


**FIGURE 1A**

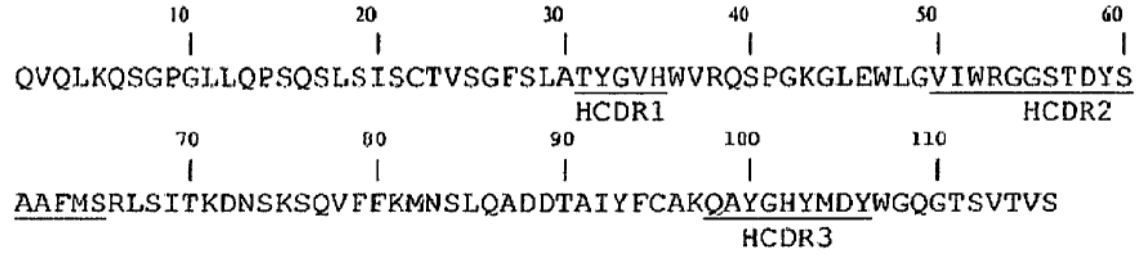



**FIGURE 1B**

VL

GATGTTTTGATGACCCAAACTCCACTCTCCCTGCCTGTCAGTCTTGGAGATCAAGCCTCC
ATCTCTTGCAGATCTAGTCAGAACATTGTACATAGTAATGGAAACACCTATTTAGAATGG
TACCTGCAGAAACCAGGCCAGTCTCCAAAGCTCCTGATCTACAAAGTTTCCAACCGATTT
TCTGGGGTCCCAGACAGGTTCAGTGGCAGTGGATCAGGGACAGATTTCACACTCAAGATC
ACCAGATTGGAGGCTGAGGATCTGGGAGTTTATTACTGCTTTCAAGGTTCACATGTTCCG
TGGACGTTCGGTGGAGGCACCAAGCTGGAAATCAAACGGGCC

FIGURE 2A

VH

CAGGTGCAGCTGAAGCAGTCAGGACCTGGCCTACTGCAGCCCTCACAGAGCCTGTCCATA
TCCTGCACAGTCTCTGGTTTCTCATTAGCTACCTATGGTGTACACTGGGTTCGCCAGTCT
CCAGGAAAGGGTCTGGAGTGGCTGGGAGTGATTTGGAGAGGTGGGAGCACAGACTACACT
GCAGCTTTCATGTCCAGACTGAGCATCACCAAGGACAACTCCAAGAGCCAAGTTTTCTTT
AAAATGAACAGTCTGCAAGCTGATGACACTGCCATTTACTTCTGTGCCAAACAGGCGTAT
CGTCACTACATGGACTACTGGGGTCAAGGAACCTCAGTCACCGTCTCC

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 WFQQRPGQSPRLIY 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 |
| hVL9 | DVLMTQSPLSLPVTLGQPASISC RSSQNIVHSNGNTYLE WYLQRPGQSPRLLIY KVSNRFS GVPDRFSGSGSGTDFTLKISRVEAEDVGVYYC FQGSHVPWT FGGGTKVEIK |
| hVL10 | DVVMTQSPLSLPVTLGQPASISC RSSQNIVHSNGNTYLE WYLQRPGQSPRRLIY KVSNRFS GVPDRFSGSGSGTDFTLKISRVEAEDVGVYYC FQGSHVPWT FGGGTKVEIK |
| hVL11 | DVVMTQTPLSLPVTLGQPASISC RSSQNIVHSNGNTYLE WYLQRPGQSPRRLIY KVSNRFS GVPDRFSGSGSGTDFTLKISRVEAEDVGVYYC FQGSHVPWT FGGGTKVEIK |
| hVL12 | DVVMTQTPLSLPVTLGQPASISC RSSQNIVHSNGNTYLE WYLQRPGQSPRRLIY KVSNRFS GVPDRFSGSGSGTDFTLKISRVEAEDVGVYYC FQGSHVPWT FGQGTKVEIK |

3/15

FIGURE 3

**Humanized VH variants**

```
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
```

**FIGURE 3 (continued)**

```
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

hVH20 EVQLVESGGGLVQPGGSLRLSCAASGFSFA TYGVH WVRQSPGKGLEWLG VIWRGGSTDYSAAFMS RLTISKDNSKNTVYFQMNSLRAEDTAVYFCAK QAYGHYMDY WGQGTSVTVSS

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

hVH26 EVQLVESGGGLVQPGGSLRLSCAASGFSFA TYGVH WVRQSPGKGLEWLG VIWRGGSTDYSAAFMS RLTISKDNSKNTVYLQMNSLRAEDTAVYFCAK QAYGHYMDY WGQGTSVTVSS

hVH27 EVQLVESGGGLVQPGGSLRLSCAASGFSFA TYGVH WVRQSPGKGLEWLG VIWRGGSTDYSAAFMS RLTISKDNSKNTVYFQMNSLRAEDTAVYYCAK QAYGHYMDY WGQGTSVTVSS

hVH28 EVQLVESGGGLVQPGGSLRLSCAASGFSFA TYGVH WVRQSPGKGLEWLG VIWRGGSTDYSAAFMS RLTISKDNSKNTVYFQMNSLRAEDTAVYYCAR QAYGHYMDY WGQGTSVTVSS

hVH29 EVQLVESGGGLVQPGGSLRLSCAASGFSFA TYGVH WVRQSPGKGLEWLG VIWRGGSTDYSAAFMS RLTISKDNSKNTVYFQMNSLRAEDTAVYFCAK QAYGHYMDY WGQGTLVTVSS
```

**Figure 3 (Continued)**

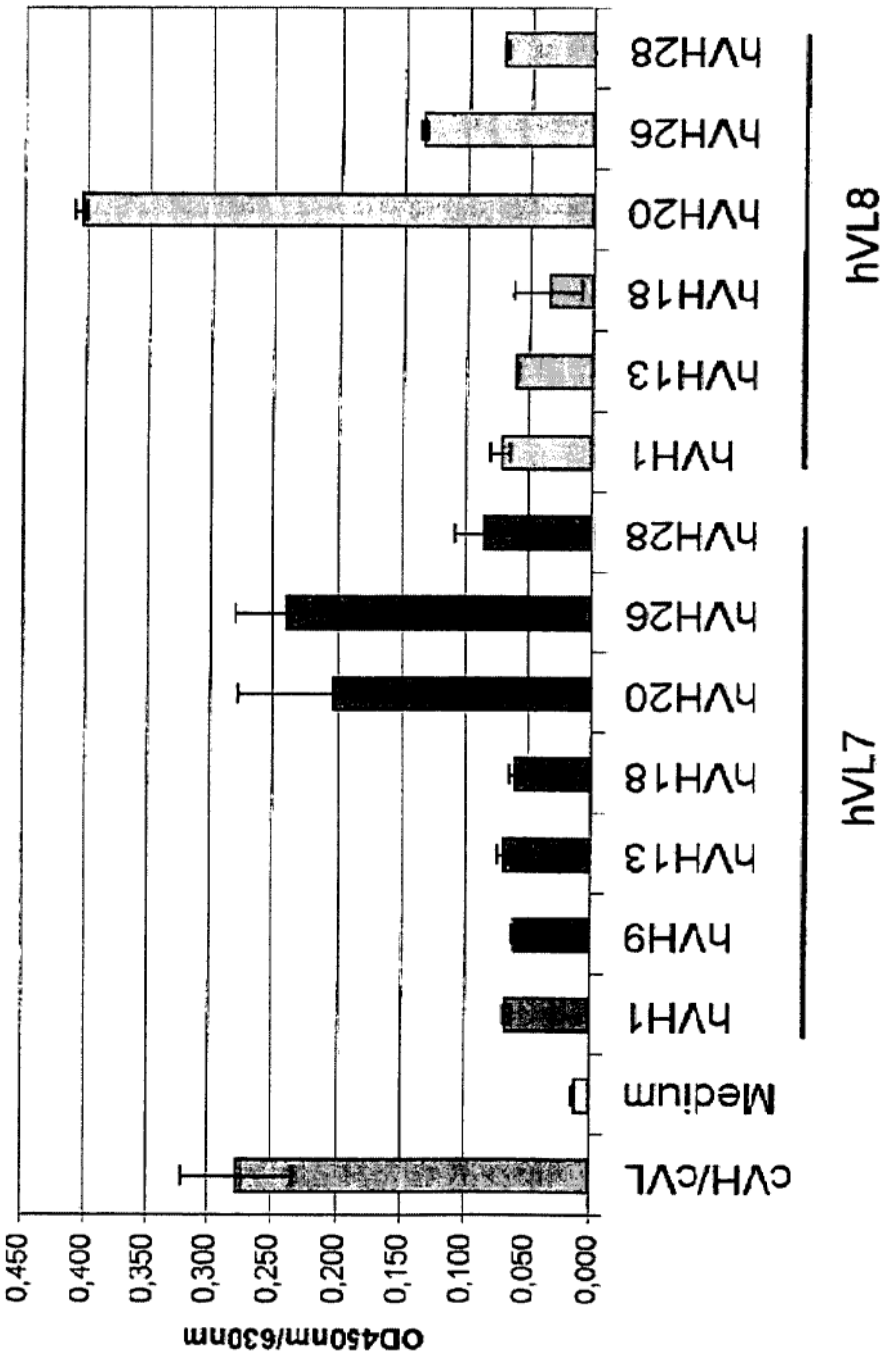

OD450nm/630nm
0,450
0,400
0,350
0,300
0,250
0,200
0,150
0,100
0,050
0,000
cVH/cVL
Medium
hVH1
hVH9
hVH13
hVH18
hVH20
hVH26
hVH28
hVL7
hVH1
hVH13
hVH18
hVH20
hVH26
hVH28
hVL8

FIGURE 4

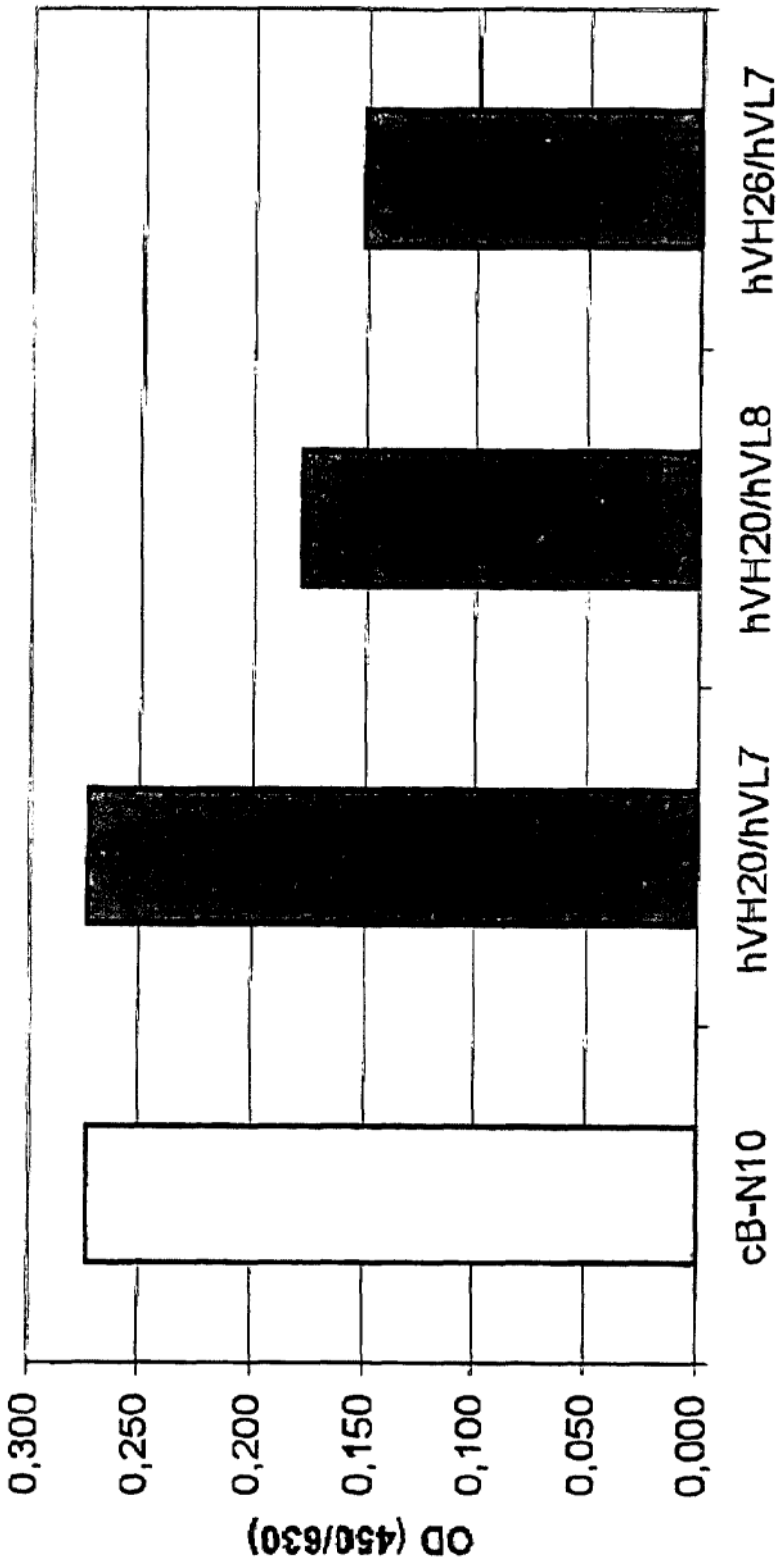

OD (450/630)
0,300
0,250
0,200
0,150
0,100
0,050
0,000
cB-N10
hVH20/hVL7
hVH20/hVL8
hVH26/hVL7

FIGURE 5

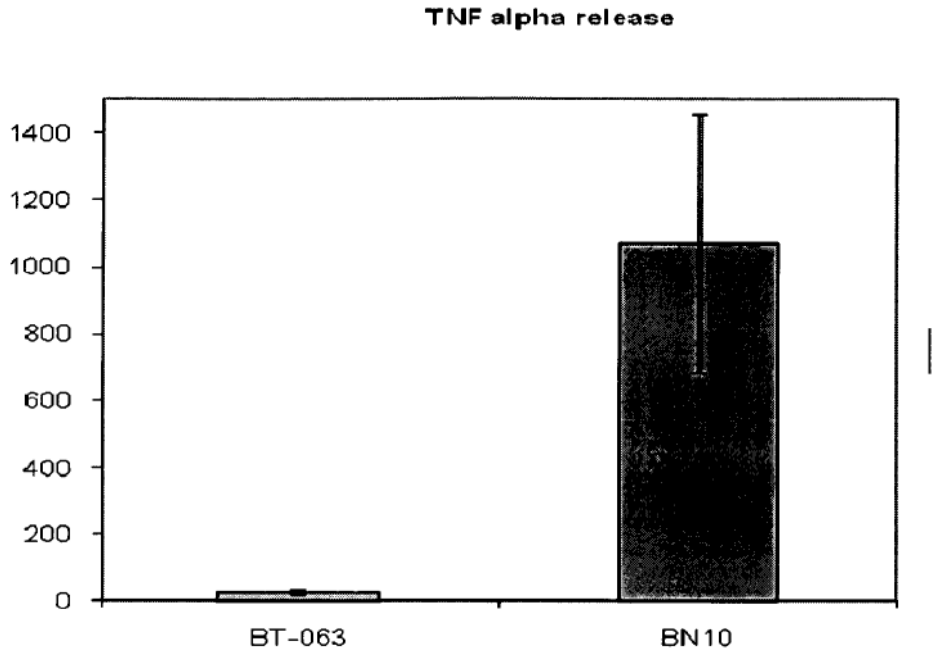



FIGURE 6A

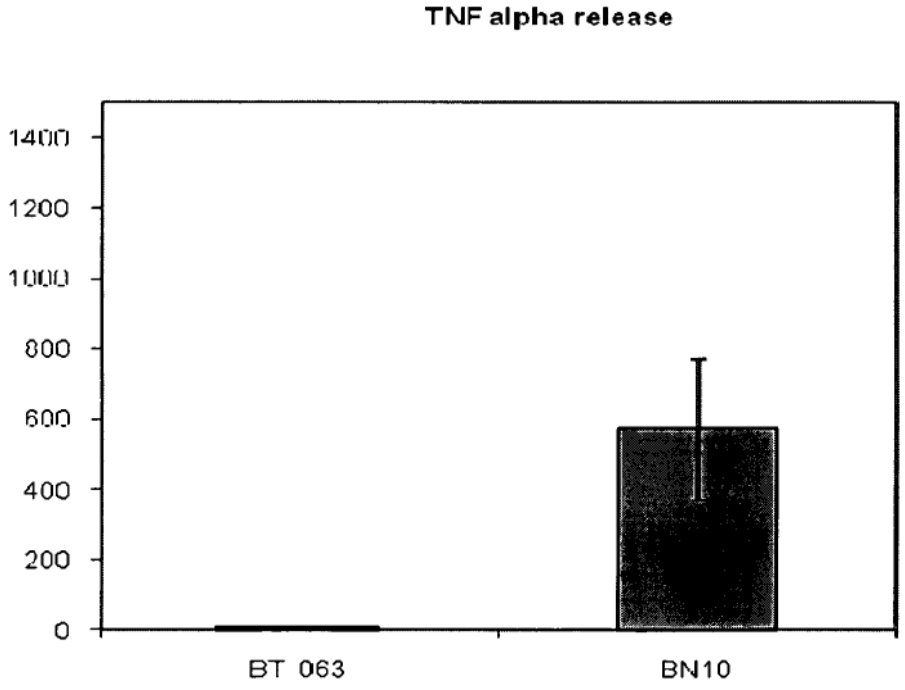



FIGURE 6B

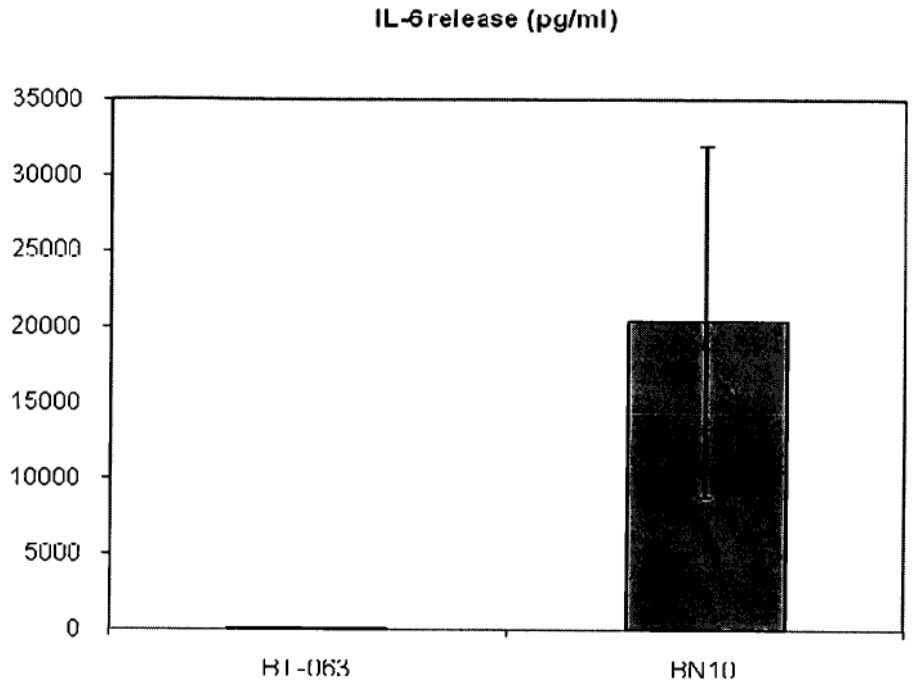



FIGURE 7A

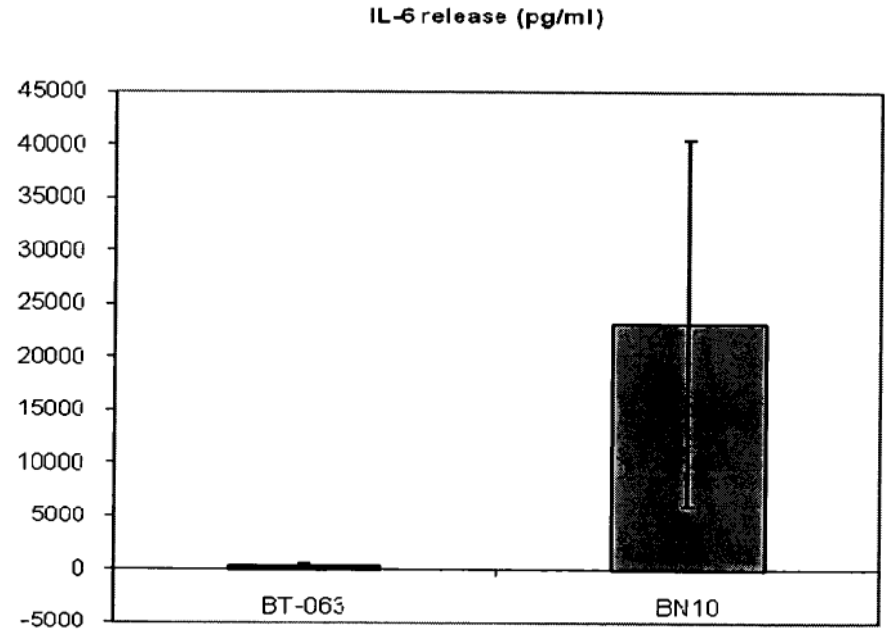



FIGURE 7B

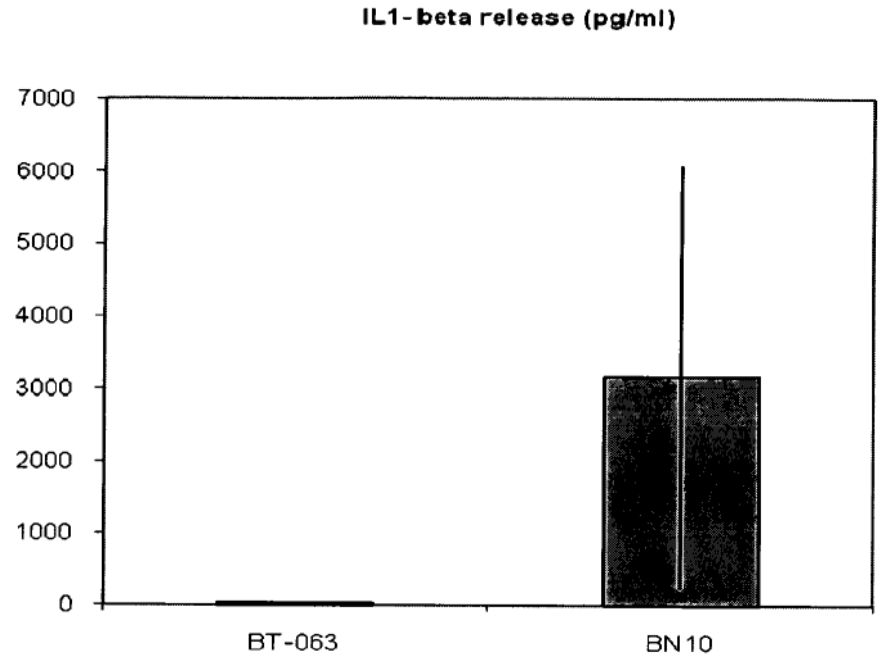



FIGURE 8A

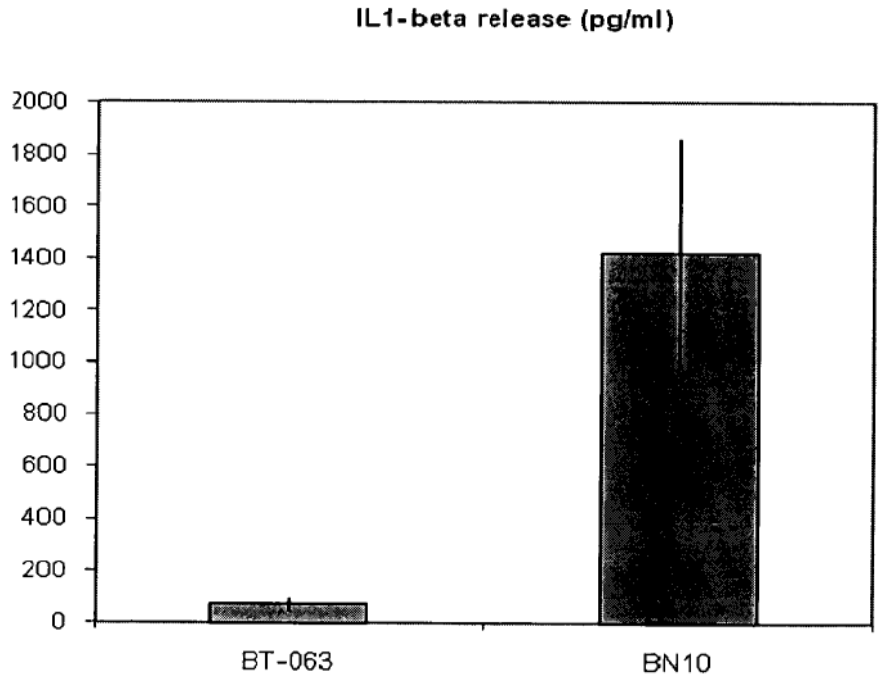



FIGURE 8B

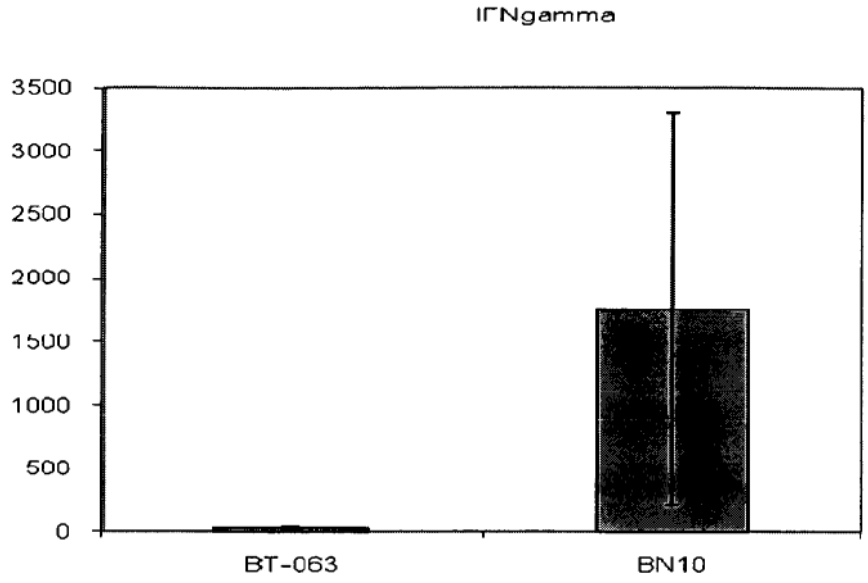



FIGURE 9A

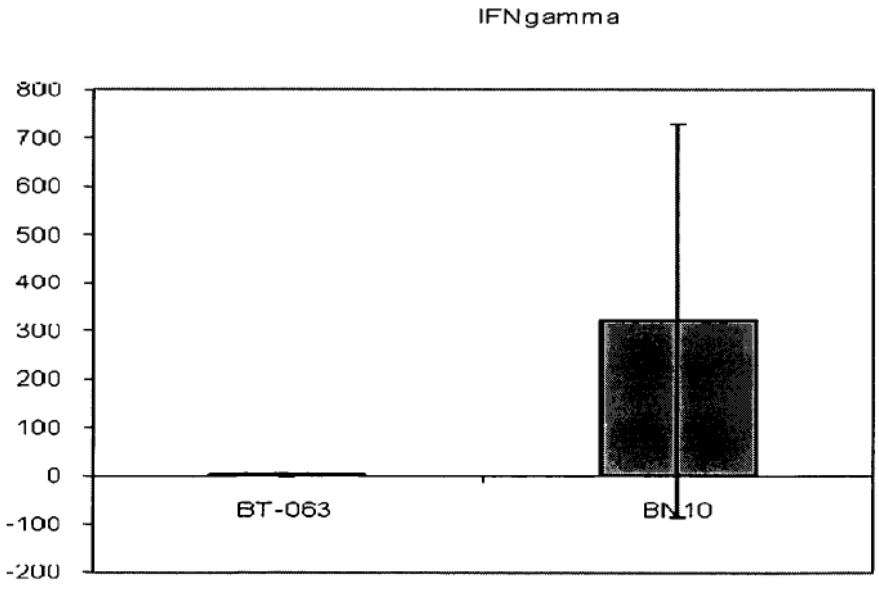



FIGURE 9B



FIGURE 10


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

**FIGURE 11**

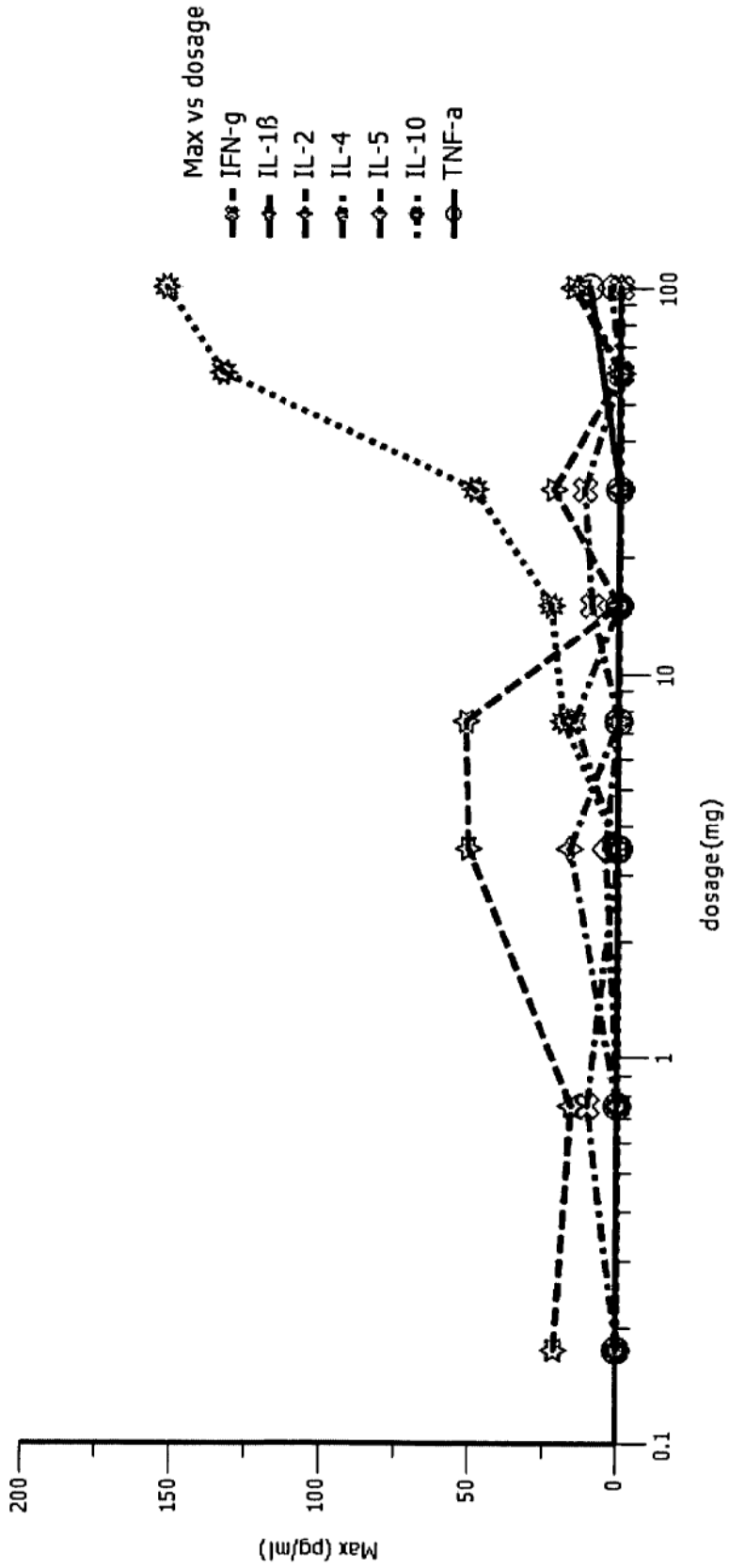

Max vs dosage
IFN-g
IL-1ß
IL-2
IL-4
IL-5
IL-10
TNF-a
Max (pg/ml)
200
150
100
50
0
0.1
1
10
100
dosage(mg)

FIGURE 12

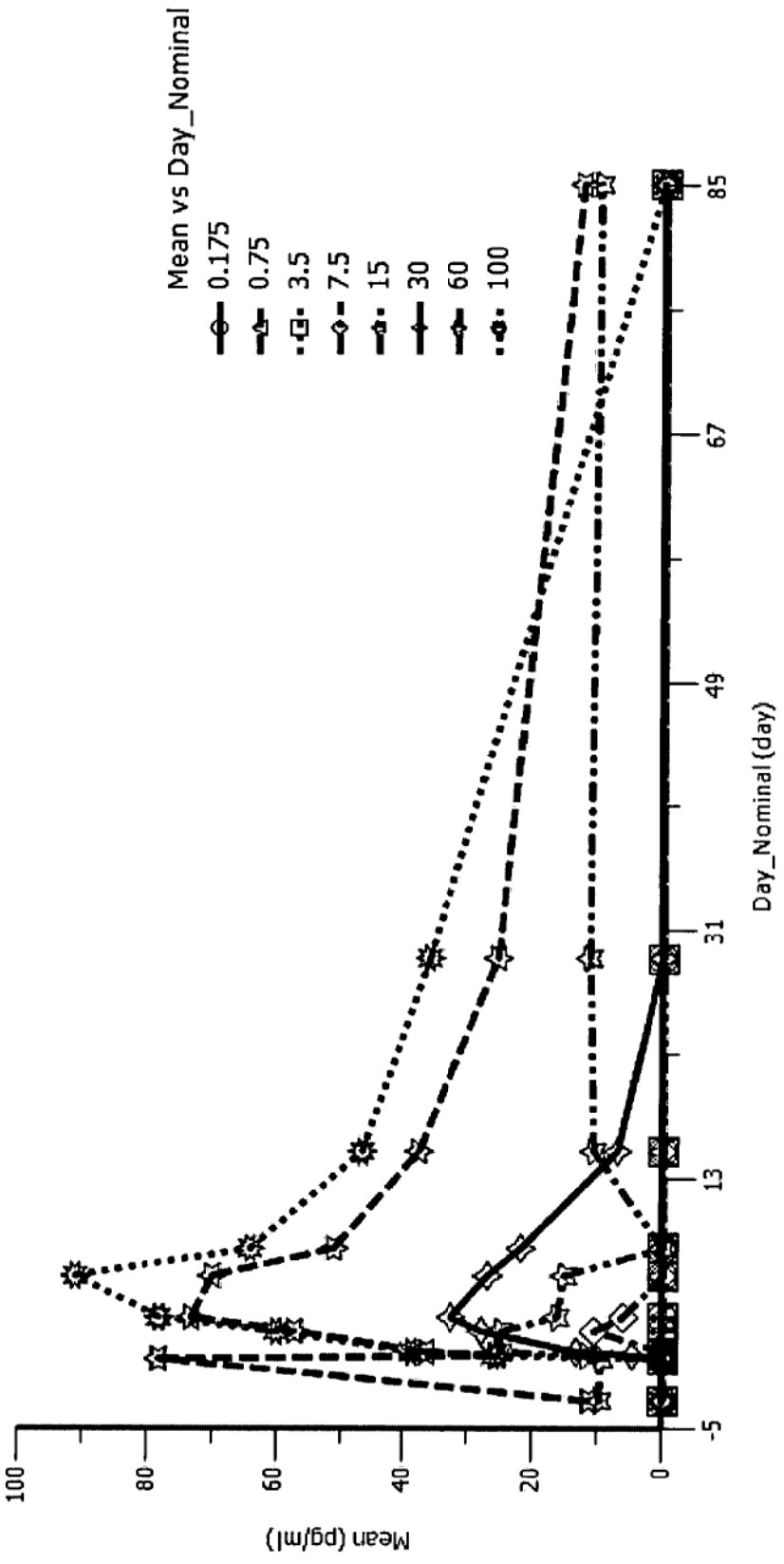

Mean vs Day_Nominal
0.175
0.75
3.5
7.5
15
30
60
100
Mean (pg/ml)
100
80
60
40
20
0
-5
13
31
49
67
85
Day_Nominal (day)

FIGURE 13