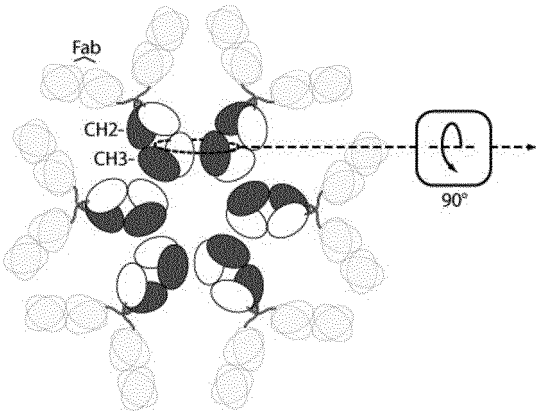
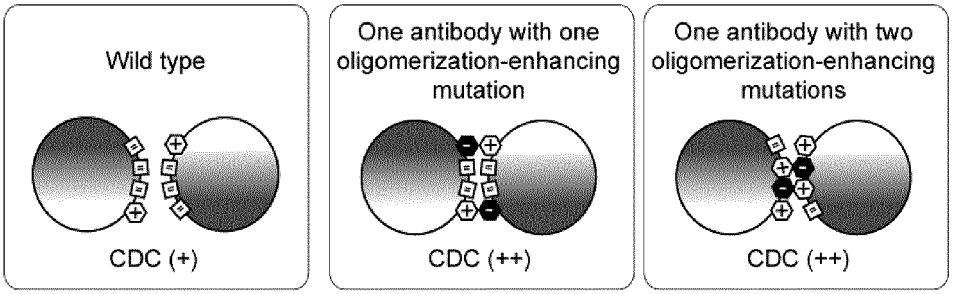
Figure 1

A) IgG molecules in hexamer formation



B) Observed effect of oligomerization-enhancing mutations on CDC



C) Observed effect of oligomerization-inhibiting mutations on CDC

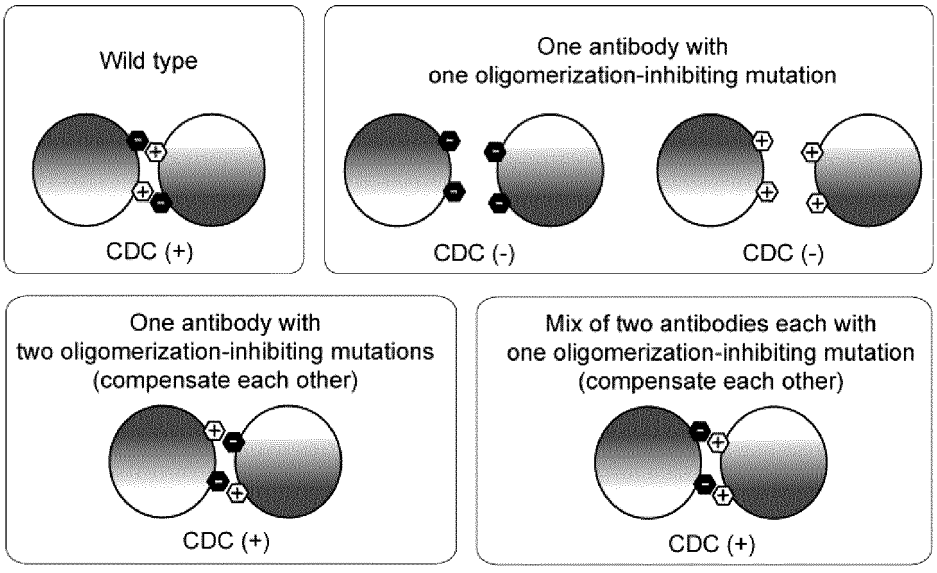


Figure 1D

D) Theoretical effect of C1q binding-inhibiting mutations on CDC

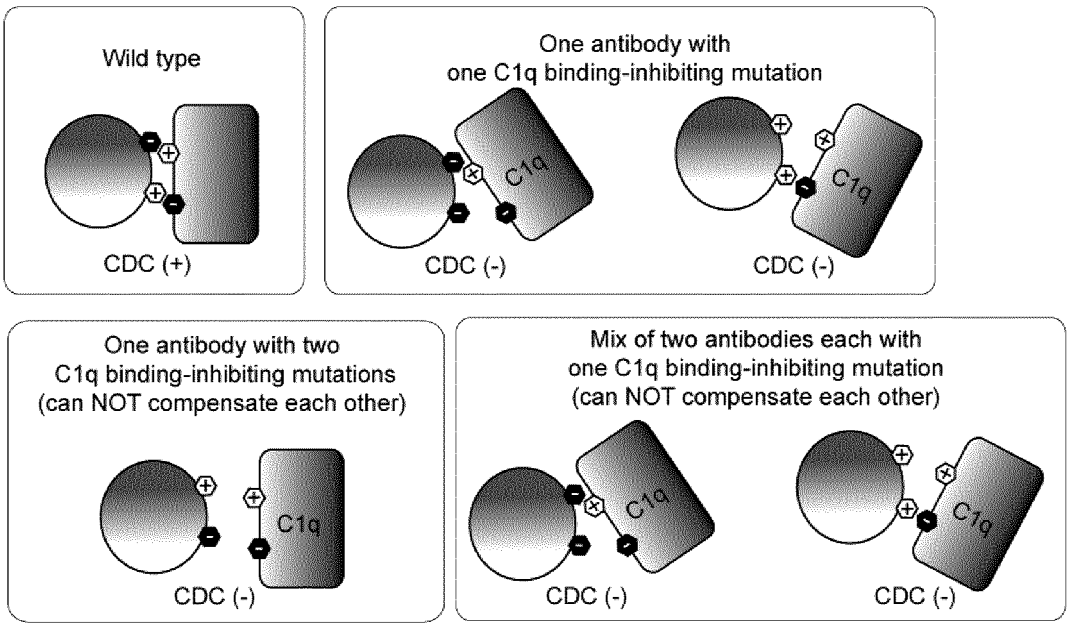


Figure 2

```
IgG1  247 PKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVL 306
IgG1f     PKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVL
IgG2      PKDTLMISRTPEVTCVVVDVSHEDPEVQFNWYVDGVEVHNAKTKPREEQFNSTFRVVSVL
IgG3      PKDTLMISRTPEVTCVVVDVSHEDPEVQFKWYVDGVEVHNAKTKPREEQYNSTFRVVSVL
IgG4      PKDTLMISRTPEVTCVVVDVSQEDPEVQFNWYVDGVEVHNAKTKPREEQFNSTYRVVSVL
IgE       SPFDLFIRKSPTITCLVVDLAPSKGTVNLTWSRASGKPVNHSTRKEEKQRNGTLTVTSTL
IgA1      ALEDLLLGSEANLTCTLTGLRDASG-VTFTWTPSSGKSAVQGP--PERDLCGCYSVSSVL
IgA2      ALEDLLLGSEANLTCTLTGLRDASG-ATFTWTPSSGKSAVQGP--PERDLCGCYSVSSVL
IgM       SFASIFLTKSTKLTCLVTDLTTYDS-VTISWTRQNGEAVKTHTNISESHPNATFSAVGEA
IgD       AVQDLWLRDKATFTCFVVGSDLKDAHLTWEVAG-KVPTGGVEEGLLERHSNGSQSQHSRL
                     : :   . .** :..    .                       * .  .     .

IgG1  307 TVLHQDWLNGKEYKCKVSNKALPAPIEKTIS-KAKGQPREPQVYTLPPSRDELTK-NQVS 364
IgG1f     TVLHQDWLNGKEYKCKVSNKALPAPIEKTIS-KAKGQPREPQVYTLPPSREEMTK-NQVS
IgG2      TVVHQDWLNGKEYKCKVSNKGLPAPIEKTIS-KTKGQPREPQVYTLPPSREEMTK-NQVS
IgG3      TVLHQDWLNGKEYKCKVSNKALPAPIEKTIS-KTKGQPREPQVYTLPPSREEMTK-NQVS
IgG4      TVLHQDWLNGKEYKCKVSNKGLPSSIEKTIS-KAKGQPREPQVYTLPPSQEEMTK-NQVS
IgE       PVGTRDWIEGETYQCRVTHPHLPRALMRSTT-KTSGPRAAPEVYAFATPEWPGSR-DKRT
IgA1      PGCAEPWNHGKTFTCTAAYPESKTPLTATLS--KSGNTFRPEVHLLPPPSEELALNELVT
IgA2      PGCAQPWNHGETFTCTAAHPELKTPLTANIT--KSGNTFRPEVHLLPPPSEELALNELVT
IgM       SICEDDWNSGERFTCTVTHTDLPSPLKQTISRPKGVALHRPDVYLLPPAREQLNLRESAT
IgD       TLPRSLWNAGTSVTCTLNHPSLPPQRLMALREPAAQAPVKLSLNLLASSDPPEAA---SW
                    .     *  *    *                              .:  :...

IgG1  365 LTCLVKGFYPSDIAVEWESNGQ--PENNYKTTPPVLDS---DGSFFLYSKLTVDKSRWQQ 419
IgG1f     LTCLVKGFYPSDIAVEWESNGQ--PENNYKTTPPVLDS---DGSFFLYSKLTVDKSRWQQ
IgG2      LTCLVKGFYPSDIAVEWESNGQ--PENNYKTTPPMLDS---DGSFFLYSKLTVDKSRWQQ
IgG3      LTCLVKGFYPSDIAVEWESSGQ--PENNYNTTPPMLDS---DGSFFLYSKLTVDKSRWQQ
IgG4      LTCLVKGFYPSDIAVEWESNGQ--PENNYKTTPPVLDS---DGSFFLYSRLTVDKSRWQE
IgE       LACLIQNFMPEDISVQWLHNEVQLPDARHSTTQPRKTK---GSGFFVFSRLEVTRAEWEQ
IgA1      LTCLARGFSPKDVLVRWLQGSQELPREKYLTWASRQEPSQGTTTFAVTSILRVAAEDWKK
IgA2      LTCLARGFSPKDVLVRWLQGSQELPREKYLTWASRQEPSQGTTTFAVTSILRVAAEDWKK
IgM       ITCLVTGFSPADVFVQWMQRGQPLSPEKYVTSAPMPEP-QAPGRYFAHSILTVSEEEWNT
IgD       LLCEVSGFSPPNILLMWLEDQREVNTSGFAPARPPPQP--GSTTFWAWSVLRVPAPPSPQ
                    : *   .* * :: : *           . .  .          :   * * *

IgG1  420 GNVFSCSVMHEALHN-HYTQKSLSLSPGK------------------ 447
IgG1f     GNVFSCSVMHEALHN-HYTQKSLSLSPGK------------------
IgG2      GNVFSCSVMHEALHN-HYTQKSLSLSPGK------------------
IgG3      GNIFSCSVMHEALHN-RFTQKSLSLSPGK------------------
IgG4      GNVFSCSVMHEALHN-HYTQKSLSLSLGK------------------
IgE       KDEFICRAVHEAASPSQTVQRAVSVNPGK------------------
IgA1      GDTFSCMVGHEALPL-AFTQKTIDRLAGKPTHVNVSVVMAEVDGTCY
IgA2      GDTFSCMVGHEALPL-AFTQKTIDRLAGKPTHVNVSVVMAEVDGTCY
IgM       GETYTCVA-HEALPN-RVTERTVDKSTGKPTLYNVSLVMSDTAGTCY
IgD       PATYTCVVSHEDSRTLLNASRSLEVSYVTDHGPMK------------
                     : * . **       ..::::.    .
```

Figure 2 (cont'd)

IgG1 = aa 130-330 of Uniprot entry P01857
IgG1f= IgG1 allotypic variant "f"
IgG2 = aa 126-326 of Uniprot entry P01859
IgG3 = aa 177-377 of Uniprot entry P01860
IgG4 = aa 127-327 of Uniprot entry P01861
IgE = aa 225-428 of Uniprot entry P01854
IgA1 = aa 133-353 of Uniprot entry P01876
IgA2 = aa 120-340 of Uniprot entry P01877
IgM = aa 230-452 of Uniprot entry P01871
IgD = aa 176-384 of Uniprot entry P01880

Figure 3A

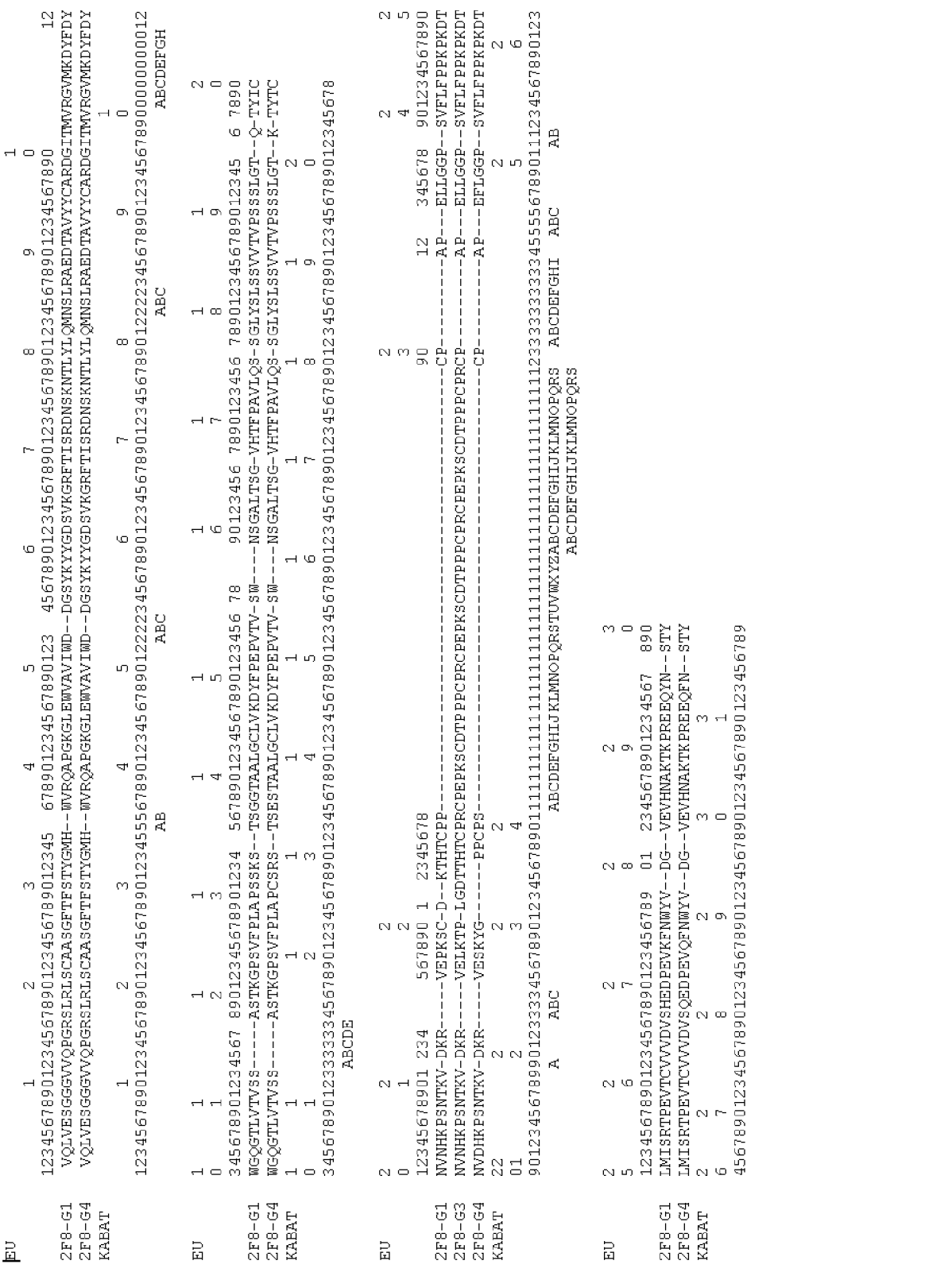


Figure 3B

```
EU          3       3       3       3       3       3       3       3       3       3       4
            0       1       2       3       4       5       6       7       8       9       0
            1234567890123456789012 3456 78901 2345678901234567  890123456789012345678901234 56  789012345678901
2F8-G1      RVVSVLTVLHQDWLNGKEYKCKVSNKALPAPI-EKTI-SKAKG-QPREPQVYTLPPSRDE--LTKNQVSLTCLVKGFYPSDIAV--EWESN-GQ--PENNYKTTPPVLDS
2F8-G4      RVVSVLTVLHQDWLNGKEYKCKVSNKGLPSSI-EKTI-SKAKG-QPREPQVYTLPPSQEE--MTKNQVSLTCLVKGFYPSDIAV--EWESN-GQ--PENNYKTTPPVLDS
KABAT       3       3       3       3       3       3       3       3       4       4
            2       3       4       5       6       7       8       9       0       1       2
            01234567890123456789011234567890123456789012345678901234567890123456789012345678
                                                A
EU          4       4       4       4       4
            0       1       2       3       4
            1  2345678901234567890123456789012345678901234567
2F8-G1      -D--GSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK
2F8-G4      -D--GSFFLYSRLTVDKSRWQEGNVFSCSVMHEALHNHYTQKSLSLSLGK
KABAT        4       4       4       4       4
             3       4       5       6       7
            901234567890123456789012345678901234567890123456789
```

Figure 4

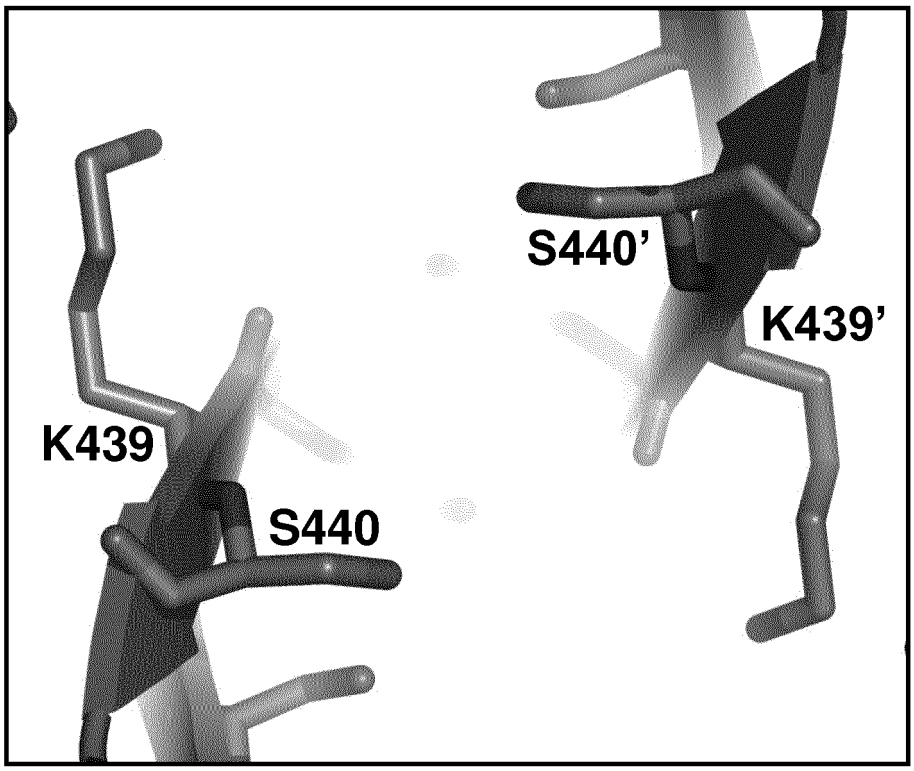


Figure 5

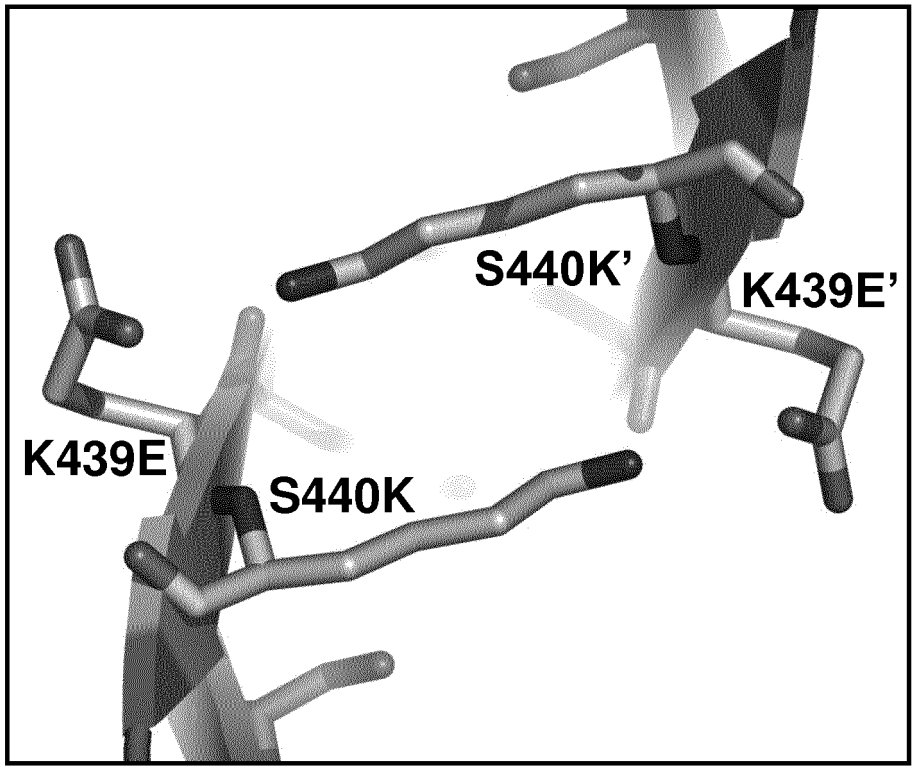


Figure 6

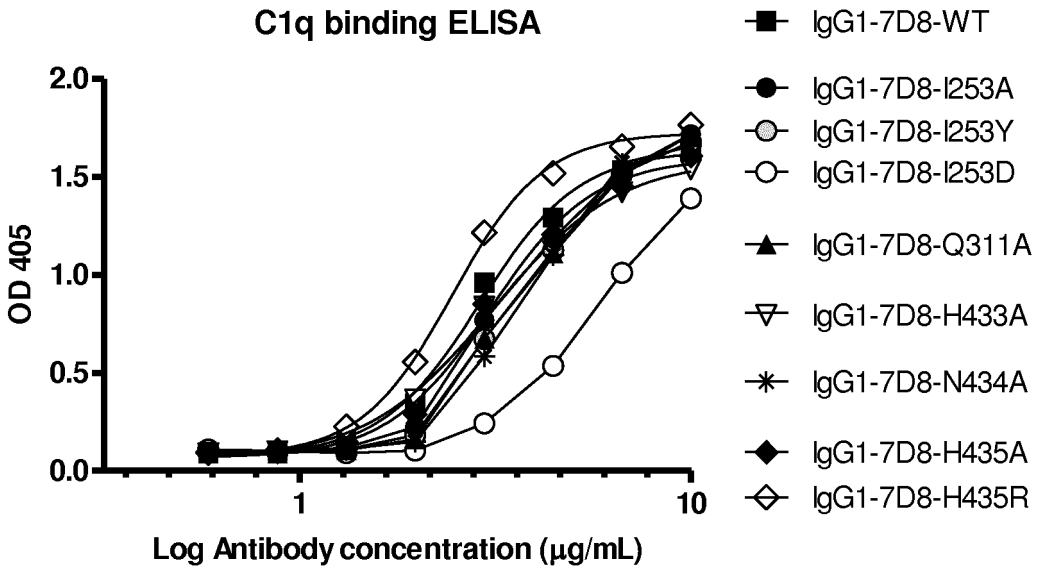


Figure 7

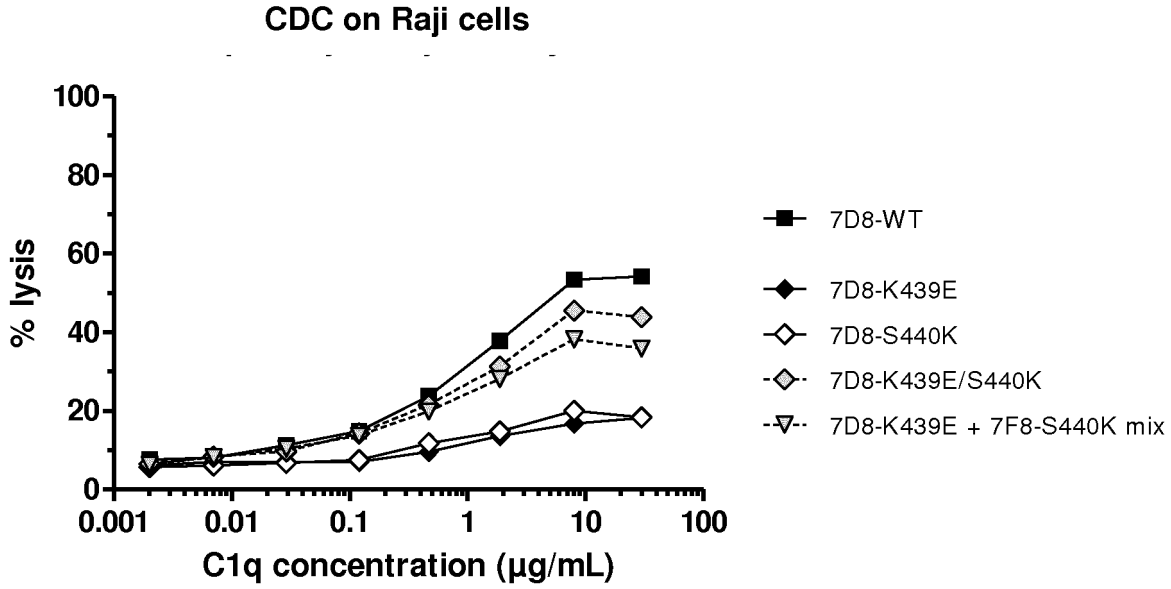


Figure 8

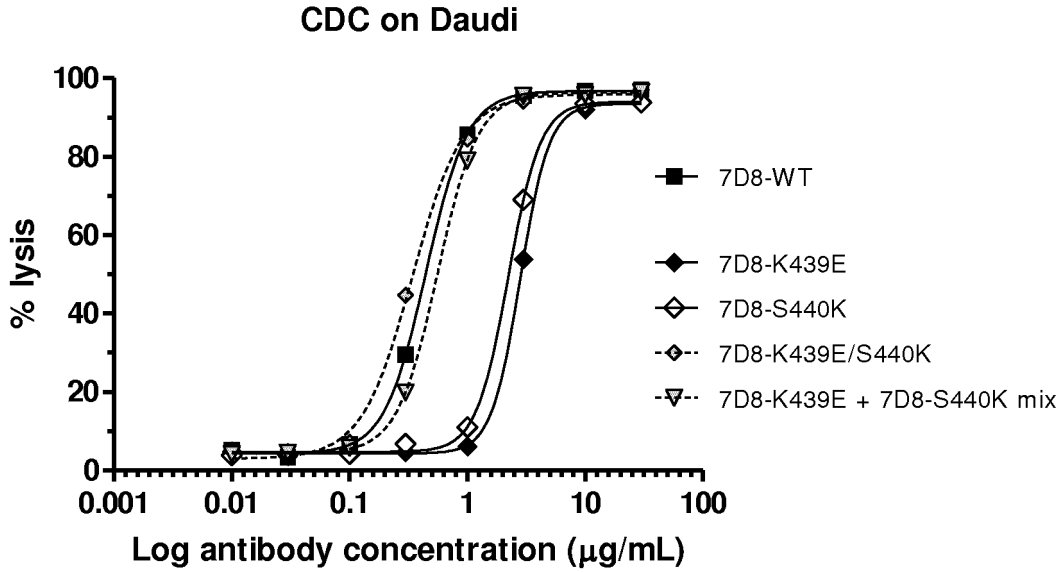

CDC on Daudi
% lysis
100
80
60
40
20
0
0.001
0.01
0.1
1
10
100
Log antibody concentration (µg/mL)
7D8-WT
7D8-K439E
7D8-S440K
7D8-K439E/S440K
7D8-K439E + 7D8-S440K mix

Figure 9A

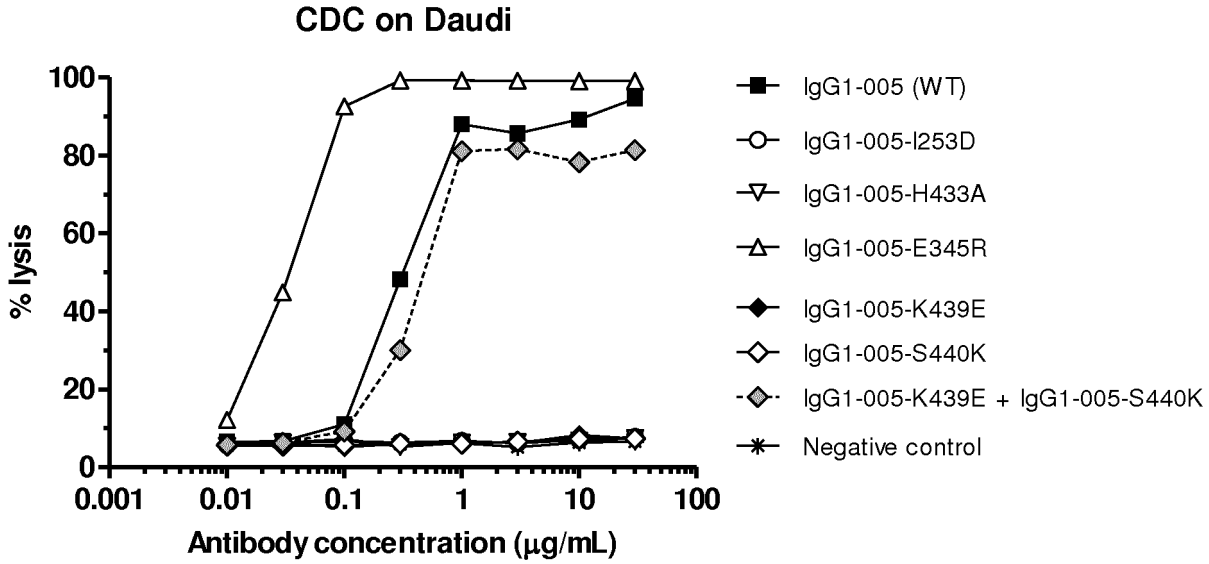


Figure 9B

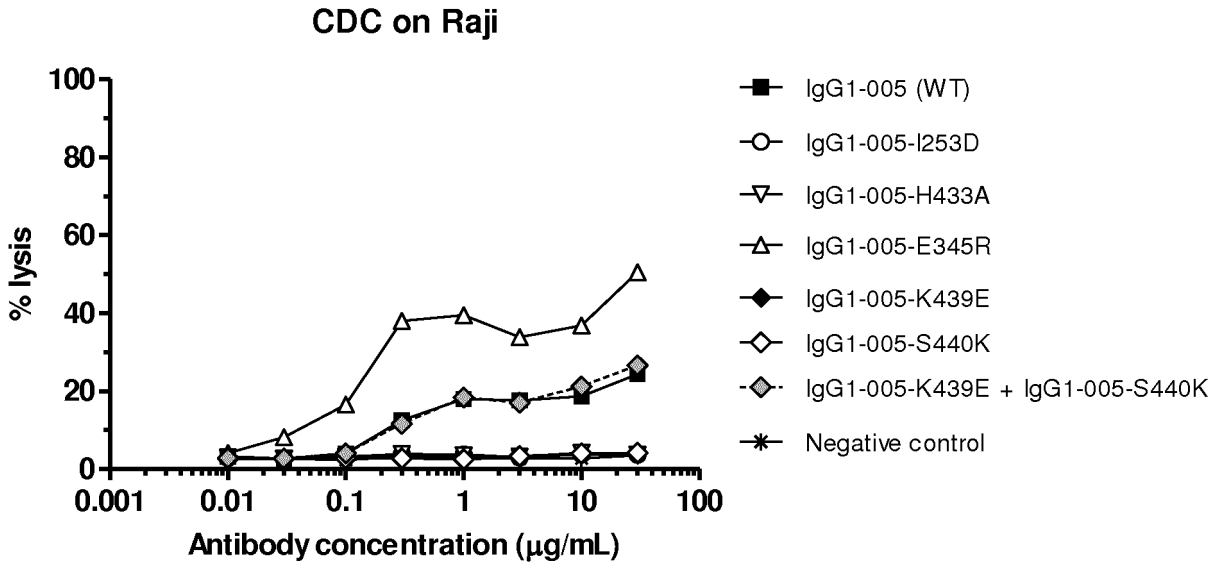


Figure 9C

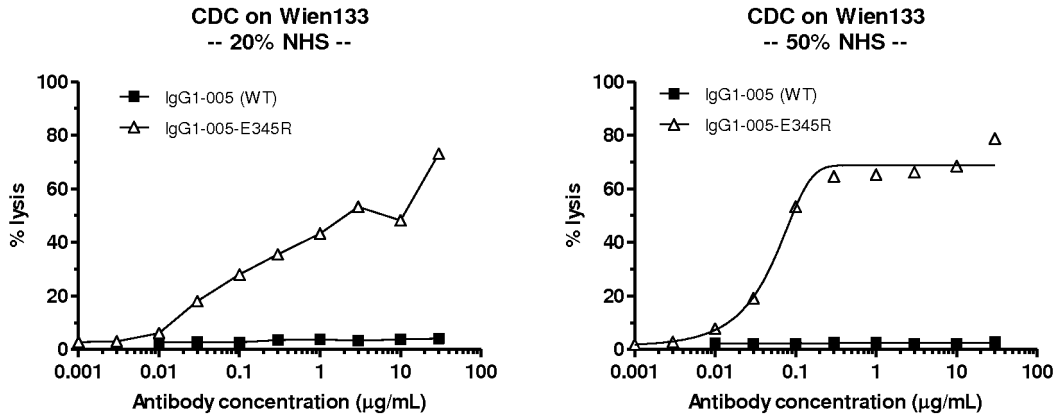


Figure 9D

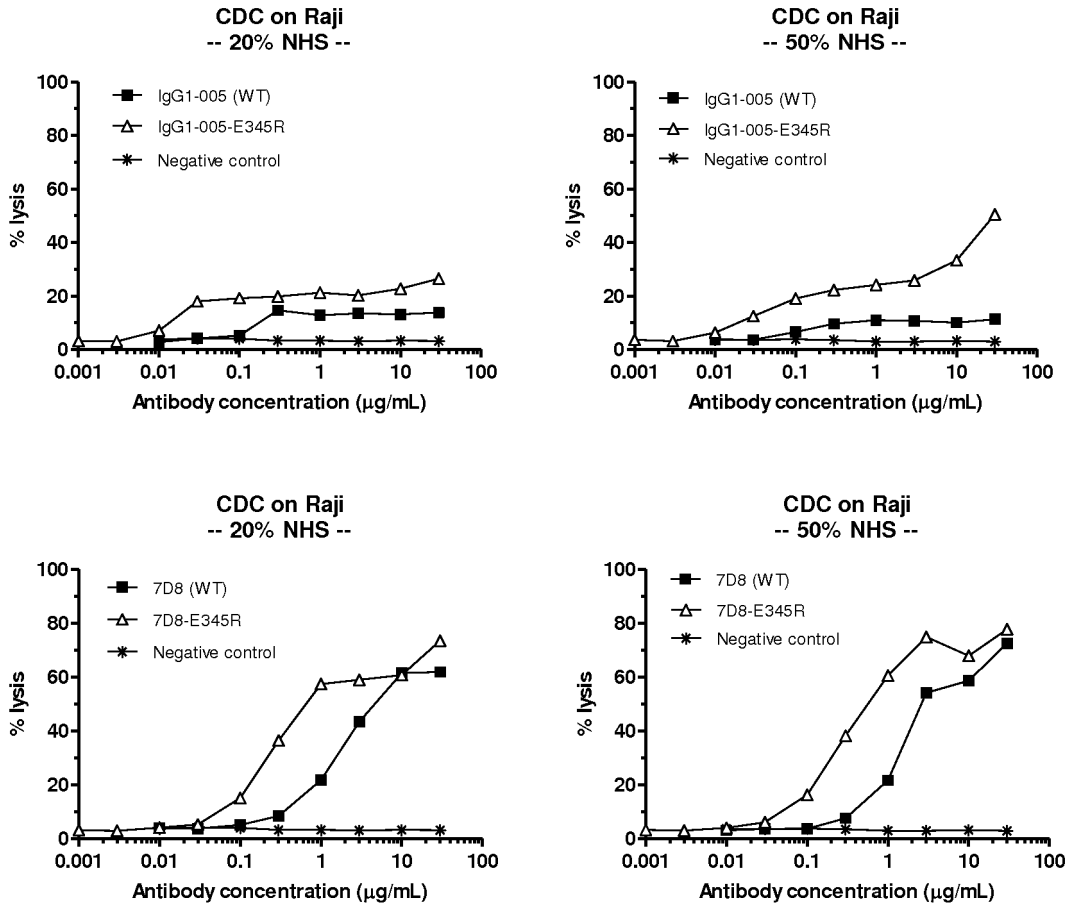


Figure 10A

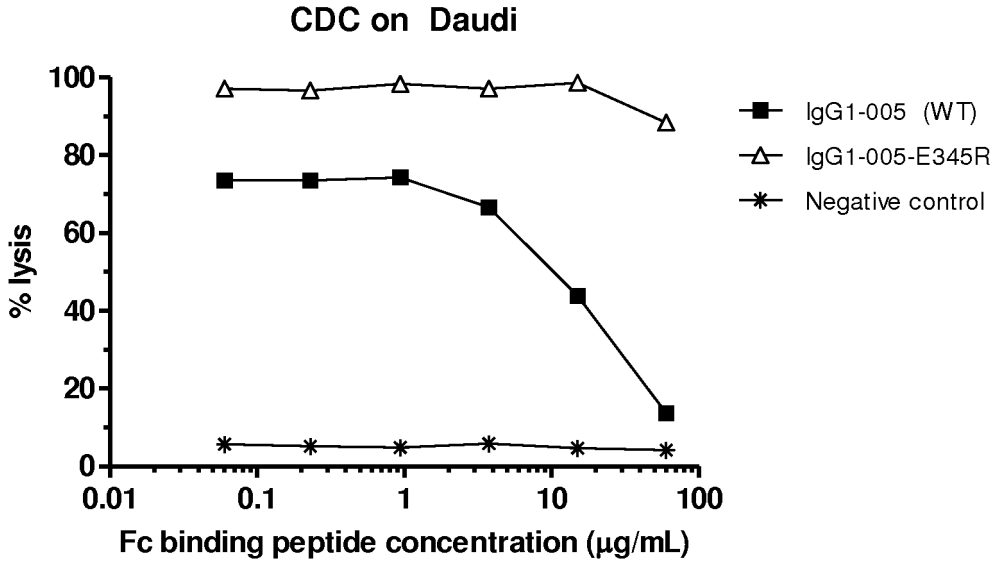


Figure 10B

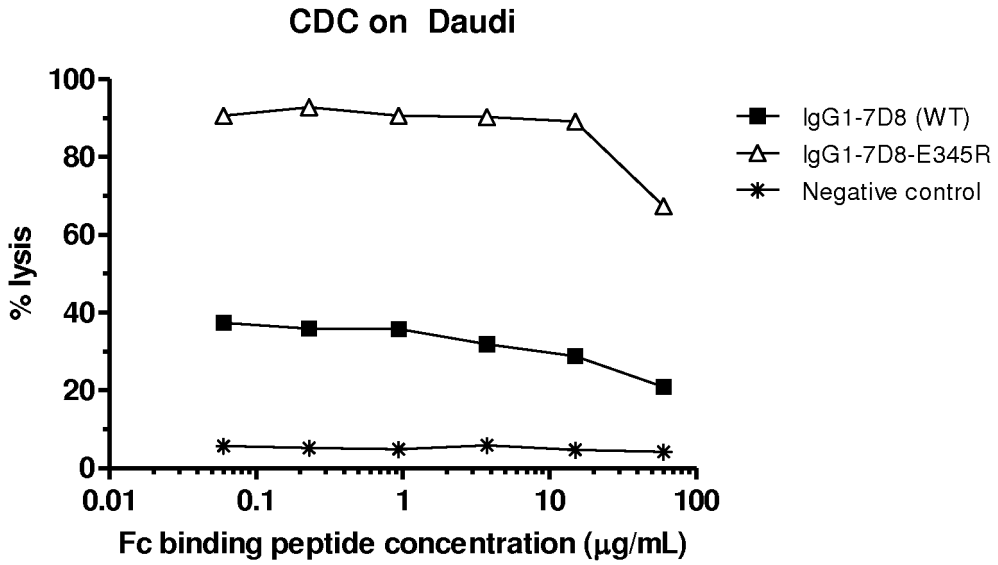


Figure 11

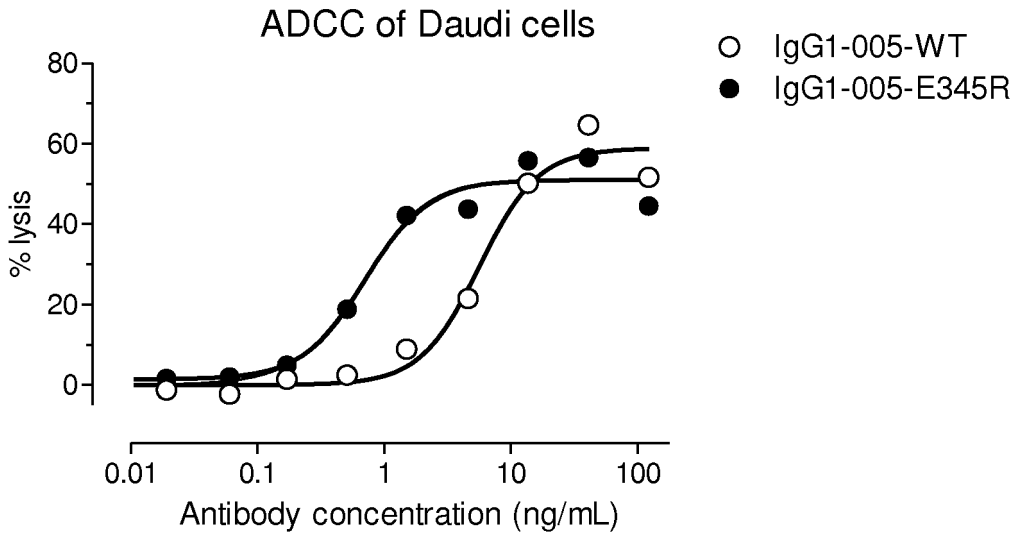

ADCC of Daudi cells
IgG1-005-WT
IgG1-005-E345R
% lysis
80
60
40
20
0
0.01
0.1
1
10
100
Antibody concentration (ng/mL)

Figure 12A

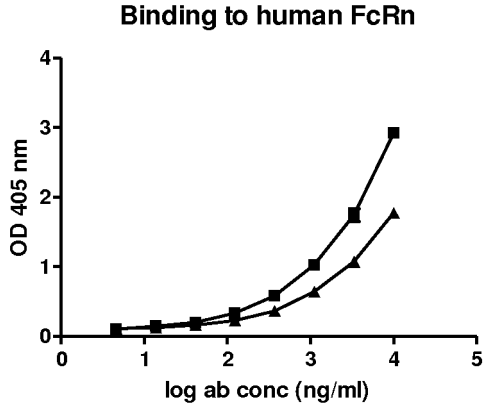


Figure 12B

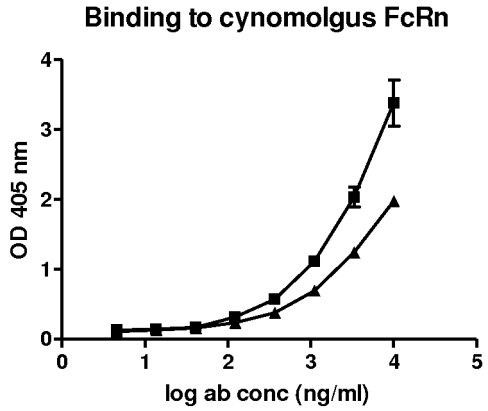


Figure 12C

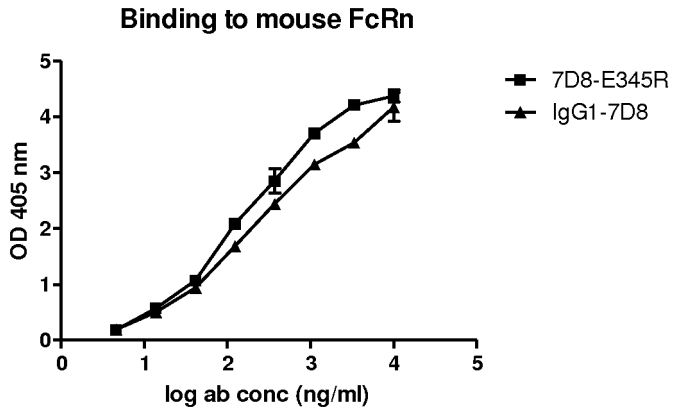


Figure 13

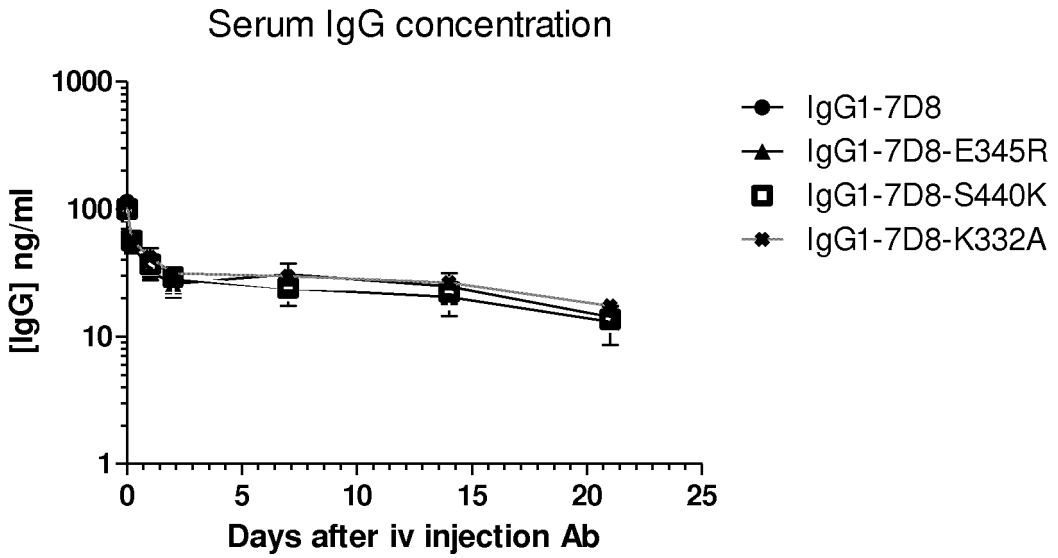

Serum IgG concentration
[IgG] ng/ml
1000
100
10
1
0
5
10
15
20
25
Days after iv injection Ab
IgG1-7D8
IgG1-7D8-E345R
IgG1-7D8-S440K
IgG1-7D8-K332A

Figure 14A

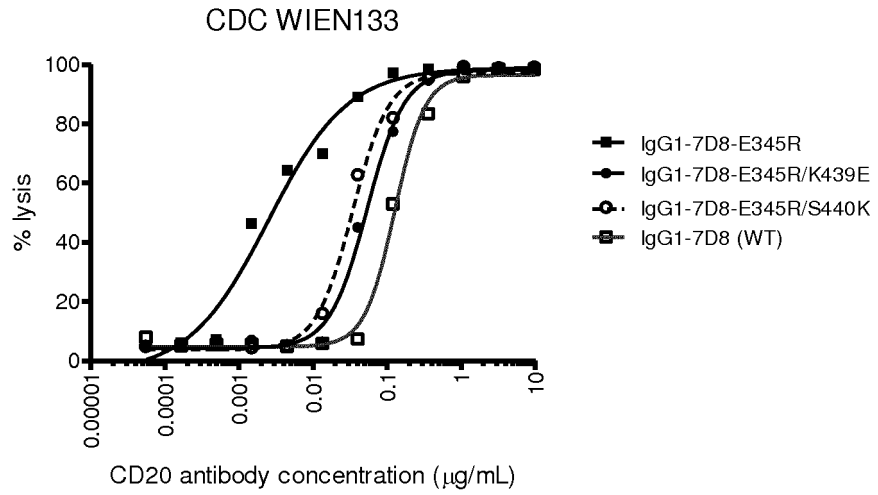


Figure 14B

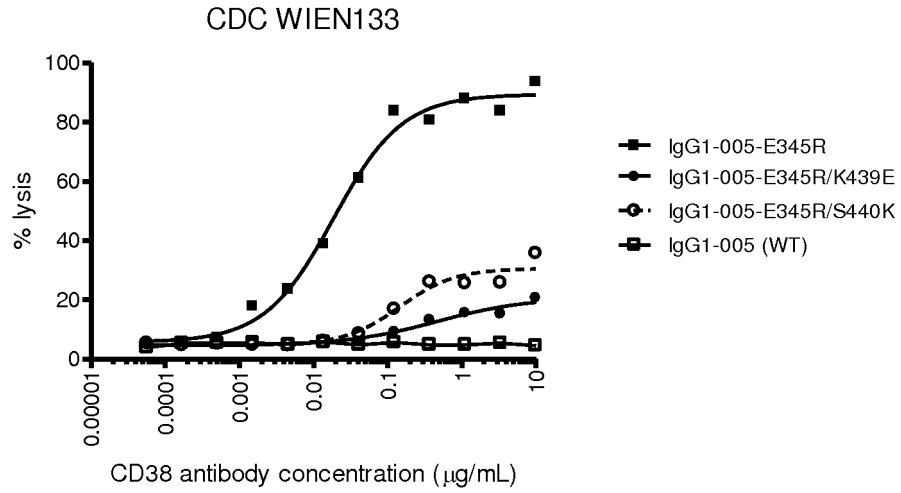


Figure 14C

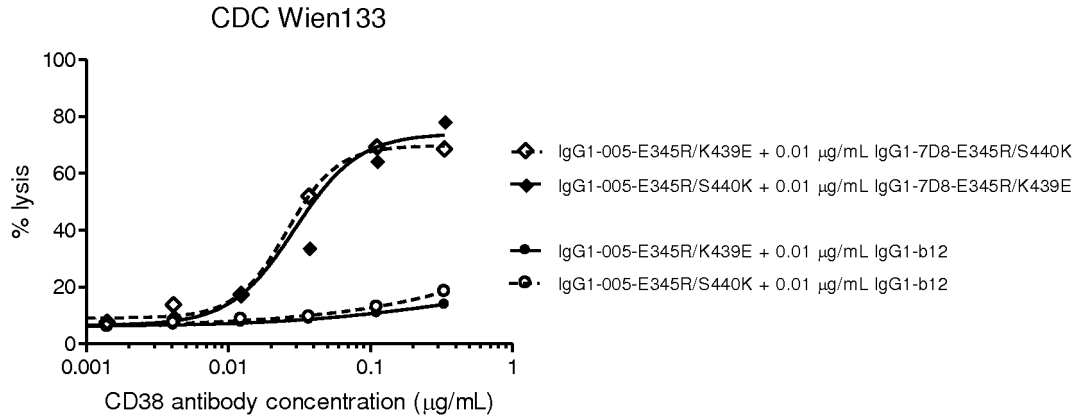


Figure 14D

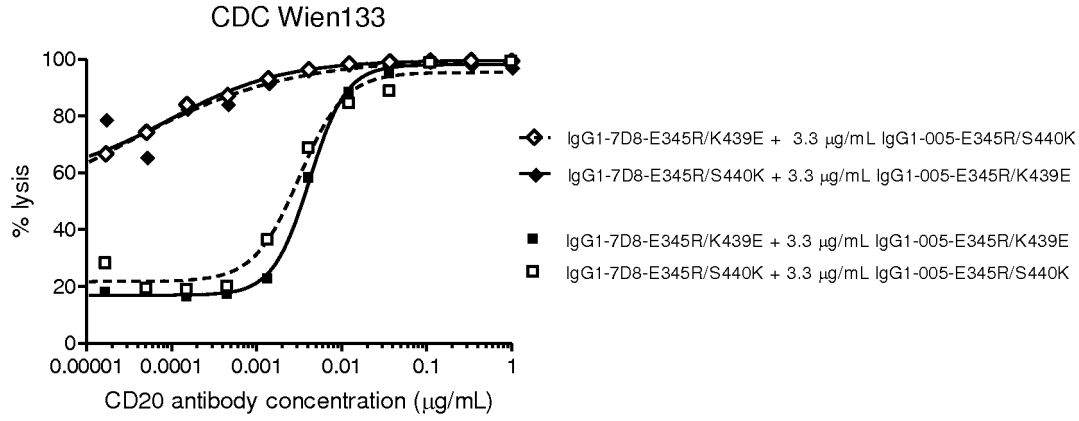


Figure 15A

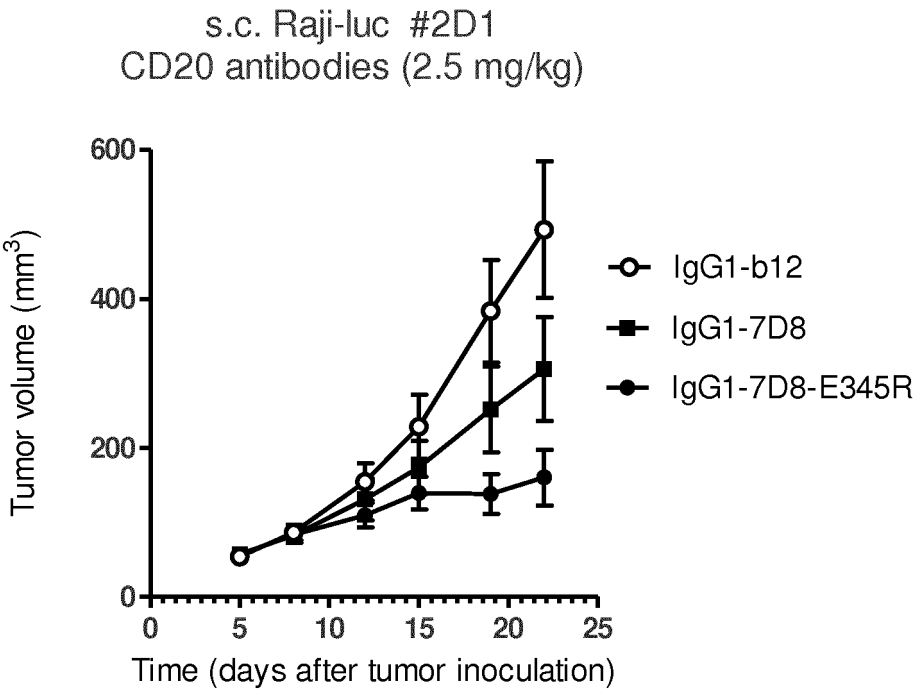


Figure 15B

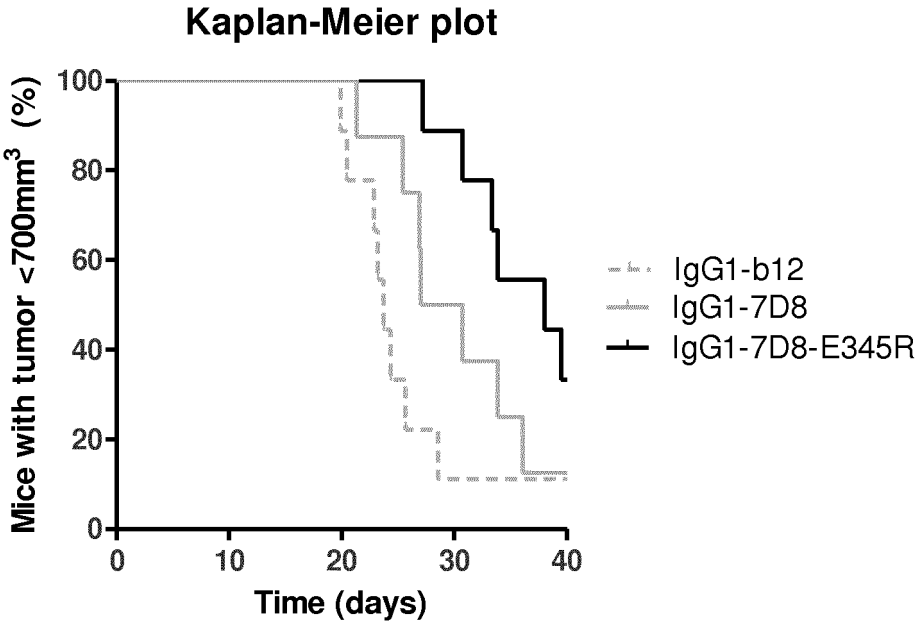


Figure 16A

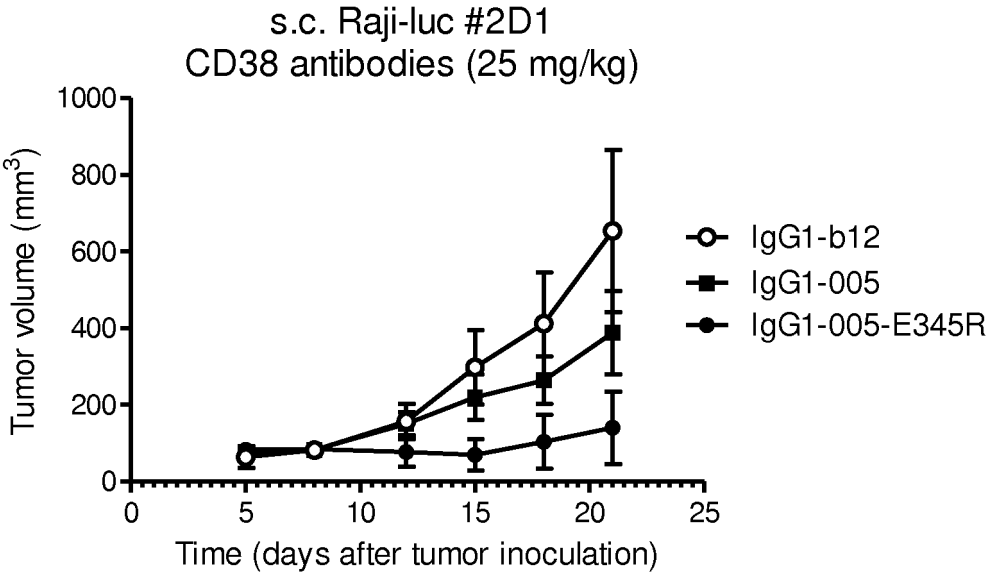


Figure 16B

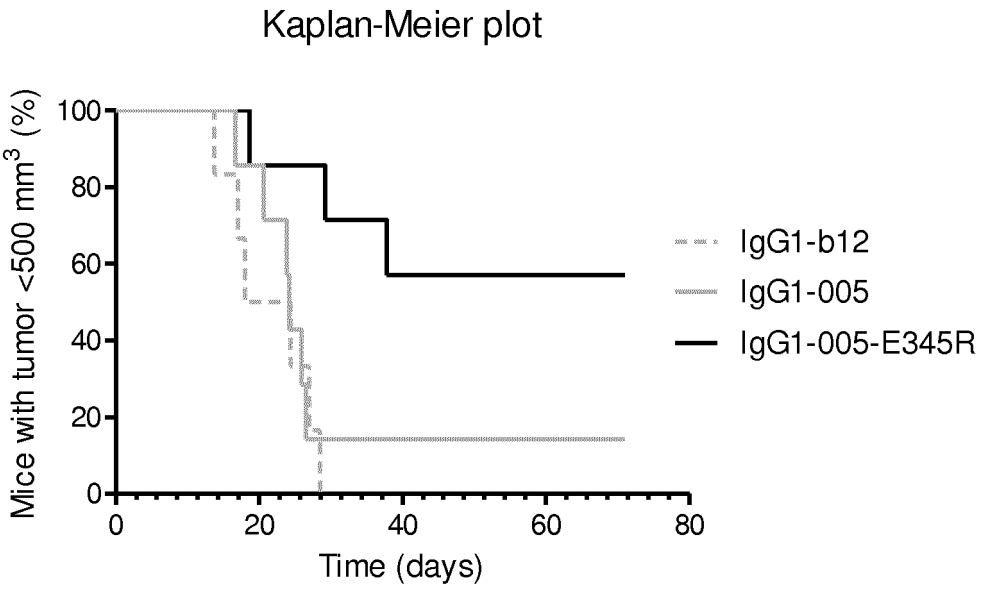


Figure 17

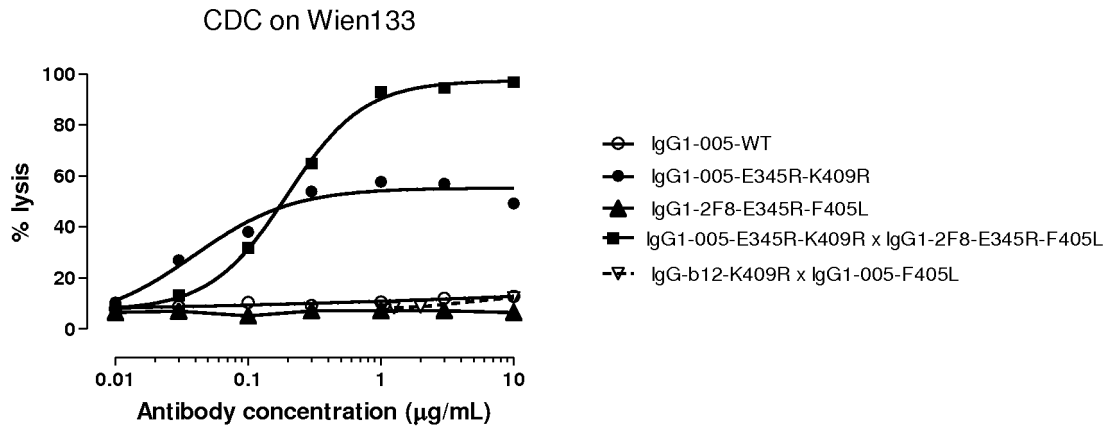

CDC on Wien133
% lysis
100
80
60
40
20
0
0.01
0.1
1
10
Antibody concentration (µg/mL)
IgG1-005-WT
IgG1-005-E345R-K409R
IgG1-2F8-E345R-F405L
IgG1-005-E345R-K409R x IgG1-2F8-E345R-F405L
IgG-b12-K409R x IgG1-005-F405L

Figure 18A

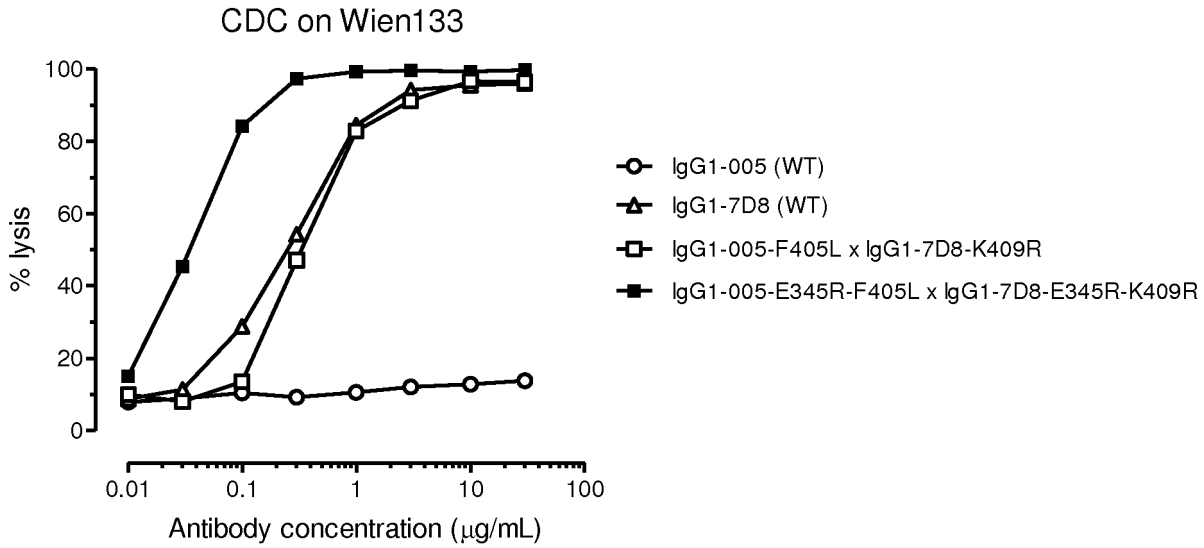


Figure 18B

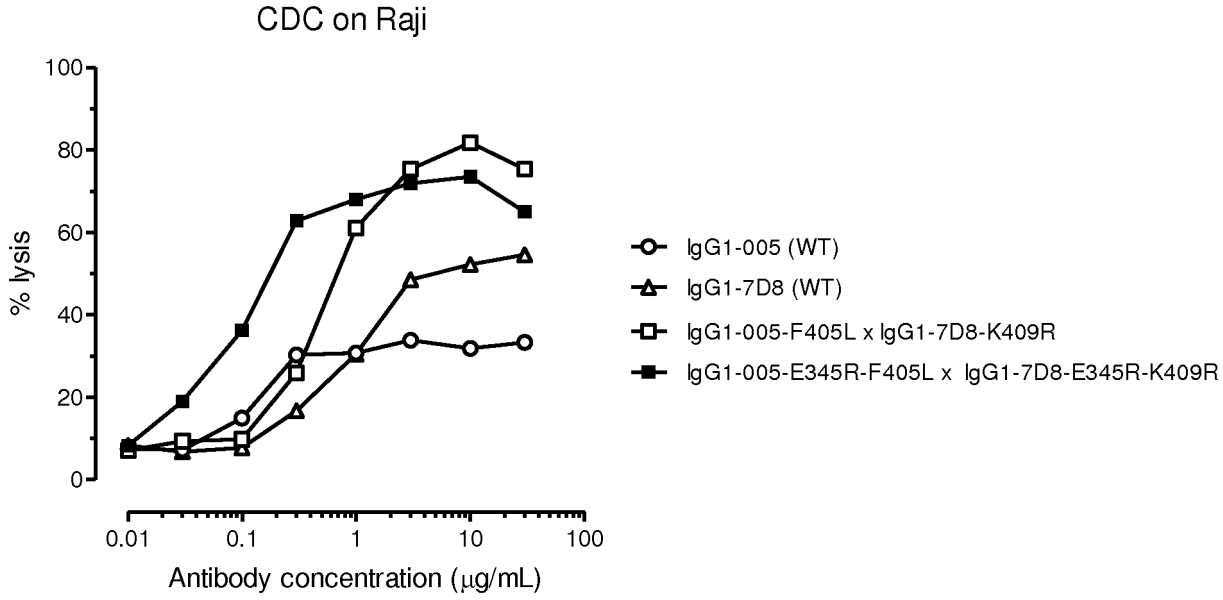


Figure 19

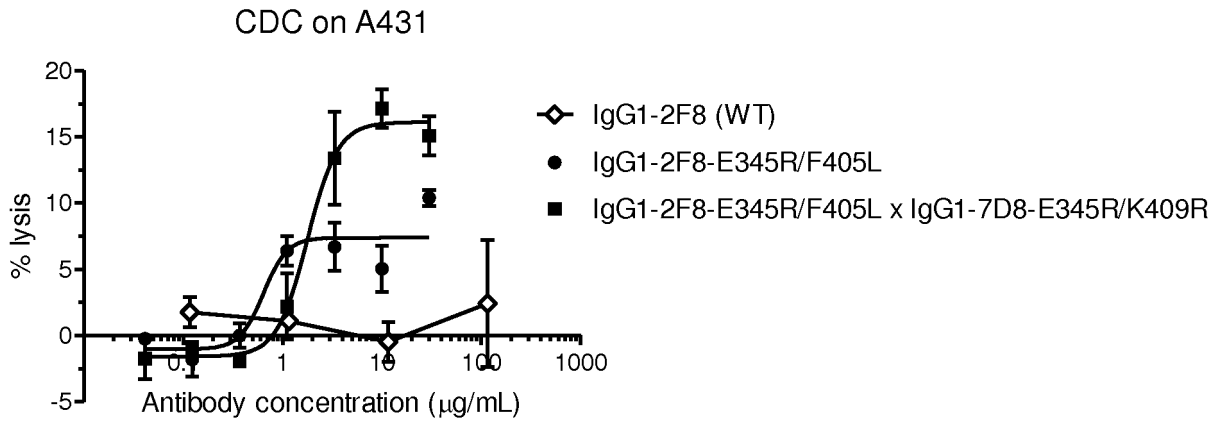

CDC on A431
% lysis
20
15
10
5
0
-5
1
10
100
1000
Antibody concentration (µg/mL)
IgG1-2F8 (WT)
IgG1-2F8-E345R/F405L
IgG1-2F8-E345R/F405L x IgG1-7D8-E345R/K409R

Figure 20

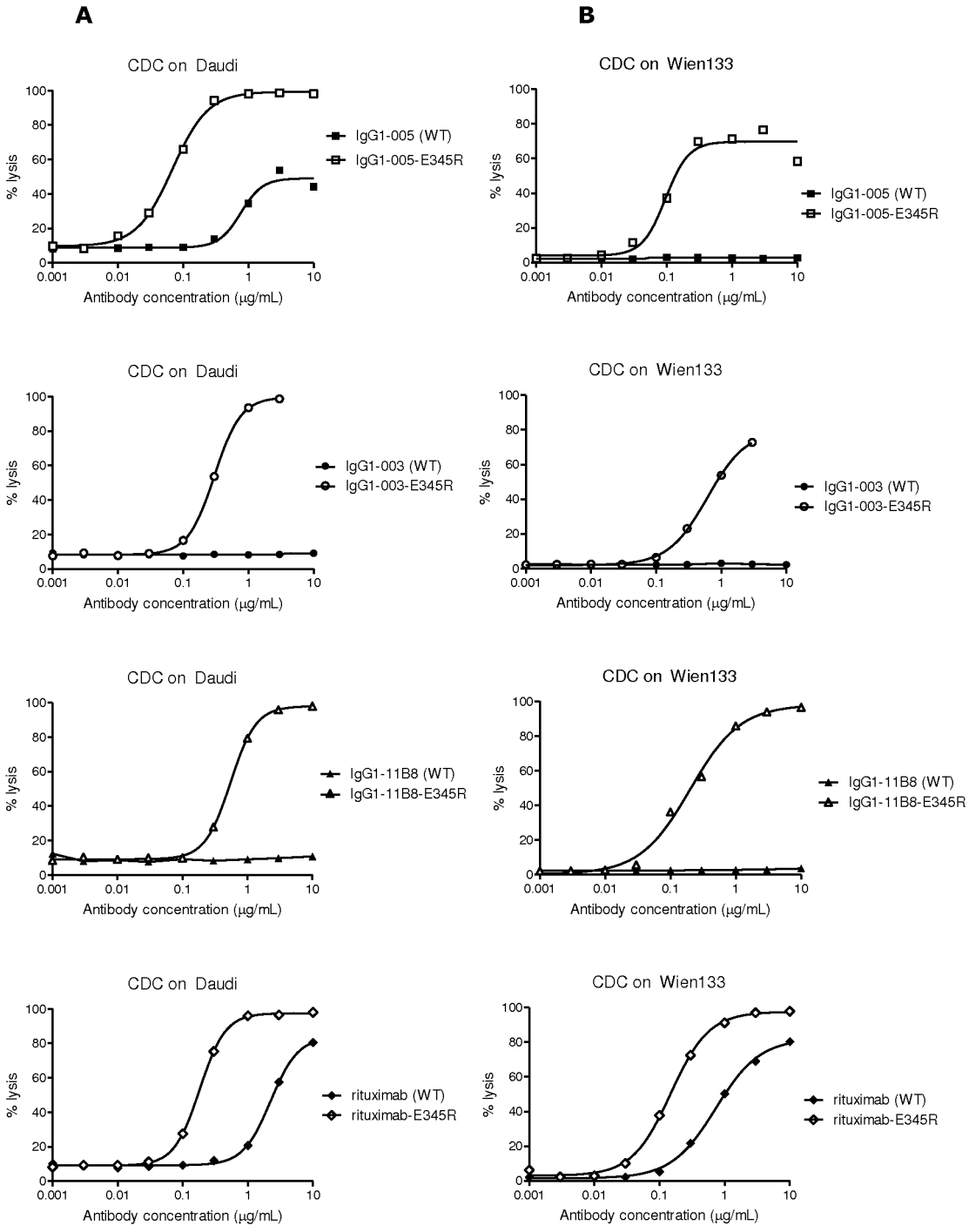

A
B
CDC on Daudi
CDC on Wien133
% lysis
Antibody concentration (µg/mL)
IgG1-005 (WT)
IgG1-005-E345R
IgG1-003 (WT)
IgG1-003-E345R
IgG1-11B8 (WT)
IgG1-11B8-E345R
rituximab (WT)
rituximab-E345R

Figure 21

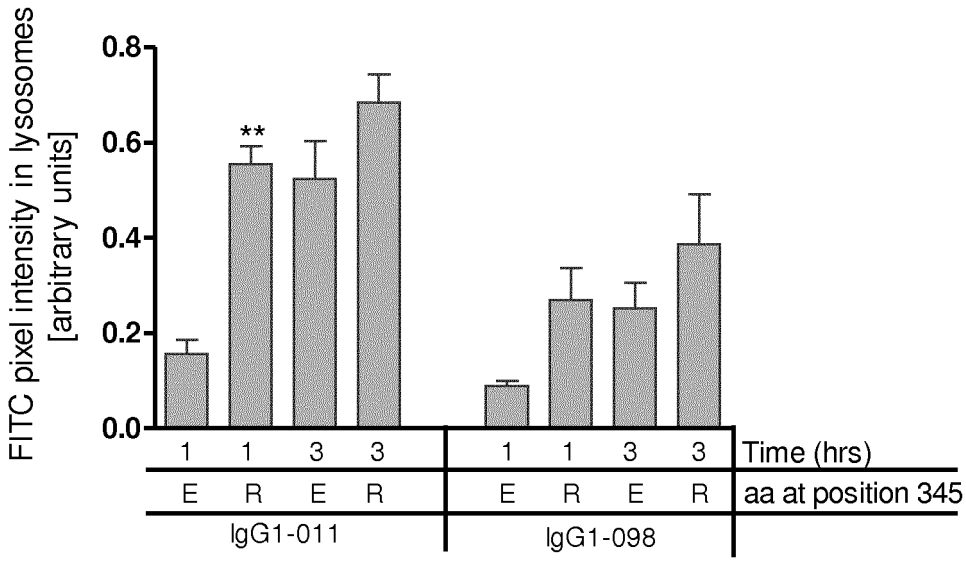


Figure 22A

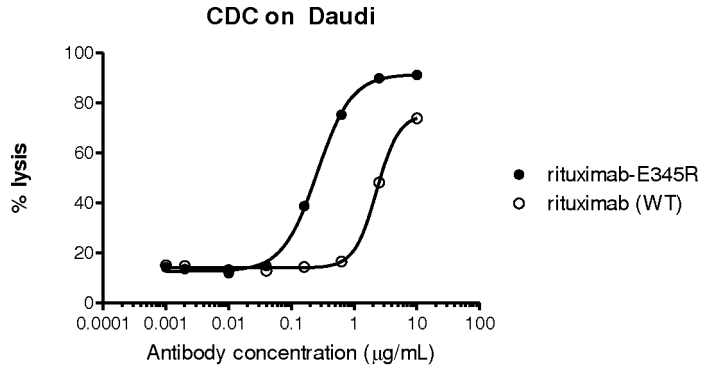


Figure 22B

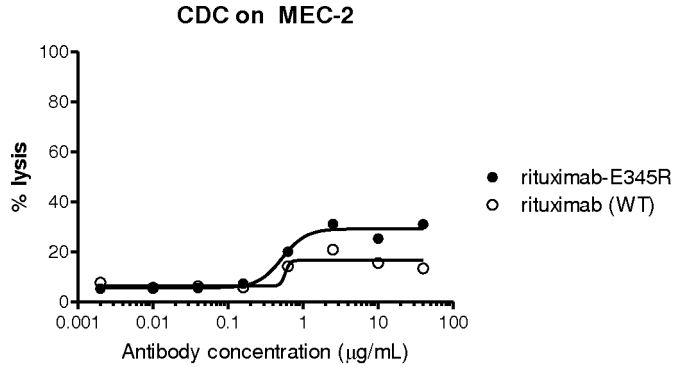


Figure 22C

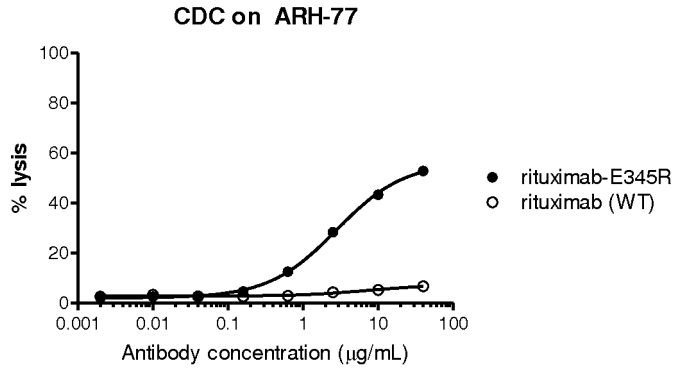


Figure 22D

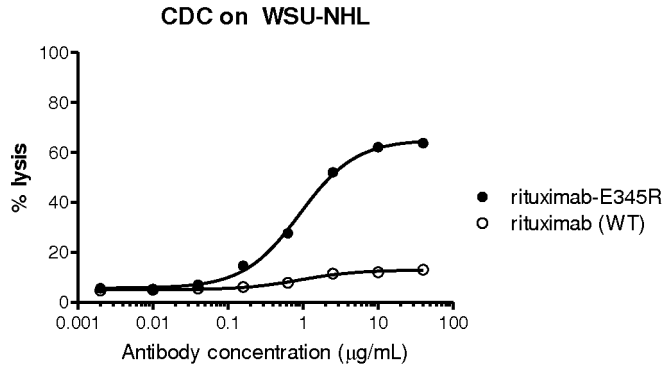


Figure 22E

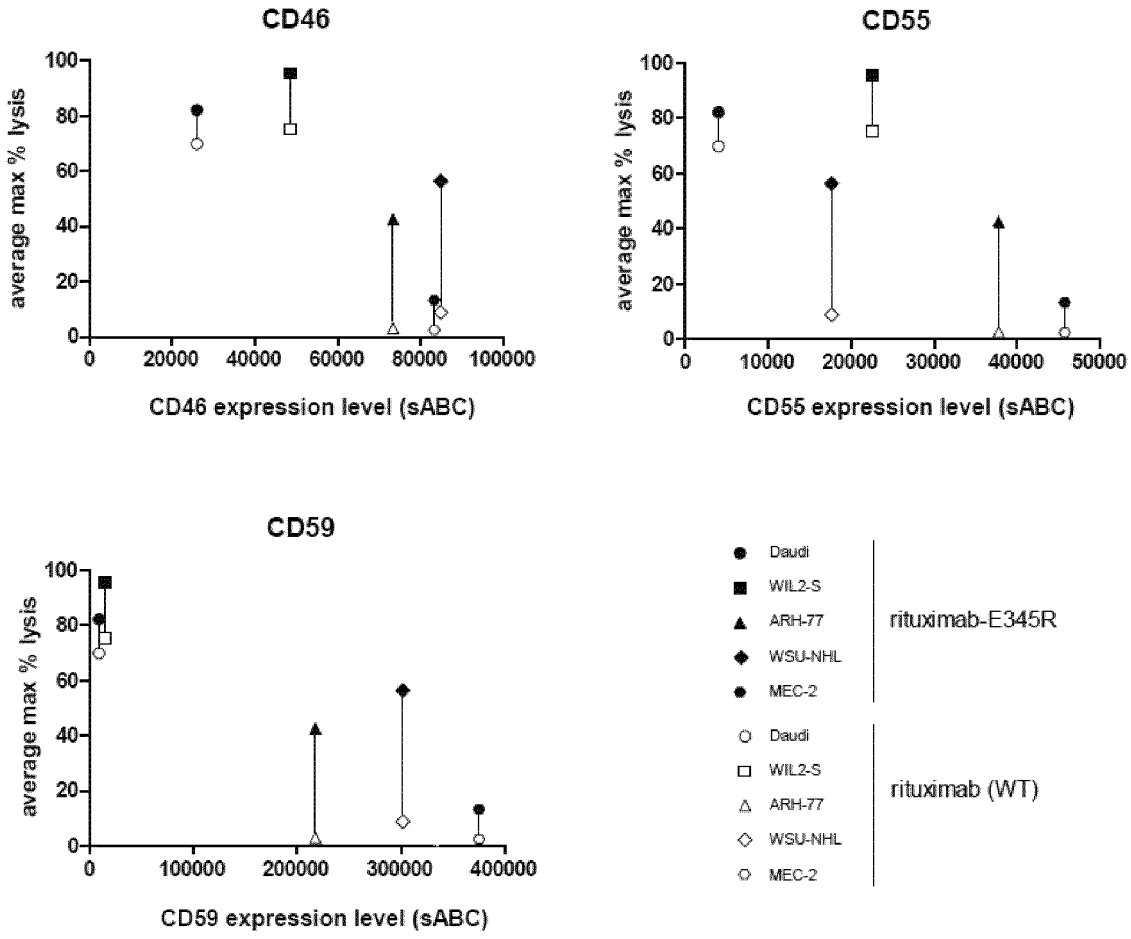
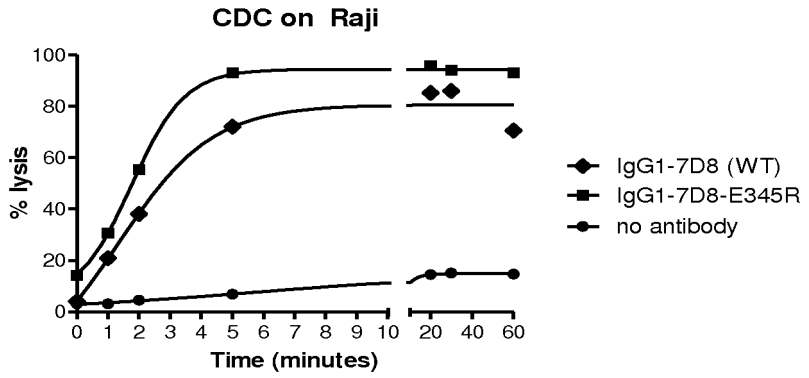
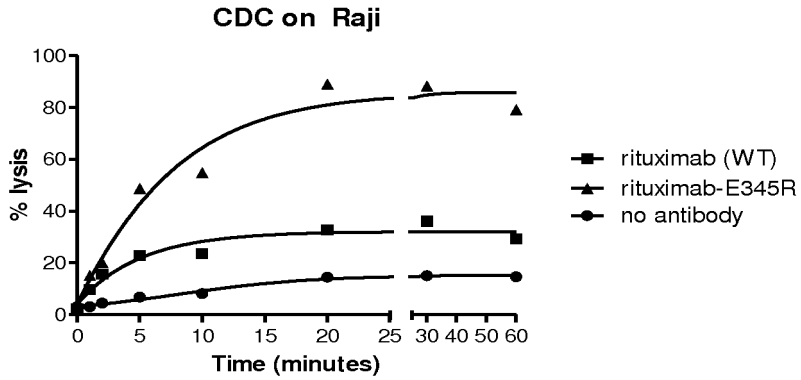

CD46
average max % lysis
100
80
60
40
20
0
0
20000
40000
60000
80000
100000
CD46 expression level (sABC)
CD55
average max % lysis
100
80
60
40
20
0
0
10000
20000
30000
40000
50000
CD55 expression level (sABC)
CD59
average max % lysis
100
80
60
40
20
0
0
100000
200000
300000
400000
CD59 expression level (sABC)
Daudi
WIL2-S
ARH-77
WSU-NHL
MEC-2
rituximab-E345R
Daudi
WIL2-S
ARH-77
WSU-NHL
MEC-2
rituximab (WT)

Figure 23

A



B



C

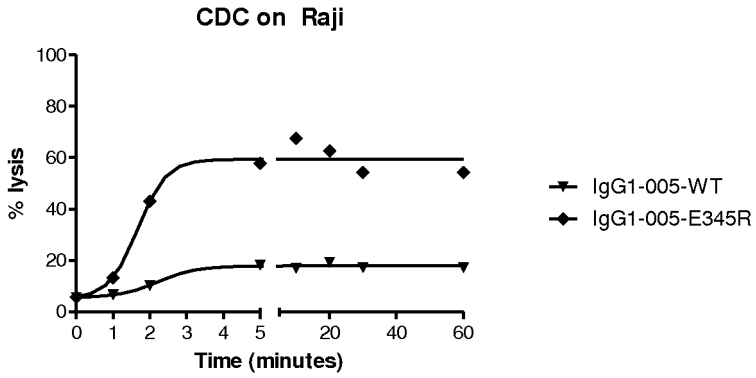


Figure 23 (cont'd)

D

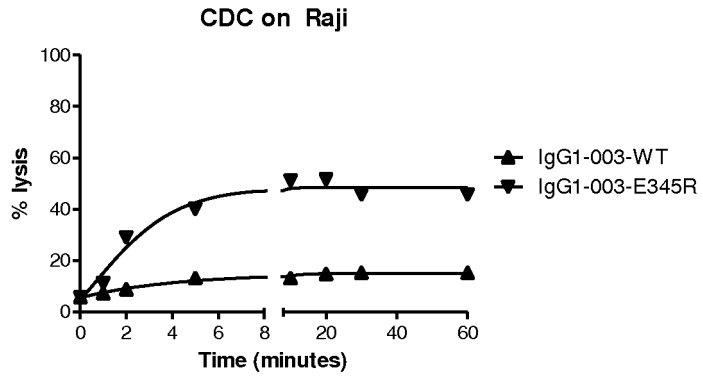


Figure 24

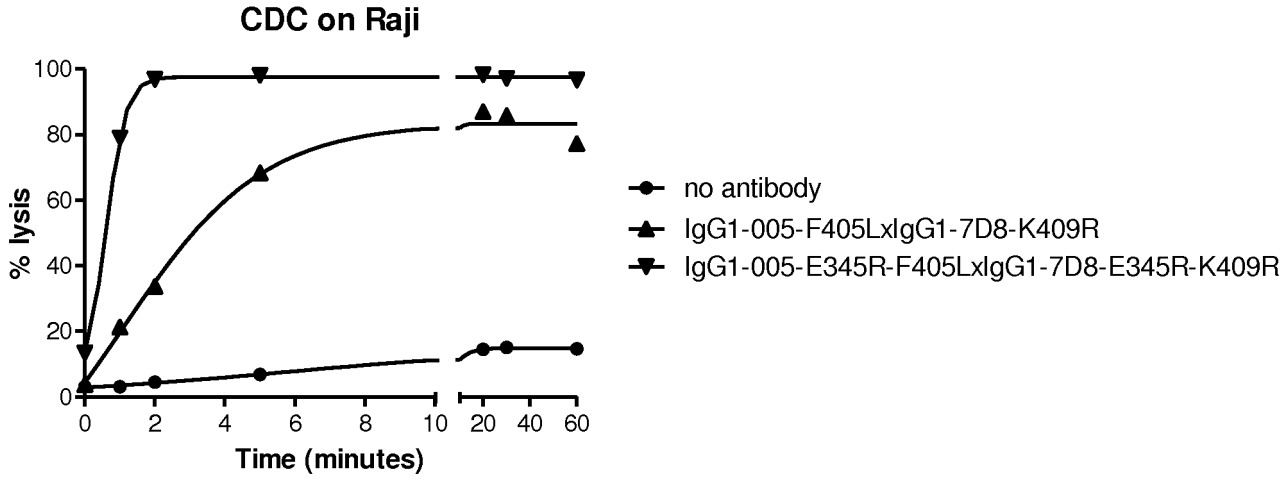


Figure 25

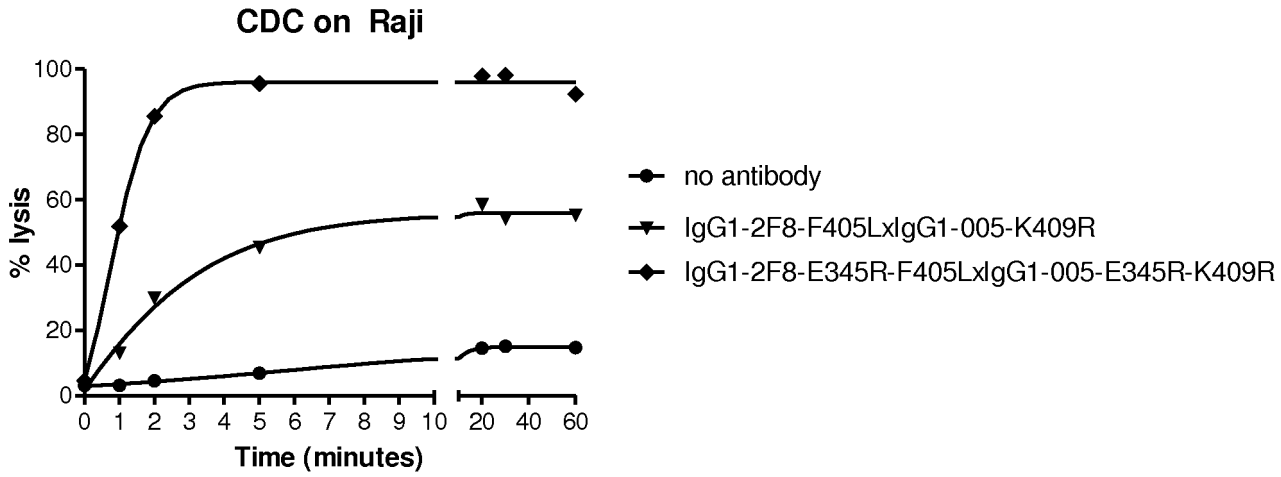

CDC on Raji
% lysis
100
80
60
40
20
0
0 1 2 3 4 5 6 7 8 9 10 20 40 60
Time (minutes)
no antibody
IgG1-2F8-F405LxIgG1-005-K409R
IgG1-2F8-E345R-F405LxIgG1-005-E345R-K409R

Figure 26

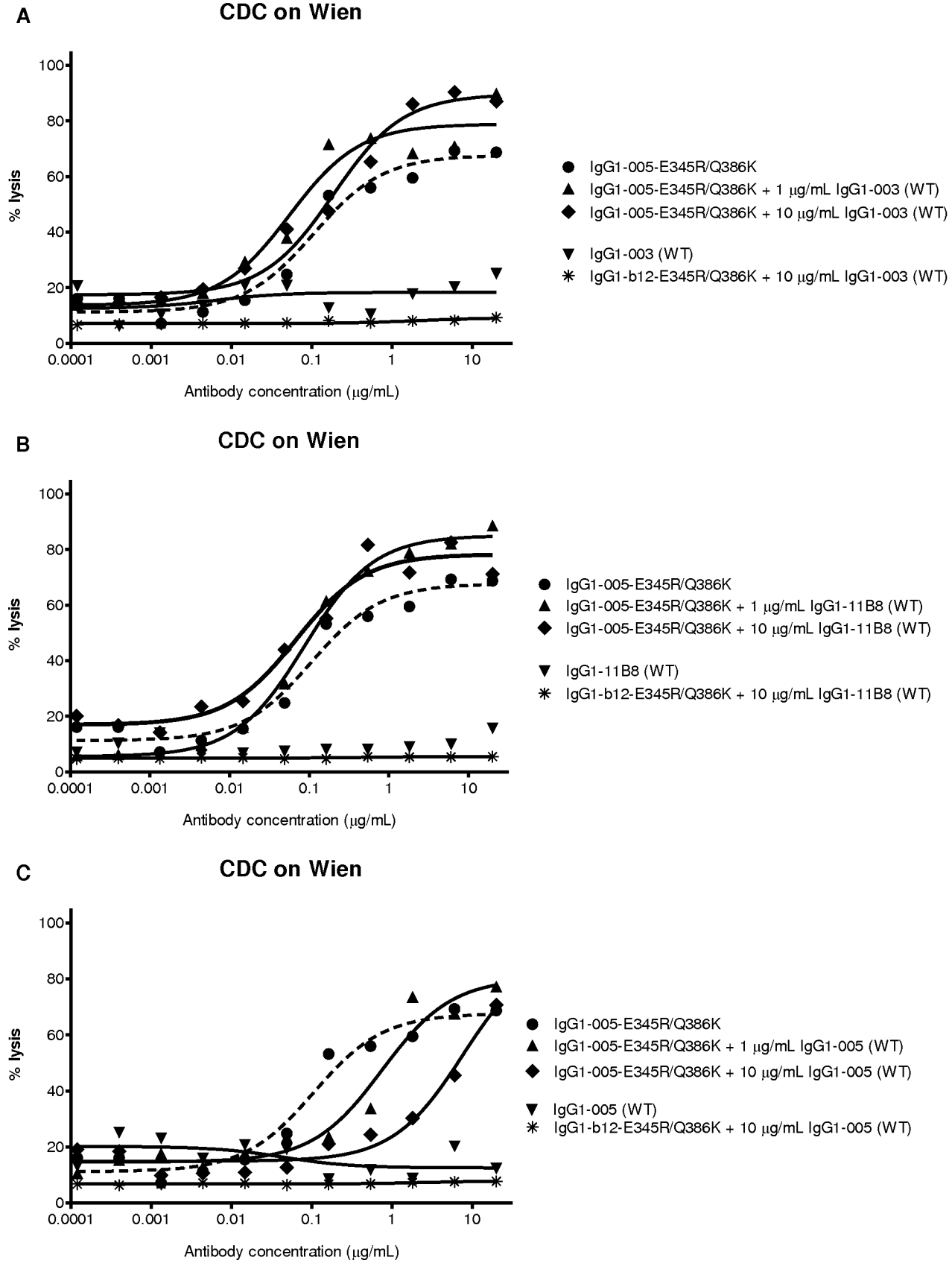

A
CDC on Wien
% lysis
Antibody concentration (µg/mL)
IgG1-005-E345R/Q386K
IgG1-005-E345R/Q386K + 1 µg/mL IgG1-003 (WT)
IgG1-005-E345R/Q386K + 10 µg/mL IgG1-003 (WT)
IgG1-003 (WT)
IgG1-b12-E345R/Q386K + 10 µg/mL IgG1-003 (WT)
B
CDC on Wien
% lysis
Antibody concentration (µg/mL)
IgG1-005-E345R/Q386K
IgG1-005-E345R/Q386K + 1 µg/mL IgG1-11B8 (WT)
IgG1-005-E345R/Q386K + 10 µg/mL IgG1-11B8 (WT)
IgG1-11B8 (WT)
IgG1-b12-E345R/Q386K + 10 µg/mL IgG1-11B8 (WT)
C
CDC on Wien
% lysis
Antibody concentration (µg/mL)
IgG1-005-E345R/Q386K
IgG1-005-E345R/Q386K + 1 µg/mL IgG1-005 (WT)
IgG1-005-E345R/Q386K + 10 µg/mL IgG1-005 (WT)
IgG1-005 (WT)
IgG1-b12-E345R/Q386K + 10 µg/mL IgG1-005 (WT)

Figure 26 (cont'd)

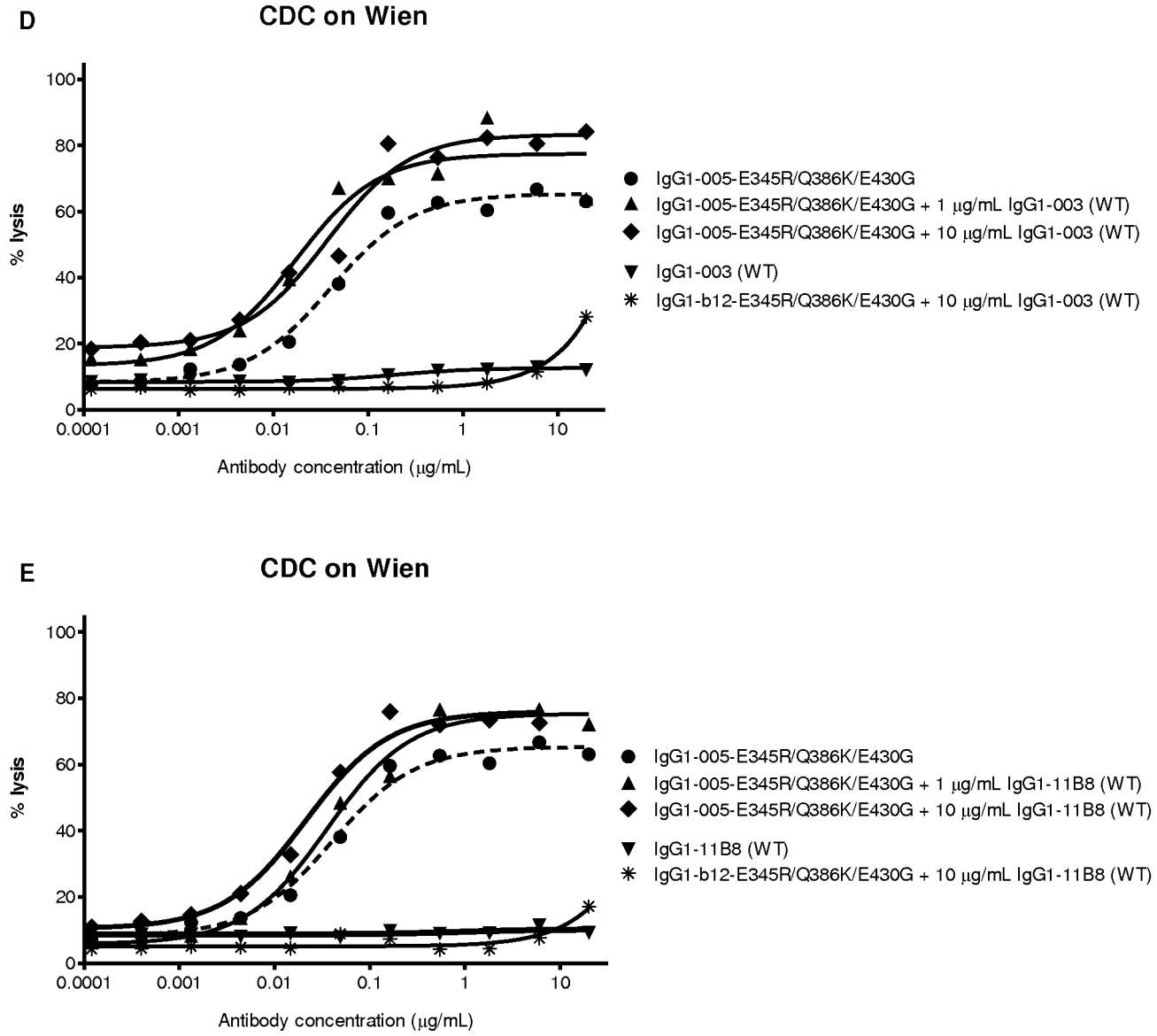


Figure 26 (cont'd)

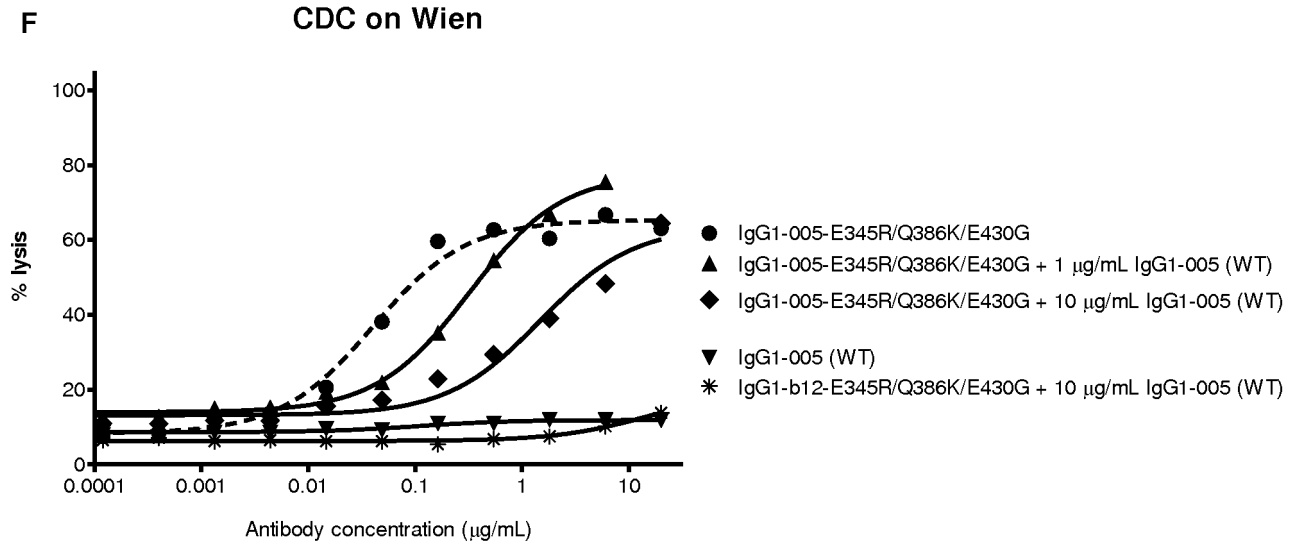


Figure 27

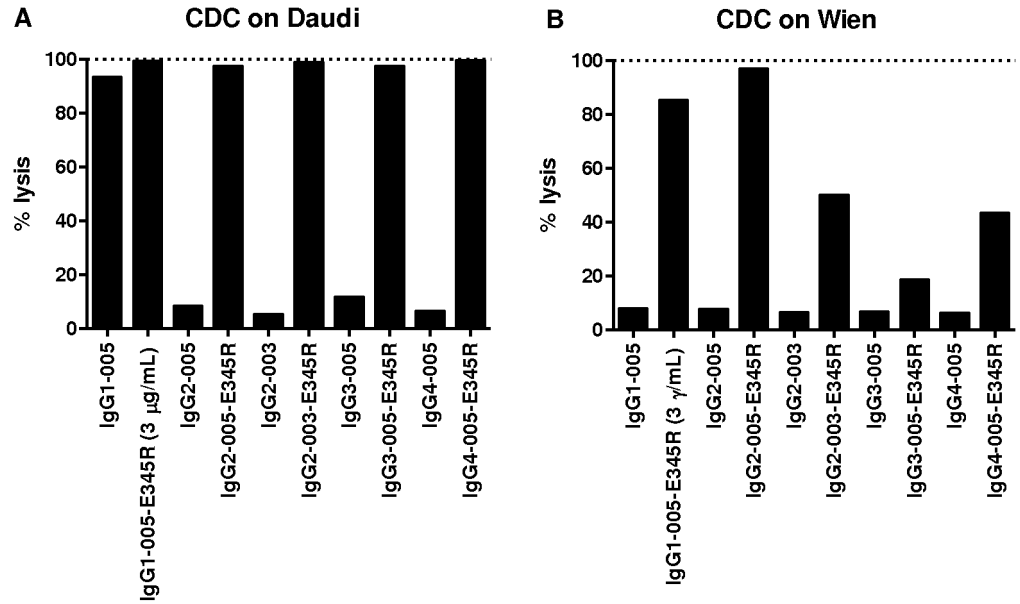


Figure 28

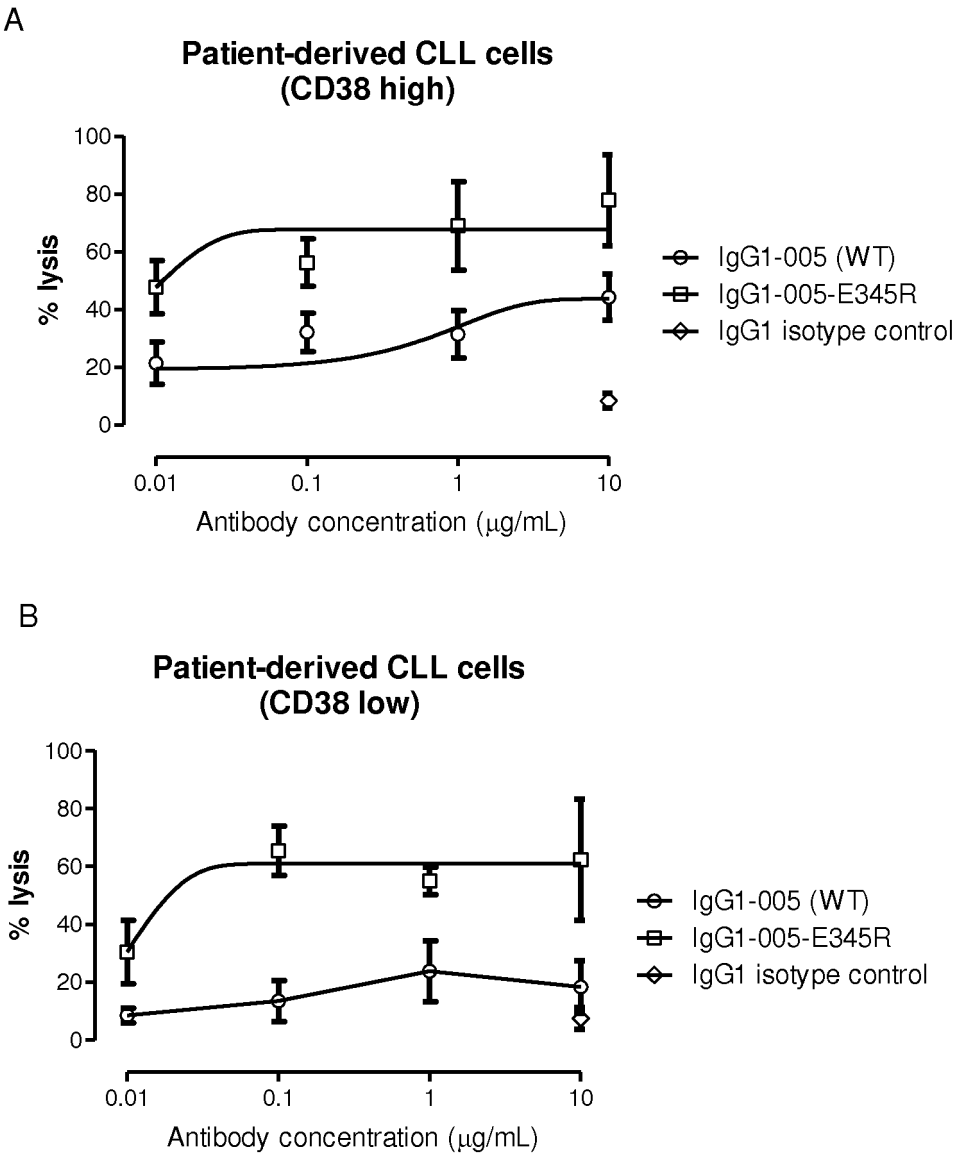
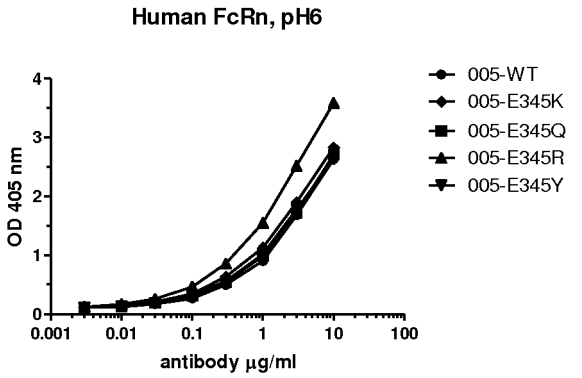
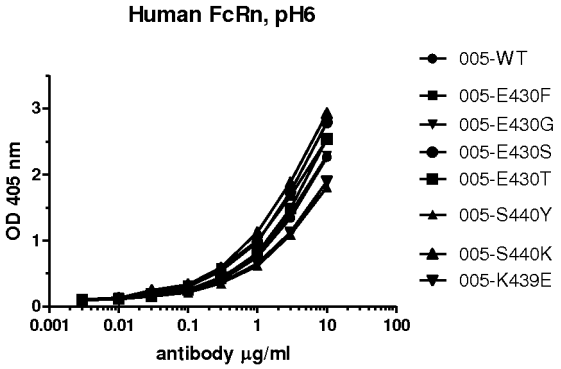
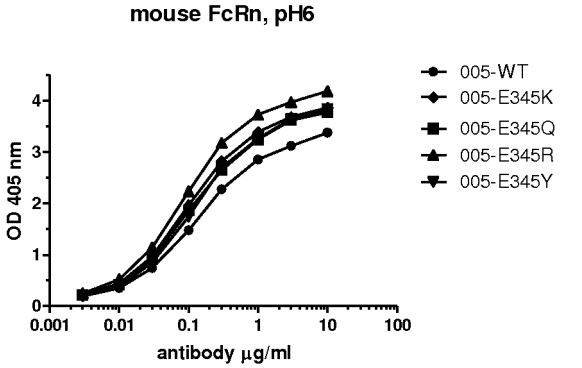
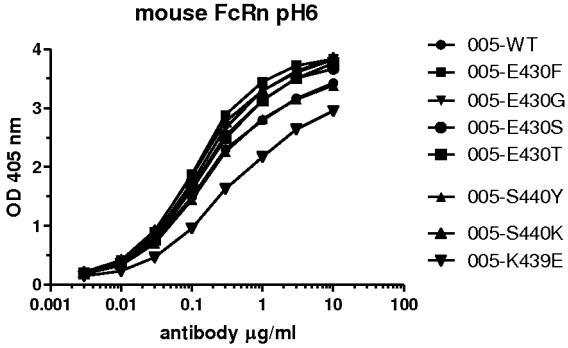

A
Patient-derived CLL cells
(CD38 high)
% lysis
100
80
60
40
20
0
0.01
0.1
1
10
Antibody concentration (µg/mL)
IgG1-005 (WT)
IgG1-005-E345R
IgG1 isotype control
B
Patient-derived CLL cells
(CD38 low)
% lysis
100
80
60
40
20
0
0.01
0.1
1
10
Antibody concentration (µg/mL)
IgG1-005 (WT)
IgG1-005-E345R
IgG1 isotype control

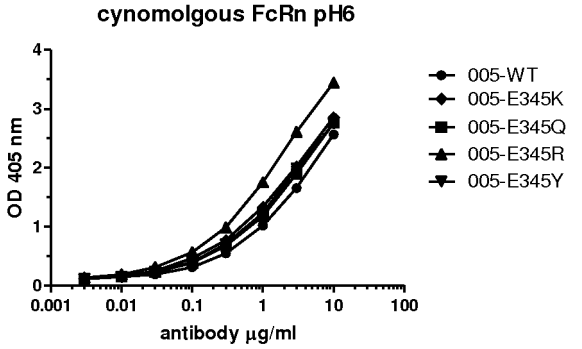
Figure 29


Human FcRn, pH6
OD 405 nm
antibody µg/ml
005-WT
005-E345K
005-E345Q
005-E345R
005-E345Y


Human FcRn, pH6
OD 405 nm
antibody µg/ml
005-WT
005-E430F
005-E430G
005-E430S
005-E430T
005-S440Y
005-S440K
005-K439E


mouse FcRn, pH6
OD 405 nm
antibody µg/ml
005-WT
005-E345K
005-E345Q
005-E345R
005-E345Y


mouse FcRn pH6
OD 405 nm
antibody µg/ml
005-WT
005-E430F
005-E430G
005-E430S
005-E430T
005-S440Y
005-S440K
005-K439E


cynomolgous FcRn pH6
OD 405 nm
antibody µg/ml
005-WT
005-E345K
005-E345Q
005-E345R
005-E345Y

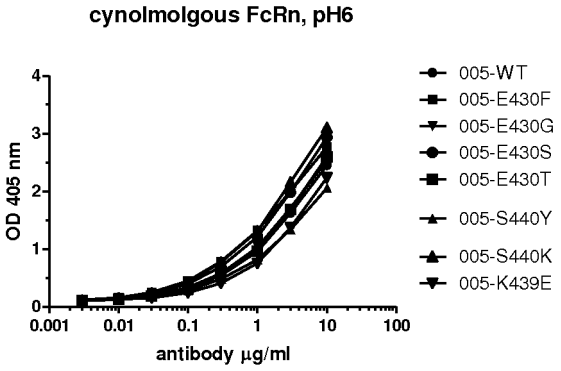

cynolmolgous FcRn, pH6
OD 405 nm
antibody µg/ml
005-WT
005-E430F
005-E430G
005-E430S
005-E430T
005-S440Y
005-S440K
005-K439E

Figure 30

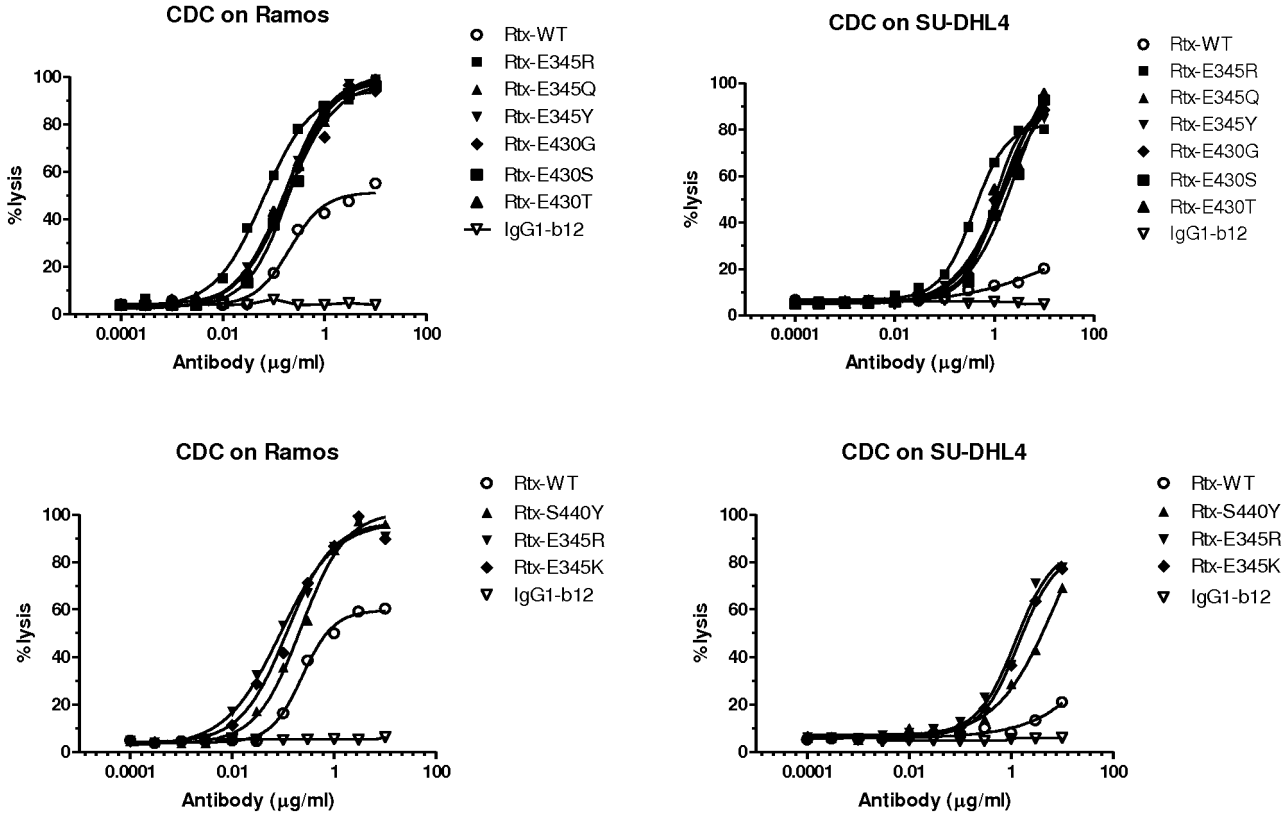


Figure 31

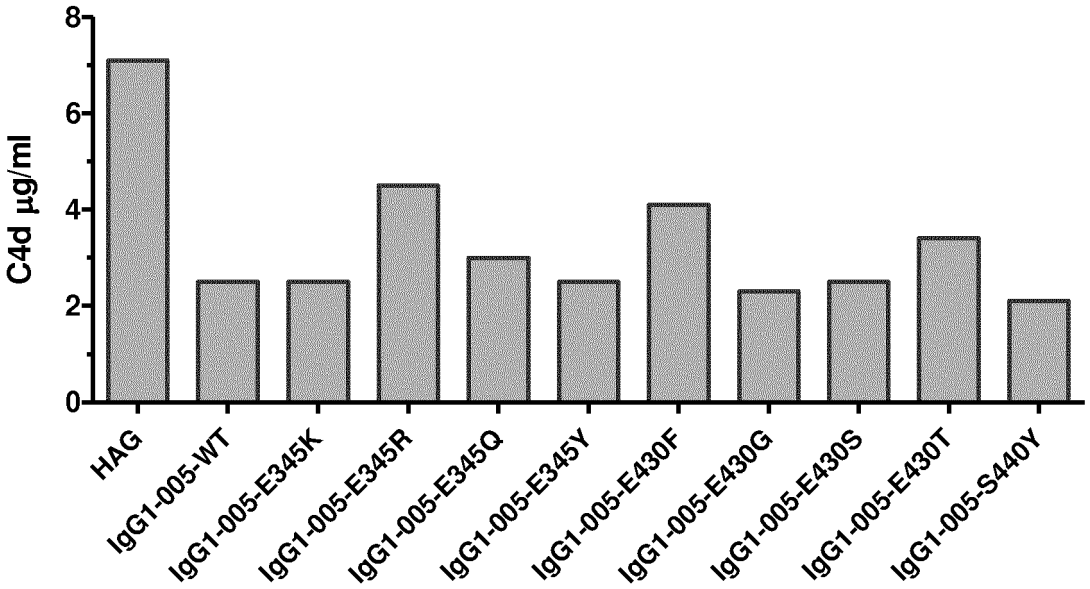


Figure 32A

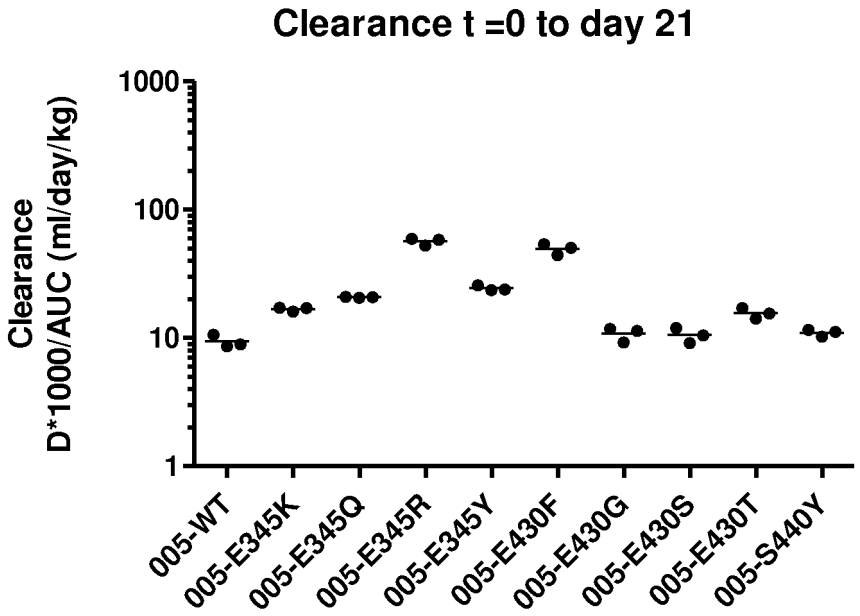


Figure 32B

