Figures

Figure 1:

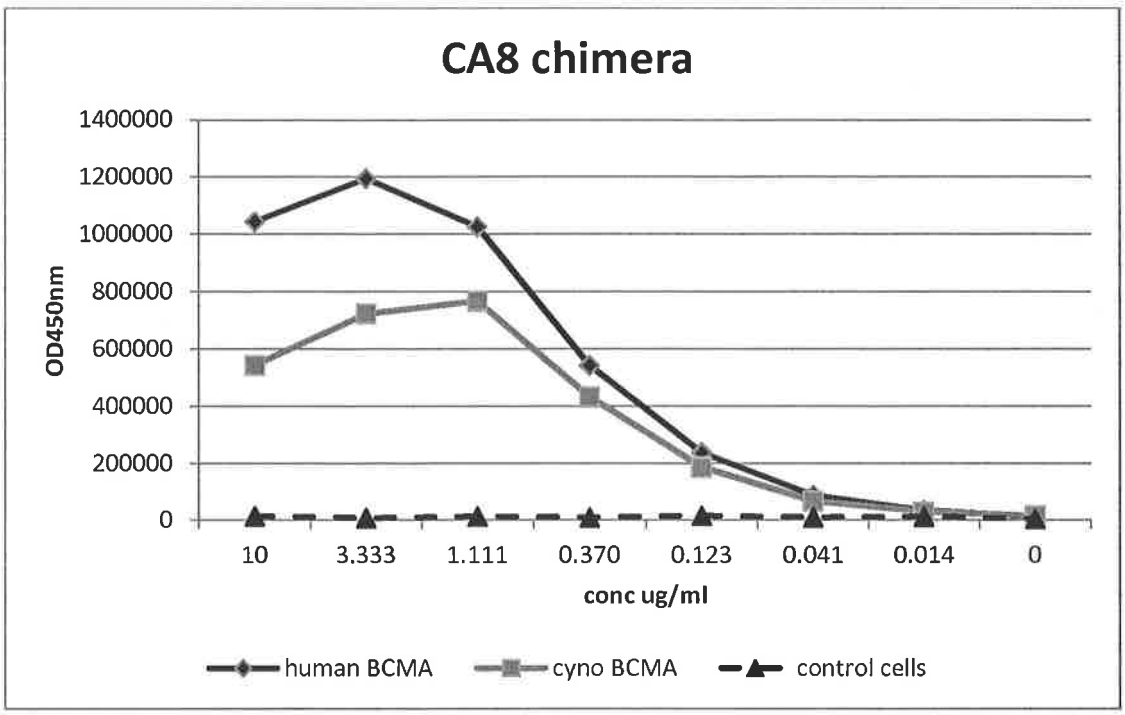


Figure 2:

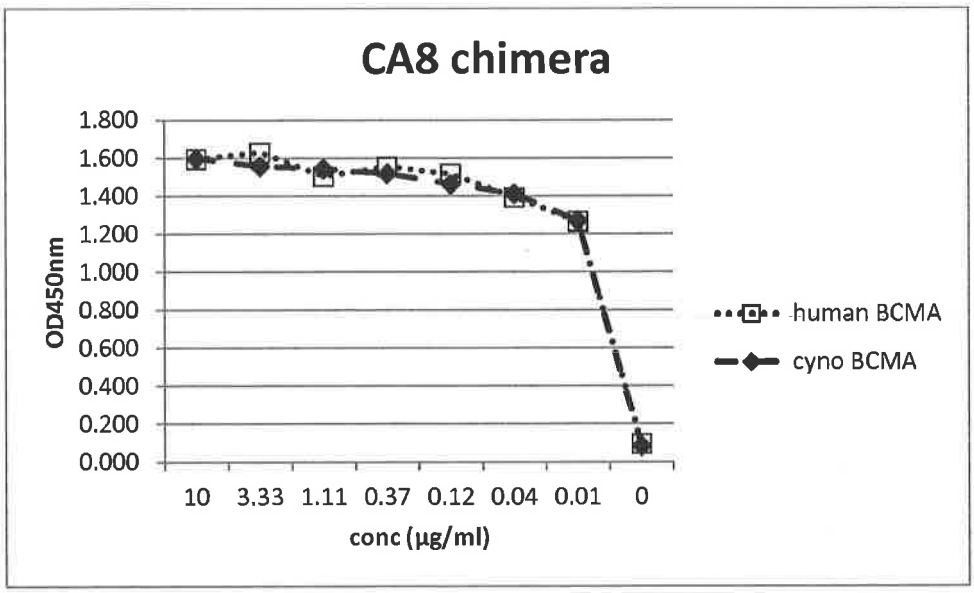

CA8 chimera
OD450nm
1.800
1.600
1.400
1.200
1.000
0.800
0.600
0.400
0.200
0.000
10
3.33
1.11
0.37
0.12
0.04
0.01
0
conc (µg/ml)
human BCMA
cyno BCMA

Figure 3:

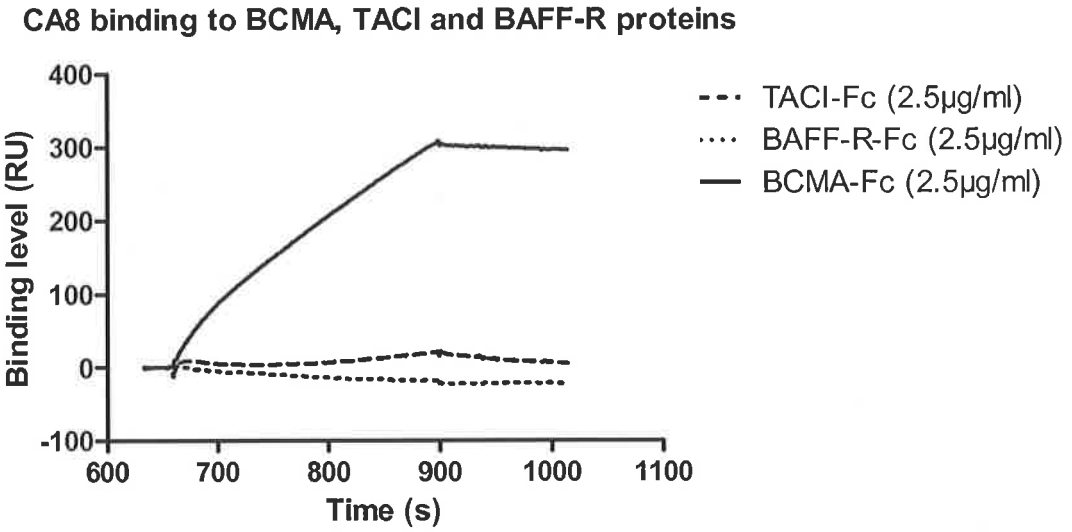

CA8 binding to BCMA, TACI and BAFF-R proteins
Binding level (RU)
400
300
200
100
0
-100
600
700
800
900
1000
1100
Time (s)
TACI-Fc (2.5µg/ml)
BAFF-R-Fc (2.5µg/ml)
BCMA-Fc (2.5µg/ml)

Figure 4:

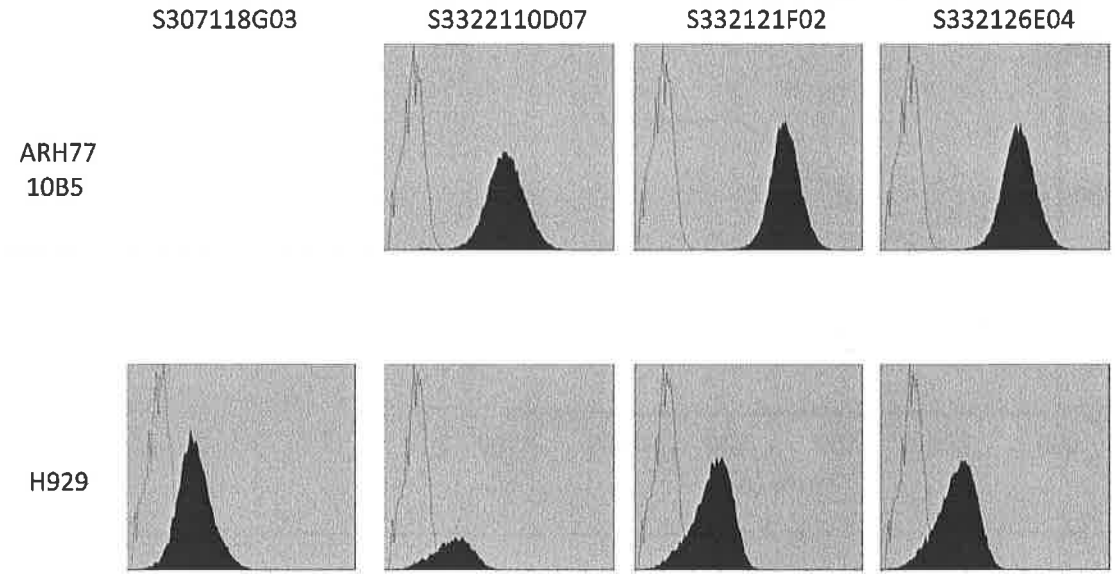

S307118G03
S3322110D07
S332121F02
S332126E04
ARH77
10B5
H929

Figure 5:

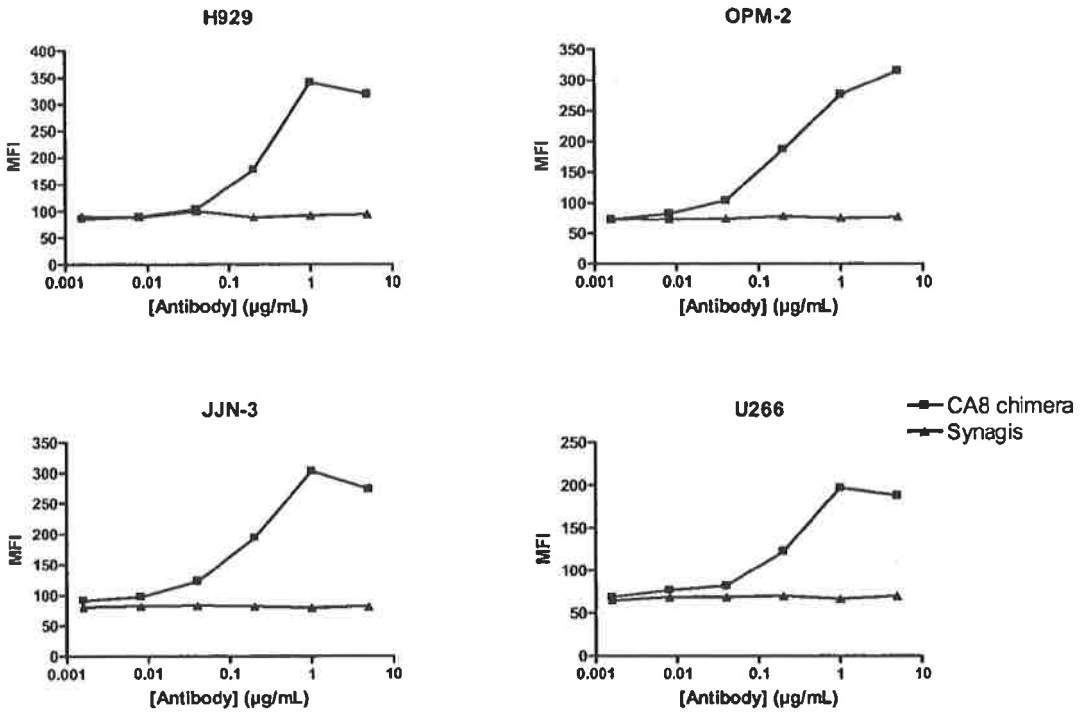
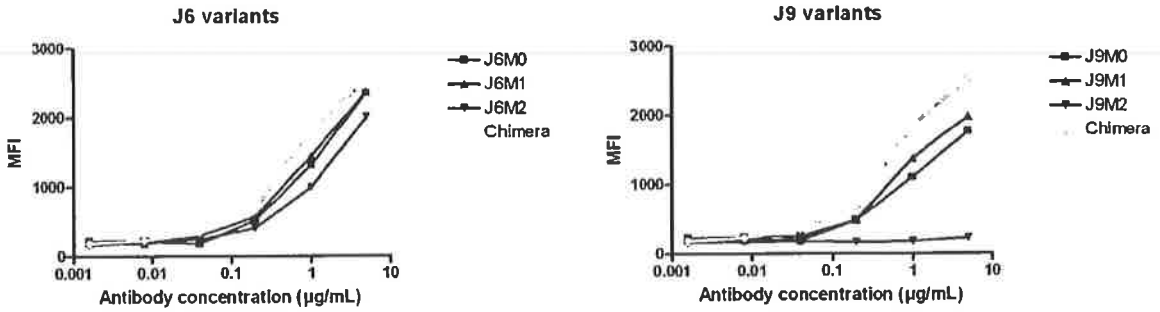


Figure 6:

A- Binding to ARH-77 10B5 cells



B - Binding to H929 cells

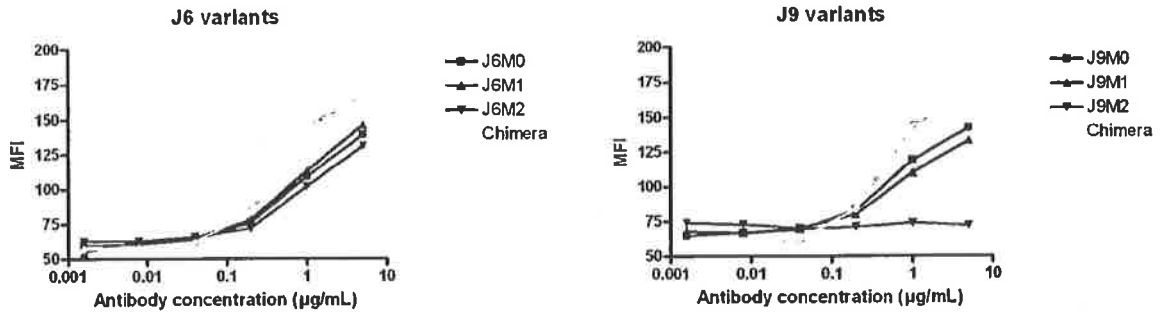
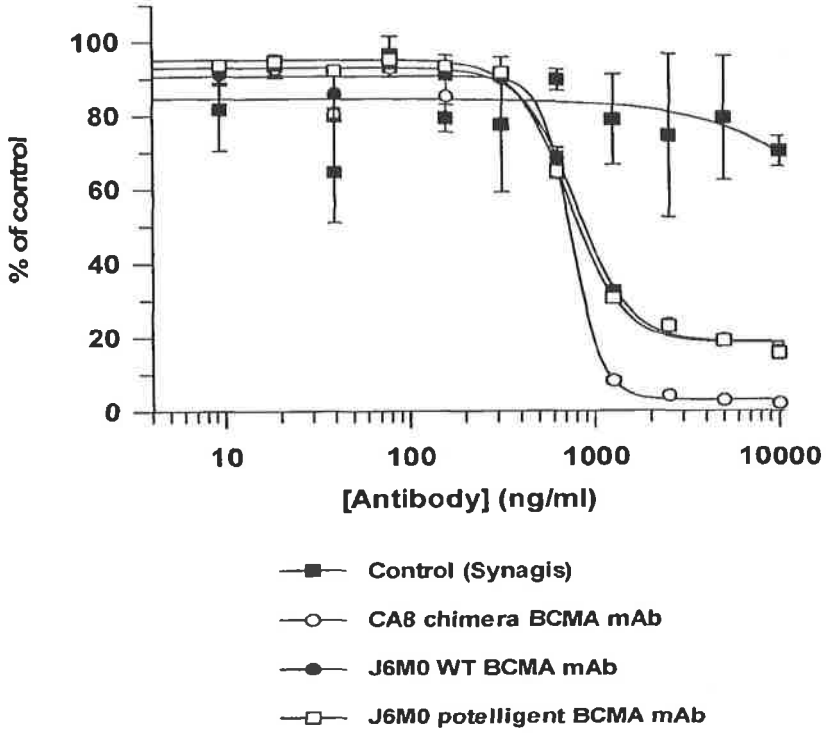
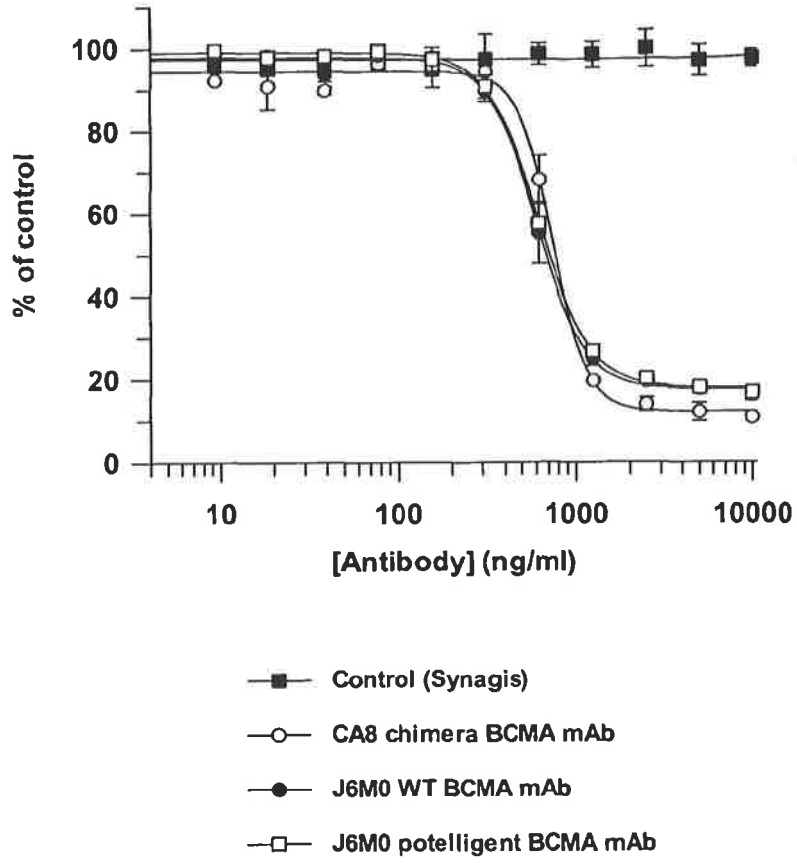


Figure 7:

(A)


100
80
60
40
20
0
% of control
10
100
1000
10000
[Antibody] (ng/ml)
Control (Synagis)
CA8 chimera BCMA mAb
J6M0 WT BCMA mAb
J6M0 potelligent BCMA mAb

(B)


100
80
60
40
20
0
% of control
10
100
1000
10000
[Antibody] (ng/ml)
Control (Synagis)
CA8 chimera BCMA mAb
J6M0 WT BCMA mAb
J6M0 potelligent BCMA mAb

(C)

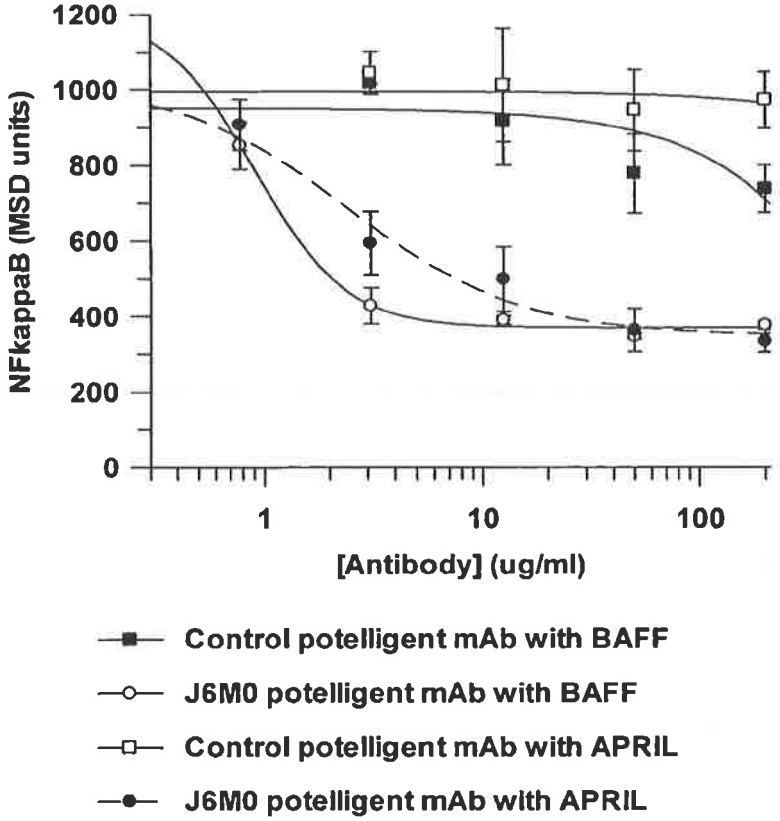
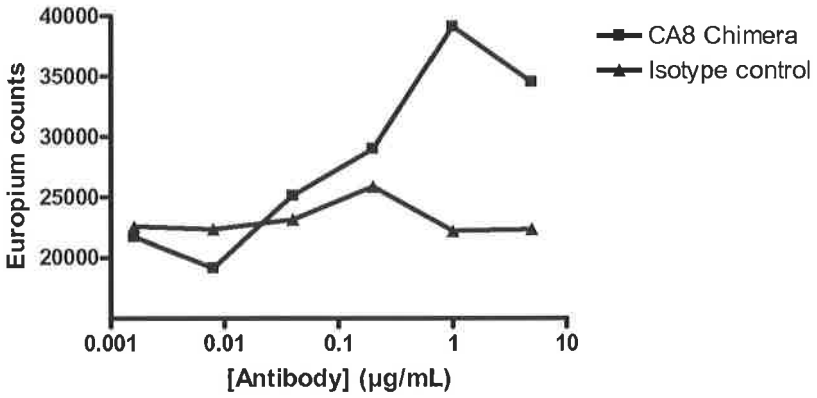

1200
1000
800
600
400
200
0
NFkappaB (MSD units)
1
10
100
[Antibody] (ug/ml)
Control potelligent mAb with BAFF
J6M0 potelligent mAb with BAFF
Control potelligent mAb with APRIL
J6M0 potelligent mAb with APRIL

Figure 8:.

(A)


40000
35000
30000
25000
20000
Europium counts
0.001
0.01
0.1
1
10
[Antibody] (µg/mL)
CA8 Chimera
Isotype control

(B)

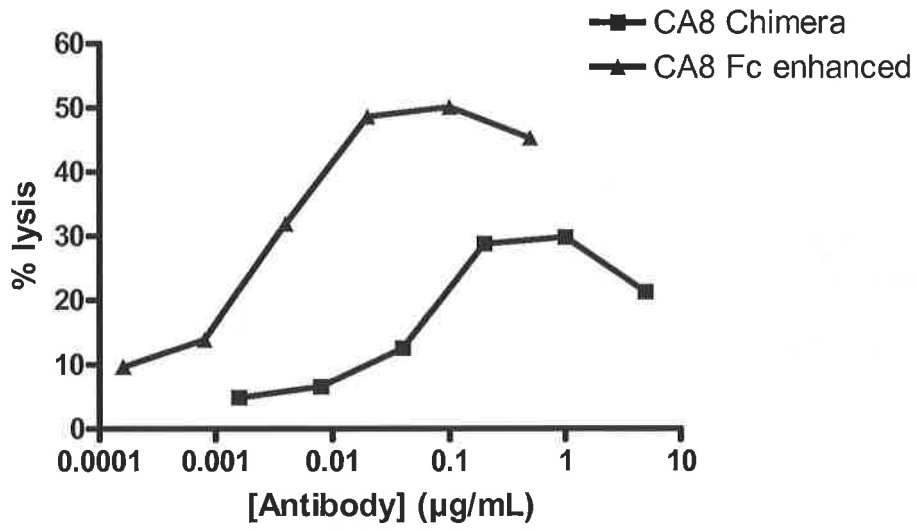
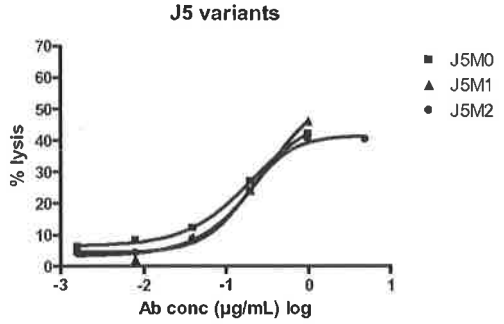
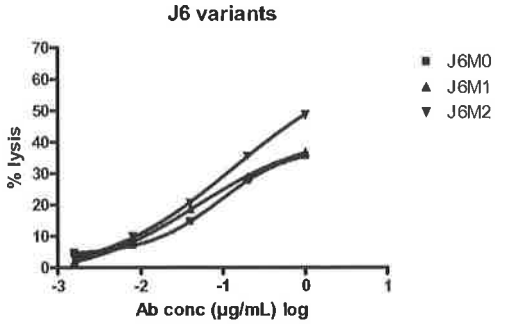

60
50
40
30
20
10
0
% lysis
0.0001
0.001
0.01
0.1
1
10
[Antibody] (µg/mL)
CA8 Chimera
CA8 Fc enhanced

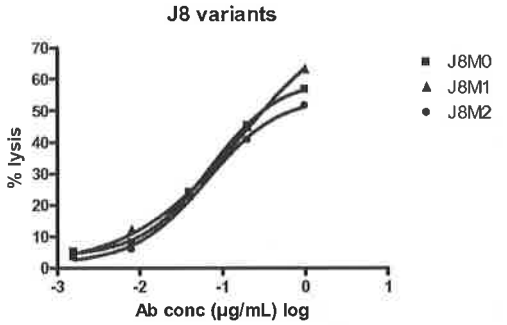
Figure 9:



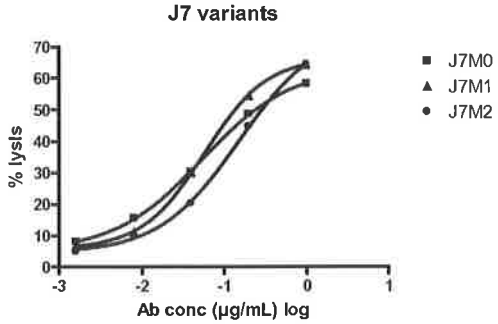
	J5M0	J5M1	J5M2
EC50	0.2087	0.3045	0.1822



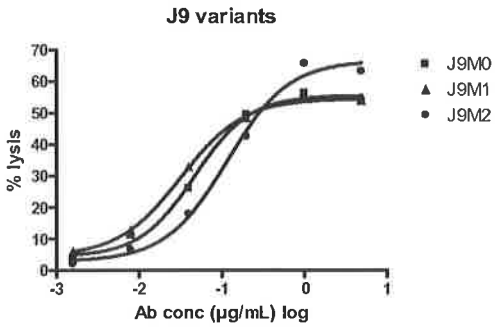
	J6M0	J6M1	J6M2
EC50	0.09187	0.04860	0.1364



	J8M0	J8M1	J8M2
EC50	0.07106	0.1734	0.06510



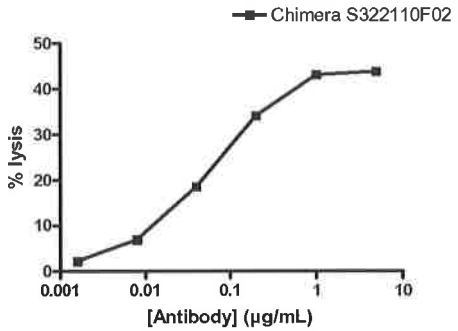
	J7M0	J7M1	J7M2
EC50	0.05386	0.05761	0.1506



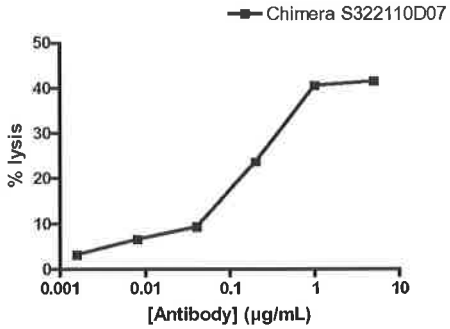
	J9M0	J9M1	J9M2
EC50	0.04738	0.03225	0.1170

Figure 10:

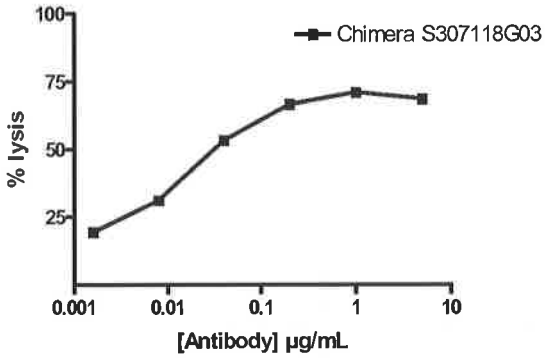
A



B



C



D

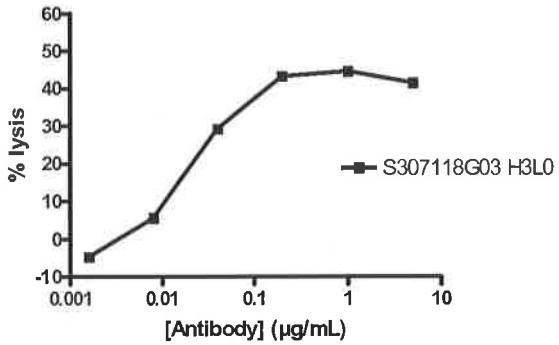


Figure 11:

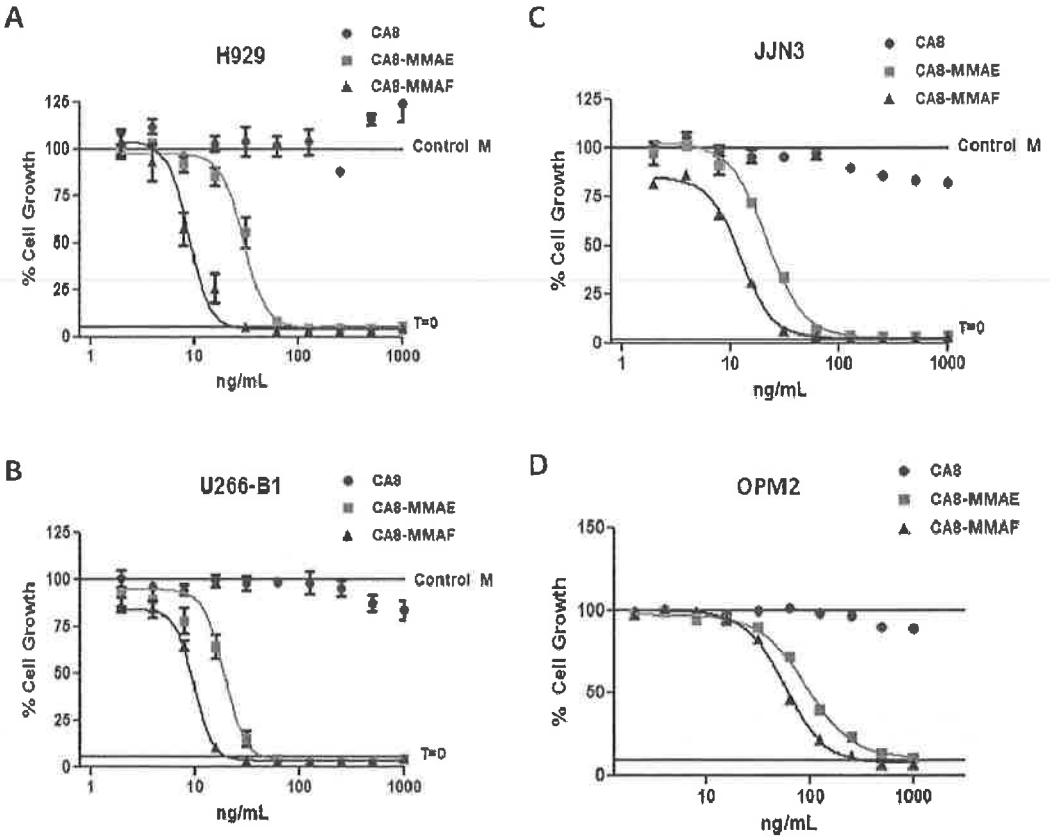

A
H929
CA8
CA8-MMAE
CA8-MMAF
Control M
T=0
% Cell Growth
ng/mL
C
JJN3
B
U266-B1
D
OPM2

Figure 12:

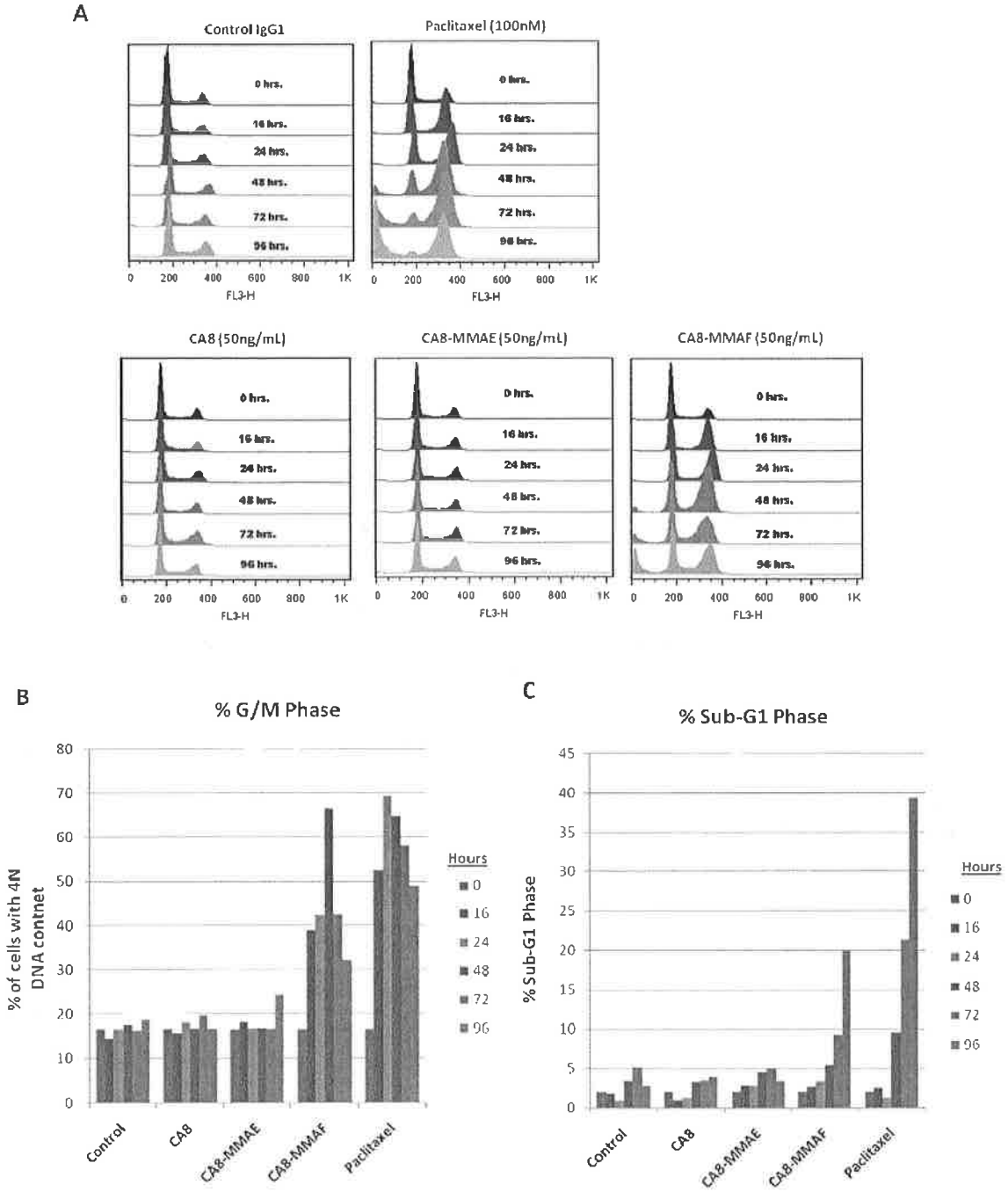

A
Control IgG1
Paclitaxel (100nM)
CA8 (50ng/mL)
CA8-MMAE (50ng/mL)
CA8-MMAF (50ng/mL)
0 hrs.
16 hrs.
24 hrs.
48 hrs.
72 hrs.
96 hrs.
0 200 400 600 800 1K
FL3-H
B
% G/M Phase
% of cells with 4N DNA contnet
Hours
0
16
24
48
72
96
Control
CA8
CA8-MMAE
CA8-MMAF
Paclitaxel
C
% Sub-G1 Phase
% Sub-G1 Phase

Figure 13:

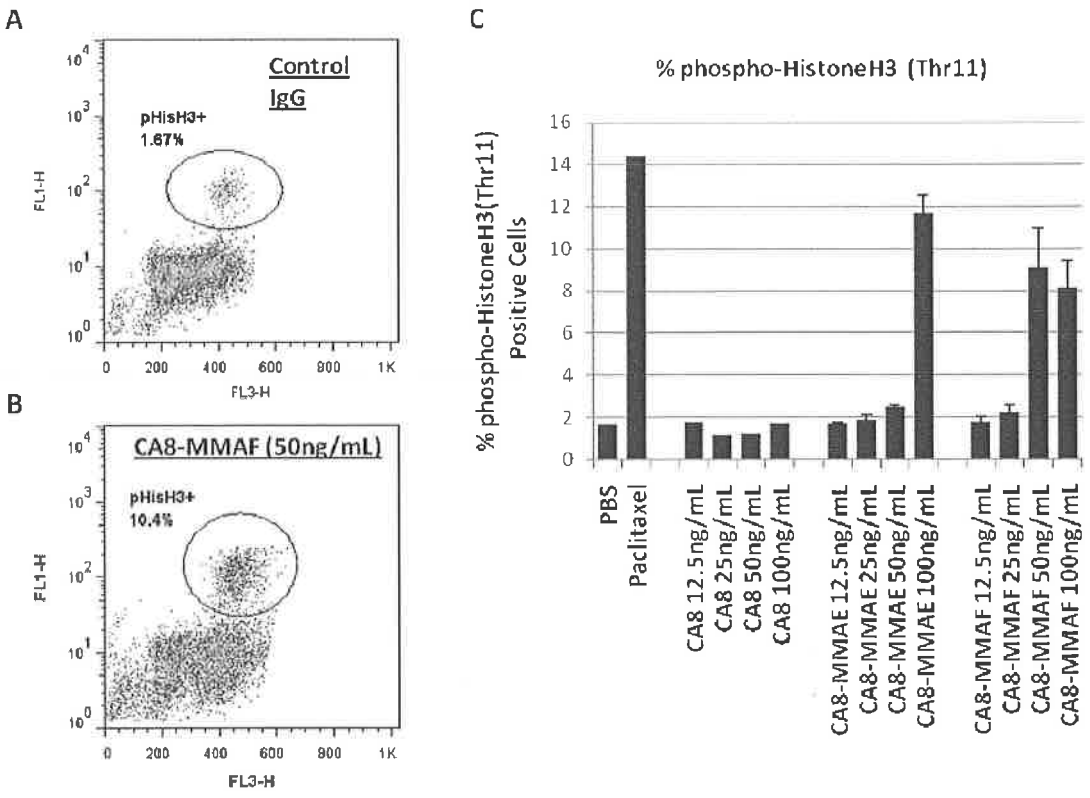

A
Control
IgG
pHisH3+
1.67%
FL1-H
FL3-H
B
CA8-MMAF (50ng/mL)
pHisH3+
10.4%
FL1-H
FL3-H
C
% phospho-HistoneH3 (Thr11)
% phospho-HistoneH3(Thr11) Positive Cells
PBS
Paclitaxel
CA8 12.5ng/mL
CA8 25ng/mL
CA8 50ng/mL
CA8 100ng/mL
CA8-MMAE 12.5ng/mL
CA8-MMAE 25ng/mL
CA8-MMAE 50ng/mL
CA8-MMAE 100ng/mL
CA8-MMAF 12.5ng/mL
CA8-MMAF 25ng/mL
CA8-MMAF 50ng/mL
CA8-MMAF 100ng/mL

Figure 14:

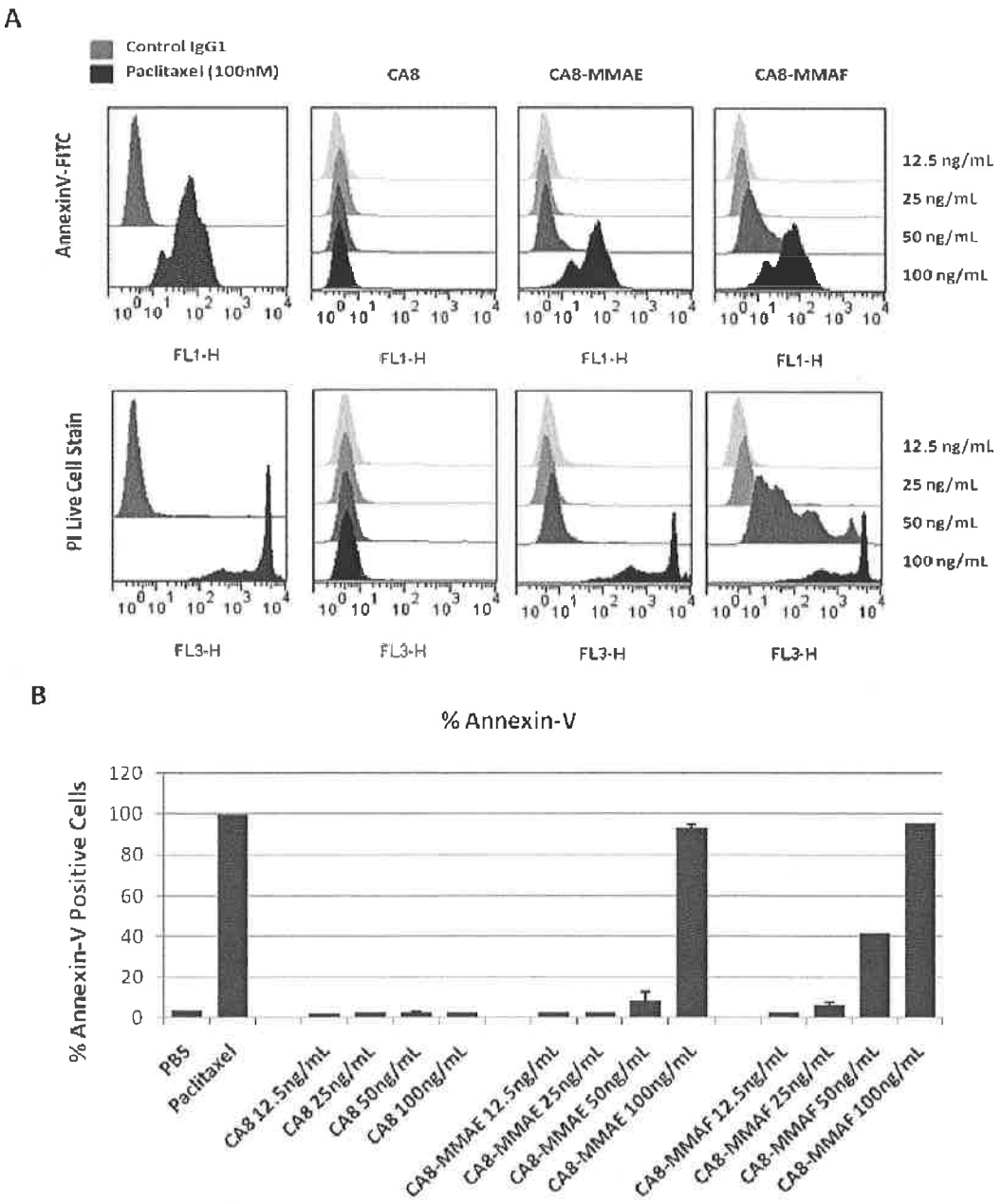

A
Control IgG1
Paclitaxel (100nM)
CA8
CA8-MMAE
CA8-MMAF
AnnexinV-FITC
PI Live Cell Stain
12.5 ng/mL
25 ng/mL
50 ng/mL
100 ng/mL
FL1-H
FL3-H
B
% Annexin-V
% Annexin-V Positive Cells
120
100
80
60
40
20
0
PBS
Paclitaxel
CA8 12.5ng/mL
CA8 25ng/mL
CA8 50ng/mL
CA8 100ng/mL
CA8-MMAE 12.5ng/mL
CA8-MMAE 25ng/mL
CA8-MMAE 50ng/mL
CA8-MMAE 100ng/mL
CA8-MMAF 12.5ng/mL
CA8-MMAF 25ng/mL
CA8-MMAF 50ng/mL
CA8-MMAF 100ng/mL

Figure 15:

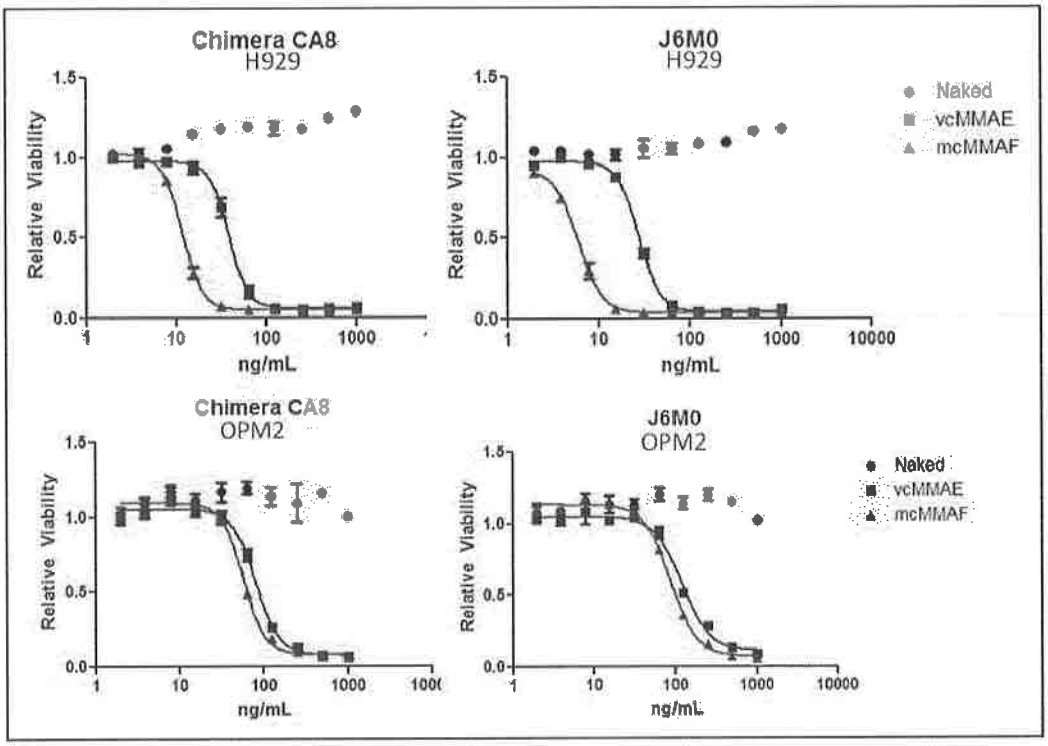

Chimera CA8
H929
J6M0
H929
Chimera CA8
OPM2
J6M0
OPM2
Relative Viability
ng/mL
Naked
vcMMAE
mcMMAF

Figure 16:

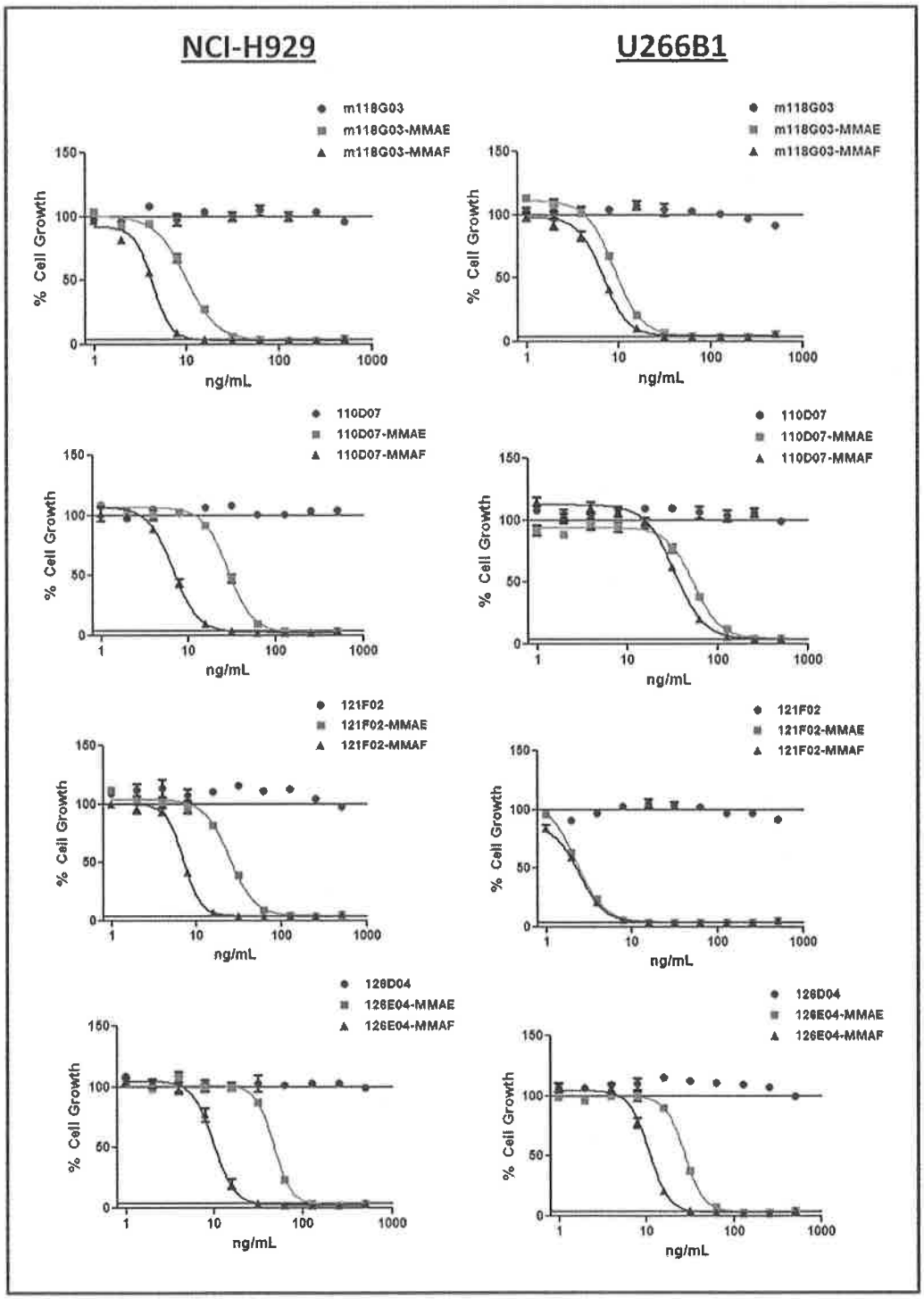

NCI-H929
U266B1
m118G03
m118G03-MMAE
m118G03-MMAF
110D07
110D07-MMAE
110D07-MMAF
121F02
121F02-MMAE
121F02-MMAF
126D04
126E04-MMAE
126E04-MMAF
% Cell Growth
ng/mL

Figure 17.

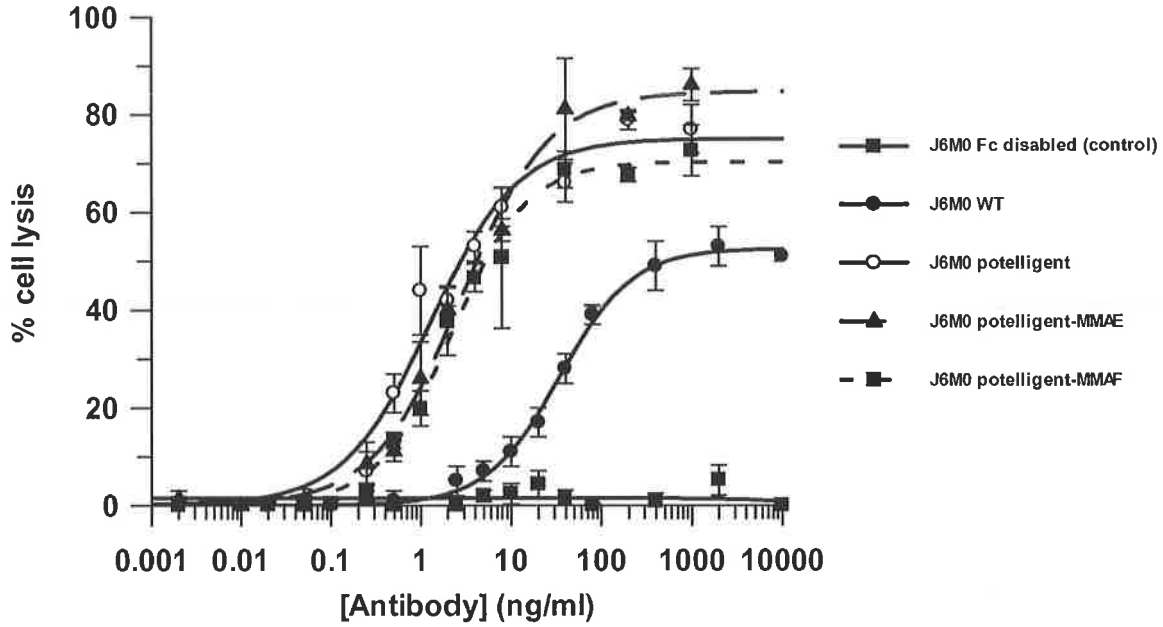
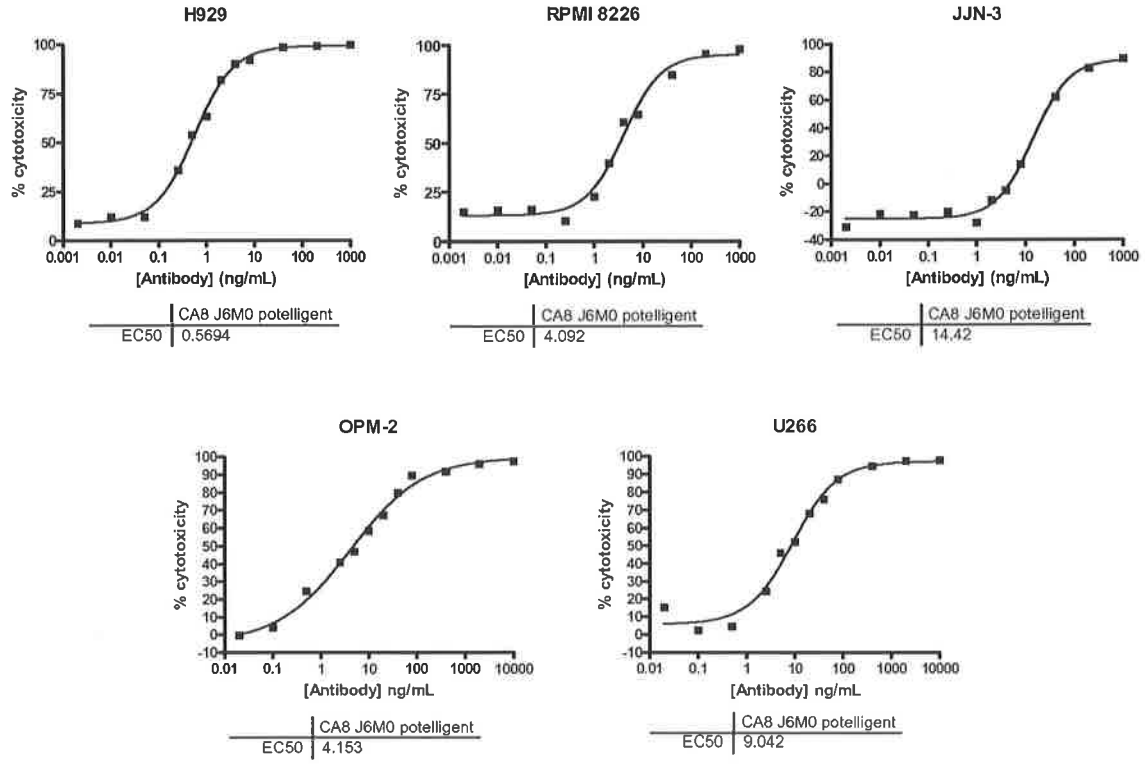


Figure 18

A



B

Figure 19.

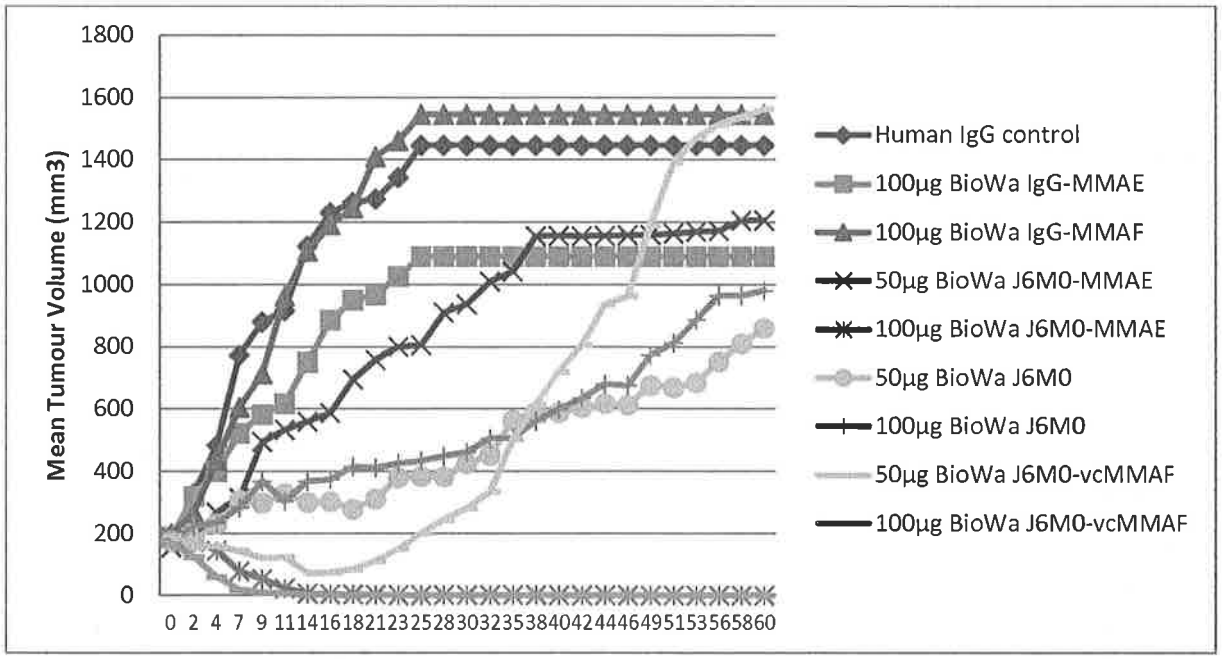
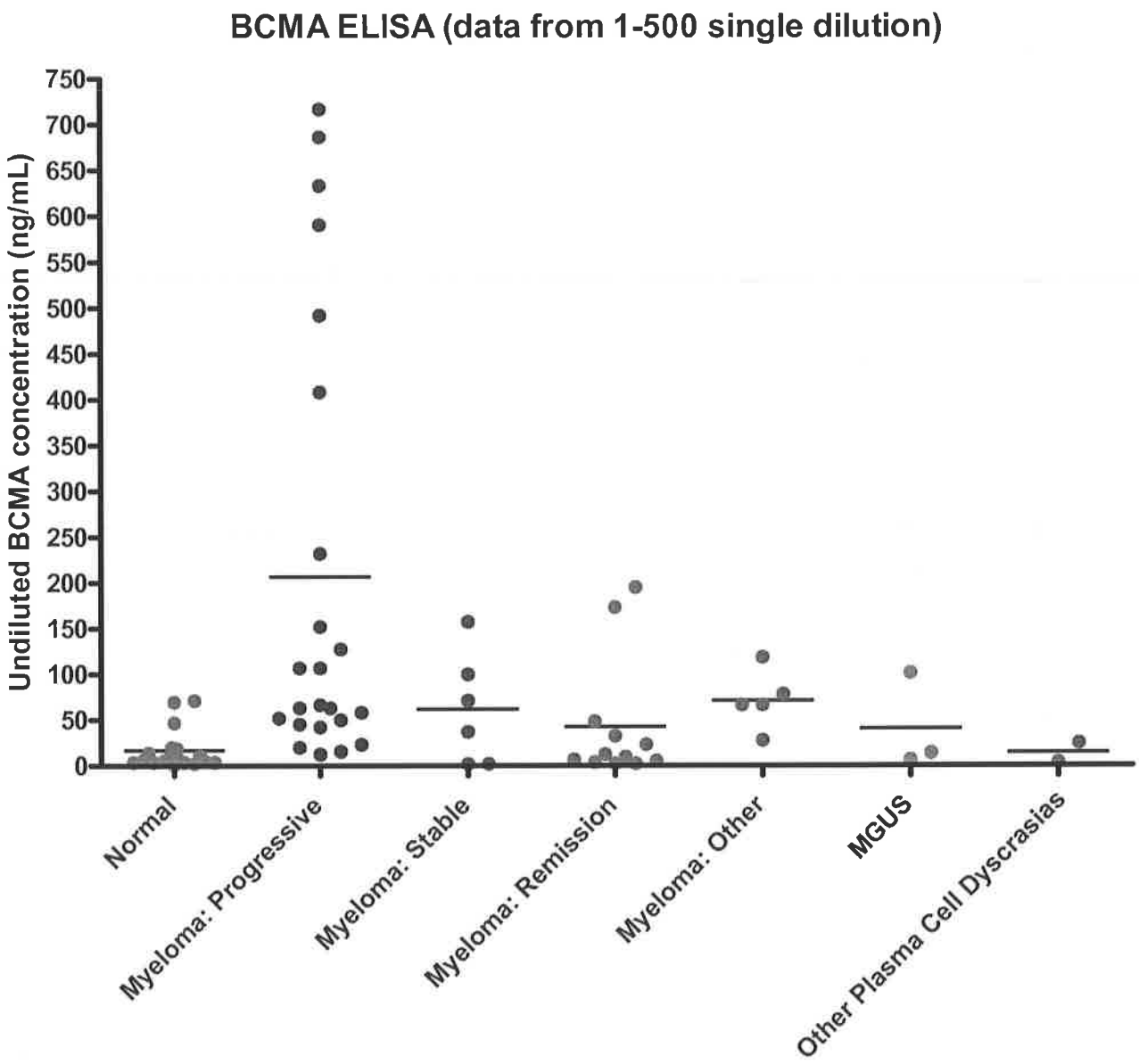

Mean Tumour Volume (mm3)
1800
1600
1400
1200
1000
800
600
400
200
0
0 2 4 7 9 11141618212325283032353840424446495153565860
Human IgG control
100µg BioWa IgG-MMAE
100µg BioWa IgG-MMAF
50µg BioWa J6M0-MMAE
100µg BioWa J6M0-MMAE
50µg BioWa J6M0
100µg BioWa J6M0
50µg BioWa J6M0-vcMMAF
100µg BioWa J6M0-vcMMAF

Figure 20



Normal: n=18
Myeloma: Progressive: n=23
Myeloma: Stable:n=6
Myeloma: Remission: n=12
Myeloma: Other: n=5
MGUS: n=3
Other PCD: n=2
***note: data above or below standards not graphed**