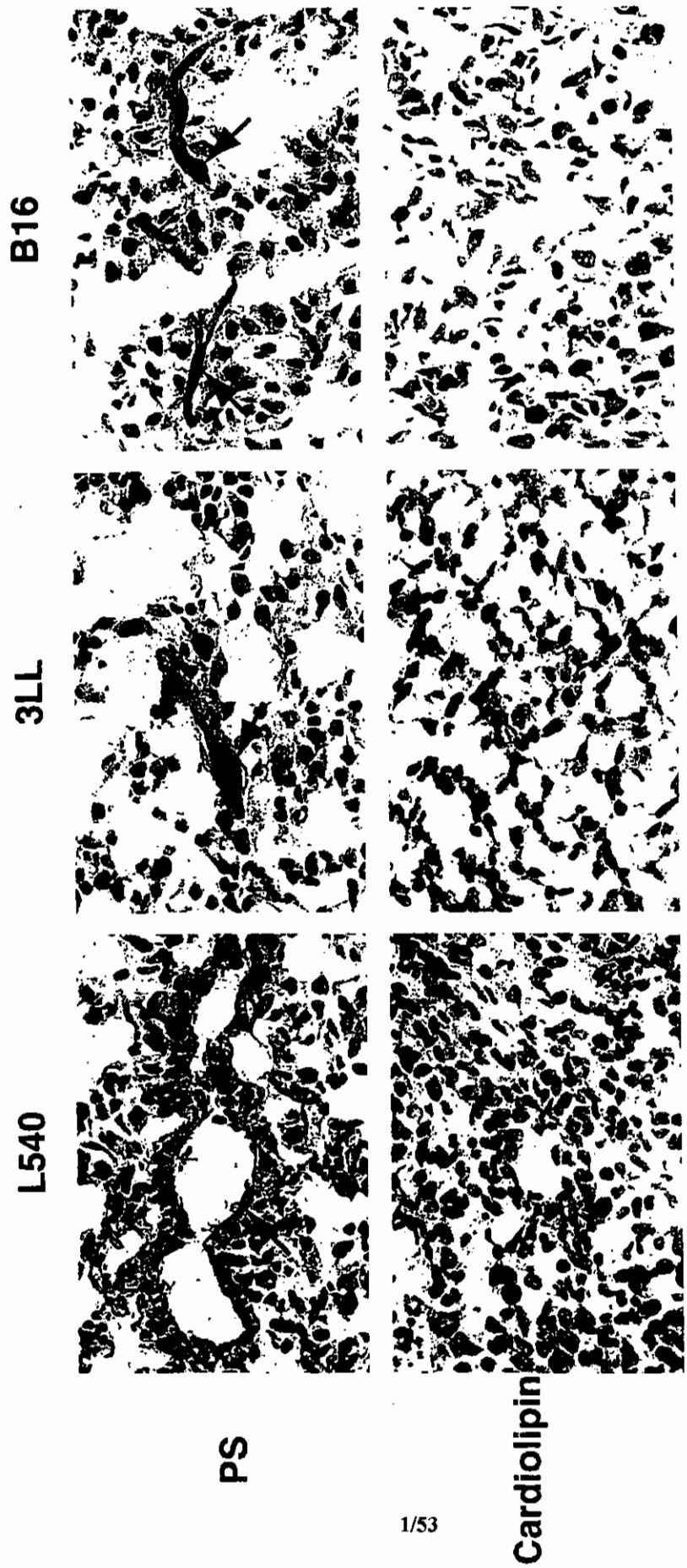


FIG. 1

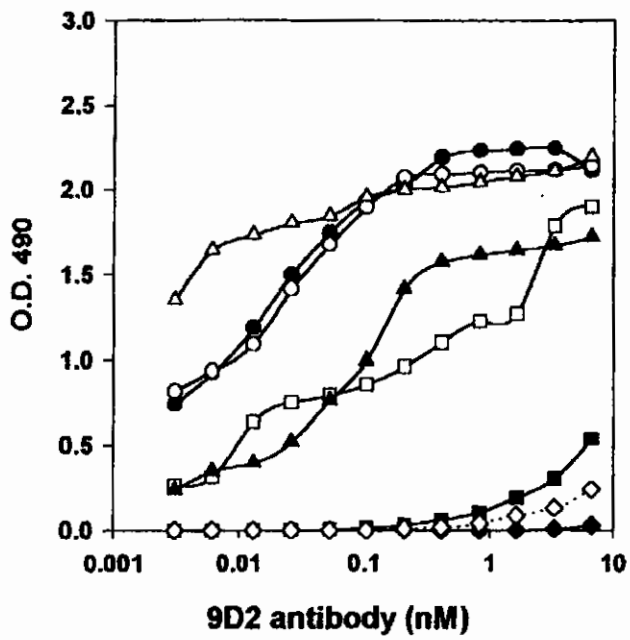

3.0
2.5
2.0
1.5
1.0
0.5
0.0
O.D. 490
0.001
0.01
0.1
1
10
9D2 antibody (nM)

FIG. 2A

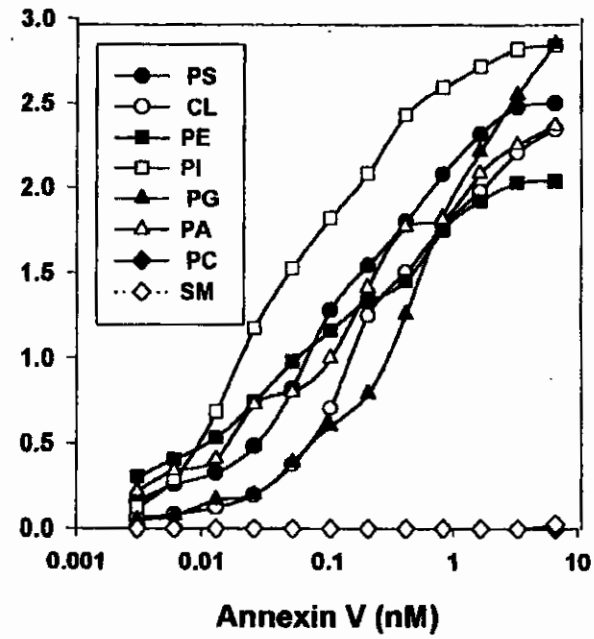

3.0
2.5
2.0
1.5
1.0
0.5
0.0
PS
CL
PE
PI
PG
PA
PC
SM
0.001
0.01
0.1
1
10
Annexin V (nM)

FIG. 2B

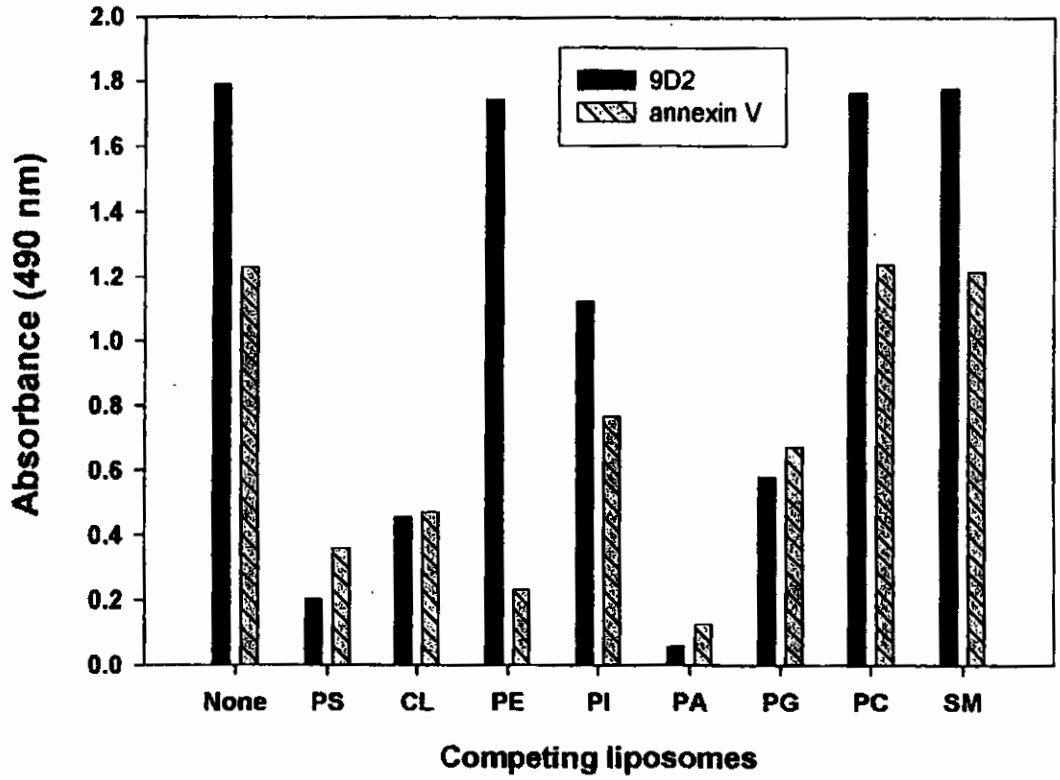

2.0
1.8
1.6
1.4
1.2
1.0
0.8
0.6
0.4
0.2
0.0
Absorbance (490 nm)
9D2
annexin V
None
PS
CL
PE
PI
PA
PG
PC
SM
Competing liposomes

FIG. 3

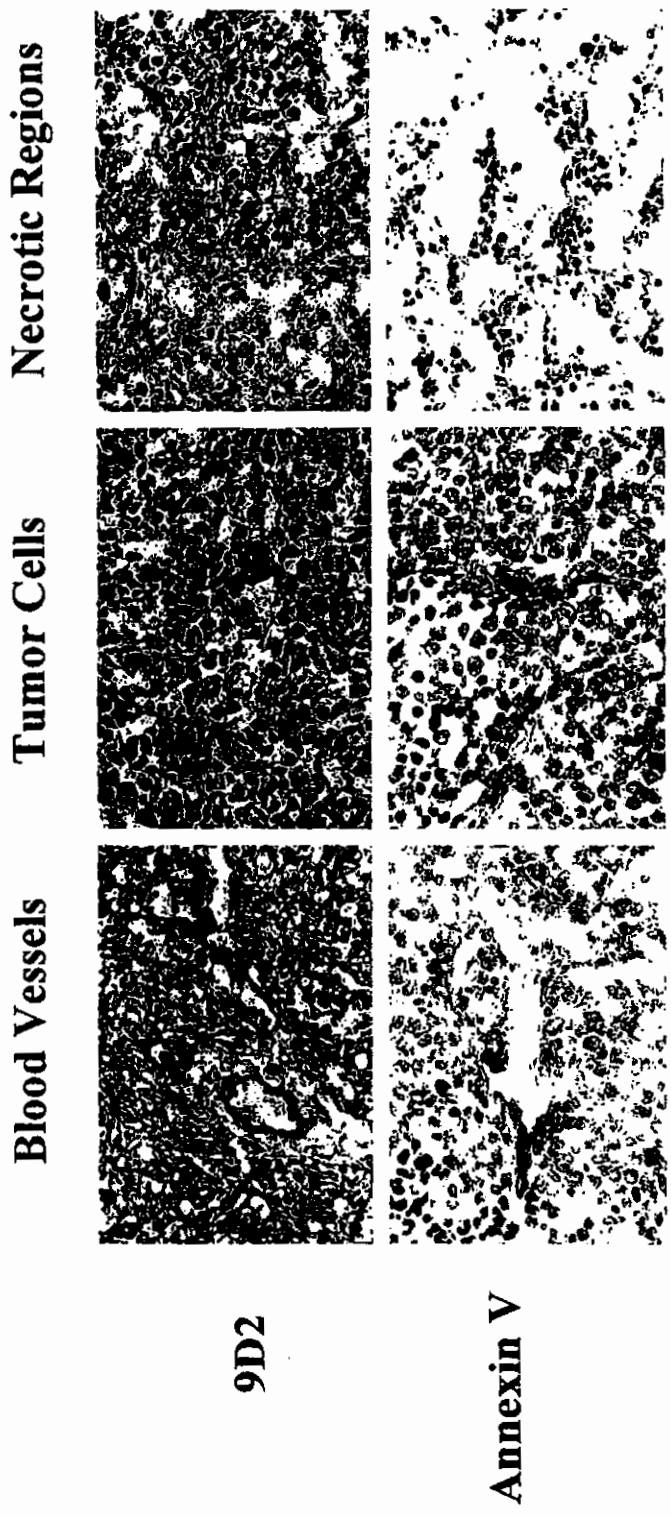


FIG. 4

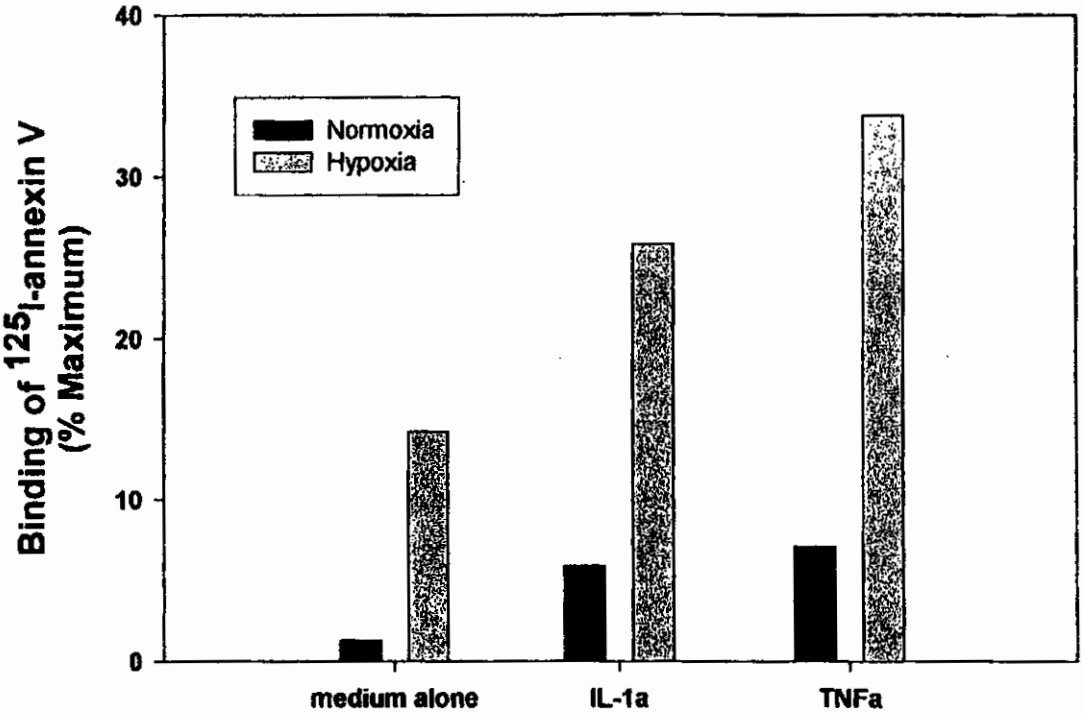

Binding of 125I-annexin V
(% Maximum)
40
30
20
10
0
Normoxia
Hypoxia
medium alone
IL-1a
TNFa

FIG. 5

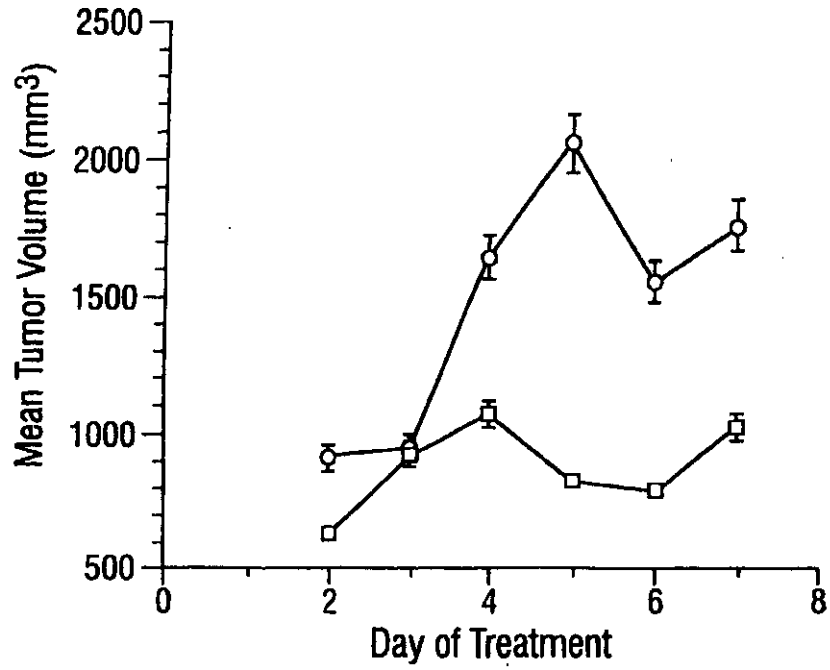

2500
2000
1500
1000
500
Mean Tumor Volume (mm3)
0
2
4
6
8
Day of Treatment

FIG. 6A

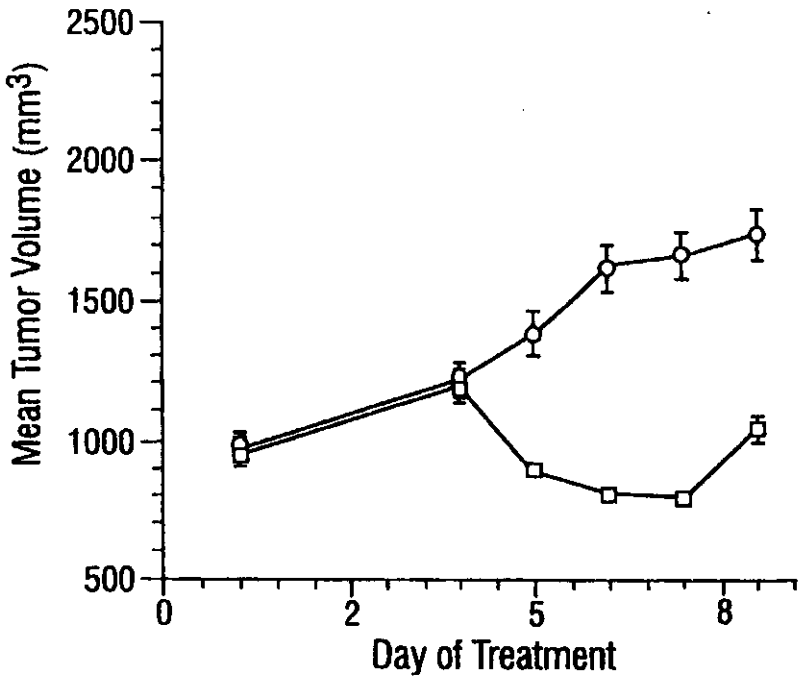

2500
2000
1500
1000
500
Mean Tumor Volume (mm3)
0
2
5
8
Day of Treatment

FIG. 6B

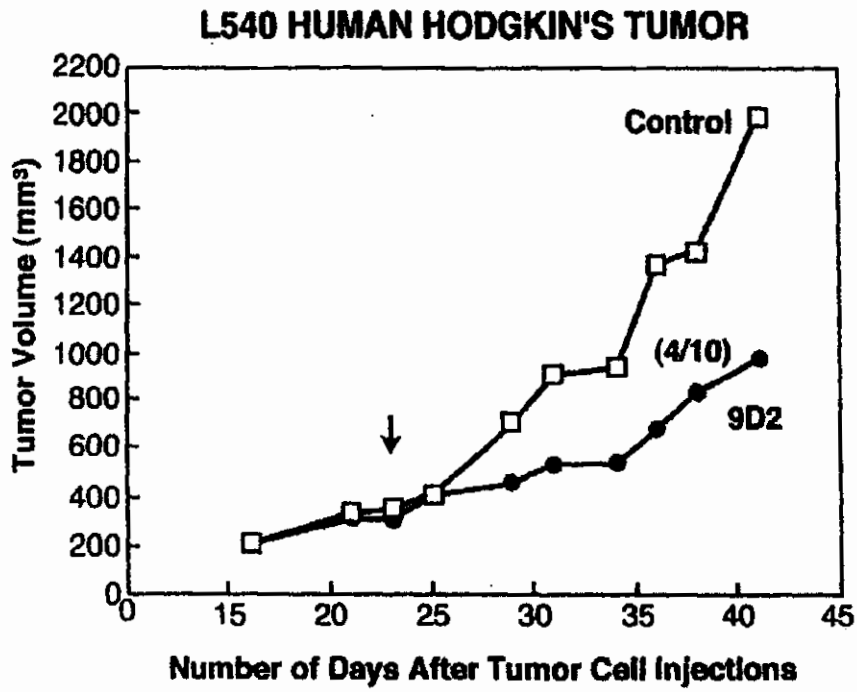

L540 HUMAN HODGKIN'S TUMOR
Tumor Volume (mm³)
2200
2000
1800
1600
1400
1200
1000
800
600
400
200
0
0
15
20
25
30
35
40
45
Number of Days After Tumor Cell Injections
Control
(4/10)
9D2

FIG. 7

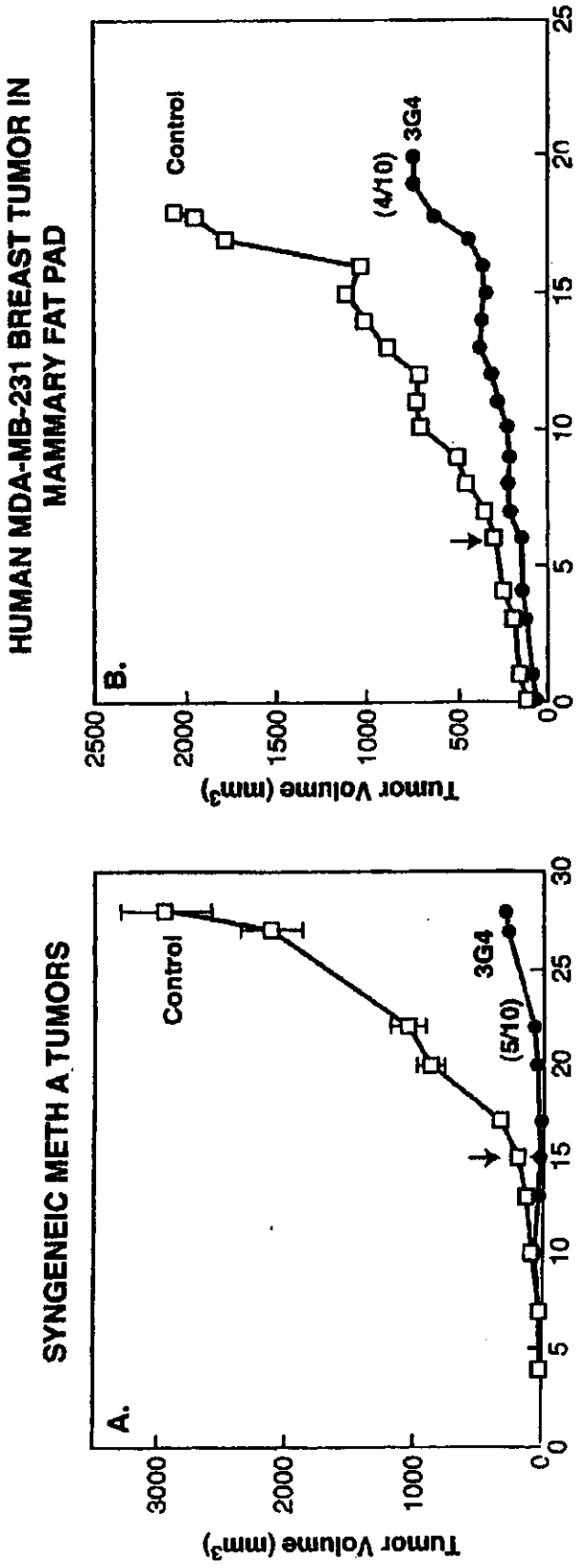


FIG. 8A

FIG. 8B

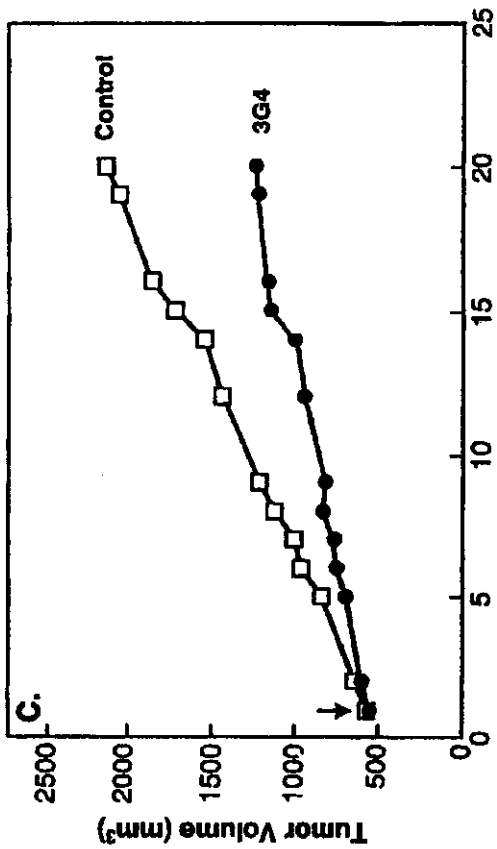


FIG. 8C

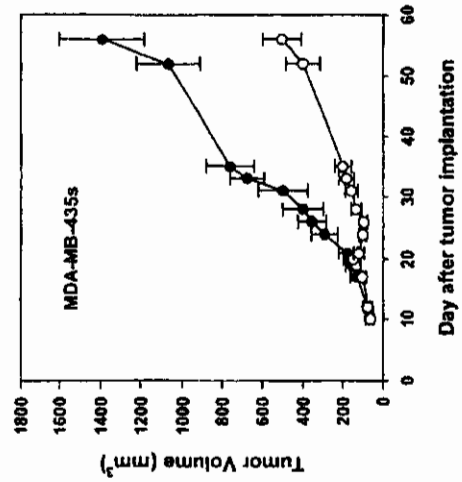


FIG. 8F

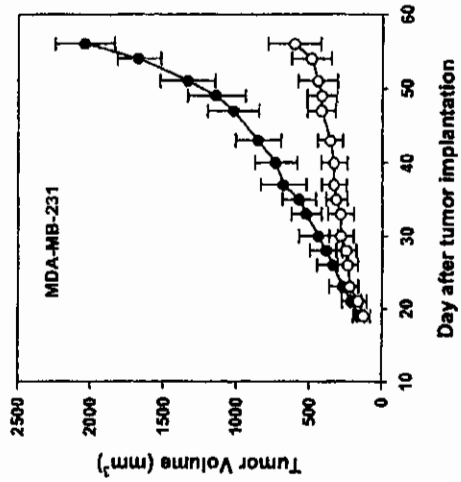


FIG. 8E

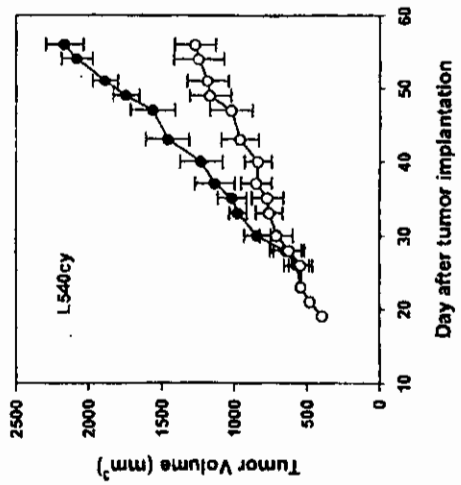


FIG. 8D

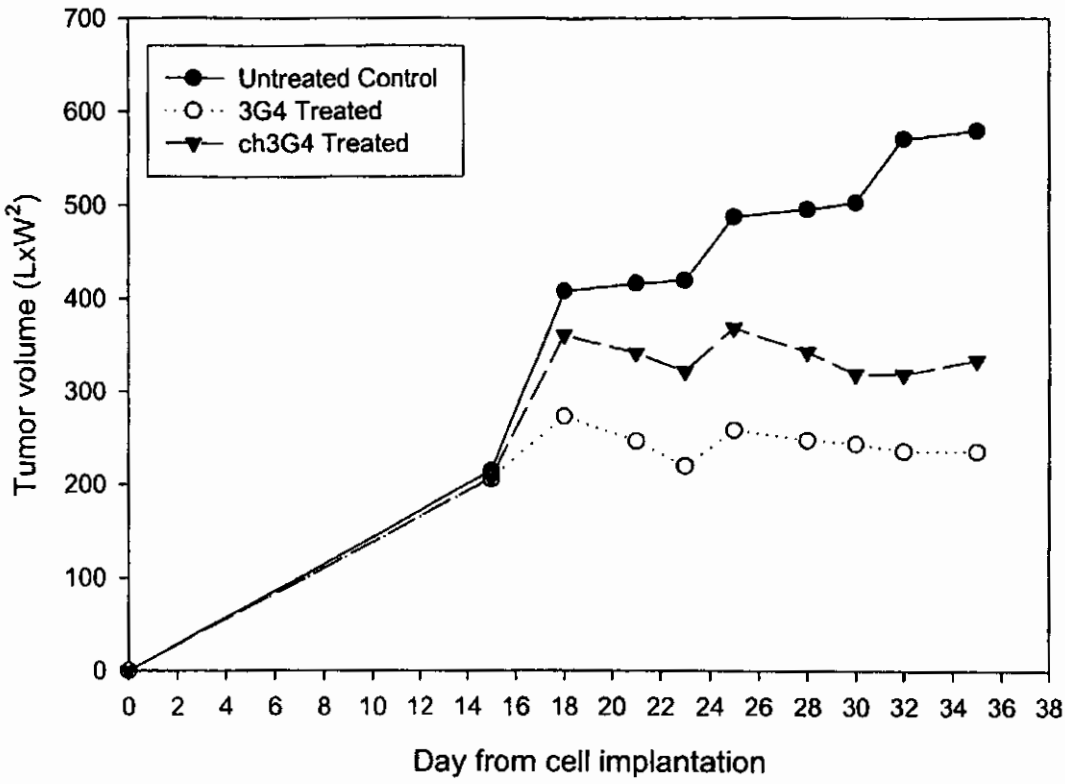

Untreated Control
3G4 Treated
ch3G4 Treated
Tumor volume (LxW²)
Day from cell implantation
0
100
200
300
400
500
600
700
0 2 4 6 8 10 12 14 16 18 20 22 24 26 28 30 32 34 36 38

FIG. 8G

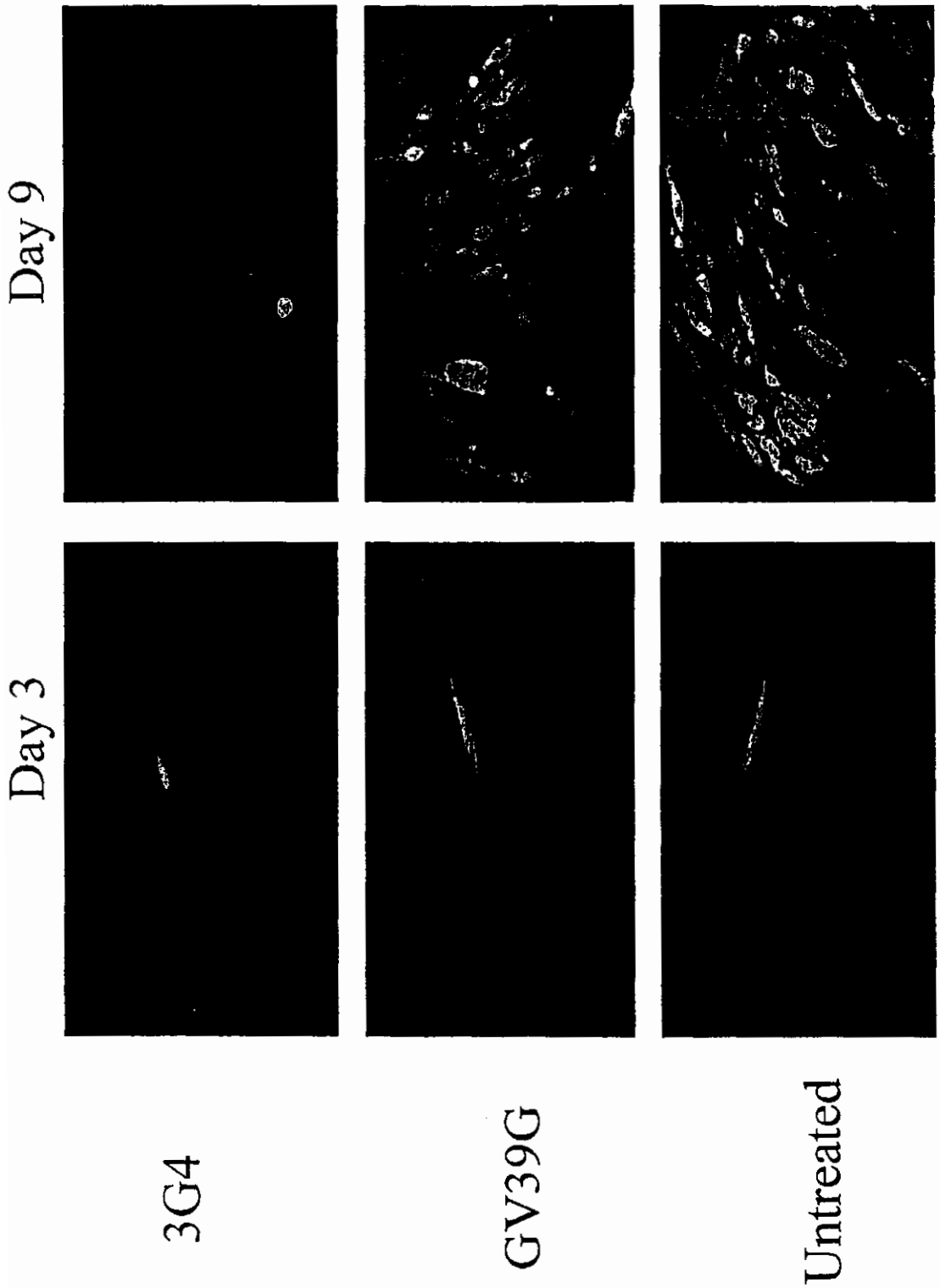


FIG. 9A

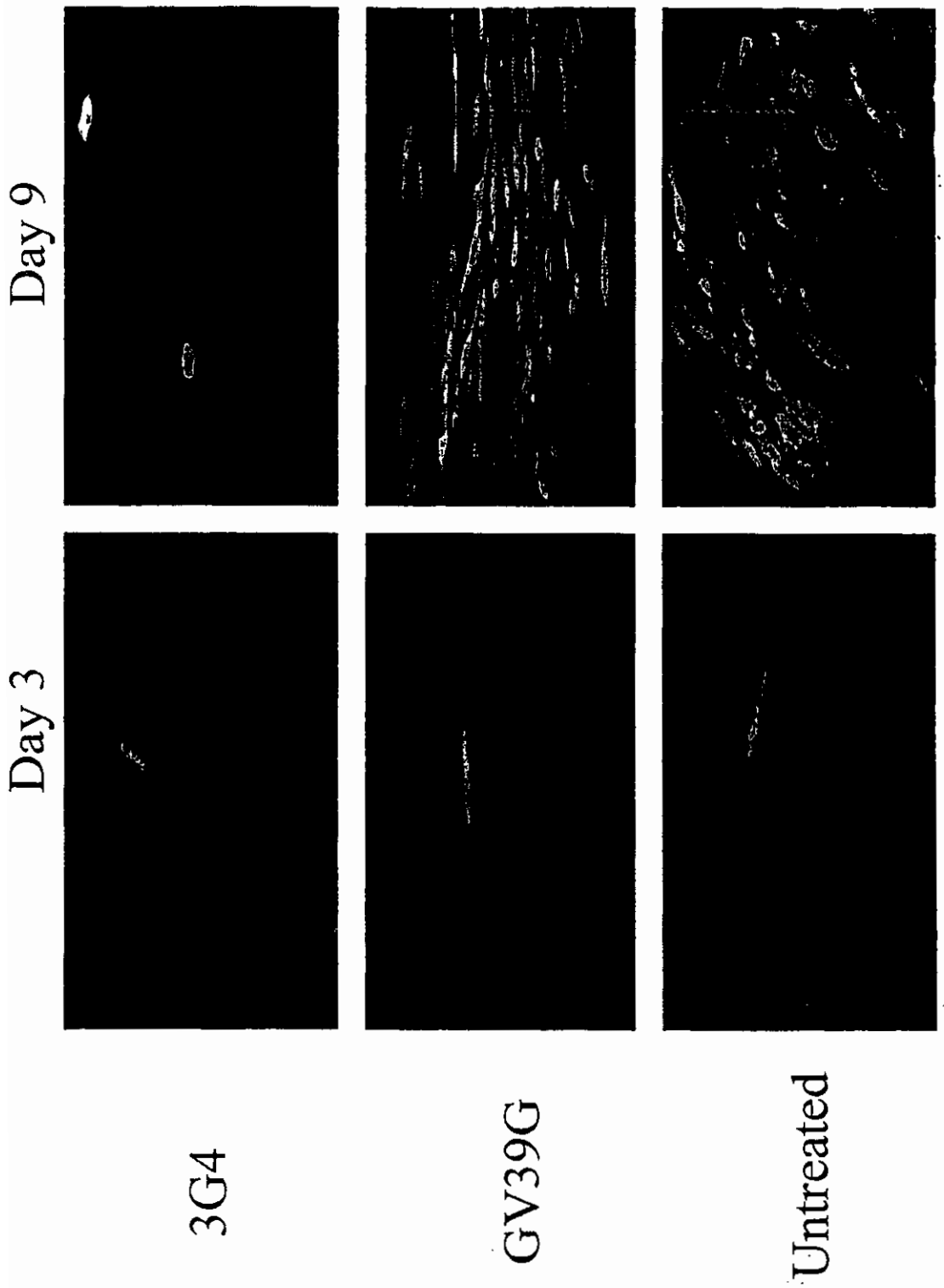


FIG. 9B

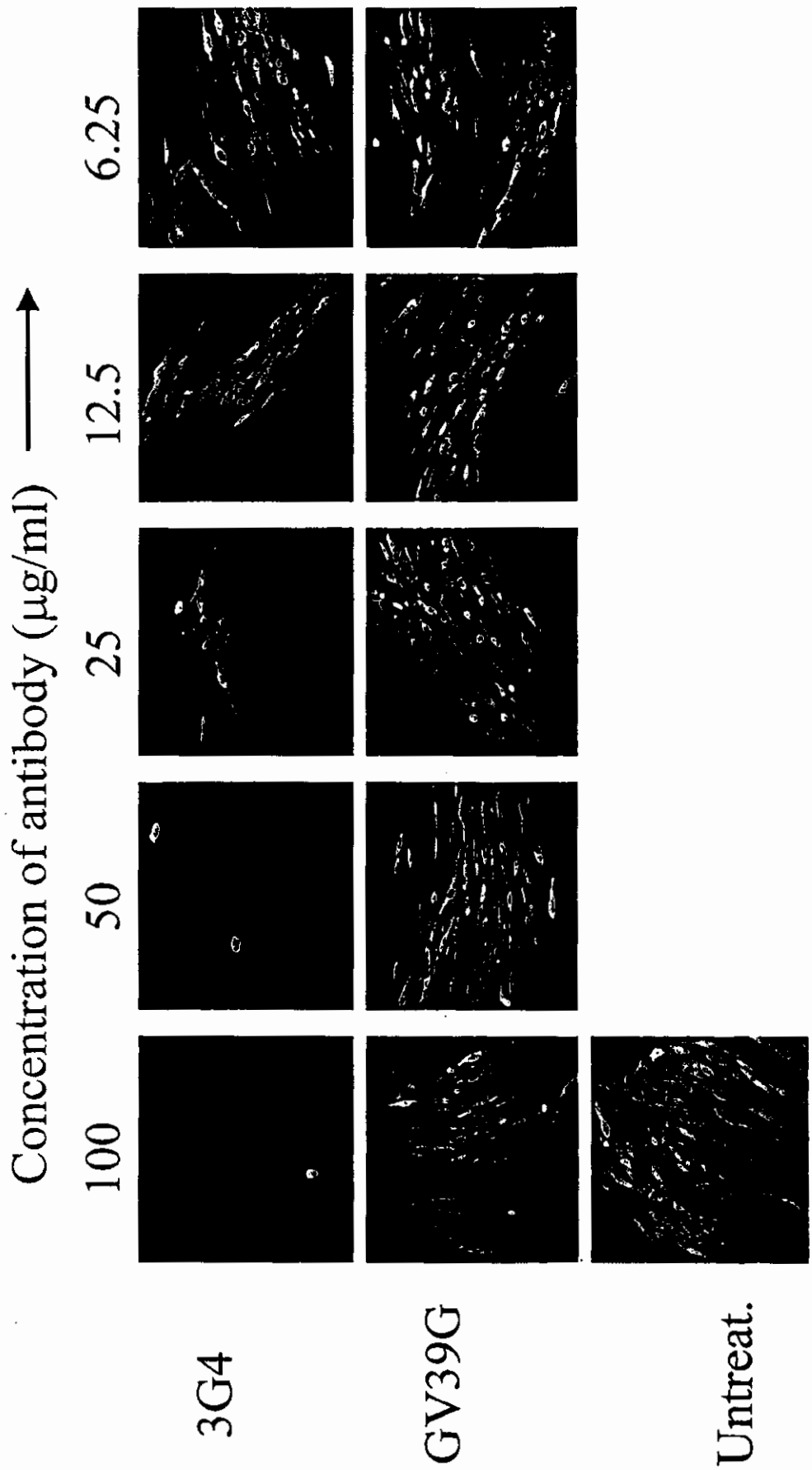

Concentration of antibody (μg/ml)
100
50
25
12.5
6.25
3G4
GV39G
Untreat.

FIG. 10

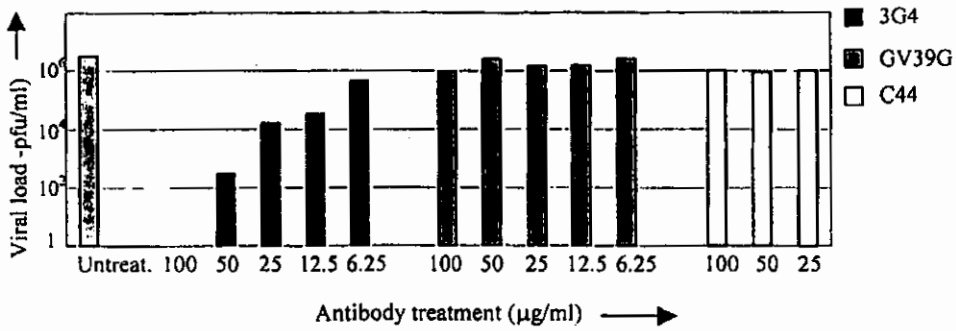


FIG. 11A

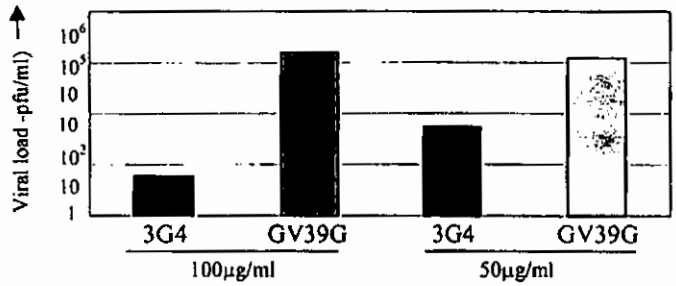


FIG. 11B

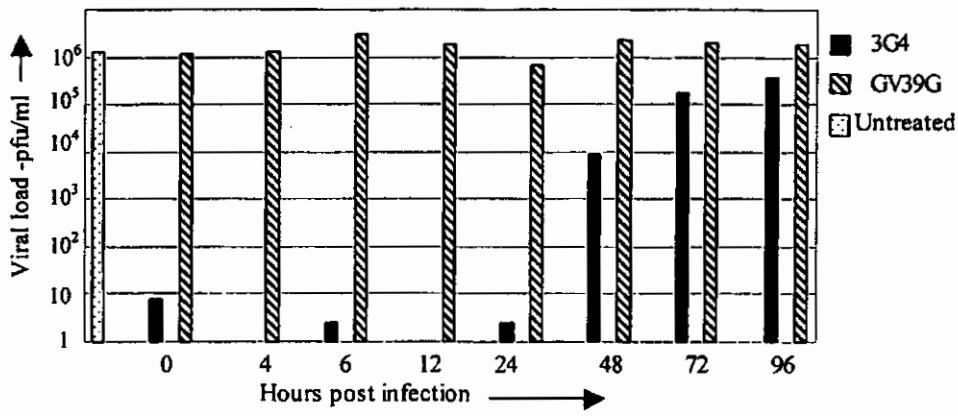

Viral load -pfu/ml
10^6
10^5
10^4
10^3
10^2
10
1
0
4
6
12
24
48
72
96
Hours post infection
3G4
GV39G
Untreated

FIG. 11C

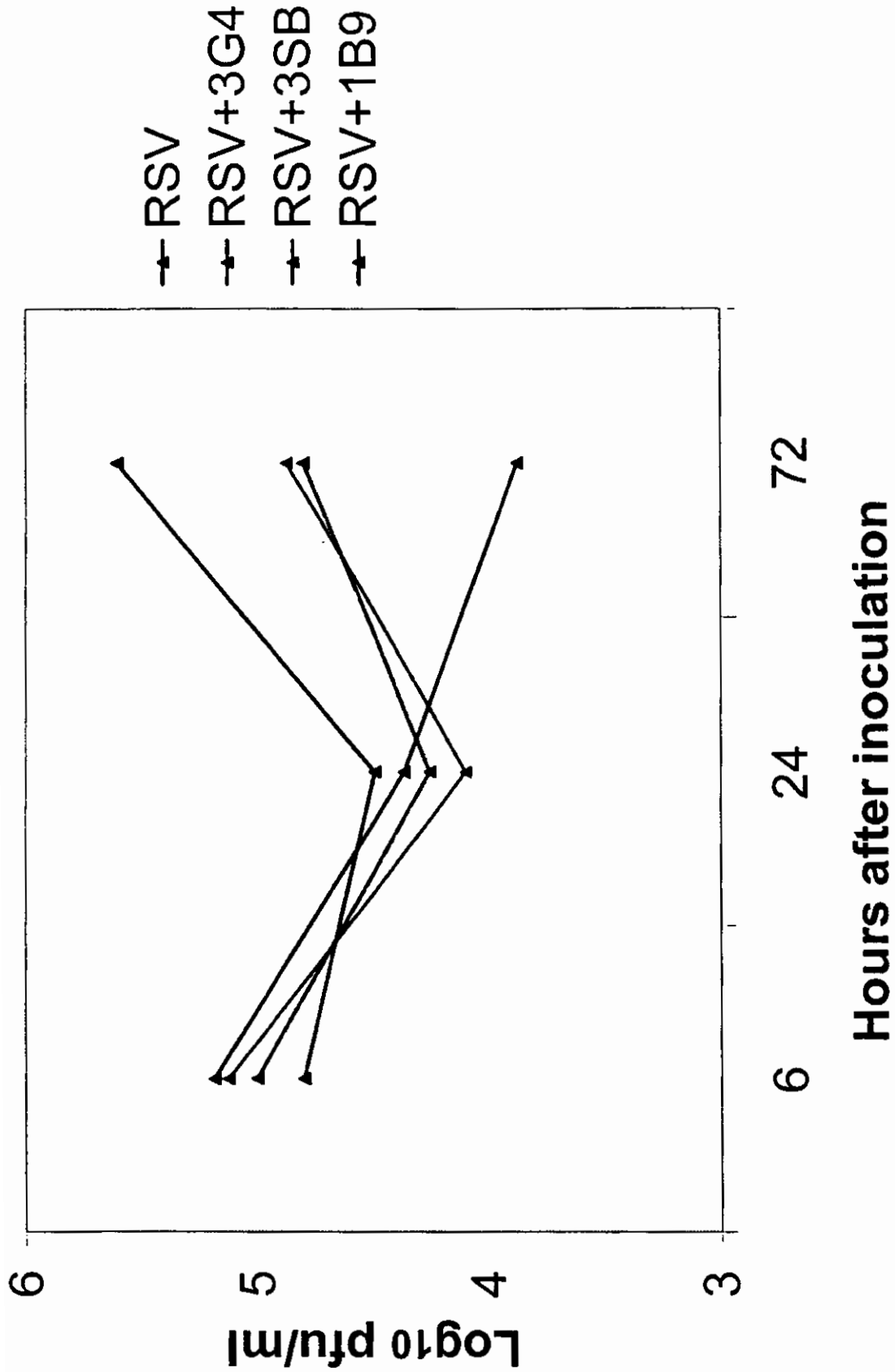

RSV
RSV+3G4
RSV+3SB
RSV+1B9
Log10 pfu/ml
6
5
4
3
6
24
72
Hours after inoculation

FIG. 12

FIG. 13A. DLB Duramycin — NH . CO . $(CH_2)_5$. NH .CO — biotin

FIG. 13B. DIB

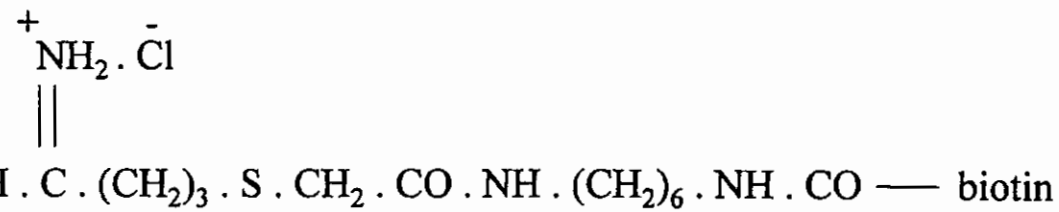


FIG. 13C. $(DLB)_4NA$

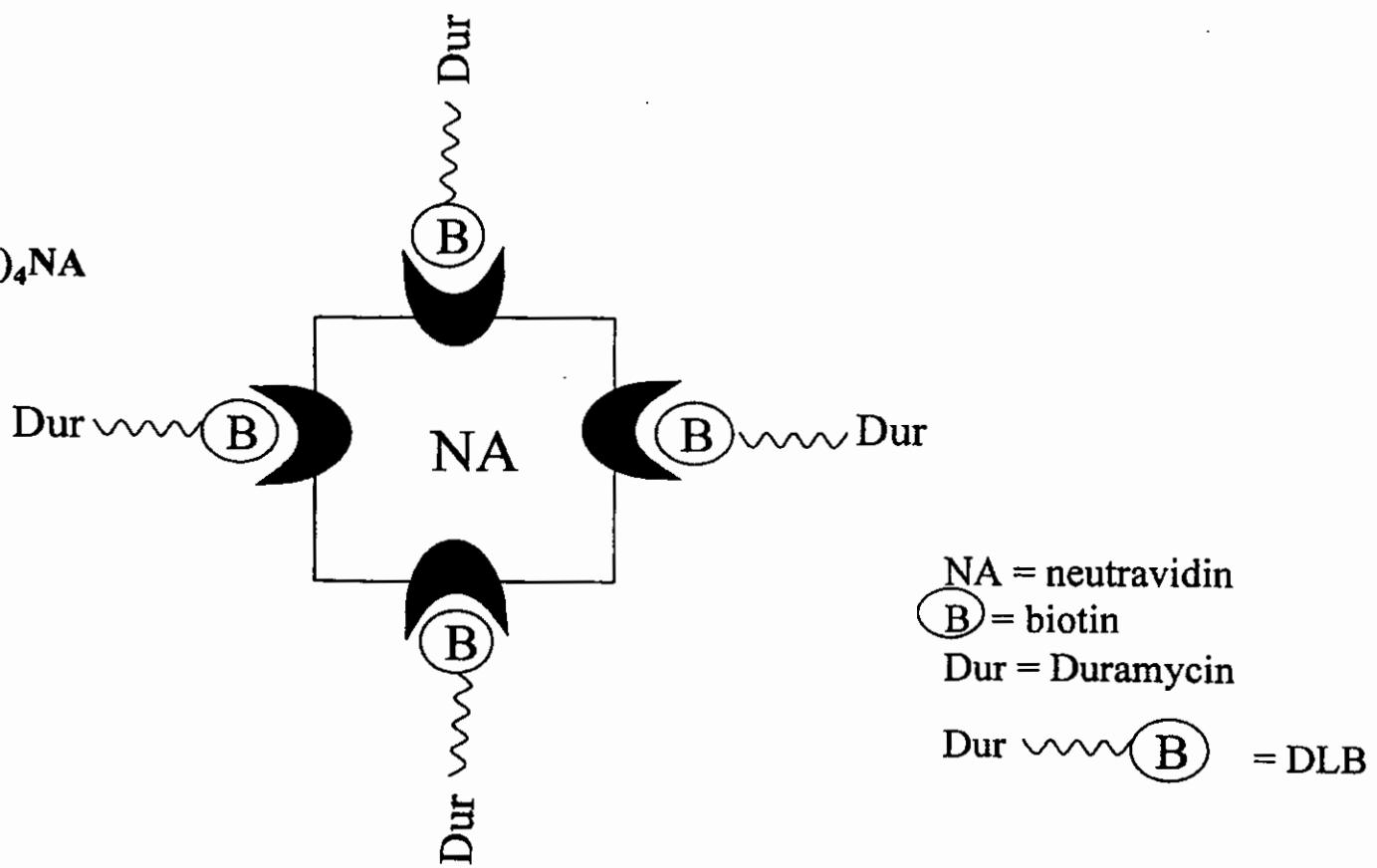
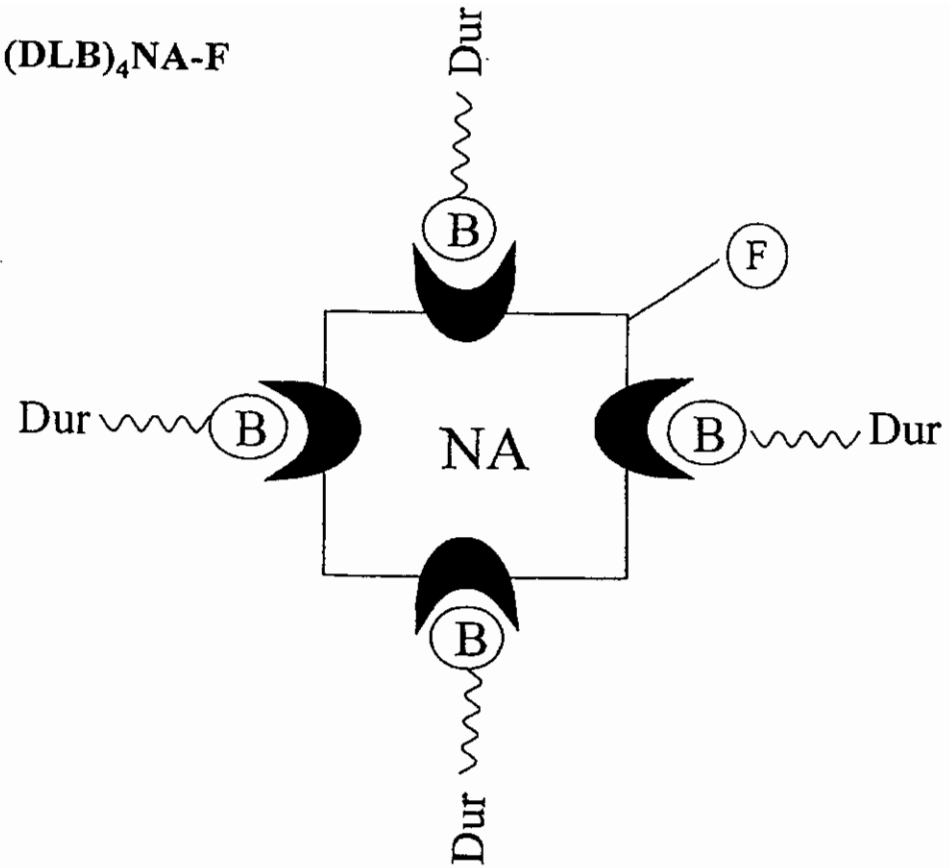


FIG. 13D. $(DLB)_4NA$-F

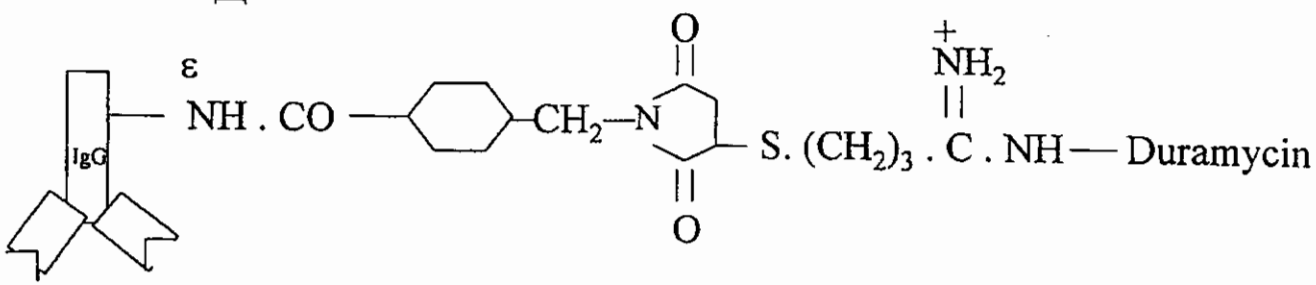


NA = neutravidin
(B) = biotin
Dur = Duramycin

Dur ~ (B) = DLB

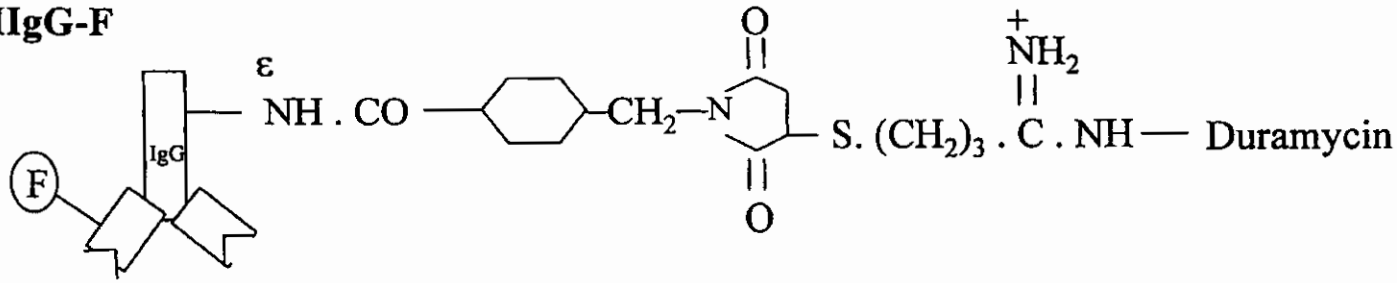
(F) = fluorescein

FIG. 13E. $(DIM)_n$ HIgG



n = 5 to 8 Duramycin residues per IgG
Monomer (150,000 Da) is shown

FIG. 13F. $(DIM)_n$ HIgG-F

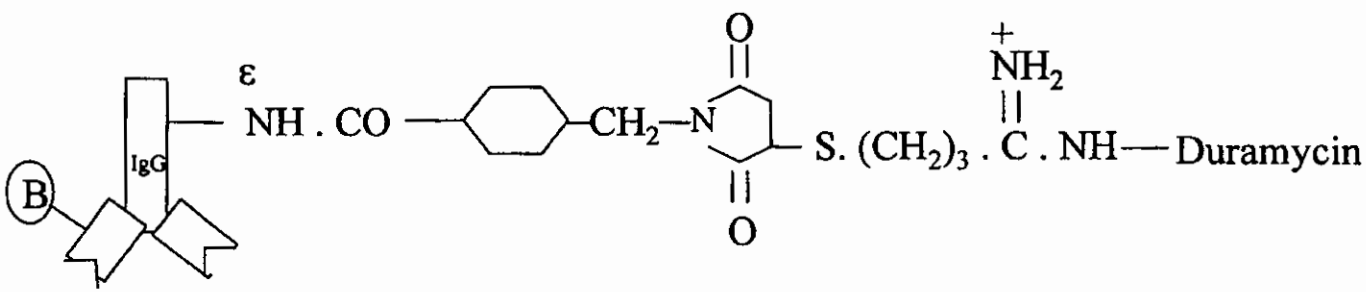


n = 5 to 8 Duramycin residues per IgG

(F) = fluorescein

Monomer (150,000 Da) is shown

FIG. 13G. $(DIM)_n$ HIgG-B



n = 5 to 8 Duramycin residues per IgG

(B) = biotin

Monomer (150,000 Da) is shown

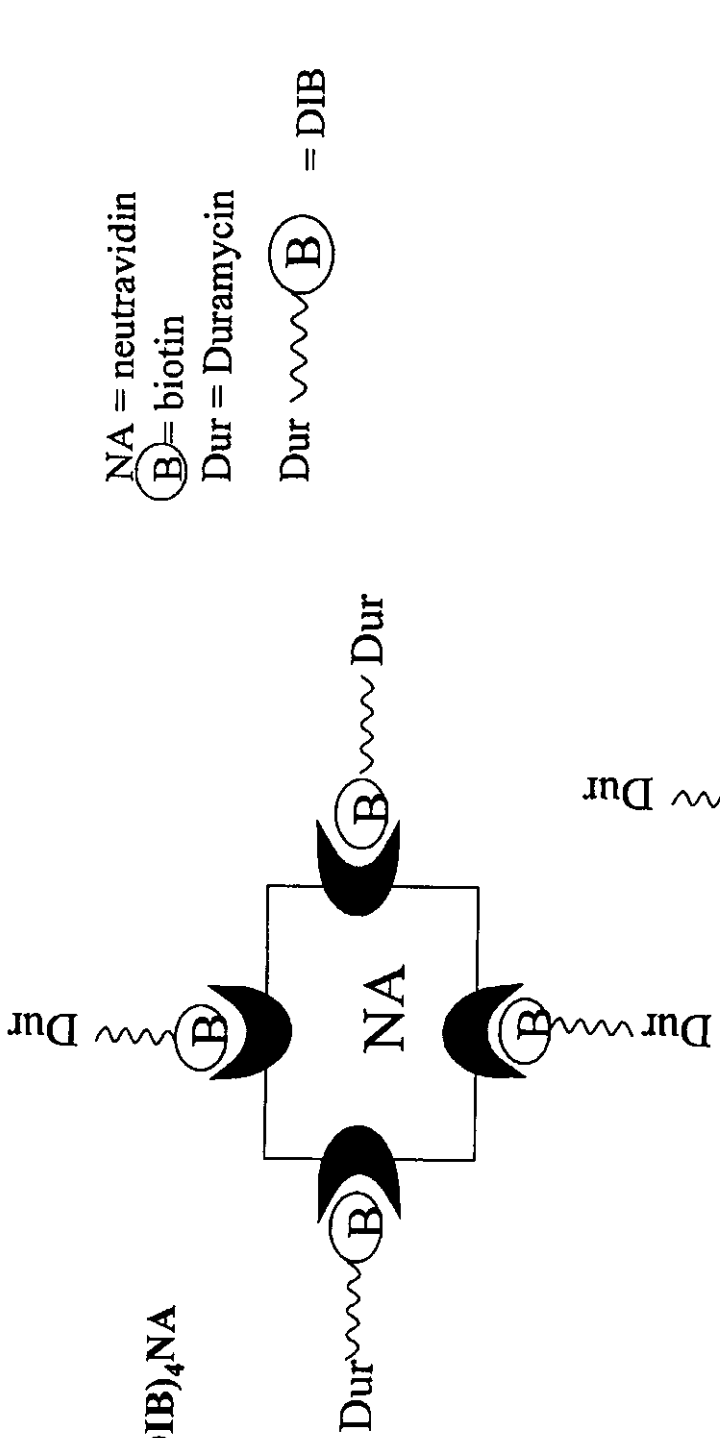


FIG. 13H. $(DIB)_4NA$

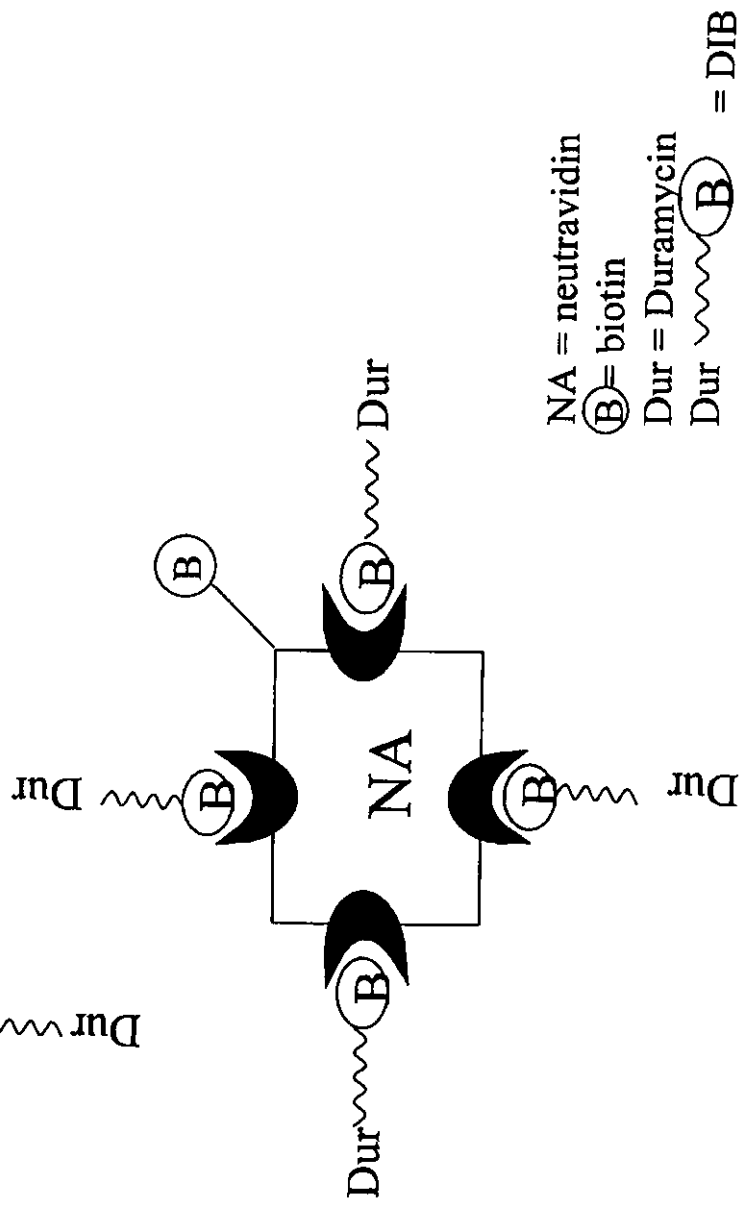


FIG. 13I. $(DIB)_4NA\text{-}B$

FIG. 13J. DS-1

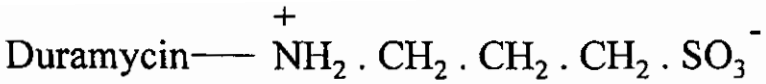


FIG. 13K. DS-2

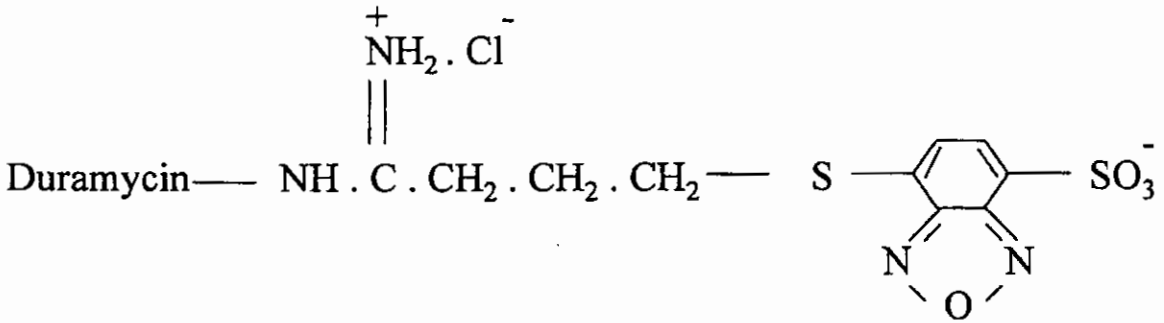


FIG. 13L. DS-3

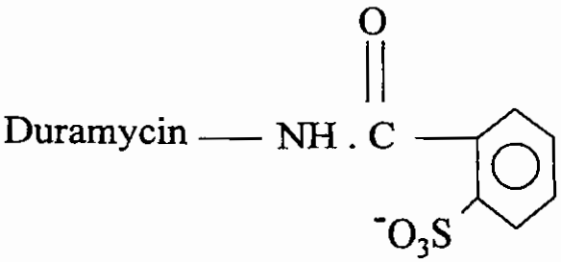


FIG. 13M. DS-4

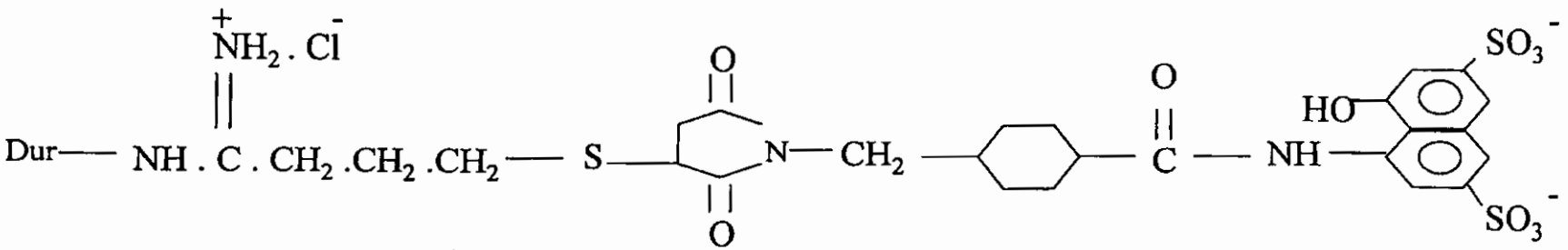
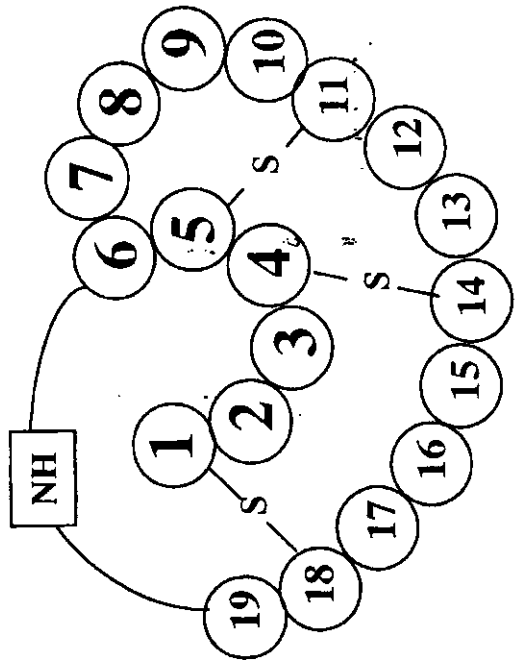


FIG. 13N. DS-5

FIG. 13O. DC-1


NH
1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
S
S
S
S

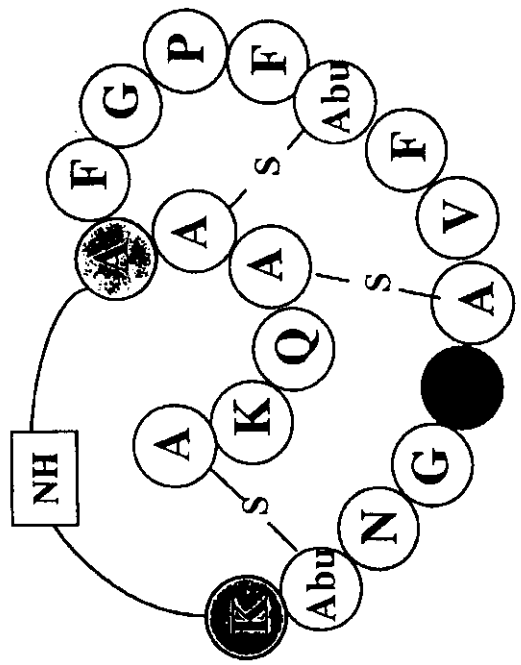

NH
A
K
Q
A
A
A
F
G
P
F
Abu
F
V
A
G
N
Abu
S
S
S
S

FIG. 13P

Lanthionine

Ala-S-Ala

cystine

β-methyllanthionine

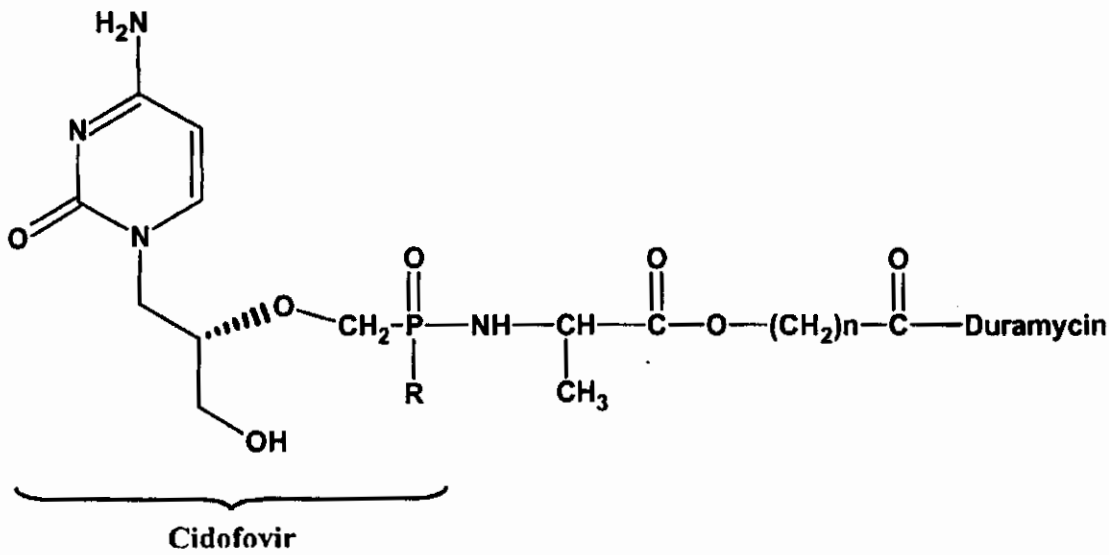
Abu-S-Ala

Lysinoalanine

Ala-NH-Lys

FIG. 13Q

FIG. 13R



R= OH, as in cidofovir, or labile hydrophobic group

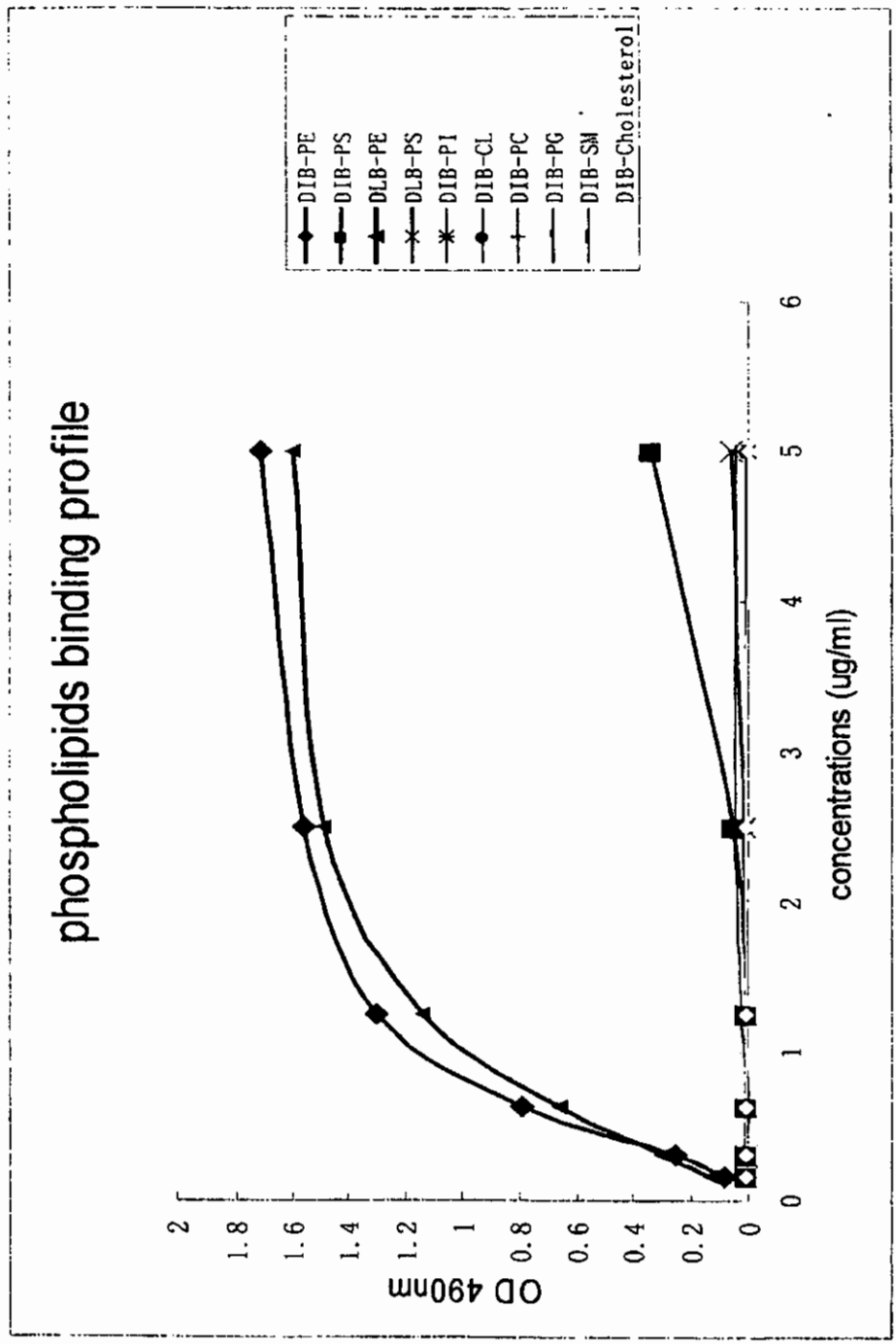

phospholipids binding profile
OD 490nm
concentrations (ug/ml)
DIB-PE
DIB-PS
DLB-PE
DLB-PS
DIB-PI
DIB-CL
DIB-PC
DIB-PG
DIB-SM
DIB-Cholesterol

FIG. 14A

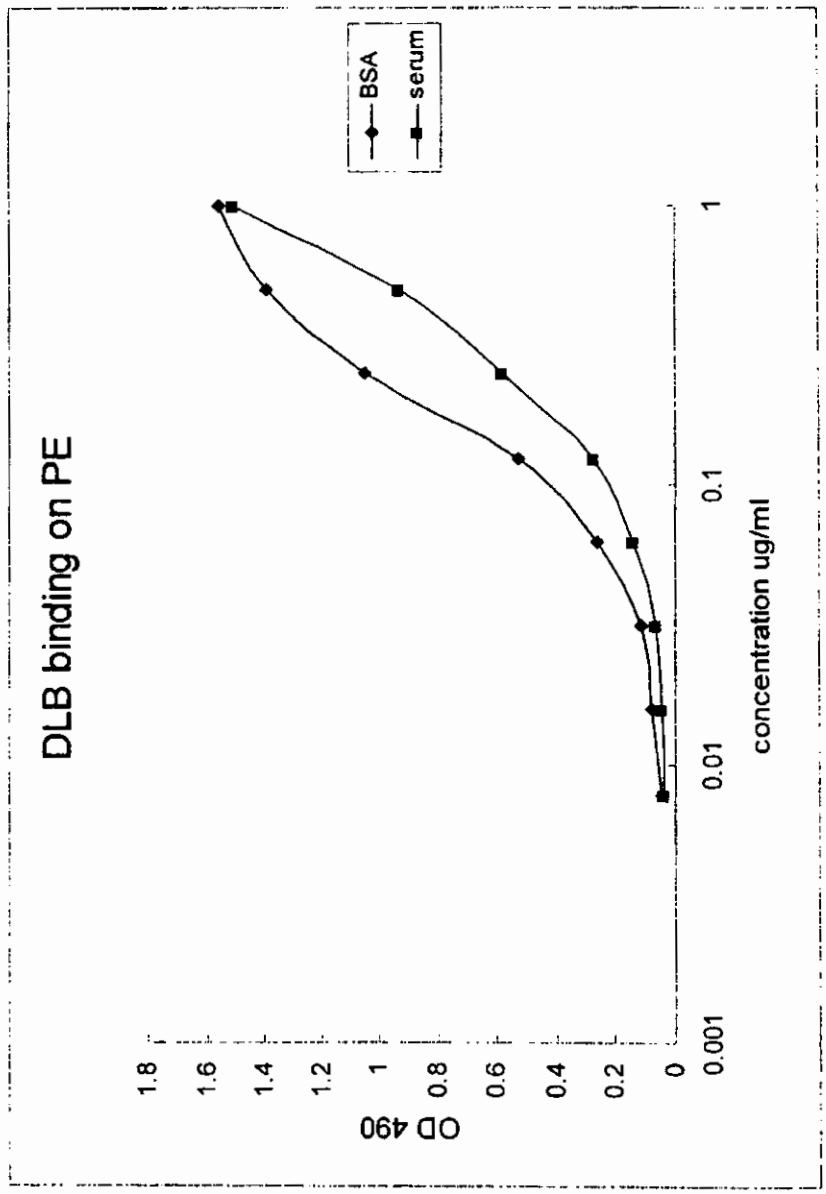

DLB binding on PE
BSA
serum
OD 490
1.8
1.6
1.4
1.2
1
0.8
0.6
0.4
0.2
0
0.001
0.01
0.1
1
concentration ug/ml

FIG. 14B

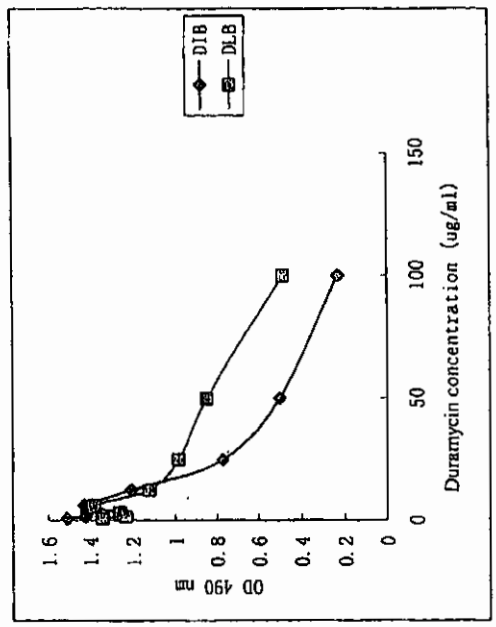


FIG. 14D

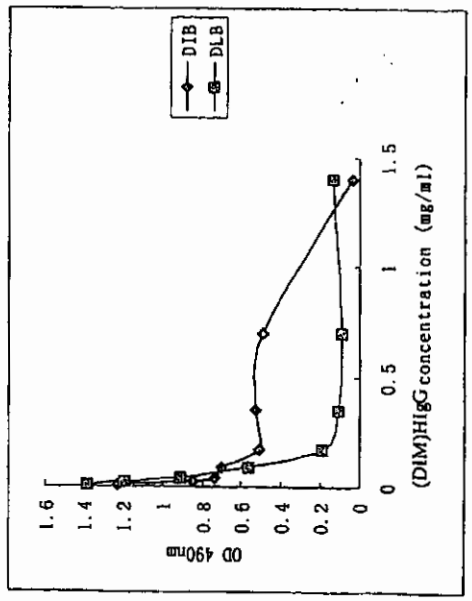


FIG. 14C

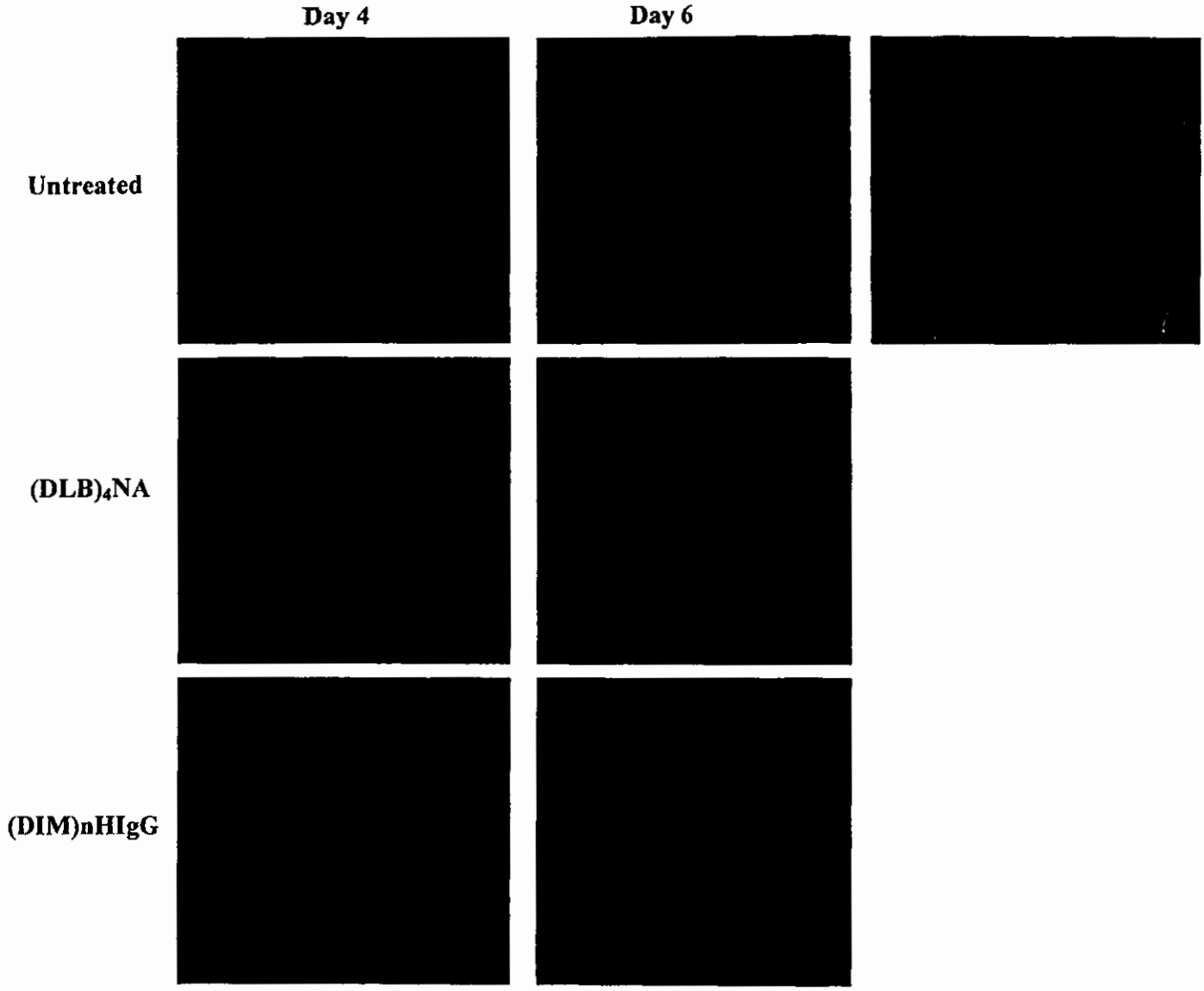


FIG. 15

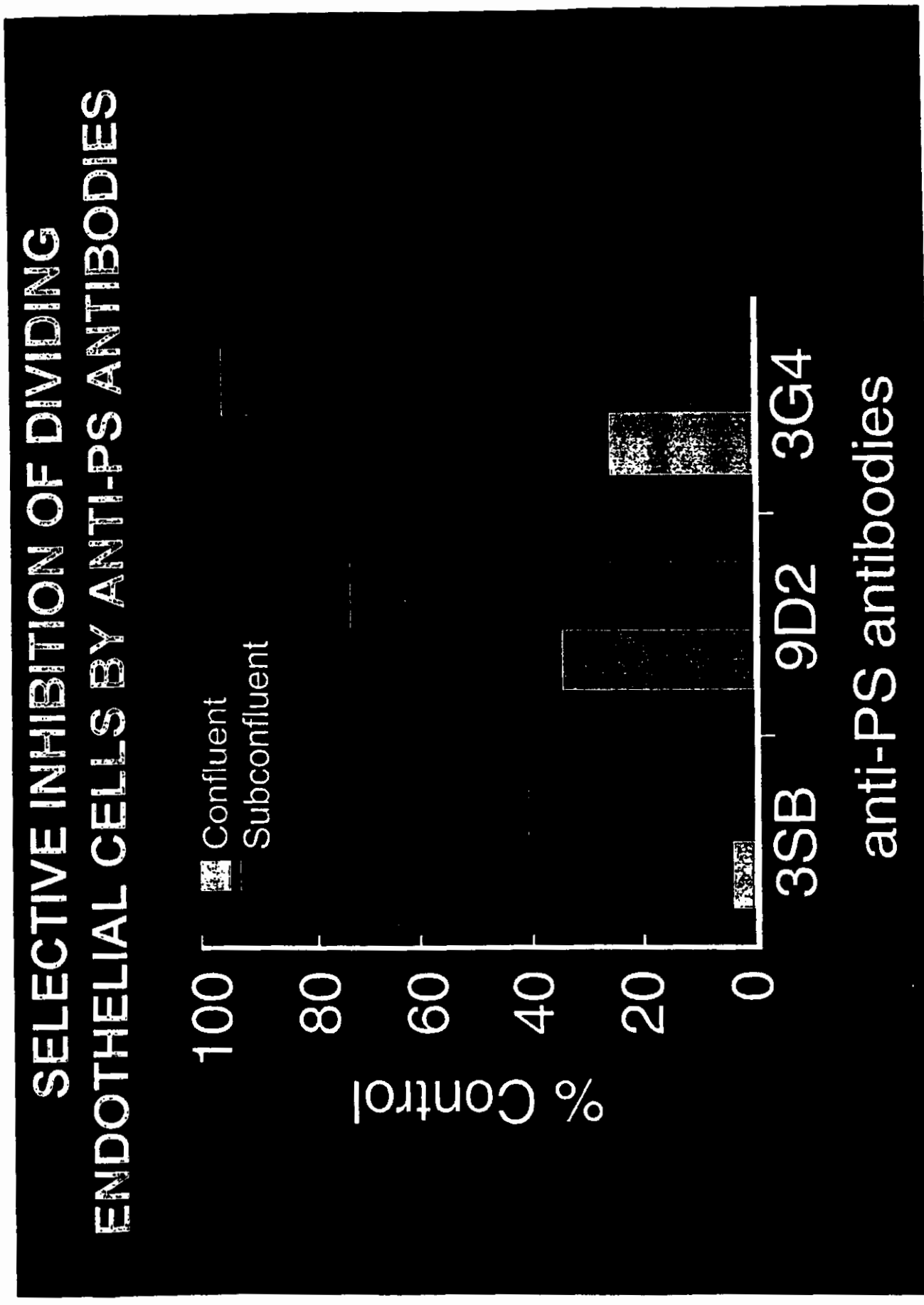

SELECTIVE INHIBITION OF DIVIDING
ENDOTHELIAL CELLS BY ANTI-PS ANTIBODIES
Confluent
Subconfluent
% Control
100
80
60
40
20
0
3SB
9D2
3G4
anti-PS antibodies

FIG. 16

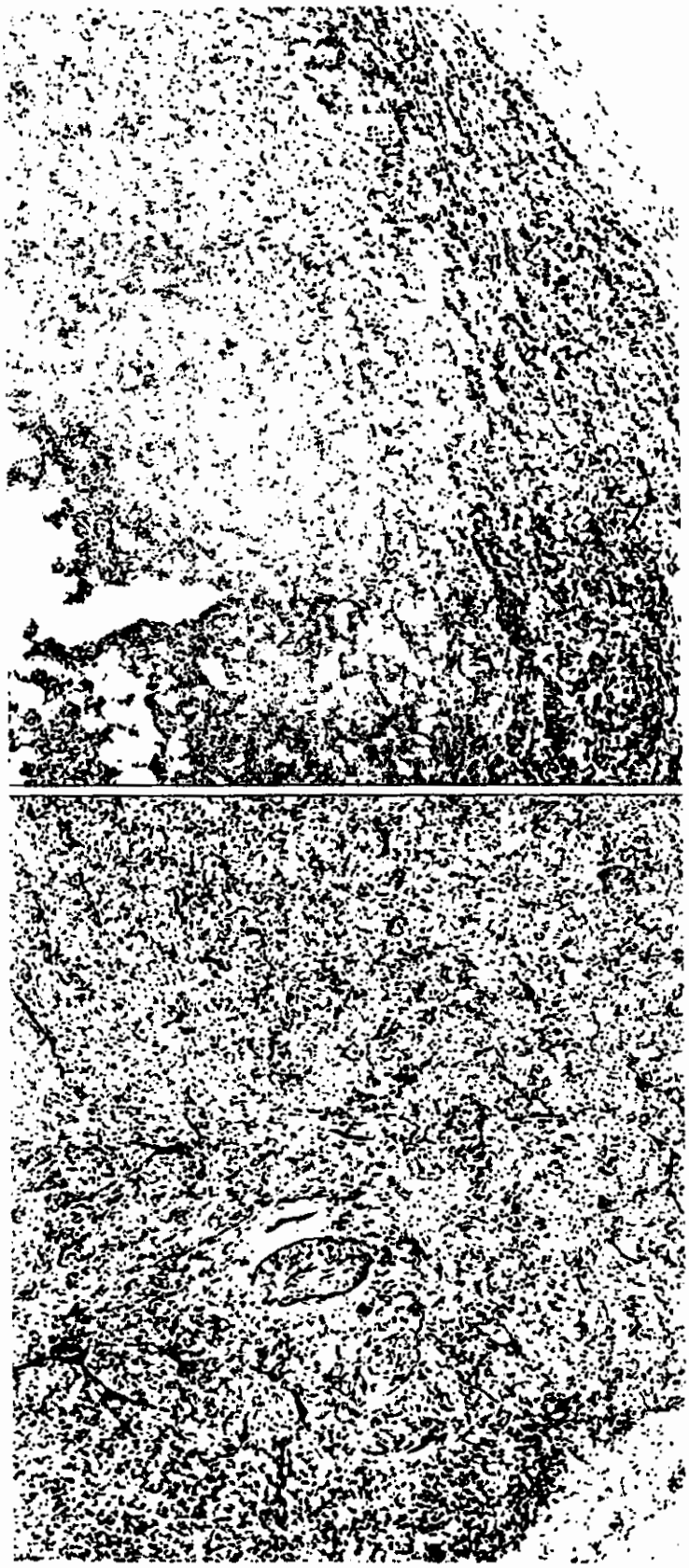


FIG. 17A

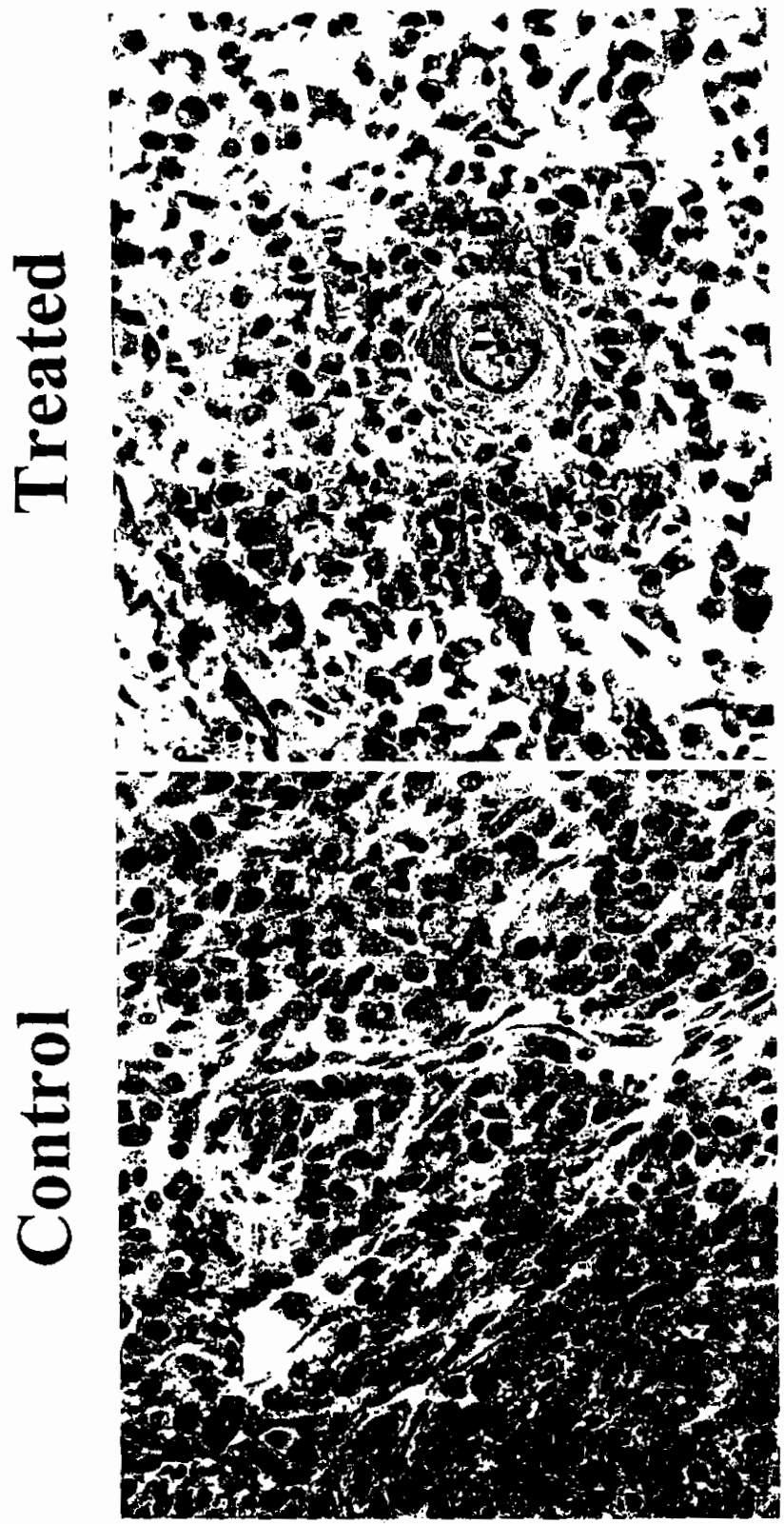


FIG. 17B

FIG. 18A

3G4-2BVH original sequence:

```
                                        M  G  W  T  W  I  F  I  L  I  L  S  V
121                                     ATG GGA TGG ACC TGG ATC TTT ATT TTA ATC CTG TCA GTA
                                        TAC CCT ACC TGG ACC TAG AAA TAA AAT TAG GAC AGT CAT
                                           PvuII
                                           --------
        T  T  G  V  H  S  E  V  Q  L  Q  Q  S  G  P  E  L  E  K  P
181     ACT ACA GGT GTC CAC TCT GAG GTC CAG CTG CAG CAG TCT GGA CCT GAG CTG GAG AAG CCT
        TGA TGT CCA CAG GTG AGA CTC CAG GTC GAC GTC GTC AGA CCT GGA CTC GAC CTC TTC GGA
        G  A  S  V  K  L  S  C  K  A  S  G  Y  S  F  T  G  Y  N  M
241     GGC GCT TCA GTG AAG CTA TCC TGC AAG GCT TCT GGT TAC TCA TTC ACT GGC TAC AAC ATG
        CCG CGA AGT CAC TTC GAT AGG ACG TTC CGA AGA CCA ATG AGT AAG TGA CCG ATG TTG TAC
        N  W  V  K  Q  S  H  G  K  S  L  E  W  I  G  H  I  D  P  Y
301     AAC TGG GTG AAA CAG AGC CAT GGA AAG AGC CTT GAA TGG ATT GGA CAT ATT GAT CCT TAC
        TTG ACC CAC TTT GTC TCG GTA CCT TTC TCG GAA CTT ACC TAA CCT GTA TAA CTA GGA ATG
        Y  G  D  T  S  Y  N  Q  K  F  R  G  K  A  T  L  T  V  D  K
361     TAT GGT GAT ACT TCC TAC AAC CAG AAG TTC AGG GGC AAG GCC ACA TTG ACT GTA GAC AAA
        ATA CCA CTA TGA AGG ATG TTG GTC TTC AAG TCC CCG TTC CGG TGT AAC TGA CAT CTG TTT
        S  S  S  T  A  Y  M  Q  L  K  S  L  T  S  E  D  S  A  V  Y
421     TCC TCC AGC ACA GCC TAC ATG CAG CTC AAG AGC CTG ACA TCT GAG GAC TCT GCA GTC TAT
        AGG AGG TCG TGT CGG ATG TAC GTC GAG TTC TCG GAC TGT AGA CTC CTG AGA CGT CAG ATA
        Y  C  V  K  G  G  Y  Y  G  H  W  Y  F  D  V  W  G  A  G  T
481     TAC TGT GTA AAG GGG GGT TAC TAC GGG CAC TGG TAC TTC GAT GTC TGG GGC GCA GGG ACC
        ATG ACA CAT TTC CCC CCA ATG ATG CCC GTG ACC ATG AAG CTA CAG ACC CCG CGT CCC TGG
          BstEII
          ----------
        T  V  T  V  S  S  A  T  T  T  A  P  S  V  Y  P  L  V  P
541     ACG GTC ACC GTC TCC TCA GCT ACA ACA ACA GCC CCA TCT GTC TAT CCC TTG GTC CCG GGC
        TGC CAG TGG CAG AGG AGT CGA TGT TGT TGT CGG GGT AGA CAG ATA GGG AAC CAG GGC CCG
        BamHI                   EcoRI                                    XhoI
        --------                --------                                 --------
601     GGA TCC CCC GGG CTG CAG GAA TTC GAT ATC AAG CTT ATC GAT ACC GTC GAC CTC GAG GGG
        CCT AGG GGG CCC GAC GTC CTT AAG CTA TAG TTC GAA TAG CTA TGG CAG CTG GAG CTC CCC
```

The RACE product 3G4-2BVH is cloned and grafted onto the human γ1 constant region at the BstEII site. Thus, it contains the mouse leader sequence and its VH is joined with the human CH1 sequence in the following way: leader/3G4VH/VSS-AST...

```
      Mouse Leader              ↓mature protein
   1  MGWTWIFILI LSVTTGVHSE VQLQQSGPEL EKPGASVKLS CKASGYSFTG
  51  YNMNWVKQSH GKSLEWIGHI DPYYGDTSYN QKFRGKATLT VDKSSSTAYM
                                                ↓BstEII graft site
 101  QLKSLTSEDS AVYYCVKGGY YGHWYFDVWG AGTTVTVSS ASTKGPSVFPL
 151  APSSKSTSG                                  ↑human γ1CH1
```

FIG. 18B

3G4-2BVL original sequence:

```
                                                                  M   D   M   R   A
                                                                  ATG GAC ATG AGG GCT
61                                                                TAC CTG TAC TCC CGA
          P   A   Q   I   L   G   F   L   L   L   L   F   P   G   T   R   C   D   I   Q
121       CCT GCA CAG ATT TTG GGC TTC TTG TTG CTC TTG TTT CCA GGT ACC AGA TGT GAC ATC CAG
          GGA CGT GTC TAA AAC CCG AAG AAC AAC GAG AAC AAA GGT CCA TGG TCT ACA CTG TAG GTC
          M   T   Q   S   P   S   S   L   S   A   S   L   G   E   R   V   S   L   T   C
181       ATG ACC CAG TCT CCA TCC TCC TTA TCT GCC TCT CTG GGA GAA AGA GTC AGT CTC ACT TGT
          TAC TGG GTC AGA GGT AGG AGG AAT AGA CGG AGA GAC CCT CTT TCT CAG TCA GAG TGA ACA
          R   A   S   Q   D   I   G   S   S   L   N   W   L   Q   Q   G   P   D   G   T
241       CGG GCA AGT CAG GAC ATT GGT AGT AGC TTA AAC TGG CTT CAG CAG GGA CCA GAT GGA ACT
          GCC CGT TCA GTC CTG TAA CCA TCA TCG AAT TTG ACC GAA GTC GTC CCT GGT CTA CCT TGA
          I   K   R   L   I   Y   A   T   S   S   L   D   S   G   V   P   K   R   F   S
301       ATT AAA CGC CTG ATC TAC GCC ACA TCC AGT TTA GAT TCT GGT GTC CCC AAA AGG TTC AGT
          TAA TTT GCG GAC TAG ATG CGG TGT AGG TCA AAT CTA AGA CCA CAG GGG TTT TCC AAG TCA
          G   S   R   S   G   S   D   Y   S   L   T   I   S   S   L   E   S   E   D   F
361       GGC AGT AGG TCT GGG TCA GAT TAT TCT CTC ACC ATC AGC AGC CTT GAG TCT GAA GAT TTT
          CCG TCA TCC AGA CCC AGT CTA ATA AGA GAG TGG TAG TCG TCG GAA CTC AGA CTT CTA AAA
          V   D   Y   Y   C   L   Q   Y   V   S   S   P   P   T   F   G   A   G   T   K
421       GTA GAC TAT TAC TGT CTA CAA TAT GTT AGT TCT CCT CCC ACG TTC GGT GCT GGG ACC AAG
          CAT CTG ATA ATG ACA GAT GTT ATA CAA TCA AGA GGA GGG TGC AAG CCA CGA CCC TGG TTC
                                                    BbsI                BamHI
                                                    -------             --------
          L   E   L   K   R   A   D   A   A   P   T   V   F   I   F   G   R   I   P
481       CTG GAG CTG AAA CGG GCT GAT GCT GCA CCA ACT GTC TTC ATC TTC GGG CGG ATC CCC CGG
          GAC CTC GAC TTT GCC CGA CTA CGA CGT GGT TGA CAG AAG TAG AAG CCC GCC TAG GGG GCC
```

The RACE product 3G4-2BVL is grafted to human κ constant region at the BbsI site. Thus, it contains the mouse leader sequence and its VL is joined withIN the human CL1 sequence in the following way: leader/3G4-VL/TVF-IFP...

```
          Mouse Leader                ↓mature protein
  1   MDMRAPAQIL GFLLLLFPGT RCDIQMTQSP SSLSASLGER VSLTCRASQD
 51   IGSSLNWLQQ GPDGTIKRLI YATSSLDSGV PKRFSGSRSG SDYSLTISSL
                                      FR4↓          ↓BbsI graft site
101   ESEDFVDYYC LQYVSSPPTF GAGTKLELKR ADAAPTVF IFPPSDEQLKSGTAS
                                                  ↑ human kappa constant
```

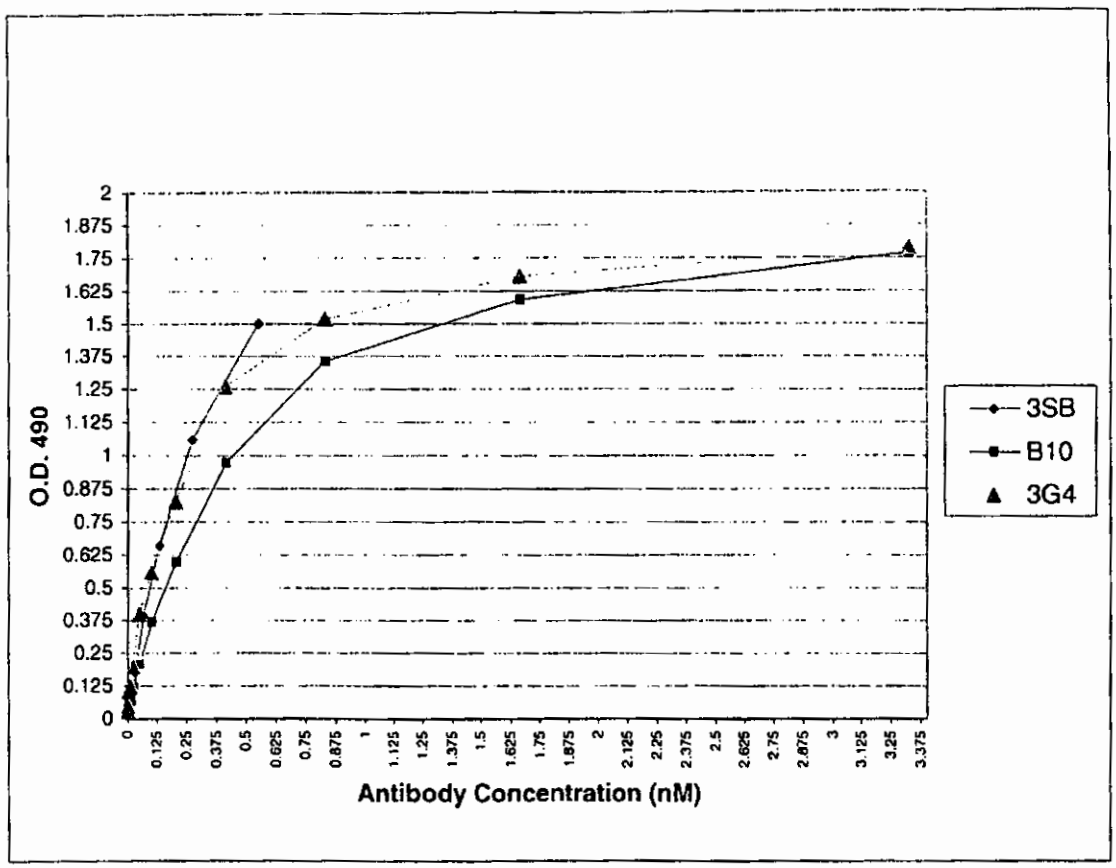

O.D. 490
2
1.875
1.75
1.625
1.5
1.375
1.25
1.125
1
0.875
0.75
0.625
0.5
0.375
0.25
0.125
0
0
0.125
0.25
0.375
0.5
0.625
0.75
0.875
1
1.125
1.25
1.375
1.5
1.625
1.75
1.875
2
2.125
2.25
2.375
2.5
2.625
2.75
2.875
3
3.125
3.25
3.375
Antibody Concentration (nM)
3SB
B10
3G4

FIG. 19A

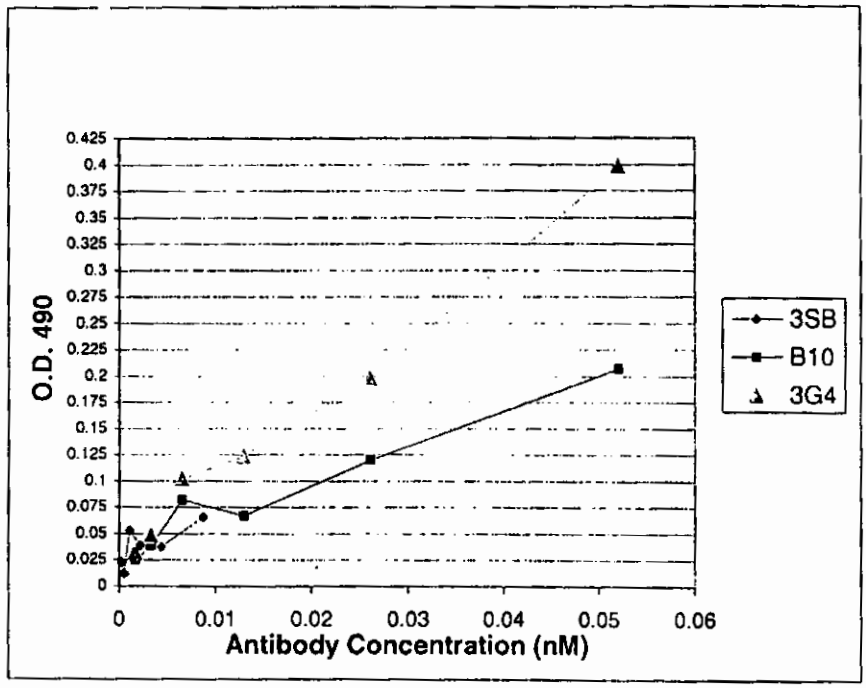

O.D. 490
0.425
0.4
0.375
0.35
0.325
0.3
0.275
0.25
0.225
0.2
0.175
0.15
0.125
0.1
0.075
0.05
0.025
0
0
0.01
0.02
0.03
0.04
0.05
0.06
Antibody Concentration (nM)
3SB
B10
3G4

FIG. 19B

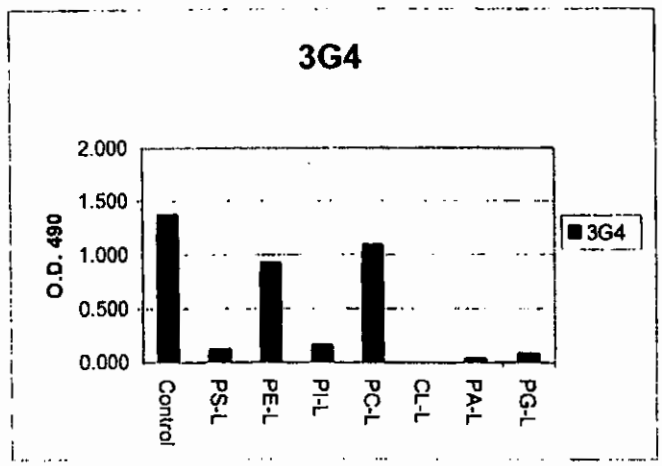

3G4
2.000
1.500
1.000
0.500
0.000
O.D. 490
3G4
Control
PS-L
PE-L
PI-L
PC-L
CL-L
PA-L
PG-L

FIG. 20

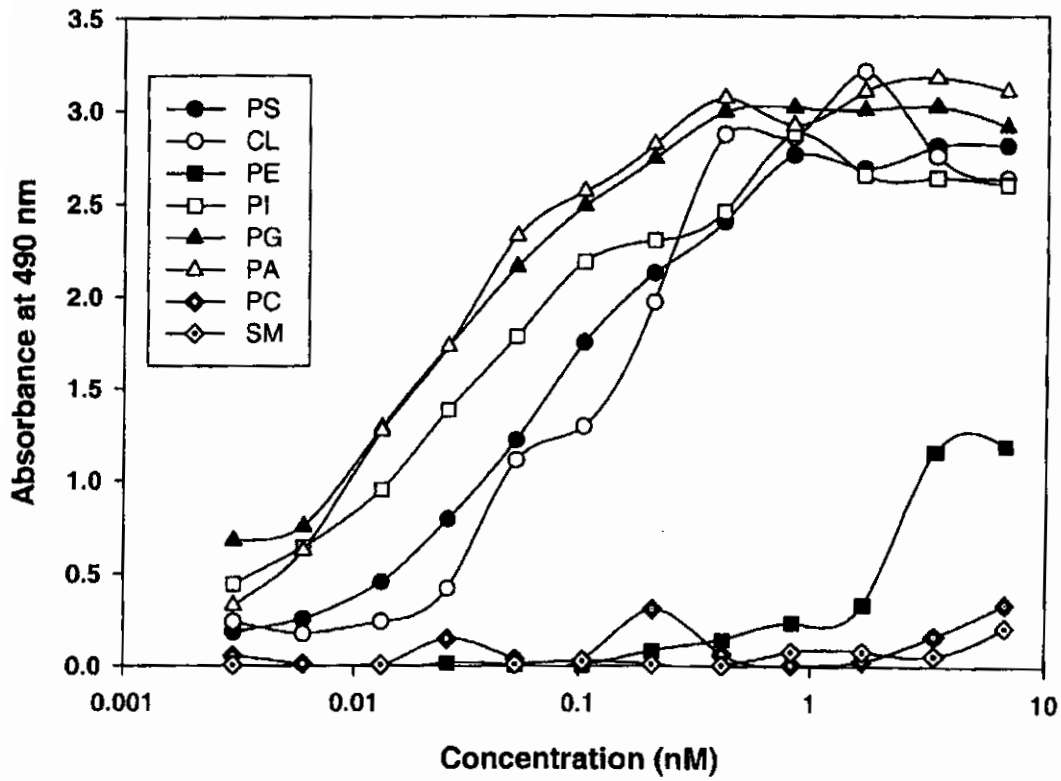

3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
Absorbance at 490 nm
PS
CL
PE
PI
PG
PA
PC
SM
0.001
0.01
0.1
1
10
Concentration (nM)

FIG. 21

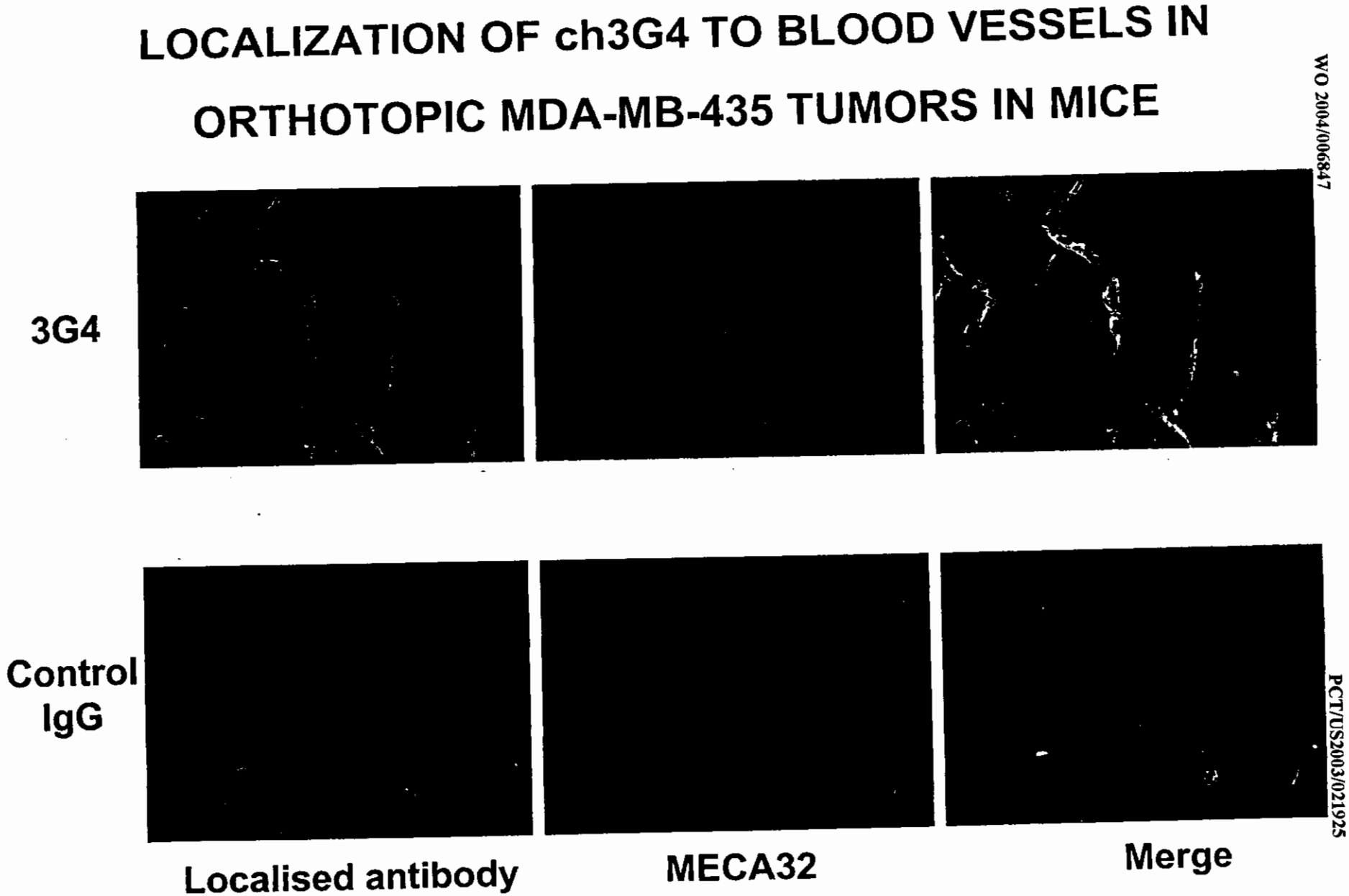

LOCALIZATION OF ch3G4 TO BLOOD VESSELS IN ORTHOTOPIC MDA-MB-435 TUMORS IN MICE
3G4
Control IgG
Localised antibody
MECA32
Merge

FIG. 22

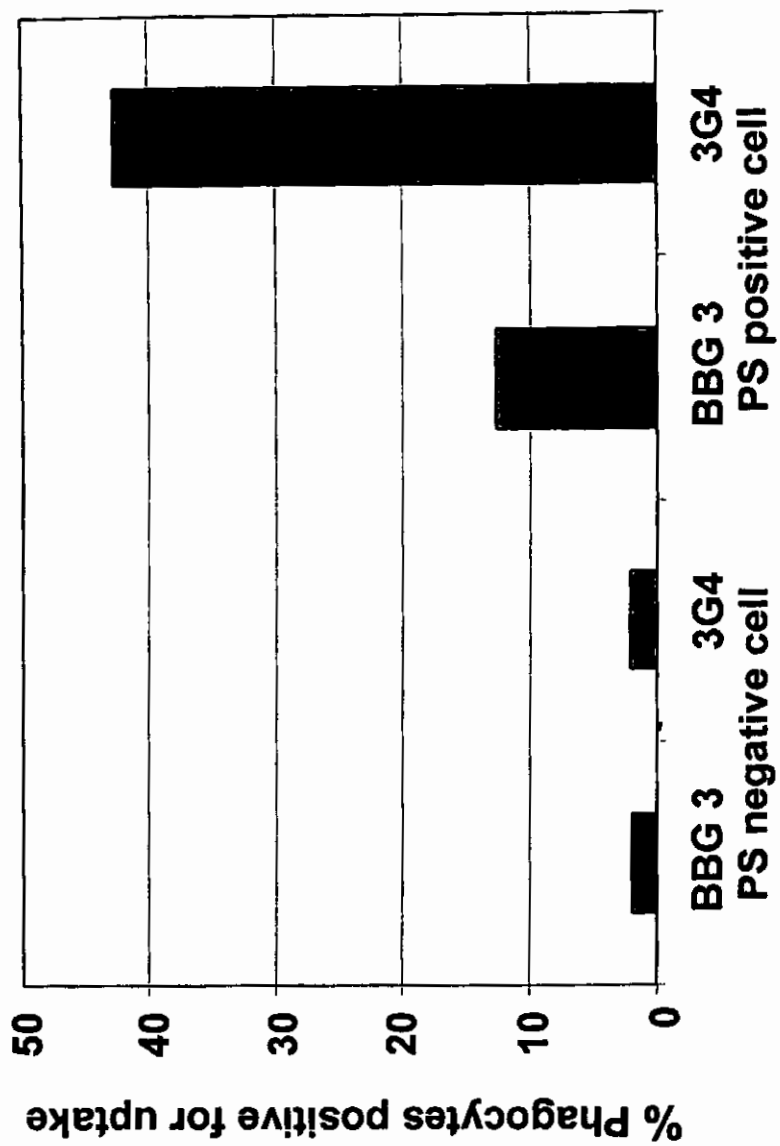

% Phagocytes positive for uptake
50
40
30
20
10
0
BBG 3 PS negative cell
3G4 PS negative cell
BBG 3 PS positive cell
3G4 PS positive cell

FIG. 23

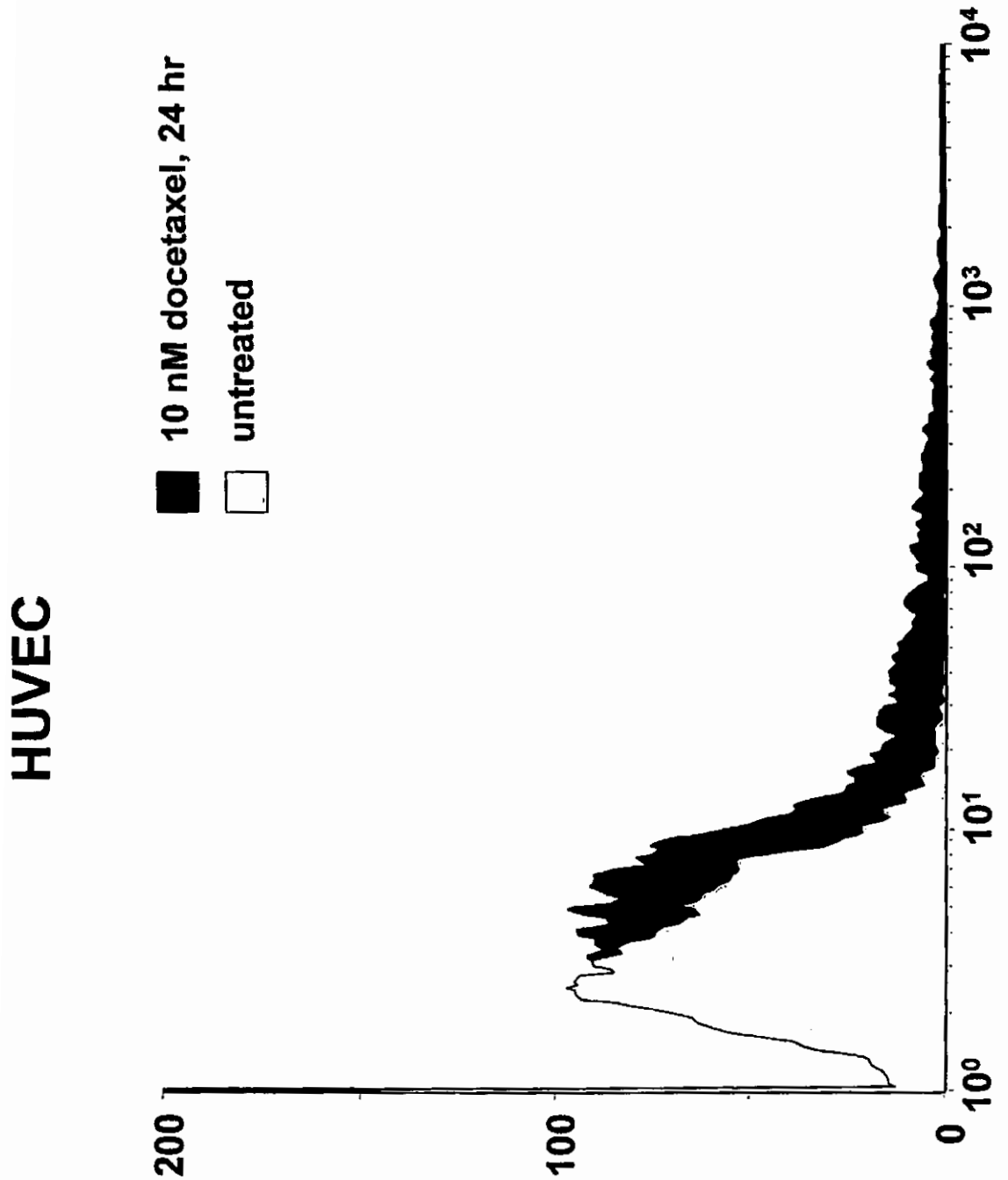

HUVEC
10 nM docetaxel, 24 hr
untreated
200
100
0
10^0
10^1
10^2
10^3
10^4

FIG. 24A

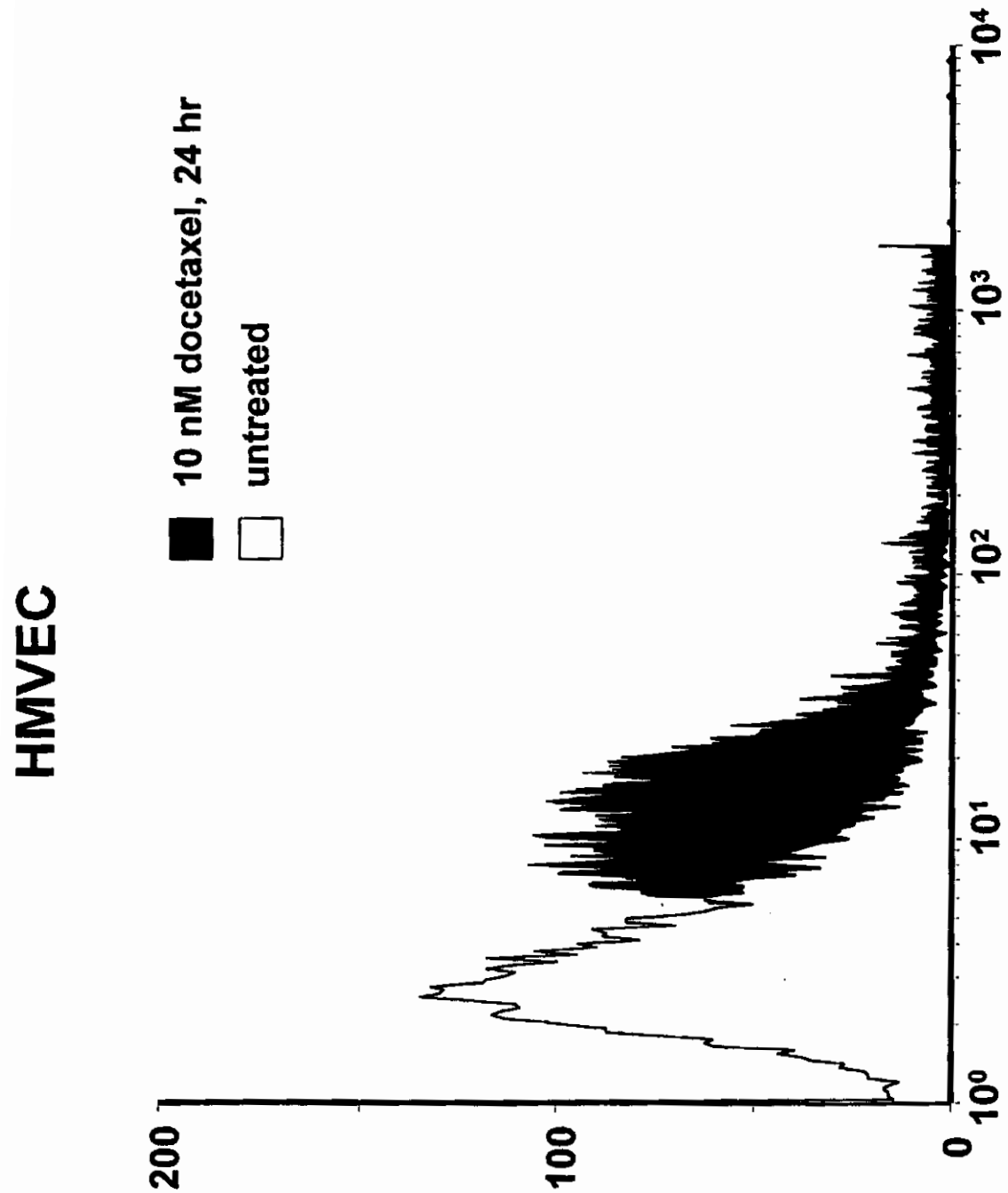

HMVEC
10 nM docetaxel, 24 hr
untreated
200
100
0
10^0
10^1
10^2
10^3
10^4

FIG. 24B

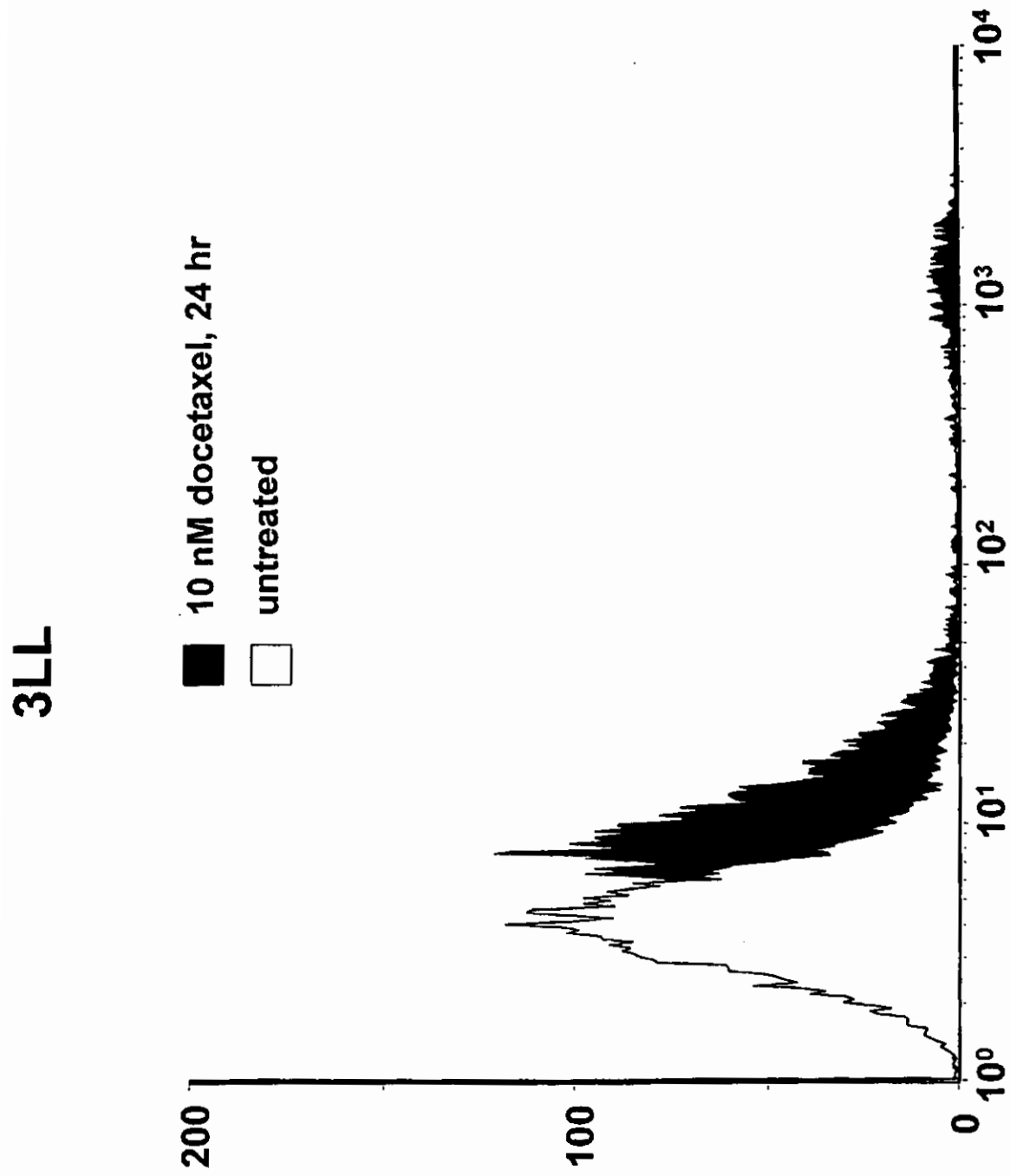

3LL
10 nM docetaxel, 24 hr
untreated
200
100
0
10^0
10^1
10^2
10^3
10^4

FIG. 25A

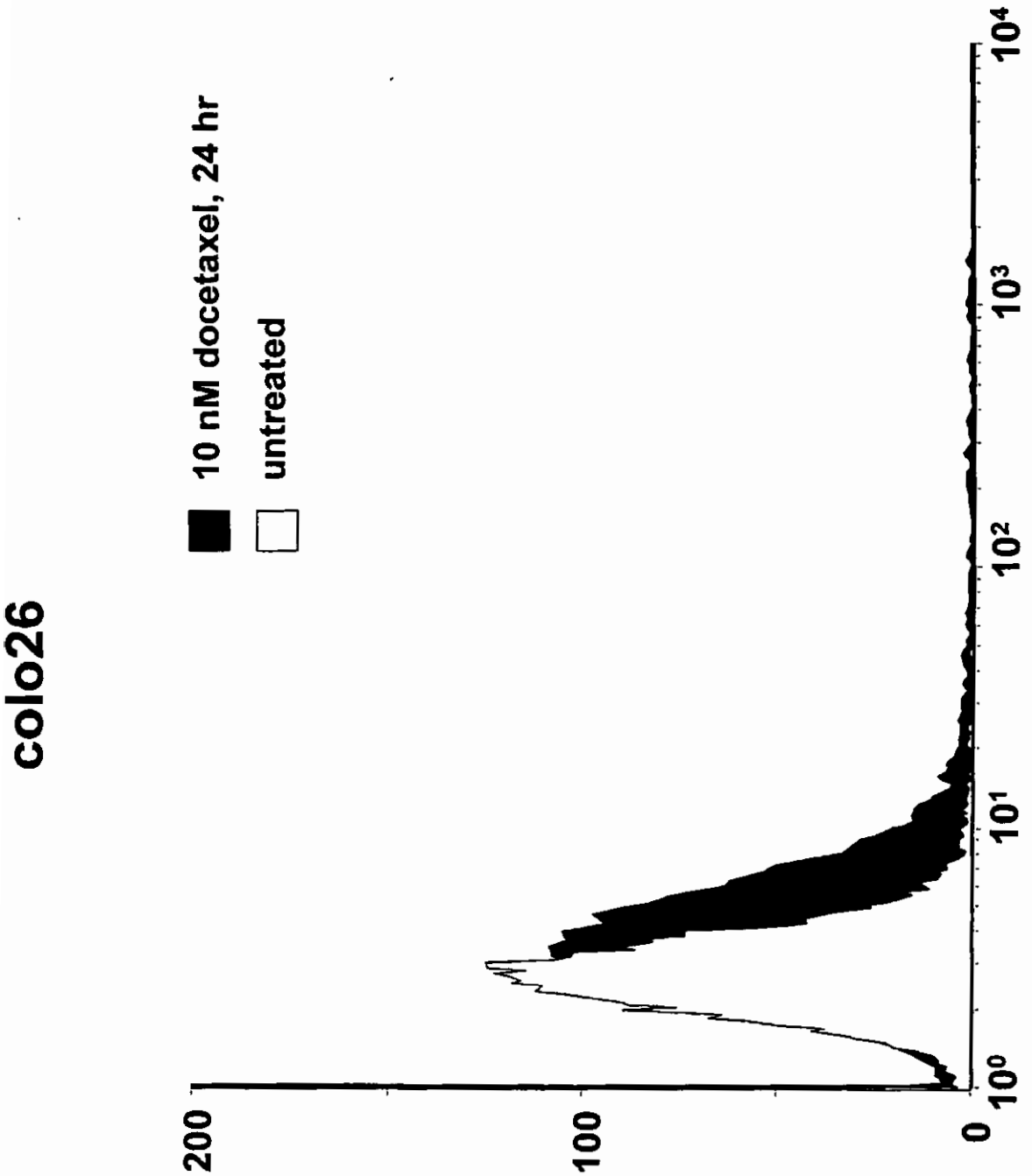

colo26
10 nM docetaxel, 24 hr
untreated
200
100
0
10^0
10^1
10^2
10^3
10^4

FIG. 25B

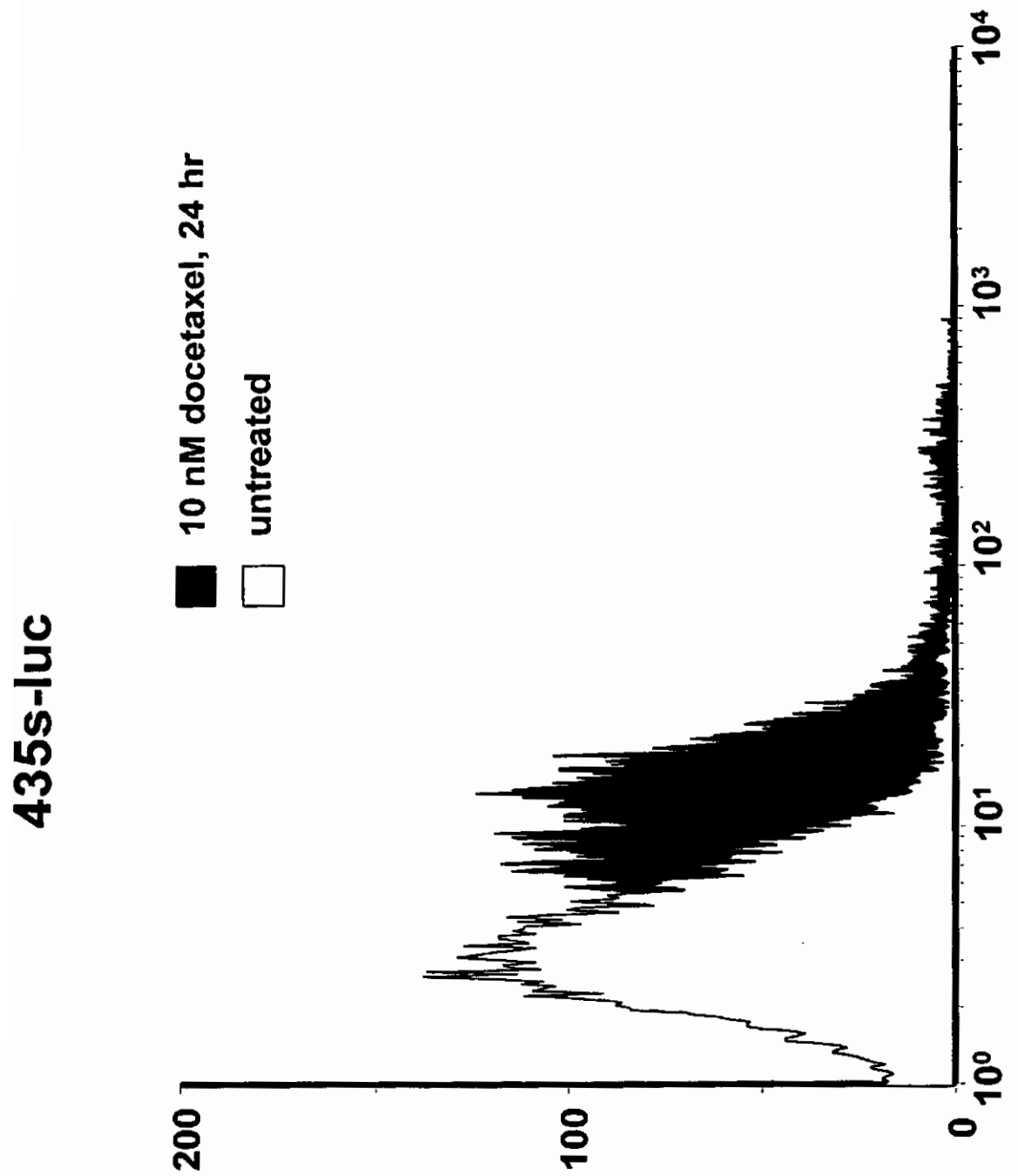

435s-luc
10 nM docetaxel, 24 hr
untreated
200
100
0
10^0
10^1
10^2
10^3
10^4

FIG. 25C

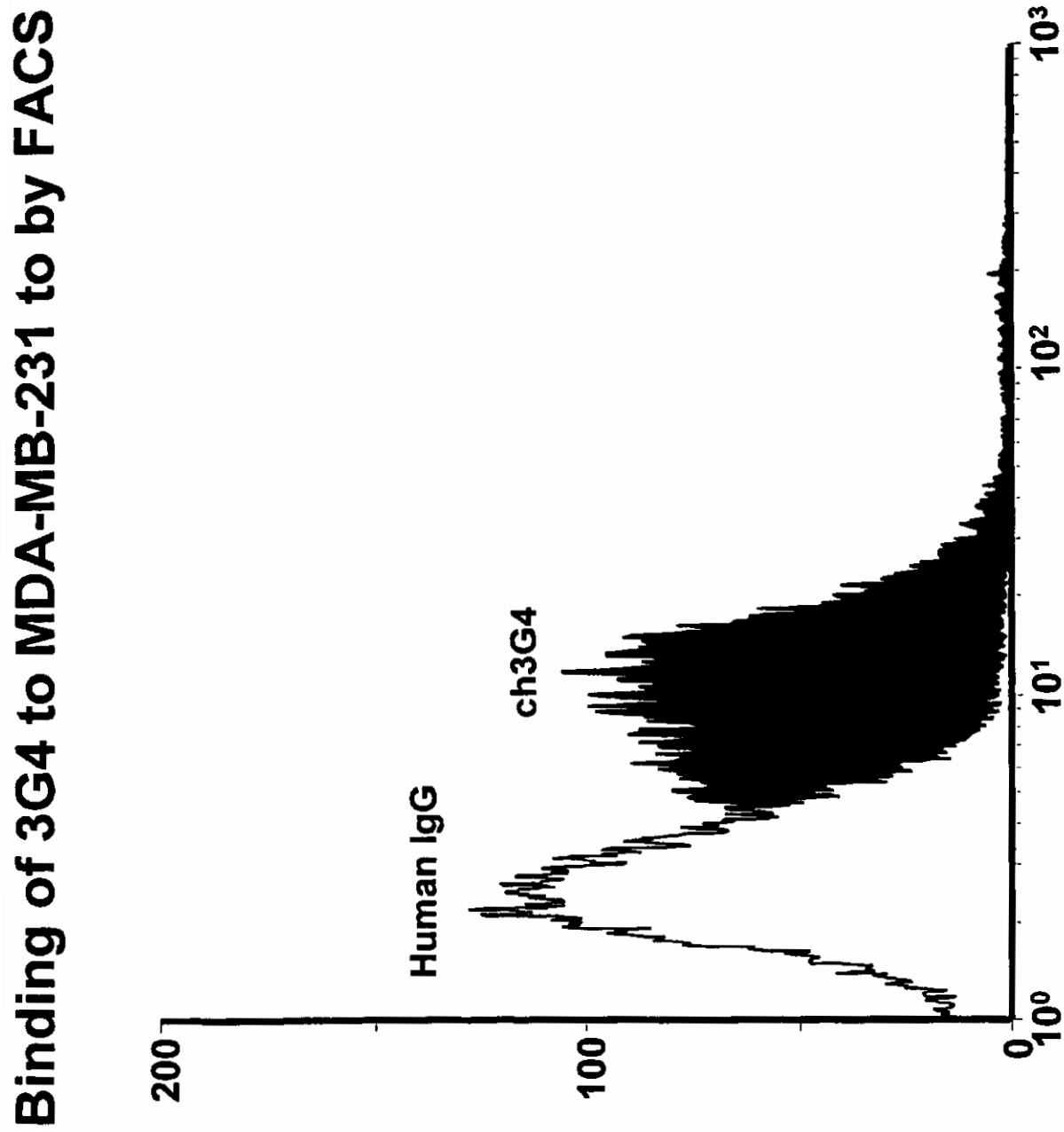

Binding of 3G4 to MDA-MB-231 to by FACS
200
100
0
Human IgG
ch3G4
10^0
10^1
10^2
10^3

FIG. 26

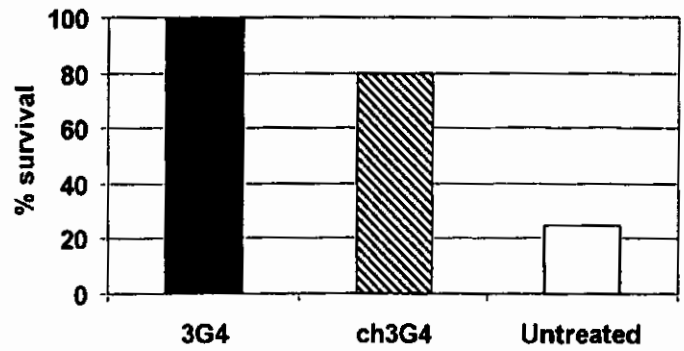


FIG. 27

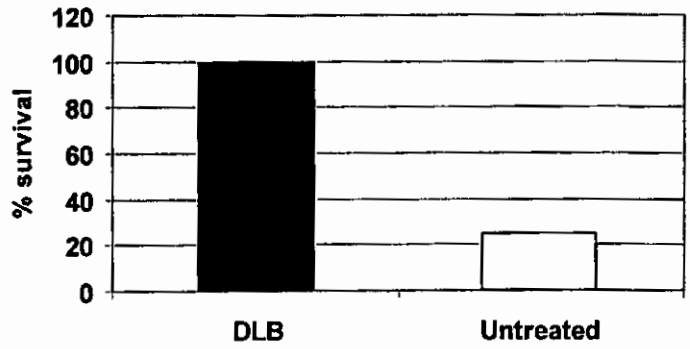


FIG. 28

FIG. 29A

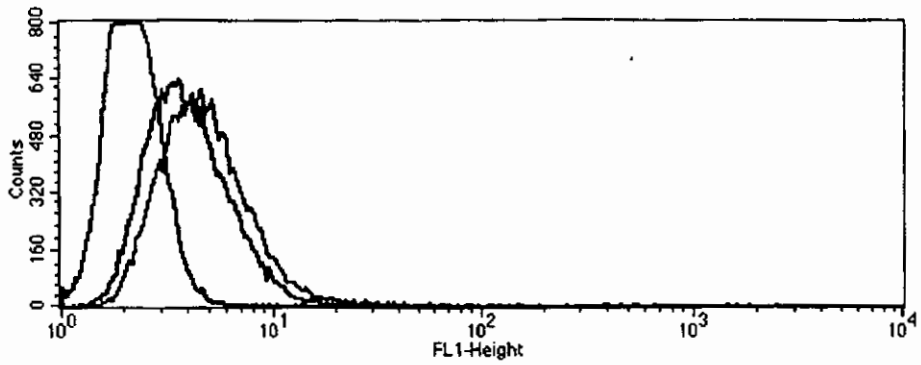
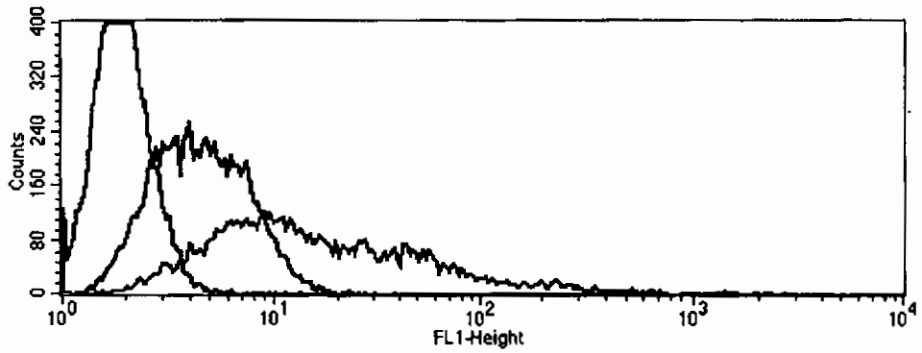


FIG. 29B



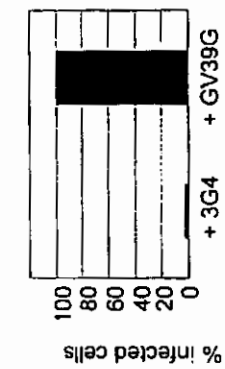


FIG. 30D

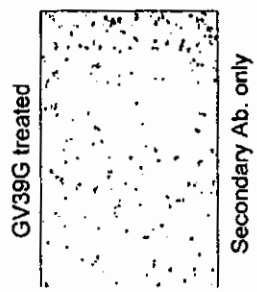


FIG. 30C

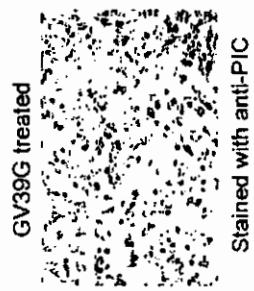


FIG. 30B

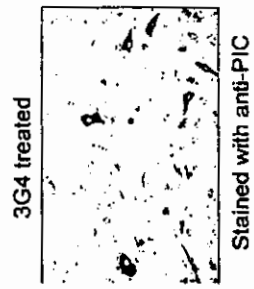


FIG. 30A

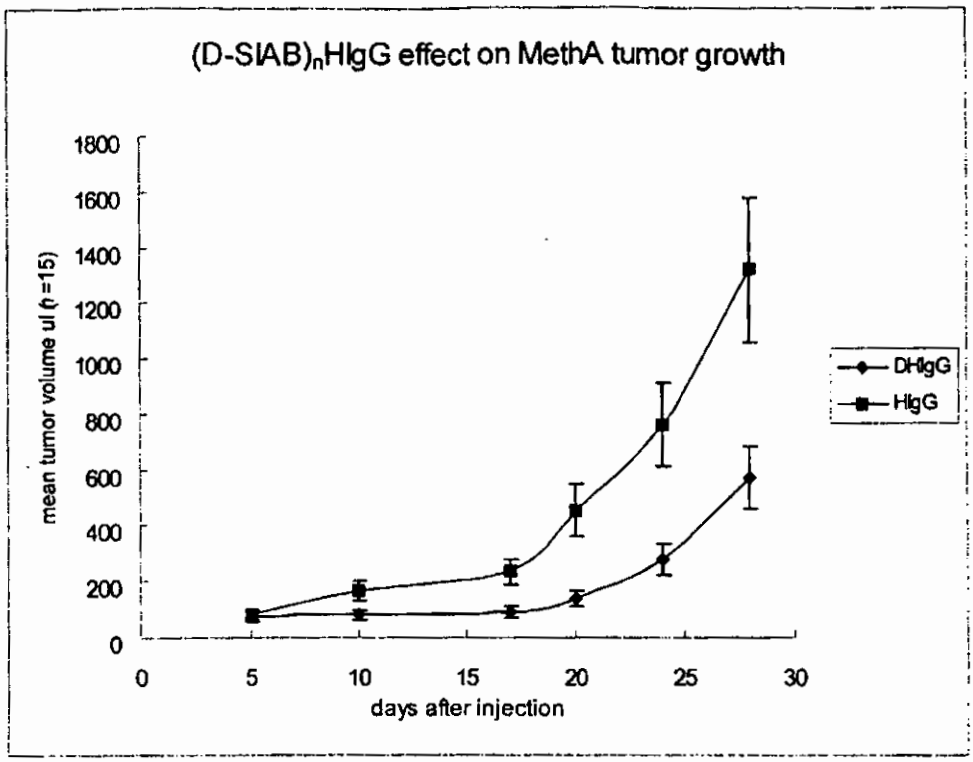

(D-SIAB)nHIgG effect on MethA tumor growth
mean tumor volume ul (n=15)
1800
1600
1400
1200
1000
800
600
400
200
0
0
5
10
15
20
25
30
days after injection
DHIgG
HIgG

FIG. 31

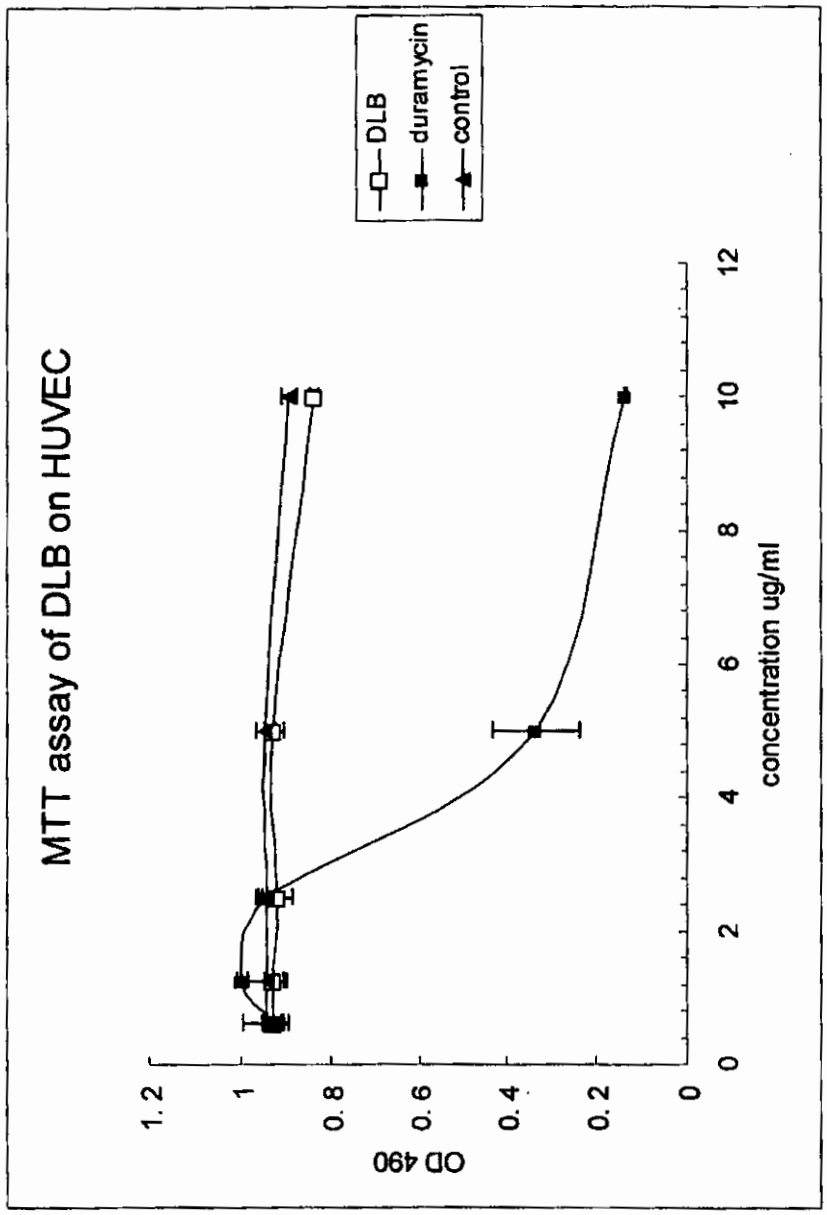

MTT assay of DLB on HUVEC
DLB
duramycin
control
OD 490
1.2
1
0.8
0.6
0.4
0.2
0
0
2
4
6
8
10
12
concentration ug/ml

FIG. 32

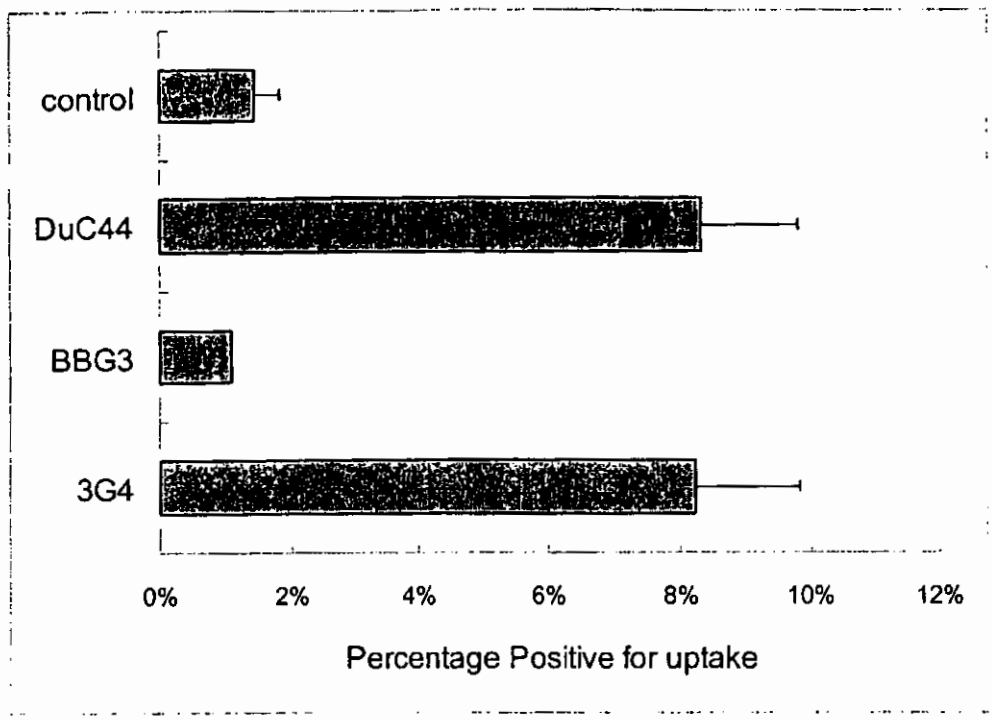

control
DuC44
BBG3
3G4
0%
2%
4%
6%
8%
10%
12%
Percentage Positive for uptake

FIG. 33