPGSRRCLFLSLFSFLIVAGATTLFCLLHFGVIGQREFFPRD
LSLISPLAQAAHVVANPQAEGLQWLNRRANALLANGVELRDNLVWPSEGLIYSQVIFKG
QGCPSHVLITHTISRIAVSYQTKVNLLSAKSPQRETPEGAEAKPWFPTIYLGGVFOLEKGDRL
SAEINRPDYLDFAEISGVYFGIIAL

Single underline represents the receptor binding sites for TNF receptor 1 and 2 – these sites can be mutated to impair interaction of TNFalpha with its receptors.

Double underline E-F LOOP-target for interaction with the adalimumab and infliximab Fab fragments. In contrast, the E-F loops are not involved in the complex interactions of TNFα with TNFR1 or TNFR2

FIG. 8

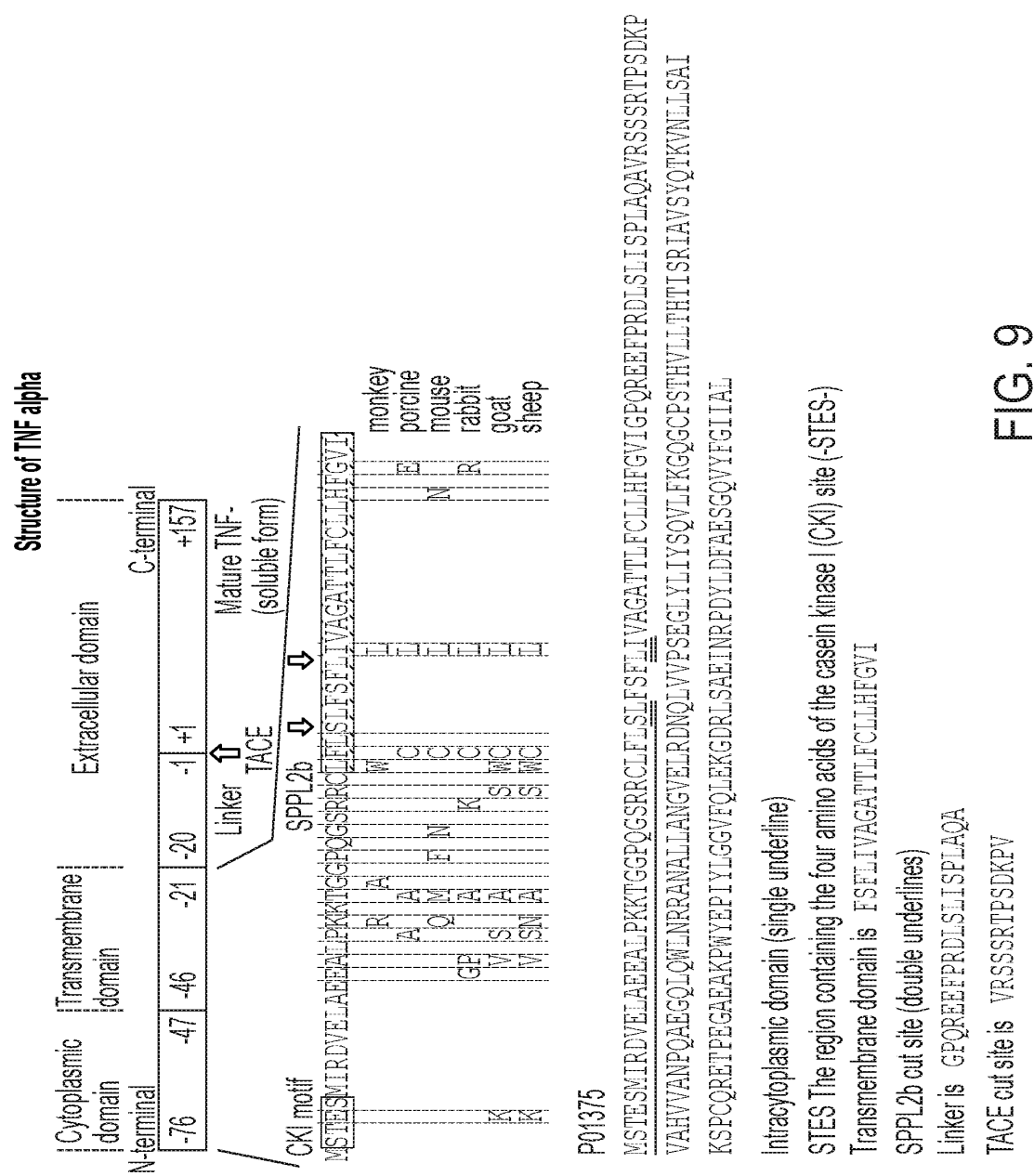


FIG. 9

atgagcactgaaaTGATCCCGGAAGGGGTCTGGACgagagggcgtcccaagaagacagggggccccagggct
ccaggcgtgcttgttcctcagcctcttctccttctgatcgtggcaggcgccaccacgctcttctTctgctgactttggagtgateggccc
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CaccagaccaagggtcaacctcctctTCgcatcaagagccccctgcagagggagacccccagggggtgagcccaagccctggtat
gagcccatctatctgggaggggtcttccagctggagaagggtgaccgactcaTcgtgagatcaatggcccgactatctTactttgcgg
agtAtgggcagggtcactttgggatcattgccctgtcg

MSTEMHPGSGSWHEEALPKKTGGPQGSRRCLFLSLFSFLIVAGATTLFFLLHFGVIGPQREEFPRDLISPLA~~Q~~AHVVAN
PQAEGLQW~~I~~NRRANALLANGVELRDNLVVPSEGLYLYSQVLFGQGCPS~~T~~HVLLTHIISRIAVSHQTKV~~N~~LLFAIKSP
CQRETPEGAFAKPWYEPYILGGVFQLEKGDRLIAEINRPDYLYFAFYGQVYFGI~~A~~LS

FIG. 10

FIG. 11A

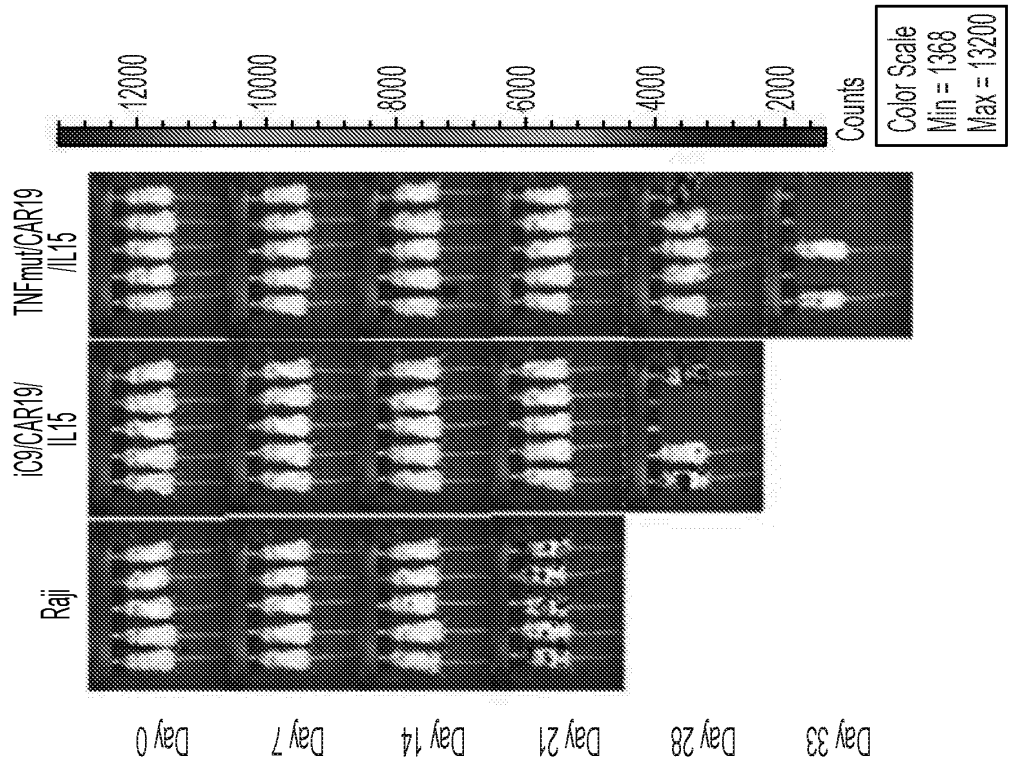


FIG. 11B

