Anti-CD30 5F11 VH

V-segment: Locus: 4-34
D segment: Locus - 7-27
J segment: JH4b

```
     Q   V   Q   L   Q   Q   W   G   A   G   L   L   K   P   S   E   T   L
1    CAG GTG CAG CTA CAG CAG TGG GGC GCA GGA CTG TTG AAG CCT TCG GAG ACC CTG

                                                        CDR1
                                                    ~~~~~~~~~~~~~~~~~~~~
     S   L   T   C   A   V   Y   G   G   S   F   S   A   Y   Y   W   S   W
55   TCC CTC ACC TGC GCT GTC TAT GGT GGG TCC TTC AGT GCT TAC TAC TGG AGC TGG

                                                            CDR2
                                                    ~~~~~~~~~~~~~~~~~~~~
     I   R   Q   P   P   G   K   G   L   E   W   I   G   D   I   N   H   G
109  ATC CGC CAG CCC CCA GGG AAG GGG CTG GAG TGG ATT GGG GAC ATC AAT CAT GGT

                        CDR2
     ~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~
     G   G   T   N   Y   N   P   S   L   K   S   R   V   T   I   S   V   D
163  GGA GGC ACC AAC TAC AAC CCG TCC CTC AAG AGT CGA GTC ACC ATA TCA GTA GAC

     T   S   K   N   Q   F   S   L   K   L   N   S   V   T   A   A   D   T
217  ACG TCC AAG AAC CAG TTC TCC CTG AAG CTG AAC TCT GTA ACC GCC GCG GAC ACG

                                    CDR3
                                ~~~~~~~~~~~~~~~~~~
     A   V   Y   Y   C   A   S   L   T   A   Y   W   G   Q   G   S   L   V
271  GCT GTG TAT TAC TGT GCG AGC CTA ACT GCC TAC TGG GGC CAG GGA AGC CTG GTC
                               D7-27/DHQ52   └→ JH4b

     T   V   S   S
325  ACC GTC TCC TCA
```

Fig. 1A

Anti-CD30 5F11 VL
V-segment: Locus: L15
J segment: JK5

```
      D   I   Q   M   T   Q   S   P   T   S   L   S   A   S   V   G   D   R
1     GAC ATC CAG ATG ACC CAG TCT CCA ACC TCA CTG TCT GCA TCT GTA GGA GAC AGA

                              CDR1
                              ~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~
      V   T   I   T   C   R   A   S   Q   G   I   S   S   W   L   T   W   Y
55    GTC ACC ATC ACT TGT CGG GCG AGT CAG GGT ATT AGC AGC TGG TTA ACC TGG TAT

                                                          CDR2
                                                          ~~~~~~~~~~~~~~~~~~~
      Q   Q   K   P   E   K   A   P   K   S   L   I   Y   A   A   S   S   L
109   CAG CAG AAA CCA GAG AAA GCC CCT AAG TCC CTG ATC TAT GCT GCA TCC AGT TTG

      CDR2
      ~~~~~~~~
      Q   S   G   V   P   S   R   F   S   G   S   G   S   G   T   D   F   T
163   CAA AGT GGG GTC CCA TCA AGG TTC AGC GGC AGT GGA TCT GGG ACA GAT TTC ACT

                                                                  CDR3
                                                                  ~~~~~~~~
      L   T   I   S   S   L   Q   P   E   D   F   A   T   Y   Y   C   Q   Q
217   CTC ACC ATC AGC AGC CTG CAG CCT GAA GAT TTT GCA ACT TAT TAC TGC CAA CAG

            CDR3
      ~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~
      Y   D   S   Y   P   I   T   F   G   Q   G   T   R   L   E   I   K
271   TAT GAT AGT TAC CCT ATC ACC TTC GGC CAA GGG ACA CGA CTG GAG ATT AAA
                        └►JK5
```

Fig. 1B

Anti-CD30 17G1 VH

V-segment: Locus: 3-07
D segment: Not Found
J segment: JH2

```
      E   V   Q   L   V   E   S   G   G   G   L   V   Q   P   G   G   S   L
1     GAG GTG CAG TTG GTG GAG TCT GGG GGA GGC TTG GTC CAG CCT GGG GGG TCC CTG

                                                        CDR1
                                                    ~~~~~~~~~~~~~~~~~~~~
      R   L   S   C   V   A   S   G   F   T   F   S   N   S   W   M   S   W
55    AGA CTC TCC TGT GTA GCC TCT GGA TTC ACC TTT AGT AAC TCT TGG ATG AGC TGG

                                                            CDR2
                                                    ~~~~~~~~~~~~~~~~~~~~
      V   R   Q   A   P   G   K   G   L   E   W   V   A   N   I   N   E   D
109   GTC CGC CAG GCT CCA GGG AAA GGG CTG GAG TGG GTG GCC AAC ATA AAC GAA GAT

                        CDR2
      ~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~
      G   S   E   K   F   Y   V   D   S   V   K   G   R   F   T   F   S   R
163   GGA AGT GAG AAA TTC TAT GTG GAC TCT GTG AAG GGC CGA TTC ACC TTC TCC AGA


      D   N   A   E   N   S   L   Y   L   Q   M   N   S   L   R   A   E   D
217   GAC AAC GCC GAG AAC TCA CTG TAT CTG CAA ATG AAC AGC CTG AGA GCC GAG GAC

                                            CDR3
                                    ~~~~~~~~~~~~~~~~~~~~~~~~~~~~
      T   A   V   Y   Y   C   A   R   V   H   W   Y   F   H   L   W   G   R
271   ACG GCT GTG TAT TAC TGT GCG AGG GTT CAT TGG TAC TTC CAT CTC TGG GGC CGT

                                        |
                                        └──► JH2

      G   T   L   V   T   V   S   S
325   GGC ACC CTG GTC ACT GTC TCC TCA
```

Fig. 2A

Anti-CD30 17G1 VL
V-segment: Locus: A27
J segment: JK1

```
      E   I   V   L   T   Q   S   P   G   T   L   S   L   S   P   G   E   R
1     GAA ATT GTG TTG ACG CAG TCT CCA GGC ACC CTG TCT TTG TCT CCA GGG GAA AGA

                                  CDR1
                          ~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~
      A   T   L   S   C   R   A   S   Q   S   V   S   S   S   Y   L   A   W
55    GCC ACC CTC TCC TGC AGG GCC AGT CAG AGT GTT AGC AGC AGC TAC TTA GCC TGG

                                                              CDR2
                                                          ~~~~~~~~~~~~~~~~
      Y   Q   Q   K   P   G   Q   A   P   R   L   L   I   Y   G   A   S   S
109   TAC CAG CAG AAA CCT GGC CAG GCT CCC AGG CTC CTC ATC TAT GGT GCA TCC AGC

          CDR2
      ~~~~~~~~~~~~
      R   A   T   G   I   P   D   R   F   S   G   S   G   S   G   T   D   F
163   AGG GCC ACT GGC ATC CCA GAC AGG TTC AGT GGC AGT GGG TCT GGG ACA GAC TTC

                                                                  CDR3
                                                                  ~~~
      T   L   T   I   S   S   L   E   P   E   D   F   A   V   Y   Y   C   Q
217   ACT CTC ACC ATC AGC AGC CTG GAG CCT GAA GAT TTT GCA GTG TAT TAC TGT CAG

                  CDR3
      ~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~
      Q   Y   G   S   S   P   W   T   F   G   Q   G   T   K   V   E   I   K
271   CAG TAT GGT AGC TCA CCG TGG ACG TTC GGC CAA GGG ACC AAG GTG GAA ATC AAA
                              |
                              └→ JK1
```

Fig. 2B

Anti-2H9 CD30 VH
V-segment: Locus: 4-34
D segment: Locus - 5-12
J segment: JH2

```
     Q   V   Q   L   Q   Q   W   G   A   G   L   L   K   P   S   E   T   L
1    CAG GTG CAG CTA CAG CAG TGG GGC GCA GGA CTG TTG AAG CCT TCG GAG ACC CTG

                                                        CDR1
                                                    ~~~~~~~~~~~~~~~~~~~
     S   L   T   C   A   V   Y   G   G   S   F   S   G   Y   Y   W   S   W
55   TCC CTC ACC TGC GCT GTC TAT GGT GGG TCC TTC AGT GGT TAC TAC TGG AGC TGG

                                                            CDR2
                                                        ~~~~~~~~~~~~~~~~~~~
     I   R   Q   P   P   G   K   G   L   E   W   I   G   E   I   N   H   S
109  ATC CGC CAG CCC CCA GGG AAG GGG CTG GAG TGG ATT GGG GAA ATC AAT CAT AGT

                    CDR2
     ~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~
     G   S   T   K   Y   T   P   S   L   K   S   R   V   T   I   S   V   D
163  GGA AGC ACC AAG TAC ACC CCG TCC CTC AAG AGC CGA GTC ACC ATA TCA GTA GAC

     T   S   K   H   Q   F   S   L   K   L   S   S   V   T   A   A   D   T
217  ACG TCC AAG CAC CAA TTC TCC CTG AAG CTG AGC TCT GTG ACC GCC GCG GAC ACG

                                        CDR3
                                    ~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~
     A   V   Y   Y   C   A   R   E   T   V   Y   Y   F   D   L   W   G   R
271  GCT GTG TAT TAC TGT GCG AGA GAG ACT GTC TAC TAC TTC GAT CTC TGG GGC CGT
                                                  |
                                                  └→ JH2

     G   T   L   V   T   V   S   S
325  GGC ACC CTG GTC ACT GTC TCC TCA
```

Fig. 3A

Anti-2H9 CD30 VL
V-segment: Locus: L6
J segment: JK1

```
      E   I   V   L   T   Q   S   P   A   T   L   S   L   S   P   G   E   R
1     GAA ATT GTG TTG ACA CAG TCT CCA GCC ACC CTG TCT TTG TCT CCA GGG GAA AGA

                                  CDR1
                  ~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~
      A   T   L   S   C   R   A   S   Q   S   V   S   S   N   L   A   W   Y
55    GCC ACC CTC TCC TGC AGG GCC AGT CAG AGT GTA AGC AGC AAC TTA GCC TGG TAC

                                                              CDR2
                                                  ~~~~~~~~~~~~~~~~~~~~
      Q   Q   K   P   G   Q   A   P   R   L   L   I   Y   D   A   S   N   R
109   CAA CAG AAA CCT GGC CAG GCT CCC AGG CTC CTC ATC TAT GAT GCA TCC AAC AGG

      CDR2
      ~~~~~~~~
      A   T   G   I   P   A   R   L   S   G   S   G   S   G   T   D   F   T
163   GCC ACT GGC ATC CCA GCC AGG CTC AGT GGC AGT GGG TCT GGG ACA GAC TTC ACT

                                                                  CDR3
                                                                  ~~~~~~~~
      L   T   I   S   S   L   E   P   E   D   F   A   V   Y   Y   C   Q   Q
217   CTC ACC ATC AGC AGC CTA GAG CCT GAA GAT TTT GCA GTT TAT TAC TGT CAA CAG

            CDR3
      ~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~
      R   S   N   W   P   W   T   F   G   Q   G   T   K   V   E   I   K
271   CGT AGC AAC TGG CCG TGG ACG TTC GGC CAA GGG ACC AAG GTG GAA ATC AAA
                  |
                  └→ JK1
```

Fig. 3B

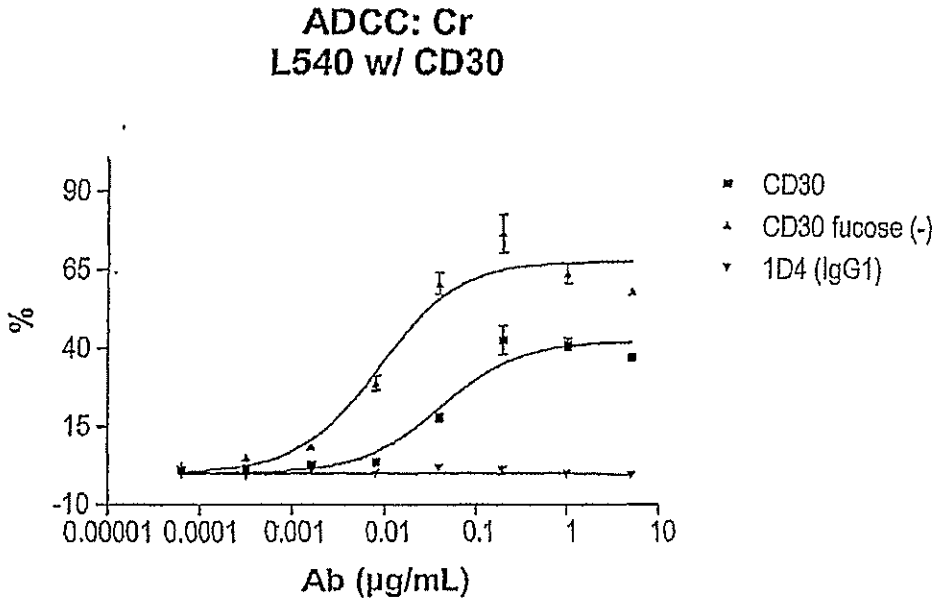

ADCC: Cr
L540 w/ CD30
90
65
40
15
-10
%
0.00001
0.0001
0.001
0.01
0.1
1
10
Ab (µg/mL)
CD30
CD30 fucose (-)
1D4 (IgG1)

Fig. 4

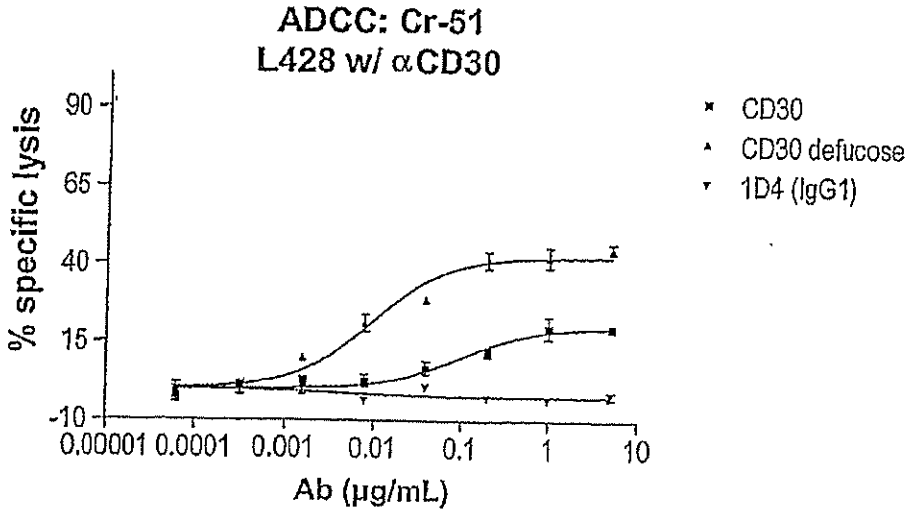

ADCC: Cr-51
L428 w/ αCD30
% specific lysis
90
65
40
15
-10
0.00001
0.0001
0.001
0.01
0.1
1
10
Ab (µg/mL)
CD30
CD30 defucose
1D4 (IgG1)

Fig. 5

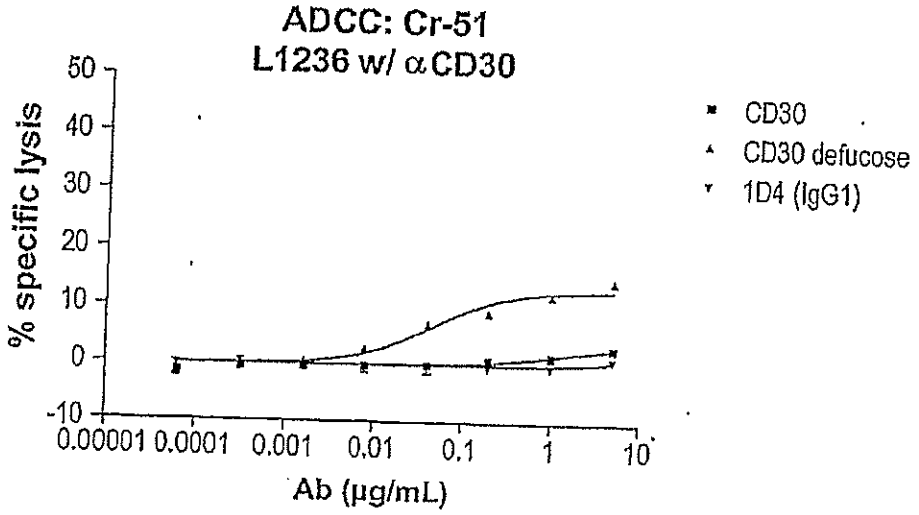

ADCC: Cr-51
L1236 w/ αCD30
% specific lysis
50
40
30
20
10
0
-10
0.00001
0.0001
0.001
0.01
0.1
1
10
Ab (µg/mL)
CD30
CD30 defucose
1D4 (IgG1)

Fig. 6

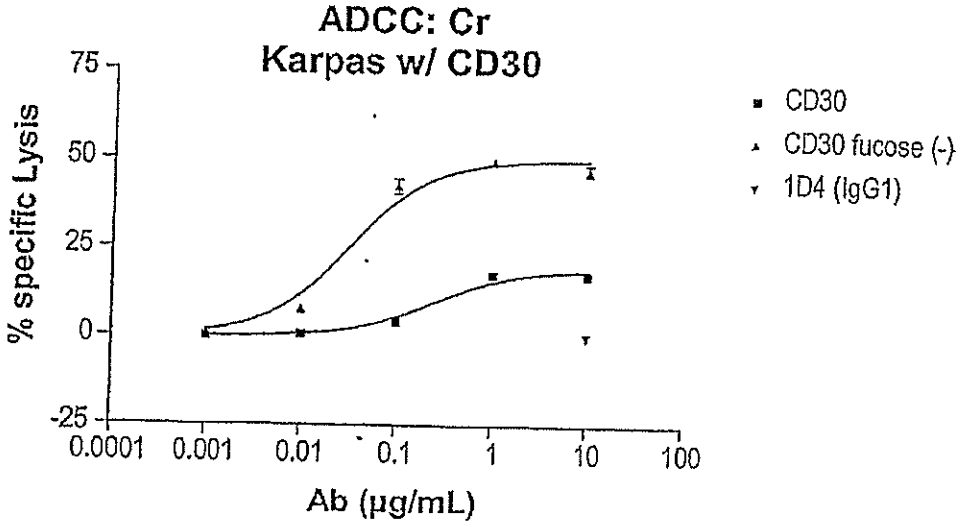

ADCC: Cr
Karpas w/ CD30
% specific Lysis
75
50
25
0
-25
0.0001
0.001
0.01
0.1
1
10
100
Ab (µg/mL)
CD30
CD30 fucose (-)
1D4 (IgG1)

Fig. 7

Heavy Chain Germline Sequences

4-34 Germline:

```
                                                                  CDR1
Q V Q L Q Q W G A G L L K P S E T L S L T C A V Y G G S F S G Y Y W S

                                                  CDR2
W I R Q P P G K G L E W I G E I N H S G S T N Y N P S L K S R V T I S

                                                  CDR3
V D T S K N Q F S L K L S S V T A A D T A V Y Y C A R
```

3-07 Germline:

```
                                                                  CDR1
                                                                  ~~~~~~~~~~
E V Q L V E S G G G L V Q P G G S L R L S C A A S G F T F S S Y W M S W

                                  CDR2
                                  ~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~
V R Q A P G K G L E W V A N I K Q D G S E K Y Y V D S V K G R F T I S R

D N A K N S L Y L Q M N S L R A E D T A V Y Y C A R
```

Fig. 8A

Light Chain Germline Sequences

L6 germline:

E I V L T Q S P A T L S L S P G E R A T L S C R A S Q S V S S Y L A
CDR1

W Y Q Q K P G Q A P R L L I Y D A S N R A T G I P A R F S G S G S G
CDR2

T D F T L T I S S L E P E D F A V Y Y C Q Q R S N W
CDR3

A27 Germline:

EIVLTQSPGTLSLSPGERATLSC *CDR1* RASQSVSSSYLA WYQQKPGQAPRLLIY *CDR2* GASSRAT

CDR3

GIPDRFSGSGSGTDFTLTISRLEPEDFAVYYC QQYGSS

L15 Germline:

DIQMTQSPSSLSASVGDRVTITC *CDR1* RASQGISSWLA WYQQKPEKAPKSLIY *CDR2* AASSLQS

GVPSRFSGSGSGTDFTLTISSLQPEDFATYYC *CDR3* QQYNSY

Fig. 8B

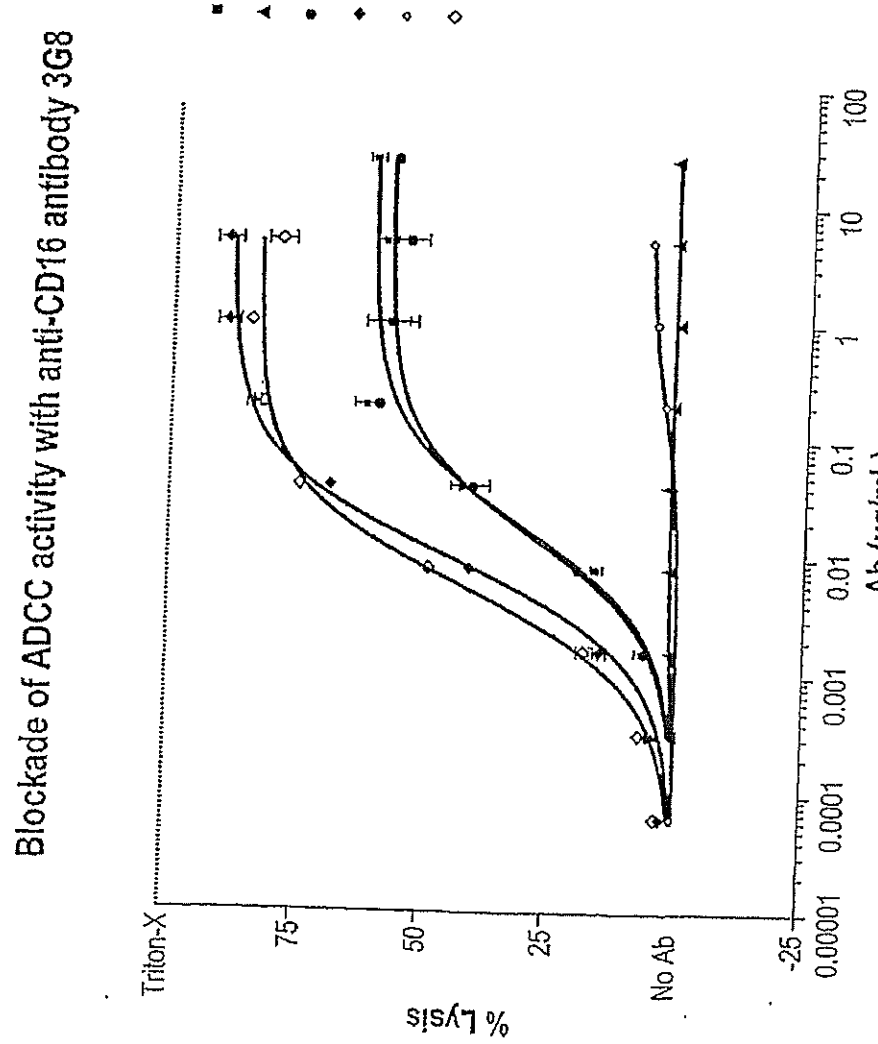
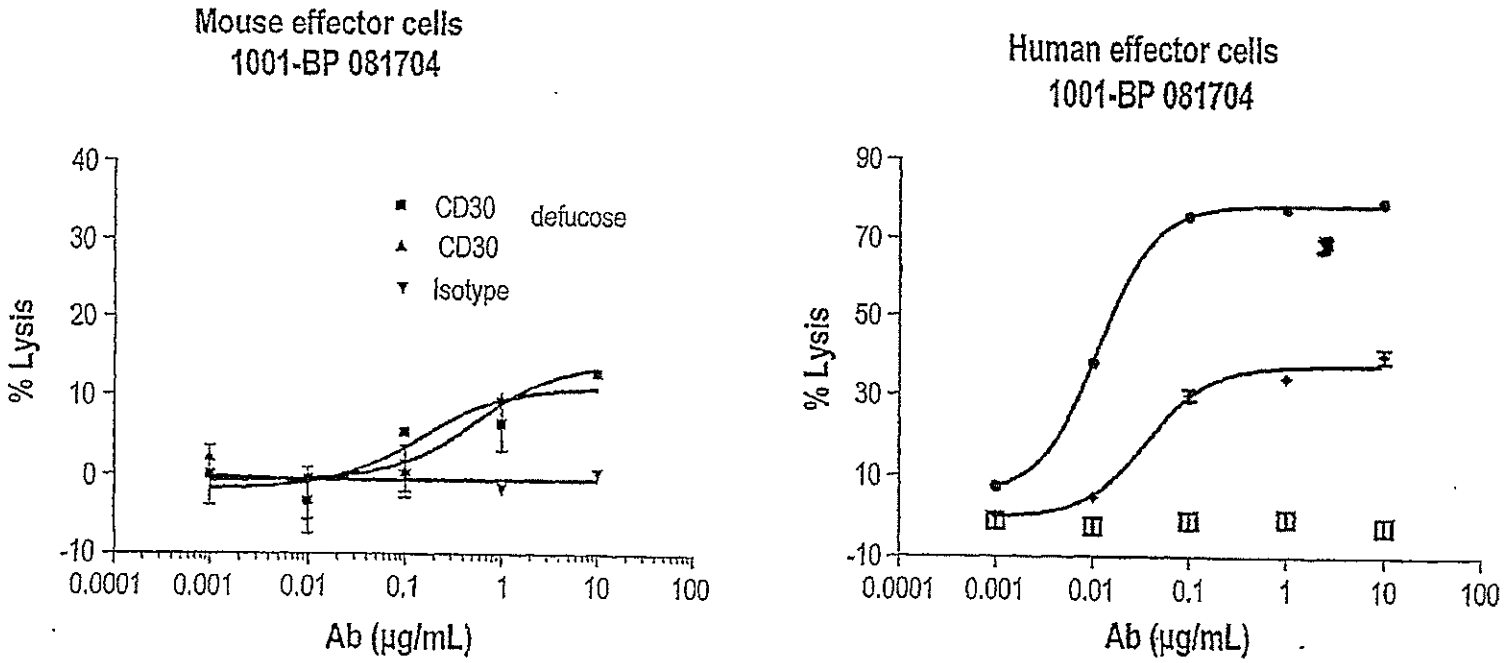

Blockade of ADCC activity with anti-CD16 antibody 3G8
Parental CD30
Parental CD30, CD16 block
Parental CD30, IgG1 block
CD30 defucose
CD30 defucose, CD16
CD30 defucose, IgG1
Triton-X
75
50
25
No Ab
-25
% Lysis
0.00001
0.0001
0.001
0.01
0.1
1
10
100
Ab (µg/mL)
EC50
0.01811
0.009528
Parental CD30
Fucose minus CD30

Fig. 9

Comparison of ADCC assay with mouse and human effector cells

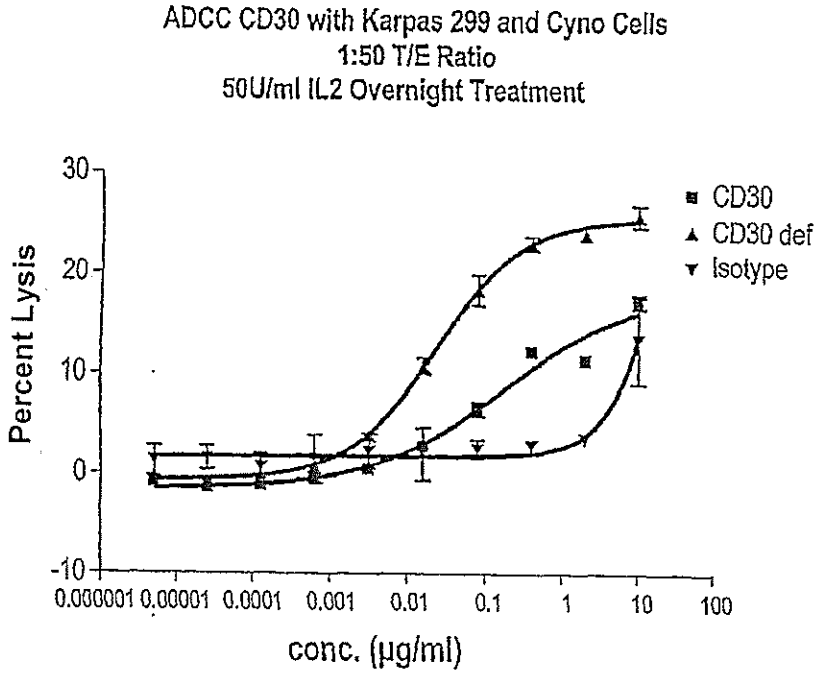


percent specific = (sample - no Ab) / (Triton-x - no Ab) x 100%

Fig. 10

ADCC assay using cynomolgus blood

Experiment #1



Experiment #2

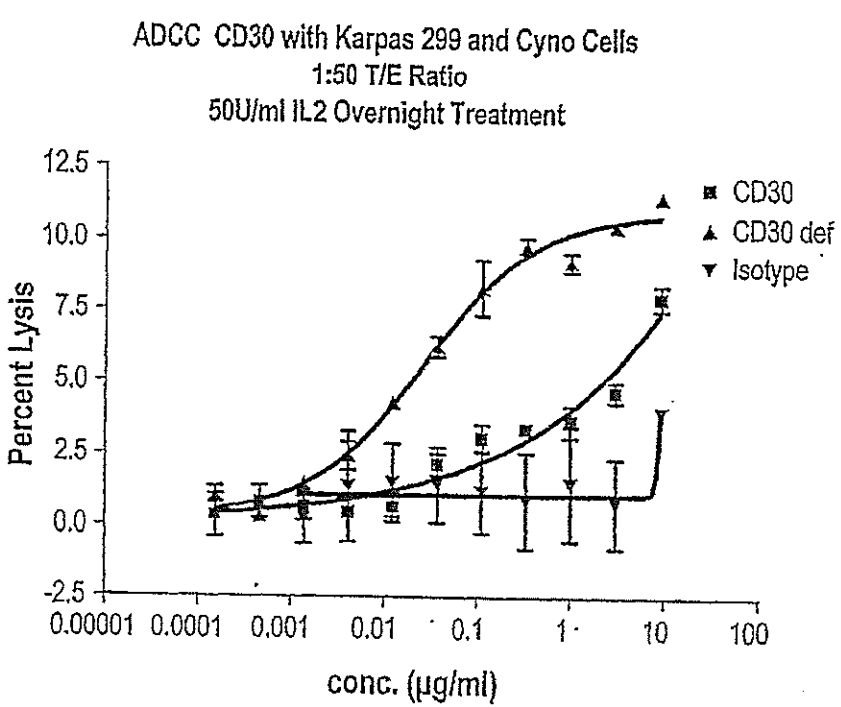


Fig. 11