Figure 1

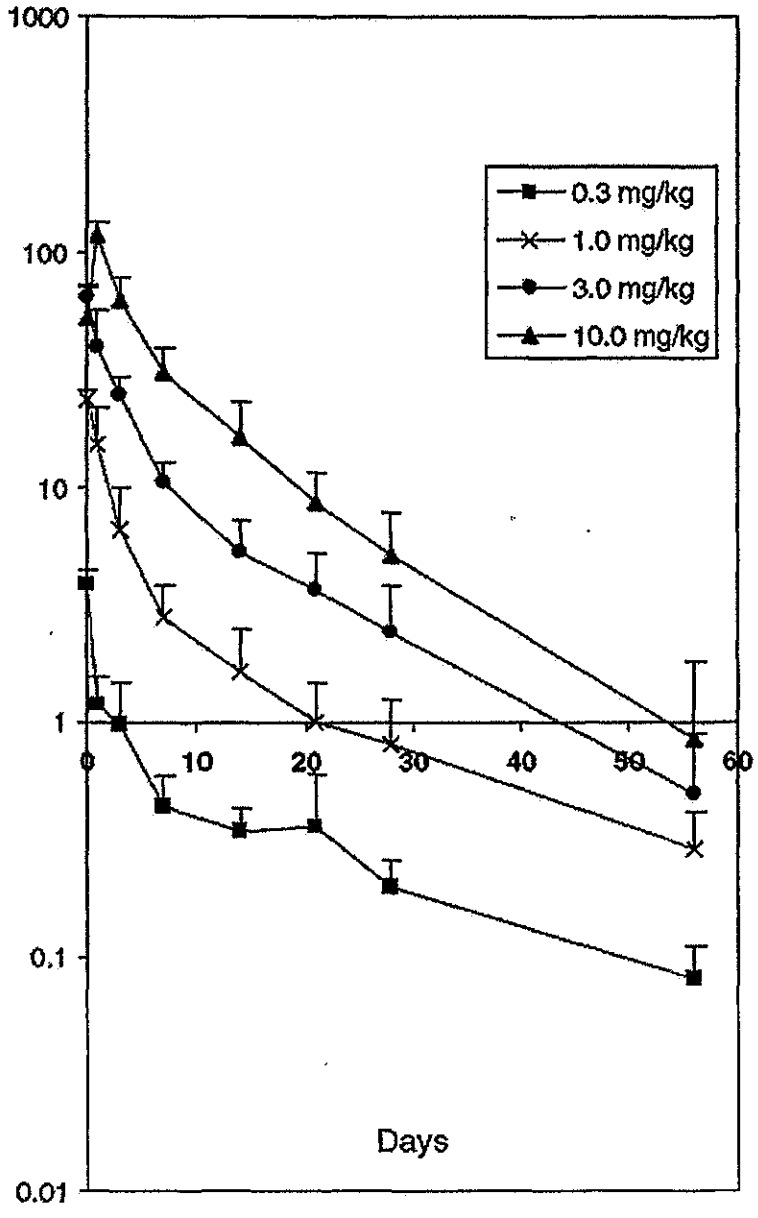

1000
100
10
1
0.1
0.01
0
10
20
30
40
50
60
Days
0.3 mg/kg
1.0 mg/kg
3.0 mg/kg
10.0 mg/kg

Figure 2

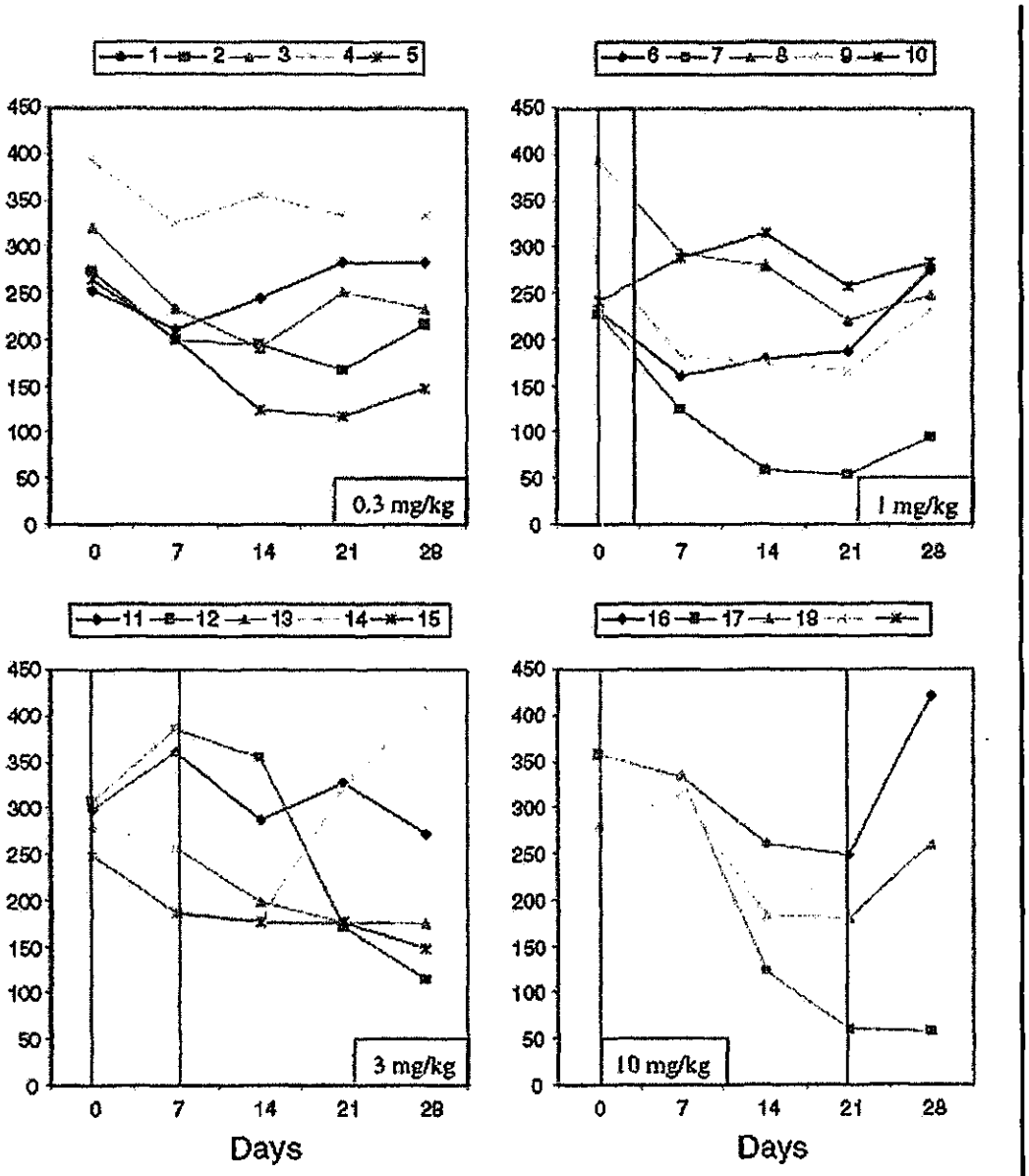

1 2 3 4 5
6 7 8 9 10
11 12 13 14 15
16 17 18
0.3 mg/kg
1 mg/kg
3 mg/kg
10 mg/kg
0 50 100 150 200 250 300 350 400 450
0 7 14 21 28
Days

Figure 3

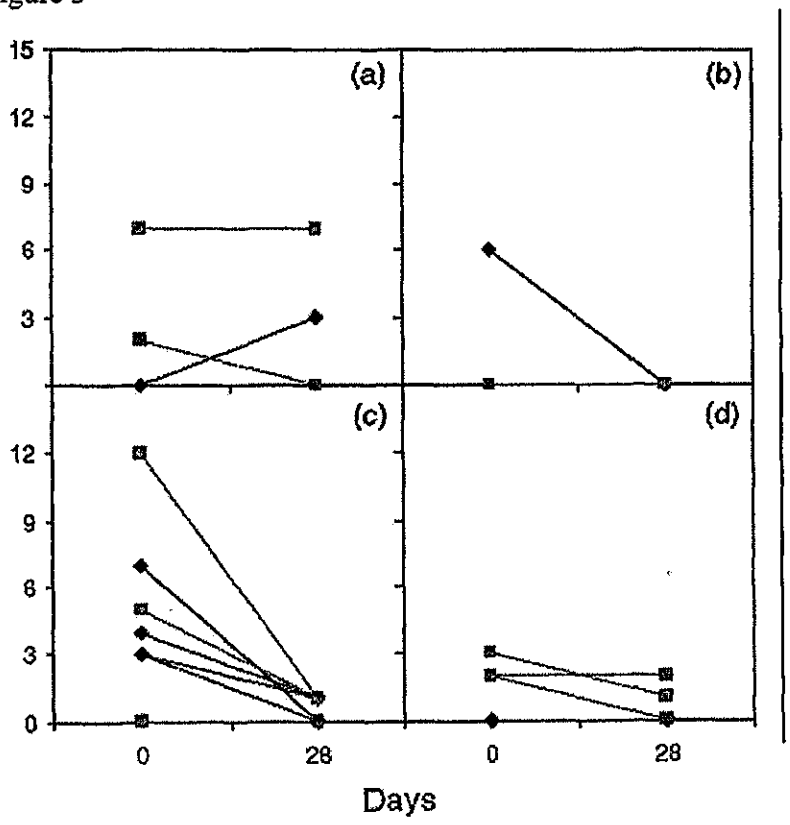


Figure 4

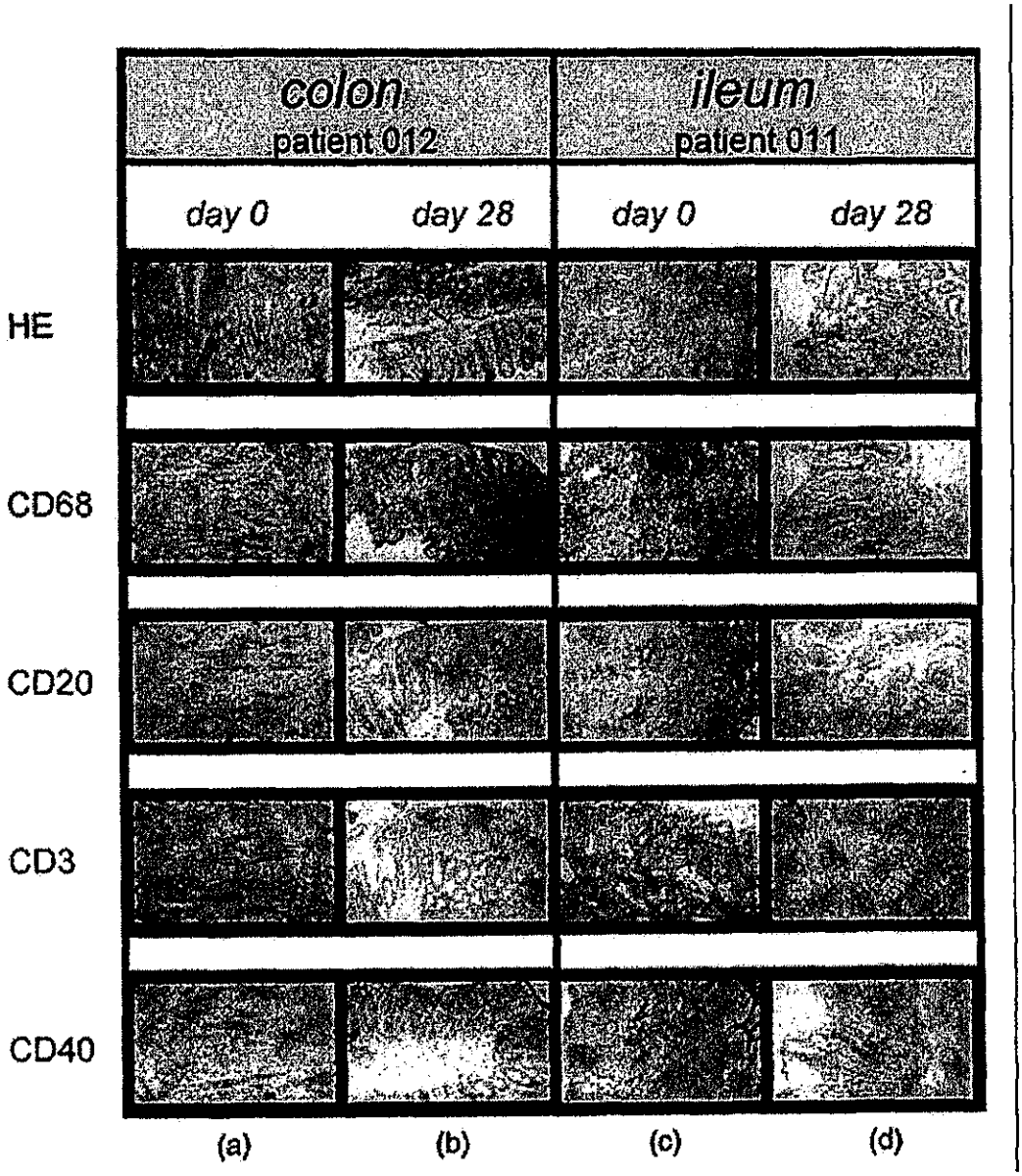

colon
patient 012
ileum
patient 011
day 0
day 28
day 0
day 28
HE
CD68
CD20
CD3
CD40
(a)
(b)
(c)
(d)

Figure 5

Mu5D12 VH region

```
Q  V  K  L     E  E  S     G  P  G     L  V  A  P     S  Q  S     L  S  I
        10             20             30             40             50             60
CAGGTCAAGC  TCGAGGAGTC  TGGACCTGGC  CTGGTGGCAC  CCTCACAGAG  CCTGTCCATC
GTCCAGTTCG  AGCTCCTCAG  ACCTGGACCG  GACCACCGTG  GGAGTGTCTC  GGACAGGTAG

T  C  T  V     S  G  F     S  L  S     R  Y  S  V     Y  W  V     R  Q  P
        70             80             90             100            110            120
ACATGCACTG  TCTCTGGGTT  CTCATTATCC  AGATATAGTG  TATACTGGGT  TCGCCAGCCT
TGTACGTGAC  AGAGACCCAA  GAGTAATAGG  TCTATATCAC  ATATGACCCA  AGCGGTCGGA

P  G  K  G     L  E  W     L  G  M     M  W  G  G     G  S  T     D  Y  N
        130            140            150            160            170            180
CCAGGAAAGG  GTCTGGAGTG  GCTGGGAATG  ATGTGGGGTG  GTGGATCCAC  AGACTATAAT
GGTCCTTTCC  CAGACCTCAC  CGACCCTTAC  TACACCCCAC  CACCTAGGTG  TCTGATATTA

S  A  L  K     S  R  L     S  I  S     K  D  T  S     K  S  Q     V  F  L
        190            200            210            220            230            240
TCAGCTCTCA  AATCCAGACT  GAGCATCAGC  AAGGACACCT  CGAAGAGCCA  GGTCTTCTTA
AGTCGAGAGT  TTAGGTCTGA  CTCGTAGTCG  TTCCTGTGGA  GCTTCTCGGT  CCAGAAGAAT

K  M  N  S     L  R  T     D  D  T     A  M  Y  Y     C  V  R     T  D  G
        250            260            270            280            290            300
AAAATGAACA  GTCTGCGAAC  TGATGACACA  GCCATGTACT  ACTGTGTCAG  AACCGATGGG
TTTTACTTGT  CAGACGCTTG  ACTACTGTGT  CGGTACATGA  TGACACAGTC  TTGGCTACCC

D  Y  W  G     Q  G  T     S  V  T     V  S  S
        310            320            330            339
GACTACTGGG  GTCAAGGAAC  CTCAGTCACC  GTCTCCTCA
CTGATGACCC  CAGTTCCTTG  GAGTCAGTGG  CAGAGGAGT
```

Mu5D12 VL region

```
E  L  Q  L     T  Q  S     P  L  S     L  P  V  S     L  G  D     Q  A  S
        10             20             30             40             50             60
GAGCTCCAGC  TGACCCAGTC  TCCACTCTCC  CTGCCTGTCA  GTCTTGGAGA  TCAAGCCTCC
CTCGAGGTCG  ACTGGGTCAG  AGGTGAGAGG  GACGGACAGT  CAGAACCTCT  AGTTCGGAGG

I  S  C  R     S  S  Q     S  L  V     N  S  N  G     N  T  Y     L  H  W
        70             80             90             100            110            120
ATCTCTTGCA  GATCTAGTCA  GAGCCTTGTA  AACAGTAATG  GAAACACCTA  TTTACATTGG
TAGAGAACGT  CTAGATCAGT  CTCGGAACAT  TTGTCATTAC  CTTTGTGGAT  AAATGTAACC

Y  L  Q  K     P  G  Q     S  P  K     L  L  I  Y     K  V  S     N  R  F
        130            140            150            160            170            180
TACCTGCAGA  AGCCAGGCCA  GTCTCCAAAG  CTCCTGATCT  ACAAAGTTTC  CAACCGATTT
ATGGACGTCT  TCGGTCCGGT  CAGAGGTTTC  GAGGACTAGA  TGTTTCAAAG  GTTGGCTAAA

S  G  V  P     D  R  F     S  G  S     G  S  G  T     D  F  T     L  K  I
        190            200            210            220            230            240
TCTGGGGTCC  CAGACAGGTT  CAGTGGCAGT  GGATCAGGGA  CAGATTTCAC  ACTCAAGATT
AGACCCCAGG  GTCTGTCCAA  GTCACCGTCA  CCTAGTCCCT  GTCTAAAGTG  TGAGTTCTAA

S  R  V  E     A  E  D     L  G  V     Y  F  C  S     Q  S  T     H  V  P
        250            260            270            280            290            300
AGCAGAGTGG  AGGCTGAGGA  TCTGGGAGTT  TATTTCTGCT  CTCAAAGTAC  ACATGTTCCG
TCGTCTCACC  TCCGACTCCT  AGACCCTCAA  ATAAAGACGA  GAGTTTCATG  TGTACAAGGC

W  T  F  G     G  G  T     K  L  E     I  K  R
        310            320            330            339
TGGACGTTCG  GTGGAGGCAC  CAAGCTGGAA  ATCAAACGT
ACCTGCAAGC  CACCTCCGTG  GTTCGACCTT  TAGTTTGCA
```

Figure 6

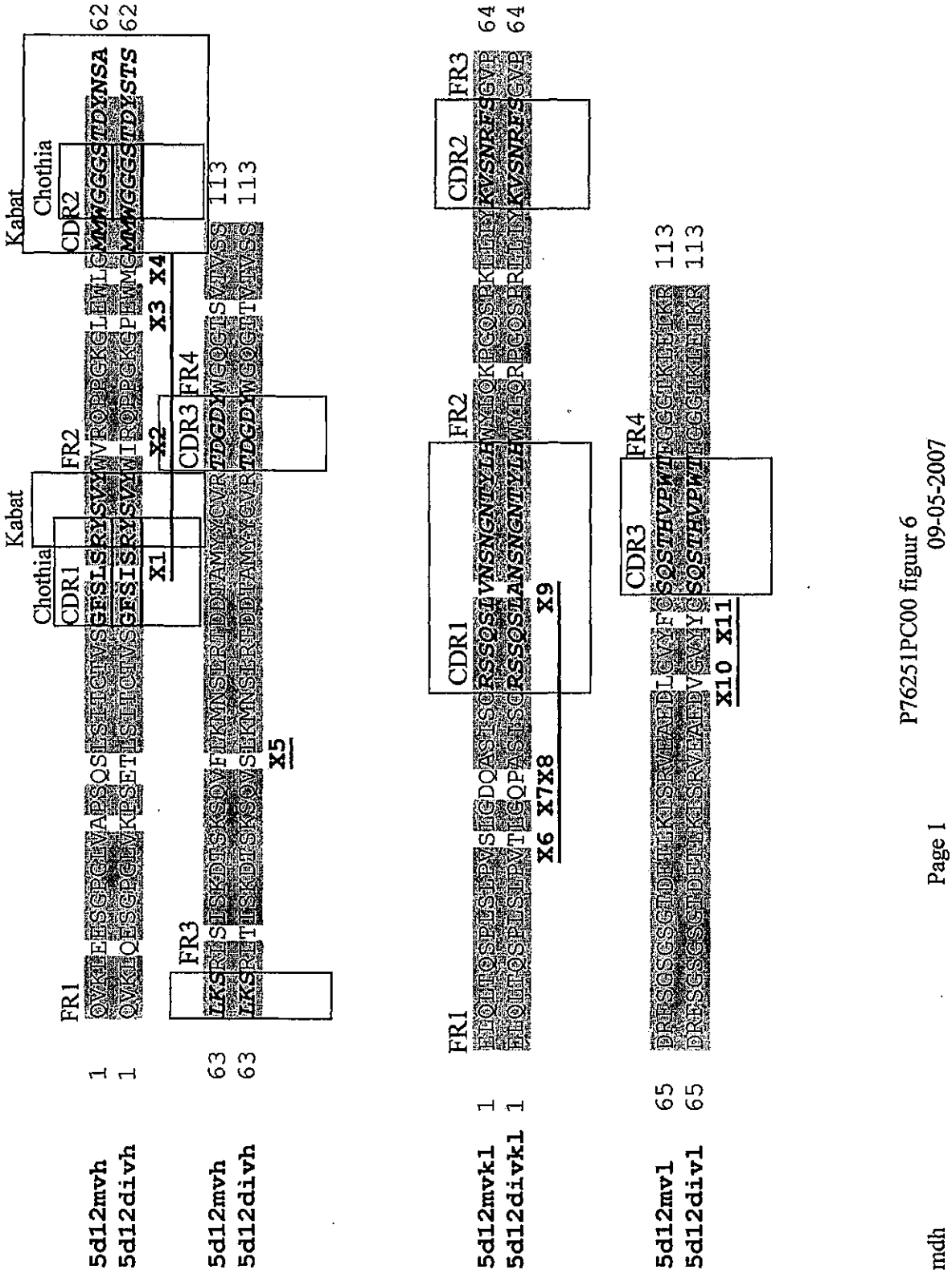

Kabat
Chothia
FR1
CDR1
FR2
CDR2
FR3
CDR3
FR4
X1
X2
X3 X4
X5
X6 X7X8
X9
X10 X11
5d12mvh
5d12divh
5d12mvkl
5d12divkl
5d12mvl
5d12divl

Figure 7

12 variants DI5D12VH

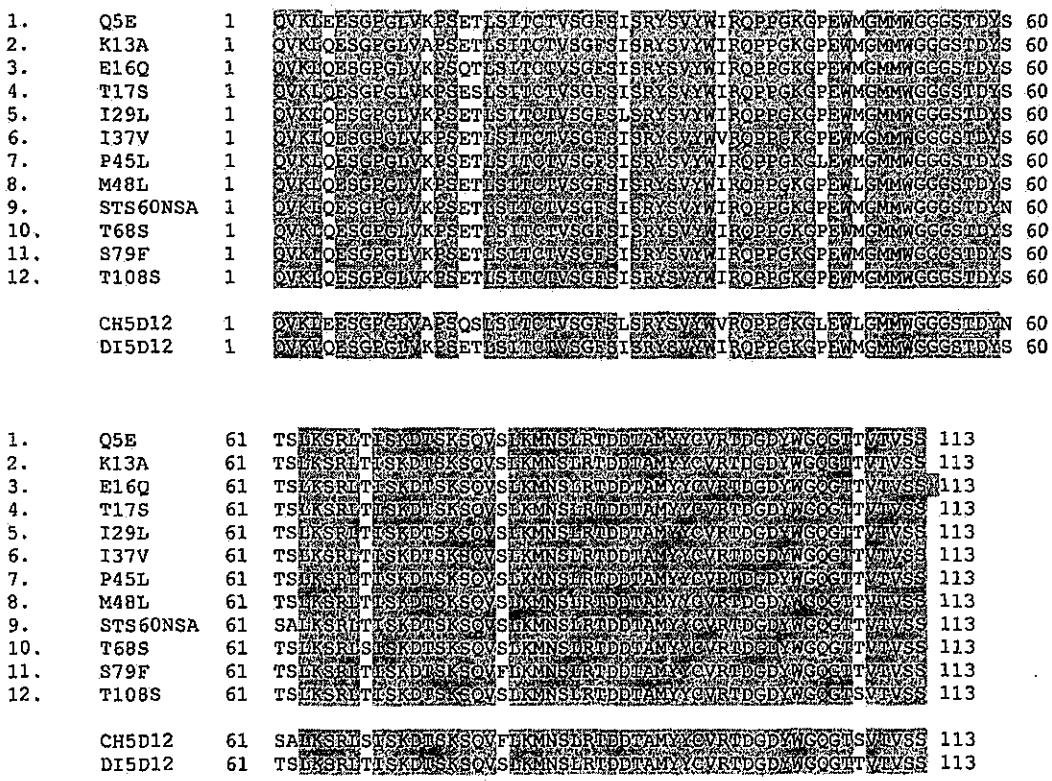
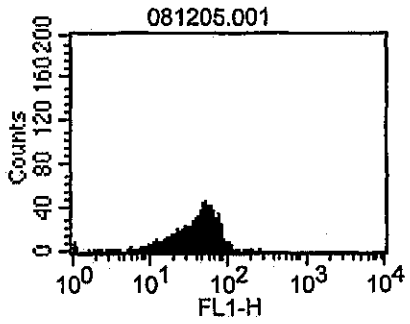


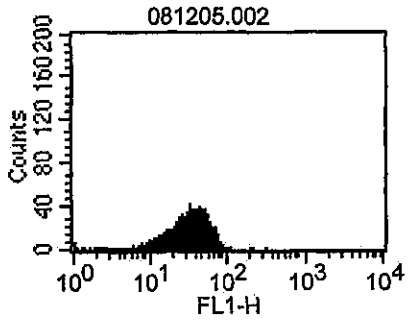
Figure 8 FACS data

Q5E



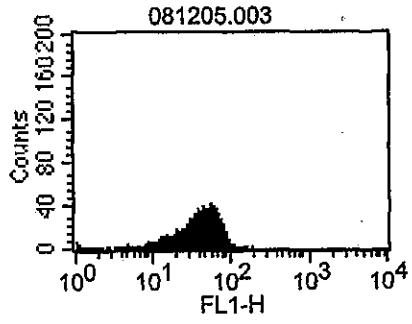
% Gated	Mean	Median
100.00	39.05	37.52

K13A



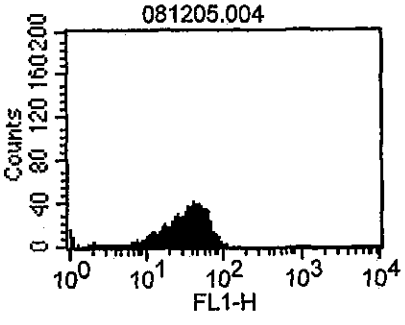
% Gated	Mean	Median
100.00	31.22	29.96

E16Q



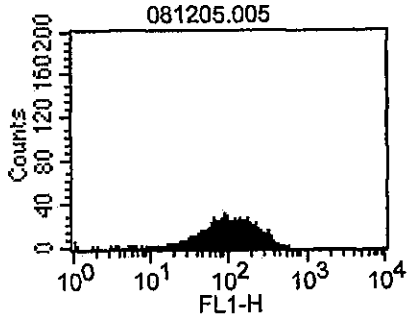
% Gated	Mean	Median
100.00	39.48	38.20

T17S



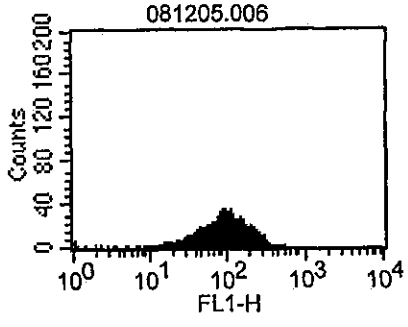
% Gated	Mean	Median
100.00	33.43	31.91

I29L



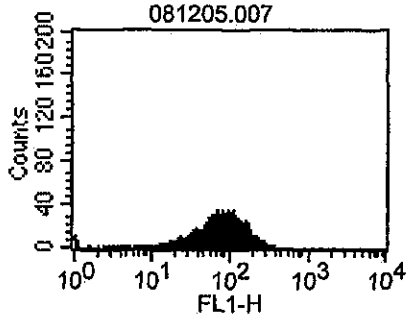
% Gated	Mean	Median
100.00	108.28	91.81

I37V



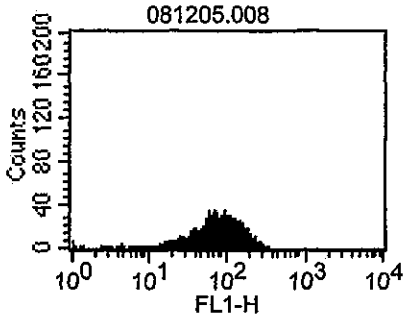
% Gated	Mean	Median
100.00	96.05	82.05

P45L



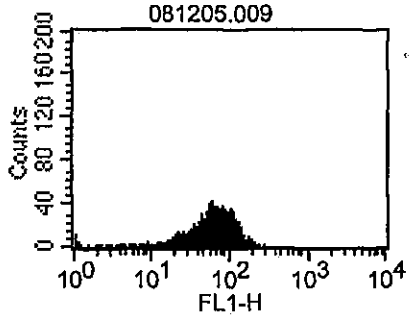
% Gated	Mean	Median
100.00	82.53	74.32

M48L



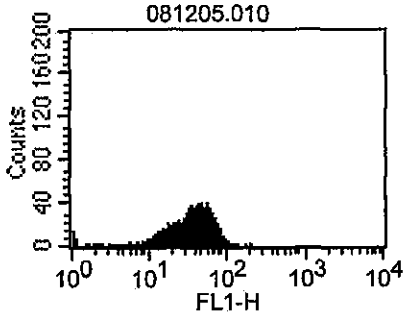
% Gated	Mean	Median
100.00	80.30	72.34

STS60NSA



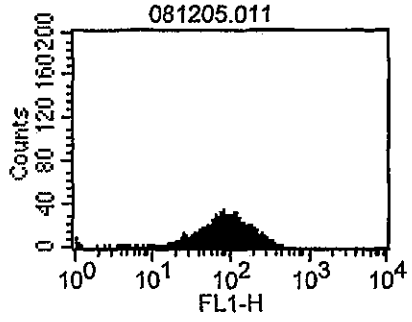
% Gated	Mean	Median
100.00	62.37	58.82

T68S



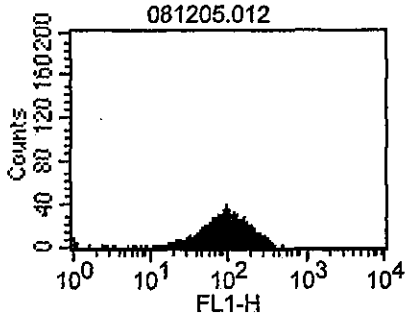
% Gated	Mean	Median
100.00	35.21	33.98

S79F



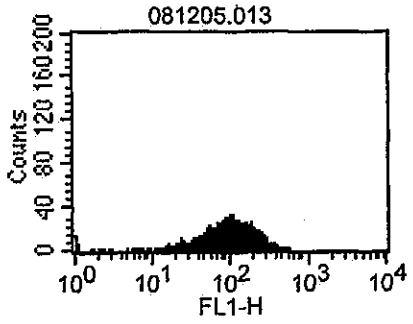
% Gated	Mean	Median
100.00	96.40	82.05

T108S



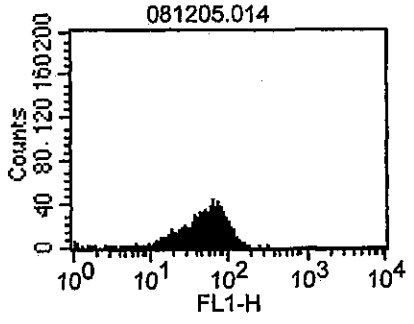
% Gated	Mean	Median
100.00	99.04	85.82

Ch5D12



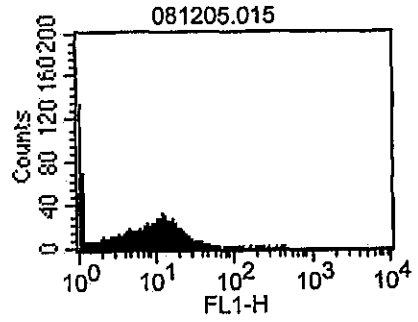
% Gated	Mean	Median
100.00	102.97	88.96

DI5D12



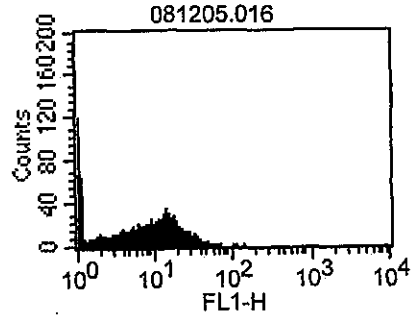
% Gated	Mean	Median
100.00	50.44	47.40

Mock Control



% Gated	Mean	Median
100.00	11.25	8.74

FACS control



% Gated	Mean	Median
100.00	10.18	8.74

Figure 9: V-L-I variants of DI5D12VH

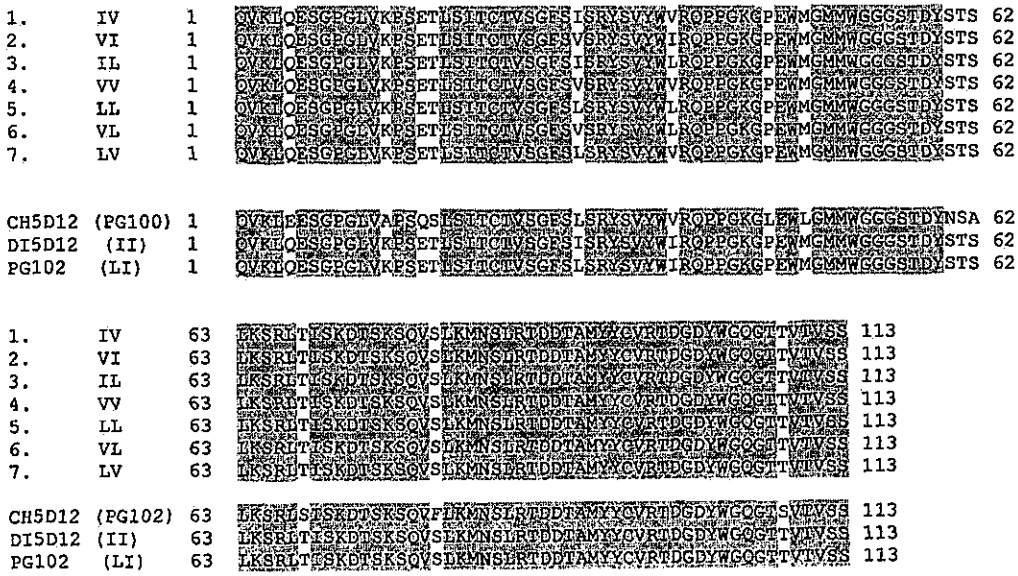


Figure 10: **Distribution of antibody productivity for GS-CHO cell lines producing the PG102 antibody and 'overgrown' 24-well plate cultures**

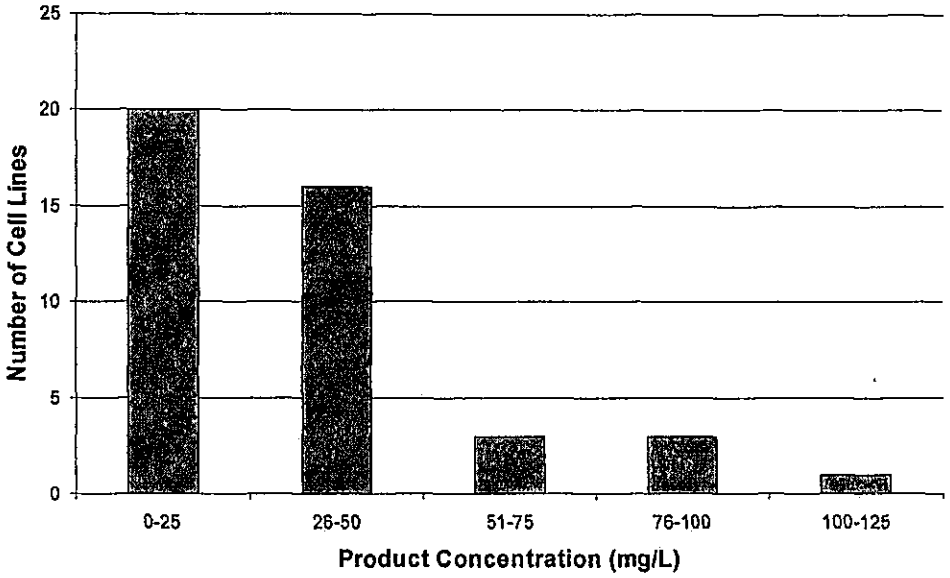
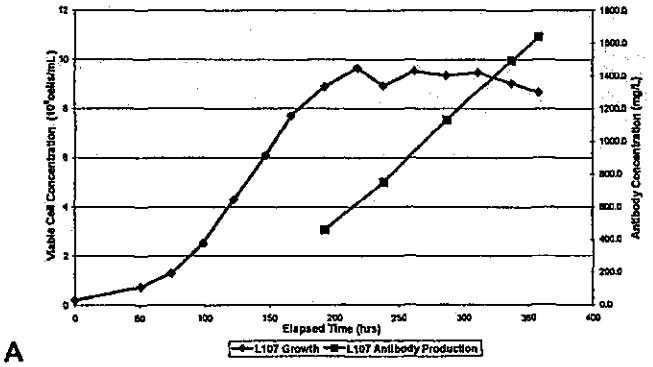
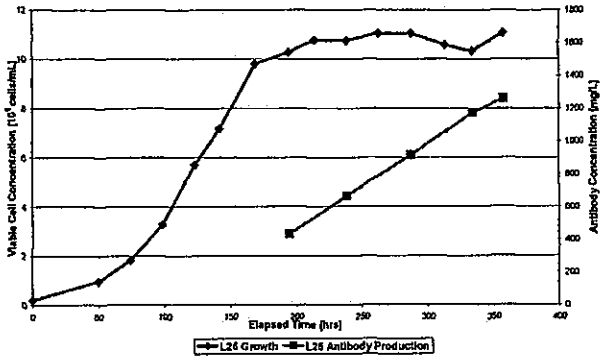


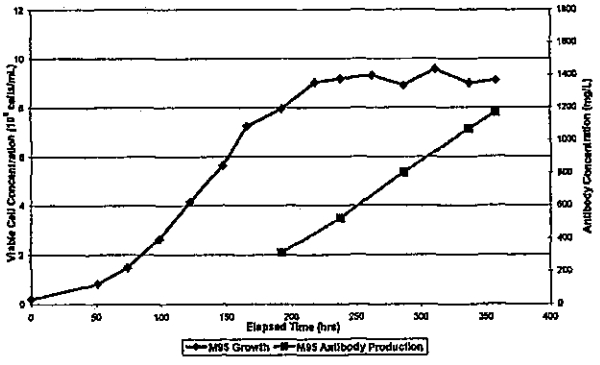
Figure 11: Growth and antibody accumulation profiles for cell lines L107 (DC1; top panel), L25 (DC2; middle panel) and M95 (DC3; lower panel) in CDACF fed-batch shake flask culture



A

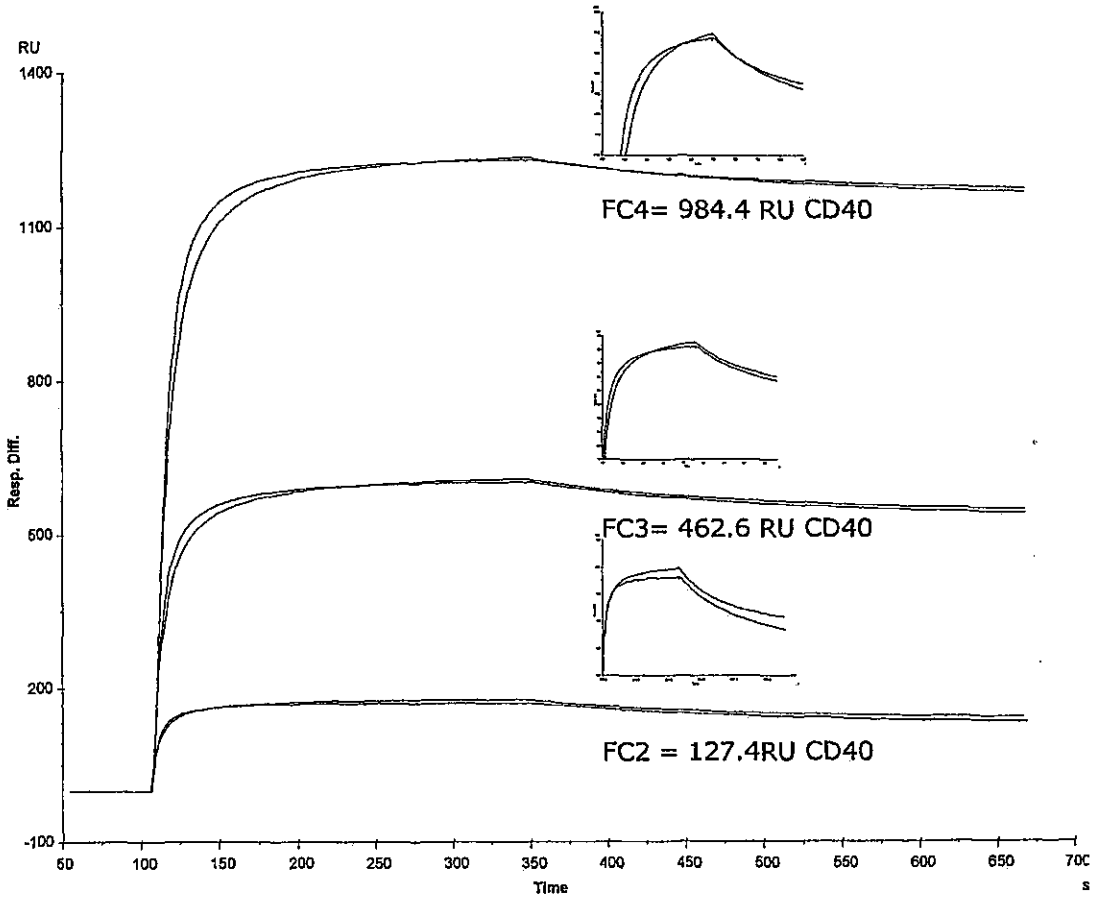


B



C

Figure 12: Comparison of the binding of PG102(red) and PG100(blue) at 10µg/mL to CD40 immobilised at 3 different levels



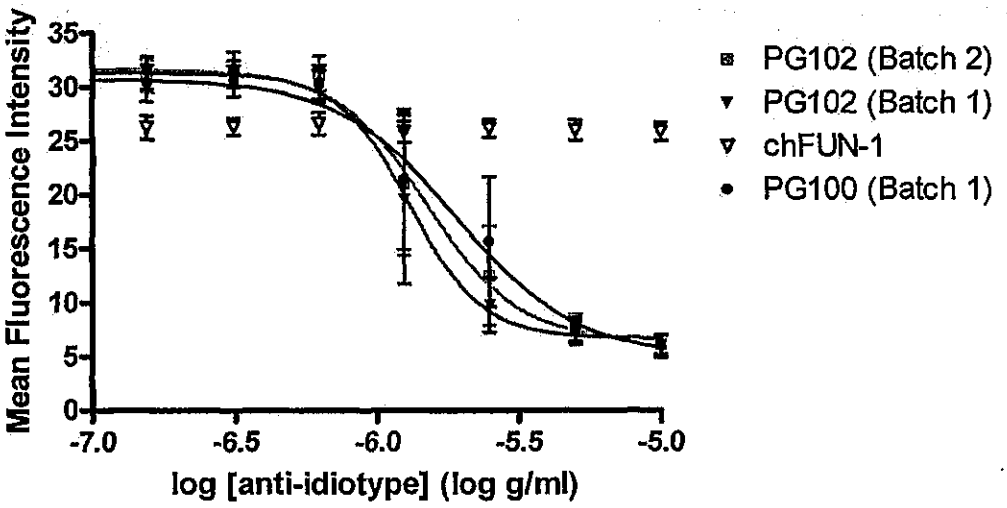


Figure 13 Inhibition of CD40 mAb binding to JY cells expressing human CD40 by the anti-idiotype mAb 173-36-1. Anti-CD40 mAbs were assayed at a concentration of 1 μg/ml. Data indicate mean ± s.e. mean of 4 separate determinations for each antibody.

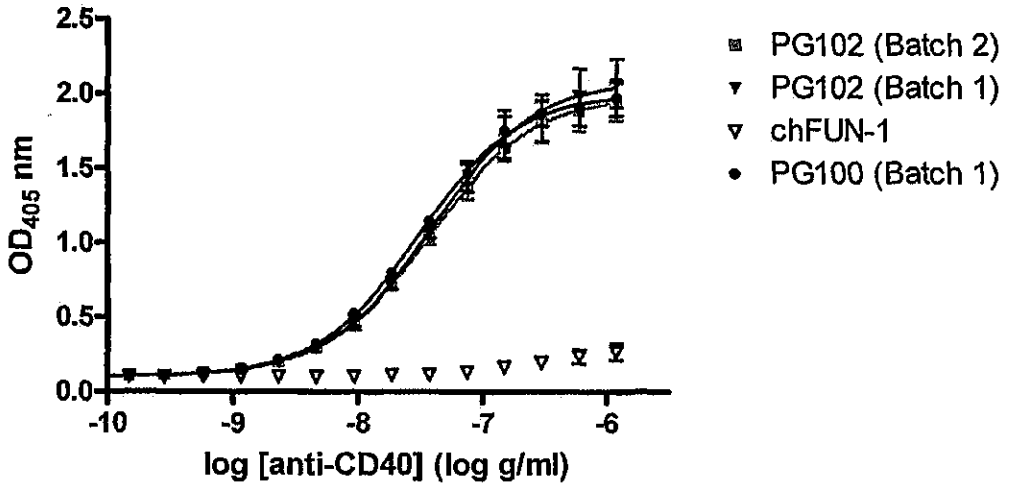


Figure 14: CD40-Fc ELISA. Concentration-related binding of PG100 and PG102 to human CD40-Fc. Plates were coated overnight with 250 ng/ml human CD40-Fc. The isotype control mAb, chFUN-1, is directed against human CD86. Data indicate mean ± s.e. mean (all n=3).

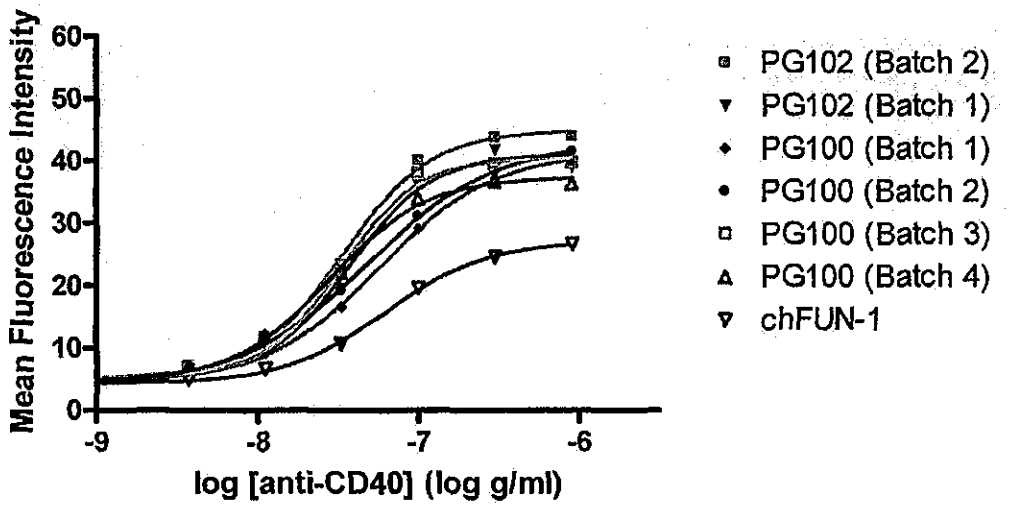


Figure 15: FACS quantification of anti-CD40 mAb binding to JY cells. PG100 and PG102 displayed comparable half-maximal binding concentrations. The anti-CD86 mAb, chFUN-1, also showed binding to JY cells in these experiments due to the surface expression of human CD86 by this cell line. Data indicate the mean of duplicate determinations for each antibody.

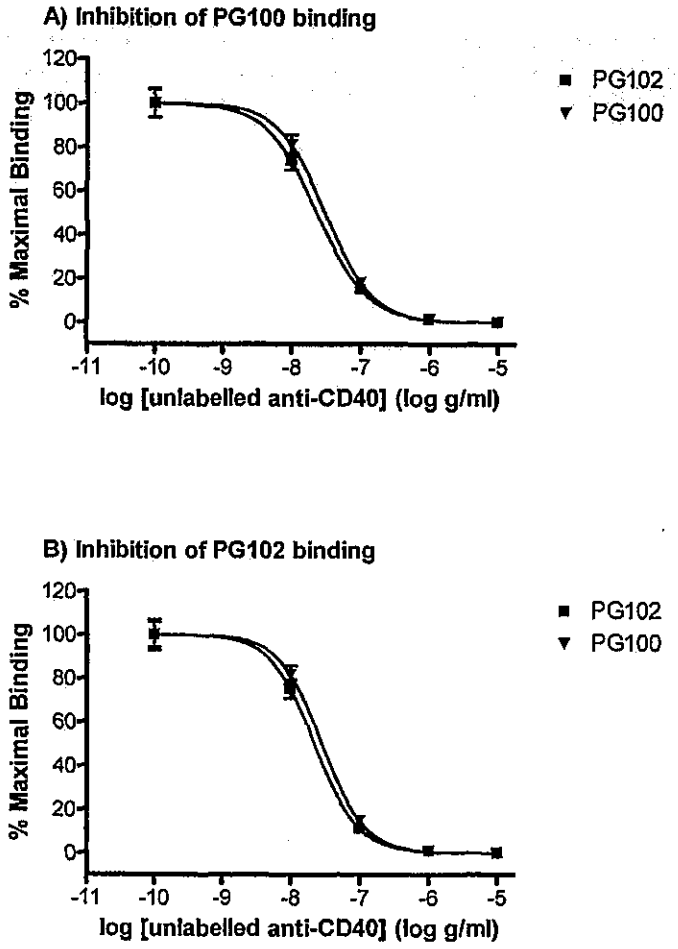


Figure 16. *Inhibition of PG100PE and PG102PE binding to JY cells by unlabelled PG100 and PG102 antibodies. Labelled PG100 (A) and PG102 (B) were incubated at 1 □g/ml in the presence of increasing concentration of competing unlabelled antibody. Labelled antibody binding was determined as mean fluorescence intensity (MFI) by flow cytometry. Maximal MFI for PG100PE and PG102PE binding was 369 fluorescence units (A) and 305 fluorescence units (B), respectively. Data indicate mean ± s.e. mean of 4 separate experiments.*

Figure 17: Inhibition of IL-8 release by THP-1 cells after co-culture with Jurkat cells.

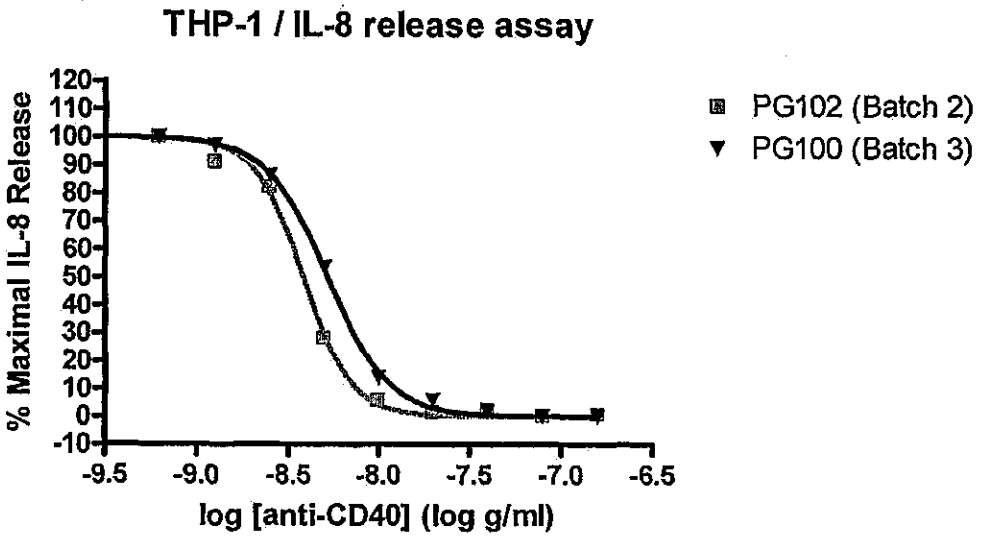


Figure 18

Protein sequence of PG102 heavy and light chain

Signal sequences are underlined, variable regions in bold.

Heavy chain:

MEWSWVFLFFLSVTTGVHS**QVKLQESGPGLVKPSETLSITCTVSGFSLSRYSVYWIRQPPGKGPE WMGMMWGGGSTDYSTSLKSRLTISKDTSKSQVSLKMNSLRTDDTAMYYCVRTDGDYWGQGTTVTV SS**ASTKGPSVFPLAPCSRSTSESTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLY SLSSVVTVPSSSLGTKTYTCNVDHKPSNTKVDKRVESKYGPPCPSCPAPEFLGGPSVFLFPPKPK DTLMISRTPEVTCVVVDVSQEDPEVQFNWYVDGVEVHNAKTKPREEQFNSTYRVVSVLTVLHQDW LNGKEYKCKVSNKGLPSSIEKTISKAKGQPREPQVYTLPPSQEEMTKNQVSLTCLVKGFYPSDIA VEWESNGQPENNYKTTPPVLDSDGSFFLYSRLTVDKSRWQEGNVFSCSVMHEALHNHYTQKSLSL SLGK

Light chain:

MSVPTQVLGLLLLWLTDARC**ELQLTQSPLSLPVTLGQPASISCRSSQSLANSNGNTYLHWYLQRP GQSPRLLIYKVSNRFSGVPDRFSGSGSGTDFTLKISRVEAEDVGVYYCSQSTHVPWTFGGGTKLE IKR**TVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNSQESVTEQDSKD STYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

DNA sequences encoding PG102 heavy and light chains

Signal sequences is indicated as underlined, variable regions in bold, and stop codons in lower case.

Heavy chain:

ATGGAGTGGTCTTGGGTGTTCCTGTTCTTCCTGTCTGTGACAACAGGAGTGCACTCT**CAGGTCAA**
GCTGCAGGAGTCTGGACCAGGACTGGTGAAGCCATCTGAGACCCTGAGCATCACCTGTACAGTGA
GCGGCTTCAGCCTCTCTAGATACAGCGTGTACTGGATCAGACAGCCACCTGGAAAGGGACCAGAG
TGGATGGGAATGATGTGGGGAGGAGGATCTACAGACTACAGCACCAGCCTGAAGTCTAGACTGAC
CATCAGCAAGGACACCTCTAAGTCTCAGGTCTCCCTGAAGATGAACTCTCTGAGAACAGACGACA
CCGCCATGTACTACTGTGTGAGAACCGACGGAGATTATTGGGGACAGGGCACAACAGTGACAGTG
TCCTCTGCCTCTACAAAGGGACCATCTGTGTTTCCACTGGCCCCATGTTCTAGATCTACCAGCGA
GTCTACAGCTGCTCTGGGATGTCTGGTGAAGGACTACTTTCCAGAGCCTGTGACAGTGTCTTGGA
ATAGTGGAGCCCTGACATCTGGAGTGCACACATTTCCAGCTGTGCTGCAGTCTAGCGGACTGTAT
TCTCTGTCCAGCGTGGTGACAGTGCCATCTTCTTCTCTGGGCACCAAGACCTACACATGTAACGT
GGACCACAAGCCATCTAACACCAAGGTGGACAAGAGAGTGGAGTCTAAGTACGGACCACCATGCC
CATCTTGTCCAGCTCCAGAGTTTCTGGGAGGACCTAGCGTGTTTCTGTTCCCCCCAAAGCCAAAG
GATACCCTGATGATCTCTAGAACCCCAGAGGTGACATGTGTGGTGGTGGATGTGTCTCAGGAGGA
TCCAGAGGTCCAGTTTAACTGGTACGTGGATGGAGTGGAGGTGCACAACGCTAAGACAAAGCCAA
GAGAGGAGCAGTTCAACAGCACATACAGAGTGGTGTCTGTGCTGACAGTGCTGCATCAGGATTGG
CTGAACGGCAAGGAATACAAGTGTAAGGTCTCCAACAAGGGCCTGCCATCTTCTATCGAGAAAAC
CATCTCTAAGGCTAAGGGACAGCCAAGGGAGCCACAGGTGTACACACTGCCACCATCTCAAGAGG
AGATGACCAAGAACCAGGTGTCCCTGACATGCCTGGTGAAGGGATTCTACCCATCTGATATCGCT
GTGGAGTGGGAGTCTAATGGACAGCCCGAGAACAACTACAAGACCACACCACCAGTGCTGGATTC
TGACGGCTCTTTCTTCCTGTACAGCAGACTGACAGTGGACAAGTCTAGATGGCAGGAGGGAAACG
TCTTTAGCTGTAGCGTGATGCATGAGGCTCTGCACAACCACTACACCCAGAAGTCTCTGTCTCTG
AGTCTGGGAAAAtgatag

Light chain:

ATGTCTGTGCCAACACAGGTGCTGGGACTGCTGCTGCTGTGGCTGACAGATGCTAGATGT**GAGCT**
GCAGCTGACACAGTCTCCACTGTCTCTGCCAGTGACACTGGGACAGCCAGCTAGCATCAGCTGTA
GAAGCTCTCAGTCTCTGGCCAACTCTAACGGCAACACATACCTGCATTGGTATCTGCAGAGACCA
GGACAGTCTCCAAGACTGCTGATCTACAAGGTGTCCAACAGATTCTCTGGAGTGCCAGACAGATT
TTCTGGCTCTGGCTCTGGAACAGACTTCACCCTGAAGATCTCTAGAGTGGAGGCTGAGGATGTGG
GAGTGTACTACTGCTCTCAGTCTACACATGTGCCATGGACATTCGGAGGAGGAACAAAGCTGGAG
ATCAAGAGAACAGTGGCTGCCCCATCTGTGTTTATCTTCCCCCCATCTGATGAGCAGCTGAAGTC
TGGAACAGCTTCTGTGGTGTGTCTGCTGAACAACTTCTACCCAAGGGAGGCTAAGGTGCAGTGGA
AGGTGGACAATGCTCTGCAGTCTGGAAACTCTCAGGAGTCTGTCACAGAGCAGGACAGCAAGGAC
TCTACCTACTCTCTGAGCAGCACACTGACACTGTCTAAGGCCGACTACGAGAAGCATAAGGTGTA
CGCCTGTGAGGTGACACATCAGGGACTGTCTAGCCCAGTGACCAAGTCTTTCAACAGAGGCGAGT
GCtgatag