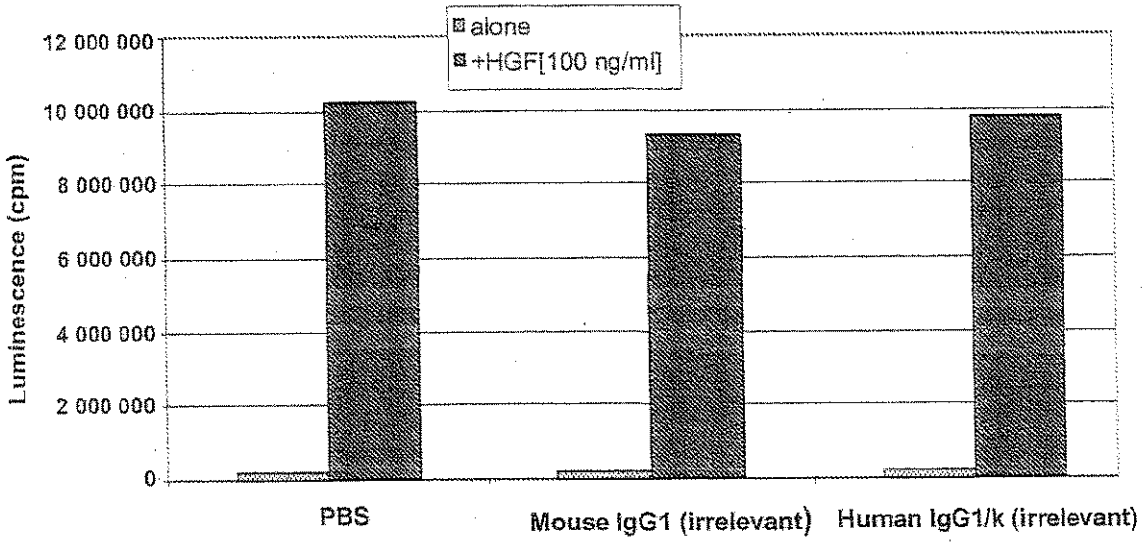

alone
+HGF[100 ng/ml]
12 000 000
10 000 000
8 000 000
6 000 000
4 000 000
2 000 000
0
Luminescence (cpm)
PBS
Mouse IgG1 (irrelevant)
Human IgG1/k (irrelevant)

FIGURE 1

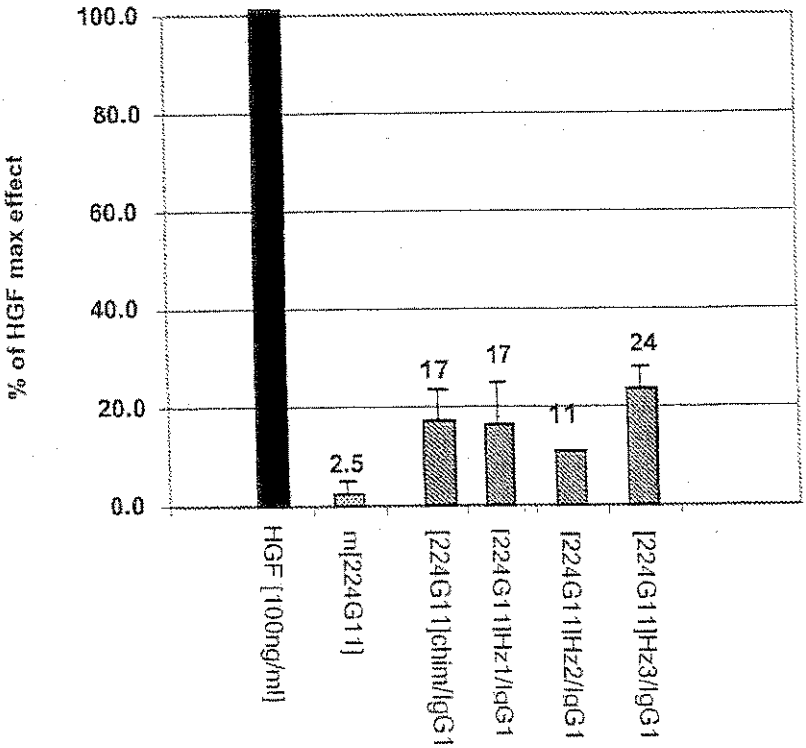


FIGURE 2A

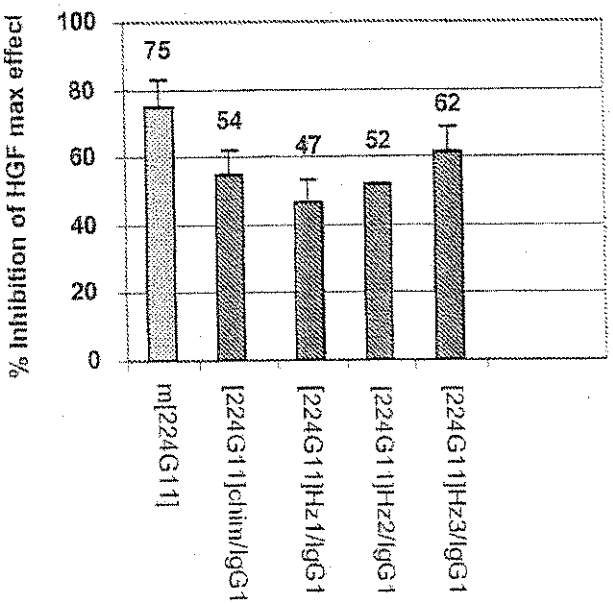


FIGURE 2B

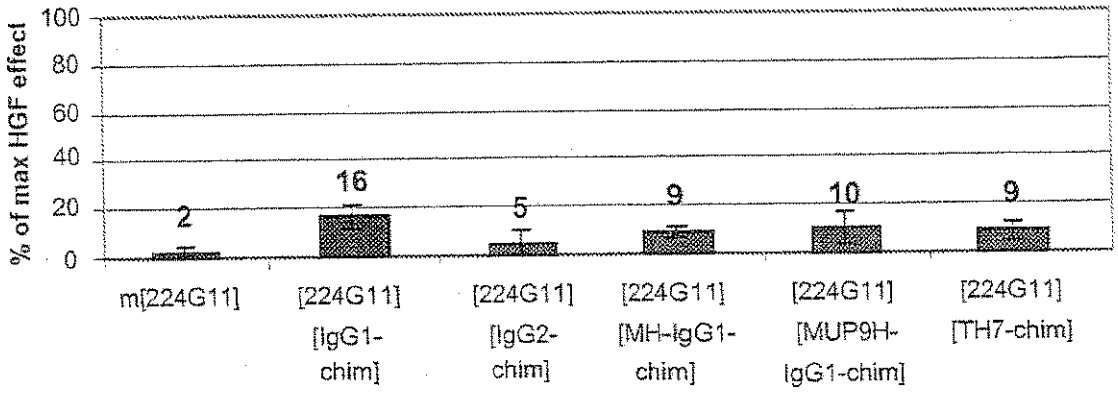


FIGURE 3A

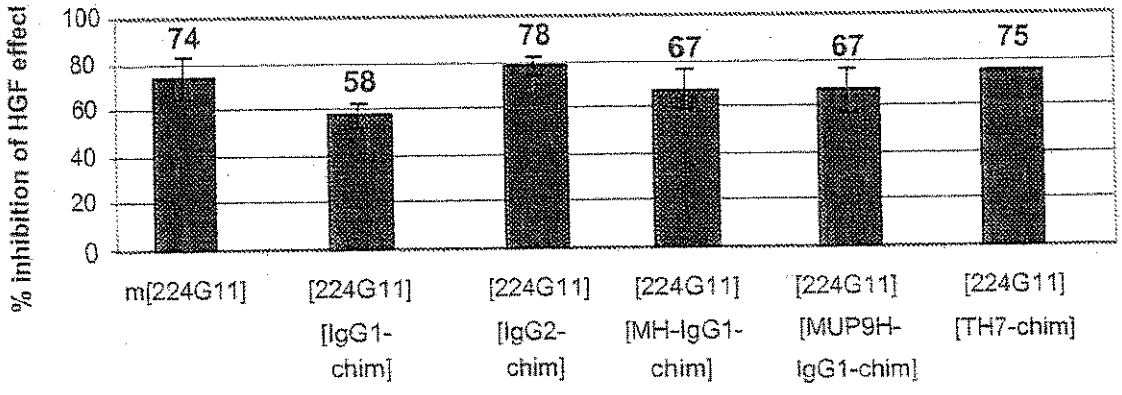


FIGURE 3B

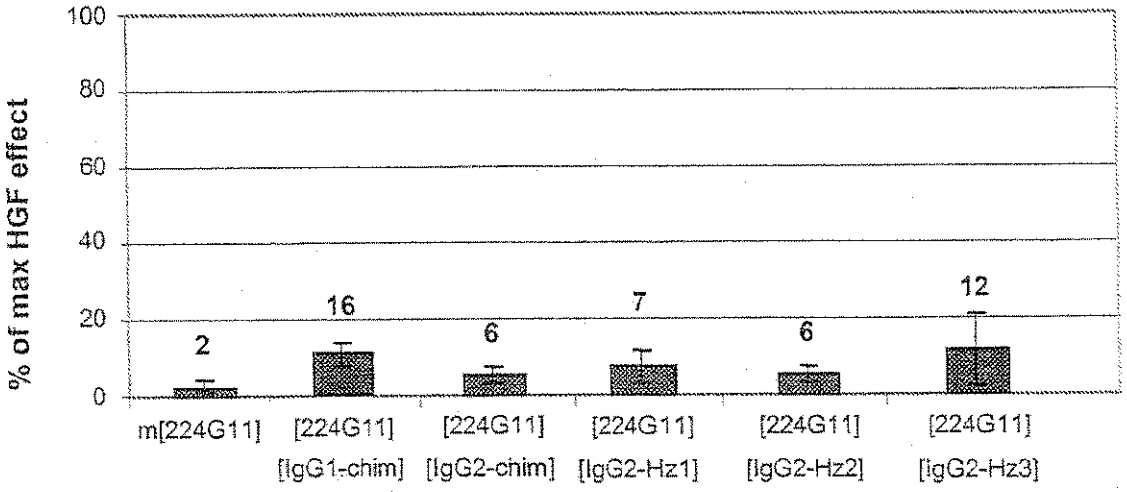


FIGURE 4A

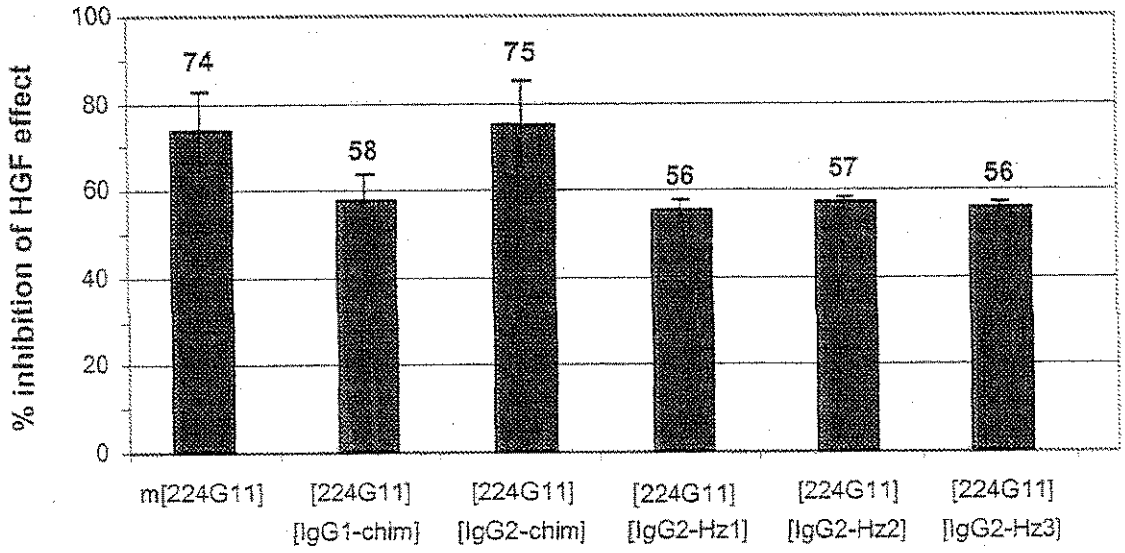


FIGURE 4B

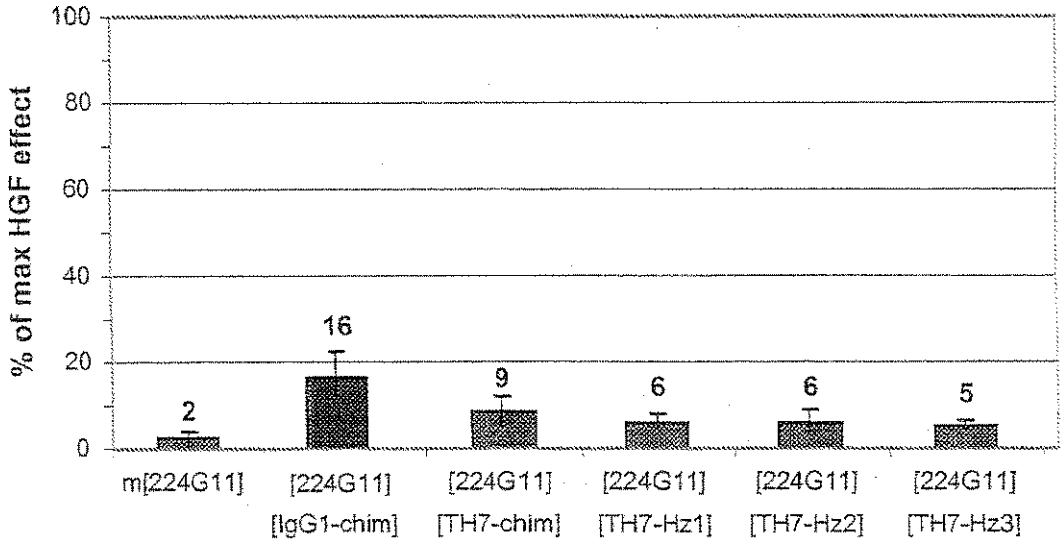


FIGURE 5A

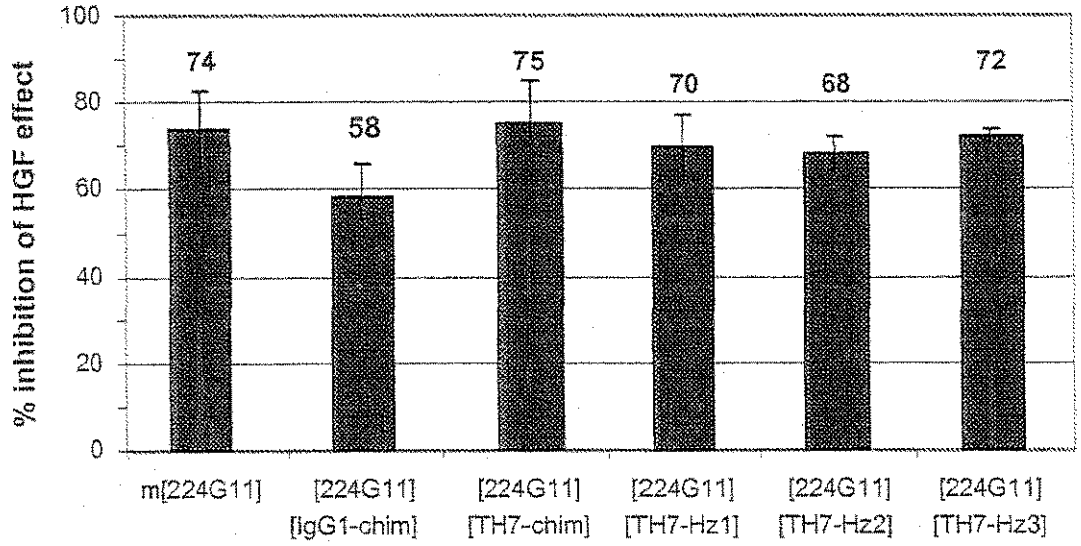


FIGURE 5B

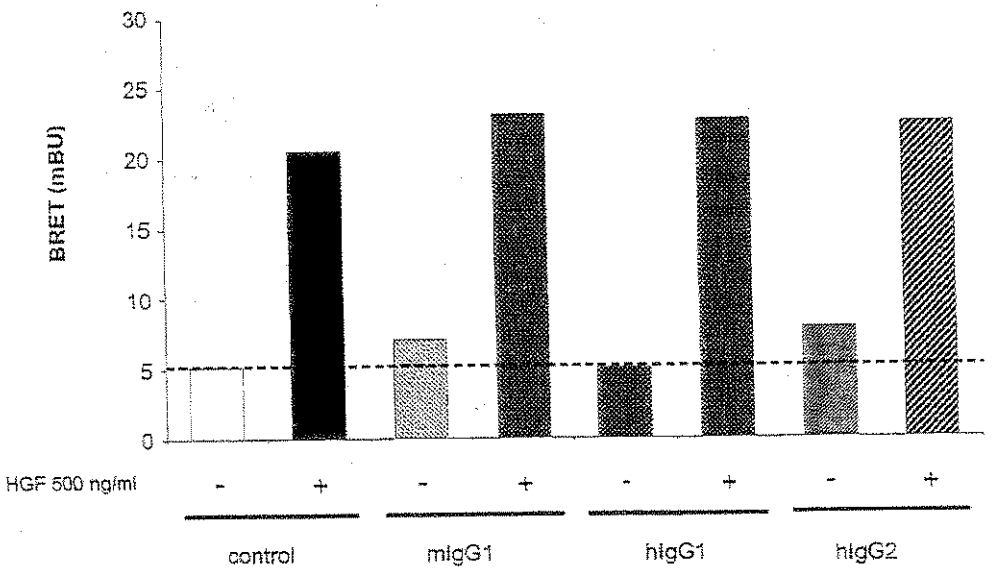


FIGURE 6A

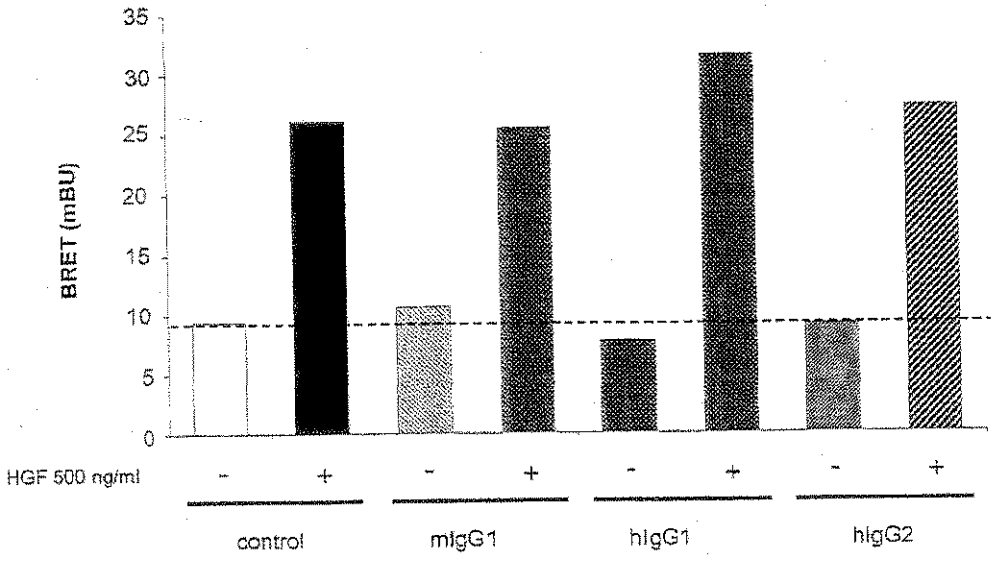


FIGURE 6B

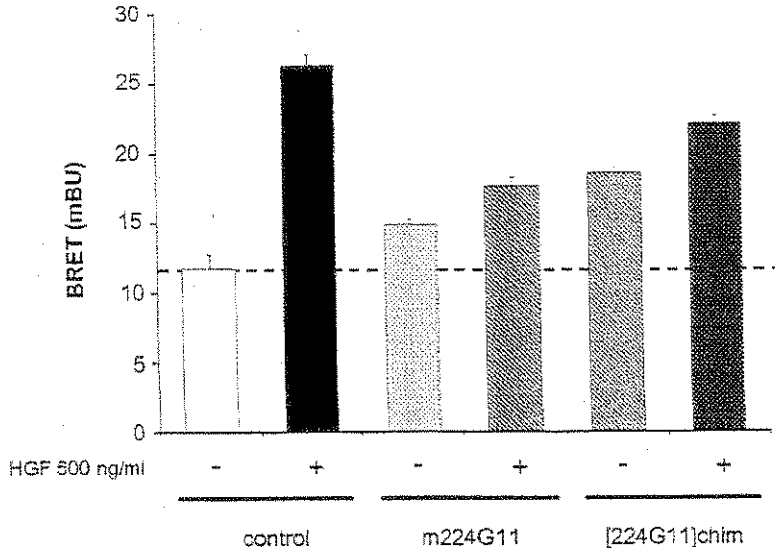


FIGURE 7A

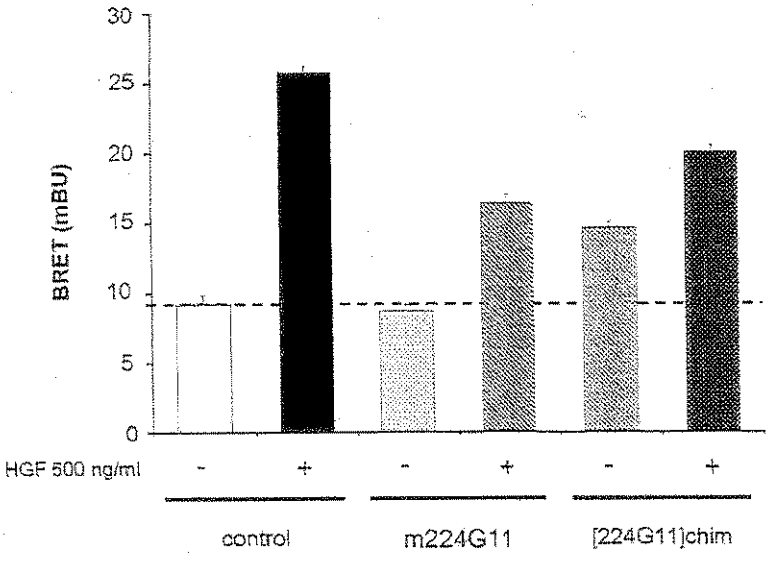


FIGURE 7B

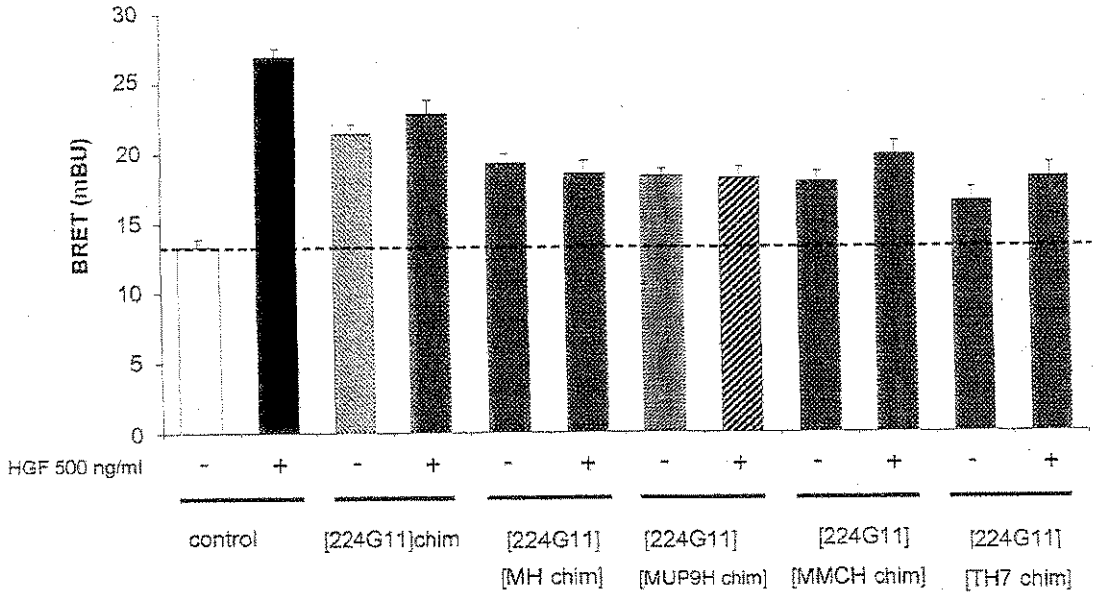


FIGURE 8A

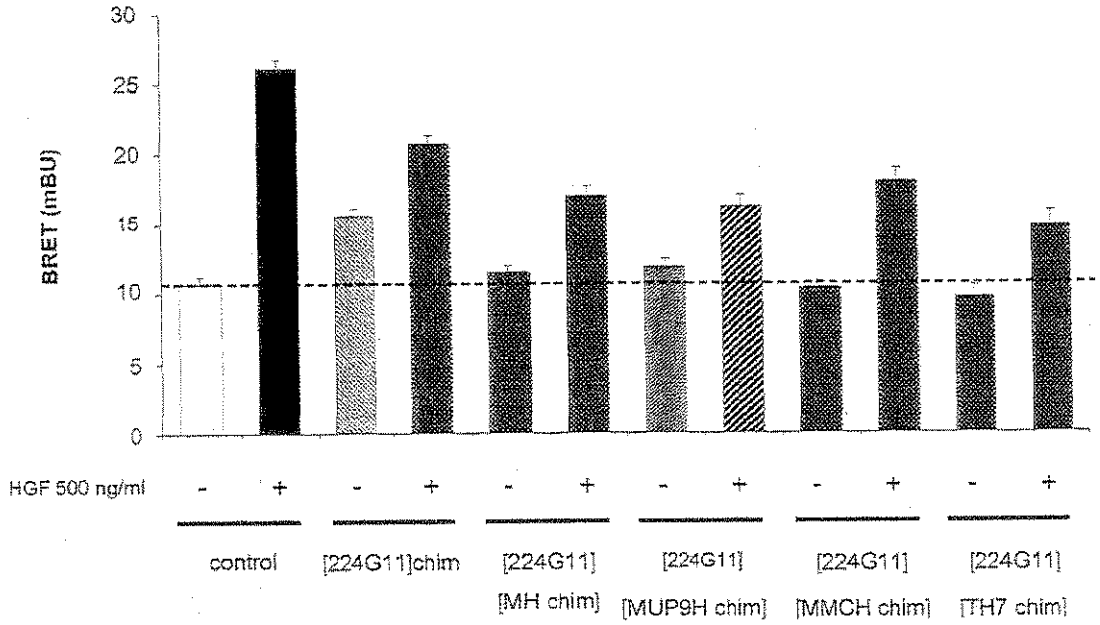


FIGURE 8B

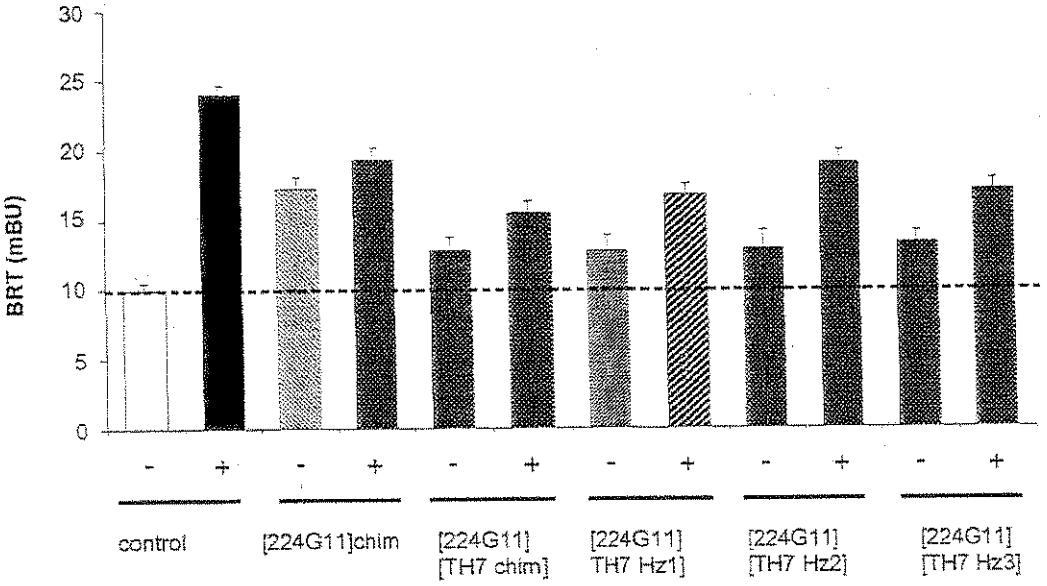


FIGURE 9A

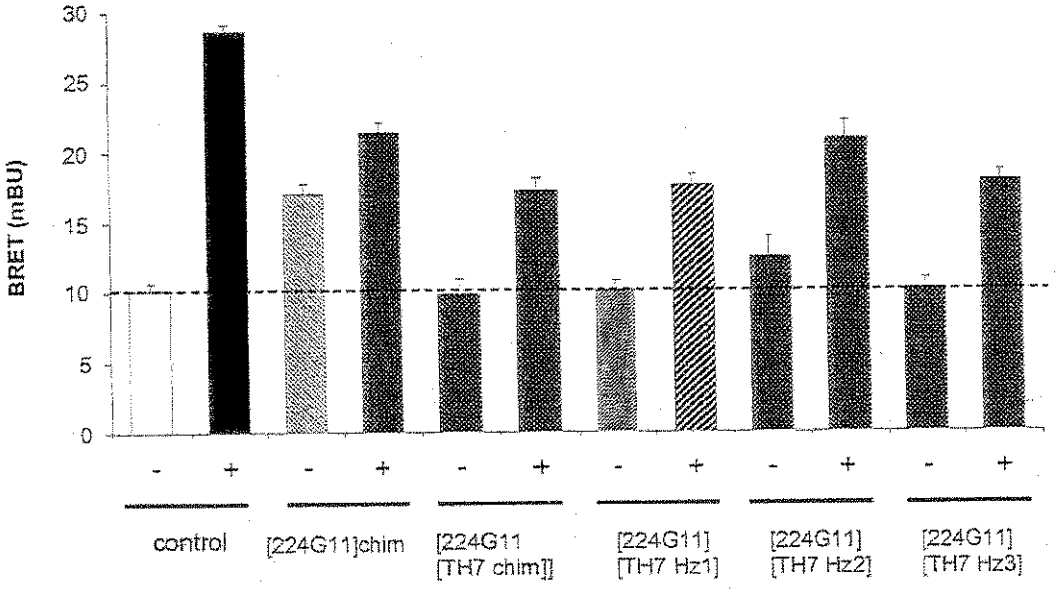


FIGURE 9B

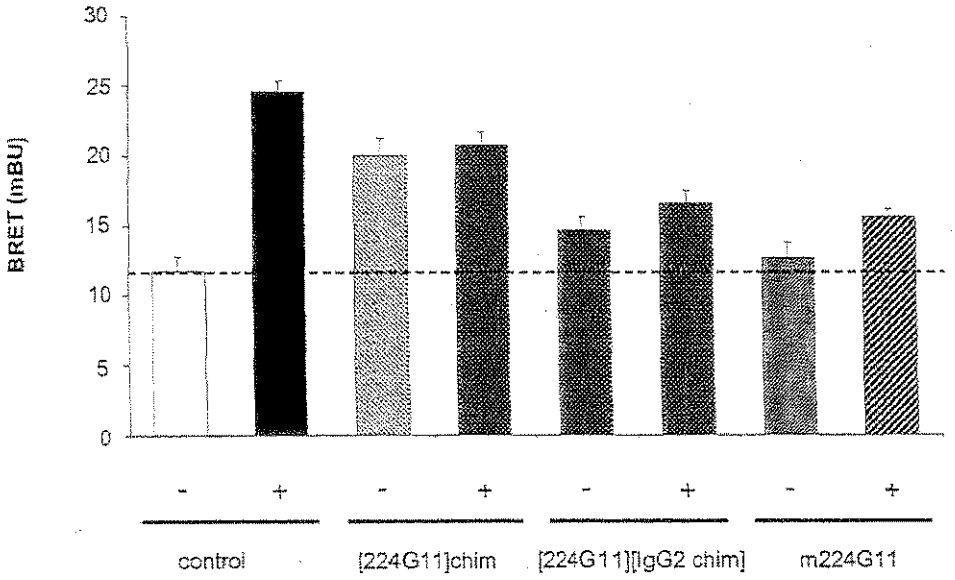


FIGURE 10A

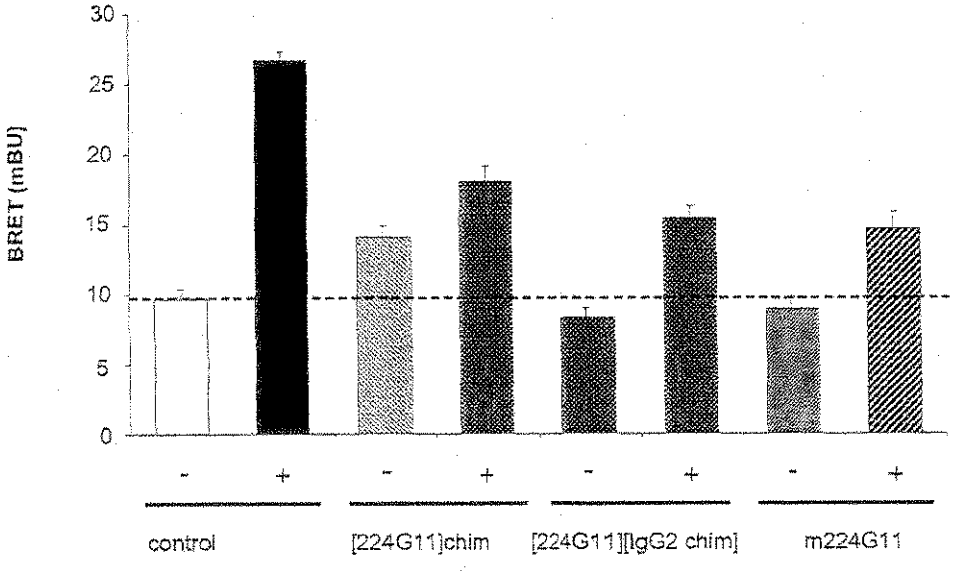
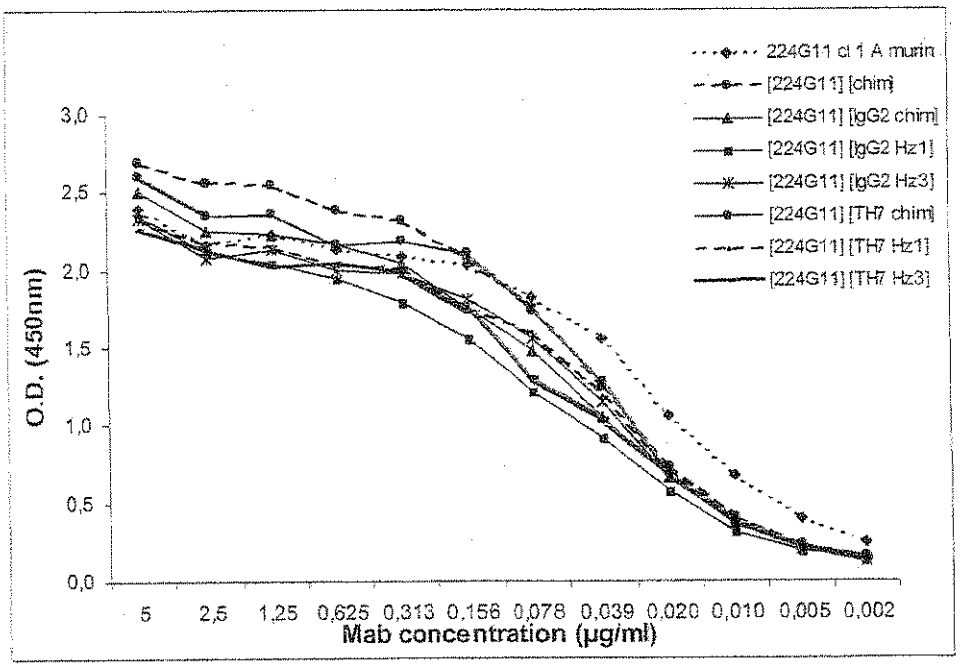


FIGURE 10B


224G11 cl 1 A murin
[224G11] [chim]
[224G11] [IgG2 chim]
[224G11] [IgG2 Hz1]
[224G11] [IgG2 Hz3]
[224G11] [TH7 chim]
[224G11] [TH7 Hz1]
[224G11] [TH7 Hz3]
O.D. (450nm)
3,0
2,5
2,0
1,5
1,0
0,5
0,0
5 2,5 1,25 0,625 0,313 0,156 0,078 0,039 0,020 0,010 0,005 0,002
Mab concentration (µg/ml)

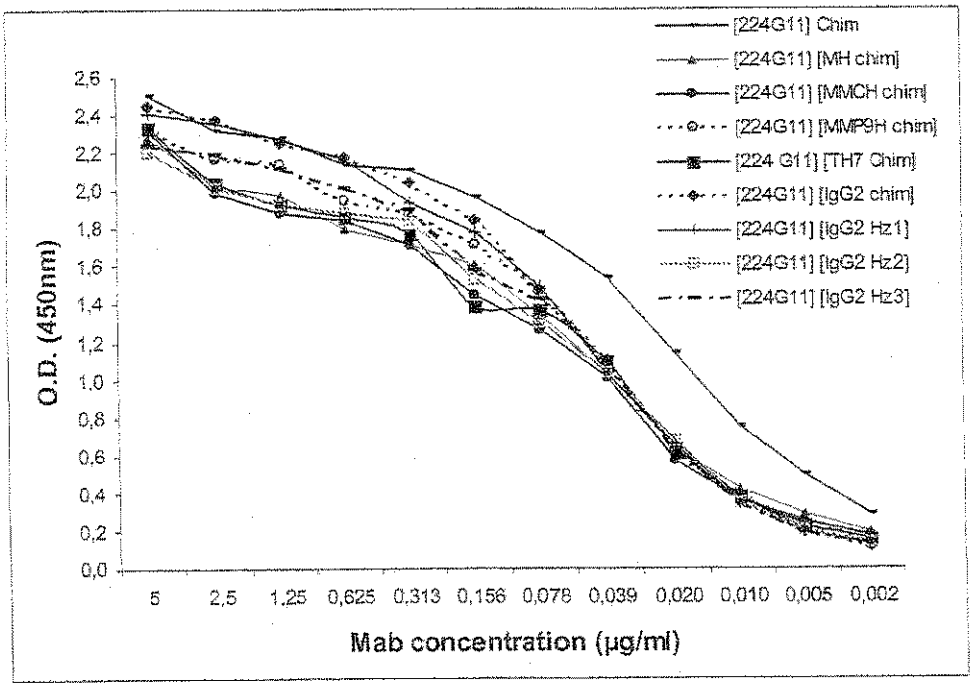

[224G11] Chim
[224G11] [MH chim]
[224G11] [MMCH chim]
[224G11] [MMP9H chim]
[224 G11] [TH7 Chim]
[224G11] [IgG2 chim]
[224G11] [IgG2 Hz1]
[224G11] [IgG2 Hz2]
[224G11] [IgG2 Hz3]
O.D. (450nm)
2,6
2,4
2,2
2,0
1,8
1,6
1,4
1,2
1,0
0,8
0,6
0,4
0,2
0,0
5 2,5 1,25 0,625 0,313 0,156 0,078 0,039 0,020 0,010 0,005 0,002
Mab concentration (µg/ml)

FIGURE 11

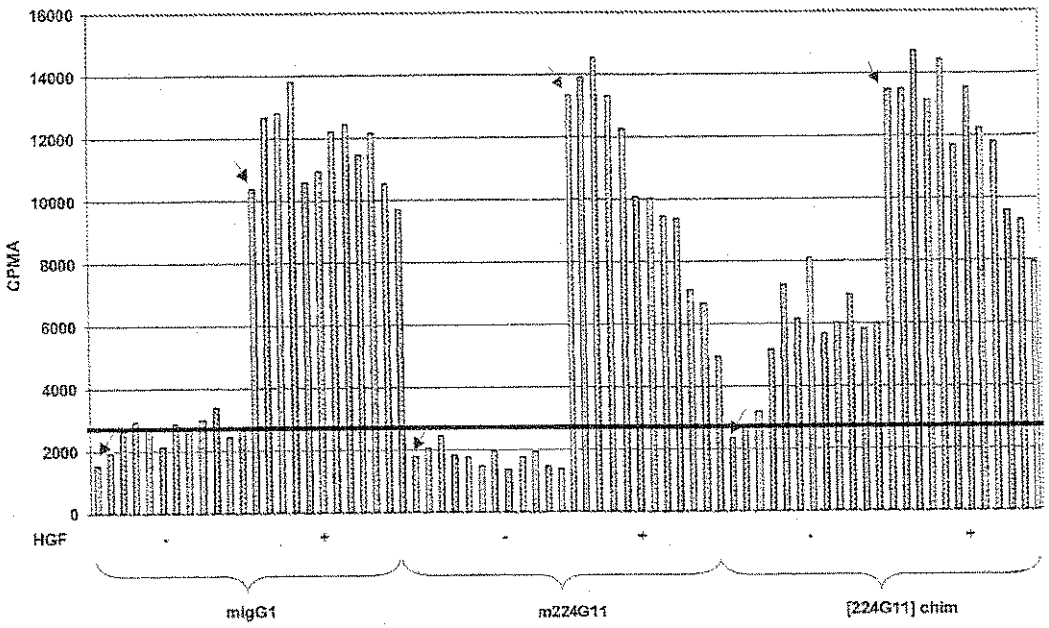


FIGURE 12

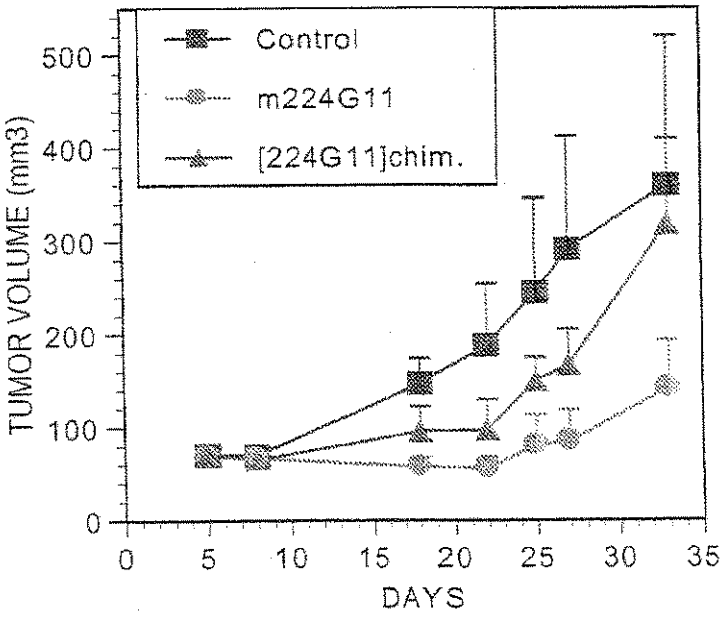


FIGURE 13

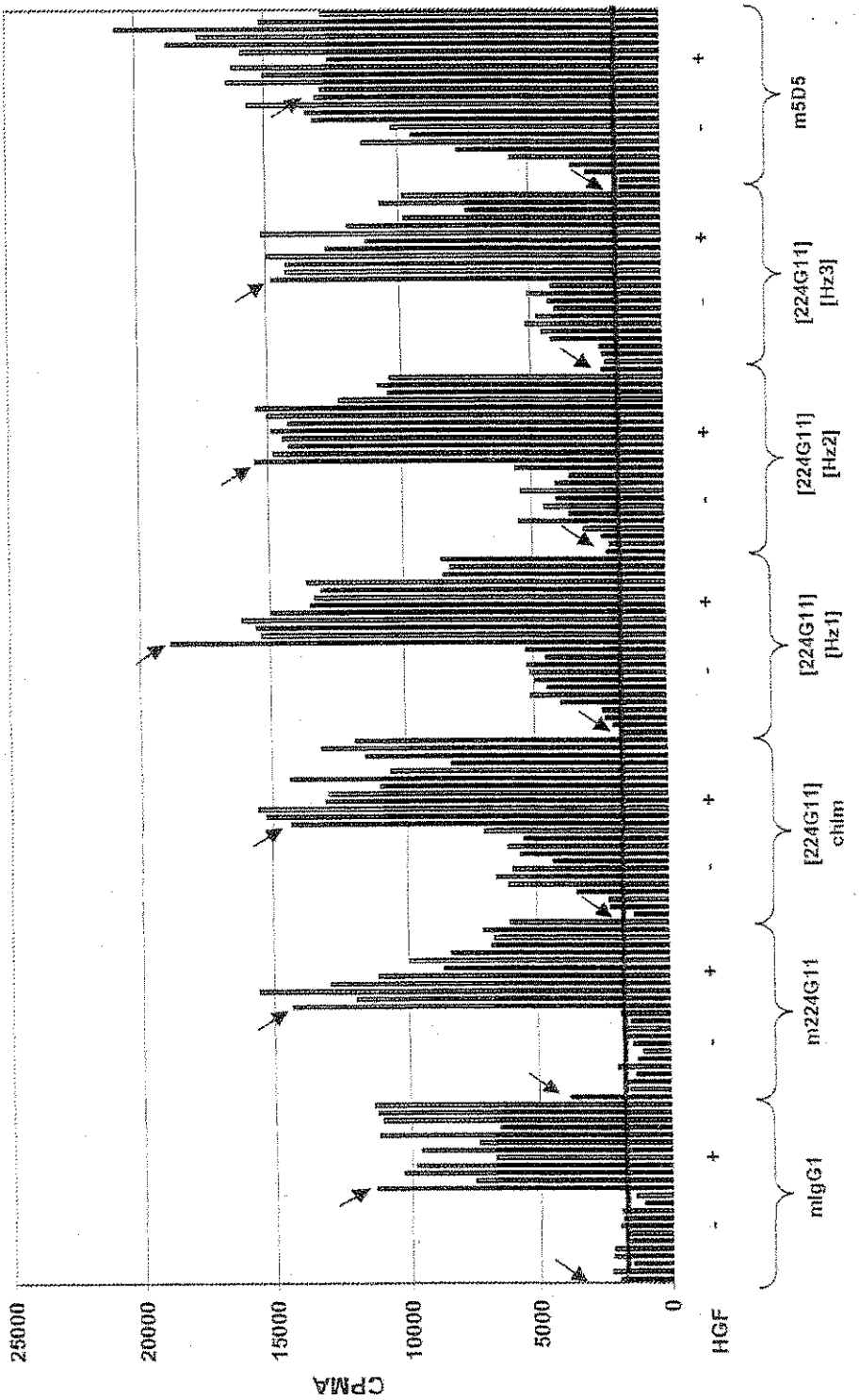

CPMA
25000
20000
15000
10000
5000
0
HGF
- + - + - + - + - +
mIgG1
m224G11
[224G11] chim
[224G11] [Hz1]
[224G11] [Hz2]
[224G11] [Hz3]
m5D5

FIGURE 14A

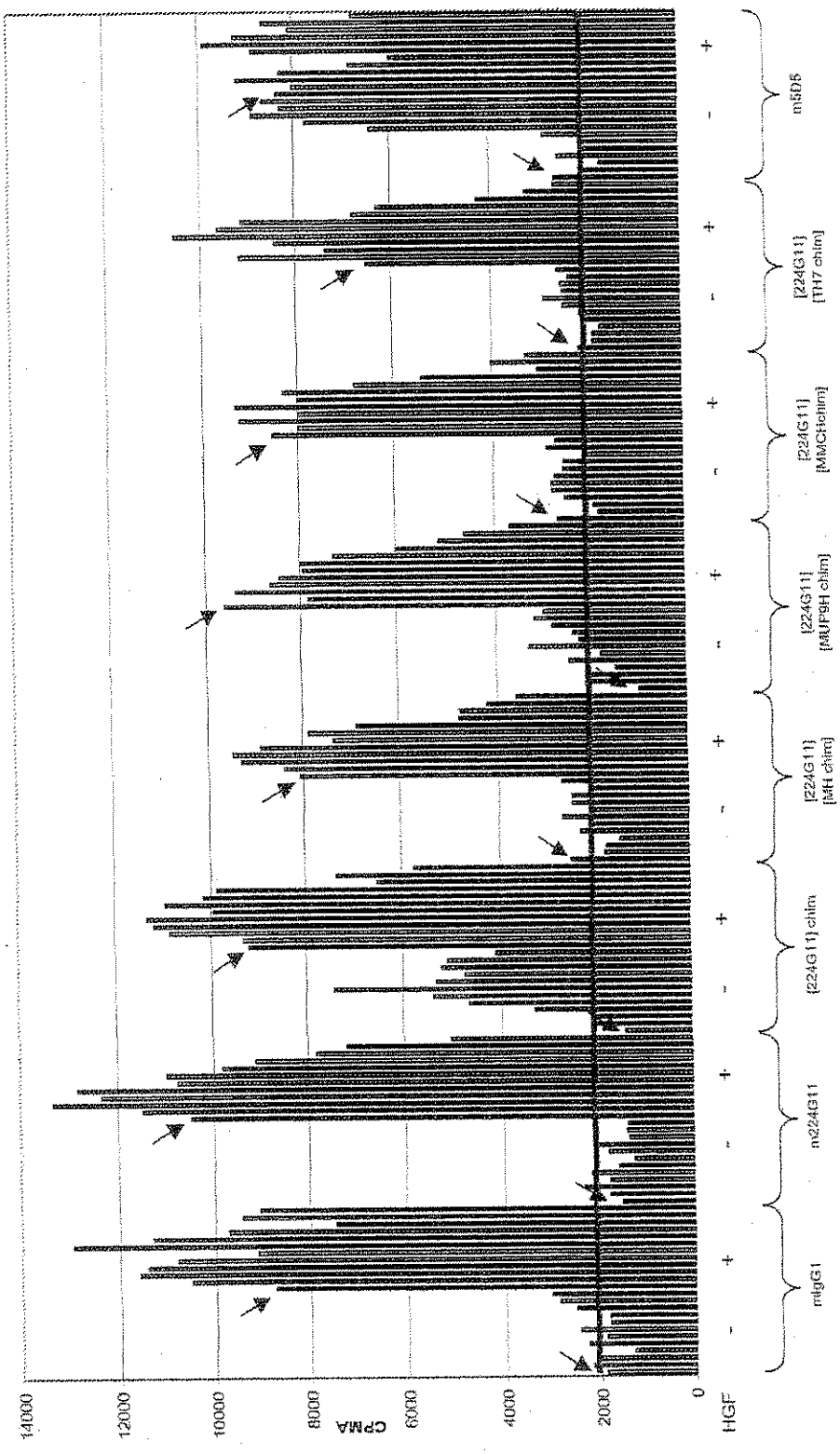

14000
12000
10000
8000
6000
4000
2000
0
CPMA
HGF
- + - + - + - + - + - +
mIgG1
m224G11
[224G11] chim
[224G11] [MH chim]
[224G11] [MUPBH chim]
[224G11] [MMCHchim]
[224G11] [TH7 chim]
m5D5

FIGURE 14B

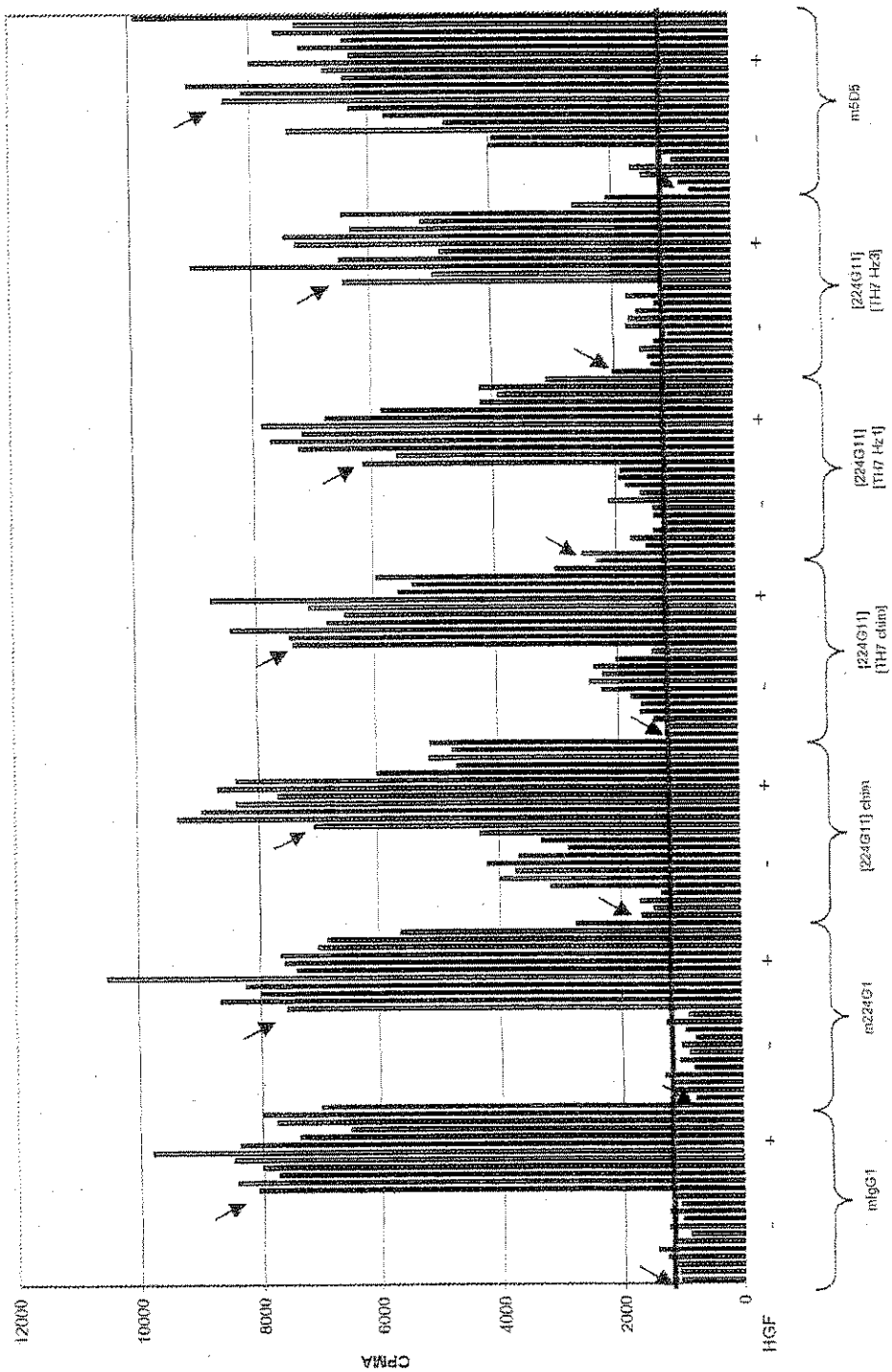

12000
10000
8000
6000
4000
2000
0
CPMA
HGF
- + - + - + - + - +
mIgG1
m224G1
[224G11] chim
[224G11] [1Hz dim]
[224G11] [1Hz Hz1]
[224G11] [1Hz Hz3]
m5D5

FIGURE 15

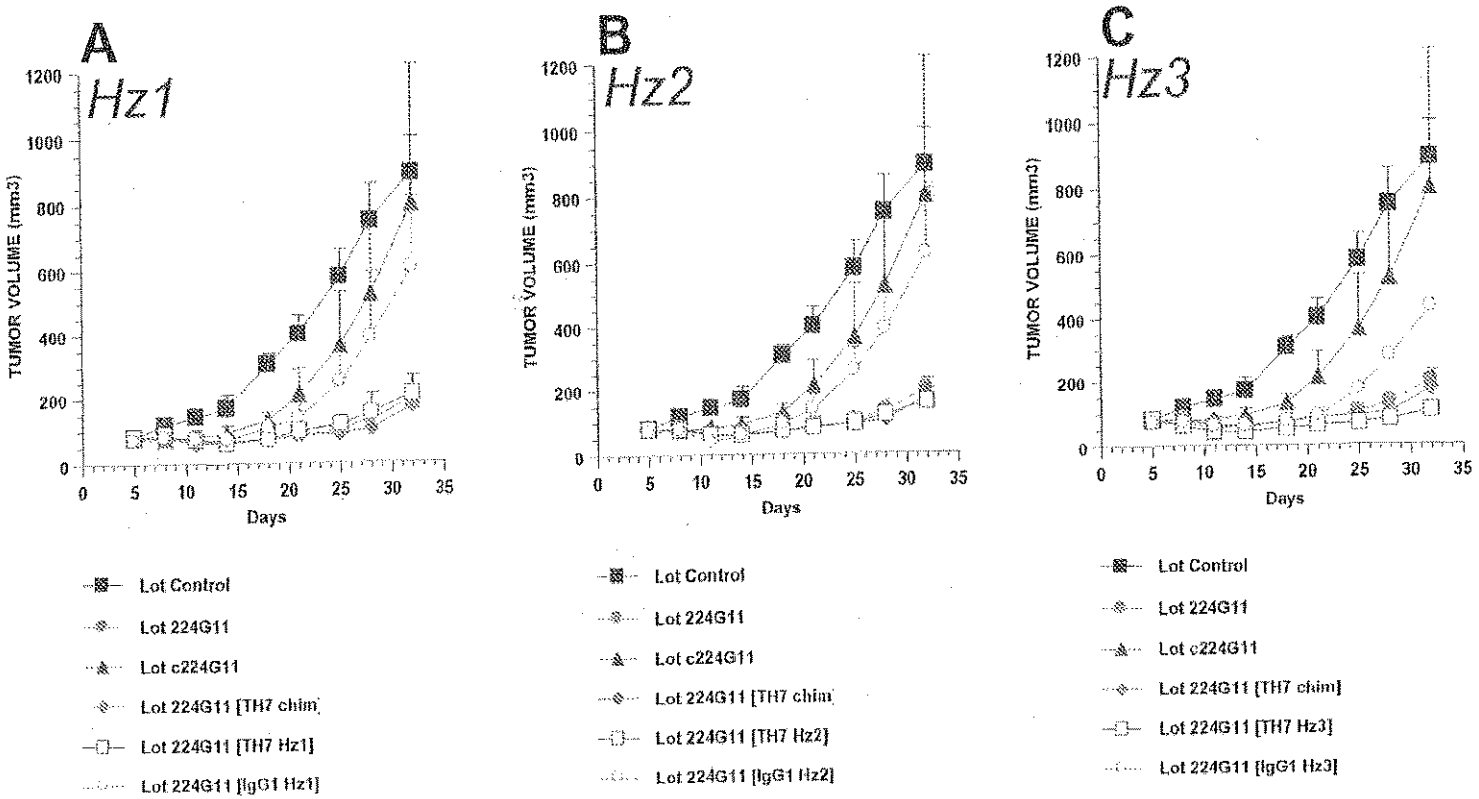

A
Hz1
B
Hz2
C
Hz3
TUMOR VOLUME (mm3)
Days
0
200
400
600
800
1000
1200
0 5 10 15 20 25 30 35
Lot Control
Lot 224G11
Lot c224G11
Lot 224G11 [TH7 chim]
Lot 224G11 [TH7 Hz1]
Lot 224G11 [IgG1 Hz1]
Lot 224G11 [TH7 Hz2]
Lot 224G11 [IgG1 Hz2]
Lot 224G11 [TH7 Hz3]
Lot 224G11 [IgG1 Hz3]

FIGURE 16

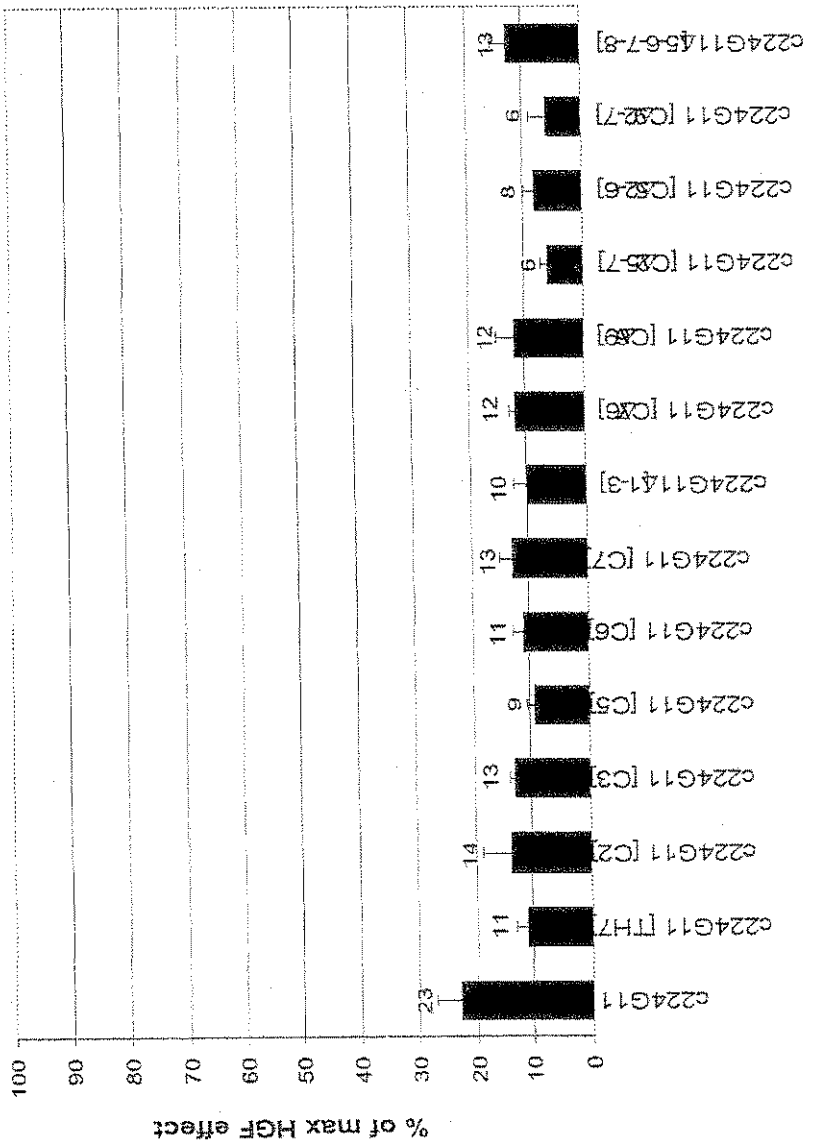

% of max HGF effect
100
90
80
70
60
50
40
30
20
10
0
c224G11
23
c224G11 [TH7]
11
c224G11 [C2]
14
c224G11 [C3]
13
c224G11 [C5]
9
c224G11 [C6]
11
c224G11 [C7]
13
c224G11[1-3]
10
c224G11 [C8]
12
c224G11 [C9]
12
c224G11 [C25-7]
9
c224G11 [C52-6]
8
c224G11 [C52-7]
6
c224G11[5-6-7-8]
13

FIGURE 17A

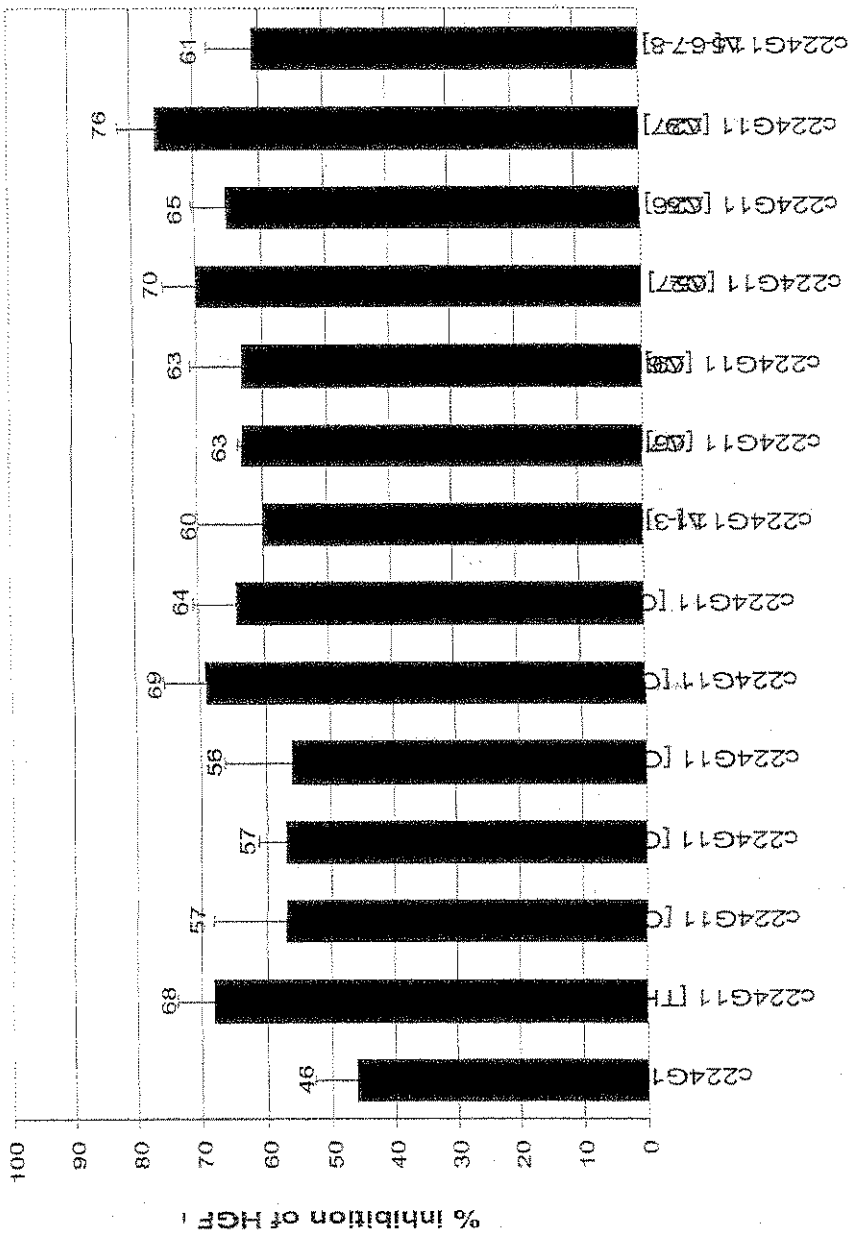

% inhibition of HGF
100
90
80
70
60
50
40
30
20
10
0
c224G1
c224G11 [TH
c224G11 [C
c224G11 [C
c224G11 [C
c224G11 [C
c224G11 [C
c224G1 Δ1-3]
c224G11 [Δ57]
c224G11 [Δ58]
c224G11 [Δ57]
c224G11 [Δ56]
c224G11 [Δ57]
c224G1 Δ5-6-7-8]
46
68
57
57
56
69
64
60
63
63
70
65
76
61

FIGURE 17B

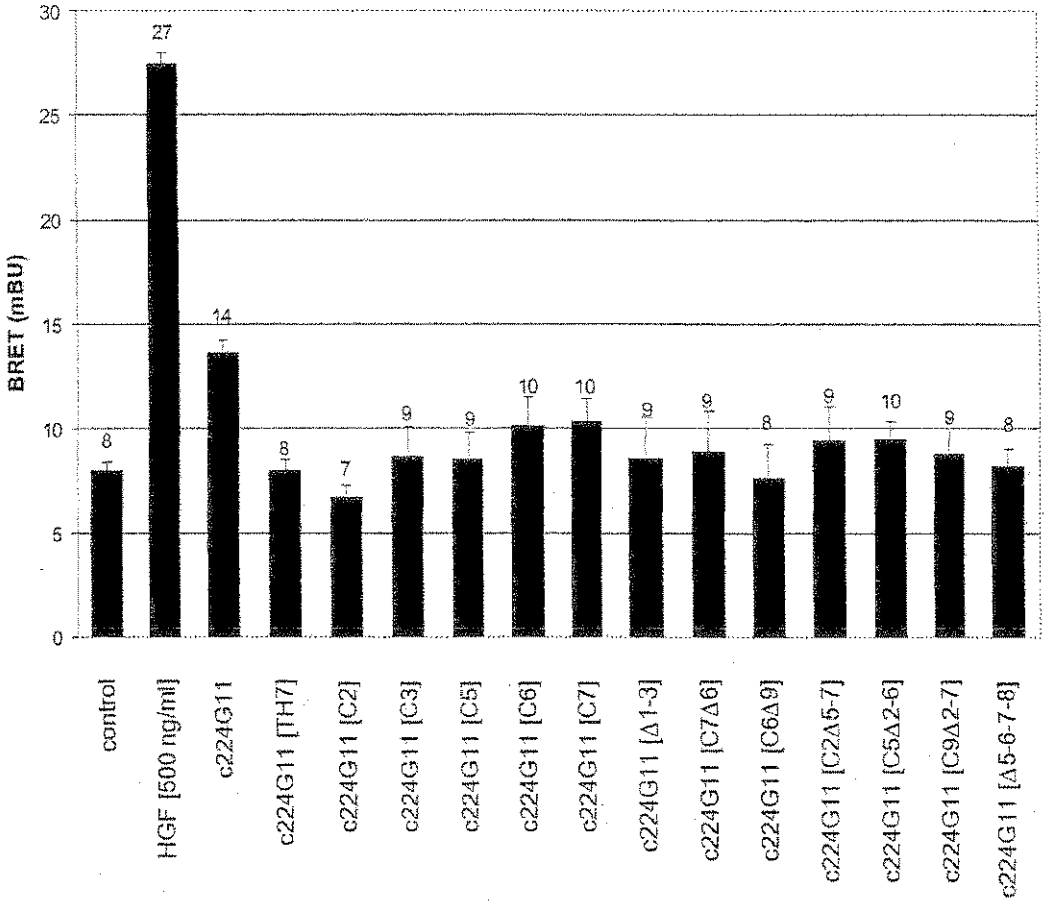
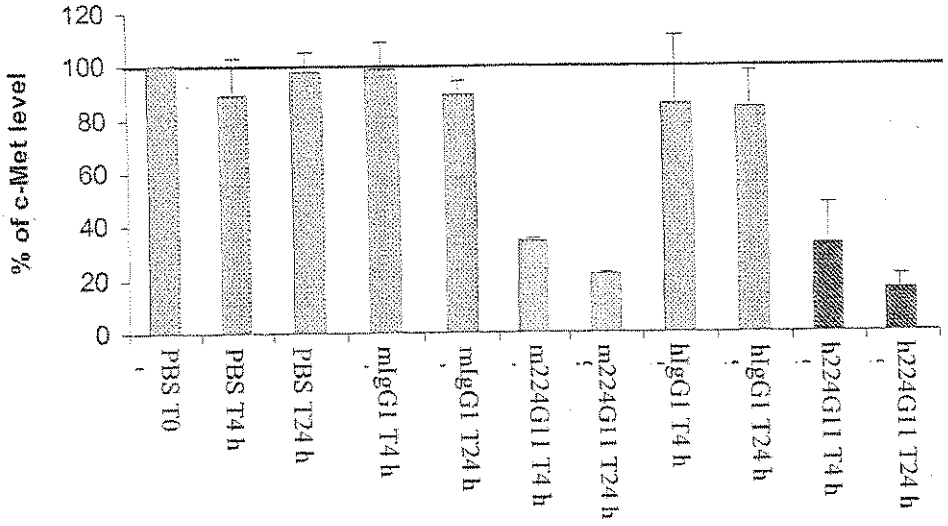

BRET (mBU)
30
25
20
15
10
5
0
8
27
14
8
7
9
9
10
10
9
9
8
9
10
9
8
control
HGF [500 ng/ml]
c224G11
c224G11 [TH7]
c224G11 [C2]
c224G11 [C3]
c224G11 [C5]
c224G11 [C6]
c224G11 [C7]
c224G11 [Δ1-3]
c224G11 [C7Δ6]
c224G11 [C6Δ9]
c224G11 [C2Δ5-7]
c224G11 [C5Δ2-6]
c224G11 [C9Δ2-7]
c224G11 [Δ5-6-7-8]

FIGURE 18

A


% of c-Met level
120
100
80
60
40
20
0
PBS T0
PBS T4 h
PBS T24 h
mIgG1 T4 h
mIgG1 T24 h
m224G11 T4 h
m224G11 T24 h
hIgG1 T4 h
hIgG1 T24 h
h224G11 T4 h
h224G11 T24 h

B

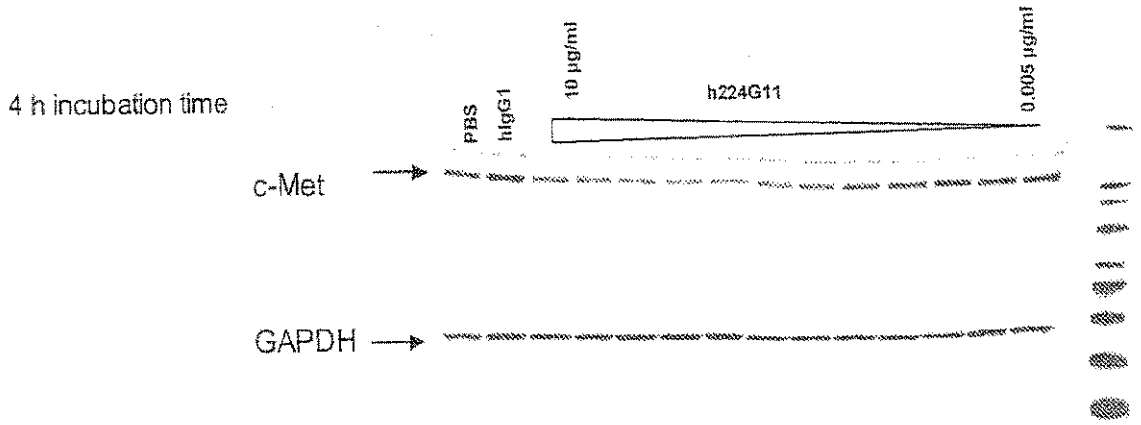
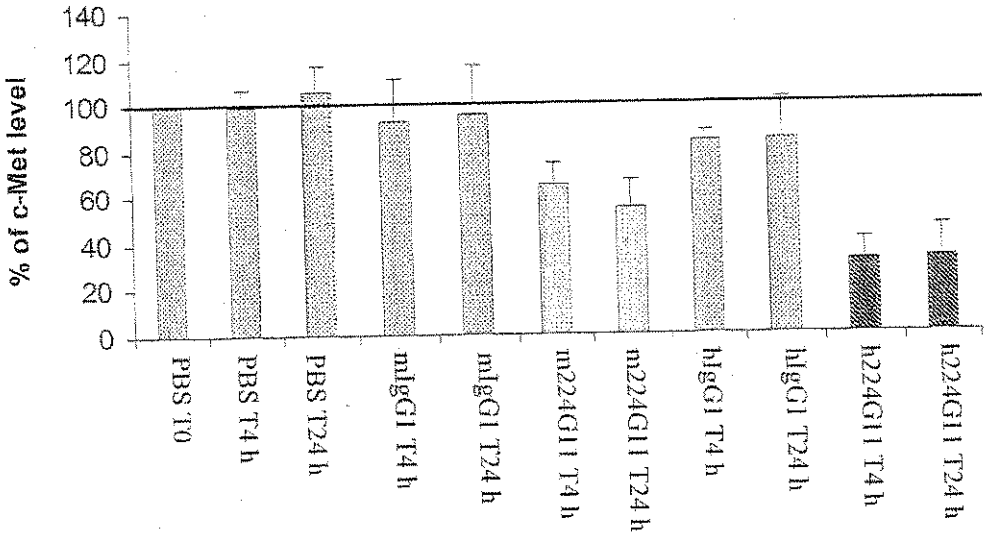

4 h incubation time
PBS
hIgG1
10 µg/ml
h224G11
0.005 µg/ml
c-Met
GAPDH

FIGURE 19

A


% of c-Met level
140
120
100
80
60
40
20
0
PBS T0
PBS T4 h
PBS T24 h
mIgG1 T4 h
mIgG1 T24 h
m224G11 T4 h
m224G11 T24 h
hIgG1 T4 h
hIgG1 T24 h
h224G11 T4 h
h224G11 T24 h

B

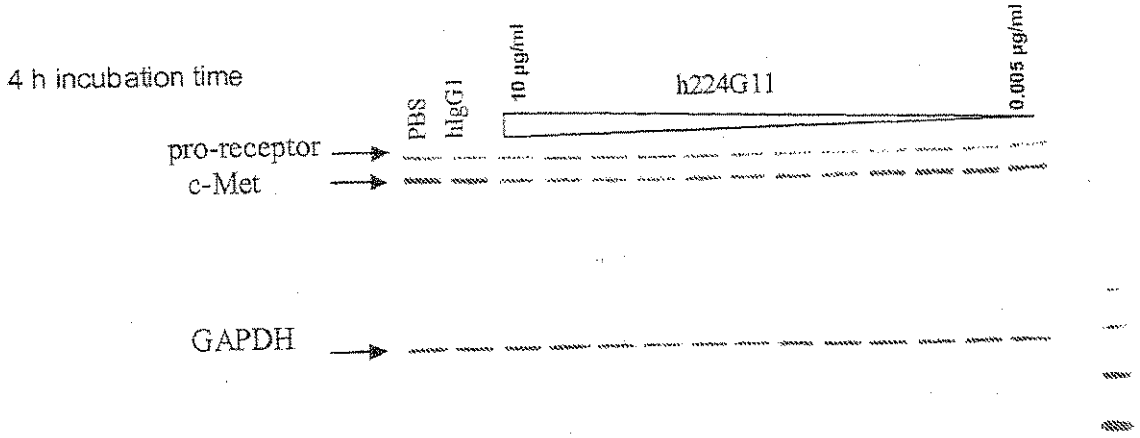

4 h incubation time
PBS
hIgG1
10 µg/ml
h224G11
0.005 µg/ml
pro-receptor
c-Met
GAPDH

FIGURE 20

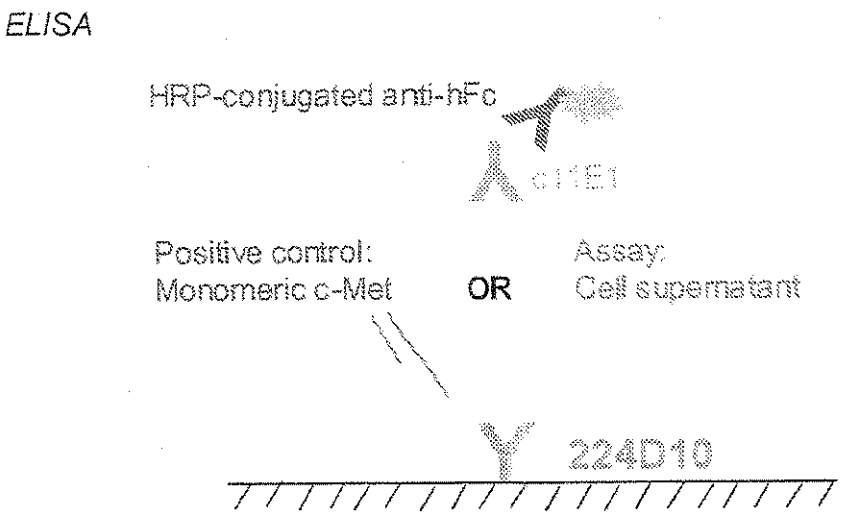


FIGURE 21

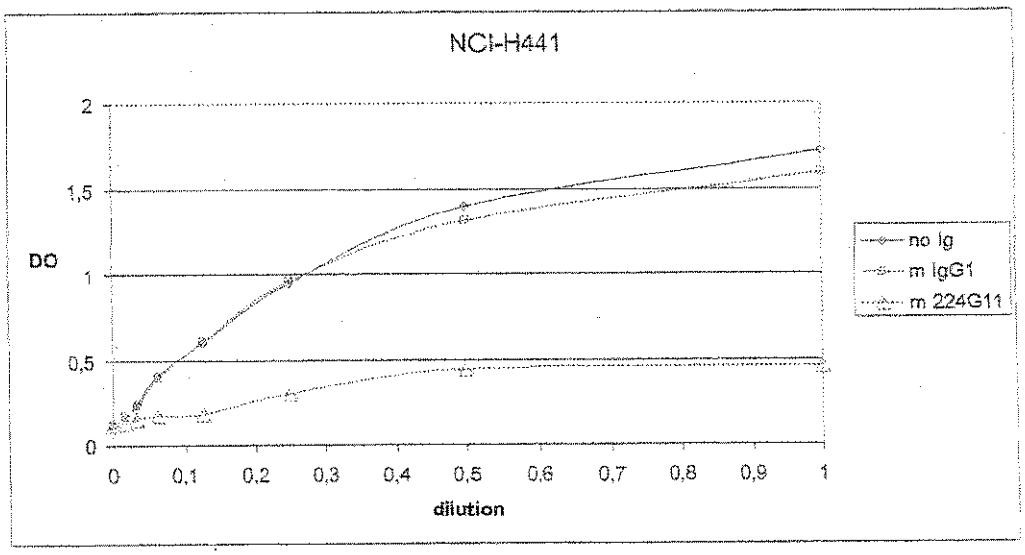


FIGURE 22

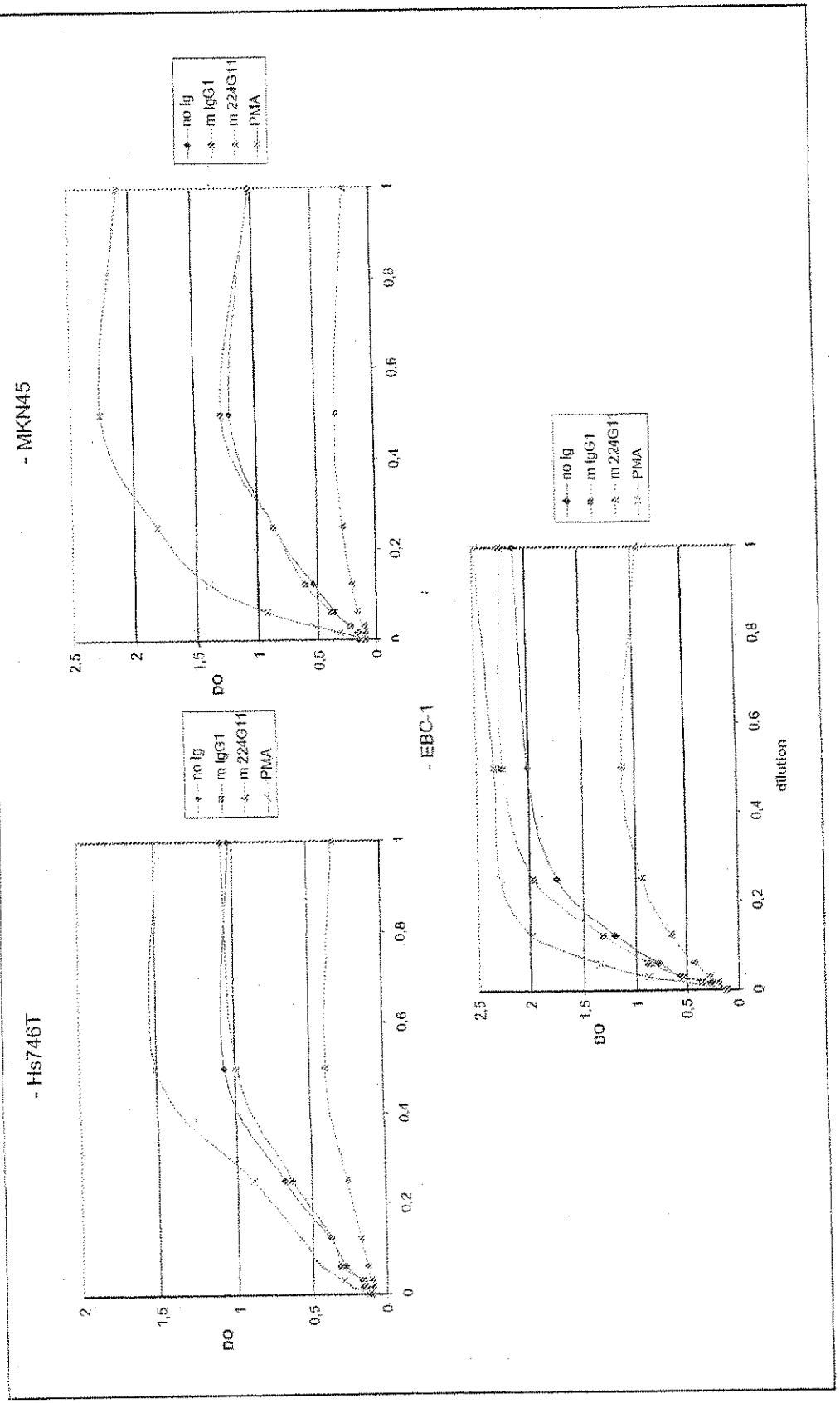


FIGURE 23

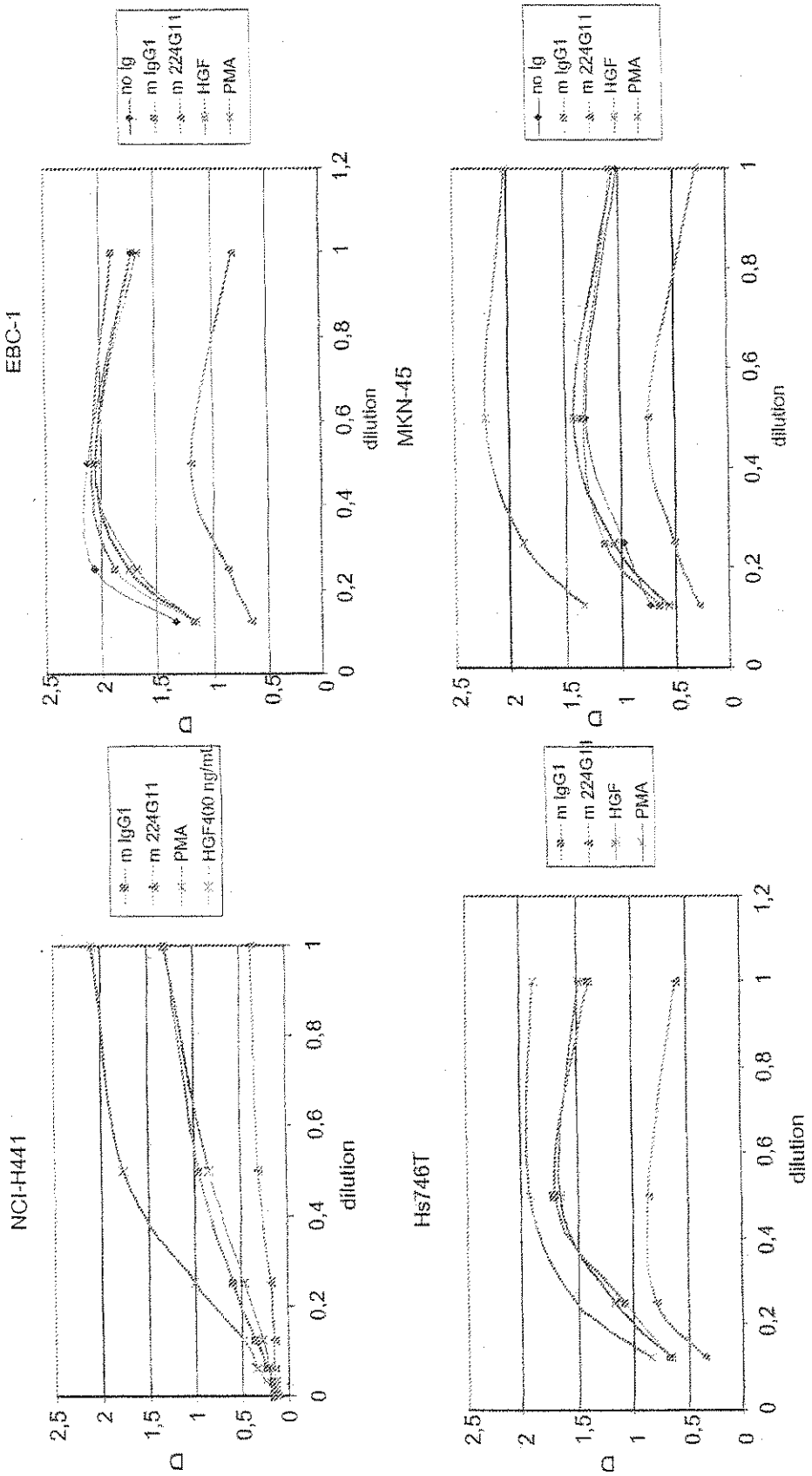

EBC-1
no Ig
m IgG1
m 224G11
HGF
PMA
MKN-45
NCI-H441
m IgG1
m 224G11
PMA
HGF400 ng/ml
Hs746T
dilution
OD

FIGURE 24

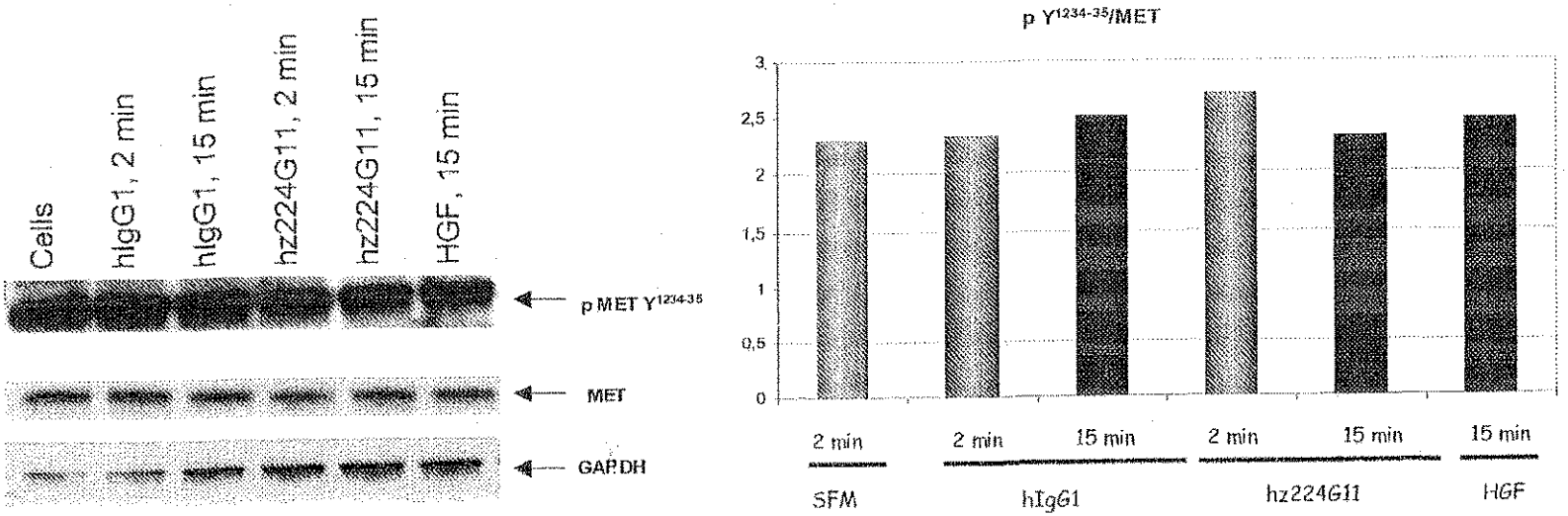

Cells
hIgG1, 2 min
hIgG1, 15 min
hz224G11, 2 min
hz224G11, 15 min
HGF, 15 min
p MET Y1234-35
MET
GAPDH
p Y1234-35/MET
3
2,5
2
1,5
1
0,5
0
2 min
2 min
15 min
2 min
15 min
15 min
SFM
hIgG1
hz224G11
HGF

FIGURE 25

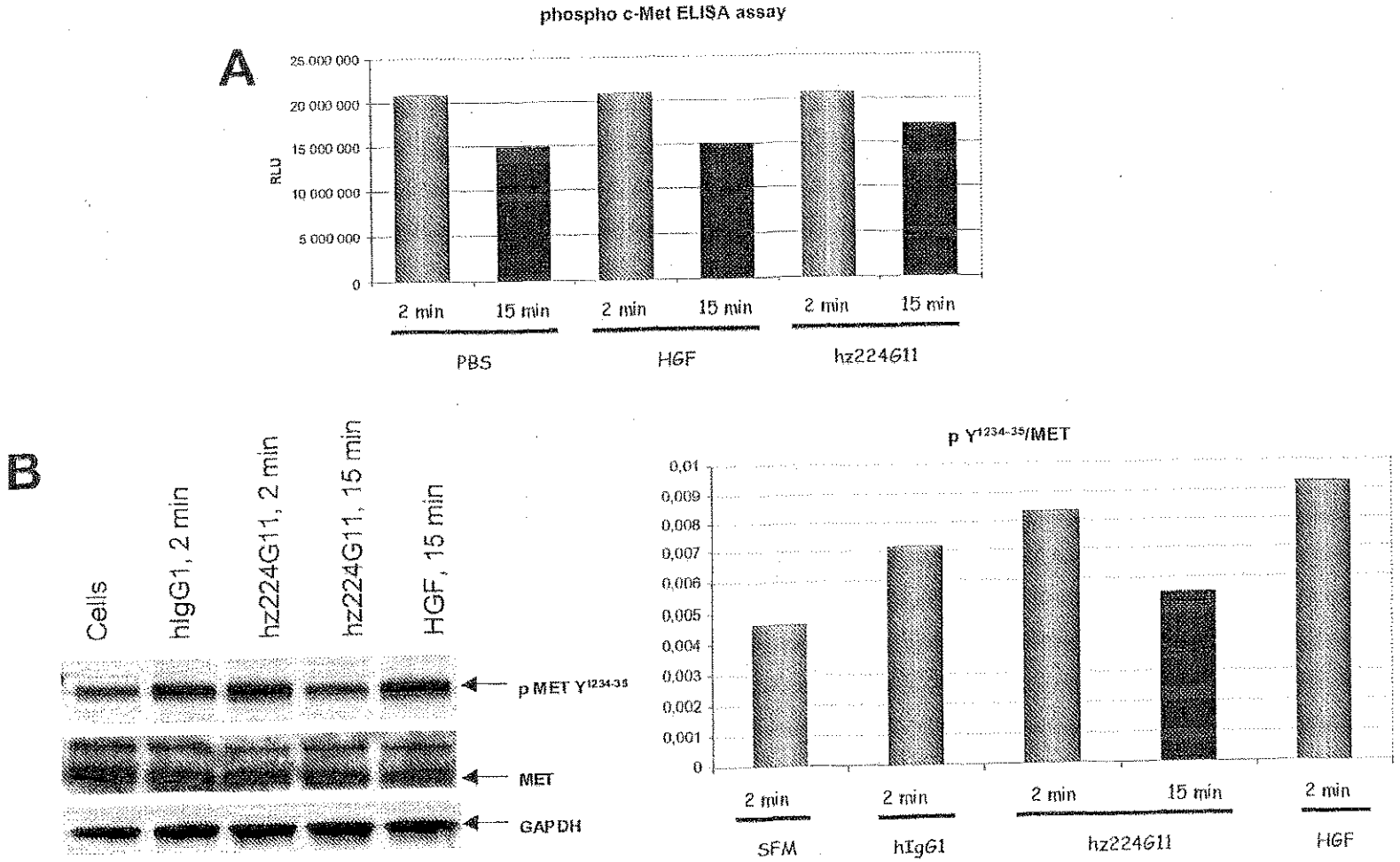

phospho c-Met ELISA assay
A
RLU
25 000 000
20 000 000
15 000 000
10 000 000
5 000 000
0
2 min
15 min
2 min
15 min
2 min
15 min
PBS
HGF
hz224G11
B
Cells
hIgG1, 2 min
hz224G11, 2 min
hz224G11, 15 min
HGF, 15 min
p MET Y1234-35
MET
GAPDH
p Y1234-35/MET
0,01
0,009
0,008
0,007
0,006
0,005
0,004
0,003
0,002
0,001
0
2 min
2 min
2 min
15 min
2 min
SFM
hIgG1
hz224G11
HGF

FIGURE 26

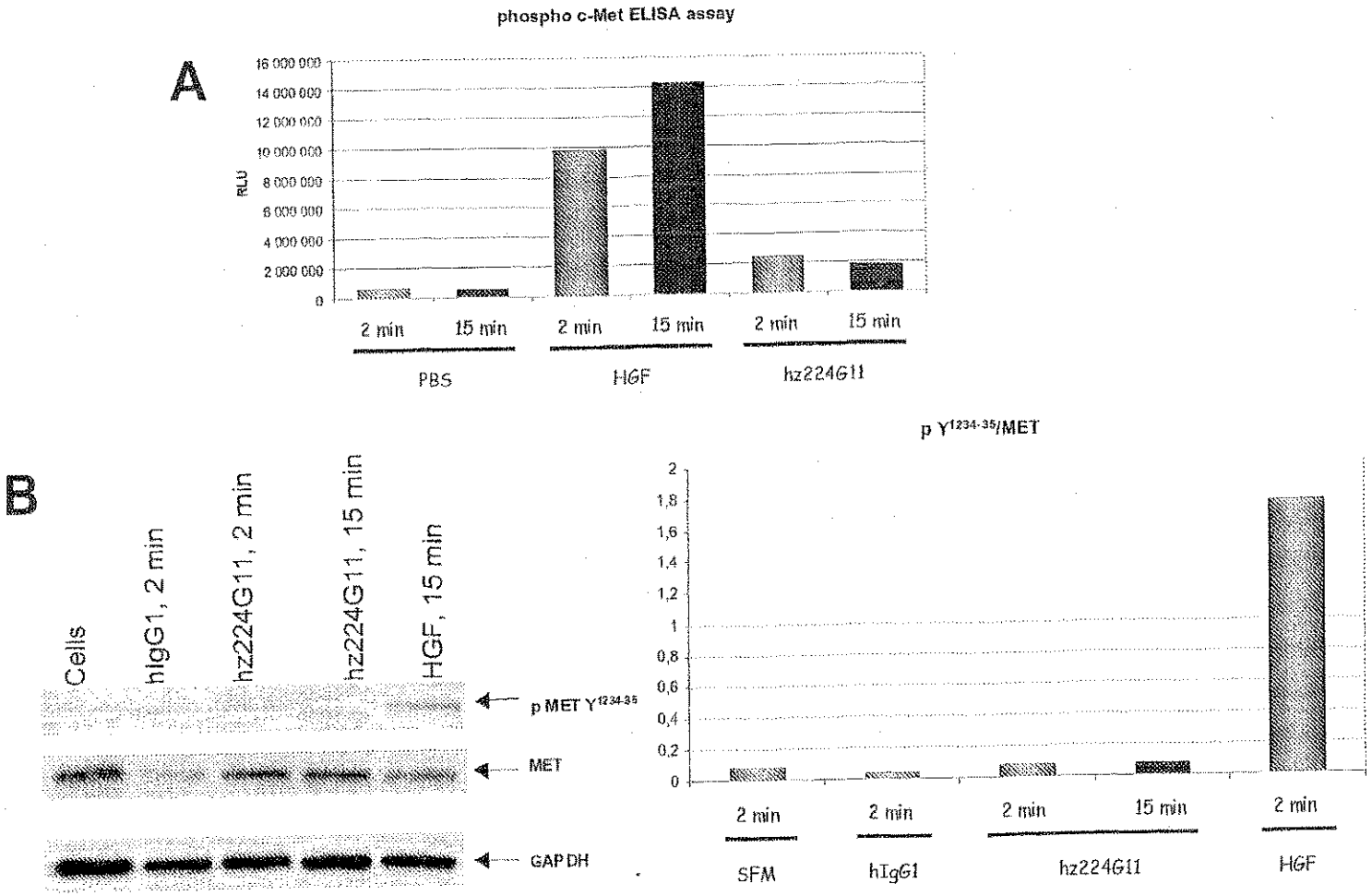

phospho c-Met ELISA assay
A
RLU
16 000 000
14 000 000
12 000 000
10 000 000
8 000 000
6 000 000
4 000 000
2 000 000
0
2 min
15 min
2 min
15 min
2 min
15 min
PBS
HGF
hz224G11
B
Cells
hIgG1, 2 min
hz224G11, 2 min
hz224G11, 15 min
HGF, 15 min
p MET Y1234-35
MET
GAPDH
p Y1234-35/MET
2
1,8
1,6
1,4
1,2
1
0,8
0,6
0,4
0,2
0
2 min
2 min
2 min
15 min
2 min
SFM
hIgG1
hz224G11
HGF

FIGURE 27

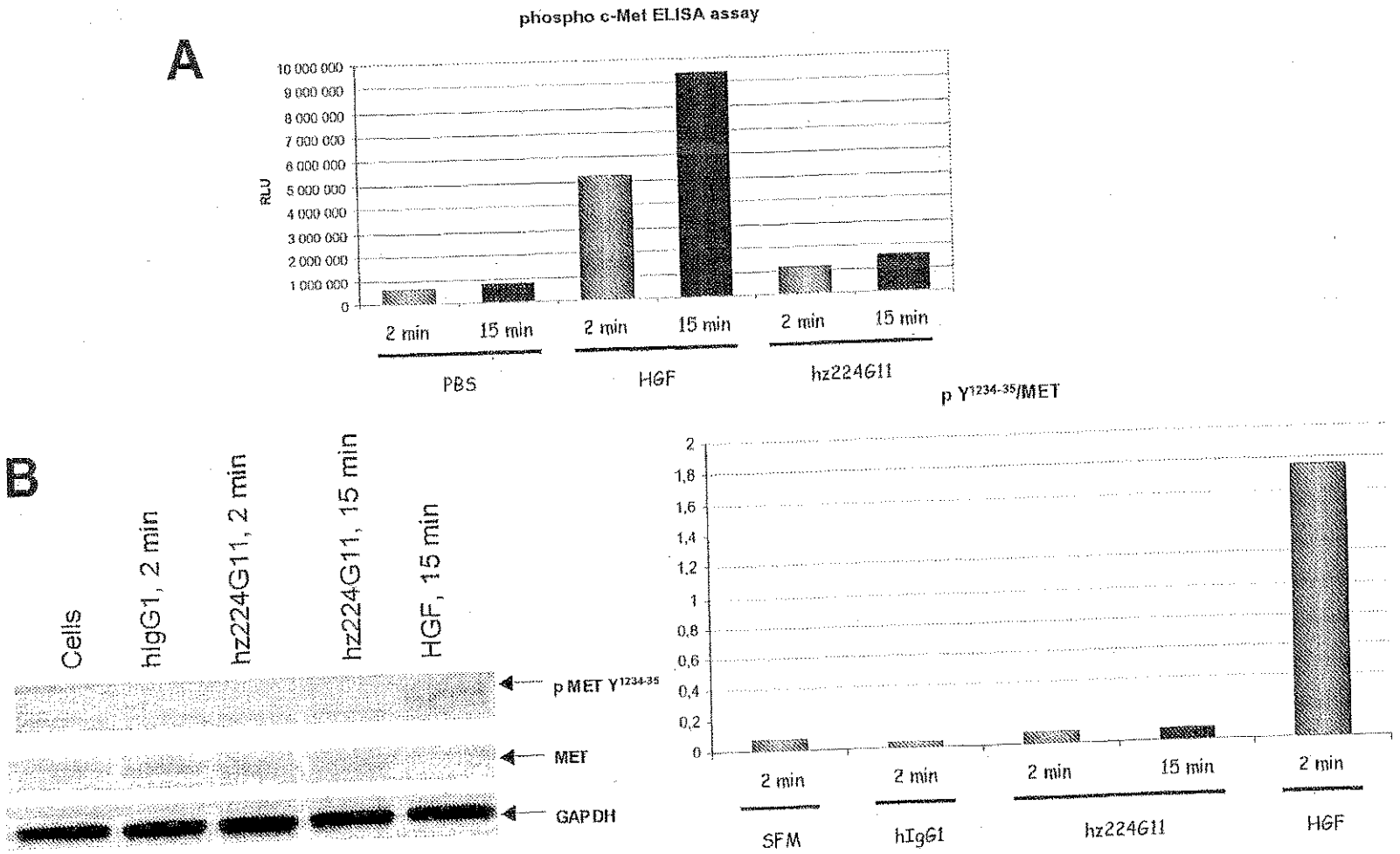

A
phospho c-Met ELISA assay
RLU
10 000 000
9 000 000
8 000 000
7 000 000
6 000 000
5 000 000
4 000 000
3 000 000
2 000 000
1 000 000
0
2 min
15 min
2 min
15 min
2 min
15 min
PBS
HGF
hz224G11
B
Cells
hIgG1, 2 min
hz224G11, 2 min
hz224G11, 15 min
HGF, 15 min
p MET Y1234-35
MET
GAPDH
p Y1234-35/MET
2
1,8
1,6
1,4
1,2
1
0,8
0,6
0,4
0,2
0
2 min
2 min
2 min
15 min
2 min
SFM
hIgG1
hz224G11
HGF

FIGURE 28

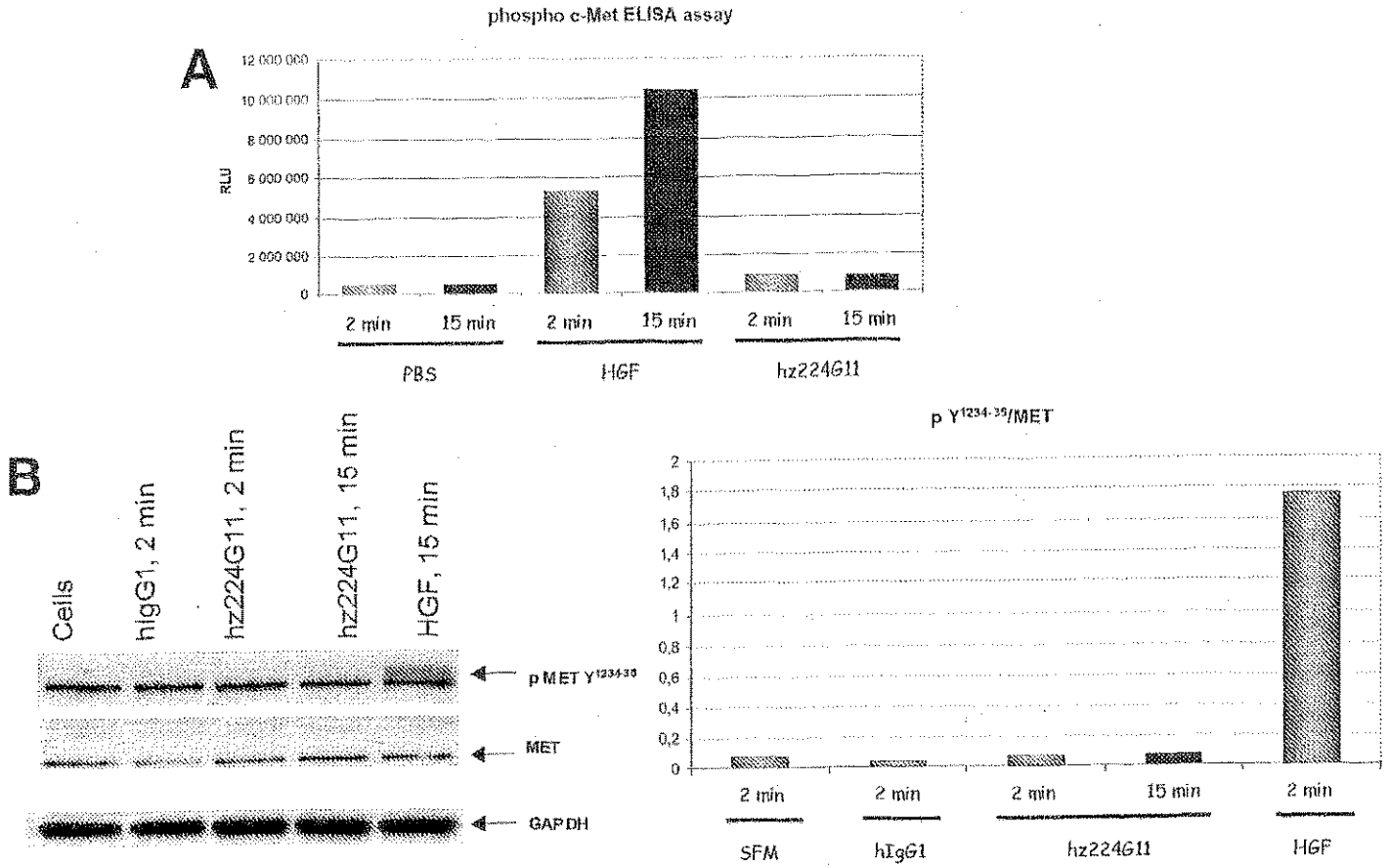

phospho c-Met ELISA assay
A
RLU
12 000 000
10 000 000
8 000 000
6 000 000
4 000 000
2 000 000
0
2 min
15 min
2 min
15 min
2 min
15 min
PBS
HGF
hz224G11
B
Cells
hIgG1, 2 min
hz224G11, 2 min
hz224G11, 15 min
HGF, 15 min
pMET Y1234-35
MET
GAPDH
p Y1234-35/MET
2
1,8
1,6
1,4
1,2
1
0,8
0,6
0,4
0,2
0
2 min
2 min
2 min
15 min
2 min
SFM
hIgG1
hz224G11
HGF

FIGURE 29

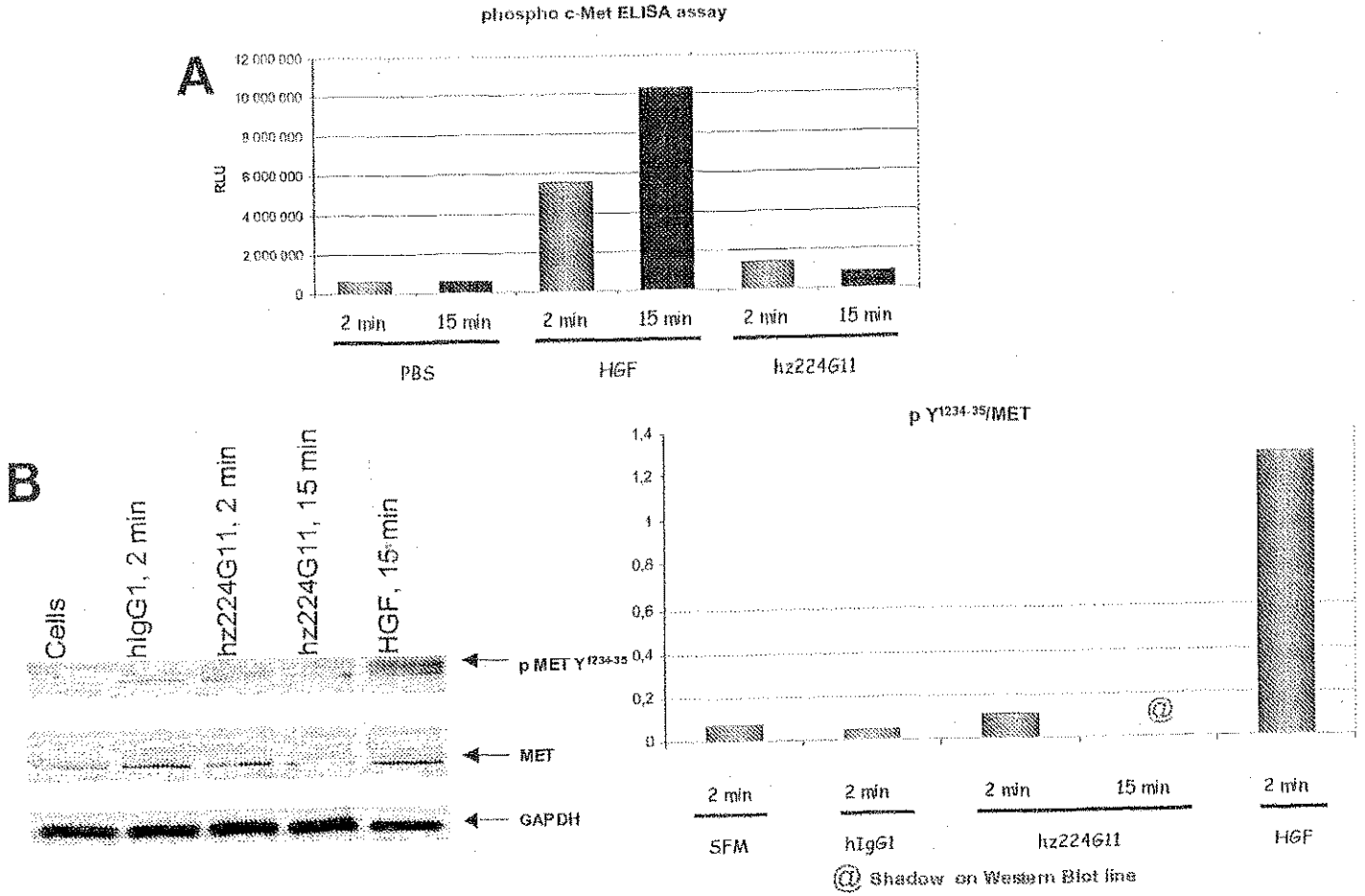

phospho c-Met ELISA assay
A
RLU
12 000 000
10 000 000
8 000 000
6 000 000
4 000 000
2 000 000
0
2 min
15 min
2 min
15 min
2 min
15 min
PBS
HGF
hz224G11
B
Cells
hIgG1, 2 min
hz224G11, 2 min
hz224G11, 15 min
HGF, 15 min
p MET Y1234-35
MET
GAPDH
p Y1234-35/MET
1,4
1,2
1
0,8
0,6
0,4
0,2
0
2 min
2 min
2 min
15 min
2 min
SFM
hIgG1
hz224G11
HGF
@ Shadow on Western Blot line

FIGURE 30

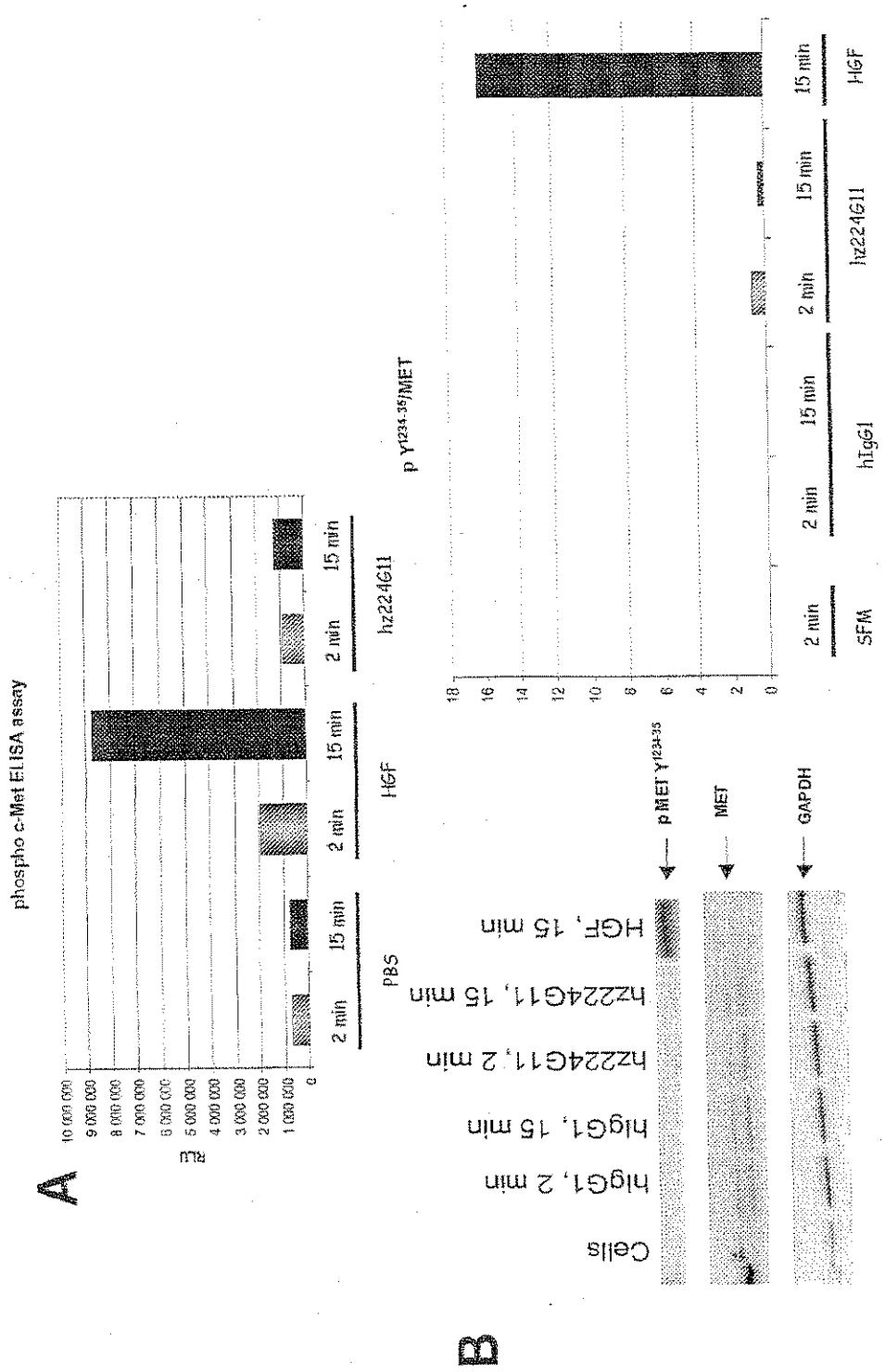

A
phospho c-Met ELISA assay
RLU
10 000 000
9 000 000
8 000 000
7 000 000
6 000 000
5 000 000
4 000 000
3 000 000
2 000 000
1 000 000
0
2 min
15 min
2 min
15 min
2 min
15 min
PBS
HGF
hz224G11
B
Cells
hIgG1, 2 min
hIgG1, 15 min
hz224G11, 2 min
hz224G11, 15 min
HGF, 15 min
p MET Y1234-35
MET
GAPDH
p Y1234-35/MET
18
16
14
12
10
8
6
4
2
0
2 min
2 min
15 min
2 min
15 min
SFM
hIgG1
hz224G11
HGF

FIGURE 31

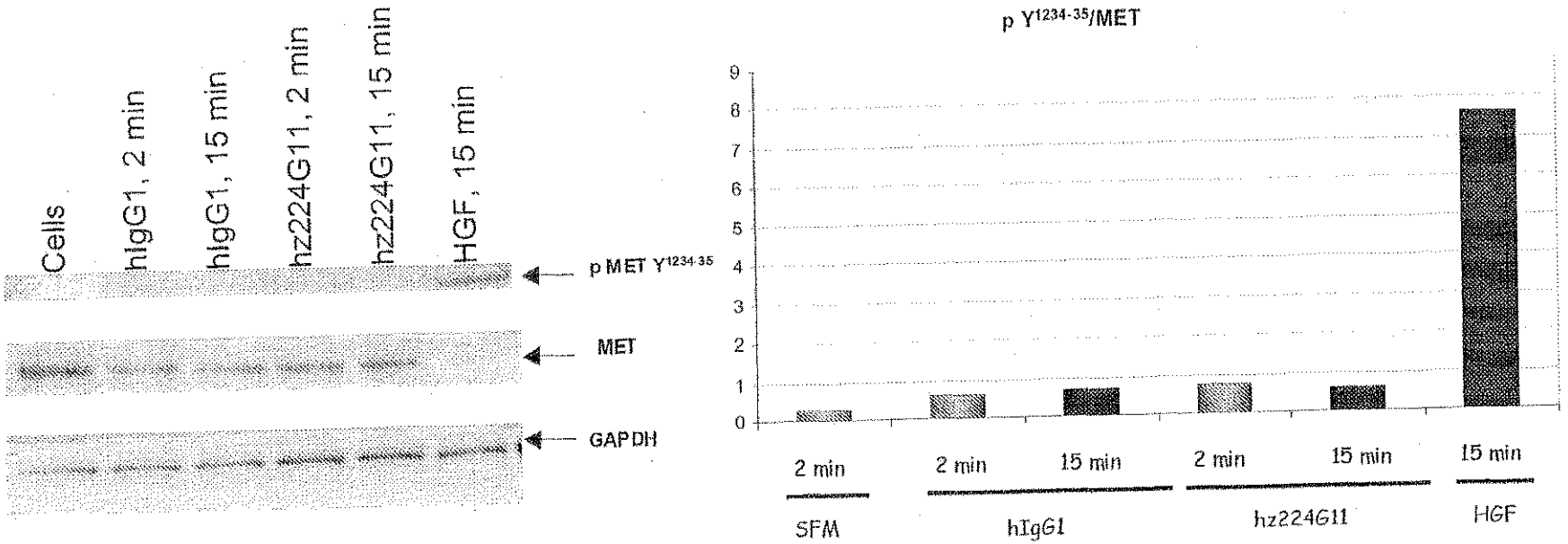

Cells
hIgG1, 2 min
hIgG1, 15 min
hz224G11, 2 min
hz224G11, 15 min
HGF, 15 min
p MET Y1234-35
MET
GAPDH
p Y1234-35/MET
9
8
7
6
5
4
3
2
1
0
2 min
2 min
15 min
2 min
15 min
15 min
SFM
hIgG1
hz224G11
HGF

FIGURE 32

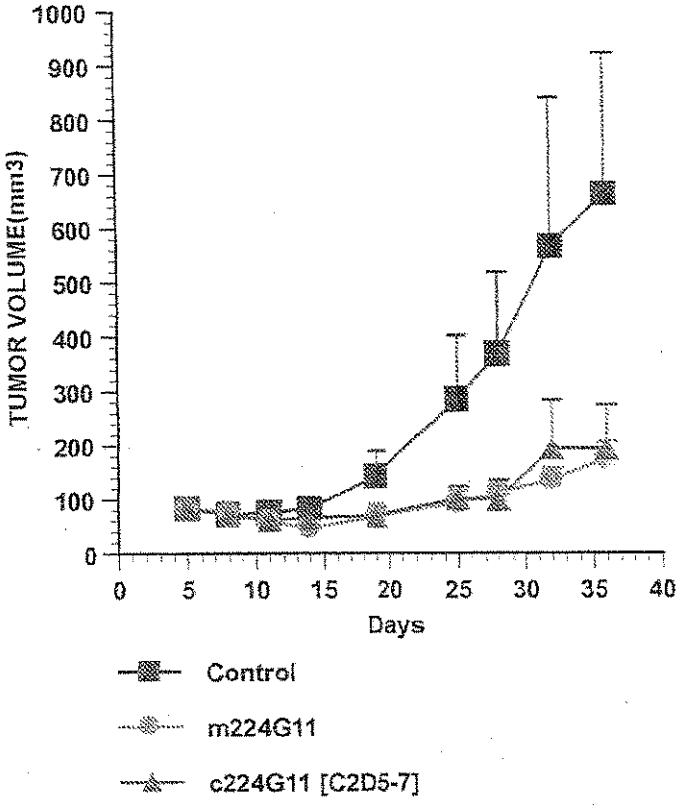

1000
900
800
700
600
500
400
300
200
100
0
TUMOR VOLUME(mm3)
0
5
10
15
20
25
30
35
40
Days
Control
m224G11
c224G11 [C2D5-7]

FIGURE 33

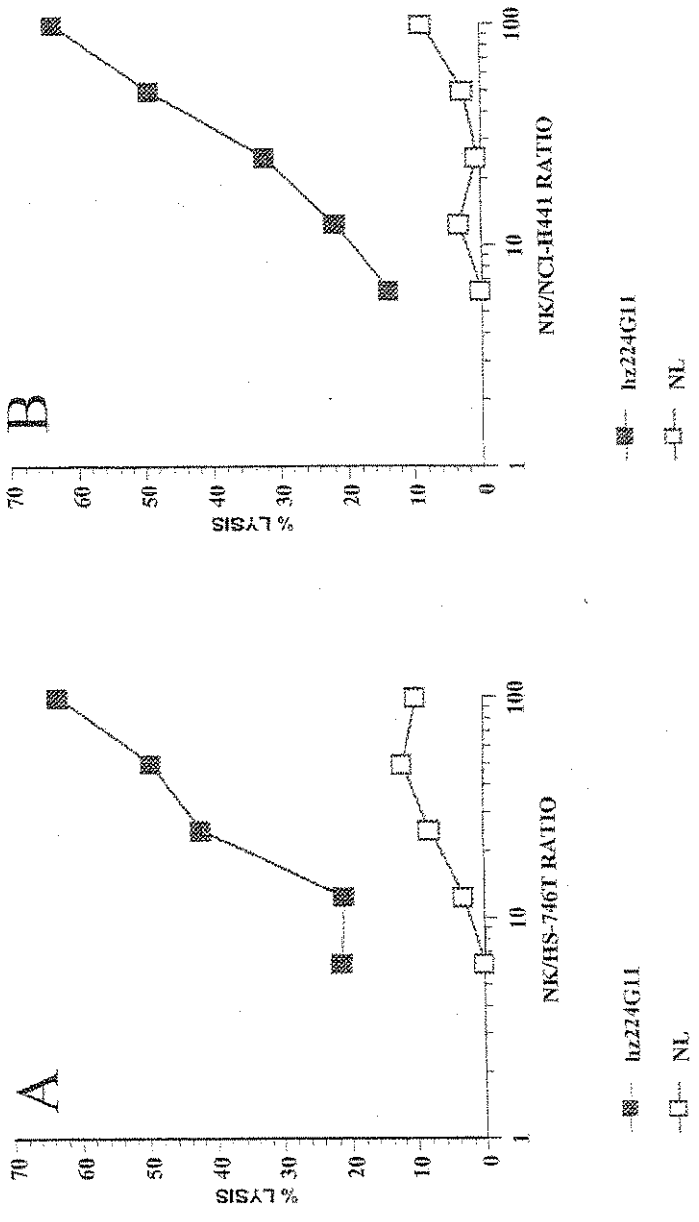
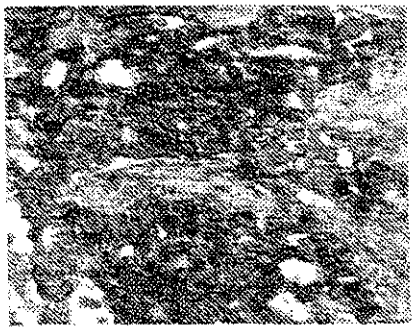

A
B
% LYSIS
NK/HS-746T RATIO
NK/NCI-H441 RATIO
hz224G11
NL
0
10
20
30
40
50
60
70
1
10
100

FIGURE 34

A



B



C



FIGURE 35