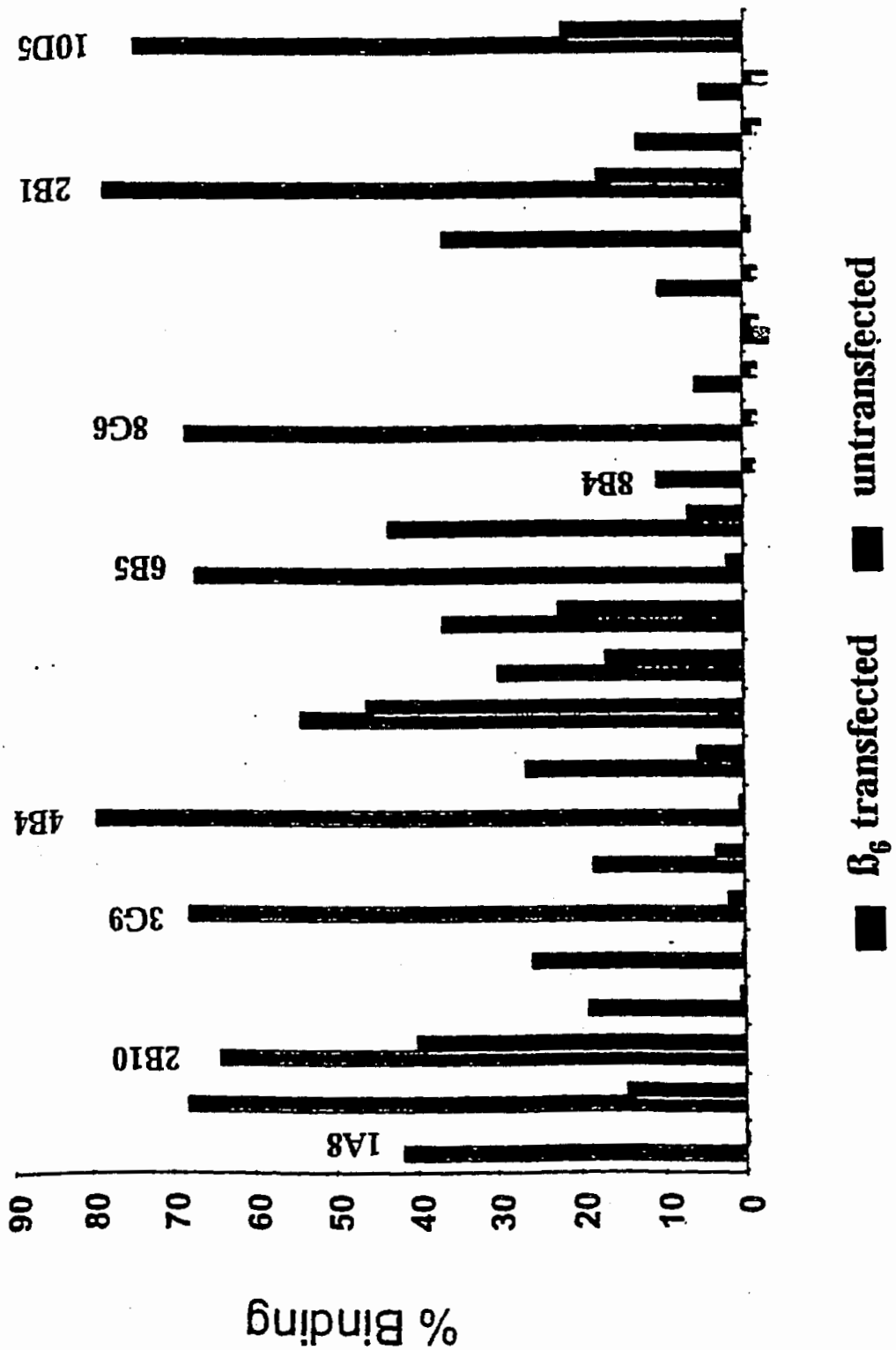

% Binding
0
10
20
30
40
50
60
70
80
90
1A8
2B10
3G9
4B4
6B5
8B4
8G6
2B1
10D5
β6 transfected
untransfected

FIG. 1A

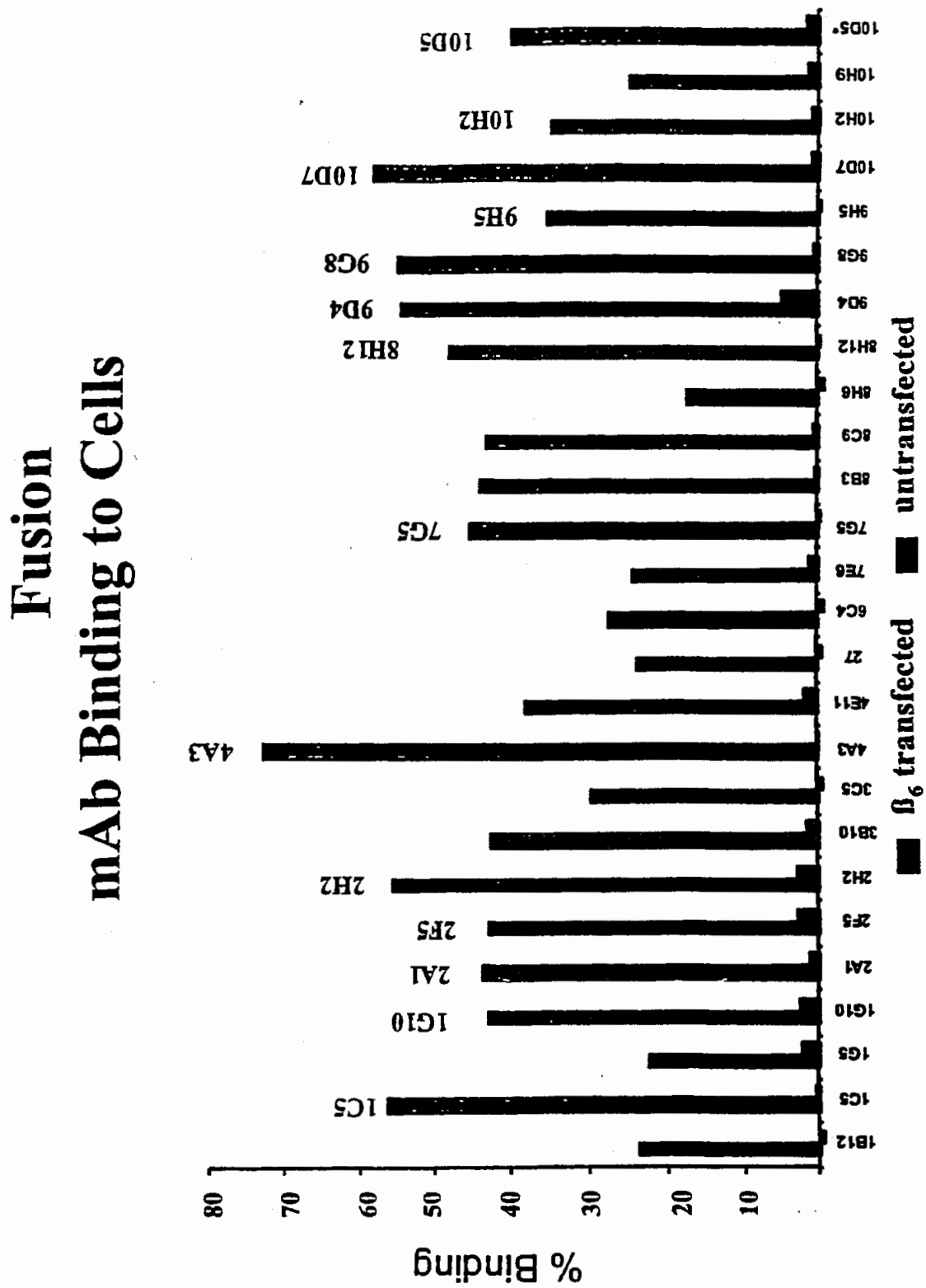

Fusion
mAb Binding to Cells
% Binding
80
70
60
50
40
30
20
10
1B12
1C5
1G5
1G10
2A1
2F5
2H2
3B10
3C5
4A3
4E11
7
6C4
7E6
7G5
8B3
8C9
8H6
8H12
9D4
9G8
9H5
10D7
10H2
10H9
10D5*
β6 transfected
untransfected

FIG. 1B

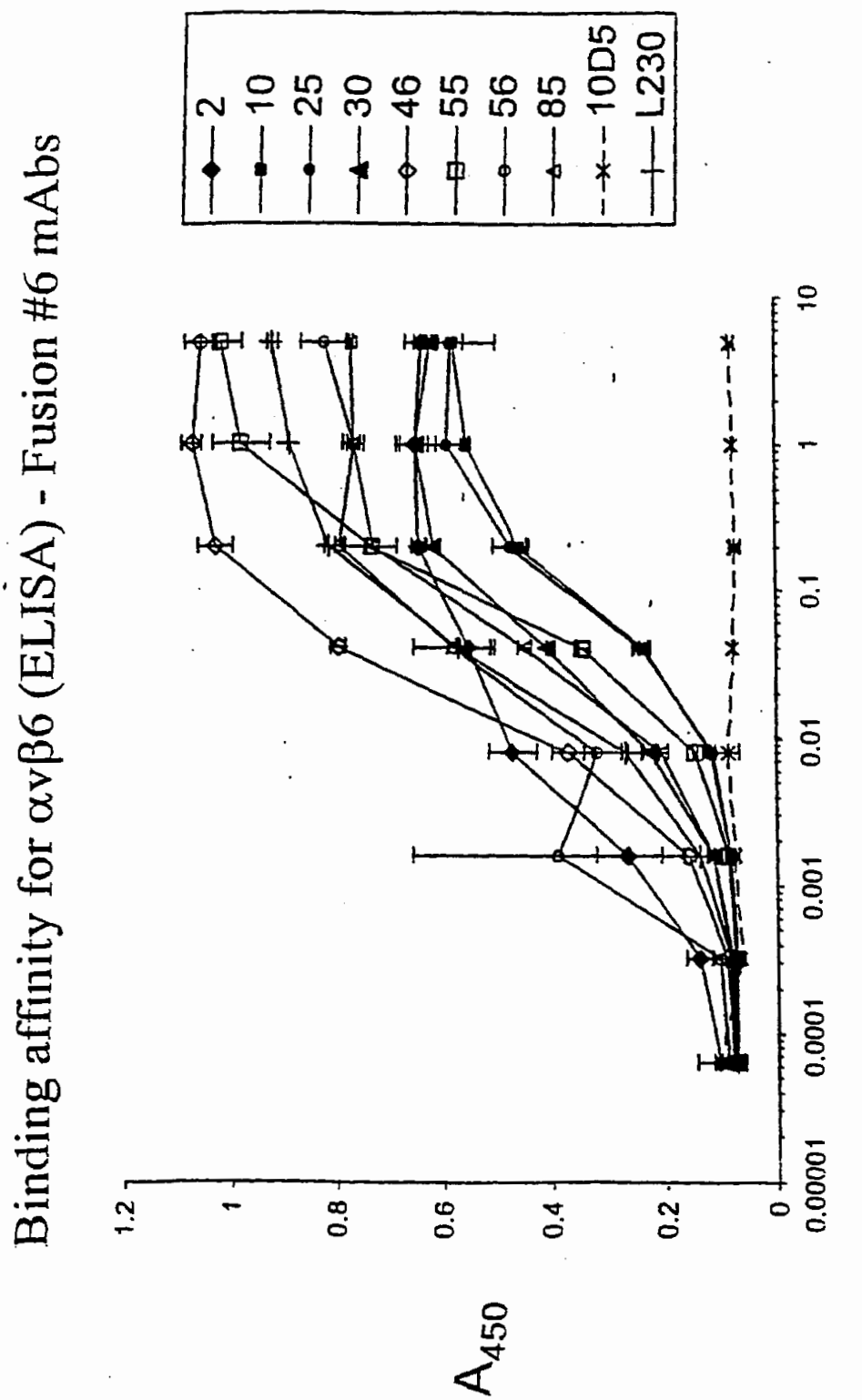

Binding affinity for αvβ6 (ELISA) - Fusion #6 mAbs
2
10
25
30
46
55
56
85
10D5
L230
A450
1.2
1
0.8
0.6
0.4
0.2
0
0.00001
0.0001
0.001
0.01
0.1
1
10
concentration (μg/mL)

FIG. 2A

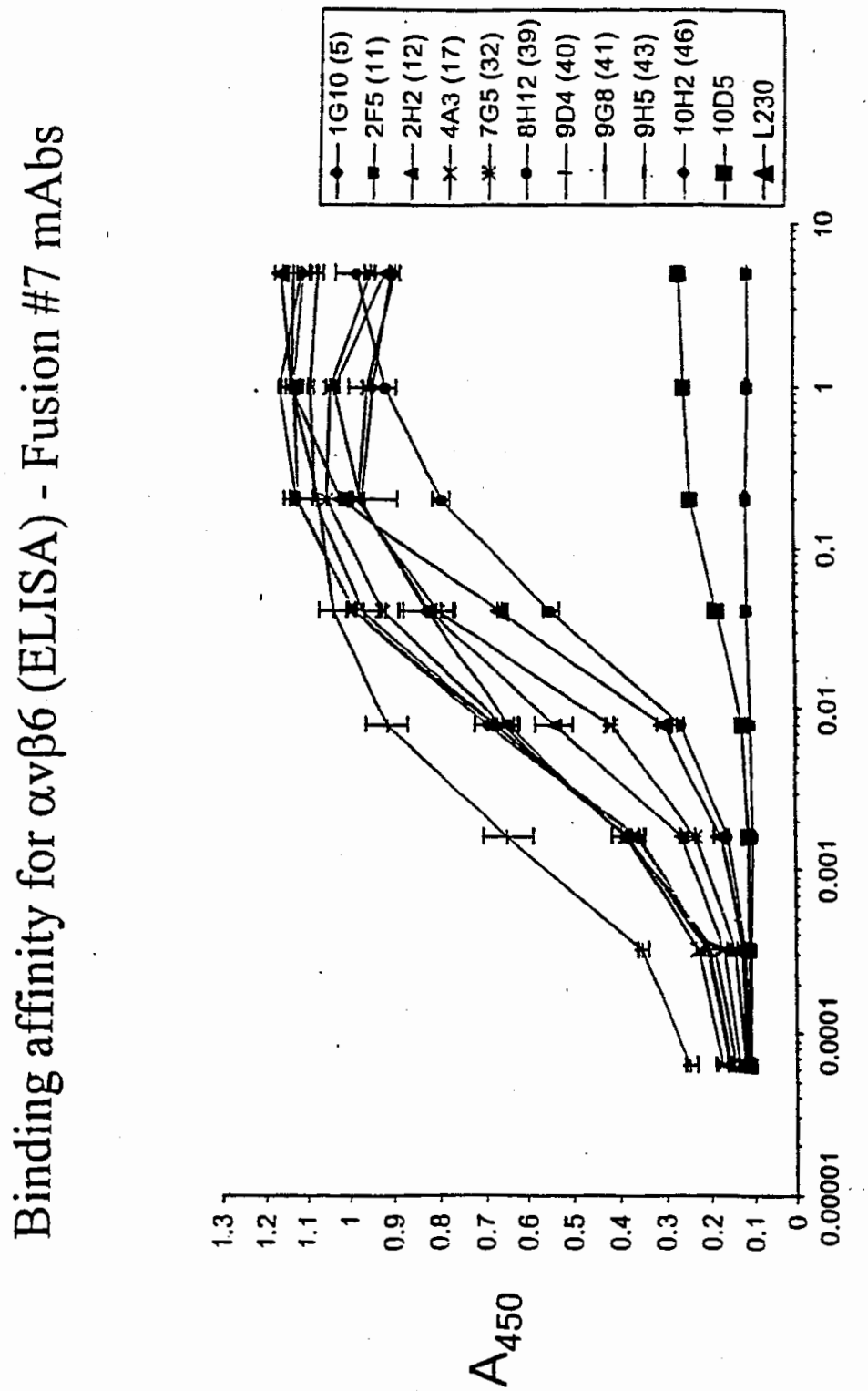

Binding affinity for αvβ6 (ELISA) - Fusion #7 mAbs
A450
concentration (μg/mL)
1G10 (5)
2F5 (11)
2H2 (12)
4A3 (17)
7G5 (32)
8H12 (39)
9D4 (40)
9G8 (41)
9H5 (43)
10H2 (46)
10D5
L230

FIG. 2B

FIGS. 3 A-F

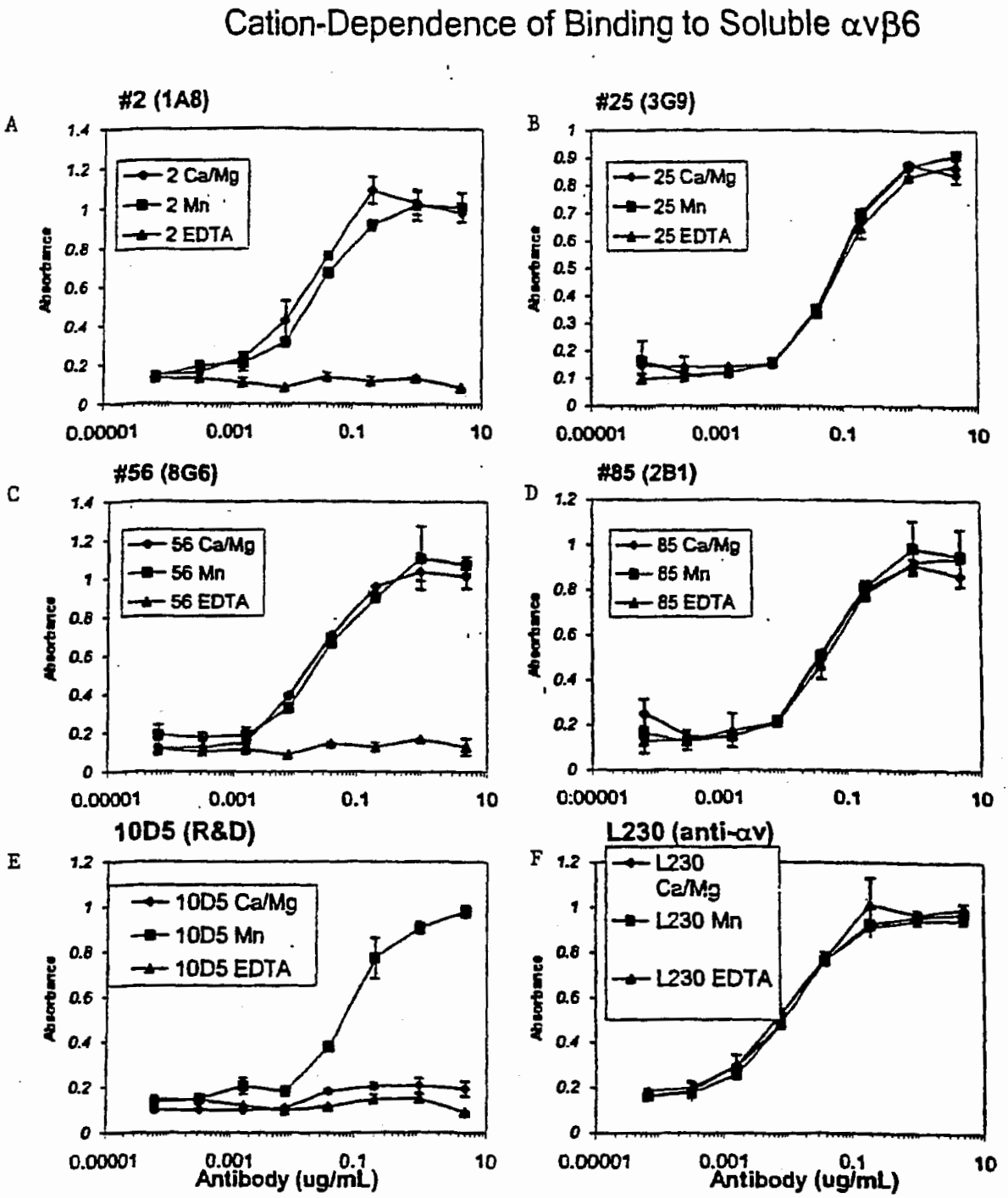
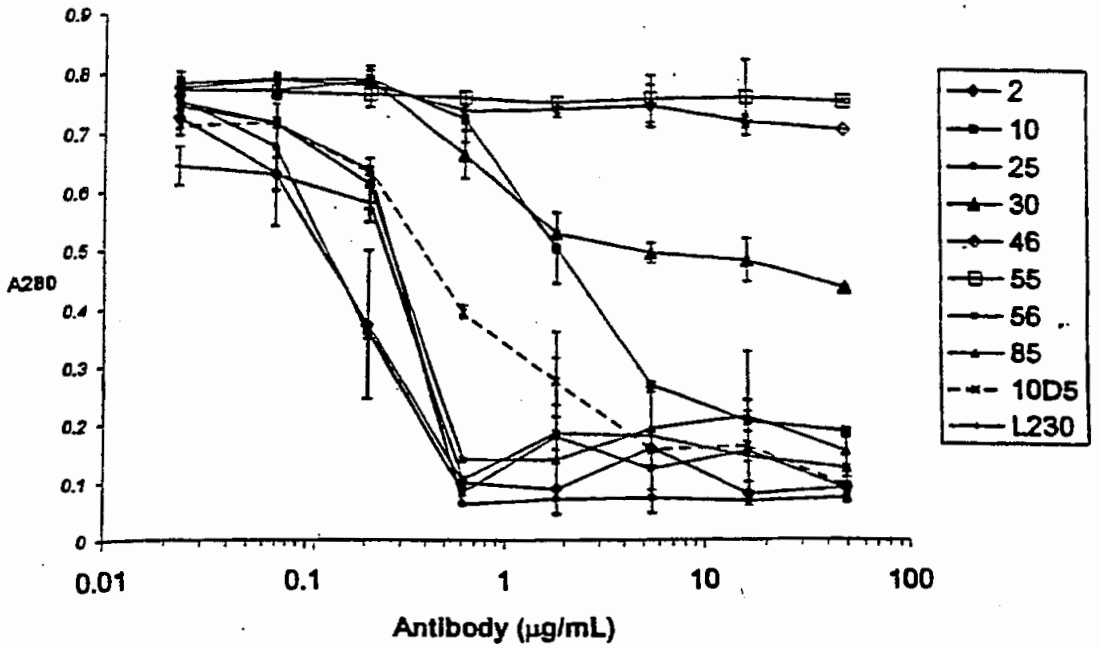

Cation-Dependence of Binding to Soluble αvβ6
A
#2 (1A8)
2 Ca/Mg
2 Mn
2 EDTA
B
#25 (3G9)
25 Ca/Mg
25 Mn
25 EDTA
C
#56 (8G6)
56 Ca/Mg
56 Mn
56 EDTA
D
#85 (2B1)
85 Ca/Mg
85 Mn
85 EDTA
E
10D5 (R&D)
10D5 Ca/Mg
10D5 Mn
10D5 EDTA
F
L230 (anti-αv)
L230 Ca/Mg
L230 Mn
L230 EDTA
Absorbance
Antibody (ug/mL)
0.00001
0.001
0.1
10

FIG. 4A


A280
0.9
0.8
0.7
0.6
0.5
0.4
0.3
0.2
0.1
0
0.01
0.1
1
10
100
Antibody (µg/mL)
2
10
25
30
46
55
56
85
10D5
L230

Inhibition of biotin-αvβ6/LAP - Fusion #7 mAbs

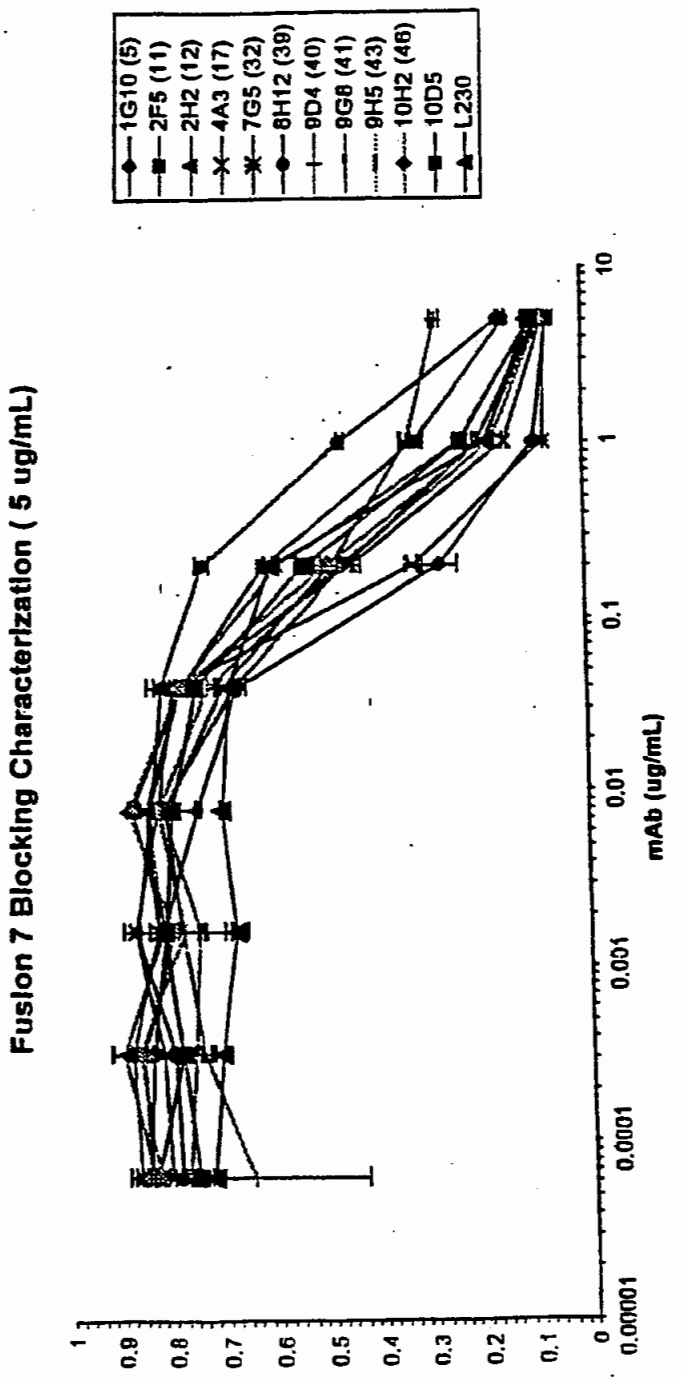
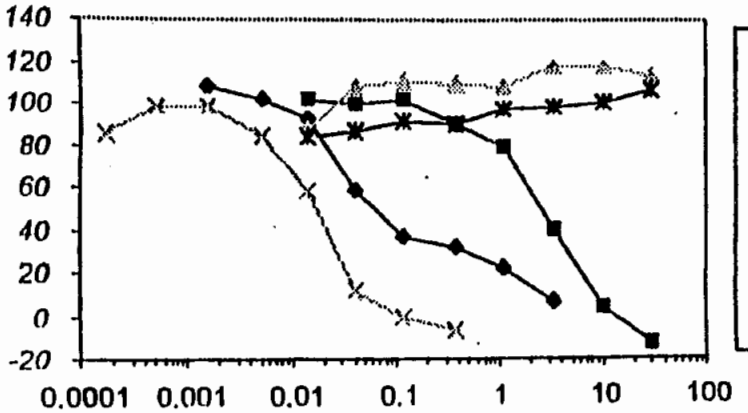
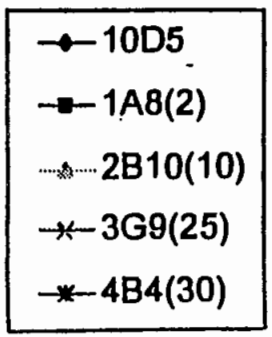


FIG. 4B

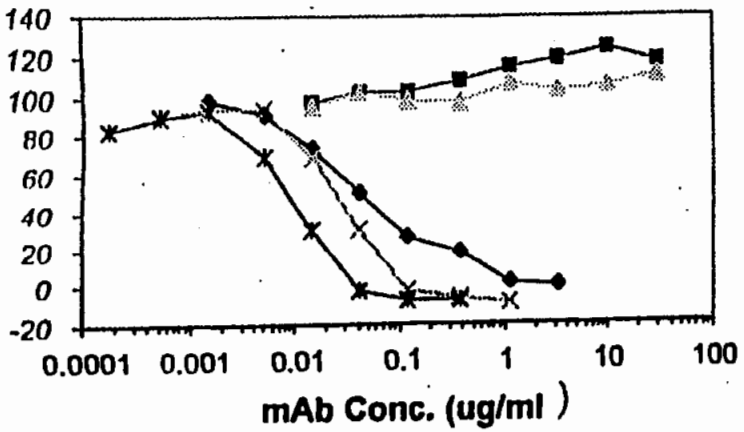
Adhesion of β6(FDC-P1)to LAP - Fusion #6 mAbs

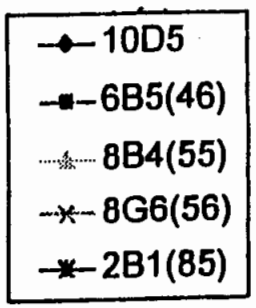




IC50s (ug/ml)
10D5: 0.064
1A8 : 2.52
2B10: >30
3G9 : 0.017
4B4 : >30

FIG. 5A





IC50s (ug/ml)
10D5: 0.042
6B5 : >30
8B4 : >30
8G6 : 0.023
2B1 : 0.008

FIG. 5B

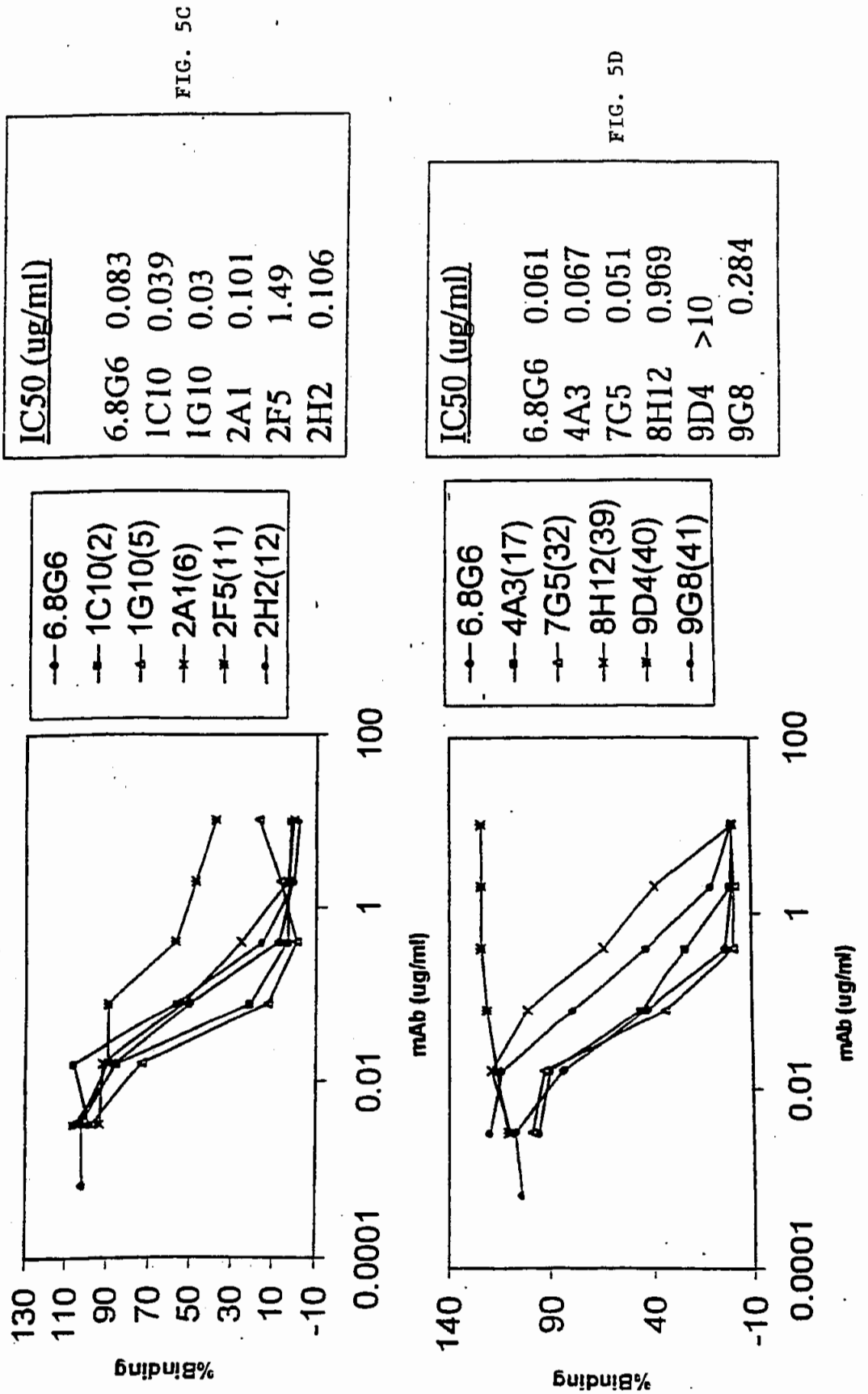

Adhesion of β6(FDC-P1)to LAP - Fusion #7 mAbs
%Binding
mAb (ug/ml)
6.8G6
1C10(2)
1G10(5)
2A1(6)
2F5(11)
2H2(12)
IC50 (ug/ml)
6.8G6 0.083
1C10 0.039
1G10 0.03
2A1 0.101
2F5 1.49
2H2 0.106
6.8G6
4A3(17)
7G5(32)
8H12(39)
9D4(40)
9G8(41)
IC50 (ug/ml)
6.8G6 0.061
4A3 0.067
7G5 0.051
8H12 0.969
9D4 >10
9G8 0.284

FIG. 5C

FIG. 5D

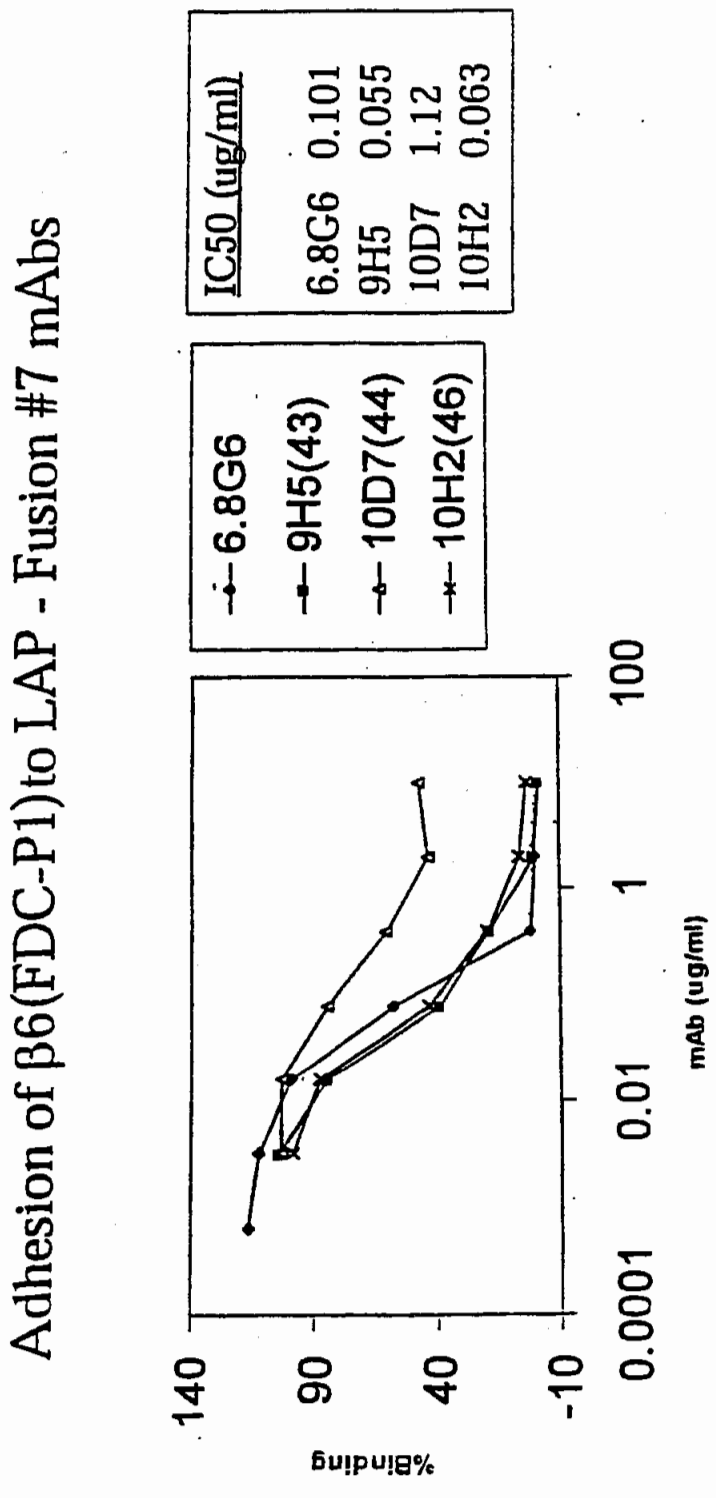
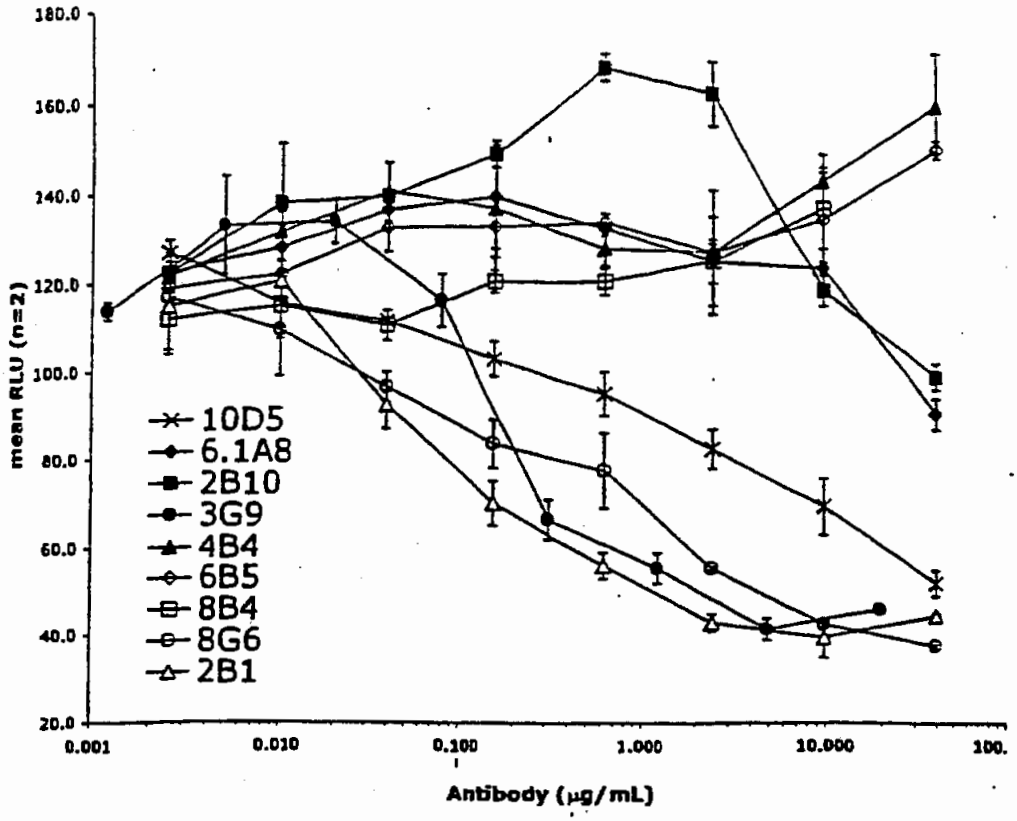

Adhesion of β6(FDC-P1)to LAP - Fusion #7 mAbs
IC50 (ug/ml)
6.8G6 0.101
9H5 0.055
10D7 1.12
10H2 0.063
6.8G6
9H5(43)
10D7(44)
10H2(46)
%Binding
140
90
40
-10
0.0001
0.01
1
100
mAb (ug/ml)

FIG. 5E

FIG. 6A


180.0
160.0
140.0
120.0
100.0
80.0
60.0
40.0
20.0
mean RLU (n=2)
0.001
0.010
0.100
1.000
10.000
100.
Antibody (µg/mL)
10D5
6.1A8
2B10
3G9
4B4
6B5
8B4
8G6
2B1

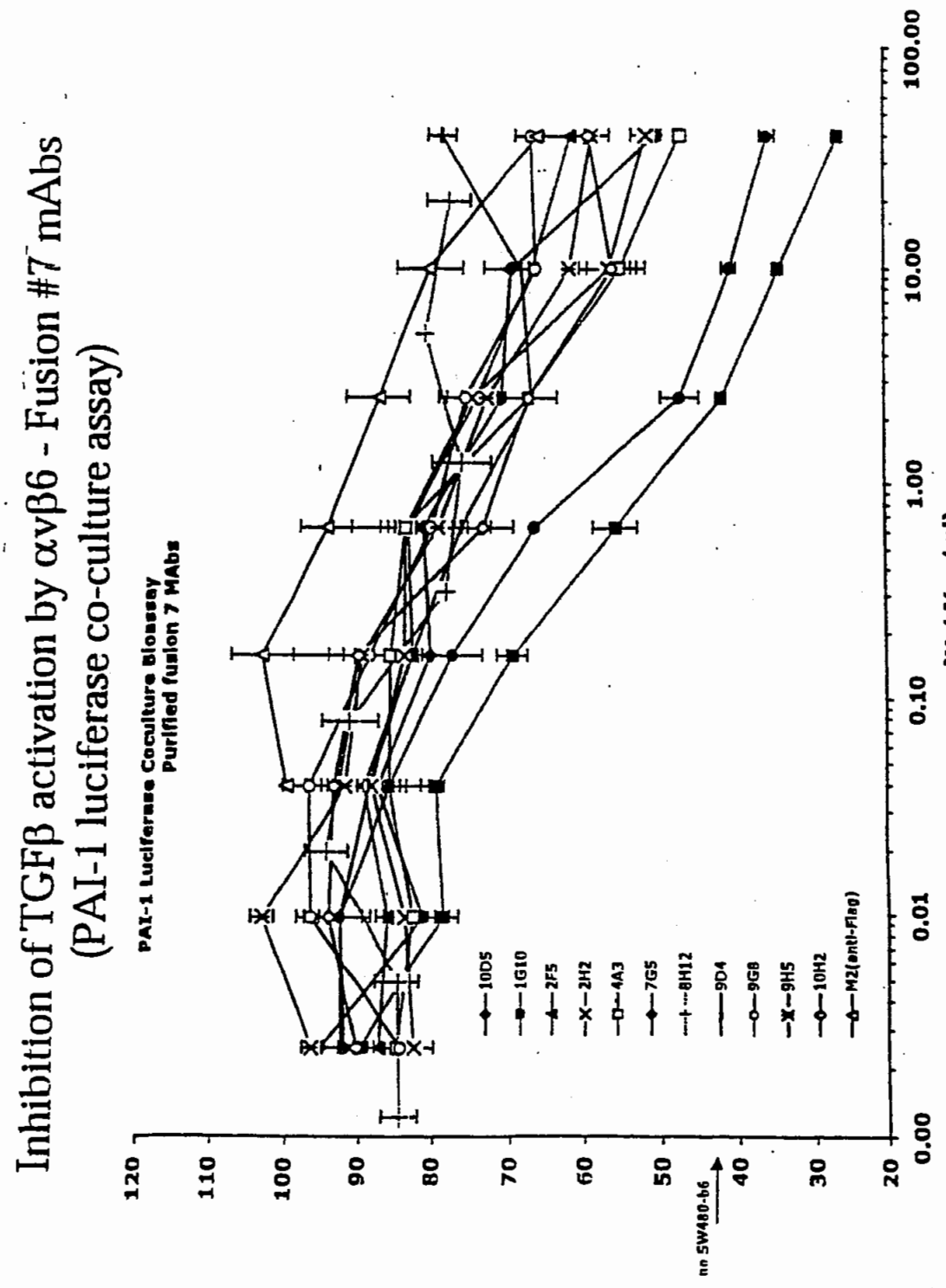

Inhibition of TGFβ activation by αvβ6 - Fusion #7 mAbs
(PAI-1 luciferase co-culture assay)
PAI-1 Luciferase Coculture Bioassay
Purified fusion 7 MAbs
10D5
1G10
2F5
2H2
4A3
7G5
8H12
9D4
9G8
9H5
10H2
M2(anti-Flag)
no SW480-b6
[Mab](ug/ml)
0.00
0.01
0.10
1.00
10.00
100.00
20
30
40
50
60
70
80
90
100
110
120

FIG. 6B

```
6.1A8      (1) QVQFQQSGPELVRPGVSVKLSCKGSSYTFTDYTMHWVKLSHAKTLEWIGVIDTYYGKTNYNQKFEGKATMTVDKSSSTAYMDLARLTSEDSAV
6.8G6-A    (1) QVQLQQSGPELVRPGVSVKISCKGSSYTFTDYAMHWVKLSHAKSLEWIGVISTYYGNTNYNQKFKGKATMTVDKSSSTAYMELARLTSEDSAV
6.8G6-B    (1) QVQLQQSGPELVRPGVSVKISCKGSSYTFTDYAMHWVKLSHAKSLEWIGVISTYYGNTNYNQKFKGKATMTVDKSSSTAYMELARLTSEDSAV
7.7G5      (1) EVQLQQSGPELVKPGASVKISCKASGYSFTGYFMNWVMQSHGKSLEWIGRIKPYNGDNFYNQKFMGKATLTVDKSSSTVHMELRSLASEDSAV
6.2B1      (1) EVKLVESGGGLVKPGGSLKLSCAASGFTFSRYVMSWVRQTPEKRLEWVASISSG-GSTYYPDSVKGRFTISRDSARNILYLQMSSLRSEDTAM
6.3G9      (1) EVMLVESGGGLVKPGGSLKLSCAASGFTFSRYVMSWVRQTPEKRLEWVASISSG-GRMYYPDTVKGRFTISRDSARNILYLQMSSLRSEDTAM
6.2B10-A   (1) QVQLQQPGAELVRPGTSVKLSCKASGYSFTSYWMNWVKQRPGQGLEWIGMIHPSISETRLNPKFKDKATLTVDTSSSTVYMQLSSPTSEDSAV
6.2B10-B   (1) QVQLQQPGAELVGPGTSVKLSCKASGYSFTSYWMNWVKQRPGQGLEWIGMIHPSISETRLNPKFKDKATLTVDTSSSTVYMQLSSPTSEDSAV
6.2G2      (1) QVQLQQSGAELARPGTSVKVSCKASGYAFTNYLIEWVKQRPGQGLEWIGVISPGSGIINYNEKFKGKATLTADKSSSTAYMQLSSLTSDDSAV
6.2A1      (1) QVQLQQSGAELVRPGTSVKVSCKASGYDFNNDLIEWVKQRPGQGLEWIAVINPGSGRTNYNEKFKGKATLTADKSSSTVYMQLSSLTSDDSAV
6.4B4-A    (1) QVQLQQSGAVLMKPGASVKISCKATGYSFTNYWIDWIKQRPGHGLEWIGENLPG-TRNNYNENFKGKATFTADPSSNTAYIQLNSLTSDDSAV
6.4B4-B    (1) QVQLQQSGAVLMKPGASVKISCKATGYSFTNYWIDWIKQRPGHGLEWIGENLPG-TRNNYNENFKGKATFTADPSSNTAYIQLNSLTSDDSAV
6.4B4-C    (1) QVQLQQSGAVLMKPGASVKISCKATGYSFTNYWMDWIKQRPGHGLEWIGENLPG-TRNNYNENFKGRATFTADPSSNTAYIQLNSLTSDDSAV
7.10H2     (1) QVQLQQSGPELVKPGASVRISCKASGYIFTSYYIHWVKQRPGQGLEWIGWIYPGNVNTKYNEKFKDKATLTADKSSSTAYMQLSSLTSEDSAV
7.9H5      (1) QVQLQQSGPELVKPGASVRISCKASGYIFTSYYIHWVKQRPGQGLEWIGWIYPGNVNTKYNEKFKDKATLTADKSSSTAYMQLSSLTSEDSAV
7.4A3-A    (1) QVQLQQSRPELVKPGASVRISCKASGYIFTSYYLHWVKQRPGQGLEWIGWIYPGNGNTKYMEKFKDKATLTSDKSSSTAYMQLSSLTSEDSAV
7.4A3-B    (1) QVQLQQSRPELVKPGASVRISCKASGYIFTSYYLHWVKQRPGQGLEWIGWIYPGNGNTKYSEKFKDKATLTSDKSSSTAYMQLSSLTSEDSAV
7.1C5-A    (1) QVQLQQSGPELVKPGASLRISCKASGYTFKSYYIHWVRQRPGQGLEWIGWIYPGNLNTKYNEKFKGKATLTADKSSSTVYMQLSSLTSEDSAV
7.1C5-B    (1) QVQLQQSGPELVKPGASLRISCKASGYTFKSYYIHWVRQRPGQGLEWIGWIYPGNLNTKYNEKFKGKATLTADKSSSTVYMQLSSLTSEDSAV
7.1G10     (1) QVQLQQSGPELVKPGASVRISCKASGYTFTSYYIHWVKQRPGQGLEWIGWLYPGKINTRYNEKFKGKATLIADKSSSTAYMQLSSLTSEDSAV

6.1A8     (94) YYCARGGFRRGDRPSLRYAMDSWGQGTSVTVSS  SEQ ID NO:19
6.8G6-A   (94) YYCARGGLRRGDRPSLRYAMDYWGQGTSVTVSS  SEQ ID NO:20
6.8G6-B   (94) YYCARGGLRRGDRPSLQYAMDYWGQGTSVTVSS  SEQ ID NO:21
7.7G5     (94) YYCARDRYG------T-YGMDYWGQGTSVTVSS  SEQ ID NO:22
6.2B1     (93) YYCARGAIYDG-----YYVFAYWGQGTLVTVSA  SEQ ID NO:23
6.3G9     (93) YYCARGSIYDG-----YYVFPYWGQGTLVTVSA  SEQ ID NO:24
6.2B10-A  (94) YYCARYLGYYTY-----YGSDCWGQGTSVTVSS  SEQ ID NO:25
6.2B10-B  (94) YYCARYLGYYTY-----YGLDYWGQGTSVTVSS  SEQ ID NO:26
6.2G2     (94) YFCAAIDYSGP------YAVDDWGQGTSVTVSS  SEQ ID NO:61
6.2A1     (94) YFCAMIYY-GPHS----YAMDYWGQGTSVTVSS  SEQ ID NO:62
6.4B4-A   (93) YYCAREALGGDY------GLDYWGQGTSLTVSS  SEQ ID NO:27
6.4B4-B   (93) YYCAREALGGDY------VLDYWGQGTSLTVSS  SEQ ID NO:28
6.4B4-C   (93) YYCAREALGGDY------GLDYWGQGTSLTVSS  SEQ ID NO:29
7.10H2    (94) YFCARHVLSGN--------FDYWGQGTTLTVSS  SEQ ID NO:30
7.9H5     (94) YFCARHVLSGN--------FDYWGQGTTLTVSS  SEQ ID NO:31
7.4A3-A   (94) YFCARHVLSGN--------FDYWGQGTTLTVSS  SEQ ID NO:32
7.4A3-B   (94) YFCARHVLSGN--------FDYWGQGTTLTVSS  SEQ ID NO:33
7.1C5-A   (94) YFCARHELNGN--------FDYWGQGTTLTVSS  SEQ ID NO:34
7.1C5-B   (94) YFCARHELNGN--------FDYWGQGTTLTVSS  SEQ ID NO:35
7.1G10    (94) YFCARHVLNGN--------FDYWGQGTTLTVSS  SEQ ID NO:36
```

FIG. 7A

```
6.1A8    (1)  DIVLTQSPASLAVSLGQRATISCRASQSVSISTSYSYIHWFQQKPGQPPKLLIKYASNLESGVPARFSGSGSGTDFTLNIHPVEEEDTAIYYC
6.8G6    (1)  DIVLTQSPASLAVSLGQRAIISCRASQSVSTSSSYSYMYWYQQKPGQSPKFLIKYASNLESGVPARFSGSGSGTDFTLNIHPVEEEDTATYYC
6.4B4    (1)  DVVMTQTPRSLPVSLGDQASMSCRSSQSLKHSNGDTYLHWYLQKPGQSPNLLIYKVSNRFSGVPDRFSGSGSGTEFTFKISRVEAEDLGVYFC
6.2A1    (1)  DIVMTQSHKFMSTVVGDRVSITCKASLDVR----TAVAWYQQKPGQSPKLLIYSASYRYTGVPDRFTGSGSGTDFTFNIRSVQAEDLAVYYC
6.2G2    (1)  DIVMTQSHKFMSTSVGDRVSVTCKASQAVN----TAVAWYQQKPGQSPKLLIYSASYQYTGVPDRFTGSGSGTDFTLTISSVQAEDLAVYYC
7.1C5    (1)  DIQMTQSPSSLSASLGERVNLTCRASQEISG-----YLSWLQQKPDGTIKRLIYAASTLDSGVPKRFSGSRSGSDYSLTISSLESEDFGDYYC
7.1G10   (1)  DIQMTQSPSSLSASLGERVSLTCRASQEISG-----YLSWLQQKPDGSIKRLIYAASTLDSGVPKRFSGSRSGADYSLTISSLESEDFADYYC
6.2B10   (1)  QIVLTQSPAIMSASPGEKVTMTCSASSSVS-----YMHWYQQKSGTSPRRWIYDTSKLASGVPARFSGSGSGTSYSLTISSMEAVDAATYYC
7.7G5    (1)  QIVLTQSPAIMSASPGEKVTMTCSASSSVS-----YMHWYQQKSGTSPKRWIYDTSKLASGVPTRFSGSGSGTSYSLTINSMEAEDAATYYC
6.2B1    (1)  QIVLTQSPAIMSASPGEKVTLTCSASSSVSSS----YLYWYQQKPGSSPKLWIYSTSNLASRVPARFSGSGSGTSYSLTISSMEAEDAASYFC
6.3G9    (1)  QIVLTQSPAIMSASPGEKVTLTCSANSSVSSS----YLYWYQQKSGSSPKLWIYSTSNLASGVPVRFSGSGSGTSFSLTISSMEAEDAASYFC

6.1A8    (93) QHSWEIPYTFGGGTKVEIK    SEQ ID NO:37
6.8G6    (93) QHNWEIPFTFGGGTKLEIK    SEQ ID NO:38
6.4B4    (94) SQSTHVPYTFGGGTRLEIK    SEQ ID NO:39
6.2A1    (89) QQHYGIPWTFGGGTKLEIK    SEQ ID NO:63
6.2G2    (89) QHHYGVPWTFGGGTKLEIK    SEQ ID NO:64
7.1C5    (89) LQYASYPYTFGGGAKLEIK    SEQ ID NO:40
7.1G10   (89) LQYATYPYTFGGGTKLEIK    SEQ ID NO:41
6.2B10   (88) QQWTSNPFTFGSGTKLGIK    SEQ ID NO:42
7.7G5    (88) QQWSSHPPTFGAGTKLELK    SEQ ID NO:43
6.2B1    (90) HQWSSYPPTFGGGTKLEIK    SEQ ID NO:44
6.3G9    (90) HQWSTYPPTFGGGTKLEIK    SEQ ID NO:45
```

FIG. 7B

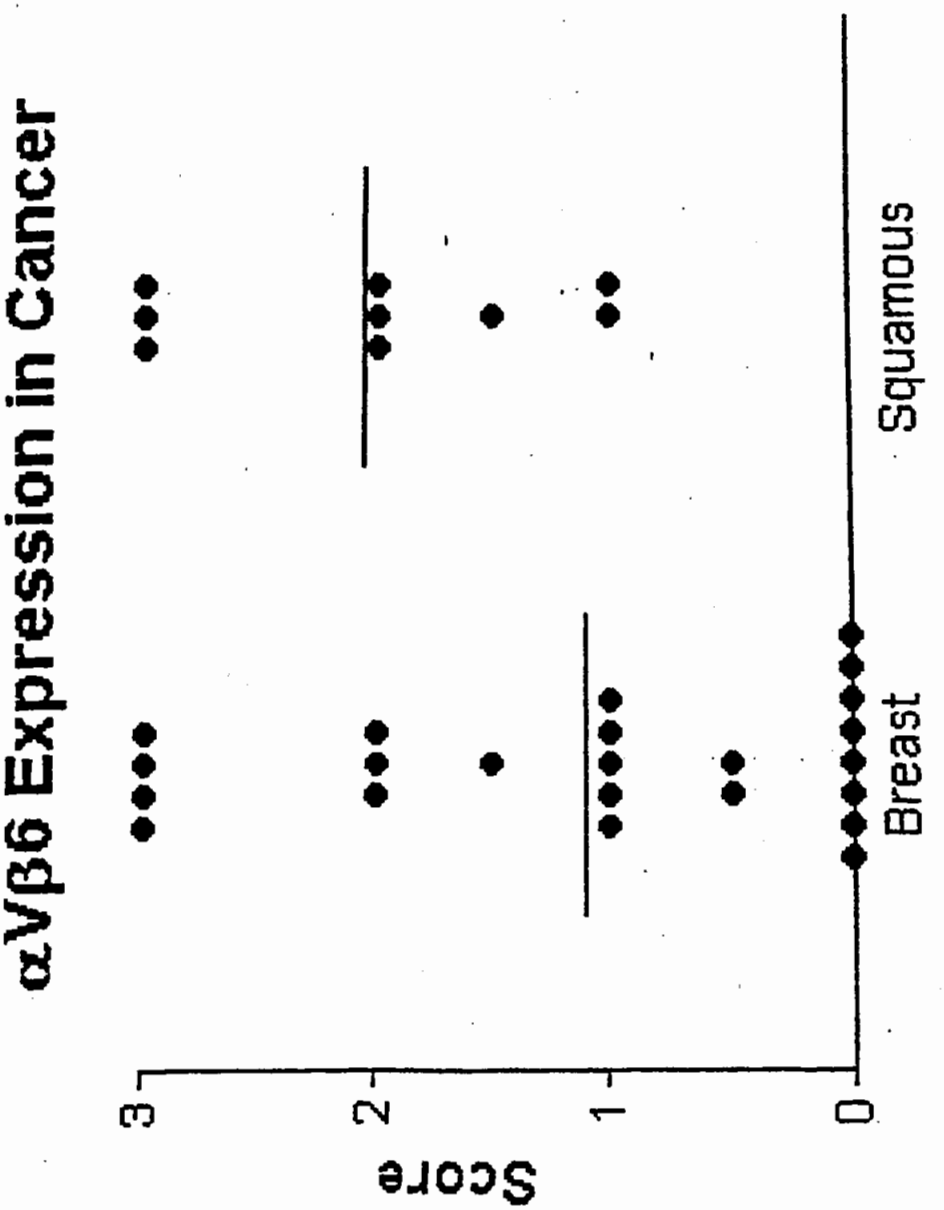

αVβ6 Expression in Cancer
Score
3
2
1
0
Breast
Squamous
Carcinoma

FIG. 8

FIG. 9A

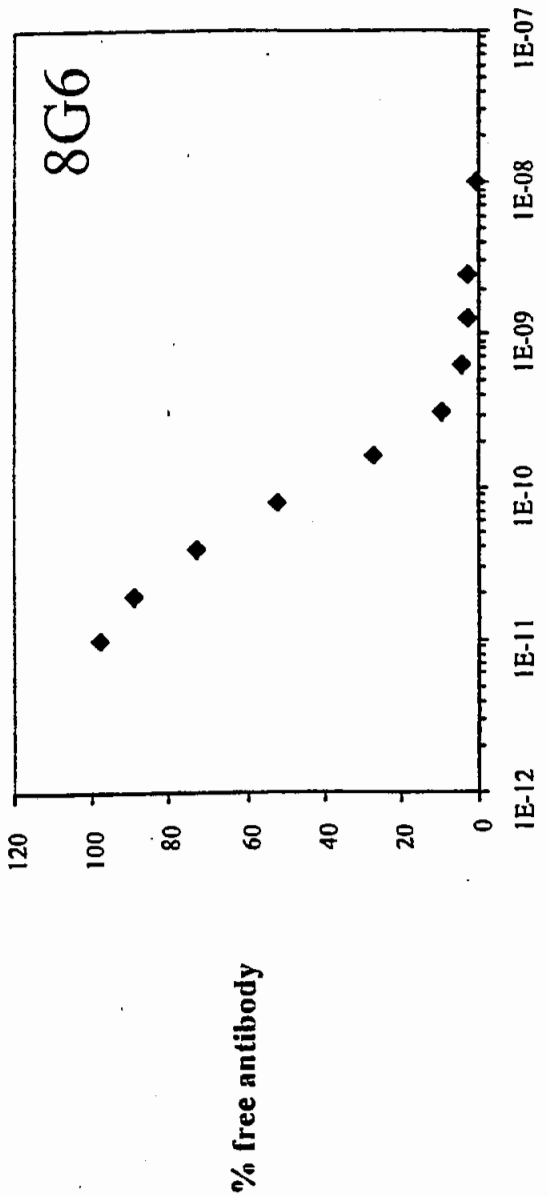

8G6
% free antibody
120
100
80
60
40
20
0
1E-12
1E-11
1E-10
1E-09
1E-08
1E-07

FIG. 9B

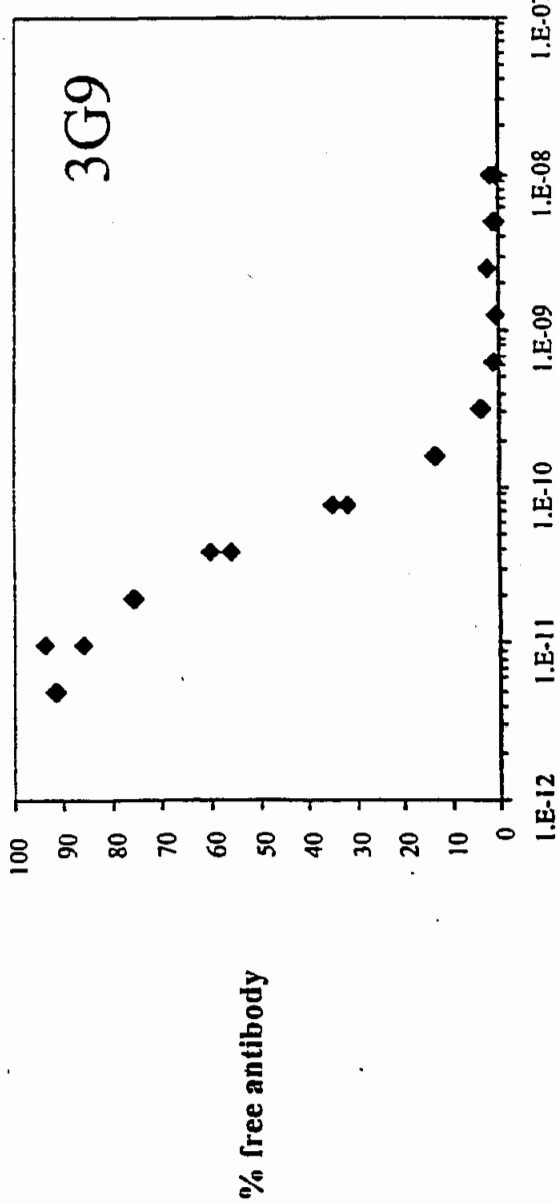

3G9
% free antibody
100
90
80
70
60
50
40
30
20
10
0
1.E-12
1.E-11
1.E-10
1.E-09
1.E-08
1.E-07
integrin concentration (M)

FIG. 10A

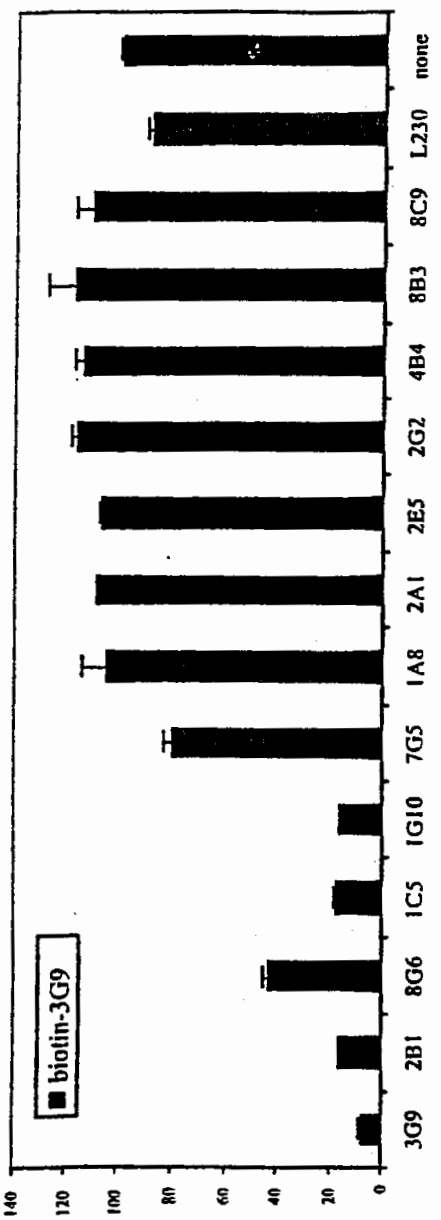
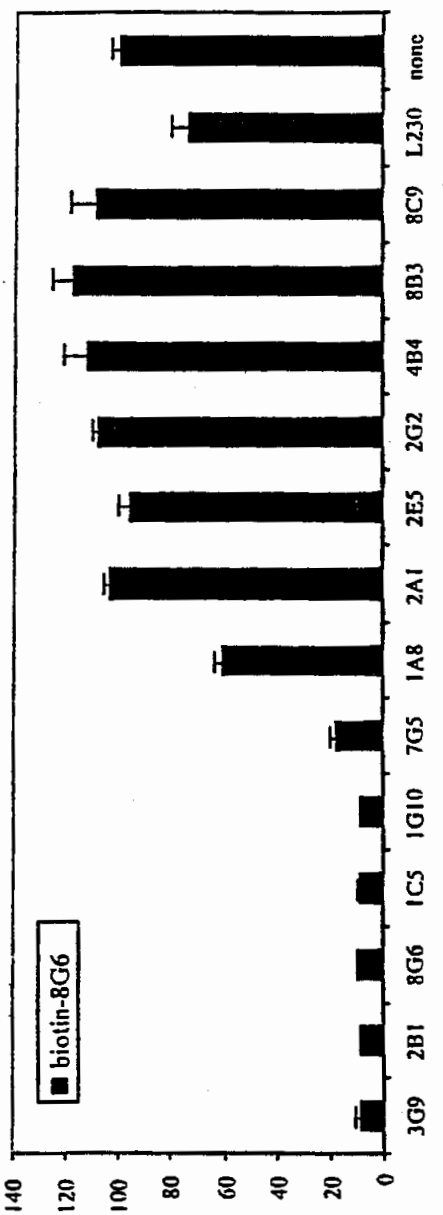


FIG. 10B



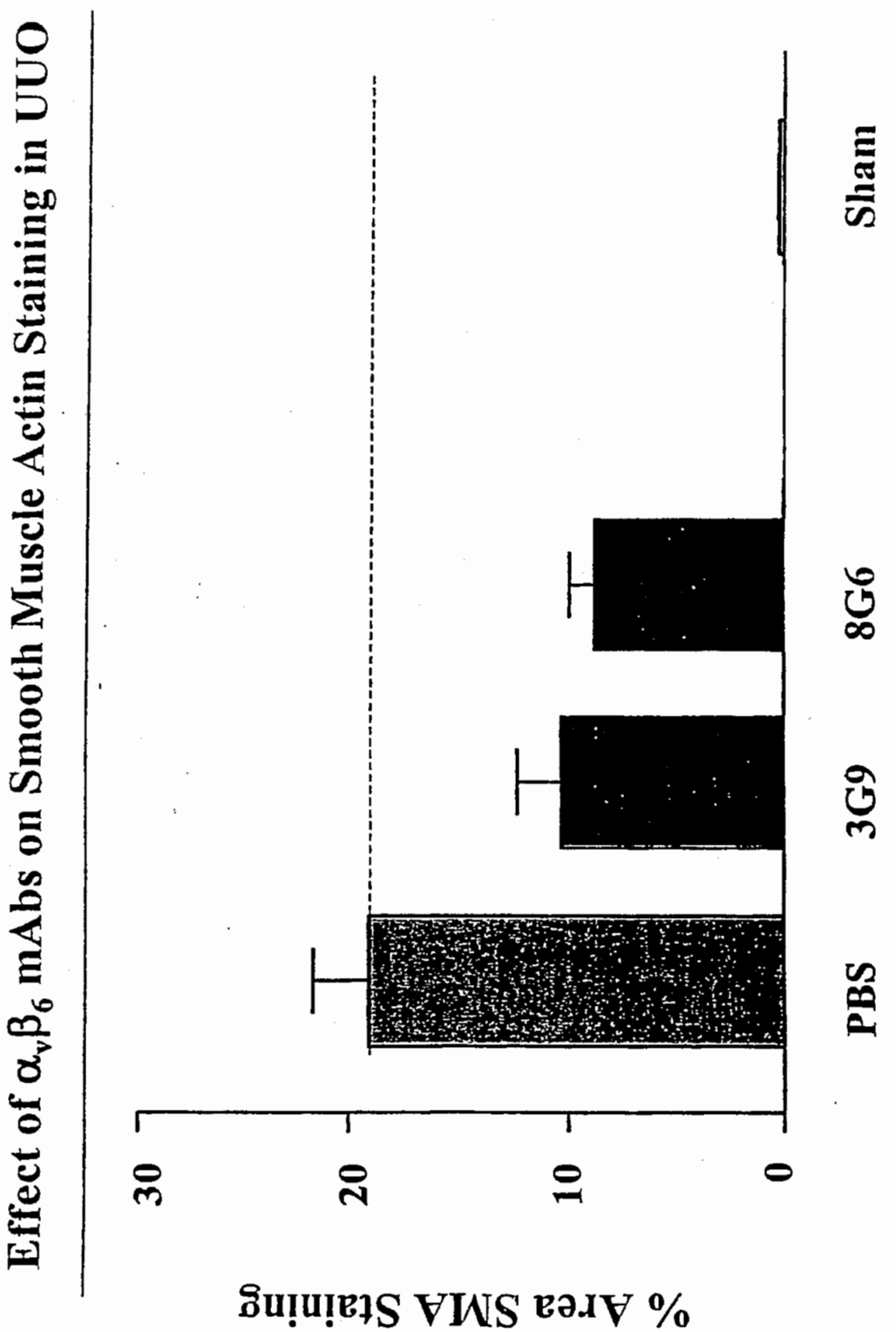

Effect of $\alpha_v\beta_6$ mAbs on Smooth Muscle Actin Staining in UUO
% Area SMA Staining
30
20
10
0
PBS
3G9
8G6
Sham

FIG. 11

FIG. 12

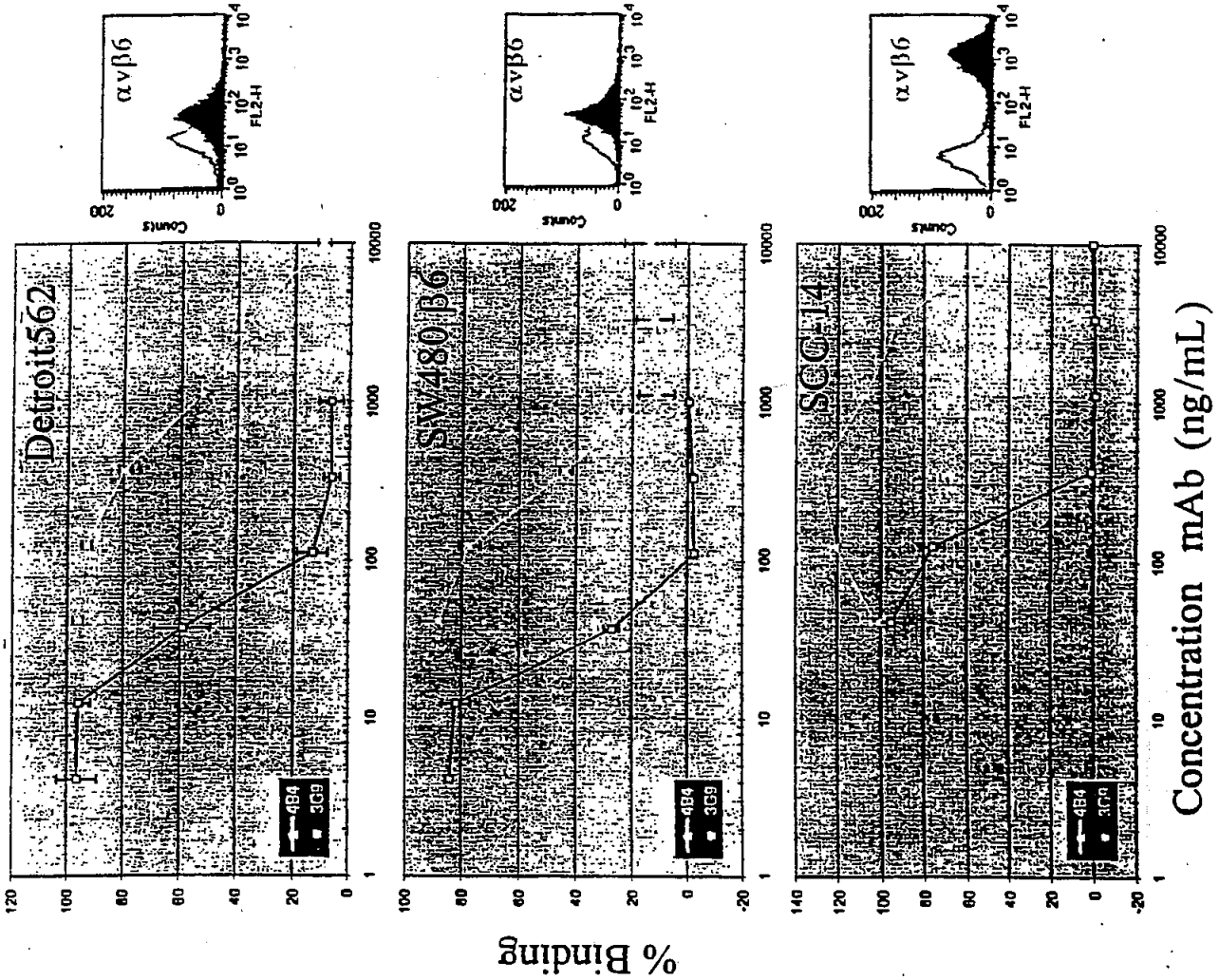
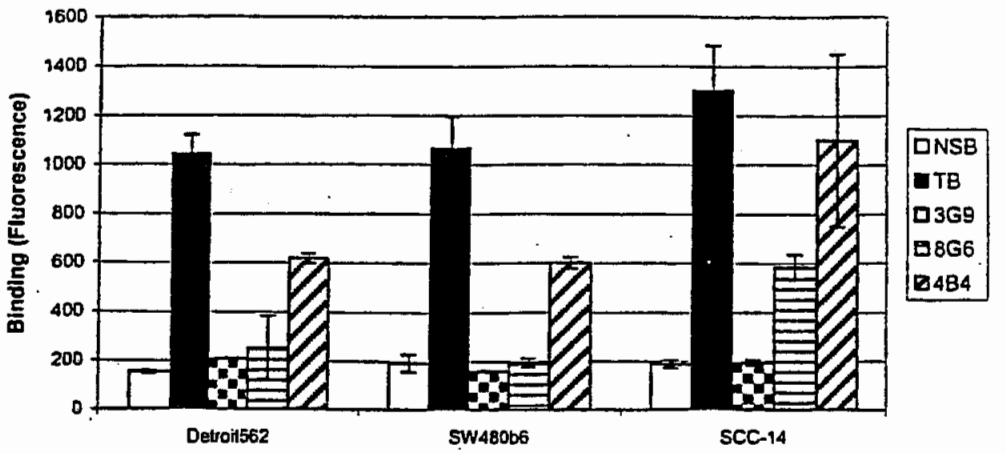

Detroit562
SW480.B6
SCC14
αvβ6
Counts
FL2-H
4B4
3G9
% Binding
Concentration mAb (ng/mL)

FIG. 13


1600
1400
1200
1000
800
600
400
200
0
Binding (Fluorescence)
Detroit562
SW480b6
SCC-14
NSB
TB
3G9
8G6
4B4

Response of the subcutaneously implanted Detroit 562, human pharynx carcinoma cell Line to avß6 mAb therapy with 3G9.

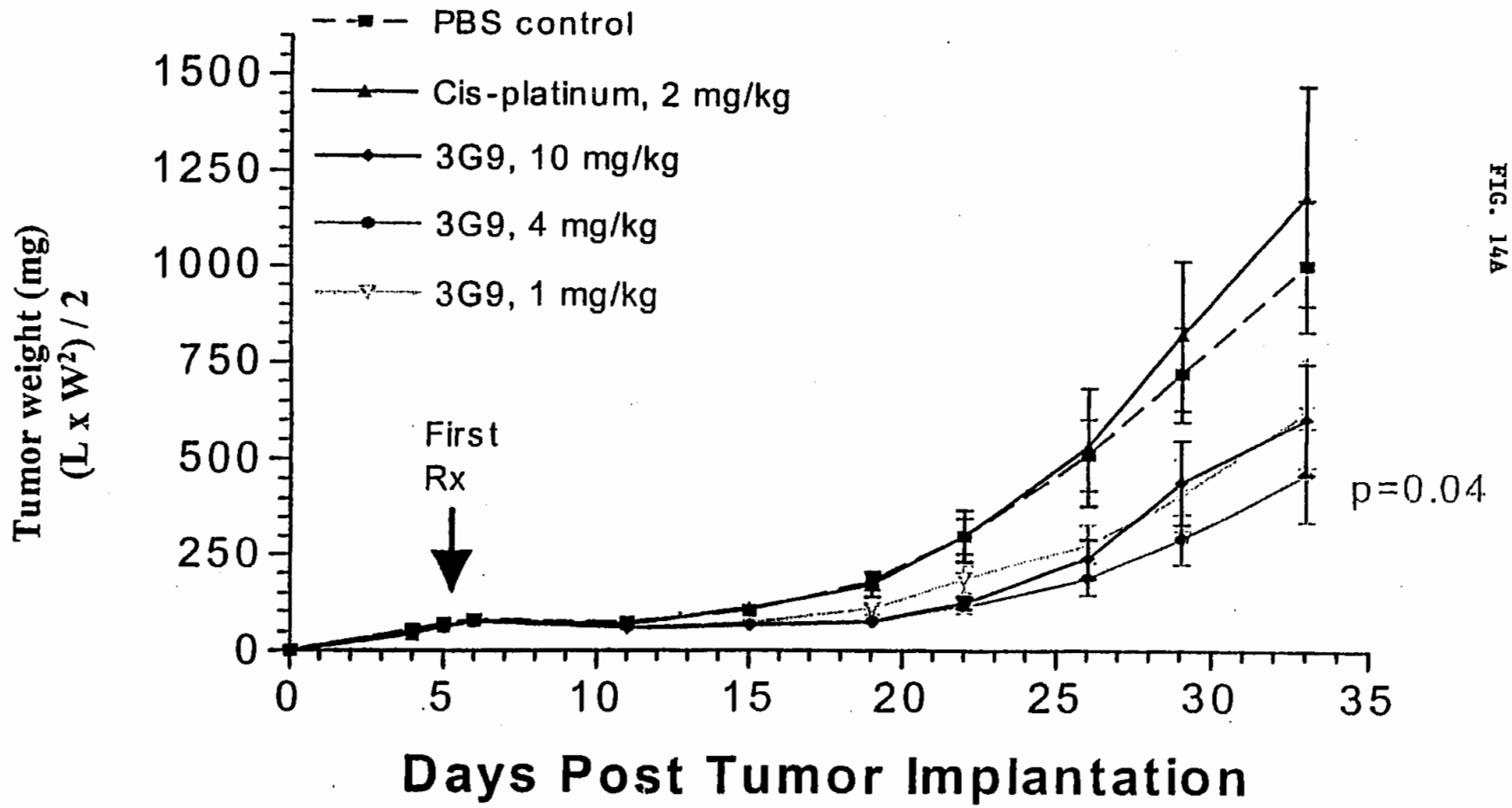
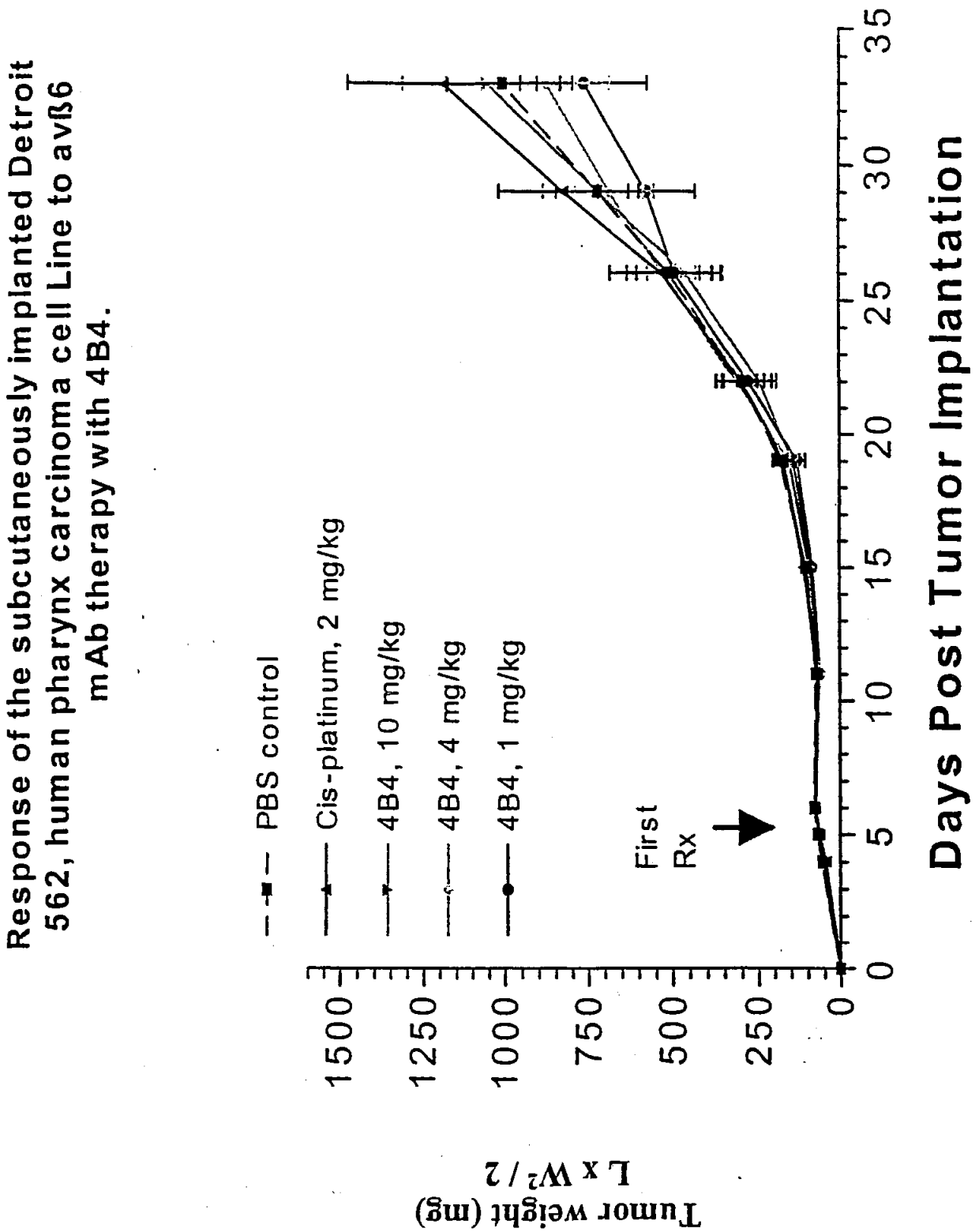


FIG. 14A

FIG. 14B


Response of the subcutaneously implanted Detroit 562, human pharynx carcinoma cell Line to avß6 mAb therapy with 4B4.
PBS control
Cis-platinum, 2 mg/kg
4B4, 10 mg/kg
4B4, 4 mg/kg
4B4, 1 mg/kg
First Rx
Tumor weight (mg)
L x W² / 2
Days Post Tumor Implantation
0
250
500
750
1000
1250
1500
0
5
10
15
20
25
30
35

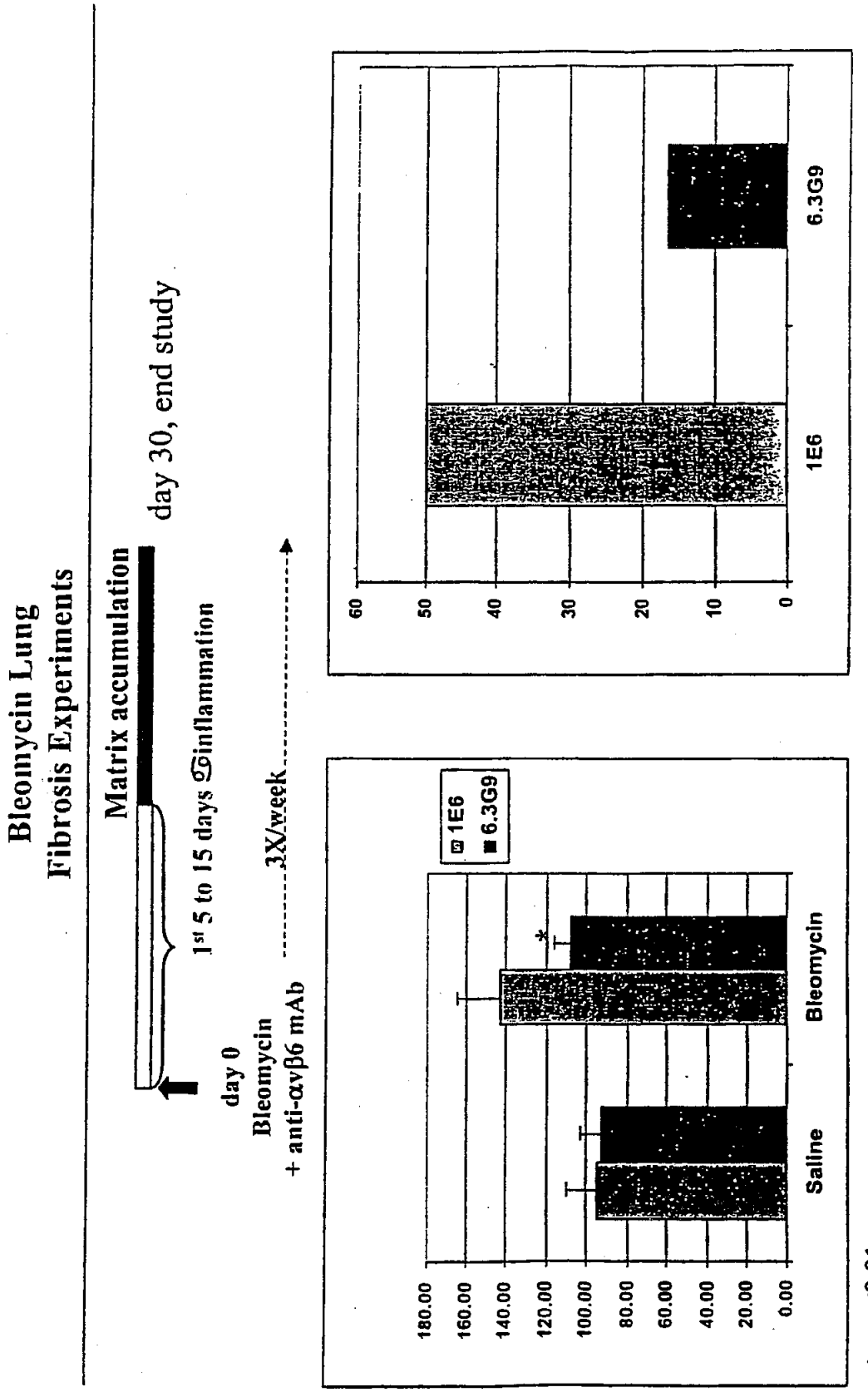

Bleomycin Lung
Fibrosis Experiments
Matrix accumulation
day 30, end study
1st 5 to 15 days Inflammation
day 0
Bleomycin
+ anti-αvβ6 mAb
3X/week
1E6
6.3G9
Saline
Bleomycin
180.00
160.00
140.00
120.00
100.00
80.00
60.00
40.00
20.00
0.00
*
60
50
40
30
20
10
0
1E6
6.3G9
* = p<0.01

FIG. 15A

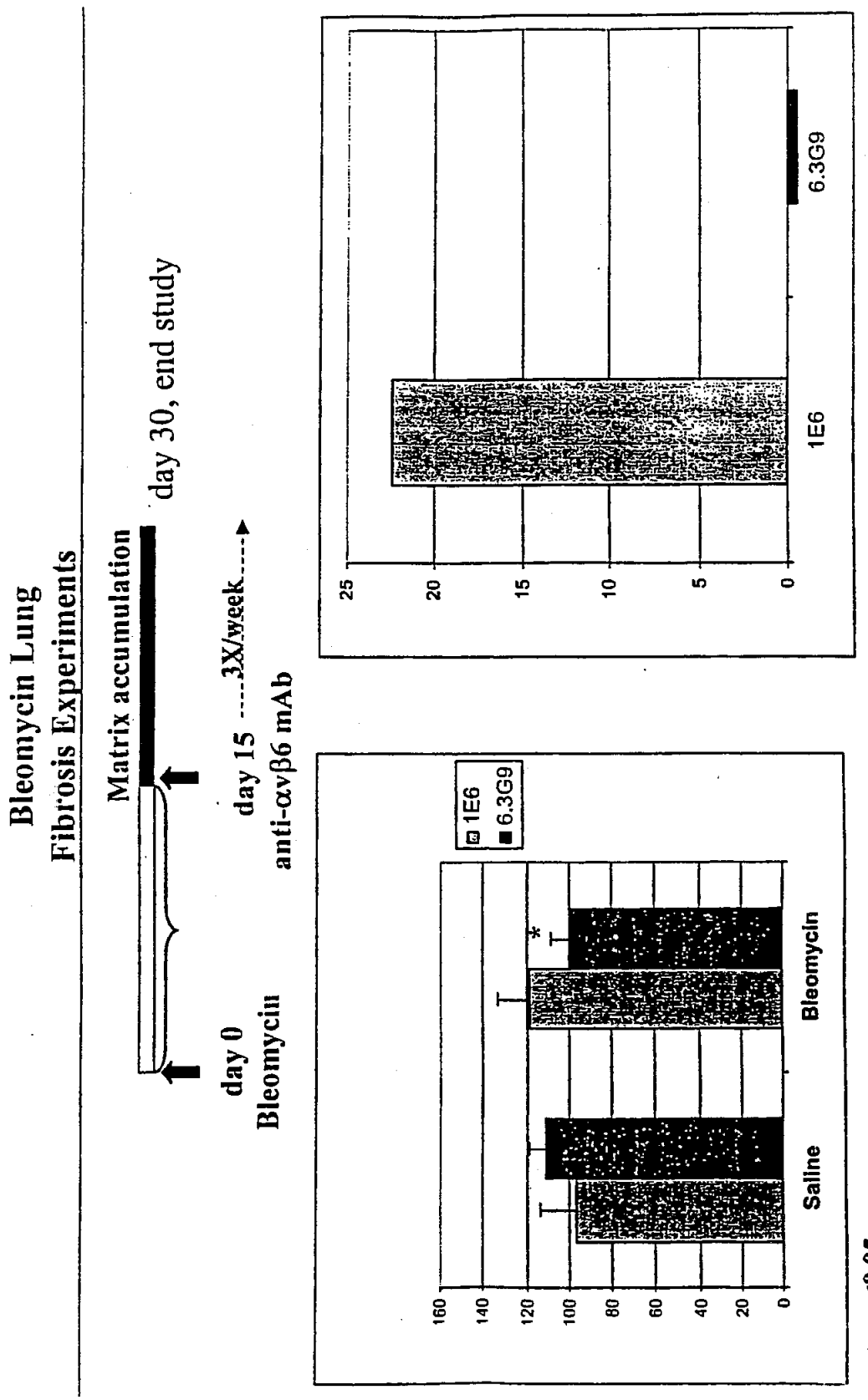

Bleomycin Lung
Fibrosis Experiments
Matrix accumulation
day 30, end study
day 15 ----3X/week---->
day 0
Bleomycin
anti-αvβ6 mAb
1E6
6.3G9
Saline
Bleomycin
* = p<0.05

FIG. 15B

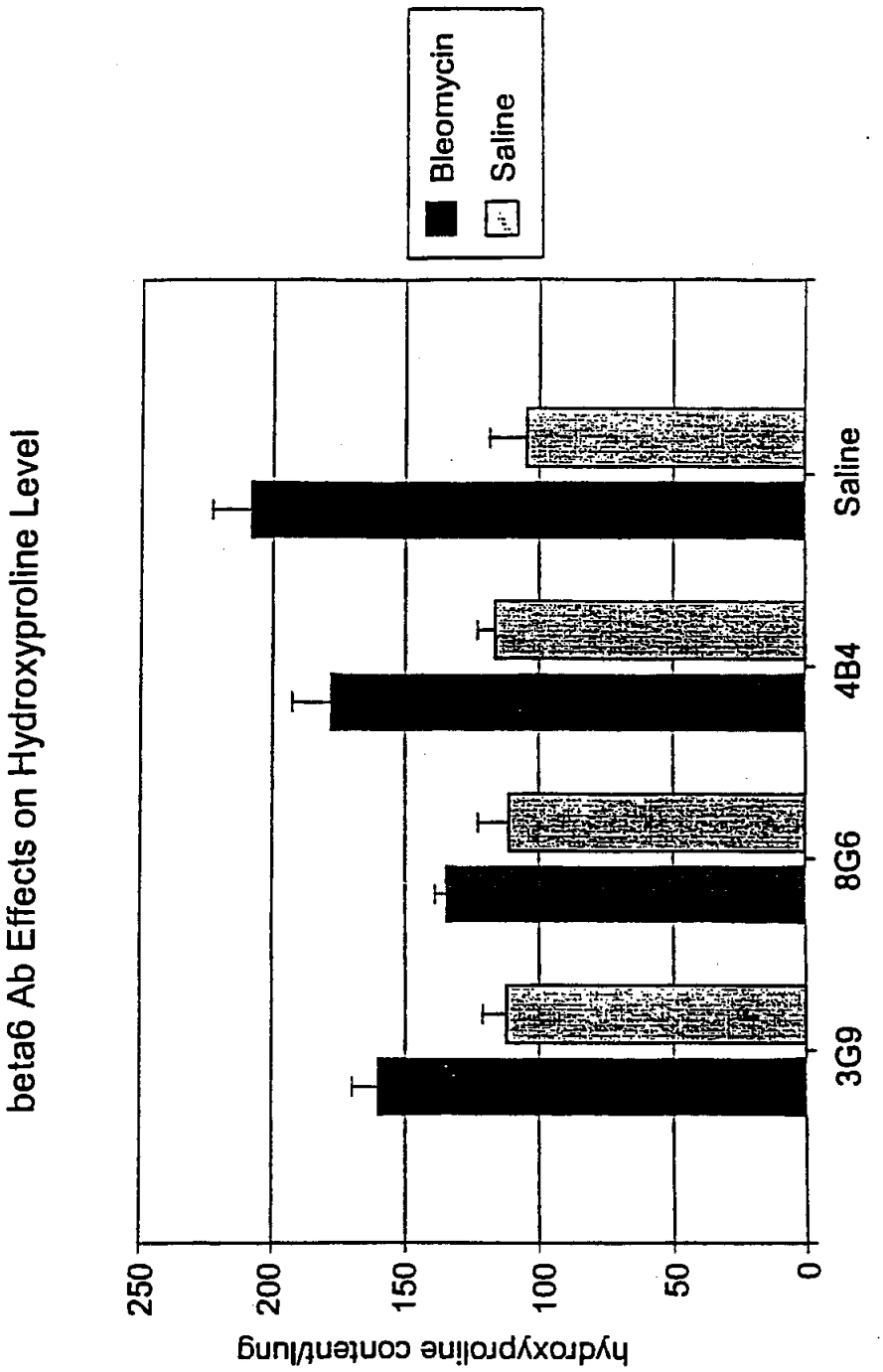

beta6 Ab Effects on Hydroxyproline Level
Bleomycin
Saline
hydroxyproline content/lung
250
200
150
100
50
0
3G9
8G6
4B4
Saline

FIG. 15C