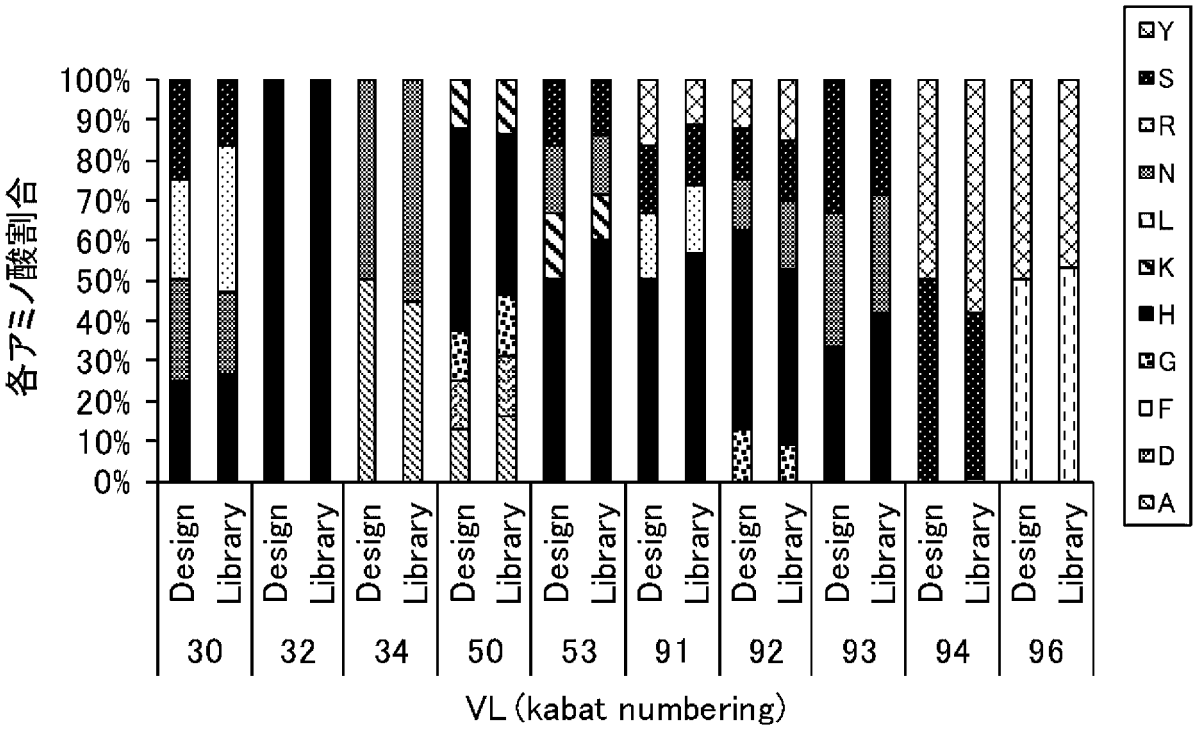
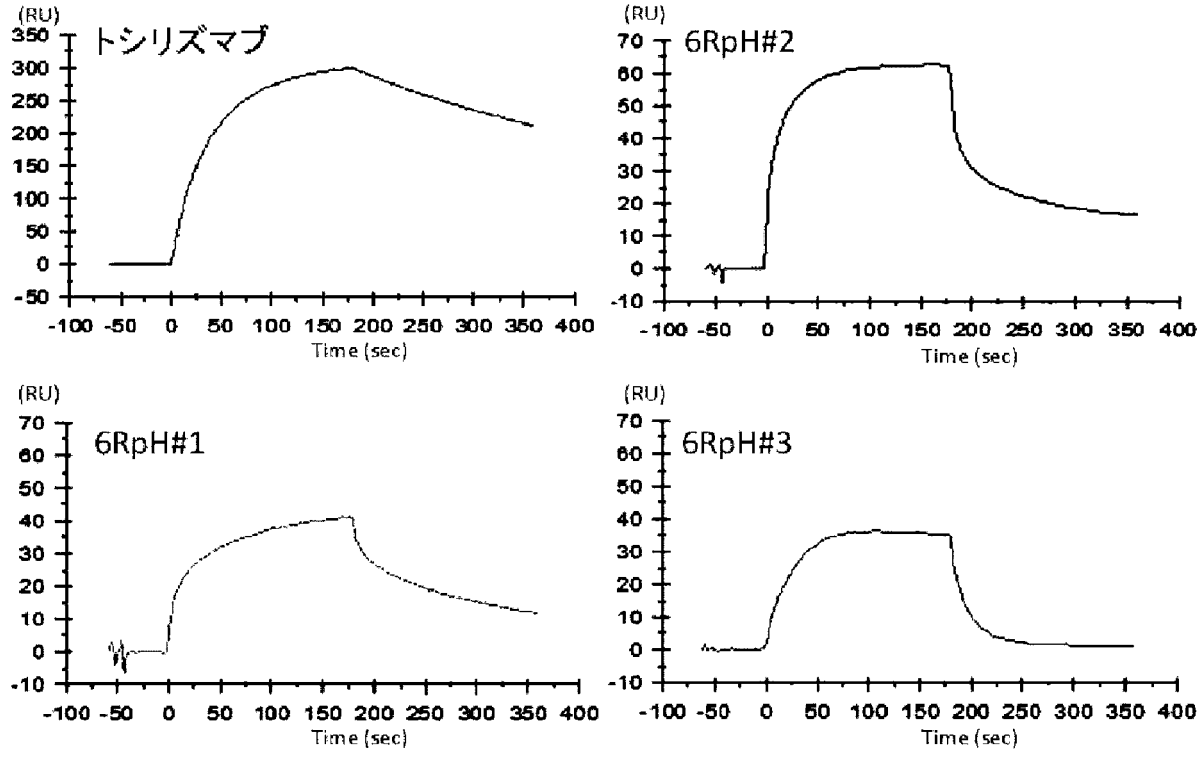
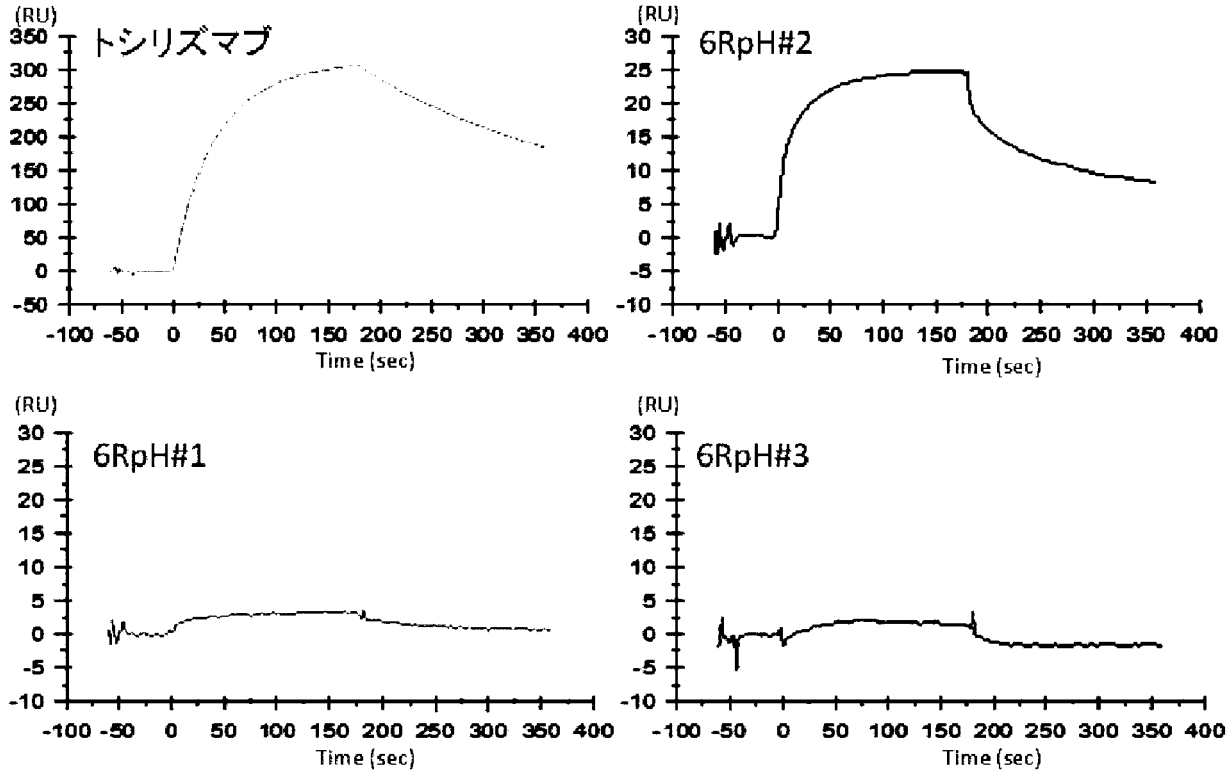
[図1]


各アミノ酸割合
100%
90%
80%
70%
60%
50%
40%
30%
20%
10%
0%
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)

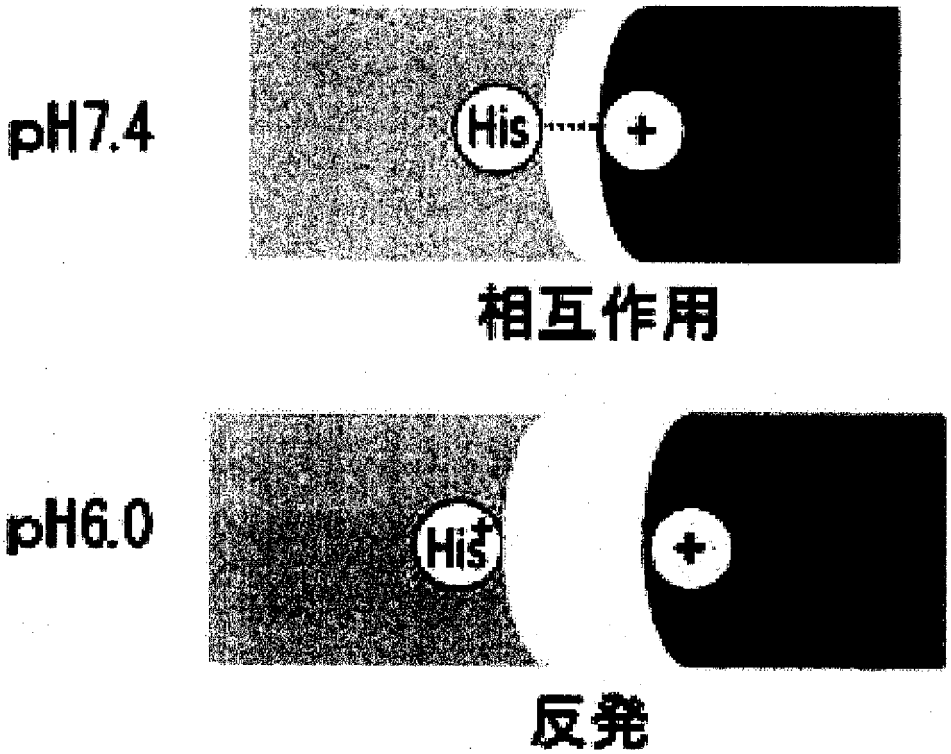
[図2]


(RU)
トシリズマブ
6RpH#2
6RpH#1
6RpH#3
Time (sec)

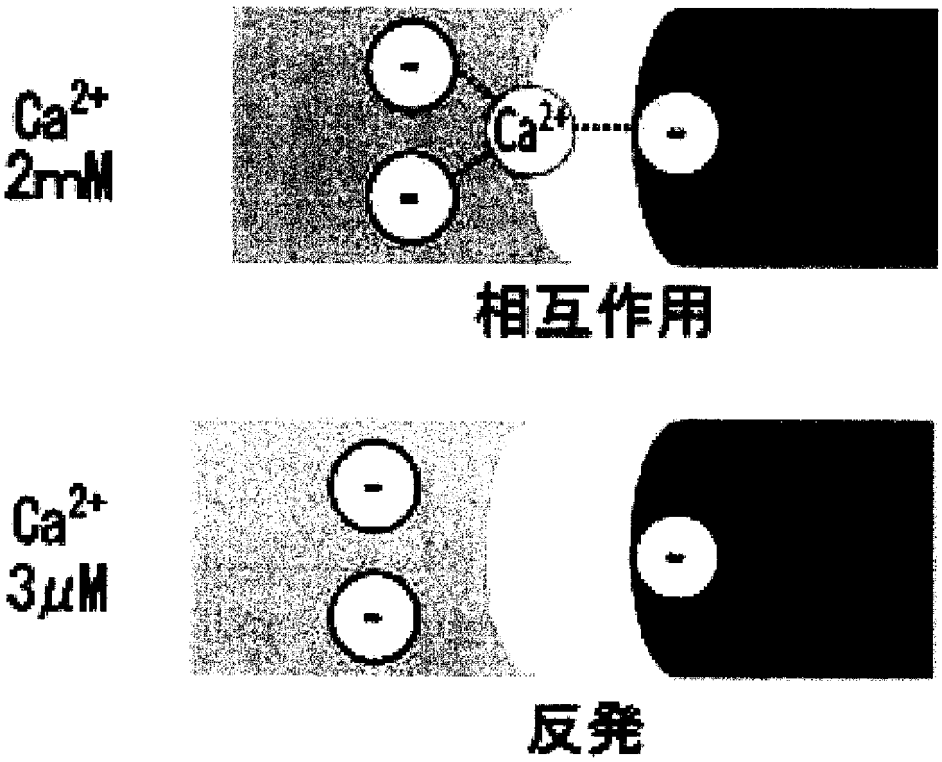
[図3]


(RU)
トシリズマブ
Time (sec)
(RU)
6RpH#2
Time (sec)
(RU)
6RpH#1
Time (sec)
(RU)
6RpH#3
Time (sec)

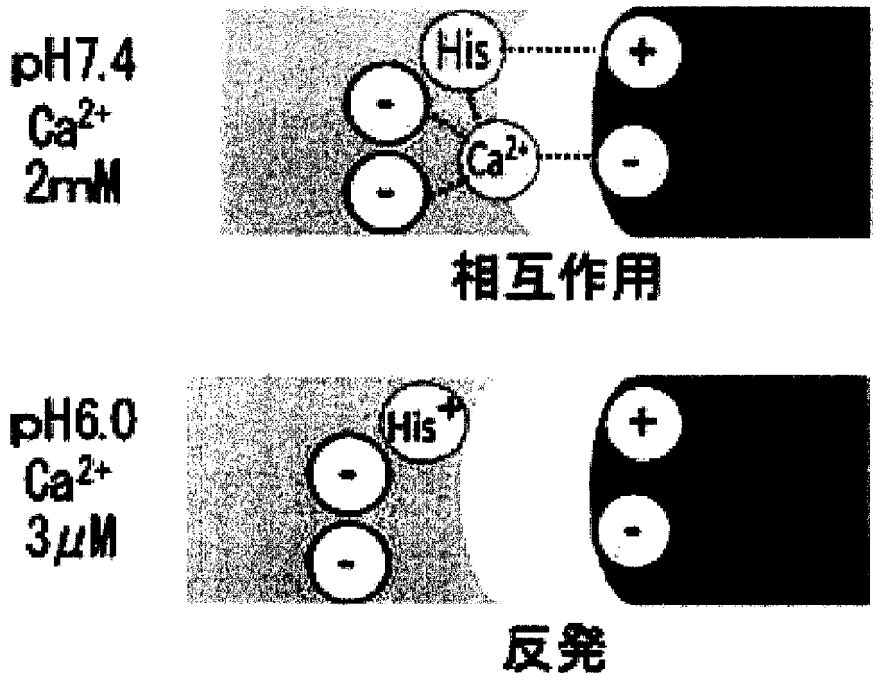
[図4A]


pH7.4
His
+
相互作用
pH6.0
His
+
反発

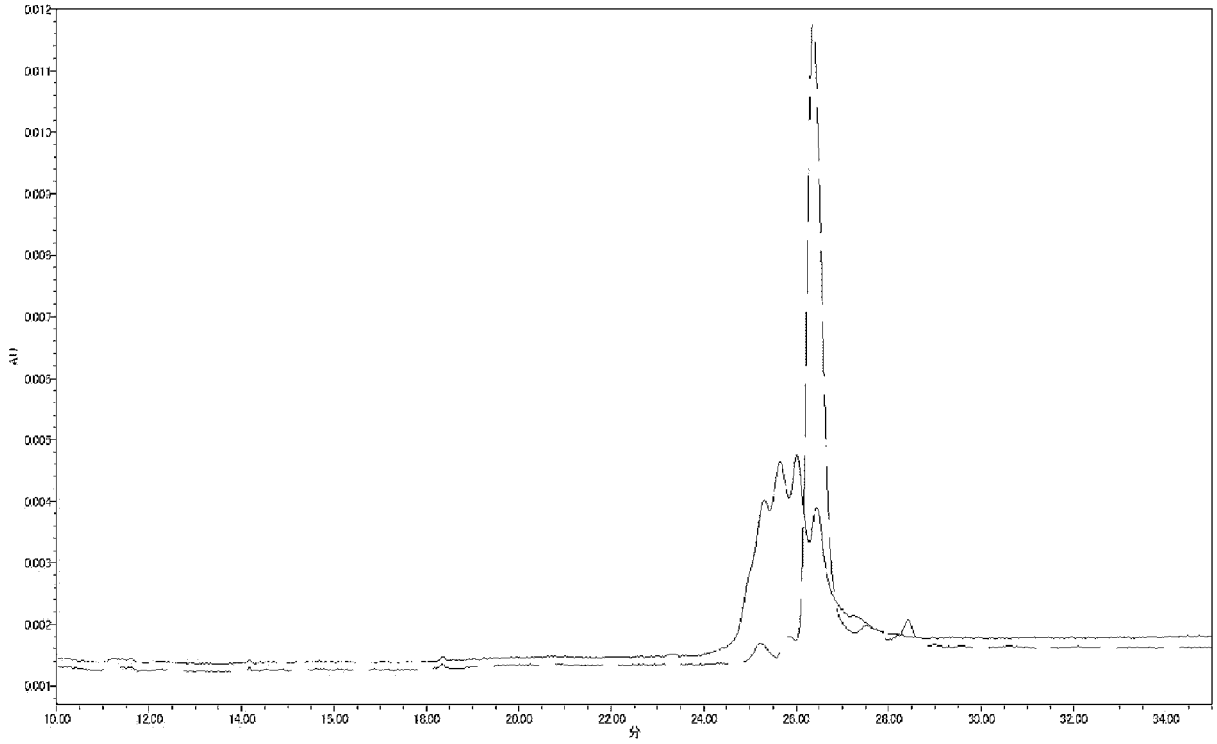
[図4B]


Ca2+
2mM
Ca2+
相互作用
Ca2+
3μM
反発

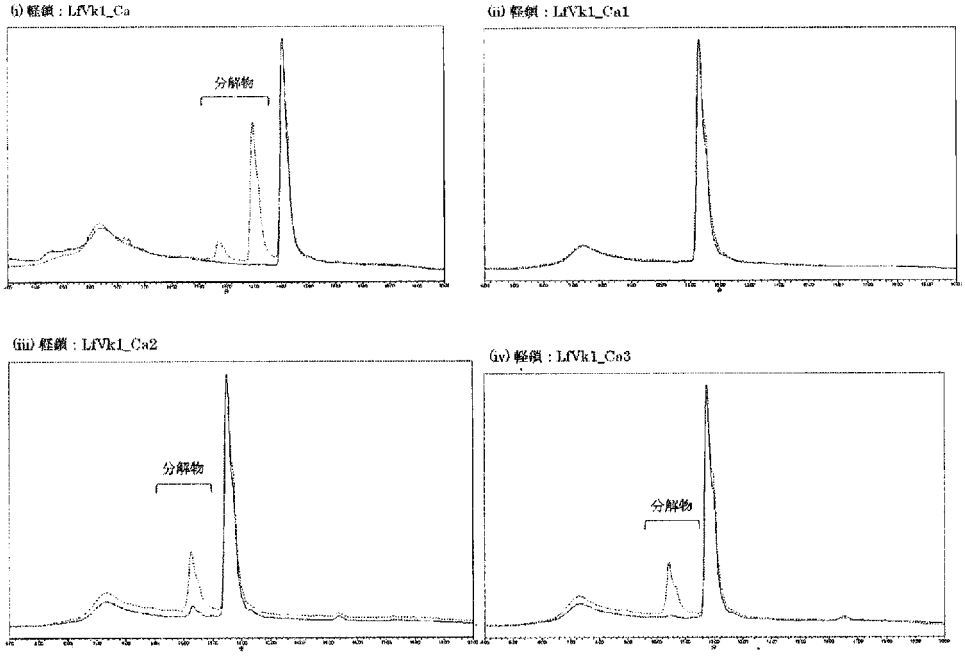
[図4C]


pH7.4
Ca2+
2mM
His
Ca2+
相互作用
pH6.0
Ca2+
3μM
His+
反発

[図5]

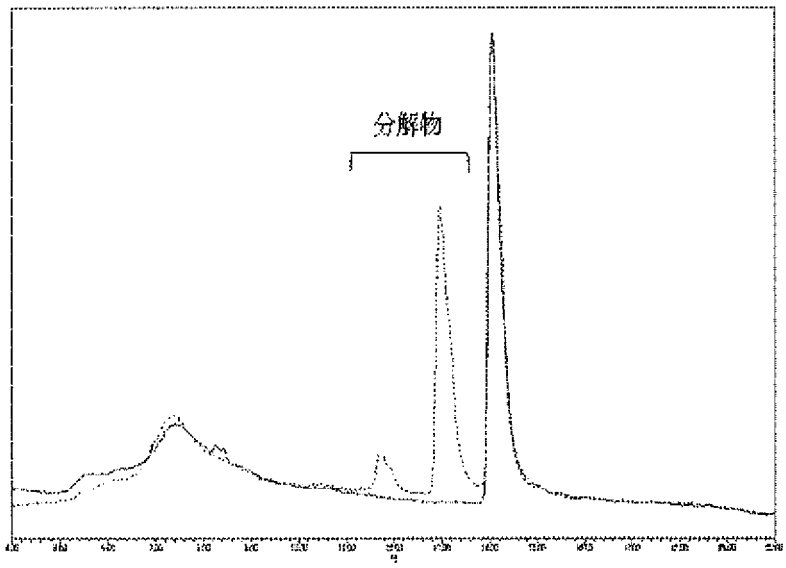

0012
0011
0010
0008
0009
0007
AU
0006
0005
0004
0003
0002
0001
10.00
12.00
14.00
16.00
18.00
20.00
22.00
24.00
26.00
28.00
30.00
32.00
34.00
分

[図6]

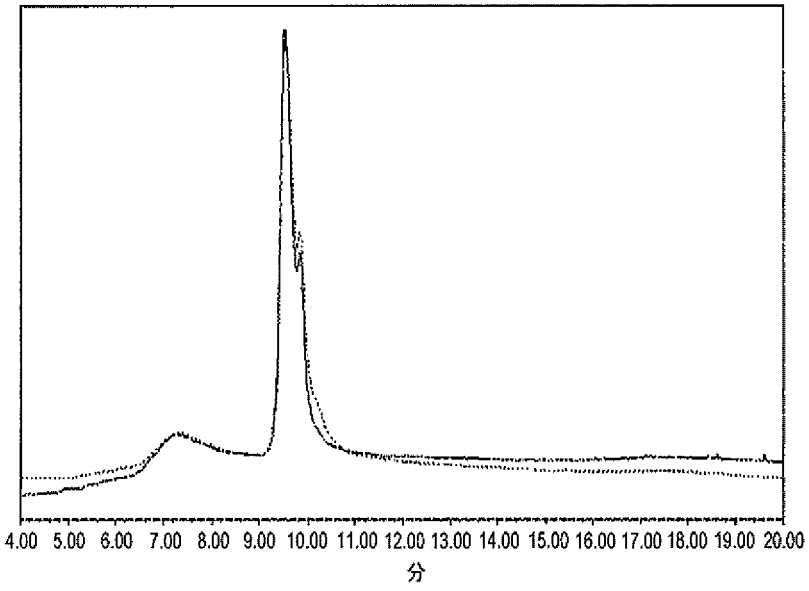

(i) 軽鎖：LfVk1_Ca
分解物
(ii) 軽鎖：LfVk1_Ca1
(iii) 軽鎖：LfVk1_Ca2
分解物
(iv) 軽鎖：LfVk1_Ca3
分解物

[図7]

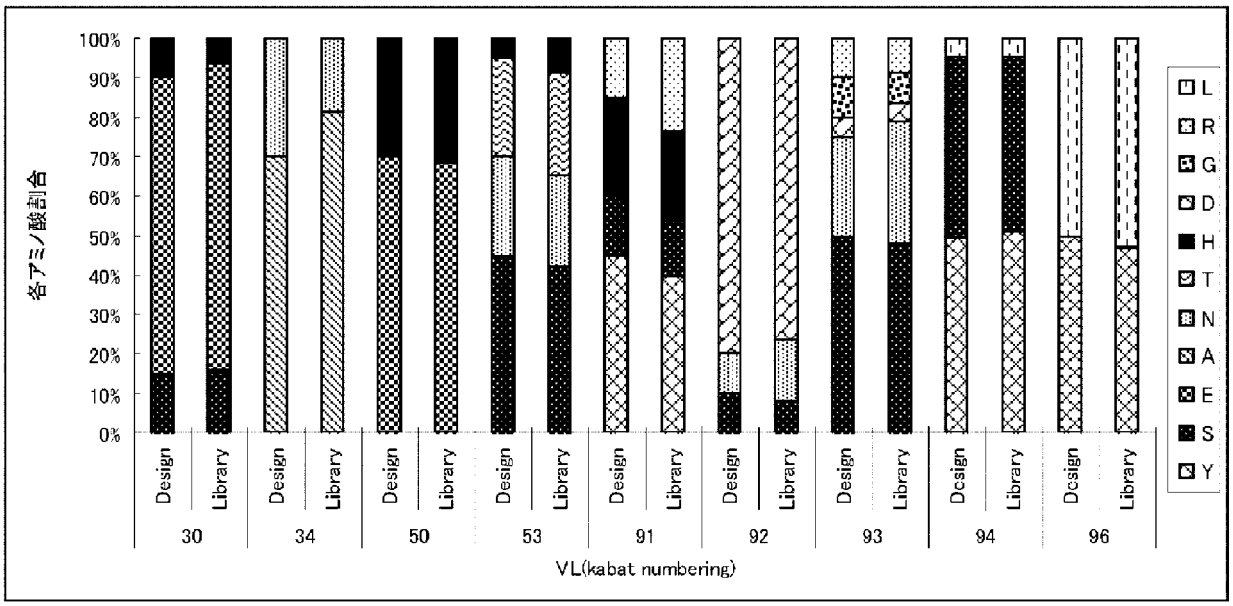
(i) 軽鎖 : LfVk1_Ca



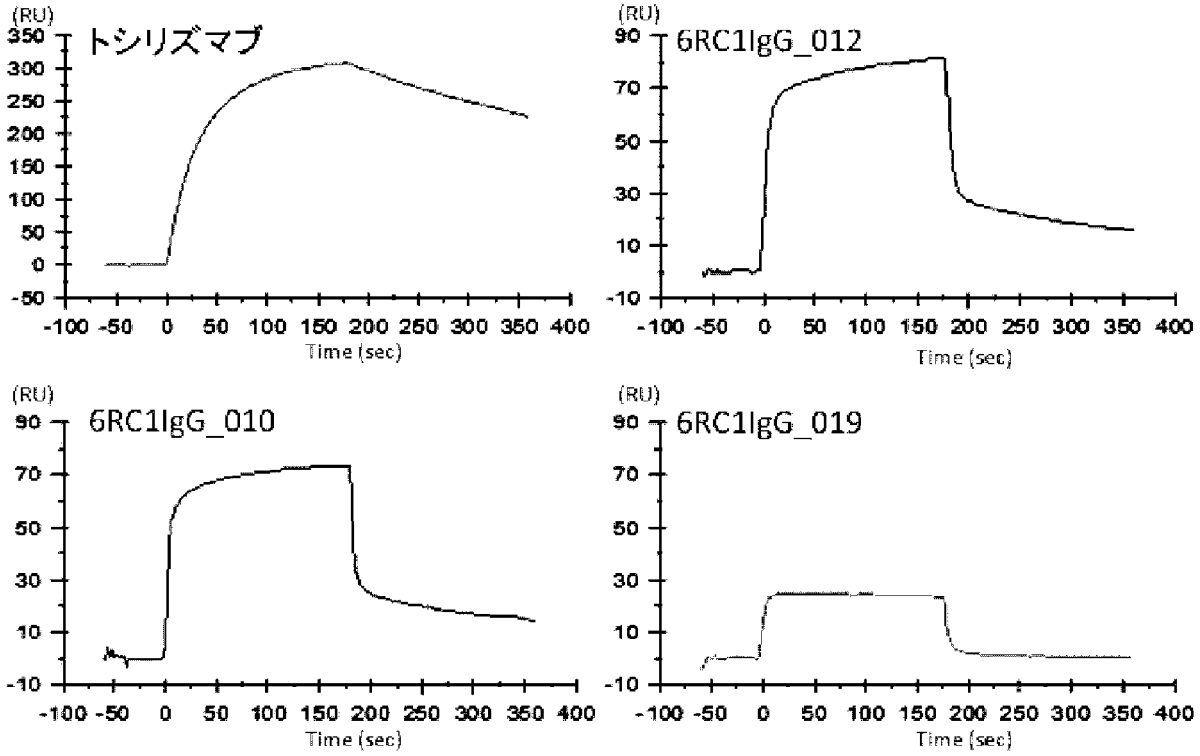
(ii)軽鎖 : LfVk1_Ca6



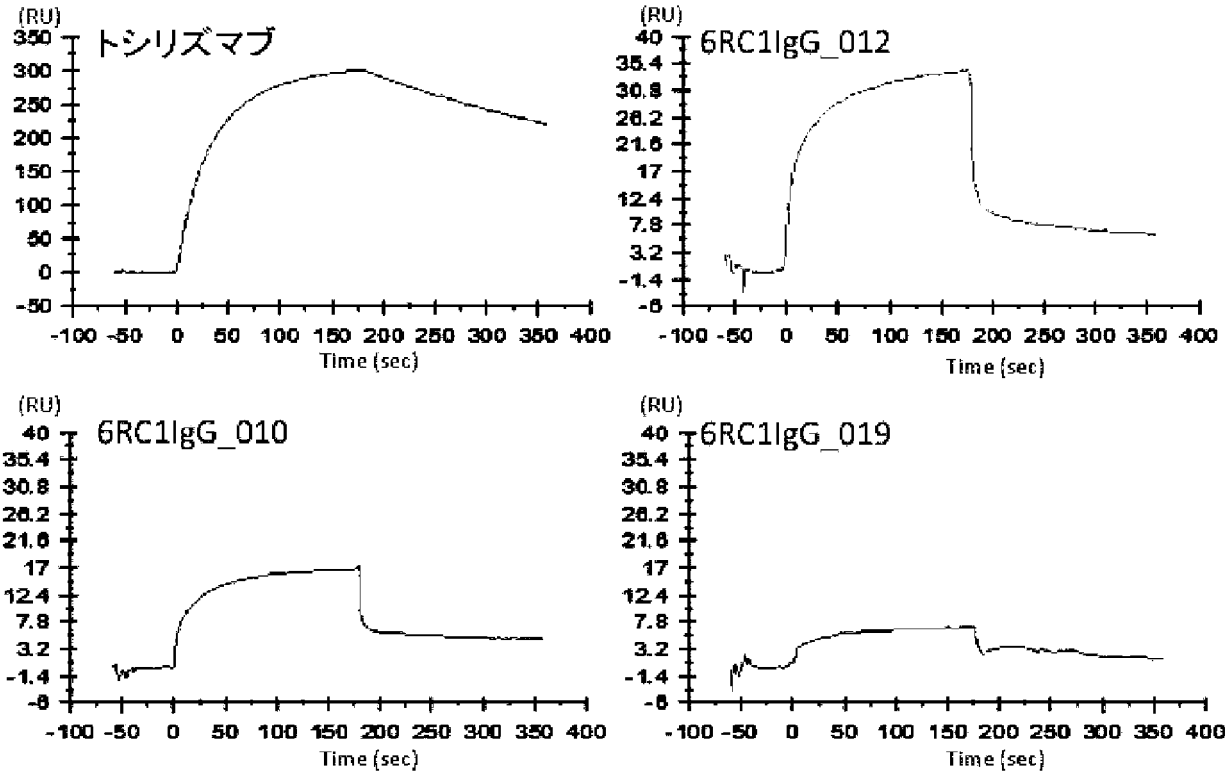
[図8]


各アミノ酸割合
100%
90%
80%
70%
60%
50%
40%
30%
20%
10%
0%
Design
Library
30
34
50
53
91
92
93
94
96
VL(kabat numbering)
L
R
G
D
H
T
N
A
E
S
Y

[図9]

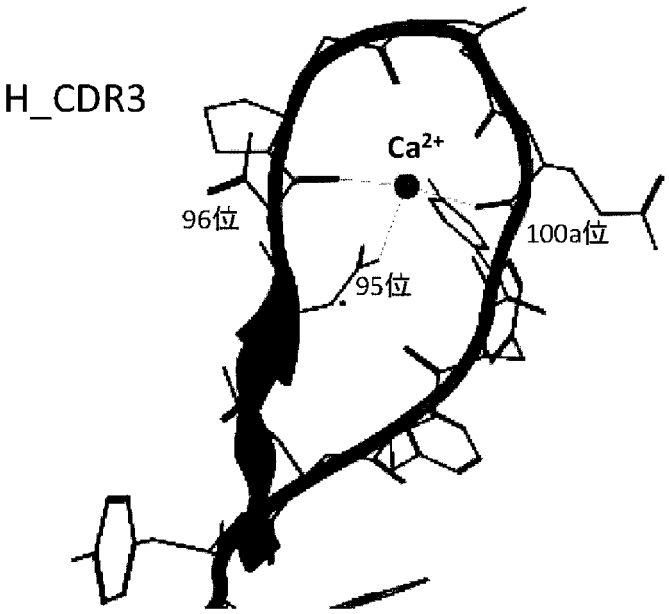

(RU)
トシリズマブ
6RC1IgG_012
6RC1IgG_010
6RC1IgG_019
Time (sec)

[図10]

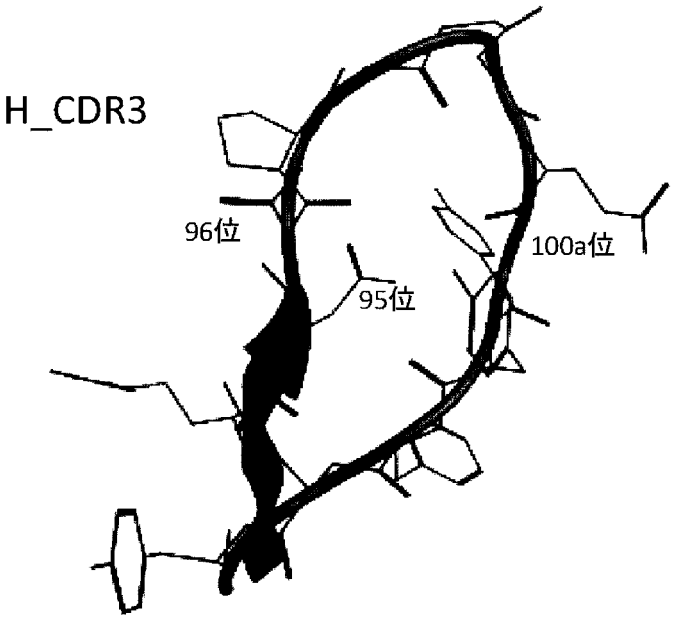

(RU)
トシリズマブ
350
300
250
200
150
100
50
0
-50
-100 -50 0 50 100 150 200 250 300 350 400
Time (sec)
(RU)
6RC1IgG_012
40
35.4
30.8
26.2
21.6
17
12.4
7.8
3.2
-1.4
-6
-100 -50 0 50 100 150 200 250 300 350 400
Time (sec)
(RU)
6RC1IgG_010
40
35.4
30.8
26.2
21.6
17
12.4
7.8
3.2
-1.4
-6
-100 -50 0 50 100 150 200 250 300 350 400
Time (sec)
(RU)
6RC1IgG_019
40
35.4
30.8
26.2
21.6
17
12.4
7.8
3.2
-1.4
-6
-100 -50 0 50 100 150 200 250 300 350 400
Time (sec)

[図11]

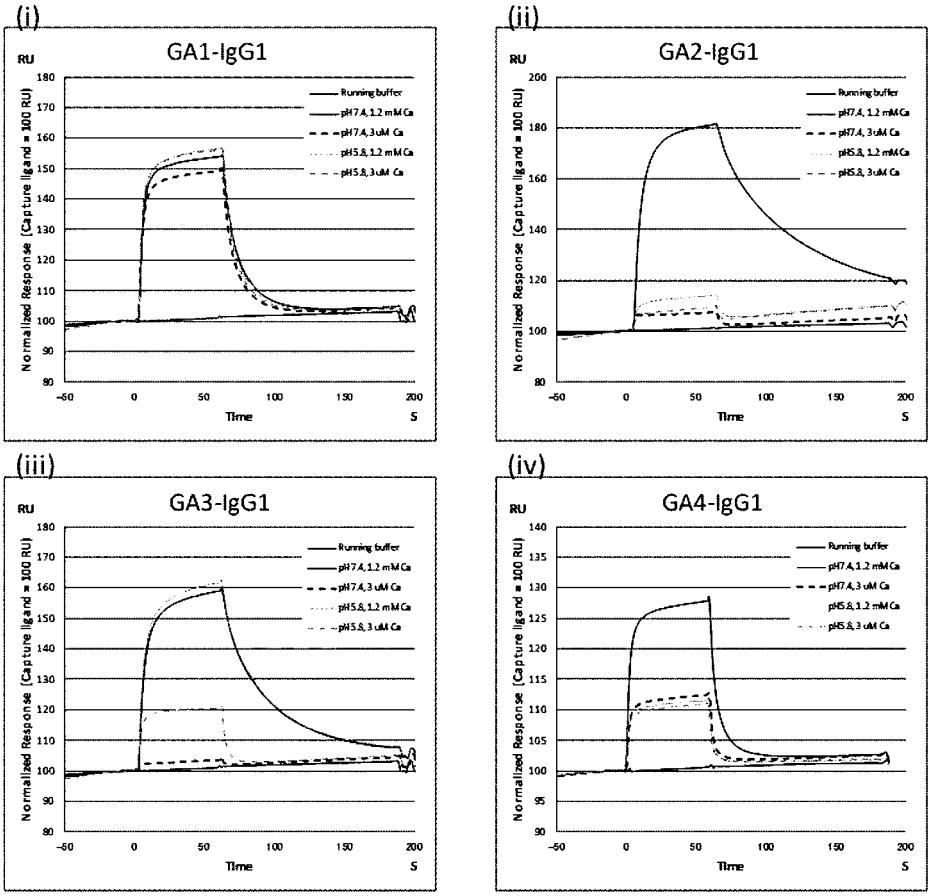
(i) カルシウムイオン存在下での結晶の構造



(ii) カルシウムイオン非存在下での結晶の構造

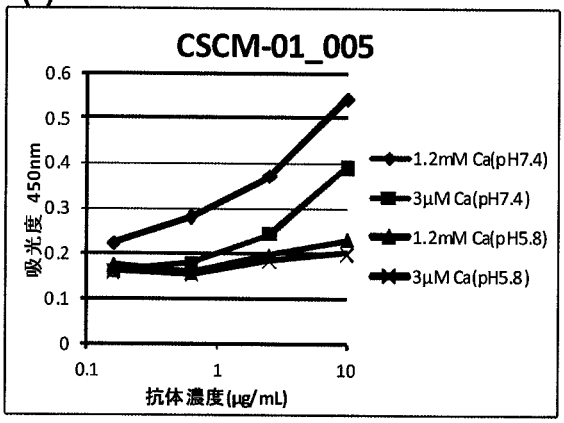


[図12]

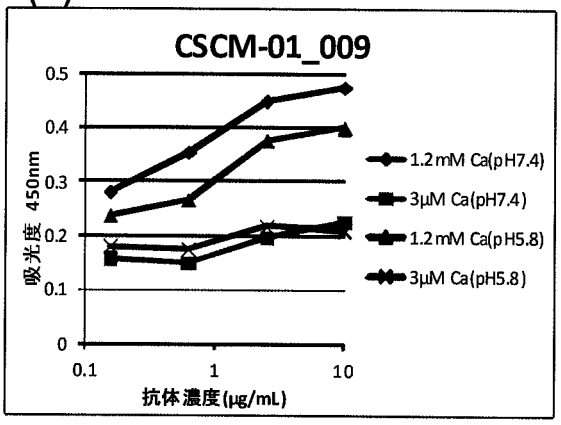

(i)
GA1-IgG1
RU
Normalized Response (Capture ligand = 100 RU)
Time
S
Running buffer
pH7.4, 1.2 mM Ca
pH7.4, 3 uM Ca
pH5.8, 1.2 mM Ca
pH5.8, 3 uM Ca
(ii)
GA2-IgG1
(iii)
GA3-IgG1
(iv)
GA4-IgG1

[図13]

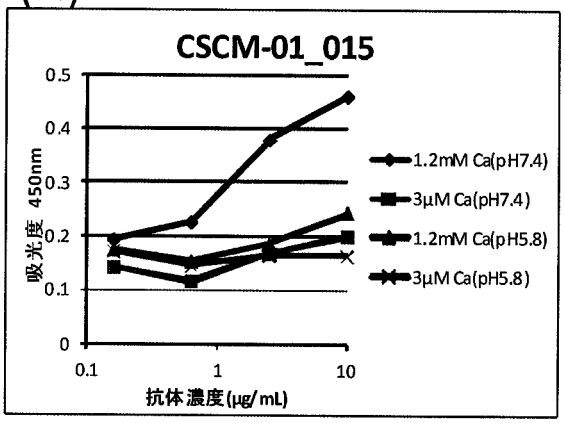
(i)



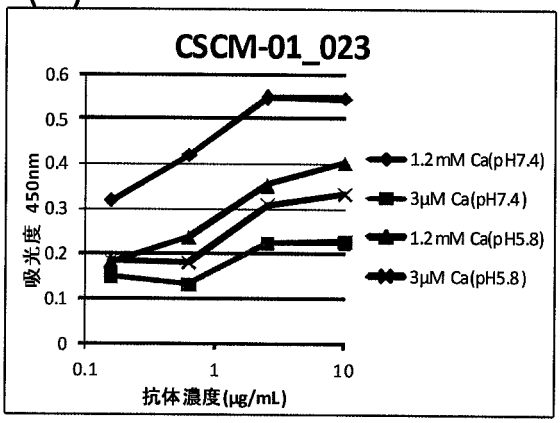
(ii)



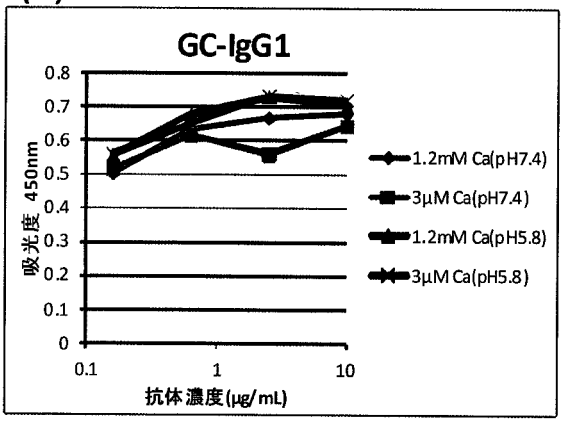
(iii)



(iv)

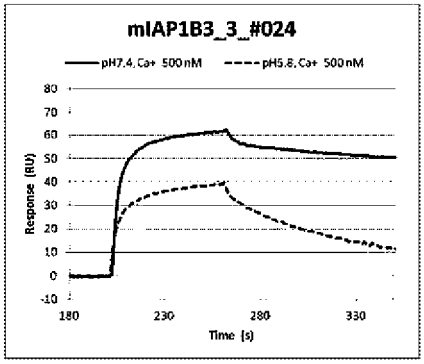


(v)

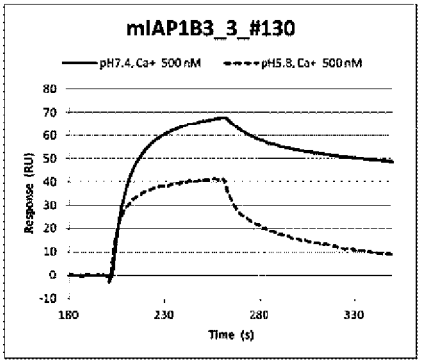


[図14]

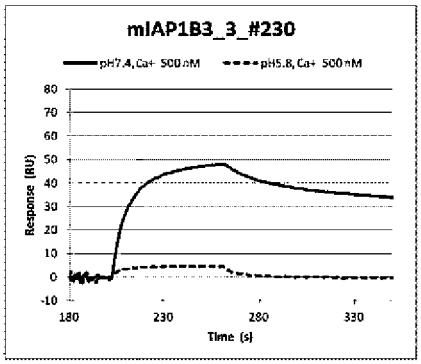
(i)



(ii)

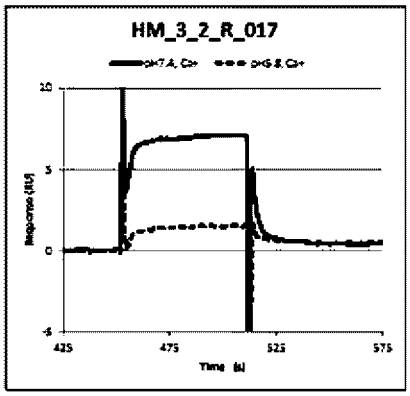


(iii)

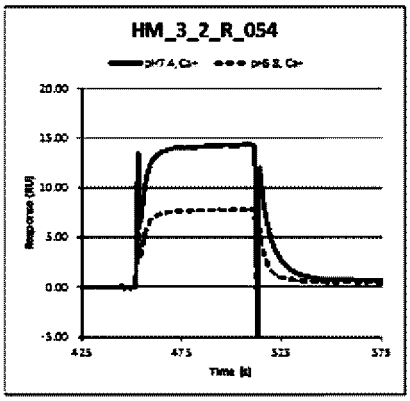


[図15]

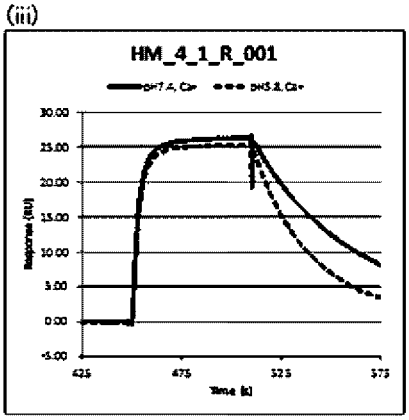
(i)



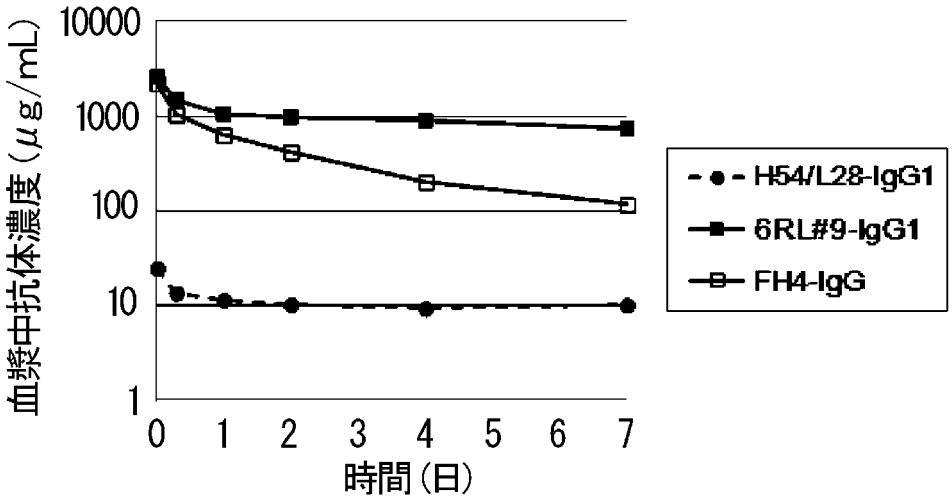
(ii)



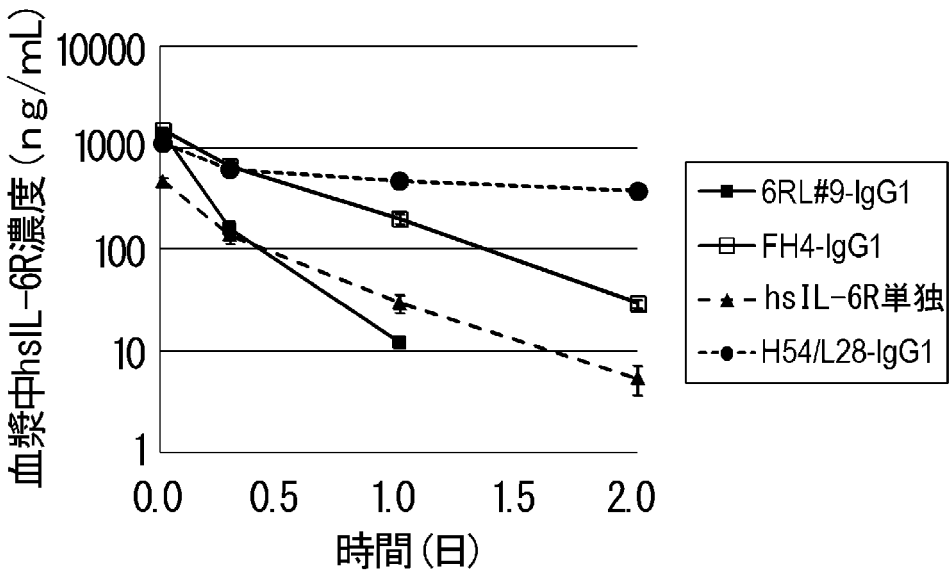
(iii)



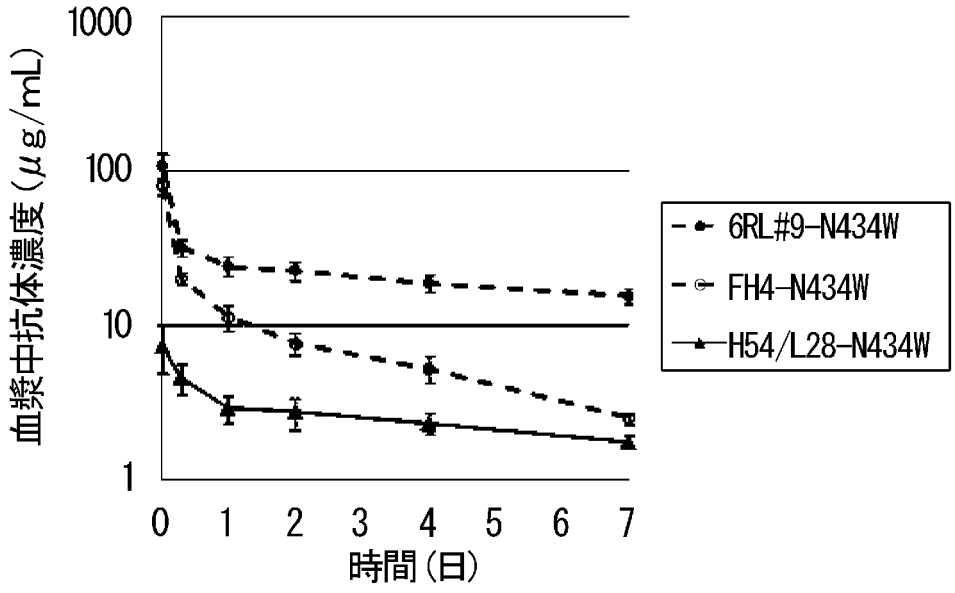
[図16]


血漿中抗体濃度（μg/mL）
10000
1000
100
10
1
0 1 2 3 4 5 6 7
時間（日）
H54/L28-IgG1
6RL#9-IgG1
FH4-IgG

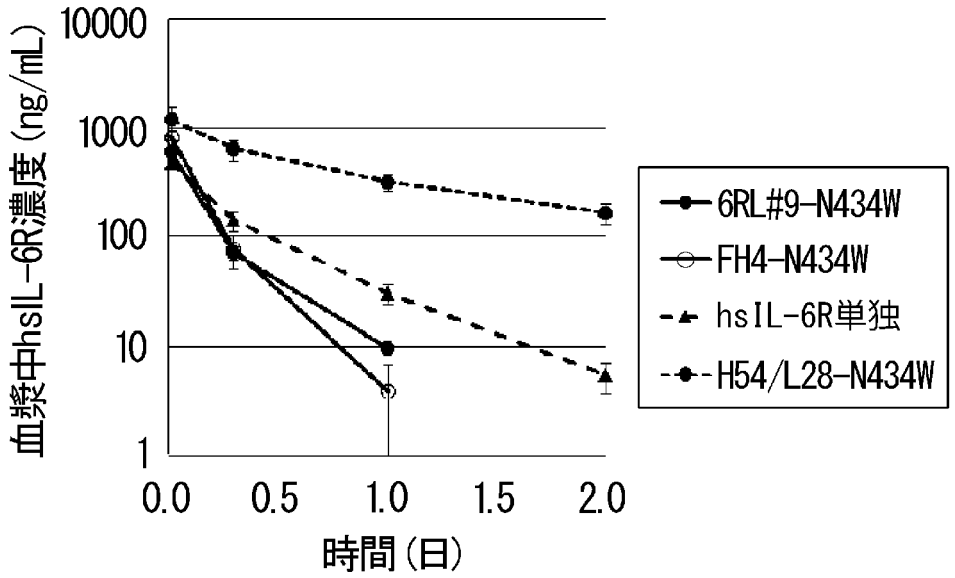
[図17]


血漿中hsIL-6R濃度（ng/mL）
10000
1000
100
10
1
0.0 0.5 1.0 1.5 2.0
時間（日）
6RL#9-IgG1
FH4-IgG1
hsIL-6R単独
H54/L28-IgG1

[図18]


血漿中抗体濃度（μg/mL）
1000
100
10
1
0 1 2 3 4 5 6 7
時間（日）
6RL#9-N434W
FH4-N434W
H54/L28-N434W

[図19]


血漿中hsIL-6R濃度 (ng/mL)
10000
1000
100
10
1
0.0
0.5
1.0
1.5
2.0
時間 (日)
6RL#9-N434W
FH4-N434W
hsIL-6R単独
H54/L28-N434W