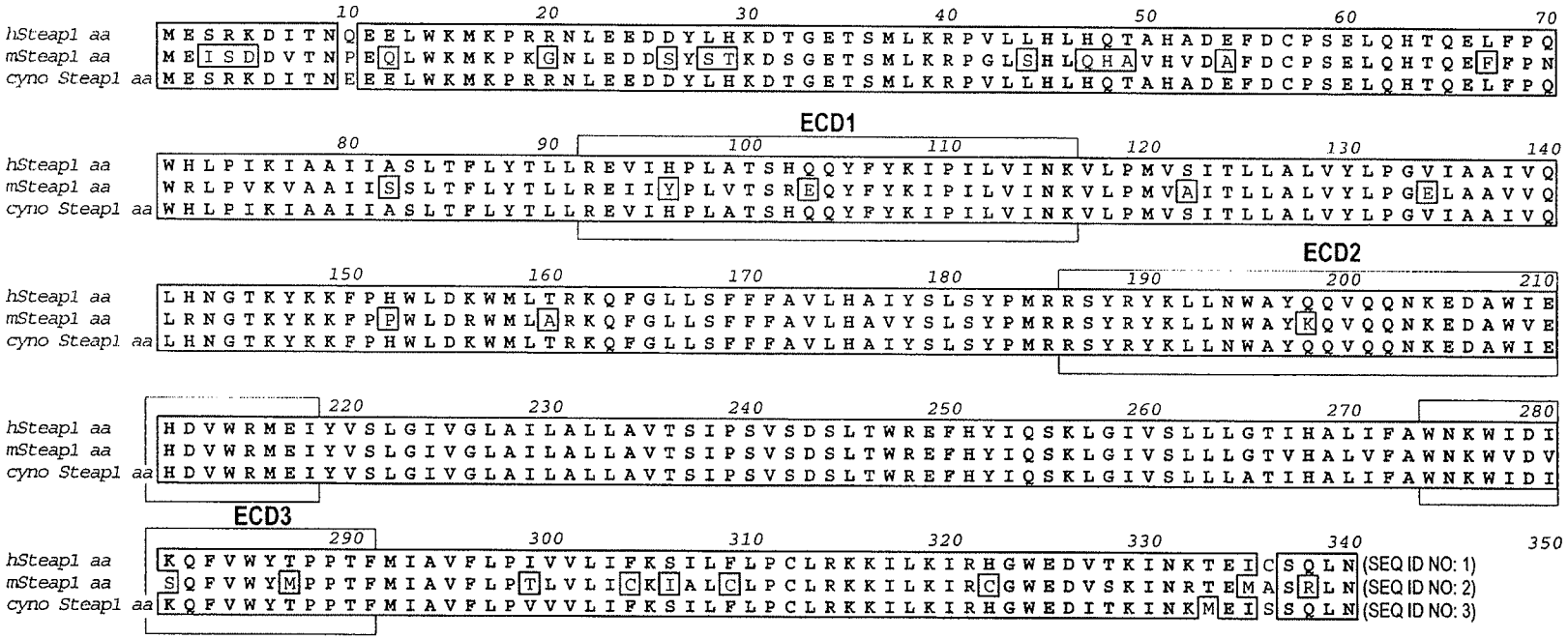
Figure 1


hSteap1 aa
mSteap1 aa
cyno Steap1 aa
ECD1
ECD2
ECD3
(SEQ ID NO: 1)
(SEQ ID NO: 2)
(SEQ ID NO: 3)

Alignment of Light Chain Sequences

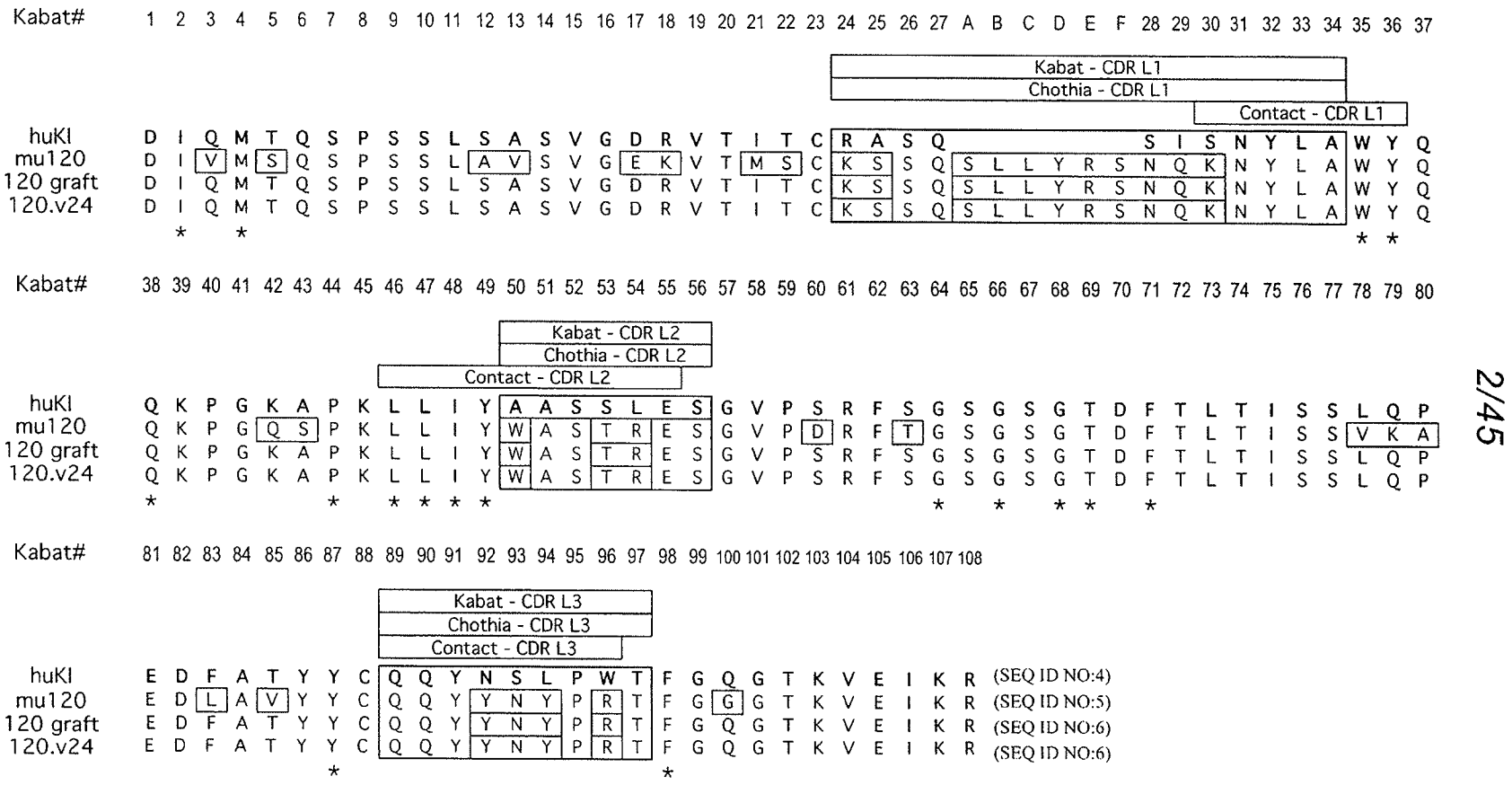


Figure 2A

Alignment of Heavy Chain Sequences

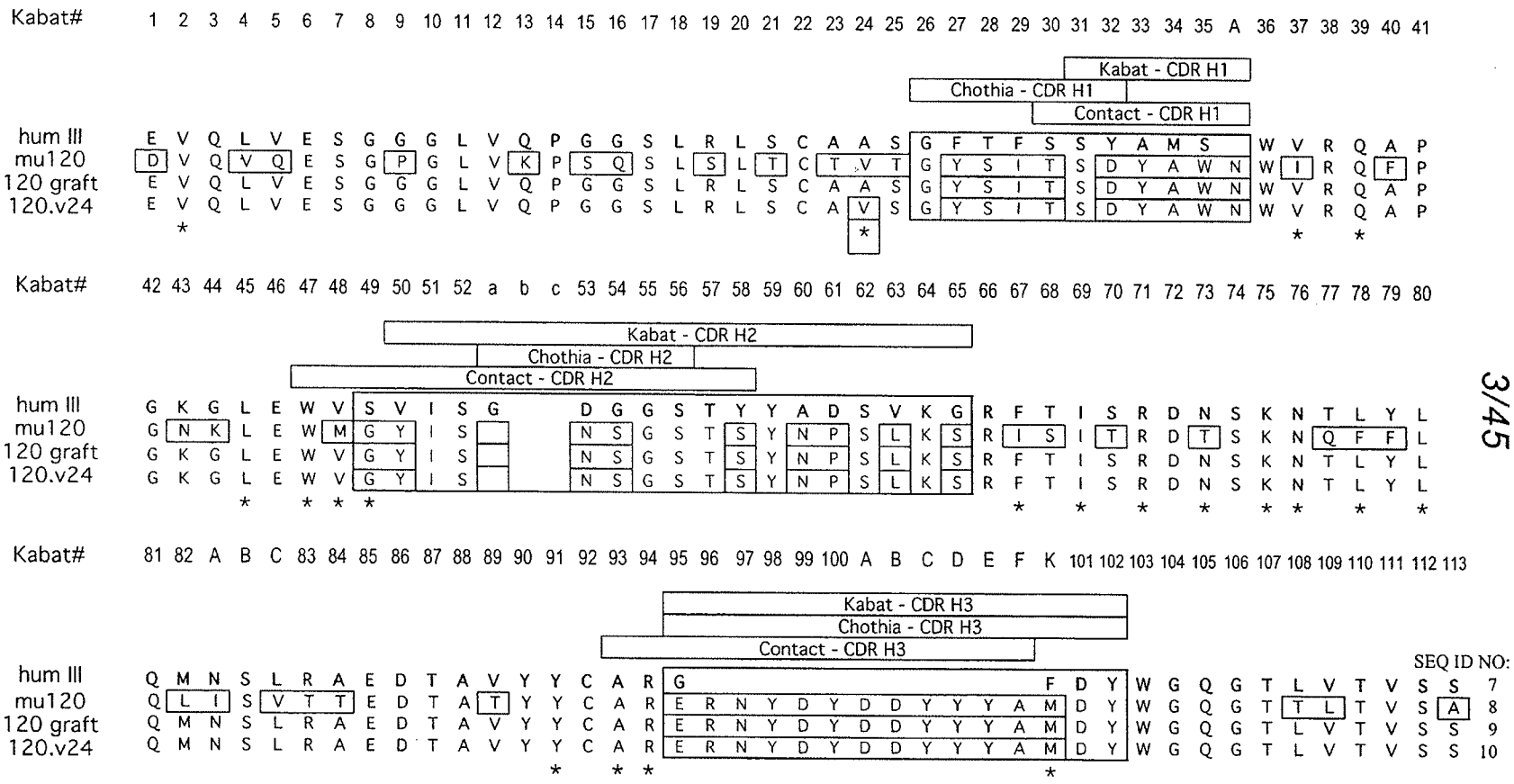


Figure 2B


I
A QVQLVQSGAEVKKPGASVKVSCKASGYTFT -H1- WVRQAPGQGLEWMG -H2-
B QVQLVQSGAEVKKPGASVKVSCKAS -H1- WVRQAPGQGLEWM -H2-
C QVQLVQSGAEVKKPGASVKVSCKAS -H1- WVRQAPGQGLEWM -H2-
D QVQLVQSGAEVKKPGASVKVSCKAS -H1- WVRQAPGQGLEWM -H2-
II
A QVQLQESGPGLVKPSQTLSLTCTVSGGSVS -H1- WIRQPPGKGLEWIG -H2-
B QVQLQESGPGLVKPSQTLSLTCTVS -H1- WIRQPPGKGLEWI -H2-
C QVQLQESGPGLVKPSQTLSLTCTVS -H1- WIRQPPGKGLEWI -H2-
D QVQLQESGPGLVKPSQTLSLTCTVS -H1- WIRQPPGKGLEWI -H2-
III
A EVQLVESGGGLVQPGGSLRLSCAASGFTFS -H1- WVRQAPGKGLEWVS -H2-
B EVQLVESGGGLVQPGGSLRVSCAAS -H1- WVRQAPGKGLEWV -H2-
C EVQLVESGGGLVQPGGSLRVSCAAS -H1- WVRQAPGKGLEWV -H2-
D EVQLVESGGGLVQPGGSLRLSCAAS -H1- WVRQAPGKGLEWV -H2-
Acceptor-1
A EVQLVESGGGLVQPGGSLRLSCAASGFNIK -H1- WVRQAPGKGLEWVS -H2-
B EVQLVESGGGLVKPGGSLRVSCAAS -H1- WVRQAPGKGLEWV -H2-
C EVQLVESGGGLVQPGGSLRLSCAAS -H1- WVRQAPGKGLEWV -H2-
Acceptor-2
A EVQLVESGGGLVQPGGSLRLSCAASGFNIK -H1- WVRQAPGKGLEWVS -H2-
B EVQLVESGGGLVQPGGSLRLSCAAS -H1- WVRQAPGKGLEWV -H2-
C EVQLVESGGELVQPGGSLRLSCAAS -H1- WVRQAPGKGLEWV -H2-
D EVQLVESGGGLVQPGGSLRLSCAAS -H1- WVRQAPGKGLEWV -H2-

Figure 3A


SEQ ID NOs:
RVTITADTSTSTAYMELSSLRSEDTAVYYCAR -H3- WGQGTLVTVSS 26, 27, 28, 29
RVTITADTSTSTAYMELSSLRSEDTAVYYCAR -H3- WGQGTLVTVSS 30, 31, 28, 29
RVTITADTSTSTAYMELSSLRSEDTAVYYCA -H3- WGQGTLVTVSS 30, 31, 32, 29
RVTITADTSTSTAYMELSSLRSEDTAVYYC -H3- WGQGTLVTVSS 30, 31, 33, 29
RVTISVDTSKNQFSLKLSSVTAADTAVVYCAR -H3- WGQGTLVTVSS 34, 35, 36, 29
RVTISVDTSKNQFSLKLSSVTAADTAVVYCAR -H3- WGQGTLVTVSS 37, 38, 36, 29
RVTISVDTSKNQFSLKLSSVTAADTAVVYCA -H3- WGQGTLVTVSS 37, 38, 39, 29
RVTISVDTSKNQFSLKLSSVTAADTAVVYC -H3- WGQGTLVTVSS 37, 38, 40, 29
RFTISRDNSKNTLYLQMNSLRAEDTAVYYCAR -H3- WGQGTLVTVSS 41, 42, 43, 29
RFTISRDNSKNTLYLQMNSLRAEDTAVYYCAR -H3- WGQGTLVTVSS 44, 45, 43, 29
RFTISRDNSKNTLYLQMNSLRAEDTAVYYCA -H3- WGQGTLVTVSS 44, 45, 46, 29
RFTISRDNSKNTLYLQMNSLRAEDTAVYYC -H3- WGQGTLVTVSS 44, 45, 47, 29
RFTISADTSKNTAYLQMNSLRAEDTAVYYCSR -H3- WGQGTLVTVSS 48, 42, 49, 29
RFTISADTSKNTAYLQMNSLRAEDTAVYYCSR -H3- WGQGTLVTVSS 44, 45, 49, 29
RFTISADTSKNTAYLQMNSLRAEDTAVYYCS -H3- WGQGTLVTVSS 44, 45, 50, 29
RFTISADTSKNTAYLQMNSLRAEDTAVYYCAR -H3- WGQGTLVTVSS 48, 42, 51, 29
RFTISADTSKNTAYLQMNSLRAEDTAVYYCAR -H3- WGQGTLVTVSS 44, 45, 51, 29
RFTISADTSKNTAYLQMNSLRAEDTAVYYCA -H3- WGQGTLVTVSS 44, 45, 52, 29
RFTISADTSKNTAYLQMNSLRAEDTAVYYC -H3- WGQGTLVTVSS 44, 45, 53, 29

Figure 3B

kv1 DIQMTQSPSSLSASVGDRVTITC -L1- WYQQKPGKAPKLLIY -L2- GVPSRFSGSGSGTDFTLTISSLQP

kv1 DIQMTQSPSSLSASVGDRVTITC -L1- WYQQKPGKAPKLLI -L2- GVPSRFSGSGSGTDFTLTISSLQP

kv2 DIVMTQSPLSLPVTPGEPASISC -L1- WYLQKPGQSPQLLIY -L2- GVPDRFSGSGSGTDFTLKISRVEA

kv3 EIVLTQSPGTLSLSPGERATLSC -L1- WYQQKPGQAPRLLIY -L2- GIPDRFSGSGSGTDFTLTISRLEP

kv4 DIVMTQSPDSLAVSLGERATINC -L1- WYQQKPGQPPKLLIY -L2- GVPDRFSGSGSGTDFTLTISSLQA

Figure 4A

EDFATYYC -L3- FGQGTKVEIK SEQ ID NOs: 54, 55, 56, 57

EDFATYYC -L3- FGQGTKVEIK SEQ ID NOs: 54, 58, 56, 57

EDVGVYYC -L3- FGQGTKVEIK SEQ ID NOs: 58, 59, 60, 57

EDFAVYYC -L3- FGQGTKVEIK SEQ ID NOs: 61, 62, 63, 57

EDVAVYYC -L3- FGQGTKVEIK SEQ ID NOs: 64, 65, 66, 57

Figure 4B

```
          230        240        250        260        270
humIgG1     PAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYV
humIgG2     PAP-PVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVQFNWYV
humIgG3     PAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVQFKWYV
humIgG4     PAPEFLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSQEDPEVQFNWYV
               ****                                  *     * *

          280        290        300        310        320
humIgG1     DGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALP
humIgG2     DGVEVHNAKTKPREEQFNSTFRVVSVLTVVHQDWLNGKEYKCKVSNKGLP
humIgG3     DGVEVHNAKTKPREEQFNSTFRVVSVLTVLHQDWLNGKEYKCKVSNKALP
humIgG4     DGVEVHNAKTKPREEQFNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKGLP
                           *   *         *                   *

          330        340        350        360        370
humIgG1     APIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAV
                                          D L
humIgG2     APIEKTISKTKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAV
humIgG3     APIEKTISKTKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAV
humIgG4     SSIEKTISKAKGQPREPQVYTLPPSQEEMTKNQVSLTCLVKGFYPSDIAV
            **        *                  *

          380        390        400        410        420
humIgG1     EWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMH
humIgG2     EWESNGQPENNYKTTPPMLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMH
humIgG3     EWESSGQPENNYNTTPPMLDSDGSFFLYSKLTVDKSRWQQGNIFSCSVMH
humIgG4     EWESNGQPENNYKTTPPVLDSDGSFFLYSRLTVDKSRWQEGNVFSCSVMH
                 *         *     *              *           *   *

          430        440
humIgG1     EALHNHYTQKSLSLSPGK  (SEQ ID NO:85)
humIgG2     EALHNHYTQKSLSLSPGK  (SEQ ID NO:86)
humIgG3     EALHNRFTQKSLSLSPGK  (SEQ ID NO:87)
humIgG4     EALHNHYTQKSLSLSLGK  (SEQ ID NO:88)
               **          *
```

A Kappa light chain constant region consensus sequence:

```
RTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWK
VDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKV
YACEVTHQGLSSPVTKSFNRGEC  (SEQ ID NO:89)
```

Figure 5

Figure 6A

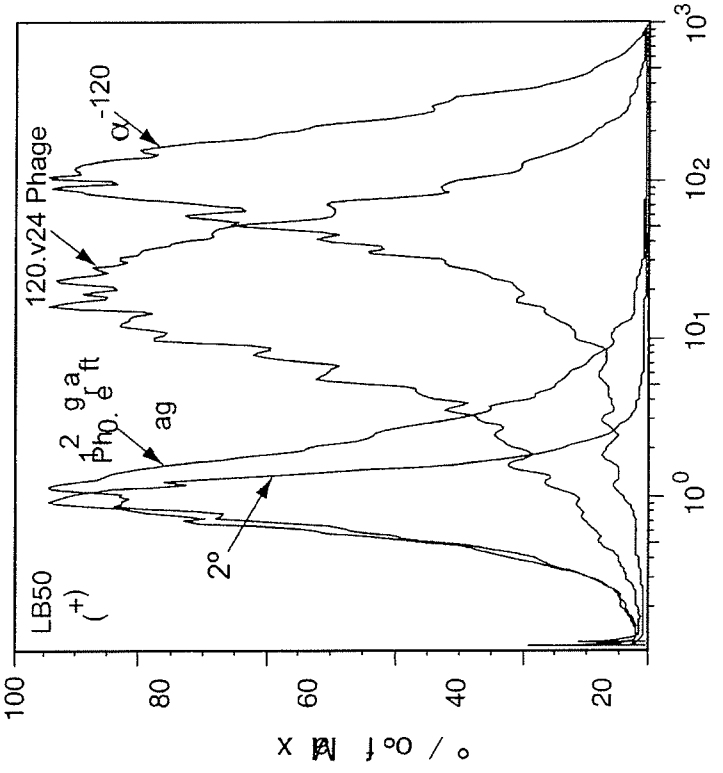


Figure 6C

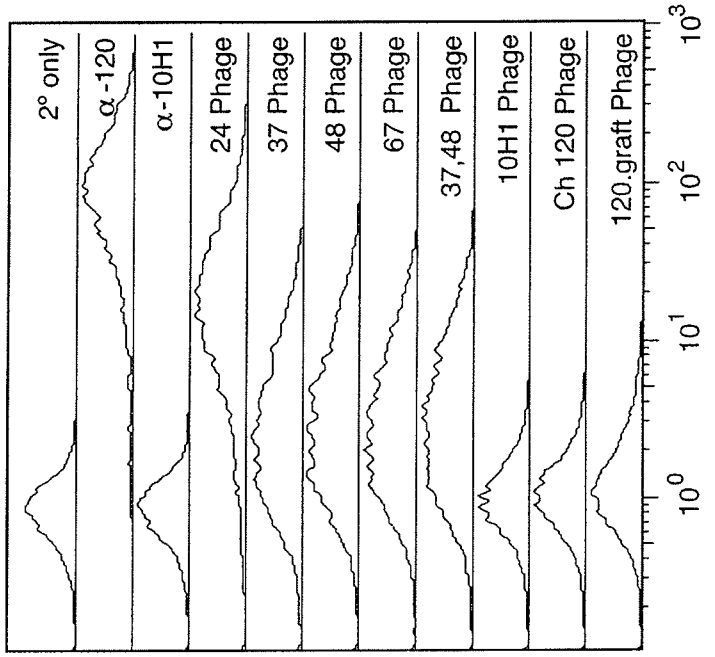


Figure 6D

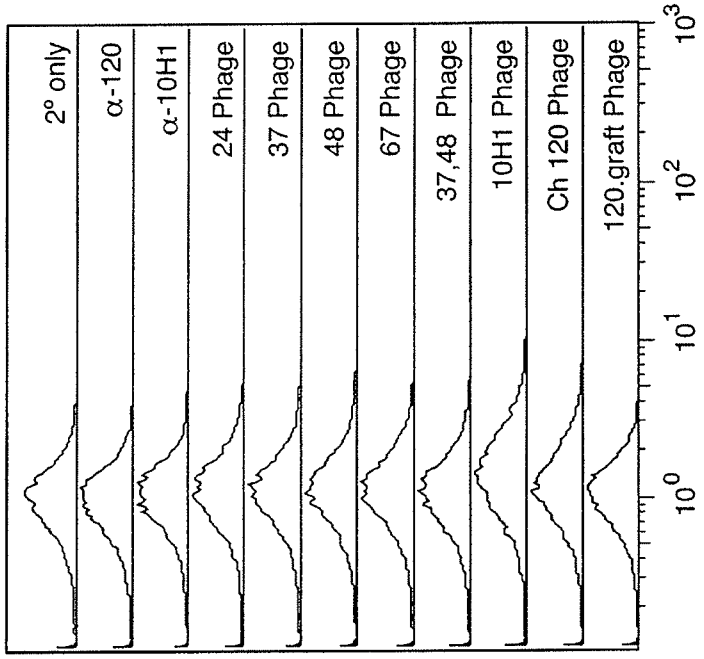
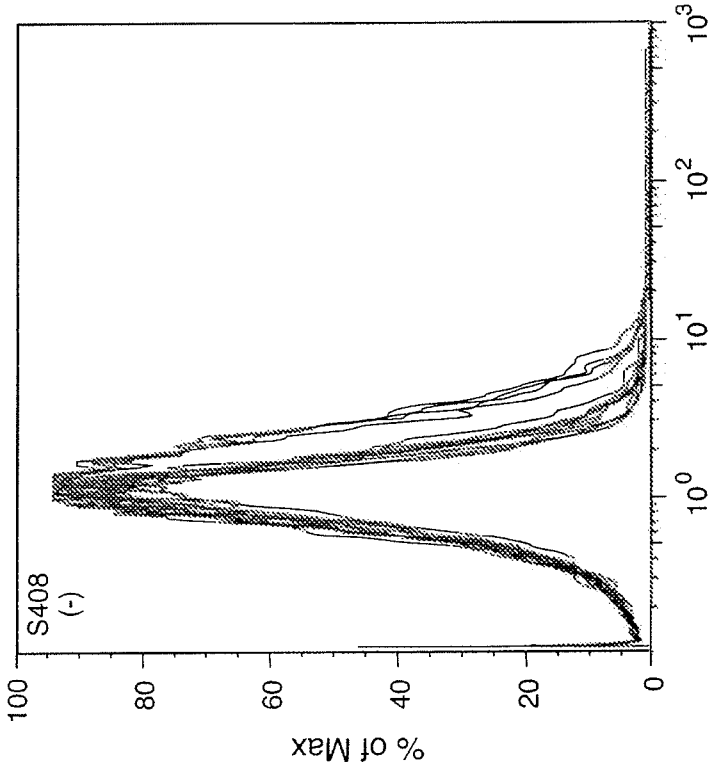


Figure 6B



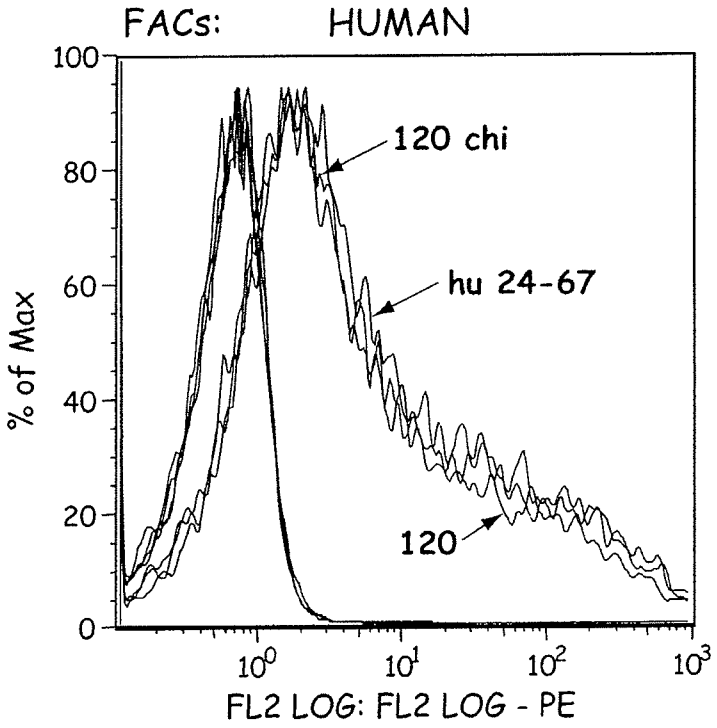


Figure 7A

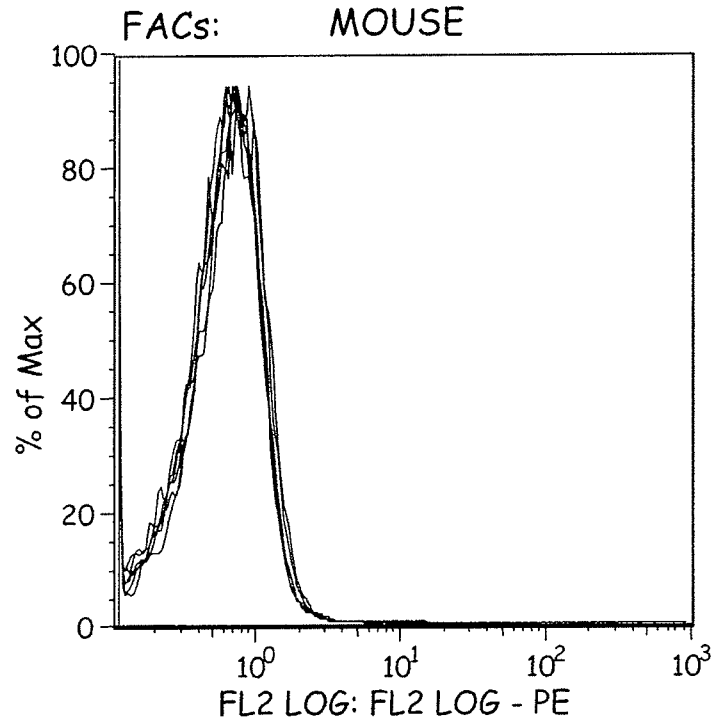


Figure 7B

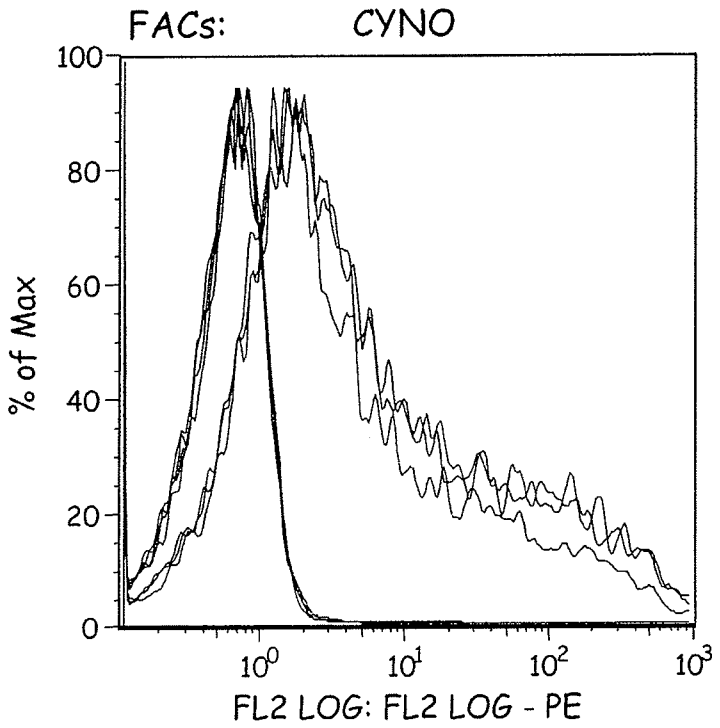


Figure 7C

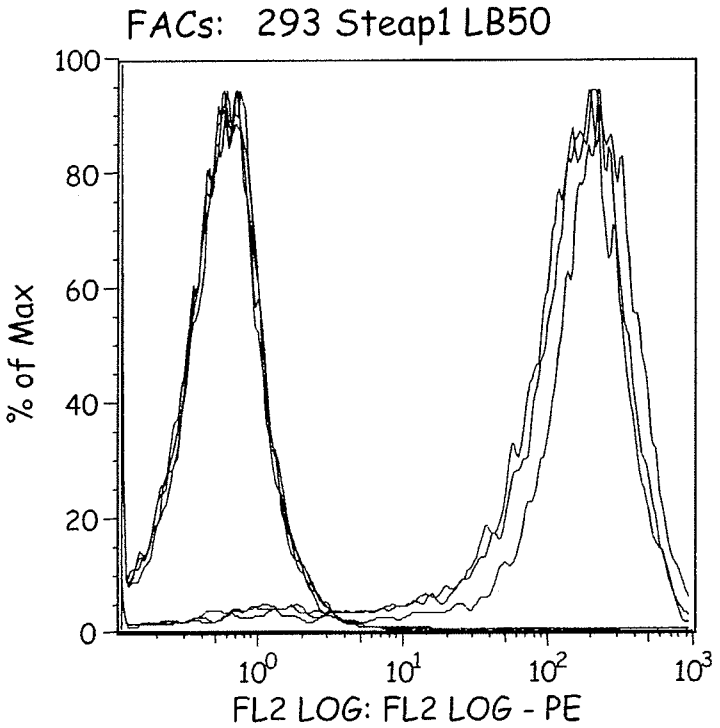


Figure 7D

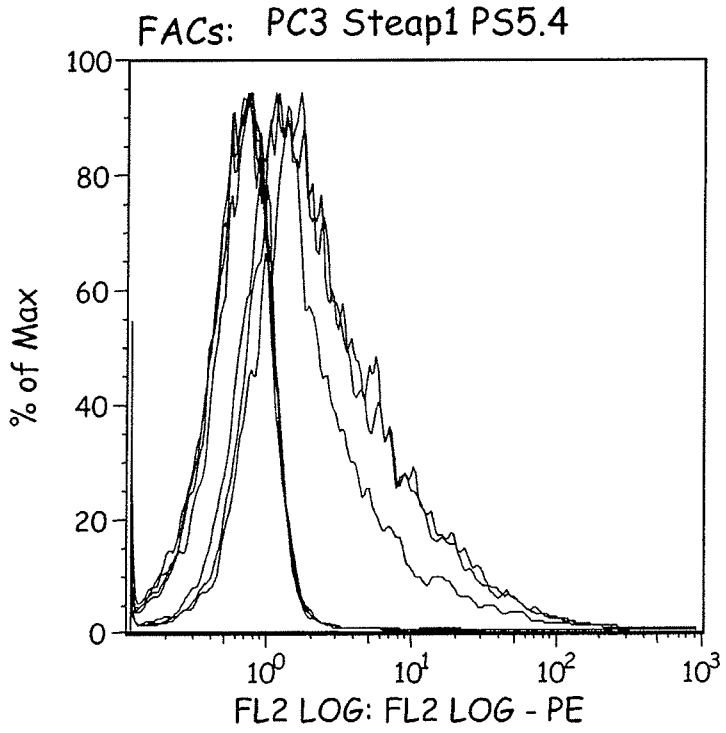


Figure 7E

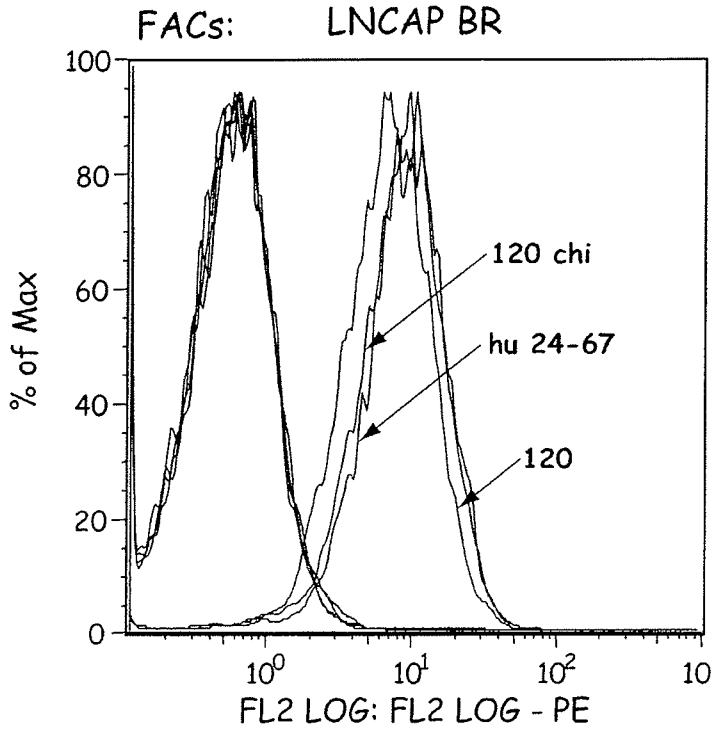


Figure 7F

Figure 8A

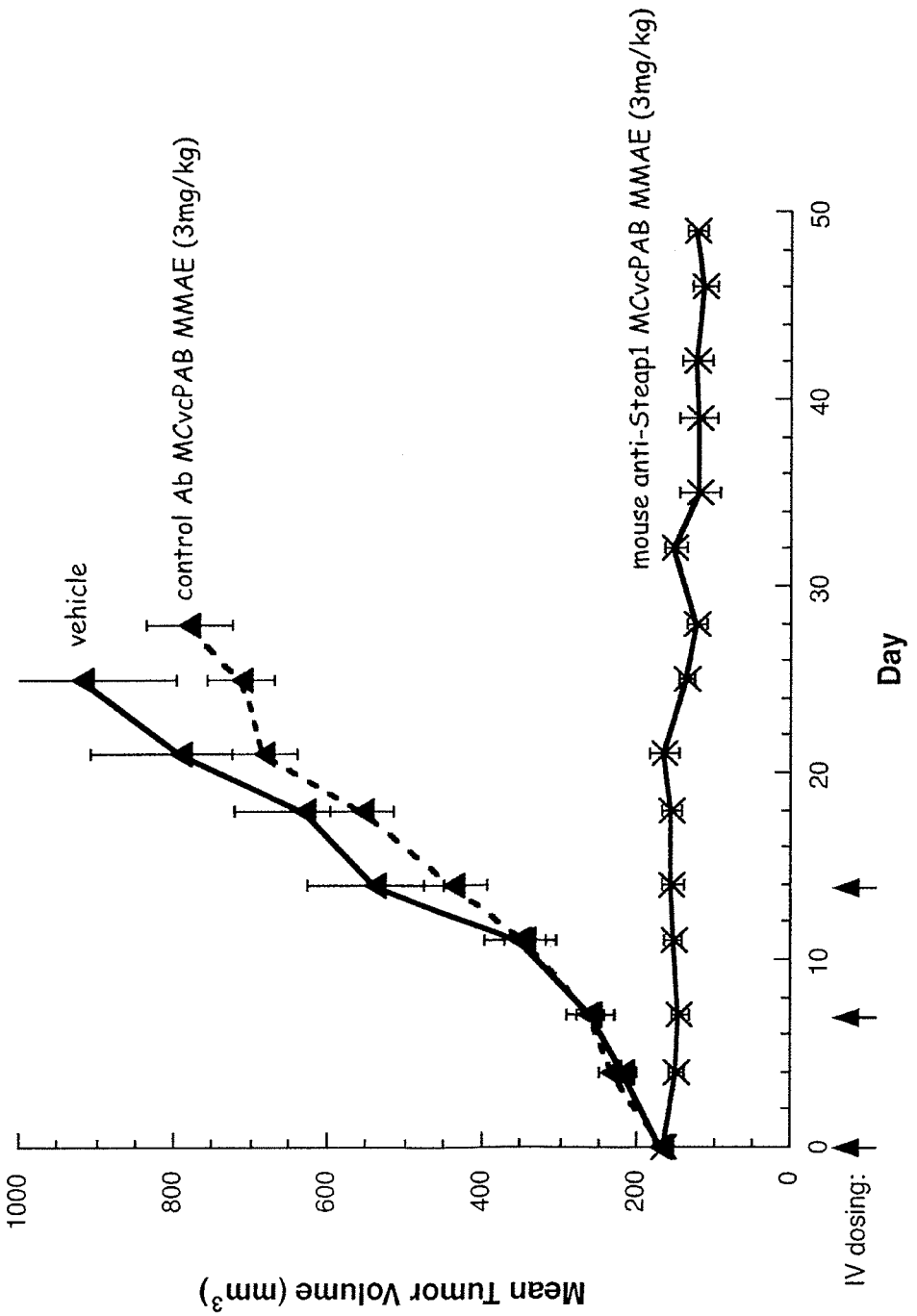

vehicle
control Ab MCvcPAB MMAE (3mg/kg)
mouse anti-Steap1 MCvcPAB MMAE (3mg/kg)
Mean Tumor Volume (mm3)
1000
800
600
400
200
0
0
10
20
30
40
50
Day
IV dosing:

Figure 8B

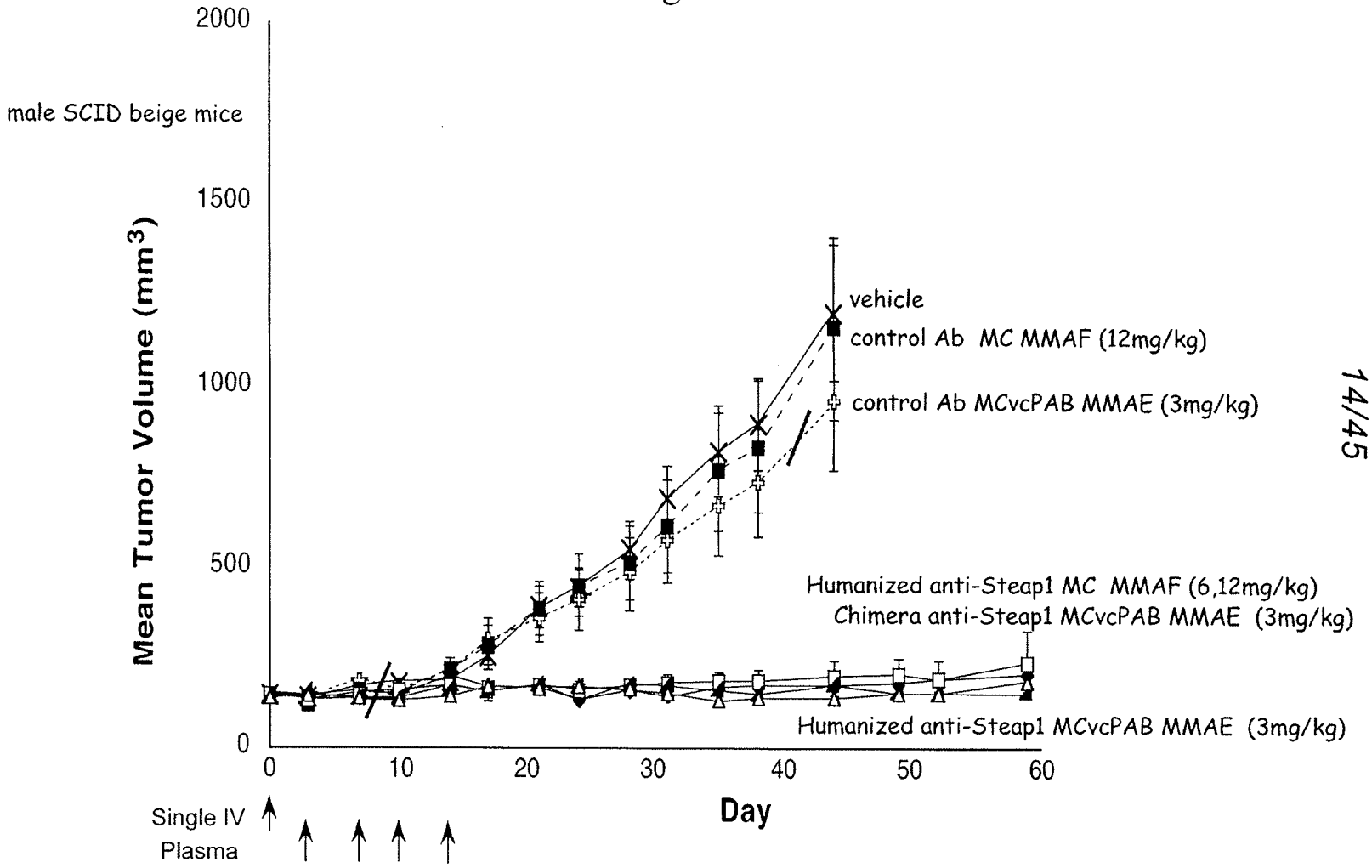

male SCID beige mice
Mean Tumor Volume (mm3)
2000
1500
1000
500
0
0
10
20
30
40
50
60
Day
vehicle
control Ab MC MMAF (12mg/kg)
control Ab MCvcPAB MMAE (3mg/kg)
Humanized anti-Steap1 MC MMAF (6,12mg/kg)
Chimera anti-Steap1 MCvcPAB MMAE (3mg/kg)
Humanized anti-Steap1 MCvcPAB MMAE (3mg/kg)
Single IV
Plasma

Figure 9

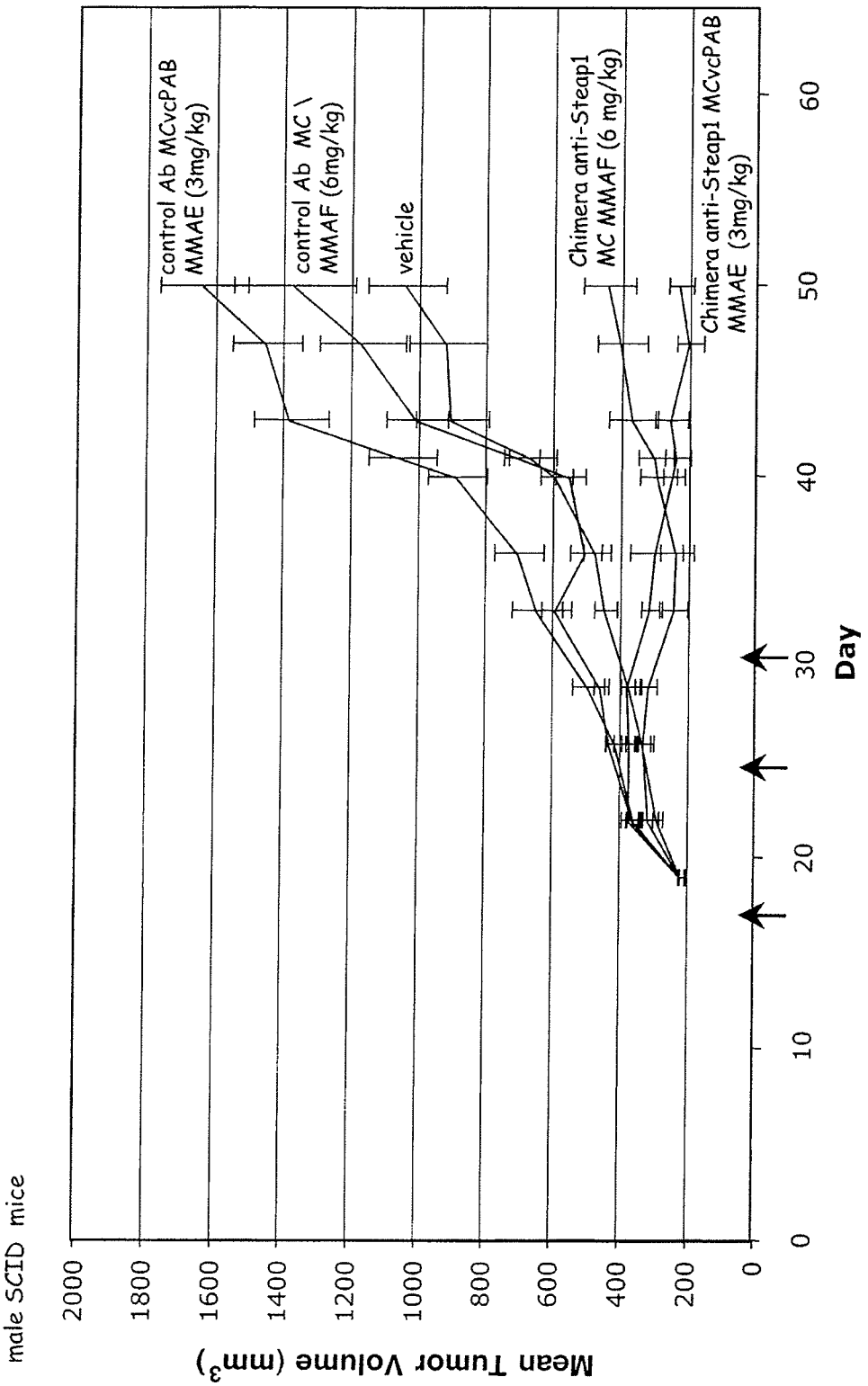

male SCID mice
Mean Tumor Volume (mm3)
2000
1800
1600
1400
1200
1000
800
600
400
200
0
0
10
20
30
40
50
60
Day
control Ab MCvcPAB MMAE (3mg/kg)
control Ab MC \ MMAF (6mg/kg)
vehicle
Chimera anti-Steap1 MC MMAF (6 mg/kg)
Chimera anti-Steap1 MCvcPAB MMAE (3mg/kg)

Figure 10

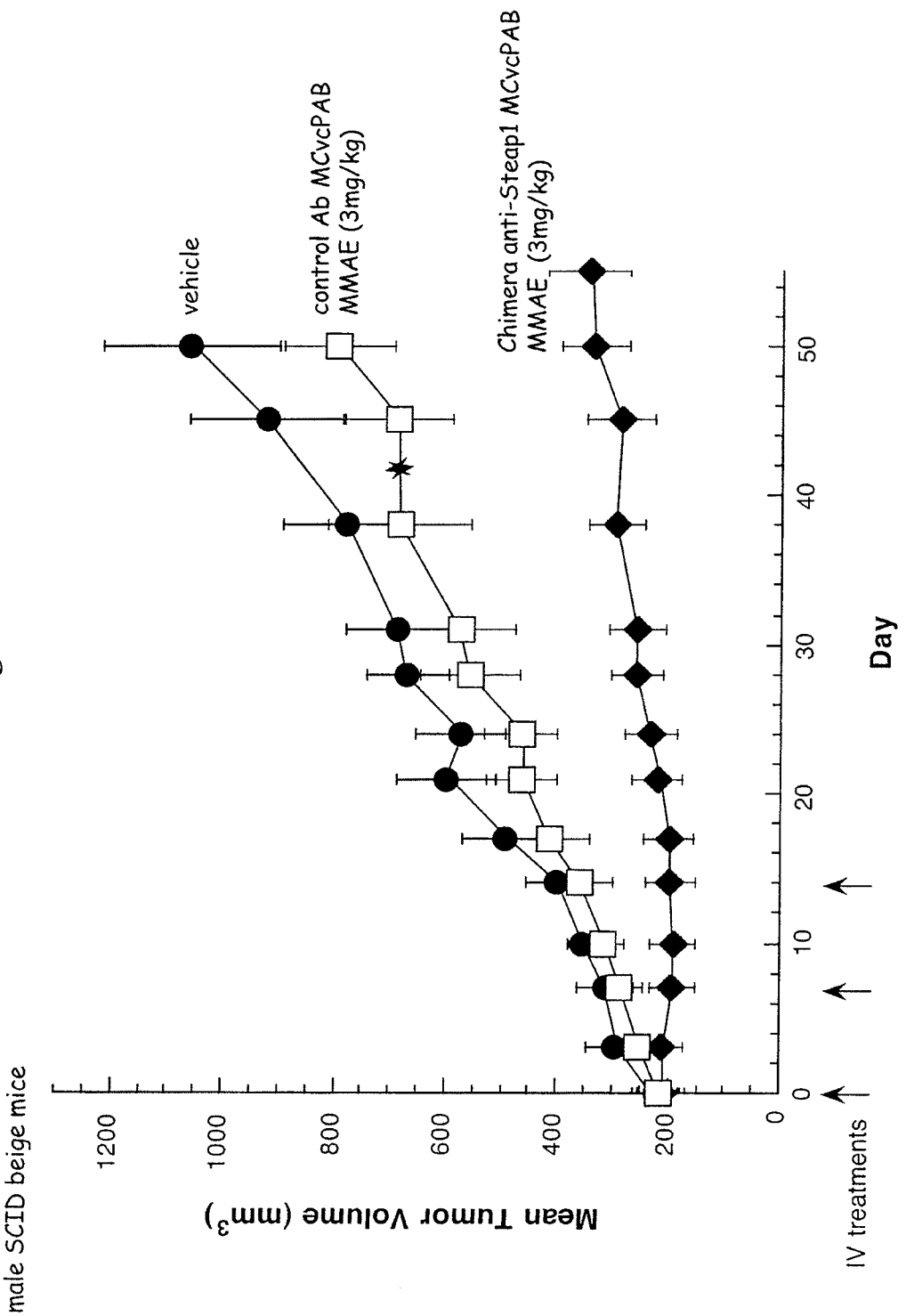
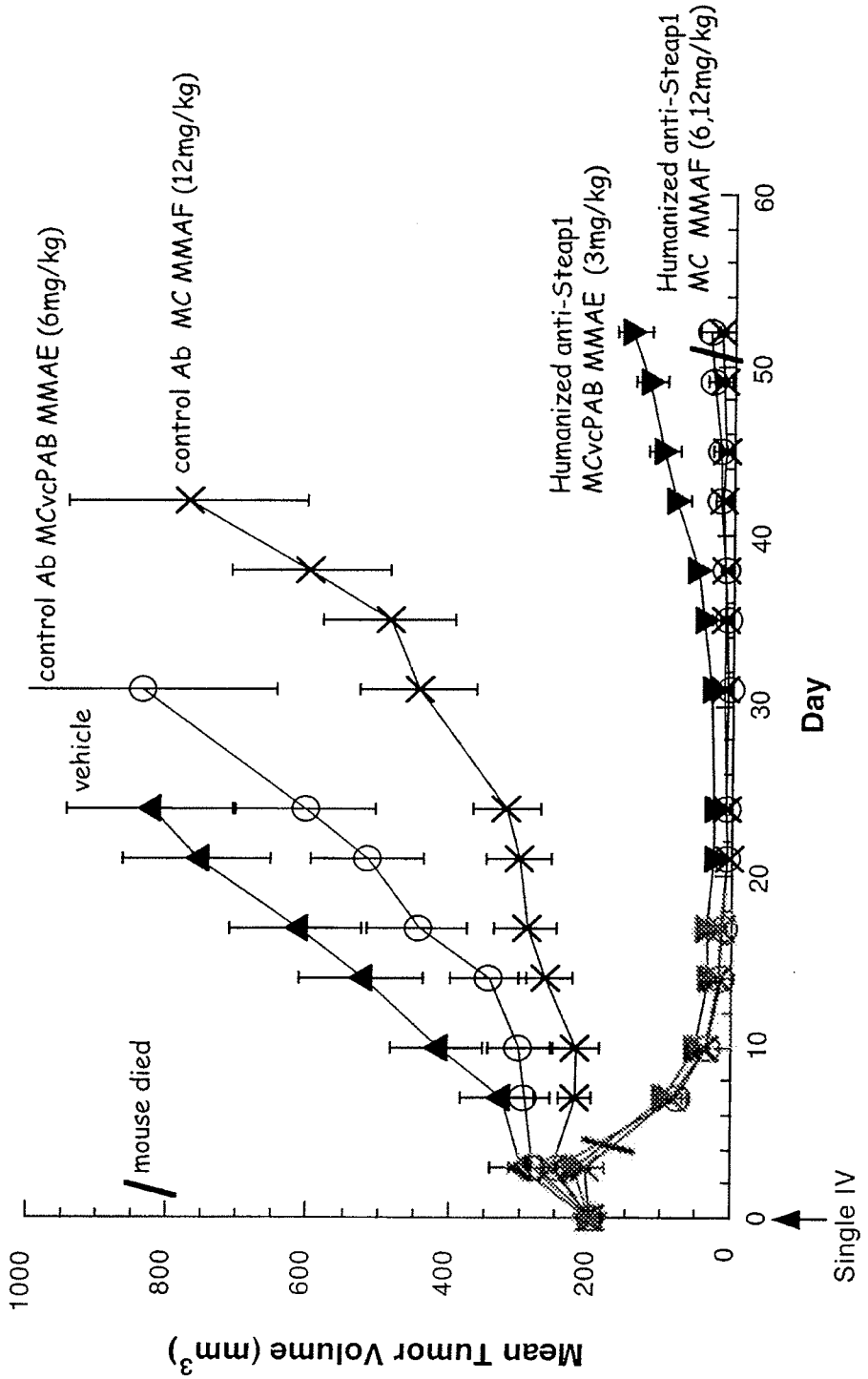

male SCID beige mice
Mean Tumor Volume (mm3)
1200
1000
800
600
400
200
0
0
10
20
30
40
50
Day
IV treatments
vehicle
control Ab MCvcPAB
MMAE (3mg/kg)
Chimera anti-Steap1 MCvcPAB
MMAE (3mg/kg)

Figure 11


Mean Tumor Volume (mm3)
1000
800
600
400
200
0
0
10
20
30
40
50
60
Day
Single IV
control Ab MCvcPAB MMAE (6mg/kg)
control Ab MC MMAF (12mg/kg)
vehicle
mouse died
Humanized anti-Steap1 MCvcPAB MMAE (3mg/kg)
Humanized anti-Steap1 MC MMAF (6,12mg/kg)

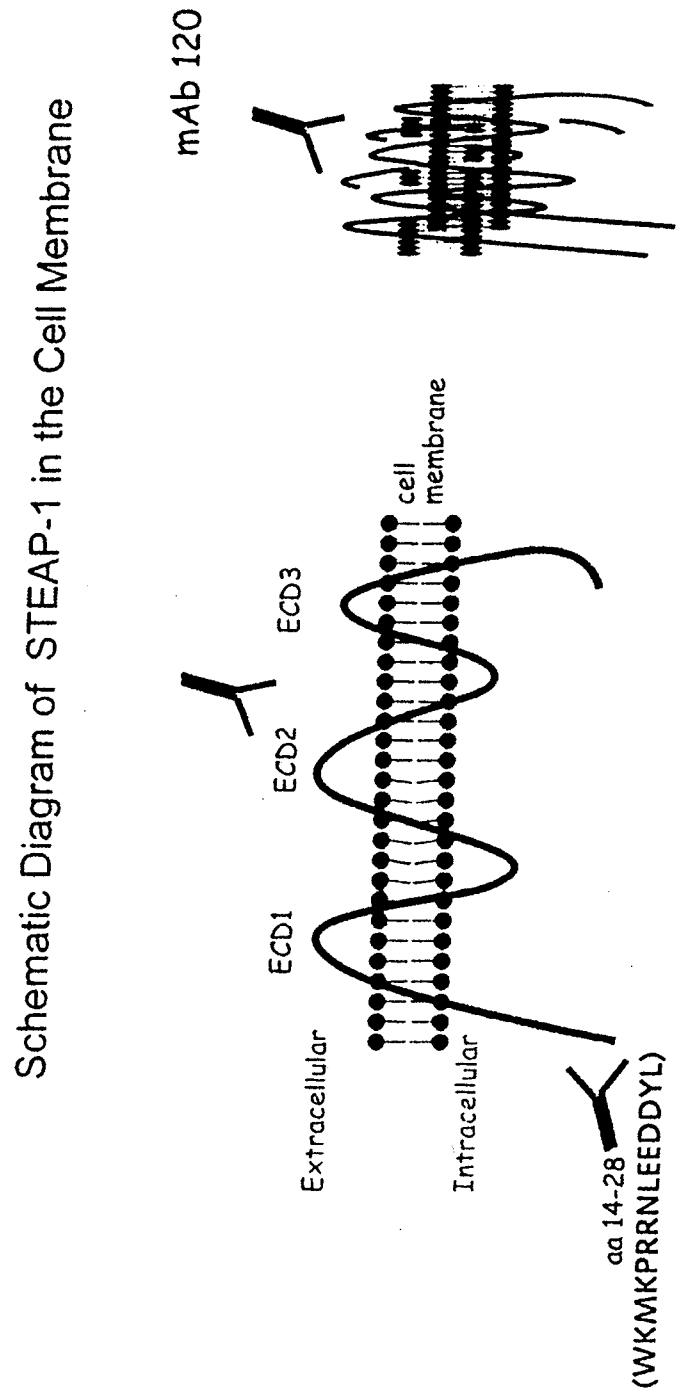

Schematic Diagram of STEAP-1 in the Cell Membrane
mAb 120
ECD1
ECD2
ECD3
cell membrane
Extracellular
Intracellular
aa 14-28
(WKMKPRRNLEEDDYL)

Figure 12

Expression of STEAP1 in prostate cancer models

Exogenous models

293 STEAP1 LB50

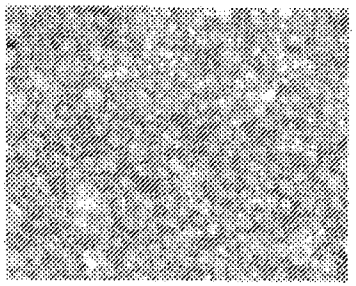


Figure 13A

PC3 STEAP1 PS5.4

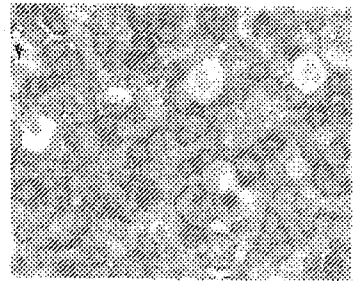


Figure 13B

Endogenous models

LN_{CaP}

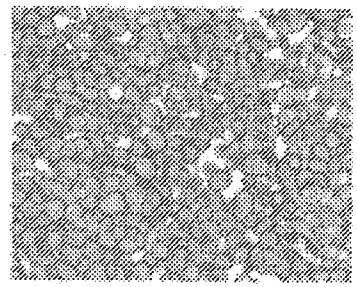


Figure 13C

LuCAP 77

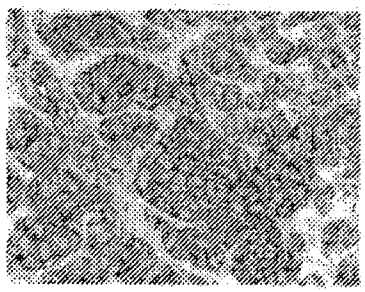


Figure 13D

Figure 14A

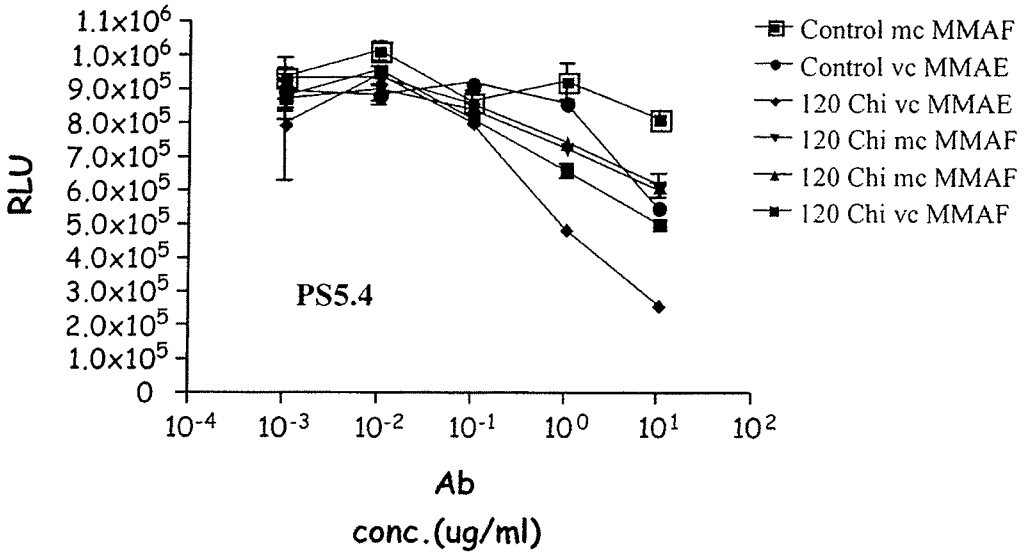


Figure 14B

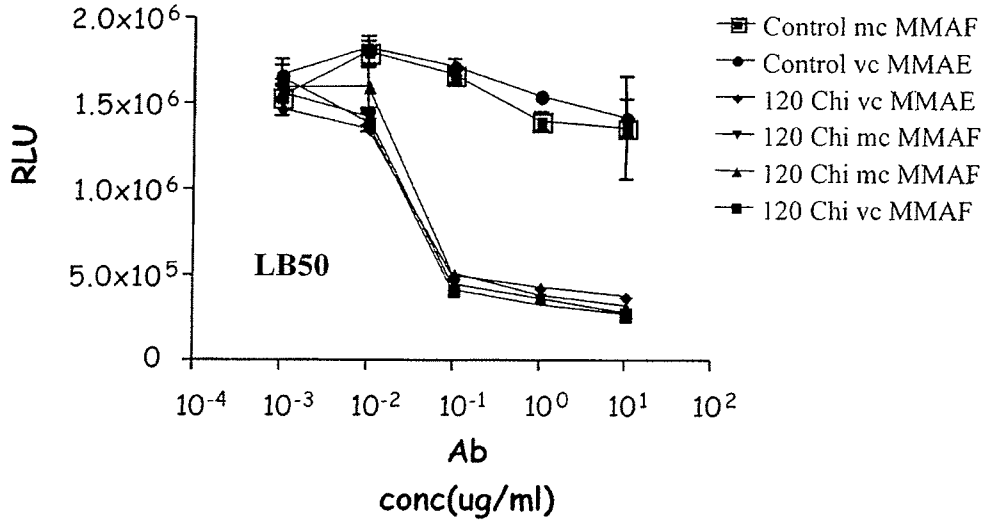


Figure 14C

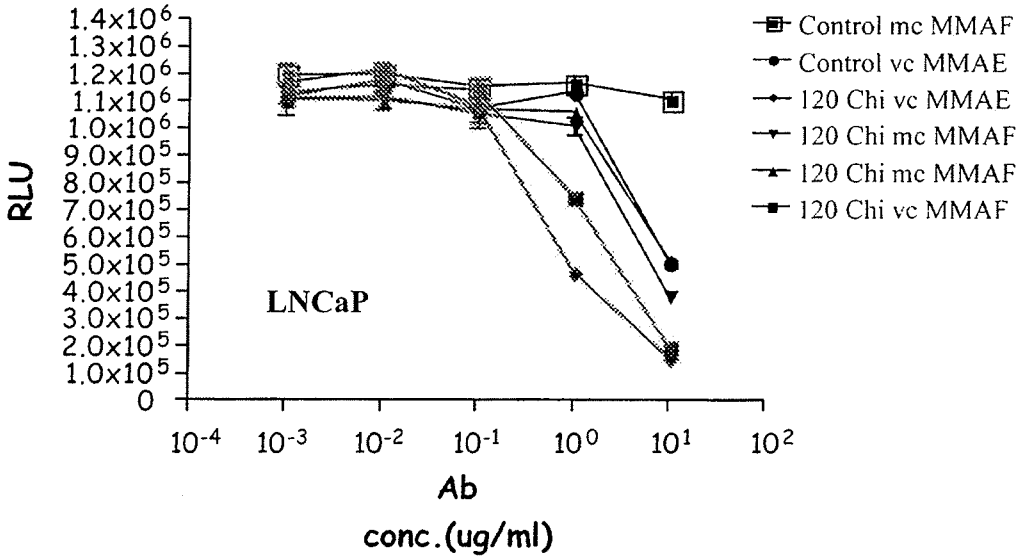


Figure 14D

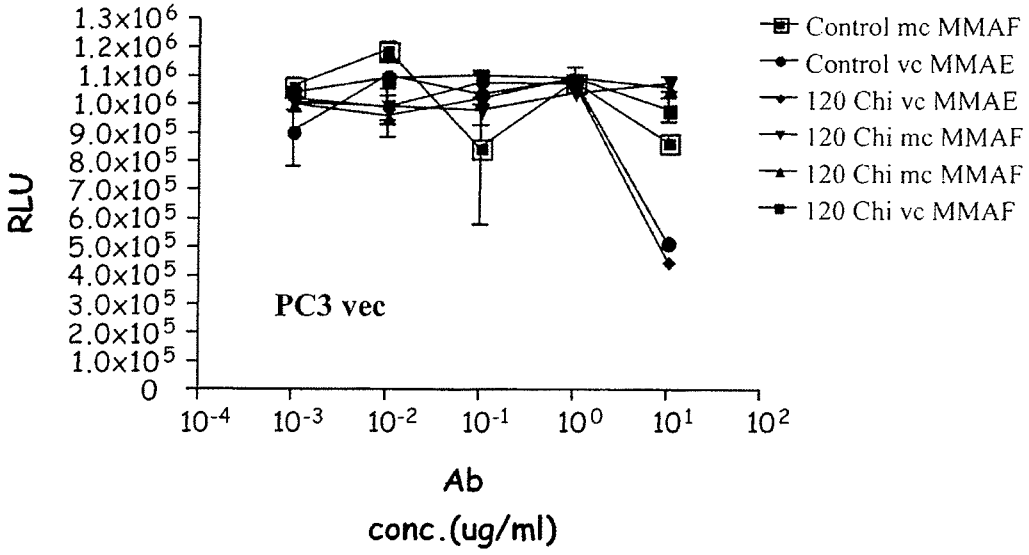


Figure 14E

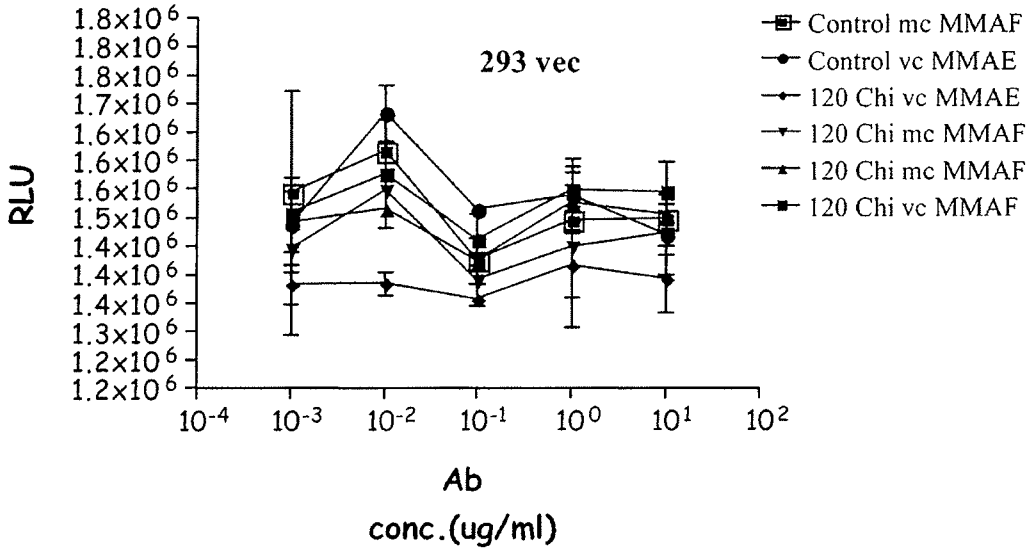

293 vec
RLU
1.8x10^6
1.8x10^6
1.8x10^6
1.7x10^6
1.6x10^6
1.6x10^6
1.6x10^6
1.5x10^6
1.4x10^6
1.4x10^6
1.4x10^6
1.3x10^6
1.2x10^6
1.2x10^6
10^-4
10^-3
10^-2
10^-1
10^0
10^1
10^2
Ab
conc.(ug/ml)
Control mc MMAF
Control vc MMAE
120 Chi vc MMAE
120 Chi mc MMAF
120 Chi mc MMAF
120 Chi vc MMAF

Figure 15

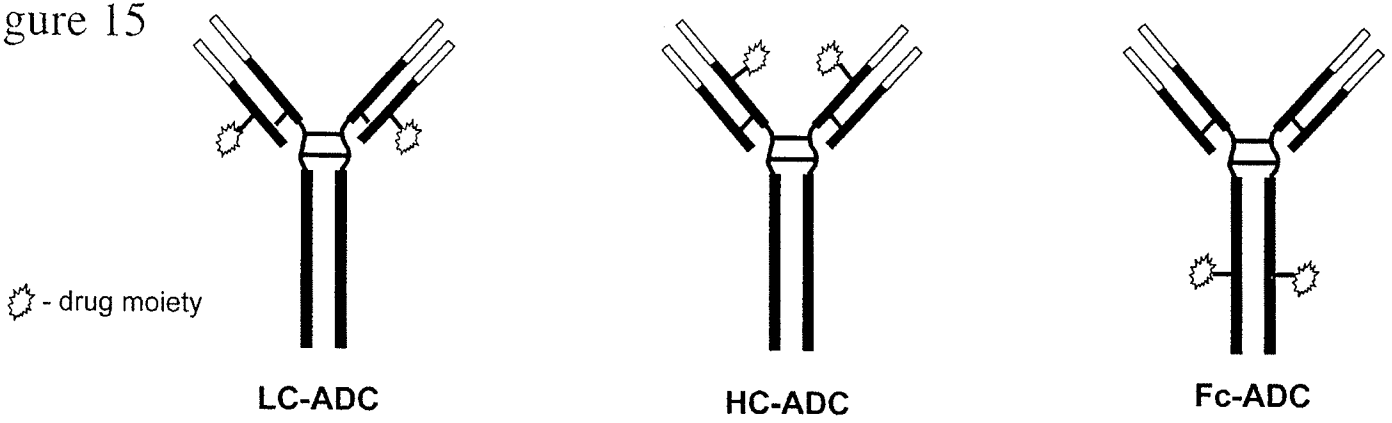
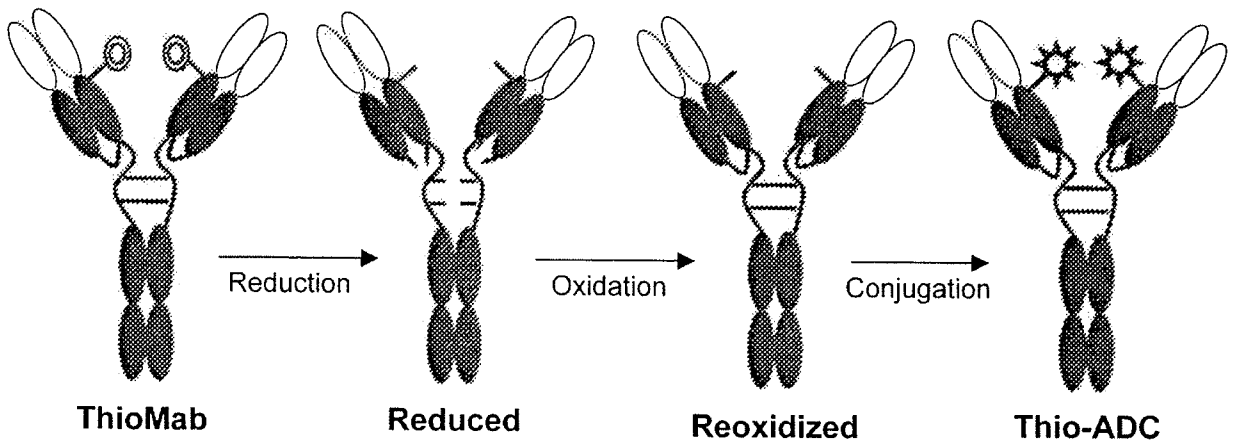


Figure 16



Thio-LC Variant (V205C) with corresponding sequential numbering

Standardized numbering >> **LC-V205C (Kabat numbering)**

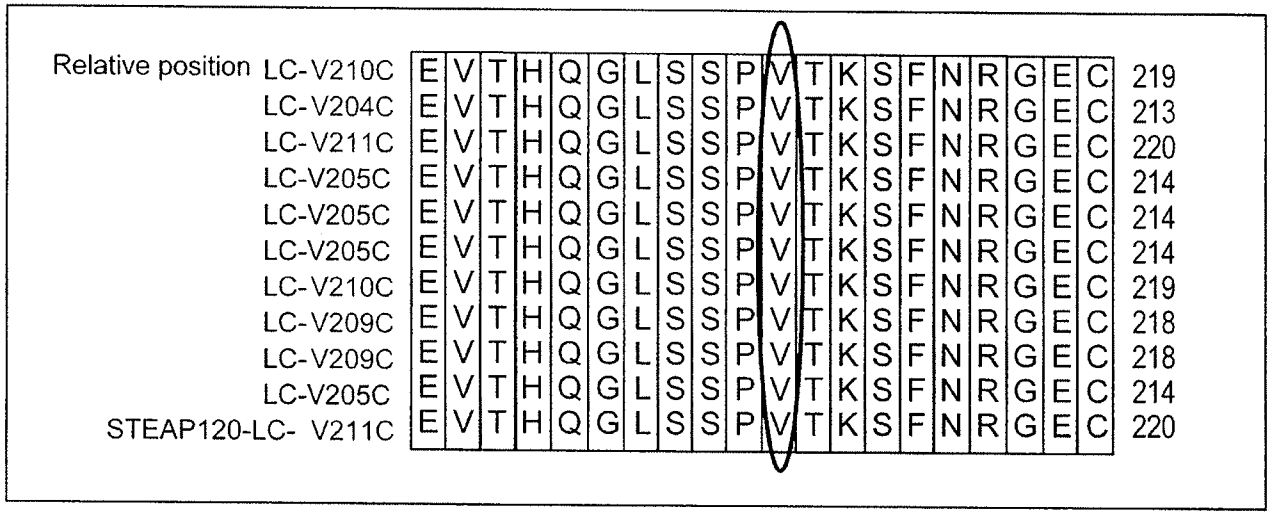


Figure 17A

Thio-HC Variant (A121C) with corresponding sequential numbering

Standardized numbering >> **HC-A118C (EU Numbering)**

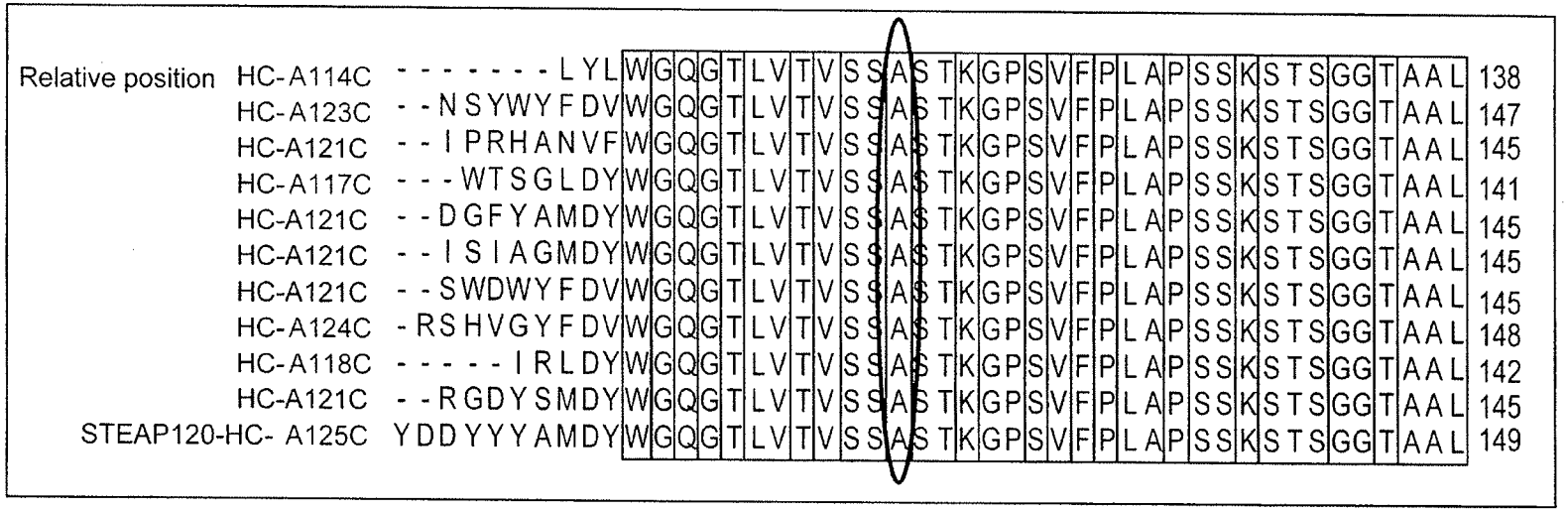


Figure 17B

Thio-Fc Variant (S400C) with corresponding sequential numbering

Standardized numbering >> **Fc-S400C (EU Numbering)**

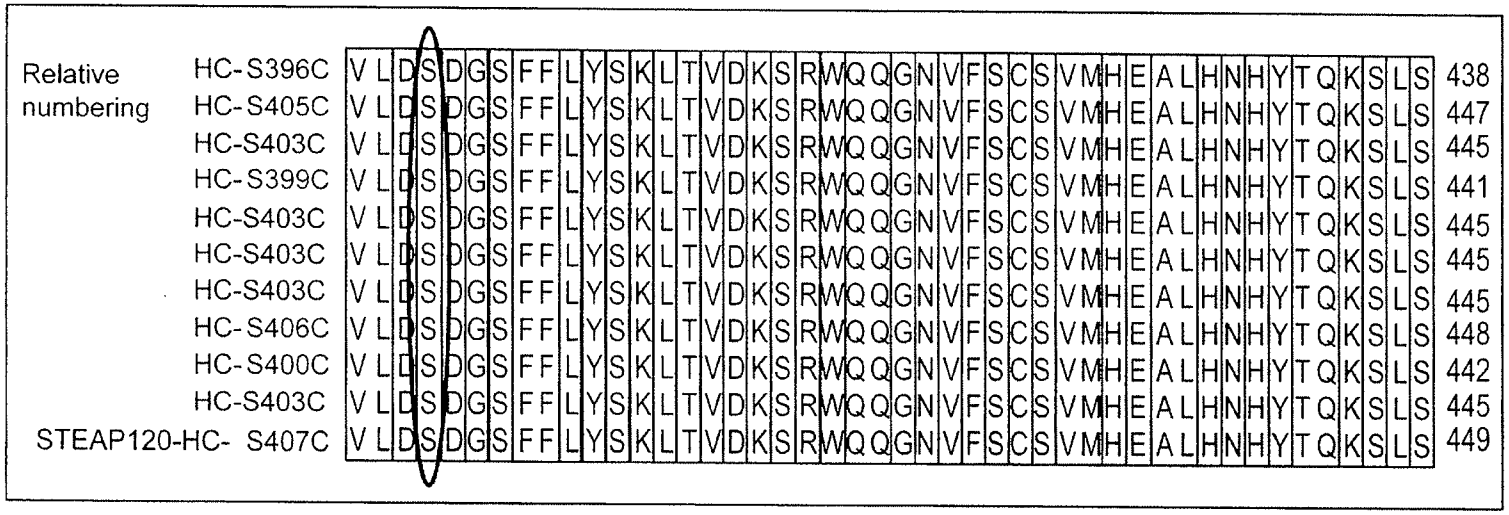


Figure 17C

Figure 18A

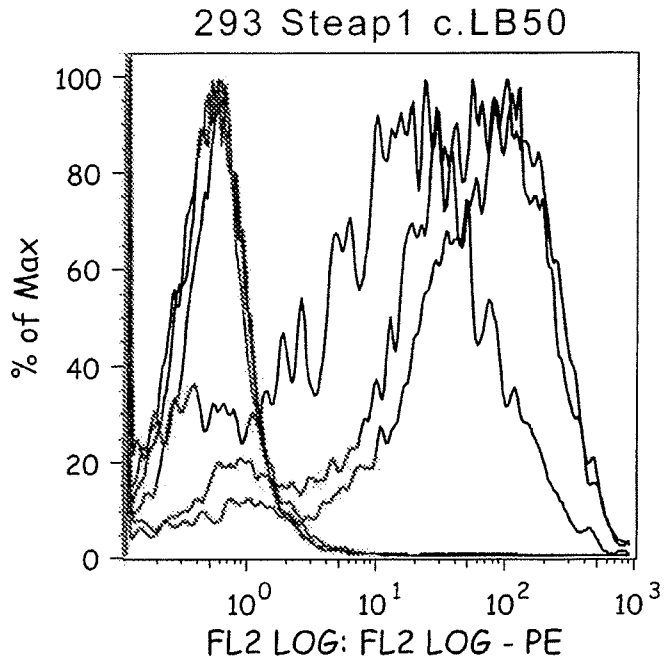


Figure 18D

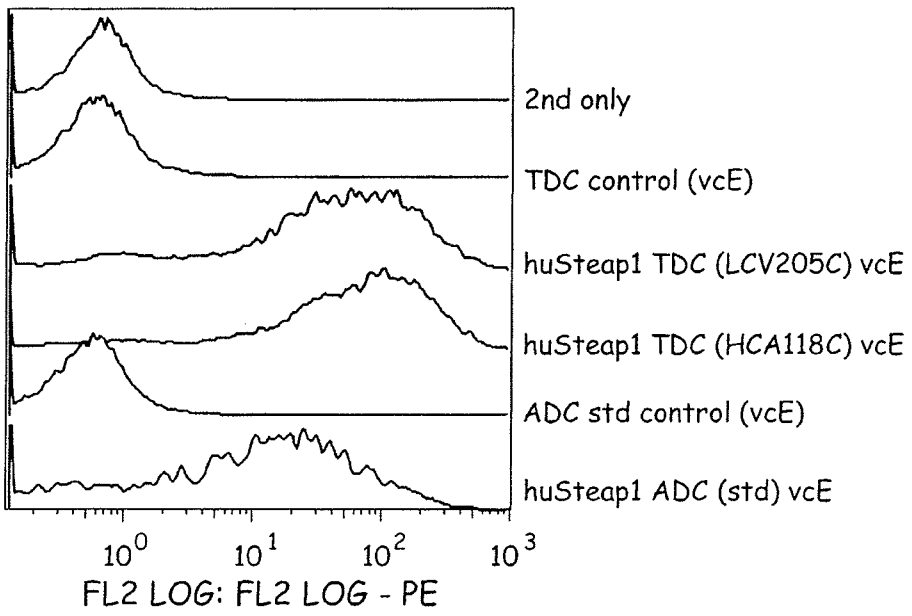


Figure 18B

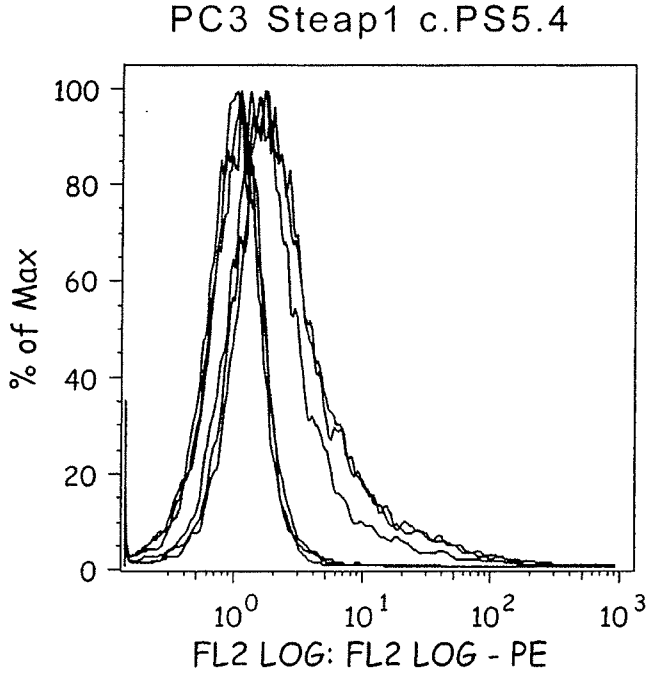


Figure 18E

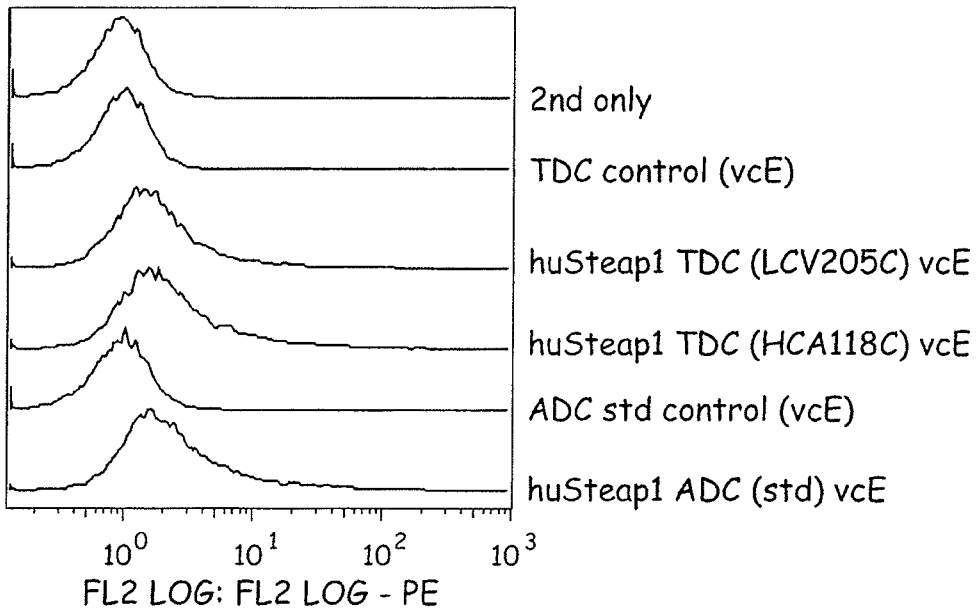


Figure 18C

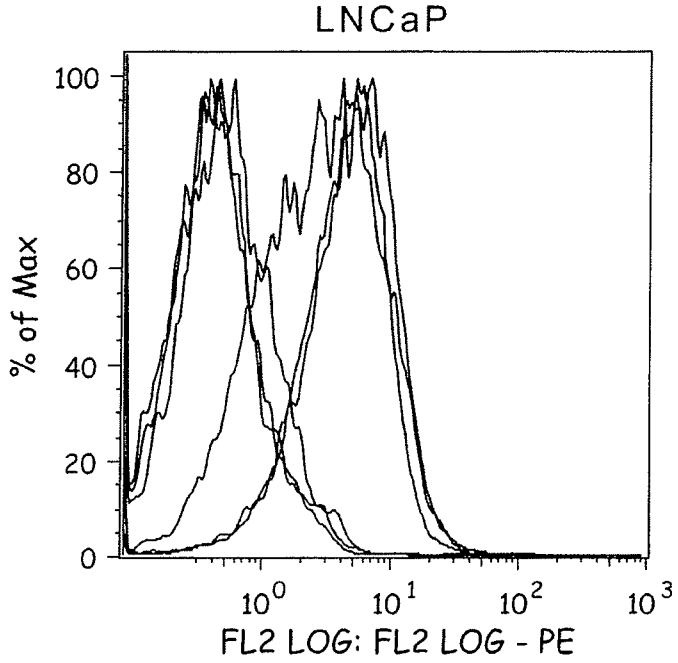


Figure 18F

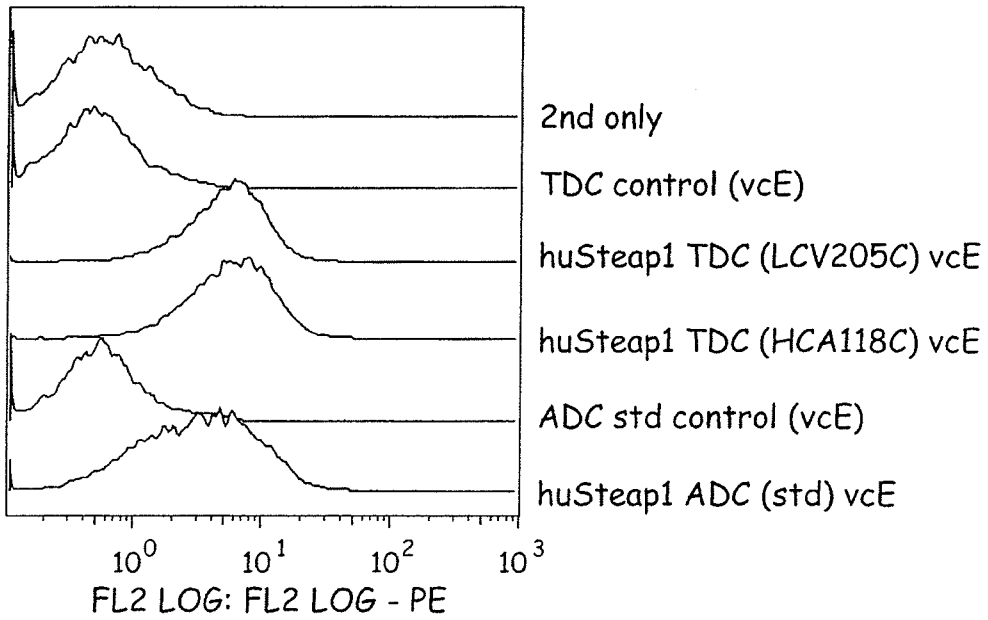


Figure 19A

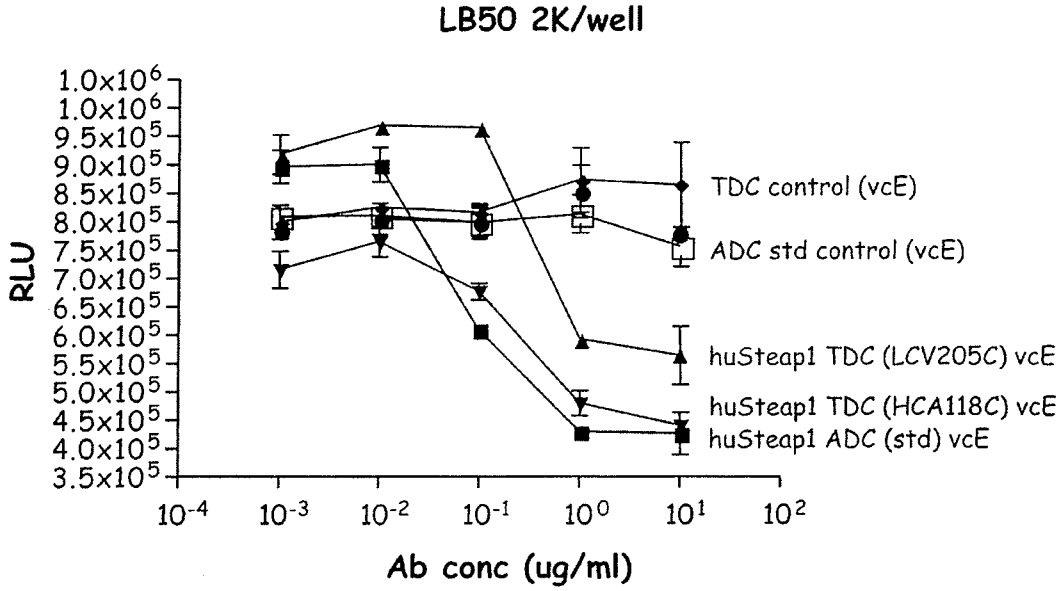


Figure 19B

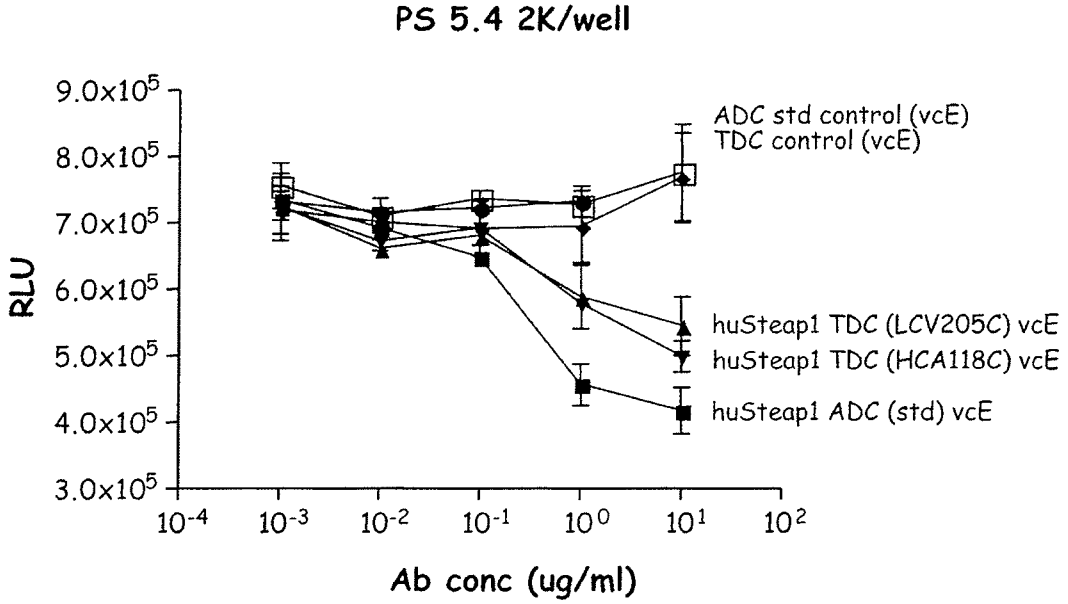
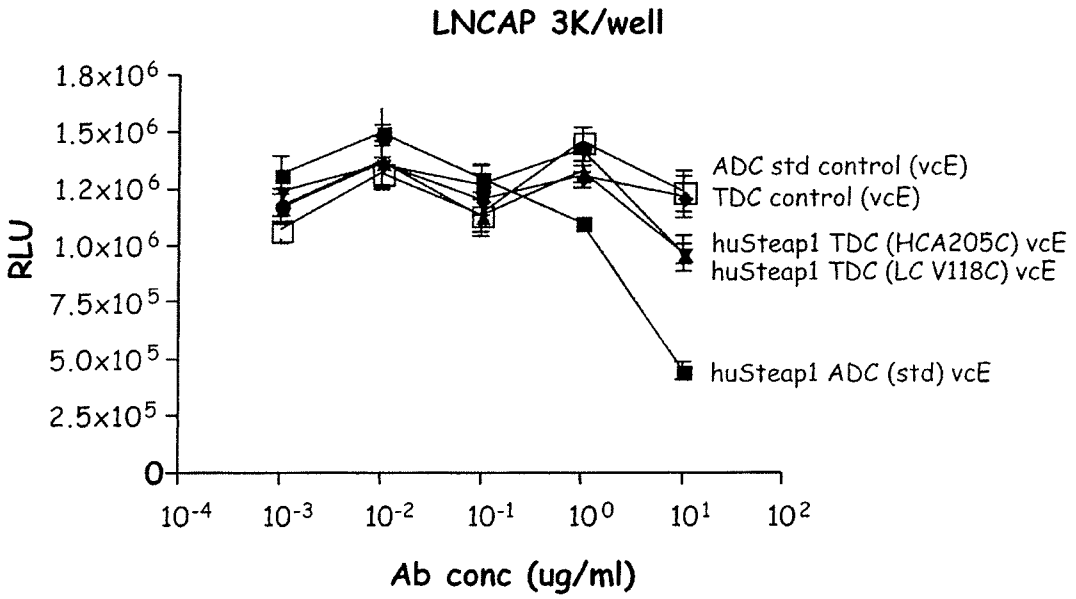


Figure 19C


LNCAP 3K/well
1.8x10^6
1.5x10^6
1.2x10^6
1.0x10^6
7.5x10^5
5.0x10^5
2.5x10^5
0
RLU
10^-4
10^-3
10^-2
10^-1
10^0
10^1
10^2
Ab conc (ug/ml)
ADC std control (vcE)
TDC control (vcE)
huSteap1 TDC (HCA205C) vcE
huSteap1 TDC (LC V118C) vcE
huSteap1 ADC (std) vcE

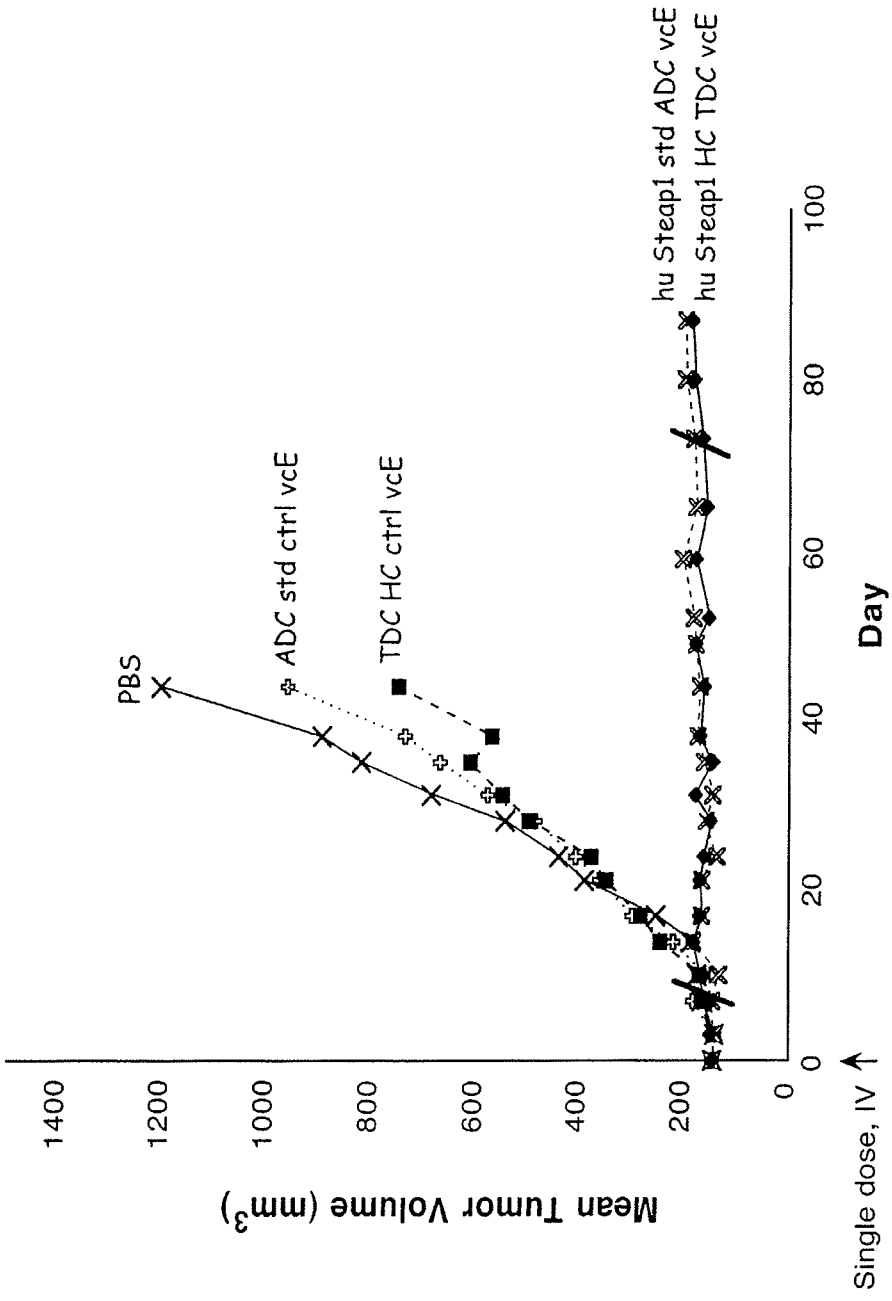

Mean Tumor Volume (mm3)
1400
1200
1000
800
600
400
200
0
0
20
40
60
80
100
Day
Single dose, IV
PBS
ADC std ctrl vcE
TDC HC ctrl vcE
hu Steap1 std ADC vcE
hu Steap1 HC TDC vcE

Figure 20

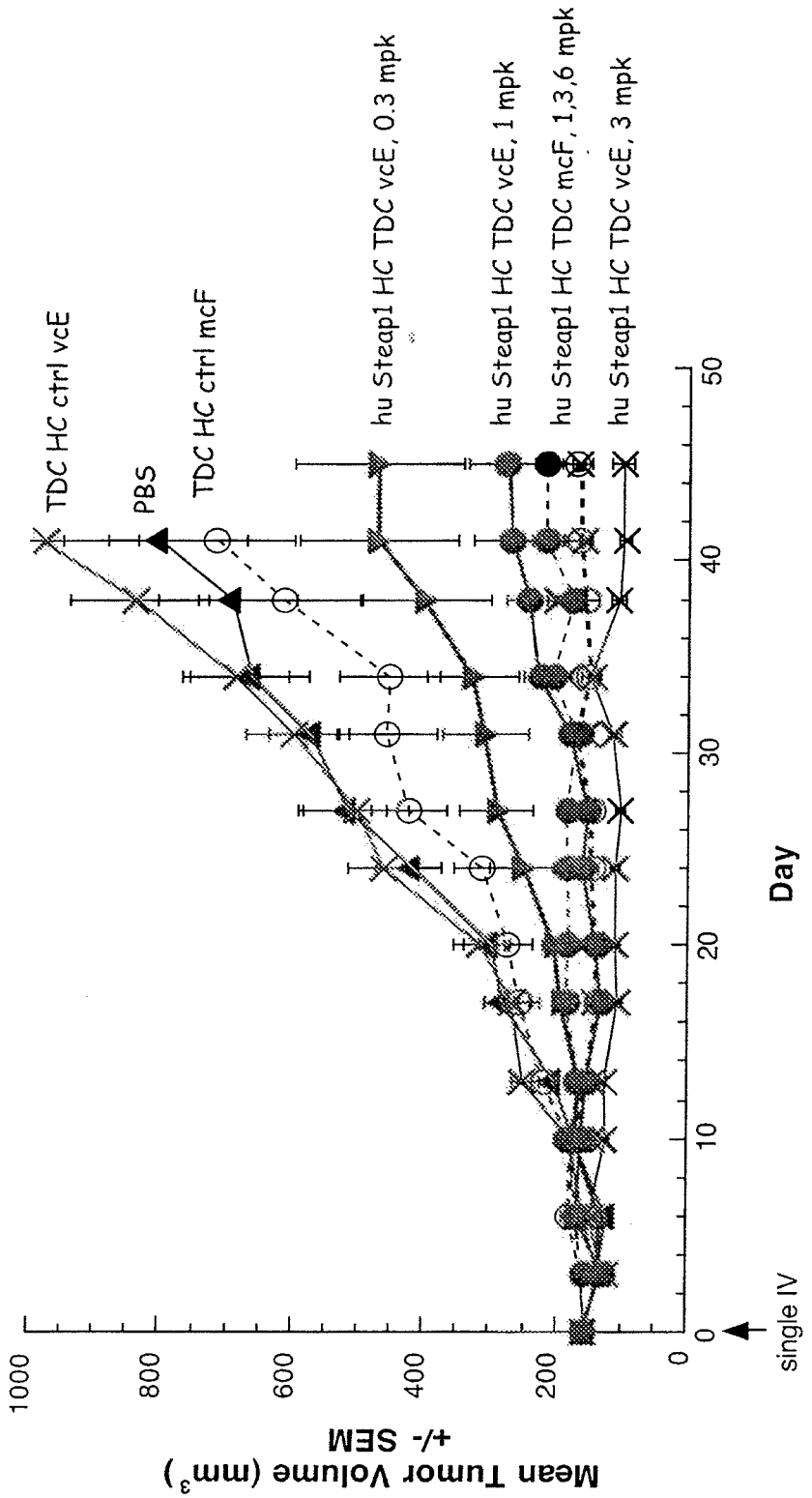

TDC HC ctrl vcE
PBS
TDC HC ctrl mcF
hu Steap1 HC TDC vcE, 0.3 mpk
hu Steap1 HC TDC vcE, 1 mpk
hu Steap1 HC TDC mcF, 1,3,6 mpk
hu Steap1 HC TDC vcE, 3 mpk
Mean Tumor Volume (mm³)
+/- SEM
1000
800
600
400
200
0
0
10
20
30
40
50
Day
single IV

Figure 21

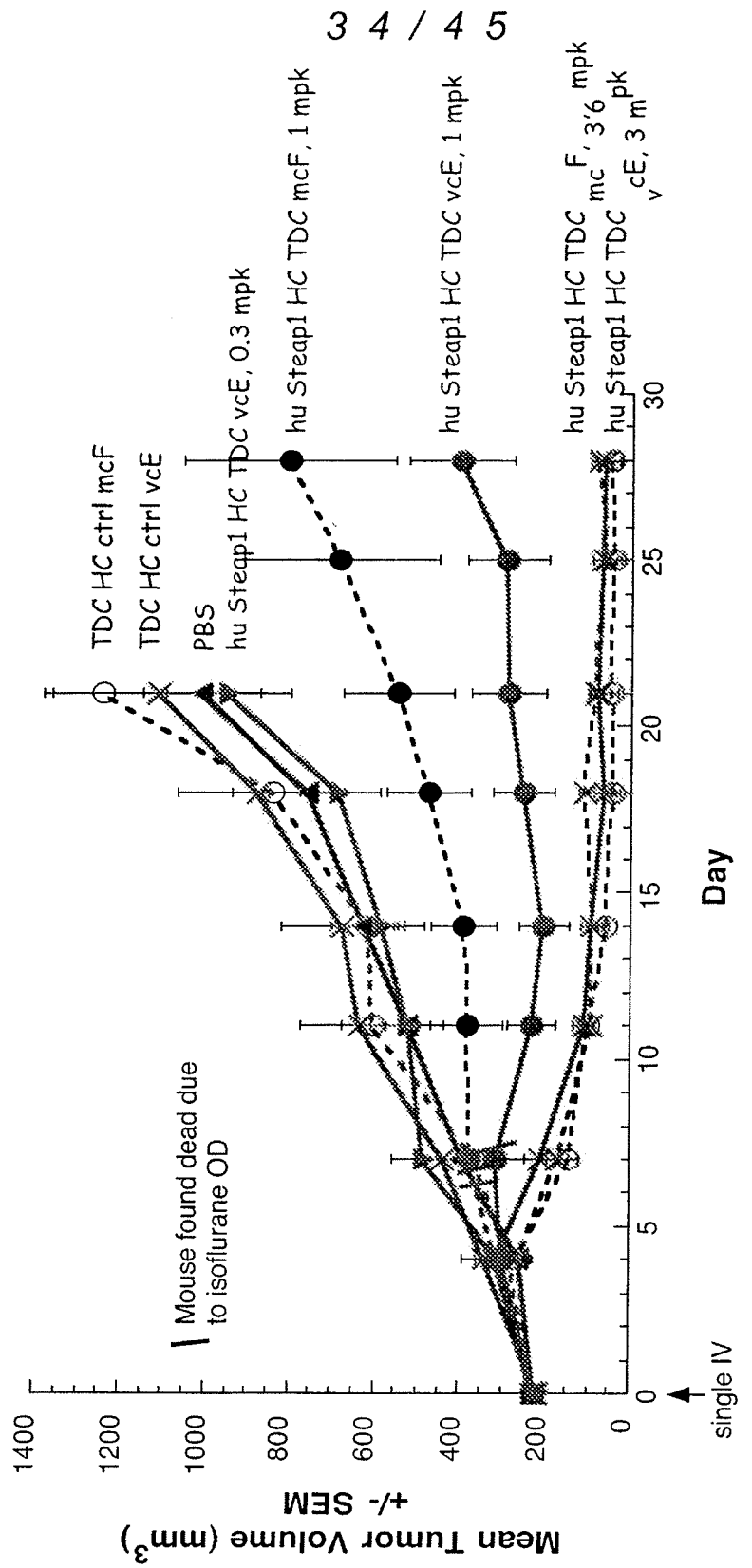

Mean Tumor Volume (mm3)
+/- SEM
Day
single IV
TDC HC ctrl mcF
TDC HC ctrl vcE
PBS
hu Steap1 HC TDC vcE, 0.3 mpk
hu Steap1 HC TDC mcF, 1 mpk
hu Steap1 HC TDC vcE, 1 mpk
hu Steap1 HC TDC mcF, 3'6 mpk
hu Steap1 HC TDC vcE, 3 mpk
Mouse found dead due to isoflurane OD

Figure 22

120 VL Differences - Kappa I vs IV

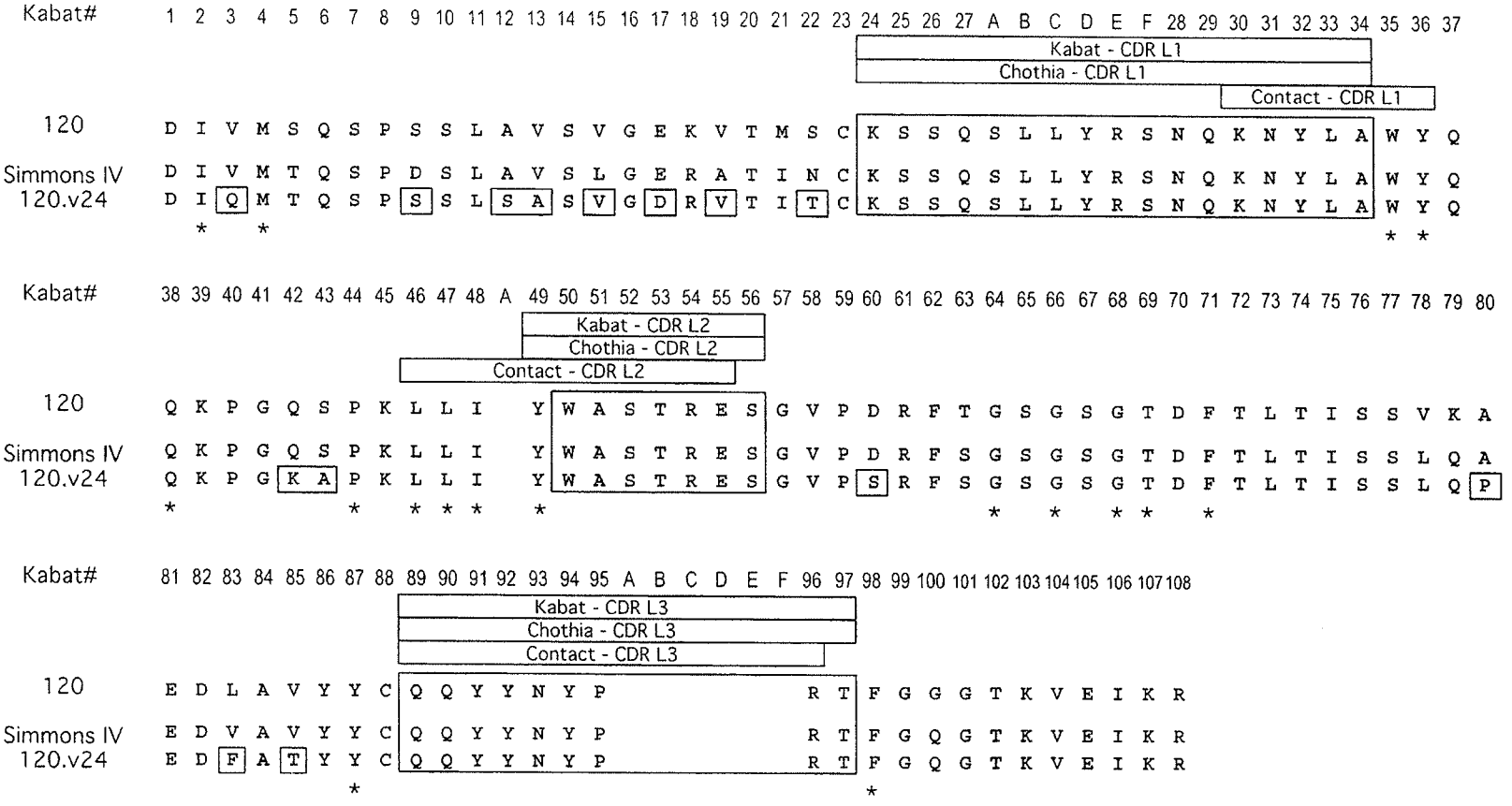


Figure 23 (PART 1)

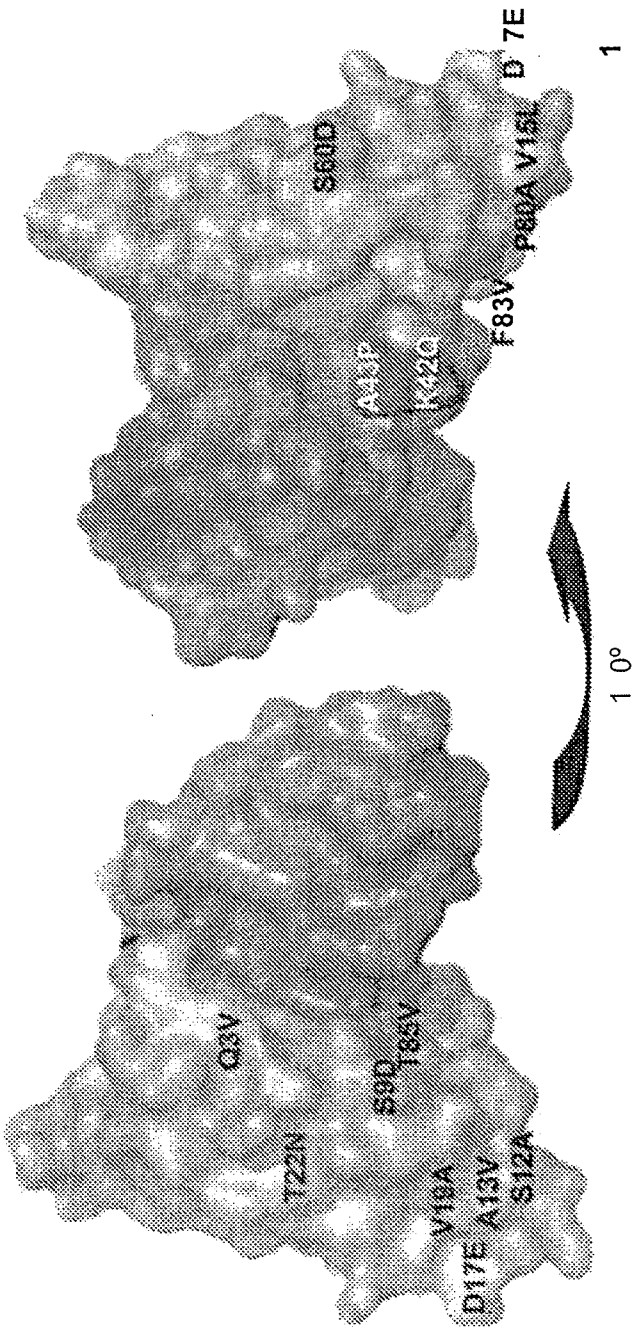


Figure 23 (PART 2)

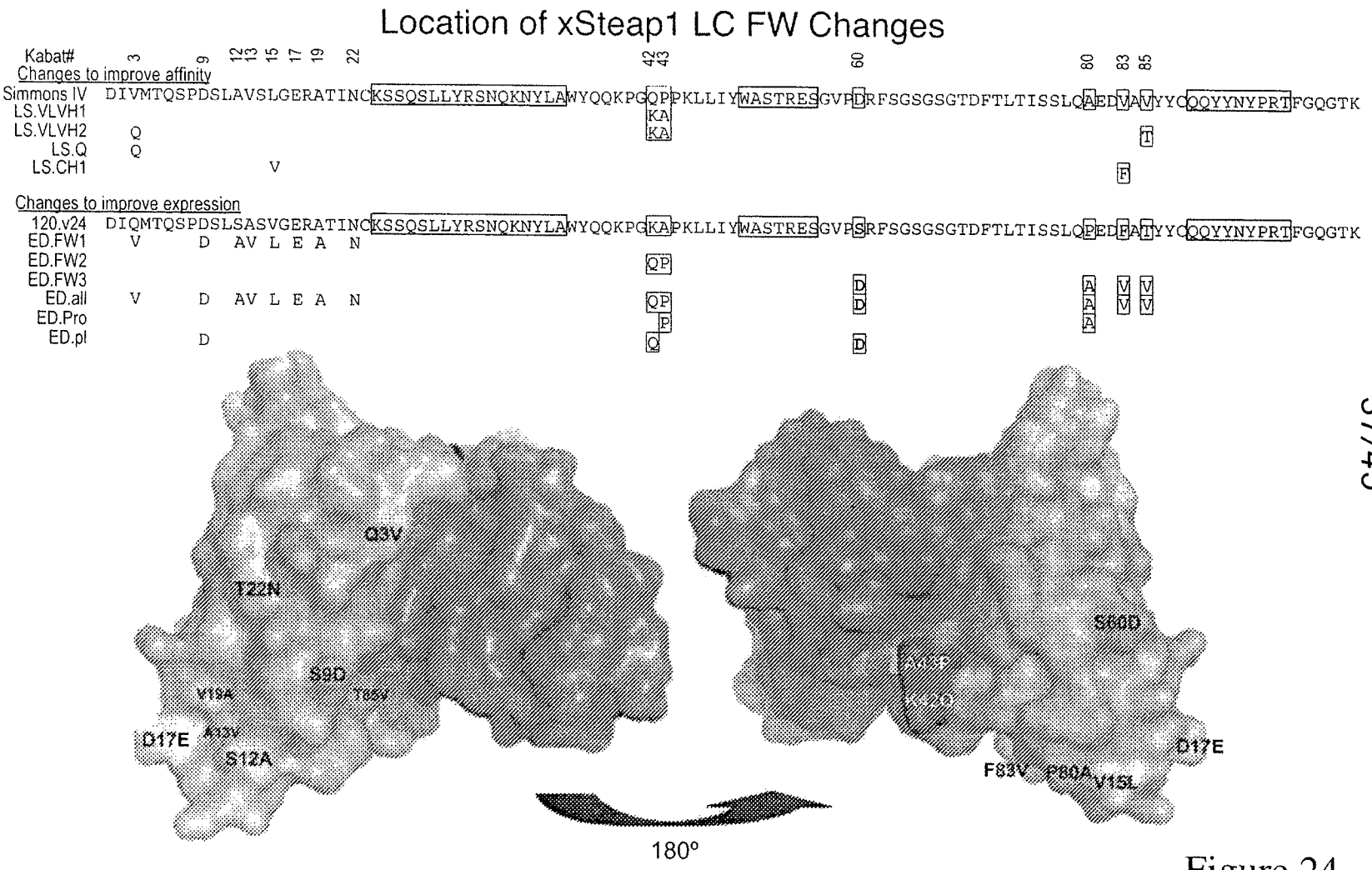

Location of xSteap1 LC FW Changes
Kabat#
Changes to improve affinity
Simmons IV DIVMTQSPDSLAVSLGERATINCKSSQSLLYRSNQKNYLAWYQQKPGQPPKLLIYWASTRESGVPDRFSGSGSGTDFTLTISSLQAEDVAVYYCQQYYNYPRTFGQGTK
LS.VLVH1
LS.VLVH2
LS.Q
LS.CH1
Changes to improve expression
120.v24 DIQMTQSPDSLSASVGERATINCKSSQSLLYRSNQKNYLAWYQQKPGKAPKLLIYWASTRESGVPSRFSGSGSGTDFTLTISSLQPEDFATYYCQQYYNYPRTFGQGTK
ED.FW1
ED.FW2
ED.FW3
ED.all
ED.Pro
ED.pl
Q3V
T22N
S9D
V19A
T65V
A43V
D17E
S12A
S60D
F83V
F80A
V15L
D17E
180°

Figure 24

Original Thio
120V24

Assay 739:
LNCaP.BR cells
KD= 1.1 nM

Figure 25A

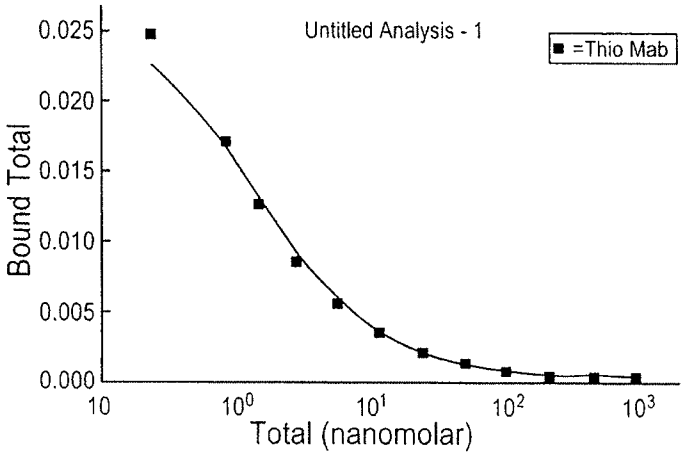
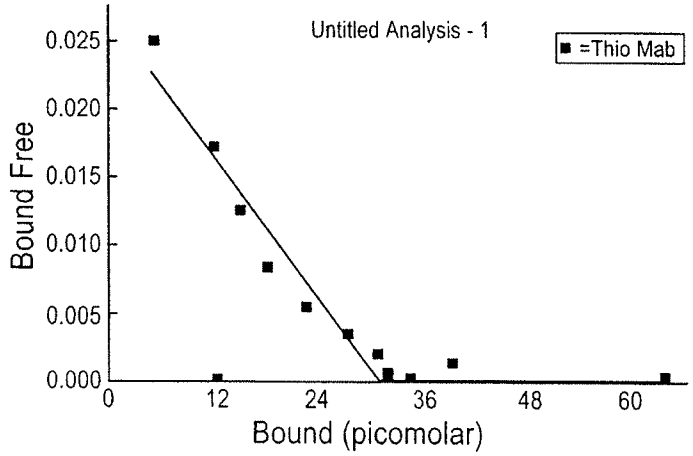


Figure 25B



Assay 740:
LNCaP.BR cells
KD= 1.7 nM

Figure 25C

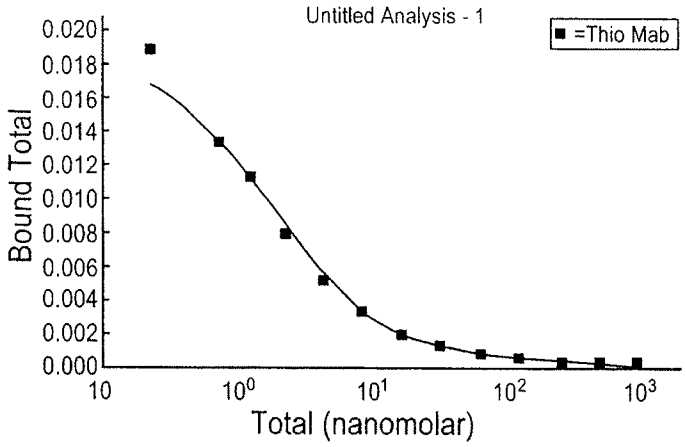


Figure 25D

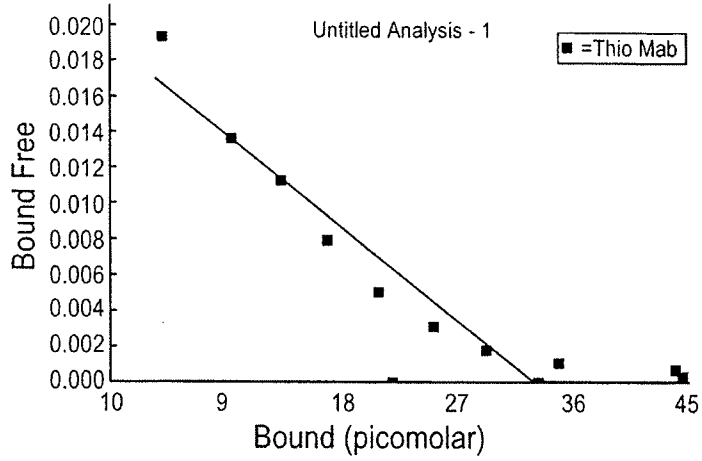


Figure 25E

120V24
Thio SGIV

Assay 733:
LNCaP.BR cells
KD= 2.3 nM

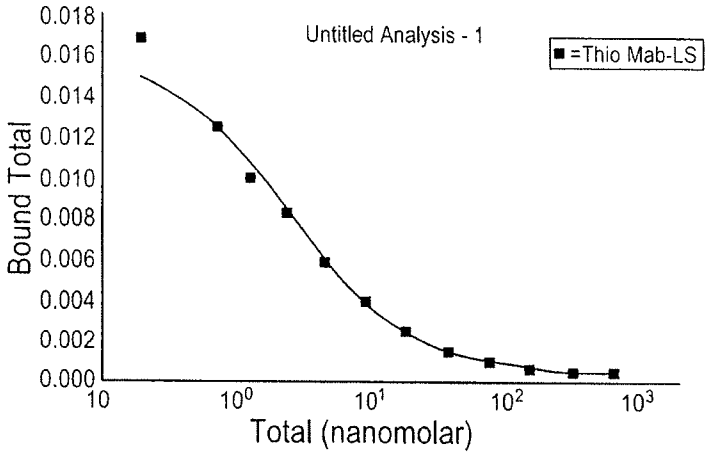


Figure 25F

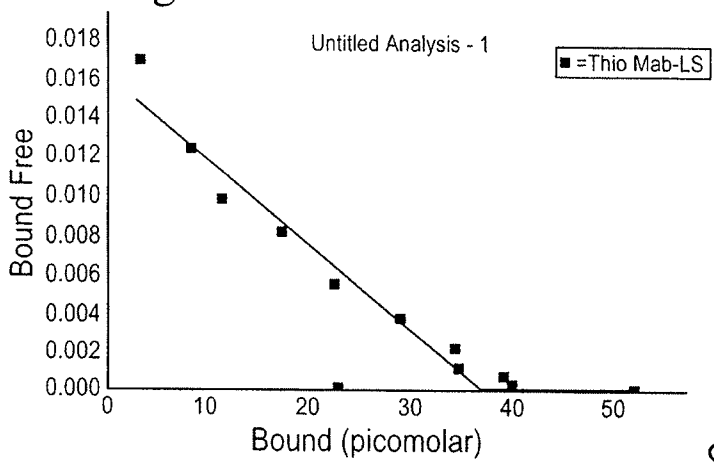


Figure 25G

Assay 734:
LNCaP.BR cells
KD= 1.9 nM

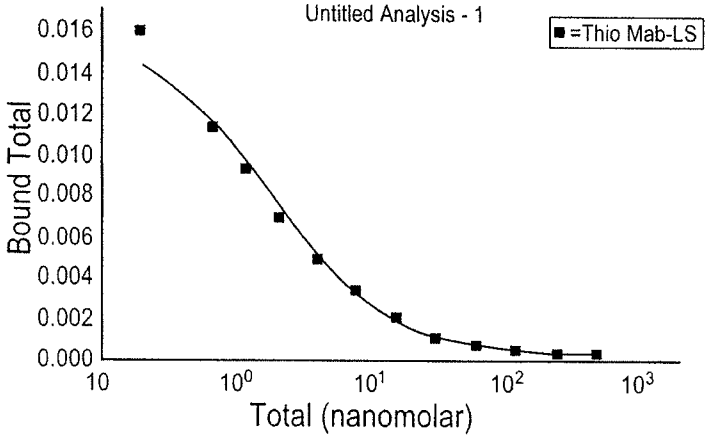


Figure 25H

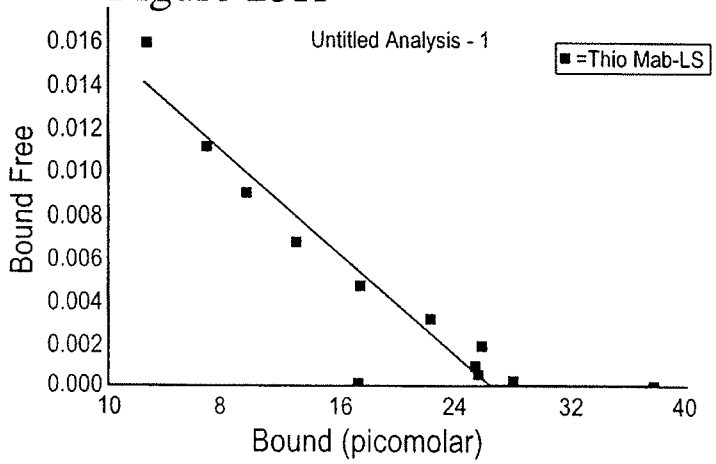


Figure 26A

Original Thio
120V24

Assay 737:
293.LB50 cells
KD= 1.7 nM

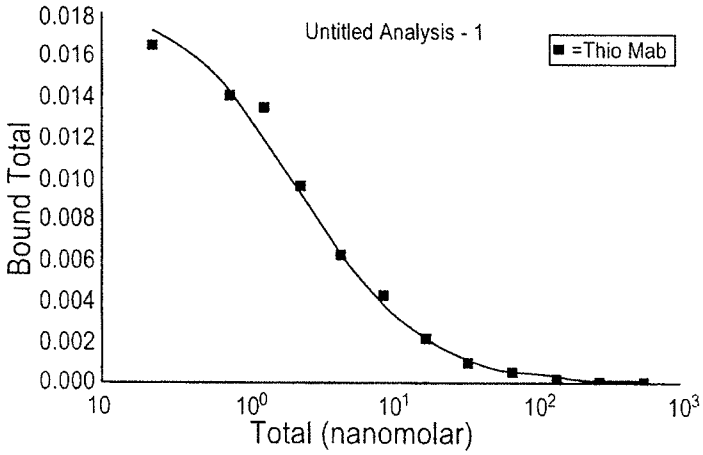


Figure 26B

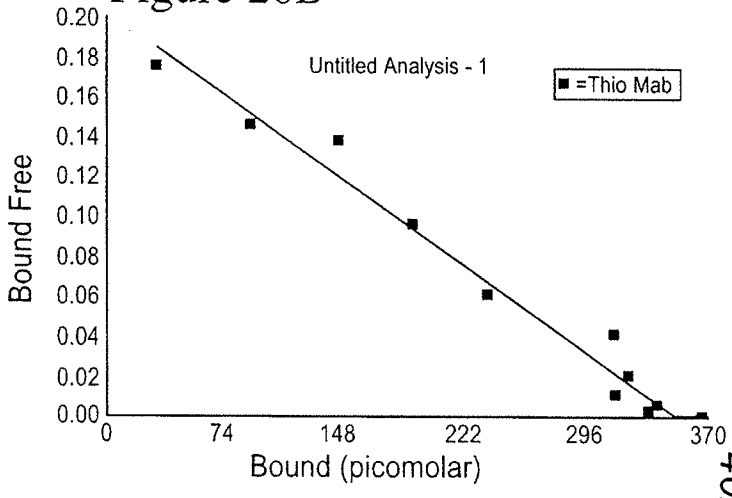


Figure 26C

Assay 738:
293.LB50 cells
KD= 2.0 nM

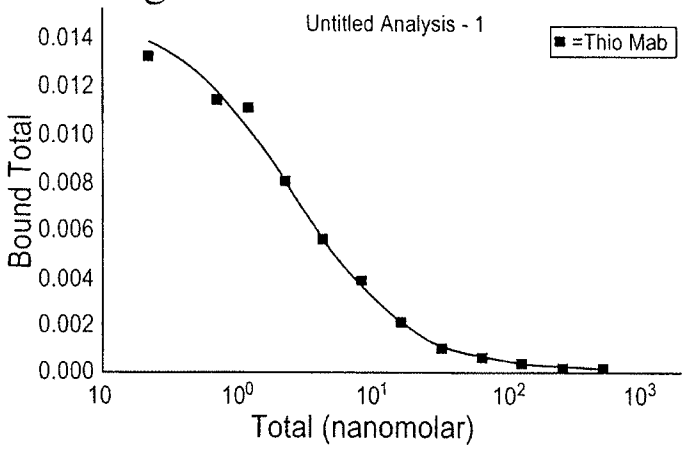


Figure 26D

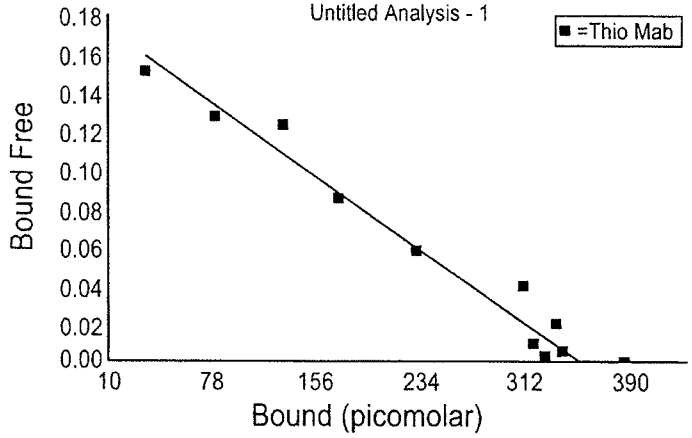


Figure 26E

120V24
Thio SGIV

Assay 735:
293.LB50 cells
KD= 2.7 nM

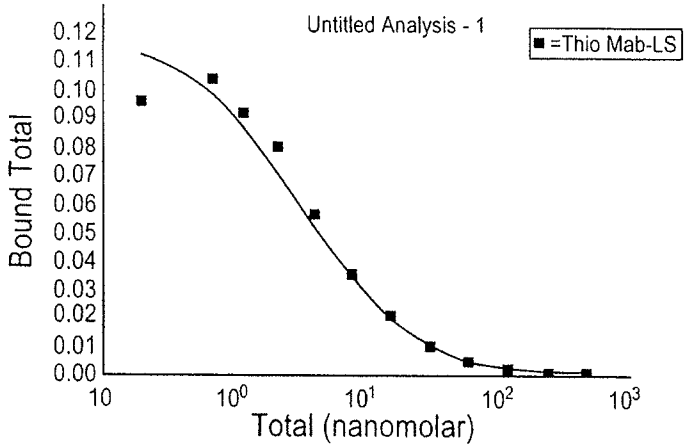


Figure 26F

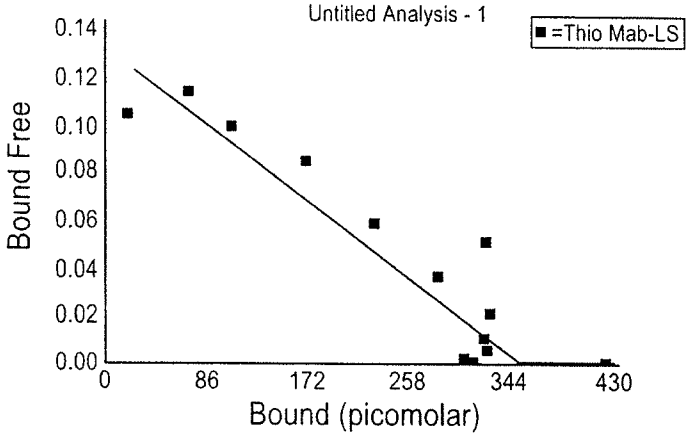


Figure 26G

Assay 736:
293.LB50 cells
KD= 2.8 nM

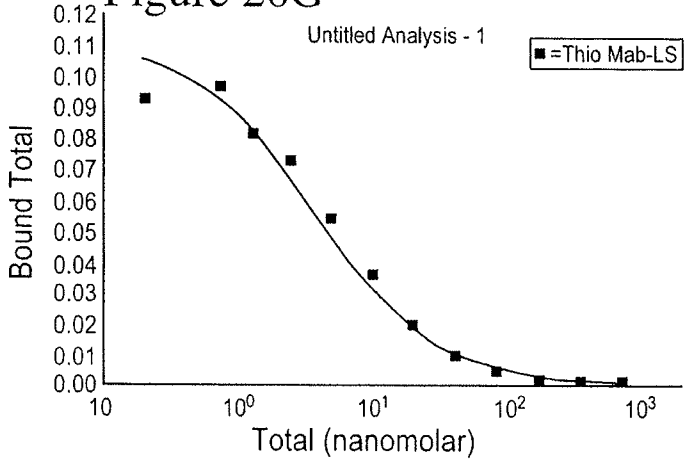
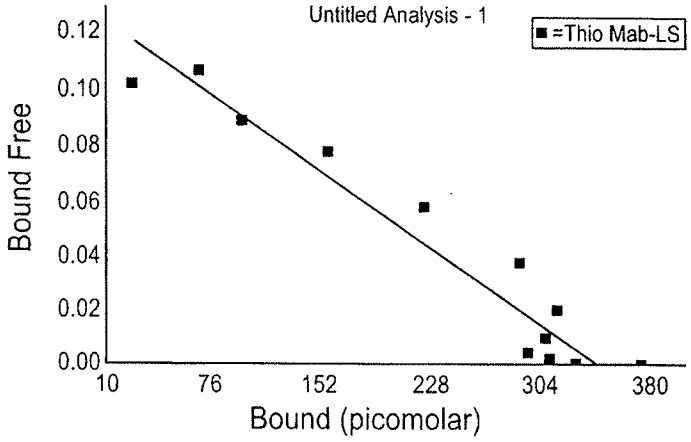


Figure 26H



Humanized Steap1 Antibody Scatchards

Scatchard Analysis

	murine α179	murine α120	Fc chimera PUR 10162)	human 120v24 PUR 11712)	orig thio PUR 12813)	thio SGIV PUR 14951)
PC3-PS5.4	~23.4 nM ~5,920	17.5 nM 187,256	9.9 nM 103,204		1.5X	
293-LB50	4.7 nM 25,368	4.7 nM 301,100	4.9 nM 252,892	2.2 nM 264,172	1.9 nM	2.8 nM
LNCaP-BR	3.3 nM 2,626	1.5 nM 37,207	0.9 nM 22,021		1.4 nM	2.1 nM

293-transient human Steap1	1.4 nM
293-transient cyno Steap1	1.1 nM

Same Affinity for human & cyno

Figure 27

Figure 28A

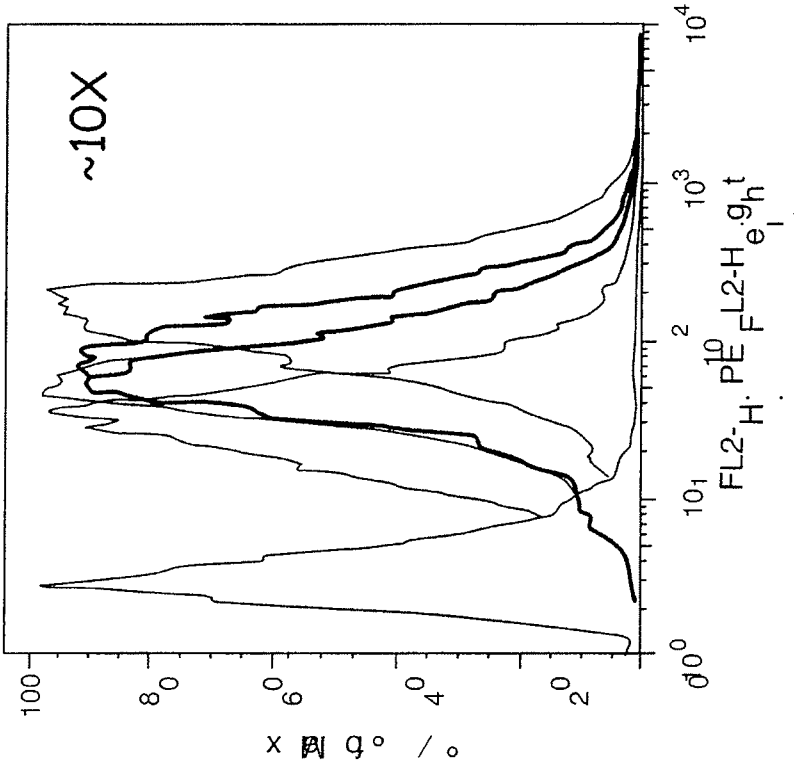


Figure 28B

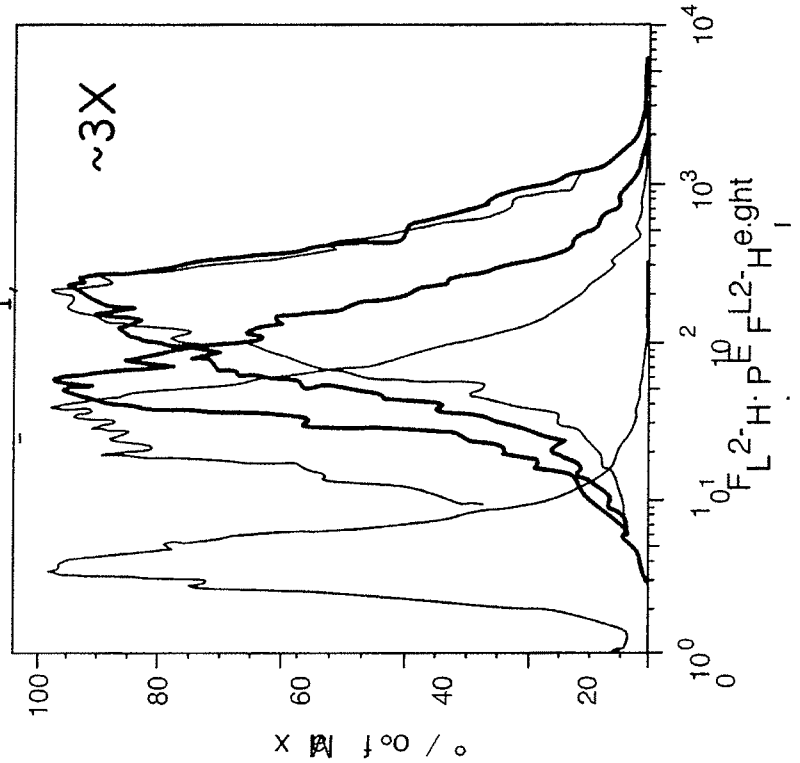


Figure 28C

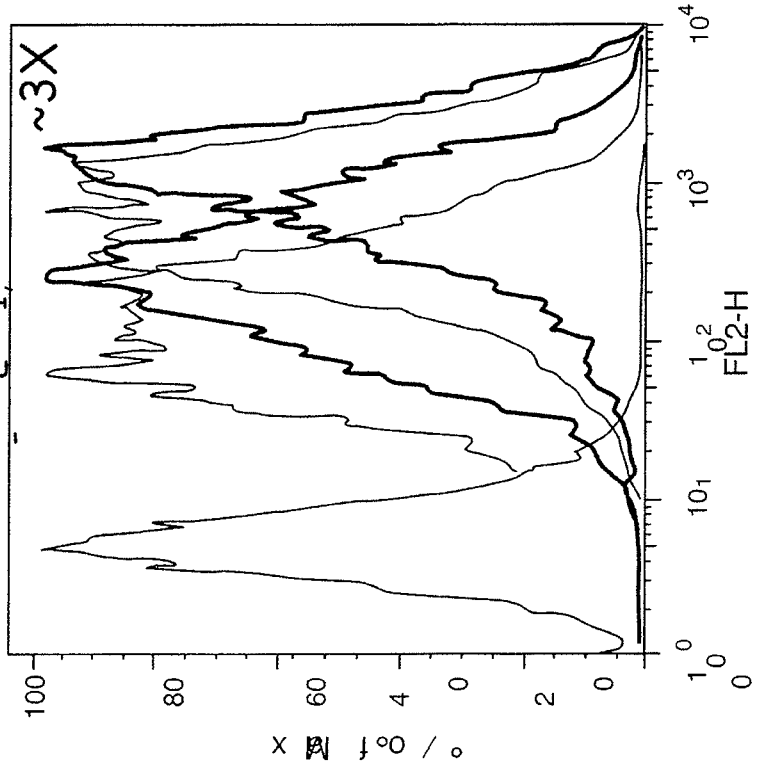
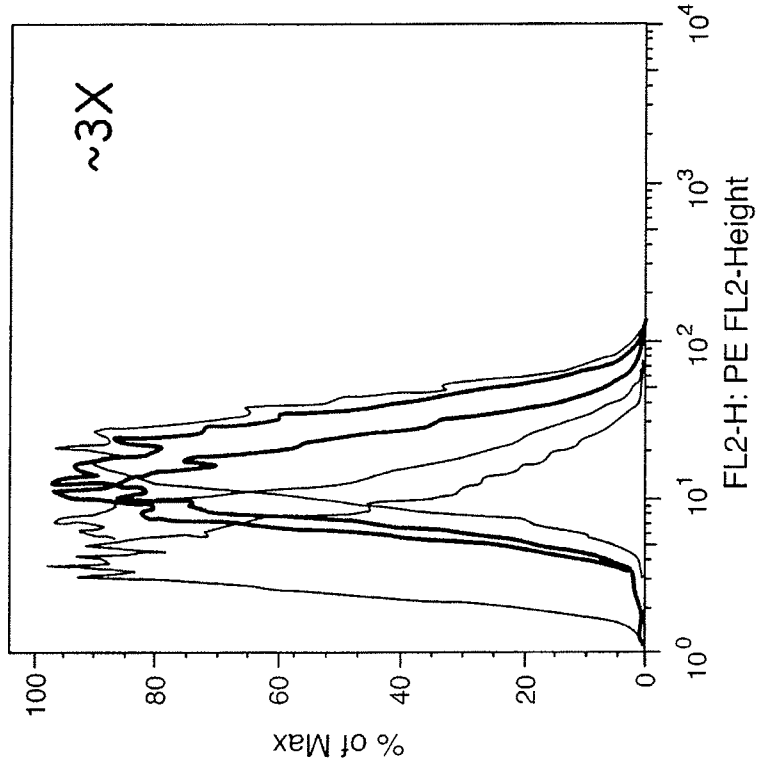


Figure 28D



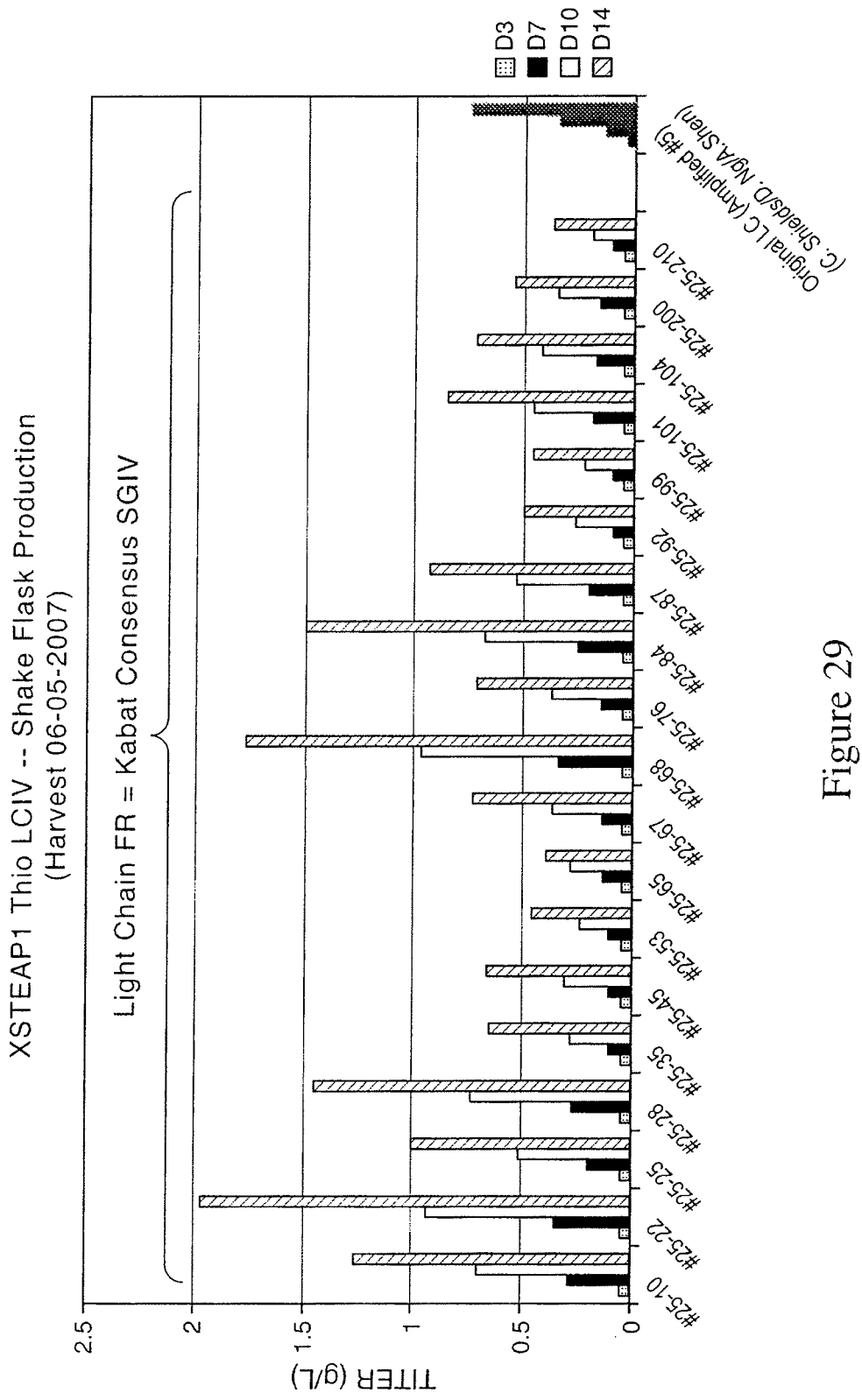

XSTEAP1 Thio LCIV -- Shake Flask Production
(Harvest 06-05-2007)
Light Chain FR = Kabat Consensus SGIV
TITER (g/L)
2.5
2
1.5
1
0.5
0
D3
D7
D10
D14
Original LC (Amplified #5)
(C. Shields/D. Ng/A.Shen)
#25-210
#25-200
#25-104
#25-101
#25-99
#25-92
#25-87
#25-84
#25-76
#25-68
#25-67
#25-65
#25-53
#25-45
#25-35
#25-28
#25-25
#25-22
#25-10

Figure 29