Fig. 1

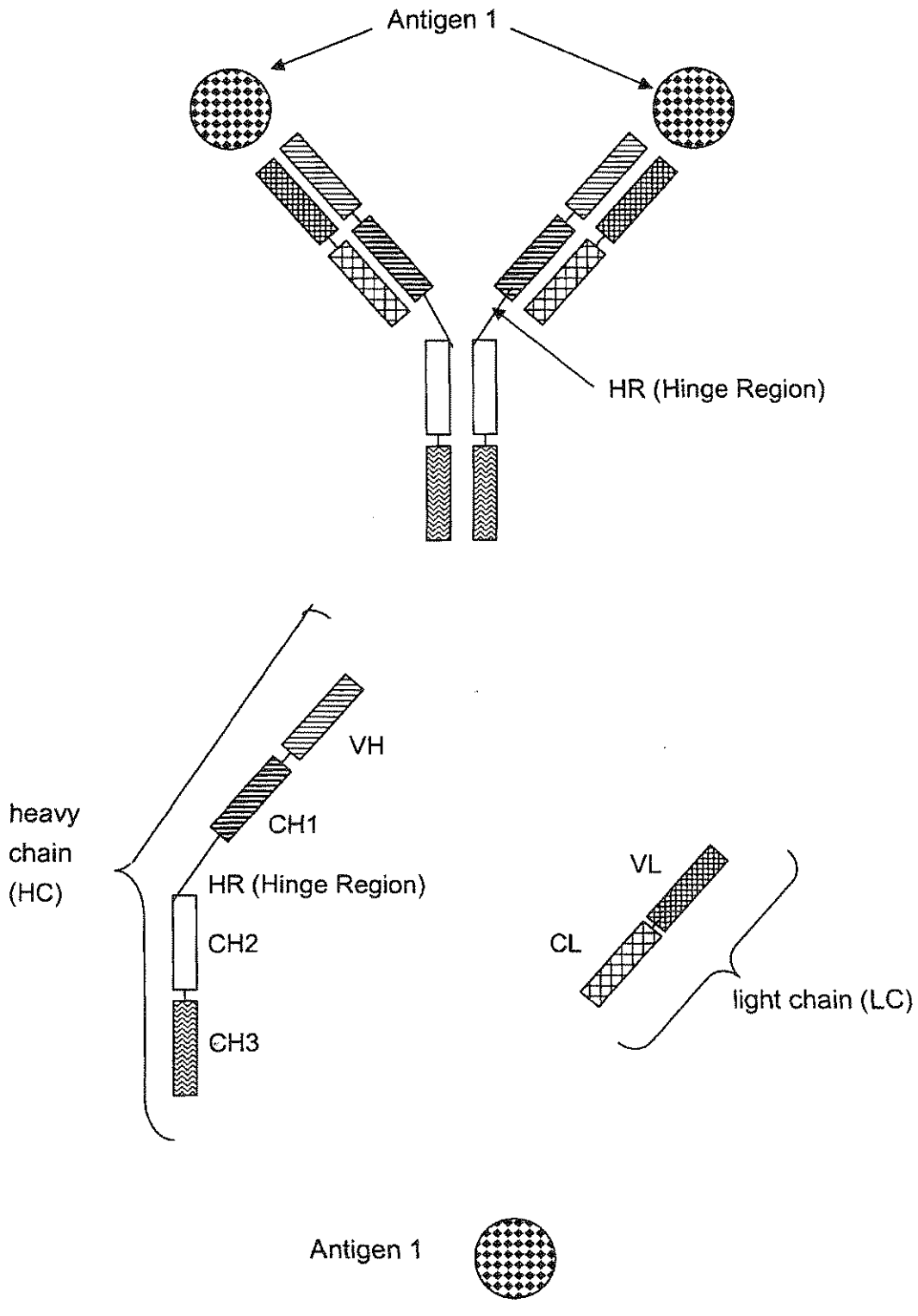
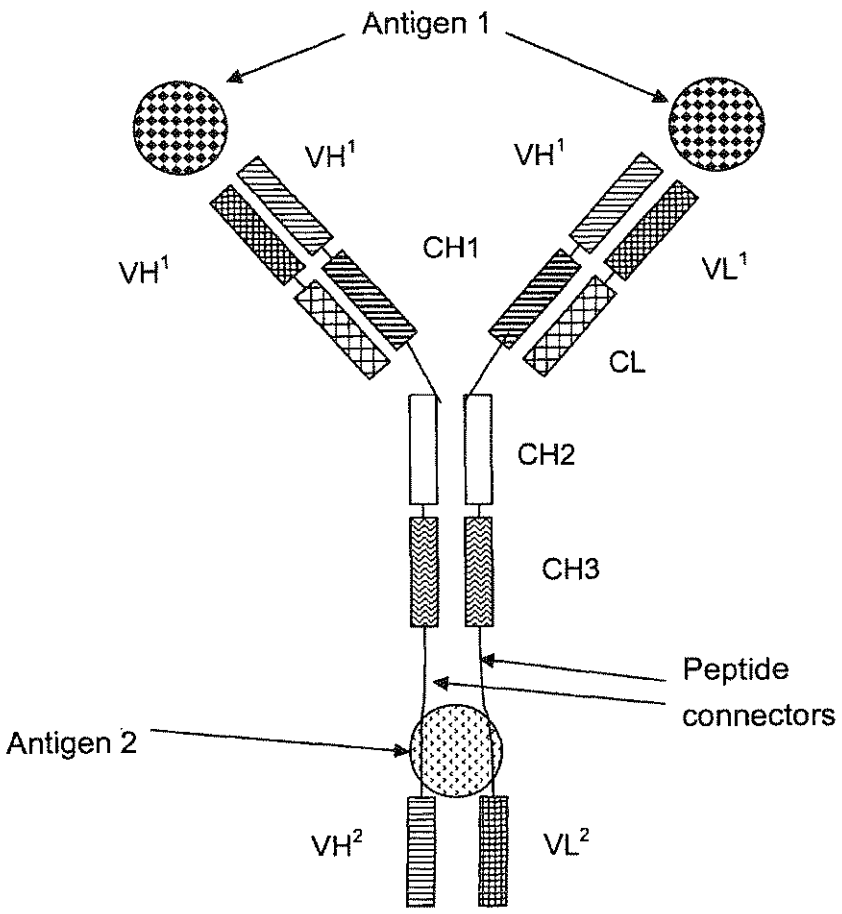
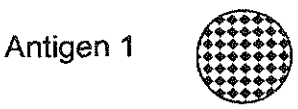

Antigen 1
HR (Hinge Region)
heavy chain (HC)
VH
CH1
HR (Hinge Region)
CH2
CH3
VL
CL
light chain (LC)
Antigen 1

Figure 2a


Antigen 1
VH1
VH1
VH1
CH1
VL1
CL
CH2
CH3
Peptide
connectors
Antigen 2
VH2
VL2


Antigen 1

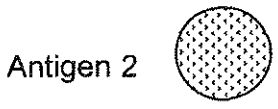

Antigen 2

Figure 2b

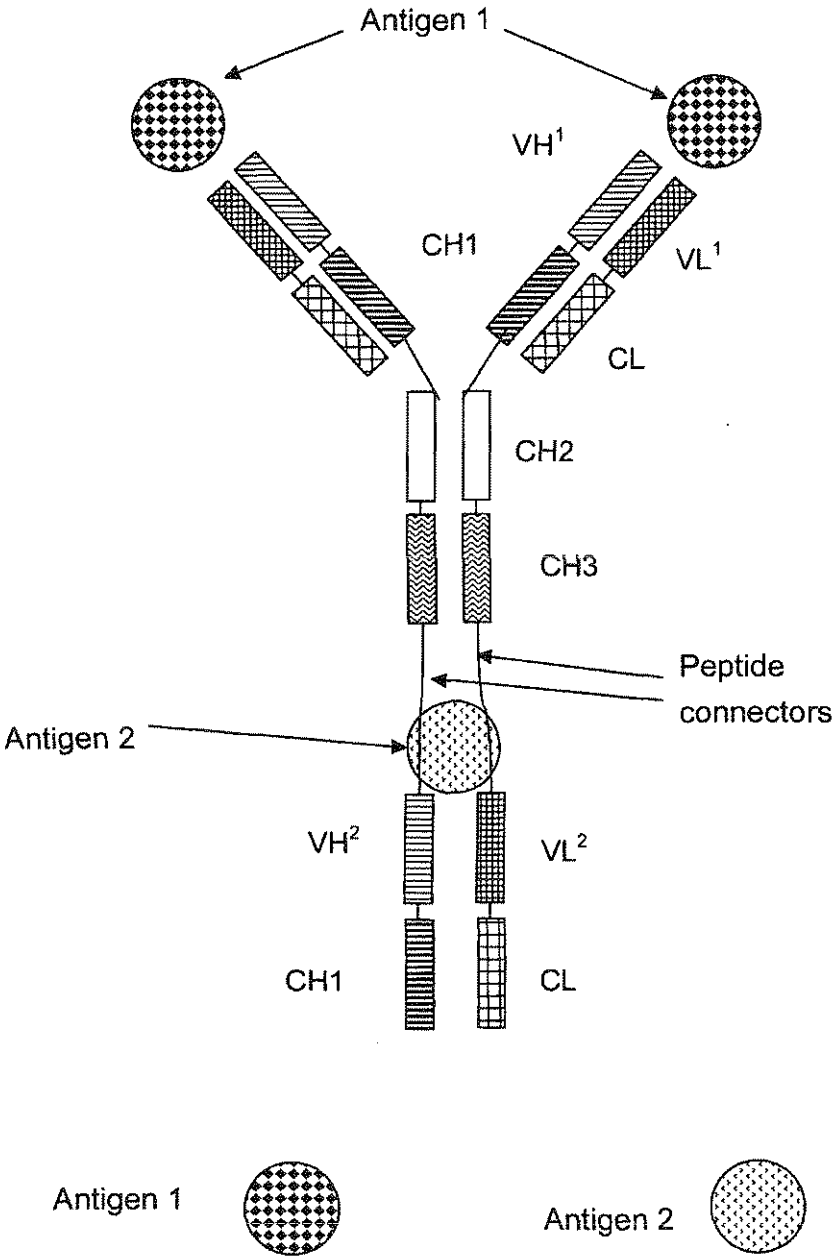
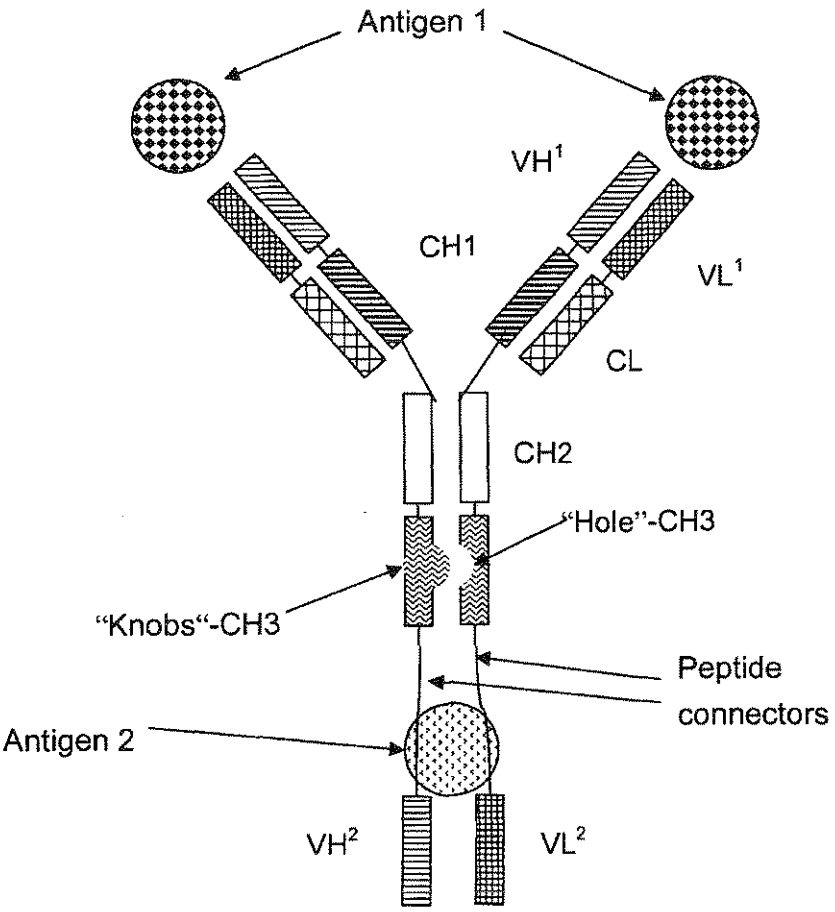

Antigen 1
VH1
CH1
VL1
CL
CH2
CH3
Peptide
connectors
Antigen 2
VH2
VL2
CH1
CL
Antigen 1
Antigen 2

Figure 3


Antigen 1
VH1
CH1
VL1
CL
CH2
"Hole"-CH3
"Knobs"-CH3
Peptide
connectors
Antigen 2
VH2
VL2


Antigen 1

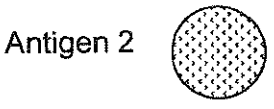

Antigen 2

Figure 4

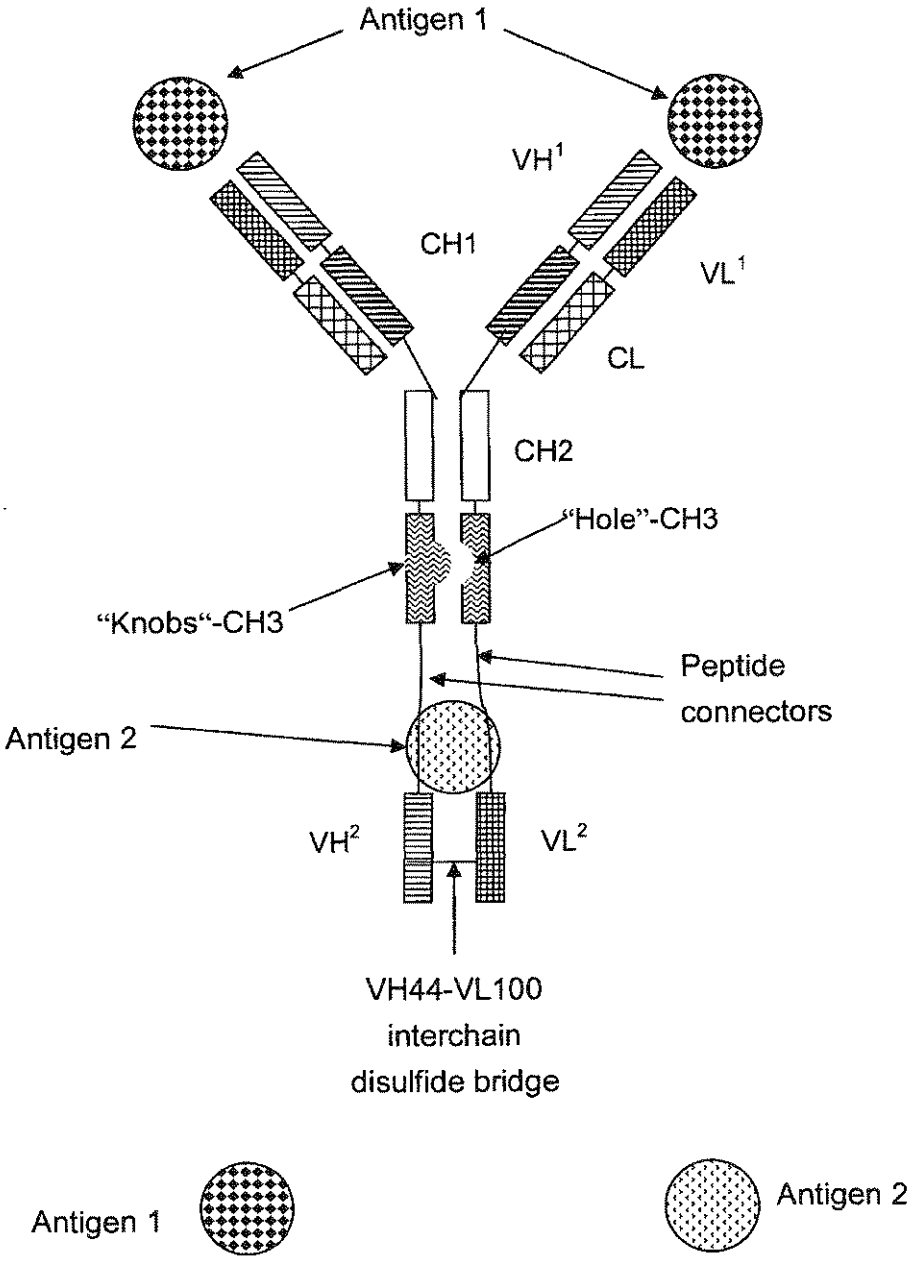

Antigen 1
VH1
CH1
VL1
CL
CH2
"Hole"-CH3
"Knobs"-CH3
Peptide
connectors
Antigen 2
VH2
VL2
VH44-VL100
interchain
disulfide bridge
Antigen 1
Antigen 2

Fig. 5

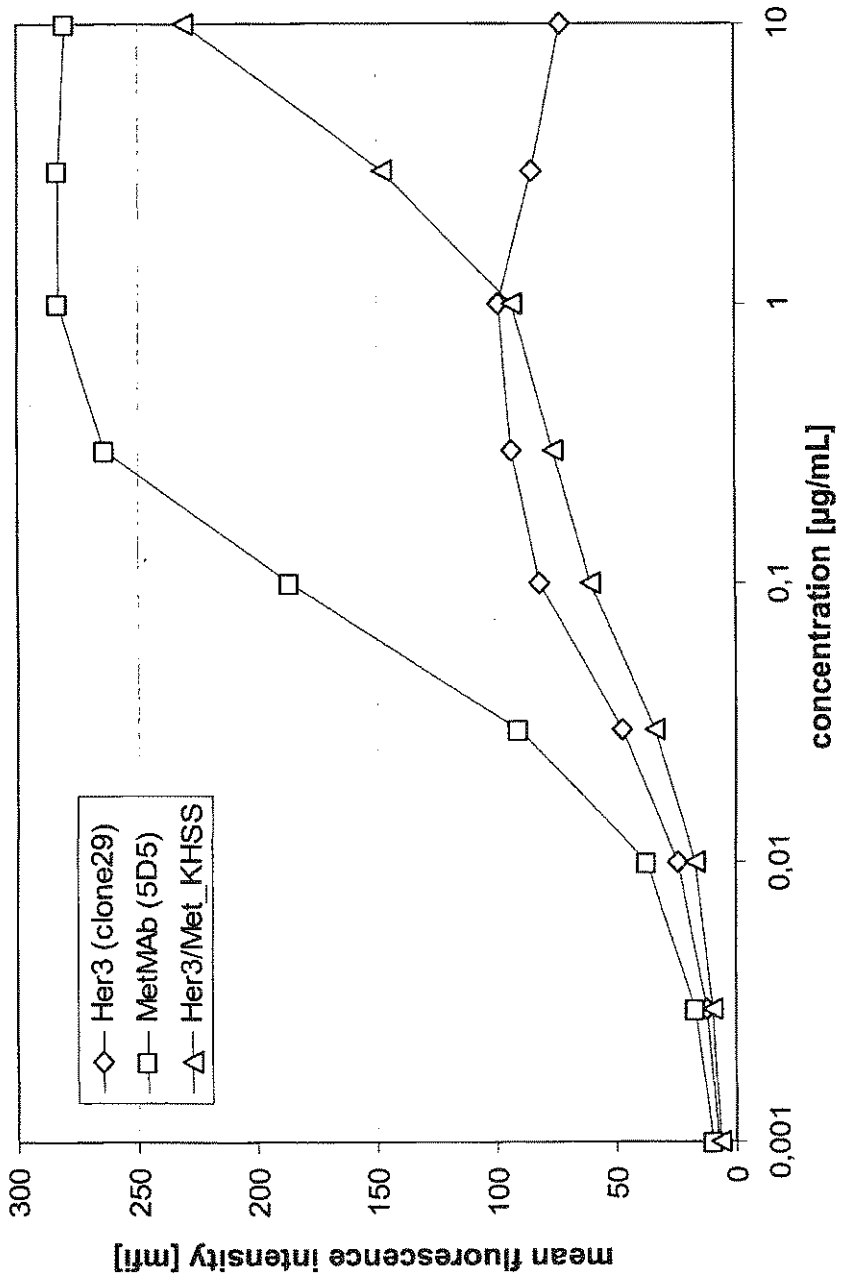

mean fluorescence intensity [mfi]
300
250
200
150
100
50
0
0,001
0,01
0,1
1
10
concentration [µg/mL]
Her3 (clone29)
MetMAb (5D5)
Her3/Met_KHSS

Fig. 6a

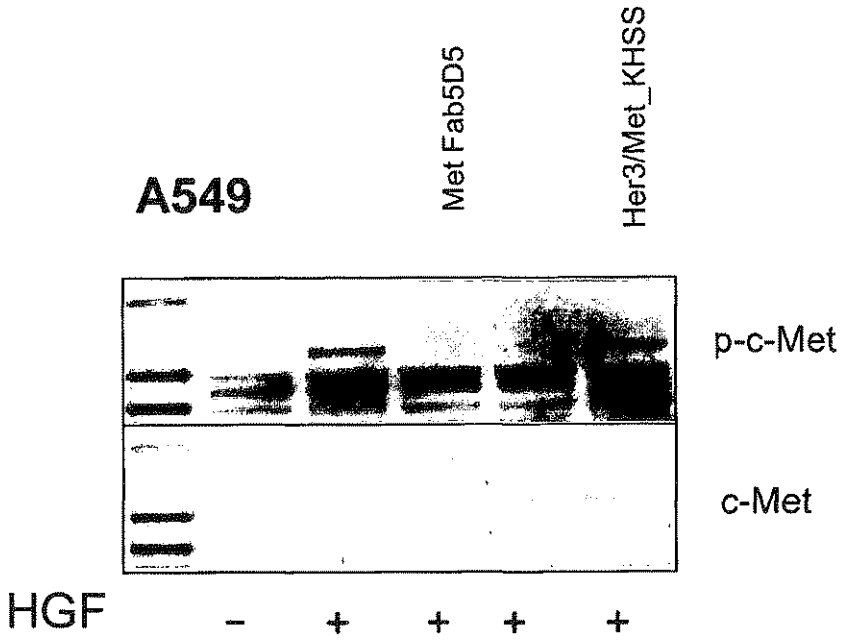

A549
Met Fab5D5
Her3/Met_KHSS
p-c-Met
c-Met
HGF
-
+
+
+
+

Fig. 6b

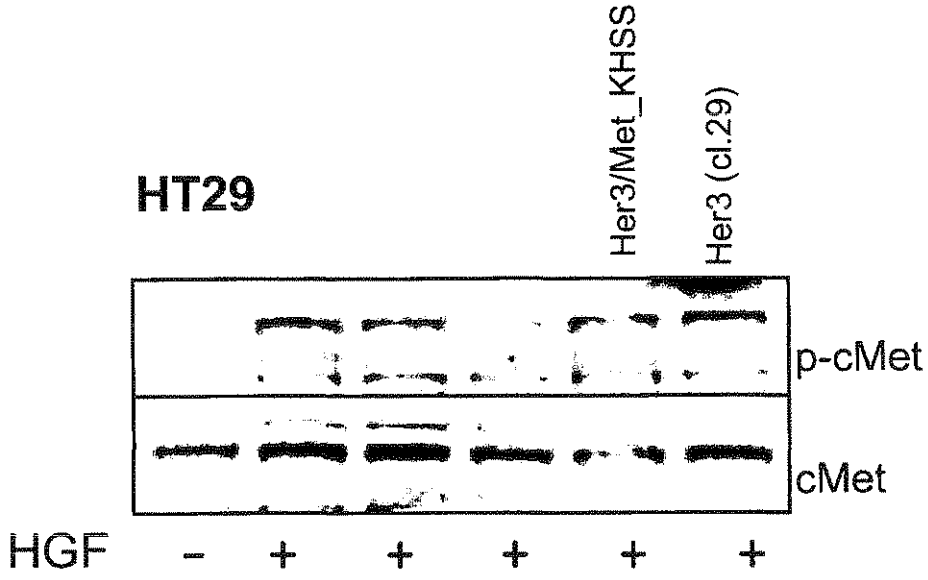
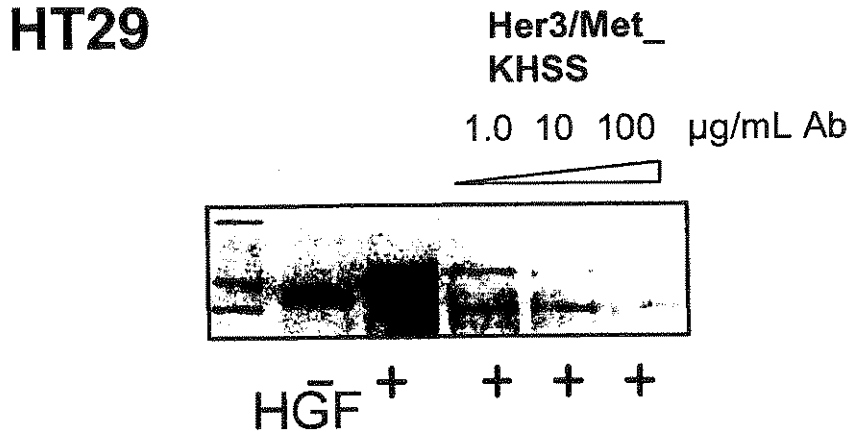

HT29
Her3/Met_KHSS
Her3 (cl.29)
p-cMet
cMet
HGF
-
+
+
+
+
+

Fig. 6c



100 ng/mL HGF, cells detached

Fig. 7a

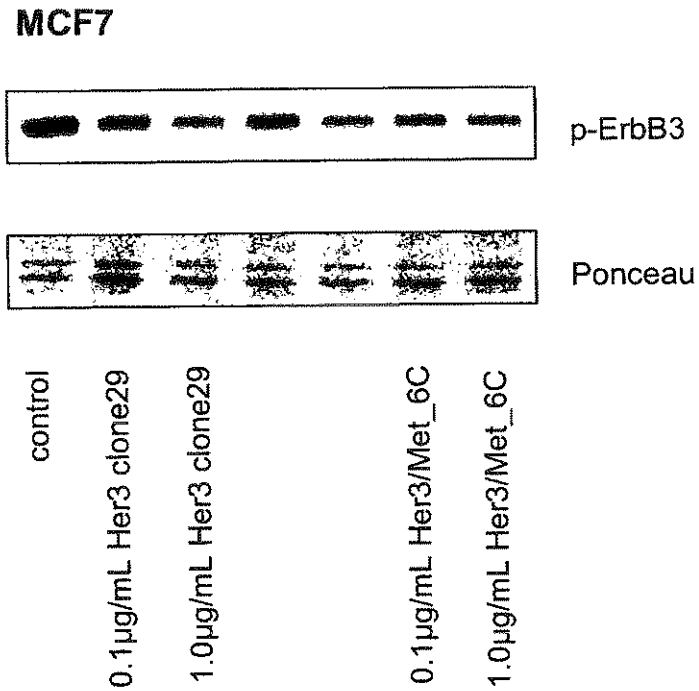
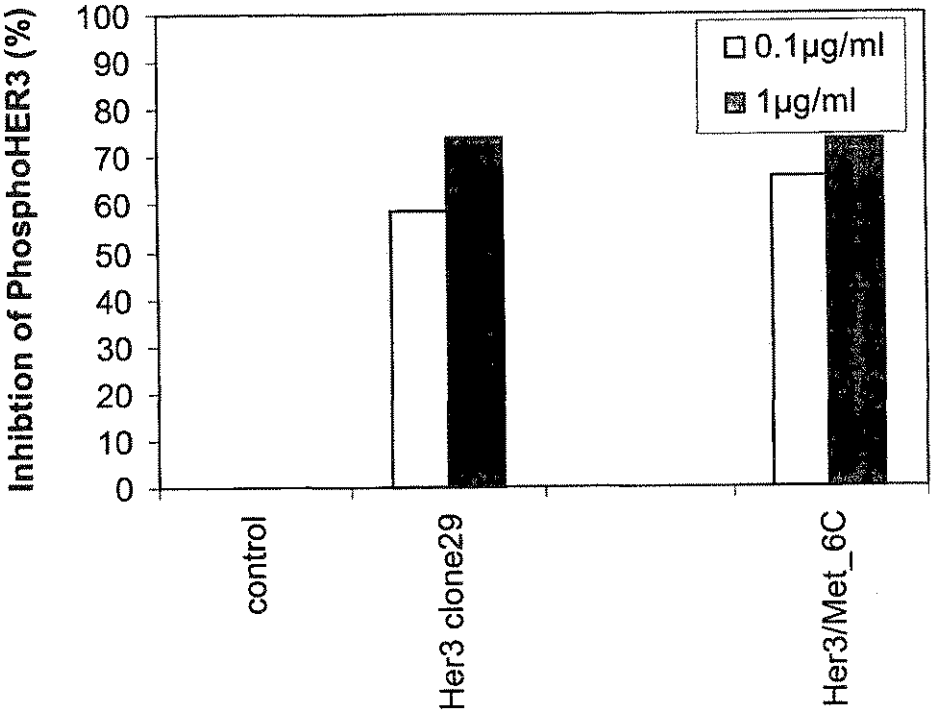


Fig. 7b


Inhibtion of PhosphoHER3 (%)
100
90
80
70
60
50
40
30
20
10
0
0.1µg/ml
1µg/ml
control
Her3 clone29
Her3/Met_6C

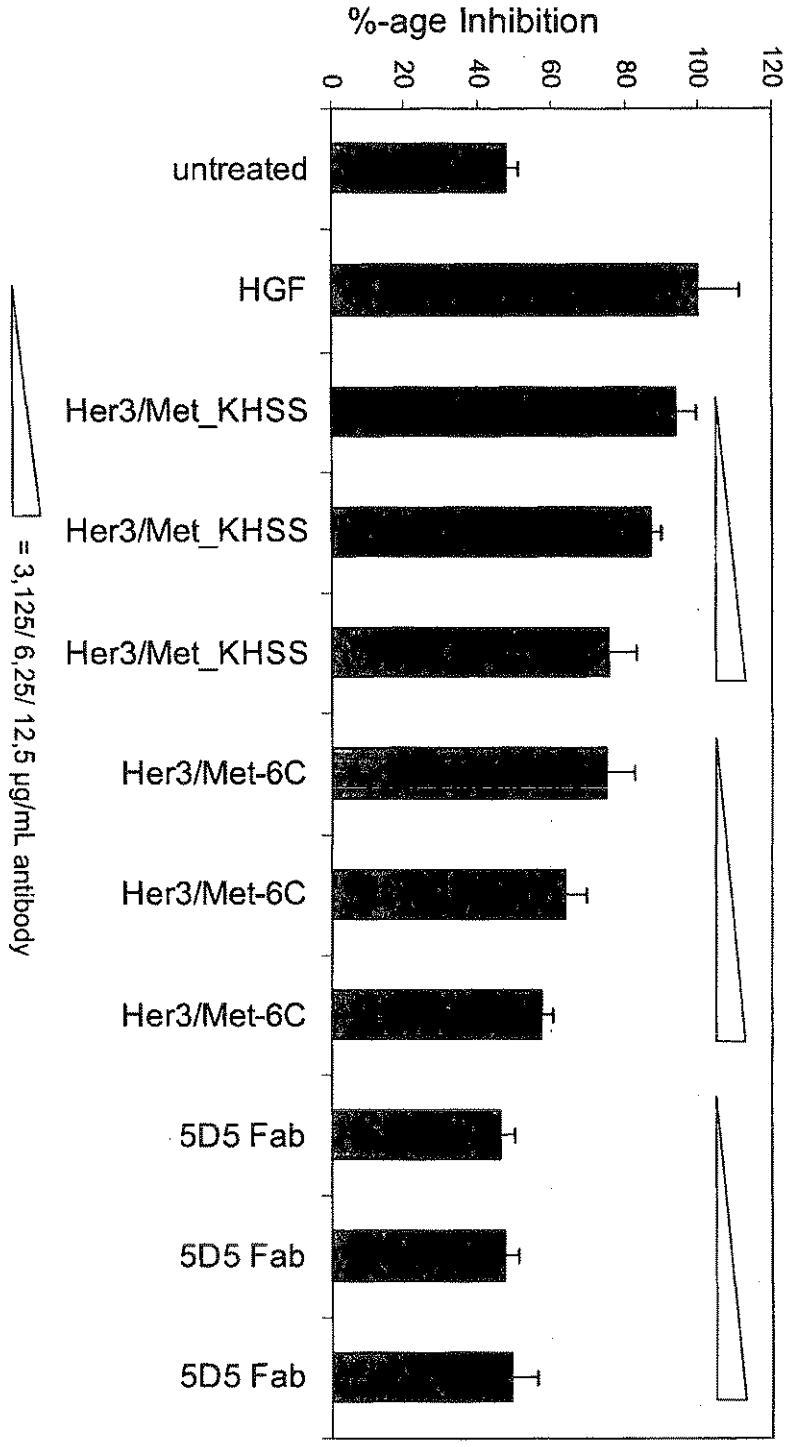

%-age Inhibition
0
20
40
60
80
100
120
untreated
HGF
Her3/Met_KHSS
Her3/Met_KHSS
Her3/Met_KHSS
Her3/Met-6C
Her3/Met-6C
Her3/Met-6C
5D5 Fab
5D5 Fab
5D5 Fab
= 3,125/ 6,25/ 12,5 µg/mL antibody

Fig. 8

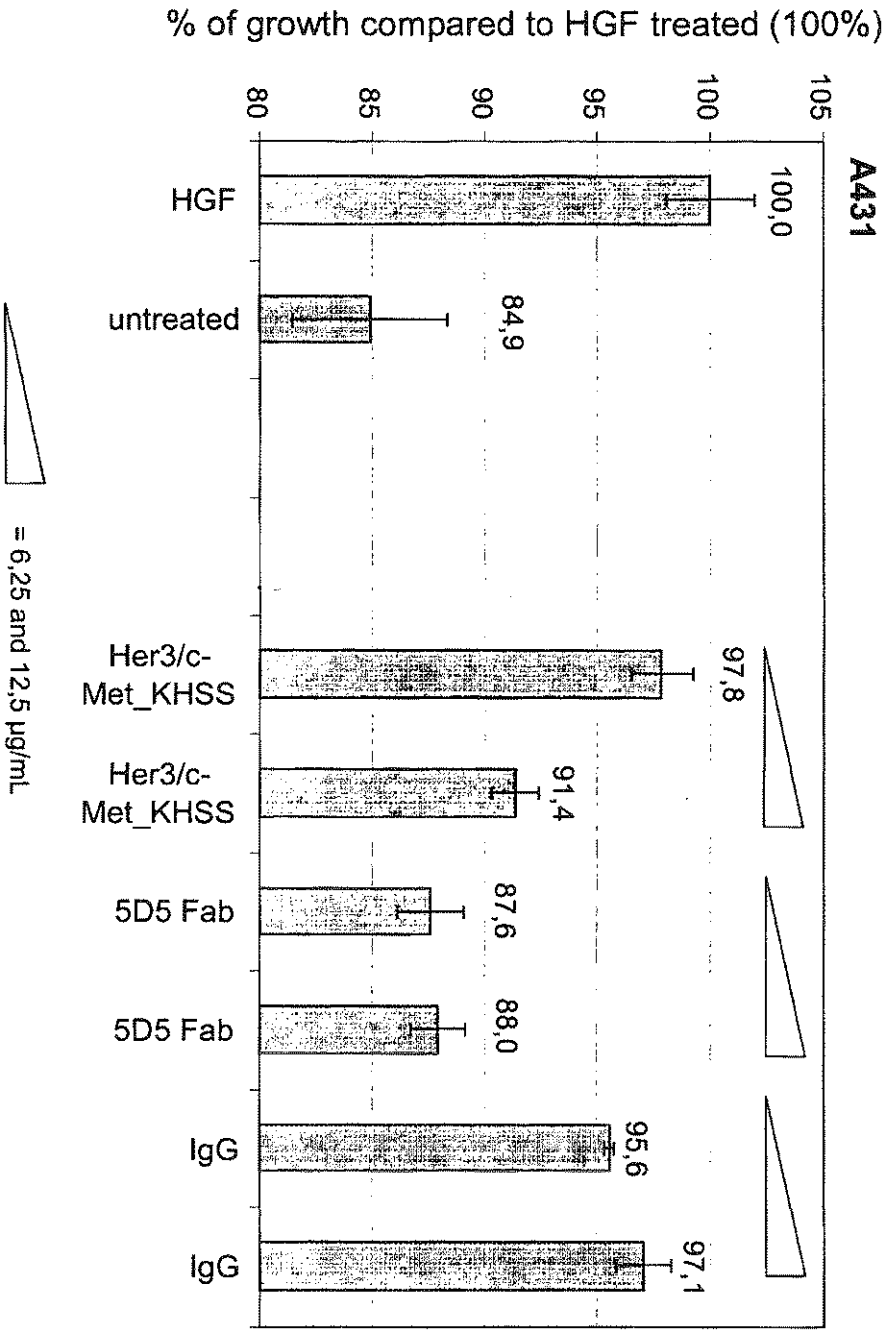

% of growth compared to HGF treated (100%)
80
85
90
95
100
105
A431
HGF
100,0
untreated
84,9
Her3/c-Met_KHSS
97,8
Her3/c-Met_KHSS
91,4
5D5 Fab
87,6
5D5 Fab
88,0
IgG
95,6
IgG
97,1
= 6,25 and 12,5 µg/mL

Fig. 9

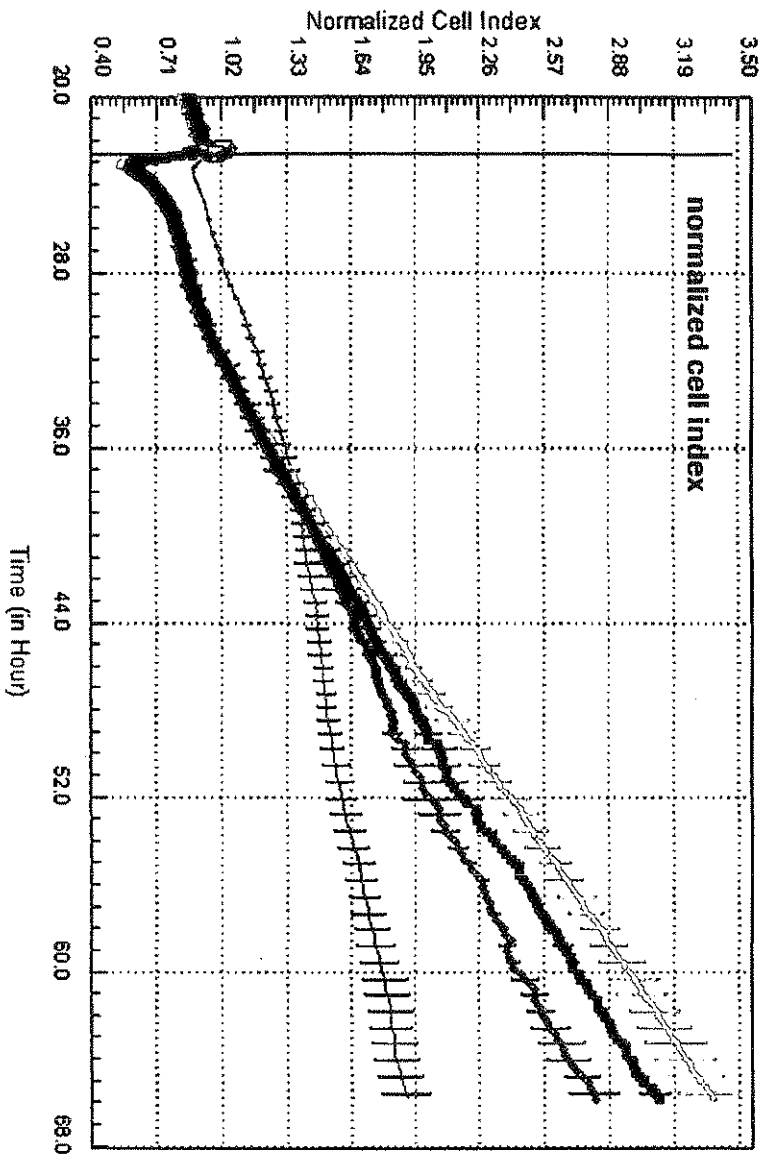

A431
normalized cell index
Normalized Cell Index
3.50
3.19
2.88
2.57
2.26
1.95
1.64
1.33
1.02
0.71
0.40
20.0
28.0
36.0
44.0
52.0
60.0
68.0
Time (in Hour)
HGF (20 ng/mL)
Her3/Met_KHSS 12,5 µg/mL
HER3/Met-6C (20 ng/mL)
control (w/o HGF)

Fig. 10