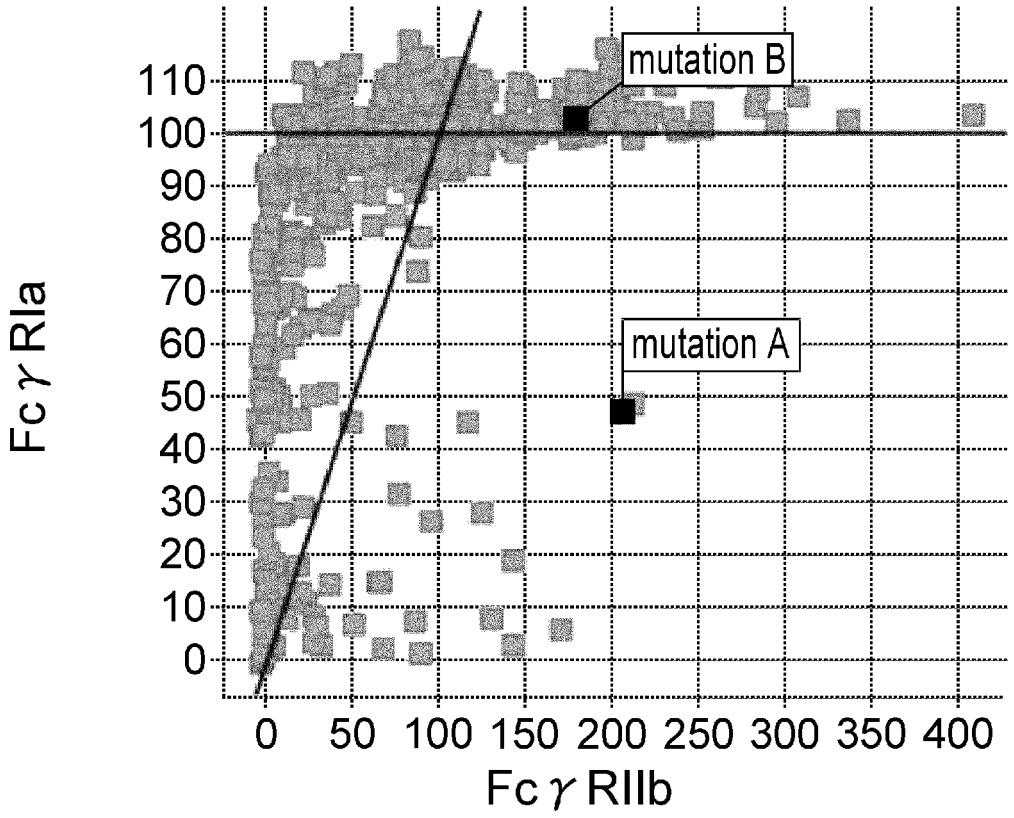
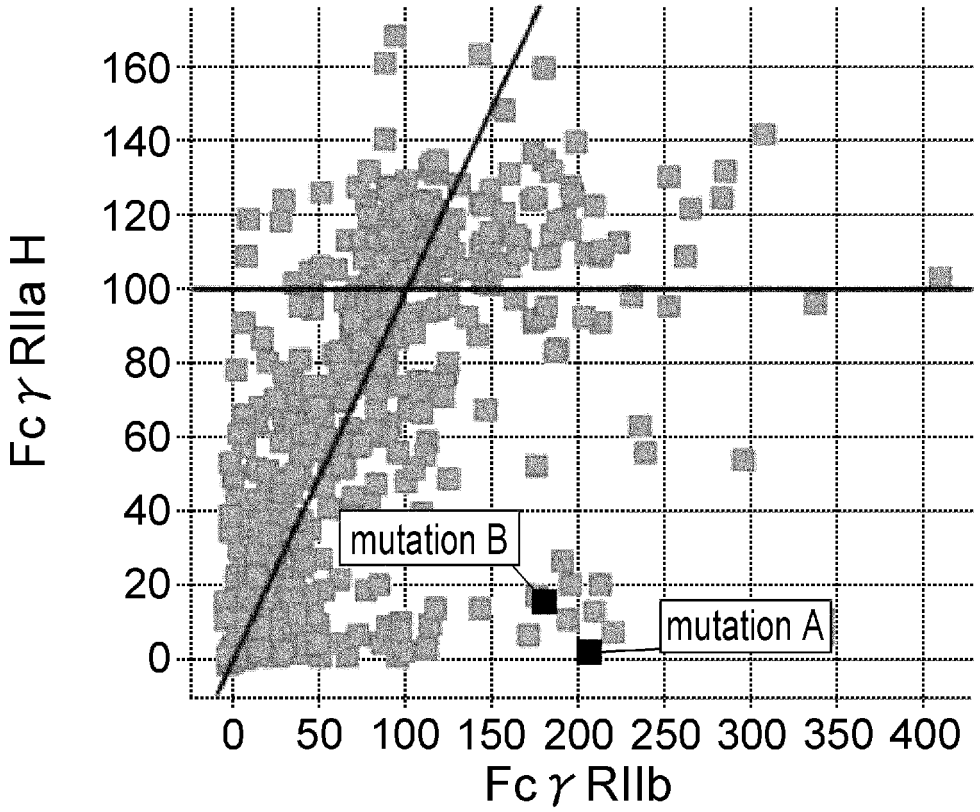
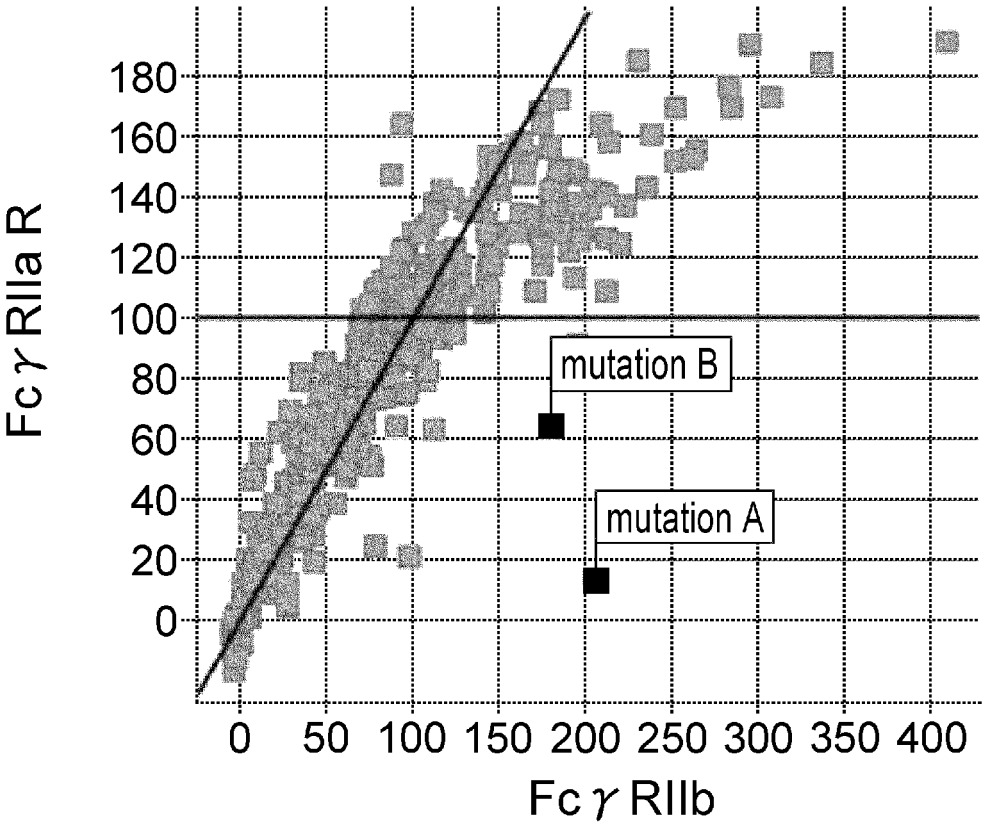
[図1]


mutation B
mutation A
110
100
90
80
70
60
50
40
30
20
10
0
0 50 100 150 200 250 300 350 400
FcγRIa
FcγRIIb

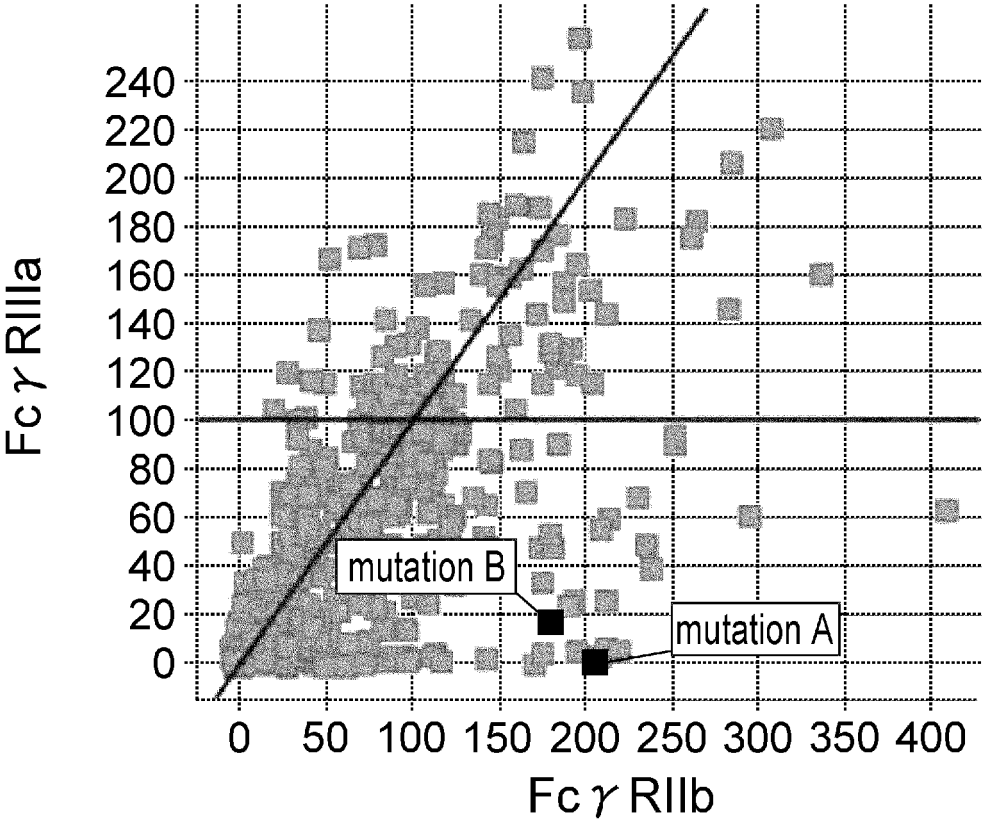
[図2]


mutation B
mutation A
160
140
120
100
80
60
40
20
0
0 50 100 150 200 250 300 350 400
FcγRIIa H
FcγRIIb

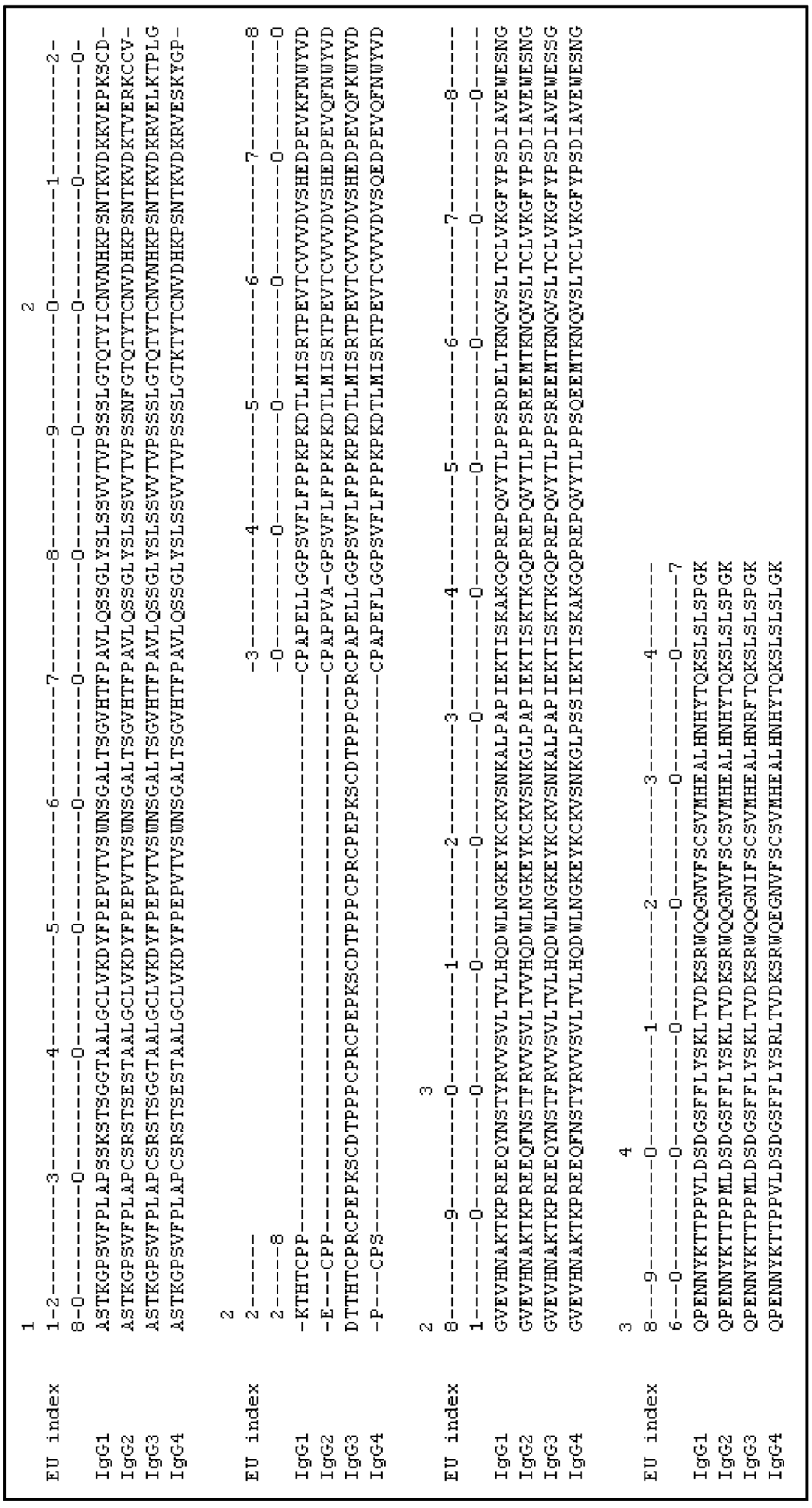
[図3]


FcγRIIa R
180
160
140
120
100
80
60
40
20
0
mutation B
mutation A
0 50 100 150 200 250 300 350 400
FcγRIIb

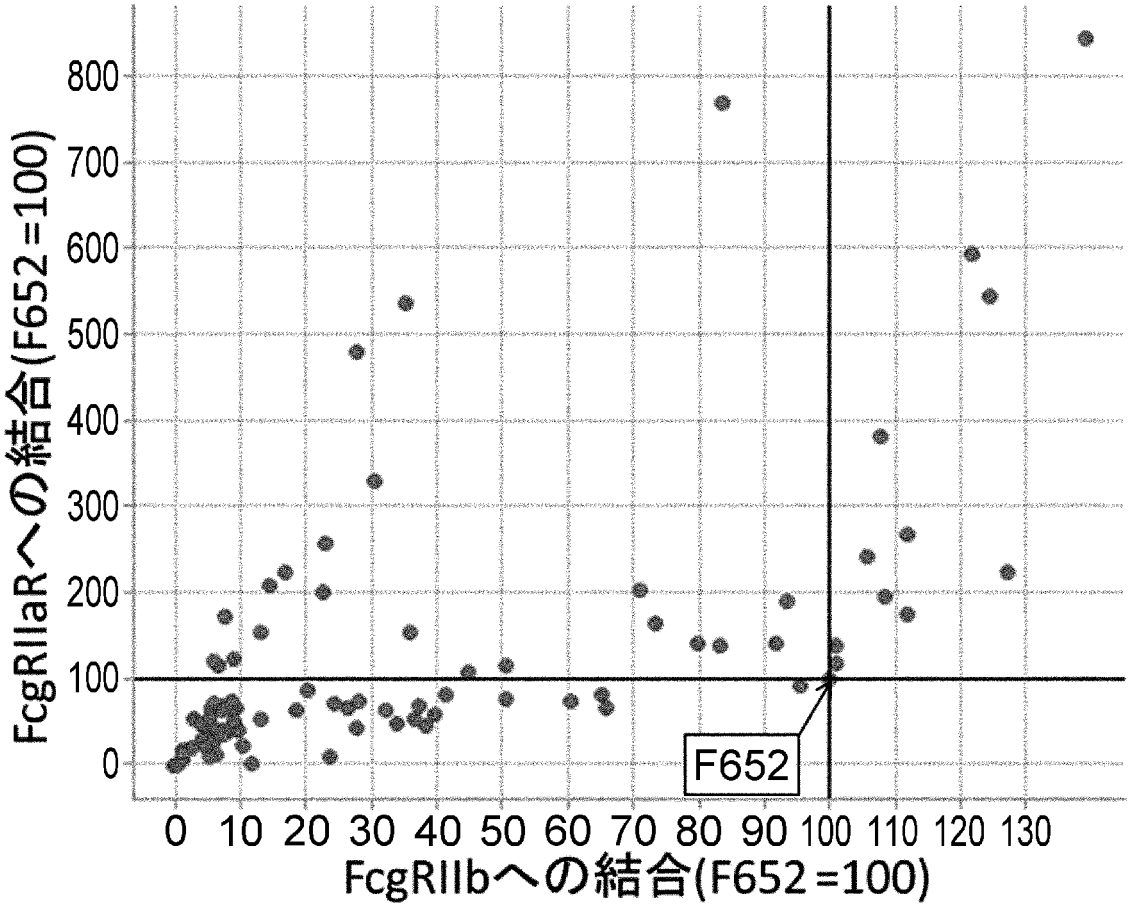
[図4]


FcγRIIIa
240
220
200
180
160
140
120
100
80
60
40
20
0
mutation B
mutation A
0 50 100 150 200 250 300 350 400
FcγRIIb

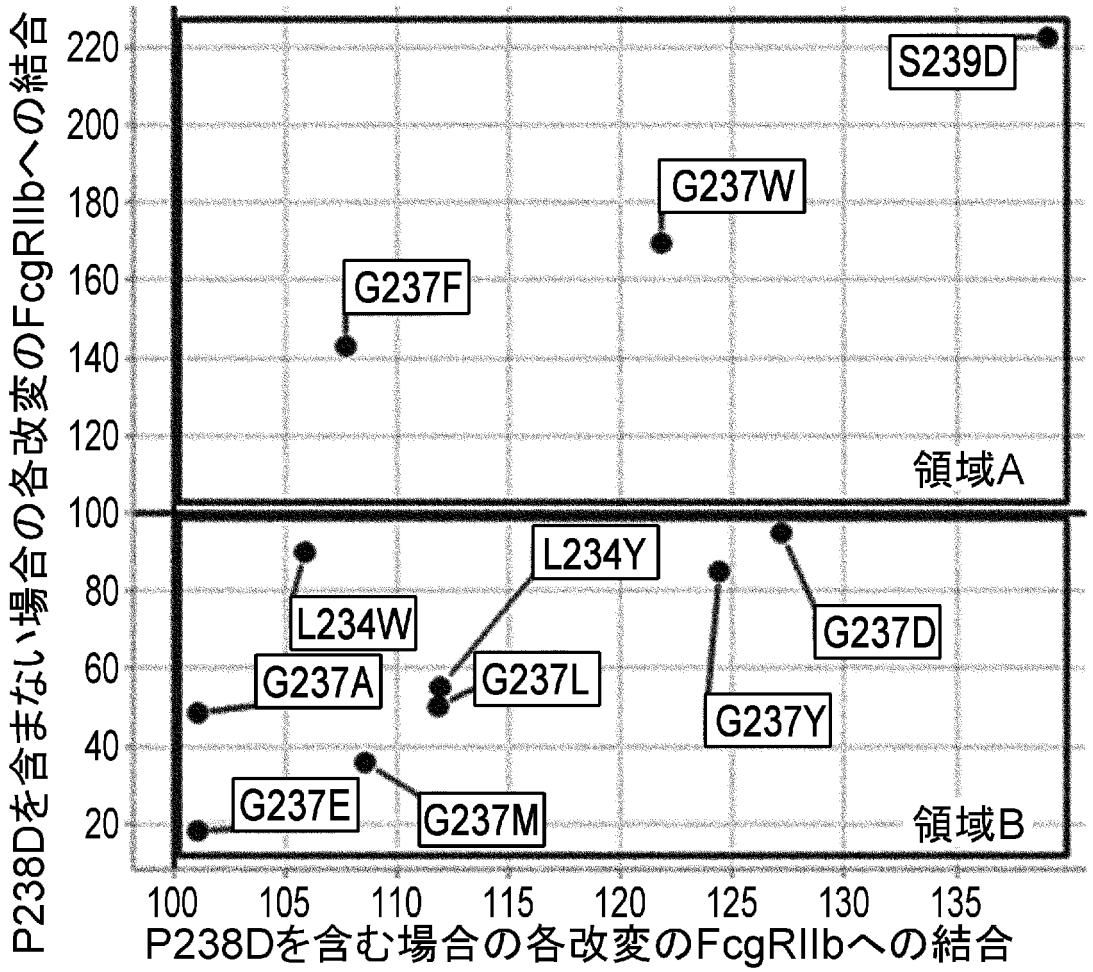
[図5]


1 2
EU index 1-2---------3---------4---------5---------6---------7---------8---------9---------0---------1---------2-
8-0---------0---------0---------0---------0---------0---------0---------0---------0---------0-
IgG1 ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCD-
IgG2 ASTKGPSVFPLAPCSRSTSESTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSNFGTQTYTCNVDHKPSNTKVDKTVERKCCV-
IgG3 ASTKGPSVFPLAPCSRSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYTCNVNHKPSNTKVDKRVELKTPLG
IgG4 ASTKGPSVFPLAPCSRSTSESTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTKTYTCNVDHKPSNTKVDKRVESKYGP-
2
EU index 2------- -3---------4---------5---------6---------7---------8
2-----8 -0---------0---------0---------0---------0
IgG1 -KTHTCPP----------CPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVD
IgG2 -E---CPP----------CPAPPVA-GPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVQFNWYVD
IgG3 DTTHTCPRCPEPKSCDTPPPCPRCPEPKSCDTPPPCPRCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVQFKWYVD
IgG4 -P---CPS----------CPAPEFLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSQEDPEVQFNWYVD
2 3
EU index 8---------9---------0---------1---------2---------3---------4---------5---------6---------7---------8-----
1---------0---------0---------0---------0---------0---------0---------0---------0---------0---------0-----
IgG1 GVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNG
IgG2 GVEVHNAKTKPREEQFNSTFRVVSVLTVVHQDWLNGKEYKCKVSNKGLPAPIEKTISKTKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNG
IgG3 GVEVHNAKTKPREEQYNSTFRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKTKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESSG
IgG4 GVEVHNAKTKPREEQFNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKGLPSSIEKTISKAKGQPREPQVYTLPPSQEEMTKNQVSLTCLVKGFYPSDIAVEWESNG
3 4
EU index 8---9---------0---------1---------2---------3---------4-------
6---0---------0---------0---------0---------0---------0-----7
IgG1 QPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK
IgG2 QPENNYKTTPPMLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNRFTQKSLSLSPGK
IgG3 QPENNYKTTPPMLDSDGSFFLYSKLTVDKSRWQQGNIFSCSVMHEALHNRFTQKSLSLSPGK
IgG4 QPENNYKTTPPVLDSDGSFFLYSRLTVDKSRWQEGNVFSCSVMHEALHNHYTQKSLSLSLGK

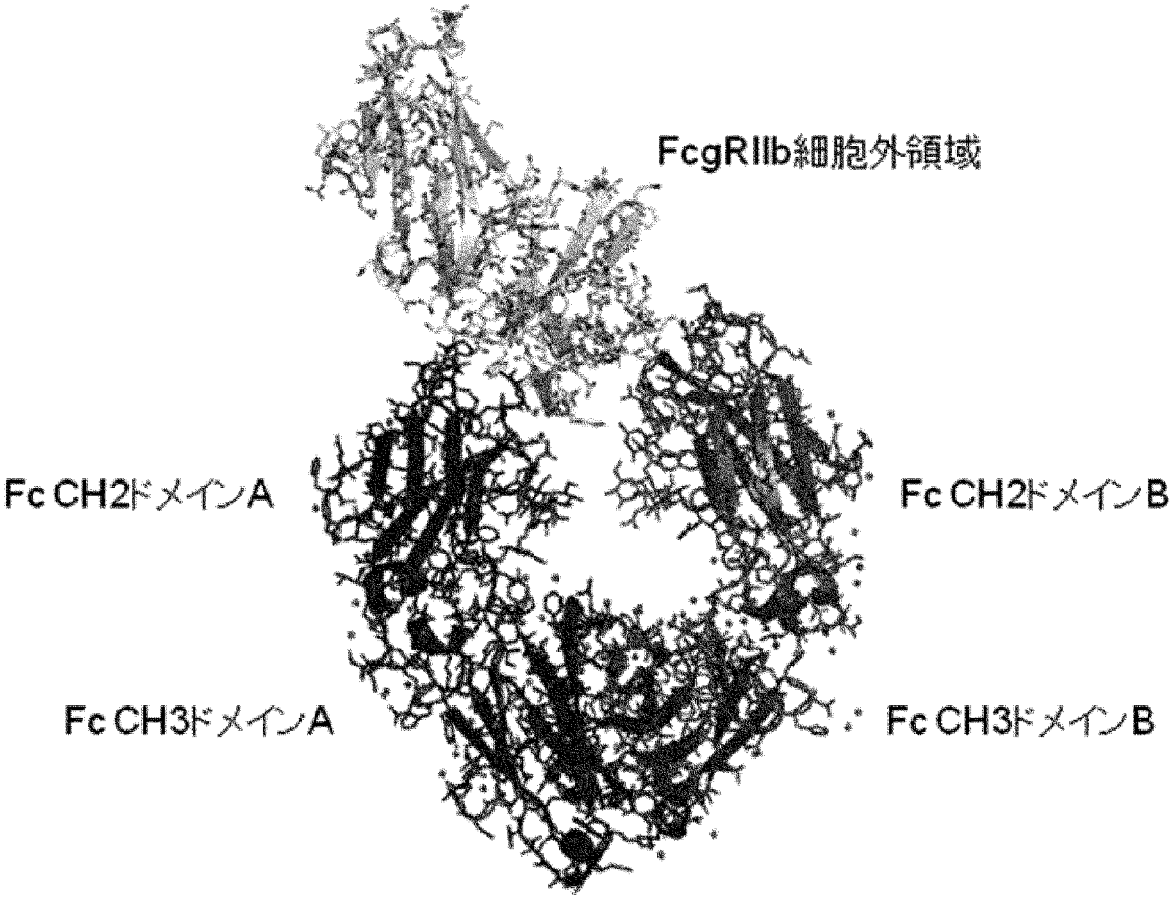
[図6]


FcgRIIaRへの結合(F652=100)
FcgRIIbへの結合(F652=100)
F652
0
100
200
300
400
500
600
700
800
0 10 20 30 40 50 60 70 80 90 100 110 120 130

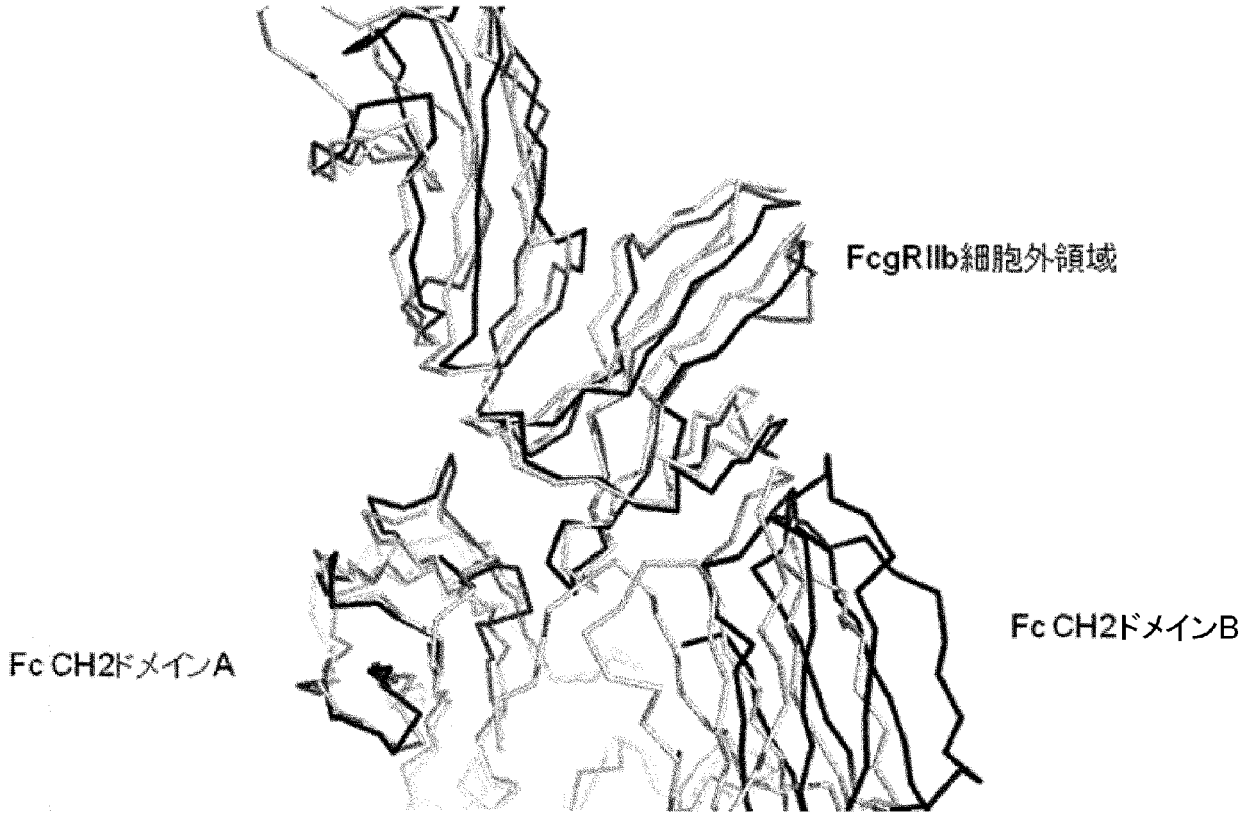
[図7]


P238Dを含まない場合の各改変のFcgRIIbへの結合
P238Dを含む場合の各改変のFcgRIIbへの結合
S239D
G237W
G237F
領域A
L234Y
L234W
G237D
G237A
G237L
G237Y
G237E
G237M
領域B
20
40
60
80
100
120
140
160
180
200
220
100 105 110 115 120 125 130 135

[図8]

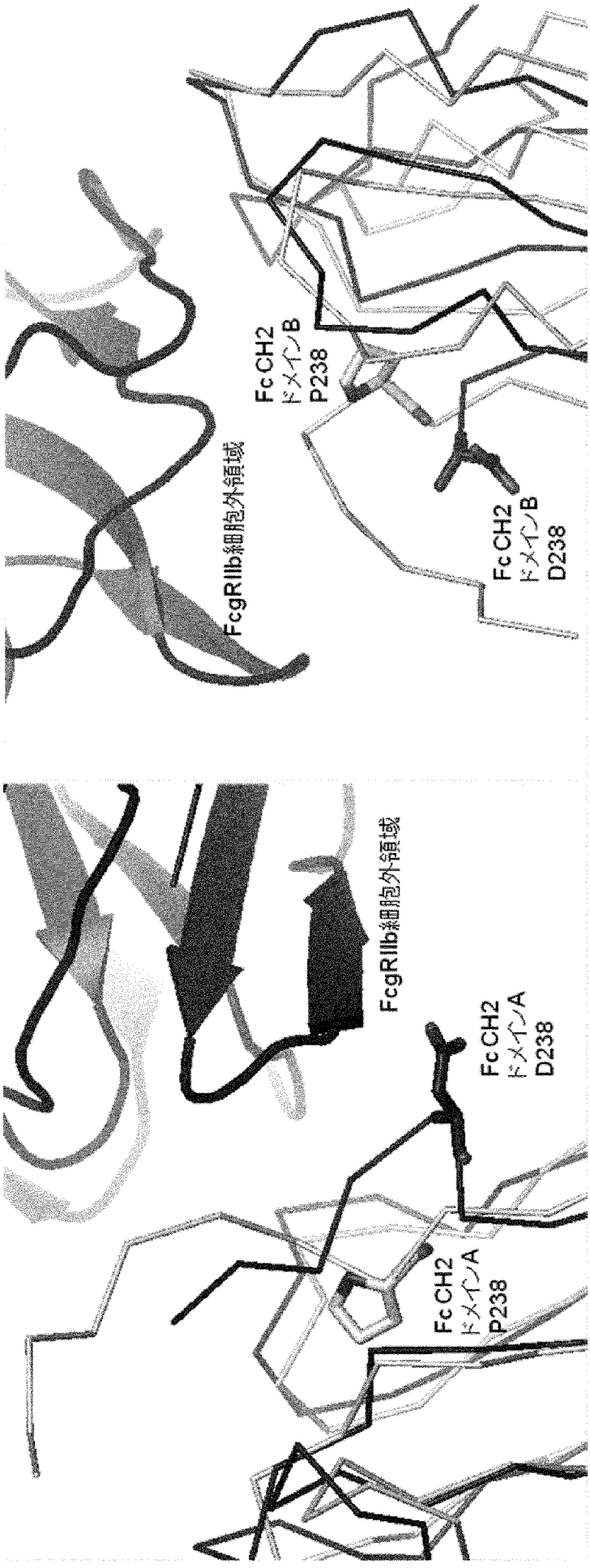


[図9]



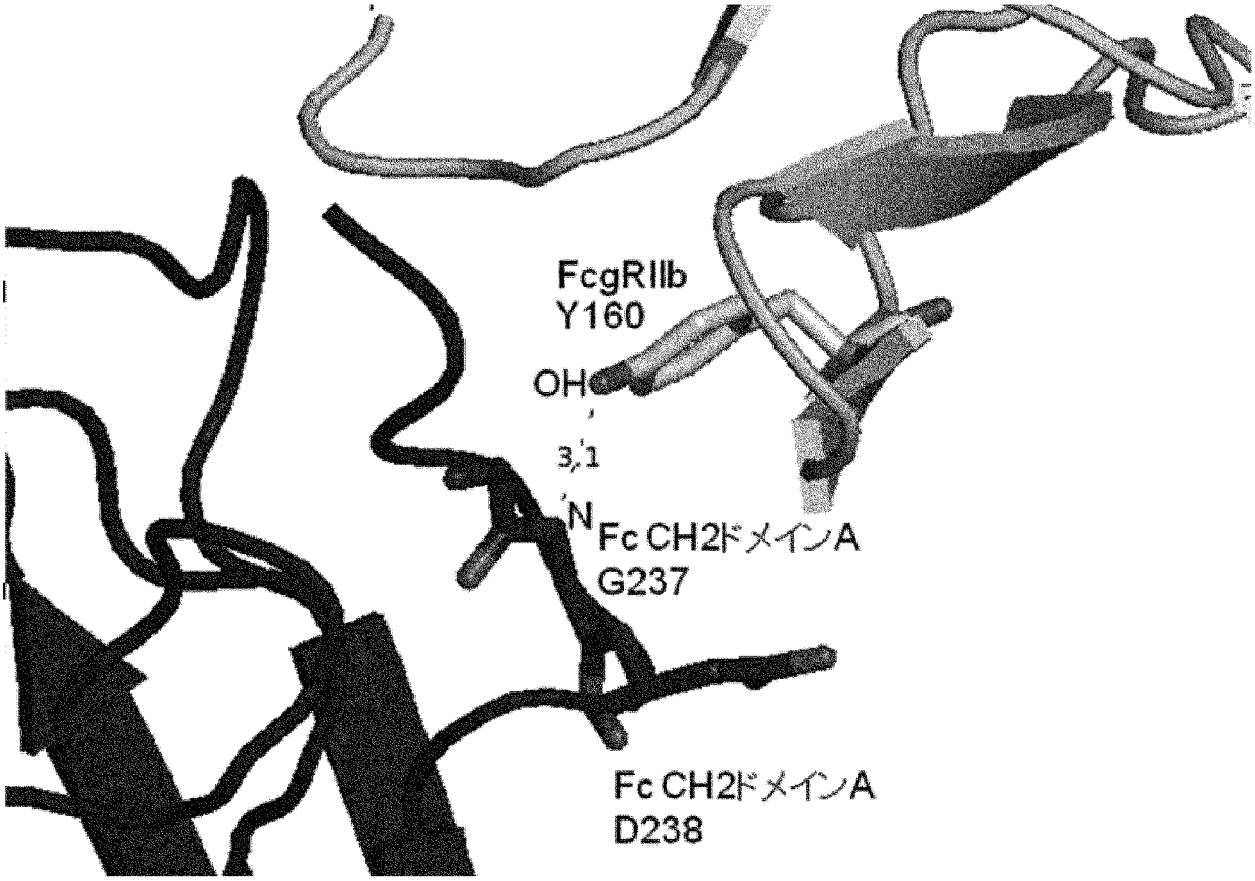
黒　Fc(P238D) / Fcγ RIIb細胞外領域複合体の 結晶構造
灰色　Fc(WT) / Fcγ RIIb 細胞外領域複合体のモデル構造

[図10]

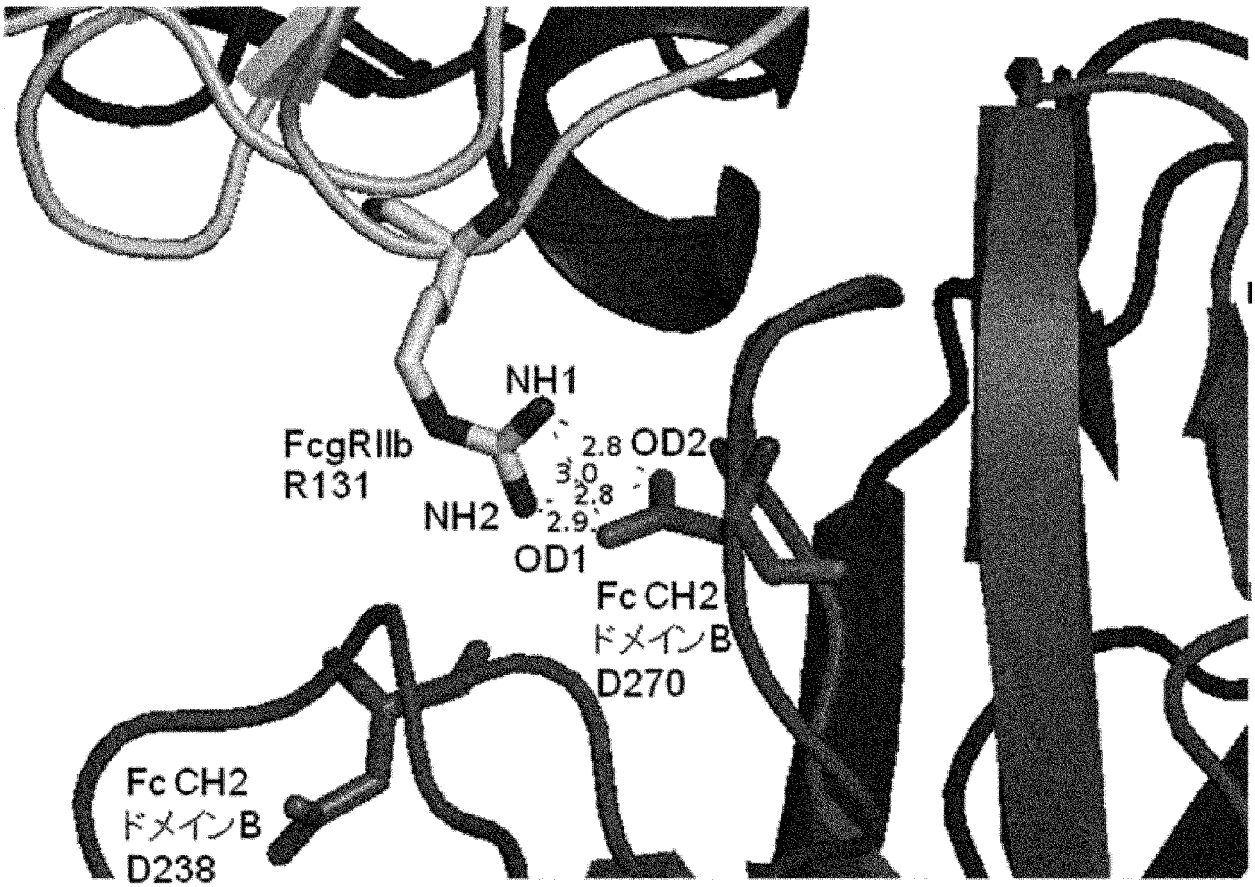


黒　Fc(P238D) / Fcγ RIIb細胞外領域複合体の結晶構造
灰色　Fc(WT) / Fcγ RIIb 細胞外領域複合体のモデル構造

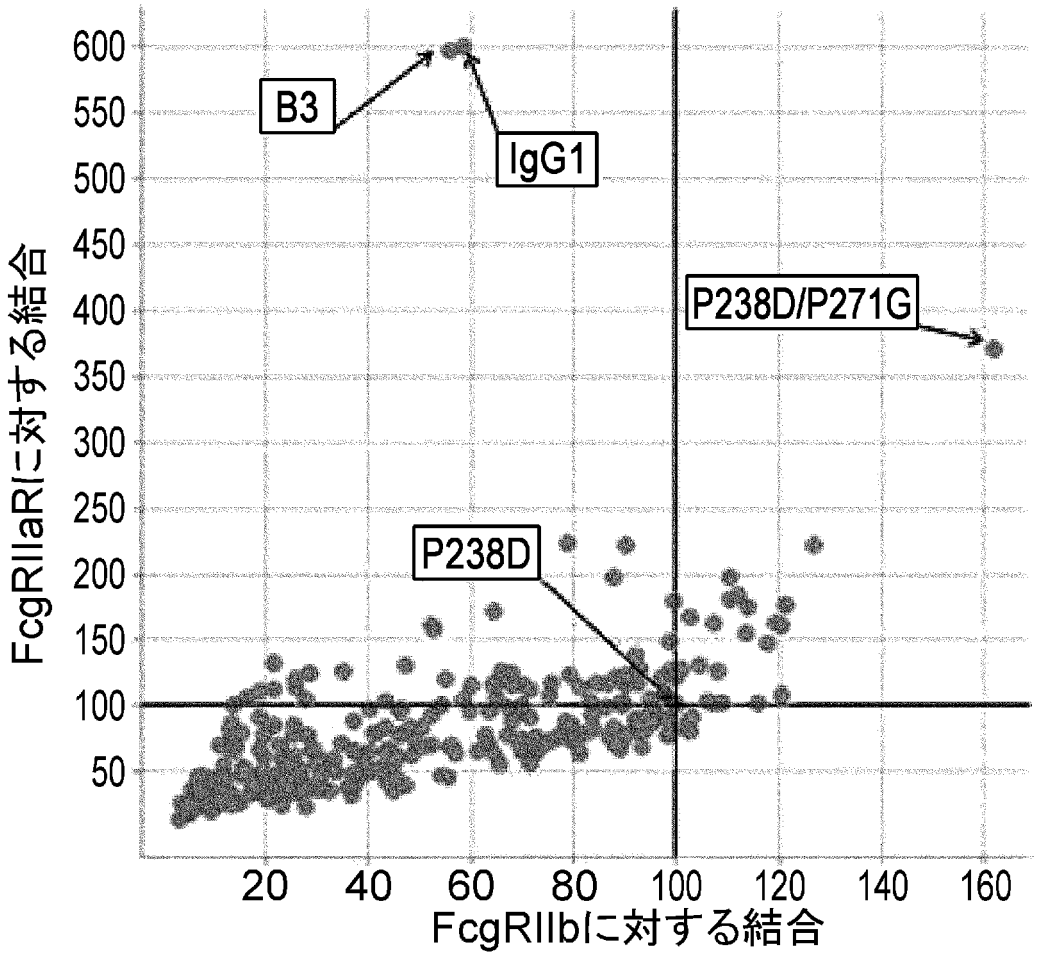
[図11]


FcgRIIb
Y160
OH
3.1
N
Fc CH2ドメインA
G237
Fc CH2ドメインA
D238

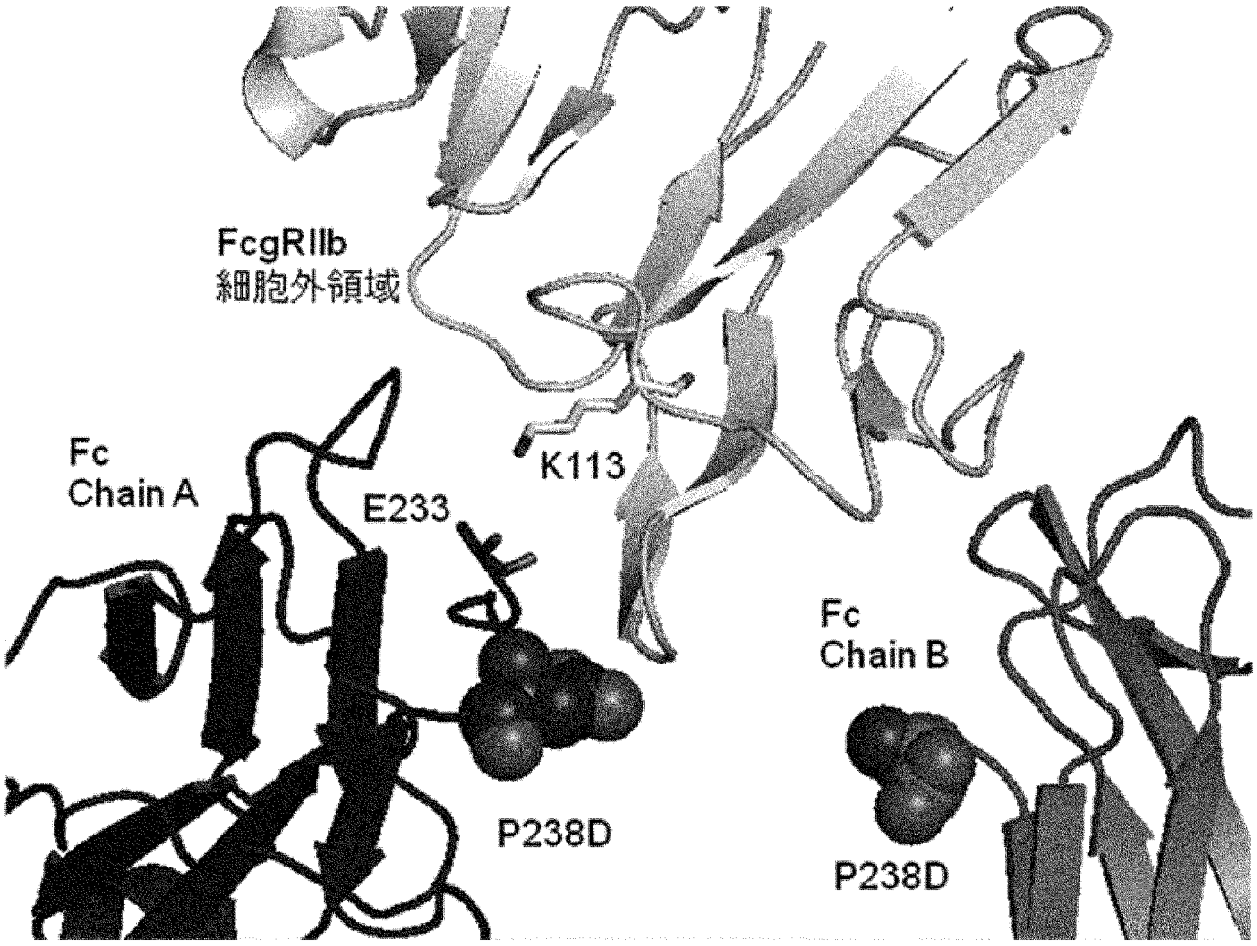
[図12]


NH1
FcgRIIb
R131
2.8
OD2
3.0
2.8
NH2
2.9
OD1
Fc CH2
ドメインB
D270
Fc CH2
ドメインB
D238

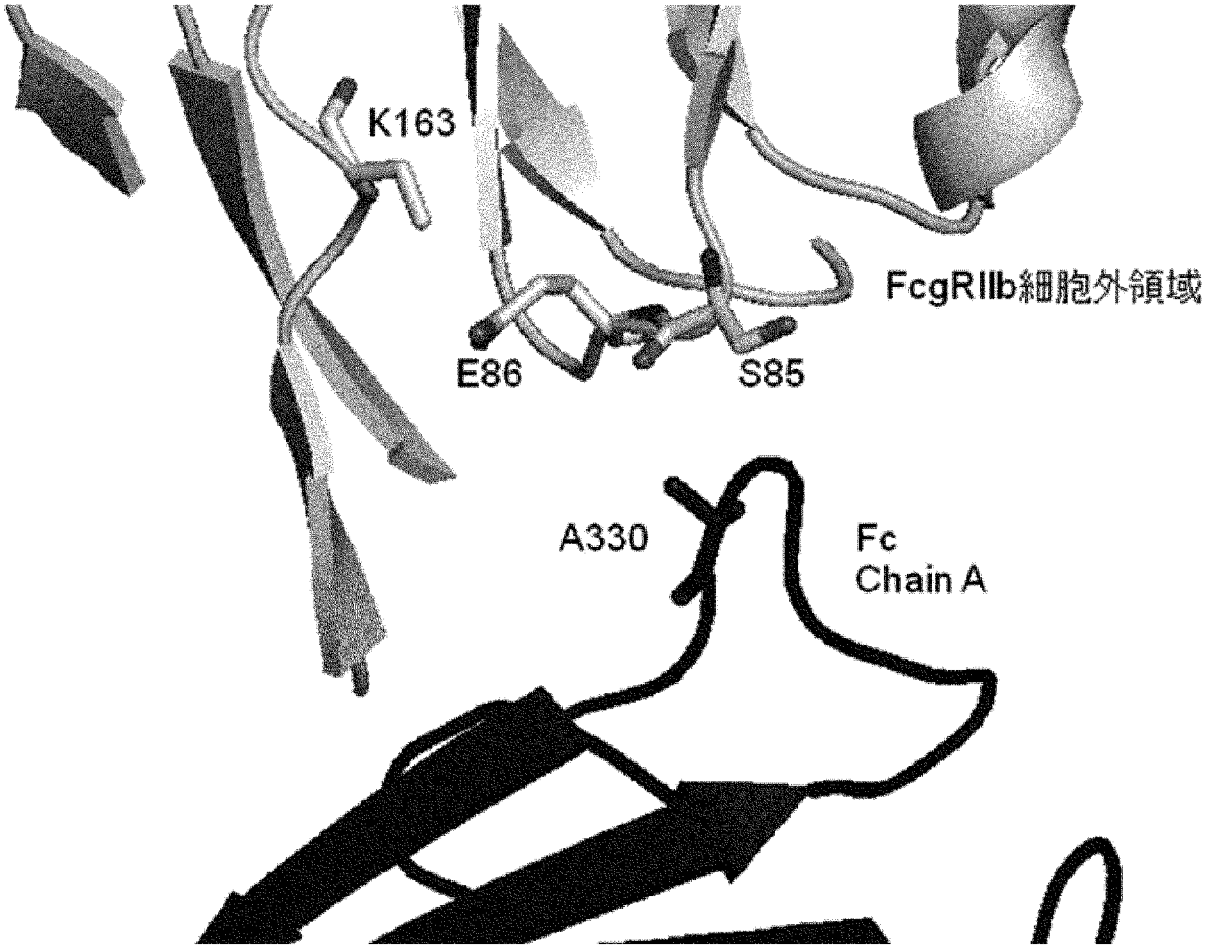
[図13]


B3
IgG1
P238D/P271G
P238D
FcgRIIaRに対する結合
FcgRIIbに対する結合
600
550
500
450
400
350
300
250
200
150
100
50
20
40
60
80
100
120
140
160

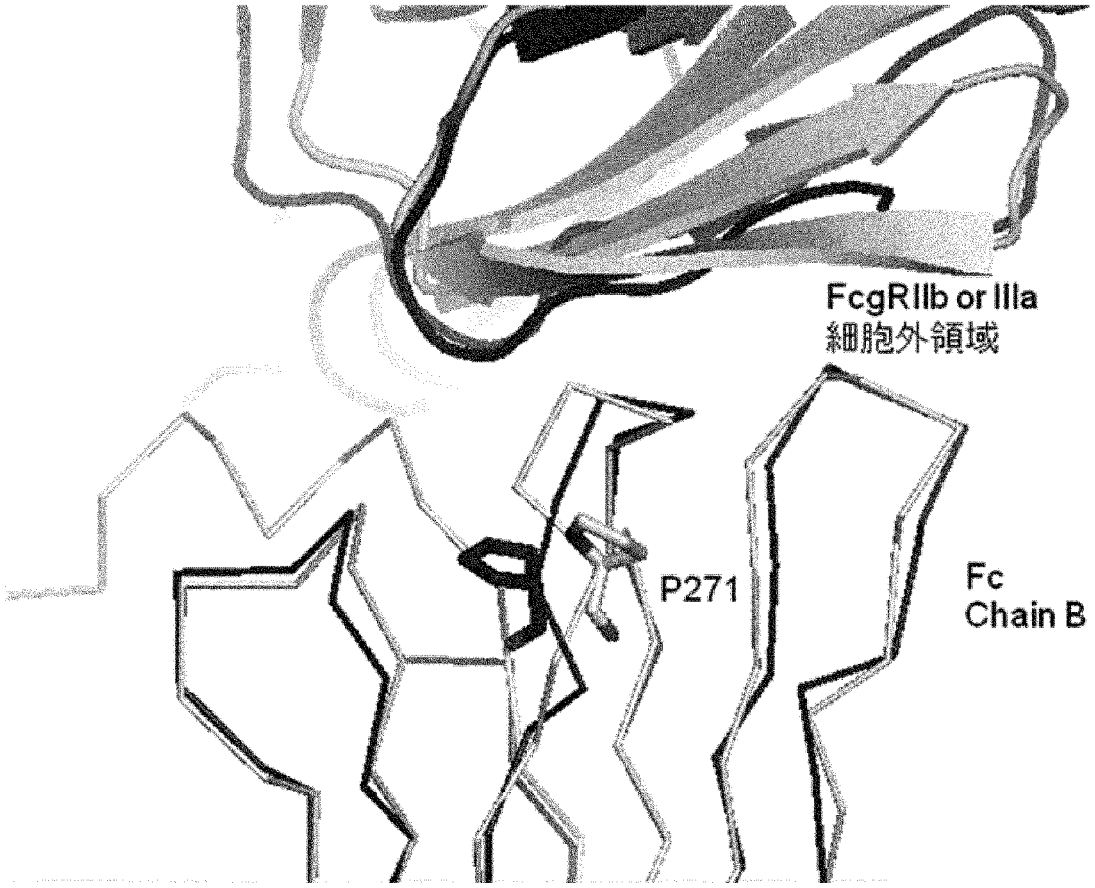
[図14]


FcgRIIb
細胞外領域
Fc
Chain A
E233
K113
P238D
Fc
Chain B
P238D

[図15]



[図16]



黒　Fc(P238D) / Fc γ RIIb細胞外領域複合体の結晶構造
灰色　Fc(WT) / Fc γ RIIIa細胞外領域複合体の結晶構造(PDB code:3SGJ)