CAGCTGCAGCTGCAGGAGTCGGGCCCAGGACTGGTGAAGCCTTCGGAGAC
CCTGTCCCTCACCTGCACTGTCTCTGGTGGCTCCATCAGCAGTAGTAGCT
ACTGGGGCTGGATCCGCCAGCCCCCAGGGAAGGGGCTGGAGTGGATTGGG
AGTATCTACTATAGTGGGAGAAACTACAACAACCCGTCCCTCAAGAGTCG
AGTCACCATATCCGTAGACACGTCCAAGAACCAGTTCTCCCTGAAGCTGA
GCTCTGTGACCGCCGCAGACACGGCTGTGTATTACTGTGCGAGACATTAC
TATGGTTCGGGGAGTTCCTACTACTACTACGATCTGGACGTCTGGGGCCA
AGGGACCACGGTCACCGTCTCCTCA

Figure 1A: DNA sequence of 22B5 heavy chain variable region (SEQ ID NO:11)

QLQLQESGPGLVKPSETLSLTCTVSGGSISSSSYWGWIRQPPGKGLEWIGSIYYSG
RNYNNPSLKSRVTISVDTSKNQFSLKLSSVTAADTAVYYCARHYYGSGSSYYYY
DLDVWGQGTTVTVSS

Figure 1B: Amino acid sequence of 22B5 heavy chain variable region (SEQ ID NO:7)

GAAATTGTGTTGACACAGTCTCCAGCCACCCTGTCTTTGTCTCCAGGGGA
AAGAGCCACCCTCTCCTGCAGGGCCAGTCAGAGTGTTAGCAGCTACTTAG
CCTGGTACCAACAGAAACCTGGCCAGGCTCCCAGGCTCCTCATCTATGAT
GCATCCAACAGGGCCACTGGCATCCCAGCCAGGTTCAGTGGCAGTGGGTC
TGGGACAGACTTCACTCTCACCATCAGCAGCCTAGAGCCTGAAGATTTTG
CAGTTTATTACTGTCAGCAGCGTAGCAACTGGCCTCTCACTTTCGGCGGA
GGGACCAAGGTGGAGATCAAA

Figure 1C: DNA sequence of 22B5 light chain variable region (SEQ ID NO:12)

EIVLTQSPATLSLSPGERATLSCRASQSVSSYLAWYQQKPGQAPRLLIYDASNRA
TGIPARFSGSGSGTDFTLTISSLEPEDFAVYYCQQRSNWPLTFGGGTKVEIK

Figure 1D: Amino acid sequence of 22B5 light chain variable region (SEQ ID NO:8)

CAGGTGCAGTTGGTGGAGTCTGGGGGAGGCGTGGTCCAGCCTGGGAGGTCCC
TGAGACTCTCCTGTGCAGCCTCTGGATTCACCTTCAGTAGTTATGCTATGCAC
TGGGTCCGCCAGGCTCCAGGCAAGGGGCTGGAGTGGGTGGCAGTTATATCAT
TTGATGGAAGCAATAAAAACTACGCAGACTCCGTGAAGGGCCGATTCACCAT
CTCCAGAGACAATTCCAAGAACACGCTGTATCTGCAAATGAACAGCCTGAGA
GCTGAGGACACGGCTATGTATTACTGTGCGAGAGAATACTGGGGAACCTACT
ACTACGGTATGGACGTCTGGGGCCAAGGGACCACGGTCACCGTCTCCTCA

Figure 1E: DNA sequence of 24C7 heavy chain variable region (SEQ ID NO:21)

QVQLVESGGGVVQPGRSLRLSCAASGFTFSSYAMHWVRQAPGKGLEWVAVISF
DGSNKNYADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAMYYCAREYWGTYY
YGMDVWGQGTTVTVSS

Figure 1F: Amino acid sequence of 24C7 heavy chain variable region (SEQ ID NO:19)

GAAATTGTGTTGACACAGTCTCCAGCCACCCTGTCTTTGTCTCCAGGGGAAAG
AGCCACCCTCTCCTGCAGGGCCAGTCAGAGTGTTAGCAACTACTTAGCCTGG
TACCAACAGAAACCTGGCCAGGCTCCCAGGCTCCTCATCTATGATGCATCCA
ACAGGGCCACTGGCATCCCAGCCAGGTTCAGTGGCAGTGGGTCTGGGACAGA
CTTCACTCTCACCATCAGCAGCCTAGAGCCTGAAGATTTTGCAGTTTATTACT
GTCAGCAGCGTACCAACTGGCCGTACACTTTTGGCCAGGGGACCAAGCTGGA
GATCAAA

Figure 1G: DNA sequence of 24C7 light chain variable region (SEQ ID NO:22)

EIVLTQSPATLSLSPGERATLSCRASQSVSNYLAWYQQKPGQAPRLLIYDASNRA
TGIPARFSGSGSGTDFTLTISSLEPEDFAVYYCQQRTNWPYTFGQGTKLEIK

Figure 1H: Amino acid sequence of 24C7 light chain variable region (SEQ ID NO:20)

CAGGTGCAGCTGGTGGAGTCTGGGGGAGGCGTGGTCCAGCCTGGGAGGTCCC
TGAGACTCTCCTGTGCAGCCTCTGGATTCCCCTTCAGTACCTATGCTATGCAC
TGGGTCCGCCAGGCTCCAGGCAAGGGGCTGGAGTGGGTGGCAGTTATATCAT
ATGATGGAAGCAATAAATACTACGCAGACTCCGTGAAGGGCCGATTCACCAT
CTCCAGAGACAATTCCAAGAACACGCTGTATCTGCAAATGAACAGCCTGAGA
GCTGAGGACACGGCTGTGTATTACTGTGCGAGAGAGTCCCCCCCCATCTACT
ACTACTACGGTATGGACGTCTGGGGCCAAGGGACCACGGTCACCGTCTCCTC
A

Figure 1I: DNA sequence of 1D9 heavy chain variable region (SEQ ID NO:31)

QVQLVESGGGVVQPGRSLRLSCAASGFPFSTYAMHWVRQAPGKGLEWVAVISY
DGSNKYYADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCARESPPIYYYY
GMDVWGQGTTVTVSS

Figure 1J: Amino acid sequence of 1D9 heavy chain variable region (SEQ ID NO:29)

GAAATTGTGTTGACACAGTCTCCAGCCACCCTGTCTTTGTCTCCAGGGGAAAG
AGCCACCCTCTCCTGCAGGGCCAGTCAGAGTGTTAGCAGCTACTTAGCCTGG
TACCAACAGAAACCTGGCCAGGCTCCCAGGCTCCTCATCTATGATGCATCCA
ACAGGGCCACTGGCATCCCAGCCAGGTTCAGTGGCAGTGGGTCTGGGACAGA
CTTCACTCTCACCATCAGCAGCCTAGAGCCTGAAGATTTTGCAGTTTATTACT
GTCAGCAGCGTAGCAACTGGCCTCGGACGTTCGGCCAAGGGACCAAGGTGG
AAATCAAA

Figure 1K: DNA sequence of 1D9 light chain variable region (SEQ ID NO:32)

EIVLTQSPATLSLSPGERATLSCRASQSVSSYLAWYQQKPGQAPRLLIYDASNRA
TGIPARFSGSGSGTDFTLTISSLEPEDFAVYYCQQRSNWPRTFGQGTKVEIK

Figure 1L: Amino acid sequence of 1D9 light chain variable region (SEQ ID NO:30)

CAGGTGCAACTGGTGGAGTCTGGGGGAGGCGTGGTCCAGCCTGGGAGGTCCC
TGAGACTCTCCTGTGCAGCCTCTGGATTCACCTTCAGTAGCTATGCTATGCAC
TGGGTCCGCCAGGCTCCAGGCAAGGGGCTGGAGTGGGTGGCAGTTATATCAT
TTGATGGAAGCACTAAATACTACGCAGACTCCGTGAAGGGCCGATTCACCAT
CTCCAGAGACAATTCCAAGAACACGCTGGATCTGCAAATGAACAGCCTGAGA
GCTGAGGACACGGCTCTGTATTACTGTGCGAGAGAATACTGGGGAACCTACT
ACTACGGGACGGACGTCTGGGGCCAAGGGACCACGGTCATCGTCTCCTCA

Figure 1M: DNA sequence of 2D2 heavy chain variable region (SEQ ID NO:41)

QVQLVESGGGVVQPGRSLRLSCAASGFTFSSYAMHWVRQAPGKGLEWVAVISF
DGSTKYYADSVKGRFTISRDNSKNTLDLQMNSLRAEDTALYYCAREYWGTYYY
GTDVWGQGTTVIVSS

Figure 1N: Amino acid sequence of 2D2 heavy chain variable region (SEQ ID NO:39)

GAAATTGTGTTGACACAGTCTCCAGCCACCCTGTCTTTGTCTCCAGGGGAAAG
AGCCACCCTCTCCTGCAGGGCCAGTCAGAGTGTTAACAGCTACTTAGCCTGG
TACCAACAGAAACCTGGCCAGGCTCCCAGGCTCCTCATCTATGATGCATCCA
ACAGGGCCACTGGCATCCCAGCCAGGTTCAGTGGCAGTGGGTCTGGGACAGA
CTTCACTCTCACCATCAGCAGCCTAGAGCCTGAAGATTTTGCAGTTTATTACT
GTCAGCAGCGTAGCAACTGGCCTCGGACGTTCGGCCAAGGGACCAAGGTGG
AAATCAAA

Figure 1O: DNA sequence of 2D2 light chain variable region (SEQ ID NO:42)

EIVLTQSPATLSLSPGERATLSCRASQSVNSYLAWYQQKPGQAPRLLIYDASNRA
TGIPARFSGSGSGTDFTLTISSLEPEDFAVYYCQQRSNWPRTFGQGTKVEIK

Figure 1P: Amino acid sequence of 2D2 light chain variable region (SEQ ID NO:40)

ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPA
VLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTHTCP
PCPAPELLGGP**D**VFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDG
VEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALP**L**P**E**EK
TISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPEN
NYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSL
SPGK

Figure 1Q: Amino acid sequence of IgG1 heavy chain constant region with S247D, A338L, and I340E mutations in bold and underlined (SEQ ID NO:43)

RTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNSQE
SVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

Figure 1R: Amino acid sequence of IgG1 light chain constant region (SEQ ID NO:44)

V_H

```
      Germline     QLQLQESGP GLVKPSETLSLTCTVSGGSISSSSYYWG WIRQPPGKGLEWI
22b5 I30S N33S     --------- ------------------------.---------------

      Germline     GSIYYSG STYYNPSLKSRVTISVDTSKNQFSLKLSSVTAADTAVYYCAR
22b5 I30S N33S     -------RN -N-------------------------------------

      Germline     QYYYGSG SYYNYYYYYGMDVWGQGTTVTVSS
22b5 I30S N33S     H.------ ...S----DL------------
```

V_κ

```
      Germline     EIVLTQSPA TLSLSPGERATLSCRASQSVSSYLAWYQQKPGQAPRLLIYD
22b5 I30S N33S     --------- ----------------------------------------

      Germline     ASNRATGIP ARFSGSGSGTDFTLTISSLEPEDFAVYYCQQRSNWPLTFGG
22b5 I30S N33S     --------- ----------------------------------------

      Germline     GTKVEIK
22b5 I30S N33S     -------
```

Figure 2

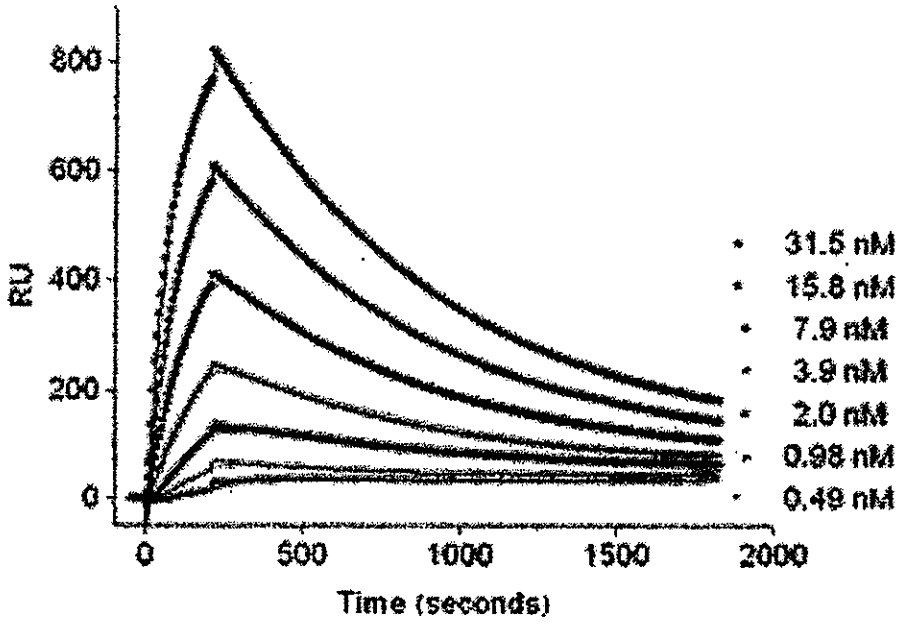

800
600
400
200
0
RU
0
500
1000
1500
2000
Time (seconds)
31.5 nM
15.8 nM
7.9 nM
3.9 nM
2.0 nM
0.98 nM
0.49 nM

Figure 3

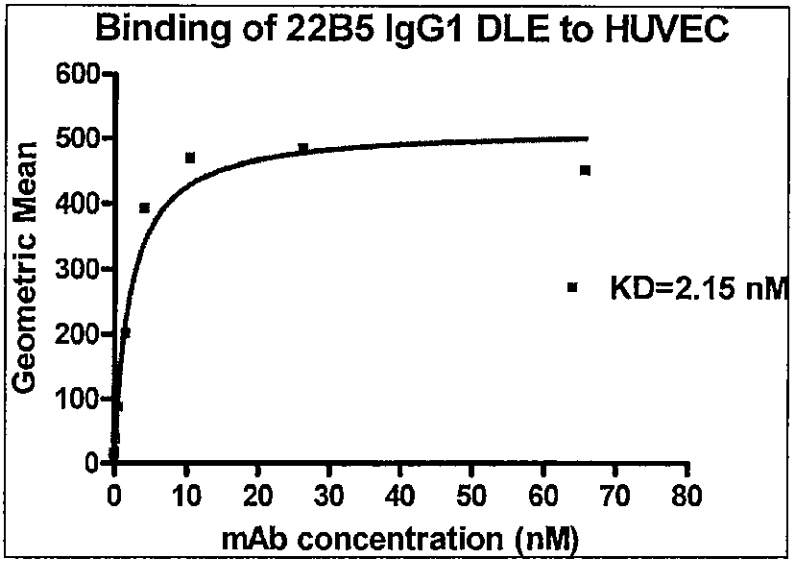

Binding of 22B5 IgG1 DLE to HUVEC
Geometric Mean
600
500
400
300
200
100
0
0
10
20
30
40
50
60
70
80
mAb concentration (nM)
KD=2.15 nM

Figure 4

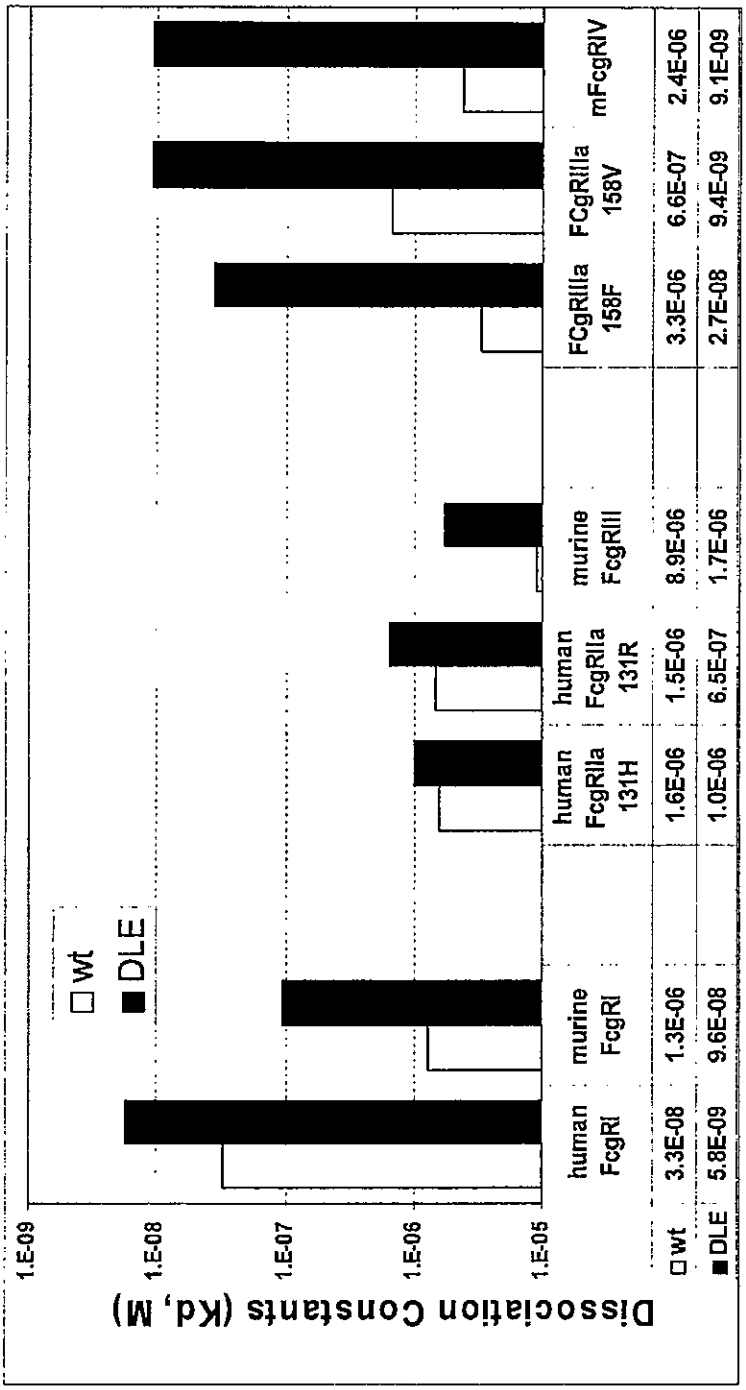
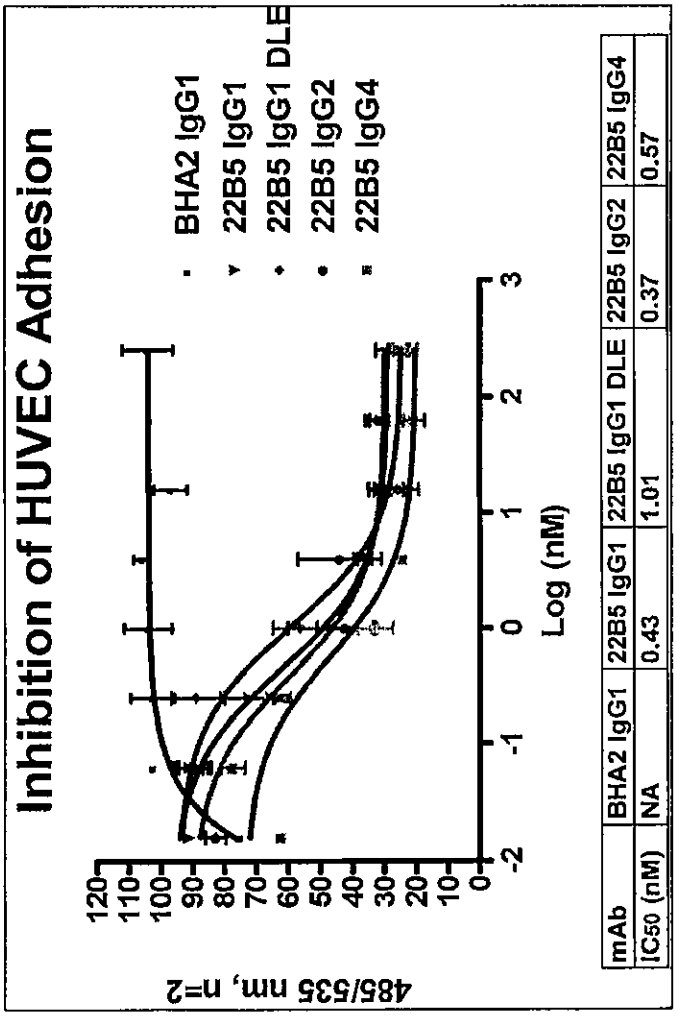

Dissociation Constants (Kd, M)
1.E-09
1.E-08
1.E-07
1.E-06
1.E-05
wt
DLE
human FcgRI
murine FcgRI
human FcgRIIa 131H
human FcgRIIa 131R
murine FcgRIII
FCgRIIIa 158F
FCgRIIIa 158V
mFcgRIV
wt 3.3E-08 1.3E-06 1.6E-06 1.5E-06 8.9E-06 3.3E-06 6.6E-07 2.4E-06
DLE 5.8E-09 9.6E-08 1.0E-06 6.5E-07 1.7E-06 2.7E-08 9.4E-09 9.1E-09

Figure 5



mAb	BHA2 IgG1	22B5 IgG1	22B5 IgG1 DLE	22B5 IgG2	22B5 IgG4
IC_{50} (nM)	NA	0.43	1.01	0.37	0.57

Figure 6

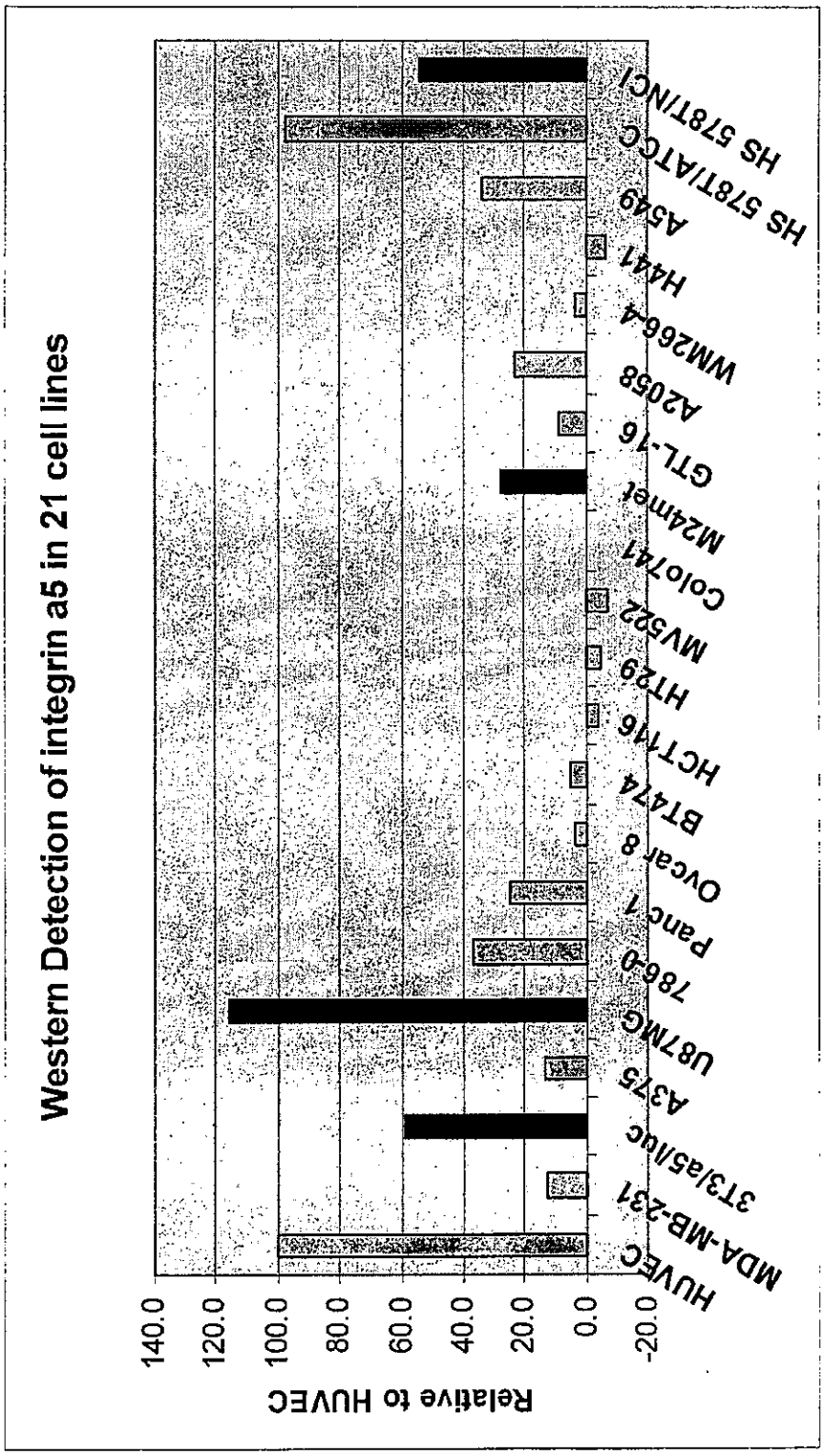
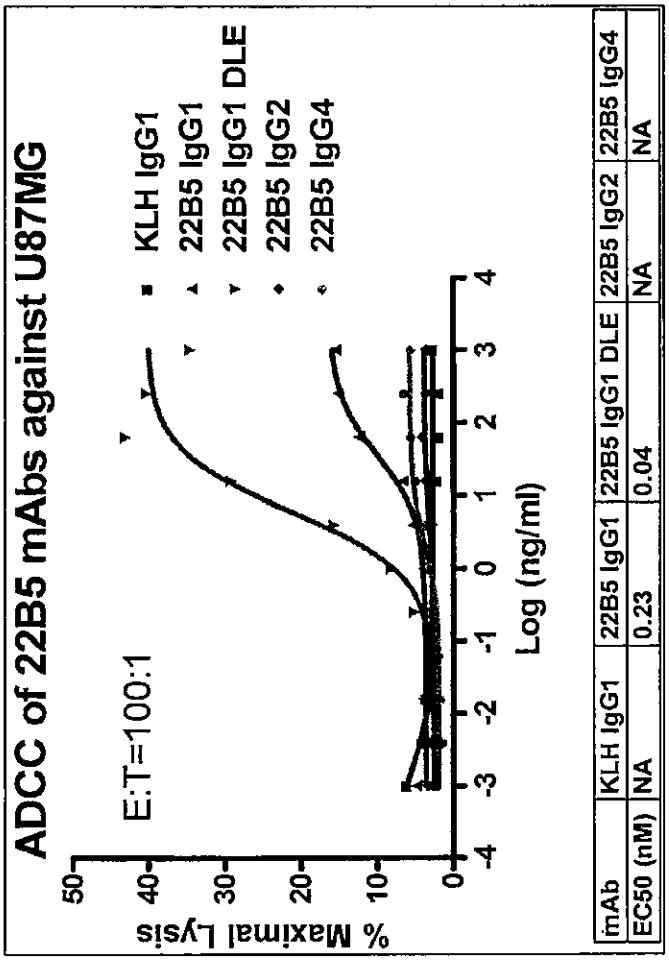

Western Detection of integrin a5 in 21 cell lines
Relative to HUVEC
140.0
120.0
100.0
80.0
60.0
40.0
20.0
0.0
-20.0
HUVEC
MDA-MB-231
3T3/a5/luc
A375
U87MG
786-0
Panc 1
Ovcar 8
BT474
HCT116
HT29
MV522
Colo741
M24met
GTL-16
A2058
WM266-4
H441
A549
HS 578T/ATCC
HS 578T/NCI

Figure 7



mAb	KLH IgG1	22B5 IgG1	22B5 IgG1 DLE	22B5 IgG2	22B5 IgG4
EC50 (nM)	NA	0.23	0.04	NA	NA

Figure 8A

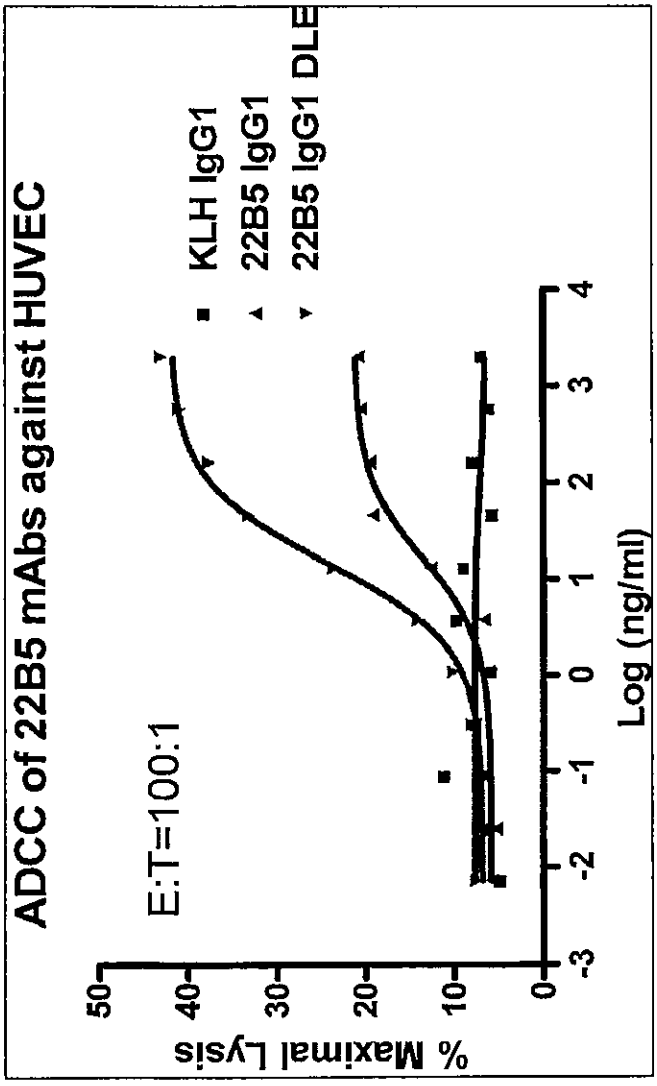

ADCC of 22B5 mAbs against HUVEC
E:T=100:1
KLH IgG1
22B5 IgG1
22B5 IgG1 DLE
% Maximal Lysis
0
10
20
30
40
50
-3
-2
-1
0
1
2
3
4
Log (ng/ml)

Figure 8B

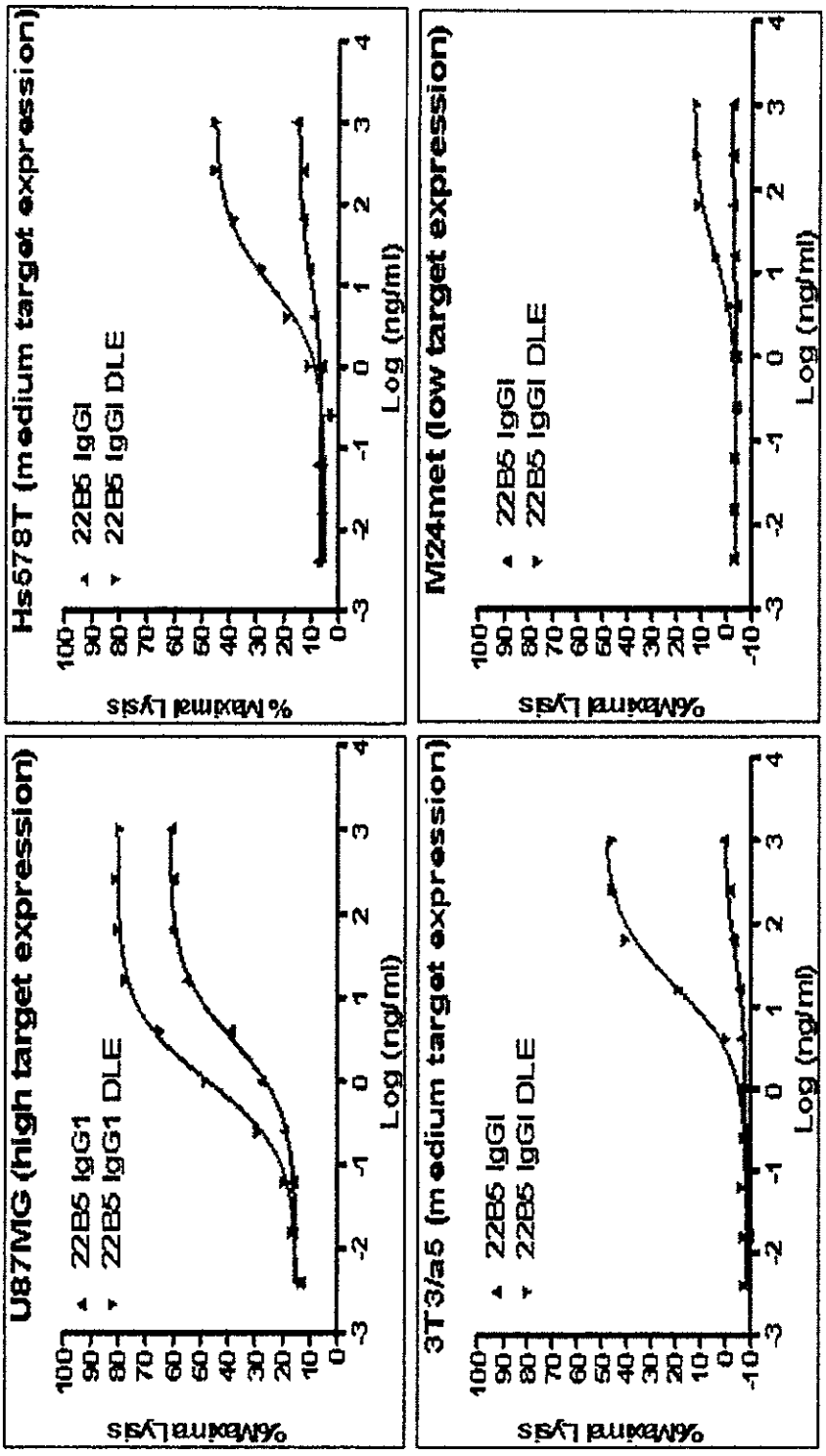

U87MG (high target expression)
22B5 IgG1
22B5 IgG1 DLE
%Maximal Lysis
Log (ng/ml)
Hs578T (medium target expression)
22B5 IgGl
22B5 IgGl DLE
% Maximal Lysis
Log (ng/ml)
3T3/a5 (medium target expression)
22B5 IgGl
22B5 IgGl DLE
%Maximal Lysis
Log (ng/ml)
M24met (low target expression)
22B5 IgGl
22B5 IgGl DLE
%Maximal Lysis
Log (ng/ml)

Figure 9

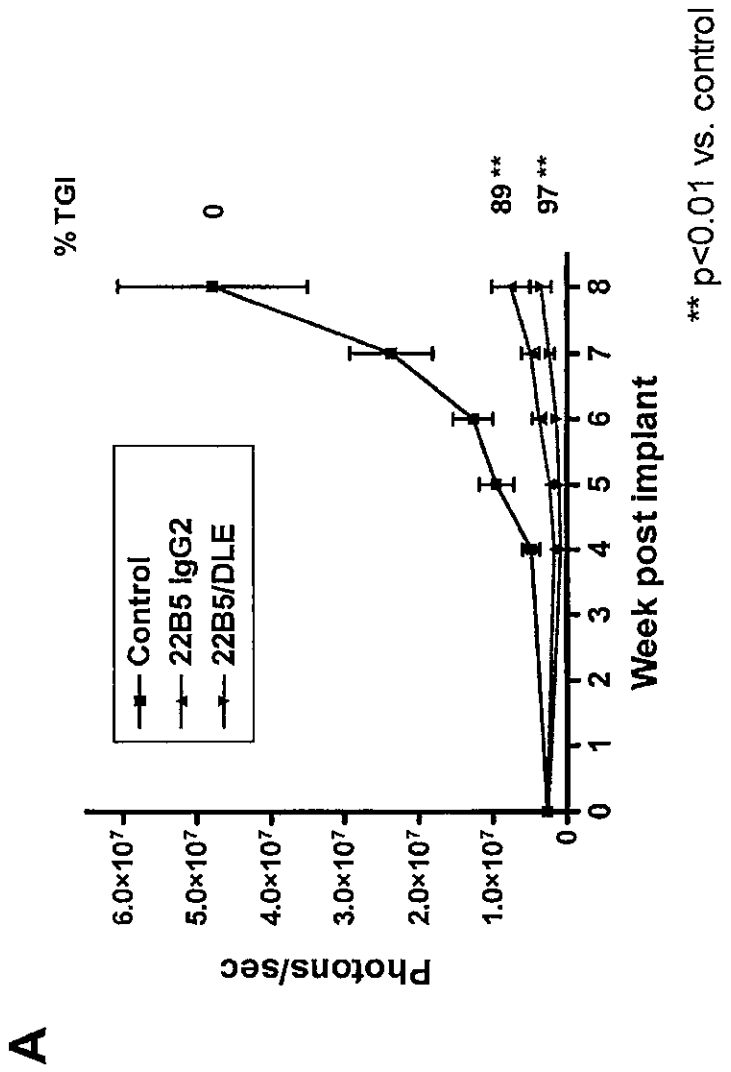

A
Photons/sec
6.0×10^7
5.0×10^7
4.0×10^7
3.0×10^7
2.0×10^7
1.0×10^7
0
0 1 2 3 4 5 6 7 8
Week post implant
Control
22B5 IgG2
22B5/DLE
% TGI
0
89 **
97 **
** p<0.01 vs. control

Figure 10A

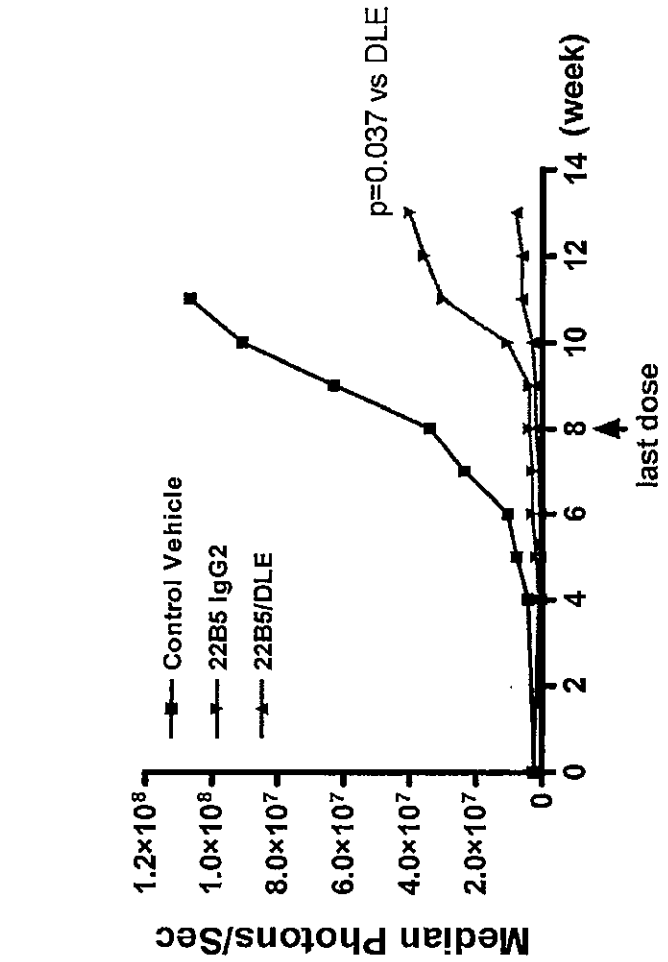
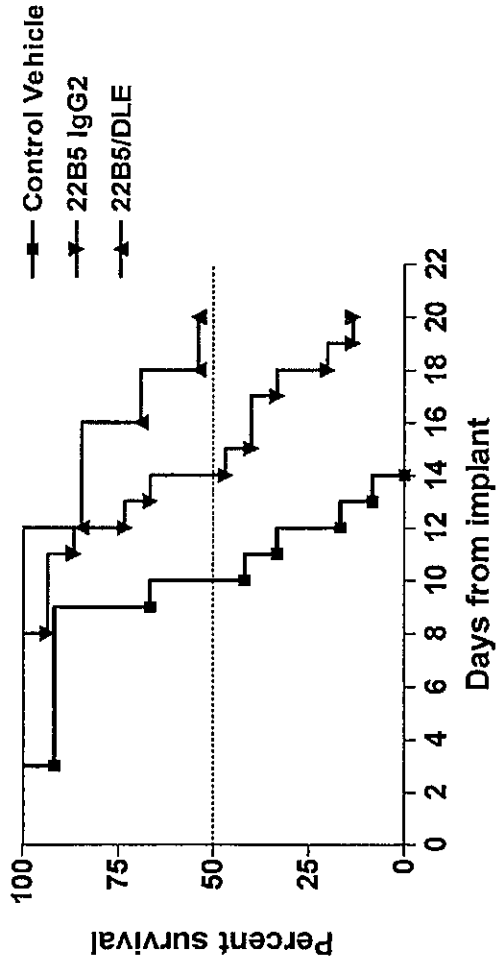
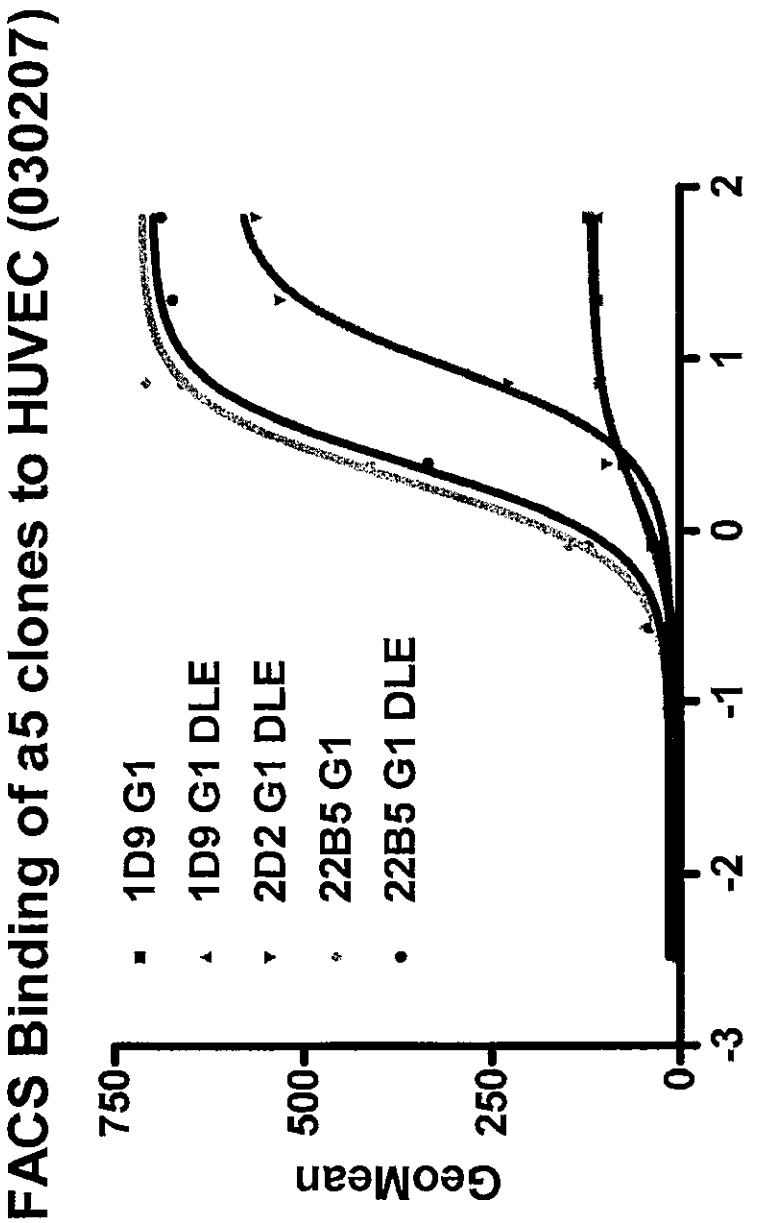

B
Median Photons/Sec
1.2×10^8
1.0×10^8
8.0×10^7
6.0×10^7
4.0×10^7
2.0×10^7
0
Control Vehicle
22B5 IgG2
22B5/DLE
p=0.037 vs DLE
last dose
0
2
4
6
8
10
12
14 (week)

Figure 10B


Control Vehicle
22B5 IgG2
22B5/DLE
Percent survival
100
75
50
25
0
0 2 4 6 8 10 12 14 16 18 20 22
Days from implant

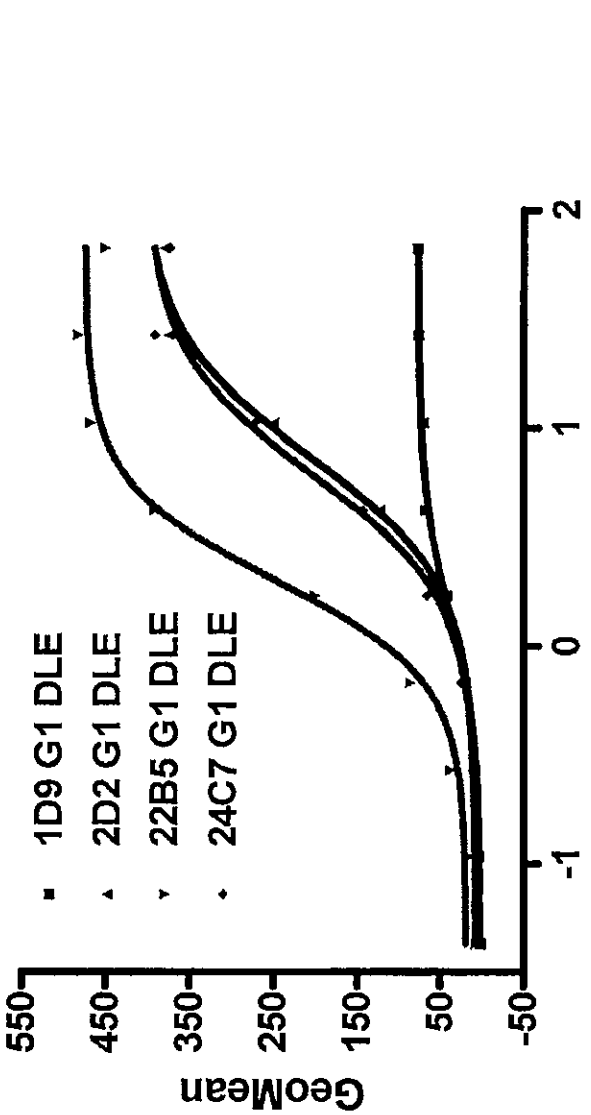
C

Figure 10C



mAb	1D9 G1	1D9 G1 DLE	2D2 G1 DLE	22B5 G1	22B5 G1 DLE
Kd (nM)	1.69	1.68	8.78	1.95	2.42
R^2	1.00	1.00	0.99	0.99	1.00

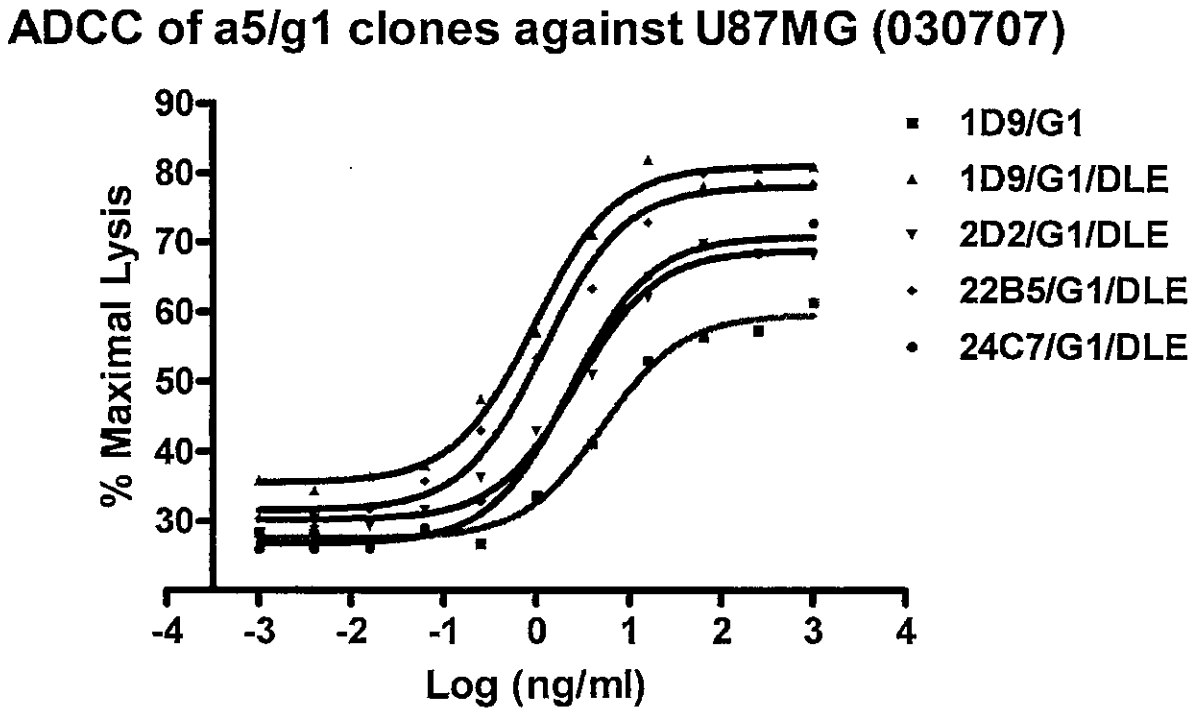
Figure 11A



mAb	1D9 G1 DLE	2D2 G1 DLE	22B5 G1 DLE	24C7 G1 DLE
Kd (nM)	1.49	7.32	1.99	6.08
R^2	1.00	1.00	1.00	0.99

Note: 24C7 unpurified

Figure 11B



mAb	1D9/G1	1D9/G1/DLE	2D2/G1/DLE	22B5/G1/DLE	24C7/G1/DLE
EC50 (ng/ml)	5.06	0.96	2.66	1.21	2.28
R^2	0.99	0.99	0.99	0.99	1.00

note: 24C7 unpurified

Figure 12

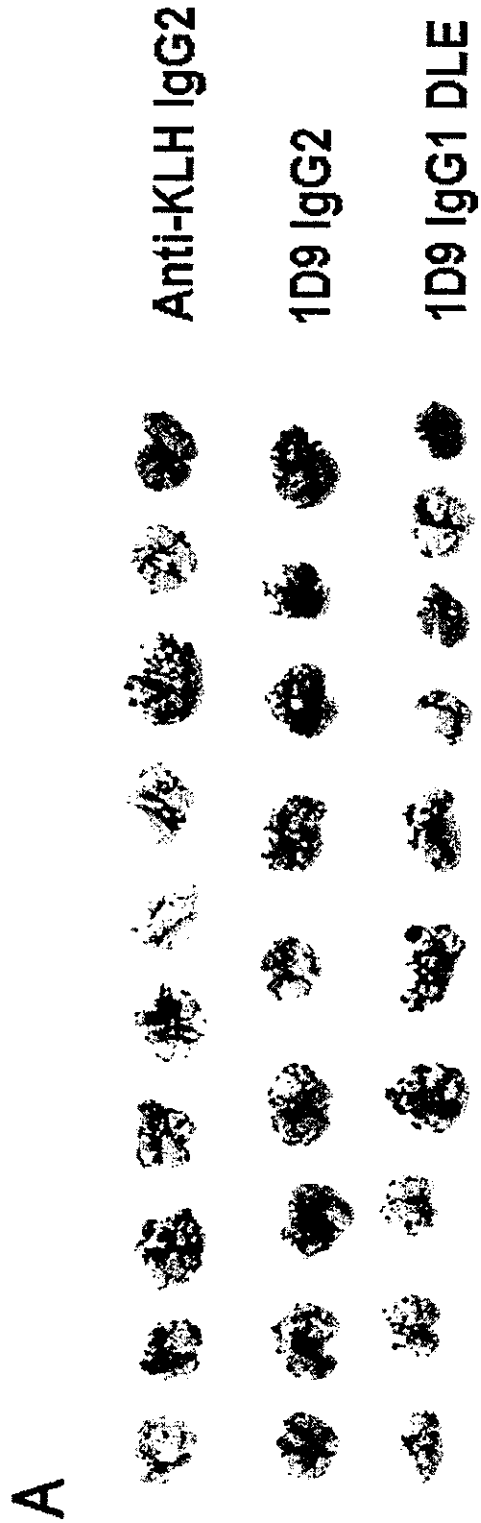


Figure 13 A

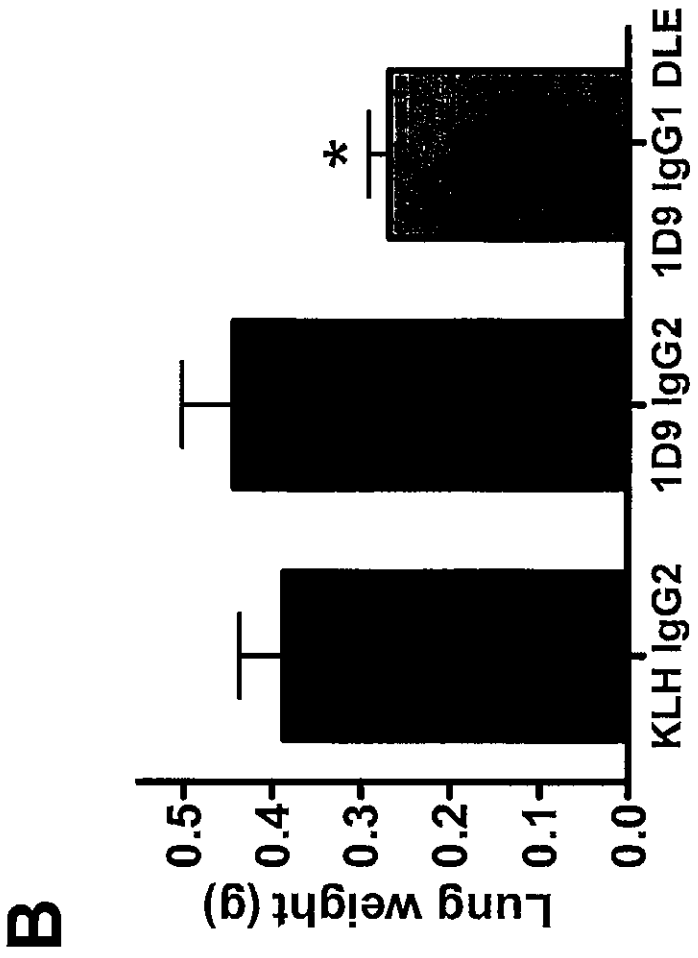


Figure 13 B

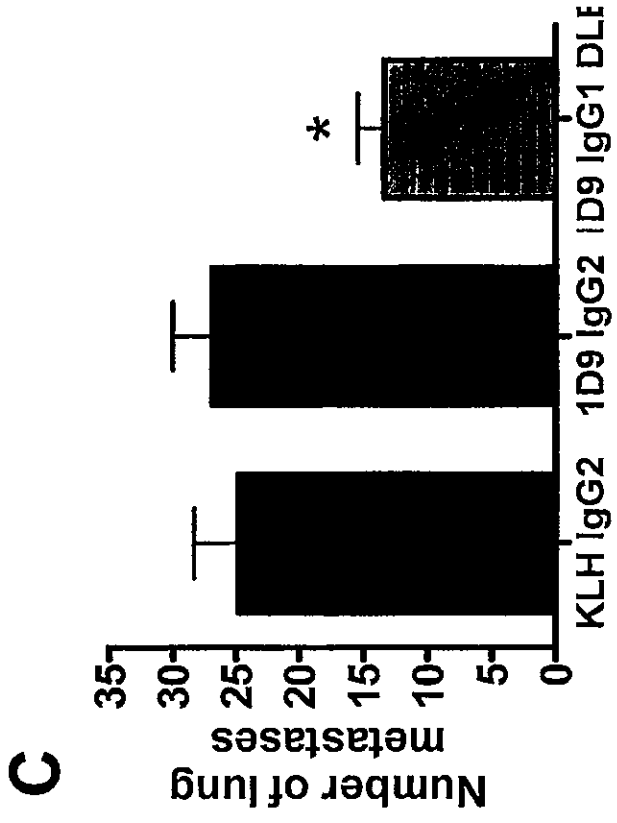

C
Number of lung metastases
35
30
25
20
15
10
5
0
*
KLH IgG2
1D9 IgG2
1D9 IgG1 DLE

Figure 13 C