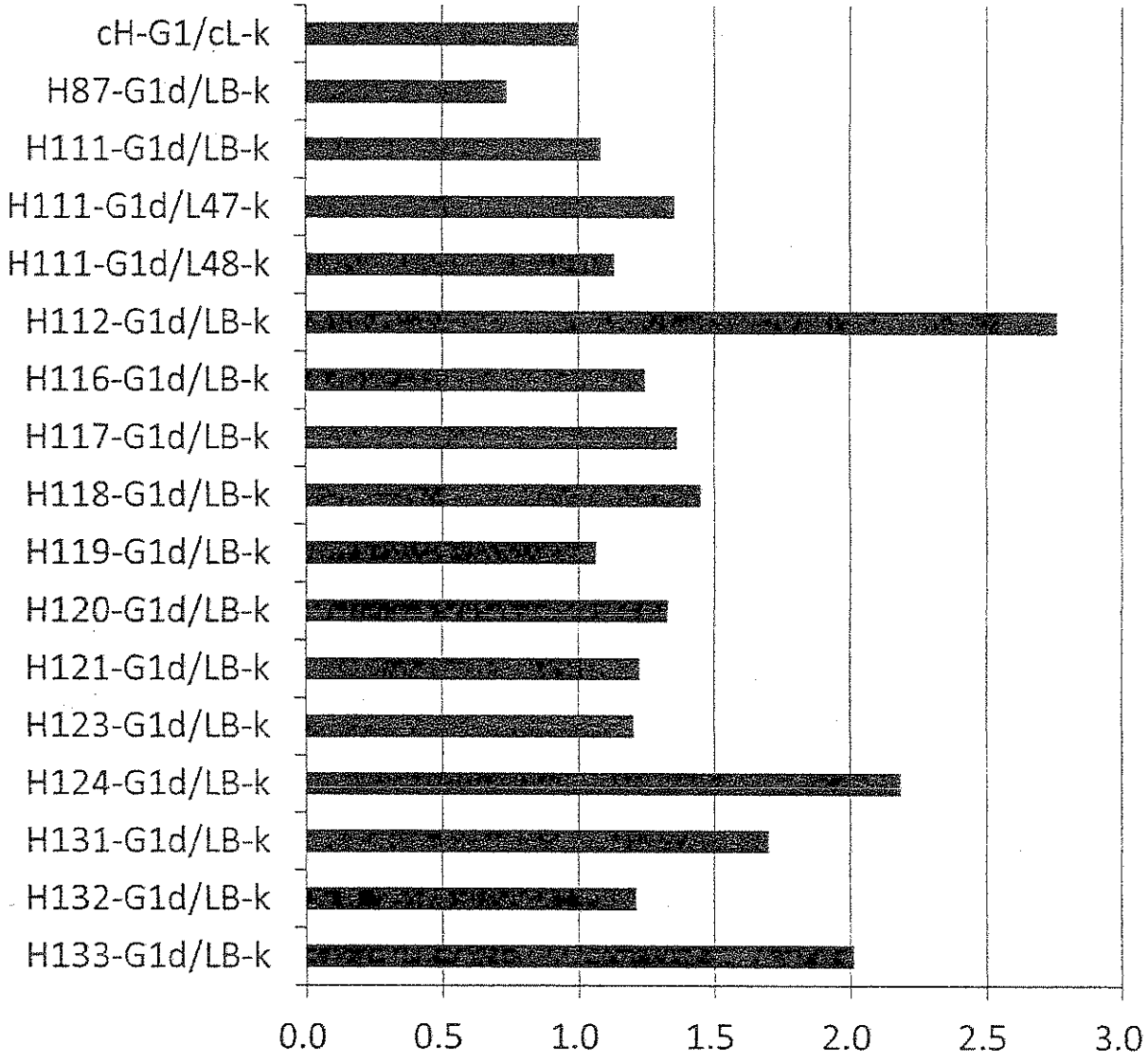

cH-G1/cL-k
H87-G1d/LB-k
H111-G1d/LB-k
H111-G1d/L47-k
H111-G1d/L48-k
H112-G1d/LB-k
H116-G1d/LB-k
H117-G1d/LB-k
H118-G1d/LB-k
H119-G1d/LB-k
H120-G1d/LB-k
H121-G1d/LB-k
H123-G1d/LB-k
H124-G1d/LB-k
H131-G1d/LB-k
H132-G1d/LB-k
H133-G1d/LB-k
0.0
0.5
1.0
1.5
2.0
2.5
3.0

FIG. 1

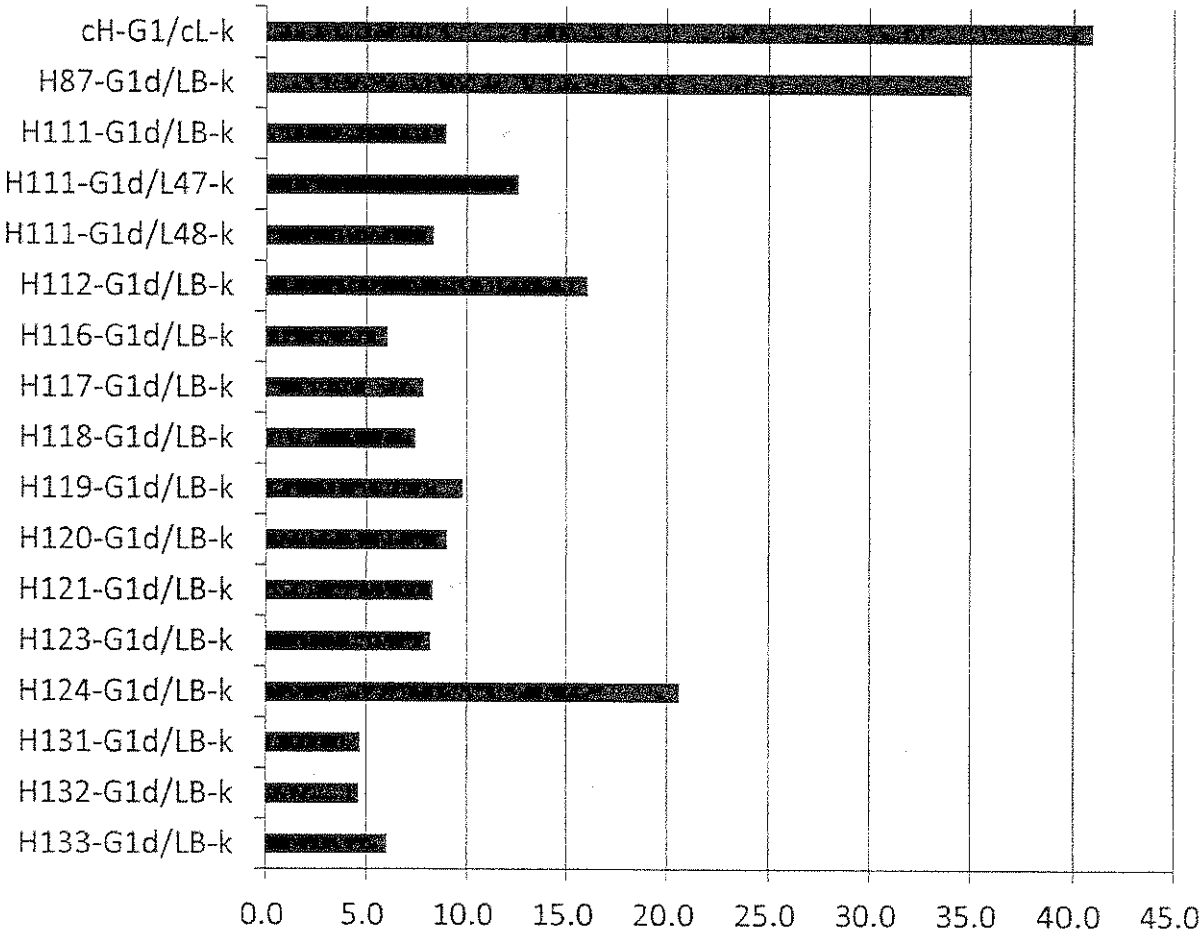

cH-G1/cL-k
H87-G1d/LB-k
H111-G1d/LB-k
H111-G1d/L47-k
H111-G1d/L48-k
H112-G1d/LB-k
H116-G1d/LB-k
H117-G1d/LB-k
H118-G1d/LB-k
H119-G1d/LB-k
H120-G1d/LB-k
H121-G1d/LB-k
H123-G1d/LB-k
H124-G1d/LB-k
H131-G1d/LB-k
H132-G1d/LB-k
H133-G1d/LB-k
0.0
5.0
10.0
15.0
20.0
25.0
30.0
35.0
40.0
45.0

FIG. 2

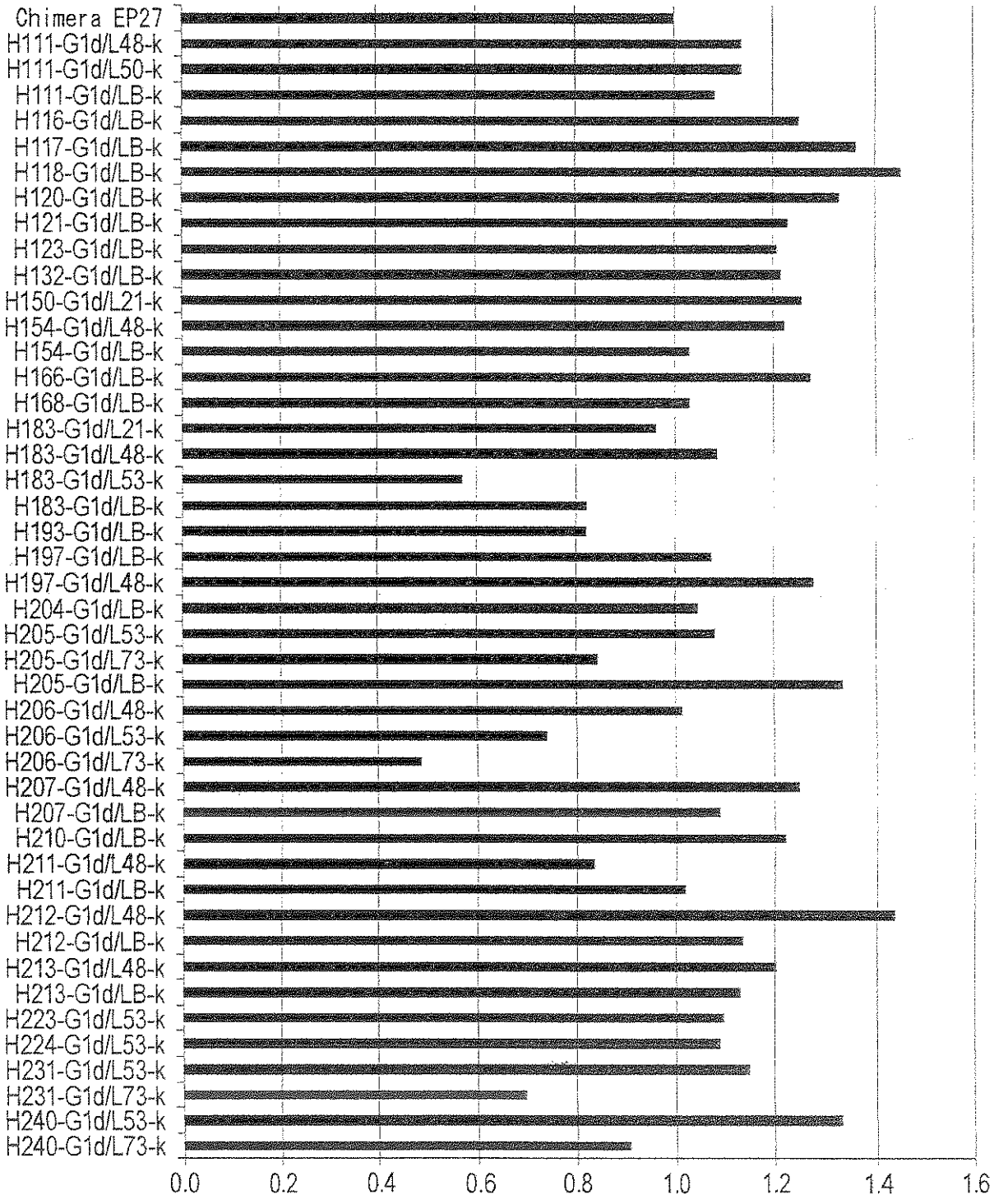

Chimera EP27
H111-G1d/L48-k
H111-G1d/L50-k
H111-G1d/LB-k
H116-G1d/LB-k
H117-G1d/LB-k
H118-G1d/LB-k
H120-G1d/LB-k
H121-G1d/LB-k
H123-G1d/LB-k
H132-G1d/LB-k
H150-G1d/L21-k
H154-G1d/L48-k
H154-G1d/LB-k
H166-G1d/LB-k
H168-G1d/LB-k
H183-G1d/L21-k
H183-G1d/L48-k
H183-G1d/L53-k
H183-G1d/LB-k
H193-G1d/LB-k
H197-G1d/LB-k
H197-G1d/L48-k
H204-G1d/LB-k
H205-G1d/L53-k
H205-G1d/L73-k
H205-G1d/LB-k
H206-G1d/L48-k
H206-G1d/L53-k
H206-G1d/L73-k
H207-G1d/L48-k
H207-G1d/LB-k
H210-G1d/LB-k
H211-G1d/L48-k
H211-G1d/LB-k
H212-G1d/L48-k
H212-G1d/LB-k
H213-G1d/L48-k
H213-G1d/LB-k
H223-G1d/L53-k
H224-G1d/L53-k
H231-G1d/L53-k
H231-G1d/L73-k
H240-G1d/L53-k
H240-G1d/L73-k
0.0
0.2
0.4
0.6
0.8
1.0
1.2
1.4
1.6

FIG. 3

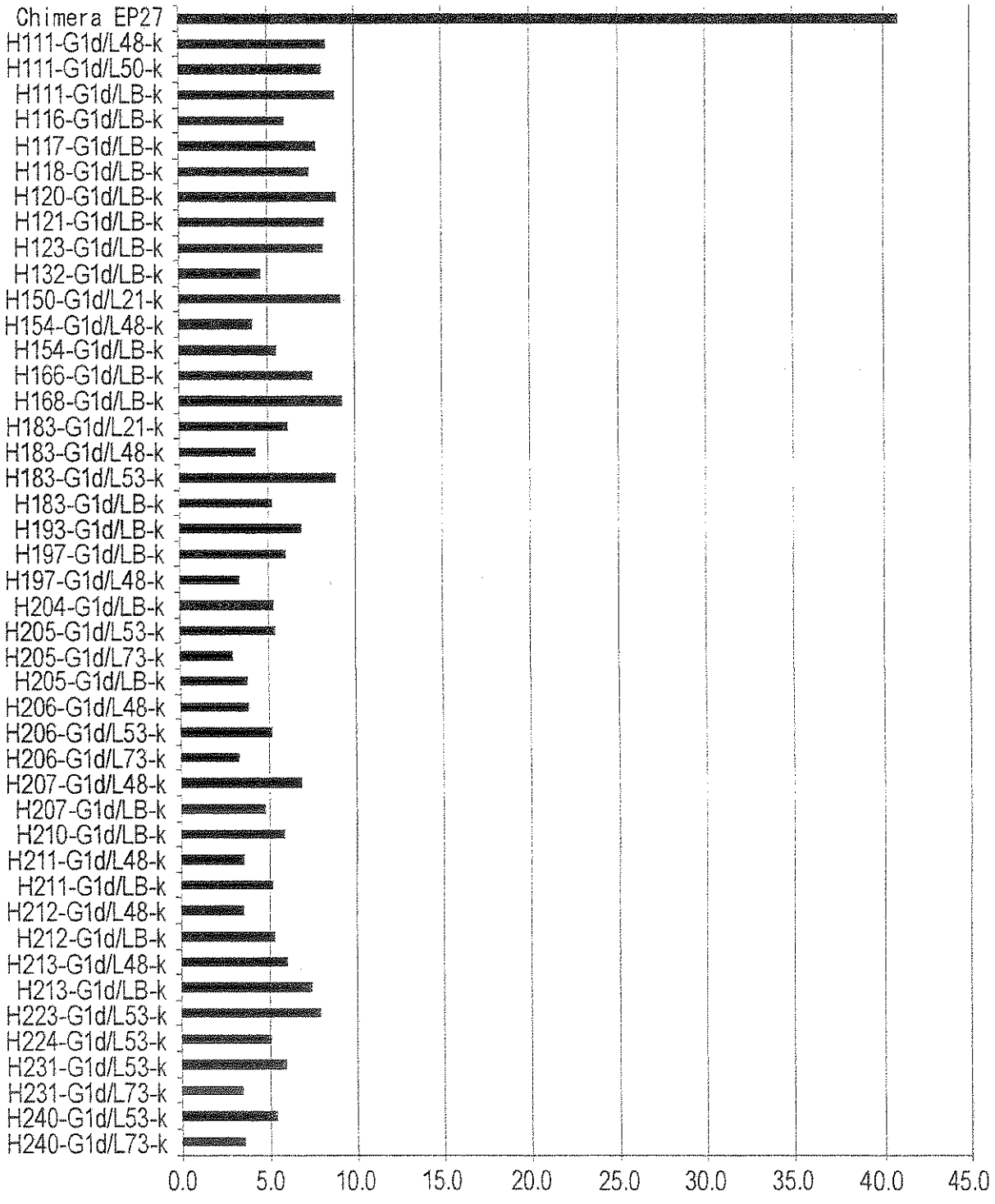

Chimera EP27
H111-G1d/L48-k
H111-G1d/L50-k
H111-G1d/LB-k
H116-G1d/LB-k
H117-G1d/LB-k
H118-G1d/LB-k
H120-G1d/LB-k
H121-G1d/LB-k
H123-G1d/LB-k
H132-G1d/LB-k
H150-G1d/L21-k
H154-G1d/L48-k
H154-G1d/LB-k
H166-G1d/LB-k
H168-G1d/LB-k
H183-G1d/L21-k
H183-G1d/L48-k
H183-G1d/L53-k
H183-G1d/LB-k
H193-G1d/LB-k
H197-G1d/LB-k
H197-G1d/L48-k
H204-G1d/LB-k
H205-G1d/L53-k
H205-G1d/L73-k
H205-G1d/LB-k
H206-G1d/L48-k
H206-G1d/L53-k
H206-G1d/L73-k
H207-G1d/L48-k
H207-G1d/LB-k
H210-G1d/LB-k
H211-G1d/L48-k
H211-G1d/LB-k
H212-G1d/L48-k
H212-G1d/LB-k
H213-G1d/L48-k
H213-G1d/LB-k
H223-G1d/L53-k
H224-G1d/L53-k
H231-G1d/L53-k
H231-G1d/L73-k
H240-G1d/L53-k
H240-G1d/L73-k
0.0
5.0
10.0
15.0
20.0
25.0
30.0
35.0
40.0
45.0

FIG. 4

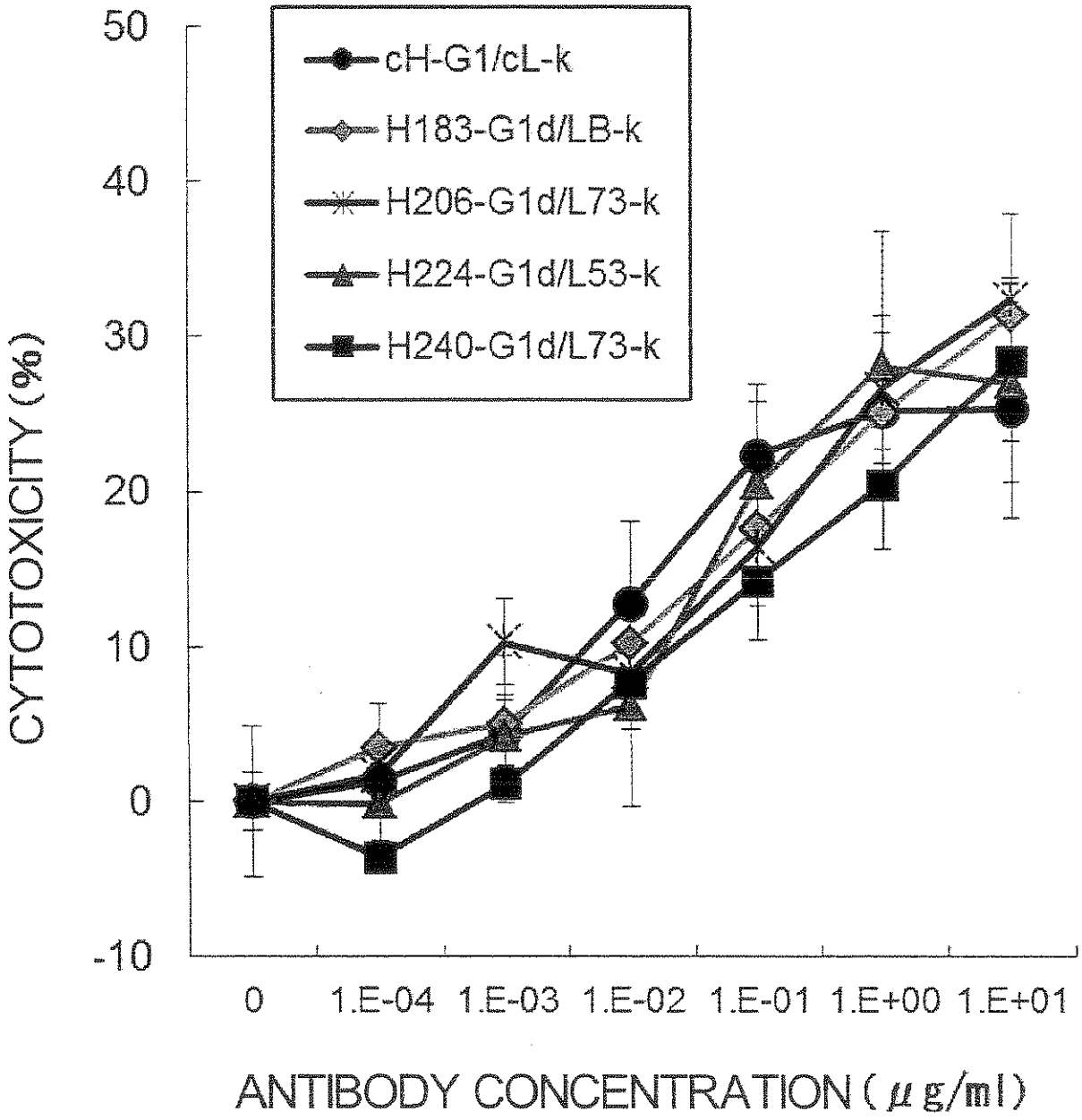

cH-G1/cL-k
H183-G1d/LB-k
H206-G1d/L73-k
H224-G1d/L53-k
H240-G1d/L73-k
CYTOTOXICITY (%)
50
40
30
20
10
0
-10
0
1.E-04
1.E-03
1.E-02
1.E-01
1.E+00
1.E+01
ANTIBODY CONCENTRATION (μg/ml)

FIG. 5

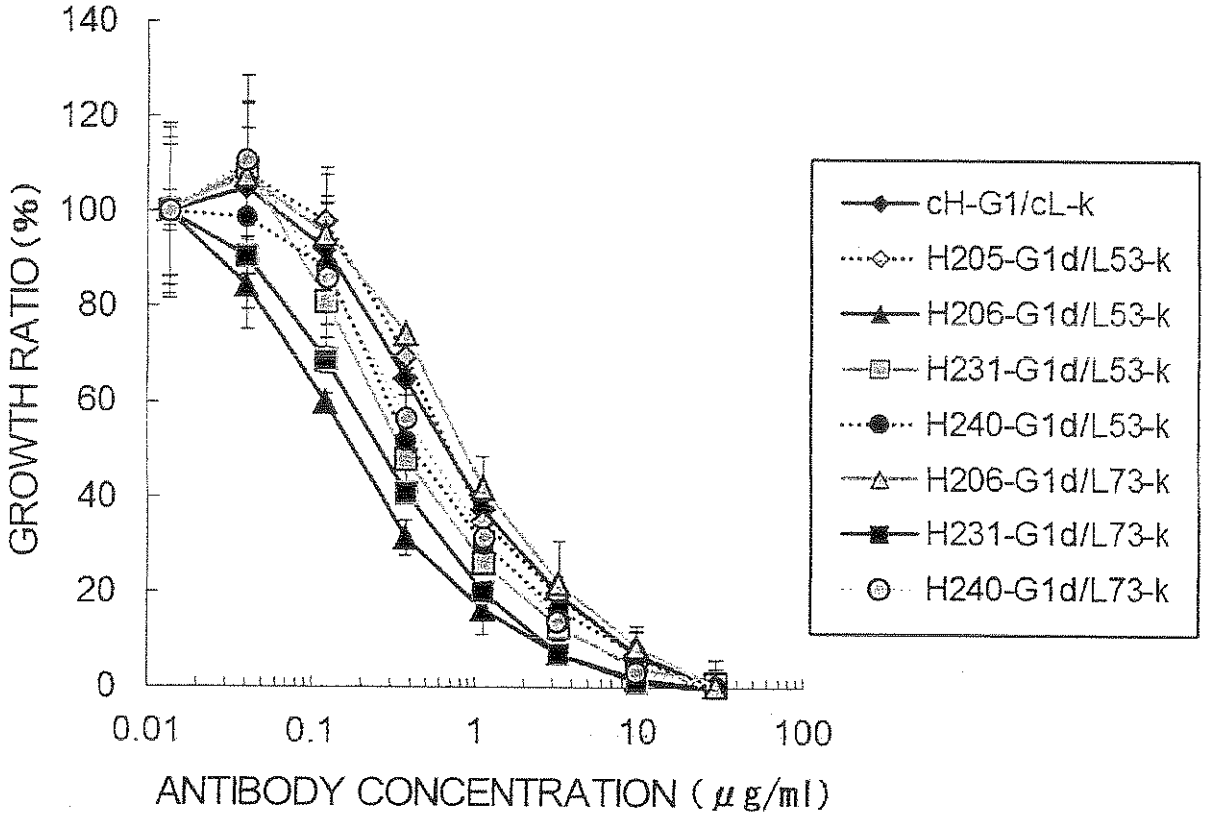

140
120
100
80
60
40
20
0
GROWTH RATIO (%)
0.01
0.1
1
10
100
ANTIBODY CONCENTRATION (μg/ml)
cH-G1/cL-k
H205-G1d/L53-k
H206-G1d/L53-k
H231-G1d/L53-k
H240-G1d/L53-k
H206-G1d/L73-k
H231-G1d/L73-k
H240-G1d/L73-k

FIG. 6

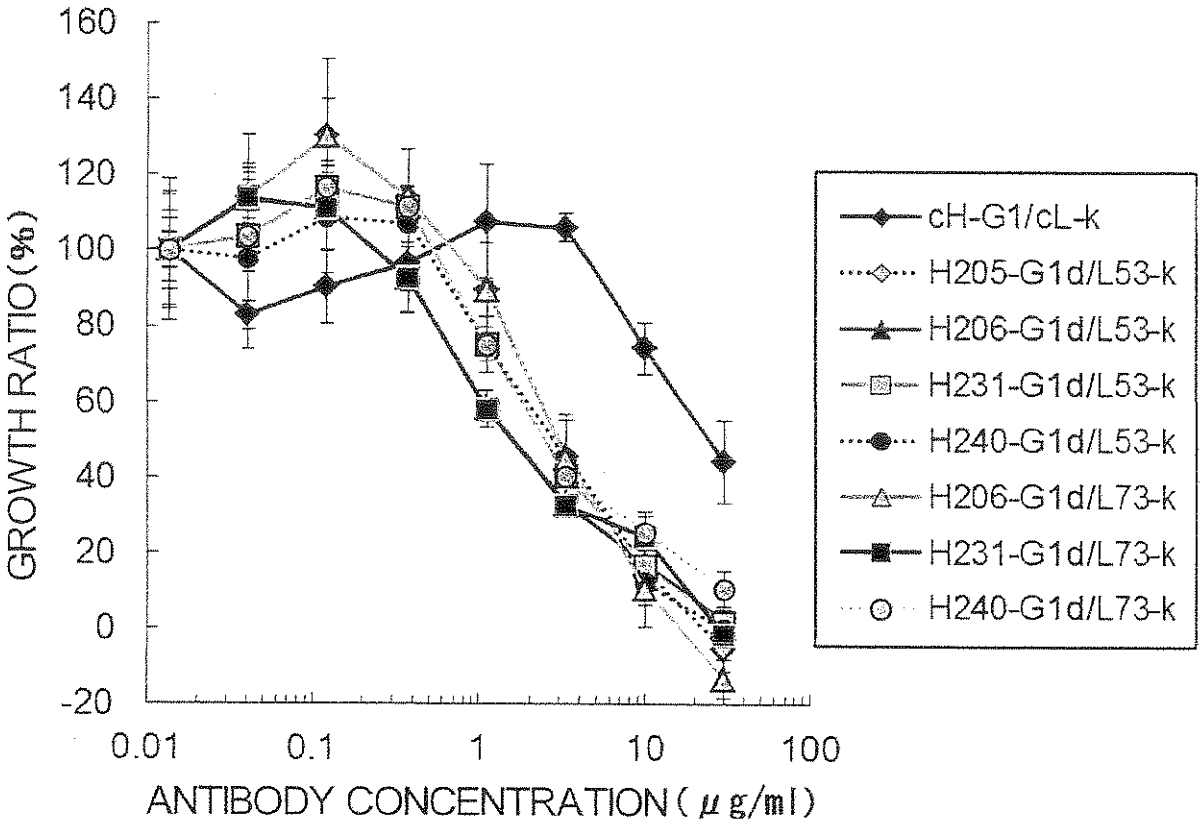

160
140
120
100
80
60
40
20
0
-20
GROWTH RATIO (%)
0.01
0.1
1
10
100
ANTIBODY CONCENTRATION (μg/ml)
cH-G1/cL-k
H205-G1d/L53-k
H206-G1d/L53-k
H231-G1d/L53-k
H240-G1d/L53-k
H206-G1d/L73-k
H231-G1d/L73-k
H240-G1d/L73-k

FIG. 7

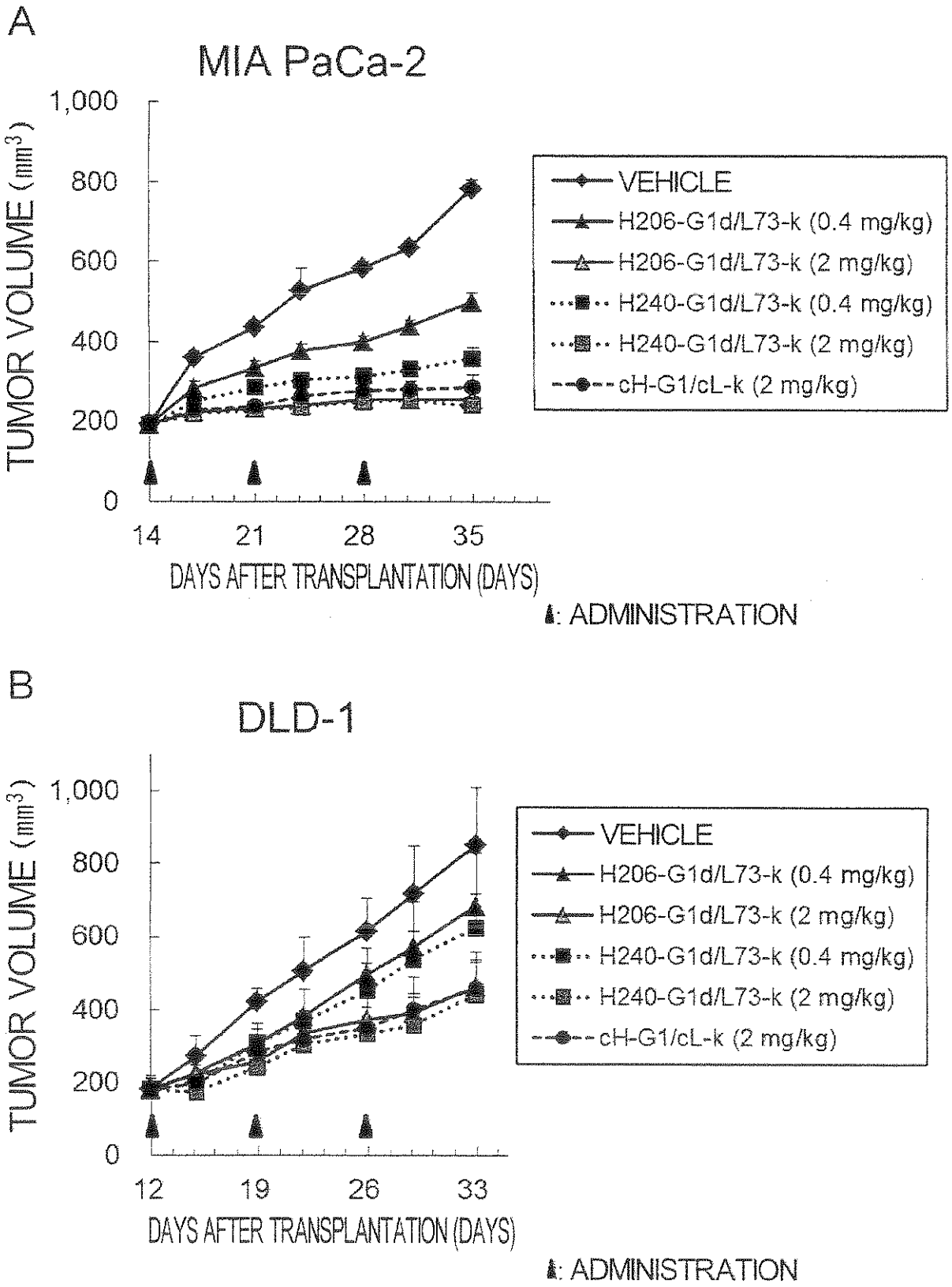
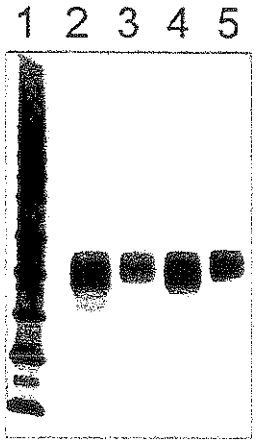

A
MIA PaCa-2
TUMOR VOLUME (mm3)
1,000
800
600
400
200
0
14
21
28
35
DAYS AFTER TRANSPLANTATION (DAYS)
VEHICLE
H206-G1d/L73-k (0.4 mg/kg)
H206-G1d/L73-k (2 mg/kg)
H240-G1d/L73-k (0.4 mg/kg)
H240-G1d/L73-k (2 mg/kg)
cH-G1/cL-k (2 mg/kg)
: ADMINISTRATION
B
DLD-1
TUMOR VOLUME (mm3)
1,000
800
600
400
200
0
12
19
26
33
DAYS AFTER TRANSPLANTATION (DAYS)
VEHICLE
H206-G1d/L73-k (0.4 mg/kg)
H206-G1d/L73-k (2 mg/kg)
H240-G1d/L73-k (0.4 mg/kg)
H240-G1d/L73-k (2 mg/kg)
cH-G1/cL-k (2 mg/kg)
: ADMINISTRATION

FIG. 8



LANE 1: MOLECULAR MARKER
LANE 2: HUMAN MATURE EREG (ELUTION FRACTION 1)
LANE 3: HUMAN MATURE EREG (ELUTION FRACTION 2)
LANE 4: CYNOMOLGUS MATURE EREG (ELUTION FRACTION 1)
LANE 5: CYNOMOLGUS MATURE EREG (ELUTION FRACTION 2)

FIG. 9

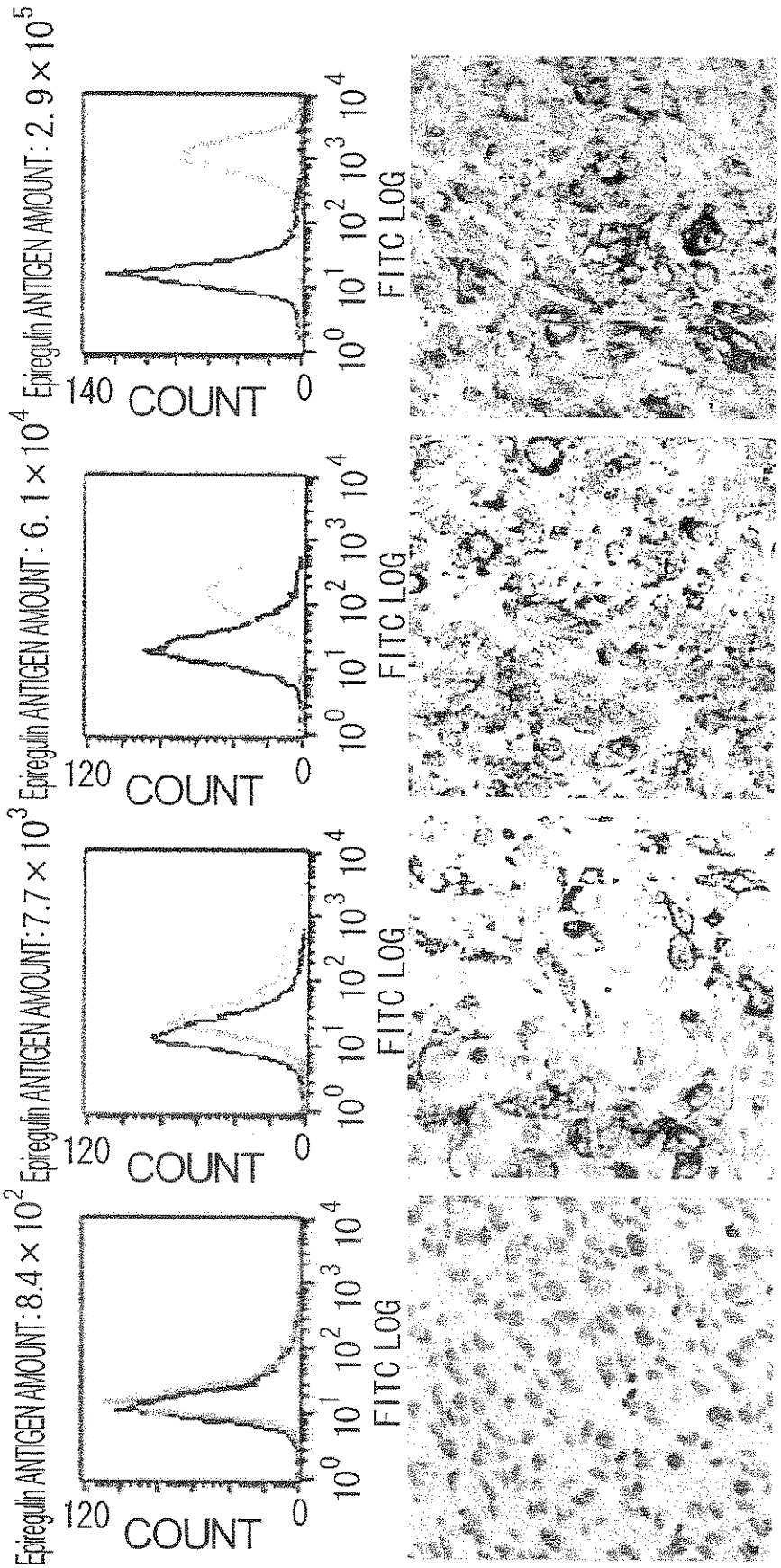

SK-HEP-1
SKE-18
SKE-23
SKE-4B2
Epiregulin ANTIGEN AMOUNT : 8.4 × 10^2
Epiregulin ANTIGEN AMOUNT : 7.7 × 10^3
Epiregulin ANTIGEN AMOUNT : 6.1 × 10^4
Epiregulin ANTIGEN AMOUNT : 2.9 × 10^5
120
140
COUNT
0
10^0 10^1 10^2 10^3 10^4
FITC LOG

FIG. 10

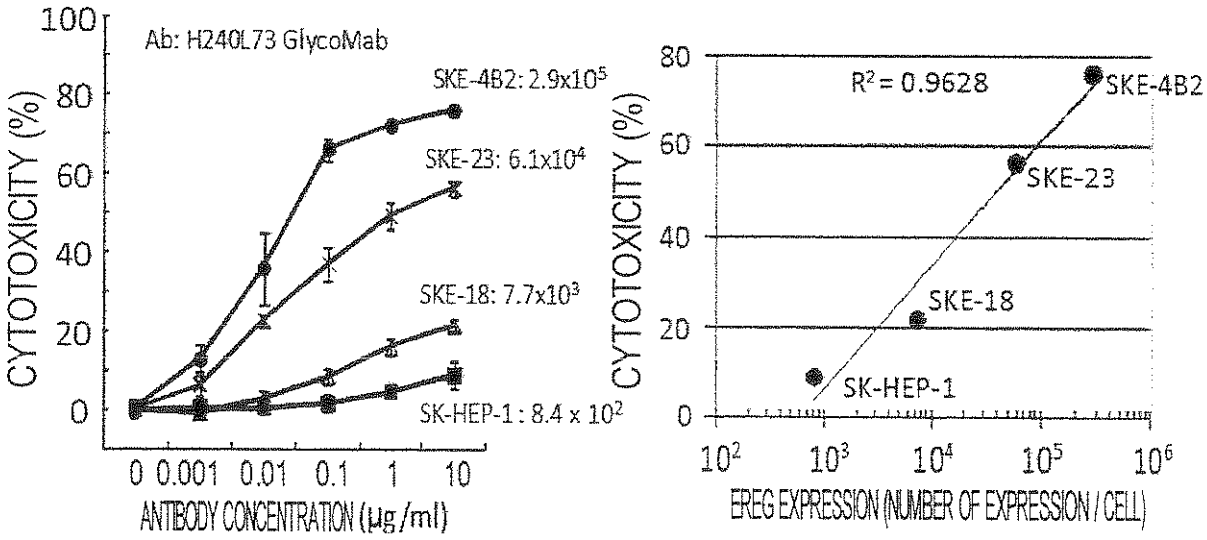

Ab: H240L73 GlycoMab
SKE-4B2: 2.9x10^5
SKE-23: 6.1x10^4
SKE-18: 7.7x10^3
SK-HEP-1 : 8.4 x 10^2
CYTOTOXICITY (%)
ANTIBODY CONCENTRATION (μg/ml)
R^2 = 0.9628
SKE-4B2
SKE-23
SKE-18
SK-HEP-1
EREG EXPRESSION (NUMBER OF EXPRESSION / CELL)

FIG. 11

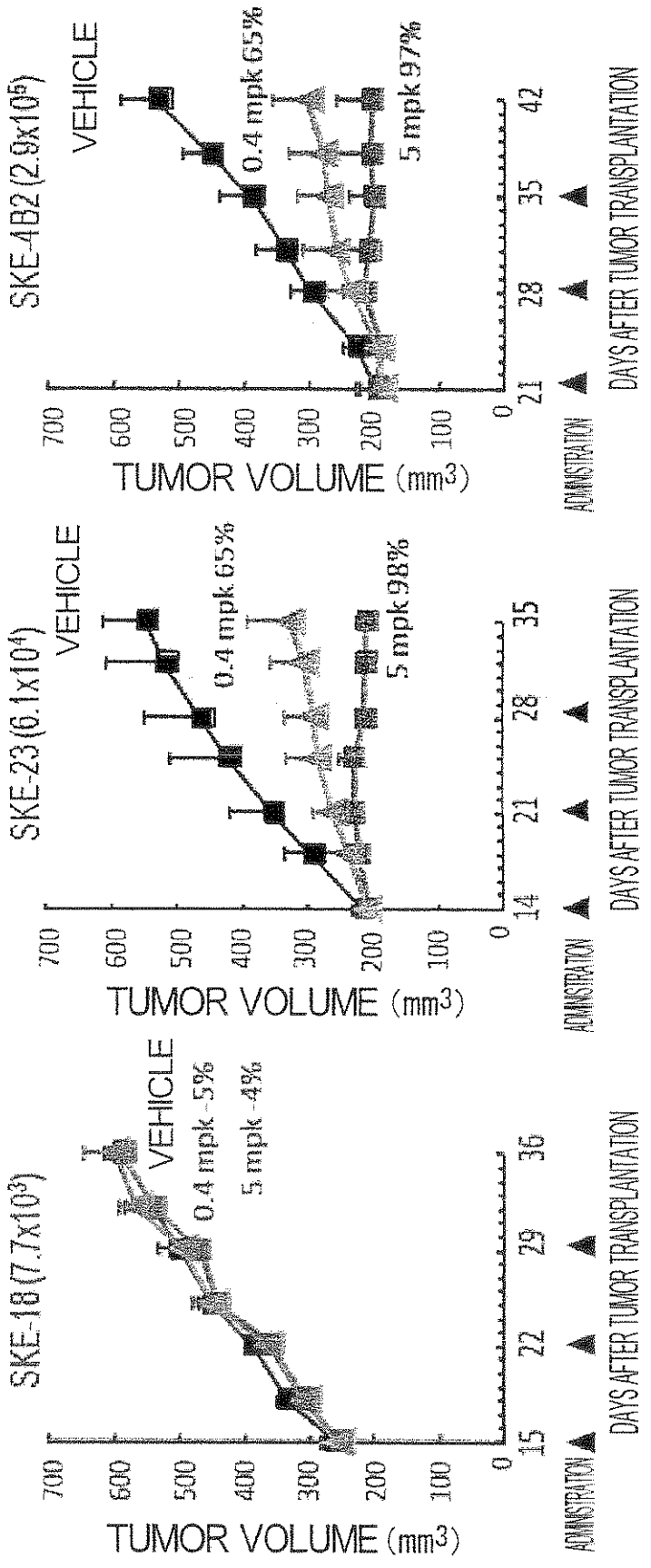

SKE-18 (7.7x10³)
VEHICLE
0.4 mpk -5%
5 mpk -4%
TUMOR VOLUME (mm³)
700
600
500
400
300
200
100
0
15
22
29
36
ADMINISTRATION
DAYS AFTER TUMOR TRANSPLANTATION
SKE-23 (6.1x10⁴)
VEHICLE
0.4 mpk 65%
5 mpk 98%
TUMOR VOLUME (mm³)
14
21
28
35
ADMINISTRATION
DAYS AFTER TUMOR TRANSPLANTATION
SKE-4B2 (2.9x10⁵)
VEHICLE
0.4 mpk 65%
5 mpk 97%
TUMOR VOLUME (mm³)
21
28
35
42
ADMINISTRATION
DAYS AFTER TUMOR TRANSPLANTATION

FIG. 12

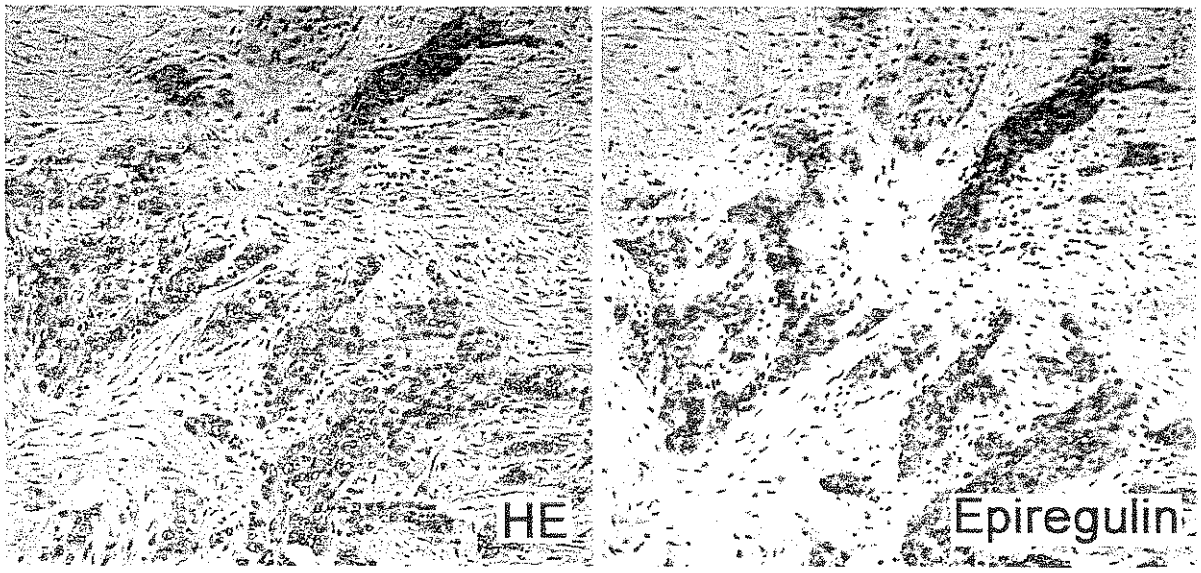


FIG. 13

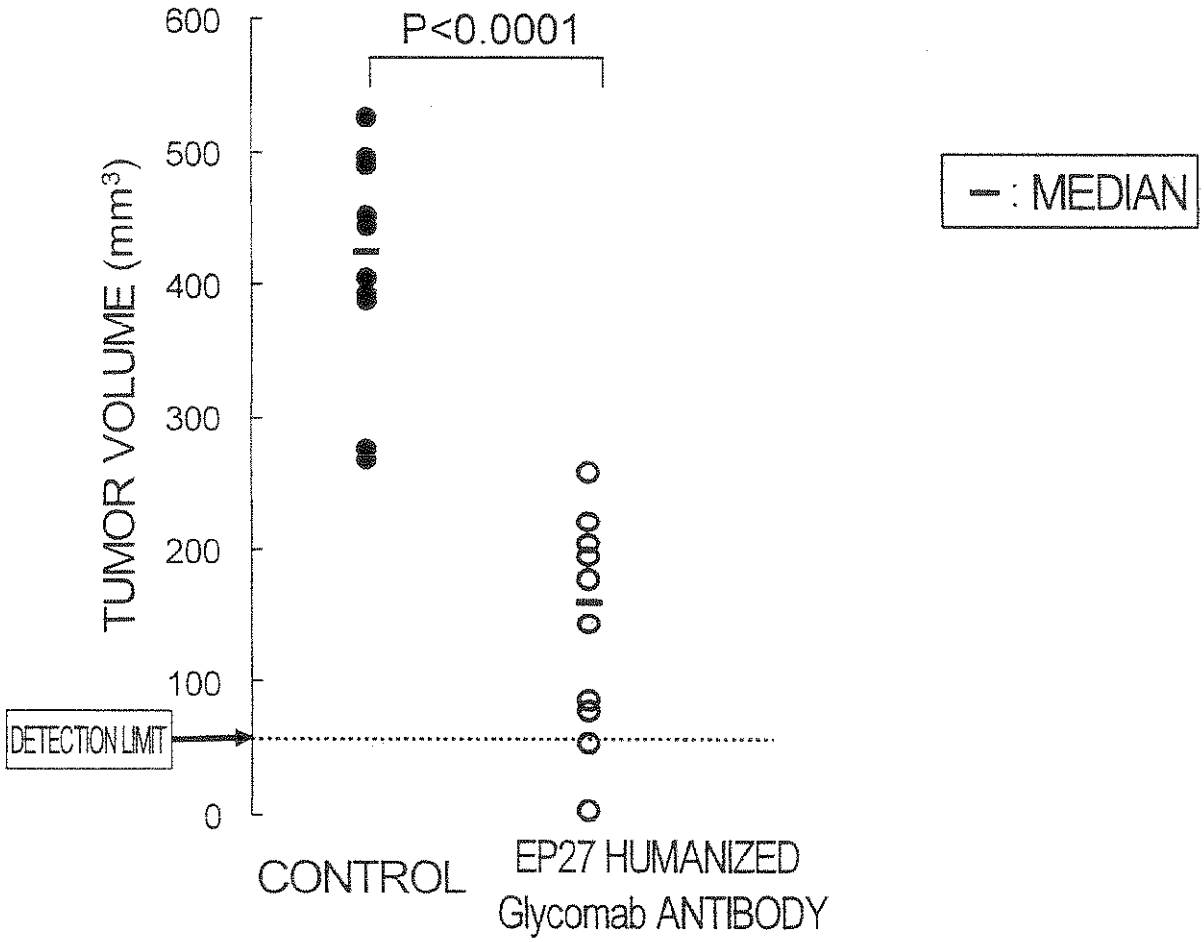

P<0.0001
600
500
400
300
200
100
0
TUMOR VOLUME (mm³)
DETECTION LIMIT
—: MEDIAN
CONTROL
EP27 HUMANIZED
Glycomab ANTIBODY

FIG. 14

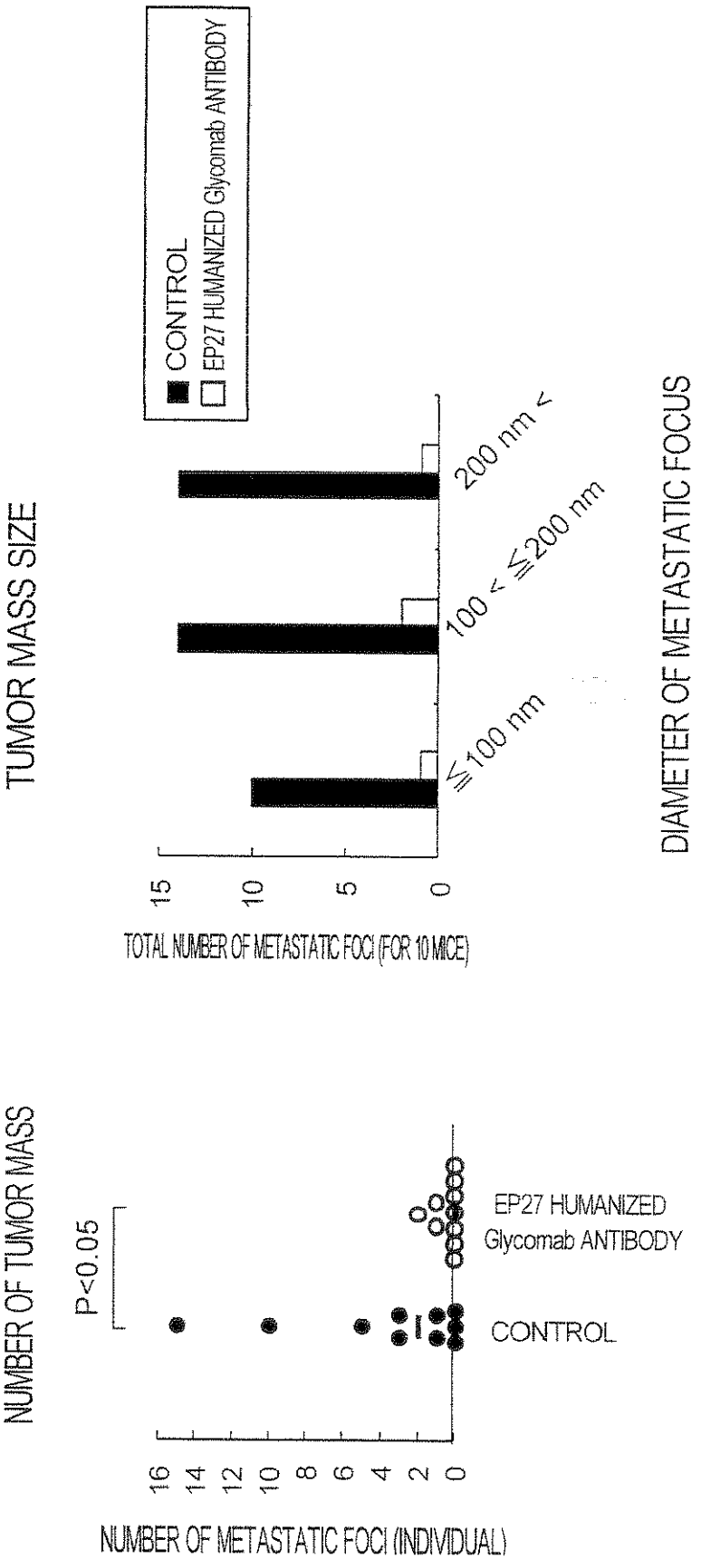

TUMOR MASS SIZE
CONTROL
EP27 HUMANIZED Glycomab ANTIBODY
200 nm <
100 < ≦200 nm
≦100 nm
15
10
5
0
TOTAL NUMBER OF METASTATIC FOCI (FOR 10 MICE)
DIAMETER OF METASTATIC FOCUS
NUMBER OF TUMOR MASS
P<0.05
EP27 HUMANIZED
Glycomab ANTIBODY
CONTROL
16
14
12
10
8
6
4
2
0
NUMBER OF METASTATIC FOCI (INDIVIDUAL)

FIG. 15

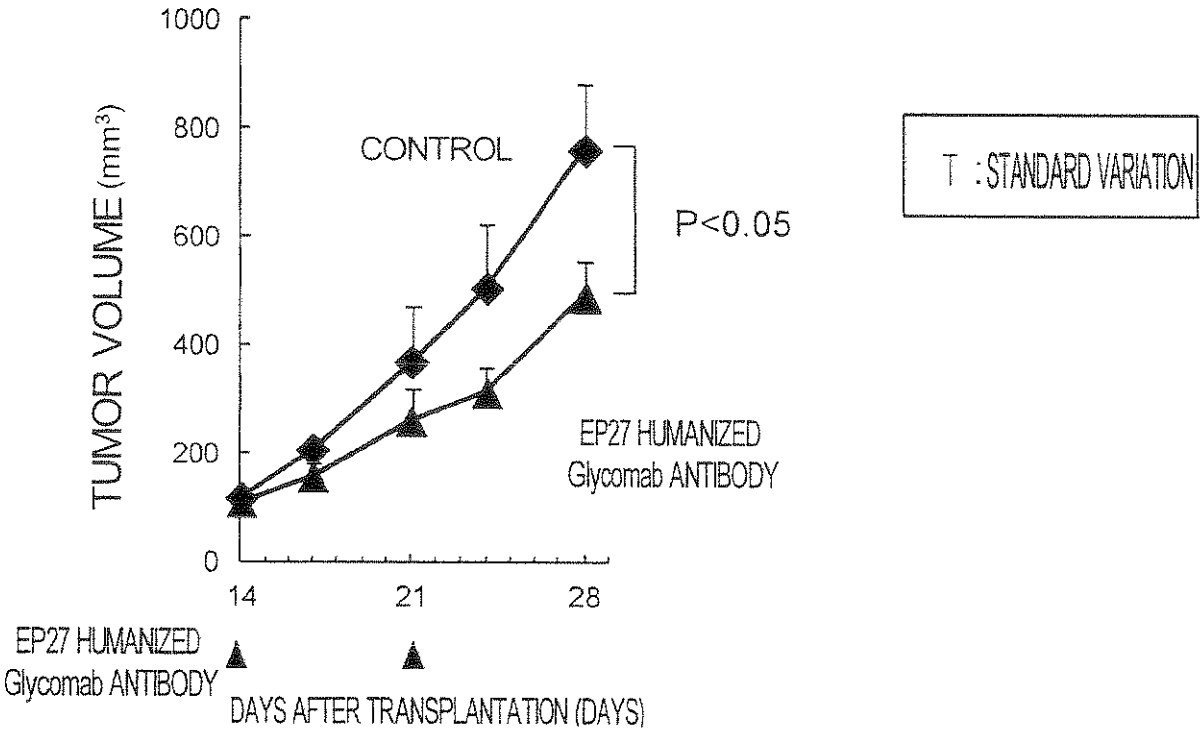

1000
800
600
400
200
0
TUMOR VOLUME (mm3)
CONTROL
P<0.05
EP27 HUMANIZED
Glycomab ANTIBODY
14
21
28
EP27 HUMANIZED
Glycomab ANTIBODY
DAYS AFTER TRANSPLANTATION (DAYS)
T :STANDARD VARIATION

FIG. 16

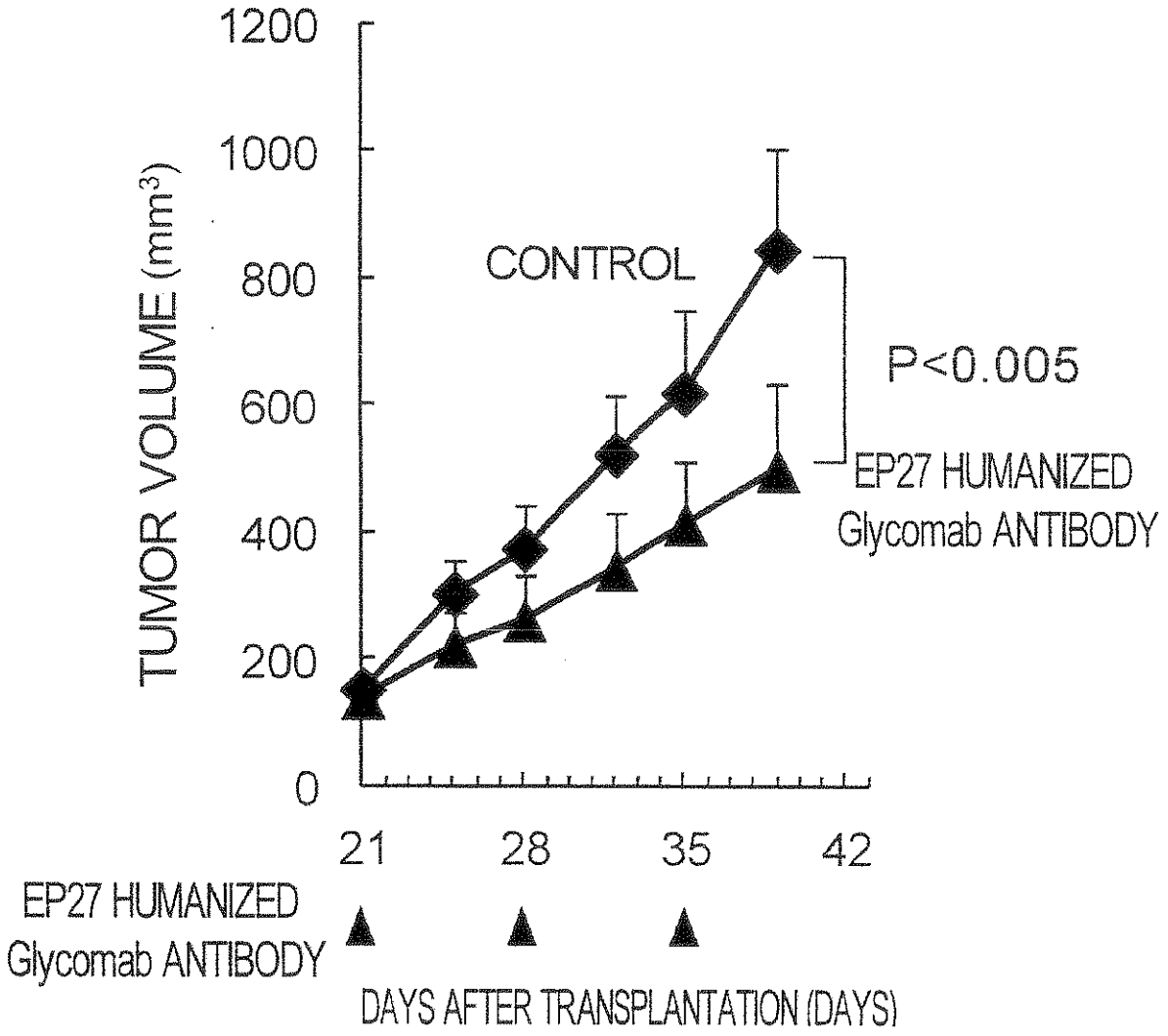
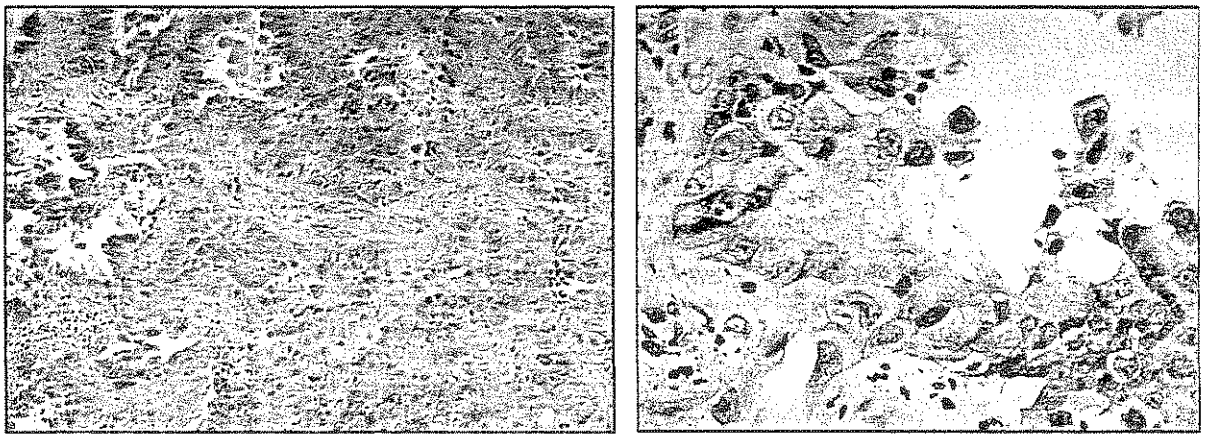

1200
1000
800
600
400
200
0
TUMOR VOLUME (mm3)
CONTROL
P<0.005
EP27 HUMANIZED
Glycomab ANTIBODY
21
28
35
42
EP27 HUMANIZED
Glycomab ANTIBODY
DAYS AFTER TRANSPLANTATION (DAYS)

FIG. 17

Clinical lung adenocarcinoma staining images



Hematoxylin-eosin staining EREG staining

FIG. 18

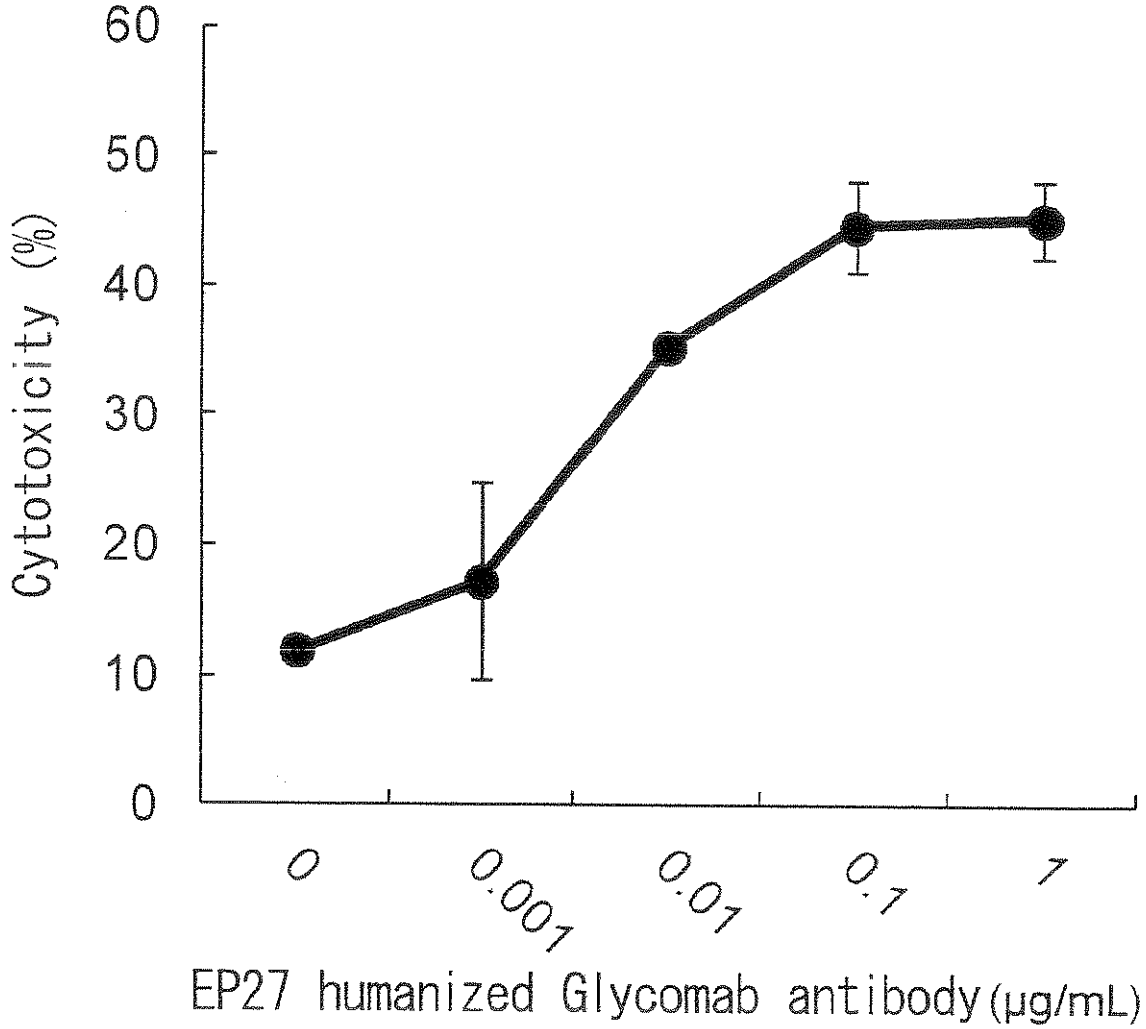

60
50
40
30
20
10
0
Cytotoxicity (%)
0
0.001
0.01
0.1
1
EP27 humanized Glycomab antibody (μg/mL)

FIG. 19

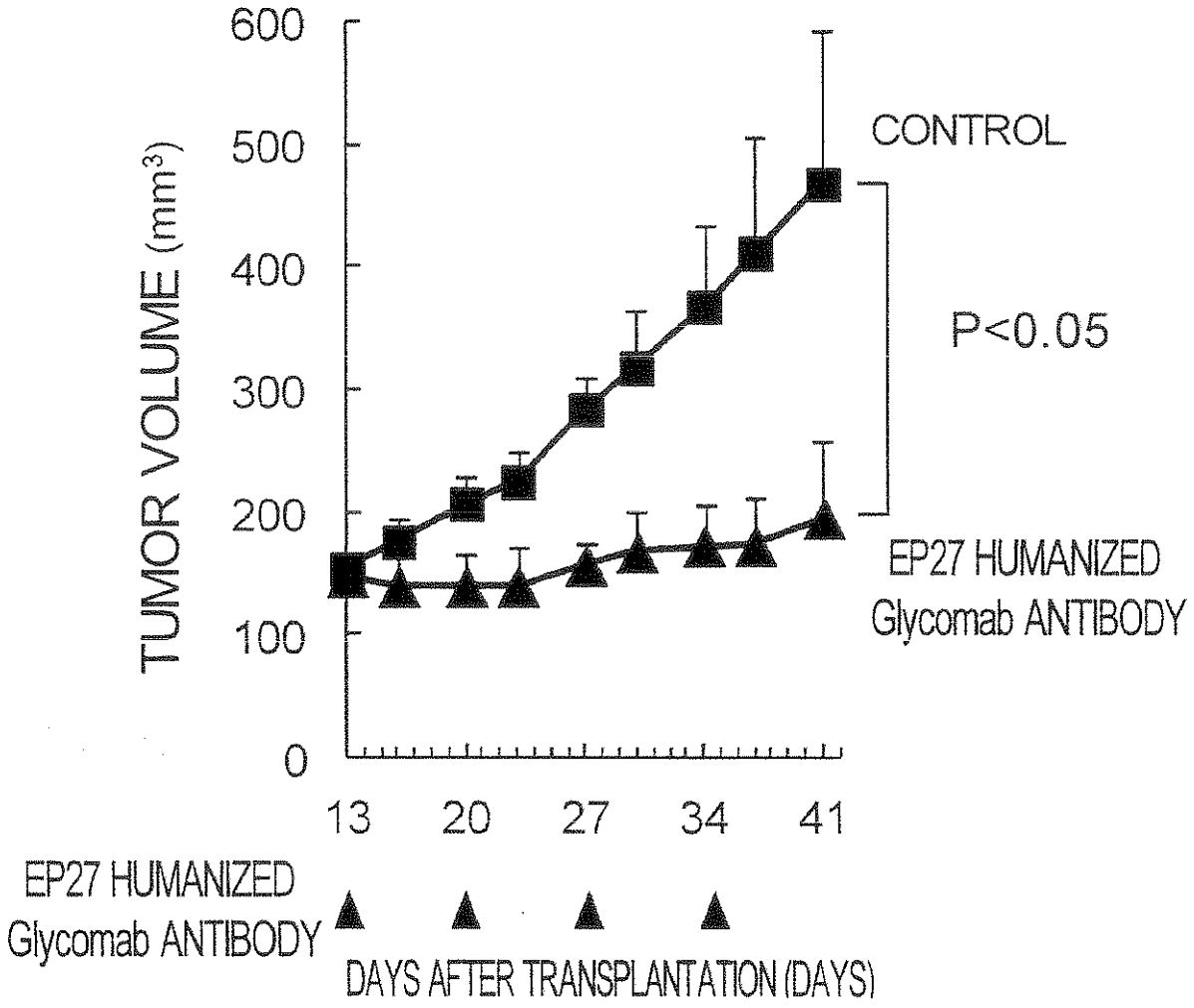
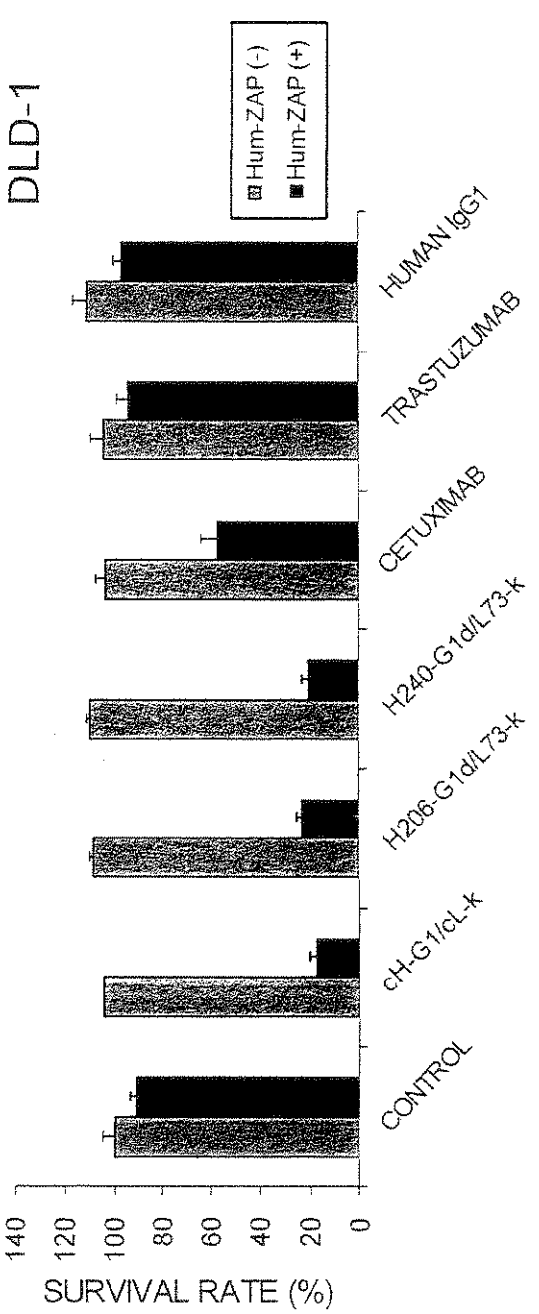

600
500
400
300
200
100
0
TUMOR VOLUME (mm3)
CONTROL
P<0.05
EP27 HUMANIZED
Glycomab ANTIBODY
13
20
27
34
41
EP27 HUMANIZED
Glycomab ANTIBODY
DAYS AFTER TRANSPLANTATION (DAYS)

FIG. 20


DLD-1
Hum-ZAP (-)
Hum-ZAP (+)
HUMAN IgG1
TRASTUZUMAB
CETUXIMAB
H240-G1d/L73-k
H206-G1d/L73-k
cH-G1/cL-k
CONTROL
140
120
100
80
60
40
20
0
SURVIVAL RATE (%)

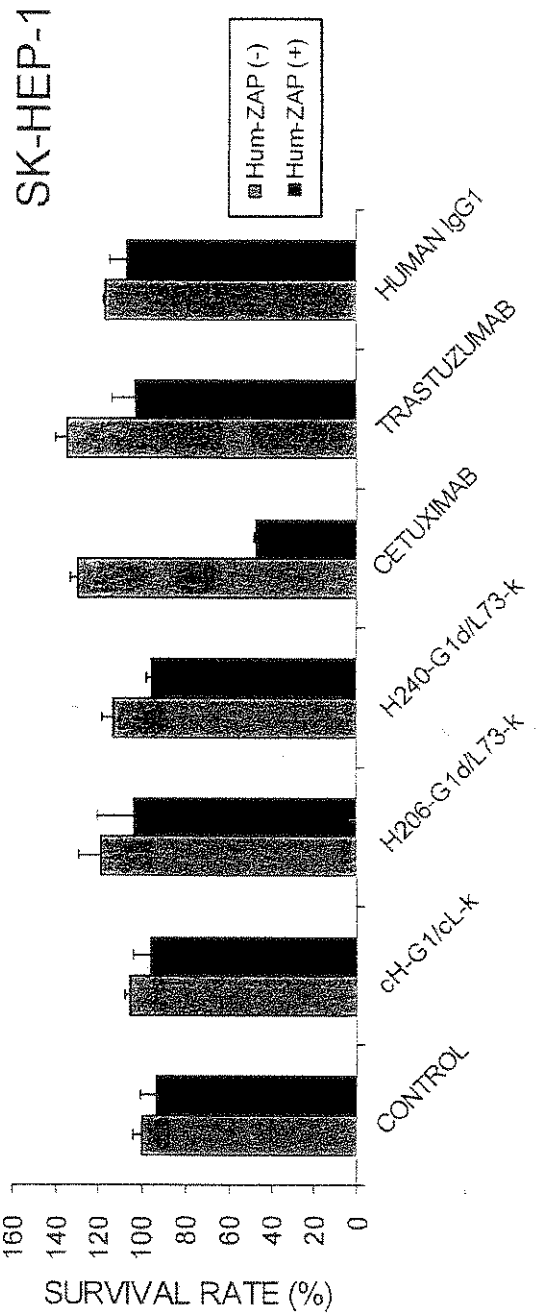

SK-HEP-1
Hum-ZAP (-)
Hum-ZAP (+)
HUMAN IgG1
TRASTUZUMAB
CETUXIMAB
H240-G1d/L73-k
H206-G1d/L73-k
cH-G1/cL-k
CONTROL
160
140
120
100
80
60
40
20
0
SURVIVAL RATE (%)

FIG. 21