Figure 1

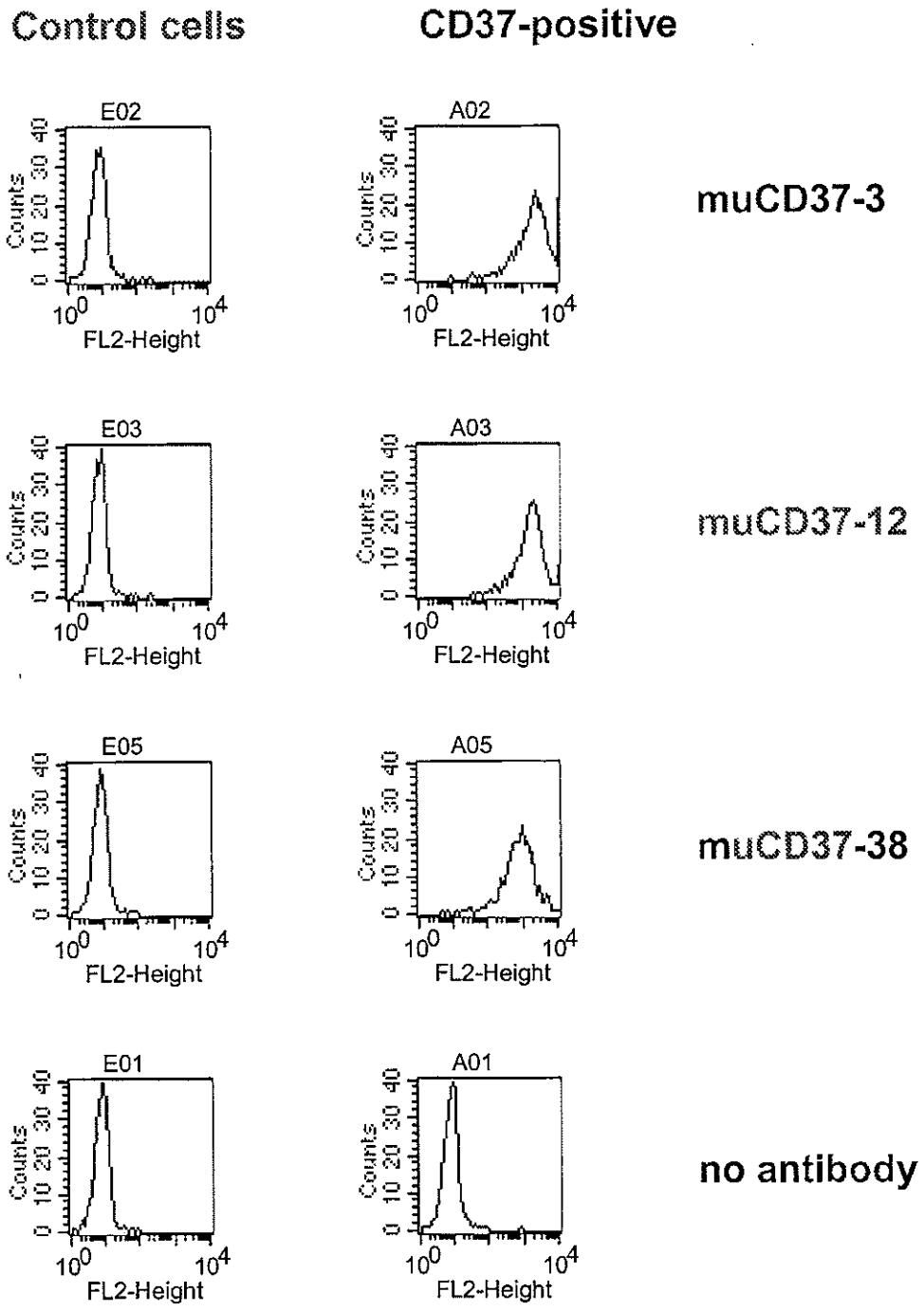

Control cells
CD37-positive
E02
A02
muCD37-3
E03
A03
muCD37-12
E05
A05
muCD37-38
E01
A01
no antibody
Counts
0 10 20 30 40
10^0
10^4
FL2-Height

Figure 2

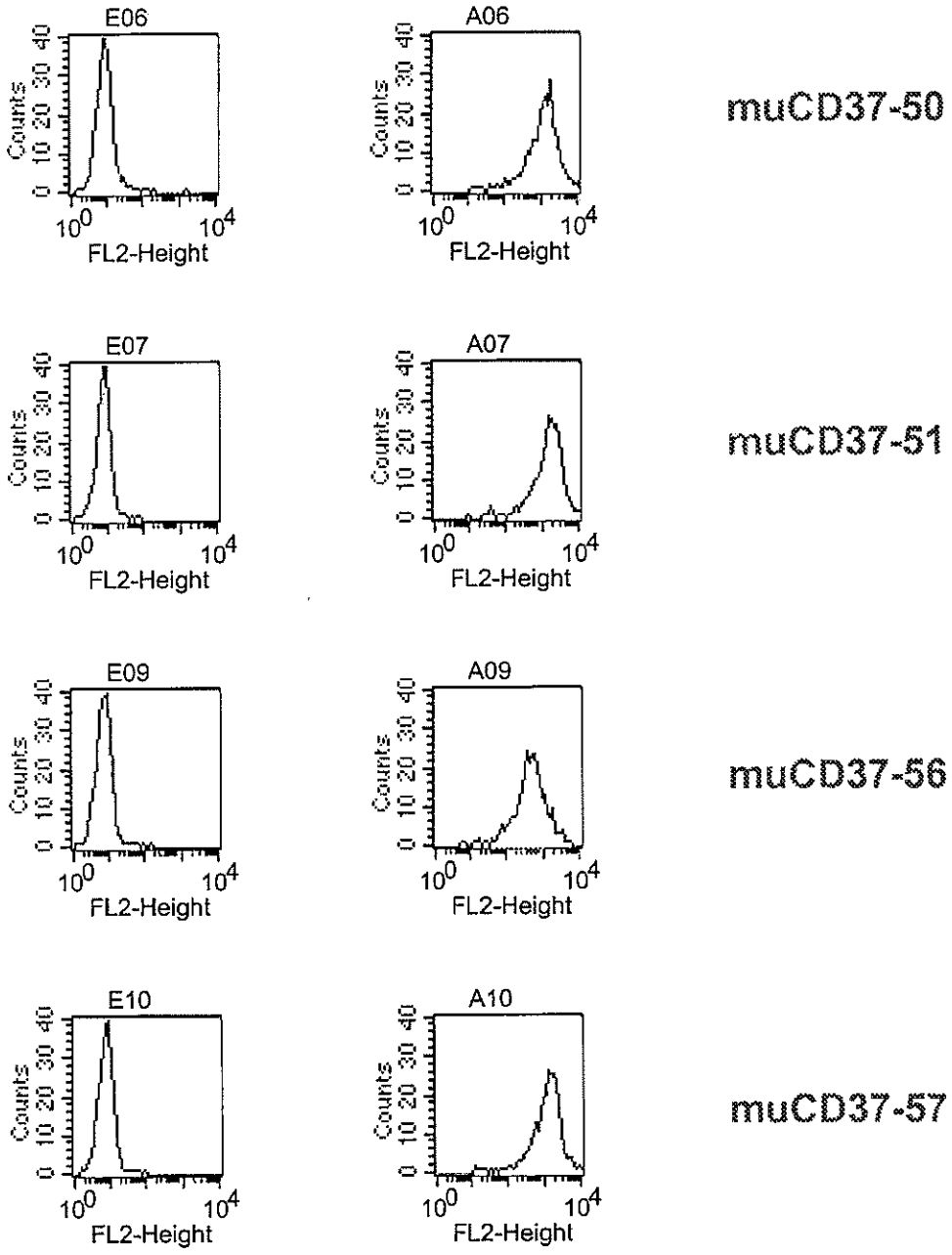
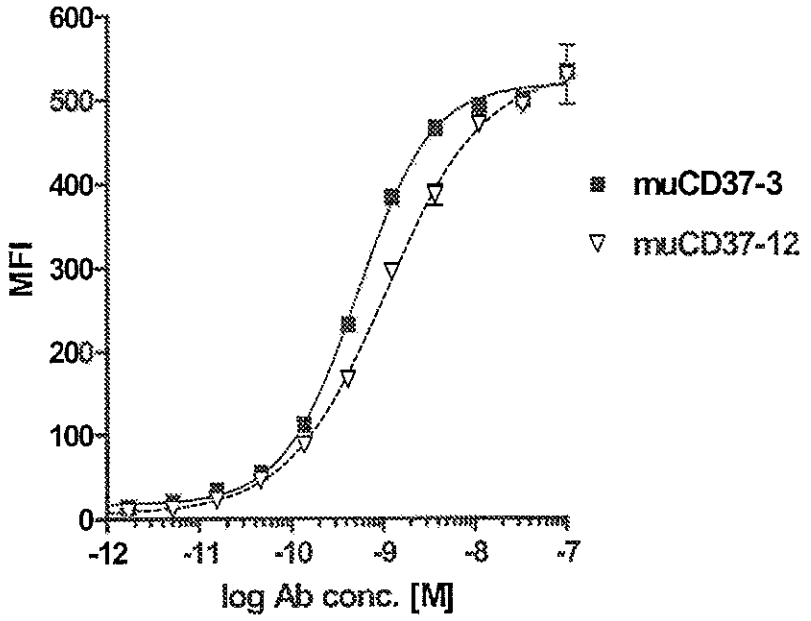

Control cells
CD37-positive
E06
A06
muCD37-50
E07
A07
muCD37-51
E09
A09
muCD37-56
E10
A10
muCD37-57
Counts
0 10 20 30 40
10^0
10^4
FL2-Height

Figure 3

A


600
500
400
300
200
100
0
MFI
-12
-11
-10
-9
-8
-7
log Ab conc. [M]
muCD37-3
muCD37-12

B

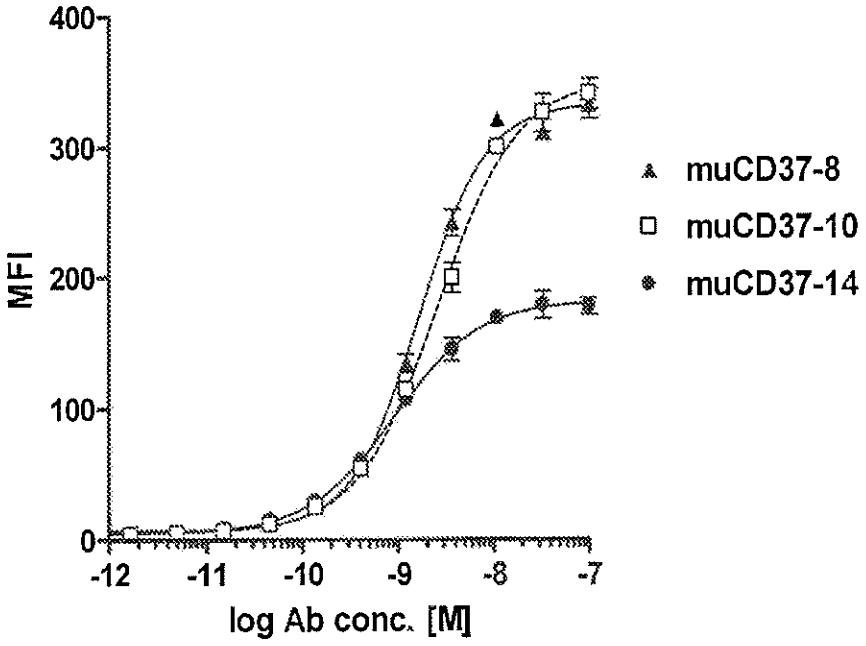

400
300
200
100
0
MFI
-12
-11
-10
-9
-8
-7
log Ab conc. [M]
muCD37-8
muCD37-10
muCD37-14

Figure 4

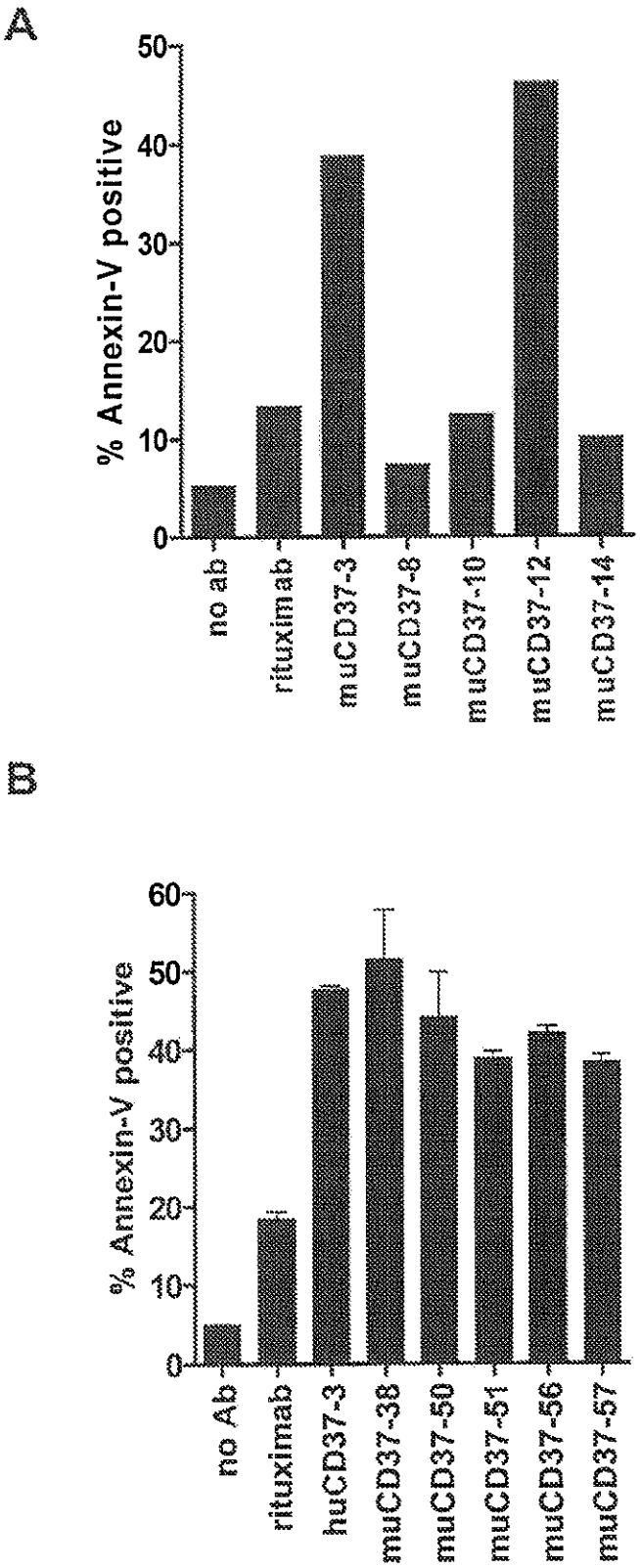

A
% Annexin-V positive
0
10
20
30
40
50
no ab
rituximab
muCD37-3
muCD37-8
muCD37-10
muCD37-12
muCD37-14
B
% Annexin-V positive
0
10
20
30
40
50
60
no Ab
rituximab
huCD37-3
muCD37-38
muCD37-50
muCD37-51
muCD37-56
muCD37-57

Figure 5

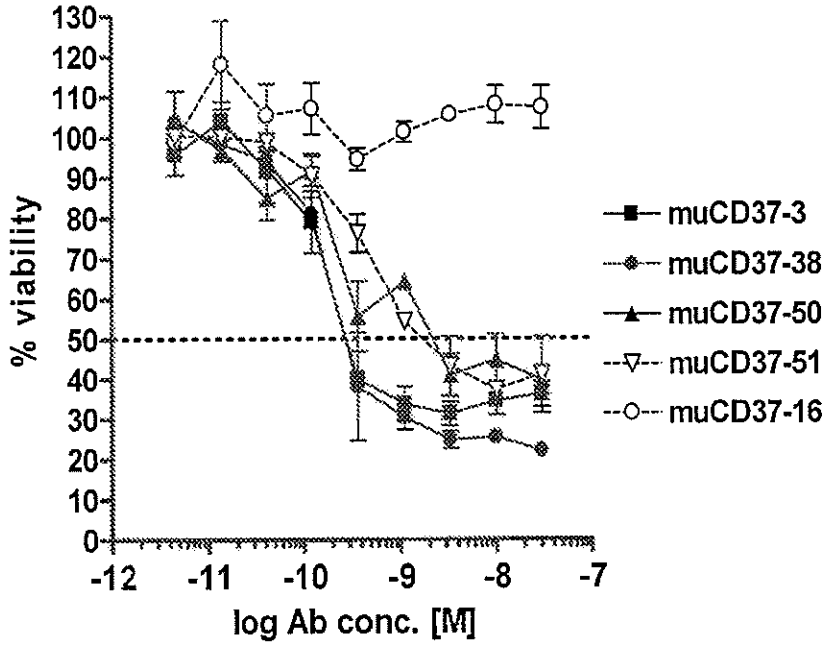

% viability
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-12
-11
-10
-9
-8
-7
log Ab conc. [M]
muCD37-3
muCD37-38
muCD37-50
muCD37-51
muCD37-16

Figure 6

A

CD37-3 V_L		
Kabat position	Murine residue	Human residue
1	D	D
3	Q	Q
9	**A**	***S***
15	V	V
18	**T**	***R***
40	**Q**	***P***
41	G	G
42	K	K
45	**Q**	***K***
57	G	G
60	S	S
67	S	S
70	**Q**	***D***
80	**S**	***P***
81	E	E
100	**G**	***Q***
103	K	K
107	K	K
108	R	R

B

CD37-3 V_H			
Kabat position	Murine residue	Human v1.00 residue	Human v1.01 residue
1	Q	Q	Q
3	Q	Q	Q
5	**K**	***Q***	***Q***
11	L	L	L
15	S	S	S
16	Q	Q	Q
17	**S**	***T***	***T***
28	S	S	S
41	P	P	P
42	G	G	G
43	K	K	K
61	**S**	***P***	**S**
62	**A**	***S***	***S***
64	K	K	K
65	S	S	S
74	S	S	S
75	K	K	K
83	**Q**	***T***	***T***
84	**T**	***A***	***A***
85	**D**	***A***	***A***
105	Q	Q	Q
108	L	L	L
112	S	S	S

Figure 7

A

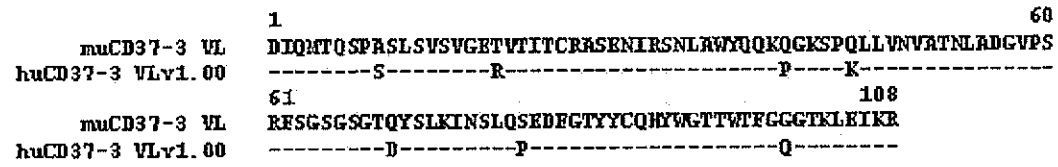
CD37-50 V_L		
Kabat position	Murine residue	Human residue
1	**D**	***E***
3	V	V
5	T	T
9	A	A
10	**I**	***T***
15	P	P
18	**K**	***R***
40	**S**	***P***
41	G	G
42	**T**	***Q***
57	G	G
60	**G**	***A***
67	S	S
77	S	S
81	E	E
100	**S**	***Q***
107	K	K
108	R	R

B

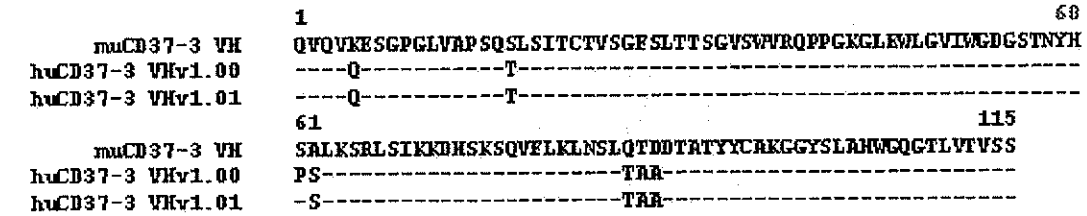
CD37-50 V_H		
Kabat position	Murine residue	Human residue
1	Q	Q
3	Q	Q
5	Q	Q
10	**D**	***G***
11	L	L
13	K	K
15	S	S
16	Q	Q
25	**T**	***S***
39	Q	Q
40	**F**	***H***
61	P	P
62	S	S
64	K	K
65	S	S
74	S	S
75	K	K
84	**T**	***A***
85	**E**	***A***
105	Q	Q
108	L	L
112	S	S

Figure 8

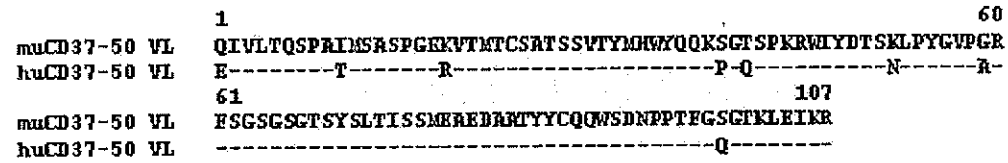
A



B



C



D

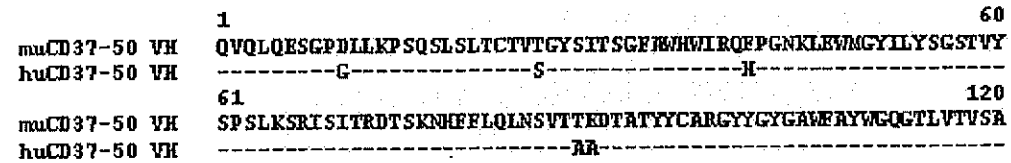
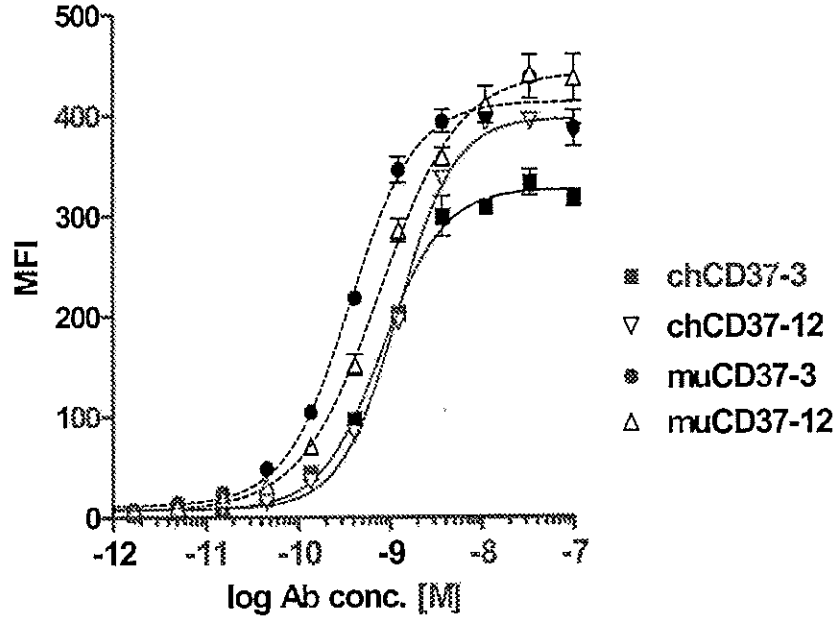


Figure 9

A


500
400
300
200
100
0
MFI
-12
-11
-10
-9
-8
-7
log Ab conc. [M]
chCD37-3
chCD37-12
muCD37-3
muCD37-12

B

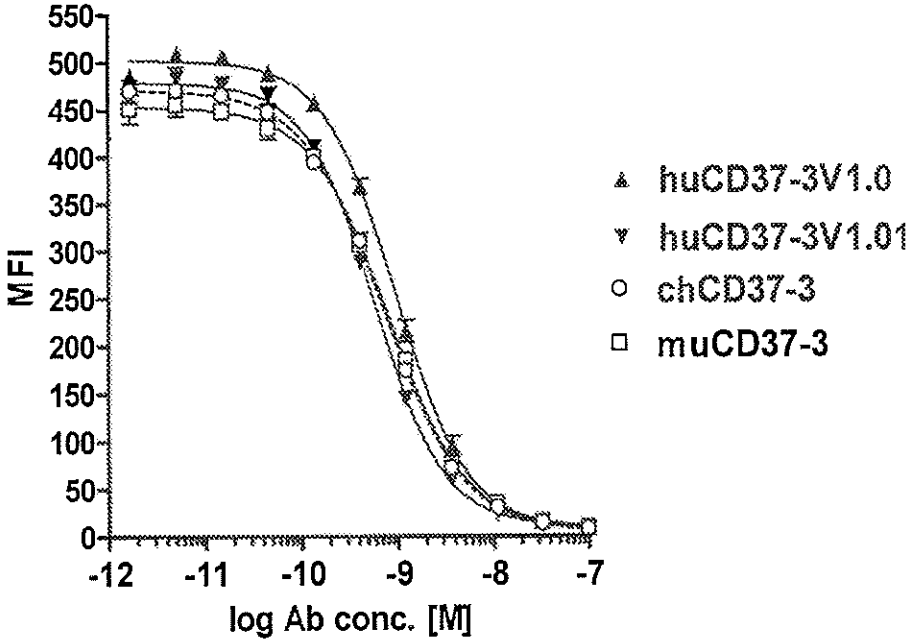

550
500
450
400
350
300
250
200
150
100
50
0
MFI
-12
-11
-10
-9
-8
-7
log Ab conc. [M]
huCD37-3V1.0
huCD37-3V1.01
chCD37-3
muCD37-3

Figure 10

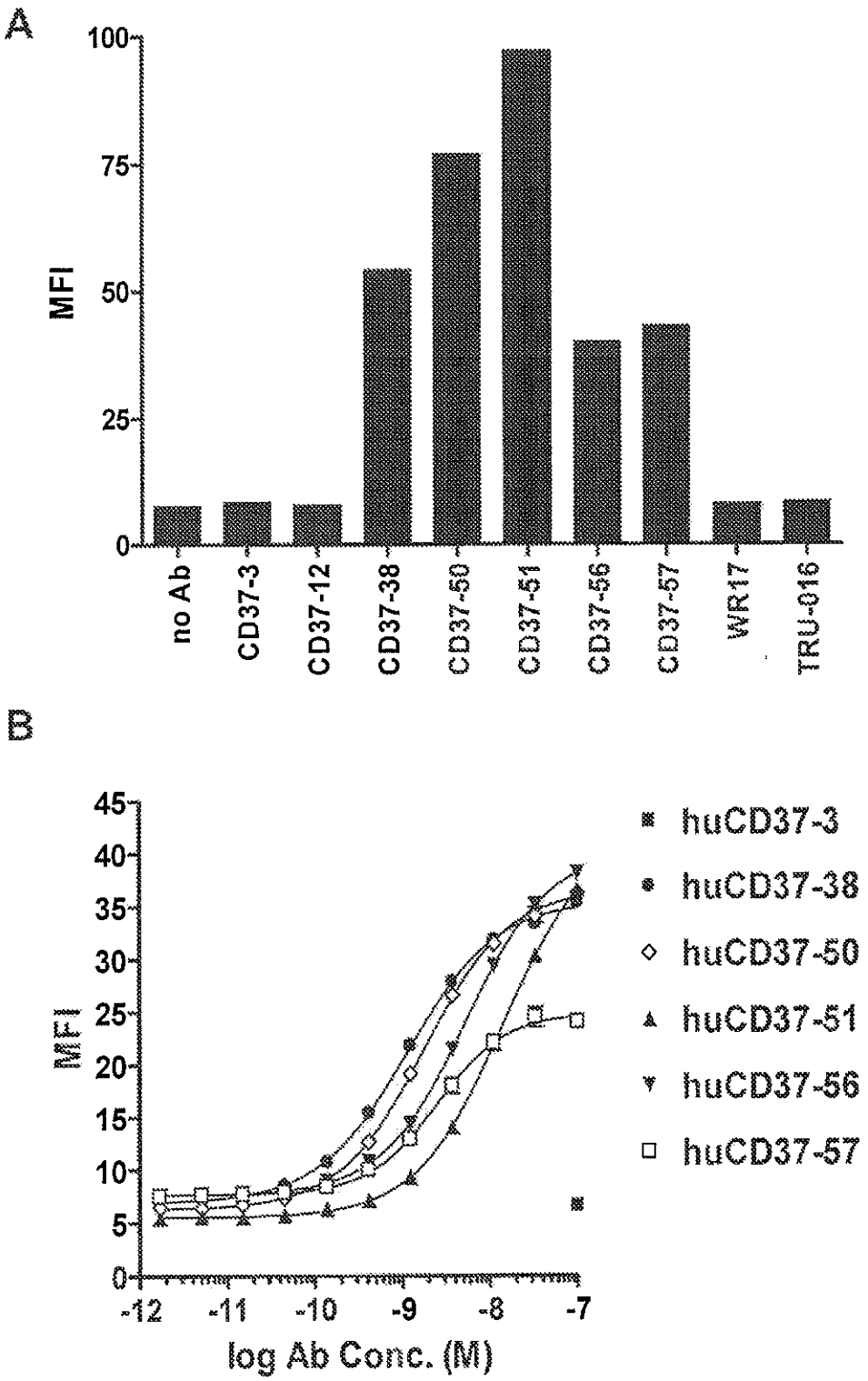

A
100
75
50
25
0
MFI
no Ab
CD37-3
CD37-12
CD37-38
CD37-50
CD37-51
CD37-56
CD37-57
WR17
TRU-016
B
45
40
35
30
25
20
15
10
5
0
MFI
-12
-11
-10
-9
-8
-7
log Ab Conc. (M)
huCD37-3
huCD37-38
huCD37-50
huCD37-51
huCD37-56
huCD37-57

Figure 11

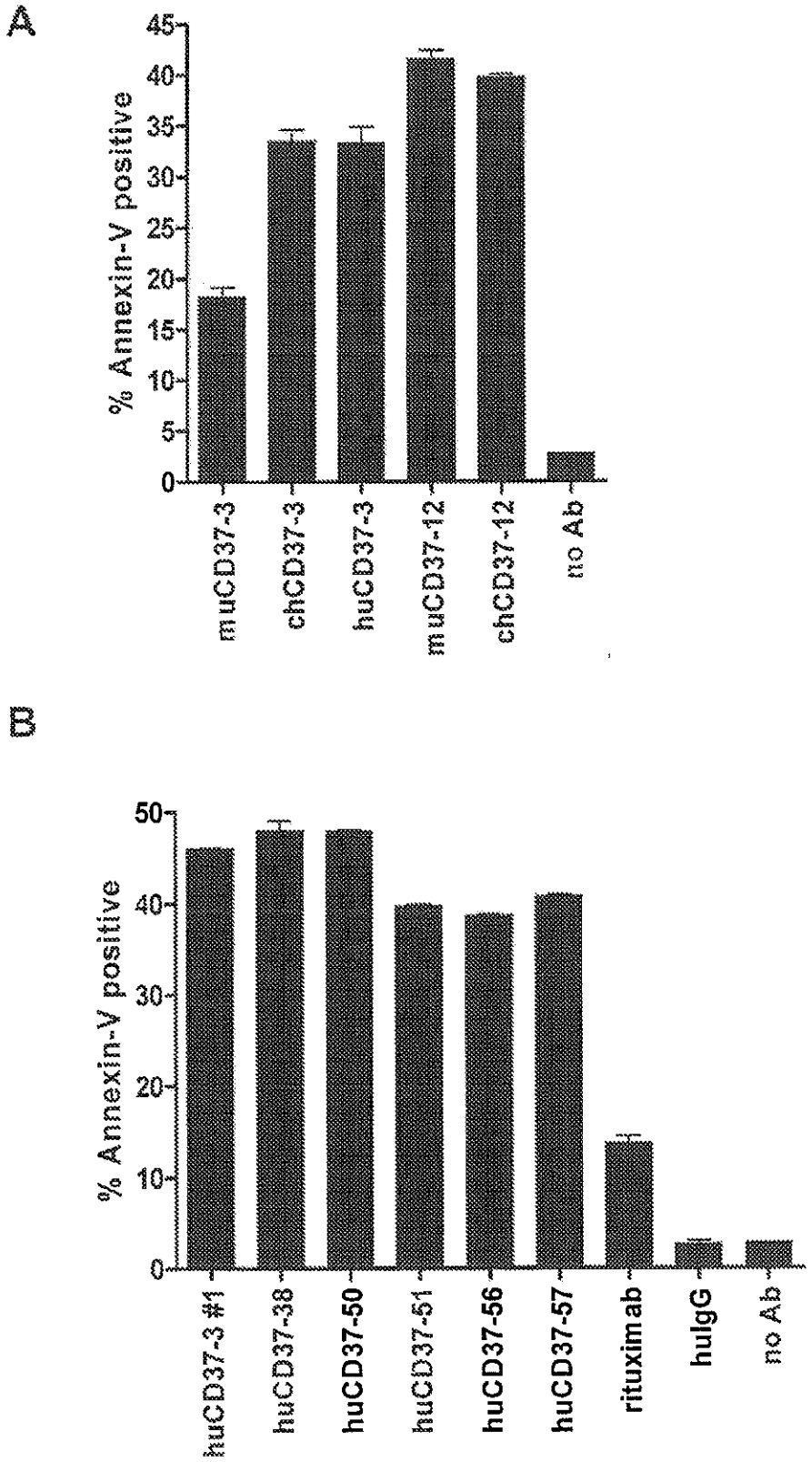
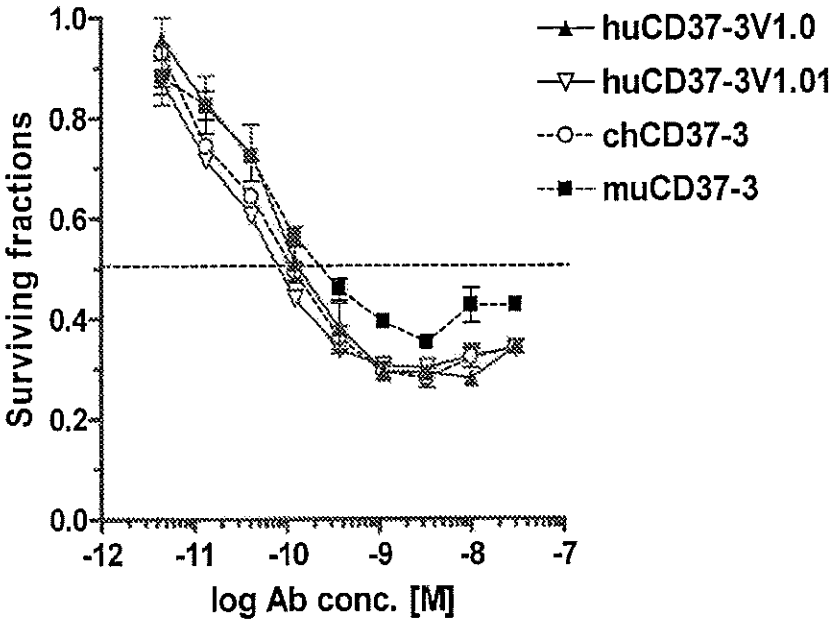

A
% Annexin-V positive
0
5
10
15
20
25
30
35
40
45
muCD37-3
chCD37-3
huCD37-3
muCD37-12
chCD37-12
no Ab
B
% Annexin-V positive
0
10
20
30
40
50
huCD37-3 #1
huCD37-38
huCD37-50
huCD37-51
huCD37-56
huCD37-57
rituximab
huIgG
no Ab

Figure 12

A


1.0
0.8
0.6
0.4
0.2
0.0
Surviving fractions
-12
-11
-10
-9
-8
-7
log Ab conc. [M]
huCD37-3V1.0
huCD37-3V1.01
chCD37-3
muCD37-3

B

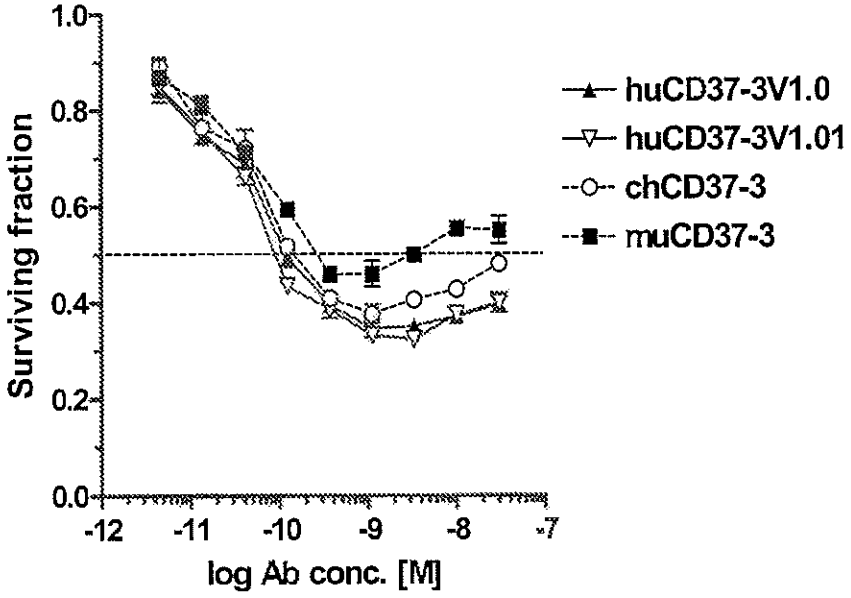
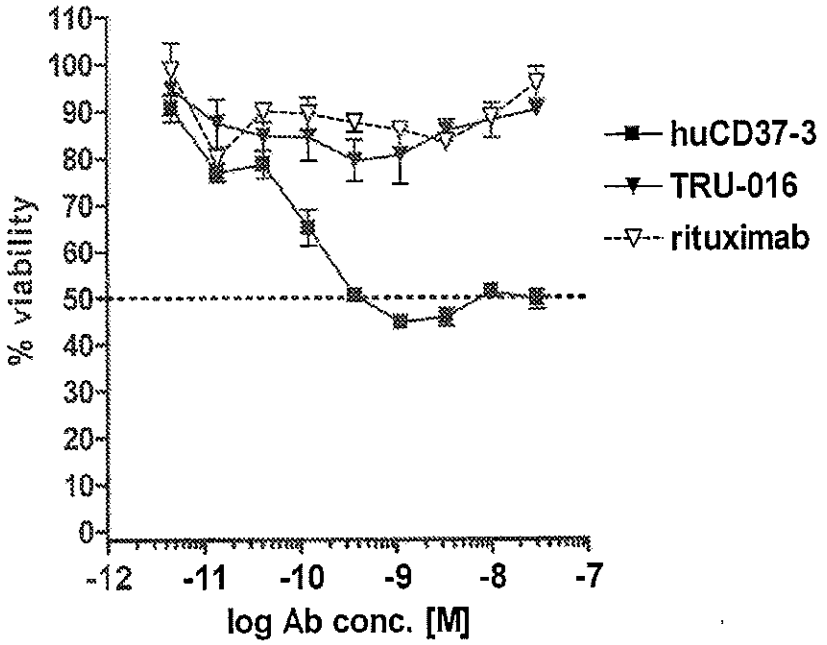

1.0
0.8
0.6
0.4
0.2
0.0
Surviving fraction
-12
-11
-10
-9
-8
-7
log Ab conc. [M]
huCD37-3V1.0
huCD37-3V1.01
chCD37-3
muCD37-3

Figure 13

A


% viability
log Ab conc. [M]
huCD37-3
TRU-016
rituximab

B

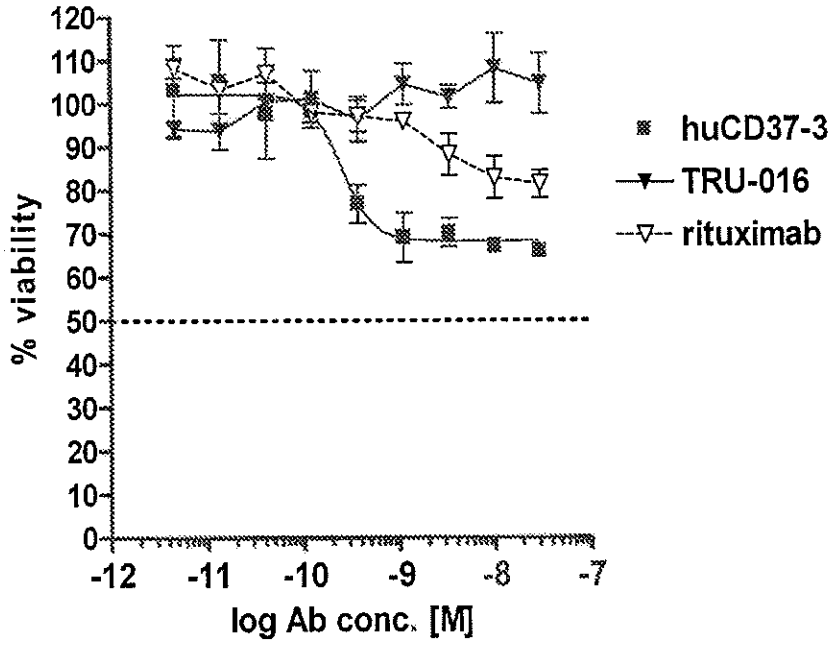
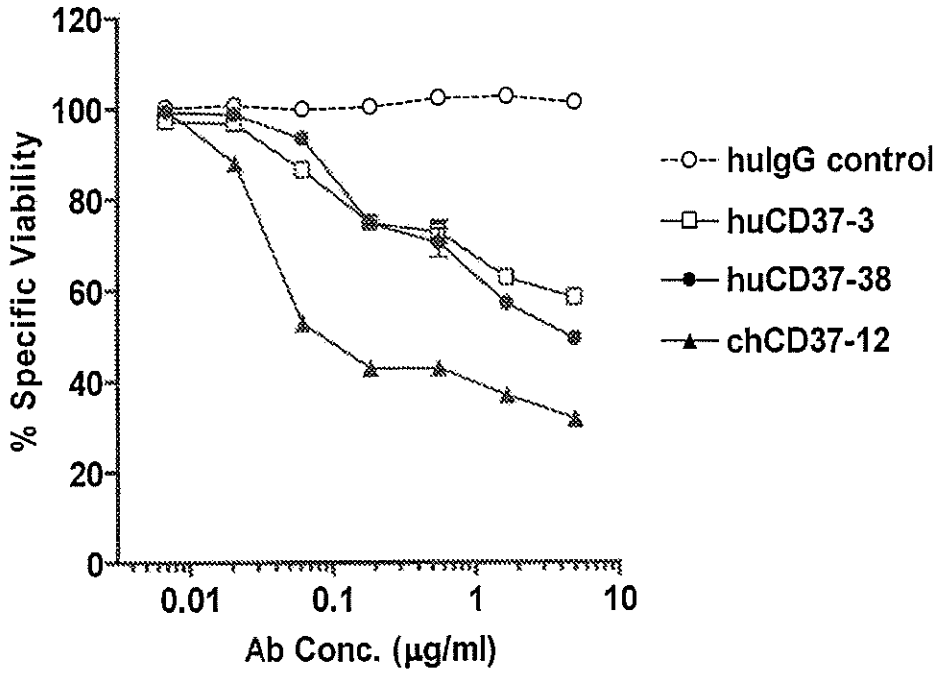

% viability
log Ab conc. [M]
huCD37-3
TRU-016
rituximab

Figure 14

A


120
100
80
60
40
20
0
% Specific Viability
0.01
0.1
1
10
Ab Conc. (µg/ml)
hulgG control
huCD37-3
huCD37-38
chCD37-12

B

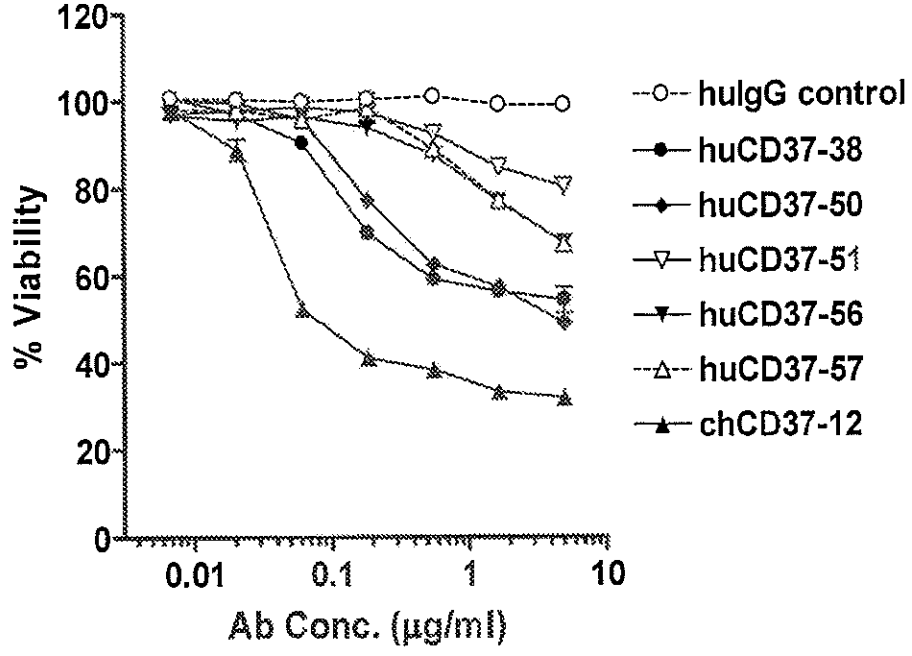

120
100
80
60
40
20
0
% Viability
0.01
0.1
1
10
Ab Conc. (µg/ml)
hulgG control
huCD37-38
huCD37-50
huCD37-51
huCD37-56
huCD37-57
chCD37-12

Figure 15

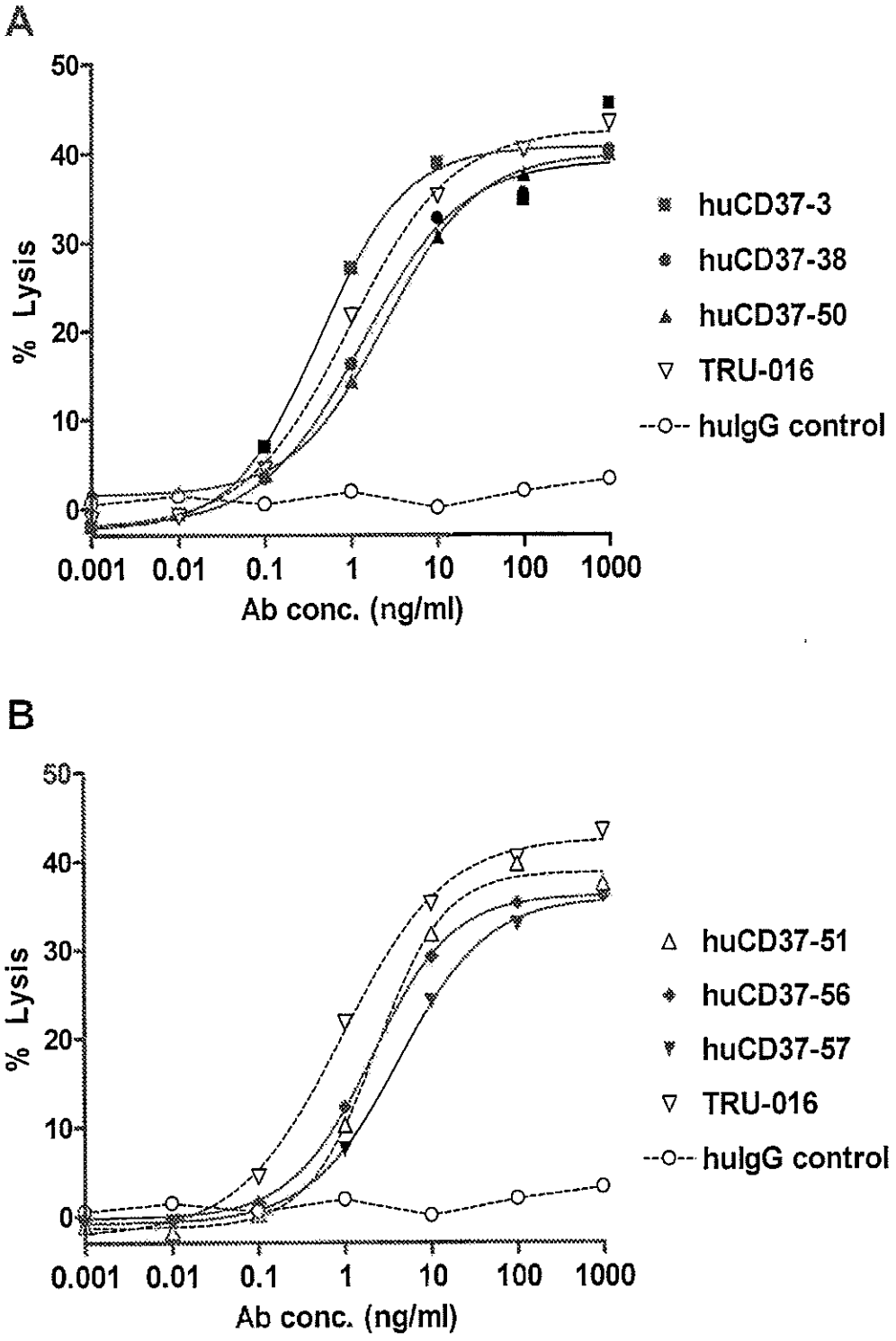

A
% Lysis
50
40
30
20
10
0
0.001
0.01
0.1
1
10
100
1000
Ab conc. (ng/ml)
huCD37-3
huCD37-38
huCD37-50
TRU-016
huIgG control
B
% Lysis
50
40
30
20
10
0
0.001
0.01
0.1
1
10
100
1000
Ab conc. (ng/ml)
huCD37-51
huCD37-56
huCD37-57
TRU-016
huIgG control

Figure 16

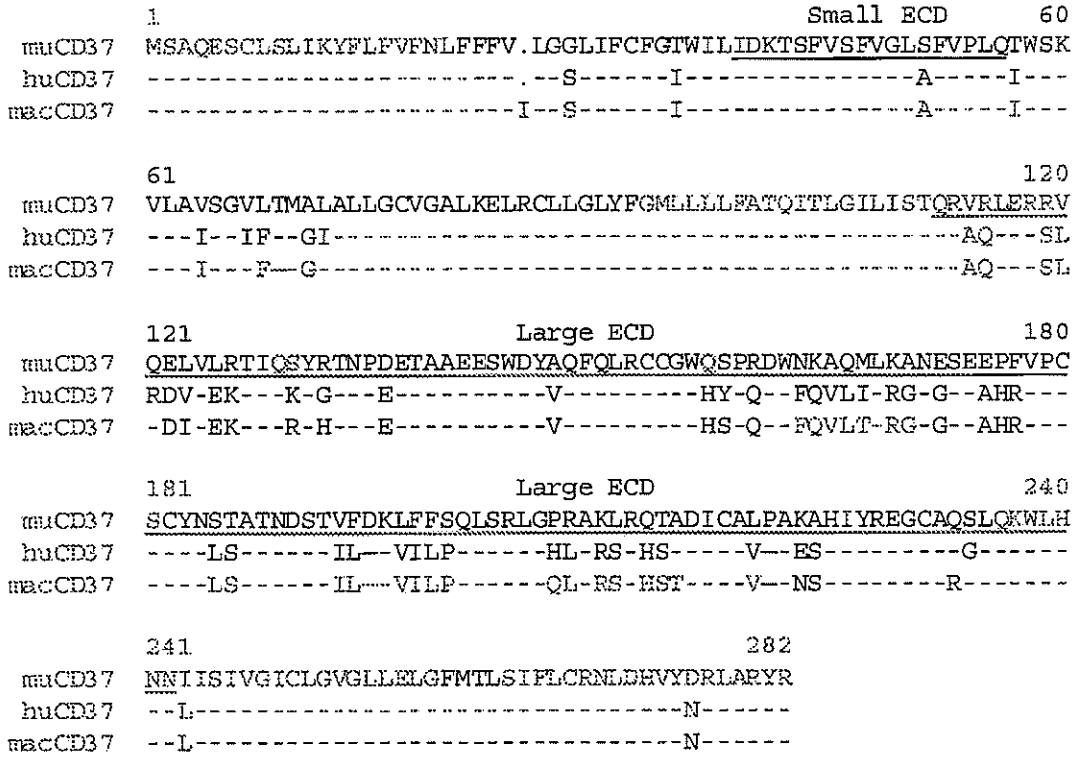

1 Small ECD 60
muCD37 MSAQESCLSLIKYFLFVFNLFFFV.LGGLIFCFGIWILIDKTSFVSFVGLSFVPLQIWSK
huCD37 ----------.--S------I----------A-----I---
macCD37 ----------I--S------I----------A-----I---
61 120
muCD37 VLAVSGVLIMALALLGCVGALKELRCLLGLYFGMLLLLFATQITLGILISTQRVRLERRV
huCD37 ---I--IF--GI----------AQ---SL
macCD37 ---I---F--G----------AQ---SL
121 Large ECD 180
muCD37 QELVLRTIQSYRTNPDETAAEESWDYAQFQLRCCGWQSPRDWNKAQMLKANESEEPFVPC
huCD37 RDV-EK---K-G---E----------V---------HY-Q--FQVLI-RG-G--AHR---
macCD37 -DI-EK---R-H---E----------V---------HS-Q--FQVLT-RG-G--AHR---
181 Large ECD 240
muCD37 SCYNSTATNDSTVFDKLFFSQLSRLGPRAKLRQTADICALPAKAHIYREGCAQSLQKWLH
huCD37 ----LS------IL--VILP------HL-RS-HS-----V--ES---------G------
macCD37 ----LS------IL--VILP------QL-RS-HST----V--NS--------R-------
241 282
muCD37 NNIISIVGICLGVGLLELGFMTLSIFLCRNLDHVYDRLARYR
huCD37 --L----------N------
macCD37 --L----------N------

Figure 17

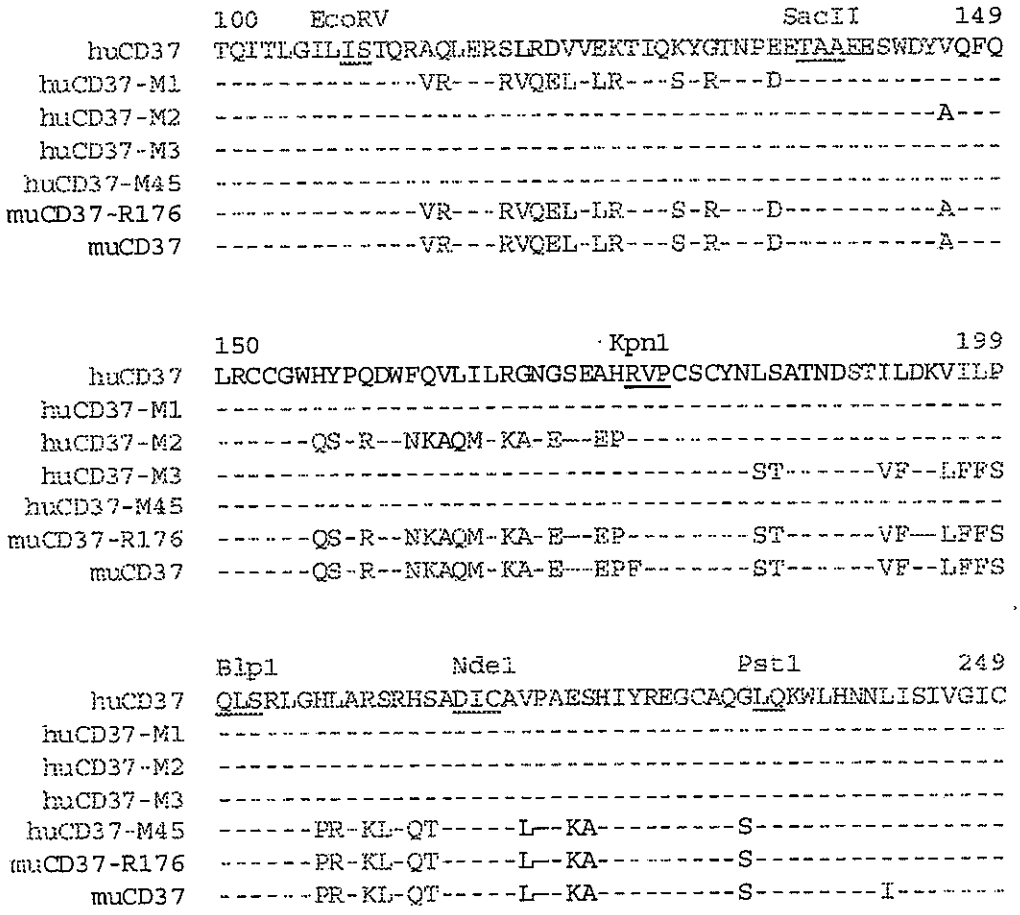
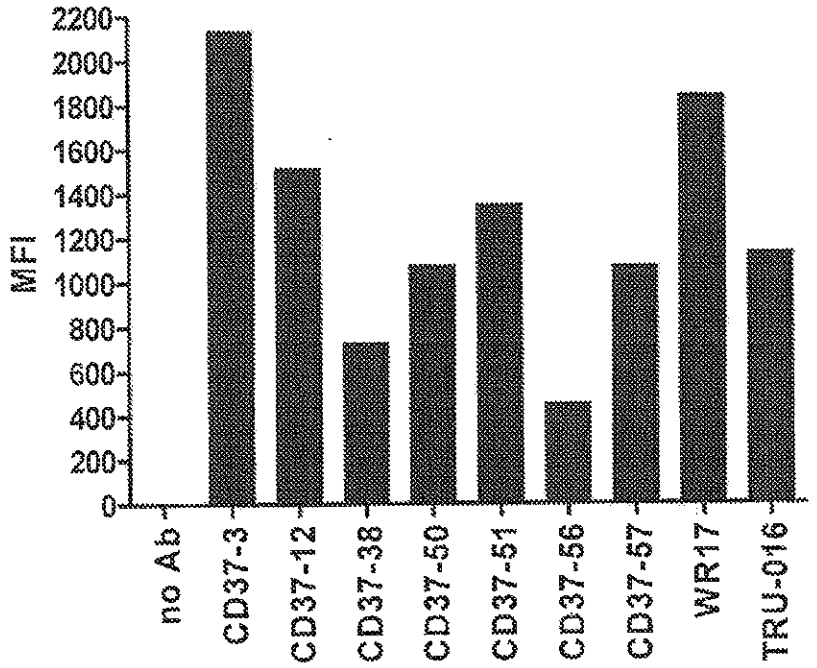

100 EcoRV SacII 149
huCD37 TQITLGILISTQRAQLERSLRDVVEKTIQKYGINPEETAAEESWDYVQFQ
huCD37-M1 ----------VR---RVQEL-LR---S-R---D----------
huCD37-M2 ----------A---
huCD37-M3 ----------
huCD37-M45 ----------
muCD37-R176 ----------VR---RVQEL-LR---S-R---D----------A---
muCD37 ----------VR---RVQEL-LR---S-R---D----------A---
150 Kpn1 199
huCD37 LRCCGWHYPQDWFQVLILRGNGSEAHRVPCSCYNLSATNDSTILDKVILP
huCD37-M1 ----------
huCD37-M2 ------QS-R--NKAQM-KA-E--EP----------
huCD37-M3 ----------ST------VF--LFFS
huCD37-M45 ----------
muCD37-R176 ------QS-R--NKAQM-KA-E--EP---------ST------VF--LFFS
muCD37 ------QS-R--NKAQM-KA-E--EPF-------ST------VF--LFFS
Blp1 Nde1 Pst1 249
huCD37 QLSRLGHLARSRHSADICAVPAESHIYREGCAQGLQKWLHNNLISIVGIC
huCD37-M1 ----------
huCD37-M2 ----------
huCD37-M3 ----------
huCD37-M45 ------PR-KL-QT-----L--KA---------S----------
muCD37-R176 ------PR-KL-QT-----L--KA---------S----------
muCD37 ------PR-KL-QT-----L--KA---------S--------I--------

Figure 18

A


MFI
2200
2000
1800
1600
1400
1200
1000
800
600
400
200
0
no Ab
CD37-3
CD37-12
CD37-38
CD37-50
CD37-51
CD37-56
CD37-57
WR17
TRU-016

B

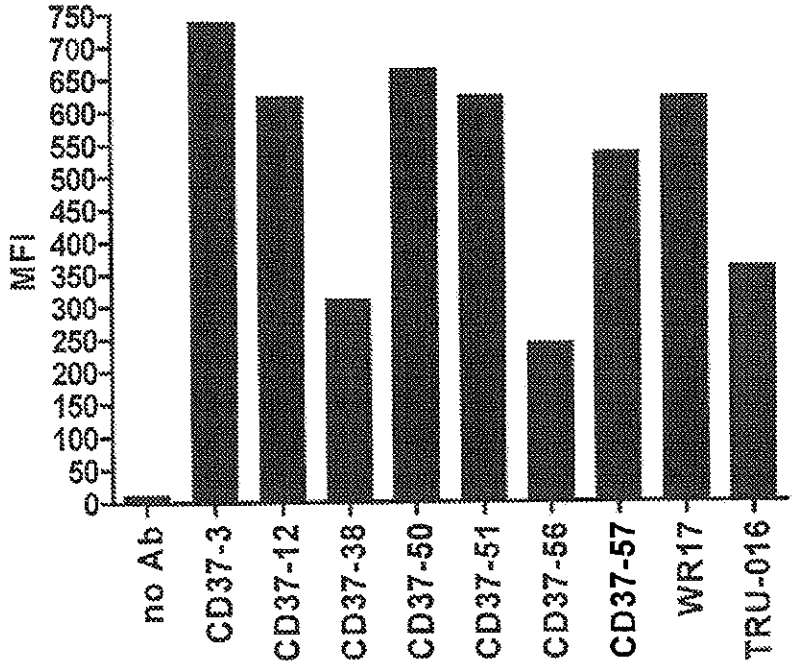
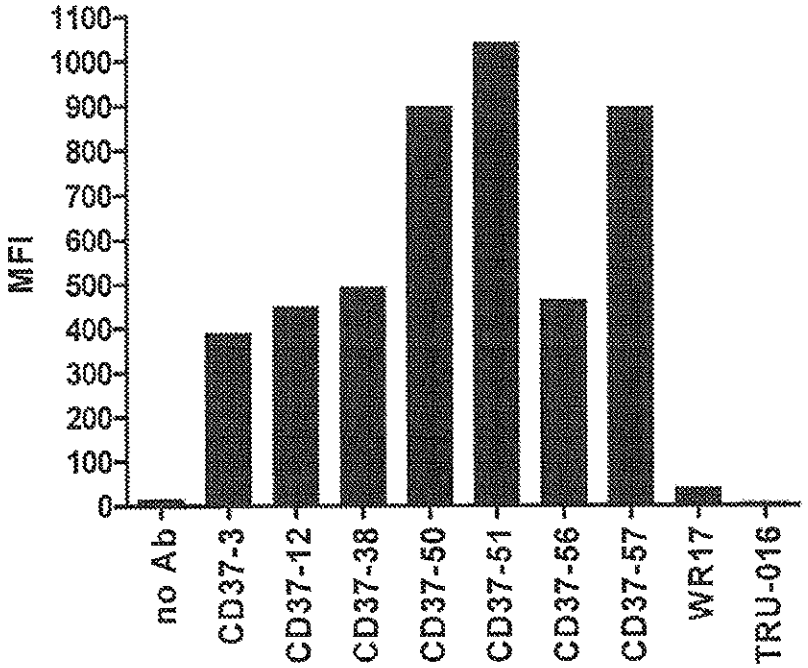

MFI
750
700
650
600
550
500
450
400
350
300
250
200
150
100
50
0
no Ab
CD37-3
CD37-12
CD37-38
CD37-50
CD37-51
CD37-56
CD37-57
WR17
TRU-016

Figure 19

A


MFI
1100
1000
900
800
700
600
500
400
300
200
100
0
no Ab
CD37-3
CD37-12
CD37-38
CD37-50
CD37-51
CD37-56
CD37-57
WR17
TRU-016

B

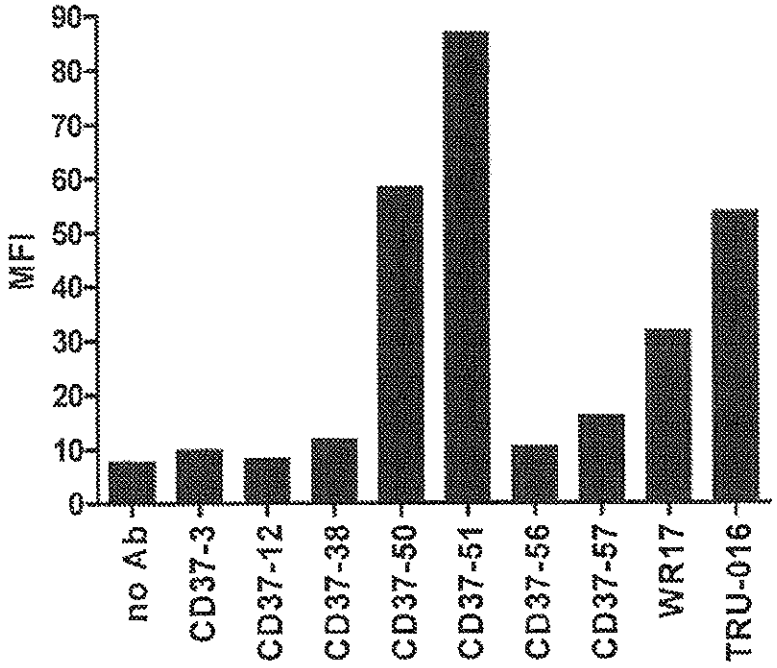
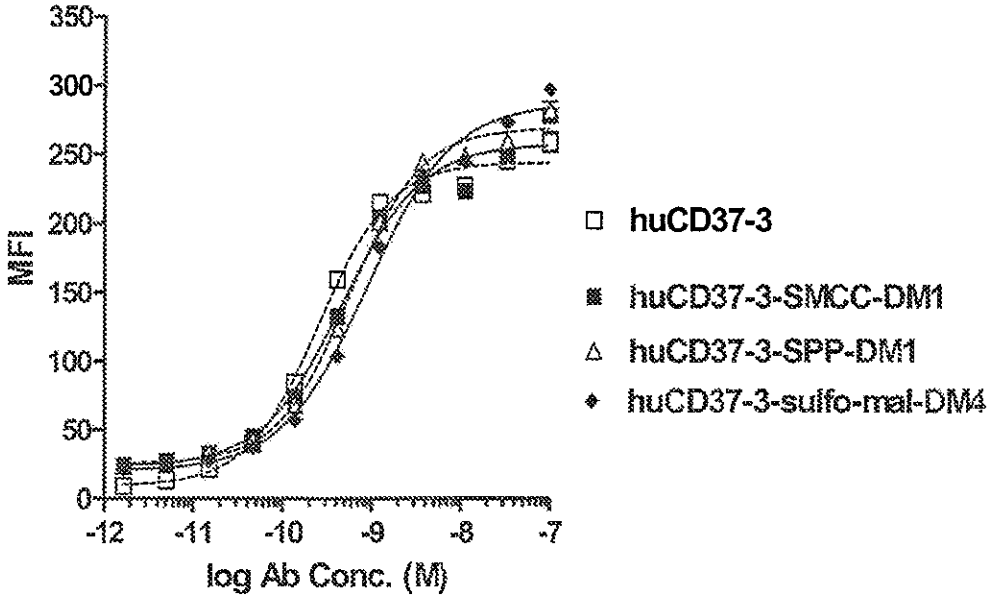

MFI
90
80
70
60
50
40
30
20
10
0
no Ab
CD37-3
CD37-12
CD37-38
CD37-50
CD37-51
CD37-56
CD37-57
WR17
TRU-016

Figure 20

A


350
300
250
200
150
100
50
0
MFI
-12
-11
-10
-9
-8
-7
log Ab Conc. (M)
huCD37-3
huCD37-3-SMCC-DM1
huCD37-3-SPP-DM1
huCD37-3-sulfo-mal-DM4

B

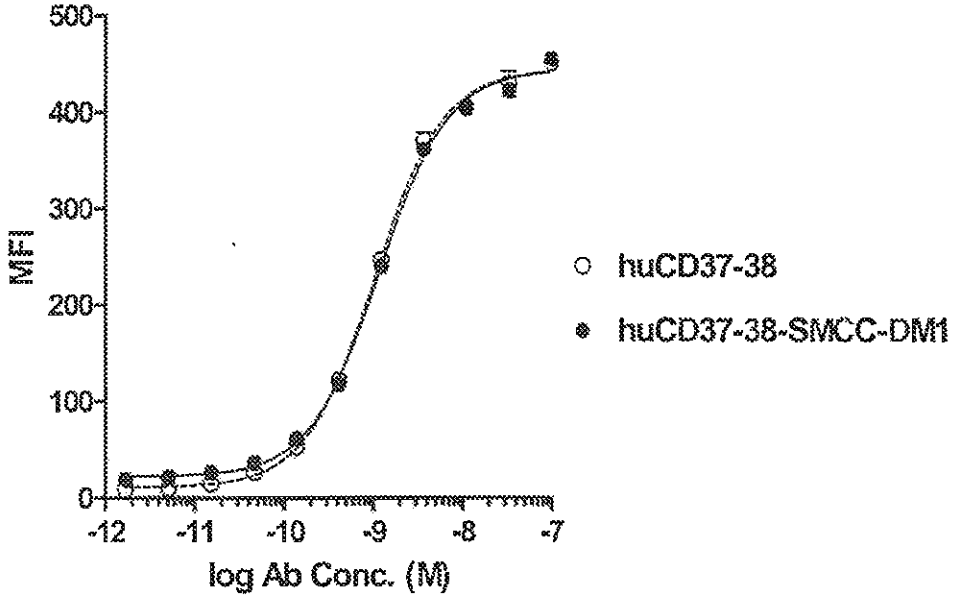
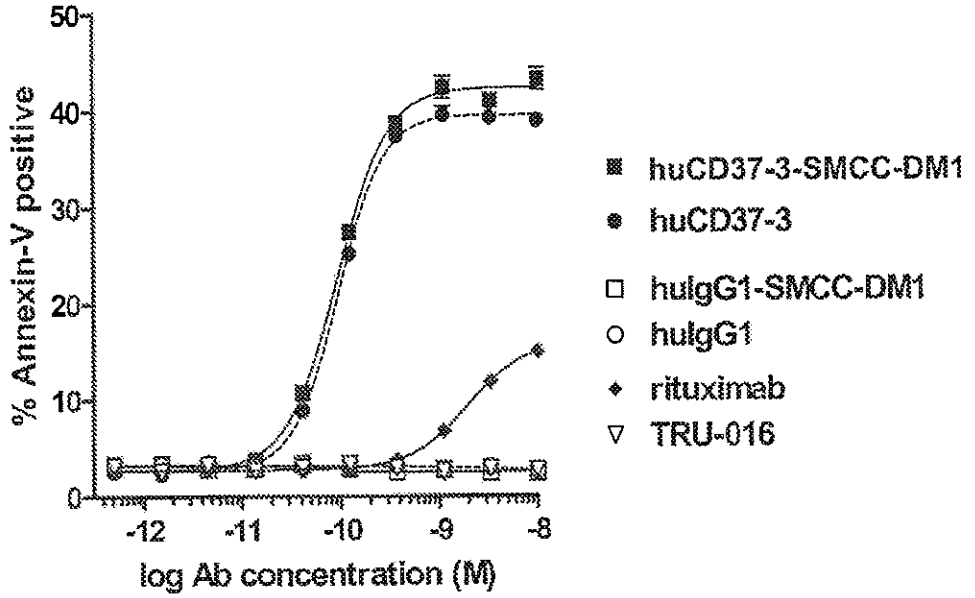

500
400
300
200
100
0
MFI
-12
-11
-10
-9
-8
-7
log Ab Conc. (M)
huCD37-38
huCD37-38-SMCC-DM1

Figure 21

A


% Annexin-V positive
50
40
30
20
10
0
-12
-11
-10
-9
-8
log Ab concentration (M)
huCD37-3-SMCC-DM1
huCD37-3
huIgG1-SMCC-DM1
huIgG1
rituximab
TRU-016

B

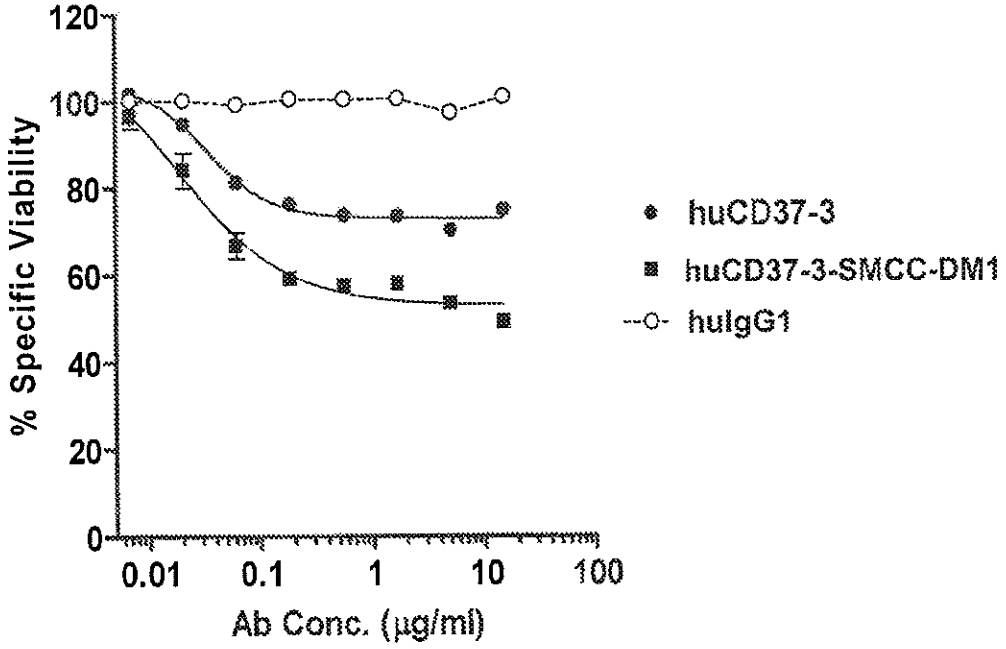
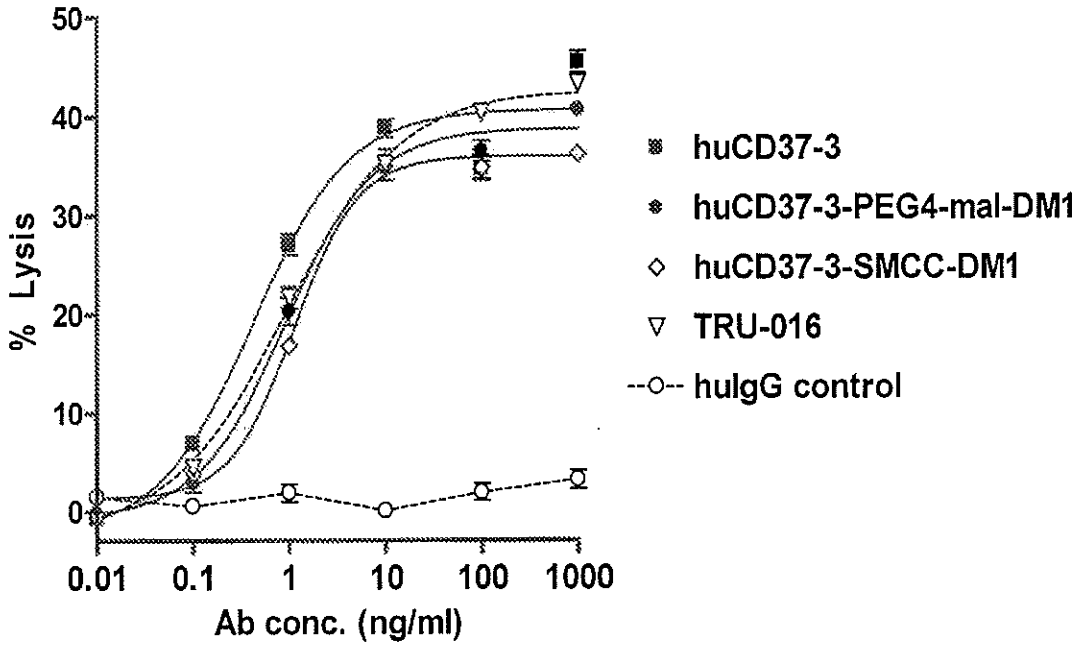

% Specific Viability
120
100
80
60
40
20
0
0.01
0.1
1
10
100
Ab Conc. (µg/ml)
huCD37-3
huCD37-3-SMCC-DM1
huIgG1

Figure 22

A


50
40
30
20
10
0
% Lysis
0.01
0.1
1
10
100
1000
Ab conc. (ng/ml)
huCD37-3
huCD37-3-PEG4-mal-DM1
huCD37-3-SMCC-DM1
TRU-016
huIgG control

B

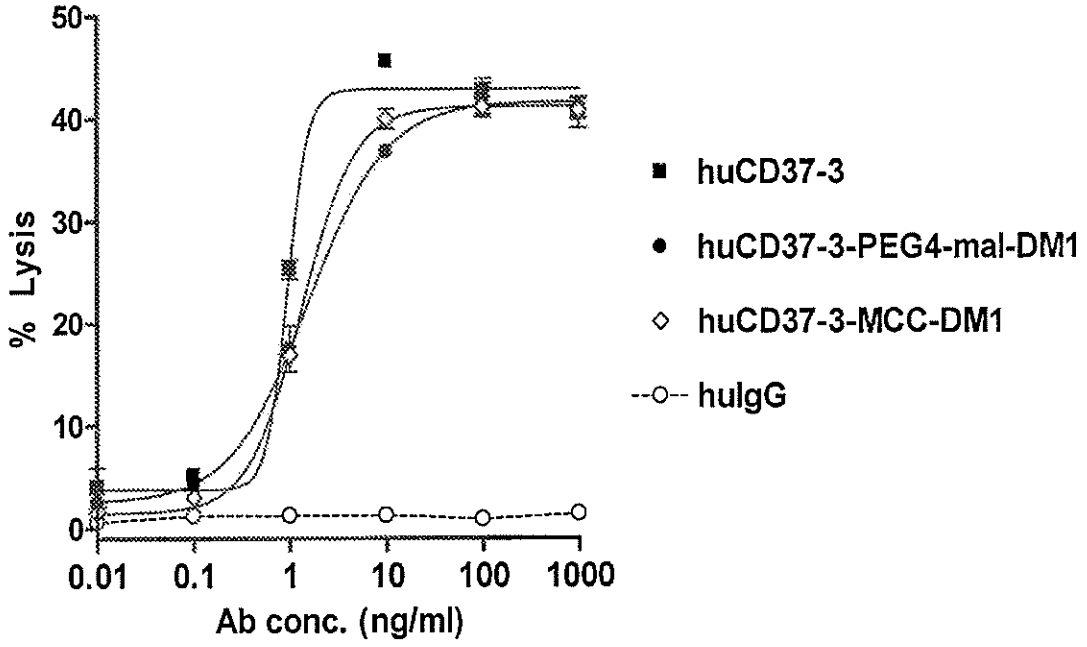
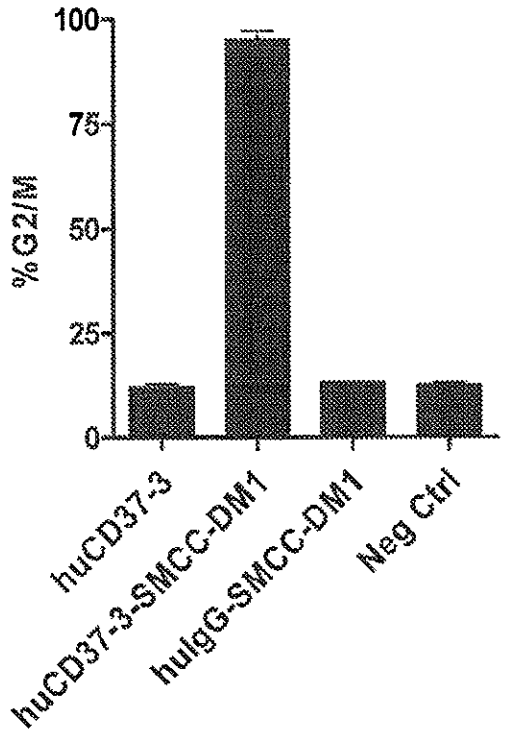

50
40
30
20
10
0
% Lysis
0.01
0.1
1
10
100
1000
Ab conc. (ng/ml)
huCD37-3
huCD37-3-PEG4-mal-DM1
huCD37-3-MCC-DM1
huIgG

Figure 23

A


100
75
50
25
0
% G2/M
huCD37-3
huCD37-3-SMCC-DM1
huIgG-SMCC-DM1
Neg Ctrl

B

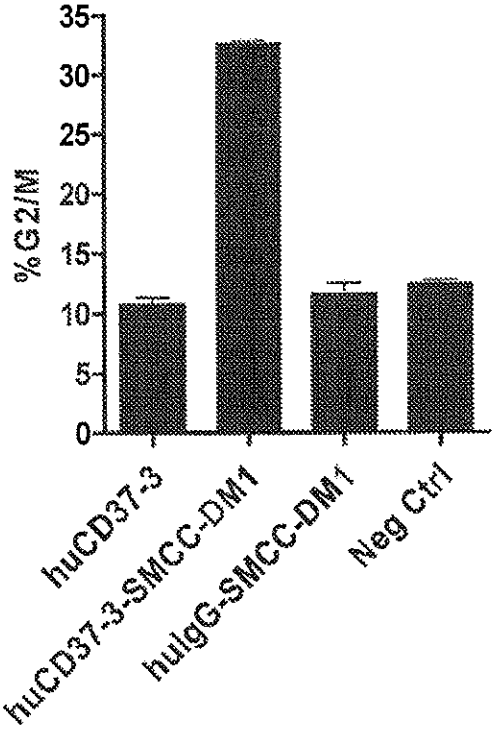
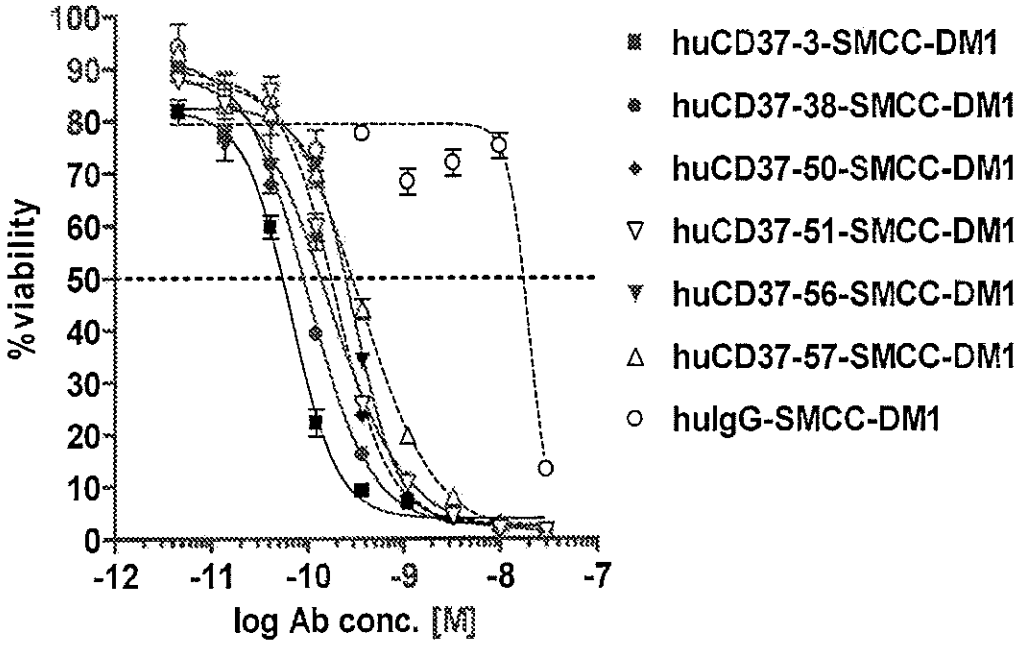

35
30
25
20
15
10
5
0
% G2/M
huCD37-3
huCD37-3-SMCC-DM1
huIgG-SMCC-DM1
Neg Ctrl

Figure 24

A


100
90
80
70
60
50
40
30
20
10
0
%viability
-12
-11
-10
-9
-8
-7
log Ab conc. [M]
huCD37-3-SMCC-DM1
huCD37-38-SMCC-DM1
huCD37-50-SMCC-DM1
huCD37-51-SMCC-DM1
huCD37-56-SMCC-DM1
huCD37-57-SMCC-DM1
huIgG-SMCC-DM1

B

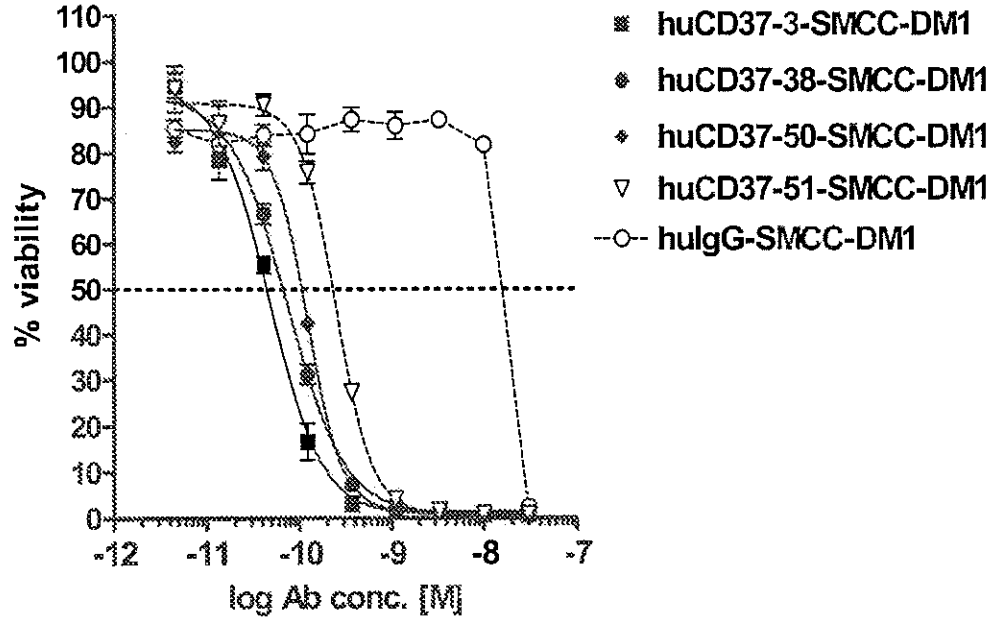
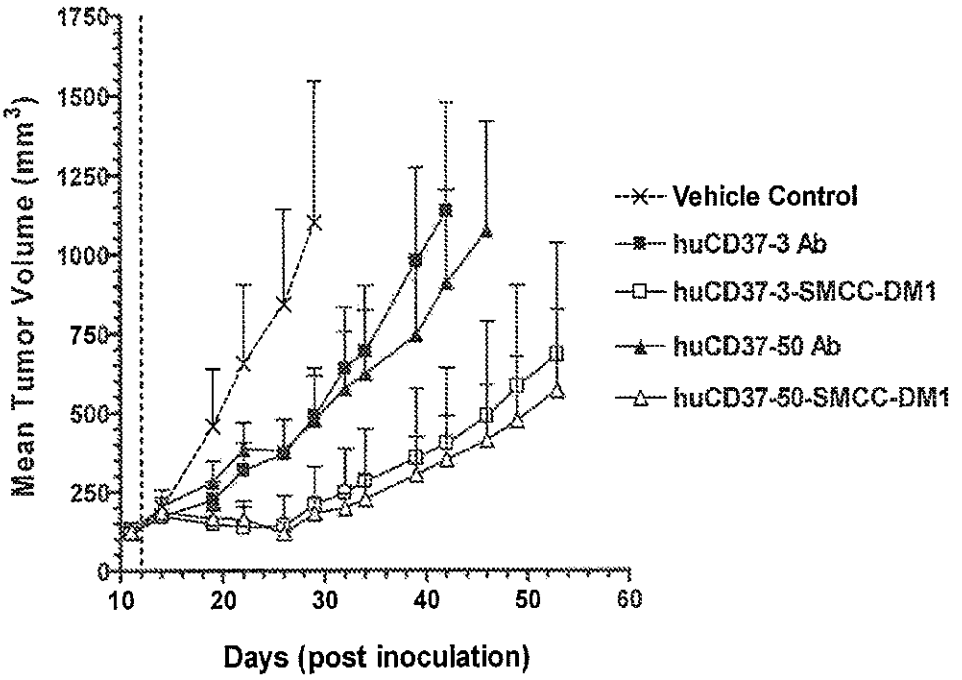

110
100
90
80
70
60
50
40
30
20
10
0
% viability
-12
-11
-10
-9
-8
-7
log Ab conc. [M]
huCD37-3-SMCC-DM1
huCD37-38-SMCC-DM1
huCD37-50-SMCC-DM1
huCD37-51-SMCC-DM1
huIgG-SMCC-DM1

Figure 25

A


Mean Tumor Volume (mm3)
1750
1500
1250
1000
750
500
250
0
10
20
30
40
50
60
Days (post inoculation)
Vehicle Control
huCD37-3 Ab
huCD37-3-SMCC-DM1
huCD37-50 Ab
huCD37-50-SMCC-DM1

B

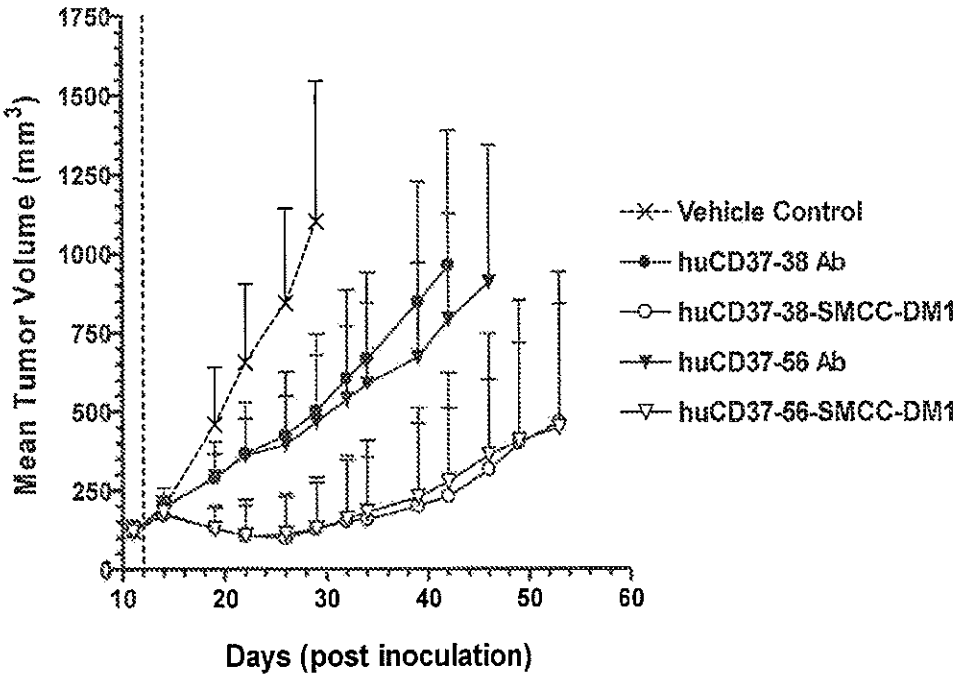

Mean Tumor Volume (mm3)
1750
1500
1250
1000
750
500
250
0
10
20
30
40
50
60
Days (post inoculation)
Vehicle Control
huCD37-38 Ab
huCD37-38-SMCC-DM1
huCD37-56 Ab
huCD37-56-SMCC-DM1

Figure 26

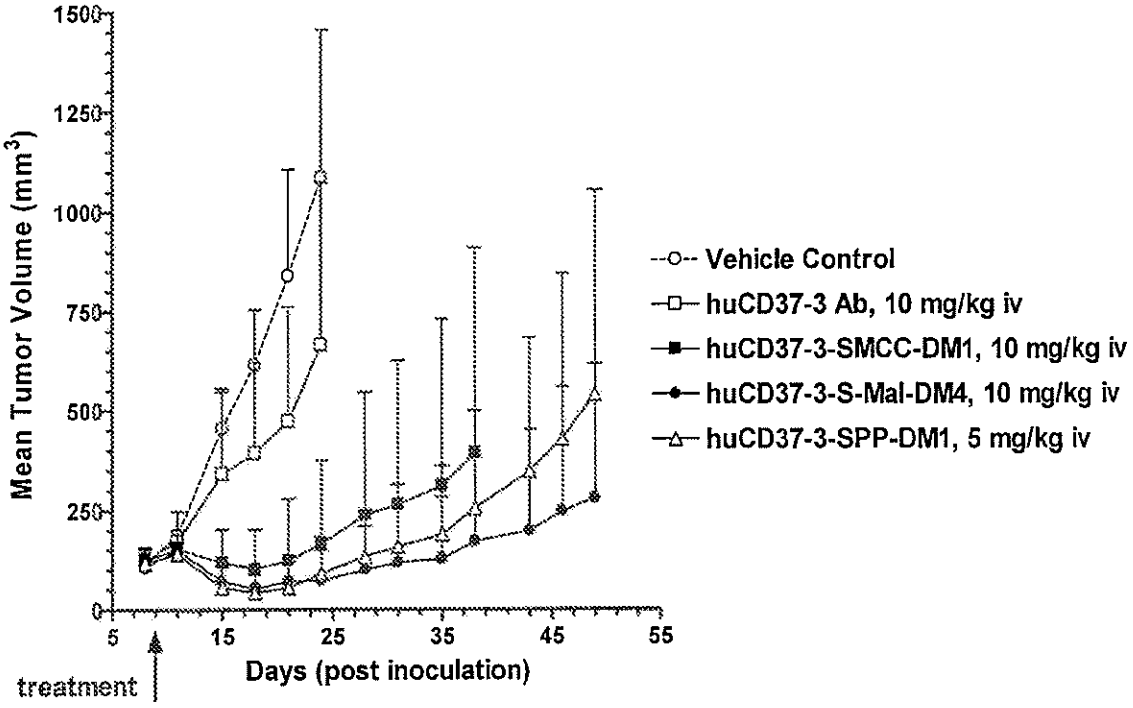

Mean Tumor Volume (mm3)
1500
1250
1000
750
500
250
0
5
15
25
35
45
55
Days (post inoculation)
treatment
Vehicle Control
huCD37-3 Ab, 10 mg/kg iv
huCD37-3-SMCC-DM1, 10 mg/kg iv
huCD37-3-S-Mal-DM4, 10 mg/kg iv
huCD37-3-SPP-DM1, 5 mg/kg iv

Figure 27

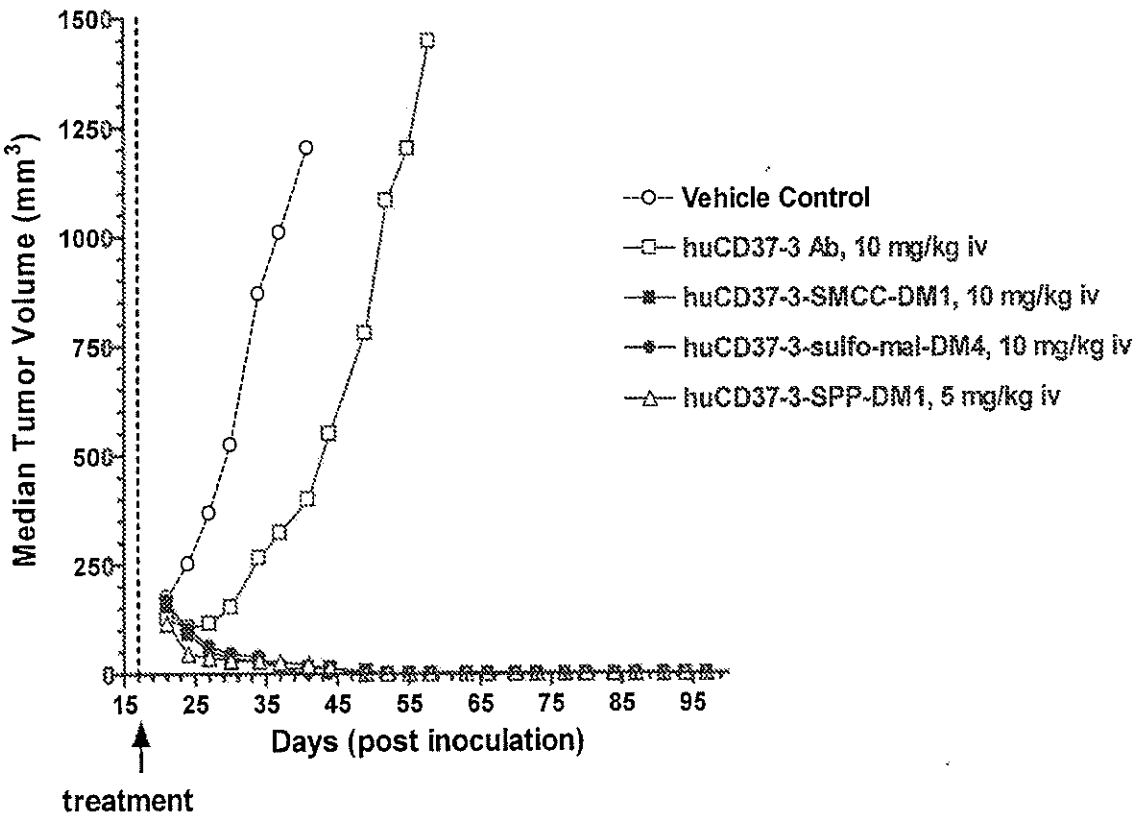

Median Tumor Volume (mm3)
1500
1250
1000
750
500
250
0
15
25
35
45
55
65
75
85
95
Days (post inoculation)
treatment
Vehicle Control
huCD37-3 Ab, 10 mg/kg iv
huCD37-3-SMCC-DM1, 10 mg/kg iv
huCD37-3-sulfo-mal-DM4, 10 mg/kg iv
huCD37-3-SPP-DM1, 5 mg/kg iv

Figure 28

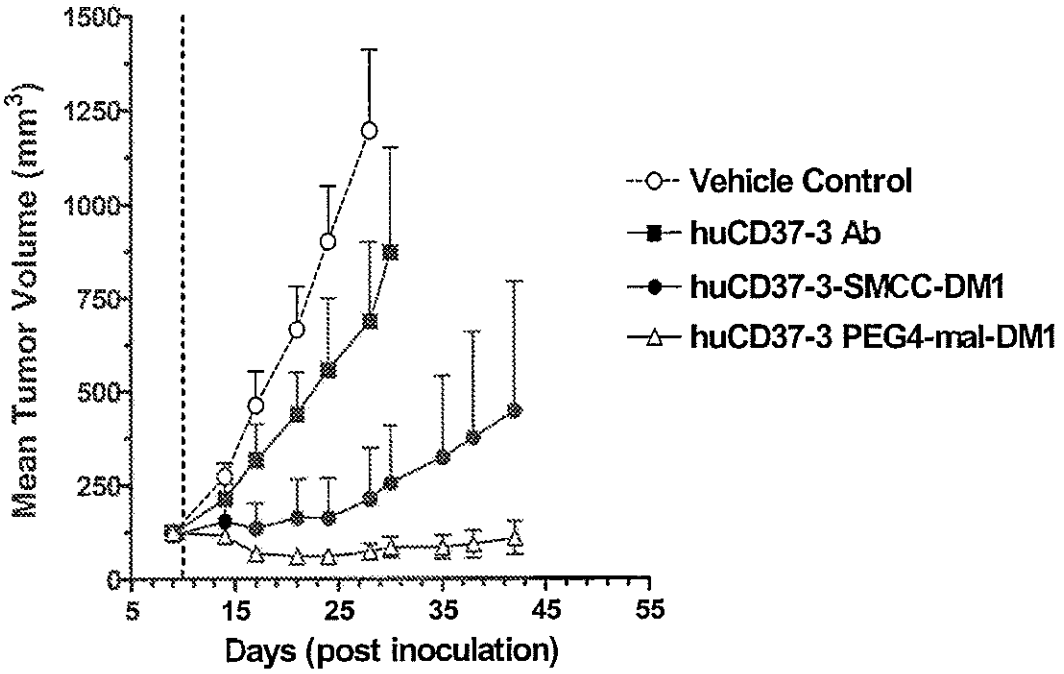

Mean Tumor Volume (mm3)
1500
1250
1000
750
500
250
0
5
15
25
35
45
55
Days (post inoculation)
Vehicle Control
huCD37-3 Ab
huCD37-3-SMCC-DM1
huCD37-3 PEG4-mal-DM1

Figure 29

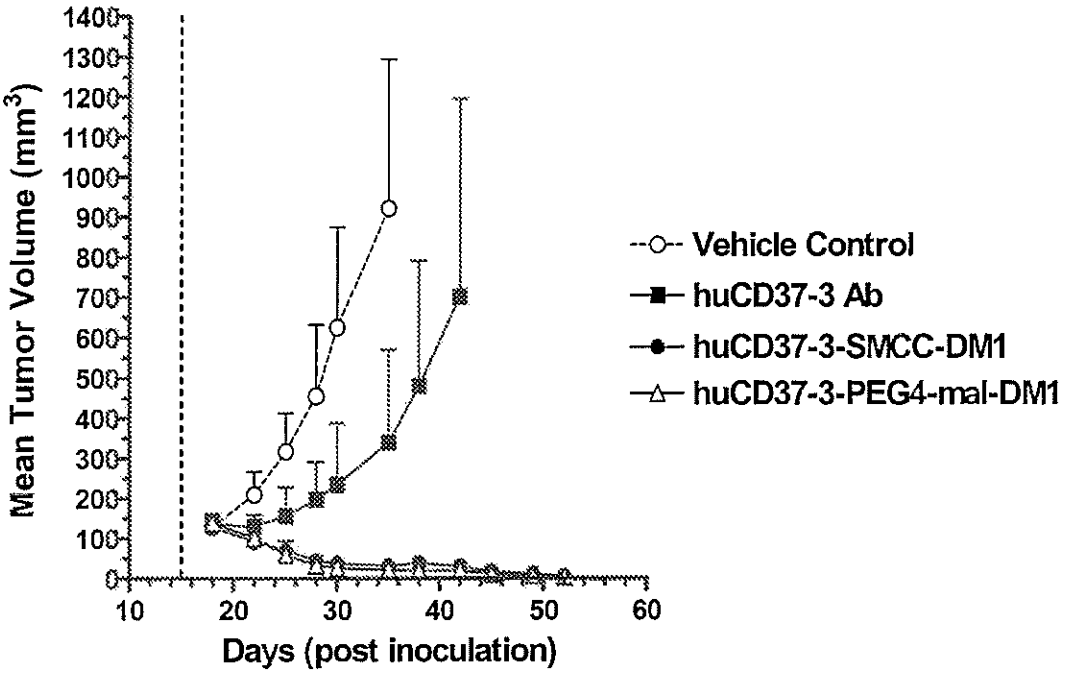

Mean Tumor Volume (mm3)
1400
1300
1200
1100
1000
900
800
700
600
500
400
300
200
100
0
10
20
30
40
50
60
Days (post inoculation)
Vehicle Control
huCD37-3 Ab
huCD37-3-SMCC-DM1
huCD37-3-PEG4-mal-DM1

Figure 30

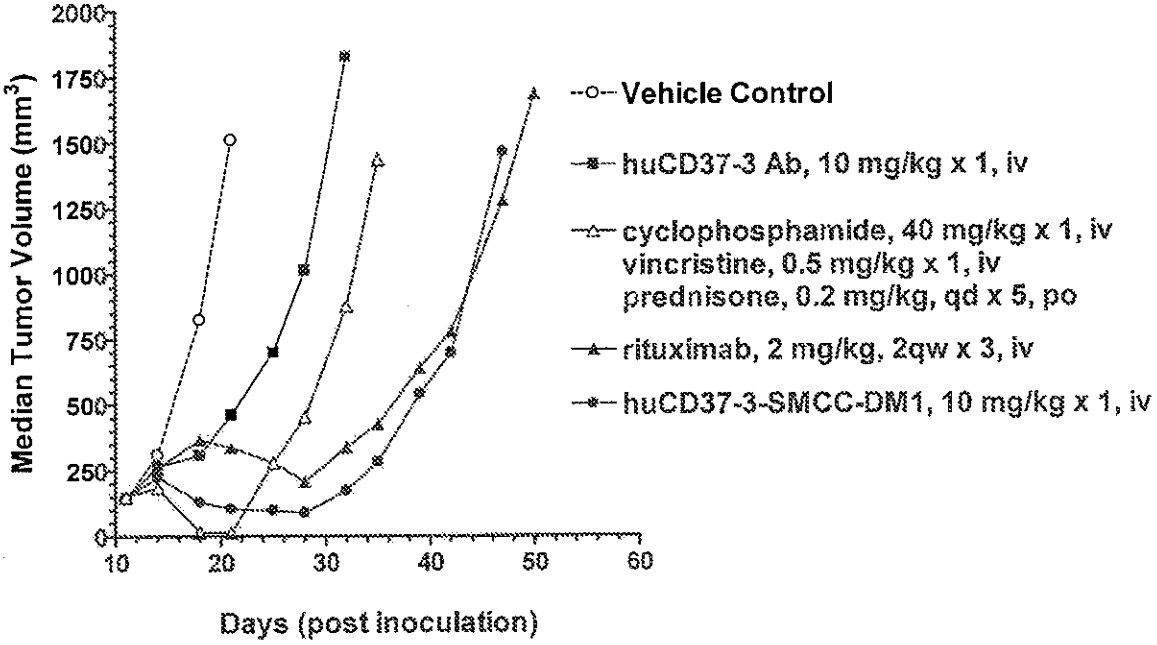

Median Tumor Volume (mm3)
2000
1750
1500
1250
1000
750
500
250
0
10
20
30
40
50
60
Days (post inoculation)
Vehicle Control
huCD37-3 Ab, 10 mg/kg x 1, iv
cyclophosphamide, 40 mg/kg x 1, iv
vincristine, 0.5 mg/kg x 1, iv
prednisone, 0.2 mg/kg, qd x 5, po
rituximab, 2 mg/kg, 2qw x 3, iv
huCD37-3-SMCC-DM1, 10 mg/kg x 1, iv

Figure 31

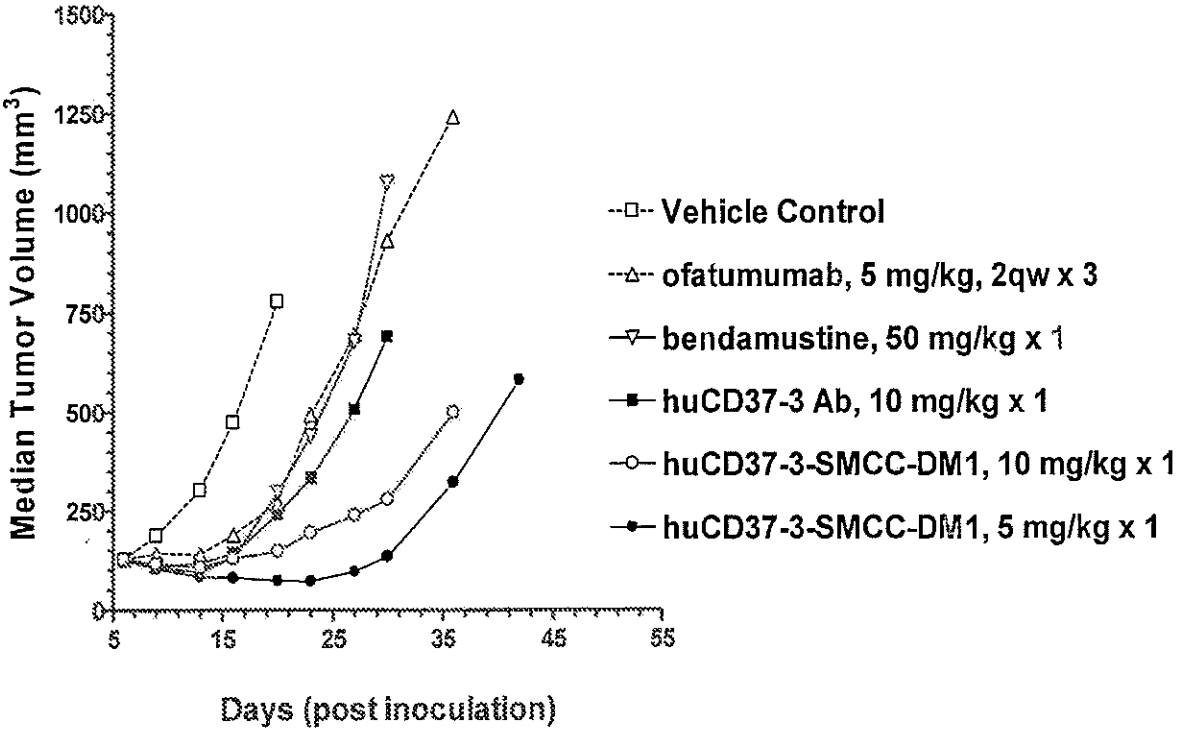
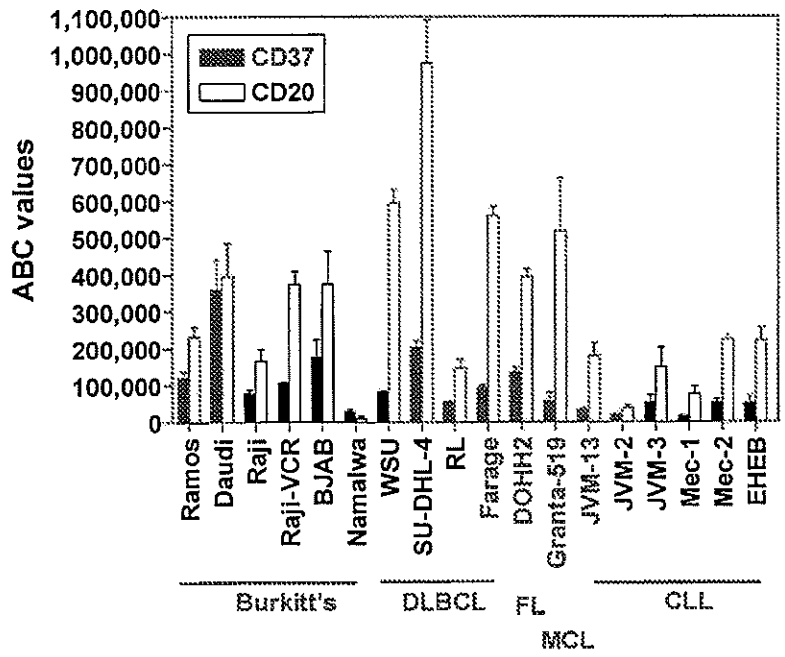
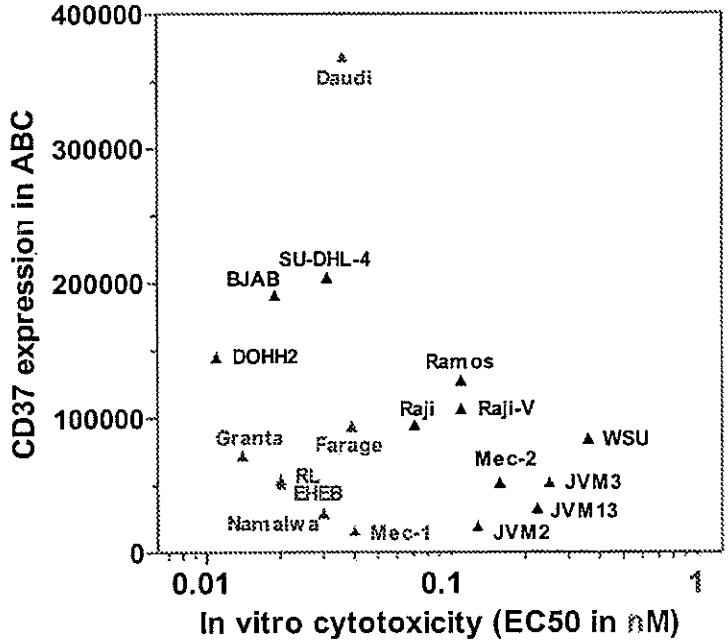

Median Tumor Volume (mm3)
1500
1250
1000
750
500
250
0
5
15
25
35
45
55
Days (post inoculation)
Vehicle Control
ofatumumab, 5 mg/kg, 2qw x 3
bendamustine, 50 mg/kg x 1
huCD37-3 Ab, 10 mg/kg x 1
huCD37-3-SMCC-DM1, 10 mg/kg x 1
huCD37-3-SMCC-DM1, 5 mg/kg x 1

Figure 32

A


1,100,000
1,000,000
900,000
800,000
700,000
600,000
500,000
400,000
300,000
200,000
100,000
0
ABC values
CD37
CD20
Ramos
Daudi
Raji
Raji-VCR
BJAB
Namalwa
WSU
SU-DHL-4
RL
Farage
DOHH2
Granta-519
JVM-13
JVM-2
JVM-3
Mec-1
Mec-2
EHEB
Burkitt's
DLBCL
FL
MCL
CLL

B


400000
300000
200000
100000
0
CD37 expression in ABC
Daudi
SU-DHL-4
BJAB
DOHH2
Ramos
Raji
Raji-V
Granta
Farage
WSU
Mec-2
RL
EHEB
JVM3
JVM13
Namalwa
Mec-1
JVM2
0.01
0.1
1
In vitro cytotoxicity (EC50 in nM)