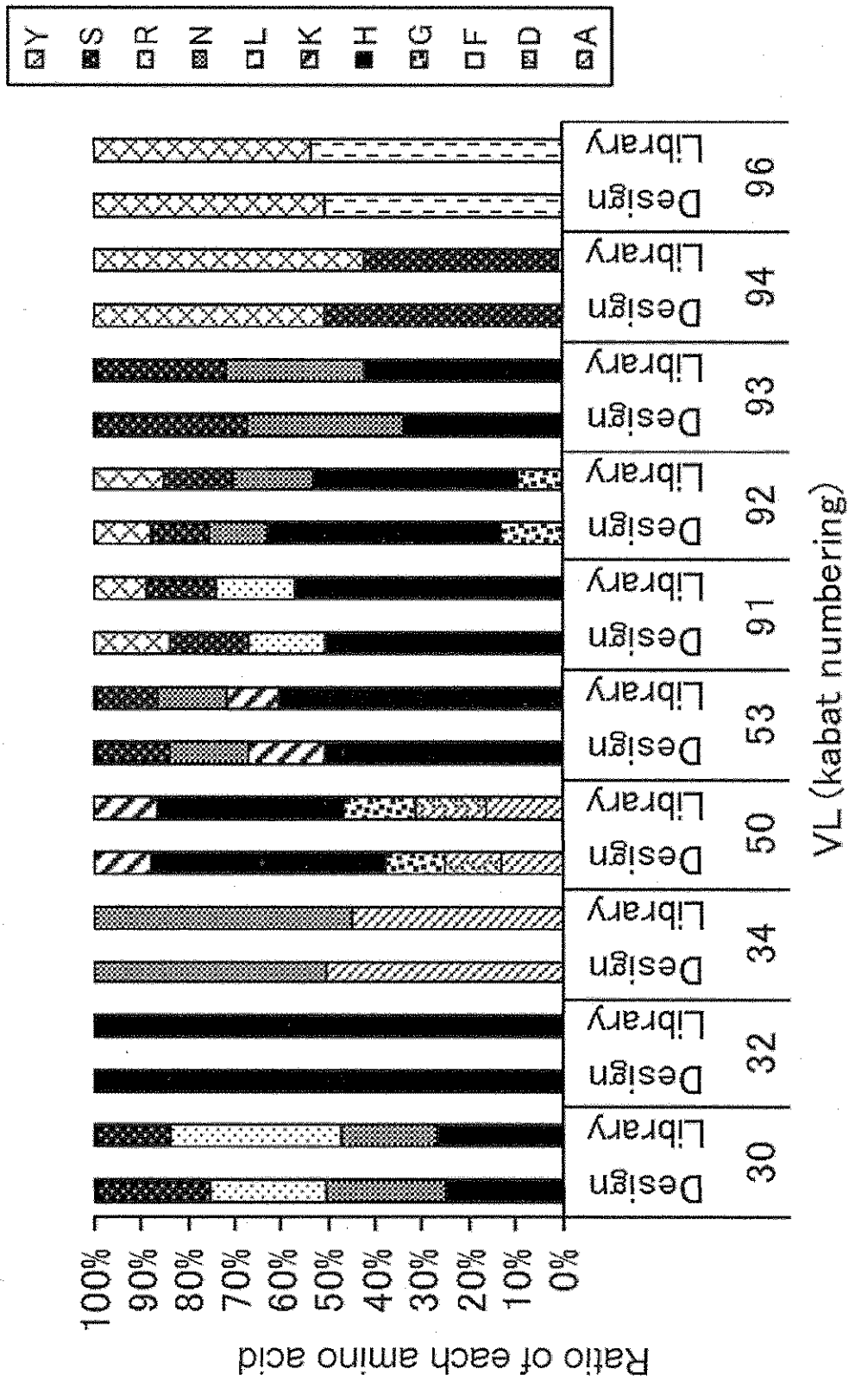

Y
S
R
N
L
K
H
G
F
D
A
Design
Library
30
32
34
50
53
91
92
93
94
96
VL (kabat numbering)
100%
90%
80%
70%
60%
50%
40%
30%
20%
10%
0%
Ratio of each amino acid

FIG.1

FIG.2

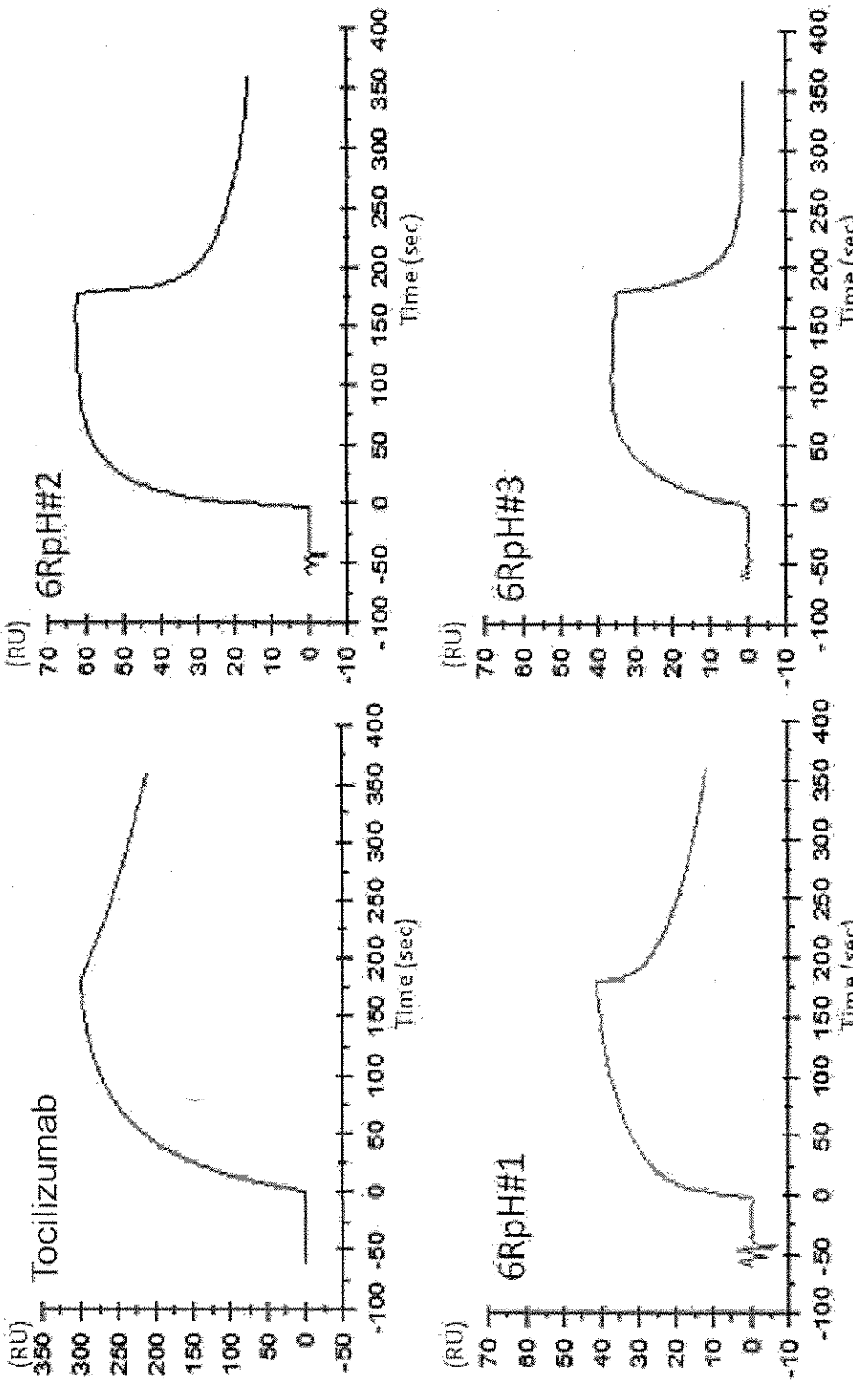


FIG.3

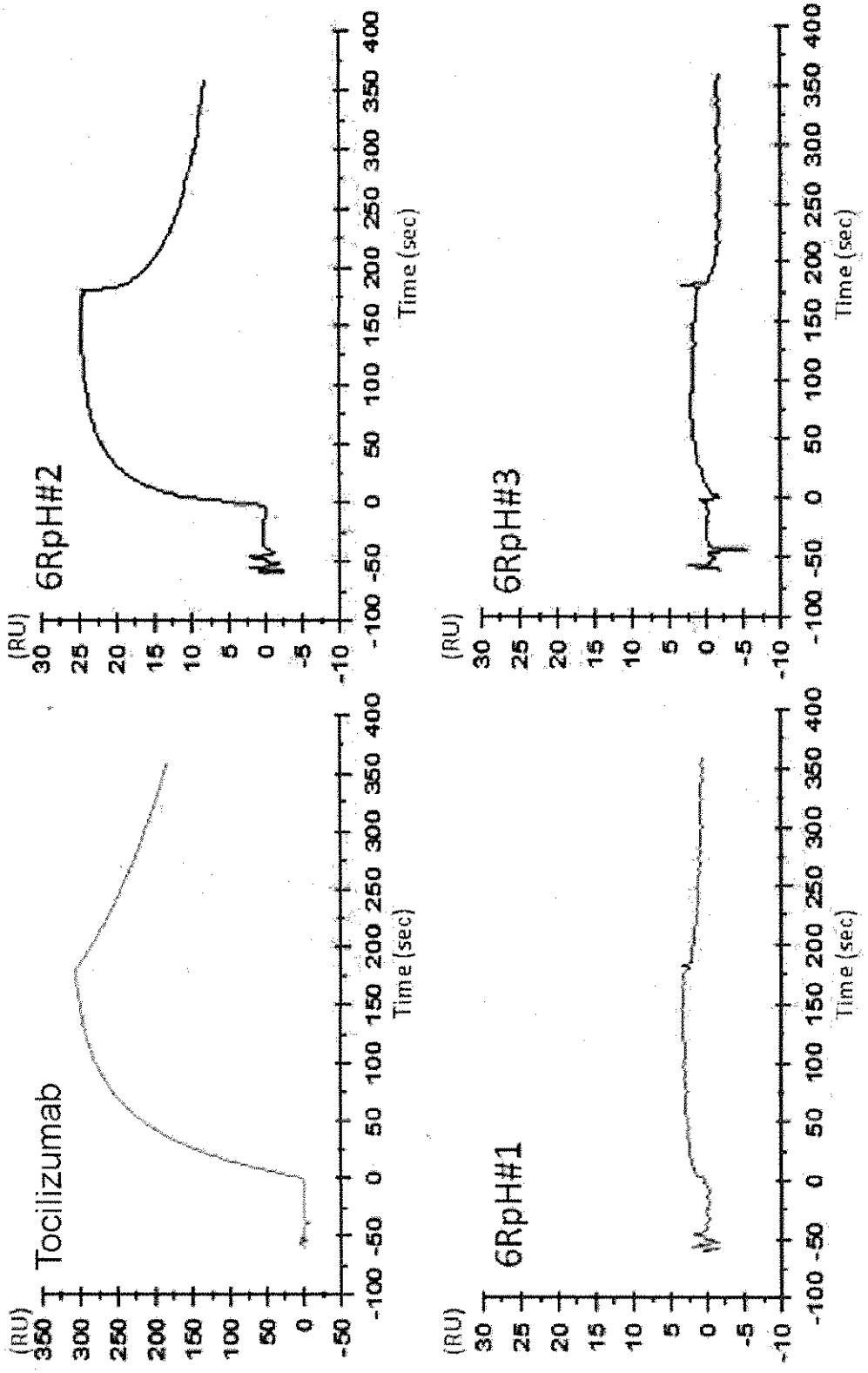


FIG.4A

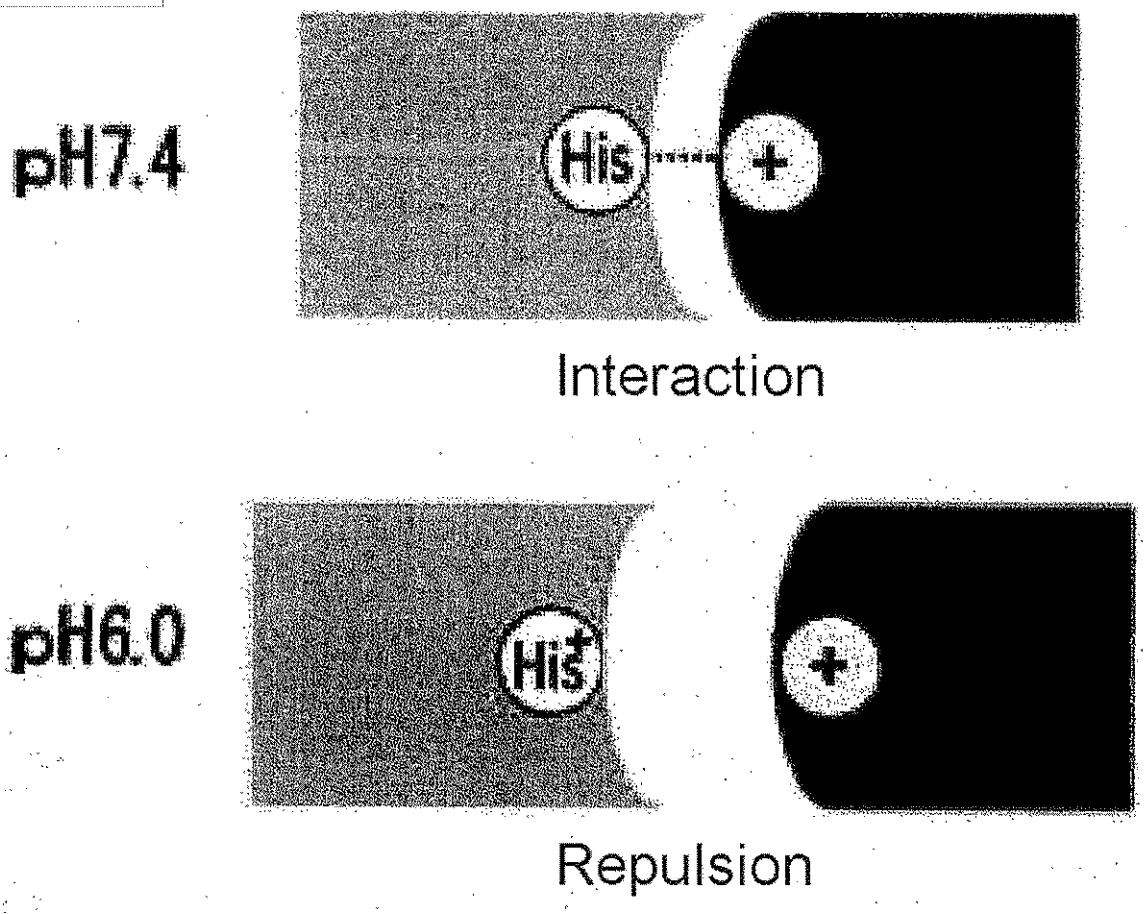


FIG.4B

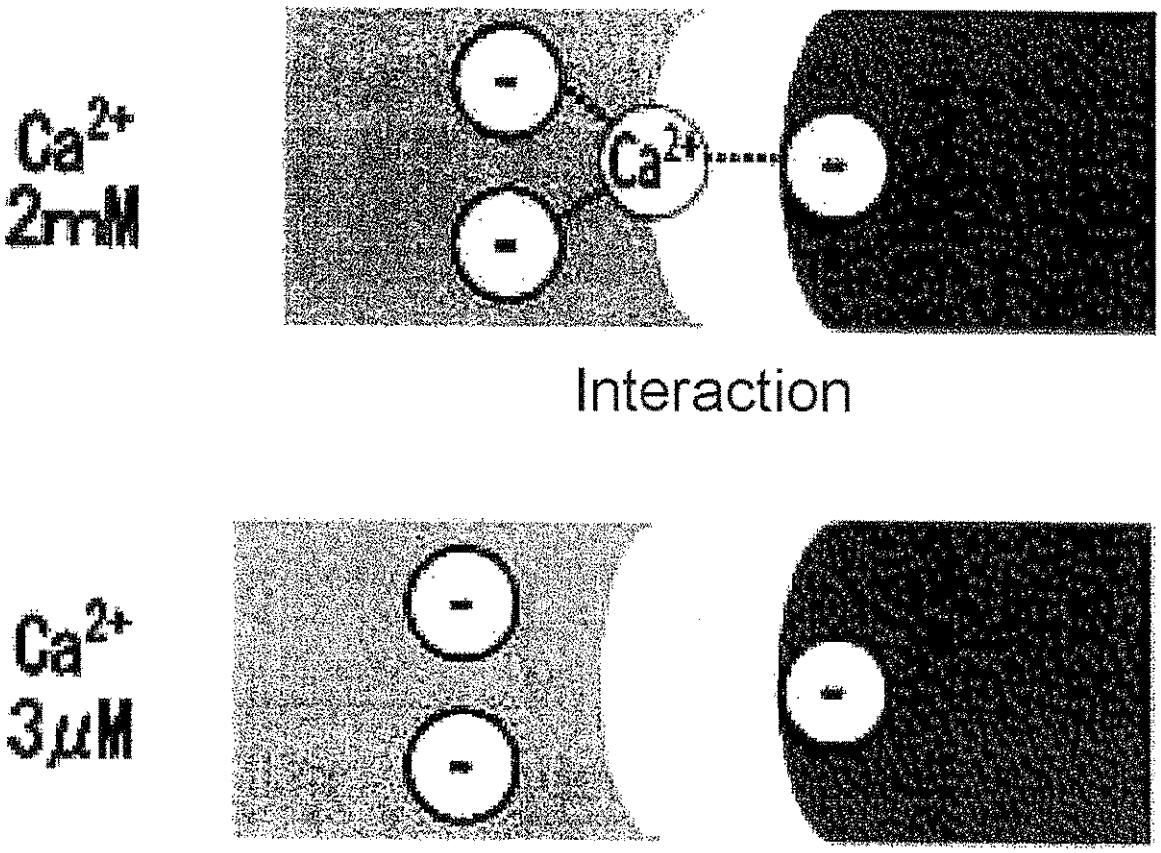


FIG.4C

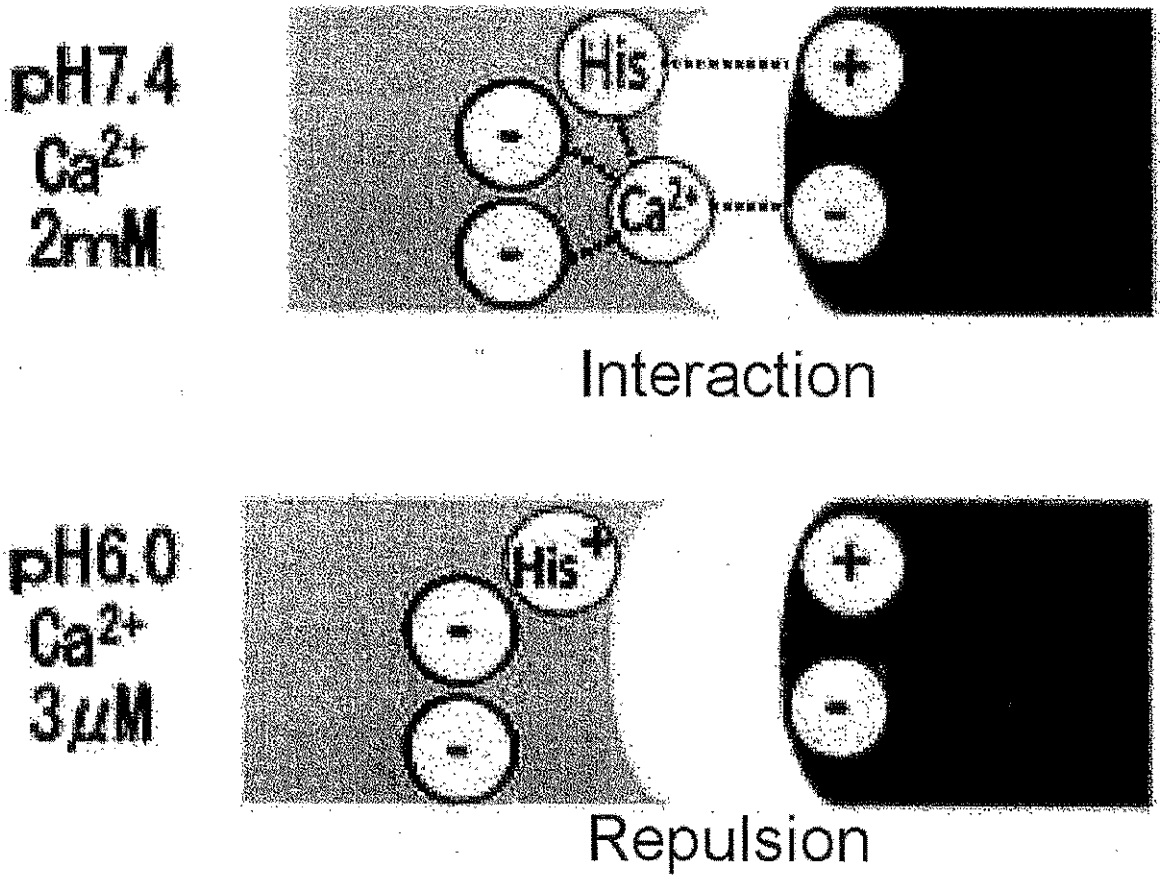


FIG.5

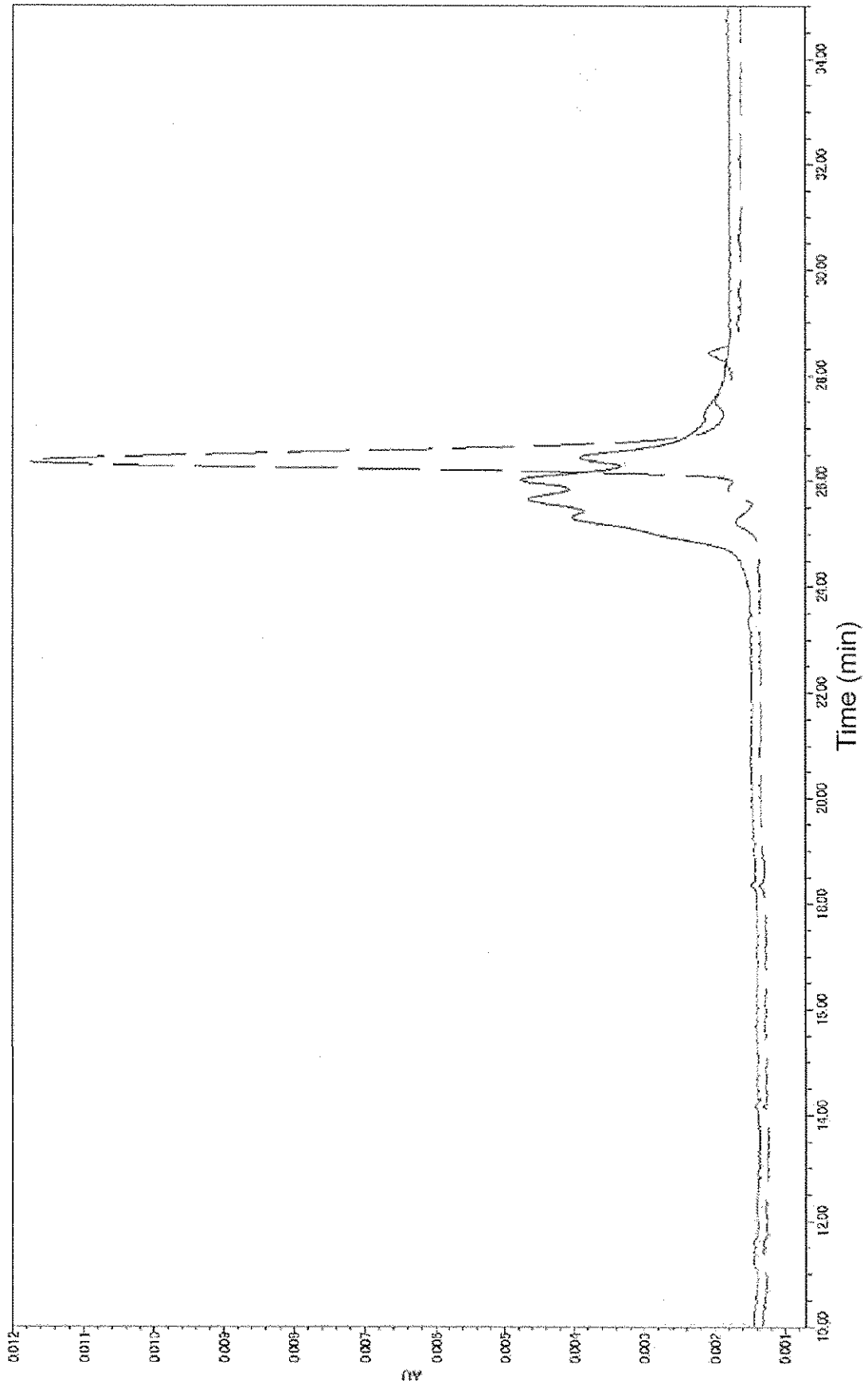

AU
0.012
0.011
0.010
0.009
0.008
0.007
0.006
0.005
0.004
0.003
0.002
0.001
10.00
12.00
14.00
16.00
18.00
20.00
22.00
24.00
26.00
28.00
30.00
32.00
34.00
Time (min)

FIG.6

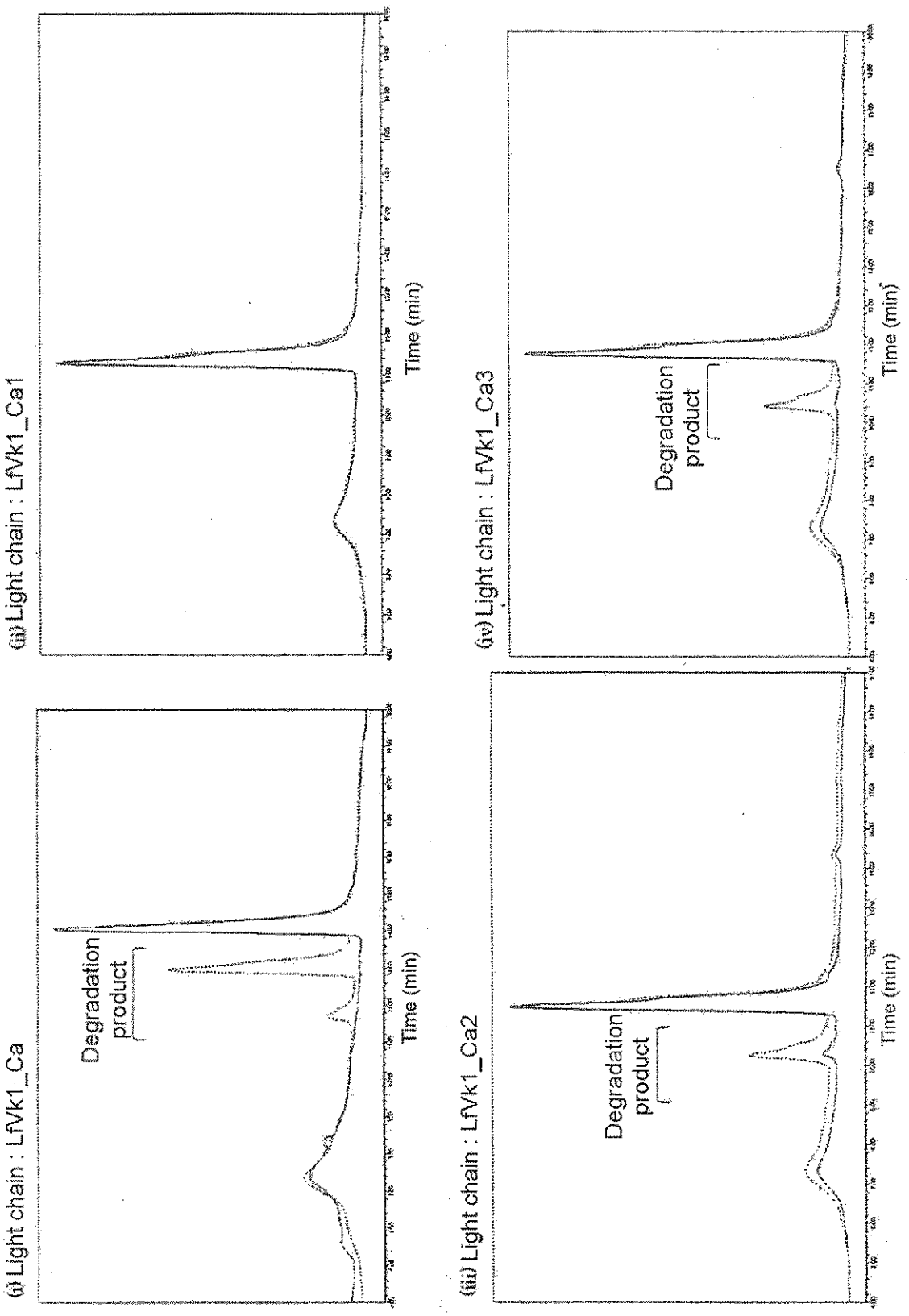
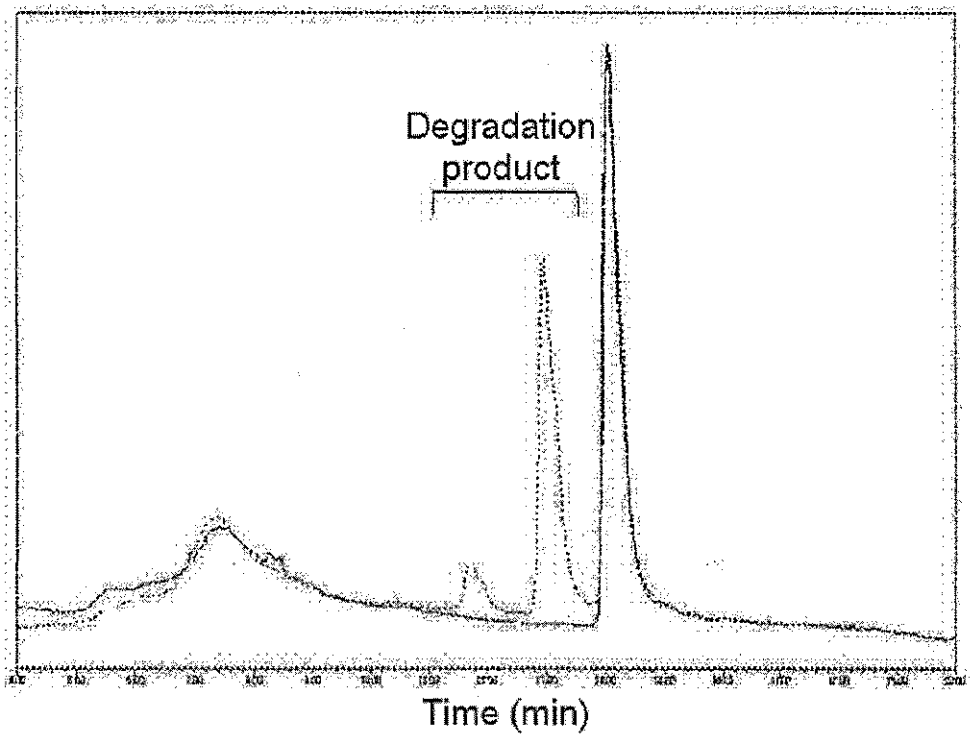
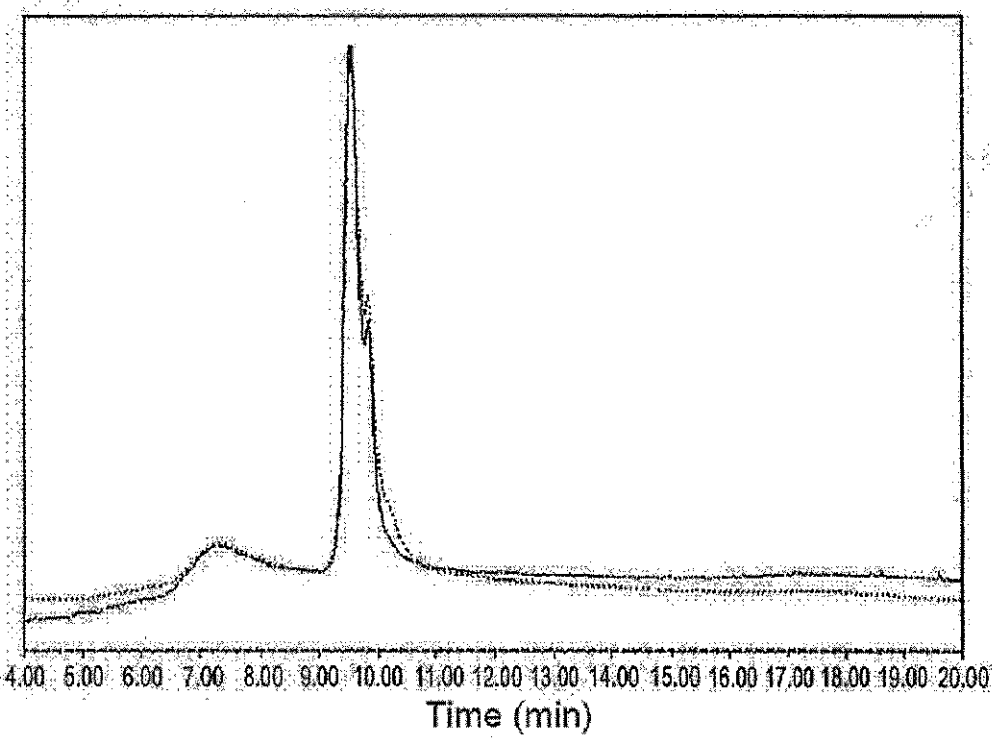

(i) Light chain : LfVk1_Ca
Degradation product
Time (min)
(ii) Light chain : LfVk1_Ca1
Time (min)
(iii) Light chain : LfVk1_Ca2
Degradation product
Time (min)
(iv) Light chain : LfVk1_Ca3
Degradation product
Time (min)

FIG.7

(i) Light chain : LfVk1_Ca



(ii) Light chain : LfVk1_Ca6



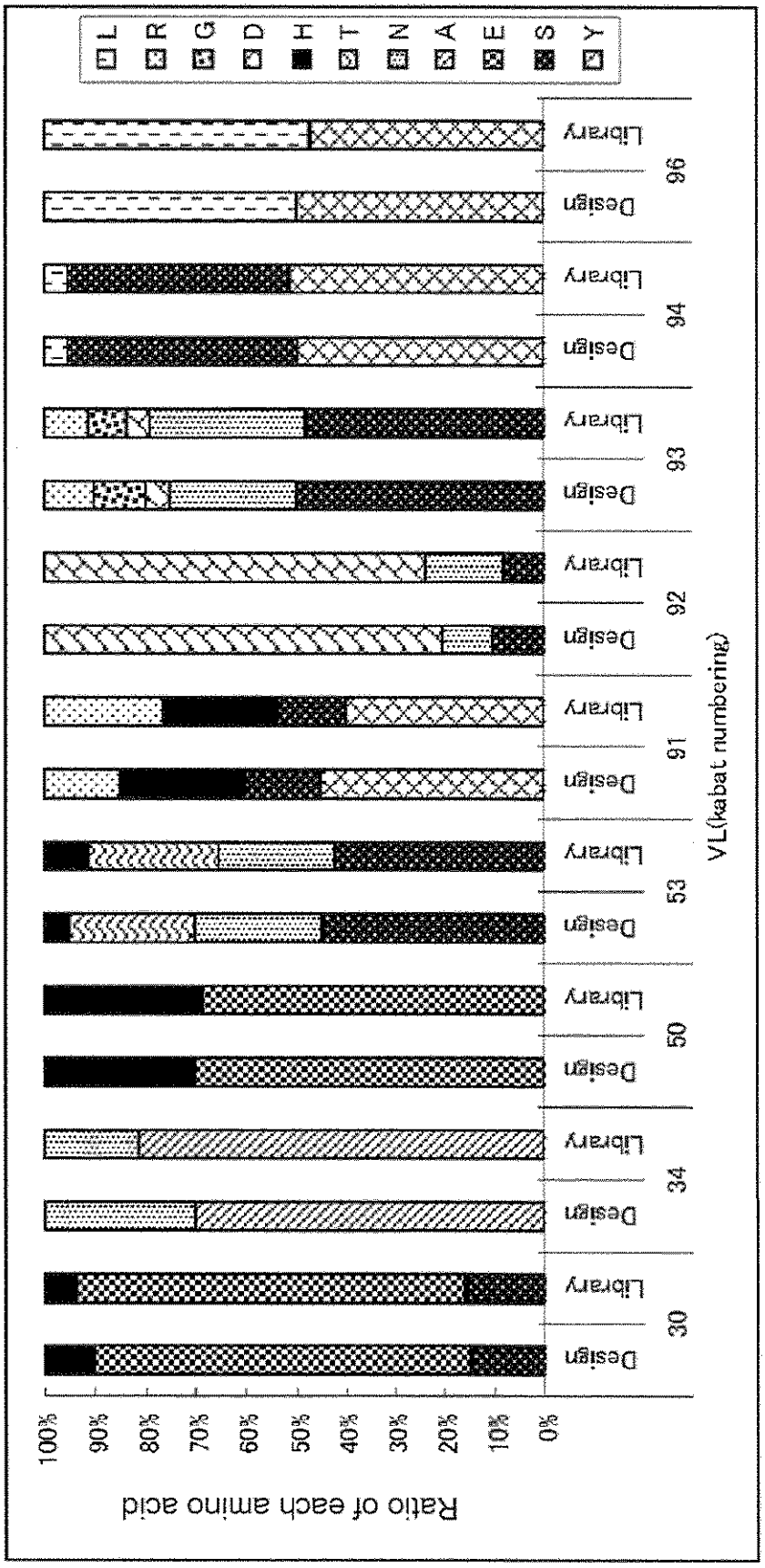

L
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E
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Y
Library
Design
96
94
93
92
91
53
50
34
30
VL(kabat numbering)
100%
90%
80%
70%
60%
50%
40%
30%
20%
10%
0%
Ratio of each amino acid

FIG.8

FIG.9

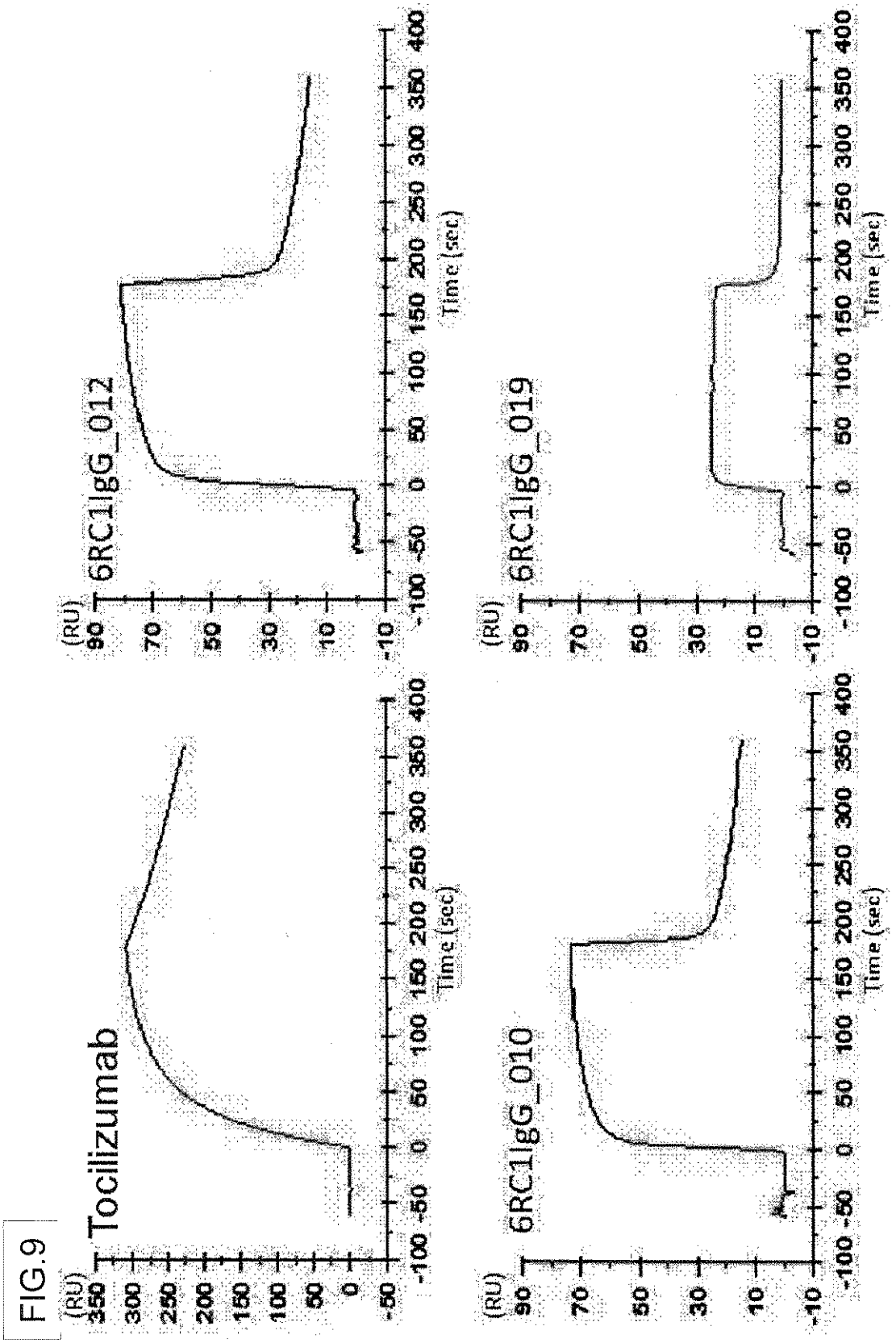

Tocilizumab
6RC1IgG_012
6RC1IgG_010
6RC1IgG_019
(RU)
Time (sec)

FIG.10

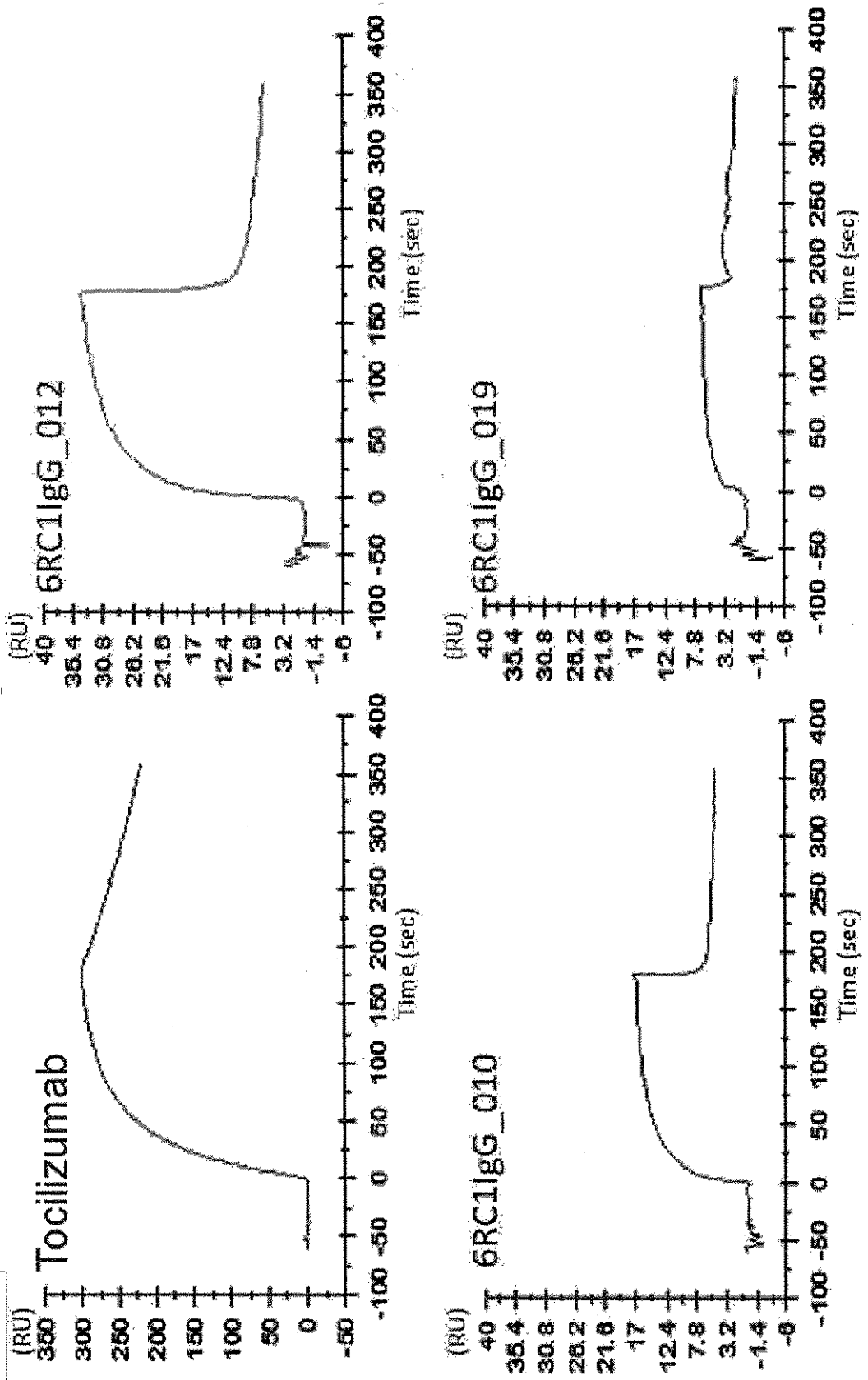
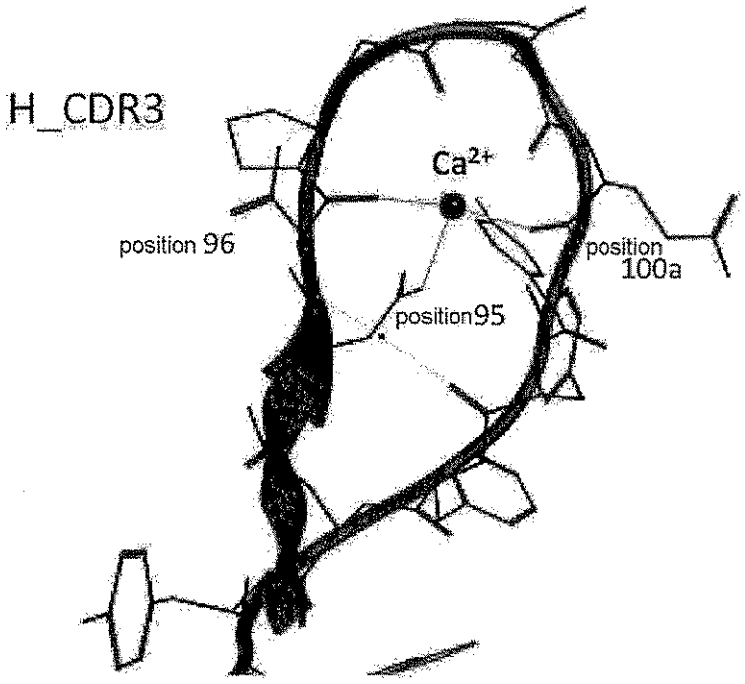

Tocilizumab
6RC1IgG_012
6RC1IgG_010
6RC1IgG_019
(RU)
Time (sec)

FIG.11

(i) Crystal structure in presence of calcium ion



(ii) Crystal structure in absence of calcium ion

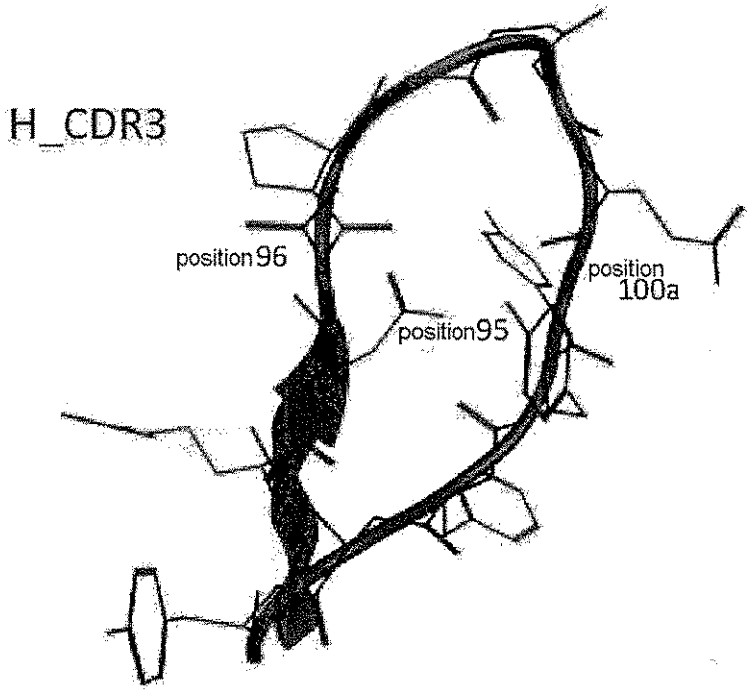


FIG.12

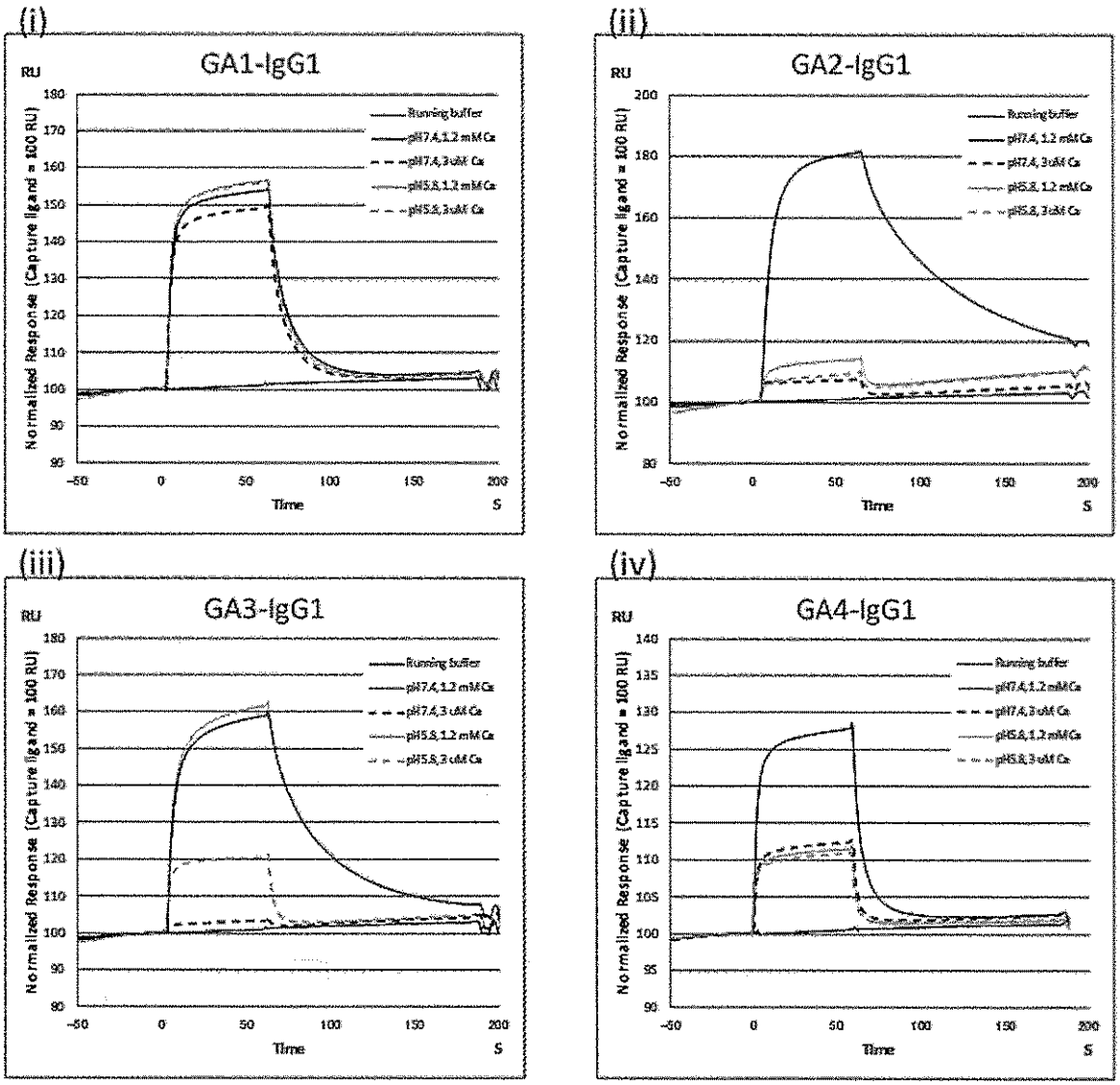
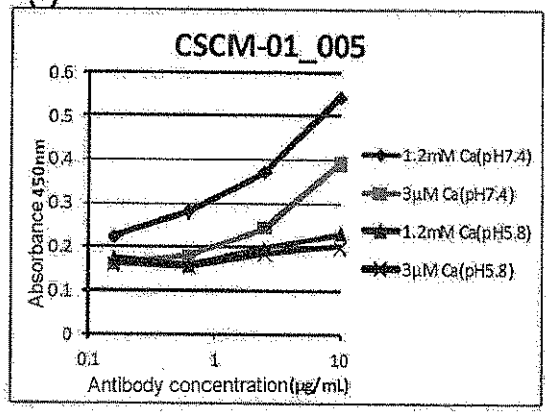
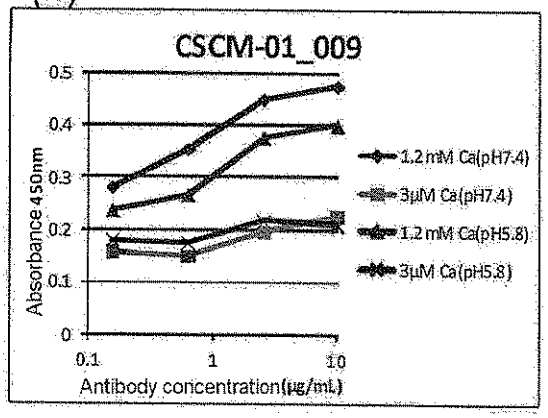

(i)
GA1-IgG1
RU
Normalized Response (Capture ligand = 100 RU)
Time
S
Running buffer
pH7.4, 1.2 mM Ca
pH7.4, 3 uM Ca
pH5.8, 1.2 mM Ca
pH5.8, 3 uM Ca
(ii)
GA2-IgG1
RU
Normalized Response (Capture ligand = 100 RU)
Time
S
Running buffer
pH7.4, 1.2 mM Ca
pH7.4, 3 uM Ca
pH5.8, 1.2 mM Ca
pH5.8, 3 uM Ca
(iii)
GA3-IgG1
RU
Normalized Response (Capture ligand = 100 RU)
Time
S
Running buffer
pH7.4, 1.2 mM Ca
pH7.4, 3 uM Ca
pH5.8, 1.2 mM Ca
pH5.8, 3 uM Ca
(iv)
GA4-IgG1
RU
Normalized Response (Capture ligand = 100 RU)
Time
S
Running buffer
pH7.4, 1.2 mM Ca
pH7.4, 3 uM Ca
pH5.8, 1.2 mM Ca
pH5.8, 3 uM Ca

FIG.13

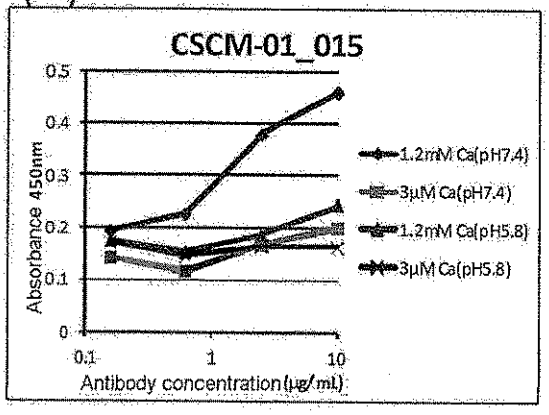
(i)



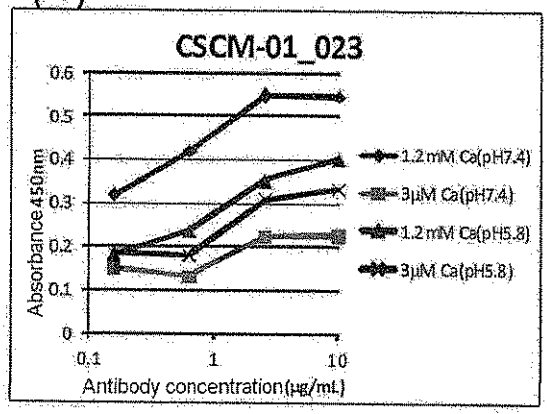
(ii)



(iii)



(iv)



(v)

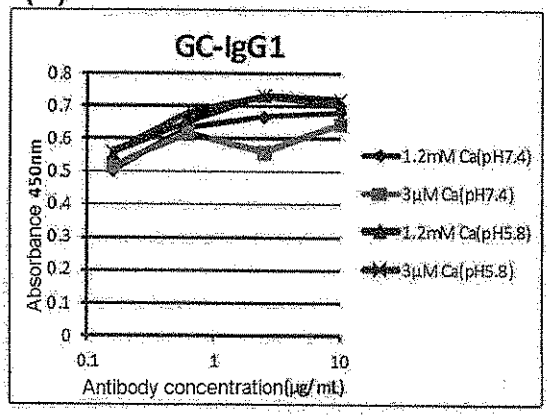
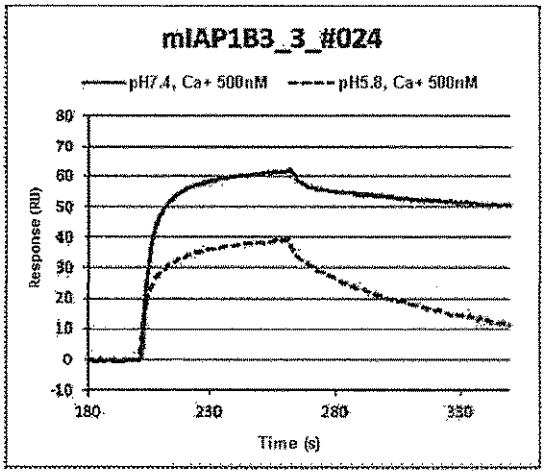
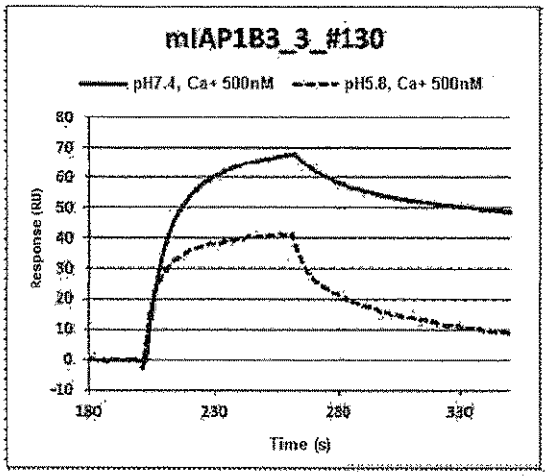


FIG.14

(i)



(ii)



(iii)

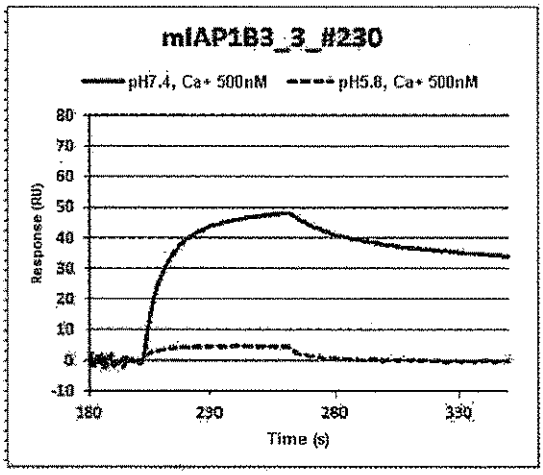
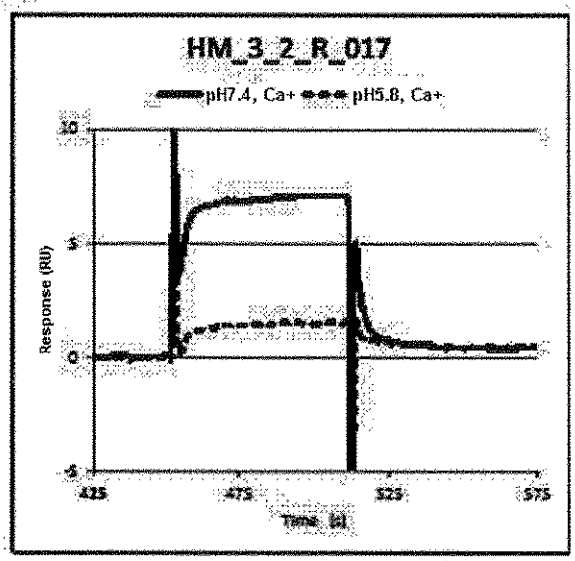
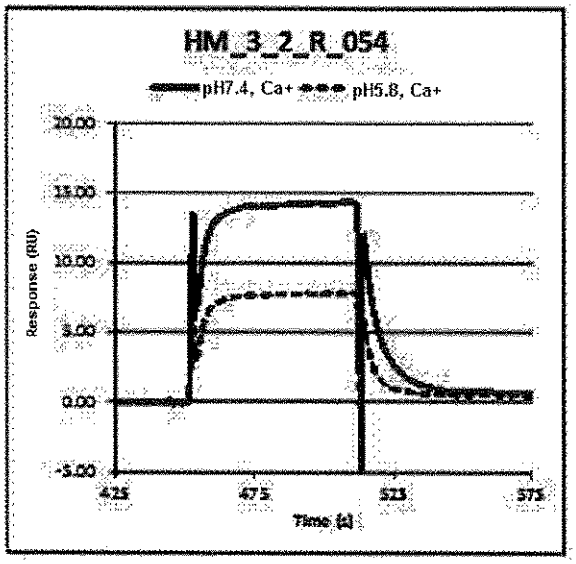


FIG.15

(i)



(ii)



(iii)

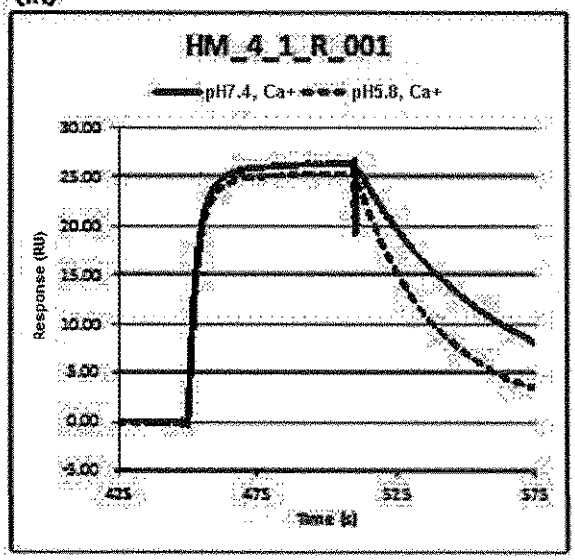


FIG.16

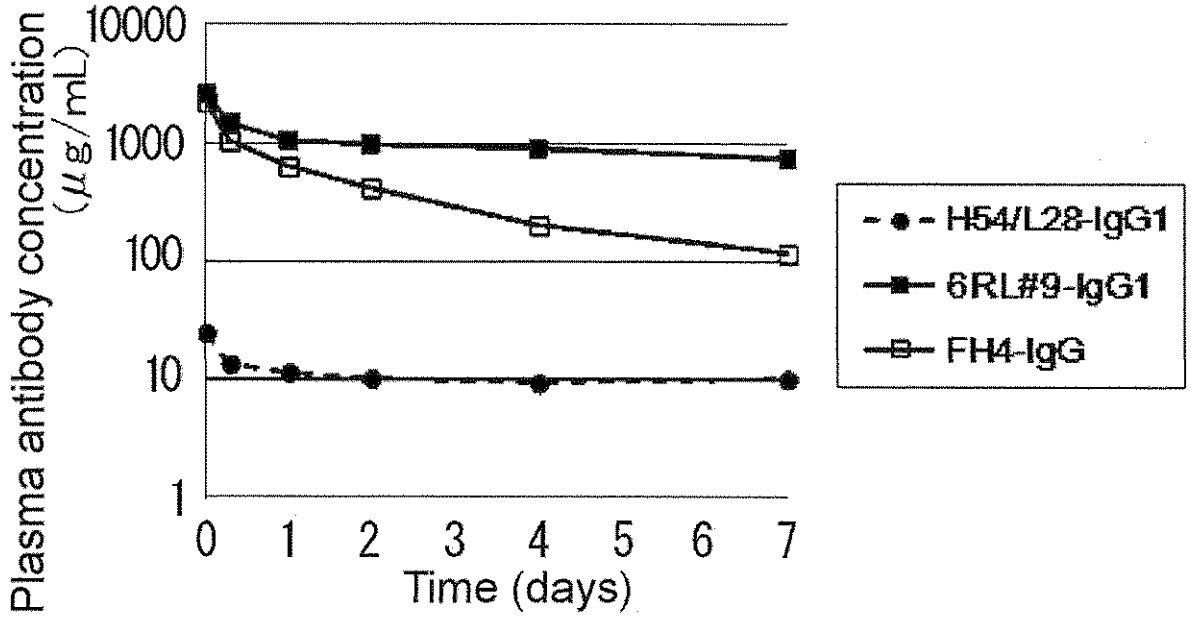

Plasma antibody concentration (μg/mL)
10000
1000
100
10
1
0
1
2
3
4
5
6
7
Time (days)
H54/L28-IgG1
6RL#9-IgG1
FH4-IgG

FIG.17

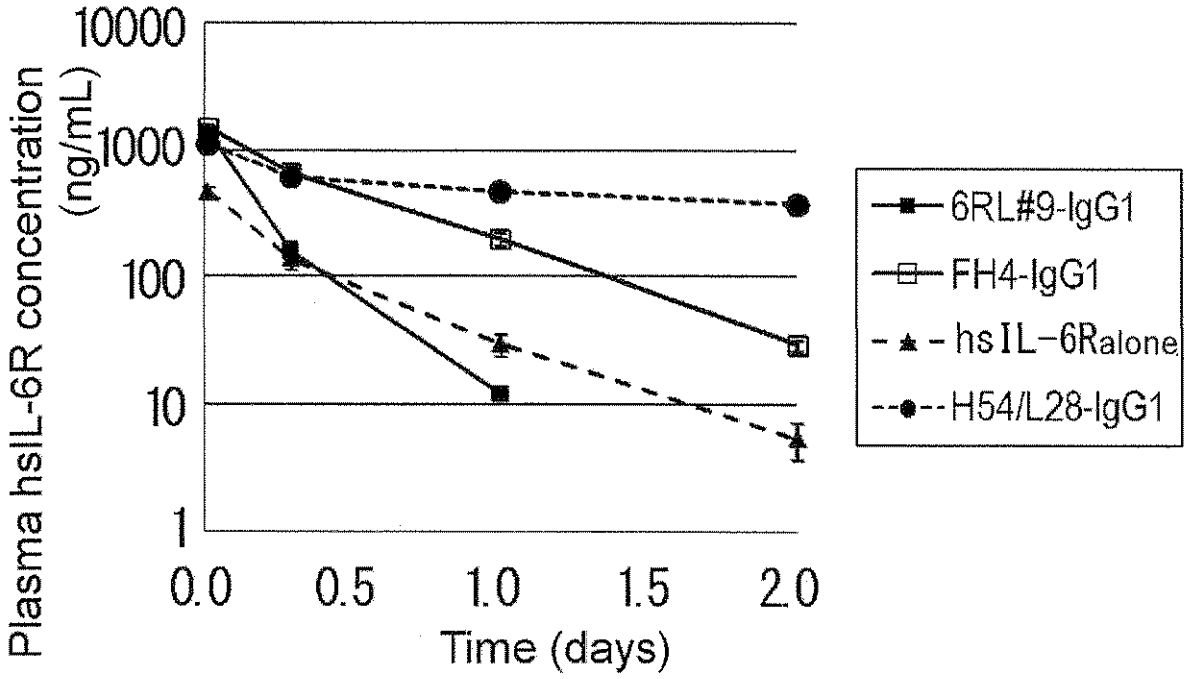

10000
1000
100
10
1
Plasma hsIL-6R concentration (ng/mL)
0.0
0.5
1.0
1.5
2.0
Time (days)
6RL#9-IgG1
FH4-IgG1
hsIL-6Ralone
H54/L28-IgG1

FIG.18

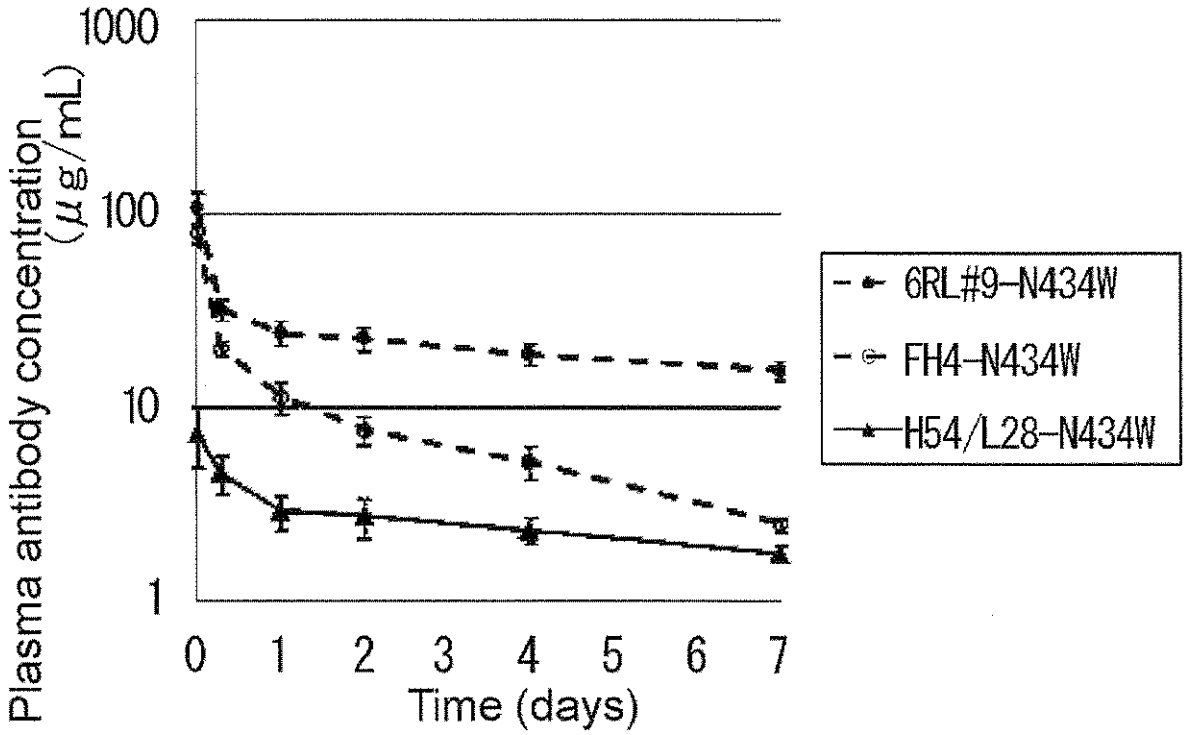
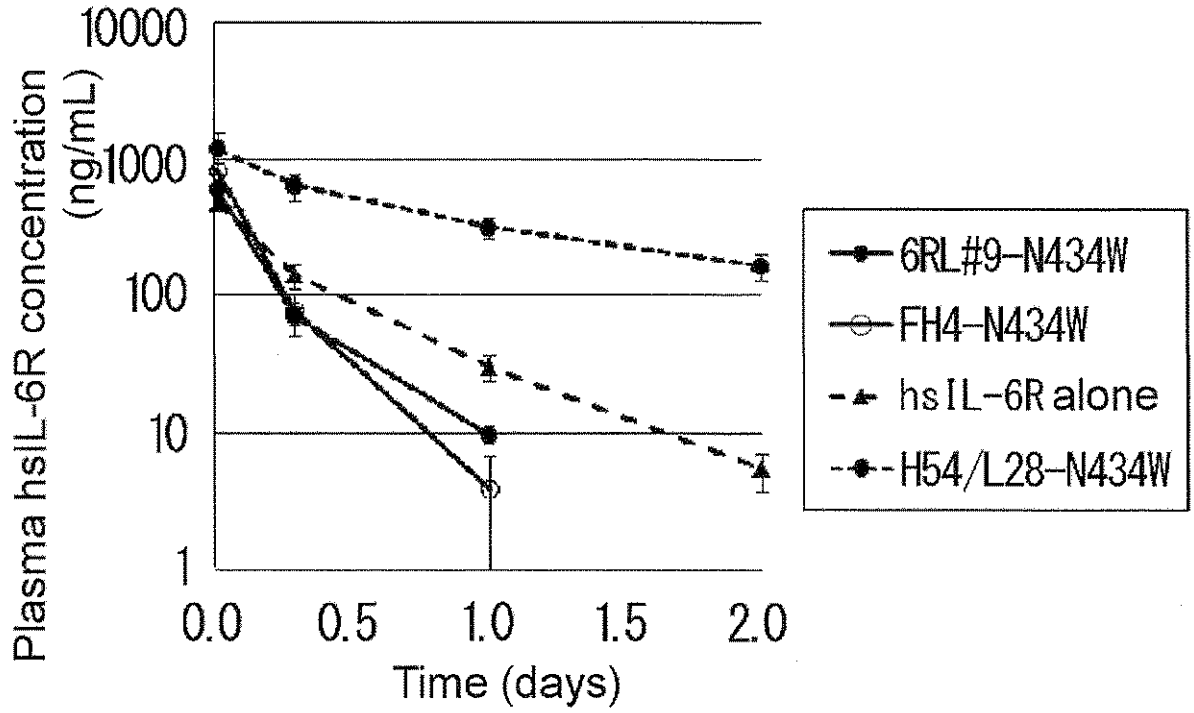

1000
100
10
1
Plasma antibody concentration (μg/mL)
0
1
2
3
4
5
6
7
Time (days)
6RL#9-N434W
FH4-N434W
H54/L28-N434W

FIG.19


10000
1000
100
10
1
Plasma hsIL-6R concentration (ng/mL)
0.0
0.5
1.0
1.5
2.0
Time (days)
6RL#9-N434W
FH4-N434W
hsIL-6R alone
H54/L28-N434W