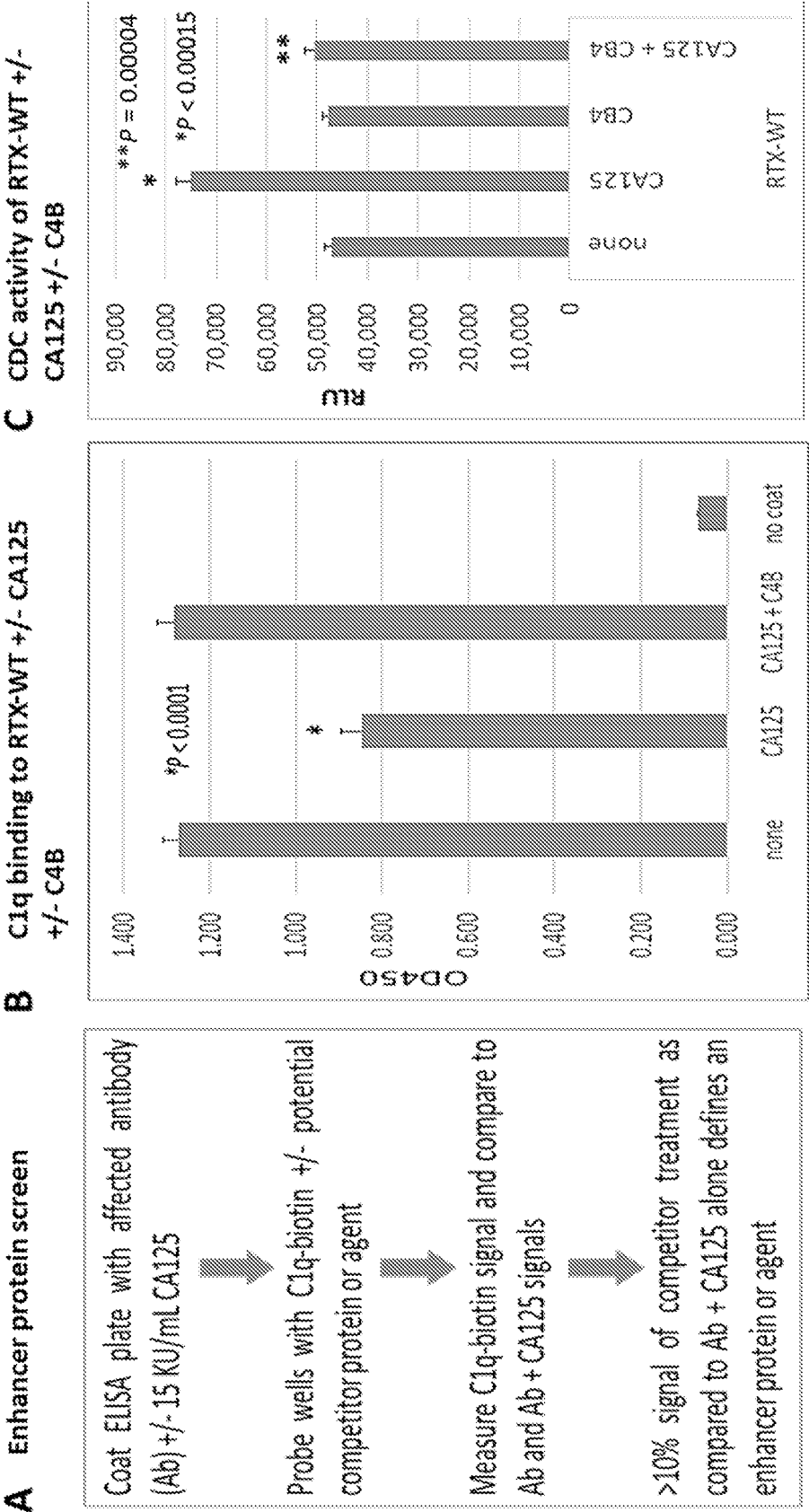


Fig 1A-C.



Re

Fig 1D.

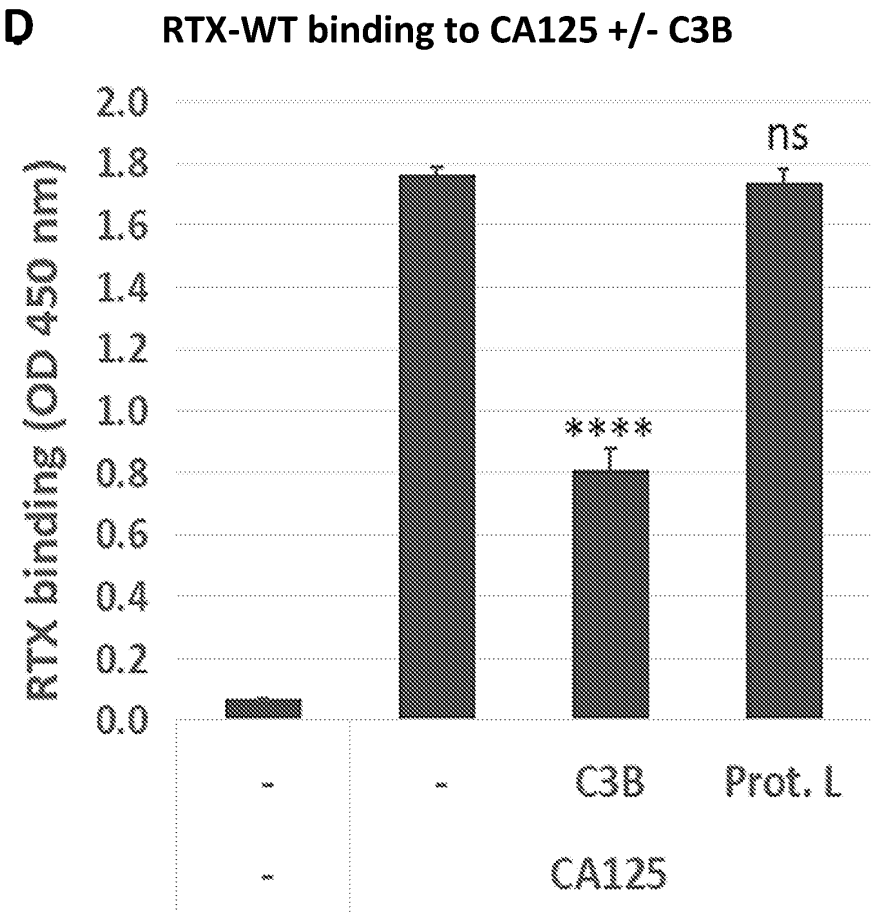
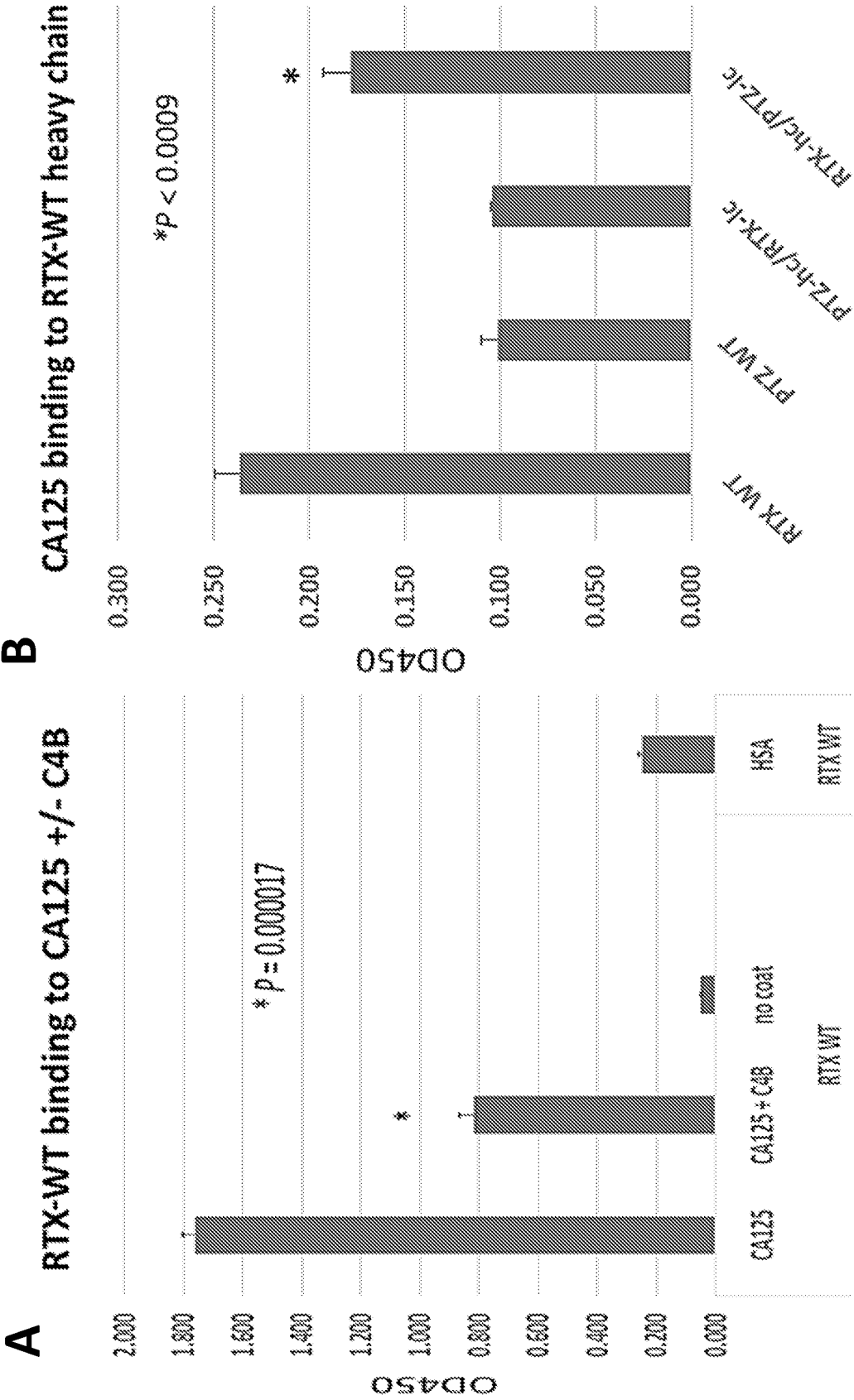


Fig 2A-B.



Re

Fig 3A.**Strategy for mutating rituximab heavy chain targeting CA125 binding site**

```

cgccgtgtattactgtgctcggtccacctactacggcggcgattggtacttcaacgtctgg
  A V Y Y C A R S T Y Y G G D W Y F N V W
ggagccggaaccactgtgaccgtgtcagccgcacccaccaagggcccacgtcttcccc
  G A G T T V T V S A A S T K G P S V F P
ctggcaccctcctccaagagcacctctgggggcacagcggccctgggctgcctggtcaag
  L A P S S K S T S G G T A A L G C L V K
gactacttccccgaaccggtgacggtgtcgtggaactcaggcggccctgaccagcggcgtg
  D Y F P E P V T V S W N S G A L T S G V
cacaccttccccggctgtcctacagtcctcaggactctactcctcagcagcgtggtgacc
  H T F P A V L Q S S G L Y S L S S V V T
gtgcccctccagcagcttgggcacccagacctacatctgcaacgtgaatcacaagcccagc
  V P S S S L G T Q T Y I C N V N H K P S
aacaccaaggtggacaagaaagttgagcccaaattcttgtgacaaaactcacacatgccca
  N T K V D K K V E P K S C D K T H T C..P.
cc

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CDR3 J Region hinge

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CGCCGTGTATTACTGTGCTCGGTCCACCTACTACGGCGGCGATTGGTACTTCAACGTCTGGGGA
GCCGGAACCACTGTGACCGTGTGAGCCgcacccaccaagggcccacgtcttccccctggcac
cctcctccaagagcacctctgggggcacagcggccctgggctgcctggtcaaggactacttccc
cgaaccggtgacggtgtcgtggaactcaggcggccctgaccagcggcgtgcacaccttccccggt
gtcctacagtcctcaggactctactcctcagcagcgtggtgaccgtgcccctccagcagcttgg
gcacccagacctacatctgcaacgtgaatcacaagcccagcaacaccaaggtggacaagaaagt
tgagcccaaattcttgtgacaaaactcacacatgccccc

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SEQ ID NO: 48 Ritux-mut-F CGCCGIGTATTACTGTGCT
SEQ ID NO: 49 Ritux-mut-R GGTGGGCATGTGTGAGTTT

```

VARIABLE REGION
constant region

Replacement Sheet

RTX-1-3	QVQLQQPGAE LVKPGASVKMSCKASGYTFTSYNMMHWVKQTPGRGLEWIGA
RTX-145	QVQLQQPGAE LVKPGASVKMSCKASGYTFTSYNMMHWVKQTPGRGLEWIGA
RTX-148	QVQLQQPGAE LVKPGASVKMSCKASGYTFTSYNMMHWVKQTPGRGLEWIGA
RTX-164	QVQLQQPGAE LVKPGASVKMSCKASGYTFTSYNMMHWVKQTPGRGLEWIGA
RTX-166	QVQLQQPGAE LVKPGASVKMSCKASGYTFTSYNMMHWVKQTPGRGLEWIGA
RTX-198	QVQLQQPGAE LVKPGASVKMSCKASGYTFTSYNMMHWVKQTPGRGLEWIGA
RTX-199	QVQLQQPGAE LVKPGASVKMSCKASGYTFTSYNMMHWVKQTPGRGLEWIGA
RTX-55	QVQLQQPGAE LVKPGASVKMSCKASGYTFTSYNMMHWVKQTPGRGLEWIGA
RTX-85	QVQLQQPGAE LVKPGASVKMSCKASGYTFTSYNMMHWVKQTPGRGLEWIGA
RTX-87	QVQLQQPGAE LVKPGASVKMSCKASGYTFTSYNMMHWVKQTPGRGLEWIGA
Rituximab	QVQLQQPGAE LVKPGASVKMSCKASGYTFTSYNMMHWVKQTPGRGLEWIGA *****
RTX-1-3	IYPGNGDTSYNQKFKGKATLTADKSSSTAYMQLSSLTSEDSAVYYCARST
RTX-145	IYPGNGDTSYNQKFKGKATLTADKSSSTAYMQLSSLTSEDSAVYYCARST
RTX-148	IYPGNGDTSYNQKFKGKATLTADKSSSTAYMQLSSLTSEDSAVYYCARST
RTX-164	IYPGNGDTSYNQKFKGKATLTADKSSSTAYMQLSSLTSEDSAVYYCARST
RTX-166	IYPGNGDTSYNQKFKGKATLTADKSSSTAYMQLSSLTSEDSAVYYCARST
RTX-198	IYPGNGDTSYNQKFKGKATLTADKSSSTAYMQLSSLTSEDSAVYYCARST
RTX-199	IYPGNGDTSYNQKFKGKATLTADKSSSTAYMQLSSLTSEDSAVYYCARST
RTX-55	IYPGNGDTSYNQKFKGKATLTADKSSSTAYMQLSSLTSEDSAVYYCARST
RTX-85	IYPGNGDTSYNQKFKGKATLTADKSSSTAYMQLSSLTSEDSAVYYCARST
RTX-87	IYPGNGDTSYNQKFKGKATLTADKSSSTAYMQLSSLTSEDSAVYYCARST
Rituximab	IYPGNGDTSYNQKFKGKATLTADKSSSTAYMQLSSLTSEDSAVYYCARST *****
RTX-1-3	YYGGDWYFNVWGAGTTVTVSAASTKGPSVFPLAPSSKSTSGGTAALGCLV
RTX-145	YYGGDWYFNVWGAGTTVTVSAASTKGPSVFPLAPSSKSTSGGTAALGCLV
RTX-148	YYGGDWYFNVWGAGTTVTVSAASTKGPSVFPLAPSSKSTSGGTAALGCLV
RTX-164	YYGGDWYFNVWGAGTTVTVSAASTKGPSVFPLAPSSKSTSGGTAALGCLV
RTX-166	YYGGDWYFNVWGAGTTVTVSAASTKGPSVFPLAPSSKSTSGGTAALGCLV
RTX-198	YYGGDWYFNVWGAGTTVTVSAASTKGPSVFPLAPSSKSTSGGTAALGCLV
RTX-199	YYGGDWYFNVWGAGTTVTVSAASTKGPSVFPLAPSSKSTSGGTAALGCLV
RTX-55	YYGGDWYFNVWGAGTTVTVSAASTKGPSVFPLAPSSKSTSGGTAALGCLV
RTX-85	YYGGDWYFNVWGAGTTVTVSAASTKGPSVFPLAPSSKSTSGGTAALGCLV
RTX-87	YYGGDWYFNVWGAGTTVTVSAASTKGPSVFPLAPSSKSTSGGTAALGCLV
Rituximab	YYGGDWYFNVWGAGTTVTVSAASTKGPSVFPLAPSSKSTSGGTAALGCLV *: *** :;*****.***.*****.***.*****
RTX-1-3	KDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSVVTVPSSSLGTQ
RTX-145	KDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSVVTVPSSSLGTQ
RTX-148	KDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSVVTVPSSSLGTQ
RTX-164	KDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSVVTVPSSSLGTQ
RTX-166	KDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSVVTVPSSSLGTQ
RTX-198	KDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSVVTVPSSSLGTQ
RTX-199	KDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSVVTVPSSSLGTQ
RTX-55	KDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSVVTVPSSSLGTQ
RTX-85	KDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSVVTVPSSSLGTQ
RTX-87	KDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSVVTVPSSSLGTQ
Rituximab	KDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSVVTVPSSSLGTQ :***** ***** *****
RTX-1-3	AYICNVNHKPSNTKVDKKVEPKSCDKTHTCPPCPAPELGGPSVFLFPPK
RTX-145	TYICNVNHKPSNTKVDKKVEPKSCDKTHTCPPCPAPELGGPSVFLFPPK
RTX-148	TYICNVNHKPSNTKVDKKVEPKSCDKTHTCPPCPAPELGGPSVFLFPPK
RTX-164	TYICNVNHKPSNTKVDKKVEPKSCDKTHTCPPCPAPELGGPSVFLFPPK
RTX-166	TYICNVNHKPSNTKVDKKVEPKSCDKTHTCPPCPAPELGGPSVFLFPPK
RTX-198	TYICNVNHKPSNTKVDKKVEPKSCDKTHTCPPCPAPELGGPSVFLFPPK
RTX-199	TYICNVNHKPSNTKVDKKVEPKSCDKTHTCPPCPAPELGGPSVFLFPPK

Fig 3B-1. alignment of RTX-MT clones

SUBSTITUTE SHEET (RULE 92bis)

Replacement Sheet 6/14

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RTX-55      TYICNVNHKPSNTKVDKKVEPKSCDKTHTCPFCPEPELLGGPSVFLFPPK
RTX-85      TYICNVNHKPSNTKVDKKVEPKSCDKTHTCPFCPEPELLGGPSVFLFPPK
RTX-87      TYICNVNHKPSNTKVDKKVEPKSCDKTHTCPFCPEPELLGGPSVFLFPPK
Rituximab   TYICNVNHKPSNTKVDKKVEPKSCDKTHTCPFCPEPELLGGPSVFLFPPK
;*****
RTX-1-3     PKDTLMI SRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQY
RTX-145     PKDTLMI SRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQY
RTX-148     PKDTLMI SRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQY
RTX-164     PKDTLMI SRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQY
RTX-166     PKDTLMI SRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQY
RTX-198     PKDTLMI SRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQY
RTX-199     PKDTLMI SRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQY
RTX-55      PKDTLMI SRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQY
RTX-85      PKDTLMI SRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQY
RTX-87      PKDTLMI SRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQY
Rituximab   PKDTLMI SRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQY
*****
RTX-1-3     NSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREP
RTX-145     NSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREP
RTX-148     NSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREP
RTX-164     NSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREP
RTX-166     NSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREP
RTX-198     NSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREP
RTX-199     NSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREP
RTX-55      NSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREP
RTX-85      NSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREP
RTX-87      NSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREP
Rituximab   NSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREP
*****
RTX-1-3     QVYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTTPP
RTX-145     QVYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTTPP
RTX-148     QVYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTTPP
RTX-164     QVYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTTPP
RTX-166     QVYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTTPP
RTX-198     QVYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTTPP
RTX-199     QVYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTTPP
RTX-55      QVYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTTPP
RTX-85      QVYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTTPP
RTX-87      QVYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTTPP
Rituximab   QVYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTTPP
*****
RTX-1-3     VLDSGDSFFLYSKLTVDKSRWQQGNVSCSVMHEALHNHYTQKSLSLSPGK
RTX-145     VLDSGDSFFLYSKLTVDKSRWQQGNVSCSVMHEALHNHYTQKSLSLSPGK
RTX-148     VLDSGDSFFLYSKLTVDKSRWQQGNVSCSVMHEALHNHYTQKSLSLSPGK
RTX-164     VLDSGDSFFLYSKLTVDKSRWQQGNVSCSVMHEALHNHYTQKSLSLSPGK
RTX-166     VLDSGDSFFLYSKLTVDKSRWQQGNVSCSVMHEALHNHYTQKSLSLSPGK
RTX-198     VLDSGDSFFLYSKLTVDKSRWQQGNVSCSVMHEALHNHYTQKSLSLSPGK
RTX-199     VLDSGDSFFLYSKLTVDKSRWQQGNVSCSVMHEALHNHYTQKSLSLSPGK
RTX-55      VLDSGDSFFLYSKLTVDKSRWQQGNVSCSVMHEALHNHYTQKSLSLSPGK
RTX-85      VLDSGDSFFLYSKLTVDKSRWQQGNVSCSVMHEALHNHYTQKSLSLSPGK
RTX-87      VLDSGDSFFLYSKLTVDKSRWQQGNVSCSVMHEALHNHYTQKSLSLSPGK
Rituximab   VLDSGDSFFLYSKLTVDKSRWQQGNVSCSVMHEALHNHYTQKSLSLSPGK
*****

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Fig 3B-2. alignment of RTX-MT clones

SUBSTITUTE SHEET (RULE 92bis)

Fig 4.

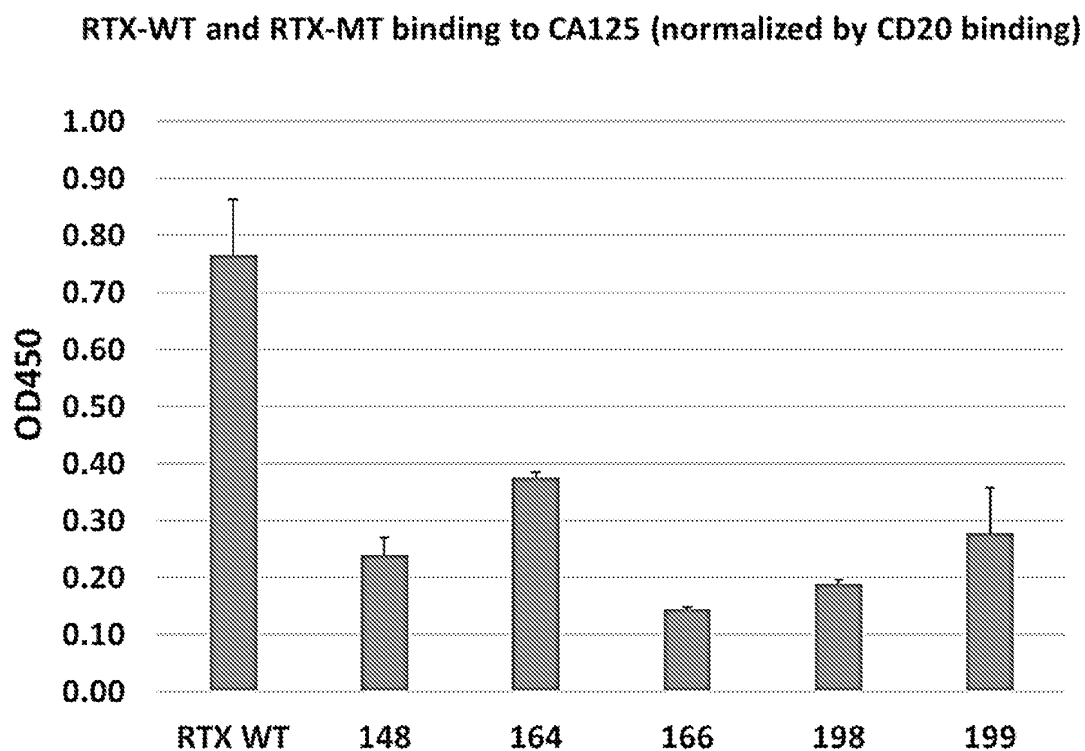


Fig 5.

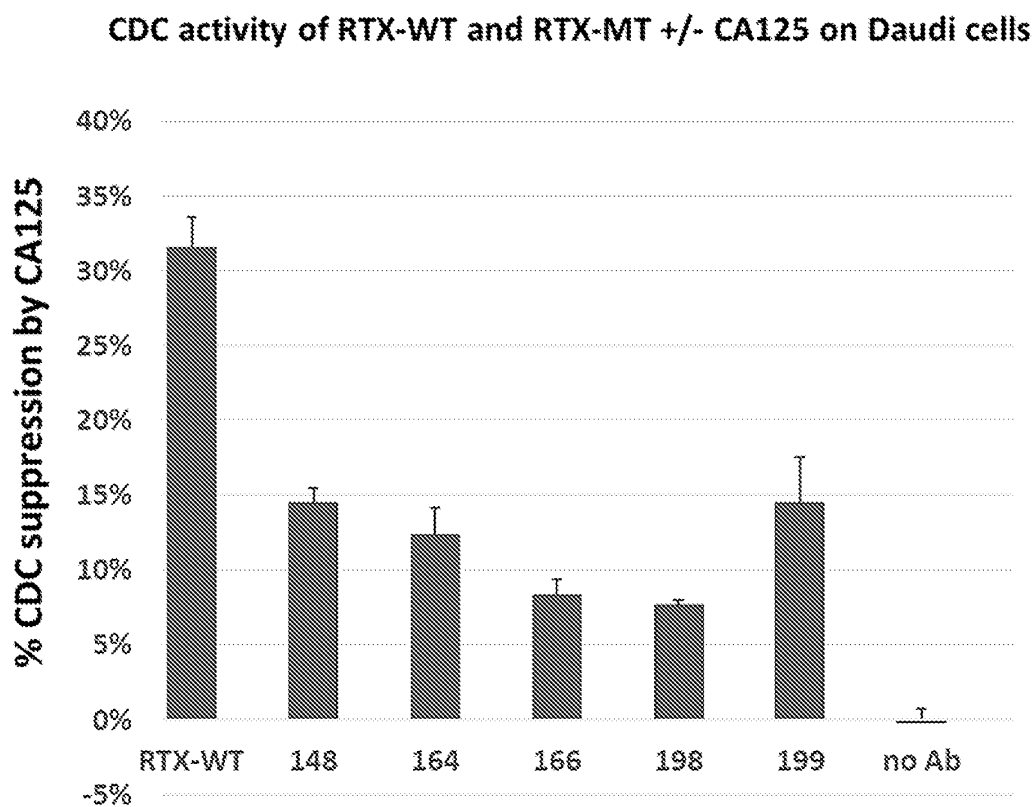


Fig 6A-B.

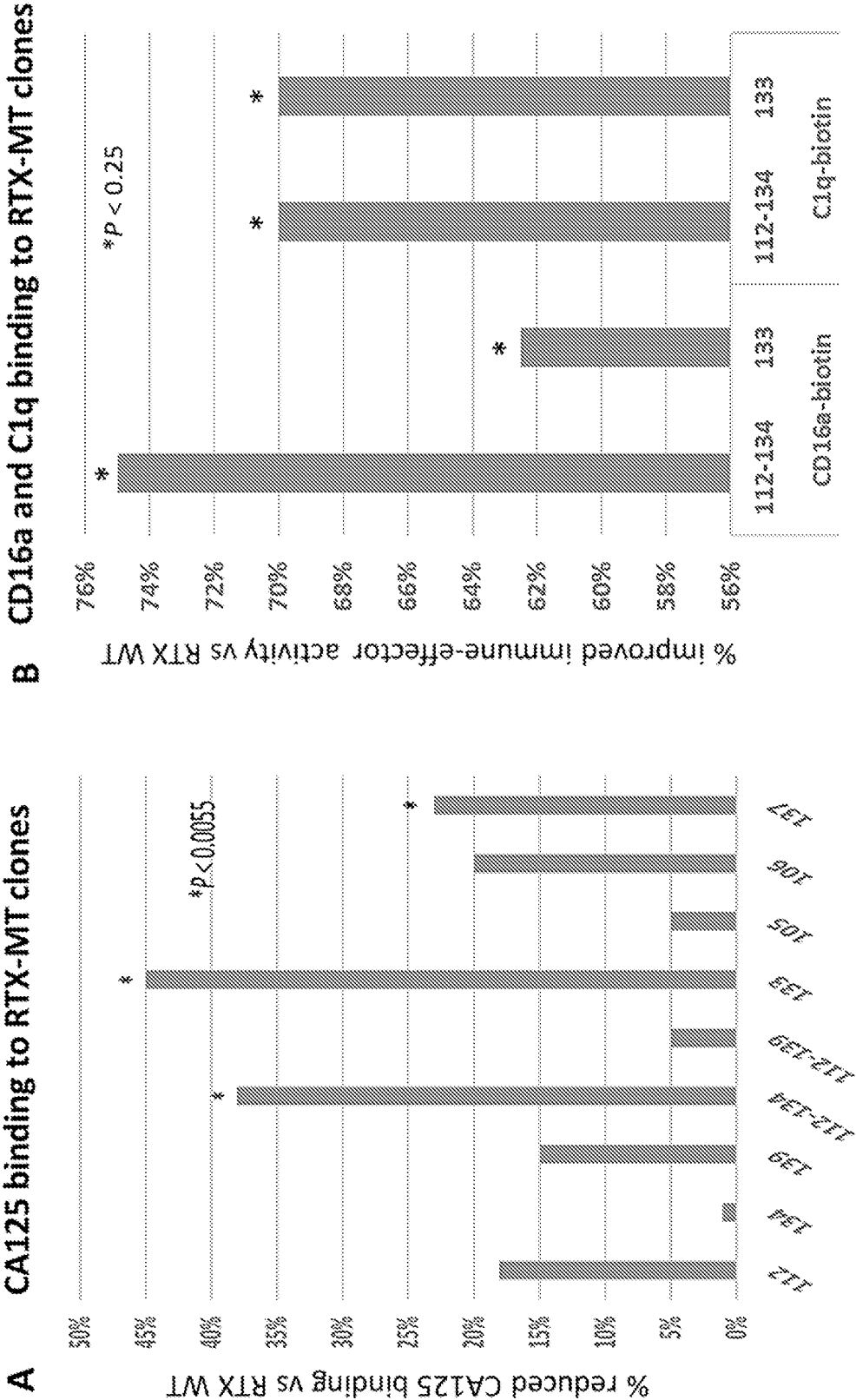


Fig 7A-B.

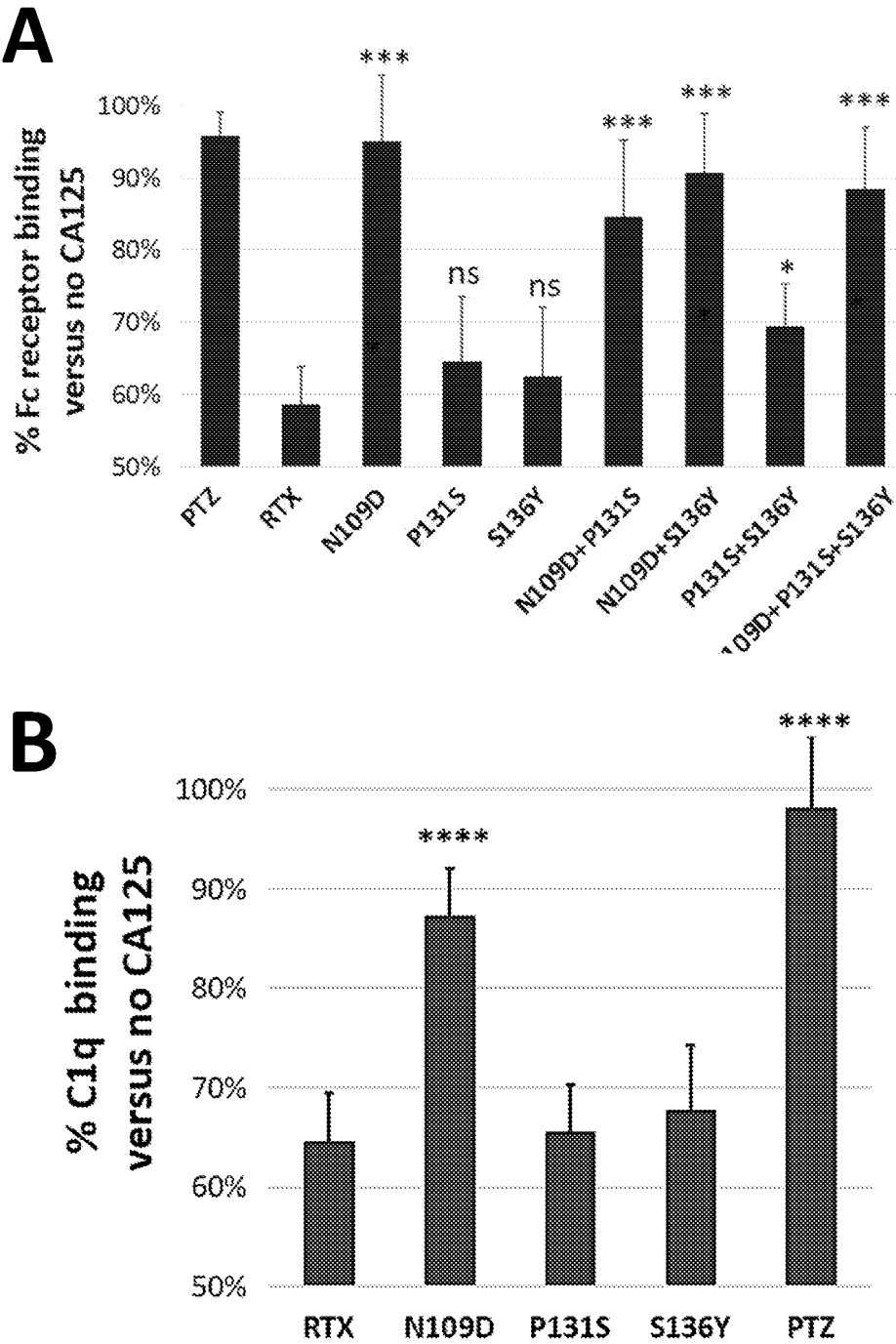
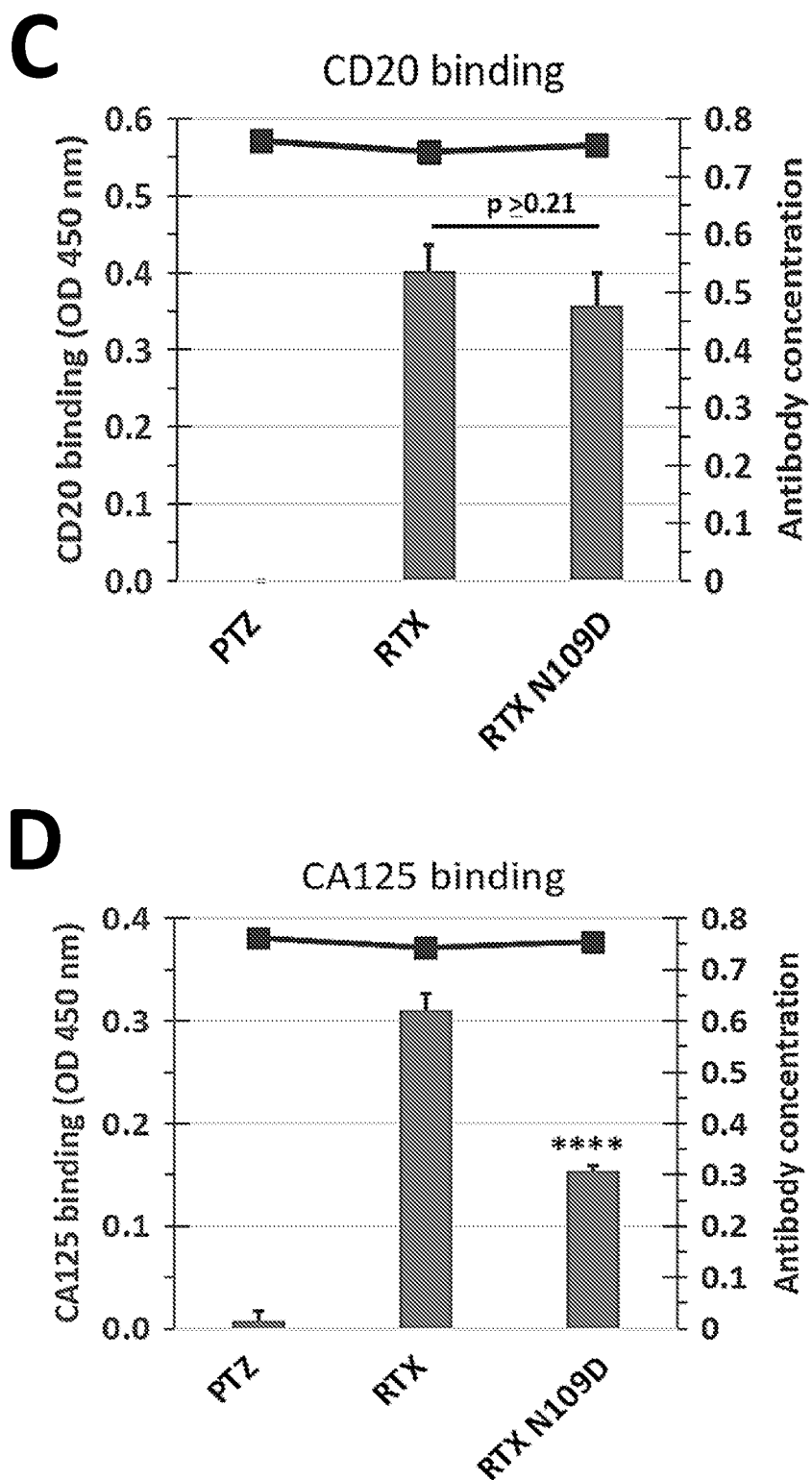


Fig 7C-D.



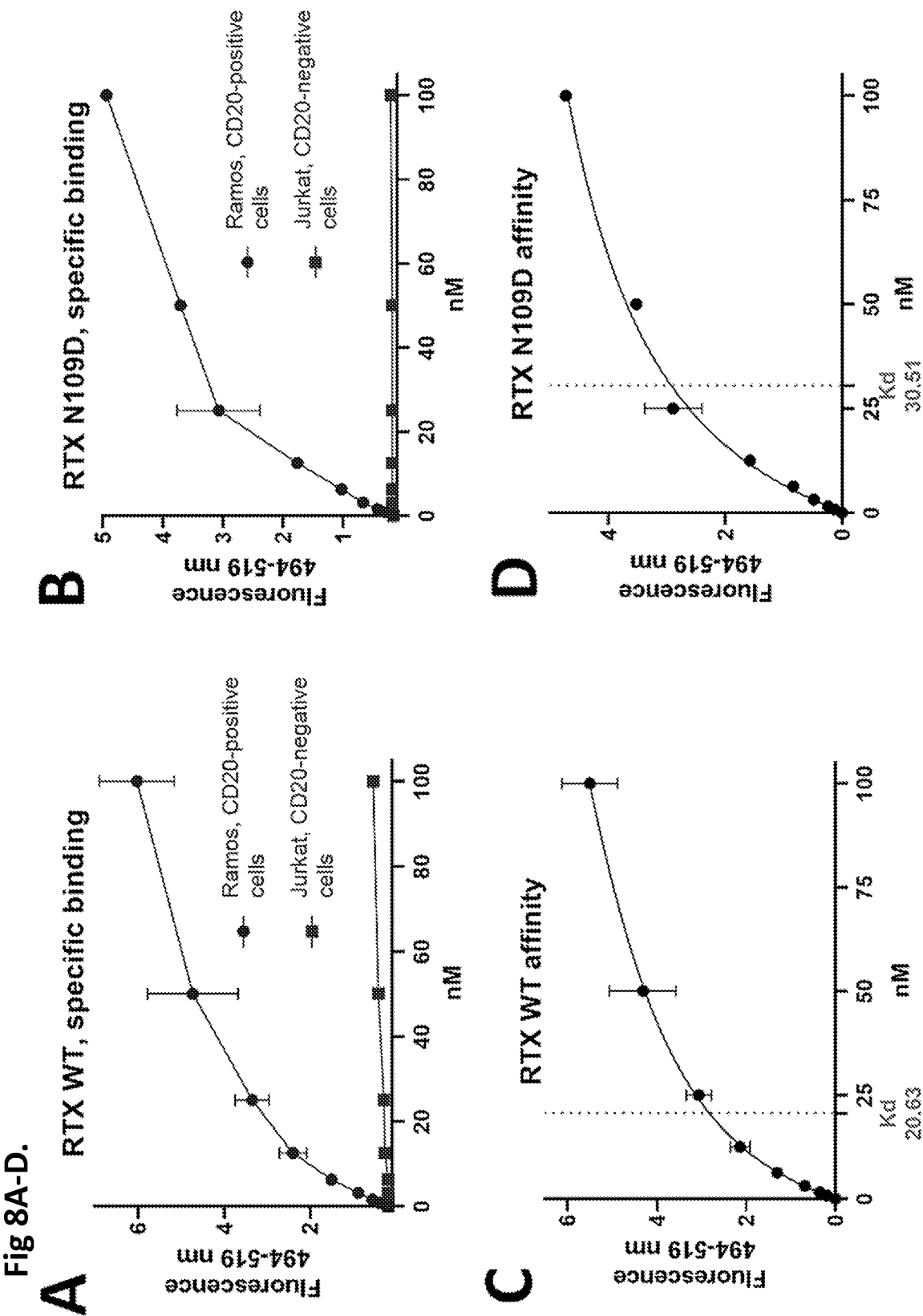


Fig 9A-B.

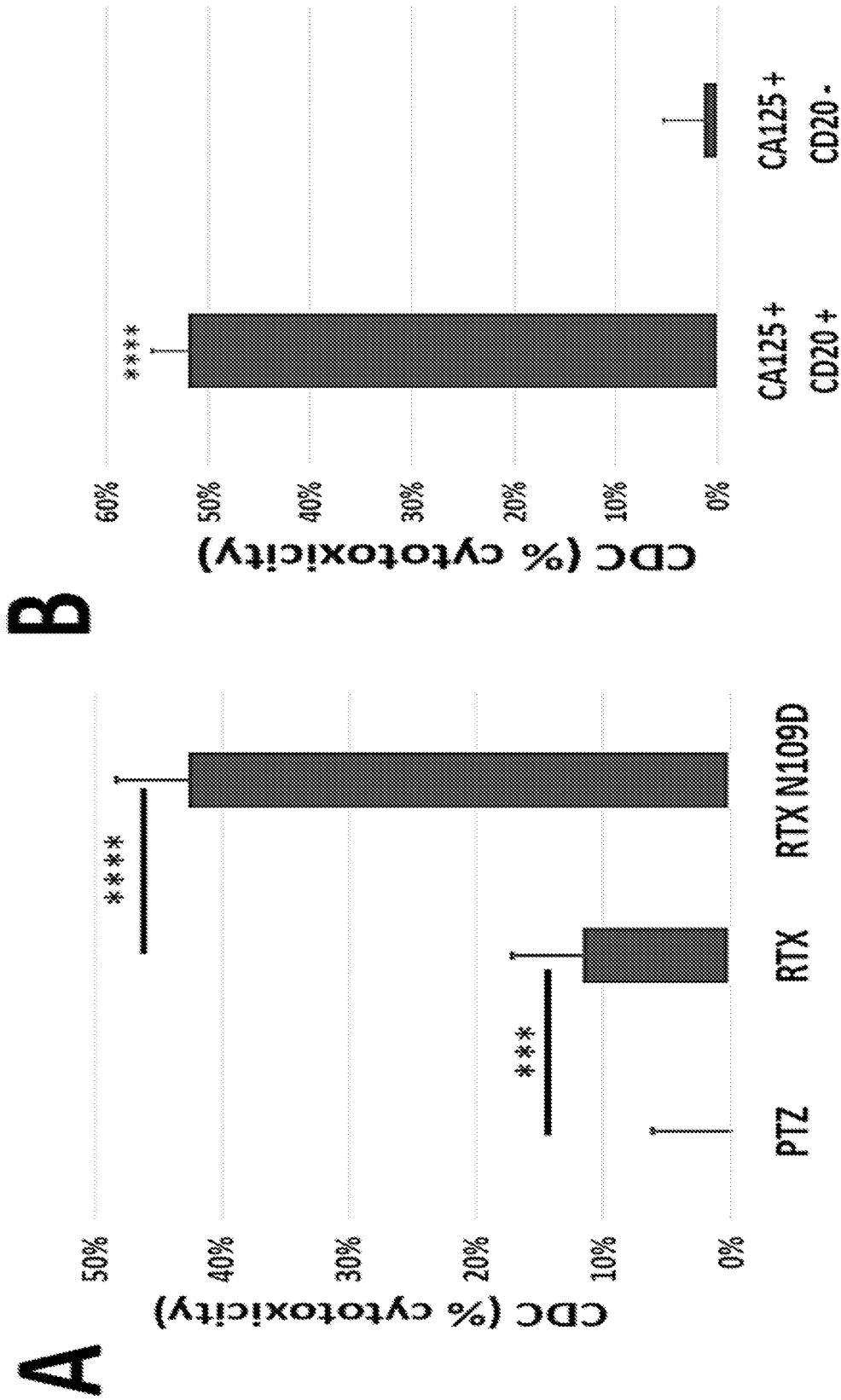


Fig 10A-B.

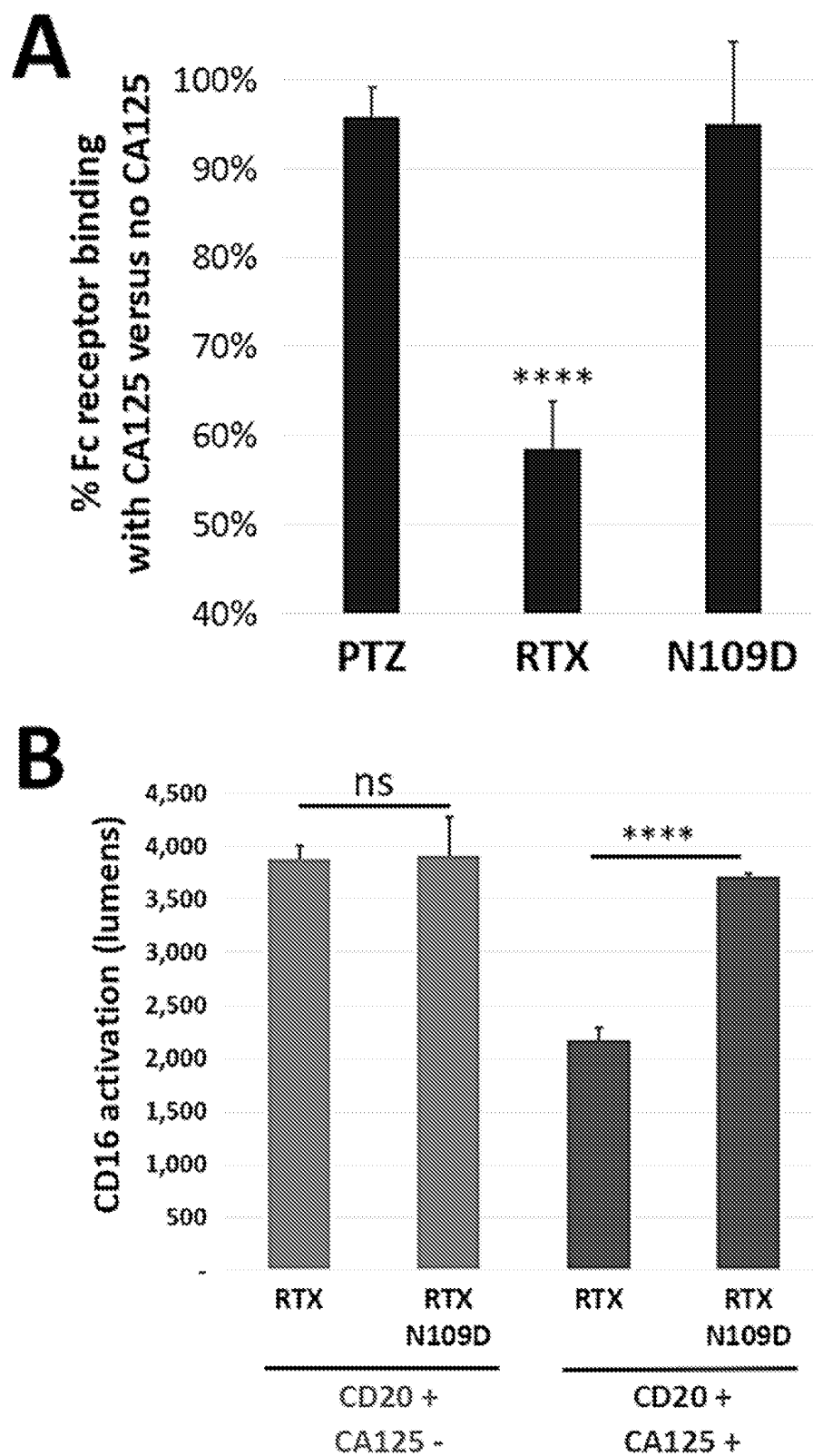


Fig 10C.

