Fig. 1

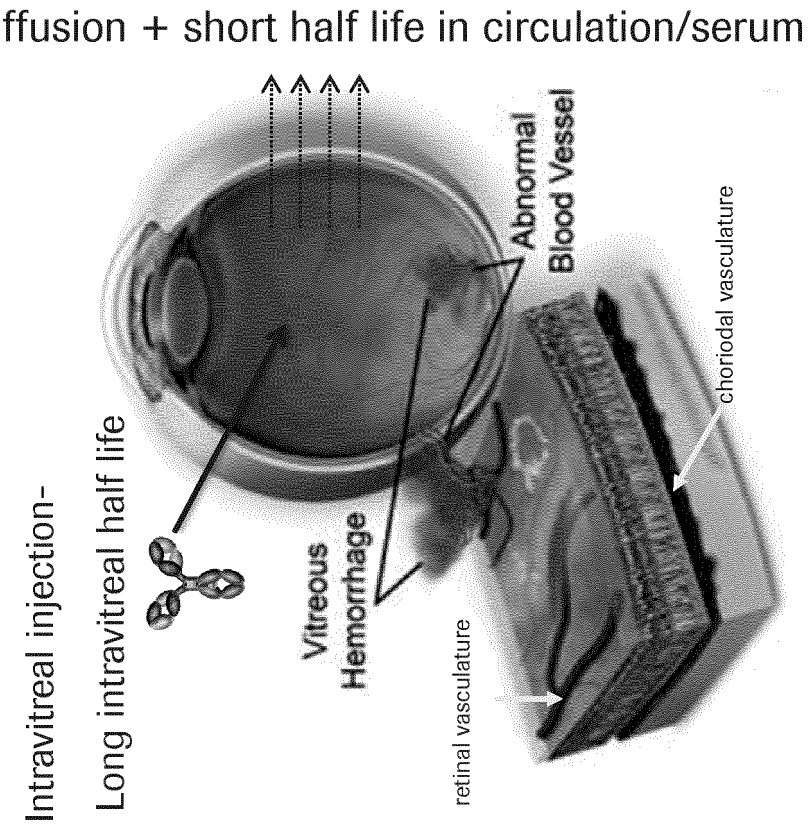

Diffusion + short half life in circulation/serum
Intravitreal injection-
Long intravitreal half life
Vitreous Hemorrhage
Abnormal Blood Vessel
retinal vasculature
choriodal vasculature

Fig. 2

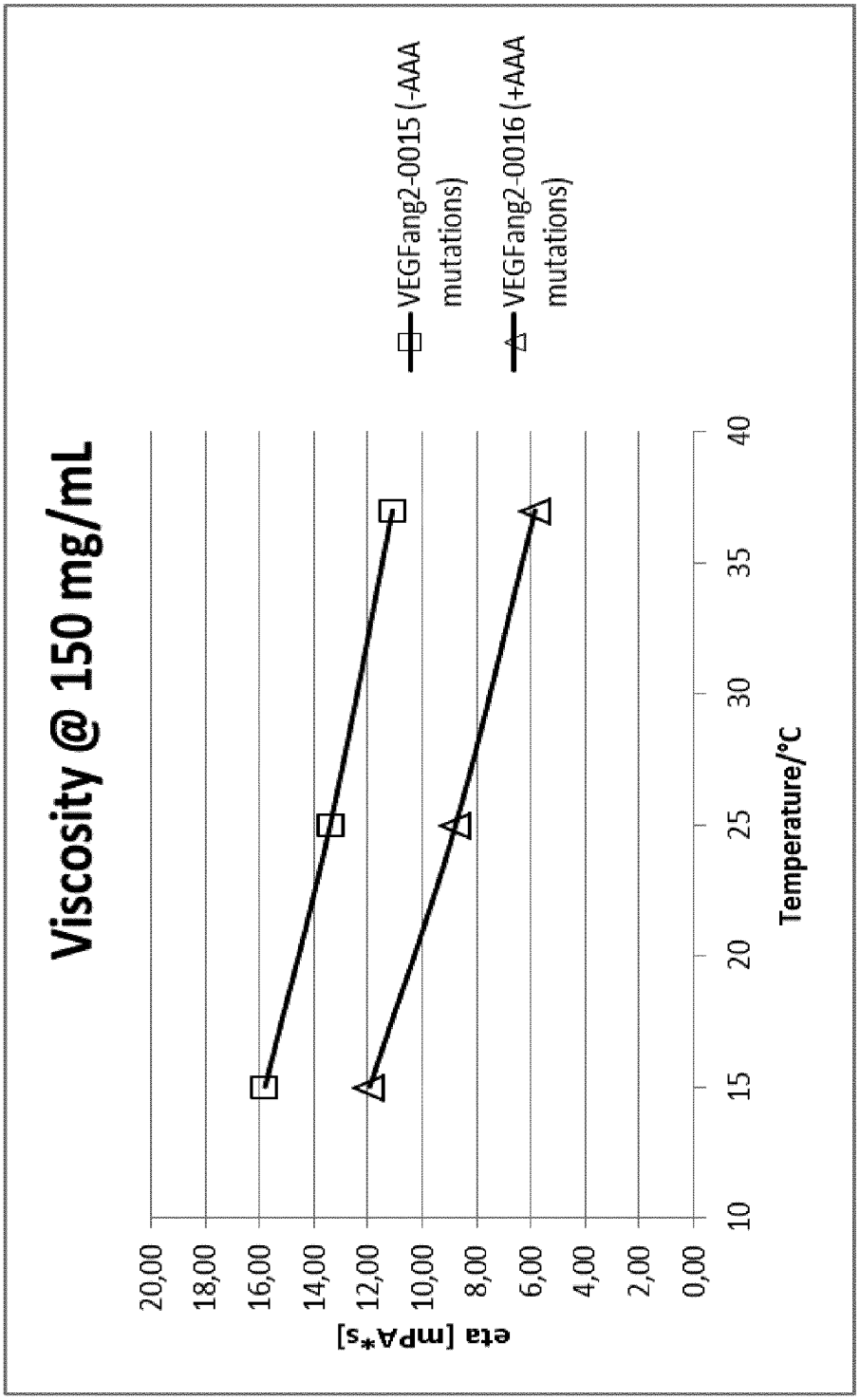

Viscosity @ 150 mg/mL
VEGFang2-0015 (-AAA mutations)
VEGFang2-0016 (+AAA mutations)
eta [mPA*s]
20,00
18,00
16,00
14,00
12,00
10,00
8,00
6,00
4,00
2,00
0,00
10
15
20
25
30
35
40
Temperature/°C

Fig. 3

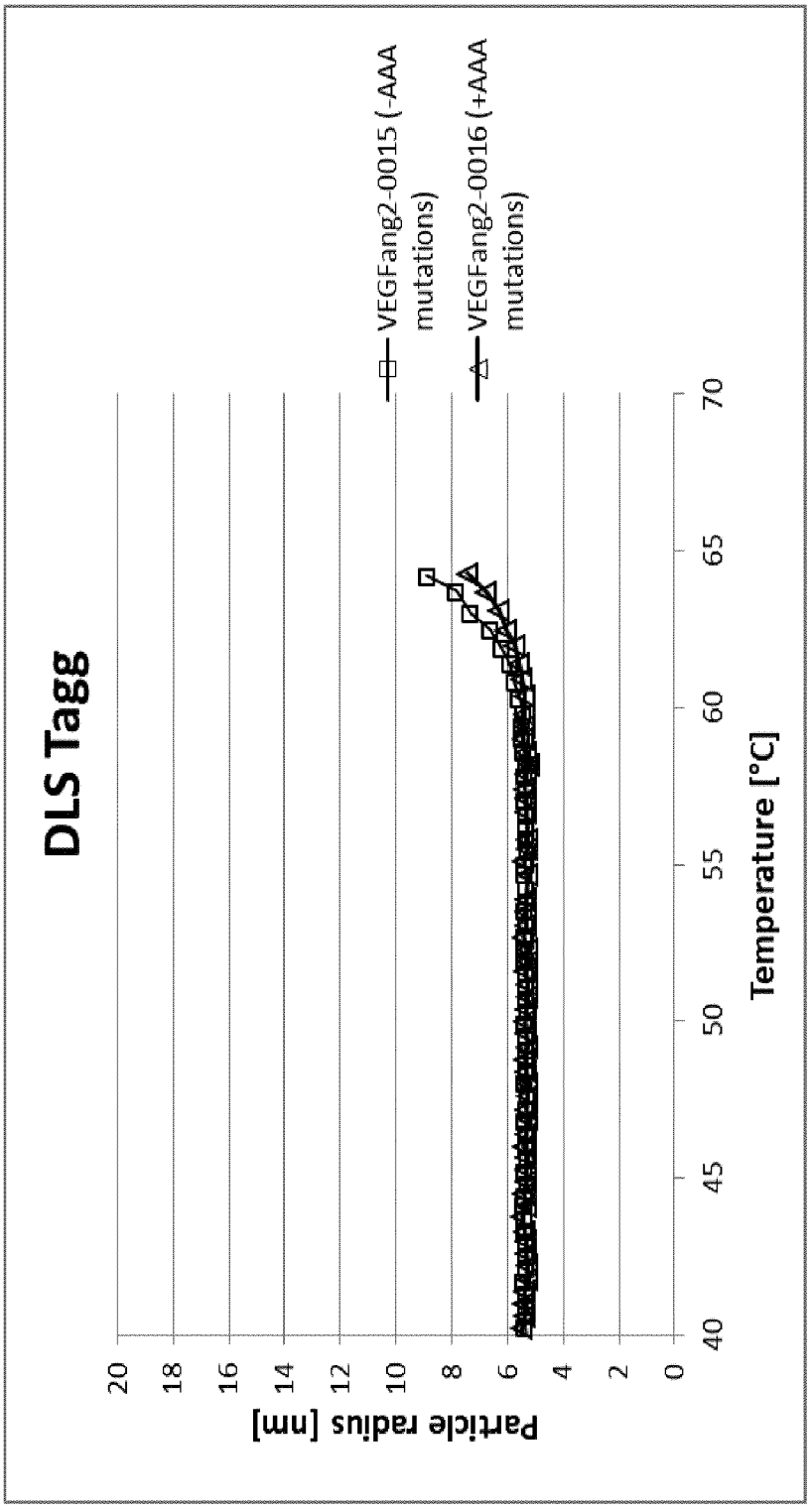

DLS Tagg
VEGFang2-0015 (-AAA mutations)
VEGFang2-0016 (+AAA mutations)
Particle radius [nm]
Temperature [°C]
0
2
4
6
8
10
12
14
16
18
20
40
45
50
55
60
65
70

Fig. 4

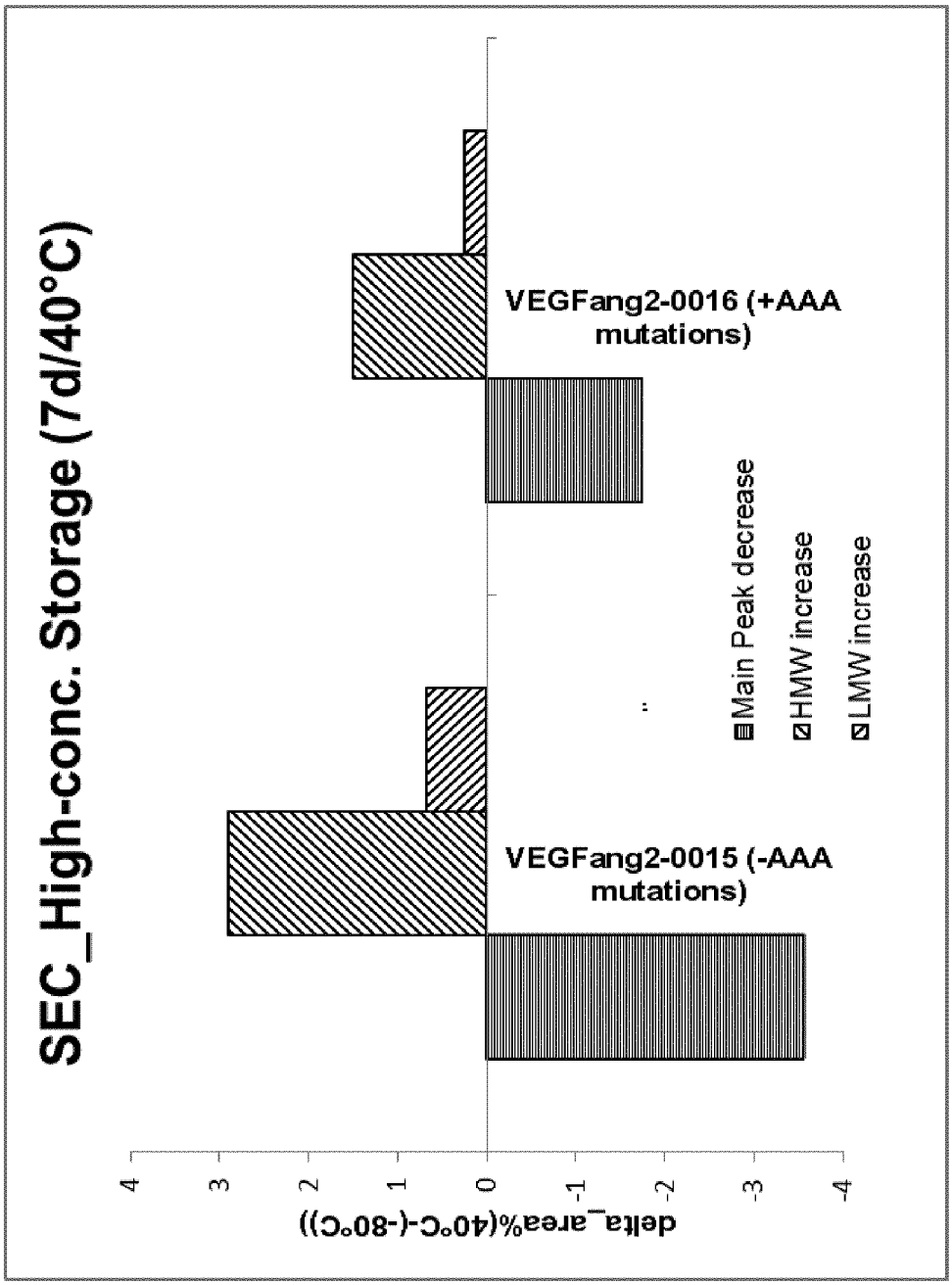

SEC_High-conc. Storage (7d/40°C)
VEGFang2-0016 (+AAA mutations)
VEGFang2-0015 (-AAA mutations)
Main Peak decrease
HMW increase
LMW increase
delta_area%(40°C-(-80°C))
4
3
2
1
0
-1
-2
-3
-4

Fig. 5A

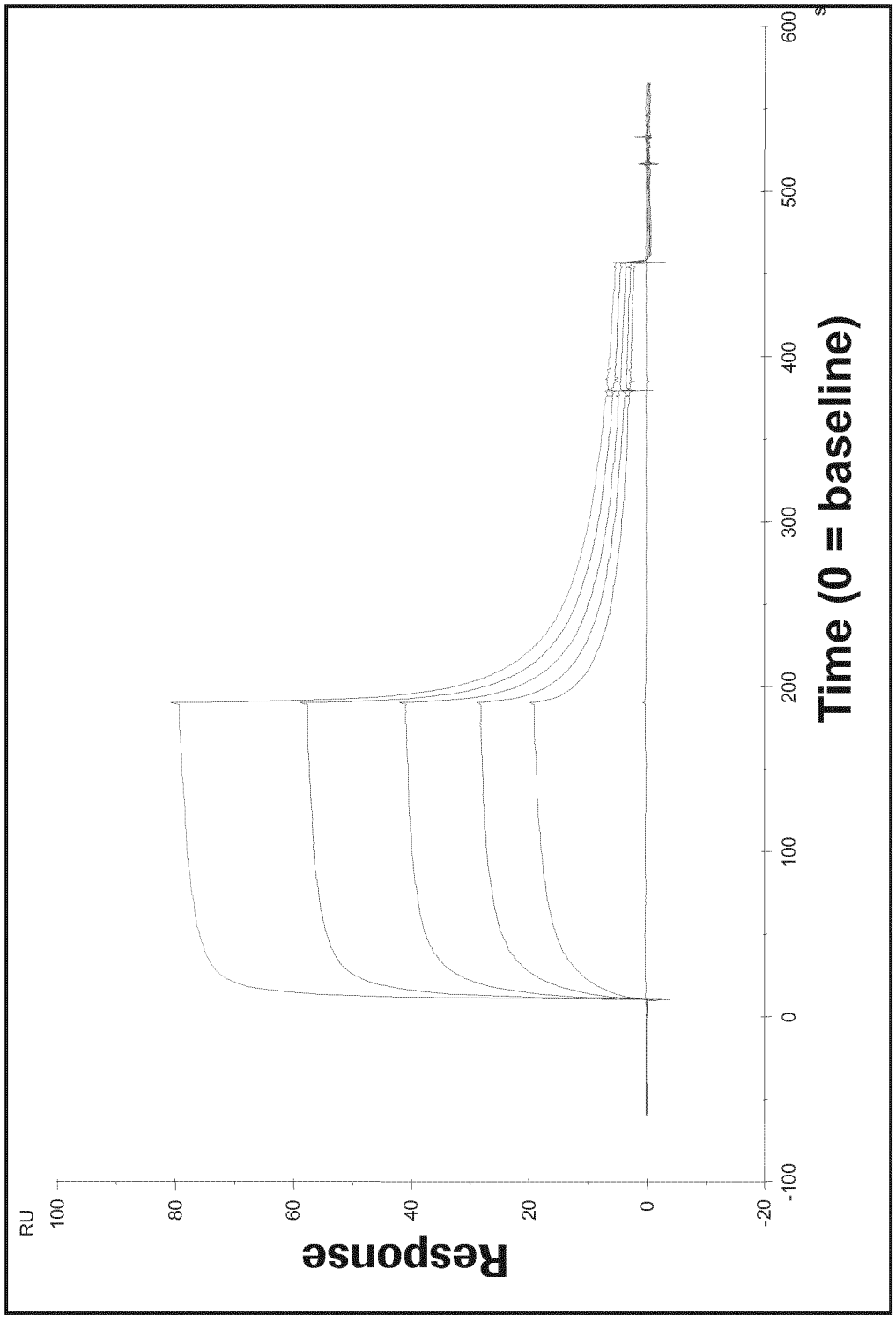

Response
RU
100
80
60
40
20
0
-20
-100
0
100
200
300
400
500
600
Time (0 = baseline)

Fig. 5B

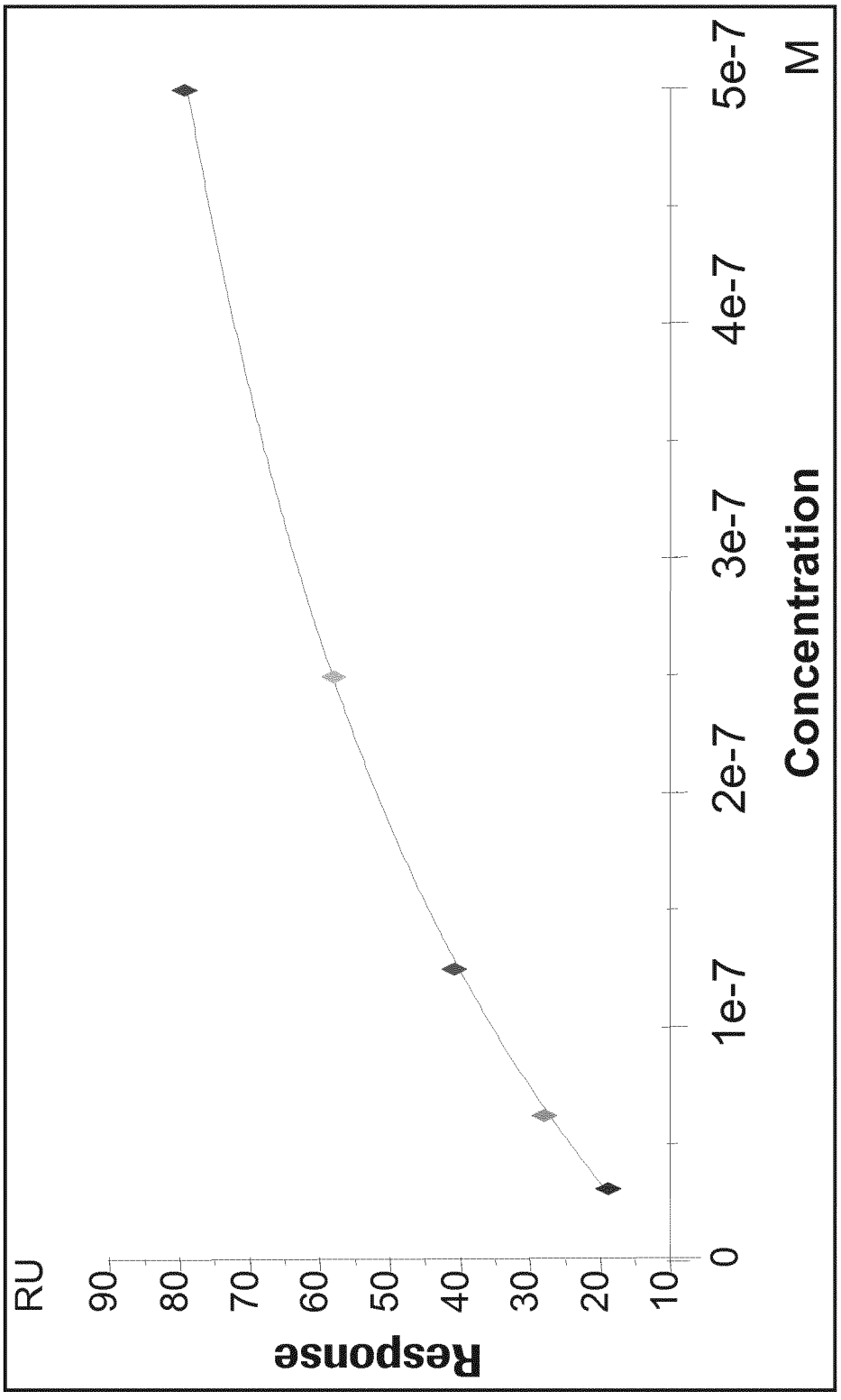

RU
90
80
70
60
50
40
30
20
10
Response
0
1e-7
2e-7
3e-7
4e-7
5e-7
M
Concentration

Fig. 5C

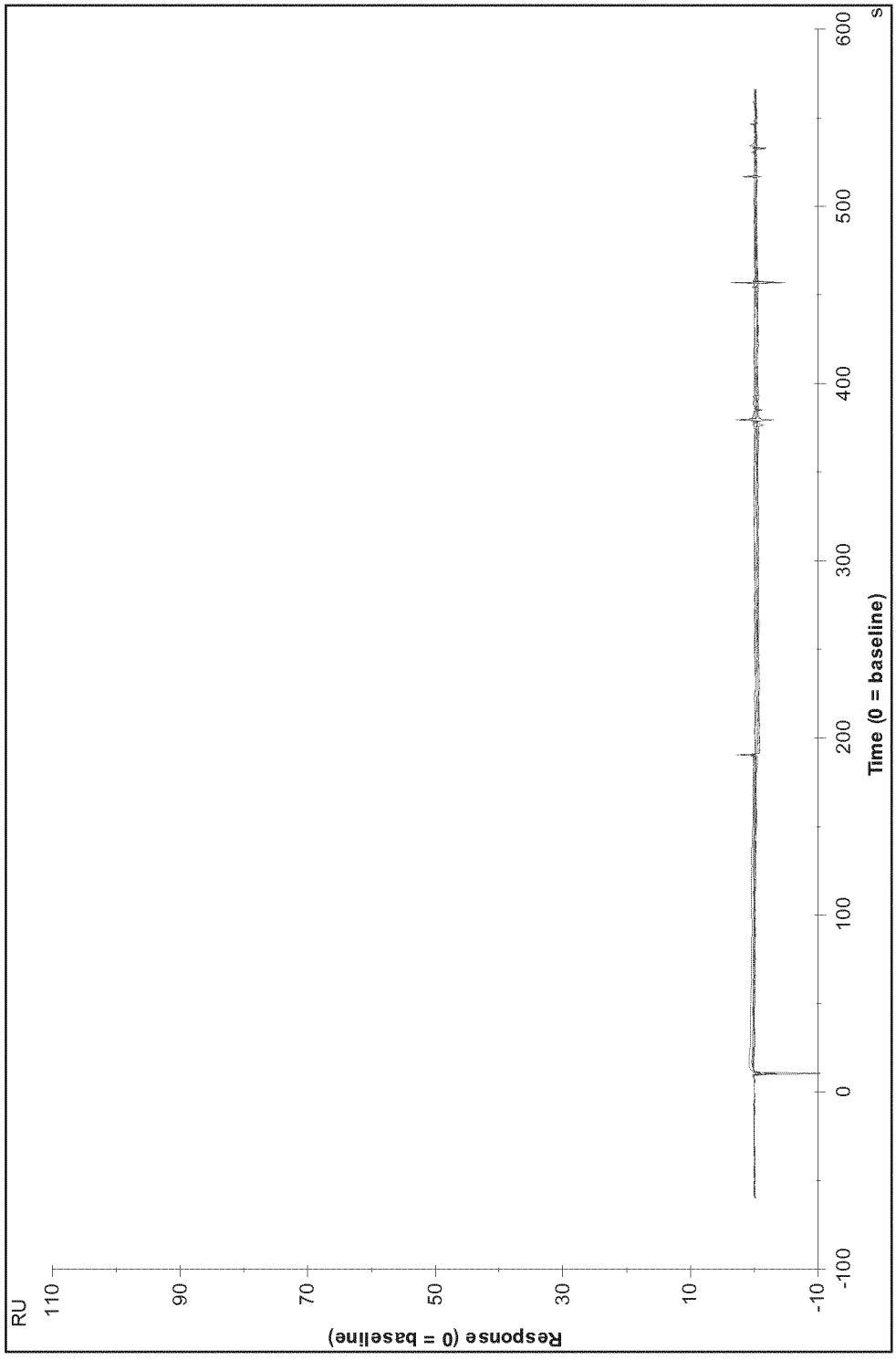

RU
110
90
70
50
30
10
-10
Response (0 = baseline)
-100
0
100
200
300
400
500
600
s
Time (0 = baseline)

Fig. 5D

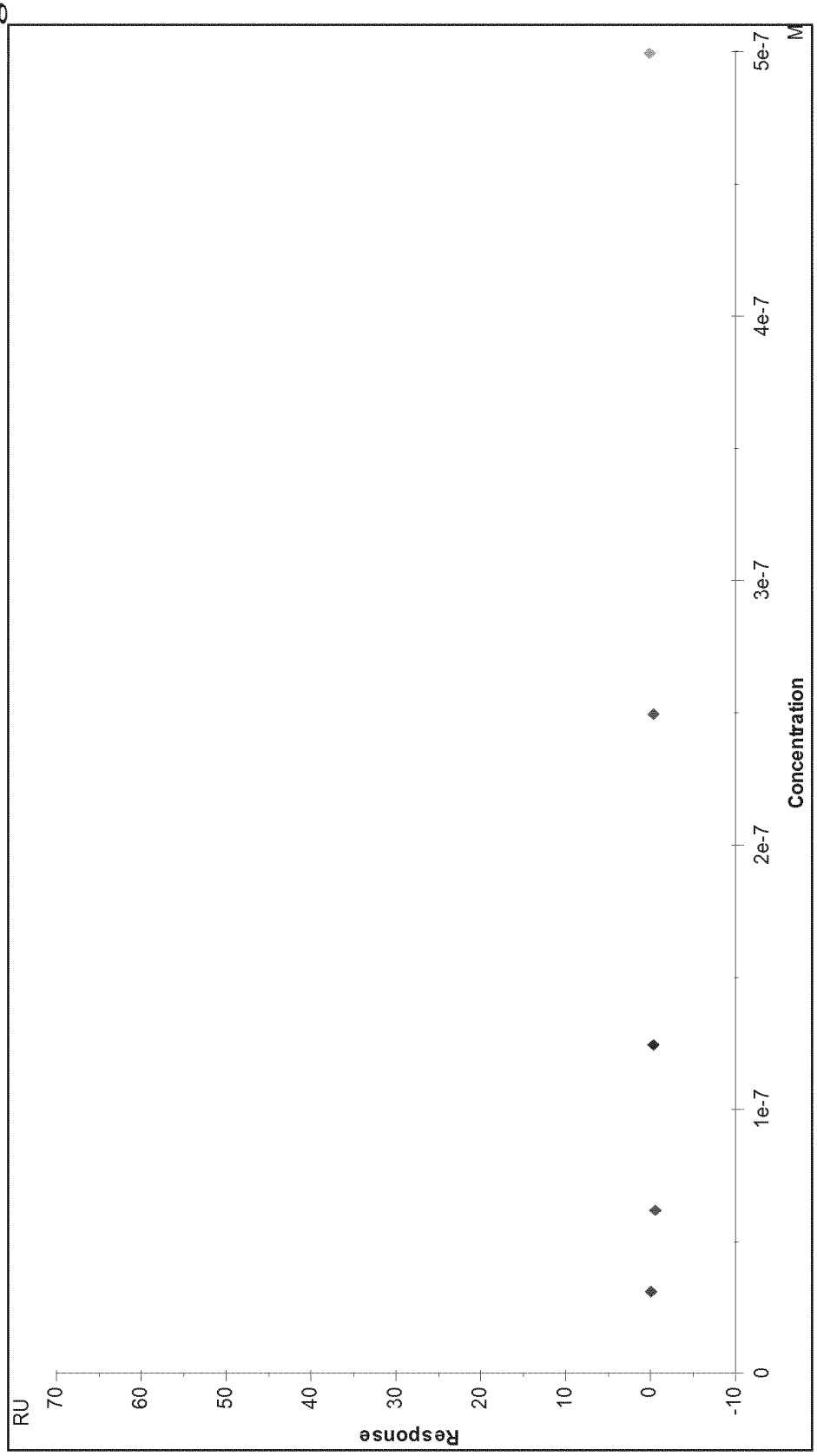

RU
70
60
50
40
30
20
10
0
-10
Response
0
1e-7
2e-7
3e-7
4e-7
5e-7
M
Concentration

Fig. 5E

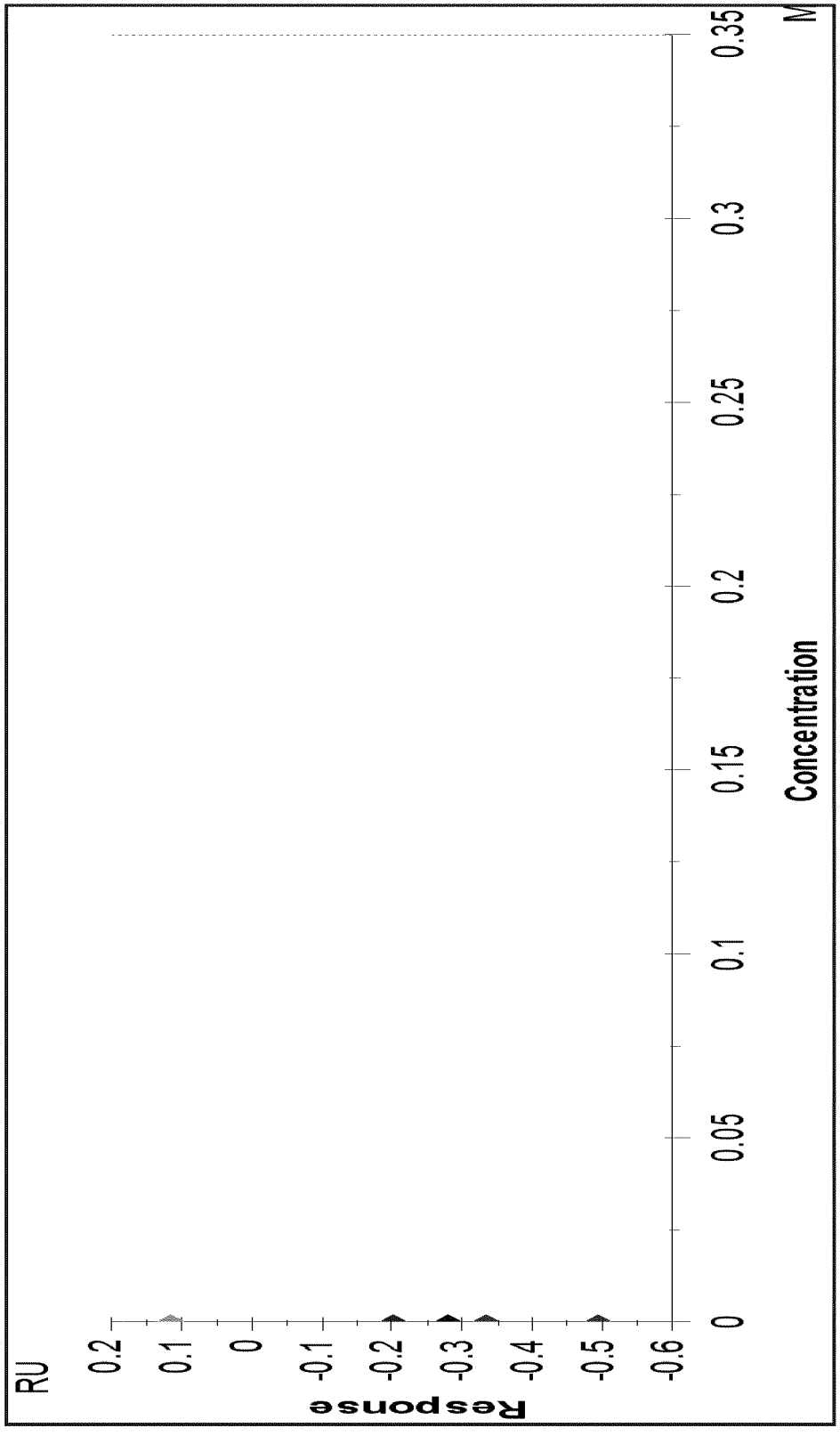

RU
0.2
0.1
0
-0.1
-0.2
-0.3
-0.4
-0.5
-0.6
Response
0
0.05
0.1
0.15
0.2
0.25
0.3
0.35
M
Concentration

Fig. 6

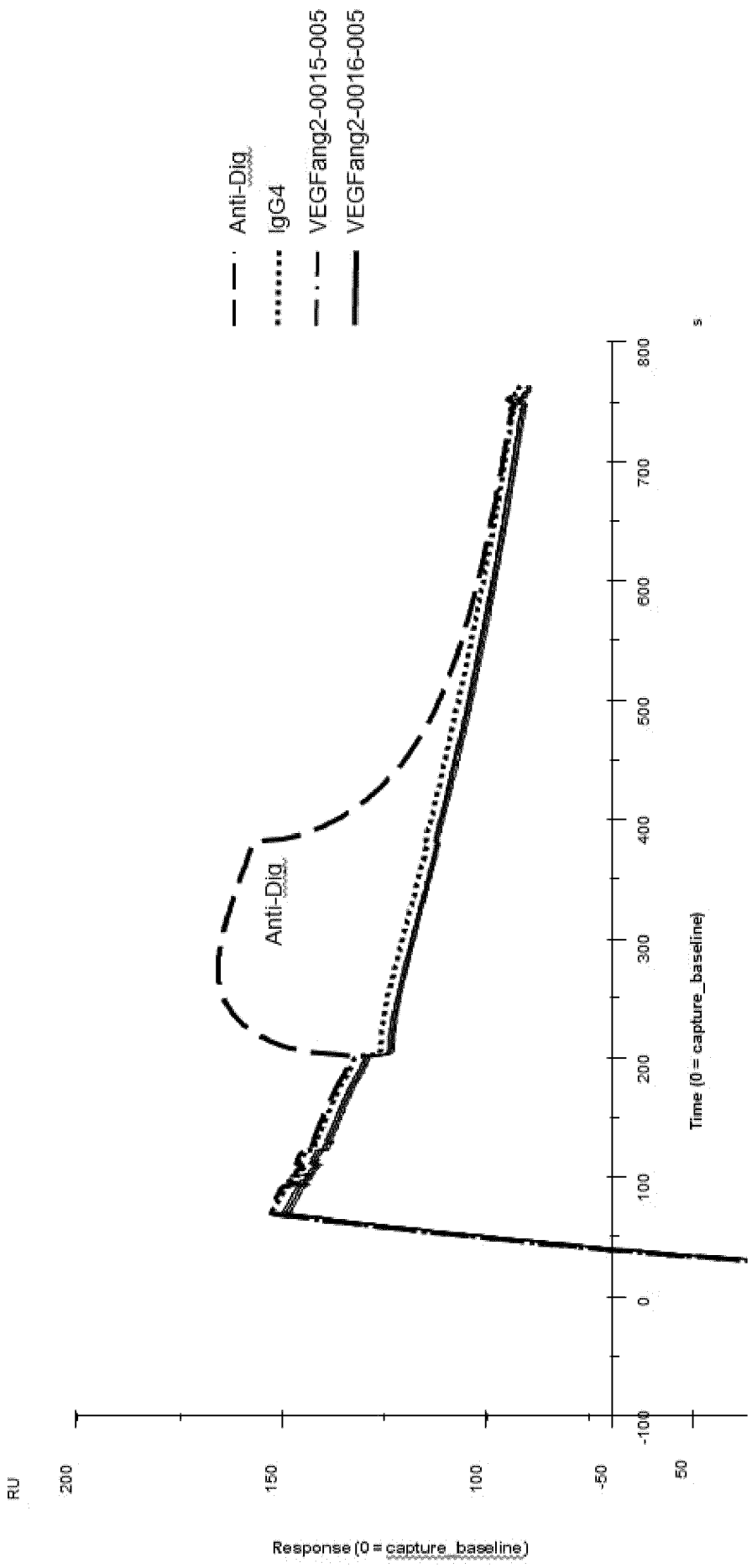

Anti-Dig
IgG4
VEGFang2-0015-005
VEGFang2-0016-005
Anti-Dig
RU
200
150
100
50
-50
-100
0
100
200
300
400
500
600
700
800
s
Time (0 = capture_baseline)
Response (0 = capture_baseline)

Fig. 7A

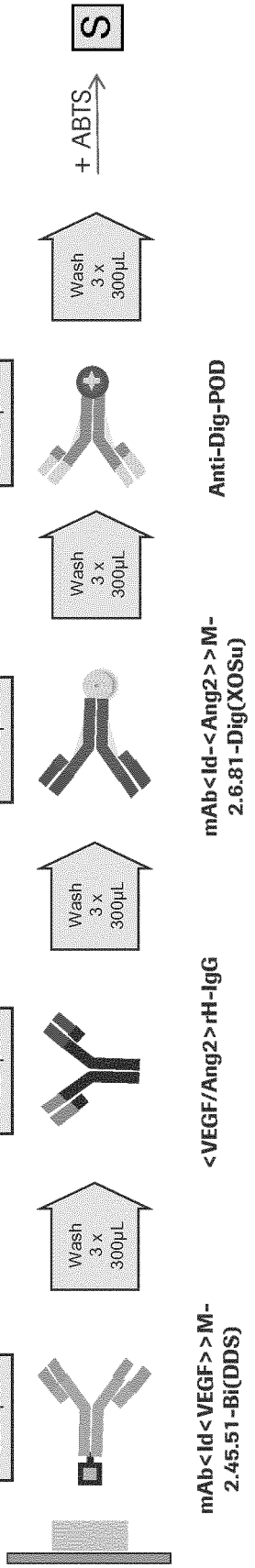

Incubation 1h at RT, 500 rpm
Wash 3 x 300µL
Incubation 1h at RT, 500 rpm
Wash 3 x 300µL
Incubation 1h at RT, 500 rpm
Wash 3 x 300µL
Incubation 1h at RT, 500 rpm
Wash 3 x 300µL
+ ABTS
S
mAb<Id<VEGF>>M-2.45.51-Bi(DDS)
<VEGF/Ang2>rH-IgG
mAb<Id-<Ang2>>M-2.6.81-Dig(XOSu)
Anti-Dig-POD

Fig. 7B

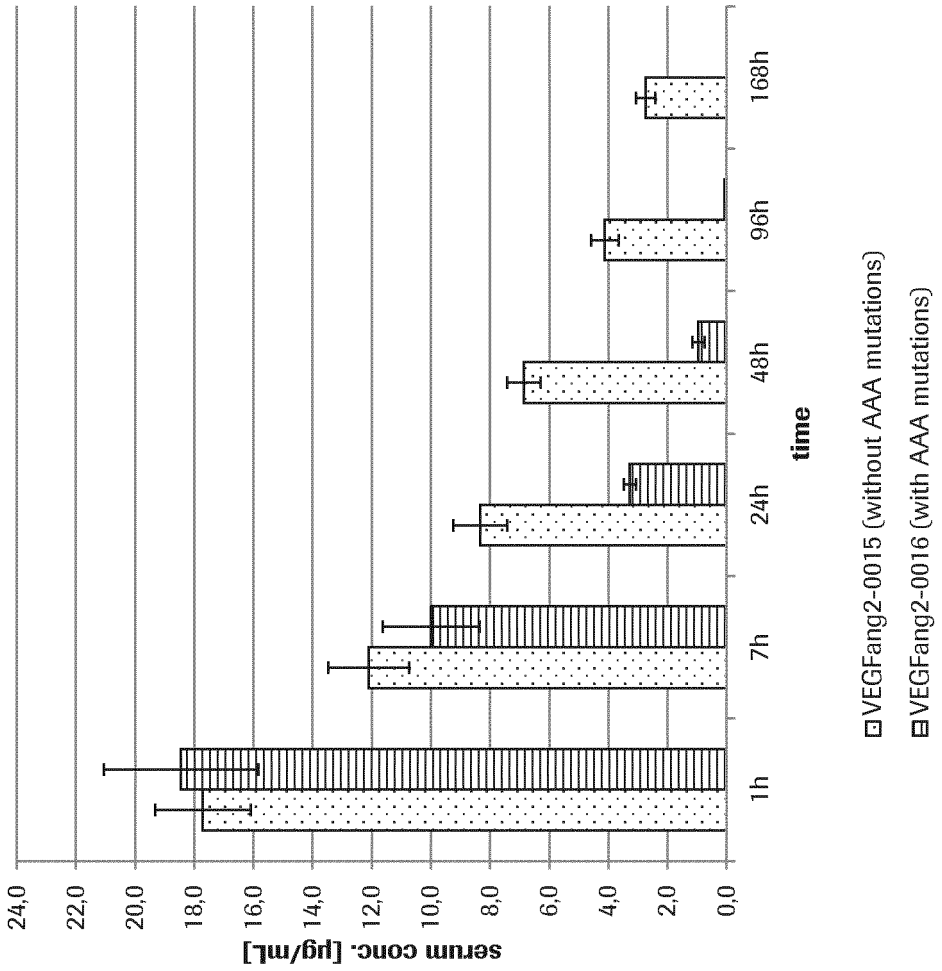

serum conc. [µg/mL]
24,0
22,0
20,0
18,0
16,0
14,0
12,0
10,0
8,0
6,0
4,0
2,0
0,0
1h
7h
24h
48h
96h
168h
time
VEGFang2-0015 (without AAA mutations)
VEGFang2-0016 (with AAA mutations)

Fig. 7C

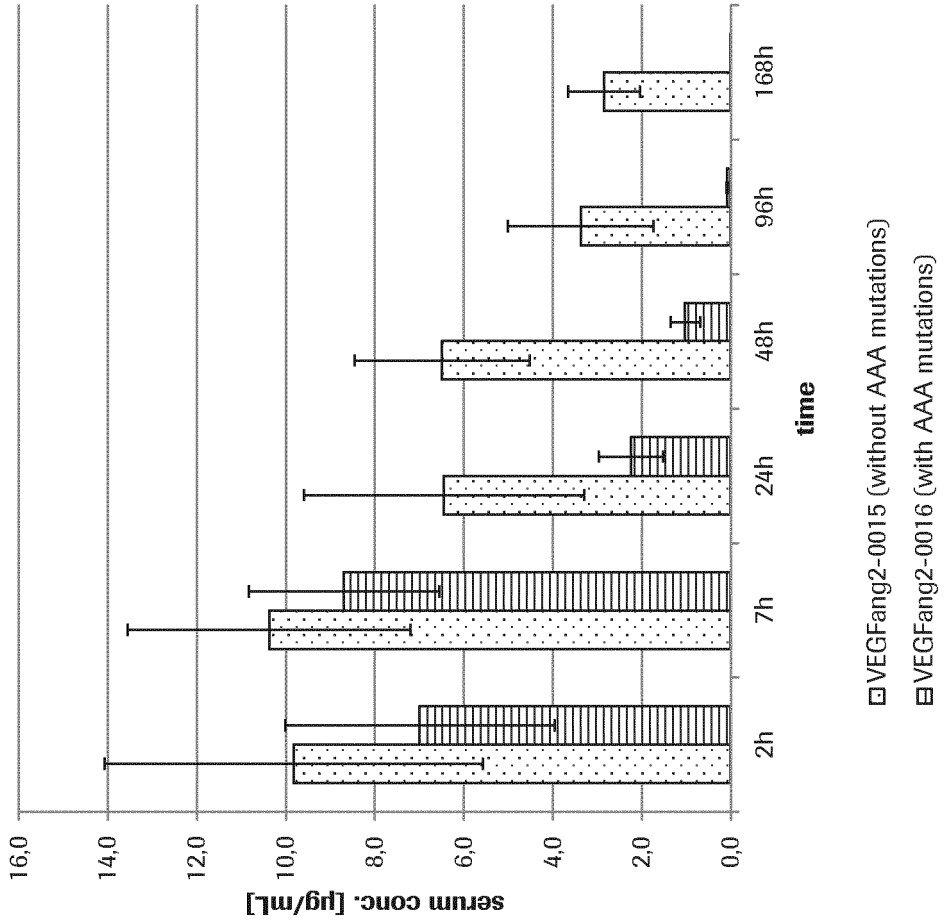

serum conc. [µg/mL]
16,0
14,0
12,0
10,0
8,0
6,0
4,0
2,0
0,0
2h
7h
24h
48h
96h
168h
time
VEGFang2-0015 (without AAA mutations)
VEGFang2-0016 (with AAA mutations)

Fig. 7D

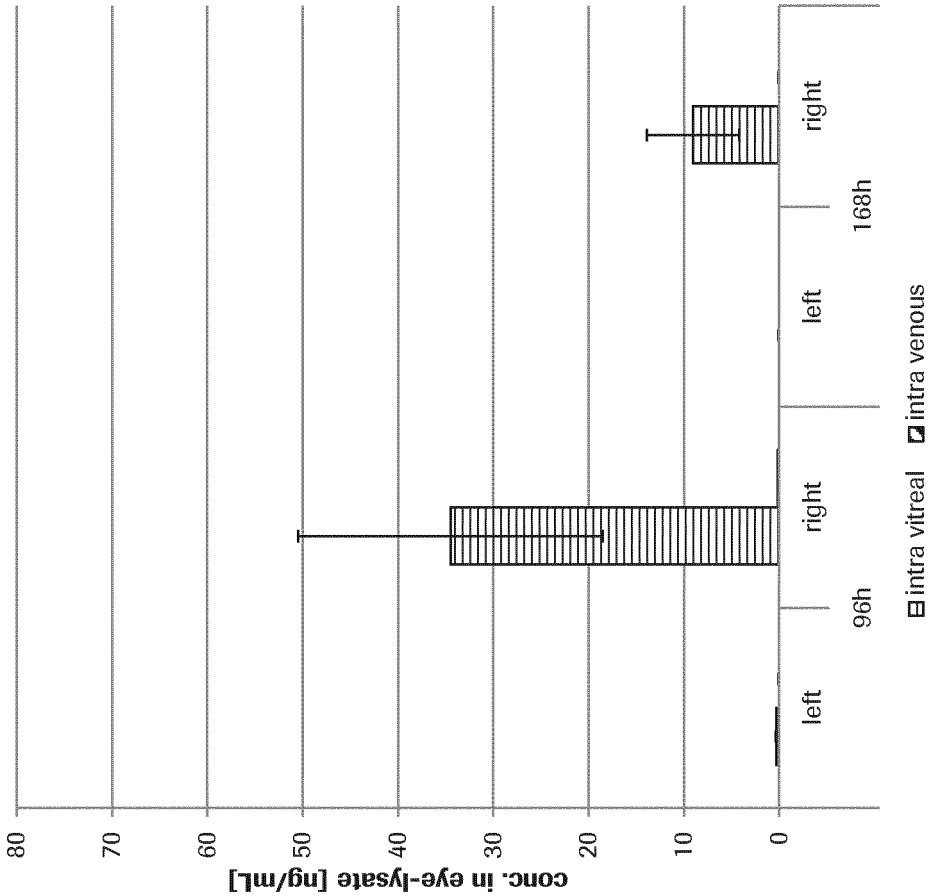
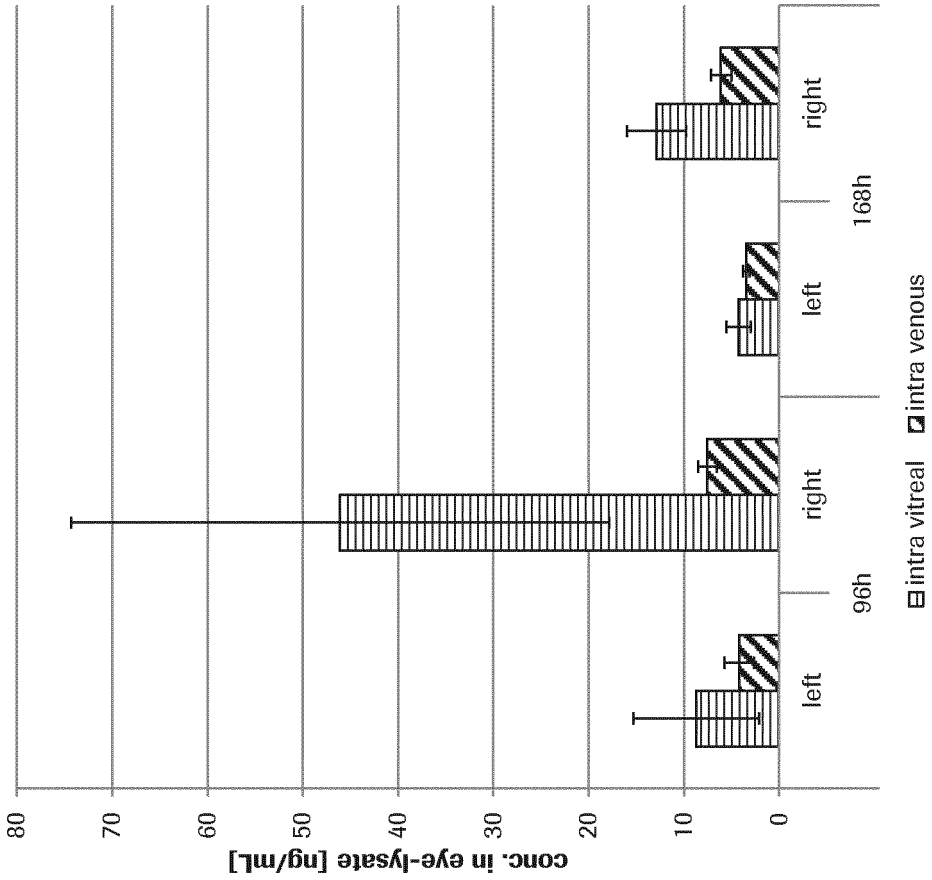

conc. in eye-lysate [ng/mL]
0
10
20
30
40
50
60
70
80
left
right
96h
left
right
168h
intra vitreal
intra venous

Fig. 7E


conc. in eye-lysate [ng/mL]
0
10
20
30
40
50
60
70
80
left
right
96h
left
right
168h
intra vitreal
intra venous