FIG. 1

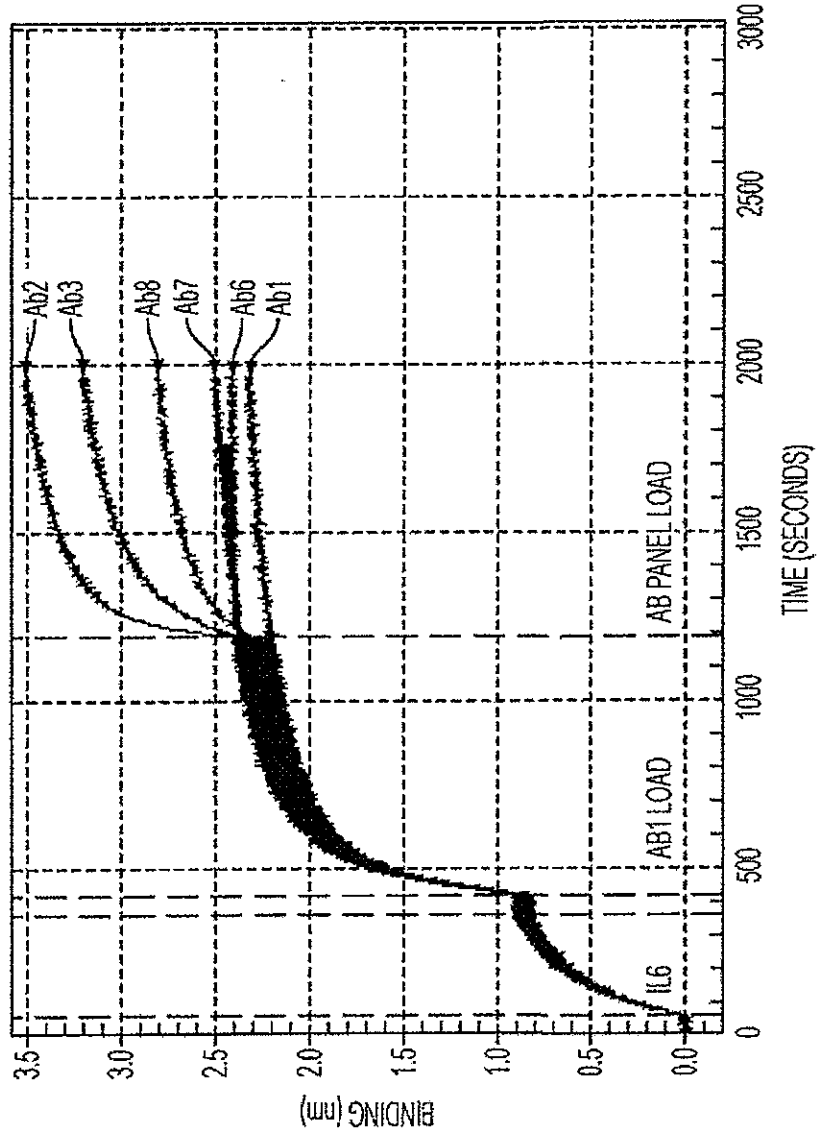

Ab2
Ab3
Ab8
Ab7
Ab6
Ab1
IL6
AB1 LOAD
AB PANEL LOAD
BINDING (nm)
TIME (SECONDS)
0.0
0.5
1.0
1.5
2.0
2.5
3.0
3.5
0
500
1000
1500
2000
2500
3000

FIG. 2

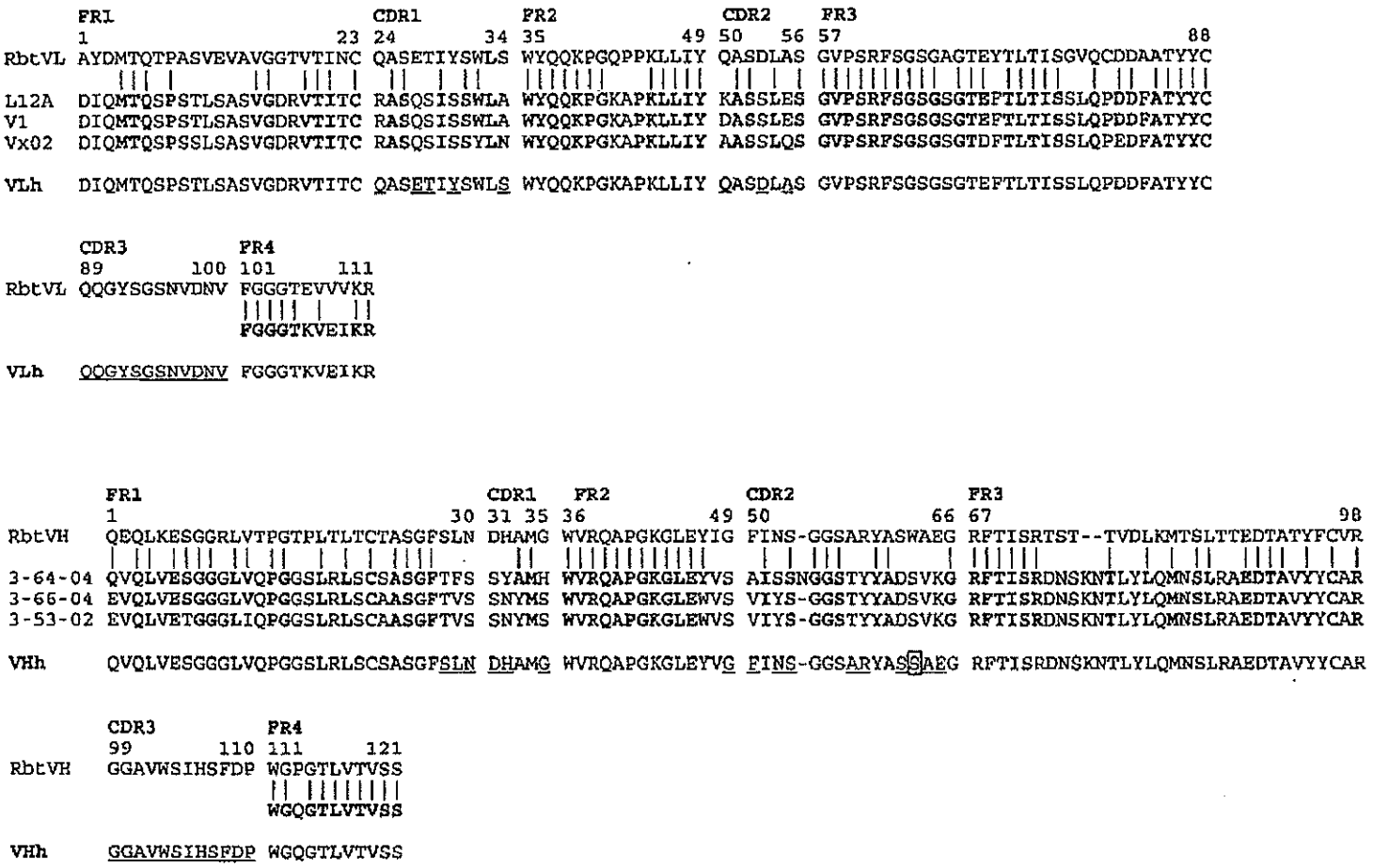

FR1 CDR1 FR2 CDR2 FR3
1 23 24 34 35 49 50 56 57 88
RbtVL AYDMTQTPASVEVAVGGTVTINC QASETIYSWLS WYQQKPGQPPKLLIY QASDLAS GVPSRFSGSGAGTEYTLTISGVQCDDAATYYC
L12A DIQMTQSPSTLSASVGDRVTITC RASQSISSWLA WYQQKPGKAPKLLIY KASSLES GVPSRFSGSGSGTEFTLTISSLQPDDFATYYC
V1 DIQMTQSPSTLSASVGDRVTITC RASQSISSWLA WYQQKPGKAPKLLIY DASSLES GVPSRFSGSGSGTEFTLTISSLQPDDFATYYC
Vx02 DIQMTQSPSSLSASVGDRVTITC RASQSISSYLN WYQQKPGKAPKLLIY AASSLQS GVPSRFSGSGSGTDFTLTISSLQPEDFATYYC
VLh DIQMTQSPSTLSASVGDRVTITC QASETIYSWLS WYQQKPGKAPKLLIY QASDLAS GVPSRFSGSGSGTEFTLTISSLQPDDFATYYC
CDR3 FR4
89 100 101 111
RbtVL QQGYSGSNVDNV FGGGTEVVVKR
FGGGTKVEIKR
VLh QQGYSGSNVDNV FGGGTKVEIKR
FR1 CDR1 FR2 CDR2 FR3
1 30 31 35 36 49 50 66 67 98
RbtVH QEQLKESGGRLVTPGTPLTLTCTASGFSLN DHAMG WVRQAPGKGLEYIG FINS-GGSARYASWAEG RFTISRTST--TVDLKMTSLTTEDTATYFCVR
3-64-04 QVQLVESGGGLVQPGGSLRLSCSASGFTFS SYAMH WVRQAPGKGLEYVS AISSNGGSTYYADSVKG RFTISRDNSKNTLYLQMNSLRAEDTAVYYCAR
3-66-04 EVQLVESGGGLVQPGGSLRLSCAASGFTVS SNYMS WVRQAPGKGLEWVS VIYS-GGSTYYADSVKG RFTISRDNSKNTLYLQMNSLRAEDTAVYYCAR
3-53-02 EVQLVETGGGLIQPGGSLRLSCAASGFTVS SNYMS WVRQAPGKGLEWVS VIYS-GGSTYYADSVKG RFTISRDNSKNTLYLQMNSLRAEDTAVYYCAR
VHh QVQLVESGGGLVQPGGSLRLSCSASGFSLN DHAMG WVRQAPGKGLEYVG FINS-GGSARYASSAEG RFTISRDNSKNTLYLQMNSLRAEDTAVYYCAR
CDR3 FR4
99 110 111 121
RbtVH GGAVWSIHSFDP WGPGTLVTVSS
WGQGTLVTVSS
VHh GGAVWSIHSFDP WGQGTLVTVSS

FIG. 3

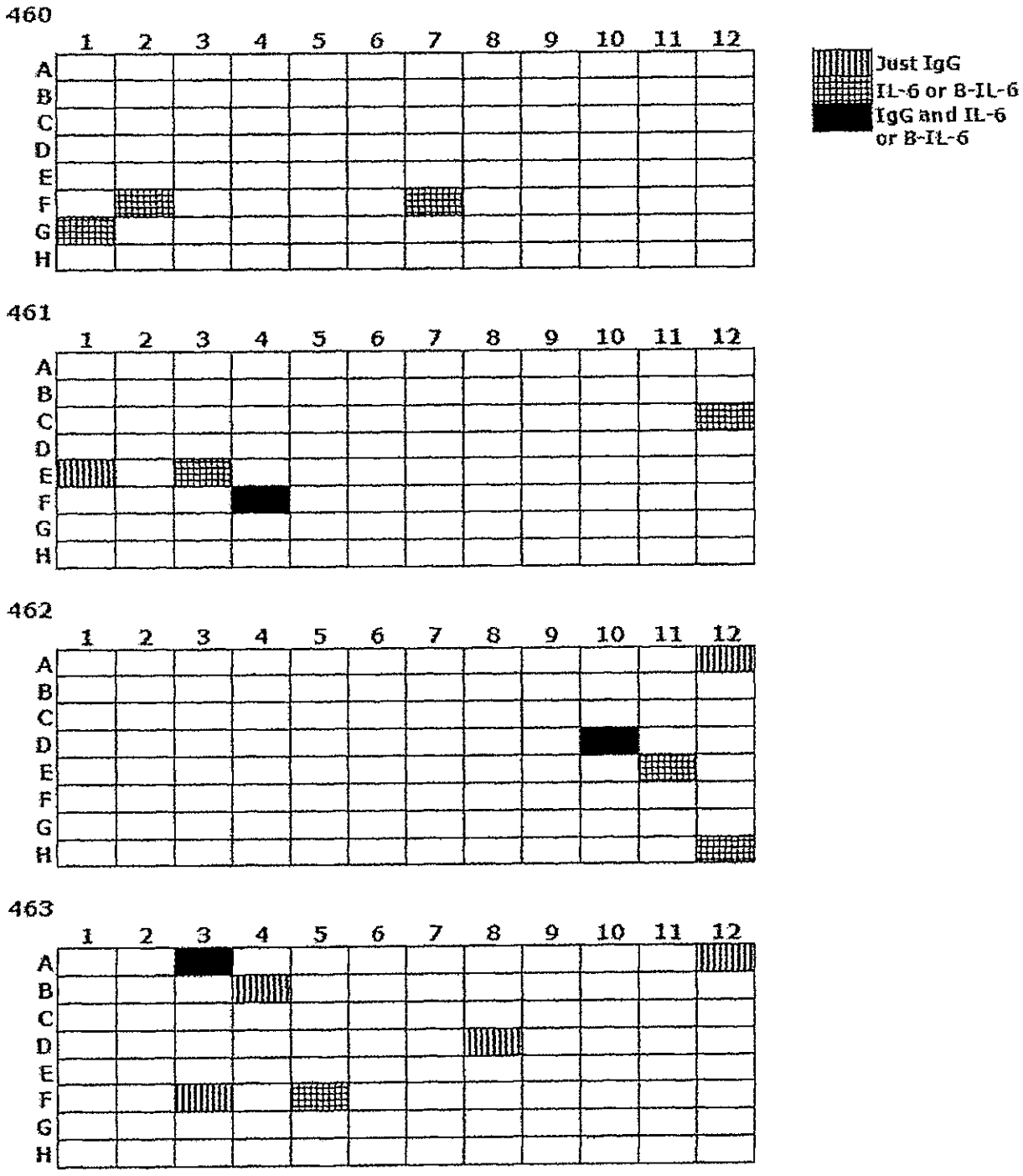

460
1 2 3 4 5 6 7 8 9 10 11 12
A
B
C
D
E
F
G
H
461
462
463
Just IgG
IL-6 or B-IL-6
IgG and IL-6 or B-IL-6

FIG. 4

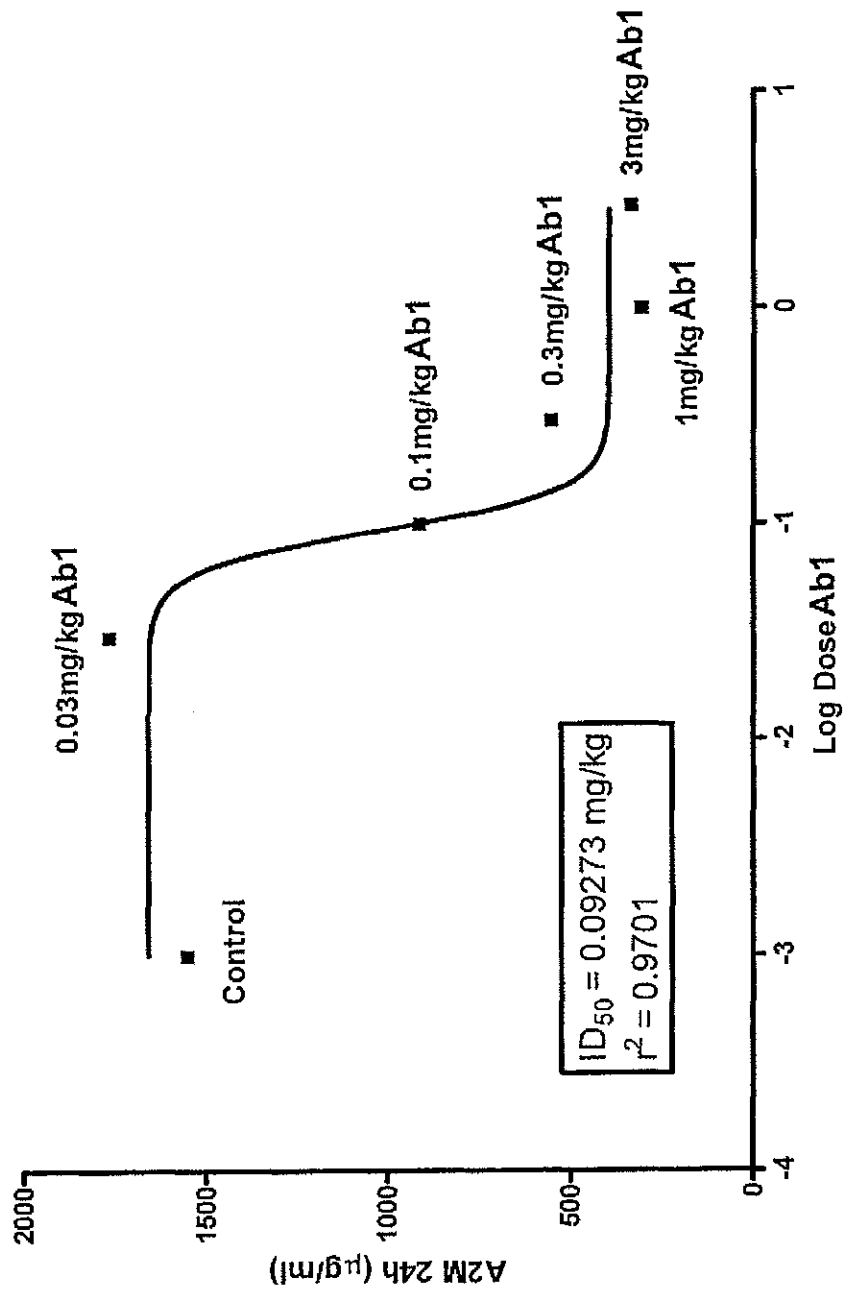

A2M 24h (µg/ml)
2000
1500
1000
500
0
-4
-3
-2
-1
0
1
Log Dose Ab1
Control
0.03mg/kg Ab1
0.1mg/kg Ab1
0.3mg/kg Ab1
1mg/kg Ab1
3mg/kg Ab1
ID50 = 0.09273 mg/kg
r2 = 0.9701

FIG. 5

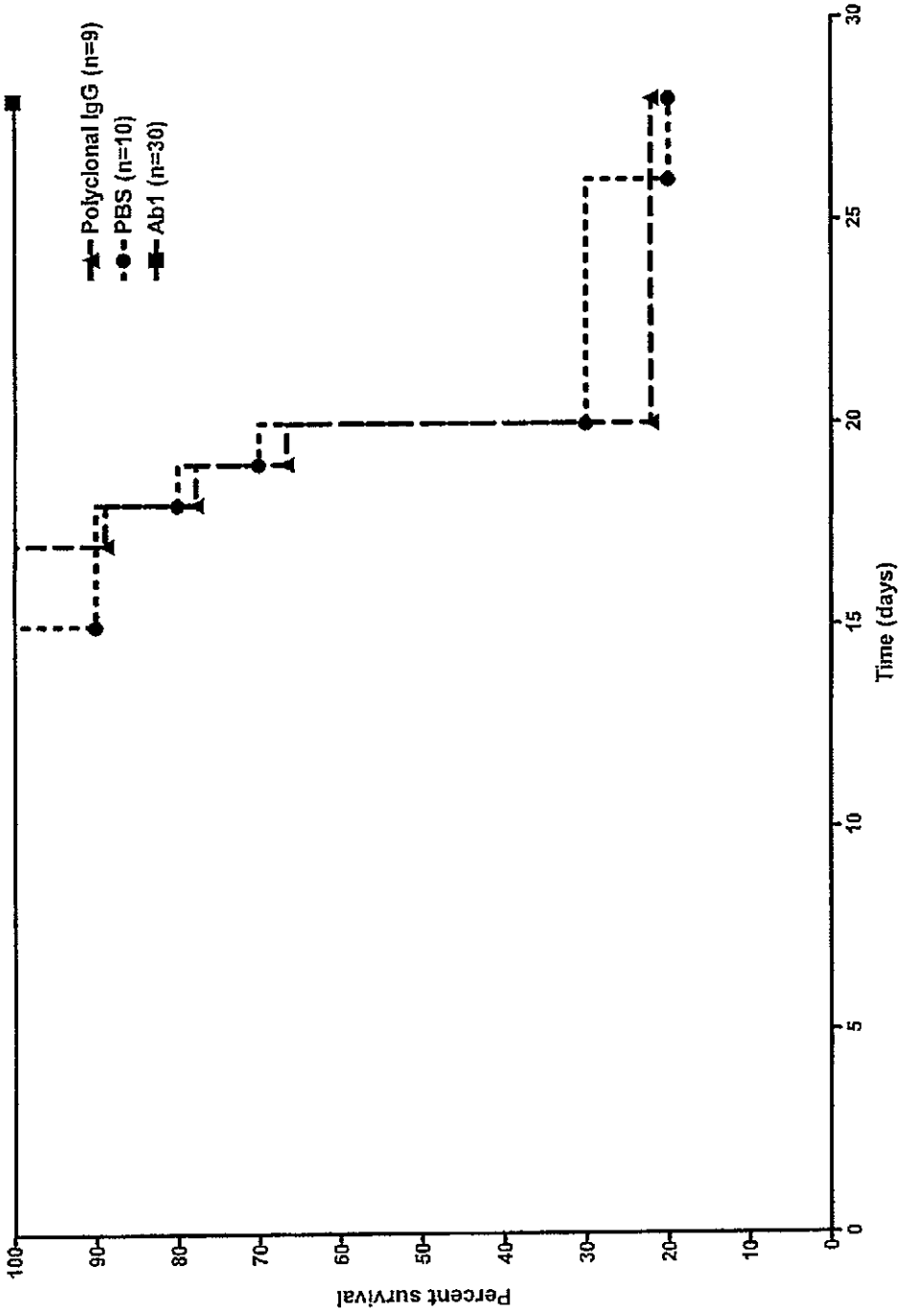

Polyclonal IgG (n=9)
PBS (n=10)
Ab1 (n=30)
Percent survival
Time (days)
100
90
80
70
60
50
40
30
20
10
0
0
5
10
15
20
25
30

FIG. 6

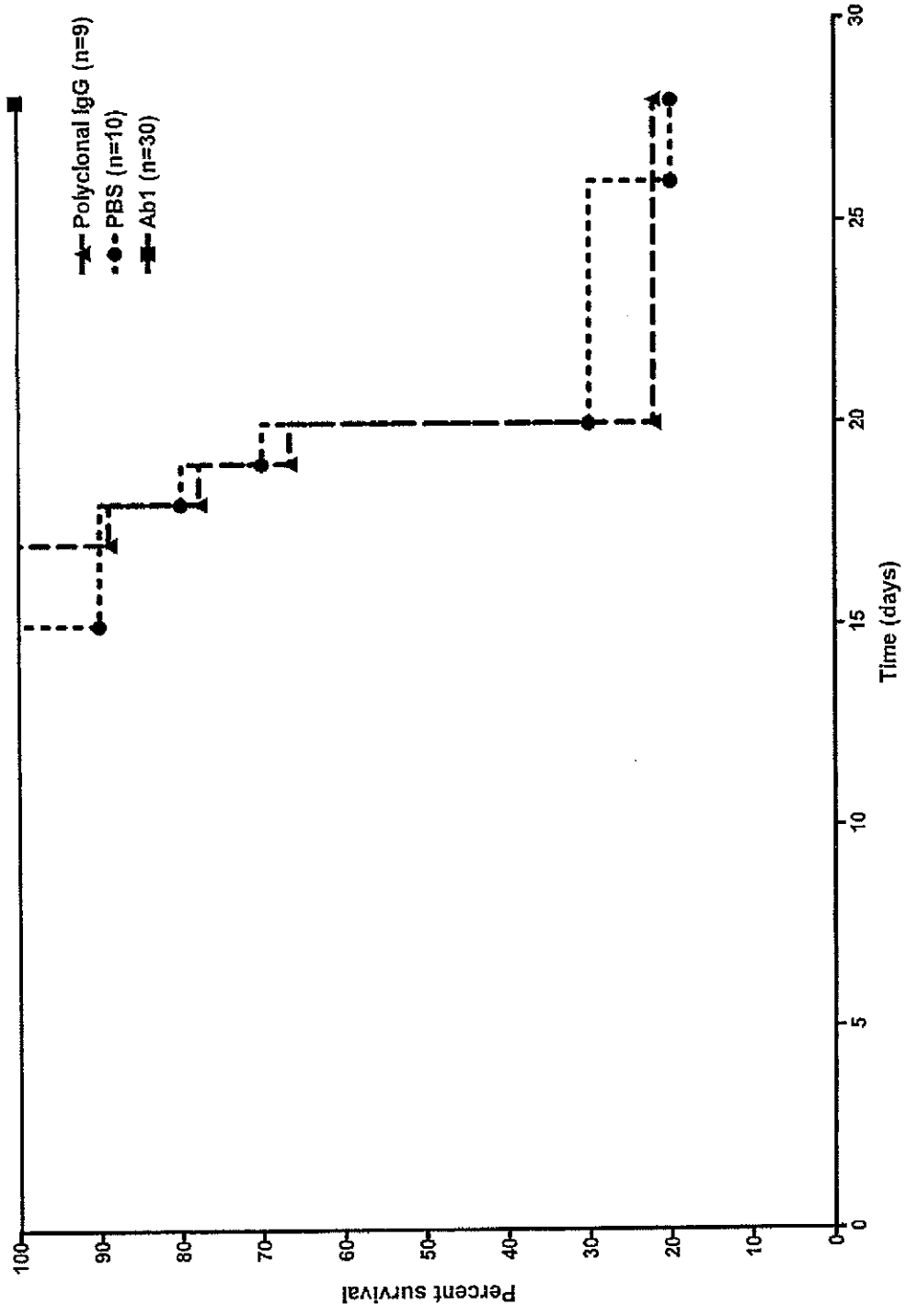

Polyclonal IgG (n=9)
PBS (n=10)
Ab1 (n=30)
Percent survival
Time (days)
100
90
80
70
60
50
40
30
20
10
0
0
5
10
15
20
25
30

FIG. 7

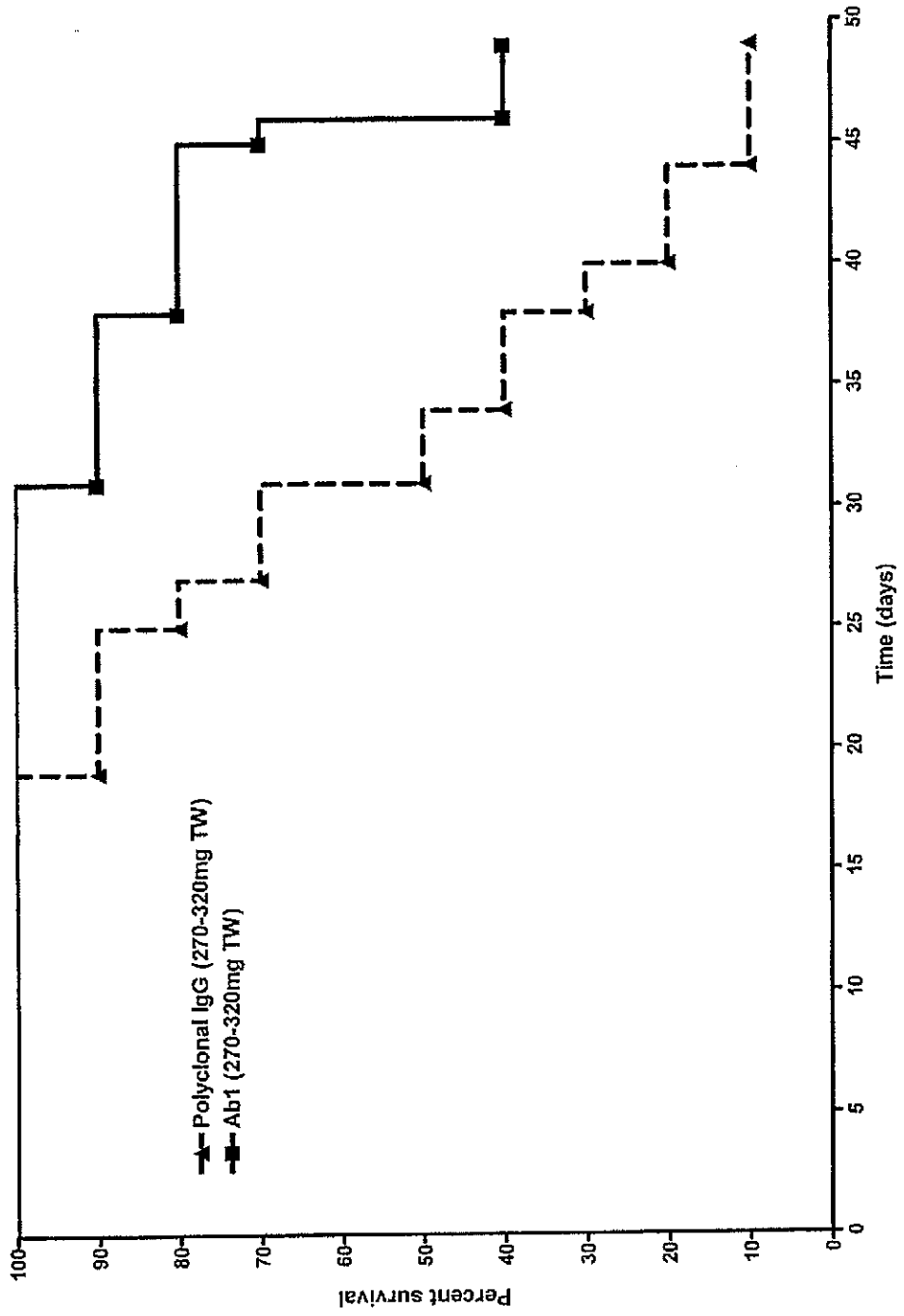

Polyclonal IgG (270-320mg TW)
Ab1 (270-320mg TW)
Percent survival
Time (days)
0
10
20
30
40
50
60
70
80
90
100
0
5
10
15
20
25
30
35
40
45
50

FIG. 8

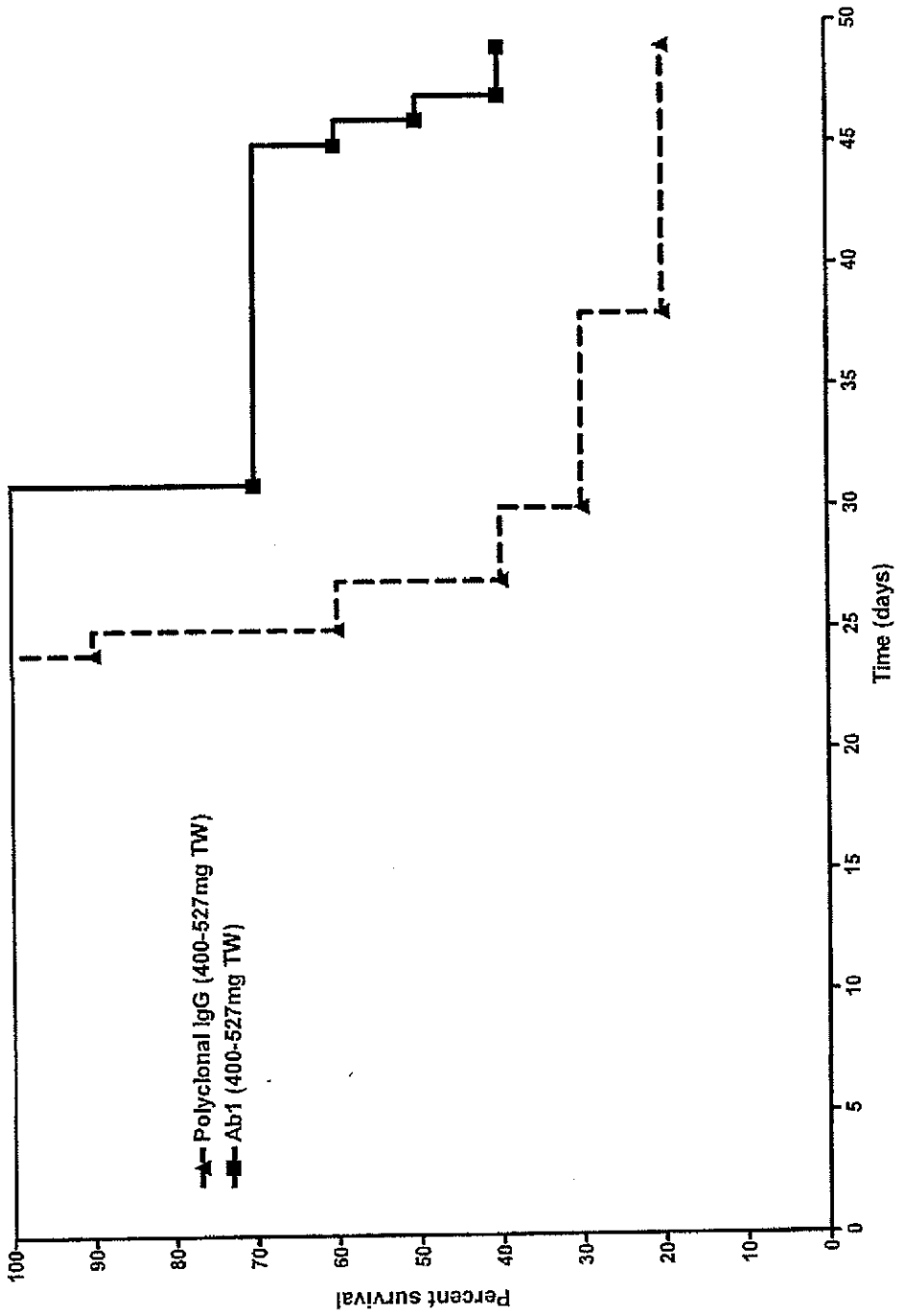

Percent survival
Time (days)
Polyclonal IgG (400-527mg TW)
Ab1 (400-527mg TW)
0
10
20
30
40
50
60
70
80
90
100
0
5
10
15
20
25
30
35
40
45
50

FIG. 9

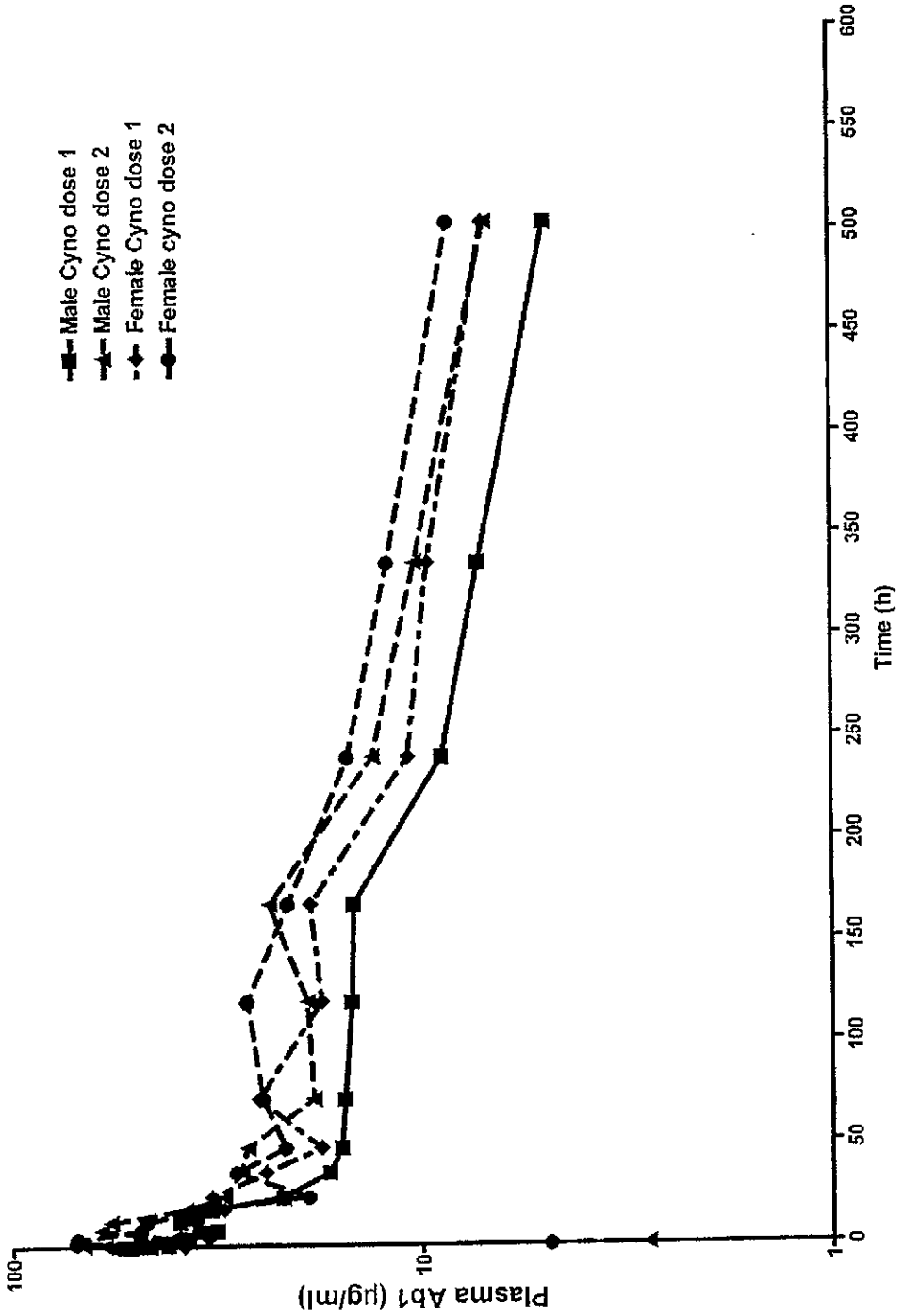

Male Cyno dose 1
Male Cyno dose 2
Female Cyno dose 1
Female cyno dose 2
Plasma Ab1 (µg/ml)
100
10
1
Time (h)
0
50
100
150
200
250
300
350
400
450
500
550
600

FIG. 10A

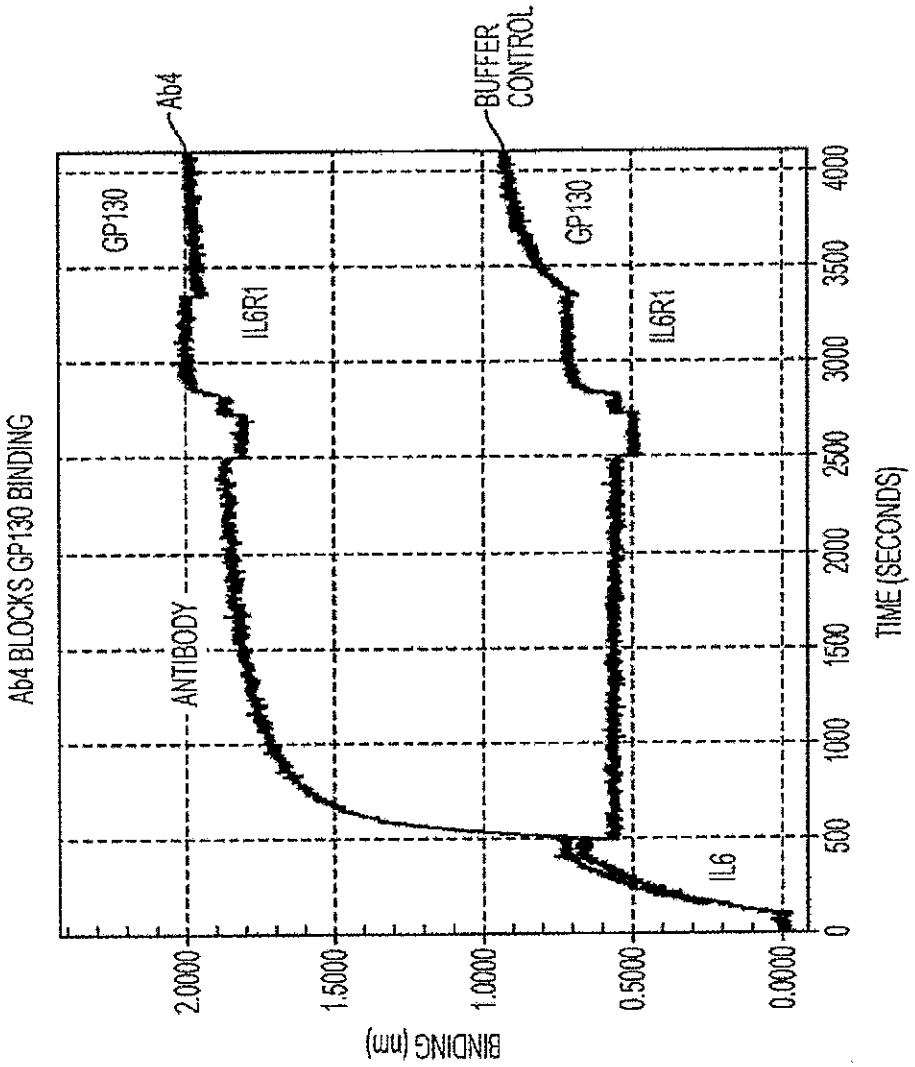

Ab4 BLOCKS GP130 BINDING
Ab4
BUFFER CONTROL
GP130
IL6R1
ANTIBODY
GP130
IL6R1
IL6
BINDING (nm)
2.0000
1.5000
1.0000
0.5000
0.0000
0
500
1000
1500
2000
2500
3000
3500
4000
TIME (SECONDS)

FIG. 10B

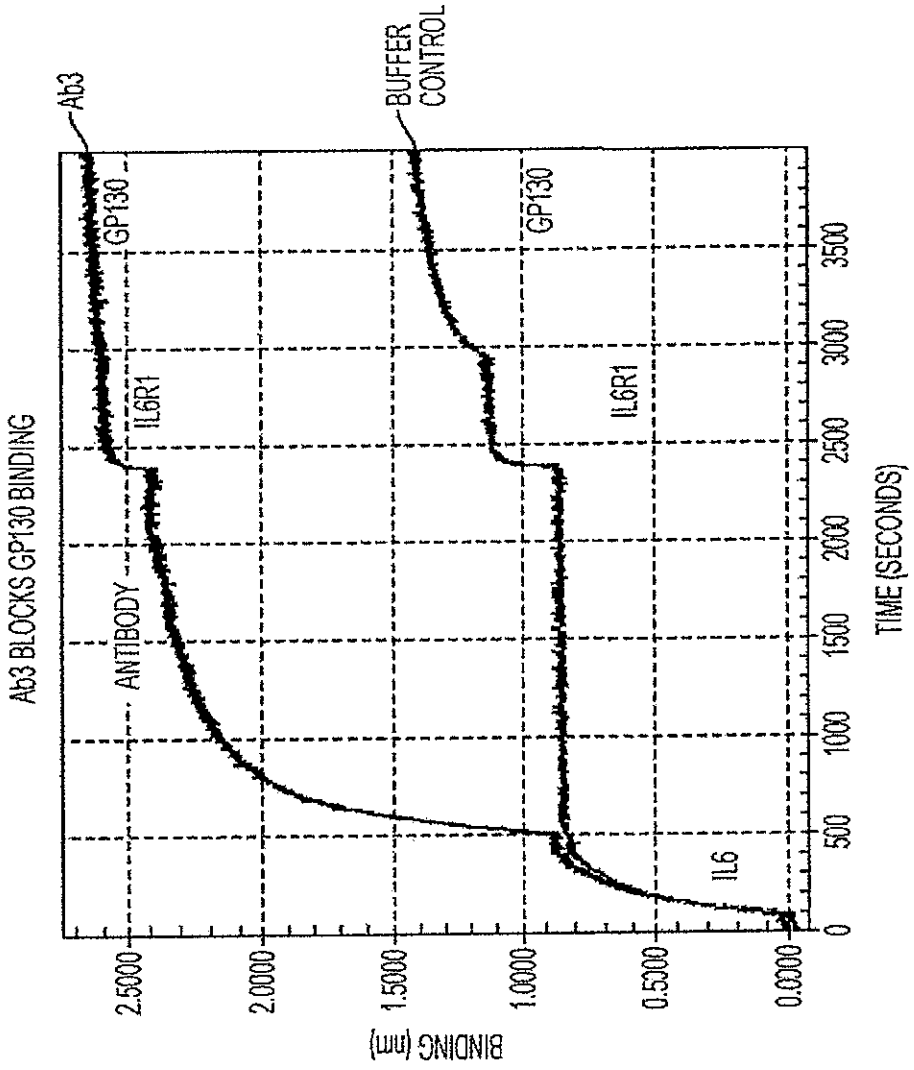

Ab3 BLOCKS GP130 BINDING
Ab3
BUFFER CONTROL
GP130
IL6R1
ANTIBODY
GP130
IL6R1
IL6
BINDING (nm)
2.5000
2.0000
1.5000
1.0000
0.5000
0.0000
0
500
1000
1500
2000
2500
3000
3500
TIME (SECONDS)

FIG. 10C

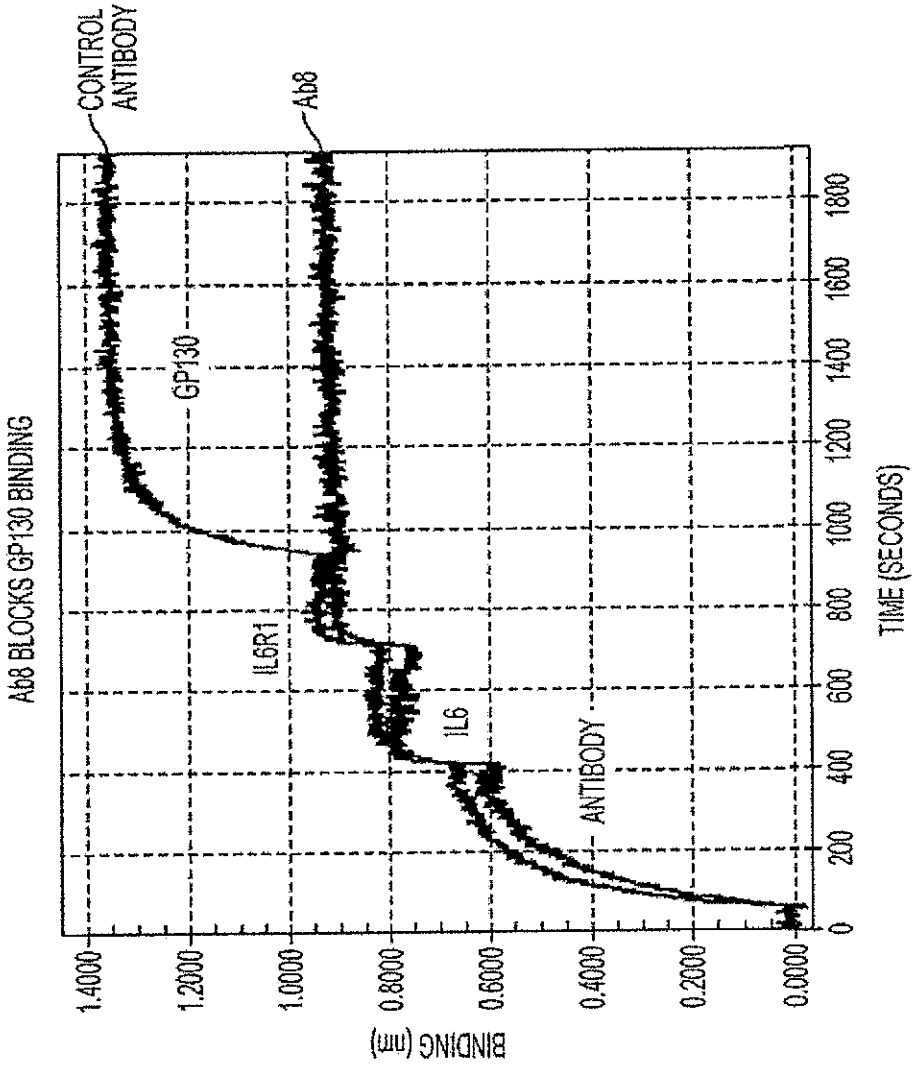

Ab8 BLOCKS GP130 BINDING
CONTROL ANTIBODY
Ab8
GP130
IL6R1
IL6
ANTIBODY
BINDING (nm)
1.4000
1.2000
1.0000
0.8000
0.6000
0.4000
0.2000
0.0000
0
200
400
600
800
1000
1200
1400
1600
1800
TIME (SECONDS)

FIG. 10D

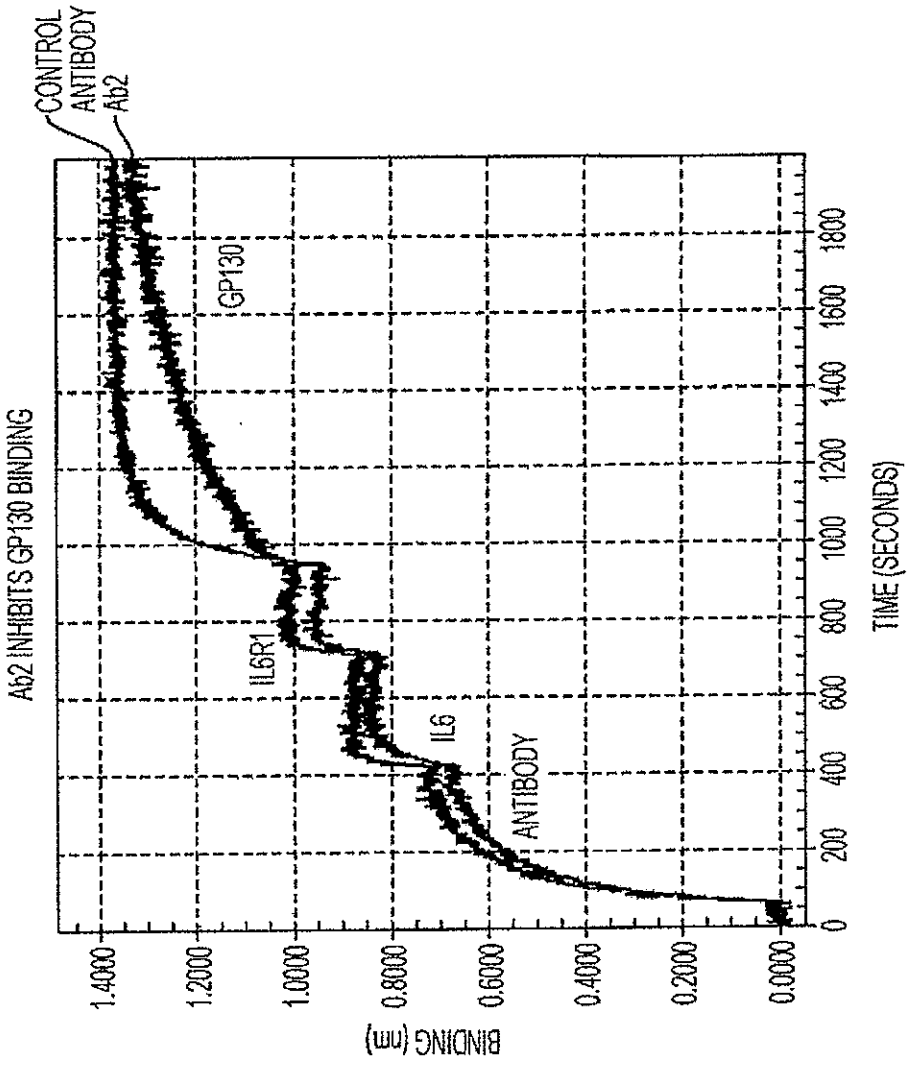

Ab2 INHIBITS GP130 BINDING
CONTROL ANTIBODY Ab2
GP130
IL6R1
IL6
ANTIBODY
BINDING (nm)
TIME (SECONDS)
0.0000
0.2000
0.4000
0.6000
0.8000
1.0000
1.2000
1.4000
0
200
400
600
800
1000
1200
1400
1600
1800

FIG. 10E

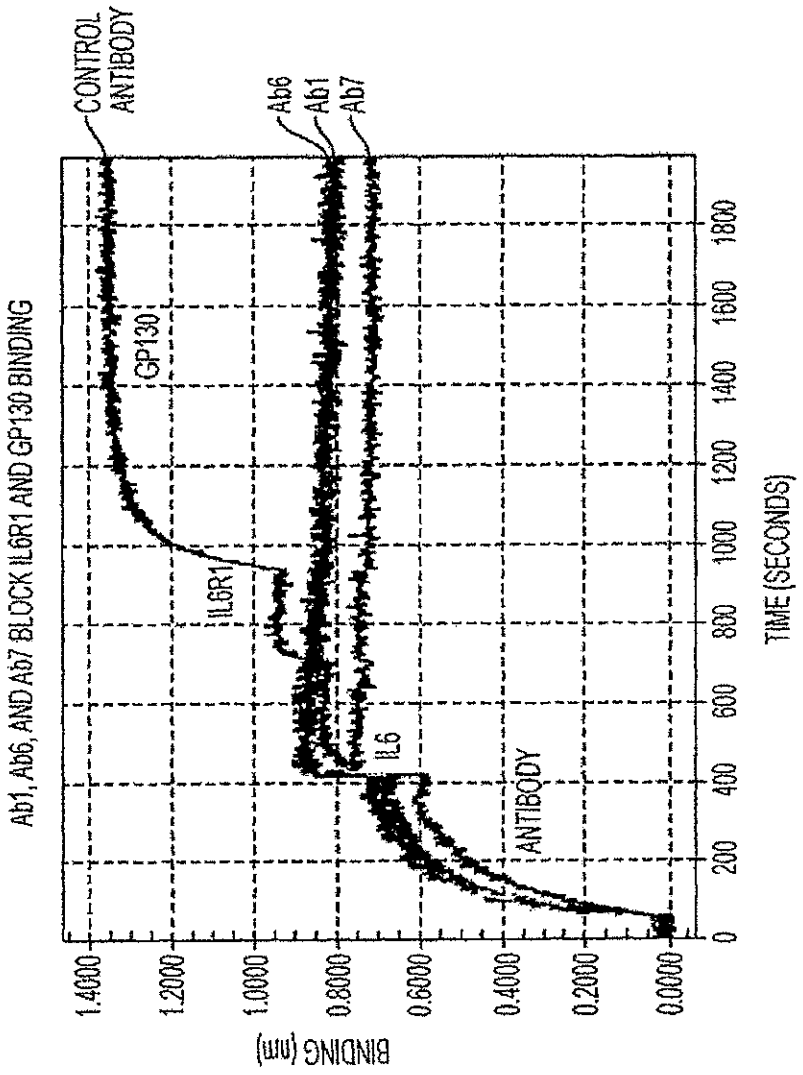

Ab1, Ab6, AND Ab7 BLOCK IL6R1 AND GP130 BINDING
CONTROL ANTIBODY
Ab6
Ab1
Ab7
GP130
IL6R1
IL6
ANTIBODY
BINDING (nm)
1.4000
1.2000
1.0000
0.8000
0.6000
0.4000
0.2000
0.0000
0
200
400
600
800
1000
1200
1400
1600
1800
TIME (SECONDS)

FIG. 11

Antibody	Blocks IL6 binding to R1	Blocks IL6 binding to GP130	Reference
Ab1	Yes	Yes	021051
Ab2	No	Partial	021050
Ab3	No	Yes	021030
Ab4	No	Yes	021050
Ab6	Yes	Yes	021051
Ab7	Yes	Yes	021051
Ab8	No	Yes	021051

FIG. 12

1 VPPGEDSKDVAAPHR (SEQ ID NO: 590)	20 ENNLNLPKMAEKDGC (SEQ ID NO: 609)	39 QMSTKVLIQFLQKKA (SEQ ID NO: 628)
2 GEDSKDVAAPHRQPL (SEQ ID NO: 591)	21 LNLPKMAEKDGCFQS (SEQ ID NO: 610)	40 TKVLIQFLQKKAKNL (SEQ ID NO: 629)
3 SKDVAAPHRQPLTSS (SEQ ID NO: 592)	22 PKMAEKDGCFQSGFN (SEQ ID NO: 611)	41 LIQFLQKKAKNLDAI (SEQ ID NO: 630)
4 VAAPHRQPLTSSERI (SEQ ID NO: 593)	23 AEKDGCFQSGFNEET (SEQ ID NO: 612)	42 FLQKKAKNLDAITTP (SEQ ID NO: 631)
5 PHRQPLTSSERIDKQ (SEQ ID NO: 594)	24 DGCFQSGFNEETCLV (SEQ ID NO: 613)	43 KKAKNLDAITTPDPT (SEQ ID NO: 632)
6 QPLTSSERIDKQIRY (SEQ ID NO: 595)	25 FQSGFNEETCLVKII (SEQ ID NO: 614)	44 KNLDAITTPDPTTNA (SEQ ID NO: 633)
7 TSSERIDKQIRYILD (SEQ ID NO: 596)	26 GFNEETCLVKIITGL (SEQ ID NO: 615)	45 DAITTPDPTTNASLL (SEQ ID NO: 634)
8 ERIDKQIRYILDGIS (SEQ ID NO: 597)	27 EETCLVKIITGLLEF (SEQ ID NO: 616)	46 TTPDPTTNASLLTKL (SEQ ID NO: 635)
9 DKQIRYILDGISALR (SEQ ID NO: 598)	28 CLVKIITGLLEFEVY (SEQ ID NO: 617)	47 DPTTNASLLTKLQAQ (SEQ ID NO: 636)
10 IRYILDGISALRKET (SEQ ID NO: 599)	29 KIITGLLEFEVYLEY (SEQ ID NO: 618)	48 TNASLLTKLQAQNQW (SEQ ID NO: 637)
11 ILDGISALRKETCNK (SEQ ID NO: 600)	30 TGLLEFEVYLEYLQN (SEQ ID NO: 619)	49 SLLTKLQAQNQWLQD (SEQ ID NO: 638)
12 GISALRKETCNKSNM (SEQ ID NO: 601)	31 LEFEVYLEYLQNRFE (SEQ ID NO: 620)	50 TKLQAQNQWLQDMTT (SEQ ID NO: 639)
13 ALRKETCNKSNMCES (SEQ ID NO: 602)	32 EVYLEYLQNRFESSE (SEQ ID NO: 621)	51 QAQNQWLQDMTTHLI (SEQ ID NO: 640)
14 KETCNKSNMCESSKE (SEQ ID NO: 603)	33 LEYLQNRFESSEEQA (SEQ ID NO: 622)	52 NQWLQDMTTHLILRS (SEQ ID NO: 641)
15 CNKSNMCESSKEALA (SEQ ID NO: 604)	34 LQNRFESSEEQARAV (SEQ ID NO: 623)	53 LQDMTTHLILRSFKE (SEQ ID NO: 642)
16 SNMCESSKEALAENN (SEQ ID NO: 605)	35 RFESSEEQARAVQMS (SEQ ID NO: 624)	54 MTTHLILRSFKEFLQ (SEQ ID NO: 643)
17 CESSKEALAENNLNL (SEQ ID NO: 606)	36 SSEEQARAVQMSTKV (SEQ ID NO: 625)	55 HLILRSFKEFLQSSL (SEQ ID NO: 644)
18 SKEALAENNLNLPKM (SEQ ID NO: 607)	37 EQARAVQMSTKVLIQ (SEQ ID NO: 626)	56 LRSFKEFLQSSLRAL (SEQ ID NO: 645)
19 ALAENNLNLPKMAEK (SEQ ID NO: 608)	38 RAVQMSTKVLIQFLQ (SEQ ID NO: 627)	57 FKEFLQSSLRALRQM (SEQ ID NO: 646)

FIG. 13

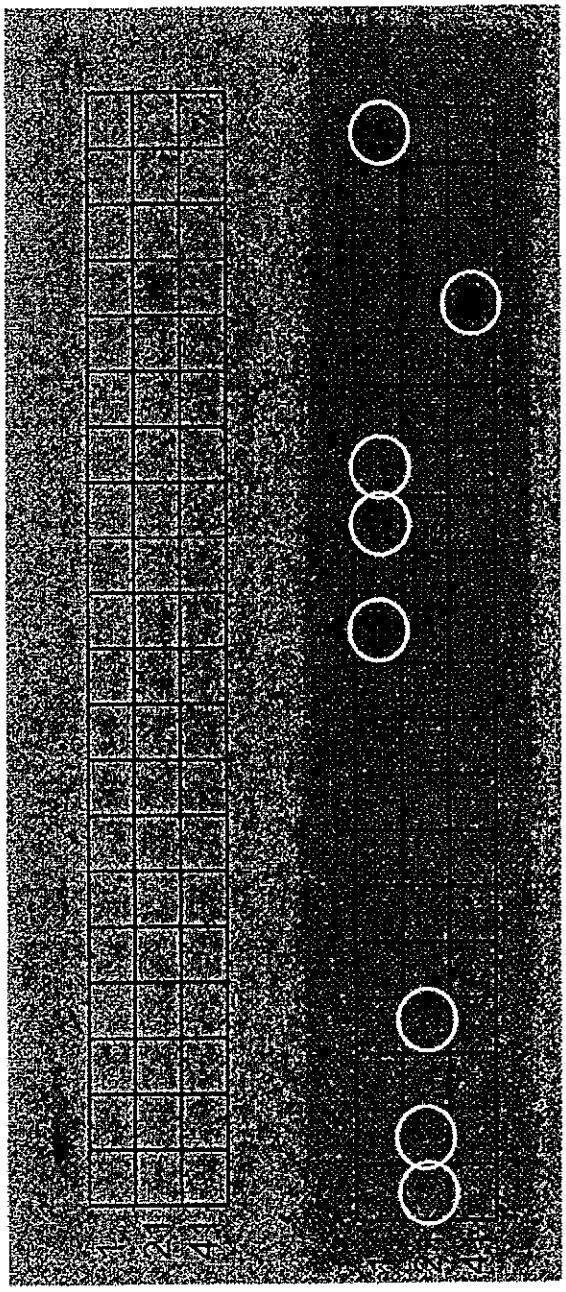


FIG. 14

