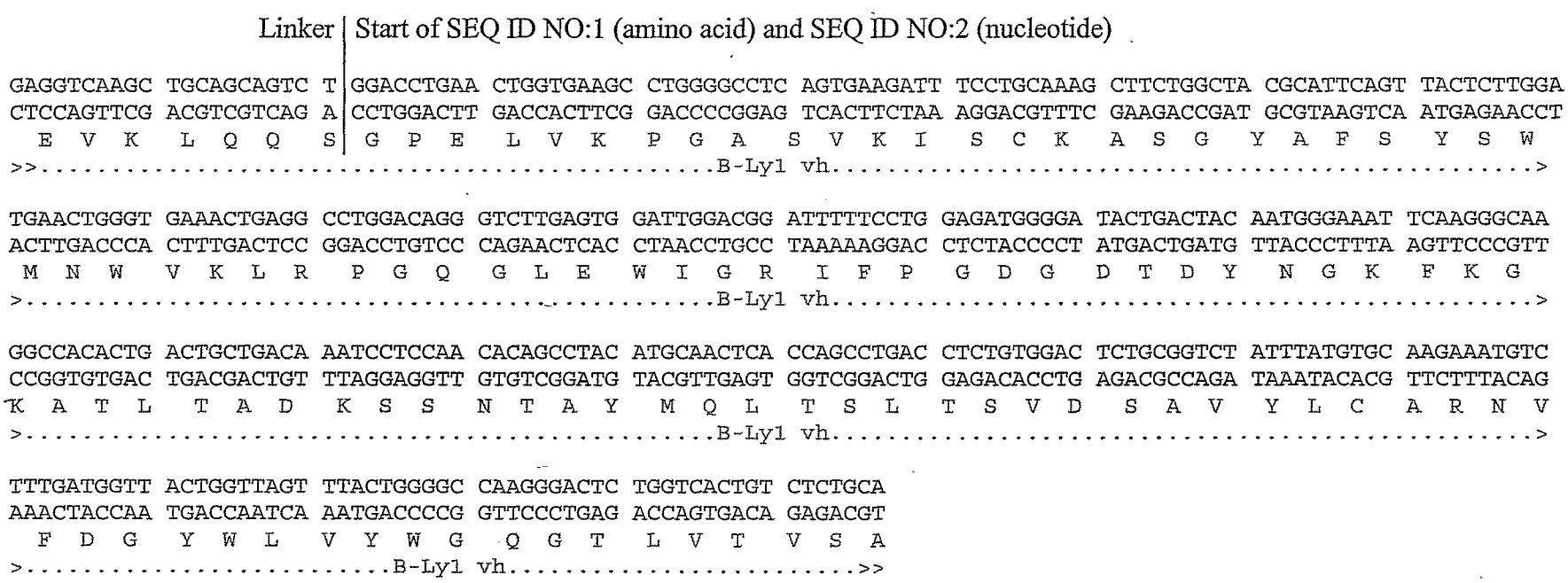

Linker | Start of SEQ ID NO:1 (amino acid) and SEQ ID NO:2 (nucleotide)
1 GAGGTCAAGC TGCAGCAGTC T|GGACCTGAA CTGGTGAAGC CTGGGGCCTC AGTGAAGATT TCCTGCAAAG CTTCTGGCTA CGCATTCAGT TACTCTTGGA
CTCCAGTTCG ACGTCGTCAG A|CCTGGACTT GACCACTTCG GACCCCGGAG TCACTTCTAA AGGACGTTTC GAAGACCGAT GCGTAAGTCA ATGAGAACCT
E V K L Q Q S| G P E L V K P G A S V K I S C K A S G Y A F S Y S W
>>.....B-Ly1 vh.....>
101 TGAACTGGGT GAAACTGAGG CCTGGACAGG GTCTTGAGTG GATTGGACGG ATTTTTCCTG GAGATGGGGA TACTGACTAC AATGGGAAAT TCAAGGGCAA
ACTTGACCCA CTTTGACTCC GGACCTGTCC CAGAACTCAC CTAACCTGCC TAAAAAGGAC CTCTACCCCT ATGACTGATG TTACCCTTTA AGTTCCCGTT
M N W V K L R P G Q G L E W I G R I F P G D G D T D Y N G K F K G
>.....B-Ly1 vh.....>
201 GGCCACACTG ACTGCTGACA AATCCTCCAA CACAGCCTAC ATGCAACTCA CCAGCCTGAC CTCTGTGGAC TCTGCGGTCT ATTTATGTGC AAGAAATGTC
CCGGTGTGAC TGACGACTGT TTAGGAGGTT GTGTCGGATG TACGTTGAGT GGTCGGACTG GAGACACCTG AGACGCCAGA TAAATACACG TTCTTTACAG
K A T L T A D K S S N T A Y M Q L T S L T S V D S A V Y L C A R N V
>.....B-Ly1 vh.....>
301 TTTGATGGTT ACTGGTTAGT TTACTGGGGC CAAGGGACTC TGGTCACTGT CTCTGCA
AAACTACCAA TGACCAATCA AATGACCCCG GTTCCCTGAG ACCAGTGACA GAGACGT
F D G Y W L V Y W G Q G T L V T V S A
>.....B-Ly1 vh.....>>

FIG. 1

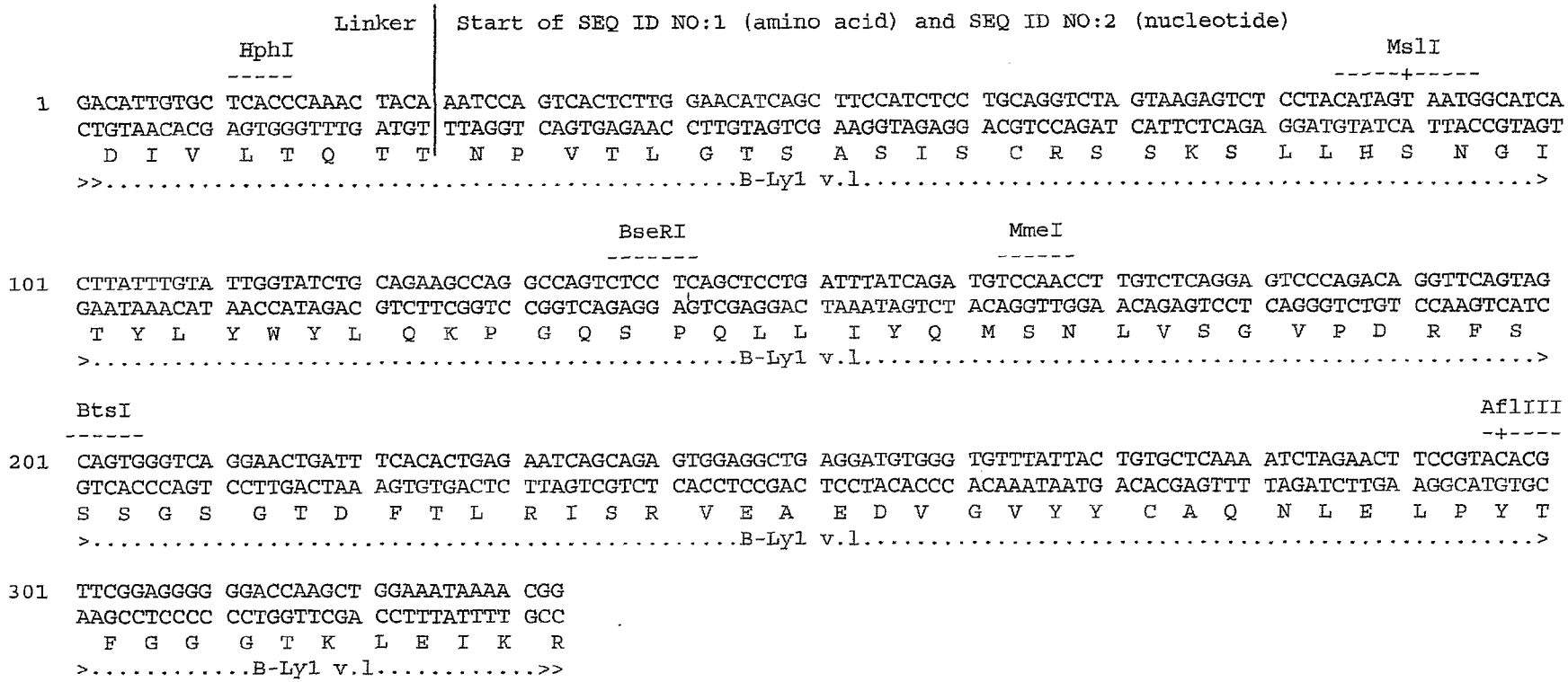

Linker
Start of SEQ ID NO:1 (amino acid) and SEQ ID NO:2 (nucleotide)
HphI
MslI
1 GACATTGTGC TCACCCAAAC TACA AATCCA GTCACTCTTG GAACATCAGC TTCCATCTCC TGCAGGTCTA GTAAGAGTCT CCTACATAGT AATGGCATCA
CTGTAACACG AGTGGGTTTG ATGT TTAGGT CAGTGAGAAC CTTGTAGTCG AAGGTAGAGG ACGTCCAGAT CATTCTCAGA GGATGTATCA TTACCGTAGT
D I V L T Q T T N P V T L G T S A S I S C R S S K S L L H S N G I
>>.....B-Ly1 v.l.....>
BseRI
MmeI
101 CTTATTTGTA TTGGTATCTG CAGAAGCCAG GCCAGTCTCC TCAGCTCCTG ATTTATCAGA TGTCCAACCT TGTCTCAGGA GTCCCAGACA GGTTCAGTAG
GAATAAACAT AACCATAGAC GTCTTCGGTC CGGTCAGAGG AGTCGAGGAC TAAATAGTCT ACAGGTTGGA ACAGAGTCCT CAGGGTCTGT CCAAGTCATC
T Y L Y W Y L Q K P G Q S P Q L L I Y Q M S N L V S G V P D R F S
>.....B-Ly1 v.l.....>
BtsI
AflIII
201 CAGTGGGTCA GGAACTGATT TCACACTGAG AATCAGCAGA GTGGAGGCTG AGGATGTGGG TGTTTATTAC TGTGCTCAAA ATCTAGAACT TCCGTACACG
GTCACCCAGT CCTTGACTAA AGTGTGACTC TTAGTCGTCT CACCTCCGAC TCCTACACCC ACAAATAATG ACACGAGTTT TAGATCTTGA AGGCATGTGC
S S G S G T D F T L R I S R V E A E D V G V Y Y C A Q N L E L P Y T
>.....B-Ly1 v.l.....>
301 TTCGGAGGGG GGACCAAGCT GGAAATAAAA CGG
AAGCCTCCCC CCTGGTTCGA CCTTTATTTT GCC
F G G G T K L E I K R
>.....B-Ly1 v.l.....>>

FIG. 2

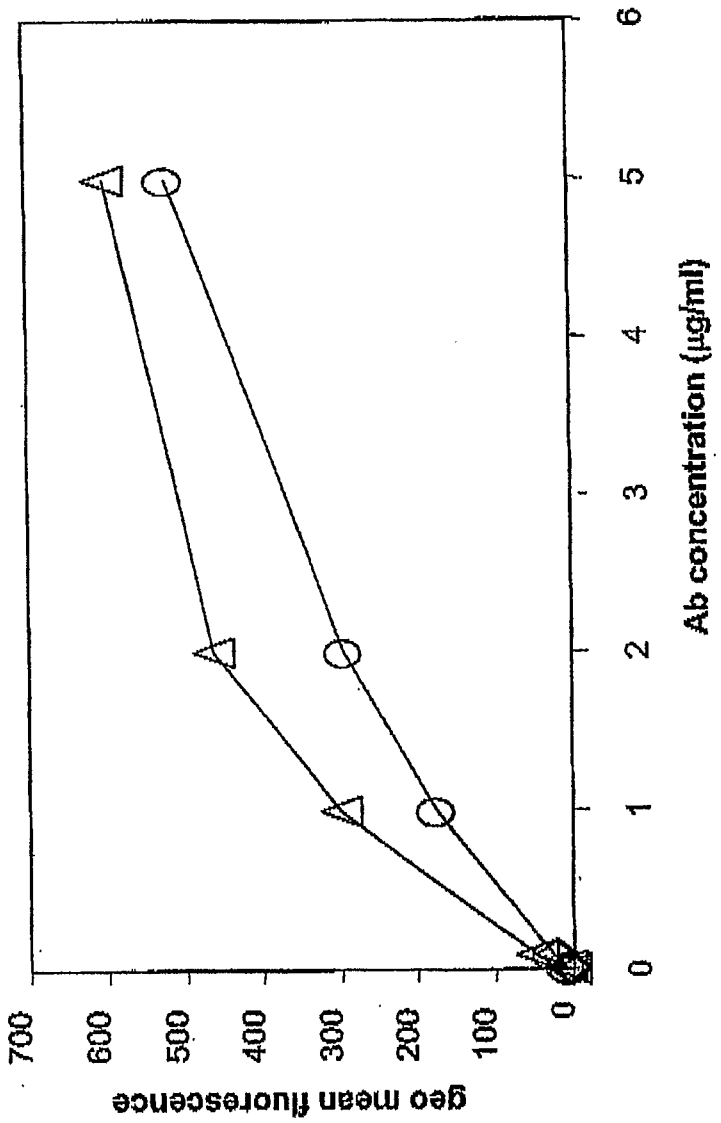

geo mean fluorescence
700
600
500
400
300
200
100
0
0
1
2
3
4
5
6
Ab concentration (µg/ml)

FIG. 3

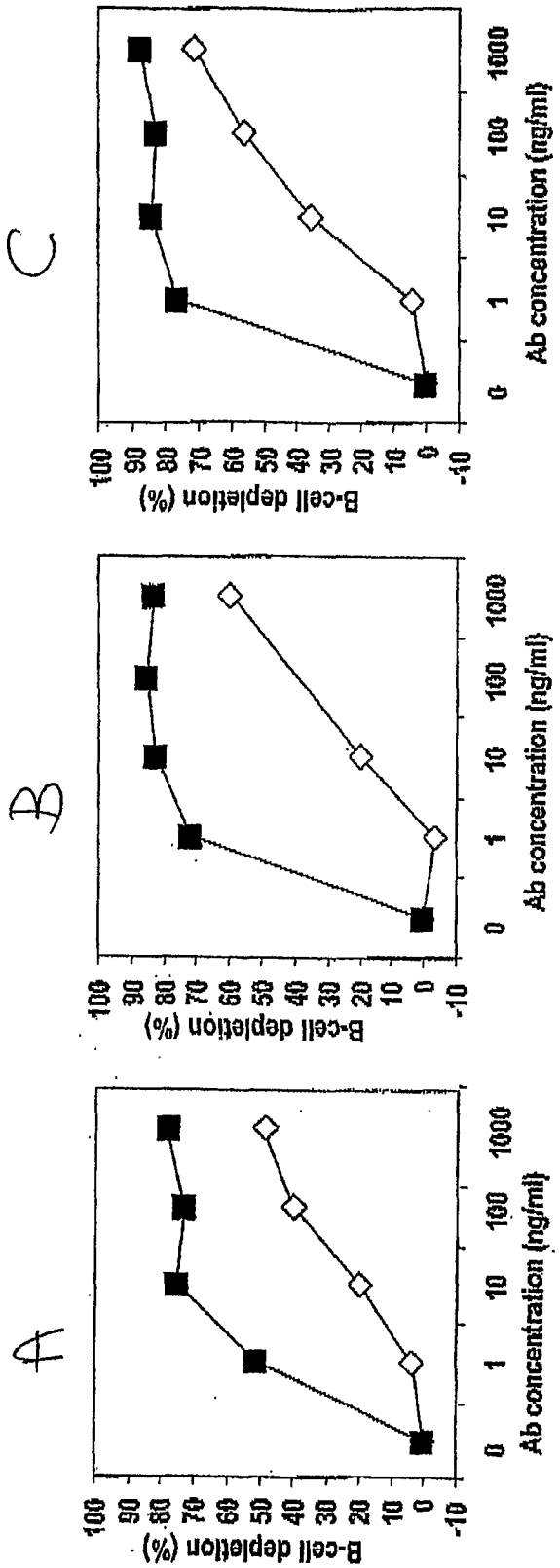

A
B
C
B-cell depletion (%)
Ab concentration (ng/ml)
100
90
80
70
60
50
40
30
20
10
0
-10
0
1
10
100
1000

FIG. 4

SapI
MluI
PstI
SEQ ID NO: 11 (nucleic acid) and SEQ ID NO: 13 (amino acid)
HindIII
StuI
PshAI
NheI
PstI
B-Ly1 h.c

FIG. 5A

```
501  CAAGGACTAC TTCCCCGAAC CGGTGACGGT GTCGTGGAAC TCAGGCGCCC TGACCAGCGG CGTGCACACC TTCCCGGCTG TCCTACAGTC CTCAGGACTC
     GTTCCTGATG AAGGGGCTTG GCCACTGCCA CAGCACCTTG AGTCCGCGGG ACTGGTCGCC GCACGTGTGG AAGGGCCGAC AGGATGTCAG GAGTCCTGAG
     V  K  D  Y     F  P  E     P  V  T     V  S  W  N     S  G  A     L  T  S     G  V  H  T     F  P  A     V  L  Q     S  S  G  L
     >.....................................................B-Ly1 h.c.....................................................>

601  TACTCCCTCA GCAGCGTGGT GACCGTGCCC TCCAGCAGCT TGGGCACCCA GACCTACATC TGCAACGTGA ATCACAAGCC CAGCAACACC AAGGTGGACA
     ATGAGGGAGT CGTCGCACCA CTGGCACGGG AGGTCGTCGA ACCCGTGGGT CTGGATGTAG ACGTTGCACT TAGTGTTCGG GTCGTTGTGG TTCCACCTGT
       Y  S  L     S  S  V     V  T  V  P     S  S  S     L  G  T     Q  T  Y  I     C  N  V     N  H  K     P  S  N  T     K  V  D
     >.....................................................B-Ly1 h.c.....................................................>

                                                                                                  AhdI
                                                                                                  ------+-----
701  AGAAAGCAGA GCCCAAATCT TGTGACAAAA CTCACACATG CCCACCGTGC CCAGCACCTG AACTCCTGGG GGGACCGTCA GTCTTCCTCT TCCCCCCAAA
     TCTTTCGTCT CGGGTTTAGA ACACTGTTTT GAGTGTGTAC GGGTGGCACG GGTCGTGGAC TTGAGGACCC CCCTGGCAGT CAGAAGGAGA AGGGGGGTTT
      K  K  A     E  P  K  S     C  D  K     T  H  T     C  P  P  C     P  A  P     E  L  L     G  G  P  S     V  F  L     F  P  P
     >.....................................................B-Ly1 h.c.....................................................>

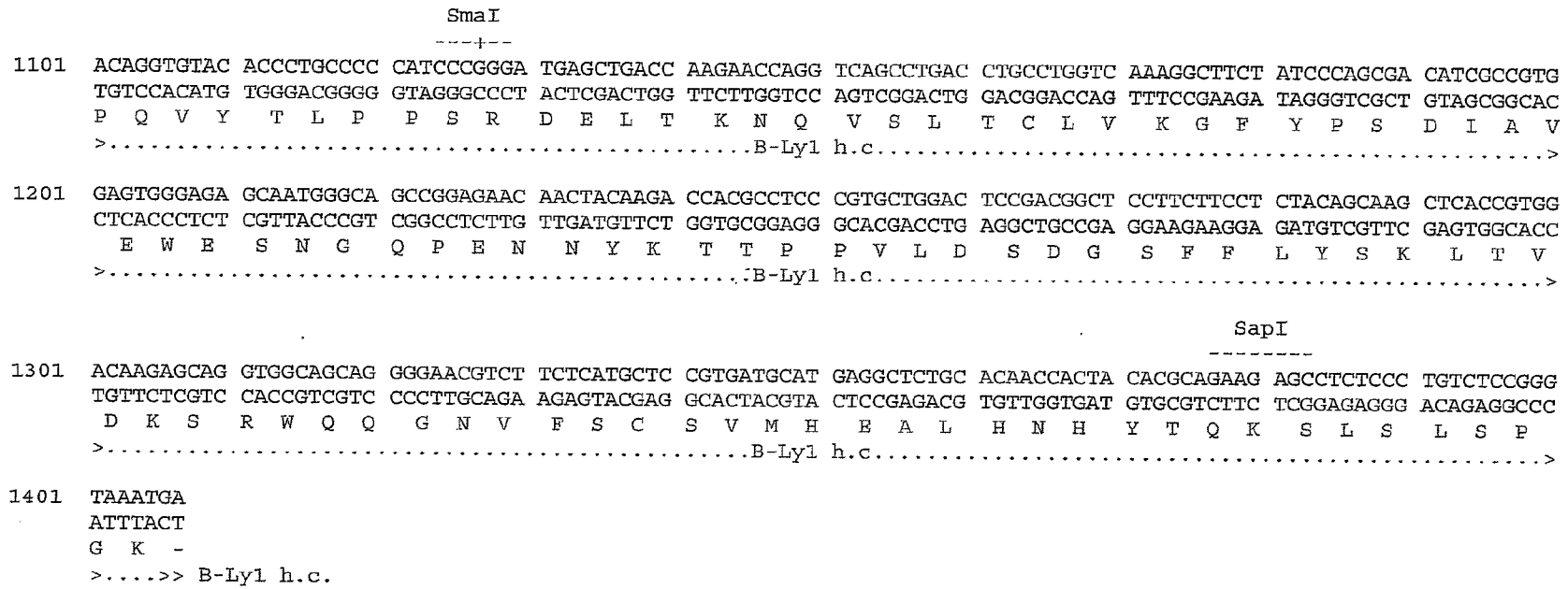
801  ACCCAAGGAC ACCCTCATGA TCTCCCGGAC CCCTGAGGTC ACATGCGTGG TGGTGGACGT GAGCCACGAA GACCCTGAGG TCAAGTTCAA CTGGTACGTG
     TGGGTTCCTG TGGGAGTACT AGAGGGCCTG GGGACTCCAG TGTACGCACC ACCACCTGCA CTCGGTGCTT CTGGGACTCC AGTTCAAGTT GACCATGCAC
     K  P  K  D     T  L  M     I  S  R     T  P  E  V     T  C  V     V  V  D     V  S  H  E     D  P  E     V  K  F     N  W  Y  V
     >.....................................................B-Ly1 h.c.....................................................>

901  GACGGCGTGG AGGTGCATAA TGCCAAGACA AAGCCGCGGG AGGAGCAGTA CAACAGCACG TACCGTGTGG TCAGCGTCCT CACCGTCCTG CACCAGGACT
     CTGCCGCACC TCCACGTATT ACGGTTCTGT TTCGGCGCCC TCCTCGTCAT GTTGTCGTGC ATGGCACACC AGTCGCAGGA GTGGCAGGAC GTGGTCCTGA
       D  G  V     E  V  H     N  A  K  T     K  P  R     E  E  Q     Y  N  S  T     Y  R  V     V  S  V     L  T  V  L     H  Q  D
     >.....................................................B-Ly1 h.c.....................................................>

1001 GGCTGAATGG CAAGGAGTAC AAGTGCAAGG TCTCCAACAA AGCCCTCCCA GCCCCCATCG AGAAAACCAT CTCCAAAGCC AAAGGGCAGC CCCGAGAACC
     CCGACTTACC GTTCCTCATG TTCACGTTCC AGAGGTTGTT TCGGGAGGGT CGGGGGTAGC TCTTTTGGTA GAGGTTTCGG TTTCCCGTCG GGGCTCTTGG
      W  L  N     G  K  E  Y     K  C  K     V  S  N     K  A  L  P     A  P  I     E  K  T     I  S  K  A     K  G  Q     P  R  E
     >.....................................................B-Ly1 h.c.....................................................>
```

SEQ ID NO: 11 (nucleic acid) and SEQ ID NO: 13 (amino acid)

FIG. 5B



SEQ ID NO: 11 (nucleic acid) and SEQ ID NO: 13 (amino acid)

FIG. 5C

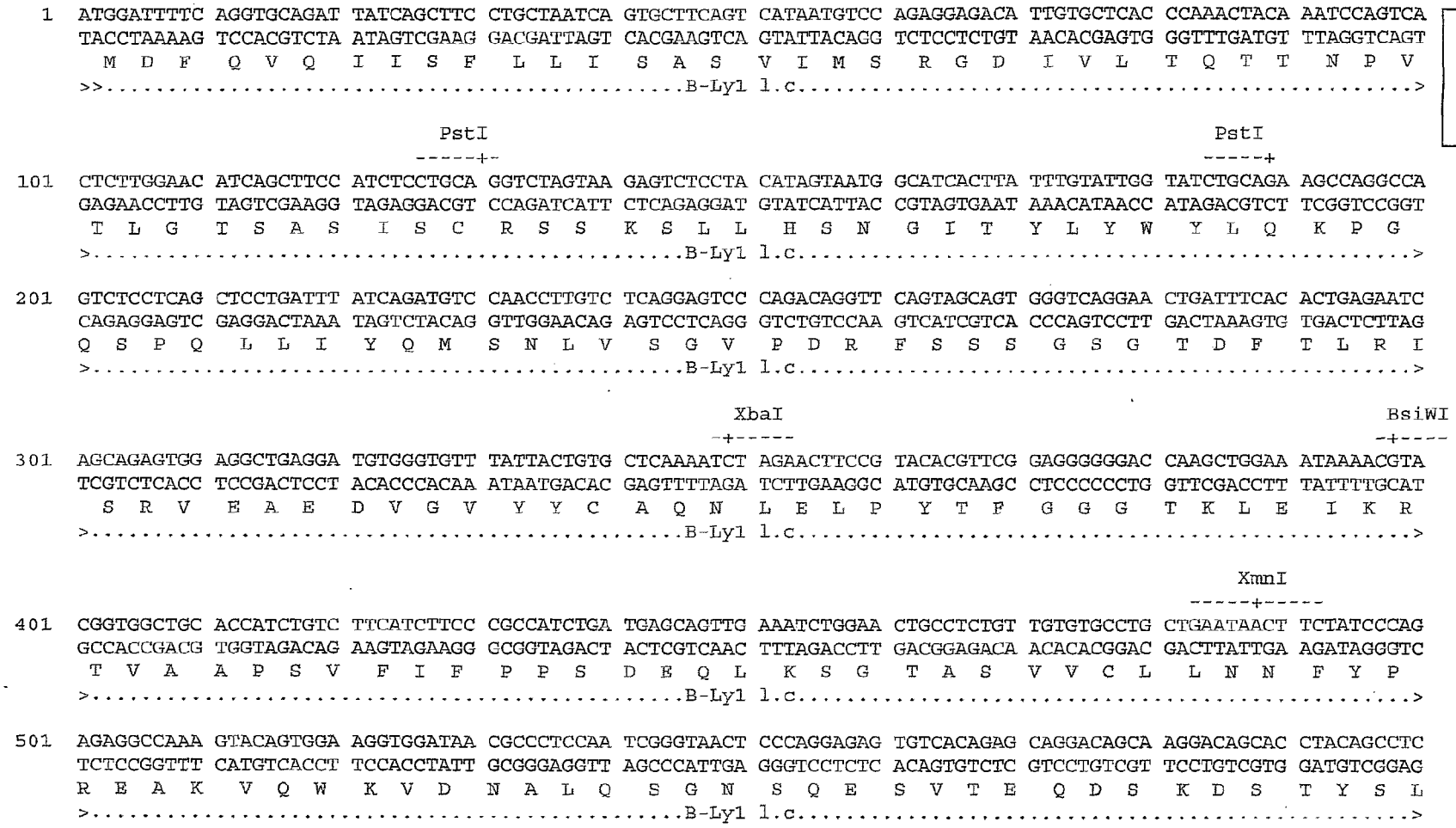

1 ATGGATTTTC AGGTGCAGAT TATCAGCTTC CTGCTAATCA GTGCTTCAGT CATAATGTCC AGAGGAGACA TTGTGCTCAC CCAAACTACA AATCCAGTCA
TACCTAAAAG TCCACGTCTA ATAGTCGAAG GACGATTAGT CACGAAGTCA GTATTACAGG TCTCCTCTGT AACACGAGTG GGTTTGATGT TTAGGTCAGT
M D F Q V Q I I S F L L I S A S V I M S R G D I V L T Q T T N P V
>>.....B-Ly1 l.c.....>
SEQ ID NO 12 (nucleic acid) and SEQ ID NO. 14 (amino acid)
PstI
PstI
101 CTCTTGGAAC ATCAGCTTCC ATCTCCTGCA GGTCTAGTAA GAGTCTCCTA CATAGTAATG GCATCACTTA TTTGTATTGG TATCTGCAGA AGCCAGGCCA
GAGAACCTTG TAGTCGAAGG TAGAGGACGT CCAGATCATT CTCAGAGGAT GTATCATTAC CGTAGTGAAT AAACATAACC ATAGACGTCT TCGGTCCGGT
T L G T S A S I S C R S S K S L L H S N G I T Y L Y W Y L Q K P G
>.....B-Ly1 l.c.....>
201 GTCTCCTCAG CTCCTGATTT ATCAGATGTC CAACCTTGTC TCAGGAGTCC CAGACAGGTT CAGTAGCAGT GGGTCAGGAA CTGATTTCAC ACTGAGAATC
CAGAGGAGTC GAGGACTAAA TAGTCTACAG GTTGGAACAG AGTCCTCAGG GTCTGTCCAA GTCATCGTCA CCCAGTCCTT GACTAAAGTG TGACTCTTAG
Q S P Q L L I Y Q M S N L V S G V P D R F S S S G S G T D F T L R I
>.....B-Ly1 l.c.....>
XbaI
BsiWI
301 AGCAGAGTGG AGGCTGAGGA TGTGGGTGTT TATTACTGTG CTCAAAATCT AGAACTTCCG TACACGTTCG GAGGGGGGAC CAAGCTGGAA ATAAAACGTA
TCGTCTCACC TCCGACTCCT ACACCCACAA ATAATGACAC GAGTTTTAGA TCTTGAAGGC ATGTGCAAGC CTCCCCCCTG GTTCGACCTT TATTTTGCAT
S R V E A E D V G V Y Y C A Q N L E L P Y T F G G G T K L E I K R
>.....B-Ly1 l.c.....>
XmnI
401 CGGTGGCTGC ACCATCTGTC TTCATCTTCC CGCCATCTGA TGAGCAGTTG AAATCTGGAA CTGCCTCTGT TGTGTGCCTG CTGAATAACT TCTATCCCAG
GCCACCGACG TGGTAGACAG AAGTAGAAGG GCGGTAGACT ACTCGTCAAC TTTAGACCTT GACGGAGACA ACACACGGAC GACTTATTGA AGATAGGGTC
T V A A P S V F I F P P S D E Q L K S G T A S V V C L L N N F Y P
>.....B-Ly1 l.c.....>
501 AGAGGCCAAA GTACAGTGGA AGGTGGATAA CGCCCTCCAA TCGGGTAACT CCCAGGAGAG TGTCACAGAG CAGGACAGCA AGGACAGCAC CTACAGCCTC
TCTCCGGTTT CATGTCACCT TCCACCTATT GCGGGAGGTT AGCCCATTGA GGGTCCTCTC ACAGTGTCTC GTCCTGTCGT TCCTGTCGTG GATGTCGGAG
R E A K V Q W K V D N A L Q S G N S Q E S V T E Q D S K D S T Y S L
>.....B-Ly1 l.c.....>

FIG. 6A

```
                                                    SacI
                                                    ------+
601  AGCAGCACCC TGACGCTGAG CAAAGCAGAC TACGAGAAAC ACAAAGTCTA CGCCTGCGAA GTCACCCATC AGGGCCTGAG CTCGCCCGTC ACAAAGAGCT
     TCGTCGTGGG ACTGCGACTC GTTTCGTCTG ATGCTCTTTG TGTTTCAGAT GCGGACGCTT CAGTGGGTAG TCCCGGACTC GAGCGGGCAG TGTTTCTCGA
       S  S  T  L  T  L   S  K  A  D   Y  E  K   H  K  V    Y  A  C  E   V  T  H   Q  G  L   S  S  P  V   T  K  S
     >.....................................B-Ly1 l.c.....................................>

701  TCAACAGGGG AGAGTGTTAG
     AGTTGTCCCC TCTCACAATC
       F  N  R   G  E  C  -
     >....B-Ly1 l.c.....>>
```

SEQ ID NO: 12 (nucleic acid) and SEQ ID NO: 14 (amino acid)

FIG 6B

A

CDR1(Kabat):	
TACTCTTGGATGAAC	SEQ ID NO: 5
TyrSerTrpMetAsn	SEQ ID NO: 15
CDR1(Chothia):	
GGCTACGCATTCAGTTAC	SEQ ID NO: 6
GlyTyrAlaPheSerTyr	SEQ ID NO: 16
CDR1(AbM):	
GGCTACGCATTCAGTTACTCTTGGATGAAC	SEQ ID NO: 7
GlyTyrAlaPheSerTyrSerTrpMetAsn	SEQ ID NO: 17

CDR2(Kabat):	
CGGATTTTTCCTGGAGATGGGGATACTGACTACAATGGGAAATTCAAGGGC	SEQ ID NO: 21
ArgIlePheProGlyAspGlyAspThrAspTyrAsnGlyLysPheLysGly	SEQ ID NO: 25
CDR2(Chothia):	
TTTCCTGGAGATGGGGATACTGAC	SEQ ID NO: 22
PheProGlyAspGlyAspThrAsp	SEQ ID NO: 26
CDR2(AbM):	
CGGATTTTTCCTGGAGATGGGGATACTGAC	SEQ ID NO: 23
ArgIlePheProGlyAspGlyAspThrAsp	SEQ ID NO: 27

CDR3(Kabat, Chothia, AbM):	
AATGTCTTTGATGGTTACTGGTTAGTTTAC	SEQ ID NO: 24
AsnValPheAspGlyTyrTrpLeuValTyr	SEQ ID NO: 28

B

CDR1(Kabat):	
AGGTCTAGTAAGAGTCTCCTACATAGTAATGGCATCACTTATTTGTAT	SEQ ID NO: 8
ArgSerSerLysSerLeuLeuHisSerAsnGlyIleThrTyrLeuTyr	SEQ ID NO: 18
CDR2(Kabat):	
CAGATGTCCAACCTTGTCTCA	SEQ ID NO: 9
GlnMetSerAsnLeuValSer	SEQ ID NO: 19
CDR3(Kabat):	
GCTCAAAATCTAGAACTTCCGTACACG	SEQ ID NO: 10
AlaGlnAsnLeuGluLeuProTyrThr	SEQ ID NO: 20

FIG. 7

1.relative percentages

	Bly-1 m1 031024 016	+ EndoH Bly-1 m1 031024 017
1053		
1256		
1282		
1298		3.70%
1339	18.60%	17.90%
1460		4.30%
1486	5.90%	5.50%
1502	5.10%	3.70%
1543	35.00%	39.20%
1622		
1647	4.60%	3.00%
1664	7%	
1680		
1688	11.00%	10.30%
1705	7.20%	7.30%
1810		
1826		
1850	5.90%	5.20%
1972		
2012		
	100%	100%

FIG. 8A

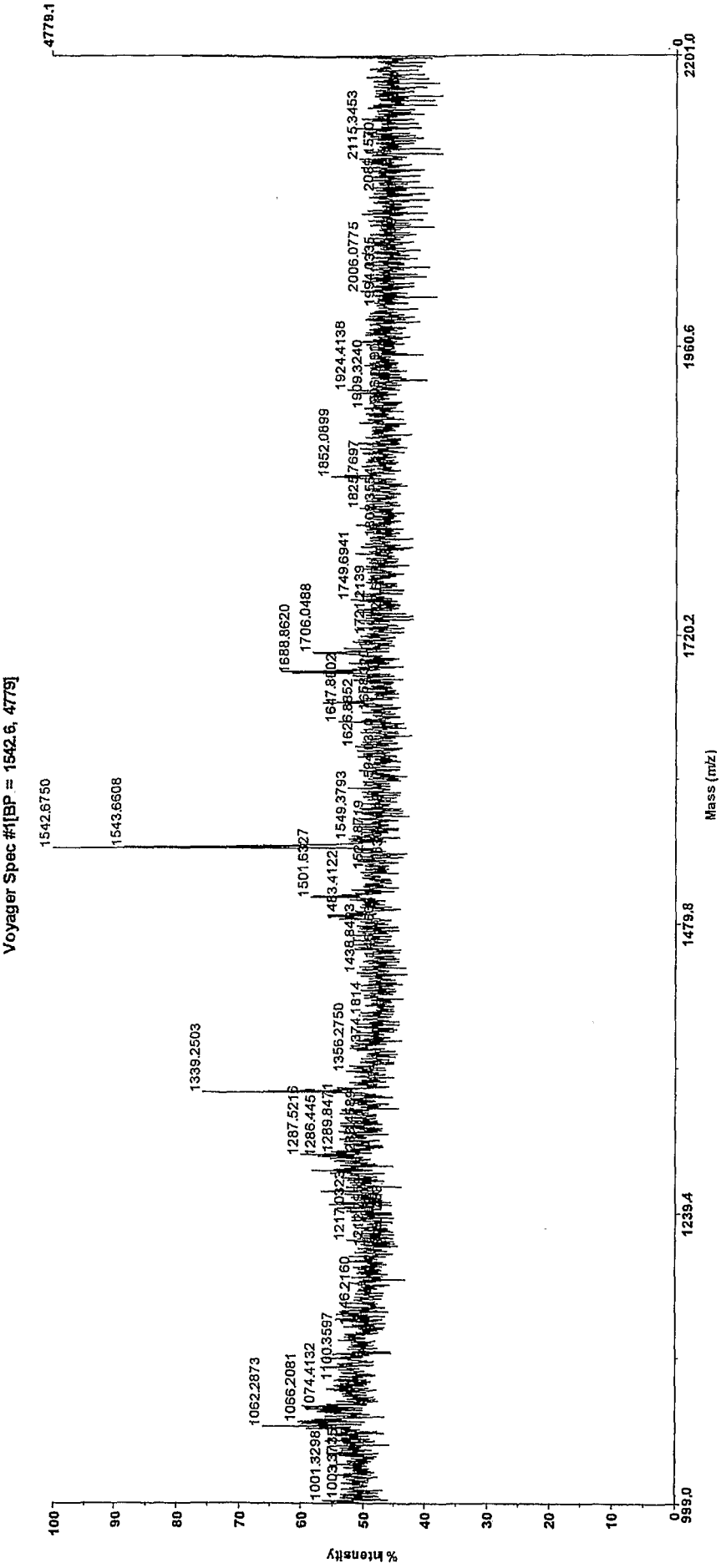

Voyager Spec #1[BP = 1542.6, 4779]
% Intensity
Mass (m/z)
100
90
80
70
60
50
40
30
20
10
0
999.0
1239.4
1479.8
1720.2
1960.6
2201.0
4778.1
1542.6750
1543.6608
1501.6327
1549.3793
1339.2503
1062.2873
1066.2081
1688.8620
1706.0488
1852.0899
1924.4138
2006.0775
2115.3453

FIG. 8B

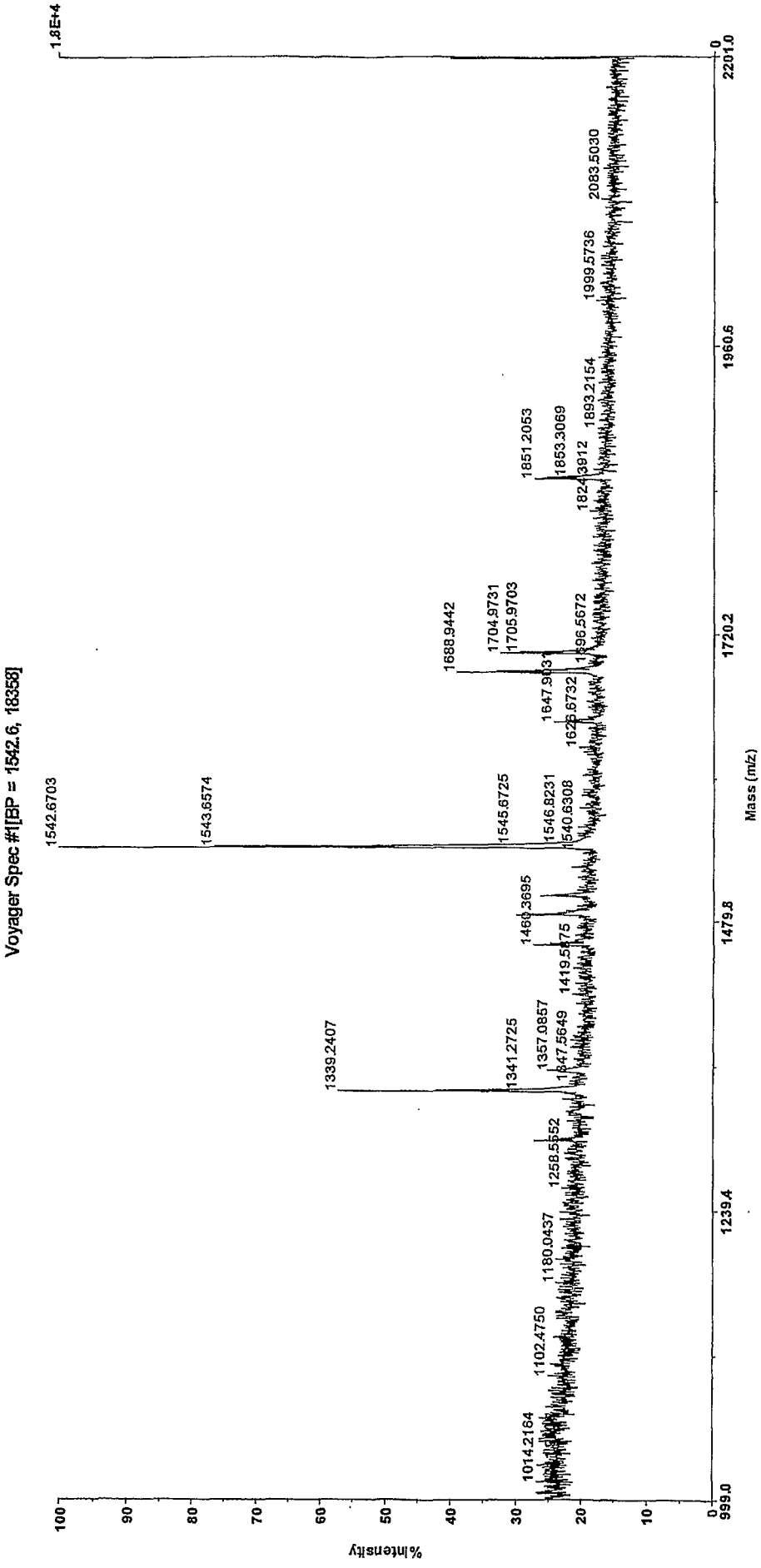

Voyager Spec #1[BP = 1542.6, 18358]
1.8E+4
0
2201.0
1960.6
1720.2
1479.8
1239.4
999.0
Mass (m/z)
%Intensity
100
90
80
70
60
50
40
30
20
10
0
1542.6703
1543.6574
1545.6725
1546.8231
1540.6308
1688.9442
1704.9731
1705.9703
1851.2053
1853.3069
1824.3912
1893.2154
1999.5736
2083.5030
1339.2407
1341.2725
1357.0857
1460.3695
1014.2164
1102.4750
1180.0437
1258.5552

FIG. 8C

Figure 9

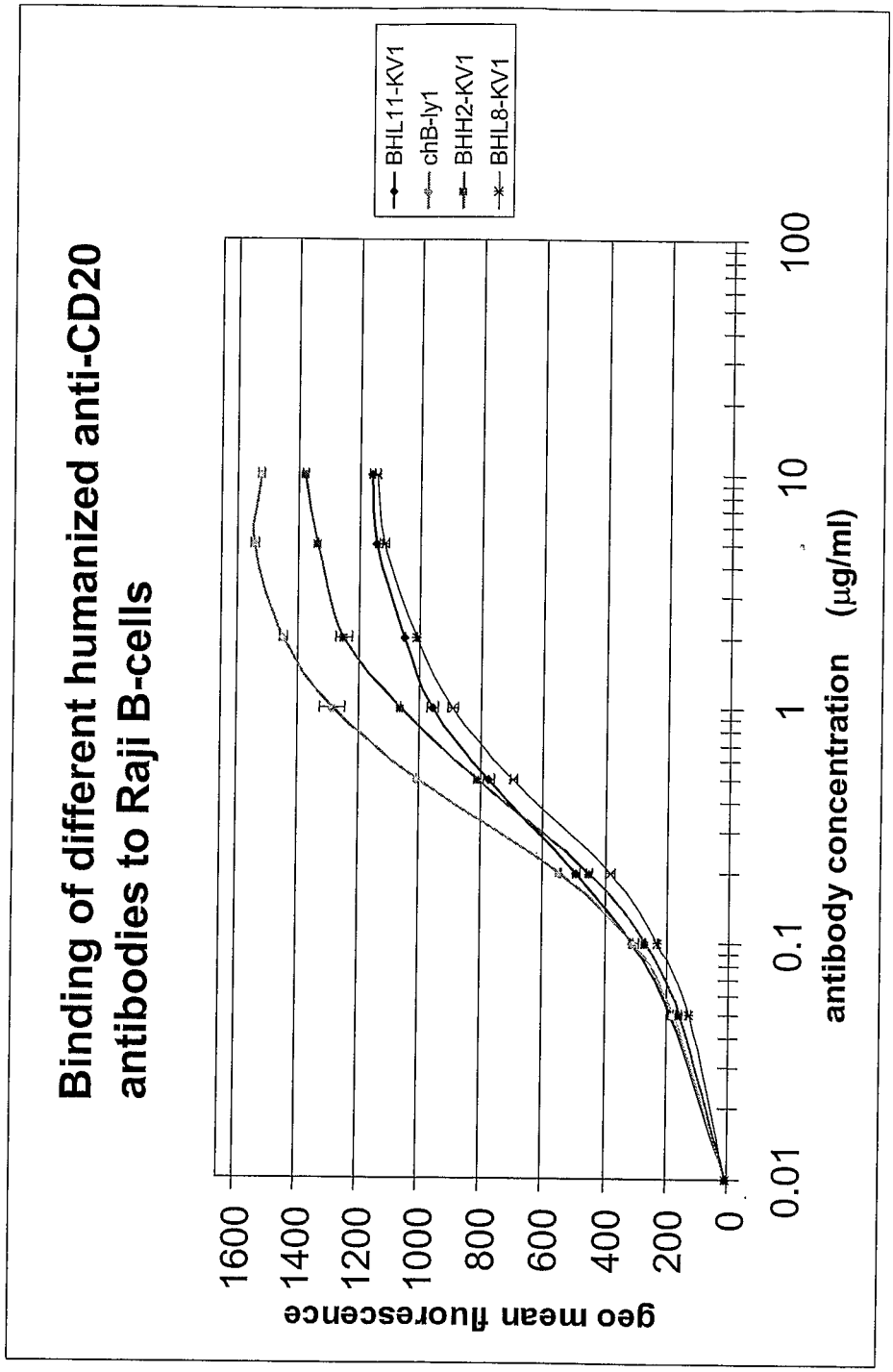

Binding of different humanized anti-CD20 antibodies to Raji B-cells
BHL11-KV1
chB-Iy1
BHH2-KV1
BHL8-KV1
geo mean fluorescence
1600
1400
1200
1000
800
600
400
200
0
0.01
0.1
1
10
100
antibody concentration (µg/ml)

Figure 10

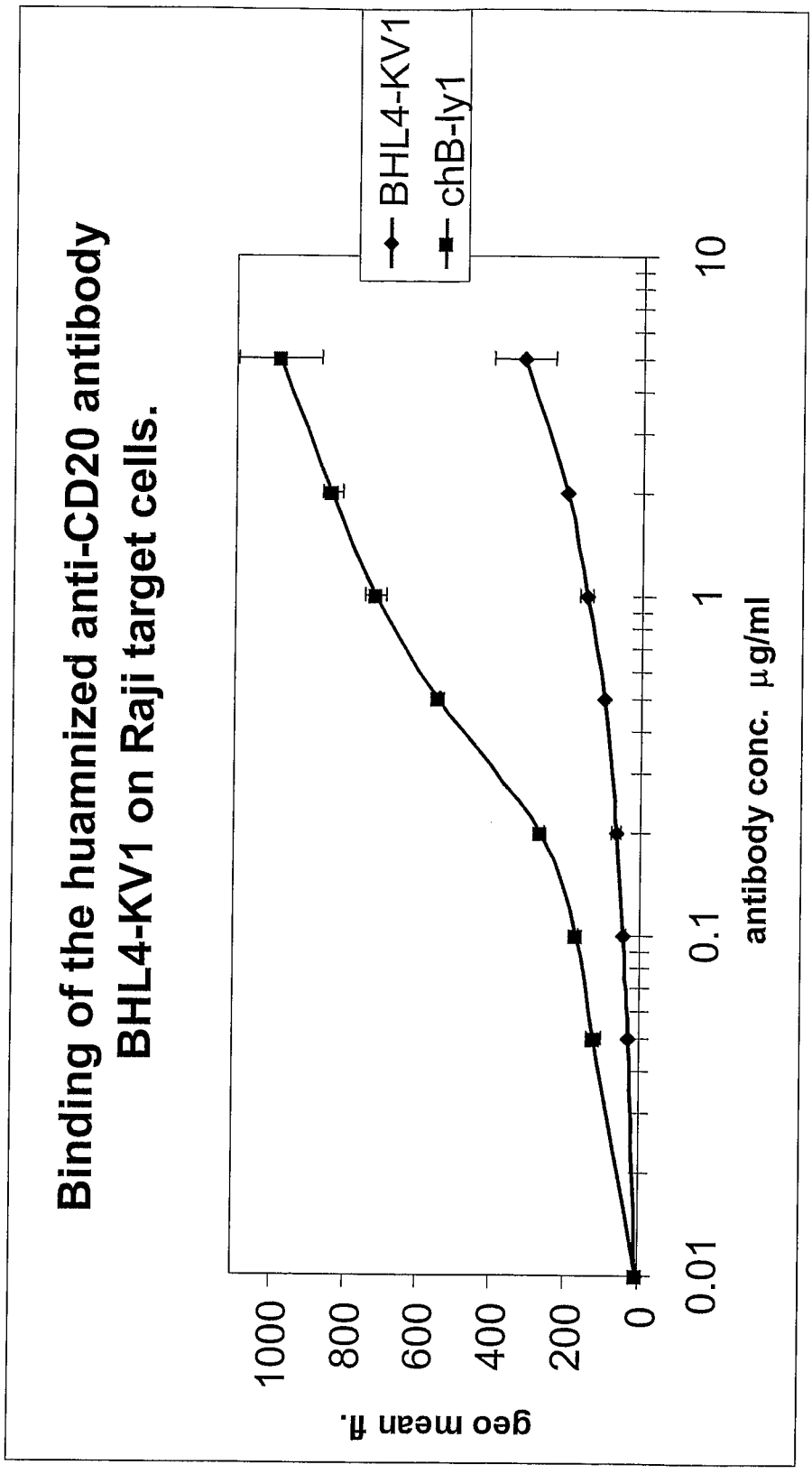

Binding of the huamnized anti-CD20 antibody
BHL4-KV1 on Raji target cells.
BHL4-KV1
chB-ly1
geo mean fl.
1000
800
600
400
200
0
0.01
0.1
1
10
antibody conc. µg/ml

Figure 11

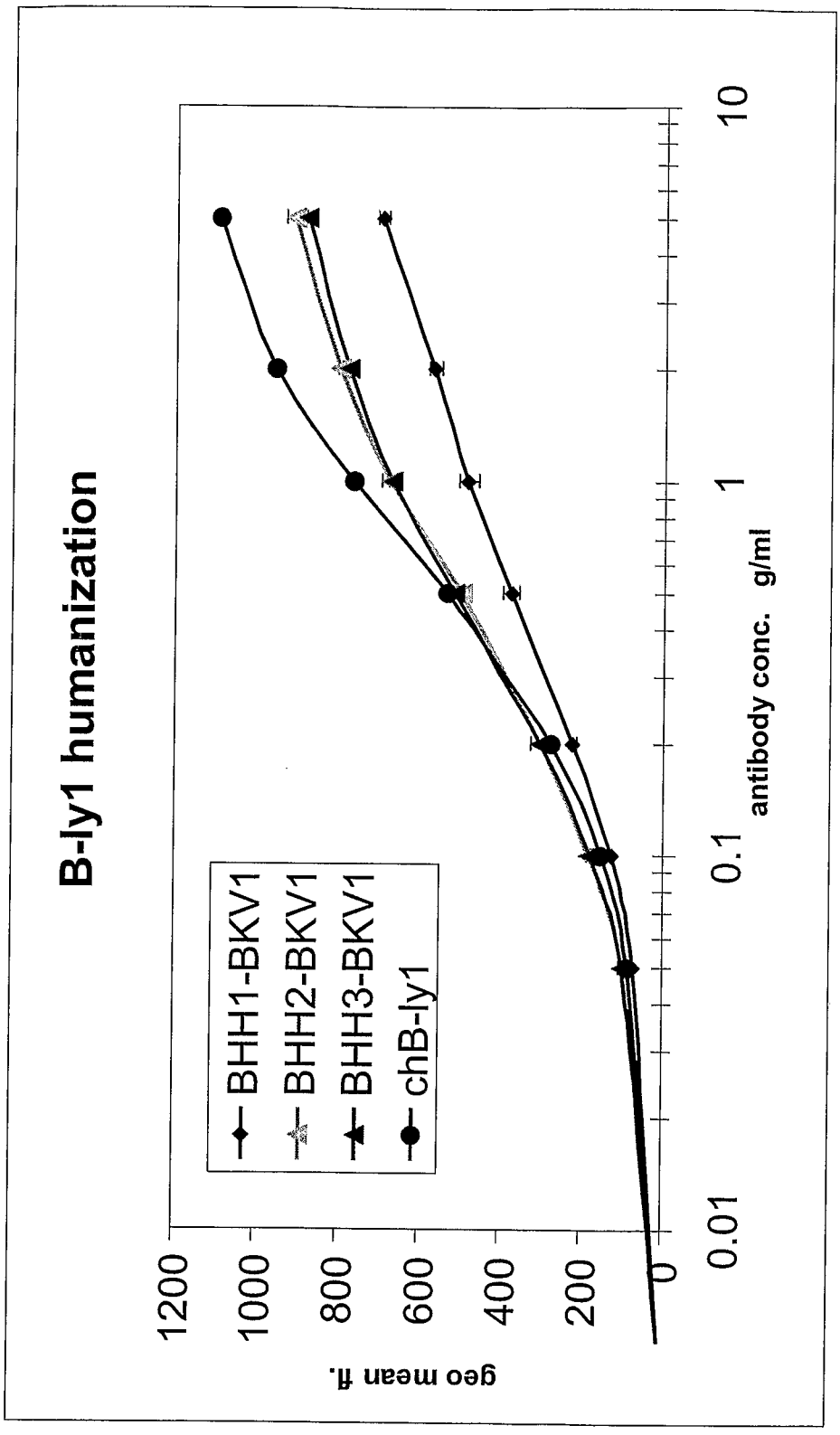

B-ly1 humanization
geo mean fl.
1200
1000
800
600
400
200
0
0.01
0.1
1
10
antibody conc. g/ml
BHH1-BKV1
BHH2-BKV1
BHH3-BKV1
chB-ly1

Figure 12

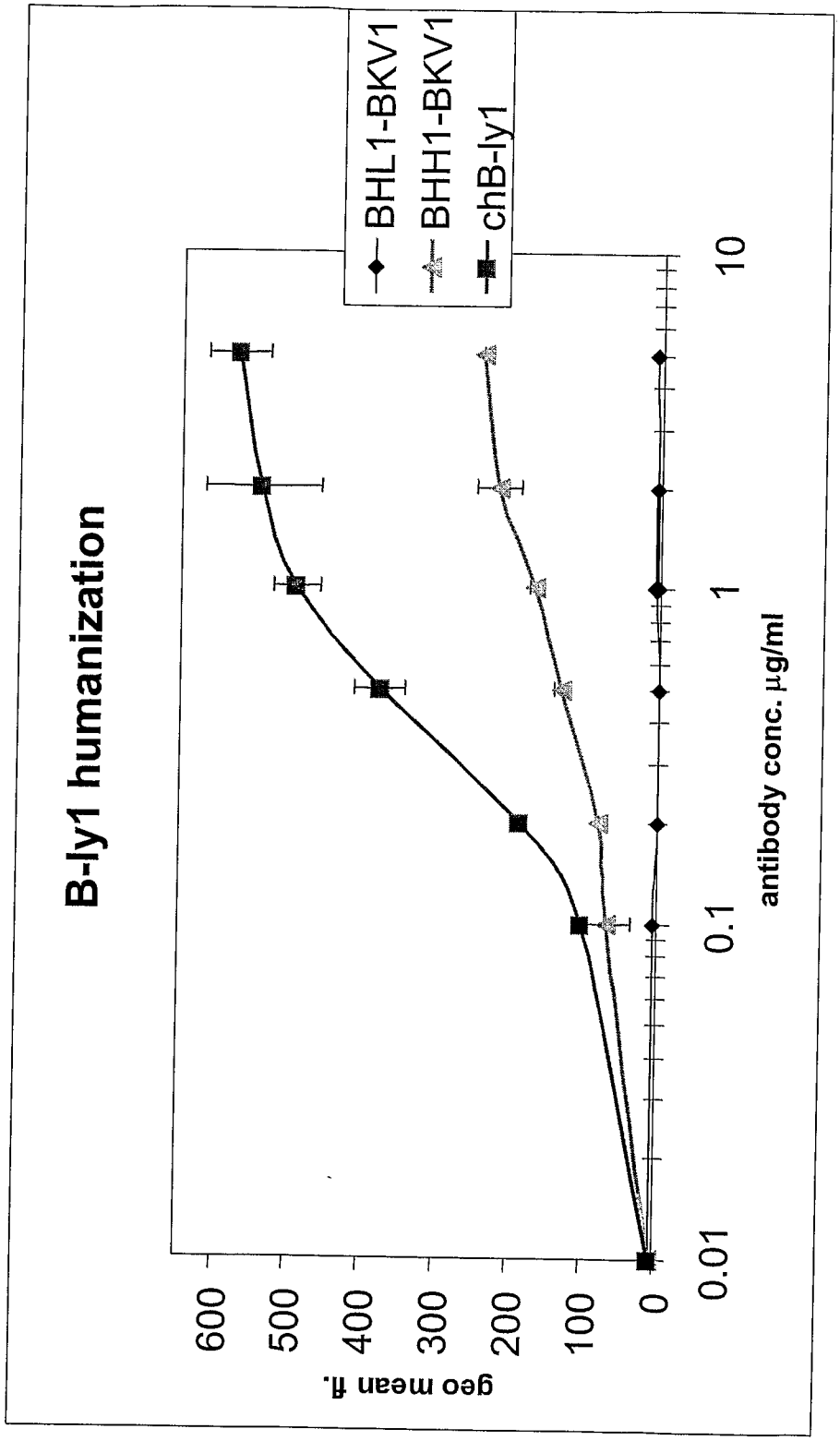

B-ly1 humanization
BHL1-BKV1
BHH1-BKV1
chB-ly1
geo mean fl.
600
500
400
300
200
100
0
0.01
0.1
1
10
antibody conc. µg/ml

Figure 13

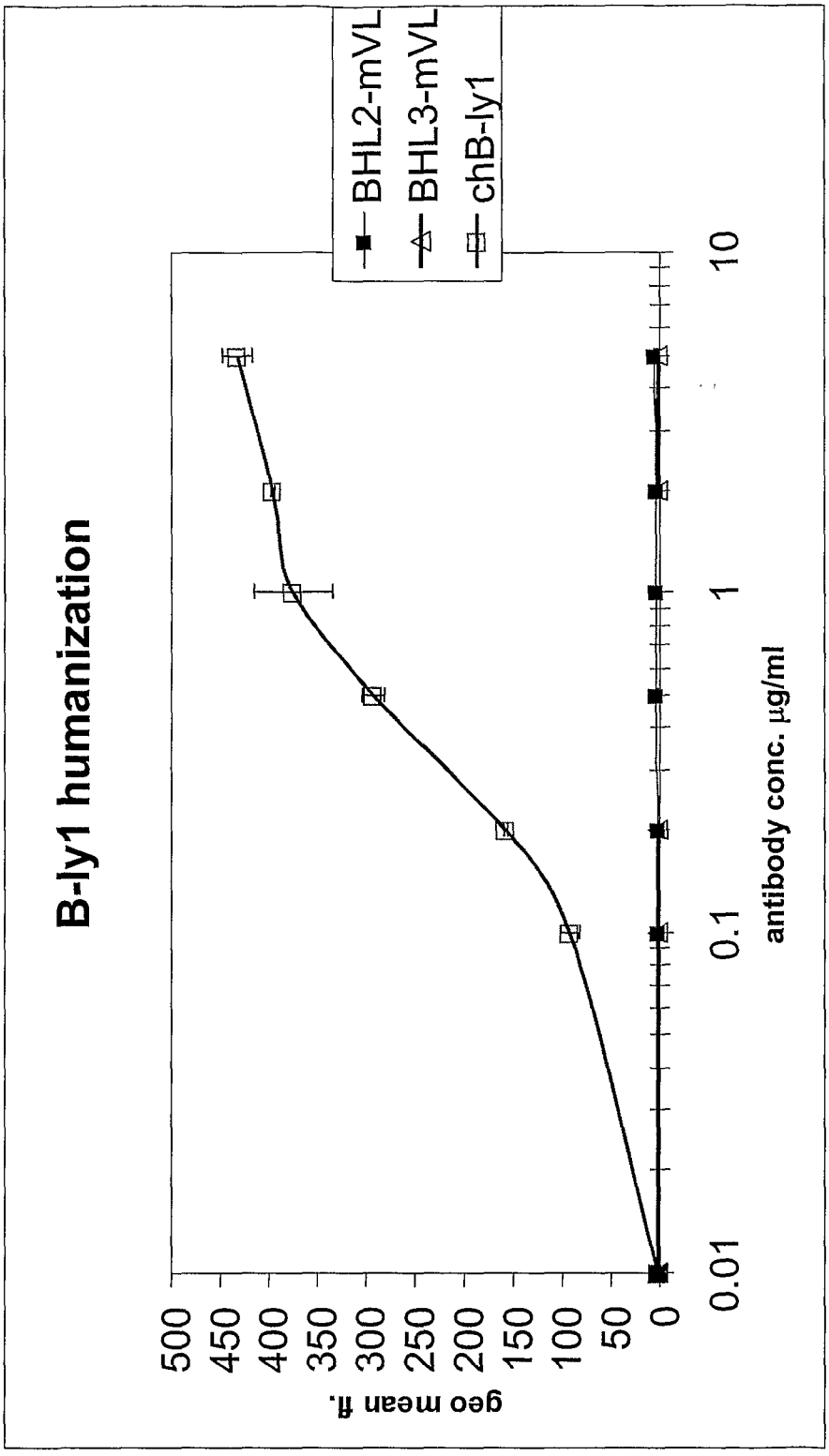

B-ly1 humanization
BHL2-mVL
BHL3-mVL
chB-ly1
geo mean fl.
500
450
400
350
300
250
200
150
100
50
0
0.01
0.1
1
10
antibody conc. µg/ml

Figure 14

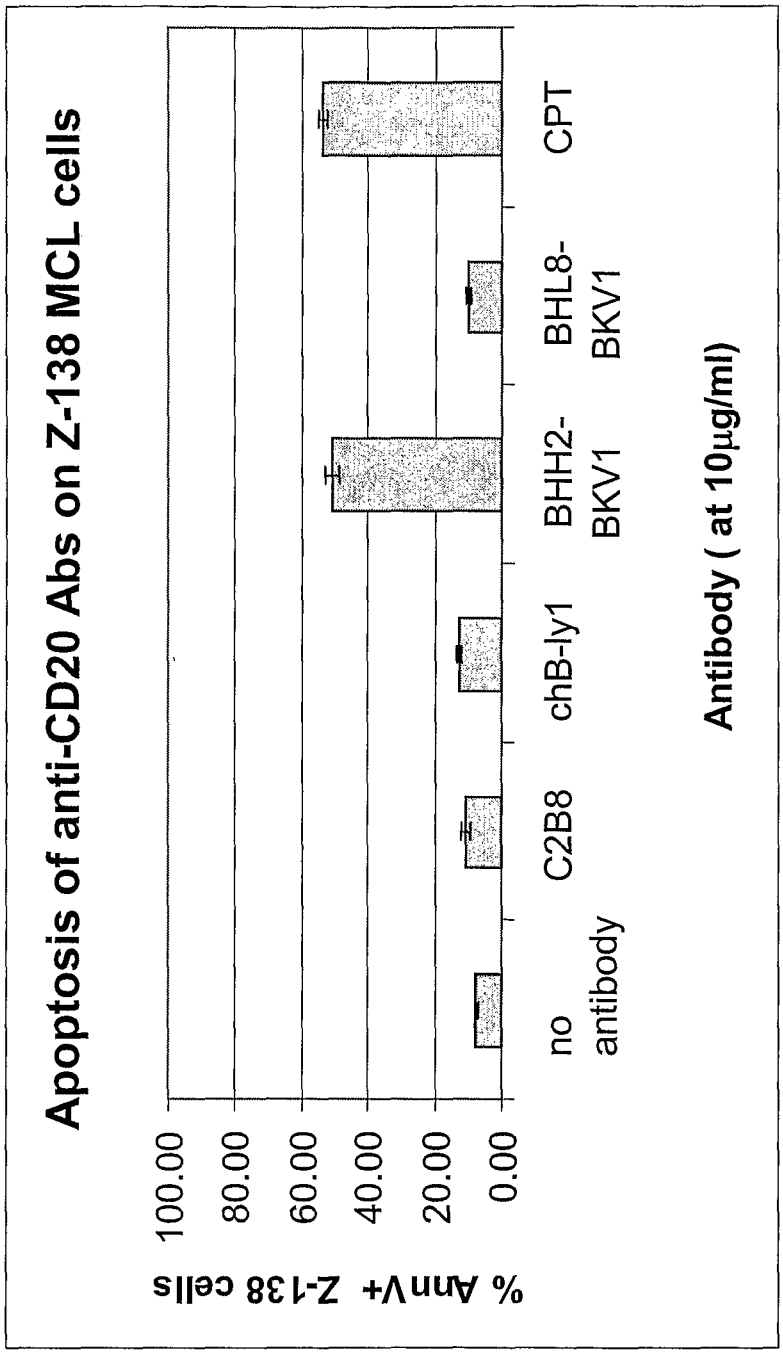
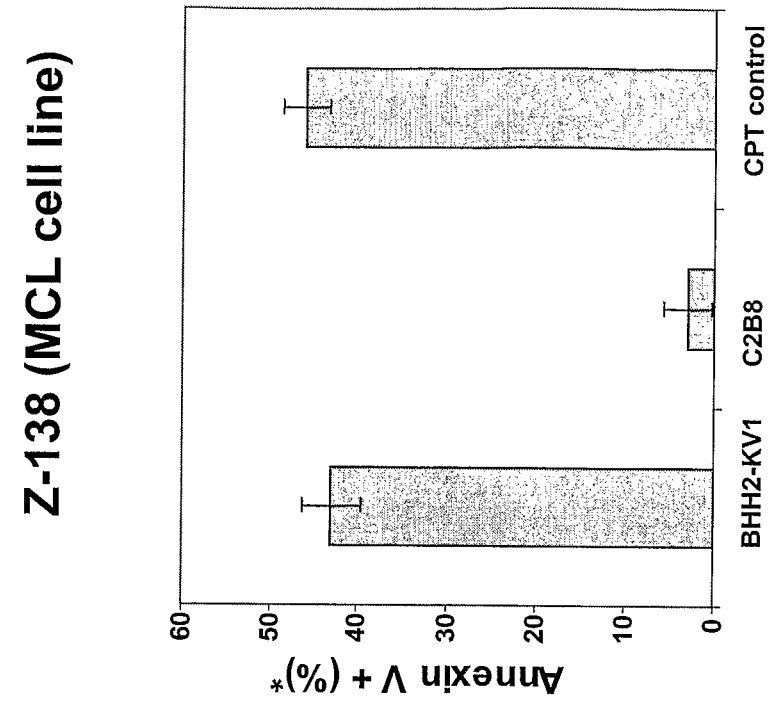

Apoptosis of anti-CD20 Abs on Z-138 MCL cells
% AnnV+ Z-138 cells
100.00
80.00
60.00
40.00
20.00
0.00
no antibody
C2B8
chB-ly1
BHH2-BKV1
BHL8-BKV1
CPT
Antibody (at 10µg/ml)

Figure15


Z-138 (MCL cell line)
Annexin V + (%)*
0
10
20
30
40
50
60
BHH2-KV1
C2B8
CPT control

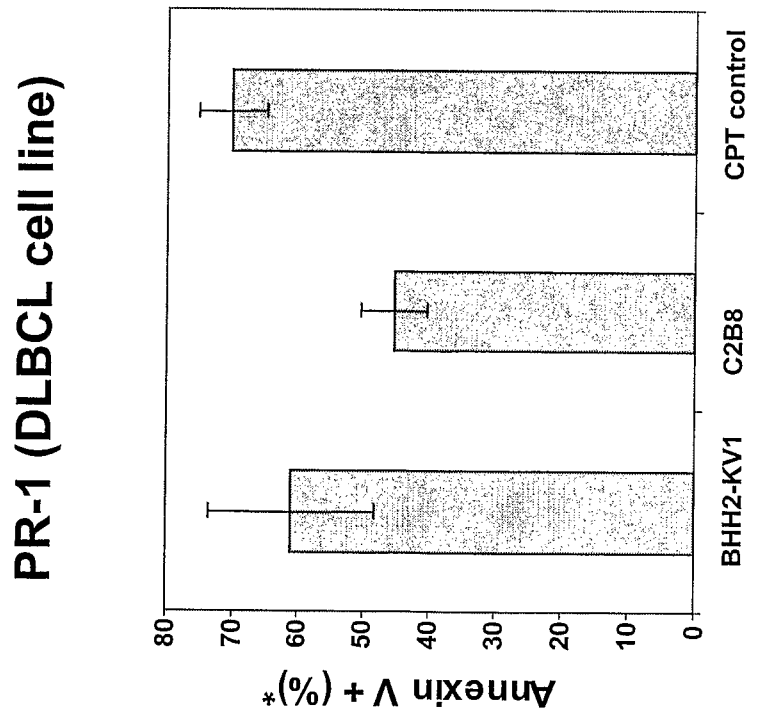

PR-1 (DLBCL cell line)
Annexin V + (%)*
0
10
20
30
40
50
60
70
80
BHH2-KV1
C2B8
CPT control

Figure 16

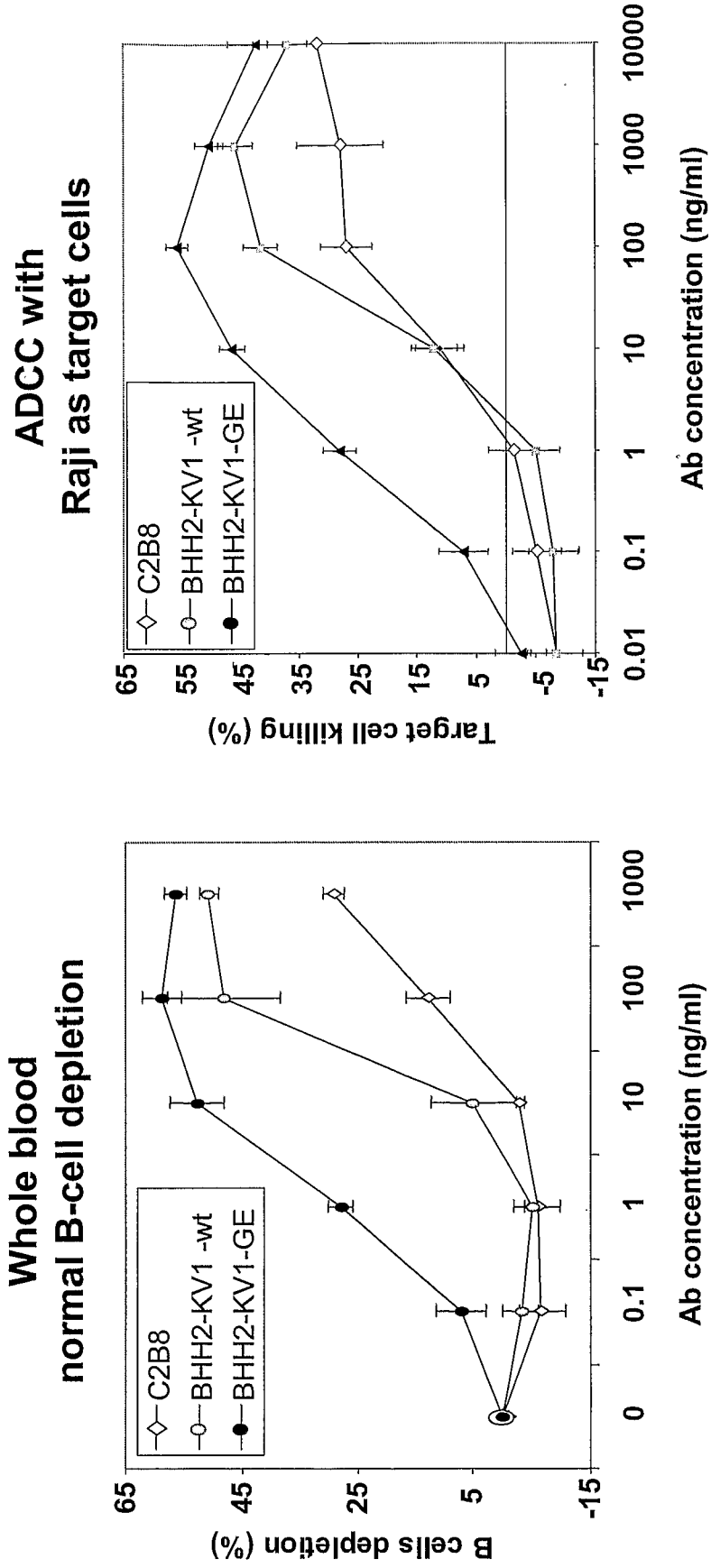

Whole blood
normal B-cell depletion
B cells depletion (%)
65
45
25
5
-15
0
0.1
1
10
100
1000
Ab concentration (ng/ml)
C2B8
BHH2-KV1 -wt
BHH2-KV1-GE
ADCC with
Raji as target cells
Target cell killing (%)
65
55
45
35
25
15
5
-5
-15
0.01
0.1
1
10
100
1000
10000
Ab concentration (ng/ml)
C2B8
BHH2-KV1 -wt
BHH2-KV1-GE

Figure 17

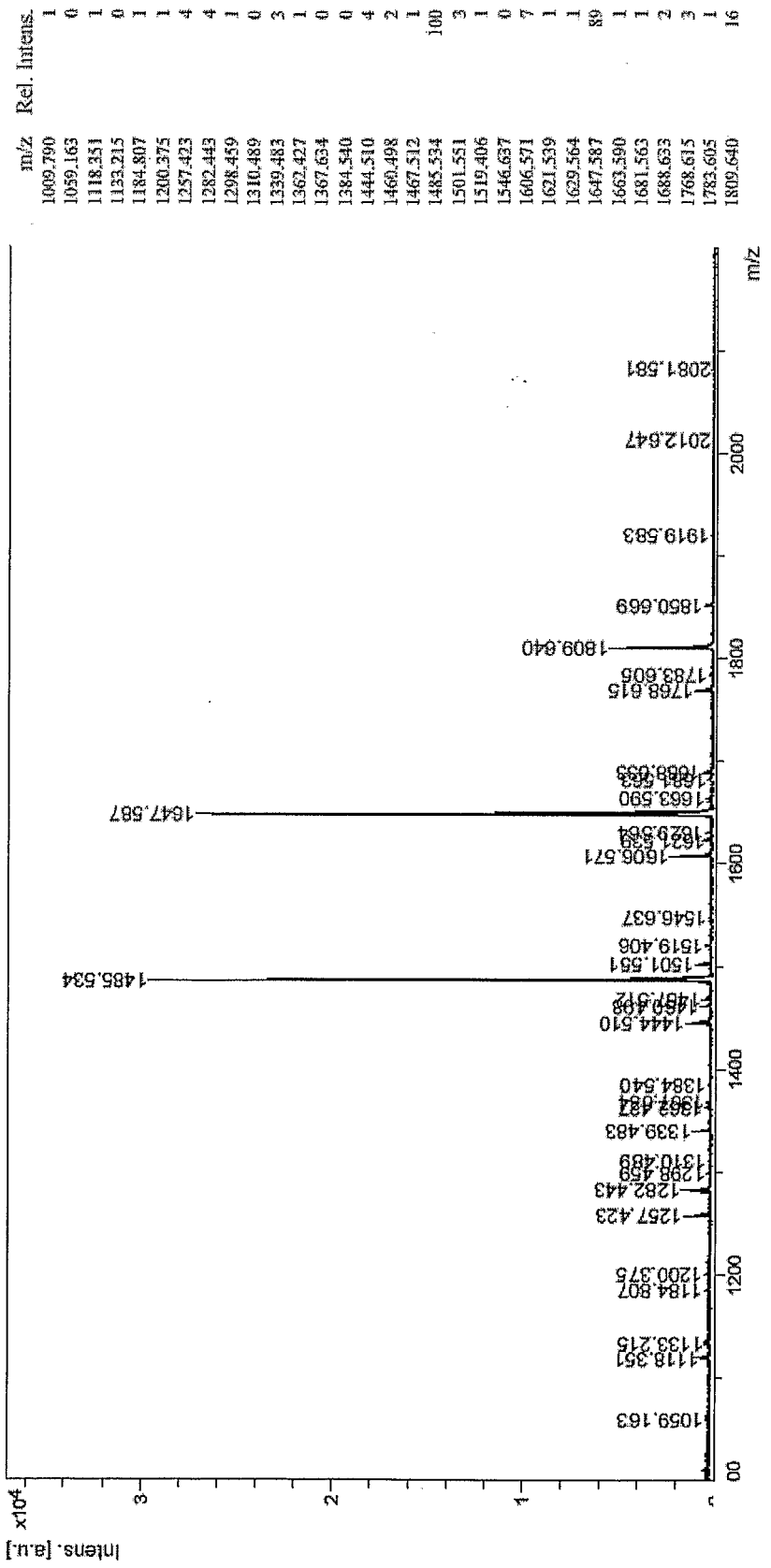

m/z Rel. Intens.
1009.790 1
1059.163 0
1118.351 1
1133.215 0
1184.807 1
1200.375 1
1257.423 4
1282.443 4
1298.459 1
1310.489 0
1339.483 3
1362.427 1
1367.634 0
1384.540 0
1444.510 4
1460.498 2
1467.512 1
1485.534 100
1501.551 3
1519.406 1
1546.637 0
1606.571 7
1621.539 1
1629.564 1
1647.587 89
1663.590 1
1681.563 1
1688.633 2
1768.615 3
1783.605 1
1809.640 16
Intens. [a.u.]
x10⁴
m/z
1059.163
1118.351
1133.215
1184.807
1200.375
1257.423
1282.443
1298.459
1310.489
1339.483
1362.427
1384.540
1444.510
1460.498
1485.534
1501.551
1519.406
1546.637
1606.571
1621.539
1629.564
1647.587
1663.590
1681.563
1688.633
1768.615
1783.605
1809.640
1850.669
1919.583
2012.647
2081.581

Figure 18

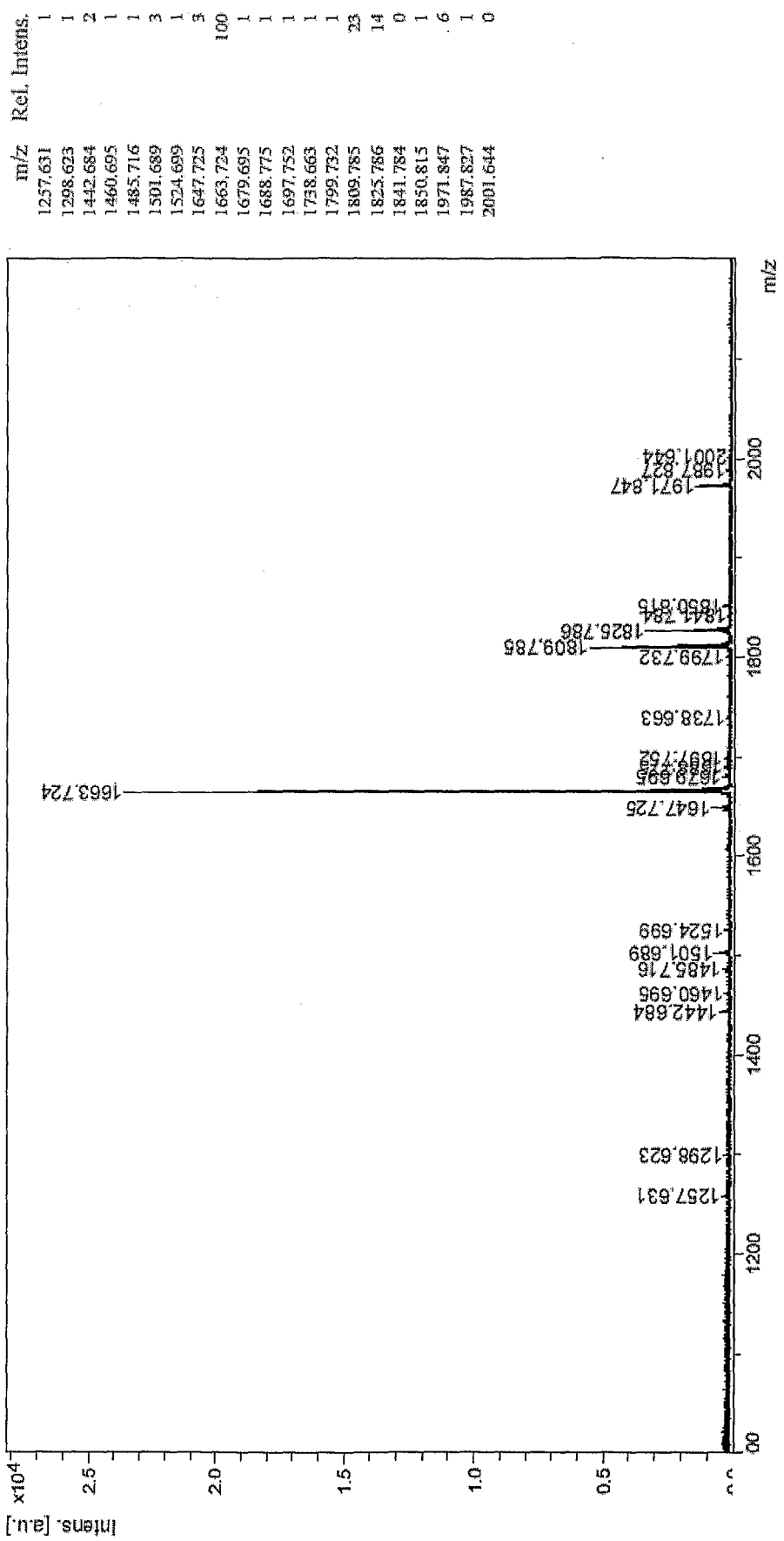

m/z Rel. Intens.
1257.631 1
1298.623 1
1442.684 2
1460.695 1
1485.716 1
1501.689 3
1524.699 1
1647.725 3
1663.724 100
1679.695 1
1688.775 1
1697.752 1
1738.663 1
1799.732 1
1809.785 23
1823.786 14
1841.784 0
1850.815 1
1971.847 6
1987.827 1
2001.644 0
Intens. [a.u.]
x10^4
2.5
2.0
1.5
1.0
0.5
0.0
m/z
1200
1400
1600
1800
2000
1257.631
1298.623
1442.684
1460.695
1485.716
1501.689
1524.699
1647.725
1663.724
1679.695
1688.775
1697.752
1738.663
1799.732
1809.785
1823.786
1841.784
1850.815
1971.847
1987.827
2001.644

Figure 19

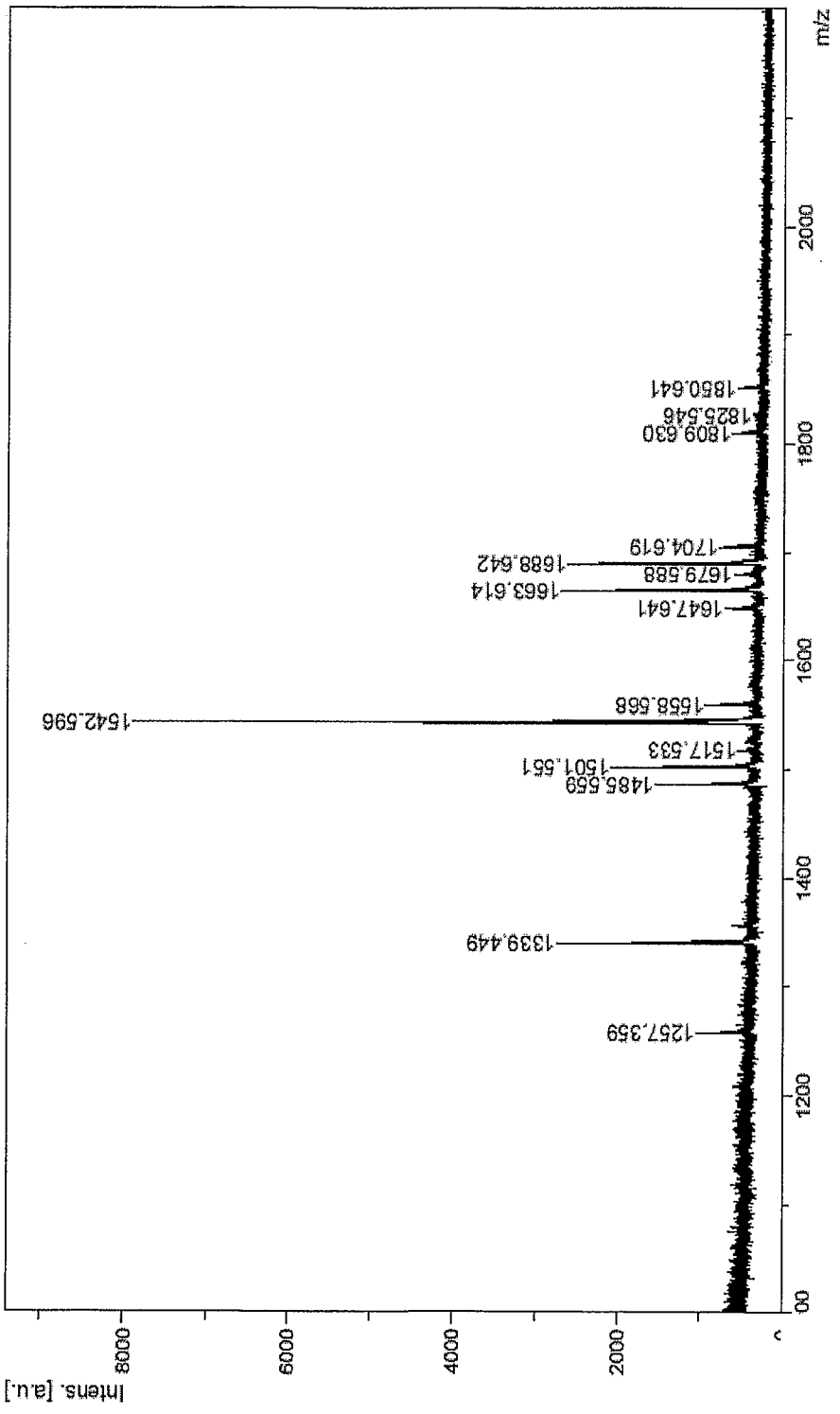

m/z Rel. Intens.
1257.359 8
1339.449 31
1485.559 16
1501.551 23
1517.533 2
1542.596 100
1558.568 8
1647.641 5
1663.614 32
1679.588 4
1688.642 31
1704.619 6
1809.630 5
1825.546 1
1850.641 4
Intens. [a.u.]
8000
6000
4000
2000
0
400
800
1200
1400
1600
1800
2000
m/z
1257.359
1339.449
1485.559
1501.551
1517.533
1542.596
1558.568
1647.641
1663.614
1679.588
1688.642
1704.619
1809.630
1825.546
1850.641

Figure 20

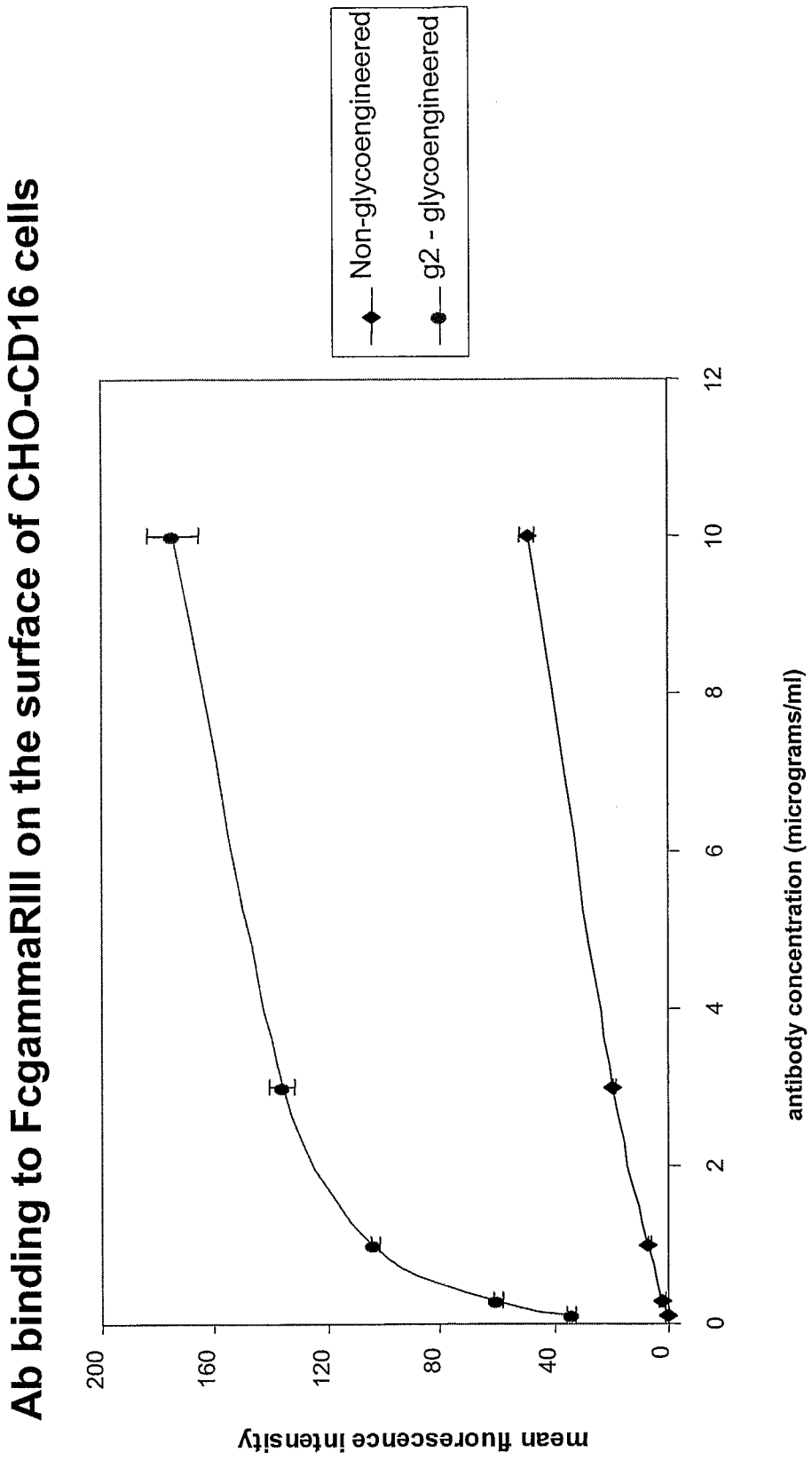
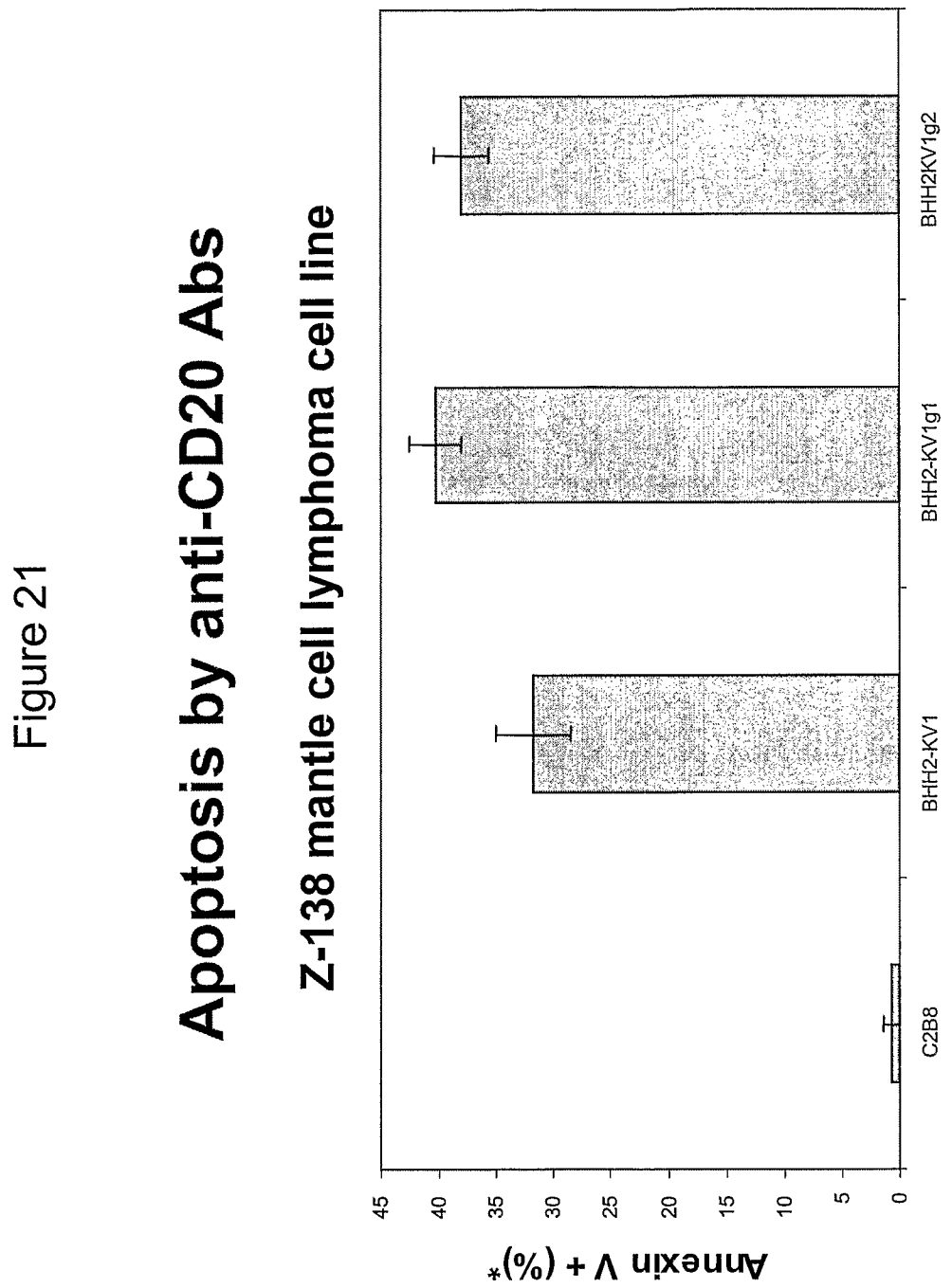

Ab binding to FcgammaRIII on the surface of CHO-CD16 cells
Non-glycoengineered
g2 - glycoengineered
mean fluorescence intensity
0
40
80
120
160
200
0
2
4
6
8
10
12
antibody concentration (micrograms/ml)

Figure 21


Apoptosis by anti-CD20 Abs
Z-138 mantle cell lymphoma cell line
Annexin V + (%)*
45
40
35
30
25
20
15
10
5
0
C2B8
BHH2-KV1
BHH2-KV1g1
BHH2KV1g2