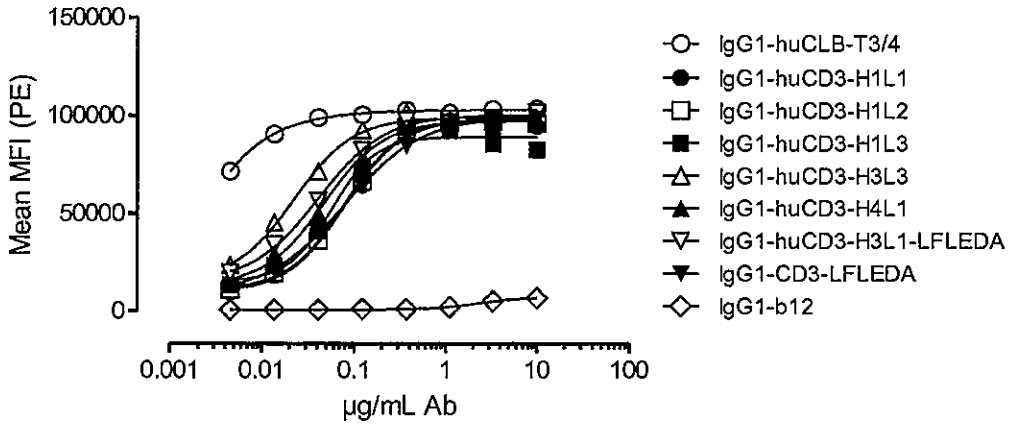
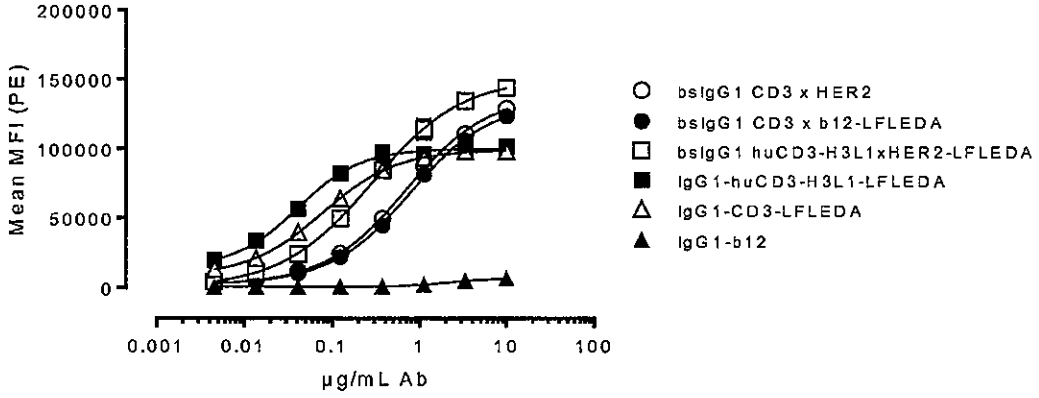
Figure 1

A



Antibody	EC50 (µg/mL)
IgG1-huCD3-H1L1	0.07
IgG1-huCD3-H1L2	0.08
IgG1-huCD3-H1L3	0.06
IgG1-huCD3-H3L3	0.02
IgG1-huCD3-H4L1	0.05
IgG1-huCD3-H3L1-LFLEDA	0.04
IgG1-CD3-LFLEDA	0.08

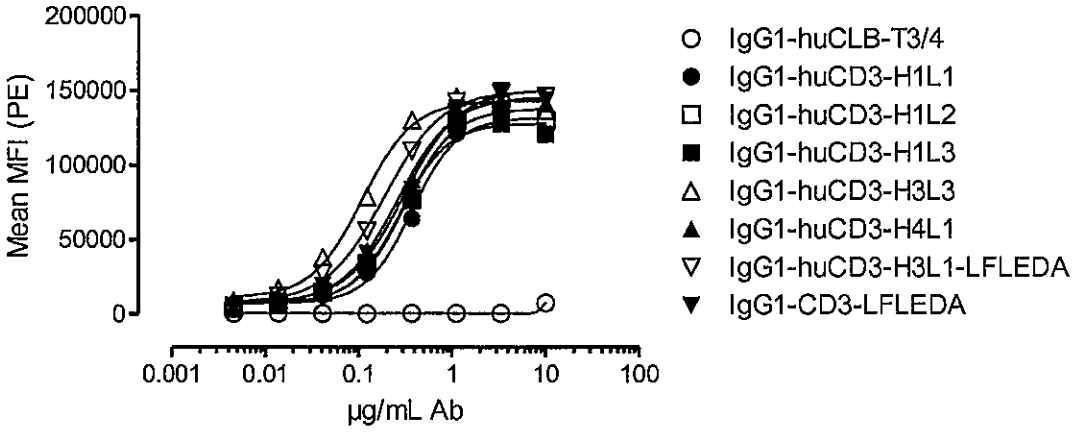
B



Antibody	EC50 (µg/mL)
bsIgG1 CD3 x HER2	0.68
bsIgG1 CD3 x b12-LFLEDA	0.75
bsIgG1 huCD3-H3L1xHER2-LFLEDA	0.28
IgG1-huCD3-H3L1-LFLEDA	0.04
IgG1-CD3-LFLEDA	0.07

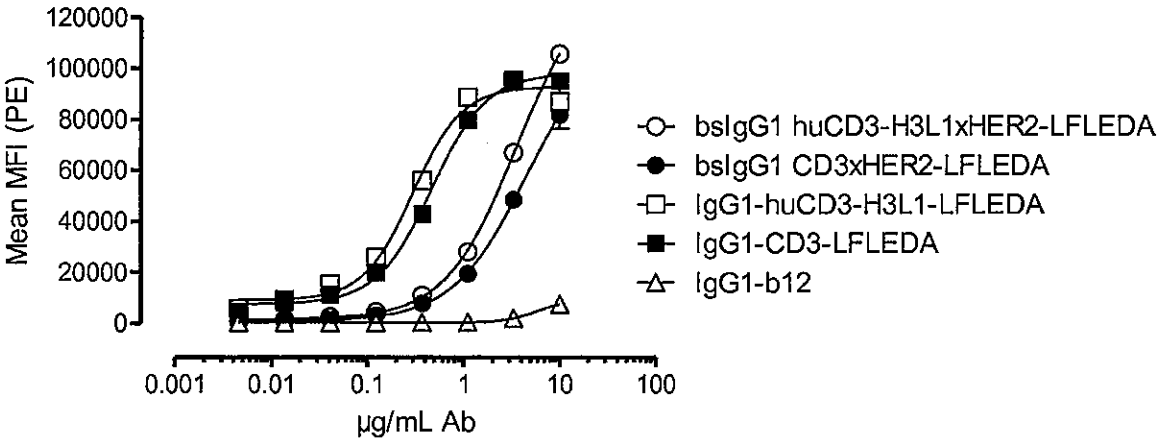
Figure 2

A



Antibody	EC50 (µg/mL)
IgG1-huCD3-H1L1	0.37
IgG1-huCD3-H1L2	0.31
IgG1-huCD3-H1L3	0.28
IgG1-huCD3-H3L3	0.11
IgG1-huCD3-H4L1	0.26
IgG1-huCD3-H3L1-LFLEDA	0.19
IgG1-CD3-LFLEDA	0.30

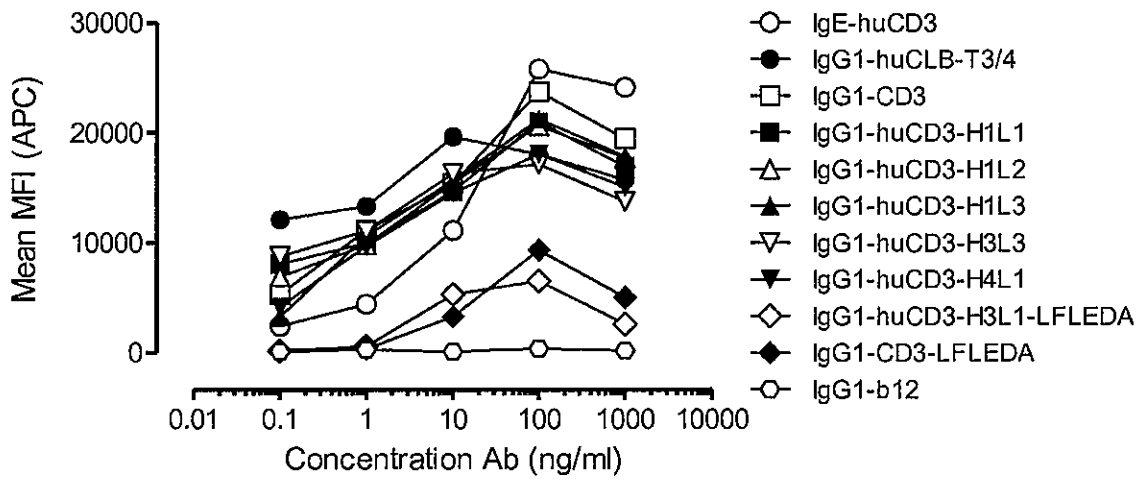
B



Antibody	EC50 (µg/mL)
bsIgG1 CD3xHER2-LFLEDA	4.46
bsIgG1 huCD3-H3L1xHER2-LFLEDA	3.54
IgG1-CD3-LFLEDA	0.47
IgG1-huCD3-H3L1-LFLEDA	0.30

Figure 3

A


30000
20000
10000
0
Mean MFI (APC)
0.01
0.1
1
10
100
1000
10000
Concentration Ab (ng/ml)
IgE-huCD3
IgG1-huCLB-T3/4
IgG1-CD3
IgG1-huCD3-H1L1
IgG1-huCD3-H1L2
IgG1-huCD3-H1L3
IgG1-huCD3-H3L3
IgG1-huCD3-H4L1
IgG1-huCD3-H3L1-LFLEDA
IgG1-CD3-LFLEDA
IgG1-b12

B

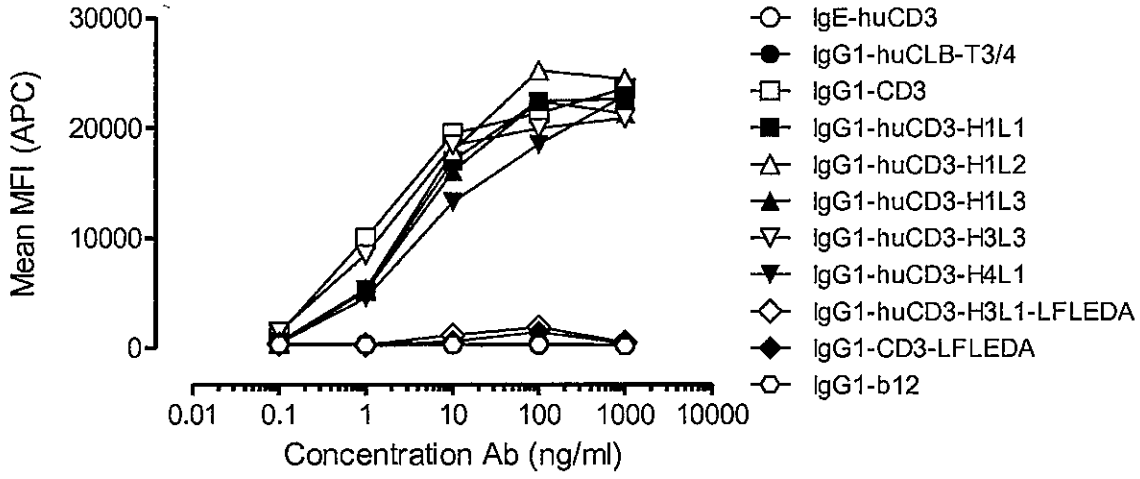
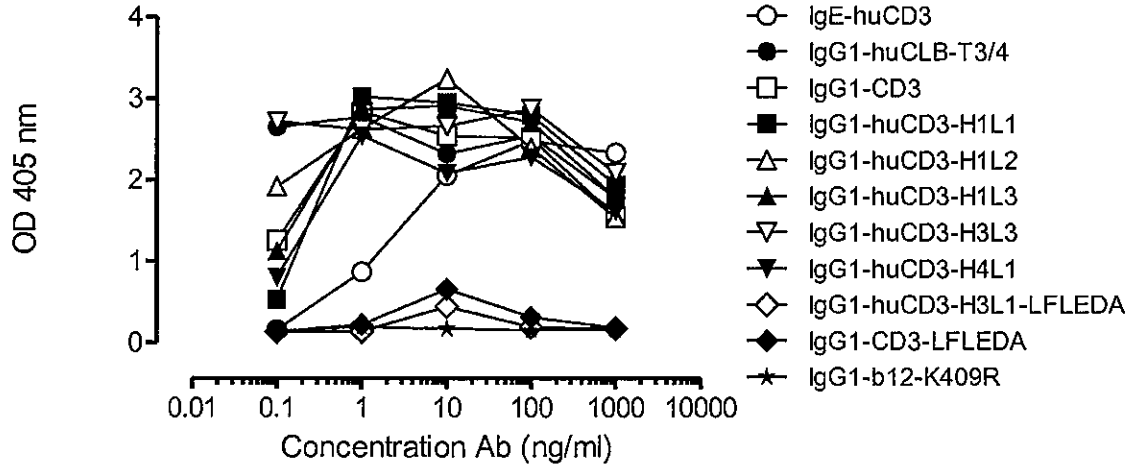

30000
20000
10000
0
Mean MFI (APC)
0.01
0.1
1
10
100
1000
10000
Concentration Ab (ng/ml)
IgE-huCD3
IgG1-huCLB-T3/4
IgG1-CD3
IgG1-huCD3-H1L1
IgG1-huCD3-H1L2
IgG1-huCD3-H1L3
IgG1-huCD3-H3L3
IgG1-huCD3-H4L1
IgG1-huCD3-H3L1-LFLEDA
IgG1-CD3-LFLEDA
IgG1-b12

Figure 4

A


OD 405 nm
4
3
2
1
0
0.01
0.1
1
10
100
1000
10000
Concentration Ab (ng/ml)
IgE-huCD3
IgG1-huCLB-T3/4
IgG1-CD3
IgG1-huCD3-H1L1
IgG1-huCD3-H1L2
IgG1-huCD3-H1L3
IgG1-huCD3-H3L3
IgG1-huCD3-H4L1
IgG1-huCD3-H3L1-LFLEDA
IgG1-CD3-LFLEDA
IgG1-b12-K409R

B

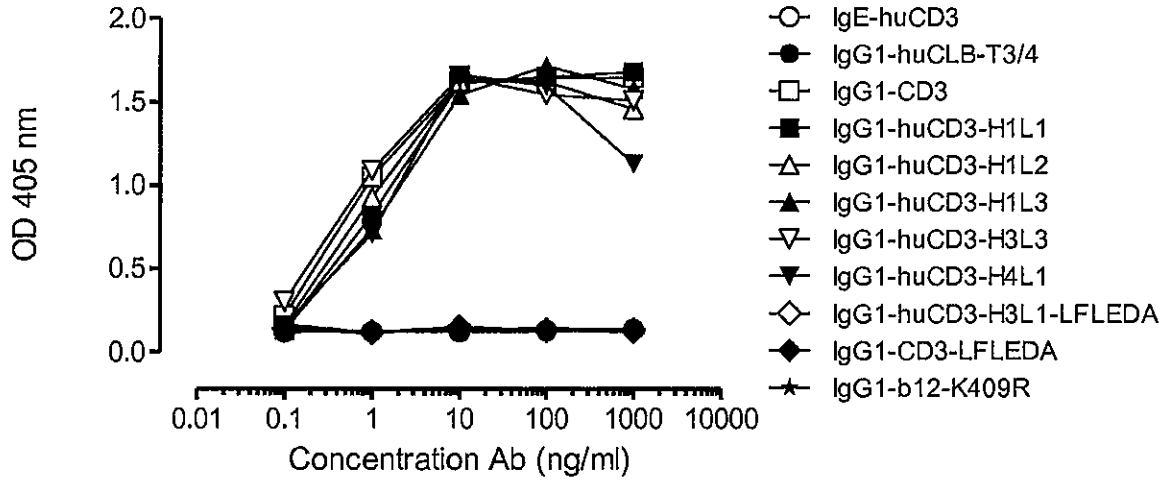
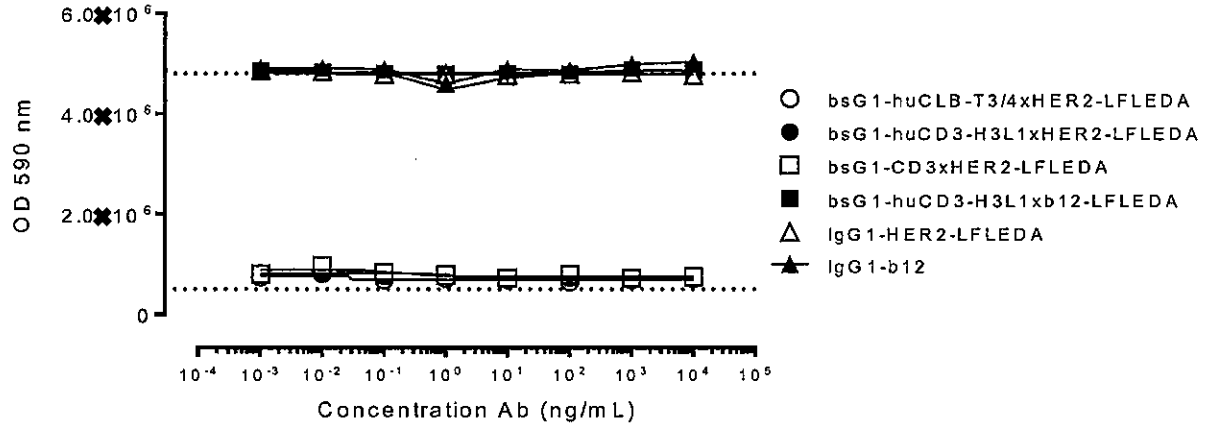

OD 405 nm
2.0
1.5
1.0
0.5
0.0
0.01
0.1
1
10
100
1000
10000
Concentration Ab (ng/ml)
IgE-huCD3
IgG1-huCLB-T3/4
IgG1-CD3
IgG1-huCD3-H1L1
IgG1-huCD3-H1L2
IgG1-huCD3-H1L3
IgG1-huCD3-H3L3
IgG1-huCD3-H4L1
IgG1-huCD3-H3L1-LFLEDA
IgG1-CD3-LFLEDA
IgG1-b12-K409R

Figure 5

A


6.0✖10⁶
4.0✖10⁶
2.0✖10⁶
0
OD 590 nm
10⁻⁴ 10⁻³ 10⁻² 10⁻¹ 10⁰ 10¹ 10² 10³ 10⁴ 10⁵
Concentration Ab (ng/mL)
bsG1-huCLB-T3/4xHER2-LFLEDA
bsG1-huCD3-H3L1xHER2-LFLEDA
bsG1-CD3xHER2-LFLEDA
bsG1-huCD3-H3L1xb12-LFLEDA
IgG1-HER2-LFLEDA
IgG1-b12

B

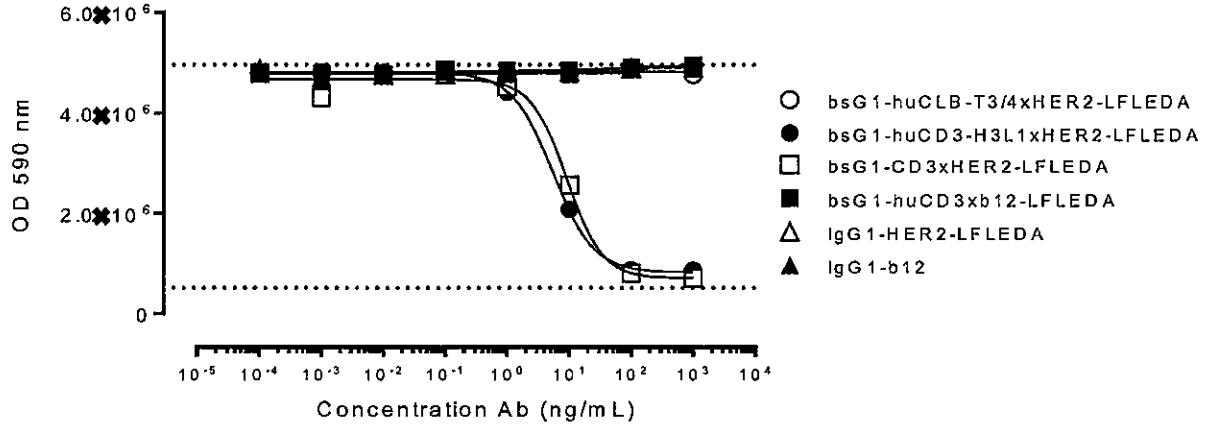
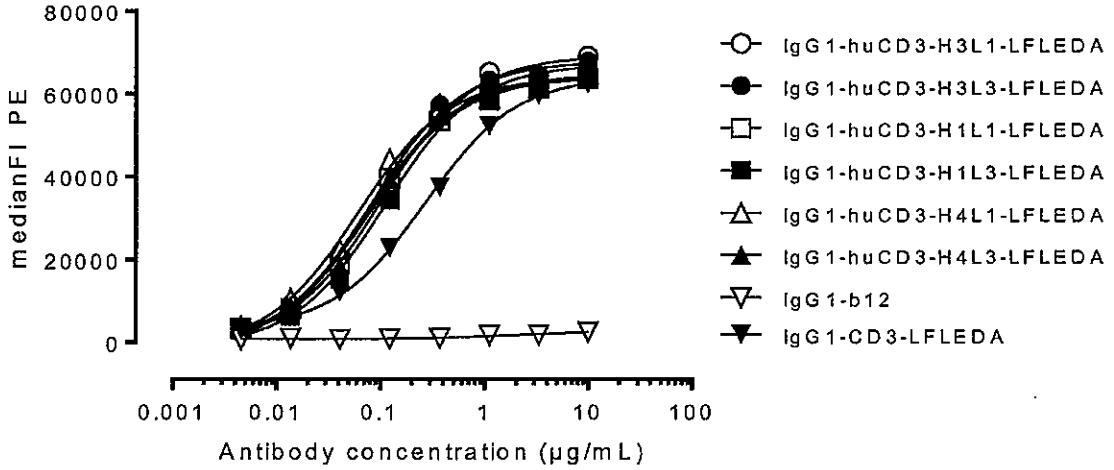

6.0✖10⁶
4.0✖10⁶
2.0✖10⁶
0
OD 590 nm
10⁻⁵ 10⁻⁴ 10⁻³ 10⁻² 10⁻¹ 10⁰ 10¹ 10² 10³ 10⁴
Concentration Ab (ng/mL)
bsG1-huCLB-T3/4xHER2-LFLEDA
bsG1-huCD3-H3L1xHER2-LFLEDA
bsG1-CD3xHER2-LFLEDA
bsG1-huCD3xb12-LFLEDA
IgG1-HER2-LFLEDA
IgG1-b12

Figure 6

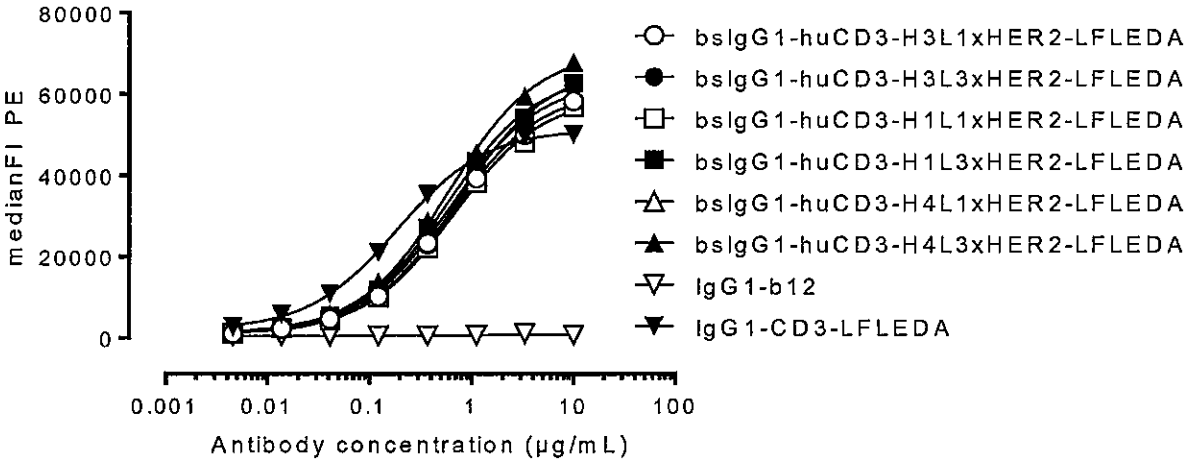
A



Antibody	EC50 (µg/mL)
IgG1-huCD3-H3L1-LFLEDA	0.10
IgG1-huCD3-H3L3- LFLEDA	0.08
IgG1-3huCD3-H1L1- LFLEDA	0.08
IgG1-huCD3-H1L3- LFLEDA	0.11
IgG1-huCD3-H4L1- LFLEDA	0.06
IgG1-huCD3-H4L3- LFLEDA	0.08
IgG1-CD3-LFLEDA	0.27

Figure 6 cont'd

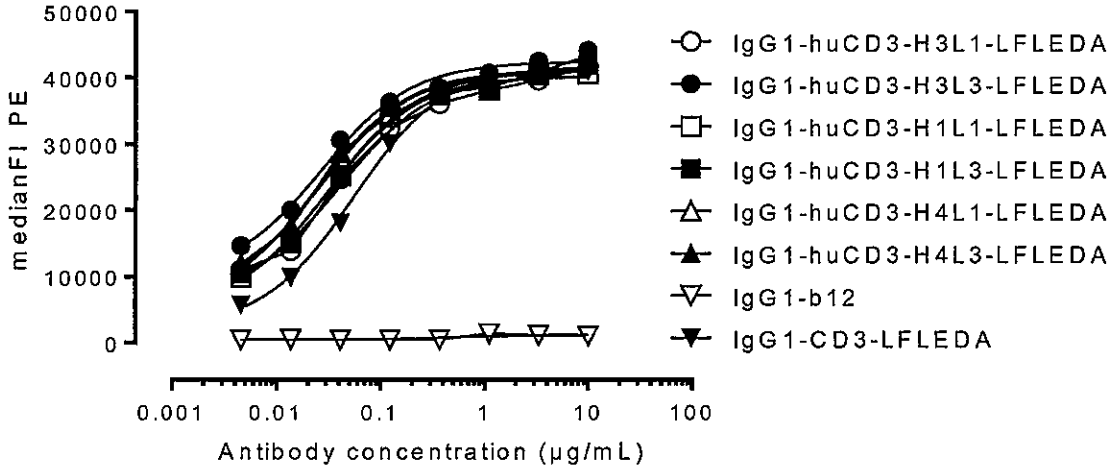
B



Antibody	EC50 (µg/mL)
bsIgG1-huCD3-H3L1xHER2-LFLEDA	0.64
bsIgG1-huCD3-H3L3xHER2-LFLEDA	0.74
bsIgG1-huCD3-H1L1xHER2-LFLEDA	0.66
bsIgG1-huCD3-H1L3xHER2-LFLEDA	0.58
bsIgG1-huCD3-H4L1xHER2-LFLEDA	0.62
bsIgG1-huCD3-H4L3xHER2-LFLEDA	0.59
IgG1-CD3-LFLEDA	0.18

Figure 7

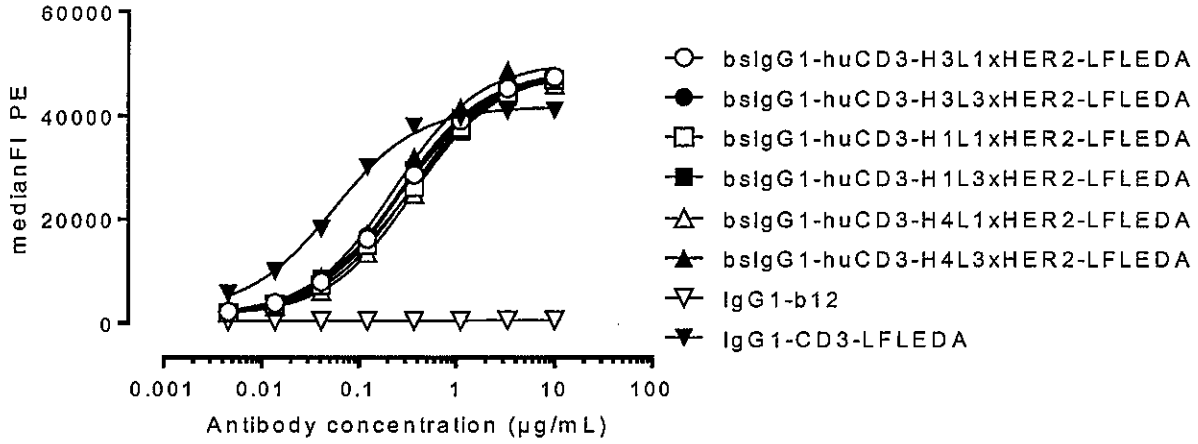
A



Antibody	EC50 (µg/mL)
IgG1-huCD3-H3L1-LFLEDA	0.04
IgG1-huCD3-H3L3-LFLEDA	0.03
IgG1-huCD3-H1L1-LFLEDA	0.03
IgG1-huCD3-H1L3-LFLEDA	0.03
IgG1-huCD3-H4L1-LFLEDA	0.03
IgG1-huCD3-H4L3-LFLEDA	0.02
IgG1-CD3-LFLEDA	0.06

Figure 7 cont'd

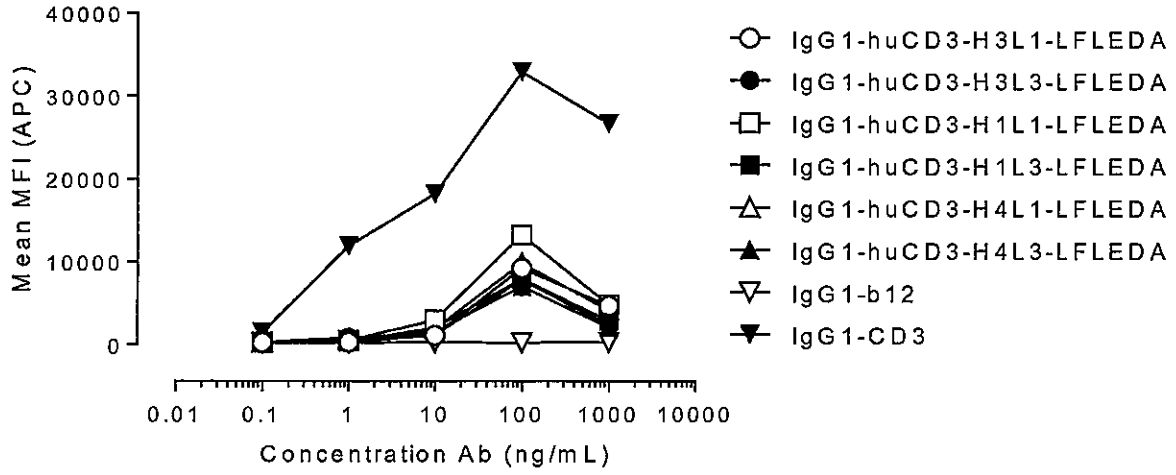
B



Antibody	EC50 (µg/mL)
bsIgG1-huCD3-H3L1xHER2-LFLEDA	0.28
bsIgG1-huCD3-H3L3xHER2-LFLEDA	0.26
bsIgG1-huCD3-H1L1xHER2-LFLEDA	0.32
bsIgG1-huCD3-H1L3xHER2-LFLEDA	0.25
bsIgG1-huCD3-H4L1xHER2-LFLEDA	0.36
bsIgG1-huCD3-H4L1xHER2-LFLEDA	0.24
IgG1-CD3-LFLEDA	0.06

Figure 8

A


40000
30000
20000
10000
0
Mean MFI (APC)
0.01
0.1
1
10
100
1000
10000
Concentration Ab (ng/mL)
IgG1-huCD3-H3L1-LFLEDA
IgG1-huCD3-H3L3-LFLEDA
IgG1-huCD3-H1L1-LFLEDA
IgG1-huCD3-H1L3-LFLEDA
IgG1-huCD3-H4L1-LFLEDA
IgG1-huCD3-H4L3-LFLEDA
IgG1-b12
IgG1-CD3

B

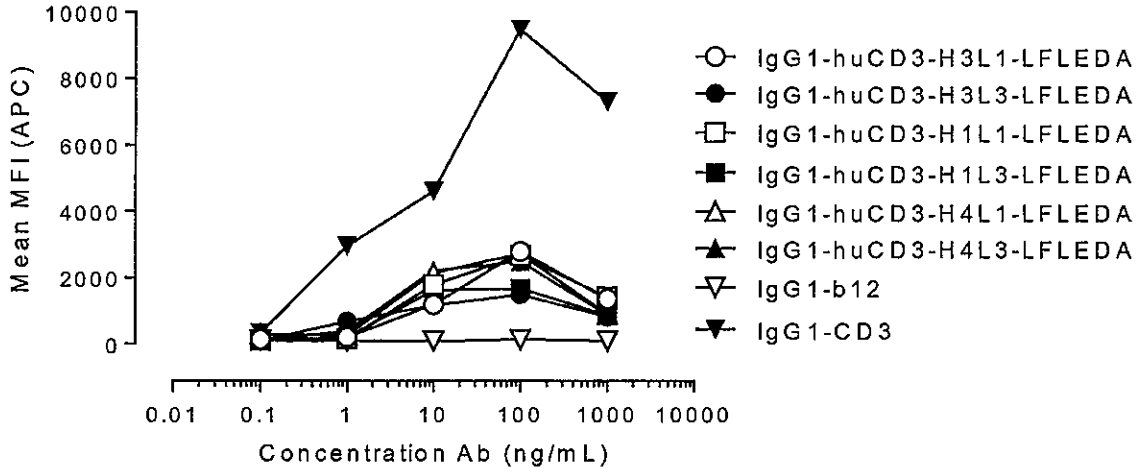
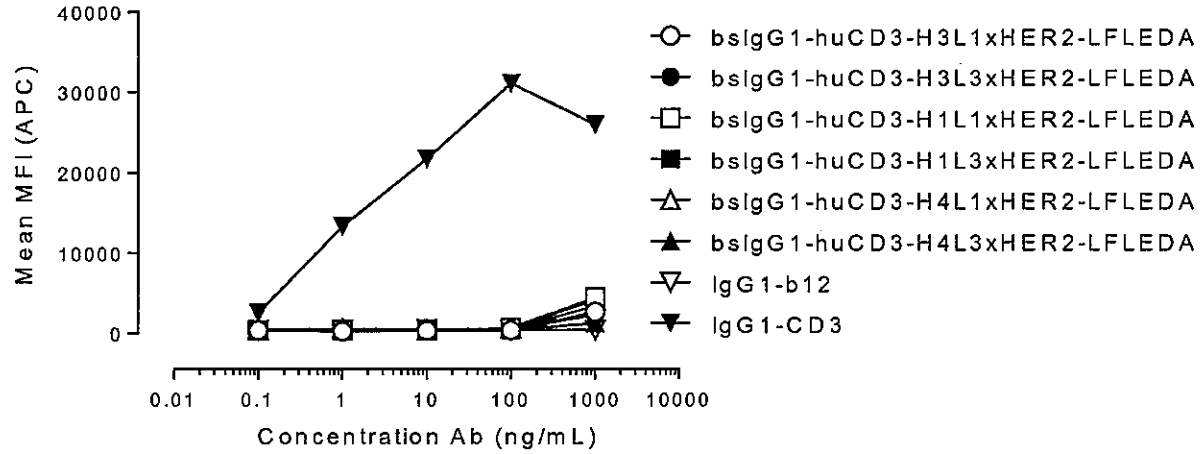

10000
8000
6000
4000
2000
0
Mean MFI (APC)
0.01
0.1
1
10
100
1000
10000
Concentration Ab (ng/mL)
IgG1-huCD3-H3L1-LFLEDA
IgG1-huCD3-H3L3-LFLEDA
IgG1-huCD3-H1L1-LFLEDA
IgG1-huCD3-H1L3-LFLEDA
IgG1-huCD3-H4L1-LFLEDA
IgG1-huCD3-H4L3-LFLEDA
IgG1-b12
IgG1-CD3

Figure 8 cont'd

C



D

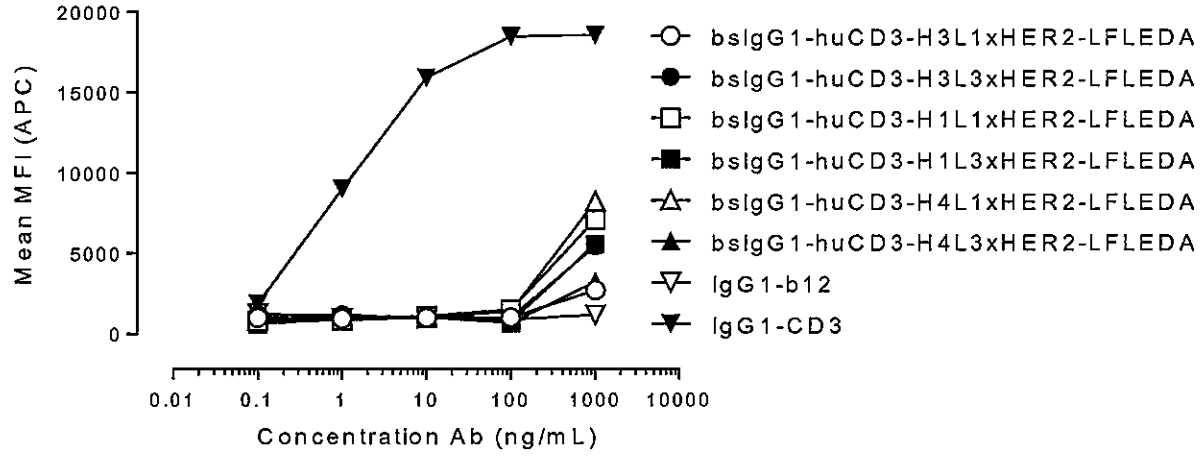
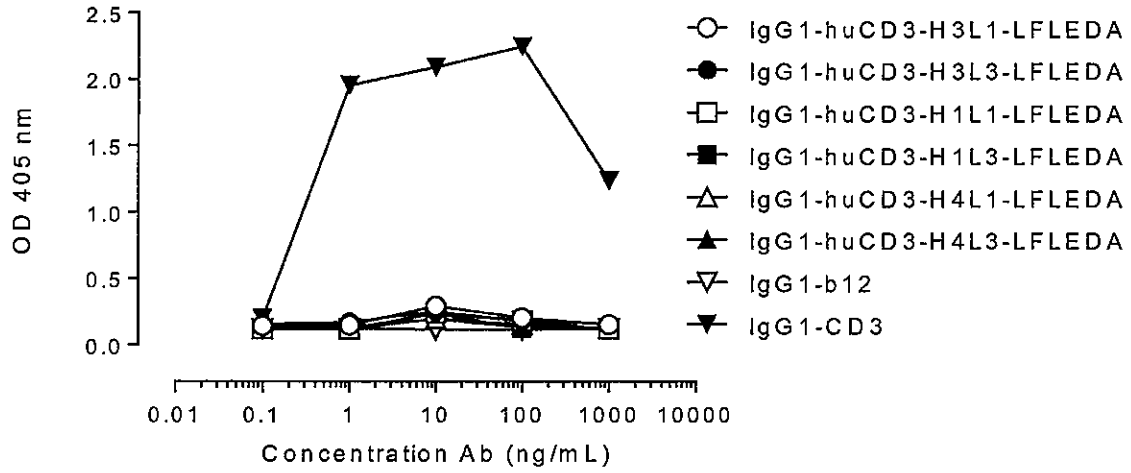


Figure 9

A


OD 405 nm
2.5
2.0
1.5
1.0
0.5
0.0
0.01
0.1
1
10
100
1000
10000
Concentration Ab (ng/mL)
IgG1-huCD3-H3L1-LFLEDA
IgG1-huCD3-H3L3-LFLEDA
IgG1-huCD3-H1L1-LFLEDA
IgG1-huCD3-H1L3-LFLEDA
IgG1-huCD3-H4L1-LFLEDA
IgG1-huCD3-H4L3-LFLEDA
IgG1-b12
IgG1-CD3

B

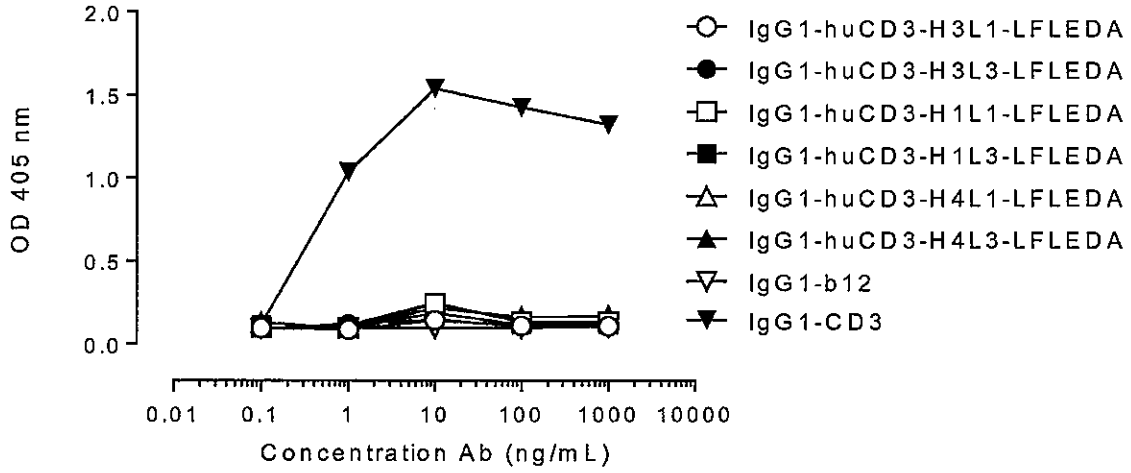
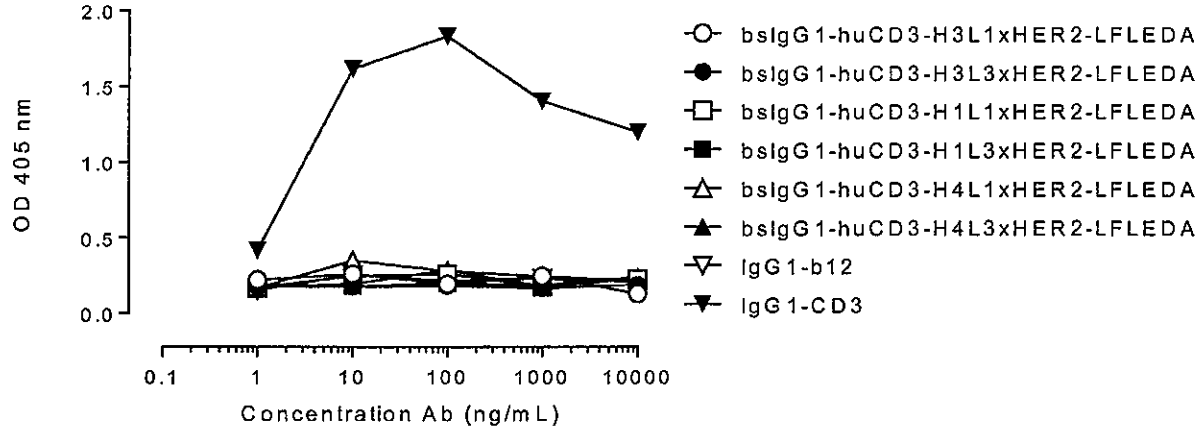

OD 405 nm
2.0
1.5
1.0
0.5
0.0
0.01
0.1
1
10
100
1000
10000
Concentration Ab (ng/mL)
IgG1-huCD3-H3L1-LFLEDA
IgG1-huCD3-H3L3-LFLEDA
IgG1-huCD3-H1L1-LFLEDA
IgG1-huCD3-H1L3-LFLEDA
IgG1-huCD3-H4L1-LFLEDA
IgG1-huCD3-H4L3-LFLEDA
IgG1-b12
IgG1-CD3

Figure 9 cont'd

C



D

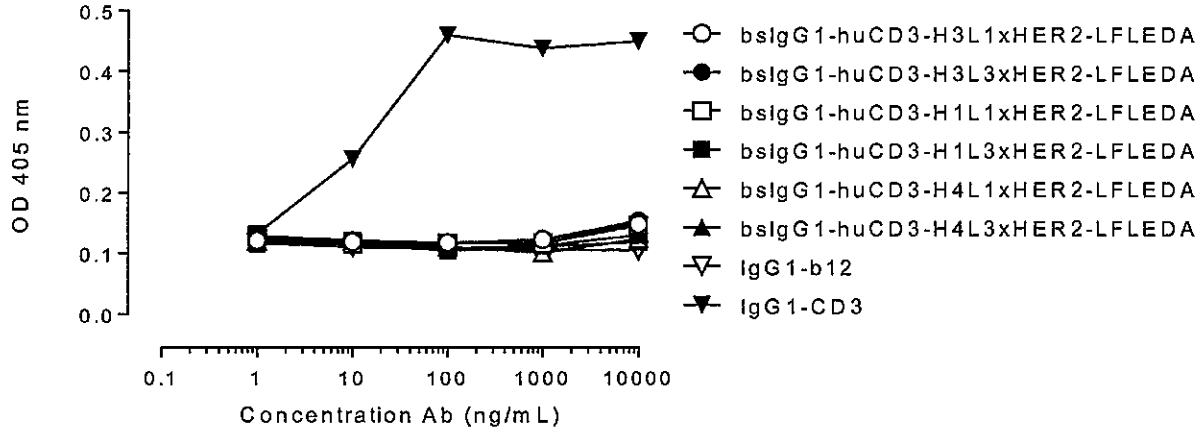
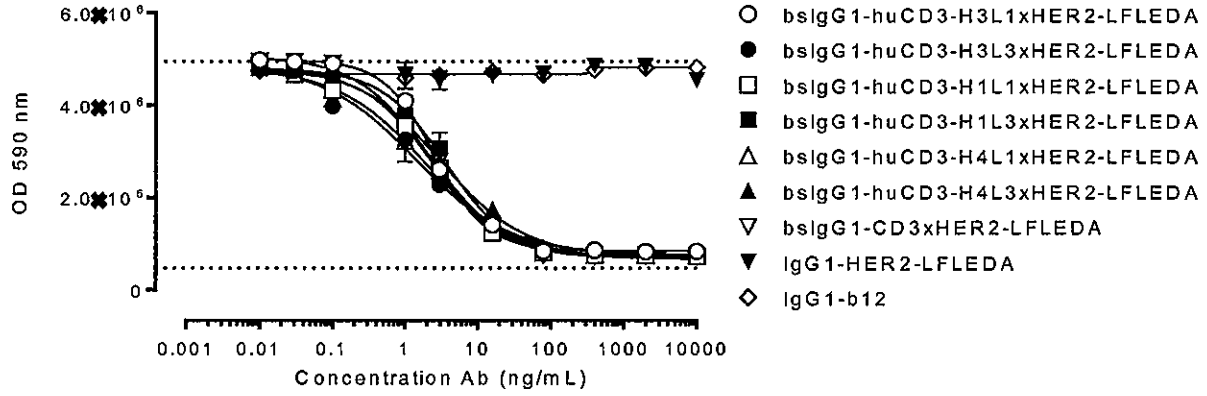


Figure 10

A


6.0✖10⁶
4.0✖10⁶
2.0✖10⁶
0
OD 590 nm
0.001 0.01 0.1 1 10 100 1000 10000
Concentration Ab (ng/mL)
bsIgG1-huCD3-H3L1xHER2-LFLEDA
bsIgG1-huCD3-H3L3xHER2-LFLEDA
bsIgG1-huCD3-H1L1xHER2-LFLEDA
bsIgG1-huCD3-H1L3xHER2-LFLEDA
bsIgG1-huCD3-H4L1xHER2-LFLEDA
bsIgG1-huCD3-H4L3xHER2-LFLEDA
bsIgG1-CD3xHER2-LFLEDA
IgG1-HER2-LFLEDA
IgG1-b12

B

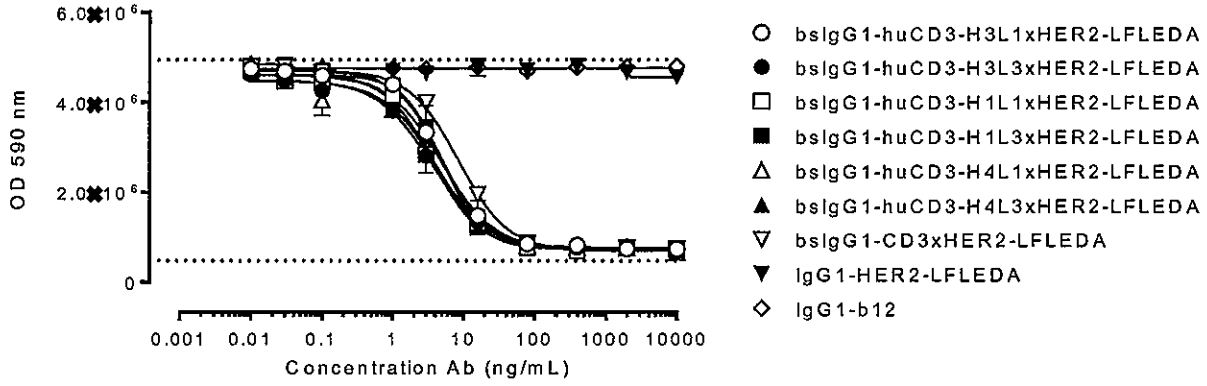

6.0✖10⁶
4.0✖10⁶
2.0✖10⁶
0
OD 590 nm
0.001 0.01 0.1 1 10 100 1000 10000
Concentration Ab (ng/mL)
bsIgG1-huCD3-H3L1xHER2-LFLEDA
bsIgG1-huCD3-H3L3xHER2-LFLEDA
bsIgG1-huCD3-H1L1xHER2-LFLEDA
bsIgG1-huCD3-H1L3xHER2-LFLEDA
bsIgG1-huCD3-H4L1xHER2-LFLEDA
bsIgG1-huCD3-H4L3xHER2-LFLEDA
bsIgG1-CD3xHER2-LFLEDA
IgG1-HER2-LFLEDA
IgG1-b12

Figure 11

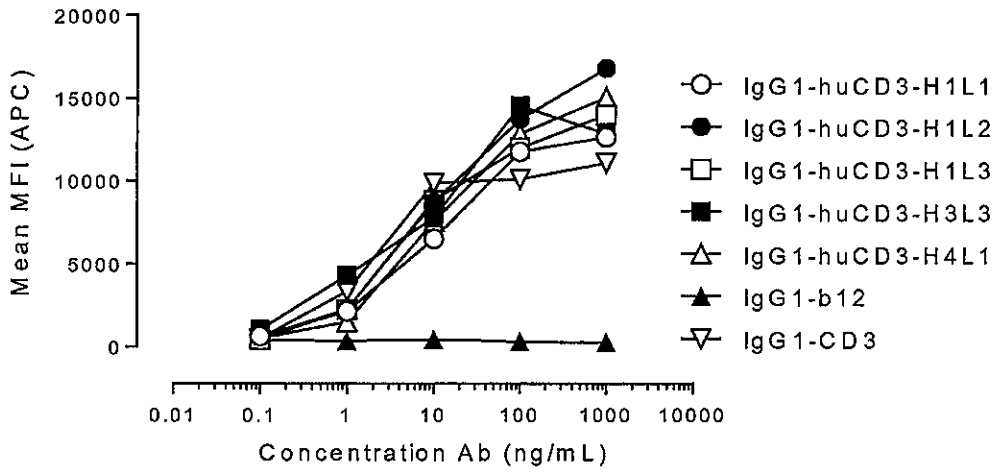
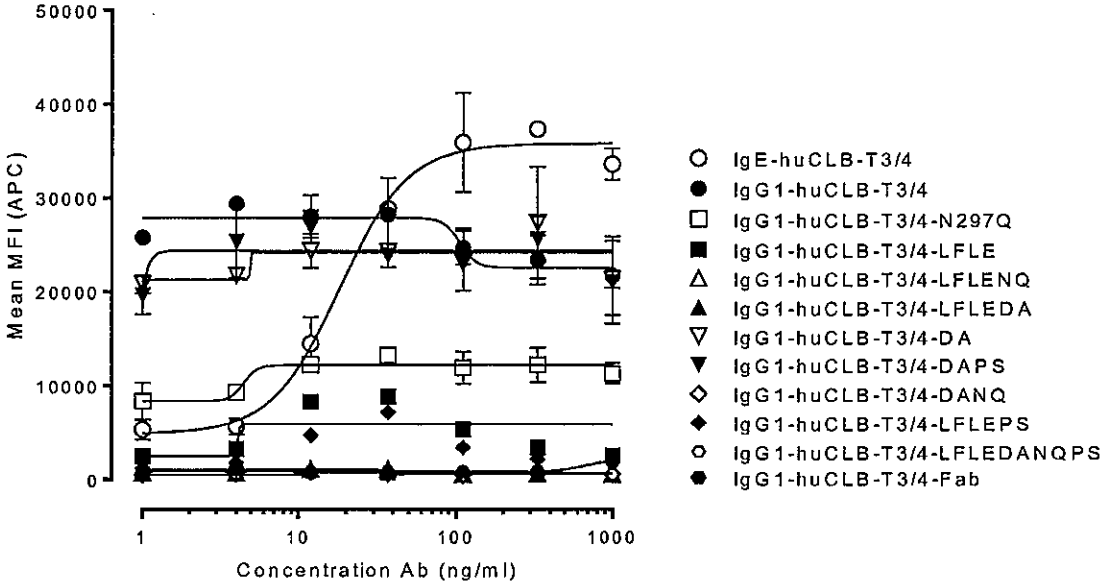

20000
15000
10000
5000
0
Mean MFI (APC)
0.01
0.1
1
10
100
1000
10000
Concentration Ab (ng/mL)
IgG1-huCD3-H1L1
IgG1-huCD3-H1L2
IgG1-huCD3-H1L3
IgG1-huCD3-H3L3
IgG1-huCD3-H4L1
IgG1-b12
IgG1-CD3

Figure 12

A


50000
40000
30000
20000
10000
0
Mean MFI (APC)
1
10
100
1000
Concentration Ab (ng/ml)
IgE-huCLB-T3/4
IgG1-huCLB-T3/4
IgG1-huCLB-T3/4-N297Q
IgG1-huCLB-T3/4-LFLE
IgG1-huCLB-T3/4-LFLENQ
IgG1-huCLB-T3/4-LFLEDA
IgG1-huCLB-T3/4-DA
IgG1-huCLB-T3/4-DAPS
IgG1-huCLB-T3/4-DANQ
IgG1-huCLB-T3/4-LFLEPS
IgG1-huCLB-T3/4-LFLEDANQPS
IgG1-huCLB-T3/4-Fab

B

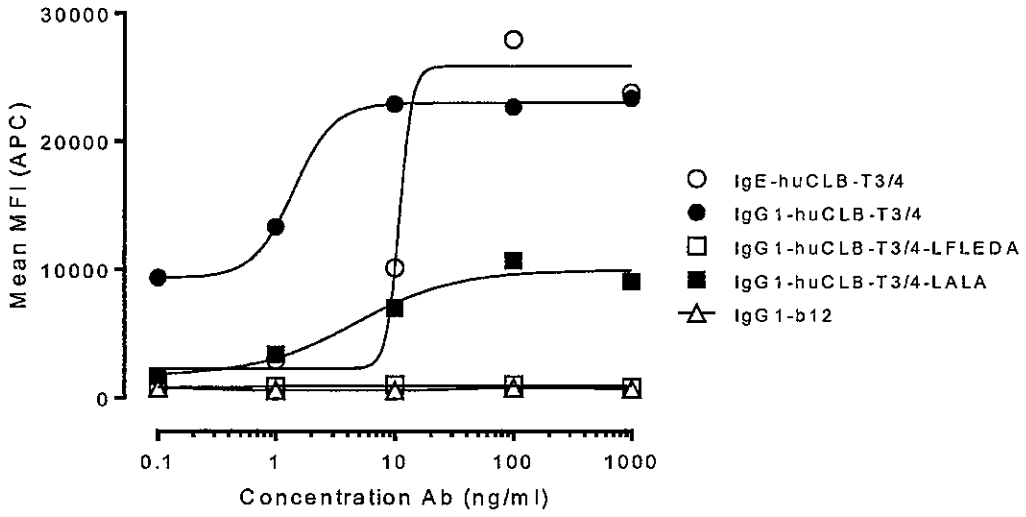
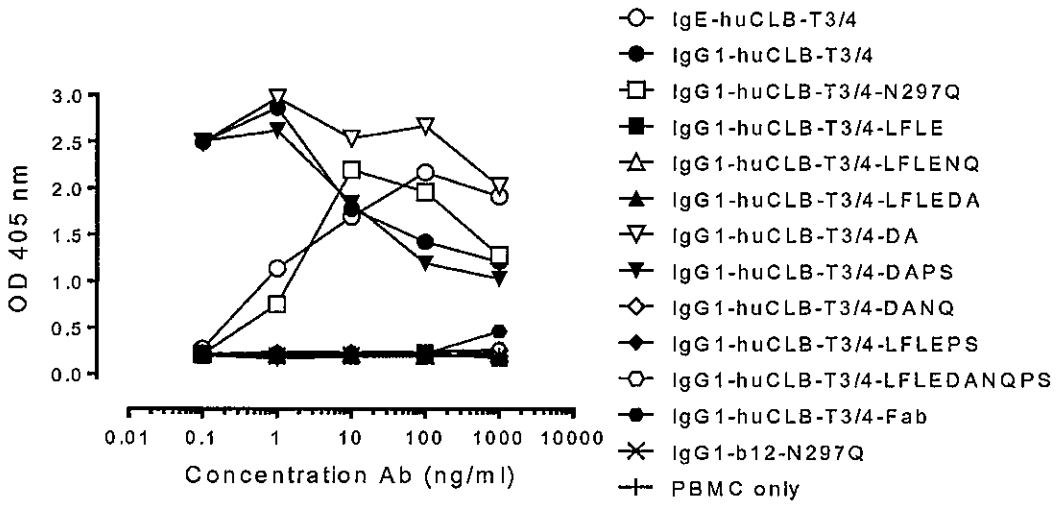

30000
20000
10000
0
Mean MFI (APC)
0.1
1
10
100
1000
Concentration Ab (ng/ml)
IgE-huCLB-T3/4
IgG1-huCLB-T3/4
IgG1-huCLB-T3/4-LFLEDA
IgG1-huCLB-T3/4-LALA
IgG1-b12

Figure 13

A


OD 405 nm
3.0
2.5
2.0
1.5
1.0
0.5
0.0
0.01
0.1
1
10
100
1000
10000
Concentration Ab (ng/ml)
IgE-huCLB-T3/4
IgG1-huCLB-T3/4
IgG1-huCLB-T3/4-N297Q
IgG1-huCLB-T3/4-LFLE
IgG1-huCLB-T3/4-LFLENQ
IgG1-huCLB-T3/4-LFLEDA
IgG1-huCLB-T3/4-DA
IgG1-huCLB-T3/4-DAPS
IgG1-huCLB-T3/4-DANQ
IgG1-huCLB-T3/4-LFLEPS
IgG1-huCLB-T3/4-LFLEDANQPS
IgG1-huCLB-T3/4-Fab
IgG1-b12-N297Q
PBMC only

B

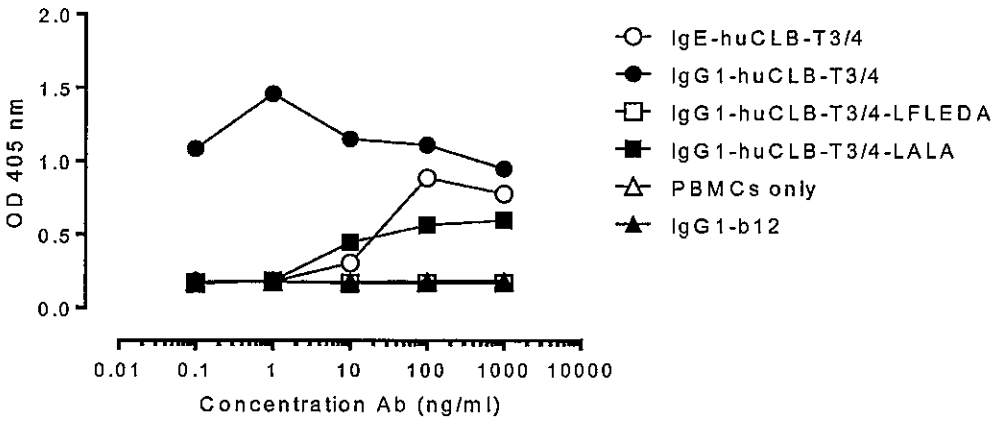
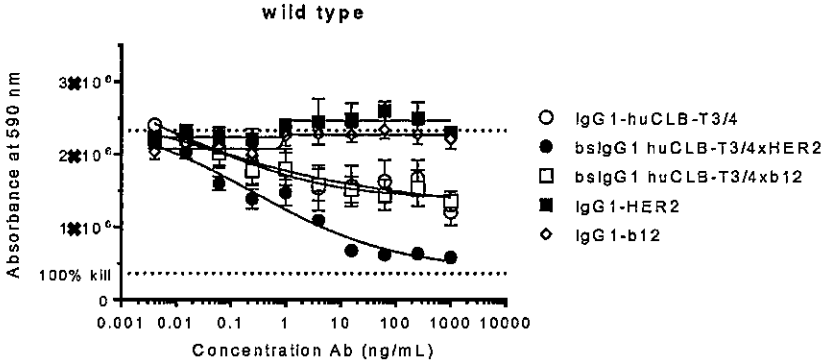

OD 405 nm
2.0
1.5
1.0
0.5
0.0
0.01
0.1
1
10
100
1000
10000
Concentration Ab (ng/ml)
IgE-huCLB-T3/4
IgG1-huCLB-T3/4
IgG1-huCLB-T3/4-LFLEDA
IgG1-huCLB-T3/4-LALA
PBMCs only
IgG1-b12

Figure 14

A


wild type
Absorbance at 590 nm
3*10^6
2*10^6
1*10^6
100% kill
0
0.001 0.01 0.1 1 10 100 1000 10000
Concentration Ab (ng/mL)
IgG1-huCLB-T3/4
bsIgG1 huCLB-T3/4xHER2
bsIgG1 huCLB-T3/4xb12
IgG1-HER2
IgG1-b12

B

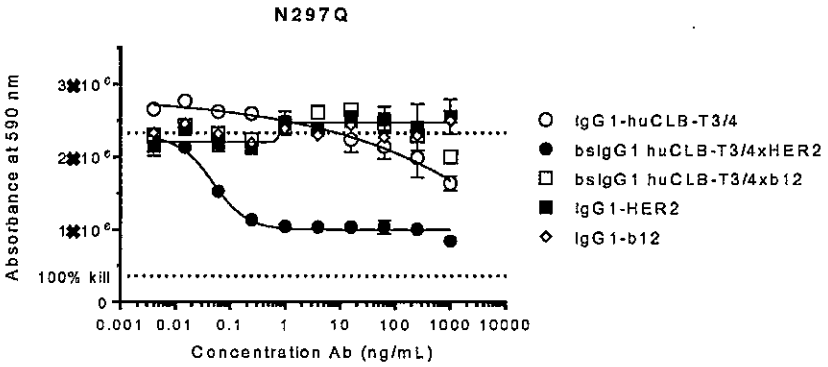
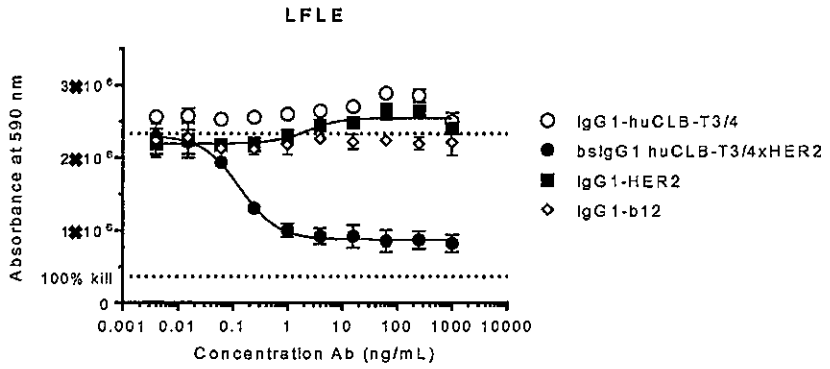

N297Q
Absorbance at 590 nm
3*10^6
2*10^6
1*10^6
100% kill
0
0.001 0.01 0.1 1 10 100 1000 10000
Concentration Ab (ng/mL)
IgG1-huCLB-T3/4
bsIgG1 huCLB-T3/4xHER2
bsIgG1 huCLB-T3/4xb12
IgG1-HER2
IgG1-b12

Figure 14 cont'd

C



D

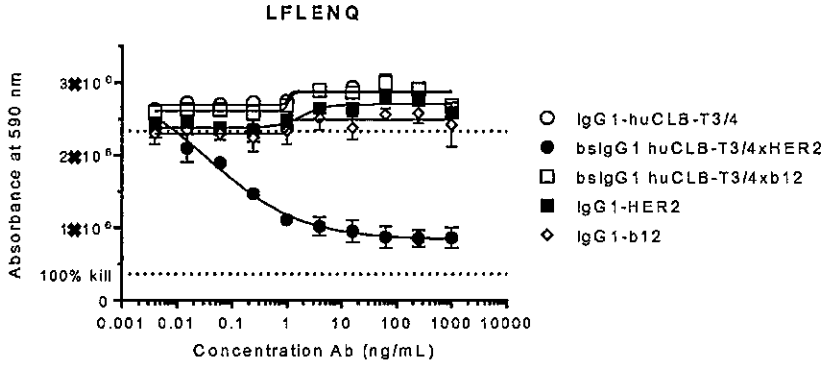
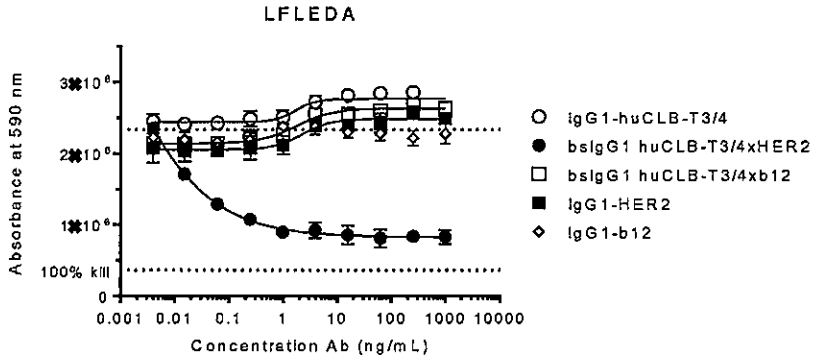
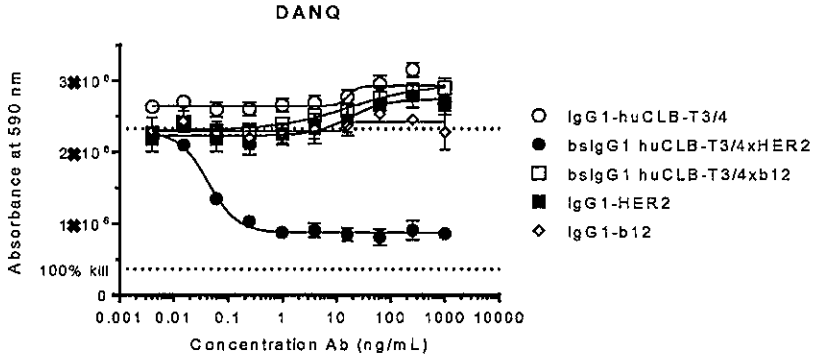


Figure 14 cont'd

E



F



G

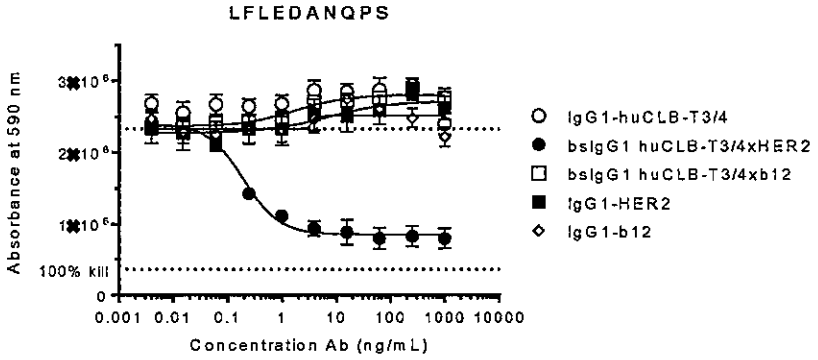
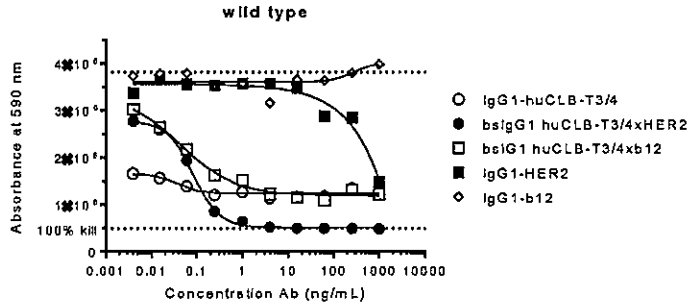
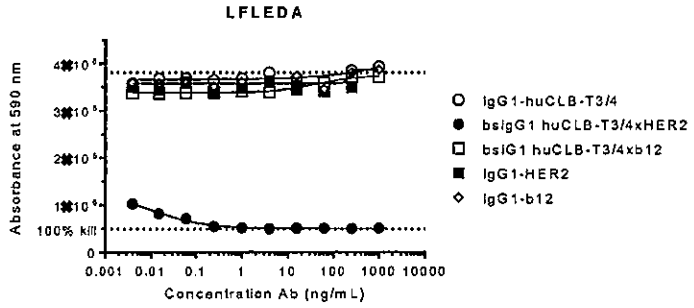


Figure 15

A



B



C

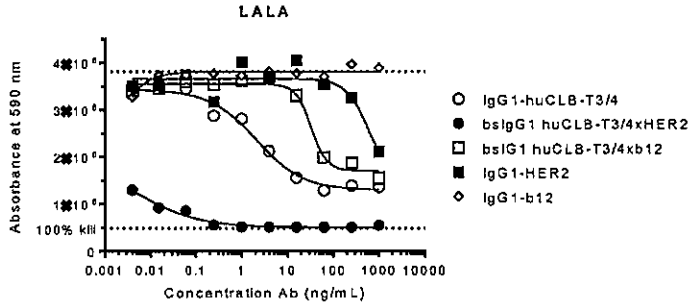
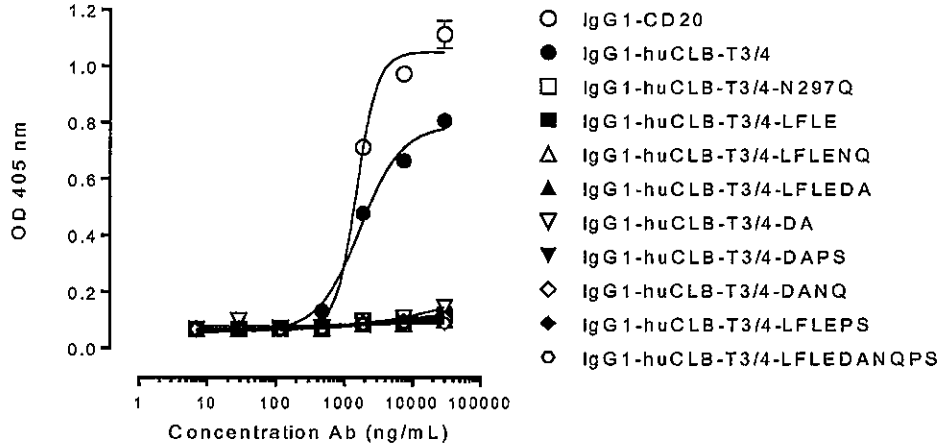


Figure 16

A


OD 405 nm
1.2
1.0
0.8
0.6
0.4
0.2
0.0
1
10
100
1000
10000
100000
Concentration Ab (ng/mL)
IgG1-CD20
IgG1-huCLB-T3/4
IgG1-huCLB-T3/4-N297Q
IgG1-huCLB-T3/4-LFLE
IgG1-huCLB-T3/4-LFLENQ
IgG1-huCLB-T3/4-LFLEDA
IgG1-huCLB-T3/4-DA
IgG1-huCLB-T3/4-DAPS
IgG1-huCLB-T3/4-DANQ
IgG1-huCLB-T3/4-LFLEPS
IgG1-huCLB-T3/4-LFLEDANQPS

B

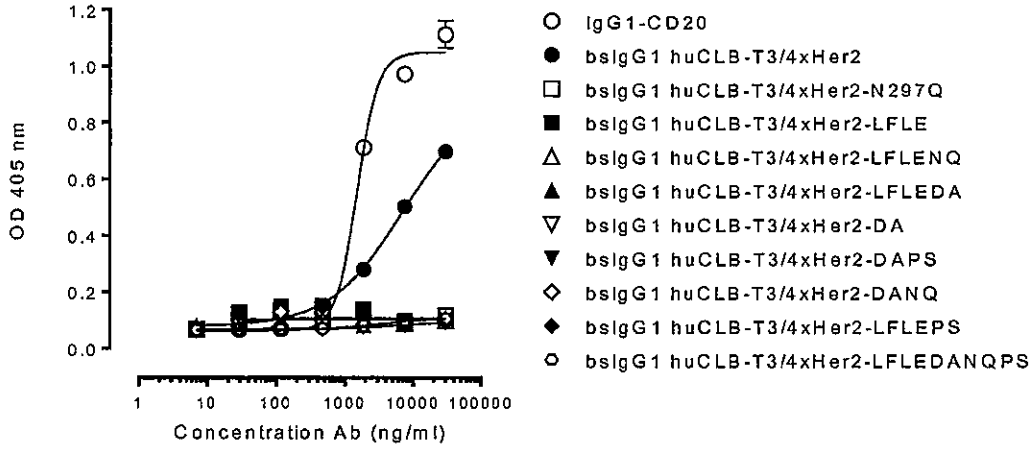
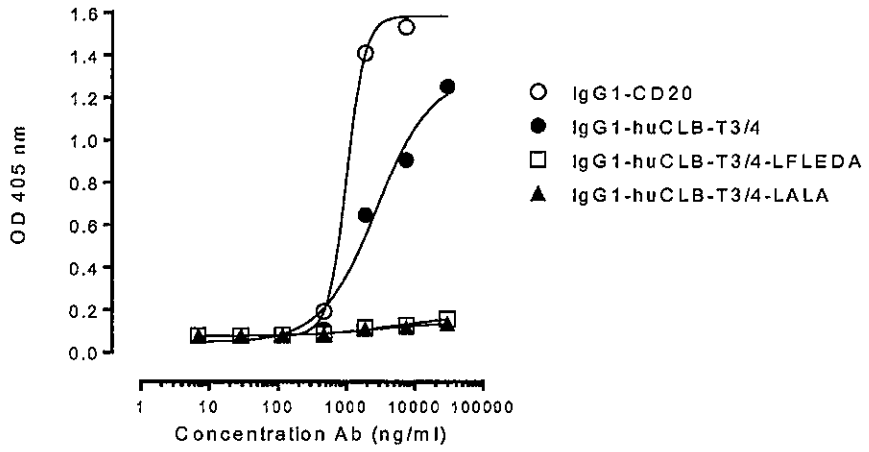

OD 405 nm
1.2
1.0
0.8
0.6
0.4
0.2
0.0
1
10
100
1000
10000
100000
Concentration Ab (ng/ml)
IgG1-CD20
bsIgG1 huCLB-T3/4xHer2
bsIgG1 huCLB-T3/4xHer2-N297Q
bsIgG1 huCLB-T3/4xHer2-LFLE
bsIgG1 huCLB-T3/4xHer2-LFLENQ
bsIgG1 huCLB-T3/4xHer2-LFLEDA
bsIgG1 huCLB-T3/4xHer2-DA
bsIgG1 huCLB-T3/4xHer2-DAPS
bsIgG1 huCLB-T3/4xHer2-DANQ
bsIgG1 huCLB-T3/4xHer2-LFLEPS
bsIgG1 huCLB-T3/4xHer2-LFLEDANQPS

Figure 16 cont'd

C



D

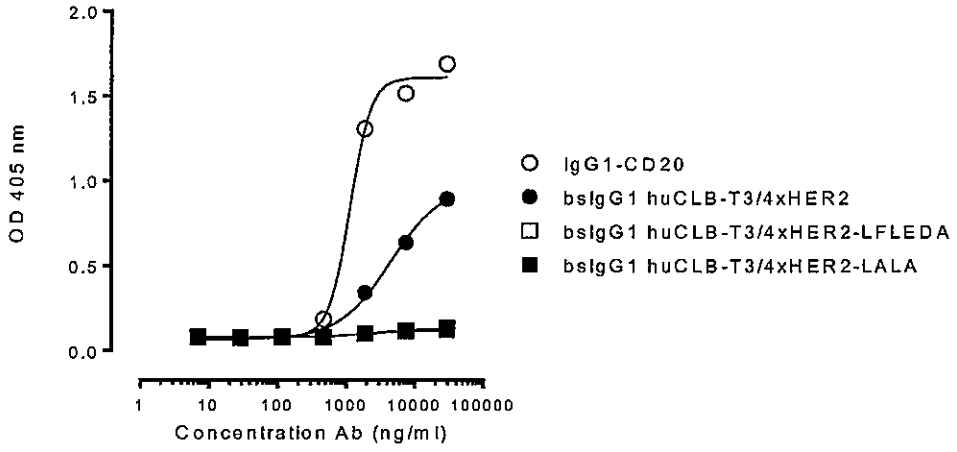
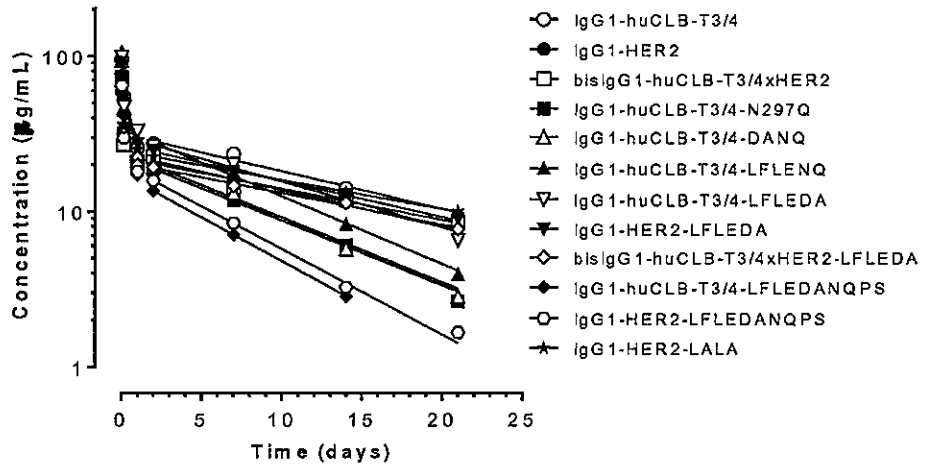


Figure 17

A


Concentration (µg/mL)
100
10
1
0
5
10
15
20
25
Time (days)
IgG1-huCLB-T3/4
IgG1-HER2
bisIgG1-huCLB-T3/4xHER2
IgG1-huCLB-T3/4-N297Q
IgG1-huCLB-T3/4-DANQ
IgG1-huCLB-T3/4-LFLENQ
IgG1-huCLB-T3/4-LFLEDA
IgG1-HER2-LFLEDA
bisIgG1-huCLB-T3/4xHER2-LFLEDA
IgG1-huCLB-T3/4-LFLEDANQPS
IgG1-HER2-LFLEDANQPS
IgG1-HER2-LALA

B

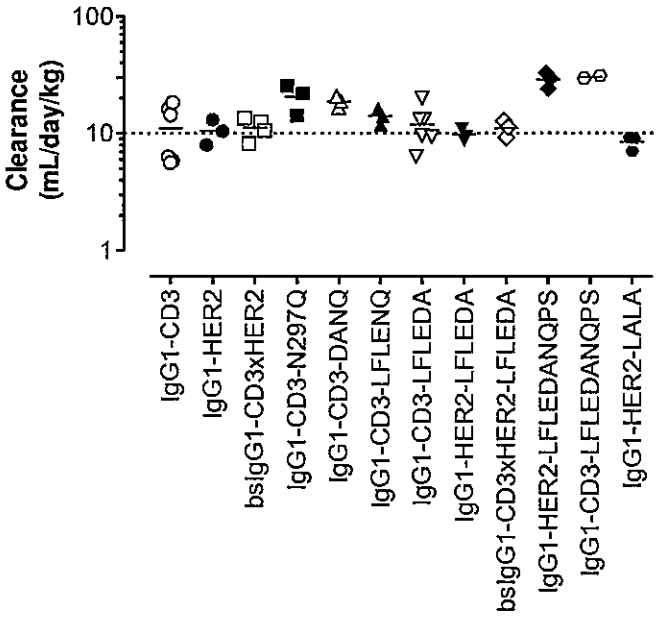

Clearance (mL/day/kg)
100
10
1
IgG1-CD3
IgG1-HER2
bsIgG1-CD3xHER2
IgG1-CD3-N297Q
IgG1-CD3-DANQ
IgG1-CD3-LFLENQ
IgG1-CD3-LFLEDA
IgG1-HER2-LFLEDA
bsIgG1-CD3xHER2-LFLEDA
IgG1-HER2-LFLEDANQPS
IgG1-CD3-LFLEDANQPS
IgG1-HER2-LALA

Figure 18

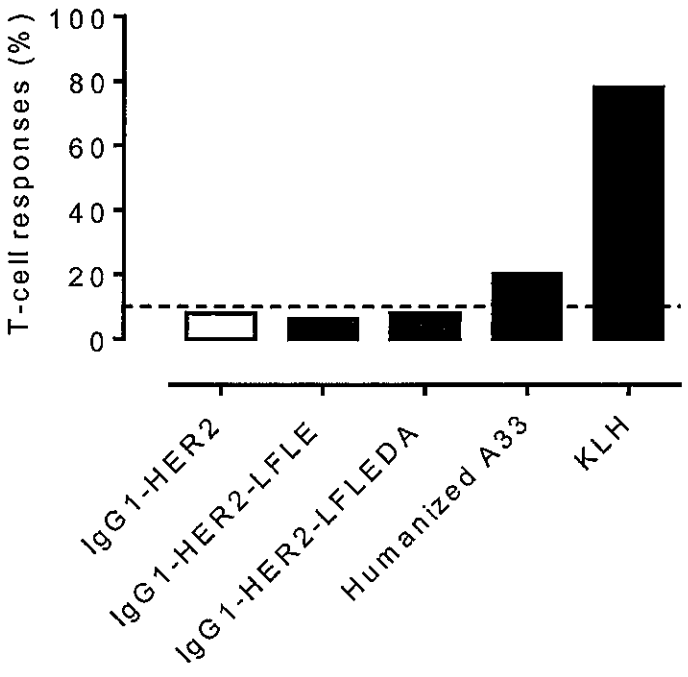

T-cell responses (%)
100
80
60
40
20
0
IgG1-HER2
IgG1-HER2-LFLE
IgG1-HER2-LFLEDA
Humanized A33
KLH

Figure 19

VH

```
VH3 EVKLVESGGGLVKPGRSLRLSCAASGFTFNTYAMNWVRQAPGKGLEWVARIRSKYNNYATYYADSVKDRFTISRDDSKSILYLQMNSLKTEDTAMYYCVRHGNFGNSYVSWFAYWGQGTLVTVSS
VH2 ----------------------------------------------------------N---------------------------------------------------------- 99%
VH4 ----------------------------------------------------------------------------------M---------- 99%
VH1 ----------Q--G------------------------------------------S------N---------------------------------------------------- 97%
```

VL

```
VL1 QAVVTQEPSFSVSPGGTVTLTCRSSTGAVTTSNYANWVQQTPGQAFRGLIGGTNKRAPGVPARFSGSLIGDKAALTITGAQADDESIYFCALWYSNLWVFGGGTKLTVL
VL2 ------------------------------------------------IL-N---------------------------------------------------- 97%
VL3 ------------------------------------------------IL-N----------------D-Y---------------------------------- 95%
```