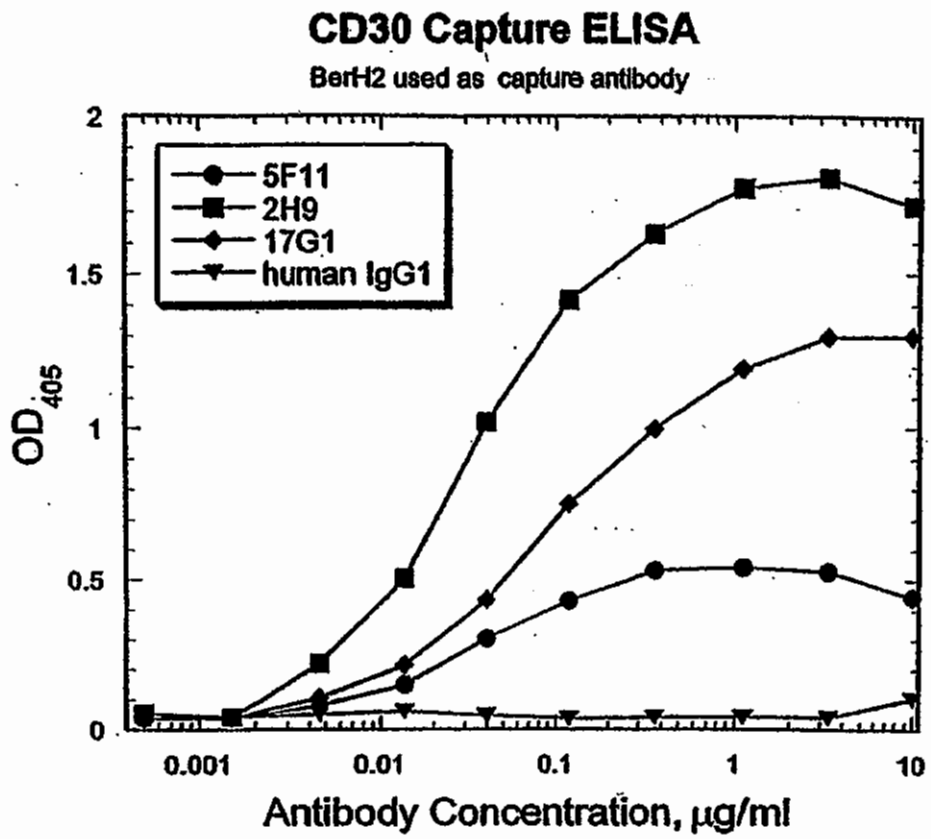

CD30 Capture ELISA
BerH2 used as capture antibody
5F11
2H9
17G1
human IgG1
OD405
2
1.5
1
0.5
0
0.001
0.01
0.1
1
10
Antibody Concentration, µg/ml

FIGURE 1

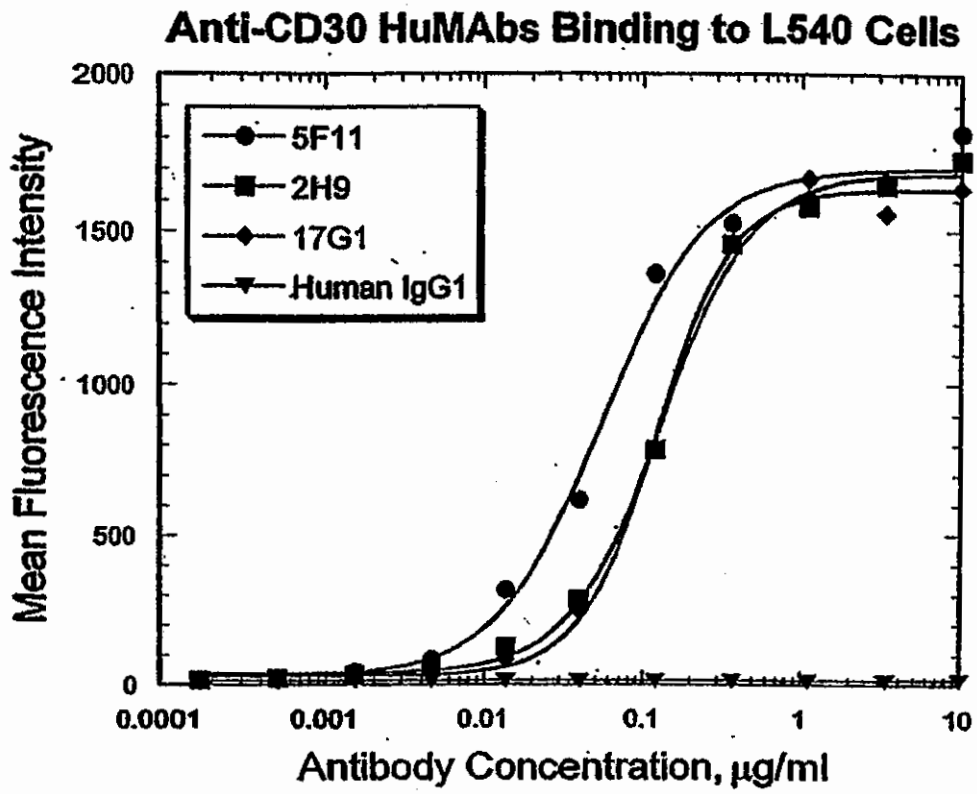

Anti-CD30 HuMAbs Binding to L540 Cells
Mean Fluorescence Intensity
2000
1500
1000
500
0
5F11
2H9
17G1
Human IgG1
0.0001
0.001
0.01
0.1
1
10
Antibody Concentration, µg/ml

FIGURE 2

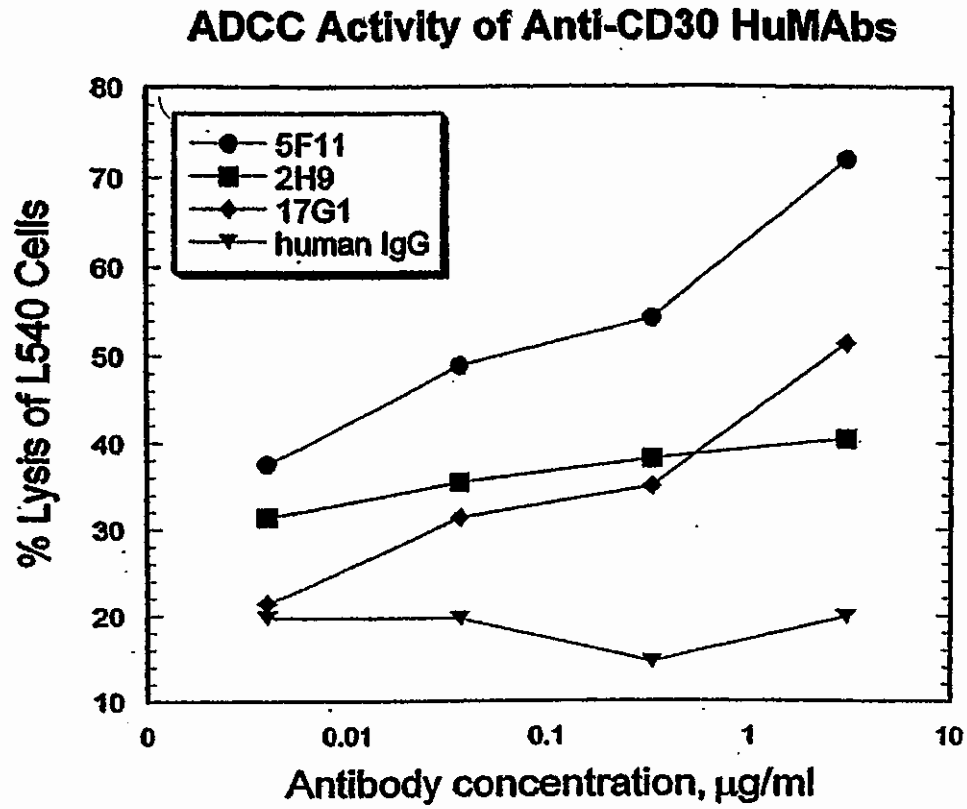

ADCC Activity of Anti-CD30 HuMAbs
% Lysis of L540 Cells
80
70
60
50
40
30
20
10
0
0.01
0.1
1
10
Antibody concentration, µg/ml
5F11
2H9
17G1
human IgG

FIGURE 3

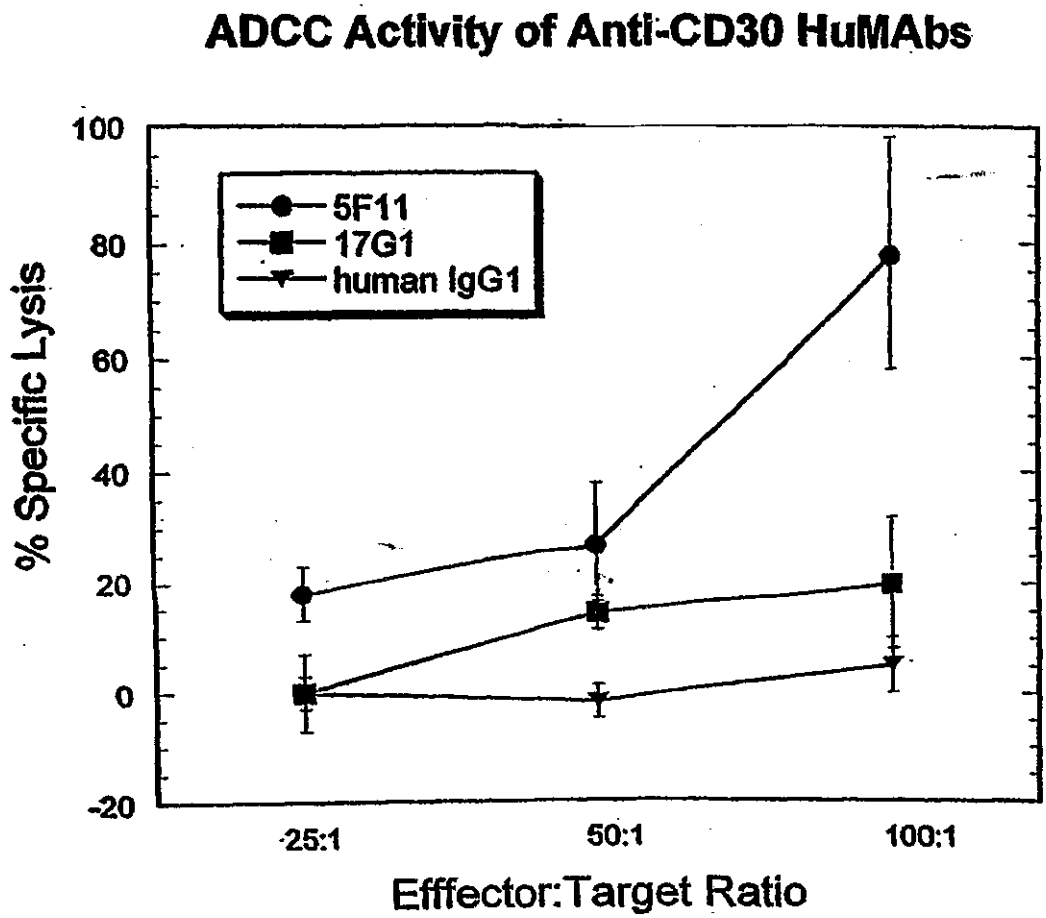
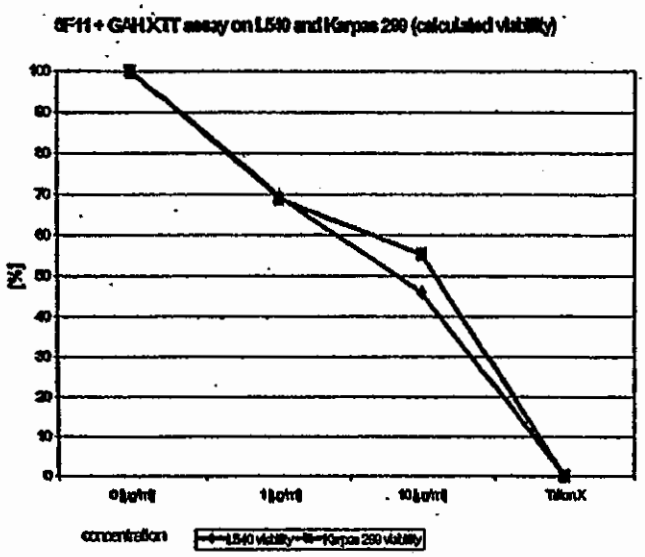

ADCC Activity of Anti-CD30 HuMAbs
% Specific Lysis
100
80
60
40
20
0
-20
5F11
17G1
human IgG1
25:1
50:1
100:1
Efffector:Target Ratio

FIGURE 4

Figure 5


6F11 + GAHXTT assay on L540 and Karpas 299 (calculated viability)
[%]
0 µg/ml
1 µg/ml
10 µg/ml
Triton X
concentration
L540 viability
Karpas 299 viability

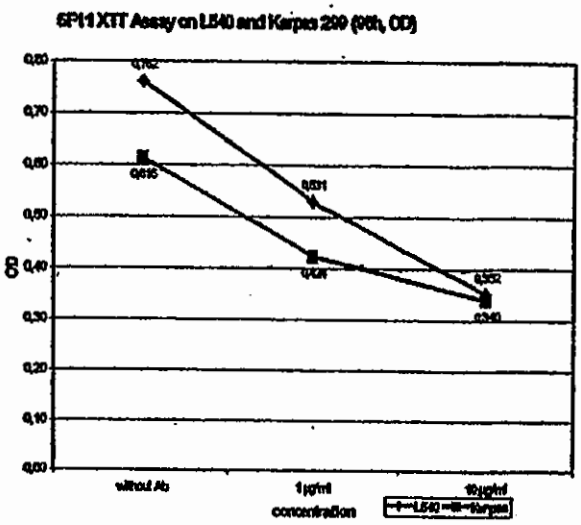

6F11 XTT Assay on L540 and Karpas 299 (96h, OD)
OD
0,762
0,615
0,631
0,426
0,352
0,340
without Ab
1 µg/ml
concentration

Figure 6: In Vivo Activity of 5F11

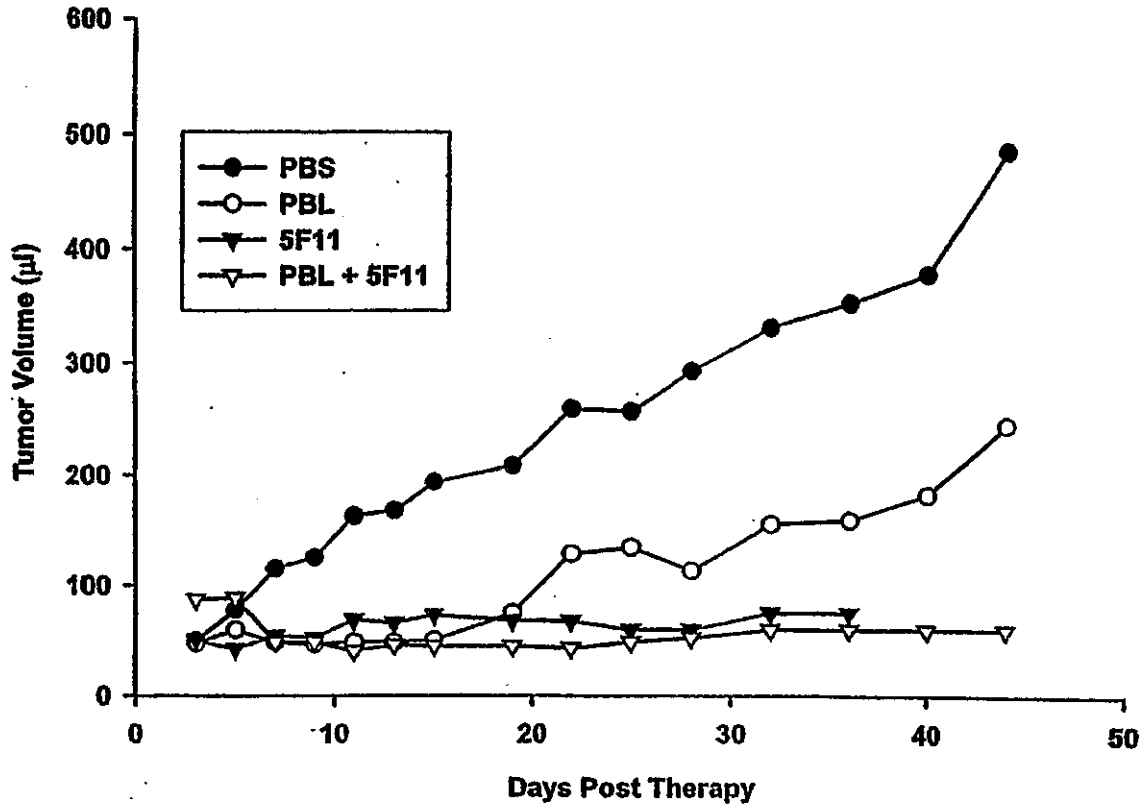


FIGURE 7

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


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

FIGURE 8

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
```

FIGURE 9

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


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

FIGURE 10

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
```

FIGURE 11

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


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

FIGURE 12

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
```

FIGURE 13

ANTI-CD30 GERMLINE SEQUENCES

VH4-34 (5F11 & 2H9 VH)

CAG GTG CAG CTA CAG CAG TGG GGC GCA GGA CTG TTG AAG CCT TCG GAG ACC
CTG TCC CTC ACC TGC GCT GTC TAT GGT GGG TCC TTC AGT GGT TAC TAC TGG
AGC TGG ATC CGC CAG CCC CCA GGG AAG GGG CTG GAG TGG ATT GGG GAA ATC
AAT CAT AGT GGA AGC ACC AAC TAC AAC CCG TCC CTC AAG AGT CGA GTC ACC
ATA TCA GTA GAC ACG TCC AAG AAC CAG TTC TCC CTG AAG CTG AGC TCT GTG
ACC GCC GCG GAC ACG GCT GTG TAT TAC TGT GCG AGA

L15 (5F11 VL)

GAC ATC CAG ATG ACC CAG TCT CCA TCC TCA CTG TCT GCA TCT GTA GGA GAC
AGA GTC ACC ATC ACT TGT CGG GCG AGT CAG GGT ATT AGC AGC TGG TTA GCC
TGG TAT CAG CAG AAA CCA GAG AAA GCC CCT AAG TCC CTG ATC TAT GCT GCA
TCC AGT TTG CAA AGT GGG GTC CCA TCA AGG TTC AGC GGC AGT GGA TCT GGG
ACA GAT TTC ACT CTC ACC ATC AGC AGC CTG CAG CCT GAA GAT TTT GCA ACT
TAT TAC TGC CAA CAG TAT AAT AGT TAC CCT

VH3-11 (17G1 VH)

GAG GTG CAG CTG GTG GAG TCT GGG GGA GGC TTG GTC CAG CCT GGG GGG TCC
CTG AGA CTC TCC TGT GCA GCC TCT GGA TTC ACC TTT AGT AGC TAT TGG ATG
AGC TGG GTC CGC CAG GCT CCA GGG AAA GGG CTG GAG TGG GTG GCC AAC ATA
AAG CAA GAT GGA AGT GAG AAA TAC TAT GTG GAC TCT GTG AAG GGC CGA TTC
ACC ATC TCC AGA GAC AAC GCC AAG AAC TCA CTG TAT CTG CAA ATG AAC AGC
CTG AGA GCC GAG GAC ACG GCT GTG TAT TAC TGT GCG AGA

A27 (17G1 VL)

GAA ATT GTG TTG ACG CAG TCT CCA GGC ACC CTG TCT TTG TCT CCA GGG GAA
AGA GCC ACC CTC TCC TGC AGG GCC AGT CAG AGT GTT AGC AGC AGC TAC TTA
GCC TGG TAC CAG CAG AAA CCT GGC CAG GCT CCC AGG CTC CTC ATC TAT GGT
GCA TCC AGC AGG GCC ACT GGC ATC CCA GAC AGG TTC AGT GGC AGT GGG TCT
GGG ACA GAC TTC ACT CTC ACC ATC AGC AGA CTG GAG CCT GAA GAT TTT GCA
GTG TAT TAC TGT CAG CAG TAT GGT AGC TCA CCT

L6 (2H9 VL)

GAA ATT GTG TTG ACA CAG TCT CCA GCC ACC CTG TCT TTG TCT CCA GGG GAA
AGA GCC ACC CTC TCC TGC AGG GCC AGT CAG AGT GTT AGC AGC TAC TTA GCC
TGG TAC CAA CAG AAA CCT GGC CAG GCT CCC AGG CTC CTC ATC TAT GAT GCA
TCC AAC AGG GCC ACT GGC ATC CCA GCC AGG TTC AGT GGC AGT GGG TCT GGG
ACA GAC TTC ACT CTC ACC ATC AGC AGC CTA GAG CCT GAA GAT TTT GCA GTT
TAT TAC TGT CAG CAG CGT AGC AAC TGG CCT

Figure 14: Epitope characterization of HuMAb 5F11

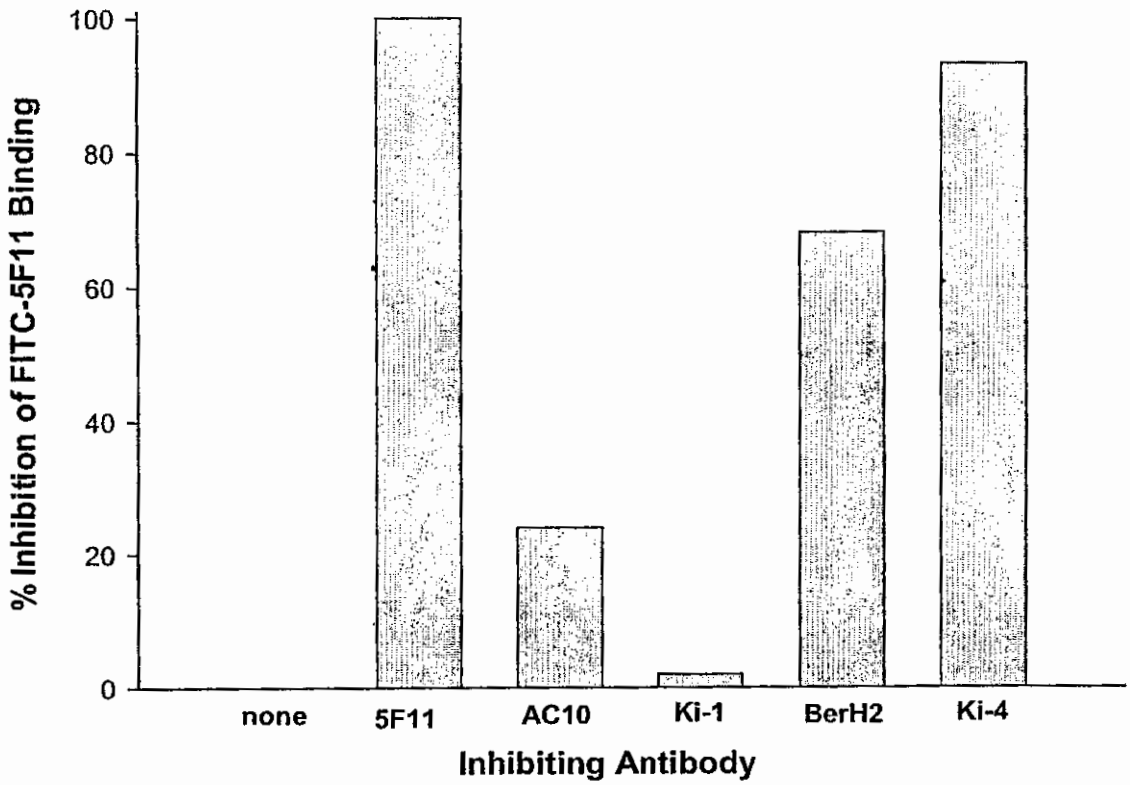


Figure 15: Effect of 5F11 treatment on disseminated L540Cy tumors in SCID mice

