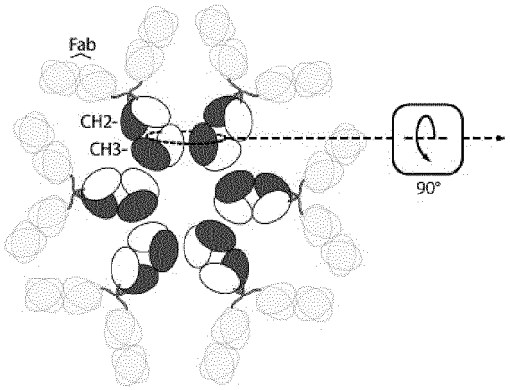
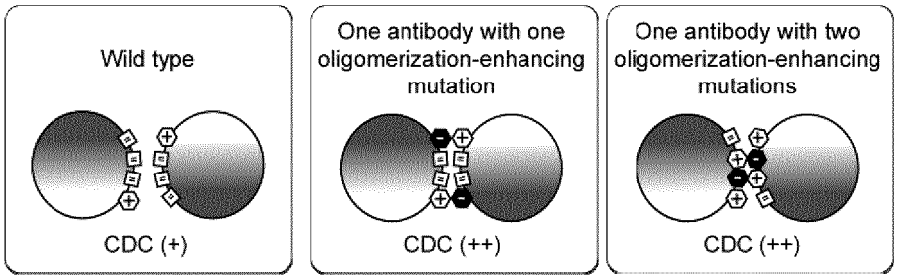
Figure 1

A) IgG molecules in hexamer formation



B) Observed effect of oligomerization-enhancing mutations on CDC



C) Observed effect of oligomerization-inhibiting mutations on CDC

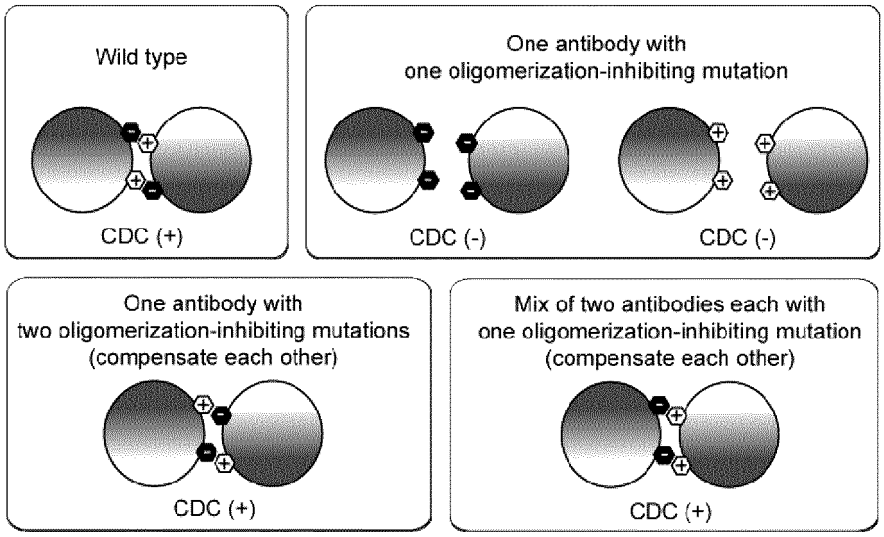


Figure 1D

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

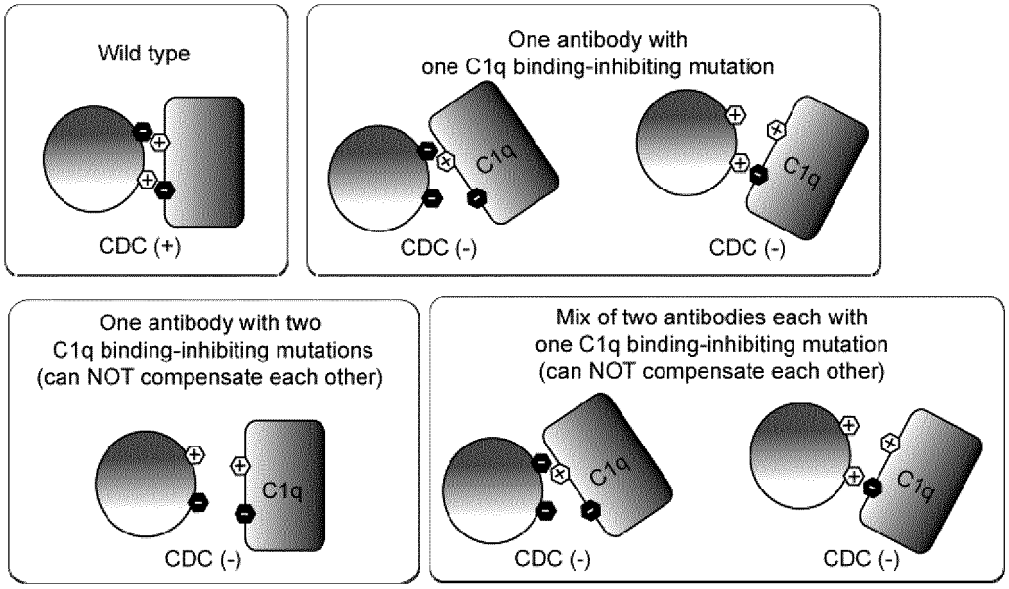


Figure 2

```
IgG1  247 PKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVL 306
IgG1f 247 PKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVL 306
IgG2  247 PKDTLMISRTPEVTCVVVDVSHEDPEVQFNWYVDGVEVHNAKTKPREEQFNSTFRVVSVL 306
IgG3  247 PKDTLMISRTPEVTCVVVDVSHEDPEVQFKWYVDGVEVHNAKTKPREEQYNSTFRVVSVL 306
hgG4  247 PKDTLMISRTPEVTCVVVDVSQEDPEVQFNWYVDGVEVHNAKTKPREEQFNSTYRVVSVL 306
          **********************:*****:*:******************:***:******

IgG1  307 TVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSRDELTKNQVSLT 366
IgG1f 307 TVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLT 366
IgG2  307 TVVHQDWLNGKEYKCKVSNKGLPAPIEKTISKTKGQPREPQVYTLPPSREEMTKNQVSLT 366
IgG3  307 TVLHQDWLNGKEYKCKVSNKALPAPIEKTISKTKGQPREPQVYTLPPSREEMTKNQVSLT 366
hgG4  307 TVLHQDWLNGKEYKCKVSNKGLPSSIEKTISKAKGQPREPQVYTLPPSQEEMTKNQVSLT 366
          **:*****************.**:.*******:***************::*:********

IgG1  367 CLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCS 426
IgG1f 367 CLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCS 426
IgG2  367 CLVKGFYPSDIAVEWESNGQPENNYKTTPPMLDSDGSFFLYSKLTVDKSRWQQGNVFSCS 426
IgG3  367 CLVKGFYPSDIAVEWESSGQPENNYNTTPPMLDSDGSFFLYSKLTVDKSRWQQGNIFSCS 426
hgG4  367 CLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSRLTVDKSRWQEGNVFSCS 426
          *****************.*******:****:***********:*********:**:****

IgG1  427 VMHEALHNHYTQKSLSLSPGK 447
IgG1f 427 VMHEALHNHYTQKSLSLSPGK 447
IgG2  427 VMHEALHNHYTQKSLSLSPGK 447
IgG3  427 VMHEALHNRFTQKSLSLSPGK 447
hgG4  427 VMHEALHNHYTQKSLSLSLGK 447
          ********::******** **
```

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

Figure 3A

```
EU                                                                                                               1
                 1         2         3           4         5           6         7         8         9         0
        12345678901234567890123456789012345  678901234567890123  45678901234567890123456789012345678901234567890           12
2F8-G1   VQLVESGGGVVQPGRSLRLSCAASGFTFSTYGMH--WVRQAPGKGLEWVAVIWD--DGSYKYYGDSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCARDGITMVRGVMKDYFDY
2F8-G4   VQLVESGGGVVQPGRSLRLSCAASGFTFSTYGMH--WVRQAPGKGLEWVAVIWD--DGSYKYYGDSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCARDGITMVRGVMKDYFDY
KABAT                                                                                                                1
                 1         2         3           4         5            6         7         8            9         0
        123456789012345678901234567890123455567890123456789012222345678901234567890123456789012222345678901234567890000000012
                                           AB                  ABC                                ABC                 ABCDEFGH

EU      1      1          1         1           1         1              1          1          1         1           2
        0      1          2         3           4         5              6          7          8         9           0
        345678901234567  89012345678901234  5678901234567890123456 78     90123456 7890123456 7890123456789012345  6 7890
2F8-G1  WGQGTLVTVSS-----ASTKGPSVFPLAPSSKS--TSGGTAALGCLVKDYFPEPVTV-SW----NSGALTSG-VHTFPAVLQS-SGLYSLSSVVTVPSSSLGT--Q-TYIC
2F8-G4  WGQGTLVTVSS-----ASTKGPSVFPLAPCSRS--TSESTAALGCLVKDYFPEPVTV-SW----NSGALTSG-VHTFPAVLQS-SGLYSLSSVVTVPSSSLGT--K-TYTC
KABAT   1      1              1         1         1         1         1         1         1         1         2
        0      1              2         3         4         5         6         7         8         9         0
        34567890123333333456789012345678901234567890123456789012345678901234567890123456789012345678901234567890123456789012345678
                  ABCDE

EU      2        2               2                                                                 2                      2         2
        0        1               2                                                                 3                      4         5
        12345678901 234      567890 1  2345678                                                    90         12   345678   901234567890
2F8-G1  NVNHKPSNTKV-DKR-----VEPKSC-D--KTHTCPP-------------------------------------------CP---------AP---ELLGGP--SVFLFPPKPKDT
2F8-G3  NVNHKPSNTKV-DKR-----VELKTP-LGDTTHTCPRCPEPKSCDTPPPCPRCPEPKSCDTPPPCPRCPEPKSCDTPPPCPRCP---------AP---ELLGGP--SVFLFPPKPKDT
2F8-G4  NVDHKPSNTKV-DKR-----VESKYG------PPCPS-------------------------------------------CP---------AP---EFLGGP--SVFLFPPKPKDT
KABAT   22          2            2          2                                                                    2           2
        01          2            3          4                                                                    5           6
        90123456789901233333456789012345678901111111111111111111111111111111111111111111112333333333334555567890111234567890123
                   A    ABC                    ABCDEFGHIJKLMNOPQRSTUVWXYZABCDEFGHIJKLMNOPQRS  ABCDEFGHI  ABC       AB
                                                                          ABCDEFGHIJKLMNOPQRS

EU      2        2         2           2           2          3
        5        6         7           8           9          0
        12345678901234567890123456789  01  2345678901234567  890
2F8-G1  LMISRTPEVTCVVVDVSHEDPEVKFNWYV--DG--VEVHNAKTKPREEQYN--STY
2F8-G4  LMISRTPEVTCVVVDVSQEDPEVQFNWYV--DG--VEVHNAKTKPREEQFN--STY
KABAT   2     2         2         2         3         3
        6     7         8         9         0         1
        4567890123456789012345678901234567890123456789012345678 9
```

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
            123456789012345678901234567890123456789012345678901234567890123456789  01234 56  789012345678901
2F8-G1      RVVSVLTVLHQDWLNGKEYKCKVSNKALPAPI-EKTI-SKAKG-QPREPQVYTLPPSRDE--LTKNQVSLTCLVKGFYPSDIAV--EWESN-GQ--PENNYKTTPPVLDS
2F8-G4      RVVSVLTVLHQDWLNGKEYKCKVSNKGLPSSI-EKTI-SKAKG-QPREPQVYTLPPSQEE--MTKNQVSLTCLVKGFYPSDIAV--EWESN-GQ--PENNYRTTPPVLDS
KABAT       3       3       3       3       3       3       3       3       4       4       4
            2       3       4       5       6       7       8       9       0       1       2
            012345678901234567890112345678901234567890123456789012345678901234567890123456789012345678
                                                  A
EU          4       4       4       4       4       4
            0       1       2       3       4
            1  2345678901234567890123456789012345678901234567890123456
2F8-G1      -D--GSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK
2F8-G4      -D--GSFFLYSRLTVDKSRWQEGNVFSCSVMHEALHNHYTQKSLSLSLGK
KABAT       4       4       4       4       4       4
            3       4       5       6       7
            901234567890123456789012345678901234567890123456789012345678
```

Figure 4

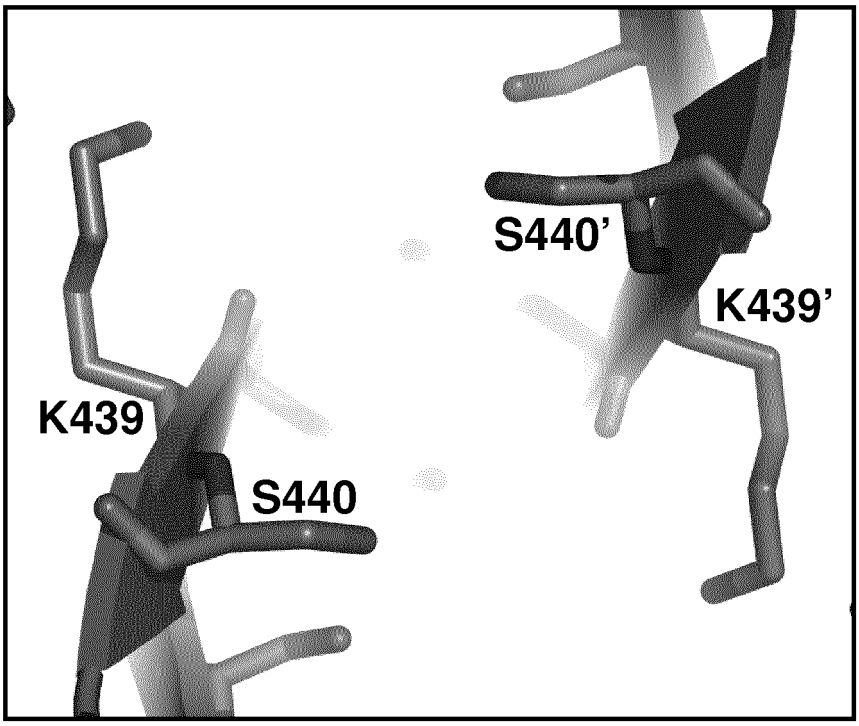


Figure 5

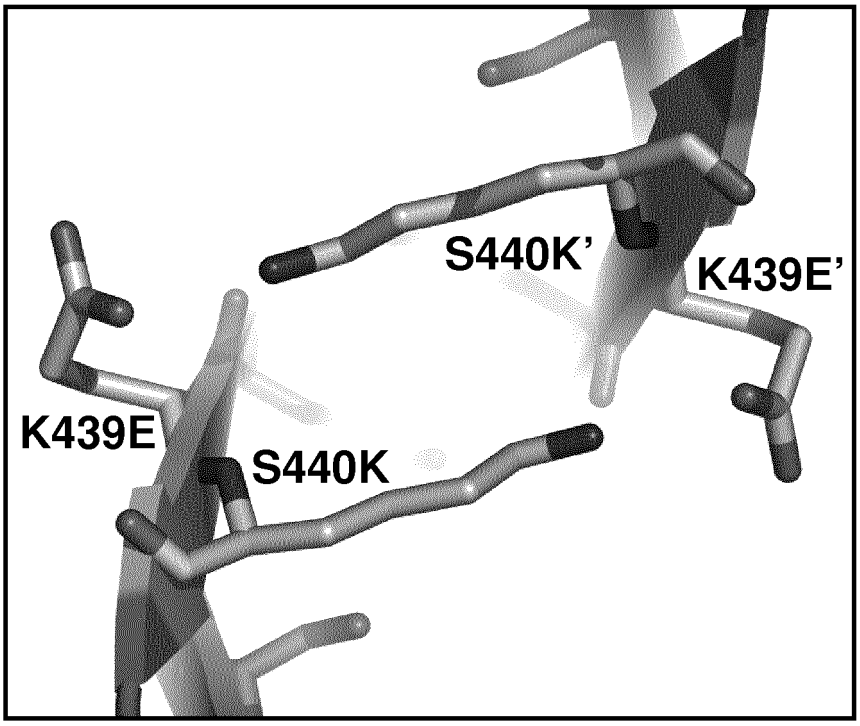


Figure 6

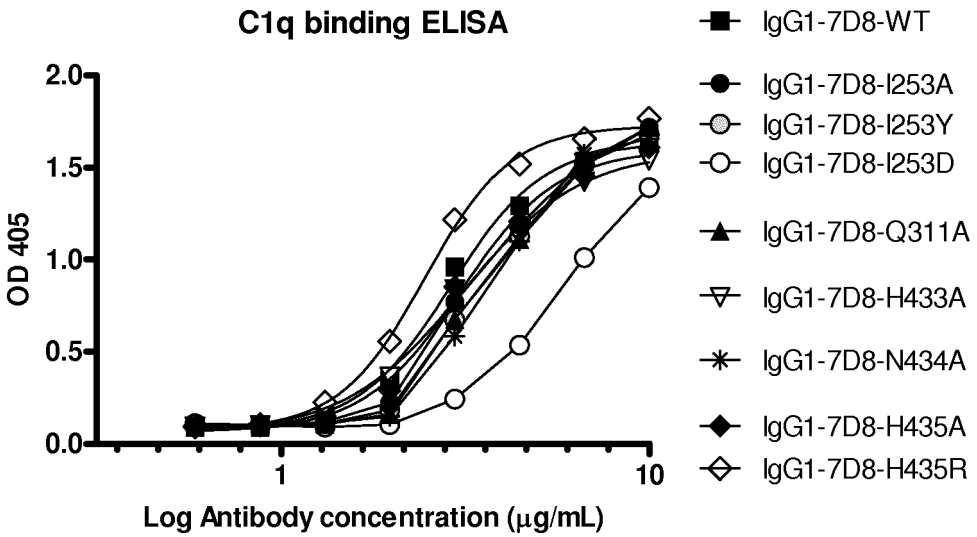


Figure 7

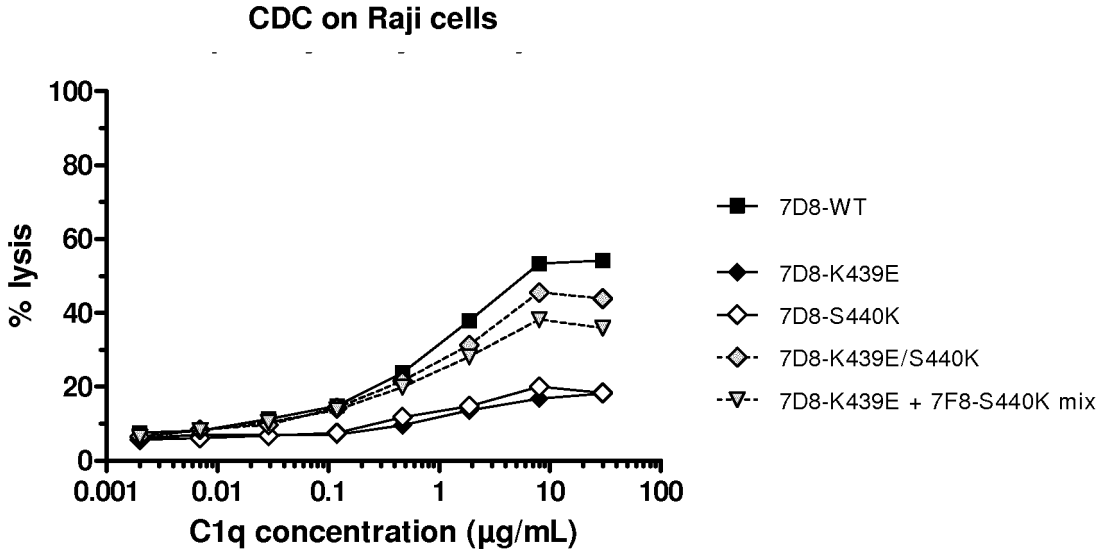


Figure 8

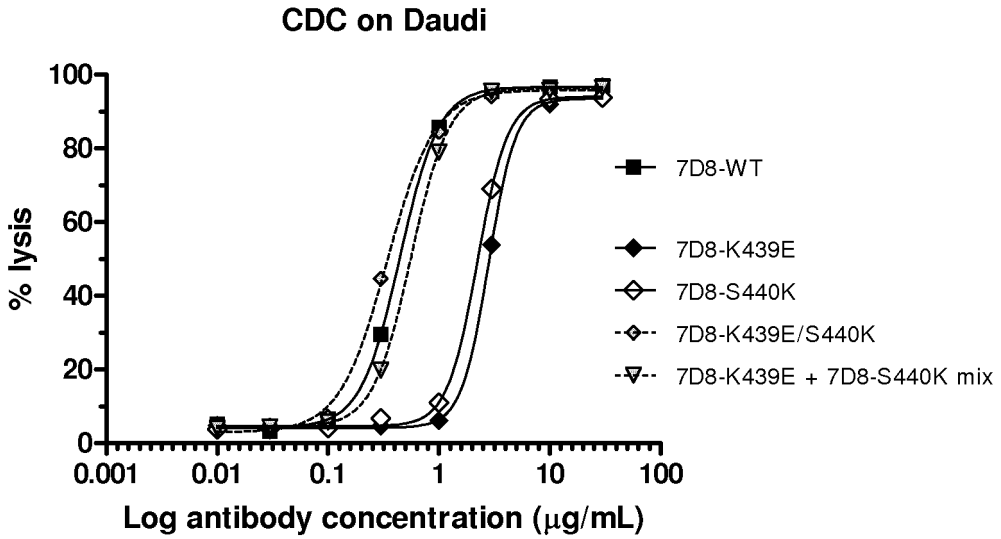

CDC on Daudi
% lysis
100
80
60
40
20
0
0.001
0.01
0.1
1
10
100
Log antibody concentration (μg/mL)
7D8-WT
7D8-K439E
7D8-S440K
7D8-K439E/S440K
7D8-K439E + 7D8-S440K mix

Figure 9A

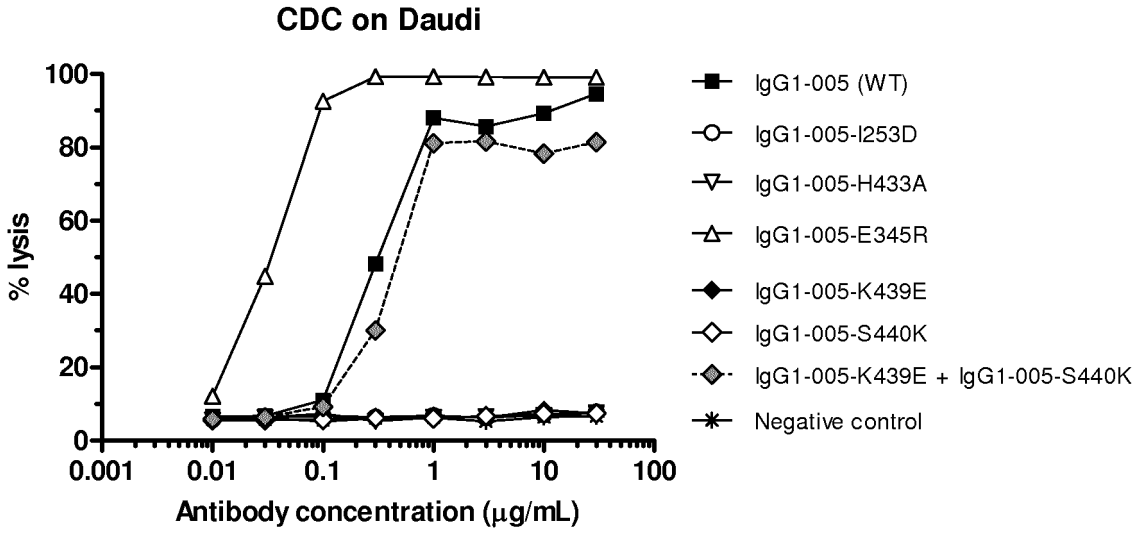


Figure 9B

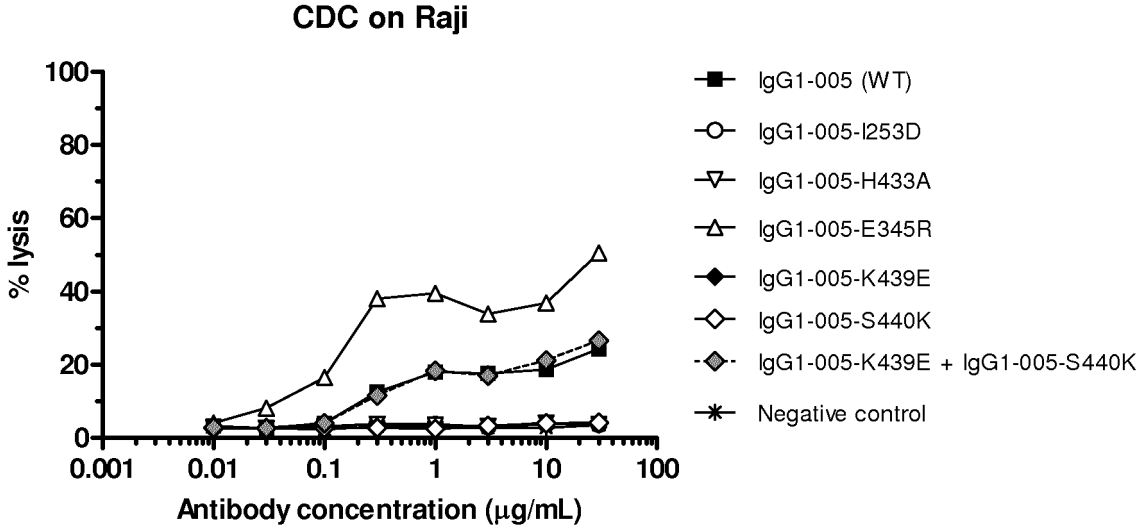


Figure 9C

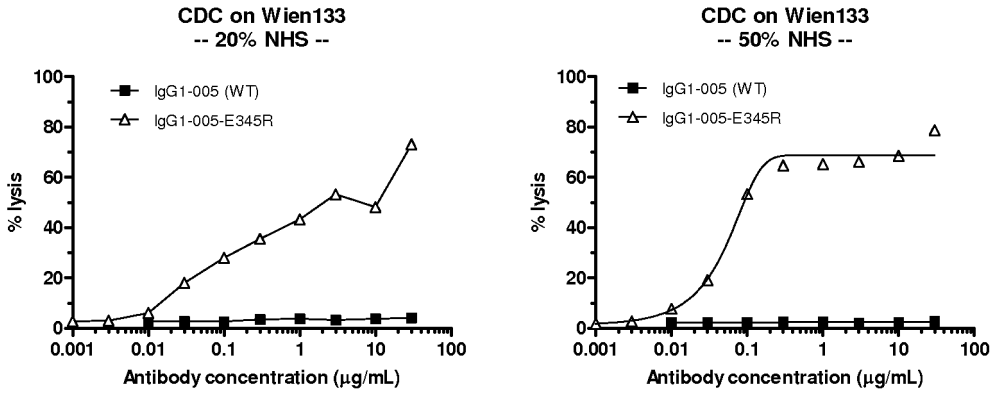


Figure 9D

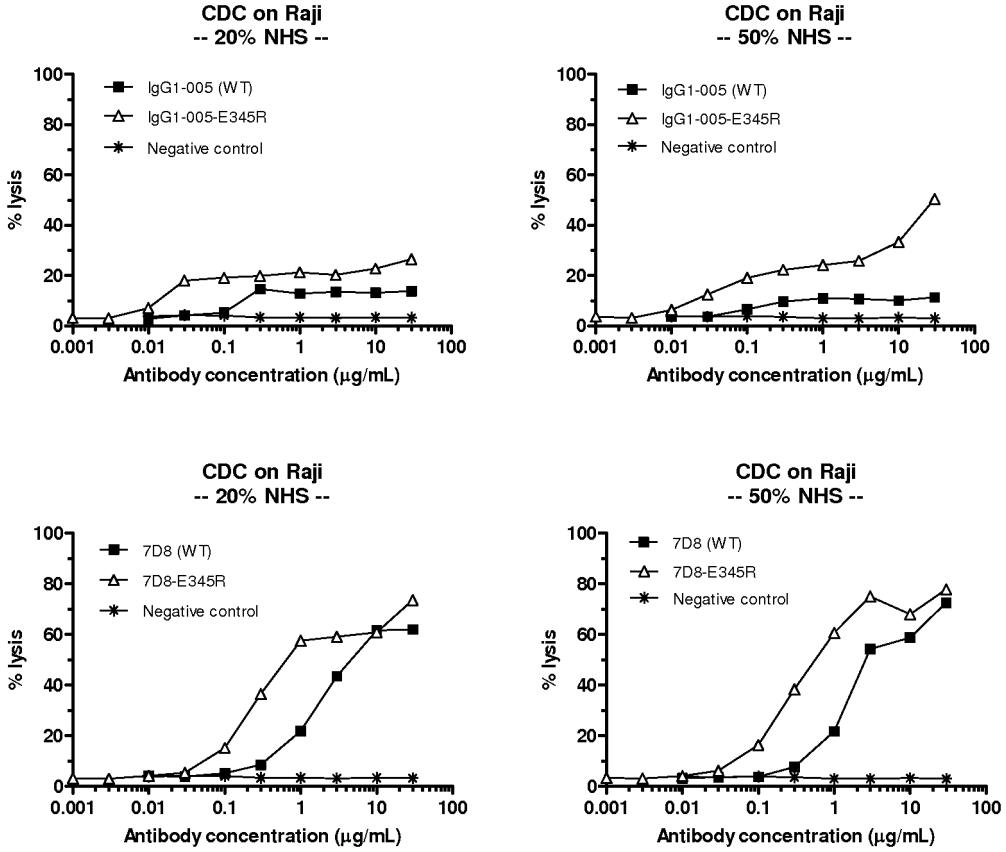


Figure 10A

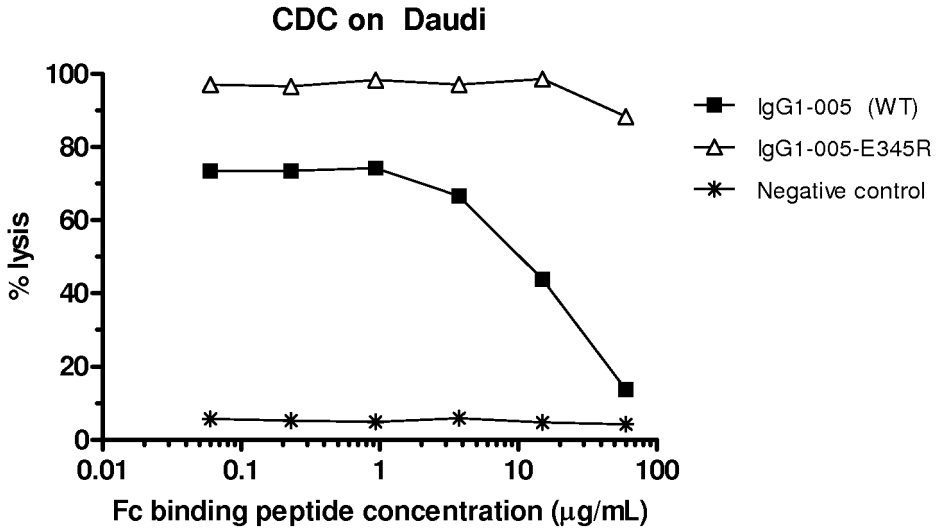


Figure 10B

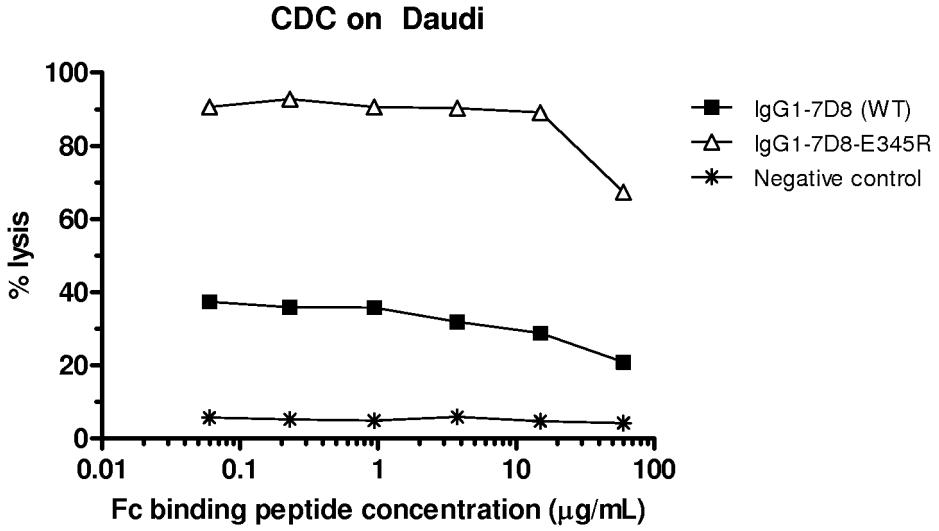


Figure 11

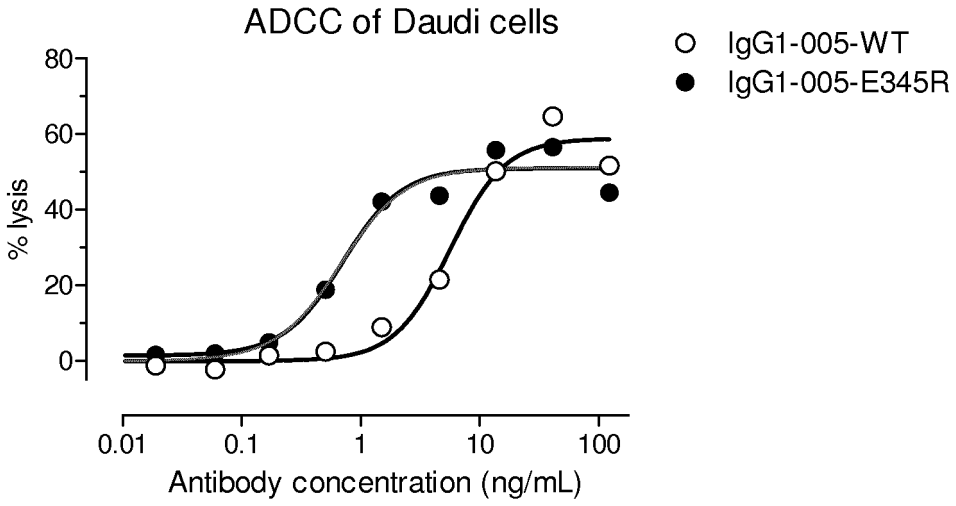

ADCC of Daudi cells
IgG1-005-WT
IgG1-005-E345R
% lysis
80
60
40
20
0
0.01
0.1
1
10
100
Antibody concentration (ng/mL)

Figure 12A

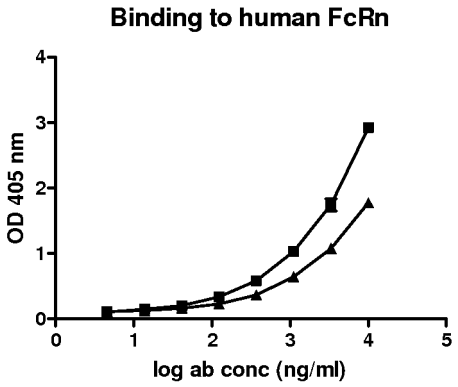


Figure 12B

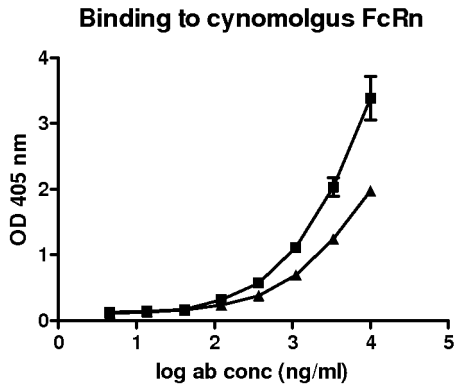


Figure 12C

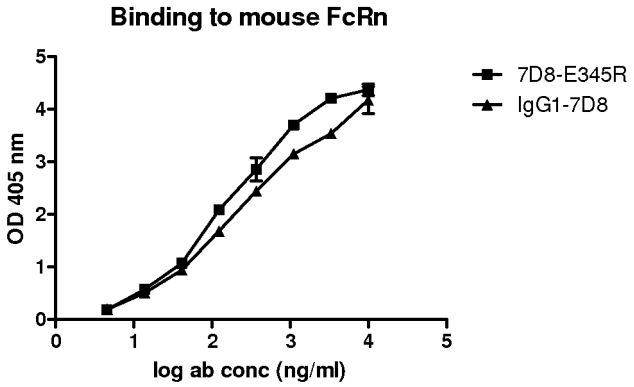


Figure 13

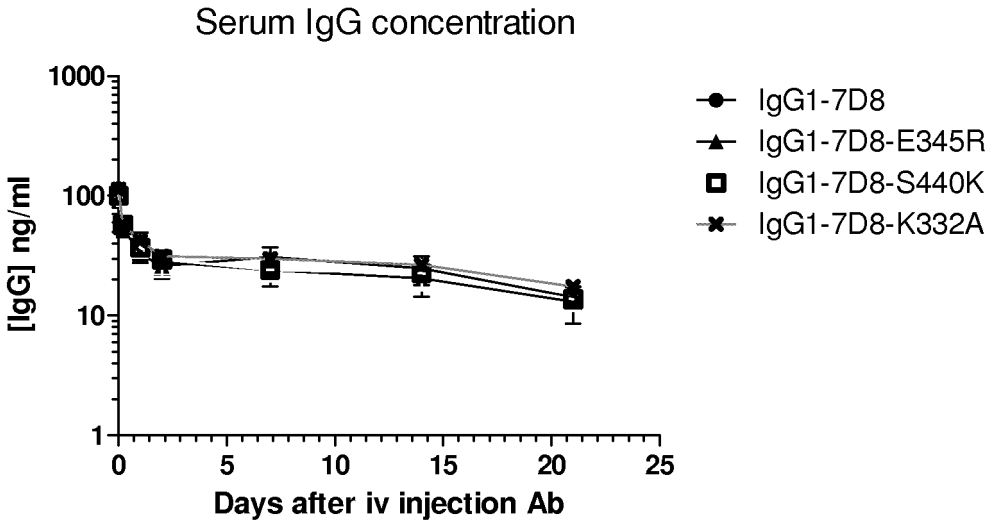

Serum IgG concentration
[IgG] ng/ml
1000
100
10
1
0
5
10
15
20
25
Days after iv injection Ab
IgG1-7D8
IgG1-7D8-E345R
IgG1-7D8-S440K
IgG1-7D8-K332A

Figure 14A

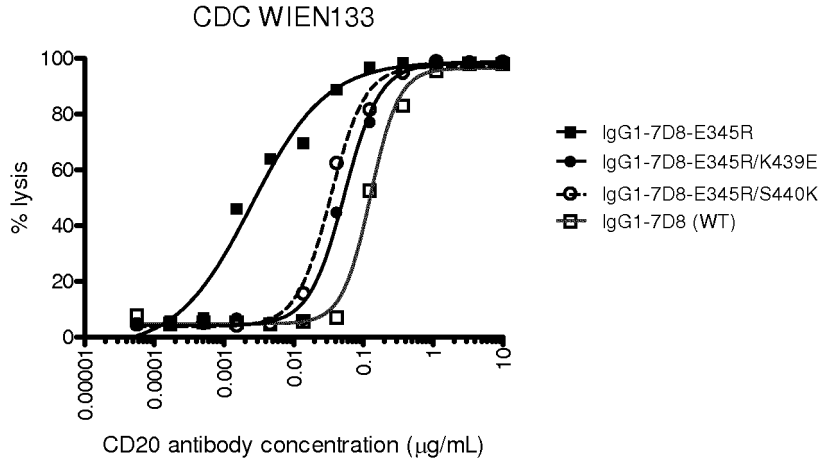


Figure 14B

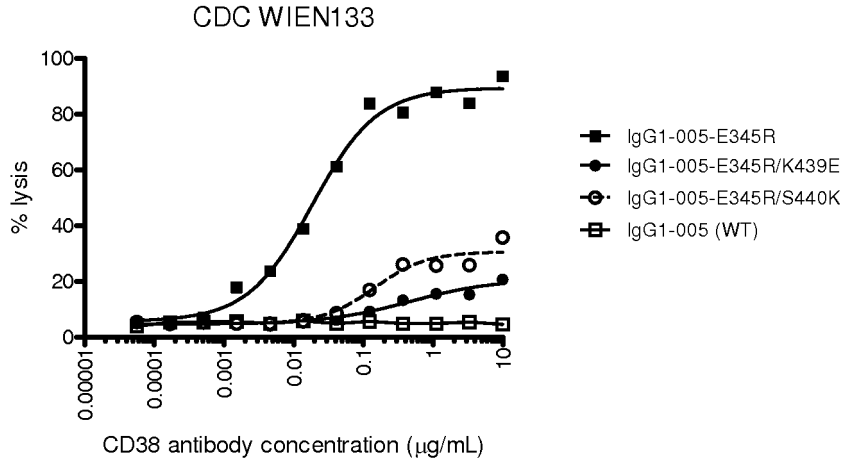


Figure 14C

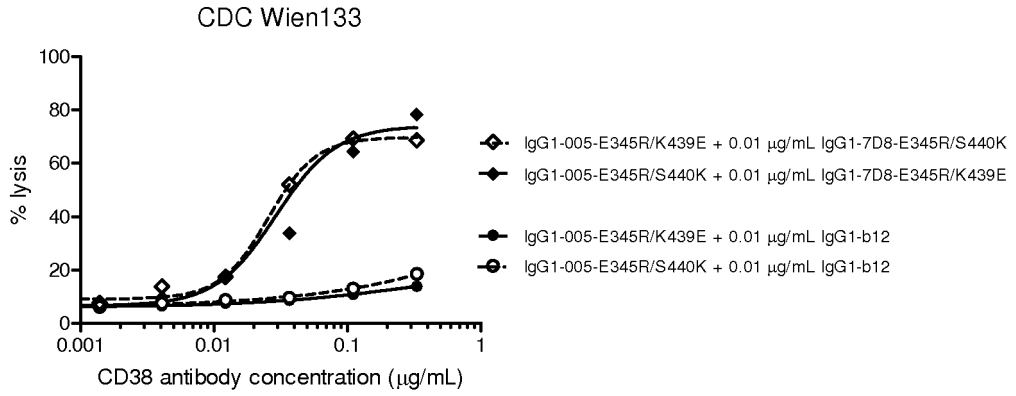


Figure 14D

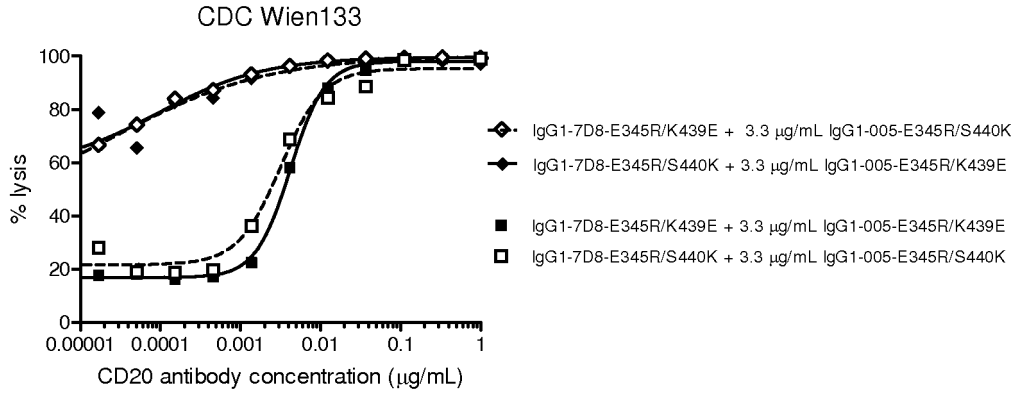


Figure 15A

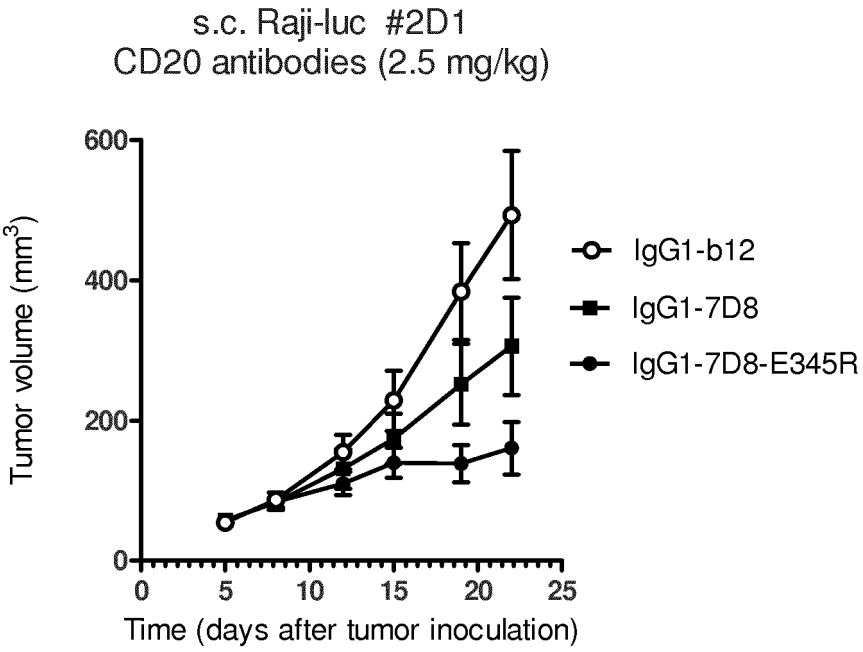


Figure 15B

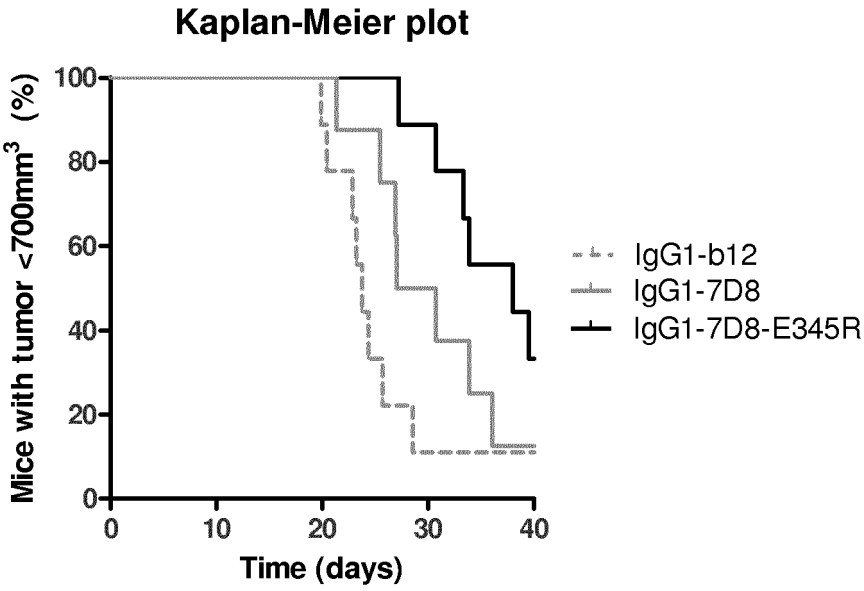


Figure 16A

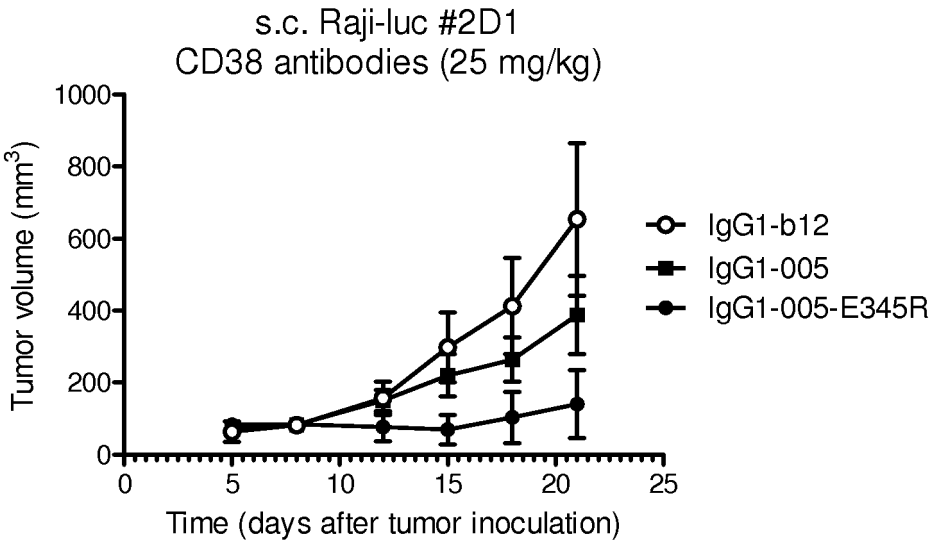


Figure 16B

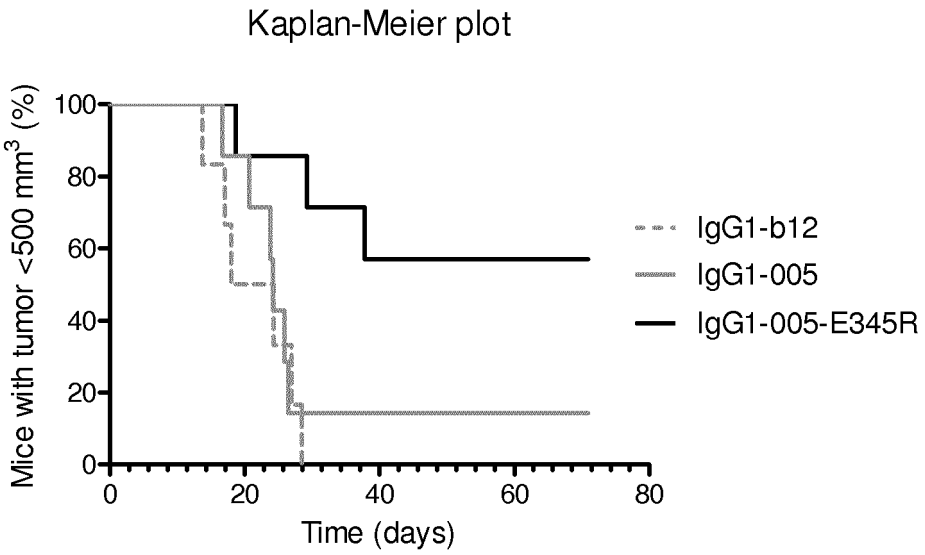


Figure 17

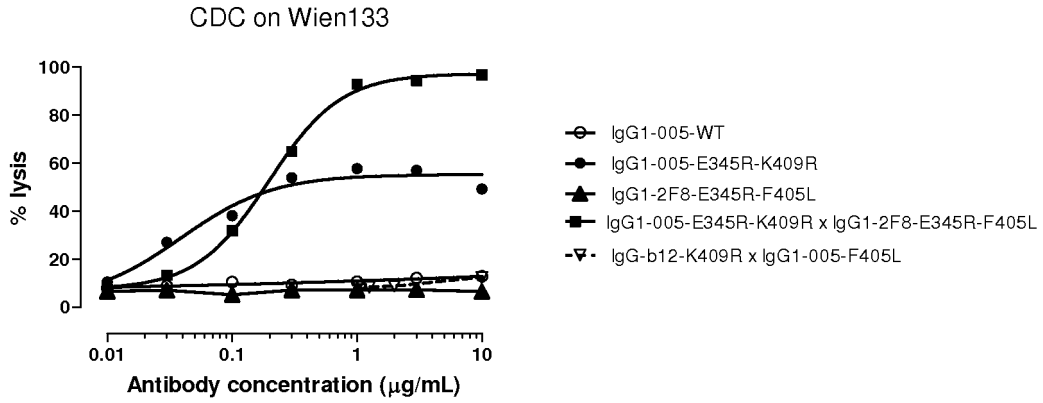

CDC on Wien133
% lysis
100
80
60
40
20
0
0.01
0.1
1
10
Antibody concentration (µg/mL)
IgG1-005-WT
IgG1-005-E345R-K409R
IgG1-2F8-E345R-F405L
IgG1-005-E345R-K409R x IgG1-2F8-E345R-F405L
IgG-b12-K409R x IgG1-005-F405L

Figure 18A

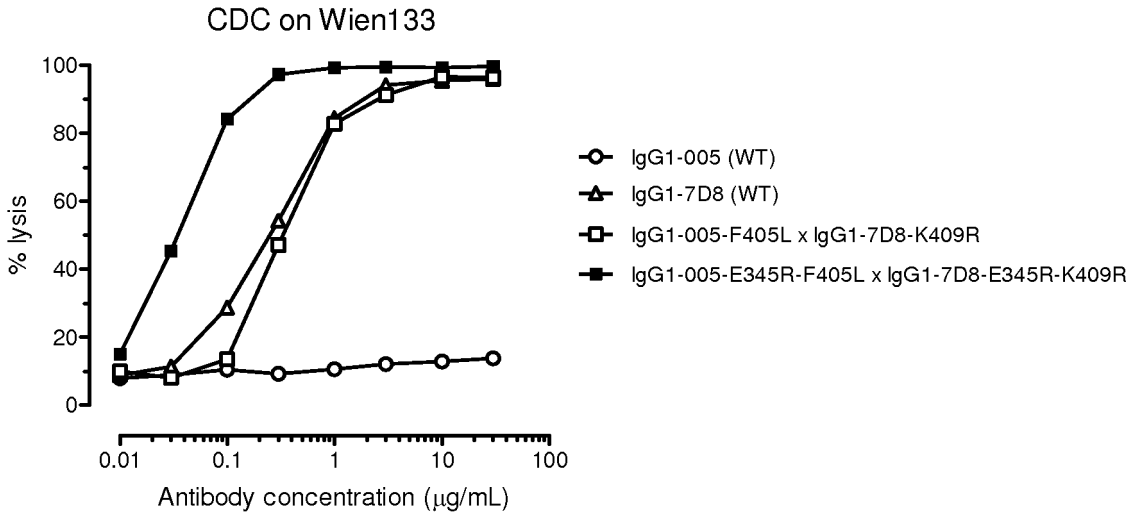


Figure 18B

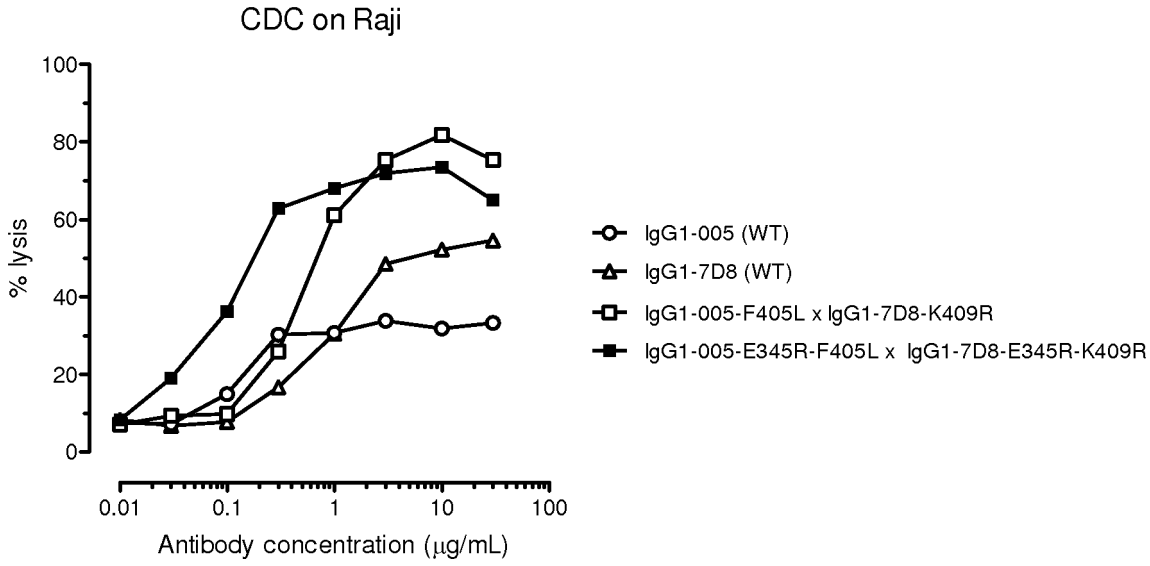


Figure 19

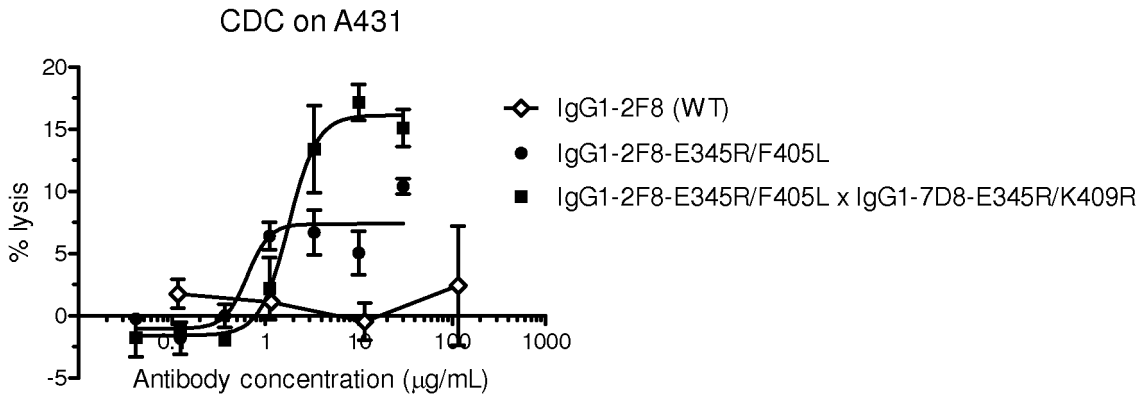

CDC on A431
% lysis
20
15
10
5
0
-5
1
1000
Antibody concentration (µg/mL)
IgG1-2F8 (WT)
IgG1-2F8-E345R/F405L
IgG1-2F8-E345R/F405L x IgG1-7D8-E345R/K409R

Figure 20

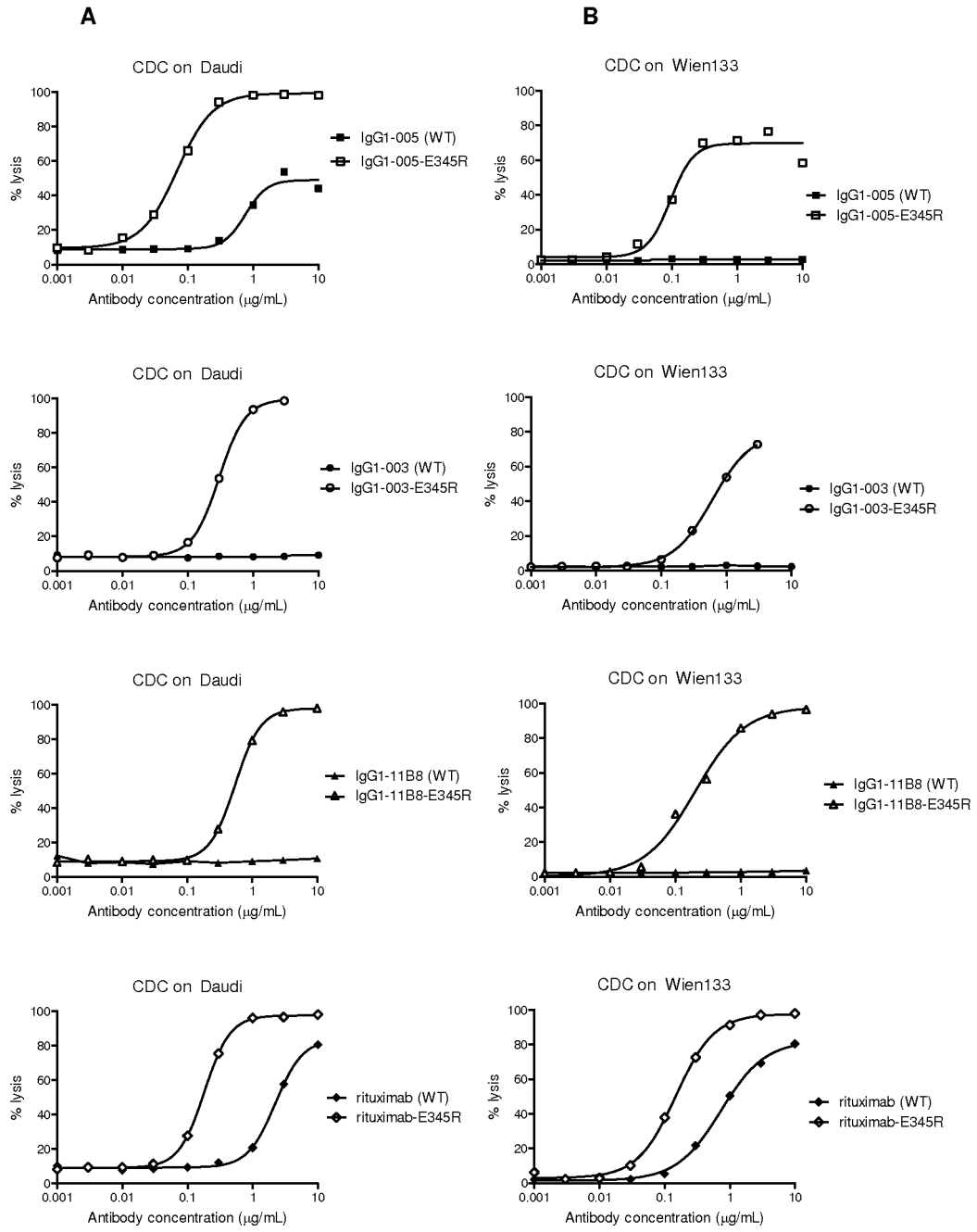

A
B
CDC on Daudi
CDC on Wien133
% lysis
Antibody concentration (µg/mL)
IgG1-005 (WT)
IgG1-005-E345R
IgG1-003 (WT)
IgG1-003-E345R
IgG1-11B8 (WT)
IgG1-11B8-E345R
rituximab (WT)
rituximab-E345R

Figure 21

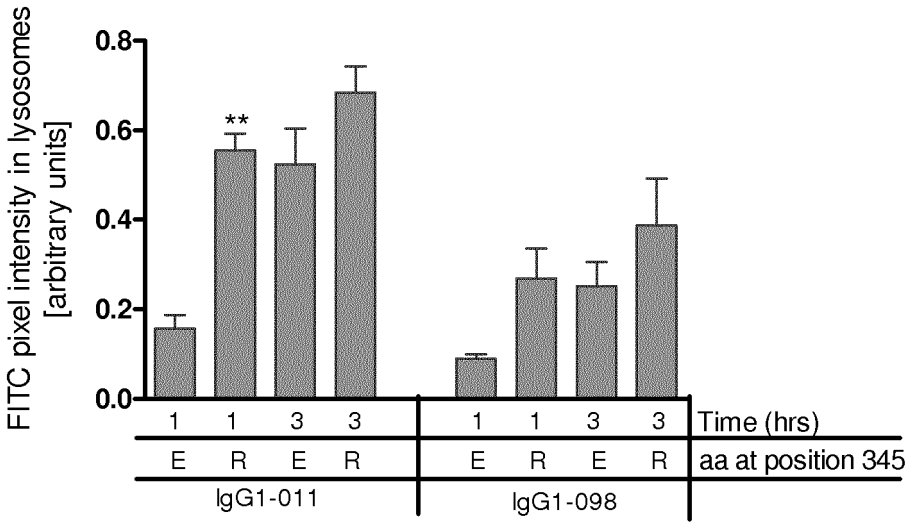


Figure 22A

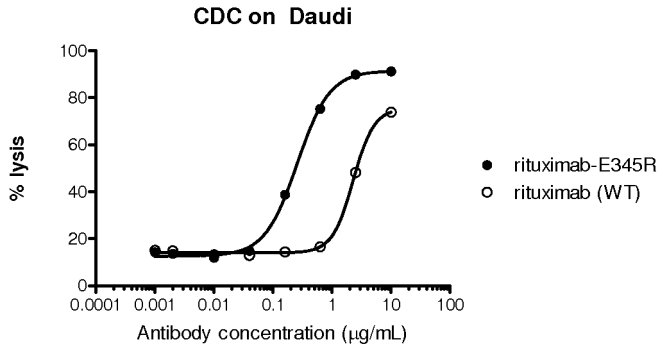


Figure 22B

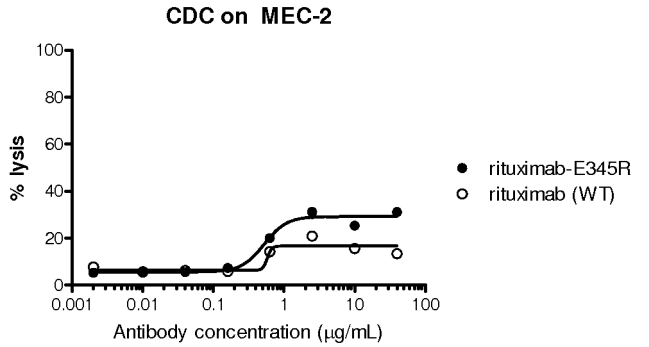


Figure 22C

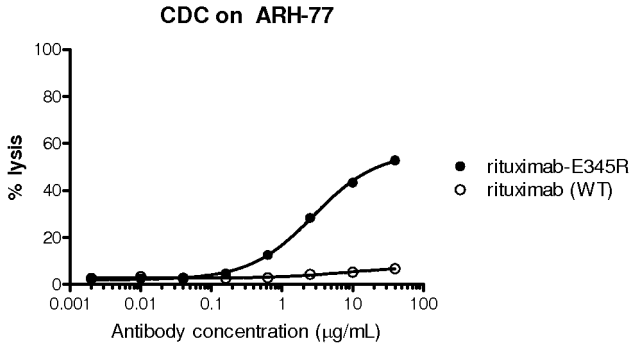


Figure 22D

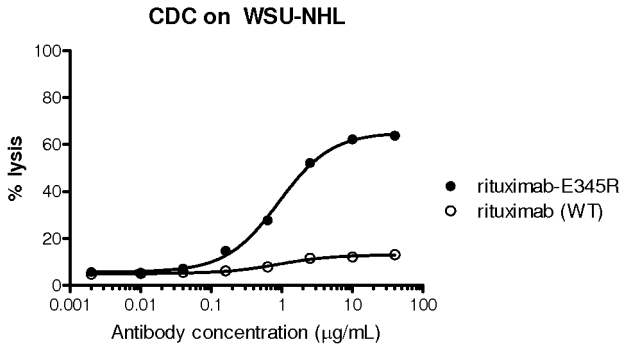


Figure 22E

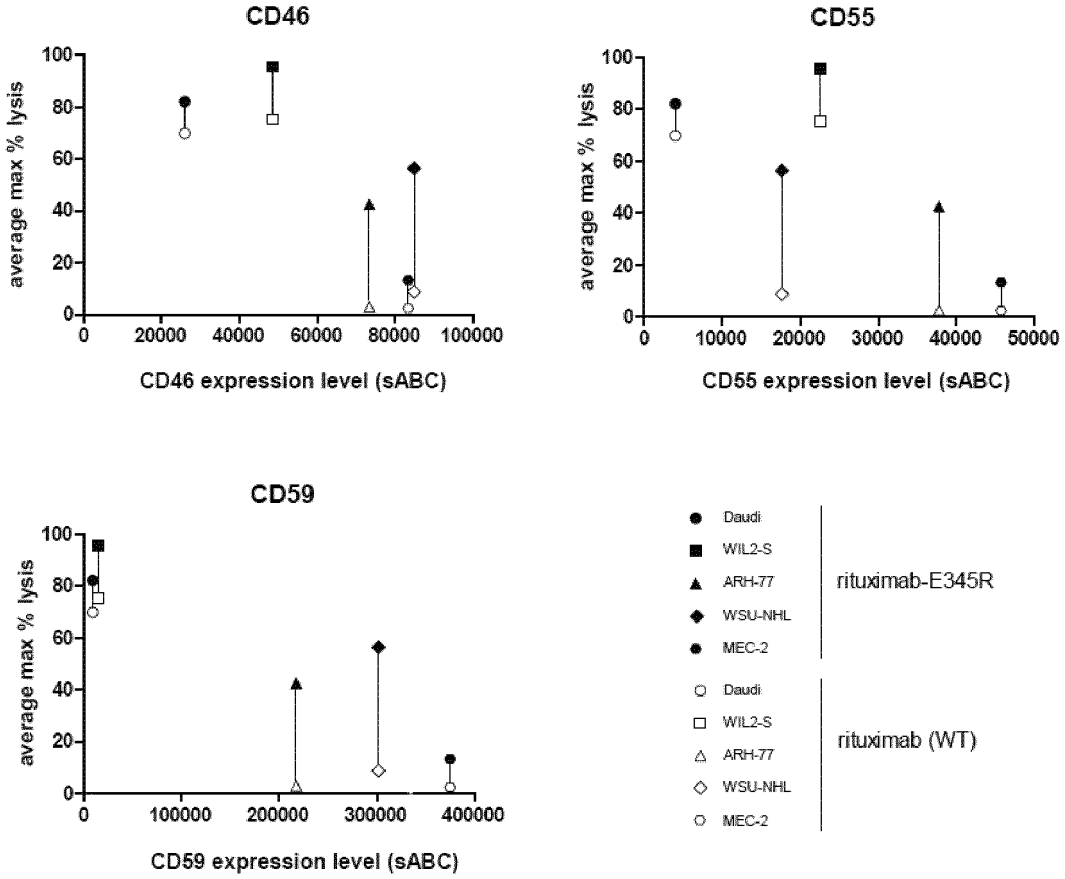
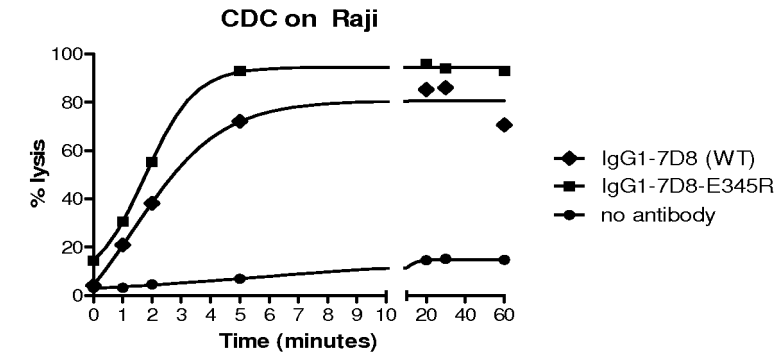
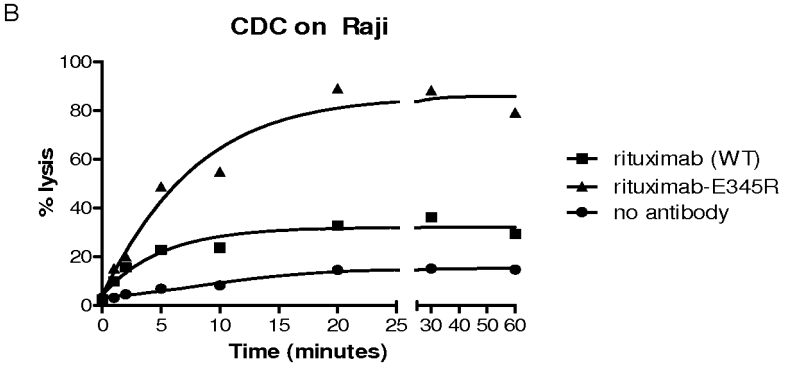

CD46
average max % lysis
CD46 expression level (sABC)
CD55
average max % lysis
CD55 expression level (sABC)
CD59
average max % lysis
CD59 expression level (sABC)
Daudi
WIL2-S
ARH-77
WSU-NHL
MEC-2
rituximab-E345R
Daudi
WIL2-S
ARH-77
WSU-NHL
MEC-2
rituximab (WT)

Figure 23

A



B



C

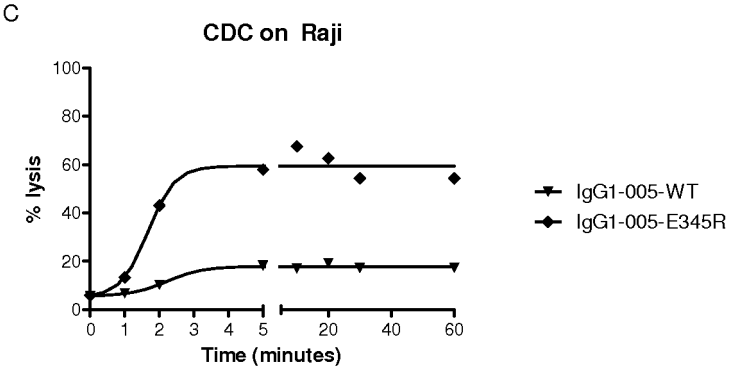


Figure 23 (cont'd)

D

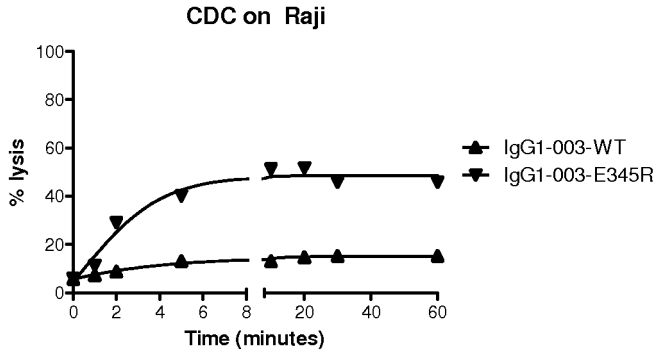


Figure 24

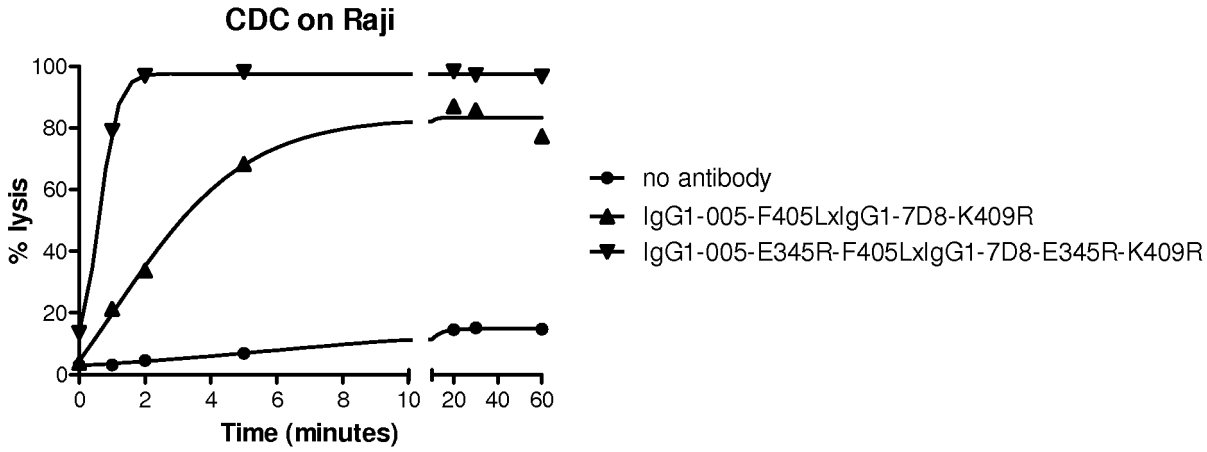


Figure 25

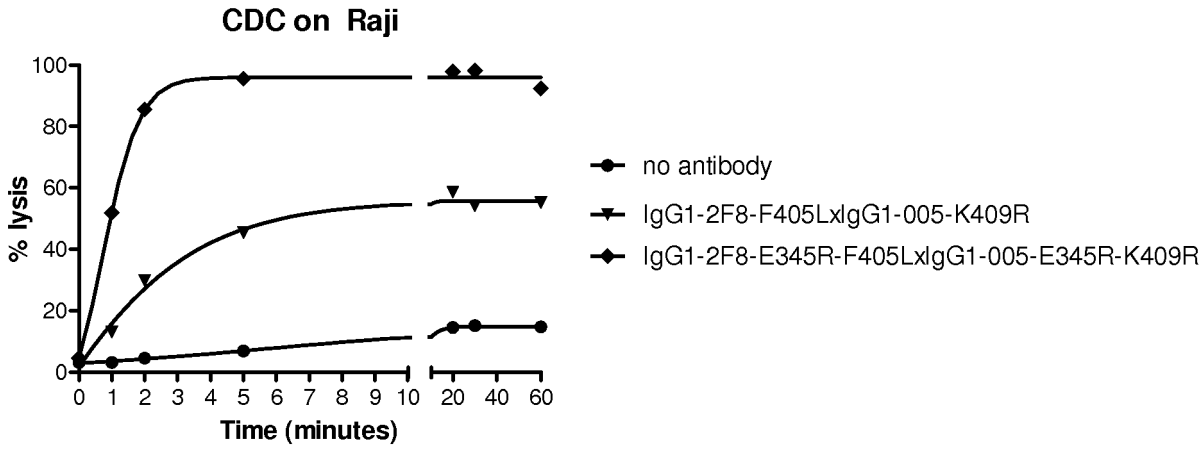

CDC on Raji
% lysis
100
80
60
40
20
0
0 1 2 3 4 5 6 7 8 9 10 20 40 60
Time (minutes)
no antibody
IgG1-2F8-F405LxIgG1-005-K409R
IgG1-2F8-E345R-F405LxIgG1-005-E345R-K409R

Figure 26

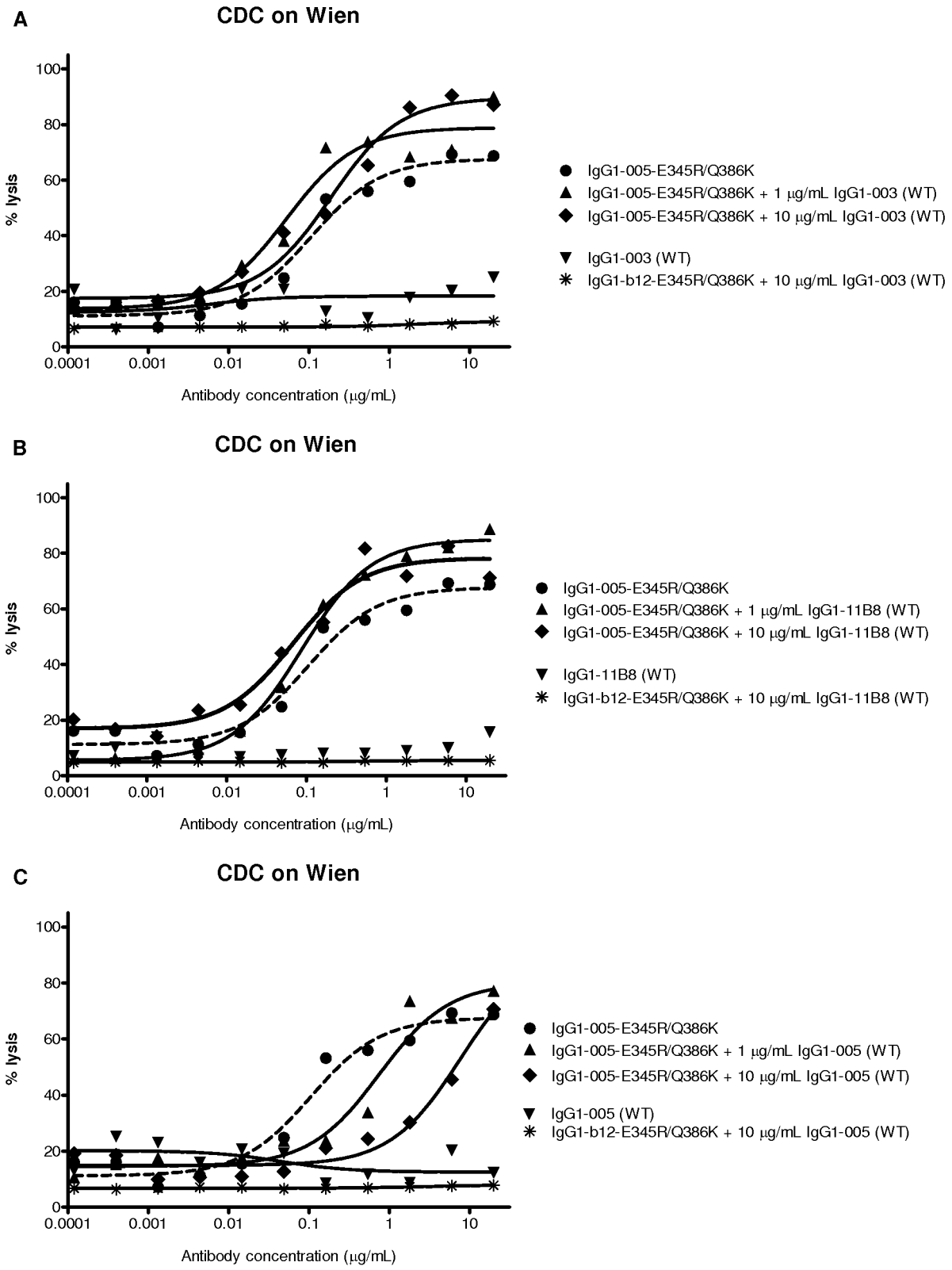

A
CDC on Wien
% lysis
Antibody concentration (µg/mL)
IgG1-005-E345R/Q386K
IgG1-005-E345R/Q386K + 1 µg/mL IgG1-003 (WT)
IgG1-005-E345R/Q386K + 10 µg/mL IgG1-003 (WT)
IgG1-003 (WT)
IgG1-b12-E345R/Q386K + 10 µg/mL IgG1-003 (WT)
B
CDC on Wien
% lysis
Antibody concentration (µg/mL)
IgG1-005-E345R/Q386K
IgG1-005-E345R/Q386K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

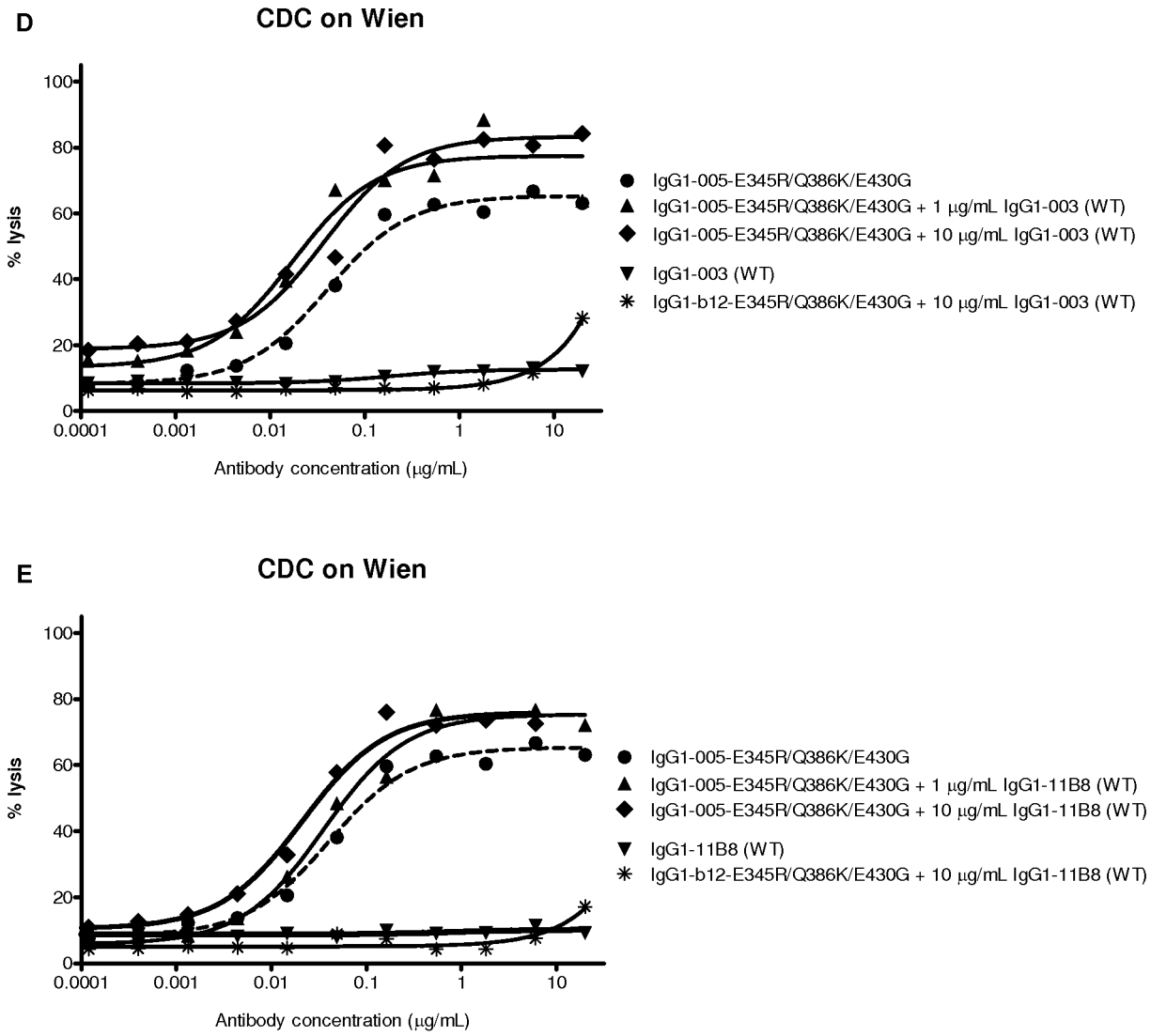


Figure 26 (cont'd)

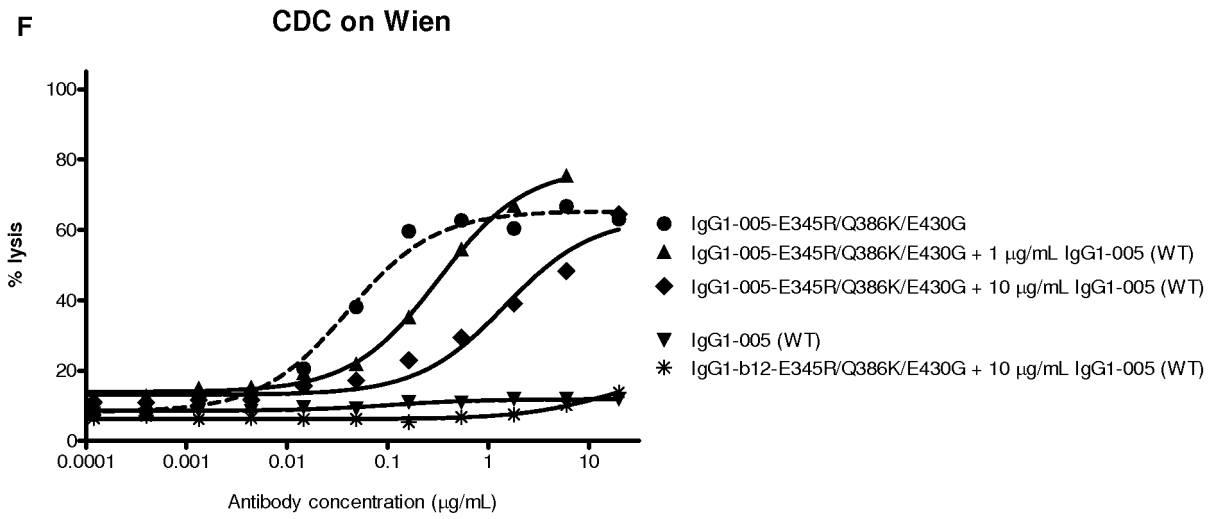


Figure 27

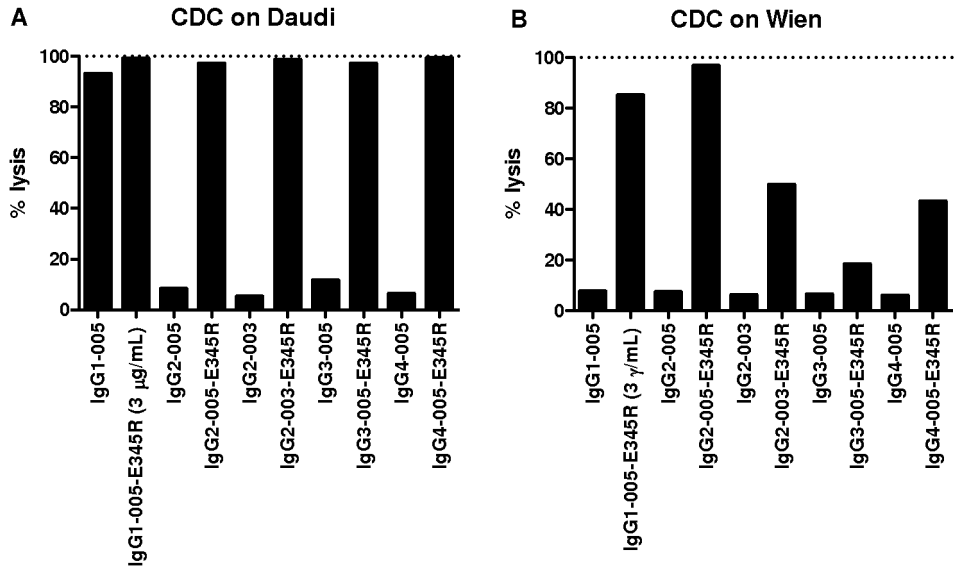
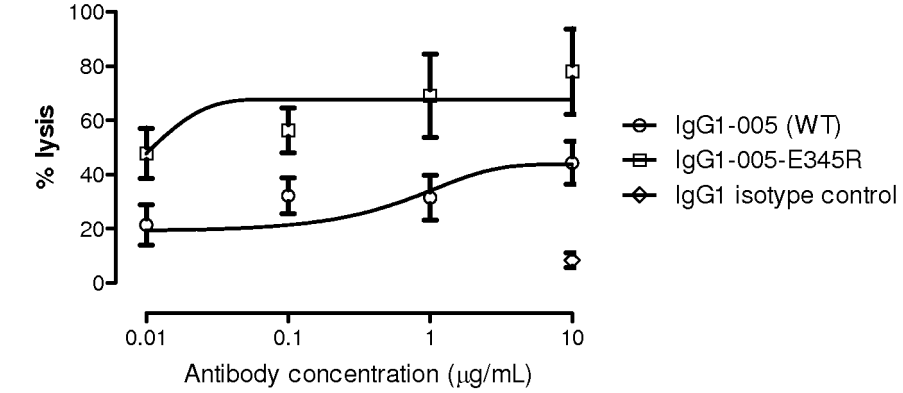
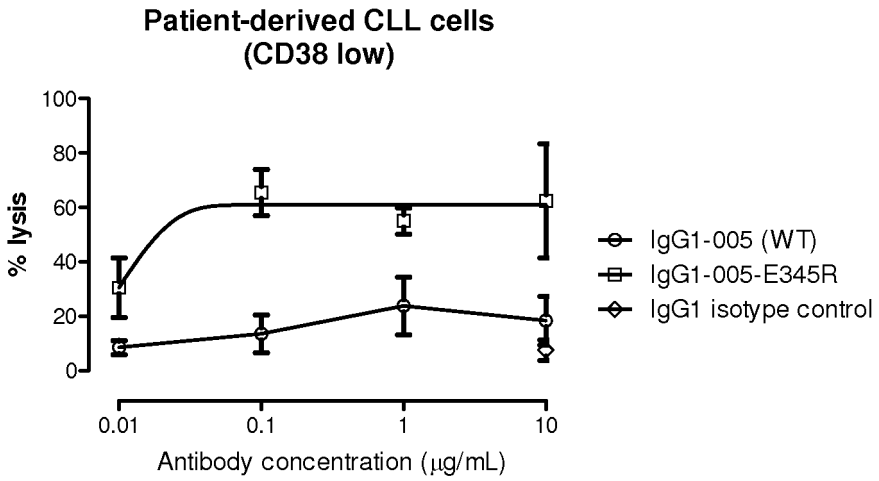


Figure 28

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