FIG. 1A

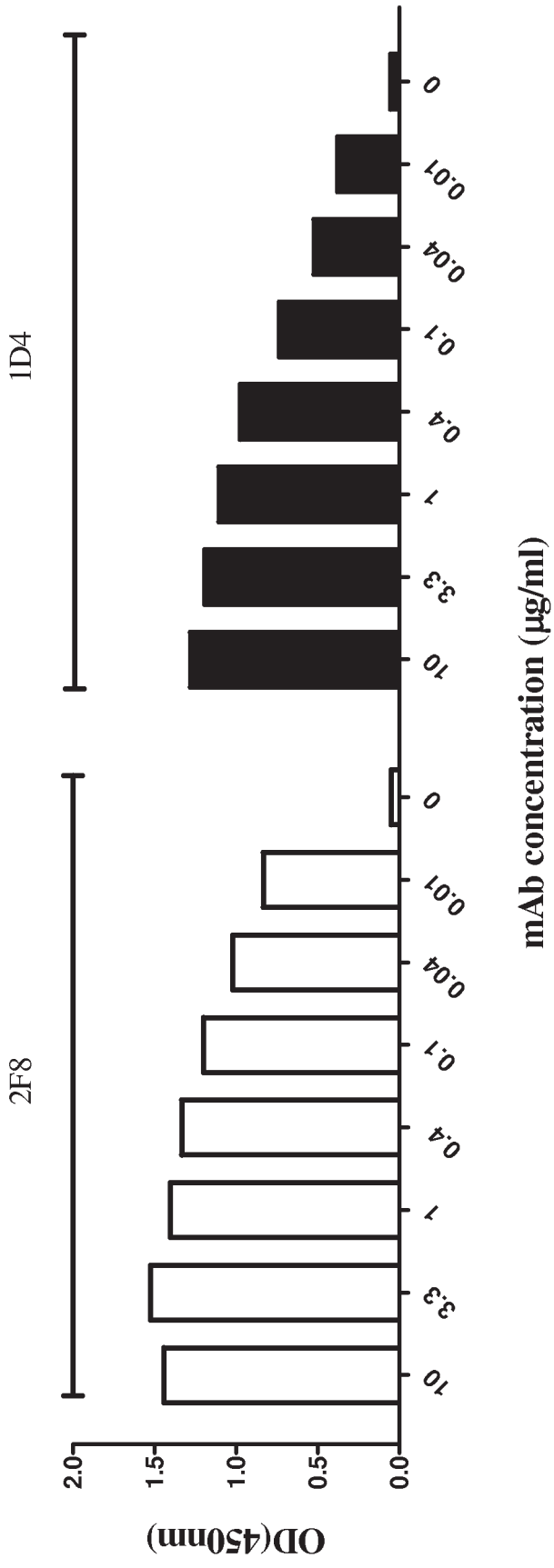

OD(450nm)
2.0
1.5
1.0
0.5
0.0
2F8
1D4
10
3.3
1
0.4
0.1
0.04
0.01
0
mAb concentration (µg/ml)

FIG. 1B

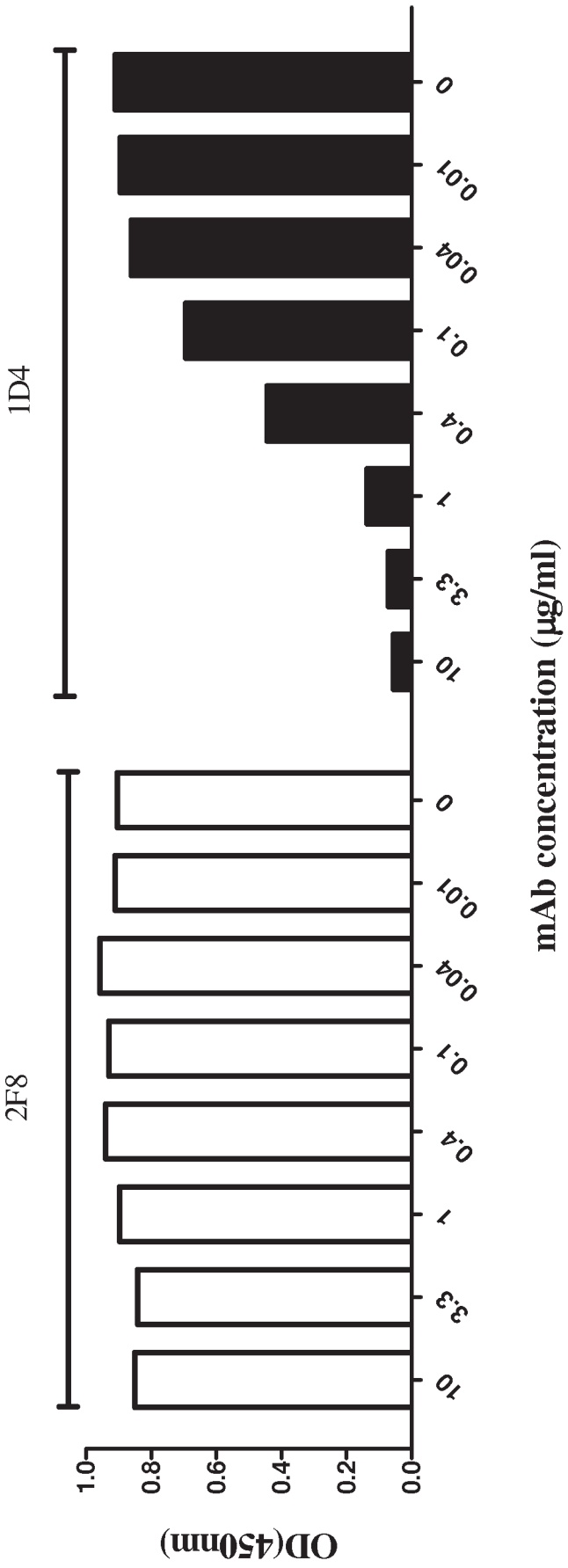

OD(450nm)
1.0
0.8
0.6
0.4
0.2
0.0
2F8
1D4
10
3.3
1
0.4
0.1
0.04
0.01
0
mAb concentration (µg/ml)

FIG. 2

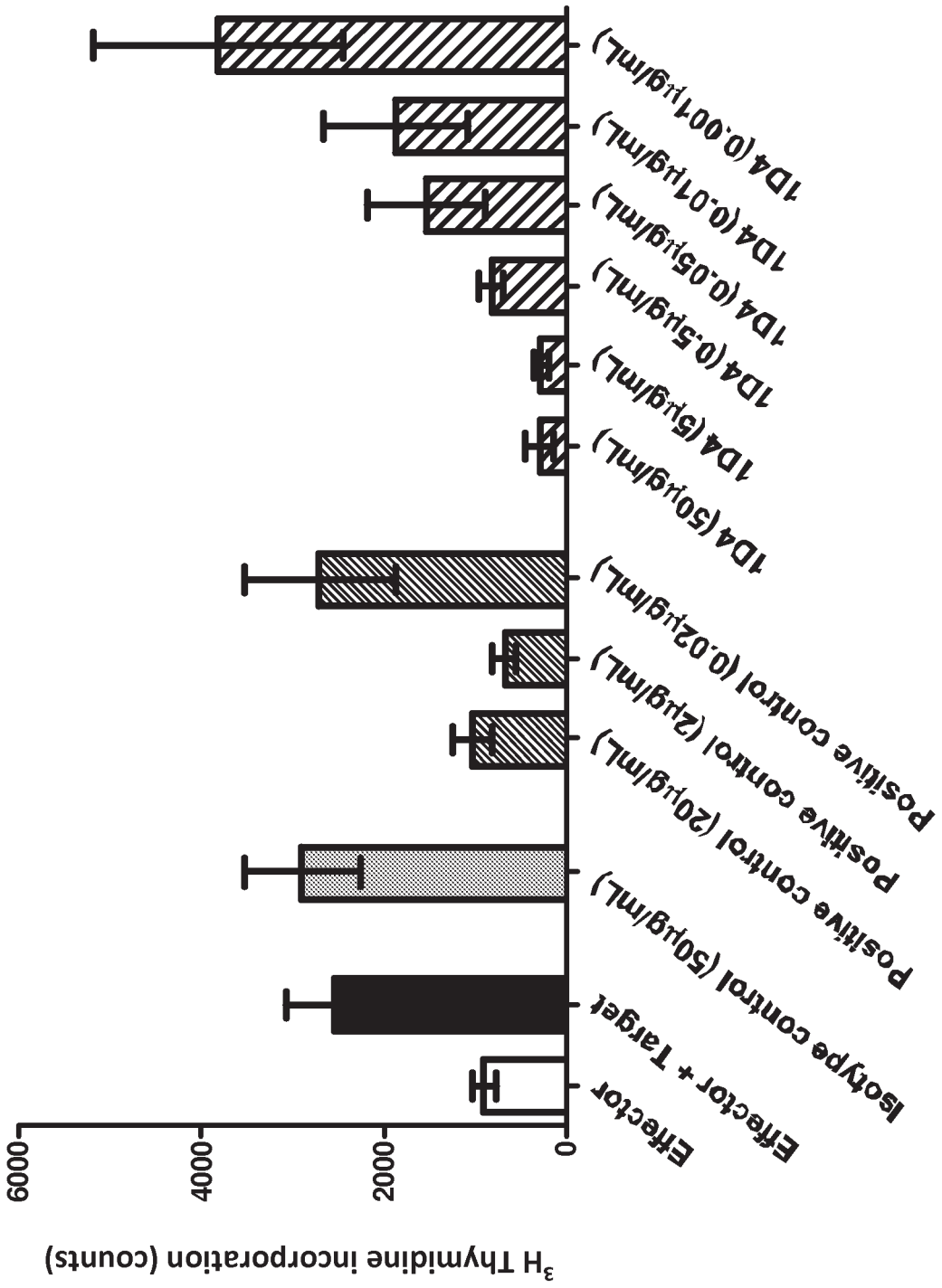

^{3}H Thymidine incorporation (counts)
6000
4000
2000
0
Effector
Effector + Target
Isotype control (50µg/mL)
Positive control (20µg/mL)
Positive control (2µg/mL)
Positive control (0.02µg/mL)
1D4 (50µg/mL)
1D4 (5µg/mL)
1D4 (0.5µg/mL)
1D4 (0.05µg/mL)
1D4 (0.01µg/mL)
1D4 (0.001µg/mL)

FIG. 3A

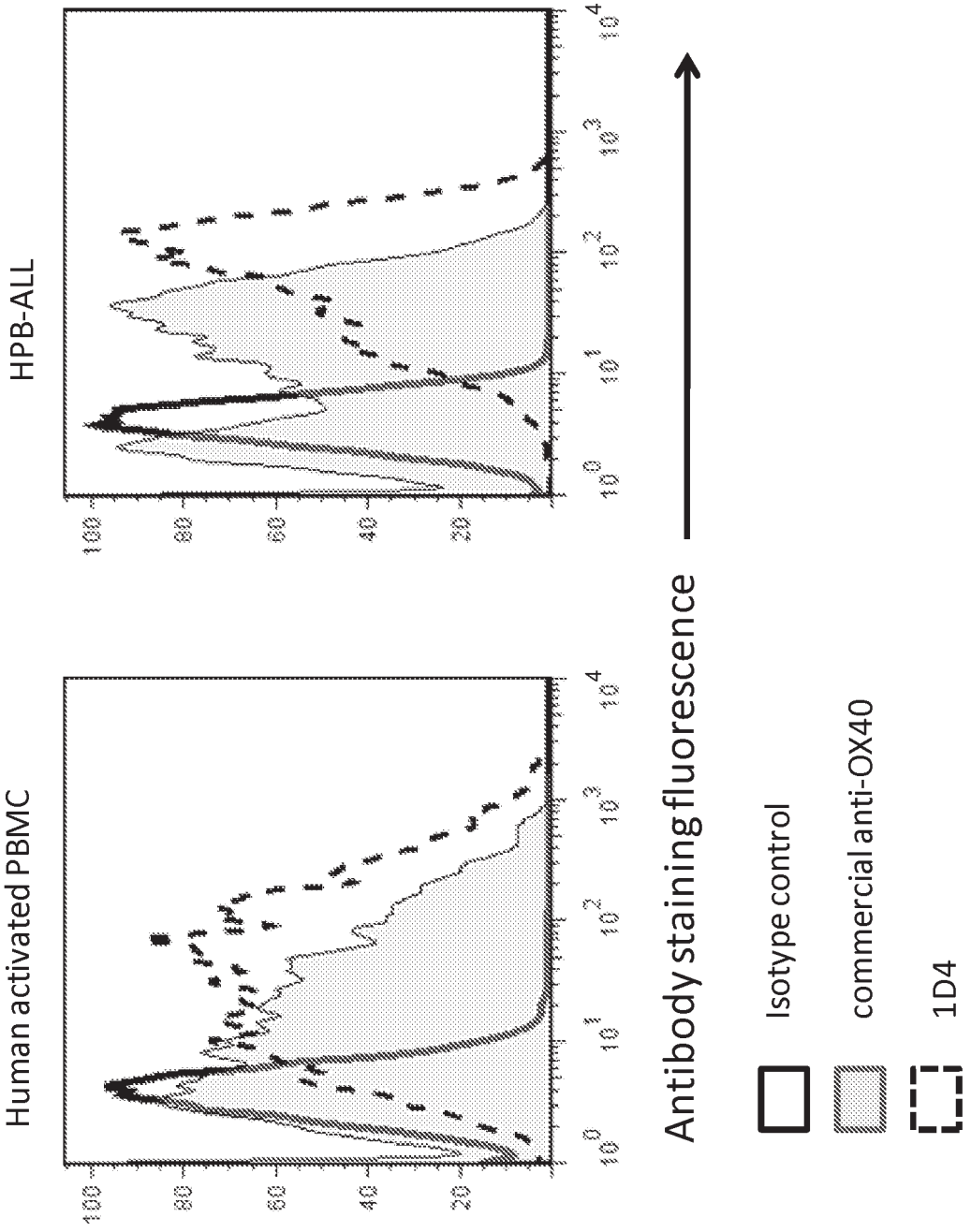

Human activated PBMC
HPB-ALL
100
80
60
40
20
10^0
10^1
10^2
10^3
10^4
Antibody staining fluorescence
Isotype control
commercial anti-OX40
1D4

FIG. 3B

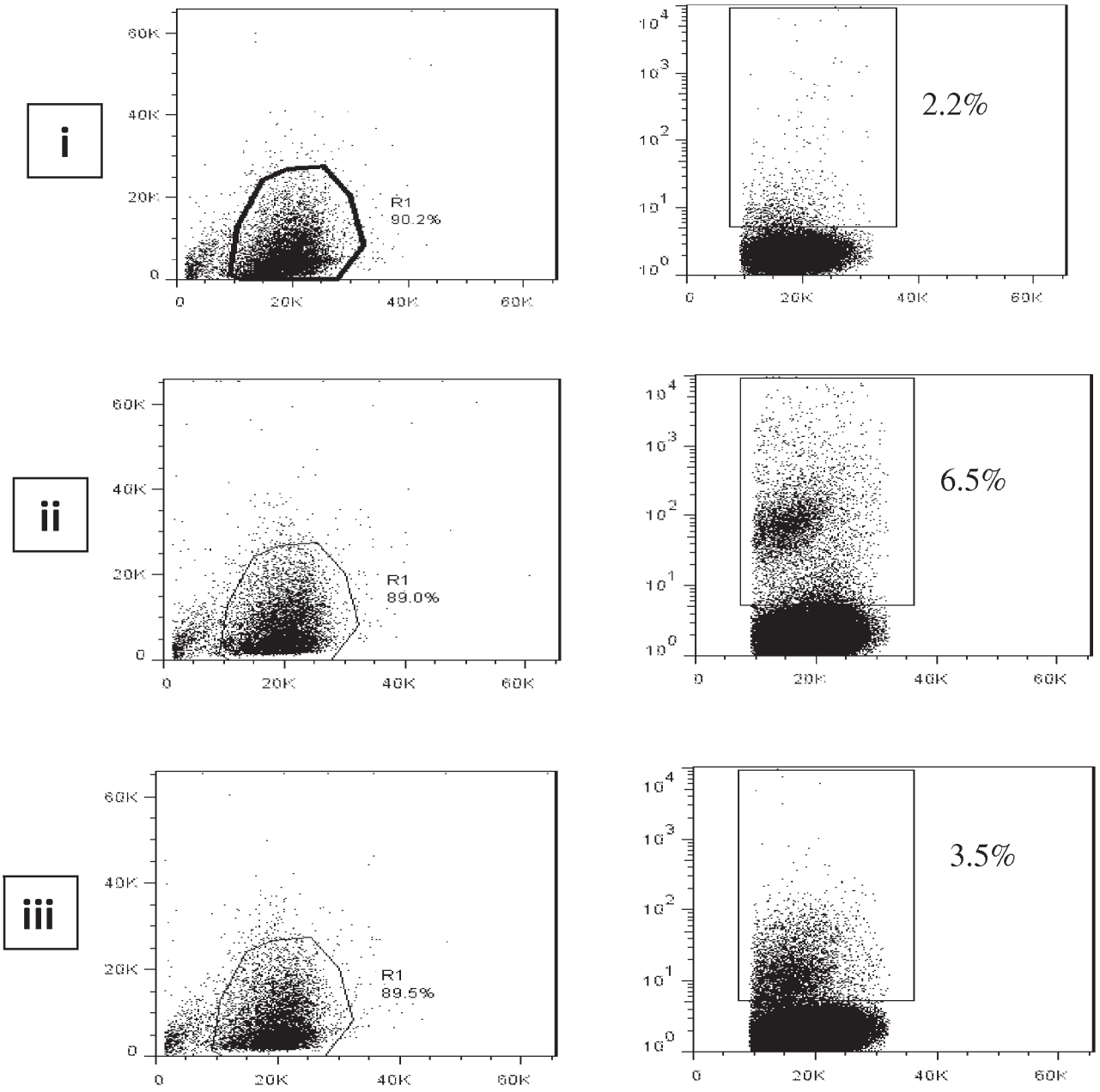

i
ii
iii
R1
90.2%
R1
89.0%
R1
89.5%
2.2%
6.5%
3.5%
0
20K
40K
60K
10^0
10^1
10^2
10^3
10^4

FIG. 4A

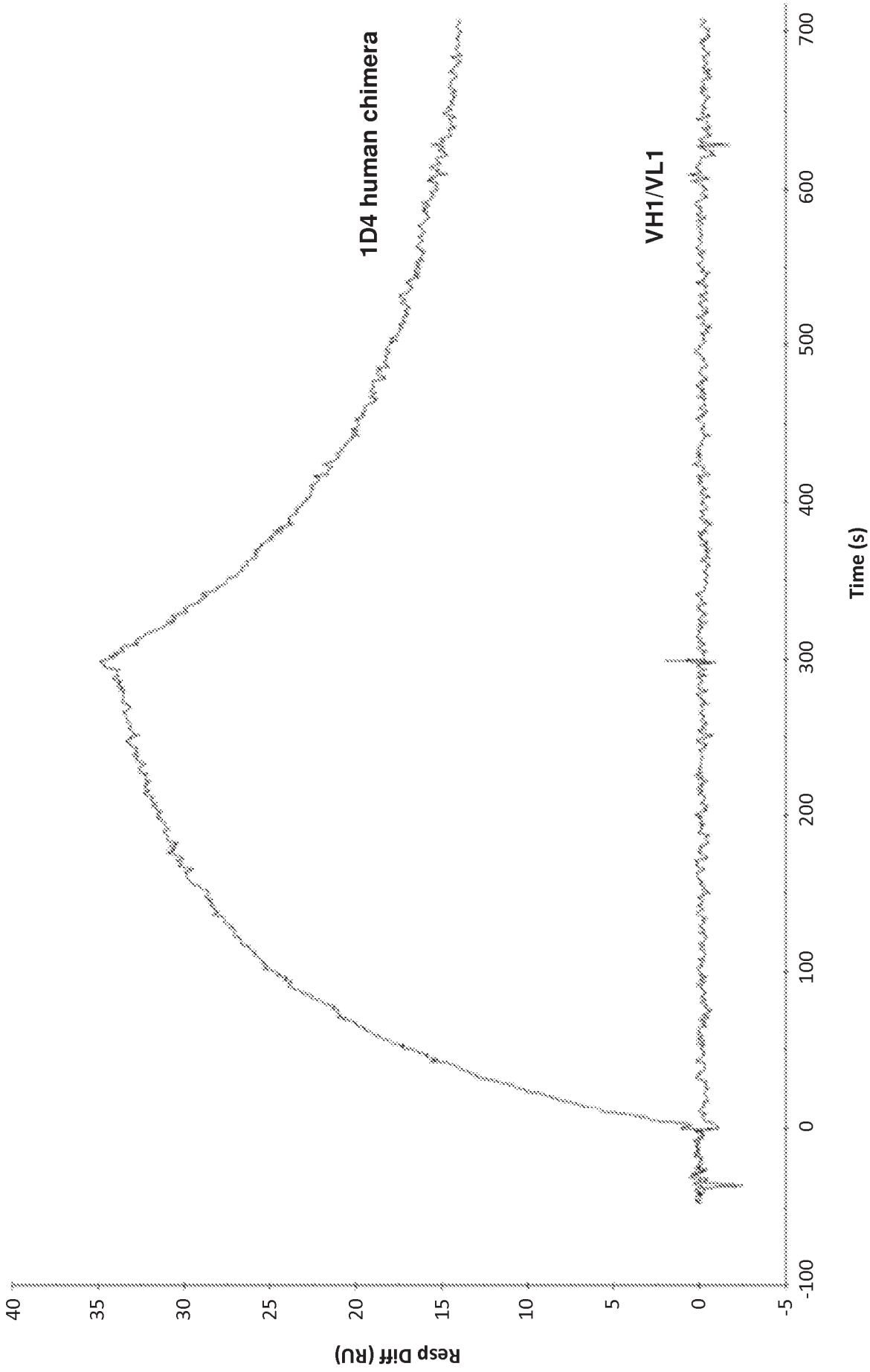

1D4 human chimera
VH1/VL1
Resp Diff (RU)
Time (s)
40
35
30
25
20
15
10
5
0
-5
-100
0
100
200
300
400
500
600
700

FIG. 4B

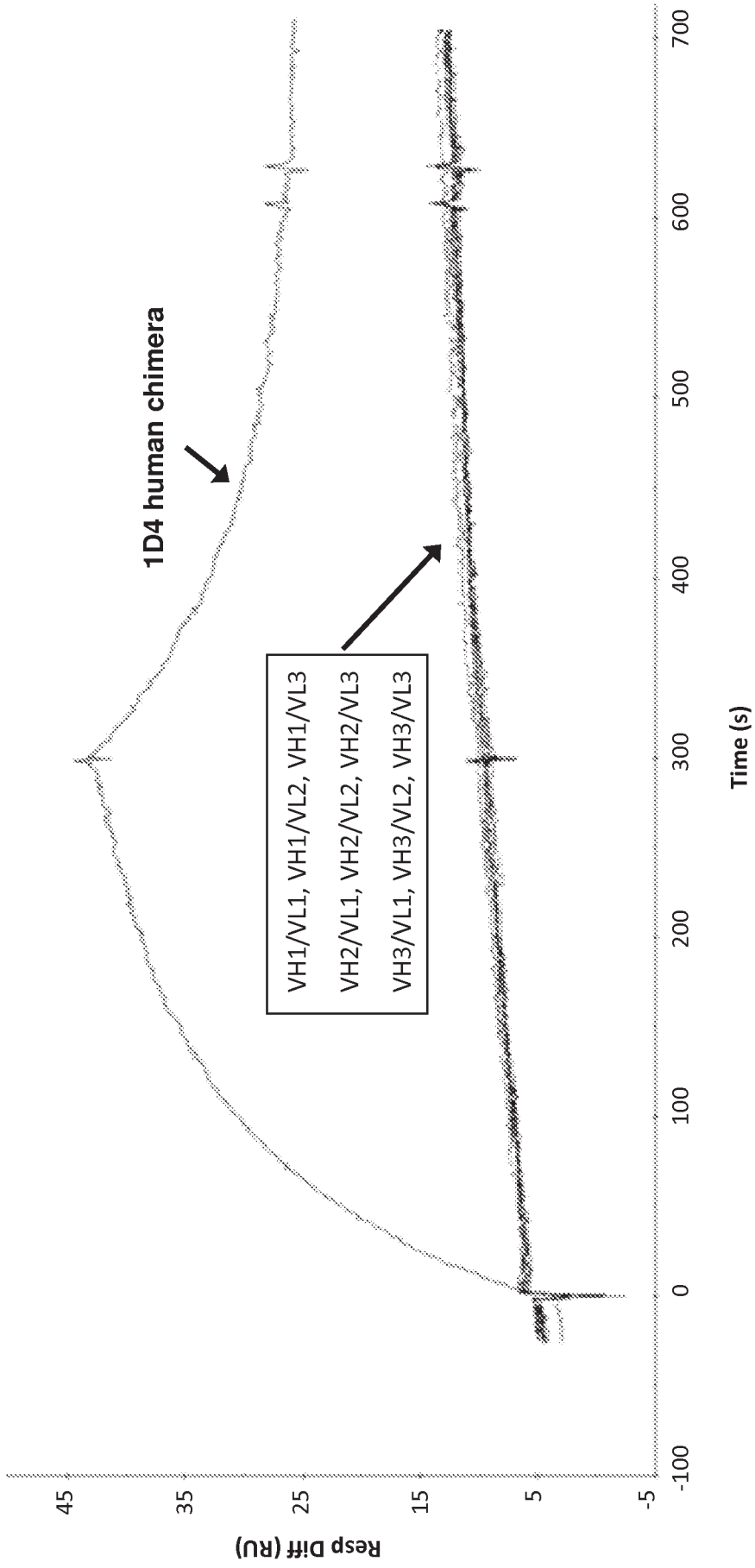

1D4 human chimera
VH1/VL1, VH1/VL2, VH1/VL3
VH2/VL1, VH2/VL2, VH2/VL3
VH3/VL1, VH3/VL2, VH3/VL3
Resp Diff (RU)
45
35
25
15
5
-5
-100
0
100
200
300
400
500
600
700
Time (s)

FIG. 4C

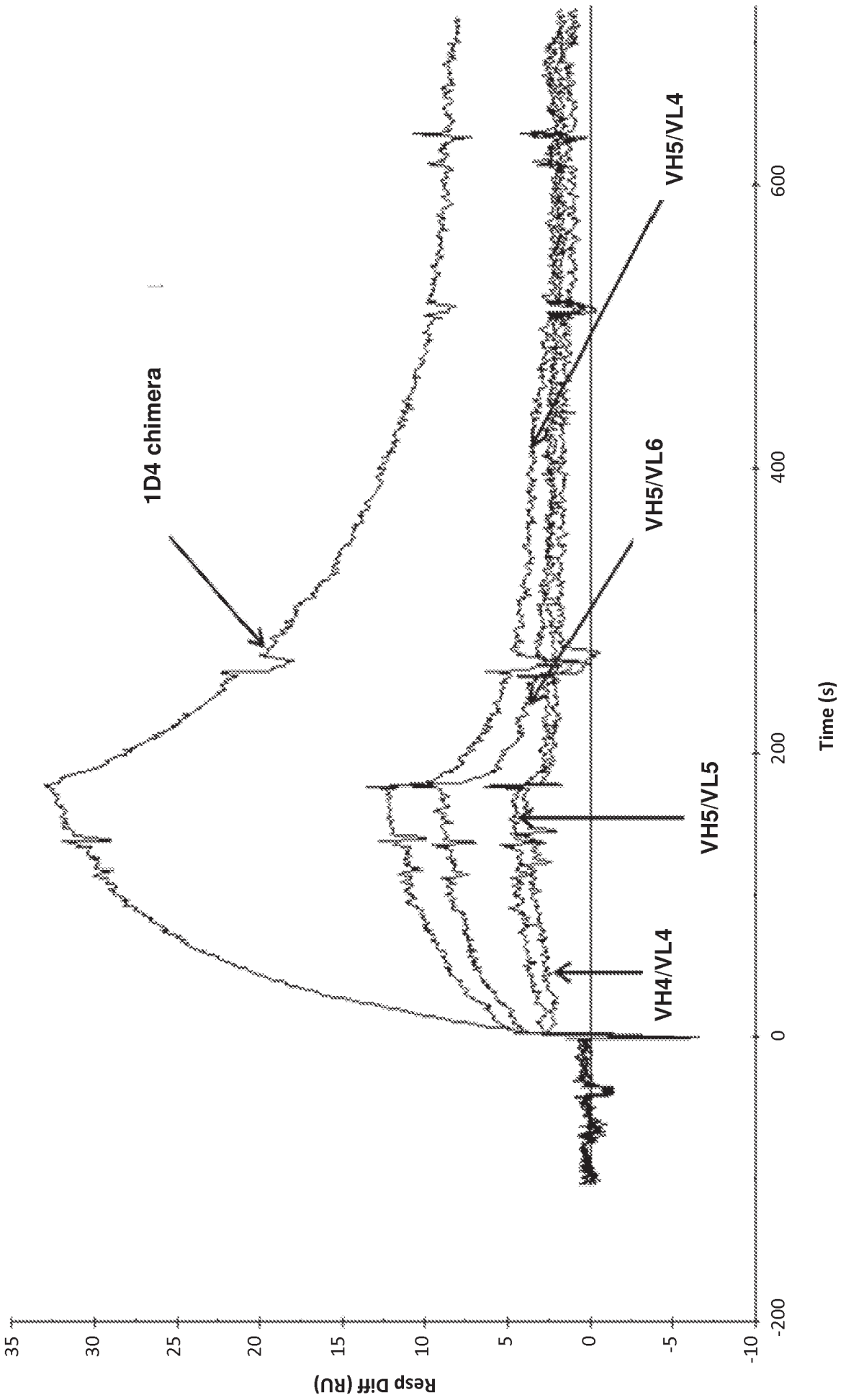

1D4 chimera
VH5/VL4
VH5/VL6
VH5/VL5
VH4/VL4
Resp Diff (RU)
Time (s)
35
30
25
20
15
10
5
0
-5
-10
-200
0
200
400
600

FIG. 4D

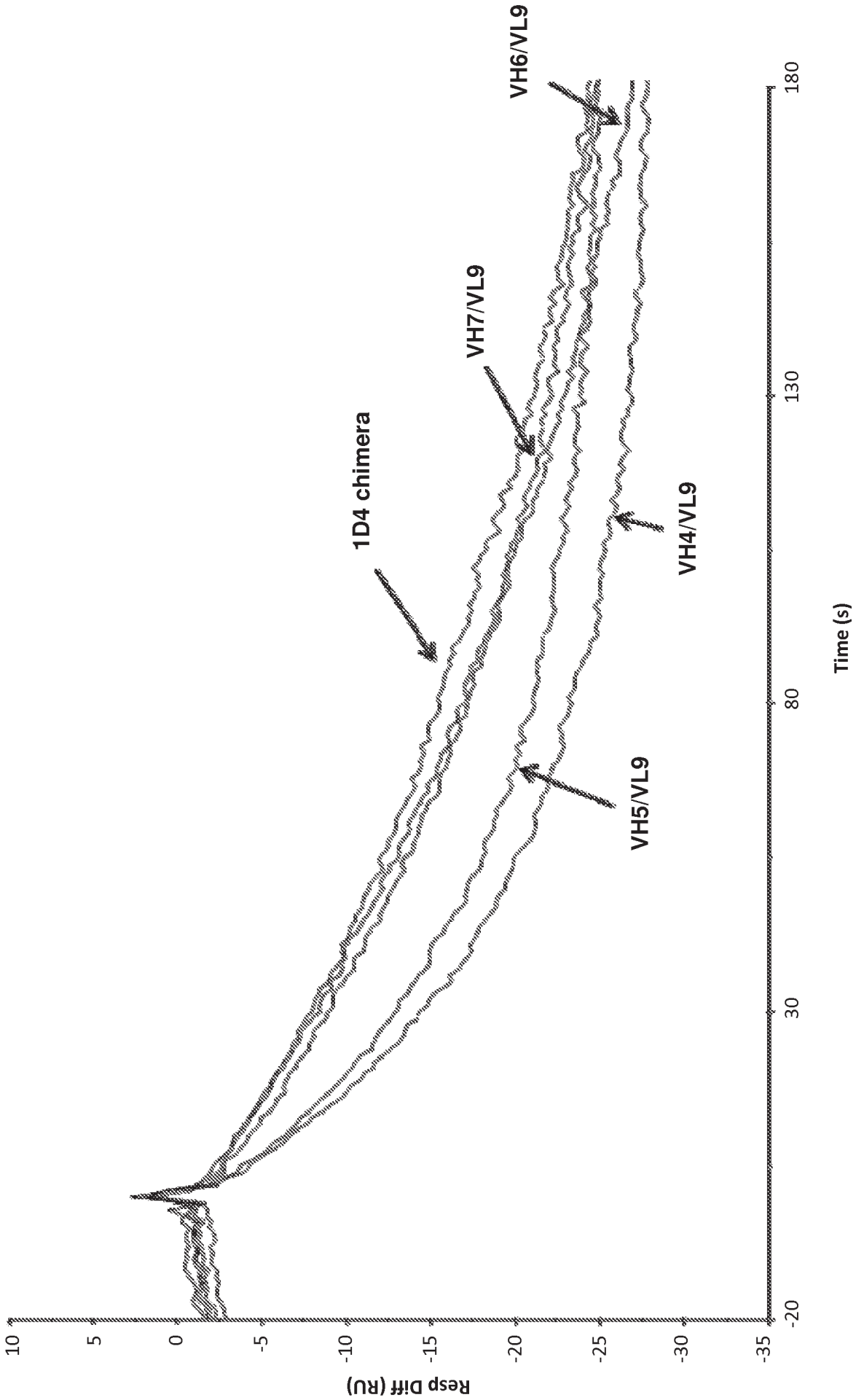

VH6/VL9
VH7/VL9
1D4 chimera
VH4/VL9
VH5/VL9
Resp Diff (RU)
Time (s)
10
5
0
-5
-10
-15
-20
-25
-30
-35
-20
30
80
130
180

FIG. 4E

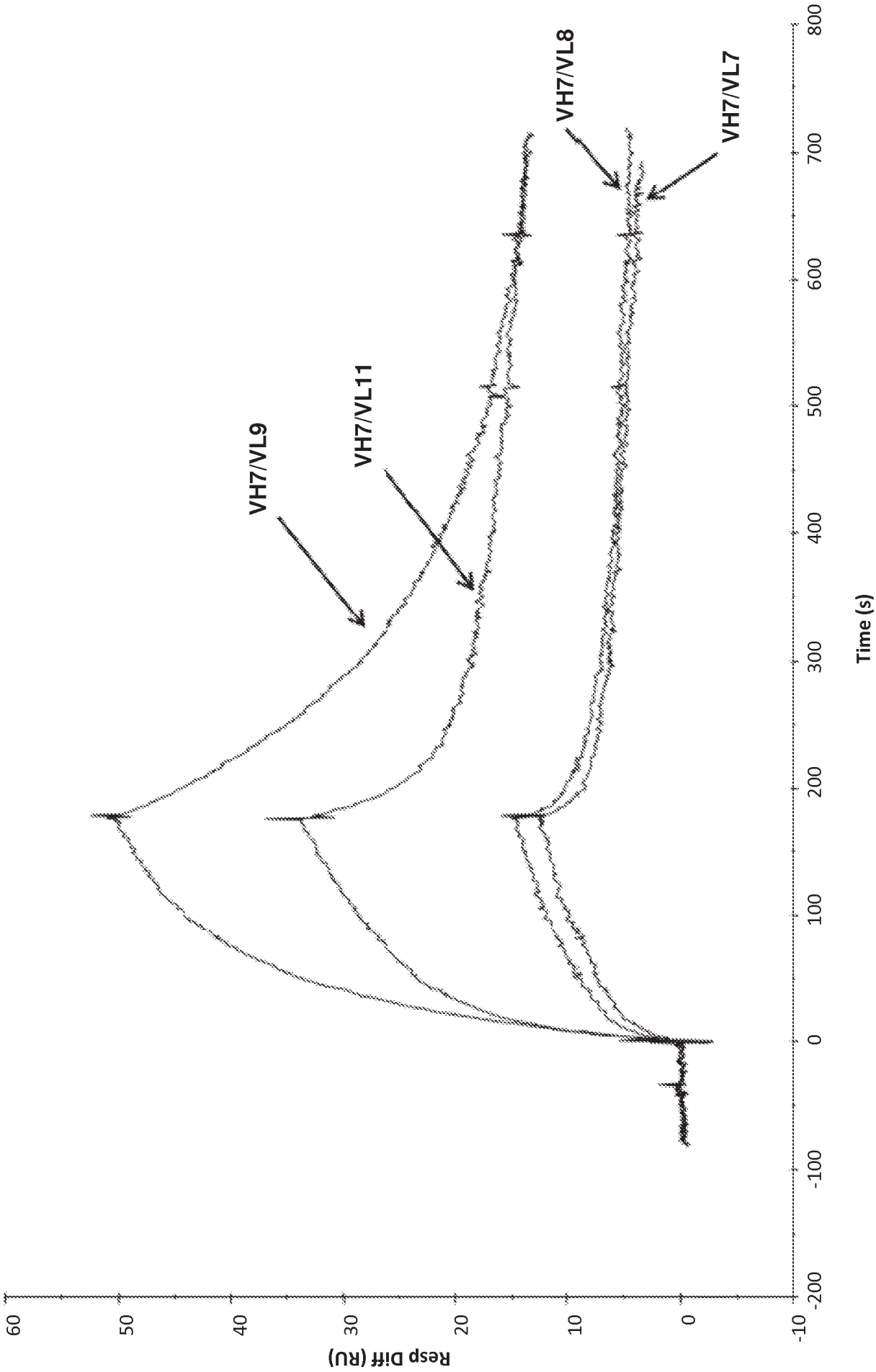

VH7/VL9
VH7/VL11
VH7/VL8
VH7/VL7
Resp Diff (RU)
60
50
40
30
20
10
0
-10
-200
-100
0
100
200
300
400
500
600
700
800
Time (s)

FIG. 4F

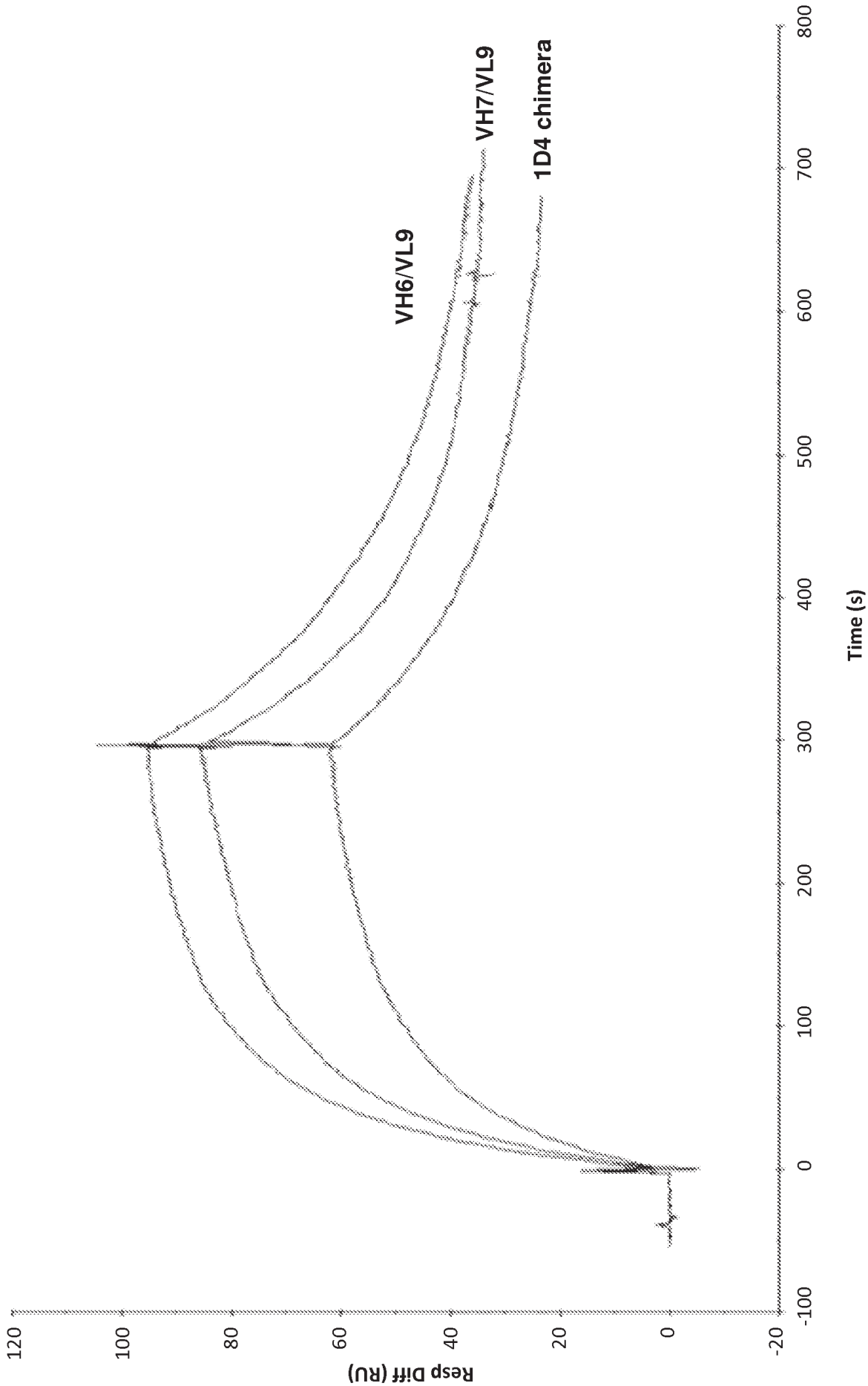

VH6/VL9
VH7/VL9
1D4 chimera
Resp Diff (RU)
Time (s)
120
100
80
60
40
20
0
-20
-100
0
100
200
300
400
500
600
700
800

FIG. 5A

```
                                10        20        30        40        50        60        70
                       ....|....|....|....|....|....|....|....|....|....|....|....|....|....|....|
Kabat VH#              12345678901234567890123456789012345ab6789012345678901 2abc3456789012345678901 2345
1D4 VH                 QVTLKESGPGILQPSQTLSLTCSFSGFSLSTSGMGVGWIRQPSGKGLEWLAHIW~~~WDDDKYYNTALKSGLTISKDTSK
Human IGHV2-70*10      QVTLKESGPALVKPTQTLTLTCTFSGFSLSTSGMRVSWIRQPPGKALEWIARID~~~WDDDKYYSTSLKTRLTISKDTSK
VH1                    QVTLKESGPALVKPTQTLTLTCTFSGFSLSTSGMGVSWIRQPPGKALEWIARIW~~~WDDDKYYSTSLKTRLTISKDTSK
VH2 [T23S]             QVTLKESGPALVKPTQTLTLTCSFSGFSLSTSGMGVSWIRQPPGKALEWIARIW~~~WDDDKYYSTSLKTRLTISKDTSK
VH3 [R50H]             QVTLKESGPALVKPTQTLTLTCTFSGFSLSTSGMGVSWIRQPPGKALEWIAHIW~~~WDDDKYYSTSLKTRLTISKDTSK
VH4 [T23S/R50H]        QVTLKESGPALVKPTQTLTLTCSFSGFSLSTSGMGVSWIRQPPGKALEWIAHIW~~~WDDDKYYSTSLKTRLTISKDTSK
VH5 [T23S/R50H/S60N/S62A]  QVTLKESGPALVKPTQTLTLTCSFSGFSLSTSGMGVSWIRQPPGKALEWIAHIW~~~WDDDKYYNTALKTRLTISKDTSK
VH6 [T23S/S35bG/R50H/S60N/S62A  QVTLKESGPALVKPTQTLTLTCSFSGFSLSTSGMGVGWIRQPPGKALEWIAHIW~~~WDDDKYYNTALKTRLTISKDTSK
VH7 [T23S/S35bG/I48L/R50H/S60N  QVTLKESGPALVKPTQTLTLTCSFSGFSLSTSGMGVGWIRQPPGKALEWLAHIW~~~WDDDKYYNTALKTRLTISKDTSK

                                    80        90        100                 110
                                ....|....|....|....|....|.............|....|...
Kabat VH#                       6789012abc3456789012345678 90abcdefghijk1234567890123
1D4 VH                          NQVFLKIASVDTTDTATYYCARIDWDGF~~~~~~~~~~~AYWGQGTLVTVSS
Human IGHV2-70*10               NQVVLTMTNMDPVDTATYYCARIYF~~~~~~~~~~~~~~DYWGQGTLVTVSS
VH1                             NQVVLTMTNMDPVDTATYYCARIDWDGF~~~~~~~~~~~AYWGQGTLVTVSS
VH2 [T23S]                      NQVVLTMTNMDPVDTATYYCARIDWDGF~~~~~~~~~~~AYWGQGTLVTVSS
VH3 [R50H]                      NQVVLTMTNMDPVDTATYYCARIDWDGF~~~~~~~~~~~AYWGQGTLVTVSS
VH4 [T23S/R50H]                 NQVVLTMTNMDPVDTATYYCARIDWDGF~~~~~~~~~~~AYWGQGTLVTVSS
VH5 [T23S/R50H/S60N/S62A]       NQVVLTMTNMDPVDTATYYCARIDWDGF~~~~~~~~~~~AYWGQGTLVTVSS
VH6 [T23S/S35bG/R50H/S60N/S62A  NQVVLTMTNMDPVDTATYYCARIDWDGF~~~~~~~~~~~AYWGQGTLVTVSS
VH7 [T23S/S35bG/I48L/R50H/S60N  NQVVLTMTNMDPVDTATYYCARIDWDGF~~~~~~~~~~~AYWGQGTLVTVSS
```

FIG. 5B

```
                                                  10        20                  30        40        50        60        70
                                                  ....|....|....|....|....|..........|....|....|....|....|....|....|....|....|
Kabat VL#                                         12345678901234567890123456 7abcdef8901234567890123456789012345678901234
1D4 VL                                            QIVLTQSPAILSASPGEKVTMTCRASS~~~~~~~SVSYMHWYQQKPGSSPKPWIYATSNLASGVPARFSGSGSGTSYSLT
Human IGKV 3-11*01                                EIVLTQSPATLSLSPGERATLSCRASQ~~~~~~SVSSYLAWYQQKPGQAPRLLIYDASNRATGIPARFSGSGSGTDFTLT
VL1                                               EIVLTQSPATLSLSPGERATLSCRASS~~~~~~SVSYYLAWYQQKPGQAPRLLIYATSNRATGIPARFSGSGSGTDFTLT
VL2 [L33M]                                        EIVLTQSPATLSLSPGERATLSCRASS~~~~~~SVSYYMAWYQQKPGQAPRLLIYATSNRATGIPARFSGSGSGTDFTLT
VL3 [F71Y]                                        EIVLTQSPATLSLSPGERATLSCRASS~~~~~~SVSYYLAWYQQKPGQAPRLLIYATSNRATGIPARFSGSGSGTDYTLT
VL4 [L33M/F71Y]                                   EIVLTQSPATLSLSPGERATLSCRASS~~~~~~SVSYYMAWYQQKPGQAPRLLIYATSNRATGIPARFSGSGSGTDYTLT
VL5 [L33M/L46P/L47W/F71Y]                         EIVLTQSPATLSLSPGERATLSCRASS~~~~~~SVSYYMAWYQQKPGQAPRPWIYATSNRATGIPARFSGSGSGTDYTLT
VL6 [E1Q/L33M/L46P/L47W/F71Y]                     QIVLTQSPATLSLSPGERATLSCRASS~~~~~~SVSYYMAWYQQKPGQAPRPWIYATSNRATGIPARFSGSGSGTDYTLT
VL7 [Y31del/L33M/F71Y]                            EIVLTQSPATLSLSPGERATLSCRASS~~~~~~~SVSYMAWYQQKPGQAPRLLIYATSNRATGIPARFSGSGSGTDYTLT
VL8 [Y31del/L33M/A34H/F71Y]                       EIVLTQSPATLSLSPGERATLSCRASS~~~~~~~SVSYMHWYQQKPGQAPRLLIYATSNRATGIPARFSGSGSGTDYTLT
VL9 [Y31del/L33M/A34H/L46P/L47W/F71Y]             EIVLTQSPATLSLSPGERATLSCRASS~~~~~~~SVSYMHWYQQKPGQAPRPWIYATSNRATGIPARFSGSGSGTDYTLT
VL10 [Y31del/L33M/R54L/T56S/F71W]                 EIVLTQSPATLSLSPGERATLSCRASS~~~~~~~SVSYMAWYQQKPGQAPRLLIYATSNLASGIPARFSGSGSGTDYTLT
VL11 [Y31del/L33M/A34H/R54L/T56S/F71Y]            EIVLTQSPATLSLSPGERATLSCRASS~~~~~~~SVSYMHWYQQKPGQAPRLLIYATSNLASGIPARFSGSGSGTDYTLT
```

```
                                                       80        90                  100
                                                       |....|....|....|....|..........|....|...
Kabat VL#                                              567890123456789012345abcdef67890123456a7
1D4 VL                                                 INRVEAEDAATYYCQQWSSNP~~~~~~WTFGGGTKLEI~K
Human IGKV 3-11*01                                     ISSLEPEDFAVYYCQQRSNWP~~~~~~WTFGQGTKVEI~K
VL1                                                    ISSLEPEDFAVYYCQQWSSNP~~~~~~WTFGQGTKVEI~K
VL2 [L33M]                                             ISSLEPEDFAVYYCQQWSSNP~~~~~~WTFGQGTKVEI~K
VL3 [F71Y]                                             ISSLEPEDFAVYYCQQWSSNP~~~~~~WTFGQGTKVEI~K
VL4 [L33M/F71Y]                                        ISSLEPEDFAVYYCQQWSSNP~~~~~~WTFGQGTKVEI~K
VL5 [L33M/L46P/L47W/F71Y]                              ISSLEPEDFAVYYCQQWSSNP~~~~~~WTFGQGTKVEI~K
VL6 [E1Q/L33M/L46P/L47W/F71Y]                          ISSLEPEDFAVYYCQQWSSNP~~~~~~WTFGQGTKVEI~K
VL7 [Y31del/L33M/F71Y]                                 ISSLEPEDFAVYYCQQWSSNP~~~~~~WTFGQGTKVEI~K
VL8 [Y31del/L33M/A34H/F71Y]                            ISSLEPEDFAVYYCQQWSSNP~~~~~~WTFGQGTKVEI~K
VL9 [Y31del/L33M/A34H/L46P/L47W/F71Y]                  ISSLEPEDFAVYYCQQWSSNP~~~~~~WTFGQGTKVEI~K
VL10 [Y31del/L33M/R54L/T56S/F71Y]                      ISSLEPEDFAVYYCQQWSSNP~~~~~~WTFGQGTKVEI~K
VL11 [Y31del/L33M/A34H/R54L/T56S/F71Y]                 ISSLEPEDFAVYYCQQWSSNP~~~~~~WTFGQGTKVEI~K
```

FIG. 6

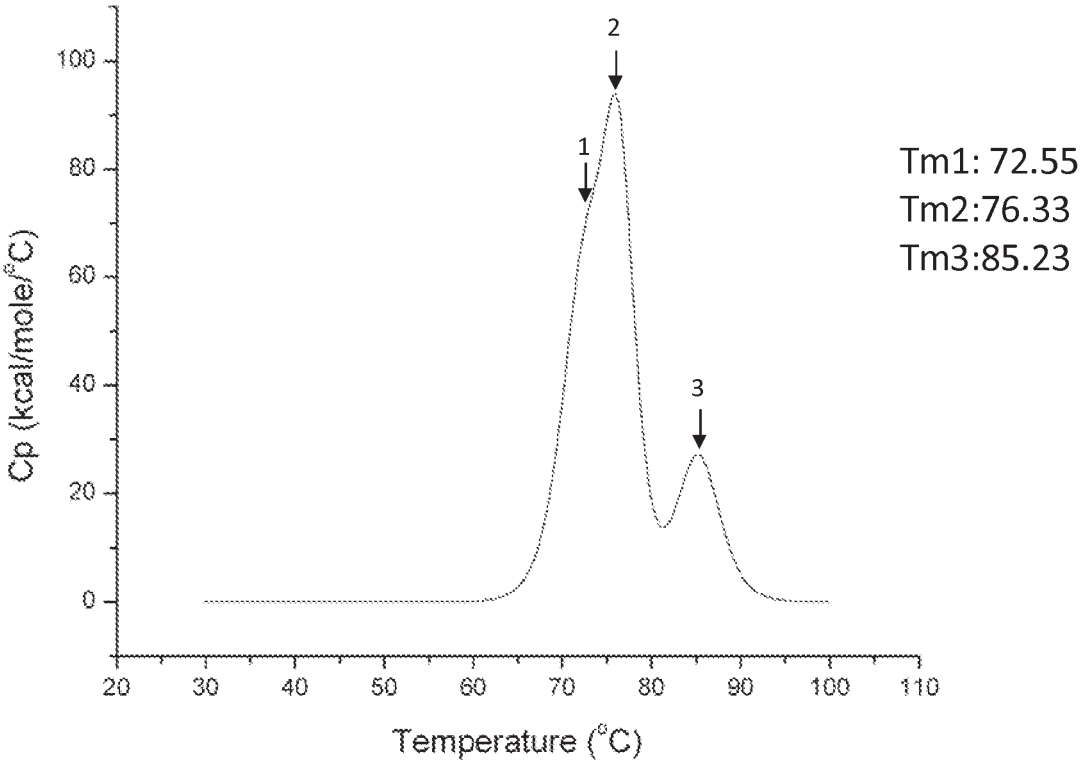


FIG. 7

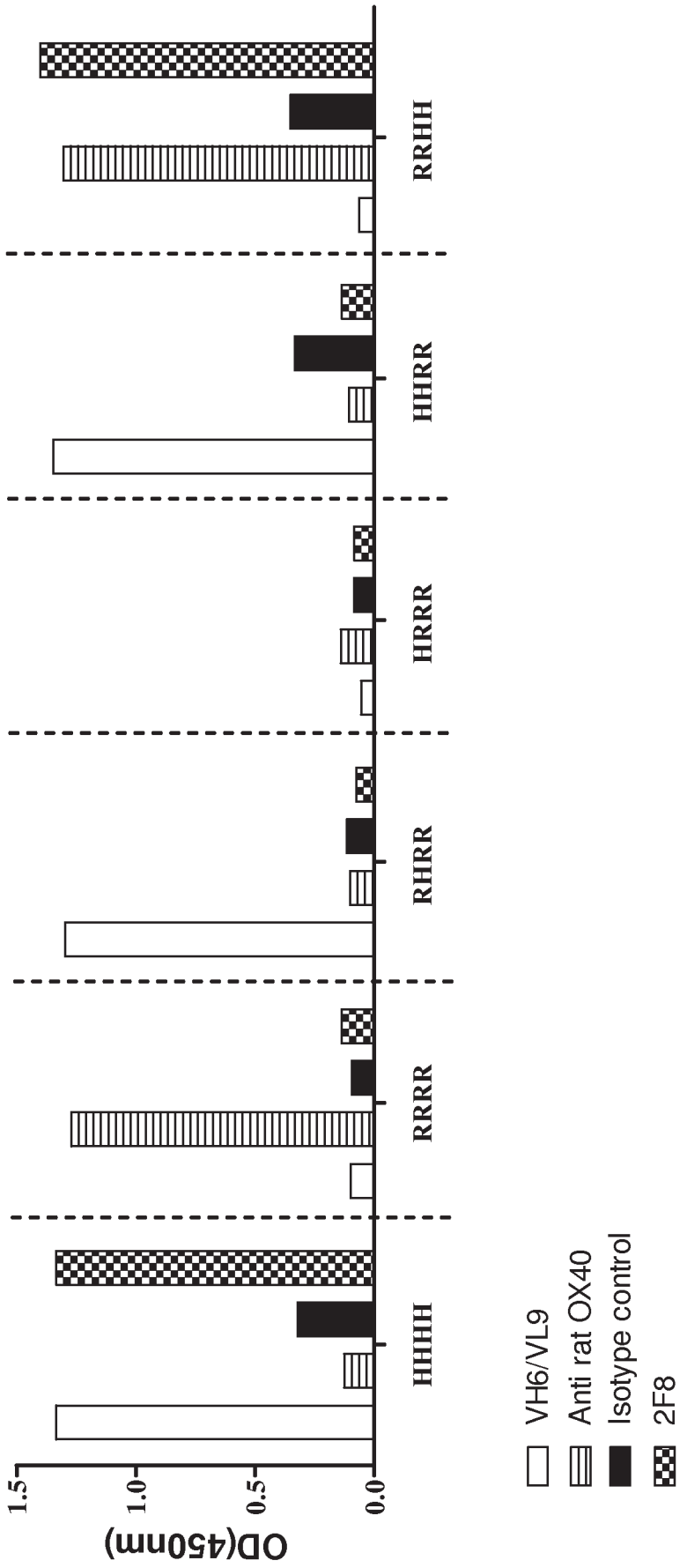

OD(450nm)
1.5
1.0
0.5
0.0
HHHH
RRRR
RHRR
HRRR
HHRR
RRHH
VH6/VL9
Anti rat OX40
Isotype control
2F8

FIG. 8A

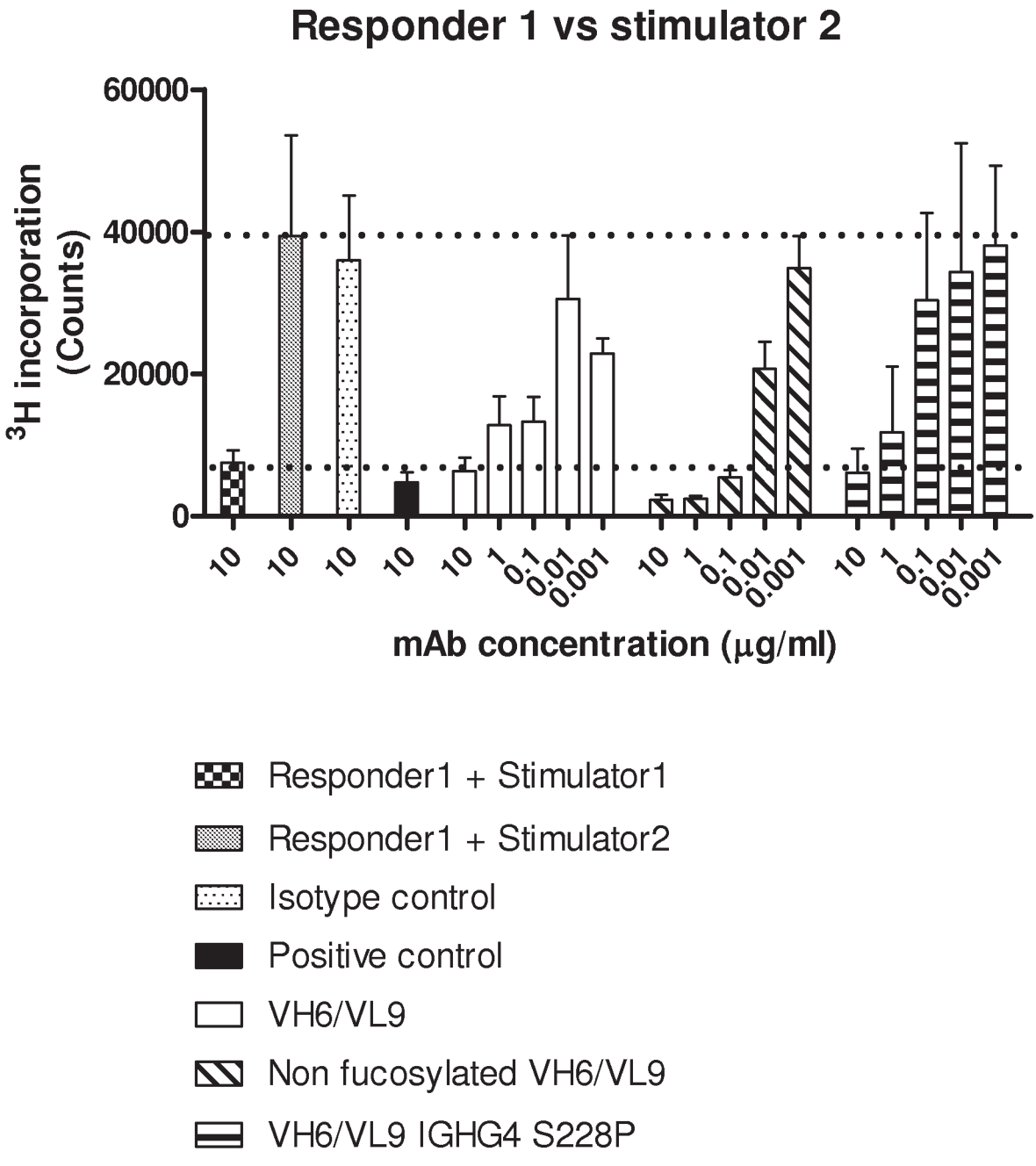

Responder 1 vs stimulator 2
60000
40000
20000
0
^{3}H incorporation (Counts)
10
10
10
10
10
1
0.1
0.01
0.001
10
1
0.1
0.01
0.001
10
1
0.1
0.01
0.001
mAb concentration (µg/ml)
Responder1 + Stimulator1
Responder1 + Stimulator2
Isotype control
Positive control
VH6/VL9
Non fucosylated VH6/VL9
VH6/VL9 IGHG4 S228P

FIG. 8B

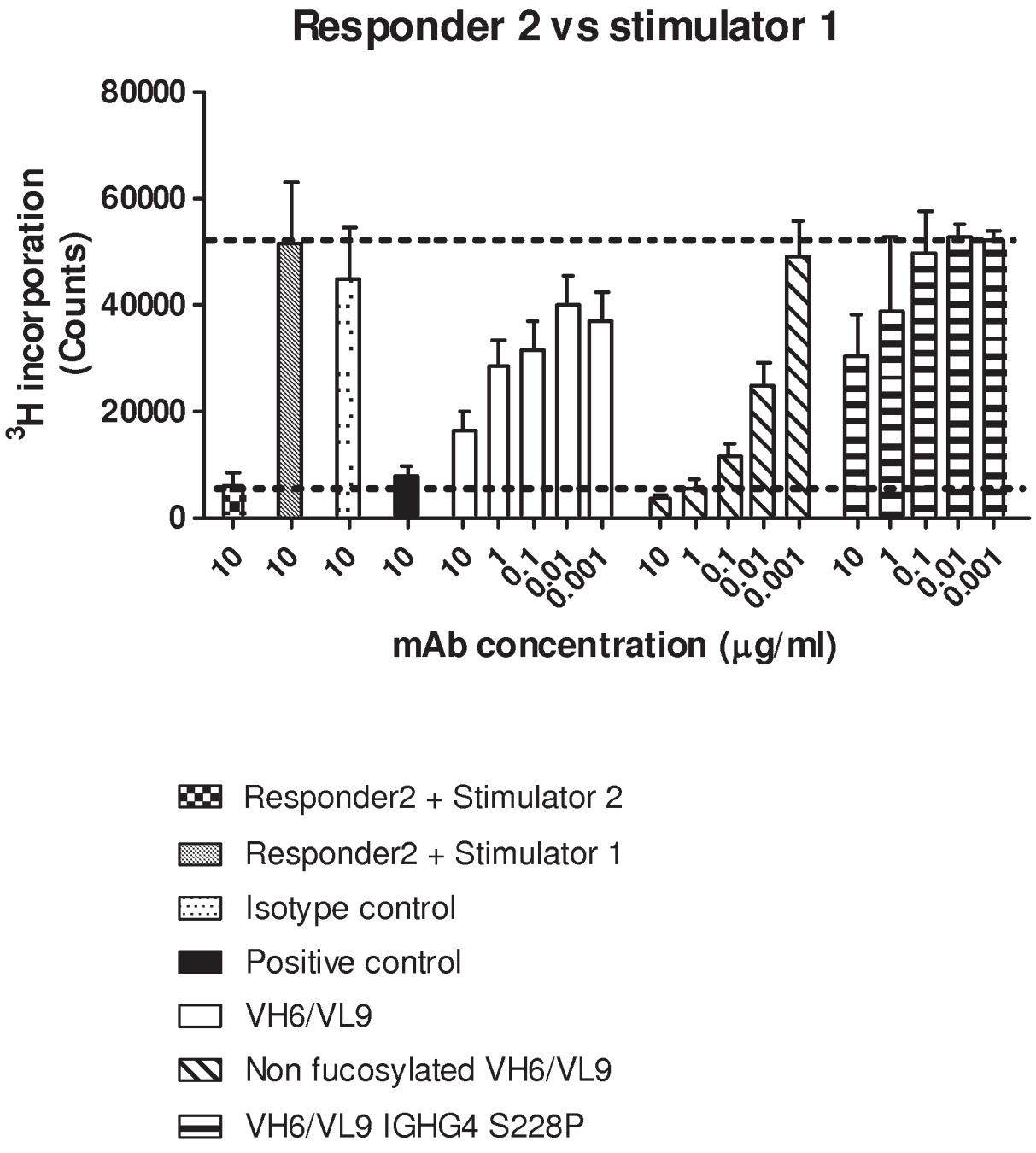
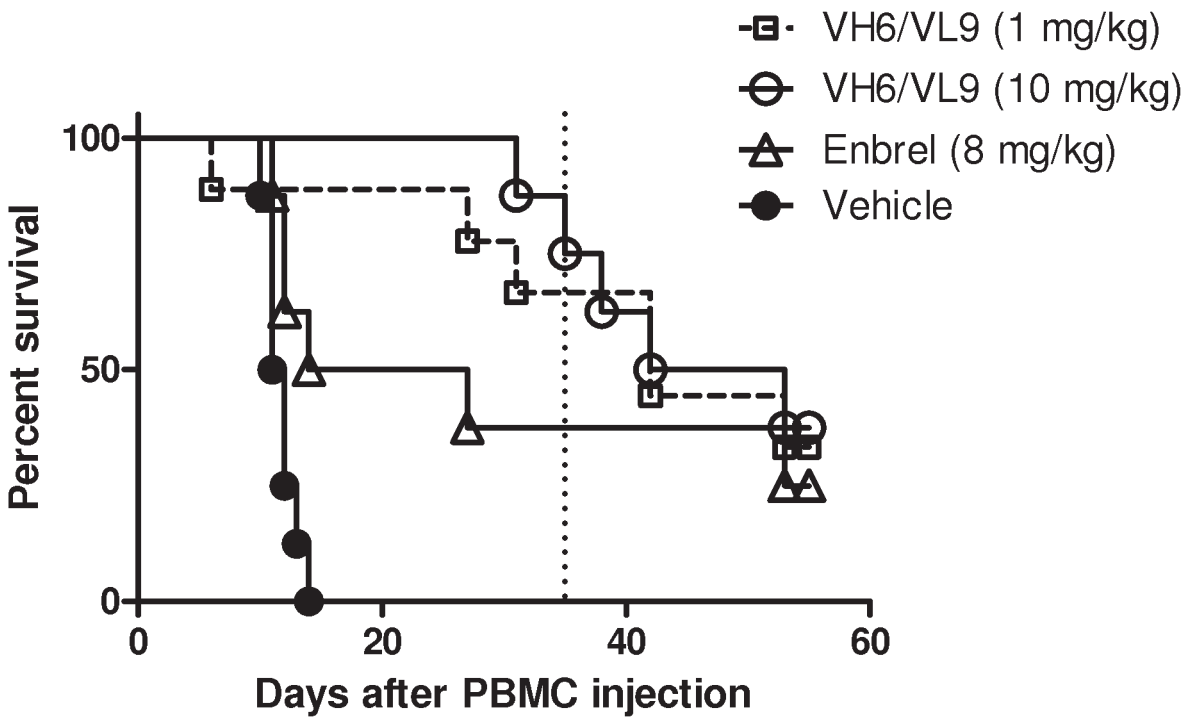

Responder 2 vs stimulator 1
80000
60000
40000
20000
0
^{3}H incorporation (Counts)
10
10
10
10
10
1
0.1
0.01
0.001
10
1
0.1
0.01
0.001
10
1
0.1
0.01
0.001
mAb concentration (µg/ml)
Responder2 + Stimulator 2
Responder2 + Stimulator 1
Isotype control
Positive control
VH6/VL9
Non fucosylated VH6/VL9
VH6/VL9 IGHG4 S228P

FIG. 9


VH6/VL9 (1 mg/kg)
VH6/VL9 (10 mg/kg)
Enbrel (8 mg/kg)
Vehicle
Percent survival
100
50
0
0
20
40
60
Days after PBMC injection