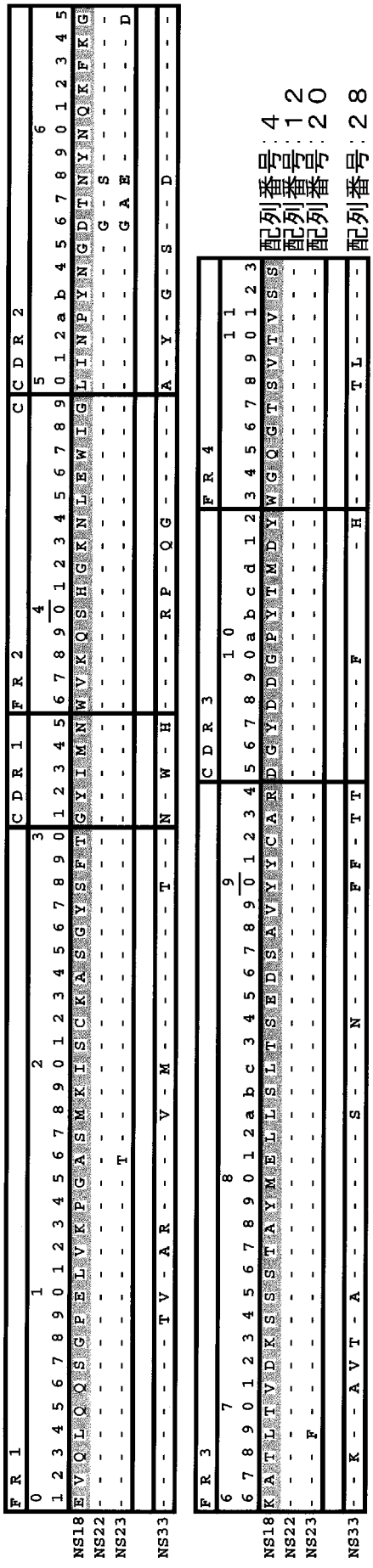
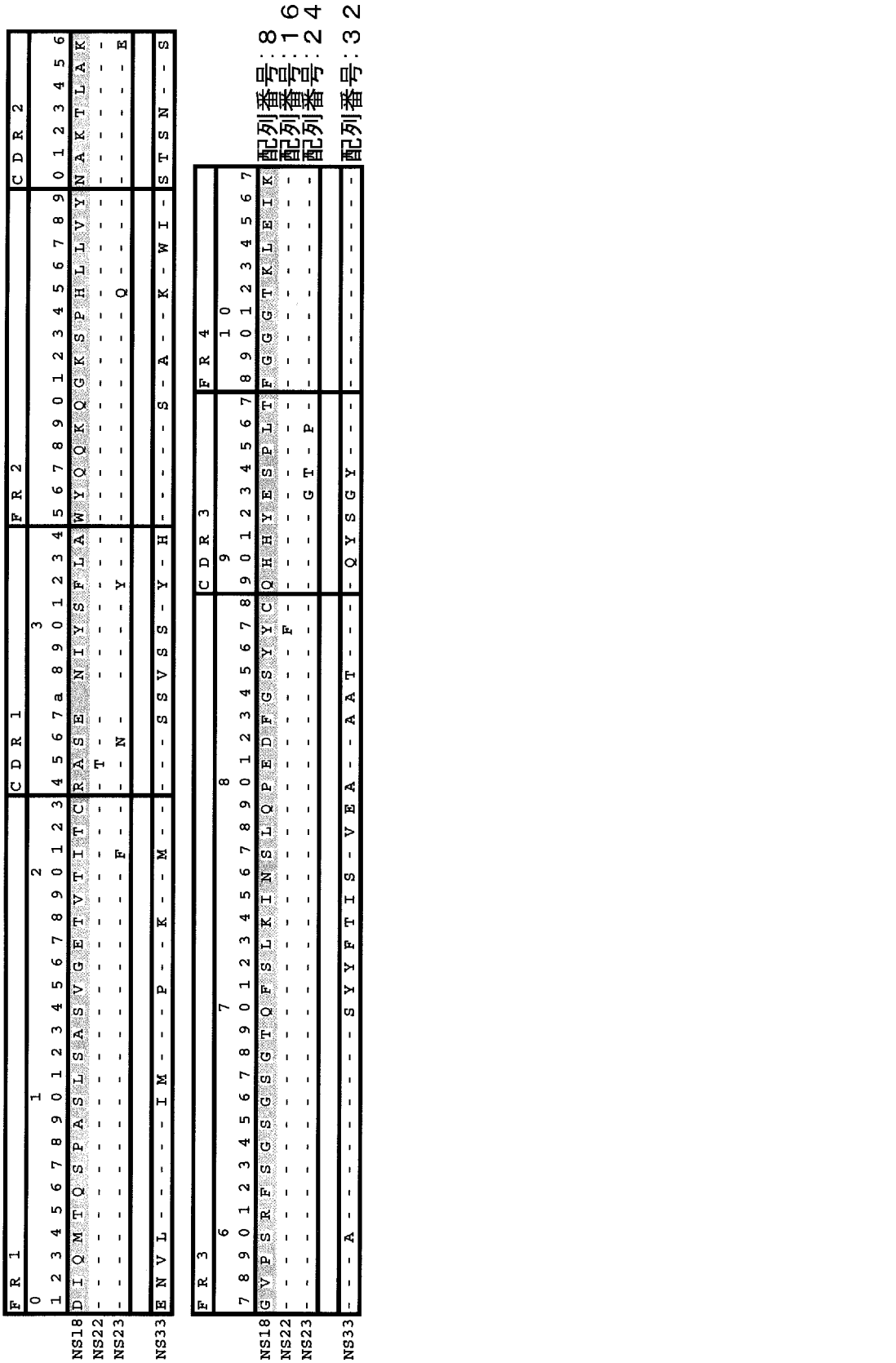
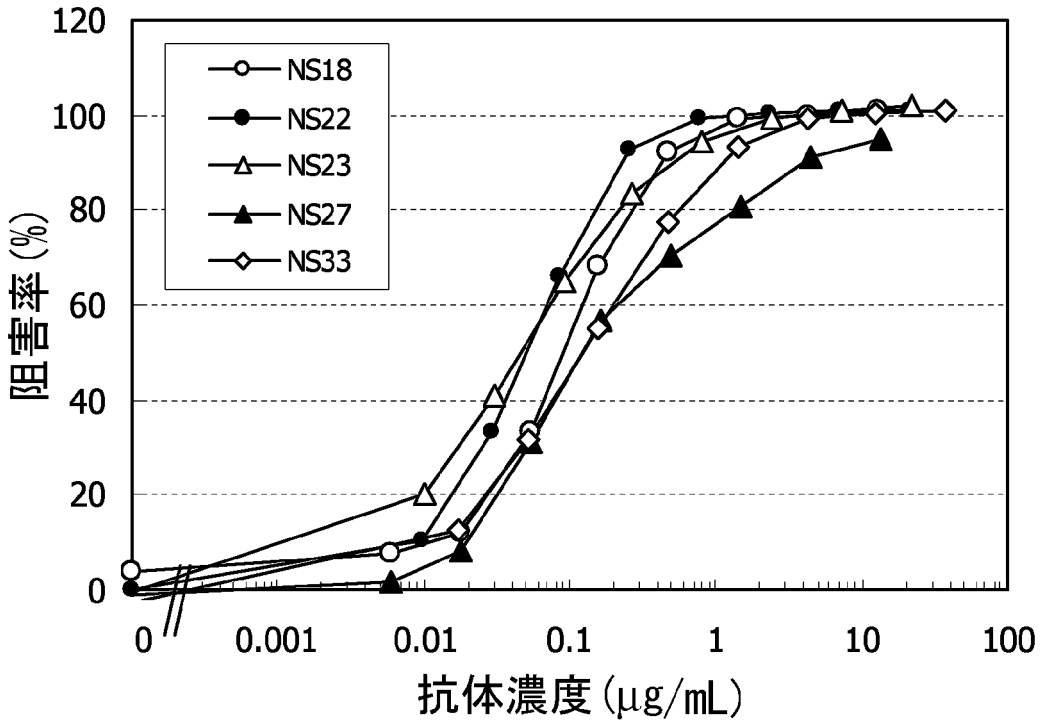
[図1]


FR1
CDR1
FR2
CDR2
FR3
CDR3
FR4
NS18
NS22
NS23
NS33
配列番号：4
配列番号：12
配列番号：20
配列番号：28

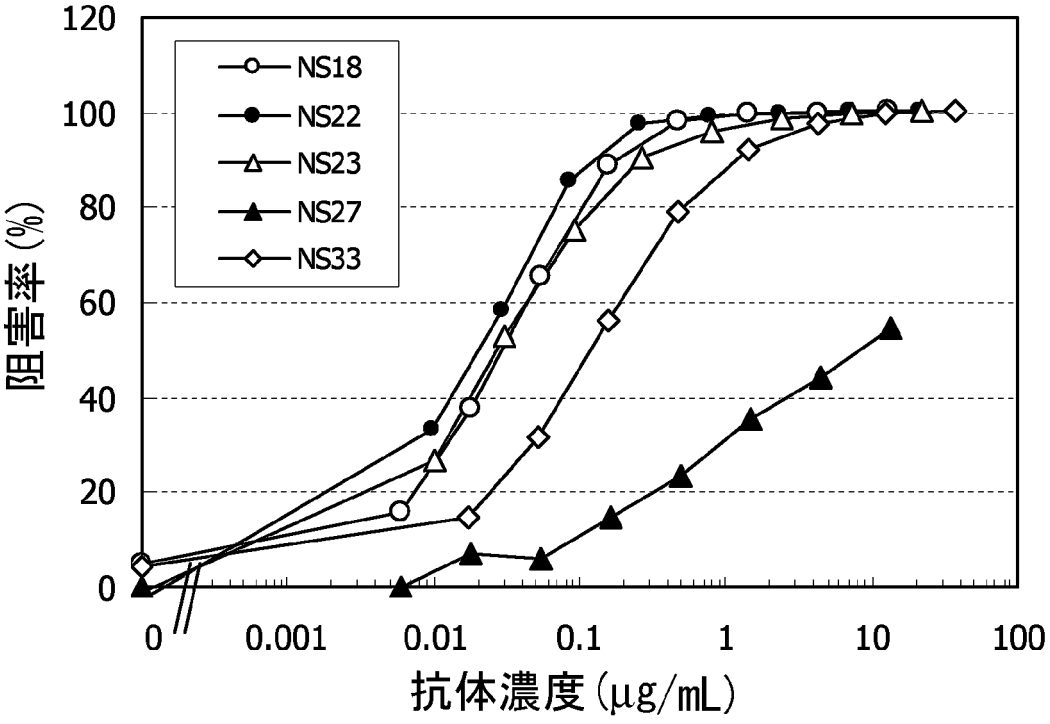
[図2]


FR 1
CDR 1
FR 2
CDR 2
FR 3
CDR 3
FR 4
NS18
NS22
NS23
NS33
配列番号：8
配列番号：16
配列番号：24
配列番号：32

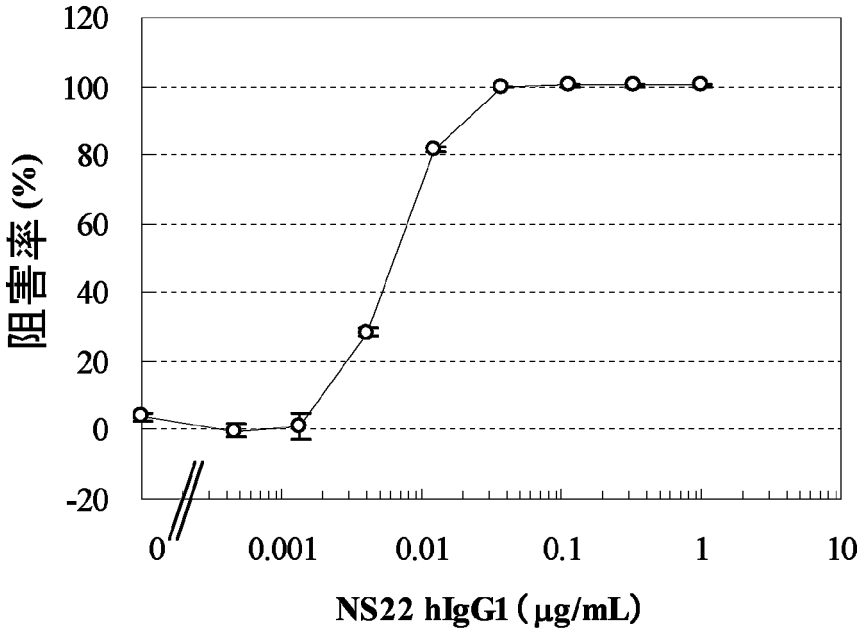
[図3]


120
100
80
60
40
20
0
阻害率(%)
NS18
NS22
NS23
NS27
NS33
0
0.001
0.01
0.1
1
10
100
抗体濃度(μg/mL)

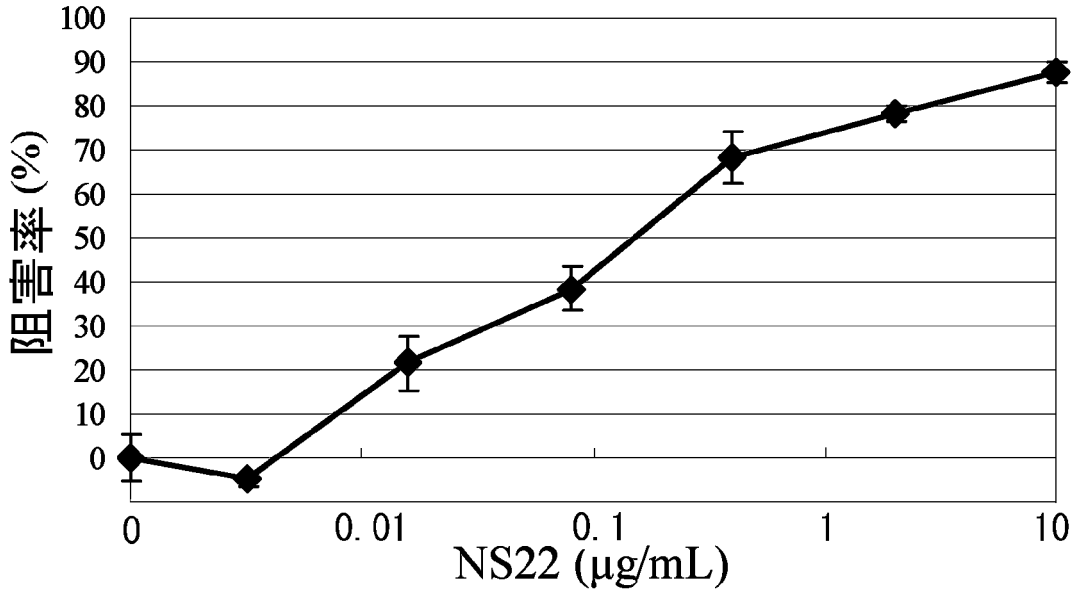
[図4]


120
100
80
60
40
20
0
阻害率(%)
NS18
NS22
NS23
NS27
NS33
0
0.001
0.01
0.1
1
10
100
抗体濃度(μg/mL)

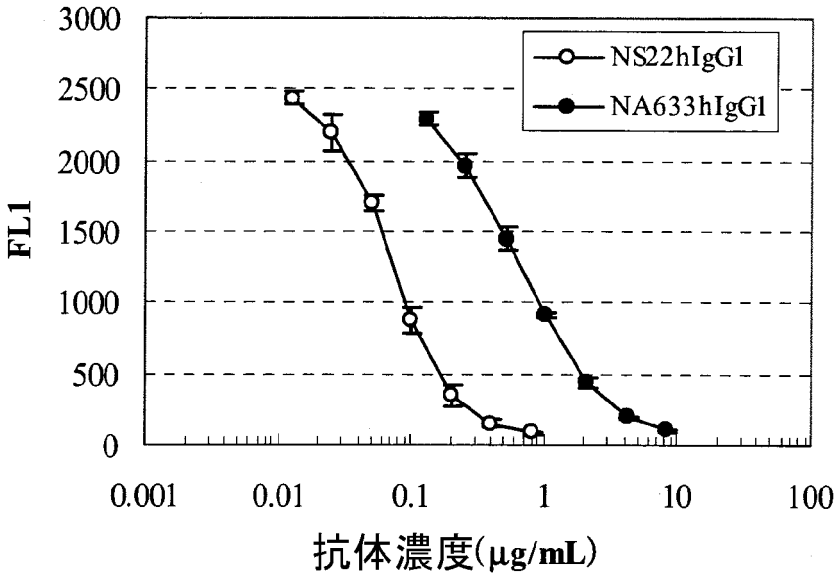
[図5]


120
100
80
60
40
20
0
-20
阻害率 (%)
0
0.001
0.01
0.1
1
10
NS22 hIgG1 (μg/mL)

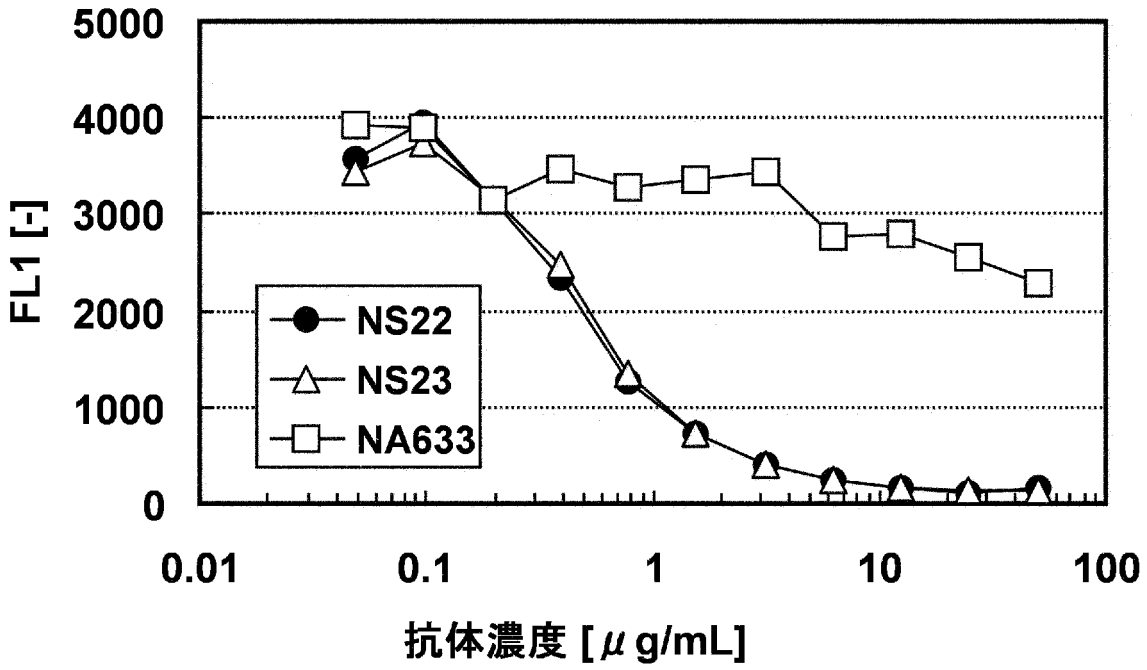
[図6]


100
90
80
70
60
50
40
30
20
10
0
阻害率 (%)
0
0. 01
0. 1
1
10
NS22 (μg/mL)

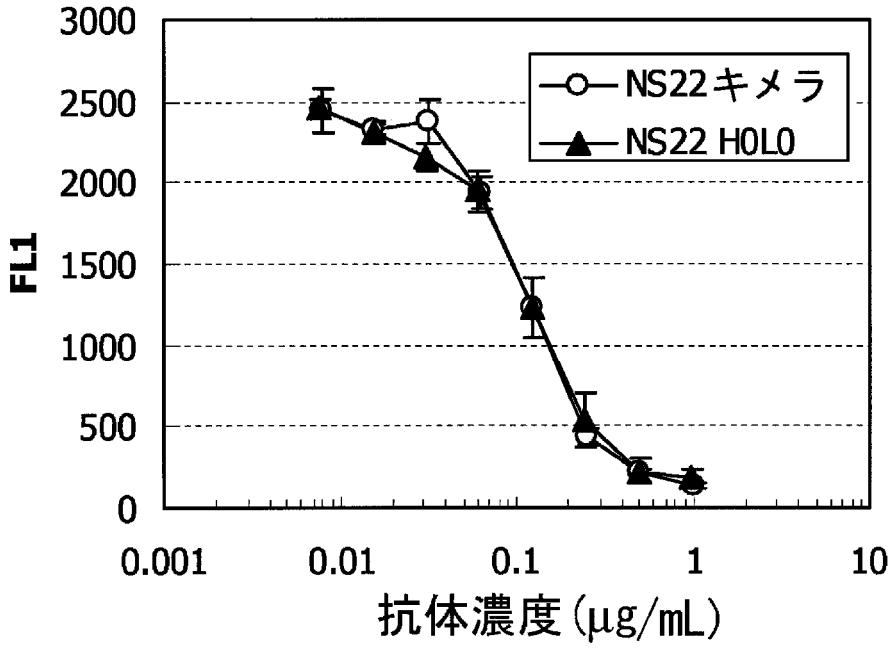
[図7]

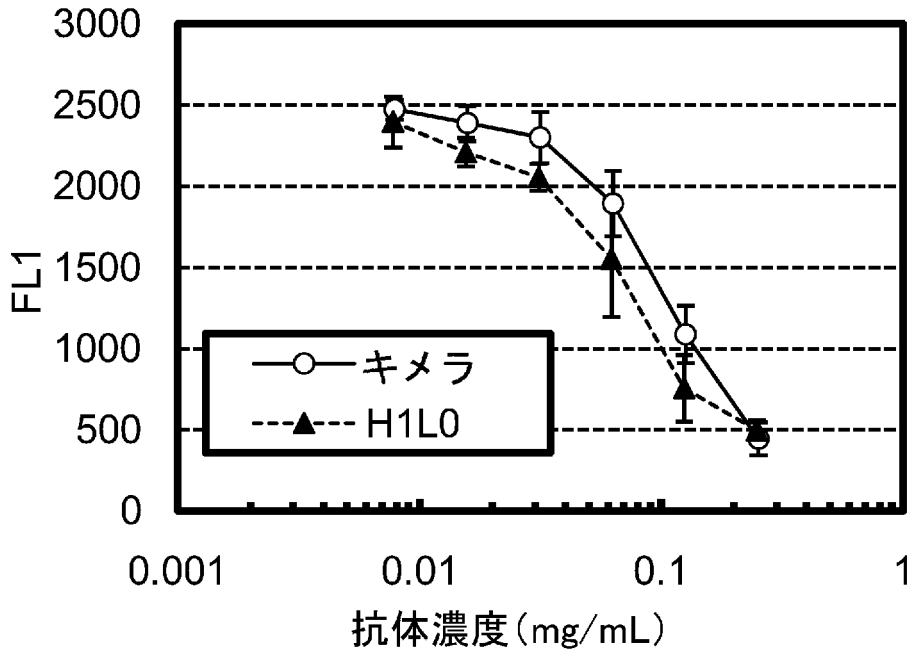

3000
2500
2000
1500
1000
500
0
FL1
NS22hIgG1
NA633hIgG1
0.001
0.01
0.1
1
10
100
抗体濃度(μg/mL)

[図8]

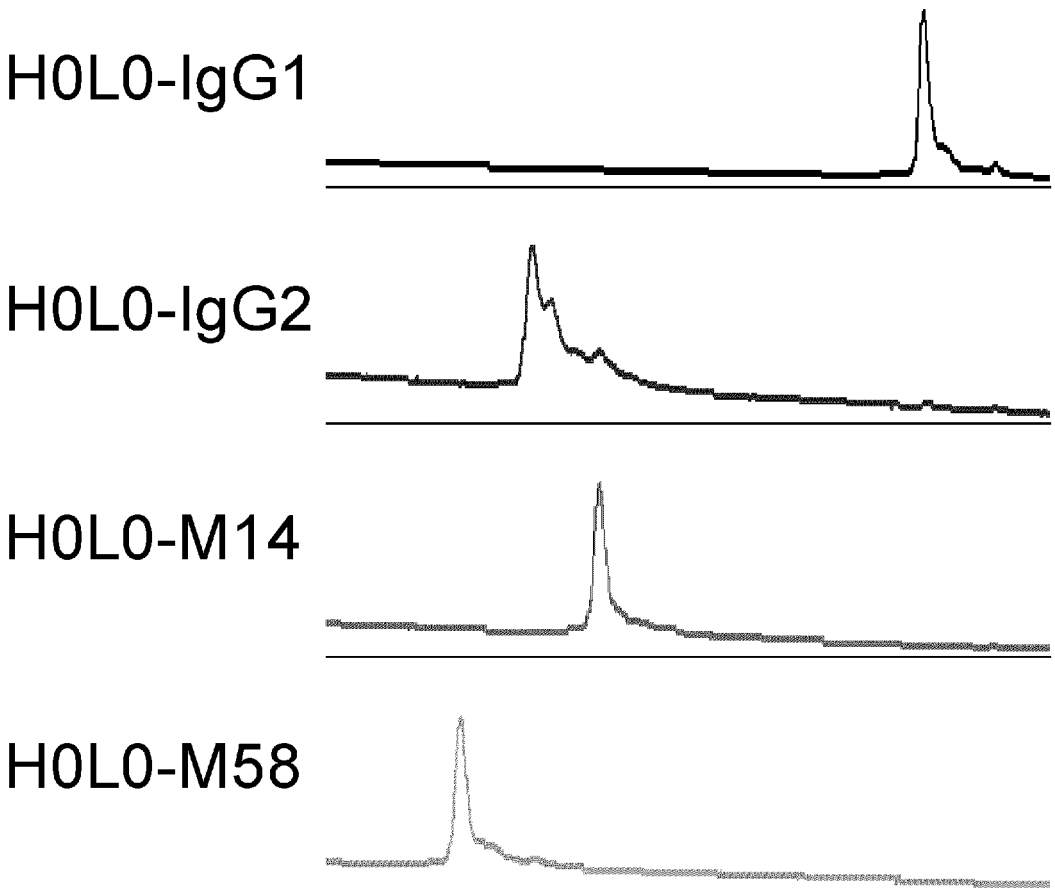

5000
4000
3000
2000
1000
0
FL1 [-]
NS22
NS23
NA633
0.01
0.1
1
10
100
抗体濃度 [μg/mL]

[図9]

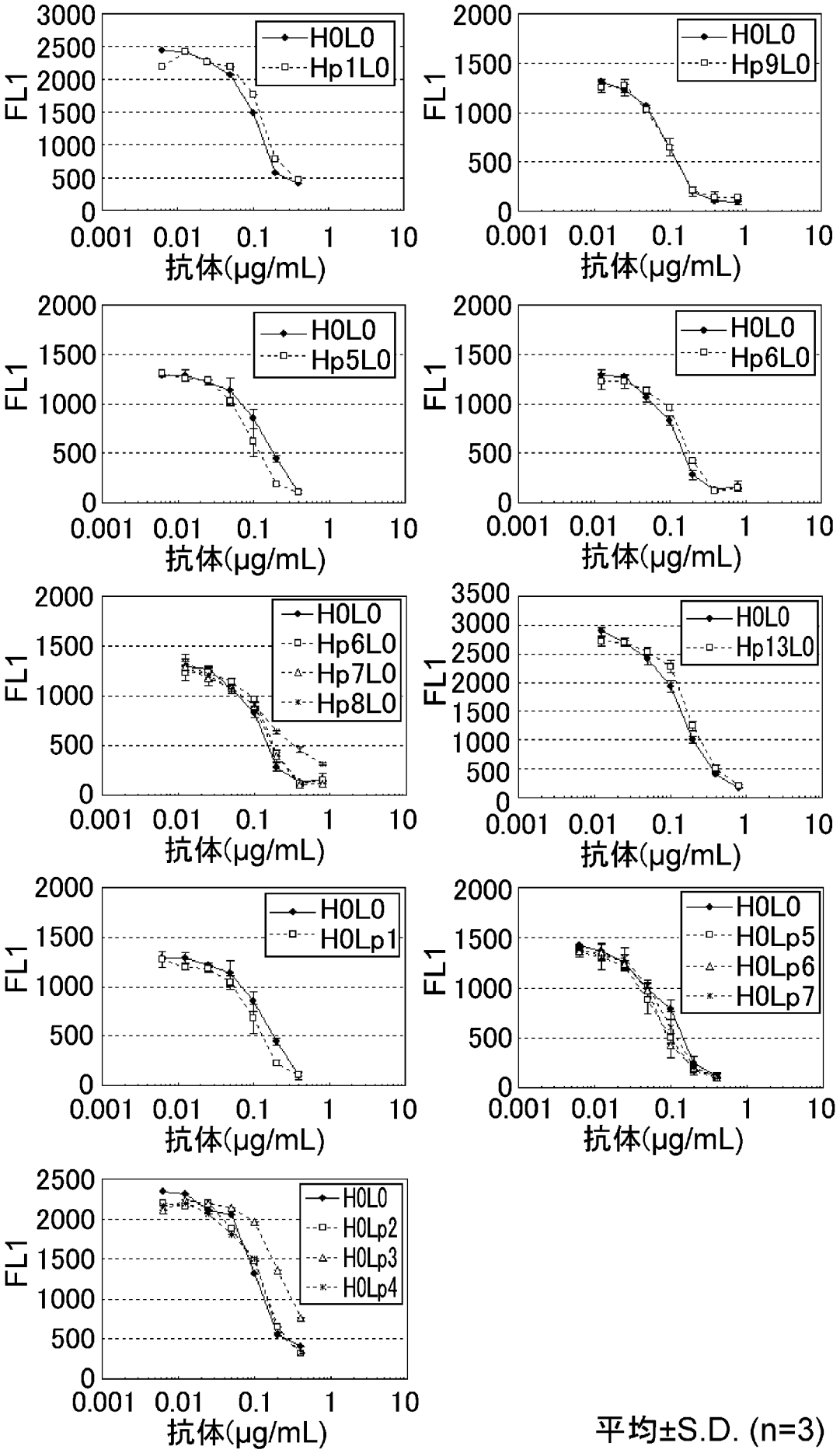

3000
2500
2000
1500
1000
500
0
FL1
NS22キメラ
NS22 H0L0
0.001
0.01
0.1
1
10
抗体濃度(μg/mL)


3000
2500
2000
1500
1000
500
0
FL1
キメラ
H1L0
0.001
0.01
0.1
1
抗体濃度(mg/mL)

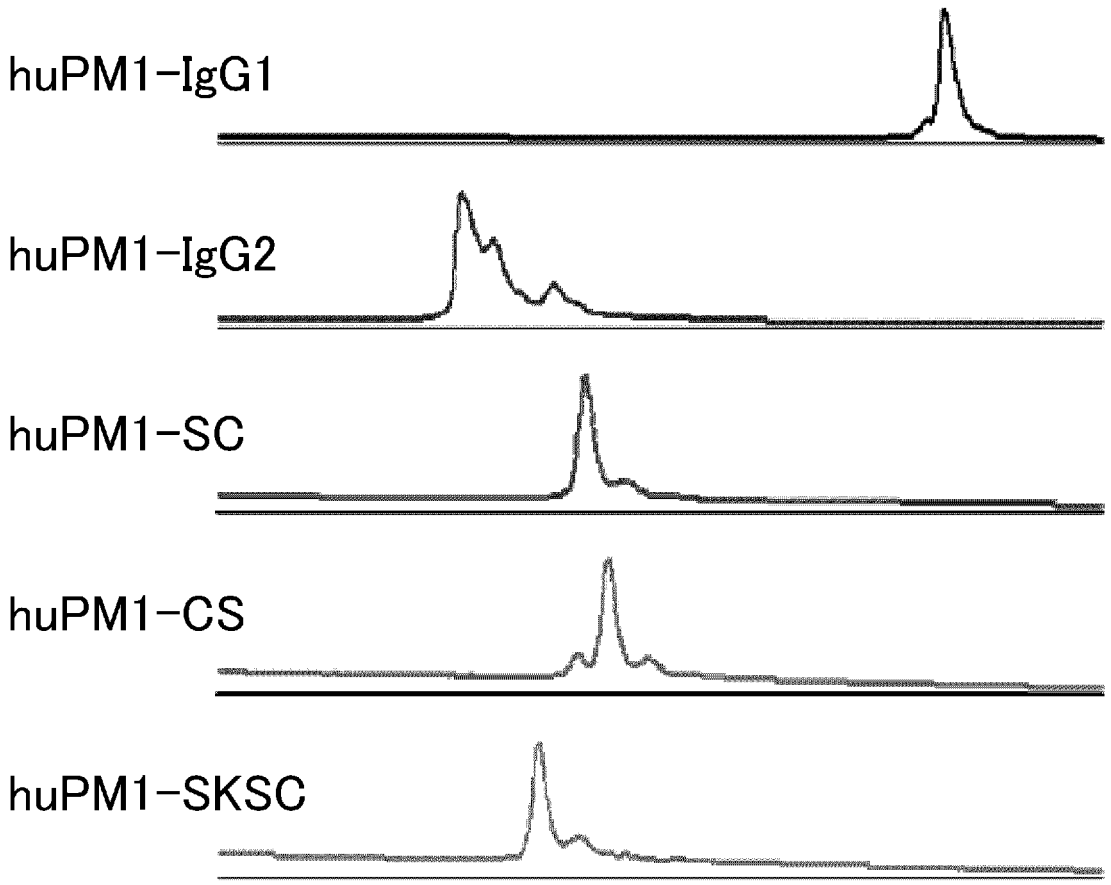
[図10]



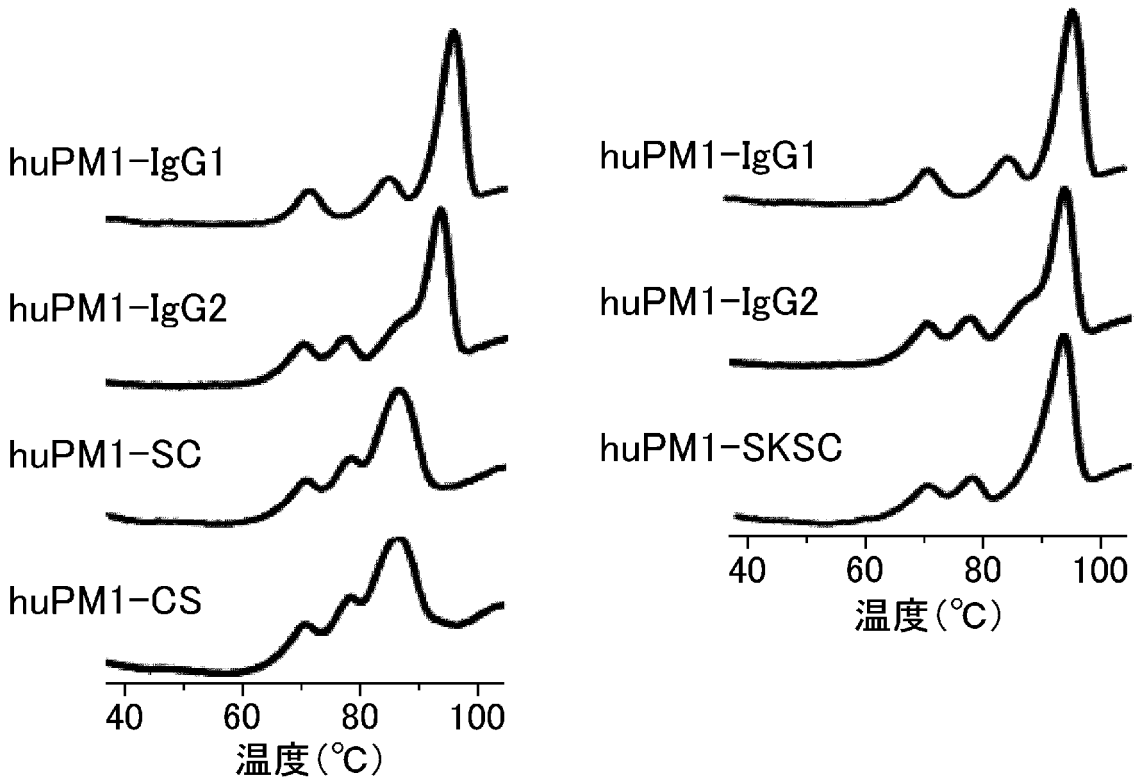
[図11]


FL1
抗体(μg/mL)
H0L0
Hp1L0
Hp9L0
Hp5L0
Hp6L0
Hp7L0
Hp8L0
Hp13L0
H0Lp1
H0Lp5
H0Lp6
H0Lp7
H0Lp2
H0Lp3
H0Lp4
平均±S.D. (n=3)

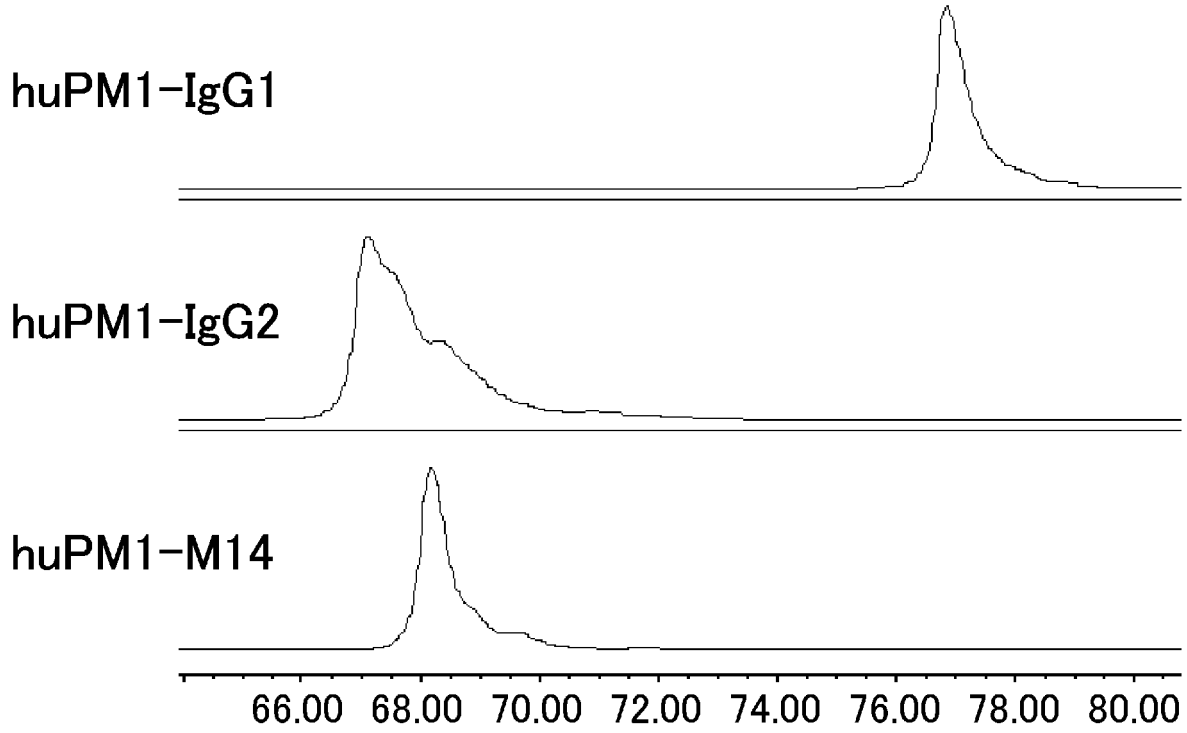
[図12]


huPM1-IgG1
huPM1-IgG2
huPM1-SC
huPM1-CS
huPM1-SKSC

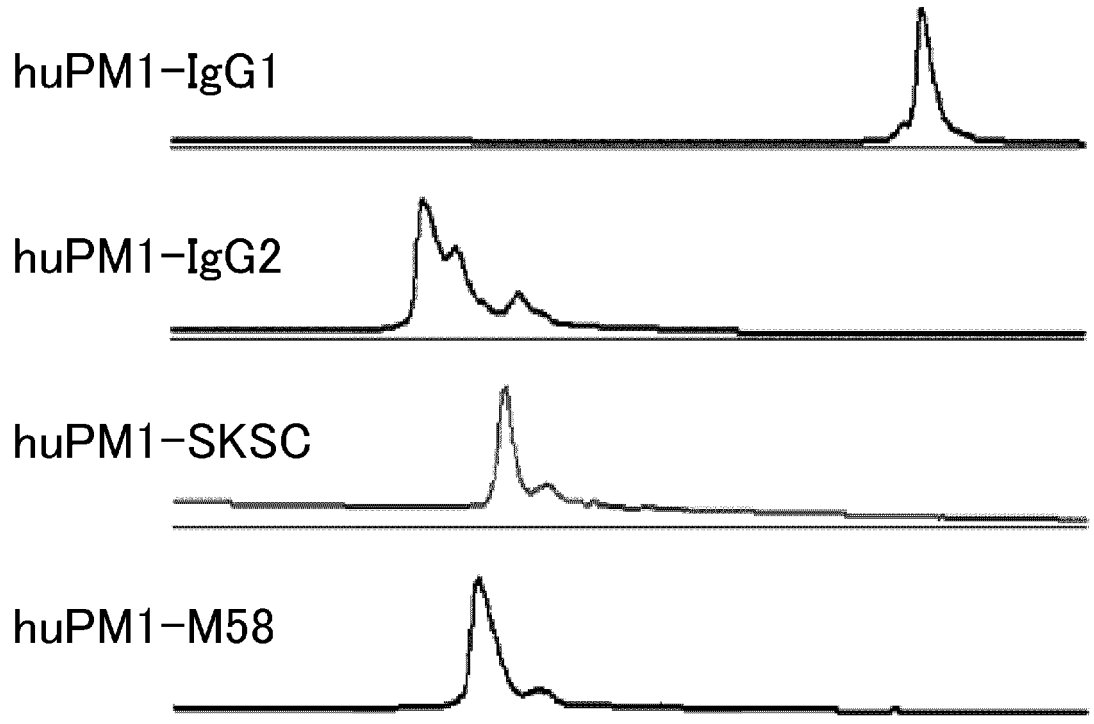
[図13]


huPM1-IgG1
huPM1-IgG2
huPM1-SC
huPM1-CS
40
60
80
100
温度(℃)
huPM1-IgG1
huPM1-IgG2
huPM1-SKSC
40
60
80
100
温度(℃)

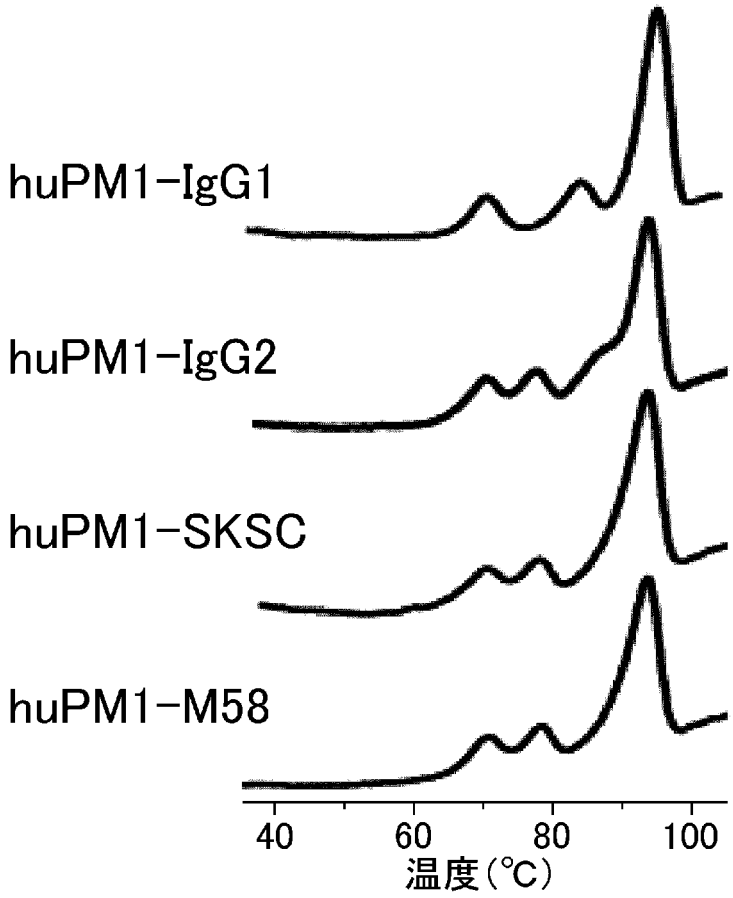
[図14]


huPM1-IgG1
huPM1-IgG2
huPM1-M14
66.00
68.00
70.00
72.00
74.00
76.00
78.00
80.00

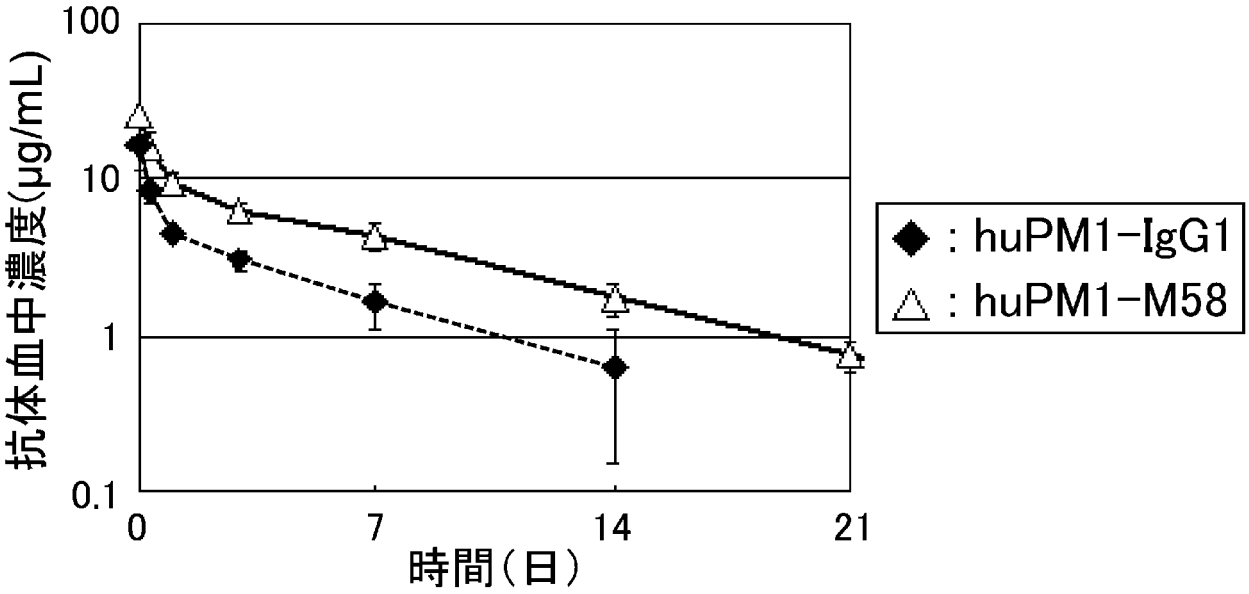
[図15]


huPM1-IgG1
huPM1-IgG2
huPM1-SKSC
huPM1-M58

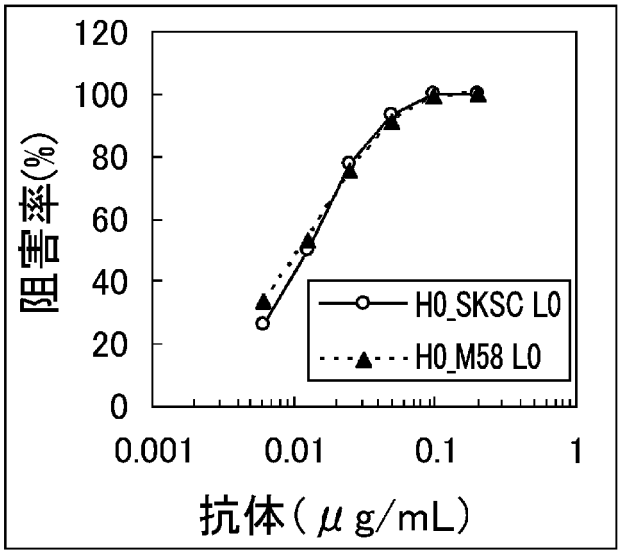
[図16]

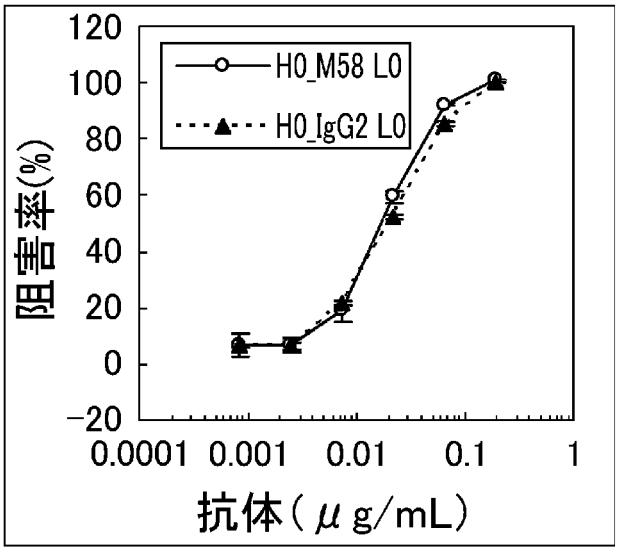

huPM1-IgG1
huPM1-IgG2
huPM1-SKSC
huPM1-M58
40
60
80
100
温度(℃)

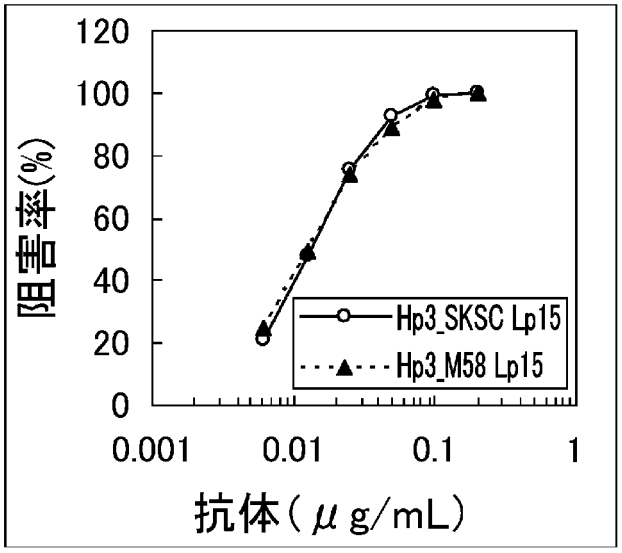
[図17]


100
10
1
0.1
抗体血中濃度(μg/mL)
0
7
14
21
時間(日)
◆ : huPM1-IgG1
△ : huPM1-M58

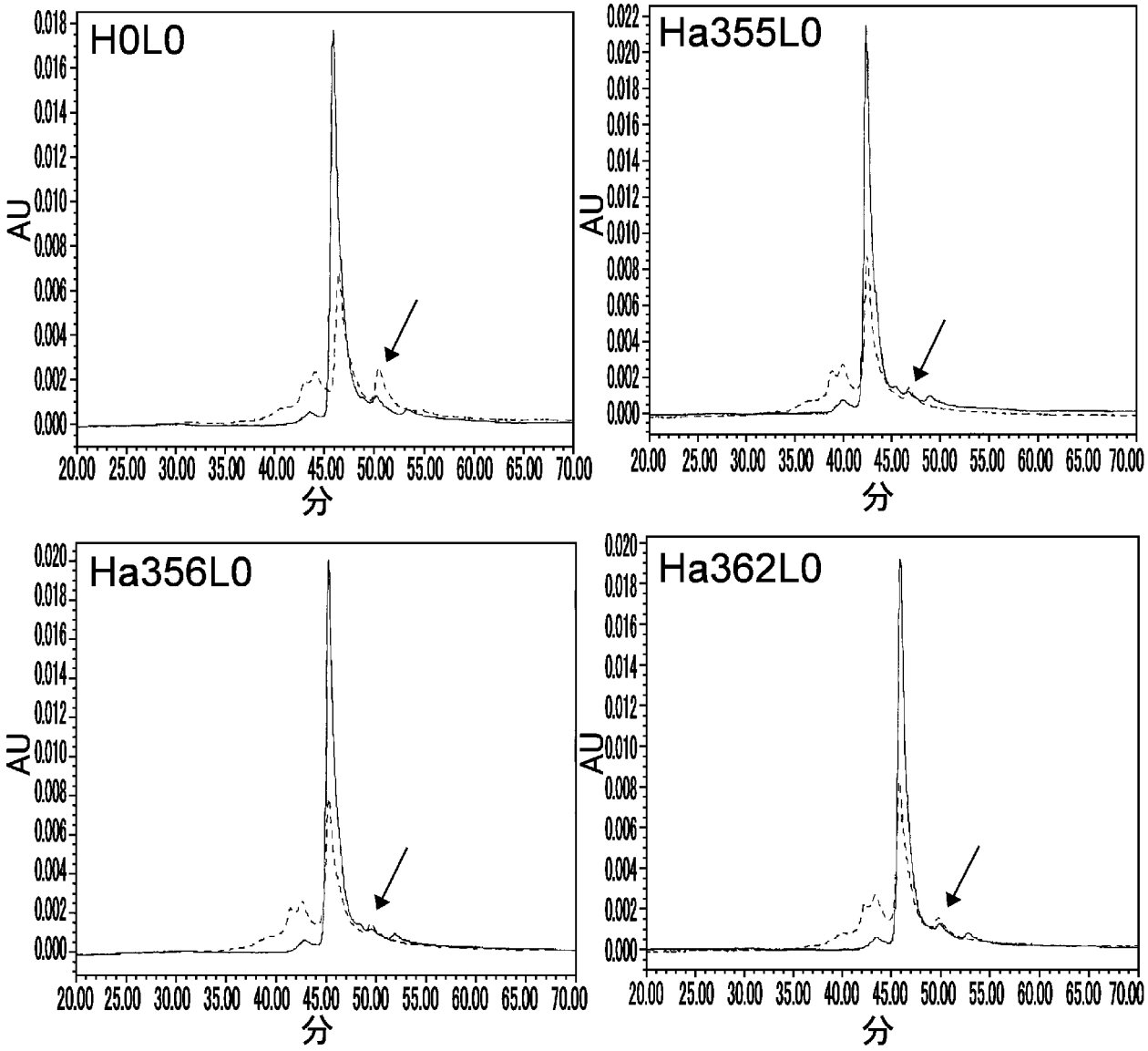
[図18]


120
100
80
60
40
20
0
阻害率(%)
H0_SKSC L0
H0_M58 L0
0.001
0.01
0.1
1
抗体(μg/mL)

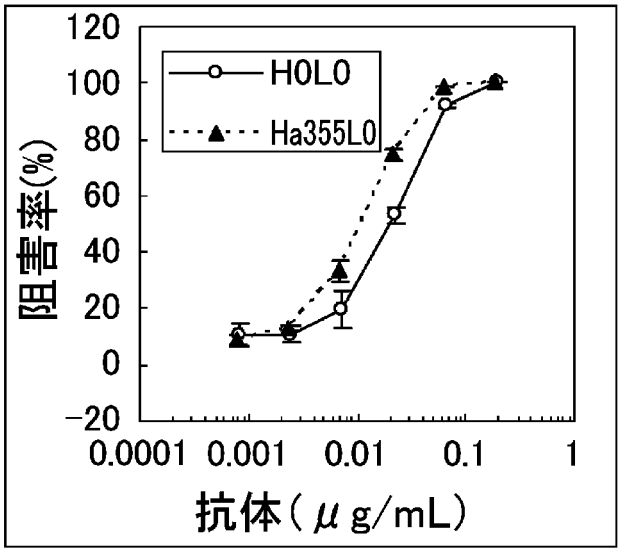

120
100
80
60
40
20
0
−20
阻害率(%)
H0_M58 L0
H0_IgG2 L0
0.0001
0.001
0.01
0.1
1
抗体(μg/mL)

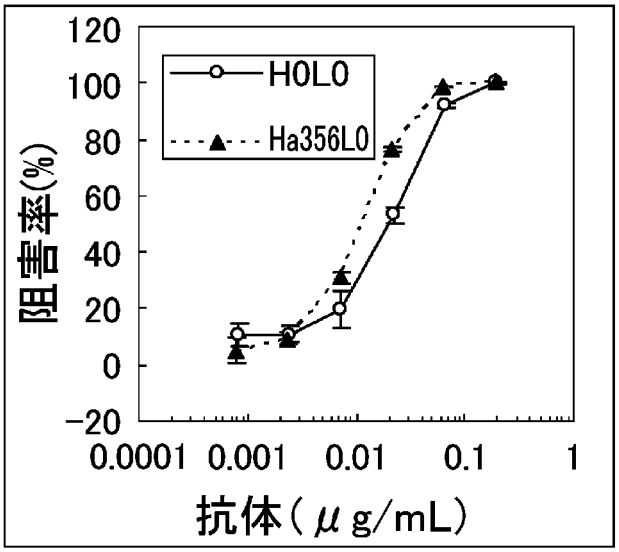

120
100
80
60
40
20
0
阻害率(%)
Hp3_SKSC Lp15
Hp3_M58 Lp15
0.001
0.01
0.1
1
抗体(μg/mL)

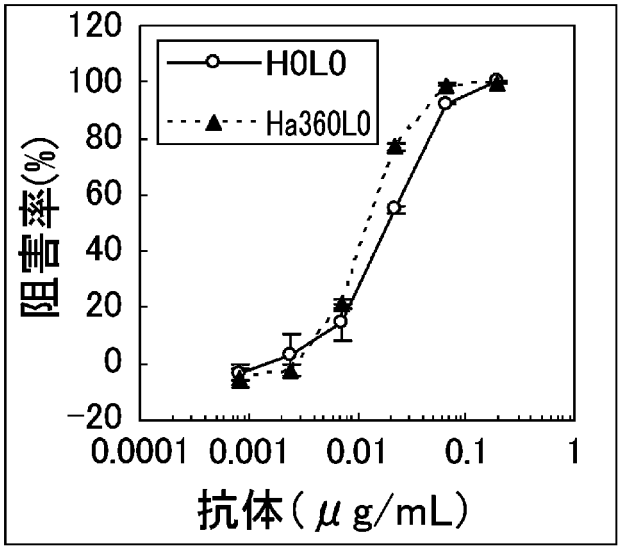
[図19]

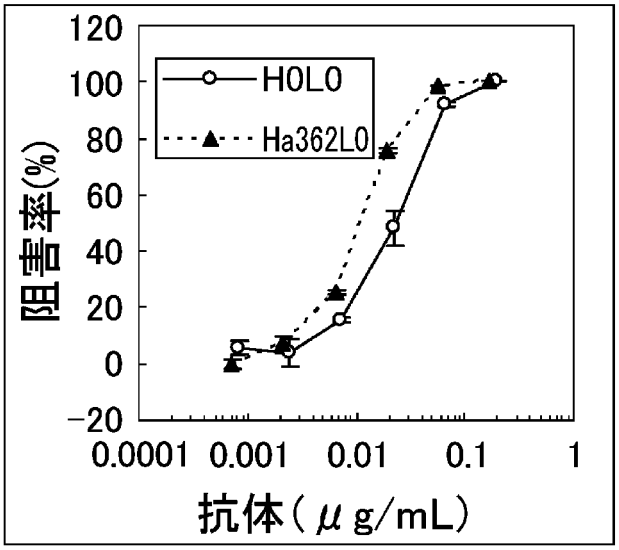

H0L0
Ha355L0
Ha356L0
Ha362L0
AU
分
20.00 25.00 30.00 35.00 40.00 45.00 50.00 55.00 60.00 65.00 70.00

[図20]

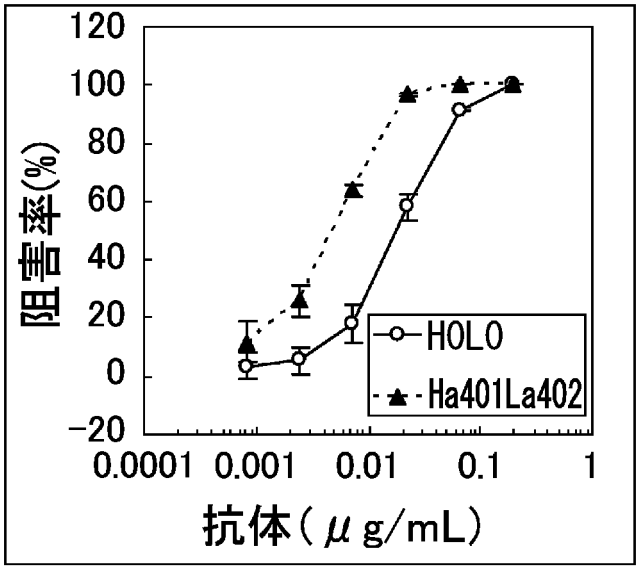

120
100
80
60
40
20
0
−20
阻害率(%)
H0L0
Ha355L0
0.0001
0.001
0.01
0.1
1
抗体(μg/mL)


120
100
80
60
40
20
0
−20
阻害率(%)
H0L0
Ha356L0
0.0001
0.001
0.01
0.1
1
抗体(μg/mL)

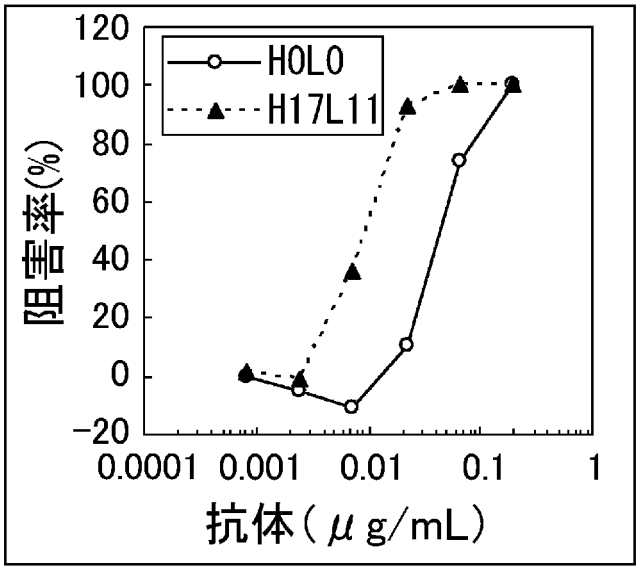

120
100
80
60
40
20
0
−20
阻害率(%)
H0L0
Ha360L0
0.0001
0.001
0.01
0.1
1
抗体(μg/mL)


120
100
80
60
40
20
0
−20
阻害率(%)
H0L0
Ha362L0
0.0001
0.001
0.01
0.1
1
抗体(μg/mL)

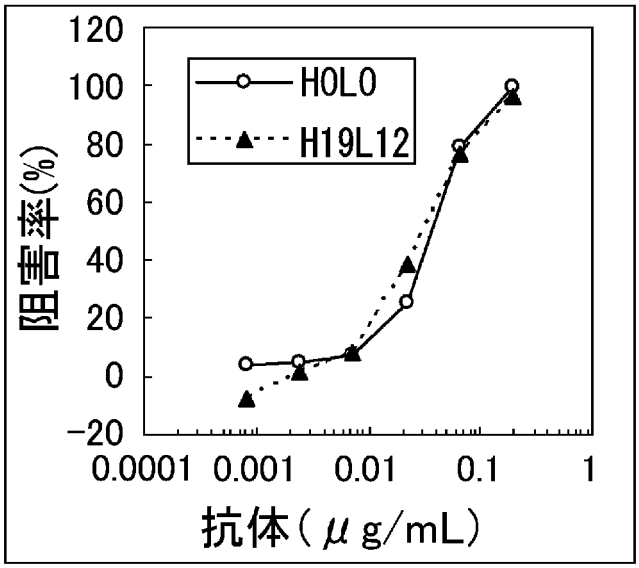
[図21]


120
100
80
60
40
20
0
−20
阻害率(%)
H0L0
Ha401La402
0.0001
0.001
0.01
0.1
1
抗体(μg/mL)

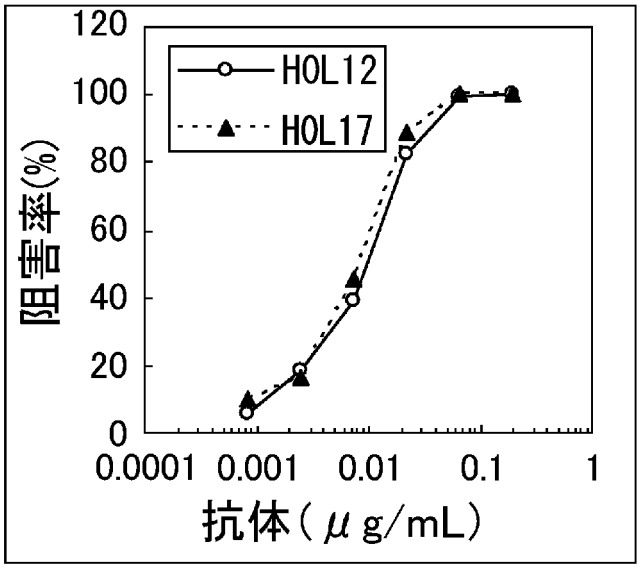
[図22]


120
100
80
60
40
20
0
−20
阻害率(%)
H0L0
H17L11
0.0001
0.001
0.01
0.1
1
抗体(μg/mL)

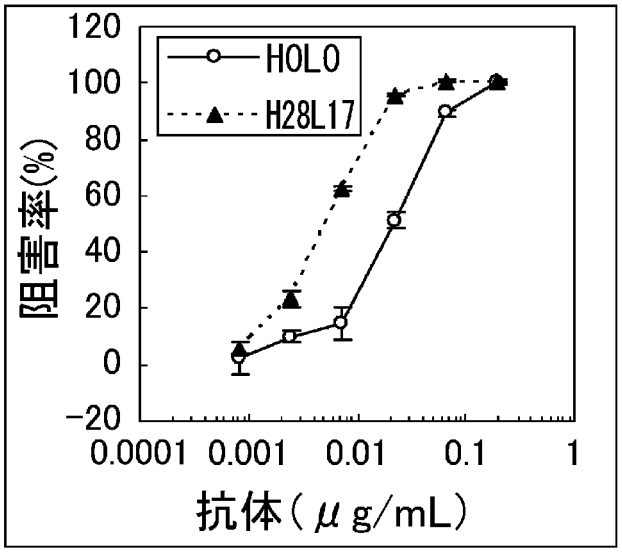
[図23]

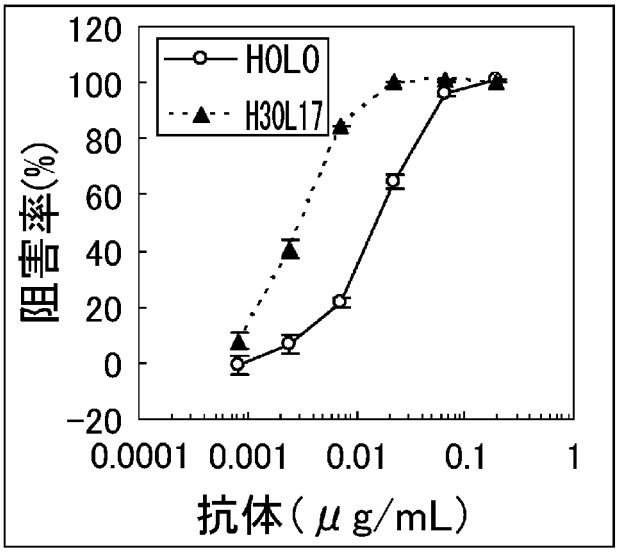

120
100
80
60
40
20
0
−20
阻害率(%)
H0L0
H19L12
0.0001
0.001
0.01
0.1
1
抗体(μg/mL)

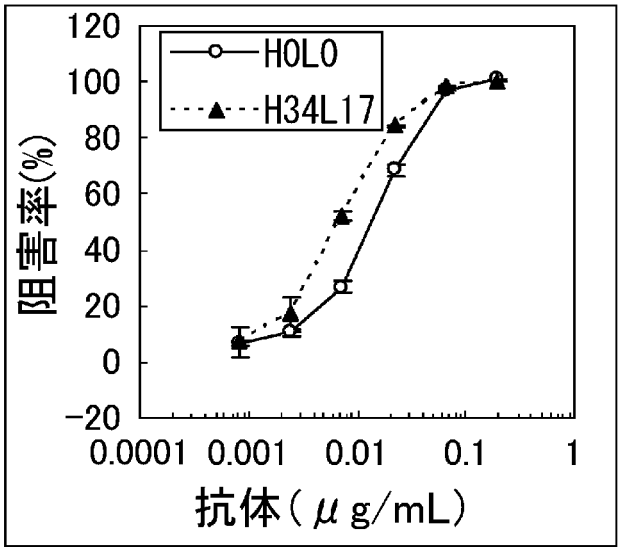
[図24]

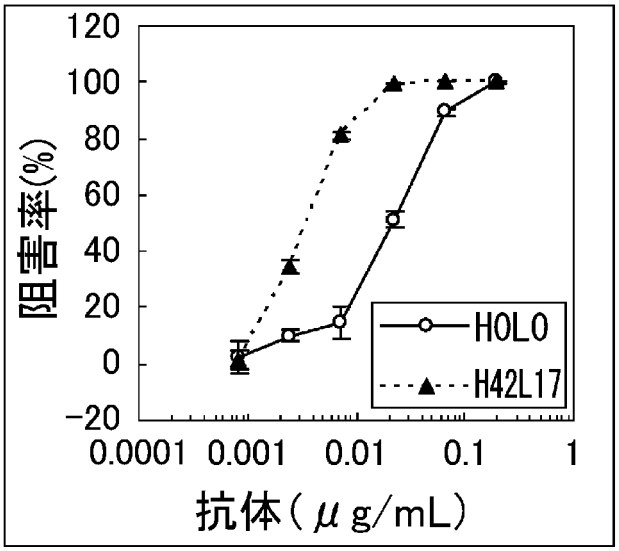

120
100
80
60
40
20
0
阻害率(%)
H0L12
H0L17
0.0001
0.001
0.01
0.1
1
抗体(μg/mL)

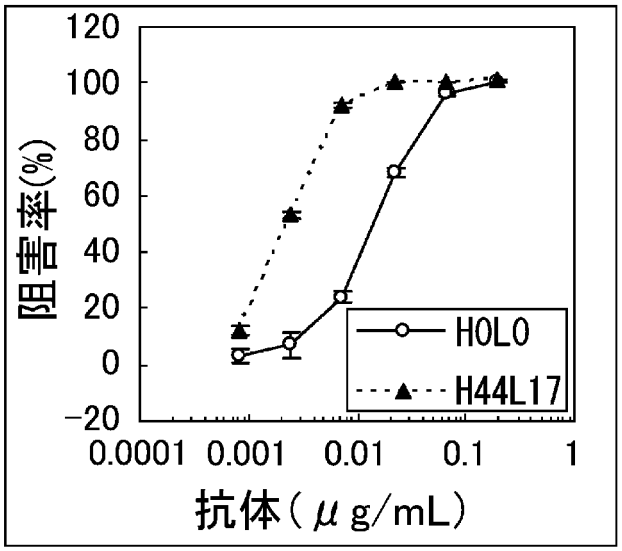
[図25-1]

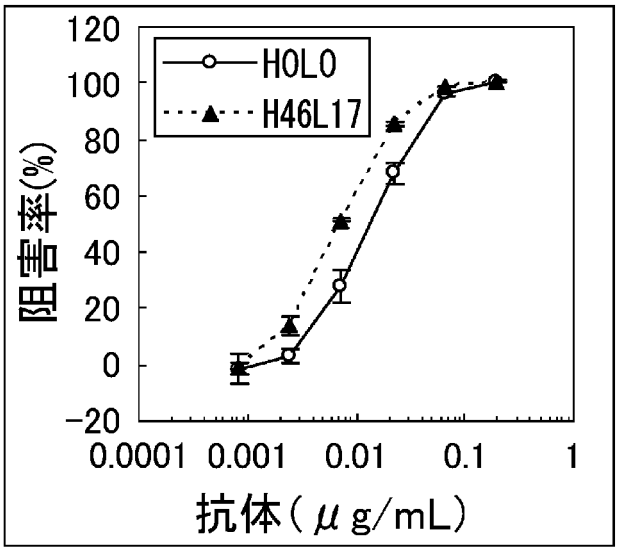

HOLO
H28L17
阻害率(%)
120
100
80
60
40
20
0
-20
0.0001
0.001
0.01
0.1
1
抗体(μg/mL)


HOLO
H30L17
阻害率(%)
120
100
80
60
40
20
0
-20
0.0001
0.001
0.01
0.1
1
抗体(μg/mL)

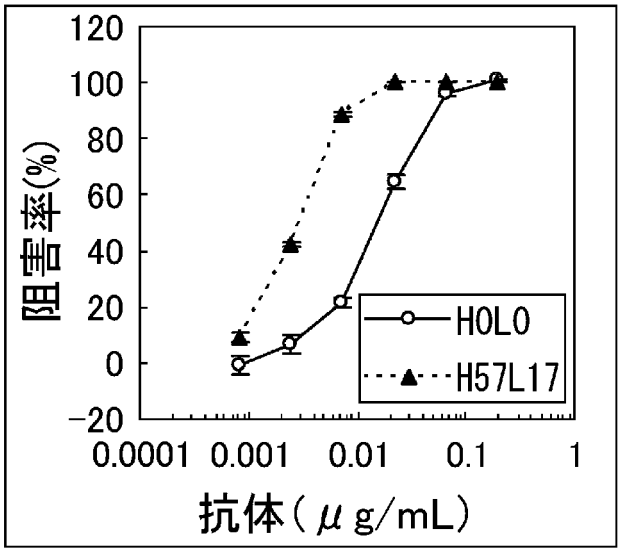

HOLO
H34L17
阻害率(%)
120
100
80
60
40
20
0
-20
0.0001
0.001
0.01
0.1
1
抗体(μg/mL)

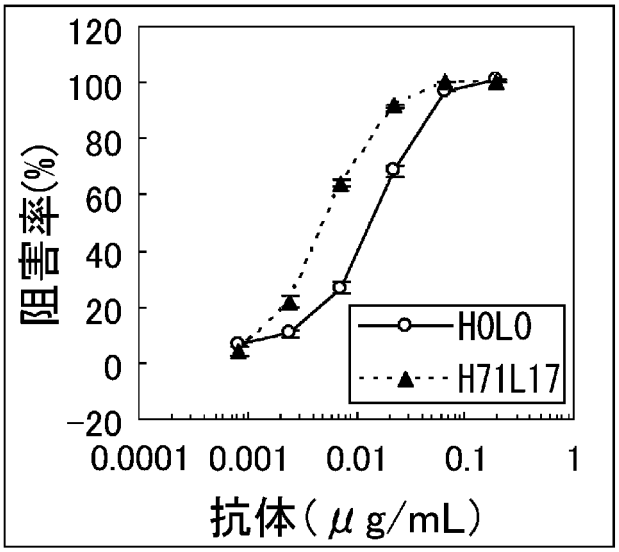

HOLO
H42L17
阻害率(%)
120
100
80
60
40
20
0
-20
0.0001
0.001
0.01
0.1
1
抗体(μg/mL)

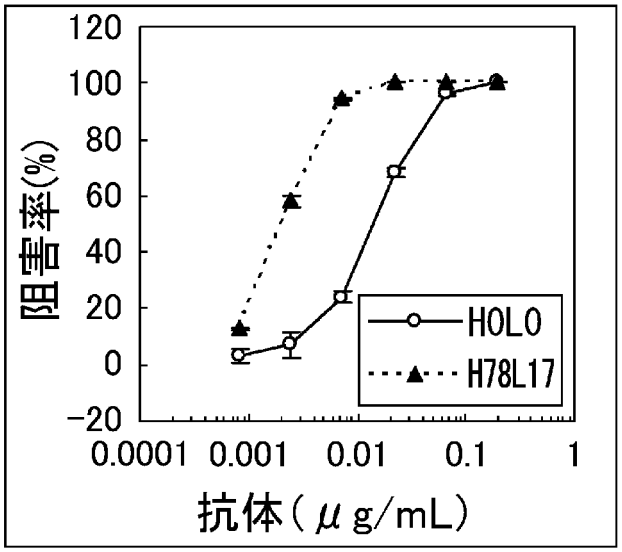

HOLO
H44L17
阻害率(%)
120
100
80
60
40
20
0
-20
0.0001
0.001
0.01
0.1
1
抗体(μg/mL)

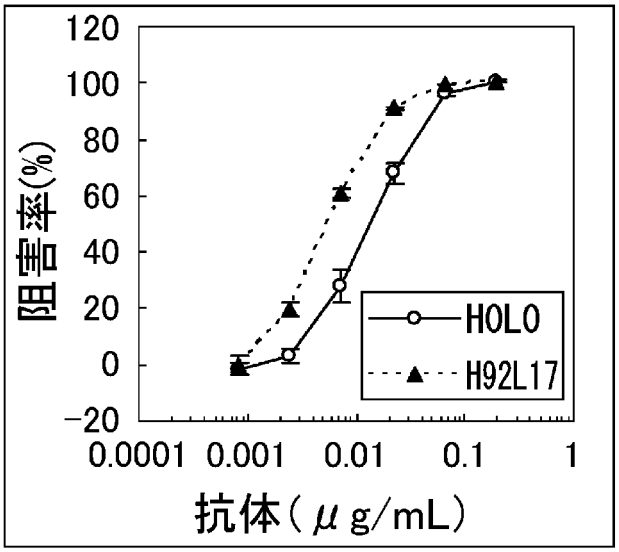

HOLO
H46L17
阻害率(%)
120
100
80
60
40
20
0
-20
0.0001
0.001
0.01
0.1
1
抗体(μg/mL)

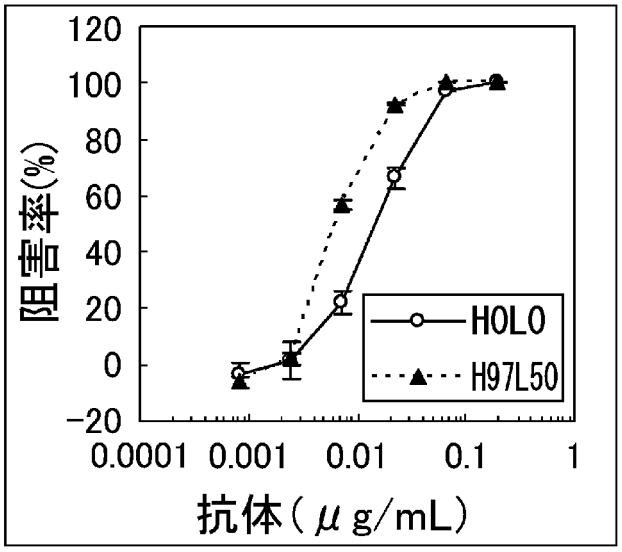
[図25-2]

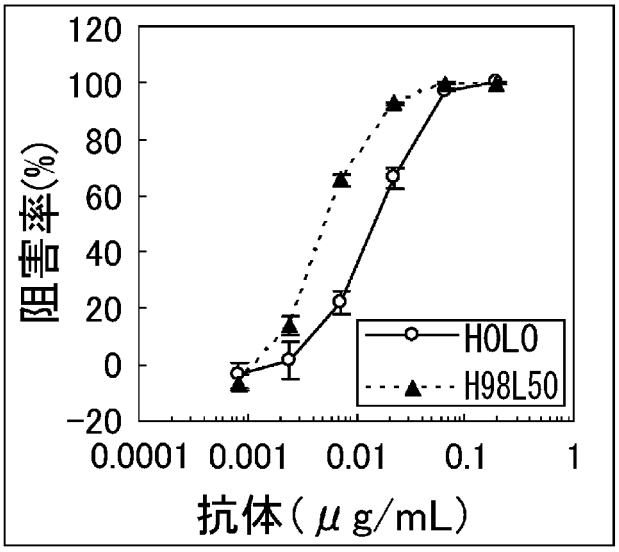

120
100
80
60
40
20
0
−20
阻害率(%)
0.0001 0.001 0.01 0.1 1
抗体(μg/mL)
H0L0
H57L17


120
100
80
60
40
20
0
−20
阻害率(%)
0.0001 0.001 0.01 0.1 1
抗体(μg/mL)
H0L0
H71L17

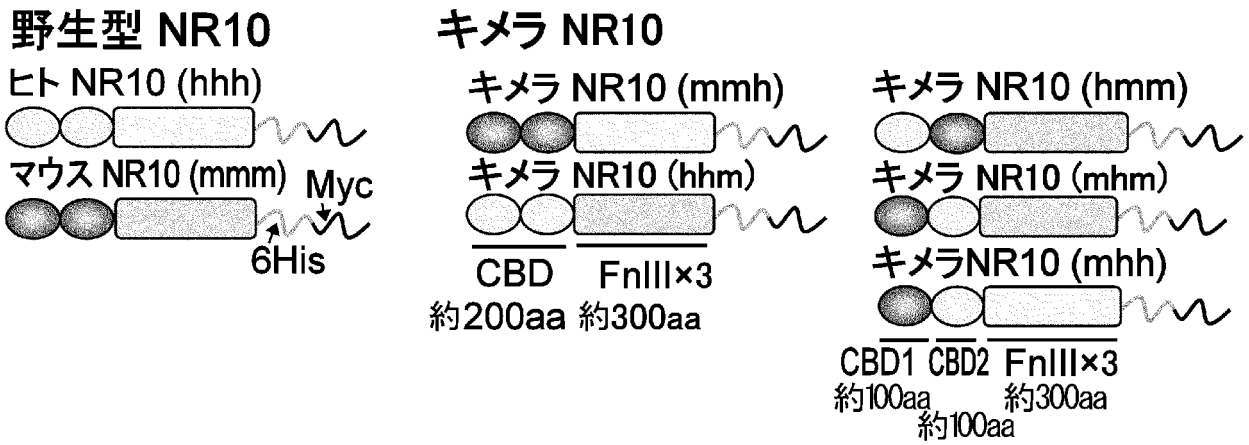

120
100
80
60
40
20
0
−20
阻害率(%)
0.0001 0.001 0.01 0.1 1
抗体(μg/mL)
H0L0
H78L17


120
100
80
60
40
20
0
−20
阻害率(%)
0.0001 0.001 0.01 0.1 1
抗体(μg/mL)
H0L0
H92L17

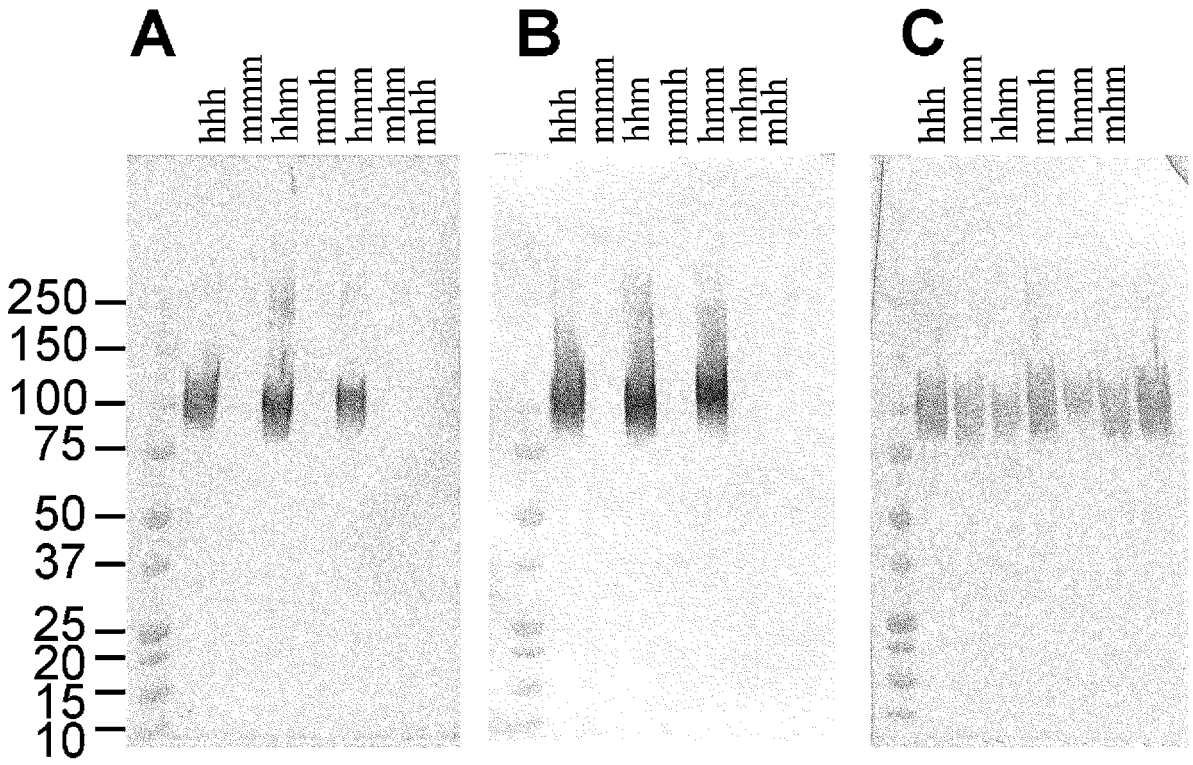

120
100
80
60
40
20
0
−20
阻害率(%)
0.0001 0.001 0.01 0.1 1
抗体(μg/mL)
H0L0
H97L50


120
100
80
60
40
20
0
−20
阻害率(%)
0.0001 0.001 0.01 0.1 1
抗体(μg/mL)
H0L0
H98L50

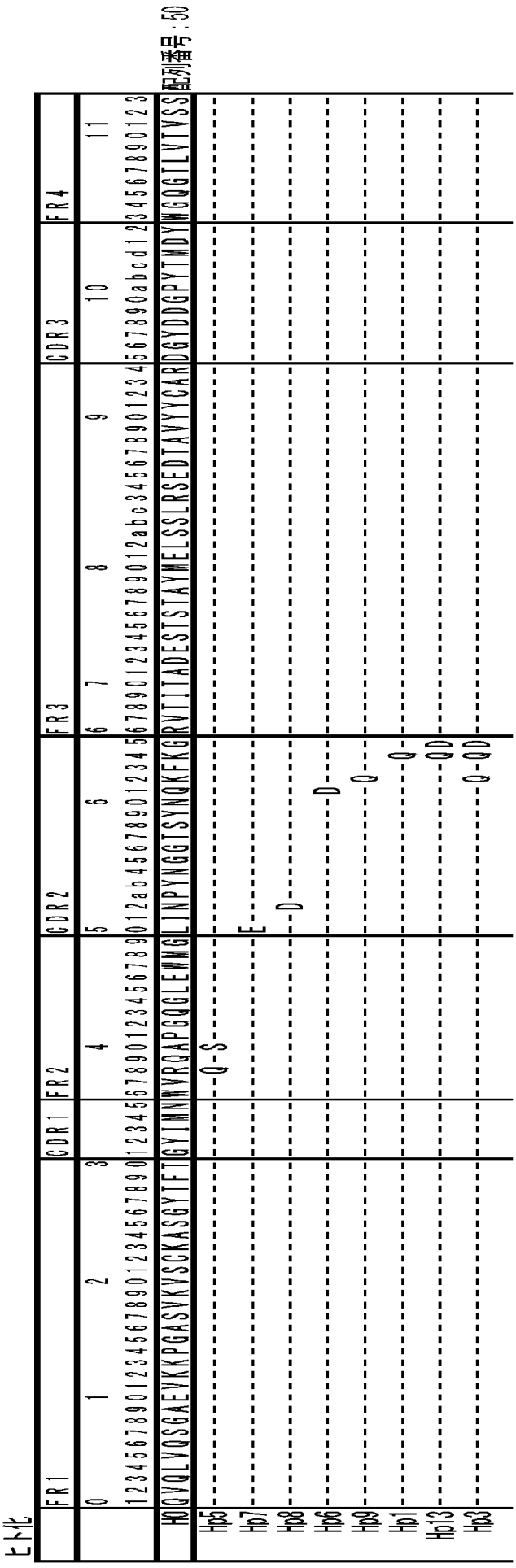
[図26]


野生型 NR10
ヒト NR10 (hhh)
マウス NR10 (mmm)
Myc
6His
キメラ NR10
キメラ NR10 (mmh)
キメラ NR10 (hhm)
CBD
FnIII×3
約200aa
約300aa
キメラ NR10 (hmm)
キメラ NR10 (mhm)
キメラNR10 (mhh)
CBD1
CBD2
FnIII×3
約100aa
約100aa
約300aa

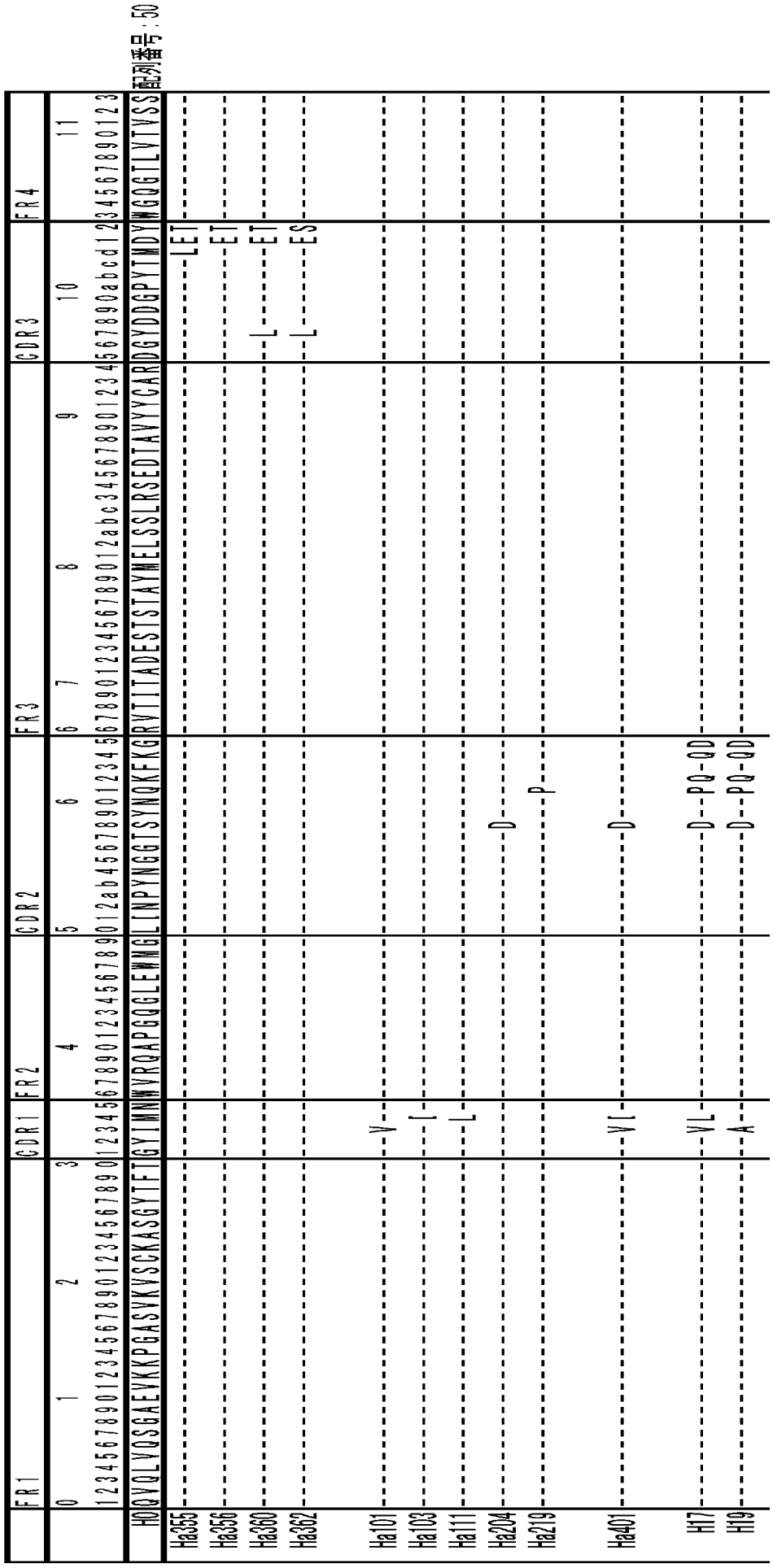
[図27]


A
B
C
hhh
mmm
hhm
mmh
hmm
mhm
mhh
250
150
100
75
50
37
25
20
15
10

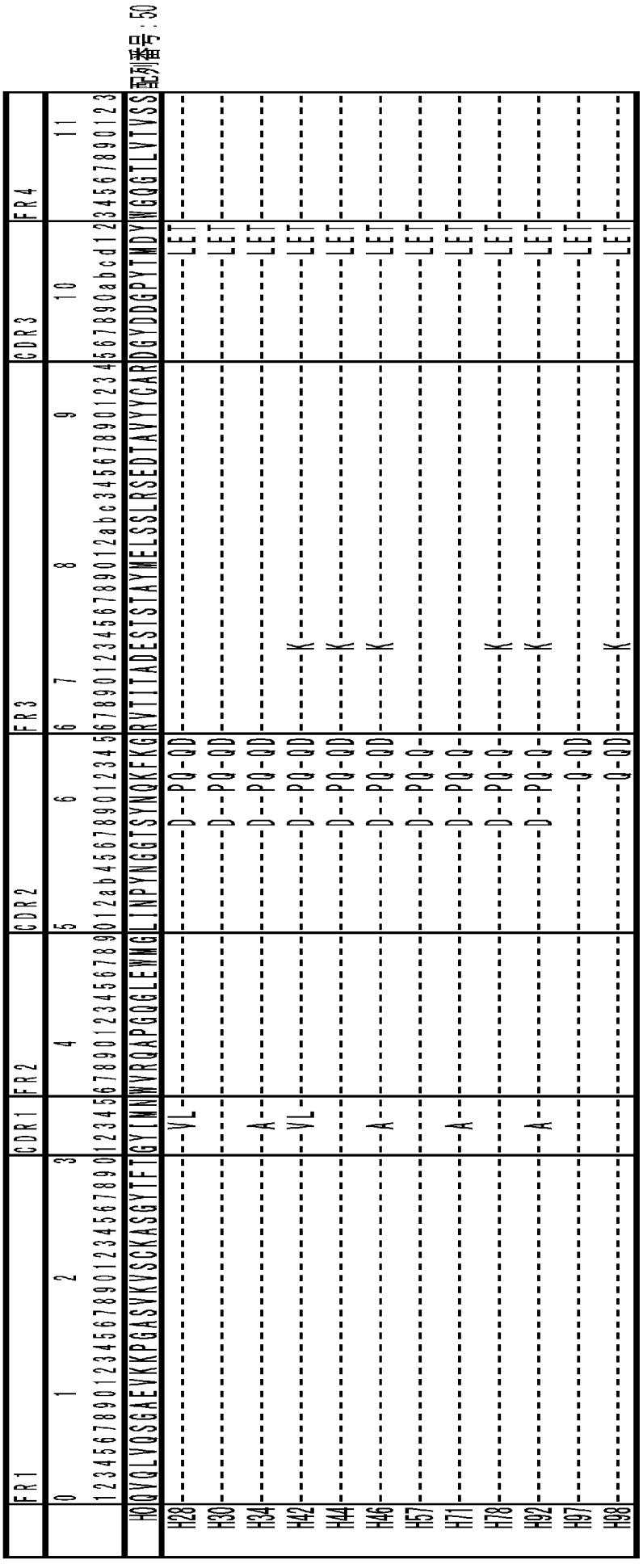
[図28-1]


ヒト化
FR1
CDR1
FR2
CDR2
FR3
CDR3
FR4
配列番号:50
HQVQLVQSGAEVKKPGASVKVSCKASGYTFTGYIMNWVRQAPGQGLEWMGLINPYNGGTSYNQKFKGRVTITADESTSTAYMELSSLRSEDTAVYYCARDGYDDGPYTMDYWGQGTLVTVSS
Hb5
Hb7
Hb8
Hb6
Hb9
Hb1
Hb13
Hb3

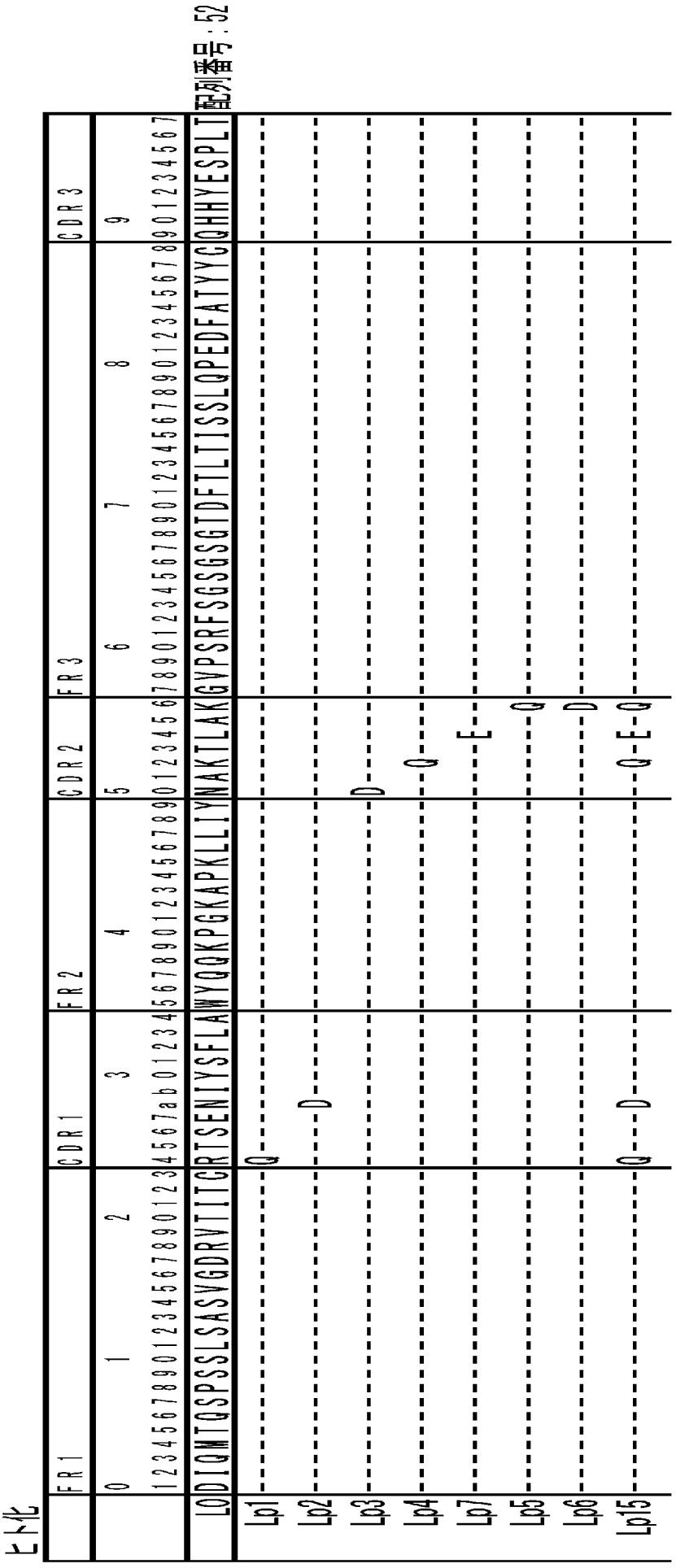
[図28-2]


配列番号:50
FR1
CDR1
FR2
CDR2
FR3
CDR3
FR4
Ha355
Ha356
Ha360
Ha362
Ha101
Ha103
Ha111
Ha204
Ha219
Ha401
H17
H19

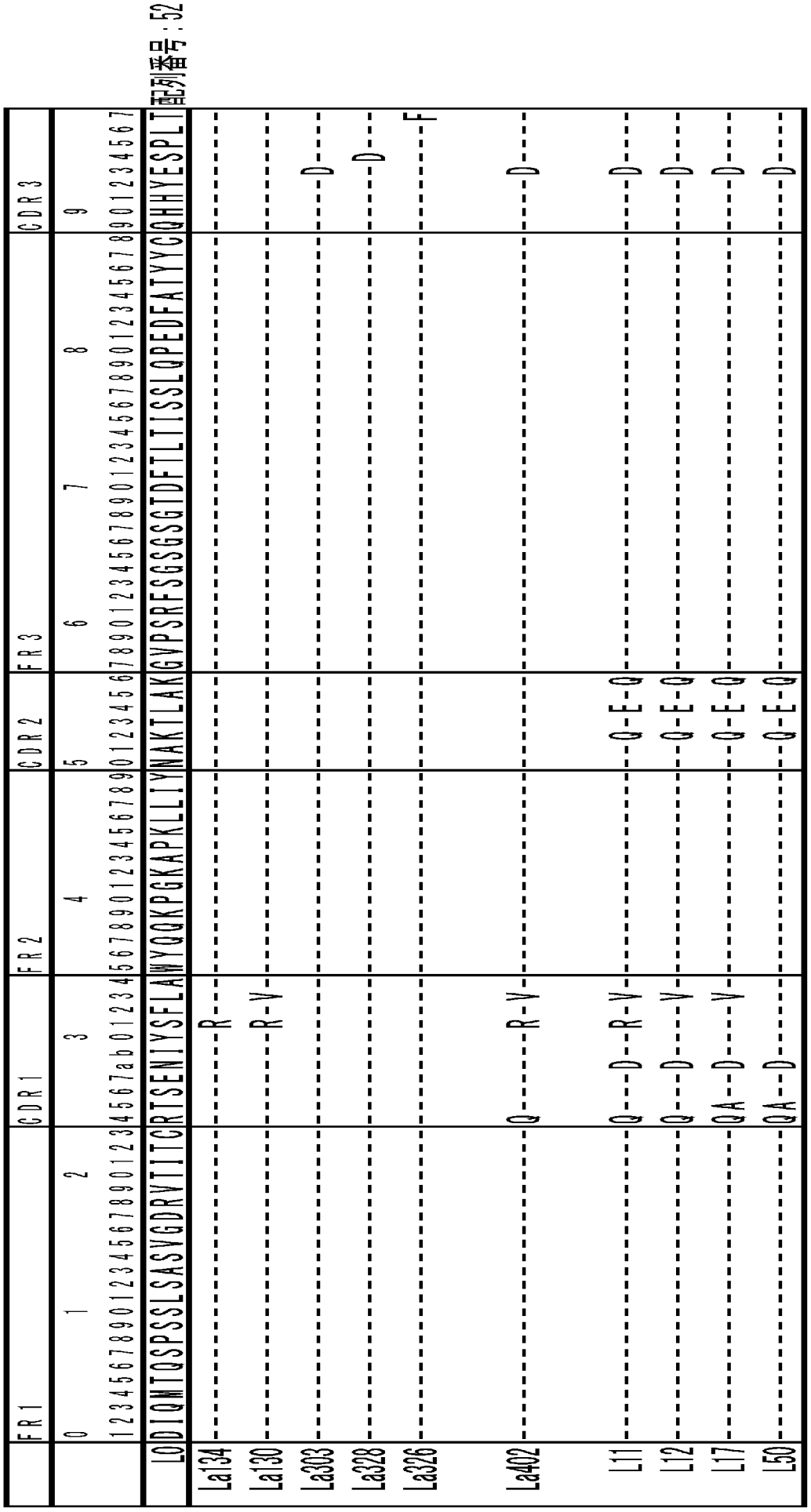
[図28-3]



[図29-1]


ヒト化
配列番号:52
FR1
CDR1
FR2
CDR2
FR3
CDR3
LODIQMTQSPSSLSASVGDRVTITCRTSENIYSFLAWYQQKPGKAPKLLIYNAKTLAKGVPSRFSGSGSGTDFTLTISSLQPEDFATYYCQHHYESPLT
Lp1
Lp2
Lp3
Lp4
Lp7
Lp5
Lp6
Lp15

[図29-2]


配列番号:52
FR1
CDR1
FR2
CDR2
FR3
CDR3
La134
La130
La303
La328
La326
La402
L11
L12
L17
L50