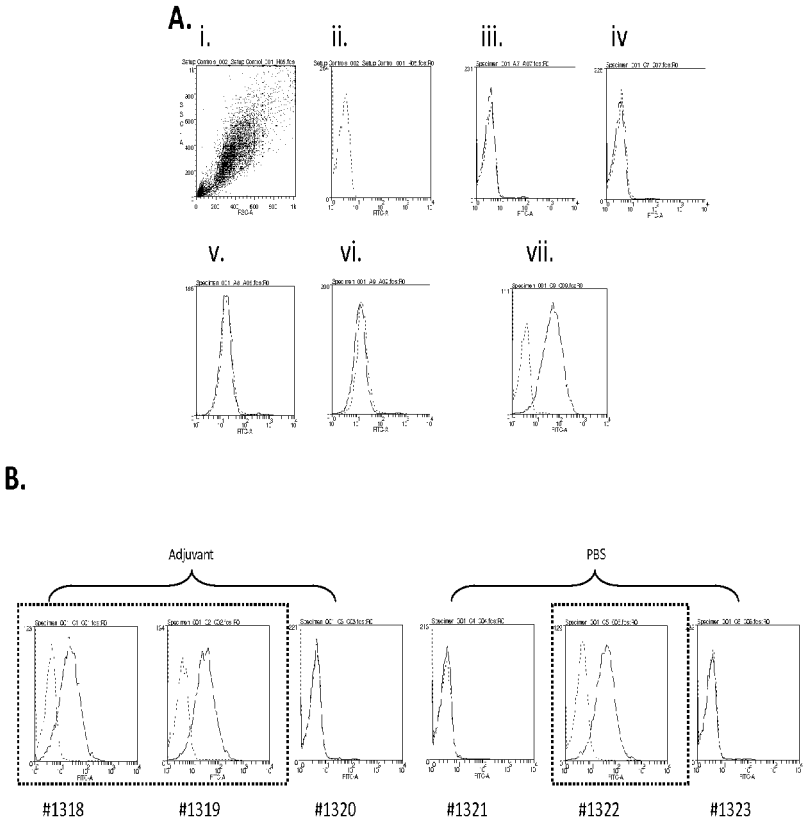

A.
i.
ii.
iii.
iv
v.
vi.
vii.
B.
Adjuvant
PBS
#1318
#1319
#1320
#1321
#1322
#1323

Figure 1

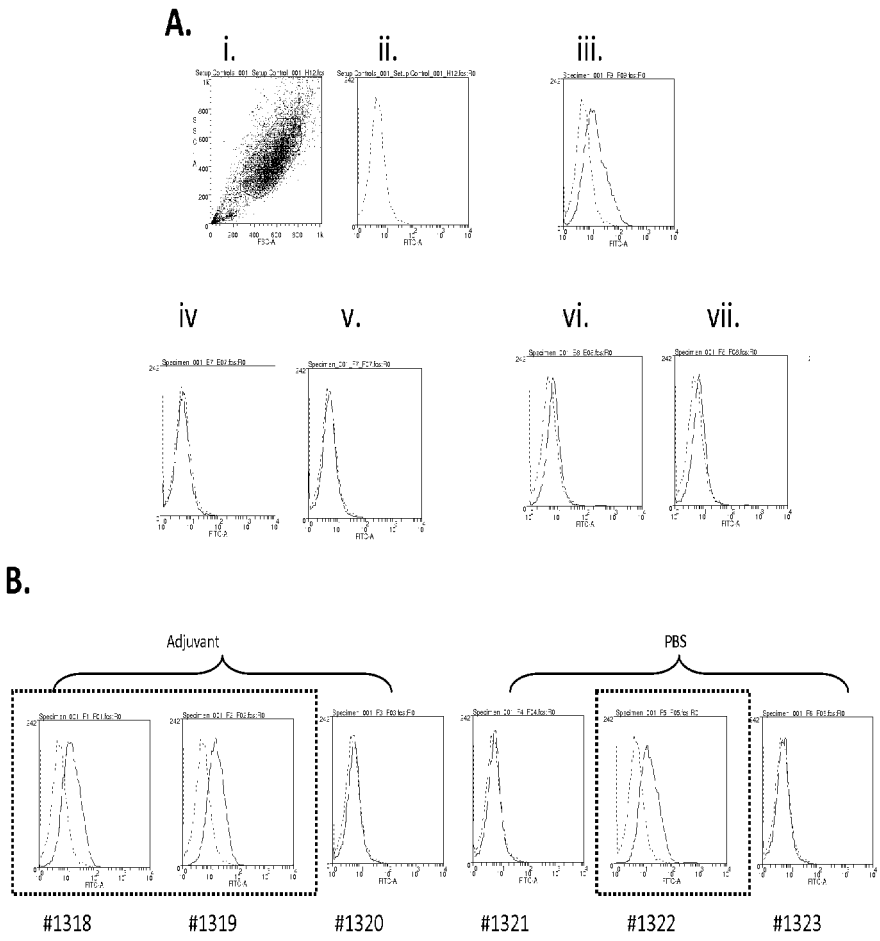

A.
i.
ii.
iii.
iv
v.
vi.
vii.
B.
Adjuvant
PBS
#1318
#1319
#1320
#1321
#1322
#1323

Figure 2

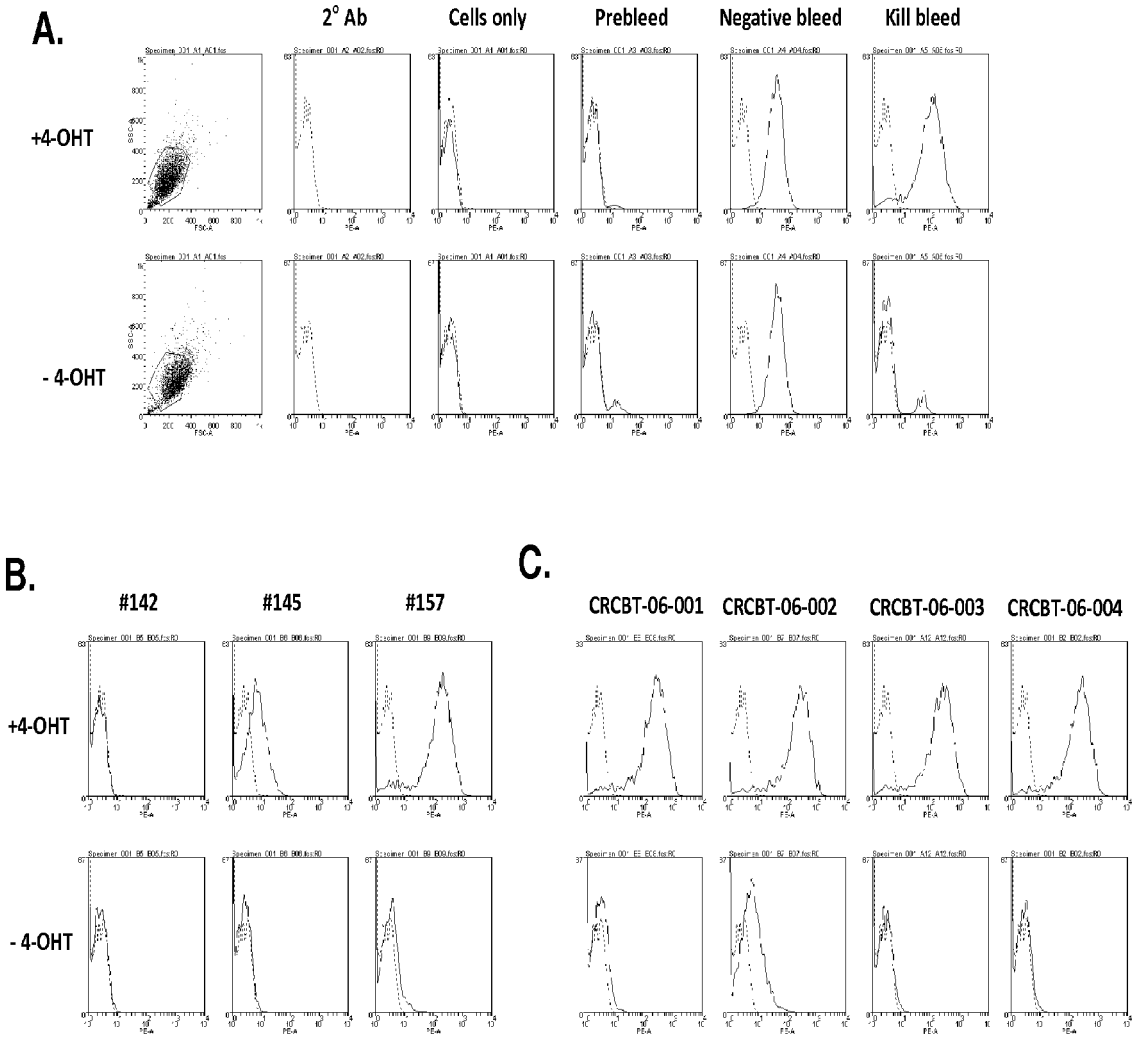

A.
2° Ab
Cells only
Prebleed
Negative bleed
Kill bleed
+4-OHT
- 4-OHT
B.
#142
#145
#157
+4-OHT
- 4-OHT
C.
CRCBT-06-001
CRCBT-06-002
CRCBT-06-003
CRCBT-06-004

Figure 3

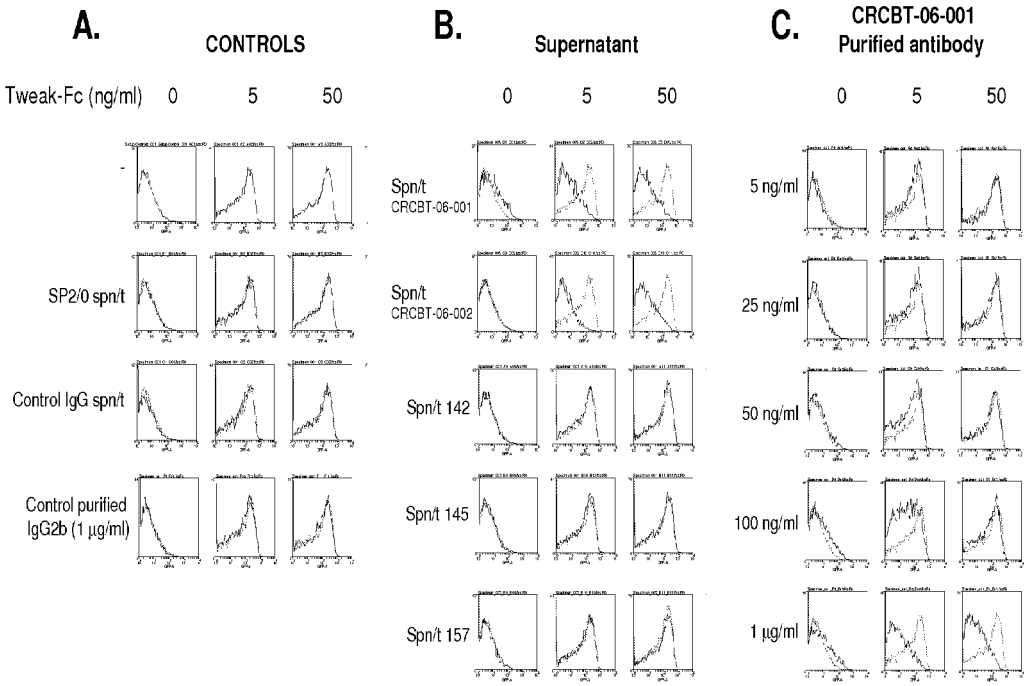

A.
CONTROLS
Tweak-Fc (ng/ml) 0 5 50
SP2/0 spn/t
Control IgG spn/t
Control purified IgG2b (1 µg/ml)
B.
Supernatant
0 5 50
Spn/t CRCBT-06-001
Spn/t CRCBT-06-002
Spn/t 142
Spn/t 145
Spn/t 157
C.
CRCBT-06-001 Purified antibody
0 5 50
5 ng/ml
25 ng/ml
50 ng/ml
100 ng/ml
1 µg/ml

Figure 4

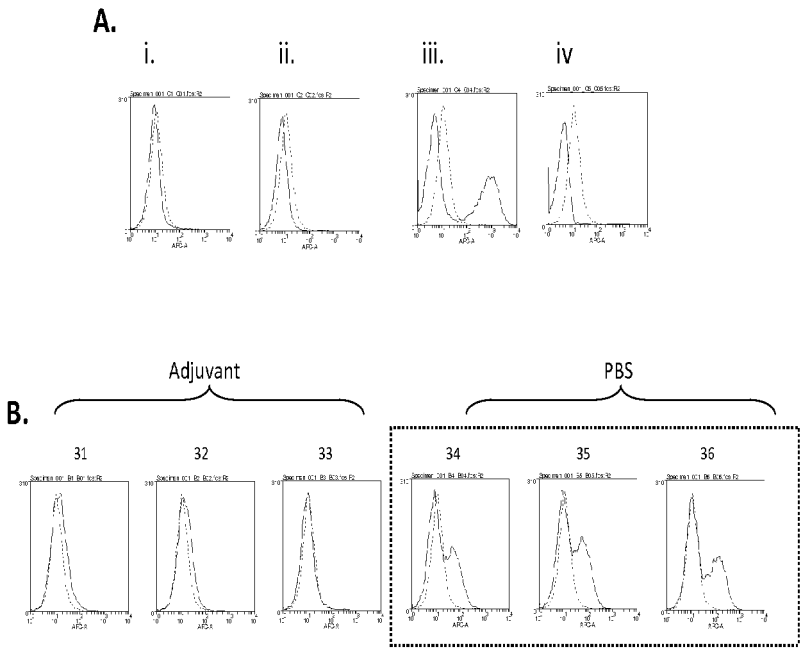


Figure 5

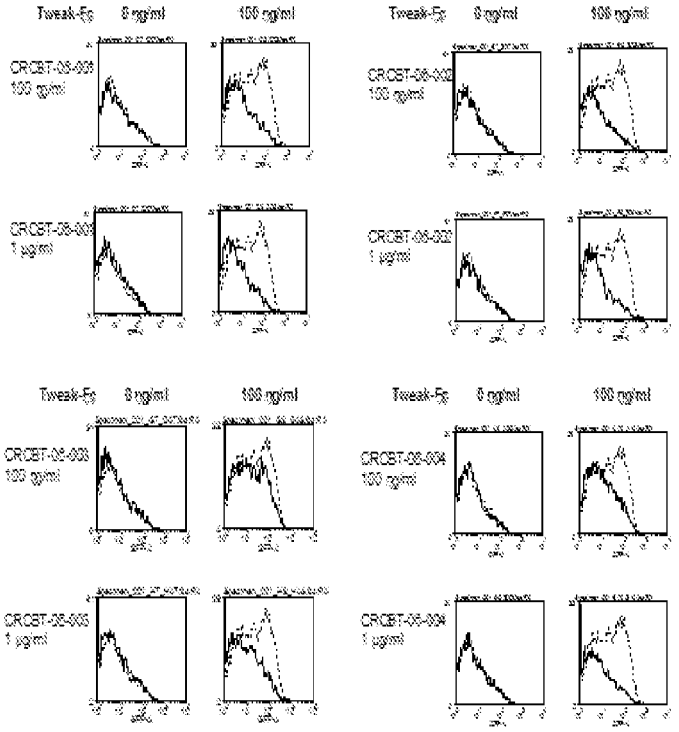

Tweak-Fc 0 ng/ml
100 ng/ml
CRCBT-06-003
100 ng/ml
CRCBT-06-003
1 µg/ml
Tweak-Fc 0 ng/ml
100 ng/ml
CRCBT-06-002
100 ng/ml
CRCBT-06-002
1 µg/ml
Tweak-Fc 0 ng/ml
100 ng/ml
CRCBT-06-005
100 ng/ml
CRCBT-06-005
1 µg/ml
Tweak-Fc 0 ng/ml
100 ng/ml
CRCBT-06-004
100 ng/ml
CRCBT-06-004
1 µg/ml

Figure 6A

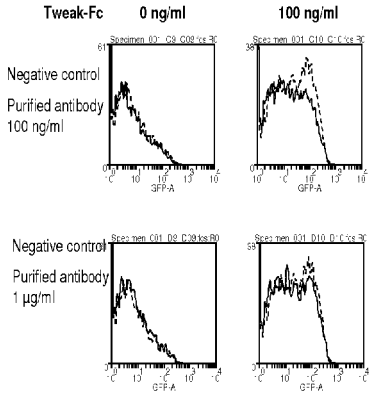


Figure 6B

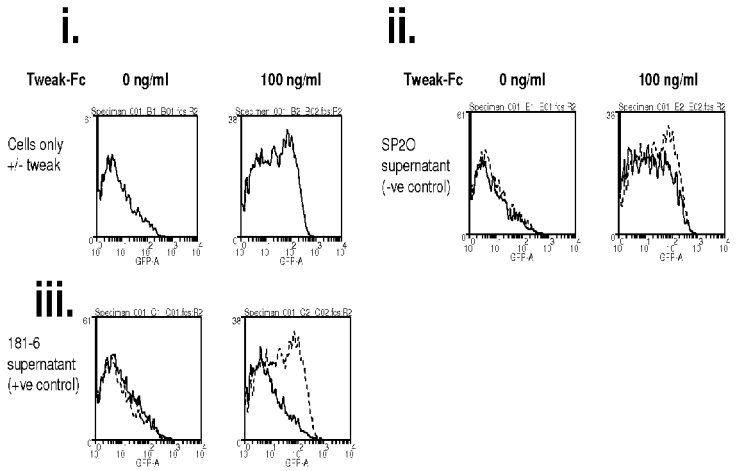
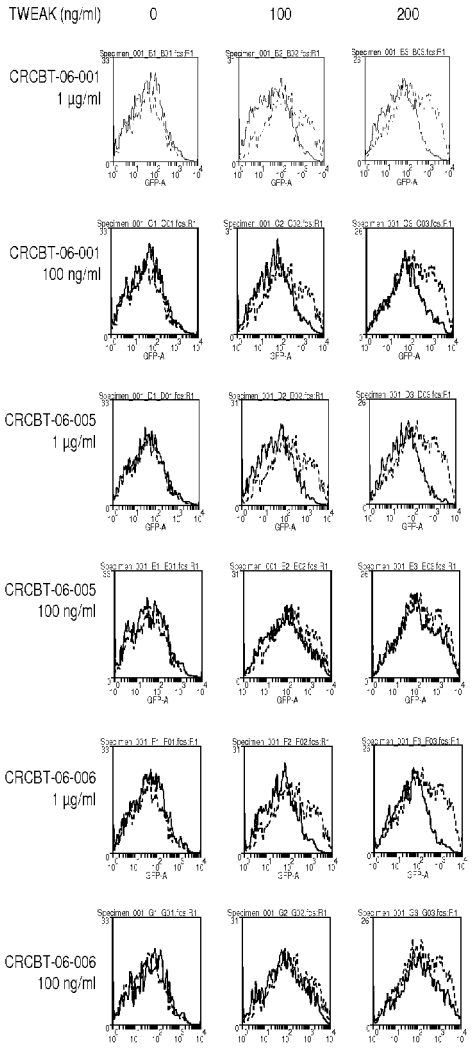


Figure 6C


TWEAK (ng/ml)
0
100
200
CRCBT-06-001
1 µg/ml
CRCBT-06-001
100 ng/ml
CRCBT-06-005
1 µg/ml
CRCBT-06-005
100 ng/ml
CRCBT-06-006
1 µg/ml
CRCBT-06-006
100 ng/ml
GFP-A

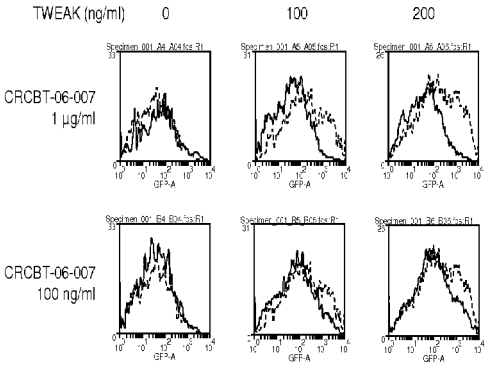

TWEAK (ng/ml)
0
100
200
CRCBT-06-007
1 µg/ml
CRCBT-06-007
100 ng/ml
GFP-A

Figure 7A

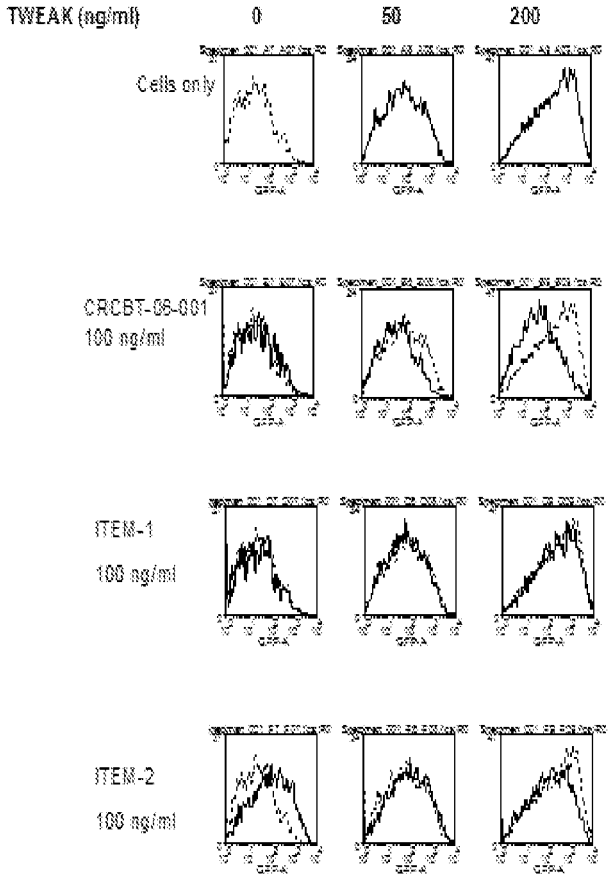

TWEAK (ng/ml)
0
50
200
Cells only
CRCBT-08-001
100 ng/ml
ITEM-1
100 ng/ml
ITEM-2
100 ng/ml

Figure 7B

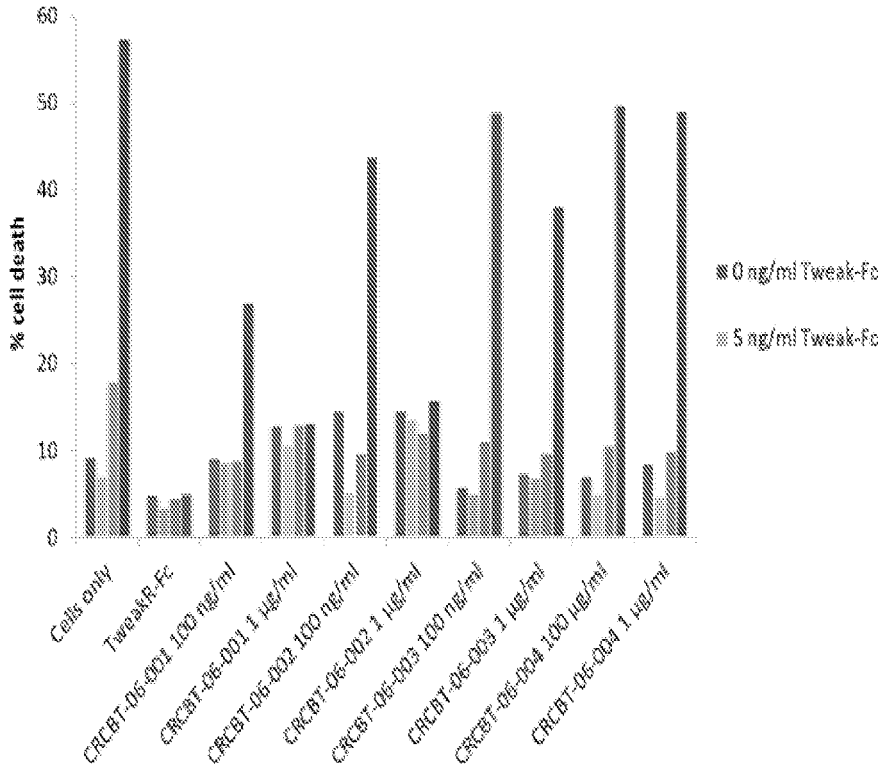

% cell death
60
50
40
30
20
10
0
0 ng/ml Tweak-Fc
5 ng/ml Tweak-Fc
Cells only
TweakR-Fc
CRCBT-06-001 100 ng/ml
CRCBT-06-001 1 µg/ml
CRCBT-06-002 100 ng/ml
CRCBT-06-002 1 µg/ml
CRCBT-06-003 100 ng/ml
CRCBT-06-003 1 µg/ml
CRCBT-06-004 100 µg/ml
CRCBT-06-004 1 µg/ml

Figure 8

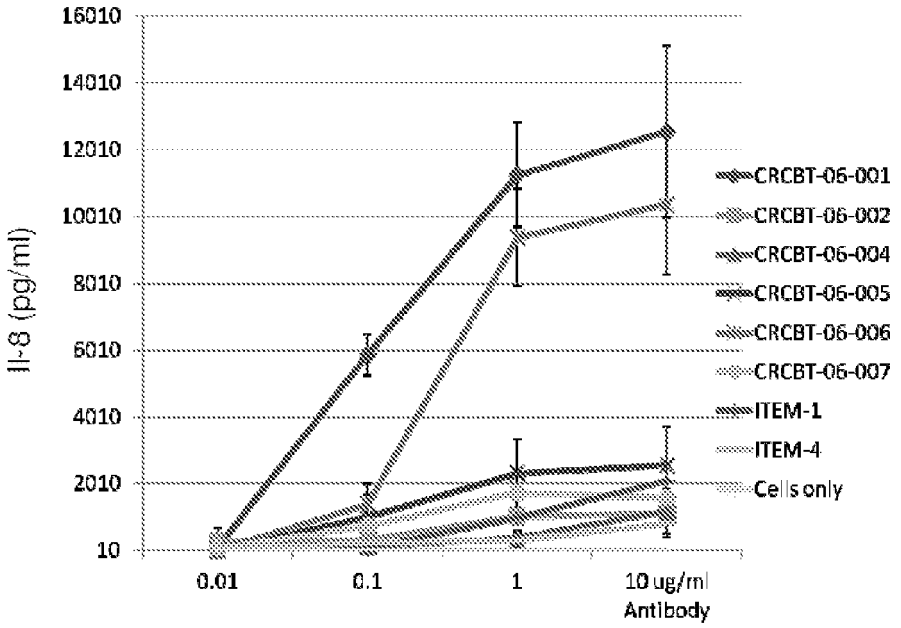


Figure 9

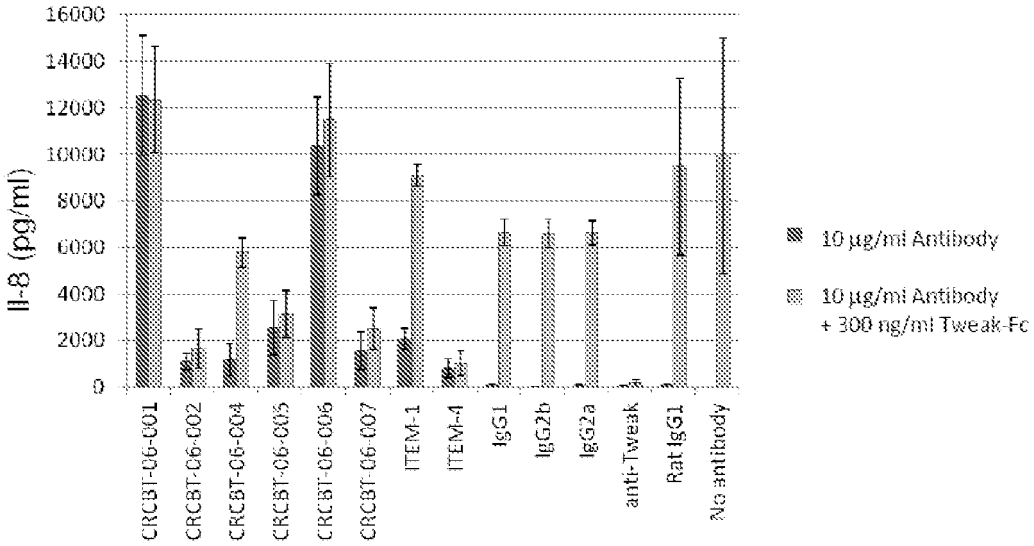


Figure 10

Light chain sequences:

	FR1	CDR1	FR2	CDR2	FR3
001	DIVMTQTPASLAVSLGQRATISC	**RASQSVSTSTYSYMH**	WYQQKPGQPPKLLIK	**YASSLES**	GVPARFSGSGSGTDFTLNIHPVEEDDTATYYC
002	DIVLTQSPASLVVSLGQRATISC	**RASQSVSTSDYSYIH**	WYQQKPGQPPKFLIK	**YASNRDS**	GVPARFSGSGSGTDFTLNIHPVEEDDTAIYYC
005	DIVLTQTTASLTVSLGQRATISC	**RASQSVSTSTYSYMH**	WYQQIPGQPPTVLIK	**YASSLES**	GVPTRFSGSGSGTDFTLNIHPVEEEDTATYYC
006	DIVITQSPASLTVSLGQRATISC	**RASQSVSTSTYSYMH**	WYQQIPGQPPTVLIK	**YASSLES**	GVPTRFSGSGSGTDFTLNIHPVEEEDTATYYC
007	DIVMTQSTASLAVSLGQRATISC	**RASQSVSTSSYSYMH**	WYQQKPGQPPKVLIK	**YASNLES**	GVPARFSGSGSGTDFTLNIHPVEEEDAATYYC

003	DIVMTQTTALMAASPGEKVTITC SVNSSI SSSYLHW	YQQKSGISPNPGFMAHPTWLLISLLASVAVDLGPLILSHSAAWRLKMLPLITVNSGVVPH	
004	DIVLTQSPALMAASPGEKVTITC SVNSSI SSSYLHW	YQQKSGISPNPGFMAHPTWLLISLLASVAVDLGPLILSHSAAWRLKMLPLITVNSGVVPH	

	CDR3	FR4	
001	**QHSWEIPYT**	FGGGTKLEIKR	SEQ ID NO: 22
002	**QHSWEIPPT**	FGAGTKLELQR	SEQ ID NO: 23
005	**QHSWEIPYT**	FGGGTKLEIKR	SEQ ID NO: 26
006	**QHSWEIPYT**	FGGGTKLEIKR	SEQ ID NO: 27
007	**QHSWEIPYT**	FGGGTKLEIKR	SEQ ID NO: 28
003		GSGTKLEIKR	SEQ ID NO: 24
004		GSGTKLEIKR	SEQ ID NO: 25

Figure 11A

Light chain sequences:

	FR1	CDR1	FR2	CDR2	FR3
001	DIVMTQTPASLAVSLGQRATISC	**RASQSVSTSTYSYMH**	WYQQKPGQPPKLLIK	**YASSLES**	GVPARFSGSGSGTDFTLNIHPVEEDDIATYYC
002	DIVLTQSPASLVVSLGQRATISC	**RASQSVSTSDYSYIH**	WYQQKPGQPPKFLIK	**YASNRDS**	GVPARFSGSGSGTDFTLNIHPVEEDDTAIYYC
005	DIVLTQTTASLIVSLGQRATISC	**RASQSVSTSTYSYMH**	WYQQTPGQPPIVLIK	**YASSLES**	GVPTRFSGSGSGTDFTLNIHPVEEDDIATYYC
006	DIVITQSPASLIVSLGQRATISC	**RASQSVSTSTYSYMH**	WYQQTPGQPPIVLIK	**YASSLES**	GVPTRFSGSGSGTDFTLNIHPVEEDDIATYYC
007	DIVMTQSTASLAVSLGQRATISC	**RASQSVSTSSYSYMH**	WYQQKPGQPPKVLIK	**YASNLES**	GVPARFSGSGSGTDFTLNIHPVEEDAATYYC
CONSENSUS	DIVXTQXXASLXVSLGQRATISC	**RASQSVSTSXYSYXH**	WYQQXPGQPPXXLIK	**YASXXXS**	GVPXRFSGSGSGTDFTLNIHPVEEXDIAXYYC
	I TP T	T M	X KL	SLE	A D T
	L ST A	D T	T TV	NRD	T E I
	M V			F	

	CDR3	FR4	
001	**QHSWEIPYT**	FGGGTKLEIKR	SEQ ID NO: 22
002	**QHSWEIPPT**	FGAGTKLELQR	SEQ ID NO: 23
005	**QHSWEIPYT**	FGGGTKLEIKR	SEQ ID NO: 26
006	**QHSWEIPYT**	FGGGTKLEIKR	SEQ ID NO: 27
007	**QHSWEIPYT**	FGGGTKLEIKR	SEQ ID NO: 28
CONSENSUS	**QHSWEIPXT**	FXGGTKLEXXR	SEQ ID NO: 14
	P	G LQ	
	Y	A IK	

Figure 11B

Heavy chain sequences:

	FR1	CDR1	FR2	CDR2	FR3
001	QVQLQQSGGGLVQPGGSMKLSCIAS	GFTFS**SYWMS**	WVRQSPEKGLEWVA	**EIRSKSDNYATHYAESVKG**	KFTISRDDSKSRFFLQMNNLRAEDTGIYYCSS
002	EVKLQQSGGGLVQPGGSMKLSCVAS	GFTFS**YYWMN**	WVRQSPEQGLEWIA	**EIRLQSNDYPTHYAESVKG**	RFTISRDDSKNSVYLQMNNLRPEDTGIYYCAC
005	QVQLQESGGGLVQPGGSMKLSCVAS	GFTFS**YYWMN**	WVRQSPEQGLEWIA	**EIRLQSNDYPTHYAESVKG**	RFTISRDDSKNSVYLQMNNLRPEDTGIYYCAC
006	QVQLQESGGGLVQPGGSMKLSCVAS	GFTFS**YYWMN**	WVRQSPEQGLEWIA	**EIRLQSNDYPTHYAESVKG**	RFTISRDDSKNSVYLQMNNLRPEDTGIYYCAC
007	QVKLEESGGVLVQPGGSMKLSCIAS	GFSFS**KYWMN**	WVRQSPEKGLEWVA	**EIRVKSNNYATHYAESVKG**	RFIISRDDSKSSVYLQMNNLRAEDTGIYYCTK
003	QVKLEQSGGGLVQPGGSMKLSCVAS	GFTFS**HYWMS**	WVRQSPEKGLEWVA	**EIRLKSDNYATHYAESVKG**	KFTISRDDSKSRLYLQMSSLRAEDTGIYYCTG
004	QVQLQQSGGGLVQPGGSMKLSCVAS	GFTFS**HYWMS**	WVRQSPEKGLEWVA	**EIRLKSDNYATHYAESVKG**	KFTISRDDSKSRLYLQMSSLRAEDTGIYYCTG

	CDR3	FR4	
001	**TYADYFHY**	WGQGTDLTVSS	SEQ ID NO: 15
002	**RYADYFDH**	WGQGTTLTVSS	SEQ ID NO: 16
005	**RYADYFDH**	WGQGTTLTVSS	SEQ ID NO: 19
006	**RYADYFDH**	WGQGTTLTVSS	SEQ ID NO: 20
007	**SYADYFDY**	WGQGTTLTVSS	SEQ ID NO: 21
003	**RYSDYFDY**	WGQGTTLTVSS	SEQ ID NO: 17
004	**RYSDYFDY**	WGQGTTLTVSS	SEQ ID NO: 18

Figure 11C

Heavy chain sequences:

	FR1	CDR1	FR2	CDR2	FR3
001	QVQLQQSGGGLVQPGGSMKLSCIAS	GFTFS**SYWMS**	WVRQSPEKGLEWVA	**EIRSKSDNYATHYAESVKG**	KFTISRDDSKSRFFLQMNNLRAEDTGIYYCSS
002	EVKLQQSGGGLVQPGGSMKLSCVAS	GFTFS**YYWMN**	WVRQSPEQGLEWIA	**EIRLQSNDYPTHYAESVKG**	RFTISRDDSKNSVYLQMNNLRPEDTGIYYCAC
005	QVQLQESGGGLVQPGGSMKLSCVAS	GFTFS**YYWMN**	WVRQSPEQGLEWIA	**EIRLQSNDYPTHYAESVKG**	RFTISRDDSKNSVYLQMNNLRPEDTGIYYCAC
006	QVQLQESGGGLVQPGGSMKLSCVAS	GFTFS**YYWMN**	WVRQSPEQGLEWIA	**EIRLQSNDYPTHYAESVKG**	RFTISRDDSKNSVYLQMNNLRPEDTGIYYCAC
007	QVKLEESGGVLVQPGGSMKLSCIAS	GFSFS**KYWMN**	WVRQSPEKGLEWVA	**EIRVKSNNYATHYAESVKG**	RFIISRDDSKSSVYLQMNNLRAEDTGIYYCTK
003	QVKLEQSGGGLVQPGGSMKLSCVAS	GFTFS**HYWMS**	WVRQSPEKGLEWVA	**EIRLKSDNYATHYAESVKG**	KFTISRDDSKSRLYLQMSSLRAEDTGIYYCTG
004	QVQLQQSGGGLVQPGGSMKLSCVAS	GFTFS**HYWMS**	WVRQSPEKGLEWVA	**EIRLKSDNYATHYAESVKG**	KFTISRDDSKSRLYLQMSSLRAEDTGIYYCTG
CONSENSUS	XVXLXXSGGXLVQPGGSMKLSCXAS	GFXFX**XYWMX**	WVRQSPEXGLEWXA	**EIRXXSXXYXTHYAESVKG**	XFXISRDDSXXXXXLQMXXLRXEDTGIYYCXX
	Q K QQ V I T SS S	Q V	VK NN A	X I	KNRFY NN P	TS
	E Q EE G V S NY N	X I	LQ DD P	R I	ESSVF SS A	AC
	K		SR E		CL	SR
	H					X

	CDR3	FR4	
001	**TYADYFHY**	WGQGTDLIVSS	SEQ ID NO: 15
002	**RYADYFDH**	WGQGTTLIVSS	SEQ ID NO: 16
005	**RYADYFDH**	WGQGTTLIVSS	SEQ ID NO: 19
006	**RYADYFDH**	WGQGTTLIVSS	SEQ ID NO: 20
007	**SYADYFDY**	WGQGTTLIVSS	SEQ ID NO: 21
003	**RYSDYFDY**	WGQGTTLIVSS	SEQ ID NO: 17
004	**RYSDYFDY**	WGQGTTLIVSS	SEQ ID NO: 18
CONSENSUS	**XYXDYFXX**	WGQGTXLIVSS	SEQ ID NO: 13
	T A HH	T	
	R S DY	D	
	S		

Figure 11D

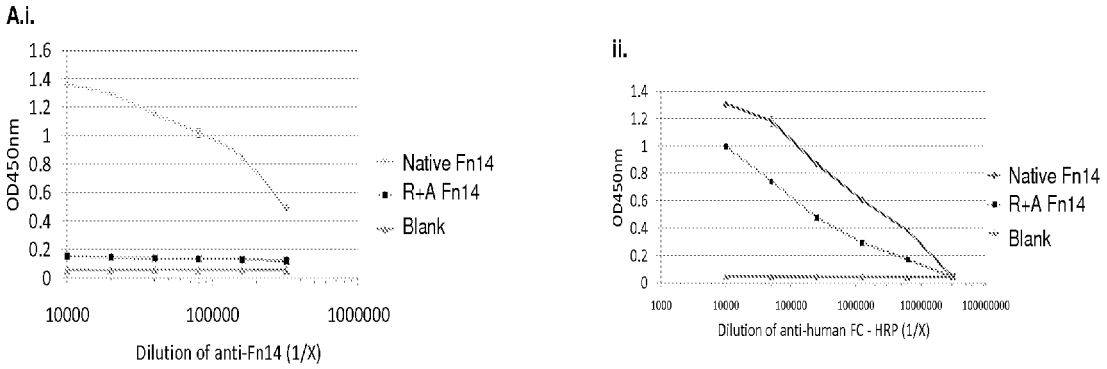

A.i.
OD450nm
1.6
1.4
1.2
1
0.8
0.6
0.4
0.2
0
10000
100000
1000000
Dilution of anti-Fn14 (1/X)
Native Fn14
R+A Fn14
Blank
ii.
OD450nm
1.4
1.2
1
0.8
0.6
0.4
0.2
0
1000
10000
100000
1000000
10000000
100000000
Dilution of anti-human FC - HRP (1/X)
Native Fn14
R+A Fn14
Blank

Figure 12A

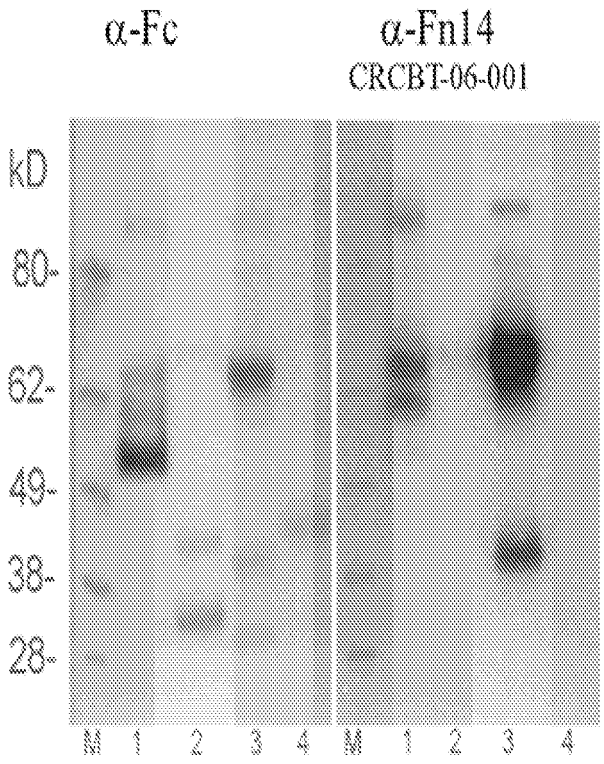


Figure 12B

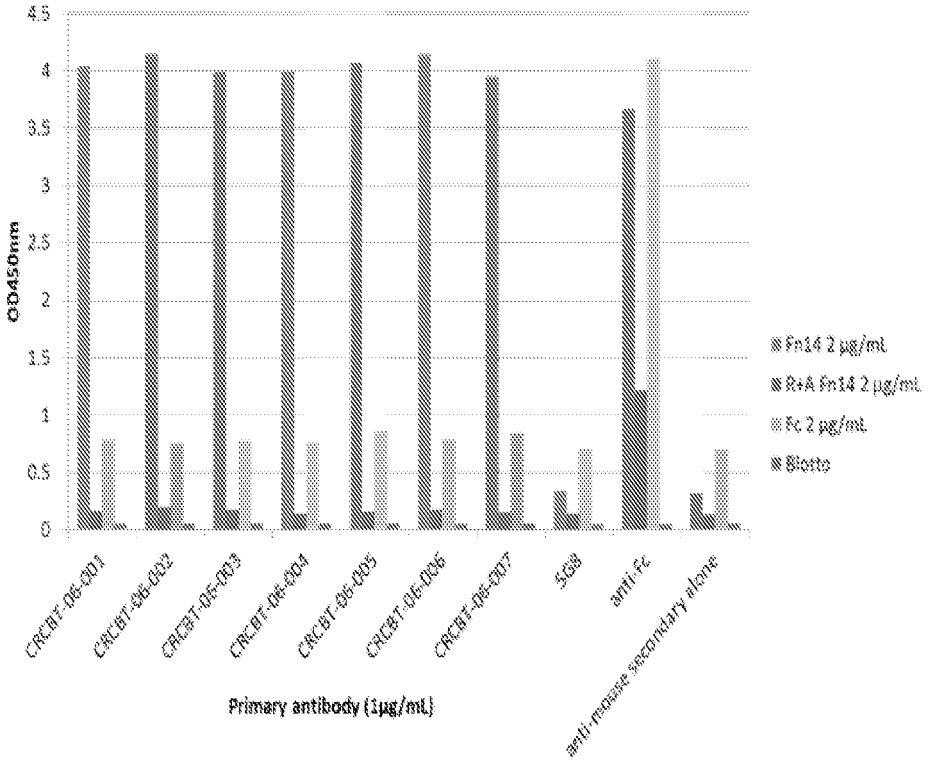

4.5
4
3.5
3
2.5
2
1.5
1
0.5
0
OD450nm
Fn14 2 µg/mL
R+A Fn14 2 µg/mL
Fc 2 µg/mL
Blank
CRCBT-06-001
CRCBT-06-002
CRCBT-06-003
CRCBT-06-004
CRCBT-06-005
CRCBT-06-006
CRCBT-06-007
SG8
anti-Fc
anti-mouse secondary alone
Primary antibody (1µg/mL)

Figure 12C

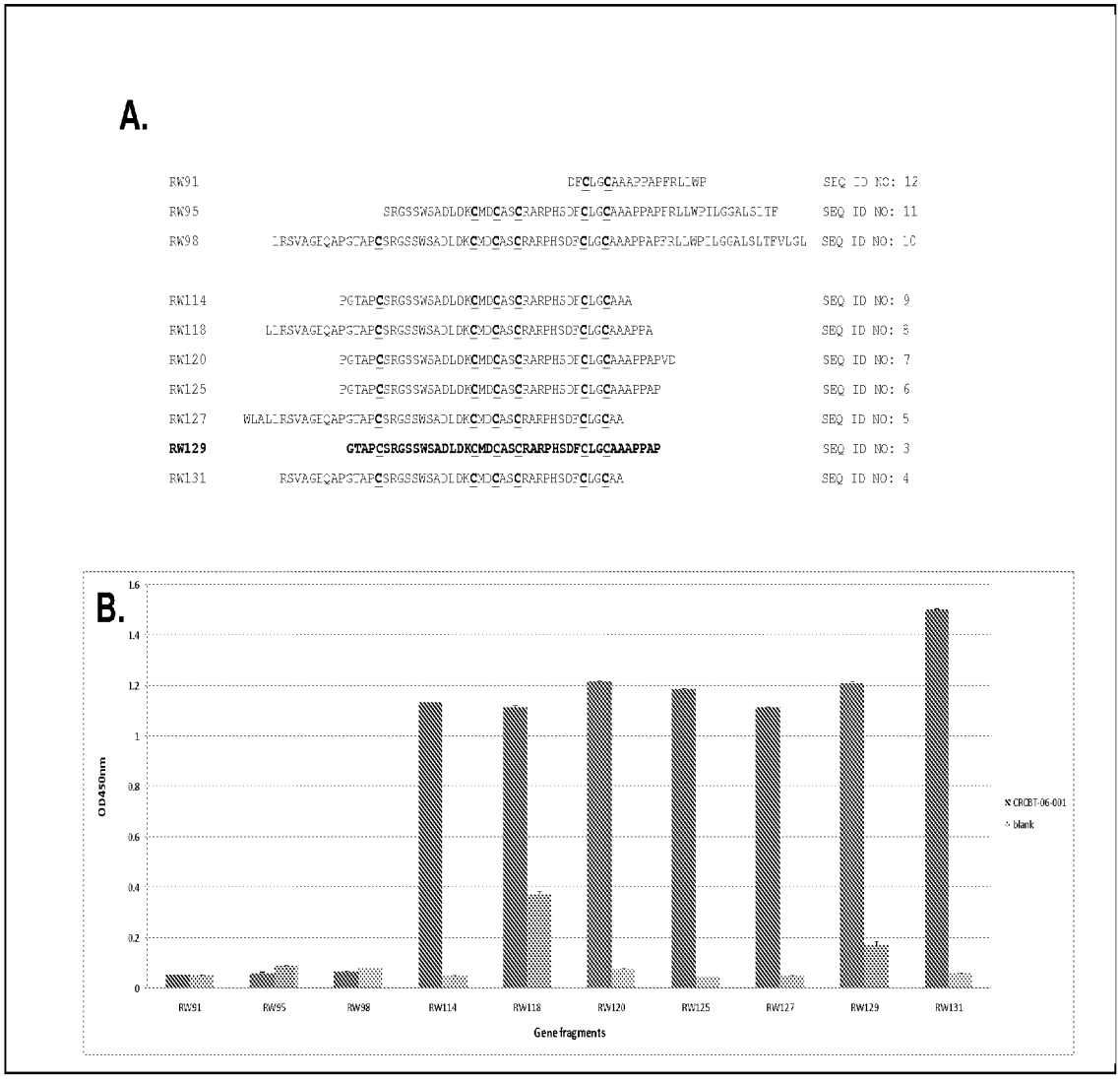

A.
RW91 DFCLGCAAAPPAPFRLLWP SEQ ID NO: 12
RW95 SRGSSWSADLDKCMDCASCRARPHSDFCLGCAAAPPAPFRLLWPILGGALSLTF SEQ ID NO: 11
RW98 LRSVAGEQAPGTAPCSRGSSWSADLDKCMDCASCRARPHSDFCLGCAAAPPAPFRLLWPILGGALSLTFVLGL SEQ ID NO: 10
RW114 PGTAPCSRGSSWSADLDKCMDCASCRARPHSDFCLGCAAA SEQ ID NO: 9
RW118 LLRSVAGEQAPGTAPCSRGSSWSADLDKCMDCASCRARPHSDFCLGCAAAPPA SEQ ID NO: 8
RW120 PGTAPCSRGSSWSADLDKCMDCASCRARPHSDFCLGCAAAPPAPVD SEQ ID NO: 7
RW125 PGTAPCSRGSSWSADLDKCMDCASCRARPHSDFCLGCAAAPPAP SEQ ID NO: 6
RW127 WLALLRSVAGEQAPGTAPCSRGSSWSADLDKCMDCASCRARPHSDFCLGCAA SEQ ID NO: 5
RW129 GTAPCSRGSSWSADLDKCMDCASCRARPHSDFCLGCAAAPPAP SEQ ID NO: 3
RW131 RSVAGEQAPGTAPCSRGSSWSADLDKCMDCASCRARPHSDFCLGCAA SEQ ID NO: 4
B.
OD450nm
1.6
1.4
1.2
1
0.8
0.6
0.4
0.2
0
RW91
RW95
RW98
RW114
RW118
RW120
RW125
RW127
RW129
RW131
Gene fragments
CRGBT-06-001
blank

Figure 13

Fn14 Ectodomain	EQAPGTAPCSRGSSWSADLDKCMDCASCRARPHSDFCLGCAAAPPAPFRL	SEQ ID NO: 2
D45A	EQAPGTAPCSRGSSWSA**A**LDKCMDCASCRARPHSDFCLGCAAAPPAPFRL	SEQ ID NO: 29
K48A	EQAPGTAPCSRGSSWSADLD**A**CMDCASCRARPHSDFCLGCAAAPPAPFRL	SEQ ID NO: 30
M50A	EQAPGTAPCSRGSSWSADLDKC**A**DCASCRARPHSDFCLGCAAAPPAPFRL	SEQ ID NO: 31
D62E	EQAPGTAPCSRGSSWSADLDKCMDCASCRARPHS**E**FCLGCAAAPPAPFRL	SEQ ID NO: 32
Fn14 Sub-domain 1	PGTAPCSRGSSWSADLDKCM	SEQ ID NO: 33
Fn14 Sub-domain 2	DCASCRARPHSDFCLGCAAA	SEQ ID NO: 34
Fn14 Sub-domain 3	ASCRARPHSDFCLG	SEQ ID NO: 35

Figure 14A

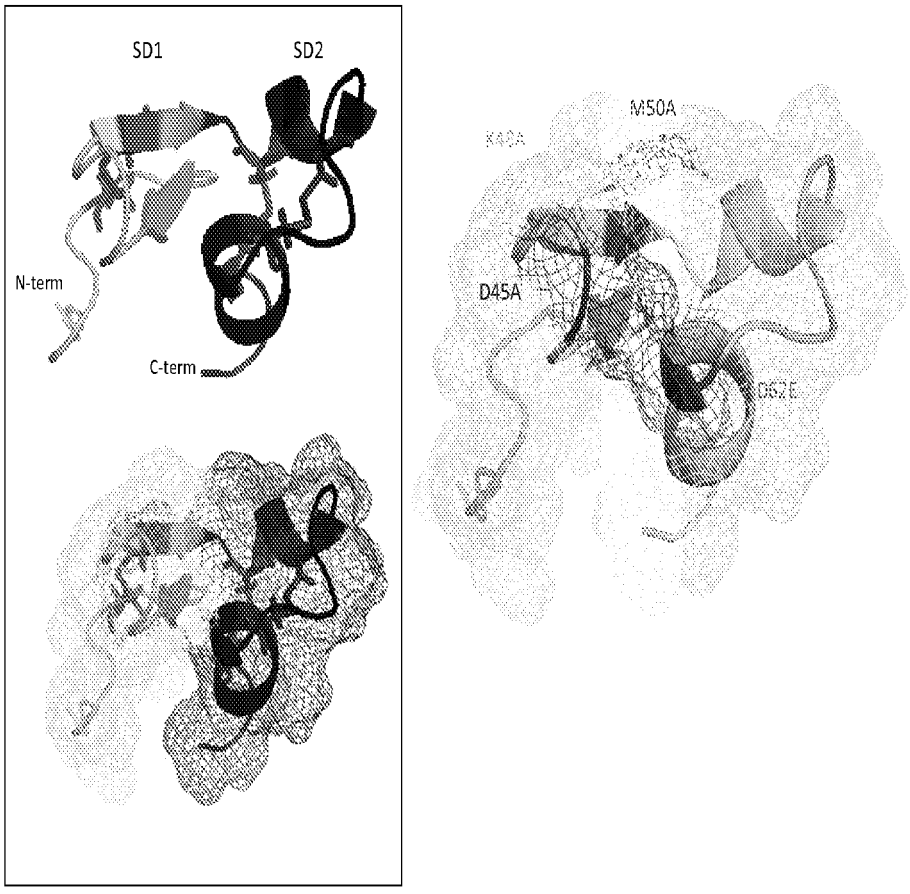


Figure 14B

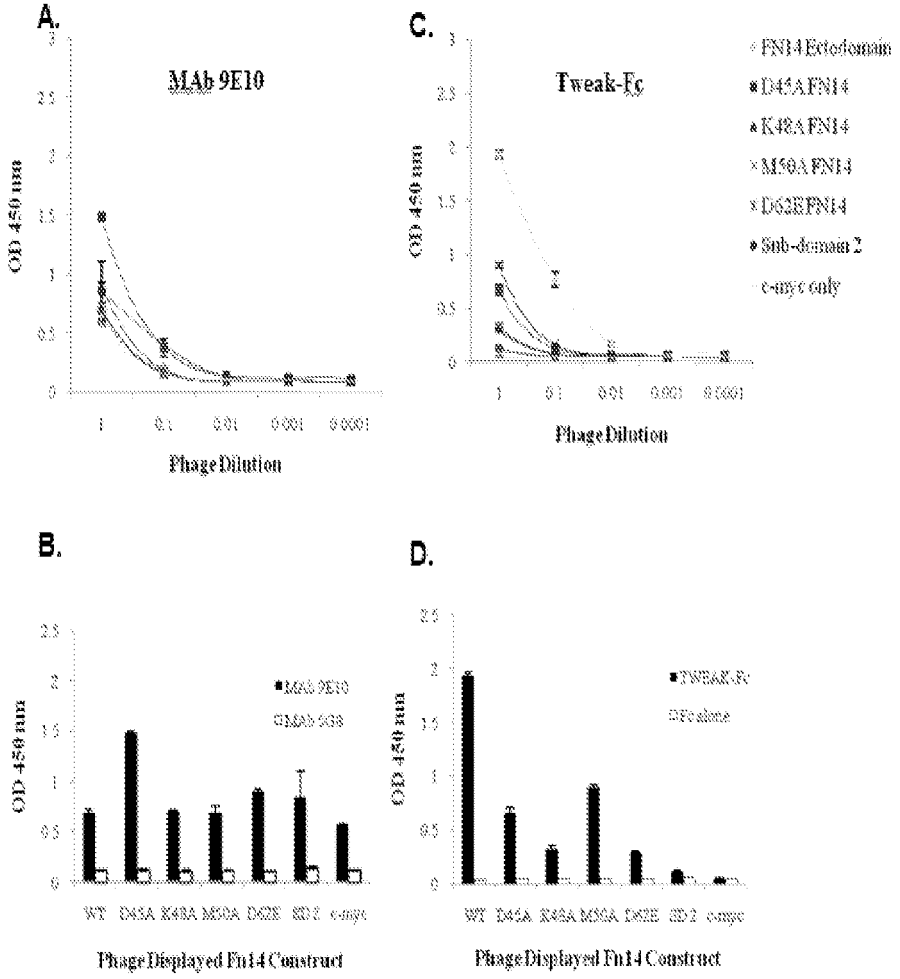

A.
MAb 9E10
OD 450 nm
Phage Dilution
C.
Tweak-Fc
FN14 Ectodomain
D45A FN14
K48A FN14
M50A FN14
D62E FN14
Sub-domain 2
c-myc only
OD 450 nm
Phage Dilution
B.
MAb 9E10
MAb 5G8
OD 450 nm
WT D45A K48A M50A D62E SD2 c-myc
Phage Displayed Fn14 Construct
D.
TWEAK-Fc
Fc alone
OD 450 nm
WT D45A K48A M50A D62E SD2 c-myc
Phage Displayed Fn14 Construct

Figure 15

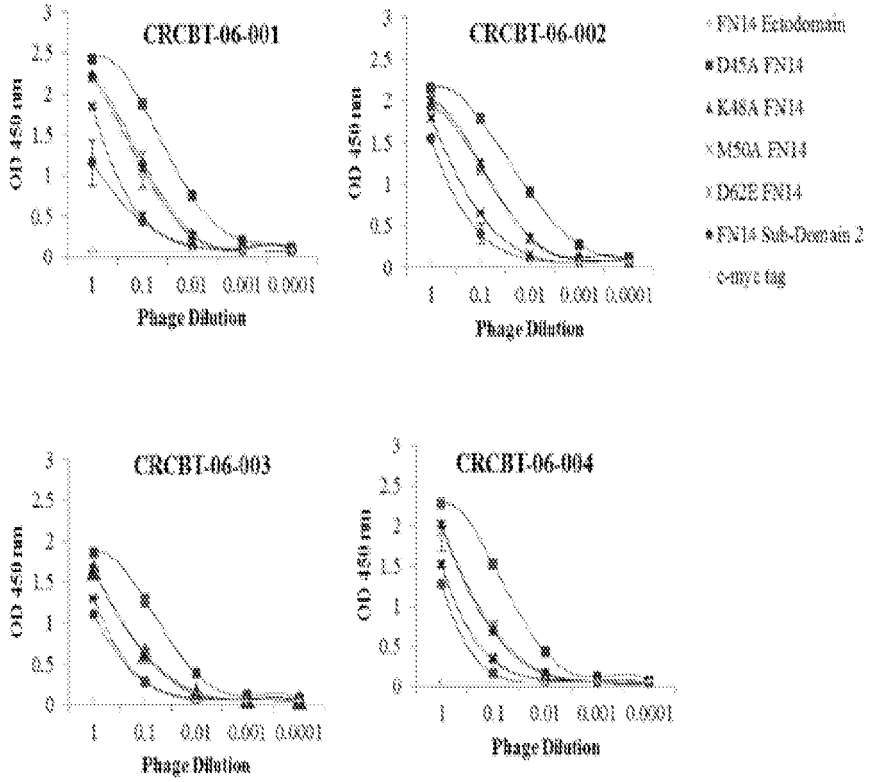

CRCBT-06-001
CRCBT-06-002
CRCBT-06-003
CRCBT-06-004
OD 450 nm
Phage Dilution
1
0.1
0.01
0.001
0.0001
FN14 Ectodomain
D45A FN14
K48A FN14
M50A FN14
D62E FN14
FN14 Sub-Domain 2
c-myc tag

Figure 16A

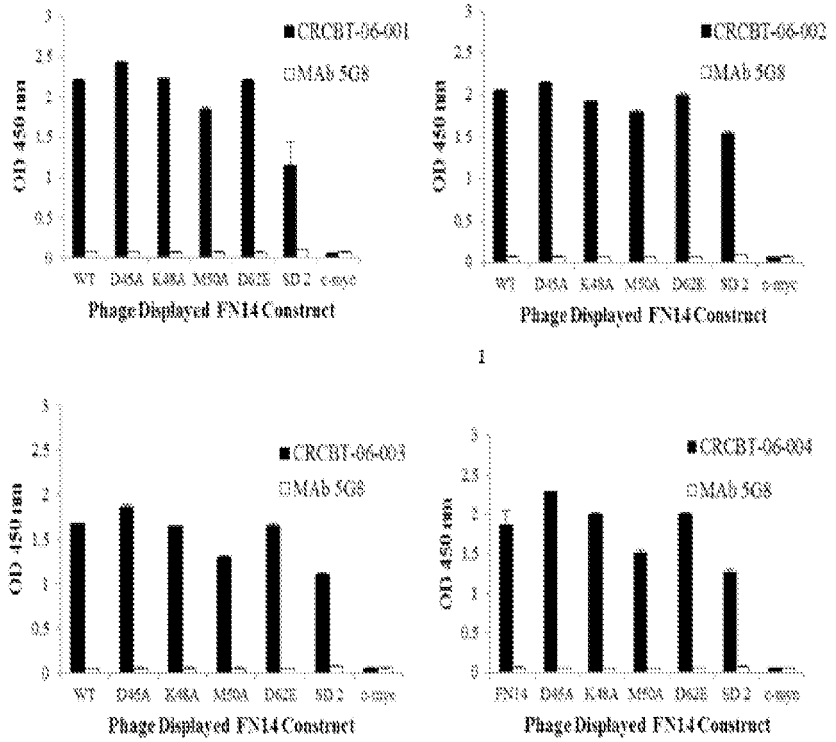

CRCBT-06-001
MAb 5G8
OD 450 nm
WT D46A K48A M50A D62E SD2 c-myc
Phage Displayed FN14 Construct
CRCBT-06-002
MAb 5G8
OD 450 nm
WT D46A K48A M50A D62E SD2 c-myc
Phage Displayed FN14 Construct
CRCBT-06-003
MAb 5G8
OD 450 nm
WT D46A K48A M50A D62E SD2 c-myc
Phage Displayed FN14 Construct
CRCBT-06-004
MAb 5G8
OD 450 nm
FN14 D46A K48A M50A D62E SD2 c-myc
Phage Displayed FN14 Construct

Figure 16B

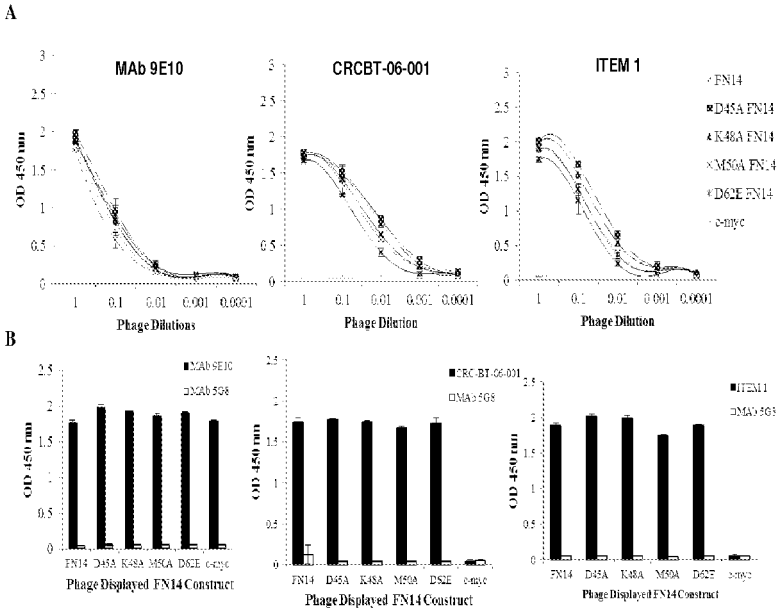

A
MAb 9E10
CRCBT-06-001
ITEM 1
FN14
D45A FN14
K48A FN14
M50A FN14
D62E FN14
c-myc
OD 450 nm
Phage Dilutions
Phage Dilution
B
MAb 9E10
MAb 5G8
CRCBT-06-001
ITEM 1
FN14
D45A
K48A
M50A
D62E
c-myc
Phage Displayed FN14 Construct

Figure 17

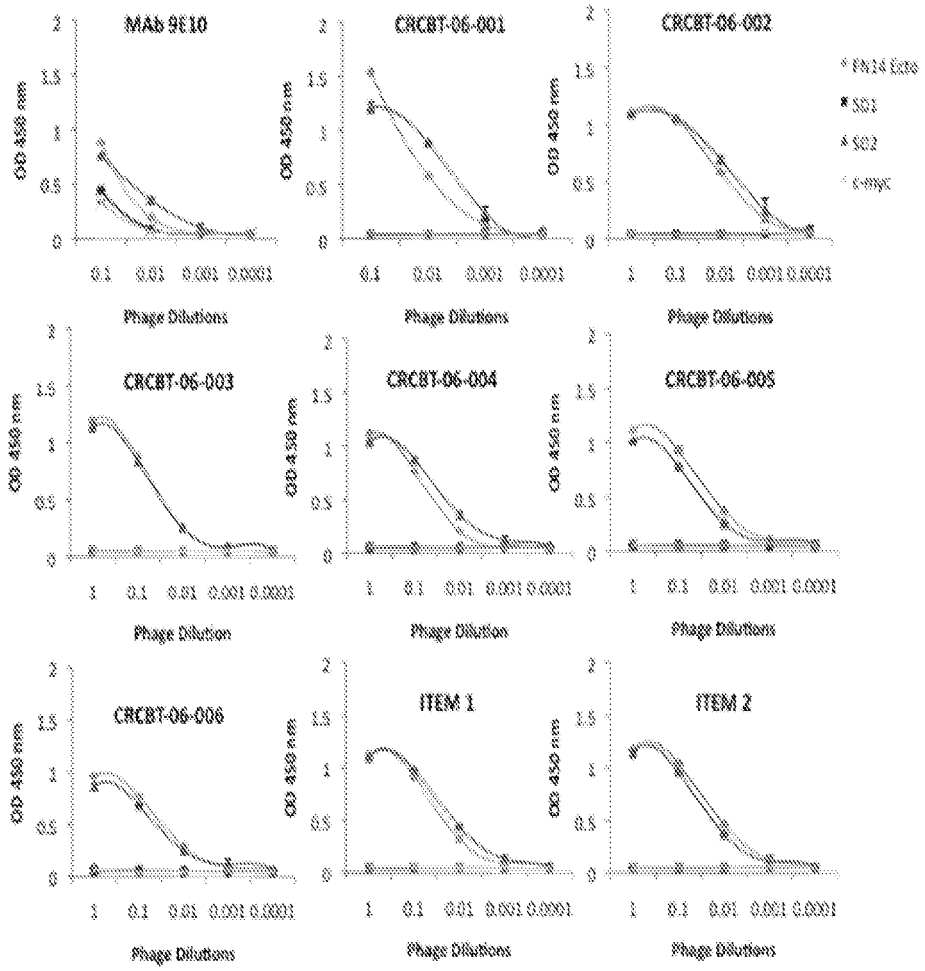

MAb 9E10
CRCBT-06-001
CRCBT-06-002
CRCBT-06-003
CRCBT-06-004
CRCBT-06-005
CRCBT-06-006
ITEM 1
ITEM 2
OD 450 nm
Phage Dilutions
Phage Dilution
S01
S02
c-myc

Figure 18A

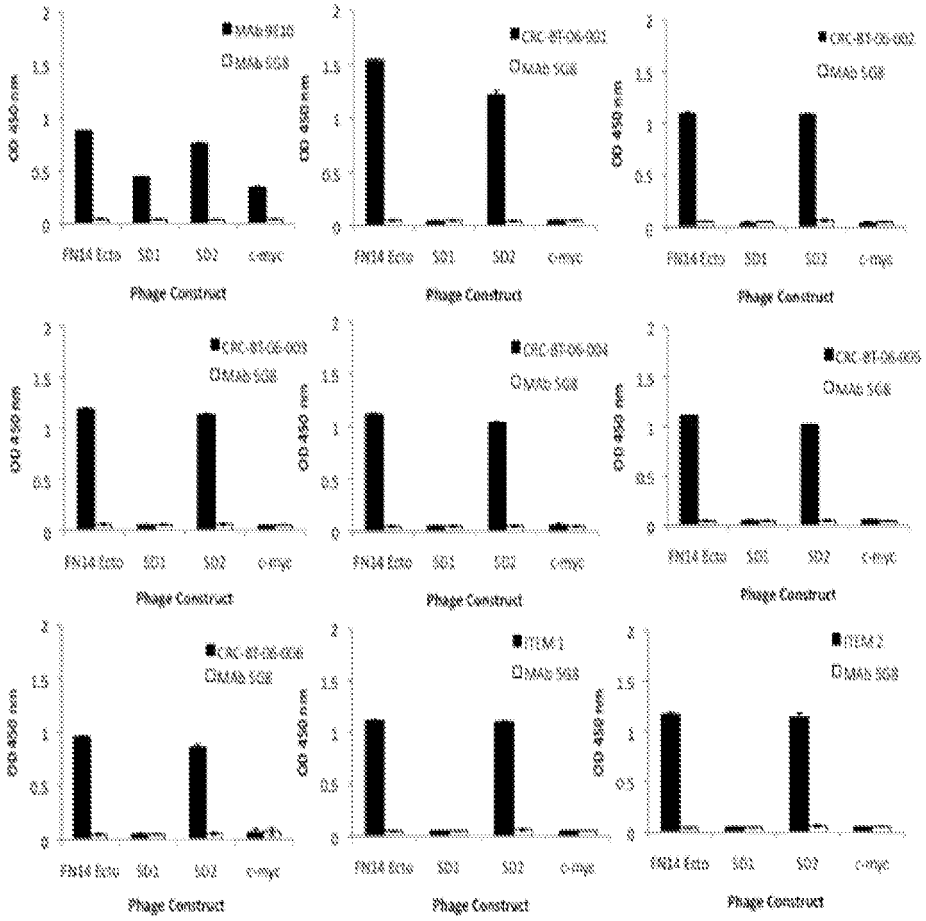


Figure 18B

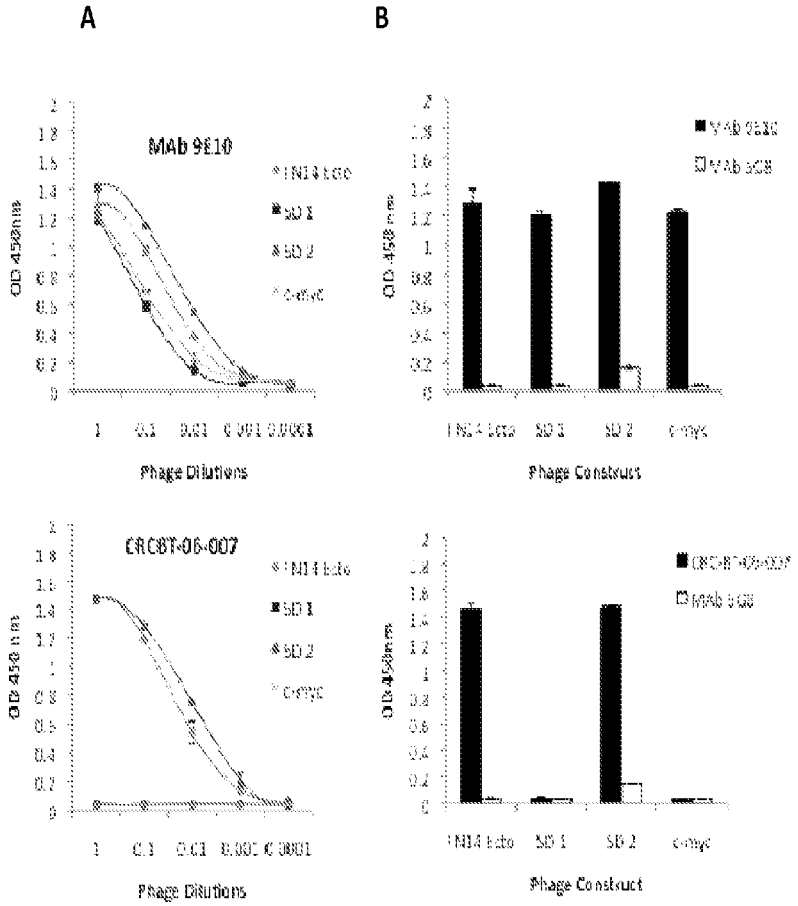
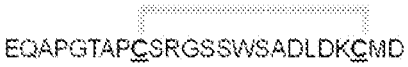

A
B
MAb 9E10
SD 1
SD 2
Phage Dilutions
Phage Construct
CRC8T-06-007
SD 1
SD 2
Phage Dilutions
Phage Construct

Figure 19

A.



B.



SEQ ID NO: 46

C.



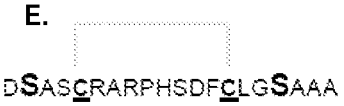
SEQ ID NO: 34

D.



SEQ ID NO: 35

E.



SEQ ID NO: 47

F.



SEQ ID NO: 48

Figure 20

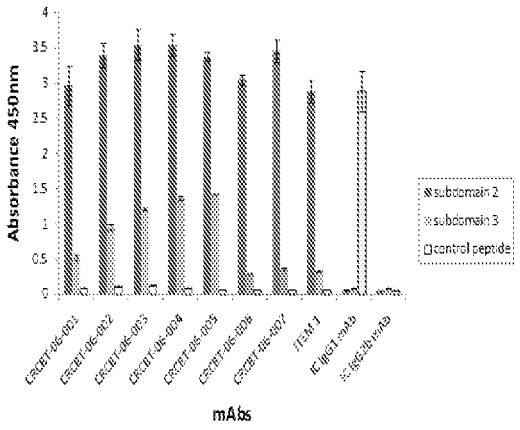


Figure 21A

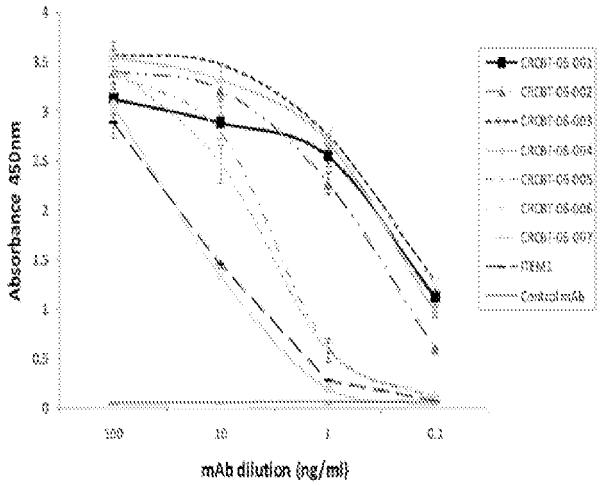


Figure 21B

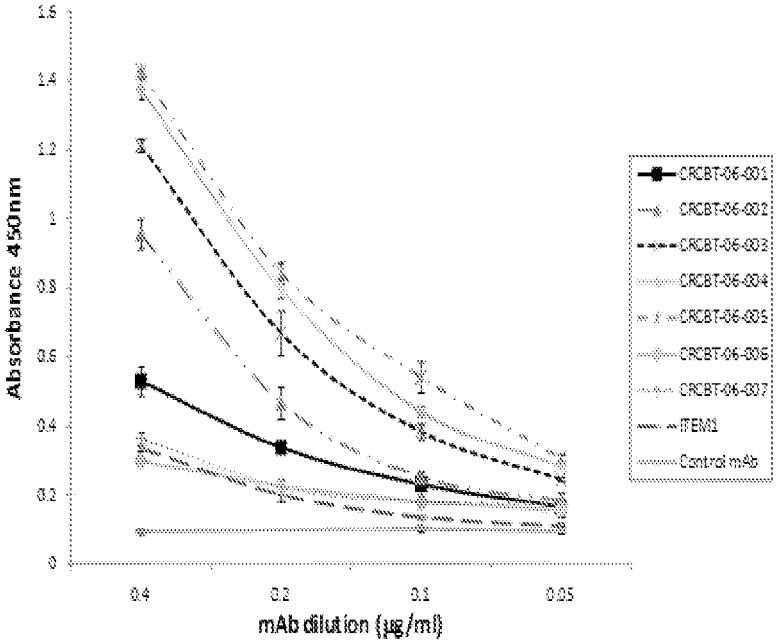

Absorbance 450nm
1.6
1.4
1.2
1
0.8
0.6
0.4
0.2
0
0.4
0.2
0.1
0.05
mAb dilution (µg/ml)
CRCBT-06-001
CRCBT-06-002
CRCBT-06-003
CRCBT-06-004
CRCBT-06-005
CRCBT-06-006
CRCBT-06-007
ITEM1
Control mAb

Figure 21C

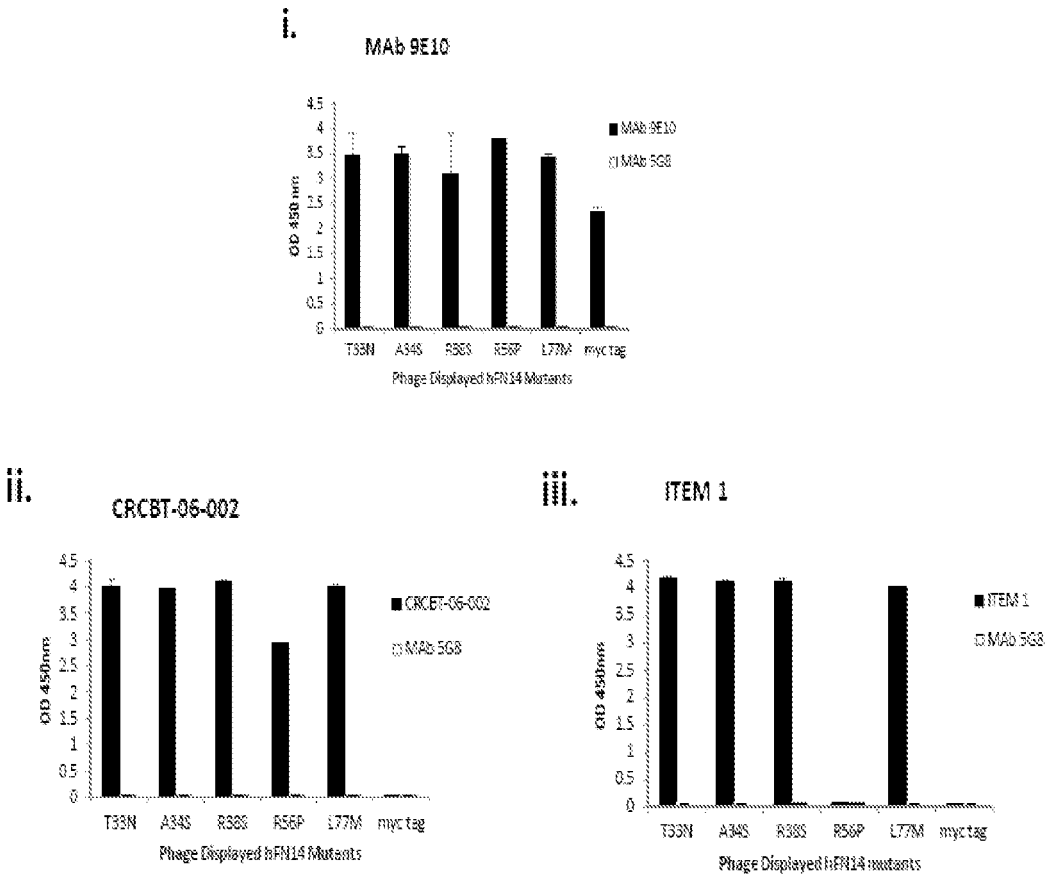

i.
MAb 9E10
OD 450 nm
MAb 9E10
MAb 5G8
T38N
A34S
R38S
R56P
L77M
myc tag
Phage Displayed hFN14 Mutants
ii.
CRCBT-06-002
OD 450nm
CRCBT-06-002
MAb 5G8
T38N
A34S
R38S
R56P
L77M
myc tag
Phage Displayed hFN14 Mutants
iii.
ITEM 1
OD 450nm
ITEM 1
MAb 5G8
T38N
A34S
R38S
R56P
L77M
myc tag
Phage Displayed hFN14 mutants

Figure 22

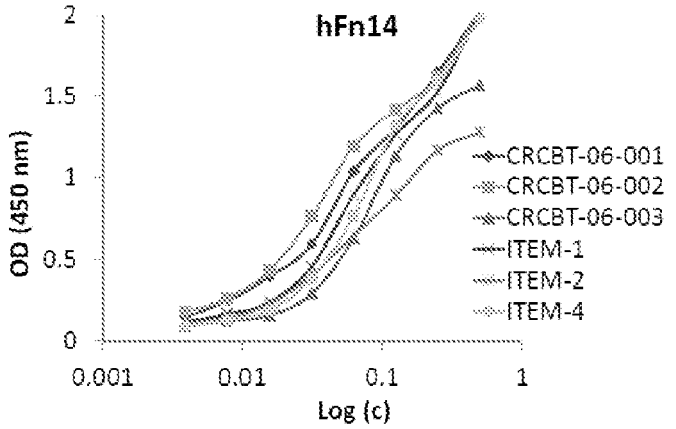


Figure 23A

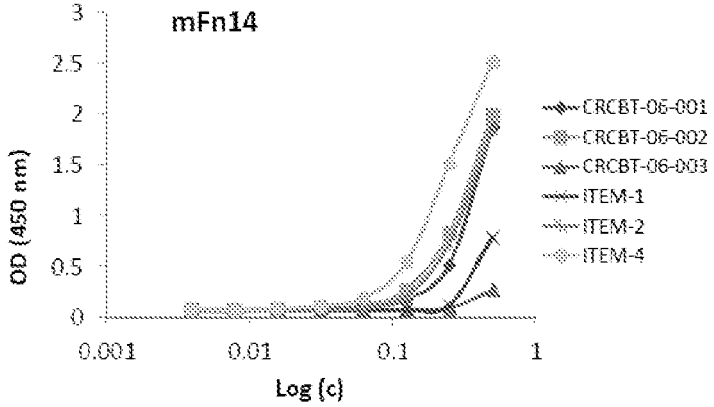


Figure 23B

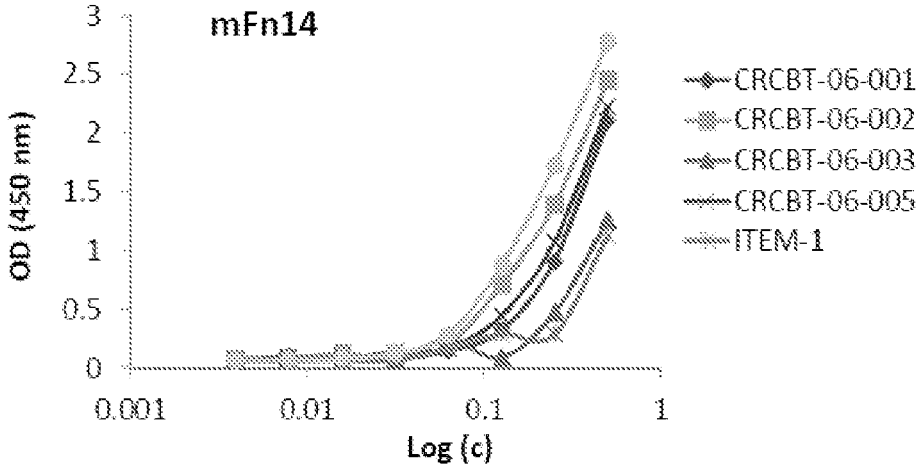


Figure 23C

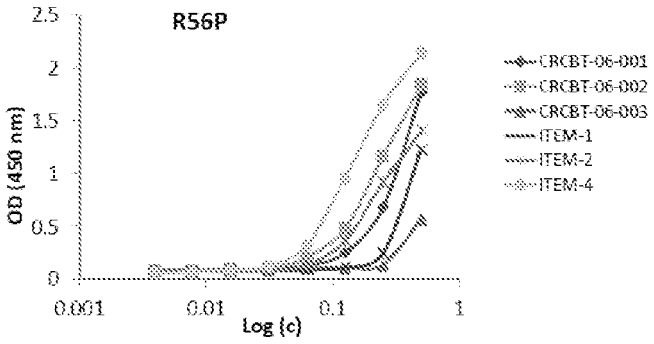


Figure 24A

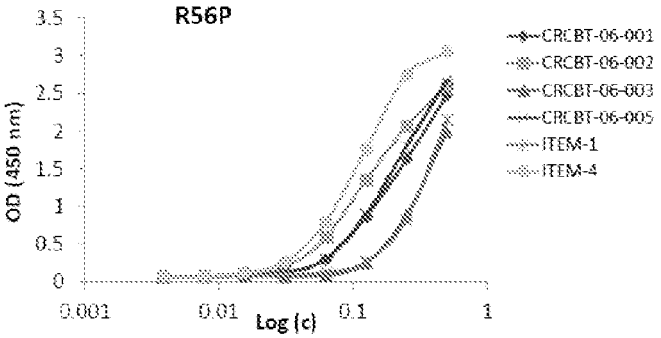


Figure 24B

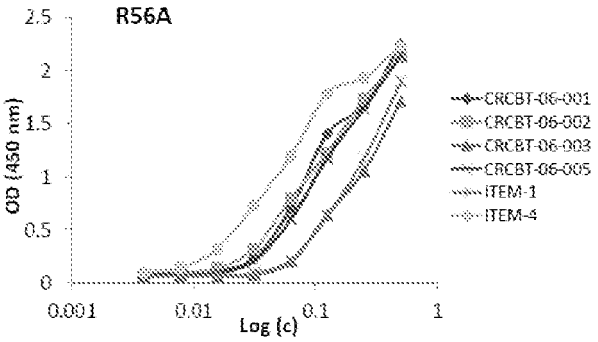


Figure 24C

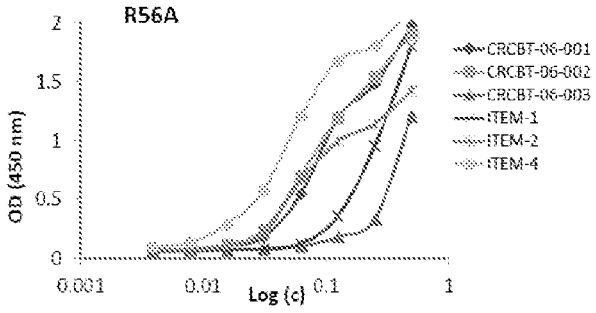


Figure 24D

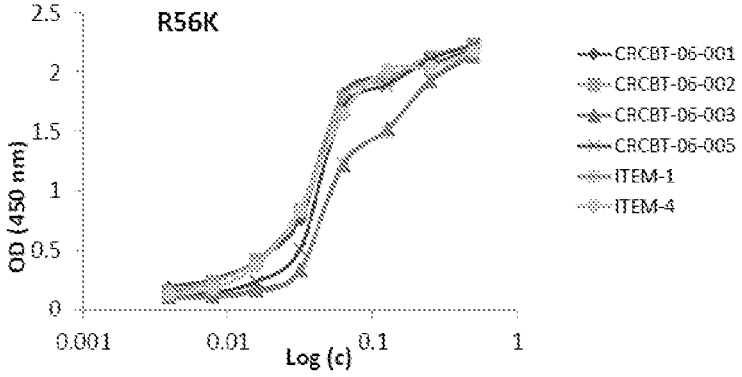


Figure 24E

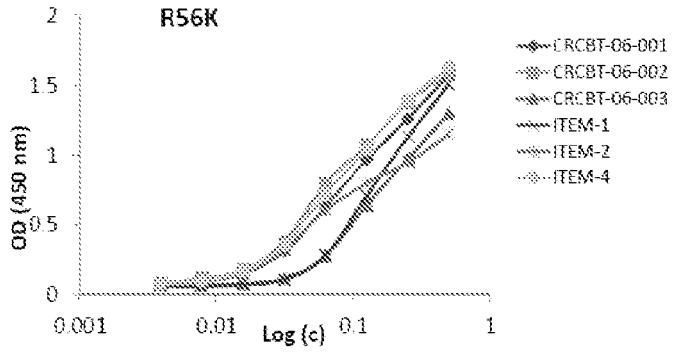


Figure 24F

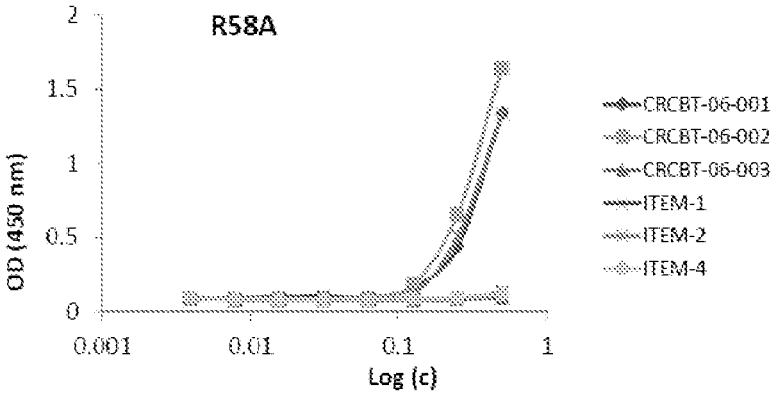


Figure 25A

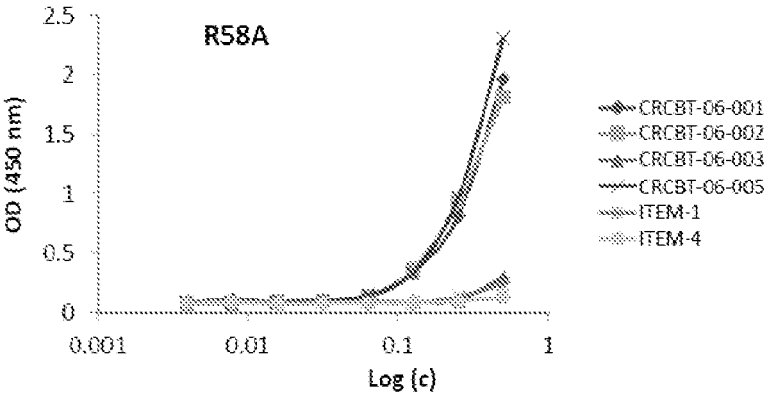


Figure 25B

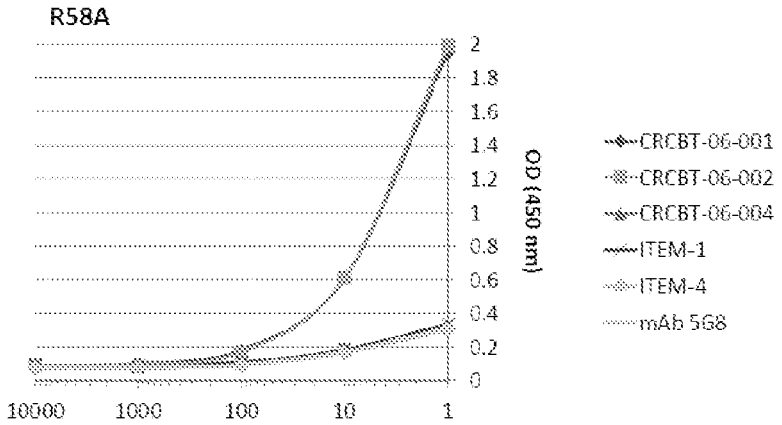


Figure 26

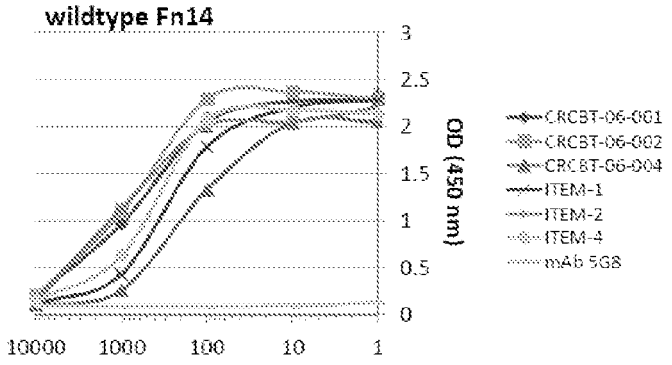


Figure 27A

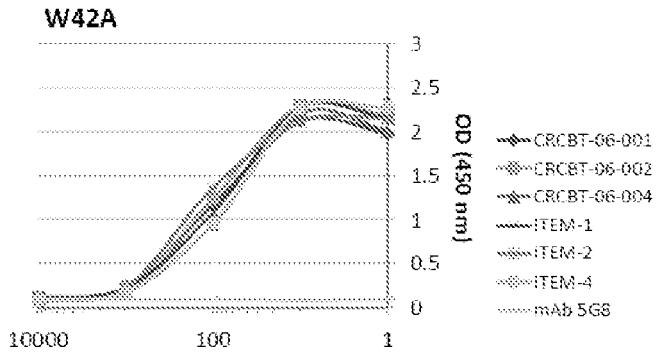


Figure 27B

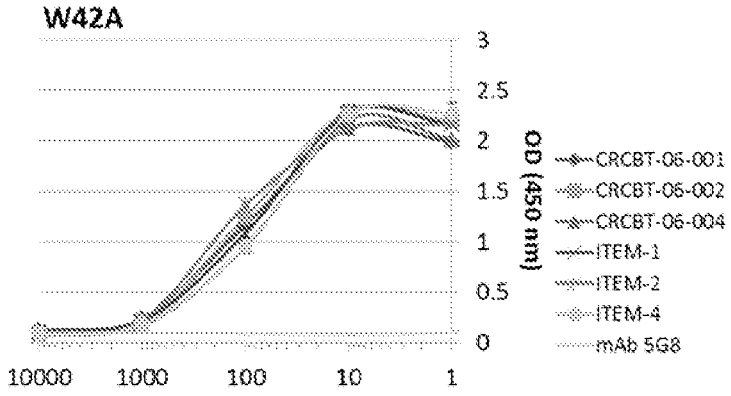


Figure 27C

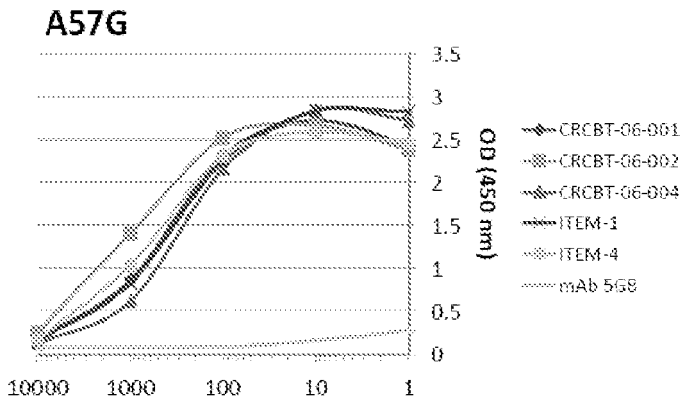


Figure 27D

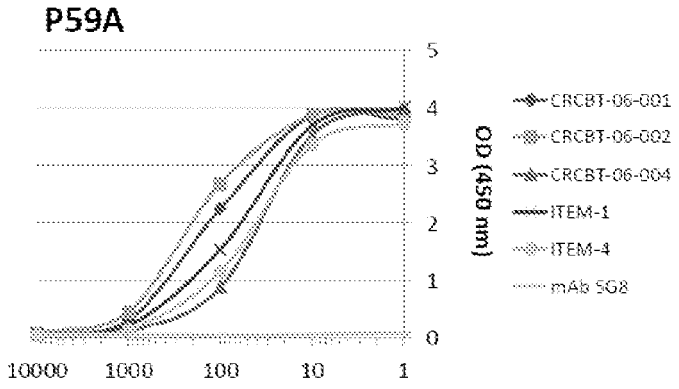


Figure 27E

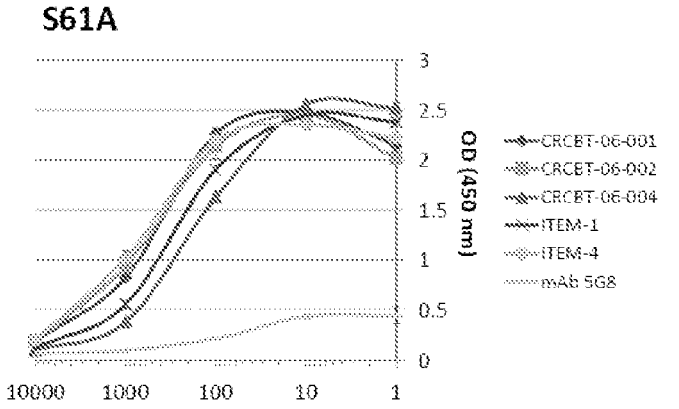


Figure 27F

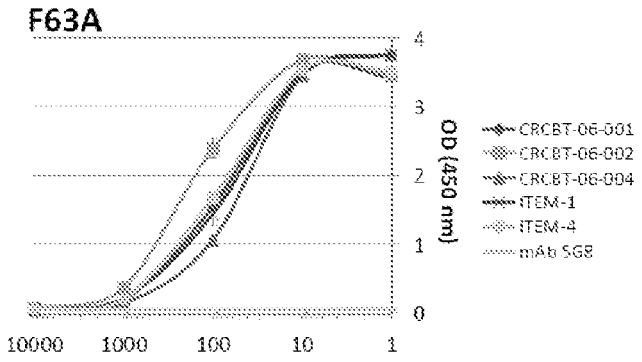


Figure 27G

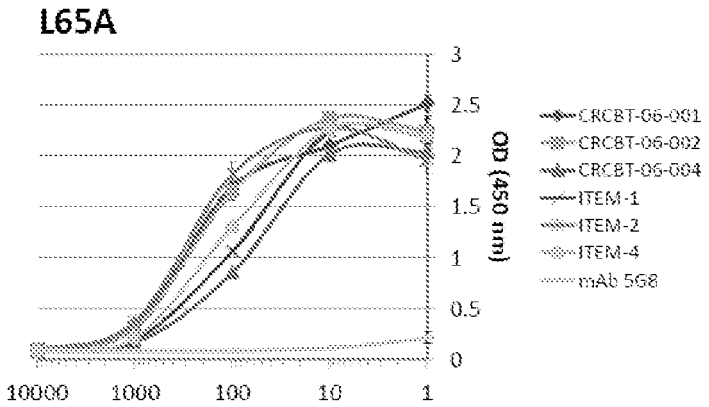


Figure 27H

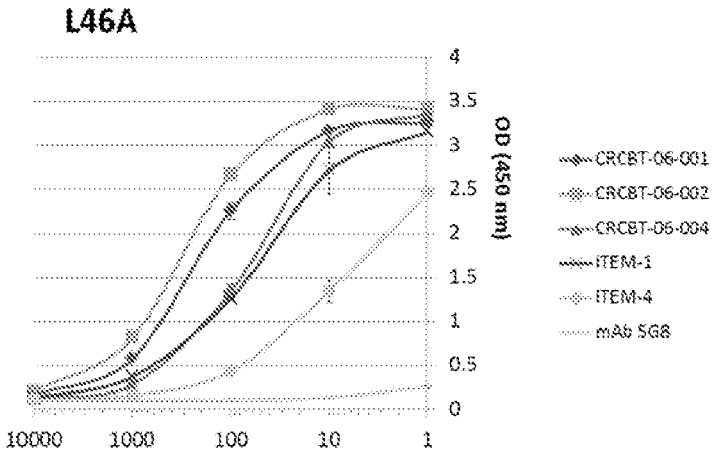


Figure 28A

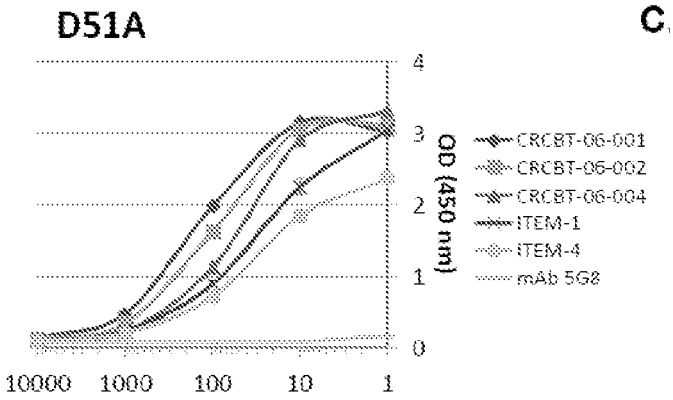


Figure 28B

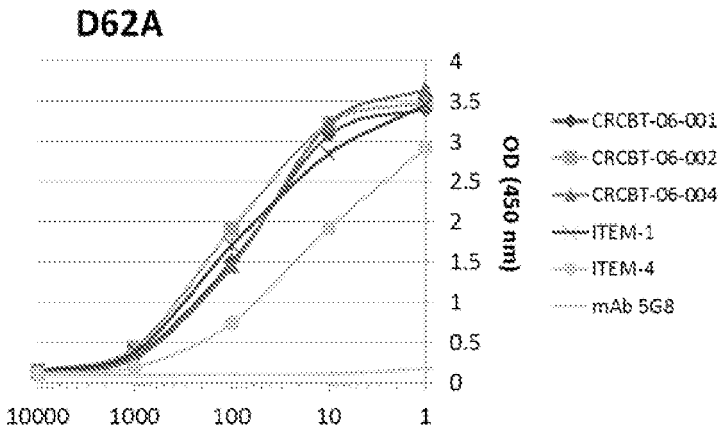


Figure 28C

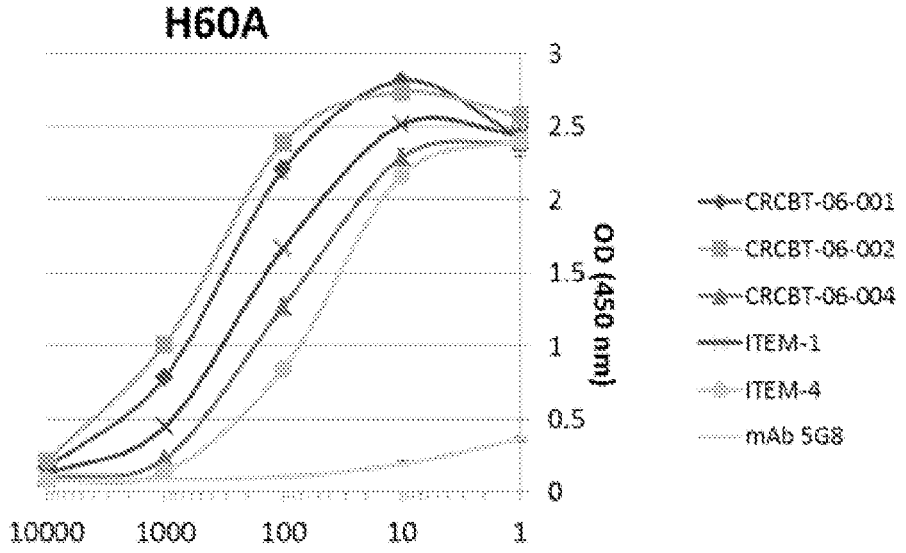


Figure 29A

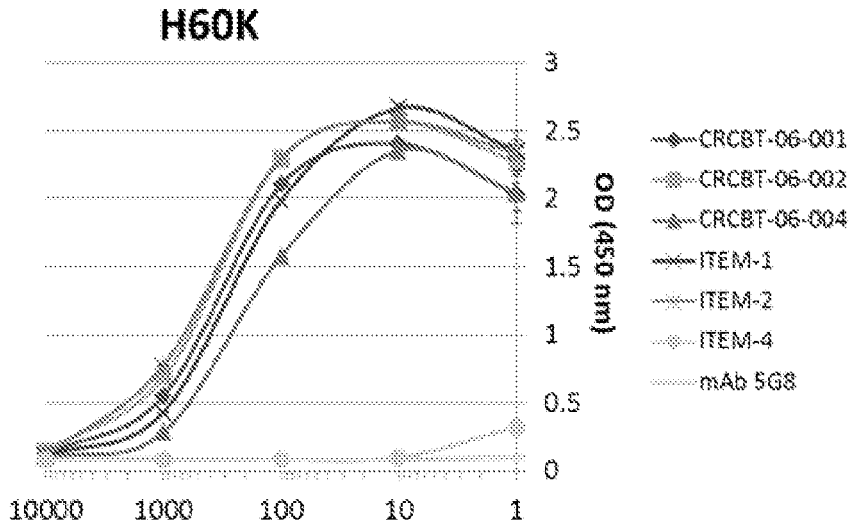


Figure 29B

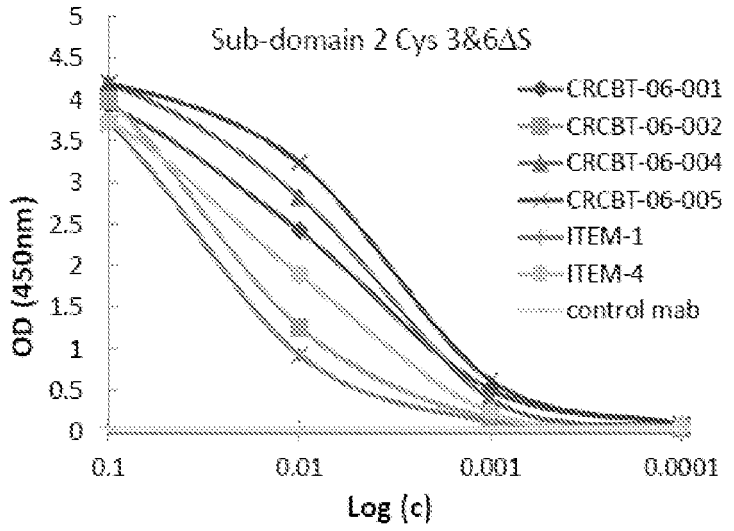


Figure 30A

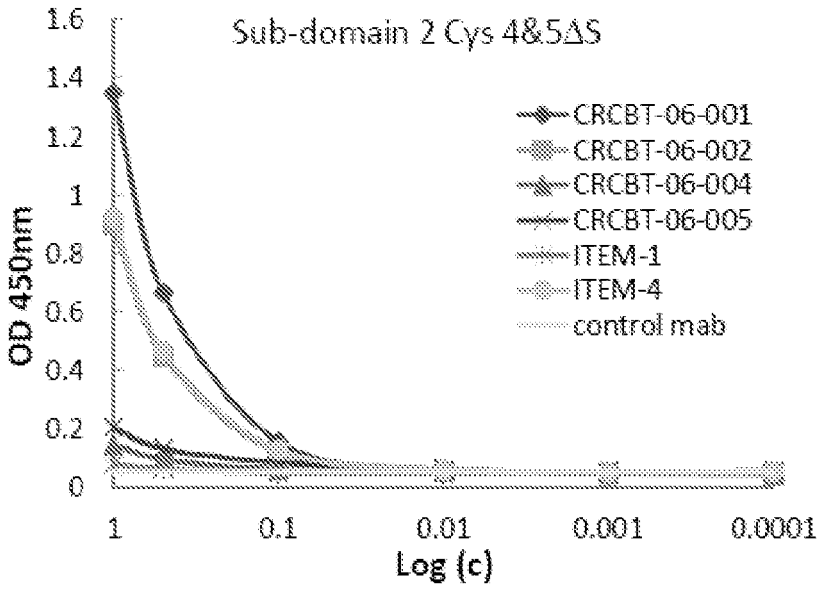


Figure 30B

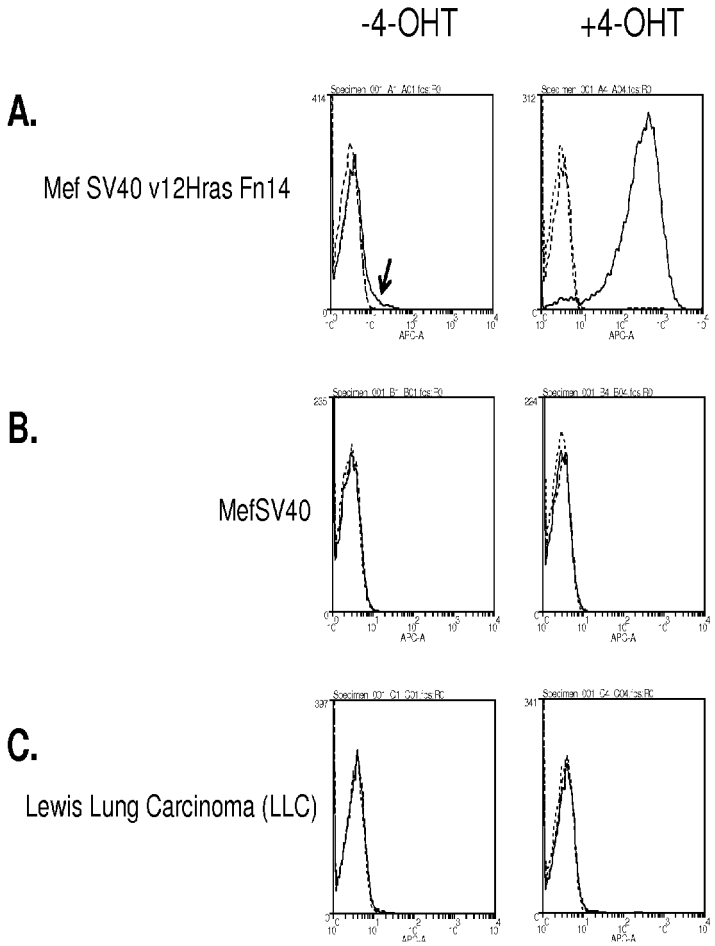

-4-OHT
+4-OHT
A.
Mef SV40 v12Hras Fn14
B.
MefSV40
C.
Lewis Lung Carcinoma (LLC)
APC-A

Figure 31

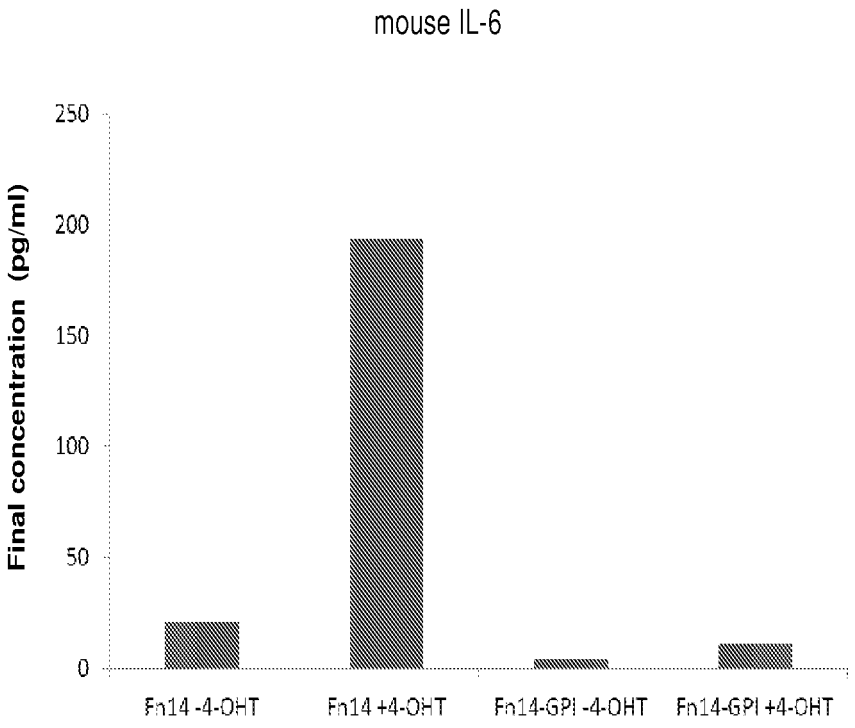

mouse IL-6
Final concentration (pg/ml)
250
200
150
100
50
0
Fn14 -4-OHT
Fn14 +4-OHT
Fn14-GPI -4-OHT
Fn14-GPI +4-OHT

Figure 32

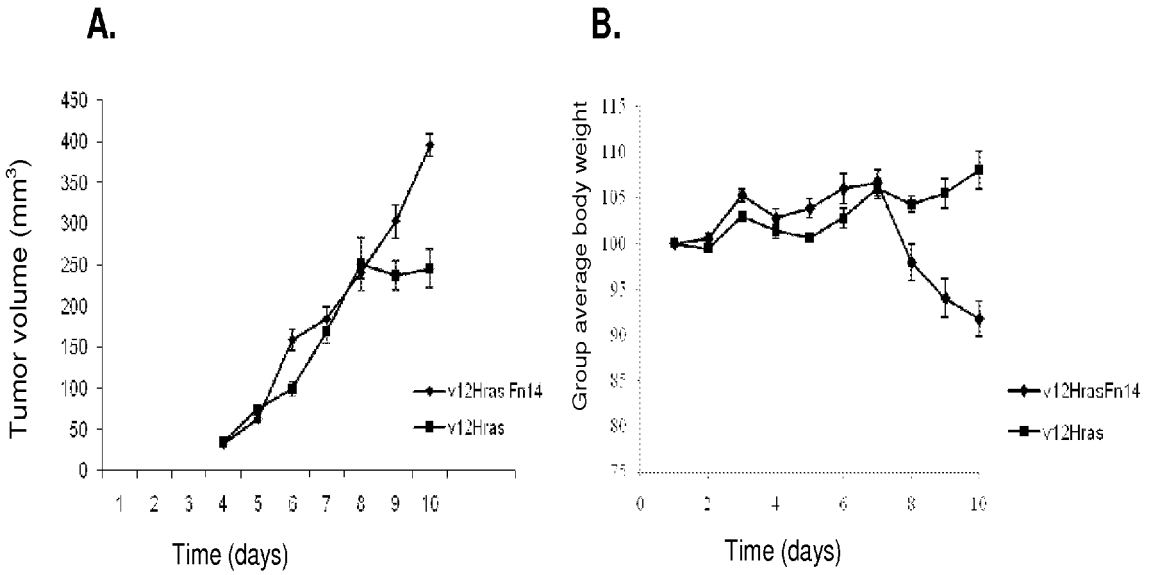

A.
B.
Tumor volume (mm3)
Time (days)
v12Hras Fn14
v12Hras
Group average body weight
Time (days)
v12HrasFn14
v12Hras

Figure 33

Protein sequence of Fn14-GPI control

1 70

MARGSLRRLLRLLVLGLWLALLRSVAGEQAPGTAPCSRGSSWSADLDKCMDCASCRARPHSDFCLGCAAA

71 126

PLAPFRLLWMTTSPGTPAPAAEETMTTSPGTPASSHYLSCTIVGIIVLIVLLIVFV SEQ ID NO: 36

Figure 34A

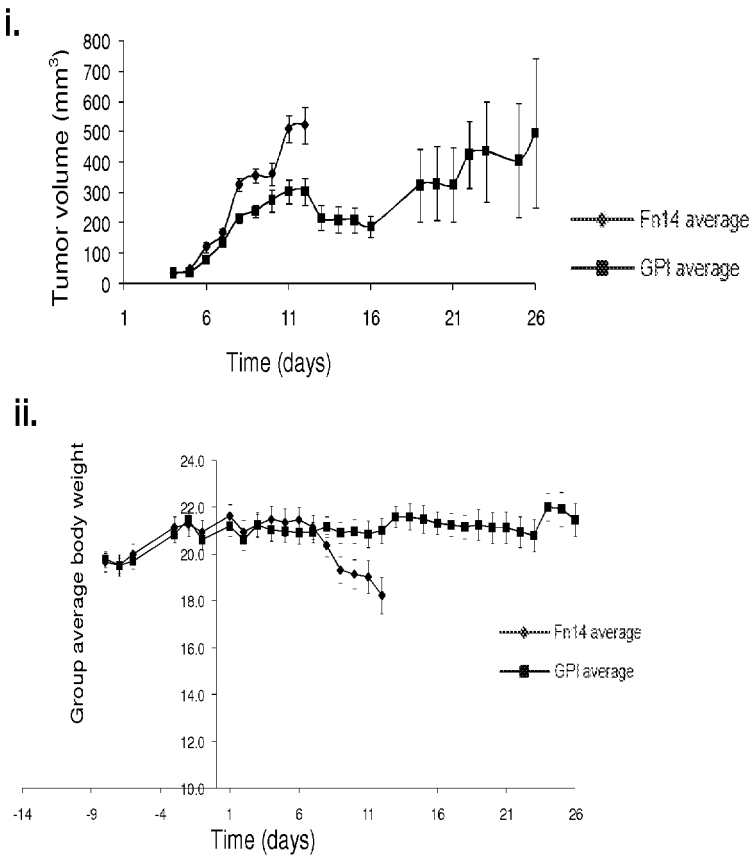

i.
Tumor volume (mm3)
800
700
600
500
400
300
200
100
0
1
6
11
16
21
26
Time (days)
Fn14 average
GPI average
ii.
Group average body weight
24.0
22.0
20.0
18.0
16.0
14.0
12.0
10.0
-14
-9
-4
1
6
11
16
21
26
Time (days)
Fn14 average
GPI average

Figure 34B

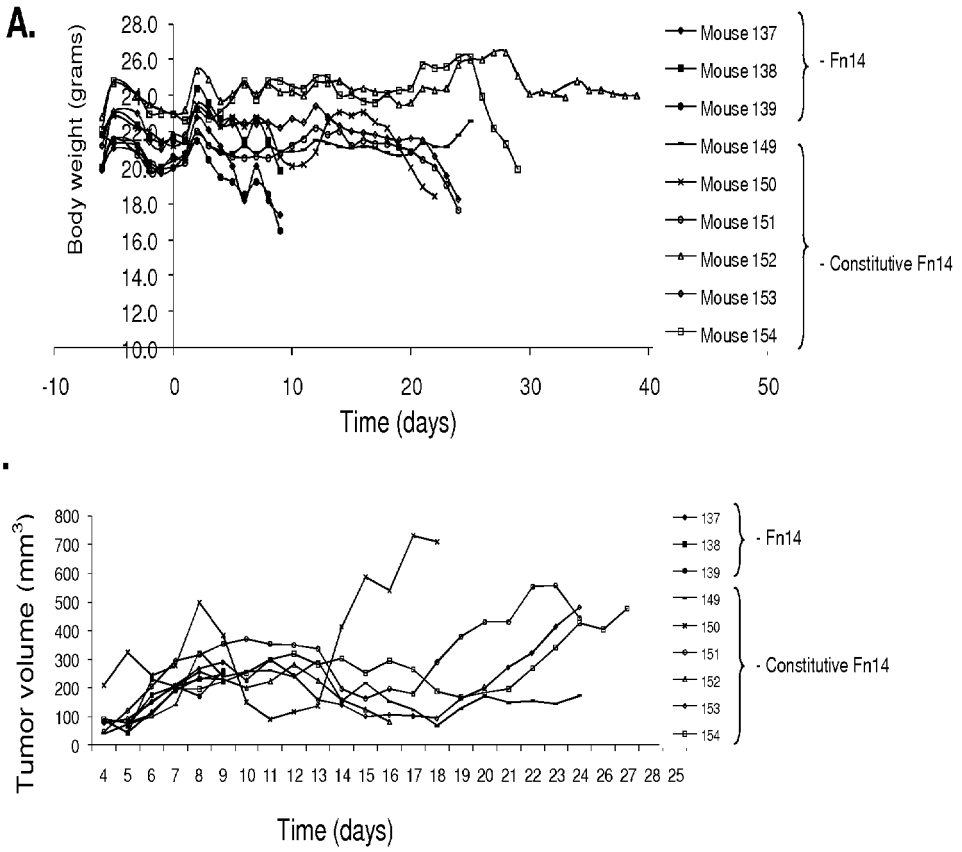

A.
Body weight (grams)
28.0
26.0
18.0
16.0
14.0
12.0
10.0
-10
0
10
20
30
40
50
Time (days)
Mouse 137
Mouse 138
Mouse 139
- Fn14
Mouse 149
Mouse 150
Mouse 151
Mouse 152
Mouse 153
Mouse 154
- Constitutive Fn14
B.
Tumor volume (mm3)
800
700
600
500
400
300
200
100
0
4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 26 27 28 25
Time (days)
137
138
139
- Fn14
149
150
151
152
153
154
- Constitutive Fn14

Figure 35

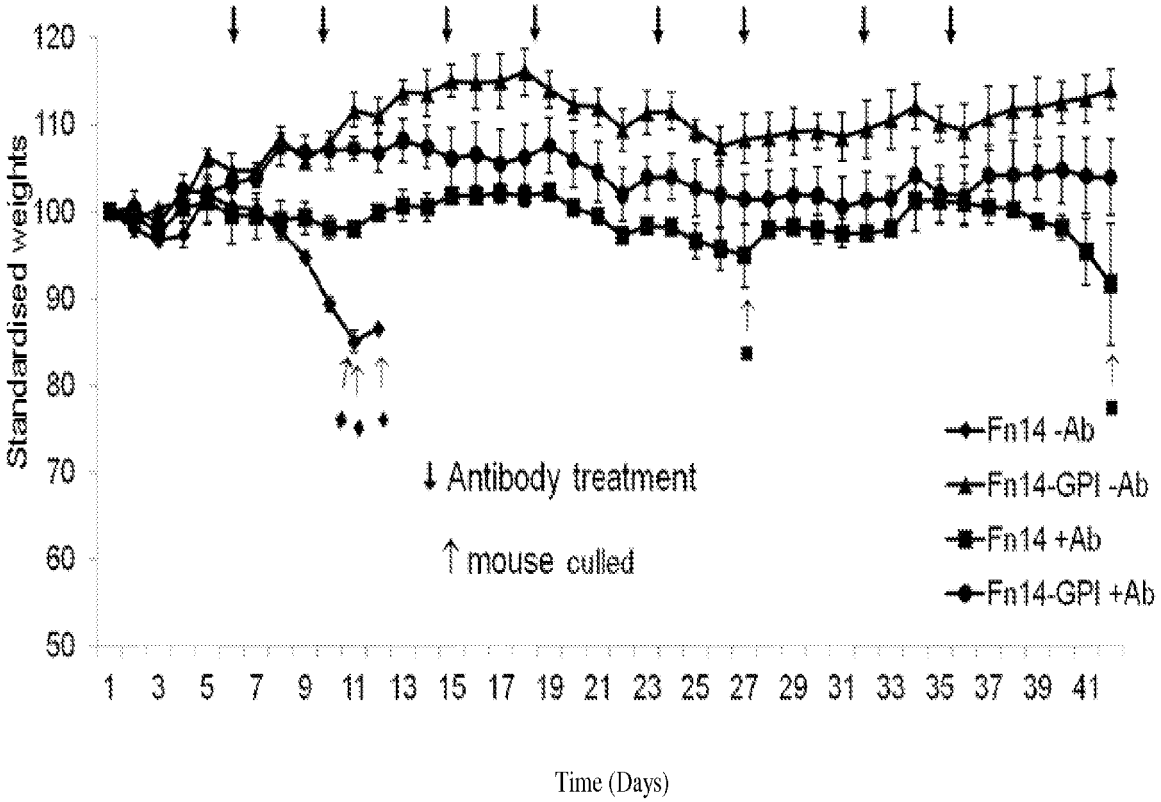

Standardised weights
120
110
100
90
80
70
60
50
1 3 5 7 9 11 13 15 17 19 21 23 25 27 29 31 33 35 37 39 41
Time (Days)
↓ Antibody treatment
↑ mouse culled
Fn14 -Ab
Fn14-GPI -Ab
Fn14 +Ab
Fn14-GPI +Ab

Figure 36

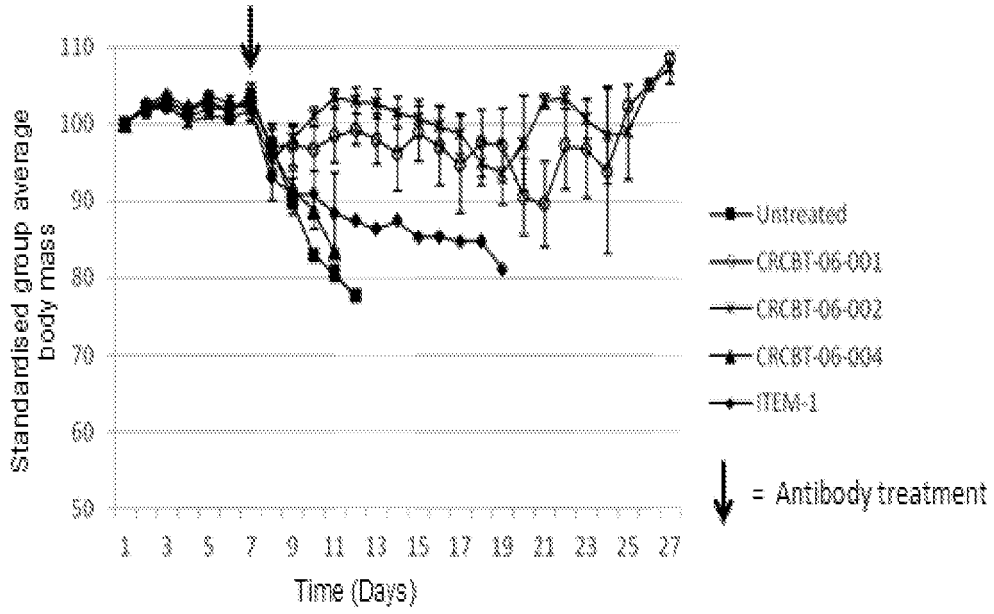

Standardised group average body mass
110
100
90
80
70
60
50
1 3 5 7 9 11 13 15 17 19 21 23 25 27
Time (Days)
Untreated
CRCBT-06-001
CRCBT-06-002
CRCBT-06-004
ITEM-1
= Antibody treatment

Figure 37A

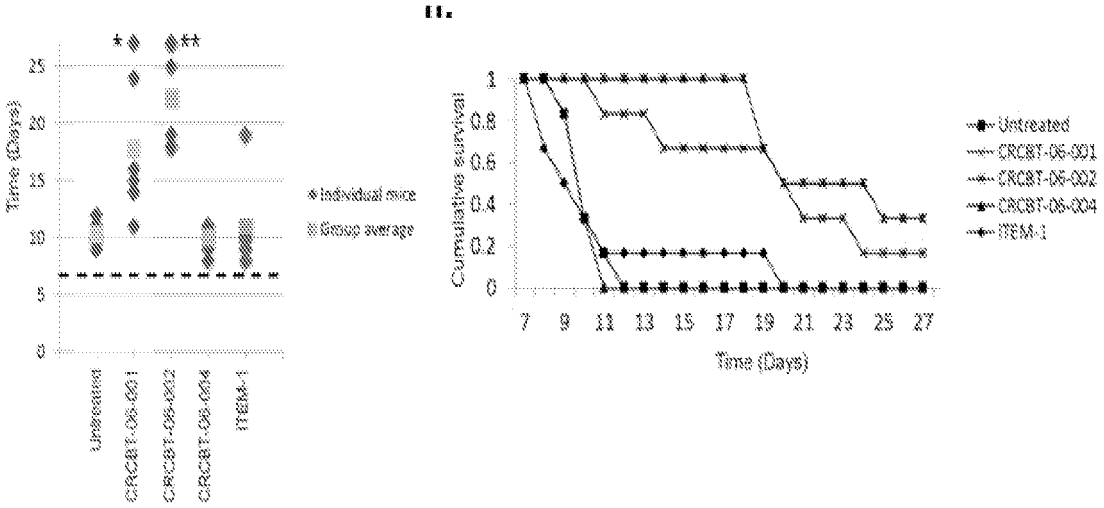

Time (Days)
Individual mice
Group average
Untreated
CRCBT-06-001
CRCBT-06-002
CRCBT-06-004
ITEM-1
Cumulative survival
Time (Days)
Untreated
CRCBT-06-001
CRCBT-06-002
CRCBT-06-004
ITEM-1

Figure 37B

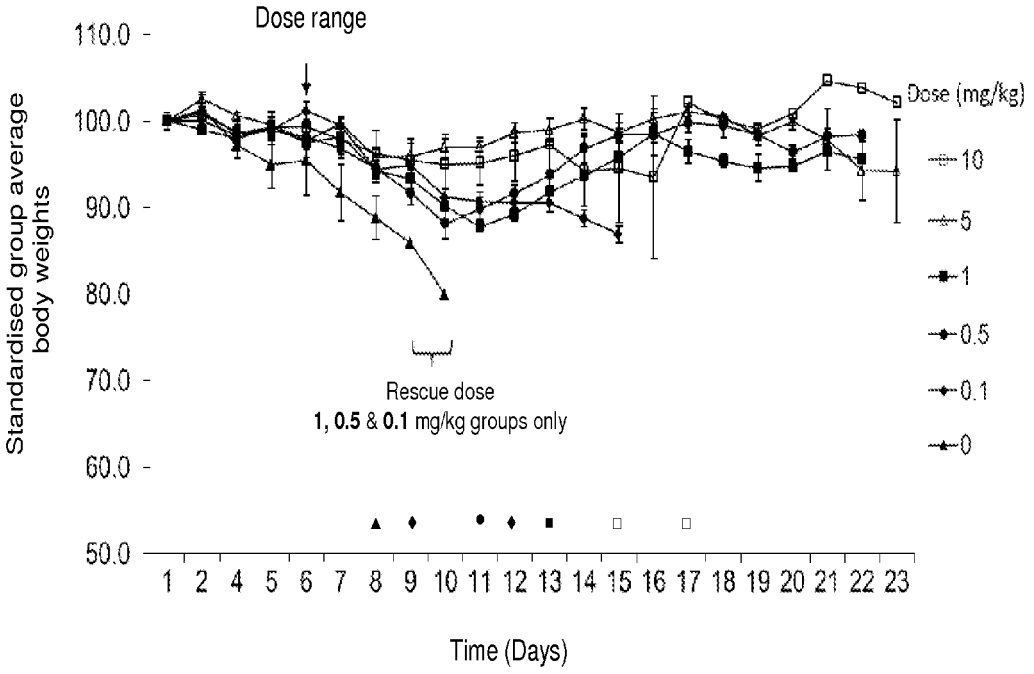

Dose range
110.0
100.0
90.0
80.0
70.0
60.0
50.0
Standardised group average body weights
Dose (mg/kg)
10
5
1
0.5
0.1
0
Rescue dose
1, 0.5 & 0.1 mg/kg groups only
1 2 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23
Time (Days)

Figure 38

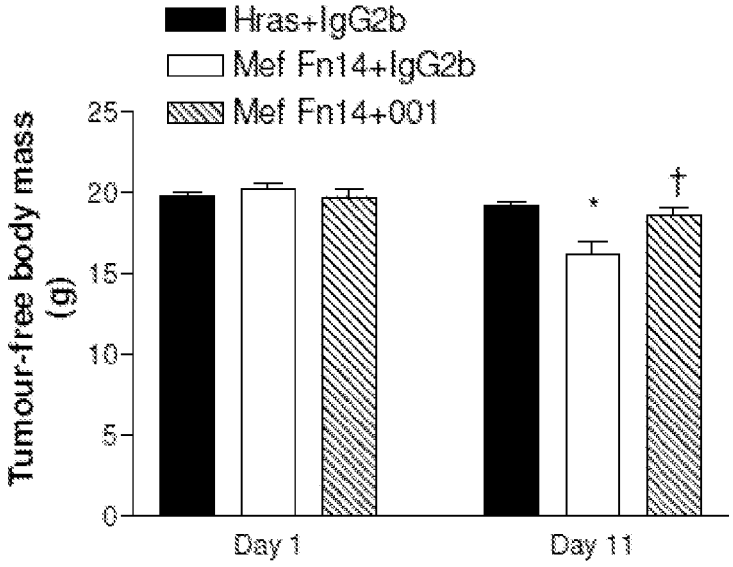


Figure 39A

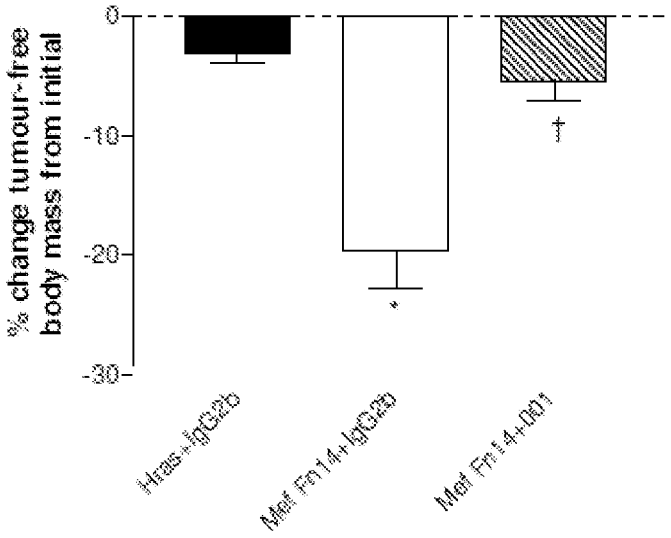


Figure 39B

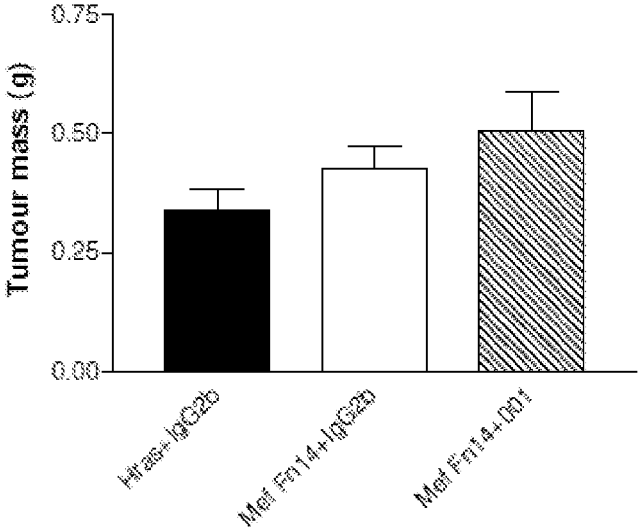


Figure 40A

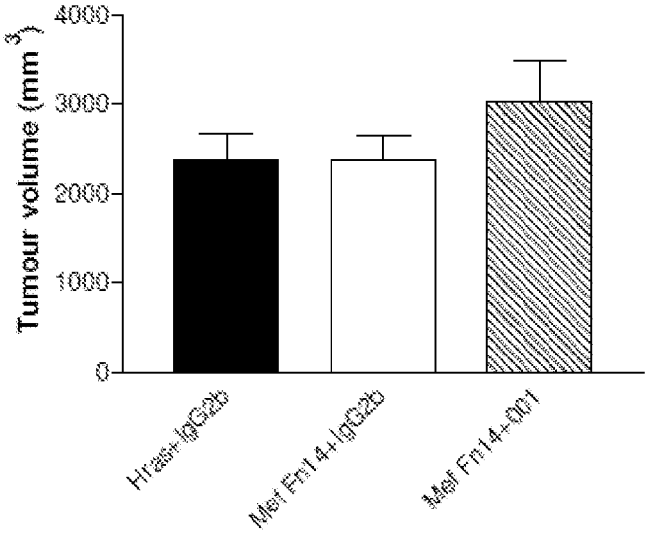


Figure 40B

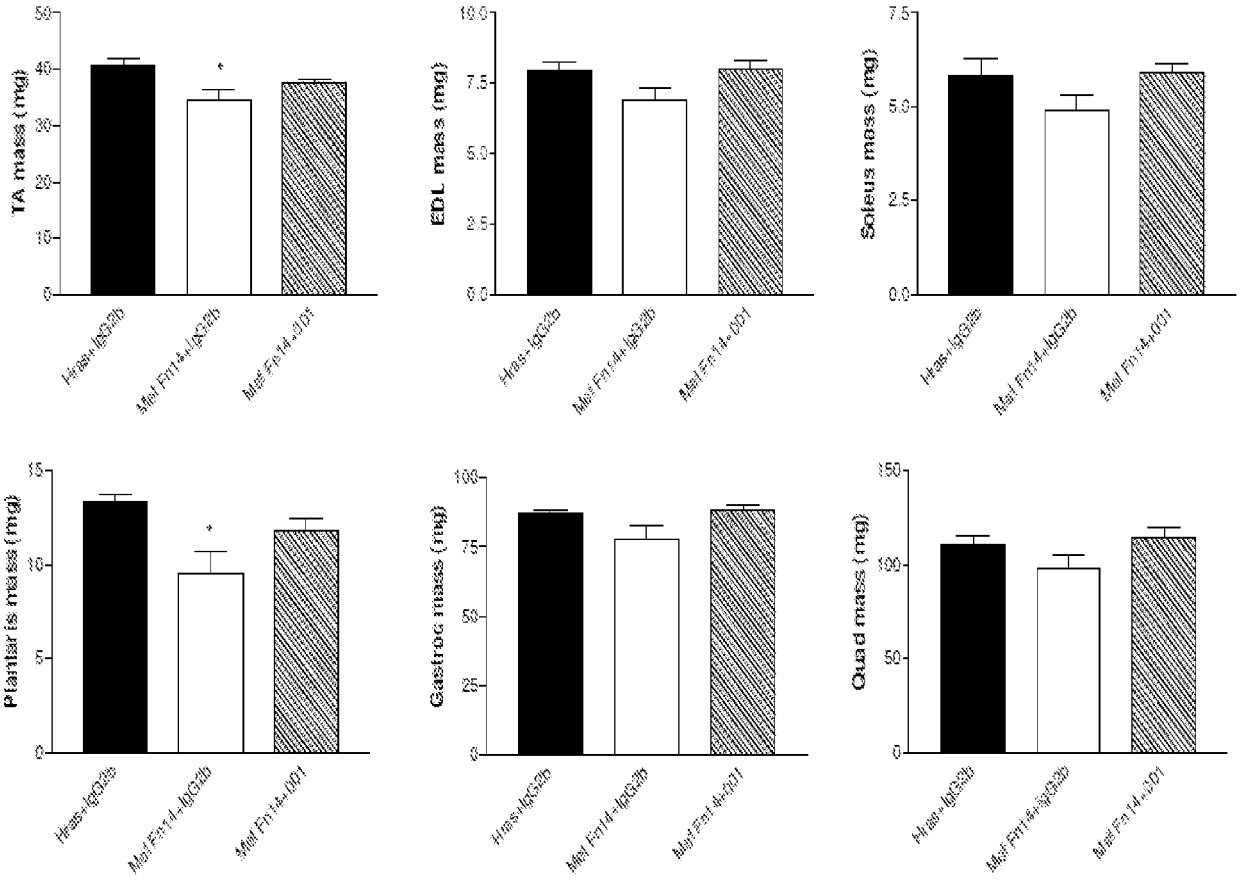

TA mass (mg)
EDL mass (mg)
Soleus mass (mg)
Plantaris mass (mg)
Gastroc mass (mg)
Quad mass (mg)
Hu-Fn14-IgG2b
Mu-Fn14-IgG2b
Mu-Fn14-001

Figure 41A

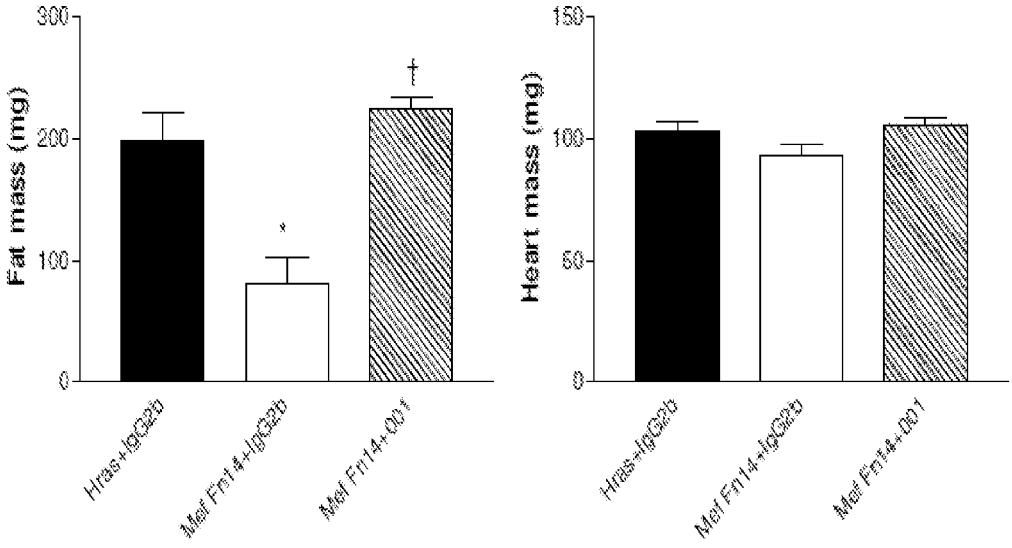

Fat mass (mg)
300
200
100
0
*
†
Hras+IgG2b
Mef Fn14+IgG2b
Mef Fn14+Dc1
Heart mass (mg)
150
100
50
0
Hras+IgG2b
Mef Fn14+IgG2b
Mef Fn14+Dc1

Figure 41B

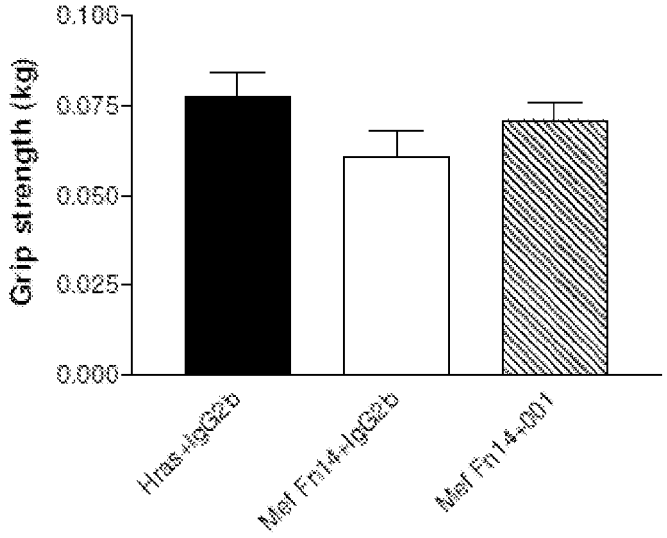


Figure 42A

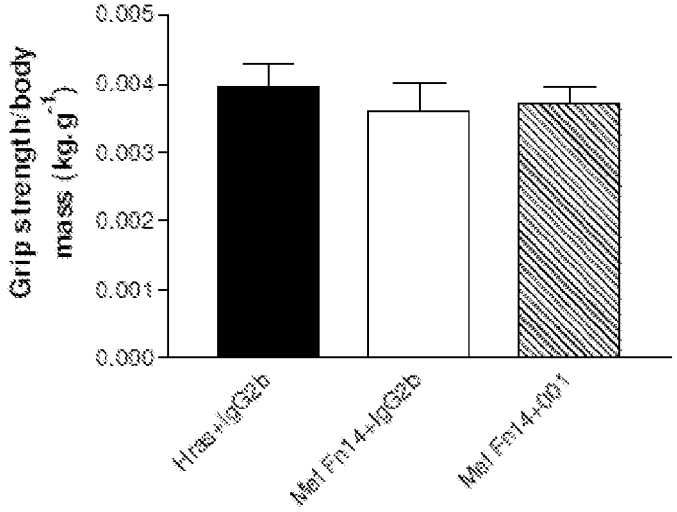


Figure 42B

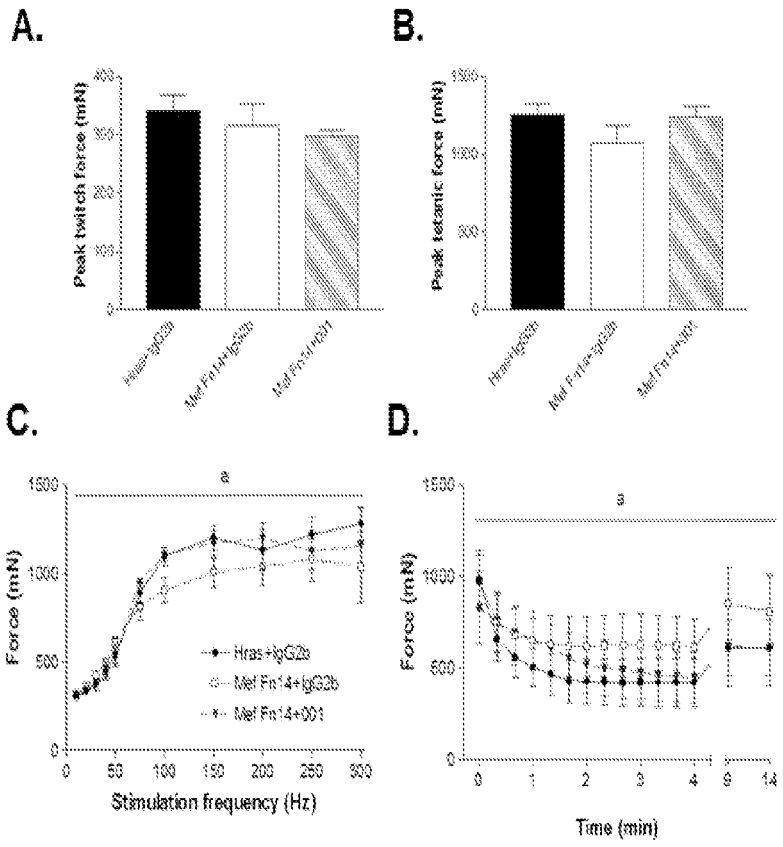

A.
B.
Peak twitch force (mN)
Peak tetanic force (mN)
C.
D.
Force (mN)
Stimulation frequency (Hz)
Time (min)
Hras+IgG2b
Mel Fn14+IgG2b
Mel Fn14+001
a

Figure 43

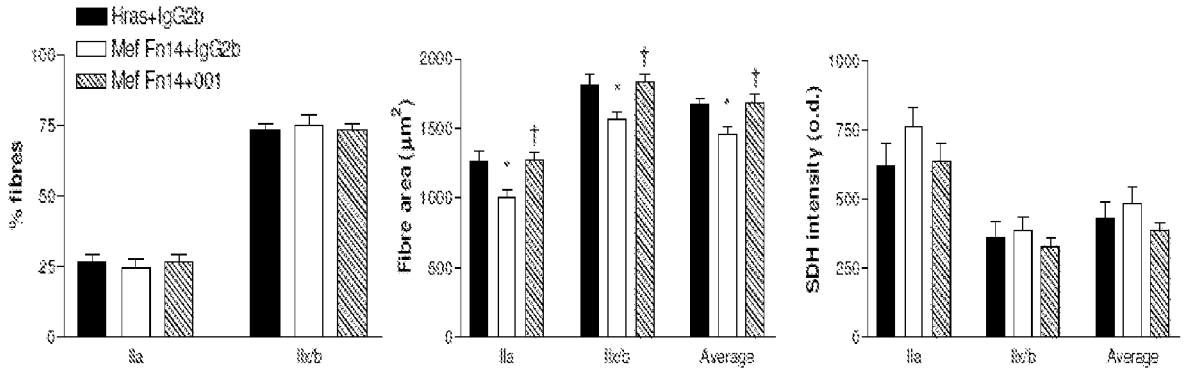

Hras+IgG2b
Mef Fn14+IgG2b
Mef Fn14+001
% fibres
Fibre area (µm²)
SDH intensity (o.d.)
IIa
IIx/b
Average

Figure 44

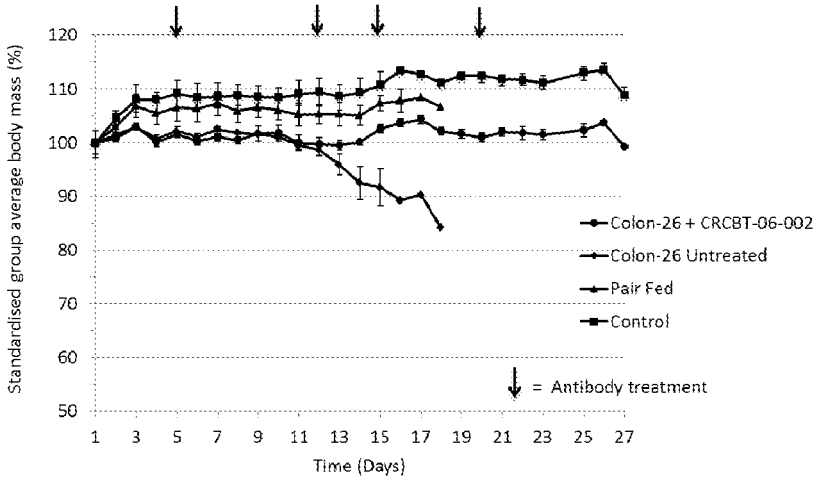


Figure 45A

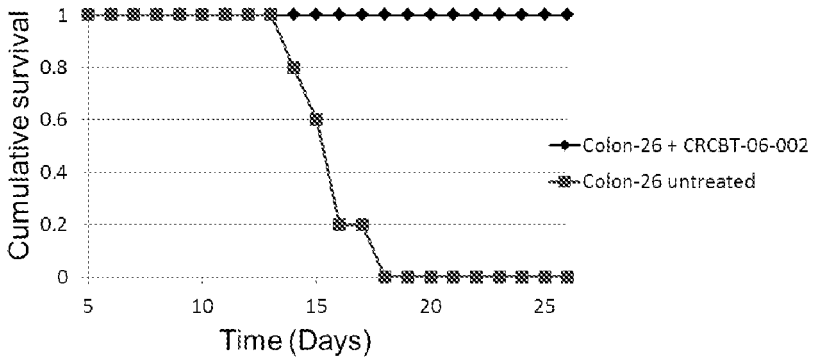


Figure 45B

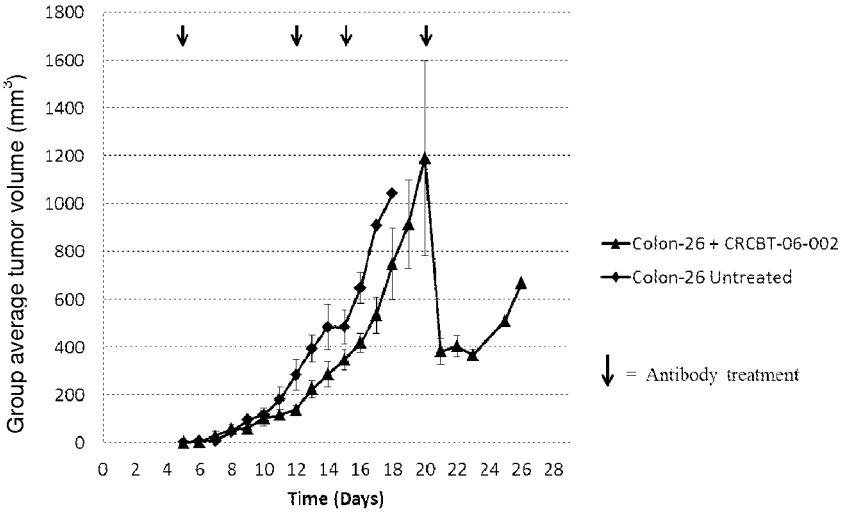


Figure 46A

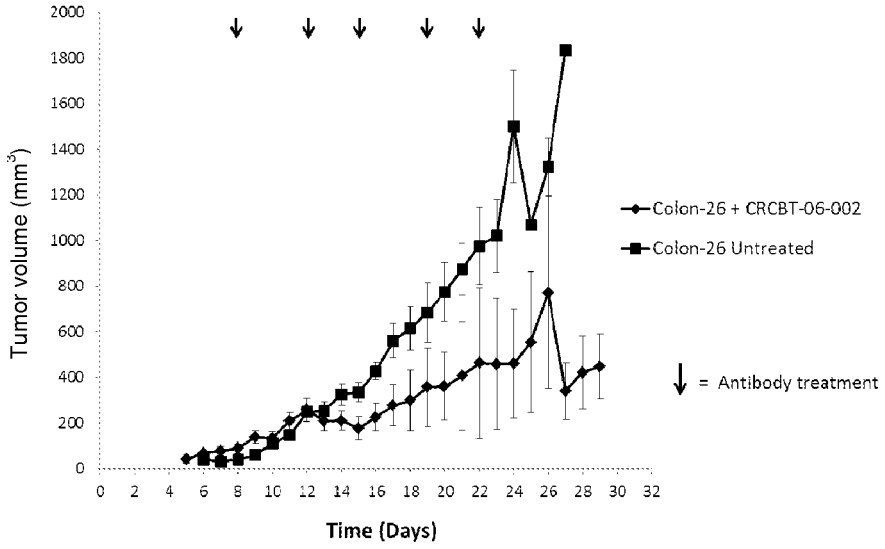


Figure 46B

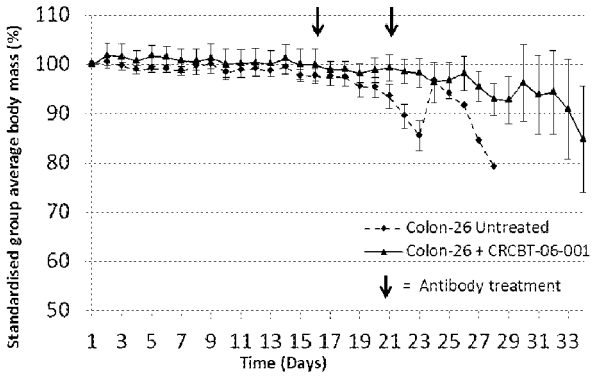


Figure 47A

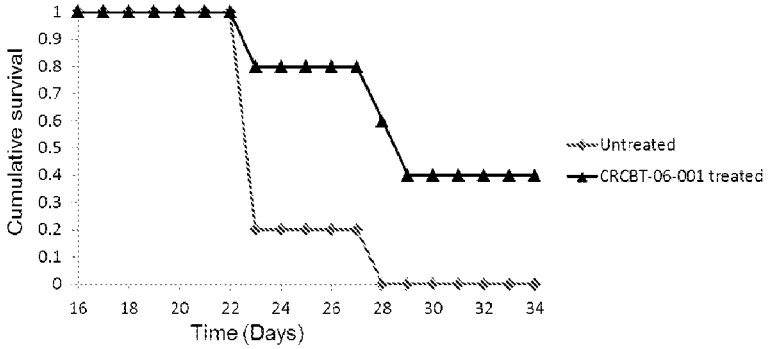


Figure 47B

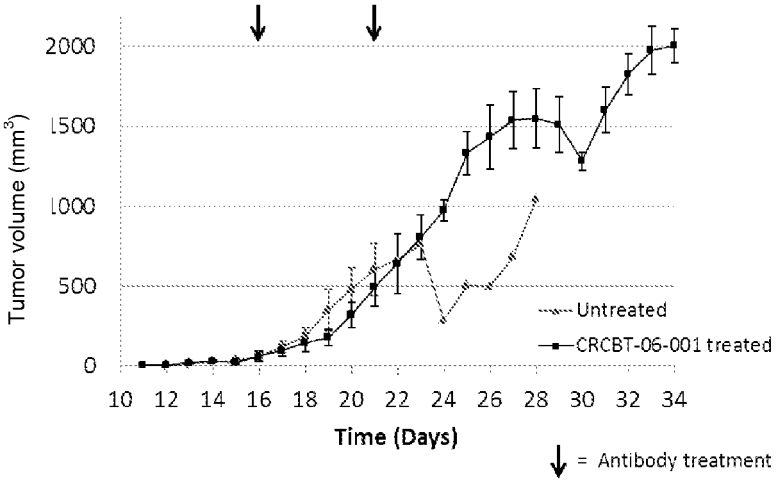


Figure 47C

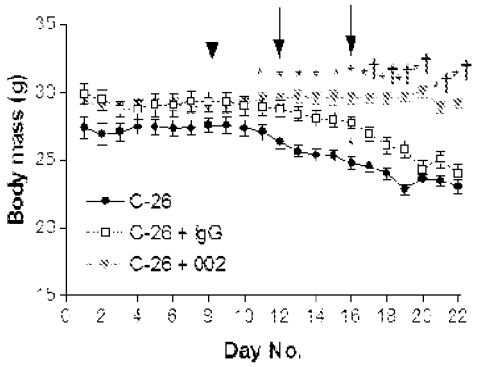


Figure 48A

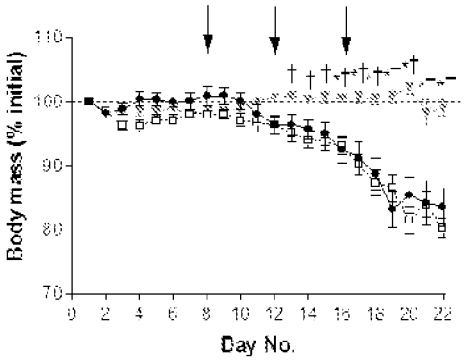


Figure 49B

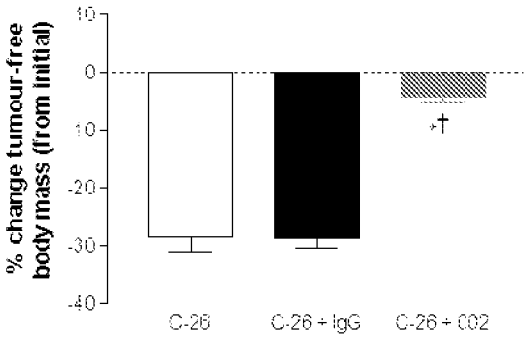


Figure 48C

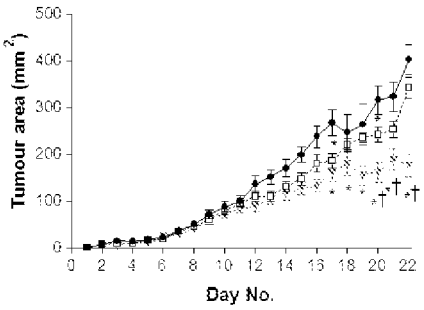


Figure 49A

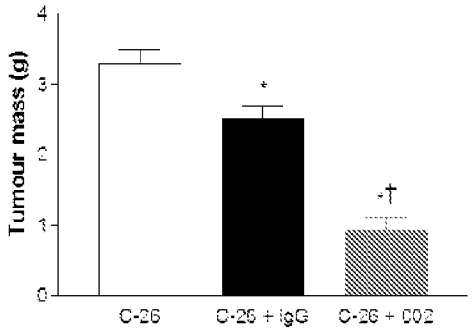


Figure 49B

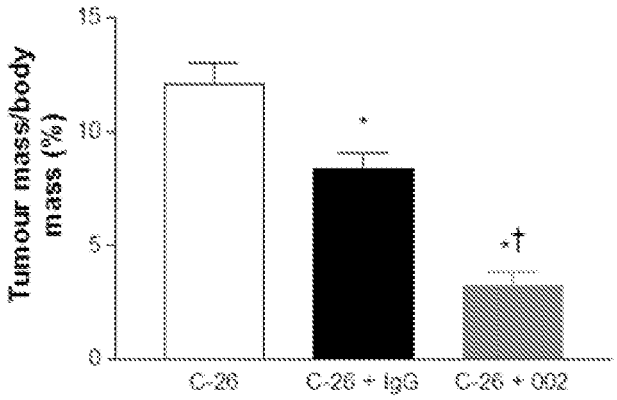


Figure 49C

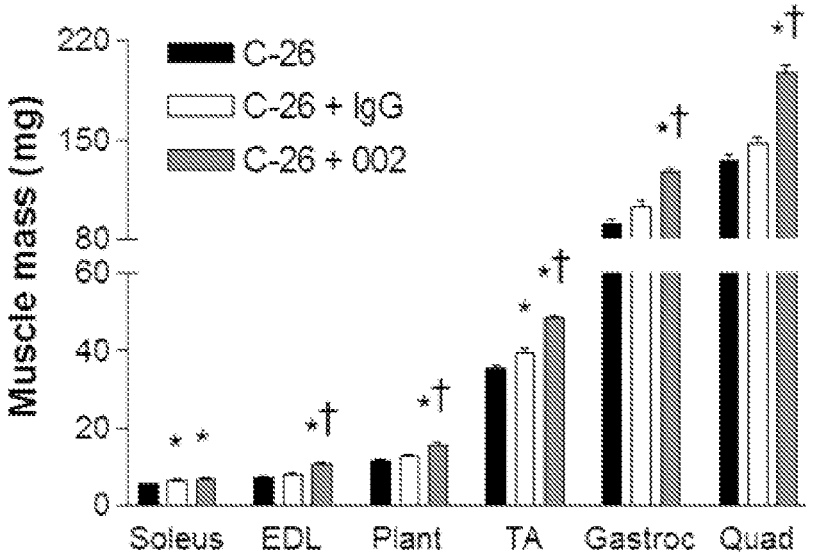


Figure 50A

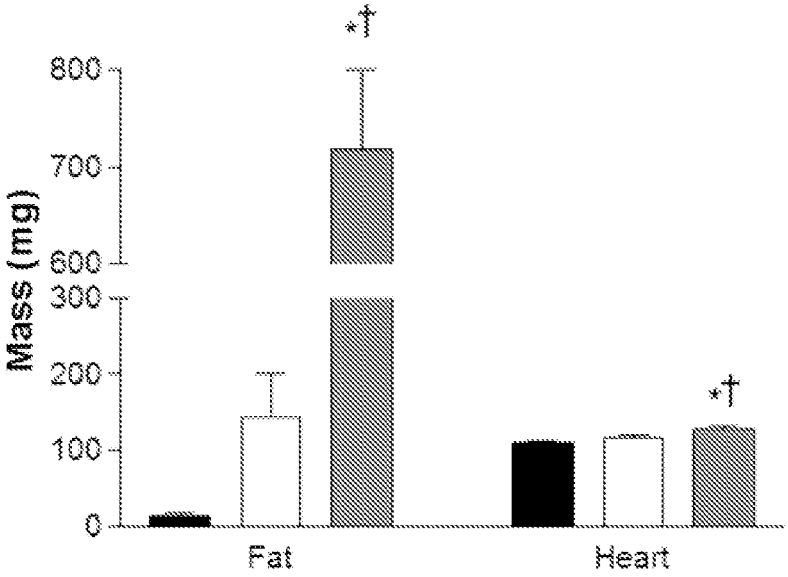


Figure 50B

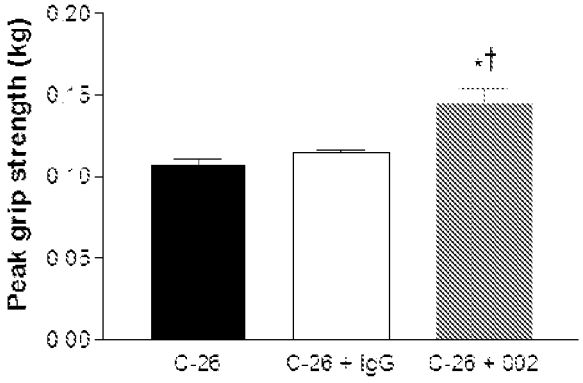


Figure 51A

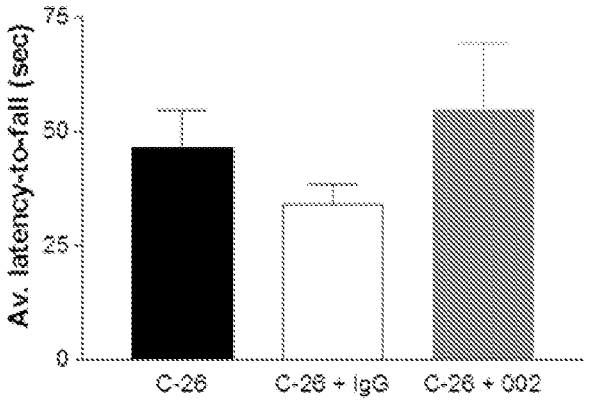


Figure 51B

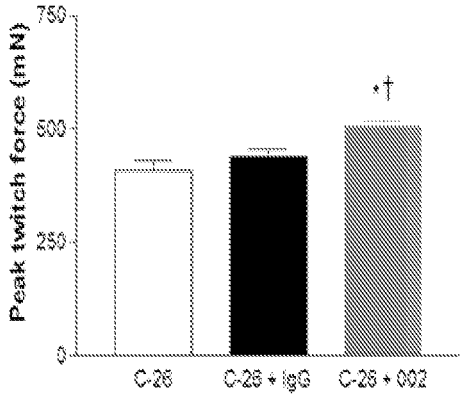


Figure 52A

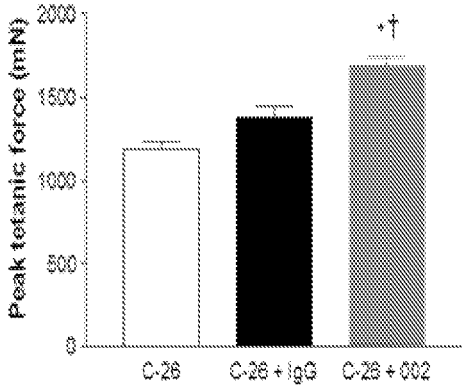


Figure 52B

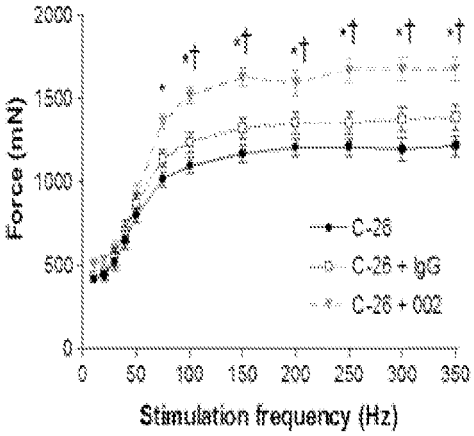


Figure 52C

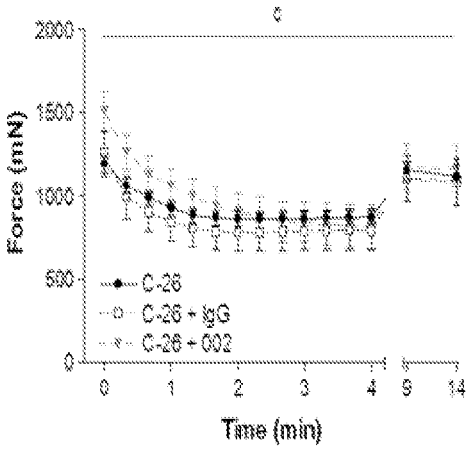


Figure 52D

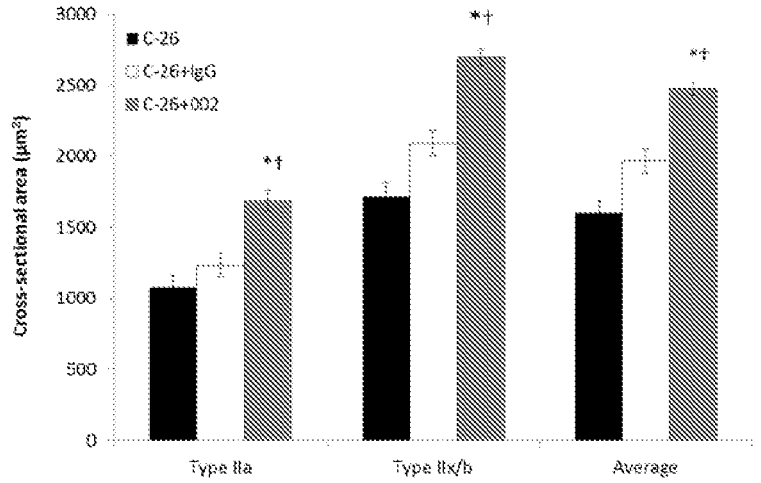


Figure 53A

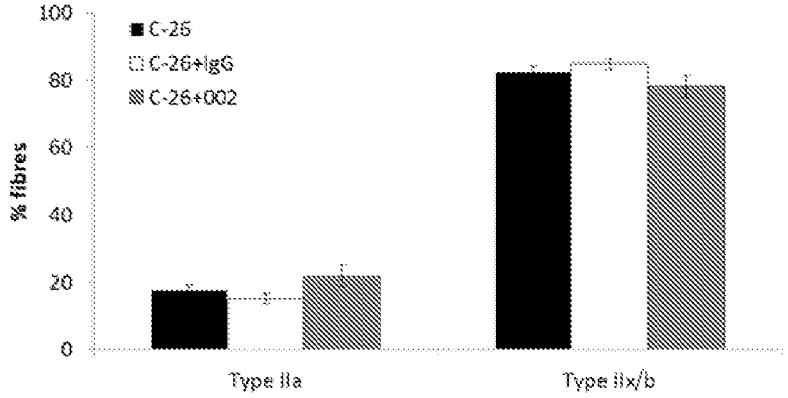


Figure 53B

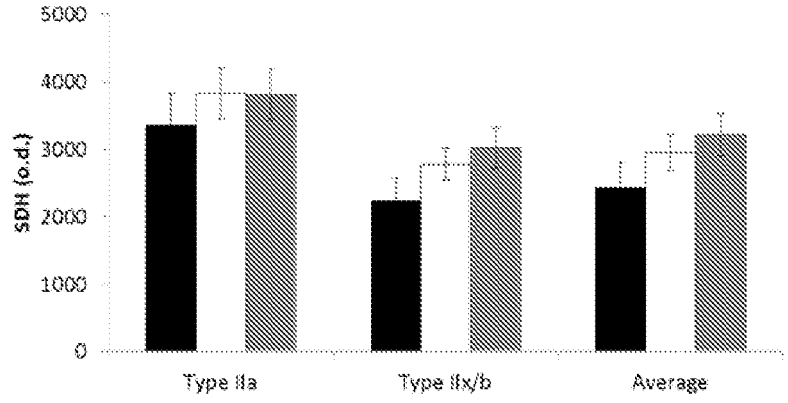


Figure 53C

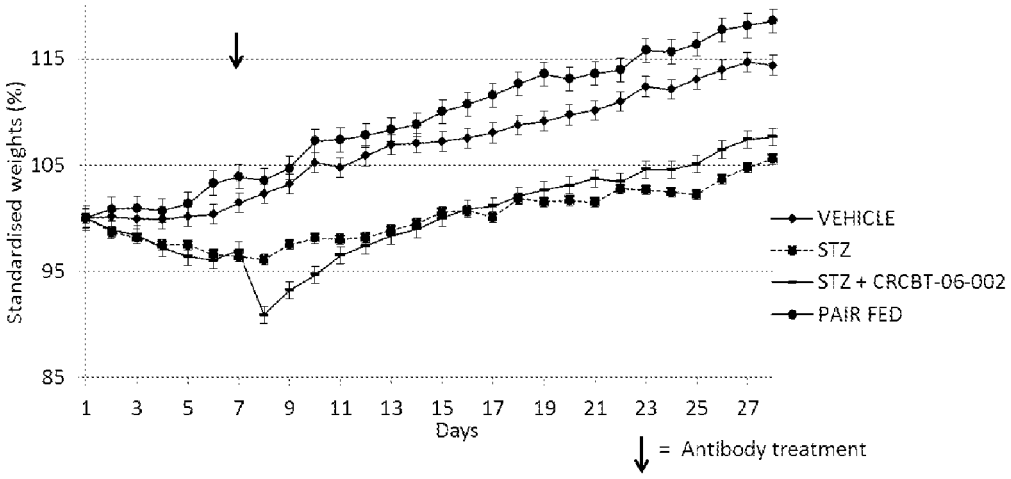


Figure 54

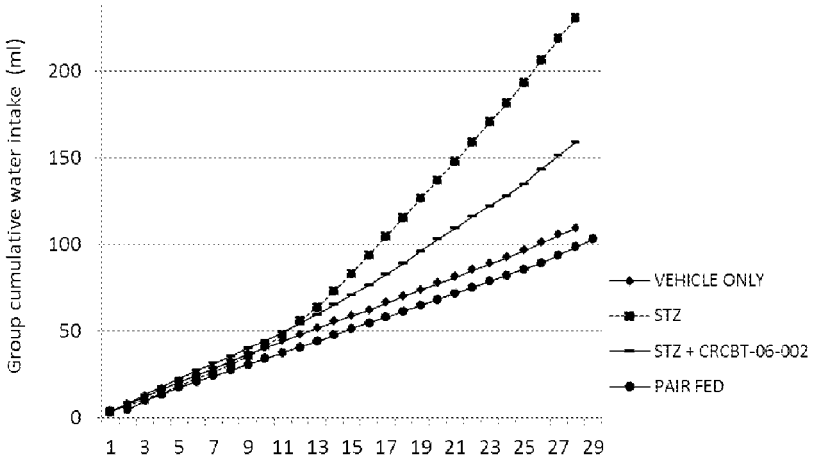


Figure 55

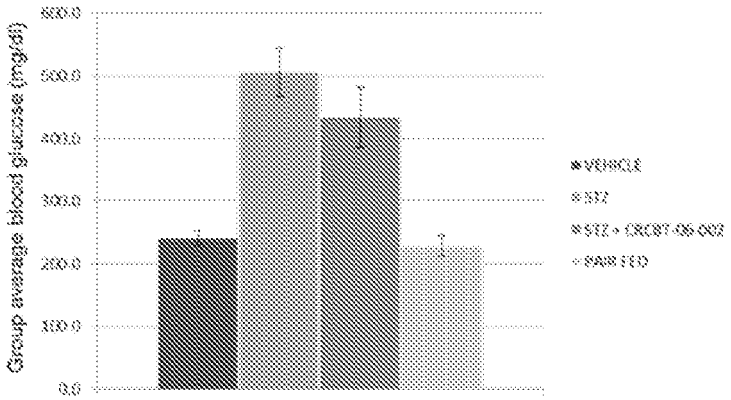


Figure 56

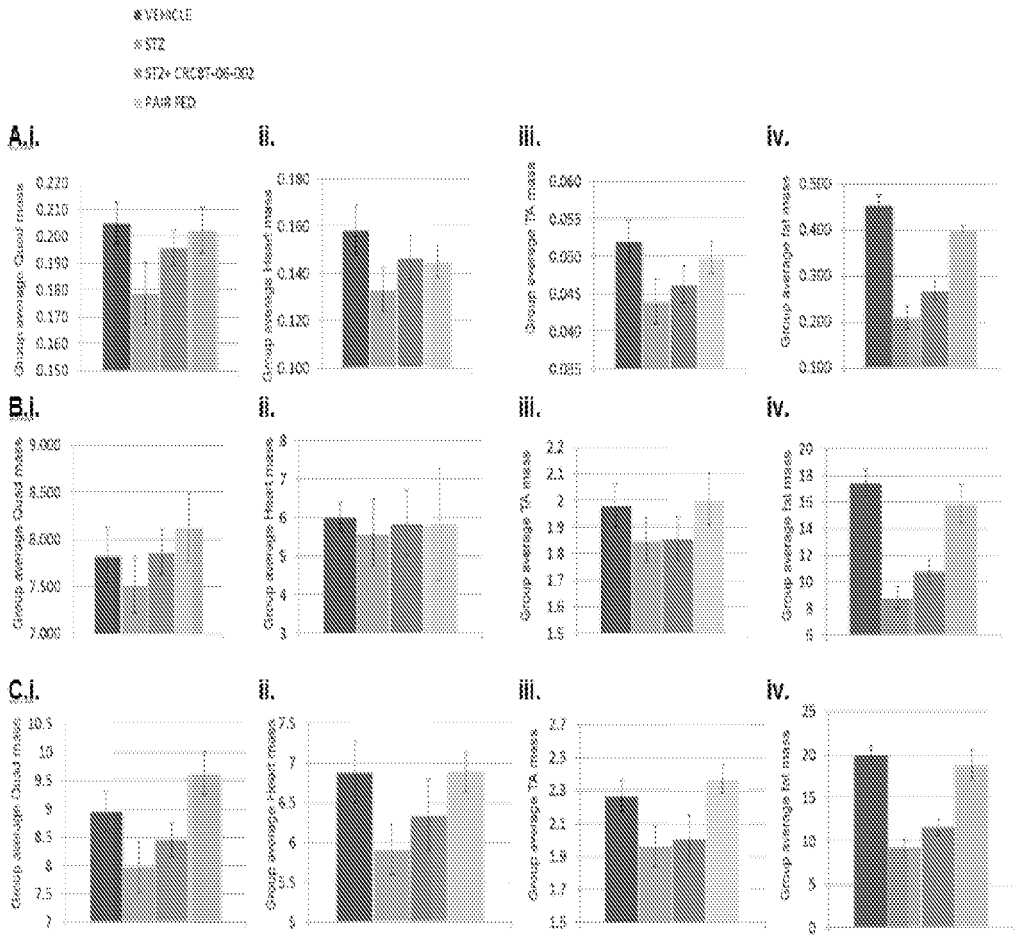

VEHICLE
STZ
STZ+ CRC87-06-002
PAIR FED
A.i.
ii.
iii.
iv.
B.i.
ii.
iii.
iv.
C.i.
ii.
iii.
iv.

Figure 57