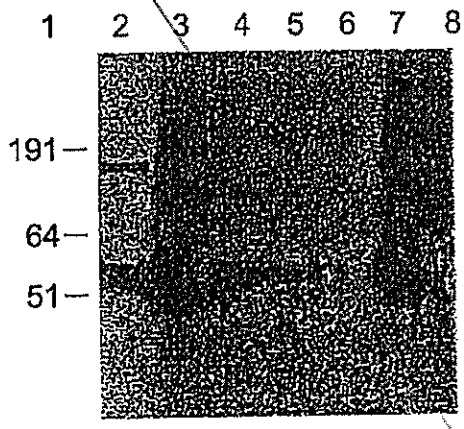


FIG. 2

FIG. 3

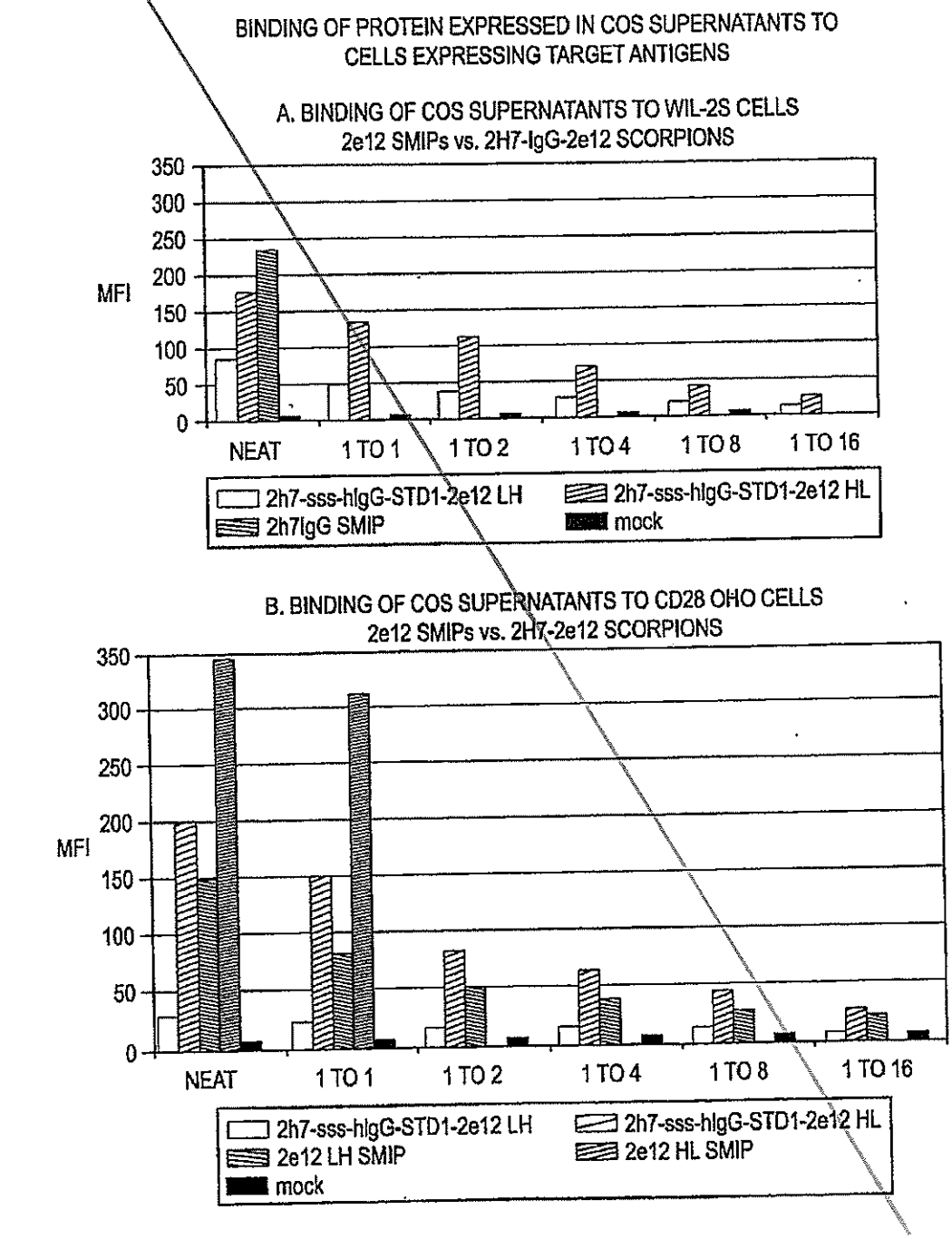

BINDING OF PROTEIN EXPRESSED IN COS SUPERNATANTS TO CELLS EXPRESSING TARGET ANTIGENS
A. BINDING OF COS SUPERNATANTS TO WIL-2S CELLS
2e12 SMIPs vs. 2H7-IgG-2e12 SCORPIONS
MFI
350
300
250
200
150
100
50
0
NEAT
1 TO 1
1 TO 2
1 TO 4
1 TO 8
1 TO 16
2h7-sss-hIgG-STD1-2e12 LH
2h7-sss-hIgG-STD1-2e12 HL
2h7IgG SMIP
mock
B. BINDING OF COS SUPERNATANTS TO CD28 OHO CELLS
2e12 SMIPs vs. 2H7-2e12 SCORPIONS
MFI
350
300
250
200
150
100
50
0
NEAT
1 TO 1
1 TO 2
1 TO 4
1 TO 8
1 TO 16
2h7-sss-hIgG-STD1-2e12 LH
2h7-sss-hIgG-STD1-2e12 HL
2e12 LH SMIP
2e12 HL SMIP
mock

FIG. 4

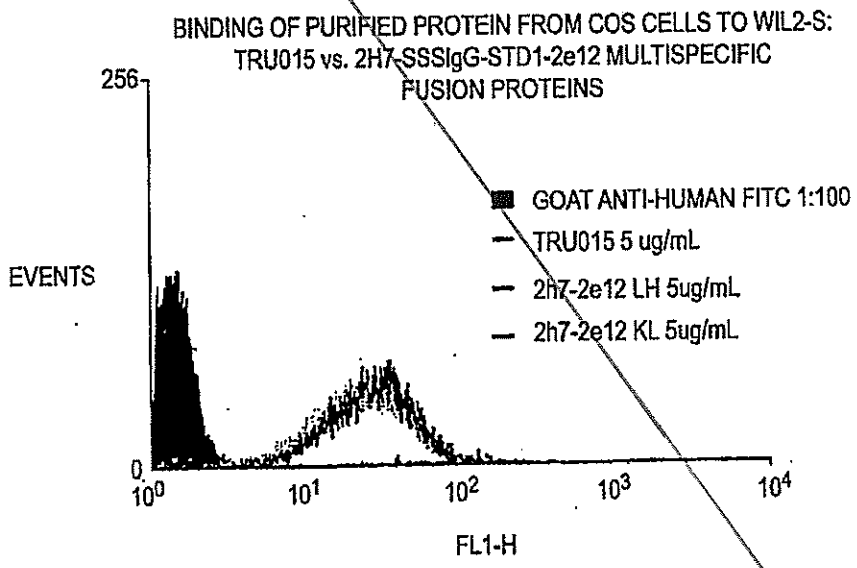

BINDING OF PURIFIED PROTEIN FROM COS CELLS TO WIL2-S:
TRU015 vs. 2H7-SSSIgG-STD1-2e12 MULTISPECIFIC
FUSION PROTEINS
256
EVENTS
0
GOAT ANTI-HUMAN FITC 1:100
TRU015 5 ug/mL
2h7-2e12 LH 5ug/mL
2h7-2e12 KL 5ug/mL
10^0
10^1
10^2
10^3
10^4
FL1-H

FIG. 5

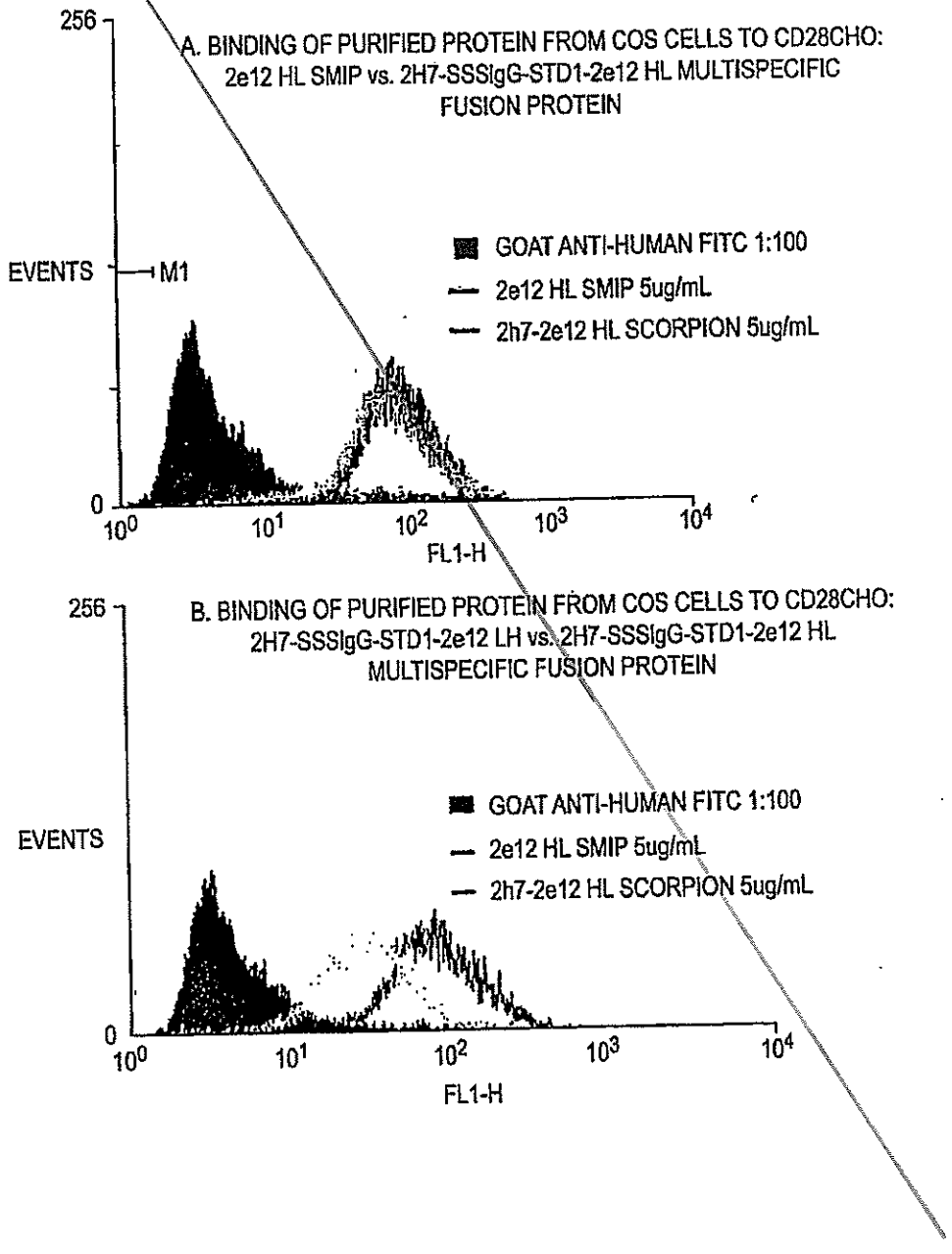

A. BINDING OF PURIFIED PROTEIN FROM COS CELLS TO CD28CHO:
2e12 HL SMIP vs. 2H7-SSSIgG-STD1-2e12 HL MULTISPECIFIC
FUSION PROTEIN
256
EVENTS
M1
0
GOAT ANTI-HUMAN FITC 1:100
2e12 HL SMIP 5ug/mL
2h7-2e12 HL SCORPION 5ug/mL
10^0
10^1
10^2
10^3
10^4
FL1-H
B. BINDING OF PURIFIED PROTEIN FROM COS CELLS TO CD28CHO:
2H7-SSSIgG-STD1-2e12 LH vs. 2H7-SSSIgG-STD1-2e12 HL
MULTISPECIFIC FUSION PROTEIN
256
EVENTS
0
GOAT ANTI-HUMAN FITC 1:100
2e12 HL SMIP 5ug/mL
2h7-2e12 HL SCORPION 5ug/mL
10^0
10^1
10^2
10^3
10^4
FL1-H

FIG. 6A

TABLE IDENTIFYING FUNCTIONAL ELEMENTS OF MULTISPECIFIC FUSION PROTEINS

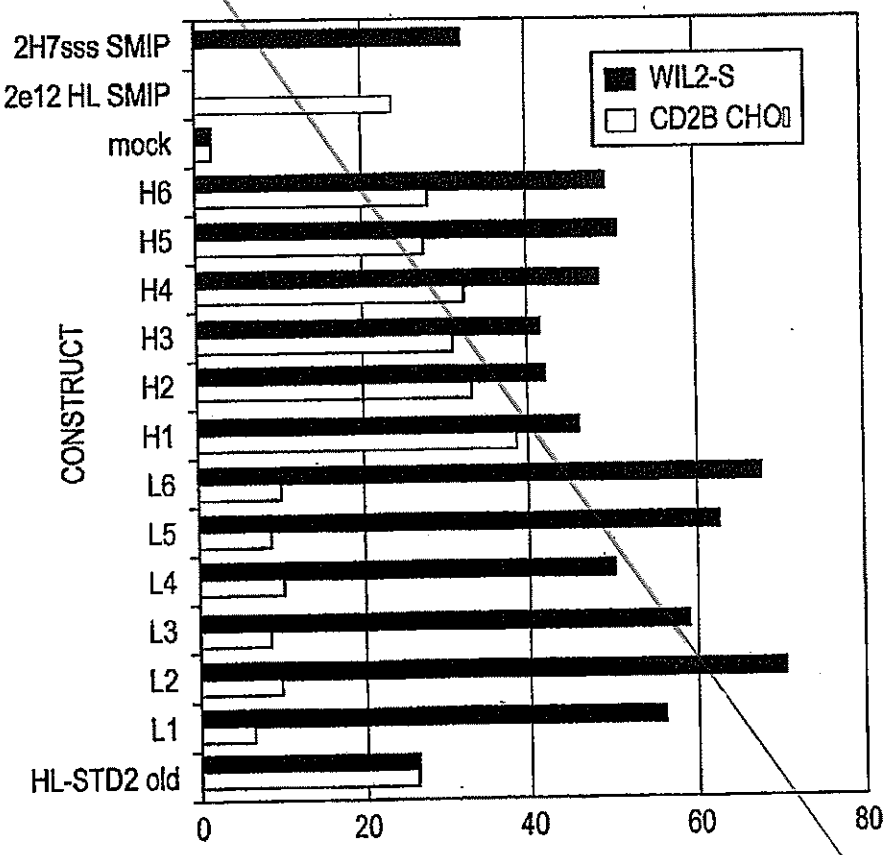


BD1 Binding Domain 1	Linker 1	EFD Effector Function Domain	Linker 2 ID	Linker Length (aa) Linker Plus R. Site	CH3 COOH	Linker 2 Sequence (- restriction site)	Fusion Junction with BD2 (L2 RS--QVQ 2e12)	BD2 Binding Domain 2
2H7 V_L-V_H	Modified hIgG1 hinge ccc->sss	hIgG1-CH2-CH3	STD	20	PGK	NYGGGGSGGGGSGGGGSG	NS QVQ	2e12 V_H-V_L
2H7 V_L-V_H	Modified hIgG1 hinge ccc->sss	hIgG1-CH2-CH3	STD2	38	PGK	NYGGGGSGGGGSGGGGSG NYGGGGSGGGGSGGGGSG	NS QVQ	2e12 V_H-V_L
2H7 V_L-V_H	Modified hIgG1 hinge ccc->sss	hIgG1-CH2-CH3	H1 L1=2e12 V_L-V_H	2 (RS)	PGK	--	NS QVQ	2e12 V_H-V_L
2H7 V_L-V_H	Modified hIgG1 hinge ccc->sss	hIgG1-CH2-CH3	H2 L2=2e12 V_L-V_H	8	PGK	GGGGSG	NS QVQ	2e12 V_H-V_L
2H7 V_L-V_H	Modified hIgG1 hinge ccc->sss	hIgG1-CH2-CH3	H3 L3=2e12 V_L-V_H	10	PGK	NYGGGGSG	NS QVQ	2e12 V_H-V_L
2H7 V_L-V_H	Modified hIgG1 hinge ccc->sss	hIgG1-CH2-CH3	H4 L4=2e12 V_L-V_H	13	PGK	GGGGSGGGGSG	NS QVQ	2e12 V_H-V_L
2H7 V_L-V_H	Modified hIgG1 hinge ccc->sss	hIgG1-CH2-CH3	H5 L5=2e12 V_L-V_H	15	PGK	NYGGGGSGGGGSG	NS QVQ	2e12 V_H-V_L
2H7 V_L-V_H	Modified hIgG1 hinge ccc->sss	hIgG1-CH2-CH3	H6 L6=2e12 V_L-V_H	18	PGK	GGGGSGGGGSGGGGSG	NS QVQ	2e12 V_H-V_L
2H7 V_L-V_H	Modified hIgG1 hinge ccc->sss	hIgG1-CH2-CH3	H7	8	PGK	GCPPCP	NS QVQ	2e12 V_H-V_L

FIG. 7

ALTERING THE LINKER AFTER THE EFD AND THE ORIENTATION OF V REGIONS IN BD2 AFFECTS BINDING EFFICIENCY OF MULTISPECIFIC FUSION PROTEINS

BINDING OF 2H7-SSShIgG-L/Hx-2e12 MULTISPECIFIC FUSION PROTEINS WITH VARIOUS LINKERS TO WIL2-S AND CD28 CHO



**ALL FUSION PROTEINS USED AT 0.72 ug/mL, PROTEIN A PURIFIED, GENERATED FROM TRANSIENT COS SUPERNATANTS.

FIG. 9

Western Blots of Multispecific Fusion Proteins With H6 Linker
A. Absence of SMIP or smaller CD28 detectable forms
B. Presence of a SMIP sized form using CD20 anti-id Fab

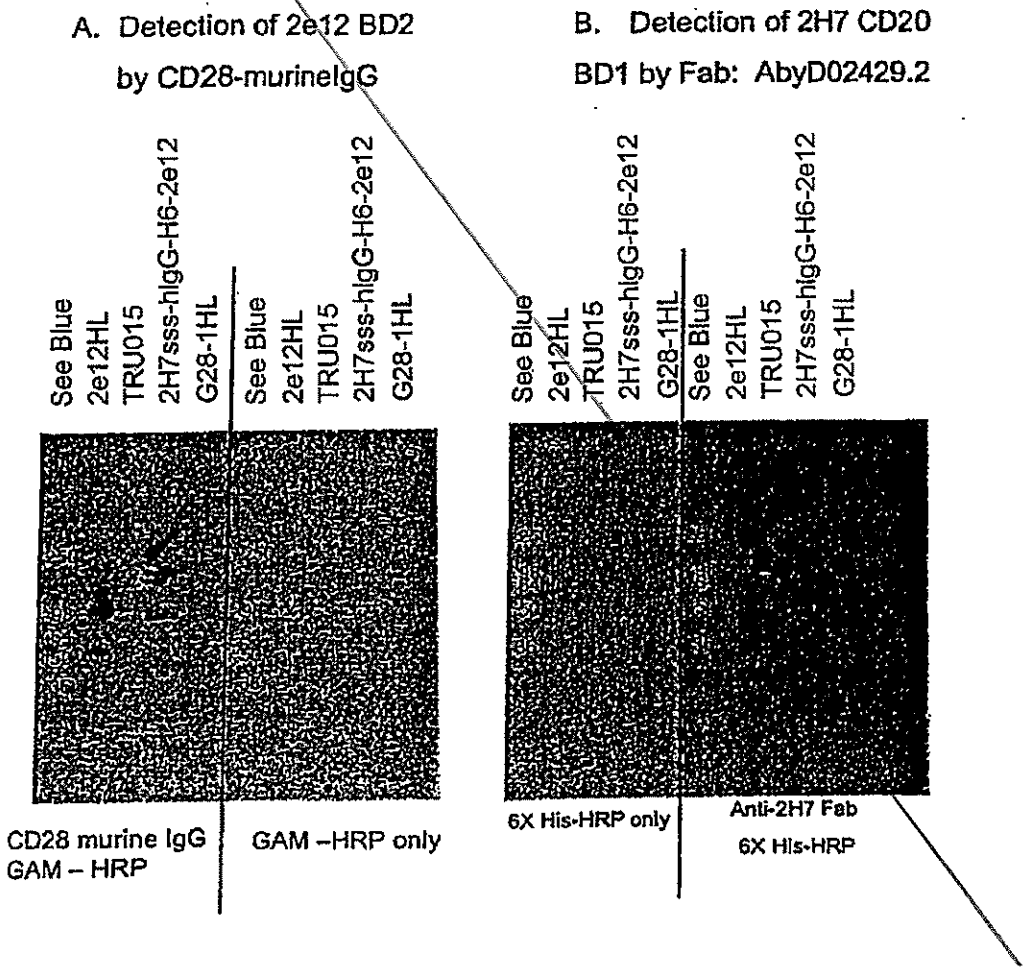
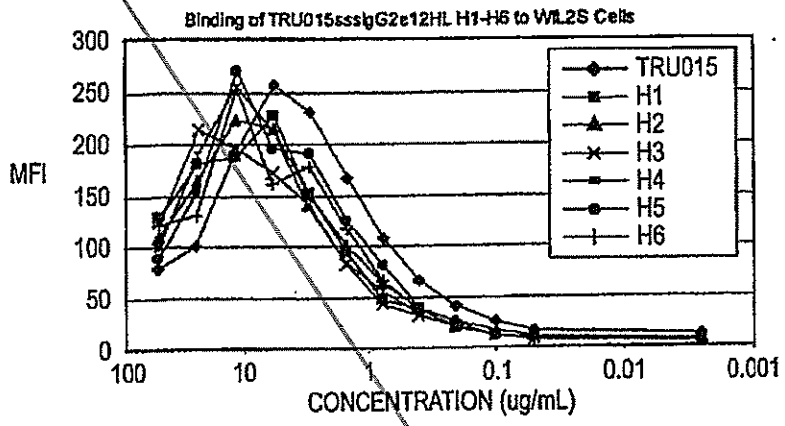


FIG. 10

A. Binding of Multispecific Fusion Proteins With Variant Linkers to WIL-2S Cells



B. Binding of Multispecific Fusion Protein With Variant Linkers to CD28 CHO Cells

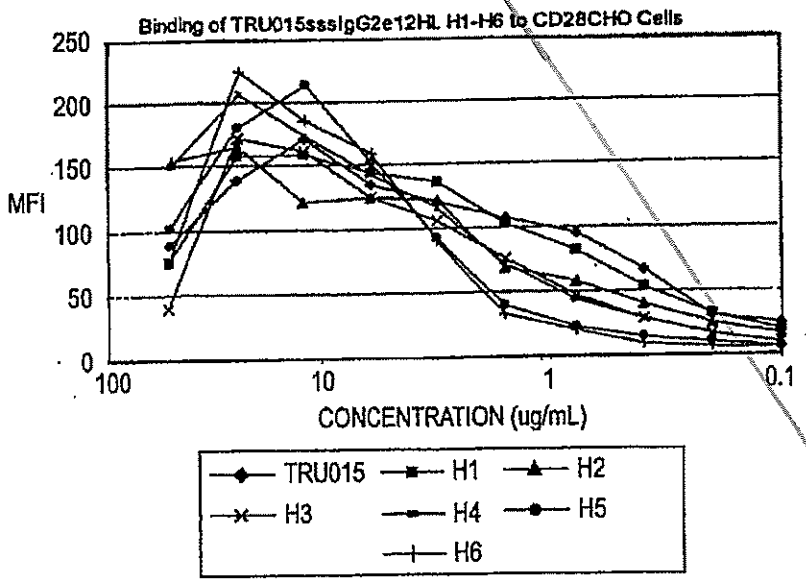


FIG. 11

Summary of SEC Fractionation of 2H7-sssIgG-2e12 HL Multispecific Fusion Proteins with Variant Linkers

Linker ID	Retention Time for POI	% POI	% Other Forms	SDS-PAGE Analysis of Cleavage at EFD/BD2 junction
H1	7.620	70.9	29.0	(Yes)
H2	7.589	67.5	32.5	(Yes)
H3	7.605	68.7	31.4	Yes
H4	7.622 (shoulder)	68.0	32.0	Yes
H5	7.933/7.680 (doublet with shoulder)	32.42/33.94	33.63	YES
H6	7.901/7.69 (doublet with shoulder)	34.5/29.3	36.1	YES
H7	7.788	84.2	15.8 (HMW)	NO

FIG. 12

Binding of [2H7-sss-hIgG-H_X-2e12 HL] Fusion Proteins with Different Linkers to Cells Expressing Target Antigen for BD1 or BD2

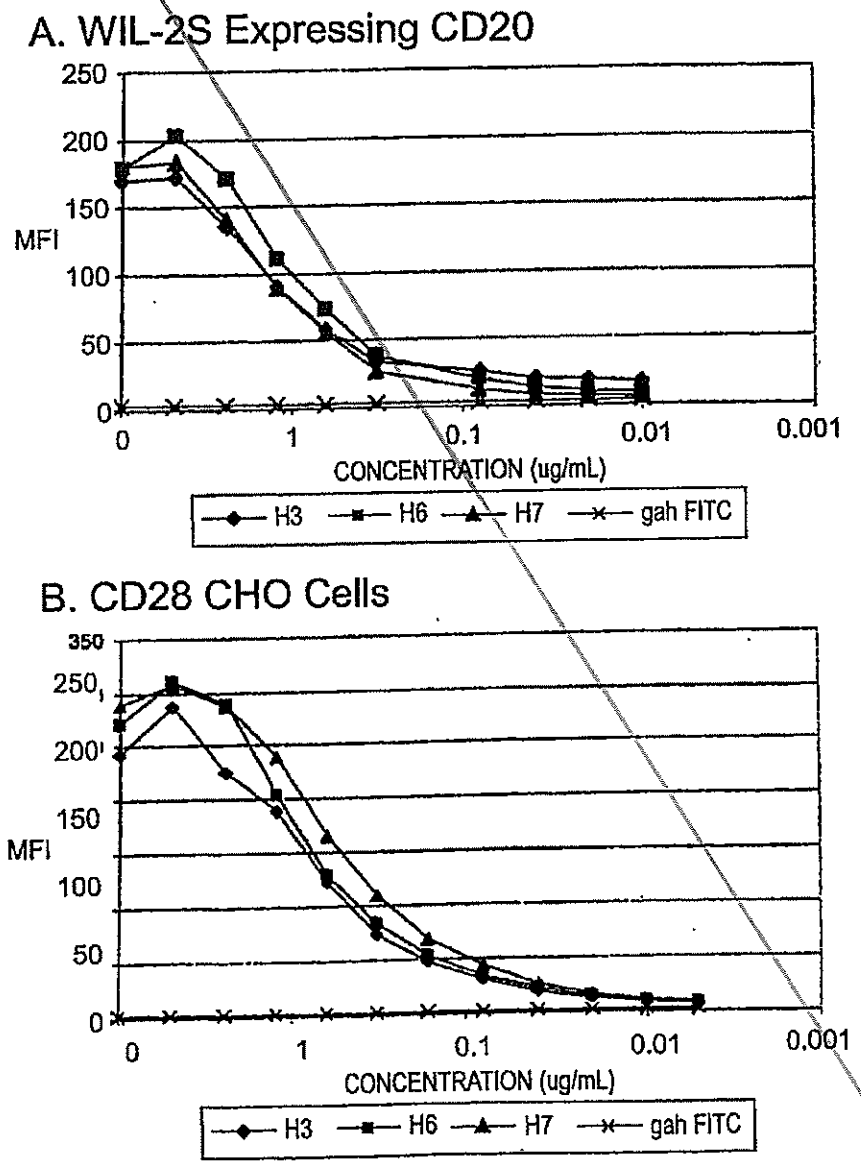


FIG. 13

Simultaneous Binding of BD1 and BD2:

Binding of [2H7-sss-hIgG-H_x-2e12 HL] Fusion Proteins with H3, H6, and H7 Linkers to WIL-2S Cells can be detected with CD28mIgG + FITC anti-mouse

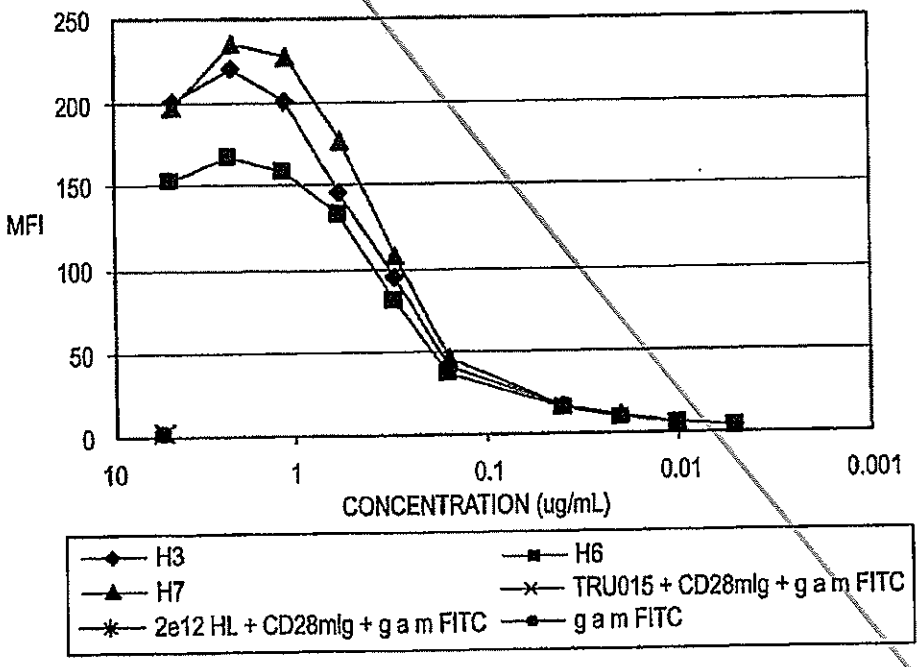
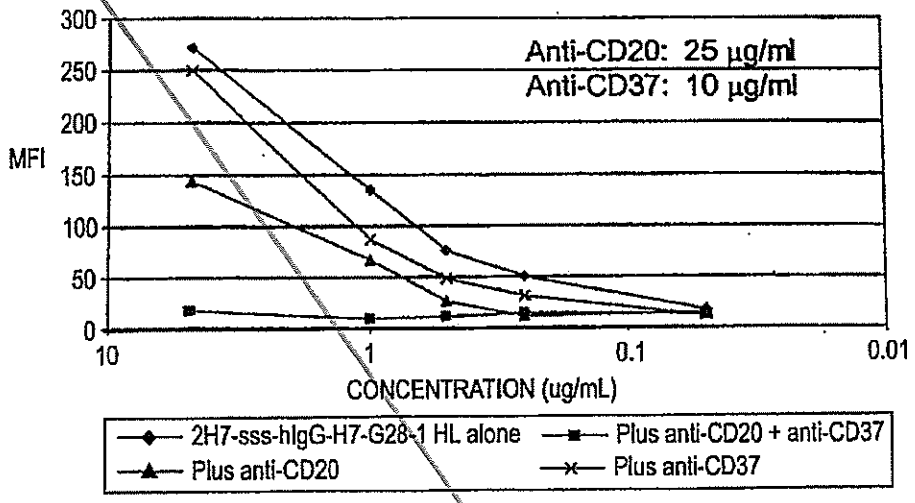


FIG. 14

A. Blocking of Binding of 2H7-sss-hIgG-H7-G28-1 HL Protein to Ramos Cells by CD20 and/or CD37 Targeted Antibodies



B. Blocking of Binding of 2H7-sss-hIgG-H7-G28-1 HL to BJAB Cells by CD20 and/or CD37 Targeted Antibodies

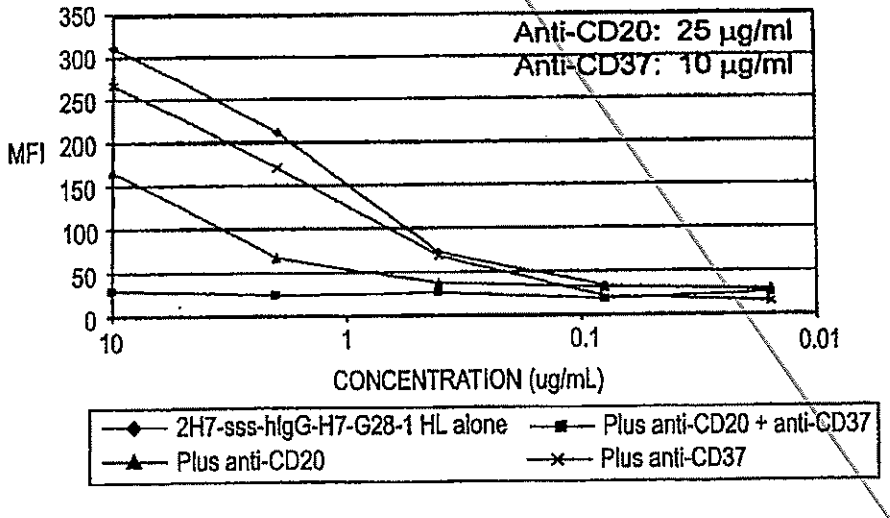


FIG. 15

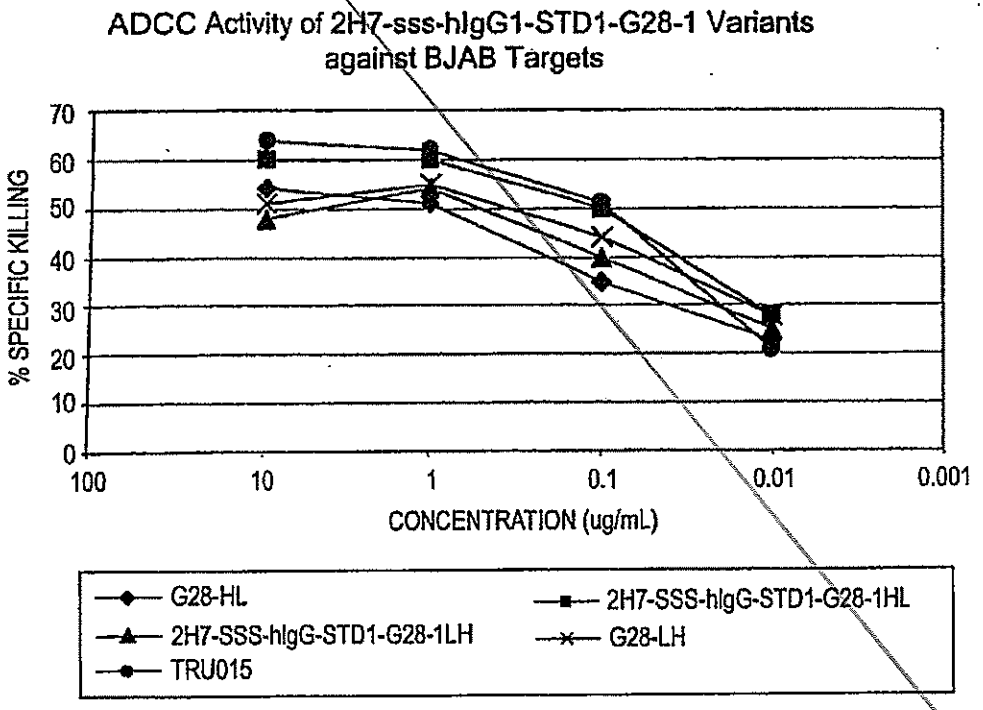

ADCC Activity of 2H7-sss-hIgG1-STD1-G28-1 Variants against BJAB Targets
% SPECIFIC KILLING
70
60
50
40
30
20
10
0
100
10
1
0.1
0.01
0.001
CONCENTRATION (ug/mL)
G28-HL
2H7-SSS-hIgG-STD1-G28-1HL
2H7-SSS-hIgG-STD1-G28-1LH
G28-LH
TRU015

FIG. 16

The Percent CD3, CD19, and CD40 Positive Lymphocytes Present in Culture after Incubation with TRU-015, G28-1 SMIP, TRU-015+G28-1 SMIP, or 2H7-sss-hIgG1-H7-G28-1 HL

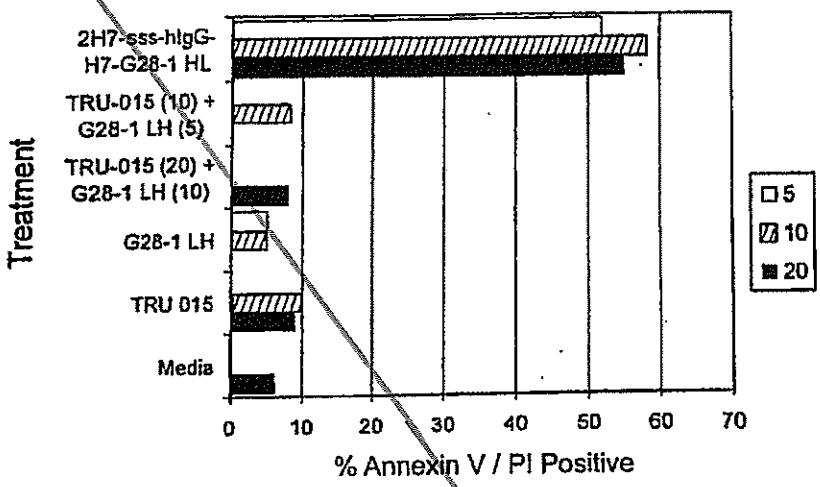
24 Hours	$CD3^+$	$CD19^+$	$CD40^+$
Media	77%	8%	7%
TRU015	76%	8.5%	7.9%
G28-1 SMIP	78%	8. 9%	7.8%
TRU015+G28-1 SMIP	76.3%	8.1%	7.5%
2H7-ssshIgG1-G28-1HL (H7)	78.4%	8.9%	7.9%

72 Hours	$CD3^+$	$CD19^+$	$CD40^+$
Media	78.5%	7.9%	7.7%
TRU015	85.2%	2.3%	2.7%
G28-1 SMIP	86.7%	2.2%	2.3%
TRU015+G28-1 SMIP	87.1%	1.1%	1.1%
2H7-ssshIgG1-G28-1 HL (H7)	96.7%	.08%	.77%

FIG. 17

The Percent Annexin and/or PI Positive B Cells in Culture after 24 Hour Incubation with Single or Multispecific Fusion Proteins.

A. Ramos Cells:



B. Daudi Cells:

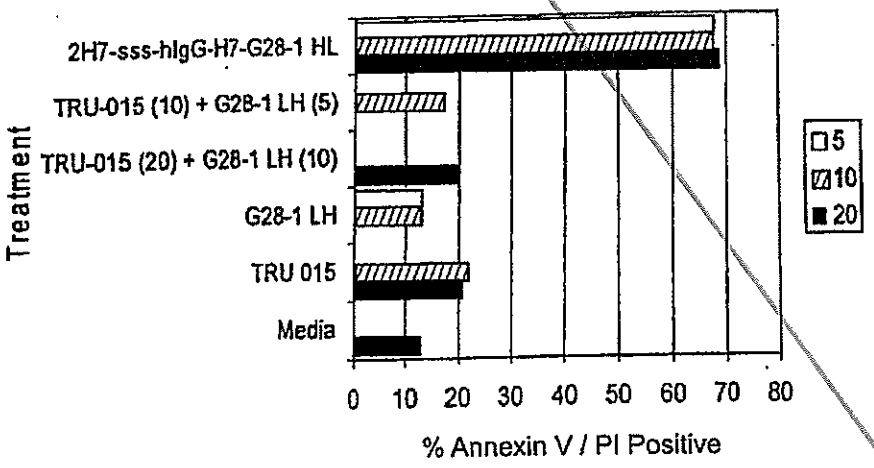


FIG. 18

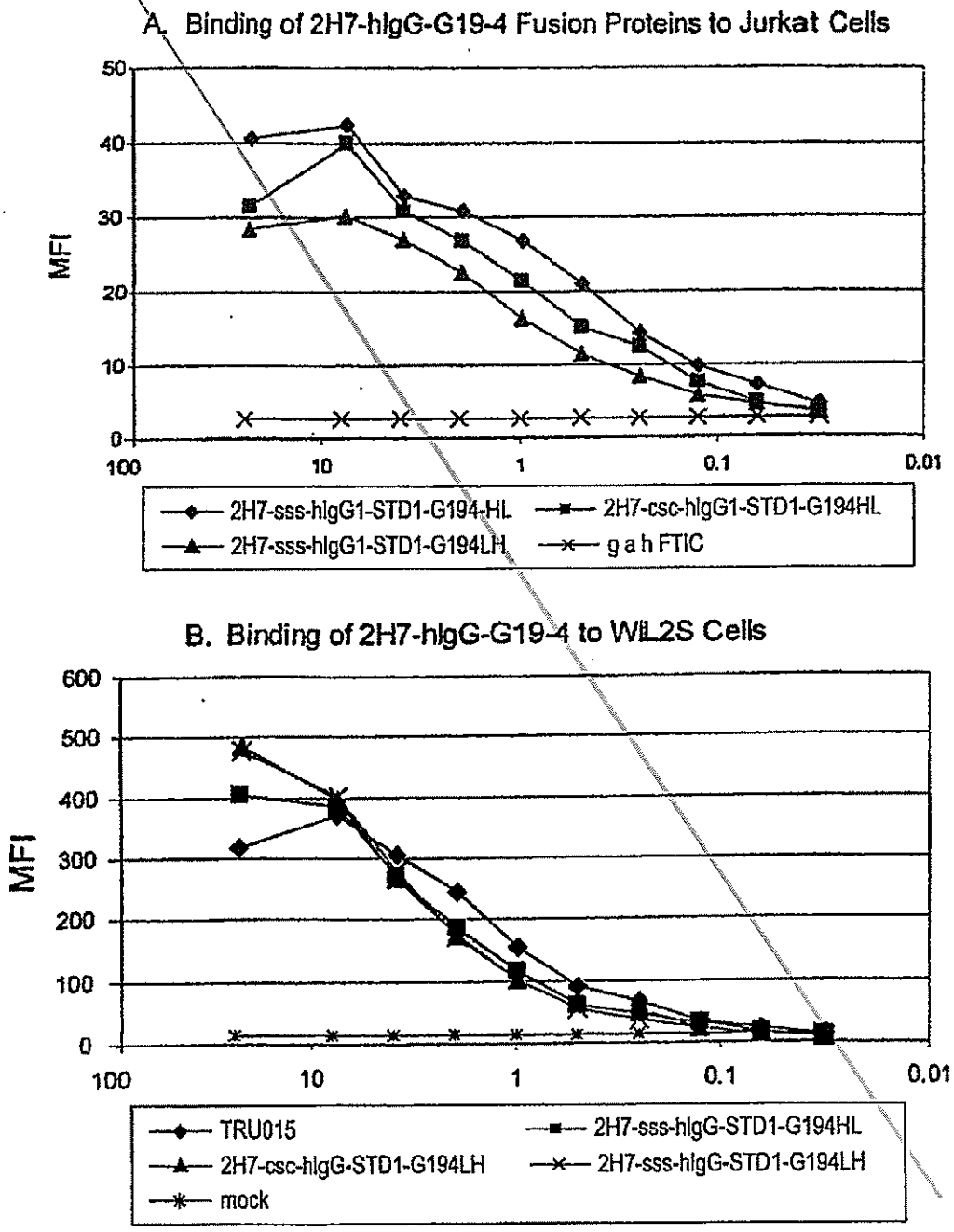
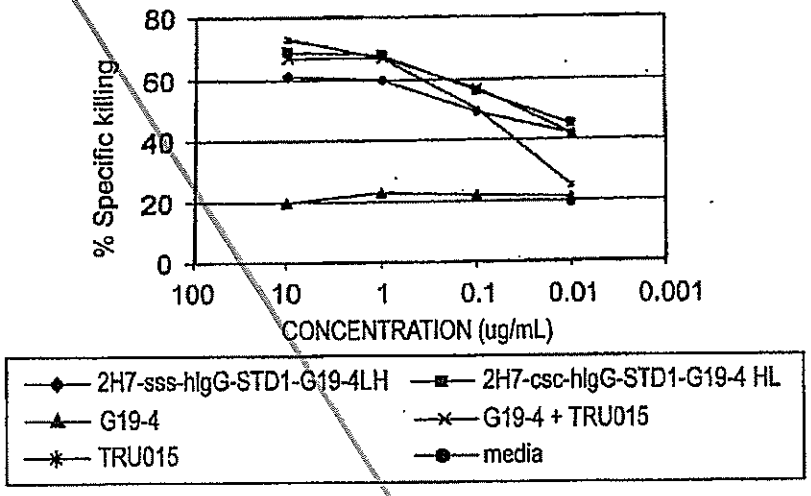

A. Binding of 2H7-hIgG-G19-4 Fusion Proteins to Jurkat Cells
MFI
50
40
30
20
10
0
100
10
1
0.1
0.01
2H7-sss-hIgG1-STD1-G194-HL
2H7-csc-hIgG1-STD1-G194HL
2H7-sss-hIgG1-STD1-G194LH
g a h FTIC
B. Binding of 2H7-hIgG-G19-4 to WIL2S Cells
MFI
600
500
400
300
200
100
0
100
10
1
0.1
0.01
TRU015
2H7-sss-hIgG-STD1-G194HL
2H7-csc-hIgG-STD1-G194LH
2H7-sss-hIgG-STD1-G194LH
mock

FIG. 19

A. ADCC Activity of 2H7-G19-4 Multispecific Fusion Proteins Against BJAB Targets Using Human PBMC Effectors at 25:1



B. ADCC Activity in NK Cell Depiated PBMC Effector Cultures Using BJAB Targets (30:1, E:T) and 2H7-G19-4 Fusion Proteins

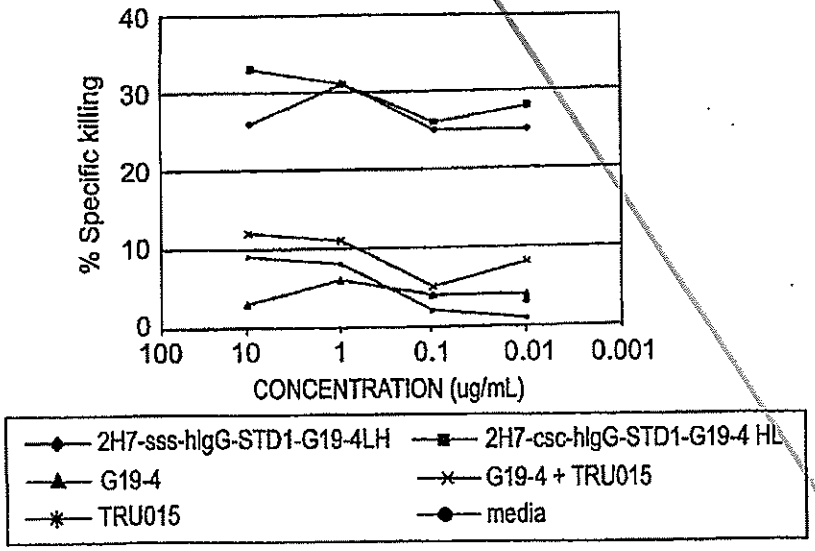


FIG. 32A

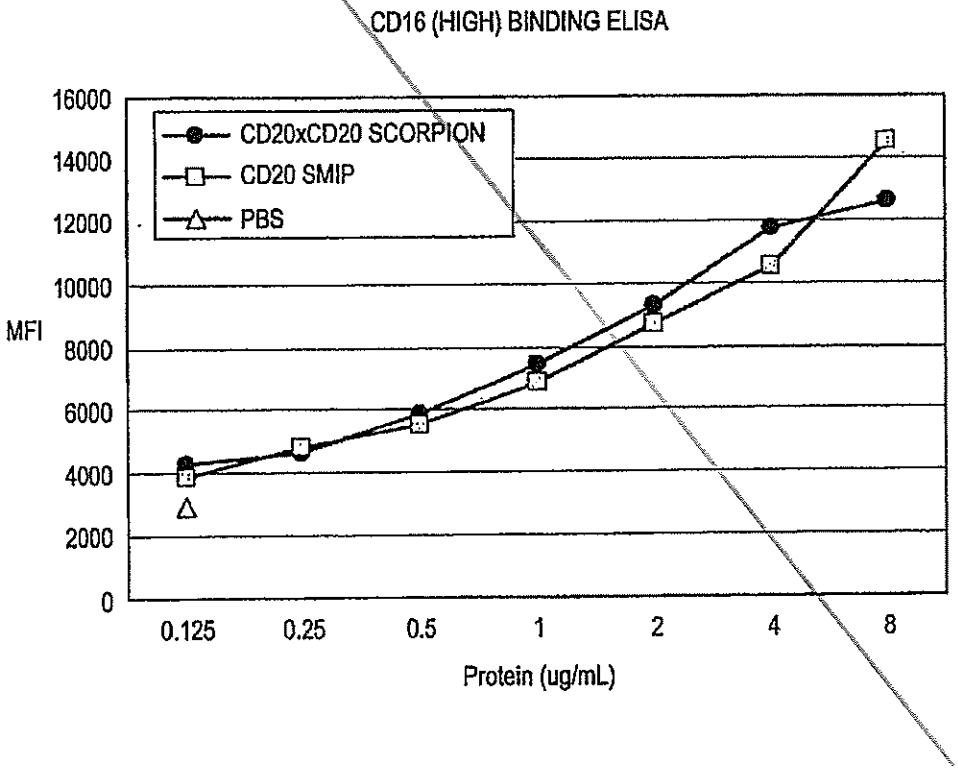

CD16 (HIGH) BINDING ELISA
CD20xCD20 SCORPION
CD20 SMIP
PBS
MFI
16000
14000
12000
10000
8000
6000
4000
2000
0
0.125
0.25
0.5
1
2
4
8
Protein (ug/mL)

FIG. 32B

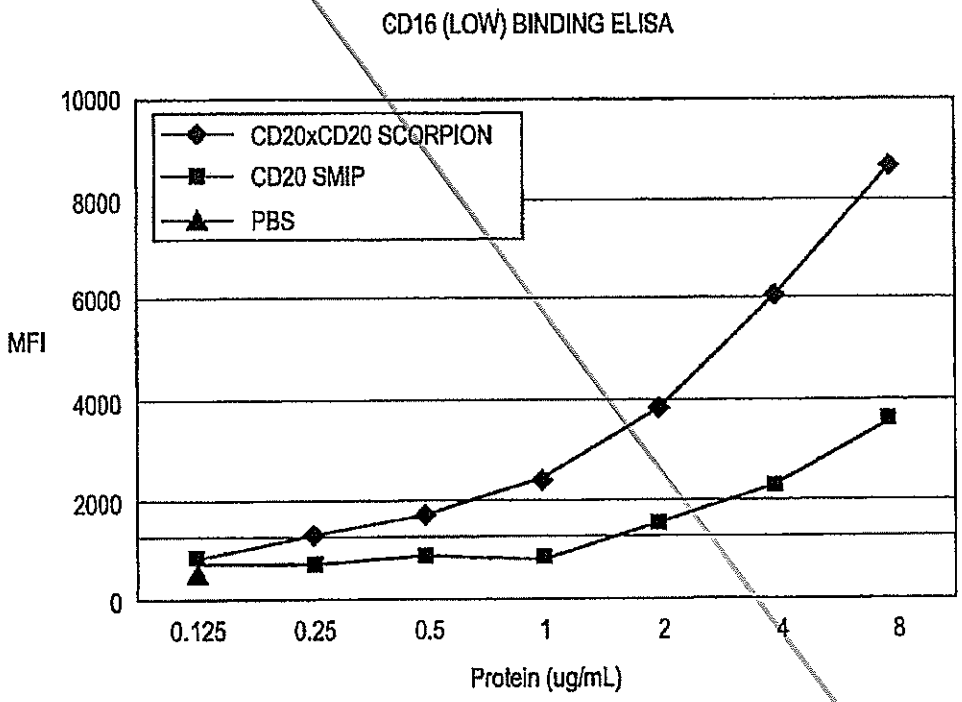

CD16 (LOW) BINDING ELISA
CD20xCD20 SCORPION
CD20 SMIP
PBS
MFI
10000
8000
6000
4000
2000
0
0.125
0.25
0.5
1
2
4
8
Protein (ug/mL)

FIG. 33

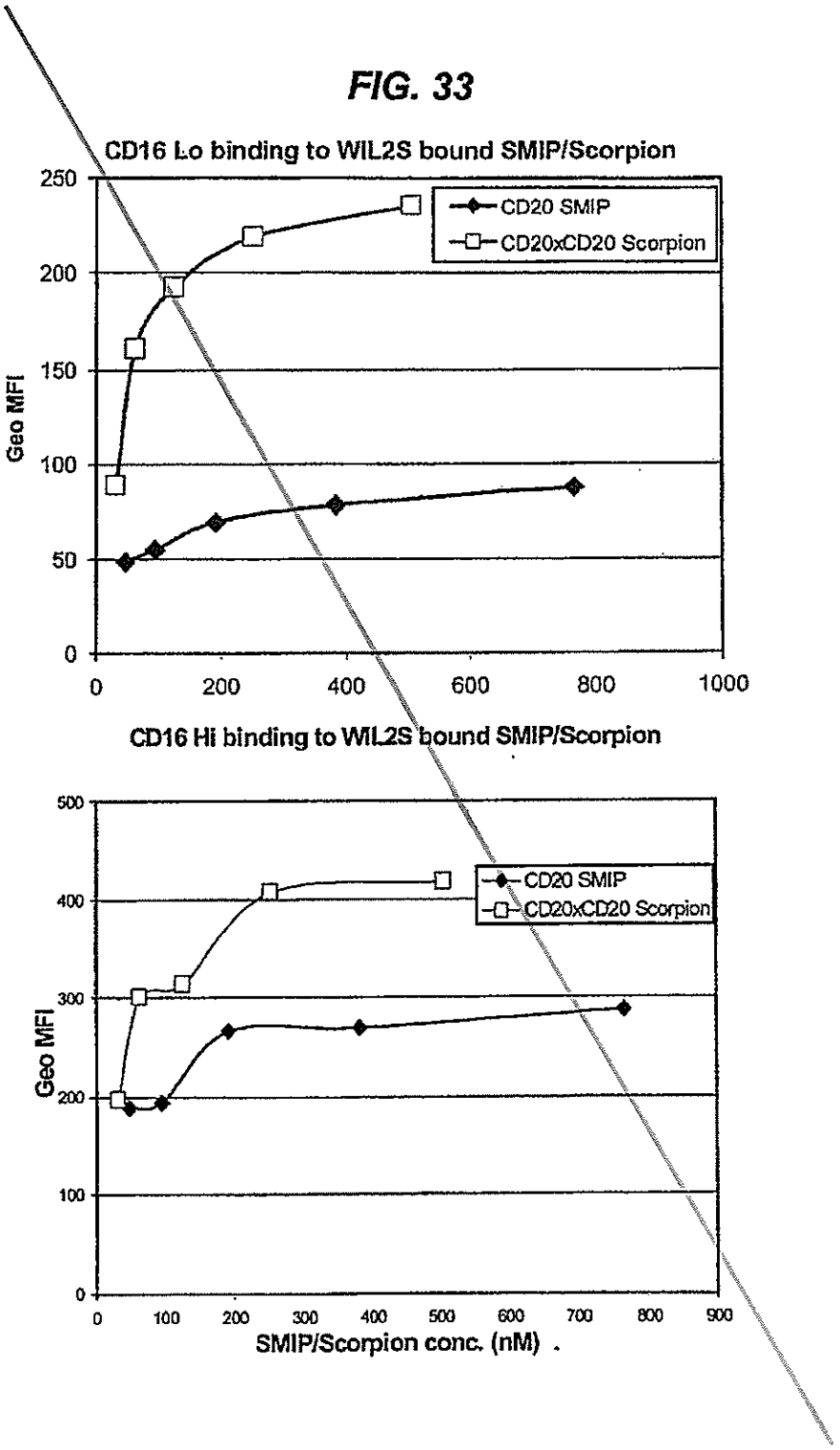

CD16 Lo binding to WIL2S bound SMIP/Scorpion
Geo MFI
250
200
150
100
50
0
0
200
400
600
800
1000
CD20 SMIP
CD20xCD20 Scorpion
CD16 Hi binding to WIL2S bound SMIP/Scorpion
Geo MFI
500
400
300
200
100
0
0
100
200
300
400
500
600
700
800
900
SMIP/Scorpion conc. (nM)
CD20 SMIP
CD20xCD20 Scorpion

FIG. 35

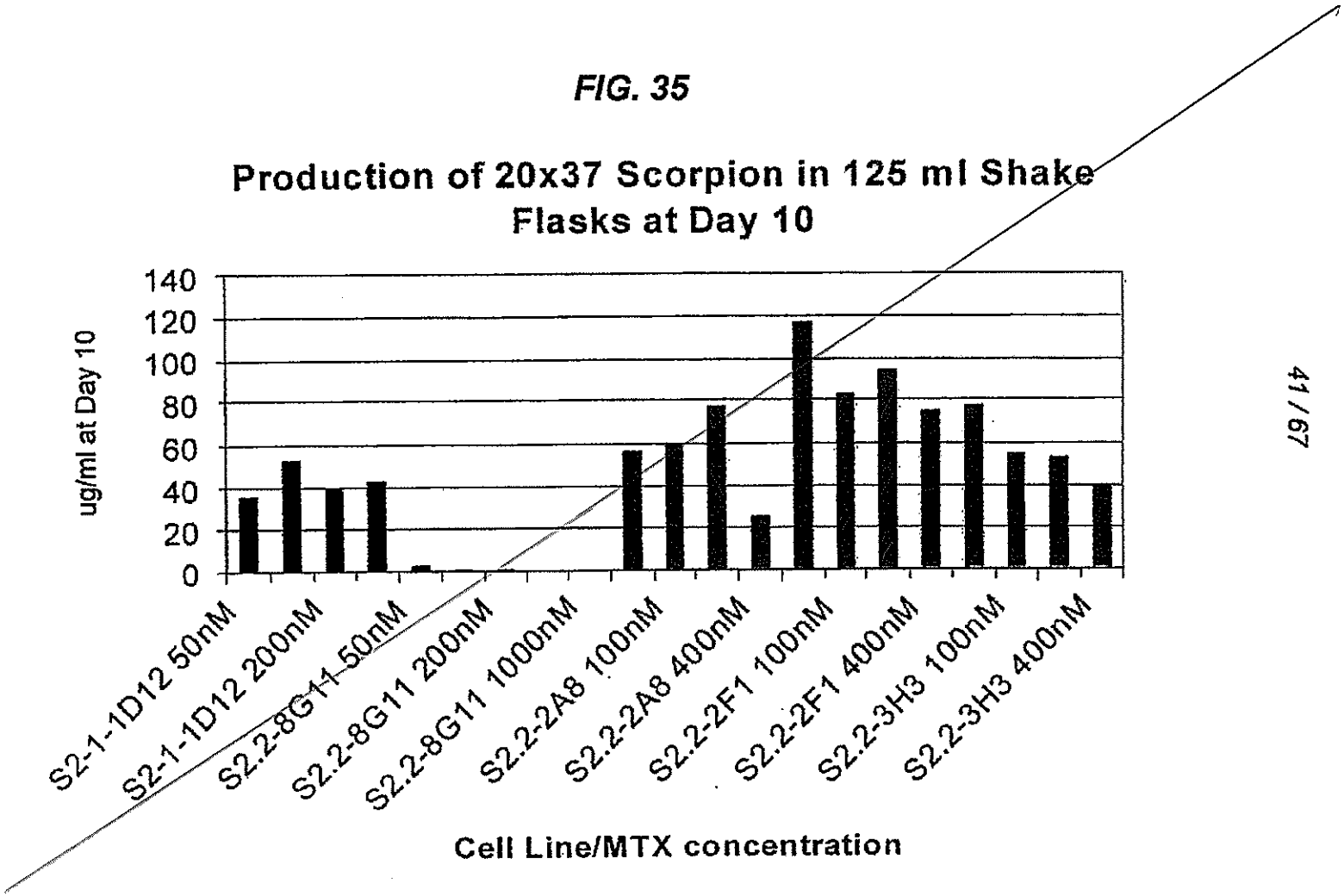

Production of 20x37 Scorpion in 125 ml Shake Flasks at Day 10
ug/ml at Day 10
140
120
100
80
60
40
20
0
S2-1-1D12 50nM
S2-1-1D12 200nM
S2.2-8G11 50nM
S2.2-8G11 200nM
S2.2-8G11 1000nM
S2.2-2A8 100nM
S2.2-2A8 400nM
S2.2-2F1 100nM
S2.2-2F1 400nM
S2.2-3H3 100nM
S2.2-3H3 400nM
Cell Line/MTX concentration

FIG. 38

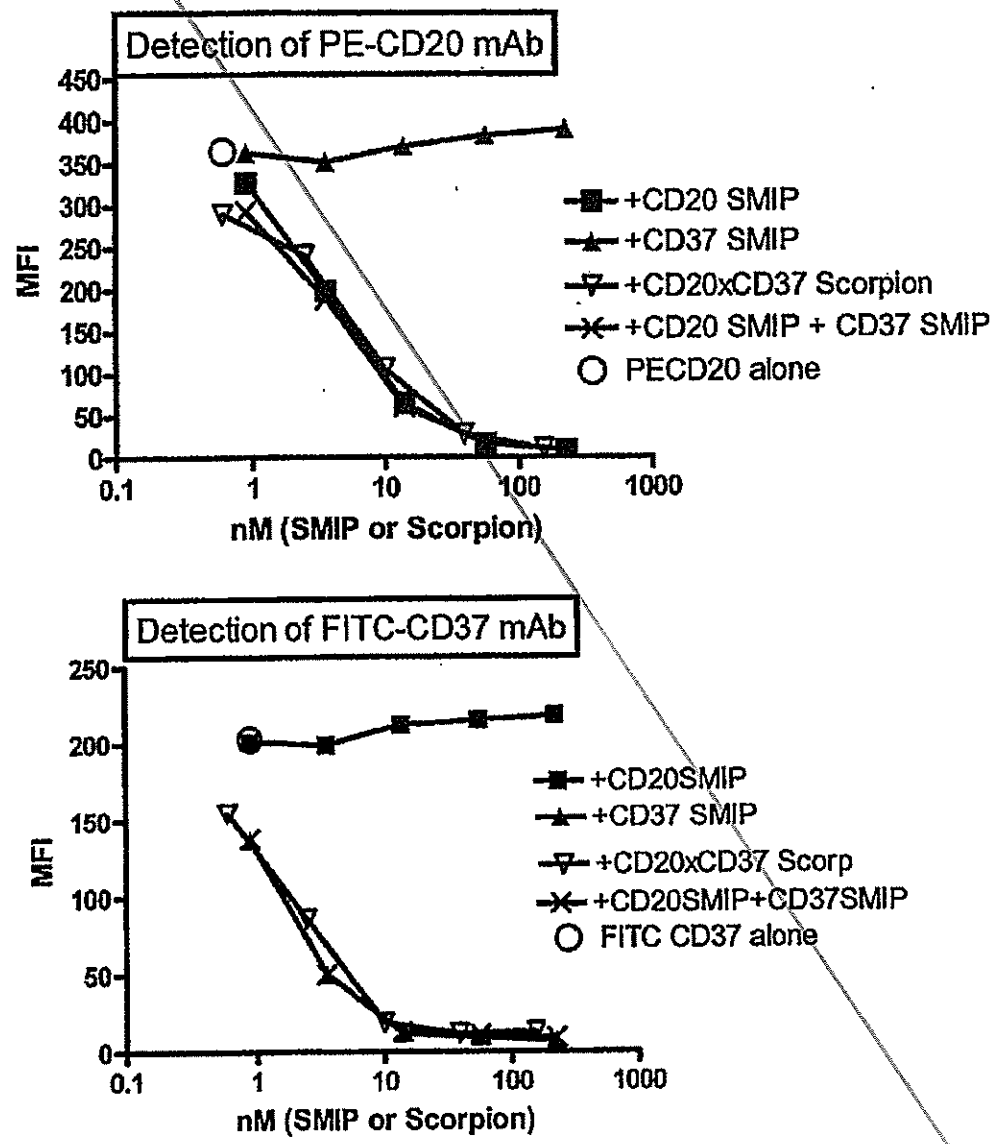

Detection of PE-CD20 mAb
MFI
450
400
350
300
250
200
150
100
50
0
0.1
1
10
100
1000
nM (SMIP or Scorpion)
+CD20 SMIP
+CD37 SMIP
+CD20xCD37 Scorpion
+CD20 SMIP + CD37 SMIP
PECD20 alone
Detection of FITC-CD37 mAb
MFI
250
200
150
100
50
0
0.1
1
10
100
1000
nM (SMIP or Scorpion)
+CD20SMIP
+CD37 SMIP
+CD20xCD37 Scorp
+CD20SMIP+CD37SMIP
FITC CD37 alone

FIG. 41

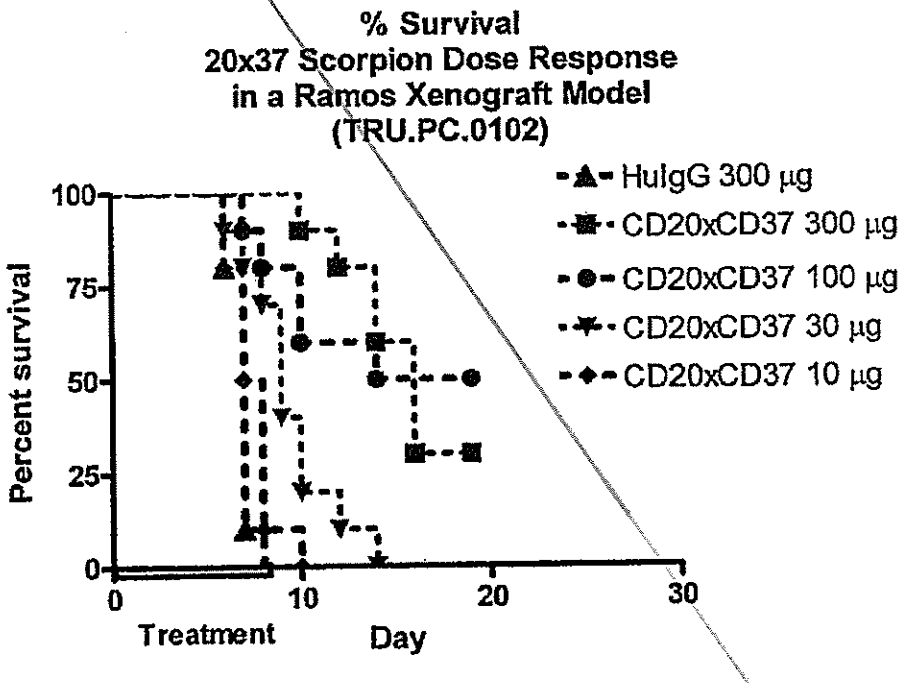

% Survival
20x37 Scorpion Dose Response
in a Ramos Xenograft Model
(TRU.PC.0102)
HuIgG 300 µg
CD20xCD37 300 µg
CD20xCD37 100 µg
CD20xCD37 30 µg
CD20xCD37 10 µg
Percent survival
100
75
50
25
0
0
10
20
30
Treatment
Day

FIG. 42

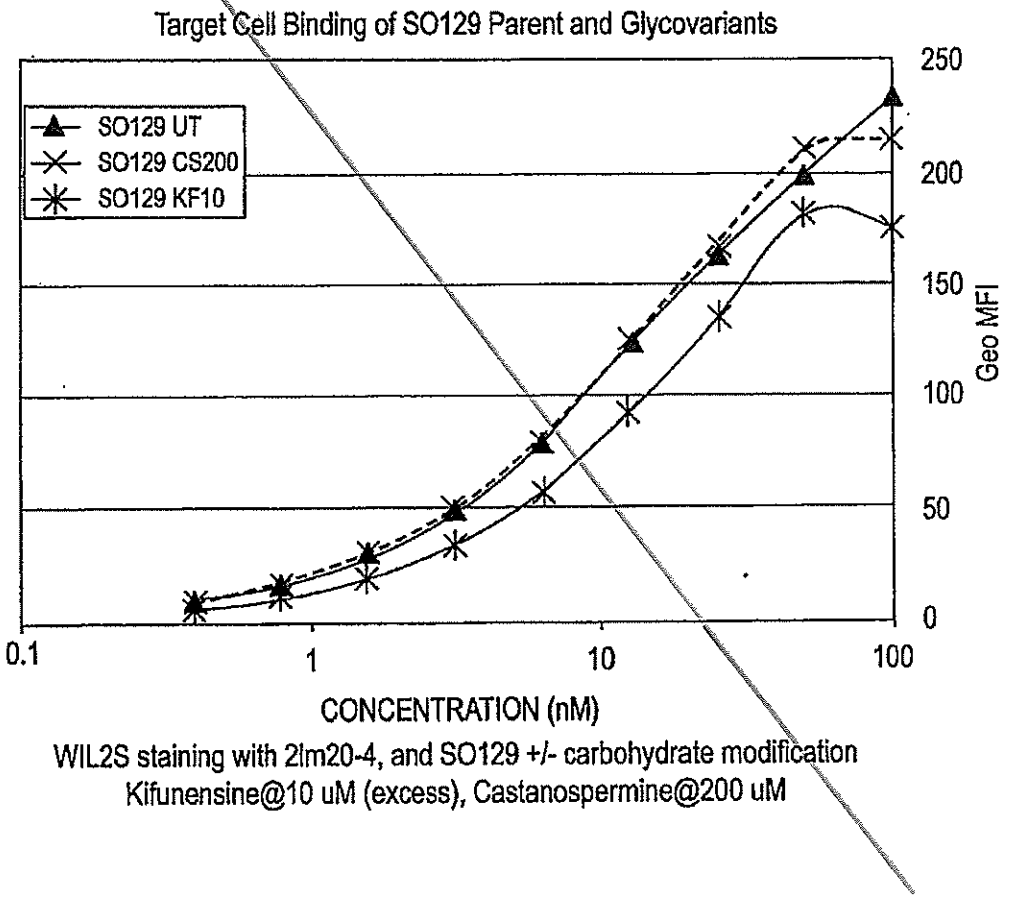
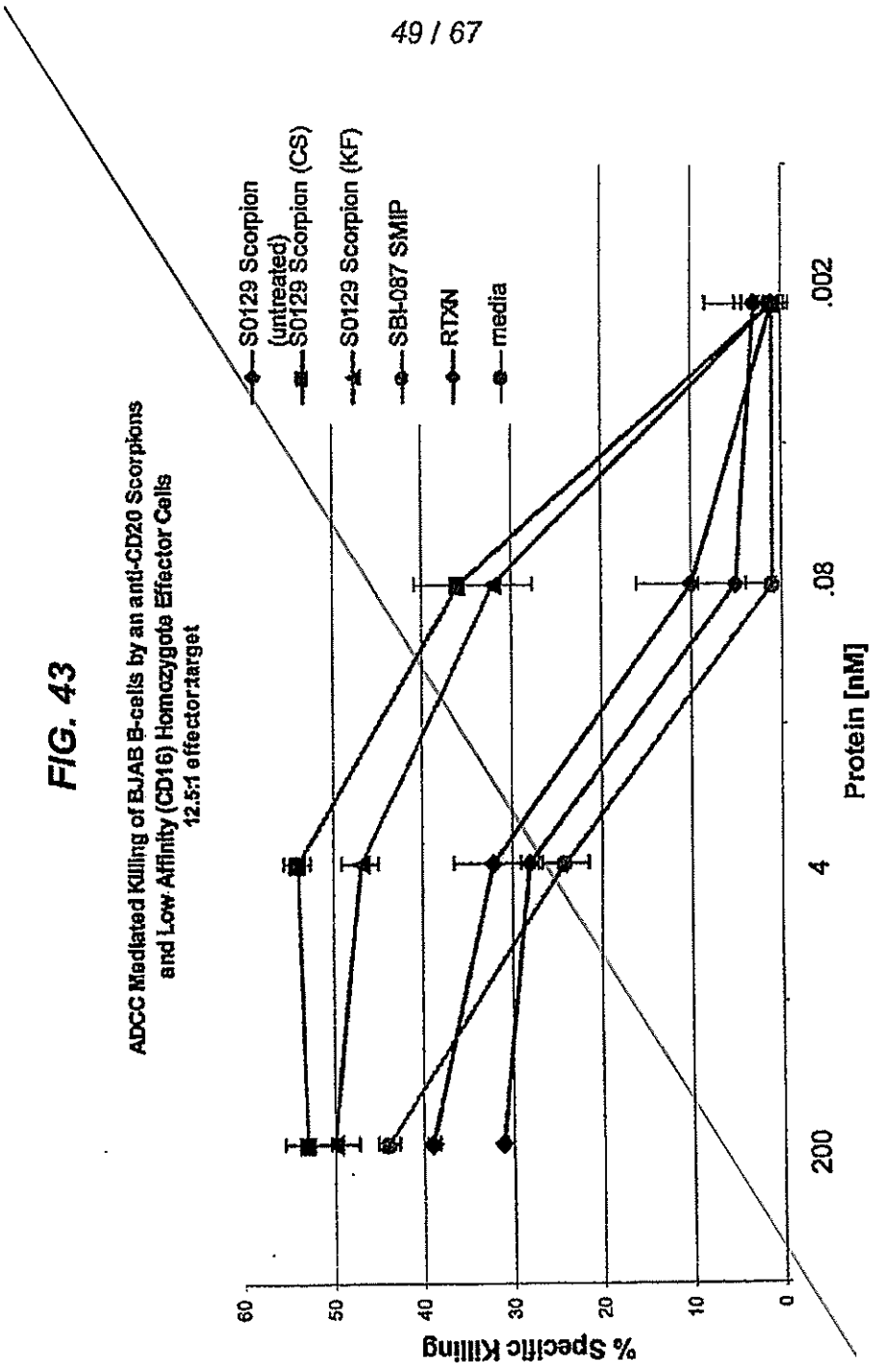

Target Cell Binding of SO129 Parent and Glycovariants
SO129 UT
SO129 CS200
SO129 KF10
250
200
150
100
50
0
Geo MFI
0.1
1
10
100
CONCENTRATION (nM)
WIL2S staining with 2Im20-4, and SO129 +/- carbohydrate modification
Kifunensine@10 uM (excess), Castanospermine@200 uM

FIG. 43


ADCC Mediated Killing of BJAB B-cells by an anti-CD20 Scorpions
and Low Affinity (CD16) Homozygote Effector Cells
12.5:1 effector:target
S0129 Scorpion (untreated)
S0129 Scorpion (CS)
S0129 Scorpion (KF)
SBI-087 SMIP
RTXN
media
% Specific Killing
0
10
20
30
40
50
60
200
4
.08
.002
Protein [nM]

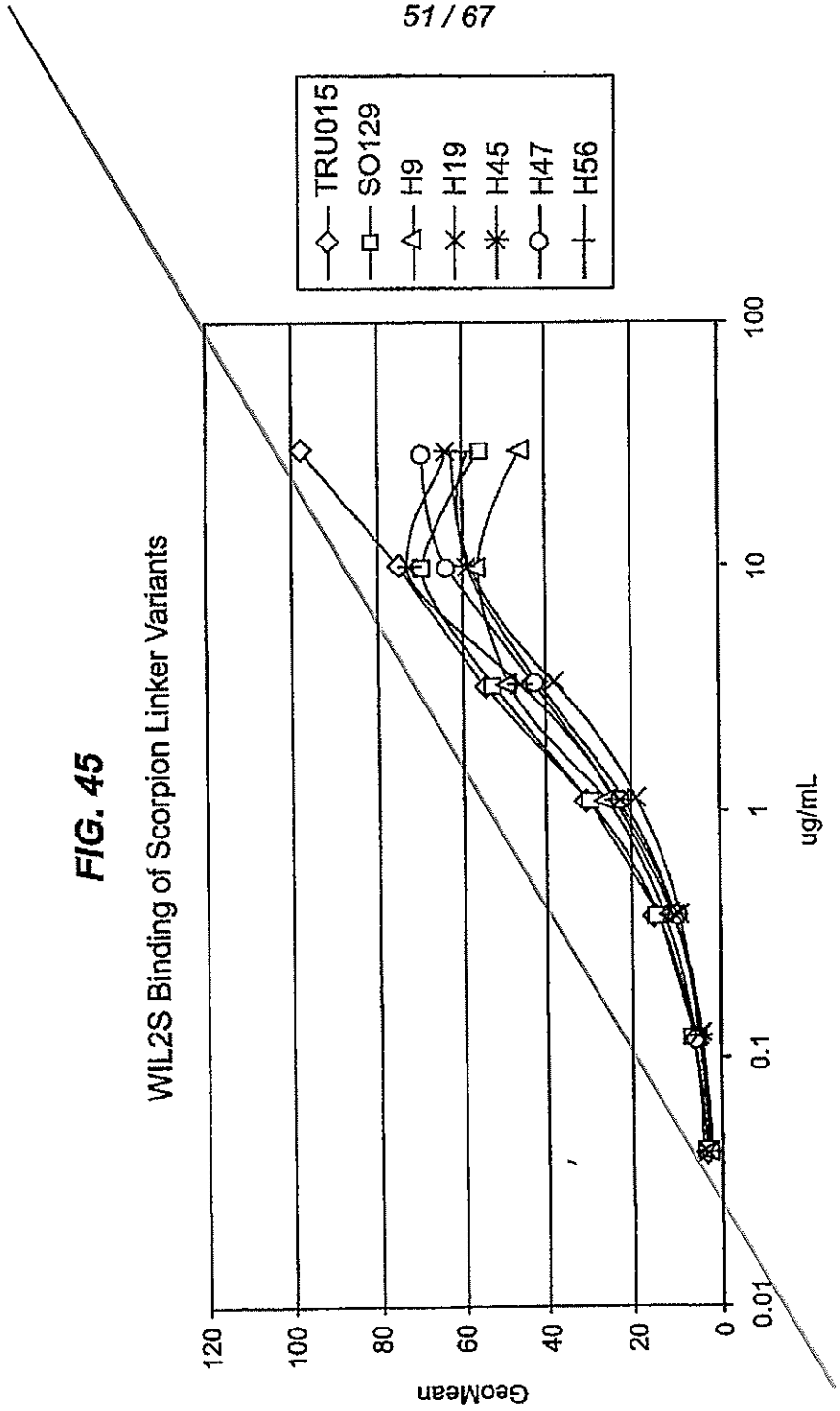

WIL2S Binding of Scorpion Linker Variants
TRU015
SO129
H9
H19
H45
H47
H56
GeoMean
120
100
80
60
40
20
0
0.01
0.1
1
10
100
ug/mL

FIG. 45

FIG. 46

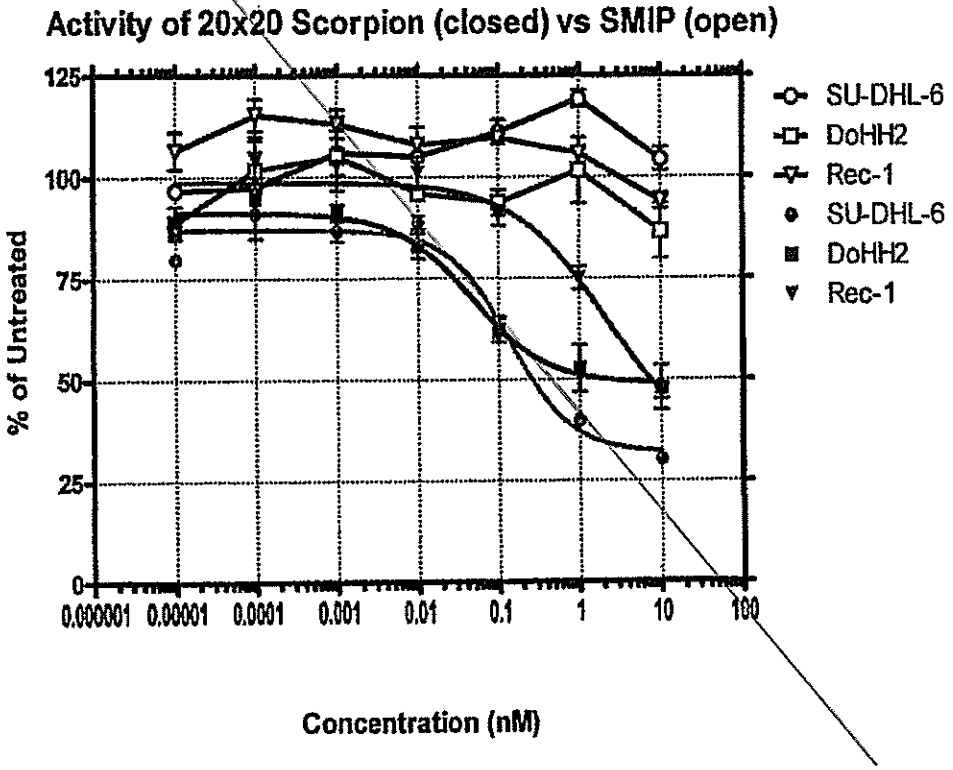

Activity of 20x20 Scorpion (closed) vs SMIP (open)
% of Untreated
125
100
75
50
25
0
0.000001
0.00001
0.0001
0.001
0.01
0.1
1
10
100
Concentration (nM)
SU-DHL-6
DoHH2
Rec-1
SU-DHL-6
DoHH2
Rec-1

FIG. 47

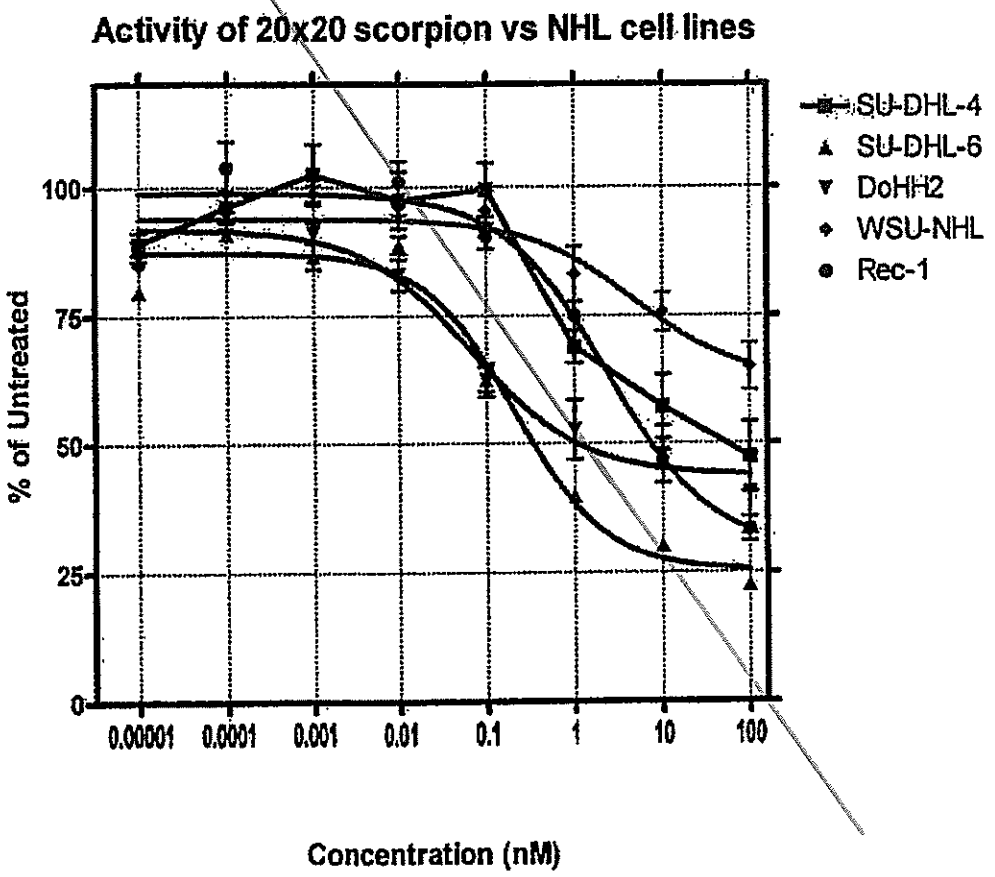

Activity of 20x20 scorpion vs NHL cell lines
% of Untreated
100
75
50
25
0
0.00001
0.0001
0.001
0.01
0.1
1
10
100
Concentration (nM)
SU-DHL-4
SU-DHL-6
DoHH2
WSU-NHL
Rec-1

FIG. 48

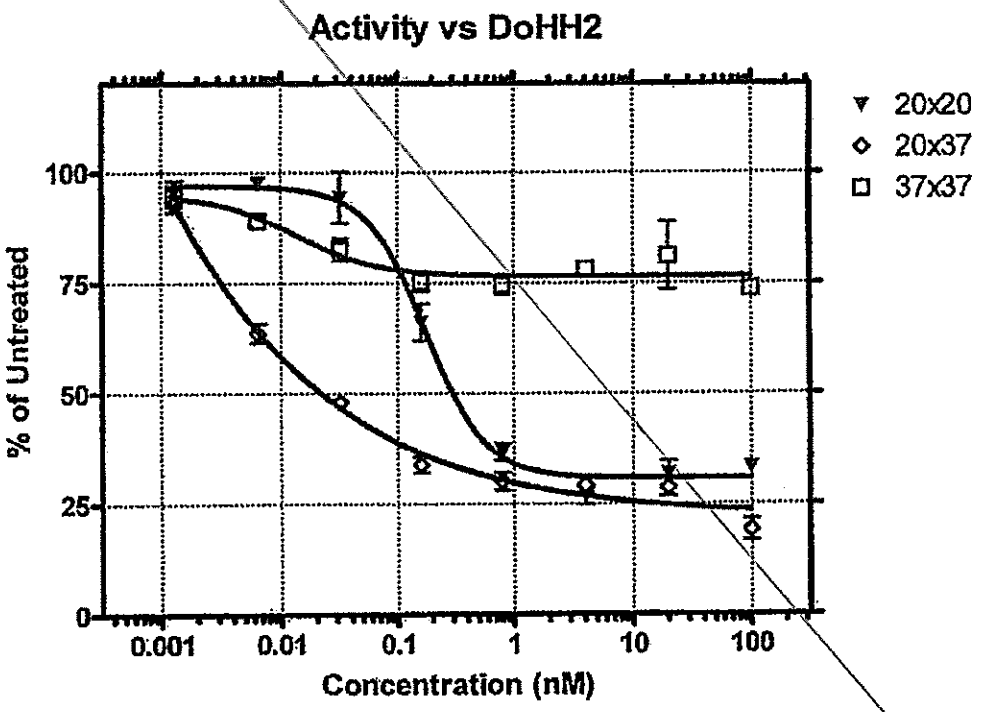

Activity vs DoHH2
% of Untreated
100
75
50
25
0
0.001
0.01
0.1
1
10
100
Concentration (nM)
20x20
20x37
37x37

FIG. 49

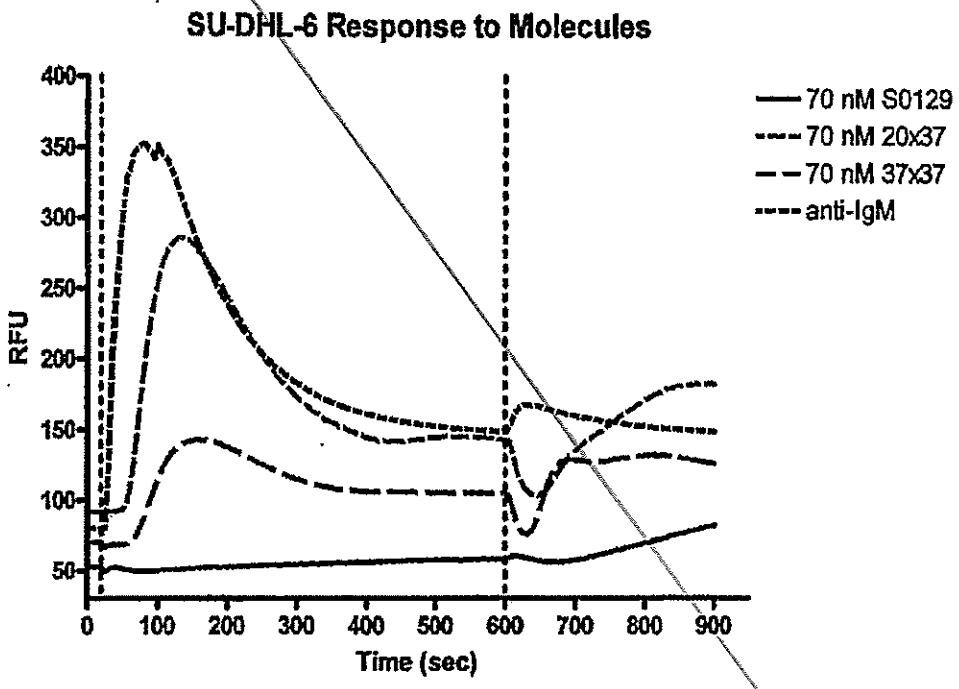
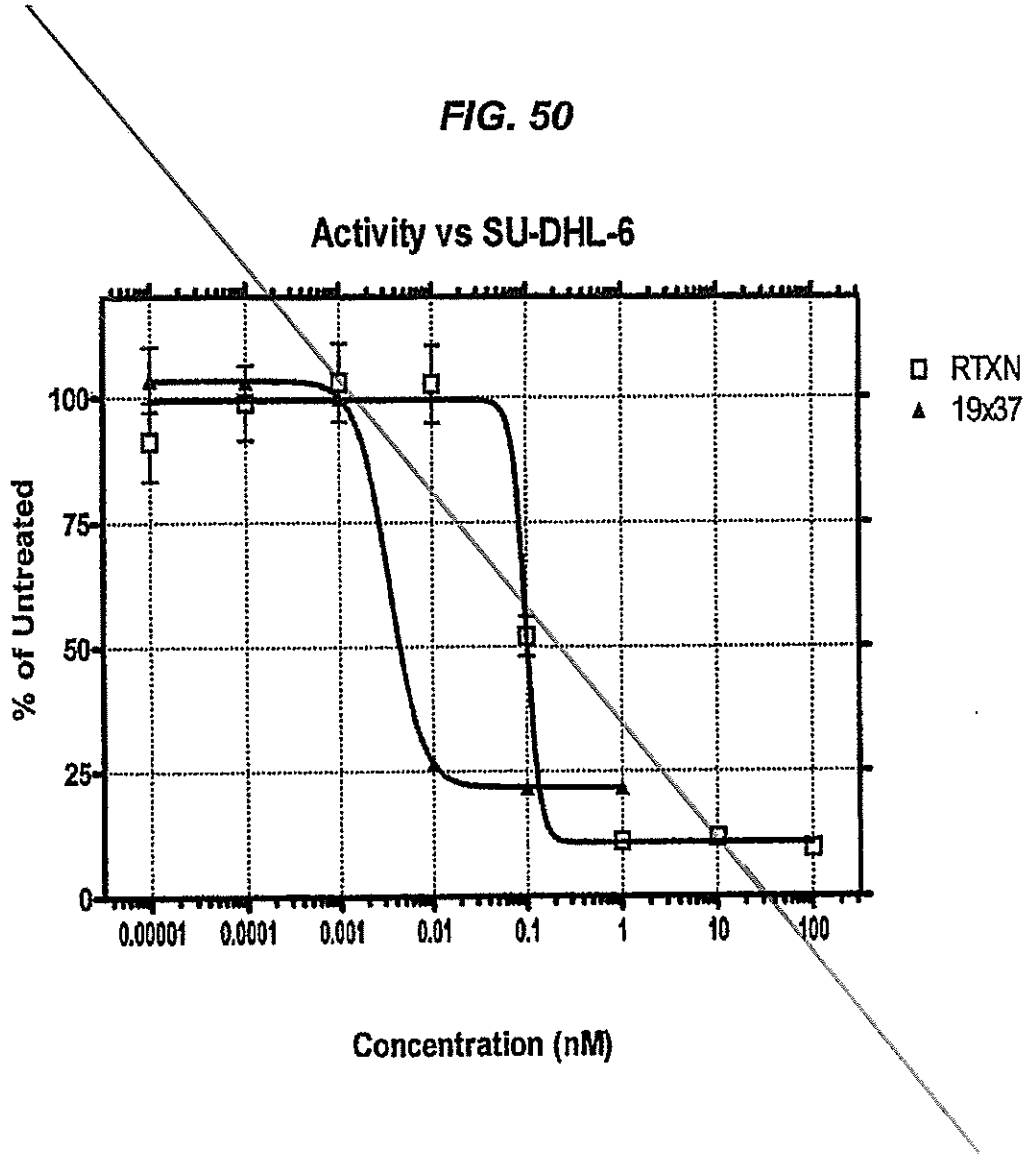

SU-DHL-6 Response to Molecules
RFU
400
350
300
250
200
150
100
50
0
100
200
300
400
500
600
700
800
900
Time (sec)
70 nM S0129
70 nM 20x37
70 nM 37x37
anti-IgM

FIG. 50


Activity vs SU-DHL-6
% of Untreated
100
75
50
25
0
0.00001
0.0001
0.001
0.01
0.1
1
10
100
Concentration (nM)
RTXN
19x37

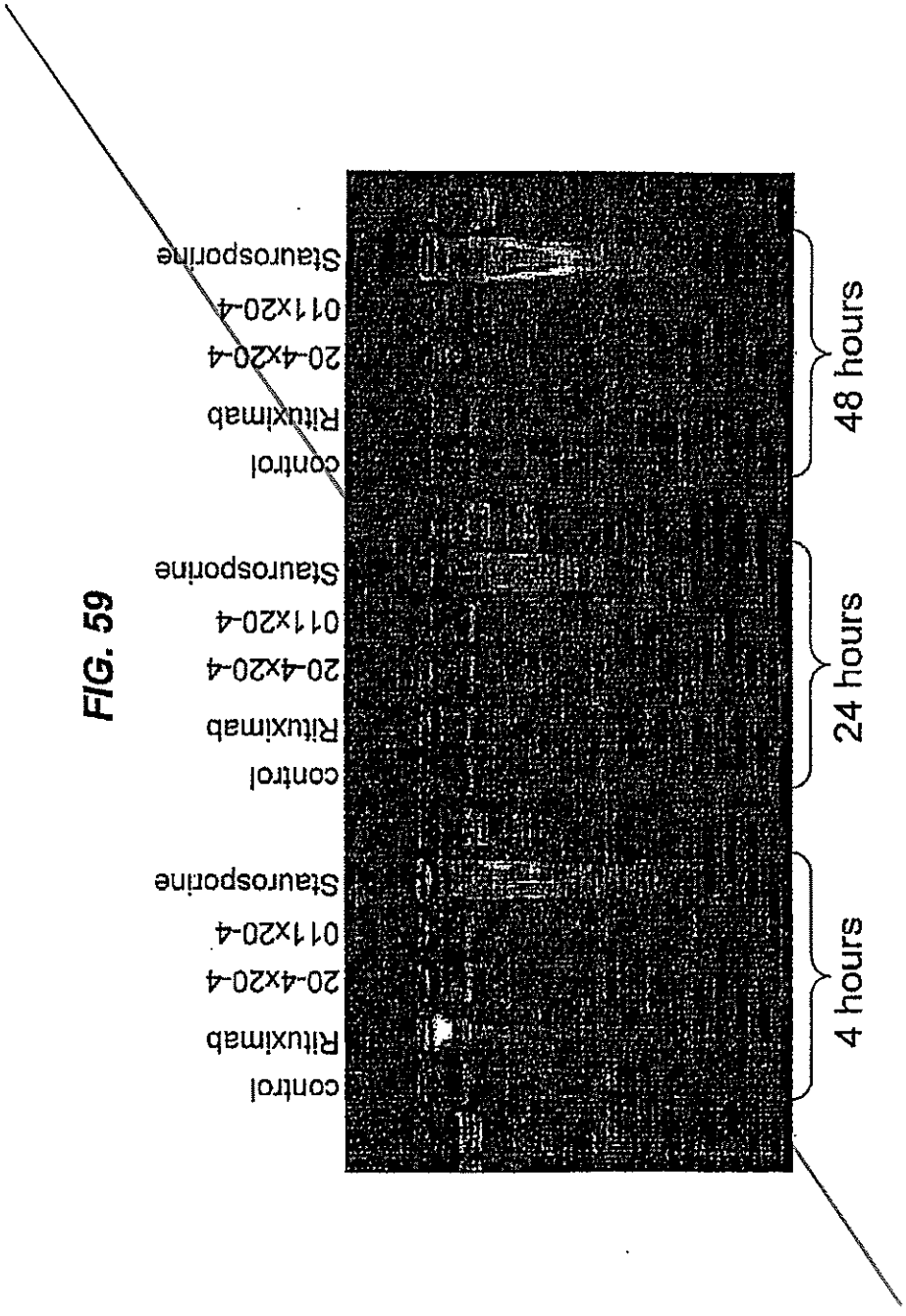
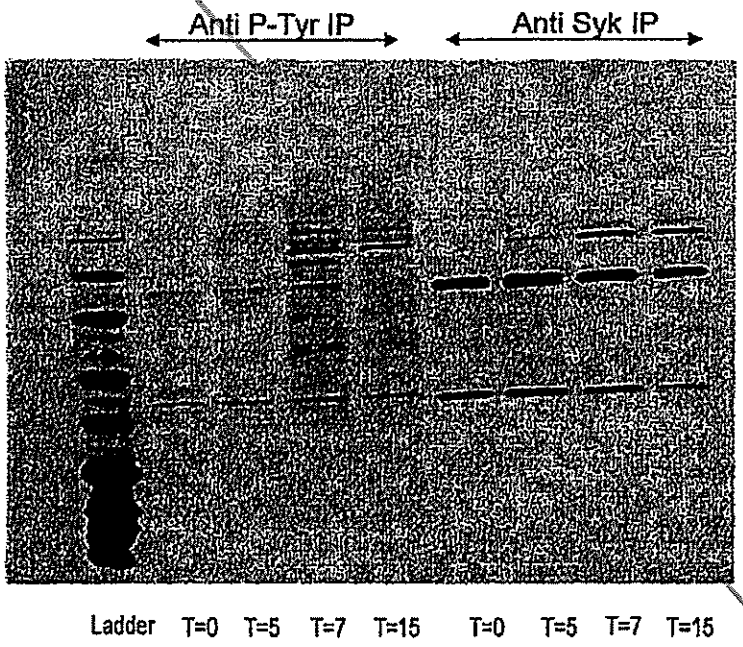

control
Rituximab
20-4x20-4
011x20-4
Staurosporine
4 hours
control
Rituximab
20-4x20-4
011x20-4
Staurosporine
24 hours
control
Rituximab
20-4x20-4
011x20-4
Staurosporine
48 hours

FIG. 59

FIG. 60

DHL6 Cells Treated with 20x37 Scorpion



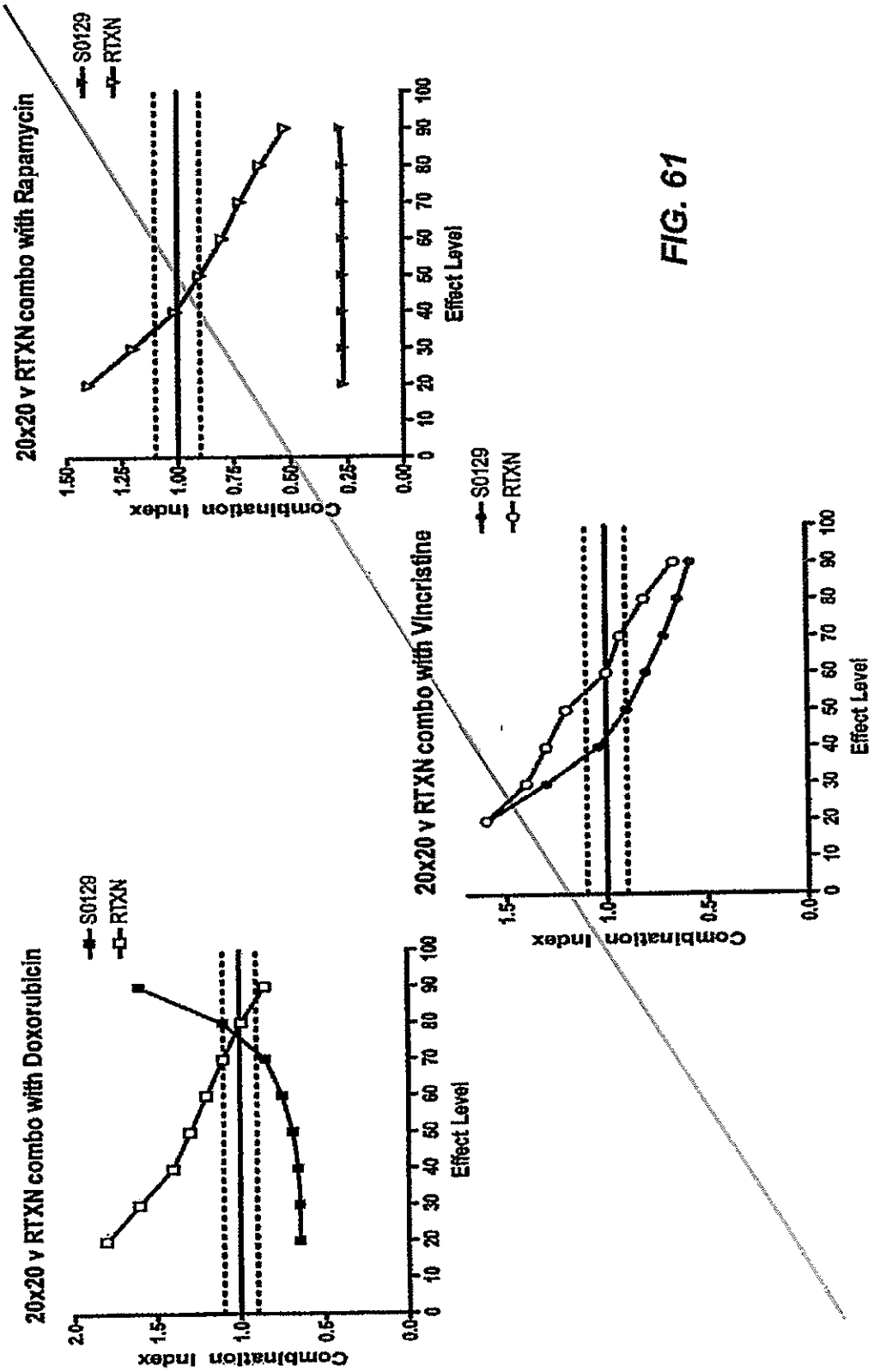

20x20 v RTXN combo with Rapamycin
S0129
RTXN
Combination Index
Effect Level
20x20 v RTXN combo with Vincristine
S0129
RTXN
Combination Index
Effect Level
20x20 v RTXN combo with Doxorubicin
S0129
RTXN
Combination Index
Effect Level

FIG. 61

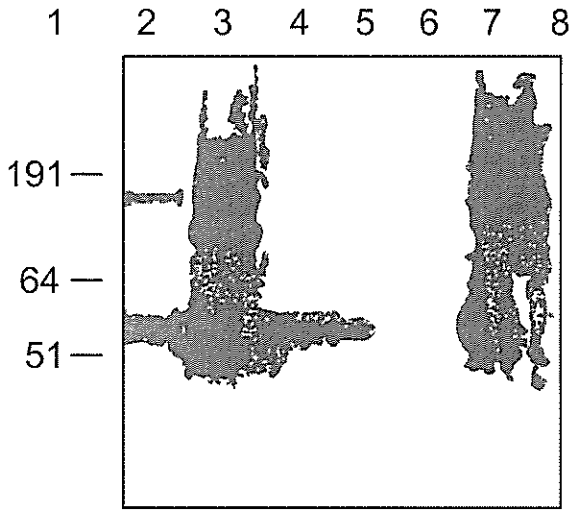


FIG. 2

FIG. 3

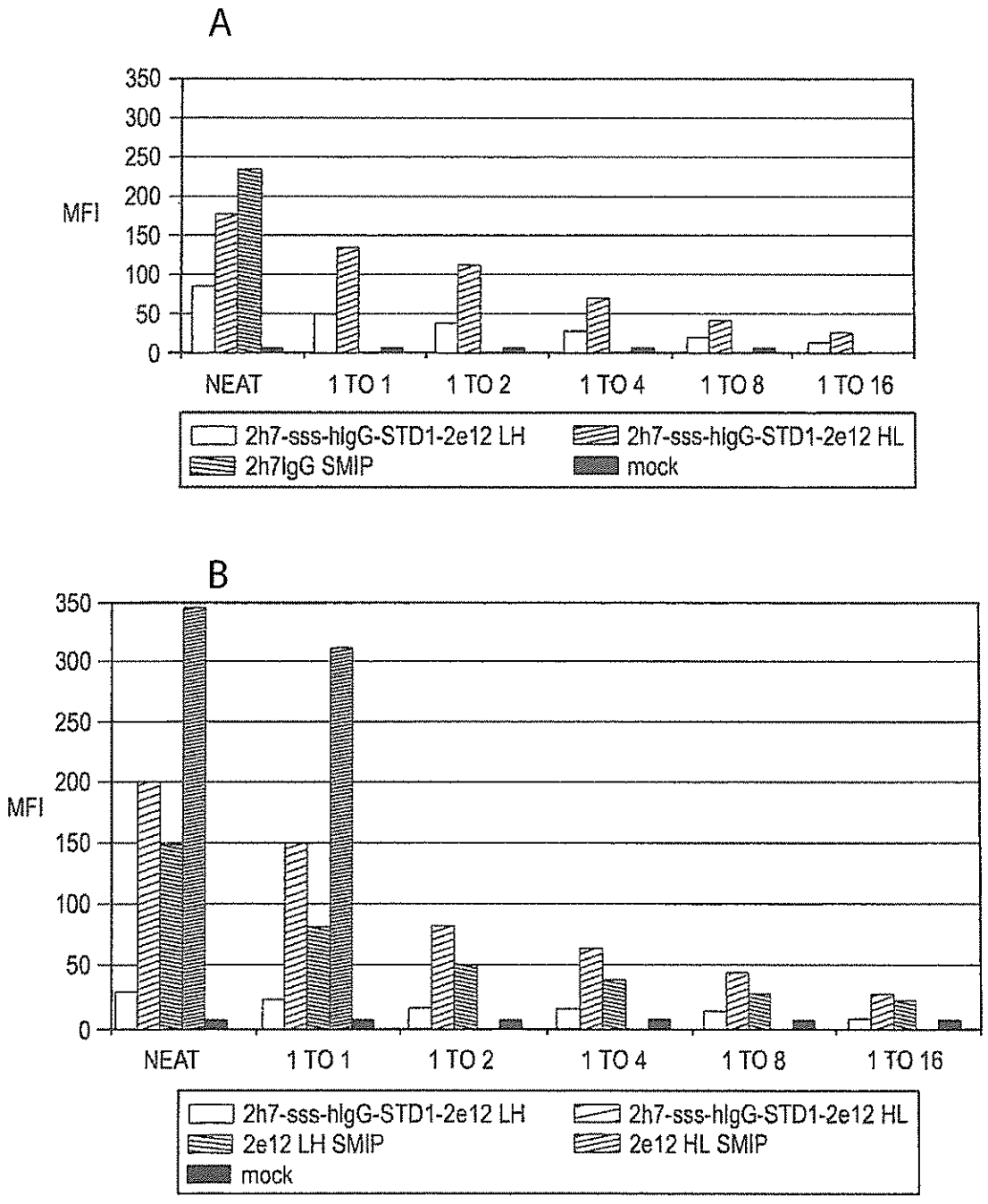

A
350
300
250
200
150
100
50
0
MFI
NEAT
1 TO 1
1 TO 2
1 TO 4
1 TO 8
1 TO 16
2h7-sss-hIgG-STD1-2e12 LH
2h7-sss-hIgG-STD1-2e12 HL
2h7IgG SMIP
mock
B
350
300
250
200
150
100
50
0
MFI
NEAT
1 TO 1
1 TO 2
1 TO 4
1 TO 8
1 TO 16
2h7-sss-hIgG-STD1-2e12 LH
2h7-sss-hIgG-STD1-2e12 HL
2e12 LH SMIP
2e12 HL SMIP
mock

FIG. 4

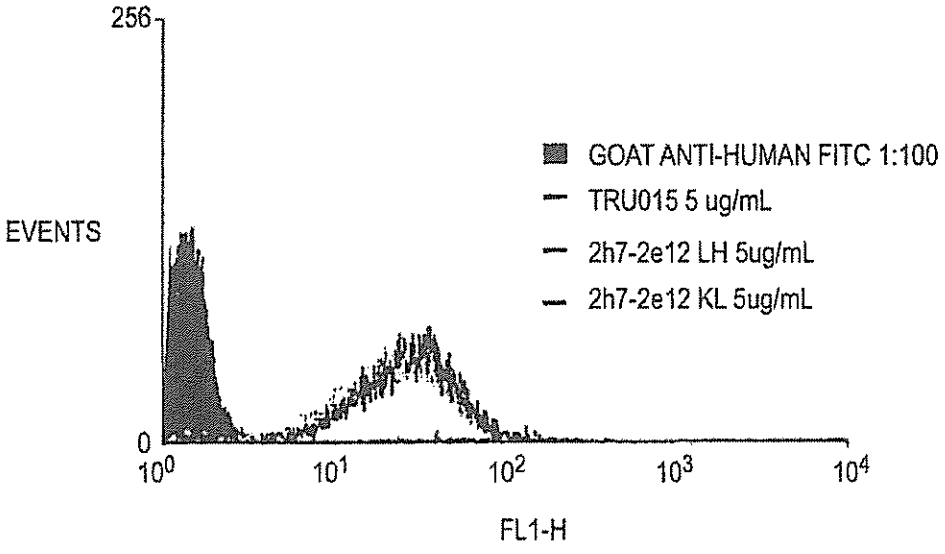

256
EVENTS
0
10^0
10^1
10^2
10^3
10^4
FL1-H
GOAT ANTI-HUMAN FITC 1:100
TRU015 5 ug/mL
2h7-2e12 LH 5ug/mL
2h7-2e12 KL 5ug/mL

FIG. 5

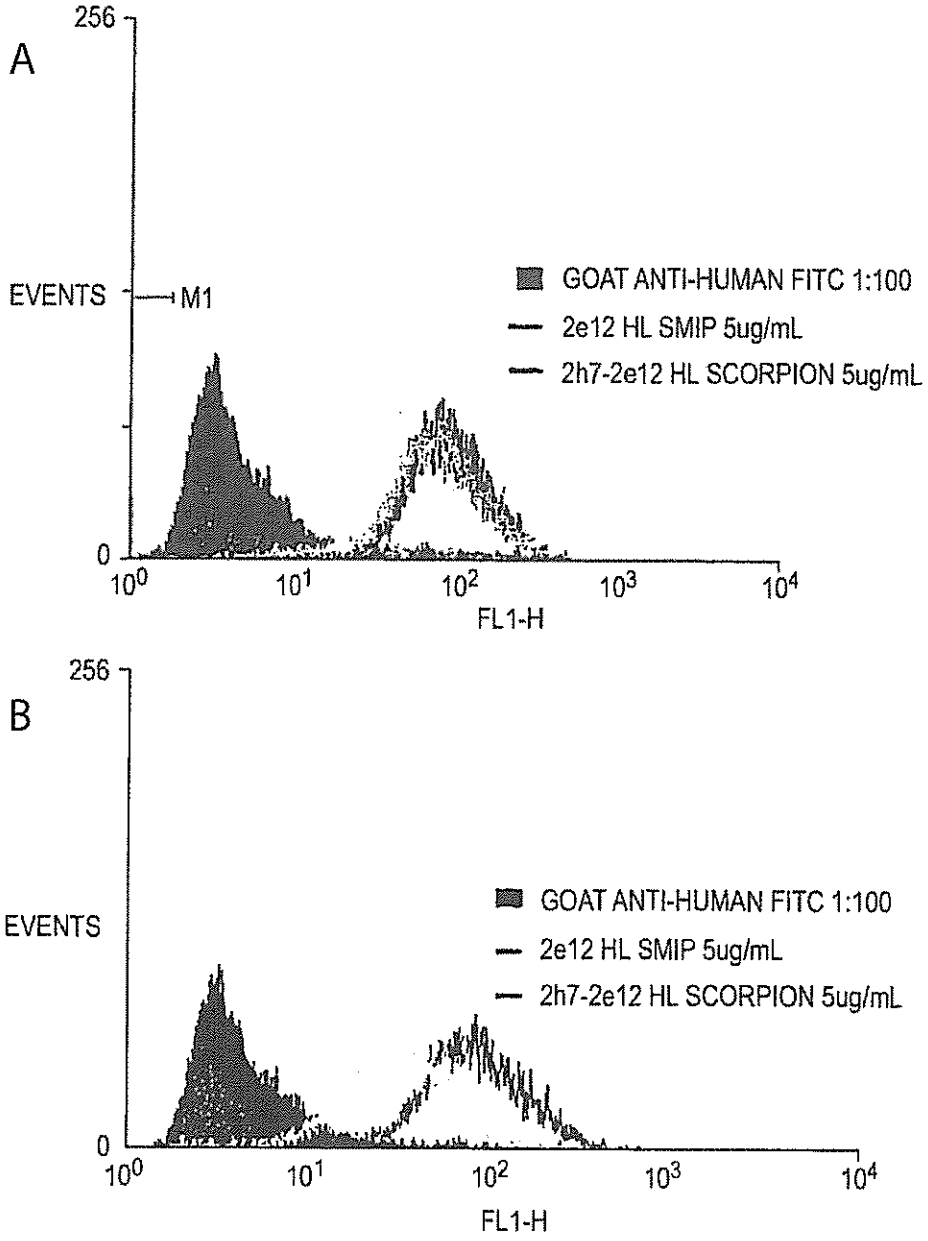

A
256
EVENTS
M1
0
10^0
10^1
10^2
10^3
10^4
FL1-H
GOAT ANTI-HUMAN FITC 1:100
2e12 HL SMIP 5ug/mL
2h7-2e12 HL SCORPION 5ug/mL
B
256
EVENTS
0
10^0
10^1
10^2
10^3
10^4
FL1-H
GOAT ANTI-HUMAN FITC 1:100
2e12 HL SMIP 5ug/mL
2h7-2e12 HL SCORPION 5ug/mL

FIG. 6A



BD1 Binding Domain 1	Linker 1	EFD Effector Function Domain	Linker 2 ID	Linker Length (aa) Linker Plus R. Site	CH3 COOH	Linker 2 Sequence (- restriction site)	Fusion Junction with BD2 (L2 RS--QVQ 2e12)	BD2 Binding Domain 2
2H7 V_L-V_H	Modified hIgGl hinge ccc->sss	hIgGl-CH2-CH3	STD	20	PGK	NYGGGGSGGGGSGGGGSG	NS QVQ	2e12 V_H-V_L
2H7 V_L-V_H	Modified hIgGl hinge ccc->sss	hIgGl-CH2-CH3	STD2	38	PGK	NYGGGGSGGGGSGGGGSG NYGGGGSGGGGSGGGGSG	NS QVQ	2e12 V_H-V_L
2H7 V_L-V_H	Modified hIgGl hinge ccc->sss	hIgGl-CH2-CH3	H1 L1=2e12 V_L-V_H	2 (RS)	PGK	---	NS QVQ	2e12 V_H-V_L
2H7 V_L-V_H	Modified hIgGl hinge ccc->sss	hIgGl-CH2-CH3	H2 L2=2e12 V_L-V_H	8	PGK	GGGGSG	NS QVQ	2e12 V_H-V_L
2H7 V_L-V_H	Modified hIgGl hinge ccc->sss	hIgGl-CH2-CH3	H3 L3=2e12 V_L-V_H	10	PGK	NYGGGGSG	NS QVQ	2e12 V_H-V_L
2H7 V_L-V_H	Modified hIgGl hinge ccc->sss	hIgGl-CH2-CH3	H4 L4=2e12 V_L-V_H	13	PGK	GGGGSGGGGSG	NS QVQ	2e12 V_H-V_L
2H7 V_L-V_H	Modified hIgGl hinge ccc->sss	hIgGl-CH2-CH3	H5 L5=2e12 V_L-V_H	15	PGK	NYGGGGSGGGGSG	NS QVQ	2e12 V_H-V_L
2H7 V_L-V_H	Modified hIgGl hinge ccc->sss	hIgGl-CH2-CH3	H6 L6=2e12 V_L-V_H	18	PGK	GGGGSGGGGSGGGGSG	NS QVQ	2e12 V_H-V_L
2H7 V_L-V_H	Modified hIgGl hinge ccc->sss	hIgGl-CH2-CH3	H7	8	PGK	GCPPCP	NS QVQ	2e12 V_H-V_L

FIG. 7

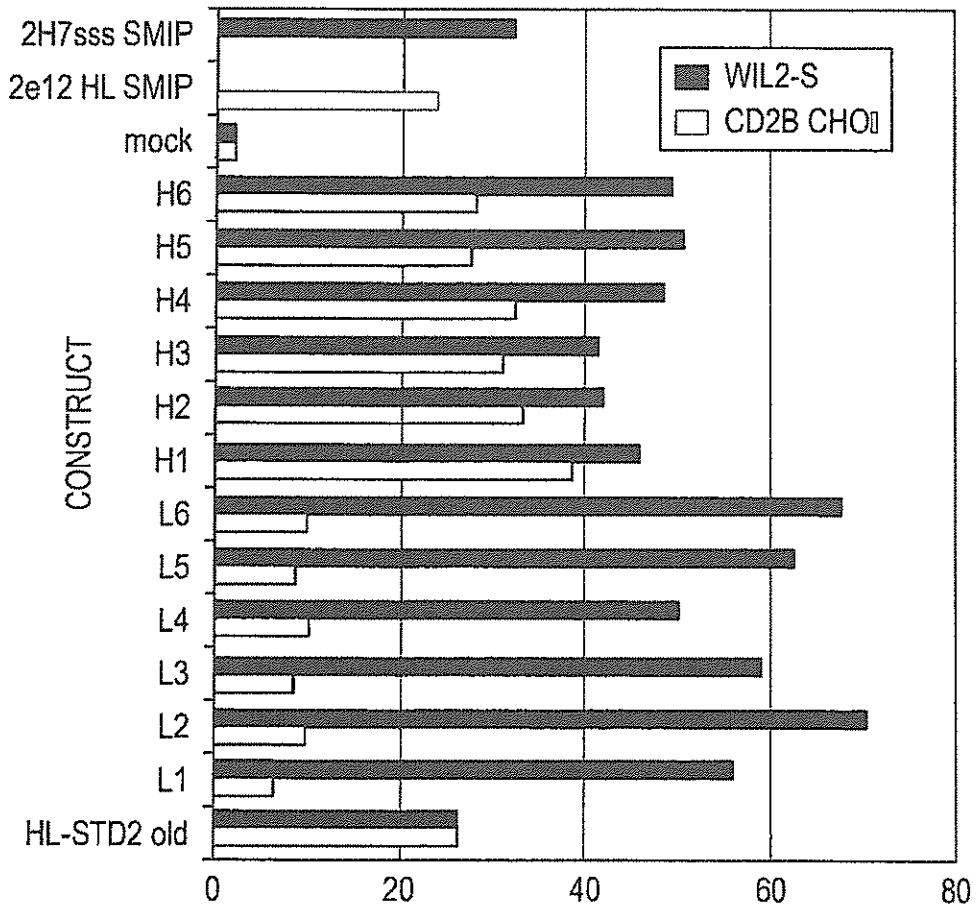

2H7sss SMIP
2e12 HL SMIP
mock
H6
H5
H4
H3
H2
H1
L6
L5
L4
L3
L2
L1
HL-STD2 old
CONSTRUCT
WIL2-S
CD2B CHO
0
20
40
60
80

FIG. 9

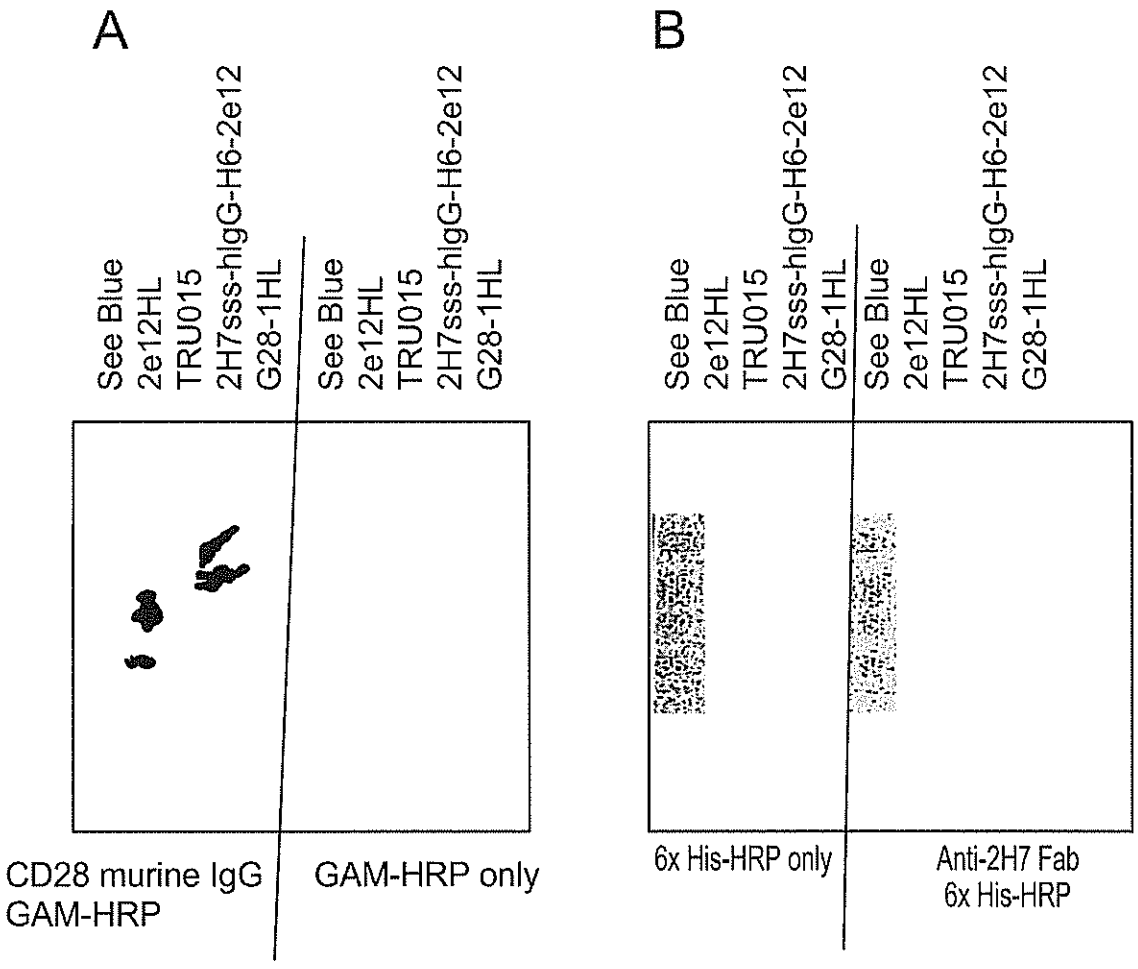

A
See Blue
2e12HL
TRU015
2H7sss-hIgG-H6-2e12
G28-1HL
See Blue
2e12HL
TRU015
2H7sss-hIgG-H6-2e12
G28-1HL
CD28 murine IgG
GAM-HRP
GAM-HRP only
B
See Blue
2e12HL
TRU015
2H7sss-hIgG-H6-2e12
G28-1HL
See Blue
2e12HL
TRU015
2H7sss-hIgG-H6-2e12
G28-1HL
6x His-HRP only
Anti-2H7 Fab
6x His-HRP

FIG. 10

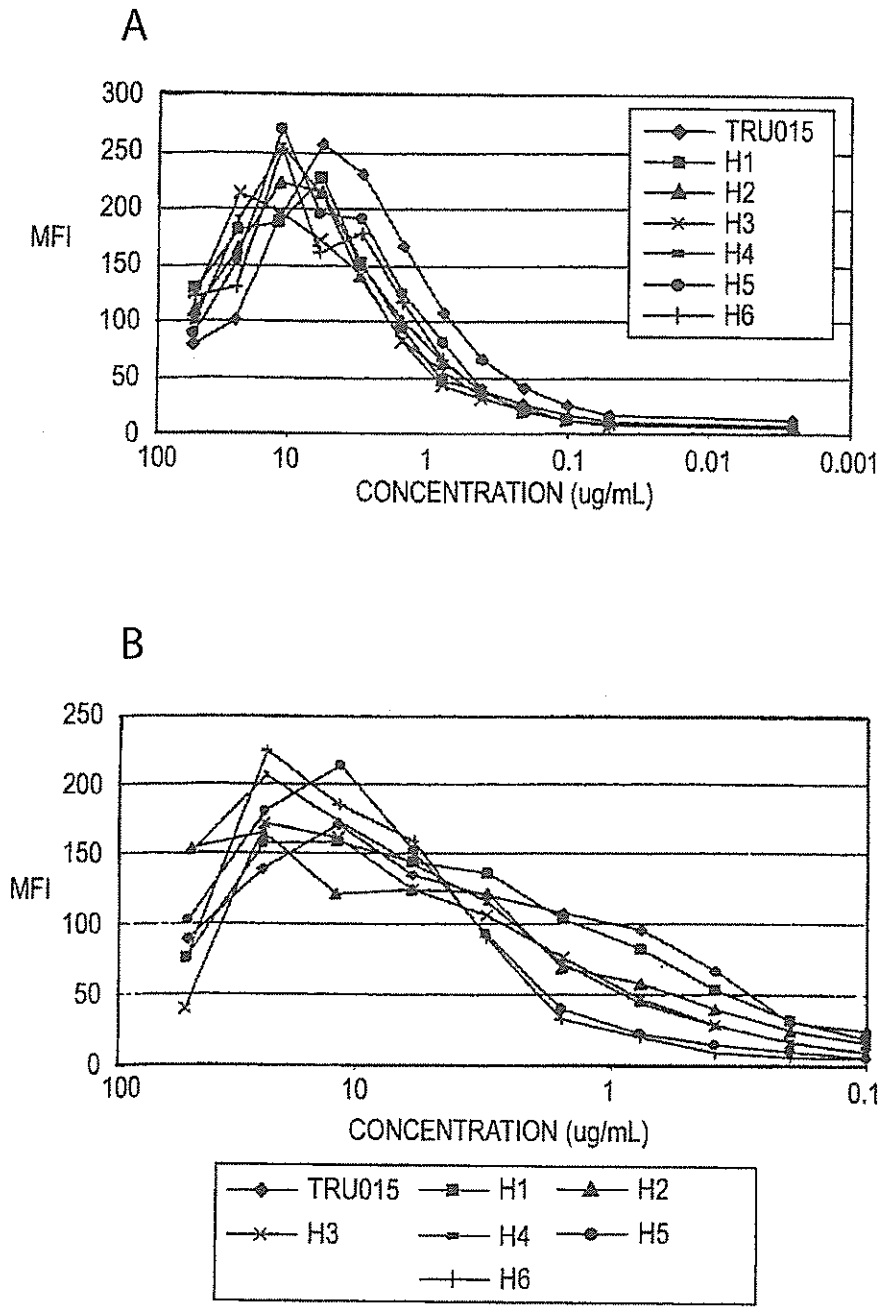

A
300
250
200
150
100
50
0
MFI
100
10
1
0.1
0.01
0.001
CONCENTRATION (ug/mL)
TRU015
H1
H2
H3
H4
H5
H6
B
250
200
150
100
50
0
MFI
100
10
1
0.1
CONCENTRATION (ug/mL)
TRU015
H1
H2
H3
H4
H5
H6

FIG. 11

Linker ID	Retention Time for POI	% POI	% Other Forms	SDS-PAGE Analysis of Cleavage at EFD/BD2 junction
H1	7.620	70.9	29.0	(Yes)
H2	7.589	67.5	32.5	(Yes)
H3	7.605	68.7	31.4	Yes
H4	7.622 (shoulder)	68.0	32.0	Yes
H5	7.933/7.680 (doublet with shoulder)	32.42/33.94	33.63	YES
H6	7.901/7.69 (doublet with shoulder)	34.5/29.3	36.1	YES
H7	7.788	84.2	15.8 (HMW)	NO

FIG. 12

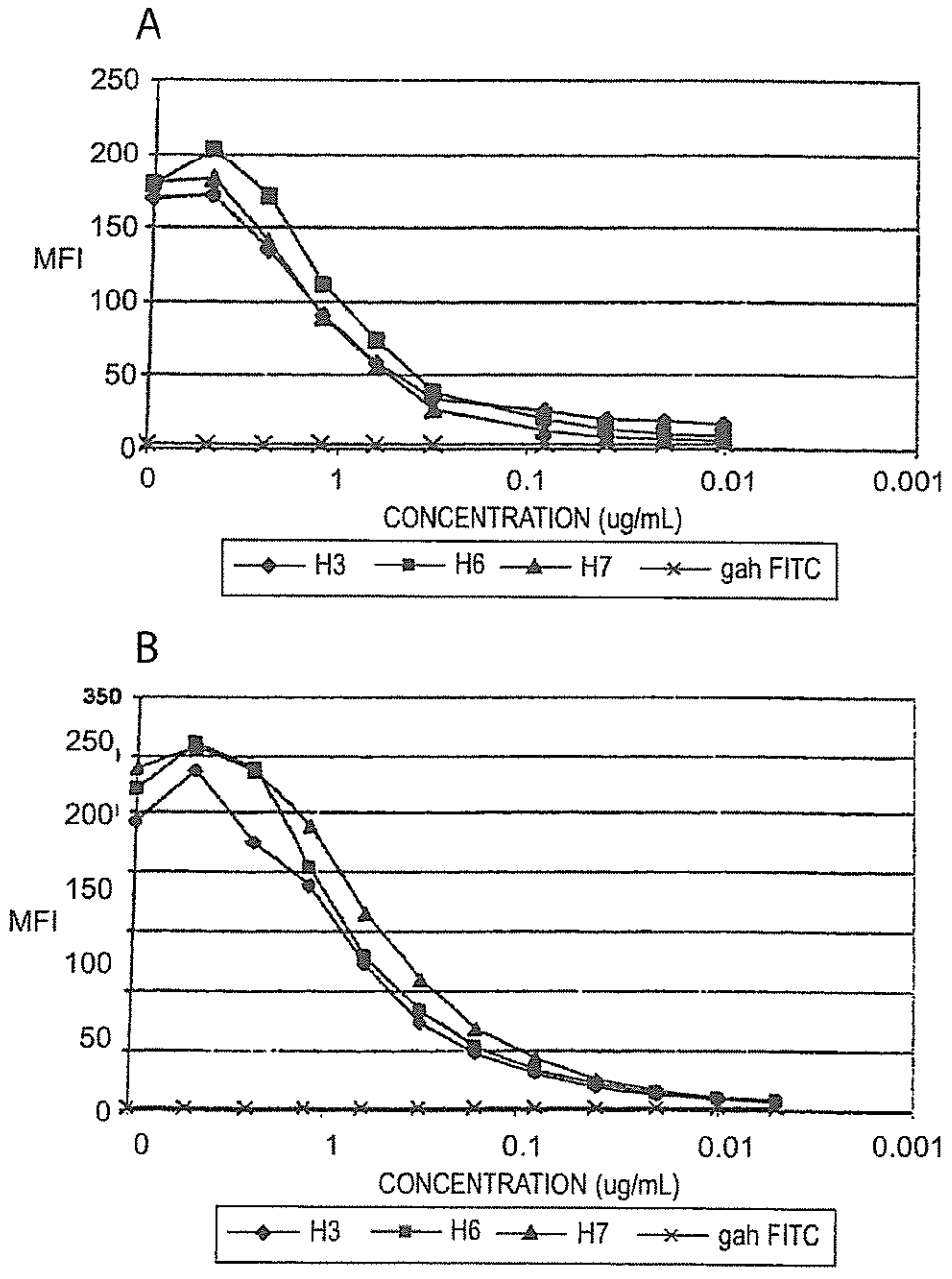

A
250
200
150
MFI
100
50
0
0
1
0.1
0.01
0.001
CONCENTRATION (ug/mL)
H3
H6
H7
gah FITC
B
350
250
200
150
MFI
100
50
0
0
1
0.1
0.01
0.001
CONCENTRATION (ug/mL)
H3
H6
H7
gah FITC

FIG. 13

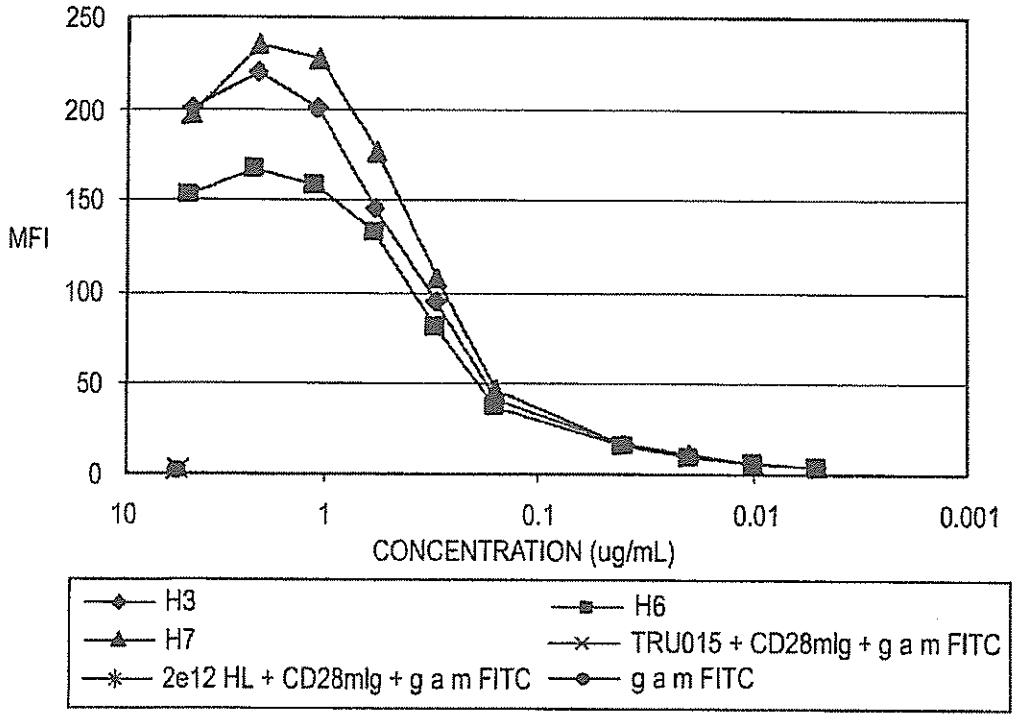

250
200
150
100
50
0
MFI
10
1
0.1
0.01
0.001
CONCENTRATION (ug/mL)
H3
H6
H7
TRU015 + CD28mlg + g a m FITC
2e12 HL + CD28mlg + g a m FITC
g a m FITC

FIG. 14

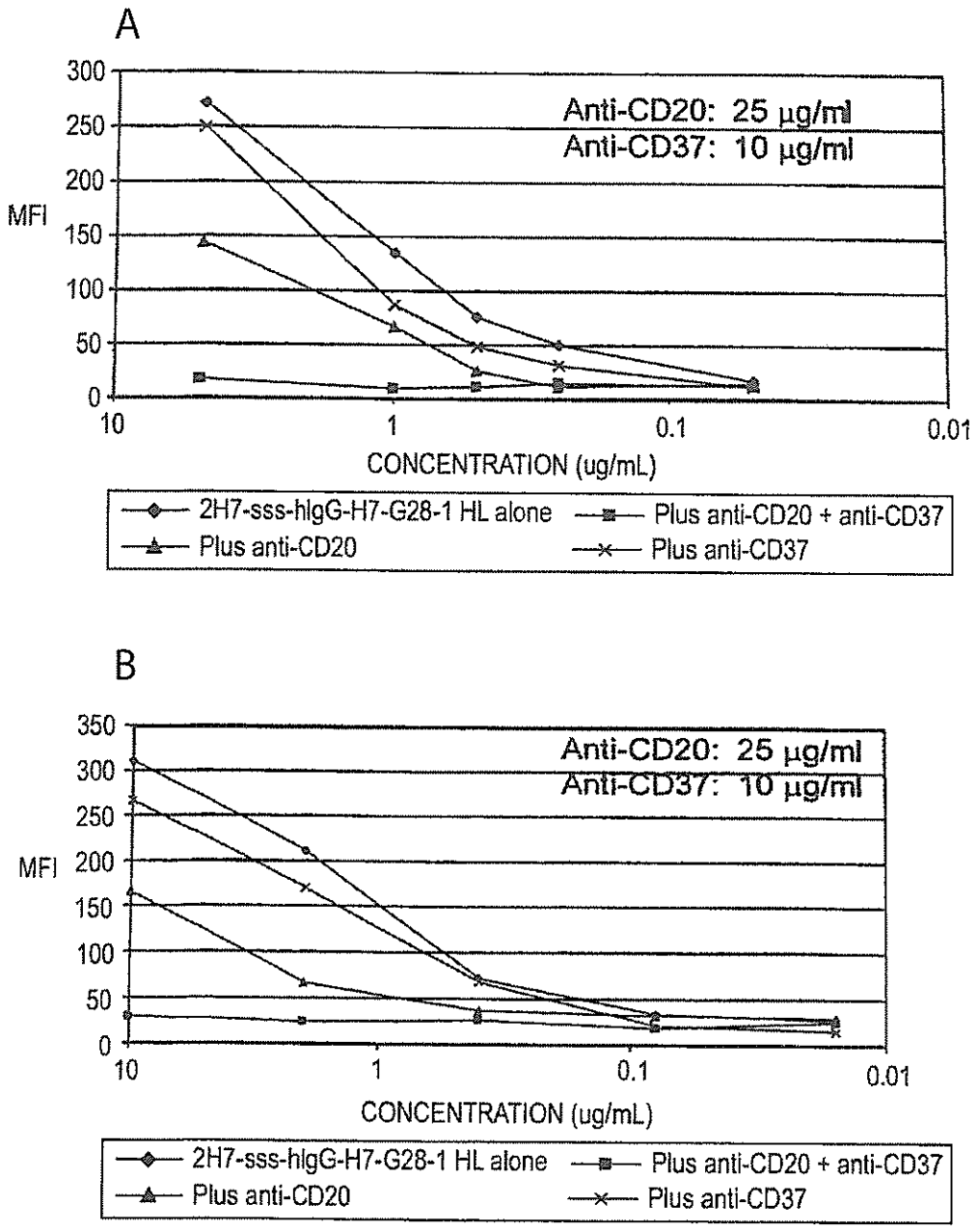

A
300
250
200
150
100
50
0
MFI
Anti-CD20: 25 µg/ml
Anti-CD37: 10 µg/ml
10
1
0.1
0.01
CONCENTRATION (ug/mL)
2H7-sss-hIgG-H7-G28-1 HL alone
Plus anti-CD20 + anti-CD37
Plus anti-CD20
Plus anti-CD37
B
350
300
250
200
150
100
50
0
MFI
Anti-CD20: 25 µg/ml
Anti-CD37: 10 µg/ml
10
1
0.1
0.01
CONCENTRATION (ug/mL)
2H7-sss-hIgG-H7-G28-1 HL alone
Plus anti-CD20 + anti-CD37
Plus anti-CD20
Plus anti-CD37

FIG. 15

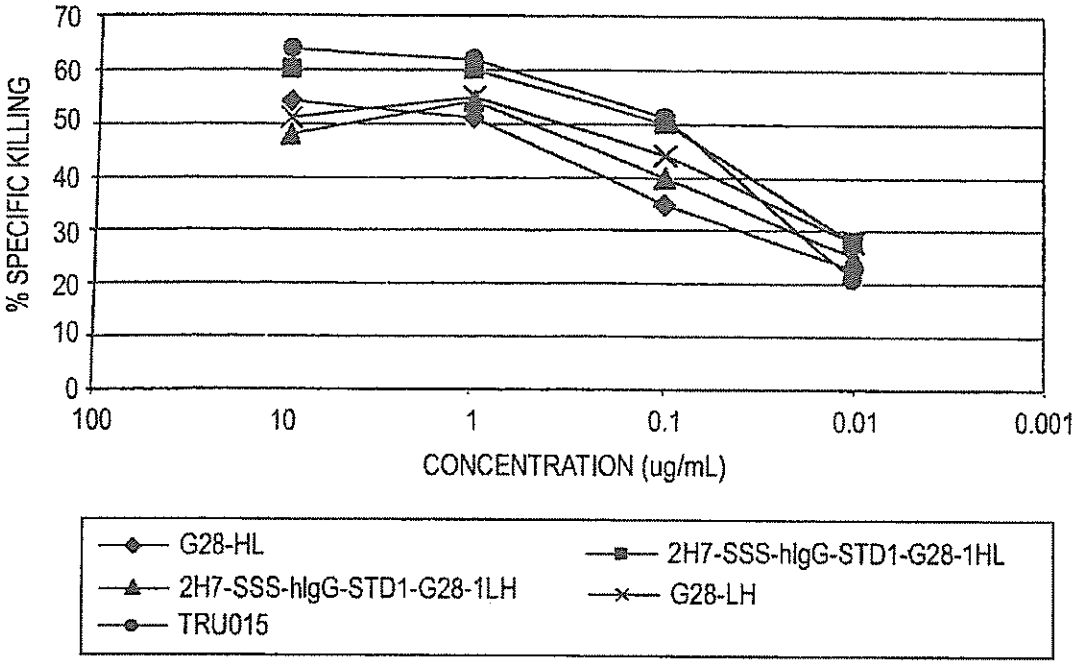

70
60
50
40
30
20
10
0
% SPECIFIC KILLING
100
10
1
0.1
0.01
0.001
CONCENTRATION (ug/mL)
G28-HL
2H7-SSS-hIgG-STD1-G28-1HL
2H7-SSS-hIgG-STD1-G28-1LH
G28-LH
TRU015

FIG. 16

24 Hours	CD3+	CD19+	CD40+
Media	77%	8%	7%
TRU015	76%	8.5%	7.9%
G28-1 SMIP	78%	8. 9%	7.8%
TRU015+G28-1 SMIP	76.3%	8.1%	7.5%
2H7-ssshlgG1-G28-1HL (H7)	78.4%	8.9%	7.9%

72 Hours	CD3+	CD19+	CD40+
Media	78.5%	7.9%	7.7%
TRU015	85.2%	2.3%	2.7%
G28-1 SMIP	86.7%	2.2%	2.3%
TRU015+G28-1 SMIP	87.1%	1.1%	1.1%
2H7-ssshlgG1-G28-1 HL (H7)	96.7%	.08%	.77%

FIG. 17

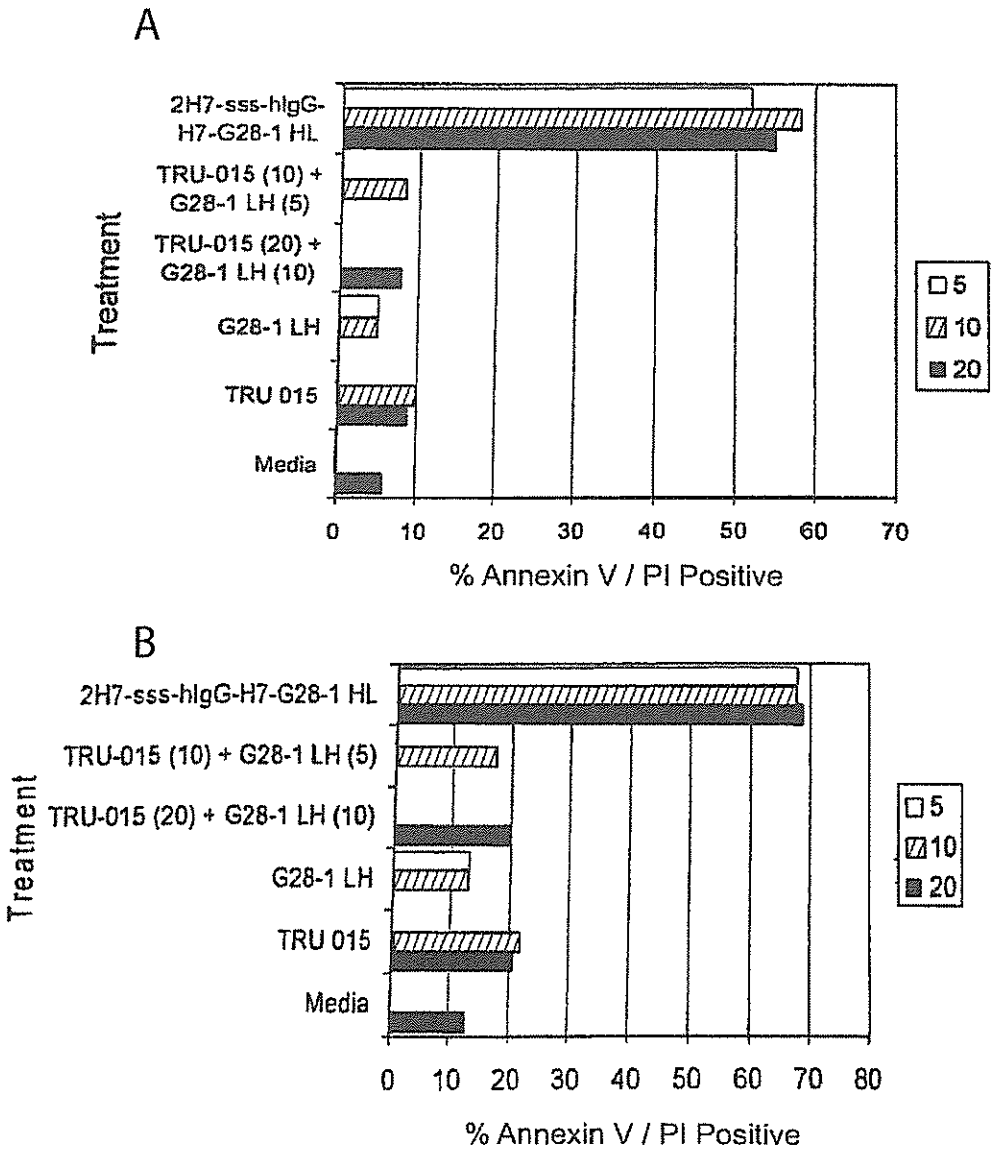

A
2H7-sss-hIgG-H7-G28-1 HL
TRU-015 (10) + G28-1 LH (5)
TRU-015 (20) + G28-1 LH (10)
G28-1 LH
TRU 015
Media
Treatment
0 10 20 30 40 50 60 70
% Annexin V / PI Positive
5
10
20
B
2H7-sss-hIgG-H7-G28-1 HL
TRU-015 (10) + G28-1 LH (5)
TRU-015 (20) + G28-1 LH (10)
G28-1 LH
TRU 015
Media
Treatment
0 10 20 30 40 50 60 70 80
% Annexin V / PI Positive
5
10
20

FIG. 18

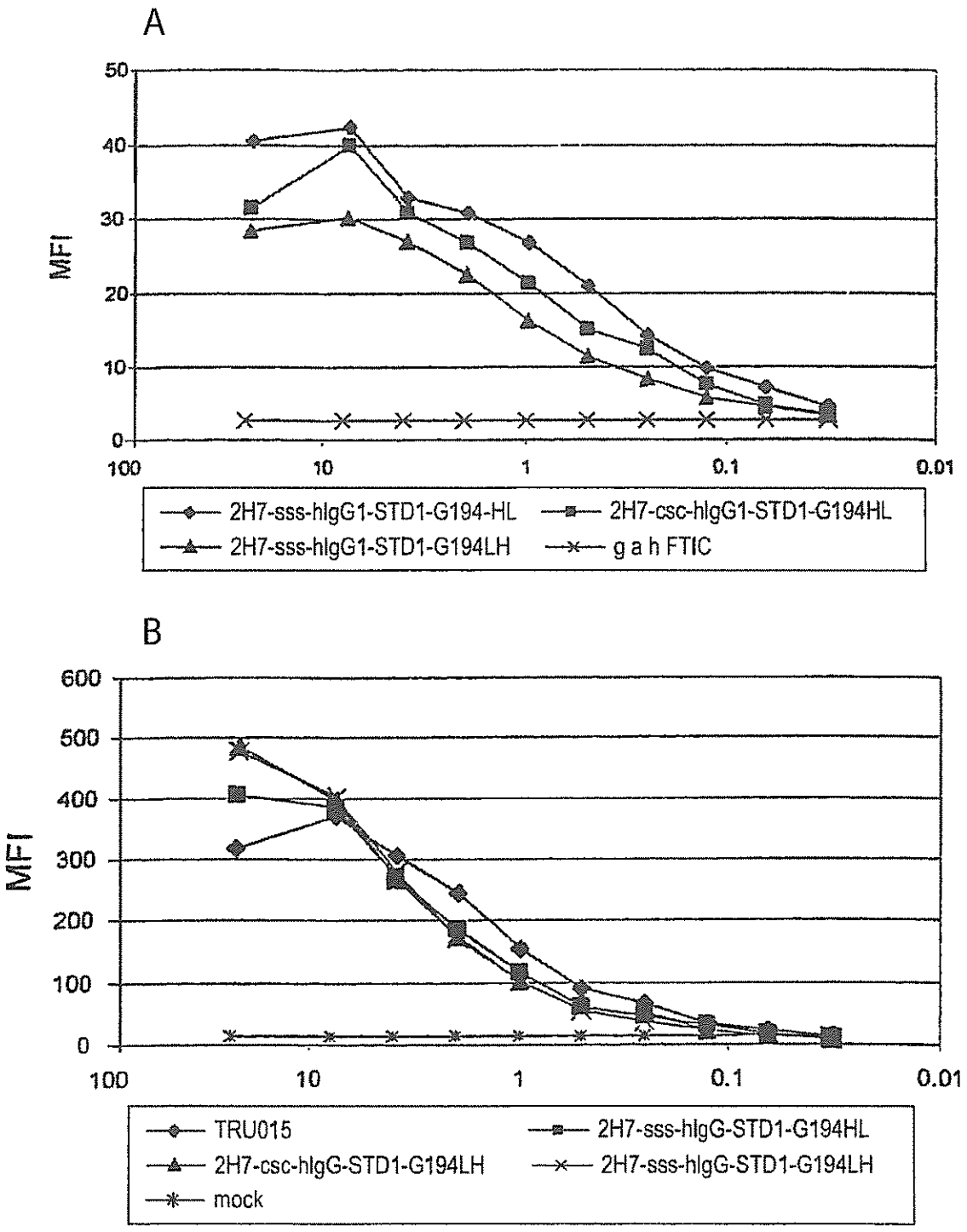
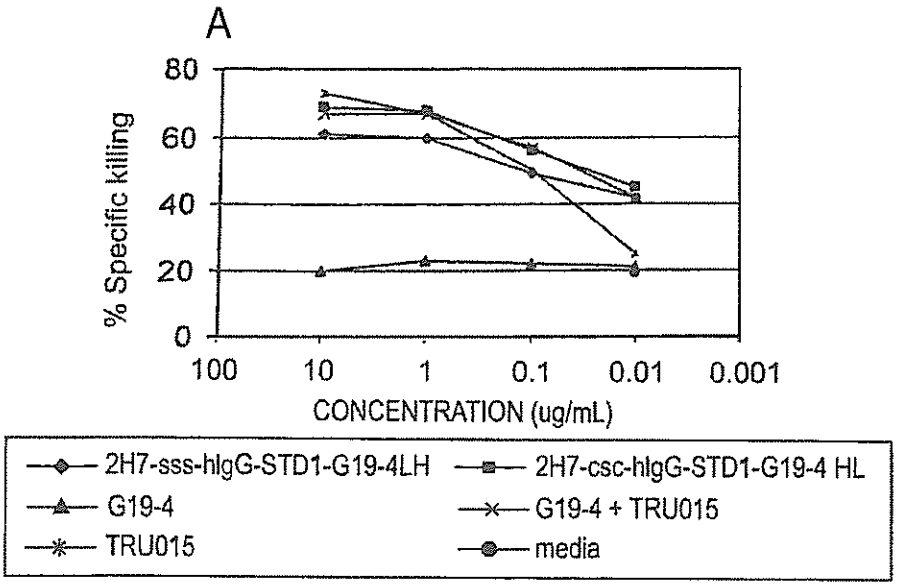

A
MFI
50
40
30
20
10
0
100
10
1
0.1
0.01
2H7-sss-hIgG1-STD1-G194-HL
2H7-csc-hIgG1-STD1-G194HL
2H7-sss-hIgG1-STD1-G194LH
g a h FTIC
B
MFI
600
500
400
300
200
100
0
100
10
1
0.1
0.01
TRU015
2H7-sss-hIgG-STD1-G194HL
2H7-csc-hIgG-STD1-G194LH
2H7-sss-hIgG-STD1-G194LH
mock

FIG. 19


A
80
60
40
20
0
% Specific killing
100
10
1
0.1
0.01
0.001
CONCENTRATION (ug/mL)
2H7-sss-hIgG-STD1-G19-4LH
2H7-csc-hIgG-STD1-G19-4 HL
G19-4
G19-4 + TRU015
TRU015
media

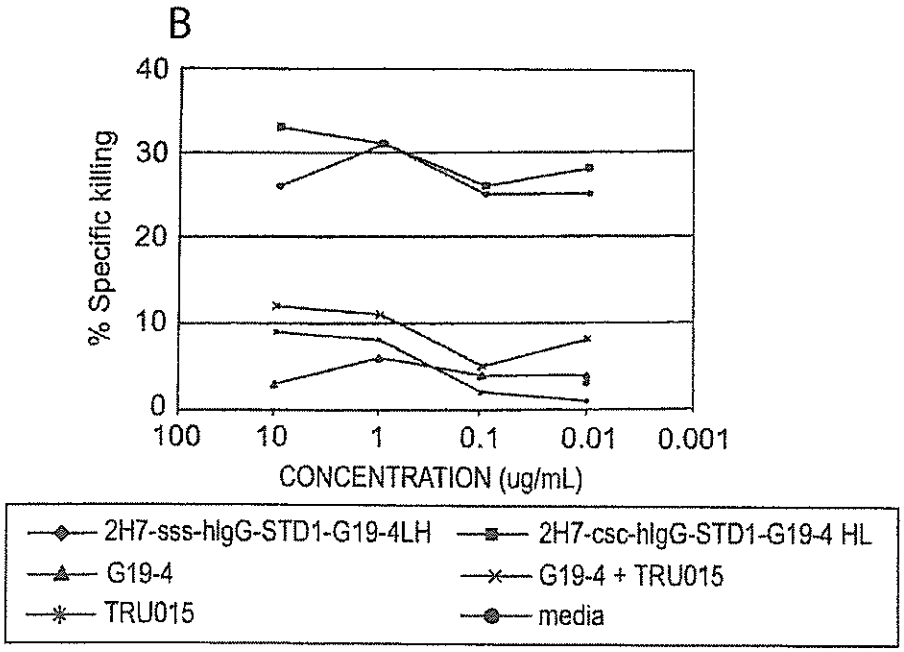

B
40
30
20
10
0
% Specific killing
100
10
1
0.1
0.01
0.001
CONCENTRATION (ug/mL)
2H7-sss-hIgG-STD1-G19-4LH
2H7-csc-hIgG-STD1-G19-4 HL
G19-4
G19-4 + TRU015
TRU015
media

FIG. 32A

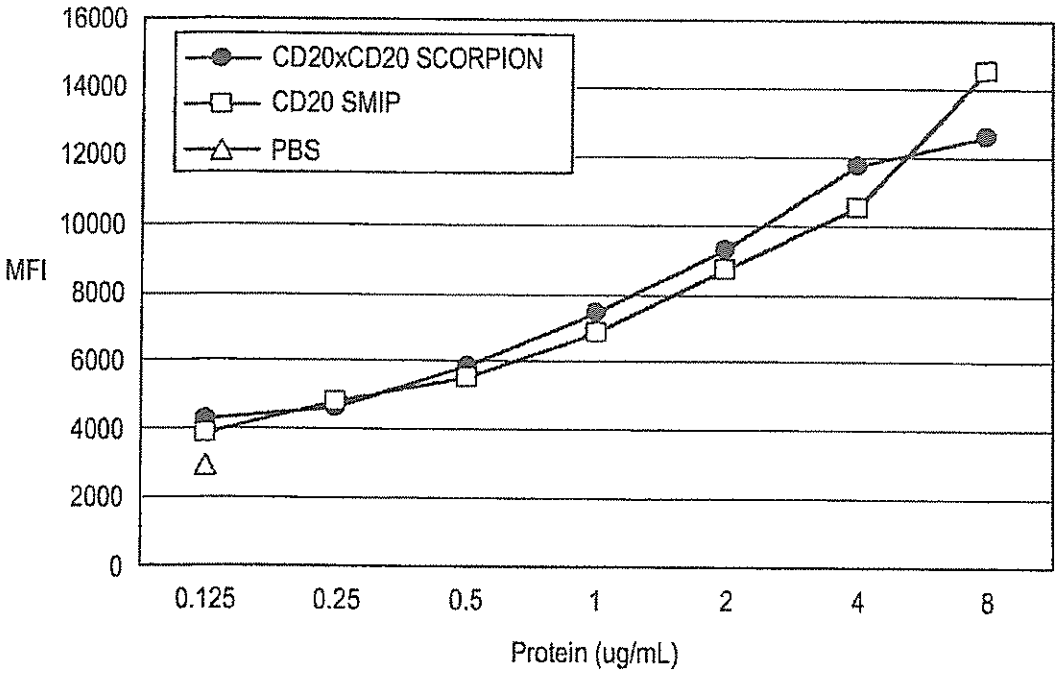

16000
14000
12000
10000
8000
6000
4000
2000
0
MFI
CD20xCD20 SCORPION
CD20 SMIP
PBS
0.125
0.25
0.5
1
2
4
8
Protein (ug/mL)

FIG. 32B

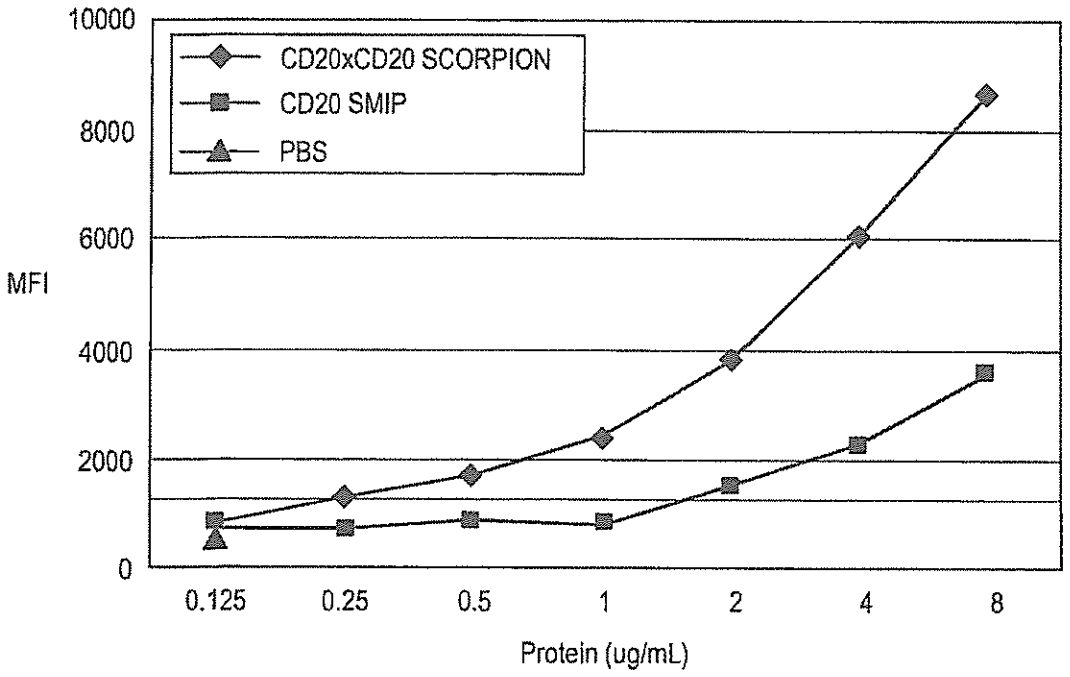

10000
8000
6000
4000
2000
0
MFI
CD20xCD20 SCORPION
CD20 SMIP
PBS
0.125
0.25
0.5
1
2
4
8
Protein (ug/mL)

FIG. 33

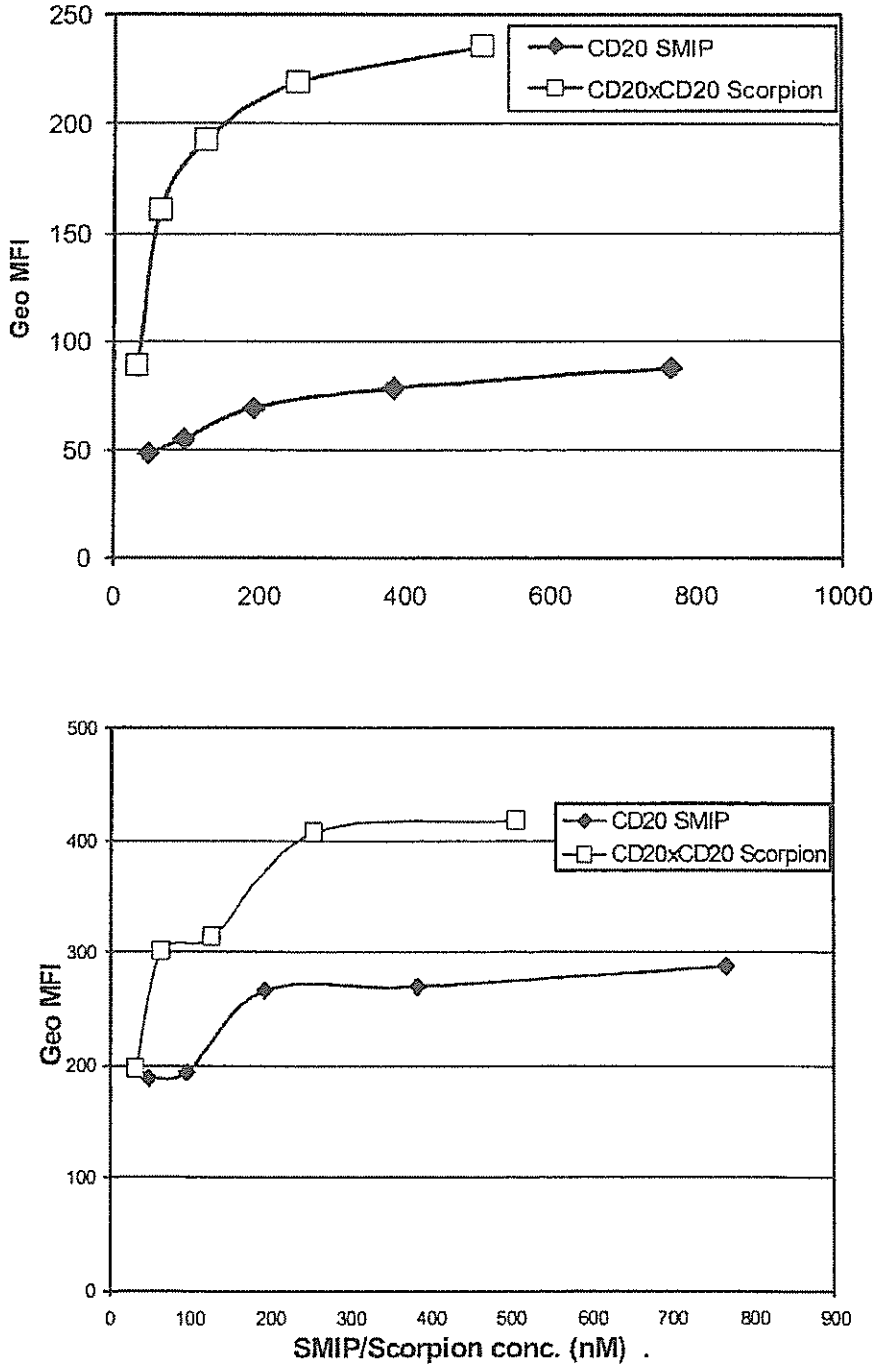

250
200
150
100
50
0
Geo MFI
0
200
400
600
800
1000
CD20 SMIP
CD20xCD20 Scorpion
500
400
300
200
100
0
Geo MFI
0
100
200
300
400
500
600
700
800
900
SMIP/Scorpion conc. (nM)
CD20 SMIP
CD20xCD20 Scorpion

FIG. 35

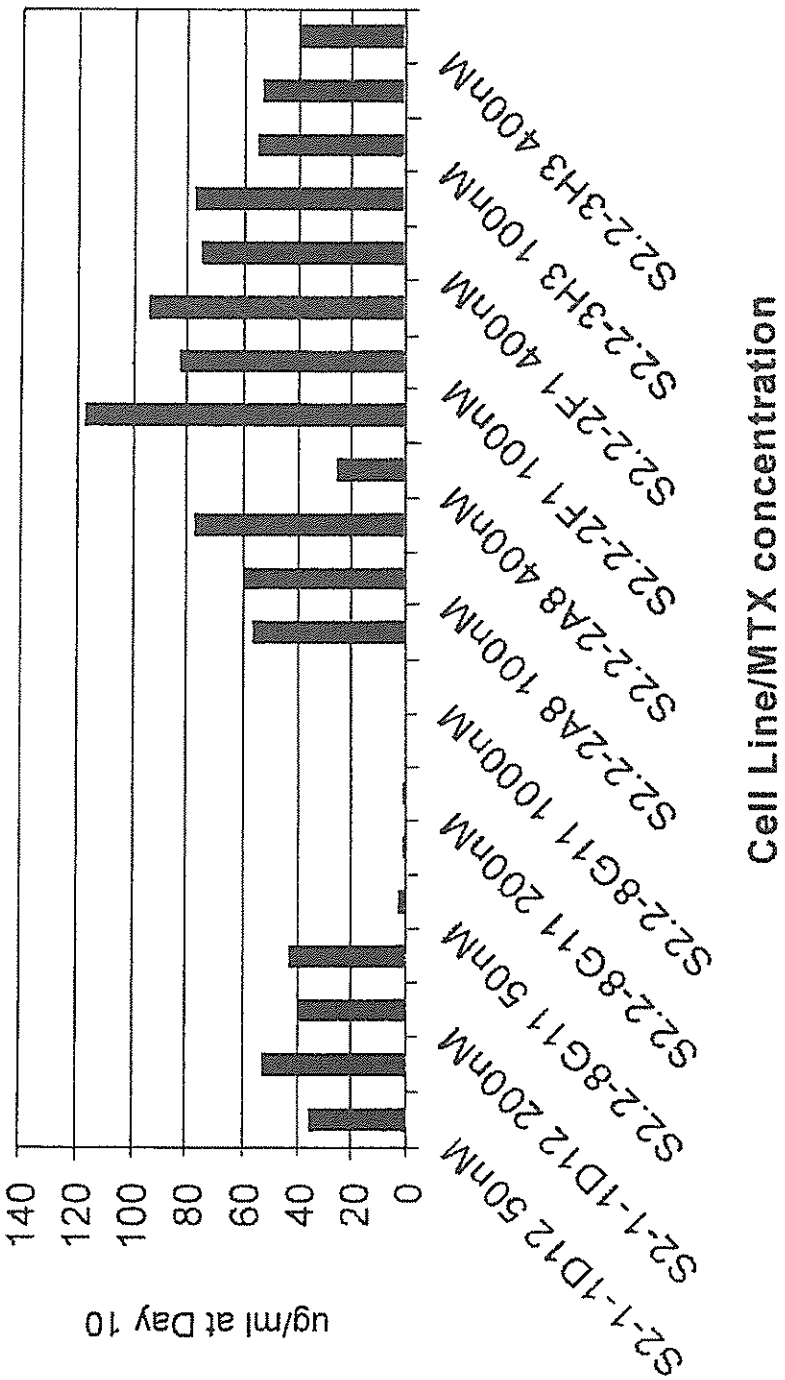
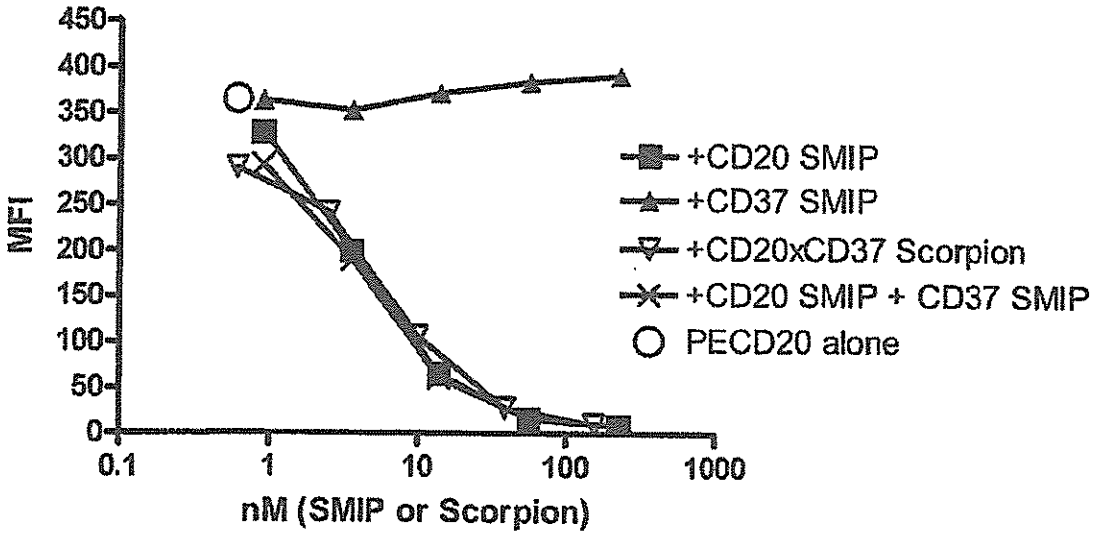

ug/ml at Day 10
0
20
40
60
80
100
120
140
S2-1-1D12 50nM
S2-1-1D12 200nM
S2.2-8G11 50nM
S2.2-8G11 200nM
S2.2-8G11 1000nM
S2.2-2A8 100nM
S2.2-2A8 400nM
S2.2-2F1 100nM
S2.2-2F1 400nM
S2.2-3H3 100nM
S2.2-3H3 400nM
Cell Line/MTX concentration

FIG. 38


450
400
350
300
250
200
150
100
50
0
MFI
0.1
1
10
100
1000
nM (SMIP or Scorpion)
+CD20 SMIP
+CD37 SMIP
+CD20xCD37 Scorpion
+CD20 SMIP + CD37 SMIP
PECD20 alone

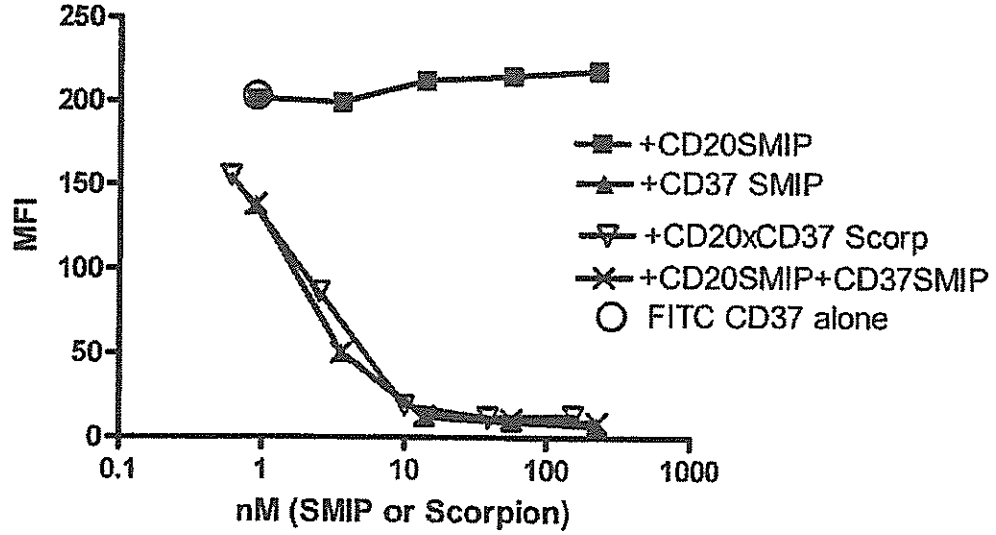

250
200
150
100
50
0
MFI
0.1
1
10
100
1000
nM (SMIP or Scorpion)
+CD20SMIP
+CD37 SMIP
+CD20xCD37 Scorp
+CD20SMIP+CD37SMIP
FITC CD37 alone

FIG. 41

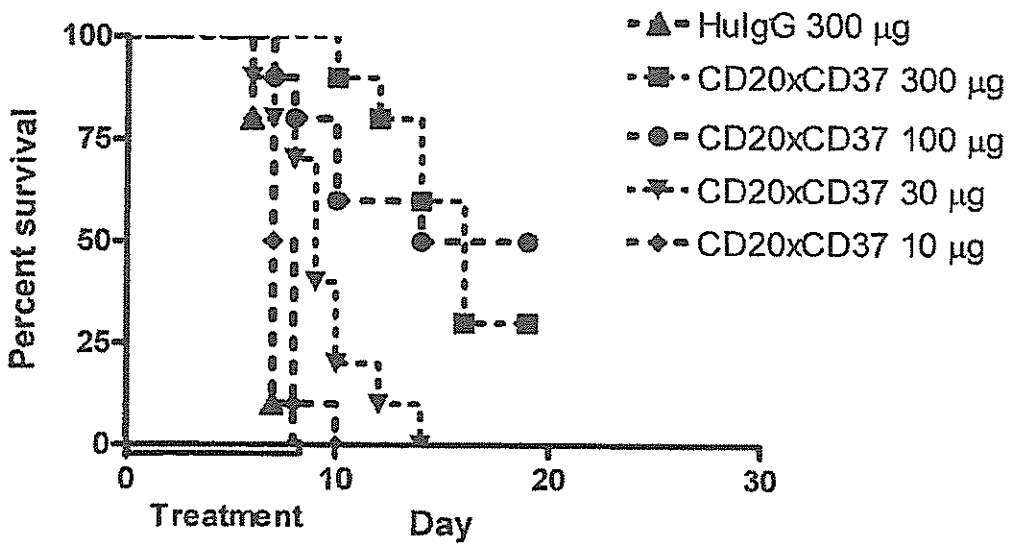

Percent survival
100
75
50
25
0
0
10
20
30
Treatment
Day
HuIgG 300 µg
CD20xCD37 300 µg
CD20xCD37 100 µg
CD20xCD37 30 µg
CD20xCD37 10 µg

FIG. 42

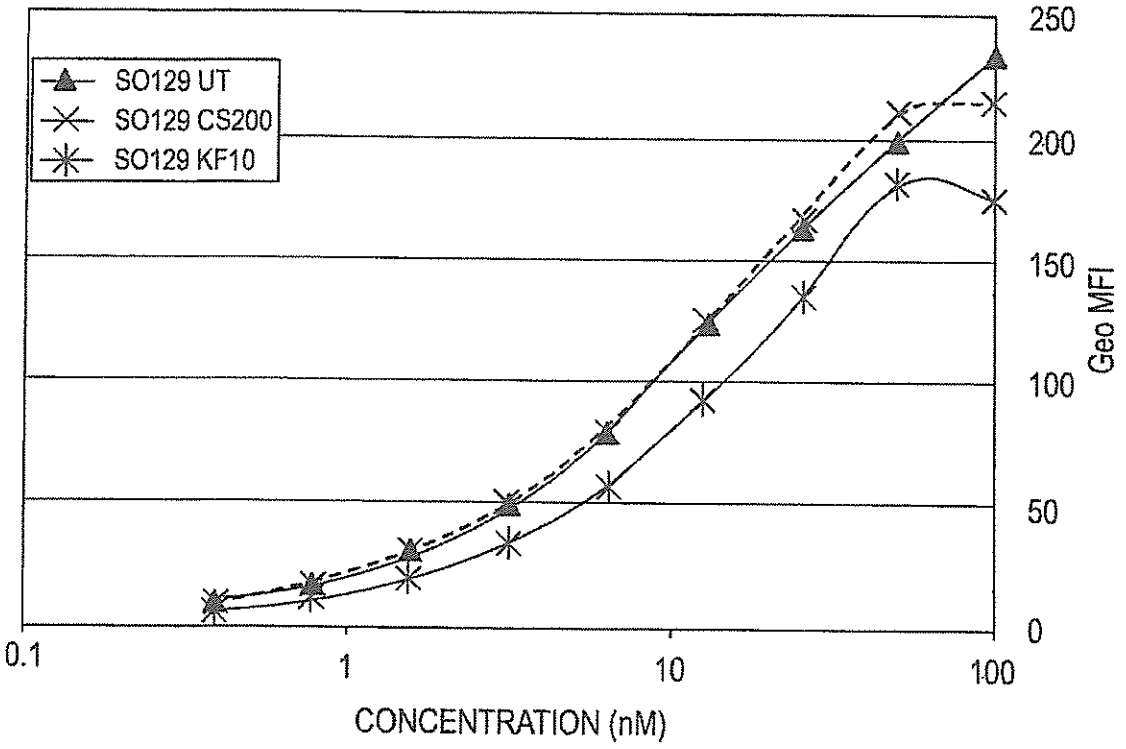

SO129 UT
SO129 CS200
SO129 KF10
250
200
150
100
50
0
Geo MFI
0.1
1
10
100
CONCENTRATION (nM)

FIG. 43

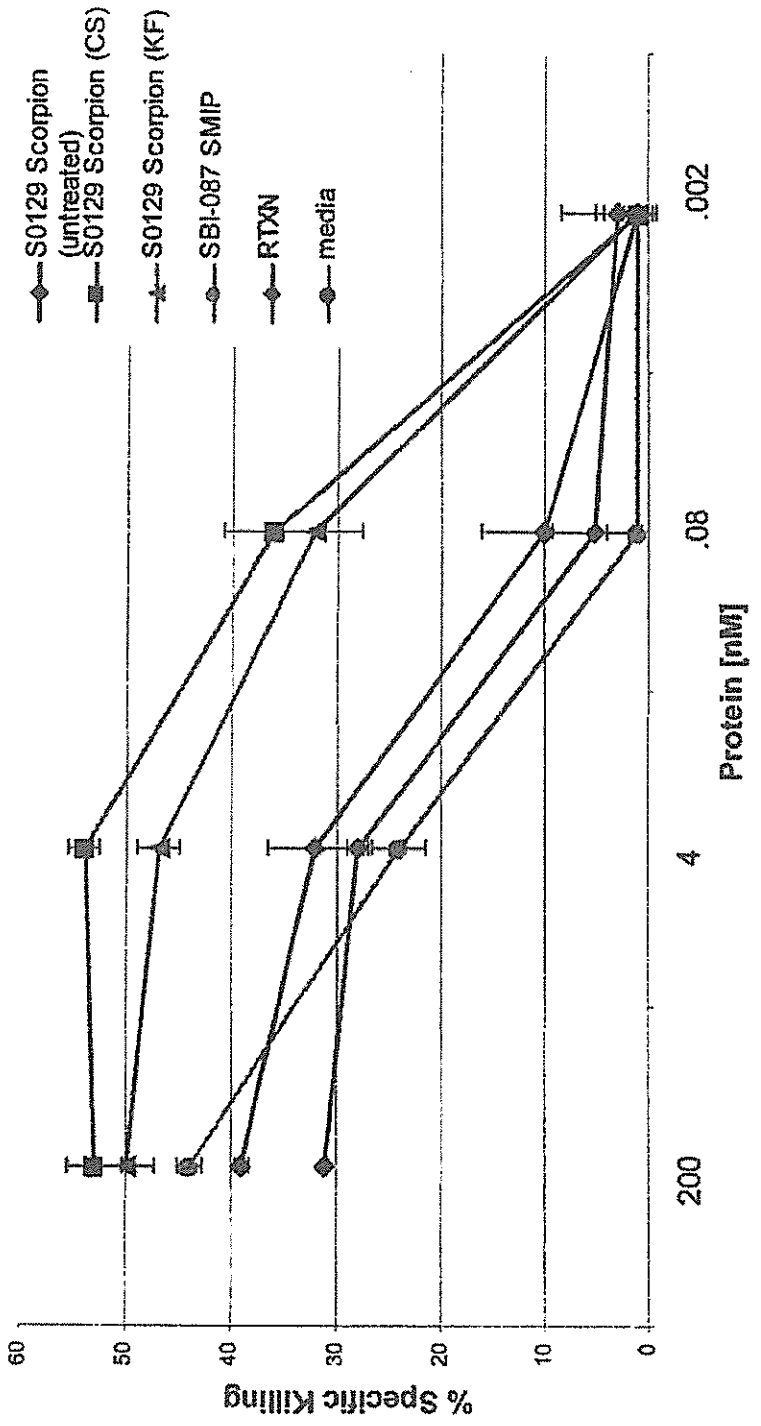

S0129 Scorpion (untreated)
S0129 Scorpion (CS)
S0129 Scorpion (KF)
SBI-087 SMIP
RTXN
media
% Specific Killing
60
50
40
30
20
10
0
200
4
.08
.002
Protein [nM]

FIG. 45

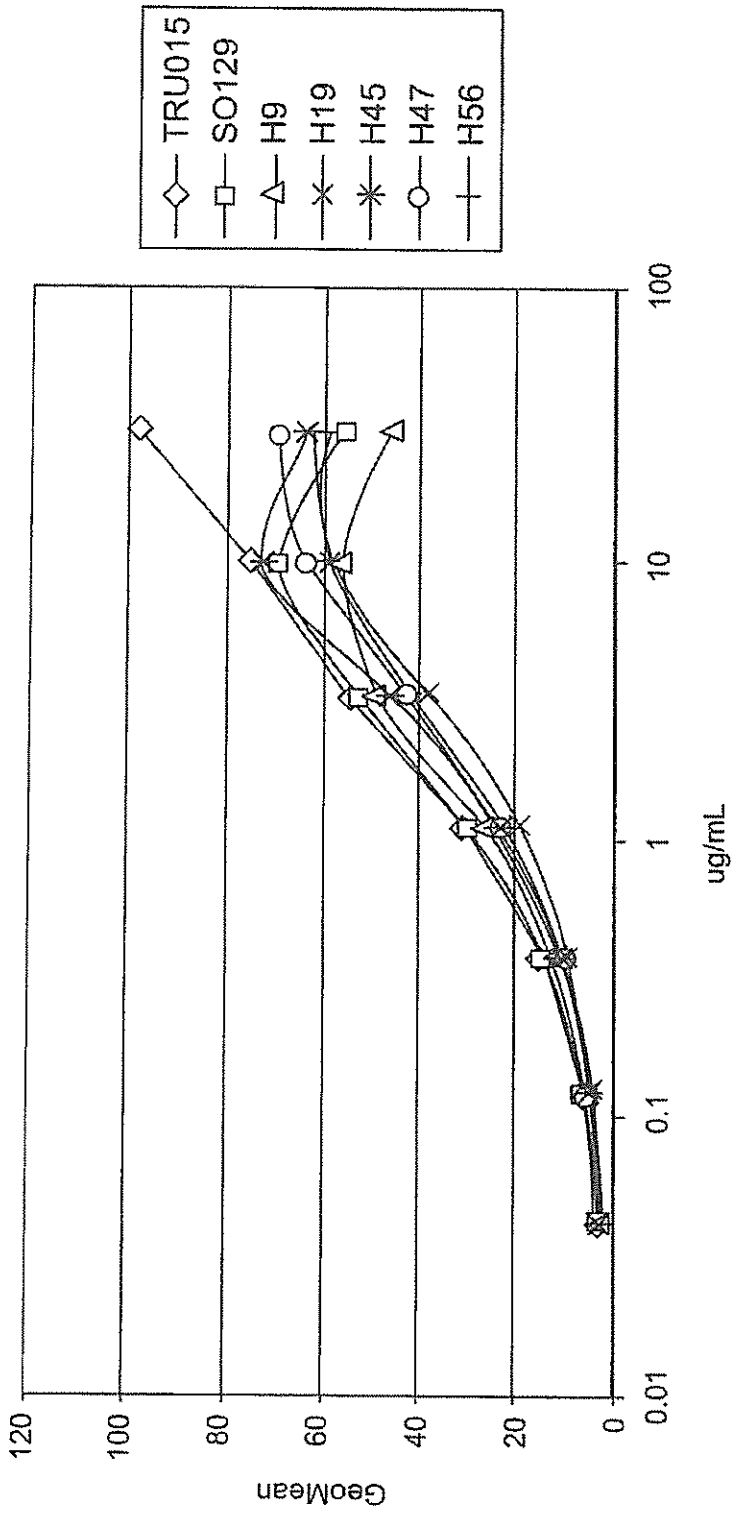

TRU015
SO129
H9
H19
H45
H47
H56
GeoMean
120
100
80
60
40
20
0
0.01
0.1
1
10
100
ug/mL

FIG. 46

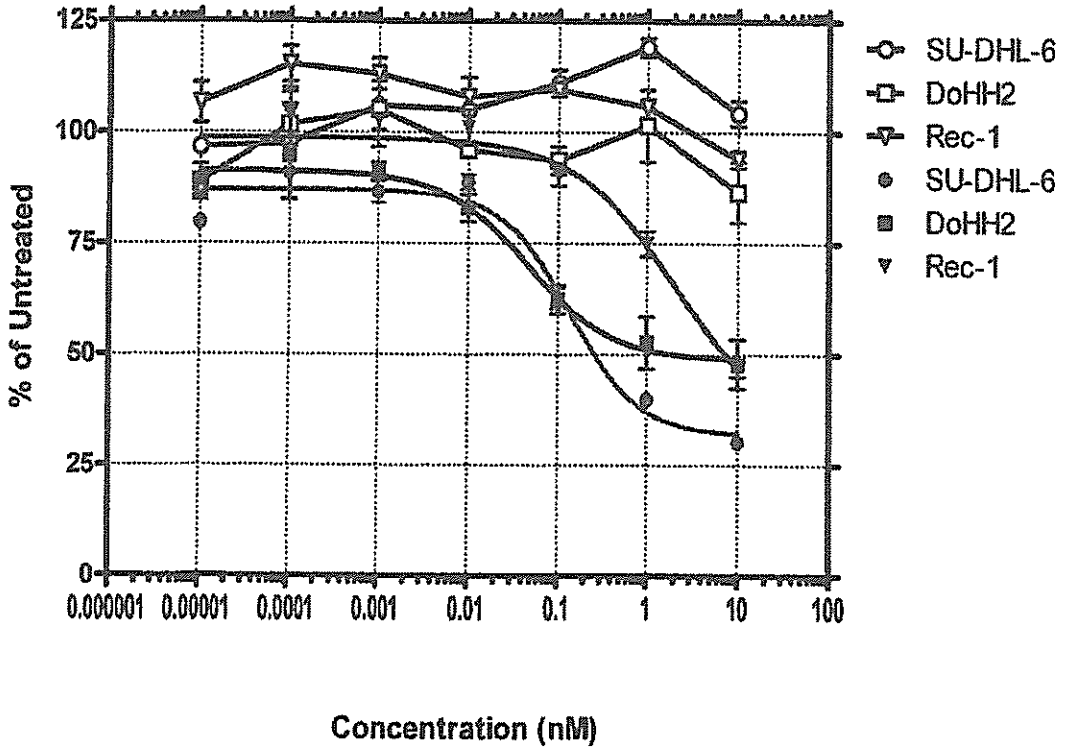

125
100
75
50
25
0
% of Untreated
0.000001
0.00001
0.0001
0.001
0.01
0.1
1
10
100
Concentration (nM)
SU-DHL-6
DoHH2
Rec-1
SU-DHL-6
DoHH2
Rec-1

FIG. 47

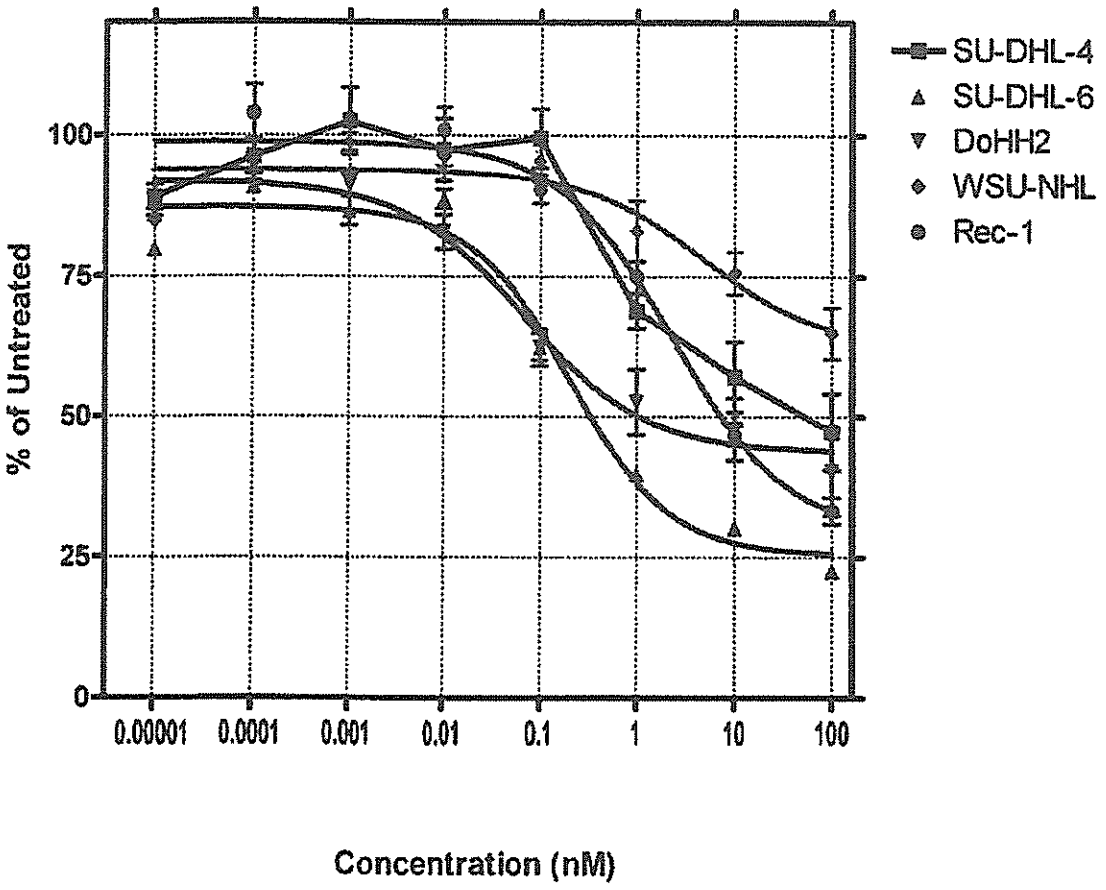

% of Untreated
100
75
50
25
0
0.00001
0.0001
0.001
0.01
0.1
1
10
100
Concentration (nM)
SU-DHL-4
SU-DHL-6
DoHH2
WSU-NHL
Rec-1

FIG. 48

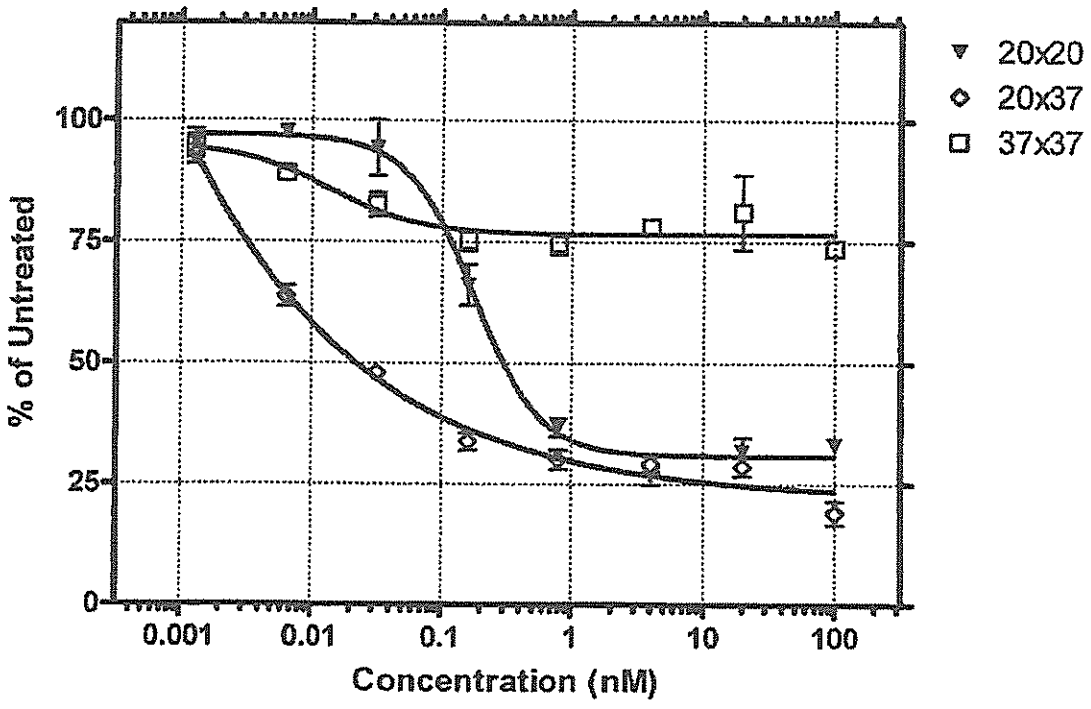

% of Untreated
100
75
50
25
0
0.001
0.01
0.1
1
10
100
Concentration (nM)
20x20
20x37
37x37

FIG. 49

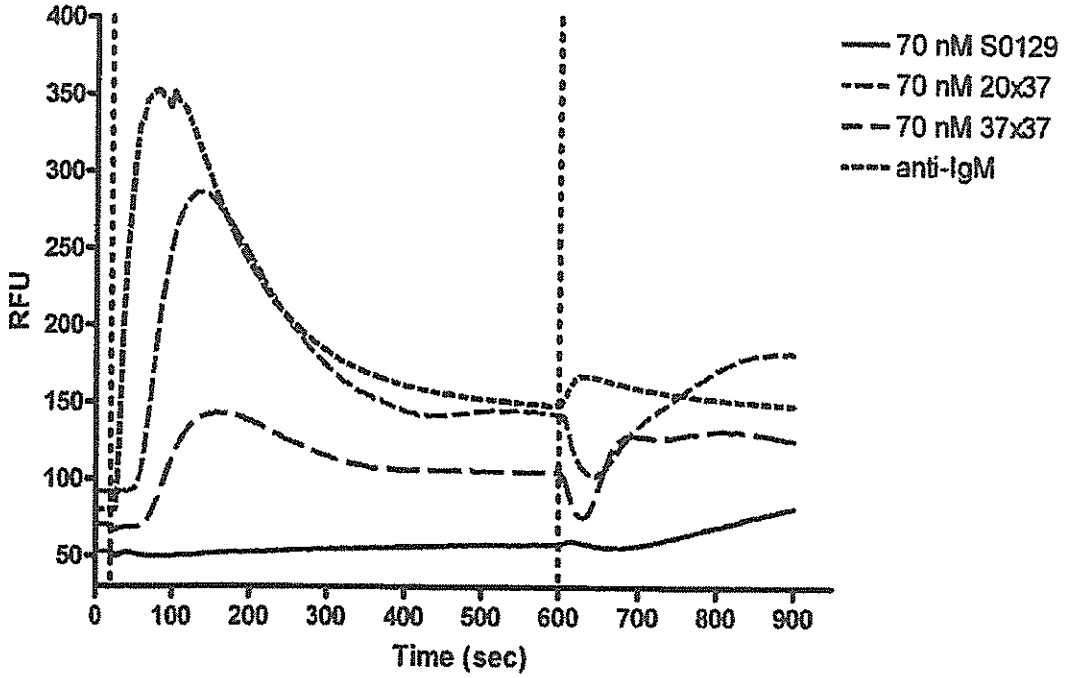

400
350
300
250
200
150
100
50
RFU
0
100
200
300
400
500
600
700
800
900
Time (sec)
70 nM S0129
70 nM 20x37
70 nM 37x37
anti-IgM

FIG. 50

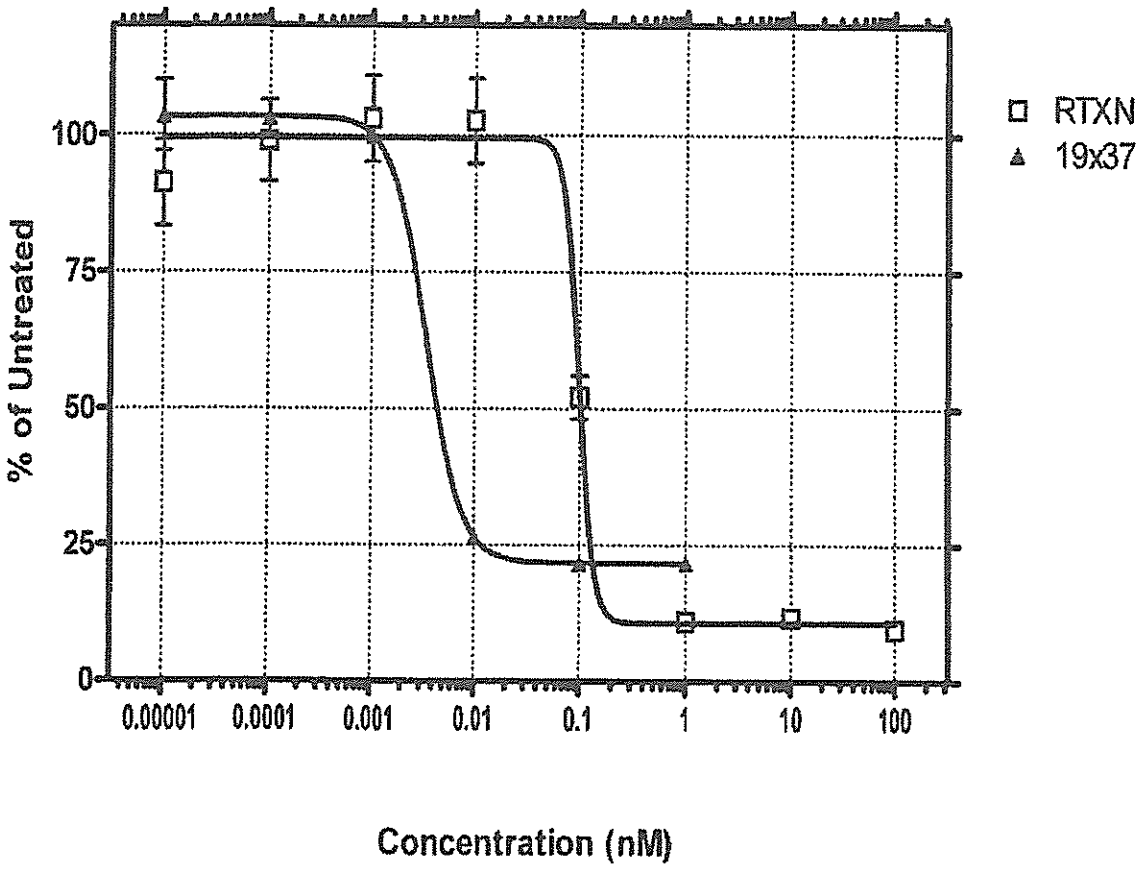

% of Untreated
100
75
50
25
0
0.00001
0.0001
0.001
0.01
0.1
1
10
100
Concentration (nM)
RTXN
19x37

FIG. 59

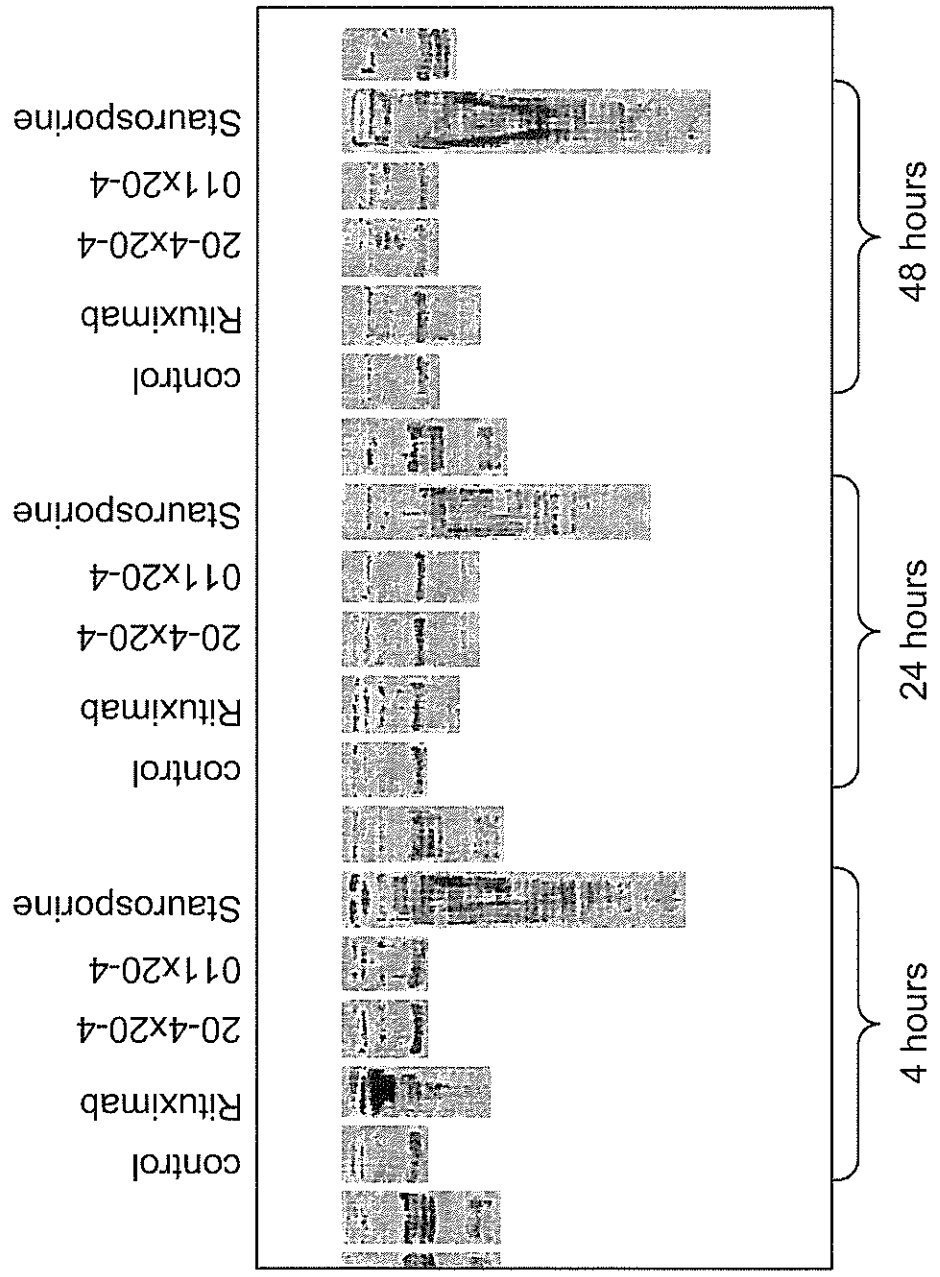
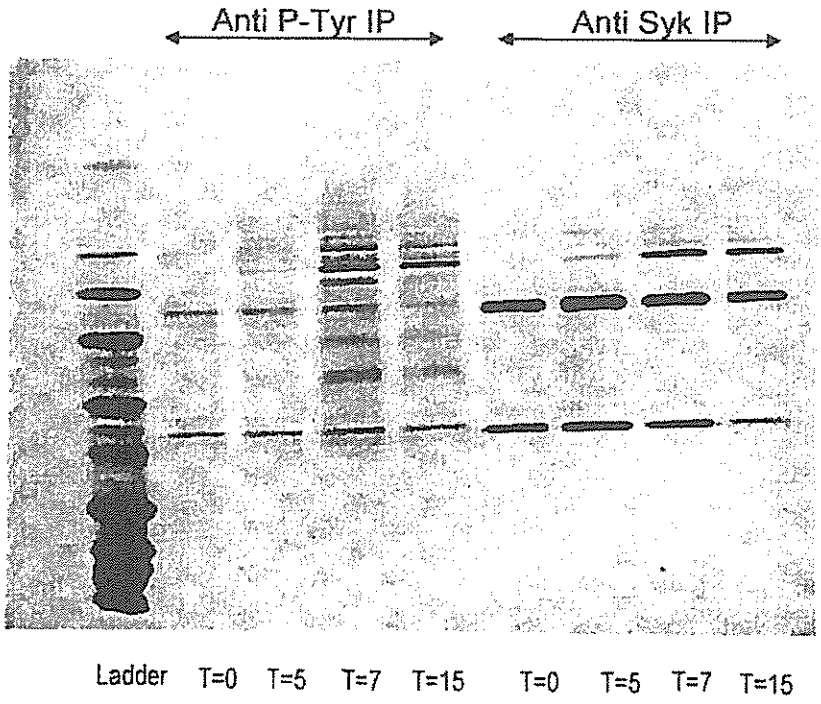
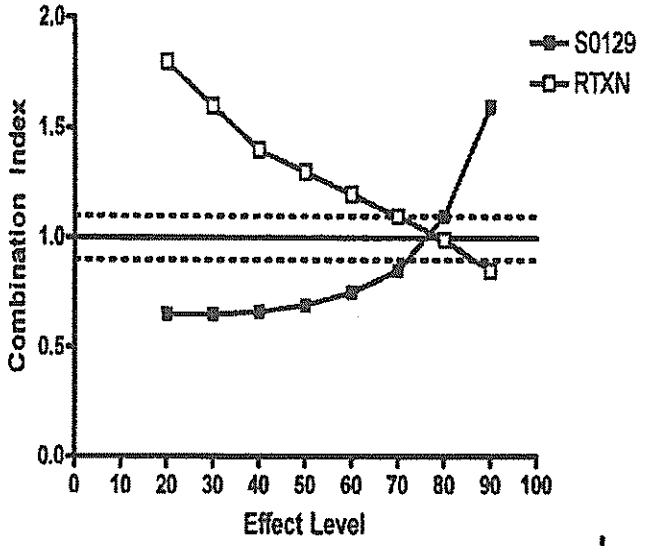
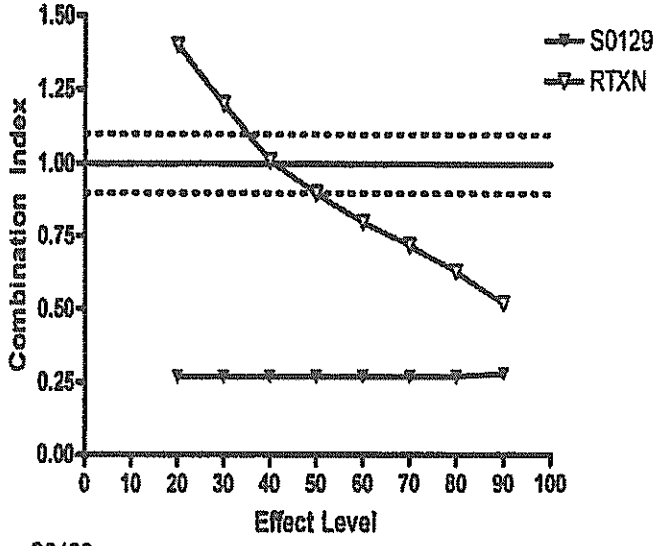

control
Rituximab
20-4x20-4
011x20-4
Staurosporine
control
Rituximab
20-4x20-4
011x20-4
Staurosporine
control
Rituximab
20-4x20-4
011x20-4
Staurosporine
4 hours
24 hours
48 hours

FIG. 60




2.0
1.5
1.0
0.5
0.0
Combination Index
0 10 20 30 40 50 60 70 80 90 100
Effect Level
S0129
RTXN


1.50
1.25
1.00
0.75
0.50
0.25
0.00
Combination Index
0 10 20 30 40 50 60 70 80 90 100
Effect Level
S0129
RTXN

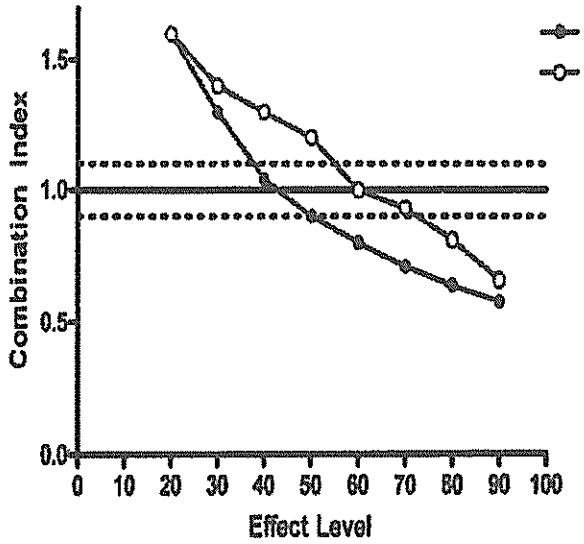

1.5
1.0
0.5
0.0
Combination Index
0 10 20 30 40 50 60 70 80 90 100
Effect Level
S0129
RTXN

FIG. 61