

Fig. 1

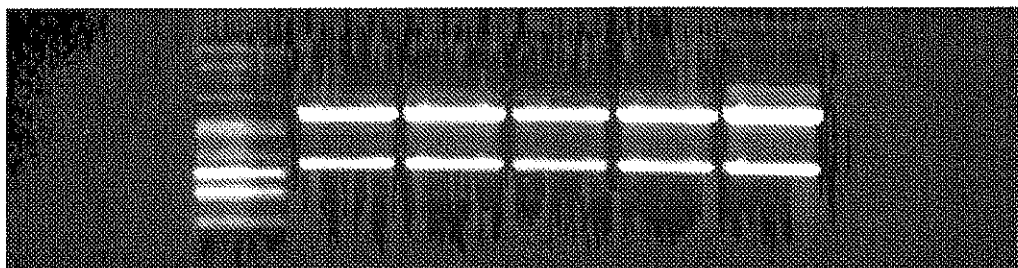


Fig. 2

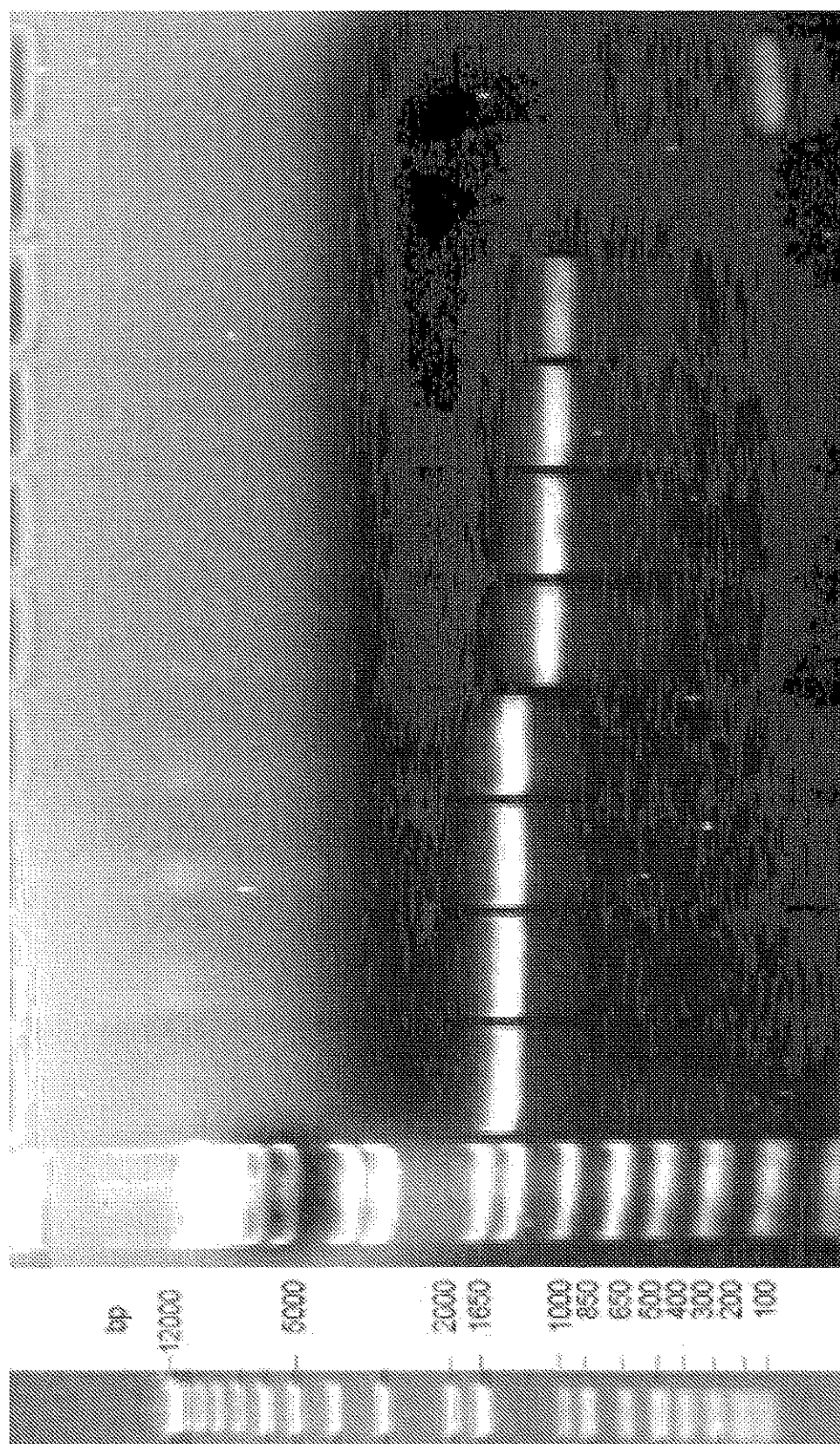


Fig. 3

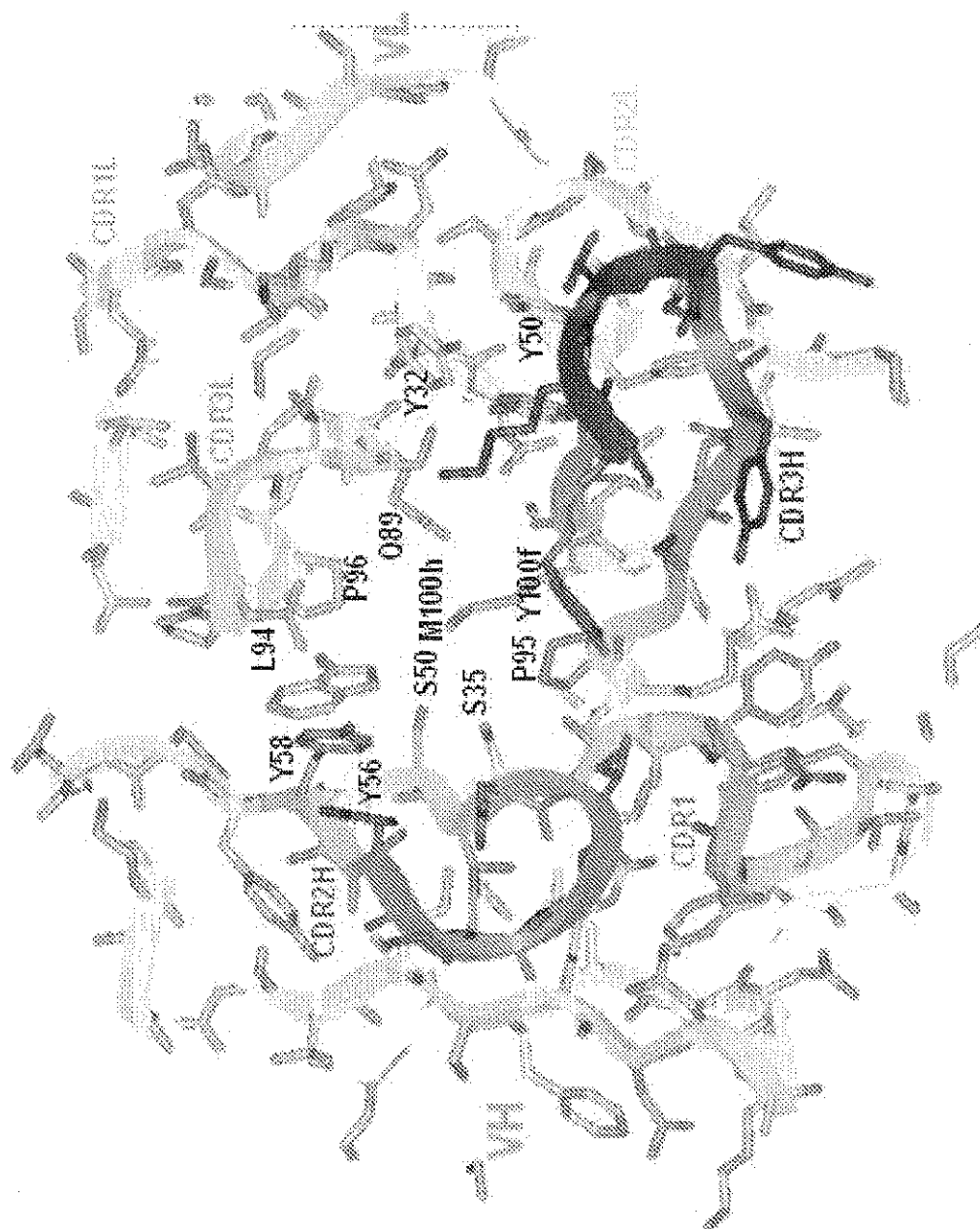


Fig. 4

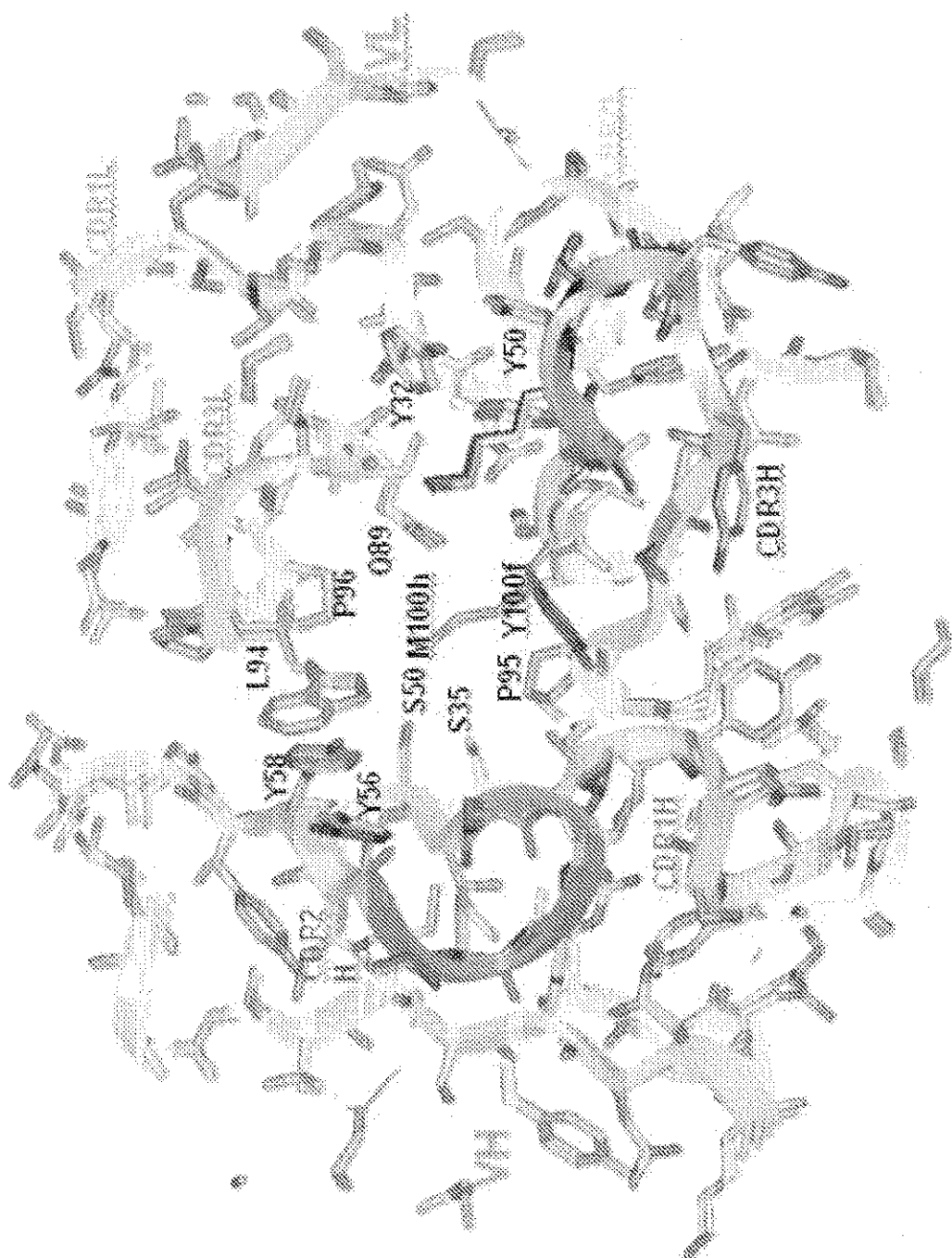


Fig. 5 a)

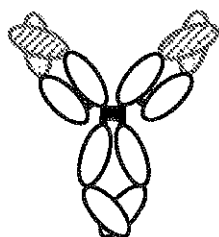


Fig. 5 b)

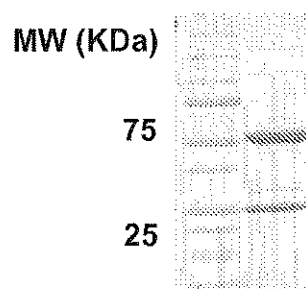


Fig. 5 c)

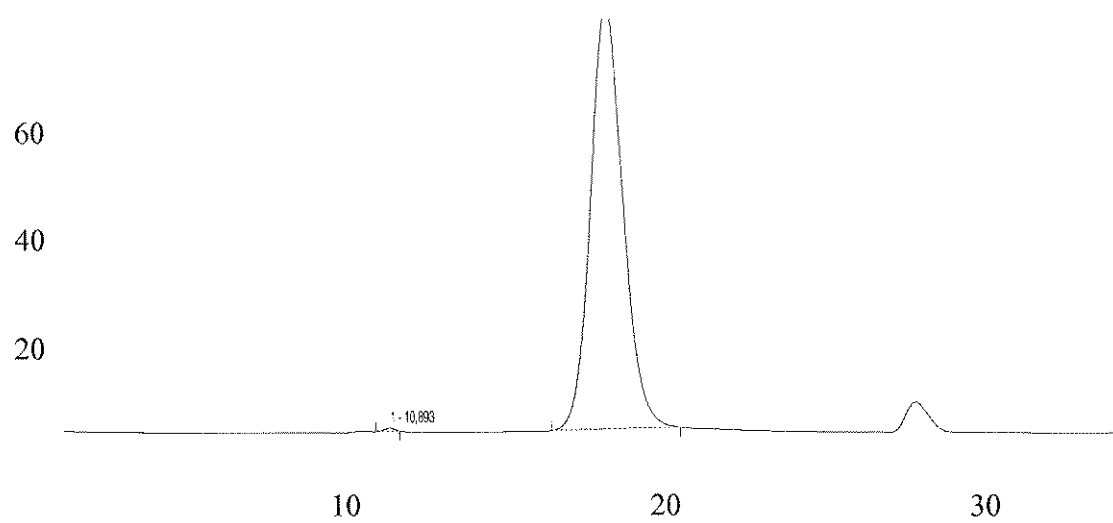


Fig. 6 a)

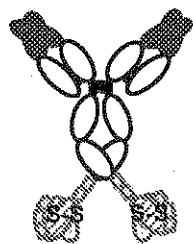


Fig. 6 b)

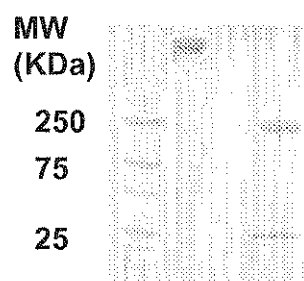


Fig. 6c)

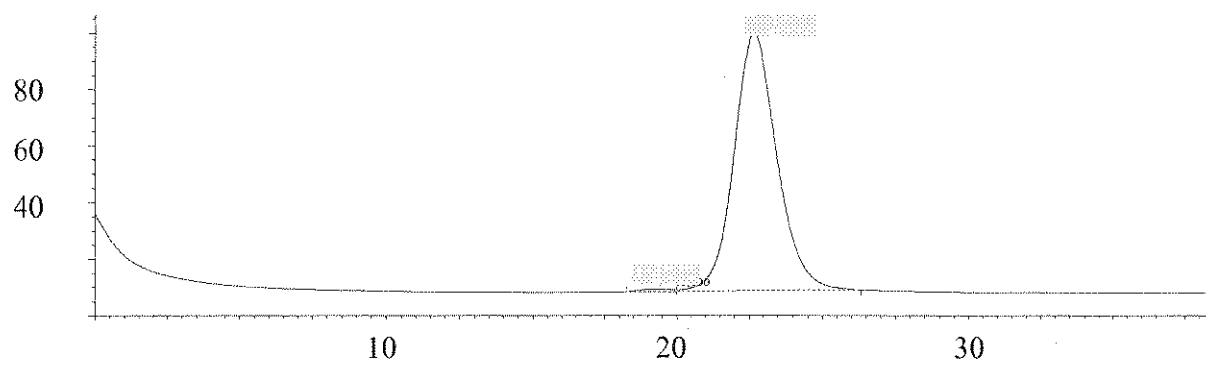


Fig. 7 a)

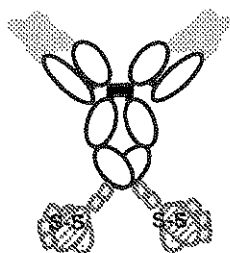


Fig. 7 b)

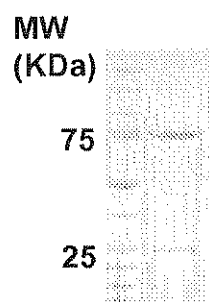


Fig. 7c)

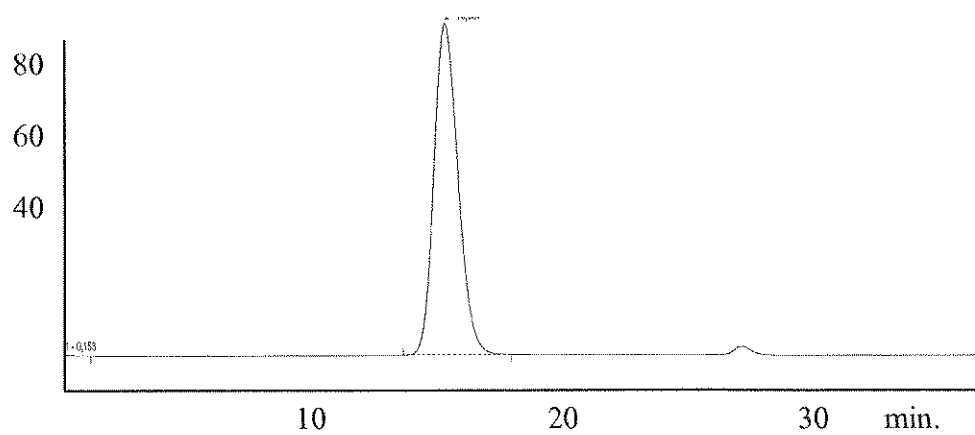


Fig. 8 a)

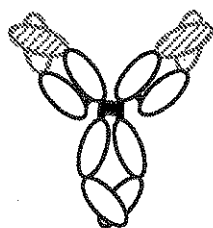


Fig. 8 b)

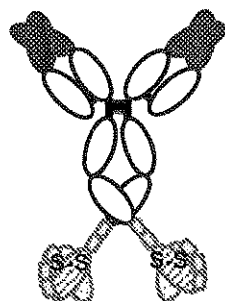


Fig. 8 c)

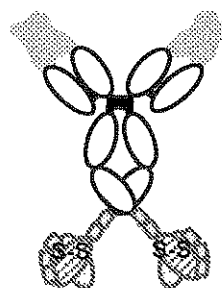


Fig. 8 d)

Construct Name	Expression mg/L
A – hu<Dig> IgG	18.8
B – <IGF1R-DIG>2321 (disulfide stabilized)	6.4
C – <Her2-DIG>2321 (disulfide-stabilized)	34.3

Fig. 9 a)

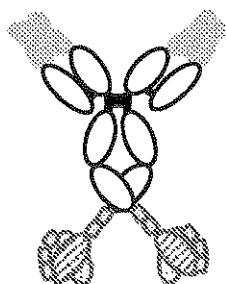


Fig. 9 b)

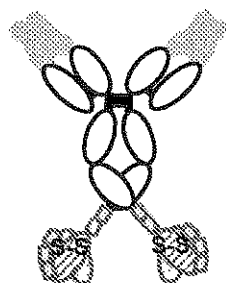


Fig. 9 c)

Sample	Σ (mg)	Aggregates
Her2DIGHu2-2320	1	22 %
Her2DIGHu2-2321	31	0 %

Fig. 10 a)

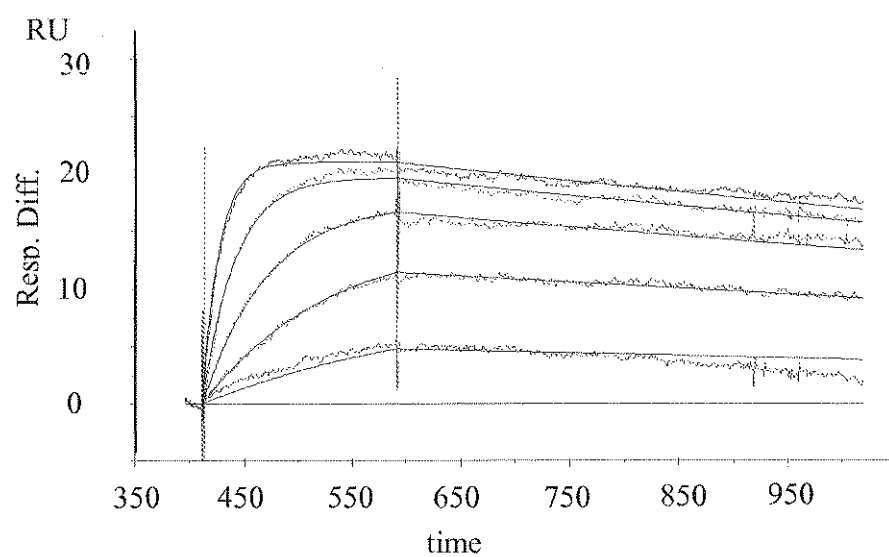


Fig. 10 b)

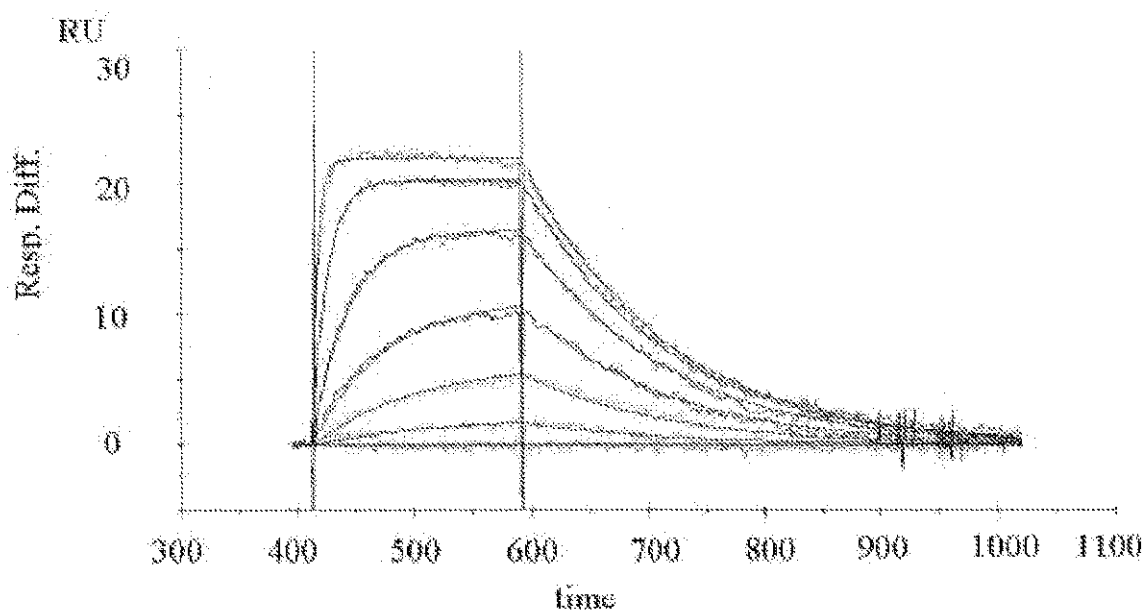


Fig. 10 c)

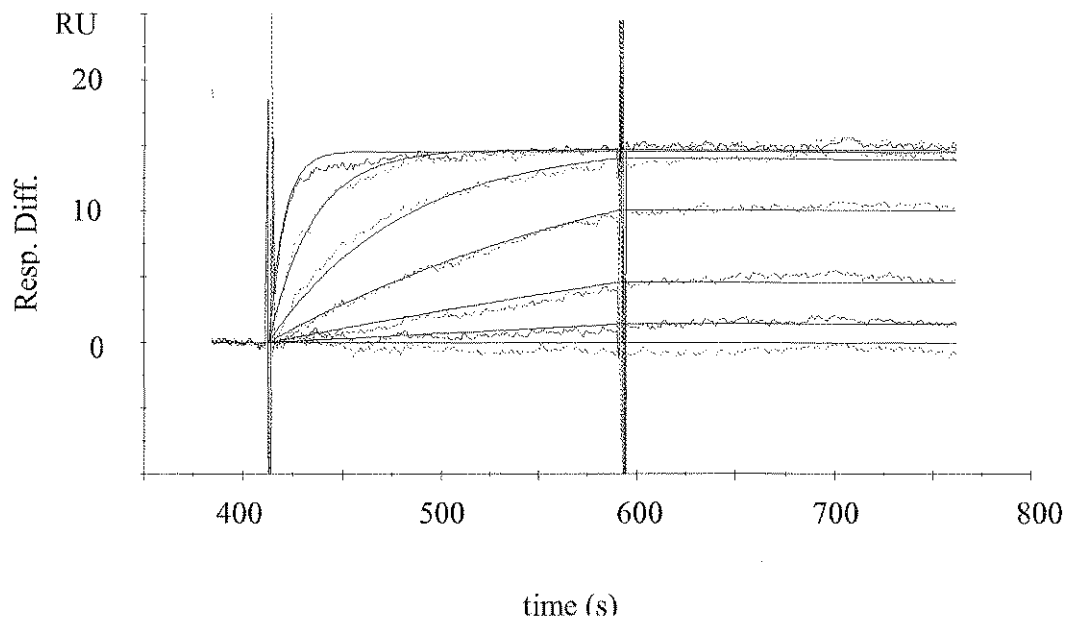


Fig. 10 d)

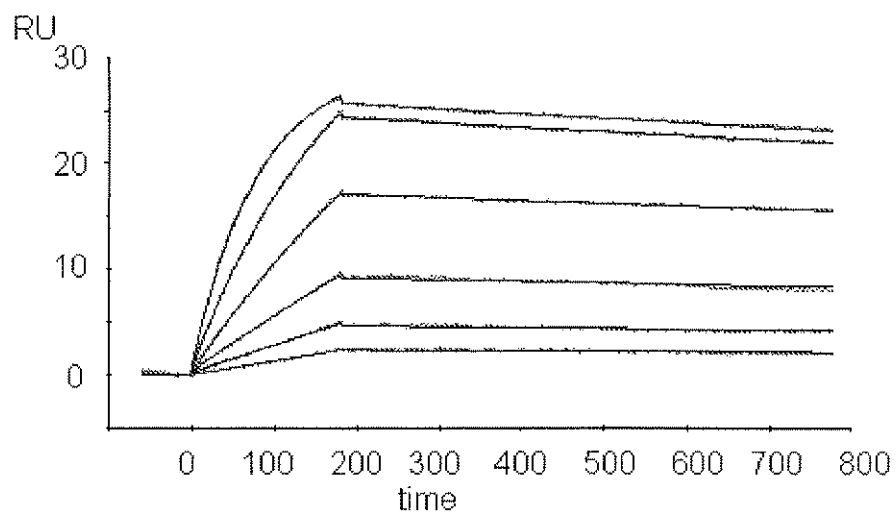


Fig. 10 e)

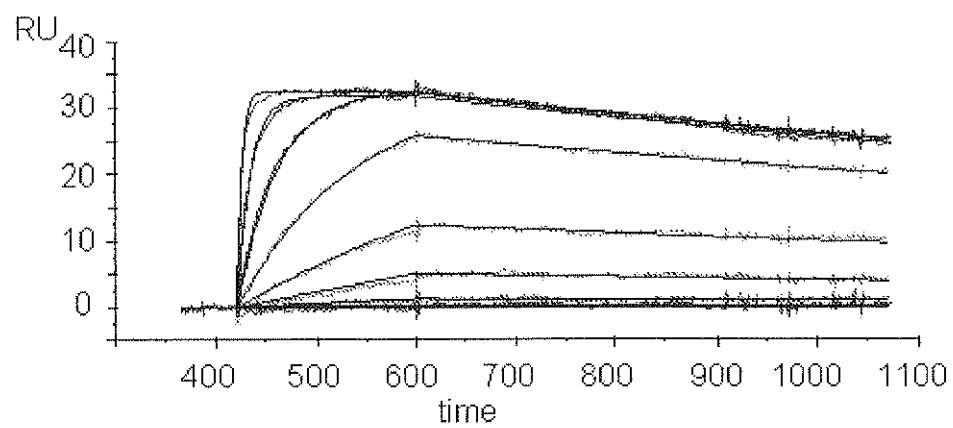


Fig. 10 f)

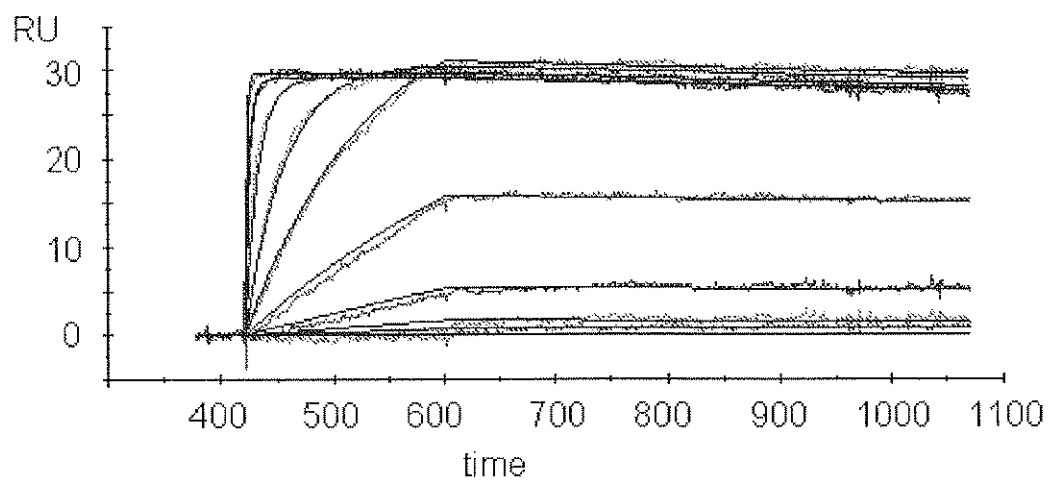


Fig. 11 a)

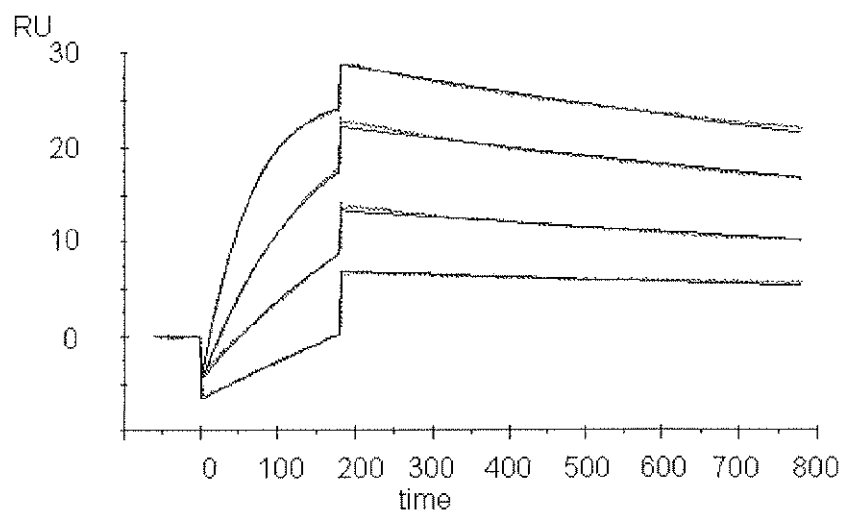


Fig. 11 b)

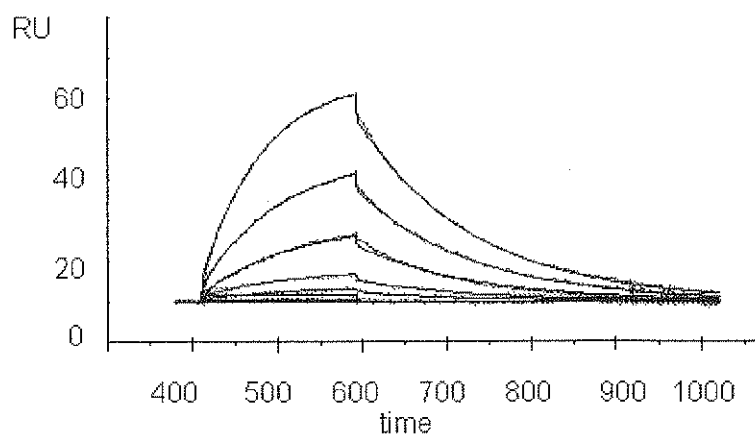


Fig. 11 c)

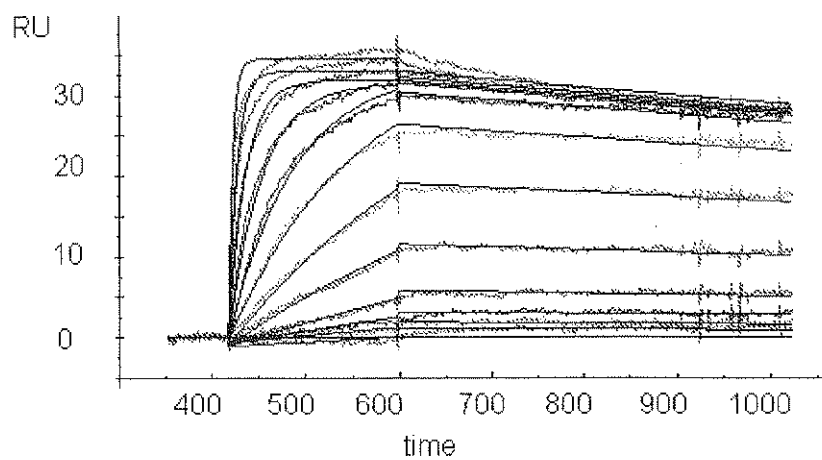


Fig. 12

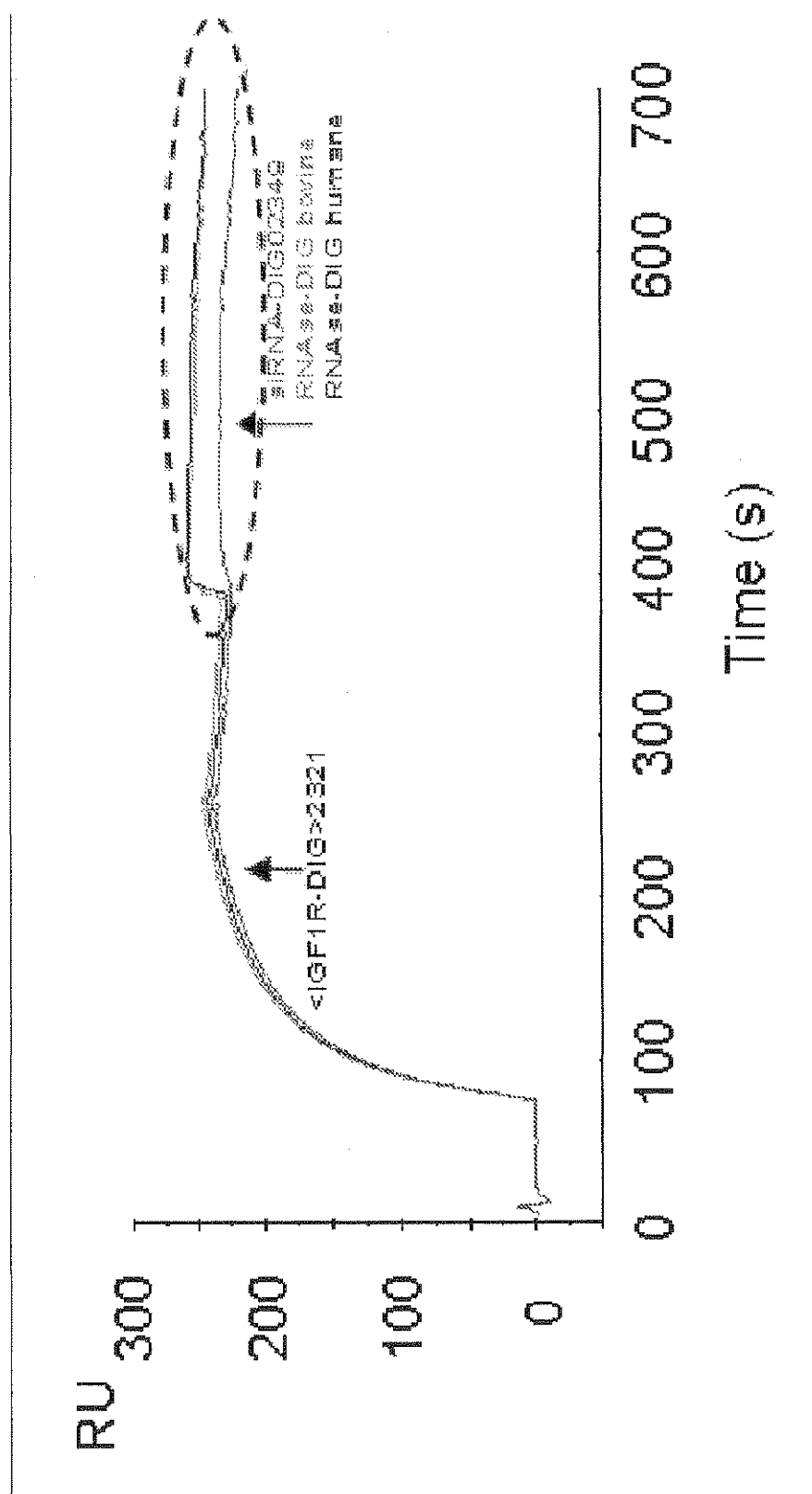


Fig. 13 a)

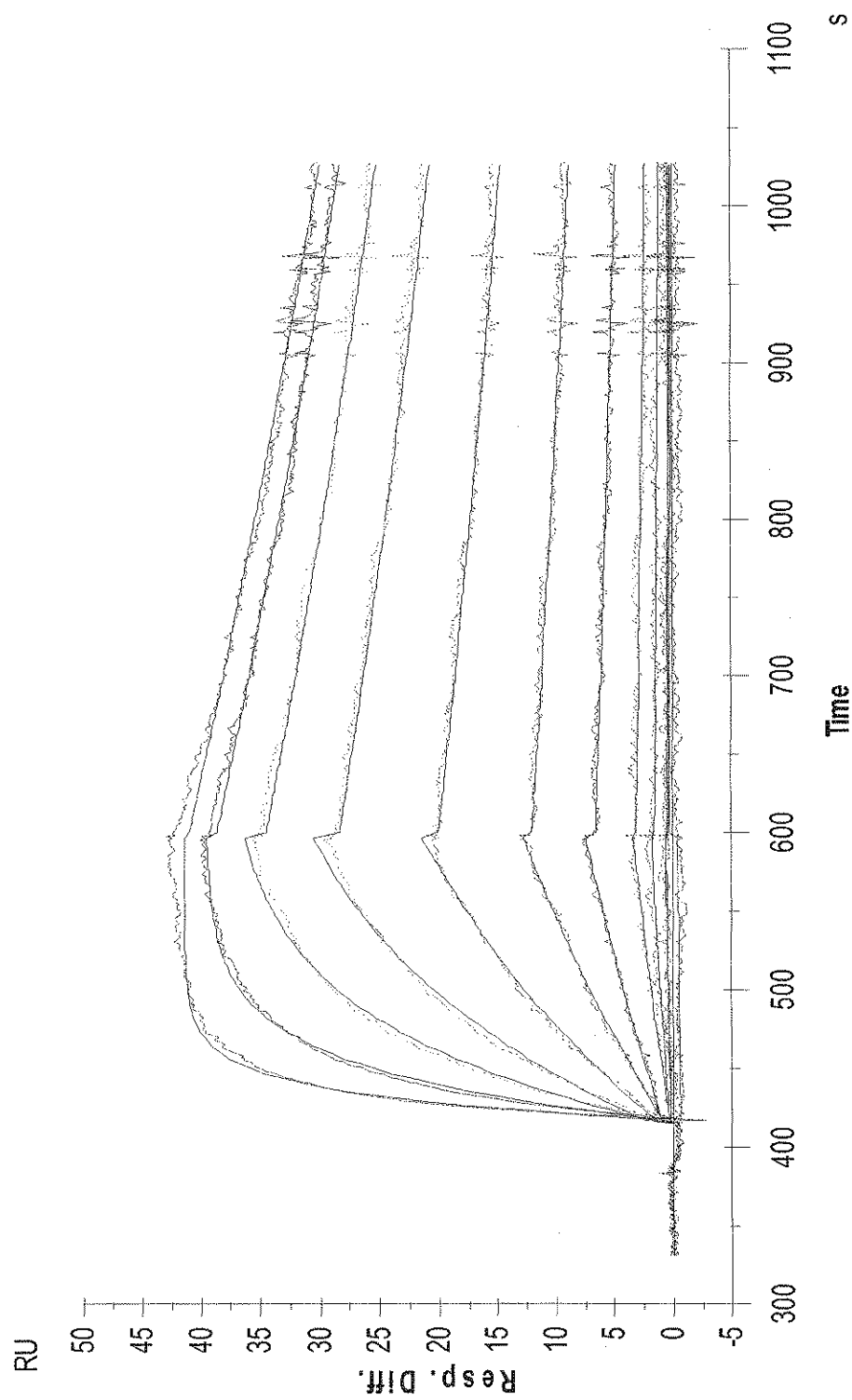


Fig. 13 b)

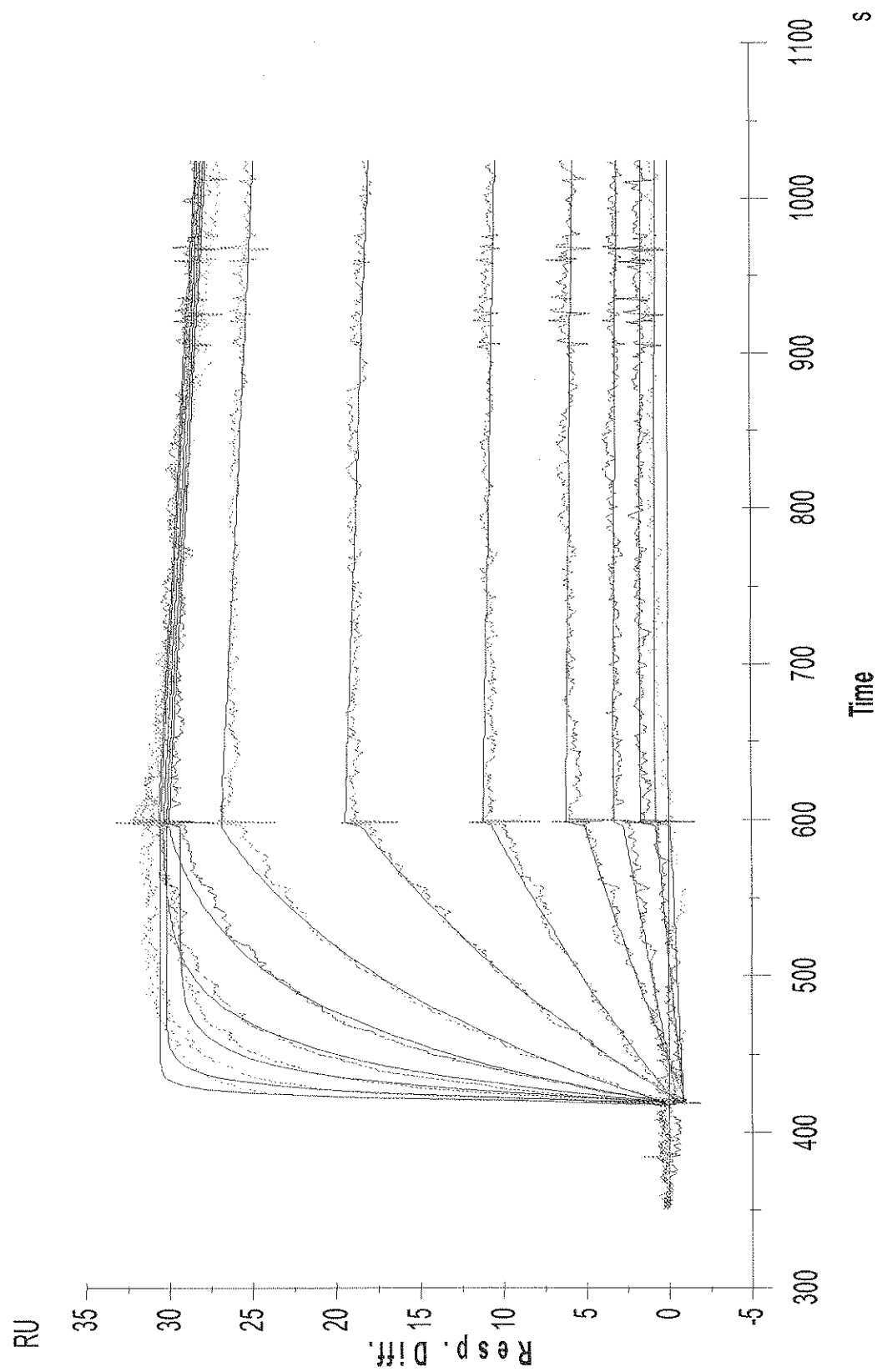


Fig. 14

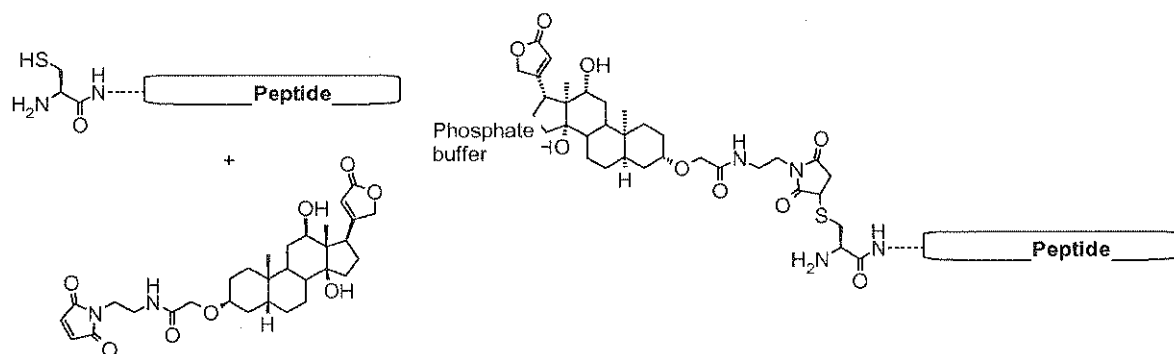


Fig. 15 a)

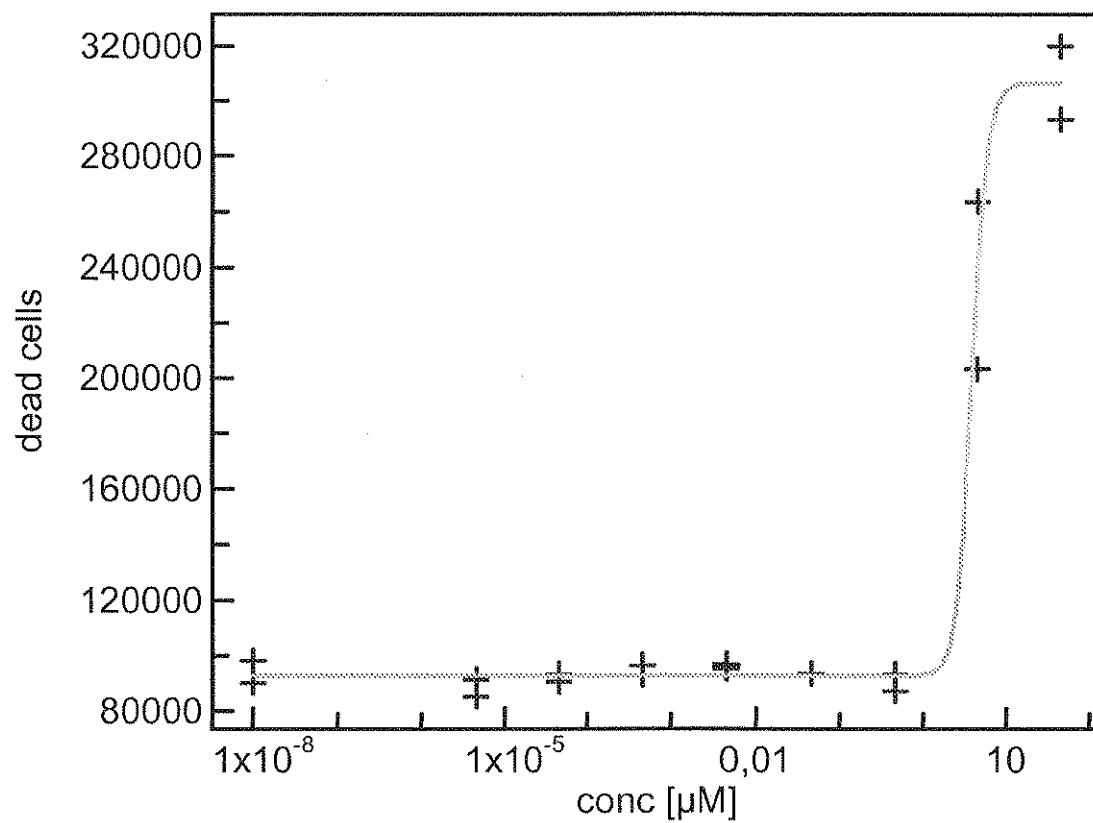


Fig. 15 b)

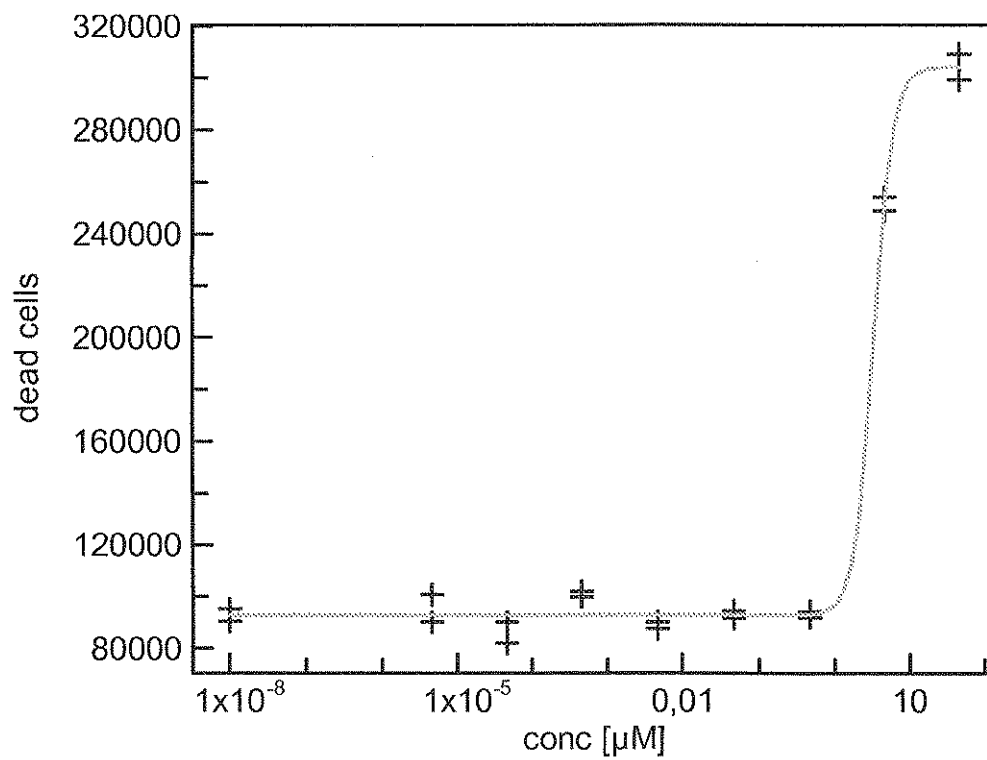


Fig. 15 c)

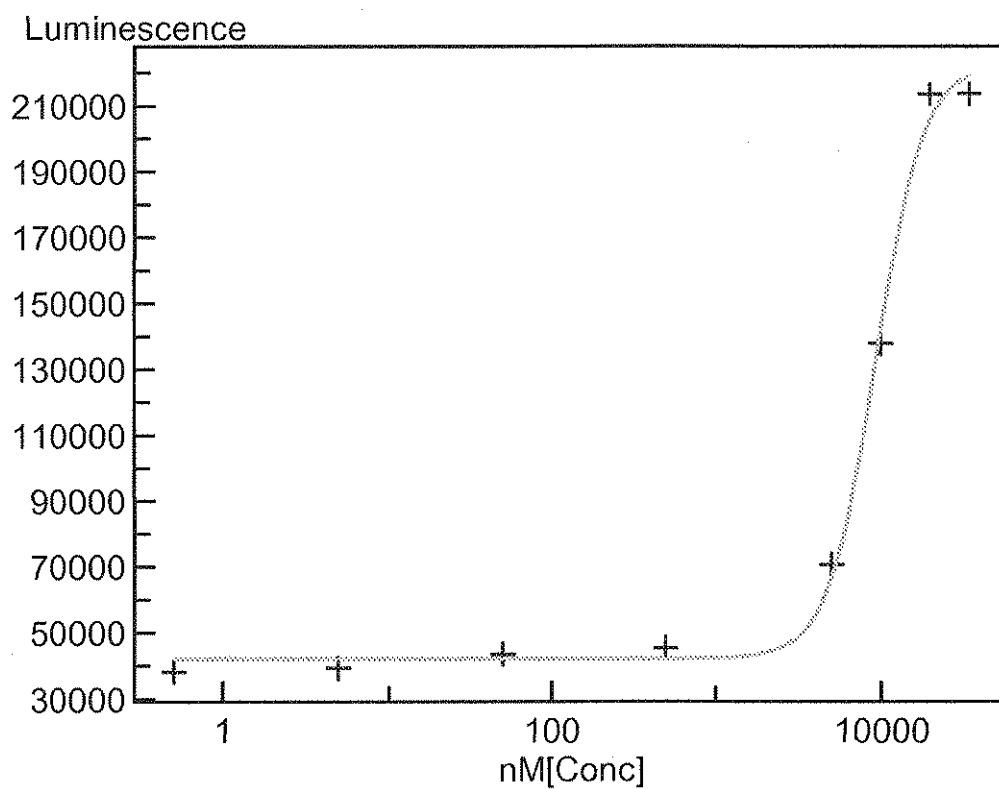


Fig. 15 d)

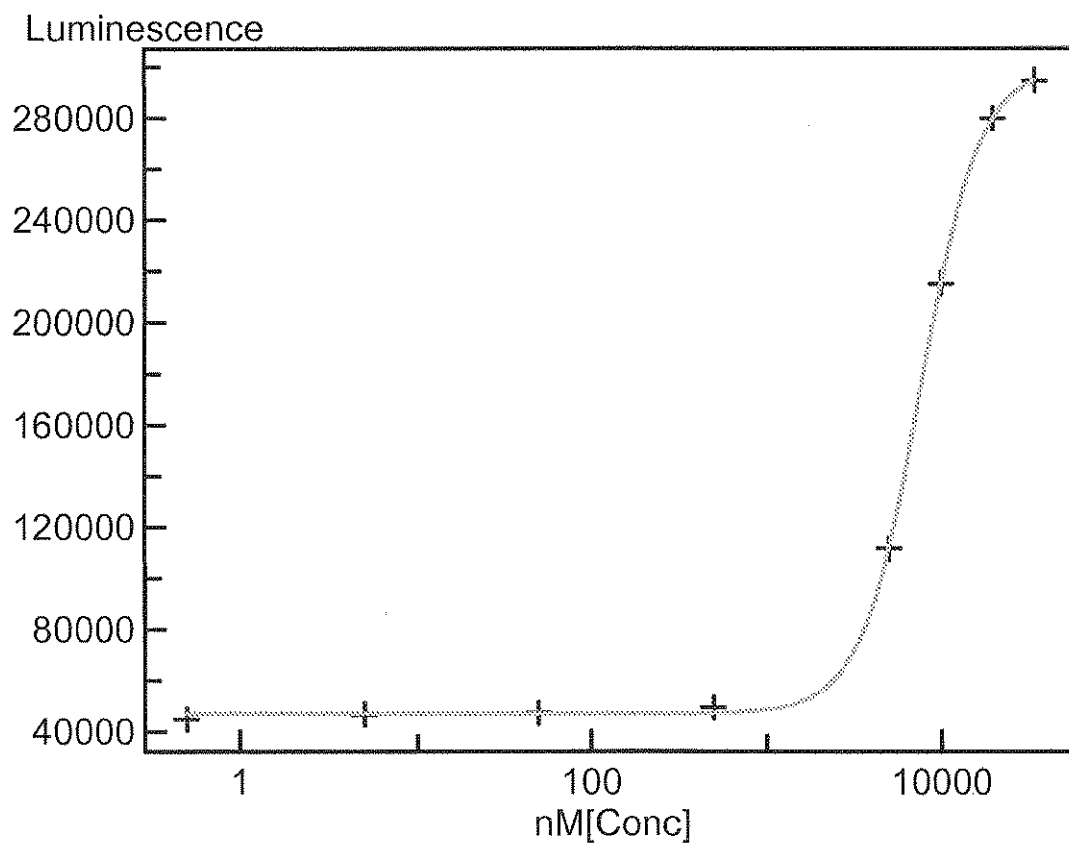


Fig. 15 e)

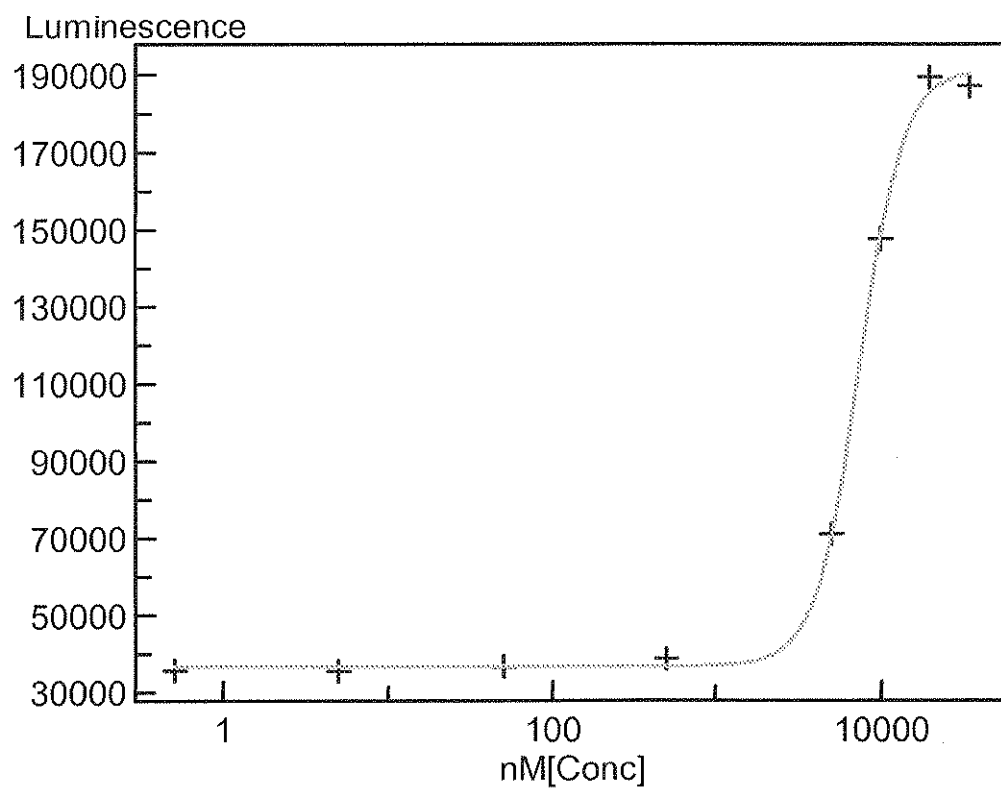


Fig. 15 f)

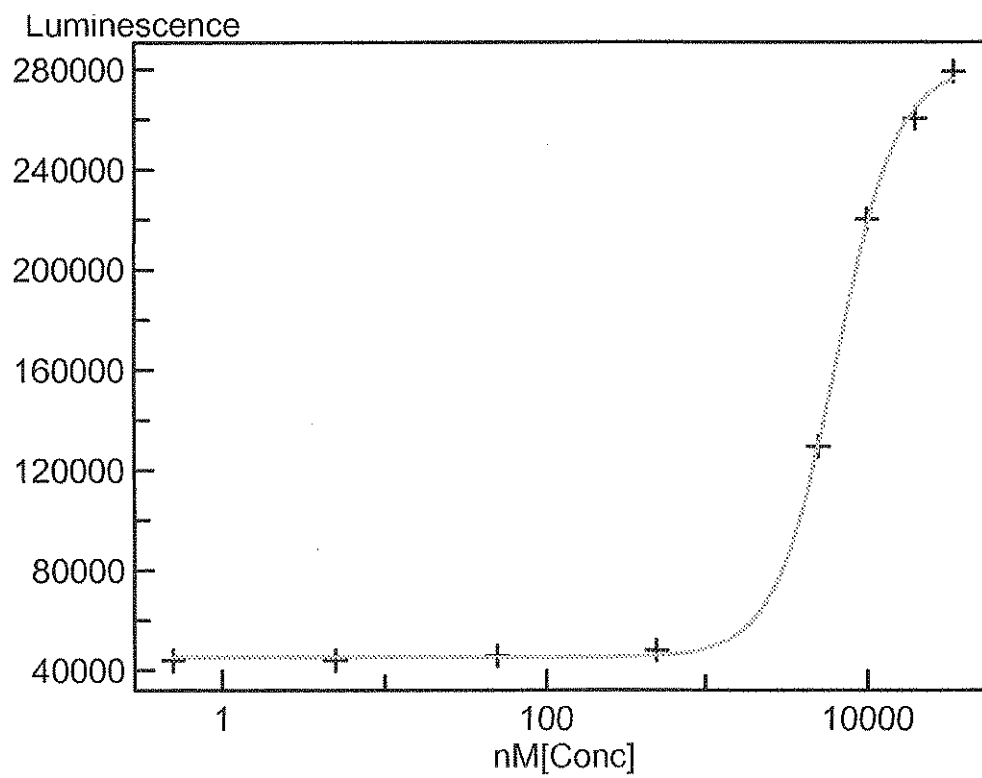
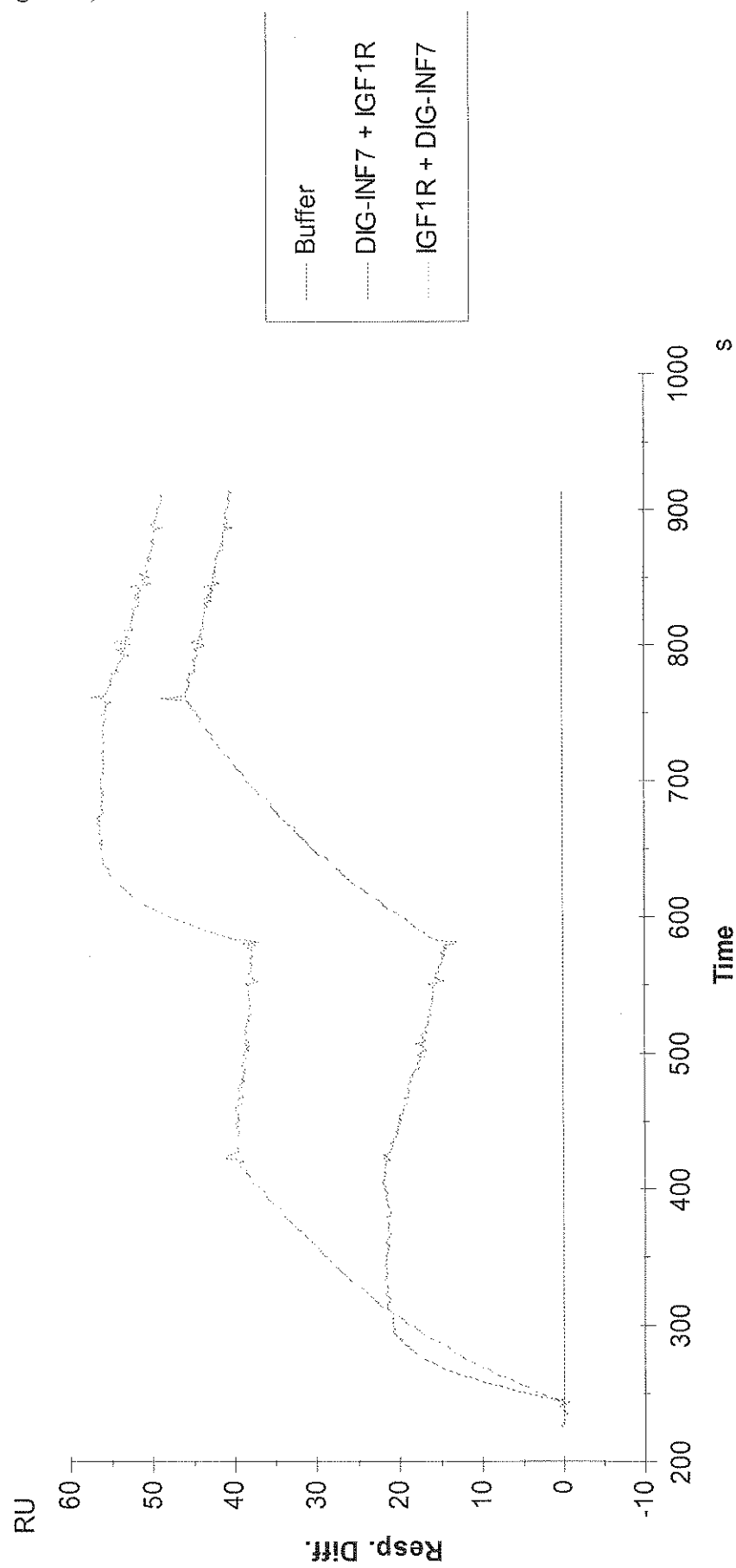
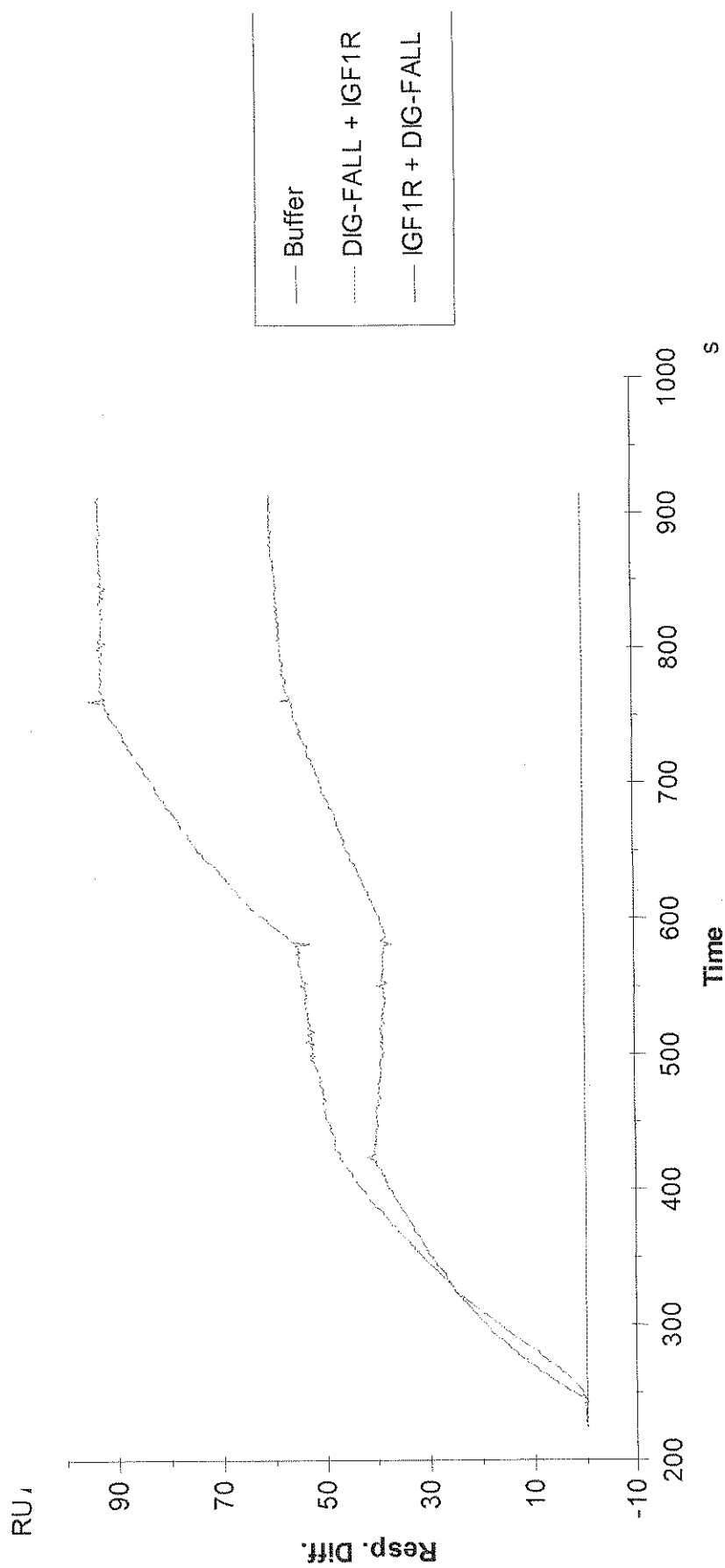


Fig. 16 a)



16 b)



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Fig. 17 a)

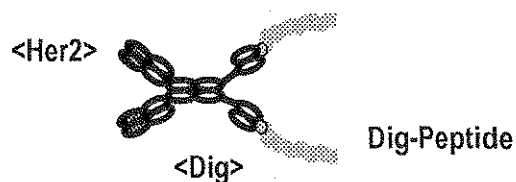


Fig. 17 b)

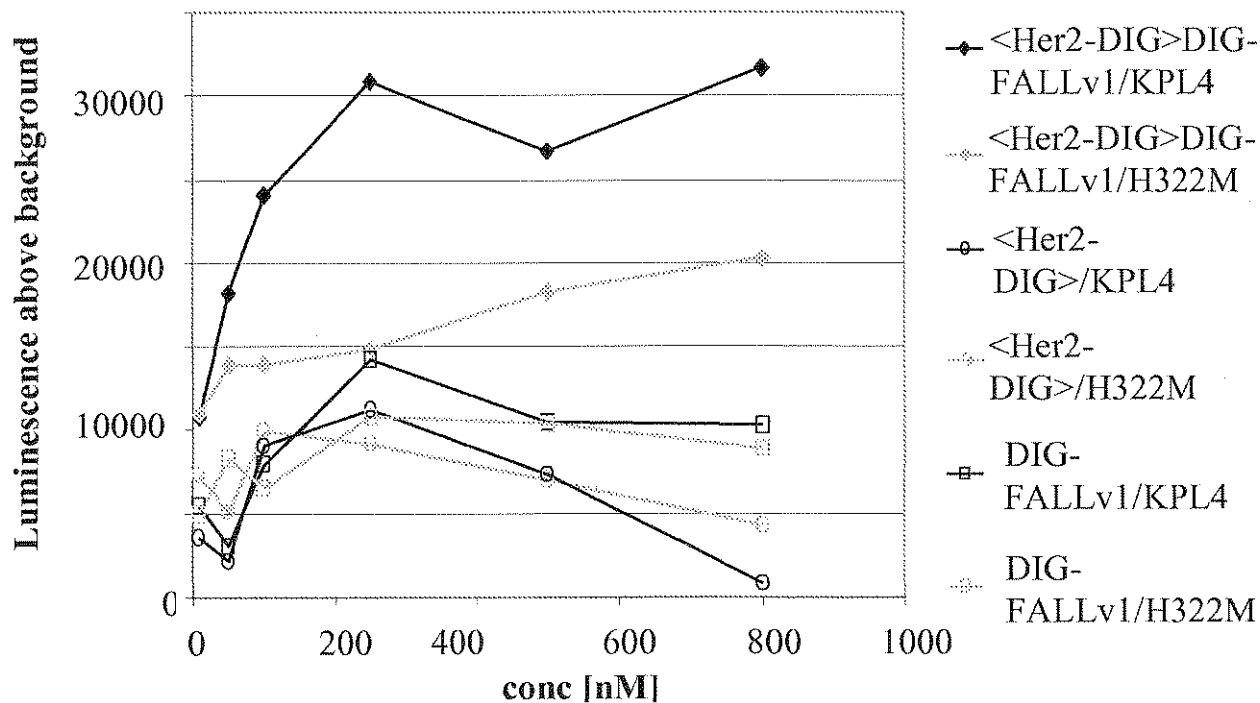


Fig. 17 c)

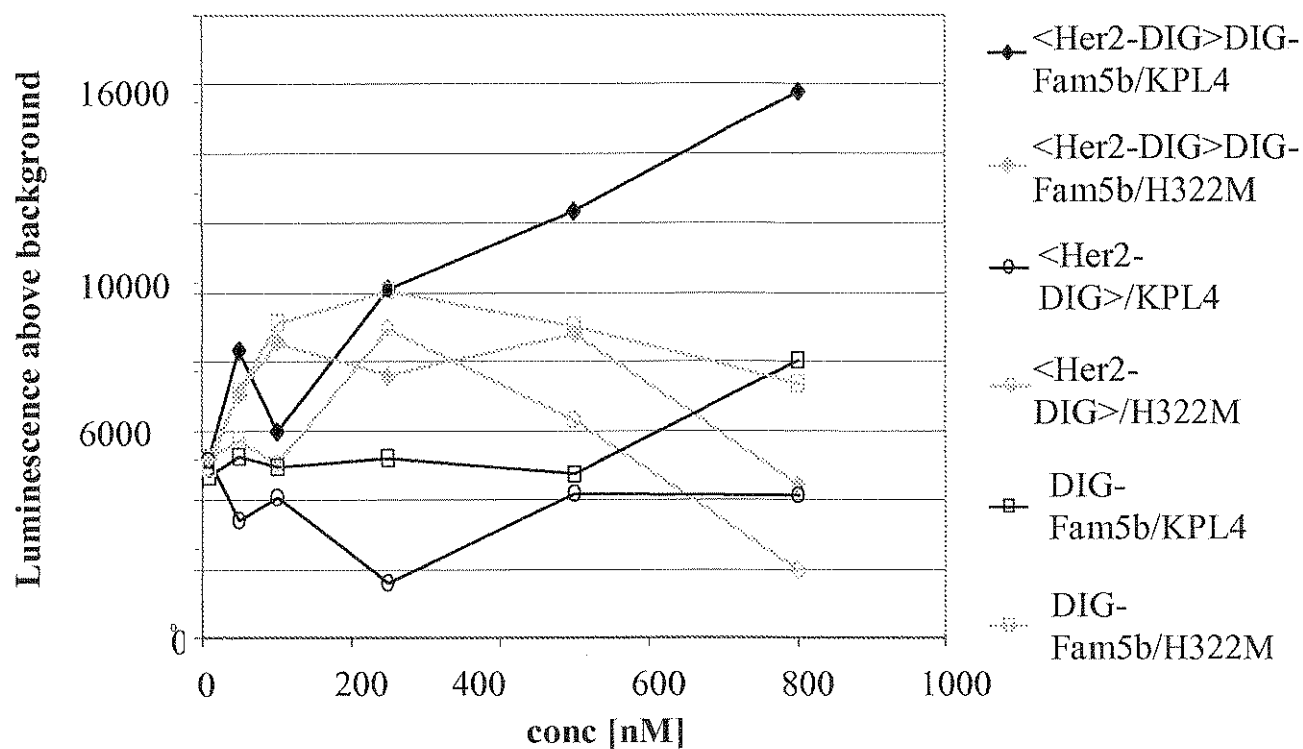


Fig. 18

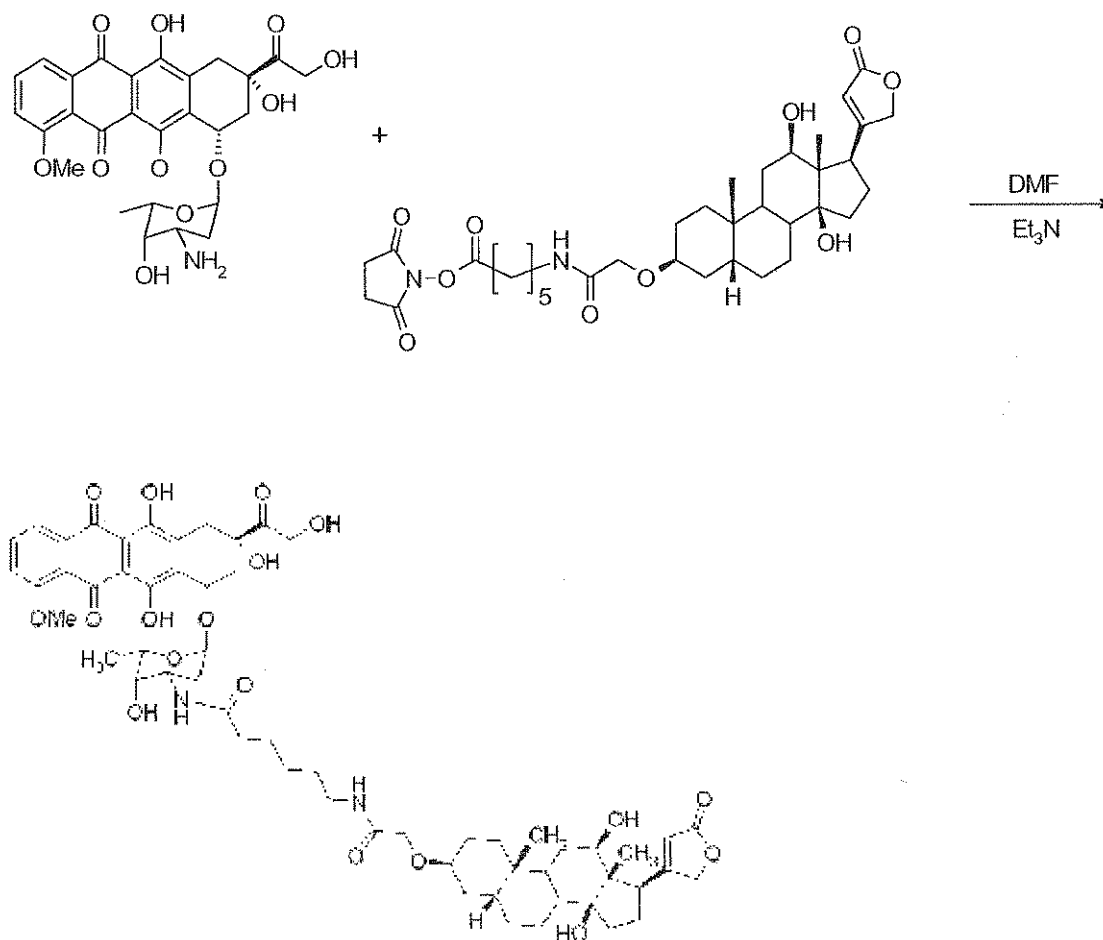


Fig. 19 a)

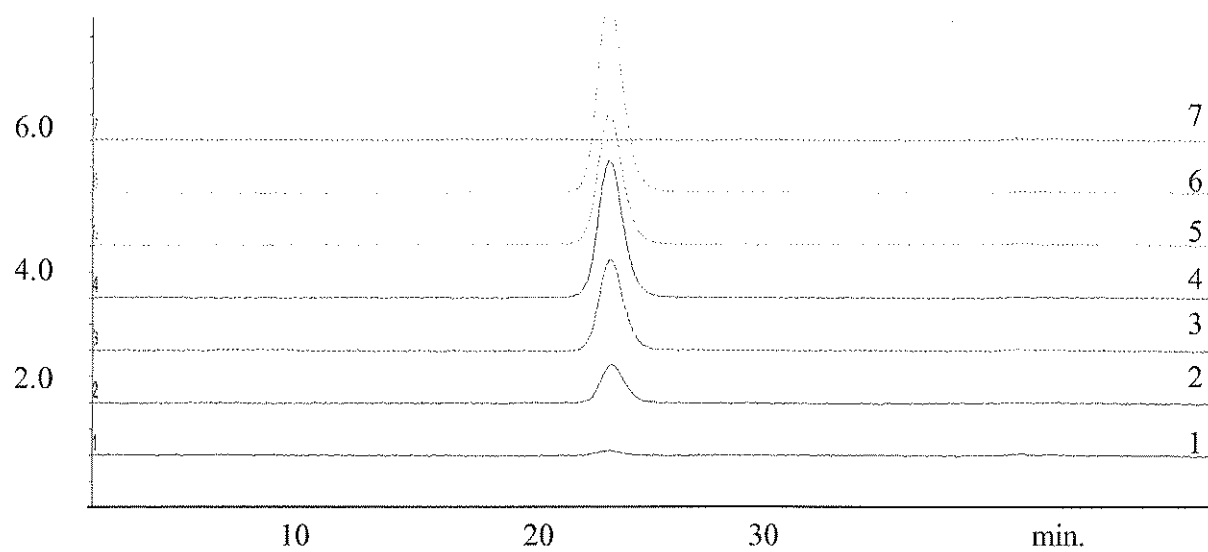


Fig. 19 b)

ratio <Her2- Dig>:Doxo	Area (Ex: 488 nm / Em: 540 nm) [mAU*min]
1:0	0
1:0,5	1,1
1:1	2,4
1:2	3,4
1:3	3,3
1:5	4,9
0:1	0

Fig. 20 a)

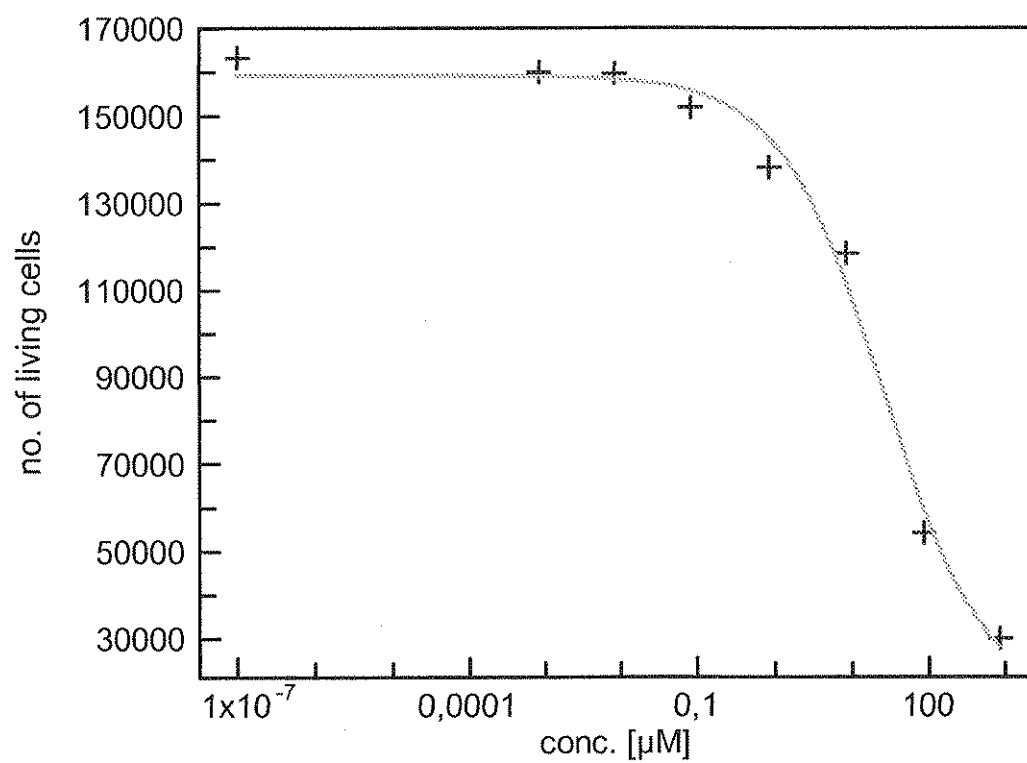


Fig. 20 b)

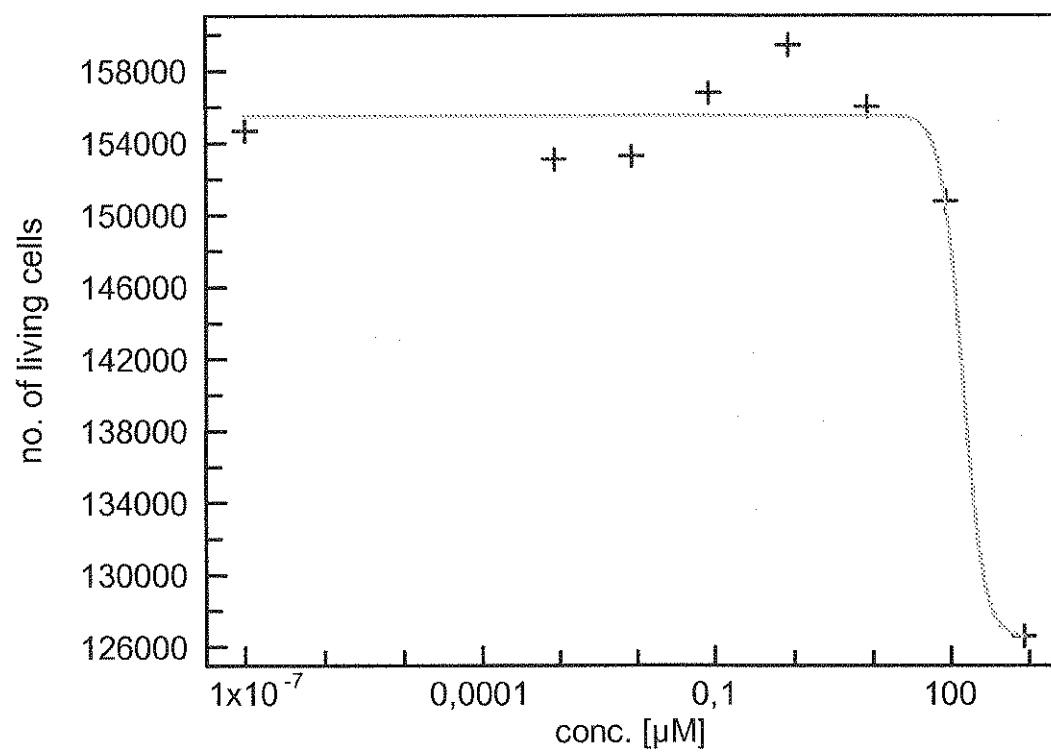


Fig. 20 c)

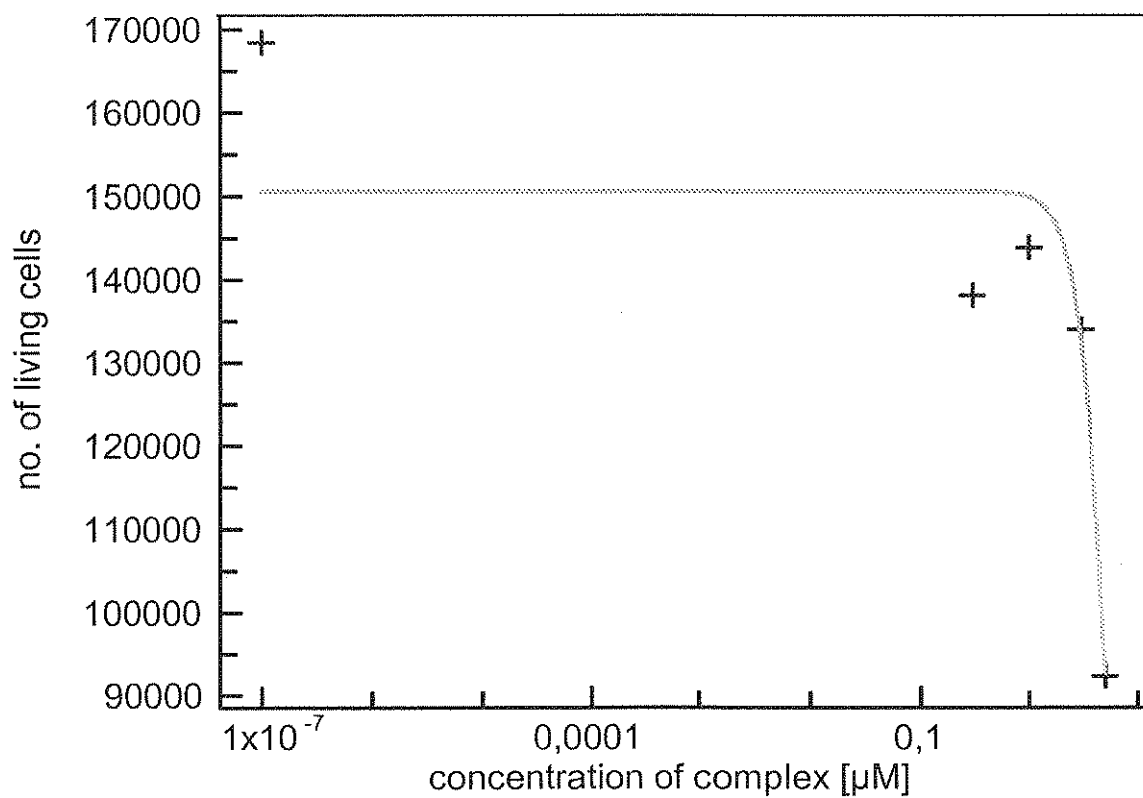


Fig. 21 a)

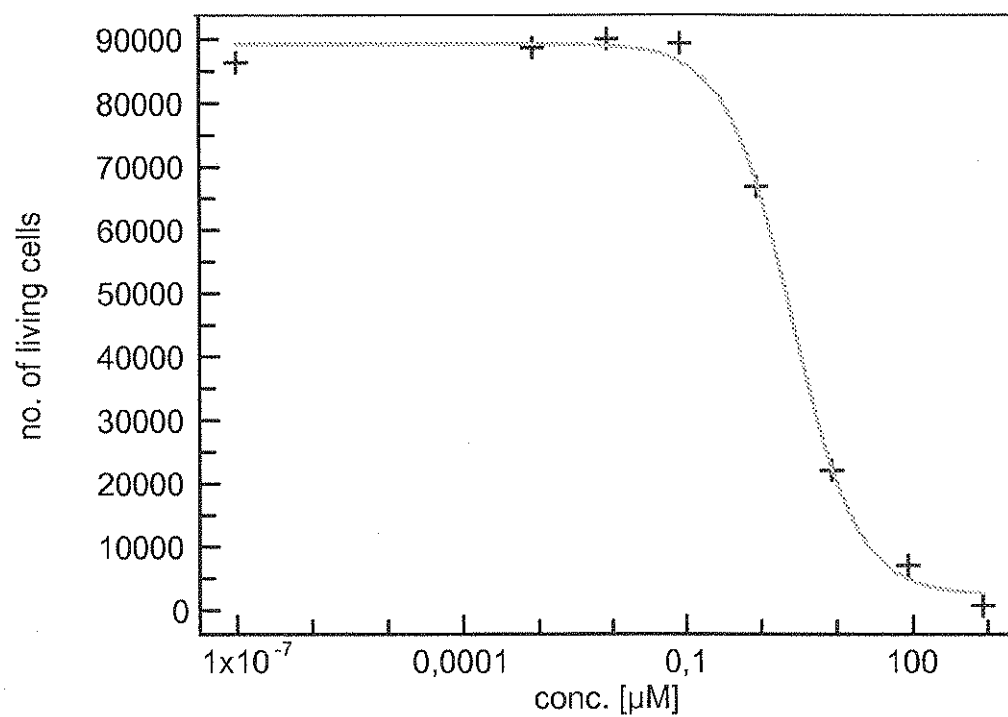


Fig. 21 b)

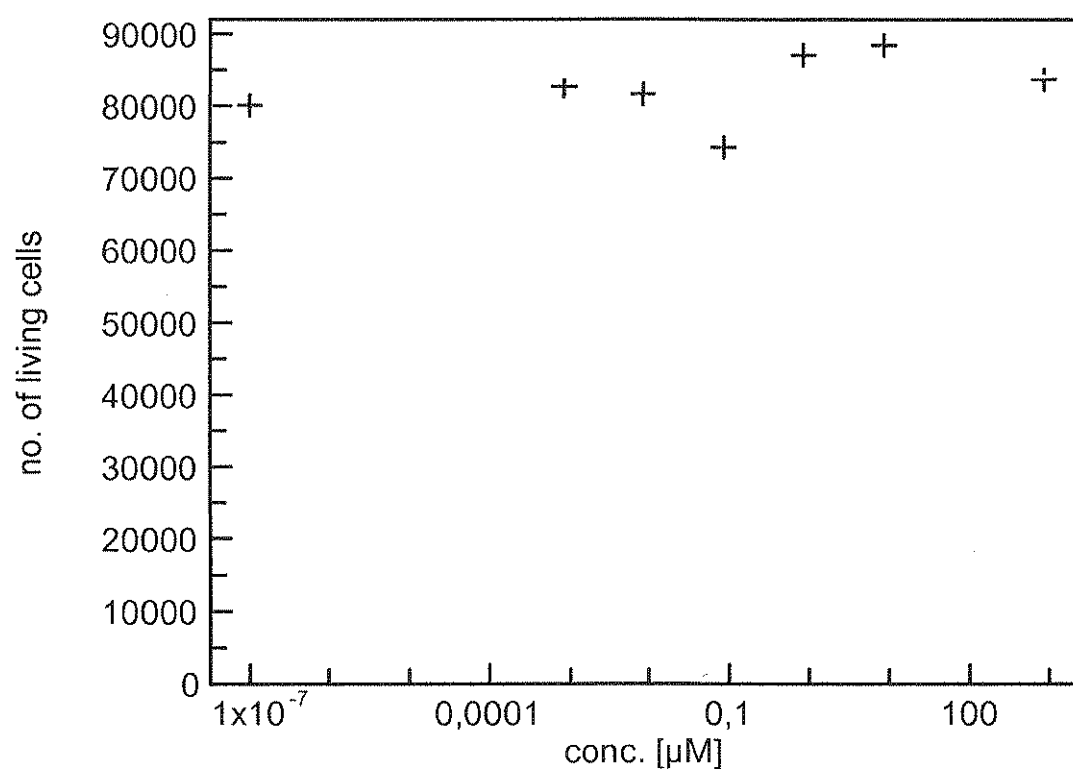


Fig. 21 c)

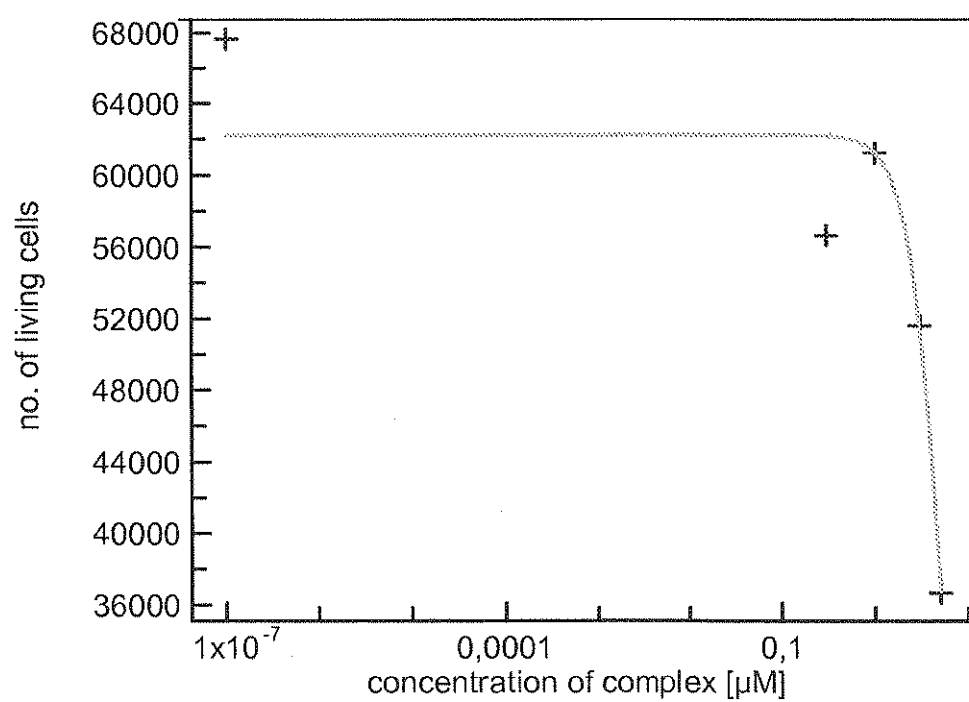


Fig. 22 a)

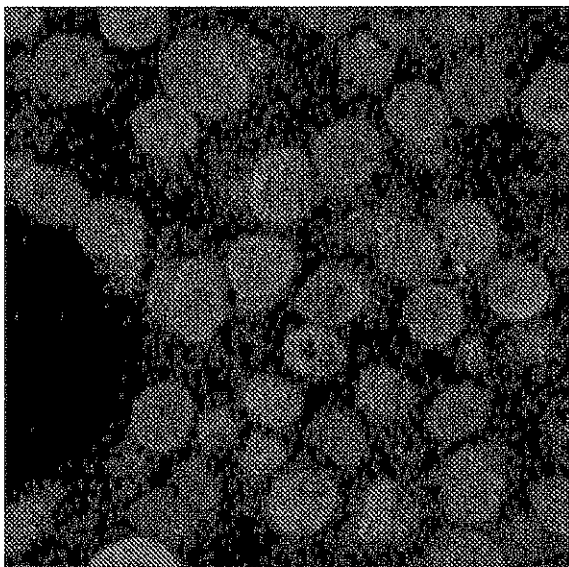


Fig. 22b)

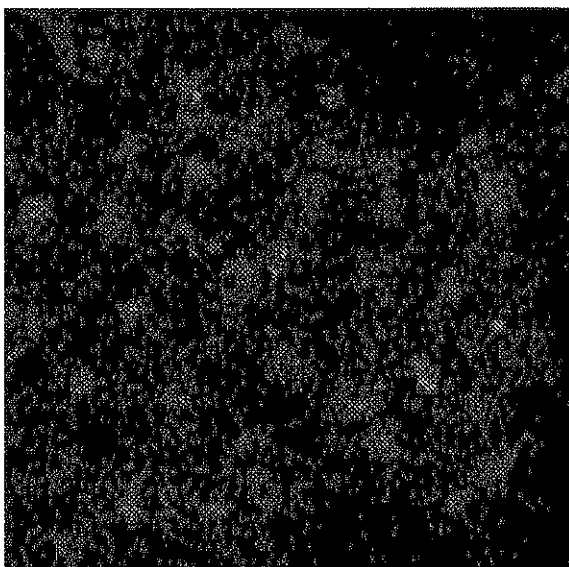


Fig. 22 c)

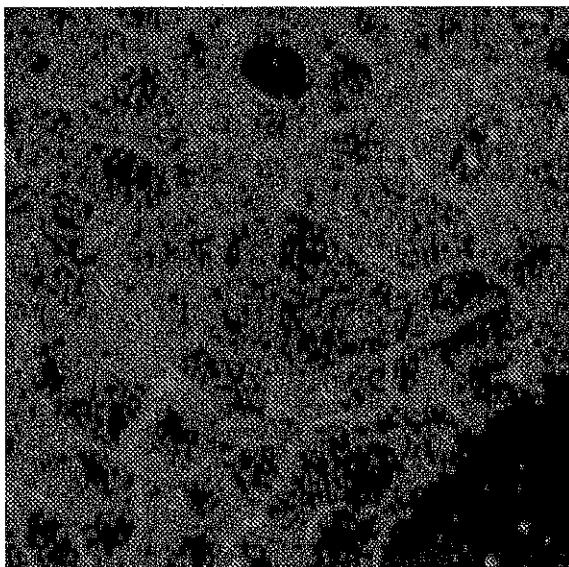


Fig. 23

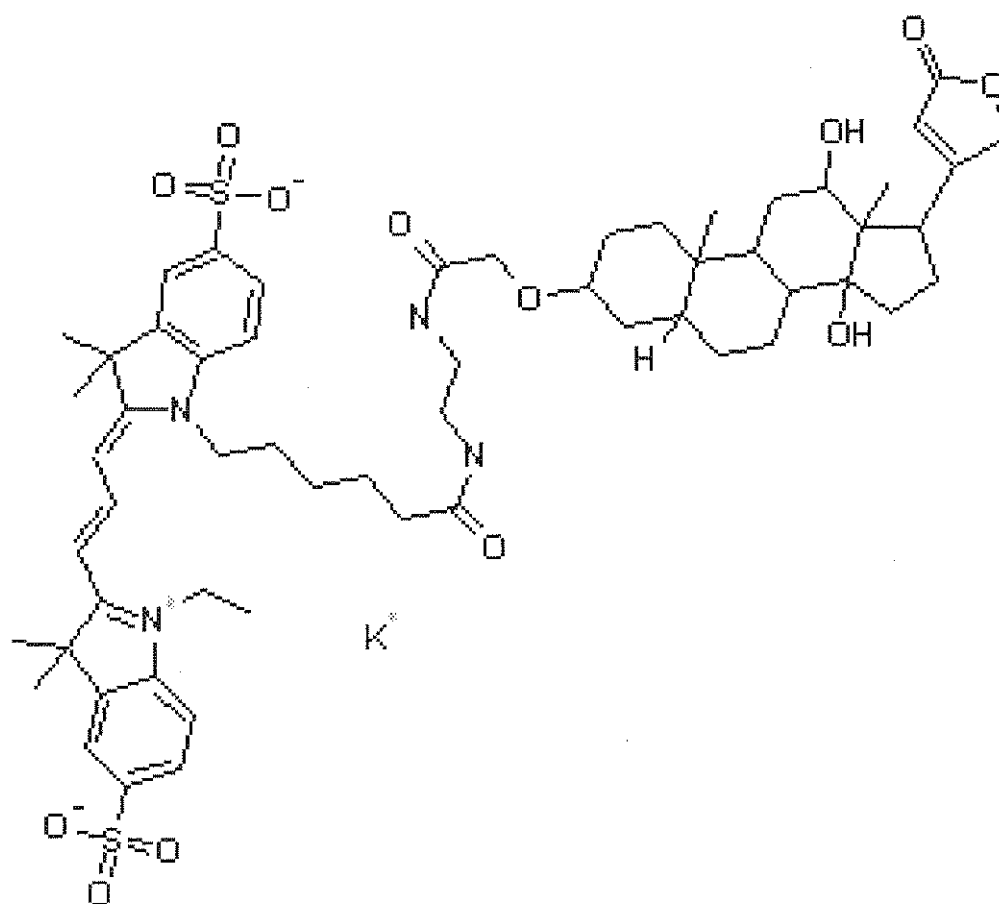


Fig. 24 a)

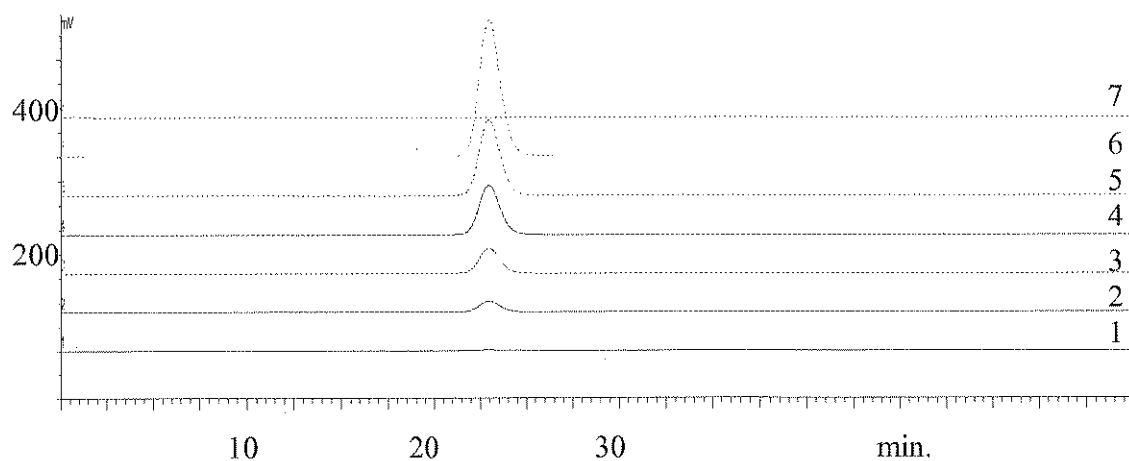


Fig. 24 b)

ratio <Her2- Dig>:Dig- Cy5	Area (Ex: 650 nm / Em: 667 nm) [mAU*min]
1:0	2
1:0,5	30
1:1	68
1:2	135
1:3	209
1:5	381
0:1	0

Fig. 25 a)

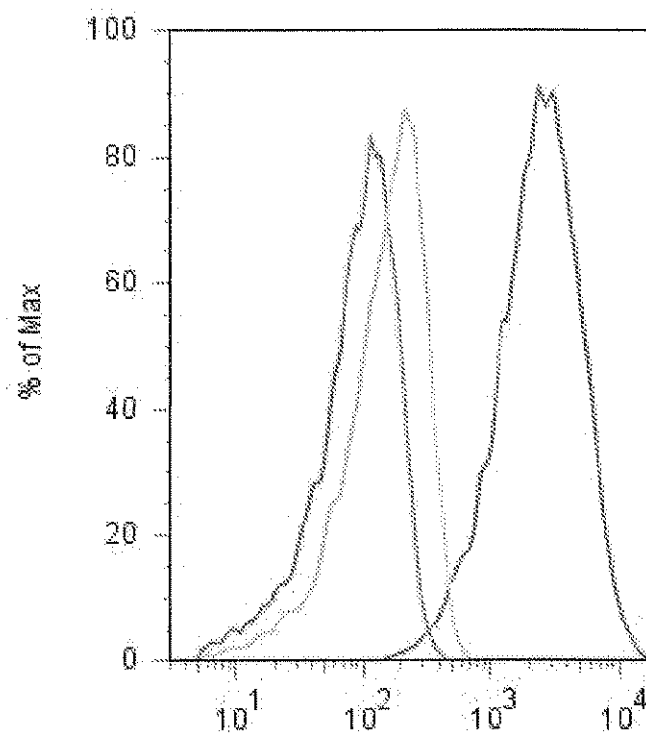


Fig. 25 b)

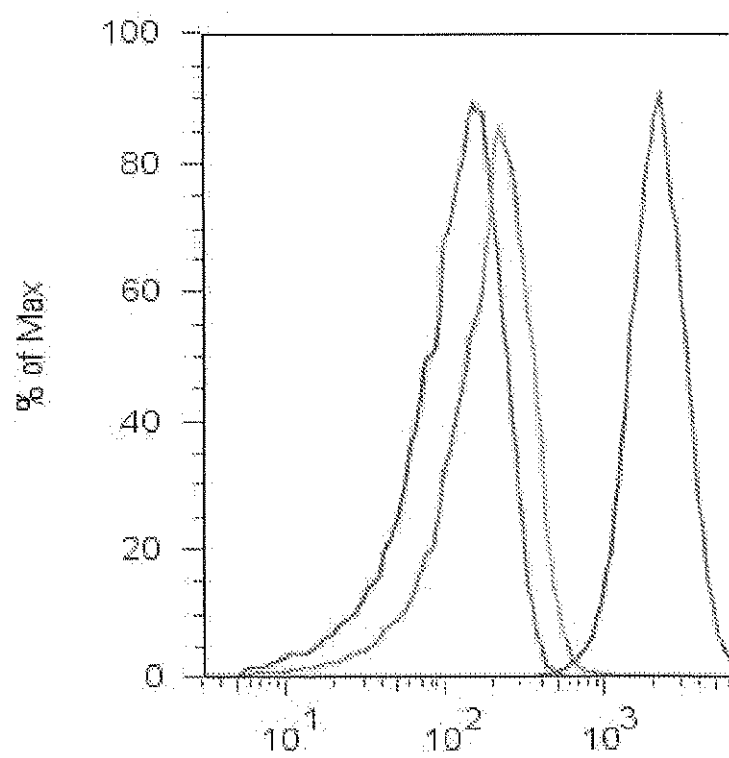


Fig. 26 a)

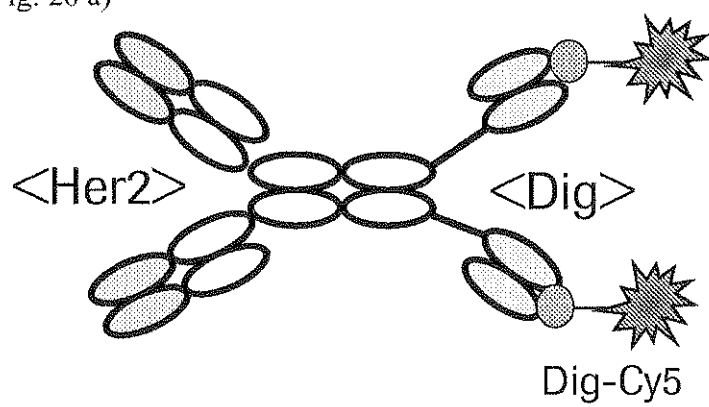


Fig. 26 b)

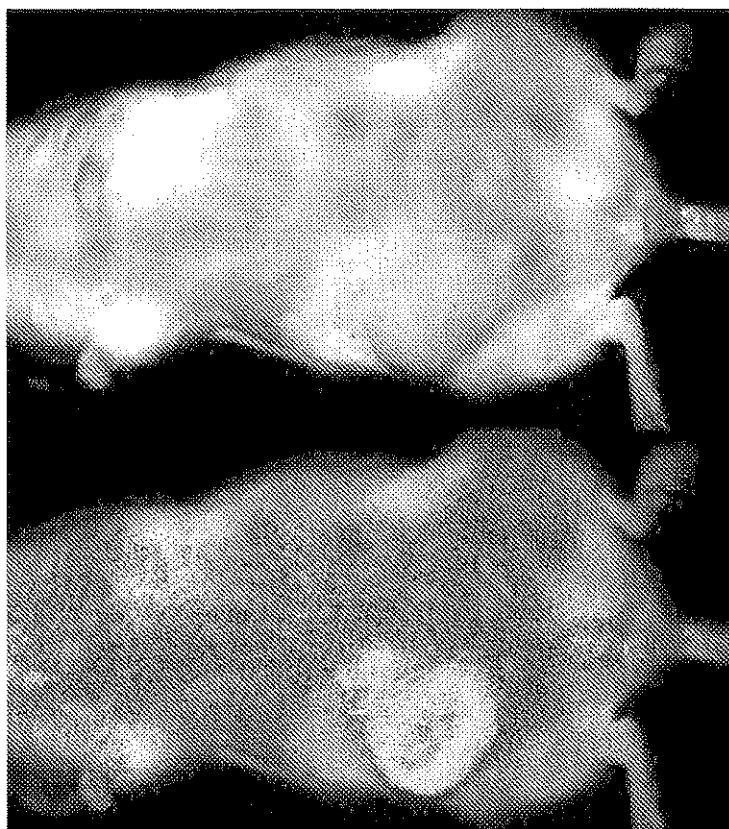


Fig. 27 a)

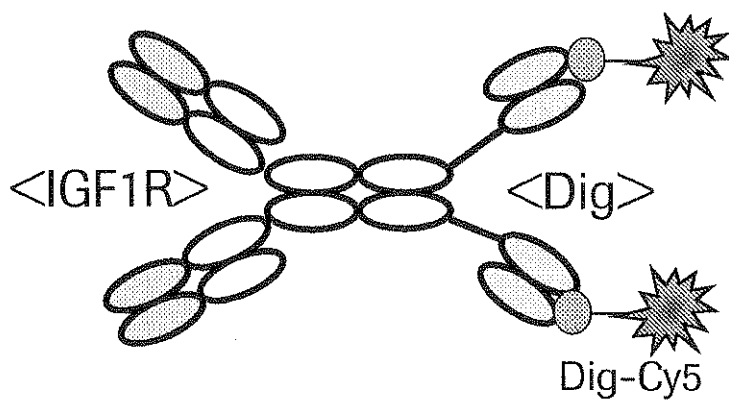


Fig 27 b)



Fig 27 c)



Fig. 28 a)

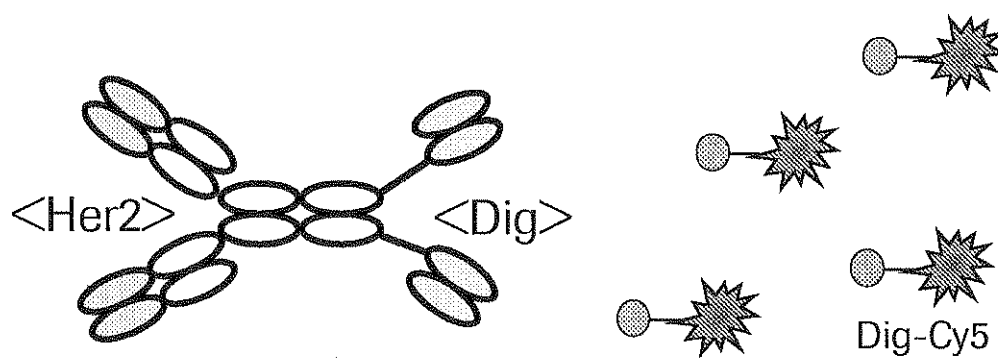


Fig. 28 b)

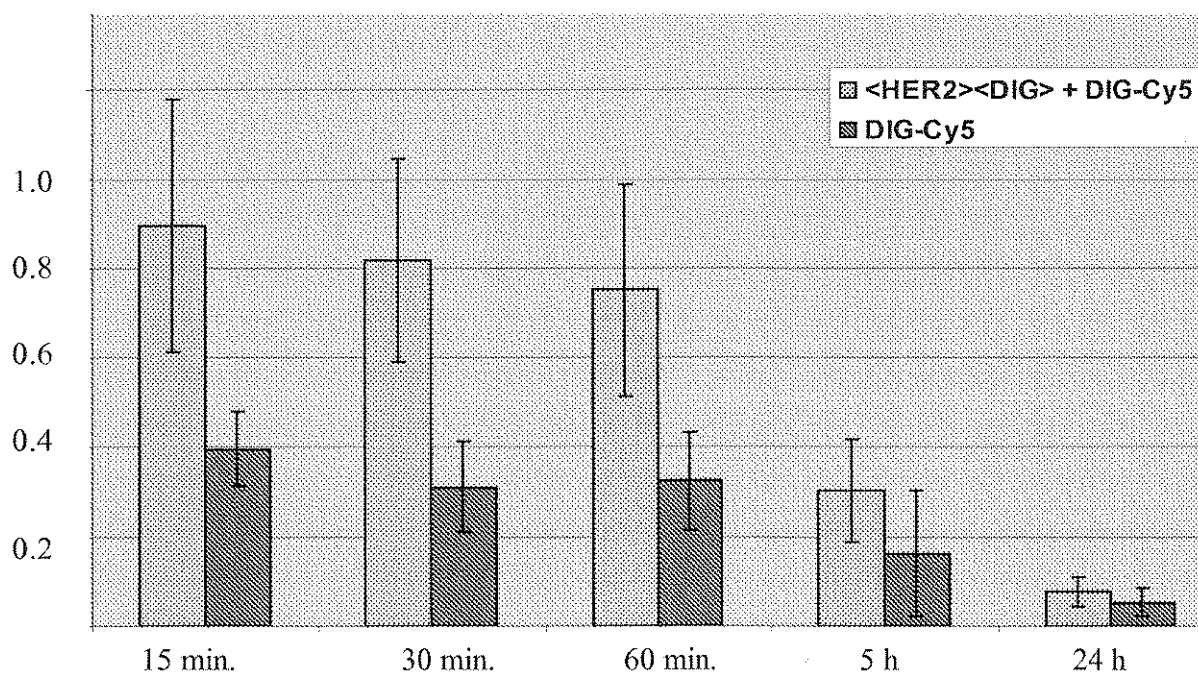


Fig. 29

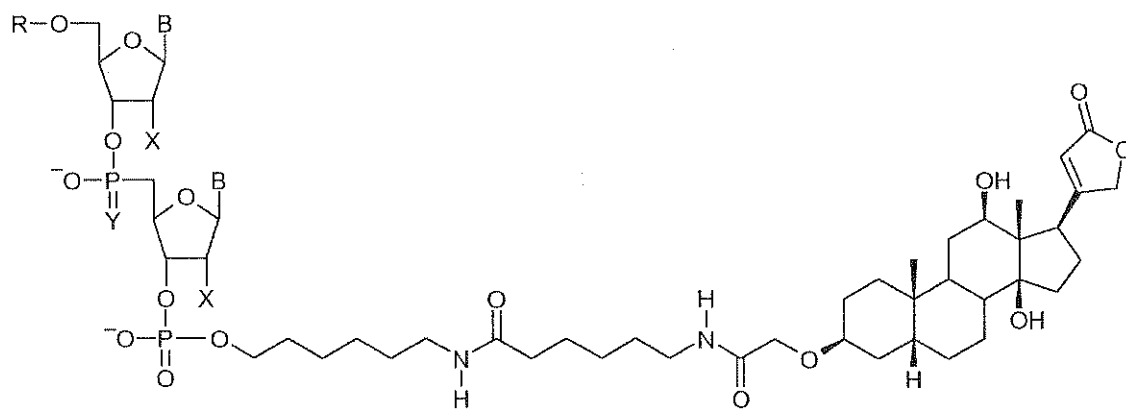


Fig. 30 a)

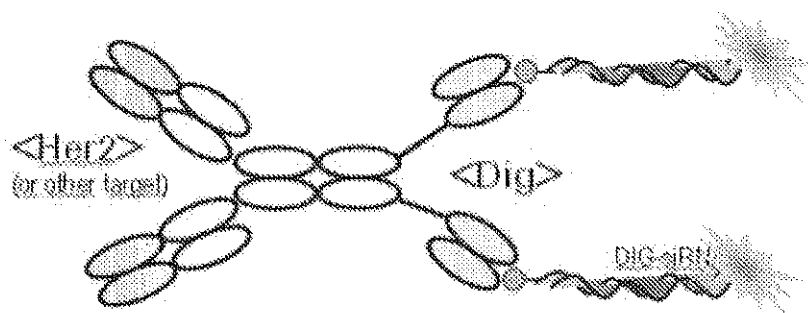


Fig. 30 b)

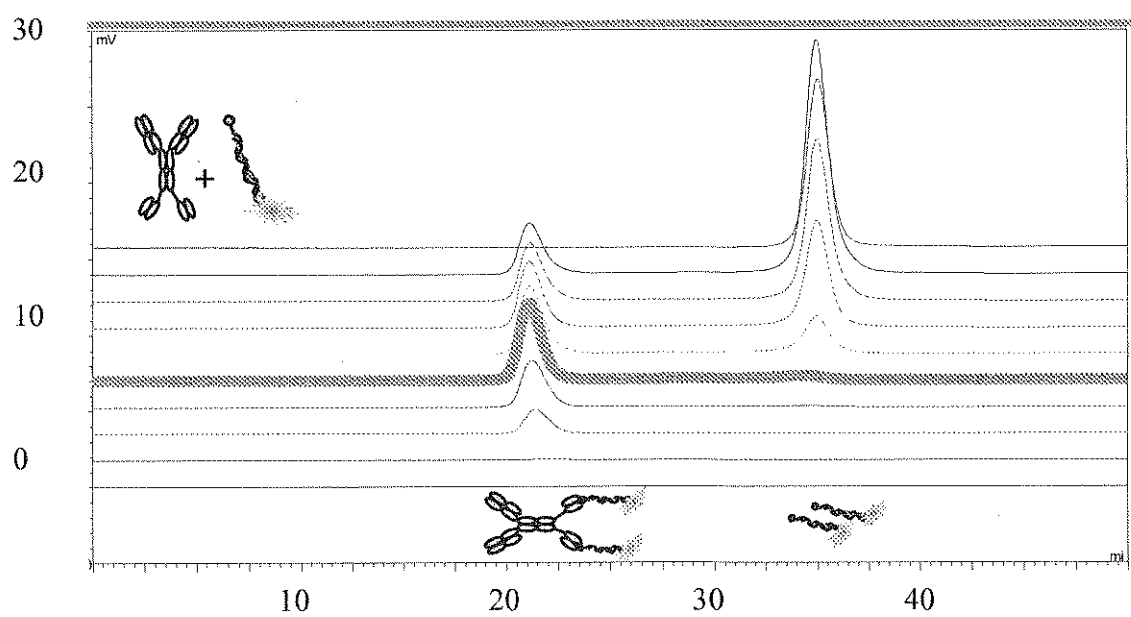


Fig. 31 a)

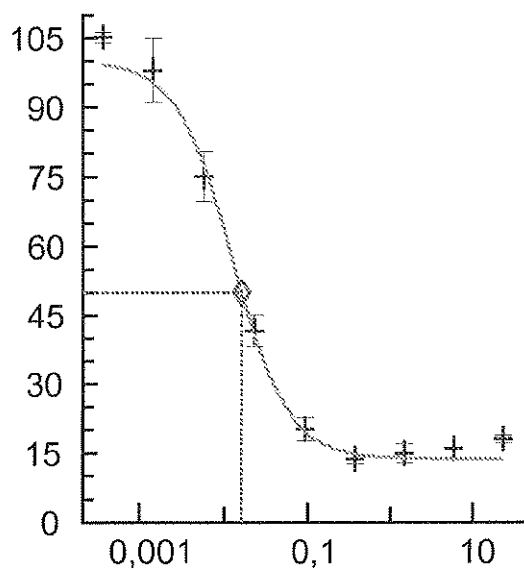


Fig. 31 b)

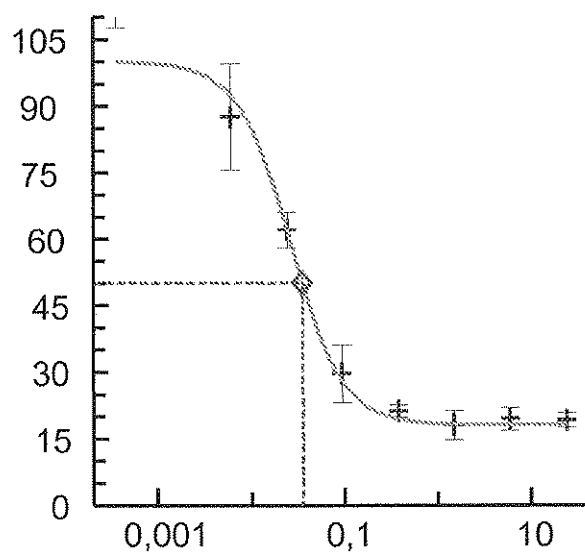


Fig. 31 c)

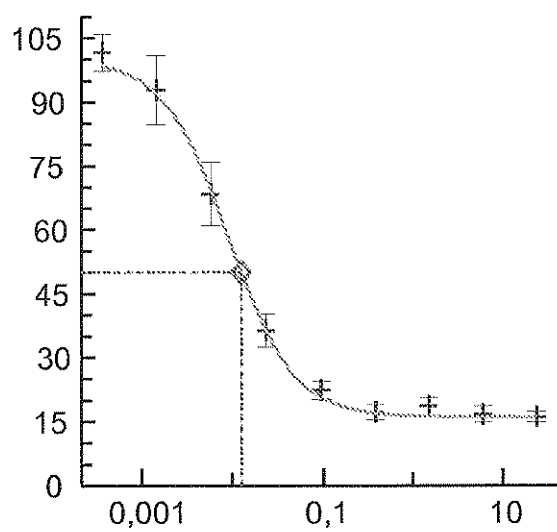


Fig. 31 d)

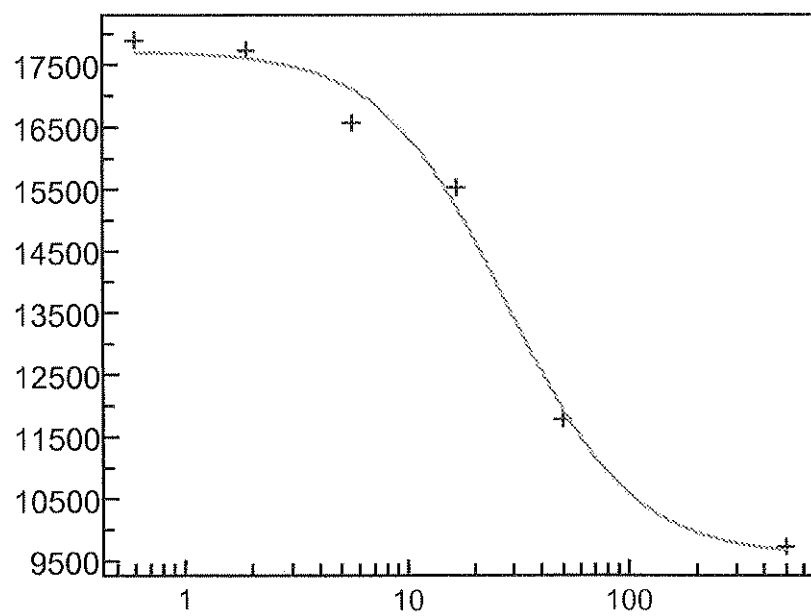


Fig. 31 e)

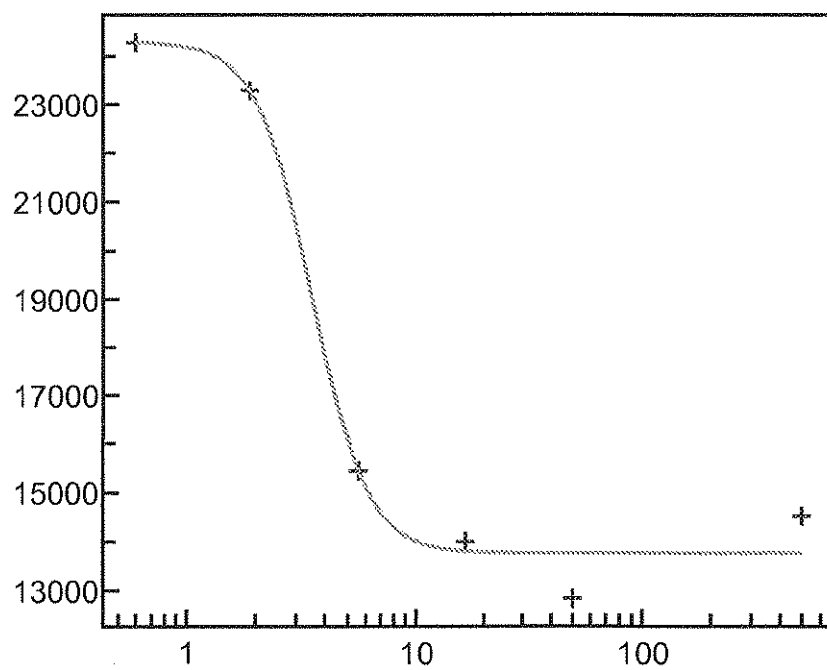


Fig. 31 f)

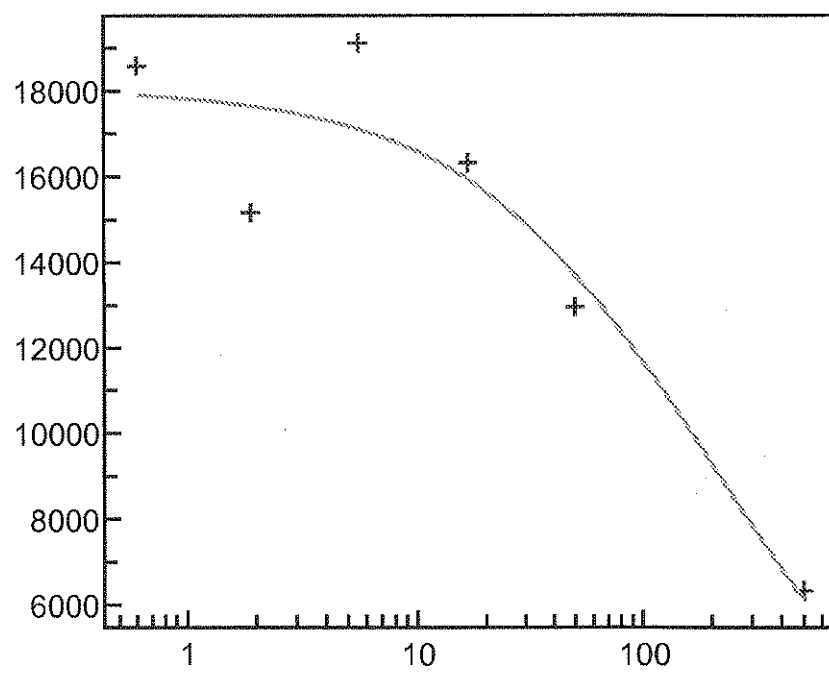


Fig. 31 g)

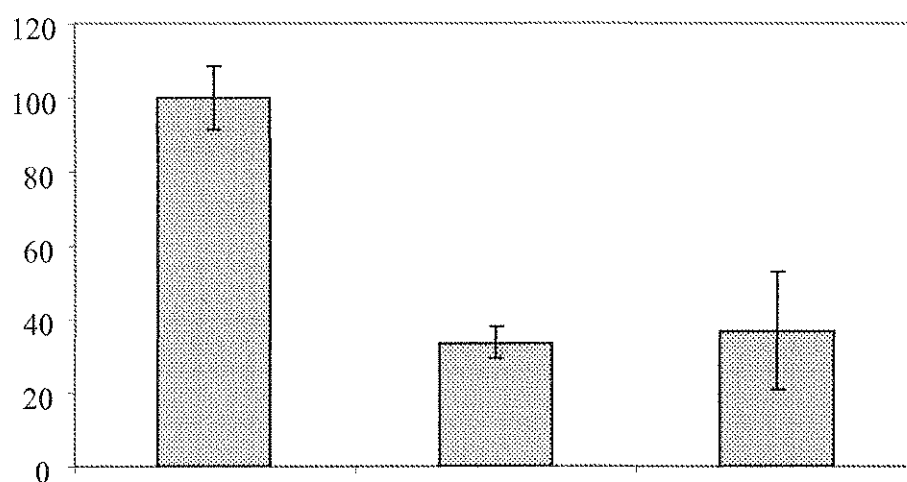


Fig. 32

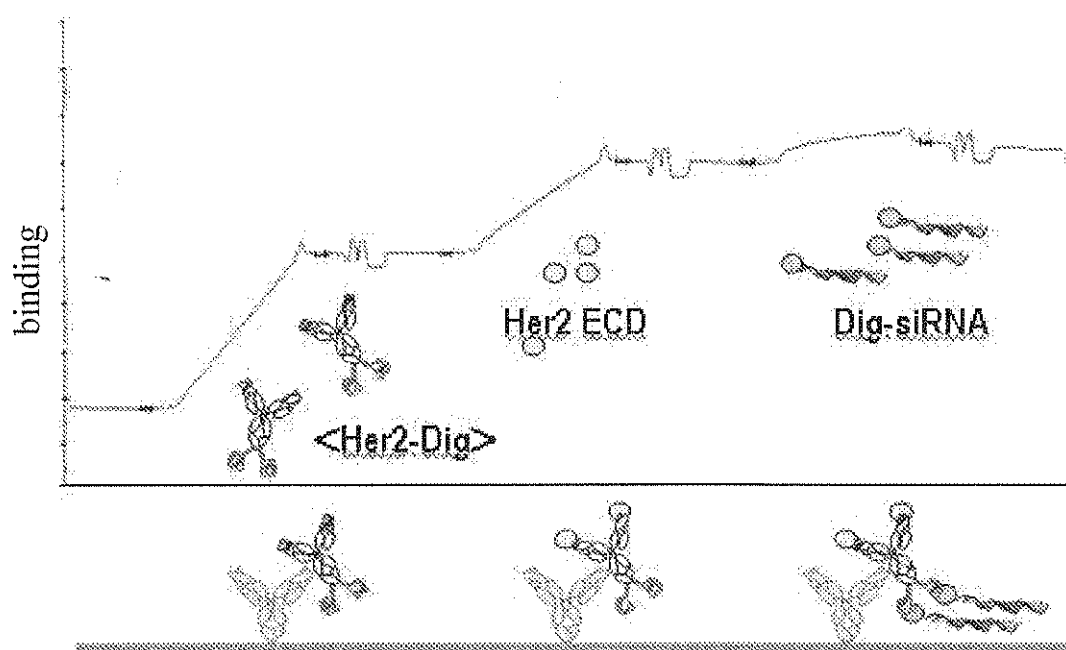


Fig. 33 a)

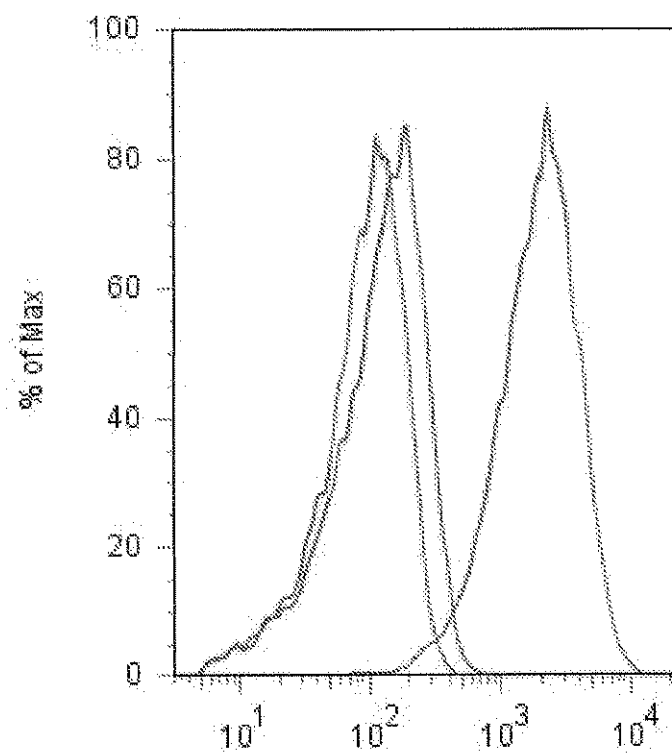


Fig. 33 b)

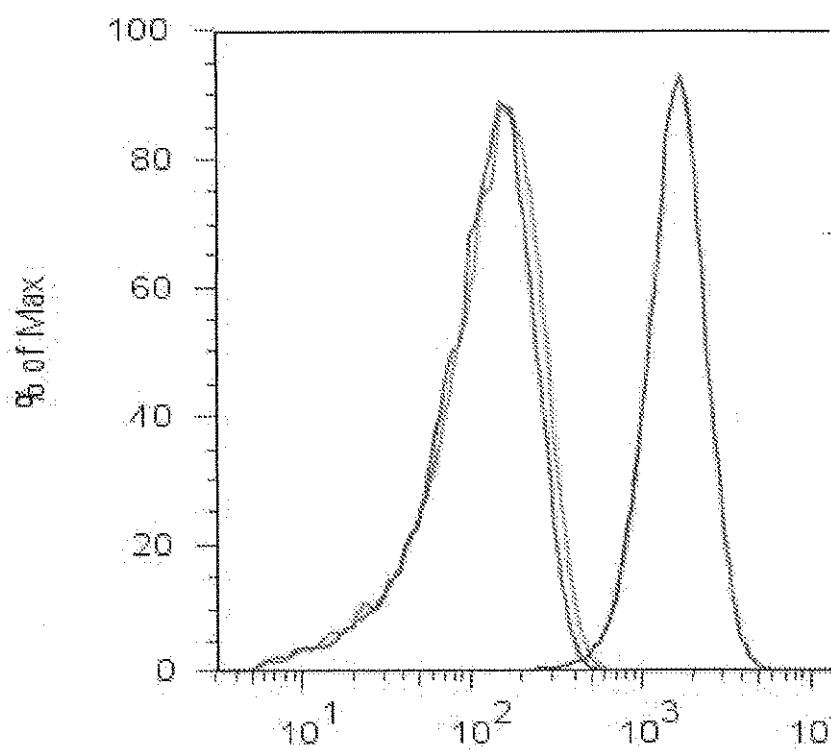


Fig. 34 a)

Fig. 34 b)

Fig. 34 c)

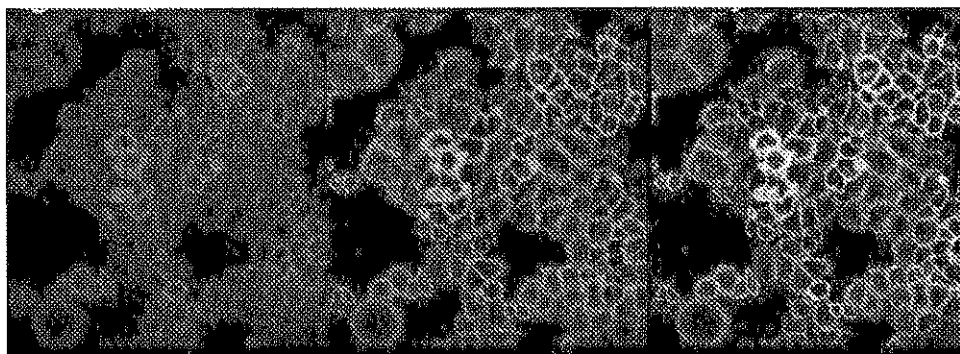


Fig. 34 d)

Fig 34 e)

Fig. 34 f)

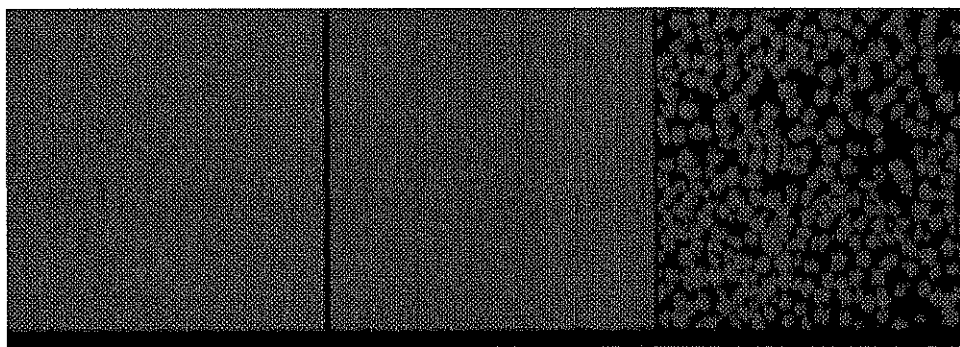


Fig. 34 g)

Fig 34 h)



Fig. 34 i)

Fig 34 j)



Fig. 35 a)

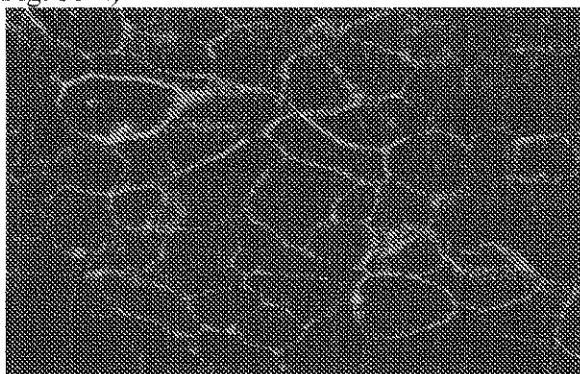


Fig. 35 b)

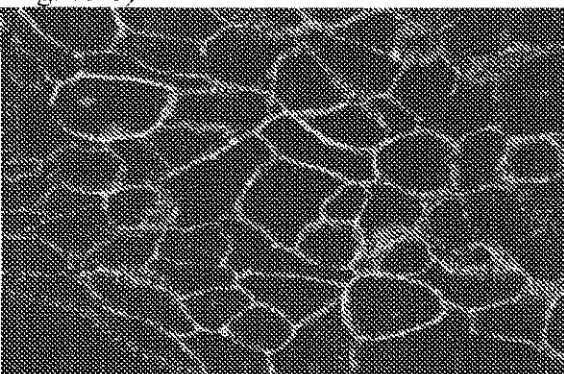


Fig. 35 c)



Fig 35 d)

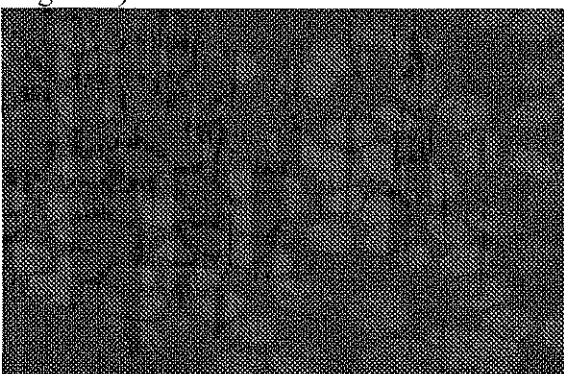


Fig. 35 e)

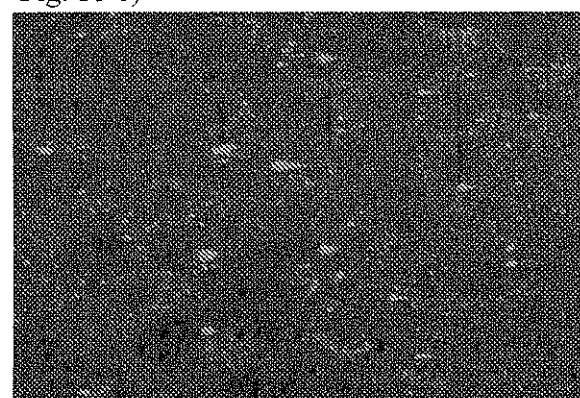


Fig 35 f)

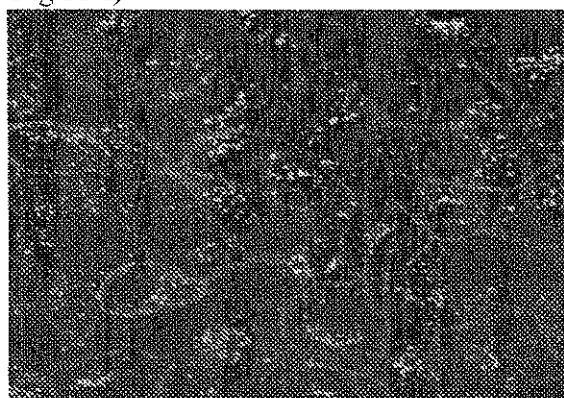


Fig. 35 g)

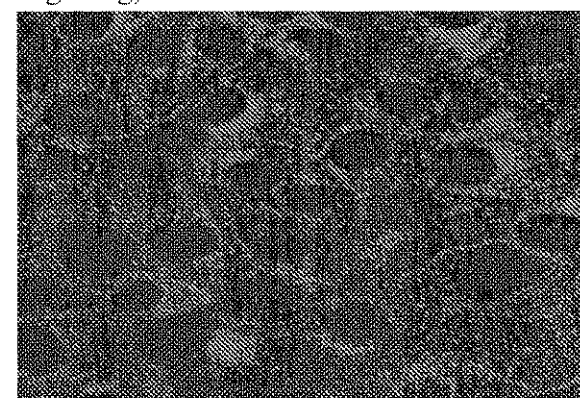


Fig 35 h)

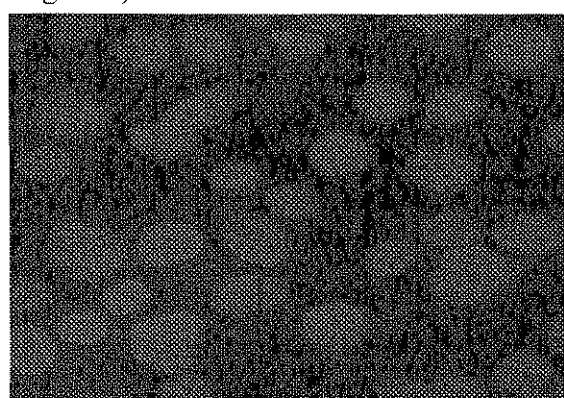


Fig. 36 a)

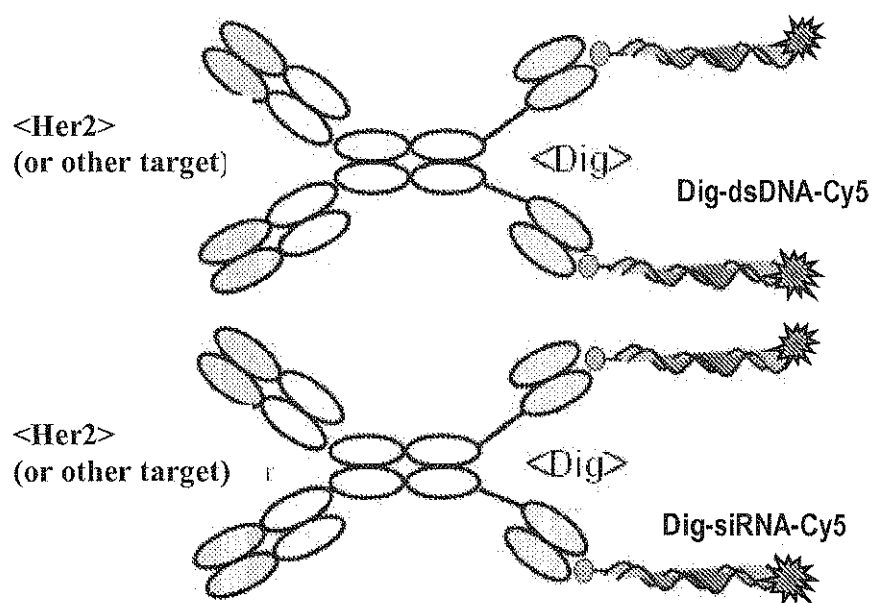


Fig. 36 b)

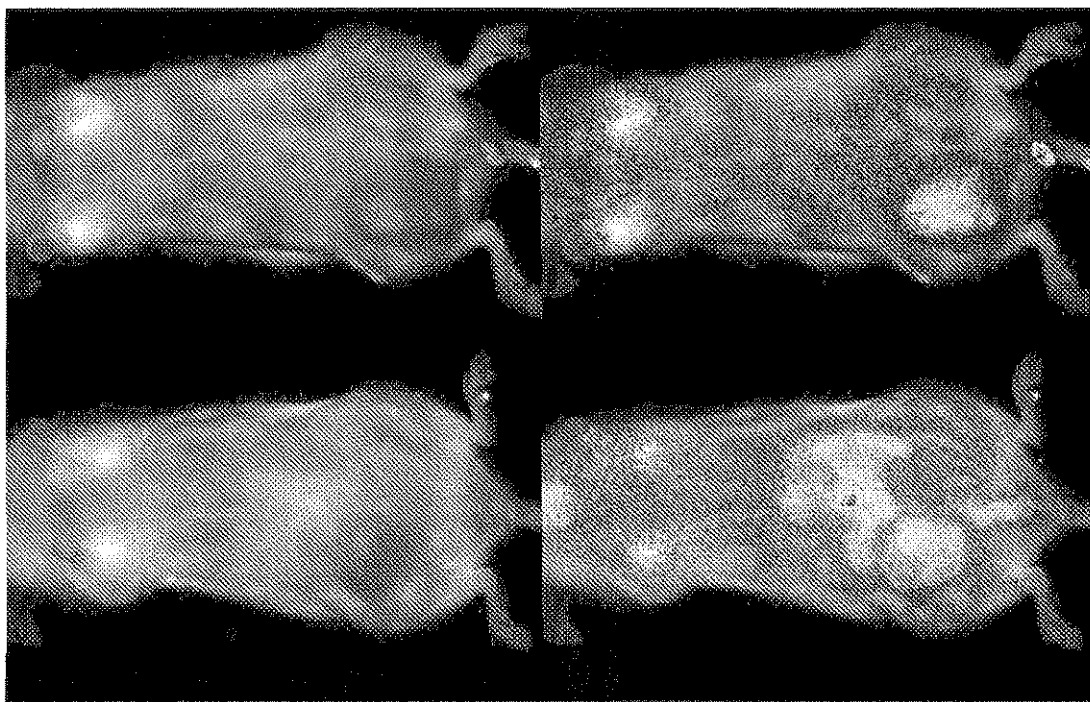


Fig. 37 a)

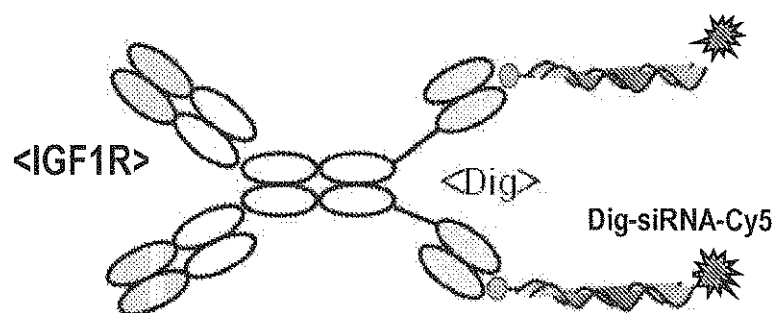


Fig. 37 b)



Fig. 38 a)

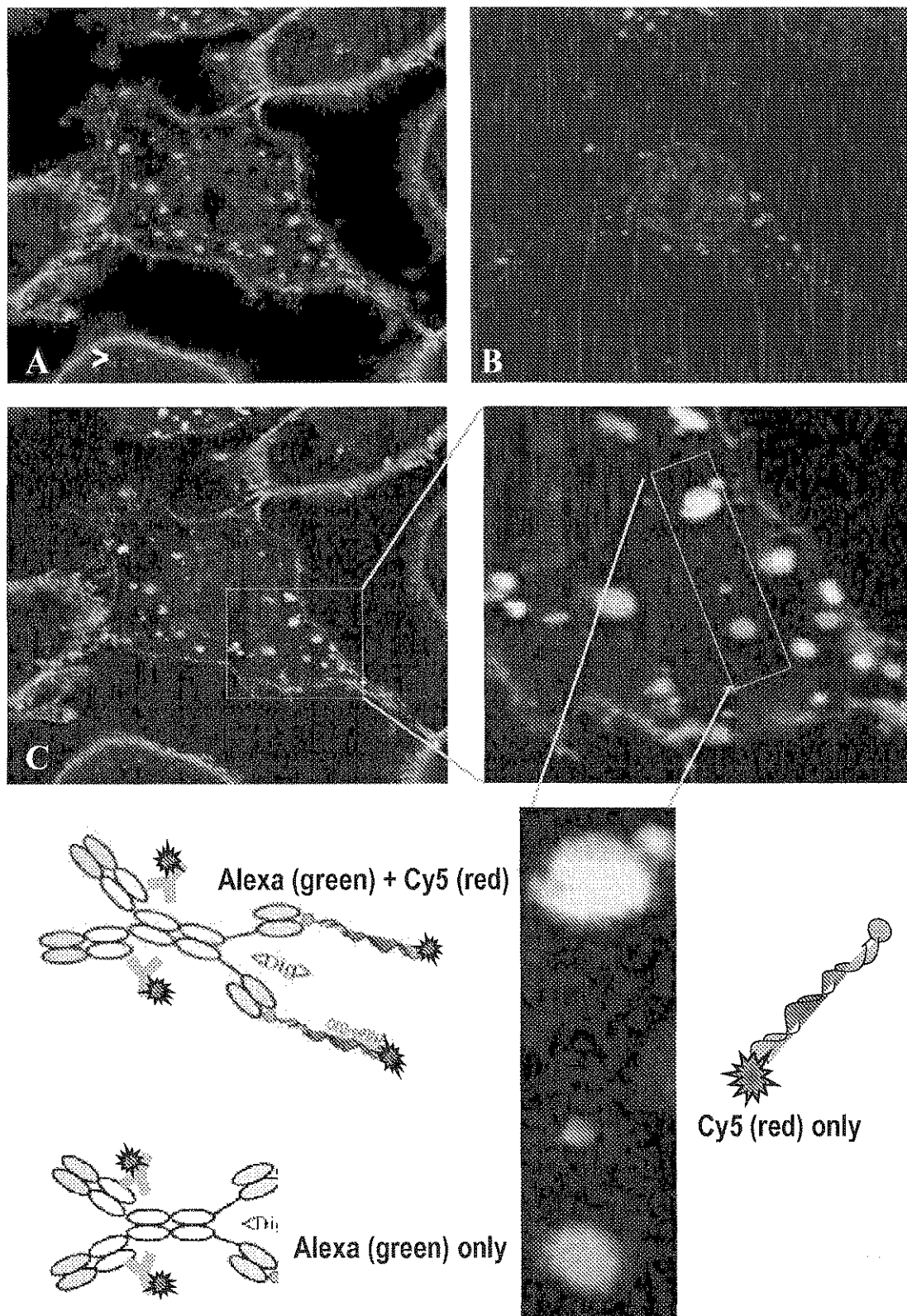


Fig. 38 b)

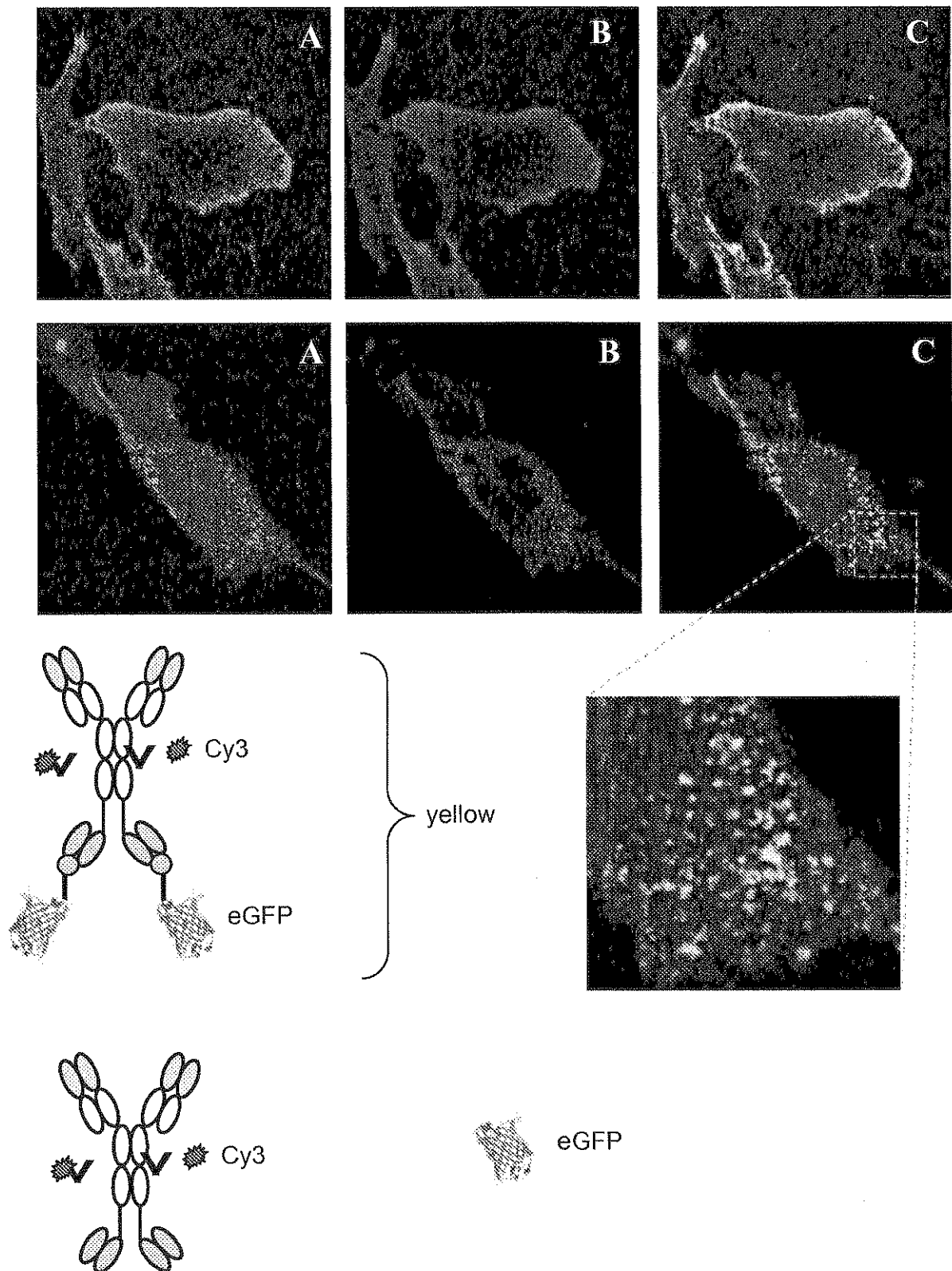


Fig. 38 c)

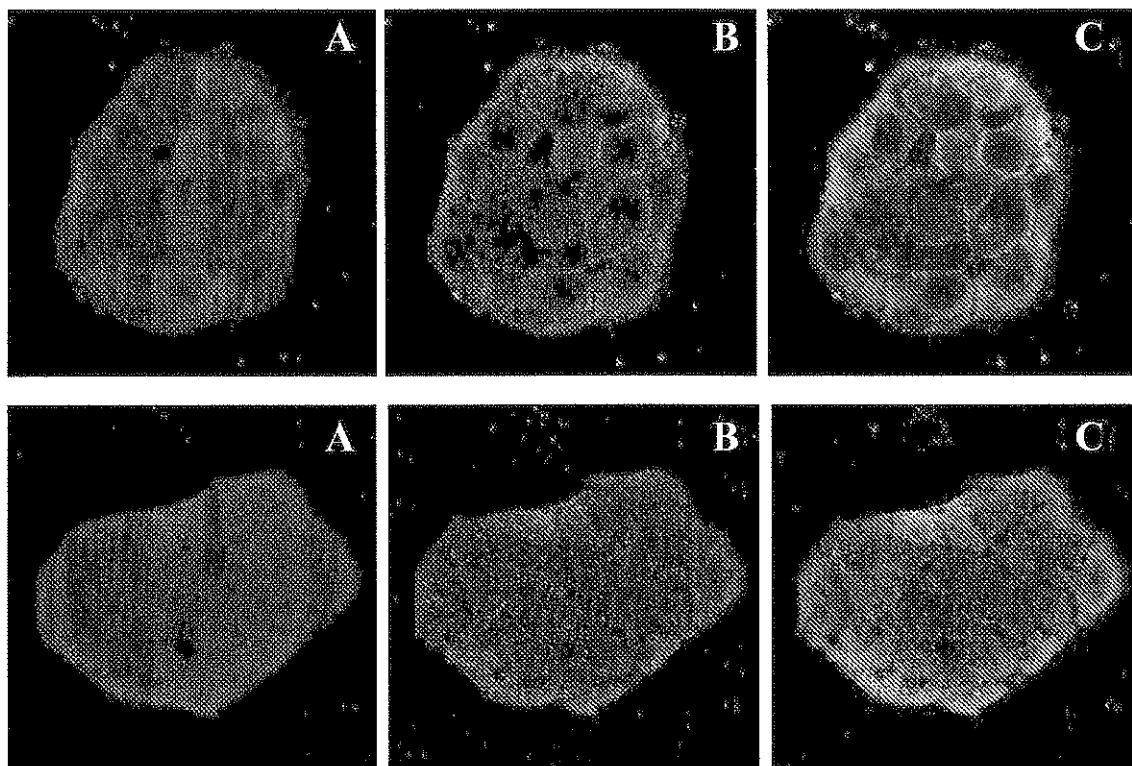


Fig. 38 d)

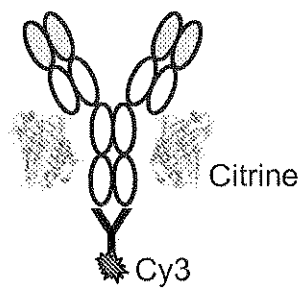
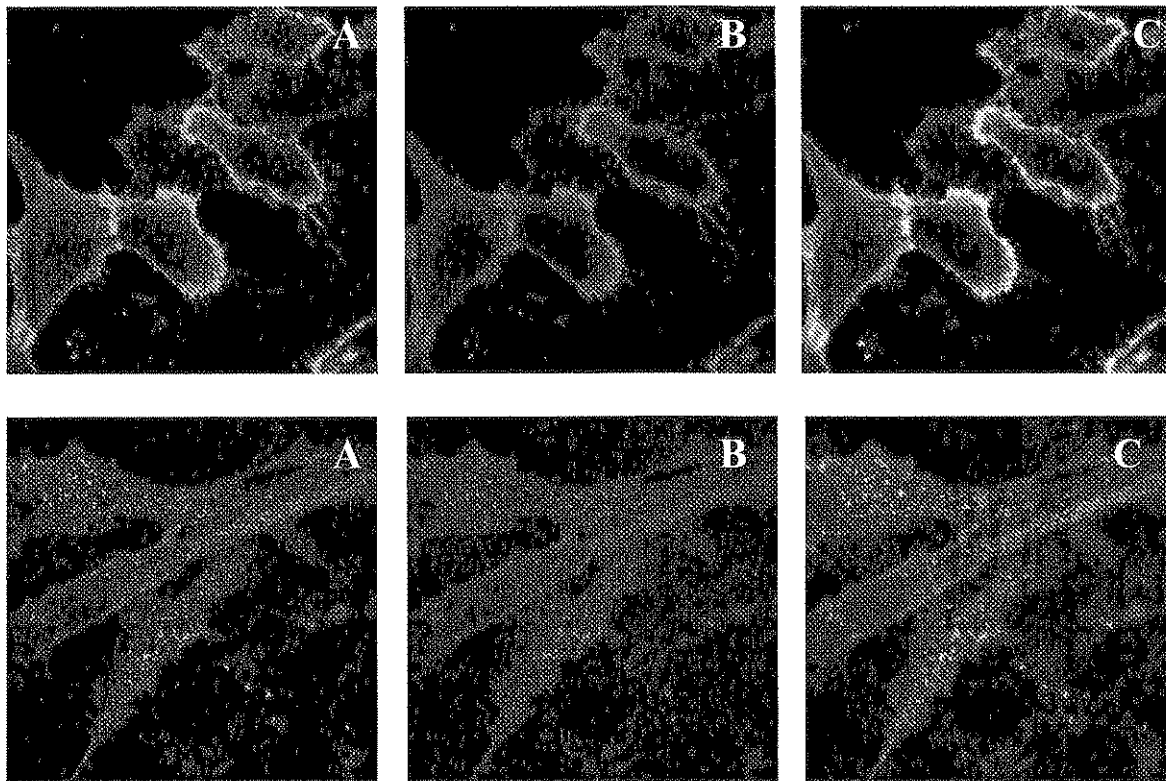


Fig. 39

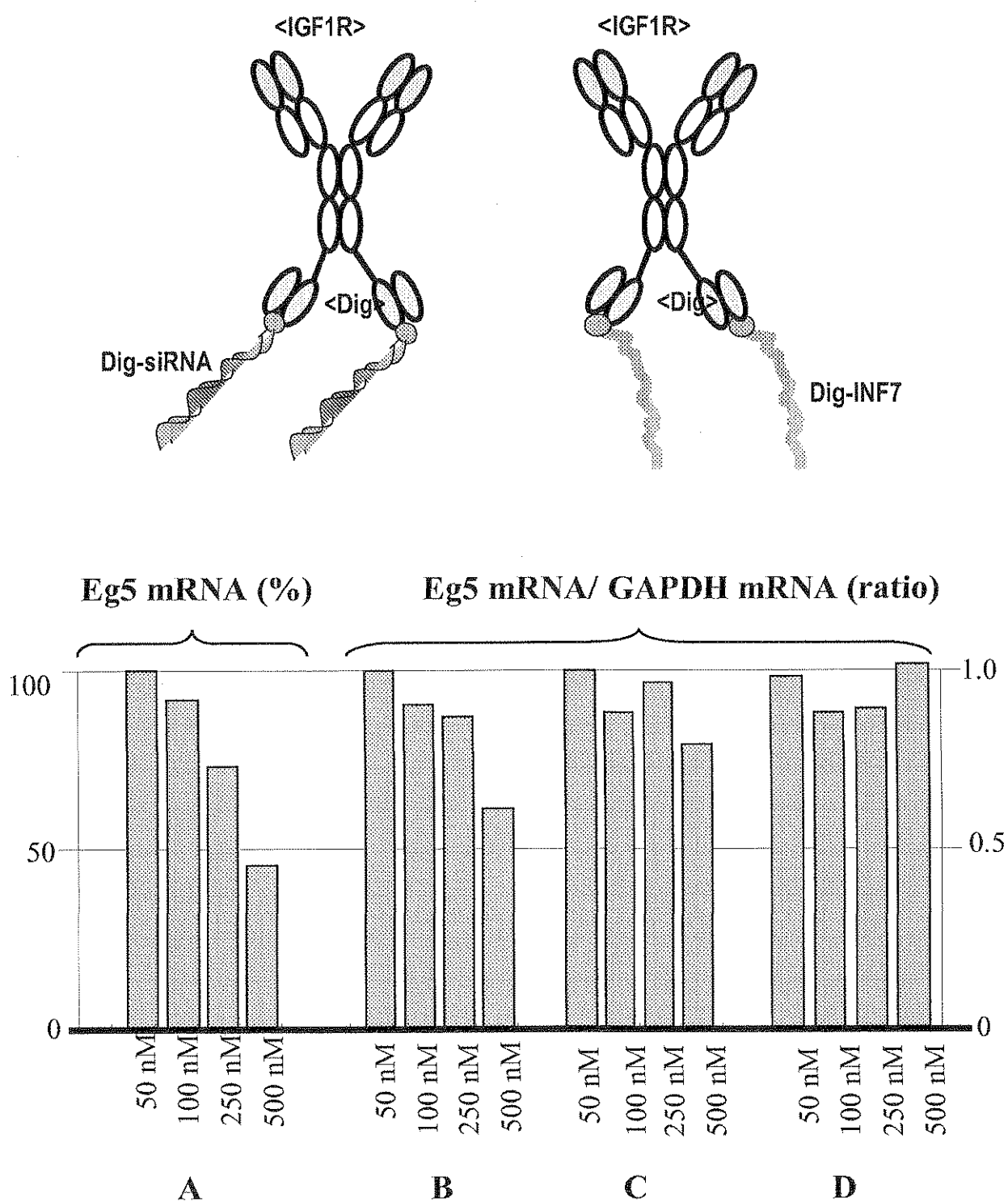


Fig. 40 a)

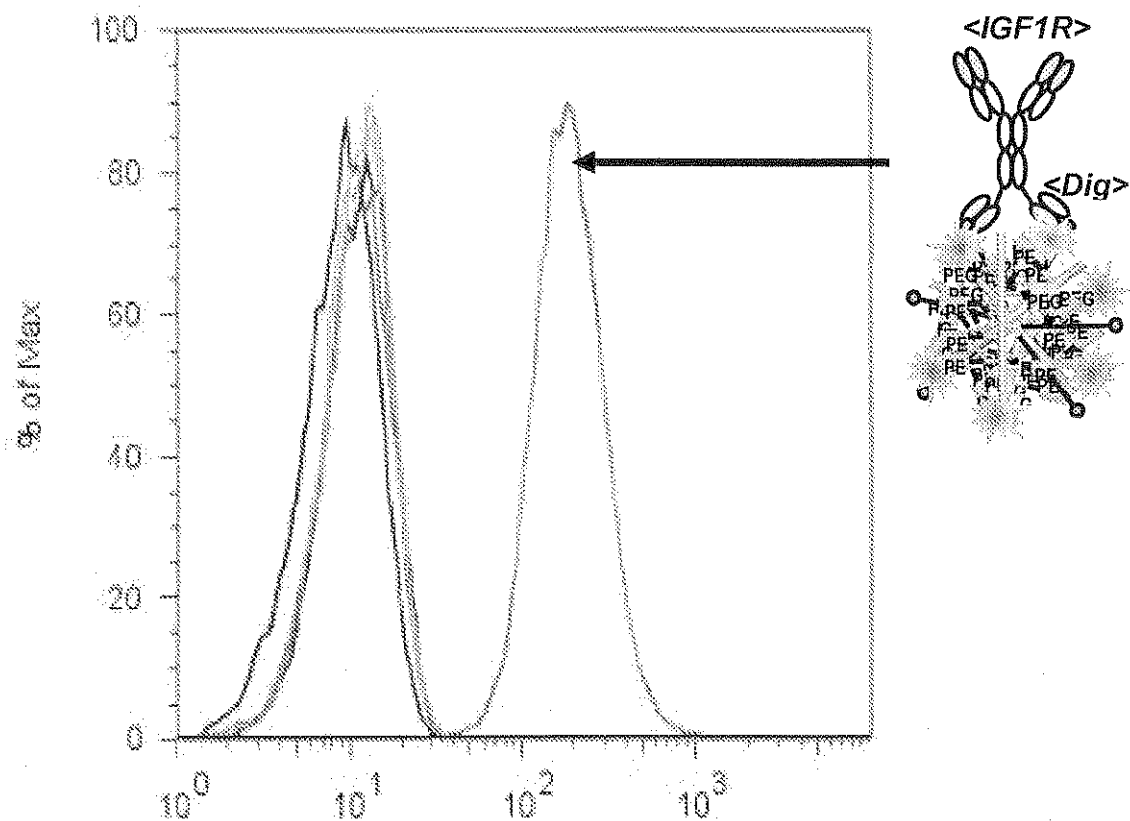


Fig. 40 b)

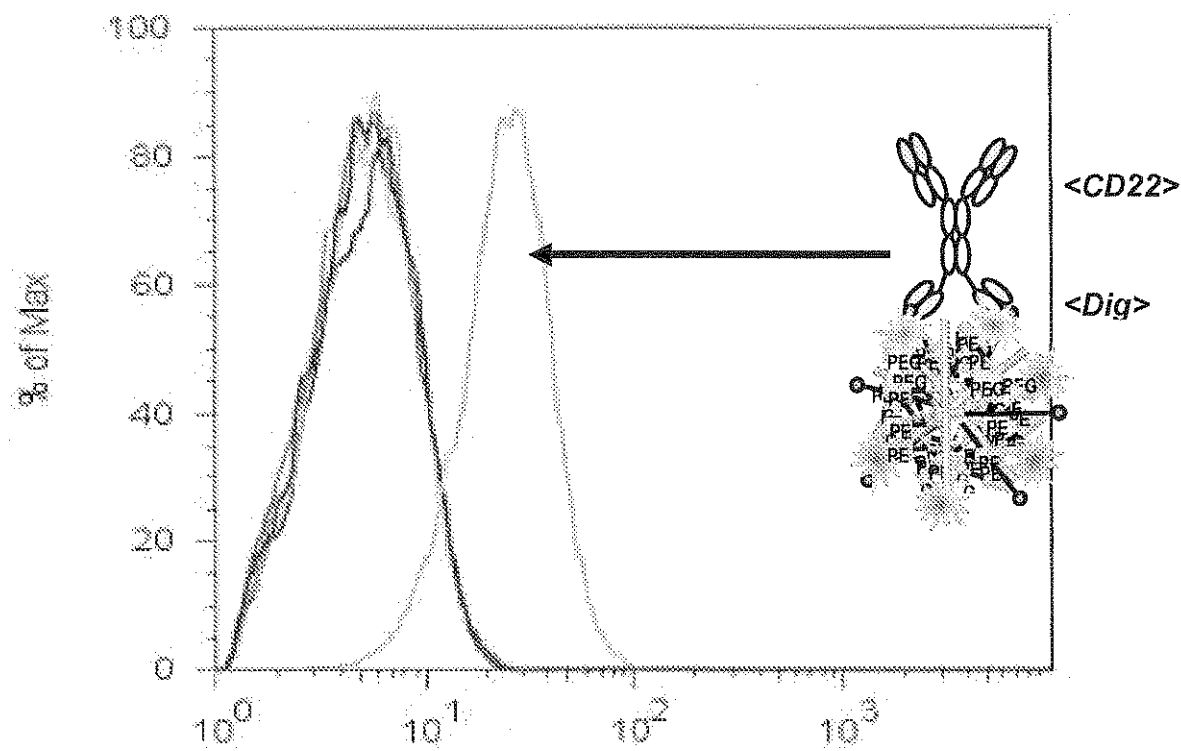


Fig. 41

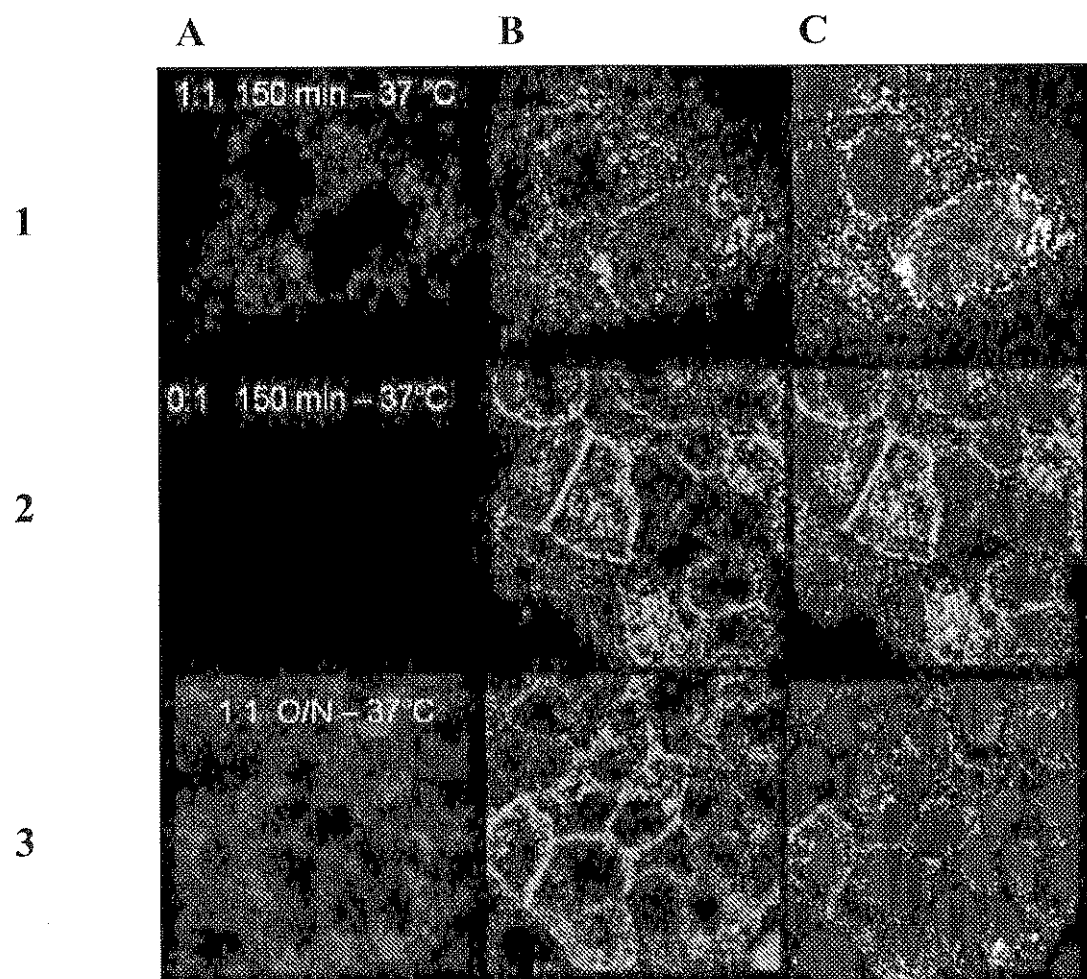


Fig. 42

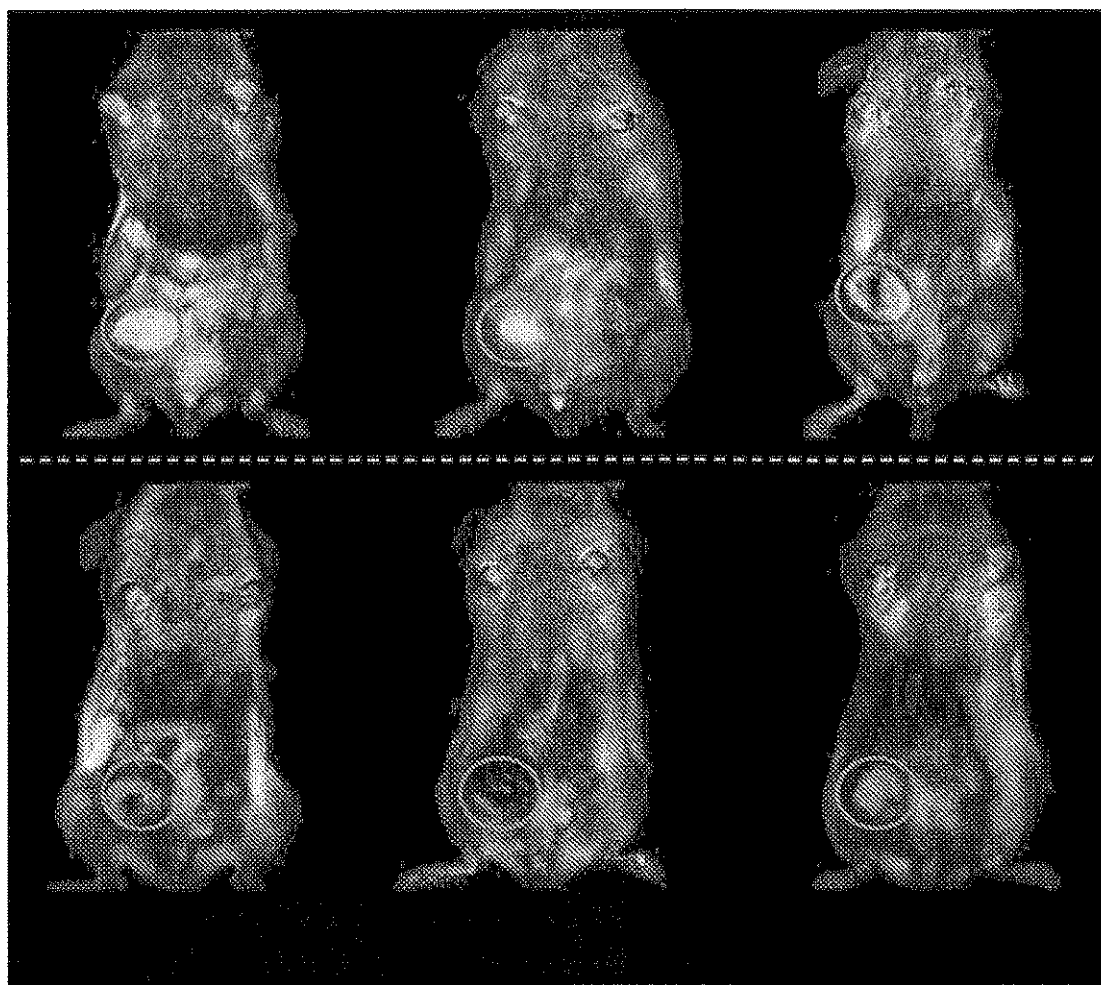


Fig. 43 a)

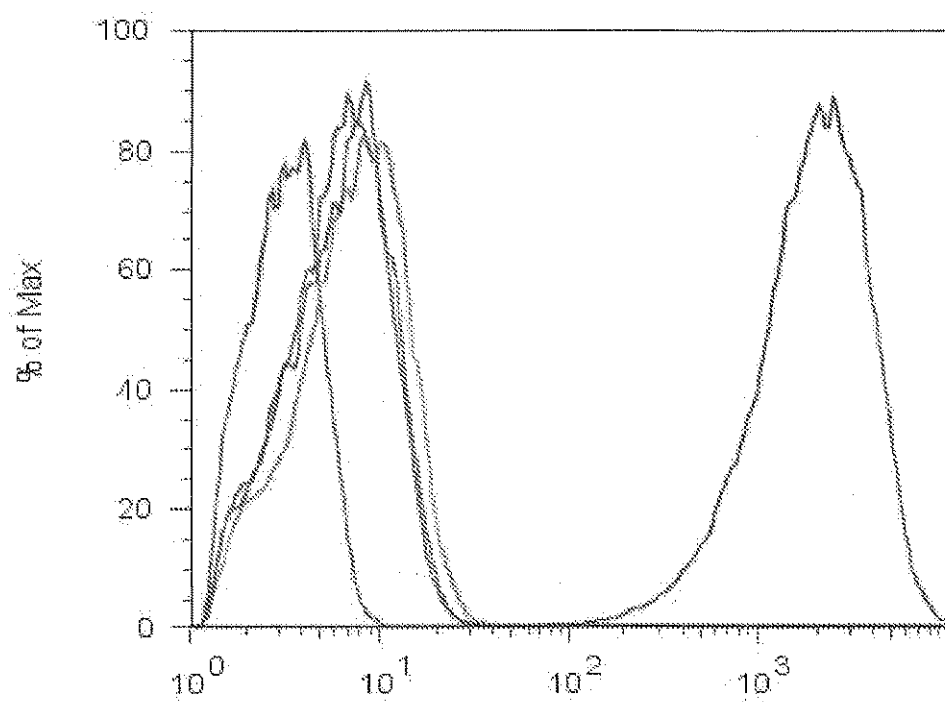


Fig. 43 b)

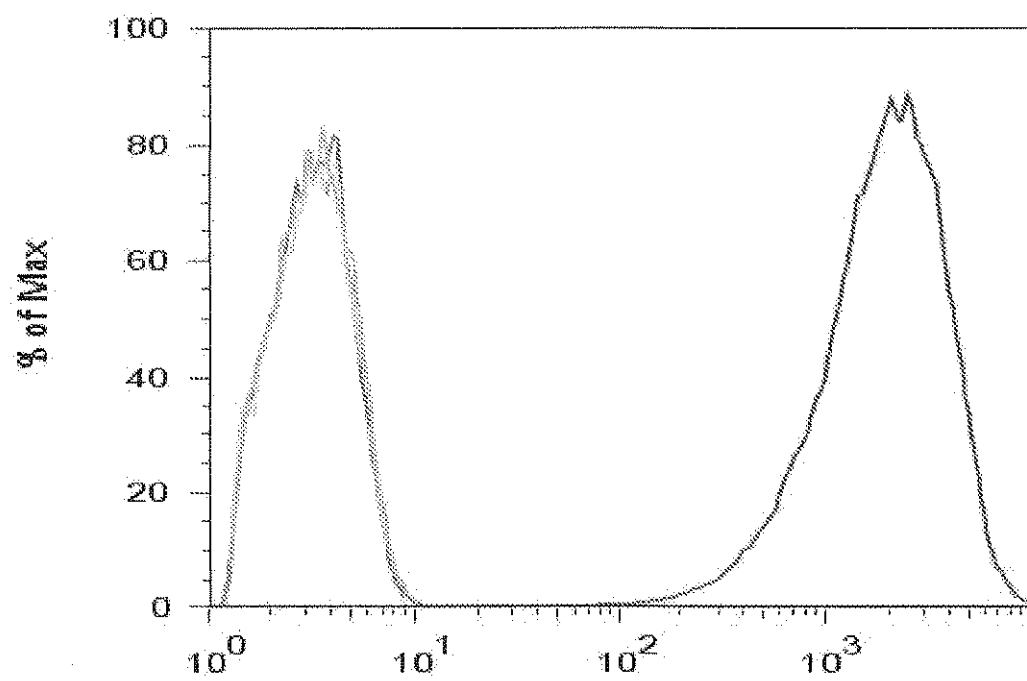


Fig. 44 a)

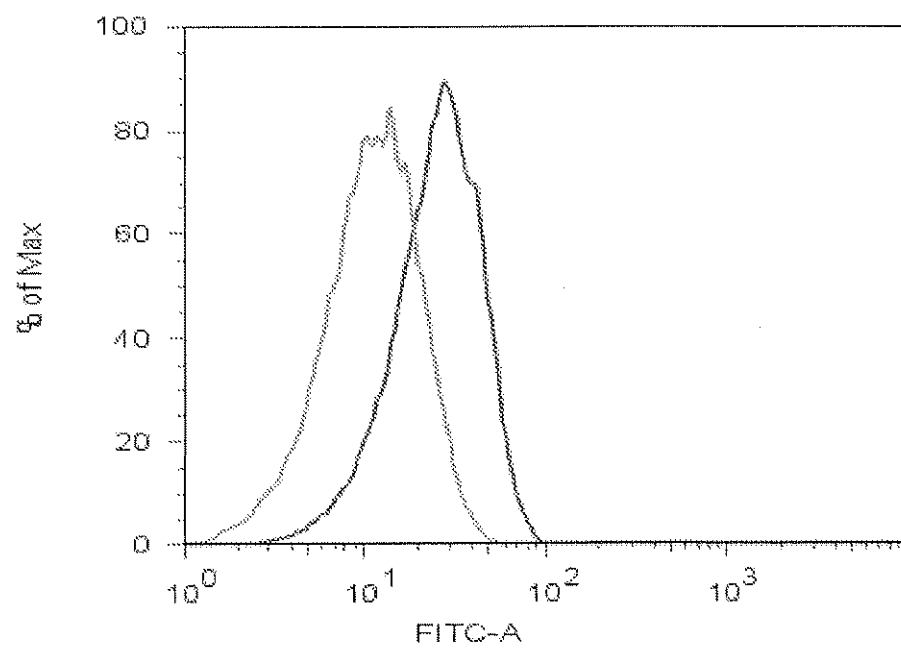


Fig. 44 b)

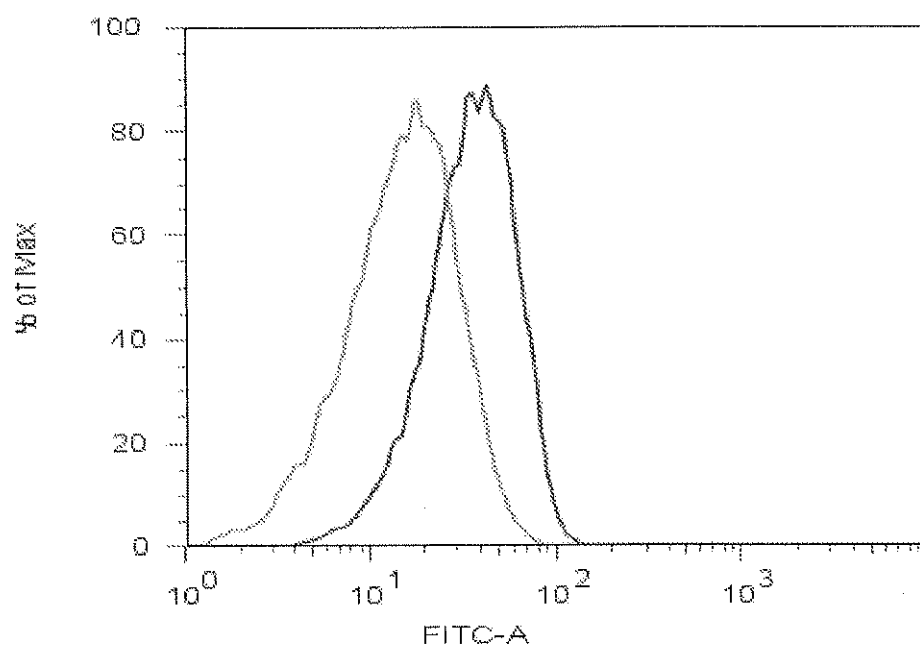


Fig 45 a)

	complex murine Fab DIG-Cy5
Data collection	
Beamline	X06SA (SLS)
Space group	P 42 21 2
Cell dimensions	
a, b, c (Å)	138.103 138.103 123.696
α , β , γ (°)	90.00 90.00 90.00
Wavelength	0.9795
Resolution (Å)	50.0-2.80
Rsym	10.1 (32.1)
I / s	26.38 (9.11)
Completeness (%)	98.1 (95.0)
Redundancy	14.7
Refinement	
Resolution (Å)	46.040 – 2.798
No. reflections (test)	29999 (1534)
Rwork / Rfree	20.340 / 23.12
No. atoms	
Protein	6660
Ligand	2x28
Water	348
B-factor (Å²)	
Protein	23.65
Ligand	16.00
Water	32.29
R.m.s deviations	
Bonds (Å)	0.006
Angles (°)	1.292
Ramachandran	
Core (%)	87.4
Disallowed (%)	0.4

Fig 45 b)

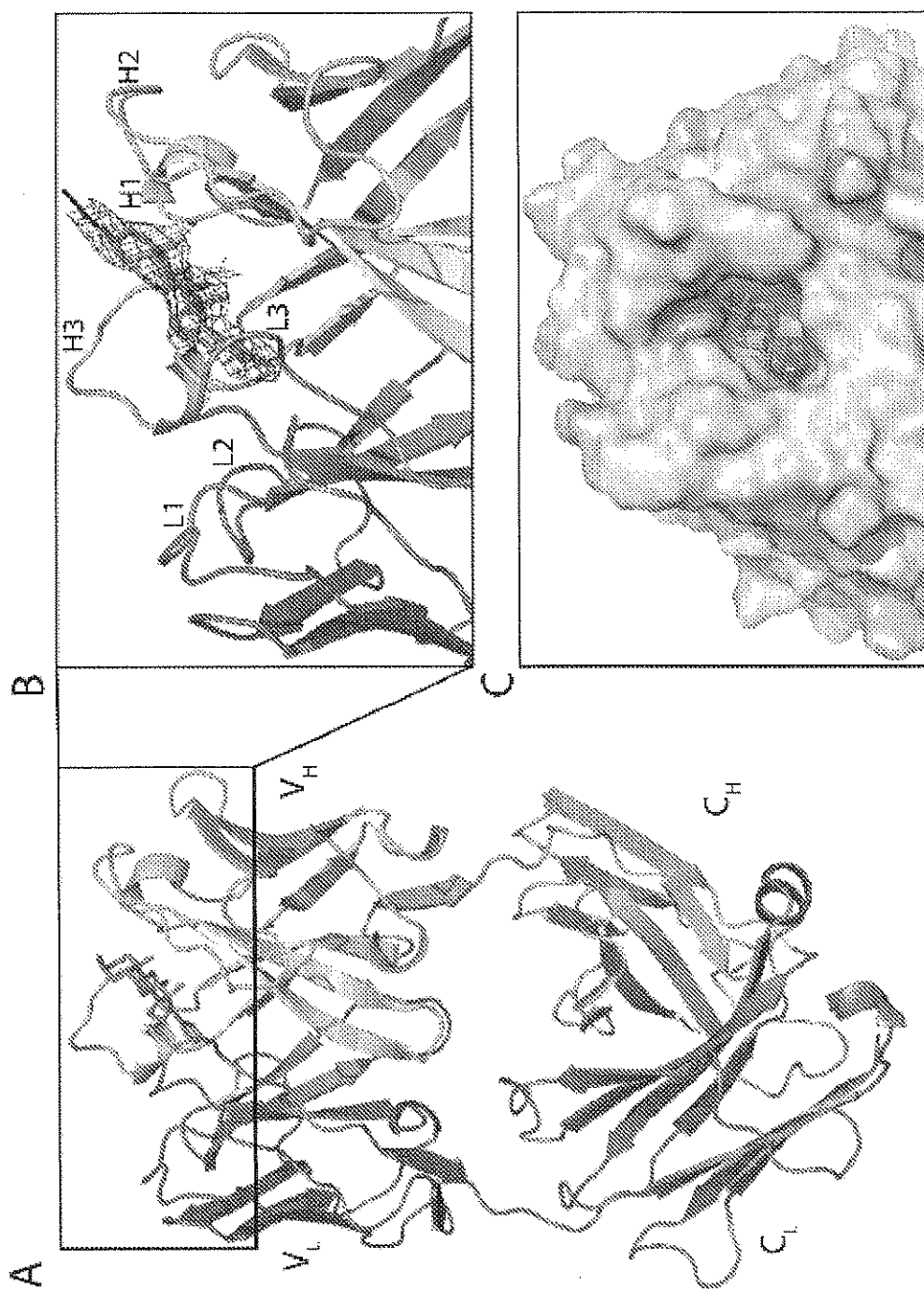


Fig. 45 c)

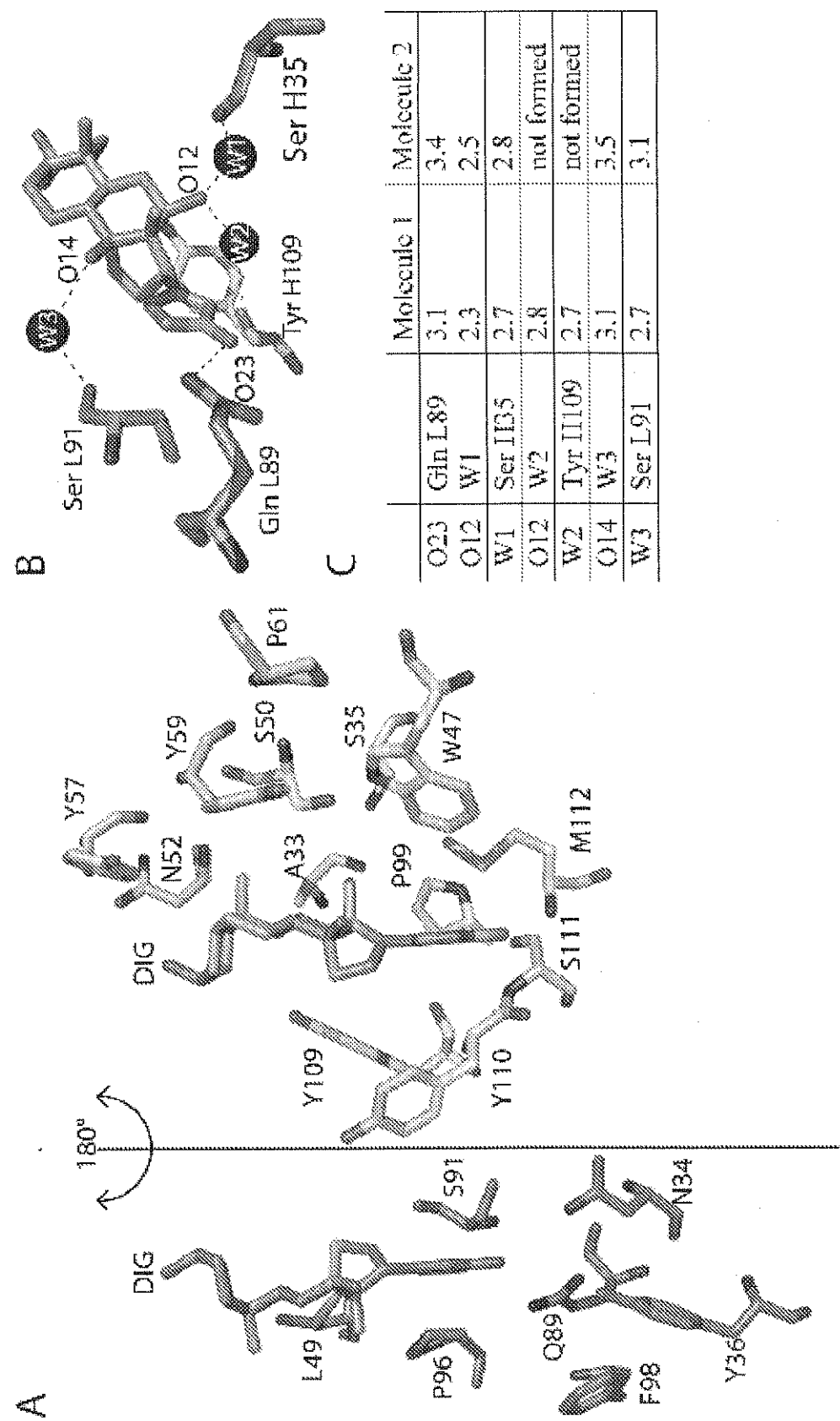


Fig. 46 a)

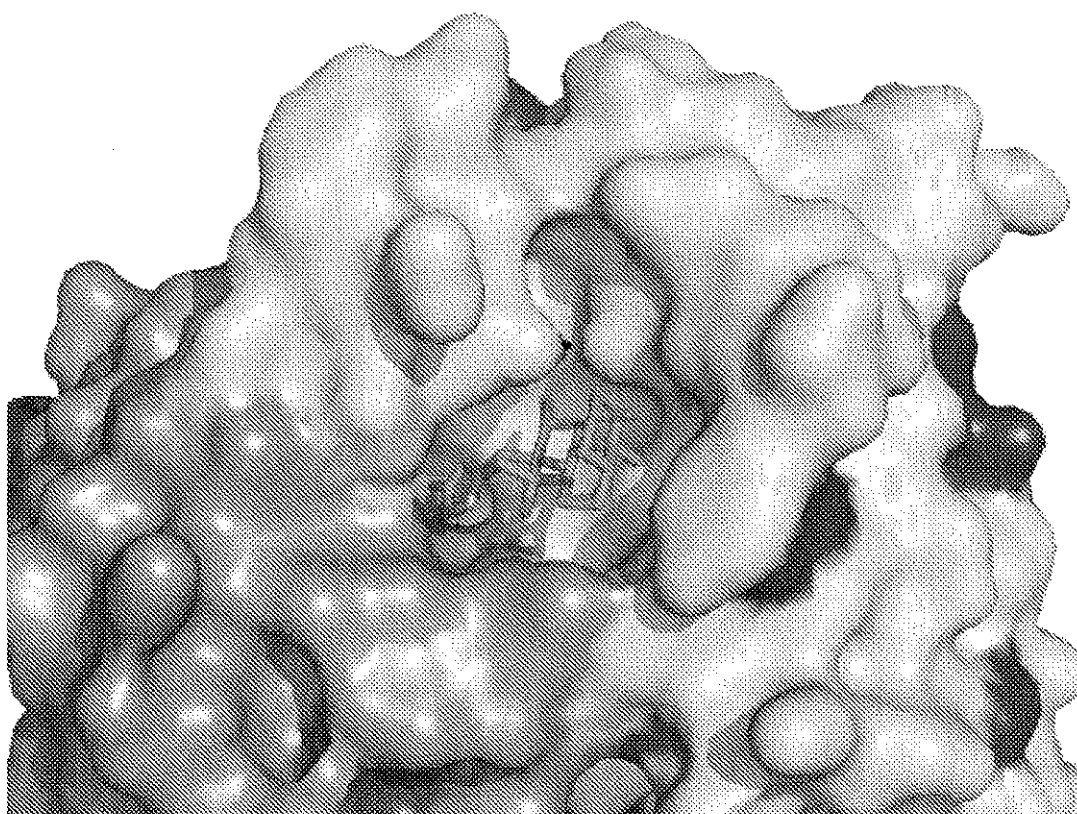


Fig. 46 b)

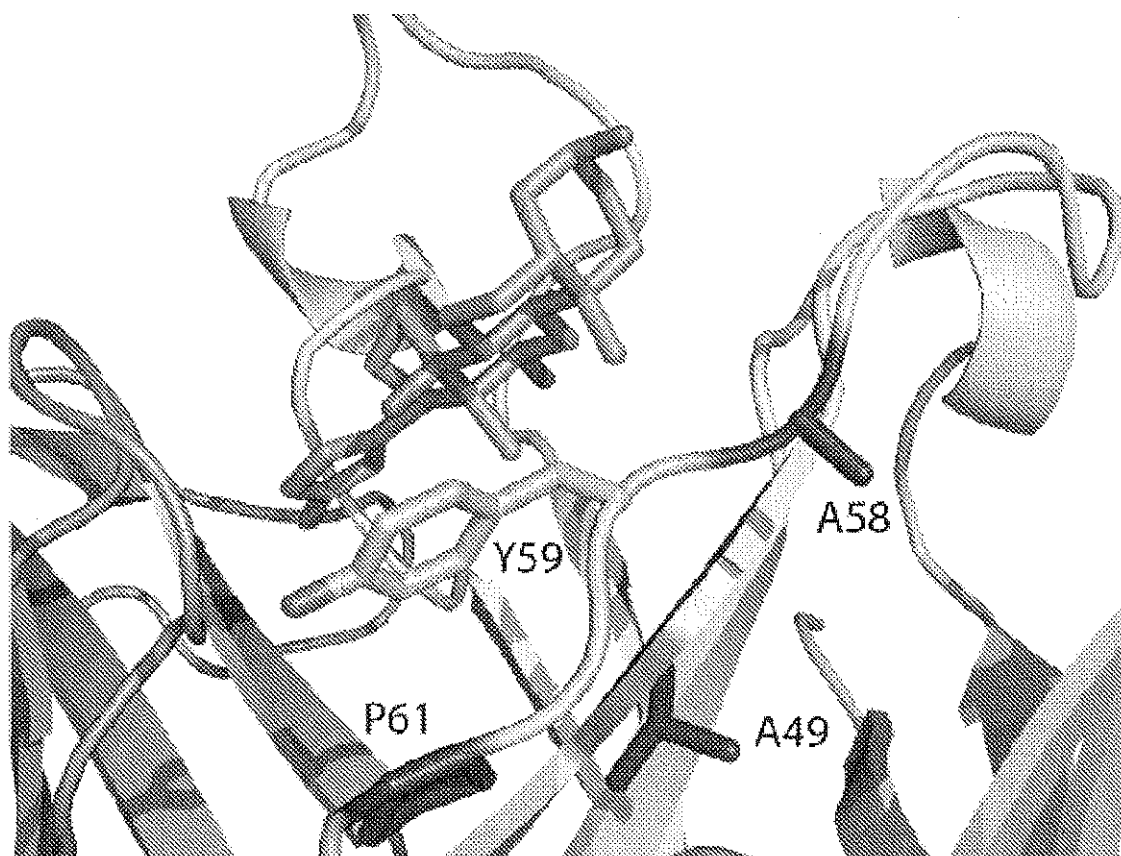


Fig. 46 c)

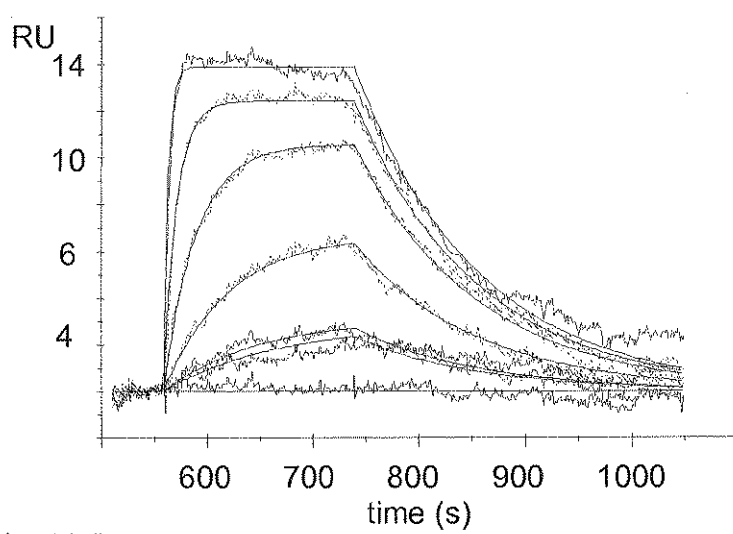


Fig. 46 d)

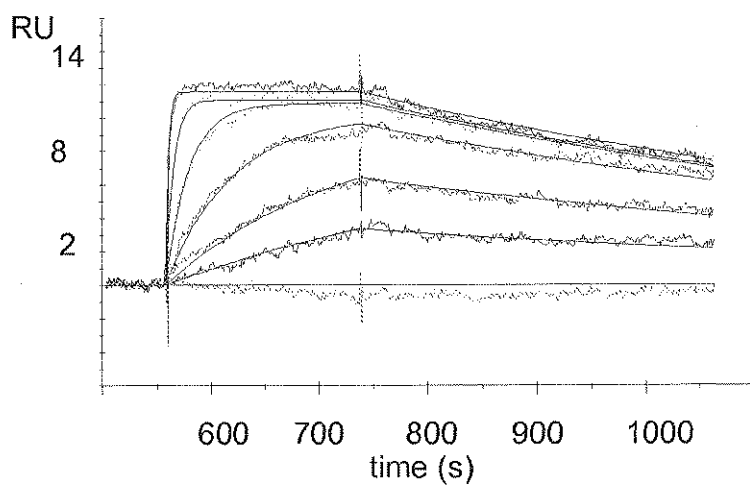


Fig. 47 a)

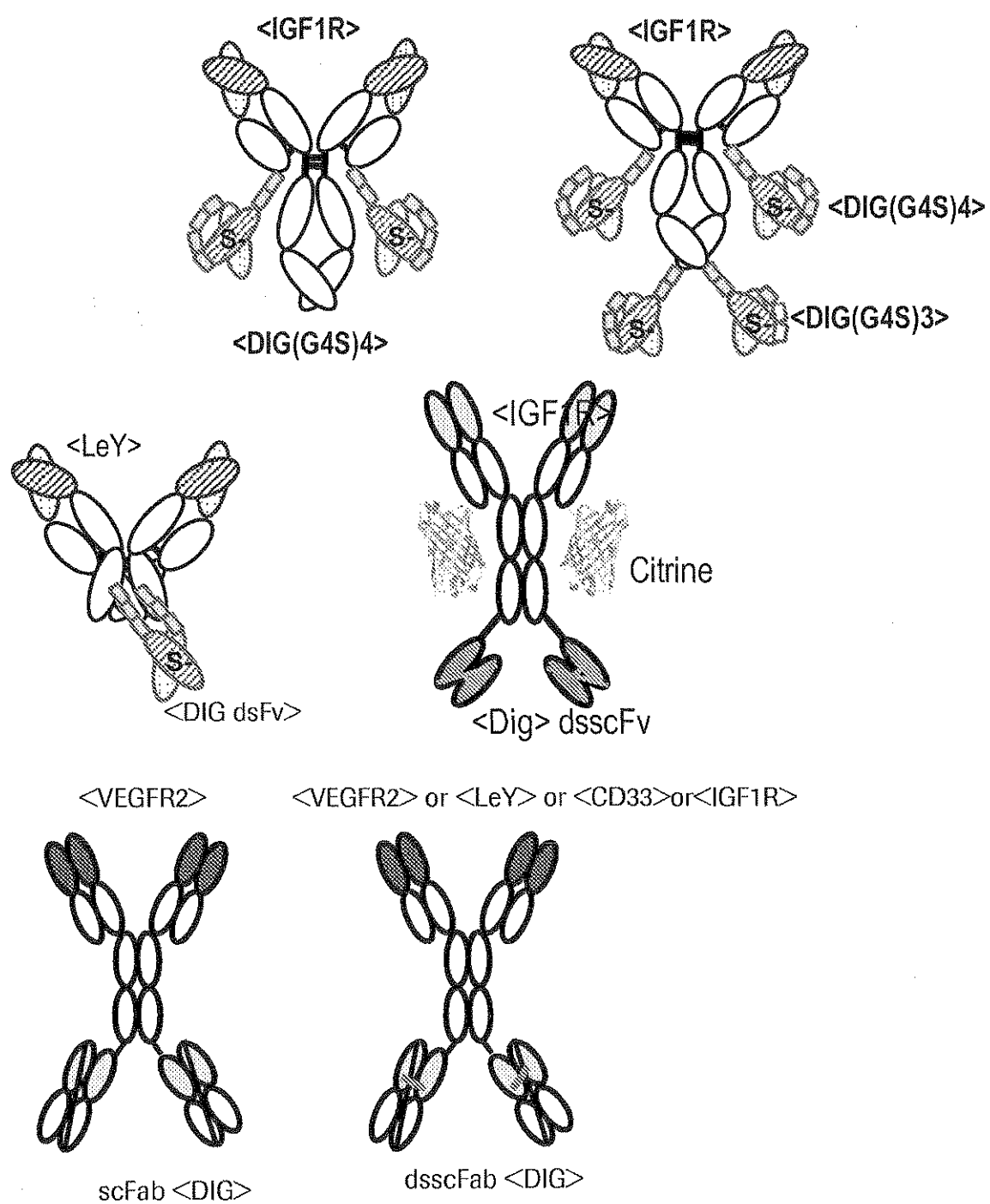


Fig 47 b)

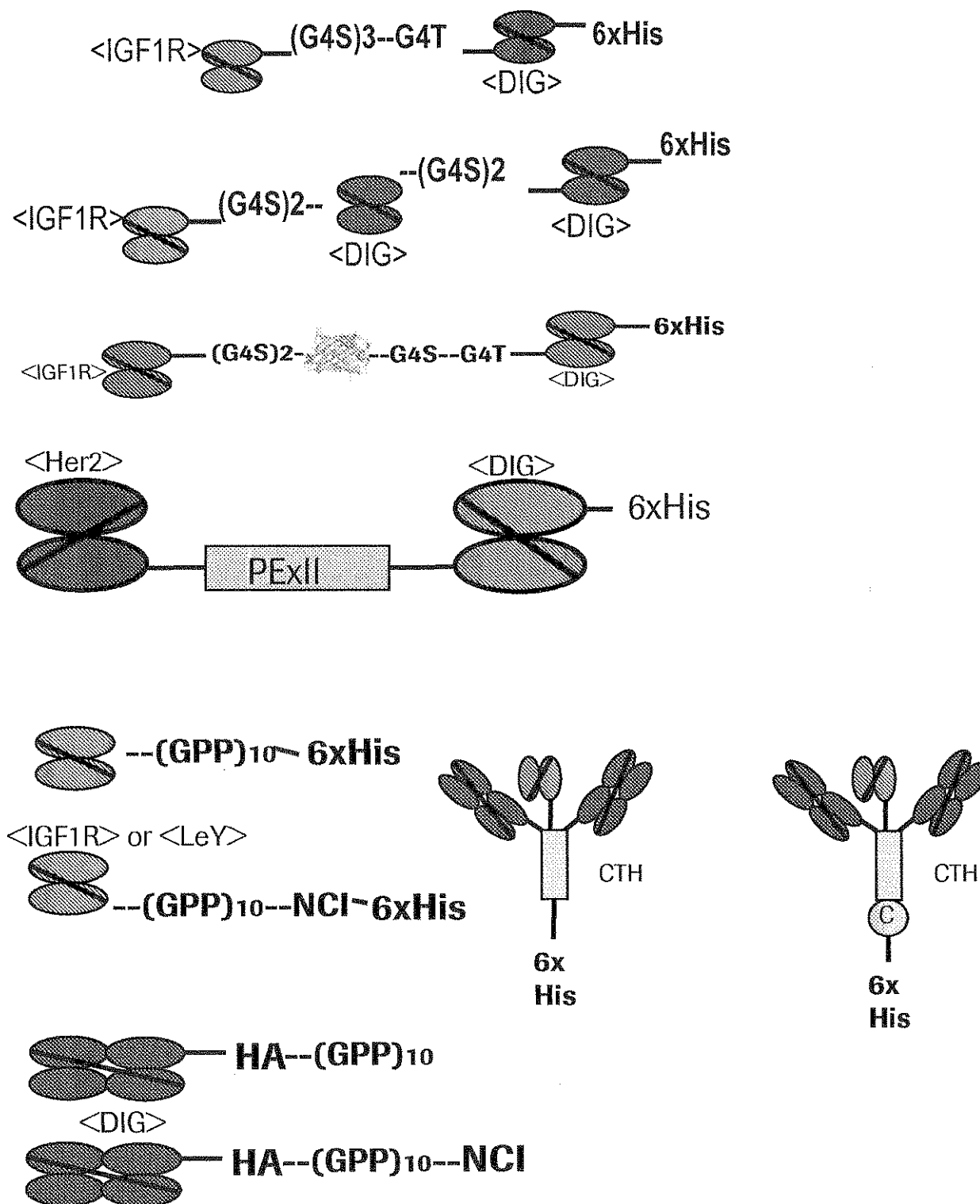


Fig. 47 c)

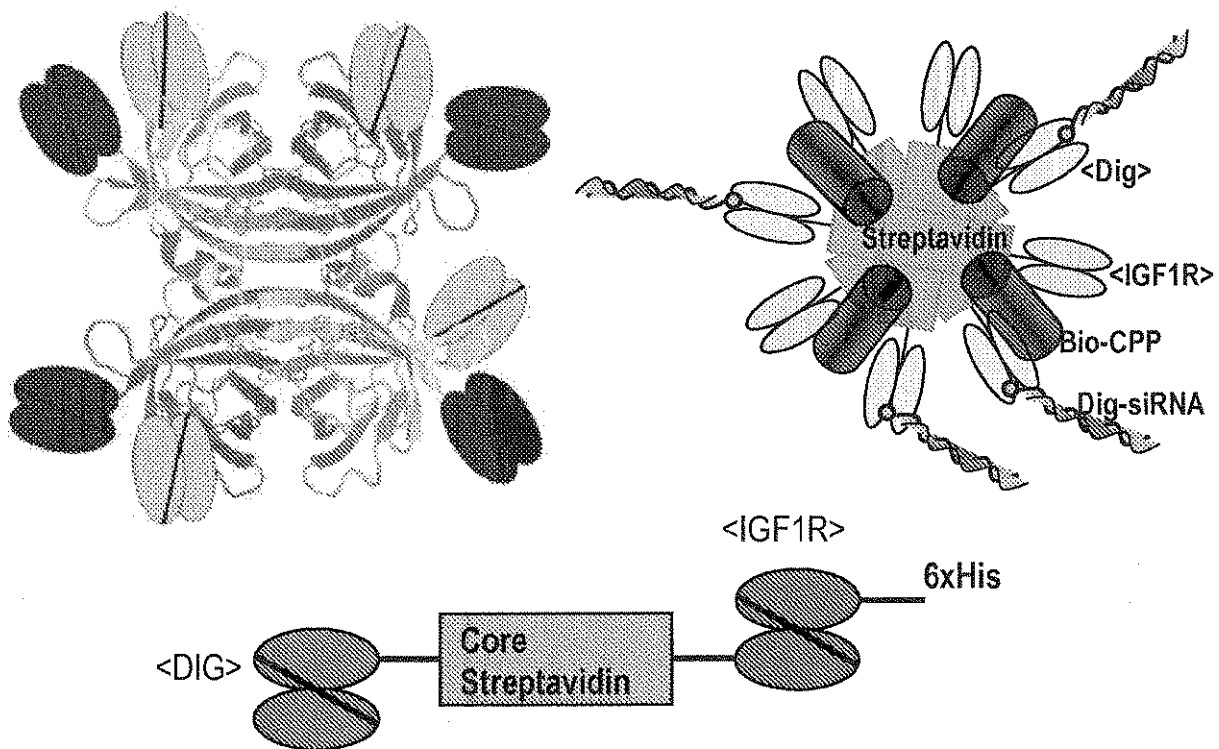


Fig. 47 d)

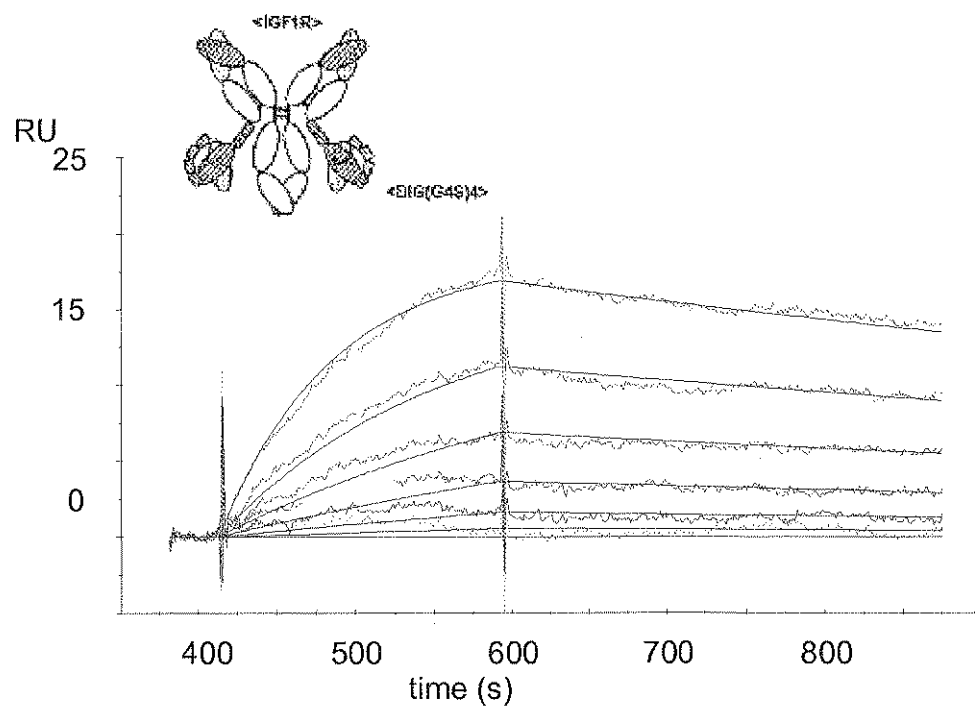


Fig. 47 e)

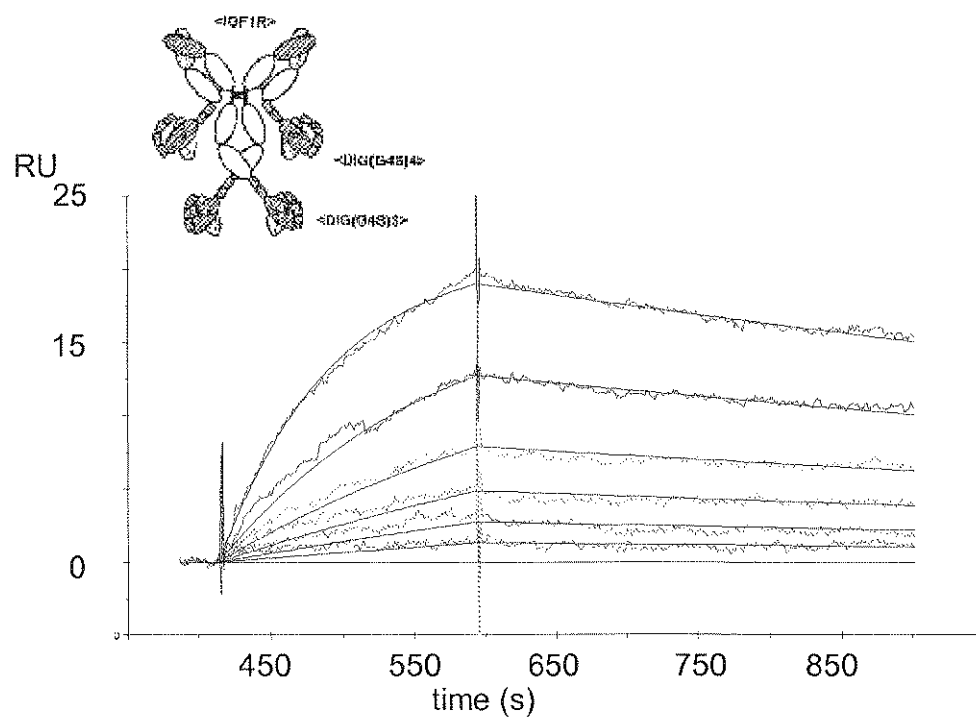


Fig. 47 f)

Affinity to siRNA-DIG	kd (1/s)	KD (nM)
<IGF1R-DIG> Dig on CH3	9,81E-03	20
<IGF1R-DIG> Dig on Ckappa	9,71E-03	23
<IGF1R-DIG-DIG> hexavalent	9,17E-03	24
Affinity to IGF-1R	kd (1/s)	KD (nM)
<IGF1R-DIG> Dig on CH3	1,09E-03	5
<IGF1R-DIG> Dig on Ckappa	7,99E-04	3
<IGF1R-DIG-DIG> hexavalent	7,64E-04	3

Affinity for DIG-siRNA		kd (1/s)	KD (nM)
<IGF1R-DIG> 2321	5,03E+0	1,17E-02	23
<IGF1R-scFab-DIG> 2321	8,32E+0	1,12E-02	14
<IGF1R-dsFab-DIG> 2321	5,79E+0	7,82E-02	14

Affinity for DIG-siRNA

Capture	Antibody	ka (1/Ms)	kd (1/s)	KD (M)
human VEGFR2-Fc	<VEGFR2(D1F7)-DIG>_001	3.44E+06	6.54E-03	1.90E-09
	<VEGFR2(D1F7)-scFab-DIG>	4.98E+06	6.70E-03	1.35E-09
	<VEGFR2(D1F7)-dsFab-DIG>	2.49E+06	9.68E-03	3.89E-09
mouse VEGFR2-Fc	<VEGFR2(D1F7)-DIG>_001	3.89E+06	6.56E-03	1.69E-09
	<VEGFR2(D1F7)-scFab-DIG>	3.21E+06	8.92E-03	2.78E-09
	<VEGFR2(D1F7)-dsFab-DIG>	2.01E+06	1.14E-02	5.65E-09

Fig. 47 g)

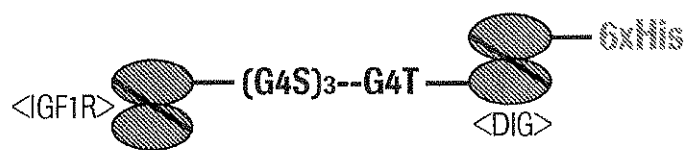


Fig. 47 h)

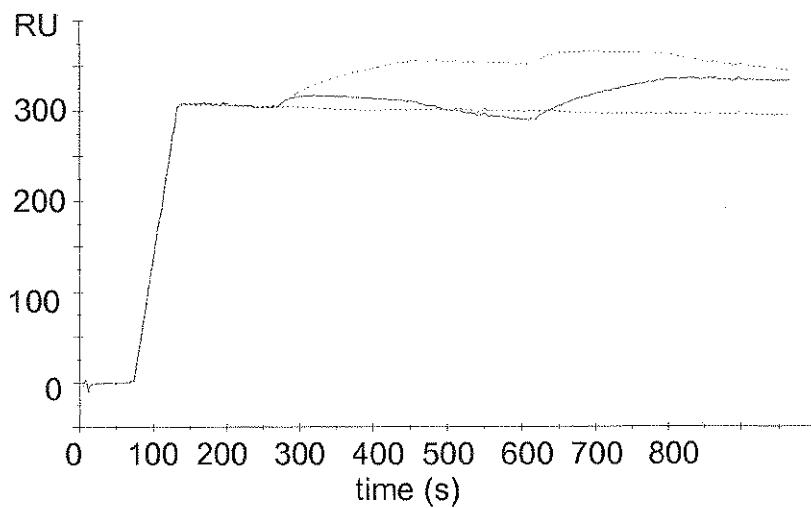


Fig. 47 i)

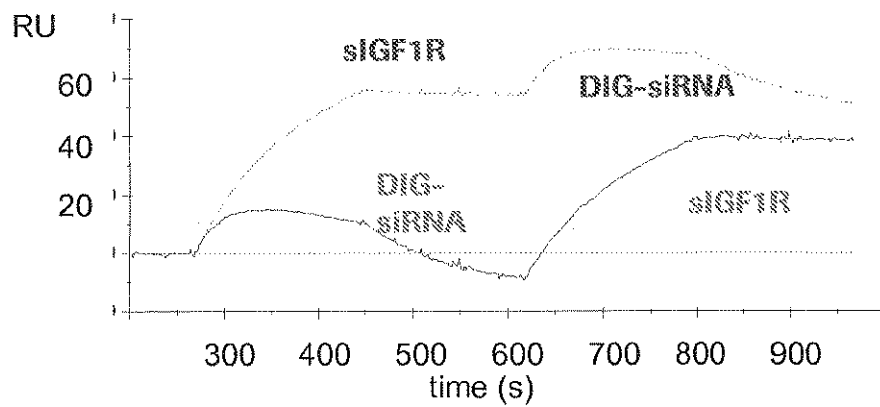


Fig. 47 j)

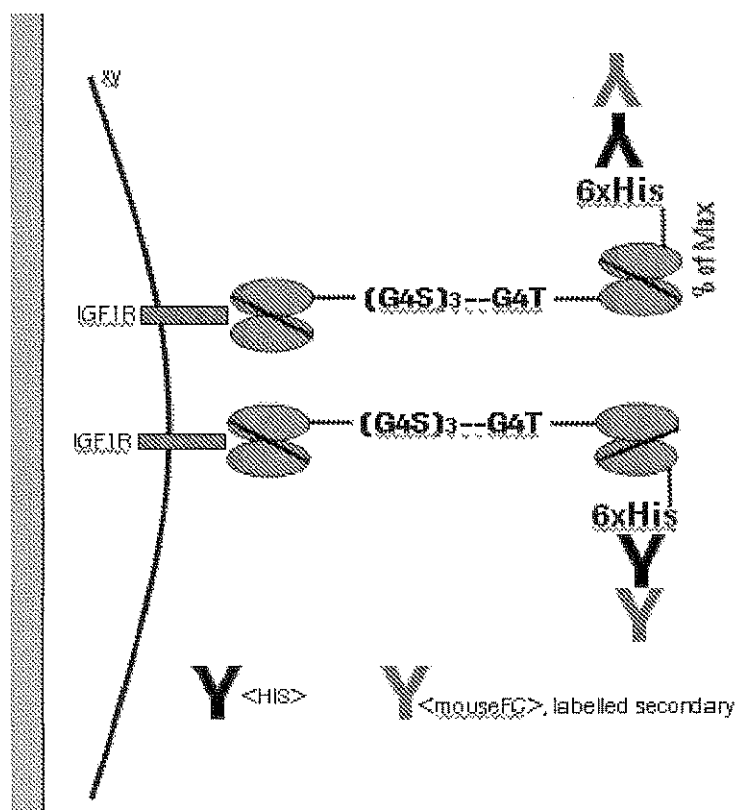
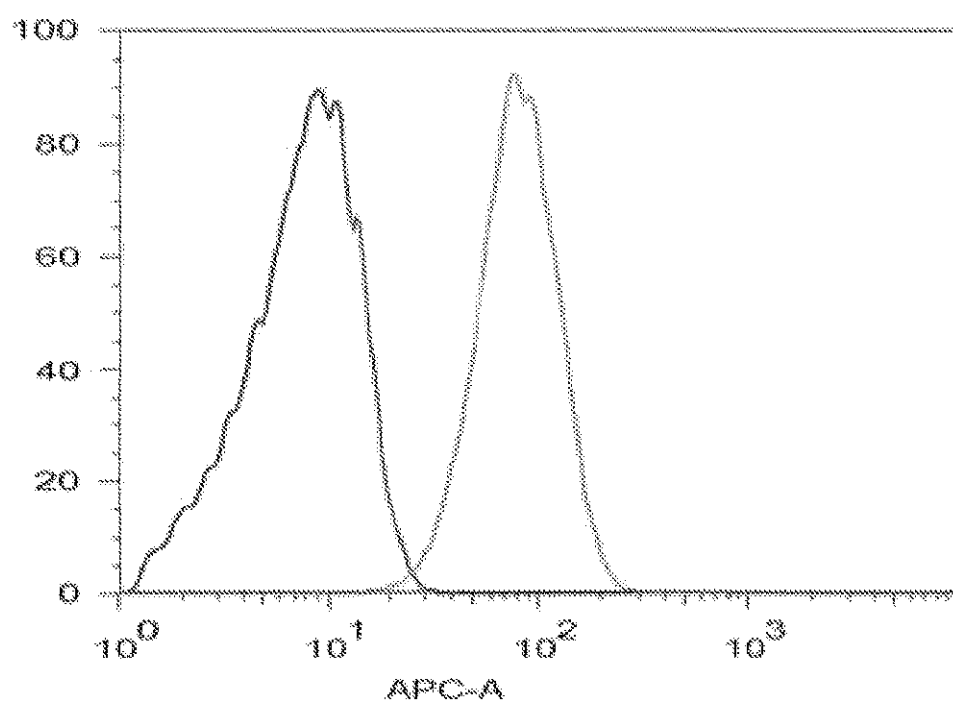


Fig 47 k)

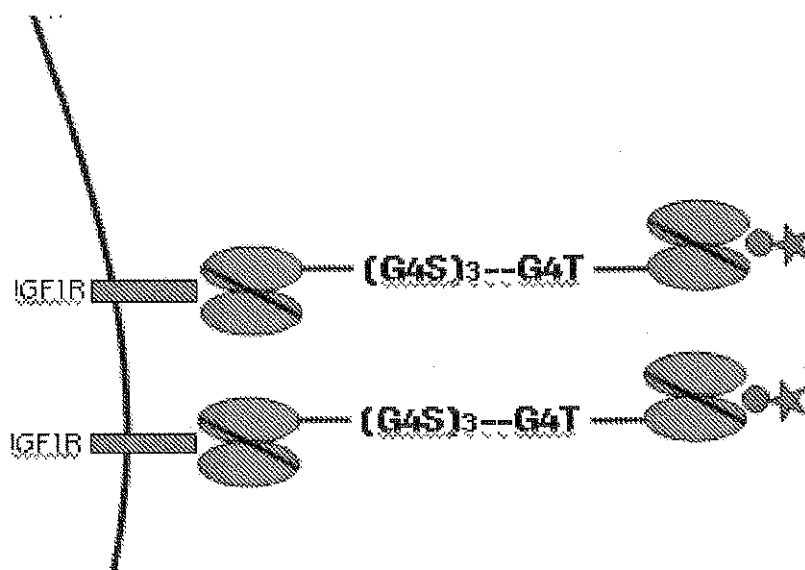
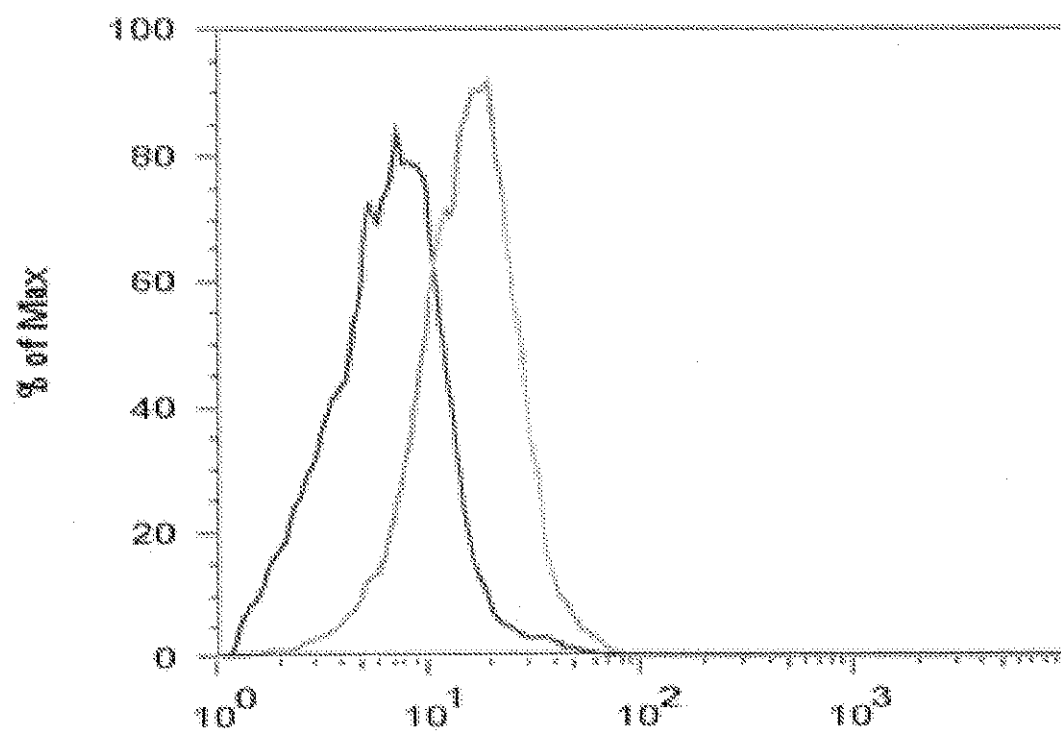


Fig. 47 l)

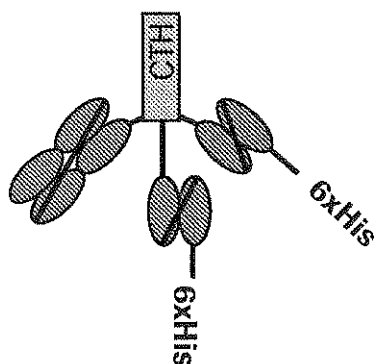


Fig. 47 n)

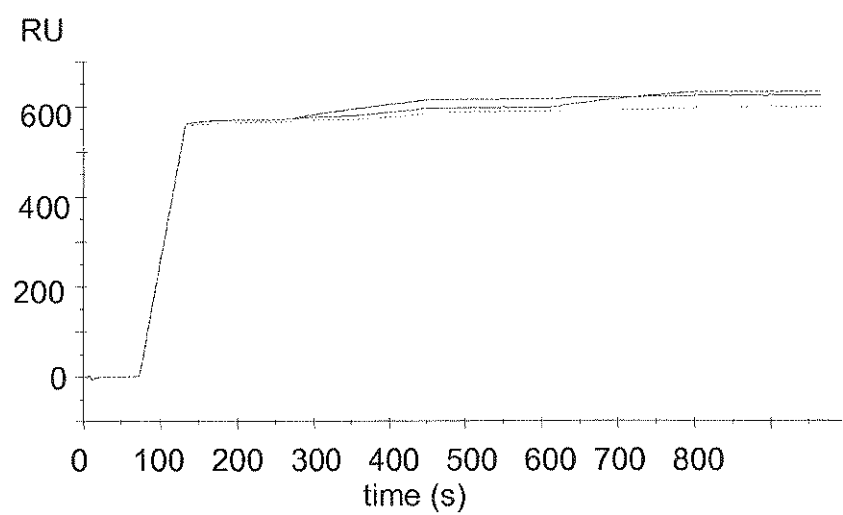


Fig. 47 m)

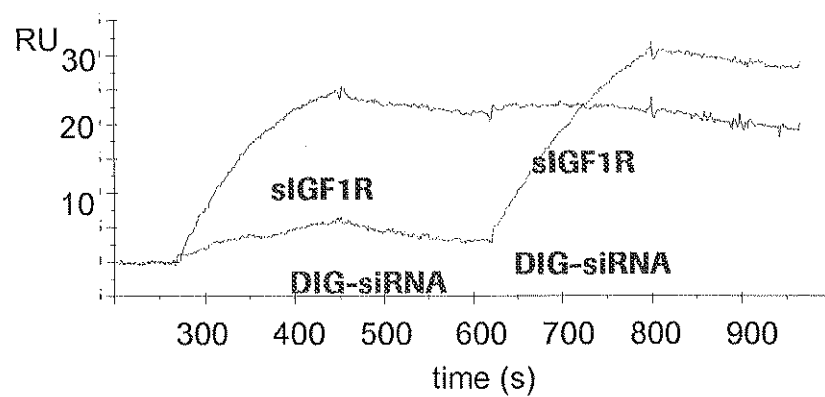


Fig. 47 o)

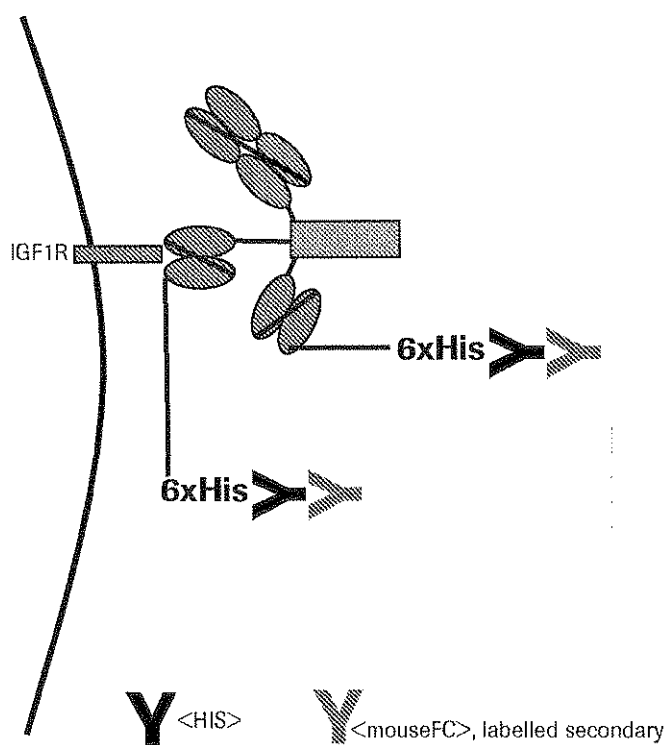
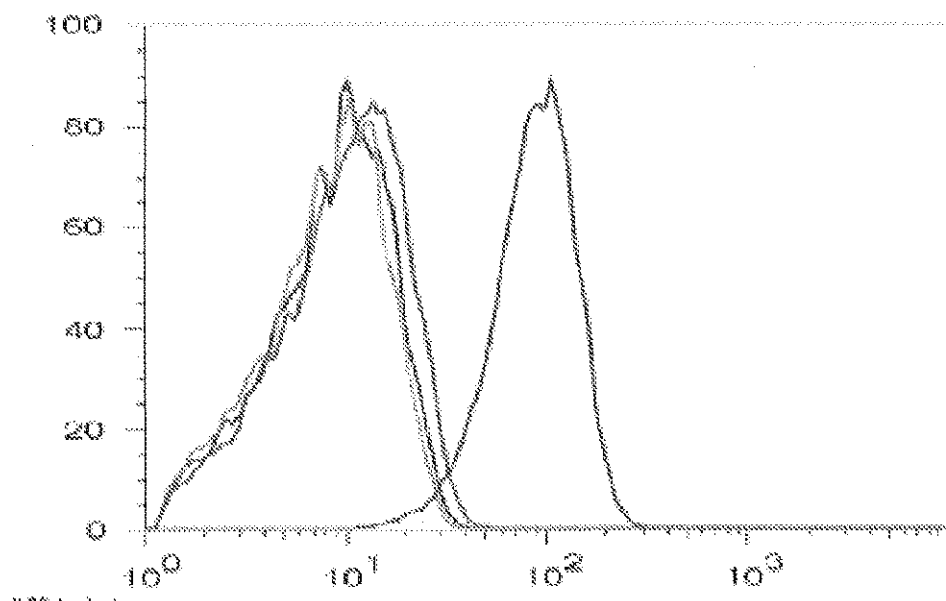


Fig. 47 p)

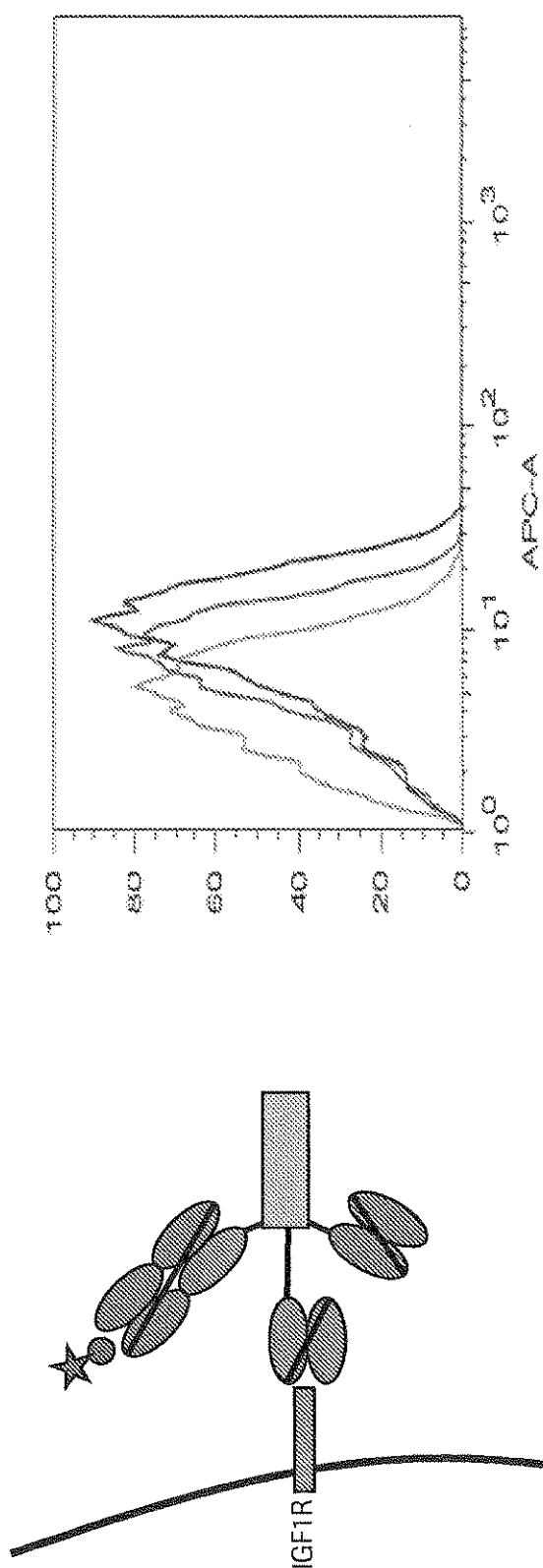


Fig. 47 q)

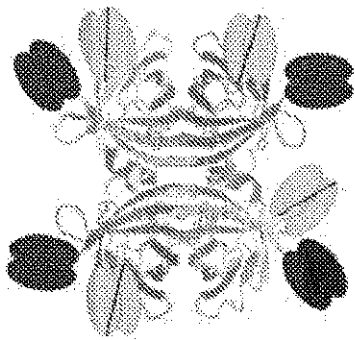


Fig. 47 r)

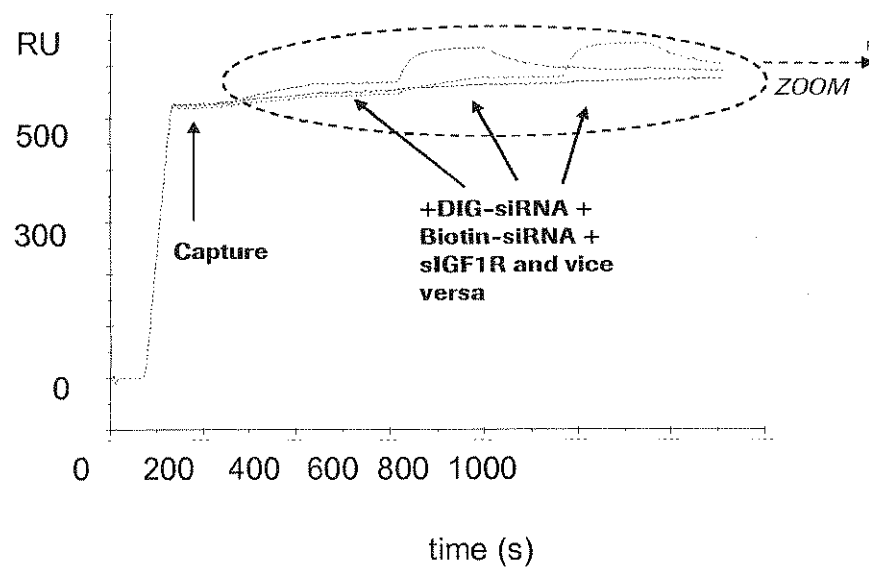


Fig. 47 s)

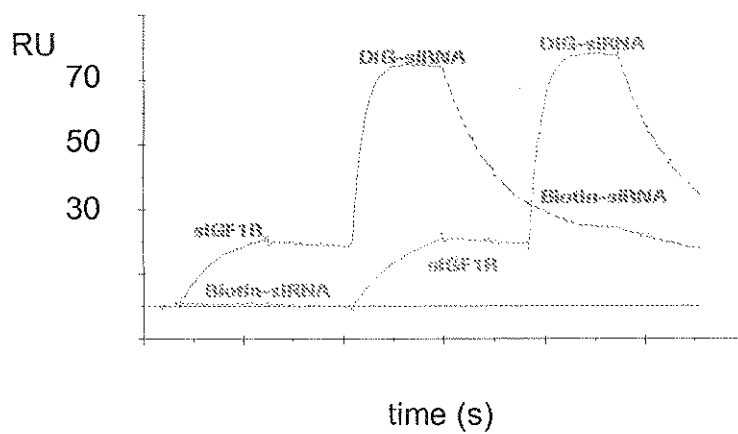


Fig 47 t)

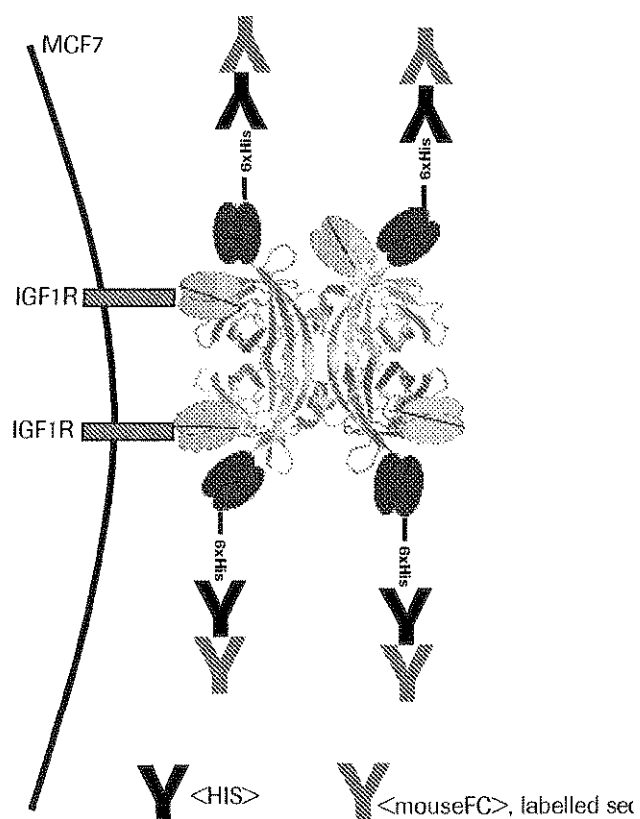
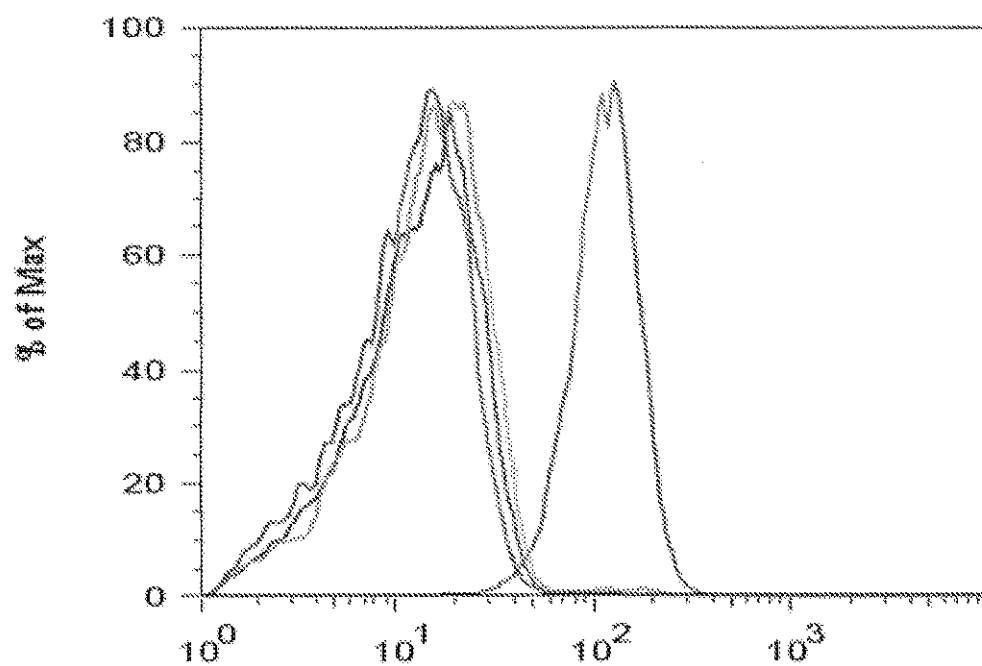


Fig. 47 u)

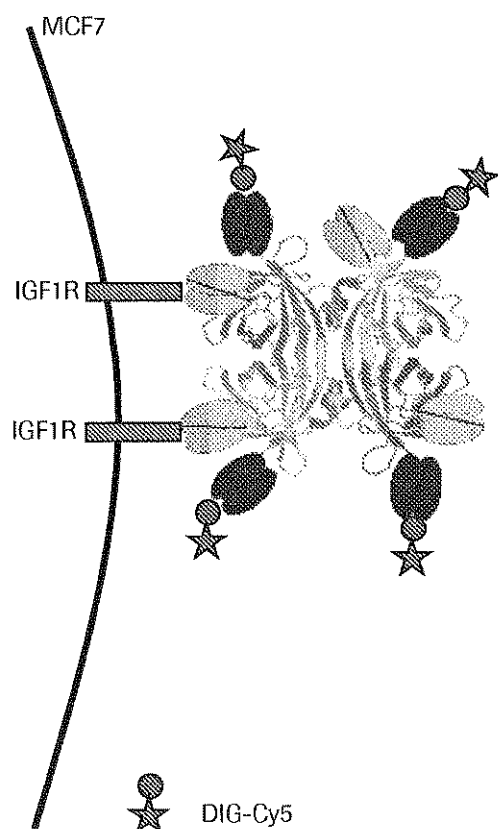
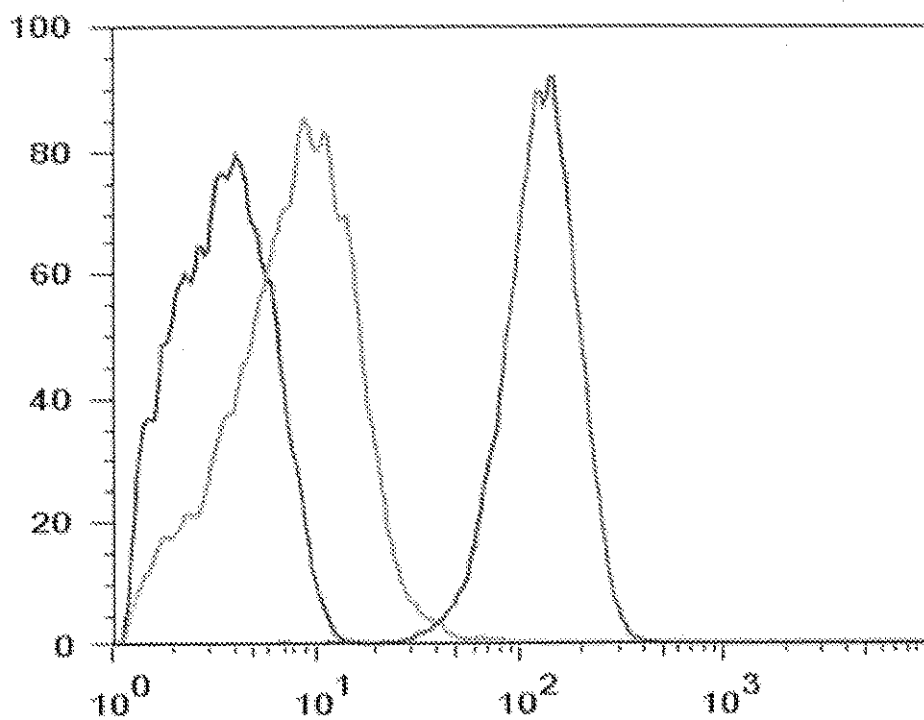


Fig. 47 v)

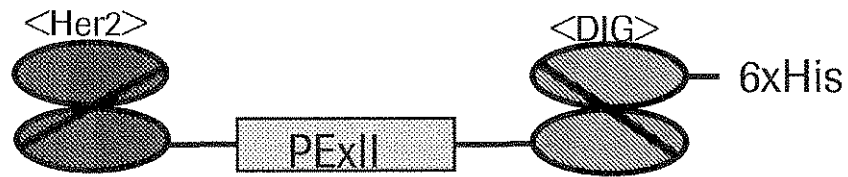


Fig. 47 w)

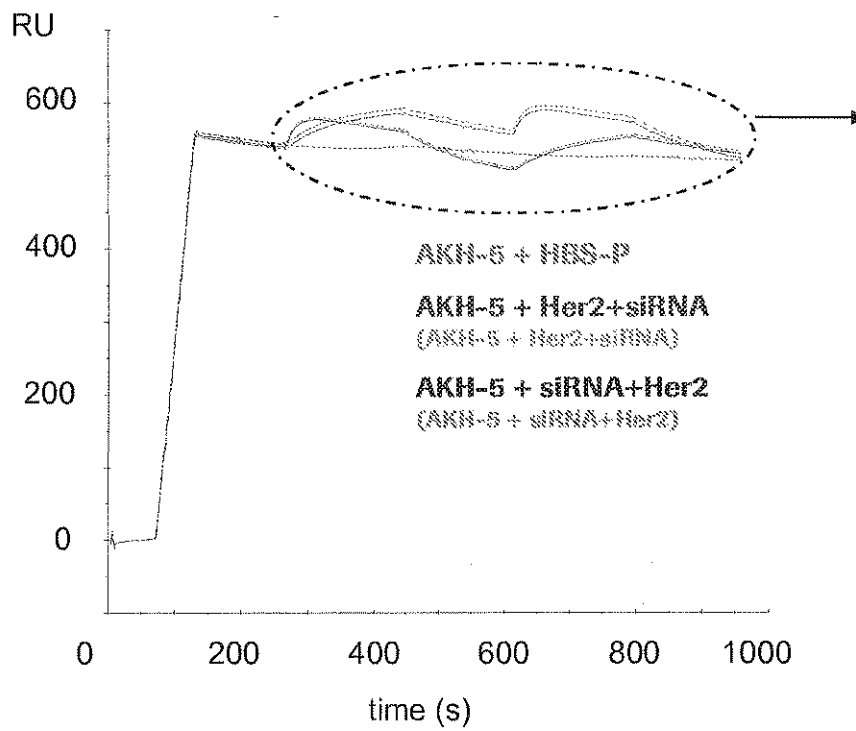


Fig. 47 x)

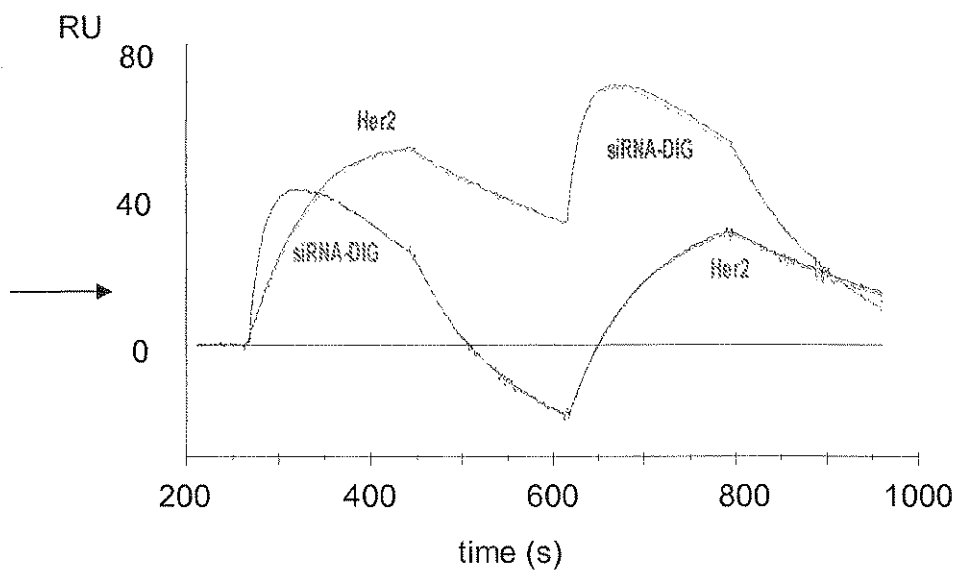


Fig. 48 a)

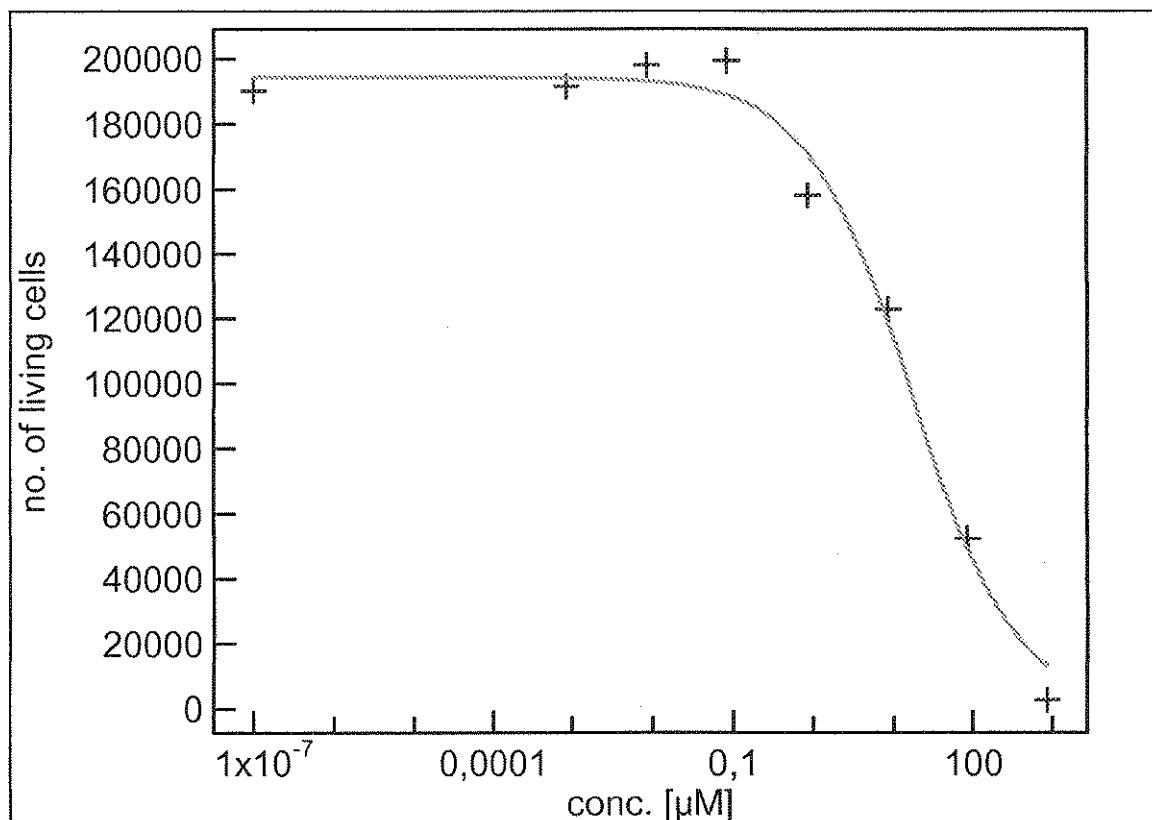


Fig. 48 b)

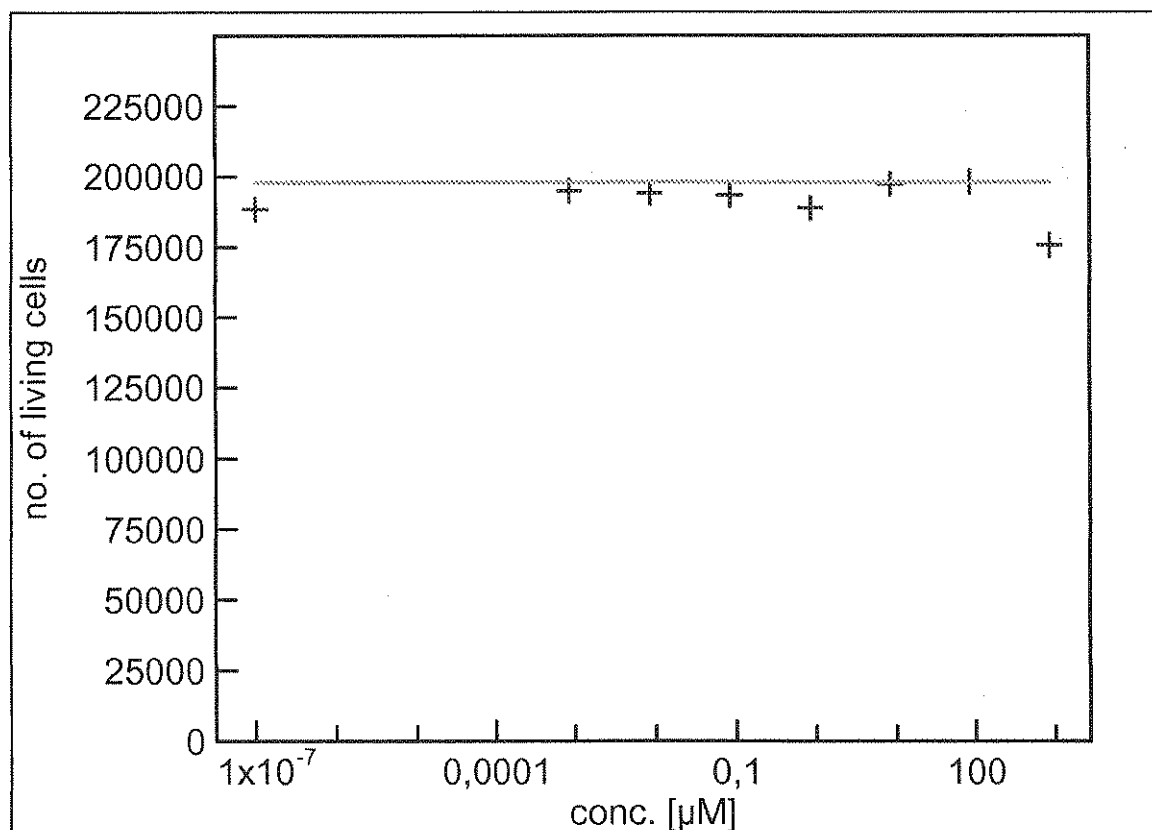


Fig. 48 c)

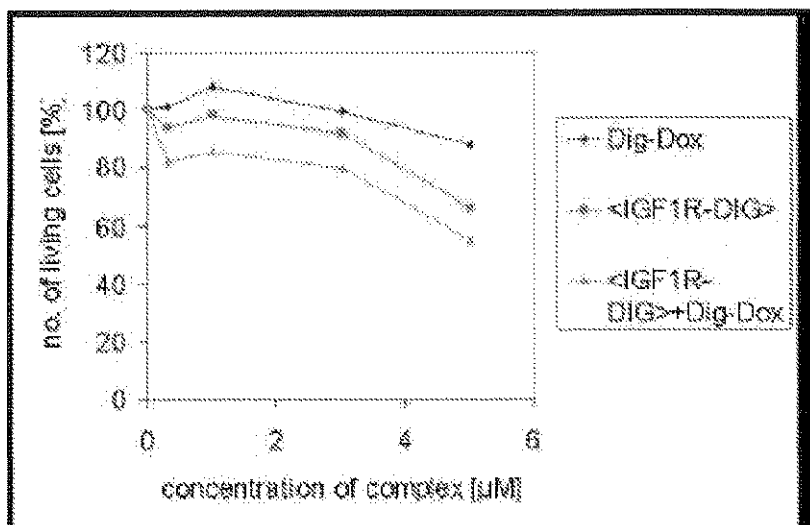


Fig. 48 d)

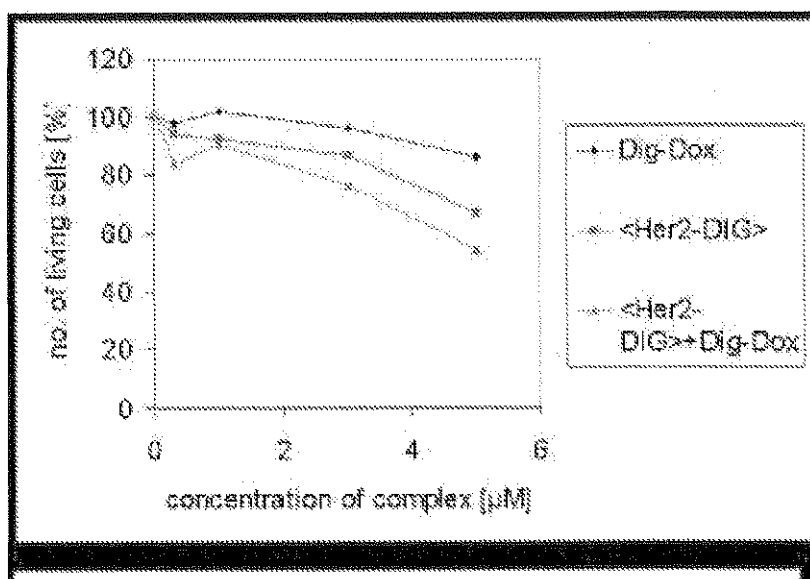


Fig. 48 e)

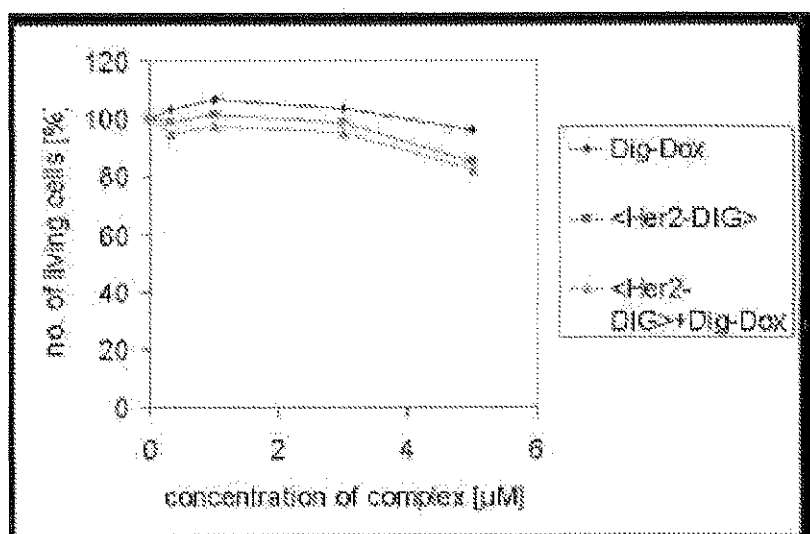


Fig. 49 a)

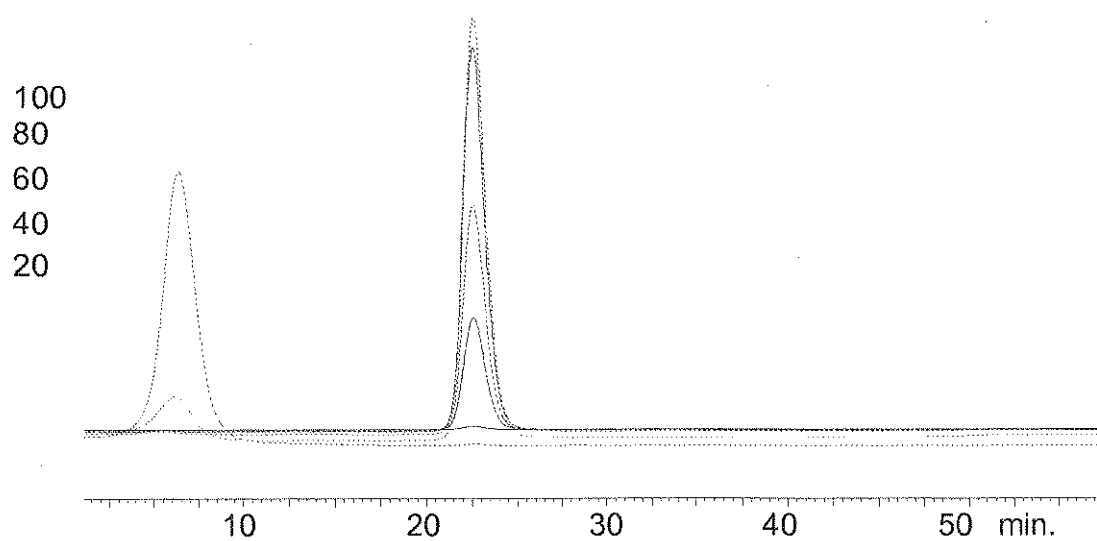


Fig. 49 b)

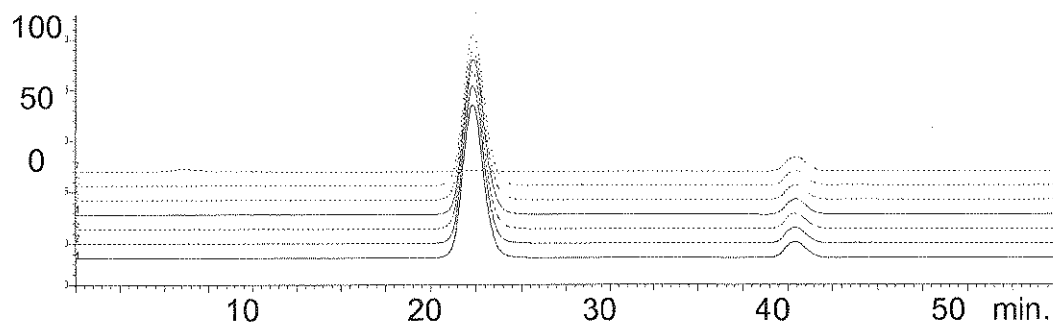


Fig. 49 c)

Molar ratio AK:DIG-Cy5	Area (Ex: 650 nm / Em: 667 nm) [mAU*min]		
	MAb Her2-DIG	MAb Her2	MAb IGF-1R
1:0	2	2	1
1:0,5	46	2	1
1:1	94	2	1
1:2	159	2	1
1:3	175	2	1
1:5	177	2	1
0:1	1	0	0

Fig. 49 d)

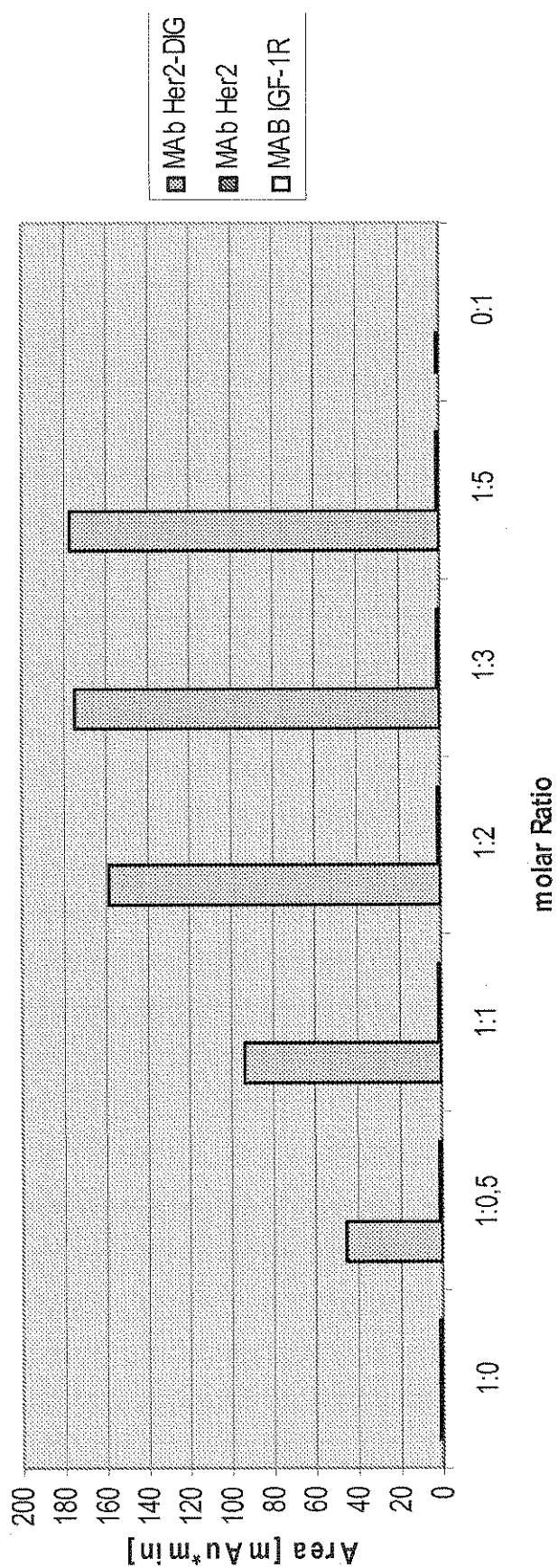


Fig. 50 a) (replacement sheet)

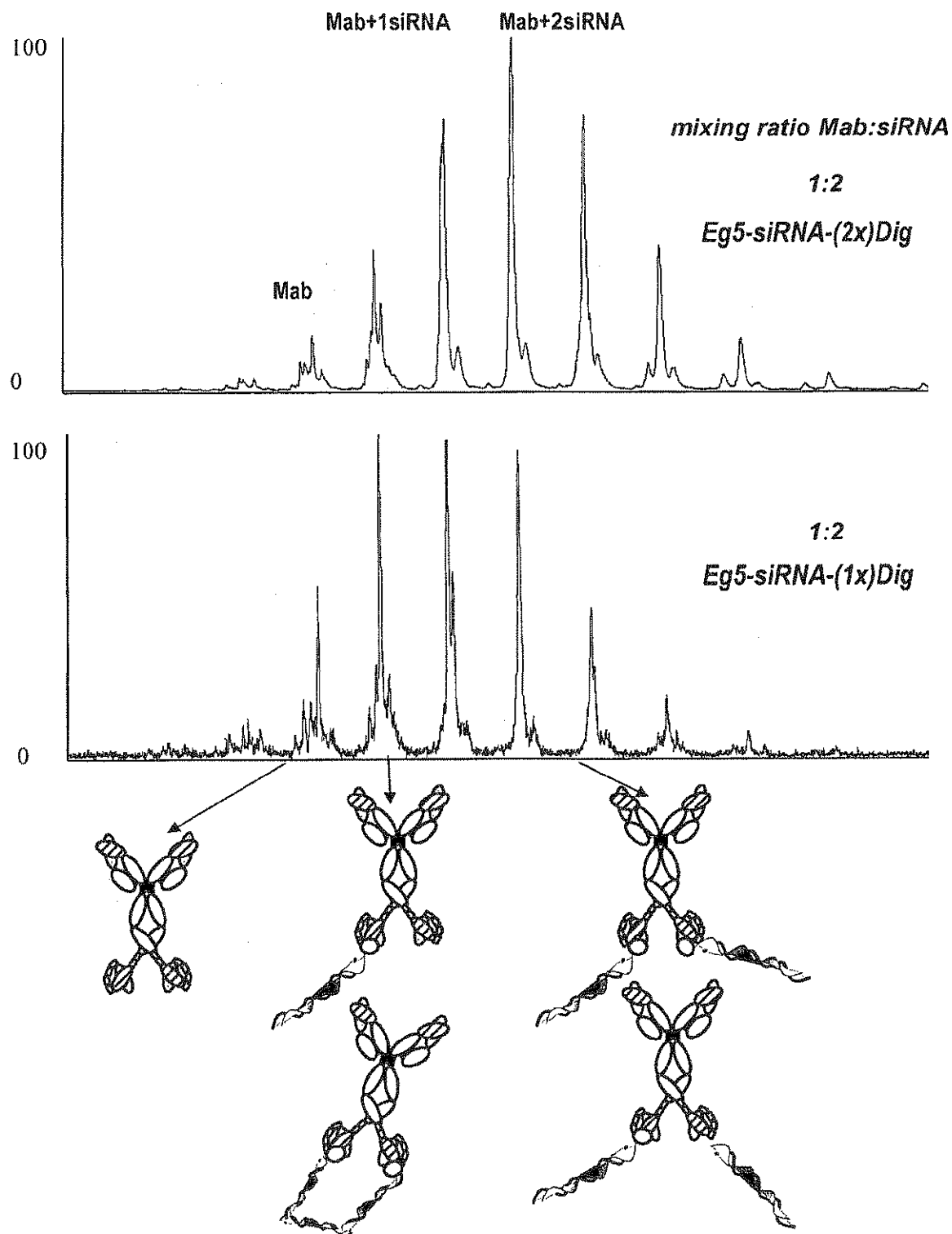


Fig. 50 b)

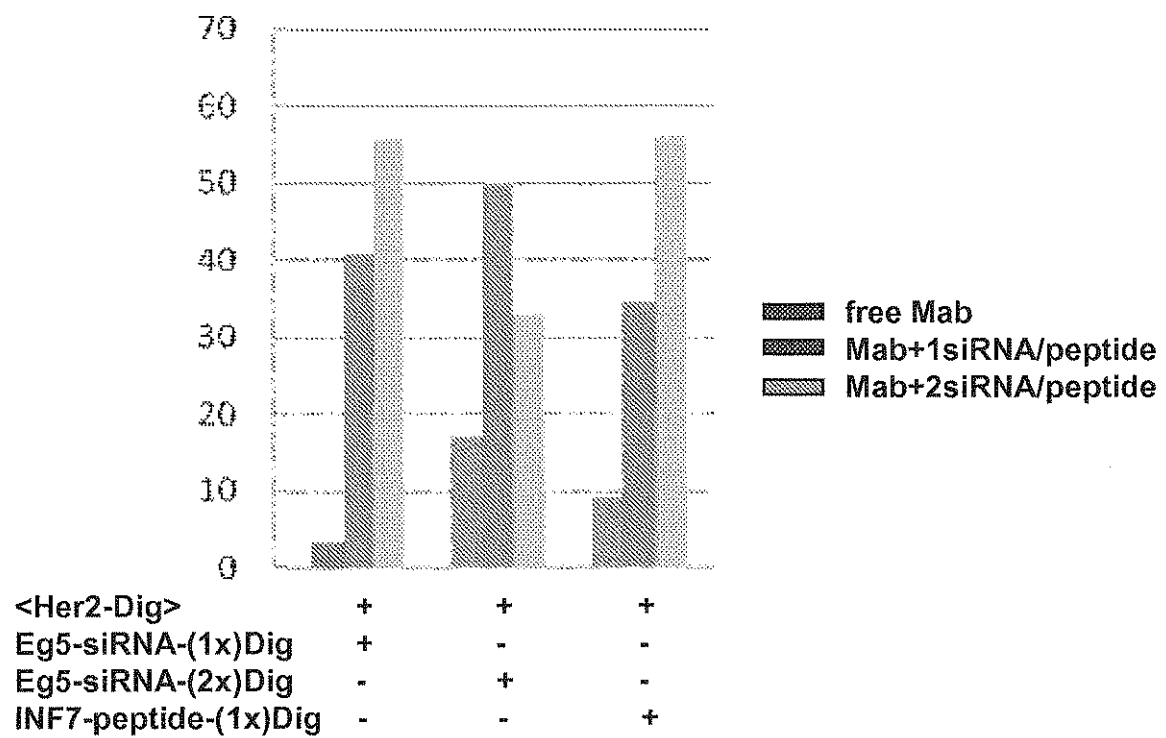


Fig. 51 a)

cell surface antigen	molecule	format
IGF1-Receptor	<IGF1R-DIG> Fv	scFv/dsscFv; Dig - CH3
IGF1-Receptor	<IGF1R-DIG> Fv	scFv/dsscFv; Dig - Ckappa
IGF1-Receptor	<IGF1R-DIG> Fv	dsscFv; Dig- CH3+Ckappa
IGF1-Receptor	<IGF1R-DIG> Fab	scFab; Dig- CH3
IGF1-Receptor	<IGF1R-DIG> Fab	dsscFab; Dig- CH3
VEGF-Receptor 2	<VEGFR2-DIG> Fv	scFv/dsscFv; Dig - CH3
VEGF-Receptor 2	<VEGFR2-DIG> Fab	scFab; Dig- CH3
VEGF-Receptor 2	<VEGFR2-DIG> Fab	dsscFab; Dig- CH3
CD33	<CD33-DIG> Fab	dsscFab; Dig- CH3
CD33	<CD33-DIG> Fv	scFv/dsscFv; Dig - CH3
LeY carbohydrate	<LeY-DIG> Fab	dsscFab; Dig- CH3
LeY carbohydrate	<LeY-DIG> Fv	scFv/dsscFv; Dig - CH3
CD22	<CD22-DIG> Fv	dsscFv; Dig - CH3
Her2	<Her2-DIG> Fv	dsscFv; Dig - CH3
CDCP1	<CDCP1-DIG> Fv	dsscFv; Dig - CH3

Fig. 51 b)

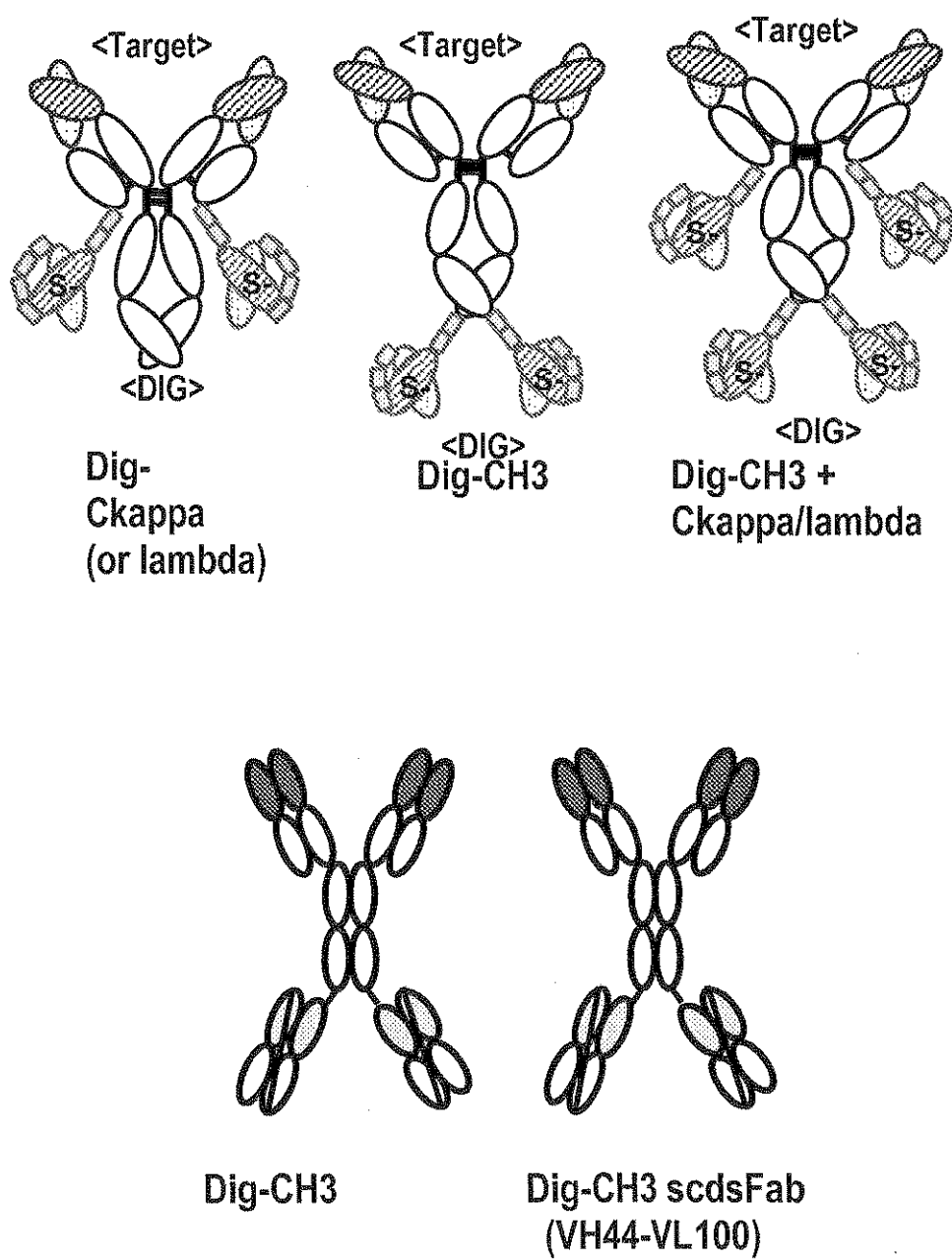


Fig. 51 c)

Capture	Antibody	k_a (1/Ms)	k_d (1/s)	KD (M)
human VEGFR2-Fc	<VEGFR2(D1F7)-DIG>_001	3.44E+06	6.54E-03	1.90E-09
	<VEGFR2(D1F7)-scFab-DIG>	4.98E+06	6.70E-03	1.35E-09
	<VEGFR2(D1F7)-dsFab-DIG>	2.49E+06	9.68E-03	3.89E-09
mouse VEGFR2-Fc	<VEGFR2(D1F7)-DIG>_001	3.89E+06	6.56E-03	1.69E-09
	<VEGFR2(D1F7)-scFab-DIG>	3.21E+06	8.92E-03	2.78E-09
	<VEGFR2(D1F7)-dsFab-DIG>	2.01E+06	1.14E-02	5.65E-09

Figure 51 d)

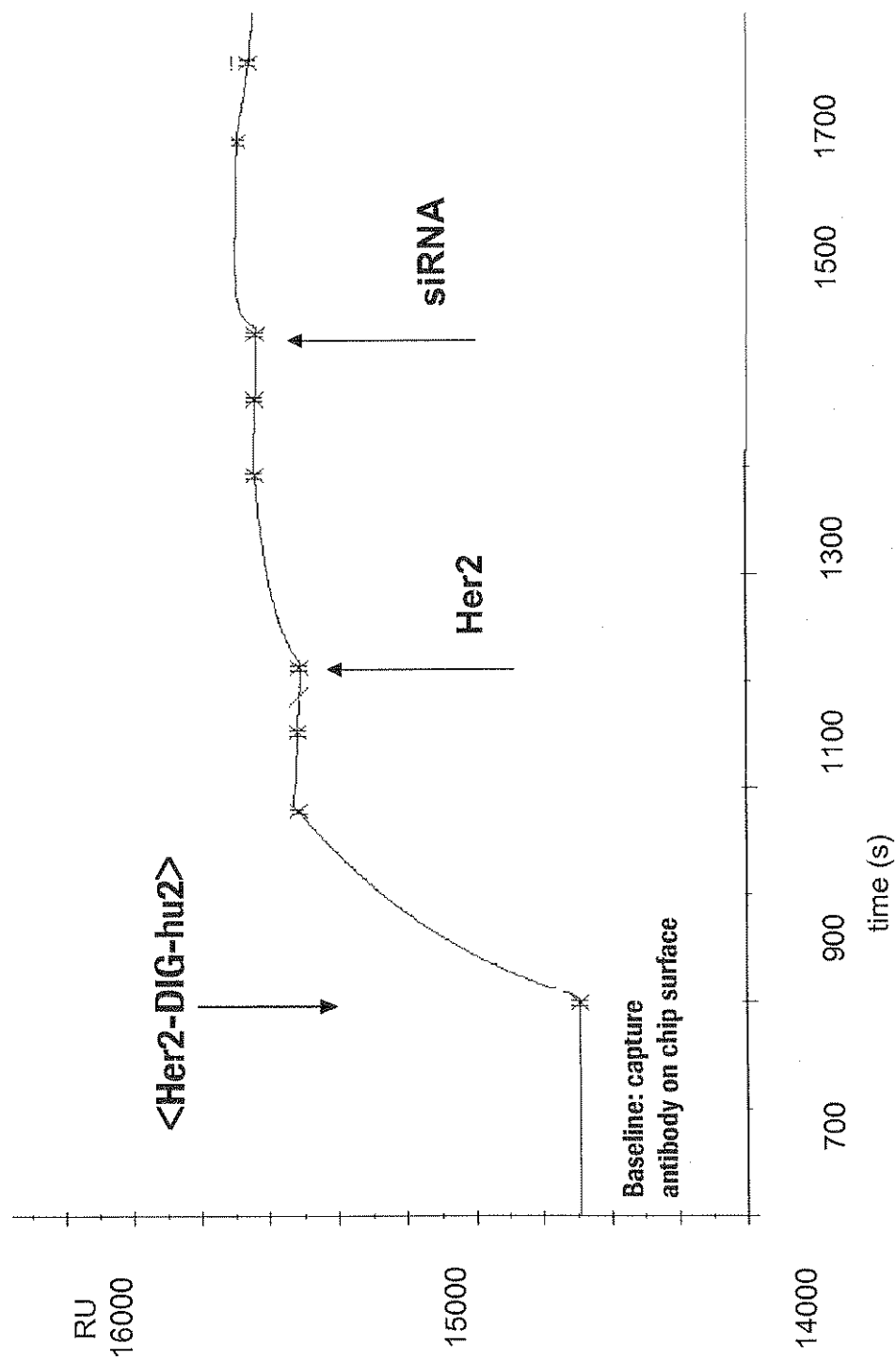


Fig. 51 e)

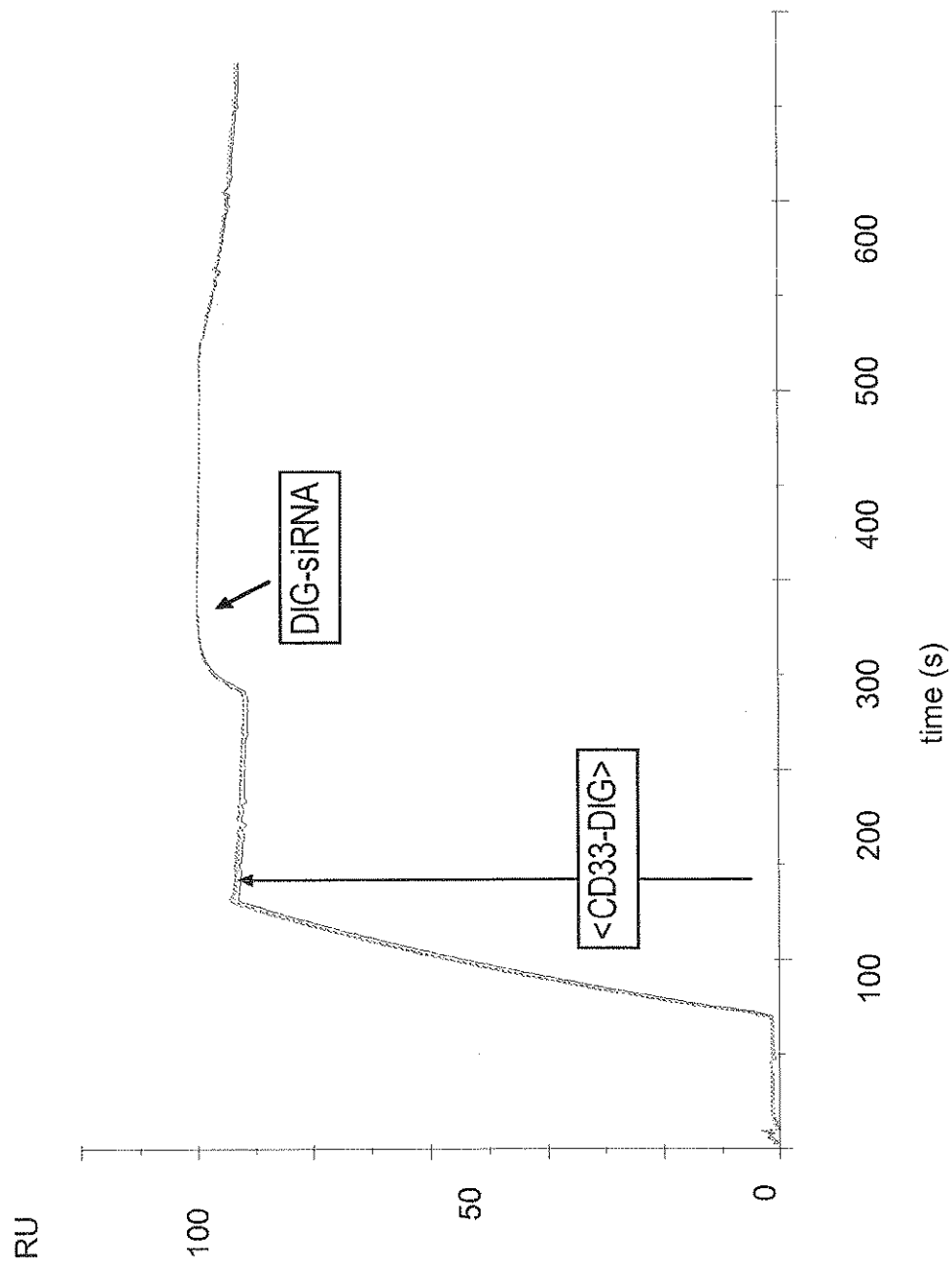


Fig. 51 f)

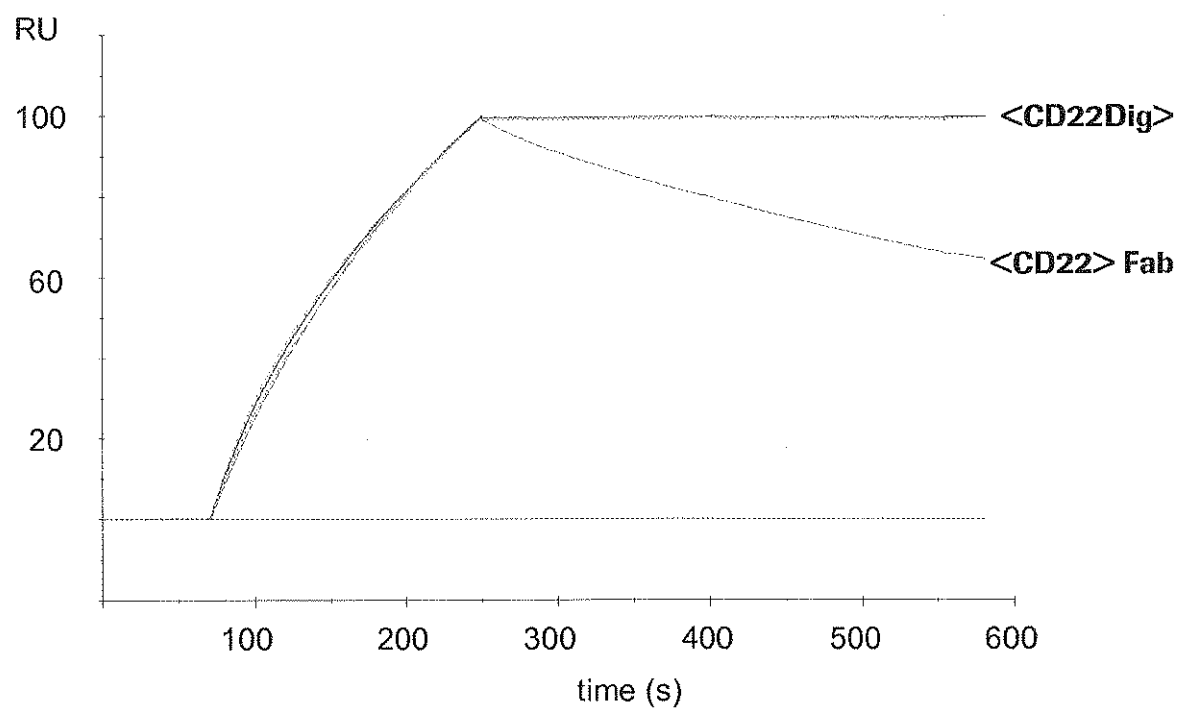


Fig. 51 g)

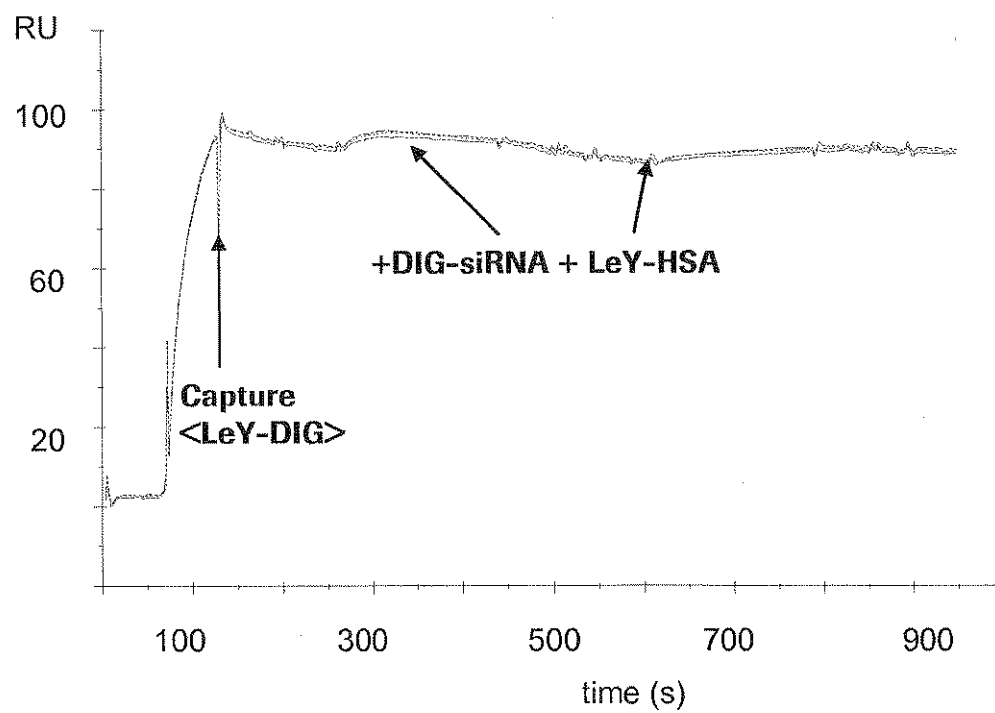


Fig. 51 h)

	k_a (1/Ms)	k_d (1/s)	KD (nM)
CDCP1-ECD	2.02E+05	1.32E-03	7
	2.02E+05	1.60E-03	8
DIG-siRNA	4.37E+05	0.0097	22
	5.54E+05	0.011	20

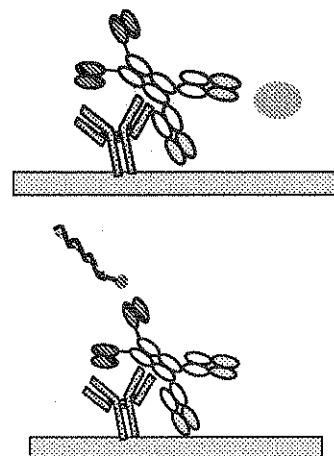


Fig. 52 a)

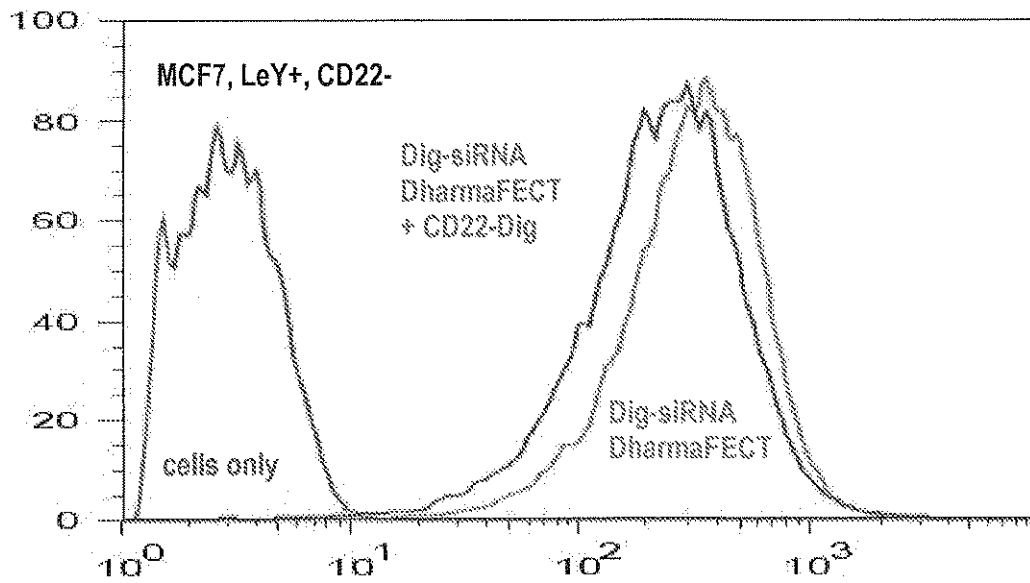


Fig. 52 b)

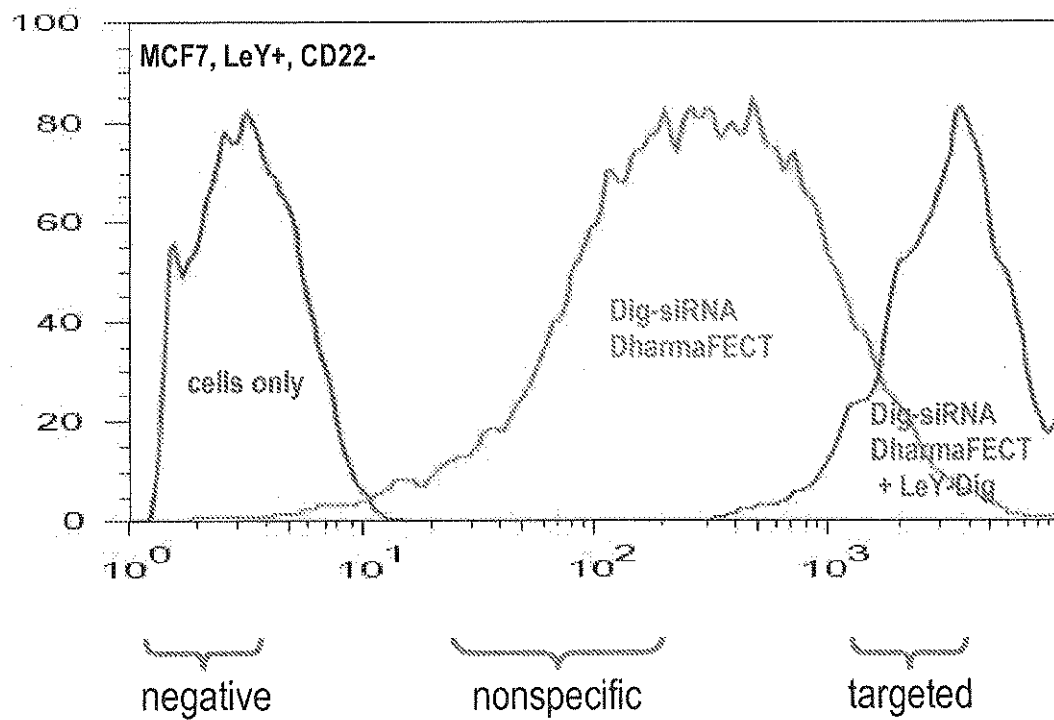


Fig. 52 c)

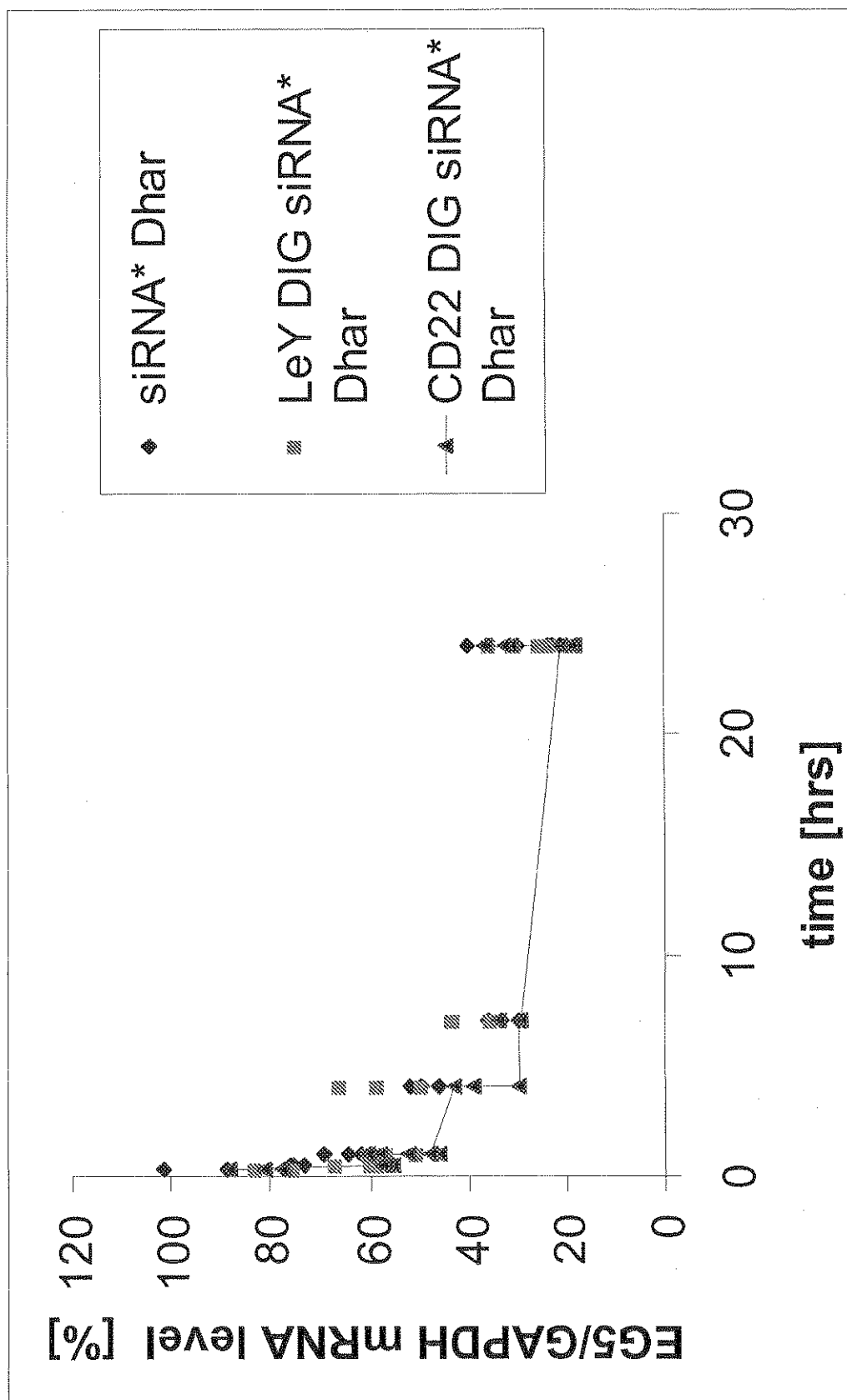


Fig. 53 a)

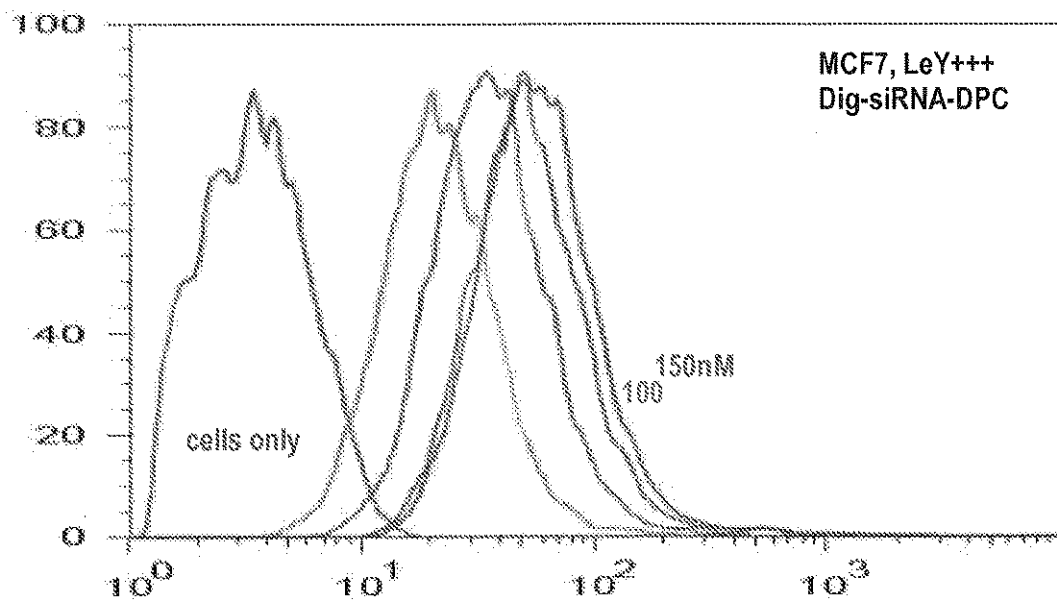


Fig. 53 b)

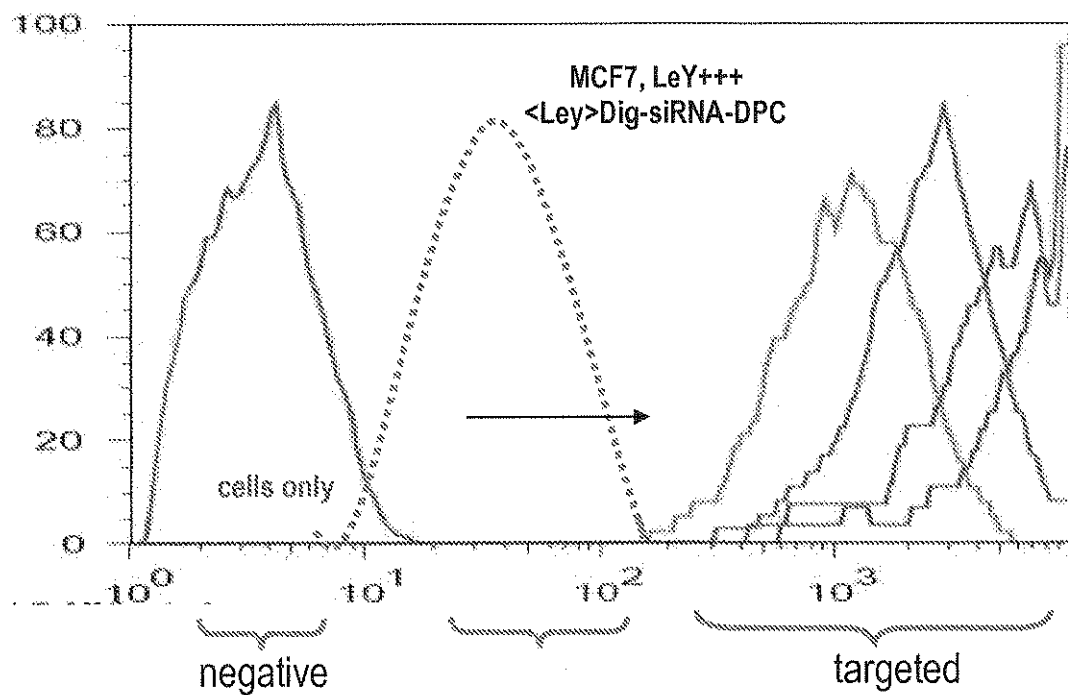


Fig. 53 c)

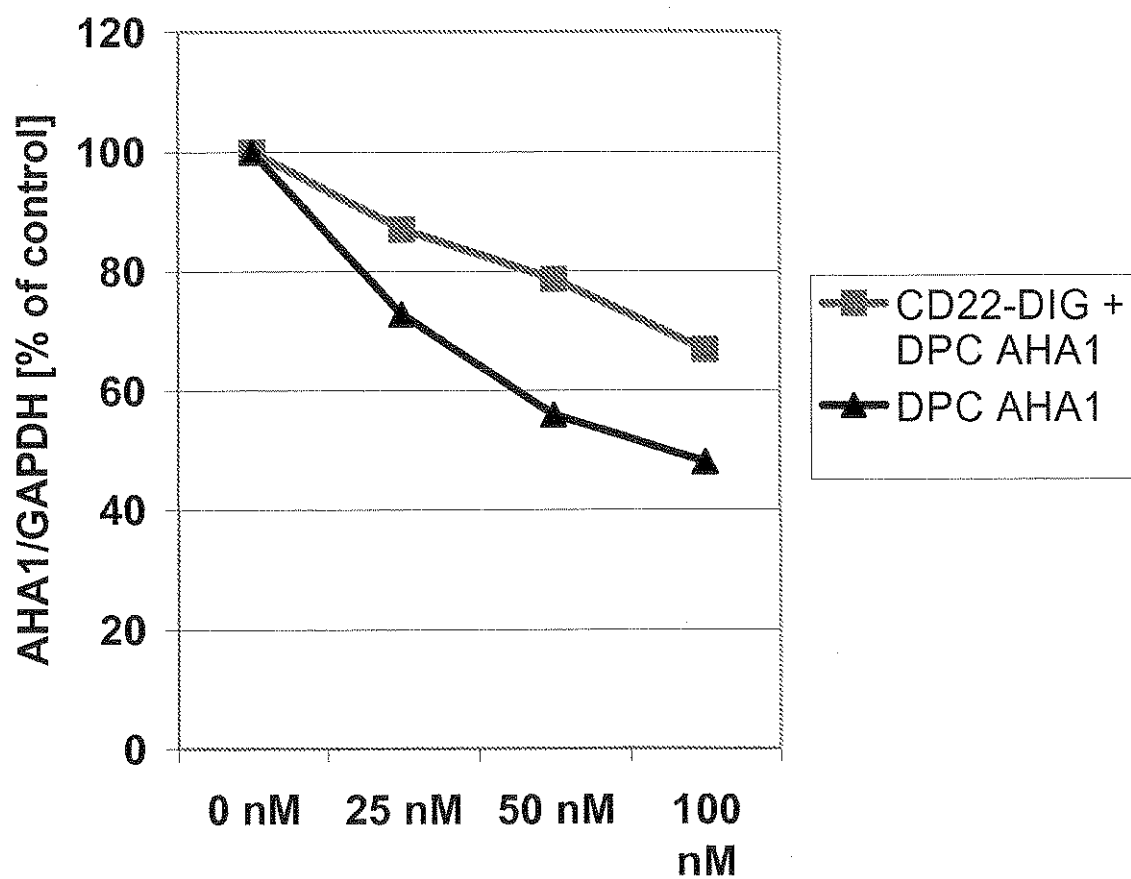


Fig. 53 d)

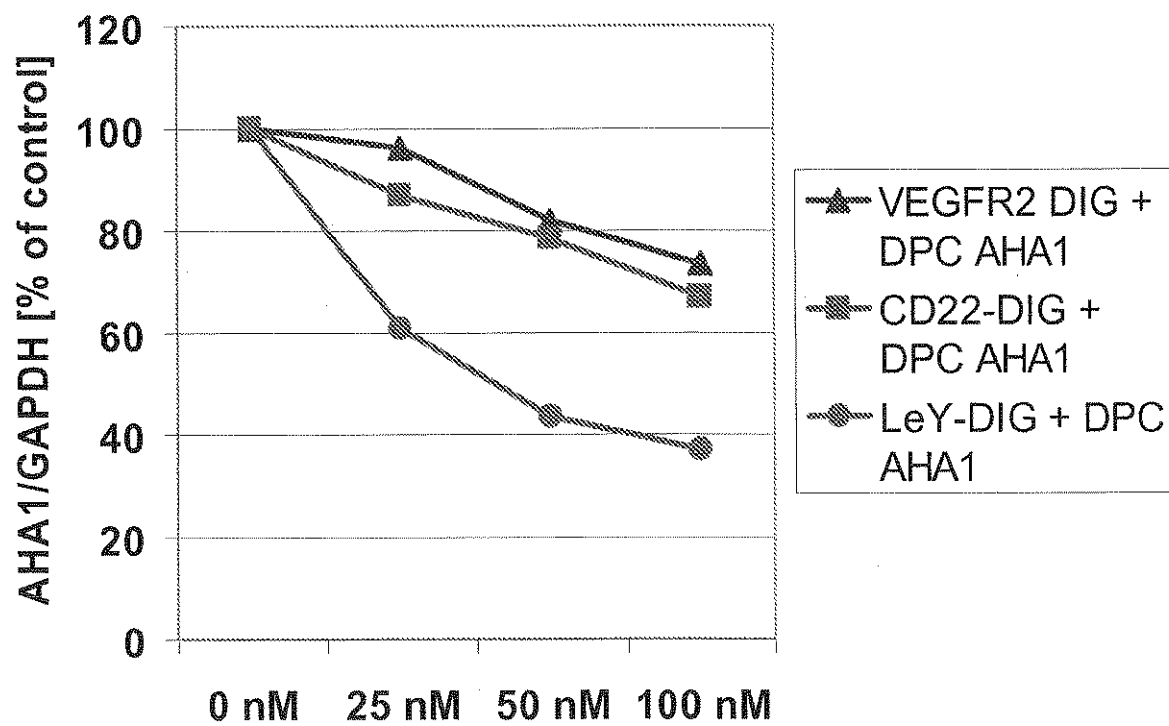


Fig. 53 e)

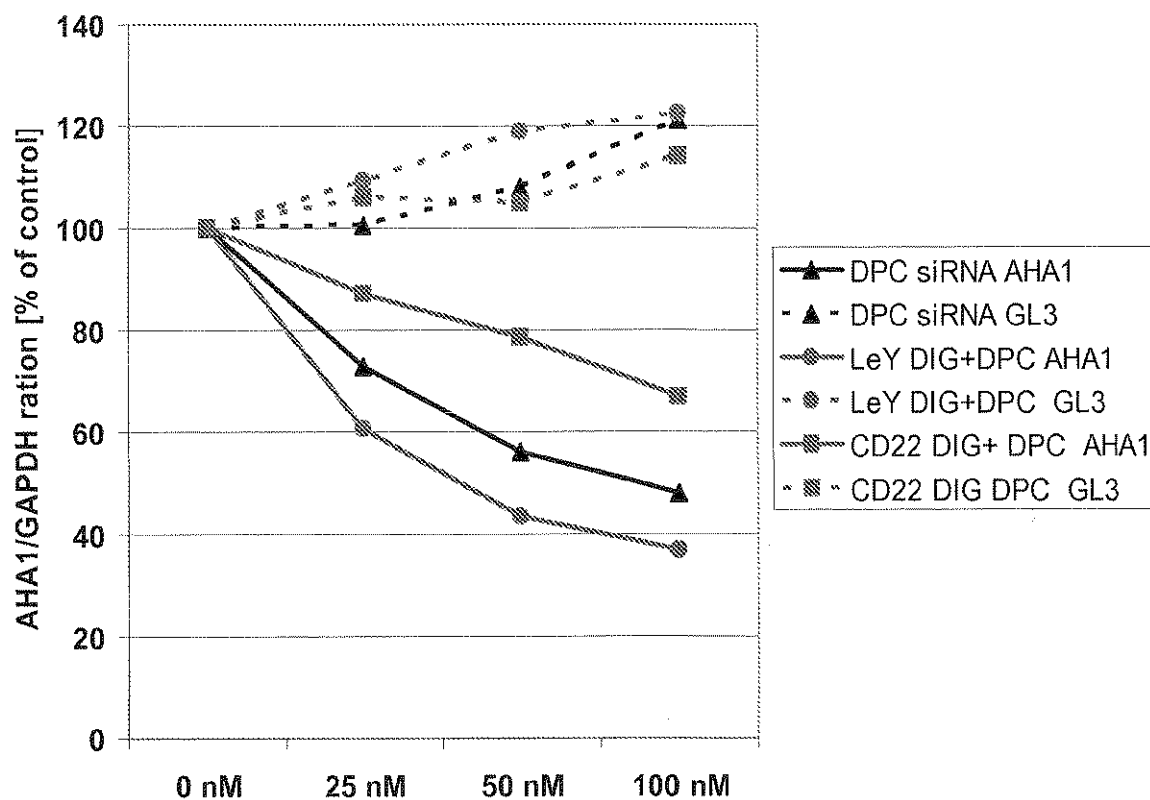


Fig. 53 f)

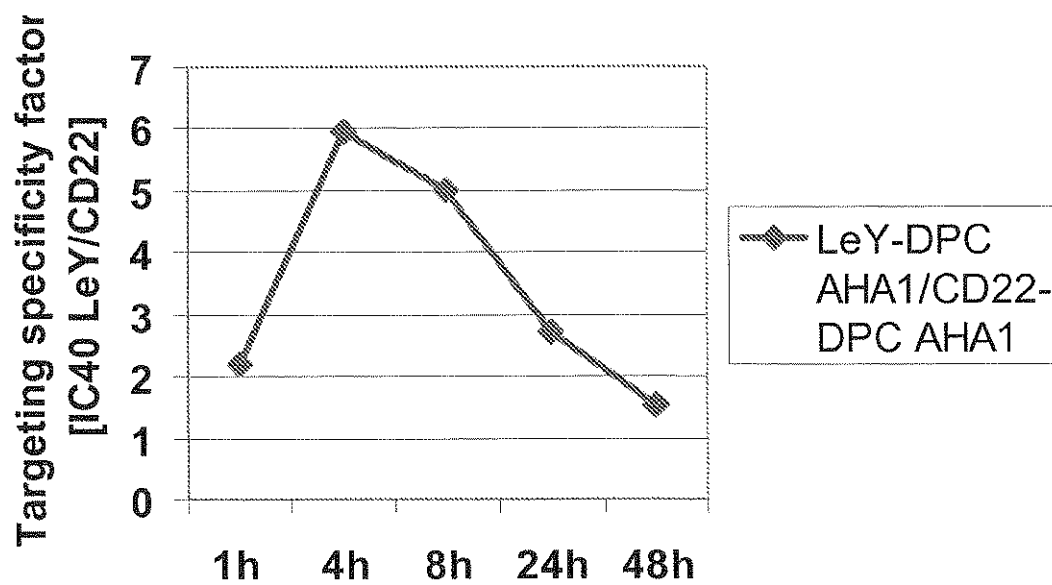


Fig. 54 a)

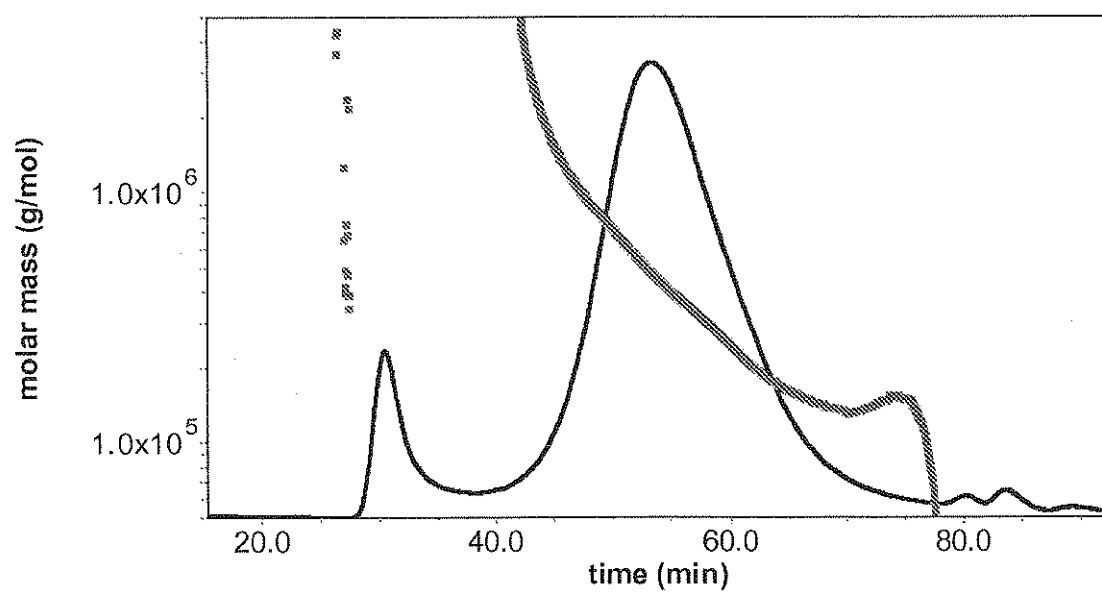


Fig. 54 b)

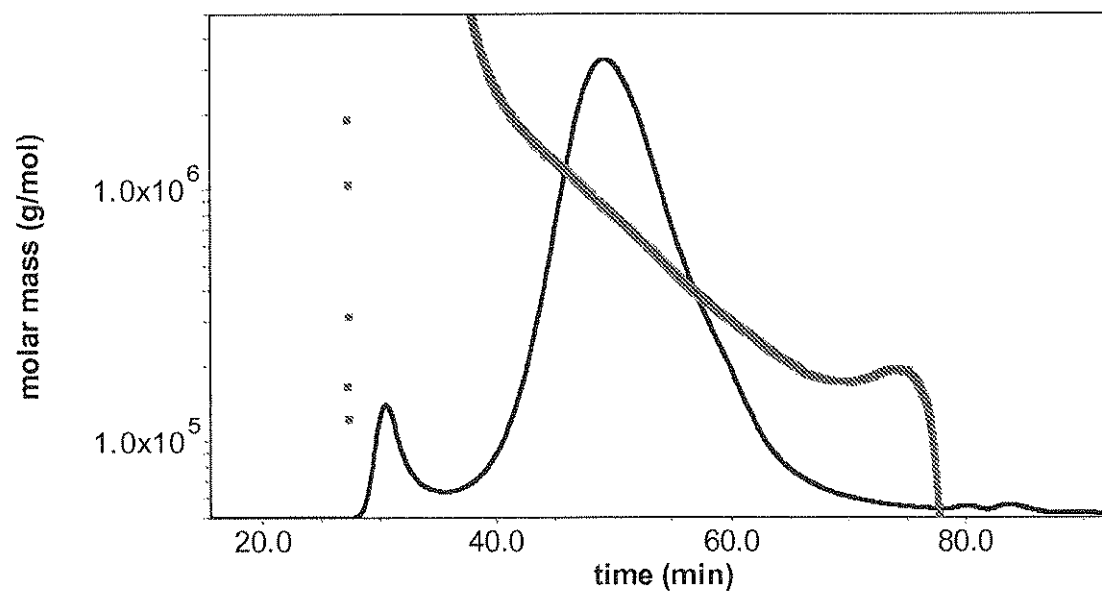


Fig. 54 c)

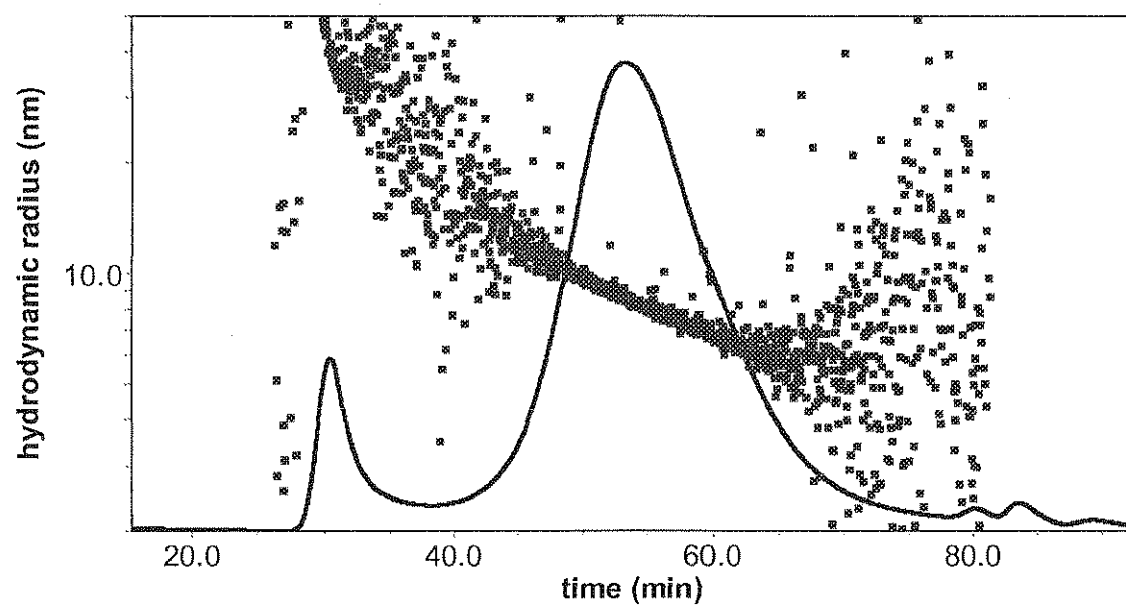


Fig. 54 d)

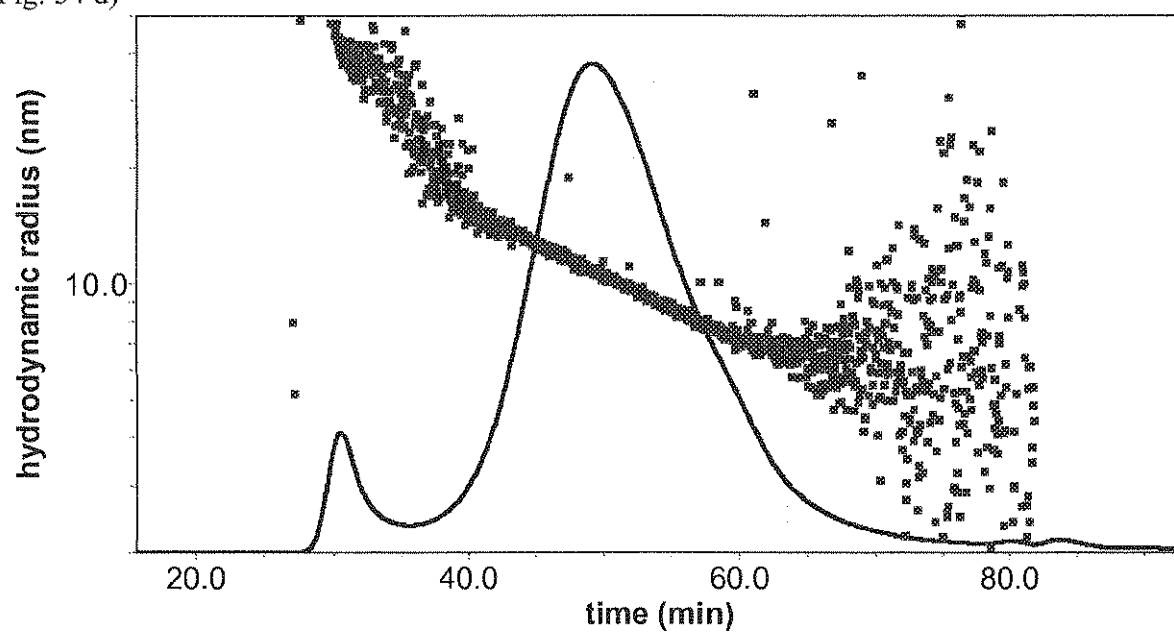


Fig. 55 a)

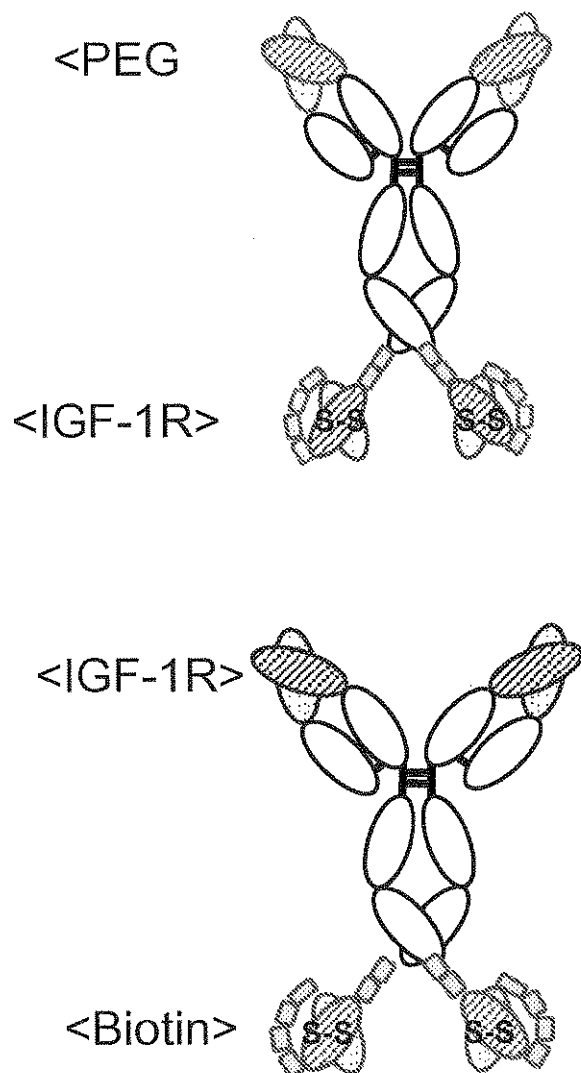


Fig. 55 b)

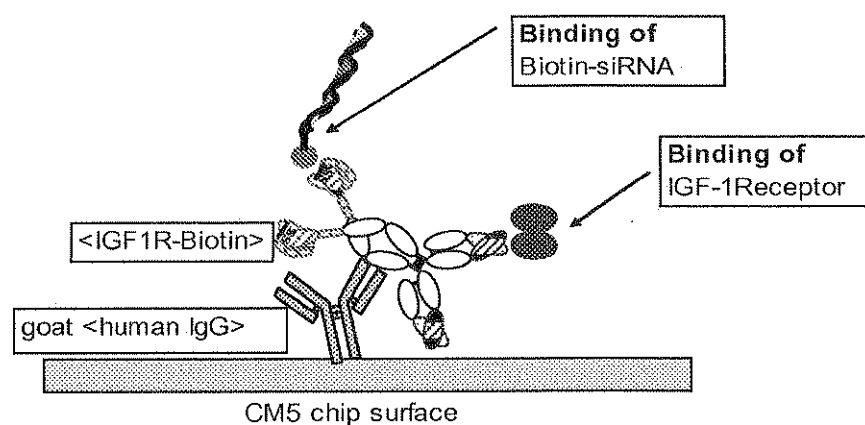


Fig. 55 c)

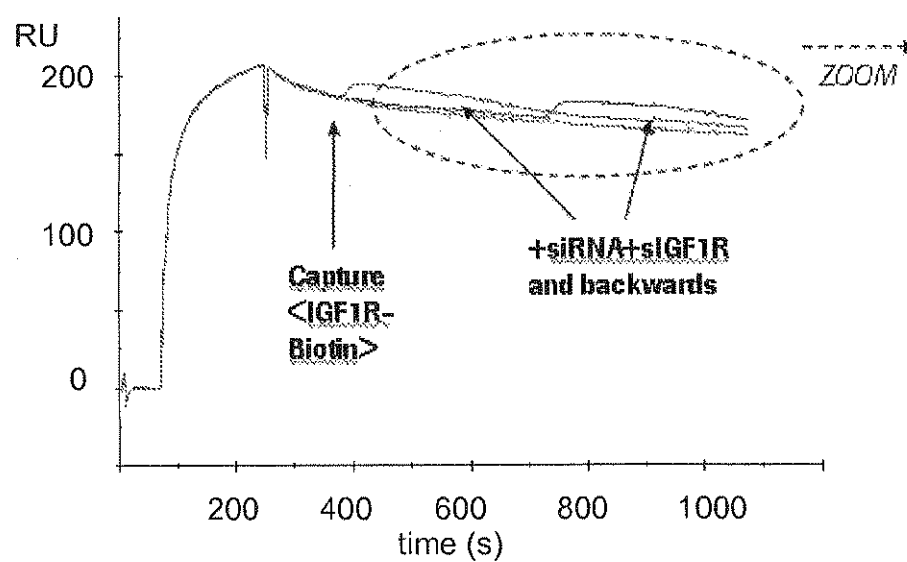


Fig. 55 d)

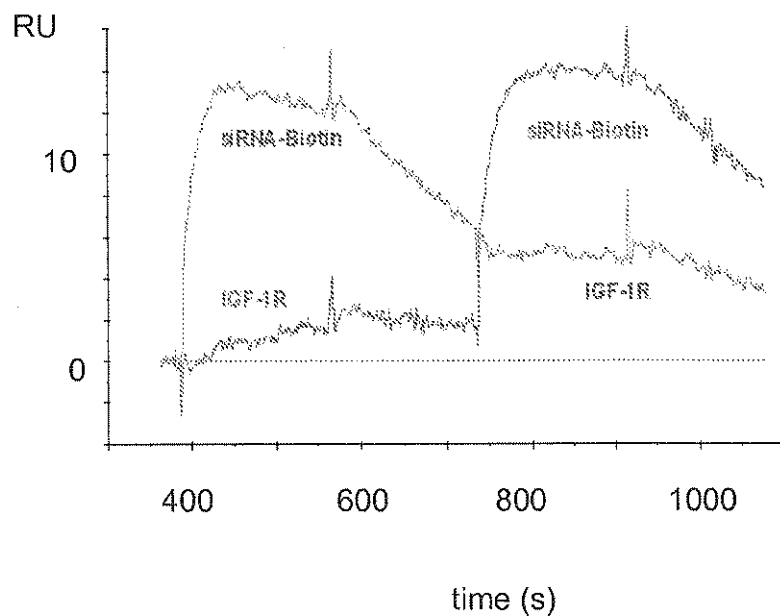


Fig. 56 a)

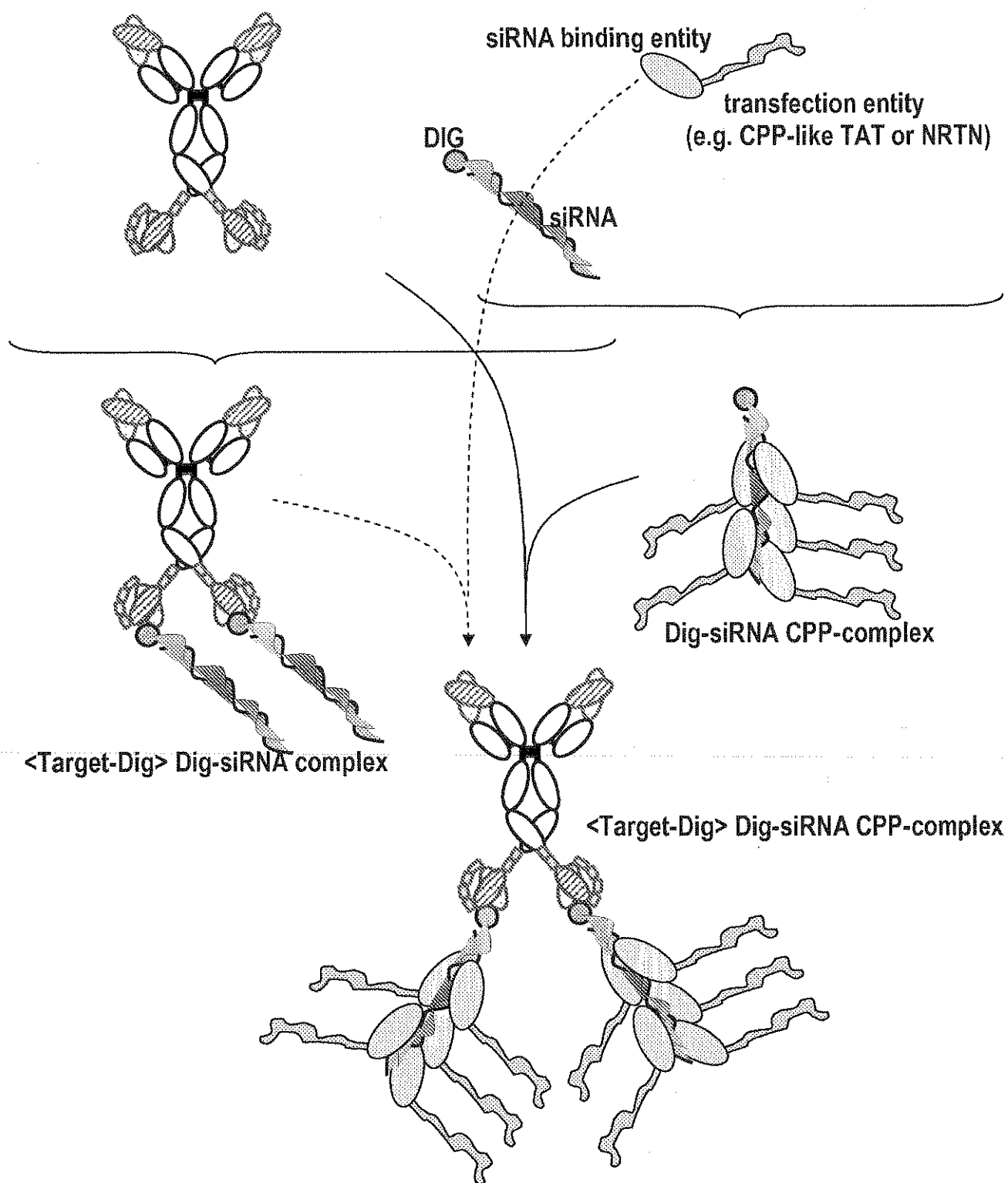


Fig. 56 b)

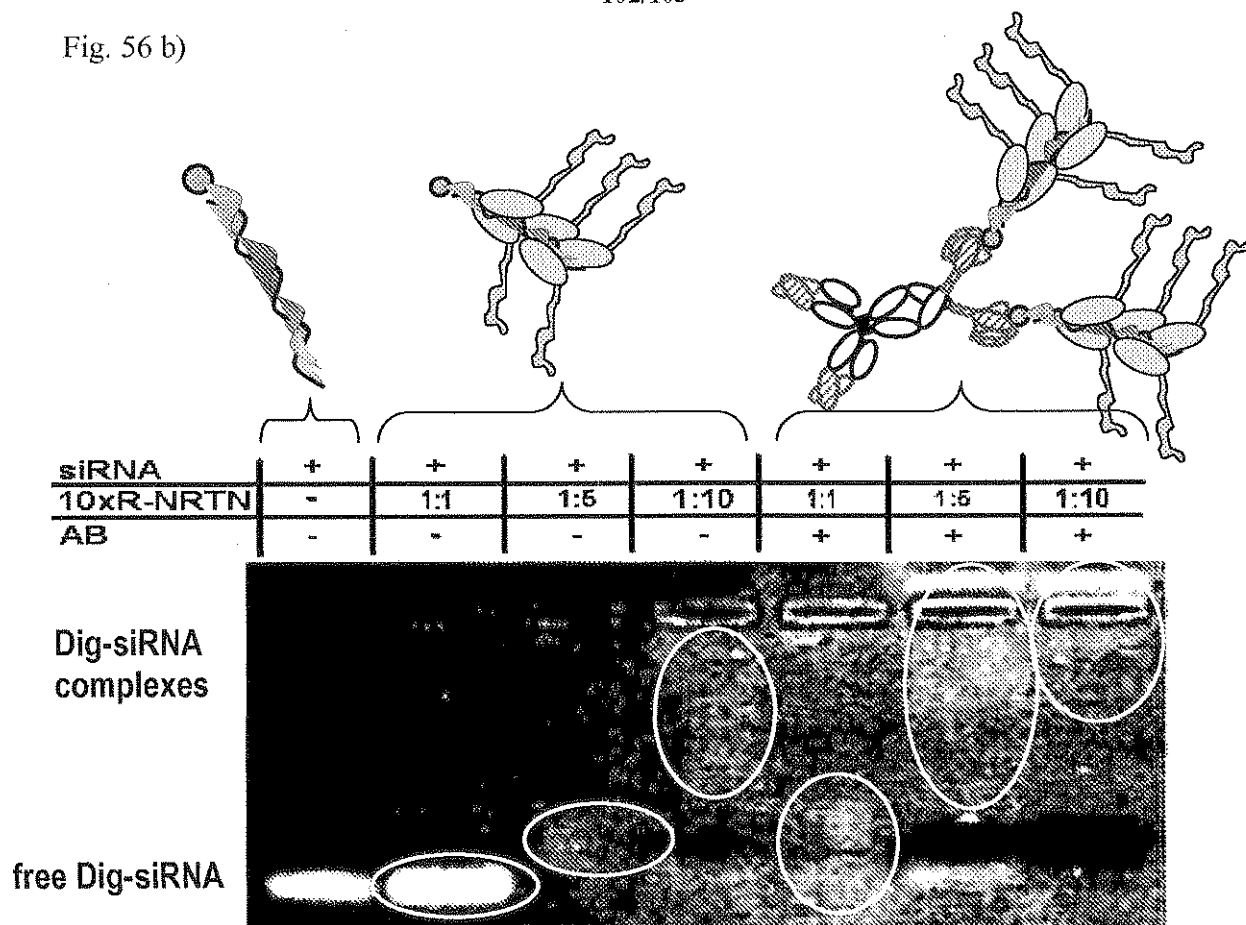


Fig. 56 c)

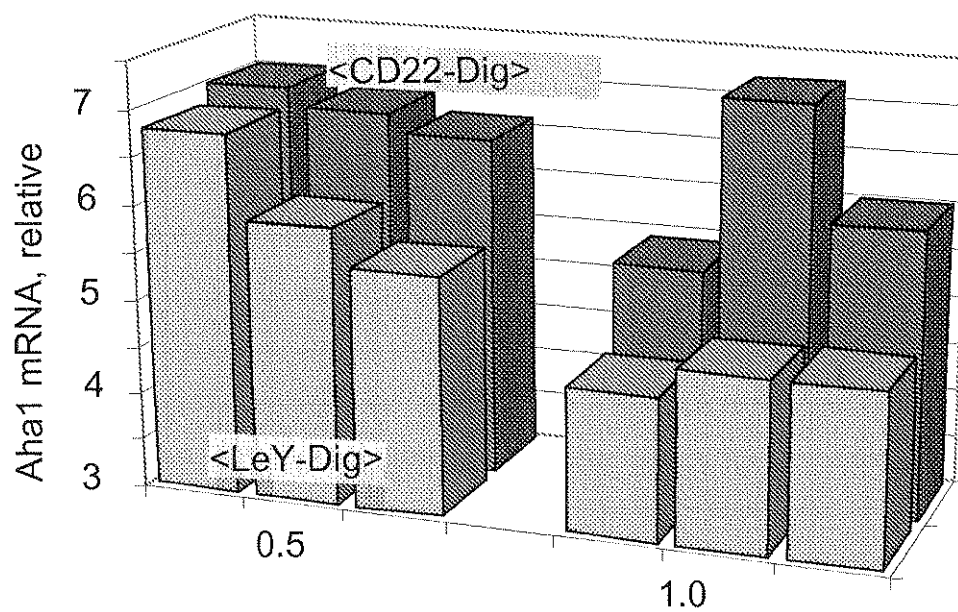


Fig. 57

