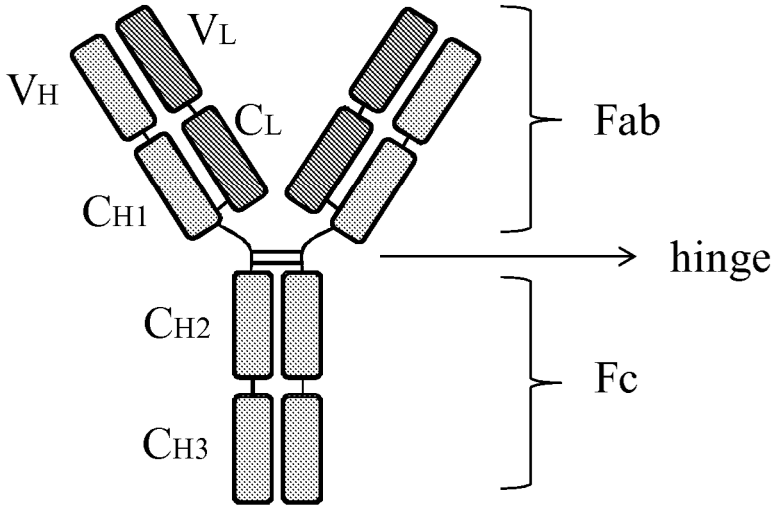
Fig. 1



Upper Hinge (Fab Region)	Core Hinge	Lower Hinge/CH2 Region ($F(ab')_2$ Region)

S(219)-C-D-$K_1T_2H_3$T-C-P-P-C-P-A-$P_4E_5L_6$L-G_7G-P-S(239)

1 Plasmin
2 Human Neutrophil Elastase (HNE)
3 Papain
4 MMP-3, MMP-12
5 Glutamyl endopeptidase I (GluV8), Cathepsin G
6 Pepsin, MMP-7
7 IdeS

Fig. 2

```
              EU 214                                                  263
hIgG1 wild-type   KVEPKSCDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVV SEQ ID
NO: 1

hIgG2 wild-type   T--R-C-VE///-------PVA/--------------------------- SEQ ID
NO: 2

hIgG1 2hDE        -------------------PVA/--D------------------------ SEQ ID
NO: 8

hIgG1 2hAA        -------------------PVA/--------------------------- SEQ ID
NO: 9

                 264                                                  313
hIgG1 wild-type   VDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDW
hIgG2 wild-type   ----------Q---------------------F---F--------V----
hIgG1 2hDE        --------------------------------------------------
hIgG1 2hAA        --------------------------------------------------

                 314                                                  363
hIgG1 wild-type   LNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSRDELTKNQV
hIgG2 wild-type   -------------G-----------T----------------E-M-----
hIgG1 2hDE        ------------------E-------------------------------
hIgG1 2hAA        ------------------AA------------------------------

                 364                                                  413
hIgG1 wild-type   SLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVD
hIgG2 wild-type   --------------S------------------M----------------
hIgG1 2hDE        --------------A-----------------------------------
hIgG1 2hAA        --------------A-----------------------------------

                 414                                  447
hIgG1 wild-type   KSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK
hIgG2 wild-type   ---------------------------------
hIgG1 2hDE        ---------------------------------
hIgG1 2hAA        ---------------------------------
```

- Denotes that the sequences are the same
/ Denotes a deletion

Fig. 3A

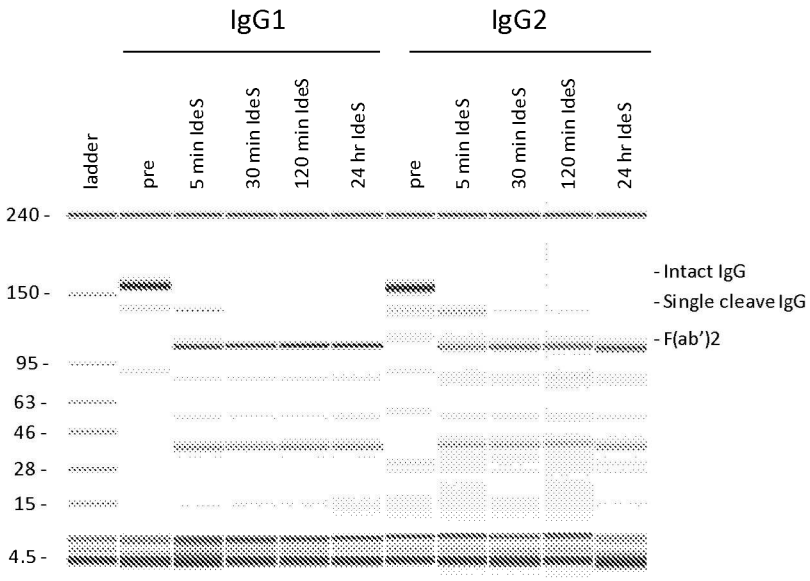

IgG1
IgG2
ladder
pre
5 min IdeS
30 min IdeS
120 min IdeS
24 hr IdeS
pre
5 min IdeS
30 min IdeS
120 min IdeS
24 hr IdeS
240 -
150 -
95 -
63 -
46 -
28 -
15 -
4.5 -
- Intact IgG
- Single cleave IgG
- F(ab')2

Fig. 3B

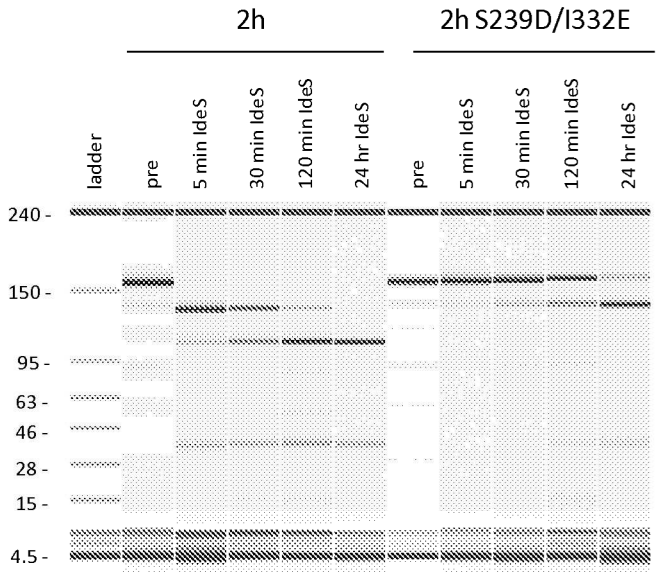

2h
2h S239D/I332E
ladder
pre
5 min IdeS
30 min IdeS
120 min IdeS
24 hr IdeS
pre
5 min IdeS
30 min IdeS
120 min IdeS
24 hr IdeS
240 -
150 -
95 -
63 -
46 -
28 -
15 -
4.5 -

Fig. 4A

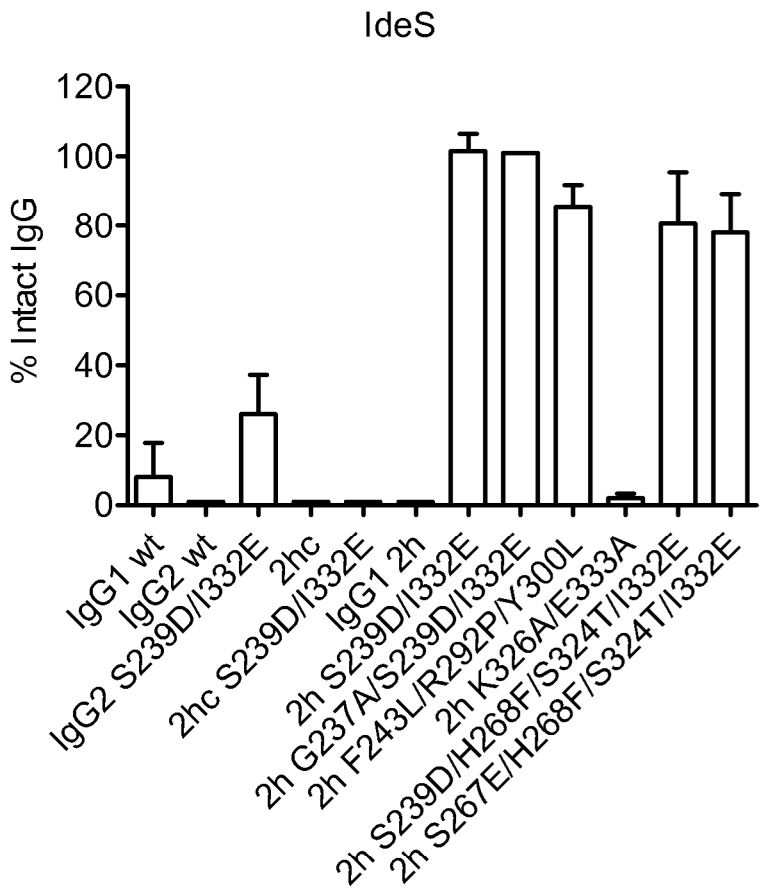

IdeS
% Intact IgG
120
100
80
60
40
20
0
IgG1 wt
IgG2 wt
IgG2 S239D/I332E
2hc
2hc S239D/I332E
IgG1 2h
2h S239D/I332E
2h G237A/S239D/I332E
2h F243L/R292P/Y300L
2h K326A/E333A
2h S239D/H268F/S324T/I332E
2h S267E/H268F/S324T/I332E

Fig. 4B

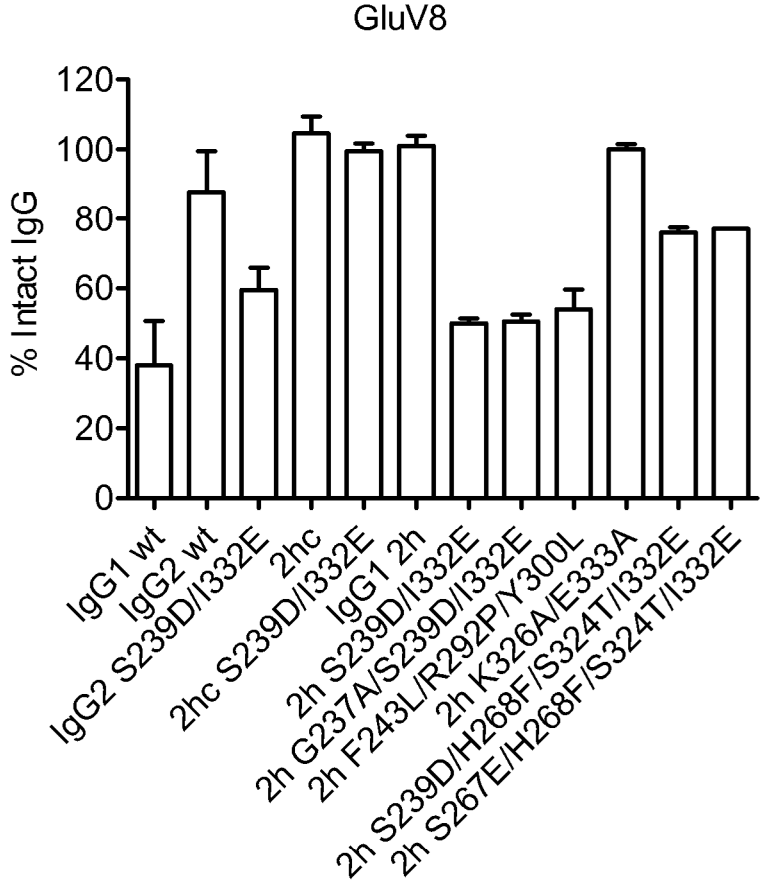

GluV8
% Intact IgG
120
100
80
60
40
20
0
IgG1 wt
IgG2 wt
IgG2 S239D/I332E
2hc
2hc S239D/I332E
IgG1 2h
2h S239D/I332E
2h G237A/S239D/I332E
2h F243L/R292P/Y300L
2h K326A/E333A
2h S239D/H268F/S324T/I332E
2h S267E/H268F/S324T/I332E

Fig. 4C

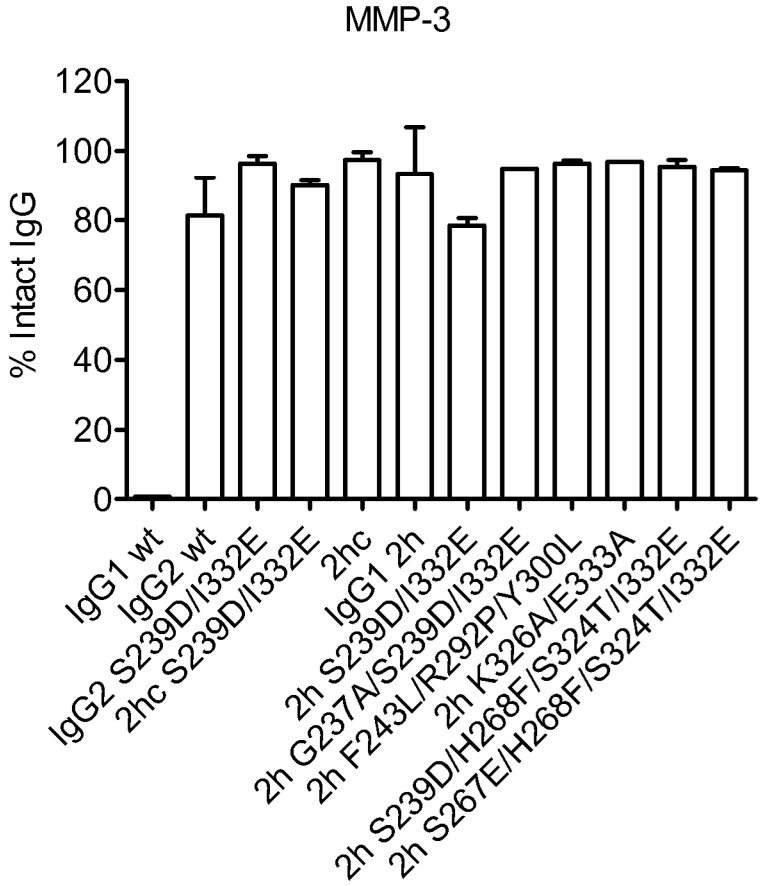

MMP-3
% Intact IgG
120
100
80
60
40
20
0
IgG1 wt
IgG2 wt
IgG2 S239D/I332E
2hc S239D/I332E
2hc
IgG1 2h
2h S239D/I332E
2h G237A/S239D/I332E
2h F243L/R292P/Y300L
2h K326A/E333A
2h S239D/H268F/S324T/I332E
2h S267E/H268F/S324T/I332E

Fig. 4D

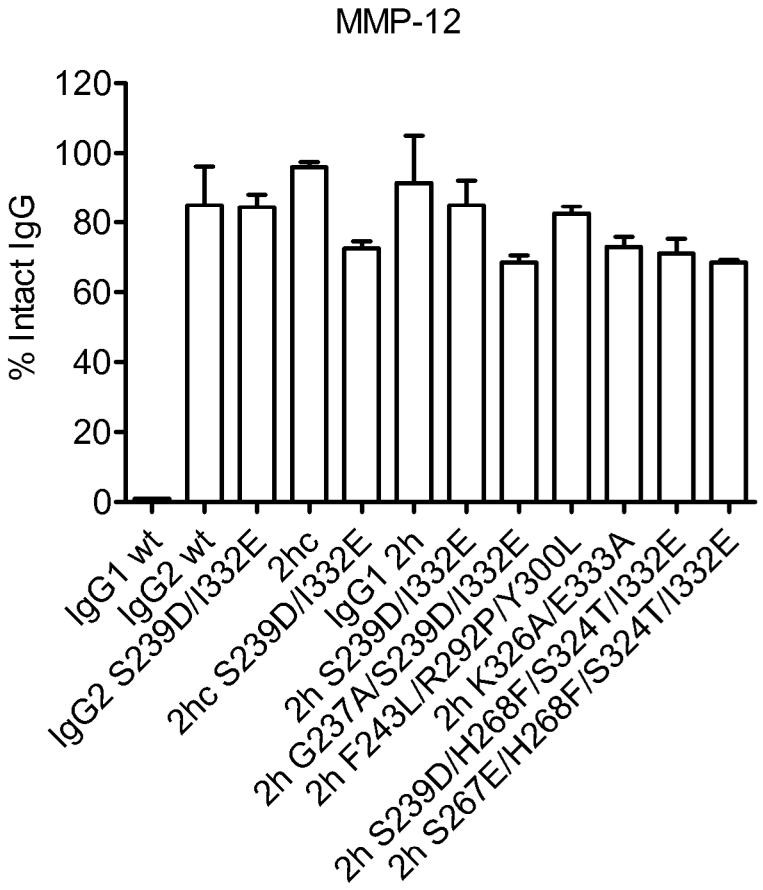

MMP-12
% Intact IgG
120
100
80
60
40
20
0
IgG1 wt
IgG2 wt
IgG2 S239D/I332E
2hc
2hc S239D/I332E
IgG1 2h
2h S239D/I332E
2h G237A/S239D/I332E
2h F243L/R292P/Y300L
2h K326A/E333A
2h S239D/H268F/S324T/I332E
2h S267E/H268F/S324T/I332E

Fig. 5A

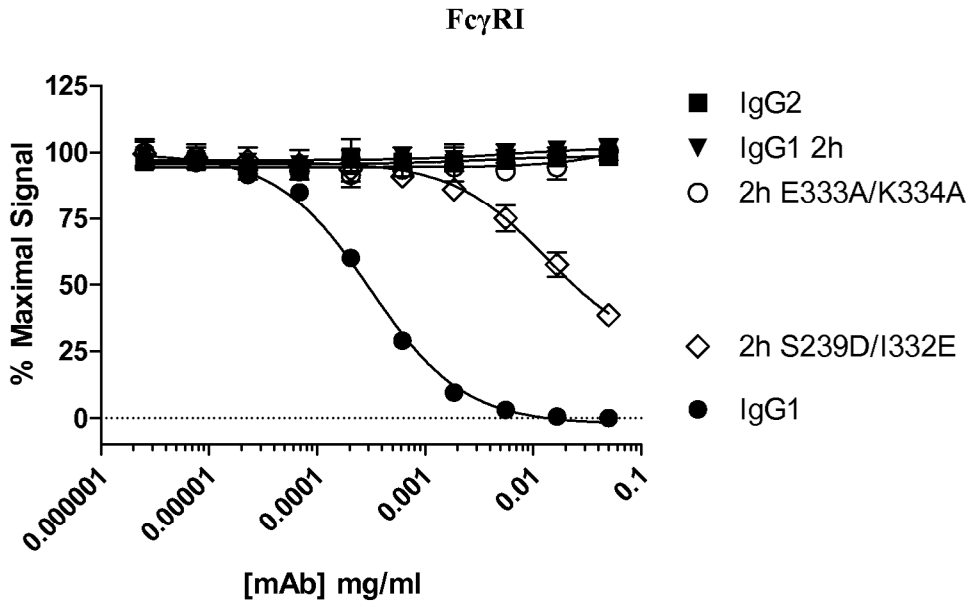

FcγRI
% Maximal Signal
125
100
75
50
25
0
0.000001
0.00001
0.0001
0.001
0.01
0.1
[mAb] mg/ml
IgG2
IgG1 2h
2h E333A/K334A
2h S239D/I332E
IgG1

Fig. 5B

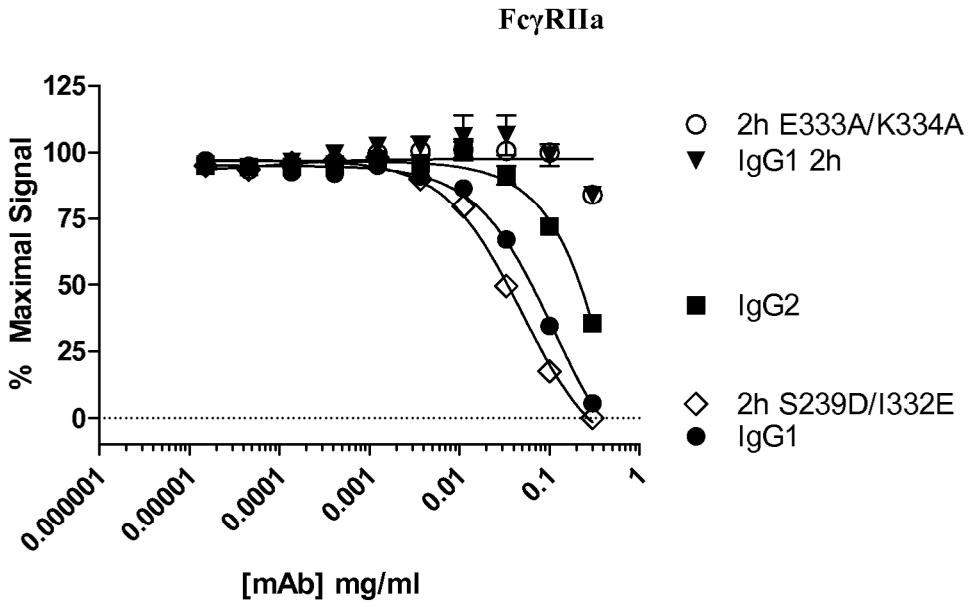

FcγRIIa
% Maximal Signal
125
100
75
50
25
0
0.000001
0.00001
0.0001
0.001
0.01
0.1
1
[mAb] mg/ml
2h E333A/K334A
IgG1 2h
IgG2
2h S239D/I332E
IgG1

Fig. 5C

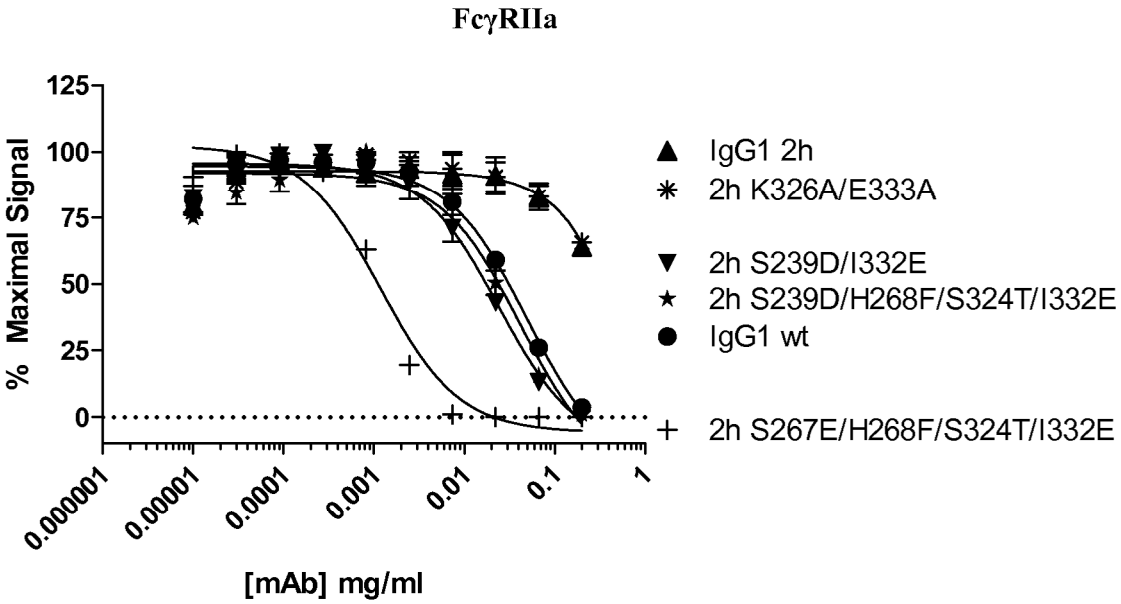

FcγRIIa
% Maximal Signal
125
100
75
50
25
0
0.000001
0.00001
0.0001
0.001
0.01
0.1
1
[mAb] mg/ml
IgG1 2h
2h K326A/E333A
2h S239D/I332E
2h S239D/H268F/S324T/I332E
IgG1 wt
2h S267E/H268F/S324T/I332E

Fig. 5D

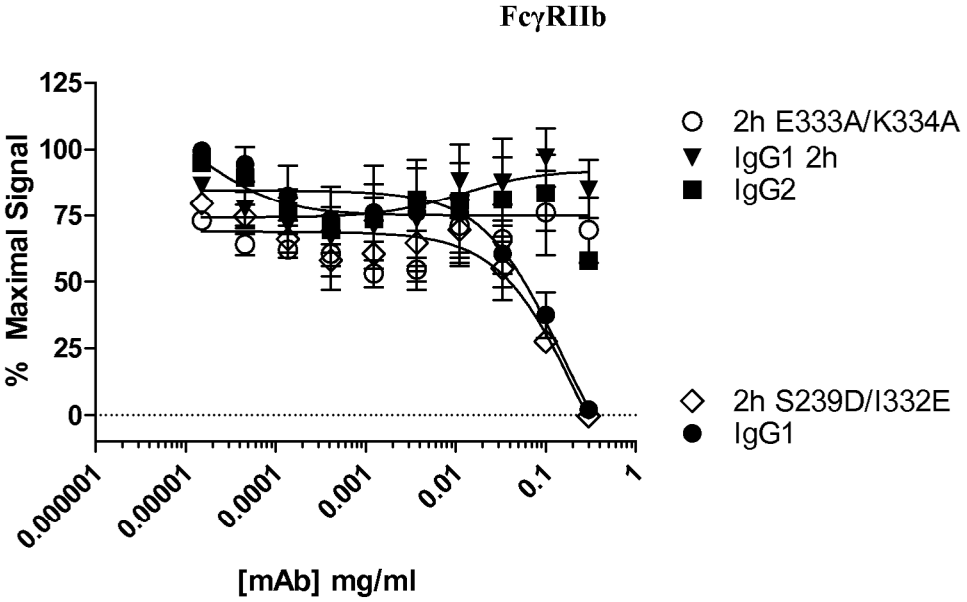

FcγRIIb
% Maximal Signal
125
100
75
50
25
0
0.000001
0.00001
0.0001
0.001
0.01
0.1
1
[mAb] mg/ml
2h E333A/K334A
IgG1 2h
IgG2
2h S239D/I332E
IgG1

Fig. 5E

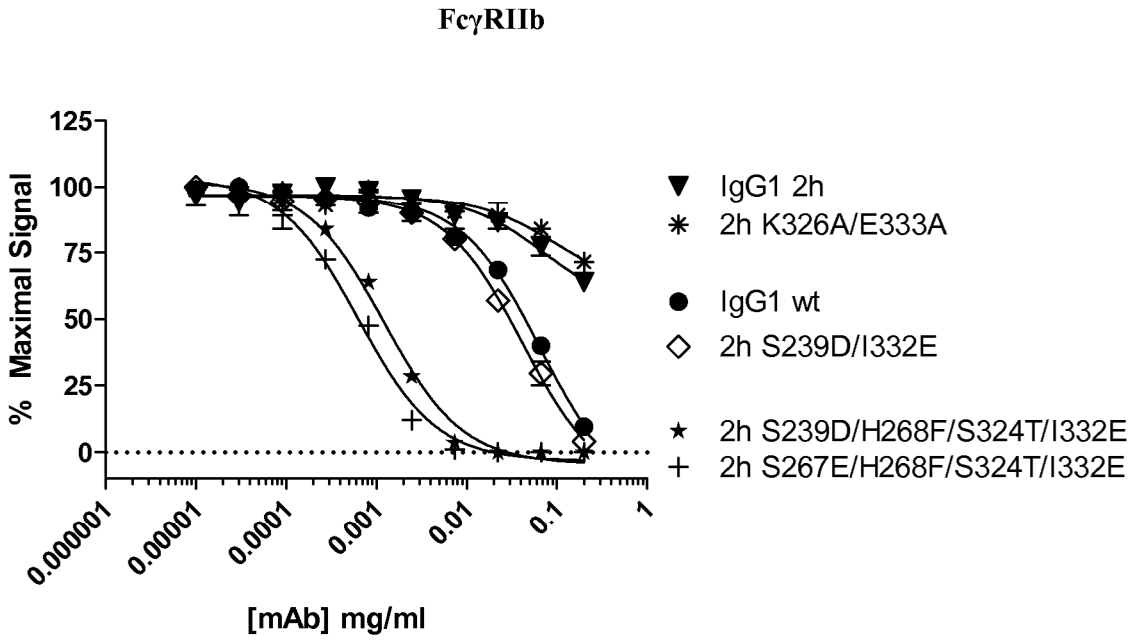

FcγRIIb
125
100
75
50
25
0
% Maximal Signal
0.000001
0.00001
0.0001
0.001
0.01
0.1
1
[mAb] mg/ml
IgG1 2h
2h K326A/E333A
IgG1 wt
2h S239D/I332E
2h S239D/H268F/S324T/I332E
2h S267E/H268F/S324T/I332E

Fig. 5F

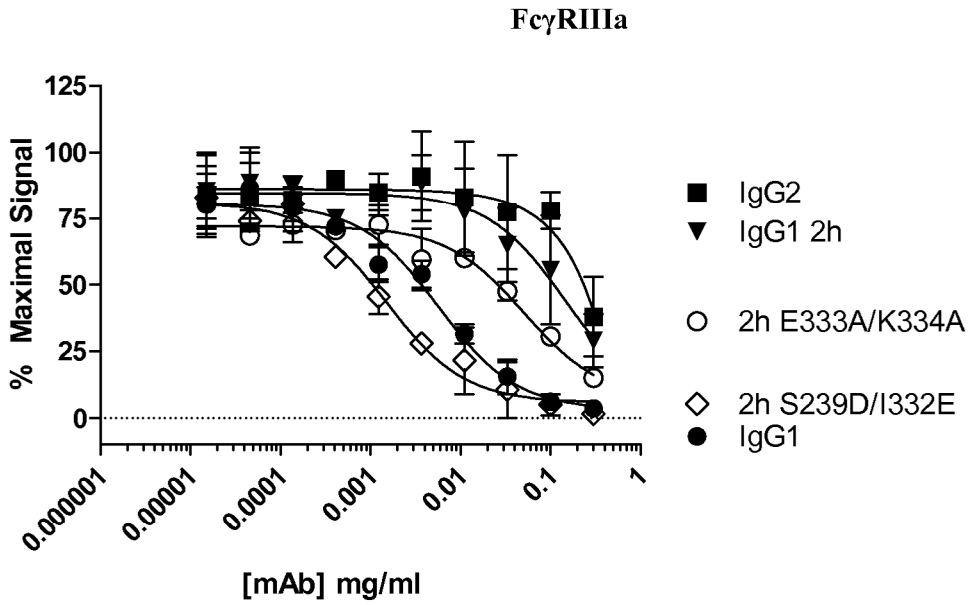

FcγRIIIa
% Maximal Signal
125
100
75
50
25
0
0.000001
0.00001
0.0001
0.001
0.01
0.1
1
[mAb] mg/ml
IgG2
IgG1 2h
2h E333A/K334A
2h S239D/I332E
IgG1

Fig. 5G

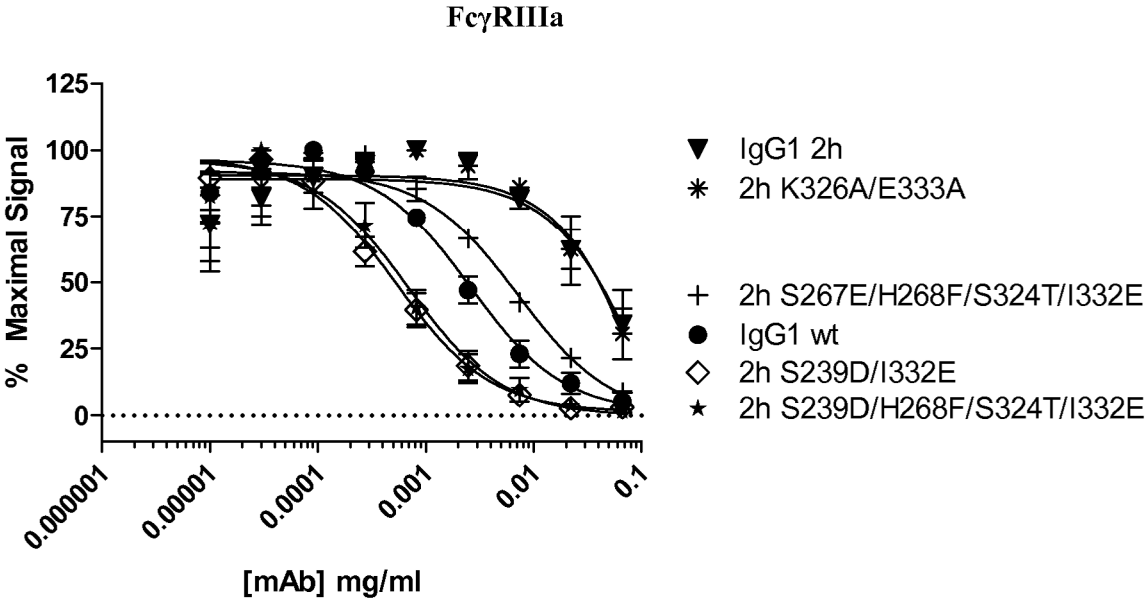

FcγRIIIa
% Maximal Signal
125
100
75
50
25
0
0.000001
0.00001
0.0001
0.001
0.01
0.1
[mAb] mg/ml
IgG1 2h
2h K326A/E333A
2h S267E/H268F/S324T/I332E
IgG1 wt
2h S239D/I332E
2h S239D/H268F/S324T/I332E

Fig. 6A

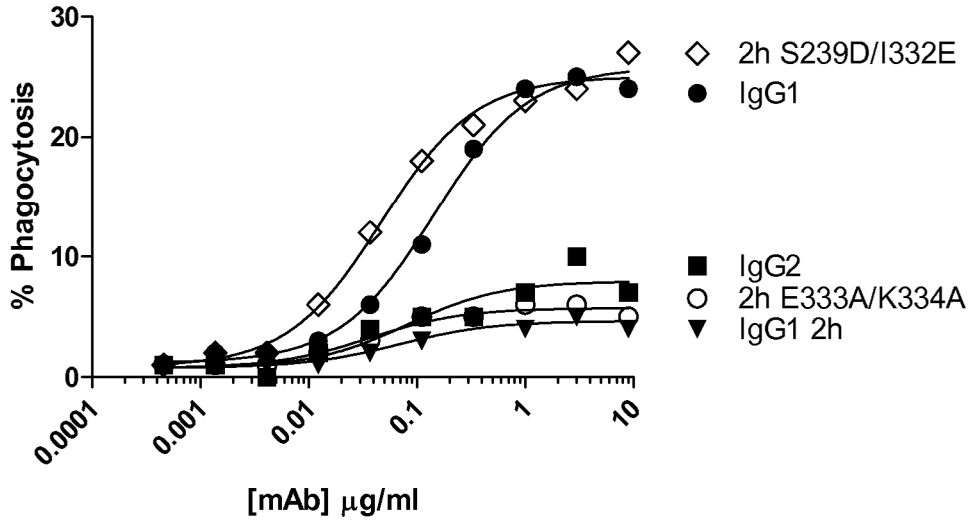

30
20
10
0
% Phagocytosis
0.0001
0.001
0.01
0.1
1
10
[mAb] μg/ml
2h S239D/I332E
IgG1
IgG2
2h E333A/K334A
IgG1 2h

Fig. 6B

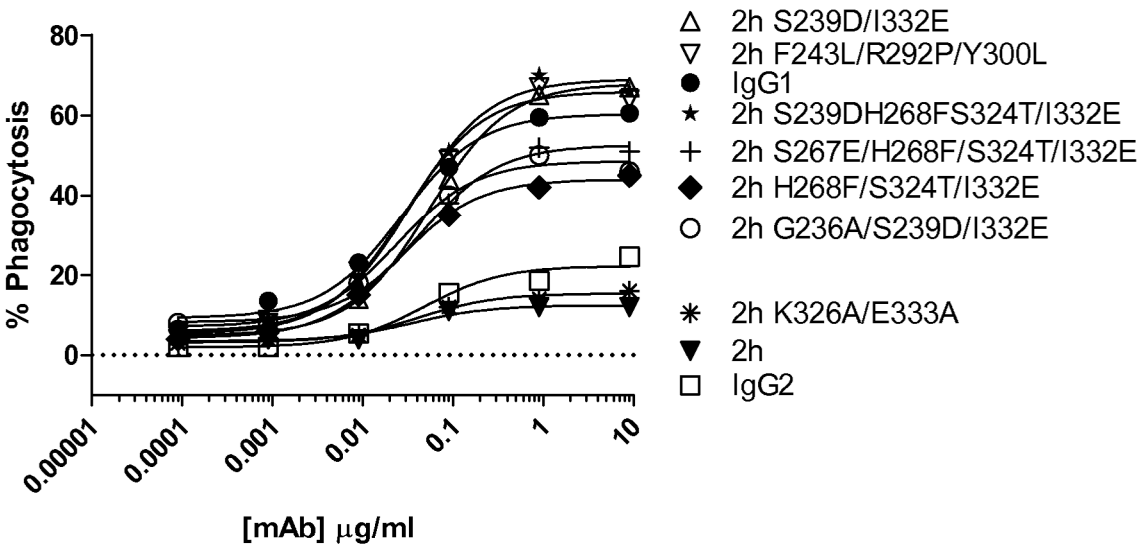

% Phagocytosis
80
60
40
20
0
0.00001
0.0001
0.001
0.01
0.1
1
10
[mAb] μg/ml
2h S239D/I332E
2h F243L/R292P/Y300L
IgG1
2h S239DH268FS324T/I332E
2h S267E/H268F/S324T/I332E
2h H268F/S324T/I332E
2h G236A/S239D/I332E
2h K326A/E333A
2h
IgG2

Fig. 6C

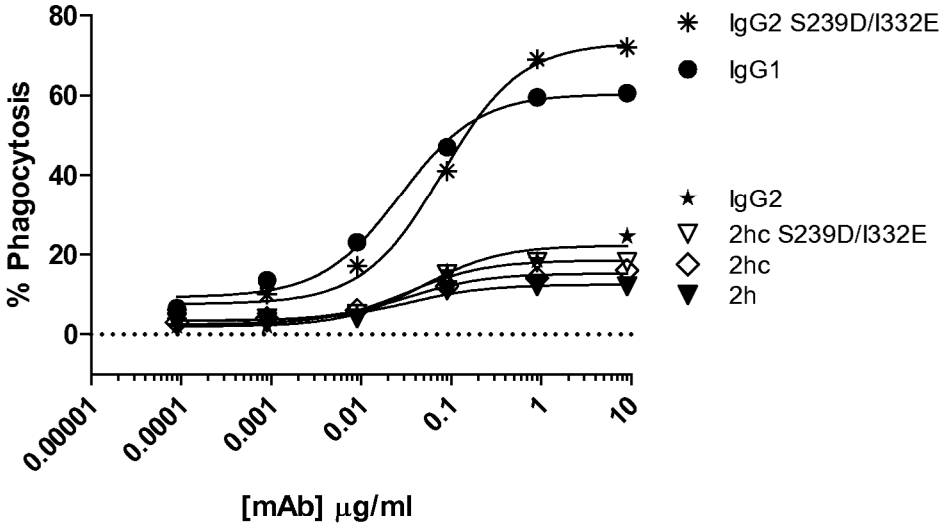

80
60
40
20
0
% Phagocytosis
0.00001
0.0001
0.001
0.01
0.1
1
10
[mAb] μg/ml
IgG2 S239D/I332E
IgG1
IgG2
2hc S239D/I332E
2hc
2h

Fig. 7A

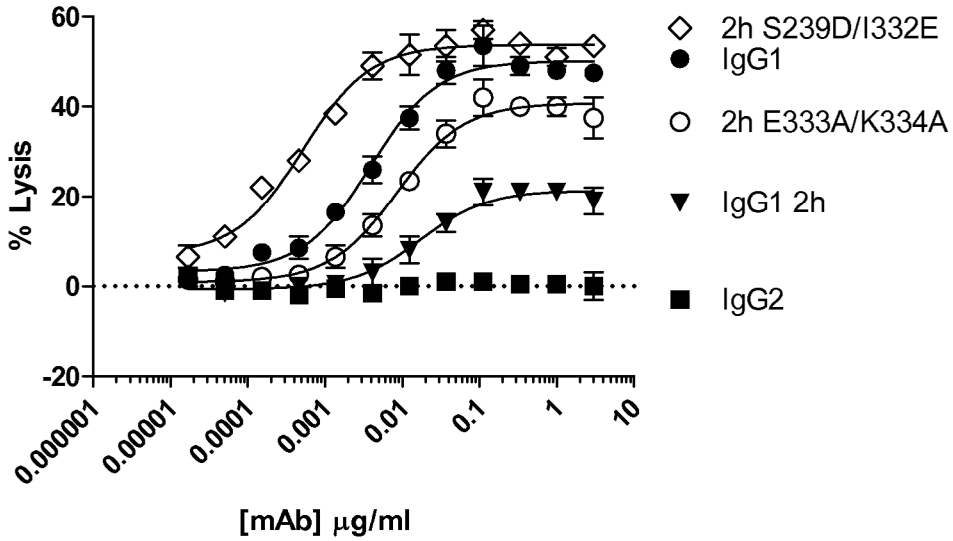

60
40
20
0
-20
% Lysis
0.000001
0.00001
0.0001
0.001
0.01
0.1
1
10
[mAb] μg/ml
2h S239D/I332E
IgG1
2h E333A/K334A
IgG1 2h
IgG2

Fig. 7B

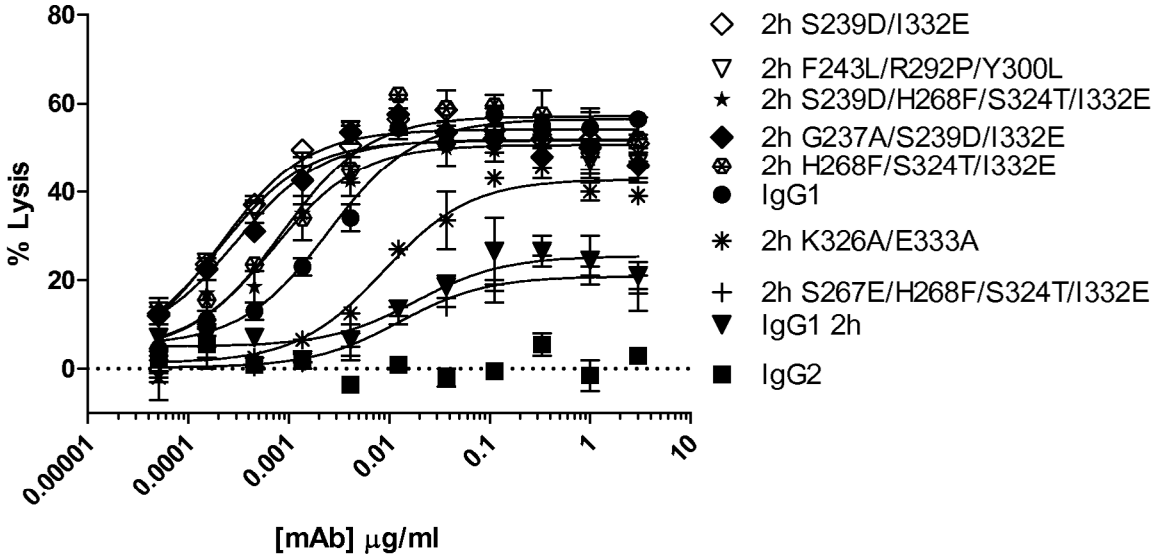

80
60
40
20
0
% Lysis
0.00001
0.0001
0.001
0.01
0.1
1
10
[mAb] μg/ml
2h S239D/I332E
2h F243L/R292P/Y300L
2h S239D/H268F/S324T/I332E
2h G237A/S239D/I332E
2h H268F/S324T/I332E
IgG1
2h K326A/E333A
2h S267E/H268F/S324T/I332E
IgG1 2h
IgG2

Fig. 7C

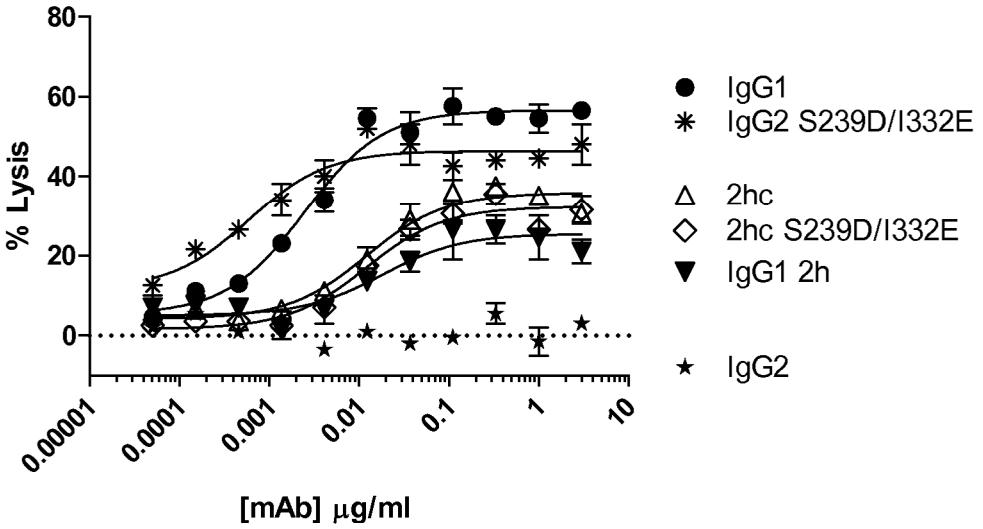
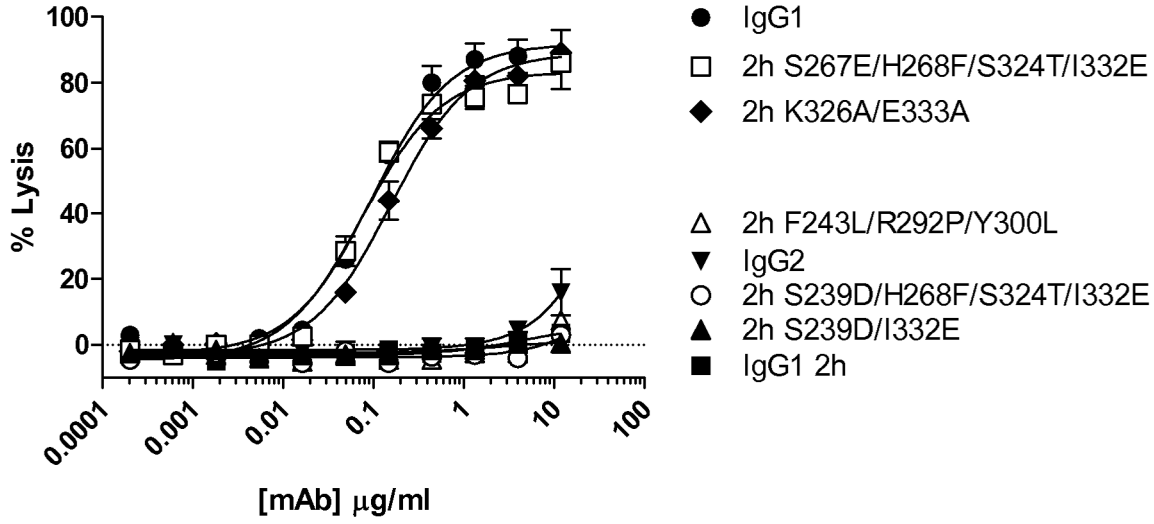

80
60
40
20
0
% Lysis
0.00001
0.0001
0.001
0.01
0.1
1
10
[mAb] μg/ml
IgG1
IgG2 S239D/I332E
2hc
2hc S239D/I332E
IgG1 2h
IgG2

Fig. 8


100
80
60
40
20
0
% Lysis
0.0001
0.001
0.01
0.1
1
10
100
[mAb] μg/ml
IgG1
2h S267E/H268F/S324T/I332E
2h K326A/E333A
2h F243L/R292P/Y300L
IgG2
2h S239D/H268F/S324T/I332E
2h S239D/I332E
IgG1 2h