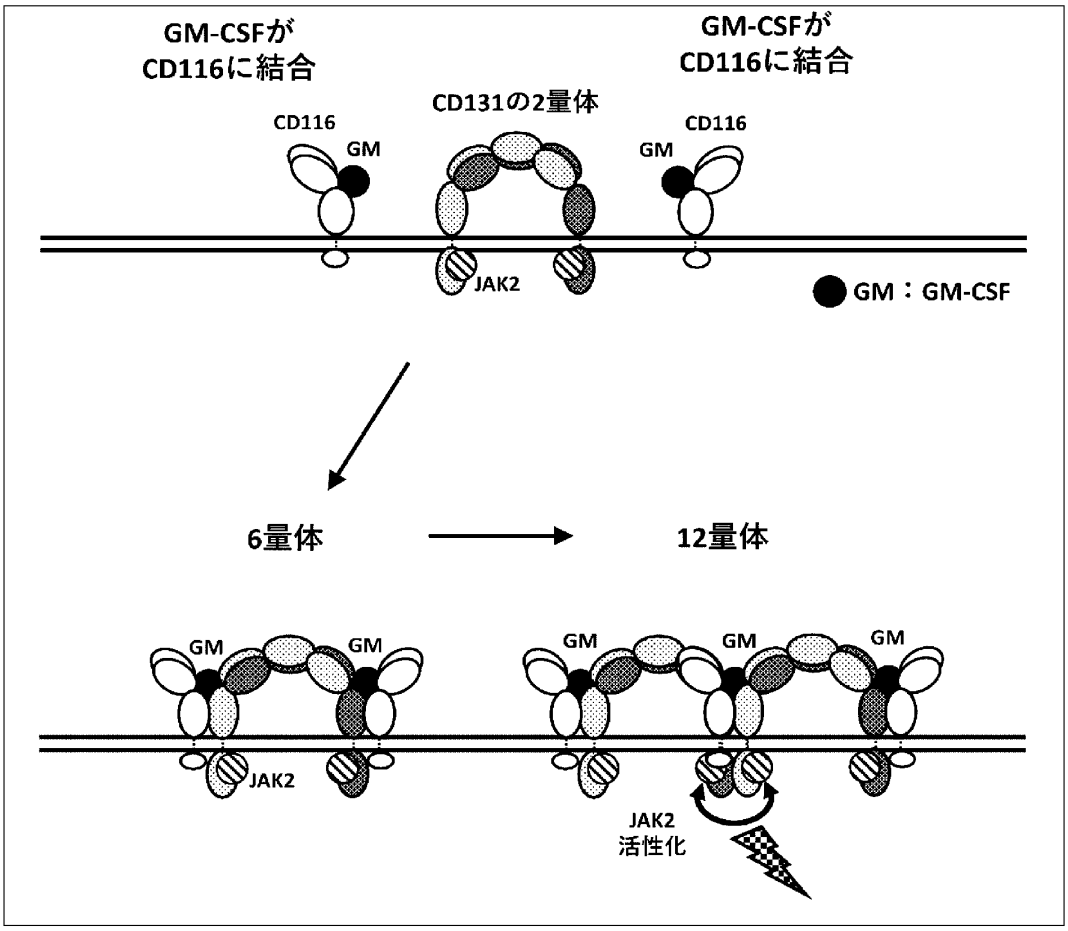
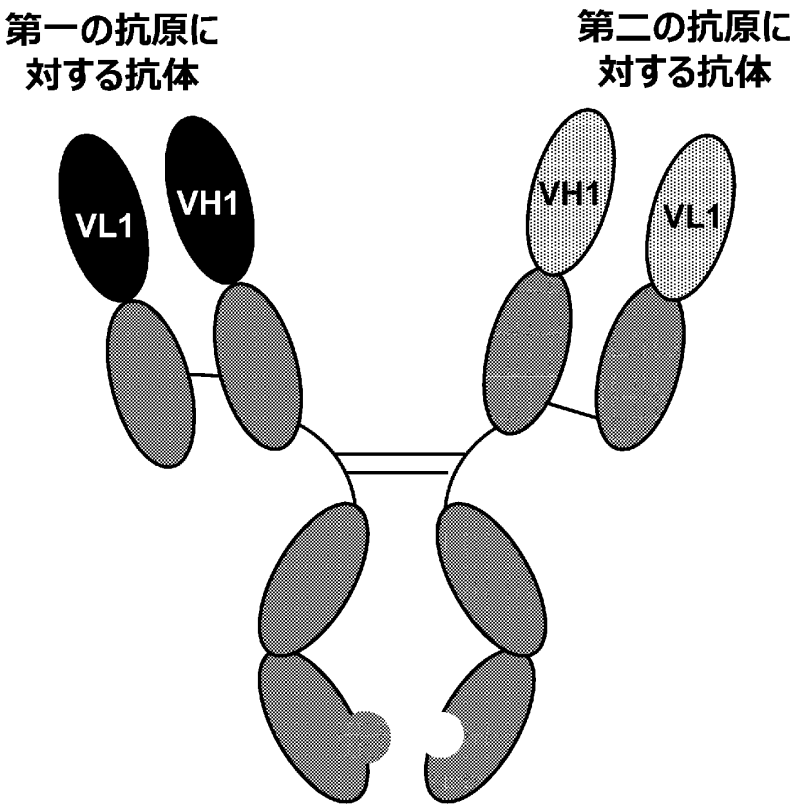
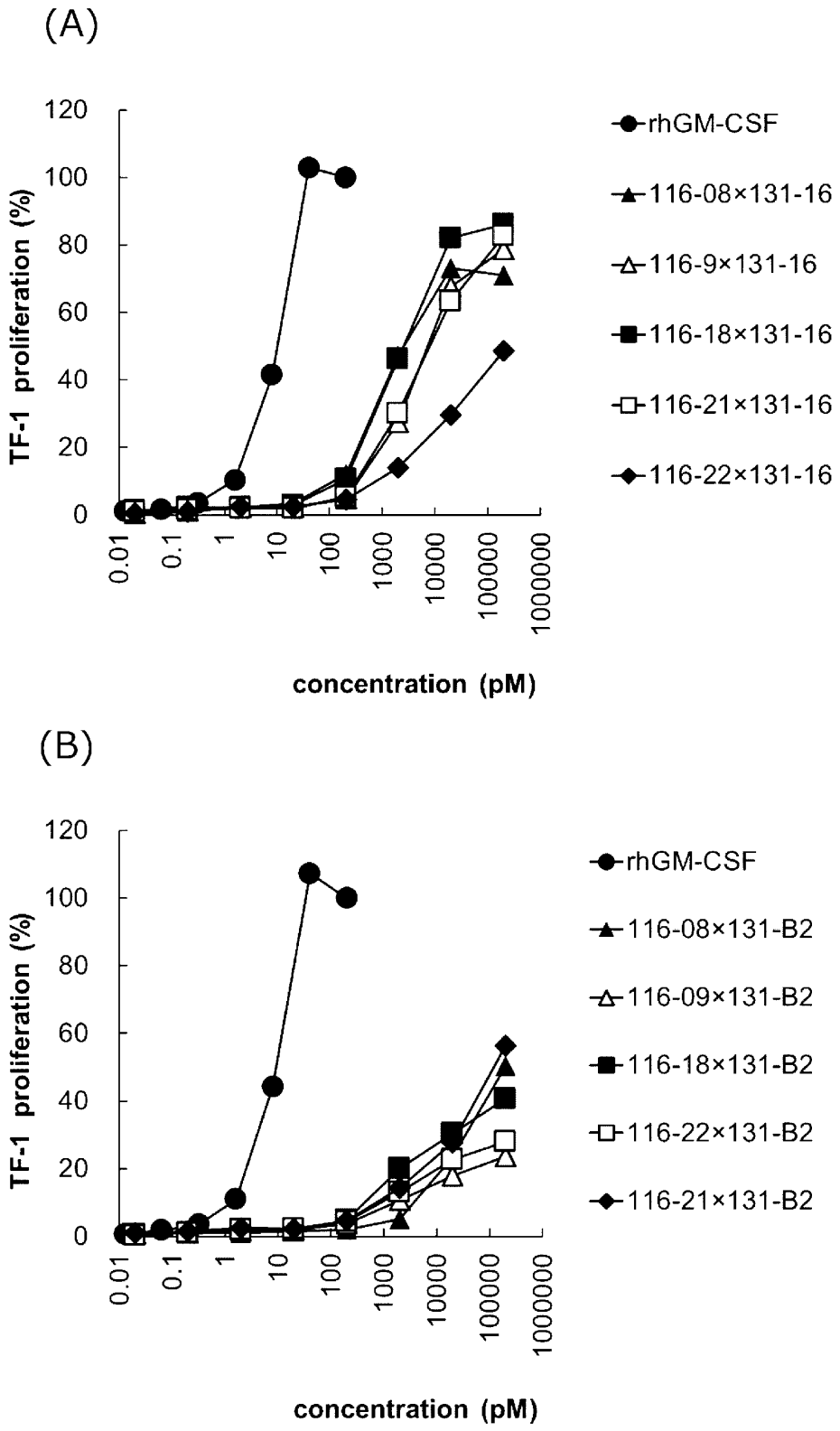
[図1]


GM-CSFが
CD116に結合
GM-CSFが
CD116に結合
CD131の2量体
CD116
GM
CD116
GM
JAK2
GM：GM-CSF
6量体
12量体
GM
GM
GM
GM
GM
JAK2
JAK2
活性化

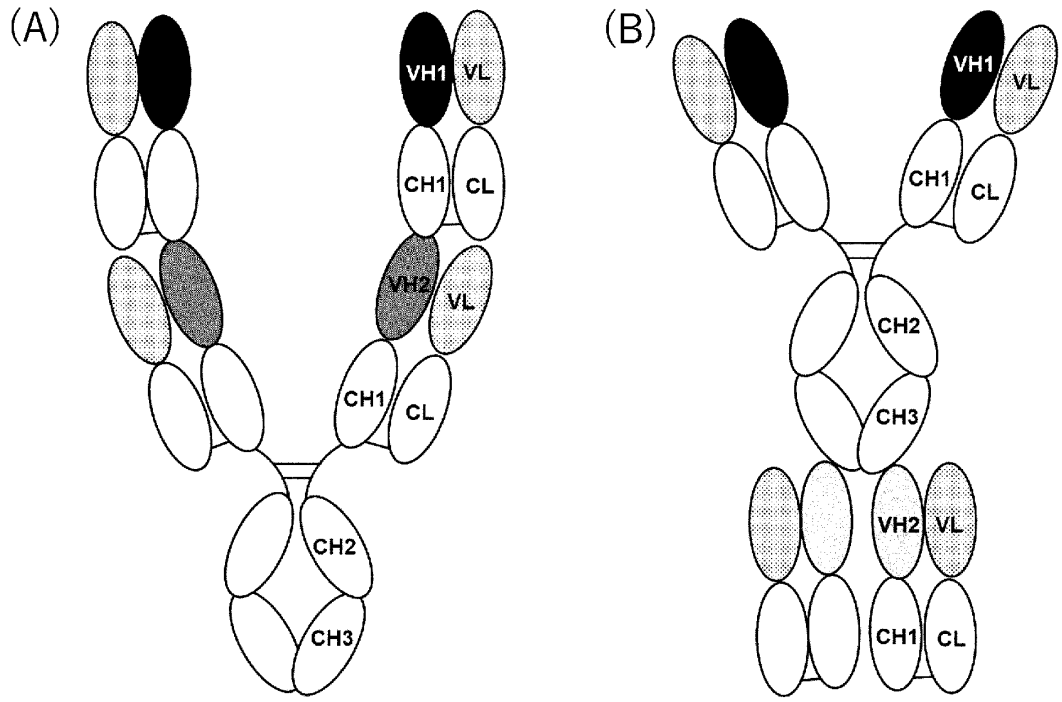
[図2]



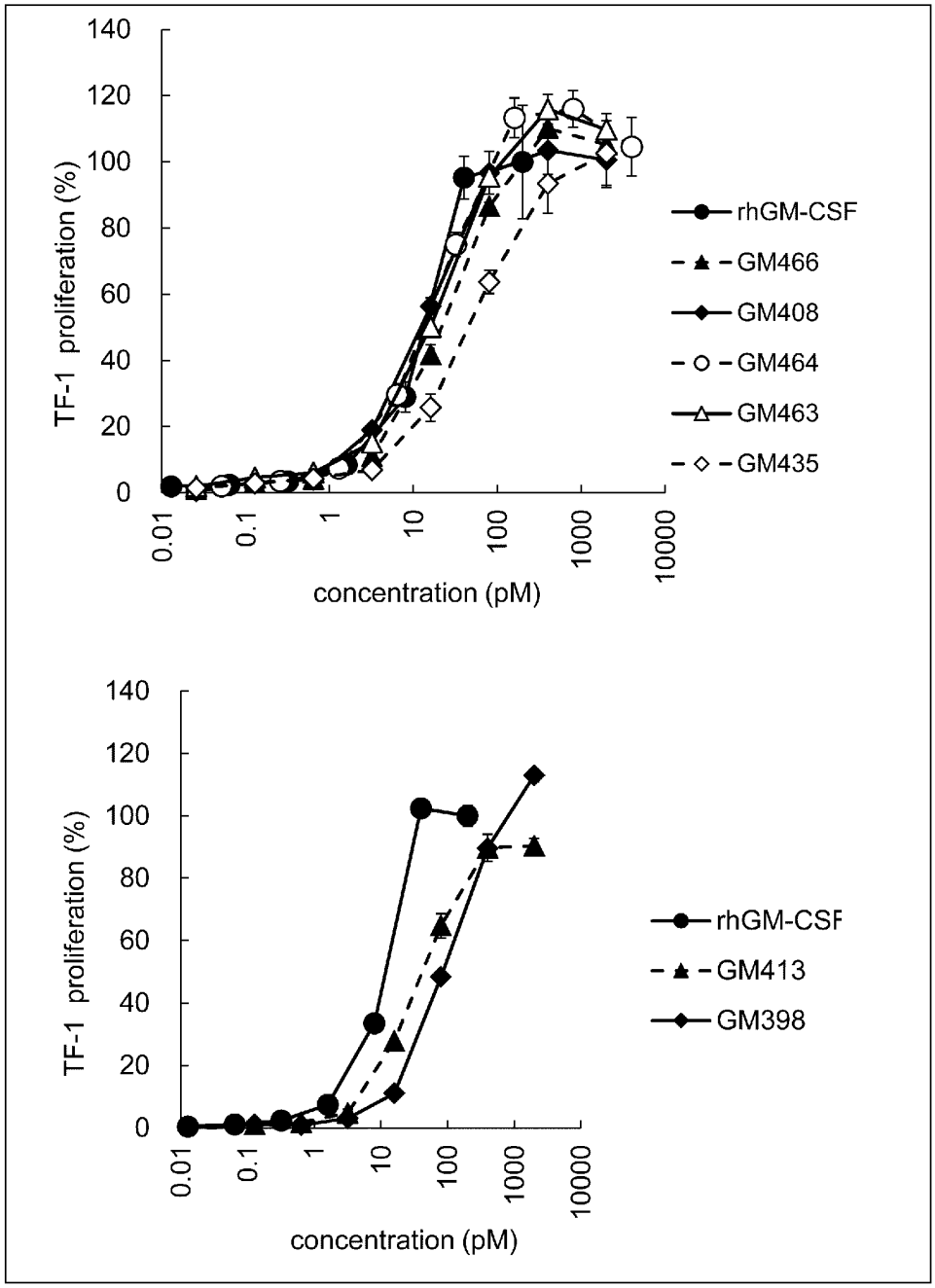
[図3]


(A)
TF-1 proliferation (%)
120
100
80
60
40
20
0
0.01
0.1
1
10
100
1000
10000
100000
1000000
concentration (pM)
rhGM-CSF
116-08×131-16
116-9×131-16
116-18×131-16
116-21×131-16
116-22×131-16
(B)
TF-1 proliferation (%)
120
100
80
60
40
20
0
0.01
0.1
1
10
100
1000
10000
100000
1000000
concentration (pM)
rhGM-CSF
116-08×131-B2
116-09×131-B2
116-18×131-B2
116-22×131-B2
116-21×131-B2

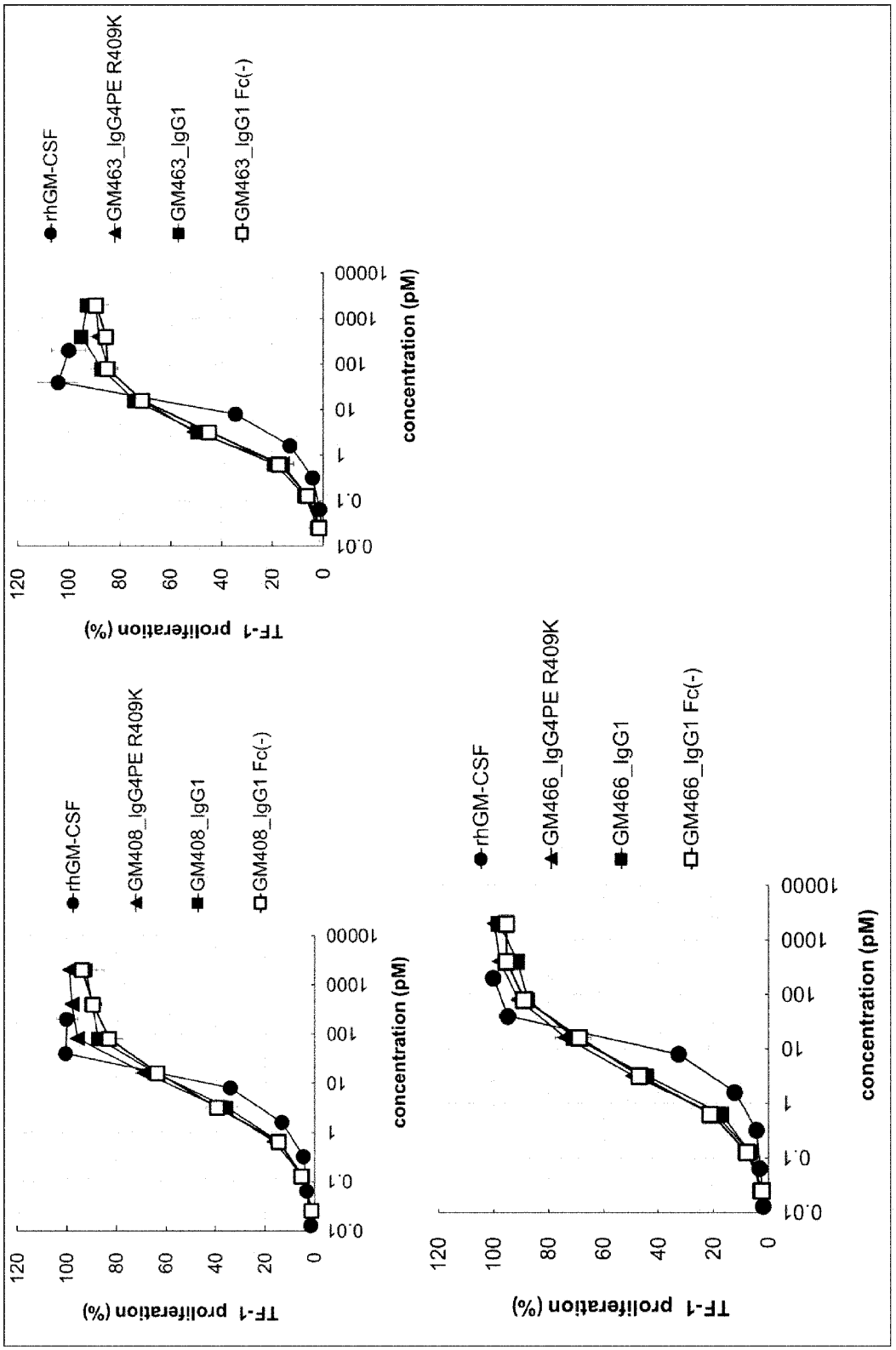
[図4]


(A)
VH1
VL
CH1
CL
VH2
VL
CH1
CL
CH2
CH3
(B)
VH1
VL
CH1
CL
CH2
CH3
VH2
VL
CH1
CL

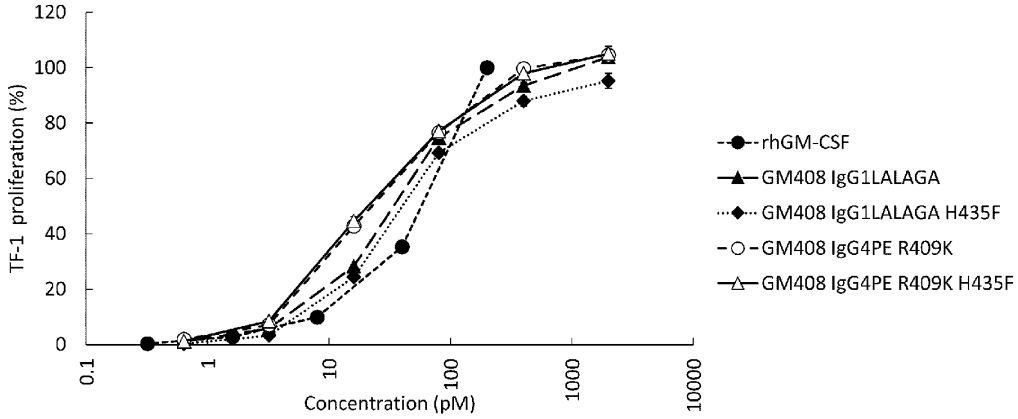
[図5]


TF-1 proliferation (%)
concentration (pM)
rhGM-CSF
GM466
GM408
GM464
GM463
GM435
TF-1 proliferation (%)
concentration (pM)
rhGM-CSF
GM413
GM398

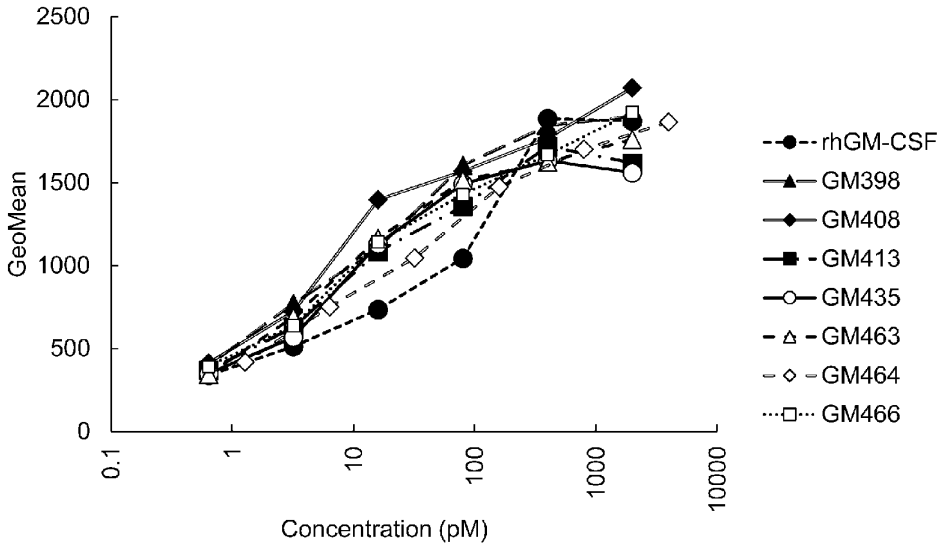
[図6]


rhGM-CSF
GM463_IgG4PE R409K
GM463_IgG1
GM463_IgG1 Fc(-)
TF-1 proliferation (%)
concentration (pM)
rhGM-CSF
GM408_IgG4PE R409K
GM408_IgG1
GM408_IgG1 Fc(-)
TF-1 proliferation (%)
concentration (pM)
rhGM-CSF
GM466_IgG4PE R409K
GM466_IgG1
GM466_IgG1 Fc(-)
TF-1 proliferation (%)
concentration (pM)

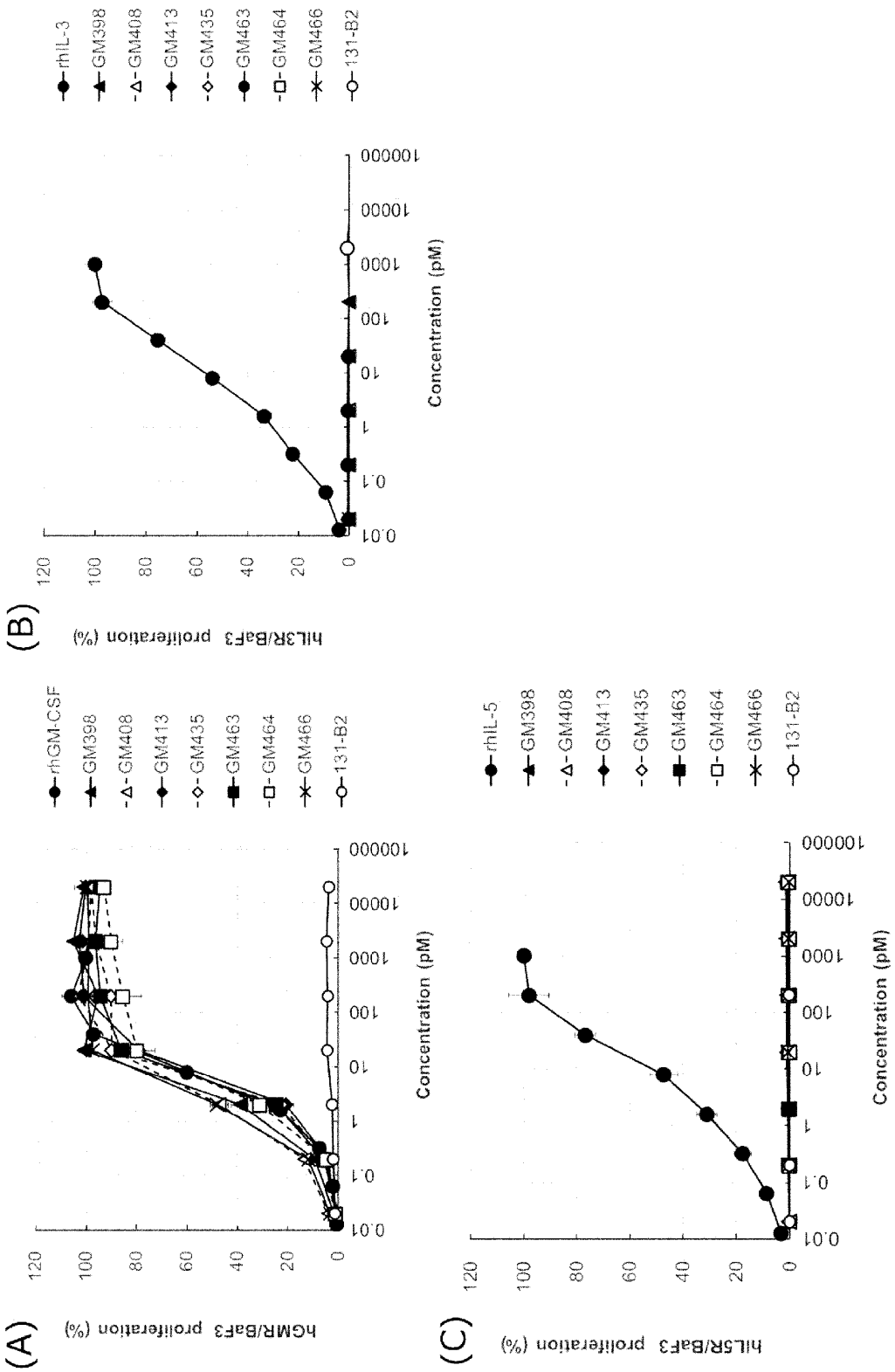
[図7]


TF-1 proliferation (%)
120
100
80
60
40
20
0
0.1
1
10
100
1000
10000
Concentration (pM)
rhGM-CSF
GM408 IgG1LALAGA
GM408 IgG1LALAGA H435F
GM408 IgG4PE R409K
GM408 IgG4PE R409K H435F

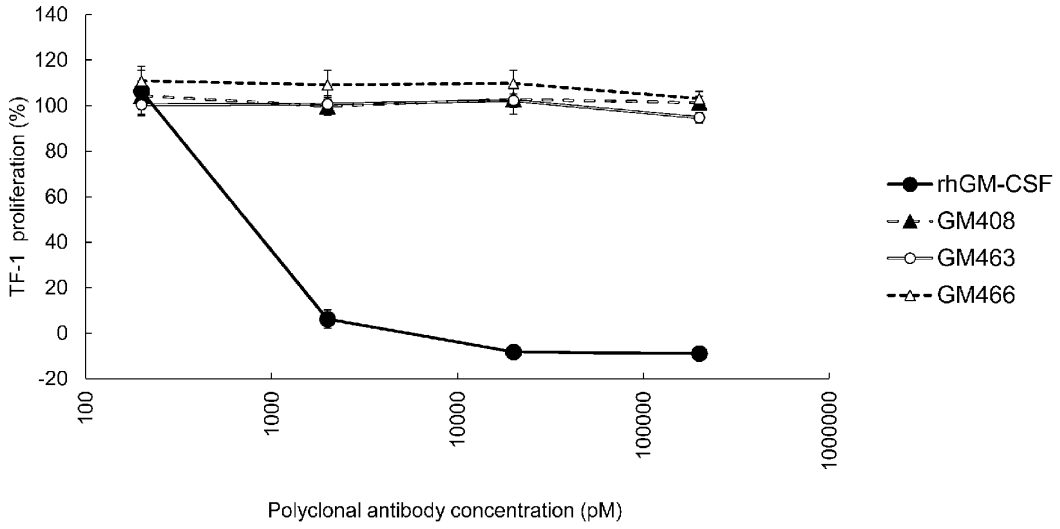
[図8]


GeoMean
2500
2000
1500
1000
500
0
0.1
1
10
100
1000
10000
Concentration (pM)
rhGM-CSF
GM398
GM408
GM413
GM435
GM463
GM464
GM466

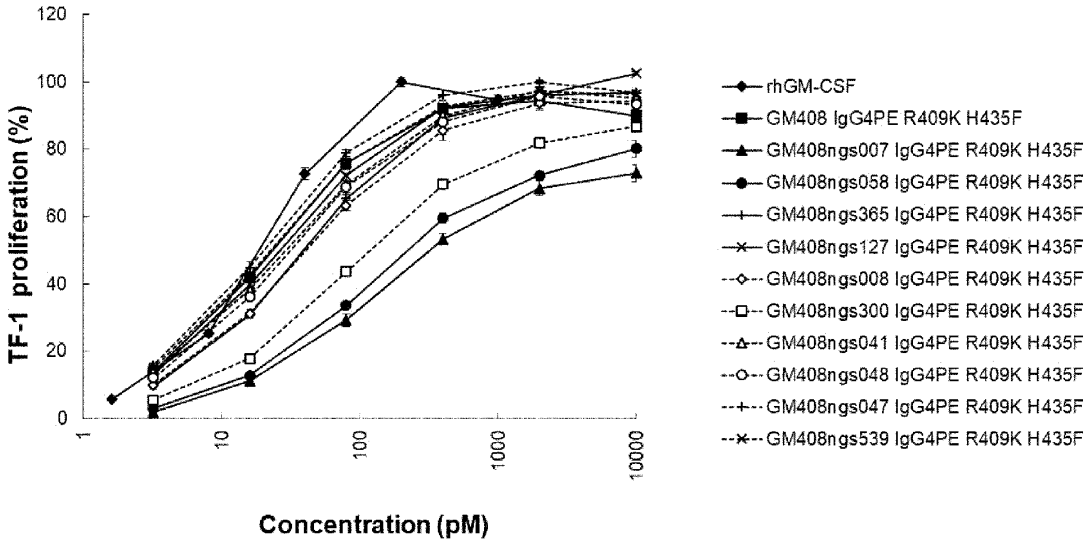
[図9]


(A)
hGMR/BaF3 proliferation (%)
rhGM-CSF
GM398
GM408
GM413
GM435
GM463
GM464
GM466
131-B2
Concentration (pM)
(B)
hIL3R/BaF3 proliferation (%)
rhIL-3
Concentration (pM)
(C)
hIL5R/BaF3 proliferation (%)
rhIL-5
Concentration (pM)

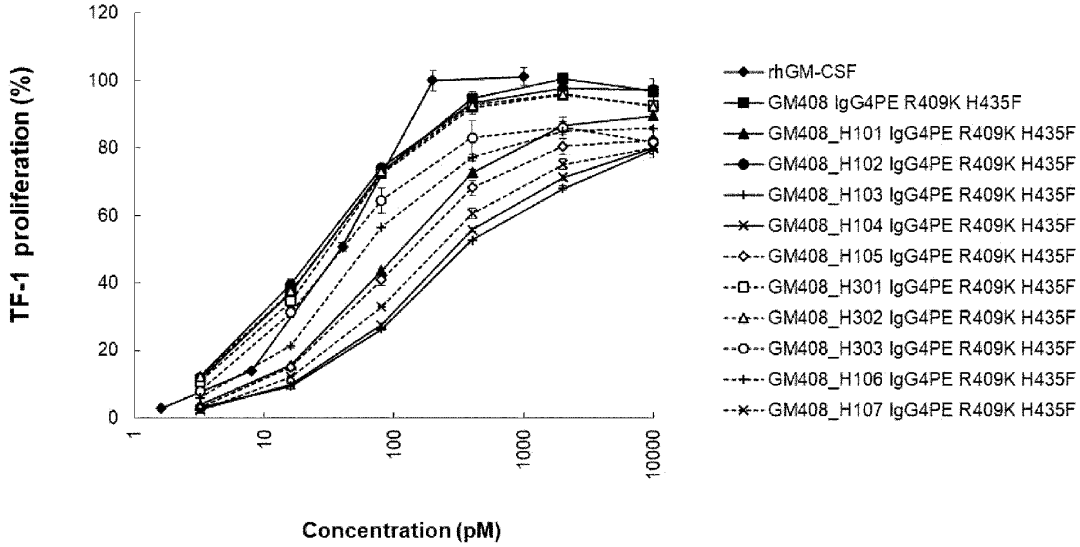
[図10]


140
120
100
80
60
40
20
0
-20
TF-1 proliferation (%)
100
1000
10000
100000
1000000
Polyclonal antibody concentration (pM)
rhGM-CSF
GM408
GM463
GM466

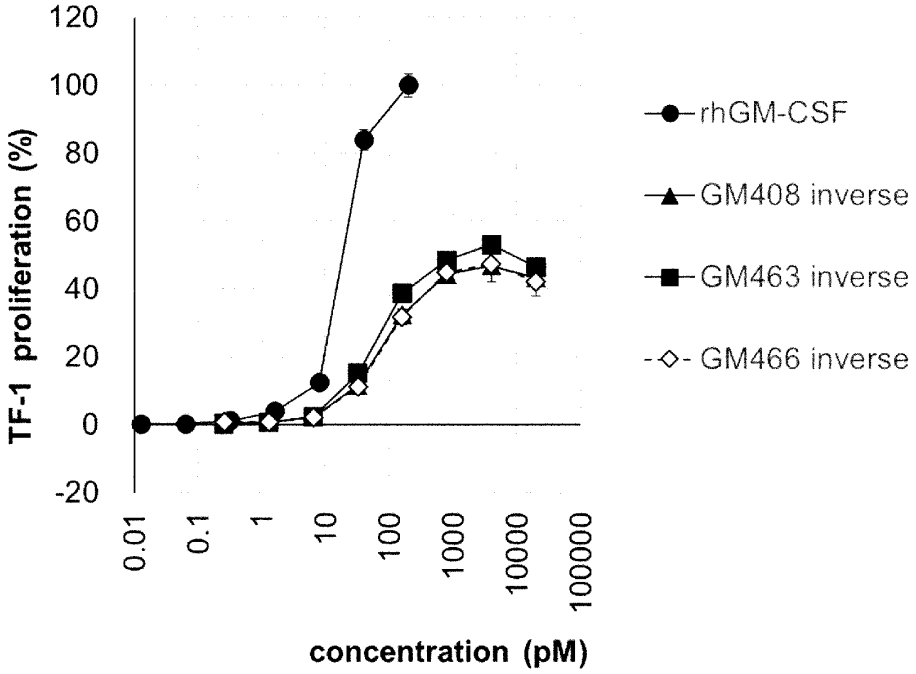
[図11]


120
100
80
60
40
20
0
TF-1 proliferation (%)
1
10
100
1000
10000
Concentration (pM)
rhGM-CSF
GM408 IgG4PE R409K H435F
GM408ngs007 IgG4PE R409K H435F
GM408ngs058 IgG4PE R409K H435F
GM408ngs365 IgG4PE R409K H435F
GM408ngs127 IgG4PE R409K H435F
GM408ngs008 IgG4PE R409K H435F
GM408ngs300 IgG4PE R409K H435F
GM408ngs041 IgG4PE R409K H435F
GM408ngs048 IgG4PE R409K H435F
GM408ngs047 IgG4PE R409K H435F
GM408ngs539 IgG4PE R409K H435F

[図12]

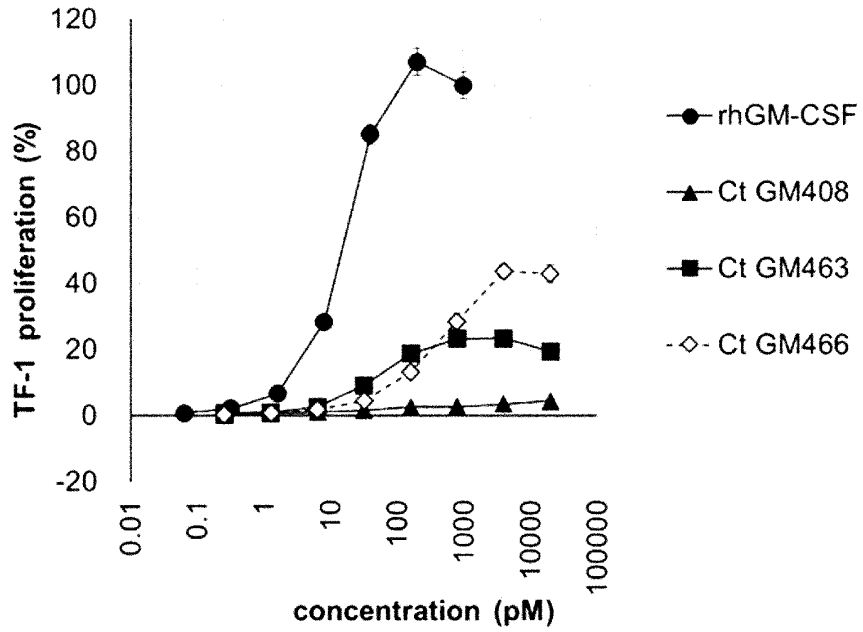

TF-1 proliferation (%)
120
100
80
60
40
20
0
1
10
100
1000
10000
Concentration (pM)
rhGM-CSF
GM408 IgG4PE R409K H435F
GM408_H101 IgG4PE R409K H435F
GM408_H102 IgG4PE R409K H435F
GM408_H103 IgG4PE R409K H435F
GM408_H104 IgG4PE R409K H435F
GM408_H105 IgG4PE R409K H435F
GM408_H301 IgG4PE R409K H435F
GM408_H302 IgG4PE R409K H435F
GM408_H303 IgG4PE R409K H435F
GM408_H106 IgG4PE R409K H435F
GM408_H107 IgG4PE R409K H435F

[図13]

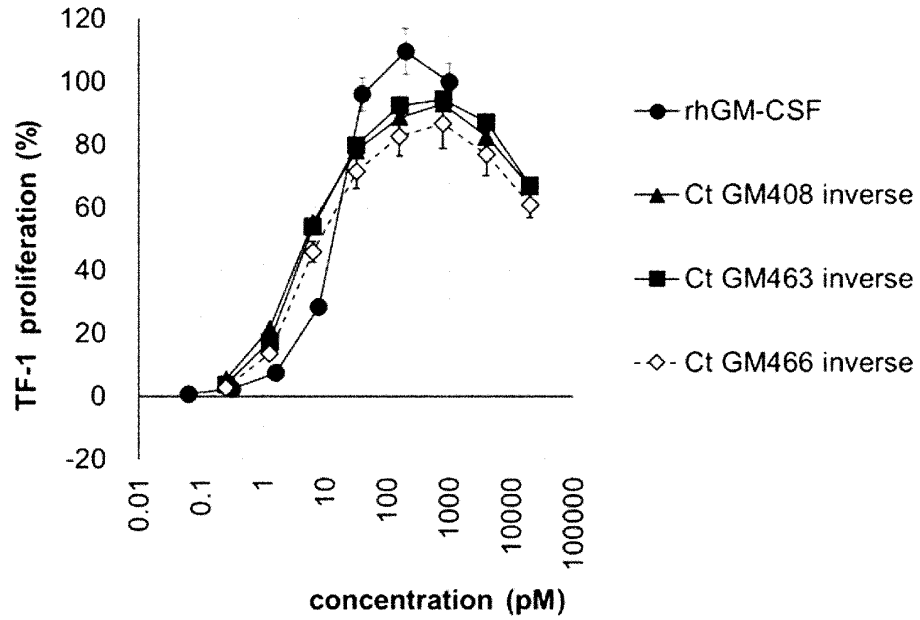

TF-1 proliferation (%)
120
100
80
60
40
20
0
-20
0.01
0.1
1
10
100
1000
10000
100000
concentration (pM)
rhGM-CSF
GM408 inverse
GM463 inverse
GM466 inverse

[図14]

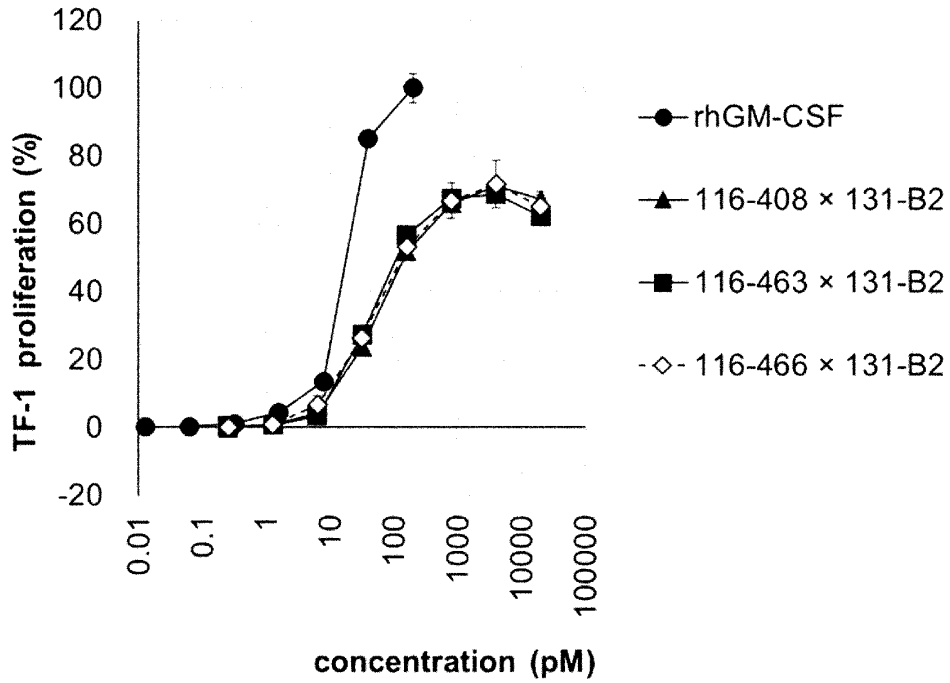
(A)


120
100
80
60
40
20
0
-20
TF-1 proliferation (%)
0.01
0.1
1
10
100
1000
10000
100000
concentration (pM)
rhGM-CSF
Ct GM408
Ct GM463
Ct GM466

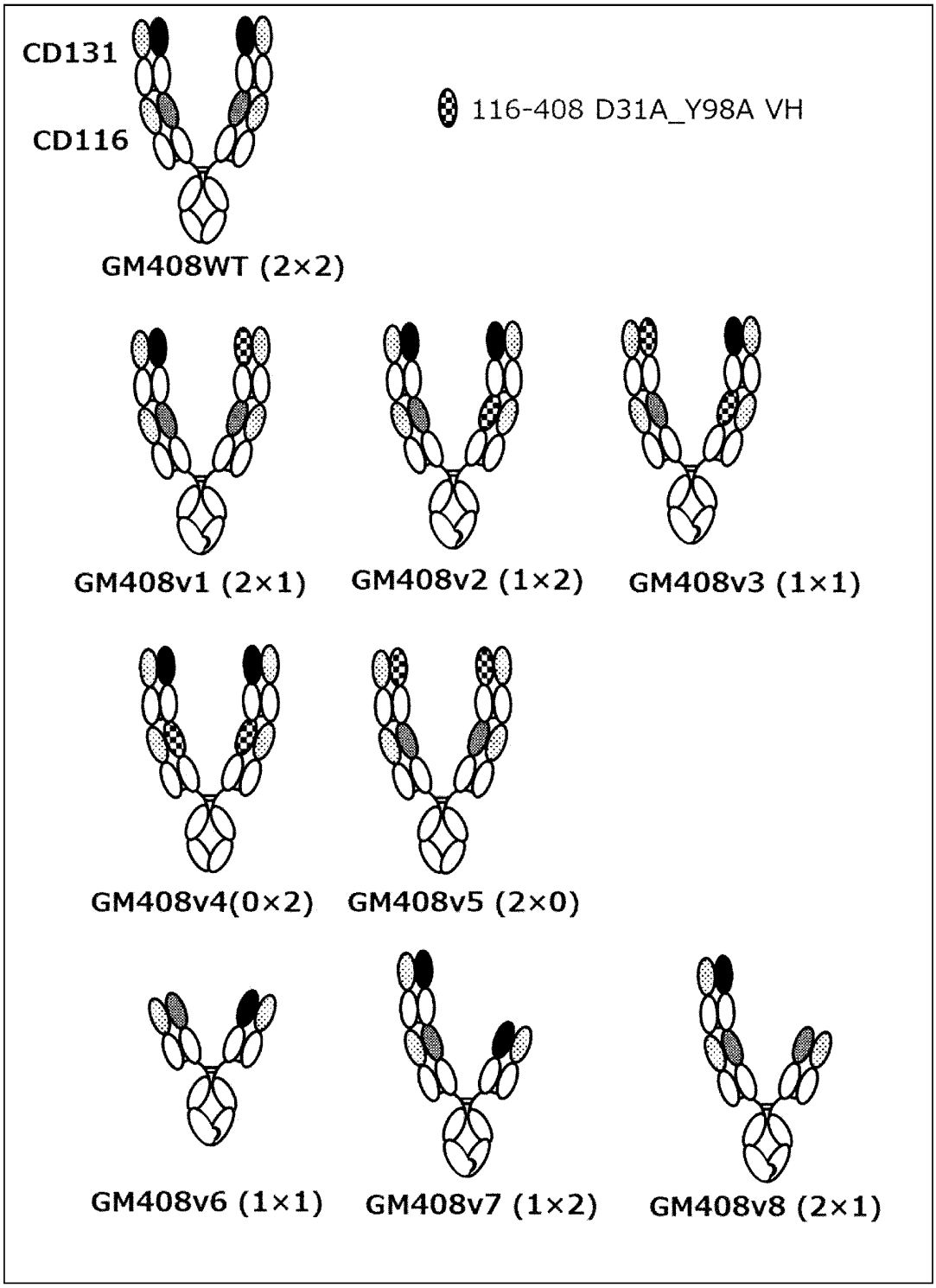
(B)


120
100
80
60
40
20
0
-20
TF-1 proliferation (%)
0.01
0.1
1
10
100
1000
10000
100000
concentration (pM)
rhGM-CSF
Ct GM408 inverse
Ct GM463 inverse
Ct GM466 inverse

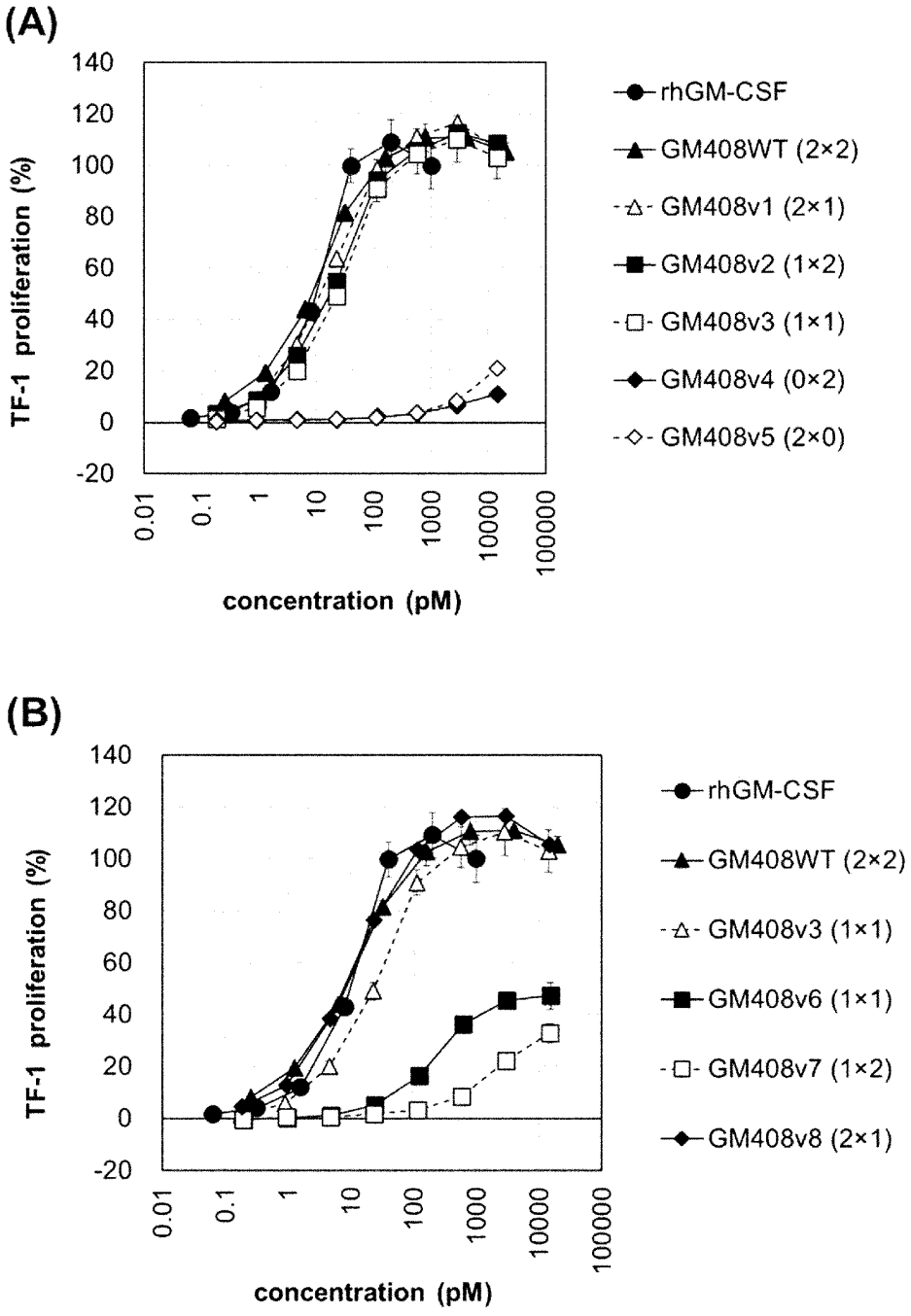
[図15]


120
100
80
60
40
20
0
-20
TF-1 proliferation (%)
0.01
0.1
1
10
100
1000
10000
100000
concentration (pM)
rhGM-CSF
116-408 × 131-B2
116-463 × 131-B2
116-466 × 131-B2

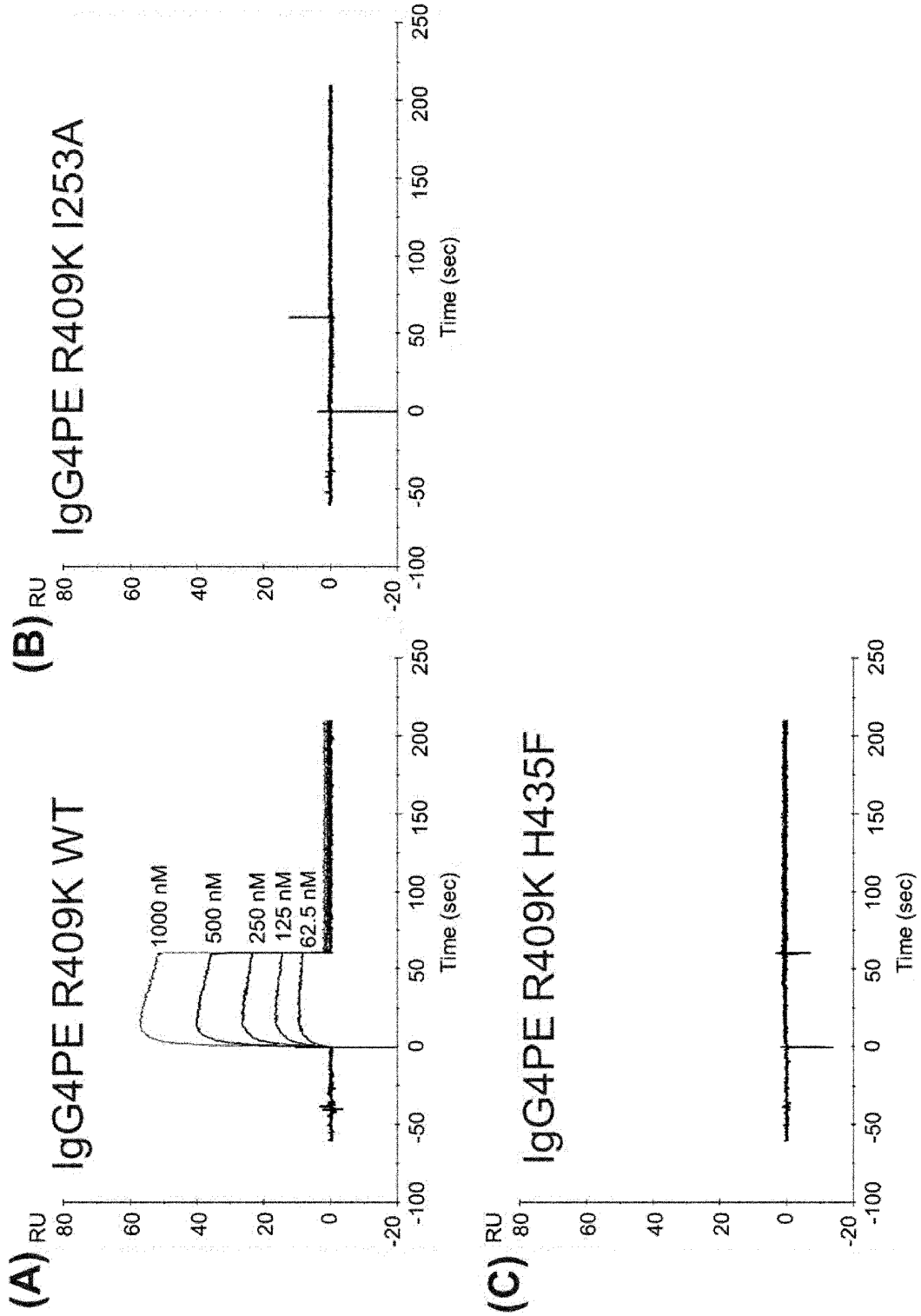
[図16]


CD131
CD116
116-408 D31A_Y98A VH
GM408WT (2×2)
GM408v1 (2×1)
GM408v2 (1×2)
GM408v3 (1×1)
GM408v4(0×2)
GM408v5 (2×0)
GM408v6 (1×1)
GM408v7 (1×2)
GM408v8 (2×1)

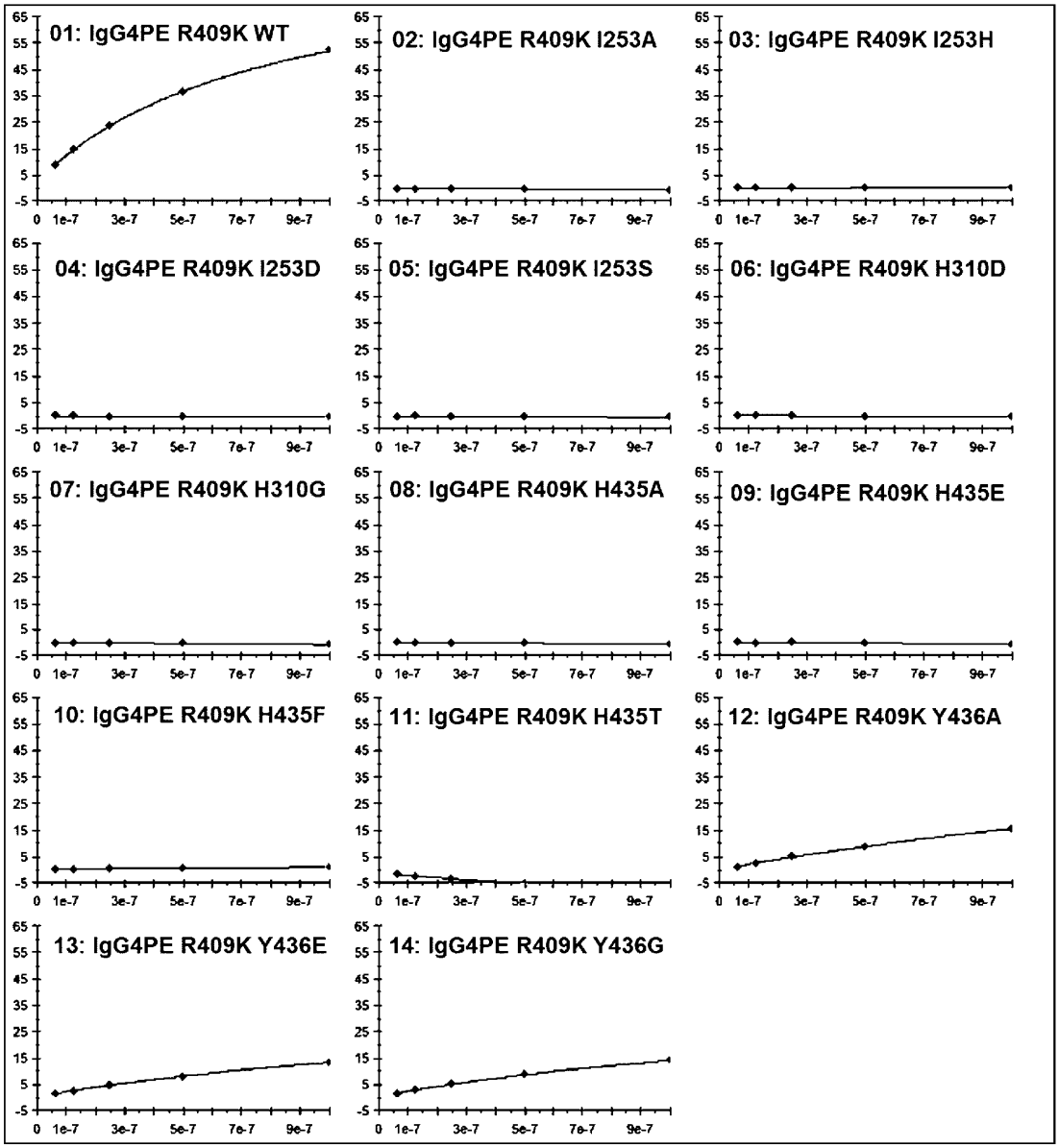
[図17]


(A)
TF-1 proliferation (%)
140
120
100
80
60
40
20
0
-20
0.01
0.1
1
10
100
1000
10000
100000
concentration (pM)
rhGM-CSF
GM408WT (2×2)
GM408v1 (2×1)
GM408v2 (1×2)
GM408v3 (1×1)
GM408v4 (0×2)
GM408v5 (2×0)
(B)
TF-1 proliferation (%)
140
120
100
80
60
40
20
0
-20
0.01
0.1
1
10
100
1000
10000
100000
concentration (pM)
rhGM-CSF
GM408WT (2×2)
GM408v3 (1×1)
GM408v6 (1×1)
GM408v7 (1×2)
GM408v8 (2×1)

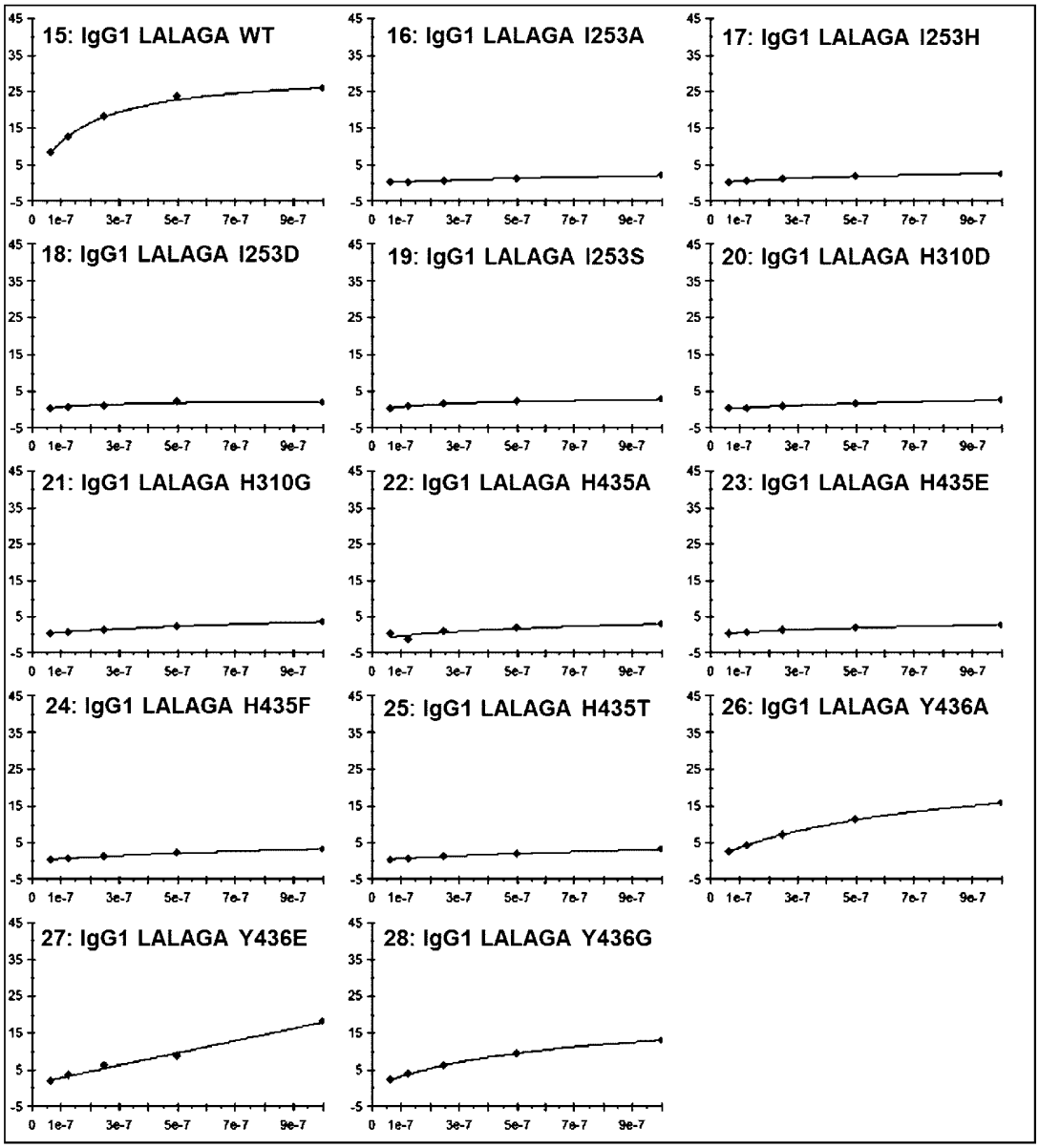
[図18]


(A)
IgG4PE R409K WT
1000 nM
500 nM
250 nM
125 nM
62.5 nM
(B)
IgG4PE R409K I253A
(C)
IgG4PE R409K H435F
RU
Time (sec)

[図19]


01: IgG4PE R409K WT
02: IgG4PE R409K I253A
03: IgG4PE R409K I253H
04: IgG4PE R409K I253D
05: IgG4PE R409K I253S
06: IgG4PE R409K H310D
07: IgG4PE R409K H310G
08: IgG4PE R409K H435A
09: IgG4PE R409K H435E
10: IgG4PE R409K H435F
11: IgG4PE R409K H435T
12: IgG4PE R409K Y436A
13: IgG4PE R409K Y436E
14: IgG4PE R409K Y436G
65
55
45
35
25
15
5
-5
0
1e-7
3e-7
5e-7
7e-7
9e-7

[図20]


15: IgG1 LALAGA WT
16: IgG1 LALAGA I253A
17: IgG1 LALAGA I253H
18: IgG1 LALAGA I253D
19: IgG1 LALAGA I253S
20: IgG1 LALAGA H310D
21: IgG1 LALAGA H310G
22: IgG1 LALAGA H435A
23: IgG1 LALAGA H435E
24: IgG1 LALAGA H435F
25: IgG1 LALAGA H435T
26: IgG1 LALAGA Y436A
27: IgG1 LALAGA Y436E
28: IgG1 LALAGA Y436G
45
35
25
15
5
-5
0
1e-7
3e-7
5e-7
7e-7
9e-7