

FIGURE 1A

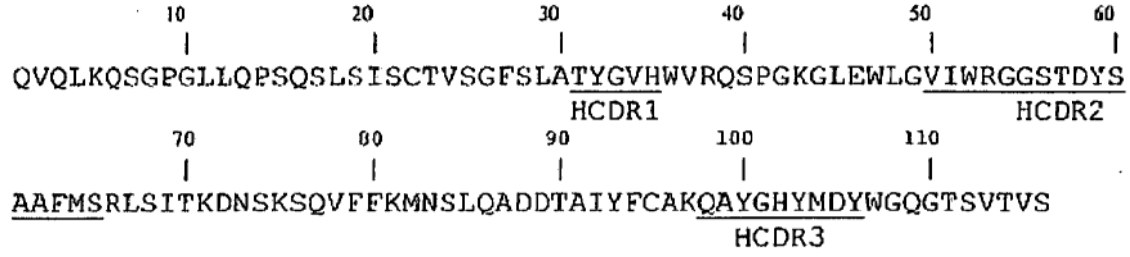


FIGURE 1B

VL

GATGTTTTGATGACCCAAACTCCACTCTCCCTGCCTGTCAGTCTTGGAGATCAAGCCTCC
ATCTCTTGCAGATCTAGTCAGAACATTGTACATAGTAATGGAAACACCTATTTAGAATGG
TACCTGCAGAAACCAGGCCAGTCTCCAAAGCTCCTGATCTACAAAGTTTCCAACCGATTT
TCTGGGGTCCCAGACAGGTTCAGTGGCAGTGGATCAGGGACAGATTTCACACTCAAGATC
ACCAGATTGGAGGCTGAGGATCTGGGAGTTTATTACTGCTTTCAAGGTTCACATGTTCCG
TGGACGTTCGGTGGAGGCACCAAGCTGGAAATCAAACGGGCC

FIGURE 2A

VH

CAGGTGCAGCTGAAGCAGTCAGGACCTGGCCTACTGCAGCCCTCACAGAGCCTGTCCATA
TCCTGCACAGTCTCTGGTTTCTCATTAGCTACCTATGGTGTACACTGGGTTCGCCAGTCT
CCAGGAAAGGGTCTGGAGTGGCTGGGAGTGATTTGGAGAGGTGGGAGCACAGACTACAGT
GCAGCTTTCATGTCCAGACTGAGCATCACCAAGGACAACTCCAAGAGCCAAGTTTTCTTT
AAAATGAACAGTCTGCAAGCTGATGACACTGCCATTTACTTCTGTGCCAAACAGGCGTAT
GGTCACTACATGGACTACTGGGGTCAAGGAACCTCAGTCACCGTCTCC

FIGURE 2B

Humanized VL variants

```
mVL   DVLMTQTPLSLPVSLGDQASISC RSSQNIVHSNGNTYLE WYLQKPGQSPKLLIY KVSNRFS GVPDRFSGSGSGTDFTLKITRLEAEDLGVYYC FQGSHVPWT FGGGTKLEIK
A17   DVVMTQSPLSLPVTLGQPASISC RSSQSLVYSDGNTYLN WFQQRPGQSPRRLIY KVSNRDS GVPDRFSGSGSGTDFTLKISRVEAEDVGVYYC MQGTHWP..
JK1                                                                                                    ..WT FGQGTKVEIK

hVL1  DVVMTQSPLSLPVTLGQPASISC RSSQNIVHSNGNTYLE WFQQRPGQSPRRLIY KVSNRFS GVPDRFSGSGSGTDFTLKISRVEAEDVGVYYC FQGSHVPWT FGQGTKVEIK
hVL2  DVLMTQSPLSLPVTLGQPASISC RSSQNIVHSNGNTYLE WFQQRPGQSPRRLIY KVSNRFS GVPDRFSGSGSGTDFTLKISRVEAEDVGVYYC FQGSHVPWT FGQGTKVEIK
hVL3  DVVMTQTPLSLPVTLGQPASISC RSSQNIVHSNGNTYLE WFQQRPGQSPRRLIY KVSNRFS GVPDRFSGSGSGTDFTLKISRVEAEDVGVYYC FQGSHVPWT FGQGTKVEIK
hVL4  DVVMTQSPLSLPVTLGQPASISC RSSQNIVHSNGNTYLE WYLQRPGQSPRRLIY KVSNRFS GVPDRFSGSGSGTDFTLKISRVEAEDVGVYYC FQGSHVPWT FGQGTKVEIK
hVL5  DVVMTQSPLSLPVTLGQPASISC RSSQNIVHSNGNTYLE WFQQRPGQSPRLLIY KVSNRFS GVPDRFSGSGSGTDFTLKISRVEAEDVGVYYC FQGSHVPWT FGQGTKVEIK
hVL6  DVVMTQSPLSLPVTLGQPASISC RSSQNIVHSNGNTYLE WFQQRPGQSPRRLIY KVSNRFS GVPDRFSGSGSGTDFTLKISRVEAEDVGVYYC FQGSHVPWT FGGGTKVEIK
hVL7  DVVMTQSPLSLPVTLGQPASISC RSSQNIVHSNGNTYLE WYLQRPGQSPRLLIY KVSNRFS GVPDRFSGSGSGTDFTLKISRVEAEDVGVYYC FQGSHVPWT FGQGTKVEIK
hVL8  DVLMTQSPLSLPVTLGQPASISC RSSQNIVHSNGNTYLE WFQQRPGQSPRLLIY KVSNRFS GVPDRFSGSGSGTDFTLKISRVEAEDVGVYYC FQGSHVPWT FGGGTKVEIK
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hVL10 DVVMTQSPLSLPVTLGQPASISC RSSQNIVHSNGNTYLE WYLQRPGQSPRRLIY KVSNRFS GVPDRFSGSGSGTDFTLKISRVEAEDVGVYYC FQGSHVPWT FGGGTKVEIK
hVL11 DVVMTQTPLSLPVTLGQPASISC RSSQNIVHSNGNTYLE WYLQRPGQSPRRLIY KVSNRFS GVPDRFSGSGSGTDFTLKISRVEAEDVGVYYC FQGSHVPWT FGGGTKVEIK
hVL12 DVVMTQTPLSLPVTLGQPASISC RSSQNIVHSNGNTYLE WYLQRPGQSPRRLIY KVSNRFS GVPDRFSGSGSGTDFTLKISRVEAEDVGVYYC FQGSHVPWT FGQGTKVEIK
```

FIGURE 3

SUBSTITUTE SHEET (RULE 26)

Humanized VH variants

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mVH     QVQLKQSGPGLLQPSQSLSISCTVSGFSLA TYGVH WVRQSPGKGLEWLG VIWRGGSTDYSAAFMS RLSITKDNSKSQVFFKMNSLQADDTAIYFCAK QAYGHYMDY WGQGTSVTVSS
3-66    EVQLVESGGGLVQPGGSLRLSCAASGFTVS SNYMS WVRQAPGKGLEWVS VIYSGGSTYYADSVKG RFTISRDNSKNTLYLQMNSLRAEDTAVYYCAR
*04
JH4                                                                                                                 ..YFDY WGQGTLVTVSS
hVH1    EVQLVESGGGLVQPGGSLRLSCAASGFTFS TYGVH WVRQAPGKGLEWVS VIWRGGSTDYSAAFMS RFTISRDNSKNTLYLQMNSLRAEDTAVYYCAR QAYGHYMDY WGQGTLVTVSS
hVH2    EVQLVESGGGLVQPGGSLRLSCAASGFSFA TYGVH WVRQAPGKGLEWVS VIWRGGSTDYSAAFMS RFTISRDNSKNTLYLQMNSLRAEDTAVYYCAR QAYGHYMDY WGQGTLVTVSS
hVH3    EVQLVESGGGLVQPGGSLRLSCAASGFTFS TYGVH WVRQSPGKGLEWVS VIWRGGSTDYSAAFMS RFTISRDNSKNTLYLQMNSLRAEDTAVYYCAR QAYGHYMDY WGQGTLVTVSS
hVH4    EVQLVESGGGLVQPGGSLRLSCAASGFTFS TYGVH WVRQAPGKGLEWLG VIWRGGSTDYSAAFMS RFTISRDNSKNTLYLQMNSLRAEDTAVYYCAR QAYGHYMDY WGQGTLVTVSS
hVH5    EVQLVESGGGLVQPGGSLRLSCAASGFTFS TYGVH WVRQAPGKGLEWVS VIWRGGSTDYSAAFMS RLTISRDNSKNTLYLQMNSLRAEDTAVYYCAR QAYGHYMDY WGQGTLVTVSS
hVH6    EVQLVESGGGLVQPGGSLRLSCAASGFTFS TYGVH WVRQAPGKGLEWVS VIWRGGSTDYSAAFMS RFTISKDNSKNTLYLQMNSLRAEDTAVYYCAR QAYGHYMDY WGQGTLVTVSS
hVH7    EVQLVESGGGLVQPGGSLRLSCAASGFTFS TYGVH WVRQAPGKGLEWVS VIWRGGSTDYSAAFMS RFTISRDNSKNTVYLQMNSLRAEDTAVYYCAR QAYGHYMDY WGQGTLVTVSS
hVH8    EVQLVESGGGLVQPGGSLRLSCAASGFTFS TYGVH WVRQAPGKGLEWVS VIWRGGSTDYSAAFMS RFTISRDNSKNTLYFQMNSLRAEDTAVYYCAR QAYGHYMDY WGQGTLVTVSS
hVH9    EVQLVESGGGLVQPGGSLRLSCAASGFTFS TYGVH WVRQAPGKGLEWVS VIWRGGSTDYSAAFMS RFTISRDNSKNTLYLQMNSLRAEDTAVYFCAK QAYGHYMDY WGQGTLVTVSS
hVH10   EVQLVESGGGLVQPGGSLRLSCAASGFTFS TYGVH WVRQAPGKGLEWVS VIWRGGSTDYSAAFMS RFTISRDNSKNTLYLQMNSLRAEDTAVYYCAK QAYGHYMDY WGQGTLVTVSS
hVH11   EVQLVESGGGLVQPGGSLRLSCAASGFTFS TYGVH WVRQAPGKGLEWVS VIWRGGSTDYSAAFMS RFTISRDNSKNTLYLQMNSLRAEDTAVYYCAR QAYGHYMDY WGQGTSVTVSS
hVH12   EVQLVESGGGLVQPGGSLRLSCAASGFTFS TYGVH WVRQAPGKGLEWLG VIWRGGSTDYSAAFMS RLTISRDNSKNTLYLQMNSLRAEDTAVYYCAR QAYGHYMDY WGQGTLVTVSS
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FIGURE 3 (continued)

SUBSTITUTE SHEET (RULE 26)

```
hVH13 EVQLVESGGGLVQPGGSLRLSCAASGFTFS TYGVH WVRQAPGKGLEWVS VIWRGGSTDYSAAFMS RFTISRDNSKNTVYFQMNSLRAEDTAVYYCAR QAYGHYMDY WGQGTLVTVSS
hVH14 EVQLVESGGGLVQPGGSLRLSCAASGFSFA TYGVH WVRQSPGKGLEWVS VIWRGGSTDYSAAFMS RFTISRDNSKNTLYLQMNSLRAEDTAVYFCAK QAYGHYMDY WGQGTLVTVSS
hVH15 EVQLVESGGGLVQPGGSLRLSCAASGFTFS TYGVH WVRQSPGKGLEWLG VIWRGGSTDYSAAFMS RFTISRDNSKNTLYLQMNSLRAEDTAVYFCAK QAYGHYMDY WGQGTSVTVSS
hVH16 EVQLVESGGGLVQPGGSLRLSCAASGFTFS TYGVH WVRQAPGKGLEWVS VIWRGGSTDYSAAFMS RFTISRDNSKNTLYFQMNSLRAEDTAVYFCAK QAYGHYMDY WGQGTLVTVSS
hVH17 EVQLVESGGGLVQPGGSLRLSCAASGFTFS TYGVH WVRQAPGKGLEWLG VIWRGGSTDYSAAFMS RFTISRDNSKNTLYLQMNSLRAEDTAVYYCAK QAYGHYMDY WGQGTSVTVSS
hVH18 EVQLVESGGGLVQPGGSLRLSCAASGFSFA TYGVH WVRQSPGKGLEWLG VIWRGGSTDYSAAFMS RLTISKDNSKNTLYLQMNSLRAEDTAVYYCAR QAYGHYMDY WGQGTLVTVSS
hVH19 EVQLVESGGGLVQPGGSLRLSCAASGFTFS TYGVH WVRQSPGKGLEWLG VIWRGGSTDYSAAFMS RLTISKDNSKNTVYFQMNSLRAEDTAVYFCAK QAYGHYMDY WGQGTSVTVSS
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hVH21 EVQLVESGGGLVQPGGSLRLSCAASGFSFA TYGVH WVRQAPGKGLEWLG VIWRGGSTDYSAAFMS RLTISKDNSKNTVYFQMNSLRAEDTAVYFCAK QAYGHYMDY WGQGTSVTVSS
hVH22 EVQLVESGGGLVQPGGSLRLSCAASGFSFA TYGVH WVRQSPGKGLEWVS VIWRGGSTDYSAAFMS RLTISKDNSKNTVYFQMNSLRAEDTAVYFCAK QAYGHYMDY WGQGTSVTVSS
hVH23 EVQLVESGGGLVQPGGSLRLSCAASGFSFA TYGVH WVRQSPGKGLEWLG VIWRGGSTDYSAAFMS RFTISKDNSKNTVYFQMNSLRAEDTAVYFCAK QAYGHYMDY WGQGTSVTVSS
hVH24 EVQLVESGGGLVQPGGSLRLSCAASGFSFA TYGVH WVRQSPGKGLEWLG VIWRGGSTDYSAAFMS RLTISRDNSKNTVYFQMNSLRAEDTAVYFCAK QAYGHYMDY WGQGTSVTVSS
hVH25 EVQLVESGGGLVQPGGSLRLSCAASGFSFA TYGVH WVRQSPGKGLEWLG VIWRGGSTDYSAAFMS RLTISKDNSKNTLYFQMNSLRAEDTAVYFCAK QAYGHYMDY WGQGTSVTVSS
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hVH27 EVQLVESGGGLVQPGGSLRLSCAASGFSFA TYGVH WVRQSPGKGLEWLG VIWRGGSTDYSAAFMS RLTISKDNSKNTVYFQMNSLRAEDTAVYYCAK QAYGHYMDY WGQGTSVTVSS
hVH28 EVQLVESGGGLVQPGGSLRLSCAASGFSFA TYGVH WVRQSPGKGLEWLG VIWRGGSTDYSAAFMS RLTISKDNSKNTVYFQMNSLRAEDTAVYYCAR QAYGHYMDY WGQGTSVTVSS
hVH29 EVQLVESGGGLVQPGGSLRLSCAASGFSFA TYGVH WVRQSPGKGLEWLG VIWRGGSTDYSAAFMS RLTISKDNSKNTVYFQMNSLRAEDTAVYFCAK QAYGHYMDY WGQGTLVTVSS
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Figure 3 (Continued)

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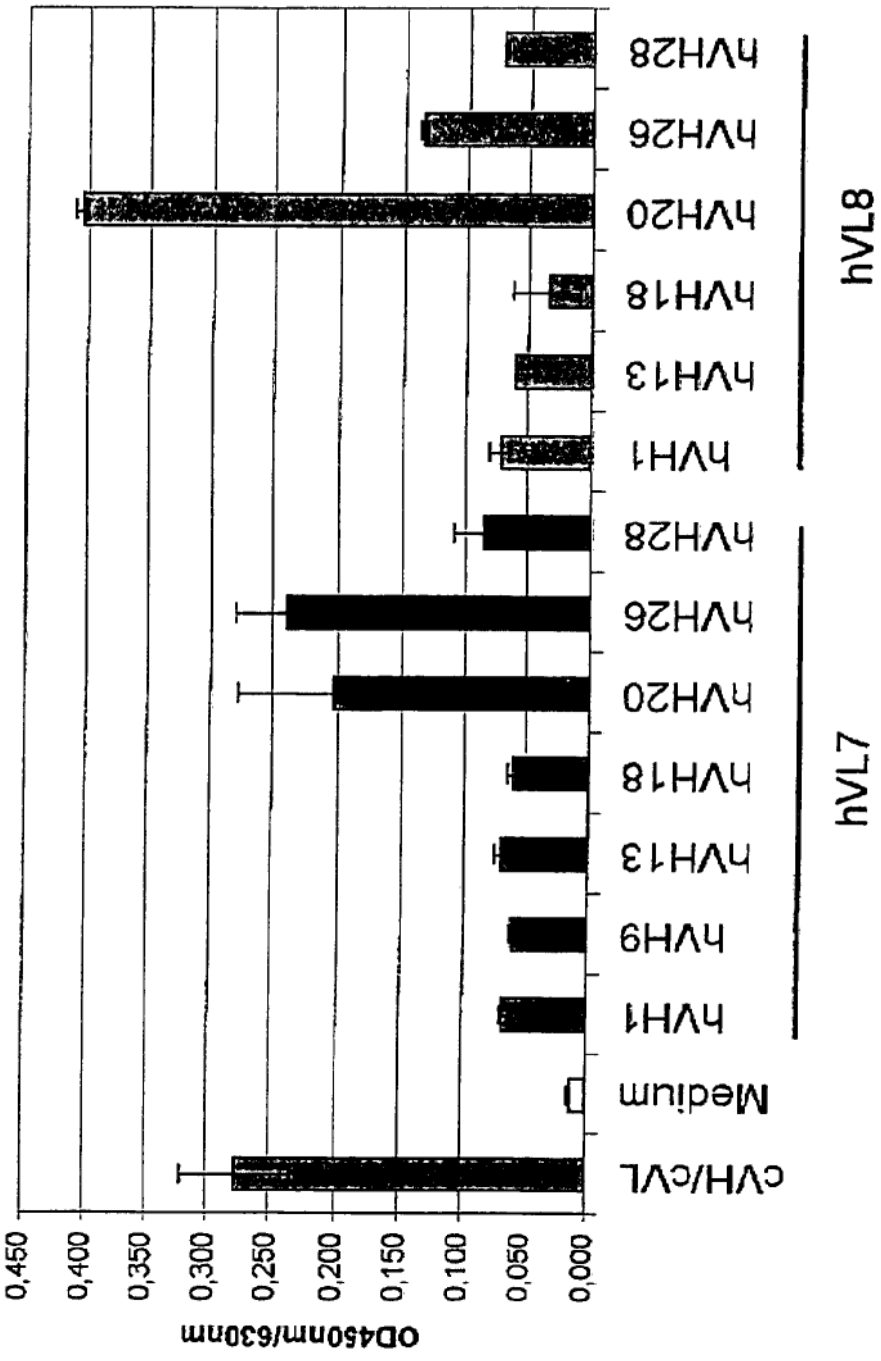

OD450nm/630nm
0,450
0,400
0,350
0,300
0,250
0,200
0,150
0,100
0,050
0,000
cVH/cVL
Medium
hVH1
hVH9
hVH13
hVH18
hVH20
hVH26
hVH28
hVL7
hVH1
hVH13
hVH18
hVH20
hVH26
hVH28
hVL8

FIGURE 4

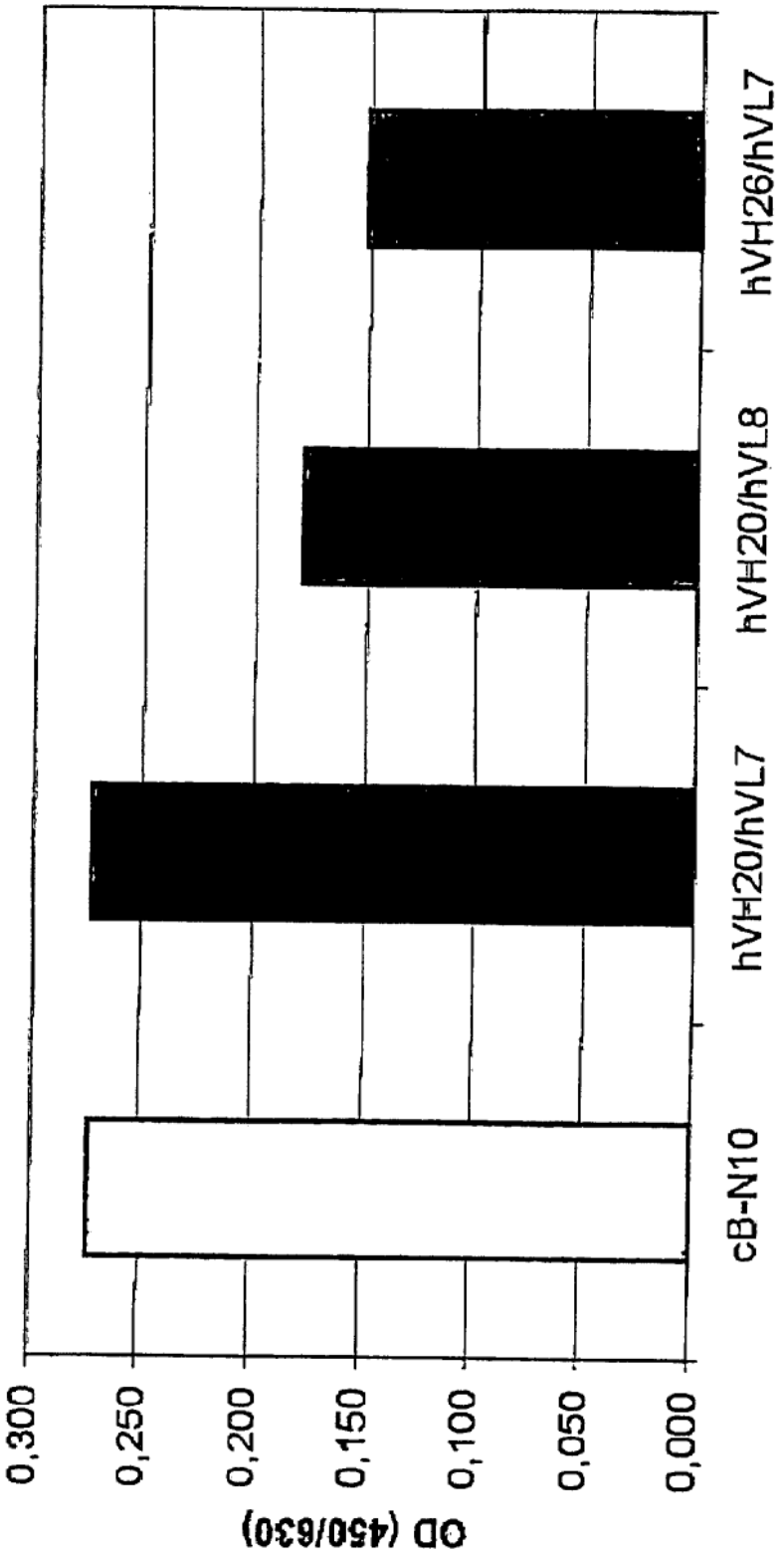

OD (450/630)
0,300
0,250
0,200
0,150
0,100
0,050
0,000
cB-N10
hVH20/hVL7
hVH20/hVL8
hVH26/hVL7

FIGURE 5

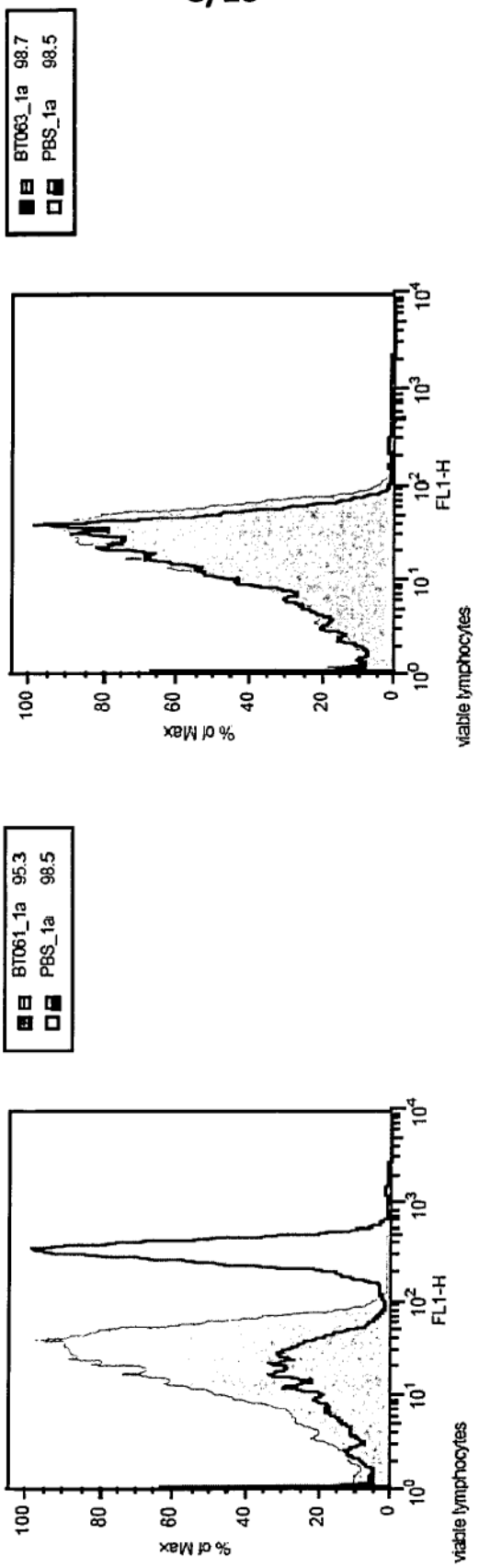

BT063_1a 98.7
PBS_1a 98.5
% of Max
viable lymphocytes
FL1-H
BT061_1a 95.3
PBS_1a 98.5
% of Max
viable lymphocytes
FL1-H

FIGURE 6

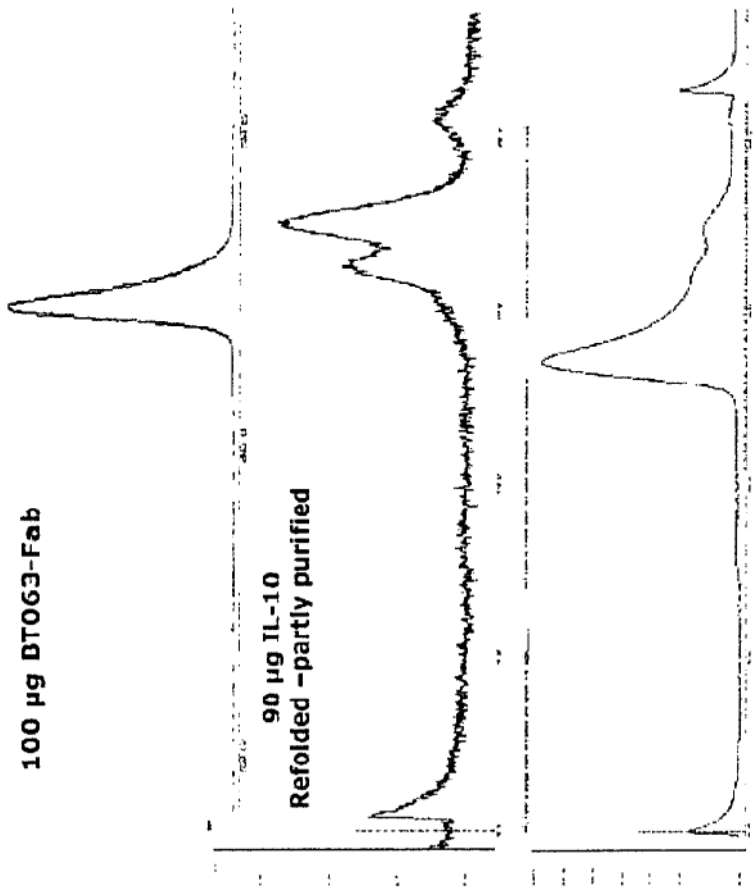


FIGURE 7



FIGURE 8

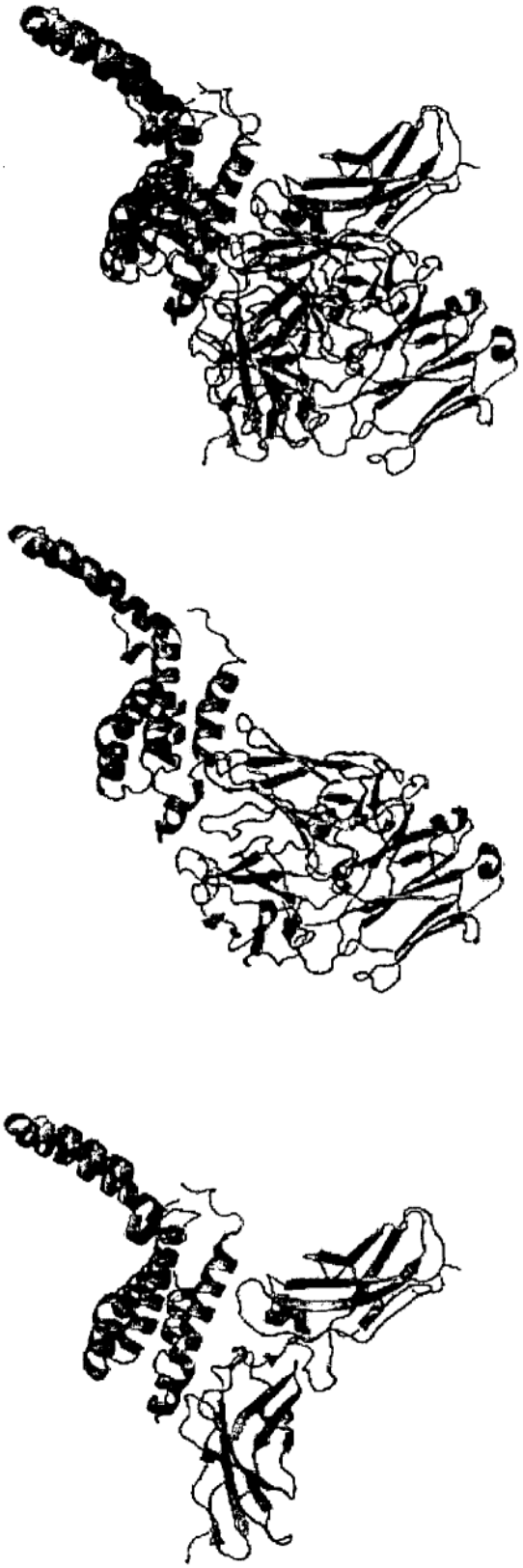

human IL-10 / IL-10R1
complex (pdb-code:1J7V)
human IL-10 / BT063-Fab
complex
overlay

FIGURE 9

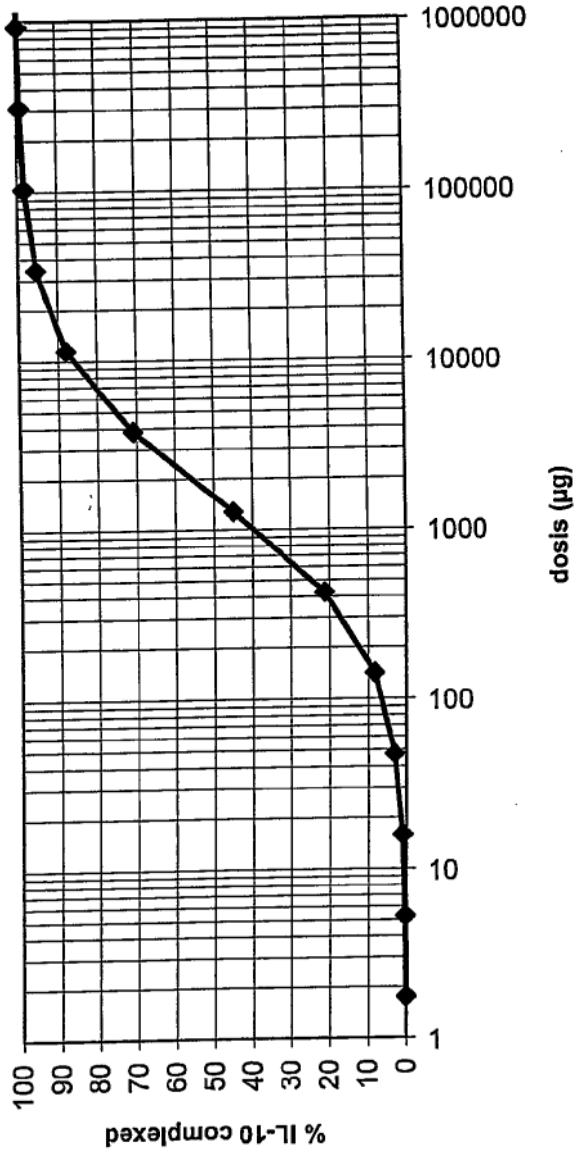

1000000
100000
10000
1000
100
10
1
dosis (µg)
100
90
80
70
60
50
40
30
20
10
0
% IL-10 complexed

FIGURE 10

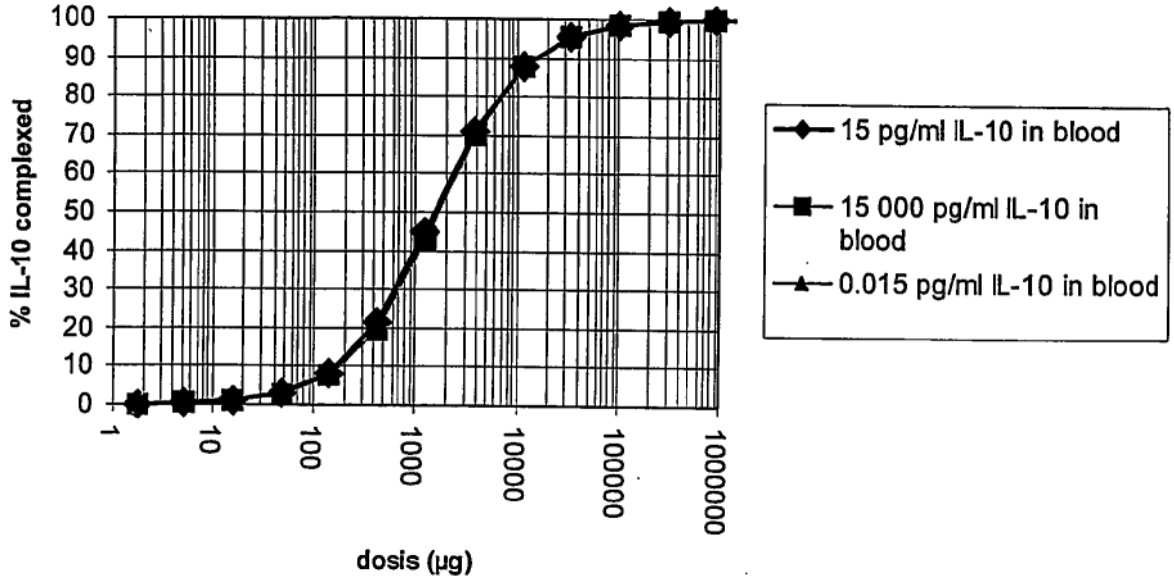


FIGURE 11

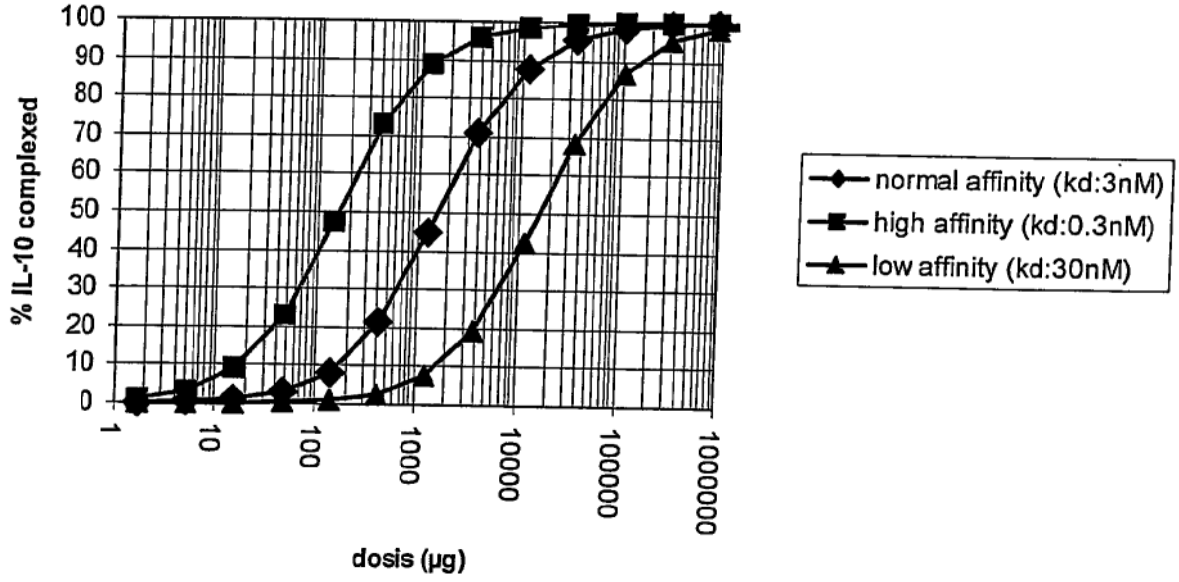


FIGURE 12

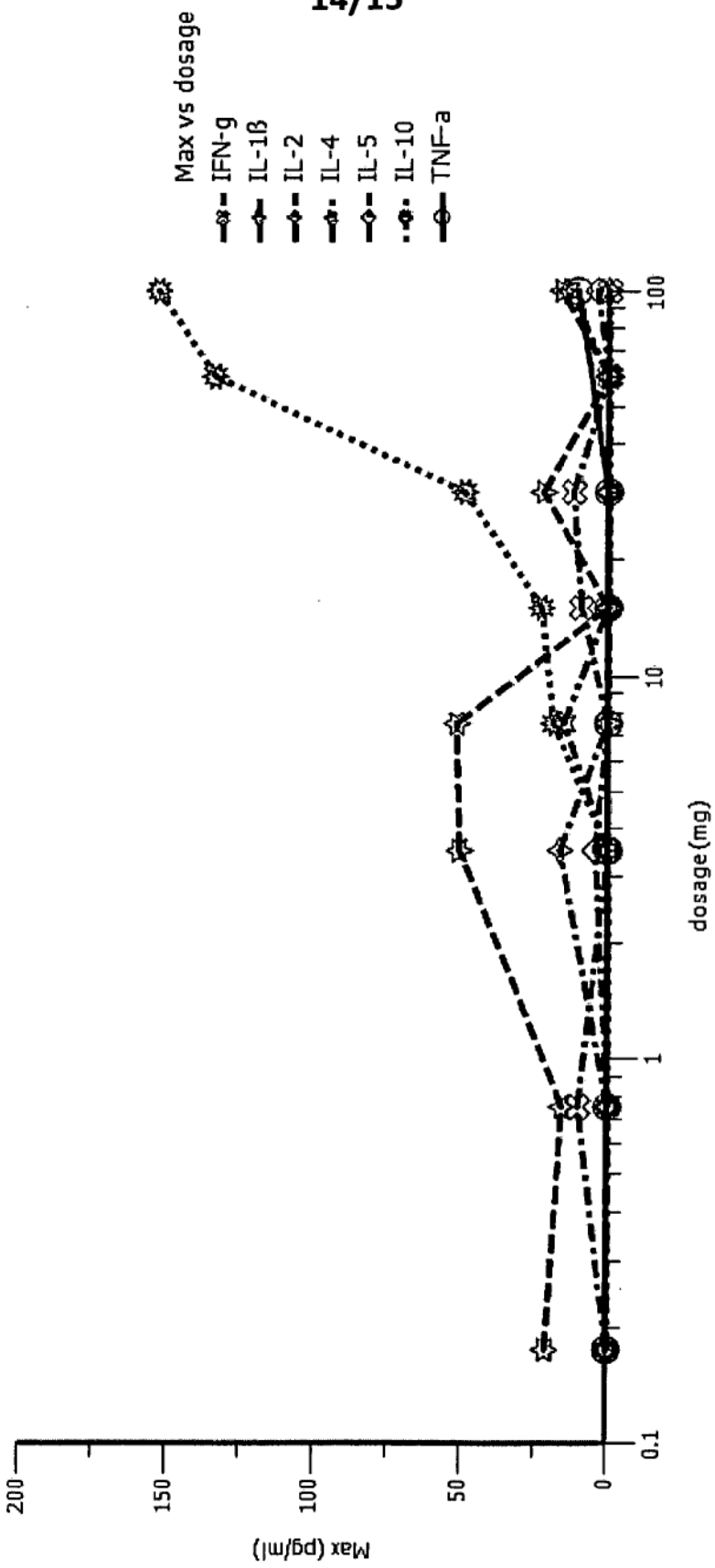

Max vs dosage
IFN-g
IL-1ß
IL-2
IL-4
IL-5
IL-10
TNF-a
Max (pg/ml)
200
150
100
50
0
0.1
1
10
100
dosage(mg)

FIGURE 13

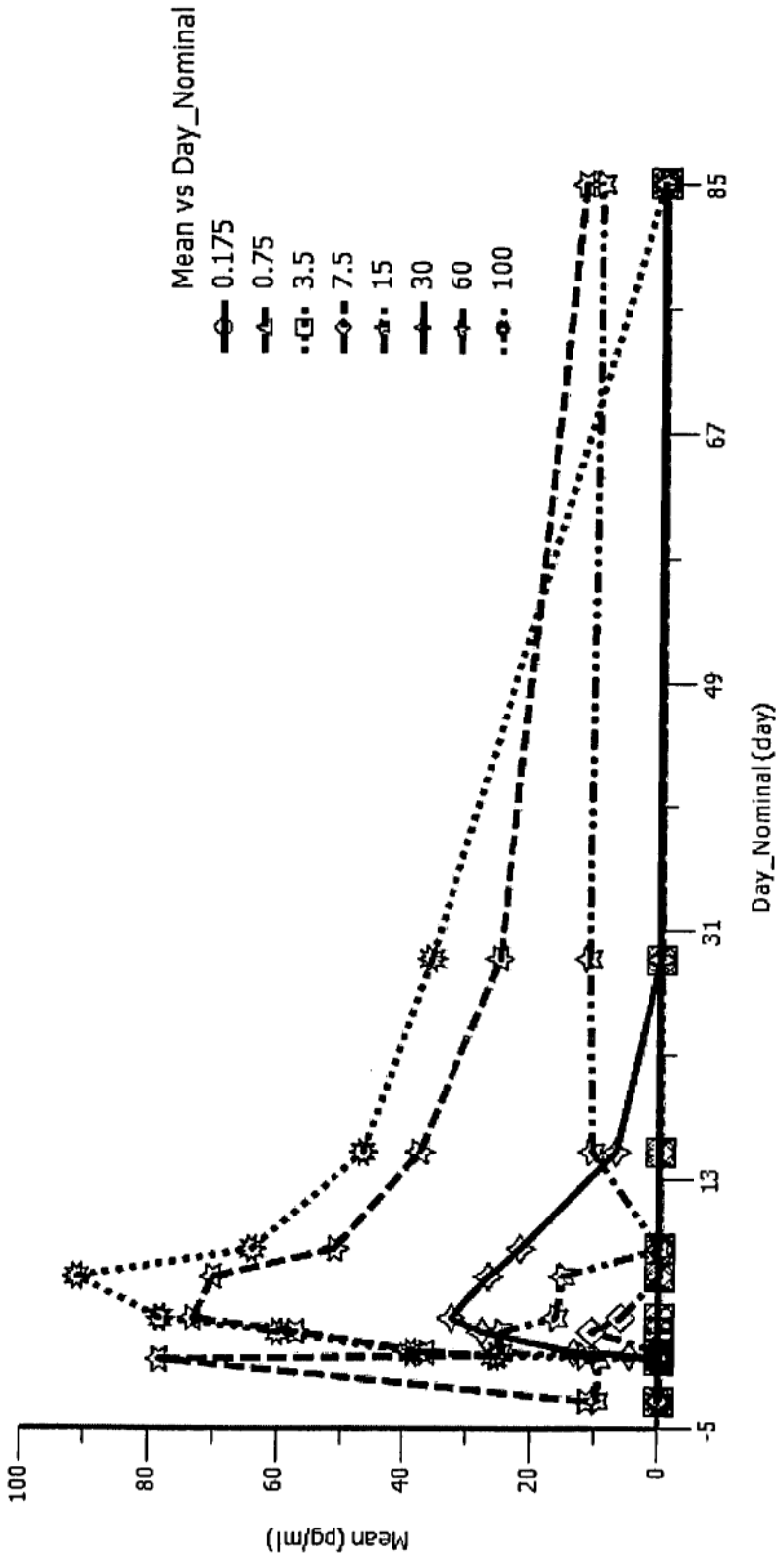

Mean vs Day_Nominal
0.175
0.75
3.5
7.5
15
30
60
100
Mean (pg/ml)
100
80
60
40
20
0
-5
13
31
49
67
85
Day_Nominal (day)

FIGURE 14