LISTADO DE SECUENCIAS

+ADw-110+AD4- F. Hoffmann-La Roche AG

+ADw-120+AD4- Moléculas de Unión A Antígeno Que Comprenden Un Trímero De Ligando de La Familia De Tnf

+ADw-130+AD4- P32429-WO

+ADw-150+AD4- EP14193260.8
+ADw-151+AD4- 14-11-2014

+ADw-150+AD4- EP15183736.6
+ADw-151+AD4- 03-09-2015

+ADw-150+AD4- EP15188142.2
+ADw-151+AD4- 02-10-2015

+ADw-160+AD4- 375

+ADw-170+AD4- PatentIn version 3.5

+ADw-210+AD4- 1
+ADw-211+AD4- 184
+ADw-212+AD4- PRT
+ADw-213+AD4- Homo sapiens

+ADw-400+AD4- 1

Arg Glu Gly Pro Glu Leu Ser Pro Asp Asp Pro Ala Gly Leu Leu Asp
1 5 10 15

Leu Arg Gln Gly Met Phe Ala Gln Leu Val Ala Gln Asn Val Leu Leu
20 25 30

Ile Asp Gly Pro Leu Ser Trp Tyr Ser Asp Pro Gly Leu Ala Gly Val
35 40 45

Ser Leu Thr Gly Gly Leu Ser Tyr Lys Glu Asp Thr Lys Glu Leu Val
50 55 60

Val Ala Lys Ala Gly Val Tyr Tyr Val Phe Phe Gln Leu Glu Leu Arg
65 70 75 80

Arg Val Val Ala Gly Glu Gly Ser Gly Ser Val Ser Leu Ala Leu His
85 90 95

Leu Gln Pro Leu Arg Ser Ala Ala Gly Ala Ala Ala Leu Ala Leu Thr
100 105 110

Val Asp Leu Pro Pro Ala Ser Ser Glu Ala Arg Asn Ser Ala Phe Gly
115 120 125

Phe Gln Gly Arg Leu Leu His Leu Ser Ala Gly Gln Arg Leu Gly Val
130 135 140

```
His Leu His Thr Glu Ala Arg Ala Arg His Ala Trp Gln Leu Thr Gln
145                 150                 155                 160


Gly Ala Thr Val Leu Gly Leu Phe Arg Val Thr Pro Glu Ile Pro Ala
                165                 170                 175


Gly Leu Pro Ser Pro Arg Ser Glu
            180


+ADw-210+AD4-  2
+ADw-211+AD4-  170
+ADw-212+AD4-  PRT
+ADw-213+AD4-  Homo sapiens

+ADw-400+AD4-  2

Leu Asp Leu Arg Gln Gly Met Phe Ala Gln Leu Val Ala Gln Asn Val
1               5                   10                  15


Leu Leu Ile Asp Gly Pro Leu Ser Trp Tyr Ser Asp Pro Gly Leu Ala
            20                  25                  30


Gly Val Ser Leu Thr Gly Gly Leu Ser Tyr Lys Glu Asp Thr Lys Glu
        35                  40                  45


Leu Val Val Ala Lys Ala Gly Val Tyr Tyr Val Phe Phe Gln Leu Glu
    50                  55                  60


Leu Arg Arg Val Val Ala Gly Glu Gly Ser Gly Ser Val Ser Leu Ala
65                  70                  75                  80


Leu His Leu Gln Pro Leu Arg Ser Ala Ala Gly Ala Ala Ala Leu Ala
                85                  90                  95


Leu Thr Val Asp Leu Pro Pro Ala Ser Ser Glu Ala Arg Asn Ser Ala
            100                 105                 110


Phe Gly Phe Gln Gly Arg Leu Leu His Leu Ser Ala Gly Gln Arg Leu
        115                 120                 125


Gly Val His Leu His Thr Glu Ala Arg Ala Arg His Ala Trp Gln Leu
    130                 135                 140


Thr Gln Gly Ala Thr Val Leu Gly Leu Phe Arg Val Thr Pro Glu Ile
145                 150                 155                 160


Pro Ala Gly Leu Pro Ser Pro Arg Ser Glu
                165                 170
```

+ADw-210+AD4- 3
+ADw-211+AD4- 175
+ADw-212+AD4- PRT
+ADw-213+AD4- Homo sapiens

+ADw-400+AD4- 3

```
Asp Pro Ala Gly Leu Leu Asp Leu Arg Gln Gly Met Phe Ala Gln Leu
1               5                  10                  15

Val Ala Gln Asn Val Leu Leu Ile Asp Gly Pro Leu Ser Trp Tyr Ser
            20                  25                  30

Asp Pro Gly Leu Ala Gly Val Ser Leu Thr Gly Gly Leu Ser Tyr Lys
        35                  40                  45

Glu Asp Thr Lys Glu Leu Val Val Ala Lys Ala Gly Val Tyr Tyr Val
    50                  55                  60

Phe Phe Gln Leu Glu Leu Arg Arg Val Val Ala Gly Glu Gly Ser Gly
65                  70                  75                  80

Ser Val Ser Leu Ala Leu His Leu Gln Pro Leu Arg Ser Ala Ala Gly
                85                  90                  95

Ala Ala Ala Leu Ala Leu Thr Val Asp Leu Pro Pro Ala Ser Ser Glu
            100                 105                 110

Ala Arg Asn Ser Ala Phe Gly Phe Gln Gly Arg Leu Leu His Leu Ser
        115                 120                 125

Ala Gly Gln Arg Leu Gly Val His Leu His Thr Glu Ala Arg Ala Arg
    130                 135                 140

His Ala Trp Gln Leu Thr Gln Gly Ala Thr Val Leu Gly Leu Phe Arg
145                 150                 155                 160

Val Thr Pro Glu Ile Pro Ala Gly Leu Pro Ser Pro Arg Ser Glu
                165                 170                 175
```

+ADw-210+AD4- 4
+ADw-211+AD4- 203
+ADw-212+AD4- PRT
+ADw-213+AD4- Homo sapiens

+ADw-400+AD4- 4

```
Pro Trp Ala Val Ser Gly Ala Arg Ala Ser Pro Gly Ser Ala Ala Ser
1               5                  10                  15
```

```
Pro Arg Leu Arg Glu Gly Pro Glu Leu Ser Pro Asp Asp Pro Ala Gly
            20                  25                  30

Leu Leu Asp Leu Arg Gln Gly Met Phe Ala Gln Leu Val Ala Gln Asn
        35                  40                  45

Val Leu Leu Ile Asp Gly Pro Leu Ser Trp Tyr Ser Asp Pro Gly Leu
    50                  55                  60

Ala Gly Val Ser Leu Thr Gly Gly Leu Ser Tyr Lys Glu Asp Thr Lys
65                  70                  75                  80

Glu Leu Val Val Ala Lys Ala Gly Val Tyr Tyr Val Phe Phe Gln Leu
                85                  90                  95

Glu Leu Arg Arg Val Val Ala Gly Glu Gly Ser Gly Ser Val Ser Leu
            100                 105                 110

Ala Leu His Leu Gln Pro Leu Arg Ser Ala Ala Gly Ala Ala Ala Leu
        115                 120                 125

Ala Leu Thr Val Asp Leu Pro Pro Ala Ser Ser Glu Ala Arg Asn Ser
    130                 135                 140

Ala Phe Gly Phe Gln Gly Arg Leu Leu His Leu Ser Ala Gly Gln Arg
145                 150                 155                 160

Leu Gly Val His Leu His Thr Glu Ala Arg Ala Arg His Ala Trp Gln
                165                 170                 175

Leu Thr Gln Gly Ala Thr Val Leu Gly Leu Phe Arg Val Thr Pro Glu
            180                 185                 190

Ile Pro Ala Gly Leu Pro Ser Pro Arg Ser Glu
        195                 200


+ADw-210+AD4-  5
+ADw-211+AD4-  378
+ADw-212+AD4-  PRT
+ADw-213+AD4-  Secuencia artificial

+ADw-220+AD4-
+ADw-223+AD4-  hu 4-1BBL (71-254) conectado mediante el enlazador (G4S)2 a
hu-4-1BBL (71-254)

+ADw-400+AD4-  5

Arg Glu Gly Pro Glu Leu Ser Pro Asp Asp Pro Ala Gly Leu Leu Asp
1               5                  10                  15
```

```
Leu Arg Gln Gly Met Phe Ala Gln Leu Val Ala Gln Asn Val Leu Leu
            20                  25                  30

Ile Asp Gly Pro Leu Ser Trp Tyr Ser Asp Pro Gly Leu Ala Gly Val
        35                  40                  45

Ser Leu Thr Gly Gly Leu Ser Tyr Lys Glu Asp Thr Lys Glu Leu Val
    50                  55                  60

Val Ala Lys Ala Gly Val Tyr Tyr Val Phe Phe Gln Leu Glu Leu Arg
65                  70                  75                  80

Arg Val Val Ala Gly Glu Gly Ser Gly Ser Val Ser Leu Ala Leu His
                85                  90                  95

Leu Gln Pro Leu Arg Ser Ala Ala Gly Ala Ala Ala Leu Ala Leu Thr
            100                 105                 110

Val Asp Leu Pro Pro Ala Ser Ser Glu Ala Arg Asn Ser Ala Phe Gly
        115                 120                 125

Phe Gln Gly Arg Leu Leu His Leu Ser Ala Gly Gln Arg Leu Gly Val
    130                 135                 140

His Leu His Thr Glu Ala Arg Ala Arg His Ala Trp Gln Leu Thr Gln
145                 150                 155                 160

Gly Ala Thr Val Leu Gly Leu Phe Arg Val Thr Pro Glu Ile Pro Ala
                165                 170                 175

Gly Leu Pro Ser Pro Arg Ser Glu Gly Gly Gly Gly Ser Gly Gly Gly
            180                 185                 190

Gly Ser Arg Glu Gly Pro Glu Leu Ser Pro Asp Asp Pro Ala Gly Leu
        195                 200                 205

Leu Asp Leu Arg Gln Gly Met Phe Ala Gln Leu Val Ala Gln Asn Val
    210                 215                 220

Leu Leu Ile Asp Gly Pro Leu Ser Trp Tyr Ser Asp Pro Gly Leu Ala
225                 230                 235                 240

Gly Val Ser Leu Thr Gly Gly Leu Ser Tyr Lys Glu Asp Thr Lys Glu
                245                 250                 255

Leu Val Val Ala Lys Ala Gly Val Tyr Tyr Val Phe Phe Gln Leu Glu
            260                 265                 270
```

```
Leu Arg Arg Val Val Ala Gly Glu Gly Ser Gly Ser Val Ser Leu Ala
        275                 280                 285

Leu His Leu Gln Pro Leu Arg Ser Ala Ala Gly Ala Ala Ala Leu Ala
    290                 295                 300

Leu Thr Val Asp Leu Pro Pro Ala Ser Ser Glu Ala Arg Asn Ser Ala
305                 310                 315                 320

Phe Gly Phe Gln Gly Arg Leu Leu His Leu Ser Ala Gly Gln Arg Leu
                325                 330                 335

Gly Val His Leu His Thr Glu Ala Arg Ala Arg His Ala Trp Gln Leu
            340                 345                 350

Thr Gln Gly Ala Thr Val Leu Gly Leu Phe Arg Val Thr Pro Glu Ile
        355                 360                 365

Pro Ala Gly Leu Pro Ser Pro Arg Ser Glu
    370                 375


+ADw-210+AD4-  6
+ADw-211+AD4-  194
+ADw-212+AD4-  PRT
+ADw-213+AD4-  Secuencia artificial

+ADw-220+AD4-
+ADw-223+AD4-  hu 4-1BBL (71-254) m+AOE-s (G4S)2

+ADw-400+AD4-  6

Arg Glu Gly Pro Glu Leu Ser Pro Asp Asp Pro Ala Gly Leu Leu Asp
1               5                   10                  15

Leu Arg Gln Gly Met Phe Ala Gln Leu Val Ala Gln Asn Val Leu Leu
            20                  25                  30

Ile Asp Gly Pro Leu Ser Trp Tyr Ser Asp Pro Gly Leu Ala Gly Val
        35                  40                  45

Ser Leu Thr Gly Gly Leu Ser Tyr Lys Glu Asp Thr Lys Glu Leu Val
    50                  55                  60

Val Ala Lys Ala Gly Val Tyr Tyr Val Phe Phe Gln Leu Glu Leu Arg
65                  70                  75                  80

Arg Val Val Ala Gly Glu Gly Ser Gly Ser Val Ser Leu Ala Leu His
                85                  90                  95
```

Leu Gln Pro Leu Arg Ser Ala Ala Gly Ala Ala Ala Leu Ala Leu Thr
100 105 110

Val Asp Leu Pro Pro Ala Ser Ser Glu Ala Arg Asn Ser Ala Phe Gly
115 120 125

Phe Gln Gly Arg Leu Leu His Leu Ser Ala Gly Gln Arg Leu Gly Val
130 135 140

His Leu His Thr Glu Ala Arg Ala Arg His Ala Trp Gln Leu Thr Gln
145 150 155 160

Gly Ala Thr Val Leu Gly Leu Phe Arg Val Thr Pro Glu Ile Pro Ala
165 170 175

Gly Leu Pro Ser Pro Arg Ser Glu Gly Gly Gly Gly Ser Gly Gly Gly
180 185 190

Gly Ser

+ADw-210+AD4- 7
+ADw-211+AD4- 5
+ADw-212+AD4- PRT
+ADw-213+AD4- Secuencia artificial

+ADw-220+AD4-
+ADw-223+AD4- CDR-H1 de FAP(28H1)

+ADw-400+AD4- 7

Ser His Ala Met Ser
1 5

+ADw-210+AD4- 8
+ADw-211+AD4- 16
+ADw-212+AD4- PRT
+ADw-213+AD4- Secuencia artificial

+ADw-220+AD4-
+ADw-223+AD4- CDR-H2 de FAP(28H1)

+ADw-400+AD4- 8

Ala Ile Trp Ala Ser Gly Glu Gln Tyr Tyr Ala Asp Ser Val Lys Gly
1 5 10 15

+ADw-210+AD4- 9
+ADw-211+AD4- 8
+ADw-212+AD4- PRT
+ADw-213+AD4- Secuencia artificial

+ADw-220+AD4-

+ADw-223+AD4- CDR-H3 de FAP(28H1)

+ADw-400+AD4- 9

Gly Trp Leu Gly Asn Phe Asp Tyr
1   5

+ADw-210+AD4- 10
+ADw-211+AD4- 12
+ADw-212+AD4- PRT
+ADw-213+AD4- Secuencia artificial

+ADw-220+AD4-
+ADw-223+AD4- CDR-L1 de FAP(28H1)

+ADw-400+AD4- 10

Arg Ala Ser Gln Ser Val Ser Arg Ser Tyr Leu Ala
1   5   10

+ADw-210+AD4- 11
+ADw-211+AD4- 7
+ADw-212+AD4- PRT
+ADw-213+AD4- Secuencia artificial

+ADw-220+AD4-
+ADw-223+AD4- CDR-L2 de FAP(28H1)

+ADw-400+AD4- 11

Gly Ala Ser Thr Arg Ala Thr
1   5

+ADw-210+AD4- 12
+ADw-211+AD4- 9
+ADw-212+AD4- PRT
+ADw-213+AD4- Secuencia artificial

+ADw-220+AD4-
+ADw-223+AD4- CDR-L3 de FAP(28H1)

+ADw-400+AD4- 12

Gln Gln Gly Gln Val Ile Pro Pro Thr
1   5

+ADw-210+AD4- 13
+ADw-211+AD4- 10
+ADw-212+AD4- PRT
+ADw-213+AD4- Secuencia artificial

+ADw-220+AD4-
+ADw-223+AD4- enlazador pept+AO0-dico (G4S)2

+ADw-400+AD4- 13

Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser
1   5   10

+ADw-210+AD4- 14
+ADw-211+AD4- 718
+ADw-212+AD4- PRT
+ADw-213+AD4- Secuencia artificial

+ADw-220+AD4-
+ADw-223+AD4- hu 4-1BBL dim+AOk-rico (71-254) m+AOE-s CH1 m+AOE-s cadena Fc pomo

+ADw-400+AD4- 14

```
Arg Glu Gly Pro Glu Leu Ser Pro Asp Asp Pro Ala Gly Leu Leu Asp
1               5                  10                  15

Leu Arg Gln Gly Met Phe Ala Gln Leu Val Ala Gln Asn Val Leu Leu
            20                  25                  30

Ile Asp Gly Pro Leu Ser Trp Tyr Ser Asp Pro Gly Leu Ala Gly Val
        35                  40                  45

Ser Leu Thr Gly Gly Leu Ser Tyr Lys Glu Asp Thr Lys Glu Leu Val
    50                  55                  60

Val Ala Lys Ala Gly Val Tyr Tyr Val Phe Phe Gln Leu Glu Leu Arg
65                  70                  75                  80

Arg Val Val Ala Gly Glu Gly Ser Gly Ser Val Ser Leu Ala Leu His
                85                  90                  95

Leu Gln Pro Leu Arg Ser Ala Ala Gly Ala Ala Ala Leu Ala Leu Thr
            100                 105                 110

Val Asp Leu Pro Pro Ala Ser Ser Glu Ala Arg Asn Ser Ala Phe Gly
        115                 120                 125

Phe Gln Gly Arg Leu Leu His Leu Ser Ala Gly Gln Arg Leu Gly Val
    130                 135                 140

His Leu His Thr Glu Ala Arg Ala Arg His Ala Trp Gln Leu Thr Gln
145                 150                 155                 160

Gly Ala Thr Val Leu Gly Leu Phe Arg Val Thr Pro Glu Ile Pro Ala
                165                 170                 175

Gly Leu Pro Ser Pro Arg Ser Glu Gly Gly Gly Gly Ser Gly Gly Gly
            180                 185                 190

Gly Ser Arg Glu Gly Pro Glu Leu Ser Pro Asp Asp Pro Ala Gly Leu
        195                 200                 205
```

```
Leu Asp Leu Arg Gln Gly Met Phe Ala Gln Leu Val Ala Gln Asn Val
    210                 215                 220

Leu Leu Ile Asp Gly Pro Leu Ser Trp Tyr Ser Asp Pro Gly Leu Ala
225                 230                 235                 240

Gly Val Ser Leu Thr Gly Gly Leu Ser Tyr Lys Glu Asp Thr Lys Glu
                245                 250                 255

Leu Val Val Ala Lys Ala Gly Val Tyr Tyr Val Phe Phe Gln Leu Glu
            260                 265                 270

Leu Arg Arg Val Val Ala Gly Glu Gly Ser Gly Ser Val Ser Leu Ala
        275                 280                 285

Leu His Leu Gln Pro Leu Arg Ser Ala Ala Gly Ala Ala Ala Leu Ala
    290                 295                 300

Leu Thr Val Asp Leu Pro Pro Ala Ser Ser Glu Ala Arg Asn Ser Ala
305                 310                 315                 320

Phe Gly Phe Gln Gly Arg Leu Leu His Leu Ser Ala Gly Gln Arg Leu
                325                 330                 335

Gly Val His Leu His Thr Glu Ala Arg Ala Arg His Ala Trp Gln Leu
            340                 345                 350

Thr Gln Gly Ala Thr Val Leu Gly Leu Phe Arg Val Thr Pro Glu Ile
        355                 360                 365

Pro Ala Gly Leu Pro Ser Pro Arg Ser Glu Gly Gly Gly Gly Ser Gly
    370                 375                 380

Gly Gly Gly Ser Ala Ser Thr Lys Gly Pro Ser Val Phe Pro Leu Ala
385                 390                 395                 400

Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu Gly Cys Leu
                405                 410                 415

Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser Trp Asn Ser Gly
            420                 425                 430

Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala Val Leu Gln Ser Ser
        435                 440                 445

Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser Ser Ser Leu
    450                 455                 460
```

```
Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys Pro Ser Asn Thr
465                 470                 475                 480

Lys Val Asp Lys Lys Val Glu Pro Lys Ser Cys Asp Lys Thr His Thr
                485                 490                 495

Cys Pro Pro Cys Pro Ala Pro Glu Ala Ala Gly Gly Pro Ser Val Phe
            500                 505                 510

Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro
        515                 520                 525

Glu Val Thr Cys Val Val Val Asp Val Ser His Glu Asp Pro Glu Val
    530                 535                 540

Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr
545                 550                 555                 560

Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg Val Val Ser Val
                565                 570                 575

Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys
            580                 585                 590

Lys Val Ser Asn Lys Ala Leu Gly Ala Pro Ile Glu Lys Thr Ile Ser
        595                 600                 605

Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro
    610                 615                 620

Cys Arg Asp Glu Leu Thr Lys Asn Gln Val Ser Leu Trp Cys Leu Val
625                 630                 635                 640

Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly
                645                 650                 655

Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp
            660                 665                 670

Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp
        675                 680                 685

Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His Glu Ala Leu His
    690                 695                 700

Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly Lys
705                 710                 715
```

+ADw-210+AD4- 15
+ADw-211+AD4- 301
+ADw-212+AD4- PRT
+ADw-213+AD4- Secuencia artificial

+ADw-220+AD4-
+ADw-223+AD4- hu 4-1BBL (71-254) -CL

+ADw-400+AD4- 15

```
Arg Glu Gly Pro Glu Leu Ser Pro Asp Asp Pro Ala Gly Leu Leu Asp
1               5                  10                  15

Leu Arg Gln Gly Met Phe Ala Gln Leu Val Ala Gln Asn Val Leu Leu
            20                  25                  30

Ile Asp Gly Pro Leu Ser Trp Tyr Ser Asp Pro Gly Leu Ala Gly Val
        35                  40                  45

Ser Leu Thr Gly Gly Leu Ser Tyr Lys Glu Asp Thr Lys Glu Leu Val
    50                  55                  60

Val Ala Lys Ala Gly Val Tyr Tyr Val Phe Phe Gln Leu Glu Leu Arg
65                  70                  75                  80

Arg Val Val Ala Gly Glu Gly Ser Gly Ser Val Ser Leu Ala Leu His
                85                  90                  95

Leu Gln Pro Leu Arg Ser Ala Ala Gly Ala Ala Ala Leu Ala Leu Thr
            100                 105                 110

Val Asp Leu Pro Pro Ala Ser Ser Glu Ala Arg Asn Ser Ala Phe Gly
        115                 120                 125

Phe Gln Gly Arg Leu Leu His Leu Ser Ala Gly Gln Arg Leu Gly Val
    130                 135                 140

His Leu His Thr Glu Ala Arg Ala Arg His Ala Trp Gln Leu Thr Gln
145                 150                 155                 160

Gly Ala Thr Val Leu Gly Leu Phe Arg Val Thr Pro Glu Ile Pro Ala
                165                 170                 175

Gly Leu Pro Ser Pro Arg Ser Glu Gly Gly Gly Gly Ser Gly Gly Gly
            180                 185                 190

Gly Ser Arg Thr Val Ala Ala Pro Ser Val Phe Ile Phe Pro Pro Ser
        195                 200                 205
```

```
Asp Glu Gln Leu Lys Ser Gly Thr Ala Ser Val Val Cys Leu Leu Asn
    210                 215                 220

Asn Phe Tyr Pro Arg Glu Ala Lys Val Gln Trp Lys Val Asp Asn Ala
225                 230                 235                 240

Leu Gln Ser Gly Asn Ser Gln Glu Ser Val Thr Glu Gln Asp Ser Lys
                245                 250                 255

Asp Ser Thr Tyr Ser Leu Ser Ser Thr Leu Thr Leu Ser Lys Ala Asp
            260                 265                 270

Tyr Glu Lys His Lys Val Tyr Ala Cys Glu Val Thr His Gln Gly Leu
        275                 280                 285

Ser Ser Pro Val Thr Lys Ser Phe Asn Arg Gly Glu Cys
    290                 295                 300


+ADw-210+AD4-  16
+ADw-211+AD4-  116
+ADw-212+AD4-  PRT
+ADw-213+AD4-  Secuencia artificial

+ADw-220+AD4-
+ADw-223+AD4-  FAP(28H1) VH

+ADw-400+AD4-  16

Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1               5                   10                  15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Ser His
            20                  25                  30

Ala Met Ser Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
        35                  40                  45

Ser Ala Ile Trp Ala Ser Gly Glu Gln Tyr Tyr Ala Asp Ser Val Lys
    50                  55                  60

Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr Leu
65                  70                  75                  80

Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys Ala
                85                  90                  95

Lys Gly Trp Leu Gly Asn Phe Asp Tyr Trp Gly Gln Gly Thr Leu Val
            100                 105                 110
```

Thr Val Ser Ser
        115

+ADw-210+AD4- 17
+ADw-211+AD4- 108
+ADw-212+AD4- PRT
+ADw-213+AD4- Secuencia artificial

+ADw-220+AD4-
+ADw-223+AD4- FAP(28H1) VL

+ADw-400+AD4- 17

Glu Ile Val Leu Thr Gln Ser Pro Gly Thr Leu Ser Leu Ser Pro Gly
1   5   10   15

Glu Arg Ala Thr Leu Ser Cys Arg Ala Ser Gln Ser Val Ser Arg Ser
            20   25   30

Tyr Leu Ala Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Arg Leu Leu
        35   40   45

Ile Ile Gly Ala Ser Thr Arg Ala Thr Gly Ile Pro Asp Arg Phe Ser
    50   55   60

Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Arg Leu Glu
65   70   75   80

Pro Glu Asp Phe Ala Val Tyr Tyr Cys Gln Gln Gly Gln Val Ile Pro
                85   90   95

Pro Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys
            100   105

+ADw-210+AD4- 18
+ADw-211+AD4- 446
+ADw-212+AD4- PRT
+ADw-213+AD4- Secuencia artificial

+ADw-220+AD4-
+ADw-223+AD4- cadena pesada de FAP(28H1) Fc agujero

+ADw-400+AD4- 18

Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1   5   10   15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Ser His
            20   25   30

Ala Met Ser Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
        35   40   45

```
Ser Ala Ile Trp Ala Ser Gly Glu Gln Tyr Tyr Ala Asp Ser Val Lys
    50                  55                  60

Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr Leu
65                  70                  75                  80

Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys Ala
                85                  90                  95

Lys Gly Trp Leu Gly Asn Phe Asp Tyr Trp Gly Gln Gly Thr Leu Val
            100                 105                 110

Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser Val Phe Pro Leu Ala
        115                 120                 125

Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu Gly Cys Leu
    130                 135                 140

Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser Trp Asn Ser Gly
145                 150                 155                 160

Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala Val Leu Gln Ser Ser
                165                 170                 175

Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser Ser Ser Leu
            180                 185                 190

Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys Pro Ser Asn Thr
        195                 200                 205

Lys Val Asp Lys Lys Val Glu Pro Lys Ser Cys Asp Lys Thr His Thr
    210                 215                 220

Cys Pro Pro Cys Pro Ala Pro Glu Ala Ala Gly Gly Pro Ser Val Phe
225                 230                 235                 240

Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro
                245                 250                 255

Glu Val Thr Cys Val Val Val Asp Val Ser His Glu Asp Pro Glu Val
            260                 265                 270

Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr
        275                 280                 285

Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg Val Val Ser Val
    290                 295                 300
```

```
Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys
305                 310                 315                 320


Lys Val Ser Asn Lys Ala Leu Gly Ala Pro Ile Glu Lys Thr Ile Ser
                325                 330                 335


Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Cys Thr Leu Pro Pro
            340                 345                 350


Ser Arg Asp Glu Leu Thr Lys Asn Gln Val Ser Leu Ser Cys Ala Val
        355                 360                 365


Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly
    370                 375                 380


Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp
385                 390                 395                 400


Gly Ser Phe Phe Leu Val Ser Lys Leu Thr Val Asp Lys Ser Arg Trp
                405                 410                 415


Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His Glu Ala Leu His
            420                 425                 430


Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly Lys
        435                 440                 445


+ADw-210+AD4-  19
+ADw-211+AD4-  215
+ADw-212+AD4-  PRT
+ADw-213+AD4-  Secuencia artificial

+ADw-220+AD4-
+ADw-223+AD4-  cadena ligera de FAP(28H1)

+ADw-400+AD4-  19

Glu Ile Val Leu Thr Gln Ser Pro Gly Thr Leu Ser Leu Ser Pro Gly
1               5                   10                  15


Glu Arg Ala Thr Leu Ser Cys Arg Ala Ser Gln Ser Val Ser Arg Ser
            20                  25                  30


Tyr Leu Ala Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Arg Leu Leu
        35                  40                  45


Ile Ile Gly Ala Ser Thr Arg Ala Thr Gly Ile Pro Asp Arg Phe Ser
    50                  55                  60
```

```
Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Arg Leu Glu
65                  70                  75                  80


Pro Glu Asp Phe Ala Val Tyr Tyr Cys Gln Gln Gly Gln Val Ile Pro
                85                  90                  95


Pro Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys Arg Thr Val Ala
            100                 105                 110


Ala Pro Ser Val Phe Ile Phe Pro Pro Ser Asp Glu Gln Leu Lys Ser
        115                 120                 125


Gly Thr Ala Ser Val Val Cys Leu Leu Asn Asn Phe Tyr Pro Arg Glu
    130                 135                 140


Ala Lys Val Gln Trp Lys Val Asp Asn Ala Leu Gln Ser Gly Asn Ser
145                 150                 155                 160


Gln Glu Ser Val Thr Glu Gln Asp Ser Lys Asp Ser Thr Tyr Ser Leu
                165                 170                 175


Ser Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu Lys His Lys Val
            180                 185                 190


Tyr Ala Cys Glu Val Thr His Gln Gly Leu Ser Ser Pro Val Thr Lys
        195                 200                 205


Ser Phe Asn Arg Gly Glu Cys
    210                 215


+ADw-210+AD4-  20
+ADw-211+AD4-  760
+ADw-212+AD4-  PRT
+ADw-213+AD4-  Homo sapiens

+ADw-400+AD4-  20

Met Lys Thr Trp Val Lys Ile Val Phe Gly Val Ala Thr Ser Ala Val
1               5                   10                  15


Leu Ala Leu Leu Val Met Cys Ile Val Leu Arg Pro Ser Arg Val His
            20                  25                  30


Asn Ser Glu Glu Asn Thr Met Arg Ala Leu Thr Leu Lys Asp Ile Leu
        35                  40                  45


Asn Gly Thr Phe Ser Tyr Lys Thr Phe Phe Pro Asn Trp Ile Ser Gly
    50                  55                  60
```

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Gln Glu Tyr Leu His Gln Ser Ala Asp Asn Asn Ile Val Leu Tyr Asn
65                  70                  75                  80

Ile Glu Thr Gly Gln Ser Tyr Thr Ile Leu Ser Asn Arg Thr Met Lys
                85                  90                  95

Ser Val Asn Ala Ser Asn Tyr Gly Leu Ser Pro Asp Arg Gln Phe Val
            100                 105                 110

Tyr Leu Glu Ser Asp Tyr Ser Lys Leu Trp Arg Tyr Ser Tyr Thr Ala
        115                 120                 125

Thr Tyr Tyr Ile Tyr Asp Leu Ser Asn Gly Glu Phe Val Arg Gly Asn
    130                 135                 140

Glu Leu Pro Arg Pro Ile Gln Tyr Leu Cys Trp Ser Pro Val Gly Ser
145                 150                 155                 160

Lys Leu Ala Tyr Val Tyr Gln Asn Asn Ile Tyr Leu Lys Gln Arg Pro
                165                 170                 175

Gly Asp Pro Pro Phe Gln Ile Thr Phe Asn Gly Arg Glu Asn Lys Ile
            180                 185                 190

Phe Asn Gly Ile Pro Asp Trp Val Tyr Glu Glu Glu Met Leu Ala Thr
        195                 200                 205

Lys Tyr Ala Leu Trp Trp Ser Pro Asn Gly Lys Phe Leu Ala Tyr Ala
    210                 215                 220

Glu Phe Asn Asp Thr Asp Ile Pro Val Ile Ala Tyr Ser Tyr Tyr Gly
225                 230                 235                 240

Asp Glu Gln Tyr Pro Arg Thr Ile Asn Ile Pro Tyr Pro Lys Ala Gly
                245                 250                 255

Ala Lys Asn Pro Val Val Arg Ile Phe Ile Ile Asp Thr Thr Tyr Pro
            260                 265                 270

Ala Tyr Val Gly Pro Gln Glu Val Pro Val Pro Ala Met Ile Ala Ser
        275                 280                 285

Ser Asp Tyr Tyr Phe Ser Trp Leu Thr Trp Val Thr Asp Glu Arg Val
    290                 295                 300

Cys Leu Gln Trp Leu Lys Arg Val Gln Asn Val Ser Val Leu Ser Ile
305                 310                 315                 320
```

```
Cys Asp Phe Arg Glu Asp Trp Gln Thr Trp Asp Cys Pro Lys Thr Gln
                325                 330                 335

Glu His Ile Glu Glu Ser Arg Thr Gly Trp Ala Gly Gly Phe Phe Val
            340                 345                 350

Ser Thr Pro Val Phe Ser Tyr Asp Ala Ile Ser Tyr Tyr Lys Ile Phe
        355                 360                 365

Ser Asp Lys Asp Gly Tyr Lys His Ile His Tyr Ile Lys Asp Thr Val
    370                 375                 380

Glu Asn Ala Ile Gln Ile Thr Ser Gly Lys Trp Glu Ala Ile Asn Ile
385                 390                 395                 400

Phe Arg Val Thr Gln Asp Ser Leu Phe Tyr Ser Ser Asn Glu Phe Glu
                405                 410                 415

Glu Tyr Pro Gly Arg Arg Asn Ile Tyr Arg Ile Ser Ile Gly Ser Tyr
            420                 425                 430

Pro Pro Ser Lys Lys Cys Val Thr Cys His Leu Arg Lys Glu Arg Cys
        435                 440                 445

Gln Tyr Tyr Thr Ala Ser Phe Ser Asp Tyr Ala Lys Tyr Tyr Ala Leu
    450                 455                 460

Val Cys Tyr Gly Pro Gly Ile Pro Ile Ser Thr Leu His Asp Gly Arg
465                 470                 475                 480

Thr Asp Gln Glu Ile Lys Ile Leu Glu Glu Asn Lys Glu Leu Glu Asn
                485                 490                 495

Ala Leu Lys Asn Ile Gln Leu Pro Lys Glu Glu Ile Lys Lys Leu Glu
            500                 505                 510

Val Asp Glu Ile Thr Leu Trp Tyr Lys Met Ile Leu Pro Pro Gln Phe
        515                 520                 525

Asp Arg Ser Lys Lys Tyr Pro Leu Leu Ile Gln Val Tyr Gly Gly Pro
    530                 535                 540

Cys Ser Gln Ser Val Arg Ser Val Phe Ala Val Asn Trp Ile Ser Tyr
545                 550                 555                 560

Leu Ala Ser Lys Glu Gly Met Val Ile Ala Leu Val Asp Gly Arg Gly
```

565 570 575

Thr Ala Phe Gln Gly Asp Lys Leu Leu Tyr Ala Val Tyr Arg Lys Leu
580 585 590

Gly Val Tyr Glu Val Glu Asp Gln Ile Thr Ala Val Arg Lys Phe Ile
595 600 605

Glu Met Gly Phe Ile Asp Glu Lys Arg Ile Ala Ile Trp Gly Trp Ser
610 615 620

Tyr Gly Gly Tyr Val Ser Ser Leu Ala Leu Ala Ser Gly Thr Gly Leu
625 630 635 640

Phe Lys Cys Gly Ile Ala Val Ala Pro Val Ser Ser Trp Glu Tyr Tyr
645 650 655

Ala Ser Val Tyr Thr Glu Arg Phe Met Gly Leu Pro Thr Lys Asp Asp
660 665 670

Asn Leu Glu His Tyr Lys Asn Ser Thr Val Met Ala Arg Ala Glu Tyr
675 680 685

Phe Arg Asn Val Asp Tyr Leu Leu Ile His Gly Thr Ala Asp Asp Asn
690 695 700

Val His Phe Gln Asn Ser Ala Gln Ile Ala Lys Ala Leu Val Asn Ala
705 710 715 720

Gln Val Asp Phe Gln Ala Met Trp Tyr Ser Asp Gln Asn His Gly Leu
725 730 735

Ser Gly Leu Ser Thr Asn His Leu Tyr Thr His Met Thr His Phe Leu
740 745 750

Lys Gln Cys Phe Ser Leu Ser Asp
755 760

+ADw-210+AD4- 21
+ADw-211+AD4- 748
+ADw-212+AD4- PRT
+ADw-213+AD4- Secuencia artificial

+ADw-220+AD4-
+ADw-223+AD4- ectodominio de hu FAP marcador Lys marcador avi

+ADw-400+AD4- 21

Arg Pro Ser Arg Val His Asn Ser Glu Glu Asn Thr Met Arg Ala Leu
1 5 10 15

```
Thr Leu Lys Asp Ile Leu Asn Gly Thr Phe Ser Tyr Lys Thr Phe Phe
            20                  25                  30

Pro Asn Trp Ile Ser Gly Gln Glu Tyr Leu His Gln Ser Ala Asp Asn
        35                  40                  45

Asn Ile Val Leu Tyr Asn Ile Glu Thr Gly Gln Ser Tyr Thr Ile Leu
    50                  55                  60

Ser Asn Arg Thr Met Lys Ser Val Asn Ala Ser Asn Tyr Gly Leu Ser
65                  70                  75                  80

Pro Asp Arg Gln Phe Val Tyr Leu Glu Ser Asp Tyr Ser Lys Leu Trp
                85                  90                  95

Arg Tyr Ser Tyr Thr Ala Thr Tyr Tyr Ile Tyr Asp Leu Ser Asn Gly
            100                 105                 110

Glu Phe Val Arg Gly Asn Glu Leu Pro Arg Pro Ile Gln Tyr Leu Cys
        115                 120                 125

Trp Ser Pro Val Gly Ser Lys Leu Ala Tyr Val Tyr Gln Asn Asn Ile
    130                 135                 140

Tyr Leu Lys Gln Arg Pro Gly Asp Pro Pro Phe Gln Ile Thr Phe Asn
145                 150                 155                 160

Gly Arg Glu Asn Lys Ile Phe Asn Gly Ile Pro Asp Trp Val Tyr Glu
                165                 170                 175

Glu Glu Met Leu Ala Thr Lys Tyr Ala Leu Trp Trp Ser Pro Asn Gly
            180                 185                 190

Lys Phe Leu Ala Tyr Ala Glu Phe Asn Asp Thr Asp Ile Pro Val Ile
        195                 200                 205

Ala Tyr Ser Tyr Tyr Gly Asp Glu Gln Tyr Pro Arg Thr Ile Asn Ile
    210                 215                 220

Pro Tyr Pro Lys Ala Gly Ala Lys Asn Pro Val Val Arg Ile Phe Ile
225                 230                 235                 240

Ile Asp Thr Thr Tyr Pro Ala Tyr Val Gly Pro Gln Glu Val Pro Val
                245                 250                 255

Pro Ala Met Ile Ala Ser Ser Asp Tyr Tyr Phe Ser Trp Leu Thr Trp
```

```
            260                 265                 270

Val Thr Asp Glu Arg Val Cys Leu Gln Trp Leu Lys Arg Val Gln Asn
        275                 280                 285

Val Ser Val Leu Ser Ile Cys Asp Phe Arg Glu Asp Trp Gln Thr Trp
    290                 295                 300

Asp Cys Pro Lys Thr Gln Glu His Ile Glu Glu Ser Arg Thr Gly Trp
305                 310                 315                 320

Ala Gly Gly Phe Phe Val Ser Thr Pro Val Phe Ser Tyr Asp Ala Ile
                325                 330                 335

Ser Tyr Tyr Lys Ile Phe Ser Asp Lys Asp Gly Tyr Lys His Ile His
            340                 345                 350

Tyr Ile Lys Asp Thr Val Glu Asn Ala Ile Gln Ile Thr Ser Gly Lys
        355                 360                 365

Trp Glu Ala Ile Asn Ile Phe Arg Val Thr Gln Asp Ser Leu Phe Tyr
    370                 375                 380

Ser Ser Asn Glu Phe Glu Glu Tyr Pro Gly Arg Arg Asn Ile Tyr Arg
385                 390                 395                 400

Ile Ser Ile Gly Ser Tyr Pro Pro Ser Lys Lys Cys Val Thr Cys His
                405                 410                 415

Leu Arg Lys Glu Arg Cys Gln Tyr Tyr Thr Ala Ser Phe Ser Asp Tyr
            420                 425                 430

Ala Lys Tyr Tyr Ala Leu Val Cys Tyr Gly Pro Gly Ile Pro Ile Ser
        435                 440                 445

Thr Leu His Asp Gly Arg Thr Asp Gln Glu Ile Lys Ile Leu Glu Glu
    450                 455                 460

Asn Lys Glu Leu Glu Asn Ala Leu Lys Asn Ile Gln Leu Pro Lys Glu
465                 470                 475                 480

Glu Ile Lys Lys Leu Glu Val Asp Glu Ile Thr Leu Trp Tyr Lys Met
                485                 490                 495

Ile Leu Pro Pro Gln Phe Asp Arg Ser Lys Lys Tyr Pro Leu Leu Ile
            500                 505                 510
```

```
Gln Val Tyr Gly Gly Pro Cys Ser Gln Ser Val Arg Ser Val Phe Ala
        515                 520                 525

Val Asn Trp Ile Ser Tyr Leu Ala Ser Lys Glu Gly Met Val Ile Ala
    530                 535                 540

Leu Val Asp Gly Arg Gly Thr Ala Phe Gln Gly Asp Lys Leu Leu Tyr
545                 550                 555                 560

Ala Val Tyr Arg Lys Leu Gly Val Tyr Glu Val Glu Asp Gln Ile Thr
                565                 570                 575

Ala Val Arg Lys Phe Ile Glu Met Gly Phe Ile Asp Glu Lys Arg Ile
            580                 585                 590

Ala Ile Trp Gly Trp Ser Tyr Gly Gly Tyr Val Ser Ser Leu Ala Leu
        595                 600                 605

Ala Ser Gly Thr Gly Leu Phe Lys Cys Gly Ile Ala Val Ala Pro Val
    610                 615                 620

Ser Ser Trp Glu Tyr Tyr Ala Ser Val Tyr Thr Glu Arg Phe Met Gly
625                 630                 635                 640

Leu Pro Thr Lys Asp Asp Asn Leu Glu His Tyr Lys Asn Ser Thr Val
                645                 650                 655

Met Ala Arg Ala Glu Tyr Phe Arg Asn Val Asp Tyr Leu Leu Ile His
            660                 665                 670

Gly Thr Ala Asp Asp Asn Val His Phe Gln Asn Ser Ala Gln Ile Ala
        675                 680                 685

Lys Ala Leu Val Asn Ala Gln Val Asp Phe Gln Ala Met Trp Tyr Ser
    690                 695                 700

Asp Gln Asn His Gly Leu Ser Gly Leu Ser Thr Asn His Leu Tyr Thr
705                 710                 715                 720

His Met Thr His Phe Leu Lys Gln Cys Phe Ser Leu Ser Asp Gly Lys
                725                 730                 735

Lys Lys Lys Lys Lys Gly His His His His His His
            740                 745

+ADw-210+AD4-  22
+ADw-211+AD4-  2244
+ADw-212+AD4-  ADN
```

+ADw-213+AD4- Secuencia artificial

+ADw-220+AD4-
+ADw-223+AD4- ectodominio de hu FAP marcador Lys marcador avi

+ADw-400+AD4- 22
cgcccttcaa gagttcataa ctctgaagaa aatacaatga gagcactcac actgaaggat 60

attttaaatg gaacattttc ttataaaaca ttttttccaa actggatttc aggacaagaa 120

tatcttcatc aatctgcaga taacaatata gtactttata atattgaaac aggacaatca 180

tataccattt tgagtaatag aaccatgaaa agtgtgaatg cttcaaatta cggcttatca 240

cctgatcggc aatttgtata tctagaaagt gattattcaa agctttggag atactcttac 300

acagcaacat attacatcta tgaccttagc aatggagaat ttgtaagagg aaatgagctt 360

cctcgtccaa ttcagtattt atgctggtcg cctgttggga gtaaattagc atatgtctat 420

caaaacaata tctatttgaa acaaagacca ggagatccac cttttcaaat aacatttaat 480

ggaagagaaa ataaaatatt taatggaatc ccagactggg tttatgaaga ggaaatgctt 540

gctacaaaat atgctctctg gtggtctcct aatggaaaat ttttggcata tgcggaattt 600

aatgatacgg atataccagt tattgcctat tcctattatg gcgatgaaca atatcctaga 660

acaataaata ttccataccc aaaggctgga gctaagaatc ccgttgttcg gatatttatt 720

atcgatacca cttaccctgc gtatgtaggt ccccaggaag tgcctgttcc agcaatgata 780

gcctcaagtg attattattt cagttggctc acgtgggtta ctgatgaacg agtatgtttg 840

cagtggctaa aaagagtcca gaatgtttcg gtcctgtcta tatgtgactt cagggaagac 900

tggcagacat gggattgtcc aaagacccag gagcatatag aagaaagcag aactggatgg 960

gctggtggat tctttgtttc aacaccagtt ttcagctatg atgccatttc gtactacaaa 1020

atatttagtg acaaggatgg ctacaaacat attcactata tcaaagacac tgtggaaaat 1080

gctattcaaa ttacaagtgg caagtgggag gccataaata tattcagagt aacacaggat 1140

tcactgtttt attctagcaa tgaatttgaa gaataccctg gaagaagaaa catctacaga 1200

attagcattg gaagctatcc tccaagcaag aagtgtgtta cttgccatct aaggaaagaa 1260

aggtgccaat attacacagc aagtttcagc gactacgcca agtactatgc acttgtctgc 1320

tacggcccag gcatccccat ttccaccctt catgatggac gcactgatca agaaattaaa 1380

atcctggaag aaaacaagga attggaaaat gctttgaaaa atatccagct gcctaaagag 1440

gaaattaaga aacttgaagt agatgaaatt actttatggt acaagatgat tcttcctcct 1500

caatttgaca gatcaaagaa gtatcccttg ctaattcaag tgtatggtgg tccctgcagt 1560

cagagtgtaa ggtctgtatt tgctgttaat tggatatctt atcttgcaag taaggaaggg 1620

atggtcattg ccttggtgga tggtcgagga acagctttcc aaggtgacaa actcctctat 1680

gcagtgtatc gaaagctggg tgtttatgaa gttgaagacc agattacagc tgtcagaaaa 1740

```
ttcatagaaa tgggtttcat tgatgaaaaa agaatagcca tatggggctg gtcctatgga     1800

ggatacgttt catcactggc ccttgcatct ggaactggtc ttttcaaatg tggtatagca     1860

gtggctccag tctccagctg ggaatattac gcgtctgtct acacagagag attcatgggt     1920

ctcccaacaa aggatgataa tcttgagcac tataagaatt caactgtgat ggcaagagca     1980

gaatatttca gaaatgtaga ctatcttctc atccacggaa cagcagatga taatgtgcac     2040

tttcaaaact cagcacagat tgctaaagct ctggttaatg cacaagtgga tttccaggca     2100

atgtggtact ctgaccagaa ccacggctta tccggcctgt ccacgaacca cttatacacc     2160

cacatgaccc acttcctaaa gcagtgtttc tctttgtcag acggcaaaaa gaaaaagaaa     2220

aagggccacc accatcacca tcac                                           2244
```

+ADw-210+AD4- 23
+ADw-211+AD4- 761
+ADw-212+AD4- PRT
+ADw-213+AD4- Mus musculus

+ADw-400+AD4- 23

```
Met Lys Thr Trp Leu Lys Thr Val Phe Gly Val Thr Thr Leu Ala Ala
1               5                  10                  15

Leu Ala Leu Val Val Ile Cys Ile Val Leu Arg Pro Ser Arg Val Tyr
            20                  25                  30

Lys Pro Glu Gly Asn Thr Lys Arg Ala Leu Thr Leu Lys Asp Ile Leu
        35                  40                  45

Asn Gly Thr Phe Ser Tyr Lys Thr Tyr Phe Pro Asn Trp Ile Ser Glu
    50                  55                  60

Gln Glu Tyr Leu His Gln Ser Glu Asp Asp Asn Ile Val Phe Tyr Asn
65                  70                  75                  80

Ile Glu Thr Arg Glu Ser Tyr Ile Ile Leu Ser Asn Ser Thr Met Lys
                85                  90                  95

Ser Val Asn Ala Thr Asp Tyr Gly Leu Ser Pro Asp Arg Gln Phe Val
            100                 105                 110

Tyr Leu Glu Ser Asp Tyr Ser Lys Leu Trp Arg Tyr Ser Tyr Thr Ala
        115                 120                 125

Thr Tyr Tyr Ile Tyr Asp Leu Gln Asn Gly Glu Phe Val Arg Gly Tyr
    130                 135                 140
```

```
Glu Leu Pro Arg Pro Ile Gln Tyr Leu Cys Trp Ser Pro Val Gly Ser
145                 150                 155                 160

Lys Leu Ala Tyr Val Tyr Gln Asn Asn Ile Tyr Leu Lys Gln Arg Pro
                165                 170                 175

Gly Asp Pro Pro Phe Gln Ile Thr Tyr Thr Gly Arg Glu Asn Arg Ile
            180                 185                 190

Phe Asn Gly Ile Pro Asp Trp Val Tyr Glu Glu Glu Met Leu Ala Thr
        195                 200                 205

Lys Tyr Ala Leu Trp Trp Ser Pro Asp Gly Lys Phe Leu Ala Tyr Val
    210                 215                 220

Glu Phe Asn Asp Ser Asp Ile Pro Ile Ile Ala Tyr Ser Tyr Tyr Gly
225                 230                 235                 240

Asp Gly Gln Tyr Pro Arg Thr Ile Asn Ile Pro Tyr Pro Lys Ala Gly
                245                 250                 255

Ala Lys Asn Pro Val Val Arg Val Phe Ile Val Asp Thr Thr Tyr Pro
            260                 265                 270

His His Val Gly Pro Met Glu Val Pro Val Pro Glu Met Ile Ala Ser
        275                 280                 285

Ser Asp Tyr Tyr Phe Ser Trp Leu Thr Trp Val Ser Ser Glu Arg Val
    290                 295                 300

Cys Leu Gln Trp Leu Lys Arg Val Gln Asn Val Ser Val Leu Ser Ile
305                 310                 315                 320

Cys Asp Phe Arg Glu Asp Trp His Ala Trp Glu Cys Pro Lys Asn Gln
                325                 330                 335

Glu His Val Glu Glu Ser Arg Thr Gly Trp Ala Gly Gly Phe Phe Val
            340                 345                 350

Ser Thr Pro Ala Phe Ser Gln Asp Ala Thr Ser Tyr Tyr Lys Ile Phe
        355                 360                 365

Ser Asp Lys Asp Gly Tyr Lys His Ile His Tyr Ile Lys Asp Thr Val
    370                 375                 380

Glu Asn Ala Ile Gln Ile Thr Ser Gly Lys Trp Glu Ala Ile Tyr Ile
385                 390                 395                 400
```

```
Phe Arg Val Thr Gln Asp Ser Leu Phe Tyr Ser Ser Asn Glu Phe Glu
                405                 410                 415

Gly Tyr Pro Gly Arg Arg Asn Ile Tyr Arg Ile Ser Ile Gly Asn Ser
            420                 425                 430

Pro Pro Ser Lys Lys Cys Val Thr Cys His Leu Arg Lys Glu Arg Cys
        435                 440                 445

Gln Tyr Tyr Thr Ala Ser Phe Ser Tyr Lys Ala Lys Tyr Tyr Ala Leu
    450                 455                 460

Val Cys Tyr Gly Pro Gly Leu Pro Ile Ser Thr Leu His Asp Gly Arg
465                 470                 475                 480

Thr Asp Gln Glu Ile Gln Val Leu Glu Glu Asn Lys Glu Leu Glu Asn
                485                 490                 495

Ser Leu Arg Asn Ile Gln Leu Pro Lys Val Glu Ile Lys Lys Leu Lys
            500                 505                 510

Asp Gly Gly Leu Thr Phe Trp Tyr Lys Met Ile Leu Pro Pro Gln Phe
        515                 520                 525

Asp Arg Ser Lys Lys Tyr Pro Leu Leu Ile Gln Val Tyr Gly Gly Pro
    530                 535                 540

Cys Ser Gln Ser Val Lys Ser Val Phe Ala Val Asn Trp Ile Thr Tyr
545                 550                 555                 560

Leu Ala Ser Lys Glu Gly Ile Val Ile Ala Leu Val Asp Gly Arg Gly
                565                 570                 575

Thr Ala Phe Gln Gly Asp Lys Phe Leu His Ala Val Tyr Arg Lys Leu
            580                 585                 590

Gly Val Tyr Glu Val Glu Asp Gln Leu Thr Ala Val Arg Lys Phe Ile
        595                 600                 605

Glu Met Gly Phe Ile Asp Glu Glu Arg Ile Ala Ile Trp Gly Trp Ser
    610                 615                 620

Tyr Gly Gly Tyr Val Ser Ser Leu Ala Leu Ala Ser Gly Thr Gly Leu
625                 630                 635                 640

Phe Lys Cys Gly Ile Ala Val Ala Pro Val Ser Ser Trp Glu Tyr Tyr
                645                 650                 655
```

```
Ala Ser Ile Tyr Ser Glu Arg Phe Met Gly Leu Pro Thr Lys Asp Asp
            660                 665                 670

Asn Leu Glu His Tyr Lys Asn Ser Thr Val Met Ala Arg Ala Glu Tyr
        675                 680                 685

Phe Arg Asn Val Asp Tyr Leu Leu Ile His Gly Thr Ala Asp Asp Asn
    690                 695                 700

Val His Phe Gln Asn Ser Ala Gln Ile Ala Lys Ala Leu Val Asn Ala
705                 710                 715                 720

Gln Val Asp Phe Gln Ala Met Trp Tyr Ser Asp Gln Asn His Gly Ile
                725                 730                 735

Ser Ser Gly Arg Ser Gln Asn His Leu Tyr Thr His Met Thr His Phe
            740                 745                 750

Leu Lys Gln Cys Phe Ser Leu Ser Asp
        755                 760


+ADw-210+AD4-  24
+ADw-211+AD4-  749
+ADw-212+AD4-  PRT
+ADw-213+AD4-  Secuencia artificial

+ADw-220+AD4-
+ADw-223+AD4-  ectodominio de FAP murino marcador Lys marcador avi

+ADw-400+AD4-  24

Arg Pro Ser Arg Val Tyr Lys Pro Glu Gly Asn Thr Lys Arg Ala Leu
1               5                  10                  15

Thr Leu Lys Asp Ile Leu Asn Gly Thr Phe Ser Tyr Lys Thr Tyr Phe
            20                  25                  30

Pro Asn Trp Ile Ser Glu Gln Glu Tyr Leu His Gln Ser Glu Asp Asp
        35                  40                  45

Asn Ile Val Phe Tyr Asn Ile Glu Thr Arg Glu Ser Tyr Ile Ile Leu
    50                  55                  60

Ser Asn Ser Thr Met Lys Ser Val Asn Ala Thr Asp Tyr Gly Leu Ser
65                  70                  75                  80

Pro Asp Arg Gln Phe Val Tyr Leu Glu Ser Asp Tyr Ser Lys Leu Trp
                85                  90                  95
```

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Arg Tyr Ser Tyr Thr Ala Thr Tyr Tyr Ile Tyr Asp Leu Gln Asn Gly
            100                 105                 110

Glu Phe Val Arg Gly Tyr Glu Leu Pro Arg Pro Ile Gln Tyr Leu Cys
        115                 120                 125

Trp Ser Pro Val Gly Ser Lys Leu Ala Tyr Val Tyr Gln Asn Asn Ile
    130                 135                 140

Tyr Leu Lys Gln Arg Pro Gly Asp Pro Pro Phe Gln Ile Thr Tyr Thr
145                 150                 155                 160

Gly Arg Glu Asn Arg Ile Phe Asn Gly Ile Pro Asp Trp Val Tyr Glu
                165                 170                 175

Glu Glu Met Leu Ala Thr Lys Tyr Ala Leu Trp Trp Ser Pro Asp Gly
            180                 185                 190

Lys Phe Leu Ala Tyr Val Glu Phe Asn Asp Ser Asp Ile Pro Ile Ile
        195                 200                 205

Ala Tyr Ser Tyr Tyr Gly Asp Gly Gln Tyr Pro Arg Thr Ile Asn Ile
    210                 215                 220

Pro Tyr Pro Lys Ala Gly Ala Lys Asn Pro Val Val Arg Val Phe Ile
225                 230                 235                 240

Val Asp Thr Thr Tyr Pro His His Val Gly Pro Met Glu Val Pro Val
                245                 250                 255

Pro Glu Met Ile Ala Ser Ser Asp Tyr Tyr Phe Ser Trp Leu Thr Trp
            260                 265                 270

Val Ser Ser Glu Arg Val Cys Leu Gln Trp Leu Lys Arg Val Gln Asn
        275                 280                 285

Val Ser Val Leu Ser Ile Cys Asp Phe Arg Glu Asp Trp His Ala Trp
    290                 295                 300

Glu Cys Pro Lys Asn Gln Glu His Val Glu Glu Ser Arg Thr Gly Trp
305                 310                 315                 320

Ala Gly Gly Phe Phe Val Ser Thr Pro Ala Phe Ser Gln Asp Ala Thr
                325                 330                 335

Ser Tyr Tyr Lys Ile Phe Ser Asp Lys Asp Gly Tyr Lys His Ile His
            340                 345                 350
```

```
Tyr Ile Lys Asp Thr Val Glu Asn Ala Ile Gln Ile Thr Ser Gly Lys
        355                 360                 365

Trp Glu Ala Ile Tyr Ile Phe Arg Val Thr Gln Asp Ser Leu Phe Tyr
    370                 375                 380

Ser Ser Asn Glu Phe Glu Gly Tyr Pro Gly Arg Arg Asn Ile Tyr Arg
385                 390                 395                 400

Ile Ser Ile Gly Asn Ser Pro Pro Ser Lys Lys Cys Val Thr Cys His
                405                 410                 415

Leu Arg Lys Glu Arg Cys Gln Tyr Tyr Thr Ala Ser Phe Ser Tyr Lys
            420                 425                 430

Ala Lys Tyr Tyr Ala Leu Val Cys Tyr Gly Pro Gly Leu Pro Ile Ser
        435                 440                 445

Thr Leu His Asp Gly Arg Thr Asp Gln Glu Ile Gln Val Leu Glu Glu
    450                 455                 460

Asn Lys Glu Leu Glu Asn Ser Leu Arg Asn Ile Gln Leu Pro Lys Val
465                 470                 475                 480

Glu Ile Lys Lys Leu Lys Asp Gly Gly Leu Thr Phe Trp Tyr Lys Met
                485                 490                 495

Ile Leu Pro Pro Gln Phe Asp Arg Ser Lys Lys Tyr Pro Leu Leu Ile
            500                 505                 510

Gln Val Tyr Gly Gly Pro Cys Ser Gln Ser Val Lys Ser Val Phe Ala
        515                 520                 525

Val Asn Trp Ile Thr Tyr Leu Ala Ser Lys Glu Gly Ile Val Ile Ala
    530                 535                 540

Leu Val Asp Gly Arg Gly Thr Ala Phe Gln Gly Asp Lys Phe Leu His
545                 550                 555                 560

Ala Val Tyr Arg Lys Leu Gly Val Tyr Glu Val Glu Asp Gln Leu Thr
                565                 570                 575

Ala Val Arg Lys Phe Ile Glu Met Gly Phe Ile Asp Glu Glu Arg Ile
            580                 585                 590

Ala Ile Trp Gly Trp Ser Tyr Gly Gly Tyr Val Ser Ser Leu Ala Leu
```

595 600 605

Ala Ser Gly Thr Gly Leu Phe Lys Cys Gly Ile Ala Val Ala Pro Val
610 615 620

Ser Ser Trp Glu Tyr Tyr Ala Ser Ile Tyr Ser Glu Arg Phe Met Gly
625 630 635 640

Leu Pro Thr Lys Asp Asp Asn Leu Glu His Tyr Lys Asn Ser Thr Val
645 650 655

Met Ala Arg Ala Glu Tyr Phe Arg Asn Val Asp Tyr Leu Leu Ile His
660 665 670

Gly Thr Ala Asp Asp Asn Val His Phe Gln Asn Ser Ala Gln Ile Ala
675 680 685

Lys Ala Leu Val Asn Ala Gln Val Asp Phe Gln Ala Met Trp Tyr Ser
690 695 700

Asp Gln Asn His Gly Ile Leu Ser Gly Arg Ser Gln Asn His Leu Tyr
705 710 715 720

Thr His Met Thr His Phe Leu Lys Gln Cys Phe Ser Leu Ser Asp Gly
725 730 735

Lys Lys Lys Lys Lys Lys Gly His His His His His His
740 745

+ADw-210+AD4- 25
+ADw-211+AD4- 2247
+ADw-212+AD4- ADN
+ADw-213+AD4- Secuencia artificial

+ADw-220+AD4-
+ADw-223+AD4- ectodominio de FAP murino marcador Lys marcador avi

+ADw-400+AD4- 25
cgtccctcaa gagtttacaa acctgaagga aacacaaaga gagctcttac cttgaaggat 60

attttaaatg gaacattctc atataaaaca tattttccca actggatttc agaacaagaa 120

tatcttcatc aatctgagga tgataacata gtattttata atattgaaac aagagaatca 180

tatatcattt tgagtaatag caccatgaaa agtgtgaatg ctacagatta tggtttgtca 240

cctgatcggc aatttgtgta tctagaaagt gattattcaa agctctggcg atattcatac 300

acagcgacat actacatcta cgaccttcag aatggggaat ttgtaagagg atacgagctc 360

cctcgtccaa ttcagtatct atgctggtcg cctgttggga gtaaattagc atatgtatat 420

caaaacaata tttatttgaa acaaagacca ggagatccac cttttcaaat aacttatact 480

ggaagagaaa atagaatatt taatggaata ccagactggg tttatgaaga ggaaatgctt 540

gccacaaaat atgctctttg gtggtctcca gatggaaaat ttttggcata tgtagaattt 600

aatgattcag atataccaat tattgcctat tcttattatg gtgatggaca gtatcctaga 660

actataaata ttccatatcc aaaggctggg gctaagaatc cggttgttcg tgtttttatt 720

gttgacacca cctaccctca ccacgtgggc ccaatggaag tgccagttcc agaaatgata 780

gcctcaagtg actattattt cagctggctc acatgggtgt ccagtgaacg agtatgcttg 840

cagtggctaa aaagagtgca gaatgtctca gtcctgtcta tatgtgattt cagggaagac 900

tggcatgcat gggaatgtcc aaagaaccag gagcatgtag aagaaagcag aacaggatgg 960

gctggtggat tctttgtttc gacaccagct tttagccagg atgccacttc ttactacaaa 1020

atatttagcg acaaggatgg ttacaaacat attcactaca tcaaagacac tgtggaaaat 1080

gctattcaaa ttacaagtgg caagtgggag gccatatata tattccgcgt aacacaggat 1140

tcactgtttt attctagcaa tgaatttgaa ggttaccctg gaagaagaaa catctacaga 1200

attagcattg gaaactctcc tccgagcaag aagtgtgtta cttgccatct aaggaaagaa 1260

aggtgccaat attacacagc aagtttcagc tacaaagcca agtactatgc actcgtctgc 1320

tatggccctg gcctccccat ttccaccctc catgatggcc gcacagacca agaaatacaa 1380

gtattagaag aaaacaaaga actggaaaat tctctgagaa atatccagct gcctaaagtg 1440

gagattaaga agctcaaaga cgggggactg actttctggt acaagatgat tctgcctcct 1500

cagtttgaca gatcaaagaa gtacccttg ctaattcaag tgtatggtgg tccttgtagc 1560

cagagtgtta agtctgtgtt tgctgttaat tggataactt atctcgcaag taaggagggg 1620

atagtcattg ccctggtaga tggtcggggc actgctttcc aaggtgacaa attcctgcat 1680

gccgtgtatc gaaaactggg tgtatatgaa gttgaggacc agctcacagc tgtcagaaaa 1740

ttcatagaaa tgggtttcat tgatgaagaa agaatagcca tatggggctg gtcctacgga 1800

ggttatgttt catccctggc ccttgcatct ggaactggtc ttttcaaatg tggcatagca 1860

gtggctccag tctccagctg ggaatattac gcatctatct actcagagag attcatgggc 1920

ctcccaacaa aggacgacaa tctcgaacac tataaaaatt caactgtgat ggcaagagca 1980

gaatatttca gaaatgtaga ctatcttctc atccacggaa cagcagatga taatgtgcac 2040

tttcagaact cagcacagat tgctaaagct ttggttaatg cacaagtgga tttccaggcg 2100

atgtggtact ctgaccagaa ccatggtata ttatctgggc gctcccagaa tcatttatat 2160

acccacatga cgcacttcct caagcaatgc ttttctttat cagacggcaa aaagaaaaag 2220

aaaaagggcc accaccatca ccatcac 2247

+ADw-210+AD4- 26

+ADw-211+AD4- 748
+ADw-212+AD4- PRT
+ADw-213+AD4- Secuencia artificial

+ADw-220+AD4-
+ADw-223+AD4- ectodominio de FAP de cinomolgo marcador Lys marcador avi

+ADw-400+AD4- 26

```
Arg Pro Pro Arg Val His Asn Ser Glu Glu Asn Thr Met Arg Ala Leu
1               5                  10                  15

Thr Leu Lys Asp Ile Leu Asn Gly Thr Phe Ser Tyr Lys Thr Phe Phe
            20                  25                  30

Pro Asn Trp Ile Ser Gly Gln Glu Tyr Leu His Gln Ser Ala Asp Asn
        35                  40                  45

Asn Ile Val Leu Tyr Asn Ile Glu Thr Gly Gln Ser Tyr Thr Ile Leu
    50                  55                  60

Ser Asn Arg Thr Met Lys Ser Val Asn Ala Ser Asn Tyr Gly Leu Ser
65                  70                  75                  80

Pro Asp Arg Gln Phe Val Tyr Leu Glu Ser Asp Tyr Ser Lys Leu Trp
                85                  90                  95

Arg Tyr Ser Tyr Thr Ala Thr Tyr Tyr Ile Tyr Asp Leu Ser Asn Gly
            100                 105                 110

Glu Phe Val Arg Gly Asn Glu Leu Pro Arg Pro Ile Gln Tyr Leu Cys
        115                 120                 125

Trp Ser Pro Val Gly Ser Lys Leu Ala Tyr Val Tyr Gln Asn Asn Ile
    130                 135                 140

Tyr Leu Lys Gln Arg Pro Gly Asp Pro Pro Phe Gln Ile Thr Phe Asn
145                 150                 155                 160

Gly Arg Glu Asn Lys Ile Phe Asn Gly Ile Pro Asp Trp Val Tyr Glu
                165                 170                 175

Glu Glu Met Leu Ala Thr Lys Tyr Ala Leu Trp Trp Ser Pro Asn Gly
            180                 185                 190

Lys Phe Leu Ala Tyr Ala Glu Phe Asn Asp Thr Asp Ile Pro Val Ile
        195                 200                 205

Ala Tyr Ser Tyr Tyr Gly Asp Glu Gln Tyr Pro Arg Thr Ile Asn Ile
    210                 215                 220
```

```
Pro Tyr Pro Lys Ala Gly Ala Lys Asn Pro Phe Val Arg Ile Phe Ile
225                 230                 235                 240

Ile Asp Thr Thr Tyr Pro Ala Tyr Val Gly Pro Gln Glu Val Pro Val
                245                 250                 255

Pro Ala Met Ile Ala Ser Ser Asp Tyr Tyr Phe Ser Trp Leu Thr Trp
            260                 265                 270

Val Thr Asp Glu Arg Val Cys Leu Gln Trp Leu Lys Arg Val Gln Asn
        275                 280                 285

Val Ser Val Leu Ser Ile Cys Asp Phe Arg Glu Asp Trp Gln Thr Trp
    290                 295                 300

Asp Cys Pro Lys Thr Gln Glu His Ile Glu Glu Ser Arg Thr Gly Trp
305                 310                 315                 320

Ala Gly Gly Phe Phe Val Ser Thr Pro Val Phe Ser Tyr Asp Ala Ile
                325                 330                 335

Ser Tyr Tyr Lys Ile Phe Ser Asp Lys Asp Gly Tyr Lys His Ile His
            340                 345                 350

Tyr Ile Lys Asp Thr Val Glu Asn Ala Ile Gln Ile Thr Ser Gly Lys
        355                 360                 365

Trp Glu Ala Ile Asn Ile Phe Arg Val Thr Gln Asp Ser Leu Phe Tyr
    370                 375                 380

Ser Ser Asn Glu Phe Glu Asp Tyr Pro Gly Arg Arg Asn Ile Tyr Arg
385                 390                 395                 400

Ile Ser Ile Gly Ser Tyr Pro Pro Ser Lys Lys Cys Val Thr Cys His
                405                 410                 415

Leu Arg Lys Glu Arg Cys Gln Tyr Tyr Thr Ala Ser Phe Ser Asp Tyr
            420                 425                 430

Ala Lys Tyr Tyr Ala Leu Val Cys Tyr Gly Pro Gly Ile Pro Ile Ser
        435                 440                 445

Thr Leu His Asp Gly Arg Thr Asp Gln Glu Ile Lys Ile Leu Glu Glu
    450                 455                 460

Asn Lys Glu Leu Glu Asn Ala Leu Lys Asn Ile Gln Leu Pro Lys Glu
```

```
465                 470                 475                 480

Glu Ile Lys Lys Leu Glu Val Asp Glu Ile Thr Leu Trp Tyr Lys Met
                485                 490                 495

Ile Leu Pro Pro Gln Phe Asp Arg Ser Lys Lys Tyr Pro Leu Leu Ile
            500                 505                 510

Gln Val Tyr Gly Gly Pro Cys Ser Gln Ser Val Arg Ser Val Phe Ala
        515                 520                 525

Val Asn Trp Ile Ser Tyr Leu Ala Ser Lys Glu Gly Met Val Ile Ala
    530                 535                 540

Leu Val Asp Gly Arg Gly Thr Ala Phe Gln Gly Asp Lys Leu Leu Tyr
545                 550                 555                 560

Ala Val Tyr Arg Lys Leu Gly Val Tyr Glu Val Glu Asp Gln Ile Thr
                565                 570                 575

Ala Val Arg Lys Phe Ile Glu Met Gly Phe Ile Asp Glu Lys Arg Ile
            580                 585                 590

Ala Ile Trp Gly Trp Ser Tyr Gly Gly Tyr Val Ser Ser Leu Ala Leu
        595                 600                 605

Ala Ser Gly Thr Gly Leu Phe Lys Cys Gly Ile Ala Val Ala Pro Val
    610                 615                 620

Ser Ser Trp Glu Tyr Tyr Ala Ser Val Tyr Thr Glu Arg Phe Met Gly
625                 630                 635                 640

Leu Pro Thr Lys Asp Asp Asn Leu Glu His Tyr Lys Asn Ser Thr Val
                645                 650                 655

Met Ala Arg Ala Glu Tyr Phe Arg Asn Val Asp Tyr Leu Leu Ile His
            660                 665                 670

Gly Thr Ala Asp Asp Asn Val His Phe Gln Asn Ser Ala Gln Ile Ala
        675                 680                 685

Lys Ala Leu Val Asn Ala Gln Val Asp Phe Gln Ala Met Trp Tyr Ser
    690                 695                 700

Asp Gln Asn His Gly Leu Ser Gly Leu Ser Thr Asn His Leu Tyr Thr
705                 710                 715                 720
```

His Met Thr His Phe Leu Lys Gln Cys Phe Ser Leu Ser Asp Gly Lys
725 730 735

Lys Lys Lys Lys Lys Gly His His His His His His
740 745

+ADw-210+AD4- 27
+ADw-211+AD4- 2244
+ADw-212+AD4- ADN
+ADw-213+AD4- Secuencia artificial

+ADw-220+AD4-
+ADw-223+AD4- ectodominio de FAP de cinomolgo marcador Lys marcador avi

+ADw-400+AD4- 27

cgccctccaa gagttcataa ctctgaagaa aatacaatga gagcactcac actgaaggat 60

attttaaatg ggacattttc ttataaaaca ttttttccaa actggatttc aggacaagaa 120

tatcttcatc aatctgcaga taacaatata gtactttata atattgaaac aggacaatca 180

tataccattt tgagtaacag aaccatgaaa agtgtgaatg cttcaaatta tggcttatca 240

cctgatcggc aatttgtata tctagaaagt gattattcaa agctttggag atactcttac 300

acagcaacat attacatcta tgaccttagc aatggagaat ttgtaagagg aaatgagctt 360

cctcgtccaa ttcagtattt atgctggtcg cctgttggga gtaaattagc atatgtctat 420

caaaacaata tctatttgaa acaaagacca ggagatccac cttttcaaat aacatttaat 480

ggaagagaaa ataaaatatt taatggaatc ccagactggg tttatgaaga ggaaatgctt 540

gctacaaaat atgctctctg gtggtctcct aatggaaaat ttttggcata tgcggaattt 600

aatgatacag atataccagt tattgcctat tcctattatg gcgatgaaca atatcccaga 660

acaataaata ttccataccc aaaggccgga gctaagaatc cttttgttcg gatatttatt 720

atcgatacca cttaccctgc gtatgtaggt ccccaggaag tgcctgttcc agcaatgata 780

gcctcaagtg attattattt cagttggctc acgtgggtta ctgatgaacg agtatgtttg 840

cagtggctaa aaagagtcca gaatgtttcg gtcttgtcta tatgtgattt cagggaagac 900

tggcagacat gggattgtcc aaagacccag gagcatatag aagaaagcag aactggatgg 960

gctggtggat tctttgtttc aacaccagtt ttcagctatg atgccatttc atactacaaa 1020

atatttagtg acaaggatgg ctacaaacat attcactata tcaaagacac tgtggaaaat 1080

gctattcaaa ttacaagtgg caagtgggag gccataaata tattcagagt aacacaggat 1140

tcactgtttt attctagcaa tgaatttgaa gattaccctg gaagaagaaa catctacaga 1200

attagcattg gaagctatcc tccaagcaag aagtgtgtta cttgccatct aaggaaagaa 1260

aggtgccaat attacacagc aagtttcagc gactacgcca agtactatgc acttgtctgc 1320

tatggcccag gcatccccat ttccaccctt catgacggac gcactgatca agaaattaaa 1380

```
atcctggaag aaaacaagga attggaaaat gctttgaaaa atatccagct gcctaaagag     1440

gaaattaaga aacttgaagt agatgaaatt actttatggt acaagatgat tcttcctcct     1500

caatttgaca gatcaaagaa gtatcccttg ctaattcaag tgtatggtgg tccctgcagt     1560

cagagtgtaa ggtctgtatt tgctgttaat tggatatctt atcttgcaag taaggaaggg     1620

atggtcattg ccttggtgga tggtcgggga acagctttcc aaggtgacaa actcctgtat     1680

gcagtgtatc gaaagctggg tgtttatgaa gttgaagacc agattacagc tgtcagaaaa     1740

ttcatagaaa tgggtttcat tgatgaaaaa agaatagcca tatggggctg gtcctatgga     1800

ggatatgttt catcactggc ccttgcatct ggaactggtc ttttcaaatg tgggatagca     1860

gtggctccag tctccagctg ggaatattac gcgtctgtct acacagagag attcatgggt     1920

ctcccaacaa aggatgataa tcttgagcac tataagaatt caactgtgat ggcaagagca     1980

gaatatttca gaaatgtaga ctatcttctc atccacggaa cagcagatga taatgtgcac     2040

tttcaaaact cagcacagat tgctaaagct ctggttaatg cacaagtgga tttccaggca     2100

atgtggtact ctgaccagaa ccacggctta tccggcctgt ccacgaacca cttatacacc     2160

cacatgaccc acttcctaaa gcagtgtttc tctttgtcag acggcaaaaa gaaaaagaaa     2220

aagggccacc accatcacca tcac                                           2244
```

+ADw-210+AD4- 28
+ADw-211+AD4- 702
+ADw-212+AD4- PRT
+ADw-213+AD4- Homo sapiens

+ADw-400+AD4- 28

```
Met Glu Ser Pro Ser Ala Pro Pro His Arg Trp Cys Ile Pro Trp Gln
1               5                  10                  15

Arg Leu Leu Leu Thr Ala Ser Leu Leu Thr Phe Trp Asn Pro Pro Thr
            20                  25                  30

Thr Ala Lys Leu Thr Ile Glu Ser Thr Pro Phe Asn Val Ala Glu Gly
        35                  40                  45

Lys Glu Val Leu Leu Leu Val His Asn Leu Pro Gln His Leu Phe Gly
    50                  55                  60

Tyr Ser Trp Tyr Lys Gly Glu Arg Val Asp Gly Asn Arg Gln Ile Ile
65                  70                  75                  80

Gly Tyr Val Ile Gly Thr Gln Gln Ala Thr Pro Gly Pro Ala Tyr Ser
                85                  90                  95

Gly Arg Glu Ile Ile Tyr Pro Asn Ala Ser Leu Leu Ile Gln Asn Ile
```

```
            100                 105                 110

Ile Gln Asn Asp Thr Gly Phe Tyr Thr Leu His Val Ile Lys Ser Asp
        115                 120                 125

Leu Val Asn Glu Glu Ala Thr Gly Gln Phe Arg Val Tyr Pro Glu Leu
    130                 135                 140

Pro Lys Pro Ser Ile Ser Ser Asn Asn Ser Lys Pro Val Glu Asp Lys
145                 150                 155                 160

Asp Ala Val Ala Phe Thr Cys Glu Pro Glu Thr Gln Asp Ala Thr Tyr
                165                 170                 175

Leu Trp Trp Val Asn Asn Gln Ser Leu Pro Val Ser Pro Arg Leu Gln
            180                 185                 190

Leu Ser Asn Gly Asn Arg Thr Leu Thr Leu Phe Asn Val Thr Arg Asn
        195                 200                 205

Asp Thr Ala Ser Tyr Lys Cys Glu Thr Gln Asn Pro Val Ser Ala Arg
    210                 215                 220

Arg Ser Asp Ser Val Ile Leu Asn Val Leu Tyr Gly Pro Asp Ala Pro
225                 230                 235                 240

Thr Ile Ser Pro Leu Asn Thr Ser Tyr Arg Ser Gly Glu Asn Leu Asn
                245                 250                 255

Leu Ser Cys His Ala Ala Ser Asn Pro Pro Ala Gln Tyr Ser Trp Phe
            260                 265                 270

Val Asn Gly Thr Phe Gln Gln Ser Thr Gln Glu Leu Phe Ile Pro Asn
        275                 280                 285

Ile Thr Val Asn Asn Ser Gly Ser Tyr Thr Cys Gln Ala His Asn Ser
    290                 295                 300

Asp Thr Gly Leu Asn Arg Thr Thr Val Thr Thr Ile Thr Val Tyr Ala
305                 310                 315                 320

Glu Pro Pro Lys Pro Phe Ile Thr Ser Asn Asn Ser Asn Pro Val Glu
                325                 330                 335

Asp Glu Asp Ala Val Ala Leu Thr Cys Glu Pro Glu Ile Gln Asn Thr
            340                 345                 350
```

```
Thr Tyr Leu Trp Trp Val Asn Asn Gln Ser Leu Pro Val Ser Pro Arg
        355                 360                 365

Leu Gln Leu Ser Asn Asp Asn Arg Thr Leu Thr Leu Leu Ser Val Thr
    370                 375                 380

Arg Asn Asp Val Gly Pro Tyr Glu Cys Gly Ile Gln Asn Lys Leu Ser
385                 390                 395                 400

Val Asp His Ser Asp Pro Val Ile Leu Asn Val Leu Tyr Gly Pro Asp
                405                 410                 415

Asp Pro Thr Ile Ser Pro Ser Tyr Thr Tyr Tyr Arg Pro Gly Val Asn
            420                 425                 430

Leu Ser Leu Ser Cys His Ala Ala Ser Asn Pro Pro Ala Gln Tyr Ser
        435                 440                 445

Trp Leu Ile Asp Gly Asn Ile Gln Gln His Thr Gln Glu Leu Phe Ile
    450                 455                 460

Ser Asn Ile Thr Glu Lys Asn Ser Gly Leu Tyr Thr Cys Gln Ala Asn
465                 470                 475                 480

Asn Ser Ala Ser Gly His Ser Arg Thr Thr Val Lys Thr Ile Thr Val
                485                 490                 495

Ser Ala Glu Leu Pro Lys Pro Ser Ile Ser Ser Asn Asn Ser Lys Pro
            500                 505                 510

Val Glu Asp Lys Asp Ala Val Ala Phe Thr Cys Glu Pro Glu Ala Gln
        515                 520                 525

Asn Thr Thr Tyr Leu Trp Trp Val Asn Gly Gln Ser Leu Pro Val Ser
    530                 535                 540

Pro Arg Leu Gln Leu Ser Asn Gly Asn Arg Thr Leu Thr Leu Phe Asn
545                 550                 555                 560

Val Thr Arg Asn Asp Ala Arg Ala Tyr Val Cys Gly Ile Gln Asn Ser
                565                 570                 575

Val Ser Ala Asn Arg Ser Asp Pro Val Thr Leu Asp Val Leu Tyr Gly
            580                 585                 590

Pro Asp Thr Pro Ile Ile Ser Pro Pro Asp Ser Ser Tyr Leu Ser Gly
        595                 600                 605
```

```
Ala Asn Leu Asn Leu Ser Cys His Ser Ala Ser Asn Pro Ser Pro Gln
    610                 615                 620

Tyr Ser Trp Arg Ile Asn Gly Ile Pro Gln Gln His Thr Gln Val Leu
625                 630                 635                 640

Phe Ile Ala Lys Ile Thr Pro Asn Asn Asn Gly Thr Tyr Ala Cys Phe
                645                 650                 655

Val Ser Asn Leu Ala Thr Gly Arg Asn Asn Ser Ile Val Lys Ser Ile
            660                 665                 670

Thr Val Ser Ala Ser Gly Thr Ser Pro Gly Leu Ser Ala Gly Ala Thr
        675                 680                 685

Val Gly Ile Met Ile Gly Val Leu Val Gly Val Ala Leu Ile
    690                 695                 700
```

+ADw-210+AD4- 29
+ADw-211+AD4- 2322
+ADw-212+AD4- PRT
+ADw-213+AD4- Homo sapiens

+ADw-400+AD4- 29

```
Met Gln Ser Gly Pro Arg Pro Pro Leu Pro Ala Pro Gly Leu Ala Leu
1               5                   10                  15

Ala Leu Thr Leu Thr Met Leu Ala Arg Leu Ala Ser Ala Ala Ser Phe
            20                  25                  30

Phe Gly Glu Asn His Leu Glu Val Pro Val Ala Thr Ala Leu Thr Asp
        35                  40                  45

Ile Asp Leu Gln Leu Gln Phe Ser Thr Ser Gln Pro Glu Ala Leu Leu
    50                  55                  60

Leu Leu Ala Ala Gly Pro Ala Asp His Leu Leu Leu Gln Leu Tyr Ser
65                  70                  75                  80

Gly Arg Leu Gln Val Arg Leu Val Leu Gly Gln Glu Glu Leu Arg Leu
                85                  90                  95

Gln Thr Pro Ala Glu Thr Leu Leu Ser Asp Ser Ile Pro His Thr Val
            100                 105                 110

Val Leu Thr Val Val Glu Gly Trp Ala Thr Leu Ser Val Asp Gly Phe
        115                 120                 125
```

```
Leu Asn Ala Ser Ser Ala Val Pro Gly Ala Pro Leu Glu Val Pro Tyr
    130                 135                 140

Gly Leu Phe Val Gly Gly Thr Gly Thr Leu Gly Leu Pro Tyr Leu Arg
145                 150                 155                 160

Gly Thr Ser Arg Pro Leu Arg Gly Cys Leu His Ala Ala Thr Leu Asn
                165                 170                 175

Gly Arg Ser Leu Leu Arg Pro Leu Thr Pro Asp Val His Glu Gly Cys
            180                 185                 190

Ala Glu Glu Phe Ser Ala Ser Asp Asp Val Ala Leu Gly Phe Ser Gly
        195                 200                 205

Pro His Ser Leu Ala Ala Phe Pro Ala Trp Gly Thr Gln Asp Glu Gly
    210                 215                 220

Thr Leu Glu Phe Thr Leu Thr Thr Gln Ser Arg Gln Ala Pro Leu Ala
225                 230                 235                 240

Phe Gln Ala Gly Gly Arg Arg Gly Asp Phe Ile Tyr Val Asp Ile Phe
                245                 250                 255

Glu Gly His Leu Arg Ala Val Val Glu Lys Gly Gln Gly Thr Val Leu
            260                 265                 270

Leu His Asn Ser Val Pro Val Ala Asp Gly Gln Pro His Glu Val Ser
        275                 280                 285

Val His Ile Asn Ala His Arg Leu Glu Ile Ser Val Asp Gln Tyr Pro
    290                 295                 300

Thr His Thr Ser Asn Arg Gly Val Leu Ser Tyr Leu Glu Pro Arg Gly
305                 310                 315                 320

Ser Leu Leu Leu Gly Gly Leu Asp Ala Glu Ala Ser Arg His Leu Gln
                325                 330                 335

Glu His Arg Leu Gly Leu Thr Pro Glu Ala Thr Asn Ala Ser Leu Leu
            340                 345                 350

Gly Cys Met Glu Asp Leu Ser Val Asn Gly Gln Arg Arg Gly Leu Arg
        355                 360                 365

Glu Ala Leu Leu Thr Arg Asn Met Ala Ala Gly Cys Arg Leu Glu Glu
    370                 375                 380
```

```
Glu Glu Tyr Glu Asp Asp Ala Tyr Gly His Tyr Glu Ala Phe Ser Thr
385                 390                 395                 400

Leu Ala Pro Glu Ala Trp Pro Ala Met Glu Leu Pro Glu Pro Cys Val
                405                 410                 415

Pro Glu Pro Gly Leu Pro Pro Val Phe Ala Asn Phe Thr Gln Leu Leu
            420                 425                 430

Thr Ile Ser Pro Leu Val Val Ala Glu Gly Gly Thr Ala Trp Leu Glu
        435                 440                 445

Trp Arg His Val Gln Pro Thr Leu Asp Leu Met Glu Ala Glu Leu Arg
    450                 455                 460

Lys Ser Gln Val Leu Phe Ser Val Thr Arg Gly Ala Arg His Gly Glu
465                 470                 475                 480

Leu Glu Leu Asp Ile Pro Gly Ala Gln Ala Arg Lys Met Phe Thr Leu
                485                 490                 495

Leu Asp Val Val Asn Arg Lys Ala Arg Phe Ile His Asp Gly Ser Glu
            500                 505                 510

Asp Thr Ser Asp Gln Leu Val Leu Glu Val Ser Val Thr Ala Arg Val
        515                 520                 525

Pro Met Pro Ser Cys Leu Arg Arg Gly Gln Thr Tyr Leu Leu Pro Ile
    530                 535                 540

Gln Val Asn Pro Val Asn Asp Pro Pro His Ile Ile Phe Pro His Gly
545                 550                 555                 560

Ser Leu Met Val Ile Leu Glu His Thr Gln Lys Pro Leu Gly Pro Glu
                565                 570                 575

Val Phe Gln Ala Tyr Asp Pro Asp Ser Ala Cys Glu Gly Leu Thr Phe
            580                 585                 590

Gln Val Leu Gly Thr Ser Ser Gly Leu Pro Val Glu Arg Arg Asp Gln
        595                 600                 605

Pro Gly Glu Pro Ala Thr Glu Phe Ser Cys Arg Glu Leu Glu Ala Gly
    610                 615                 620

Ser Leu Val Tyr Val His Arg Gly Gly Pro Ala Gln Asp Leu Thr Phe
```

625 630 635 640

Arg Val Ser Asp Gly Leu Gln Ala Ser Pro Pro Ala Thr Leu Lys Val
645 650 655

Val Ala Ile Arg Pro Ala Ile Gln Ile His Arg Ser Thr Gly Leu Arg
660 665 670

Leu Ala Gln Gly Ser Ala Met Pro Ile Leu Pro Ala Asn Leu Ser Val
675 680 685

Glu Thr Asn Ala Val Gly Gln Asp Val Ser Val Leu Phe Arg Val Thr
690 695 700

Gly Ala Leu Gln Phe Gly Glu Leu Gln Lys Gln Gly Ala Gly Gly Val
705 710 715 720

Glu Gly Ala Glu Trp Trp Ala Thr Gln Ala Phe His Gln Arg Asp Val
725 730 735

Glu Gln Gly Arg Val Arg Tyr Leu Ser Thr Asp Pro Gln His His Ala
740 745 750

Tyr Asp Thr Val Glu Asn Leu Ala Leu Glu Val Gln Val Gly Gln Glu
755 760 765

Ile Leu Ser Asn Leu Ser Phe Pro Val Thr Ile Gln Arg Ala Thr Val
770 775 780

Trp Met Leu Arg Leu Glu Pro Leu His Thr Gln Asn Thr Gln Gln Glu
785 790 795 800

Thr Leu Thr Thr Ala His Leu Glu Ala Thr Leu Glu Glu Ala Gly Pro
805 810 815

Ser Pro Pro Thr Phe His Tyr Glu Val Val Gln Ala Pro Arg Lys Gly
820 825 830

Asn Leu Gln Leu Gln Gly Thr Arg Leu Ser Asp Gly Gln Gly Phe Thr
835 840 845

Gln Asp Asp Ile Gln Ala Gly Arg Val Thr Tyr Gly Ala Thr Ala Arg
850 855 860

Ala Ser Glu Ala Val Glu Asp Thr Phe Arg Phe Arg Val Thr Ala Pro
865 870 875 880

```
Pro Tyr Phe Ser Pro Leu Tyr Thr Phe Pro Ile His Ile Gly Gly Asp
                885                 890                 895

Pro Asp Ala Pro Val Leu Thr Asn Val Leu Leu Val Val Pro Glu Gly
            900                 905                 910

Gly Glu Gly Val Leu Ser Ala Asp His Leu Phe Val Lys Ser Leu Asn
        915                 920                 925

Ser Ala Ser Tyr Leu Tyr Glu Val Met Glu Arg Pro Arg His Gly Arg
    930                 935                 940

Leu Ala Trp Arg Gly Thr Gln Asp Lys Thr Thr Met Val Thr Ser Phe
945                 950                 955                 960

Thr Asn Glu Asp Leu Leu Arg Gly Arg Leu Val Tyr Gln His Asp Asp
                965                 970                 975

Ser Glu Thr Thr Glu Asp Asp Ile Pro Phe Val Ala Thr Arg Gln Gly
            980                 985                 990

Glu Ser Ser Gly Asp Met Ala Trp  Glu Glu Val Arg Gly  Val Phe Arg
        995                 1000                1005

Val Ala  Ile Gln Pro Val Asn  Asp His Ala Pro Val  Gln Thr Ile
    1010                1015                1020

Ser Arg  Ile Phe His Val Ala  Arg Gly Gly Arg Arg  Leu Leu Thr
    1025                1030                1035

Thr Asp  Asp Val Ala Phe Ser  Asp Ala Asp Ser Gly  Phe Ala Asp
    1040                1045                1050

Ala Gln  Leu Val Leu Thr Arg  Lys Asp Leu Leu Phe  Gly Ser Ile
    1055                1060                1065

Val Ala  Val Asp Glu Pro Thr  Arg Pro Ile Tyr Arg  Phe Thr Gln
    1070                1075                1080

Glu Asp  Leu Arg Lys Arg Arg  Val Leu Phe Val His  Ser Gly Ala
    1085                1090                1095

Asp Arg  Gly Trp Ile Gln Leu  Gln Val Ser Asp Gly  Gln His Gln
    1100                1105                1110

Ala Thr  Ala Leu Leu Glu Val  Gln Ala Ser Glu Pro  Tyr Leu Arg
    1115                1120                1125
```

```
Val Ala  Asn Gly Ser Ser Leu  Val Val Pro Gln Gly  Gly Gln Gly
    1130                1135                1140

Thr Ile  Asp Thr Ala Val Leu  His Leu Asp Thr Asn  Leu Asp Ile
    1145                1150                1155

Arg Ser  Gly Asp Glu Val His  Tyr His Val Thr Ala  Gly Pro Arg
    1160                1165                1170

Trp Gly  Gln Leu Val Arg Ala  Gly Gln Pro Ala Thr  Ala Phe Ser
    1175                1180                1185

Gln Gln  Asp Leu Leu Asp Gly  Ala Val Leu Tyr Ser  His Asn Gly
    1190                1195                1200

Ser Leu  Ser Pro Arg Asp Thr  Met Ala Phe Ser Val  Glu Ala Gly
    1205                1210                1215

Pro Val  His Thr Asp Ala Thr  Leu Gln Val Thr Ile  Ala Leu Glu
    1220                1225                1230

Gly Pro  Leu Ala Pro Leu Lys  Leu Val Arg His Lys  Lys Ile Tyr
    1235                1240                1245

Val Phe  Gln Gly Glu Ala Ala  Glu Ile Arg Arg Asp  Gln Leu Glu
    1250                1255                1260

Ala Ala  Gln Glu Ala Val Pro  Pro Ala Asp Ile Val  Phe Ser Val
    1265                1270                1275

Lys Ser  Pro Pro Ser Ala Gly  Tyr Leu Val Met Val  Ser Arg Gly
    1280                1285                1290

Ala Leu  Ala Asp Glu Pro Pro  Ser Leu Asp Pro Val  Gln Ser Phe
    1295                1300                1305

Ser Gln  Glu Ala Val Asp Thr  Gly Arg Val Leu Tyr  Leu His Ser
    1310                1315                1320

Arg Pro  Glu Ala Trp Ser Asp  Ala Phe Ser Leu Asp  Val Ala Ser
    1325                1330                1335

Gly Leu  Gly Ala Pro Leu Glu  Gly Val Leu Val Glu  Leu Glu Val
    1340                1345                1350

Leu Pro  Ala Ala Ile Pro Leu  Glu Ala Gln Asn Phe  Ser Val Pro
    1355                1360                1365
```

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Glu Gly  Gly Ser Leu Thr Leu  Ala Pro Pro Leu Leu  Arg Val Ser
    1370                1375                1380

Gly Pro  Tyr Phe Pro Thr Leu  Leu Gly Leu Ser Leu  Gln Val Leu
    1385                1390                1395

Glu Pro  Pro Gln His Gly Ala  Leu Gln Lys Glu Asp  Gly Pro Gln
    1400                1405                1410

Ala Arg  Thr Leu Ser Ala Phe  Ser Trp Arg Met Val  Glu Glu Gln
    1415                1420                1425

Leu Ile  Arg Tyr Val His Asp  Gly Ser Glu Thr Leu  Thr Asp Ser
    1430                1435                1440

Phe Val  Leu Met Ala Asn Ala  Ser Glu Met Asp Arg  Gln Ser His
    1445                1450                1455

Pro Val  Ala Phe Thr Val Thr  Val Leu Pro Val Asn  Asp Gln Pro
    1460                1465                1470

Pro Ile  Leu Thr Thr Asn Thr  Gly Leu Gln Met Trp  Glu Gly Ala
    1475                1480                1485

Thr Ala  Pro Ile Pro Ala Glu  Ala Leu Arg Ser Thr  Asp Gly Asp
    1490                1495                1500

Ser Gly  Ser Glu Asp Leu Val  Tyr Thr Ile Glu Gln  Pro Ser Asn
    1505                1510                1515

Gly Arg  Val Val Leu Arg Gly  Ala Pro Gly Thr Glu  Val Arg Ser
    1520                1525                1530

Phe Thr  Gln Ala Gln Leu Asp  Gly Gly Leu Val Leu  Phe Ser His
    1535                1540                1545

Arg Gly  Thr Leu Asp Gly Gly  Phe Arg Phe Arg Leu  Ser Asp Gly
    1550                1555                1560

Glu His  Thr Ser Pro Gly His  Phe Phe Arg Val Thr  Ala Gln Lys
    1565                1570                1575

Gln Val  Leu Leu Ser Leu Lys  Gly Ser Gln Thr Leu  Thr Val Cys
    1580                1585                1590

Pro Gly  Ser Val Gln Pro Leu  Ser Ser Gln Thr Leu  Arg Ala Ser
```

1595 1600 1605

Ser Ser Ala Gly Thr Asp Pro Gln Leu Leu Leu Tyr Arg Val Val
1610 1615 1620

Arg Gly Pro Gln Leu Gly Arg Leu Phe His Ala Gln Gln Asp Ser
1625 1630 1635

Thr Gly Glu Ala Leu Val Asn Phe Thr Gln Ala Glu Val Tyr Ala
1640 1645 1650

Gly Asn Ile Leu Tyr Glu His Glu Met Pro Pro Glu Pro Phe Trp
1655 1660 1665

Glu Ala His Asp Thr Leu Glu Leu Gln Leu Ser Ser Pro Pro Ala
1670 1675 1680

Arg Asp Val Ala Ala Thr Leu Ala Val Ala Val Ser Phe Glu Ala
1685 1690 1695

Ala Cys Pro Gln Arg Pro Ser His Leu Trp Lys Asn Lys Gly Leu
1700 1705 1710

Trp Val Pro Glu Gly Gln Arg Ala Arg Ile Thr Val Ala Ala Leu
1715 1720 1725

Asp Ala Ser Asn Leu Leu Ala Ser Val Pro Ser Pro Gln Arg Ser
1730 1735 1740

Glu His Asp Val Leu Phe Gln Val Thr Gln Phe Pro Ser Arg Gly
1745 1750 1755

Gln Leu Leu Val Ser Glu Glu Pro Leu His Ala Gly Gln Pro His
1760 1765 1770

Phe Leu Gln Ser Gln Leu Ala Ala Gly Gln Leu Val Tyr Ala His
1775 1780 1785

Gly Gly Gly Gly Thr Gln Gln Asp Gly Phe His Phe Arg Ala His
1790 1795 1800

Leu Gln Gly Pro Ala Gly Ala Ser Val Ala Gly Pro Gln Thr Ser
1805 1810 1815

Glu Ala Phe Ala Ile Thr Val Arg Asp Val Asn Glu Arg Pro Pro
1820 1825 1830

```
Gln Pro  Gln Ala Ser Val Pro  Leu Arg Leu Thr Arg  Gly Ser Arg
    1835                 1840                 1845

Ala Pro  Ile Ser Arg Ala Gln  Leu Ser Val Val Asp  Pro Asp Ser
    1850                 1855                 1860

Ala Pro  Gly Glu Ile Glu Tyr  Glu Val Gln Arg Ala  Pro His Asn
    1865                 1870                 1875

Gly Phe  Leu Ser Leu Val Gly  Gly Gly Leu Gly Pro  Val Thr Arg
    1880                 1885                 1890

Phe Thr  Gln Ala Asp Val Asp  Ser Gly Arg Leu Ala  Phe Val Ala
    1895                 1900                 1905

Asn Gly  Ser Ser Val Ala Gly  Ile Phe Gln Leu Ser  Met Ser Asp
    1910                 1915                 1920

Gly Ala  Ser Pro Pro Leu Pro  Met Ser Leu Ala Val  Asp Ile Leu
    1925                 1930                 1935

Pro Ser  Ala Ile Glu Val Gln  Leu Arg Ala Pro Leu  Glu Val Pro
    1940                 1945                 1950

Gln Ala  Leu Gly Arg Ser Ser  Leu Ser Gln Gln Gln  Leu Arg Val
    1955                 1960                 1965

Val Ser  Asp Arg Glu Glu Pro  Glu Ala Ala Tyr Arg  Leu Ile Gln
    1970                 1975                 1980

Gly Pro  Gln Tyr Gly His Leu  Leu Val Gly Gly Arg  Pro Thr Ser
    1985                 1990                 1995

Ala Phe  Ser Gln Phe Gln Ile  Asp Gln Gly Glu Val  Val Phe Ala
    2000                 2005                 2010

Phe Thr  Asn Phe Ser Ser Ser  His Asp His Phe Arg  Val Leu Ala
    2015                 2020                 2025

Leu Ala  Arg Gly Val Asn Ala  Ser Ala Val Val Asn  Val Thr Val
    2030                 2035                 2040

Arg Ala  Leu Leu His Val Trp  Ala Gly Gly Pro Trp  Pro Gln Gly
    2045                 2050                 2055

Ala Thr  Leu Arg Leu Asp Pro  Thr Val Leu Asp Ala  Gly Glu Leu
    2060                 2065                 2070
```

```
Ala Asn  Arg Thr Gly Ser Val  Pro Arg Phe Arg Leu  Leu Glu Gly
    2075                 2080                 2085

Pro Arg  His Gly Arg Val Val  Arg Val Pro Arg Ala  Arg Thr Glu
    2090                 2095                 2100

Pro Gly  Gly Ser Gln Leu Val  Glu Gln Phe Thr Gln  Gln Asp Leu
    2105                 2110                 2115

Glu Asp  Gly Arg Leu Gly Leu  Glu Val Gly Arg Pro  Glu Gly Arg
    2120                 2125                 2130

Ala Pro  Gly Pro Ala Gly Asp  Ser Leu Thr Leu Glu  Leu Trp Ala
    2135                 2140                 2145

Gln Gly  Val Pro Pro Ala Val  Ala Ser Leu Asp Phe  Ala Thr Glu
    2150                 2155                 2160

Pro Tyr  Asn Ala Ala Arg Pro  Tyr Ser Val Ala Leu  Leu Ser Val
    2165                 2170                 2175

Pro Glu  Ala Ala Arg Thr Glu  Ala Gly Lys Pro Glu  Ser Ser Thr
    2180                 2185                 2190

Pro Thr  Gly Glu Pro Gly Pro  Met Ala Ser Ser Pro  Glu Pro Ala
    2195                 2200                 2205

Val Ala  Lys Gly Gly Phe Leu  Ser Phe Leu Glu Ala  Asn Met Phe
    2210                 2215                 2220

Ser Val  Ile Ile Pro Met Cys  Leu Val Leu Leu Leu  Leu Ala Leu
    2225                 2230                 2235

Ile Leu  Pro Leu Leu Phe Tyr  Leu Arg Lys Arg Asn  Lys Thr Gly
    2240                 2245                 2250

Lys His  Asp Val Gln Val Leu  Thr Ala Lys Pro Arg  Asn Gly Leu
    2255                 2260                 2265

Ala Gly  Asp Thr Glu Thr Phe  Arg Lys Val Glu Pro  Gly Gln Ala
    2270                 2275                 2280

Ile Pro  Leu Thr Ala Val Pro  Gly Gln Gly Pro Pro  Pro Gly Gly
    2285                 2290                 2295

Gln Pro  Asp Pro Glu Leu Leu  Gln Phe Cys Arg Thr  Pro Asn Pro
    2300                 2305                 2310
```

```
Ala Leu  Lys Asn Gly Gln Tyr  Trp Val
    2315                2320


+ADw-210+AD4-  30
+ADw-211+AD4-  1210
+ADw-212+AD4-  PRT
+ADw-213+AD4-  Homo sapiens

+ADw-400+AD4-  30

Met Arg Pro Ser Gly Thr Ala Gly Ala Ala Leu Leu Ala Leu Leu Ala
1               5                  10                  15


Ala Leu Cys Pro Ala Ser Arg Ala Leu Glu Glu Lys Lys Val Cys Gln
            20                  25                  30


Gly Thr Ser Asn Lys Leu Thr Gln Leu Gly Thr Phe Glu Asp His Phe
        35                  40                  45


Leu Ser Leu Gln Arg Met Phe Asn Asn Cys Glu Val Val Leu Gly Asn
    50                  55                  60


Leu Glu Ile Thr Tyr Val Gln Arg Asn Tyr Asp Leu Ser Phe Leu Lys
65                  70                  75                  80


Thr Ile Gln Glu Val Ala Gly Tyr Val Leu Ile Ala Leu Asn Thr Val
                85                  90                  95


Glu Arg Ile Pro Leu Glu Asn Leu Gln Ile Ile Arg Gly Asn Met Tyr
            100                 105                 110


Tyr Glu Asn Ser Tyr Ala Leu Ala Val Leu Ser Asn Tyr Asp Ala Asn
        115                 120                 125


Lys Thr Gly Leu Lys Glu Leu Pro Met Arg Asn Leu Gln Glu Ile Leu
    130                 135                 140


His Gly Ala Val Arg Phe Ser Asn Asn Pro Ala Leu Cys Asn Val Glu
145                 150                 155                 160


Ser Ile Gln Trp Arg Asp Ile Val Ser Ser Asp Phe Leu Ser Asn Met
                165                 170                 175


Ser Met Asp Phe Gln Asn His Leu Gly Ser Cys Gln Lys Cys Asp Pro
            180                 185                 190


Ser Cys Pro Asn Gly Ser Cys Trp Gly Ala Gly Glu Glu Asn Cys Gln
        195                 200                 205
```

```
Lys Leu Thr Lys Ile Ile Cys Ala Gln Gln Cys Ser Gly Arg Cys Arg
    210                 215                 220

Gly Lys Ser Pro Ser Asp Cys Cys His Asn Gln Cys Ala Ala Gly Cys
225                 230                 235                 240

Thr Gly Pro Arg Glu Ser Asp Cys Leu Val Cys Arg Lys Phe Arg Asp
                245                 250                 255

Glu Ala Thr Cys Lys Asp Thr Cys Pro Pro Leu Met Leu Tyr Asn Pro
            260                 265                 270

Thr Thr Tyr Gln Met Asp Val Asn Pro Glu Gly Lys Tyr Ser Phe Gly
        275                 280                 285

Ala Thr Cys Val Lys Lys Cys Pro Arg Asn Tyr Val Val Thr Asp His
    290                 295                 300

Gly Ser Cys Val Arg Ala Cys Gly Ala Asp Ser Tyr Glu Met Glu Glu
305                 310                 315                 320

Asp Gly Val Arg Lys Cys Lys Lys Cys Glu Gly Pro Cys Arg Lys Val
                325                 330                 335

Cys Asn Gly Ile Gly Ile Gly Glu Phe Lys Asp Ser Leu Ser Ile Asn
            340                 345                 350

Ala Thr Asn Ile Lys His Phe Lys Asn Cys Thr Ser Ile Ser Gly Asp
        355                 360                 365

Leu His Ile Leu Pro Val Ala Phe Arg Gly Asp Ser Phe Thr His Thr
    370                 375                 380

Pro Pro Leu Asp Pro Gln Glu Leu Asp Ile Leu Lys Thr Val Lys Glu
385                 390                 395                 400

Ile Thr Gly Phe Leu Leu Ile Gln Ala Trp Pro Glu Asn Arg Thr Asp
                405                 410                 415

Leu His Ala Phe Glu Asn Leu Glu Ile Ile Arg Gly Arg Thr Lys Gln
            420                 425                 430

His Gly Gln Phe Ser Leu Ala Val Val Ser Leu Asn Ile Thr Ser Leu
        435                 440                 445

Gly Leu Arg Ser Leu Lys Glu Ile Ser Asp Gly Asp Val Ile Ile Ser
```

```
    450                 455                 460

Gly Asn Lys Asn Leu Cys Tyr Ala Asn Thr Ile Asn Trp Lys Lys Leu
465                 470                 475                 480

Phe Gly Thr Ser Gly Gln Lys Thr Lys Ile Ile Ser Asn Arg Gly Glu
                485                 490                 495

Asn Ser Cys Lys Ala Thr Gly Gln Val Cys His Ala Leu Cys Ser Pro
            500                 505                 510

Glu Gly Cys Trp Gly Pro Glu Pro Arg Asp Cys Val Ser Cys Arg Asn
        515                 520                 525

Val Ser Arg Gly Arg Glu Cys Val Asp Lys Cys Asn Leu Leu Glu Gly
    530                 535                 540

Glu Pro Arg Glu Phe Val Glu Asn Ser Glu Cys Ile Gln Cys His Pro
545                 550                 555                 560

Glu Cys Leu Pro Gln Ala Met Asn Ile Thr Cys Thr Gly Arg Gly Pro
                565                 570                 575

Asp Asn Cys Ile Gln Cys Ala His Tyr Ile Asp Gly Pro His Cys Val
            580                 585                 590

Lys Thr Cys Pro Ala Gly Val Met Gly Glu Asn Asn Thr Leu Val Trp
        595                 600                 605

Lys Tyr Ala Asp Ala Gly His Val Cys His Leu Cys His Pro Asn Cys
    610                 615                 620

Thr Tyr Gly Cys Thr Gly Pro Gly Leu Glu Gly Cys Pro Thr Asn Gly
625                 630                 635                 640

Pro Lys Ile Pro Ser Ile Ala Thr Gly Met Val Gly Ala Leu Leu Leu
                645                 650                 655

Leu Leu Val Val Ala Leu Gly Ile Gly Leu Phe Met Arg Arg Arg His
            660                 665                 670

Ile Val Arg Lys Arg Thr Leu Arg Arg Leu Leu Gln Glu Arg Glu Leu
        675                 680                 685

Val Glu Pro Leu Thr Pro Ser Gly Glu Ala Pro Asn Gln Ala Leu Leu
    690                 695                 700
```

```
Arg Ile Leu Lys Glu Thr Glu Phe Lys Lys Ile Lys Val Leu Gly Ser
705                 710                 715                 720

Gly Ala Phe Gly Thr Val Tyr Lys Gly Leu Trp Ile Pro Glu Gly Glu
                725                 730                 735

Lys Val Lys Ile Pro Val Ala Ile Lys Glu Leu Arg Glu Ala Thr Ser
            740                 745                 750

Pro Lys Ala Asn Lys Glu Ile Leu Asp Glu Ala Tyr Val Met Ala Ser
        755                 760                 765

Val Asp Asn Pro His Val Cys Arg Leu Leu Gly Ile Cys Leu Thr Ser
    770                 775                 780

Thr Val Gln Leu Ile Thr Gln Leu Met Pro Phe Gly Cys Leu Leu Asp
785                 790                 795                 800

Tyr Val Arg Glu His Lys Asp Asn Ile Gly Ser Gln Tyr Leu Leu Asn
                805                 810                 815

Trp Cys Val Gln Ile Ala Lys Gly Met Asn Tyr Leu Glu Asp Arg Arg
            820                 825                 830

Leu Val His Arg Asp Leu Ala Ala Arg Asn Val Leu Val Lys Thr Pro
        835                 840                 845

Gln His Val Lys Ile Thr Asp Phe Gly Leu Ala Lys Leu Leu Gly Ala
    850                 855                 860

Glu Glu Lys Glu Tyr His Ala Glu Gly Gly Lys Val Pro Ile Lys Trp
865                 870                 875                 880

Met Ala Leu Glu Ser Ile Leu His Arg Ile Tyr Thr His Gln Ser Asp
                885                 890                 895

Val Trp Ser Tyr Gly Val Thr Val Trp Glu Leu Met Thr Phe Gly Ser
            900                 905                 910

Lys Pro Tyr Asp Gly Ile Pro Ala Ser Glu Ile Ser Ser Ile Leu Glu
        915                 920                 925

Lys Gly Glu Arg Leu Pro Gln Pro Pro Ile Cys Thr Ile Asp Val Tyr
    930                 935                 940

Met Ile Met Val Lys Cys Trp Met Ile Asp Ala Asp Ser Arg Pro Lys
945                 950                 955                 960
```

```
Phe Arg Glu Leu Ile Ile Glu Phe Ser Lys Met Ala Arg Asp Pro Gln
               965                 970                 975

Arg Tyr Leu Val Ile Gln Gly Asp Glu Arg Met His Leu Pro Ser Pro
           980                 985                 990

Thr Asp Ser Asn Phe Tyr Arg Ala  Leu Met Asp Glu Glu  Asp Met Asp
       995                 1000                1005

Asp Val  Val Asp Ala Asp Glu  Tyr Leu Ile Pro Gln  Gln Gly Phe
   1010                1015                1020

Phe Ser  Ser Pro Ser Thr Ser  Arg Thr Pro Leu Leu  Ser Ser Leu
   1025                1030                1035

Ser Ala  Thr Ser Asn Asn Ser  Thr Val Ala Cys Ile  Asp Arg Asn
   1040                1045                1050

Gly Leu  Gln Ser Cys Pro Ile  Lys Glu Asp Ser Phe  Leu Gln Arg
   1055                1060                1065

Tyr Ser  Ser Asp Pro Thr Gly  Ala Leu Thr Glu Asp  Ser Ile Asp
   1070                1075                1080

Asp Thr  Phe Leu Pro Val Pro  Glu Tyr Ile Asn Gln  Ser Val Pro
   1085                1090                1095

Lys Arg  Pro Ala Gly Ser Val  Gln Asn Pro Val Tyr  His Asn Gln
   1100                1105                1110

Pro Leu  Asn Pro Ala Pro Ser  Arg Asp Pro His Tyr  Gln Asp Pro
   1115                1120                1125

His Ser  Thr Ala Val Gly Asn  Pro Glu Tyr Leu Asn  Thr Val Gln
   1130                1135                1140

Pro Thr  Cys Val Asn Ser Thr  Phe Asp Ser Pro Ala  His Trp Ala
   1145                1150                1155

Gln Lys  Gly Ser His Gln Ile  Ser Leu Asp Asn Pro  Asp Tyr Gln
   1160                1165                1170

Gln Asp  Phe Phe Pro Lys Glu  Ala Lys Pro Asn Gly  Ile Phe Lys
   1175                1180                1185

Gly Ser  Thr Ala Glu Asn Ala  Glu Tyr Leu Arg Val  Ala Pro Gln
   1190                1195                1200
```

```
Ser Ser  Glu Phe Ile Gly Ala
    1205                1210


+ADw-210+AD4-  31
+ADw-211+AD4-  556
+ADw-212+AD4-  PRT
+ADw-213+AD4-  Homo sapiens

+ADw-400+AD4-  31

Met Pro Pro Pro Arg Leu Leu Phe Phe Leu Leu Phe Leu Thr Pro Met
1               5                  10                  15


Glu Val Arg Pro Glu Glu Pro Leu Val Val Lys Val Glu Glu Gly Asp
            20                  25                  30


Asn Ala Val Leu Gln Cys Leu Lys Gly Thr Ser Asp Gly Pro Thr Gln
        35                  40                  45


Gln Leu Thr Trp Ser Arg Glu Ser Pro Leu Lys Pro Phe Leu Lys Leu
    50                  55                  60


Ser Leu Gly Leu Pro Gly Leu Gly Ile His Met Arg Pro Leu Ala Ile
65                  70                  75                  80


Trp Leu Phe Ile Phe Asn Val Ser Gln Gln Met Gly Gly Phe Tyr Leu
                85                  90                  95


Cys Gln Pro Gly Pro Pro Ser Glu Lys Ala Trp Gln Pro Gly Trp Thr
            100                 105                 110


Val Asn Val Glu Gly Ser Gly Glu Leu Phe Arg Trp Asn Val Ser Asp
        115                 120                 125


Leu Gly Gly Leu Gly Cys Gly Leu Lys Asn Arg Ser Ser Glu Gly Pro
    130                 135                 140


Ser Ser Pro Ser Gly Lys Leu Met Ser Pro Lys Leu Tyr Val Trp Ala
145                 150                 155                 160


Lys Asp Arg Pro Glu Ile Trp Glu Gly Glu Pro Pro Cys Leu Pro Pro
                165                 170                 175


Arg Asp Ser Leu Asn Gln Ser Leu Ser Gln Asp Leu Thr Met Ala Pro
            180                 185                 190


Gly Ser Thr Leu Trp Leu Ser Cys Gly Val Pro Pro Asp Ser Val Ser
        195                 200                 205
```

```
Arg Gly Pro Leu Ser Trp Thr His Val His Pro Lys Gly Pro Lys Ser
    210                 215                 220

Leu Leu Ser Leu Glu Leu Lys Asp Asp Arg Pro Ala Arg Asp Met Trp
225                 230                 235                 240

Val Met Glu Thr Gly Leu Leu Leu Pro Arg Ala Thr Ala Gln Asp Ala
                245                 250                 255

Gly Lys Tyr Tyr Cys His Arg Gly Asn Leu Thr Met Ser Phe His Leu
            260                 265                 270

Glu Ile Thr Ala Arg Pro Val Leu Trp His Trp Leu Leu Arg Thr Gly
        275                 280                 285

Gly Trp Lys Val Ser Ala Val Thr Leu Ala Tyr Leu Ile Phe Cys Leu
    290                 295                 300

Cys Ser Leu Val Gly Ile Leu His Leu Gln Arg Ala Leu Val Leu Arg
305                 310                 315                 320

Arg Lys Arg Lys Arg Met Thr Asp Pro Thr Arg Arg Phe Phe Lys Val
                325                 330                 335

Thr Pro Pro Pro Gly Ser Gly Pro Gln Asn Gln Tyr Gly Asn Val Leu
            340                 345                 350

Ser Leu Pro Thr Pro Thr Ser Gly Leu Gly Arg Ala Gln Arg Trp Ala
        355                 360                 365

Ala Gly Leu Gly Gly Thr Ala Pro Ser Tyr Gly Asn Pro Ser Ser Asp
    370                 375                 380

Val Gln Ala Asp Gly Ala Leu Gly Ser Arg Ser Pro Pro Gly Val Gly
385                 390                 395                 400

Pro Glu Glu Glu Glu Gly Glu Gly Tyr Glu Glu Pro Asp Ser Glu Glu
                405                 410                 415

Asp Ser Glu Phe Tyr Glu Asn Asp Ser Asn Leu Gly Gln Asp Gln Leu
            420                 425                 430

Ser Gln Asp Gly Ser Gly Tyr Glu Asn Pro Glu Asp Glu Pro Leu Gly
        435                 440                 445

Pro Glu Asp Glu Asp Ser Phe Ser Asn Ala Glu Ser Tyr Glu Asn Glu
```

450 455 460

Asp Glu Glu Leu Thr Gln Pro Val Ala Arg Thr Met Asp Phe Leu Ser
465 470 475 480

Pro His Gly Ser Ala Trp Asp Pro Ser Arg Glu Ala Thr Ser Leu Gly
485 490 495

Ser Gln Ser Tyr Glu Asp Met Arg Gly Ile Leu Tyr Ala Ala Pro Gln
500 505 510

Leu Arg Ser Ile Arg Gly Gln Pro Gly Pro Asn His Glu Glu Asp Ala
515 520 525

Asp Ser Tyr Glu Asn Met Asp Asn Pro Asp Gly Pro Asp Pro Ala Trp
530 535 540

Gly Gly Gly Gly Arg Met Gly Thr Trp Ser Thr Arg
545 550 555

+ADw-210+AD4- 32
+ADw-211+AD4- 297
+ADw-212+AD4- PRT
+ADw-213+AD4- Homo sapiens

+ADw-400+AD4- 32

Met Thr Thr Pro Arg Asn Ser Val Asn Gly Thr Phe Pro Ala Glu Pro
1 5 10 15

Met Lys Gly Pro Ile Ala Met Gln Ser Gly Pro Lys Pro Leu Phe Arg
20 25 30

Arg Met Ser Ser Leu Val Gly Pro Thr Gln Ser Phe Phe Met Arg Glu
35 40 45

Ser Lys Thr Leu Gly Ala Val Gln Ile Met Asn Gly Leu Phe His Ile
50 55 60

Ala Leu Gly Gly Leu Leu Met Ile Pro Ala Gly Ile Tyr Ala Pro Ile
65 70 75 80

Cys Val Thr Val Trp Tyr Pro Leu Trp Gly Gly Ile Met Tyr Ile Ile
85 90 95

Ser Gly Ser Leu Leu Ala Ala Thr Glu Lys Asn Ser Arg Lys Cys Leu
100 105 110

Val Lys Gly Lys Met Ile Met Asn Ser Leu Ser Leu Phe Ala Ala Ile

115 120 125

Ser Gly Met Ile Leu Ser Ile Met Asp Ile Leu Asn Ile Lys Ile Ser
130 135 140

His Phe Leu Lys Met Glu Ser Leu Asn Phe Ile Arg Ala His Thr Pro
145 150 155 160

Tyr Ile Asn Ile Tyr Asn Cys Glu Pro Ala Asn Pro Ser Glu Lys Asn
165 170 175

Ser Pro Ser Thr Gln Tyr Cys Tyr Ser Ile Gln Ser Leu Phe Leu Gly
180 185 190

Ile Leu Ser Val Met Leu Ile Phe Ala Phe Phe Gln Glu Leu Val Ile
195 200 205

Ala Gly Ile Val Glu Asn Glu Trp Lys Arg Thr Cys Ser Arg Pro Lys
210 215 220

Ser Asn Ile Val Leu Leu Ser Ala Glu Glu Lys Lys Glu Gln Thr Ile
225 230 235 240

Glu Ile Lys Glu Glu Val Val Gly Leu Thr Glu Thr Ser Ser Gln Pro
245 250 255

Lys Asn Glu Glu Asp Ile Glu Ile Ile Pro Ile Gln Glu Glu Glu Glu
260 265 270

Glu Glu Thr Glu Thr Asn Phe Pro Glu Pro Pro Gln Asp Gln Glu Ser
275 280 285

Ser Pro Ile Glu Asn Asp Ser Ser Pro
290 295

+ADw-210+AD4- 33
+ADw-211+AD4- 364
+ADw-212+AD4- PRT
+ADw-213+AD4- Homo sapiens

+ADw-400+AD4- 33

Met Pro Leu Leu Leu Leu Leu Pro Leu Leu Trp Ala Gly Ala Leu Ala
1 5 10 15

Met Asp Pro Asn Phe Trp Leu Gln Val Gln Glu Ser Val Thr Val Gln
20 25 30

Glu Gly Leu Cys Val Leu Val Pro Cys Thr Phe Phe His Pro Ile Pro

```
        35                  40                  45

Tyr Tyr Asp Lys Asn Ser Pro Val His Gly Tyr Trp Phe Arg Glu Gly
    50                  55                  60

Ala Ile Ile Ser Arg Asp Ser Pro Val Ala Thr Asn Lys Leu Asp Gln
65                  70                  75                  80

Glu Val Gln Glu Glu Thr Gln Gly Arg Phe Arg Leu Leu Gly Asp Pro
                85                  90                  95

Ser Arg Asn Asn Cys Ser Leu Ser Ile Val Asp Ala Arg Arg Arg Asp
            100                 105                 110

Asn Gly Ser Tyr Phe Phe Arg Met Glu Arg Gly Ser Thr Lys Tyr Ser
        115                 120                 125

Tyr Lys Ser Pro Gln Leu Ser Val His Val Thr Asp Leu Thr His Arg
    130                 135                 140

Pro Lys Ile Leu Ile Pro Gly Thr Leu Glu Pro Gly His Ser Lys Asn
145                 150                 155                 160

Leu Thr Cys Ser Val Ser Trp Ala Cys Glu Gln Gly Thr Pro Pro Ile
                165                 170                 175

Phe Ser Trp Leu Ser Ala Ala Pro Thr Ser Leu Gly Pro Arg Thr Thr
            180                 185                 190

His Ser Ser Val Leu Ile Ile Thr Pro Arg Pro Gln Asp His Gly Thr
        195                 200                 205

Asn Leu Thr Cys Gln Val Lys Phe Ala Gly Ala Gly Val Thr Thr Glu
    210                 215                 220

Arg Thr Ile Gln Leu Asn Val Thr Tyr Val Pro Gln Asn Pro Thr Thr
225                 230                 235                 240

Gly Ile Phe Pro Gly Asp Gly Ser Gly Lys Gln Glu Thr Arg Ala Gly
                245                 250                 255

Val Val His Gly Ala Ile Gly Gly Ala Gly Val Thr Ala Leu Leu Ala
            260                 265                 270

Leu Cys Leu Cys Leu Ile Phe Phe Ile Val Lys Thr His Arg Arg Lys
        275                 280                 285
```

Ala Ala Arg Thr Ala Val Gly Arg Asn Asp Thr His Pro Thr Thr Gly
290 295 300

Ser Ala Ser Pro Lys His Gln Lys Lys Ser Lys Leu His Gly Pro Thr
305 310 315 320

Glu Thr Ser Ser Cys Ser Gly Ala Ala Pro Thr Val Glu Met Asp Glu
325 330 335

Glu Leu His Tyr Ala Ser Leu Asn Phe His Gly Met Asn Pro Ser Lys
340 345 350

Asp Thr Ser Thr Glu Tyr Ser Glu Val Arg Thr Gln
355 360

+ADw-210+AD4- 34
+ADw-211+AD4- 205
+ADw-212+AD4- PRT
+ADw-213+AD4- Homo sapiens

+ADw-400+AD4- 34

Met Thr Pro Pro Glu Arg Leu Phe Leu Pro Arg Val Cys Gly Thr Thr
1 5 10 15

Leu His Leu Leu Leu Leu Gly Leu Leu Leu Val Leu Leu Pro Gly Ala
20 25 30

Gln Gly Leu Pro Gly Val Gly Leu Thr Pro Ser Ala Ala Gln Thr Ala
35 40 45

Arg Gln His Pro Lys Met His Leu Ala His Ser Thr Leu Lys Pro Ala
50 55 60

Ala His Leu Ile Gly Asp Pro Ser Lys Gln Asn Ser Leu Leu Trp Arg
65 70 75 80

Ala Asn Thr Asp Arg Ala Phe Leu Gln Asp Gly Phe Ser Leu Ser Asn
85 90 95

Asn Ser Leu Leu Val Pro Thr Ser Gly Ile Tyr Phe Val Tyr Ser Gln
100 105 110

Val Val Phe Ser Gly Lys Ala Tyr Ser Pro Lys Ala Thr Ser Ser Pro
115 120 125

Leu Tyr Leu Ala His Glu Val Gln Leu Phe Ser Ser Gln Tyr Pro Phe
130 135 140

```
His Val Pro Leu Leu Ser Ser Gln Lys Met Val Tyr Pro Gly Leu Gln
145                 150                 155                 160


Glu Pro Trp Leu His Ser Met Tyr His Gly Ala Ala Phe Gln Leu Thr
                165                 170                 175


Gln Gly Asp Gln Leu Ser Thr His Thr Asp Gly Ile Pro His Leu Val
            180                 185                 190


Leu Ser Pro Ser Thr Val Phe Phe Gly Ala Phe Ala Leu
        195                 200                 205


+ADw-210+AD4-  35
+ADw-211+AD4-  233
+ADw-212+AD4-  PRT
+ADw-213+AD4-  Homo sapiens

+ADw-400+AD4-  35

Met Ser Thr Glu Ser Met Ile Arg Asp Val Glu Leu Ala Glu Glu Ala
1               5                   10                  15


Leu Pro Lys Lys Thr Gly Gly Pro Gln Gly Ser Arg Arg Cys Leu Phe
            20                  25                  30


Leu Ser Leu Phe Ser Phe Leu Ile Val Ala Gly Ala Thr Thr Leu Phe
        35                  40                  45


Cys Leu Leu His Phe Gly Val Ile Gly Pro Gln Arg Glu Glu Phe Pro
    50                  55                  60


Arg Asp Leu Ser Leu Ile Ser Pro Leu Ala Gln Ala Val Arg Ser Ser
65                  70                  75                  80


Ser Arg Thr Pro Ser Asp Lys Pro Val Ala His Val Val Ala Asn Pro
                85                  90                  95


Gln Ala Glu Gly Gln Leu Gln Trp Leu Asn Arg Arg Ala Asn Ala Leu
            100                 105                 110


Leu Ala Asn Gly Val Glu Leu Arg Asp Asn Gln Leu Val Val Pro Ser
        115                 120                 125


Glu Gly Leu Tyr Leu Ile Tyr Ser Gln Val Leu Phe Lys Gly Gln Gly
    130                 135                 140


Cys Pro Ser Thr His Val Leu Leu Thr His Thr Ile Ser Arg Ile Ala
145                 150                 155                 160
```

```
Val Ser Tyr Gln Thr Lys Val Asn Leu Leu Ser Ala Ile Lys Ser Pro
                165                 170                 175


Cys Gln Arg Glu Thr Pro Glu Gly Ala Glu Ala Lys Pro Trp Tyr Glu
            180                 185                 190


Pro Ile Tyr Leu Gly Gly Val Phe Gln Leu Glu Lys Gly Asp Arg Leu
        195                 200                 205


Ser Ala Glu Ile Asn Arg Pro Asp Tyr Leu Asp Phe Ala Glu Ser Gly
    210                 215                 220


Gln Val Tyr Phe Gly Ile Ile Ala Leu
225                 230


+ADw-210+AD4-  36
+ADw-211+AD4-  244
+ADw-212+AD4-  PRT
+ADw-213+AD4-  Homo sapiens

+ADw-400+AD4-  36

Met Gly Ala Leu Gly Leu Glu Gly Arg Gly Gly Arg Leu Gln Gly Arg
1               5                   10                  15


Gly Ser Leu Leu Leu Ala Val Ala Gly Ala Thr Ser Leu Val Thr Leu
            20                  25                  30


Leu Leu Ala Val Pro Ile Thr Val Leu Ala Val Leu Ala Leu Val Pro
        35                  40                  45


Gln Asp Gln Gly Gly Leu Val Thr Glu Thr Ala Asp Pro Gly Ala Gln
    50                  55                  60


Ala Gln Gln Gly Leu Gly Phe Gln Lys Leu Pro Glu Glu Glu Pro Glu
65                  70                  75                  80


Thr Asp Leu Ser Pro Gly Leu Pro Ala Ala His Leu Ile Gly Ala Pro
                85                  90                  95


Leu Lys Gly Gln Gly Leu Gly Trp Glu Thr Thr Lys Glu Gln Ala Phe
            100                 105                 110


Leu Thr Ser Gly Thr Gln Phe Ser Asp Ala Glu Gly Leu Ala Leu Pro
        115                 120                 125


Gln Asp Gly Leu Tyr Tyr Leu Tyr Cys Leu Val Gly Tyr Arg Gly Arg
    130                 135                 140
```

```
Ala Pro Pro Gly Gly Gly Asp Pro Gln Gly Arg Ser Val Thr Leu Arg
145                 150                 155                 160


Ser Ser Leu Tyr Arg Ala Gly Gly Ala Tyr Gly Pro Gly Thr Pro Glu
                165                 170                 175


Leu Leu Leu Glu Gly Ala Glu Thr Val Thr Pro Val Leu Asp Pro Ala
            180                 185                 190


Arg Arg Gln Gly Tyr Gly Pro Leu Trp Tyr Thr Ser Val Gly Phe Gly
        195                 200                 205


Gly Leu Val Gln Leu Arg Arg Gly Glu Arg Val Tyr Val Asn Ile Ser
    210                 215                 220


His Pro Asp Met Val Asp Phe Ala Arg Gly Lys Thr Phe Phe Gly Ala
225                 230                 235                 240


Val Met Val Gly



+ADw-210+AD4-  37
+ADw-211+AD4-  183
+ADw-212+AD4-  PRT
+ADw-213+AD4-  Homo sapiens

+ADw-400+AD4-  37

Met Glu Arg Val Gln Pro Leu Glu Glu Asn Val Gly Asn Ala Ala Arg
1               5                   10                  15


Pro Arg Phe Glu Arg Asn Lys Leu Leu Leu Val Ala Ser Val Ile Gln
            20                  25                  30


Gly Leu Gly Leu Leu Leu Cys Phe Thr Tyr Ile Cys Leu His Phe Ser
        35                  40                  45


Ala Leu Gln Val Ser His Arg Tyr Pro Arg Ile Gln Ser Ile Lys Val
    50                  55                  60


Gln Phe Thr Glu Tyr Lys Lys Glu Lys Gly Phe Ile Leu Thr Ser Gln
65                  70                  75                  80


Lys Glu Asp Glu Ile Met Lys Val Gln Asn Asn Ser Val Ile Ile Asn
                85                  90                  95


Cys Asp Gly Phe Tyr Leu Ile Ser Leu Lys Gly Tyr Phe Ser Gln Glu
            100                 105                 110
```

```
Val Asn Ile Ser Leu His Tyr Gln Lys Asp Glu Glu Pro Leu Phe Gln
        115                 120                 125

Leu Lys Lys Val Arg Ser Val Asn Ser Leu Met Val Ala Ser Leu Thr
    130                 135                 140

Tyr Lys Asp Lys Val Tyr Leu Asn Val Thr Thr Asp Asn Thr Ser Leu
145                 150                 155                 160

Asp Asp Phe His Val Asn Gly Gly Glu Leu Ile Leu Ile His Gln Asn
                165                 170                 175

Pro Gly Glu Phe Cys Val Leu
            180


+ADw-210+AD4-  38
+ADw-211+AD4-  261
+ADw-212+AD4-  PRT
+ADw-213+AD4-  Homo sapiens

+ADw-400+AD4-  38

Met Ile Glu Thr Tyr Asn Gln Thr Ser Pro Arg Ser Ala Ala Thr Gly
1               5                   10                  15

Leu Pro Ile Ser Met Lys Ile Phe Met Tyr Leu Leu Thr Val Phe Leu
            20                  25                  30

Ile Thr Gln Met Ile Gly Ser Ala Leu Phe Ala Val Tyr Leu His Arg
        35                  40                  45

Arg Leu Asp Lys Ile Glu Asp Glu Arg Asn Leu His Glu Asp Phe Val
    50                  55                  60

Phe Met Lys Thr Ile Gln Arg Cys Asn Thr Gly Glu Arg Ser Leu Ser
65                  70                  75                  80

Leu Leu Asn Cys Glu Glu Ile Lys Ser Gln Phe Glu Gly Phe Val Lys
                85                  90                  95

Asp Ile Met Leu Asn Lys Glu Glu Thr Lys Lys Glu Asn Ser Phe Glu
            100                 105                 110

Met Gln Lys Gly Asp Gln Asn Pro Gln Ile Ala Ala His Val Ile Ser
        115                 120                 125

Glu Ala Ser Ser Lys Thr Thr Ser Val Leu Gln Trp Ala Glu Lys Gly
    130                 135                 140
```

```
Tyr Tyr Thr Met Ser Asn Asn Leu Val Thr Leu Glu Asn Gly Lys Gln
145                 150                 155                 160


Leu Thr Val Lys Arg Gln Gly Leu Tyr Tyr Ile Tyr Ala Gln Val Thr
                165                 170                 175


Phe Cys Ser Asn Arg Glu Ala Ser Ser Gln Ala Pro Phe Ile Ala Ser
            180                 185                 190


Leu Cys Leu Lys Ser Pro Gly Arg Phe Glu Arg Ile Leu Leu Arg Ala
        195                 200                 205


Ala Asn Thr His Ser Ser Ala Lys Pro Cys Gly Gln Gln Ser Ile His
    210                 215                 220


Leu Gly Gly Val Phe Glu Leu Gln Pro Gly Ala Ser Val Phe Val Asn
225                 230                 235                 240


Val Thr Asp Pro Ser Gln Val Ser His Gly Thr Gly Phe Thr Ser Phe
                245                 250                 255


Gly Leu Leu Lys Leu
            260


+ADw-210+AD4-  39
+ADw-211+AD4-  281
+ADw-212+AD4-  PRT
+ADw-213+AD4-  Homo sapiens

+ADw-400+AD4-  39

Met Gln Gln Pro Phe Asn Tyr Pro Tyr Pro Gln Ile Tyr Trp Val Asp
1               5                   10                  15


Ser Ser Ala Ser Ser Pro Trp Ala Pro Pro Gly Thr Val Leu Pro Cys
            20                  25                  30


Pro Thr Ser Val Pro Arg Arg Pro Gly Gln Arg Arg Pro Pro Pro Pro
        35                  40                  45


Pro Pro Pro Pro Pro Leu Pro Pro Pro Pro Pro Pro Pro Pro Leu Pro
    50                  55                  60


Pro Leu Pro Leu Pro Pro Leu Lys Lys Arg Gly Asn His Ser Thr Gly
65                  70                  75                  80


Leu Cys Leu Leu Val Met Phe Phe Met Val Leu Val Ala Leu Val Gly
                85                  90                  95
```

```
Leu Gly Leu Gly Met Phe Gln Leu Phe His Leu Gln Lys Glu Leu Ala
            100                 105                 110

Glu Leu Arg Glu Ser Thr Ser Gln Met His Thr Ala Ser Ser Leu Glu
        115                 120                 125

Lys Gln Ile Gly His Pro Ser Pro Pro Pro Glu Lys Lys Glu Leu Arg
    130                 135                 140

Lys Val Ala His Leu Thr Gly Lys Ser Asn Ser Arg Ser Met Pro Leu
145                 150                 155                 160

Glu Trp Glu Asp Thr Tyr Gly Ile Val Leu Leu Ser Gly Val Lys Tyr
                165                 170                 175

Lys Lys Gly Gly Leu Val Ile Asn Glu Thr Gly Leu Tyr Phe Val Tyr
            180                 185                 190

Ser Lys Val Tyr Phe Arg Gly Gln Ser Cys Asn Asn Leu Pro Leu Ser
        195                 200                 205

His Lys Val Tyr Met Arg Asn Ser Lys Tyr Pro Gln Asp Leu Val Met
    210                 215                 220

Met Glu Gly Lys Met Met Ser Tyr Cys Thr Thr Gly Gln Met Trp Ala
225                 230                 235                 240

Arg Ser Ser Tyr Leu Gly Ala Val Phe Asn Leu Thr Ser Ala Asp His
                245                 250                 255

Leu Tyr Val Asn Val Ser Glu Leu Ser Leu Val Asn Phe Glu Glu Ser
            260                 265                 270

Gln Thr Phe Phe Gly Leu Tyr Lys Leu
        275                 280


+ADw-210+AD4-  40
+ADw-211+AD4-  193
+ADw-212+AD4-  PRT
+ADw-213+AD4-  Homo sapiens

+ADw-400+AD4-  40

Met Pro Glu Glu Gly Ser Gly Cys Ser Val Arg Arg Arg Pro Tyr Gly
1               5                   10                  15

Cys Val Leu Arg Ala Ala Leu Val Pro Leu Val Ala Gly Leu Val Ile
            20                  25                  30
```

```
Cys Leu Val Val Cys Ile Gln Arg Phe Ala Gln Ala Gln Gln Gln Leu
        35                  40                  45

Pro Leu Glu Ser Leu Gly Trp Asp Val Ala Glu Leu Gln Leu Asn His
    50                  55                  60

Thr Gly Pro Gln Gln Asp Pro Arg Leu Tyr Trp Gln Gly Gly Pro Ala
65                  70                  75                  80

Leu Gly Arg Ser Phe Leu His Gly Pro Glu Leu Asp Lys Gly Gln Leu
                85                  90                  95

Arg Ile His Arg Asp Gly Ile Tyr Met Val His Ile Gln Val Thr Leu
            100                 105                 110

Ala Ile Cys Ser Ser Thr Thr Ala Ser Arg His His Pro Thr Thr Leu
        115                 120                 125

Ala Val Gly Ile Cys Ser Pro Ala Ser Arg Ser Ile Ser Leu Leu Arg
    130                 135                 140

Leu Ser Phe His Gln Gly Cys Thr Ile Ala Ser Gln Arg Leu Thr Pro
145                 150                 155                 160

Leu Ala Arg Gly Asp Thr Leu Cys Thr Asn Leu Thr Gly Thr Leu Leu
                165                 170                 175

Pro Ser Arg Asn Thr Asp Glu Thr Phe Phe Gly Val Gln Trp Val Arg
            180                 185                 190

Pro
```

+ADw-210+AD4- 41
+ADw-211+AD4- 234
+ADw-212+AD4- PRT
+ADw-213+AD4- Homo sapiens

+ADw-400+AD4- 41

```
Met Asp Pro Gly Leu Gln Gln Ala Leu Asn Gly Met Ala Pro Pro Gly
1               5                   10                  15

Asp Thr Ala Met His Val Pro Ala Gly Ser Val Ala Ser His Leu Gly
            20                  25                  30

Thr Thr Ser Arg Ser Tyr Phe Tyr Leu Thr Thr Ala Thr Leu Ala Leu
        35                  40                  45
```

```
Cys Leu Val Phe Thr Val Ala Thr Ile Met Val Leu Val Val Gln Arg
    50                  55                  60

Thr Asp Ser Ile Pro Asn Ser Pro Asp Asn Val Pro Leu Lys Gly Gly
65                  70                  75                  80

Asn Cys Ser Glu Asp Leu Leu Cys Ile Leu Lys Arg Ala Pro Phe Lys
                85                  90                  95

Lys Ser Trp Ala Tyr Leu Gln Val Ala Lys His Leu Asn Lys Thr Lys
            100                 105                 110

Leu Ser Trp Asn Lys Asp Gly Ile Leu His Gly Val Arg Tyr Gln Asp
        115                 120                 125

Gly Asn Leu Val Ile Gln Phe Pro Gly Leu Tyr Phe Ile Ile Cys Gln
    130                 135                 140

Leu Gln Phe Leu Val Gln Cys Pro Asn Asn Ser Val Asp Leu Lys Leu
145                 150                 155                 160

Glu Leu Leu Ile Asn Lys His Ile Lys Lys Gln Ala Leu Val Thr Val
                165                 170                 175

Cys Glu Ser Gly Met Gln Thr Lys His Val Tyr Gln Asn Leu Ser Gln
            180                 185                 190

Phe Leu Leu Asp Tyr Leu Gln Val Asn Thr Thr Ile Ser Val Asn Val
        195                 200                 205

Asp Thr Phe Gln Tyr Ile Asp Thr Ser Thr Phe Pro Leu Glu Asn Val
    210                 215                 220

Leu Ser Ile Phe Leu Tyr Ser Asn Ser Asp
225                 230


+ADw-210+AD4-  42
+ADw-211+AD4-  254
+ADw-212+AD4-  PRT
+ADw-213+AD4-  Homo sapiens

+ADw-400+AD4-  42

Met Glu Tyr Ala Ser Asp Ala Ser Leu Asp Pro Glu Ala Pro Trp Pro
1               5                   10                  15

Pro Ala Pro Arg Ala Arg Ala Cys Arg Val Leu Pro Trp Ala Leu Val
            20                  25                  30
```

```
Ala Gly Leu Leu Leu Leu Leu Leu Leu Ala Ala Ala Cys Ala Val Phe
        35                  40                  45

Leu Ala Cys Pro Trp Ala Val Ser Gly Ala Arg Ala Ser Pro Gly Ser
    50                  55                  60

Ala Ala Ser Pro Arg Leu Arg Glu Gly Pro Glu Leu Ser Pro Asp Asp
65                  70                  75                  80

Pro Ala Gly Leu Leu Asp Leu Arg Gln Gly Met Phe Ala Gln Leu Val
                85                  90                  95

Ala Gln Asn Val Leu Leu Ile Asp Gly Pro Leu Ser Trp Tyr Ser Asp
            100                 105                 110

Pro Gly Leu Ala Gly Val Ser Leu Thr Gly Gly Leu Ser Tyr Lys Glu
        115                 120                 125

Asp Thr Lys Glu Leu Val Val Ala Lys Ala Gly Val Tyr Tyr Val Phe
    130                 135                 140

Phe Gln Leu Glu Leu Arg Arg Val Val Ala Gly Glu Gly Ser Gly Ser
145                 150                 155                 160

Val Ser Leu Ala Leu His Leu Gln Pro Leu Arg Ser Ala Ala Gly Ala
                165                 170                 175

Ala Ala Leu Ala Leu Thr Val Asp Leu Pro Pro Ala Ser Ser Glu Ala
            180                 185                 190

Arg Asn Ser Ala Phe Gly Phe Gln Gly Arg Leu Leu His Leu Ser Ala
        195                 200                 205

Gly Gln Arg Leu Gly Val His Leu His Thr Glu Ala Arg Ala Arg His
    210                 215                 220

Ala Trp Gln Leu Thr Gln Gly Ala Thr Val Leu Gly Leu Phe Arg Val
225                 230                 235                 240

Thr Pro Glu Ile Pro Ala Gly Leu Pro Ser Pro Arg Ser Glu
                245                 250

+ADw-210+AD4-  43
+ADw-211+AD4-  281
+ADw-212+AD4-  PRT
+ADw-213+AD4-  Homo sapiens

+ADw-400+AD4-  43
```

```
Met Ala Met Met Glu Val Gln Gly Gly Pro Ser Leu Gly Gln Thr Cys
1               5                  10                  15

Val Leu Ile Val Ile Phe Thr Val Leu Leu Gln Ser Leu Cys Val Ala
            20                  25                  30

Val Thr Tyr Val Tyr Phe Thr Asn Glu Leu Lys Gln Met Gln Asp Lys
        35                  40                  45

Tyr Ser Lys Ser Gly Ile Ala Cys Phe Leu Lys Glu Asp Asp Ser Tyr
    50                  55                  60

Trp Asp Pro Asn Asp Glu Glu Ser Met Asn Ser Pro Cys Trp Gln Val
65                  70                  75                  80

Lys Trp Gln Leu Arg Gln Leu Val Arg Lys Met Ile Leu Arg Thr Ser
                85                  90                  95

Glu Glu Thr Ile Ser Thr Val Gln Glu Lys Gln Gln Asn Ile Ser Pro
            100                 105                 110

Leu Val Arg Glu Arg Gly Pro Gln Arg Val Ala Ala His Ile Thr Gly
        115                 120                 125

Thr Arg Gly Arg Ser Asn Thr Leu Ser Ser Pro Asn Ser Lys Asn Glu
    130                 135                 140

Lys Ala Leu Gly Arg Lys Ile Asn Ser Trp Glu Ser Ser Arg Ser Gly
145                 150                 155                 160

His Ser Phe Leu Ser Asn Leu His Leu Arg Asn Gly Glu Leu Val Ile
                165                 170                 175

His Glu Lys Gly Phe Tyr Tyr Ile Tyr Ser Gln Thr Tyr Phe Arg Phe
            180                 185                 190

Gln Glu Glu Ile Lys Glu Asn Thr Lys Asn Asp Lys Gln Met Val Gln
        195                 200                 205

Tyr Ile Tyr Lys Tyr Thr Ser Tyr Pro Asp Pro Ile Leu Leu Met Lys
    210                 215                 220

Ser Ala Arg Asn Ser Cys Trp Ser Lys Asp Ala Glu Tyr Gly Leu Tyr
225                 230                 235                 240

Ser Ile Tyr Gln Gly Gly Ile Phe Glu Leu Lys Glu Asn Asp Arg Ile
                245                 250                 255
```

```
Phe Val Ser Val Thr Asn Glu His Leu Ile Asp Met Asp His Glu Ala
            260                 265                 270


Ser Phe Phe Gly Ala Phe Leu Val Gly
        275                 280


+ADw-210+AD4-  44
+ADw-211+AD4-  317
+ADw-212+AD4-  PRT
+ADw-213+AD4-  Homo sapiens

+ADw-400+AD4-  44

Met Arg Arg Ala Ser Arg Asp Tyr Thr Lys Tyr Leu Arg Gly Ser Glu
1               5                   10                  15


Glu Met Gly Gly Gly Pro Gly Ala Pro His Glu Gly Pro Leu His Ala
            20                  25                  30


Pro Pro Pro Pro Ala Pro His Gln Pro Pro Ala Ala Ser Arg Ser Met
        35                  40                  45


Phe Val Ala Leu Leu Gly Leu Gly Leu Gly Gln Val Val Cys Ser Val
    50                  55                  60


Ala Leu Phe Phe Tyr Phe Arg Ala Gln Met Asp Pro Asn Arg Ile Ser
65                  70                  75                  80


Glu Asp Gly Thr His Cys Ile Tyr Arg Ile Leu Arg Leu His Glu Asn
                85                  90                  95


Ala Asp Phe Gln Asp Thr Thr Leu Glu Ser Gln Asp Thr Lys Leu Ile
            100                 105                 110


Pro Asp Ser Cys Arg Arg Ile Lys Gln Ala Phe Gln Gly Ala Val Gln
        115                 120                 125


Lys Glu Leu Gln His Ile Val Gly Ser Gln His Ile Arg Ala Glu Lys
    130                 135                 140


Ala Met Val Asp Gly Ser Trp Leu Asp Leu Ala Lys Arg Ser Lys Leu
145                 150                 155                 160


Glu Ala Gln Pro Phe Ala His Leu Thr Ile Asn Ala Thr Asp Ile Pro
                165                 170                 175


Ser Gly Ser His Lys Val Ser Leu Ser Ser Trp Tyr His Asp Arg Gly
            180                 185                 190
```

```
Trp Ala Lys Ile Ser Asn Met Thr Phe Ser Asn Gly Lys Leu Ile Val
        195                 200                 205

Asn Gln Asp Gly Phe Tyr Tyr Leu Tyr Ala Asn Ile Cys Phe Arg His
    210                 215                 220

His Glu Thr Ser Gly Asp Leu Ala Thr Glu Tyr Leu Gln Leu Met Val
225                 230                 235                 240

Tyr Val Thr Lys Thr Ser Ile Lys Ile Pro Ser Ser His Thr Leu Met
                245                 250                 255

Lys Gly Gly Ser Thr Lys Tyr Trp Ser Gly Asn Ser Glu Phe His Phe
            260                 265                 270

Tyr Ser Ile Asn Val Gly Gly Phe Phe Lys Leu Arg Ser Gly Glu Glu
        275                 280                 285

Ile Ser Ile Glu Val Ser Asn Pro Ser Leu Leu Asp Pro Asp Gln Asp
    290                 295                 300

Ala Thr Tyr Phe Gly Ala Phe Lys Val Arg Asp Ile Asp
305                 310                 315


+ADw-210+AD4-  45
+ADw-211+AD4-  249
+ADw-212+AD4-  PRT
+ADw-213+AD4-  Homo sapiens

+ADw-400+AD4-  45

Met Ala Ala Arg Arg Ser Gln Arg Arg Arg Gly Arg Arg Gly Glu Pro
1               5                   10                  15

Gly Thr Ala Leu Leu Val Pro Leu Ala Leu Gly Leu Gly Leu Ala Leu
            20                  25                  30

Ala Cys Leu Gly Leu Leu Leu Ala Val Val Ser Leu Gly Ser Arg Ala
        35                  40                  45

Ser Leu Ser Ala Gln Glu Pro Ala Gln Glu Glu Leu Val Ala Glu Glu
    50                  55                  60

Asp Gln Asp Pro Ser Glu Leu Asn Pro Gln Thr Glu Glu Ser Gln Asp
65                  70                  75                  80

Pro Ala Pro Phe Leu Asn Arg Leu Val Arg Pro Arg Arg Ser Ala Pro
                85                  90                  95
```

```
Lys Gly Arg Lys Thr Arg Ala Arg Arg Ala Ile Ala Ala His Tyr Glu
            100                 105                 110

Val His Pro Arg Pro Gly Gln Asp Gly Ala Gln Ala Gly Val Asp Gly
        115                 120                 125

Thr Val Ser Gly Trp Glu Glu Ala Arg Ile Asn Ser Ser Ser Pro Leu
    130                 135                 140

Arg Tyr Asn Arg Gln Ile Gly Glu Phe Ile Val Thr Arg Ala Gly Leu
145                 150                 155                 160

Tyr Tyr Leu Tyr Cys Gln Val His Phe Asp Glu Gly Lys Ala Val Tyr
                165                 170                 175

Leu Lys Leu Asp Leu Leu Val Asp Gly Val Leu Ala Leu Arg Cys Leu
            180                 185                 190

Glu Glu Phe Ser Ala Thr Ala Ala Ser Ser Leu Gly Pro Gln Leu Arg
        195                 200                 205

Leu Cys Gln Val Ser Gly Leu Leu Ala Leu Arg Pro Gly Ser Ser Leu
    210                 215                 220

Arg Ile Arg Thr Leu Pro Trp Ala His Leu Lys Ala Ala Pro Phe Leu
225                 230                 235                 240

Thr Tyr Phe Gly Leu Phe Gln Val His
                245


+ADw-210+AD4-  46
+ADw-211+AD4-  250
+ADw-212+AD4-  PRT
+ADw-213+AD4-  Homo sapiens

+ADw-400+AD4-  46

Met Pro Ala Ser Ser Pro Phe Leu Leu Ala Pro Lys Gly Pro Pro Gly
1               5                   10                  15

Asn Met Gly Gly Pro Val Arg Glu Pro Ala Leu Ser Val Ala Leu Trp
            20                  25                  30

Leu Ser Trp Gly Ala Ala Leu Gly Ala Val Ala Cys Ala Met Ala Leu
        35                  40                  45

Leu Thr Gln Gln Thr Glu Leu Gln Ser Leu Arg Arg Glu Val Ser Arg
    50                  55                  60
```

```
Leu Gln Gly Thr Gly Gly Pro Ser Gln Asn Gly Glu Gly Tyr Pro Trp
65                  70                  75                  80

Gln Ser Leu Pro Glu Gln Ser Ser Asp Ala Leu Glu Ala Trp Glu Asn
                85                  90                  95

Gly Glu Arg Ser Arg Lys Arg Arg Ala Val Leu Thr Gln Lys Gln Lys
            100                 105                 110

Lys Gln His Ser Val Leu His Leu Val Pro Ile Asn Ala Thr Ser Lys
        115                 120                 125

Asp Asp Ser Asp Val Thr Glu Val Met Trp Gln Pro Ala Leu Arg Arg
    130                 135                 140

Gly Arg Gly Leu Gln Ala Gln Gly Tyr Gly Val Arg Ile Gln Asp Ala
145                 150                 155                 160

Gly Val Tyr Leu Leu Tyr Ser Gln Val Leu Phe Gln Asp Val Thr Phe
                165                 170                 175

Thr Met Gly Gln Val Val Ser Arg Glu Gly Gln Gly Arg Gln Glu Thr
            180                 185                 190

Leu Phe Arg Cys Ile Arg Ser Met Pro Ser His Pro Asp Arg Ala Tyr
        195                 200                 205

Asn Ser Cys Tyr Ser Ala Gly Val Phe His Leu His Gln Gly Asp Ile
    210                 215                 220

Leu Ser Val Ile Ile Pro Arg Ala Arg Ala Lys Leu Asn Leu Ser Pro
225                 230                 235                 240

His Gly Thr Phe Leu Gly Phe Val Lys Leu
                245                 250


+ADw-210+AD4-  47
+ADw-211+AD4-  285
+ADw-212+AD4-  PRT
+ADw-213+AD4-  Homo sapiens

+ADw-400+AD4-  47

Met Asp Asp Ser Thr Glu Arg Glu Gln Ser Arg Leu Thr Ser Cys Leu
1               5                   10                  15

Lys Lys Arg Glu Glu Met Lys Leu Lys Glu Cys Val Ser Ile Leu Pro
            20                  25                  30
```

```
Arg Lys Glu Ser Pro Ser Val Arg Ser Ser Lys Asp Gly Lys Leu Leu
        35                  40                  45

Ala Ala Thr Leu Leu Leu Ala Leu Leu Ser Cys Cys Leu Thr Val Val
    50                  55                  60

Ser Phe Tyr Gln Val Ala Ala Leu Gln Gly Asp Leu Ala Ser Leu Arg
65                  70                  75                  80

Ala Glu Leu Gln Gly His His Ala Glu Lys Leu Pro Ala Gly Ala Gly
                85                  90                  95

Ala Pro Lys Ala Gly Leu Glu Glu Ala Pro Ala Val Thr Ala Gly Leu
            100                 105                 110

Lys Ile Phe Glu Pro Pro Ala Pro Gly Glu Gly Asn Ser Ser Gln Asn
        115                 120                 125

Ser Arg Asn Lys Arg Ala Val Gln Gly Pro Glu Glu Thr Val Thr Gln
    130                 135                 140

Asp Cys Leu Gln Leu Ile Ala Asp Ser Glu Thr Pro Thr Ile Gln Lys
145                 150                 155                 160

Gly Ser Tyr Thr Phe Val Pro Trp Leu Leu Ser Phe Lys Arg Gly Ser
                165                 170                 175

Ala Leu Glu Glu Lys Glu Asn Lys Ile Leu Val Lys Glu Thr Gly Tyr
            180                 185                 190

Phe Phe Ile Tyr Gly Gln Val Leu Tyr Thr Asp Lys Thr Tyr Ala Met
        195                 200                 205

Gly His Leu Ile Gln Arg Lys Lys Val His Val Phe Gly Asp Glu Leu
    210                 215                 220

Ser Leu Val Thr Leu Phe Arg Cys Ile Gln Asn Met Pro Glu Thr Leu
225                 230                 235                 240

Pro Asn Asn Ser Cys Tyr Ser Ala Gly Ile Ala Lys Leu Glu Glu Gly
                245                 250                 255

Asp Glu Leu Gln Leu Ala Ile Pro Arg Glu Asn Ala Gln Ile Ser Leu
            260                 265                 270

Asp Gly Asp Val Thr Phe Phe Gly Ala Leu Lys Leu Leu
        275                 280                 285
```

+ADw-210+AD4- 48
+ADw-211+AD4- 240
+ADw-212+AD4- PRT
+ADw-213+AD4- Homo sapiens

+ADw-400+AD4- 48

```
Met Glu Glu Ser Val Val Arg Pro Ser Val Phe Val Val Asp Gly Gln
1               5                  10                  15

Thr Asp Ile Pro Phe Thr Arg Leu Gly Arg Ser His Arg Arg Gln Ser
            20                  25                  30

Cys Ser Val Ala Arg Val Gly Leu Gly Leu Leu Leu Leu Leu Met Gly
        35                  40                  45

Ala Gly Leu Ala Val Gln Gly Trp Phe Leu Leu Gln Leu His Trp Arg
    50                  55                  60

Leu Gly Glu Met Val Thr Arg Leu Pro Asp Gly Pro Ala Gly Ser Trp
65                  70                  75                  80

Glu Gln Leu Ile Gln Glu Arg Arg Ser His Glu Val Asn Pro Ala Ala
                85                  90                  95

His Leu Thr Gly Ala Asn Ser Ser Leu Thr Gly Ser Gly Gly Pro Leu
            100                 105                 110

Leu Trp Glu Thr Gln Leu Gly Leu Ala Phe Leu Arg Gly Leu Ser Tyr
        115                 120                 125

His Asp Gly Ala Leu Val Val Thr Lys Ala Gly Tyr Tyr Tyr Ile Tyr
    130                 135                 140

Ser Lys Val Gln Leu Gly Gly Val Gly Cys Pro Leu Gly Leu Ala Ser
145                 150                 155                 160

Thr Ile Thr His Gly Leu Tyr Lys Arg Thr Pro Arg Tyr Pro Glu Glu
                165                 170                 175

Leu Glu Leu Leu Val Ser Gln Gln Ser Pro Cys Gly Arg Ala Thr Ser
            180                 185                 190

Ser Ser Arg Val Trp Trp Asp Ser Ser Phe Leu Gly Gly Val Val His
        195                 200                 205

Leu Glu Ala Gly Glu Lys Val Val Val Arg Val Leu Asp Glu Arg Leu
    210                 215                 220
```

```
Val Arg Leu Arg Asp Gly Thr Arg Ser Tyr Phe Gly Ala Phe Met Val
225                 230                 235                 240


+ADw-210+AD4-  49
+ADw-211+AD4-  251
+ADw-212+AD4-  PRT
+ADw-213+AD4-  Homo sapiens

+ADw-400+AD4-  49

Met Ala Glu Asp Leu Gly Leu Ser Phe Gly Glu Thr Ala Ser Val Glu
1               5                   10                  15


Met Leu Pro Glu His Gly Ser Cys Arg Pro Lys Ala Arg Ser Ser Ser
            20                  25                  30


Ala Arg Trp Ala Leu Thr Cys Cys Leu Val Leu Leu Pro Phe Leu Ala
        35                  40                  45


Gly Leu Thr Thr Tyr Leu Leu Val Ser Gln Leu Arg Ala Gln Gly Glu
    50                  55                  60


Ala Cys Val Gln Phe Gln Ala Leu Lys Gly Gln Glu Phe Ala Pro Ser
65                  70                  75                  80


His Gln Gln Val Tyr Ala Pro Leu Arg Ala Asp Gly Asp Lys Pro Arg
                85                  90                  95


Ala His Leu Thr Val Val Arg Gln Thr Pro Thr Gln His Phe Lys Asn
            100                 105                 110


Gln Phe Pro Ala Leu His Trp Glu His Glu Leu Gly Leu Ala Phe Thr
        115                 120                 125


Lys Asn Arg Met Asn Tyr Thr Asn Lys Phe Leu Leu Ile Pro Glu Ser
    130                 135                 140


Gly Asp Tyr Phe Ile Tyr Ser Gln Val Thr Phe Arg Gly Met Thr Ser
145                 150                 155                 160


Glu Cys Ser Glu Ile Arg Gln Ala Gly Arg Pro Asn Lys Pro Asp Ser
                165                 170                 175


Ile Thr Val Val Ile Thr Lys Val Thr Asp Ser Tyr Pro Glu Pro Thr
            180                 185                 190


Gln Leu Leu Met Gly Thr Lys Ser Val Cys Glu Val Gly Ser Asn Trp
        195                 200                 205
```

```
Phe Gln Pro Ile Tyr Leu Gly Ala Met Phe Ser Leu Gln Glu Gly Asp
    210                 215                 220

Lys Leu Met Val Asn Val Ser Asp Ile Ser Leu Val Asp Tyr Thr Lys
225                 230                 235                 240

Glu Asp Lys Thr Phe Phe Gly Ala Phe Leu Leu
                245                 250

+ADw-210+AD4-  50
+ADw-211+AD4-  199
+ADw-212+AD4-  PRT
+ADw-213+AD4-  Homo sapiens

+ADw-400+AD4-  50

Met Thr Leu His Pro Ser Pro Ile Thr Cys Glu Phe Leu Phe Ser Thr
1               5                   10                  15

Ala Leu Ile Ser Pro Lys Met Cys Leu Ser His Leu Glu Asn Met Pro
            20                  25                  30

Leu Ser His Ser Arg Thr Gln Gly Ala Gln Arg Ser Ser Trp Lys Leu
        35                  40                  45

Trp Leu Phe Cys Ser Ile Val Met Leu Leu Phe Leu Cys Ser Phe Ser
    50                  55                  60

Trp Leu Ile Phe Ile Phe Leu Gln Leu Glu Thr Ala Lys Glu Pro Cys
65                  70                  75                  80

Met Ala Lys Phe Gly Pro Leu Pro Ser Lys Trp Gln Met Ala Ser Ser
                85                  90                  95

Glu Pro Pro Cys Val Asn Lys Val Ser Asp Trp Lys Leu Glu Ile Leu
            100                 105                 110

Gln Asn Gly Leu Tyr Leu Ile Tyr Gly Gln Val Ala Pro Asn Ala Asn
        115                 120                 125

Tyr Asn Asp Val Ala Pro Phe Glu Val Arg Leu Tyr Lys Asn Lys Asp
    130                 135                 140

Met Ile Gln Thr Leu Thr Asn Lys Ser Lys Ile Gln Asn Val Gly Gly
145                 150                 155                 160

Thr Tyr Glu Leu His Val Gly Asp Thr Ile Asp Leu Ile Phe Asn Ser
                165                 170                 175
```

```
Glu His Gln Val Leu Lys Asn Asn Thr Tyr Trp Gly Ile Ile Leu Leu
            180                 185                 190


Ala Asn Pro Gln Phe Ile Ser
        195


+ADw-210+AD4-  51
+ADw-211+AD4-  391
+ADw-212+AD4-  PRT
+ADw-213+AD4-  Homo sapiens

+ADw-400+AD4-  51

Met Gly Tyr Pro Glu Val Glu Arg Arg Glu Leu Leu Pro Ala Ala Ala
1               5                   10                  15


Pro Arg Glu Arg Gly Ser Gln Gly Cys Gly Cys Gly Gly Ala Pro Ala
            20                  25                  30


Arg Ala Gly Glu Gly Asn Ser Cys Leu Leu Phe Leu Gly Phe Phe Gly
        35                  40                  45


Leu Ser Leu Ala Leu His Leu Leu Thr Leu Cys Cys Tyr Leu Glu Leu
    50                  55                  60


Arg Ser Glu Leu Arg Arg Glu Arg Gly Ala Glu Ser Arg Leu Gly Gly
65                  70                  75                  80


Ser Gly Thr Pro Gly Thr Ser Gly Thr Leu Ser Ser Leu Gly Gly Leu
                85                  90                  95


Asp Pro Asp Ser Pro Ile Thr Ser His Leu Gly Gln Pro Ser Pro Lys
            100                 105                 110


Gln Gln Pro Leu Glu Pro Gly Glu Ala Ala Leu His Ser Asp Ser Gln
        115                 120                 125


Asp Gly His Gln Met Ala Leu Leu Asn Phe Phe Phe Pro Asp Glu Lys
    130                 135                 140


Pro Tyr Ser Glu Glu Glu Ser Arg Arg Val Arg Arg Asn Lys Arg Ser
145                 150                 155                 160


Lys Ser Asn Glu Gly Ala Asp Gly Pro Val Lys Asn Lys Lys Lys Gly
                165                 170                 175


Lys Lys Ala Gly Pro Pro Gly Pro Asn Gly Pro Pro Gly Pro Pro Gly
            180                 185                 190
```

```
Pro Pro Gly Pro Gln Gly Pro Pro Gly Ile Pro Gly Ile Pro Gly Ile
        195                 200                 205

Pro Gly Thr Thr Val Met Gly Pro Pro Gly Pro Pro Gly Pro Pro Gly
    210                 215                 220

Pro Gln Gly Pro Pro Gly Leu Gln Gly Pro Ser Gly Ala Ala Asp Lys
225                 230                 235                 240

Ala Gly Thr Arg Glu Asn Gln Pro Ala Val Val His Leu Gln Gly Gln
                245                 250                 255

Gly Ser Ala Ile Gln Val Lys Asn Asp Leu Ser Gly Gly Val Leu Asn
            260                 265                 270

Asp Trp Ser Arg Ile Thr Met Asn Pro Lys Val Phe Lys Leu His Pro
        275                 280                 285

Arg Ser Gly Glu Leu Glu Val Leu Val Asp Gly Thr Tyr Phe Ile Tyr
    290                 295                 300

Ser Gln Val Glu Val Tyr Tyr Ile Asn Phe Thr Asp Phe Ala Ser Tyr
305                 310                 315                 320

Glu Val Val Val Asp Glu Lys Pro Phe Leu Gln Cys Thr Arg Ser Ile
                325                 330                 335

Glu Thr Gly Lys Thr Asn Tyr Asn Thr Cys Tyr Thr Ala Gly Val Cys
            340                 345                 350

Leu Leu Lys Ala Arg Gln Lys Ile Ala Val Lys Met Val His Ala Asp
        355                 360                 365

Ile Ser Ile Asn Met Ser Lys His Thr Thr Phe Phe Gly Ala Ile Arg
    370                 375                 380

Leu Gly Glu Ala Pro Ala Ser
385                 390


+ADw-210+AD4-  52
+ADw-211+AD4-  205
+ADw-212+AD4-  PRT
+ADw-213+AD4-  Homo sapiens

+ADw-400+AD4-  52

Ala Cys Pro Trp Ala Val Ser Gly Ala Arg Ala Ser Pro Gly Ser Ala
1               5                   10                  15
```

```
Ala Ser Pro Arg Leu Arg Glu Gly Pro Glu Leu Ser Pro Asp Asp Pro
            20                  25                  30

Ala Gly Leu Leu Asp Leu Arg Gln Gly Met Phe Ala Gln Leu Val Ala
        35                  40                  45

Gln Asn Val Leu Leu Ile Asp Gly Pro Leu Ser Trp Tyr Ser Asp Pro
    50                  55                  60

Gly Leu Ala Gly Val Ser Leu Thr Gly Gly Leu Ser Tyr Lys Glu Asp
65                  70                  75                  80

Thr Lys Glu Leu Val Val Ala Lys Ala Gly Val Tyr Tyr Val Phe Phe
                85                  90                  95

Gln Leu Glu Leu Arg Arg Val Val Ala Gly Glu Gly Ser Gly Ser Val
            100                 105                 110

Ser Leu Ala Leu His Leu Gln Pro Leu Arg Ser Ala Ala Gly Ala Ala
        115                 120                 125

Ala Leu Ala Leu Thr Val Asp Leu Pro Pro Ala Ser Ser Glu Ala Arg
    130                 135                 140

Asn Ser Ala Phe Gly Phe Gln Gly Arg Leu Leu His Leu Ser Ala Gly
145                 150                 155                 160

Gln Arg Leu Gly Val His Leu His Thr Glu Ala Arg Ala Arg His Ala
                165                 170                 175

Trp Gln Leu Thr Gln Gly Ala Thr Val Leu Gly Leu Phe Arg Val Thr
            180                 185                 190

Pro Glu Ile Pro Ala Gly Leu Pro Ser Pro Arg Ser Glu
        195                 200                 205


+ADw-210+AD4-  53
+ADw-211+AD4-  133
+ADw-212+AD4-  PRT
+ADw-213+AD4-  Homo sapiens

+ADw-400+AD4-  53

Gln Val Ser His Arg Tyr Pro Arg Ile Gln Ser Ile Lys Val Gln Phe
1               5                   10                  15

Thr Glu Tyr Lys Lys Glu Lys Gly Phe Ile Leu Thr Ser Gln Lys Glu
            20                  25                  30
```

```
Asp Glu Ile Met Lys Val Gln Asn Asn Ser Val Ile Ile Asn Cys Asp
        35                  40                  45

Gly Phe Tyr Leu Ile Ser Leu Lys Gly Tyr Phe Ser Gln Glu Val Asn
    50                  55                  60

Ile Ser Leu His Tyr Gln Lys Asp Glu Glu Pro Leu Phe Gln Leu Lys
65                  70                  75                  80

Lys Val Arg Ser Val Asn Ser Leu Met Val Ala Ser Leu Thr Tyr Lys
                85                  90                  95

Asp Lys Val Tyr Leu Asn Val Thr Thr Asp Asn Thr Ser Leu Asp Asp
            100                 105                 110

Phe His Val Asn Gly Gly Glu Leu Ile Leu Ile His Gln Asn Pro Gly
        115                 120                 125

Glu Phe Cys Val Leu
    130


+ADw-210+AD4-  54
+ADw-211+AD4-  132
+ADw-212+AD4-  PRT
+ADw-213+AD4-  Homo sapiens

+ADw-400+AD4-  54

Val Ser His Arg Tyr Pro Arg Ile Gln Ser Ile Lys Val Gln Phe Thr
1               5                   10                  15

Glu Tyr Lys Lys Glu Lys Gly Phe Ile Leu Thr Ser Gln Lys Glu Asp
            20                  25                  30

Glu Ile Met Lys Val Gln Asn Asn Ser Val Ile Ile Asn Cys Asp Gly
        35                  40                  45

Phe Tyr Leu Ile Ser Leu Lys Gly Tyr Phe Ser Gln Glu Val Asn Ile
    50                  55                  60

Ser Leu His Tyr Gln Lys Asp Glu Glu Pro Leu Phe Gln Leu Lys Lys
65                  70                  75                  80

Val Arg Ser Val Asn Ser Leu Met Val Ala Ser Leu Thr Tyr Lys Asp
                85                  90                  95

Lys Val Tyr Leu Asn Val Thr Thr Asp Asn Thr Ser Leu Asp Asp Phe
            100                 105                 110
```

His Val Asn Gly Gly Glu Leu Ile Leu Ile His Gln Asn Pro Gly Glu
        115   120   125

Phe Cys Val Leu
    130

+ADw-210+AD4- 55
+ADw-211+AD4- 10
+ADw-212+AD4- PRT
+ADw-213+AD4- Secuencia artificial

+ADw-220+AD4-
+ADw-223+AD4- Enlazador pept+AO0-dico (SG4)2

+ADw-400+AD4- 55

Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly
1   5   10

+ADw-210+AD4- 56
+ADw-211+AD4- 14
+ADw-212+AD4- PRT
+ADw-213+AD4- Secuencia artificial

+ADw-220+AD4-
+ADw-223+AD4- Enlazador pept+AO0-dico

+ADw-400+AD4- 56

Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly
1   5   10

+ADw-210+AD4- 57
+ADw-211+AD4- 10
+ADw-212+AD4- PRT
+ADw-213+AD4- Secuencia artificial

+ADw-220+AD4-
+ADw-223+AD4- Enlazador pept+AO0-dico

+ADw-400+AD4- 57

Gly Ser Pro Gly Ser Ser Ser Ser Gly Ser
1   5   10

+ADw-210+AD4- 58
+ADw-211+AD4- 20
+ADw-212+AD4- PRT
+ADw-213+AD4- Secuencia artificial

+ADw-220+AD4-
+ADw-223+AD4- Enlazador pept+AO0-dico

+ADw-400+AD4- 58

Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly

1 5 10 15

Gly Gly Gly Ser
20

+ADw-210+AD4- 59
+ADw-211+AD4- 8
+ADw-212+AD4- PRT
+ADw-213+AD4- Secuencia artificial

+ADw-220+AD4-
+ADw-223+AD4- Enlazador pept+AO0-dico

+ADw-400+AD4- 59

Gly Ser Gly Ser Gly Asn Gly Ser
1 5

+ADw-210+AD4- 60
+ADw-211+AD4- 8
+ADw-212+AD4- PRT
+ADw-213+AD4- Secuencia artificial

+ADw-220+AD4-
+ADw-223+AD4- Enlazador pept+AO0-dico

+ADw-400+AD4- 60

Gly Gly Ser Gly Ser Gly Ser Gly
1 5

+ADw-210+AD4- 61
+ADw-211+AD4- 6
+ADw-212+AD4- PRT
+ADw-213+AD4- Secuencia artificial

+ADw-220+AD4-
+ADw-223+AD4- Enlazador pept+AO0-dico

+ADw-400+AD4- 61

Gly Gly Ser Gly Ser Gly
1 5

+ADw-210+AD4- 62
+ADw-211+AD4- 4
+ADw-212+AD4- PRT
+ADw-213+AD4- Secuencia artificial

+ADw-220+AD4-
+ADw-223+AD4- Enlazador pept+AO0-dico

+ADw-400+AD4- 62

Gly Gly Ser Gly
1

+ADw-210+AD4- 63
+ADw-211+AD4- 8
+ADw-212+AD4- PRT
+ADw-213+AD4- Secuencia artificial

+ADw-220+AD4-
+ADw-223+AD4- Enlazador pept+AO0-dico

+ADw-400+AD4- 63

Gly Gly Ser Gly Asn Gly Ser Gly
1 5

+ADw-210+AD4- 64
+ADw-211+AD4- 8
+ADw-212+AD4- PRT
+ADw-213+AD4- Secuencia artificial

+ADw-220+AD4-
+ADw-223+AD4- Enlazador pept+AO0-dico

+ADw-400+AD4- 64

Gly Gly Asn Gly Ser Gly Ser Gly
1 5

+ADw-210+AD4- 65
+ADw-211+AD4- 6
+ADw-212+AD4- PRT
+ADw-213+AD4- Secuencia artificial

+ADw-220+AD4-
+ADw-223+AD4- Enlazador pept+AO0-dico

+ADw-400+AD4- 65

Gly Gly Asn Gly Ser Gly
1 5

+ADw-210+AD4- 66
+ADw-211+AD4- 2154
+ADw-212+AD4- ADN
+ADw-213+AD4- Secuencia artificial

+ADw-220+AD4-
+ADw-223+AD4- hu 4-1BBL dim+AOk-rico(71-254)-CH1 Fc de cadena de pomo

+ADw-400+AD4- 66
agagagggcc ctgagctgag ccccgatgat cctgctggac tgctggacct gcggcagggc 60

atgtttgctc agctggtggc ccagaacgtg ctgctgatcg atggcccccc gtcctggtac 120

agcgatcctg gactggctgg cgtgtcactg acaggcggcc tgagctacaa agaggacacc 180

aaagaactgg tggtggccaa ggccggcgtg tactacgtgt tctttcagct ggaactgcgg 240

agagtggtgg ccggcgaagg atctggctct gtgtctctgg ccctgcatct gcagcctctg 300

agaagcgctg ctggcgctgc agctctggca ctgacagtgg atctgcctcc tgccagctcc 360

gaggcccgga atagcgcatt tgggtttcaa ggcaggctgc tgcacctgtc tgccggccag 420

aggctgggag tgcatctgca cacagaggcc agggctagac acgcctggca gctgacacag 480

ggcgctacag tgctgggcct gttcagagtg acccccgaga ttccagccgg cctgccttct 540

ccaagaagcg aaggcggagg cggatctggc ggcggaggat ctagagaggg acccgaactg 600

tcccctgacg atccagccgg gctgctggat ctgagacagg gaatgttcgc ccagctggtg 660

gctcagaatg tgctgctgat tgacggacct ctgagctggt actccgaccc agggctggca 720

ggggtgtccc tgactggggg actgtcctac aaagaagata caaaagaact ggtggtggct 780

aaagctgggg tgtactatgt gtttttttcag ctggaactga ggcgggtggt ggctggggag 840

ggctcaggat ctgtgtccct ggctctgcat ctgcagccac tgcgctctgc tgctggcgca 900

gctgcactgg ctctgactgt ggacctgcca ccagcctcta gcgaggccag aaacagcgcc 960

ttcgggttcc aaggacgcct gctgcatctg agcgccggac agcgcctggg agtgcatctg 1020

catactgaag ccagagcccg gcatgcttgg cagctgactc agggggcaac tgtgctggga 1080

ctgtttcgcg tgacacctga gatccctgcc ggactgccaa gccctagatc agaaggggggc 1140

ggaggaagcg gagggggagg aagtgctagc accaagggcc ctagcgtgtt ccctctggcc 1200

cctagcagca agagcacaag tggaggaaca gccgccctgg gctgcctggt caaggactac 1260

ttccccgagc ccgtgaccgt gtcctggaat tctggcgccc tgacaagcgg cgtgcacaca 1320

tttccagccg tgctgcagag cagcggcctg tactctctga gcagcgtcgt gaccgtgccc 1380

tctagctctc tgggcaccca gacctacatc tgcaacgtga accacaagcc cagcaacacc 1440

aaagtggaca agaaggtgga acccaagagc tgcgacaaga cccacacctg tccccccttgc 1500

cctgcccctg aagctgctgg tggcccttcc gtgttcctgt tccccccaaa gcccaaggac 1560

accctgatga tcagccggac ccccgaagtg acctgcgtgg tggtcgatgt gtcccacgag 1620

gaccctgaag tgaagttcaa ttggtacgtg gacggcgtgg aagtgcacaa tgccaagacc 1680

aagccgcggg aggagcagta caacagcacg taccgtgtgg tcagcgtcct caccgtcctg 1740

caccaggact ggctgaatgg caaggagtac aagtgcaagg tctccaacaa agccctcggc 1800

gcccccatcg agaaaaccat ctccaaagcc aaagggcagc cccgagaacc acaggtgtac 1860

accctgcccc catgccggga tgagctgacc aagaaccagg tcagcctgtg gtgcctggtc 1920

aaaggcttct atcccagcga catcgccgtg gagtgggaga gcaatgggca gccggagaac 1980

aactacaaga ccacgcctcc cgtgctggac tccgacggct ccttcttcct ctacagcaag 2040

ctcaccgtgg acaagagcag gtggcagcag gggaacgtct tctcatgctc cgtgatgcat 2100

gaggctctgc acaaccacta cacgcagaag agcctctccc tgtctccggg taaa 2154

+ADw-210+AD4- 67
+ADw-211+AD4- 903

+ADw-212+AD4- ADN
+ADw-213+AD4- Secuencia artificial

+ADw-220+AD4-
+ADw-223+AD4- Hu 4-1BBL monom+AOk-rico (71-254)-CL

+ADw-400+AD4- 67

agagagggcc ctgagctgag ccccgatgat cctgctggac tgctggacct gcggcagggc 60

atgtttgctc agctggtggc ccagaacgtg ctgctgatcg atggcccccc gtcctggtac 120

agcgatcctg gactggctgg cgtgtcactg acaggcggcc tgagctacaa agaggacacc 180

aaagaactgg tggtggccaa ggccggcgtg tactacgtgt tctttcagct ggaactgcgg 240

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agaagcgctg ctggcgctgc agctctggca ctgacagtgg atctgcctcc tgccagctcc 360

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aggctgggag tgcatctgca cacagaggcc agggctagac acgcctggca gctgacacag 480

ggcgctacag tgctgggcct gttcagagtg acccccgaga ttccagccgg cctgccttct 540

ccaagaagcg aaggcggagg cggatctggc ggcggaggat ctcgtacggt ggctgcacca 600

tctgtcttca tcttcccgcc atctgatgag cagttgaaat ctggaactgc ctctgttgtg 660

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tgcgaagtca cccatcaggg cctgagctcg cccgtcacaa agagcttcaa caggggagag 900

tgt 903

+ADw-210+AD4- 68
+ADw-211+AD4- 1338
+ADw-212+AD4- ADN
+ADw-213+AD4- Secuencia artificial

+ADw-220+AD4-
+ADw-223+AD4- FAP (28H1) cadena pesada de Fc agujero

+ADw-400+AD4- 68

gaagtgcagc tgctggaatc cggcggaggc ctggtgcagc ctggcggatc tctgagactg 60

tcctgcgccg cctccggctt caccttctcc tcccacgcca tgtcctgggt ccgacaggct 120

cctggcaaag gcctggaatg ggtgtccgcc atctgggcct ccggcgagca gtactacgcc 180

gactctgtga agggccggtt caccatctcc cgggacaact ccaagaacac cctgtacctg 240

cagatgaact ccctgcgggc cgaggacacc gccgtgtact actgtgccaa gggctggctg 300

ggcaacttcg actactgggg acagggcacc ctggtcaccg tgtccagcgc tagcaccaag 360

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aaaactcaca catgcccacc gtgcccagca cctgaagctg caggggggacc gtcagtcttc 720

ctcttccccc caaaacccaa ggacaccctc atgatctccc ggacccctga ggtcacatgc 780

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gtggtcagcg tcctcaccgt cctgcaccag gactggctga atggcaagga gtacaagtgc 960

aaggtctcca acaaagccct cggcgccccc atcgagaaaa ccatctccaa agccaaaggg 1020

cagccccgag aaccacaggt gtgcaccctg cccccatccc gggatgagct gaccaagaac 1080

caggtcagcc tctcgtgcgc agtcaaaggc ttctatccca gcgacatcgc cgtggagtgg 1140

gagagcaatg ggcagccgga gaacaactac aagaccacgc ctcccgtgct ggactccgac 1200

ggctccttct tcctcgtgag caagctcacc gtggacaaga gcaggtggca gcaggggaac 1260

gtcttctcat gctccgtgat gcatgaggct ctgcacaacc actacacgca gaagagcctc 1320

tccctgtctc cgggtaaa 1338

+ADw-210+AD4- 69
+ADw-211+AD4- 645
+ADw-212+AD4- ADN
+ADw-213+AD4- Secuencia artificial

+ADw-220+AD4-
+ADw-223+AD4- cadena ligera de FAP(28H1)

+ADw-400+AD4- 69
gagatcgtgc tgacccagtc ccccggcacc ctgtctctga gccctggcga gagagccacc 60

ctgtcctgca gagcctccca gtccgtgtcc cggtcctacc tcgcctggta tcagcagaag 120

cccggccagg cccctcggct gctgatcatc ggcgcctcta ccagagccac cggcatccct 180

gaccggttct ccggctctgg ctccggcacc gacttcaccc tgaccatctc ccggctggaa 240

cccgaggact tcgccgtgta ctactgccag cagggccagg tcatccctcc caccttggc 300

cagggcacca aggtggaaat caagcgtacg gtggctgcac catctgtctt catcttcccg 360

ccatctgatg agcagttgaa atctggaact gcctctgttg tgtgcctgct gaataacttc 420

tatcccagag aggccaaagt acagtggaag gtggataacg ccctccaatc gggtaactcc 480

caggagagtg tcacagagca ggacagcaag gacagcacct acagcctcag cagcaccctg 540

acgctgagca aagcagacta cgagaaacac aaagtctacg cctgcgaagt cacccatcag 600

ggcctgagct cgcccgtcac aaagagcttc aacaggggag agtgt 645

+ADw-210+AD4- 70
+ADw-211+AD4- 309
+ADw-212+AD4- PRT
+ADw-213+AD4- Mus musculus

+ADw-400+AD4- 70

```
Met Asp Gln His Thr Leu Asp Val Glu Asp Thr Ala Asp Ala Arg His
1               5                  10                  15

Pro Ala Gly Thr Ser Cys Pro Ser Asp Ala Ala Leu Leu Arg Asp Thr
            20                  25                  30

Gly Leu Leu Ala Asp Ala Ala Leu Leu Ser Asp Thr Val Arg Pro Thr
        35                  40                  45

Asn Ala Ala Leu Pro Thr Asp Ala Ala Tyr Pro Ala Val Asn Val Arg
    50                  55                  60

Asp Arg Glu Ala Ala Trp Pro Pro Ala Leu Asn Phe Cys Ser Arg His
65                  70                  75                  80

Pro Lys Leu Tyr Gly Leu Val Ala Leu Val Leu Leu Leu Leu Ile Ala
                85                  90                  95

Ala Cys Val Pro Ile Phe Thr Arg Thr Glu Pro Arg Pro Ala Leu Thr
            100                 105                 110

Ile Thr Thr Ser Pro Asn Leu Gly Thr Arg Glu Asn Asn Ala Asp Gln
        115                 120                 125

Val Thr Pro Val Ser His Ile Gly Cys Pro Asn Thr Thr Gln Gln Gly
    130                 135                 140

Ser Pro Val Phe Ala Lys Leu Leu Ala Lys Asn Gln Ala Ser Leu Cys
145                 150                 155                 160

Asn Thr Thr Leu Asn Trp His Ser Gln Asp Gly Ala Gly Ser Ser Tyr
                165                 170                 175

Leu Ser Gln Gly Leu Arg Tyr Glu Glu Asp Lys Lys Glu Leu Val Val
            180                 185                 190

Asp Ser Pro Gly Leu Tyr Tyr Val Phe Leu Glu Leu Lys Leu Ser Pro
        195                 200                 205

Thr Phe Thr Asn Thr Gly His Lys Val Gln Gly Trp Val Ser Leu Val
    210                 215                 220
```

Leu Gln Ala Lys Pro Gln Val Asp Asp Phe Asp Asn Leu Ala Leu Thr
225 230 235 240

Val Glu Leu Phe Pro Cys Ser Met Glu Asn Lys Leu Val Asp Arg Ser
245 250 255

Trp Ser Gln Leu Leu Leu Leu Lys Ala Gly His Arg Leu Ser Val Gly
260 265 270

Leu Arg Ala Tyr Leu His Gly Ala Gln Asp Ala Tyr Arg Asp Trp Glu
275 280 285

Leu Ser Tyr Pro Asn Thr Thr Ser Phe Gly Leu Phe Leu Val Lys Pro
290 295 300

Asp Asn Pro Trp Glu
305

+ADw-210+AD4- 71
+ADw-211+AD4- 2298
+ADw-212+AD4- ADN
+ADw-213+AD4- Secuencia artificial

+ADw-220+AD4-
+ADw-223+AD4- 4-1BBL dim+AOk-rico (71-254) -CH1-cadena Fc pomo

+ADw-400+AD4- 71
agaaccgagc ccagacccgc cctgaccatc accaccagcc ctaacctggg caccagagag 60

aacaacgccg accaagtgac ccccgtgtcc cacatcggca gccccaatac cacacagcag 120

ggcagccctg tgttcgccaa gctgctggcc aagaaccagg ccagcctgag caacaccacc 180

ctgaactggc acagccagga tggcgccgga agcagctatc tgagccaggg cctgagatac 240

gaagaggaca agaaagaact ggtggtggac agccctggcc tgtactacgt gttcctggaa 300

ctgaagctga gccccacctt caccaacacc ggccacaagg tgcagggctg ggtgtcactg 360

gtgctgcagg ccaaacccca ggtggacgac ttcgacaacc tggccctgac cgtggaactg 420

ttccccagca gcatggaaaa caagctggtg gatcggagct ggtcccagct tctgctgctg 480

aaggccggac acagactgag cgtgggcctg agggcttatc tgcacggcgc ccaggacgcc 540

tacagagact gggagctgag ctaccccaac acaaccagct tcggcctgtt cctcgtgaag 600

cccgacaacc cttgggaagg cggcggagga tctggcggag gcggatctag aacagagcct 660

cggcctgccc tgacaattac cacatccccc aatctgggca cccgggaaaa caatgcagat 720

caagtgacac ctgtgtctca tattggctcc ccaaacacta cccagcaggg ctcccccgtg 780

tttgctaaac tgctggctaa aaatcaggcc tccctgtcta acacaacact gaactggcac 840

tcccaggacg gcgctggcag ctcttacctg agtcagggac tgcgctatga ggaagataag 900

aaagaactgg tggtggattc ccccggactg tactatgtgt ttctggaact gaaactgtcc 960

cctaccttta caaataccgg gcacaaagtg cagggatggg tgtccctggt gctgcaggct 1020

aagcctcagg tggacgattt tgataatctg gctctgacag tggaactgtt tcctagcagc 1080

atggaaaaca agctggtgga cagaagctgg tcccagctcc tgctgctgaa ggccggacac 1140

agactgagcg tgggcctgag agcctatctg cacggcgccc aggacgccta cagagactgg 1200

gagctgagct accccaacac aaccagcttc ggcctgttcc tcgtgaagcc cgacaaccct 1260

tgggaaggcg gcggaggatc tggcggaggc ggatccagag ctgatgctgc ccctaccgtg 1320

tccatcttcc cacccagcag cgagcagctg acatctgggg gagctagcgt cgtgtgcttc 1380

ctgaacaact tctaccccaa ggacatcaac gtgaagtgga agatcgacgg cagcgagcgg 1440

cagaacggcg tgctgaatag ctggaccgac caggacagca aggactccac ctacagcatg 1500

agcagcaccc tgaccctgac caaggacgag tacgagcggc acaacagcta cacatgcgag 1560

gccacccaca agaccagcac cagccccatc gtgaagtcct tcaaccggaa cgagtgcgtg 1620

cccagagact gcggctgcaa gccttgcatc tgcaccgtgc ctgaggtgtc cagcgtgttc 1680

atcttcccac ccaagcccaa ggacgtgctg accatcaccc tgacacccaa agtgacctgc 1740

gtggtggtgg ccatcagcaa ggatgacccc gaggtgcagt tcagttggtt cgtggacgac 1800

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agagtgaaca gcgccgcctt tggcgccccc atcgagaaaa ccatctccaa gaccaagggc 1980

agacccaagg ccccccaggt gtacacaatc cccccaccca aagaacagat ggccaaggac 2040

aaggtgtccc tgacctgcat gatcaccaat ttcttcccag aggatatcac cgtggaatgg 2100

cagtggaacg gccagcccgc cgagaactac gacaacaccc agcctatcat ggacaccgac 2160

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accttcacct gtagcgtgct gcacgagggc ctgcacaacc accacaccga gaagtccctg 2280

tcccacagcc ctggcaag 2298

+ADw-210+AD4- 72
+ADw-211+AD4- 954
+ADw-212+AD4- ADN
+ADw-213+AD4- Secuencia artificial

+ADw-220+AD4-
+ADw-223+AD4- fusi+APM-n de mu 4-1BBL monom+AOk-rico (71-254) -CL

+ADw-400+AD4- 72
agaaccgagc ccagacccgc cctgaccatc accaccagcc ctaacctggg caccagagag 60

aacaacgccg accaagtgac ccccgtgtcc cacatcggca gccccaatac cacacagcag 120

ggcagccctg tgttcgccaa gctgctggcc aagaaccagg ccagcctgag caacaccacc 180

ctgaactggc acagccagga tggcgccgga agcagctatc tgagccaggg cctgagatac 240

gaagaggaca agaaagaact ggtggtggac agccctggcc tgtactacgt gttcctggaa 300

ctgaagctga gccccacctt caccaacacc ggccacaagg tgcagggctg ggtgtcactg 360

gtgctgcagg ccaaacccca ggtggacgac ttcgacaacc tggccctgac cgtggaactg 420

ttccccagca gcatggaaaa caagctggtg gatcggagct ggtcccagct tctgctgctg 480

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cccgacaacc cttgggaagg cggcggaggc tccggaggag gcggaagcgc taagaccacc 660

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agcagctccg tgaccgtgcc tagcagcacc tggcccagcc agacagtgac ctgcaacgtg 900

gcccaccctg ccagcagcac caaggtggac aagaaaatcg tgccccggga ctgc 954

+ADw-210+AD4- 73
+ADw-211+AD4- 1320
+ADw-212+AD4- ADN
+ADw-213+AD4- Secuencia artificial

+ADw-220+AD4-
+ADw-223+AD4- FAP cadena pesada de Fc KK

+ADw-400+AD4- 73
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tcctgcgccg cctccggctt caccttctcc tcccacgcca tgtcctgggt ccgacaggct 120

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agcctgagca gcggcgtgca cacctttcca gccgtgctgc agagcgacct gtacaccctg 540

agcagctccg tgaccgtgcc tagcagcacc tggcccagcc agacagtgac ctgcaacgtg 600

gcccaccctg ccagcagcac caaggtggac aagaaaatcg tgccccggga ctgcggctgc 660

aagccctgca tctgcaccgt gcccgaggtg tccagcgtgt tcatcttccc acccaagccc 720

aaggacgtgc tgaccatcac cctgaccccc aaagtgacct gcgtggtggt ggccatcagc 780

aaggacgacc ccgaggtgca gttctcttgg tttgtggacg acgtggaggt gcacacagcc 840

cagacaaagc cccgggagga acagatcaac agcaccttca gaagcgtgtc cgagctgccc 900

atcatgcacc aggactggct gaacggcaaa gaattcaagt gcagagtgaa cagcgccgcc 960

ttcggcgccc ccatcgagaa aaccatcagc aagaccaagg gcagacccaa ggcccccccag 1020

gtgtacacca tccccccacc caaaaaacag atggccaagg acaaggtgtc cctgacctgc 1080

atgatcacca acttttccc cgaggacatc accgtggagt ggcagtggaa tggccagccc 1140

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ctgcacgagg gcctgcacaa ccaccacacc gagaagtccc tgagccactc ccccggcaag 1320

+ADw-210+AD4- 74
+ADw-211+AD4- 645
+ADw-212+AD4- ADN
+ADw-213+AD4- Secuencia artificial

+ADw-220+AD4-
+ADw-223+AD4- cadena ligera de FAP

+ADw-400+AD4- 74
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ctgtcctgca gagcctccca gtccgtgtcc cggtcctacc tcgcctggta tcagcagaag 120

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ctgaacagtt ggactgatca ggacagcaaa gacagcacct acagcatgag cagcaccctc 540

acgttgacca aggacgagta tgaacgacat aacagctata cctgtgaggc cactcacaag 600

acatcaactt cacccattgt caagagcttc aacaggaatg agtgt 645

+ADw-210+AD4- 75
+ADw-211+AD4- 766
+ADw-212+AD4- PRT
+ADw-213+AD4- Secuencia artificial

+ADw-220+AD4-
+ADw-223+AD4- mu 4-1BBL dim+AOk-rico (71-254)-CH1-cadena pesada Fc DD

+ADw-400+AD4- 75

```
Arg Thr Glu Pro Arg Pro Ala Leu Thr Ile Thr Thr Ser Pro Asn Leu
1               5                  10                  15

Gly Thr Arg Glu Asn Asn Ala Asp Gln Val Thr Pro Val Ser His Ile
            20                  25                  30

Gly Ser Pro Asn Thr Thr Gln Gln Gly Ser Pro Val Phe Ala Lys Leu
        35                  40                  45

Leu Ala Lys Asn Gln Ala Ser Leu Ser Asn Thr Thr Leu Asn Trp His
    50                  55                  60

Ser Gln Asp Gly Ala Gly Ser Ser Tyr Leu Ser Gln Gly Leu Arg Tyr
65                  70                  75                  80

Glu Glu Asp Lys Lys Glu Leu Val Val Asp Ser Pro Gly Leu Tyr Tyr
                85                  90                  95

Val Phe Leu Glu Leu Lys Leu Ser Pro Thr Phe Thr Asn Thr Gly His
            100                 105                 110

Lys Val Gln Gly Trp Val Ser Leu Val Leu Gln Ala Lys Pro Gln Val
        115                 120                 125

Asp Asp Phe Asp Asn Leu Ala Leu Thr Val Glu Leu Phe Pro Ser Ser
    130                 135                 140

Met Glu Asn Lys Leu Val Asp Arg Ser Trp Ser Gln Leu Leu Leu Leu
145                 150                 155                 160

Lys Ala Gly His Arg Leu Ser Val Gly Leu Arg Ala Tyr Leu His Gly
                165                 170                 175

Ala Gln Asp Ala Tyr Arg Asp Trp Glu Leu Ser Tyr Pro Asn Thr Thr
            180                 185                 190

Ser Phe Gly Leu Phe Leu Val Lys Pro Asp Asn Pro Trp Glu Gly Gly
        195                 200                 205

Gly Gly Ser Gly Gly Gly Gly Ser Arg Thr Glu Pro Arg Pro Ala Leu
    210                 215                 220

Thr Ile Thr Thr Ser Pro Asn Leu Gly Thr Arg Glu Asn Asn Ala Asp
225                 230                 235                 240

Gln Val Thr Pro Val Ser His Ile Gly Ser Pro Asn Thr Thr Gln Gln
                245                 250                 255
```

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Gly Ser Pro Val Phe Ala Lys Leu Leu Ala Lys Asn Gln Ala Ser Leu
            260                 265                 270

Ser Asn Thr Thr Leu Asn Trp His Ser Gln Asp Gly Ala Gly Ser Ser
        275                 280                 285

Tyr Leu Ser Gln Gly Leu Arg Tyr Glu Glu Asp Lys Lys Glu Leu Val
    290                 295                 300

Val Asp Ser Pro Gly Leu Tyr Tyr Val Phe Leu Glu Leu Lys Leu Ser
305                 310                 315                 320

Pro Thr Phe Thr Asn Thr Gly His Lys Val Gln Gly Trp Val Ser Leu
                325                 330                 335

Val Leu Gln Ala Lys Pro Gln Val Asp Asp Phe Asp Asn Leu Ala Leu
            340                 345                 350

Thr Val Glu Leu Phe Pro Ser Ser Met Glu Asn Lys Leu Val Asp Arg
        355                 360                 365

Ser Trp Ser Gln Leu Leu Leu Leu Lys Ala Gly His Arg Leu Ser Val
    370                 375                 380

Gly Leu Arg Ala Tyr Leu His Gly Ala Gln Asp Ala Tyr Arg Asp Trp
385                 390                 395                 400

Glu Leu Ser Tyr Pro Asn Thr Thr Ser Phe Gly Leu Phe Leu Val Lys
                405                 410                 415

Pro Asp Asn Pro Trp Glu Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser
            420                 425                 430

Arg Ala Asp Ala Ala Pro Thr Val Ser Ile Phe Pro Pro Ser Ser Glu
        435                 440                 445

Gln Leu Thr Ser Gly Gly Ala Ser Val Val Cys Phe Leu Asn Asn Phe
    450                 455                 460

Tyr Pro Lys Asp Ile Asn Val Lys Trp Lys Ile Asp Gly Ser Glu Arg
465                 470                 475                 480

Gln Asn Gly Val Leu Asn Ser Trp Thr Asp Gln Asp Ser Lys Asp Ser
                485                 490                 495

Thr Tyr Ser Met Ser Ser Thr Leu Thr Leu Thr Lys Asp Glu Tyr Glu
            500                 505                 510
```

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Arg His Asn Ser Tyr Thr Cys Glu Ala Thr His Lys Thr Ser Thr Ser
        515                 520                 525

Pro Ile Val Lys Ser Phe Asn Arg Asn Glu Cys Val Pro Arg Asp Cys
    530                 535                 540

Gly Cys Lys Pro Cys Ile Cys Thr Val Pro Glu Val Ser Ser Val Phe
545                 550                 555                 560

Ile Phe Pro Pro Lys Pro Lys Asp Val Leu Thr Ile Thr Leu Thr Pro
                565                 570                 575

Lys Val Thr Cys Val Val Val Ala Ile Ser Lys Asp Asp Pro Glu Val
            580                 585                 590

Gln Phe Ser Trp Phe Val Asp Asp Val Glu Val His Thr Ala Gln Thr
        595                 600                 605

Lys Pro Arg Glu Glu Gln Ile Asn Ser Thr Phe Arg Ser Val Ser Glu
    610                 615                 620

Leu Pro Ile Met His Gln Asp Trp Leu Asn Gly Lys Glu Phe Lys Cys
625                 630                 635                 640

Arg Val Asn Ser Ala Ala Phe Gly Ala Pro Ile Glu Lys Thr Ile Ser
                645                 650                 655

Lys Thr Lys Gly Arg Pro Lys Ala Pro Gln Val Tyr Thr Ile Pro Pro
            660                 665                 670

Pro Lys Glu Gln Met Ala Lys Asp Lys Val Ser Leu Thr Cys Met Ile
        675                 680                 685

Thr Asn Phe Phe Pro Glu Asp Ile Thr Val Glu Trp Gln Trp Asn Gly
    690                 695                 700

Gln Pro Ala Glu Asn Tyr Asp Asn Thr Gln Pro Ile Met Asp Thr Asp
705                 710                 715                 720

Gly Ser Tyr Phe Val Tyr Ser Asp Leu Asn Val Gln Lys Ser Asn Trp
                725                 730                 735

Glu Ala Gly Asn Thr Phe Thr Cys Ser Val Leu His Glu Gly Leu His
            740                 745                 750

Asn His His Thr Glu Lys Ser Leu Ser His Ser Pro Gly Lys
```

755 760 765

+ADw-210+AD4- 76
+ADw-211+AD4- 318
+ADw-212+AD4- PRT
+ADw-213+AD4- Secuencia artificial

+ADw-220+AD4-
+ADw-223+AD4- fusi+APM-n de mu 4-1BBL monom+AOk-rico (71-254) -CL

+ADw-400+AD4- 76

Arg Thr Glu Pro Arg Pro Ala Leu Thr Ile Thr Thr Ser Pro Asn Leu
1 5 10 15

Gly Thr Arg Glu Asn Asn Ala Asp Gln Val Thr Pro Val Ser His Ile
20 25 30

Gly Ser Pro Asn Thr Thr Gln Gln Gly Ser Pro Val Phe Ala Lys Leu
35 40 45

Leu Ala Lys Asn Gln Ala Ser Leu Ser Asn Thr Thr Leu Asn Trp His
50 55 60

Ser Gln Asp Gly Ala Gly Ser Ser Tyr Leu Ser Gln Gly Leu Arg Tyr
65 70 75 80

Glu Glu Asp Lys Lys Glu Leu Val Val Asp Ser Pro Gly Leu Tyr Tyr
85 90 95

Val Phe Leu Glu Leu Lys Leu Ser Pro Thr Phe Thr Asn Thr Gly His
100 105 110

Lys Val Gln Gly Trp Val Ser Leu Val Leu Gln Ala Lys Pro Gln Val
115 120 125

Asp Asp Phe Asp Asn Leu Ala Leu Thr Val Glu Leu Phe Pro Ser Ser
130 135 140

Met Glu Asn Lys Leu Val Asp Arg Ser Trp Ser Gln Leu Leu Leu Leu
145 150 155 160

Lys Ala Gly His Arg Leu Ser Val Gly Leu Arg Ala Tyr Leu His Gly
165 170 175

Ala Gln Asp Ala Tyr Arg Asp Trp Glu Leu Ser Tyr Pro Asn Thr Thr
180 185 190

Ser Phe Gly Leu Phe Leu Val Lys Pro Asp Asn Pro Trp Glu Gly Gly
195 200 205

```
Gly Gly Ser Gly Gly Gly Gly Ser Ala Lys Thr Thr Pro Pro Ser Val
    210                 215                 220

Tyr Pro Leu Ala Pro Gly Ser Ala Ala Gln Thr Asn Ser Met Val Thr
225                 230                 235                 240

Leu Gly Cys Leu Val Lys Gly Tyr Phe Pro Glu Pro Val Thr Val Thr
                245                 250                 255

Trp Asn Ser Gly Ser Leu Ser Ser Gly Val His Thr Phe Pro Ala Val
            260                 265                 270

Leu Gln Ser Asp Leu Tyr Thr Leu Ser Ser Ser Val Thr Val Pro Ser
        275                 280                 285

Ser Thr Trp Pro Ser Gln Thr Val Thr Cys Asn Val Ala His Pro Ala
    290                 295                 300

Ser Ser Thr Lys Val Asp Lys Lys Ile Val Pro Arg Asp Cys
305                 310                 315


+ADw-210+AD4-  77
+ADw-211+AD4-  440
+ADw-212+AD4-  PRT
+ADw-213+AD4-  Secuencia artificial

+ADw-220+AD4-
+ADw-223+AD4-  cadena pesada de anti-FAP Fc KK

+ADw-400+AD4-  77

Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1               5                  10                  15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Ser His
            20                  25                  30

Ala Met Ser Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
        35                  40                  45

Ser Ala Ile Trp Ala Ser Gly Glu Gln Tyr Tyr Ala Asp Ser Val Lys
    50                  55                  60

Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr Leu
65                  70                  75                  80

Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys Ala
                85                  90                  95
```

```
Lys Gly Trp Leu Gly Asn Phe Asp Tyr Trp Gly Gln Gly Thr Leu Val
            100                 105                 110

Thr Val Ser Ser Ala Lys Thr Thr Pro Pro Ser Val Tyr Pro Leu Ala
        115                 120                 125

Pro Gly Ser Ala Ala Gln Thr Asn Ser Met Val Thr Leu Gly Cys Leu
    130                 135                 140

Val Lys Gly Tyr Phe Pro Glu Pro Val Thr Val Thr Trp Asn Ser Gly
145                 150                 155                 160

Ser Leu Ser Ser Gly Val His Thr Phe Pro Ala Val Leu Gln Ser Asp
                165                 170                 175

Leu Tyr Thr Leu Ser Ser Ser Val Thr Val Pro Ser Ser Thr Trp Pro
            180                 185                 190

Ser Gln Thr Val Thr Cys Asn Val Ala His Pro Ala Ser Ser Thr Lys
        195                 200                 205

Val Asp Lys Lys Ile Val Pro Arg Asp Cys Gly Cys Lys Pro Cys Ile
    210                 215                 220

Cys Thr Val Pro Glu Val Ser Ser Val Phe Ile Phe Pro Pro Lys Pro
225                 230                 235                 240

Lys Asp Val Leu Thr Ile Thr Leu Thr Pro Lys Val Thr Cys Val Val
                245                 250                 255

Val Ala Ile Ser Lys Asp Asp Pro Glu Val Gln Phe Ser Trp Phe Val
            260                 265                 270

Asp Asp Val Glu Val His Thr Ala Gln Thr Lys Pro Arg Glu Glu Gln
        275                 280                 285

Ile Asn Ser Thr Phe Arg Ser Val Ser Glu Leu Pro Ile Met His Gln
    290                 295                 300

Asp Trp Leu Asn Gly Lys Glu Phe Lys Cys Arg Val Asn Ser Ala Ala
305                 310                 315                 320

Phe Gly Ala Pro Ile Glu Lys Thr Ile Ser Lys Thr Lys Gly Arg Pro
                325                 330                 335

Lys Ala Pro Gln Val Tyr Thr Ile Pro Pro Pro Lys Lys Gln Met Ala
            340                 345                 350
```

```
Lys Asp Lys Val Ser Leu Thr Cys Met Ile Thr Asn Phe Phe Pro Glu
        355                 360                 365

Asp Ile Thr Val Glu Trp Gln Trp Asn Gly Gln Pro Ala Glu Asn Tyr
    370                 375                 380

Lys Asn Thr Gln Pro Ile Met Lys Thr Asp Gly Ser Tyr Phe Val Tyr
385                 390                 395                 400

Ser Lys Leu Asn Val Gln Lys Ser Asn Trp Glu Ala Gly Asn Thr Phe
                405                 410                 415

Thr Cys Ser Val Leu His Glu Gly Leu His Asn His His Thr Glu Lys
            420                 425                 430

Ser Leu Ser His Ser Pro Gly Lys
        435                 440


+ADw-210+AD4-  78
+ADw-211+AD4-  215
+ADw-212+AD4-  PRT
+ADw-213+AD4-  Secuencia artificial

+ADw-220+AD4-
+ADw-223+AD4-  cadena ligera de anti-FAP

+ADw-400+AD4-  78

Glu Ile Val Leu Thr Gln Ser Pro Gly Thr Leu Ser Leu Ser Pro Gly
1               5                   10                  15

Glu Arg Ala Thr Leu Ser Cys Arg Ala Ser Gln Ser Val Ser Arg Ser
            20                  25                  30

Tyr Leu Ala Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Arg Leu Leu
        35                  40                  45

Ile Ile Gly Ala Ser Thr Arg Ala Thr Gly Ile Pro Asp Arg Phe Ser
    50                  55                  60

Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Arg Leu Glu
65                  70                  75                  80

Pro Glu Asp Phe Ala Val Tyr Tyr Cys Gln Gln Gly Gln Val Ile Pro
                85                  90                  95

Pro Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys Arg Ala Asp Ala
            100                 105                 110
```

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Ala Pro Thr Val Ser Ile Phe Pro Pro Ser Ser Glu Gln Leu Thr Ser
        115                 120                 125


Gly Gly Ala Ser Val Val Cys Phe Leu Asn Asn Phe Tyr Pro Lys Asp
    130                 135                 140


Ile Asn Val Lys Trp Lys Ile Asp Gly Ser Glu Arg Gln Asn Gly Val
145                 150                 155                 160


Leu Asn Ser Trp Thr Asp Gln Asp Ser Lys Asp Ser Thr Tyr Ser Met
                165                 170                 175


Ser Ser Thr Leu Thr Leu Thr Lys Asp Glu Tyr Glu Arg His Asn Ser
            180                 185                 190


Tyr Thr Cys Glu Ala Thr His Lys Thr Ser Thr Ser Pro Ile Val Lys
        195                 200                 205


Ser Phe Asn Arg Asn Glu Cys
    210                 215


+ADw-210+AD4-  79
+ADw-211+AD4-  1335
+ADw-212+AD4-  ADN
+ADw-213+AD4-  Secuencia artificial

+ADw-220+AD4-
+ADw-223+AD4-  cadena pesada de DP47 Fc agujero

+ADw-400+AD4-  79
gaggtgcaat tgttggagtc tgggggaggc ttggtacagc ctgggggtc cctgagactc       60

tcctgtgcag cctccggatt cacctttagc agttatgcca tgagctgggt ccgccaggct      120

ccagggaagg ggctggagtg ggtctcagct attagtggta gtggtggtag cacatactac      180

gcagactccg tgaagggccg gttcaccatc tccagagaca attccaagaa cacgctgtat      240

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ggatttgact actggggcca aggaaccctg gtcaccgtct cgagtgctag caccaagggc      360

ccatcggtct tccccctggc accctcctcc aagagcacct ctgggggcac agcggccctg      420

ggctgcctgg tcaaggacta cttccccgaa ccggtgacgg tgtcgtggaa ctcaggcgcc      480

ctgaccagcg gcgtgcacac cttcccggct gtcctacagt cctcaggact ctactccctc      540

agcagcgtgg tgaccgtgcc ctccagcagc ttgggcaccc agacctacat ctgcaacgtg      600

aatcacaagc ccagcaacac caaggtggac aagaaagttg agcccaaatc ttgtgacaaa      660

actcacacat gcccaccgtg cccagcacct gaagctgcag ggggaccgtc agtcttcctc      720

ttcccccaa aacccaagga caccctcatg atctcccgga cccctgaggt cacatgcgtg      780
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gtcagcgtcc tcaccgtcct gcaccaggac tggctgaatg gcaaggagta caagtgcaag 960

gtctccaaca aagccctcgg cgcccccatc gagaaaacca tctccaaagc caaagggcag 1020

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ctgtctccgg gtaaa 1335

+ADw-210+AD4- 80
+ADw-211+AD4- 645
+ADw-212+AD4- ADN
+ADw-213+AD4- Secuencia artificial

+ADw-220+AD4-
+ADw-223+AD4- cadena ligera de DP47

+ADw-400+AD4- 80
gaaatcgtgt taacgcagtc tccaggcacc ctgtctttgt ctccagggga aagagccacc 60

ctctcttgca gggccagtca gagtgttagc agcagctact tagcctggta ccagcagaaa 120

cctggccagg ctcccaggct cctcatctat ggagcatcca gcagggccac tggcatccca 180

gacaggttca gtggcagtgg atccgggaca gacttcactc tcaccatcag cagactggag 240

cctgaagatt ttgcagtgta ttactgtcag cagtatggta gctcaccgct gacgttcggc 300

caggggacca aagtggaaat caaacgtacg gtggctgcac catctgtctt catcttcccg 360

ccatctgatg agcagttgaa atctggaact gcctctgttg tgtgcctgct gaataacttc 420

tatcccagag aggccaaagt acagtggaag gtggataacg ccctccaatc gggtaactcc 480

caggagagtg tcacagagca ggacagcaag gacagcacct acagcctcag cagcaccctg 540

acgctgagca aagcagacta cgagaaacac aaagtctacg cctgcgaagt cacccatcag 600

ggcctgagct cgcccgtcac aaagagcttc aacaggggag agtgt 645

+ADw-210+AD4- 81
+ADw-211+AD4- 445
+ADw-212+AD4- PRT
+ADw-213+AD4- Secuencia artificial

+ADw-220+AD4-
+ADw-223+AD4- cadena pesada de DP47 Fc agujero

+ADw-400+AD4- 81

```
Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1               5                  10                  15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Ser Tyr
            20                  25                  30

Ala Met Ser Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
        35                  40                  45

Ser Ala Ile Ser Gly Ser Gly Gly Ser Thr Tyr Tyr Ala Asp Ser Val
    50                  55                  60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65                  70                  75                  80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95

Ala Lys Gly Ser Gly Phe Asp Tyr Trp Gly Gln Gly Thr Leu Val Thr
            100                 105                 110

Val Ser Ser Ala Ser Thr Lys Gly Pro Ser Val Phe Pro Leu Ala Pro
        115                 120                 125

Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu Gly Cys Leu Val
    130                 135                 140

Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser Trp Asn Ser Gly Ala
145                 150                 155                 160

Leu Thr Ser Gly Val His Thr Phe Pro Ala Val Leu Gln Ser Ser Gly
                165                 170                 175

Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser Ser Ser Leu Gly
            180                 185                 190

Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys Pro Ser Asn Thr Lys
        195                 200                 205

Val Asp Lys Lys Val Glu Pro Lys Ser Cys Asp Lys Thr His Thr Cys
    210                 215                 220

Pro Pro Cys Pro Ala Pro Glu Ala Ala Gly Gly Pro Ser Val Phe Leu
225                 230                 235                 240

Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu
                245                 250                 255
```

```
Val Thr Cys Val Val Val Asp Val Ser His Glu Asp Pro Glu Val Lys
            260                 265                 270

Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys
        275                 280                 285

Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg Val Val Ser Val Leu
    290                 295                 300

Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys
305                 310                 315                 320

Val Ser Asn Lys Ala Leu Gly Ala Pro Ile Glu Lys Thr Ile Ser Lys
                325                 330                 335

Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Cys Thr Leu Pro Pro Ser
            340                 345                 350

Arg Asp Glu Leu Thr Lys Asn Gln Val Ser Leu Ser Cys Ala Val Lys
        355                 360                 365

Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln
    370                 375                 380

Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly
385                 390                 395                 400

Ser Phe Phe Leu Val Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln
                405                 410                 415

Gln Gly Asn Val Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn
            420                 425                 430

His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly Lys
        435                 440                 445


+ADw-210+AD4-  82
+ADw-211+AD4-  215
+ADw-212+AD4-  PRT
+ADw-213+AD4-  Secuencia artificial

+ADw-220+AD4-
+ADw-223+AD4-  cadena ligera de DP47

+ADw-400+AD4-  82

Glu Ile Val Leu Thr Gln Ser Pro Gly Thr Leu Ser Leu Ser Pro Gly
1               5                  10                  15
```

```
Glu Arg Ala Thr Leu Ser Cys Arg Ala Ser Gln Ser Val Ser Ser Ser
            20                  25                  30

Tyr Leu Ala Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Arg Leu Leu
        35                  40                  45

Ile Tyr Gly Ala Ser Ser Arg Ala Thr Gly Ile Pro Asp Arg Phe Ser
    50                  55                  60

Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Arg Leu Glu
65                  70                  75                  80

Pro Glu Asp Phe Ala Val Tyr Tyr Cys Gln Gln Tyr Gly Ser Ser Pro
                85                  90                  95

Leu Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys Arg Thr Val Ala
            100                 105                 110

Ala Pro Ser Val Phe Ile Phe Pro Pro Ser Asp Glu Gln Leu Lys Ser
        115                 120                 125

Gly Thr Ala Ser Val Val Cys Leu Leu Asn Asn Phe Tyr Pro Arg Glu
    130                 135                 140

Ala Lys Val Gln Trp Lys Val Asp Asn Ala Leu Gln Ser Gly Asn Ser
145                 150                 155                 160

Gln Glu Ser Val Thr Glu Gln Asp Ser Lys Asp Ser Thr Tyr Ser Leu
                165                 170                 175

Ser Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu Lys His Lys Val
            180                 185                 190

Tyr Ala Cys Glu Val Thr His Gln Gly Leu Ser Ser Pro Val Thr Lys
        195                 200                 205

Ser Phe Asn Arg Gly Glu Cys
    210                 215


+ADw-210+AD4-  83
+ADw-211+AD4-  163
+ADw-212+AD4-  PRT
+ADw-213+AD4-  Homo sapiens

+ADw-400+AD4-  83

Leu Gln Asp Pro Cys Ser Asn Cys Pro Ala Gly Thr Phe Cys Asp Asn
1               5                   10                  15
```

```
Asn Arg Asn Gln Ile Cys Ser Pro Cys Pro Pro Asn Ser Phe Ser Ser
            20                  25                  30

Ala Gly Gly Gln Arg Thr Cys Asp Ile Cys Arg Gln Cys Lys Gly Val
        35                  40                  45

Phe Arg Thr Arg Lys Glu Cys Ser Ser Thr Ser Asn Ala Glu Cys Asp
    50                  55                  60

Cys Thr Pro Gly Phe His Cys Leu Gly Ala Gly Cys Ser Met Cys Glu
65                  70                  75                  80

Gln Asp Cys Lys Gln Gly Gln Glu Leu Thr Lys Lys Gly Cys Lys Asp
                85                  90                  95

Cys Cys Phe Gly Thr Phe Asn Asp Gln Lys Arg Gly Ile Cys Arg Pro
            100                 105                 110

Trp Thr Asn Cys Ser Leu Asp Gly Lys Ser Val Leu Val Asn Gly Thr
        115                 120                 125

Lys Glu Arg Asp Val Val Cys Gly Pro Ser Pro Ala Asp Leu Ser Pro
    130                 135                 140

Gly Ala Ser Ser Val Thr Pro Pro Ala Pro Ala Arg Glu Pro Gly His
145                 150                 155                 160

Ser Pro Gln



+ADw-210+AD4-  84
+ADw-211+AD4-  163
+ADw-212+AD4-  PRT
+ADw-213+AD4-  Cinomolgo

+ADw-400+AD4-  84

Leu Gln Asp Leu Cys Ser Asn Cys Pro Ala Gly Thr Phe Cys Asp Asn
1               5                   10                  15

Asn Arg Ser Gln Ile Cys Ser Pro Cys Pro Pro Asn Ser Phe Ser Ser
            20                  25                  30

Ala Gly Gly Gln Arg Thr Cys Asp Ile Cys Arg Gln Cys Lys Gly Val
        35                  40                  45

Phe Lys Thr Arg Lys Glu Cys Ser Ser Thr Ser Asn Ala Glu Cys Asp
    50                  55                  60
```

```
Cys Ile Ser Gly Tyr His Cys Leu Gly Ala Glu Cys Ser Met Cys Glu
65                  70                  75                  80


Gln Asp Cys Lys Gln Gly Gln Glu Leu Thr Lys Lys Gly Cys Lys Asp
                85                  90                  95


Cys Cys Phe Gly Thr Phe Asn Asp Gln Lys Arg Gly Ile Cys Arg Pro
            100                 105                 110


Trp Thr Asn Cys Ser Leu Asp Gly Lys Ser Val Leu Val Asn Gly Thr
        115                 120                 125


Lys Glu Arg Asp Val Val Cys Gly Pro Ser Pro Ala Asp Leu Ser Pro
    130                 135                 140


Gly Ala Ser Ser Ala Thr Pro Pro Ala Pro Ala Arg Glu Pro Gly His
145                 150                 155                 160


Ser Pro Gln



+ADw-210+AD4-  85
+ADw-211+AD4-  164
+ADw-212+AD4-  PRT
+ADw-213+AD4-  Mus musculus

+ADw-400+AD4-  85

Val Gln Asn Ser Cys Asp Asn Cys Gln Pro Gly Thr Phe Cys Arg Lys
1               5                   10                  15


Tyr Asn Pro Val Cys Lys Ser Cys Pro Pro Ser Thr Phe Ser Ser Ile
            20                  25                  30


Gly Gly Gln Pro Asn Cys Asn Ile Cys Arg Val Cys Ala Gly Tyr Phe
        35                  40                  45


Arg Phe Lys Lys Phe Cys Ser Ser Thr His Asn Ala Glu Cys Glu Cys
    50                  55                  60


Ile Glu Gly Phe His Cys Leu Gly Pro Gln Cys Thr Arg Cys Glu Lys
65                  70                  75                  80


Asp Cys Arg Pro Gly Gln Glu Leu Thr Lys Gln Gly Cys Lys Thr Cys
                85                  90                  95


Ser Leu Gly Thr Phe Asn Asp Gln Asn Gly Thr Gly Val Cys Arg Pro
            100                 105                 110
```

Trp Thr Asn Cys Ser Leu Asp Gly Arg Ser Val Leu Lys Thr Gly Thr
115 120 125

Thr Glu Lys Asp Val Val Cys Gly Pro Pro Val Val Ser Phe Ser Pro
130 135 140

Ser Thr Thr Ile Ser Val Thr Pro Glu Gly Gly Pro Gly Gly His Ser
145 150 155 160

Leu Gln Val Leu

+ADw-210+AD4- 86
+ADw-211+AD4- 681
+ADw-212+AD4- ADN
+ADw-213+AD4- Secuencia artificial

+ADw-220+AD4-
+ADw-223+AD4- cadena Fc agujero

+ADw-400+AD4- 86
gacaaaactc acacatgccc accgtgccca gcacctgaac tcctgggggg accgtcagtc 60

ttcctcttcc ccccaaaacc caaggacacc ctcatgatct cccggacccc tgaggtcaca 120

tgcgtggtgg tggacgtgag ccacgaagac cctgaggtca agttcaactg gtacgtggac 180

ggcgtggagg tgcataatgc caagacaaag ccgcgggagg agcagtacaa cagcacgtac 240

cgtgtggtca gcgtcctcac cgtcctgcac caggactggc tgaatggcaa ggagtacaag 300

tgcaaggtct ccaacaaagc cctcccagcc cccatcgaga aaaccatctc caaagccaaa 360

gggcagcccc gagaaccaca ggtgtgcacc ctgcccccat cccgggatga gctgaccaag 420

aaccaggtca gcctctcgtg cgcagtcaaa ggcttctatc ccagcgacat cgccgtggag 480

tgggagagca atgggcagcc ggagaacaac tacaagacca cgcctcccgt gctggactcc 540

gacggctcct tcttcctcgt gagcaagctc accgtggaca agagcaggtg gcagcagggg 600

aacgtcttct catgctccgt gatgcatgag gctctgcaca accactacac gcagaagagc 660

ctctccctgt ctccgggtaa a 681

+ADw-210+AD4- 87
+ADw-211+AD4- 1266
+ADw-212+AD4- ADN
+ADw-213+AD4- Secuencia artificial

+ADw-220+AD4-
+ADw-223+AD4- fusi+APM-n de hu 4-1BB Fc pomo

+ADw-400+AD4- 87
ctgcaggacc cctgcagcaa ctgccctgcc ggcaccttct gcgacaacaa ccggaaccag 60

atctgcagcc cctgcccccc caacagcttc agctctgccg gcggacagcg gacctgcgac 120

atctgcagac agtgcaaggg cgtgttcaga acccggaaag agtgcagcag caccagcaac 180

gccgagtgcg actgcacccc cggcttccat tgtctgggag ccggctgcag catgtgcgag 240

caggactgca agcagggcca ggaactgacc aagaagggct gcaaggactg ctgcttcggc 300

accttcaacg accagaagcg gggcatctgc cggccctgga ccaactgtag cctggacggc 360

aagagcgtgc tggtcaacgg caccaaagaa cgggacgtcg tgtgcggccc cagccctgct 420

gatctgtctc ctggggccag cagcgtgacc cctcctgccc ctgccagaga gcctggccac 480

tctcctcagg tcgacgaaca gttatatttt cagggcggct cacccaaatc tgcagacaaa 540

actcacacat gcccaccgtg cccagcacct gaactcctgg ggggaccgtc agtcttcctc 600

ttcccccaa aacccaagga caccctcatg atctcccgga cccctgaggt cacatgcgtg 660

gtggtggacg tgagccacga agaccctgag gtcaagttca actggtacgt ggacggcgtg 720

gaggtgcata atgccaagac aaagccgcgg gaggagcagt acaacagcac gtaccgtgtg 780

gtcagcgtcc tcaccgtcct gcaccaggac tggctgaatg gcaaggagta caagtgcaag 840

gtctccaaca aagccctccc agcccccatc gagaaaacca tctccaaagc caaagggcag 900

ccccgagaac cacaggtgta caccctgccc ccatgccggg atgagctgac caagaaccag 960

gtcagcctgt ggtgcctggt caaaggcttc tatcccagcg acatcgccgt ggagtgggag 1020

agcaatgggc agccggagaa caactacaag accacgcctc ccgtgctgga ctccgacggc 1080

tccttcttcc tctacagcaa gctcaccgtg gacaagagca ggtggcagca ggggaacgtc 1140

ttctcatgct ccgtgatgca tgaggctctg cacaaccact acacgcagaa gagcctctcc 1200

ctgtctccgg gtaaatccgg aggcctgaac gacatcttcg aggcccagaa gattgaatgg 1260

cacgag 1266

+ADw-210+AD4- 88
+ADw-211+AD4- 1266
+ADw-212+AD4- ADN
+ADw-213+AD4- Secuencia artificial

+ADw-220+AD4-
+ADw-223+AD4- Fusi+APM-n de 4-1BB de cinomolgo Fc pomo

+ADw-400+AD4- 88
ttgcaggatc tgtgtagtaa ctgcccagct ggtacattct gtgataataa caggagtcag 60

atttgcagtc cctgtcctcc aaatagtttc tccagcgcag gtggacaaag gacctgtgac 120

atatgcaggc agtgtaaagg tgttttcaag accaggaagg agtgttcctc caccagcaat 180

gcagagtgtg actgcatttc agggtatcac tgcctggggg cagagtgcag catgtgtgaa 240

caggattgta aacaaggtca agaattgaca aaaaaaggtt gtaaagactg ttgctttggg 300

acatttaatg accagaaacg tggcatctgt cgcccctgga caaactgttc tttggatgga 360

aagtctgtgc ttgtgaatgg gacgaaggag agggacgtgg tctgcggacc atctccagcc 420

gacctctctc caggagcatc ctctgcgacc ccgcctgccc ctgcgagaga gccaggacac 480

tctccgcagg tcgacgaaca gttatatttt cagggcggct cacccaaatc tgcagacaaa 540

actcacacat gcccaccgtg cccagcacct gaactcctgg ggggaccgtc agtcttcctc 600

ttcccccaa aacccaagga caccctcatg atctcccgga cccctgaggt cacatgcgtg 660

gtggtggacg tgagccacga agaccctgag gtcaagttca actggtacgt ggacggcgtg 720

gaggtgcata atgccaagac aaagccgcgg gaggagcagt acaacagcac gtaccgtgtg 780

gtcagcgtcc tcaccgtcct gcaccaggac tggctgaatg gcaaggagta caagtgcaag 840

gtctccaaca aagccctccc agcccccatc gagaaaacca tctccaaagc caaagggcag 900

ccccgagaac cacaggtgta caccctgccc ccatgccggg atgagctgac caagaaccag 960

gtcagcctgt ggtgcctggt caaaggcttc tatcccagcg acatcgccgt ggagtgggag 1020

agcaatgggc agccggagaa caactacaag accacgcctc ccgtgctgga ctccgacggc 1080

tccttcttcc tctacagcaa gctcaccgtg gacaagagca ggtggcagca ggggaacgtc 1140

ttctcatgct ccgtgatgca tgaggctctg cacaaccact acacgcagaa gagcctctcc 1200

ctgtctccgg gtaaatccgg aggcctgaac gacatcttcg aggcccagaa gattgaatgg 1260

cacgag 1266

+ADw-210+AD4- 89
+ADw-211+AD4- 1269
+ADw-212+AD4- ADN
+ADw-213+AD4- Secuencia artificial

+ADw-220+AD4-
+ADw-223+AD4- Fusi+APM-n de 4-1BB murino Fc pomo

+ADw-400+AD4- 89
gtgcagaaca gctgcgacaa ctgccagccc ggcaccttct gccggaagta caaccccgtg 60

tgcaagagct gccccccag caccttcagc agcatcggcg gccagcccaa ctgcaacatc 120

tgcagagtgt gcgccggcta cttccggttc aagaagttct gcagcagcac ccacaacgcc 180

gagtgcgagt gcatcgaggg cttccactgc ctgggccccc agtgcaccag atgcgagaag 240

gactgcagac ccggccagga actgaccaag cagggctgta agacctgcag cctgggcacc 300

ttcaacgacc agaacgggac cggcgtgtgc cggccttgga ccaattgcag cctggacggg 360

agaagcgtgc tgaaaaccgg caccaccgag aaggacgtcg tgtgcggccc tcccgtggtg 420

tccttcagcc ctagcaccac catcagcgtg acccctgaag gcggccctgg cggacactct 480

ctgcaggtcc tggtcgacga acagttatat tttcagggcg gctcacccaa atctgcagac 540

aaaactcaca catgcccacc gtgcccagca cctgaactcc tgggggggacc gtcagtcttc 600

ctcttccccc caaaacccaa ggacaccctc atgatctccc ggacccctga ggtcacatgc 660

gtggtggtgg acgtgagcca cgaagaccct gaggtcaagt tcaactggta cgtggacggc 720

gtggaggtgc ataatgccaa gacaaagccg cgggaggagc agtacaacag cacgtaccgt 780

gtggtcagcg tcctcaccgt cctgcaccag gactggctga atggcaagga gtacaagtgc 840

aaggtctcca acaaagccct cccagccccc atcgagaaaa ccatctccaa agccaaaggg 900

cagccccgag aaccacaggt gtacaccctg cccccatgcc gggatgagct gaccaagaac 960

caggtcagcc tgtggtgcct ggtcaaaggc ttctatccca gcgacatcgc cgtggagtgg 1020

gagagcaatg ggcagccgga gaacaactac aagaccacgc ctcccgtgct ggactccgac 1080

ggctccttct tcctctacag caagctcacc gtggacaaga gcaggtggca gcaggggaac 1140

gtcttctcat gctccgtgat gcatgaggct ctgcacaacc actacacgca gaagagcctc 1200

tccctgtctc cgggtaaatc cggaggcctg aacgacatct tcgaggccca gaagattgaa 1260

tggcacgag 1269

+ADw-210+AD4- 90
+ADw-211+AD4- 227
+ADw-212+AD4- PRT
+ADw-213+AD4- Secuencia artificial

+ADw-220+AD4-
+ADw-223+AD4- cadena Fc agujero

+ADw-400+AD4- 90

Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly
1 5 10 15

Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met
20 25 30

Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His
35 40 45

Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val
50 55 60

His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr
65 70 75 80

Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly
85 90 95

Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile
100 105 110

Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val

115 120 125

Cys Thr Leu Pro Pro Ser Arg Asp Glu Leu Thr Lys Asn Gln Val Ser
130 135 140

Leu Ser Cys Ala Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu
145 150 155 160

Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro
165 170 175

Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Val Ser Lys Leu Thr Val
180 185 190

Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met
195 200 205

His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser
210 215 220

Pro Gly Lys
225

+ADw-210+AD4- 91
+ADw-211+AD4- 422
+ADw-212+AD4- PRT
+ADw-213+AD4- Secuencia artificial

+ADw-220+AD4-
+ADw-223+AD4- Fusi+APM-n de 4-1BB humano Fc pomo

+ADw-400+AD4- 91

Leu Gln Asp Pro Cys Ser Asn Cys Pro Ala Gly Thr Phe Cys Asp Asn
1 5 10 15

Asn Arg Asn Gln Ile Cys Ser Pro Cys Pro Pro Asn Ser Phe Ser Ser
20 25 30

Ala Gly Gly Gln Arg Thr Cys Asp Ile Cys Arg Gln Cys Lys Gly Val
35 40 45

Phe Arg Thr Arg Lys Glu Cys Ser Ser Thr Ser Asn Ala Glu Cys Asp
50 55 60

Cys Thr Pro Gly Phe His Cys Leu Gly Ala Gly Cys Ser Met Cys Glu
65 70 75 80

Gln Asp Cys Lys Gln Gly Gln Glu Leu Thr Lys Lys Gly Cys Lys Asp
85 90 95

```
Cys Cys Phe Gly Thr Phe Asn Asp Gln Lys Arg Gly Ile Cys Arg Pro
            100                 105                 110

Trp Thr Asn Cys Ser Leu Asp Gly Lys Ser Val Leu Val Asn Gly Thr
        115                 120                 125

Lys Glu Arg Asp Val Val Cys Gly Pro Ser Pro Ala Asp Leu Ser Pro
    130                 135                 140

Gly Ala Ser Ser Val Thr Pro Pro Ala Pro Ala Arg Glu Pro Gly His
145                 150                 155                 160

Ser Pro Gln Val Asp Glu Gln Leu Tyr Phe Gln Gly Gly Ser Pro Lys
                165                 170                 175

Ser Ala Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu
            180                 185                 190

Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr
        195                 200                 205

Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val
    210                 215                 220

Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val
225                 230                 235                 240

Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser
                245                 250                 255

Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu
            260                 265                 270

Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala
        275                 280                 285

Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro
    290                 295                 300

Gln Val Tyr Thr Leu Pro Pro Cys Arg Asp Glu Leu Thr Lys Asn Gln
305                 310                 315                 320

Val Ser Leu Trp Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala
                325                 330                 335

Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr
```

340 345 350

Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu
355 360 365

Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser
370 375 380

Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser
385 390 395 400

Leu Ser Pro Gly Lys Ser Gly Gly Leu Asn Asp Ile Phe Glu Ala Gln
405 410 415

Lys Ile Glu Trp His Glu
420

+ADw-210+AD4- 92
+ADw-211+AD4- 422
+ADw-212+AD4- PRT
+ADw-213+AD4- Secuencia artificial

+ADw-220+AD4-
+ADw-223+AD4- Fusi+APM-n de 4-1BB de cinomolgo Fc pomo

+ADw-400+AD4- 92

Leu Gln Asp Leu Cys Ser Asn Cys Pro Ala Gly Thr Phe Cys Asp Asn
1 5 10 15

Asn Arg Ser Gln Ile Cys Ser Pro Cys Pro Pro Asn Ser Phe Ser Ser
20 25 30

Ala Gly Gly Gln Arg Thr Cys Asp Ile Cys Arg Gln Cys Lys Gly Val
35 40 45

Phe Lys Thr Arg Lys Glu Cys Ser Ser Thr Ser Asn Ala Glu Cys Asp
50 55 60

Cys Ile Ser Gly Tyr His Cys Leu Gly Ala Glu Cys Ser Met Cys Glu
65 70 75 80

Gln Asp Cys Lys Gln Gly Gln Glu Leu Thr Lys Lys Gly Cys Lys Asp
85 90 95

Cys Cys Phe Gly Thr Phe Asn Asp Gln Lys Arg Gly Ile Cys Arg Pro
100 105 110

Trp Thr Asn Cys Ser Leu Asp Gly Lys Ser Val Leu Val Asn Gly Thr
115 120 125

```
Lys Glu Arg Asp Val Val Cys Gly Pro Ser Pro Ala Asp Leu Ser Pro
    130                 135                 140

Gly Ala Ser Ser Ala Thr Pro Pro Ala Pro Ala Arg Glu Pro Gly His
145                 150                 155                 160

Ser Pro Gln Val Asp Glu Gln Leu Tyr Phe Gln Gly Gly Ser Pro Lys
                165                 170                 175

Ser Ala Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu
            180                 185                 190

Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr
        195                 200                 205

Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val
    210                 215                 220

Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val
225                 230                 235                 240

Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser
                245                 250                 255

Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu
            260                 265                 270

Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala
        275                 280                 285

Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro
    290                 295                 300

Gln Val Tyr Thr Leu Pro Pro Cys Arg Asp Glu Leu Thr Lys Asn Gln
305                 310                 315                 320

Val Ser Leu Trp Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala
                325                 330                 335

Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr
            340                 345                 350

Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu
        355                 360                 365

Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser
```

370 375 380

Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser
385 390 395 400

Leu Ser Pro Gly Lys Ser Gly Gly Leu Asn Asp Ile Phe Glu Ala Gln
405 410 415

Lys Ile Glu Trp His Glu
420

+ADw-210+AD4- 93
+ADw-211+AD4- 423
+ADw-212+AD4- PRT
+ADw-213+AD4- Secuencia artificial

+ADw-220+AD4-
+ADw-223+AD4- Fusi+APM-n de 4-1BB murino Fc pomo

+ADw-400+AD4- 93

Val Gln Asn Ser Cys Asp Asn Cys Gln Pro Gly Thr Phe Cys Arg Lys
1 5 10 15

Tyr Asn Pro Val Cys Lys Ser Cys Pro Pro Ser Thr Phe Ser Ser Ile
20 25 30

Gly Gly Gln Pro Asn Cys Asn Ile Cys Arg Val Cys Ala Gly Tyr Phe
35 40 45

Arg Phe Lys Lys Phe Cys Ser Ser Thr His Asn Ala Glu Cys Glu Cys
50 55 60

Ile Glu Gly Phe His Cys Leu Gly Pro Gln Cys Thr Arg Cys Glu Lys
65 70 75 80

Asp Cys Arg Pro Gly Gln Glu Leu Thr Lys Gln Gly Cys Lys Thr Cys
85 90 95

Ser Leu Gly Thr Phe Asn Asp Gln Asn Gly Thr Gly Val Cys Arg Pro
100 105 110

Trp Thr Asn Cys Ser Leu Asp Gly Arg Ser Val Leu Lys Thr Gly Thr
115 120 125

Thr Glu Lys Asp Val Val Cys Gly Pro Pro Val Val Ser Phe Ser Pro
130 135 140

Ser Thr Thr Ile Ser Val Thr Pro Glu Gly Gly Pro Gly Gly His Ser
145 150 155 160

```
Leu Gln Val Leu Val Asp Glu Gln Leu Tyr Phe Gln Gly Gly Ser Pro
                165                 170                 175

Lys Ser Ala Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu
            180                 185                 190

Leu Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp
        195                 200                 205

Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp
    210                 215                 220

Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly
225                 230                 235                 240

Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn
                245                 250                 255

Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp
            260                 265                 270

Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro
        275                 280                 285

Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu
    290                 295                 300

Pro Gln Val Tyr Thr Leu Pro Pro Cys Arg Asp Glu Leu Thr Lys Asn
305                 310                 315                 320

Gln Val Ser Leu Trp Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile
                325                 330                 335

Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr
            340                 345                 350

Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys
        355                 360                 365

Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys
    370                 375                 380

Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu
385                 390                 395                 400

Ser Leu Ser Pro Gly Lys Ser Gly Gly Leu Asn Asp Ile Phe Glu Ala
```

405 410 415

Gln Lys Ile Glu Trp His Glu
420

+ADw-210+AD4- 94
+ADw-211+AD4- 594
+ADw-212+AD4- ADN
+ADw-213+AD4- Secuencia artificial

+ADw-220+AD4-
+ADw-223+AD4- 4-1BB humano marcado con His

+ADw-400+AD4- 94
ctgcaggacc cctgcagcaa ctgccctgcc ggcaccttct gcgacaacaa ccggaaccag 60

atctgcagcc cctgcccccc caacagcttc agctctgccg gcggacagcg gacctgcgac 120

atctgcagac agtgcaaggg cgtgttcaga acccggaaag agtgcagcag caccagcaac 180

gccgagtgcg actgcacccc cggcttccat tgtctgggag ccggctgcag catgtgcgag 240

caggactgca agcagggcca ggaactgacc aagaagggct gcaaggactg ctgcttcggc 300

accttcaacg accagaagcg gggcatctgc cggccctgga ccaactgtag cctggacggc 360

aagagcgtgc tggtcaacgg caccaaagaa cgggacgtcg tgtgcggccc cagccctgct 420

gatctgtctc ctggggccag cagcgtgacc cctcctgccc ctgccagaga gcctggccac 480

tctcctcagg tcgacgaaca gttatatttt cagggcggct caggcctgaa cgacatcttc 540

gaggcccaga agatcgagtg gcacgaggct cgagctcacc accatcacca tcac 594

+ADw-210+AD4- 95
+ADw-211+AD4- 198
+ADw-212+AD4- PRT
+ADw-213+AD4- Secuencia artificial

+ADw-220+AD4-
+ADw-223+AD4- 4-1BB humano marcado con His

+ADw-400+AD4- 95

Leu Gln Asp Pro Cys Ser Asn Cys Pro Ala Gly Thr Phe Cys Asp Asn
1 5 10 15

Asn Arg Asn Gln Ile Cys Ser Pro Cys Pro Pro Asn Ser Phe Ser Ser
20 25 30

Ala Gly Gly Gln Arg Thr Cys Asp Ile Cys Arg Gln Cys Lys Gly Val
35 40 45

Phe Arg Thr Arg Lys Glu Cys Ser Ser Thr Ser Asn Ala Glu Cys Asp
50 55 60

```
Cys Thr Pro Gly Phe His Cys Leu Gly Ala Gly Cys Ser Met Cys Glu
65                  70                  75                  80


Gln Asp Cys Lys Gln Gly Gln Glu Leu Thr Lys Lys Gly Cys Lys Asp
                85                  90                  95


Cys Cys Phe Gly Thr Phe Asn Asp Gln Lys Arg Gly Ile Cys Arg Pro
            100                 105                 110


Trp Thr Asn Cys Ser Leu Asp Gly Lys Ser Val Leu Val Asn Gly Thr
        115                 120                 125


Lys Glu Arg Asp Val Val Cys Gly Pro Ser Pro Ala Asp Leu Ser Pro
    130                 135                 140


Gly Ala Ser Ser Val Thr Pro Pro Ala Pro Ala Arg Glu Pro Gly His
145                 150                 155                 160


Ser Pro Gln Val Asp Glu Gln Leu Tyr Phe Gln Gly Gly Ser Gly Leu
                165                 170                 175


Asn Asp Ile Phe Glu Ala Gln Lys Ile Glu Trp His Glu Ala Arg Ala
            180                 185                 190


His His His His His His
        195


+ADw-210+AD4-  96
+ADw-211+AD4-  178
+ADw-212+AD4-  PRT
+ADw-213+AD4-  Homo sapiens

+ADw-400+AD4-  96

Arg Glu Gly Pro Glu Leu Ser Pro Asp Asp Pro Ala Gly Leu Leu Asp
1               5                   10                  15


Leu Arg Gln Gly Met Phe Ala Gln Leu Val Ala Gln Asn Val Leu Leu
            20                  25                  30


Ile Asp Gly Pro Leu Ser Trp Tyr Ser Asp Pro Gly Leu Ala Gly Val
        35                  40                  45


Ser Leu Thr Gly Gly Leu Ser Tyr Lys Glu Asp Thr Lys Glu Leu Val
    50                  55                  60


Val Ala Lys Ala Gly Val Tyr Tyr Val Phe Phe Gln Leu Glu Leu Arg
65                  70                  75                  80
```

```
Arg Val Val Ala Gly Glu Gly Ser Gly Ser Val Ser Leu Ala Leu His
                85                  90                  95

Leu Gln Pro Leu Arg Ser Ala Ala Gly Ala Ala Ala Leu Ala Leu Thr
            100                 105                 110

Val Asp Leu Pro Pro Ala Ser Ser Glu Ala Arg Asn Ser Ala Phe Gly
        115                 120                 125

Phe Gln Gly Arg Leu Leu His Leu Ser Ala Gly Gln Arg Leu Gly Val
    130                 135                 140

His Leu His Thr Glu Ala Arg Ala Arg His Ala Trp Gln Leu Thr Gln
145                 150                 155                 160

Gly Ala Thr Val Leu Gly Leu Phe Arg Val Thr Pro Glu Ile Pro Ala
                165                 170                 175

Gly Leu


+ADw-210+AD4-  97
+ADw-211+AD4-  366
+ADw-212+AD4-  PRT
+ADw-213+AD4-  Secuencia artificial

+ADw-220+AD4-
+ADw-223+AD4-  hu 4-1BBL dim+AOk-rico conectado mediante (G4S)2

+ADw-400+AD4-  97

Arg Glu Gly Pro Glu Leu Ser Pro Asp Asp Pro Ala Gly Leu Leu Asp
1               5                  10                  15

Leu Arg Gln Gly Met Phe Ala Gln Leu Val Ala Gln Asn Val Leu Leu
            20                  25                  30

Ile Asp Gly Pro Leu Ser Trp Tyr Ser Asp Pro Gly Leu Ala Gly Val
        35                  40                  45

Ser Leu Thr Gly Gly Leu Ser Tyr Lys Glu Asp Thr Lys Glu Leu Val
    50                  55                  60

Val Ala Lys Ala Gly Val Tyr Tyr Val Phe Phe Gln Leu Glu Leu Arg
65                  70                  75                  80

Arg Val Val Ala Gly Glu Gly Ser Gly Ser Val Ser Leu Ala Leu His
                85                  90                  95

Leu Gln Pro Leu Arg Ser Ala Ala Gly Ala Ala Ala Leu Ala Leu Thr
```

```
            100                 105                 110

Val Asp Leu Pro Pro Ala Ser Ser Glu Ala Arg Asn Ser Ala Phe Gly
        115                 120                 125

Phe Gln Gly Arg Leu Leu His Leu Ser Ala Gly Gln Arg Leu Gly Val
    130                 135                 140

His Leu His Thr Glu Ala Arg Ala Arg His Ala Trp Gln Leu Thr Gln
145                 150                 155                 160

Gly Ala Thr Val Leu Gly Leu Phe Arg Val Thr Pro Glu Ile Pro Ala
                165                 170                 175

Gly Leu Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Arg Glu Gly Pro
            180                 185                 190

Glu Leu Ser Pro Asp Asp Pro Ala Gly Leu Leu Asp Leu Arg Gln Gly
        195                 200                 205

Met Phe Ala Gln Leu Val Ala Gln Asn Val Leu Leu Ile Asp Gly Pro
    210                 215                 220

Leu Ser Trp Tyr Ser Asp Pro Gly Leu Ala Gly Val Ser Leu Thr Gly
225                 230                 235                 240

Gly Leu Ser Tyr Lys Glu Asp Thr Lys Glu Leu Val Val Ala Lys Ala
                245                 250                 255

Gly Val Tyr Tyr Val Phe Phe Gln Leu Glu Leu Arg Arg Val Val Ala
            260                 265                 270

Gly Glu Gly Ser Gly Ser Val Ser Leu Ala Leu His Leu Gln Pro Leu
        275                 280                 285

Arg Ser Ala Ala Gly Ala Ala Ala Leu Ala Leu Thr Val Asp Leu Pro
    290                 295                 300

Pro Ala Ser Ser Glu Ala Arg Asn Ser Ala Phe Gly Phe Gln Gly Arg
305                 310                 315                 320

Leu Leu His Leu Ser Ala Gly Gln Arg Leu Gly Val His Leu His Thr
                325                 330                 335

Glu Ala Arg Ala Arg His Ala Trp Gln Leu Thr Gln Gly Ala Thr Val
            340                 345                 350
```

Leu Gly Leu Phe Arg Val Thr Pro Glu Ile Pro Ala Gly Leu
355 360 365

+ADw-210+AD4- 98
+ADw-211+AD4- 360
+ADw-212+AD4- PRT
+ADw-213+AD4- Secuencia artificial

+ADw-220+AD4-
+ADw-223+AD4- hu 4-1BBL dim+AOk-rico (80-254) conectado mediante enlazador (G4S)2

+ADw-400+AD4- 98

Asp Pro Ala Gly Leu Leu Asp Leu Arg Gln Gly Met Phe Ala Gln Leu
1 5 10 15

Val Ala Gln Asn Val Leu Leu Ile Asp Gly Pro Leu Ser Trp Tyr Ser
20 25 30

Asp Pro Gly Leu Ala Gly Val Ser Leu Thr Gly Gly Leu Ser Tyr Lys
35 40 45

Glu Asp Thr Lys Glu Leu Val Val Ala Lys Ala Gly Val Tyr Tyr Val
50 55 60

Phe Phe Gln Leu Glu Leu Arg Arg Val Val Ala Gly Glu Gly Ser Gly
65 70 75 80

Ser Val Ser Leu Ala Leu His Leu Gln Pro Leu Arg Ser Ala Ala Gly
85 90 95

Ala Ala Ala Leu Ala Leu Thr Val Asp Leu Pro Pro Ala Ser Ser Glu
100 105 110

Ala Arg Asn Ser Ala Phe Gly Phe Gln Gly Arg Leu Leu His Leu Ser
115 120 125

Ala Gly Gln Arg Leu Gly Val His Leu His Thr Glu Ala Arg Ala Arg
130 135 140

His Ala Trp Gln Leu Thr Gln Gly Ala Thr Val Leu Gly Leu Phe Arg
145 150 155 160

Val Thr Pro Glu Ile Pro Ala Gly Leu Pro Ser Pro Arg Ser Glu Gly
165 170 175

Gly Gly Gly Ser Gly Gly Gly Gly Ser Asp Pro Ala Gly Leu Leu Asp
180 185 190

Leu Arg Gln Gly Met Phe Ala Gln Leu Val Ala Gln Asn Val Leu Leu

195 200 205

Ile Asp Gly Pro Leu Ser Trp Tyr Ser Asp Pro Gly Leu Ala Gly Val
210 215 220

Ser Leu Thr Gly Gly Leu Ser Tyr Lys Glu Asp Thr Lys Glu Leu Val
225 230 235 240

Val Ala Lys Ala Gly Val Tyr Tyr Val Phe Phe Gln Leu Glu Leu Arg
245 250 255

Arg Val Val Ala Gly Glu Gly Ser Gly Ser Val Ser Leu Ala Leu His
260 265 270

Leu Gln Pro Leu Arg Ser Ala Ala Gly Ala Ala Ala Leu Ala Leu Thr
275 280 285

Val Asp Leu Pro Pro Ala Ser Ser Glu Ala Arg Asn Ser Ala Phe Gly
290 295 300

Phe Gln Gly Arg Leu Leu His Leu Ser Ala Gly Gln Arg Leu Gly Val
305 310 315 320

His Leu His Thr Glu Ala Arg Ala Arg His Ala Trp Gln Leu Thr Gln
325 330 335

Gly Ala Thr Val Leu Gly Leu Phe Arg Val Thr Pro Glu Ile Pro Ala
340 345 350

Gly Leu Pro Ser Pro Arg Ser Glu
355 360

+ADw-210+AD4- 99
+ADw-211+AD4- 416
+ADw-212+AD4- PRT
+ADw-213+AD4- Secuencia artificial

+ADw-220+AD4-
+ADw-223+AD4- hu 4-1BBL dim+AOk-rico (52-254) conectado mediante enlazador (G4S)2

+ADw-400+AD4- 99

Pro Trp Ala Val Ser Gly Ala Arg Ala Ser Pro Gly Ser Ala Ala Ser
1 5 10 15

Pro Arg Leu Arg Glu Gly Pro Glu Leu Ser Pro Asp Asp Pro Ala Gly
20 25 30

Leu Leu Asp Leu Arg Gln Gly Met Phe Ala Gln Leu Val Ala Gln Asn
35 40 45

```
Val Leu Leu Ile Asp Gly Pro Leu Ser Trp Tyr Ser Asp Pro Gly Leu
    50                  55                  60

Ala Gly Val Ser Leu Thr Gly Gly Leu Ser Tyr Lys Glu Asp Thr Lys
65                  70                  75                  80

Glu Leu Val Val Ala Lys Ala Gly Val Tyr Tyr Val Phe Phe Gln Leu
                85                  90                  95

Glu Leu Arg Arg Val Val Ala Gly Glu Gly Ser Gly Ser Val Ser Leu
            100                 105                 110

Ala Leu His Leu Gln Pro Leu Arg Ser Ala Ala Gly Ala Ala Ala Leu
        115                 120                 125

Ala Leu Thr Val Asp Leu Pro Pro Ala Ser Ser Glu Ala Arg Asn Ser
    130                 135                 140

Ala Phe Gly Phe Gln Gly Arg Leu Leu His Leu Ser Ala Gly Gln Arg
145                 150                 155                 160

Leu Gly Val His Leu His Thr Glu Ala Arg Ala Arg His Ala Trp Gln
                165                 170                 175

Leu Thr Gln Gly Ala Thr Val Leu Gly Leu Phe Arg Val Thr Pro Glu
            180                 185                 190

Ile Pro Ala Gly Leu Pro Ser Pro Arg Ser Glu Gly Gly Gly Gly Ser
        195                 200                 205

Gly Gly Gly Gly Ser Pro Trp Ala Val Ser Gly Ala Arg Ala Ser Pro
    210                 215                 220

Gly Ser Ala Ala Ser Pro Arg Leu Arg Glu Gly Pro Glu Leu Ser Pro
225                 230                 235                 240

Asp Asp Pro Ala Gly Leu Leu Asp Leu Arg Gln Gly Met Phe Ala Gln
                245                 250                 255

Leu Val Ala Gln Asn Val Leu Leu Ile Asp Gly Pro Leu Ser Trp Tyr
            260                 265                 270

Ser Asp Pro Gly Leu Ala Gly Val Ser Leu Thr Gly Gly Leu Ser Tyr
        275                 280                 285

Lys Glu Asp Thr Lys Glu Leu Val Val Ala Lys Ala Gly Val Tyr Tyr
```

290 295 300

Val Phe Phe Gln Leu Glu Leu Arg Arg Val Val Ala Gly Glu Gly Ser
305 310 315 320

Gly Ser Val Ser Leu Ala Leu His Leu Gln Pro Leu Arg Ser Ala Ala
325 330 335

Gly Ala Ala Ala Leu Ala Leu Thr Val Asp Leu Pro Pro Ala Ser Ser
340 345 350

Glu Ala Arg Asn Ser Ala Phe Gly Phe Gln Gly Arg Leu Leu His Leu
355 360 365

Ser Ala Gly Gln Arg Leu Gly Val His Leu His Thr Glu Ala Arg Ala
370 375 380

Arg His Ala Trp Gln Leu Thr Gln Gly Ala Thr Val Leu Gly Leu Phe
385 390 395 400

Arg Val Thr Pro Glu Ile Pro Ala Gly Leu Pro Ser Pro Arg Ser Glu
405 410 415

+ADw-210+AD4- 100
+ADw-211+AD4- 5
+ADw-212+AD4- PRT
+ADw-213+AD4- Secuencia artificial

+ADw-220+AD4-
+ADw-223+AD4- CDR-H1 de FAP(4B9)

+ADw-400+AD4- 100

Ser Tyr Ala Met Ser
1 5

+ADw-210+AD4- 101
+ADw-211+AD4- 17
+ADw-212+AD4- PRT
+ADw-213+AD4- Secuencia artificial

+ADw-220+AD4-
+ADw-223+AD4- CDR-H2 de FAP(4B9)

+ADw-400+AD4- 101

Ala Ile Ile Gly Ser Gly Ala Ser Thr Tyr Tyr Ala Asp Ser Val Lys
1 5 10 15

Gly

+ADw-210+AD4- 102
+ADw-211+AD4- 8
+ADw-212+AD4- PRT
+ADw-213+AD4- Secuencia artificial

+ADw-220+AD4-
+ADw-223+AD4- CDR-H3 de FAP(4B9)

+ADw-400+AD4- 102

Gly Trp Phe Gly Gly Phe Asn Tyr
1 5

+ADw-210+AD4- 103
+ADw-211+AD4- 12
+ADw-212+AD4- PRT
+ADw-213+AD4- Secuencia artificial

+ADw-220+AD4-
+ADw-223+AD4- CDR-L1 de FAP(4B9)

+ADw-400+AD4- 103

Arg Ala Ser Gln Ser Val Thr Ser Ser Tyr Leu Ala
1 5 10

+ADw-210+AD4- 104
+ADw-211+AD4- 7
+ADw-212+AD4- PRT
+ADw-213+AD4- Secuencia artificial

+ADw-220+AD4-
+ADw-223+AD4- CDR-L2 de FAP(4B9)

+ADw-400+AD4- 104

Val Gly Ser Arg Arg Ala Thr
1 5

+ADw-210+AD4- 105
+ADw-211+AD4- 9
+ADw-212+AD4- PRT
+ADw-213+AD4- Secuencia artificial

+ADw-220+AD4-
+ADw-223+AD4- CDR-L3 de FAP(4B9)

+ADw-400+AD4- 105

Gln Gln Gly Ile Met Leu Pro Pro Thr
1 5

+ADw-210+AD4- 106
+ADw-211+AD4- 117
+ADw-212+AD4- PRT
+ADw-213+AD4- Secuencia artificial

+ADw-220+AD4-
+ADw-223+AD4- FAP(4B9) VH

+ADw-400+AD4- 106

```
Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1               5                  10                  15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Ser Tyr
            20                  25                  30

Ala Met Ser Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
        35                  40                  45

Ser Ala Ile Ile Gly Ser Gly Ala Ser Thr Tyr Tyr Ala Asp Ser Val
    50                  55                  60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65                  70                  75                  80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95

Ala Lys Gly Trp Phe Gly Gly Phe Asn Tyr Trp Gly Gln Gly Thr Leu
            100                 105                 110

Val Thr Val Ser Ser
        115
```

+ADw-210+AD4- 107
+ADw-211+AD4- 108
+ADw-212+AD4- PRT
+ADw-213+AD4- Secuencia artificial

+ADw-220+AD4-
+ADw-223+AD4- FAP(4B9) VL

+ADw-400+AD4- 107

```
Glu Ile Val Leu Thr Gln Ser Pro Gly Thr Leu Ser Leu Ser Pro Gly
1               5                  10                  15

Glu Arg Ala Thr Leu Ser Cys Arg Ala Ser Gln Ser Val Thr Ser Ser
            20                  25                  30

Tyr Leu Ala Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Arg Leu Leu
        35                  40                  45

Ile Asn Val Gly Ser Arg Arg Ala Thr Gly Ile Pro Asp Arg Phe Ser
    50                  55                  60

Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Arg Leu Glu
65                  70                  75                  80
```

```
Pro Glu Asp Phe Ala Val Tyr Tyr Cys Gln Gln Gly Ile Met Leu Pro
                85                  90                  95

Pro Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys
            100                 105
```

+ADw-210+AD4- 108
+ADw-211+AD4- 718
+ADw-212+AD4- PRT
+ADw-213+AD4- Secuencia artificial

+ADw-220+AD4-
+ADw-223+AD4- hu 4-1BBL dim+AOk-rico (71-254) - CH1+ACo- cadena Fc pomo

+ADw-400+AD4- 108

```
Arg Glu Gly Pro Glu Leu Ser Pro Asp Asp Pro Ala Gly Leu Leu Asp
1               5                  10                  15

Leu Arg Gln Gly Met Phe Ala Gln Leu Val Ala Gln Asn Val Leu Leu
            20                  25                  30

Ile Asp Gly Pro Leu Ser Trp Tyr Ser Asp Pro Gly Leu Ala Gly Val
        35                  40                  45

Ser Leu Thr Gly Gly Leu Ser Tyr Lys Glu Asp Thr Lys Glu Leu Val
    50                  55                  60

Val Ala Lys Ala Gly Val Tyr Tyr Val Phe Phe Gln Leu Glu Leu Arg
65                  70                  75                  80

Arg Val Val Ala Gly Glu Gly Ser Gly Ser Val Ser Leu Ala Leu His
                85                  90                  95

Leu Gln Pro Leu Arg Ser Ala Ala Gly Ala Ala Ala Leu Ala Leu Thr
            100                 105                 110

Val Asp Leu Pro Pro Ala Ser Ser Glu Ala Arg Asn Ser Ala Phe Gly
        115                 120                 125

Phe Gln Gly Arg Leu Leu His Leu Ser Ala Gly Gln Arg Leu Gly Val
    130                 135                 140

His Leu His Thr Glu Ala Arg Ala Arg His Ala Trp Gln Leu Thr Gln
145                 150                 155                 160

Gly Ala Thr Val Leu Gly Leu Phe Arg Val Thr Pro Glu Ile Pro Ala
                165                 170                 175
```

```
Gly Leu Pro Ser Pro Arg Ser Glu Gly Gly Gly Gly Ser Gly Gly Gly
            180                 185                 190

Gly Ser Arg Glu Gly Pro Glu Leu Ser Pro Asp Asp Pro Ala Gly Leu
        195                 200                 205

Leu Asp Leu Arg Gln Gly Met Phe Ala Gln Leu Val Ala Gln Asn Val
    210                 215                 220

Leu Leu Ile Asp Gly Pro Leu Ser Trp Tyr Ser Asp Pro Gly Leu Ala
225                 230                 235                 240

Gly Val Ser Leu Thr Gly Gly Leu Ser Tyr Lys Glu Asp Thr Lys Glu
                245                 250                 255

Leu Val Val Ala Lys Ala Gly Val Tyr Tyr Val Phe Phe Gln Leu Glu
            260                 265                 270

Leu Arg Arg Val Val Ala Gly Glu Gly Ser Gly Ser Val Ser Leu Ala
        275                 280                 285

Leu His Leu Gln Pro Leu Arg Ser Ala Ala Gly Ala Ala Ala Leu Ala
    290                 295                 300

Leu Thr Val Asp Leu Pro Pro Ala Ser Ser Glu Ala Arg Asn Ser Ala
305                 310                 315                 320

Phe Gly Phe Gln Gly Arg Leu Leu His Leu Ser Ala Gly Gln Arg Leu
                325                 330                 335

Gly Val His Leu His Thr Glu Ala Arg Ala Arg His Ala Trp Gln Leu
            340                 345                 350

Thr Gln Gly Ala Thr Val Leu Gly Leu Phe Arg Val Thr Pro Glu Ile
        355                 360                 365

Pro Ala Gly Leu Pro Ser Pro Arg Ser Glu Gly Gly Gly Gly Ser Gly
    370                 375                 380

Gly Gly Gly Ser Ala Ser Thr Lys Gly Pro Ser Val Phe Pro Leu Ala
385                 390                 395                 400

Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu Gly Cys Leu
                405                 410                 415

Val Glu Asp Tyr Phe Pro Glu Pro Val Thr Val Ser Trp Asn Ser Gly
            420                 425                 430
```

```
Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala Val Leu Gln Ser Ser
        435                 440                 445

Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser Ser Ser Leu
    450                 455                 460

Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys Pro Ser Asn Thr
465                 470                 475                 480

Lys Val Asp Glu Lys Val Glu Pro Lys Ser Cys Asp Lys Thr His Thr
                485                 490                 495

Cys Pro Pro Cys Pro Ala Pro Glu Ala Ala Gly Gly Pro Ser Val Phe
            500                 505                 510

Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro
        515                 520                 525

Glu Val Thr Cys Val Val Val Asp Val Ser His Glu Asp Pro Glu Val
    530                 535                 540

Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr
545                 550                 555                 560

Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg Val Val Ser Val
                565                 570                 575

Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys
            580                 585                 590

Lys Val Ser Asn Lys Ala Leu Gly Ala Pro Ile Glu Lys Thr Ile Ser
        595                 600                 605

Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro
    610                 615                 620

Cys Arg Asp Glu Leu Thr Lys Asn Gln Val Ser Leu Trp Cys Leu Val
625                 630                 635                 640

Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly
                645                 650                 655

Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp
            660                 665                 670

Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp
```

675 680 685

Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His Glu Ala Leu His
690 695 700

Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly Lys
705 710 715

+ADw-210+AD4- 109
+ADw-211+AD4- 301
+ADw-212+AD4- PRT
+ADw-213+AD4- Secuencia artificial

+ADw-220+AD4-
+ADw-223+AD4- Hu 4-1BBL monom+AOk-rico (71-254)-CL+ACo-

+ADw-400+AD4- 109

Arg Glu Gly Pro Glu Leu Ser Pro Asp Asp Pro Ala Gly Leu Leu Asp
1 5 10 15

Leu Arg Gln Gly Met Phe Ala Gln Leu Val Ala Gln Asn Val Leu Leu
20 25 30

Ile Asp Gly Pro Leu Ser Trp Tyr Ser Asp Pro Gly Leu Ala Gly Val
35 40 45

Ser Leu Thr Gly Gly Leu Ser Tyr Lys Glu Asp Thr Lys Glu Leu Val
50 55 60

Val Ala Lys Ala Gly Val Tyr Tyr Val Phe Phe Gln Leu Glu Leu Arg
65 70 75 80

Arg Val Val Ala Gly Glu Gly Ser Gly Ser Val Ser Leu Ala Leu His
85 90 95

Leu Gln Pro Leu Arg Ser Ala Ala Gly Ala Ala Ala Leu Ala Leu Thr
100 105 110

Val Asp Leu Pro Pro Ala Ser Ser Glu Ala Arg Asn Ser Ala Phe Gly
115 120 125

Phe Gln Gly Arg Leu Leu His Leu Ser Ala Gly Gln Arg Leu Gly Val
130 135 140

His Leu His Thr Glu Ala Arg Ala Arg His Ala Trp Gln Leu Thr Gln
145 150 155 160

Gly Ala Thr Val Leu Gly Leu Phe Arg Val Thr Pro Glu Ile Pro Ala
165 170 175

```
Gly Leu Pro Ser Pro Arg Ser Glu Gly Gly Gly Gly Ser Gly Gly Gly
            180                 185                 190

Gly Ser Arg Thr Val Ala Ala Pro Ser Val Phe Ile Phe Pro Pro Ser
        195                 200                 205

Asp Arg Lys Leu Lys Ser Gly Thr Ala Ser Val Val Cys Leu Leu Asn
    210                 215                 220

Asn Phe Tyr Pro Arg Glu Ala Lys Val Gln Trp Lys Val Asp Asn Ala
225                 230                 235                 240

Leu Gln Ser Gly Asn Ser Gln Glu Ser Val Thr Glu Gln Asp Ser Lys
                245                 250                 255

Asp Ser Thr Tyr Ser Leu Ser Ser Thr Leu Thr Leu Ser Lys Ala Asp
            260                 265                 270

Tyr Glu Lys His Lys Val Tyr Ala Cys Glu Val Thr His Gln Gly Leu
        275                 280                 285

Ser Ser Pro Val Thr Lys Ser Phe Asn Arg Gly Glu Cys
    290                 295                 300


+ADw-210+AD4-  110
+ADw-211+AD4-  296
+ADw-212+AD4-  PRT
+ADw-213+AD4-  Secuencia artificial

+ADw-220+AD4-
+ADw-223+AD4-  hu 4-1BBL monom+AOk-rico (71-254) -(G4S)1- CL+ACo-

+ADw-400+AD4-  110

Arg Glu Gly Pro Glu Leu Ser Pro Asp Asp Pro Ala Gly Leu Leu Asp
1               5                  10                  15

Leu Arg Gln Gly Met Phe Ala Gln Leu Val Ala Gln Asn Val Leu Leu
            20                  25                  30

Ile Asp Gly Pro Leu Ser Trp Tyr Ser Asp Pro Gly Leu Ala Gly Val
        35                  40                  45

Ser Leu Thr Gly Gly Leu Ser Tyr Lys Glu Asp Thr Lys Glu Leu Val
    50                  55                  60

Val Ala Lys Ala Gly Val Tyr Tyr Val Phe Phe Gln Leu Glu Leu Arg
65                  70                  75                  80
```

```
Arg Val Val Ala Gly Glu Gly Ser Gly Ser Val Ser Leu Ala Leu His
                85                  90                  95

Leu Gln Pro Leu Arg Ser Ala Ala Gly Ala Ala Ala Leu Ala Leu Thr
            100                 105                 110

Val Asp Leu Pro Pro Ala Ser Ser Glu Ala Arg Asn Ser Ala Phe Gly
        115                 120                 125

Phe Gln Gly Arg Leu Leu His Leu Ser Ala Gly Gln Arg Leu Gly Val
    130                 135                 140

His Leu His Thr Glu Ala Arg Ala Arg His Ala Trp Gln Leu Thr Gln
145                 150                 155                 160

Gly Ala Thr Val Leu Gly Leu Phe Arg Val Thr Pro Glu Ile Pro Ala
                165                 170                 175

Gly Leu Pro Ser Pro Arg Ser Glu Gly Gly Gly Gly Ser Arg Thr Val
            180                 185                 190

Ala Ala Pro Ser Val Phe Ile Phe Pro Pro Ser Asp Arg Lys Leu Lys
        195                 200                 205

Ser Gly Thr Ala Ser Val Val Cys Leu Leu Asn Asn Phe Tyr Pro Arg
    210                 215                 220

Glu Ala Lys Val Gln Trp Lys Val Asp Asn Ala Leu Gln Ser Gly Asn
225                 230                 235                 240

Ser Gln Glu Ser Val Thr Glu Gln Asp Ser Lys Asp Ser Thr Tyr Ser
                245                 250                 255

Leu Ser Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu Lys His Lys
            260                 265                 270

Val Tyr Ala Cys Glu Val Thr His Gln Gly Leu Ser Ser Pro Val Thr
        275                 280                 285

Lys Ser Phe Asn Arg Gly Glu Cys
    290                 295


+ADw-210+AD4-  111
+ADw-211+AD4-  756
+ADw-212+AD4-  PRT
+ADw-213+AD4-  Secuencia artificial

+ADw-220+AD4-
```

+ADw-223+AD4- hu 4-1BBL dim+AOk-rico (52-254) - CH1+ACo- cadena Fc pomo

+ADw-400+AD4- 111

```
Pro Trp Ala Val Ser Gly Ala Arg Ala Ser Pro Gly Ser Ala Ala Ser
1               5                  10                  15

Pro Arg Leu Arg Glu Gly Pro Glu Leu Ser Pro Asp Asp Pro Ala Gly
            20                  25                  30

Leu Leu Asp Leu Arg Gln Gly Met Phe Ala Gln Leu Val Ala Gln Asn
        35                  40                  45

Val Leu Leu Ile Asp Gly Pro Leu Ser Trp Tyr Ser Asp Pro Gly Leu
    50                  55                  60

Ala Gly Val Ser Leu Thr Gly Gly Leu Ser Tyr Lys Glu Asp Thr Lys
65                  70                  75                  80

Glu Leu Val Val Ala Lys Ala Gly Val Tyr Tyr Val Phe Phe Gln Leu
                85                  90                  95

Glu Leu Arg Arg Val Val Ala Gly Glu Gly Ser Gly Ser Val Ser Leu
            100                 105                 110

Ala Leu His Leu Gln Pro Leu Arg Ser Ala Ala Gly Ala Ala Ala Leu
        115                 120                 125

Ala Leu Thr Val Asp Leu Pro Pro Ala Ser Ser Glu Ala Arg Asn Ser
    130                 135                 140

Ala Phe Gly Phe Gln Gly Arg Leu Leu His Leu Ser Ala Gly Gln Arg
145                 150                 155                 160

Leu Gly Val His Leu His Thr Glu Ala Arg Ala Arg His Ala Trp Gln
                165                 170                 175

Leu Thr Gln Gly Ala Thr Val Leu Gly Leu Phe Arg Val Thr Pro Glu
            180                 185                 190

Ile Pro Ala Gly Leu Pro Ser Pro Arg Ser Glu Gly Gly Gly Gly Ser
        195                 200                 205

Gly Gly Gly Gly Ser Pro Trp Ala Val Ser Gly Ala Arg Ala Ser Pro
    210                 215                 220

Gly Ser Ala Ala Ser Pro Arg Leu Arg Glu Gly Pro Glu Leu Ser Pro
225                 230                 235                 240
```

```
Asp Asp Pro Ala Gly Leu Leu Asp Leu Arg Gln Gly Met Phe Ala Gln
                245                 250                 255

Leu Val Ala Gln Asn Val Leu Leu Ile Asp Gly Pro Leu Ser Trp Tyr
            260                 265                 270

Ser Asp Pro Gly Leu Ala Gly Val Ser Leu Thr Gly Gly Leu Ser Tyr
        275                 280                 285

Lys Glu Asp Thr Lys Glu Leu Val Val Ala Lys Ala Gly Val Tyr Tyr
    290                 295                 300

Val Phe Phe Gln Leu Glu Leu Arg Arg Val Val Ala Gly Glu Gly Ser
305                 310                 315                 320

Gly Ser Val Ser Leu Ala Leu His Leu Gln Pro Leu Arg Ser Ala Ala
                325                 330                 335

Gly Ala Ala Ala Leu Ala Leu Thr Val Asp Leu Pro Pro Ala Ser Ser
            340                 345                 350

Glu Ala Arg Asn Ser Ala Phe Gly Phe Gln Gly Arg Leu Leu His Leu
        355                 360                 365

Ser Ala Gly Gln Arg Leu Gly Val His Leu His Thr Glu Ala Arg Ala
    370                 375                 380

Arg His Ala Trp Gln Leu Thr Gln Gly Ala Thr Val Leu Gly Leu Phe
385                 390                 395                 400

Arg Val Thr Pro Glu Ile Pro Ala Gly Leu Pro Ser Pro Arg Ser Glu
                405                 410                 415

Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Ala Ser Thr Lys Gly Pro
            420                 425                 430

Ser Val Phe Pro Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr
        435                 440                 445

Ala Ala Leu Gly Cys Leu Val Glu Asp Tyr Phe Pro Glu Pro Val Thr
    450                 455                 460

Val Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro
465                 470                 475                 480

Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr
                485                 490                 495
```

```
Val Pro Ser Ser Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn
            500                 505                 510

His Lys Pro Ser Asn Thr Lys Val Asp Glu Lys Val Glu Pro Lys Ser
        515                 520                 525

Cys Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Ala Ala
    530                 535                 540

Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu
545                 550                 555                 560

Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser
                565                 570                 575

His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu
            580                 585                 590

Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr
        595                 600                 605

Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn
    610                 615                 620

Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Gly Ala Pro
625                 630                 635                 640

Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln
                645                 650                 655

Val Tyr Thr Leu Pro Pro Cys Arg Asp Glu Leu Thr Lys Asn Gln Val
            660                 665                 670

Ser Leu Trp Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val
        675                 680                 685

Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro
    690                 695                 700

Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr
705                 710                 715                 720

Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val
                725                 730                 735

Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu
```

740 745 750

Ser Pro Gly Lys
755

+ADw-210+AD4- 112
+ADw-211+AD4- 320
+ADw-212+AD4- PRT
+ADw-213+AD4- Secuencia artificial

+ADw-220+AD4-
+ADw-223+AD4- Hu 4-1BBL monom+AOk-rico (52-254)-CL+ACo-

+ADw-400+AD4- 112

Pro Trp Ala Val Ser Gly Ala Arg Ala Ser Pro Gly Ser Ala Ala Ser
1 5 10 15

Pro Arg Leu Arg Glu Gly Pro Glu Leu Ser Pro Asp Asp Pro Ala Gly
20 25 30

Leu Leu Asp Leu Arg Gln Gly Met Phe Ala Gln Leu Val Ala Gln Asn
35 40 45

Val Leu Leu Ile Asp Gly Pro Leu Ser Trp Tyr Ser Asp Pro Gly Leu
50 55 60

Ala Gly Val Ser Leu Thr Gly Gly Leu Ser Tyr Lys Glu Asp Thr Lys
65 70 75 80

Glu Leu Val Val Ala Lys Ala Gly Val Tyr Tyr Val Phe Phe Gln Leu
85 90 95

Glu Leu Arg Arg Val Val Ala Gly Glu Gly Ser Gly Ser Val Ser Leu
100 105 110

Ala Leu His Leu Gln Pro Leu Arg Ser Ala Ala Gly Ala Ala Ala Leu
115 120 125

Ala Leu Thr Val Asp Leu Pro Pro Ala Ser Ser Glu Ala Arg Asn Ser
130 135 140

Ala Phe Gly Phe Gln Gly Arg Leu Leu His Leu Ser Ala Gly Gln Arg
145 150 155 160

Leu Gly Val His Leu His Thr Glu Ala Arg Ala Arg His Ala Trp Gln
165 170 175

Leu Thr Gln Gly Ala Thr Val Leu Gly Leu Phe Arg Val Thr Pro Glu
180 185 190

```
Ile Pro Ala Gly Leu Pro Ser Pro Arg Ser Glu Gly Gly Gly Gly Ser
        195                 200                 205

Gly Gly Gly Gly Ser Arg Thr Val Ala Ala Pro Ser Val Phe Ile Phe
    210                 215                 220

Pro Pro Ser Asp Arg Lys Leu Lys Ser Gly Thr Ala Ser Val Val Cys
225                 230                 235                 240

Leu Leu Asn Asn Phe Tyr Pro Arg Glu Ala Lys Val Gln Trp Lys Val
                245                 250                 255

Asp Asn Ala Leu Gln Ser Gly Asn Ser Gln Glu Ser Val Thr Glu Gln
            260                 265                 270

Asp Ser Lys Asp Ser Thr Tyr Ser Leu Ser Ser Thr Leu Thr Leu Ser
        275                 280                 285

Lys Ala Asp Tyr Glu Lys His Lys Val Tyr Ala Cys Glu Val Thr His
    290                 295                 300

Gln Gly Leu Ser Ser Pro Val Thr Lys Ser Phe Asn Arg Gly Glu Cys
305                 310                 315                 320
```

+ADw-210+AD4- 113
+ADw-211+AD4- 700
+ADw-212+AD4- PRT
+ADw-213+AD4- Secuencia artificial

+ADw-220+AD4-
+ADw-223+AD4- hu 4-1BBL dim+AOk-rico (80-254) - CH1+ACo- cadena Fc pomo

+ADw-400+AD4- 113

```
Asp Pro Ala Gly Leu Leu Asp Leu Arg Gln Gly Met Phe Ala Gln Leu
1               5                   10                  15

Val Ala Gln Asn Val Leu Leu Ile Asp Gly Pro Leu Ser Trp Tyr Ser
            20                  25                  30

Asp Pro Gly Leu Ala Gly Val Ser Leu Thr Gly Gly Leu Ser Tyr Lys
        35                  40                  45

Glu Asp Thr Lys Glu Leu Val Val Ala Lys Ala Gly Val Tyr Tyr Val
    50                  55                  60

Phe Phe Gln Leu Glu Leu Arg Arg Val Val Ala Gly Glu Gly Ser Gly
65                  70                  75                  80
```

```
Ser Val Ser Leu Ala Leu His Leu Gln Pro Leu Arg Ser Ala Ala Gly
                85                  90                  95

Ala Ala Ala Leu Ala Leu Thr Val Asp Leu Pro Pro Ala Ser Ser Glu
            100                 105                 110

Ala Arg Asn Ser Ala Phe Gly Phe Gln Gly Arg Leu Leu His Leu Ser
        115                 120                 125

Ala Gly Gln Arg Leu Gly Val His Leu His Thr Glu Ala Arg Ala Arg
    130                 135                 140

His Ala Trp Gln Leu Thr Gln Gly Ala Thr Val Leu Gly Leu Phe Arg
145                 150                 155                 160

Val Thr Pro Glu Ile Pro Ala Gly Leu Pro Ser Pro Arg Ser Glu Gly
                165                 170                 175

Gly Gly Gly Ser Gly Gly Gly Gly Ser Asp Pro Ala Gly Leu Leu Asp
            180                 185                 190

Leu Arg Gln Gly Met Phe Ala Gln Leu Val Ala Gln Asn Val Leu Leu
        195                 200                 205

Ile Asp Gly Pro Leu Ser Trp Tyr Ser Asp Pro Gly Leu Ala Gly Val
    210                 215                 220

Ser Leu Thr Gly Gly Leu Ser Tyr Lys Glu Asp Thr Lys Glu Leu Val
225                 230                 235                 240

Val Ala Lys Ala Gly Val Tyr Tyr Val Phe Phe Gln Leu Glu Leu Arg
                245                 250                 255

Arg Val Val Ala Gly Glu Gly Ser Gly Ser Val Ser Leu Ala Leu His
            260                 265                 270

Leu Gln Pro Leu Arg Ser Ala Ala Gly Ala Ala Ala Leu Ala Leu Thr
        275                 280                 285

Val Asp Leu Pro Pro Ala Ser Ser Glu Ala Arg Asn Ser Ala Phe Gly
    290                 295                 300

Phe Gln Gly Arg Leu Leu His Leu Ser Ala Gly Gln Arg Leu Gly Val
305                 310                 315                 320

His Leu His Thr Glu Ala Arg Ala Arg His Ala Trp Gln Leu Thr Gln
                325                 330                 335
```

```
Gly Ala Thr Val Leu Gly Leu Phe Arg Val Thr Pro Glu Ile Pro Ala
            340                 345                 350

Gly Leu Pro Ser Pro Arg Ser Glu Gly Gly Gly Gly Ser Gly Gly Gly
        355                 360                 365

Gly Ser Ala Ser Thr Lys Gly Pro Ser Val Phe Pro Leu Ala Pro Ser
    370                 375                 380

Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu Gly Cys Leu Val Glu
385                 390                 395                 400

Asp Tyr Phe Pro Glu Pro Val Thr Val Ser Trp Asn Ser Gly Ala Leu
                405                 410                 415

Thr Ser Gly Val His Thr Phe Pro Ala Val Leu Gln Ser Ser Gly Leu
            420                 425                 430

Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser Ser Ser Leu Gly Thr
        435                 440                 445

Gln Thr Tyr Ile Cys Asn Val Asn His Lys Pro Ser Asn Thr Lys Val
    450                 455                 460

Asp Glu Lys Val Glu Pro Lys Ser Cys Asp Lys Thr His Thr Cys Pro
465                 470                 475                 480

Pro Cys Pro Ala Pro Glu Ala Ala Gly Gly Pro Ser Val Phe Leu Phe
                485                 490                 495

Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val
            500                 505                 510

Thr Cys Val Val Val Asp Val Ser His Glu Asp Pro Glu Val Lys Phe
        515                 520                 525

Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys Pro
    530                 535                 540

Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg Val Val Ser Val Leu Thr
545                 550                 555                 560

Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val
                565                 570                 575

Ser Asn Lys Ala Leu Gly Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala
```

580 585 590

Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Cys Arg
595 600 605

Asp Glu Leu Thr Lys Asn Gln Val Ser Leu Trp Cys Leu Val Lys Gly
610 615 620

Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro
625 630 635 640

Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser
645 650 655

Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln Gln
660 665 670

Gly Asn Val Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn His
675 680 685

Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly Lys
690 695 700

+ADw-210+AD4- 114
+ADw-211+AD4- 292
+ADw-212+AD4- PRT
+ADw-213+AD4- Secuencia artificial

+ADw-220+AD4-
+ADw-223+AD4- Hu 4-1BBL monom+AOk-rico (80-254)-CL+ACo-

+ADw-400+AD4- 114

Asp Pro Ala Gly Leu Leu Asp Leu Arg Gln Gly Met Phe Ala Gln Leu
1 5 10 15

Val Ala Gln Asn Val Leu Leu Ile Asp Gly Pro Leu Ser Trp Tyr Ser
20 25 30

Asp Pro Gly Leu Ala Gly Val Ser Leu Thr Gly Gly Leu Ser Tyr Lys
35 40 45

Glu Asp Thr Lys Glu Leu Val Val Ala Lys Ala Gly Val Tyr Tyr Val
50 55 60

Phe Phe Gln Leu Glu Leu Arg Arg Val Val Ala Gly Glu Gly Ser Gly
65 70 75 80

Ser Val Ser Leu Ala Leu His Leu Gln Pro Leu Arg Ser Ala Ala Gly
85 90 95

```
Ala Ala Ala Leu Ala Leu Thr Val Asp Leu Pro Pro Ala Ser Ser Glu
            100                 105                 110

Ala Arg Asn Ser Ala Phe Gly Phe Gln Gly Arg Leu Leu His Leu Ser
        115                 120                 125

Ala Gly Gln Arg Leu Gly Val His Leu His Thr Glu Ala Arg Ala Arg
    130                 135                 140

His Ala Trp Gln Leu Thr Gln Gly Ala Thr Val Leu Gly Leu Phe Arg
145                 150                 155                 160

Val Thr Pro Glu Ile Pro Ala Gly Leu Pro Ser Pro Arg Ser Glu Gly
                165                 170                 175

Gly Gly Gly Ser Gly Gly Gly Gly Ser Arg Thr Val Ala Ala Pro Ser
            180                 185                 190

Val Phe Ile Phe Pro Pro Ser Asp Arg Lys Leu Lys Ser Gly Thr Ala
        195                 200                 205

Ser Val Val Cys Leu Leu Asn Asn Phe Tyr Pro Arg Glu Ala Lys Val
    210                 215                 220

Gln Trp Lys Val Asp Asn Ala Leu Gln Ser Gly Asn Ser Gln Glu Ser
225                 230                 235                 240

Val Thr Glu Gln Asp Ser Lys Asp Ser Thr Tyr Ser Leu Ser Ser Thr
                245                 250                 255

Leu Thr Leu Ser Lys Ala Asp Tyr Glu Lys His Lys Val Tyr Ala Cys
            260                 265                 270

Glu Val Thr His Gln Gly Leu Ser Ser Pro Val Thr Lys Ser Phe Asn
        275                 280                 285

Arg Gly Glu Cys
    290


+ADw-210+AD4-  115
+ADw-211+AD4-  722
+ADw-212+AD4-  PRT
+ADw-213+AD4-  Secuencia artificial

+ADw-220+AD4-
+ADw-223+AD4-  hu 4-1BBL dim+AOk-rico (71-254) - CL+ACo- cadena Fc pomo

+ADw-400+AD4-  115
```

```
Arg Glu Gly Pro Glu Leu Ser Pro Asp Asp Pro Ala Gly Leu Leu Asp
1               5                  10                  15

Leu Arg Gln Gly Met Phe Ala Gln Leu Val Ala Gln Asn Val Leu Leu
            20                  25                  30

Ile Asp Gly Pro Leu Ser Trp Tyr Ser Asp Pro Gly Leu Ala Gly Val
        35                  40                  45

Ser Leu Thr Gly Gly Leu Ser Tyr Lys Glu Asp Thr Lys Glu Leu Val
    50                  55                  60

Val Ala Lys Ala Gly Val Tyr Tyr Val Phe Phe Gln Leu Glu Leu Arg
65                  70                  75                  80

Arg Val Val Ala Gly Glu Gly Ser Gly Ser Val Ser Leu Ala Leu His
                85                  90                  95

Leu Gln Pro Leu Arg Ser Ala Ala Gly Ala Ala Ala Leu Ala Leu Thr
            100                 105                 110

Val Asp Leu Pro Pro Ala Ser Ser Glu Ala Arg Asn Ser Ala Phe Gly
        115                 120                 125

Phe Gln Gly Arg Leu Leu His Leu Ser Ala Gly Gln Arg Leu Gly Val
    130                 135                 140

His Leu His Thr Glu Ala Arg Ala Arg His Ala Trp Gln Leu Thr Gln
145                 150                 155                 160

Gly Ala Thr Val Leu Gly Leu Phe Arg Val Thr Pro Glu Ile Pro Ala
                165                 170                 175

Gly Leu Pro Ser Pro Arg Ser Glu Gly Gly Gly Gly Ser Gly Gly Gly
            180                 185                 190

Gly Ser Arg Glu Gly Pro Glu Leu Ser Pro Asp Asp Pro Ala Gly Leu
        195                 200                 205

Leu Asp Leu Arg Gln Gly Met Phe Ala Gln Leu Val Ala Gln Asn Val
    210                 215                 220

Leu Leu Ile Asp Gly Pro Leu Ser Trp Tyr Ser Asp Pro Gly Leu Ala
225                 230                 235                 240

Gly Val Ser Leu Thr Gly Gly Leu Ser Tyr Lys Glu Asp Thr Lys Glu
                245                 250                 255
```

```
Leu Val Val Ala Lys Ala Gly Val Tyr Tyr Val Phe Phe Gln Leu Glu
            260                 265                 270

Leu Arg Arg Val Val Ala Gly Glu Gly Ser Gly Ser Val Ser Leu Ala
        275                 280                 285

Leu His Leu Gln Pro Leu Arg Ser Ala Ala Gly Ala Ala Ala Leu Ala
    290                 295                 300

Leu Thr Val Asp Leu Pro Pro Ala Ser Ser Glu Ala Arg Asn Ser Ala
305                 310                 315                 320

Phe Gly Phe Gln Gly Arg Leu Leu His Leu Ser Ala Gly Gln Arg Leu
                325                 330                 335

Gly Val His Leu His Thr Glu Ala Arg Ala Arg His Ala Trp Gln Leu
            340                 345                 350

Thr Gln Gly Ala Thr Val Leu Gly Leu Phe Arg Val Thr Pro Glu Ile
        355                 360                 365

Pro Ala Gly Leu Pro Ser Pro Arg Ser Glu Gly Gly Gly Gly Ser Gly
    370                 375                 380

Gly Gly Gly Ser Arg Thr Val Ala Ala Pro Ser Val Phe Ile Phe Pro
385                 390                 395                 400

Pro Ser Asp Arg Lys Leu Lys Ser Gly Thr Ala Ser Val Val Cys Leu
                405                 410                 415

Leu Asn Asn Phe Tyr Pro Arg Glu Ala Lys Val Gln Trp Lys Val Asp
            420                 425                 430

Asn Ala Leu Gln Ser Gly Asn Ser Gln Glu Ser Val Thr Glu Gln Asp
        435                 440                 445

Ser Lys Asp Ser Thr Tyr Ser Leu Ser Ser Thr Leu Thr Leu Ser Lys
    450                 455                 460

Ala Asp Tyr Glu Lys His Lys Val Tyr Ala Cys Glu Val Thr His Gln
465                 470                 475                 480

Gly Leu Ser Ser Pro Val Thr Lys Ser Phe Asn Arg Gly Glu Cys Asp
                485                 490                 495

Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Ala Ala Gly Gly
```

```
            500                 505                 510

Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile
        515                 520                 525

Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His Glu
    530                 535                 540

Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val His
545                 550                 555                 560

Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg
                565                 570                 575

Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys
            580                 585                 590

Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Gly Ala Pro Ile Glu
        595                 600                 605

Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr
    610                 615                 620

Thr Leu Pro Pro Cys Arg Asp Glu Leu Thr Lys Asn Gln Val Ser Leu
625                 630                 635                 640

Trp Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp
                645                 650                 655

Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val
            660                 665                 670

Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp
        675                 680                 685

Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His
    690                 695                 700

Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro
705                 710                 715                 720

Gly Lys
```

+ADw-210+AD4- 116
+ADw-211+AD4- 297
+ADw-212+AD4- PRT
+ADw-213+AD4- Secuencia artificial

+ADw-220+AD4-
+ADw-223+AD4- hu 4-1BBL monom+AOk-rico (71-254) -CH1+ACo-

+ADw-400+AD4- 116

```
Arg Glu Gly Pro Glu Leu Ser Pro Asp Asp Pro Ala Gly Leu Leu Asp
1               5                  10                  15

Leu Arg Gln Gly Met Phe Ala Gln Leu Val Ala Gln Asn Val Leu Leu
            20                  25                  30

Ile Asp Gly Pro Leu Ser Trp Tyr Ser Asp Pro Gly Leu Ala Gly Val
        35                  40                  45

Ser Leu Thr Gly Gly Leu Ser Tyr Lys Glu Asp Thr Lys Glu Leu Val
    50                  55                  60

Val Ala Lys Ala Gly Val Tyr Tyr Val Phe Phe Gln Leu Glu Leu Arg
65                  70                  75                  80

Arg Val Val Ala Gly Glu Gly Ser Gly Ser Val Ser Leu Ala Leu His
                85                  90                  95

Leu Gln Pro Leu Arg Ser Ala Ala Gly Ala Ala Ala Leu Ala Leu Thr
            100                 105                 110

Val Asp Leu Pro Pro Ala Ser Ser Glu Ala Arg Asn Ser Ala Phe Gly
        115                 120                 125

Phe Gln Gly Arg Leu Leu His Leu Ser Ala Gly Gln Arg Leu Gly Val
    130                 135                 140

His Leu His Thr Glu Ala Arg Ala Arg His Ala Trp Gln Leu Thr Gln
145                 150                 155                 160

Gly Ala Thr Val Leu Gly Leu Phe Arg Val Thr Pro Glu Ile Pro Ala
                165                 170                 175

Gly Leu Pro Ser Pro Arg Ser Glu Gly Gly Gly Gly Ser Gly Gly Gly
            180                 185                 190

Gly Ser Ala Ser Thr Lys Gly Pro Ser Val Phe Pro Leu Ala Pro Ser
        195                 200                 205

Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu Gly Cys Leu Val Glu
    210                 215                 220

Asp Tyr Phe Pro Glu Pro Val Thr Val Ser Trp Asn Ser Gly Ala Leu
```

225 230 235 240

Thr Ser Gly Val His Thr Phe Pro Ala Val Leu Gln Ser Ser Gly Leu
245 250 255

Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser Ser Ser Leu Gly Thr
260 265 270

Gln Thr Tyr Ile Cys Asn Val Asn His Lys Pro Ser Asn Thr Lys Val
275 280 285

Asp Glu Lys Val Glu Pro Lys Ser Cys
290 295

+ADw-210+AD4- 117
+ADw-211+AD4- 722
+ADw-212+AD4- PRT
+ADw-213+AD4- Secuencia artificial

+ADw-220+AD4-
+ADw-223+AD4- hu 4-1BBL dim+AOk-rico (71-254) - CL cadena Fc pomo

+ADw-400+AD4- 117

Arg Glu Gly Pro Glu Leu Ser Pro Asp Asp Pro Ala Gly Leu Leu Asp
1 5 10 15

Leu Arg Gln Gly Met Phe Ala Gln Leu Val Ala Gln Asn Val Leu Leu
20 25 30

Ile Asp Gly Pro Leu Ser Trp Tyr Ser Asp Pro Gly Leu Ala Gly Val
35 40 45

Ser Leu Thr Gly Gly Leu Ser Tyr Lys Glu Asp Thr Lys Glu Leu Val
50 55 60

Val Ala Lys Ala Gly Val Tyr Tyr Val Phe Phe Gln Leu Glu Leu Arg
65 70 75 80

Arg Val Val Ala Gly Glu Gly Ser Gly Ser Val Ser Leu Ala Leu His
85 90 95

Leu Gln Pro Leu Arg Ser Ala Ala Gly Ala Ala Ala Leu Ala Leu Thr
100 105 110

Val Asp Leu Pro Pro Ala Ser Ser Glu Ala Arg Asn Ser Ala Phe Gly
115 120 125

Phe Gln Gly Arg Leu Leu His Leu Ser Ala Gly Gln Arg Leu Gly Val
130 135 140

```
His Leu His Thr Glu Ala Arg Ala Arg His Ala Trp Gln Leu Thr Gln
145                 150                 155                 160

Gly Ala Thr Val Leu Gly Leu Phe Arg Val Thr Pro Glu Ile Pro Ala
                165                 170                 175

Gly Leu Pro Ser Pro Arg Ser Glu Gly Gly Gly Gly Ser Gly Gly Gly
            180                 185                 190

Gly Ser Arg Glu Gly Pro Glu Leu Ser Pro Asp Asp Pro Ala Gly Leu
        195                 200                 205

Leu Asp Leu Arg Gln Gly Met Phe Ala Gln Leu Val Ala Gln Asn Val
    210                 215                 220

Leu Leu Ile Asp Gly Pro Leu Ser Trp Tyr Ser Asp Pro Gly Leu Ala
225                 230                 235                 240

Gly Val Ser Leu Thr Gly Gly Leu Ser Tyr Lys Glu Asp Thr Lys Glu
                245                 250                 255

Leu Val Val Ala Lys Ala Gly Val Tyr Tyr Val Phe Phe Gln Leu Glu
            260                 265                 270

Leu Arg Arg Val Val Ala Gly Glu Gly Ser Gly Ser Val Ser Leu Ala
        275                 280                 285

Leu His Leu Gln Pro Leu Arg Ser Ala Ala Gly Ala Ala Ala Leu Ala
    290                 295                 300

Leu Thr Val Asp Leu Pro Pro Ala Ser Ser Glu Ala Arg Asn Ser Ala
305                 310                 315                 320

Phe Gly Phe Gln Gly Arg Leu Leu His Leu Ser Ala Gly Gln Arg Leu
                325                 330                 335

Gly Val His Leu His Thr Glu Ala Arg Ala Arg His Ala Trp Gln Leu
            340                 345                 350

Thr Gln Gly Ala Thr Val Leu Gly Leu Phe Arg Val Thr Pro Glu Ile
        355                 360                 365

Pro Ala Gly Leu Pro Ser Pro Arg Ser Glu Gly Gly Gly Gly Ser Gly
    370                 375                 380

Gly Gly Gly Ser Arg Thr Val Ala Ala Pro Ser Val Phe Ile Phe Pro
```

```
385                 390                 395                 400

Pro Ser Asp Glu Gln Leu Lys Ser Gly Thr Ala Ser Val Val Cys Leu
                405                 410                 415

Leu Asn Asn Phe Tyr Pro Arg Glu Ala Lys Val Gln Trp Lys Val Asp
            420                 425                 430

Asn Ala Leu Gln Ser Gly Asn Ser Gln Glu Ser Val Thr Glu Gln Asp
        435                 440                 445

Ser Lys Asp Ser Thr Tyr Ser Leu Ser Ser Thr Leu Thr Leu Ser Lys
    450                 455                 460

Ala Asp Tyr Glu Lys His Lys Val Tyr Ala Cys Glu Val Thr His Gln
465                 470                 475                 480

Gly Leu Ser Ser Pro Val Thr Lys Ser Phe Asn Arg Gly Glu Cys Asp
                485                 490                 495

Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Ala Ala Gly Gly
            500                 505                 510

Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile
        515                 520                 525

Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His Glu
    530                 535                 540

Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val His
545                 550                 555                 560

Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg
                565                 570                 575

Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys
            580                 585                 590

Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Gly Ala Pro Ile Glu
        595                 600                 605

Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr
    610                 615                 620

Thr Leu Pro Pro Cys Arg Asp Glu Leu Thr Lys Asn Gln Val Ser Leu
625                 630                 635                 640
```

```
Trp Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp
                645                 650                 655

Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val
            660                 665                 670

Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp
        675                 680                 685

Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His
    690                 695                 700

Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro
705                 710                 715                 720

Gly Lys
```

+ADw-210+AD4- 118
+ADw-211+AD4- 297
+ADw-212+AD4- PRT
+ADw-213+AD4- Secuencia artificial

+ADw-220+AD4-
+ADw-223+AD4- hu 4-1BBL monom+AOk-rico (71-254) - CH1

+ADw-400+AD4- 118

```
Arg Glu Gly Pro Glu Leu Ser Pro Asp Asp Pro Ala Gly Leu Leu Asp
1               5                   10                  15

Leu Arg Gln Gly Met Phe Ala Gln Leu Val Ala Gln Asn Val Leu Leu
            20                  25                  30

Ile Asp Gly Pro Leu Ser Trp Tyr Ser Asp Pro Gly Leu Ala Gly Val
        35                  40                  45

Ser Leu Thr Gly Gly Leu Ser Tyr Lys Glu Asp Thr Lys Glu Leu Val
    50                  55                  60

Val Ala Lys Ala Gly Val Tyr Tyr Val Phe Phe Gln Leu Glu Leu Arg
65                  70                  75                  80

Arg Val Val Ala Gly Glu Gly Ser Gly Ser Val Ser Leu Ala Leu His
                85                  90                  95

Leu Gln Pro Leu Arg Ser Ala Ala Gly Ala Ala Ala Leu Ala Leu Thr
            100                 105                 110

Val Asp Leu Pro Pro Ala Ser Ser Glu Ala Arg Asn Ser Ala Phe Gly
```

115 120 125

Phe Gln Gly Arg Leu Leu His Leu Ser Ala Gly Gln Arg Leu Gly Val
130 135 140

His Leu His Thr Glu Ala Arg Ala Arg His Ala Trp Gln Leu Thr Gln
145 150 155 160

Gly Ala Thr Val Leu Gly Leu Phe Arg Val Thr Pro Glu Ile Pro Ala
165 170 175

Gly Leu Pro Ser Pro Arg Ser Glu Gly Gly Gly Gly Ser Gly Gly Gly
180 185 190

Gly Ser Ala Ser Thr Lys Gly Pro Ser Val Phe Pro Leu Ala Pro Ser
195 200 205

Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu Gly Cys Leu Val Lys
210 215 220

Asp Tyr Phe Pro Glu Pro Val Thr Val Ser Trp Asn Ser Gly Ala Leu
225 230 235 240

Thr Ser Gly Val His Thr Phe Pro Ala Val Leu Gln Ser Ser Gly Leu
245 250 255

Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser Ser Ser Leu Gly Thr
260 265 270

Gln Thr Tyr Ile Cys Asn Val Asn His Lys Pro Ser Asn Thr Lys Val
275 280 285

Asp Lys Lys Val Glu Pro Lys Ser Cys
290 295

+ADw-210+AD4- 119
+ADw-211+AD4- 710
+ADw-212+AD4- PRT
+ADw-213+AD4- Secuencia artificial

+ADw-220+AD4-
+ADw-223+AD4- hu 4-1BBL dim+AOk-rico (71-248) - CL+ACo- cadena Fc pomo

+ADw-400+AD4- 119

Arg Glu Gly Pro Glu Leu Ser Pro Asp Asp Pro Ala Gly Leu Leu Asp
1 5 10 15

Leu Arg Gln Gly Met Phe Ala Gln Leu Val Ala Gln Asn Val Leu Leu
20 25 30

```
Ile Asp Gly Pro Leu Ser Trp Tyr Ser Asp Pro Gly Leu Ala Gly Val
        35                  40                  45

Ser Leu Thr Gly Gly Leu Ser Tyr Lys Glu Asp Thr Lys Glu Leu Val
    50                  55                  60

Val Ala Lys Ala Gly Val Tyr Tyr Val Phe Phe Gln Leu Glu Leu Arg
65                  70                  75                  80

Arg Val Val Ala Gly Glu Gly Ser Gly Ser Val Ser Leu Ala Leu His
                85                  90                  95

Leu Gln Pro Leu Arg Ser Ala Ala Gly Ala Ala Ala Leu Ala Leu Thr
            100                 105                 110

Val Asp Leu Pro Pro Ala Ser Ser Glu Ala Arg Asn Ser Ala Phe Gly
        115                 120                 125

Phe Gln Gly Arg Leu Leu His Leu Ser Ala Gly Gln Arg Leu Gly Val
    130                 135                 140

His Leu His Thr Glu Ala Arg Ala Arg His Ala Trp Gln Leu Thr Gln
145                 150                 155                 160

Gly Ala Thr Val Leu Gly Leu Phe Arg Val Thr Pro Glu Ile Pro Ala
                165                 170                 175

Gly Leu Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Arg Glu Gly Pro
            180                 185                 190

Glu Leu Ser Pro Asp Asp Pro Ala Gly Leu Leu Asp Leu Arg Gln Gly
        195                 200                 205

Met Phe Ala Gln Leu Val Ala Gln Asn Val Leu Leu Ile Asp Gly Pro
    210                 215                 220

Leu Ser Trp Tyr Ser Asp Pro Gly Leu Ala Gly Val Ser Leu Thr Gly
225                 230                 235                 240

Gly Leu Ser Tyr Lys Glu Asp Thr Lys Glu Leu Val Val Ala Lys Ala
                245                 250                 255

Gly Val Tyr Tyr Val Phe Phe Gln Leu Glu Leu Arg Arg Val Val Ala
            260                 265                 270

Gly Glu Gly Ser Gly Ser Val Ser Leu Ala Leu His Leu Gln Pro Leu
```

275 280 285

Arg Ser Ala Ala Gly Ala Ala Ala Leu Ala Leu Thr Val Asp Leu Pro
290 295 300

Pro Ala Ser Ser Glu Ala Arg Asn Ser Ala Phe Gly Phe Gln Gly Arg
305 310 315 320

Leu Leu His Leu Ser Ala Gly Gln Arg Leu Gly Val His Leu His Thr
325 330 335

Glu Ala Arg Ala Arg His Ala Trp Gln Leu Thr Gln Gly Ala Thr Val
340 345 350

Leu Gly Leu Phe Arg Val Thr Pro Glu Ile Pro Ala Gly Leu Gly Gly
355 360 365

Gly Gly Ser Gly Gly Gly Gly Ser Arg Thr Val Ala Ala Pro Ser Val
370 375 380

Phe Ile Phe Pro Pro Ser Asp Arg Lys Leu Lys Ser Gly Thr Ala Ser
385 390 395 400

Val Val Cys Leu Leu Asn Asn Phe Tyr Pro Arg Glu Ala Lys Val Gln
405 410 415

Trp Lys Val Asp Asn Ala Leu Gln Ser Gly Asn Ser Gln Glu Ser Val
420 425 430

Thr Glu Gln Asp Ser Lys Asp Ser Thr Tyr Ser Leu Ser Ser Thr Leu
435 440 445

Thr Leu Ser Lys Ala Asp Tyr Glu Lys His Lys Val Tyr Ala Cys Glu
450 455 460

Val Thr His Gln Gly Leu Ser Ser Pro Val Thr Lys Ser Phe Asn Arg
465 470 475 480

Gly Glu Cys Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu
485 490 495

Ala Ala Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp
500 505 510

Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp
515 520 525

Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly
530 535 540

Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn
545 550 555 560

Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp
565 570 575

Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Gly
580 585 590

Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu
595 600 605

Pro Gln Val Tyr Thr Leu Pro Pro Cys Arg Asp Glu Leu Thr Lys Asn
610 615 620

Gln Val Ser Leu Trp Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile
625 630 635 640

Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr
645 650 655

Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys
660 665 670

Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys
675 680 685

Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu
690 695 700

Ser Leu Ser Pro Gly Lys
705 710

+ADw-210+AD4- 120
+ADw-211+AD4- 291
+ADw-212+AD4- PRT
+ADw-213+AD4- Secuencia artificial

+ADw-220+AD4-
+ADw-223+AD4- hu 4-1BBL monom+AOk-rico (71-248) - CH1+ACo-

+ADw-400+AD4- 120

Arg Glu Gly Pro Glu Leu Ser Pro Asp Asp Pro Ala Gly Leu Leu Asp
1 5 10 15

Leu Arg Gln Gly Met Phe Ala Gln Leu Val Ala Gln Asn Val Leu Leu

```
            20                  25                  30

Ile Asp Gly Pro Leu Ser Trp Tyr Ser Asp Pro Gly Leu Ala Gly Val
        35                  40                  45

Ser Leu Thr Gly Gly Leu Ser Tyr Lys Glu Asp Thr Lys Glu Leu Val
    50                  55                  60

Val Ala Lys Ala Gly Val Tyr Tyr Val Phe Phe Gln Leu Glu Leu Arg
65                  70                  75                  80

Arg Val Val Ala Gly Glu Gly Ser Gly Ser Val Ser Leu Ala Leu His
                85                  90                  95

Leu Gln Pro Leu Arg Ser Ala Ala Gly Ala Ala Ala Leu Ala Leu Thr
            100                 105                 110

Val Asp Leu Pro Pro Ala Ser Ser Glu Ala Arg Asn Ser Ala Phe Gly
        115                 120                 125

Phe Gln Gly Arg Leu Leu His Leu Ser Ala Gly Gln Arg Leu Gly Val
    130                 135                 140

His Leu His Thr Glu Ala Arg Ala Arg His Ala Trp Gln Leu Thr Gln
145                 150                 155                 160

Gly Ala Thr Val Leu Gly Leu Phe Arg Val Thr Pro Glu Ile Pro Ala
                165                 170                 175

Gly Leu Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Ala Ser Thr Lys
            180                 185                 190

Gly Pro Ser Val Phe Pro Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly
        195                 200                 205

Gly Thr Ala Ala Leu Gly Cys Leu Val Glu Asp Tyr Phe Pro Glu Pro
    210                 215                 220

Val Thr Val Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr
225                 230                 235                 240

Phe Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val
                245                 250                 255

Val Thr Val Pro Ser Ser Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn
            260                 265                 270
```

Val Asn His Lys Pro Ser Asn Thr Lys Val Asp Glu Lys Val Glu Pro
        275   280   285

Lys Ser Cys
    290

+ADw-210+AD4- 121
+ADw-211+AD4- 833
+ADw-212+AD4- PRT
+ADw-213+AD4- Secuencia artificial

+ADw-220+AD4-
+ADw-223+AD4- cadena Fc agujero de anti-FAP (28H1) fusionada a hu 4-1BBL dim+AOk-rico (71-254)

+ADw-400+AD4- 121

Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1   5   10   15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Ser His
            20   25   30

Ala Met Ser Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
        35   40   45

Ser Ala Ile Trp Ala Ser Gly Glu Gln Tyr Tyr Ala Asp Ser Val Lys
    50   55   60

Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr Leu
65   70   75   80

Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys Ala
                85   90   95

Lys Gly Trp Leu Gly Asn Phe Asp Tyr Trp Gly Gln Gly Thr Leu Val
            100   105   110

Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser Val Phe Pro Leu Ala
        115   120   125

Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu Gly Cys Leu
    130   135   140

Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser Trp Asn Ser Gly
145   150   155   160

Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala Val Leu Gln Ser Ser
                165   170   175

```
Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser Ser Ser Leu
            180                 185                 190

Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys Pro Ser Asn Thr
        195                 200                 205

Lys Val Asp Lys Lys Val Glu Pro Lys Ser Cys Asp Lys Thr His Thr
    210                 215                 220

Cys Pro Pro Cys Pro Ala Pro Glu Ala Ala Gly Gly Pro Ser Val Phe
225                 230                 235                 240

Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro
                245                 250                 255

Glu Val Thr Cys Val Val Val Asp Val Ser His Glu Asp Pro Glu Val
            260                 265                 270

Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr
        275                 280                 285

Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg Val Val Ser Val
    290                 295                 300

Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys
305                 310                 315                 320

Lys Val Ser Asn Lys Ala Leu Gly Ala Pro Ile Glu Lys Thr Ile Ser
                325                 330                 335

Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Cys Thr Leu Pro Pro
            340                 345                 350

Ser Arg Asp Glu Leu Thr Lys Asn Gln Val Ser Leu Ser Cys Ala Val
        355                 360                 365

Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly
    370                 375                 380

Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp
385                 390                 395                 400

Gly Ser Phe Phe Leu Val Ser Lys Leu Thr Val Asp Lys Ser Arg Trp
                405                 410                 415

Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His Glu Ala Leu His
            420                 425                 430
```

```
Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly Gly Gly Gly
        435                 440                 445

Gly Ser Gly Gly Gly Gly Ser Arg Glu Gly Pro Glu Leu Ser Pro Asp
    450                 455                 460

Asp Pro Ala Gly Leu Leu Asp Leu Arg Gln Gly Met Phe Ala Gln Leu
465                 470                 475                 480

Val Ala Gln Asn Val Leu Leu Ile Asp Gly Pro Leu Ser Trp Tyr Ser
                485                 490                 495

Asp Pro Gly Leu Ala Gly Val Ser Leu Thr Gly Gly Leu Ser Tyr Lys
            500                 505                 510

Glu Asp Thr Lys Glu Leu Val Val Ala Lys Ala Gly Val Tyr Tyr Val
        515                 520                 525

Phe Phe Gln Leu Glu Leu Arg Arg Val Val Ala Gly Glu Gly Ser Gly
    530                 535                 540

Ser Val Ser Leu Ala Leu His Leu Gln Pro Leu Arg Ser Ala Ala Gly
545                 550                 555                 560

Ala Ala Ala Leu Ala Leu Thr Val Asp Leu Pro Pro Ala Ser Ser Glu
                565                 570                 575

Ala Arg Asn Ser Ala Phe Gly Phe Gln Gly Arg Leu Leu His Leu Ser
            580                 585                 590

Ala Gly Gln Arg Leu Gly Val His Leu His Thr Glu Ala Arg Ala Arg
        595                 600                 605

His Ala Trp Gln Leu Thr Gln Gly Ala Thr Val Leu Gly Leu Phe Arg
    610                 615                 620

Val Thr Pro Glu Ile Pro Ala Gly Leu Pro Ser Pro Arg Ser Glu Gly
625                 630                 635                 640

Gly Gly Gly Ser Gly Gly Gly Gly Ser Arg Glu Gly Pro Glu Leu Ser
                645                 650                 655

Pro Asp Asp Pro Ala Gly Leu Leu Asp Leu Arg Gln Gly Met Phe Ala
            660                 665                 670

Gln Leu Val Ala Gln Asn Val Leu Leu Ile Asp Gly Pro Leu Ser Trp
        675                 680                 685
```

```
Tyr Ser Asp Pro Gly Leu Ala Gly Val Ser Leu Thr Gly Gly Leu Ser
    690                 695                 700

Tyr Lys Glu Asp Thr Lys Glu Leu Val Val Ala Lys Ala Gly Val Tyr
705                 710                 715                 720

Tyr Val Phe Phe Gln Leu Glu Leu Arg Arg Val Val Ala Gly Glu Gly
                725                 730                 735

Ser Gly Ser Val Ser Leu Ala Leu His Leu Gln Pro Leu Arg Ser Ala
            740                 745                 750

Ala Gly Ala Ala Ala Leu Ala Leu Thr Val Asp Leu Pro Pro Ala Ser
        755                 760                 765

Ser Glu Ala Arg Asn Ser Ala Phe Gly Phe Gln Gly Arg Leu Leu His
    770                 775                 780

Leu Ser Ala Gly Gln Arg Leu Gly Val His Leu His Thr Glu Ala Arg
785                 790                 795                 800

Ala Arg His Ala Trp Gln Leu Thr Gln Gly Ala Thr Val Leu Gly Leu
                805                 810                 815

Phe Arg Val Thr Pro Glu Ile Pro Ala Gly Leu Pro Ser Pro Arg Ser
            820                 825                 830

Glu
```

+ADw-210+AD4- 122
+ADw-211+AD4- 639
+ADw-212+AD4- PRT
+ADw-213+AD4- Secuencia artificial

+ADw-220+AD4-
+ADw-223+AD4- ADN de cadena de Fc pomo de anti-FAP (28H1) fusionada a hu 4-1BBL monom+AOk-rico
(71-254)

+ADw-400+AD4- 122

```
Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1               5                   10                  15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Ser His
            20                  25                  30

Ala Met Ser Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
```

```
        35                  40                  45

Ser Ala Ile Trp Ala Ser Gly Glu Gln Tyr Tyr Ala Asp Ser Val Lys
    50                  55                  60

Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr Leu
65                  70                  75                  80

Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys Ala
                85                  90                  95

Lys Gly Trp Leu Gly Asn Phe Asp Tyr Trp Gly Gln Gly Thr Leu Val
            100                 105                 110

Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser Val Phe Pro Leu Ala
        115                 120                 125

Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu Gly Cys Leu
    130                 135                 140

Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser Trp Asn Ser Gly
145                 150                 155                 160

Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala Val Leu Gln Ser Ser
                165                 170                 175

Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser Ser Ser Leu
            180                 185                 190

Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys Pro Ser Asn Thr
        195                 200                 205

Lys Val Asp Lys Lys Val Glu Pro Lys Ser Cys Asp Lys Thr His Thr
    210                 215                 220

Cys Pro Pro Cys Pro Ala Pro Glu Ala Ala Gly Gly Pro Ser Val Phe
225                 230                 235                 240

Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro
                245                 250                 255

Glu Val Thr Cys Val Val Val Asp Val Ser His Glu Asp Pro Glu Val
            260                 265                 270

Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr
        275                 280                 285
```

```
Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg Val Val Ser Val
    290                 295                 300

Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys
305                 310                 315                 320

Lys Val Ser Asn Lys Ala Leu Gly Ala Pro Ile Glu Lys Thr Ile Ser
                325                 330                 335

Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro
            340                 345                 350

Cys Arg Asp Glu Leu Thr Lys Asn Gln Val Ser Leu Trp Cys Leu Val
        355                 360                 365

Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly
    370                 375                 380

Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp
385                 390                 395                 400

Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp
                405                 410                 415

Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His Glu Ala Leu His
            420                 425                 430

Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly Gly Gly Gly
        435                 440                 445

Gly Ser Gly Gly Gly Gly Ser Arg Glu Gly Pro Glu Leu Ser Pro Asp
    450                 455                 460

Asp Pro Ala Gly Leu Leu Asp Leu Arg Gln Gly Met Phe Ala Gln Leu
465                 470                 475                 480

Val Ala Gln Asn Val Leu Leu Ile Asp Gly Pro Leu Ser Trp Tyr Ser
                485                 490                 495

Asp Pro Gly Leu Ala Gly Val Ser Leu Thr Gly Gly Leu Ser Tyr Lys
            500                 505                 510

Glu Asp Thr Lys Glu Leu Val Val Ala Lys Ala Gly Val Tyr Tyr Val
        515                 520                 525

Phe Phe Gln Leu Glu Leu Arg Arg Val Val Ala Gly Glu Gly Ser Gly
    530                 535                 540
```

```
Ser Val Ser Leu Ala Leu His Leu Gln Pro Leu Arg Ser Ala Ala Gly
545                 550                 555                 560


Ala Ala Ala Leu Ala Leu Thr Val Asp Leu Pro Pro Ala Ser Ser Glu
                565                 570                 575


Ala Arg Asn Ser Ala Phe Gly Phe Gln Gly Arg Leu Leu His Leu Ser
            580                 585                 590


Ala Gly Gln Arg Leu Gly Val His Leu His Thr Glu Ala Arg Ala Arg
        595                 600                 605


His Ala Trp Gln Leu Thr Gln Gly Ala Thr Val Leu Gly Leu Phe Arg
    610                 615                 620


Val Thr Pro Glu Ile Pro Ala Gly Leu Pro Ser Pro Arg Ser Glu
625                 630                 635


+ADw-210+AD4-  123
+ADw-211+AD4-  834
+ADw-212+AD4-  PRT
+ADw-213+AD4-  Secuencia artificial

+ADw-220+AD4-
+ADw-223+AD4-  cadena Fc agujero de anti-FAP (4B9) fusionada a hu 4-1BBL
dim+AOk-rico (71-254)

+ADw-400+AD4-  123

Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1               5                   10                  15


Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Ser Tyr
            20                  25                  30


Ala Met Ser Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
        35                  40                  45


Ser Ala Ile Ile Gly Ser Gly Ala Ser Thr Tyr Tyr Ala Asp Ser Val
    50                  55                  60


Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65                  70                  75                  80


Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95


Ala Lys Gly Trp Phe Gly Gly Phe Asn Tyr Trp Gly Gln Gly Thr Leu
            100                 105                 110
```

```
Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser Val Phe Pro Leu
        115                 120                 125

Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu Gly Cys
    130                 135                 140

Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser Trp Asn Ser
145                 150                 155                 160

Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala Val Leu Gln Ser
                165                 170                 175

Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser Ser Ser
            180                 185                 190

Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys Pro Ser Asn
        195                 200                 205

Thr Lys Val Asp Lys Lys Val Glu Pro Lys Ser Cys Asp Lys Thr His
    210                 215                 220

Thr Cys Pro Pro Cys Pro Ala Pro Glu Ala Ala Gly Gly Pro Ser Val
225                 230                 235                 240

Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr
                245                 250                 255

Pro Glu Val Thr Cys Val Val Val Asp Val Ser His Glu Asp Pro Glu
            260                 265                 270

Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala Lys
        275                 280                 285

Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg Val Val Ser
    290                 295                 300

Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys
305                 310                 315                 320

Cys Lys Val Ser Asn Lys Ala Leu Gly Ala Pro Ile Glu Lys Thr Ile
                325                 330                 335

Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Cys Thr Leu Pro
            340                 345                 350

Pro Ser Arg Asp Glu Leu Thr Lys Asn Gln Val Ser Leu Ser Cys Ala
        355                 360                 365
```

```
Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn
    370                 375                 380

Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser
385                 390                 395                 400

Asp Gly Ser Phe Phe Leu Val Ser Lys Leu Thr Val Asp Lys Ser Arg
                405                 410                 415

Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His Glu Ala Leu
            420                 425                 430

His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly Gly Gly
        435                 440                 445

Gly Gly Ser Gly Gly Gly Gly Ser Arg Glu Gly Pro Glu Leu Ser Pro
    450                 455                 460

Asp Asp Pro Ala Gly Leu Leu Asp Leu Arg Gln Gly Met Phe Ala Gln
465                 470                 475                 480

Leu Val Ala Gln Asn Val Leu Leu Ile Asp Gly Pro Leu Ser Trp Tyr
                485                 490                 495

Ser Asp Pro Gly Leu Ala Gly Val Ser Leu Thr Gly Gly Leu Ser Tyr
            500                 505                 510

Lys Glu Asp Thr Lys Glu Leu Val Val Ala Lys Ala Gly Val Tyr Tyr
        515                 520                 525

Val Phe Phe Gln Leu Glu Leu Arg Arg Val Val Ala Gly Glu Gly Ser
    530                 535                 540

Gly Ser Val Ser Leu Ala Leu His Leu Gln Pro Leu Arg Ser Ala Ala
545                 550                 555                 560

Gly Ala Ala Ala Leu Ala Leu Thr Val Asp Leu Pro Pro Ala Ser Ser
                565                 570                 575

Glu Ala Arg Asn Ser Ala Phe Gly Phe Gln Gly Arg Leu Leu His Leu
            580                 585                 590

Ser Ala Gly Gln Arg Leu Gly Val His Leu His Thr Glu Ala Arg Ala
        595                 600                 605

Arg His Ala Trp Gln Leu Thr Gln Gly Ala Thr Val Leu Gly Leu Phe
```

610 615 620

Arg Val Thr Pro Glu Ile Pro Ala Gly Leu Pro Ser Pro Arg Ser Glu
625 630 635 640

Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Arg Glu Gly Pro Glu Leu
645 650 655

Ser Pro Asp Asp Pro Ala Gly Leu Leu Asp Leu Arg Gln Gly Met Phe
660 665 670

Ala Gln Leu Val Ala Gln Asn Val Leu Leu Ile Asp Gly Pro Leu Ser
675 680 685

Trp Tyr Ser Asp Pro Gly Leu Ala Gly Val Ser Leu Thr Gly Gly Leu
690 695 700

Ser Tyr Lys Glu Asp Thr Lys Glu Leu Val Val Ala Lys Ala Gly Val
705 710 715 720

Tyr Tyr Val Phe Phe Gln Leu Glu Leu Arg Arg Val Val Ala Gly Glu
725 730 735

Gly Ser Gly Ser Val Ser Leu Ala Leu His Leu Gln Pro Leu Arg Ser
740 745 750

Ala Ala Gly Ala Ala Ala Leu Ala Leu Thr Val Asp Leu Pro Pro Ala
755 760 765

Ser Ser Glu Ala Arg Asn Ser Ala Phe Gly Phe Gln Gly Arg Leu Leu
770 775 780

His Leu Ser Ala Gly Gln Arg Leu Gly Val His Leu His Thr Glu Ala
785 790 795 800

Arg Ala Arg His Ala Trp Gln Leu Thr Gln Gly Ala Thr Val Leu Gly
805 810 815

Leu Phe Arg Val Thr Pro Glu Ile Pro Ala Gly Leu Pro Ser Pro Arg
820 825 830

Ser Glu

+ADw-210+AD4- 124
+ADw-211+AD4- 640
+ADw-212+AD4- PRT
+ADw-213+AD4- Secuencia artificial

+ADw-220+AD4-
+ADw-223+AD4- ADN de cadena de Fc pomo de anti-FAP (4B9) fusionada a hu 4-1BBL monom+AOk-rico
(71-254)

+ADw-400+AD4- 124

```
Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1               5                  10                  15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Ser Tyr
            20                  25                  30

Ala Met Ser Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
        35                  40                  45

Ser Ala Ile Ile Gly Ser Gly Ala Ser Thr Tyr Tyr Ala Asp Ser Val
    50                  55                  60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65                  70                  75                  80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95

Ala Lys Gly Trp Phe Gly Gly Phe Asn Tyr Trp Gly Gln Gly Thr Leu
            100                 105                 110

Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser Val Phe Pro Leu
        115                 120                 125

Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu Gly Cys
    130                 135                 140

Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser Trp Asn Ser
145                 150                 155                 160

Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala Val Leu Gln Ser
                165                 170                 175

Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser Ser Ser
            180                 185                 190

Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys Pro Ser Asn
        195                 200                 205

Thr Lys Val Asp Lys Lys Val Glu Pro Lys Ser Cys Asp Lys Thr His
    210                 215                 220
```

```
Thr Cys Pro Pro Cys Pro Ala Pro Glu Ala Ala Gly Gly Pro Ser Val
225                 230                 235                 240

Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr
                245                 250                 255

Pro Glu Val Thr Cys Val Val Val Asp Val Ser His Glu Asp Pro Glu
            260                 265                 270

Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala Lys
        275                 280                 285

Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg Val Val Ser
    290                 295                 300

Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys
305                 310                 315                 320

Cys Lys Val Ser Asn Lys Ala Leu Gly Ala Pro Ile Glu Lys Thr Ile
                325                 330                 335

Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro
            340                 345                 350

Pro Cys Arg Asp Glu Leu Thr Lys Asn Gln Val Ser Leu Trp Cys Leu
        355                 360                 365

Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn
    370                 375                 380

Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser
385                 390                 395                 400

Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg
                405                 410                 415

Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His Glu Ala Leu
            420                 425                 430

His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly Gly Gly
        435                 440                 445

Gly Gly Ser Gly Gly Gly Gly Ser Arg Glu Gly Pro Glu Leu Ser Pro
    450                 455                 460

Asp Asp Pro Ala Gly Leu Leu Asp Leu Arg Gln Gly Met Phe Ala Gln
465                 470                 475                 480
```

```
Leu Val Ala Gln Asn Val Leu Leu Ile Asp Gly Pro Leu Ser Trp Tyr
                485                 490                 495

Ser Asp Pro Gly Leu Ala Gly Val Ser Leu Thr Gly Gly Leu Ser Tyr
            500                 505                 510

Lys Glu Asp Thr Lys Glu Leu Val Val Ala Lys Ala Gly Val Tyr Tyr
        515                 520                 525

Val Phe Phe Gln Leu Glu Leu Arg Arg Val Val Ala Gly Glu Gly Ser
    530                 535                 540

Gly Ser Val Ser Leu Ala Leu His Leu Gln Pro Leu Arg Ser Ala Ala
545                 550                 555                 560

Gly Ala Ala Ala Leu Ala Leu Thr Val Asp Leu Pro Pro Ala Ser Ser
                565                 570                 575

Glu Ala Arg Asn Ser Ala Phe Gly Phe Gln Gly Arg Leu Leu His Leu
            580                 585                 590

Ser Ala Gly Gln Arg Leu Gly Val His Leu His Thr Glu Ala Arg Ala
        595                 600                 605

Arg His Ala Trp Gln Leu Thr Gln Gly Ala Thr Val Leu Gly Leu Phe
    610                 615                 620

Arg Val Thr Pro Glu Ile Pro Ala Gly Leu Pro Ser Pro Arg Ser Glu
625                 630                 635                 640


+ADw-210+AD4-  125
+ADw-211+AD4-  215
+ADw-212+AD4-  PRT
+ADw-213+AD4-  Secuencia artificial

+ADw-220+AD4-
+ADw-223+AD4-  cadena ligera de anti-FAP (4B9)

+ADw-400+AD4-  125

Glu Ile Val Leu Thr Gln Ser Pro Gly Thr Leu Ser Leu Ser Pro Gly
1               5                   10                  15

Glu Arg Ala Thr Leu Ser Cys Arg Ala Ser Gln Ser Val Thr Ser Ser
            20                  25                  30

Tyr Leu Ala Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Arg Leu Leu
        35                  40                  45
```

```
Ile Asn Val Gly Ser Arg Arg Ala Thr Gly Ile Pro Asp Arg Phe Ser
    50                  55                  60

Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Arg Leu Glu
65                  70                  75                  80

Pro Glu Asp Phe Ala Val Tyr Tyr Cys Gln Gln Gly Ile Met Leu Pro
                85                  90                  95

Pro Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys Arg Thr Val Ala
            100                 105                 110

Ala Pro Ser Val Phe Ile Phe Pro Pro Ser Asp Glu Gln Leu Lys Ser
        115                 120                 125

Gly Thr Ala Ser Val Val Cys Leu Leu Asn Asn Phe Tyr Pro Arg Glu
    130                 135                 140

Ala Lys Val Gln Trp Lys Val Asp Asn Ala Leu Gln Ser Gly Asn Ser
145                 150                 155                 160

Gln Glu Ser Val Thr Glu Gln Asp Ser Lys Asp Ser Thr Tyr Ser Leu
                165                 170                 175

Ser Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu Lys His Lys Val
            180                 185                 190

Tyr Ala Cys Glu Val Thr His Gln Gly Leu Ser Ser Pro Val Thr Lys
        195                 200                 205

Ser Phe Asn Arg Gly Glu Cys
    210                 215


+ADw-210+AD4-  126
+ADw-211+AD4-  822
+ADw-212+AD4-  PRT
+ADw-213+AD4-  Secuencia artificial

+ADw-220+AD4-
+ADw-223+AD4-  cadena Fc agujero de anti-FAP (4B9) fusionada a hu 4-1BBL
dim+AOk-rico (71-248)

+ADw-400+AD4-  126

Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1               5                   10                  15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Ser Tyr
            20                  25                  30
```

```
Ala Met Ser Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
        35                  40                  45

Ser Ala Ile Ile Gly Ser Gly Ala Ser Thr Tyr Tyr Ala Asp Ser Val
    50                  55                  60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65                  70                  75                  80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95

Ala Lys Gly Trp Phe Gly Gly Phe Asn Tyr Trp Gly Gln Gly Thr Leu
            100                 105                 110

Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser Val Phe Pro Leu
        115                 120                 125

Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu Gly Cys
    130                 135                 140

Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser Trp Asn Ser
145                 150                 155                 160

Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala Val Leu Gln Ser
                165                 170                 175

Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser Ser Ser
            180                 185                 190

Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys Pro Ser Asn
        195                 200                 205

Thr Lys Val Asp Lys Lys Val Glu Pro Lys Ser Cys Asp Lys Thr His
    210                 215                 220

Thr Cys Pro Pro Cys Pro Ala Pro Glu Ala Ala Gly Gly Pro Ser Val
225                 230                 235                 240

Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr
                245                 250                 255

Pro Glu Val Thr Cys Val Val Val Asp Val Ser His Glu Asp Pro Glu
            260                 265                 270

Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala Lys
        275                 280                 285
```

```
Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg Val Val Ser
    290                 295                 300

Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys
305                 310                 315                 320

Cys Lys Val Ser Asn Lys Ala Leu Gly Ala Pro Ile Glu Lys Thr Ile
                325                 330                 335

Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Cys Thr Leu Pro
            340                 345                 350

Pro Ser Arg Asp Glu Leu Thr Lys Asn Gln Val Ser Leu Ser Cys Ala
        355                 360                 365

Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn
    370                 375                 380

Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser
385                 390                 395                 400

Asp Gly Ser Phe Phe Leu Val Ser Lys Leu Thr Val Asp Lys Ser Arg
                405                 410                 415

Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His Glu Ala Leu
            420                 425                 430

His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly Gly Gly
        435                 440                 445

Gly Gly Ser Gly Gly Gly Gly Ser Arg Glu Gly Pro Glu Leu Ser Pro
    450                 455                 460

Asp Asp Pro Ala Gly Leu Leu Asp Leu Arg Gln Gly Met Phe Ala Gln
465                 470                 475                 480

Leu Val Ala Gln Asn Val Leu Leu Ile Asp Gly Pro Leu Ser Trp Tyr
                485                 490                 495

Ser Asp Pro Gly Leu Ala Gly Val Ser Leu Thr Gly Gly Leu Ser Tyr
            500                 505                 510

Lys Glu Asp Thr Lys Glu Leu Val Val Ala Lys Ala Gly Val Tyr Tyr
        515                 520                 525

Val Phe Phe Gln Leu Glu Leu Arg Arg Val Val Ala Gly Glu Gly Ser
```

530 535 540

Gly Ser Val Ser Leu Ala Leu His Leu Gln Pro Leu Arg Ser Ala Ala
545 550 555 560

Gly Ala Ala Ala Leu Ala Leu Thr Val Asp Leu Pro Pro Ala Ser Ser
565 570 575

Glu Ala Arg Asn Ser Ala Phe Gly Phe Gln Gly Arg Leu Leu His Leu
580 585 590

Ser Ala Gly Gln Arg Leu Gly Val His Leu His Thr Glu Ala Arg Ala
595 600 605

Arg His Ala Trp Gln Leu Thr Gln Gly Ala Thr Val Leu Gly Leu Phe
610 615 620

Arg Val Thr Pro Glu Ile Pro Ala Gly Leu Gly Gly Gly Gly Ser Gly
625 630 635 640

Gly Gly Gly Ser Arg Glu Gly Pro Glu Leu Ser Pro Asp Asp Pro Ala
645 650 655

Gly Leu Leu Asp Leu Arg Gln Gly Met Phe Ala Gln Leu Val Ala Gln
660 665 670

Asn Val Leu Leu Ile Asp Gly Pro Leu Ser Trp Tyr Ser Asp Pro Gly
675 680 685

Leu Ala Gly Val Ser Leu Thr Gly Gly Leu Ser Tyr Lys Glu Asp Thr
690 695 700

Lys Glu Leu Val Val Ala Lys Ala Gly Val Tyr Tyr Val Phe Phe Gln
705 710 715 720

Leu Glu Leu Arg Arg Val Val Ala Gly Glu Gly Ser Gly Ser Val Ser
725 730 735

Leu Ala Leu His Leu Gln Pro Leu Arg Ser Ala Ala Gly Ala Ala Ala
740 745 750

Leu Ala Leu Thr Val Asp Leu Pro Pro Ala Ser Ser Glu Ala Arg Asn
755 760 765

Ser Ala Phe Gly Phe Gln Gly Arg Leu Leu His Leu Ser Ala Gly Gln
770 775 780

```
Arg Leu Gly Val His Leu His Thr Glu Ala Arg Ala Arg His Ala Trp
785                 790                 795                 800


Gln Leu Thr Gln Gly Ala Thr Val Leu Gly Leu Phe Arg Val Thr Pro
                805                 810                 815


Glu Ile Pro Ala Gly Leu
            820


+ADw-210+AD4-  127
+ADw-211+AD4-  634
+ADw-212+AD4-  PRT
+ADw-213+AD4-  Secuencia artificial

+ADw-220+AD4-
+ADw-223+AD4-  ADN de cadena de Fc pomo de anti-FAP (4B9) fusionada a hu 4-1BBL
monom+AOk-rico
       (71-248)

+ADw-400+AD4-  127

Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1               5                   10                  15


Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Ser Tyr
            20                  25                  30


Ala Met Ser Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
        35                  40                  45


Ser Ala Ile Ile Gly Ser Gly Ala Ser Thr Tyr Tyr Ala Asp Ser Val
    50                  55                  60


Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65                  70                  75                  80


Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95


Ala Lys Gly Trp Phe Gly Gly Phe Asn Tyr Trp Gly Gln Gly Thr Leu
            100                 105                 110


Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser Val Phe Pro Leu
        115                 120                 125


Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu Gly Cys
    130                 135                 140


Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser Trp Asn Ser
145                 150                 155                 160
```

```
Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala Val Leu Gln Ser
                165                 170                 175

Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser Ser Ser
            180                 185                 190

Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys Pro Ser Asn
        195                 200                 205

Thr Lys Val Asp Lys Lys Val Glu Pro Lys Ser Cys Asp Lys Thr His
    210                 215                 220

Thr Cys Pro Pro Cys Pro Ala Pro Glu Ala Ala Gly Gly Pro Ser Val
225                 230                 235                 240

Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr
                245                 250                 255

Pro Glu Val Thr Cys Val Val Val Asp Val Ser His Glu Asp Pro Glu
            260                 265                 270

Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala Lys
        275                 280                 285

Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg Val Val Ser
    290                 295                 300

Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys
305                 310                 315                 320

Cys Lys Val Ser Asn Lys Ala Leu Gly Ala Pro Ile Glu Lys Thr Ile
                325                 330                 335

Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro
            340                 345                 350

Pro Cys Arg Asp Glu Leu Thr Lys Asn Gln Val Ser Leu Trp Cys Leu
        355                 360                 365

Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn
    370                 375                 380

Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser
385                 390                 395                 400

Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg
                405                 410                 415
```

```
Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His Glu Ala Leu
            420                 425                 430

His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly Gly Gly
        435                 440                 445

Gly Gly Ser Gly Gly Gly Gly Ser Arg Glu Gly Pro Glu Leu Ser Pro
    450                 455                 460

Asp Asp Pro Ala Gly Leu Leu Asp Leu Arg Gln Gly Met Phe Ala Gln
465                 470                 475                 480

Leu Val Ala Gln Asn Val Leu Leu Ile Asp Gly Pro Leu Ser Trp Tyr
                485                 490                 495

Ser Asp Pro Gly Leu Ala Gly Val Ser Leu Thr Gly Gly Leu Ser Tyr
            500                 505                 510

Lys Glu Asp Thr Lys Glu Leu Val Val Ala Lys Ala Gly Val Tyr Tyr
        515                 520                 525

Val Phe Phe Gln Leu Glu Leu Arg Arg Val Val Ala Gly Glu Gly Ser
    530                 535                 540

Gly Ser Val Ser Leu Ala Leu His Leu Gln Pro Leu Arg Ser Ala Ala
545                 550                 555                 560

Gly Ala Ala Ala Leu Ala Leu Thr Val Asp Leu Pro Pro Ala Ser Ser
                565                 570                 575

Glu Ala Arg Asn Ser Ala Phe Gly Phe Gln Gly Arg Leu Leu His Leu
            580                 585                 590

Ser Ala Gly Gln Arg Leu Gly Val His Leu His Thr Glu Ala Arg Ala
        595                 600                 605

Arg His Ala Trp Gln Leu Thr Gln Gly Ala Thr Val Leu Gly Leu Phe
    610                 615                 620

Arg Val Thr Pro Glu Ile Pro Ala Gly Leu
625                 630
```

+ADw-210+AD4- 128
+ADw-211+AD4- 5
+ADw-212+AD4- PRT
+ADw-213+AD4- Secuencia artificial

+ADw-220+AD4-
+ADw-223+AD4- Enlazador pept+AO0-dico G4S

+ADw-400+AD4- 128

Gly Gly Gly Gly Ser
1 5

+ADw-210+AD4- 129
+ADw-211+AD4- 2166
+ADw-212+AD4- ADN
+ADw-213+AD4- Secuencia artificial

+ADw-220+AD4-
+ADw-223+AD4- hu 4-1BBL dim+AOk-rico (71-254) - CL+ACo- cadena Fc pomo

+ADw-400+AD4- 129

agagagggcc ctgagctgag ccccgatgat cctgctggac tgctggacct gcggcagggc 60

atgtttgctc agctggtggc ccagaacgtg ctgctgatcg atggcccccc gtcctggtac 120

agcgatcctg gactggctgg cgtgtcactg acaggcggcc tgagctacaa agaggacacc 180

aaagaactgg tggtggccaa ggccggcgtg tactacgtgt tctttcagct ggaactgcgg 240

agagtggtgg ccggcgaagg atctggctct gtgtctctgg ccctgcatct gcagcctctg 300

agaagcgctg ctggcgctgc agctctggca ctgacagtgg atctgcctcc tgccagctcc 360

gaggcccgga atagcgcatt tgggtttcaa ggcaggctgc tgcacctgtc tgccggccag 420

aggctgggag tgcatctgca cacagaggcc agggctagac acgcctggca gctgacacag 480

ggcgctacag tgctgggcct gttcagagtg acccccgaga ttccagccgg cctgccttct 540

ccaagaagcg aaggcggagg cggatctggc ggcggaggat ctagagaggg acccgaactg 600

tcccctgacg atccagccgg gctgctggat ctgagacagg gaatgttcgc ccagctggtg 660

gctcagaatg tgctgctgat tgacggacct ctgagctggt actccgaccc agggctggca 720

ggggtgtccc tgactggggg actgtcctac aaagaagata caaaagaact ggtggtggct 780

aaagctgggg tgtactatgt gtttttttcag ctggaactga ggcgggtggt ggctggggag 840

ggctcaggat ctgtgtccct ggctctgcat ctgcagccac tgcgctctgc tgctggcgca 900

gctgcactgg ctctgactgt ggacctgcca ccagcctcta gcgaggccag aaacagcgcc 960

ttcgggttcc aaggacgcct gctgcatctg agcgccggac agcgcctggg agtgcatctg 1020

catactgaag ccagagcccg gcatgcttgg cagctgactc agggggcaac tgtgctggga 1080

ctgtttcgcg tgacacctga gatccctgcc ggactgccaa gccctagatc agaaggggggc 1140

ggaggttccg gagggggagg atctcgtacg gtggctgcac catctgtctt tatcttccca 1200

cccagcgacc ggaagctgaa gtctggcaca gccagcgtcg tgtgcctgct gaataacttc 1260

taccccgcg aggccaaggt gcagtggaag gtggacaatg ccctgcagag cggcaacagc 1320

caggaaagcg tgaccgagca ggacagcaag gactccacct acagcctgag cagcaccctg 1380

accctgagca aggccgacta cgagaagcac aaggtgtacg cctgcgaagt gacccaccag 1440

ggcctgtcta gccccgtgac caagagcttc aaccggggcg agtgcgacaa gacccacacc 1500

tgtcctccat gccctgcccc tgaagctgct ggcggcccta gcgtgttcct gttcccccca 1560

aagcccaagg acaccctgat gatcagccgg acccctgaag tgacctgcgt ggtggtggat 1620

gtgtcccacg aggaccctga agtgaagttc aattggtacg tggacggcgt ggaagtgcac 1680

aatgccaaga ccaagccgcg ggaggagcag tacaacagca cgtaccgtgt ggtcagcgtc 1740

ctcaccgtcc tgcaccagga ctggctgaat ggcaaggagt acaagtgcaa ggtctccaac 1800

aaagccctcg gcgcccccat cgagaaaacc atctccaaag ccaaagggca gccccgagaa 1860

ccacaggtgt acaccctgcc cccatgccgg gatgagctga ccaagaacca ggtcagcctg 1920

tggtgcctgg tcaaaggctt ctatcccagc gacatcgccg tggagtggga gagcaatggg 1980

cagccggaga acaactacaa gaccacgcct cccgtgctgg actccgacgg ctccttcttc 2040

ctctacagca agctcaccgt ggacaagagc aggtggcagc aggggaacgt cttctcatgc 2100

tccgtgatgc atgaggctct gcacaaccac tacacgcaga agagcctctc cctgtctccg 2160

ggtaaa 2166

+ADw-210+AD4- 130
+ADw-211+AD4- 891
+ADw-212+AD4- ADN
+ADw-213+AD4- Secuencia artificial

+ADw-220+AD4-
+ADw-223+AD4- hu 4-1BBL monom+AOk-rico (71-254) -CH1+ACo-

+ADw-400+AD4- 130
agagagggcc ctgagctgag ccccgatgat cctgctggac tgctggacct gcggcagggc 60

atgtttgctc agctggtggc ccagaacgtg ctgctgatcg atggcccccc gtcctggtac 120

agcgatcctg gactggctgg cgtgtcactg acaggcggcc tgagctacaa agaggacacc 180

aaagaactgg tggtggccaa ggccggcgtg tactacgtgt tctttcagct ggaactgcgg 240

agagtggtgg ccggcgaagg atctggctct gtgtctctgg ccctgcatct gcagcctctg 300

agaagcgctg ctggcgctgc agctctggct ctgacagtgg atctgcctcc tgccagctcc 360

gaggcccgga atagcgcatt tgggtttcaa ggccggctgc tgcacctgtc tgccggccag 420

agactgggag tgcatctgca cacagaggcc agagccaggc acgcctggca gctgacacag 480

ggcgctacag tgctgggcct gttcagagtg acccccgaga ttcctgccgg cctgcctagc 540

cctagatctg aaggcggcgg aggttccgga ggcggaggat ctgctagcac aaagggcccc 600

agcgtgttcc ctctggcccc tagcagcaag agcacatctg gcggaacagc cgccctgggc 660

tgcctggtgg aagattactt ccccgagccc gtgaccgtgt cctggaattc tggcgccctg 720

acaagcggcg tgcacacctt tccagccgtg ctgcagagca gcggcctgta ctctctgagc 780

agcgtcgtga cagtgcccag cagctctctg ggcacccaga cctacatctg caacgtgaac 840

cacaagccca gcaacaccaa ggtggacgag aaggtggaac ccaagtcctg c 891

+ADw-210+AD4- 131
+ADw-211+AD4- 2154
+ADw-212+AD4- ADN
+ADw-213+AD4- Secuencia artificial

+ADw-220+AD4-
+ADw-223+AD4- hu 4-1BBL dim+AOk-rico (71-254) - CH1+ACo- cadena Fc pomo

+ADw-400+AD4- 131
agagagggcc ctgagctgag ccccgatgat cctgctggac tgctggacct gcggcagggc 60

atgtttgctc agctggtggc ccagaacgtg ctgctgatcg atggcccccc gtcctggtac 120

agcgatcctg gactggctgg cgtgtcactg acaggcggcc tgagctacaa agaggacacc 180

aaagaactgg tggtggccaa ggccggcgtg tactacgtgt tctttcagct ggaactgcgg 240

agagtggtgg ccggcgaagg atctggctct gtgtctctgg ccctgcatct gcagcctctg 300

agaagcgctg ctggcgctgc agctctggca ctgacagtgg atctgcctcc tgccagctcc 360

gaggcccgga atagcgcatt tgggtttcaa ggcaggctgc tgcacctgtc tgccggccag 420

aggctgggag tgcatctgca cacagaggcc agggctagac acgcctggca gctgacacag 480

ggcgctacag tgctgggcct gttcagagtg acccccgaga ttccagccgg cctgccttct 540

ccaagaagcg aaggcggagg cggatctggc ggcggaggat ctagagaggg acccgaactg 600

tcccctgacg atccagccgg gctgctggat ctgagacagg gaatgttcgc ccagctggtg 660

gctcagaatg tgctgctgat tgacggacct ctgagctggt actccgaccc agggctggca 720

ggggtgtccc tgactggggg actgtcctac aaagaagata caaaagaact ggtggtggct 780

aaagctgggg tgtactatgt gttttttcag ctggaactga ggcgggtggt ggctggggag 840

ggctcaggat ctgtgtccct ggctctgcat ctgcagccac tgcgctctgc tgctggcgca 900

gctgcactgg ctctgactgt ggacctgcca ccagcctcta gcgaggccag aaacagcgcc 960

ttcgggttcc aaggacgcct gctgcatctg agcgccggac agcgcctggg agtgcatctg 1020

catactgaag ccagagcccg gcatgcttgg cagctgactc agggggcaac tgtgctggga 1080

ctgtttcgcg tgacacctga gatccctgcc ggactgccaa gccctagatc agaagggggc 1140

ggaggaagcg gagggggagg aagtgctagc accaagggcc cctccgtgtt ccccctggcc 1200

cccagcagca agagcaccag cggcggcaca gccgctctgg gctgcctggt cgaggactac 1260

ttccccgagc ccgtgaccgt gtcctggaac agcggagccc tgacctccgg cgtgcacacc 1320

ttccccgccg tgctgcagag ttctggcctg tatagcctga gcagcgtggt caccgtgcct 1380

tctagcagcc tgggcaccca gacctacatc tgcaacgtga accacaagcc cagcaacacc 1440

aaggtggacg agaaggtgga gcccaagagc tgcgacaaaa ctcacacatg cccaccgtgc 1500

ccagcacctg aagctgcagg gggaccgtca gtcttcctct tccccccaaa acccaaggac 1560

accctcatga tctcccggac ccctgaggtc acatgcgtgg tggtggacgt gagccacgaa 1620

gaccctgagg tcaagttcaa ctggtacgtg gacggcgtgg aggtgcataa tgccaagaca 1680

aagccgcggg aggagcagta caacagcacg taccgtgtgg tcagcgtcct caccgtcctg 1740

caccaggact ggctgaatgg caaggagtac aagtgcaagg tctccaacaa agccctcggc 1800

gcccccatcg agaaaaccat ctccaaagcc aaagggcagc cccgagaacc acaggtgtac 1860

accctgcccc catgccggga tgagctgacc aagaaccagg tcagcctgtg gtgcctggtc 1920

aaaggcttct atcccagcga catcgccgtg gagtgggaga gcaatgggca gccggagaac 1980

aactacaaga ccacgcctcc cgtgctggac tccgacggct ccttcttcct ctacagcaag 2040

ctcaccgtgg acaagagcag gtggcagcag gggaacgtct tctcatgctc cgtgatgcat 2100

gaggctctgc acaaccacta cacgcagaag agcctctccc tgtctccggg taaa 2154

+ADw-210+AD4- 132
+ADw-211+AD4- 903
+ADw-212+AD4- ADN
+ADw-213+AD4- Secuencia artificial

+ADw-220+AD4-
+ADw-223+AD4- Hu 4-1BBL monom+AOk-rico (71-254)-CL+ACo-

+ADw-400+AD4- 132
agagagggcc ctgagctgag ccccgatgat cctgctggac tgctggacct gcggcagggc 60

atgtttgctc agctggtggc ccagaacgtg ctgctgatcg atggcccccc gtcctggtac 120

agcgatcctg gactggctgg cgtgtcactg acaggcggcc tgagctacaa agaggacacc 180

aaagaactgg tggtggccaa ggccggcgtg tactacgtgt tctttcagct ggaactgcgg 240

agagtggtgg ccggcgaagg atctggctct gtgtctctgg ccctgcatct gcagcctctg 300

agaagcgctg ctggcgctgc agctctggca ctgacagtgg atctgcctcc tgccagctcc 360

gaggcccgga atagcgcatt tgggtttcaa ggcaggctgc tgcacctgtc tgccggccag 420

aggctgggag tgcatctgca cacagaggcc agggctagac acgcctggca gctgacacag 480

ggcgctacag tgctgggcct gttcagagtg acccccgaga ttccagccgg cctgccttct 540

ccaagaagcg aaggcggagg cggatctggc ggcggaggat ctcgtacggt ggctgcacca 600

tctgtcttca tcttcccgcc atctgatcgg aagttgaaat ctggaactgc ctctgttgtg 660

tgcctgctga ataacttcta tcccagagag gccaaagtac agtggaaggt ggataacgcc 720

ctccaatcgg gtaactccca ggagagtgtc acagagcagg acagcaagga cagcacctac 780

agcctcagca gcaccctgac gctgagcaaa gcagactacg agaaacacaa agtctacgcc 840

tgcgaagtca cccatcaggg cctgagctcg cccgtcacaa agagcttcaa caggggagag 900

tgt 903

+ADw-210+AD4- 133
+ADw-211+AD4- 1350
+ADw-212+AD4- ADN
+ADw-213+AD4- Secuencia artificial

+ADw-220+AD4-
+ADw-223+AD4- cadena de agujero de Fc anti-FAP(28H1) (VHCL)

+ADw-400+AD4- 133
gaagtgcagc tgctggaatc cggcggaggc ctggtgcagc ctggcggatc tctgagactg 60

tcctgcgccg cctccggctt caccttctcc tcccacgcca tgtcctgggt ccgacaggct 120

cctggcaaag gcctggaatg ggtgtccgcc atctgggcct ccggcgagca gtactacgcc 180

gactctgtga agggccggtt caccatctcc cgggacaact ccaagaacac cctgtacctg 240

cagatgaact ccctgcgggc cgaggacacc gccgtgtact actgtgccaa gggctggctg 300

ggcaacttcg actactgggg acagggcacc ctggtcaccg tgtccagcgc tagcgtggcc 360

gctcccagcg tgttcatctt cccacccagc gacgagcagc tgaagtccgg cacagccagc 420

gtggtgtgcc tgctgaacaa cttctacccc cgcgaggcca aggtgcagtg gaaggtggac 480

aacgccctgc agagcggcaa cagccaggaa tccgtgaccg agcaggacag caaggactcc 540

acctacagcc tgagcagcac cctgaccctg agcaaggccg actacgagaa gcacaaggtg 600

tacgcctgcg aagtgaccca ccagggcctg tccagccccg tgaccaagag cttcaaccgg 660

ggcgagtgcg acaagaccca cacctgtccc ccttgccctg cccctgaagc tgctggtggc 720

ccttccgtgt tcctgttccc cccaaagccc aaggacaccc tgatgatcag ccggaccccc 780

gaagtgacct gcgtggtggt cgatgtgtcc cacgaggacc ctgaagtgaa gttcaattgg 840

tacgtggacg gcgtggaagt gcacaatgcc aagaccaagc cgcgggagga gcagtacaac 900

agcacgtacc gtgtggtcag cgtcctcacc gtcctgcacc aggactggct gaatggcaag 960

gagtacaagt gcaaggtctc caacaaagcc ctcggcgccc ccatcgagaa aaccatctcc 1020

aaagccaaag ggcagccccg agaaccacag gtgtgcaccc tgcccccatc ccgggatgag 1080

ctgaccaaga accaggtcag cctctcgtgc gcagtcaaag gcttctatcc cagcgacatc 1140

gccgtggagt gggagagcaa tgggcagccg gagaacaact acaagaccac gcctcccgtg 1200

ctggactccg acggctcctt cttcctcgtg agcaagctca ccgtggacaa gagcaggtgg 1260

cagcagggga acgtcttctc atgctccgtg atgcatgagg ctctgcacaa ccactacacg 1320

cagaagagcc tctccctgtc tccgggtaaa 1350

+ADw-210+AD4- 134
+ADw-211+AD4- 639

+ADw-212+AD4- ADN
+ADw-213+AD4- Secuencia artificial

+ADw-220+AD4-
+ADw-223+AD4- cadena ligera de anti-FAP(28H1) (VHCL)

+ADw-400+AD4- 134

gagatcgtgc tgacccagtc tcccggcacc ctgagcctga gccctggcga gagagccacc 60

ctgagctgca gagccagcca gagcgtgagc cggagctacc tggcctggta tcagcagaag 120

cccggccagg cccccagact gctgatcatc ggcgccagca cccgggccac cggcatcccc 180

gatagattca gcggcagcgg ctccggcacc gacttcaccc tgaccatcag ccggctggaa 240

cccgaggact tcgccgtgta ctactgccag cagggccagg tgatcccccc caccttcggc 300

cagggcacca aggtggaaat caagagcagc gcttccacca aaggcccttc cgtgtttcct 360

ctggctccta gctccaagtc cacctctgga ggcaccgctg ctctcggatg cctcgtgaag 420

gattattttc ctgagcctgt gacagtgtcc tggaatagcg gagcactgac ctctggagtg 480

catactttcc ccgctgtgct gcagtcctct ggactgtaca gcctgagcag cgtggtgaca 540

gtgcccagca gcagcctggg cacccagacc tacatctgca acgtgaacca caagcccagc 600

aacaccaagg tggacaagaa ggtggaaccc aagtcttgt 639

+ADw-210+AD4- 135
+ADw-211+AD4- 450
+ADw-212+AD4- PRT
+ADw-213+AD4- Secuencia artificial

+ADw-220+AD4-
+ADw-223+AD4- cadena de agujero de Fc anti-FAP(28H1) (VHCL)

+ADw-400+AD4- 135

Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Ser His
20 25 30

Ala Met Ser Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Ser Ala Ile Trp Ala Ser Gly Glu Gln Tyr Tyr Ala Asp Ser Val Lys
50 55 60

Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr Leu
65 70 75 80

Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys Ala
85 90 95

```
Lys Gly Trp Leu Gly Asn Phe Asp Tyr Trp Gly Gln Gly Thr Leu Val
            100                 105                 110

Thr Val Ser Ser Ala Ser Val Ala Ala Pro Ser Val Phe Ile Phe Pro
        115                 120                 125

Pro Ser Asp Glu Gln Leu Lys Ser Gly Thr Ala Ser Val Val Cys Leu
    130                 135                 140

Leu Asn Asn Phe Tyr Pro Arg Glu Ala Lys Val Gln Trp Lys Val Asp
145                 150                 155                 160

Asn Ala Leu Gln Ser Gly Asn Ser Gln Glu Ser Val Thr Glu Gln Asp
                165                 170                 175

Ser Lys Asp Ser Thr Tyr Ser Leu Ser Ser Thr Leu Thr Leu Ser Lys
            180                 185                 190

Ala Asp Tyr Glu Lys His Lys Val Tyr Ala Cys Glu Val Thr His Gln
        195                 200                 205

Gly Leu Ser Ser Pro Val Thr Lys Ser Phe Asn Arg Gly Glu Cys Asp
    210                 215                 220

Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Ala Ala Gly Gly
225                 230                 235                 240

Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile
                245                 250                 255

Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His Glu
            260                 265                 270

Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val His
        275                 280                 285

Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg
    290                 295                 300

Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys
305                 310                 315                 320

Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Gly Ala Pro Ile Glu
                325                 330                 335

Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Cys
            340                 345                 350
```

```
Thr Leu Pro Pro Ser Arg Asp Glu Leu Thr Lys Asn Gln Val Ser Leu
        355                 360                 365


Ser Cys Ala Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp
    370                 375                 380


Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val
385                 390                 395                 400


Leu Asp Ser Asp Gly Ser Phe Phe Leu Val Ser Lys Leu Thr Val Asp
                405                 410                 415


Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His
            420                 425                 430


Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro
        435                 440                 445


Gly Lys
    450


+ADw-210+AD4-  136
+ADw-211+AD4-  213
+ADw-212+AD4-  PRT
+ADw-213+AD4-  Secuencia artificial

+ADw-220+AD4-
+ADw-223+AD4-  cadena ligera de anti-FAP(28H1) (VHCL)

+ADw-400+AD4-  136

Glu Ile Val Leu Thr Gln Ser Pro Gly Thr Leu Ser Leu Ser Pro Gly
1               5                   10                  15


Glu Arg Ala Thr Leu Ser Cys Arg Ala Ser Gln Ser Val Ser Arg Ser
            20                  25                  30


Tyr Leu Ala Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Arg Leu Leu
        35                  40                  45


Ile Ile Gly Ala Ser Thr Arg Ala Thr Gly Ile Pro Asp Arg Phe Ser
    50                  55                  60


Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Arg Leu Glu
65                  70                  75                  80


Pro Glu Asp Phe Ala Val Tyr Tyr Cys Gln Gln Gly Gln Val Ile Pro
                85                  90                  95
```

Pro Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys Ser Ser Ala Ser
100 105 110

Thr Lys Gly Pro Ser Val Phe Pro Leu Ala Pro Ser Ser Lys Ser Thr
115 120 125

Ser Gly Gly Thr Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro
130 135 140

Glu Pro Val Thr Val Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val
145 150 155 160

His Thr Phe Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser
165 170 175

Ser Val Val Thr Val Pro Ser Ser Ser Leu Gly Thr Gln Thr Tyr Ile
180 185 190

Cys Asn Val Asn His Lys Pro Ser Asn Thr Lys Val Asp Lys Lys Val
195 200 205

Glu Pro Lys Ser Cys
210

+ADw-210+AD4- 137
+ADw-211+AD4- 1572
+ADw-212+AD4- ADN
+ADw-213+AD4- Secuencia artificial

+ADw-220+AD4-
+ADw-223+AD4- hu 4-1BBL monom+AOk-rico (71-254) - CH1+ACo- cadena Fc pomo

+ADw-400+AD4- 137
agagagggcc ctgagctgag ccccgatgat cctgctggac tgctggacct gcggcagggc 60

atgtttgctc agctggtggc ccagaacgtg ctgctgatcg atggcccccc gtcctggtac 120

agcgatcctg gactggctgg cgtgtcactg acaggcggcc tgagctacaa agaggacacc 180

aaagaactgg tggtggccaa ggccggcgtg tactacgtgt tctttcagct ggaactgcgg 240

agagtggtgg ccggcgaagg atctggctct gtgtctctgg ccctgcatct gcagcctctg 300

agaagcgctg ctggcgctgc agctctggct ctgacagtgg atctgcctcc tgccagctcc 360

gaggcccgga atagcgcatt tgggtttcaa ggccggctgc tgcacctgtc tgccggccag 420

agactgggag tgcatctgca cacagaggcc agagccaggc acgcctggca gctgacacag 480

ggcgctacag tgctgggcct gttcagagtg acccccgaga ttcctgccgg cctgcctagc 540

cctagatctg aaggcggcgg aggttccgga ggcggaggat ctgctagcac caagggcccc 600

tccgtgttcc ccctggcccc cagcagcaag agcaccagcg gcggcacagc cgctctgggc 660

tgcctggtcg aggactactt ccccgagccc gtgaccgtgt cctggaacag cggagccctg 720

acctccggcg tgcacacctt ccccgccgtg ctgcagagtt ctggcctgta tagcctgagc 780

agcgtggtca ccgtgccttc tagcagcctg ggcacccaga cctacatctg caacgtgaac 840

cacaagccca gcaacaccaa ggtggacgag aaggtggagc ccaagagctg cgacaaaact 900

cacacatgcc caccgtgccc agcacctgaa gctgcagggg gaccgtcagt cttcctcttc 960

cccccaaaac ccaaggacac cctcatgatc tcccggaccc ctgaggtcac atgcgtggtg 1020

gtggacgtga gccacgaaga ccctgaggtc aagttcaact ggtacgtgga cggcgtggag 1080

gtgcataatg ccaagacaaa gccgcgggag gagcagtaca acagcacgta ccgtgtggtc 1140

agcgtcctca ccgtcctgca ccaggactgg ctgaatggca aggagtacaa gtgcaaggtc 1200

tccaacaaag ccctcggcgc ccccatcgag aaaaccatct ccaaagccaa agggcagccc 1260

cgagaaccac aggtgtacac cctgccccca tgccgggatg agctgaccaa gaaccaggtc 1320

agcctgtggt gcctggtcaa aggcttctat cccagcgaca tcgccgtgga gtgggagagc 1380

aatgggcagc cggagaacaa ctacaagacc acgcctcccg tgctggactc cgacggctcc 1440

ttcttcctct acagcaagct caccgtggac aagagcaggt ggcagcaggg gaacgtcttc 1500

tcatgctccg tgatgcatga ggctctgcac aaccactaca cgcagaagag cctctccctg 1560

tctccgggta aa 1572

+ADw-210+AD4- 138
+ADw-211+AD4- 1485
+ADw-212+AD4- ADN
+ADw-213+AD4- Secuencia artificial

+ADw-220+AD4-
+ADw-223+AD4- Hu 4-1BBL dim+AOk-rico (71-254)-CL+ACo-

+ADw-400+AD4- 138
agagagggcc ctgagctgag ccccgatgat cctgctggac tgctggacct gcggcagggc 60

atgtttgctc agctggtggc ccagaacgtg ctgctgatcg atggcccccc gtcctggtac 120

agcgatcctg gactggctgg cgtgtcactg acaggcggcc tgagctacaa agaggacacc 180

aaagaactgg tggtggccaa ggccggcgtg tactacgtgt tctttcagct ggaactgcgg 240

agagtggtgg ccggcgaagg atctggctct gtgtctctgg ccctgcatct gcagcctctg 300

agaagcgctg ctggcgctgc agctctggca ctgacagtgg atctgcctcc tgccagctcc 360

gaggcccgga atagcgcatt tgggtttcaa ggcaggctgc tgcacctgtc tgccggccag 420

aggctgggag tgcatctgca cacagaggcc agggctagac acgcctggca gctgacacag 480

ggcgctacag tgctgggcct gttcagagtg acccccgaga ttccagccgg cctgccttct 540

ccaagaagcg aaggcggagg cggatctggc ggcggaggat ctagagaggg acccgaactg 600

tcccctgacg atccagccgg gctgctggat ctgagacagg gaatgttcgc ccagctggtg 660

gctcagaatg tgctgctgat tgacggacct ctgagctggt actccgaccc agggctggca 720

ggggtgtccc tgactggggg actgtcctac aaagaagata caaaagaact ggtggtggct 780

aaagctgggg tgtactatgt gttttttcag ctggaactga ggcgggtggt ggctggggag 840

ggctcaggat ctgtgtccct ggctctgcat ctgcagccac tgcgctctgc tgctggcgca 900

gctgcactgg ctctgactgt ggacctgcca ccagcctcta gcgaggccag aaacagcgcc 960

ttcgggttcc aaggacgcct gctgcatctg agcgccggac agcgcctggg agtgcatctg 1020

catactgaag ccagagcccg gcatgcttgg cagctgactc agggggcaac tgtgctggga 1080

ctgtttcgcg tgacacctga gatccctgcc ggactgccaa gccctagatc agaaggggc 1140

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tatcccagag aggccaaagt acagtggaag gtggataacg ccctccaatc gggtaactcc 1320

caggagagtg tcacagagca ggacagcaag gacagcacct acagcctcag cagcaccctg 1380

acgctgagca aagcagacta cgagaaacac aaagtctacg cctgcgaagt cacccatcag 1440

ggcctgagct cgcccgtcac aaagagcttc aacaggggag agtgt 1485

+ADw-210+AD4- 139
+ADw-211+AD4- 718
+ADw-212+AD4- PRT
+ADw-213+AD4- Secuencia artificial

+ADw-220+AD4-
+ADw-223+AD4- hu 4-1BBL monom+AOk-rico (71-254) - CL+ACo- cadena Fc pomo

+ADw-400+AD4- 139

Arg Glu Gly Pro Glu Leu Ser Pro Asp Asp Pro Ala Gly Leu Leu Asp
1 5 10 15

Leu Arg Gln Gly Met Phe Ala Gln Leu Val Ala Gln Asn Val Leu Leu
20 25 30

Ile Asp Gly Pro Leu Ser Trp Tyr Ser Asp Pro Gly Leu Ala Gly Val
35 40 45

Ser Leu Thr Gly Gly Leu Ser Tyr Lys Glu Asp Thr Lys Glu Leu Val
50 55 60

Val Ala Lys Ala Gly Val Tyr Tyr Val Phe Phe Gln Leu Glu Leu Arg
65 70 75 80

Arg Val Val Ala Gly Glu Gly Ser Gly Ser Val Ser Leu Ala Leu His
85 90 95

```
Leu Gln Pro Leu Arg Ser Ala Ala Gly Ala Ala Ala Leu Ala Leu Thr
            100                 105                 110

Val Asp Leu Pro Pro Ala Ser Ser Glu Ala Arg Asn Ser Ala Phe Gly
        115                 120                 125

Phe Gln Gly Arg Leu Leu His Leu Ser Ala Gly Gln Arg Leu Gly Val
    130                 135                 140

His Leu His Thr Glu Ala Arg Ala Arg His Ala Trp Gln Leu Thr Gln
145                 150                 155                 160

Gly Ala Thr Val Leu Gly Leu Phe Arg Val Thr Pro Glu Ile Pro Ala
                165                 170                 175

Gly Leu Pro Ser Pro Arg Ser Glu Gly Gly Gly Gly Ser Gly Gly Gly
            180                 185                 190

Gly Ser Arg Glu Gly Pro Glu Leu Ser Pro Asp Asp Pro Ala Gly Leu
        195                 200                 205

Leu Asp Leu Arg Gln Gly Met Phe Ala Gln Leu Val Ala Gln Asn Val
    210                 215                 220

Leu Leu Ile Asp Gly Pro Leu Ser Trp Tyr Ser Asp Pro Gly Leu Ala
225                 230                 235                 240

Gly Val Ser Leu Thr Gly Gly Leu Ser Tyr Lys Glu Asp Thr Lys Glu
                245                 250                 255

Leu Val Val Ala Lys Ala Gly Val Tyr Tyr Val Phe Phe Gln Leu Glu
            260                 265                 270

Leu Arg Arg Val Val Ala Gly Glu Gly Ser Gly Ser Val Ser Leu Ala
        275                 280                 285

Leu His Leu Gln Pro Leu Arg Ser Ala Ala Gly Ala Ala Ala Leu Ala
    290                 295                 300

Leu Thr Val Asp Leu Pro Pro Ala Ser Ser Glu Ala Arg Asn Ser Ala
305                 310                 315                 320

Phe Gly Phe Gln Gly Arg Leu Leu His Leu Ser Ala Gly Gln Arg Leu
                325                 330                 335

Gly Val His Leu His Thr Glu Ala Arg Ala Arg His Ala Trp Gln Leu
```

```
            340                 345                 350

Thr Gln Gly Ala Thr Val Leu Gly Leu Phe Arg Val Thr Pro Glu Ile
        355                 360                 365

Pro Ala Gly Leu Pro Ser Pro Arg Ser Glu Gly Gly Gly Gly Ser Gly
    370                 375                 380

Gly Gly Gly Ser Ala Ser Thr Lys Gly Pro Ser Val Phe Pro Leu Ala
385                 390                 395                 400

Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu Gly Cys Leu
                405                 410                 415

Val Glu Asp Tyr Phe Pro Glu Pro Val Thr Val Ser Trp Asn Ser Gly
            420                 425                 430

Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala Val Leu Gln Ser Ser
        435                 440                 445

Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser Ser Ser Leu
    450                 455                 460

Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys Pro Ser Asn Thr
465                 470                 475                 480

Lys Val Asp Glu Lys Val Glu Pro Lys Ser Cys Asp Lys Thr His Thr
                485                 490                 495

Cys Pro Pro Cys Pro Ala Pro Glu Ala Ala Gly Gly Pro Ser Val Phe
            500                 505                 510

Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro
        515                 520                 525

Glu Val Thr Cys Val Val Val Asp Val Ser His Glu Asp Pro Glu Val
    530                 535                 540

Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr
545                 550                 555                 560

Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg Val Val Ser Val
                565                 570                 575

Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys
            580                 585                 590
```

```
Lys Val Ser Asn Lys Ala Leu Gly Ala Pro Ile Glu Lys Thr Ile Ser
        595                 600                 605

Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro
    610                 615                 620

Cys Arg Asp Glu Leu Thr Lys Asn Gln Val Ser Leu Trp Cys Leu Val
625                 630                 635                 640

Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly
                645                 650                 655

Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp
            660                 665                 670

Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp
        675                 680                 685

Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His Glu Ala Leu His
    690                 695                 700

Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly Lys
705                 710                 715


+ADw-210+AD4-  140
+ADw-211+AD4-  495
+ADw-212+AD4-  PRT
+ADw-213+AD4-  Secuencia artificial

+ADw-220+AD4-
+ADw-223+AD4-  Hu 4-1BBL dim+AOk-rico (71-254)-CL+ACo-

+ADw-400+AD4-  140

Arg Glu Gly Pro Glu Leu Ser Pro Asp Asp Pro Ala Gly Leu Leu Asp
1               5                  10                  15

Leu Arg Gln Gly Met Phe Ala Gln Leu Val Ala Gln Asn Val Leu Leu
            20                  25                  30

Ile Asp Gly Pro Leu Ser Trp Tyr Ser Asp Pro Gly Leu Ala Gly Val
        35                  40                  45

Ser Leu Thr Gly Gly Leu Ser Tyr Lys Glu Asp Thr Lys Glu Leu Val
    50                  55                  60

Val Ala Lys Ala Gly Val Tyr Tyr Val Phe Phe Gln Leu Glu Leu Arg
65                  70                  75                  80

Arg Val Val Ala Gly Glu Gly Ser Gly Ser Val Ser Leu Ala Leu His
```

```
                85                  90                  95

Leu Gln Pro Leu Arg Ser Ala Ala Gly Ala Ala Ala Leu Ala Leu Thr
            100                 105                 110

Val Asp Leu Pro Pro Ala Ser Ser Glu Ala Arg Asn Ser Ala Phe Gly
        115                 120                 125

Phe Gln Gly Arg Leu Leu His Leu Ser Ala Gly Gln Arg Leu Gly Val
    130                 135                 140

His Leu His Thr Glu Ala Arg Ala Arg His Ala Trp Gln Leu Thr Gln
145                 150                 155                 160

Gly Ala Thr Val Leu Gly Leu Phe Arg Val Thr Pro Glu Ile Pro Ala
                165                 170                 175

Gly Leu Pro Ser Pro Arg Ser Glu Gly Gly Gly Gly Ser Gly Gly Gly
            180                 185                 190

Gly Ser Arg Glu Gly Pro Glu Leu Ser Pro Asp Asp Pro Ala Gly Leu
        195                 200                 205

Leu Asp Leu Arg Gln Gly Met Phe Ala Gln Leu Val Ala Gln Asn Val
    210                 215                 220

Leu Leu Ile Asp Gly Pro Leu Ser Trp Tyr Ser Asp Pro Gly Leu Ala
225                 230                 235                 240

Gly Val Ser Leu Thr Gly Gly Leu Ser Tyr Lys Glu Asp Thr Lys Glu
                245                 250                 255

Leu Val Val Ala Lys Ala Gly Val Tyr Tyr Val Phe Phe Gln Leu Glu
            260                 265                 270

Leu Arg Arg Val Val Ala Gly Glu Gly Ser Gly Ser Val Ser Leu Ala
        275                 280                 285

Leu His Leu Gln Pro Leu Arg Ser Ala Ala Gly Ala Ala Ala Leu Ala
    290                 295                 300

Leu Thr Val Asp Leu Pro Pro Ala Ser Ser Glu Ala Arg Asn Ser Ala
305                 310                 315                 320

Phe Gly Phe Gln Gly Arg Leu Leu His Leu Ser Ala Gly Gln Arg Leu
                325                 330                 335
```

Gly Val His Leu His Thr Glu Ala Arg Ala Arg His Ala Trp Gln Leu
340 345 350

Thr Gln Gly Ala Thr Val Leu Gly Leu Phe Arg Val Thr Pro Glu Ile
355 360 365

Pro Ala Gly Leu Pro Ser Pro Arg Ser Glu Gly Gly Gly Gly Ser Gly
370 375 380

Gly Gly Gly Ser Arg Thr Val Ala Ala Pro Ser Val Phe Ile Phe Pro
385 390 395 400

Pro Ser Asp Arg Lys Leu Lys Ser Gly Thr Ala Ser Val Val Cys Leu
405 410 415

Leu Asn Asn Phe Tyr Pro Arg Glu Ala Lys Val Gln Trp Lys Val Asp
420 425 430

Asn Ala Leu Gln Ser Gly Asn Ser Gln Glu Ser Val Thr Glu Gln Asp
435 440 445

Ser Lys Asp Ser Thr Tyr Ser Leu Ser Ser Thr Leu Thr Leu Ser Lys
450 455 460

Ala Asp Tyr Glu Lys His Lys Val Tyr Ala Cys Glu Val Thr His Gln
465 470 475 480

Gly Leu Ser Ser Pro Val Thr Lys Ser Phe Asn Arg Gly Glu Cys
485 490 495

+ADw-210+AD4- 141
+ADw-211+AD4- 2499
+ADw-212+AD4- ADN
+ADw-213+AD4- Secuencia artificial

+ADw-220+AD4-
+ADw-223+AD4- cadena Fc agujero de anti-FAP (28H1) fusionada a hu 4-1BBL dim+AOk-rico (71-254)

+ADw-400+AD4- 141
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+ADw-210+AD4- 142
+ADw-211+AD4- 1917
+ADw-212+AD4- ADN
+ADw-213+AD4- Secuencia artificial

+ADw-220+AD4-
+ADw-223+AD4- ADN de cadena de Fc pomo de anti-FAP (28H1) fusionada a hu 4-1BBL monom+AOk-rico
(71-254)

+ADw-400+AD4- 142
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+ADw-210+AD4- 143
+ADw-211+AD4- 888
+ADw-212+AD4- ADN
+ADw-213+AD4- Secuencia artificial

+ADw-220+AD4-
+ADw-223+AD4- hu 4-1BBL monom+AOk-rico (71-254) -(G4S)1- CL+ACo-

+ADw-400+AD4- 143
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+ADw-210+AD4- 144

+ADw-211+AD4- 2028
+ADw-212+AD4- ADN
+ADw-213+AD4- Secuencia artificial

+ADw-220+AD4-
+ADw-223+AD4- +AFs-anti-FAP (28H1)+AF0-2 cadena de Fc agujero

+ADw-400+AD4- 144

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gtggacaaga gcaggtggca gcaggggaac gtcttctcat gctccgtgat gcatgaggct     1980

ctgcacaacc actacacgca gaagagcctc tccctgtctc cgggtaaa                  2028


+ADw-210+AD4-  145
+ADw-211+AD4-  676
+ADw-212+AD4-  PRT
+ADw-213+AD4-  Secuencia artificial

+ADw-220+AD4-
+ADw-223+AD4-  +AFs-anti-FAP (28H1)+AF0-2 cadena de Fc agujero

+ADw-400+AD4-  145

Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1               5                  10                  15


Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Ser His
            20                  25                  30


Ala Met Ser Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
        35                  40                  45


Ser Ala Ile Trp Ala Ser Gly Glu Gln Tyr Tyr Ala Asp Ser Val Lys
    50                  55                  60


Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr Leu
65                  70                  75                  80


Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys Ala
                85                  90                  95


Lys Gly Trp Leu Gly Asn Phe Asp Tyr Trp Gly Gln Gly Thr Leu Val
            100                 105                 110


Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser Val Phe Pro Leu Ala
        115                 120                 125


Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu Gly Cys Leu
    130                 135                 140


Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser Trp Asn Ser Gly
145                 150                 155                 160
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Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala Val Leu Gln Ser Ser
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Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser Ser Ser Leu
            180                 185                 190

Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys Pro Ser Asn Thr
        195                 200                 205

Lys Val Asp Lys Lys Val Glu Pro Lys Ser Cys Asp Gly Gly Gly Gly
    210                 215                 220

Ser Gly Gly Gly Gly Ser Glu Val Gln Leu Leu Glu Ser Gly Gly Gly
225                 230                 235                 240

Leu Val Gln Pro Gly Gly Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly
                245                 250                 255

Phe Thr Phe Ser Ser His Ala Met Ser Trp Val Arg Gln Ala Pro Gly
            260                 265                 270

Lys Gly Leu Glu Trp Val Ser Ala Ile Trp Ala Ser Gly Glu Gln Tyr
        275                 280                 285

Tyr Ala Asp Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser
    290                 295                 300

Lys Asn Thr Leu Tyr Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr
305                 310                 315                 320

Ala Val Tyr Tyr Cys Ala Lys Gly Trp Leu Gly Asn Phe Asp Tyr Trp
                325                 330                 335

Gly Gln Gly Thr Leu Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro
            340                 345                 350

Ser Val Phe Pro Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr
        355                 360                 365

Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr
    370                 375                 380

Val Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro
385                 390                 395                 400

Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr
                405                 410                 415
```

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Val Pro Ser Ser Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn
            420                 425                 430

His Lys Pro Ser Asn Thr Lys Val Asp Lys Lys Val Glu Pro Lys Ser
        435                 440                 445

Cys Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Ala Ala
    450                 455                 460

Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu
465                 470                 475                 480

Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser
                485                 490                 495

His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu
            500                 505                 510

Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr
        515                 520                 525

Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn
    530                 535                 540

Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Gly Ala Pro
545                 550                 555                 560

Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln
                565                 570                 575

Val Cys Thr Leu Pro Pro Ser Arg Asp Glu Leu Thr Lys Asn Gln Val
            580                 585                 590

Ser Leu Ser Cys Ala Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val
        595                 600                 605

Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro
    610                 615                 620

Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Val Ser Lys Leu Thr
625                 630                 635                 640

Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val
                645                 650                 655

Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu
```

660 665 670

Ser Pro Gly Lys
675

+ADw-210+AD4- 146
+ADw-211+AD4- 2514
+ADw-212+AD4- ADN
+ADw-213+AD4- Secuencia artificial

+ADw-220+AD4-
+ADw-223+AD4- hu 4-1BBL dim+AOk-rico (71-254) - FAP (VHCL+ACo-) cadena Fc pomo

+ADw-400+AD4- 146
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+ADw-210+AD4- 147
+ADw-211+AD4- 1221
+ADw-212+AD4- ADN
+ADw-213+AD4- Secuencia artificial

+ADw-220+AD4-
+ADw-223+AD4- Hu 4-1BBL monom+AOk-rico (71-254) +IBM-FAP (VLCH1+ACo-)

+ADw-400+AD4- 147
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aaagaactgg tggtggccaa ggccggcgtg tactacgtgt tctttcagct ggaactgcgg 240

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agaagcgctg ctggcgctgc agctctggct ctgacagtgg atctgcctcc tgccagctcc 360

gaggcccgga atagcgcatt tgggtttcaa ggccggctgc tgcacctgtc tgccggccag 420

agactgggag tgcatctgca cacagaggcc agagccaggc acgcctggca gctgacacag 480

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ggcgctacag tgctgggcct gttcagagtg acccccgaga ttcctgccgg cctgcctagc      540

cctagatctg aaggcggcgg aggttccgga ggcggaggat ctgagatcgt gctgacccag      600

tctcccggca ccctgagcct gagccctggc gagagagcca ccctgagctg cagagccagc      660

cagagcgtga gccggagcta cctggcctgg tatcagcaga agcccggcca ggcccccaga      720

ctgctgatca tcggcgccag cacccgggcc accggcatcc ccgatagatt cagcggcagc      780

ggctccggca ccgacttcac cctgaccatc agccggctgg aacccgagga cttcgccgtg      840

tactactgcc agcagggcca ggtgatcccc cccaccttcg gccagggcac caaggtggaa      900

atcaagtcct ctgctagcac aaagggcccc agcgtgttcc ctctggcccc tagcagcaag      960

agcacatctg gcggaacagc cgccctgggc tgcctggtgg aagattactt ccccgagccc     1020

gtgaccgtgt cctggaattc tggcgccctg acaagcggcg tgcacacctt tccagccgtg     1080

ctgcagagca gcggcctgta ctctctgagc agcgtcgtga cagtgcccag cagctctctg     1140

ggcacccaga cctacatctg caacgtgaac cacaagccca gcaacaccaa ggtggacgag     1200

aaggtggaac ccaagtcctg c                                               1221
```

+ADw-210+AD4- 148
+ADw-211+AD4- 838
+ADw-212+AD4- PRT
+ADw-213+AD4- Secuencia artificial

+ADw-220+AD4-
+ADw-223+AD4- hu 4-1BBL dim+AOk-rico (71-254) - FAP (VHCL+ACo-) cadena Fc pomo

+ADw-400+AD4- 148

```
Arg Glu Gly Pro Glu Leu Ser Pro Asp Asp Pro Ala Gly Leu Leu Asp
1               5                  10                  15

Leu Arg Gln Gly Met Phe Ala Gln Leu Val Ala Gln Asn Val Leu Leu
            20                  25                  30

Ile Asp Gly Pro Leu Ser Trp Tyr Ser Asp Pro Gly Leu Ala Gly Val
        35                  40                  45

Ser Leu Thr Gly Gly Leu Ser Tyr Lys Glu Asp Thr Lys Glu Leu Val
    50                  55                  60

Val Ala Lys Ala Gly Val Tyr Tyr Val Phe Phe Gln Leu Glu Leu Arg
65                  70                  75                  80

Arg Val Val Ala Gly Glu Gly Ser Gly Ser Val Ser Leu Ala Leu His
                85                  90                  95

Leu Gln Pro Leu Arg Ser Ala Ala Gly Ala Ala Ala Leu Ala Leu Thr
            100                 105                 110
```

```
Val Asp Leu Pro Pro Ala Ser Ser Glu Ala Arg Asn Ser Ala Phe Gly
        115                 120                 125

Phe Gln Gly Arg Leu Leu His Leu Ser Ala Gly Gln Arg Leu Gly Val
    130                 135                 140

His Leu His Thr Glu Ala Arg Ala Arg His Ala Trp Gln Leu Thr Gln
145                 150                 155                 160

Gly Ala Thr Val Leu Gly Leu Phe Arg Val Thr Pro Glu Ile Pro Ala
                165                 170                 175

Gly Leu Pro Ser Pro Arg Ser Glu Gly Gly Gly Gly Ser Gly Gly Gly
            180                 185                 190

Gly Ser Arg Glu Gly Pro Glu Leu Ser Pro Asp Asp Pro Ala Gly Leu
        195                 200                 205

Leu Asp Leu Arg Gln Gly Met Phe Ala Gln Leu Val Ala Gln Asn Val
    210                 215                 220

Leu Leu Ile Asp Gly Pro Leu Ser Trp Tyr Ser Asp Pro Gly Leu Ala
225                 230                 235                 240

Gly Val Ser Leu Thr Gly Gly Leu Ser Tyr Lys Glu Asp Thr Lys Glu
                245                 250                 255

Leu Val Val Ala Lys Ala Gly Val Tyr Tyr Val Phe Phe Gln Leu Glu
            260                 265                 270

Leu Arg Arg Val Val Ala Gly Glu Gly Ser Gly Ser Val Ser Leu Ala
        275                 280                 285

Leu His Leu Gln Pro Leu Arg Ser Ala Ala Gly Ala Ala Ala Leu Ala
    290                 295                 300

Leu Thr Val Asp Leu Pro Pro Ala Ser Ser Glu Ala Arg Asn Ser Ala
305                 310                 315                 320

Phe Gly Phe Gln Gly Arg Leu Leu His Leu Ser Ala Gly Gln Arg Leu
                325                 330                 335

Gly Val His Leu His Thr Glu Ala Arg Ala Arg His Ala Trp Gln Leu
            340                 345                 350

Thr Gln Gly Ala Thr Val Leu Gly Leu Phe Arg Val Thr Pro Glu Ile
```

```
        355                 360                 365

Pro Ala Gly Leu Pro Ser Pro Arg Ser Glu Gly Gly Gly Gly Ser Gly
    370                 375                 380

Gly Gly Gly Ser Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Val
385                 390                 395                 400

Gln Pro Gly Gly Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr
                405                 410                 415

Phe Ser Ser His Ala Met Ser Trp Val Arg Gln Ala Pro Gly Lys Gly
            420                 425                 430

Leu Glu Trp Val Ser Ala Ile Trp Ala Ser Gly Glu Gln Tyr Tyr Ala
        435                 440                 445

Asp Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn
    450                 455                 460

Thr Leu Tyr Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val
465                 470                 475                 480

Tyr Tyr Cys Ala Lys Gly Trp Leu Gly Asn Phe Asp Tyr Trp Gly Gln
                485                 490                 495

Gly Thr Leu Val Thr Val Ser Ser Ala Ser Val Ala Ala Pro Ser Val
            500                 505                 510

Phe Ile Phe Pro Pro Ser Asp Arg Lys Leu Lys Ser Gly Thr Ala Ser
        515                 520                 525

Val Val Cys Leu Leu Asn Asn Phe Tyr Pro Arg Glu Ala Lys Val Gln
    530                 535                 540

Trp Lys Val Asp Asn Ala Leu Gln Ser Gly Asn Ser Gln Glu Ser Val
545                 550                 555                 560

Thr Glu Gln Asp Ser Lys Asp Ser Thr Tyr Ser Leu Ser Ser Thr Leu
                565                 570                 575

Thr Leu Ser Lys Ala Asp Tyr Glu Lys His Lys Val Tyr Ala Cys Glu
            580                 585                 590

Val Thr His Gln Gly Leu Ser Ser Pro Val Thr Lys Ser Phe Asn Arg
        595                 600                 605
```

```
Gly Glu Cys Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu
    610                 615                 620

Ala Ala Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp
625                 630                 635                 640

Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp
                645                 650                 655

Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly
            660                 665                 670

Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn
        675                 680                 685

Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp
    690                 695                 700

Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Gly
705                 710                 715                 720

Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu
                725                 730                 735

Pro Gln Val Tyr Thr Leu Pro Pro Cys Arg Asp Glu Leu Thr Lys Asn
            740                 745                 750

Gln Val Ser Leu Trp Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile
        755                 760                 765

Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr
    770                 775                 780

Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys
785                 790                 795                 800

Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys
                805                 810                 815

Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu
            820                 825                 830

Ser Leu Ser Pro Gly Lys
        835
```

+ADw-210+AD4- 149
+ADw-211+AD4- 407
+ADw-212+AD4- PRT

+ADw-213+AD4- Secuencia artificial

+ADw-220+AD4-
+ADw-223+AD4- Hu 4-1BBL monom+AOk-rico (71-254) +IBM-FAP (VLCH1+ACo-)

+ADw-400+AD4- 149

```
Arg Glu Gly Pro Glu Leu Ser Pro Asp Asp Pro Ala Gly Leu Leu Asp
1               5                  10                  15

Leu Arg Gln Gly Met Phe Ala Gln Leu Val Ala Gln Asn Val Leu Leu
            20                  25                  30

Ile Asp Gly Pro Leu Ser Trp Tyr Ser Asp Pro Gly Leu Ala Gly Val
        35                  40                  45

Ser Leu Thr Gly Gly Leu Ser Tyr Lys Glu Asp Thr Lys Glu Leu Val
    50                  55                  60

Val Ala Lys Ala Gly Val Tyr Tyr Val Phe Phe Gln Leu Glu Leu Arg
65                  70                  75                  80

Arg Val Val Ala Gly Glu Gly Ser Gly Ser Val Ser Leu Ala Leu His
                85                  90                  95

Leu Gln Pro Leu Arg Ser Ala Ala Gly Ala Ala Ala Leu Ala Leu Thr
            100                 105                 110

Val Asp Leu Pro Pro Ala Ser Ser Glu Ala Arg Asn Ser Ala Phe Gly
        115                 120                 125

Phe Gln Gly Arg Leu Leu His Leu Ser Ala Gly Gln Arg Leu Gly Val
    130                 135                 140

His Leu His Thr Glu Ala Arg Ala Arg His Ala Trp Gln Leu Thr Gln
145                 150                 155                 160

Gly Ala Thr Val Leu Gly Leu Phe Arg Val Thr Pro Glu Ile Pro Ala
                165                 170                 175

Gly Leu Pro Ser Pro Arg Ser Glu Gly Gly Gly Gly Ser Gly Gly Gly
            180                 185                 190

Gly Ser Glu Ile Val Leu Thr Gln Ser Pro Gly Thr Leu Ser Leu Ser
        195                 200                 205

Pro Gly Glu Arg Ala Thr Leu Ser Cys Arg Ala Ser Gln Ser Val Ser
    210                 215                 220
```

```
Arg Ser Tyr Leu Ala Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Arg
225                 230                 235                 240

Leu Leu Ile Ile Gly Ala Ser Thr Arg Ala Thr Gly Ile Pro Asp Arg
                245                 250                 255

Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Arg
            260                 265                 270

Leu Glu Pro Glu Asp Phe Ala Val Tyr Tyr Cys Gln Gln Gly Gln Val
        275                 280                 285

Ile Pro Pro Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys Ser Ser
    290                 295                 300

Ala Ser Thr Lys Gly Pro Ser Val Phe Pro Leu Ala Pro Ser Ser Lys
305                 310                 315                 320

Ser Thr Ser Gly Gly Thr Ala Ala Leu Gly Cys Leu Val Glu Asp Tyr
                325                 330                 335

Phe Pro Glu Pro Val Thr Val Ser Trp Asn Ser Gly Ala Leu Thr Ser
            340                 345                 350

Gly Val His Thr Phe Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser
        355                 360                 365

Leu Ser Ser Val Val Thr Val Pro Ser Ser Ser Leu Gly Thr Gln Thr
    370                 375                 380

Tyr Ile Cys Asn Val Asn His Lys Pro Ser Asn Thr Lys Val Asp Glu
385                 390                 395                 400

Lys Val Glu Pro Lys Ser Cys
                405
```

+ADw-210+AD4- 150
+ADw-211+AD4- 2268
+ADw-212+AD4- ADN
+ADw-213+AD4- Secuencia artificial

+ADw-220+AD4-
+ADw-223+AD4- hu 4-1BBL dim+AOk-rico (52-254) - CH1+ACo- cadena Fc pomo

+ADw-400+AD4- 150

```
ccttgggctg tgtctggcgc tagagcctct cctggatctg ccgccagccc cagactgaga       60

gagggacctg agctgagccc cgatgatcct gccggactgc tggatctgag acagggcatg      120

ttcgcccagc tggtggccca gaacgtgctg ctgatcgatg gccccctgtc ctggtacagc      180
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gtggtggccg gcgagggatc tggatctgtg tctctggccc tgcatctgca gcccctgaga 360
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agagcctctc ctggatctgc cgccagcccc agactgagag agggacctga gctgagcccc 720
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gtggacaaga gcaggtggca gcaggggaac gtcttctcat gctccgtgat gcatgaggct 2220

ctgcacaacc actacacgca gaagagcctc tccctgtctc cgggtaaa 2268

+ADw-210+AD4- 151
+ADw-211+AD4- 960
+ADw-212+AD4- ADN
+ADw-213+AD4- Secuencia artificial

+ADw-220+AD4-
+ADw-223+AD4- Hu 4-1BBL monom+AOk-rico (52-254)-CL+ACo-

+ADw-400+AD4- 151
ccttgggctg tgtctggcgc tagagcctct cctggatctg ccgccagccc cagactgaga 60

gagggacctg agctgagccc cgatgatcct gccggactgc tggatctgag acagggcatg 120

ttcgcccagc tggtggccca gaacgtgctg ctgatcgatg gccccctgtc ctggtacagc 180

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caatcgggta actcccagga gagtgtcaca gagcaggaca gcaaggacag cacctacagc 840

ctcagcagca ccctgacgct gagcaaagca gactacgaga aacacaaagt ctacgcctgc 900

gaagtcaccc atcagggcct gagctcgccc gtcacaaaga gcttcaacag gggagagtgt 960

+ADw-210+AD4- 152
+ADw-211+AD4- 2100
+ADw-212+AD4- ADN
+ADw-213+AD4- Secuencia artificial

+ADw-220+AD4-
+ADw-223+AD4- hu 4-1BBL dim+AOk-rico (80-254) - CH1+ACo- cadena Fc pomo

+ADw-400+AD4- 152
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gtgctgctga tcgatggccc cctgagctgg tacagcgatc ctggactggc tggcgtgtca 120

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agcaagctca ccgtggacaa gagcaggtgg cagcagggga acgtcttctc atgctccgtg     2040
```

atgcatgagg ctctgcacaa ccactacacg cagaagagcc tctccctgtc tccgggtaaa 2100

+ADw-210+AD4- 153
+ADw-211+AD4- 876
+ADw-212+AD4- ADN
+ADw-213+AD4- Secuencia artificial

+ADw-220+AD4-
+ADw-223+AD4- Hu 4-1BBL monom+AOk-rico (80-254)-CL+ACo-

+ADw-400+AD4- 153
gatcctgccg gcctgctgga tctgcggcag ggaatgtttg cccagctggt ggcccagaac 60

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ctgacaggcg gcctgagcta caaagaggac accaaagaac tggtggtggc caaggccggc 180

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gtcacagagc aggacagcaa ggacagcacc tacagcctca gcagcaccct gacgctgagc 780

aaagcagact acgagaaaca caaagtctac gcctgcgaag tcacccatca gggcctgagc 840

tcgcccgtca caaagagctt caacagggga gagtgt 876

+ADw-210+AD4- 154
+ADw-211+AD4- 1317
+ADw-212+AD4- ADN
+ADw-213+AD4- Secuencia artificial

+ADw-220+AD4-
+ADw-223+AD4- ADN de cadena KK de Fc de DP47

+ADw-400+AD4- 154
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caccctgcca gcagcaccaa ggtggacaag aaaatcgtgc cccgggactg cggctgcaag 660

ccctgcatct gcaccgtgcc cgaggtgtcc agcgtgttca tcttcccacc caagcccaag 720

gacgtgctga ccatcaccct gacccccaaa gtgacctgcg tggtggtggc catcagcaag 780

gacgaccccg aggtgcagtt ctcttggttt gtggacgacg tggaggtgca cacagcccag 840

acaaagcccc gggaggaaca gatcaacagc accttcagaa gcgtgtccga gctgcccatc 900

atgcaccagg actggctgaa cggcaaagaa ttcaagtgca gagtgaacag cgccgccttc 960

ggcgccccca tcgagaaaac catcagcaag accaagggca gacccaaggc cccccaggtg 1020

tacaccatcc ccccacccaa aaaacagatg gccaaggaca aggtgtccct gacctgcatg 1080

atcaccaact ttttccccga ggacatcacc gtggagtggc agtggaatgg ccagcccgcc 1140

gagaactaca agaacaccca gcccatcatg aagaccgacg gcagctactt cgtgtacagc 1200

aagctgaacg tgcagaagtc caactgggag gccggcaaca ccttcacctg tagcgtgctg 1260

cacgagggcc tgcacaacca ccacaccgag aagtccctga gccactcccc cggcaag 1317

+ADw-210+AD4- 155
+ADw-211+AD4- 645
+ADw-212+AD4- ADN
+ADw-213+AD4- Secuencia artificial

+ADw-220+AD4-
+ADw-223+AD4- ADN de cadena ligera de DP47

+ADw-400+AD4- 155
gaaatcgtgt taacgcagtc tccaggcacc ctgtctttgt ctccagggga aagagccacc 60

ctctcttgca gggccagtca gagtgttagc agcagctact tagcctggta ccagcagaaa 120

cctggccagg ctcccaggct cctcatctat ggagcatcca gcagggccac tggcatccca 180

gacaggttca gtggcagtgg atccgggaca gacttcactc tcaccatcag cagactggag 240

cctgaagatt ttgcagtgta ttactgtcag cagtatggta gctcaccgct gacgttcggc 300

caggggacca aagtggaaat caaacgtgcc gatgctgcac caactgtatc gattttccca 360

ccatccagtg agcagttaac atctggaggt gcctcagtcg tgtgcttctt gaacaacttc 420

taccccaaag acatcaatgt caagtggaag attgatggca gtgaacgaca aaatggcgtc 480

ctgaacagtt ggactgatca ggacagcaaa gacagcacct acagcatgag cagcaccctc 540

acgttgacca aggacgagta tgaacgacat aacagctata cctgtgaggc cactcacaag 600

acatcaactt cacccattgt caagagcttc aacaggaatg agtgt 645

+ADw-210+AD4- 156
+ADw-211+AD4- 439
+ADw-212+AD4- PRT
+ADw-213+AD4- Secuencia artificial

+ADw-220+AD4-
+ADw-223+AD4- cadena KK de Fc de DP47

+ADw-400+AD4- 156

Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Ser Tyr
20 25 30

Ala Met Ser Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Ser Ala Ile Ser Gly Ser Gly Gly Ser Thr Tyr Tyr Ala Asp Ser Val
50 55 60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65 70 75 80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Lys Gly Ser Gly Phe Asp Tyr Trp Gly Gln Gly Thr Leu Val Thr
100 105 110

Val Ser Ser Ala Lys Thr Thr Pro Pro Ser Val Tyr Pro Leu Ala Pro
115 120 125

Gly Ser Ala Ala Gln Thr Asn Ser Met Val Thr Leu Gly Cys Leu Val
130 135 140

Lys Gly Tyr Phe Pro Glu Pro Val Thr Val Thr Trp Asn Ser Gly Ser
145 150 155 160

Leu Ser Ser Gly Val His Thr Phe Pro Ala Val Leu Gln Ser Asp Leu
165 170 175

Tyr Thr Leu Ser Ser Ser Val Thr Val Pro Ser Ser Thr Trp Pro Ser
180 185 190

Gln Thr Val Thr Cys Asn Val Ala His Pro Ala Ser Ser Thr Lys Val

```
        195                 200                 205

Asp Lys Lys Ile Val Pro Arg Asp Cys Gly Cys Lys Pro Cys Ile Cys
    210                 215                 220

Thr Val Pro Glu Val Ser Ser Val Phe Ile Phe Pro Pro Lys Pro Lys
225                 230                 235                 240

Asp Val Leu Thr Ile Thr Leu Thr Pro Lys Val Thr Cys Val Val Val
                245                 250                 255

Ala Ile Ser Lys Asp Asp Pro Glu Val Gln Phe Ser Trp Phe Val Asp
            260                 265                 270

Asp Val Glu Val His Thr Ala Gln Thr Lys Pro Arg Glu Glu Gln Ile
        275                 280                 285

Asn Ser Thr Phe Arg Ser Val Ser Glu Leu Pro Ile Met His Gln Asp
    290                 295                 300

Trp Leu Asn Gly Lys Glu Phe Lys Cys Arg Val Asn Ser Ala Ala Phe
305                 310                 315                 320

Gly Ala Pro Ile Glu Lys Thr Ile Ser Lys Thr Lys Gly Arg Pro Lys
                325                 330                 335

Ala Pro Gln Val Tyr Thr Ile Pro Pro Pro Lys Lys Gln Met Ala Lys
            340                 345                 350

Asp Lys Val Ser Leu Thr Cys Met Ile Thr Asn Phe Phe Pro Glu Asp
        355                 360                 365

Ile Thr Val Glu Trp Gln Trp Asn Gly Gln Pro Ala Glu Asn Tyr Lys
    370                 375                 380

Asn Thr Gln Pro Ile Met Lys Thr Asp Gly Ser Tyr Phe Val Tyr Ser
385                 390                 395                 400

Lys Leu Asn Val Gln Lys Ser Asn Trp Glu Ala Gly Asn Thr Phe Thr
                405                 410                 415

Cys Ser Val Leu His Glu Gly Leu His Asn His His Thr Glu Lys Ser
            420                 425                 430

Leu Ser His Ser Pro Gly Lys
        435
```

+ADw-210+AD4- 157
+ADw-211+AD4- 215
+ADw-212+AD4- PRT
+ADw-213+AD4- Secuencia artificial

+ADw-220+AD4-
+ADw-223+AD4- cadena ligera de DP47

+ADw-400+AD4- 157

```
Glu Ile Val Leu Thr Gln Ser Pro Gly Thr Leu Ser Leu Ser Pro Gly
1               5                  10                  15

Glu Arg Ala Thr Leu Ser Cys Arg Ala Ser Gln Ser Val Ser Ser Ser
            20                  25                  30

Tyr Leu Ala Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Arg Leu Leu
        35                  40                  45

Ile Tyr Gly Ala Ser Ser Arg Ala Thr Gly Ile Pro Asp Arg Phe Ser
    50                  55                  60

Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Arg Leu Glu
65                  70                  75                  80

Pro Glu Asp Phe Ala Val Tyr Tyr Cys Gln Gln Tyr Gly Ser Ser Pro
                85                  90                  95

Leu Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys Arg Ala Asp Ala
            100                 105                 110

Ala Pro Thr Val Ser Ile Phe Pro Pro Ser Ser Glu Gln Leu Thr Ser
        115                 120                 125

Gly Gly Ala Ser Val Val Cys Phe Leu Asn Asn Phe Tyr Pro Lys Asp
    130                 135                 140

Ile Asn Val Lys Trp Lys Ile Asp Gly Ser Glu Arg Gln Asn Gly Val
145                 150                 155                 160

Leu Asn Ser Trp Thr Asp Gln Asp Ser Lys Asp Ser Thr Tyr Ser Met
                165                 170                 175

Ser Ser Thr Leu Thr Leu Thr Lys Asp Glu Tyr Glu Arg His Asn Ser
            180                 185                 190

Tyr Thr Cys Glu Ala Thr His Lys Thr Ser Thr Ser Pro Ile Val Lys
        195                 200                 205

Ser Phe Asn Arg Asn Glu Cys
```

210 215

+ADw-210+AD4- 158
+ADw-211+AD4- 2298
+ADw-212+AD4- ADN
+ADw-213+AD4- Secuencia artificial

+ADw-220+AD4-
+ADw-223+AD4- 4-1BBL murino dim+AOk-rico (104-309, C160S) +IBM- cadena DD de Fc de CL

+ADw-400+AD4- 158
agaaccgagc ccagacccgc cctgaccatc accaccagcc ctaacctggg caccagagag 60

aacaacgccg accaagtgac ccccgtgtcc cacatcggct gccccaatac cacacagcag 120

ggcagccctg tgttcgccaa gctgctggcc aagaaccagg ccagcctgag caacaccacc 180

ctgaactggc acagccagga tggcgccgga agcagctatc tgagccaggg cctgagatac 240

gaagaggaca agaaagaact ggtggtggac agccctggcc tgtactacgt gttcctggaa 300

ctgaagctga gccccacctt caccaacacc ggccacaagg tgcagggctg ggtgtcactg 360

gtgctgcagg ccaaacccca ggtggacgac ttcgacaacc tggccctgac cgtggaactg 420

ttcccctgca gcatggaaaa caagctggtg gatcggagct ggtcccagct tctgctgctg 480

aaggccggac acagactgag cgtgggcctg agggcttatc tgcacggcgc ccaggacgcc 540

tacagagact gggagctgag ctaccccaac acaaccagct tcggcctgtt cctcgtgaag 600

cccgacaacc cttgggaagg cggcggaggc tccggaggag gcggatctag aacagagcct 660

cggcctgccc tgacaattac cacatccccc aatctgggca cccgggaaaa caatgcagat 720

caagtgacac ctgtgtctca tattgggtgc cccaacacta cccagcaggg gtccccagtg 780

tttgctaaac tgctggctaa aaatcaggcc tccctgtcta acacaacact gaattggcat 840

agtcaggacg gggctggcag cagctacctg tctcagggac tgcgctatga ggaagataag 900

aaagaactgg tggtggattc ccccggactg tactatgtgt ttctggaact gaaactgtcc 960

cctaccttta caaataccgg gcacaaagtg cagggatggg tgtccctggt gctgcaggct 1020

aagcctcagg tggacgattt tgataatctg gctctgacag tggaactgtt tccttgctct 1080

atggaaaaca aactggtgga ccgctcttgg agccagttgc tgctgctgaa agctggccac 1140

cggctgtctg tgggactgag agcatacctg catggggcac aggatgccta ccgggattgg 1200

gaactgtcct accctaacac tacttccttc ggactgttcc tcgtgaaacc tgataatccc 1260

tgggagggcg gaggcggaag tggcggaggg ggatccagag ctgatgctgc ccctaccgtg 1320

tccatcttcc cacccagcag cgagcagctg acatctgggg gagctagcgt cgtgtgcttc 1380

ctgaacaact tctaccccaa ggacatcaac gtgaagtgga agatcgacgg cagcgagcgg 1440

cagaacggcg tgctgaatag ctggaccgac caggacagca aggactccac ctacagcatg 1500

agcagcaccc tgaccctgac caaggacgag tacgagcggc acaacagcta cacatgcgag 1560

gccacccaca agaccagcac cagccccatc gtgaagtcct tcaaccggaa cgagtgcgtg 1620

cccagagact gcggctgcaa gccttgcatc tgcaccgtgc ctgaggtgtc cagcgtgttc 1680

atcttcccac ccaagcccaa ggacgtgctg accatcaccc tgacacccaa agtgacctgc 1740

gtggtggtgg ccatcagcaa ggatgacccc gaggtgcagt tcagttggtt cgtggacgac 1800

gtggaagtgc acaccgctca gaccaagccc agagaggaac agatcaacag caccttcaga 1860

agcgtgtccg agctgcccat catgcaccag gactggctga acggcaaaga attcaagtgc 1920

agagtgaaca gcgccgcctt tggcgccct atcgagaaaa ccatctccaa gaccaagggc 1980

agacccaagg ccccccaggt gtacacaatc cccccaccca aagaacagat ggccaaggac 2040

aaggtgtccc tgacctgcat gatcaccaat ttcttcccag aggatatcac cgtggaatgg 2100

cagtggaacg gccagcccgc cgagaactac gacaacaccc agcctatcat ggacaccgac 2160

ggctcctact tcgtgtacag cgacctgaac gtgcagaagt ccaactggga ggccggcaac 2220

accttcacct gtagcgtgct gcacgagggc ctgcacaacc accacaccga gaagtccctg 2280

tcccacagcc ctggcaag 2298

+ADw-210+AD4- 159
+ADw-211+AD4- 954
+ADw-212+AD4- ADN
+ADw-213+AD4- Secuencia artificial

+ADw-220+AD4-
+ADw-223+AD4- ADN de 4-1BBL murino monom+AOk-rico (104-309, C160S) - CH1

+ADw-400+AD4- 159
agaaccgagc ccagacccgc cctgaccatc accaccagcc ctaacctggg caccagagag 60

aacaacgccg accaagtgac ccccgtgtcc cacatcggct gccccaatac cacacagcag 120

ggcagccctg tgttcgccaa gctgctggcc aagaaccagg ccagcctgag caacaccacc 180

ctgaactggc acagccagga tggcgccgga agcagctatc tgagccaggg cctgagatac 240

gaagaggaca agaaagaact ggtggtggac agccctggcc tgtactacgt gttcctggaa 300

ctgaagctga gccccacctt caccaacacc ggccacaagg tgcagggctg ggtgtcactg 360

gtgctgcagg ccaaacccca ggtggacgac ttcgacaacc tggccctgac cgtggaactg 420

ttcccctgca gcatggaaaa caagctggtg gatcggagct ggtcccagct tctgctgctg 480

aaggccggac acagactgag cgtgggcctg agggcttatc tgcacggcgc ccaggacgcc 540

tacagagact gggagctgag ctaccccaac acaaccagct tcggcctgtt cctcgtgaag 600

cccgacaacc cttgggaagg cggcggaggc tccggaggag gcggaagcgc taagaccacc 660

ccccccagcg tgtaccctct ggcccctgga tctgccgccc agaccaacag catggtgacc 720

ctgggctgcc tggtgaaggg ctacttcccc gagcctgtga ccgtgacctg gaacagcggc 780

agcctgagca gcggcgtgca cacctttcca gccgtgctgc agagcgacct gtacaccctg 840

agcagctccg tgaccgtgcc tagcagcacc tggcccagcc agacagtgac ctgcaacgtg 900

gcccaccctg ccagcagcac caaggtggac aagaaaatcg tgccccggga ctgc 954

+ADw-210+AD4- 160
+ADw-211+AD4- 766
+ADw-212+AD4- PRT
+ADw-213+AD4- Secuencia artificial

+ADw-220+AD4-
+ADw-223+AD4- 4-1BBL murino dim+AOk-rico (104-309, C160S) +IBM- cadena DD de Fc de CL

+ADw-400+AD4- 160

Arg Thr Glu Pro Arg Pro Ala Leu Thr Ile Thr Thr Ser Pro Asn Leu
1 5 10 15

Gly Thr Arg Glu Asn Asn Ala Asp Gln Val Thr Pro Val Ser His Ile
20 25 30

Gly Cys Pro Asn Thr Thr Gln Gln Gly Ser Pro Val Phe Ala Lys Leu
35 40 45

Leu Ala Lys Asn Gln Ala Ser Leu Ser Asn Thr Thr Leu Asn Trp His
50 55 60

Ser Gln Asp Gly Ala Gly Ser Ser Tyr Leu Ser Gln Gly Leu Arg Tyr
65 70 75 80

Glu Glu Asp Lys Lys Glu Leu Val Val Asp Ser Pro Gly Leu Tyr Tyr
85 90 95

Val Phe Leu Glu Leu Lys Leu Ser Pro Thr Phe Thr Asn Thr Gly His
100 105 110

Lys Val Gln Gly Trp Val Ser Leu Val Leu Gln Ala Lys Pro Gln Val
115 120 125

Asp Asp Phe Asp Asn Leu Ala Leu Thr Val Glu Leu Phe Pro Cys Ser
130 135 140

Met Glu Asn Lys Leu Val Asp Arg Ser Trp Ser Gln Leu Leu Leu Leu
145 150 155 160

Lys Ala Gly His Arg Leu Ser Val Gly Leu Arg Ala Tyr Leu His Gly
165 170 175

```
Ala Gln Asp Ala Tyr Arg Asp Trp Glu Leu Ser Tyr Pro Asn Thr Thr
            180                 185                 190

Ser Phe Gly Leu Phe Leu Val Lys Pro Asp Asn Pro Trp Glu Gly Gly
        195                 200                 205

Gly Gly Ser Gly Gly Gly Gly Ser Arg Thr Glu Pro Arg Pro Ala Leu
    210                 215                 220

Thr Ile Thr Thr Ser Pro Asn Leu Gly Thr Arg Glu Asn Asn Ala Asp
225                 230                 235                 240

Gln Val Thr Pro Val Ser His Ile Gly Cys Pro Asn Thr Thr Gln Gln
                245                 250                 255

Gly Ser Pro Val Phe Ala Lys Leu Leu Ala Lys Asn Gln Ala Ser Leu
            260                 265                 270

Ser Asn Thr Thr Leu Asn Trp His Ser Gln Asp Gly Ala Gly Ser Ser
        275                 280                 285

Tyr Leu Ser Gln Gly Leu Arg Tyr Glu Glu Asp Lys Lys Glu Leu Val
    290                 295                 300

Val Asp Ser Pro Gly Leu Tyr Tyr Val Phe Leu Glu Leu Lys Leu Ser
305                 310                 315                 320

Pro Thr Phe Thr Asn Thr Gly His Lys Val Gln Gly Trp Val Ser Leu
                325                 330                 335

Val Leu Gln Ala Lys Pro Gln Val Asp Asp Phe Asp Asn Leu Ala Leu
            340                 345                 350

Thr Val Glu Leu Phe Pro Cys Ser Met Glu Asn Lys Leu Val Asp Arg
        355                 360                 365

Ser Trp Ser Gln Leu Leu Leu Leu Lys Ala Gly His Arg Leu Ser Val
    370                 375                 380

Gly Leu Arg Ala Tyr Leu His Gly Ala Gln Asp Ala Tyr Arg Asp Trp
385                 390                 395                 400

Glu Leu Ser Tyr Pro Asn Thr Thr Ser Phe Gly Leu Phe Leu Val Lys
                405                 410                 415

Pro Asp Asn Pro Trp Glu Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser
            420                 425                 430
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```
Arg Ala Asp Ala Ala Pro Thr Val Ser Ile Phe Pro Pro Ser Ser Glu
        435                 440                 445

Gln Leu Thr Ser Gly Gly Ala Ser Val Val Cys Phe Leu Asn Asn Phe
    450                 455                 460

Tyr Pro Lys Asp Ile Asn Val Lys Trp Lys Ile Asp Gly Ser Glu Arg
465                 470                 475                 480

Gln Asn Gly Val Leu Asn Ser Trp Thr Asp Gln Asp Ser Lys Asp Ser
                485                 490                 495

Thr Tyr Ser Met Ser Ser Thr Leu Thr Leu Thr Lys Asp Glu Tyr Glu
            500                 505                 510

Arg His Asn Ser Tyr Thr Cys Glu Ala Thr His Lys Thr Ser Thr Ser
        515                 520                 525

Pro Ile Val Lys Ser Phe Asn Arg Asn Glu Cys Val Pro Arg Asp Cys
    530                 535                 540

Gly Cys Lys Pro Cys Ile Cys Thr Val Pro Glu Val Ser Ser Val Phe
545                 550                 555                 560

Ile Phe Pro Pro Lys Pro Lys Asp Val Leu Thr Ile Thr Leu Thr Pro
                565                 570                 575

Lys Val Thr Cys Val Val Val Ala Ile Ser Lys Asp Asp Pro Glu Val
            580                 585                 590

Gln Phe Ser Trp Phe Val Asp Asp Val Glu Val His Thr Ala Gln Thr
        595                 600                 605

Lys Pro Arg Glu Glu Gln Ile Asn Ser Thr Phe Arg Ser Val Ser Glu
    610                 615                 620

Leu Pro Ile Met His Gln Asp Trp Leu Asn Gly Lys Glu Phe Lys Cys
625                 630                 635                 640

Arg Val Asn Ser Ala Ala Phe Gly Ala Pro Ile Glu Lys Thr Ile Ser
                645                 650                 655

Lys Thr Lys Gly Arg Pro Lys Ala Pro Gln Val Tyr Thr Ile Pro Pro
            660                 665                 670

Pro Lys Glu Gln Met Ala Lys Asp Lys Val Ser Leu Thr Cys Met Ile
        675                 680                 685
```

```
Thr Asn Phe Phe Pro Glu Asp Ile Thr Val Glu Trp Gln Trp Asn Gly
    690                 695                 700

Gln Pro Ala Glu Asn Tyr Asp Asn Thr Gln Pro Ile Met Asp Thr Asp
705                 710                 715                 720

Gly Ser Tyr Phe Val Tyr Ser Asp Leu Asn Val Gln Lys Ser Asn Trp
                725                 730                 735

Glu Ala Gly Asn Thr Phe Thr Cys Ser Val Leu His Glu Gly Leu His
            740                 745                 750

Asn His His Thr Glu Lys Ser Leu Ser His Ser Pro Gly Lys
        755                 760                 765


+ADw-210+AD4-  161
+ADw-211+AD4-  318
+ADw-212+AD4-  PRT
+ADw-213+AD4-  Secuencia artificial

+ADw-220+AD4-
+ADw-223+AD4-  ADN de 4-1BBL murino monom+AOk-rico (104-309, C160S) - CH1

+ADw-400+AD4-  161

Arg Thr Glu Pro Arg Pro Ala Leu Thr Ile Thr Thr Ser Pro Asn Leu
1               5                   10                  15

Gly Thr Arg Glu Asn Asn Ala Asp Gln Val Thr Pro Val Ser His Ile
            20                  25                  30

Gly Cys Pro Asn Thr Thr Gln Gln Gly Ser Pro Val Phe Ala Lys Leu
        35                  40                  45

Leu Ala Lys Asn Gln Ala Ser Leu Ser Asn Thr Thr Leu Asn Trp His
    50                  55                  60

Ser Gln Asp Gly Ala Gly Ser Ser Tyr Leu Ser Gln Gly Leu Arg Tyr
65                  70                  75                  80

Glu Glu Asp Lys Lys Glu Leu Val Val Asp Ser Pro Gly Leu Tyr Tyr
                85                  90                  95

Val Phe Leu Glu Leu Lys Leu Ser Pro Thr Phe Thr Asn Thr Gly His
            100                 105                 110

Lys Val Gln Gly Trp Val Ser Leu Val Leu Gln Ala Lys Pro Gln Val
        115                 120                 125
```

Asp Asp Phe Asp Asn Leu Ala Leu Thr Val Glu Leu Phe Pro Cys Ser
130 135 140

Met Glu Asn Lys Leu Val Asp Arg Ser Trp Ser Gln Leu Leu Leu Leu
145 150 155 160

Lys Ala Gly His Arg Leu Ser Val Gly Leu Arg Ala Tyr Leu His Gly
165 170 175

Ala Gln Asp Ala Tyr Arg Asp Trp Glu Leu Ser Tyr Pro Asn Thr Thr
180 185 190

Ser Phe Gly Leu Phe Leu Val Lys Pro Asp Asn Pro Trp Glu Gly Gly
195 200 205

Gly Gly Ser Gly Gly Gly Gly Ser Ala Lys Thr Thr Pro Pro Ser Val
210 215 220

Tyr Pro Leu Ala Pro Gly Ser Ala Ala Gln Thr Asn Ser Met Val Thr
225 230 235 240

Leu Gly Cys Leu Val Lys Gly Tyr Phe Pro Glu Pro Val Thr Val Thr
245 250 255

Trp Asn Ser Gly Ser Leu Ser Ser Gly Val His Thr Phe Pro Ala Val
260 265 270

Leu Gln Ser Asp Leu Tyr Thr Leu Ser Ser Ser Val Thr Val Pro Ser
275 280 285

Ser Thr Trp Pro Ser Gln Thr Val Thr Cys Asn Val Ala His Pro Ala
290 295 300

Ser Ser Thr Lys Val Asp Lys Lys Ile Val Pro Arg Asp Cys
305 310 315

+ADw-210+AD4- 162
+ADw-211+AD4- 1341
+ADw-212+AD4- ADN
+ADw-213+AD4- Secuencia artificial

+ADw-220+AD4-
+ADw-223+AD4- ADN de +AFs-anti-FAP (28H1)+AF0-2 cadena de Fc agujero

+ADw-400+AD4- 162
gaggtgcagc tgctcgaaag cggcggagga ctggtgcagc ctggcggcag cctgagactg 60

tcttgcgccg ccagcggctt caccttcagc agctacgcca tgagctgggt ccgccaggcc 120

cctggcaagg gactggaatg ggtgtccgcc atcatcggct ctggcgccag cacctactac 180

gccgacagcg tgaagggccg gttcaccatc agccgggaca acagcaagaa caccctgtac 240

ctgcagatga acagcctgcg ggccgaggac accgccgtgt actactgcgc caagggatgg 300

ttcggcggct tcaactactg gggacagggc accctggtca cagtgtccag cgctagcacc 360

aagggcccct ccgtgttccc cctggccccc agcagcaaga gcaccagcgg cggcacagcc 420

gctctgggct gcctggtcaa ggactacttc cccgagcccg tgaccgtgtc ctggaacagc 480

ggagccctga cctccggcgt gcacaccttc cccgccgtgc tgcagagttc tggcctgtat 540

agcctgagca gcgtggtcac cgtgccttct agcagcctgg gcacccagac ctacatctgc 600

aacgtgaacc acaagcccag caacaccaag gtggacaaga aggtggagcc caagagctgc 660

gacaaaactc acacatgccc accgtgccca gcacctgaag ctgcaggggg accgtcagtc 720

ttcctcttcc ccccaaaacc caaggacacc ctcatgatct cccggacccc tgaggtcaca 780

tgcgtggtgg tggacgtgag ccacgaagac cctgaggtca agttcaactg gtacgtggac 840

ggcgtggagg tgcataatgc caagacaaag ccgcgggagg agcagtacaa cagcacgtac 900

cgtgtggtca gcgtcctcac cgtcctgcac caggactggc tgaatggcaa ggagtacaag 960

tgcaaggtct ccaacaaagc cctcggcgcc cccatcgaga aaaccatctc caaagccaaa 1020

gggcagcccc gagaaccaca ggtgtgcacc ctgcccccat cccgggatga gctgaccaag 1080

aaccaggtca gcctctcgtg cgcagtcaaa ggcttctatc ccagcgacat cgccgtggag 1140

tgggagagca atgggcagcc ggagaacaac tacaagacca cgcctcccgt gctggactcc 1200

gacggctcct tcttcctcgt gagcaagctc accgtggaca agagcaggtg gcagcagggg 1260

aacgtcttct catgctccgt gatgcatgag gctctgcaca accactacac gcagaagagc 1320

ctctccctgt ctccgggtaa a 1341

+ADw-210+AD4- 163
+ADw-211+AD4- 645
+ADw-212+AD4- ADN
+ADw-213+AD4- Secuencia artificial

+ADw-220+AD4-
+ADw-223+AD4- ADN de cadena ligera de anti-FAP (4B9)

+ADw-400+AD4- 163
gagatcgtgc tgacccagtc ccccggcacc ctgtctctga gccctggcga gagagccacc 60

ctgtcctgca gagcctccca gtccgtgacc tcctcctacc tcgcctggta tcagcagaag 120

cccggccagg cccctcggct gctgatcaac gtgggcagtc ggagagccac cggcatccct 180

gaccggttct ccggctctgg ctccggcacc gacttcaccc tgaccatctc ccggctggaa 240

cccgaggact tcgccgtgta ctactgccag cagggcatca tgctgccccc cacctttggc 300

cagggcacca aggtggaaat caagcgtacg gtggctgcac catctgtctt catcttcccg 360

ccatctgatg agcagttgaa atctggaact gcctctgttg tgtgcctgct gaataacttc 420

tatcccagag aggccaaagt acagtggaag gtggataacg ccctccaatc gggtaactcc 480

caggagagtg tcacagagca ggacagcaag gacagcacct acagcctcag cagcaccctg 540

acgctgagca aagcagacta cgagaaacac aaagtctacg cctgcgaagt cacccatcag 600

ggcctgagct cgcccgtcac aaagagcttc aacaggggag agtgt 645

+ADw-210+AD4- 164
+ADw-211+AD4- 447
+ADw-212+AD4- PRT
+ADw-213+AD4- Secuencia artificial

+ADw-220+AD4-
+ADw-223+AD4- cadena de agujero de Fc anti-FAP(4B9)

+ADw-400+AD4- 164

Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
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Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Ser Tyr
20 25 30

Ala Met Ser Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Ser Ala Ile Ile Gly Ser Gly Ala Ser Thr Tyr Tyr Ala Asp Ser Val
50 55 60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65 70 75 80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Lys Gly Trp Phe Gly Gly Phe Asn Tyr Trp Gly Gln Gly Thr Leu
100 105 110

Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser Val Phe Pro Leu
115 120 125

Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu Gly Cys
130 135 140

Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser Trp Asn Ser
145 150 155 160

Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala Val Leu Gln Ser
165 170 175

```
Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser Ser Ser
            180                 185                 190

Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys Pro Ser Asn
        195                 200                 205

Thr Lys Val Asp Lys Lys Val Glu Pro Lys Ser Cys Asp Lys Thr His
    210                 215                 220

Thr Cys Pro Pro Cys Pro Ala Pro Glu Ala Ala Gly Gly Pro Ser Val
225                 230                 235                 240

Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr
                245                 250                 255

Pro Glu Val Thr Cys Val Val Val Asp Val Ser His Glu Asp Pro Glu
            260                 265                 270

Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala Lys
        275                 280                 285

Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg Val Val Ser
    290                 295                 300

Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys
305                 310                 315                 320

Cys Lys Val Ser Asn Lys Ala Leu Gly Ala Pro Ile Glu Lys Thr Ile
                325                 330                 335

Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Cys Thr Leu Pro
            340                 345                 350

Pro Ser Arg Asp Glu Leu Thr Lys Asn Gln Val Ser Leu Ser Cys Ala
        355                 360                 365

Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn
    370                 375                 380

Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser
385                 390                 395                 400

Asp Gly Ser Phe Phe Leu Val Ser Lys Leu Thr Val Asp Lys Ser Arg
                405                 410                 415

Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His Glu Ala Leu
```

420 425 430

His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly Lys
435 440 445

+ADw-210+AD4- 165
+ADw-211+AD4- 2166
+ADw-212+AD4- ADN
+ADw-213+AD4- Secuencia artificial

+ADw-220+AD4-
+ADw-223+AD4- ADN de hu 4-1BBL dim+AOk-rico (71-254) - CL cadena Fc pomo

+ADw-400+AD4- 165
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+ADw-210+AD4- 166
+ADw-211+AD4- 891
+ADw-212+AD4- ADN
+ADw-213+AD4- Secuencia artificial

+ADw-220+AD4-
+ADw-223+AD4- ADN de hu 4-1BBL monom+AOk-rico (71-254) - CH1

+ADw-400+AD4- 166
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+ADw-210+AD4- 167
+ADw-211+AD4- 2502
+ADw-212+AD4- ADN
+ADw-213+AD4- Secuencia artificial

+ADw-220+AD4-
+ADw-223+AD4- cadena Fc agujero de anti-FAP (4B9) fusionada a hu 4-1BBL dim+AOk-rico (71-254)
ADN

+ADw-400+AD4- 167
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+ADw-210+AD4- 168
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+ADw-213+AD4- Secuencia artificial

+ADw-220+AD4-
+ADw-223+AD4- ADN de cadena de Fc pomo de anti-FAP (4B9) fusionada a hu 4-1BBL monom+AOk-rico
(71-254)

+ADw-400+AD4- 168
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+ADw-210+AD4- 169
+ADw-211+AD4- 2130
+ADw-212+AD4- ADN
+ADw-213+AD4- Secuencia artificial

+ADw-220+AD4-
+ADw-223+AD4- ADN de hu 4-1BBL dim+AOk-rico (71-248) - CL+ACo- cadena de Fc pomo

+ADw-400+AD4- 169
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+ADw-210+AD4- 170
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+ADw-212+AD4- ADN
+ADw-213+AD4- Secuencia artificial

+ADw-220+AD4-
+ADw-223+AD4- ADN de hu 4-1BBL monom+AOk-rico (71-248) - CH1+ACo-

+ADw-400+AD4- 170
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+ADw-210+AD4- 171
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+ADw-213+AD4- Secuencia artificial

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+ADw-223+AD4- ADN de hu 4-1BBL dim+AOk-rico (71-248) - CL cadena Fc pomo

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+ADw-210+AD4- 172
+ADw-211+AD4- 873
+ADw-212+AD4- ADN
+ADw-213+AD4- Secuencia artificial

+ADw-220+AD4-
+ADw-223+AD4- ADN de hu 4-1BBL monom+AOk-rico (71-248) - CH1

+ADw-400+AD4- 172
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agcagcagcc tgggcaccca gacctacatc tgcaacgtga accacaagcc cagcaacacc 840

aaggtggaca agaaggtgga acccaagtct tgt 873

+ADw-210+AD4- 173
+ADw-211+AD4- 710
+ADw-212+AD4- PRT
+ADw-213+AD4- Secuencia artificial

+ADw-220+AD4-
+ADw-223+AD4- hu 4-1BBL dim+AOk-rico (71-248) - CL cadena Fc pomo

+ADw-400+AD4- 173

Arg Glu Gly Pro Glu Leu Ser Pro Asp Asp Pro Ala Gly Leu Leu Asp
1 5 10 15

Leu Arg Gln Gly Met Phe Ala Gln Leu Val Ala Gln Asn Val Leu Leu
20 25 30

Ile Asp Gly Pro Leu Ser Trp Tyr Ser Asp Pro Gly Leu Ala Gly Val
35 40 45

```
Ser Leu Thr Gly Gly Leu Ser Tyr Lys Glu Asp Thr Lys Glu Leu Val
    50                  55                  60

Val Ala Lys Ala Gly Val Tyr Tyr Val Phe Phe Gln Leu Glu Leu Arg
65                  70                  75                  80

Arg Val Val Ala Gly Glu Gly Ser Gly Ser Val Ser Leu Ala Leu His
                85                  90                  95

Leu Gln Pro Leu Arg Ser Ala Ala Gly Ala Ala Ala Leu Ala Leu Thr
            100                 105                 110

Val Asp Leu Pro Pro Ala Ser Ser Glu Ala Arg Asn Ser Ala Phe Gly
        115                 120                 125

Phe Gln Gly Arg Leu Leu His Leu Ser Ala Gly Gln Arg Leu Gly Val
    130                 135                 140

His Leu His Thr Glu Ala Arg Ala Arg His Ala Trp Gln Leu Thr Gln
145                 150                 155                 160

Gly Ala Thr Val Leu Gly Leu Phe Arg Val Thr Pro Glu Ile Pro Ala
                165                 170                 175

Gly Leu Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Arg Glu Gly Pro
            180                 185                 190

Glu Leu Ser Pro Asp Asp Pro Ala Gly Leu Leu Asp Leu Arg Gln Gly
        195                 200                 205

Met Phe Ala Gln Leu Val Ala Gln Asn Val Leu Leu Ile Asp Gly Pro
    210                 215                 220

Leu Ser Trp Tyr Ser Asp Pro Gly Leu Ala Gly Val Ser Leu Thr Gly
225                 230                 235                 240

Gly Leu Ser Tyr Lys Glu Asp Thr Lys Glu Leu Val Val Ala Lys Ala
                245                 250                 255

Gly Val Tyr Tyr Val Phe Phe Gln Leu Glu Leu Arg Arg Val Val Ala
            260                 265                 270

Gly Glu Gly Ser Gly Ser Val Ser Leu Ala Leu His Leu Gln Pro Leu
        275                 280                 285

Arg Ser Ala Ala Gly Ala Ala Ala Leu Ala Leu Thr Val Asp Leu Pro
```

290 295 300

Pro Ala Ser Ser Glu Ala Arg Asn Ser Ala Phe Gly Phe Gln Gly Arg
305 310 315 320

Leu Leu His Leu Ser Ala Gly Gln Arg Leu Gly Val His Leu His Thr
325 330 335

Glu Ala Arg Ala Arg His Ala Trp Gln Leu Thr Gln Gly Ala Thr Val
340 345 350

Leu Gly Leu Phe Arg Val Thr Pro Glu Ile Pro Ala Gly Leu Gly Gly
355 360 365

Gly Gly Ser Gly Gly Gly Gly Ser Arg Thr Val Ala Ala Pro Ser Val
370 375 380

Phe Ile Phe Pro Pro Ser Asp Glu Gln Leu Lys Ser Gly Thr Ala Ser
385 390 395 400

Val Val Cys Leu Leu Asn Asn Phe Tyr Pro Arg Glu Ala Lys Val Gln
405 410 415

Trp Lys Val Asp Asn Ala Leu Gln Ser Gly Asn Ser Gln Glu Ser Val
420 425 430

Thr Glu Gln Asp Ser Lys Asp Ser Thr Tyr Ser Leu Ser Ser Thr Leu
435 440 445

Thr Leu Ser Lys Ala Asp Tyr Glu Lys His Lys Val Tyr Ala Cys Glu
450 455 460

Val Thr His Gln Gly Leu Ser Ser Pro Val Thr Lys Ser Phe Asn Arg
465 470 475 480

Gly Glu Cys Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu
485 490 495

Ala Ala Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp
500 505 510

Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp
515 520 525

Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly
530 535 540

```
Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn
545                 550                 555                 560


Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp
                565                 570                 575


Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Gly
            580                 585                 590


Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu
        595                 600                 605


Pro Gln Val Tyr Thr Leu Pro Pro Cys Arg Asp Glu Leu Thr Lys Asn
    610                 615                 620


Gln Val Ser Leu Trp Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile
625                 630                 635                 640


Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr
                645                 650                 655


Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys
            660                 665                 670


Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys
        675                 680                 685


Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu
    690                 695                 700


Ser Leu Ser Pro Gly Lys
705                 710


+ADw-210+AD4-  174
+ADw-211+AD4-  291
+ADw-212+AD4-  PRT
+ADw-213+AD4-  Secuencia artificial

+ADw-220+AD4-
+ADw-223+AD4-  hu 4-1BBL monom+AOk-rico (71-248) - CH1

+ADw-400+AD4-  174

Arg Glu Gly Pro Glu Leu Ser Pro Asp Asp Pro Ala Gly Leu Leu Asp
1                5                  10                  15


Leu Arg Gln Gly Met Phe Ala Gln Leu Val Ala Gln Asn Val Leu Leu
            20                  25                  30


Ile Asp Gly Pro Leu Ser Trp Tyr Ser Asp Pro Gly Leu Ala Gly Val
```

```
        35                  40                  45

Ser Leu Thr Gly Gly Leu Ser Tyr Lys Glu Asp Thr Lys Glu Leu Val
    50                  55                  60

Val Ala Lys Ala Gly Val Tyr Tyr Val Phe Phe Gln Leu Glu Leu Arg
65                  70                  75                  80

Arg Val Val Ala Gly Glu Gly Ser Gly Ser Val Ser Leu Ala Leu His
                85                  90                  95

Leu Gln Pro Leu Arg Ser Ala Ala Gly Ala Ala Ala Leu Ala Leu Thr
            100                 105                 110

Val Asp Leu Pro Pro Ala Ser Ser Glu Ala Arg Asn Ser Ala Phe Gly
        115                 120                 125

Phe Gln Gly Arg Leu Leu His Leu Ser Ala Gly Gln Arg Leu Gly Val
    130                 135                 140

His Leu His Thr Glu Ala Arg Ala Arg His Ala Trp Gln Leu Thr Gln
145                 150                 155                 160

Gly Ala Thr Val Leu Gly Leu Phe Arg Val Thr Pro Glu Ile Pro Ala
                165                 170                 175

Gly Leu Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Ala Ser Thr Lys
            180                 185                 190

Gly Pro Ser Val Phe Pro Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly
        195                 200                 205

Gly Thr Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro
    210                 215                 220

Val Thr Val Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr
225                 230                 235                 240

Phe Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val
                245                 250                 255

Val Thr Val Pro Ser Ser Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn
            260                 265                 270

Val Asn His Lys Pro Ser Asn Thr Lys Val Asp Lys Lys Val Glu Pro
        275                 280                 285
```

Lys Ser Cys
290

+ADw-210+AD4- 175
+ADw-211+AD4- 2466
+ADw-212+AD4- ADN
+ADw-213+AD4- Secuencia artificial

+ADw-220+AD4-
+ADw-223+AD4- cadena Fc agujero de anti-FAP (4B9) fusionada a hu 4-1BBL dim+AOk-rico (71-248)
ADN

+ADw-400+AD4- 175
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ggactg 2466

+ADw-210+AD4- 176
+ADw-211+AD4- 1902
+ADw-212+AD4- ADN
+ADw-213+AD4- Secuencia artificial

+ADw-220+AD4-
+ADw-223+AD4- ADN de cadena de Fc pomo de anti-FAP (4B9) fusionada a hu 4-1BBL monom+AOk-rico
(71-248)

+ADw-400+AD4- 176
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ctgggcctgt tcagagtgac ccccgagatt ccagccggcc tg 1902

+ADw-210+AD4- 177
+ADw-211+AD4- 2496
+ADw-212+AD4- ADN
+ADw-213+AD4- Secuencia artificial

+ADw-220+AD4-
+ADw-223+AD4- ADN de cadena de Fc agujero de DP47 fusionada a hu 4-1BBL dim+AOk-rico (71-254)

+ADw-400+AD4- 177
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attgacggac ctctgagctg gtactccgac ccagggctgg caggggtgtc cctgactggg 2100

ggactgtcct acaaagaaga tacaaaagaa ctggtggtgg ctaaagctgg ggtgtactat 2160

gtgtttttc agctggaact gaggcgggtg gtggctgggg agggctcagg atctgtgtcc 2220

ctggctctgc atctgcagcc actgcgctct gctgctggcg cagctgcact ggctctgact 2280

gtggacctgc caccagcctc tagcgaggcc agaaacagcg ccttcgggtt ccaaggacgc 2340

ctgctgcatc tgagcgccgg acagcgcctg ggagtgcatc tgcatactga agccagagcc 2400

cggcatgctt ggcagctgac tcaggggca actgtgctgg gactgtttcg cgtgacacct 2460

gagatccctg ccggactgcc aagccctaga tcagaa 2496

+ADw-210+AD4- 178
+ADw-211+AD4- 1914
+ADw-212+AD4- ADN
+ADw-213+AD4- Secuencia artificial

+ADw-220+AD4-
+ADw-223+AD4- ADN de cadena de Fc pomo de DP47 fusionada a hu 4-1BBL monom+AOk-rico (71-254)

+ADw-400+AD4- 178
gaggtgcaat tgttggagtc tgggggaggc ttggtacagc ctgggggtc cctgagactc 60

tcctgtgcag cctccggatt cacctttagc agttatgcca tgagctgggt ccgccaggct 120

ccagggaagg ggctggagtg ggtctcagct attagtggta gtggtggtag cacatactac 180

gcagactccg tgaagggccg gttcaccatc tccagagaca attccaagaa cacgctgtat 240

ctgcagatga acagcctgag agccgaggac acggccgtat attactgtgc gaaaggcagc 300

ggatttgact actggggcca aggaaccctg gtcaccgtct cgagtgctag caccaagggc 360

ccatcggtct tcccctggc accctcctcc aagagcacct ctgggggcac agcggccctg 420

ggctgcctgg tcaaggacta cttccccgaa ccggtgacgg tgtcgtggaa ctcaggcgcc 480

ctgaccagcg gcgtgcacac cttcccggct gtcctacagt cctcaggact ctactccctc 540

agcagcgtgg tgaccgtgcc ctccagcagc ttgggcaccc agacctacat ctgcaacgtg 600

aatcacaagc ccagcaacac caaggtggac aagaaagttg agcccaaatc ttgtgacaaa 660

actcacacat gcccaccgtg cccagcacct gaagctgcag ggggaccgtc agtcttcctc 720

ttccccccaa aacccaagga caccctcatg atctcccgga cccctgaggt cacatgcgtg 780

gtggtggacg tgagccacga agaccctgag gtcaagttca actggtacgt ggacggcgtg 840

gaggtgcata atgccaagac aaagccgcgg gaggagcagt acaacagcac gtaccgtgtg 900

gtcagcgtcc tcaccgtcct gcaccaggac tggctgaatg gcaaggagta caagtgcaag 960

gtctccaaca aagccctcgg cgcccccatc gagaaaacca tctccaaagc caaagggcag 1020

ccccgagaac cacaggtgta caccctgccc ccctgcagag atgagctgac caagaaccag 1080

gtgtccctgt ggtgtctggt caagggcttc taccccagcg atatcgccgt ggagtgggag 1140

agcaacggcc agcctgagaa caactacaag accacccccc ctgtgctgga cagcgacggc 1200

agcttcttcc tgtactccaa actgaccgtg gacaagagcc ggtggcagca gggcaacgtg 1260

ttcagctgca gcgtgatgca cgaggccctg cacaaccact acacccagaa gtccctgagc 1320

ctgagccccg gcggaggcgg cggaagcgga ggaggaggat ccagagaggg ccctgagctg 1380

agccccgatg atcctgctgg actgctggac ctgcggcagg gcatgtttgc tcagctggtg 1440

gcccagaacg tgctgctgat cgatggcccc ctgtcctggt acagcgatcc tggactggct 1500

ggcgtgtcac tgacaggcgg cctgagctac aaagaggaca ccaaagaact ggtggtggcc 1560

aaggccggcg tgtactacgt gttctttcag ctggaactgc ggagagtggt ggccggcgaa 1620

ggatctggct ctgtgtctct ggccctgcat ctgcagcctc tgagaagcgc tgctggcgct 1680

gcagctctgg cactgacagt ggatctgcct cctgccagct ccgaggcccg gaatagcgca 1740

tttgggtttc aaggcaggct gctgcacctg tctgccggcc agaggctggg agtgcatctg 1800

cacacagagg ccagggctag acacgcctgg cagctgacac agggcgctac agtgctgggc 1860

ctgttcagag tgacccccga gattccagcc ggcctgcctt ctccaagaag cgaa 1914

+ADw-210+AD4- 179
+ADw-211+AD4- 834
+ADw-212+AD4- PRT
+ADw-213+AD4- Secuencia artificial

+ADw-220+AD4-
+ADw-223+AD4- cadena de Fc agujero de DP47 fusionada a hu 4-1BBL dim+AOk-rico (71-254)

+ADw-400+AD4- 179

Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Ser Tyr
20 25 30

Ala Met Ser Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Ser Ala Ile Ile Gly Ser Gly Ala Ser Thr Tyr Tyr Ala Asp Ser Val
50 55 60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65 70 75 80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys

```
                85                  90                  95

Ala Lys Gly Trp Phe Gly Gly Phe Asn Tyr Trp Gly Gln Gly Thr Leu
            100                 105                 110

Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser Val Phe Pro Leu
        115                 120                 125

Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu Gly Cys
    130                 135                 140

Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser Trp Asn Ser
145                 150                 155                 160

Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala Val Leu Gln Ser
                165                 170                 175

Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser Ser Ser
            180                 185                 190

Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys Pro Ser Asn
        195                 200                 205

Thr Lys Val Asp Lys Lys Val Glu Pro Lys Ser Cys Asp Lys Thr His
    210                 215                 220

Thr Cys Pro Pro Cys Pro Ala Pro Glu Ala Ala Gly Gly Pro Ser Val
225                 230                 235                 240

Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr
                245                 250                 255

Pro Glu Val Thr Cys Val Val Val Asp Val Ser His Glu Asp Pro Glu
            260                 265                 270

Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala Lys
        275                 280                 285

Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg Val Val Ser
    290                 295                 300

Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys
305                 310                 315                 320

Cys Lys Val Ser Asn Lys Ala Leu Gly Ala Pro Ile Glu Lys Thr Ile
                325                 330                 335
```

```
Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Cys Thr Leu Pro
            340                 345                 350

Pro Ser Arg Asp Glu Leu Thr Lys Asn Gln Val Ser Leu Ser Cys Ala
        355                 360                 365

Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn
    370                 375                 380

Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser
385                 390                 395                 400

Asp Gly Ser Phe Phe Leu Val Ser Lys Leu Thr Val Asp Lys Ser Arg
                405                 410                 415

Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His Glu Ala Leu
            420                 425                 430

His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly Gly Gly
        435                 440                 445

Gly Gly Ser Gly Gly Gly Gly Ser Arg Glu Gly Pro Glu Leu Ser Pro
    450                 455                 460

Asp Asp Pro Ala Gly Leu Leu Asp Leu Arg Gln Gly Met Phe Ala Gln
465                 470                 475                 480

Leu Val Ala Gln Asn Val Leu Leu Ile Asp Gly Pro Leu Ser Trp Tyr
                485                 490                 495

Ser Asp Pro Gly Leu Ala Gly Val Ser Leu Thr Gly Gly Leu Ser Tyr
            500                 505                 510

Lys Glu Asp Thr Lys Glu Leu Val Val Ala Lys Ala Gly Val Tyr Tyr
        515                 520                 525

Val Phe Phe Gln Leu Glu Leu Arg Arg Val Val Ala Gly Glu Gly Ser
    530                 535                 540

Gly Ser Val Ser Leu Ala Leu His Leu Gln Pro Leu Arg Ser Ala Ala
545                 550                 555                 560

Gly Ala Ala Ala Leu Ala Leu Thr Val Asp Leu Pro Pro Ala Ser Ser
                565                 570                 575

Glu Ala Arg Asn Ser Ala Phe Gly Phe Gln Gly Arg Leu Leu His Leu
            580                 585                 590
```

```
Ser Ala Gly Gln Arg Leu Gly Val His Leu His Thr Glu Ala Arg Ala
        595                 600                 605

Arg His Ala Trp Gln Leu Thr Gln Gly Ala Thr Val Leu Gly Leu Phe
    610                 615                 620

Arg Val Thr Pro Glu Ile Pro Ala Gly Leu Pro Ser Pro Arg Ser Glu
625                 630                 635                 640

Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Arg Glu Gly Pro Glu Leu
                645                 650                 655

Ser Pro Asp Asp Pro Ala Gly Leu Leu Asp Leu Arg Gln Gly Met Phe
            660                 665                 670

Ala Gln Leu Val Ala Gln Asn Val Leu Leu Ile Asp Gly Pro Leu Ser
        675                 680                 685

Trp Tyr Ser Asp Pro Gly Leu Ala Gly Val Ser Leu Thr Gly Gly Leu
    690                 695                 700

Ser Tyr Lys Glu Asp Thr Lys Glu Leu Val Val Ala Lys Ala Gly Val
705                 710                 715                 720

Tyr Tyr Val Phe Phe Gln Leu Glu Leu Arg Arg Val Val Ala Gly Glu
                725                 730                 735

Gly Ser Gly Ser Val Ser Leu Ala Leu His Leu Gln Pro Leu Arg Ser
            740                 745                 750

Ala Ala Gly Ala Ala Ala Leu Ala Leu Thr Val Asp Leu Pro Pro Ala
        755                 760                 765

Ser Ser Glu Ala Arg Asn Ser Ala Phe Gly Phe Gln Gly Arg Leu Leu
    770                 775                 780

His Leu Ser Ala Gly Gln Arg Leu Gly Val His Leu His Thr Glu Ala
785                 790                 795                 800

Arg Ala Arg His Ala Trp Gln Leu Thr Gln Gly Ala Thr Val Leu Gly
                805                 810                 815

Leu Phe Arg Val Thr Pro Glu Ile Pro Ala Gly Leu Pro Ser Pro Arg
            820                 825                 830

Ser Glu
```

+ADw-210+AD4- 180
+ADw-211+AD4- 640
+ADw-212+AD4- PRT
+ADw-213+AD4- Secuencia artificial

+ADw-220+AD4-
+ADw-223+AD4- cadena de Fc pomo de DP47 fusionada a hu 4-1BBL monom+AOk-rico (71-254)

+ADw-400+AD4- 180

```
Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1               5                  10                  15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Ser Tyr
            20                  25                  30

Ala Met Ser Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
        35                  40                  45

Ser Ala Ile Ile Gly Ser Gly Ala Ser Thr Tyr Tyr Ala Asp Ser Val
    50                  55                  60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65                  70                  75                  80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95

Ala Lys Gly Trp Phe Gly Gly Phe Asn Tyr Trp Gly Gln Gly Thr Leu
            100                 105                 110

Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser Val Phe Pro Leu
        115                 120                 125

Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu Gly Cys
    130                 135                 140

Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser Trp Asn Ser
145                 150                 155                 160

Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala Val Leu Gln Ser
                165                 170                 175

Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser Ser Ser
            180                 185                 190

Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys Pro Ser Asn
        195                 200                 205
```

```
Thr Lys Val Asp Lys Lys Val Glu Pro Lys Ser Cys Asp Lys Thr His
    210                 215                 220

Thr Cys Pro Pro Cys Pro Ala Pro Glu Ala Ala Gly Gly Pro Ser Val
225                 230                 235                 240

Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr
                245                 250                 255

Pro Glu Val Thr Cys Val Val Val Asp Val Ser His Glu Asp Pro Glu
            260                 265                 270

Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala Lys
        275                 280                 285

Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg Val Val Ser
    290                 295                 300

Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys
305                 310                 315                 320

Cys Lys Val Ser Asn Lys Ala Leu Gly Ala Pro Ile Glu Lys Thr Ile
                325                 330                 335

Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro
            340                 345                 350

Pro Cys Arg Asp Glu Leu Thr Lys Asn Gln Val Ser Leu Trp Cys Leu
        355                 360                 365

Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn
    370                 375                 380

Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser
385                 390                 395                 400

Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg
                405                 410                 415

Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His Glu Ala Leu
            420                 425                 430

His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly Gly Gly
        435                 440                 445

Gly Gly Ser Gly Gly Gly Gly Ser Arg Glu Gly Pro Glu Leu Ser Pro
```

450 455 460

Asp Asp Pro Ala Gly Leu Leu Asp Leu Arg Gln Gly Met Phe Ala Gln
465 470 475 480

Leu Val Ala Gln Asn Val Leu Leu Ile Asp Gly Pro Leu Ser Trp Tyr
485 490 495

Ser Asp Pro Gly Leu Ala Gly Val Ser Leu Thr Gly Gly Leu Ser Tyr
500 505 510

Lys Glu Asp Thr Lys Glu Leu Val Val Ala Lys Ala Gly Val Tyr Tyr
515 520 525

Val Phe Phe Gln Leu Glu Leu Arg Arg Val Val Ala Gly Glu Gly Ser
530 535 540

Gly Ser Val Ser Leu Ala Leu His Leu Gln Pro Leu Arg Ser Ala Ala
545 550 555 560

Gly Ala Ala Ala Leu Ala Leu Thr Val Asp Leu Pro Pro Ala Ser Ser
565 570 575

Glu Ala Arg Asn Ser Ala Phe Gly Phe Gln Gly Arg Leu Leu His Leu
580 585 590

Ser Ala Gly Gln Arg Leu Gly Val His Leu His Thr Glu Ala Arg Ala
595 600 605

Arg His Ala Trp Gln Leu Thr Gln Gly Ala Thr Val Leu Gly Leu Phe
610 615 620

Arg Val Thr Pro Glu Ile Pro Ala Gly Leu Pro Ser Pro Arg Ser Glu
625 630 635 640

+ADw-210+AD4- 181
+ADw-211+AD4- 1335
+ADw-212+AD4- ADN
+ADw-213+AD4- Secuencia artificial

+ADw-220+AD4-
+ADw-223+AD4- DP47 heavy chain (hu IgG1 PGLALA) DNA

+ADw-400+AD4- 181
gaggtgcaat tgttggagtc tgggggaggc ttggtacagc ctgggggtc cctgagactc 60

tcctgtgcag cctccggatt cacctttagc agttatgcca tgagctgggt ccgccaggct 120

ccagggaagg ggctggagtg ggtctcagct attagtggta gtggtggtag cacatactac 180

gcagactccg tgaagggccg gttcaccatc tccagagaca attccaagaa cacgctgtat 240

ctgcagatga acagcctgag agccgaggac acggccgtat attactgtgc gaaaggcagc 300

ggatttgact actggggcca aggaaccctg gtcaccgtct cgagtgctag caccaagggc 360

ccatcggtct tcccccctggc accctcctcc aagagcacct ctgggggcac agcggccctg 420

ggctgcctgg tcaaggacta cttccccgaa ccggtgacgg tgtcgtggaa ctcaggcgcc 480

ctgaccagcg gcgtgcacac cttcccggct gtcctacagt cctcaggact ctactccctc 540

agcagcgtgg tgaccgtgcc ctccagcagc ttgggcaccc agacctacat ctgcaacgtg 600

aatcacaagc ccagcaacac caaggtggac aagaaagttg agcccaaatc ttgtgacaaa 660

actcacacat gcccaccgtg cccagcacct gaagctgcag ggggaccgtc agtcttcctc 720

ttccccccaa aacccaagga caccctcatg atctcccgga cccctgaggt cacatgcgtg 780

gtggtggacg tgagccacga agaccctgag gtcaagttca actggtacgt ggacggcgtg 840

gaggtgcata atgccaagac aaagccgcgg gaggagcagt acaacagcac gtaccgtgtg 900

gtcagcgtcc tcaccgtcct gcaccaggac tggctgaatg gcaaggagta caagtgcaag 960

gtctccaaca aagccctcgg cgcccccatc gagaaaacca tctccaaagc caaagggcag 1020

ccccgagaac cacaggtgta caccctgccc ccatcccggg atgagctgac caagaaccag 1080

gtcagcctga cctgcctggt caaaggcttc tatcccagcg acatcgccgt ggagtgggag 1140

agcaatgggc agccggagaa caactacaag accacgcctc ccgtgctgga ctccgacggc 1200

tccttcttcc tctacagcaa gctcaccgtg gacaagagca ggtggcagca ggggaacgtc 1260

ttctcatgct ccgtgatgca tgaggctctg cacaaccact acacgcagaa gagcctctcc 1320

ctgtctccgg gtaaa 1335

+ADw-210+AD4- 182
+ADw-211+AD4- 445
+ADw-212+AD4- PRT
+ADw-213+AD4- Secuencia artificial

+ADw-220+AD4-
+ADw-223+AD4- DP47 heavy chain (hu IgG1 PGLALA)

+ADw-400+AD4- 182

Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Ser Tyr
20 25 30

Ala Met Ser Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Ser Ala Ile Ser Gly Ser Gly Gly Ser Thr Tyr Tyr Ala Asp Ser Val

50 55 60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65 70 75 80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Lys Gly Ser Gly Phe Asp Tyr Trp Gly Gln Gly Thr Leu Val Thr
100 105 110

Val Ser Ser Ala Ser Thr Lys Gly Pro Ser Val Phe Pro Leu Ala Pro
115 120 125

Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu Gly Cys Leu Val
130 135 140

Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser Trp Asn Ser Gly Ala
145 150 155 160

Leu Thr Ser Gly Val His Thr Phe Pro Ala Val Leu Gln Ser Ser Gly
165 170 175

Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser Ser Ser Leu Gly
180 185 190

Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys Pro Ser Asn Thr Lys
195 200 205

Val Asp Lys Lys Val Glu Pro Lys Ser Cys Asp Lys Thr His Thr Cys
210 215 220

Pro Pro Cys Pro Ala Pro Glu Ala Ala Gly Gly Pro Ser Val Phe Leu
225 230 235 240

Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu
245 250 255

Val Thr Cys Val Val Val Asp Val Ser His Glu Asp Pro Glu Val Lys
260 265 270

Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys
275 280 285

Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg Val Val Ser Val Leu
290 295 300

```
Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys
305                 310                 315                 320

Val Ser Asn Lys Ala Leu Gly Ala Pro Ile Glu Lys Thr Ile Ser Lys
                325                 330                 335

Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser
            340                 345                 350

Arg Asp Glu Leu Thr Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys
        355                 360                 365

Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln
    370                 375                 380

Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly
385                 390                 395                 400

Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln
                405                 410                 415

Gln Gly Asn Val Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn
            420                 425                 430

His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly Lys
        435                 440                 445


+ADw-210+AD4-  183
+ADw-211+AD4-  189
+ADw-212+AD4-  PRT
+ADw-213+AD4-  Secuencia artificial

+ADw-220+AD4-
+ADw-223+AD4-  hu 4-1BBL monom+AOk-rico (71-254) m+AOE-s enlazador (G4S)1

+ADw-400+AD4-  183

Arg Glu Gly Pro Glu Leu Ser Pro Asp Asp Pro Ala Gly Leu Leu Asp
1               5                   10                  15

Leu Arg Gln Gly Met Phe Ala Gln Leu Val Ala Gln Asn Val Leu Leu
            20                  25                  30

Ile Asp Gly Pro Leu Ser Trp Tyr Ser Asp Pro Gly Leu Ala Gly Val
        35                  40                  45

Ser Leu Thr Gly Gly Leu Ser Tyr Lys Glu Asp Thr Lys Glu Leu Val
    50                  55                  60

Val Ala Lys Ala Gly Val Tyr Tyr Val Phe Phe Gln Leu Glu Leu Arg
```

65 70 75 80

Arg Val Val Ala Gly Glu Gly Ser Gly Ser Val Ser Leu Ala Leu His
85 90 95

Leu Gln Pro Leu Arg Ser Ala Ala Gly Ala Ala Ala Leu Ala Leu Thr
100 105 110

Val Asp Leu Pro Pro Ala Ser Ser Glu Ala Arg Asn Ser Ala Phe Gly
115 120 125

Phe Gln Gly Arg Leu Leu His Leu Ser Ala Gly Gln Arg Leu Gly Val
130 135 140

His Leu His Thr Glu Ala Arg Ala Arg His Ala Trp Gln Leu Thr Gln
145 150 155 160

Gly Ala Thr Val Leu Gly Leu Phe Arg Val Thr Pro Glu Ile Pro Ala
165 170 175

Gly Leu Pro Ser Pro Arg Ser Glu Gly Gly Gly Gly Ser
180 185

+ADw-210+AD4- 184
+ADw-211+AD4- 188
+ADw-212+AD4- PRT
+ADw-213+AD4- Secuencia artificial

+ADw-220+AD4-
+ADw-223+AD4- hu 4-1BBL monom+AOk-rico (71-248) m+AOE-s enlazador (G4S)2

+ADw-400+AD4- 184

Arg Glu Gly Pro Glu Leu Ser Pro Asp Asp Pro Ala Gly Leu Leu Asp
1 5 10 15

Leu Arg Gln Gly Met Phe Ala Gln Leu Val Ala Gln Asn Val Leu Leu
20 25 30

Ile Asp Gly Pro Leu Ser Trp Tyr Ser Asp Pro Gly Leu Ala Gly Val
35 40 45

Ser Leu Thr Gly Gly Leu Ser Tyr Lys Glu Asp Thr Lys Glu Leu Val
50 55 60

Val Ala Lys Ala Gly Val Tyr Tyr Val Phe Phe Gln Leu Glu Leu Arg
65 70 75 80

Arg Val Val Ala Gly Glu Gly Ser Gly Ser Val Ser Leu Ala Leu His
85 90 95

```
Leu Gln Pro Leu Arg Ser Ala Ala Gly Ala Ala Ala Leu Ala Leu Thr
            100                 105                 110


Val Asp Leu Pro Pro Ala Ser Ser Glu Ala Arg Asn Ser Ala Phe Gly
        115                 120                 125


Phe Gln Gly Arg Leu Leu His Leu Ser Ala Gly Gln Arg Leu Gly Val
    130                 135                 140


His Leu His Thr Glu Ala Arg Ala Arg His Ala Trp Gln Leu Thr Gln
145                 150                 155                 160


Gly Ala Thr Val Leu Gly Leu Phe Arg Val Thr Pro Glu Ile Pro Ala
                165                 170                 175


Gly Leu Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser
            180                 185


+ADw-210+AD4-  185
+ADw-211+AD4-  183
+ADw-212+AD4-  PRT
+ADw-213+AD4-  Secuencia artificial

+ADw-220+AD4-
+ADw-223+AD4-  hu 4-1BBL monom+AOk-rico (71-248) m+AOE-s enlazador (G4S)1

+ADw-400+AD4-  185

Arg Glu Gly Pro Glu Leu Ser Pro Asp Asp Pro Ala Gly Leu Leu Asp
1               5                   10                  15


Leu Arg Gln Gly Met Phe Ala Gln Leu Val Ala Gln Asn Val Leu Leu
            20                  25                  30


Ile Asp Gly Pro Leu Ser Trp Tyr Ser Asp Pro Gly Leu Ala Gly Val
        35                  40                  45


Ser Leu Thr Gly Gly Leu Ser Tyr Lys Glu Asp Thr Lys Glu Leu Val
    50                  55                  60


Val Ala Lys Ala Gly Val Tyr Tyr Val Phe Phe Gln Leu Glu Leu Arg
65                  70                  75                  80


Arg Val Val Ala Gly Glu Gly Ser Gly Ser Val Ser Leu Ala Leu His
                85                  90                  95


Leu Gln Pro Leu Arg Ser Ala Ala Gly Ala Ala Ala Leu Ala Leu Thr
            100                 105                 110
```

Val Asp Leu Pro Pro Ala Ser Ser Glu Ala Arg Asn Ser Ala Phe Gly
115 120 125

Phe Gln Gly Arg Leu Leu His Leu Ser Ala Gly Gln Arg Leu Gly Val
130 135 140

His Leu His Thr Glu Ala Arg Ala Arg His Ala Trp Gln Leu Thr Gln
145 150 155 160

Gly Ala Thr Val Leu Gly Leu Phe Arg Val Thr Pro Glu Ile Pro Ala
165 170 175

Gly Leu Gly Gly Gly Gly Ser
180

+ADw-210+AD4- 186
+ADw-211+AD4- 1602
+ADw-212+AD4- ADN
+ADw-213+AD4- Secuencia artificial

+ADw-220+AD4-
+ADw-223+AD4- ADN de cadena de Fc pomo de ant+AO0-geno CD19 humano marcador avi

+ADw-400+AD4- 186
cccgaggaac ccctggtcgt gaaggtggaa gagggcgaca atgccgtgct gcagtgcctg 60

aagggcacct ccgatggccc tacccagcag ctgacctggt ccagagagag ccccctgaag 120

cccttcctga agctgtctct gggcctgcct ggcctgggca tccatatgag gcctctggcc 180

atctggctgt tcatcttcaa cgtgtcccag cagatgggcg gcttctacct gtgtcagcct 240

ggccccccat ctgagaaggc ttggcagcct ggctggaccg tgaacgtgga aggatccggc 300

gagctgttcc ggtggaacgt gtccgatctg ggcggcctgg gatgcggcct gaagaacaga 360

tctagcgagg gccccagcag ccccagcggc aaactgatga gccccaagct gtacgtgtgg 420

gccaaggaca gacccgagat ctgggagggc gagcctcctt gcctgccccc tagagacagc 480

ctgaaccaga gcctgagcca ggacctgaca atggcccctg gcagcacact gtggctgagc 540

tgtggcgtgc cacccgactc tgtgtctaga ggccctctga gctggaccca cgtgcaccct 600

aagggcccta agagcctgct gagcctggaa ctgaaggacg acaggcccgc cagagatatg 660

tgggtcatgg aaaccggcct gctgctgcct agagccacag cccaggatgc cggcaagtac 720

tactgccaca gaggcaacct gaccatgagc ttccacctgg aaatcaccgc cagacccgtg 780

ctgtggcact ggctgctgag aacaggcggc tggaaggtcg acgctagcgg tggtagtccg 840

acacctccga cacccggggg tggttctgca gacaaaactc acacatgccc accgtgccca 900

gcacctgaag ccgcaggggg accgtcagtc ttcctcttcc ccccaaaacc caaggacacc 960

ctcatgatct cccggacccc tgaggtcaca tgcgtggtgg tggacgtgag ccacgaagac 1020

cctgaggtca agttcaactg gtacgtggac ggcgtggagg tgcataatgc caagacaaag 1080

ccgcgggagg agcagtacaa cagcacgtac cgtgtggtca gcgtcctcac cgtcctgcac 1140

caggactggc tgaatggcaa ggagtacaag tgcaaggtct ccaacaaagc cctcggagcc 1200

cccatcgaga aaaccatctc caaagccaaa gggcagcccc gagaaccaca ggtgtacacc 1260

ctgcccccat gccgggatga gctgaccaag aaccaggtca gcctgtggtg cctggtcaaa 1320

ggcttctatc ccagcgacat cgccgtggag tgggagagca atgggcagcc ggagaacaac 1380

tacaagacca cgcctcccgt gctggactcc gacggctcct tcttcctcta cagcaagctc 1440

accgtggaca agagcaggtg gcagcagggg aacgtcttct catgctccgt gatgcatgag 1500

gctctgcaca accactacac gcagaagagc ctctccctgt ctccgggtaa atccggaggc 1560

ctgaacgaca tcttcgaggc ccagaagatt gaatggcacg ag 1602

+ADw-210+AD4- 187
+ADw-211+AD4- 534
+ADw-212+AD4- PRT
+ADw-213+AD4- Secuencia artificial

+ADw-220+AD4-
+ADw-223+AD4- cadena de Fc pomo de ant+AO0-geno CD19 humano marcador avi

+ADw-400+AD4- 187

Pro Glu Glu Pro Leu Val Val Lys Val Glu Glu Gly Asp Asn Ala Val
1 5 10 15

Leu Gln Cys Leu Lys Gly Thr Ser Asp Gly Pro Thr Gln Gln Leu Thr
20 25 30

Trp Ser Arg Glu Ser Pro Leu Lys Pro Phe Leu Lys Leu Ser Leu Gly
35 40 45

Leu Pro Gly Leu Gly Ile His Met Arg Pro Leu Ala Ile Trp Leu Phe
50 55 60

Ile Phe Asn Val Ser Gln Gln Met Gly Gly Phe Tyr Leu Cys Gln Pro
65 70 75 80

Gly Pro Pro Ser Glu Lys Ala Trp Gln Pro Gly Trp Thr Val Asn Val
85 90 95

Glu Gly Ser Gly Glu Leu Phe Arg Trp Asn Val Ser Asp Leu Gly Gly
100 105 110

Leu Gly Cys Gly Leu Lys Asn Arg Ser Ser Glu Gly Pro Ser Ser Pro
115 120 125

```
Ser Gly Lys Leu Met Ser Pro Lys Leu Tyr Val Trp Ala Lys Asp Arg
    130                 135                 140

Pro Glu Ile Trp Glu Gly Glu Pro Pro Cys Leu Pro Pro Arg Asp Ser
145                 150                 155                 160

Leu Asn Gln Ser Leu Ser Gln Asp Leu Thr Met Ala Pro Gly Ser Thr
                165                 170                 175

Leu Trp Leu Ser Cys Gly Val Pro Pro Asp Ser Val Ser Arg Gly Pro
            180                 185                 190

Leu Ser Trp Thr His Val His Pro Lys Gly Pro Lys Ser Leu Leu Ser
        195                 200                 205

Leu Glu Leu Lys Asp Asp Arg Pro Ala Arg Asp Met Trp Val Met Glu
    210                 215                 220

Thr Gly Leu Leu Leu Pro Arg Ala Thr Ala Gln Asp Ala Gly Lys Tyr
225                 230                 235                 240

Tyr Cys His Arg Gly Asn Leu Thr Met Ser Phe His Leu Glu Ile Thr
                245                 250                 255

Ala Arg Pro Val Leu Trp His Trp Leu Leu Arg Thr Gly Gly Trp Lys
            260                 265                 270

Val Asp Ala Ser Gly Gly Ser Pro Thr Pro Pro Thr Pro Gly Gly Gly
        275                 280                 285

Ser Ala Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Ala
    290                 295                 300

Ala Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr
305                 310                 315                 320

Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val
                325                 330                 335

Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val
            340                 345                 350

Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser
        355                 360                 365

Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu
    370                 375                 380
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Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Gly Ala
385                 390                 395                 400

Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro
                405                 410                 415

Gln Val Tyr Thr Leu Pro Pro Cys Arg Asp Glu Leu Thr Lys Asn Gln
            420                 425                 430

Val Ser Leu Trp Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala
        435                 440                 445

Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr
    450                 455                 460

Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu
465                 470                 475                 480

Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser
                485                 490                 495

Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser
            500                 505                 510

Leu Ser Pro Gly Lys Ser Gly Gly Leu Asn Asp Ile Phe Glu Ala Gln
        515                 520                 525

Lys Ile Glu Trp His Glu
    530


+ADw-210+AD4-  188
+ADw-211+AD4-  1605
+ADw-212+AD4-  ADN
+ADw-213+AD4-  Secuencia artificial

+ADw-220+AD4-
+ADw-223+AD4-  ADN de cadena de Fc pomo de ant+AO0-geno CD19 de cinomolgo marcador
avi

+ADw-400+AD4-  188
ccccaggaac ccctggtcgt gaaggtggaa gagggcgaca atgccgtgct ccagtgcctg       60

gaaggcacct ccgatggccc tacacagcag ctcgtgtggt gcagagacag ccccttcgag      120

cccttcctga acctgtctct gggcctgcct ggcatgggca tcagaatggg ccctctgggc      180

atctggctgc tgatcttcaa cgtgtccaac cagaccggcg gcttctacct gtgtcagcct      240

ggcctgccaa gcgagaaggc ttggcagcct ggatggaccg tgtccgtgga aggatctggc      300

gagctgttcc ggtggaacgt gtccgatctg ggcggcctgg gatgcggcct gaagaacaga      360
```

agcagcgagg gccctagcag ccccagcggc aagctgaata gcagccagct gtacgtgtgg 420

gccaaggaca gacccgagat gtgggagggc gagcctgtgt gtggcccccc tagagatagc 480

ctgaaccaga gcctgagcca ggacctgaca atggcccctg gcagcacact gtggctgagc 540

tgtggcgtgc cacccgactc tgtgtccaga ggccctctga gctggacaca cgtgcggcca 600

aagggcccta agagcagcct gctgagcctg gaactgaagg acgaccggcc cgaccgggat 660

atgtgggtgg tggatacagg cctgctgctg accagagcca cagcccagga tgccggcaag 720

tactactgcc acagaggcaa ctggaccaag agcttttacc tggaaatcac cgccagaccc 780

gccctgtggc actggctgct gagaatcgga ggctggaagg tcgacgctag cggtggtagt 840

ccgacacctc cgacacccgg gggtggttct gcagacaaaa ctcacacatg cccaccgtgc 900

ccagcacctg aagccgcagg gggaccgtca gtcttcctct tccccccaaa acccaaggac 960

accctcatga tctcccggac ccctgaggtc acatgcgtgg tggtggacgt gagccacgaa 1020

gaccctgagg tcaagttcaa ctggtacgtg gacggcgtgg aggtgcataa tgccaagaca 1080

aagccgcggg aggagcagta caacagcacg taccgtgtgg tcagcgtcct caccgtcctg 1140

caccaggact ggctgaatgg caaggagtac aagtgcaagg tctccaacaa agccctcgga 1200

gcccccatcg agaaaaccat ctccaaagcc aaagggcagc cccgagaacc acaggtgtac 1260

accctgcccc catgccggga tgagctgacc aagaaccagg tcagcctgtg gtgcctggtc 1320

aaaggcttct atcccagcga catcgccgtg gagtgggaga gcaatgggca gccggagaac 1380

aactacaaga ccacgcctcc cgtgctggac tccgacggct ccttcttcct ctacagcaag 1440

ctcaccgtgg acaagagcag gtggcagcag gggaacgtct tctcatgctc cgtgatgcat 1500

gaggctctgc acaaccacta cacgcagaag agcctctccc tgtctccggg taaatccgga 1560

ggcctgaacg acatcttcga ggcccagaag attgaatggc acgag 1605

+ADw-210+AD4- 189
+ADw-211+AD4- 535
+ADw-212+AD4- PRT
+ADw-213+AD4- Secuencia artificial

+ADw-220+AD4-
+ADw-223+AD4- cadena de Fc pomo de ant+AO0-geno CD19 de cinomolgo marcador avi

+ADw-400+AD4- 189

Pro Gln Glu Pro Leu Val Val Lys Val Glu Glu Gly Asp Asn Ala Val
1 5 10 15

Leu Gln Cys Leu Glu Gly Thr Ser Asp Gly Pro Thr Gln Gln Leu Val
20 25 30

Trp Cys Arg Asp Ser Pro Phe Glu Pro Phe Leu Asn Leu Ser Leu Gly

```
        35                  40                  45

Leu Pro Gly Met Gly Ile Arg Met Gly Pro Leu Gly Ile Trp Leu Leu
    50                  55                  60

Ile Phe Asn Val Ser Asn Gln Thr Gly Gly Phe Tyr Leu Cys Gln Pro
65                  70                  75                  80

Gly Leu Pro Ser Glu Lys Ala Trp Gln Pro Gly Trp Thr Val Ser Val
                85                  90                  95

Glu Gly Ser Gly Glu Leu Phe Arg Trp Asn Val Ser Asp Leu Gly Gly
            100                 105                 110

Leu Gly Cys Gly Leu Lys Asn Arg Ser Ser Glu Gly Pro Ser Ser Pro
        115                 120                 125

Ser Gly Lys Leu Asn Ser Ser Gln Leu Tyr Val Trp Ala Lys Asp Arg
    130                 135                 140

Pro Glu Met Trp Glu Gly Glu Pro Val Cys Gly Pro Pro Arg Asp Ser
145                 150                 155                 160

Leu Asn Gln Ser Leu Ser Gln Asp Leu Thr Met Ala Pro Gly Ser Thr
                165                 170                 175

Leu Trp Leu Ser Cys Gly Val Pro Pro Asp Ser Val Ser Arg Gly Pro
            180                 185                 190

Leu Ser Trp Thr His Val Arg Pro Lys Gly Pro Lys Ser Ser Leu Leu
        195                 200                 205

Ser Leu Glu Leu Lys Asp Asp Arg Pro Asp Arg Asp Met Trp Val Val
    210                 215                 220

Asp Thr Gly Leu Leu Leu Thr Arg Ala Thr Ala Gln Asp Ala Gly Lys
225                 230                 235                 240

Tyr Tyr Cys His Arg Gly Asn Trp Thr Lys Ser Phe Tyr Leu Glu Ile
                245                 250                 255

Thr Ala Arg Pro Ala Leu Trp His Trp Leu Leu Arg Ile Gly Gly Trp
            260                 265                 270

Lys Val Asp Ala Ser Gly Gly Ser Pro Thr Pro Pro Thr Pro Gly Gly
        275                 280                 285
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Gly Ser Ala Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu
    290                 295                 300

Ala Ala Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp
305                 310                 315                 320

Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp
                325                 330                 335

Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly
            340                 345                 350

Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn
        355                 360                 365

Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp
    370                 375                 380

Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Gly
385                 390                 395                 400

Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu
                405                 410                 415

Pro Gln Val Tyr Thr Leu Pro Pro Cys Arg Asp Glu Leu Thr Lys Asn
            420                 425                 430

Gln Val Ser Leu Trp Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile
        435                 440                 445

Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr
    450                 455                 460

Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys
465                 470                 475                 480

Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys
                485                 490                 495

Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu
            500                 505                 510

Ser Leu Ser Pro Gly Lys Ser Gly Gly Leu Asn Asp Ile Phe Glu Ala
        515                 520                 525

Gln Lys Ile Glu Trp His Glu
    530                 535
```

+ADw-210+AD4- 190
+ADw-211+AD4- 6
+ADw-212+AD4- PRT
+ADw-213+AD4- Secuencia artificial

+ADw-220+AD4-
+ADw-223+AD4- CD19 humanizado (8B8) HVR-L1

+ADw-400+AD4- 190

Asn Ser Asn Gly Asn Thr
1 5

+ADw-210+AD4- 191
+ADw-211+AD4- 4
+ADw-212+AD4- PRT
+ADw-213+AD4- Secuencia artificial

+ADw-220+AD4-
+ADw-223+AD4- CD19 humanizado (8B8) HVR-H2

+ADw-400+AD4- 191

Lys Phe Asn Gly
1

+ADw-210+AD4- 192
+ADw-211+AD4- 10
+ADw-212+AD4- PRT
+ADw-213+AD4- Secuencia artificial

+ADw-220+AD4-
+ADw-223+AD4- CD19 humanizado (8B8) var. 1 a 9 HVR-H2

+ADw-400+AD4- 192

Thr Glu Lys Phe Gln Gly Arg Val Thr Met
1 5 10

+ADw-210+AD4- 193
+ADw-211+AD4- 8
+ADw-212+AD4- PRT
+ADw-213+AD4- Secuencia artificial

+ADw-220+AD4-
+ADw-223+AD4- CD19 (8B8) humanizado var.5 HVR-L1

+ADw-400+AD4- 193

Leu Glu Asn Pro Asn Gly Asn Thr
1 5

+ADw-210+AD4- 194
+ADw-211+AD4- 8
+ADw-212+AD4- PRT
+ADw-213+AD4- Secuencia artificial

+ADw-220+AD4-

+ADw-223+AD4- CD19 (8B8) humanizado var.9 HVR-L1

+ADw-400+AD4- 194

Leu Glu Asn Pro Ser Gly Asn Thr
1 5

+ADw-210+AD4- 195
+ADw-211+AD4- 5
+ADw-212+AD4- PRT
+ADw-213+AD4- Secuencia artificial

+ADw-220+AD4-
+ADw-223+AD4- CD19 (8B8-018) CDR-H1

+ADw-400+AD4- 195

Asp Tyr Ile Met His
1 5

+ADw-210+AD4- 196
+ADw-211+AD4- 17
+ADw-212+AD4- PRT
+ADw-213+AD4- Secuencia artificial

+ADw-220+AD4-
+ADw-223+AD4- CD19 (8B8-018) CDR-H2

+ADw-400+AD4- 196

Tyr Ile Asn Pro Tyr Asn Asp Gly Ser Lys Tyr Thr Glu Lys Phe Gln
1 5 10 15

Gly

+ADw-210+AD4- 197
+ADw-211+AD4- 12
+ADw-212+AD4- PRT
+ADw-213+AD4- Secuencia artificial

+ADw-220+AD4-
+ADw-223+AD4- CD19 (8B8-018) CDR-H3

+ADw-400+AD4- 197

Gly Thr Tyr Tyr Tyr Gly Ser Ala Leu Phe Asp Tyr
1 5 10

+ADw-210+AD4- 198
+ADw-211+AD4- 16
+ADw-212+AD4- PRT
+ADw-213+AD4- Secuencia artificial

+ADw-220+AD4-
+ADw-223+AD4- CD19 (8B8-018) CDR-L1

+ADw-400+AD4- 198

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Lys Ser Ser Gln Ser Leu Glu Asn Pro Asn Gly Asn Thr Tyr Leu Asn
1               5                   10                  15


+ADw-210+AD4-  199
+ADw-211+AD4-  7
+ADw-212+AD4-  PRT
+ADw-213+AD4-  Secuencia artificial

+ADw-220+AD4-
+ADw-223+AD4-  CD19 (8B8-018) CDR-L2

+ADw-400+AD4-  199

Arg Val Ser Lys Arg Phe Ser
1               5


+ADw-210+AD4-  200
+ADw-211+AD4-  9
+ADw-212+AD4-  PRT
+ADw-213+AD4-  Secuencia artificial

+ADw-220+AD4-
+ADw-223+AD4-  CD19 (8B8-018) CDR-L3

+ADw-400+AD4-  200

Leu Gln Leu Thr His Val Pro Tyr Thr
1               5


+ADw-210+AD4-  201
+ADw-211+AD4-  121
+ADw-212+AD4-  PRT
+ADw-213+AD4-  Secuencia artificial

+ADw-220+AD4-
+ADw-223+AD4-  CD19 (8B8-018) VH

+ADw-400+AD4-  201

Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1               5                   10                  15


Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Asp Tyr
            20                  25                  30


Ile Met His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
        35                  40                  45


Gly Tyr Ile Asn Pro Tyr Asn Asp Gly Ser Lys Tyr Thr Glu Lys Phe
    50                  55                  60


Gln Gly Arg Val Thr Met Thr Ser Asp Thr Ser Ile Ser Thr Ala Tyr
65                  70                  75                  80
```

Met Glu Leu Ser Arg Leu Arg Ser Asp Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Gly Thr Tyr Tyr Tyr Gly Ser Ala Leu Phe Asp Tyr Trp Gly
100 105 110

Gln Gly Thr Thr Val Thr Val Ser Ser
115 120

+ADw-210+AD4- 202
+ADw-211+AD4- 112
+ADw-212+AD4- PRT
+ADw-213+AD4- Secuencia artificial

+ADw-220+AD4-
+ADw-223+AD4- CD19 (8B8-018) VL

+ADw-400+AD4- 202

Asp Ile Val Met Thr Gln Thr Pro Leu Ser Leu Ser Val Thr Pro Gly
1 5 10 15

Gln Pro Ala Ser Ile Ser Cys Lys Ser Ser Gln Ser Leu Glu Asn Pro
20 25 30

Asn Gly Asn Thr Tyr Leu Asn Trp Tyr Leu Gln Lys Pro Gly Gln Ser
35 40 45

Pro Gln Leu Leu Ile Tyr Arg Val Ser Lys Arg Phe Ser Gly Val Pro
50 55 60

Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile
65 70 75 80

Ser Arg Val Glu Ala Glu Asp Val Gly Val Tyr Tyr Cys Leu Gln Leu
85 90 95

Thr His Val Pro Tyr Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys
100 105 110

+ADw-210+AD4- 203
+ADw-211+AD4- 1353
+ADw-212+AD4- ADN
+ADw-213+AD4- Secuencia artificial

+ADw-220+AD4-
+ADw-223+AD4- ADN de cadena Fc agujero de anti-CD19(8B8-018)

+ADw-400+AD4- 203
caggtccagc tggtgcagtc cggcgccgag gtcaagaaac ccggggcttc tgtgaaggtt 60

tcatgcaagg caagcggata caccttcacc gactatatca tgcattgggt caggcaggcc 120

cctggccaag gtctcgaatg gatgggctac attaacccat ataatgatgg ctccaaatac 180

accgagaagt ttcagggaag agtcactatg acatctgaca ccagtatcag cactgcttac 240

atggagctgt cccgccttcg gtctgatgac accgcagtgt attactgtgc caggggcaca 300

tattactacg gctcagctct gttcgactat tgggggcagg gaaccacagt aaccgtgagc 360

tccgctagca ccaagggccc ctccgtgttc cccctggccc ccagcagcaa gagcaccagc 420

ggcggcacag ccgctctggg ctgcctggtc aaggactact tccccgagcc cgtgaccgtg 480

tcctggaaca gcggagccct gacctccggc gtgcacacct tccccgccgt gctgcagagt 540

tctggcctgt atagcctgag cagcgtggtc accgtgcctt ctagcagcct gggcacccag 600

acctacatct gcaacgtgaa ccacaagccc agcaacacca aggtggacaa gaaggtggag 660

cccaagagct gcgacaaaac tcacacatgc ccaccgtgcc cagcacctga agctgcaggg 720

ggaccgtcag tcttcctctt cccccaaaa cccaaggaca ccctcatgat ctcccggacc 780

cctgaggtca catgcgtggt ggtggacgtg agccacgaag accctgaggt caagttcaac 840

tggtacgtgg acggcgtgga ggtgcataat gccaagacaa agccgcggga ggagcagtac 900

aacagcacgt accgtgtggt cagcgtcctc accgtcctgc accaggactg gctgaatggc 960

aaggagtaca agtgcaaggt ctccaacaaa gccctcggcg cccccatcga gaaaaccatc 1020

tccaaagcca aagggcagcc ccgagaacca caggtgtgca ccctgccccc atcccgggat 1080

gagctgacca agaaccaggt cagcctctcg tgcgcagtca aaggcttcta tcccagcgac 1140

atcgccgtgg agtgggagag caatgggcag ccggagaaca actacaagac cacgcctccc 1200

gtgctggact ccgacggctc cttcttcctc gtgagcaagc tcaccgtgga caagagcagg 1260

tggcagcagg ggaacgtctt ctcatgctcc gtgatgcatg aggctctgca caaccactac 1320

acgcagaaga gcctctccct gtctccgggt aaa 1353

+ADw-210+AD4- 204
+ADw-211+AD4- 657
+ADw-212+AD4- ADN
+ADw-213+AD4- Secuencia artificial

+ADw-220+AD4-
+ADw-223+AD4- ADN de cadena ligera de anti-CD19(8B8-018)

+ADw-400+AD4- 204
gacatcgtca tgacccagac acccctgtcc ctctctgtga cccctggcca gccagcctca 60

attagctgca agtcctctca aagtctggag aaccccaatg ggaacactta ccttaattgg 120

tatctgcaga aacccggaca atcccctcaa ctcctgatct acagggtctc taagagattc 180

tcaggcgtgc cagatcgctt tagcggttcc gggtctggca cagacttcac cttgaagatt 240

agtcgggttg aagctgagga tgtgggagtc tattactgtc tgcagctcac tcatgtgccc 300

tacacctttg gtcagggcac aaaactggag atcaagcgga ccgtggccgc tccctccgtg 360

ttcatcttcc caccctccga cgagcagctg aagtccggca ccgccagcgt ggtgtgcctg 420

ctgaacaact tctacccccg cgaggccaag gtgcagtgga aggtggacaa cgccctgcag 480

tccggcaact cccaggaatc cgtgaccgag caggactcca aggacagcac ctactccctg 540

tcctccaccc tgaccctgtc caaggccgac tacgagaagc acaaggtgta cgcctgcgaa 600

gtgacccacc agggcctgtc cagccccgtg accaagtcct tcaaccgggg cgagtgc 657

+ADw-210+AD4- 205
+ADw-211+AD4- 451
+ADw-212+AD4- PRT
+ADw-213+AD4- Secuencia artificial

+ADw-220+AD4-
+ADw-223+AD4- cadena Fc agujero de anti-CD19(8B8-018)

+ADw-400+AD4- 205

Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Asp Tyr
20 25 30

Ile Met His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
35 40 45

Gly Tyr Ile Asn Pro Tyr Asn Asp Gly Ser Lys Tyr Thr Glu Lys Phe
50 55 60

Gln Gly Arg Val Thr Met Thr Ser Asp Thr Ser Ile Ser Thr Ala Tyr
65 70 75 80

Met Glu Leu Ser Arg Leu Arg Ser Asp Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Gly Thr Tyr Tyr Tyr Gly Ser Ala Leu Phe Asp Tyr Trp Gly
100 105 110

Gln Gly Thr Thr Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser
115 120 125

Val Phe Pro Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala
130 135 140

Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val
145 150 155 160

Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala

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                165                 170                 175

Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val
            180                 185                 190

Pro Ser Ser Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His
        195                 200                 205

Lys Pro Ser Asn Thr Lys Val Asp Lys Lys Val Glu Pro Lys Ser Cys
    210                 215                 220

Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Ala Ala Gly
225                 230                 235                 240

Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met
                245                 250                 255

Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His
            260                 265                 270

Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val
        275                 280                 285

His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr
    290                 295                 300

Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly
305                 310                 315                 320

Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Gly Ala Pro Ile
                325                 330                 335

Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val
            340                 345                 350

Cys Thr Leu Pro Pro Ser Arg Asp Glu Leu Thr Lys Asn Gln Val Ser
        355                 360                 365

Leu Ser Cys Ala Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu
    370                 375                 380

Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro
385                 390                 395                 400

Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Val Ser Lys Leu Thr Val
                405                 410                 415
```

Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met
420 425 430

His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser
435 440 445

Pro Gly Lys
450

+ADw-210+AD4- 206
+ADw-211+AD4- 219
+ADw-212+AD4- PRT
+ADw-213+AD4- Secuencia artificial

+ADw-220+AD4-
+ADw-223+AD4- cadena ligera de anti-CD19(8B8-018)

+ADw-400+AD4- 206

Asp Ile Val Met Thr Gln Thr Pro Leu Ser Leu Ser Val Thr Pro Gly
1 5 10 15

Gln Pro Ala Ser Ile Ser Cys Lys Ser Ser Gln Ser Leu Glu Asn Pro
20 25 30

Asn Gly Asn Thr Tyr Leu Asn Trp Tyr Leu Gln Lys Pro Gly Gln Ser
35 40 45

Pro Gln Leu Leu Ile Tyr Arg Val Ser Lys Arg Phe Ser Gly Val Pro
50 55 60

Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile
65 70 75 80

Ser Arg Val Glu Ala Glu Asp Val Gly Val Tyr Tyr Cys Leu Gln Leu
85 90 95

Thr His Val Pro Tyr Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys
100 105 110

Arg Thr Val Ala Ala Pro Ser Val Phe Ile Phe Pro Pro Ser Asp Glu
115 120 125

Gln Leu Lys Ser Gly Thr Ala Ser Val Val Cys Leu Leu Asn Asn Phe
130 135 140

Tyr Pro Arg Glu Ala Lys Val Gln Trp Lys Val Asp Asn Ala Leu Gln
145 150 155 160

Ser Gly Asn Ser Gln Glu Ser Val Thr Glu Gln Asp Ser Lys Asp Ser

165 170 175

Thr Tyr Ser Leu Ser Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu
180 185 190

Lys His Lys Val Tyr Ala Cys Glu Val Thr His Gln Gly Leu Ser Ser
195 200 205

Pro Val Thr Lys Ser Phe Asn Arg Gly Glu Cys
210 215

+ADw-210+AD4- 207
+ADw-211+AD4- 2514
+ADw-212+AD4- ADN
+ADw-213+AD4- Secuencia artificial

+ADw-220+AD4-
+ADw-223+AD4- ADN de cadena Fc agujero ligando dim+AOk-rico de anti-CD19(8B8-018)

+ADw-400+AD4- 207
caggtccagc tggtgcagtc cggcgccgag gtcaagaaac ccggggcttc tgtgaaggtt 60

tcatgcaagg caagcggata caccttcacc gactatatca tgcattgggt caggcaggcc 120

cctggccaag gtctcgaatg gatgggctac attaacccat ataatgatgg ctccaaatac 180

accgagaagt ttcagggaag agtcactatg acatctgaca ccagtatcag cactgcttac 240

atggagctgt cccgccttcg gtctgatgac accgcagtgt attactgtgc caggggcaca 300

tattactacg gctcagctct gttcgactat tgggggcagg gaaccacagt aaccgtgagc 360

tccgctagca ccaagggccc ctccgtgttc cccctggccc ccagcagcaa gagcaccagc 420

ggcggcacag ccgctctggg ctgcctggtc aaggactact tccccgagcc cgtgaccgtg 480

tcctggaaca gcggagccct gacctccggc gtgcacacct tccccgccgt gctgcagagt 540

tctggcctgt atagcctgag cagcgtggtc accgtgcctt ctagcagcct gggcacccag 600

acctacatct gcaacgtgaa ccacaagccc agcaacacca aggtggacaa gaaggtggag 660

cccaagagct gcgacaaaac tcacacatgc ccaccgtgcc cagcacctga agctgcaggg 720

ggaccgtcag tcttcctctt cccccccaaaa cccaaggaca ccctcatgat ctcccggacc 780

cctgaggtca catgcgtggt ggtggacgtg agccacgaag accctgaggt caagttcaac 840

tggtacgtgg acggcgtgga ggtgcataat gccaagacaa agccgcggga ggagcagtac 900

aacagcacgt accgtgtggt cagcgtcctc accgtcctgc accaggactg gctgaatggc 960

aaggagtaca agtgcaaggt ctccaacaaa gccctcggcg cccccatcga gaaaaccatc 1020

tccaaagcca aagggcagcc ccgagaacca caggtgtgca ccctgccccc atcccgggat 1080

gagctgacca agaaccaggt cagcctctcg tgcgcagtca aaggcttcta tcccagcgac 1140

atcgccgtgg agtgggagag caatgggcag ccggagaaca actacaagac cacgcctccc 1200

gtgctggact ccgacggctc cttcttcctc gtgagcaagc tcaccgtgga caagagcagg 1260

tggcagcagg ggaacgtctt ctcatgctcc gtgatgcatg aggctctgca caaccactac 1320

acgcagaaga gcctctccct gtctccgggt ggaggcggcg gaagcggagg aggaggatcc 1380

agagagggcc ctgagctgag ccccgatgat cctgctggac tgctggacct gcggcagggc 1440

atgtttgctc agctggtggc ccagaacgtg ctgctgatcg atggcccccc gtcctggtac 1500

agcgatcctg gactggctgg cgtgtcactg acaggcggcc tgagctacaa agaggacacc 1560

aaagaactgg tggtggccaa ggccggcgtg tactacgtgt tctttcagct ggaactgcgg 1620

agagtggtgg ccggcgaagg atctggctct gtgtctctgg ccctgcatct gcagcctctg 1680

agaagcgctg ctggcgctgc agctctggca ctgacagtgg atctgcctcc tgccagctcc 1740

gaggcccgga atagcgcatt tgggtttcaa ggcaggctgc tgcacctgtc tgccggccag 1800

aggctgggag tgcatctgca cacagaggcc agggctagac acgcctggca gctgacacag 1860

ggcgctacag tgctgggcct gttcagagtg acccccgaga ttccagccgg cctgccttct 1920

ccaagaagcg aaggcggagg cggatctggc ggcggaggat ctagagaggg acccgaactg 1980

tcccctgacg atccagccgg gctgctggat ctgagacagg gaatgttcgc ccagctggtg 2040

gctcagaatg tgctgctgat tgacggacct ctgagctggt actccgaccc agggctggca 2100

ggggtgtccc tgactggggg actgtcctac aaagaagata caaaagaact ggtggtggct 2160

aaagctgggg tgtactatgt gtttttttcag ctggaactga ggcgggtggt ggctggggag 2220

ggctcaggat ctgtgtccct ggctctgcat ctgcagccac tgcgctctgc tgctggcgca 2280

gctgcactgg ctctgactgt ggacctgcca ccagcctcta gcgaggccag aaacagcgcc 2340

ttcgggttcc aaggacgcct gctgcatctg agcgccggac agcgcctggg agtgcatctg 2400

catactgaag ccagagcccg gcatgcttgg cagctgactc agggggcaac tgtgctggga 2460

ctgtttcgcg tgacacctga gatccctgcc ggactgccaa gccctagatc agaa 2514

+ADw-210+AD4- 208
+ADw-211+AD4- 1932
+ADw-212+AD4- ADN
+ADw-213+AD4- Secuencia artificial

+ADw-220+AD4-
+ADw-223+AD4- ADN de anti-CD19(8B8-018) ligando monom+AOk-rico de Fc pomo

+ADw-400+AD4- 208
caggtccagc tggtgcagtc cggcgccgag gtcaagaaac ccggggcttc tgtgaaggtt 60

tcatgcaagg caagcggata caccttcacc gactatatca tgcattgggt caggcaggcc 120

cctggccaag gtctcgaatg gatgggctac attaacccat ataatgatgg ctccaaatac 180

accgagaagt ttcagggaag agtcactatg acatctgaca ccagtatcag cactgcttac 240

atggagctgt cccgccttcg gtctgatgac accgcagtgt attactgtgc caggggcaca 300

tattactacg gctcagctct gttcgactat tgggggcagg gaaccacagt aaccgtgagc 360

tccgctagca ccaagggccc atcggtcttc cccctggcac cctcctccaa gagcacctct 420

gggggcacag cggccctggg ctgcctggtc aaggactact tccccgaacc ggtgacggtg 480

tcgtggaact caggcgccct gaccagcggc gtgcacacct tcccggctgt cctacagtcc 540

tcaggactct actccctcag cagcgtggtg accgtgccct ccagcagctt gggcacccag 600

acctacatct gcaacgtgaa tcacaagccc agcaacacca aggtggacaa gaaagttgag 660

cccaaatctt gtgacaaaac tcacacatgc ccaccgtgcc cagcacctga agctgcaggg 720

ggaccgtcag tcttcctctt cccccaaaa cccaaggaca ccctcatgat ctcccggacc 780

cctgaggtca catgcgtggt ggtggacgtg agccacgaag accctgaggt caagttcaac 840

tggtacgtgg acggcgtgga ggtgcataat gccaagacaa agccgcggga ggagcagtac 900

aacagcacgt accgtgtggt cagcgtcctc accgtcctgc accaggactg gctgaatggc 960

aaggagtaca agtgcaaggt ctccaacaaa gccctcggcg cccccatcga gaaaaccatc 1020

tccaaagcca aagggcagcc ccgagaacca caggtgtaca ccctgccccc ctgcagagat 1080

gagctgacca agaaccaggt gtccctgtgg tgtctggtca agggcttcta ccccagcgat 1140

atcgccgtgg agtgggagag caacggccag cctgagaaca actacaagac cacccccct 1200

gtgctggaca gcgacggcag cttcttcctg tactccaaac tgaccgtgga caagagccgg 1260

tggcagcagg gcaacgtgtt cagctgcagc gtgatgcacg aggccctgca caaccactac 1320

acccagaagt ccctgagcct gagccccggc ggaggcggcg gaagcggagg aggaggatcc 1380

agagagggcc ctgagctgag ccccgatgat cctgctggac tgctggacct gcggcagggc 1440

atgtttgctc agctggtggc ccagaacgtg ctgctgatcg atggcccccc gtcctggtac 1500

agcgatcctg gactggctgg cgtgtcactg acaggcggcc tgagctacaa agaggacacc 1560

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aggctgggag tgcatctgca cacagaggcc agggctagac acgcctggca gctgacacag 1860

ggcgctacag tgctgggcct gttcagagtg acccccgaga ttccagccgg cctgccttct 1920

ccaagaagcg aa 1932

+ADw-210+AD4- 209
+ADw-211+AD4- 838
+ADw-212+AD4- PRT
+ADw-213+AD4- Secuencia artificial

+ADw-220+AD4-
+ADw-223+AD4- cadena Fc agujero ligando dim+AOk-rico de anti-CD19(8B8-018)

+ADw-400+AD4- 209

```
Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1               5                  10                  15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Asp Tyr
            20                  25                  30

Ile Met His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
        35                  40                  45

Gly Tyr Ile Asn Pro Tyr Asn Asp Gly Ser Lys Tyr Thr Glu Lys Phe
    50                  55                  60

Gln Gly Arg Val Thr Met Thr Ser Asp Thr Ser Ile Ser Thr Ala Tyr
65                  70                  75                  80

Met Glu Leu Ser Arg Leu Arg Ser Asp Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95

Ala Arg Gly Thr Tyr Tyr Tyr Gly Ser Ala Leu Phe Asp Tyr Trp Gly
            100                 105                 110

Gln Gly Thr Thr Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser
        115                 120                 125

Val Phe Pro Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala
    130                 135                 140

Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val
145                 150                 155                 160

Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala
                165                 170                 175

Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val
            180                 185                 190

Pro Ser Ser Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His
        195                 200                 205

Lys Pro Ser Asn Thr Lys Val Asp Lys Lys Val Glu Pro Lys Ser Cys
    210                 215                 220

Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Ala Ala Gly
```

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225                 230                 235                 240

Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met
                245                 250                 255

Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His
            260                 265                 270

Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val
        275                 280                 285

His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr
    290                 295                 300

Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly
305                 310                 315                 320

Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Gly Ala Pro Ile
                325                 330                 335

Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val
            340                 345                 350

Cys Thr Leu Pro Pro Ser Arg Asp Glu Leu Thr Lys Asn Gln Val Ser
        355                 360                 365

Leu Ser Cys Ala Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu
    370                 375                 380

Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro
385                 390                 395                 400

Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Val Ser Lys Leu Thr Val
                405                 410                 415

Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met
            420                 425                 430

His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser
        435                 440                 445

Pro Gly Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Arg Glu Gly Pro
    450                 455                 460

Glu Leu Ser Pro Asp Asp Pro Ala Gly Leu Leu Asp Leu Arg Gln Gly
465                 470                 475                 480
```

```
Met Phe Ala Gln Leu Val Ala Gln Asn Val Leu Leu Ile Asp Gly Pro
                485                 490                 495

Leu Ser Trp Tyr Ser Asp Pro Gly Leu Ala Gly Val Ser Leu Thr Gly
            500                 505                 510

Gly Leu Ser Tyr Lys Glu Asp Thr Lys Glu Leu Val Val Ala Lys Ala
        515                 520                 525

Gly Val Tyr Tyr Val Phe Phe Gln Leu Glu Leu Arg Arg Val Val Ala
    530                 535                 540

Gly Glu Gly Ser Gly Ser Val Ser Leu Ala Leu His Leu Gln Pro Leu
545                 550                 555                 560

Arg Ser Ala Ala Gly Ala Ala Ala Leu Ala Leu Thr Val Asp Leu Pro
                565                 570                 575

Pro Ala Ser Ser Glu Ala Arg Asn Ser Ala Phe Gly Phe Gln Gly Arg
            580                 585                 590

Leu Leu His Leu Ser Ala Gly Gln Arg Leu Gly Val His Leu His Thr
        595                 600                 605

Glu Ala Arg Ala Arg His Ala Trp Gln Leu Thr Gln Gly Ala Thr Val
    610                 615                 620

Leu Gly Leu Phe Arg Val Thr Pro Glu Ile Pro Ala Gly Leu Pro Ser
625                 630                 635                 640

Pro Arg Ser Glu Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Arg Glu
                645                 650                 655

Gly Pro Glu Leu Ser Pro Asp Asp Pro Ala Gly Leu Leu Asp Leu Arg
            660                 665                 670

Gln Gly Met Phe Ala Gln Leu Val Ala Gln Asn Val Leu Leu Ile Asp
        675                 680                 685

Gly Pro Leu Ser Trp Tyr Ser Asp Pro Gly Leu Ala Gly Val Ser Leu
    690                 695                 700

Thr Gly Gly Leu Ser Tyr Lys Glu Asp Thr Lys Glu Leu Val Val Ala
705                 710                 715                 720

Lys Ala Gly Val Tyr Tyr Val Phe Phe Gln Leu Glu Leu Arg Arg Val
                725                 730                 735
```

```
Val Ala Gly Glu Gly Ser Gly Ser Val Ser Leu Ala Leu His Leu Gln
            740                 745                 750


Pro Leu Arg Ser Ala Ala Gly Ala Ala Ala Leu Ala Leu Thr Val Asp
        755                 760                 765


Leu Pro Pro Ala Ser Ser Glu Ala Arg Asn Ser Ala Phe Gly Phe Gln
    770                 775                 780


Gly Arg Leu Leu His Leu Ser Ala Gly Gln Arg Leu Gly Val His Leu
785                 790                 795                 800


His Thr Glu Ala Arg Ala Arg His Ala Trp Gln Leu Thr Gln Gly Ala
                805                 810                 815


Thr Val Leu Gly Leu Phe Arg Val Thr Pro Glu Ile Pro Ala Gly Leu
            820                 825                 830


Pro Ser Pro Arg Ser Glu
        835


+ADw-210+AD4-  210
+ADw-211+AD4-  644
+ADw-212+AD4-  PRT
+ADw-213+AD4-  Secuencia artificial

+ADw-220+AD4-
+ADw-223+AD4-  anti-CD19(8B8-018) ligando monom+AOk-rico de Fc pomo

+ADw-400+AD4-  210

Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1               5                   10                  15


Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Asp Tyr
            20                  25                  30


Ile Met His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
        35                  40                  45


Gly Tyr Ile Asn Pro Tyr Asn Asp Gly Ser Lys Tyr Thr Glu Lys Phe
    50                  55                  60


Gln Gly Arg Val Thr Met Thr Ser Asp Thr Ser Ile Ser Thr Ala Tyr
65                  70                  75                  80


Met Glu Leu Ser Arg Leu Arg Ser Asp Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95
```

```
Ala Arg Gly Thr Tyr Tyr Tyr Gly Ser Ala Leu Phe Asp Tyr Trp Gly
            100                 105                 110

Gln Gly Thr Thr Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser
        115                 120                 125

Val Phe Pro Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala
    130                 135                 140

Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val
145                 150                 155                 160

Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala
                165                 170                 175

Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val
            180                 185                 190

Pro Ser Ser Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His
        195                 200                 205

Lys Pro Ser Asn Thr Lys Val Asp Lys Lys Val Glu Pro Lys Ser Cys
    210                 215                 220

Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Ala Ala Gly
225                 230                 235                 240

Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met
                245                 250                 255

Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His
            260                 265                 270

Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val
        275                 280                 285

His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr
    290                 295                 300

Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly
305                 310                 315                 320

Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Gly Ala Pro Ile
                325                 330                 335

Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val
            340                 345                 350
```

```
Tyr Thr Leu Pro Pro Cys Arg Asp Glu Leu Thr Lys Asn Gln Val Ser
        355                 360                 365

Leu Trp Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu
    370                 375                 380

Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro
385                 390                 395                 400

Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val
                405                 410                 415

Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met
            420                 425                 430

His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser
        435                 440                 445

Pro Gly Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Arg Glu Gly Pro
    450                 455                 460

Glu Leu Ser Pro Asp Asp Pro Ala Gly Leu Leu Asp Leu Arg Gln Gly
465                 470                 475                 480

Met Phe Ala Gln Leu Val Ala Gln Asn Val Leu Leu Ile Asp Gly Pro
                485                 490                 495

Leu Ser Trp Tyr Ser Asp Pro Gly Leu Ala Gly Val Ser Leu Thr Gly
            500                 505                 510

Gly Leu Ser Tyr Lys Glu Asp Thr Lys Glu Leu Val Val Ala Lys Ala
        515                 520                 525

Gly Val Tyr Tyr Val Phe Phe Gln Leu Glu Leu Arg Arg Val Val Ala
    530                 535                 540

Gly Glu Gly Ser Gly Ser Val Ser Leu Ala Leu His Leu Gln Pro Leu
545                 550                 555                 560

Arg Ser Ala Ala Gly Ala Ala Ala Leu Ala Leu Thr Val Asp Leu Pro
                565                 570                 575

Pro Ala Ser Ser Glu Ala Arg Asn Ser Ala Phe Gly Phe Gln Gly Arg
            580                 585                 590

Leu Leu His Leu Ser Ala Gly Gln Arg Leu Gly Val His Leu His Thr
        595                 600                 605
```

Glu Ala Arg Ala Arg His Ala Trp Gln Leu Thr Gln Gly Ala Thr Val
610 615 620

Leu Gly Leu Phe Arg Val Thr Pro Glu Ile Pro Ala Gly Leu Pro Ser
625 630 635 640

Pro Arg Ser Glu

+ADw-210+AD4- 211
+ADw-211+AD4- 2478
+ADw-212+AD4- ADN
+ADw-213+AD4- Secuencia artificial

+ADw-220+AD4-
+ADw-223+AD4- ADN de cadena Fc agujero ligando dim+AOk-rico (71-248) de anti-CD19(8B8-018)

+ADw-400+AD4- 211
caggtccagc tggtgcagtc cggcgccgag gtcaagaaac ccggggcttc tgtgaaggtt 60

tcatgcaagg caagcggata caccttcacc gactatatca tgcattgggt caggcaggcc 120

cctggccaag gtctcgaatg gatgggctac attaacccat ataatgatgg ctccaaatac 180

accgagaagt ttcagggaag agtcactatg acatctgaca ccagtatcag cactgcttac 240

atggagctgt cccgccttcg gtctgatgac accgcagtgt attactgtgc caggggcaca 300

tattactacg gctcagctct gttcgactat tgggggcagg gaaccacagt aaccgtgagc 360

tccgctagca ccaagggccc ctccgtgttc cccctggccc ccagcagcaa gagcaccagc 420

ggcggcacag ccgctctggg ctgcctggtc aaggactact tccccgagcc cgtgaccgtg 480

tcctggaaca gcggagccct gacctccggc gtgcacacct tccccgccgt gctgcagagt 540

tctggcctgt atagcctgag cagcgtggtc accgtgcctt ctagcagcct gggcacccag 600

acctacatct gcaacgtgaa ccacaagccc agcaacacca aggtggacaa gaaggtggag 660

cccaagagct gcgacaaaac tcacacatgc ccaccgtgcc cagcacctga agctgcaggg 720

ggaccgtcag tcttcctctt cccccccaaaa cccaaggaca ccctcatgat ctcccggacc 780

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aacagcacgt accgtgtggt cagcgtcctc accgtcctgc accaggactg gctgaatggc 960

aaggagtaca agtgcaaggt ctccaacaaa gccctcggcg cccccatcga gaaaaccatc 1020

tccaaagcca aagggcagcc ccgagaacca caggtgtgca ccctgccccc atcccgggat 1080

gagctgacca agaaccaggt cagcctctcg tgcgcagtca aaggcttcta tcccagcgac 1140

atcgccgtgg agtgggagag caatgggcag ccggagaaca actacaagac cacgcctccc 1200

gtgctggact ccgacggctc cttcttcctc gtgagcaagc tcaccgtgga caagagcagg 1260

tggcagcagg ggaacgtctt ctcatgctcc gtgatgcatg aggctctgca caaccactac 1320

acgcagaaga gcctctccct gtctccgggt ggaggcggcg gaagcggagg aggaggatcc 1380

agagagggcc ctgagctgag ccctgatgat cctgccggac tgctggacct gcggcaggga 1440

atgtttgccc agctggtggc ccagaacgtg ctgctgatcg atggcccccc gtcctggtac 1500

agcgatcctg gactggctgg cgtgtcactg acaggcggcc tgagctacaa agaggacacc 1560

aaagaactgg tggtggccaa ggccggcgtg tactacgtgt tctttcagct ggaactgcgg 1620

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agatctgctg ctggcgccgc tgctctggca ctgacagtgg atctgcctcc tgccagcagc 1740

gaggcccgga atagcgcatt tgggtttcaa ggcaggctgc tgcacctgtc tgccggccag 1800

aggctgggag tgcatctgca cacagaggcc agggctagac acgcctggca gctgacacag 1860

ggcgctacag tgctgggcct gttcagagtg acccccgaga ttccagcagg cctgggaggc 1920

ggcggatctg gcggcggagg atctagagaa ggacccgagc tgtcccccga cgatcccgct 1980

gggctgctgg atctgagaca gggcatgttc gctcagctgg tggctcagaa tgtgctgctg 2040

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ggactgtcct acaaagaaga tacaaaagaa ctggtggtgg ctaaagctgg ggtgtactat 2160

gtgttttttc agctggaact gaggcgggtg gtggctgggg agggctcagg atctgtgtcc 2220

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ctgctgcatc tgagcgccgg acagcgcctg ggagtgcatc tgcatactga agccagagcc 2400

cggcatgctt ggcagctgac tcaggggca actgtgctgg gactgtttcg cgtgacacct 2460

gagatcccag ccgggctc 2478

+ADw-210+AD4- 212
+ADw-211+AD4- 1914
+ADw-212+AD4- ADN
+ADw-213+AD4- Secuencia artificial

+ADw-220+AD4-
+ADw-223+AD4- ADN de anti-CD19(8B8-018) ligando monom+AOk-rico (71-248) de Fc pomo

+ADw-400+AD4- 212
caggtccagc tggtgcagtc cggcgccgag gtcaagaaac ccggggcttc tgtgaaggtt 60

tcatgcaagg caagcggata caccttcacc gactatatca tgcattgggt caggcaggcc 120

cctggccaag gtctcgaatg gatgggctac attaacccat ataatgatgg ctccaaatac 180

accgagaagt ttcagggaag agtcactatg acatctgaca ccagtatcag cactgcttac 240

atggagctgt cccgccttcg gtctgatgac accgcagtgt attactgtgc caggggcaca 300

tattactacg gctcagctct gttcgactat tgggggcagg gaaccacagt aaccgtgagc 360

tccgctagca ccaagggccc atcggtcttc cccctggcac cctcctccaa gagcacctct 420

gggggcacag cggccctggg ctgcctggtc aaggactact tccccgaacc ggtgacggtg 480

tcgtggaact caggcgccct gaccagcggc gtgcacacct tcccggctgt cctacagtcc 540

tcaggactct actccctcag cagcgtggtg accgtgccct ccagcagctt gggcacccag 600

acctacatct gcaacgtgaa tcacaagccc agcaacacca aggtggacaa gaaagttgag 660

cccaaatctt gtgacaaaac tcacacatgc ccaccgtgcc cagcacctga agctgcaggg 720

ggaccgtcag tcttcctctt cccccaaaa cccaaggaca ccctcatgat ctcccggacc 780

cctgaggtca catgcgtggt ggtggacgtg agccacgaag accctgaggt caagttcaac 840

tggtacgtgg acggcgtgga ggtgcataat gccaagacaa agccgcggga ggagcagtac 900

aacagcacgt accgtgtggt cagcgtcctc accgtcctgc accaggactg gctgaatggc 960

aaggagtaca agtgcaaggt ctccaacaaa gccctcggcg cccccatcga gaaaaccatc 1020

tccaaagcca aagggcagcc ccgagaacca caggtgtaca ccctgccccc ctgcagagat 1080

gagctgacca agaaccaggt gtccctgtgg tgtctggtca agggcttcta ccccagcgat 1140

atcgccgtgg agtgggagag caacggccag cctgagaaca actacaagac cacccccct 1200

gtgctggaca gcgacggcag cttcttcctg tactccaaac tgaccgtgga caagagccgg 1260

tggcagcagg gcaacgtgtt cagctgcagc gtgatgcacg aggccctgca caaccactac 1320

acccagaagt ccctgagcct gagccccggc ggaggcggcg gaagcggagg aggaggatcc 1380

agagagggcc ctgagctgag ccctgatgat cctgccggac tgctggacct gcggcaggga 1440

atgtttgccc agctggtggc ccagaacgtg ctgctgatcg atggcccct gtcctggtac 1500

agcgatcctg gactggctgg cgtgtcactg acaggcggcc tgagctacaa agaggacacc 1560

aaagaactgg tggtggccaa ggccggcgtg tactacgtgt tctttcagct ggaactgcgg 1620

agagtggtgg ccggcgaagg atctggctct gtgtctctgg ccctgcatct gcagcctctg 1680

agatctgctg ctggcgccgc tgctctggca ctgacagtgg atctgcctcc tgccagcagc 1740

gaggcccgga atagcgcatt tgggtttcaa ggcaggctgc tgcacctgtc tgccggccag 1800

aggctgggag tgcatctgca cacagaggcc agggctagac acgcctggca gctgacacag 1860

ggcgctacag tgctgggcct gttcagagtg acccccgaga ttcctgccgg gctc 1914

+ADw-210+AD4- 213
+ADw-211+AD4- 826
+ADw-212+AD4- PRT
+ADw-213+AD4- Secuencia artificial

+ADw-220+AD4-

+ADw-223+AD4- cadena Fc agujero ligando dim+AOk-rico (71-248) de anti-CD19(8B8-018)

+ADw-400+AD4- 213

```
Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1               5                  10                  15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Asp Tyr
            20                  25                  30

Ile Met His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
        35                  40                  45

Gly Tyr Ile Asn Pro Tyr Asn Asp Gly Ser Lys Tyr Thr Glu Lys Phe
    50                  55                  60

Gln Gly Arg Val Thr Met Thr Ser Asp Thr Ser Ile Ser Thr Ala Tyr
65                  70                  75                  80

Met Glu Leu Ser Arg Leu Arg Ser Asp Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95

Ala Arg Gly Thr Tyr Tyr Tyr Gly Ser Ala Leu Phe Asp Tyr Trp Gly
            100                 105                 110

Gln Gly Thr Thr Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser
        115                 120                 125

Val Phe Pro Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala
    130                 135                 140

Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val
145                 150                 155                 160

Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala
                165                 170                 175

Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val
            180                 185                 190

Pro Ser Ser Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His
        195                 200                 205

Lys Pro Ser Asn Thr Lys Val Asp Lys Lys Val Glu Pro Lys Ser Cys
    210                 215                 220

Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Ala Ala Gly
225                 230                 235                 240
```

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Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met
                245                 250                 255

Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His
            260                 265                 270

Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val
        275                 280                 285

His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr
    290                 295                 300

Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly
305                 310                 315                 320

Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Gly Ala Pro Ile
                325                 330                 335

Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val
            340                 345                 350

Cys Thr Leu Pro Pro Ser Arg Asp Glu Leu Thr Lys Asn Gln Val Ser
        355                 360                 365

Leu Ser Cys Ala Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu
    370                 375                 380

Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro
385                 390                 395                 400

Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Val Ser Lys Leu Thr Val
                405                 410                 415

Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met
            420                 425                 430

His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser
        435                 440                 445

Pro Gly Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Arg Glu Gly Pro
    450                 455                 460

Glu Leu Ser Pro Asp Asp Pro Ala Gly Leu Leu Asp Leu Arg Gln Gly
465                 470                 475                 480

Met Phe Ala Gln Leu Val Ala Gln Asn Val Leu Leu Ile Asp Gly Pro
```

485 490 495

Leu Ser Trp Tyr Ser Asp Pro Gly Leu Ala Gly Val Ser Leu Thr Gly
500 505 510

Gly Leu Ser Tyr Lys Glu Asp Thr Lys Glu Leu Val Val Ala Lys Ala
515 520 525

Gly Val Tyr Tyr Val Phe Phe Gln Leu Glu Leu Arg Arg Val Val Ala
530 535 540

Gly Glu Gly Ser Gly Ser Val Ser Leu Ala Leu His Leu Gln Pro Leu
545 550 555 560

Arg Ser Ala Ala Gly Ala Ala Ala Leu Ala Leu Thr Val Asp Leu Pro
565 570 575

Pro Ala Ser Ser Glu Ala Arg Asn Ser Ala Phe Gly Phe Gln Gly Arg
580 585 590

Leu Leu His Leu Ser Ala Gly Gln Arg Leu Gly Val His Leu His Thr
595 600 605

Glu Ala Arg Ala Arg His Ala Trp Gln Leu Thr Gln Gly Ala Thr Val
610 615 620

Leu Gly Leu Phe Arg Val Thr Pro Glu Ile Pro Ala Gly Leu Gly Gly
625 630 635 640

Gly Gly Ser Gly Gly Gly Gly Ser Arg Glu Gly Pro Glu Leu Ser Pro
645 650 655

Asp Asp Pro Ala Gly Leu Leu Asp Leu Arg Gln Gly Met Phe Ala Gln
660 665 670

Leu Val Ala Gln Asn Val Leu Leu Ile Asp Gly Pro Leu Ser Trp Tyr
675 680 685

Ser Asp Pro Gly Leu Ala Gly Val Ser Leu Thr Gly Gly Leu Ser Tyr
690 695 700

Lys Glu Asp Thr Lys Glu Leu Val Val Ala Lys Ala Gly Val Tyr Tyr
705 710 715 720

Val Phe Phe Gln Leu Glu Leu Arg Arg Val Val Ala Gly Glu Gly Ser
725 730 735

Gly Ser Val Ser Leu Ala Leu His Leu Gln Pro Leu Arg Ser Ala Ala
740 745 750

Gly Ala Ala Ala Leu Ala Leu Thr Val Asp Leu Pro Pro Ala Ser Ser
755 760 765

Glu Ala Arg Asn Ser Ala Phe Gly Phe Gln Gly Arg Leu Leu His Leu
770 775 780

Ser Ala Gly Gln Arg Leu Gly Val His Leu His Thr Glu Ala Arg Ala
785 790 795 800

Arg His Ala Trp Gln Leu Thr Gln Gly Ala Thr Val Leu Gly Leu Phe
805 810 815

Arg Val Thr Pro Glu Ile Pro Ala Gly Leu
820 825

+ADw-210+AD4- 214
+ADw-211+AD4- 638
+ADw-212+AD4- PRT
+ADw-213+AD4- Secuencia artificial

+ADw-220+AD4-
+ADw-223+AD4- anti-CD19(8B8-018) ligando monom+AOk-rico (71-248) de Fc pomo

+ADw-400+AD4- 214

Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Asp Tyr
20 25 30

Ile Met His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
35 40 45

Gly Tyr Ile Asn Pro Tyr Asn Asp Gly Ser Lys Tyr Thr Glu Lys Phe
50 55 60

Gln Gly Arg Val Thr Met Thr Ser Asp Thr Ser Ile Ser Thr Ala Tyr
65 70 75 80

Met Glu Leu Ser Arg Leu Arg Ser Asp Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Gly Thr Tyr Tyr Tyr Gly Ser Ala Leu Phe Asp Tyr Trp Gly
100 105 110

Gln Gly Thr Thr Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser

```
        115                 120                 125

Val Phe Pro Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala
    130                 135                 140

Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val
145                 150                 155                 160

Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala
                165                 170                 175

Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val
            180                 185                 190

Pro Ser Ser Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His
        195                 200                 205

Lys Pro Ser Asn Thr Lys Val Asp Lys Lys Val Glu Pro Lys Ser Cys
    210                 215                 220

Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Ala Ala Gly
225                 230                 235                 240

Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met
                245                 250                 255

Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His
            260                 265                 270

Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val
        275                 280                 285

His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr
    290                 295                 300

Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly
305                 310                 315                 320

Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Gly Ala Pro Ile
                325                 330                 335

Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val
            340                 345                 350

Tyr Thr Leu Pro Pro Cys Arg Asp Glu Leu Thr Lys Asn Gln Val Ser
        355                 360                 365
```

```
Leu Trp Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu
    370                 375                 380

Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro
385                 390                 395                 400

Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val
                405                 410                 415

Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met
            420                 425                 430

His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser
        435                 440                 445

Pro Gly Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Arg Glu Gly Pro
    450                 455                 460

Glu Leu Ser Pro Asp Asp Pro Ala Gly Leu Leu Asp Leu Arg Gln Gly
465                 470                 475                 480

Met Phe Ala Gln Leu Val Ala Gln Asn Val Leu Leu Ile Asp Gly Pro
                485                 490                 495

Leu Ser Trp Tyr Ser Asp Pro Gly Leu Ala Gly Val Ser Leu Thr Gly
            500                 505                 510

Gly Leu Ser Tyr Lys Glu Asp Thr Lys Glu Leu Val Val Ala Lys Ala
        515                 520                 525

Gly Val Tyr Tyr Val Phe Phe Gln Leu Glu Leu Arg Arg Val Val Ala
    530                 535                 540

Gly Glu Gly Ser Gly Ser Val Ser Leu Ala Leu His Leu Gln Pro Leu
545                 550                 555                 560

Arg Ser Ala Ala Gly Ala Ala Ala Leu Ala Leu Thr Val Asp Leu Pro
                565                 570                 575

Pro Ala Ser Ser Glu Ala Arg Asn Ser Ala Phe Gly Phe Gln Gly Arg
            580                 585                 590

Leu Leu His Leu Ser Ala Gly Gln Arg Leu Gly Val His Leu His Thr
        595                 600                 605

Glu Ala Arg Ala Arg His Ala Trp Gln Leu Thr Gln Gly Ala Thr Val
    610                 615                 620
```

Leu Gly Leu Phe Arg Val Thr Pro Glu Ile Pro Ala Gly Leu
625 630 635

+ADw-210+AD4- 215
+ADw-211+AD4- 363
+ADw-212+AD4- ADN
+ADw-213+AD4- Secuencia artificial

+ADw-220+AD4-
+ADw-223+AD4- ADN de secuencia nucleot+AO0-dica CD19 (8B8) VH clon progenitor

+ADw-400+AD4- 215
gaggtccagc tgcagcagtc tggacctgag ctggtaaagc ctggggcttc agtgaagatg 60

gcctgcaagg cttctggata cacattcact gactatatta tgcactgggt gaagcagaag 120

actgggcagg gccttgagtg gattggatat attaatcctt acaatgatgg ttctaagtac 180

actgagaagt tcaacggcaa ggccacactg acttcagaca aatcttccat cacagcctac 240

atggagctca gcagcctgac ctctgaggac tctgcggtct attactgtgc aagagggacc 300

tattattatg gtagcgccct ctttgactac tggggccaag gcaccactct cacagtctcc 360

tcg 363

+ADw-210+AD4- 216
+ADw-211+AD4- 336
+ADw-212+AD4- ADN
+ADw-213+AD4- Secuencia artificial

+ADw-220+AD4-
+ADw-223+AD4- ADN de secuencia nucleot+AO0-dica CD19 (8B8) VL clon progenitor

+ADw-400+AD4- 216
gatgctgtga tgacccaaac tccactctcc ctgcctgtca gtcttggaga tcaagcctcc 60

atctcttgca ggtctagtca gagccttgaa aacagtaatg gaaacaccta tttgaactgg 120

tacctccaga aaccaggcca gtctccacaa ctcctgatct acagggtttc caaacgattt 180

tctggggtcc tagacaggtt cagtggtagt ggatcaggga cagatttcac actgaaaatc 240

agcagagtgg aggctgagga tttgggagtt tatttctgcc tacaacttac acatgtcccg 300

tacacgttcg gaggggggac caagctggaa ataaaa 336

+ADw-210+AD4- 217
+ADw-211+AD4- 94
+ADw-212+AD4- ADN
+ADw-213+AD4- Secuencia artificial

+ADw-220+AD4-
+ADw-223+AD4- 43-45: 40+AKAAJQ- Y, 6+AKAAJQ- A/S/T/G/P/D/N/E/Q/V, 49-51: 40+AKAAJQ- N, 6 +ACU-
A/S/T/Y/G/P/D/E/Q/V, 55-57: 25+AKAAJQ- S/T/Q/E, 61-63: 25+AKAAJQ- S/T/Q/E

+ADw-220+AD4-

+ADw-221+AD4- misc+AF8-feature
+ADw-222+AD4- (43)..(45)
+ADw-223+AD4- n es a, c, g o t

+ADw-220+AD4-
+ADw-221+AD4- misc+AF8-feature
+ADw-222+AD4- (49)..(51)
+ADw-223+AD4- n es a, c, g o t

+ADw-220+AD4-
+ADw-221+AD4- misc+AF8-feature
+ADw-222+AD4- (55)..(57)
+ADw-223+AD4- n es a, c, g o t

+ADw-220+AD4-
+ADw-221+AD4- misc+AF8-feature
+ADw-222+AD4- (61)..(63)
+ADw-223+AD4- n es a, c, g o t

+ADw-400+AD4- 217
cagctgcggg ctctgacccg gtttctggag ataccagttc agnnncgtnn ngccnnngga 60

nnnttccaga gattggctgg atttgcaaga aatg   94

+ADw-210+AD4- 218
+ADw-211+AD4- 99
+ADw-212+AD4- ADN
+ADw-213+AD4- Secuencia artificial

+ADw-220+AD4-
+ADw-223+AD4- 40-42: 30+AKAAJQ- R, 20+AKAAJQ- E, 5+AKAAJQ- A/S/T/Y/G/P/D/N/Q/V.
49-51: 30+AKAAJQ- K, 20+AKAAJQ- S,
       5+AKAAJQ- A/N/T/Y/G/P/D/E/Q/V, 55-57: 40+AKAAJQ- F, 5+AKAAJQ-
A/S/T/Y/G/P/D/E/Q/V/I/L,
       58-60: 40+AKAAJQ- S, 6,6+AKAAJQ- A/T/Y/G/P/D/E/Q/V, 67-69: 50+AKAAJQ- P,
50+AKAAJQ- L

+ADw-220+AD4-
+ADw-221+AD4- misc+AF8-feature
+ADw-222+AD4- (40)..(42)
+ADw-223+AD4- n es a, c, g o t

+ADw-220+AD4-
+ADw-221+AD4- misc+AF8-feature
+ADw-222+AD4- (49)..(51)
+ADw-223+AD4- n es a, c, g o t

+ADw-220+AD4-
+ADw-221+AD4- misc+AF8-feature
+ADw-222+AD4- (55)..(57)
+ADw-223+AD4- n es a, c, g o t

+ADw-220+AD4-
+ADw-221+AD4- misc+AF8-feature
+ADw-222+AD4- (58)..(60)
+ADw-223+AD4- n es a, c, g o t

+ADw-220+AD4-
+ADw-221+AD4- misc+AF8-feature
+ADw-222+AD4- (67)..(69)
+ADw-223+AD4- n es a, c, g o t

+ADw-400+AD4- 218
ctccagaaac cgggtcagag cccgcagctg ctgatctacn nngtatctnn ncgcnnnnnn 60

ggcgttnnng atcgtttcag cggttctgga tccggcacc   99

+ADw-210+AD4- 219
+ADw-211+AD4- 99
+ADw-212+AD4- ADN
+ADw-213+AD4- Secuencia artificial

+ADw-220+AD4-
+ADw-223+AD4- 40-42: 52+AKAAJQ- H, 4+AKAAJQ- G/A/S/P/T/N/Y/D/E/Q/V/I 46-48:
30+AKAAJQ- I, 15+AKAAJQ- Y, 5+AKAAJQ-
       G/A/S/T/P/N/H/D/E/Q/V, 49-51: 52+AKAAJQ- Y, 4+AKAAJQ-
G/A/S/P/T/N/H/D/E/Q/V/I,
       52-54: 30+AKAAJQ- D, 15+AKAAJQ- G, 5+AKAAJQ- A/S/P/Y/N/H/D/E/Q/V/I, 55-57:
52+AKAAJQ- T, 4+AKAAJQ-
       G/A/S/P/Y/N/H/D/E/Q/V/I, 61-63: 52+AKAAJQ- T, 4+AKAAJQ-
G/A/S/P/Y/N/H/D/E/Q/V/I

+ADw-220+AD4-
+ADw-221+AD4- misc+AF8-feature
+ADw-222+AD4- (40)..(42)
+ADw-223+AD4- n es a, c, g o t

+ADw-220+AD4-
+ADw-221+AD4- misc+AF8-feature
+ADw-222+AD4- (46)..(48)
+ADw-223+AD4- n es a, c, g o t

+ADw-220+AD4-
+ADw-221+AD4- misc+AF8-feature
+ADw-222+AD4- (49)..(51)
+ADw-223+AD4- n es a, c, g o t

+ADw-220+AD4-
+ADw-221+AD4- misc+AF8-feature
+ADw-222+AD4- (52)..(54)
+ADw-223+AD4- n es a, c, g o t

+ADw-220+AD4-
+ADw-221+AD4- misc+AF8-feature
+ADw-222+AD4- (55)..(57)
+ADw-223+AD4- n es a, c, g o t

+ADw-220+AD4-
+ADw-221+AD4- misc+AF8-feature
+ADw-222+AD4- (61)..(63)
+ADw-223+AD4- n es a, c, g o t

+ADw-400+AD4- 219
catccactcc agaccctggc ccggggcctg acgaacccan nncatnnnnn nnnnnnngaa 60

nnngtaacca gatgctttgc agctcacttt aacggaagc   99

+ADw-210+AD4- 220
+ADw-211+AD4- 99
+ADw-212+AD4- ADN
+ADw-213+AD4- Secuencia artificial

+ADw-220+AD4-
+ADw-223+AD4- 34-36: 45+AKAAJQ- Y, 5+ACU- otros, 40-42: 52+AKAAJQ- N, 4+AKAAJQ-
otros, 46-48: 40+AKAAJQ- Y,
       5+ACU- otros, 49-51: 30+AKAAJQ- N, 15+AKAAJQ- S, 5+ACU- otros, 52-54:
30+AKAAJQ- D, 15+AKAAJQ- G,
       5+ACU- otros, 55-57: 52+AKAAJQ- G, 4+AKAAJQ- otros, 61-63: 30+AKAAJQ- K,
15+AKAAJQ- N, 4+AKAAJQ-
       otros, 70-72: 30+AKAAJQ- E, 15+AKAAJQ- Q, 5+ACU- otros

+ADw-220+AD4-
+ADw-221+AD4- misc+AF8-feature
+ADw-222+AD4- (34)..(36)
+ADw-223+AD4- n es a, c, g o t

+ADw-220+AD4-
+ADw-221+AD4- misc+AF8-feature
+ADw-222+AD4- (40)..(42)
+ADw-223+AD4- n es a, c, g o t

+ADw-220+AD4-
+ADw-221+AD4- misc+AF8-feature
+ADw-222+AD4- (46)..(48)
+ADw-223+AD4- n es a, c, g o t

+ADw-220+AD4-
+ADw-221+AD4- misc+AF8-feature
+ADw-222+AD4- (49)..(51)
+ADw-223+AD4- n es a, c, g o t

+ADw-220+AD4-
+ADw-221+AD4- misc+AF8-feature
+ADw-222+AD4- (52)..(54)
+ADw-223+AD4- n es a, c, g o t

+ADw-220+AD4-
+ADw-221+AD4- misc+AF8-feature
+ADw-222+AD4- (55)..(57)
+ADw-223+AD4- n es a, c, g o t

+ADw-220+AD4-
+ADw-221+AD4- misc+AF8-feature
+ADw-222+AD4- (61)..(63)
+ADw-223+AD4- n es a, c, g o t

+ADw-220+AD4-
+ADw-221+AD4- misc+AF8-feature
+ADw-222+AD4- (70)..(72)
+ADw-223+AD4- n es a, c, g o t

+ADw-400+AD4- 220
caggccccgg gccagggtct ggagtggatg ggcnnnattn nnccannnnn nnnnnnntcc   60

nnntataccn nnaaattcca gggccgcgtc acgatgacc   99

+ADw-210+AD4- 221
+ADw-211+AD4- 33
+ADw-212+AD4- ADN
+ADw-213+AD4- Secuencia artificial

+ADw-220+AD4-

+ADw-223+AD4- CD19 H3 inverso constante

+ADw-400+AD4- 221
cgtcaccggt tcggggaagt agtccttgac cag   33

+ADw-210+AD4- 222
+ADw-211+AD4- 26
+ADw-212+AD4- ADN
+ADw-213+AD4- Secuencia artificial

+ADw-220+AD4-
+ADw-223+AD4- LMB3

+ADw-400+AD4- 222
caggaaacag ctatgaccat gattac   26

+ADw-210+AD4- 223
+ADw-211+AD4- 33
+ADw-212+AD4- ADN
+ADw-213+AD4- Secuencia artificial

+ADw-220+AD4-
+ADw-223+AD4- CD19 L1 directo constante

+ADw-400+AD4- 223
tggtatctcc agaaaccggg tcagagcccg cag   33

+ADw-210+AD4- 224
+ADw-211+AD4- 84
+ADw-212+AD4- ADN
+ADw-213+AD4- Secuencia artificial

+ADw-220+AD4-
+ADw-223+AD4- 34-36: 52+AKAAJQ- Y, 4+AKAAJQ- otros, 37-39: 52+AKAAJQ- P, 4+AKAAJQ-
otros, 40-42: 42+AKAAJQ- V,
       10+AKAAJQ- L, 4+AKAAJQ- otros, 43-45: 52+AKAAJQ- H, 4+AKAAJQ- otros, 46-48:
42+AKAAJQ- T, 10+AKAAJQ- I,
       4+AKAAJQ- otros, 49-51: 45+AKAAJQ- L, 11+AKAAJQ- G, 4+AKAAJQ- otros

+ADw-220+AD4-
+ADw-221+AD4- misc+AF8-feature
+ADw-222+AD4- (34)..(36)
+ADw-223+AD4- n es a, c, g o t

+ADw-220+AD4-
+ADw-221+AD4- misc+AF8-feature
+ADw-222+AD4- (37)..(39)
+ADw-223+AD4- n es a, c, g o t

+ADw-220+AD4-
+ADw-221+AD4- misc+AF8-feature
+ADw-222+AD4- (40)..(42)
+ADw-223+AD4- n es a, c, g o t

+ADw-220+AD4-
+ADw-221+AD4- misc+AF8-feature
+ADw-222+AD4- (43)..(45)
+ADw-223+AD4- n es a, c, g o t

+ADw-220+AD4-
+ADw-221+AD4- misc+AF8-feature
+ADw-222+AD4- (46)..(48)
+ADw-223+AD4- n es a, c, g o t

+ADw-220+AD4-
+ADw-221+AD4- misc+AF8-feature
+ADw-222+AD4- (49)..(51)
+ADw-223+AD4- n es a, c, g o t

+ADw-400+AD4- 224
tttaatttcc agtttagttc cttgaccgaa ggtnnnnnnn nnnnnnnnnn nctgcagaca 60

atagtagacg ccaacgtctt cagc 84

+ADw-210+AD4- 225
+ADw-211+AD4- 35
+ADw-212+AD4- ADN
+ADw-213+AD4- Secuencia artificial

+ADw-220+AD4-
+ADw-223+AD4- CD19 L3 directo constante

+ADw-400+AD4- 225
accttcggtc aaggaactaa actggaaatt aaacg 35

+ADw-210+AD4- 226
+ADw-211+AD4- 107
+ADw-212+AD4- ADN
+ADw-213+AD4- Secuencia artificial

+ADw-220+AD4-
+ADw-223+AD4- pos. 59-61: 50+AKAAJQ- L, 3,8+AKAAJQ- otros, 62-64: 50+AKAAJQ- A, 4,2+AKAAJQ- otros, 65-67:
50+AKAAJQ- S, 4,2+AKAAJQ- otros, 68-70: 50+AKAAJQ- G, 4,2+AKAAJQ- otros, 71-73: 50+AKAAJQ- Y, 4,2+AKAAJQ-
otros, 74-76: 50+AKAAJQ- Y, 4,2+AKAAJQ- otros, 77-79: 50+AKAAJQ- Y, 4,2+AKAAJQ- otros,
80-82: 50+AKAAJQ- T, 4,2+AKAAJQ- otros, 83-85: 50+AKAAJQ- G, 4,2+AKAAJQ- otros.

+ADw-220+AD4-
+ADw-221+AD4- misc+AF8-feature
+ADw-222+AD4- (54)..(58)
+ADw-223+AD4- n es a, c, g, o t

+ADw-220+AD4-
+ADw-221+AD4- misc+AF8-feature
+ADw-222+AD4- (59)..(61)
+ADw-223+AD4- n es a, c, g o t

+ADw-220+AD4-
+ADw-221+AD4- misc+AF8-feature
+ADw-222+AD4- (62)..(64)
+ADw-223+AD4- n es a, c, g o t

+ADw-220+AD4-
+ADw-221+AD4- misc+AF8-feature
+ADw-222+AD4- (65)..(67)
+ADw-223+AD4- n es a, c, g o t

+ADw-220+AD4-
+ADw-221+AD4- misc+AF8-feature
+ADw-222+AD4- (68)..(70)
+ADw-223+AD4- n es a, c, g o t

+ADw-220+AD4-
+ADw-221+AD4- misc+AF8-feature
+ADw-222+AD4- (71)..(73)
+ADw-223+AD4- n es a, c, g o t

+ADw-220+AD4-
+ADw-221+AD4- misc+AF8-feature
+ADw-222+AD4- (74)..(76)
+ADw-223+AD4- n es a, c, g o t

+ADw-220+AD4-
+ADw-221+AD4- misc+AF8-feature
+ADw-222+AD4- (77)..(79)
+ADw-223+AD4- n es a, c, g o t

+ADw-220+AD4-
+ADw-221+AD4- misc+AF8-feature
+ADw-222+AD4- (80)..(82)
+ADw-223+AD4- n es a, c, g o t

+ADw-220+AD4-
+ADw-221+AD4- misc+AF8-feature
+ADw-222+AD4- (83)..(85)
+ADw-223+AD4- n es a, c, g o t

+ADw-400+AD4- 226
ttggtgctag cagagcttac ggtcaccgtg gtaccttggc cccagtaatc aaannnnnnn 60

nnnnnnnnnn nnnnnnnnnn gcgtgcacaa tagtaaacag cggtgtc 107

+ADw-210+AD4- 227
+ADw-211+AD4- 1615
+ADw-212+AD4- ADN
+ADw-213+AD4- Secuencia artificial

+ADw-220+AD4-
+ADw-223+AD4- ADN de marcador SNAP ECD de CD19 humano-PDGFR

+ADw-400+AD4- 227
ggccgccgct agcggcatcg actacaagga cgacgatgac aaggccggca tcgatgccat 60

catggacaaa gactgcgaaa tgaagcgcac caccctggat agccctctgg gcaagctgga 120

actgtctggg tgcgaacagg gcctgcacga gatcaagctg ctgggcaaag gaacatctgc 180

cgccgacgcc gtggaagtgc ctgccccagc cgccgtgctg ggcggaccag agccactgat 240

gcaggccacc gcctggctca acgcctactt tcaccagcct gaggccatcg aggagttccc 300

tgtgccagcc ctgcaccacc cagtgttcca gcaggagagc tttacccgcc aggtgctgtg 360

gaaactgctg aaagtggtga agttcggaga ggtcatcagc taccagcagc tggccgccct 420

ggccggcaat cccgccgcca ccgccgccgt gaaaaccgcc ctgagcggaa atcccgtgcc 480

cattctgatc ccctgccacc gggtggtgtc tagctctggc gccgtggggg gctacgaggg 540

cgggctcgcc gtgaaagagt ggctgctggc ccacgagggc cacagactgg gcaagcctgg 600

gctgggtgat atccccgagg aacccctggt cgtgaaggtg gaagagggcg acaatgccgt 660

gctgcagtgc ctgaagggca cctccgatgg ccctacccag cagctgacct ggtccagaga 720

gagccccctg aagcccttcc tgaagctgtc tctgggcctg cctggcctgg gcatccatat 780

gaggcctctg gccatctggc tgttcatctt caacgtgtcc cagcagatgg gcggcttcta 840

cctgtgtcag cctggccccc catctgagaa ggcttggcag cctggctgga ccgtgaacgt 900

ggaaggatcc ggcgagctgt tccggtggaa cgtgtccgat ctgggcggcc tgggatgcgg 960

cctgaagaac agatctagcg agggccccag cagccccagc ggcaaactga tgagccccaa 1020

gctgtacgtg tgggccaagg acagacccga gatctgggag ggcgagcctc cttgcctgcc 1080

ccctagagac agcctgaacc agagcctgag ccaggacctg acaatggccc ctggcagcac 1140

actgtggctg agctgtggcg tgccacccga ctctgtgtct agaggccctc tgagctggac 1200

ccacgtgcac cctaagggcc ctaagagcct gctgagcctg gaactgaagg acgacaggcc 1260

cgccagagat atgtgggtca tggaaaccgg cctgctgctg cctagagcca cagcccagga 1320

tgccggcaag tactactgcc acagaggcaa cctgaccatg agcttccacc tggaaatcac 1380

cgccagaccc gtgctgtggc actggctgct gagaacaggc ggctggaagg tcgacgaaca 1440

aaaactcatc tcagaagagg atctgaatgc tgtgggccag gacacgcagg aggtcatcgt 1500

ggtgccacac tccttgccct ttaaggtggt ggtgatctca gccatcctgg ccctggtggt 1560

gctcaccatc atctccctta tcatcctcat catgctttgg cagaagaagc cacgt 1615

+ADw-210+AD4- 228
+ADw-211+AD4- 1620
+ADw-212+AD4- ADN
+ADw-213+AD4- Secuencia artificial

+ADw-220+AD4-
+ADw-223+AD4- ADN de marcador SNAP ECD de CD19 de cinomolgo-PDGFR

+ADw-400+AD4- 228
ccggccgccg ctagcggcat cgactacaag gacgacgatg acaaggccgg catcgatgcc 60

atcatggaca aagactgcga aatgaagcgc accaccctgg atagccctct gggcaagctg 120

gaactgtctg ggtgcgaaca gggcctgcac gagatcaagc tgctgggcaa aggaacatct 180

gccgccgacg ccgtggaagt gcctgcccca gccgccgtgc tgggcggacc agagccactg 240

atgcaggcca ccgcctggct caacgcctac tttcaccagc ctgaggccat cgaggagttc 300

cctgtgccag ccctgcacca cccagtgttc cagcaggaga gctttacccg ccaggtgctg 360

tggaaactgc tgaaagtggt gaagttcgga gaggtcatca gctaccagca gctggccgcc 420

ctggccggca atcccgccgc caccgccgcc gtgaaaaccg ccctgagcgg aaatcccgtg 480

cccattctga tcccctgcca ccgggtggtg tctagctctg gcgccgtggg gggctacgag 540

ggcgggctcg ccgtgaaaga gtggctgctg gcccacgagg gccacagact gggcaagcct 600

gggctgggtg atatccccca ggaacccctg gtcgtgaagg tggaagaggg cgacaatgcc 660

gtgctccagt gtctcgaggg cacctccgat ggccctacac agcagctcgt gtggtgcaga 720

gacagcccct tcgagccctt cctgaacctg tctctgggcc tgcctggcat gggcatcaga 780

atgggccctc tgggcatctg gctgctgatc ttcaacgtgt ccaaccagac cggcggcttc 840

tacctgtgtc agcctggcct gccaagcgag aaggcttggc agcctggatg gaccgtgtcc 900

gtggaaggat ctggcgagct gttccggtgg aacgtgtccg atctgggcgg cctgggatgc 960

ggcctgaaga acagaagcag cgagggccct agcagcccca gcggcaagct gaatagcagc 1020

cagctgtacg tgtgggccaa ggacagaccc gagatgtggg agggcgagcc tgtgtgtggc 1080

ccccctagag atagcctgaa ccagagcctg agccaggacc tgacaatggc ccctggcagc 1140

acactgtggc tgagctgtgg cgtgccaccc gactctgtgt ccagaggccc tctgagctgg 1200

acacacgtgc ggcctaaggg ccctaagagc agcctgctga gcctggaact gaaggacgac 1260

cggcccgacc gggatatgtg ggtggtggat acaggcctgc tgctgaccag agccacagcc 1320

caggatgccg gcaagtacta ctgccacaga ggcaactgga ccaagagctt ttacctggaa 1380

atcaccgcca gacccgccct gtggcactgg ctgctgagaa tcggaggctg gaaggtcgac 1440

gagcagaagc tgatctccga agaggacctg aacgccgtgg gccaggatac ccaggaagtg 1500

atcgtggtgc cccacagcct gcccttcaag gtggtcgtga tcagcgccat tctggccctg 1560

gtggtgctga ccatcatcag cctgatcatc ctgattatgc tgtggcagaa aaagccccgc 1620

+ADw-210+AD4- 229
+ADw-211+AD4- 539
+ADw-212+AD4- PRT
+ADw-213+AD4- Secuencia artificial

+ADw-220+AD4-
+ADw-223+AD4- marcador SNAP ECD de CD19 humano-PDGFR

+ADw-400+AD4- 229

Pro Ala Ala Ala Ser Gly Ile Asp Tyr Lys Asp Asp Asp Asp Lys Ala
1 5 10 15

Gly Ile Asp Ala Ile Met Asp Lys Asp Cys Glu Met Lys Arg Thr Thr
20 25 30

Leu Asp Ser Pro Leu Gly Lys Leu Glu Leu Ser Gly Cys Glu Gln Gly
35 40 45

Leu His Glu Ile Lys Leu Leu Gly Lys Gly Thr Ser Ala Ala Asp Ala
50 55 60

```
Val Glu Val Pro Ala Pro Ala Ala Val Leu Gly Gly Pro Glu Pro Leu
65                  70                  75                  80

Met Gln Ala Thr Ala Trp Leu Asn Ala Tyr Phe His Gln Pro Glu Ala
                85                  90                  95

Ile Glu Glu Phe Pro Val Pro Ala Leu His His Pro Val Phe Gln Gln
            100                 105                 110

Glu Ser Phe Thr Arg Gln Val Leu Trp Lys Leu Leu Lys Val Val Lys
        115                 120                 125

Phe Gly Glu Val Ile Ser Tyr Gln Gln Leu Ala Ala Leu Ala Gly Asn
    130                 135                 140

Pro Ala Ala Thr Ala Ala Val Lys Thr Ala Leu Ser Gly Asn Pro Val
145                 150                 155                 160

Pro Ile Leu Ile Pro Cys His Arg Val Val Ser Ser Ser Gly Ala Val
                165                 170                 175

Gly Gly Tyr Glu Gly Gly Leu Ala Val Lys Glu Trp Leu Leu Ala His
            180                 185                 190

Glu Gly His Arg Leu Gly Lys Pro Gly Leu Gly Asp Ile Pro Glu Glu
        195                 200                 205

Pro Leu Val Val Lys Val Glu Glu Gly Asp Asn Ala Val Leu Gln Cys
    210                 215                 220

Leu Lys Gly Thr Ser Asp Gly Pro Thr Gln Gln Leu Thr Trp Ser Arg
225                 230                 235                 240

Glu Ser Pro Leu Lys Pro Phe Leu Lys Leu Ser Leu Gly Leu Pro Gly
                245                 250                 255

Leu Gly Ile His Met Arg Pro Leu Ala Ile Trp Leu Phe Ile Phe Asn
            260                 265                 270

Val Ser Gln Gln Met Gly Gly Phe Tyr Leu Cys Gln Pro Gly Pro Pro
        275                 280                 285

Ser Glu Lys Ala Trp Gln Pro Gly Trp Thr Val Asn Val Glu Gly Ser
    290                 295                 300

Gly Glu Leu Phe Arg Trp Asn Val Ser Asp Leu Gly Gly Leu Gly Cys
```

305 310 315 320

Gly Leu Lys Asn Arg Ser Ser Glu Gly Pro Ser Ser Pro Ser Gly Lys
325 330 335

Leu Met Ser Pro Lys Leu Tyr Val Trp Ala Lys Asp Arg Pro Glu Ile
340 345 350

Trp Glu Gly Glu Pro Pro Cys Leu Pro Pro Arg Asp Ser Leu Asn Gln
355 360 365

Ser Leu Ser Gln Asp Leu Thr Met Ala Pro Gly Ser Thr Leu Trp Leu
370 375 380

Ser Cys Gly Val Pro Pro Asp Ser Val Ser Arg Gly Pro Leu Ser Trp
385 390 395 400

Thr His Val His Pro Lys Gly Pro Lys Ser Leu Leu Ser Leu Glu Leu
405 410 415

Lys Asp Asp Arg Pro Ala Arg Asp Met Trp Val Met Glu Thr Gly Leu
420 425 430

Leu Leu Pro Arg Ala Thr Ala Gln Asp Ala Gly Lys Tyr Tyr Cys His
435 440 445

Arg Gly Asn Leu Thr Met Ser Phe His Leu Glu Ile Thr Ala Arg Pro
450 455 460

Val Leu Trp His Trp Leu Leu Arg Thr Gly Gly Trp Lys Val Asp Glu
465 470 475 480

Gln Lys Leu Ile Ser Glu Glu Asp Leu Asn Ala Val Gly Gln Asp Thr
485 490 495

Gln Glu Val Ile Val Val Pro His Ser Leu Pro Phe Lys Val Val Val
500 505 510

Ile Ser Ala Ile Leu Ala Leu Val Val Leu Thr Ile Ile Ser Leu Ile
515 520 525

Ile Leu Ile Met Leu Trp Gln Lys Lys Pro Arg
530 535

+ADw-210+AD4- 230
+ADw-211+AD4- 540
+ADw-212+AD4- PRT
+ADw-213+AD4- Secuencia artificial

+ADw-220+AD4-
+ADw-223+AD4- marcador SNAP ECD de CD19 de cinomolgo-PDGFR

+ADw-400+AD4- 230

```
Pro Ala Ala Ala Ser Gly Ile Asp Tyr Lys Asp Asp Asp Asp Lys Ala
1               5                   10                  15

Gly Ile Asp Ala Ile Met Asp Lys Asp Cys Glu Met Lys Arg Thr Thr
            20                  25                  30

Leu Asp Ser Pro Leu Gly Lys Leu Glu Leu Ser Gly Cys Glu Gln Gly
        35                  40                  45

Leu His Glu Ile Lys Leu Leu Gly Lys Gly Thr Ser Ala Ala Asp Ala
    50                  55                  60

Val Glu Val Pro Ala Pro Ala Ala Val Leu Gly Gly Pro Glu Pro Leu
65                  70                  75                  80

Met Gln Ala Thr Ala Trp Leu Asn Ala Tyr Phe His Gln Pro Glu Ala
                85                  90                  95

Ile Glu Glu Phe Pro Val Pro Ala Leu His His Pro Val Phe Gln Gln
            100                 105                 110

Glu Ser Phe Thr Arg Gln Val Leu Trp Lys Leu Leu Lys Val Val Lys
        115                 120                 125

Phe Gly Glu Val Ile Ser Tyr Gln Gln Leu Ala Ala Leu Ala Gly Asn
    130                 135                 140

Pro Ala Ala Thr Ala Ala Val Lys Thr Ala Leu Ser Gly Asn Pro Val
145                 150                 155                 160

Pro Ile Leu Ile Pro Cys His Arg Val Val Ser Ser Ser Gly Ala Val
                165                 170                 175

Gly Gly Tyr Glu Gly Gly Leu Ala Val Lys Glu Trp Leu Leu Ala His
            180                 185                 190

Glu Gly His Arg Leu Gly Lys Pro Gly Leu Gly Asp Ile Pro Gln Glu
        195                 200                 205

Pro Leu Val Val Lys Val Glu Glu Gly Asp Asn Ala Val Leu Gln Cys
    210                 215                 220

Leu Glu Gly Thr Ser Asp Gly Pro Thr Gln Gln Leu Val Trp Cys Arg
```

```
225                 230                 235                 240

Asp Ser Pro Phe Glu Pro Phe Leu Asn Leu Ser Leu Gly Leu Pro Gly
                245                 250                 255

Met Gly Ile Arg Met Gly Pro Leu Gly Ile Trp Leu Leu Ile Phe Asn
            260                 265                 270

Val Ser Asn Gln Thr Gly Gly Phe Tyr Leu Cys Gln Pro Gly Leu Pro
        275                 280                 285

Ser Glu Lys Ala Trp Gln Pro Gly Trp Thr Val Ser Val Glu Gly Ser
    290                 295                 300

Gly Glu Leu Phe Arg Trp Asn Val Ser Asp Leu Gly Gly Leu Gly Cys
305                 310                 315                 320

Gly Leu Lys Asn Arg Ser Ser Glu Gly Pro Ser Ser Pro Ser Gly Lys
                325                 330                 335

Leu Asn Ser Ser Gln Leu Tyr Val Trp Ala Lys Asp Arg Pro Glu Met
            340                 345                 350

Trp Glu Gly Glu Pro Val Cys Gly Pro Pro Arg Asp Ser Leu Asn Gln
        355                 360                 365

Ser Leu Ser Gln Asp Leu Thr Met Ala Pro Gly Ser Thr Leu Trp Leu
    370                 375                 380

Ser Cys Gly Val Pro Pro Asp Ser Val Ser Arg Gly Pro Leu Ser Trp
385                 390                 395                 400

Thr His Val Arg Pro Lys Gly Pro Lys Ser Ser Leu Leu Ser Leu Glu
                405                 410                 415

Leu Lys Asp Asp Arg Pro Asp Arg Asp Met Trp Val Val Asp Thr Gly
            420                 425                 430

Leu Leu Leu Thr Arg Ala Thr Ala Gln Asp Ala Gly Lys Tyr Tyr Cys
        435                 440                 445

His Arg Gly Asn Trp Thr Lys Ser Phe Tyr Leu Glu Ile Thr Ala Arg
    450                 455                 460

Pro Ala Leu Trp His Trp Leu Leu Arg Ile Gly Gly Trp Lys Val Asp
465                 470                 475                 480
```

Glu Gln Lys Leu Ile Ser Glu Glu Asp Leu Asn Ala Val Gly Gln Asp
485 490 495

Thr Gln Glu Val Ile Val Val Pro His Ser Leu Pro Phe Lys Val Val
500 505 510

Val Ile Ser Ala Ile Leu Ala Leu Val Val Leu Thr Ile Ile Ser Leu
515 520 525

Ile Ile Leu Ile Met Leu Trp Gln Lys Lys Pro Arg
530 535 540

+ADw-210+AD4- 231
+ADw-211+AD4- 16
+ADw-212+AD4- PRT
+ADw-213+AD4- Secuencia artificial

+ADw-220+AD4-
+ADw-223+AD4- CD19 (8B8-5H09) CDR-L1

+ADw-400+AD4- 231

Lys Ser Ser Gln Ser Leu Glu Ser Ser Thr Gly Asn Thr Tyr Leu Asn
1 5 10 15

+ADw-210+AD4- 232
+ADw-211+AD4- 7
+ADw-212+AD4- PRT
+ADw-213+AD4- Secuencia artificial

+ADw-220+AD4-
+ADw-223+AD4- CD19 (8B8-5H09) CDR-L2

+ADw-400+AD4- 232

Arg Val Ser Lys Arg Phe Ser
1 5

+ADw-210+AD4- 233
+ADw-211+AD4- 9
+ADw-212+AD4- PRT
+ADw-213+AD4- Secuencia artificial

+ADw-220+AD4-
+ADw-223+AD4- CD19 (8B8-5H09) CDR-L3

+ADw-400+AD4- 233

Leu Gln Leu Ile Asp Tyr Pro Val Thr
1 5

+ADw-210+AD4- 234
+ADw-211+AD4- 5
+ADw-212+AD4- PRT
+ADw-213+AD4- Secuencia artificial

+ADw-220+AD4-
+ADw-223+AD4- CD19 (8B8-5H09) CDR-H1

+ADw-400+AD4- 234

Asp Tyr Ile Met His
1 5

+ADw-210+AD4- 235
+ADw-211+AD4- 17
+ADw-212+AD4- PRT
+ADw-213+AD4- Secuencia artificial

+ADw-220+AD4-
+ADw-223+AD4- CD19 (8B8-5H09) CDR-H2

+ADw-400+AD4- 235

Tyr Ile Asn Pro Tyr Asn Asp Gly Ser Lys Tyr Thr Glu Lys Phe Gln
1 5 10 15

Gly

+ADw-210+AD4- 236
+ADw-211+AD4- 12
+ADw-212+AD4- PRT
+ADw-213+AD4- Secuencia artificial

+ADw-220+AD4-
+ADw-223+AD4- CDR-H3 de CDR(8B8-5H09)

+ADw-400+AD4- 236

Gly Thr Tyr Tyr Tyr Gly Ser Ala Leu Phe Asp Tyr
1 5 10

+ADw-210+AD4- 237
+ADw-211+AD4- 16
+ADw-212+AD4- PRT
+ADw-213+AD4- Secuencia artificial

+ADw-220+AD4-
+ADw-223+AD4- CD19 (8B8-7H07) CDR-L1

+ADw-400+AD4- 237

Lys Ser Ser Gln Ser Leu Glu Thr Ser Thr Gly Asn Thr Tyr Leu Asn
1 5 10 15

+ADw-210+AD4- 238
+ADw-211+AD4- 7
+ADw-212+AD4- PRT
+ADw-213+AD4- Secuencia artificial

+ADw-220+AD4-
+ADw-223+AD4- CD19 (8B8-7H07) CDR-L2

+ADw-400+AD4- 238

Arg Val Ser Lys Arg Phe Ser
1   5

+ADw-210+AD4- 239
+ADw-211+AD4- 9
+ADw-212+AD4- PRT
+ADw-213+AD4- Secuencia artificial

+ADw-220+AD4-
+ADw-223+AD4- CD19 (8B8-7H07) CDR-L3

+ADw-400+AD4- 239

Leu Gln Ala Thr His Ile Pro Tyr Thr
1   5

+ADw-210+AD4- 240
+ADw-211+AD4- 5
+ADw-212+AD4- PRT
+ADw-213+AD4- Secuencia artificial

+ADw-220+AD4-
+ADw-223+AD4- CD19 (8B8-7H07) CDR-H1

+ADw-400+AD4- 240

Asp Tyr Ile Met His
1   5

+ADw-210+AD4- 241
+ADw-211+AD4- 17
+ADw-212+AD4- PRT
+ADw-213+AD4- Secuencia artificial

+ADw-220+AD4-
+ADw-223+AD4- CD19 (8B8-7H07) CDR-H2

+ADw-400+AD4- 241

Tyr Ile Asn Pro Tyr Asn Asp Gly Ser Lys Tyr Thr Glu Lys Phe Gln
1   5   10   15

Gly

+ADw-210+AD4- 242
+ADw-211+AD4- 12
+ADw-212+AD4- PRT
+ADw-213+AD4- Secuencia artificial

+ADw-220+AD4-
+ADw-223+AD4- CD19 (8B8-7H07) CDR-H3

+ADw-400+AD4- 242

Gly Thr Tyr Tyr Tyr Gly Ser Glu Leu Phe Asp Tyr

1 5 10

+ADw-210+AD4- 243
+ADw-211+AD4- 16
+ADw-212+AD4- PRT
+ADw-213+AD4- Secuencia artificial

+ADw-220+AD4-
+ADw-223+AD4- CD19 (8B8-2B03) CDR-L1

+ADw-400+AD4- 243

Lys Ser Ser Gln Ser Leu Glu Thr Ser Thr Gly Asn Thr Tyr Leu Asn
1 5 10 15

+ADw-210+AD4- 244
+ADw-211+AD4- 7
+ADw-212+AD4- PRT
+ADw-213+AD4- Secuencia artificial

+ADw-220+AD4-
+ADw-223+AD4- CD19 (8B8-2B03) CDR-L2

+ADw-400+AD4- 244

Arg Val Ser Lys Arg Phe Ser
1 5

+ADw-210+AD4- 245
+ADw-211+AD4- 9
+ADw-212+AD4- PRT
+ADw-213+AD4- Secuencia artificial

+ADw-220+AD4-
+ADw-223+AD4- CD19 (8B8-2B03) CDR-L3

+ADw-400+AD4- 245

Leu Gln Leu Thr His Val Pro Tyr Thr
1 5

+ADw-210+AD4- 246
+ADw-211+AD4- 5
+ADw-212+AD4- PRT
+ADw-213+AD4- Secuencia artificial

+ADw-220+AD4-
+ADw-223+AD4- CD19 (8B8-2B03) CDR-H1

+ADw-400+AD4- 246

Asp Tyr Ile Thr His
1 5

+ADw-210+AD4- 247
+ADw-211+AD4- 17
+ADw-212+AD4- PRT
+ADw-213+AD4- Secuencia artificial

+ADw-220+AD4-
+ADw-223+AD4- CD19 (8B8-2B03) CDR-H2

+ADw-400+AD4- 247

Tyr Ile Asn Pro Tyr Asn Asp Gly Ser Lys Tyr Thr Glu Lys Phe Gln
1 5 10 15

Gly

+ADw-210+AD4- 248
+ADw-211+AD4- 12
+ADw-212+AD4- PRT
+ADw-213+AD4- Secuencia artificial

+ADw-220+AD4-
+ADw-223+AD4- CD19 (8B8-2B03) CDR-H3

+ADw-400+AD4- 248

Gly Thr Tyr Tyr Tyr Gly Pro Asp Leu Phe Asp Tyr
1 5 10

+ADw-210+AD4- 249
+ADw-211+AD4- 16
+ADw-212+AD4- PRT
+ADw-213+AD4- Secuencia artificial

+ADw-220+AD4-
+ADw-223+AD4- CD19 (8B8-2B11) CDR-L1

+ADw-400+AD4- 249

Lys Ser Ser Gln Ser Leu Glu Thr Ser Thr Gly Thr Thr Tyr Leu Asn
1 5 10 15

+ADw-210+AD4- 250
+ADw-211+AD4- 7
+ADw-212+AD4- PRT
+ADw-213+AD4- Secuencia artificial

+ADw-220+AD4-
+ADw-223+AD4- CD19 (8B8-2B11) CDR-L2

+ADw-400+AD4- 250

Arg Val Ser Lys Arg Phe Ser
1 5

+ADw-210+AD4- 251
+ADw-211+AD4- 9
+ADw-212+AD4- PRT
+ADw-213+AD4- Secuencia artificial

+ADw-220+AD4-
+ADw-223+AD4- CD19 (8B8-2B11) CDR-L3

+ADw-400+AD4- 251

Leu Gln Leu Leu Glu Asp Pro Tyr Thr
1   5

+ADw-210+AD4- 252
+ADw-211+AD4- 5
+ADw-212+AD4- PRT
+ADw-213+AD4- Secuencia artificial

+ADw-220+AD4-
+ADw-223+AD4- CD19 (8B8-2B11) CDR-H1

+ADw-400+AD4- 252

Asp Tyr Ile Met His
1   5

+ADw-210+AD4- 253
+ADw-211+AD4- 17
+ADw-212+AD4- PRT
+ADw-213+AD4- Secuencia artificial

+ADw-220+AD4-
+ADw-223+AD4- CD19 (8B8-2B11) CDR-H2

+ADw-400+AD4- 253

Tyr Ile Asn Pro Tyr Asn Asp Gly Ser Lys Tyr Thr Glu Lys Phe Gln
1   5   10   15

Gly

+ADw-210+AD4- 254
+ADw-211+AD4- 12
+ADw-212+AD4- PRT
+ADw-213+AD4- Secuencia artificial

+ADw-220+AD4-
+ADw-223+AD4- CD19 (8B8-2B11) CDR-H3

+ADw-400+AD4- 254

Gly Thr Tyr Tyr Tyr Gly Pro Gln Leu Phe Asp Tyr
1   5   10

+ADw-210+AD4- 255
+ADw-211+AD4- 16
+ADw-212+AD4- PRT
+ADw-213+AD4- Secuencia artificial

+ADw-220+AD4-
+ADw-223+AD4- CD19 (8B8-5A07) CDR-L1

+ADw-400+AD4- 255

Lys Ser Ser Gln Ser Leu Glu Thr Ser Thr Gly Asn Thr Tyr Leu Asn
1   5   10   15

+ADw-210+AD4- 256
+ADw-211+AD4- 7
+ADw-212+AD4- PRT
+ADw-213+AD4- Secuencia artificial

+ADw-220+AD4-
+ADw-223+AD4- CD19 (8B8-5A07) CDR-L2

+ADw-400+AD4- 256

Arg Val Ser Lys Arg Phe Ser
1   5

+ADw-210+AD4- 257
+ADw-211+AD4- 9
+ADw-212+AD4- PRT
+ADw-213+AD4- Secuencia artificial

+ADw-220+AD4-
+ADw-223+AD4- CD19 (8B8-5A07) CDR-L3

+ADw-400+AD4- 257

Leu Gln Pro Gly His Tyr Pro Gly Thr
1   5

+ADw-210+AD4- 258
+ADw-211+AD4- 5
+ADw-212+AD4- PRT
+ADw-213+AD4- Secuencia artificial

+ADw-220+AD4-
+ADw-223+AD4- CD19 (8B8-5A07) CDR-H1

+ADw-400+AD4- 258

Asp Tyr Ile Met His
1   5

+ADw-210+AD4- 259
+ADw-211+AD4- 17
+ADw-212+AD4- PRT
+ADw-213+AD4- Secuencia artificial

+ADw-220+AD4-
+ADw-223+AD4- CD19 (8B8-5A07) CDR-H2

+ADw-400+AD4- 259

Tyr Ile Asn Pro Tyr Asn Asp Gly Ser Lys Tyr Thr Glu Lys Phe Gln
1   5   10   15

Gly

+ADw-210+AD4- 260
+ADw-211+AD4- 12
+ADw-212+AD4- PRT
+ADw-213+AD4- Secuencia artificial

+ADw-220+AD4-
+ADw-223+AD4- CD19 (8B8-5A07) CDR-H3

+ADw-400+AD4- 260

Gly Thr Tyr Tyr Tyr Gly Ser Ala Leu Phe Asp Tyr
1 5 10

+ADw-210+AD4- 261
+ADw-211+AD4- 16
+ADw-212+AD4- PRT
+ADw-213+AD4- Secuencia artificial

+ADw-220+AD4-
+ADw-223+AD4- CD19 (8B8-5B08) CDR-L1

+ADw-400+AD4- 261

Lys Ser Ser Gln Ser Leu Glu Thr Ser Thr Gly Asn Thr Tyr Leu Asn
1 5 10 15

+ADw-210+AD4- 262
+ADw-211+AD4- 7
+ADw-212+AD4- PRT
+ADw-213+AD4- Secuencia artificial

+ADw-220+AD4-
+ADw-223+AD4- CD19 (8B8-5B08) CDR-L2

+ADw-400+AD4- 262

Arg Val Ser Lys Arg Phe Ser
1 5

+ADw-210+AD4- 263
+ADw-211+AD4- 9
+ADw-212+AD4- PRT
+ADw-213+AD4- Secuencia artificial

+ADw-220+AD4-
+ADw-223+AD4- CD19 (8B8-5B08) CDR-L3

+ADw-400+AD4- 263

Leu Gln Leu Asp Ser Tyr Pro Asn Thr
1 5

+ADw-210+AD4- 264
+ADw-211+AD4- 5
+ADw-212+AD4- PRT
+ADw-213+AD4- Secuencia artificial

+ADw-220+AD4-

+ADw-223+AD4- CD19 (8B8-5B08) CDR-H1

+ADw-400+AD4- 264

Asp Tyr Ile Met His
1   5

+ADw-210+AD4- 265
+ADw-211+AD4- 17
+ADw-212+AD4- PRT
+ADw-213+AD4- Secuencia artificial

+ADw-220+AD4-
+ADw-223+AD4- CD19 (8B8-5B08) CDR-H2

+ADw-400+AD4- 265

Tyr Ile Asn Pro Tyr Asn Asp Gly Ser Lys Tyr Thr Glu Lys Phe Gln
1   5   10   15

Gly

+ADw-210+AD4- 266
+ADw-211+AD4- 12
+ADw-212+AD4- PRT
+ADw-213+AD4- Secuencia artificial

+ADw-220+AD4-
+ADw-223+AD4- CD19 (8B8-5B08) CDR-H3

+ADw-400+AD4- 266

Gly Thr Tyr Tyr Tyr Gly Pro Gln Leu Phe Asp Tyr
1   5   10

+ADw-210+AD4- 267
+ADw-211+AD4- 16
+ADw-212+AD4- PRT
+ADw-213+AD4- Secuencia artificial

+ADw-220+AD4-
+ADw-223+AD4- CD19 (8B8-5D08) CDR-L1

+ADw-400+AD4- 267

Lys Ser Ser Gln Ser Leu Glu Thr Ser Thr Gly Asn Thr Tyr Leu Asn
1   5   10   15

+ADw-210+AD4- 268
+ADw-211+AD4- 7
+ADw-212+AD4- PRT
+ADw-213+AD4- Secuencia artificial

+ADw-220+AD4-
+ADw-223+AD4- CD19 (8B8-5D08) CDR-L2

+ADw-400+AD4- 268

Arg Val Ser Lys Arg Phe Ser
1 5

+ADw-210+AD4- 269
+ADw-211+AD4- 9
+ADw-212+AD4- PRT
+ADw-213+AD4- Secuencia artificial

+ADw-220+AD4-
+ADw-223+AD4- CD19 (8B8-5D08) CDR-L3

+ADw-400+AD4- 269

Leu Gln Leu Thr His Glu Pro Tyr Thr
1 5

+ADw-210+AD4- 270
+ADw-211+AD4- 5
+ADw-212+AD4- PRT
+ADw-213+AD4- Secuencia artificial

+ADw-220+AD4-
+ADw-223+AD4- CD19 (8B8-5D08) CDR-H1

+ADw-400+AD4- 270

Asp Tyr Ile Met His
1 5

+ADw-210+AD4- 271
+ADw-211+AD4- 17
+ADw-212+AD4- PRT
+ADw-213+AD4- Secuencia artificial

+ADw-220+AD4-
+ADw-223+AD4- CD19 (8B8-5D08) CDR-H2

+ADw-400+AD4- 271

Tyr Ile Asn Pro Tyr Asn Asp Gly Ser Lys Tyr Thr Glu Lys Phe Gln
1 5 10 15

Gly

+ADw-210+AD4- 272
+ADw-211+AD4- 12
+ADw-212+AD4- PRT
+ADw-213+AD4- Secuencia artificial

+ADw-220+AD4-
+ADw-223+AD4- CD19 (8B8-5D08) CDR-H3

+ADw-400+AD4- 272

Gly Thr Tyr Tyr Tyr Gly Ser Glu Leu Phe Asp Tyr
1 5 10

+ADw-210+AD4- 273
+ADw-211+AD4- 657
+ADw-212+AD4- ADN
+ADw-213+AD4- Secuencia artificial

+ADw-220+AD4-
+ADw-223+AD4- ADN de CD19 (8B8) cadena ligera progenitora

+ADw-400+AD4- 273
gatgctgtga tgacccaaac tccactctcc ctgcctgtca gtcttggaga tcaagcctcc 60

atctcttgca ggtctagtca gagccttgaa aacagtaatg gaaacaccta tttgaactgg 120

tacctccaga aaccaggcca gtctccacaa ctcctgatct acagggtttc caaacgattt 180

tctggggtcc tagacaggtt cagtggtagt ggatcaggga cagatttcac actgaaaatc 240

agcagagtgg aggctgagga tttgggagtt tatttctgcc tacaacttac acatgtcccg 300

tacacgttcg gaggggggac caagctggaa ataaaacgta cggtggctgc accatctgtc 360

ttcatcttcc cgccatctga tgagcagttg aaatctggaa ctgcctctgt tgtgtgcctg 420

ctgaataact tctatcccag agaggccaaa gtacagtgga aggtggataa cgccctccaa 480

tcgggtaact cccaggagag tgtcacagag caggacagca aggacagcac ctacagcctc 540

agcagcaccc tgacgctgag caaagcagac tacgagaaac acaaagtcta cgcctgcgaa 600

gtcacccatc agggcctgag ctcgcccgtc acaaagagct tcaacagggg agagtgt 657

+ADw-210+AD4- 274
+ADw-211+AD4- 1353
+ADw-212+AD4- ADN
+ADw-213+AD4- Secuencia artificial

+ADw-220+AD4-
+ADw-223+AD4- ADN de CD19 (8B8) cadena pesada progenitora

+ADw-400+AD4- 274
gaggtccagc tgcagcagtc tggacctgag ctggtaaagc ctggggcttc agtgaagatg 60

gcctgcaagg cttctggata cacattcact gactatatta tgcactgggt gaagcagaag 120

actgggcagg gccttgagtg gattggatat attaatcctt acaatgatgg ttctaagtac 180

actgagaagt tcaacggcaa ggccacactg acttcagaca aatcttccat cacagcctac 240

atggagctca gcagcctgac ctctgaggac tctgcggtct attactgtgc aagagggacc 300

tattattatg gtagcgccct ctttgactac tggggccaag gcaccactct cacagtctcc 360

tcggctagca ccaagggccc atcggtcttc cccctggcac cctcctccaa gagcacctct 420

gggggcacag cggccctggg ctgcctggtc aaggactact tccccgaacc ggtgacggtg 480

tcgtggaact caggcgccct gaccagcggc gtgcacacct tcccggctgt cctacagtcc 540

tcaggactct actccctcag cagcgtggtg accgtgccct ccagcagctt gggcacccag 600

acctacatct gcaacgtgaa tcacaagccc agcaacacca aggtggacaa gaaagttgag 660

cccaaatctt gtgacaaaac tcacacatgc ccaccgtgcc cagcacctga agctgcaggg 720

ggaccgtcag tcttcctctt cccccaaaa cccaaggaca ccctcatgat ctcccggacc 780

cctgaggtca catgcgtggt ggtggacgtg agccacgaag accctgaggt caagttcaac 840

tggtacgtgg acggcgtgga ggtgcataat gccaagacaa agccgcggga ggagcagtac 900

aacagcacgt accgtgtggt cagcgtcctc accgtcctgc accaggactg gctgaatggc 960

aaggagtaca agtgcaaggt ctccaacaaa gccctcggcg cccccatcga gaaaaccatc 1020

tccaaagcca aagggcagcc ccgagaacca caggtgtaca ccctgccccc atcccgggat 1080

gagctgacca agaaccaggt cagcctgacc tgcctggtca aaggcttcta tcccagcgac 1140

atcgccgtgg agtgggagag caatgggcag ccggagaaca actacaagac cacgcctccc 1200

gtgctggact ccgacggctc cttcttcctc tacagcaagc tcaccgtgga caagagcagg 1260

tggcagcagg ggaacgtctt ctcatgctcc gtgatgcatg aggctctgca caaccactac 1320

acgcagaaga gcctctccct gtctccgggt aaa 1353

+ADw-210+AD4- 275
+ADw-211+AD4- 219
+ADw-212+AD4- PRT
+ADw-213+AD4- Secuencia artificial

+ADw-220+AD4-
+ADw-223+AD4- CD19 (8B8) cadena ligera progenitora

+ADw-400+AD4- 275

Asp Ala Val Met Thr Gln Thr Pro Leu Ser Leu Pro Val Ser Leu Gly
1 5 10 15

Asp Gln Ala Ser Ile Ser Cys Arg Ser Ser Gln Ser Leu Glu Asn Ser
20 25 30

Asn Gly Asn Thr Tyr Leu Asn Trp Tyr Leu Gln Lys Pro Gly Gln Ser
35 40 45

Pro Gln Leu Leu Ile Tyr Arg Val Ser Lys Arg Phe Ser Gly Val Leu
50 55 60

Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile
65 70 75 80

Ser Arg Val Glu Ala Glu Asp Leu Gly Val Tyr Phe Cys Leu Gln Leu
85 90 95

Thr His Val Pro Tyr Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys
100 105 110

```
Arg Thr Val Ala Ala Pro Ser Val Phe Ile Phe Pro Pro Ser Asp Glu
        115                 120                 125

Gln Leu Lys Ser Gly Thr Ala Ser Val Val Cys Leu Leu Asn Asn Phe
    130                 135                 140

Tyr Pro Arg Glu Ala Lys Val Gln Trp Lys Val Asp Asn Ala Leu Gln
145                 150                 155                 160

Ser Gly Asn Ser Gln Glu Ser Val Thr Glu Gln Asp Ser Lys Asp Ser
                165                 170                 175

Thr Tyr Ser Leu Ser Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu
            180                 185                 190

Lys His Lys Val Tyr Ala Cys Glu Val Thr His Gln Gly Leu Ser Ser
        195                 200                 205

Pro Val Thr Lys Ser Phe Asn Arg Gly Glu Cys
    210                 215


+ADw-210+AD4-  276
+ADw-211+AD4-  451
+ADw-212+AD4-  PRT
+ADw-213+AD4-  Secuencia artificial

+ADw-220+AD4-
+ADw-223+AD4-  CD19 (8B8) cadena pesada progenitora

+ADw-400+AD4-  276

Glu Val Gln Leu Gln Gln Ser Gly Pro Glu Leu Val Lys Pro Gly Ala
1               5                   10                  15

Ser Val Lys Met Ala Cys Lys Ala Ser Gly Tyr Thr Phe Thr Asp Tyr
            20                  25                  30

Ile Met His Trp Val Lys Gln Lys Thr Gly Gln Gly Leu Glu Trp Ile
        35                  40                  45

Gly Tyr Ile Asn Pro Tyr Asn Asp Gly Ser Lys Tyr Thr Glu Lys Phe
    50                  55                  60

Asn Gly Lys Ala Thr Leu Thr Ser Asp Lys Ser Ser Ile Thr Ala Tyr
65                  70                  75                  80

Met Glu Leu Ser Ser Leu Thr Ser Glu Asp Ser Ala Val Tyr Tyr Cys
                85                  90                  95
```

```
Ala Arg Gly Thr Tyr Tyr Tyr Gly Ser Ala Leu Phe Asp Tyr Trp Gly
            100                 105                 110

Gln Gly Thr Thr Leu Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser
        115                 120                 125

Val Phe Pro Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala
    130                 135                 140

Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val
145                 150                 155                 160

Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala
                165                 170                 175

Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val
            180                 185                 190

Pro Ser Ser Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His
        195                 200                 205

Lys Pro Ser Asn Thr Lys Val Asp Lys Lys Val Glu Pro Lys Ser Cys
    210                 215                 220

Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Ala Ala Gly
225                 230                 235                 240

Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met
                245                 250                 255

Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His
            260                 265                 270

Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val
        275                 280                 285

His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr
    290                 295                 300

Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly
305                 310                 315                 320

Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Gly Ala Pro Ile
                325                 330                 335

Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val
            340                 345                 350
```

```
Tyr Thr Leu Pro Pro Ser Arg Asp Glu Leu Thr Lys Asn Gln Val Ser
        355                 360                 365

Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu
    370                 375                 380

Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro
385                 390                 395                 400

Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val
                405                 410                 415

Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met
            420                 425                 430

His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser
        435                 440                 445

Pro Gly Lys
    450
```

+ADw-210+AD4- 277
+ADw-211+AD4- 657
+ADw-212+AD4- ADN
+ADw-213+AD4- Secuencia artificial

+ADw-220+AD4-
+ADw-223+AD4- ADN de cadena ligera de CD19 (8B8-2B11)

+ADw-400+AD4- 277

```
gatattgtca tgactcaaac tccactgtct ctgtccgtga ccccgggtca gccagcgagc       60

atttcttgca aatccagcca atctctggaa acctccaccg gcaccacgta cctgaactgg      120

tatctccaga aaccgggtca gagcccgcag ctgctgatct accgtgtatc taagcgcttc      180

tccggcgttc ctgatcgttt cagcggttct ggatccggca ccgactttac tctgaaaatc      240

agccgtgtgg aagctgaaga cgttggcgtc tactattgtc tgcagctgct ggaagatcca      300

tacaccttcg gtcaaggaac gaaactggaa attaaacgta cggtggctgc accatctgtc      360

ttcatcttcc cgccatctga tgagcagttg aaatctggaa ctgcctctgt tgtgtgcctg      420

ctgaataact tctatcccag agaggccaaa gtacagtgga aggtggataa cgccctccaa      480

tcgggtaact cccaggagag tgtcacagag caggacagca aggacagcac ctacagcctc      540

agcagcaccc tgacgctgag caaagcagac tacgagaaac acaaagtcta cgcctgcgaa      600

gtcacccatc agggcctgag ctcgcccgtc acaaagagct tcaacagggg agagtgt         657
```

+ADw-210+AD4- 278

+ADw-211+AD4- 1353
+ADw-212+AD4- ADN
+ADw-213+AD4- Secuencia artificial

+ADw-220+AD4-
+ADw-223+AD4- ADN de cadena pesada de CD19 (8B8-2B11)

+ADw-400+AD4- 278

caggtgcaat tggttcaatc tggtgctgaa gtaaaaaaac cgggcgcttc cgttaaagtg 60

agctgcaaag catctggtta caccttcact gactatatca tgcactgggt tcgtcaggcc 120

ccgggccagg gtctggagtg gatgggctac attaacccat acaacgacgg ttccaaatat 180

accgagaaat tccagggccg cgtcacgatg accagcgaca cttctatctc caccgcgtac 240

atggaactgt ctagactgcg ttctgacgac accgctgttt actattgtgc acgcggtacc 300

tactactacg gtccacagct gtttgattac tggggccaag gtaccacggt gaccgtaagc 360

tctgctagca ccaagggccc atcggtcttc cccctggcac cctcctccaa gagcacctct 420

gggggcacag cggccctggg ctgcctggtc aaggactact tccccgaacc ggtgacggtg 480

tcgtggaact caggcgccct gaccagcggc gtgcacacct tcccggctgt cctacagtcc 540

tcaggactct actccctcag cagcgtggtg accgtgccct ccagcagctt gggcacccag 600

acctacatct gcaacgtgaa tcacaagccc agcaacacca aggtggacaa gaaagttgag 660

cccaaatctt gtgacaaaac tcacacatgc ccaccgtgcc cagcacctga agctgcaggg 720

ggaccgtcag tcttcctctt cccccaaaa cccaaggaca ccctcatgat ctcccggacc 780

cctgaggtca catgcgtggt ggtggacgtg agccacgaag accctgaggt caagttcaac 840

tggtacgtgg acggcgtgga ggtgcataat gccaagacaa agccgcggga ggagcagtac 900

aacagcacgt accgtgtggt cagcgtcctc accgtcctgc accaggactg gctgaatggc 960

aaggagtaca agtgcaaggt ctccaacaaa gccctcggcg cccccatcga gaaaaccatc 1020

tccaaagcca aagggcagcc ccgagaacca caggtgtaca ccctgccccc atcccgggat 1080

gagctgacca agaaccaggt cagcctgacc tgcctggtca aaggcttcta tcccagcgac 1140

atcgccgtgg agtgggagag caatgggcag ccggagaaca actacaagac cacgcctccc 1200

gtgctggact ccgacggctc cttcttcctc tacagcaagc tcaccgtgga caagagcagg 1260

tggcagcagg ggaacgtctt ctcatgctcc gtgatgcatg aggctctgca caaccactac 1320

acgcagaaga gcctctccct gtctccgggt aaa 1353

+ADw-210+AD4- 279
+ADw-211+AD4- 219
+ADw-212+AD4- PRT
+ADw-213+AD4- Secuencia artificial

+ADw-220+AD4-
+ADw-223+AD4- cadena ligera de CD19 (8B8-2B11)

+ADw-400+AD4- 279

```
Asp Ile Val Met Thr Gln Thr Pro Leu Ser Leu Ser Val Thr Pro Gly
1               5                  10                  15

Gln Pro Ala Ser Ile Ser Cys Lys Ser Ser Gln Ser Leu Glu Thr Ser
            20                  25                  30

Thr Gly Thr Thr Tyr Leu Asn Trp Tyr Leu Gln Lys Pro Gly Gln Ser
        35                  40                  45

Pro Gln Leu Leu Ile Tyr Arg Val Ser Lys Arg Phe Ser Gly Val Pro
    50                  55                  60

Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile
65                  70                  75                  80

Ser Arg Val Glu Ala Glu Asp Val Gly Val Tyr Tyr Cys Leu Gln Leu
                85                  90                  95

Leu Glu Asp Pro Tyr Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys
            100                 105                 110

Arg Thr Val Ala Ala Pro Ser Val Phe Ile Phe Pro Pro Ser Asp Glu
        115                 120                 125

Gln Leu Lys Ser Gly Thr Ala Ser Val Val Cys Leu Leu Asn Asn Phe
    130                 135                 140

Tyr Pro Arg Glu Ala Lys Val Gln Trp Lys Val Asp Asn Ala Leu Gln
145                 150                 155                 160

Ser Gly Asn Ser Gln Glu Ser Val Thr Glu Gln Asp Ser Lys Asp Ser
                165                 170                 175

Thr Tyr Ser Leu Ser Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu
            180                 185                 190

Lys His Lys Val Tyr Ala Cys Glu Val Thr His Gln Gly Leu Ser Ser
        195                 200                 205

Pro Val Thr Lys Ser Phe Asn Arg Gly Glu Cys
    210                 215
```

+ADw-210+AD4- 280
+ADw-211+AD4- 451
+ADw-212+AD4- PRT
+ADw-213+AD4- Secuencia artificial

+ADw-220+AD4-
+ADw-223+AD4- cadena pesada de CD19 (8B8-2B11)

+ADw-400+AD4- 280

```
Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1               5                  10                  15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Asp Tyr
            20                  25                  30

Ile Met His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
        35                  40                  45

Gly Tyr Ile Asn Pro Tyr Asn Asp Gly Ser Lys Tyr Thr Glu Lys Phe
    50                  55                  60

Gln Gly Arg Val Thr Met Thr Ser Asp Thr Ser Ile Ser Thr Ala Tyr
65                  70                  75                  80

Met Glu Leu Ser Arg Leu Arg Ser Asp Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95

Ala Arg Gly Thr Tyr Tyr Tyr Gly Pro Gln Leu Phe Asp Tyr Trp Gly
            100                 105                 110

Gln Gly Thr Thr Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser
        115                 120                 125

Val Phe Pro Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala
    130                 135                 140

Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val
145                 150                 155                 160

Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala
                165                 170                 175

Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val
            180                 185                 190

Pro Ser Ser Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His
        195                 200                 205

Lys Pro Ser Asn Thr Lys Val Asp Lys Lys Val Glu Pro Lys Ser Cys
    210                 215                 220

Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Ala Ala Gly
225                 230                 235                 240
```

```
Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met
                245                 250                 255

Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His
            260                 265                 270

Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val
        275                 280                 285

His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr
    290                 295                 300

Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly
305                 310                 315                 320

Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Gly Ala Pro Ile
                325                 330                 335

Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val
            340                 345                 350

Tyr Thr Leu Pro Pro Ser Arg Asp Glu Leu Thr Lys Asn Gln Val Ser
        355                 360                 365

Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu
    370                 375                 380

Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro
385                 390                 395                 400

Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val
                405                 410                 415

Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met
            420                 425                 430

His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser
        435                 440                 445

Pro Gly Lys
    450


+ADw-210+AD4-  281
+ADw-211+AD4-  657
+ADw-212+AD4-  ADN
+ADw-213+AD4-  Secuencia artificial
```

+ADw-220+AD4-
+ADw-223+AD4- ADN de cadena ligera de CD19 (8B8-7H07)

+ADw-400+AD4- 281
gatattgtta tgactcaaac tccactgtct ctgtccgtga ccccgggtca gccagcgagc 60

atttcttgca aatccagcca atctctggaa acctccaccg gcaacacgta cctgaactgg 120

tatctccaga aaccgggtca gagcccgcag ctgctgatct accgtgtatc taagcgcttc 180

tccggcgttc ctgatcgttt cagcggttct ggatccggca ccgactttac tctgaaaatc 240

agccgtgtgg aagctgaaga cgttggcgtc tactattgtc tgcaggcaac ccatatccca 300

tacaccttcg gtcaaggaac taaactggaa attaaacgta cggtggctgc accatctgtc 360

ttcatcttcc cgccatctga tgagcagttg aaatctggaa ctgcctctgt tgtgtgcctg 420

ctgaataact tctatcccag agaggccaaa gtacagtgga aggtggataa cgccctccaa 480

tcgggtaact cccaggagag tgtcacagag caggacagca aggacagcac ctacagcctc 540

agcagcaccc tgacgctgag caaagcagac tacgagaaac acaaagtcta cgcctgcgaa 600

gtcacccatc agggcctgag ctcgcccgtc acaaagagct tcaacagggg agagtgt 657

+ADw-210+AD4- 282
+ADw-211+AD4- 1353
+ADw-212+AD4- ADN
+ADw-213+AD4- Secuencia artificial

+ADw-220+AD4-
+ADw-223+AD4- ADN de cadena pesada de CD19 (8B8-7H07)

+ADw-400+AD4- 282
caggtgcaat tggttcaatc tggtgctgaa gtaaaaaaac cgggcgcttc cgttaaagtg 60

agctgcaaag catctggtta caccttcact gactatatca tgcactgggt tcgtcaggcc 120

ccgggccagg gtctggagtg gatgggctac attaacccat acaacgacgg ttccaaatat 180

accgagaaat tccagggccg cgtcacgatg accagcgaca cttctatctc caccgcgtac 240

atggaactgt ctagactgcg ttctgacgac accgctgttt actattgtgc acgcggtacc 300

tactactacg gttctgaact gtttgattac tggggccaag gtaccacggt gaccgtaagc 360

tctgctagca ccaagggccc atcggtcttc cccctggcac cctcctccaa gagcacctct 420

gggggcacag cggccctggg ctgcctggtc aaggactact tccccgaacc ggtgacggtg 480

tcgtggaact caggcgccct gaccagcggc gtgcacacct tcccggctgt cctacagtcc 540

tcaggactct actccctcag cagcgtggtg accgtgccct ccagcagctt gggcacccag 600

acctacatct gcaacgtgaa tcacaagccc agcaacacca aggtggacaa gaaagttgag 660

cccaaatctt gtgacaaaac tcacacatgc ccaccgtgcc cagcacctga agctgcaggg 720

ggaccgtcag tcttcctctt cccccaaaa cccaaggaca ccctcatgat ctcccggacc 780

cctgaggtca catgcgtggt ggtggacgtg agccacgaag accctgaggt caagttcaac 840

tggtacgtgg acggcgtgga ggtgcataat gccaagacaa agccgcggga ggagcagtac 900

aacagcacgt accgtgtggt cagcgtcctc accgtcctgc accaggactg gctgaatggc 960

aaggagtaca agtgcaaggt ctccaacaaa gccctcggcg cccccatcga gaaaaccatc 1020

tccaaagcca aagggcagcc ccgagaacca caggtgtaca ccctgccccc atcccgggat 1080

gagctgacca agaaccaggt cagcctgacc tgcctggtca aaggcttcta tcccagcgac 1140

atcgccgtgg agtgggagag caatgggcag ccggagaaca actacaagac cacgcctccc 1200

gtgctggact ccgacggctc cttcttcctc tacagcaagc tcaccgtgga caagagcagg 1260

tggcagcagg ggaacgtctt ctcatgctcc gtgatgcatg aggctctgca caaccactac 1320

acgcagaaga gcctctccct gtctccgggt aaa 1353

+ADw-210+AD4- 283
+ADw-211+AD4- 219
+ADw-212+AD4- PRT
+ADw-213+AD4- Secuencia artificial

+ADw-220+AD4-
+ADw-223+AD4- cadena ligera de CD19 (8B8-7H07)

+ADw-400+AD4- 283

Asp Ile Val Met Thr Gln Thr Pro Leu Ser Leu Ser Val Thr Pro Gly
1 5 10 15

Gln Pro Ala Ser Ile Ser Cys Lys Ser Ser Gln Ser Leu Glu Thr Ser
20 25 30

Thr Gly Asn Thr Tyr Leu Asn Trp Tyr Leu Gln Lys Pro Gly Gln Ser
35 40 45

Pro Gln Leu Leu Ile Tyr Arg Val Ser Lys Arg Phe Ser Gly Val Pro
50 55 60

Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile
65 70 75 80

Ser Arg Val Glu Ala Glu Asp Val Gly Val Tyr Tyr Cys Leu Gln Ala
85 90 95

Thr His Ile Pro Tyr Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys
100 105 110

Arg Thr Val Ala Ala Pro Ser Val Phe Ile Phe Pro Pro Ser Asp Glu
115 120 125

Gln Leu Lys Ser Gly Thr Ala Ser Val Val Cys Leu Leu Asn Asn Phe

130 135 140

Tyr Pro Arg Glu Ala Lys Val Gln Trp Lys Val Asp Asn Ala Leu Gln
145 150 155 160

Ser Gly Asn Ser Gln Glu Ser Val Thr Glu Gln Asp Ser Lys Asp Ser
165 170 175

Thr Tyr Ser Leu Ser Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu
180 185 190

Lys His Lys Val Tyr Ala Cys Glu Val Thr His Gln Gly Leu Ser Ser
195 200 205

Pro Val Thr Lys Ser Phe Asn Arg Gly Glu Cys
210 215

+ADw-210+AD4- 284
+ADw-211+AD4- 451
+ADw-212+AD4- PRT
+ADw-213+AD4- Secuencia artificial

+ADw-220+AD4-
+ADw-223+AD4- cadena pesada de CD19 (8B8-7H07)

+ADw-400+AD4- 284

Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Asp Tyr
20 25 30

Ile Met His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
35 40 45

Gly Tyr Ile Asn Pro Tyr Asn Asp Gly Ser Lys Tyr Thr Glu Lys Phe
50 55 60

Gln Gly Arg Val Thr Met Thr Ser Asp Thr Ser Ile Ser Thr Ala Tyr
65 70 75 80

Met Glu Leu Ser Arg Leu Arg Ser Asp Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Gly Thr Tyr Tyr Tyr Gly Ser Glu Leu Phe Asp Tyr Trp Gly
100 105 110

Gln Gly Thr Thr Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser
115 120 125

```
Val Phe Pro Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala
    130                 135                 140

Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val
145                 150                 155                 160

Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala
                165                 170                 175

Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val
            180                 185                 190

Pro Ser Ser Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His
        195                 200                 205

Lys Pro Ser Asn Thr Lys Val Asp Lys Lys Val Glu Pro Lys Ser Cys
    210                 215                 220

Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Ala Ala Gly
225                 230                 235                 240

Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met
                245                 250                 255

Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His
            260                 265                 270

Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val
        275                 280                 285

His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr
    290                 295                 300

Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly
305                 310                 315                 320

Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Gly Ala Pro Ile
                325                 330                 335

Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val
            340                 345                 350

Tyr Thr Leu Pro Pro Ser Arg Asp Glu Leu Thr Lys Asn Gln Val Ser
        355                 360                 365

Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu
```

370 375 380

Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro
385 390 395 400

Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val
405 410 415

Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met
420 425 430

His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser
435 440 445

Pro Gly Lys
450

+ADw-210+AD4- 285
+ADw-211+AD4- 657
+ADw-212+AD4- ADN
+ADw-213+AD4- Secuencia artificial

+ADw-220+AD4-
+ADw-223+AD4- ADN de cadena ligera de CD19 (8B8-2B03)

+ADw-220+AD4-
+ADw-221+AD4- misc+AF8-feature
+ADw-222+AD4- (320)..(321)
+ADw-223+AD4- n es a, c, g, o t

+ADw-400+AD4- 285
gatattgtta tgactcaaac tccactgtct ctgtccgtga ccccgggtca gccagcgagc 60

atttcttgca aatccagcca atctctggaa acctccaccg gcaacacgta cctgaactgg 120

tatctccaga aaccgggtca gagcccgcag ctgctgatct accgtgtatc taagcgcttc 180

tccggcgttc ctgatcgttt cagcggttct ggatccggca ccgactttac tctgaaaatc 240

agccgtgtgg aagctgaaga cgttggcgtc tactattgtc tgcagttgac ccacgttccg 300

tacaccttcg gtcaaggaan naaactggaa attaaacgta cggtggctgc accatctgtc 360

ttcatcttcc cgccatctga tgagcagttg aaatctggaa ctgcctctgt tgtgtgcctg 420

ctgaataact tctatcccag agaggccaaa gtacagtgga aggtggataa cgccctccaa 480

tcgggtaact cccaggagag tgtcacagag caggacagca aggacagcac ctacagcctc 540

agcagcaccc tgacgctgag caaagcagac tacgagaaac acaaagtcta cgcctgcgaa 600

gtcacccatc agggcctgag ctcgcccgtc acaaagagct tcaacagggg agagtgt 657

+ADw-210+AD4- 286
+ADw-211+AD4- 1353

+ADw-212+AD4- ADN
+ADw-213+AD4- Secuencia artificial

+ADw-220+AD4-
+ADw-223+AD4- ADN de cadena pesada de CD19 (8B8-2B03)

+ADw-400+AD4- 286

caggtgcaat tggttcaatc tggtgctgaa gtaaaaaaac cgggcgcttc cgttaaagtg 60

agctgcaaag catctggtta caccttcact gactatatca cgcactgggt tcgtcaggcc 120

ccgggccagg gtctggagtg gatgggctac attaacccat acaacgacgg ttccaaatat 180

accgagaaat tccagggccg cgtcacgatg accagcgaca cttctatctc caccgcgtac 240

atggaactgt ctagactgcg ttctgacgac accgctgttt actattgtgc acgcggtacc 300

tactactacg gtccagatct gtttgattac tggggccaag gtaccacggt gaccgtaagc 360

tctgctagca ccaagggccc atcggtcttc cccctggcac cctcctccaa gagcacctct 420

gggggcacag cggccctggg ctgcctggtc aaggactact tccccgaacc ggtgacggtg 480

tcgtggaact caggcgccct gaccagcggc gtgcacacct tcccggctgt cctacagtcc 540

tcaggactct actccctcag cagcgtggtg accgtgccct ccagcagctt gggcacccag 600

acctacatct gcaacgtgaa tcacaagccc agcaacacca aggtggacaa gaaagttgag 660

cccaaatctt gtgacaaaac tcacacatgc ccaccgtgcc cagcacctga agctgcaggg 720

ggaccgtcag tcttcctctt cccccaaaa cccaaggaca ccctcatgat ctcccggacc 780

cctgaggtca catgcgtggt ggtggacgtg agccacgaag accctgaggt caagttcaac 840

tggtacgtgg acggcgtgga ggtgcataat gccaagacaa agccgcggga ggagcagtac 900

aacagcacgt accgtgtggt cagcgtcctc accgtcctgc accaggactg gctgaatggc 960

aaggagtaca agtgcaaggt ctccaacaaa gccctcggcg cccccatcga gaaaaccatc 1020

tccaaagcca aagggcagcc ccgagaacca caggtgtaca ccctgccccc atcccgggat 1080

gagctgacca agaaccaggt cagcctgacc tgcctggtca aaggcttcta tcccagcgac 1140

atcgccgtgg agtgggagag caatgggcag ccggagaaca actacaagac cacgcctccc 1200

gtgctggact ccgacggctc cttcttcctc tacagcaagc tcaccgtgga caagagcagg 1260

tggcagcagg ggaacgtctt ctcatgctcc gtgatgcatg aggctctgca caaccactac 1320

acgcagaaga gcctctccct gtctccgggt aaa 1353

+ADw-210+AD4- 287
+ADw-211+AD4- 219
+ADw-212+AD4- PRT
+ADw-213+AD4- Secuencia artificial

+ADw-220+AD4-
+ADw-223+AD4- cadena ligera de CD19 (8B8-2B03)

+ADw-220+AD4-
+ADw-221+AD4- misc+AF8-feature
+ADw-222+AD4- (107)..(107)
+ADw-223+AD4- Xaa puede ser cualquier amino+AOE-cido de origen natural

+ADw-400+AD4- 287

```
Asp Ile Val Met Thr Gln Thr Pro Leu Ser Leu Ser Val Thr Pro Gly
1               5                  10                  15

Gln Pro Ala Ser Ile Ser Cys Lys Ser Ser Gln Ser Leu Glu Thr Ser
            20                  25                  30

Thr Gly Asn Thr Tyr Leu Asn Trp Tyr Leu Gln Lys Pro Gly Gln Ser
        35                  40                  45

Pro Gln Leu Leu Ile Tyr Arg Val Ser Lys Arg Phe Ser Gly Val Pro
    50                  55                  60

Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile
65                  70                  75                  80

Ser Arg Val Glu Ala Glu Asp Val Gly Val Tyr Tyr Cys Leu Gln Leu
                85                  90                  95

Thr His Val Pro Tyr Thr Phe Gly Gln Gly Xaa Lys Leu Glu Ile Lys
            100                 105                 110

Arg Thr Val Ala Ala Pro Ser Val Phe Ile Phe Pro Pro Ser Asp Glu
        115                 120                 125

Gln Leu Lys Ser Gly Thr Ala Ser Val Val Cys Leu Leu Asn Asn Phe
    130                 135                 140

Tyr Pro Arg Glu Ala Lys Val Gln Trp Lys Val Asp Asn Ala Leu Gln
145                 150                 155                 160

Ser Gly Asn Ser Gln Glu Ser Val Thr Glu Gln Asp Ser Lys Asp Ser
                165                 170                 175

Thr Tyr Ser Leu Ser Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu
            180                 185                 190

Lys His Lys Val Tyr Ala Cys Glu Val Thr His Gln Gly Leu Ser Ser
        195                 200                 205

Pro Val Thr Lys Ser Phe Asn Arg Gly Glu Cys
    210                 215
```

+ADw-210+AD4- 288
+ADw-211+AD4- 451
+ADw-212+AD4- PRT
+ADw-213+AD4- Secuencia artificial

+ADw-220+AD4-
+ADw-223+AD4- cadena pesada de CD19 (8B8-2B03)

+ADw-400+AD4- 288

```
Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1               5                  10                  15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Asp Tyr
            20                  25                  30

Ile Thr His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
        35                  40                  45

Gly Tyr Ile Asn Pro Tyr Asn Asp Gly Ser Lys Tyr Thr Glu Lys Phe
    50                  55                  60

Gln Gly Arg Val Thr Met Thr Ser Asp Thr Ser Ile Ser Thr Ala Tyr
65                  70                  75                  80

Met Glu Leu Ser Arg Leu Arg Ser Asp Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95

Ala Arg Gly Thr Tyr Tyr Tyr Gly Pro Asp Leu Phe Asp Tyr Trp Gly
            100                 105                 110

Gln Gly Thr Thr Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser
        115                 120                 125

Val Phe Pro Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala
    130                 135                 140

Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val
145                 150                 155                 160

Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala
                165                 170                 175

Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val
            180                 185                 190

Pro Ser Ser Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His
        195                 200                 205

Lys Pro Ser Asn Thr Lys Val Asp Lys Lys Val Glu Pro Lys Ser Cys
```

```
    210                 215                 220

Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Ala Ala Gly
225                 230                 235                 240

Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met
                245                 250                 255

Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His
            260                 265                 270

Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val
        275                 280                 285

His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr
    290                 295                 300

Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly
305                 310                 315                 320

Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Gly Ala Pro Ile
                325                 330                 335

Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val
            340                 345                 350

Tyr Thr Leu Pro Pro Ser Arg Asp Glu Leu Thr Lys Asn Gln Val Ser
        355                 360                 365

Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu
    370                 375                 380

Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro
385                 390                 395                 400

Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val
                405                 410                 415

Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met
            420                 425                 430

His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser
        435                 440                 445

Pro Gly Lys
    450
```

+ADw-210+AD4- 289
+ADw-211+AD4- 657
+ADw-212+AD4- ADN
+ADw-213+AD4- Secuencia artificial

+ADw-220+AD4-
+ADw-223+AD4- ADN de cadena ligera de CD19 (8B8-5A07)

+ADw-400+AD4- 289
gatattgtta tgactcaaac tccactgtct ctgtccgtga ccccgggtca gccagcgagc 60

atttcttgca aatccagcca atctctggaa acctccaccg gcaacacgta cctgaactgg 120

tatctccaga aaccgggtca gagcccgcag ctgctgatct accgtgtatc taagcgcttc 180

tccggcgttc ctgatcgttt cagcggttct ggatccggca ccgactttac tctgaaaatc 240

agccgtgtgg aagctgaaga cgttggcgtc tactattgtc tgcagccagg tcattaccca 300

ggtaccttcg gtcaaggaac taaactggaa attaaacgta cggtggctgc accatctgtc 360

ttcatcttcc cgccatctga tgagcagttg aaatctggaa ctgcctctgt tgtgtgcctg 420

ctgaataact tctatcccag agaggccaaa gtacagtgga aggtggataa cgccctccaa 480

tcgggtaact cccaggagag tgtcacagag caggacagca aggacagcac ctacagcctc 540

agcagcaccc tgacgctgag caaagcagac tacgagaaac acaaagtcta cgcctgcgaa 600

gtcacccatc agggcctgag ctcgcccgtc acaaagagct tcaacagggg agagtgt 657

+ADw-210+AD4- 290
+ADw-211+AD4- 1353
+ADw-212+AD4- ADN
+ADw-213+AD4- Secuencia artificial

+ADw-220+AD4-
+ADw-223+AD4- ADN de cadena pesada de CD19 (8B8-5A07)

+ADw-400+AD4- 290
caggtgcaat tggttcaatc tggtgctgaa gtaaaaaaac cgggcgcttc cgttaaagtg 60

agctgcaaag catctggtta caccttcact gactatatca tgcactgggt tcgtcaggcc 120

ccgggccagg gtctggagtg gatgggctac attaacccat acaacgacgg ttccaaatat 180

accgagaaat tccagggccg cgtcacgatg accagcgaca cttctatctc caccgcgtac 240

atggaactgt ctagactgcg ttctgacgac accgctgttt actattgtgc acgcggtact 300

tactactacg gttccgccct ctttgattac tggggccaag gtaccacggt gaccgtaagc 360

tctgctagca ccaagggccc atcggtcttc cccctggcac cctcctccaa gagcacctct 420

gggggcacag cggccctggg ctgcctggtc aaggactact tccccgaacc ggtgacggtg 480

tcgtggaact caggcgccct gaccagcggc gtgcacacct tcccggctgt cctacagtcc 540

tcaggactct actccctcag cagcgtggtg accgtgccct ccagcagctt gggcacccag 600

acctacatct gcaacgtgaa tcacaagccc agcaacacca aggtggacaa gaaagttgag 660

```
cccaaatctt gtgacaaaac tcacacatgc ccaccgtgcc cagcacctga agctgcaggg      720

ggaccgtcag tcttcctctt ccccccaaaa cccaaggaca ccctcatgat ctcccggacc      780

cctgaggtca catgcgtggt ggtggacgtg agccacgaag accctgaggt caagttcaac      840

tggtacgtgg acggcgtgga ggtgcataat gccaagacaa agccgcggga ggagcagtac      900

aacagcacgt accgtgtggt cagcgtcctc accgtcctgc accaggactg gctgaatggc      960

aaggagtaca agtgcaaggt ctccaacaaa gccctcggcg cccccatcga gaaaaccatc     1020

tccaaagcca aagggcagcc ccgagaacca caggtgtaca ccctgccccc atcccgggat     1080

gagctgacca agaaccaggt cagcctgacc tgcctggtca aaggcttcta tcccagcgac     1140

atcgccgtgg agtgggagag caatgggcag ccggagaaca actacaagac cacgcctccc     1200

gtgctggact ccgacggctc cttcttcctc tacagcaagc tcaccgtgga caagagcagg     1260

tggcagcagg ggaacgtctt ctcatgctcc gtgatgcatg aggctctgca caaccactac     1320

acgcagaaga gcctctccct gtctccgggt aaa                                  1353


+ADw-210+AD4-  291
+ADw-211+AD4-  219
+ADw-212+AD4-  PRT
+ADw-213+AD4-  Secuencia artificial

+ADw-220+AD4-
+ADw-223+AD4-  cadena ligera de CD19 (8B8-5A07)

+ADw-400+AD4-  291

Asp Ile Val Met Thr Gln Thr Pro Leu Ser Leu Ser Val Thr Pro Gly
1               5                  10                  15


Gln Pro Ala Ser Ile Ser Cys Lys Ser Ser Gln Ser Leu Glu Thr Ser
            20                  25                  30


Thr Gly Asn Thr Tyr Leu Asn Trp Tyr Leu Gln Lys Pro Gly Gln Ser
        35                  40                  45


Pro Gln Leu Leu Ile Tyr Arg Val Ser Lys Arg Phe Ser Gly Val Pro
    50                  55                  60


Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile
65                  70                  75                  80


Ser Arg Val Glu Ala Glu Asp Val Gly Val Tyr Tyr Cys Leu Gln Pro
                85                  90                  95


Gly His Tyr Pro Gly Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys
            100                 105                 110
```

```
Arg Thr Val Ala Ala Pro Ser Val Phe Ile Phe Pro Pro Ser Asp Glu
        115                 120                 125


Gln Leu Lys Ser Gly Thr Ala Ser Val Val Cys Leu Leu Asn Asn Phe
    130                 135                 140


Tyr Pro Arg Glu Ala Lys Val Gln Trp Lys Val Asp Asn Ala Leu Gln
145                 150                 155                 160


Ser Gly Asn Ser Gln Glu Ser Val Thr Glu Gln Asp Ser Lys Asp Ser
                165                 170                 175


Thr Tyr Ser Leu Ser Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu
            180                 185                 190


Lys His Lys Val Tyr Ala Cys Glu Val Thr His Gln Gly Leu Ser Ser
        195                 200                 205


Pro Val Thr Lys Ser Phe Asn Arg Gly Glu Cys
    210                 215


+ADw-210+AD4-  292
+ADw-211+AD4-  451
+ADw-212+AD4-  PRT
+ADw-213+AD4-  Secuencia artificial

+ADw-220+AD4-
+ADw-223+AD4-  cadena pesada de CD19 (8B8-5A07)

+ADw-400+AD4-  292

Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1               5                   10                  15


Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Asp Tyr
            20                  25                  30


Ile Met His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
        35                  40                  45


Gly Tyr Ile Asn Pro Tyr Asn Asp Gly Ser Lys Tyr Thr Glu Lys Phe
    50                  55                  60


Gln Gly Arg Val Thr Met Thr Ser Asp Thr Ser Ile Ser Thr Ala Tyr
65                  70                  75                  80


Met Glu Leu Ser Arg Leu Arg Ser Asp Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95


Ala Arg Gly Thr Tyr Tyr Tyr Gly Ser Ala Leu Phe Asp Tyr Trp Gly
```

```
            100                 105                 110

Gln Gly Thr Thr Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser
        115                 120                 125

Val Phe Pro Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala
    130                 135                 140

Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val
145                 150                 155                 160

Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala
                165                 170                 175

Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val
            180                 185                 190

Pro Ser Ser Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His
        195                 200                 205

Lys Pro Ser Asn Thr Lys Val Asp Lys Lys Val Glu Pro Lys Ser Cys
    210                 215                 220

Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Ala Ala Gly
225                 230                 235                 240

Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met
                245                 250                 255

Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His
            260                 265                 270

Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val
        275                 280                 285

His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr
    290                 295                 300

Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly
305                 310                 315                 320

Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Gly Ala Pro Ile
                325                 330                 335

Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val
            340                 345                 350
```

Tyr Thr Leu Pro Pro Ser Arg Asp Glu Leu Thr Lys Asn Gln Val Ser
355 360 365

Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu
370 375 380

Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro
385 390 395 400

Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val
405 410 415

Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met
420 425 430

His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser
435 440 445

Pro Gly Lys
450

+ADw-210+AD4- 293
+ADw-211+AD4- 657
+ADw-212+AD4- ADN
+ADw-213+AD4- Secuencia artificial

+ADw-220+AD4-
+ADw-223+AD4- ADN de cadena ligera de CD19 (8B8-5D08)

+ADw-400+AD4- 293
gatattgtta tgactcaaac tccactgtct ctgtccgtga ccccgggtca gccagcgagc 60

atttcttgca aatccagcca atctctggaa acctccaccg gcaacacgta cctgaactgg 120

tatctccaga aaccgggtca gagcccgcag ctgctgatct accgtgtatc taagcgcttc 180

tccggcgttc ctgatcgttt cagcggttct ggatccggca ccgactttac tctgaaaatc 240

agccgtgtgg aagctgaaga cgttggcgtc tactattgtc tgcagctgac ccatgaacca 300

tacaccttcg gtcaaggaac taaactggaa attaaacgta cggtggctgc accatctgtc 360

ttcatcttcc cgccatctga tgagcagttg aaatctggaa ctgcctctgt tgtgtgcctg 420

ctgaataact tctatcccag agaggccaaa gtacagtgga aggtggataa cgccctccaa 480

tcgggtaact cccaggagag tgtcacagag caggacagca aggacagcac ctacagcctc 540

agcagcaccc tgacgctgag caaagcagac tacgagaaac acaaagtcta cgcctgcgaa 600

gtcacccatc agggcctgag ctcgcccgtc acaaagagct tcaacagggg agagtgt 657

+ADw-210+AD4- 294
+ADw-211+AD4- 1353
+ADw-212+AD4- ADN

+ADw-213+AD4- Secuencia artificial

+ADw-220+AD4-
+ADw-223+AD4- ADN de cadena pesada de CD19 (8B8-5D08)

+ADw-400+AD4- 294
caggtgcaat tggttcaatc tggtgctgaa gtaaaaaaac cgggcgcttc cgttaaagtg 60

agctgcaaag catctggtta caccttcact gactatatca tgcactgggt tcgtcaggcc 120

ccgggccagg gtctggagtg gatgggctac attaacccat acaacgacgg ttccaaatat 180

accgagaaat tccagggccg cgtcacgatg accagcgaca cttctatctc caccgcgtac 240

atggaactgt ctagactgcg ttctgacgac accgctgttt actattgtgc acgcggtacc 300

tactactacg gttctgaact gtttgattac tggggccaag gtaccacggt gaccgtaagc 360

tctgctagca ccaagggccc atcggtcttc cccctggcac cctcctccaa gagcacctct 420

gggggcacag cggccctggg ctgcctggtc aaggactact tccccgaacc ggtgacggtg 480

tcgtggaact caggcgccct gaccagcggc gtgcacacct tcccggctgt cctacagtcc 540

tcaggactct actccctcag cagcgtggtg accgtgccct ccagcagctt gggcacccag 600

acctacatct gcaacgtgaa tcacaagccc agcaacacca aggtggacaa gaaagttgag 660

cccaaatctt gtgacaaaac tcacacatgc ccaccgtgcc cagcacctga agctgcaggg 720

ggaccgtcag tcttcctctt cccccaaaa cccaaggaca ccctcatgat ctcccggacc 780

cctgaggtca catgcgtggt ggtggacgtg agccacgaag accctgaggt caagttcaac 840

tggtacgtgg acggcgtgga ggtgcataat gccaagacaa agccgcggga ggagcagtac 900

aacagcacgt accgtgtggt cagcgtcctc accgtcctgc accaggactg gctgaatggc 960

aaggagtaca agtgcaaggt ctccaacaaa gccctcggcg cccccatcga gaaaaccatc 1020

tccaaagcca aagggcagcc ccgagaacca caggtgtaca ccctgccccc atcccgggat 1080

gagctgacca agaaccaggt cagcctgacc tgcctggtca aaggcttcta tcccagcgac 1140

atcgccgtgg agtgggagag caatgggcag ccggagaaca actacaagac cacgcctccc 1200

gtgctggact ccgacggctc cttcttcctc tacagcaagc tcaccgtgga caagagcagg 1260

tggcagcagg ggaacgtctt ctcatgctcc gtgatgcatg aggctctgca caaccactac 1320

acgcagaaga gcctctccct gtctccgggt aaa 1353

+ADw-210+AD4- 295
+ADw-211+AD4- 219
+ADw-212+AD4- PRT
+ADw-213+AD4- Secuencia artificial

+ADw-220+AD4-
+ADw-223+AD4- cadena ligera de CD19 (8B8-5D08)

+ADw-400+AD4- 295

```
Asp Ile Val Met Thr Gln Thr Pro Leu Ser Leu Ser Val Thr Pro Gly
1               5                  10                  15

Gln Pro Ala Ser Ile Ser Cys Lys Ser Ser Gln Ser Leu Glu Thr Ser
            20                  25                  30

Thr Gly Asn Thr Tyr Leu Asn Trp Tyr Leu Gln Lys Pro Gly Gln Ser
        35                  40                  45

Pro Gln Leu Leu Ile Tyr Arg Val Ser Lys Arg Phe Ser Gly Val Pro
    50                  55                  60

Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile
65                  70                  75                  80

Ser Arg Val Glu Ala Glu Asp Val Gly Val Tyr Tyr Cys Leu Gln Leu
                85                  90                  95

Thr His Glu Pro Tyr Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys
            100                 105                 110

Arg Thr Val Ala Ala Pro Ser Val Phe Ile Phe Pro Pro Ser Asp Glu
        115                 120                 125

Gln Leu Lys Ser Gly Thr Ala Ser Val Val Cys Leu Leu Asn Asn Phe
    130                 135                 140

Tyr Pro Arg Glu Ala Lys Val Gln Trp Lys Val Asp Asn Ala Leu Gln
145                 150                 155                 160

Ser Gly Asn Ser Gln Glu Ser Val Thr Glu Gln Asp Ser Lys Asp Ser
                165                 170                 175

Thr Tyr Ser Leu Ser Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu
            180                 185                 190

Lys His Lys Val Tyr Ala Cys Glu Val Thr His Gln Gly Leu Ser Ser
        195                 200                 205

Pro Val Thr Lys Ser Phe Asn Arg Gly Glu Cys
    210                 215
```

+ADw-210+AD4- 296
+ADw-211+AD4- 451
+ADw-212+AD4- PRT
+ADw-213+AD4- Secuencia artificial

+ADw-220+AD4-
+ADw-223+AD4- cadena pesada de CD19 (8B8-5D08)

+ADw-400+AD4- 296

```
Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1               5                   10                  15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Asp Tyr
            20                  25                  30

Ile Met His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
        35                  40                  45

Gly Tyr Ile Asn Pro Tyr Asn Asp Gly Ser Lys Tyr Thr Glu Lys Phe
    50                  55                  60

Gln Gly Arg Val Thr Met Thr Ser Asp Thr Ser Ile Ser Thr Ala Tyr
65                  70                  75                  80

Met Glu Leu Ser Arg Leu Arg Ser Asp Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95

Ala Arg Gly Thr Tyr Tyr Tyr Gly Ser Glu Leu Phe Asp Tyr Trp Gly
            100                 105                 110

Gln Gly Thr Thr Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser
        115                 120                 125

Val Phe Pro Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala
    130                 135                 140

Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val
145                 150                 155                 160

Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala
                165                 170                 175

Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val
            180                 185                 190

Pro Ser Ser Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His
        195                 200                 205

Lys Pro Ser Asn Thr Lys Val Asp Lys Lys Val Glu Pro Lys Ser Cys
    210                 215                 220

Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Ala Ala Gly
225                 230                 235                 240
```

```
Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met
                245                 250                 255

Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His
            260                 265                 270

Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val
        275                 280                 285

His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr
    290                 295                 300

Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly
305                 310                 315                 320

Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Gly Ala Pro Ile
                325                 330                 335

Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val
            340                 345                 350

Tyr Thr Leu Pro Pro Ser Arg Asp Glu Leu Thr Lys Asn Gln Val Ser
        355                 360                 365

Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu
    370                 375                 380

Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro
385                 390                 395                 400

Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val
                405                 410                 415

Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met
            420                 425                 430

His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser
        435                 440                 445

Pro Gly Lys
    450
```

+ADw-210+AD4- 297
+ADw-211+AD4- 657
+ADw-212+AD4- ADN
+ADw-213+AD4- Secuencia artificial

+ADw-220+AD4-
+ADw-223+AD4- ADN de cadena ligera de CD19 (8B8-5B08)

+ADw-400+AD4- 297
gatattgtta tgactcaaac tccactgtct ctgtccgtga ccccgggtca gccagcgagc 60

atttcttgca aatccagcca atctctggaa acctccaccg gcaacacgta cctgaactgg 120

tatctccaga aaccgggtca gagcccgcag ctgctgatct accgtgtatc taagcgcttc 180

tccggcgttc ctgatcgttt cagcggttct ggatccggca ccgactttac tctgaaaatc 240

agccgtgtgg aagctgaaga cgttggcgtc tactattgtc tgcagctgga ttcttaccca 300

aacaccttcg gtcaaggaac taaactggaa attaaacgta cggtggctgc accatctgtc 360

ttcatcttcc cgccatctga tgagcagttg aaatctggaa ctgcctctgt tgtgtgcctg 420

ctgaataact tctatcccag agaggccaaa gtacagtgga aggtggataa cgccctccaa 480

tcgggtaact cccaggagag tgtcacagag caggacagca aggacagcac ctacagcctc 540

agcagcaccc tgacgctgag caaagcagac tacgagaaac acaaagtcta cgcctgcgaa 600

gtcacccatc agggcctgag ctcgcccgtc acaaagagct tcaacagggg agagtgt 657

+ADw-210+AD4- 298
+ADw-211+AD4- 1353
+ADw-212+AD4- ADN
+ADw-213+AD4- Secuencia artificial

+ADw-220+AD4-
+ADw-223+AD4- ADN de cadena pesada de CD19 (8B8-5B08)

+ADw-400+AD4- 298
caggtgcaat tggttcaatc tggtgctgaa gtaaaaaaac cgggcgcttc cgttaaagtg 60

agctgcaaag catctggtta caccttcact gactatatca tgcactgggt tcgtcaggcc 120

ccgggccagg gtctggagtg gatgggctac attaacccat acaacgacgg ttccaaatat 180

accgagaaat tccagggccg cgtcacgatg accagcgaca cttctatctc caccgcgtac 240

atggaactgt ctagactgcg ttctgacgac accgctgttt actattgtgc acgcggtacc 300

tactactacg gtccacagct gtttgattac tggggccaag gtaccacggt gaccgtaagc 360

tctgctagca ccaagggccc atcggtcttc cccctggcac cctcctccaa gagcacctct 420

gggggcacag cggccctggg ctgcctggtc aaggactact tccccgaacc ggtgacggtg 480

tcgtggaact caggcgccct gaccagcggc gtgcacacct tcccggctgt cctacagtcc 540

tcaggactct actccctcag cagcgtggtg accgtgccct ccagcagctt gggcacccag 600

acctacatct gcaacgtgaa tcacaagccc agcaacacca aggtggacaa gaaagttgag 660

cccaaatctt gtgacaaaac tcacacatgc ccaccgtgcc cagcacctga agctgcaggg 720

ggaccgtcag tcttcctctt ccccccaaaa cccaaggaca ccctcatgat ctcccggacc 780

cctgaggtca catgcgtggt ggtggacgtg agccacgaag accctgaggt caagttcaac 840

tggtacgtgg acggcgtgga ggtgcataat gccaagacaa agccgcggga ggagcagtac 900

aacagcacgt accgtgtggt cagcgtcctc accgtcctgc accaggactg gctgaatggc 960

aaggagtaca agtgcaaggt ctccaacaaa gccctcggcg cccccatcga gaaaaccatc 1020

tccaaagcca aagggcagcc ccgagaacca caggtgtaca ccctgccccc atcccgggat 1080

gagctgacca agaaccaggt cagcctgacc tgcctggtca aaggcttcta tcccagcgac 1140

atcgccgtgg agtgggagag caatgggcag ccggagaaca actacaagac cacgcctccc 1200

gtgctggact ccgacggctc cttcttcctc tacagcaagc tcaccgtgga caagagcagg 1260

tggcagcagg ggaacgtctt ctcatgctcc gtgatgcatg aggctctgca caaccactac 1320

acgcagaaga gcctctccct gtctccgggt aaa 1353

+ADw-210+AD4- 299
+ADw-211+AD4- 219
+ADw-212+AD4- PRT
+ADw-213+AD4- Secuencia artificial

+ADw-220+AD4-
+ADw-223+AD4- cadena ligera de CD19 (8B8-5B08)

+ADw-400+AD4- 299

Asp Ile Val Met Thr Gln Thr Pro Leu Ser Leu Ser Val Thr Pro Gly
1 5 10 15

Gln Pro Ala Ser Ile Ser Cys Lys Ser Ser Gln Ser Leu Glu Thr Ser
20 25 30

Thr Gly Asn Thr Tyr Leu Asn Trp Tyr Leu Gln Lys Pro Gly Gln Ser
35 40 45

Pro Gln Leu Leu Ile Tyr Arg Val Ser Lys Arg Phe Ser Gly Val Pro
50 55 60

Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile
65 70 75 80

Ser Arg Val Glu Ala Glu Asp Val Gly Val Tyr Tyr Cys Leu Gln Leu
85 90 95

Asp Ser Tyr Pro Asn Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys
100 105 110

Arg Thr Val Ala Ala Pro Ser Val Phe Ile Phe Pro Pro Ser Asp Glu
115 120 125

Gln Leu Lys Ser Gly Thr Ala Ser Val Val Cys Leu Leu Asn Asn Phe
130 135 140

```
Tyr Pro Arg Glu Ala Lys Val Gln Trp Lys Val Asp Asn Ala Leu Gln
145                 150                 155                 160


Ser Gly Asn Ser Gln Glu Ser Val Thr Glu Gln Asp Ser Lys Asp Ser
                165                 170                 175


Thr Tyr Ser Leu Ser Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu
            180                 185                 190


Lys His Lys Val Tyr Ala Cys Glu Val Thr His Gln Gly Leu Ser Ser
        195                 200                 205


Pro Val Thr Lys Ser Phe Asn Arg Gly Glu Cys
    210                 215


+ADw-210+AD4-  300
+ADw-211+AD4-  451
+ADw-212+AD4-  PRT
+ADw-213+AD4-  Secuencia artificial

+ADw-220+AD4-
+ADw-223+AD4-  cadena pesada de CD19 (8B8-5B08)

+ADw-400+AD4-  300

Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1               5                   10                  15


Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Asp Tyr
            20                  25                  30


Ile Met His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
        35                  40                  45


Gly Tyr Ile Asn Pro Tyr Asn Asp Gly Ser Lys Tyr Thr Glu Lys Phe
    50                  55                  60


Gln Gly Arg Val Thr Met Thr Ser Asp Thr Ser Ile Ser Thr Ala Tyr
65                  70                  75                  80


Met Glu Leu Ser Arg Leu Arg Ser Asp Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95


Ala Arg Gly Thr Tyr Tyr Tyr Gly Pro Gln Leu Phe Asp Tyr Trp Gly
            100                 105                 110


Gln Gly Thr Thr Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser
        115                 120                 125
```

```
Val Phe Pro Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala
    130                 135                 140

Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val
145                 150                 155                 160

Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala
                165                 170                 175

Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val
            180                 185                 190

Pro Ser Ser Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His
        195                 200                 205

Lys Pro Ser Asn Thr Lys Val Asp Lys Lys Val Glu Pro Lys Ser Cys
    210                 215                 220

Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Ala Ala Gly
225                 230                 235                 240

Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met
                245                 250                 255

Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His
            260                 265                 270

Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val
        275                 280                 285

His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr
    290                 295                 300

Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly
305                 310                 315                 320

Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Gly Ala Pro Ile
                325                 330                 335

Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val
            340                 345                 350

Tyr Thr Leu Pro Pro Ser Arg Asp Glu Leu Thr Lys Asn Gln Val Ser
        355                 360                 365

Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu
    370                 375                 380
```

Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro
385 390 395 400

Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val
405 410 415

Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met
420 425 430

His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser
435 440 445

Pro Gly Lys
450

+ADw-210+AD4- 301
+ADw-211+AD4- 657
+ADw-212+AD4- ADN
+ADw-213+AD4- Secuencia artificial

+ADw-220+AD4-
+ADw-223+AD4- ADN de cadena ligera de CD19 (8B8-5H09)

+ADw-400+AD4- 301
gatattgtta tgactcaaac tccactgtct ctgtccgtga ccccgggtca gccagcgagc 60

atttcttgca aatccagcca atctctggaa tcttccaccg gcaacacgta cctgaactgg 120

tatctccaga aaccgggtca gagcccgcag ctgctgatct accgtgtatc taagcgcttc 180

tccggcgttc ctgatcgttt cagcggttct ggatccggca ccgactttac tctgaaaatc 240

agccgtgtgg aagctgaaga cgttggcgtc tactattgtc tgcagctgat cgattaccca 300

gttaccttcg gtcaaggaac taaactggaa attaaacgta cggtggctgc accatctgtc 360

ttcatcttcc cgccatctga tgagcagttg aaatctggaa ctgcctctgt tgtgtgcctg 420

ctgaataact tctatcccag agaggccaaa gtacagtgga aggtggataa cgccctccaa 480

tcgggtaact cccaggagag tgtcacagag caggacagca aggacagcac ctacagcctc 540

agcagcaccc tgacgctgag caaagcagac tacgagaaac acaaagtcta cgcctgcgaa 600

gtcacccatc agggcctgag ctcgcccgtc acaaagagct tcaacagggg agagtgt 657

+ADw-210+AD4- 302
+ADw-211+AD4- 1353
+ADw-212+AD4- ADN
+ADw-213+AD4- Secuencia artificial

+ADw-220+AD4-
+ADw-223+AD4- ADN de cadena pesada de CD19 (8B8-5H09)

+ADw-400+AD4- 302
caggtgcaat tggttcaatc tggtgctgaa gtaaaaaaac cgggcgcttc cgttaaagtg 60

agctgcaaag catctggtta caccttcact gactatatca tgcactgggt tcgtcaggcc 120

ccgggccagg gtctggagtg gatgggctac attaacccat acaacgacgg ttccaaatat 180

accgagaaat tccagggccg cgtcacgatg accagcgaca cttctatctc caccgcgtac 240

atggaactgt ctagactgcg ttctgacgac accgctgttt actattgtgc acgcggtacc 300

tactactacg gttctgcact gtttgattac tggggccaag gtaccacggt gaccgtaagc 360

tctgctagca ccaagggccc atcggtcttc cccctggcac cctcctccaa gagcacctct 420

gggggcacag cggccctggg ctgcctggtc aaggactact tccccgaacc ggtgacggtg 480

tcgtggaact caggcgccct gaccagcggc gtgcacacct tcccggctgt cctacagtcc 540

tcaggactct actccctcag cagcgtggtg accgtgccct ccagcagctt gggcacccag 600

acctacatct gcaacgtgaa tcacaagccc agcaacacca aggtggacaa gaaagttgag 660

cccaaatctt gtgacaaaac tcacacatgc ccaccgtgcc cagcacctga agctgcaggg 720

ggaccgtcag tcttcctctt cccccaaaa cccaaggaca ccctcatgat ctcccggacc 780

cctgaggtca catgcgtggt ggtggacgtg agccacgaag accctgaggt caagttcaac 840

tggtacgtgg acggcgtgga ggtgcataat gccaagacaa agccgcggga ggagcagtac 900

aacagcacgt accgtgtggt cagcgtcctc accgtcctgc accaggactg gctgaatggc 960

aaggagtaca agtgcaaggt ctccaacaaa gccctcggcg cccccatcga gaaaaccatc 1020

tccaaagcca aagggcagcc ccgagaacca caggtgtaca ccctgccccc atcccgggat 1080

gagctgacca agaaccaggt cagcctgacc tgcctggtca aaggcttcta tcccagcgac 1140

atcgccgtgg agtgggagag caatgggcag ccggagaaca actacaagac cacgcctccc 1200

gtgctggact ccgacggctc cttcttcctc tacagcaagc tcaccgtgga caagagcagg 1260

tggcagcagg ggaacgtctt ctcatgctcc gtgatgcatg aggctctgca caaccactac 1320

acgcagaaga gcctctccct gtctccgggt aaa 1353

+ADw-210+AD4- 303
+ADw-211+AD4- 219
+ADw-212+AD4- PRT
+ADw-213+AD4- Secuencia artificial

+ADw-220+AD4-
+ADw-223+AD4- cadena ligera de CD19 (8B8-5H09)

+ADw-400+AD4- 303

Asp Ile Val Met Thr Gln Thr Pro Leu Ser Leu Ser Val Thr Pro Gly
1 5 10 15

Gln Pro Ala Ser Ile Ser Cys Lys Ser Ser Gln Ser Leu Glu Ser Ser
20 25 30

```
Thr Gly Asn Thr Tyr Leu Asn Trp Tyr Leu Gln Lys Pro Gly Gln Ser
        35                  40                  45

Pro Gln Leu Leu Ile Tyr Arg Val Ser Lys Arg Phe Ser Gly Val Pro
    50                  55                  60

Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile
65                  70                  75                  80

Ser Arg Val Glu Ala Glu Asp Val Gly Val Tyr Tyr Cys Leu Gln Leu
                85                  90                  95

Ile Asp Tyr Pro Val Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys
            100                 105                 110

Arg Thr Val Ala Ala Pro Ser Val Phe Ile Phe Pro Pro Ser Asp Glu
        115                 120                 125

Gln Leu Lys Ser Gly Thr Ala Ser Val Val Cys Leu Leu Asn Asn Phe
    130                 135                 140

Tyr Pro Arg Glu Ala Lys Val Gln Trp Lys Val Asp Asn Ala Leu Gln
145                 150                 155                 160

Ser Gly Asn Ser Gln Glu Ser Val Thr Glu Gln Asp Ser Lys Asp Ser
                165                 170                 175

Thr Tyr Ser Leu Ser Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu
            180                 185                 190

Lys His Lys Val Tyr Ala Cys Glu Val Thr His Gln Gly Leu Ser Ser
        195                 200                 205

Pro Val Thr Lys Ser Phe Asn Arg Gly Glu Cys
    210                 215


+ADw-210+AD4-  304
+ADw-211+AD4-  451
+ADw-212+AD4-  PRT
+ADw-213+AD4-  Secuencia artificial

+ADw-220+AD4-
+ADw-223+AD4-  cadena pesada de CD19 (8B8-5H09)

+ADw-400+AD4-  304

Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1               5                   10                  15
```

```
Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Asp Tyr
            20                  25                  30

Ile Met His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
        35                  40                  45

Gly Tyr Ile Asn Pro Tyr Asn Asp Gly Ser Lys Tyr Thr Glu Lys Phe
    50                  55                  60

Gln Gly Arg Val Thr Met Thr Ser Asp Thr Ser Ile Ser Thr Ala Tyr
65                  70                  75                  80

Met Glu Leu Ser Arg Leu Arg Ser Asp Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95

Ala Arg Gly Thr Tyr Tyr Tyr Gly Ser Ala Leu Phe Asp Tyr Trp Gly
            100                 105                 110

Gln Gly Thr Thr Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser
        115                 120                 125

Val Phe Pro Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala
    130                 135                 140

Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val
145                 150                 155                 160

Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala
                165                 170                 175

Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val
            180                 185                 190

Pro Ser Ser Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His
        195                 200                 205

Lys Pro Ser Asn Thr Lys Val Asp Lys Lys Val Glu Pro Lys Ser Cys
    210                 215                 220

Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Ala Ala Gly
225                 230                 235                 240

Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met
                245                 250                 255

Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His
            260                 265                 270
```

Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val
275 280 285

His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr
290 295 300

Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly
305 310 315 320

Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Gly Ala Pro Ile
325 330 335

Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val
340 345 350

Tyr Thr Leu Pro Pro Ser Arg Asp Glu Leu Thr Lys Asn Gln Val Ser
355 360 365

Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu
370 375 380

Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro
385 390 395 400

Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val
405 410 415

Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met
420 425 430

His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser
435 440 445

Pro Gly Lys
450

+ADw-210+AD4- 305
+ADw-211+AD4- 1353
+ADw-212+AD4- ADN
+ADw-213+AD4- Secuencia artificial

+ADw-220+AD4-
+ADw-223+AD4- ADN de cadena Fc agujero de CD19(8B8-2B11)

+ADw-400+AD4- 305
caggtgcaat tggttcaatc tggtgctgaa gtaaaaaaac cgggcgcttc cgttaaagtg 60

agctgcaaag catctggtta caccttcact gactatatca tgcactgggt tcgtcaggcc 120

ccgggccagg gtctggagtg gatgggctac attaacccat acaacgacgg ttccaaatat 180

```
accgagaaat tccagggccg cgtcacgatg accagcgaca cttctatctc caccgcgtac      240

atggaactgt ctagactgcg ttctgacgac accgctgttt actattgtgc acgcggtacc      300

tactactacg gtccacagct gtttgattac tggggccaag gtaccacggt gaccgtaagc      360

tctgctagca ccaagggccc ctccgtgttc cccctggccc ccagcagcaa gagcaccagc      420

ggcggcacag ccgctctggg ctgcctggtc aaggactact tccccgagcc cgtgaccgtg      480

tcctggaaca gcggagccct gacctccggc gtgcacacct tccccgccgt gctgcagagt      540

tctggcctgt atagcctgag cagcgtggtc accgtgcctt ctagcagcct gggcacccag      600

acctacatct gcaacgtgaa ccacaagccc agcaacacca aggtggacaa gaaggtggag      660

cccaagagct gcgacaaaac tcacacatgc ccaccgtgcc cagcacctga agctgcaggg      720

ggaccgtcag tcttcctctt ccccccaaaa cccaaggaca ccctcatgat ctcccggacc      780

cctgaggtca catgcgtggt ggtggacgtg agccacgaag accctgaggt caagttcaac      840

tggtacgtgg acggcgtgga ggtgcataat gccaagacaa agccgcggga ggagcagtac      900

aacagcacgt accgtgtggt cagcgtcctc accgtcctgc accaggactg gctgaatggc      960

aaggagtaca agtgcaaggt ctccaacaaa gccctcggcg cccccatcga gaaaaccatc     1020

tccaaagcca aagggcagcc ccgagaacca caggtgtgca ccctgccccc atcccgggat     1080

gagctgacca agaaccaggt cagcctctcg tgcgcagtca aaggcttcta tcccagcgac     1140

atcgccgtgg agtgggagag caatgggcag ccggagaaca actacaagac cacgcctccc     1200

gtgctggact ccgacggctc cttcttcctc gtgagcaagc tcaccgtgga caagagcagg     1260

tggcagcagg ggaacgtctt ctcatgctcc gtgatgcatg aggctctgca caaccactac     1320

acgcagaaga gcctctccct gtctccgggt aaa                                  1353


+ADw-210+AD4-  306
+ADw-211+AD4-  451
+ADw-212+AD4-  PRT
+ADw-213+AD4-  Secuencia artificial

+ADw-220+AD4-
+ADw-223+AD4-  cadena Fc agujero de CD19(8B8-2B11)

+ADw-400+AD4-  306

Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1               5                  10                  15


Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Asp Tyr
            20                  25                  30


Ile Met His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
        35                  40                  45
```

```
Gly Tyr Ile Asn Pro Tyr Asn Asp Gly Ser Lys Tyr Thr Glu Lys Phe
    50                  55                  60

Gln Gly Arg Val Thr Met Thr Ser Asp Thr Ser Ile Ser Thr Ala Tyr
65                  70                  75                  80

Met Glu Leu Ser Arg Leu Arg Ser Asp Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95

Ala Arg Gly Thr Tyr Tyr Tyr Gly Pro Gln Leu Phe Asp Tyr Trp Gly
            100                 105                 110

Gln Gly Thr Thr Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser
        115                 120                 125

Val Phe Pro Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala
    130                 135                 140

Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val
145                 150                 155                 160

Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala
                165                 170                 175

Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val
            180                 185                 190

Pro Ser Ser Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His
        195                 200                 205

Lys Pro Ser Asn Thr Lys Val Asp Lys Lys Val Glu Pro Lys Ser Cys
    210                 215                 220

Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Ala Ala Gly
225                 230                 235                 240

Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met
                245                 250                 255

Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His
            260                 265                 270

Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val
        275                 280                 285

His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr
    290                 295                 300
```

Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly
305 310 315 320

Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Gly Ala Pro Ile
325 330 335

Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val
340 345 350

Cys Thr Leu Pro Pro Ser Arg Asp Glu Leu Thr Lys Asn Gln Val Ser
355 360 365

Leu Ser Cys Ala Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu
370 375 380

Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro
385 390 395 400

Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Val Ser Lys Leu Thr Val
405 410 415

Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met
420 425 430

His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser
435 440 445

Pro Gly Lys
450

+ADw-210+AD4- 307
+ADw-211+AD4- 2514
+ADw-212+AD4- ADN
+ADw-213+AD4- Secuencia artificial

+ADw-220+AD4-
+ADw-223+AD4- ADN de cadena de ligando dim+AOk-rico de Fc agujero de CD19(8B8-2B11)

+ADw-400+AD4- 307
caggtgcaat tggttcaatc tggtgctgaa gtaaaaaaac cgggcgcttc cgttaaagtg 60

agctgcaaag catctggtta caccttcact gactatatca tgcactgggt tcgtcaggcc 120

ccgggccagg gtctggagtg gatgggctac attaacccat acaacgacgg ttccaaatat 180

accgagaaat tccagggccg cgtcacgatg accagcgaca cttctatctc caccgcgtac 240

atggaactgt ctagactgcg ttctgacgac accgctgttt actattgtgc acgcggtacc 300

tactactacg gtccacagct gtttgattac tggggccaag gtaccacggt gaccgtaagc 360

tctgctagca ccaagggccc ctccgtgttc cccctggccc ccagcagcaa gagcaccagc 420

ggcggcacag ccgctctggg ctgcctggtc aaggactact tccccgagcc cgtgaccgtg 480

tcctggaaca gcggagccct gacctccggc gtgcacacct tccccgccgt gctgcagagt 540

tctggcctgt atagcctgag cagcgtggtc accgtgcctt ctagcagcct gggcacccag 600

acctacatct gcaacgtgaa ccacaagccc agcaacacca aggtggacaa gaaggtggag 660

cccaagagct gcgacaaaac tcacacatgc ccaccgtgcc cagcacctga agctgcaggg 720

ggaccgtcag tcttcctctt cccccaaaa cccaaggaca ccctcatgat ctcccggacc 780

cctgaggtca catgcgtggt ggtggacgtg agccacgaag accctgaggt caagttcaac 840

tggtacgtgg acggcgtgga ggtgcataat gccaagacaa agccgcggga ggagcagtac 900

aacagcacgt accgtgtggt cagcgtcctc accgtcctgc accaggactg gctgaatggc 960

aaggagtaca agtgcaaggt ctccaacaaa gccctcggcg cccccatcga gaaaaccatc 1020

tccaaagcca aagggcagcc ccgagaacca caggtgtgca ccctgccccc atcccgggat 1080

gagctgacca agaaccaggt cagcctctcg tgcgcagtca aaggcttcta tcccagcgac 1140

atcgccgtgg agtgggagag caatgggcag ccggagaaca actacaagac cacgcctccc 1200

gtgctggact ccgacggctc cttcttcctc gtgagcaagc tcaccgtgga caagagcagg 1260

tggcagcagg ggaacgtctt ctcatgctcc gtgatgcatg aggctctgca caaccactac 1320

acgcagaaga gcctctccct gtctccgggt ggaggcggcg gaagcggagg aggaggatcc 1380

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ggcgctacag tgctgggcct gttcagagtg acccccgaga ttccagccgg cctgccttct 1920

ccaagaagcg aaggcggagg cggatctggc ggcggaggat ctagagaggg acccgaactg 1980

tcccctgacg atccagccgg gctgctggat ctgagacagg gaatgttcgc ccagctggtg 2040

gctcagaatg tgctgctgat tgacggacct ctgagctggt actccgaccc agggctggca 2100

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aaagctgggg tgtactatgt gtttttcag ctggaactga ggcgggtggt ggctggggag 2220

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gctgcactgg ctctgactgt ggacctgcca ccagcctcta gcgaggccag aaacagcgcc 2340

ttcgggttcc aaggacgcct gctgcatctg agcgccggac agcgcctggg agtgcatctg 2400

catactgaag ccagagcccg gcatgcttgg cagctgactc agggggcaac tgtgctggga 2460

ctgtttcgcg tgacacctga gatccctgcc ggactgccaa gccctagatc agaa 2514

+ADw-210+AD4- 308
+ADw-211+AD4- 1932
+ADw-212+AD4- ADN
+ADw-213+AD4- Secuencia artificial

+ADw-220+AD4-
+ADw-223+AD4- ADN de ligando mon+APM-erico de Fc pomo de CD19(8B8-2B11)

+ADw-400+AD4- 308
caggtgcaat tggttcaatc tggtgctgaa gtaaaaaaac cgggcgcttc cgttaaagtg 60

agctgcaaag catctggtta caccttcact gactatatca tgcactgggt tcgtcaggcc 120

ccgggccagg gtctggagtg gatgggctac attaacccat acaacgacgg ttccaaatat 180

accgagaaat tccagggccg cgtcacgatg accagcgaca cttctatctc caccgcgtac 240

atggaactgt ctagactgcg ttctgacgac accgctgttt actattgtgc acgcggtacc 300

tactactacg gtccacagct gtttgattac tggggccaag gtaccacggt gaccgtaagc 360

tctgctagca ccaagggccc atcggtcttc cccctggcac cctcctccaa gagcacctct 420

gggggcacag cggccctggg ctgcctggtc aaggactact tccccgaacc ggtgacggtg 480

tcgtggaact caggcgccct gaccagcggc gtgcacacct tcccggctgt cctacagtcc 540

tcaggactct actccctcag cagcgtggtg accgtgccct ccagcagctt gggcacccag 600

acctacatct gcaacgtgaa tcacaagccc agcaacacca aggtggacaa gaaagttgag 660

cccaaatctt gtgacaaaac tcacacatgc ccaccgtgcc cagcacctga agctgcaggg 720

ggaccgtcag tcttcctctt cccccaaaa cccaaggaca ccctcatgat ctcccggacc 780

cctgaggtca catgcgtggt ggtggacgtg agccacgaag accctgaggt caagttcaac 840

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aaggagtaca agtgcaaggt ctccaacaaa gccctcggcg cccccatcga gaaaaccatc 1020

tccaaagcca aagggcagcc ccgagaacca caggtgtaca ccctgccccc ctgcagagat 1080

gagctgacca agaaccaggt gtccctgtgg tgtctggtca agggcttcta ccccagcgat 1140

atcgccgtgg agtgggagag caacggccag cctgagaaca actacaagac cacccccct 1200

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agagagggcc ctgagctgag ccccgatgat cctgctggac tgctggacct gcggcagggc 1440

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aggctgggag tgcatctgca cacagaggcc agggctagac acgcctggca gctgacacag 1860

ggcgctacag tgctgggcct gttcagagtg acccccgaga ttccagccgg cctgccttct 1920

ccaagaagcg aa 1932

+ADw-210+AD4- 309
+ADw-211+AD4- 838
+ADw-212+AD4- PRT
+ADw-213+AD4- Secuencia artificial

+ADw-220+AD4-
+ADw-223+AD4- cadena de ligando dim+AOk-rico de Fc agujero de CD19(8B8-2B11)

+ADw-400+AD4- 309

Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Asp Tyr
20 25 30

Ile Met His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
35 40 45

Gly Tyr Ile Asn Pro Tyr Asn Asp Gly Ser Lys Tyr Thr Glu Lys Phe
50 55 60

Gln Gly Arg Val Thr Met Thr Ser Asp Thr Ser Ile Ser Thr Ala Tyr
65 70 75 80

Met Glu Leu Ser Arg Leu Arg Ser Asp Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Gly Thr Tyr Tyr Tyr Gly Pro Gln Leu Phe Asp Tyr Trp Gly
100 105 110

Gln Gly Thr Thr Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser

```
        115                 120                 125

Val Phe Pro Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala
    130                 135                 140

Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val
145                 150                 155                 160

Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala
                165                 170                 175

Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val
            180                 185                 190

Pro Ser Ser Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His
        195                 200                 205

Lys Pro Ser Asn Thr Lys Val Asp Lys Lys Val Glu Pro Lys Ser Cys
    210                 215                 220

Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Ala Ala Gly
225                 230                 235                 240

Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met
                245                 250                 255

Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His
            260                 265                 270

Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val
        275                 280                 285

His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr
    290                 295                 300

Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly
305                 310                 315                 320

Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Gly Ala Pro Ile
                325                 330                 335

Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val
            340                 345                 350

Cys Thr Leu Pro Pro Ser Arg Asp Glu Leu Thr Lys Asn Gln Val Ser
        355                 360                 365
```

```
Leu Ser Cys Ala Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu
    370                 375                 380

Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro
385                 390                 395                 400

Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Val Ser Lys Leu Thr Val
                405                 410                 415

Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met
            420                 425                 430

His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser
        435                 440                 445

Pro Gly Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Arg Glu Gly Pro
    450                 455                 460

Glu Leu Ser Pro Asp Asp Pro Ala Gly Leu Leu Asp Leu Arg Gln Gly
465                 470                 475                 480

Met Phe Ala Gln Leu Val Ala Gln Asn Val Leu Leu Ile Asp Gly Pro
                485                 490                 495

Leu Ser Trp Tyr Ser Asp Pro Gly Leu Ala Gly Val Ser Leu Thr Gly
            500                 505                 510

Gly Leu Ser Tyr Lys Glu Asp Thr Lys Glu Leu Val Val Ala Lys Ala
        515                 520                 525

Gly Val Tyr Tyr Val Phe Phe Gln Leu Glu Leu Arg Arg Val Val Ala
    530                 535                 540

Gly Glu Gly Ser Gly Ser Val Ser Leu Ala Leu His Leu Gln Pro Leu
545                 550                 555                 560

Arg Ser Ala Ala Gly Ala Ala Ala Leu Ala Leu Thr Val Asp Leu Pro
                565                 570                 575

Pro Ala Ser Ser Glu Ala Arg Asn Ser Ala Phe Gly Phe Gln Gly Arg
            580                 585                 590

Leu Leu His Leu Ser Ala Gly Gln Arg Leu Gly Val His Leu His Thr
        595                 600                 605

Glu Ala Arg Ala Arg His Ala Trp Gln Leu Thr Gln Gly Ala Thr Val
    610                 615                 620
```

```
Leu Gly Leu Phe Arg Val Thr Pro Glu Ile Pro Ala Gly Leu Pro Ser
625                 630                 635                 640

Pro Arg Ser Glu Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Arg Glu
                645                 650                 655

Gly Pro Glu Leu Ser Pro Asp Asp Pro Ala Gly Leu Leu Asp Leu Arg
            660                 665                 670

Gln Gly Met Phe Ala Gln Leu Val Ala Gln Asn Val Leu Leu Ile Asp
        675                 680                 685

Gly Pro Leu Ser Trp Tyr Ser Asp Pro Gly Leu Ala Gly Val Ser Leu
    690                 695                 700

Thr Gly Gly Leu Ser Tyr Lys Glu Asp Thr Lys Glu Leu Val Val Ala
705                 710                 715                 720

Lys Ala Gly Val Tyr Tyr Val Phe Phe Gln Leu Glu Leu Arg Arg Val
                725                 730                 735

Val Ala Gly Glu Gly Ser Gly Ser Val Ser Leu Ala Leu His Leu Gln
            740                 745                 750

Pro Leu Arg Ser Ala Ala Gly Ala Ala Ala Leu Ala Leu Thr Val Asp
        755                 760                 765

Leu Pro Pro Ala Ser Ser Glu Ala Arg Asn Ser Ala Phe Gly Phe Gln
    770                 775                 780

Gly Arg Leu Leu His Leu Ser Ala Gly Gln Arg Leu Gly Val His Leu
785                 790                 795                 800

His Thr Glu Ala Arg Ala Arg His Ala Trp Gln Leu Thr Gln Gly Ala
                805                 810                 815

Thr Val Leu Gly Leu Phe Arg Val Thr Pro Glu Ile Pro Ala Gly Leu
            820                 825                 830

Pro Ser Pro Arg Ser Glu
        835
```

+ADw-210+AD4- 310
+ADw-211+AD4- 644
+ADw-212+AD4- PRT
+ADw-213+AD4- Secuencia artificial

+ADw-220+AD4-

+ADw-223+AD4- ligando mon+APM-erico de Fc pomo de CD19(8B8-2B11)

+ADw-400+AD4- 310

```
Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1               5                  10                  15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Asp Tyr
            20                  25                  30

Ile Met His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
        35                  40                  45

Gly Tyr Ile Asn Pro Tyr Asn Asp Gly Ser Lys Tyr Thr Glu Lys Phe
    50                  55                  60

Gln Gly Arg Val Thr Met Thr Ser Asp Thr Ser Ile Ser Thr Ala Tyr
65                  70                  75                  80

Met Glu Leu Ser Arg Leu Arg Ser Asp Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95

Ala Arg Gly Thr Tyr Tyr Tyr Gly Pro Gln Leu Phe Asp Tyr Trp Gly
            100                 105                 110

Gln Gly Thr Thr Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser
        115                 120                 125

Val Phe Pro Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala
    130                 135                 140

Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val
145                 150                 155                 160

Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala
                165                 170                 175

Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val
            180                 185                 190

Pro Ser Ser Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His
        195                 200                 205

Lys Pro Ser Asn Thr Lys Val Asp Lys Lys Val Glu Pro Lys Ser Cys
    210                 215                 220

Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Ala Ala Gly
225                 230                 235                 240
```

```
Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met
                245                 250                 255

Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His
            260                 265                 270

Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val
        275                 280                 285

His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr
    290                 295                 300

Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly
305                 310                 315                 320

Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Gly Ala Pro Ile
                325                 330                 335

Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val
            340                 345                 350

Tyr Thr Leu Pro Pro Cys Arg Asp Glu Leu Thr Lys Asn Gln Val Ser
        355                 360                 365

Leu Trp Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu
    370                 375                 380

Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro
385                 390                 395                 400

Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val
                405                 410                 415

Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met
            420                 425                 430

His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser
        435                 440                 445

Pro Gly Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Arg Glu Gly Pro
    450                 455                 460

Glu Leu Ser Pro Asp Asp Pro Ala Gly Leu Leu Asp Leu Arg Gln Gly
465                 470                 475                 480

Met Phe Ala Gln Leu Val Ala Gln Asn Val Leu Leu Ile Asp Gly Pro
                485                 490                 495
```

Leu Ser Trp Tyr Ser Asp Pro Gly Leu Ala Gly Val Ser Leu Thr Gly
500 505 510

Gly Leu Ser Tyr Lys Glu Asp Thr Lys Glu Leu Val Val Ala Lys Ala
515 520 525

Gly Val Tyr Tyr Val Phe Phe Gln Leu Glu Leu Arg Arg Val Val Ala
530 535 540

Gly Glu Gly Ser Gly Ser Val Ser Leu Ala Leu His Leu Gln Pro Leu
545 550 555 560

Arg Ser Ala Ala Gly Ala Ala Ala Leu Ala Leu Thr Val Asp Leu Pro
565 570 575

Pro Ala Ser Ser Glu Ala Arg Asn Ser Ala Phe Gly Phe Gln Gly Arg
580 585 590

Leu Leu His Leu Ser Ala Gly Gln Arg Leu Gly Val His Leu His Thr
595 600 605

Glu Ala Arg Ala Arg His Ala Trp Gln Leu Thr Gln Gly Ala Thr Val
610 615 620

Leu Gly Leu Phe Arg Val Thr Pro Glu Ile Pro Ala Gly Leu Pro Ser
625 630 635 640

Pro Arg Ser Glu

+ADw-210+AD4- 311
+ADw-211+AD4- 2478
+ADw-212+AD4- ADN
+ADw-213+AD4- Secuencia artificial

+ADw-220+AD4-
+ADw-223+AD4- ADN de cadena de ligando dim+AOk-rico (71-248) de Fc agujero de CD19(8B8-2B11)

+ADw-400+AD4- 311
caggtgcaat tggttcaatc tggtgctgaa gtaaaaaaac cgggcgcttc cgttaaagtg 60

agctgcaaag catctggtta caccttcact gactatatca tgcactgggt tcgtcaggcc 120

ccgggccagg gtctggagtg gatgggctac attaacccat acaacgacgg ttccaaatat 180

accgagaaat tccagggccg cgtcacgatg accagcgaca cttctatctc caccgcgtac 240

atggaactgt ctagactgcg ttctgacgac accgctgttt actattgtgc acgcggtacc 300

tactactacg gtccacagct gtttgattac tggggccaag gtaccacggt gaccgtaagc 360

tctgctagca ccaagggccc ctccgtgttc cccctggccc ccagcagcaa gagcaccagc 420

ggcggcacag ccgctctggg ctgcctggtc aaggactact tccccgagcc cgtgaccgtg 480

tcctggaaca gcggagccct gacctccggc gtgcacacct tccccgccgt gctgcagagt 540

tctggcctgt atagcctgag cagcgtggtc accgtgcctt ctagcagcct gggcacccag 600

acctacatct gcaacgtgaa ccacaagccc agcaacacca aggtggacaa gaaggtggag 660

cccaagagct gcgacaaaac tcacacatgc ccaccgtgcc cagcacctga agctgcaggg 720

ggaccgtcag tcttcctctt cccccaaaa cccaaggaca ccctcatgat ctcccggacc 780

cctgaggtca catgcgtggt ggtggacgtg agccacgaag accctgaggt caagttcaac 840

tggtacgtgg acggcgtgga ggtgcataat gccaagacaa agccgcggga ggagcagtac 900

aacagcacgt accgtgtggt cagcgtcctc accgtcctgc accaggactg gctgaatggc 960

aaggagtaca agtgcaaggt ctccaacaaa gccctcggcg cccccatcga gaaaaccatc 1020

tccaaagcca aagggcagcc ccgagaacca caggtgtgca ccctgccccc atcccgggat 1080

gagctgacca agaaccaggt cagcctctcg tgcgcagtca aaggcttcta tcccagcgac 1140

atcgccgtgg agtgggagag caatgggcag ccggagaaca actacaagac cacgcctccc 1200

gtgctggact ccgacggctc cttcttcctc gtgagcaagc tcaccgtgga caagagcagg 1260

tggcagcagg ggaacgtctt ctcatgctcc gtgatgcatg aggctctgca caaccactac 1320

acgcagaaga gcctctccct gtctccgggt ggaggcggcg gaagcggagg aggaggatcc 1380

agagagggcc ctgagctgag ccctgatgat cctgccggac tgctggacct gcggcaggga 1440

atgtttgccc agctggtggc ccagaacgtg ctgctgatcg atggcccccc gtcctggtac 1500

agcgatcctg gactggctgg cgtgtcactg acaggcggcc tgagctacaa agaggacacc 1560

aaagaactgg tggtggccaa ggccggcgtg tactacgtgt tctttcagct ggaactgcgg 1620

agagtggtgg ccggcgaagg atctggctct gtgtctctgg ccctgcatct gcagcctctg 1680

agatctgctg ctggcgccgc tgctctggca ctgacagtgg atctgcctcc tgccagcagc 1740

gaggcccgga atagcgcatt tgggtttcaa ggcaggctgc tgcacctgtc tgccggccag 1800

aggctgggag tgcatctgca cacagaggcc agggctagac acgcctggca gctgacacag 1860

ggcgctacag tgctgggcct gttcagagtg acccccgaga ttccagcagg cctgggaggc 1920

ggcggatctg gcggcggagg atctagagaa ggacccgagc tgtcccccga cgatcccgct 1980

gggctgctgg atctgagaca gggcatgttc gctcagctgg tggctcagaa tgtgctgctg 2040

attgacggac ctctgagctg gtactccgac ccagggctgg caggggtgtc cctgactggg 2100

ggactgtcct acaaagaaga tacaaaagaa ctggtggtgg ctaaagctgg ggtgtactat 2160

gtgtttttttc agctggaact gaggcgggtg gtggctgggg agggctcagg atctgtgtcc 2220

ctggctctgc atctgcagcc actgcgctct gcagcagggg ctgcagcact ggccctgact 2280

gtggacctgc ccccagcttc ttccgaggcc agaaacagcg ccttcgggtt ccaaggacgc 2340

ctgctgcatc tgagcgccgg acagcgcctg ggagtgcatc tgcatactga agccagagcc 2400

cggcatgctt ggcagctgac tcaggggca actgtgctgg gactgtttcg cgtgacacct 2460

gagatcccag ccgggctc 2478

+ADw-210+AD4- 312
+ADw-211+AD4- 1914
+ADw-212+AD4- ADN
+ADw-213+AD4- Secuencia artificial

+ADw-220+AD4-
+ADw-223+AD4- ADN de ligando mon+APM-erico de Fc pomo (71-248) de CD19(8B8-2B11)

+ADw-400+AD4- 312
caggtgcaat tggttcaatc tggtgctgaa gtaaaaaaac cgggcgcttc cgttaaagtg 60

agctgcaaag catctggtta caccttcact gactatatca tgcactgggt tcgtcaggcc 120

ccgggccagg gtctggagtg gatgggctac attaacccat acaacgacgg ttccaaatat 180

accgagaaat tccagggccg cgtcacgatg accagcgaca cttctatctc caccgcgtac 240

atggaactgt ctagactgcg ttctgacgac accgctgttt actattgtgc acgcggtacc 300

tactactacg gtccacagct gtttgattac tggggccaag gtaccacggt gaccgtaagc 360

tctgctagca ccaagggccc atcggtcttc cccctggcac cctcctccaa gagcacctct 420

gggggcacag cggccctggg ctgcctggtc aaggactact tccccgaacc ggtgacggtg 480

tcgtggaact caggcgccct gaccagcggc gtgcacacct tcccggctgt cctacagtcc 540

tcaggactct actccctcag cagcgtggtg accgtgccct ccagcagctt gggcacccag 600

acctacatct gcaacgtgaa tcacaagccc agcaacacca aggtggacaa gaaagttgag 660

cccaaatctt gtgacaaaac tcacacatgc ccaccgtgcc cagcacctga agctgcaggg 720

ggaccgtcag tcttcctctt ccccccaaaa cccaaggaca ccctcatgat ctcccggacc 780

cctgaggtca catgcgtggt ggtggacgtg agccacgaag accctgaggt caagttcaac 840

tggtacgtgg acggcgtgga ggtgcataat gccaagacaa agccgcggga ggagcagtac 900

aacagcacgt accgtgtggt cagcgtcctc accgtcctgc accaggactg gctgaatggc 960

aaggagtaca agtgcaaggt ctccaacaaa gccctcggcg cccccatcga gaaaaccatc 1020

tccaaagcca aagggcagcc ccgagaacca caggtgtaca ccctgccccc ctgcagagat 1080

gagctgacca agaaccaggt gtccctgtgg tgtctggtca agggcttcta ccccagcgat 1140

atcgccgtgg agtgggagag caacggccag cctgagaaca actacaagac cacccccct 1200

gtgctggaca gcgacggcag cttcttcctg tactccaaac tgaccgtgga caagagccgg 1260

tggcagcagg gcaacgtgtt cagctgcagc gtgatgcacg aggccctgca caaccactac 1320

acccagaagt ccctgagcct gagccccggc ggaggcggcg gaagcggagg aggaggatcc 1380

agagagggcc ctgagctgag ccctgatgat cctgccggac tgctggacct gcggcaggga 1440

atgtttgccc agctggtggc ccagaacgtg ctgctgatcg atggcccccc gtcctggtac 1500

agcgatcctg gactggctgg cgtgtcactg acaggcggcc tgagctacaa agaggacacc 1560

aaagaactgg tggtggccaa ggccggcgtg tactacgtgt tctttcagct ggaactgcgg 1620

agagtggtgg ccggcgaagg atctggctct gtgtctctgg ccctgcatct gcagcctctg 1680

agatctgctg ctggcgccgc tgctctggca ctgacagtgg atctgcctcc tgccagcagc 1740

gaggcccgga atagcgcatt tgggtttcaa ggcaggctgc tgcacctgtc tgccggccag 1800

aggctgggag tgcatctgca cacagaggcc agggctagac acgcctggca gctgacacag 1860

ggcgctacag tgctgggcct gttcagagtg acccccgaga ttcctgccgg gctc 1914

+ADw-210+AD4- 313
+ADw-211+AD4- 826
+ADw-212+AD4- PRT
+ADw-213+AD4- Secuencia artificial

+ADw-220+AD4-
+ADw-223+AD4- cadena de ligando dim+AOk-rico (71-248) de Fc agujero de CD19(8B8-2B11)

+ADw-400+AD4- 313

Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Asp Tyr
20 25 30

Ile Met His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
35 40 45

Gly Tyr Ile Asn Pro Tyr Asn Asp Gly Ser Lys Tyr Thr Glu Lys Phe
50 55 60

Gln Gly Arg Val Thr Met Thr Ser Asp Thr Ser Ile Ser Thr Ala Tyr
65 70 75 80

Met Glu Leu Ser Arg Leu Arg Ser Asp Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Gly Thr Tyr Tyr Tyr Gly Pro Gln Leu Phe Asp Tyr Trp Gly
100 105 110

Gln Gly Thr Thr Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser
115 120 125

```
Val Phe Pro Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala
    130                 135                 140

Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val
145                 150                 155                 160

Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala
                165                 170                 175

Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val
            180                 185                 190

Pro Ser Ser Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His
        195                 200                 205

Lys Pro Ser Asn Thr Lys Val Asp Lys Lys Val Glu Pro Lys Ser Cys
    210                 215                 220

Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Ala Ala Gly
225                 230                 235                 240

Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met
                245                 250                 255

Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His
            260                 265                 270

Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val
        275                 280                 285

His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr
    290                 295                 300

Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly
305                 310                 315                 320

Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Gly Ala Pro Ile
                325                 330                 335

Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val
            340                 345                 350

Cys Thr Leu Pro Pro Ser Arg Asp Glu Leu Thr Lys Asn Gln Val Ser
        355                 360                 365

Leu Ser Cys Ala Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu
```

```
    370                 375                 380

Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro
385                 390                 395                 400

Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Val Ser Lys Leu Thr Val
                405                 410                 415

Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met
            420                 425                 430

His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser
        435                 440                 445

Pro Gly Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Arg Glu Gly Pro
    450                 455                 460

Glu Leu Ser Pro Asp Asp Pro Ala Gly Leu Leu Asp Leu Arg Gln Gly
465                 470                 475                 480

Met Phe Ala Gln Leu Val Ala Gln Asn Val Leu Leu Ile Asp Gly Pro
                485                 490                 495

Leu Ser Trp Tyr Ser Asp Pro Gly Leu Ala Gly Val Ser Leu Thr Gly
            500                 505                 510

Gly Leu Ser Tyr Lys Glu Asp Thr Lys Glu Leu Val Val Ala Lys Ala
        515                 520                 525

Gly Val Tyr Tyr Val Phe Phe Gln Leu Glu Leu Arg Arg Val Val Ala
    530                 535                 540

Gly Glu Gly Ser Gly Ser Val Ser Leu Ala Leu His Leu Gln Pro Leu
545                 550                 555                 560

Arg Ser Ala Ala Gly Ala Ala Ala Leu Ala Leu Thr Val Asp Leu Pro
                565                 570                 575

Pro Ala Ser Ser Glu Ala Arg Asn Ser Ala Phe Gly Phe Gln Gly Arg
            580                 585                 590

Leu Leu His Leu Ser Ala Gly Gln Arg Leu Gly Val His Leu His Thr
        595                 600                 605

Glu Ala Arg Ala Arg His Ala Trp Gln Leu Thr Gln Gly Ala Thr Val
    610                 615                 620
```

```
Leu Gly Leu Phe Arg Val Thr Pro Glu Ile Pro Ala Gly Leu Gly Gly
625                 630                 635                 640

Gly Gly Ser Gly Gly Gly Gly Ser Arg Glu Gly Pro Glu Leu Ser Pro
                645                 650                 655

Asp Asp Pro Ala Gly Leu Leu Asp Leu Arg Gln Gly Met Phe Ala Gln
            660                 665                 670

Leu Val Ala Gln Asn Val Leu Leu Ile Asp Gly Pro Leu Ser Trp Tyr
        675                 680                 685

Ser Asp Pro Gly Leu Ala Gly Val Ser Leu Thr Gly Gly Leu Ser Tyr
    690                 695                 700

Lys Glu Asp Thr Lys Glu Leu Val Val Ala Lys Ala Gly Val Tyr Tyr
705                 710                 715                 720

Val Phe Phe Gln Leu Glu Leu Arg Arg Val Val Ala Gly Glu Gly Ser
                725                 730                 735

Gly Ser Val Ser Leu Ala Leu His Leu Gln Pro Leu Arg Ser Ala Ala
            740                 745                 750

Gly Ala Ala Ala Leu Ala Leu Thr Val Asp Leu Pro Pro Ala Ser Ser
        755                 760                 765

Glu Ala Arg Asn Ser Ala Phe Gly Phe Gln Gly Arg Leu Leu His Leu
    770                 775                 780

Ser Ala Gly Gln Arg Leu Gly Val His Leu His Thr Glu Ala Arg Ala
785                 790                 795                 800

Arg His Ala Trp Gln Leu Thr Gln Gly Ala Thr Val Leu Gly Leu Phe
                805                 810                 815

Arg Val Thr Pro Glu Ile Pro Ala Gly Leu
            820                 825


+ADw-210+AD4-  314
+ADw-211+AD4-  638
+ADw-212+AD4-  PRT
+ADw-213+AD4-  Secuencia artificial

+ADw-220+AD4-
+ADw-223+AD4-  ligando mon+APM-erico de Fc pomo (71-248) de CD19(8B8-2B11)

+ADw-400+AD4-  314

Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
```

```
1               5                   10                  15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Asp Tyr
            20                  25                  30

Ile Met His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
        35                  40                  45

Gly Tyr Ile Asn Pro Tyr Asn Asp Gly Ser Lys Tyr Thr Glu Lys Phe
    50                  55                  60

Gln Gly Arg Val Thr Met Thr Ser Asp Thr Ser Ile Ser Thr Ala Tyr
65                  70                  75                  80

Met Glu Leu Ser Arg Leu Arg Ser Asp Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95

Ala Arg Gly Thr Tyr Tyr Tyr Gly Pro Gln Leu Phe Asp Tyr Trp Gly
            100                 105                 110

Gln Gly Thr Thr Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser
        115                 120                 125

Val Phe Pro Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala
    130                 135                 140

Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val
145                 150                 155                 160

Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala
                165                 170                 175

Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val
            180                 185                 190

Pro Ser Ser Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His
        195                 200                 205

Lys Pro Ser Asn Thr Lys Val Asp Lys Lys Val Glu Pro Lys Ser Cys
    210                 215                 220

Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Ala Ala Gly
225                 230                 235                 240

Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met
                245                 250                 255
```

```
Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His
            260                 265                 270

Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val
        275                 280                 285

His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr
    290                 295                 300

Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly
305                 310                 315                 320

Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Gly Ala Pro Ile
                325                 330                 335

Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val
            340                 345                 350

Tyr Thr Leu Pro Pro Cys Arg Asp Glu Leu Thr Lys Asn Gln Val Ser
        355                 360                 365

Leu Trp Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu
    370                 375                 380

Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro
385                 390                 395                 400

Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val
                405                 410                 415

Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met
            420                 425                 430

His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser
        435                 440                 445

Pro Gly Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Arg Glu Gly Pro
    450                 455                 460

Glu Leu Ser Pro Asp Asp Pro Ala Gly Leu Leu Asp Leu Arg Gln Gly
465                 470                 475                 480

Met Phe Ala Gln Leu Val Ala Gln Asn Val Leu Leu Ile Asp Gly Pro
                485                 490                 495

Leu Ser Trp Tyr Ser Asp Pro Gly Leu Ala Gly Val Ser Leu Thr Gly
            500                 505                 510
```

Gly Leu Ser Tyr Lys Glu Asp Thr Lys Glu Leu Val Val Ala Lys Ala
515 520 525

Gly Val Tyr Tyr Val Phe Phe Gln Leu Glu Leu Arg Arg Val Val Ala
530 535 540

Gly Glu Gly Ser Gly Ser Val Ser Leu Ala Leu His Leu Gln Pro Leu
545 550 555 560

Arg Ser Ala Ala Gly Ala Ala Ala Leu Ala Leu Thr Val Asp Leu Pro
565 570 575

Pro Ala Ser Ser Glu Ala Arg Asn Ser Ala Phe Gly Phe Gln Gly Arg
580 585 590

Leu Leu His Leu Ser Ala Gly Gln Arg Leu Gly Val His Leu His Thr
595 600 605

Glu Ala Arg Ala Arg His Ala Trp Gln Leu Thr Gln Gly Ala Thr Val
610 615 620

Leu Gly Leu Phe Arg Val Thr Pro Glu Ile Pro Ala Gly Leu
625 630 635

+ADw-210+AD4- 315
+ADw-211+AD4- 1353
+ADw-212+AD4- ADN
+ADw-213+AD4- Secuencia artificial

+ADw-220+AD4-
+ADw-223+AD4- CD19(8B8-018) heavy chain (huIgG1 PGLALA) DNA

+ADw-400+AD4- 315
caggtccagc tggtgcagtc cggcgccgag gtcaagaaac ccggggcttc tgtgaaggtt 60

tcatgcaagg caagcggata caccttcacc gactatatca tgcattgggt caggcaggcc 120

cctggccaag gtctcgaatg gatgggctac attaacccat ataatgatgg ctccaaatac 180

accgagaagt ttcagggaag agtcactatg acatctgaca ccagtatcag cactgcttac 240

atggagctgt cccgccttcg gtctgatgac accgcagtgt attactgtgc caggggcaca 300

tattactacg gctcagctct gttcgactat tgggggcagg gaaccacagt aaccgtgagc 360

tccgcaagta ctaagggccc atcggtcttc cccctggcac cctcctccaa gagcacctct 420

gggggcacag cggccctggg ctgcctggtc aaggactact tccccgaacc ggtgacggtg 480

tcgtggaact caggcgccct gaccagcggc gtgcacacct tcccggctgt cctacagtcc 540

tcaggactct actccctcag cagcgtggtg accgtgccct ccagcagctt gggcacccag 600

acctacatct gcaacgtgaa tcacaagccc agcaacacca aggtggacaa gaaagttgag 660

```
cccaaatctt gtgacaaaac tcacacatgc ccaccgtgcc cagcacctga agcagctggg      720

ggaccgtcag tcttcctctt ccccccaaaa cccaaggaca ccctcatgat ctcccggacc      780

cctgaggtca catgcgtggt ggtggacgtg agccacgaag accctgaggt caagttcaac      840

tggtacgtgg acggcgtgga ggtgcataat gccaagacaa agccgcggga ggagcagtac      900

aacagcacgt accgtgtggt cagcgtcctc accgtcctgc accaggactg gctgaatggc      960

aaggagtaca agtgcaaggt ctccaacaaa gccctcggag cccccatcga gaaaaccatc     1020

tccaaagcca aagggcagcc ccgagaacca caggtgtaca ccctgccccc atcccgggat     1080

gagctgacca agaaccaggt cagcctgacc tgcctggtca aaggcttcta tcccagcgac     1140

atcgccgtgg agtgggagag caatgggcag ccggagaaca actacaagac cacgcctccc     1200

gtgctggact ccgacggctc cttcttcctc tacagcaagc tcaccgtgga caagagcagg     1260

tggcagcagg ggaacgtctt ctcatgctcc gtgatgcatg aggctctgca caaccactac     1320

acgcagaaga gcctctccct gtccccgggc aaa                                  1353


+ADw-210+AD4-  316
+ADw-211+AD4-  451
+ADw-212+AD4-  PRT
+ADw-213+AD4-  Secuencia artificial

+ADw-220+AD4-
+ADw-223+AD4-  CD19(8B8-018) heavy chain (huIgG1 PGLALA)

+ADw-400+AD4-  316

Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1               5                   10                  15


Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Asp Tyr
            20                  25                  30


Ile Met His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
        35                  40                  45


Gly Tyr Ile Asn Pro Tyr Asn Asp Gly Ser Lys Tyr Thr Glu Lys Phe
    50                  55                  60


Gln Gly Arg Val Thr Met Thr Ser Asp Thr Ser Ile Ser Thr Ala Tyr
65                  70                  75                  80


Met Glu Leu Ser Arg Leu Arg Ser Asp Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95


Ala Arg Gly Thr Tyr Tyr Tyr Gly Ser Ala Leu Phe Asp Tyr Trp Gly
            100                 105                 110
```

```
Gln Gly Thr Thr Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser
        115                 120                 125

Val Phe Pro Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala
    130                 135                 140

Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val
145                 150                 155                 160

Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala
                165                 170                 175

Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val
            180                 185                 190

Pro Ser Ser Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His
        195                 200                 205

Lys Pro Ser Asn Thr Lys Val Asp Lys Lys Val Glu Pro Lys Ser Cys
    210                 215                 220

Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Ala Ala Gly
225                 230                 235                 240

Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met
                245                 250                 255

Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His
            260                 265                 270

Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val
        275                 280                 285

His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr
    290                 295                 300

Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly
305                 310                 315                 320

Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Gly Ala Pro Ile
                325                 330                 335

Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val
            340                 345                 350

Tyr Thr Leu Pro Pro Ser Arg Asp Glu Leu Thr Lys Asn Gln Val Ser
        355                 360                 365
```

```
Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu
    370                 375                 380

Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro
385                 390                 395                 400

Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val
                405                 410                 415

Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met
            420                 425                 430

His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser
        435                 440                 445

Pro Gly Lys
    450


+ADw-210+AD4-  317
+ADw-211+AD4-  140
+ADw-212+AD4-  PRT
+ADw-213+AD4-  Secuencia artificial

+ADw-220+AD4-
+ADw-223+AD4-  anti-mu CEA T84.66 VH

+ADw-400+AD4-  317

Met Lys Cys Ser Trp Val Ile Phe Phe Leu Met Ala Val Val Thr Gly
1               5                   10                  15

Val Asn Ser Glu Val Gln Leu Gln Gln Ser Gly Ala Glu Leu Val Glu
            20                  25                  30

Pro Gly Ala Ser Val Lys Leu Ser Cys Thr Ala Ser Gly Phe Asn Ile
        35                  40                  45

Lys Asp Thr Tyr Met His Trp Val Lys Gln Arg Pro Glu Gln Gly Leu
    50                  55                  60

Glu Trp Ile Gly Arg Ile Asp Pro Ala Asn Gly Asn Ser Lys Tyr Val
65                  70                  75                  80

Pro Lys Phe Gln Gly Lys Ala Thr Ile Thr Ala Asp Thr Ser Ser Asn
                85                  90                  95

Thr Ala Tyr Leu Gln Leu Thr Ser Leu Thr Ser Glu Asp Thr Ala Val
            100                 105                 110
```

Tyr Tyr Cys Ala Pro Phe Gly Tyr Tyr Val Ser Asp Tyr Ala Met Ala
115 120 125

Tyr Trp Gly Gln Gly Thr Ser Val Thr Val Ser Ser
130 135 140

+ADw-210+AD4- 318
+ADw-211+AD4- 131
+ADw-212+AD4- PRT
+ADw-213+AD4- Secuencia artificial

+ADw-220+AD4-
+ADw-223+AD4- anti-mu CEA T84.66 VL

+ADw-400+AD4- 318

Met Glu Thr Asp Thr Leu Leu Leu Trp Val Leu Leu Leu Trp Val Pro
1 5 10 15

Gly Ser Thr Gly Asp Ile Val Leu Thr Gln Ser Pro Ala Ser Leu Ala
20 25 30

Val Ser Leu Gly Gln Arg Ala Thr Met Ser Cys Arg Ala Gly Glu Ser
35 40 45

Val Asp Ile Phe Gly Val Gly Phe Leu His Trp Tyr Gln Gln Lys Pro
50 55 60

Gly Gln Pro Pro Lys Leu Leu Ile Tyr Arg Ala Ser Asn Leu Glu Ser
65 70 75 80

Gly Ile Pro Val Arg Phe Ser Gly Thr Gly Ser Arg Thr Asp Phe Thr
85 90 95

Leu Ile Ile Asp Pro Val Glu Ala Asp Asp Val Ala Thr Tyr Tyr Cys
100 105 110

Gln Gln Thr Asn Glu Asp Pro Tyr Thr Phe Gly Gly Gly Thr Lys Leu
115 120 125

Glu Ile Lys
130

+ADw-210+AD4- 319
+ADw-211+AD4- 392
+ADw-212+AD4- ADN
+ADw-213+AD4- Secuencia artificial

+ADw-220+AD4-
+ADw-223+AD4- Secuencia de armaz+APM-n aceptor de cadena pesada

+ADw-400+AD4- 319
taaggggctt cctagtccta aggctgagga agggatcctg gtttagttaa agaggatttt 60

attcacccct gtgtcctctc cacaggtgtc cagtcccagg tccagctggt gcaatctggg 120

gctgaggtga agaagcctgg gtcctcggtg aaggtctcct gcaaggcttc tggaggcacc 180

ttcagcagct atactatcag ctgggtgcga caggcccctg gacaagggct tgagtggatg 240

ggaaggatca tccctatcct tggtacagca aactacgcac agaagttcca gggcagagtc 300

acgattaccg cggacaaatc cacgagcaca gcctacatgg agctgagcag cctgagatct 360

gaggacacgg ccgtgtatta ctgtgcgaga ga   392

+ADw-210+AD4- 320
+ADw-211+AD4- 797
+ADw-212+AD4- ADN
+ADw-213+AD4- Secuencia artificial

+ADw-220+AD4-
+ADw-223+AD4- Secuencia de armaz+APM-n aceptor de cadena ligera

+ADw-400+AD4- 320
ctgcagctgg aagctcagct cccacccagc tgctttgcat gtccctccca gctgccctac 60

cttccagagc ccatatcaat gcctgtgtca gagccctggg gaggaactgc tcagttagga 120

cccagaggga accatggaag ccccagctca gcttctcttc ctcctgctac tctggctccc 180

aggtgagggg aacatgaggt ggttttgcac attagtgaaa actcttgcca cctctgctca 240

gcaagaaata taattaaaat tcaaagtata tcaacaattt tggctctact caaagacagt 300

tggtttgatc ttgattacat gagtgcattt ctgttttatt tccaatttca gataccaccg 360

gagaaattgt gttgacacag tctccagcca ccctgtcttt gtctccaggg gaaagagcca 420

ccctctcctg cagggccagt cagagtgtta gcagctactt agcctggtac caacagaaac 480

ctggccaggc tcccaggctc ctcatctatg atgcatccaa cagggccact ggcatcccag 540

ccaggttcag tggcagtggg tctgggacag acttcactct caccatcagc agcctagagc 600

ctgaagattt tgcagtttat tactgtcagc agcgtagcaa ctggcctccc acagtgattc 660

cacatgaaac aaaaacccca acaagaccat cagtgtttac tagattatta taccagctgc 720

ttcctttaca gacagctagt ggggtggcca ctcagtgtta gcatctcagc tctatttggc 780

cattttggag ttcaagt   797

+ADw-210+AD4- 321
+ADw-211+AD4- 5
+ADw-212+AD4- PRT
+ADw-213+AD4- Secuencia artificial

+ADw-220+AD4-
+ADw-223+AD4- CEA (T84.66-LCHA) CDR-H1

+ADw-400+AD4- 321

Asp Thr Tyr Met His
1 5

+ADw-210+AD4- 322
+ADw-211+AD4- 17
+ADw-212+AD4- PRT
+ADw-213+AD4- Secuencia artificial

+ADw-220+AD4-
+ADw-223+AD4- CEA(T84.66-LCHA) CDR-H2

+ADw-400+AD4- 322

Arg Ile Asp Pro Ala Asn Gly Asn Ser Lys Tyr Val Pro Lys Phe Gln
1 5 10 15

Gly

+ADw-210+AD4- 323
+ADw-211+AD4- 12
+ADw-212+AD4- PRT
+ADw-213+AD4- Secuencia artificial

+ADw-220+AD4-
+ADw-223+AD4- CEA(T84.66-LCHA) CDR-H3

+ADw-400+AD4- 323

Phe Gly Tyr Tyr Val Ser Asp Tyr Ala Met Ala Tyr
1 5 10

+ADw-210+AD4- 324
+ADw-211+AD4- 15
+ADw-212+AD4- PRT
+ADw-213+AD4- Secuencia artificial

+ADw-220+AD4-
+ADw-223+AD4- CEA(T84.66-LCHA) CDR-L1

+ADw-400+AD4- 324

Arg Ala Gly Glu Ser Val Asp Ile Phe Gly Val Gly Phe Leu His
1 5 10 15

+ADw-210+AD4- 325
+ADw-211+AD4- 7
+ADw-212+AD4- PRT
+ADw-213+AD4- Secuencia artificial

+ADw-220+AD4-
+ADw-223+AD4- CEA(T84.66-LCHA) CDR-L2

+ADw-400+AD4- 325

Arg Ala Ser Asn Arg Ala Thr
1 5

+ADw-210+AD4- 326
+ADw-211+AD4- 9
+ADw-212+AD4- PRT
+ADw-213+AD4- Secuencia artificial

+ADw-220+AD4-
+ADw-223+AD4- CEA(T84.66-LCHA) CDR-L3

+ADw-400+AD4- 326

```
Gln Gln Thr Asn Glu Asp Pro Tyr Thr
1               5
```

+ADw-210+AD4- 327
+ADw-211+AD4- 121
+ADw-212+AD4- PRT
+ADw-213+AD4- Secuencia artificial

+ADw-220+AD4-
+ADw-223+AD4- VH de uni+APM-n a CEA progenitora

+ADw-400+AD4- 327

```
Glu Val Gln Leu Gln Gln Ser Gly Ala Glu Leu Val Glu Pro Gly Ala
1               5                   10                  15

Ser Val Lys Leu Ser Cys Thr Ala Ser Gly Phe Asn Ile Lys Asp Thr
            20                  25                  30

Tyr Met His Trp Val Lys Gln Arg Pro Glu Gln Gly Leu Glu Trp Ile
        35                  40                  45

Gly Arg Ile Asp Pro Ala Asn Gly Asn Ser Lys Tyr Val Pro Lys Phe
    50                  55                  60

Gln Gly Lys Ala Thr Ile Thr Ala Asp Thr Ser Ser Asn Thr Ala Tyr
65                  70                  75                  80

Leu Gln Leu Thr Ser Leu Thr Ser Glu Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95

Ala Pro Phe Gly Tyr Tyr Val Ser Asp Tyr Ala Met Ala Tyr Trp Gly
            100                 105                 110

Gln Gly Thr Ser Val Thr Val Ser Ser
        115                 120
```

+ADw-210+AD4- 328
+ADw-211+AD4- 111
+ADw-212+AD4- PRT
+ADw-213+AD4- Secuencia artificial

+ADw-220+AD4-
+ADw-223+AD4- VL de uni+APM-n a CEA progenitora

+ADw-400+AD4- 328

```
Asp Ile Val Leu Thr Gln Ser Pro Ala Ser Leu Ala Val Ser Leu Gly
1               5                  10                  15

Gln Arg Ala Thr Met Ser Cys Arg Ala Gly Glu Ser Val Asp Ile Phe
            20                  25                  30

Gly Val Gly Phe Leu His Trp Tyr Gln Gln Lys Pro Gly Gln Pro Pro
        35                  40                  45

Lys Leu Leu Ile Tyr Arg Ala Ser Asn Leu Glu Ser Gly Ile Pro Val
    50                  55                  60

Arg Phe Ser Gly Thr Gly Ser Arg Thr Asp Phe Thr Leu Ile Ile Asp
65                  70                  75                  80

Pro Val Glu Ala Asp Asp Val Ala Thr Tyr Tyr Cys Gln Gln Thr Asn
                85                  90                  95

Glu Asp Pro Tyr Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys
            100                 105                 110
```

+ADw-210+AD4- 329
+ADw-211+AD4- 242
+ADw-212+AD4- PRT
+ADw-213+AD4- Secuencia artificial

+ADw-220+AD4-
+ADw-223+AD4- CEA(T84.66-LCHA) VH

+ADw-400+AD4- 329

```
Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ser
1               5                  10                  15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Phe Asn Ile Lys Asp Thr
            20                  25                  30

Tyr Met His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
        35                  40                  45

Gly Arg Ile Asp Pro Ala Asn Gly Asn Ser Lys Tyr Val Pro Lys Phe
    50                  55                  60

Gln Gly Arg Val Thr Ile Thr Ala Asp Thr Ser Thr Ser Thr Ala Tyr
65                  70                  75                  80
```

```
Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95

Ala Pro Phe Gly Tyr Tyr Val Ser Asp Tyr Ala Met Ala Tyr Trp Gly
            100                 105                 110

Gln Gly Thr Leu Val Thr Val Ser Ser Gln Val Gln Leu Val Gln Ser
        115                 120                 125

Gly Ala Glu Val Lys Lys Pro Gly Ser Ser Val Lys Val Ser Cys Lys
    130                 135                 140

Ala Ser Gly Phe Asn Ile Lys Asp Thr Tyr Met His Trp Val Arg Gln
145                 150                 155                 160

Ala Pro Gly Gln Gly Leu Glu Trp Met Gly Arg Ile Asp Pro Ala Asn
                165                 170                 175

Gly Asn Ser Lys Tyr Val Pro Lys Phe Gln Gly Arg Val Thr Ile Thr
            180                 185                 190

Ala Asp Thr Ser Thr Ser Thr Ala Tyr Met Glu Leu Ser Ser Leu Arg
        195                 200                 205

Ser Glu Asp Thr Ala Val Tyr Tyr Cys Ala Pro Phe Gly Tyr Tyr Val
    210                 215                 220

Ser Asp Tyr Ala Met Ala Tyr Trp Gly Gln Gly Thr Leu Val Thr Val
225                 230                 235                 240

Ser Ser
```

+ADw-210+AD4- 330
+ADw-211+AD4- 111
+ADw-212+AD4- PRT
+ADw-213+AD4- Secuencia artificial

+ADw-220+AD4-
+ADw-223+AD4- CEA(T84.66-LCHA) VL

+ADw-400+AD4- 330

```
Glu Ile Val Leu Thr Gln Ser Pro Ala Thr Leu Ser Leu Ser Pro Gly
1               5                   10                  15

Glu Arg Ala Thr Leu Ser Cys Arg Ala Gly Glu Ser Val Asp Ile Phe
            20                  25                  30

Gly Val Gly Phe Leu His Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro
```

35 40 45

Arg Leu Leu Ile Tyr Arg Ala Ser Asn Arg Ala Thr Gly Ile Pro Ala
50 55 60

Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser
65 70 75 80

Ser Leu Glu Pro Glu Asp Phe Ala Val Tyr Tyr Cys Gln Gln Thr Asn
85 90 95

Glu Asp Pro Tyr Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys
100 105 110

+ADw-210+AD4- 331
+ADw-211+AD4- 1353
+ADw-212+AD4- ADN
+ADw-213+AD4- Secuencia artificial

+ADw-220+AD4-
+ADw-223+AD4- ADN de cadena Fc agujero de CEA(T84.66-LCHA)

+ADw-400+AD4- 331
caggtgcagc tggtgcagtc tggcgccgaa gtgaagaaac ccggcagcag cgtgaaggtg 60

tcctgcaagg ccagcggctt caacatcaag gacacctaca tgcactgggt gcgccaggcc 120

cctggacagg gactggaatg gatgggcaga atcgaccccg ccaacggcaa cagcaaatac 180

gtgcccaagt tccagggcag agtgaccatc accgccgaca ccagcacctc caccgcctac 240

atggaactga gcagcctgcg gagcgaggac accgccgtgt actactgtgc ccccttcggc 300

tactacgtgt ccgactacgc catggcctat tggggccagg gcacactcgt gaccgtgtcc 360

tctgctagca ccaagggccc ctccgtgttc cccctggccc ccagcagcaa gagcaccagc 420

ggcggcacag ccgctctggg ctgcctggtc aaggactact tccccgagcc cgtgaccgtg 480

tcctggaaca gcggagccct gacctccggc gtgcacacct tccccgccgt gctgcagagt 540

tctggcctgt atagcctgag cagcgtggtc accgtgcctt ctagcagcct gggcacccag 600

acctacatct gcaacgtgaa ccacaagccc agcaacacca aggtggacaa gaaggtggag 660

cccaagagct gcgacaaaac tcacacatgc ccaccgtgcc cagcacctga agctgcaggg 720

ggaccgtcag tcttcctctt cccccaaaa cccaaggaca ccctcatgat ctcccggacc 780

cctgaggtca catgcgtggt ggtggacgtg agccacgaag accctgaggt caagttcaac 840

tggtacgtgg acggcgtgga ggtgcataat gccaagacaa agccgcggga ggagcagtac 900

aacagcacgt accgtgtggt cagcgtcctc accgtcctgc accaggactg gctgaatggc 960

aaggagtaca agtgcaaggt ctccaacaaa gccctcggcg cccccatcga gaaaaccatc 1020

tccaaagcca aagggcagcc ccgagaacca caggtgtgca ccctgccccc atcccgggat 1080

gagctgacca agaaccaggt cagcctctcg tgcgcagtca aaggcttcta tcccagcgac 1140

atcgccgtgg agtgggagag caatgggcag ccggagaaca actacaagac cacgcctccc 1200

gtgctggact ccgacggctc cttcttcctc gtgagcaagc tcaccgtgga caagagcagg 1260

tggcagcagg ggaacgtctt ctcatgctcc gtgatgcatg aggctctgca caaccactac 1320

acgcagaaga gcctctccct gtctccgggt aaa 1353

+ADw-210+AD4- 332
+ADw-211+AD4- 654
+ADw-212+AD4- ADN
+ADw-213+AD4- Secuencia artificial

+ADw-220+AD4-
+ADw-223+AD4- ADN de cadena ligera de CEA(T84.66-LCHA)

+ADw-400+AD4- 332
gagatcgtgc tgacccagag ccctgccacc ctgtcactgt ctccaggcga gagagccacc 60

ctgagctgta gagccggcga gagcgtggac atcttcggcg tgggatttct gcactggtat 120

cagcagaagc ccggccaggc ccccagactg ctgatctaca gagccagcaa ccgggccaca 180

ggcatccccg ccagattttc tggctctggc agcggcaccg acttcaccct gacaatcagc 240

agcctggaac ccgaggactt cgccgtgtac tactgccagc agaccaacga ggacccctac 300

acctttggcc agggcaccaa gctggaaatc aagcgtacgg tggctgcacc atctgtcttc 360

atcttcccgc catctgatga gcagttgaaa tctggaactg cctctgttgt gtgcctgctg 420

aataacttct atcccagaga ggccaaagta cagtggaagg tggataacgc cctccaatcg 480

ggtaactccc aggagagtgt cacagagcag gacagcaagg acagcaccta cagcctcagc 540

agcaccctga cgctgagcaa agcagactac gagaaacaca aagtctacgc ctgcgaagtc 600

acccatcagg gcctgagctc gcccgtcaca aagagcttca acaggggaga gtgt 654

+ADw-210+AD4- 333
+ADw-211+AD4- 451
+ADw-212+AD4- PRT
+ADw-213+AD4- Secuencia artificial

+ADw-220+AD4-
+ADw-223+AD4- CEA (T84.66-LCHA) cadena de Fc agujero

+ADw-400+AD4- 333

Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ser
1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Phe Asn Ile Lys Asp Thr
20 25 30

Tyr Met His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met

```
        35                  40                  45

Gly Arg Ile Asp Pro Ala Asn Gly Asn Ser Lys Tyr Val Pro Lys Phe
    50                  55                  60

Gln Gly Arg Val Thr Ile Thr Ala Asp Thr Ser Thr Ser Thr Ala Tyr
65                  70                  75                  80

Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95

Ala Pro Phe Gly Tyr Tyr Val Ser Asp Tyr Ala Met Ala Tyr Trp Gly
            100                 105                 110

Gln Gly Thr Leu Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser
        115                 120                 125

Val Phe Pro Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala
    130                 135                 140

Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val
145                 150                 155                 160

Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala
                165                 170                 175

Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val
            180                 185                 190

Pro Ser Ser Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His
        195                 200                 205

Lys Pro Ser Asn Thr Lys Val Asp Lys Lys Val Glu Pro Lys Ser Cys
    210                 215                 220

Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Ala Ala Gly
225                 230                 235                 240

Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met
                245                 250                 255

Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His
            260                 265                 270

Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val
        275                 280                 285
```

```
His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr
    290                 295                 300

Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly
305                 310                 315                 320

Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Gly Ala Pro Ile
                325                 330                 335

Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val
            340                 345                 350

Cys Thr Leu Pro Pro Ser Arg Asp Glu Leu Thr Lys Asn Gln Val Ser
        355                 360                 365

Leu Ser Cys Ala Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu
    370                 375                 380

Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro
385                 390                 395                 400

Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Val Ser Lys Leu Thr Val
                405                 410                 415

Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met
            420                 425                 430

His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser
        435                 440                 445

Pro Gly Lys
    450


+ADw-210+AD4-  334
+ADw-211+AD4-  218
+ADw-212+AD4-  PRT
+ADw-213+AD4-  Secuencia artificial

+ADw-220+AD4-
+ADw-223+AD4-  CEA (T84.66-LCHA) cadena ligera

+ADw-400+AD4-  334

Glu Ile Val Leu Thr Gln Ser Pro Ala Thr Leu Ser Leu Ser Pro Gly
1               5                   10                  15

Glu Arg Ala Thr Leu Ser Cys Arg Ala Gly Glu Ser Val Asp Ile Phe
            20                  25                  30

Gly Val Gly Phe Leu His Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro
```

35 40 45

Arg Leu Leu Ile Tyr Arg Ala Ser Asn Arg Ala Thr Gly Ile Pro Ala
50 55 60

Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser
65 70 75 80

Ser Leu Glu Pro Glu Asp Phe Ala Val Tyr Tyr Cys Gln Gln Thr Asn
85 90 95

Glu Asp Pro Tyr Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys Arg
100 105 110

Thr Val Ala Ala Pro Ser Val Phe Ile Phe Pro Pro Ser Asp Glu Gln
115 120 125

Leu Lys Ser Gly Thr Ala Ser Val Val Cys Leu Leu Asn Asn Phe Tyr
130 135 140

Pro Arg Glu Ala Lys Val Gln Trp Lys Val Asp Asn Ala Leu Gln Ser
145 150 155 160

Gly Asn Ser Gln Glu Ser Val Thr Glu Gln Asp Ser Lys Asp Ser Thr
165 170 175

Tyr Ser Leu Ser Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu Lys
180 185 190

His Lys Val Tyr Ala Cys Glu Val Thr His Gln Gly Leu Ser Ser Pro
195 200 205

Val Thr Lys Ser Phe Asn Arg Gly Glu Cys
210 215

+ADw-210+AD4- 335
+ADw-211+AD4- 2514
+ADw-212+AD4- ADN
+ADw-213+AD4- Secuencia artificial

+ADw-220+AD4-
+ADw-223+AD4- ADN de CEA (T84.66-LCHA) cadena de 4-1BBL dim+AOk-rico de Fc agujero (71-254)

+ADw-400+AD4- 335
caggtgcagc tggtgcagtc tggcgccgaa gtgaagaaac ccggcagcag cgtgaaggtg 60

tcctgcaagg ccagcggctt caacatcaag gacacctaca tgcactgggt gcgccaggcc 120

cctggacagg gactggaatg gatgggcaga atcgaccccg ccaacggcaa cagcaaatac 180

gtgcccaagt tccagggcag agtgaccatc accgccgaca ccagcacctc caccgcctac 240
atggaactga gcagcctgcg gagcgaggac accgccgtgt actactgtgc ccccttcggc 300
tactacgtgt ccgactacgc catggcctat tggggccagg gcacactcgt gaccgtgtcc 360
tctgctagca ccaagggccc ctccgtgttc cccctggccc ccagcagcaa gagcaccagc 420
ggcggcacag ccgctctggg ctgcctggtc aaggactact tccccgagcc cgtgaccgtg 480
tcctggaaca gcggagccct gacctccggc gtgcacacct tccccgccgt gctgcagagt 540
tctggcctgt atagcctgag cagcgtggtc accgtgcctt ctagcagcct gggcacccag 600
acctacatct gcaacgtgaa ccacaagccc agcaacacca aggtggacaa gaaggtggag 660
cccaagagct gcgacaaaac tcacacatgc ccaccgtgcc cagcacctga agctgcaggg 720
ggaccgtcag tcttcctctt cccccccaaaa cccaaggaca ccctcatgat ctcccggacc 780
cctgaggtca catgcgtggt ggtggacgtg agccacgaag accctgaggt caagttcaac 840
tggtacgtgg acggcgtgga ggtgcataat gccaagacaa agccgcggga ggagcagtac 900
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ctgtttcgcg tgacacctga gatccctgcc ggactgccaa gccctagatc agaa 2514

+ADw-210+AD4- 336
+ADw-211+AD4- 1932
+ADw-212+AD4- ADN
+ADw-213+AD4- Secuencia artificial

+ADw-220+AD4-
+ADw-223+AD4- ADN de anti-CEA (T84.66-LCHA) Fc pomo 41-1BBL (71-254) monom+AOk-rico

+ADw-400+AD4- 336
caggtgcagc tggtgcagtc tggcgccgaa gtgaagaaac ccggcagcag cgtgaaggtg 60

tcctgcaagg ccagcggctt caacatcaag gacacctaca tgcactgggt gcgccaggcc 120

cctggacagg gactggaatg gatgggcaga atcgaccccg ccaacggcaa cagcaaatac 180

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tctgctagca ccaagggccc atcggtcttc cccctggcac cctcctccaa gagcacctct 420

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tcgtggaact caggcgccct gaccagcggc gtgcacacct tcccggctgt cctacagtcc 540

tcaggactct actccctcag cagcgtggtg accgtgccct ccagcagctt gggcacccag 600

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ggcgctacag tgctgggcct gttcagagtg acccccgaga ttccagccgg cctgccttct 1920

ccaagaagcg aa 1932

+ADw-210+AD4- 337
+ADw-211+AD4- 838
+ADw-212+AD4- PRT
+ADw-213+AD4- Secuencia artificial

+ADw-220+AD4-
+ADw-223+AD4- CEA (T84.66-LCHA) cadena de 4-1BBL dim+AOk-rico de Fc agujero (71-254)

+ADw-400+AD4- 337

Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ser
1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Phe Asn Ile Lys Asp Thr
20 25 30

Tyr Met His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
35 40 45

Gly Arg Ile Asp Pro Ala Asn Gly Asn Ser Lys Tyr Val Pro Lys Phe
50 55 60

Gln Gly Arg Val Thr Ile Thr Ala Asp Thr Ser Thr Ser Thr Ala Tyr
65 70 75 80

Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

```
Ala Pro Phe Gly Tyr Tyr Val Ser Asp Tyr Ala Met Ala Tyr Trp Gly
            100                 105                 110

Gln Gly Thr Leu Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser
        115                 120                 125

Val Phe Pro Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala
    130                 135                 140

Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val
145                 150                 155                 160

Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala
                165                 170                 175

Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val
            180                 185                 190

Pro Ser Ser Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His
        195                 200                 205

Lys Pro Ser Asn Thr Lys Val Asp Lys Lys Val Glu Pro Lys Ser Cys
    210                 215                 220

Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Ala Ala Gly
225                 230                 235                 240

Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met
                245                 250                 255

Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His
            260                 265                 270

Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val
        275                 280                 285

His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr
    290                 295                 300

Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly
305                 310                 315                 320

Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Gly Ala Pro Ile
                325                 330                 335

Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val
```

340 345 350

Cys Thr Leu Pro Pro Ser Arg Asp Glu Leu Thr Lys Asn Gln Val Ser
355 360 365

Leu Ser Cys Ala Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu
370 375 380

Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro
385 390 395 400

Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Val Ser Lys Leu Thr Val
405 410 415

Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met
420 425 430

His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser
435 440 445

Pro Gly Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Arg Glu Gly Pro
450 455 460

Glu Leu Ser Pro Asp Asp Pro Ala Gly Leu Leu Asp Leu Arg Gln Gly
465 470 475 480

Met Phe Ala Gln Leu Val Ala Gln Asn Val Leu Leu Ile Asp Gly Pro
485 490 495

Leu Ser Trp Tyr Ser Asp Pro Gly Leu Ala Gly Val Ser Leu Thr Gly
500 505 510

Gly Leu Ser Tyr Lys Glu Asp Thr Lys Glu Leu Val Val Ala Lys Ala
515 520 525

Gly Val Tyr Tyr Val Phe Phe Gln Leu Glu Leu Arg Arg Val Val Ala
530 535 540

Gly Glu Gly Ser Gly Ser Val Ser Leu Ala Leu His Leu Gln Pro Leu
545 550 555 560

Arg Ser Ala Ala Gly Ala Ala Ala Leu Ala Leu Thr Val Asp Leu Pro
565 570 575

Pro Ala Ser Ser Glu Ala Arg Asn Ser Ala Phe Gly Phe Gln Gly Arg
580 585 590

```
Leu Leu His Leu Ser Ala Gly Gln Arg Leu Gly Val His Leu His Thr
        595                 600                 605

Glu Ala Arg Ala Arg His Ala Trp Gln Leu Thr Gln Gly Ala Thr Val
    610                 615                 620

Leu Gly Leu Phe Arg Val Thr Pro Glu Ile Pro Ala Gly Leu Pro Ser
625                 630                 635                 640

Pro Arg Ser Glu Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Arg Glu
                645                 650                 655

Gly Pro Glu Leu Ser Pro Asp Asp Pro Ala Gly Leu Leu Asp Leu Arg
            660                 665                 670

Gln Gly Met Phe Ala Gln Leu Val Ala Gln Asn Val Leu Leu Ile Asp
        675                 680                 685

Gly Pro Leu Ser Trp Tyr Ser Asp Pro Gly Leu Ala Gly Val Ser Leu
    690                 695                 700

Thr Gly Gly Leu Ser Tyr Lys Glu Asp Thr Lys Glu Leu Val Val Ala
705                 710                 715                 720

Lys Ala Gly Val Tyr Tyr Val Phe Phe Gln Leu Glu Leu Arg Arg Val
                725                 730                 735

Val Ala Gly Glu Gly Ser Gly Ser Val Ser Leu Ala Leu His Leu Gln
            740                 745                 750

Pro Leu Arg Ser Ala Ala Gly Ala Ala Ala Leu Ala Leu Thr Val Asp
        755                 760                 765

Leu Pro Pro Ala Ser Ser Glu Ala Arg Asn Ser Ala Phe Gly Phe Gln
    770                 775                 780

Gly Arg Leu Leu His Leu Ser Ala Gly Gln Arg Leu Gly Val His Leu
785                 790                 795                 800

His Thr Glu Ala Arg Ala Arg His Ala Trp Gln Leu Thr Gln Gly Ala
                805                 810                 815

Thr Val Leu Gly Leu Phe Arg Val Thr Pro Glu Ile Pro Ala Gly Leu
            820                 825                 830

Pro Ser Pro Arg Ser Glu
        835
```

+ADw-210+AD4- 338
+ADw-211+AD4- 644
+ADw-212+AD4- PRT
+ADw-213+AD4- Secuencia artificial

+ADw-220+AD4-
+ADw-223+AD4- cadena anti-CEA (T84.66-LCHA) Fc pomo 4-1BBL (71-254) monom+AOk-rico

+ADw-400+AD4- 338

```
Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ser
1               5                  10                  15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Phe Asn Ile Lys Asp Thr
            20                  25                  30

Tyr Met His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
        35                  40                  45

Gly Arg Ile Asp Pro Ala Asn Gly Asn Ser Lys Tyr Val Pro Lys Phe
    50                  55                  60

Gln Gly Arg Val Thr Ile Thr Ala Asp Thr Ser Thr Ser Thr Ala Tyr
65                  70                  75                  80

Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95

Ala Pro Phe Gly Tyr Tyr Val Ser Asp Tyr Ala Met Ala Tyr Trp Gly
            100                 105                 110

Gln Gly Thr Leu Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser
        115                 120                 125

Val Phe Pro Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala
    130                 135                 140

Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val
145                 150                 155                 160

Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala
                165                 170                 175

Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val
            180                 185                 190

Pro Ser Ser Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His
        195                 200                 205
```

```
Lys Pro Ser Asn Thr Lys Val Asp Lys Lys Val Glu Pro Lys Ser Cys
    210                 215                 220

Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Ala Ala Gly
225                 230                 235                 240

Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met
                245                 250                 255

Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His
            260                 265                 270

Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val
        275                 280                 285

His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr
    290                 295                 300

Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly
305                 310                 315                 320

Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Gly Ala Pro Ile
                325                 330                 335

Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val
            340                 345                 350

Tyr Thr Leu Pro Pro Cys Arg Asp Glu Leu Thr Lys Asn Gln Val Ser
        355                 360                 365

Leu Trp Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu
    370                 375                 380

Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro
385                 390                 395                 400

Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val
                405                 410                 415

Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met
            420                 425                 430

His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser
        435                 440                 445

Pro Gly Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Arg Glu Gly Pro
    450                 455                 460
```

Glu Leu Ser Pro Asp Asp Pro Ala Gly Leu Leu Asp Leu Arg Gln Gly
465 470 475 480

Met Phe Ala Gln Leu Val Ala Gln Asn Val Leu Leu Ile Asp Gly Pro
485 490 495

Leu Ser Trp Tyr Ser Asp Pro Gly Leu Ala Gly Val Ser Leu Thr Gly
500 505 510

Gly Leu Ser Tyr Lys Glu Asp Thr Lys Glu Leu Val Val Ala Lys Ala
515 520 525

Gly Val Tyr Tyr Val Phe Phe Gln Leu Glu Leu Arg Arg Val Val Ala
530 535 540

Gly Glu Gly Ser Gly Ser Val Ser Leu Ala Leu His Leu Gln Pro Leu
545 550 555 560

Arg Ser Ala Ala Gly Ala Ala Ala Leu Ala Leu Thr Val Asp Leu Pro
565 570 575

Pro Ala Ser Ser Glu Ala Arg Asn Ser Ala Phe Gly Phe Gln Gly Arg
580 585 590

Leu Leu His Leu Ser Ala Gly Gln Arg Leu Gly Val His Leu His Thr
595 600 605

Glu Ala Arg Ala Arg His Ala Trp Gln Leu Thr Gln Gly Ala Thr Val
610 615 620

Leu Gly Leu Phe Arg Val Thr Pro Glu Ile Pro Ala Gly Leu Pro Ser
625 630 635 640

Pro Arg Ser Glu

+ADw-210+AD4- 339
+ADw-211+AD4- 2478
+ADw-212+AD4- ADN
+ADw-213+AD4- Secuencia artificial

+ADw-220+AD4-
+ADw-223+AD4- ADN de CEA (T84.66-LCHA) cadena de 4-1BBL dim+AOk-rico de Fc agujero (71-248)

+ADw-400+AD4- 339
caggtgcagc tggtgcagtc tggcgccgaa gtgaagaaac ccggcagcag cgtgaaggtg 60

tcctgcaagg ccagcggctt caacatcaag gacacctaca tgcactgggt gcgccaggcc 120

cctggacagg gactggaatg gatgggcaga atcgaccccg ccaacggcaa cagcaaatac 180
gtgcccaagt tccagggcag agtgaccatc accgccgaca ccagcacctc caccgcctac 240
atggaactga gcagcctgcg gagcgaggac accgccgtgt actactgtgc ccccttcggc 300
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cggcatgctt ggcagctgac tcaggggca actgtgctgg gactgtttcg cgtgacacct 2460

gagatcccag ccgggctc 2478

+ADw-210+AD4- 340
+ADw-211+AD4- 1914
+ADw-212+AD4- ADN
+ADw-213+AD4- Secuencia artificial

+ADw-220+AD4-
+ADw-223+AD4- cadena de ADN de anti-CEA (T84.66-LCHA) Fc pomo 4-1BBL (71-248) monom+AOk-rico

+ADw-400+AD4- 340
caggtgcagc tggtgcagtc tggcgccgaa gtgaagaaac ccggcagcag cgtgaaggtg 60

tcctgcaagg ccagcggctt caacatcaag gacacctaca tgcactgggt gcgccaggcc 120

cctggacagg gactggaatg gatgggcaga atcgaccccg ccaacggcaa cagcaaatac 180

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tctgctagca ccaagggccc atcggtcttc cccctggcac cctcctccaa gagcacctct 420

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ggcgctacag tgctgggcct gttcagagtg acccccgaga ttcctgccgg gctc 1914

+ADw-210+AD4- 341
+ADw-211+AD4- 826
+ADw-212+AD4- PRT
+ADw-213+AD4- Secuencia artificial

+ADw-220+AD4-
+ADw-223+AD4- CEA (T84.66-LCHA) cadena de 4-1BBL dim+AOk-rico de Fc agujero (71-248)

+ADw-400+AD4- 341

Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ser
1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Phe Asn Ile Lys Asp Thr
20 25 30

Tyr Met His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
35 40 45

Gly Arg Ile Asp Pro Ala Asn Gly Asn Ser Lys Tyr Val Pro Lys Phe
50 55 60

Gln Gly Arg Val Thr Ile Thr Ala Asp Thr Ser Thr Ser Thr Ala Tyr
65 70 75 80

Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys

85 90 95

Ala Pro Phe Gly Tyr Tyr Val Ser Asp Tyr Ala Met Ala Tyr Trp Gly
100 105 110

Gln Gly Thr Leu Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser
115 120 125

Val Phe Pro Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala
130 135 140

Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val
145 150 155 160

Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala
165 170 175

Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val
180 185 190

Pro Ser Ser Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His
195 200 205

Lys Pro Ser Asn Thr Lys Val Asp Lys Lys Val Glu Pro Lys Ser Cys
210 215 220

Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Ala Ala Gly
225 230 235 240

Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met
245 250 255

Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His
260 265 270

Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val
275 280 285

His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr
290 295 300

Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly
305 310 315 320

Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Gly Ala Pro Ile
325 330 335

```
Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val
            340                 345                 350

Cys Thr Leu Pro Pro Ser Arg Asp Glu Leu Thr Lys Asn Gln Val Ser
        355                 360                 365

Leu Ser Cys Ala Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu
    370                 375                 380

Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro
385                 390                 395                 400

Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Val Ser Lys Leu Thr Val
                405                 410                 415

Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met
            420                 425                 430

His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser
        435                 440                 445

Pro Gly Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Arg Glu Gly Pro
    450                 455                 460

Glu Leu Ser Pro Asp Asp Pro Ala Gly Leu Leu Asp Leu Arg Gln Gly
465                 470                 475                 480

Met Phe Ala Gln Leu Val Ala Gln Asn Val Leu Leu Ile Asp Gly Pro
                485                 490                 495

Leu Ser Trp Tyr Ser Asp Pro Gly Leu Ala Gly Val Ser Leu Thr Gly
            500                 505                 510

Gly Leu Ser Tyr Lys Glu Asp Thr Lys Glu Leu Val Val Ala Lys Ala
        515                 520                 525

Gly Val Tyr Tyr Val Phe Phe Gln Leu Glu Leu Arg Arg Val Val Ala
    530                 535                 540

Gly Glu Gly Ser Gly Ser Val Ser Leu Ala Leu His Leu Gln Pro Leu
545                 550                 555                 560

Arg Ser Ala Ala Gly Ala Ala Ala Leu Ala Leu Thr Val Asp Leu Pro
                565                 570                 575

Pro Ala Ser Ser Glu Ala Arg Asn Ser Ala Phe Gly Phe Gln Gly Arg
            580                 585                 590
```

```
Leu Leu His Leu Ser Ala Gly Gln Arg Leu Gly Val His Leu His Thr
        595                 600                 605

Glu Ala Arg Ala Arg His Ala Trp Gln Leu Thr Gln Gly Ala Thr Val
    610                 615                 620

Leu Gly Leu Phe Arg Val Thr Pro Glu Ile Pro Ala Gly Leu Gly Gly
625                 630                 635                 640

Gly Gly Ser Gly Gly Gly Gly Ser Arg Glu Gly Pro Glu Leu Ser Pro
                645                 650                 655

Asp Asp Pro Ala Gly Leu Leu Asp Leu Arg Gln Gly Met Phe Ala Gln
            660                 665                 670

Leu Val Ala Gln Asn Val Leu Leu Ile Asp Gly Pro Leu Ser Trp Tyr
        675                 680                 685

Ser Asp Pro Gly Leu Ala Gly Val Ser Leu Thr Gly Gly Leu Ser Tyr
    690                 695                 700

Lys Glu Asp Thr Lys Glu Leu Val Val Ala Lys Ala Gly Val Tyr Tyr
705                 710                 715                 720

Val Phe Phe Gln Leu Glu Leu Arg Arg Val Val Ala Gly Glu Gly Ser
                725                 730                 735

Gly Ser Val Ser Leu Ala Leu His Leu Gln Pro Leu Arg Ser Ala Ala
            740                 745                 750

Gly Ala Ala Ala Leu Ala Leu Thr Val Asp Leu Pro Pro Ala Ser Ser
        755                 760                 765

Glu Ala Arg Asn Ser Ala Phe Gly Phe Gln Gly Arg Leu Leu His Leu
    770                 775                 780

Ser Ala Gly Gln Arg Leu Gly Val His Leu His Thr Glu Ala Arg Ala
785                 790                 795                 800

Arg His Ala Trp Gln Leu Thr Gln Gly Ala Thr Val Leu Gly Leu Phe
                805                 810                 815

Arg Val Thr Pro Glu Ile Pro Ala Gly Leu
            820                 825
```

+ADw-210+AD4- 342
+ADw-211+AD4- 638

+ADw-212+AD4- PRT
+ADw-213+AD4- Secuencia artificial

+ADw-220+AD4-
+ADw-223+AD4- cadena de anti-CEA (T84.66-LCHA) Fc pomo 4-1BBL (71-248) monom+AOk-rico

+ADw-400+AD4- 342

```
Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ser
1               5                   10                  15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Phe Asn Ile Lys Asp Thr
            20                  25                  30

Tyr Met His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
        35                  40                  45

Gly Arg Ile Asp Pro Ala Asn Gly Asn Ser Lys Tyr Val Pro Lys Phe
    50                  55                  60

Gln Gly Arg Val Thr Ile Thr Ala Asp Thr Ser Thr Ser Thr Ala Tyr
65                  70                  75                  80

Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95

Ala Pro Phe Gly Tyr Tyr Val Ser Asp Tyr Ala Met Ala Tyr Trp Gly
            100                 105                 110

Gln Gly Thr Leu Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser
        115                 120                 125

Val Phe Pro Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala
    130                 135                 140

Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val
145                 150                 155                 160

Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala
                165                 170                 175

Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val
            180                 185                 190

Pro Ser Ser Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His
        195                 200                 205

Lys Pro Ser Asn Thr Lys Val Asp Lys Lys Val Glu Pro Lys Ser Cys
    210                 215                 220
```

```
Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Ala Ala Gly
225                 230                 235                 240

Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met
                245                 250                 255

Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His
            260                 265                 270

Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val
        275                 280                 285

His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr
    290                 295                 300

Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly
305                 310                 315                 320

Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Gly Ala Pro Ile
                325                 330                 335

Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val
            340                 345                 350

Tyr Thr Leu Pro Pro Cys Arg Asp Glu Leu Thr Lys Asn Gln Val Ser
        355                 360                 365

Leu Trp Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu
    370                 375                 380

Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro
385                 390                 395                 400

Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val
                405                 410                 415

Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met
            420                 425                 430

His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser
        435                 440                 445

Pro Gly Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Arg Glu Gly Pro
    450                 455                 460

Glu Leu Ser Pro Asp Asp Pro Ala Gly Leu Leu Asp Leu Arg Gln Gly
```

465 470 475 480

Met Phe Ala Gln Leu Val Ala Gln Asn Val Leu Leu Ile Asp Gly Pro
485 490 495

Leu Ser Trp Tyr Ser Asp Pro Gly Leu Ala Gly Val Ser Leu Thr Gly
500 505 510

Gly Leu Ser Tyr Lys Glu Asp Thr Lys Glu Leu Val Val Ala Lys Ala
515 520 525

Gly Val Tyr Tyr Val Phe Phe Gln Leu Glu Leu Arg Arg Val Val Ala
530 535 540

Gly Glu Gly Ser Gly Ser Val Ser Leu Ala Leu His Leu Gln Pro Leu
545 550 555 560

Arg Ser Ala Ala Gly Ala Ala Ala Leu Ala Leu Thr Val Asp Leu Pro
565 570 575

Pro Ala Ser Ser Glu Ala Arg Asn Ser Ala Phe Gly Phe Gln Gly Arg
580 585 590

Leu Leu His Leu Ser Ala Gly Gln Arg Leu Gly Val His Leu His Thr
595 600 605

Glu Ala Arg Ala Arg His Ala Trp Gln Leu Thr Gln Gly Ala Thr Val
610 615 620

Leu Gly Leu Phe Arg Val Thr Pro Glu Ile Pro Ala Gly Leu
625 630 635

+ADw-210+AD4- 343
+ADw-211+AD4- 1353
+ADw-212+AD4- ADN
+ADw-213+AD4- Secuencia artificial

+ADw-220+AD4-
+ADw-223+AD4- ADN de cadena Fc agujero de CEA(T84.66)

+ADw-400+AD4- 343
gaggtgcagc tgcagcagtc tggcgccgaa ctggtggaac ctggcgcctc tgtgaagctg 60

agctgtaccg ccagcggctt caacatcaag gacacctaca tgcactgggt caagcagcgg 120

cctgagcagg gcctggaatg gatcggcaga atcgaccccg ccaacggcaa cagcaaatac 180

gtgcccaagt tccagggcaa ggccaccatc accgccgaca ccagcagcaa cacagcctac 240

ctgcagctga ccagcctgac ctccgaggac accgccgtgt actactgcgc ccccttcggc 300

tactacgtgt ccgactacgc catggcctat tggggccagg gcacaagcgt gaccgtgtcc 360

tctgctagca ccaagggccc ctccgtgttc cccctggccc ccagcagcaa gagcaccagc 420

ggcggcacag ccgctctggg ctgcctggtc aaggactact tccccgagcc cgtgaccgtg 480

tcctggaaca gcggagccct gacctccggc gtgcacacct tccccgccgt gctgcagagt 540

tctggcctgt atagcctgag cagcgtggtc accgtgcctt ctagcagcct gggcacccag 600

acctacatct gcaacgtgaa ccacaagccc agcaacacca aggtggacaa gaaggtggag 660

cccaagagct gcgacaaaac tcacacatgc ccaccgtgcc cagcacctga agctgcaggg 720

ggaccgtcag tcttcctctt cccccaaaa cccaaggaca ccctcatgat ctcccggacc 780

cctgaggtca catgcgtggt ggtggacgtg agccacgaag accctgaggt caagttcaac 840

tggtacgtgg acggcgtgga ggtgcataat gccaagacaa agccgcggga ggagcagtac 900

aacagcacgt accgtgtggt cagcgtcctc accgtcctgc accaggactg gctgaatggc 960

aaggagtaca agtgcaaggt ctccaacaaa gccctcggcg cccccatcga gaaaaccatc 1020

tccaaagcca aagggcagcc ccgagaacca caggtgtgca ccctgccccc atcccgggat 1080

gagctgacca agaaccaggt cagcctctcg tgcgcagtca aaggcttcta tcccagcgac 1140

atcgccgtgg agtgggagag caatgggcag ccggagaaca actacaagac cacgcctccc 1200

gtgctggact ccgacggctc cttcttcctc gtgagcaagc tcaccgtgga caagagcagg 1260

tggcagcagg ggaacgtctt ctcatgctcc gtgatgcatg aggctctgca caaccactac 1320

acgcagaaga gcctctccct gtctccgggt aaa 1353

+ADw-210+AD4- 344
+ADw-211+AD4- 654
+ADw-212+AD4- ADN
+ADw-213+AD4- Secuencia artificial

+ADw-220+AD4-
+ADw-223+AD4- ADN de cadena ligera de anti-CEA(T84.66)

+ADw-400+AD4- 344
gacatcgtgc tgacccagag ccctgcctct ctggccgtgt ctctgggaca gagggccacc 60

atgtcttgca gagccggcga gagcgtggac atcttcggcg tgggatttct gcactggtat 120

cagcagaagc ccggccagcc ccccaagctg ctgatctaca gagccagcaa cctggaaagc 180

ggcatccccg tgcggtttag cggcaccggc agcagaaccg acttcaccct gatcatcgac 240

cccgtggaag ccgacgacgt ggccacctac tactgccagc agaccaacga ggacccctac 300

acctttggcg gaggcaccaa gctggaaatc aagcgtacgg tggctgcacc atctgtcttc 360

atcttcccgc catctgatga gcagttgaaa tctggaactg cctctgttgt gtgcctgctg 420

aataacttct atcccagaga ggccaaagta cagtggaagg tggataacgc cctccaatcg 480

ggtaactccc aggagagtgt cacagagcag gacagcaagg acagcaccta cagcctcagc 540

agcaccctga cgctgagcaa agcagactac gagaaacaca aagtctacgc ctgcgaagtc 600

acccatcagg gcctgagctc gcccgtcaca aagagcttca acaggggaga gtgt 654

+ADw-210+AD4- 345
+ADw-211+AD4- 451
+ADw-212+AD4- PRT
+ADw-213+AD4- Secuencia artificial

+ADw-220+AD4-
+ADw-223+AD4- CEA (T84.66) cadena de Fc agujero

+ADw-400+AD4- 345

Glu Val Gln Leu Gln Gln Ser Gly Ala Glu Leu Val Glu Pro Gly Ala
1 5 10 15

Ser Val Lys Leu Ser Cys Thr Ala Ser Gly Phe Asn Ile Lys Asp Thr
20 25 30

Tyr Met His Trp Val Lys Gln Arg Pro Glu Gln Gly Leu Glu Trp Ile
35 40 45

Gly Arg Ile Asp Pro Ala Asn Gly Asn Ser Lys Tyr Val Pro Lys Phe
50 55 60

Gln Gly Lys Ala Thr Ile Thr Ala Asp Thr Ser Ser Asn Thr Ala Tyr
65 70 75 80

Leu Gln Leu Thr Ser Leu Thr Ser Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Pro Phe Gly Tyr Tyr Val Ser Asp Tyr Ala Met Ala Tyr Trp Gly
100 105 110

Gln Gly Thr Ser Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser
115 120 125

Val Phe Pro Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala
130 135 140

Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val
145 150 155 160

Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala
165 170 175

Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val
180 185 190

```
Pro Ser Ser Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His
        195                 200                 205

Lys Pro Ser Asn Thr Lys Val Asp Lys Lys Val Glu Pro Lys Ser Cys
    210                 215                 220

Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Ala Ala Gly
225                 230                 235                 240

Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met
                245                 250                 255

Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His
            260                 265                 270

Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val
        275                 280                 285

His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr
    290                 295                 300

Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly
305                 310                 315                 320

Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Gly Ala Pro Ile
                325                 330                 335

Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val
            340                 345                 350

Cys Thr Leu Pro Pro Ser Arg Asp Glu Leu Thr Lys Asn Gln Val Ser
        355                 360                 365

Leu Ser Cys Ala Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu
    370                 375                 380

Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro
385                 390                 395                 400

Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Val Ser Lys Leu Thr Val
                405                 410                 415

Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met
            420                 425                 430

His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser
        435                 440                 445
```

Pro Gly Lys
450

+ADw-210+AD4- 346
+ADw-211+AD4- 218
+ADw-212+AD4- PRT
+ADw-213+AD4- Secuencia artificial

+ADw-220+AD4-
+ADw-223+AD4- CEA (T84.66) cadena ligera

+ADw-400+AD4- 346

Asp Ile Val Leu Thr Gln Ser Pro Ala Ser Leu Ala Val Ser Leu Gly
1 5 10 15

Gln Arg Ala Thr Met Ser Cys Arg Ala Gly Glu Ser Val Asp Ile Phe
20 25 30

Gly Val Gly Phe Leu His Trp Tyr Gln Gln Lys Pro Gly Gln Pro Pro
35 40 45

Lys Leu Leu Ile Tyr Arg Ala Ser Asn Leu Glu Ser Gly Ile Pro Val
50 55 60

Arg Phe Ser Gly Thr Gly Ser Arg Thr Asp Phe Thr Leu Ile Ile Asp
65 70 75 80

Pro Val Glu Ala Asp Asp Val Ala Thr Tyr Tyr Cys Gln Gln Thr Asn
85 90 95

Glu Asp Pro Tyr Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys Arg
100 105 110

Thr Val Ala Ala Pro Ser Val Phe Ile Phe Pro Pro Ser Asp Glu Gln
115 120 125

Leu Lys Ser Gly Thr Ala Ser Val Val Cys Leu Leu Asn Asn Phe Tyr
130 135 140

Pro Arg Glu Ala Lys Val Gln Trp Lys Val Asp Asn Ala Leu Gln Ser
145 150 155 160

Gly Asn Ser Gln Glu Ser Val Thr Glu Gln Asp Ser Lys Asp Ser Thr
165 170 175

Tyr Ser Leu Ser Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu Lys
180 185 190

His Lys Val Tyr Ala Cys Glu Val Thr His Gln Gly Leu Ser Ser Pro
195 200 205

Val Thr Lys Ser Phe Asn Arg Gly Glu Cys
210 215

+ADw-210+AD4- 347
+ADw-211+AD4- 2514
+ADw-212+AD4- ADN
+ADw-213+AD4- Secuencia artificial

+ADw-220+AD4-
+ADw-223+AD4- ADN de CEA (T84.66) cadena de 4-1BBL dim+AOk-rico de Fc agujero (71-254)

+ADw-400+AD4- 347
gaggtgcagc tgcagcagtc tggcgccgaa ctggtggaac ctggcgcctc tgtgaagctg 60

agctgtaccg ccagcggctt caacatcaag gacacctaca tgcactgggt caagcagcgg 120

cctgagcagg gcctggaatg gatcggcaga atcgaccccg ccaacggcaa cagcaaatac 180

gtgcccaagt tccagggcaa ggccaccatc accgccgaca ccagcagcaa cacagcctac 240

ctgcagctga ccagcctgac ctccgaggac accgccgtgt actactgcgc ccccttcggc 300

tactacgtgt ccgactacgc catggcctat tggggccagg gcacaagcgt gaccgtgtcc 360

tctgctagca ccaagggccc ctccgtgttc cccctggccc ccagcagcaa gagcaccagc 420

ggcggcacag ccgctctggg ctgcctggtc aaggactact tccccgagcc cgtgaccgtg 480

tcctggaaca gcggagccct gacctccggc gtgcacacct tccccgccgt gctgcagagt 540

tctggcctgt atagcctgag cagcgtggtc accgtgcctt ctagcagcct gggcacccag 600

acctacatct gcaacgtgaa ccacaagccc agcaacacca aggtggacaa gaaggtggag 660

cccaagagct gcgacaaaac tcacacatgc ccaccgtgcc cagcacctga agctgcaggg 720

ggaccgtcag tcttcctctt cccccaaaa cccaaggaca ccctcatgat ctcccggacc 780

cctgaggtca catgcgtggt ggtggacgtg agccacgaag accctgaggt caagttcaac 840

tggtacgtgg acggcgtgga ggtgcataat gccaagacaa agccgcggga ggagcagtac 900

aacagcacgt accgtgtggt cagcgtcctc accgtcctgc accaggactg gctgaatggc 960

aaggagtaca agtgcaaggt ctccaacaaa gccctcggcg cccccatcga gaaaaccatc 1020

tccaaagcca aagggcagcc ccgagaacca caggtgtgca ccctgccccc atcccgggat 1080

gagctgacca agaaccaggt cagcctctcg tgcgcagtca aaggcttcta tcccagcgac 1140

atcgccgtgg agtgggagag caatgggcag ccggagaaca actacaagac cacgcctccc 1200

gtgctggact ccgacggctc cttcttcctc gtgagcaagc tcaccgtgga caagagcagg 1260

tggcagcagg ggaacgtctt ctcatgctcc gtgatgcatg aggctctgca caaccactac 1320

acgcagaaga gcctctccct gtctccgggt ggaggcggcg gaagcggagg aggaggatcc 1380

agagagggcc ctgagctgag ccccgatgat cctgctggac tgctggacct gcggcagggc 1440

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agcgatcctg gactggctgg cgtgtcactg acaggcggcc tgagctacaa agaggacacc 1560

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gaggcccgga atagcgcatt tgggtttcaa ggcaggctgc tgcacctgtc tgccggccag 1800

aggctgggag tgcatctgca cacagaggcc agggctagac acgcctggca gctgacacag 1860

ggcgctacag tgctgggcct gttcagagtg acccccgaga ttccagccgg cctgccttct 1920

ccaagaagcg aaggcggagg cggatctggc ggcggaggat ctagagaggg acccgaactg 1980

tcccctgacg atccagccgg gctgctggat ctgagacagg gaatgttcgc ccagctggtg 2040

gctcagaatg tgctgctgat tgacggacct ctgagctggt actccgaccc agggctggca 2100

ggggtgtccc tgactggggg actgtcctac aaagaagata caaaagaact ggtggtggct 2160

aaagctgggg tgtactatgt gtttttttcag ctggaactga ggcgggtggt ggctggggag 2220

ggctcaggat ctgtgtccct ggctctgcat ctgcagccac tgcgctctgc tgctggcgca 2280

gctgcactgg ctctgactgt ggacctgcca ccagcctcta gcgaggccag aaacagcgcc 2340

ttcgggttcc aaggacgcct gctgcatctg agcgccggac agcgcctggg agtgcatctg 2400

catactgaag ccagagcccg gcatgcttgg cagctgactc agggggcaac tgtgctggga 2460

ctgtttcgcg tgacacctga gatccctgcc ggactgccaa gccctagatc agaa 2514

+ADw-210+AD4- 348
+ADw-211+AD4- 1932
+ADw-212+AD4- ADN
+ADw-213+AD4- Secuencia artificial

+ADw-220+AD4-
+ADw-223+AD4- ADN de CEA (T84.66) cadena de 4-1BBL monom+AOk-rico de Fc pomo (72-254)

+ADw-400+AD4- 348
gaggtgcagc tgcagcagtc tggcgccgaa ctggtggaac ctggcgcctc tgtgaagctg 60

agctgtaccg ccagcggctt caacatcaag gacacctaca tgcactgggt caagcagcgg 120

cctgagcagg gcctggaatg gatcggcaga atcgaccccg ccaacggcaa cagcaaatac 180

gtgcccaagt tccagggcaa ggccaccatc accgccgaca ccagcagcaa cacagcctac 240

ctgcagctga ccagcctgac ctccgaggac accgccgtgt actactgcgc ccccttcggc 300

tactacgtgt ccgactacgc catggcctat tggggccagg gcacaagcgt gaccgtgtcc 360

tctgctagca ccaagggccc atcggtcttc cccctggcac cctcctccaa gagcacctct 420

```
gggggcacag cggccctggg ctgcctggtc aaggactact tccccgaacc ggtgacggtg      480
tcgtggaact caggcgccct gaccagcggc gtgcacacct tcccggctgt cctacagtcc      540
tcaggactct actccctcag cagcgtggtg accgtgccct ccagcagctt gggcacccag      600
acctacatct gcaacgtgaa tcacaagccc agcaacacca aggtggacaa gaaagttgag      660
cccaaatctt gtgacaaaac tcacacatgc ccaccgtgcc cagcacctga agctgcaggg      720
ggaccgtcag tcttcctctt cccccaaaa cccaaggaca ccctcatgat ctcccggacc      780
cctgaggtca catgcgtggt ggtggacgtg agccacgaag accctgaggt caagttcaac      840
tggtacgtgg acggcgtgga ggtgcataat gccaagacaa agccgcggga ggagcagtac      900
aacagcacgt accgtgtggt cagcgtcctc accgtcctgc accaggactg gctgaatggc      960
aaggagtaca agtgcaaggt ctccaacaaa gccctcggcg cccccatcga gaaaaccatc     1020
tccaaagcca aagggcagcc ccgagaacca caggtgtaca ccctgccccc ctgcagagat     1080
gagctgacca agaaccaggt gtccctgtgg tgtctggtca agggcttcta ccccagcgat     1140
atcgccgtgg agtgggagag caacggccag cctgagaaca actacaagac cacccccct      1200
gtgctggaca gcgacggcag cttcttcctg tactccaaac tgaccgtgga caagagccgg     1260
tggcagcagg gcaacgtgtt cagctgcagc gtgatgcacg aggccctgca caaccactac     1320
acccagaagt ccctgagcct gagccccggc ggaggcggcg gaagcggagg aggaggatcc     1380
agagagggcc ctgagctgag ccccgatgat cctgctggac tgctggacct gcggcagggc     1440
atgtttgctc agctggtggc ccagaacgtg ctgctgatcg atggcccct gtcctggtac      1500
agcgatcctg gactggctgg cgtgtcactg acaggcggcc tgagctacaa agaggacacc     1560
aaagaactgg tggtggccaa ggccggcgtg tactacgtgt tctttcagct ggaactgcgg     1620
agagtggtgg ccggcgaagg atctggctct gtgtctctgg ccctgcatct gcagcctctg     1680
agaagcgctg ctggcgctgc agctctggca ctgacagtgg atctgcctcc tgccagctcc     1740
gaggcccgga atagcgcatt tgggtttcaa ggcaggctgc tgcacctgtc tgccggccag     1800
aggctgggag tgcatctgca cacagaggcc agggctagac acgcctggca gctgacacag     1860
ggcgctacag tgctgggcct gttcagagtg acccccgaga ttccagccgg cctgccttct     1920
ccaagaagcg aa                                                         1932
```

+ADw-210+AD4- 349
+ADw-211+AD4- 838
+ADw-212+AD4- PRT
+ADw-213+AD4- Secuencia artificial

+ADw-220+AD4-
+ADw-223+AD4- CEA (T84.66) cadena de 4-1BBL dim+AOk-rico de Fc agujero (71-254)

+ADw-400+AD4- 349

```
Glu Val Gln Leu Gln Gln Ser Gly Ala Glu Leu Val Glu Pro Gly Ala
1               5                  10                  15

Ser Val Lys Leu Ser Cys Thr Ala Ser Gly Phe Asn Ile Lys Asp Thr
            20                  25                  30

Tyr Met His Trp Val Lys Gln Arg Pro Glu Gln Gly Leu Glu Trp Ile
        35                  40                  45

Gly Arg Ile Asp Pro Ala Asn Gly Asn Ser Lys Tyr Val Pro Lys Phe
    50                  55                  60

Gln Gly Lys Ala Thr Ile Thr Ala Asp Thr Ser Ser Asn Thr Ala Tyr
65                  70                  75                  80

Leu Gln Leu Thr Ser Leu Thr Ser Glu Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95

Ala Pro Phe Gly Tyr Tyr Val Ser Asp Tyr Ala Met Ala Tyr Trp Gly
            100                 105                 110

Gln Gly Thr Ser Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser
        115                 120                 125

Val Phe Pro Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala
    130                 135                 140

Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val
145                 150                 155                 160

Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala
                165                 170                 175

Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val
            180                 185                 190

Pro Ser Ser Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His
        195                 200                 205

Lys Pro Ser Asn Thr Lys Val Asp Lys Lys Val Glu Pro Lys Ser Cys
    210                 215                 220

Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Ala Ala Gly
225                 230                 235                 240

Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met
                245                 250                 255
```

```
Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His
            260                 265                 270

Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val
        275                 280                 285

His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr
    290                 295                 300

Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly
305                 310                 315                 320

Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Gly Ala Pro Ile
                325                 330                 335

Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val
            340                 345                 350

Cys Thr Leu Pro Pro Ser Arg Asp Glu Leu Thr Lys Asn Gln Val Ser
        355                 360                 365

Leu Ser Cys Ala Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu
    370                 375                 380

Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro
385                 390                 395                 400

Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Val Ser Lys Leu Thr Val
                405                 410                 415

Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met
            420                 425                 430

His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser
        435                 440                 445

Pro Gly Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Arg Glu Gly Pro
    450                 455                 460

Glu Leu Ser Pro Asp Asp Pro Ala Gly Leu Leu Asp Leu Arg Gln Gly
465                 470                 475                 480

Met Phe Ala Gln Leu Val Ala Gln Asn Val Leu Leu Ile Asp Gly Pro
                485                 490                 495

Leu Ser Trp Tyr Ser Asp Pro Gly Leu Ala Gly Val Ser Leu Thr Gly
```

```
            500                 505                 510

Gly Leu Ser Tyr Lys Glu Asp Thr Lys Glu Leu Val Val Ala Lys Ala
        515                 520                 525

Gly Val Tyr Tyr Val Phe Phe Gln Leu Glu Leu Arg Arg Val Val Ala
    530                 535                 540

Gly Glu Gly Ser Gly Ser Val Ser Leu Ala Leu His Leu Gln Pro Leu
545                 550                 555                 560

Arg Ser Ala Ala Gly Ala Ala Ala Leu Ala Leu Thr Val Asp Leu Pro
                565                 570                 575

Pro Ala Ser Ser Glu Ala Arg Asn Ser Ala Phe Gly Phe Gln Gly Arg
            580                 585                 590

Leu Leu His Leu Ser Ala Gly Gln Arg Leu Gly Val His Leu His Thr
        595                 600                 605

Glu Ala Arg Ala Arg His Ala Trp Gln Leu Thr Gln Gly Ala Thr Val
    610                 615                 620

Leu Gly Leu Phe Arg Val Thr Pro Glu Ile Pro Ala Gly Leu Pro Ser
625                 630                 635                 640

Pro Arg Ser Glu Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Arg Glu
                645                 650                 655

Gly Pro Glu Leu Ser Pro Asp Asp Pro Ala Gly Leu Leu Asp Leu Arg
            660                 665                 670

Gln Gly Met Phe Ala Gln Leu Val Ala Gln Asn Val Leu Leu Ile Asp
        675                 680                 685

Gly Pro Leu Ser Trp Tyr Ser Asp Pro Gly Leu Ala Gly Val Ser Leu
    690                 695                 700

Thr Gly Gly Leu Ser Tyr Lys Glu Asp Thr Lys Glu Leu Val Val Ala
705                 710                 715                 720

Lys Ala Gly Val Tyr Tyr Val Phe Phe Gln Leu Glu Leu Arg Arg Val
                725                 730                 735

Val Ala Gly Glu Gly Ser Gly Ser Val Ser Leu Ala Leu His Leu Gln
            740                 745                 750
```

```
Pro Leu Arg Ser Ala Ala Gly Ala Ala Ala Leu Ala Leu Thr Val Asp
        755                 760                 765

Leu Pro Pro Ala Ser Ser Glu Ala Arg Asn Ser Ala Phe Gly Phe Gln
    770                 775                 780

Gly Arg Leu Leu His Leu Ser Ala Gly Gln Arg Leu Gly Val His Leu
785                 790                 795                 800

His Thr Glu Ala Arg Ala Arg His Ala Trp Gln Leu Thr Gln Gly Ala
                805                 810                 815

Thr Val Leu Gly Leu Phe Arg Val Thr Pro Glu Ile Pro Ala Gly Leu
            820                 825                 830

Pro Ser Pro Arg Ser Glu
        835


+ADw-210+AD4-  350
+ADw-211+AD4-  644
+ADw-212+AD4-  PRT
+ADw-213+AD4-  Secuencia artificial

+ADw-220+AD4-
+ADw-223+AD4-  CEA (T84.66) cadena de 4-1BBL monom+AOk-rico de Fc pomo (71-254)

+ADw-400+AD4-  350

Glu Val Gln Leu Gln Gln Ser Gly Ala Glu Leu Val Glu Pro Gly Ala
1               5                   10                  15

Ser Val Lys Leu Ser Cys Thr Ala Ser Gly Phe Asn Ile Lys Asp Thr
            20                  25                  30

Tyr Met His Trp Val Lys Gln Arg Pro Glu Gln Gly Leu Glu Trp Ile
        35                  40                  45

Gly Arg Ile Asp Pro Ala Asn Gly Asn Ser Lys Tyr Val Pro Lys Phe
    50                  55                  60

Gln Gly Lys Ala Thr Ile Thr Ala Asp Thr Ser Ser Asn Thr Ala Tyr
65                  70                  75                  80

Leu Gln Leu Thr Ser Leu Thr Ser Glu Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95

Ala Pro Phe Gly Tyr Tyr Val Ser Asp Tyr Ala Met Ala Tyr Trp Gly
            100                 105                 110

Gln Gly Thr Ser Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser
```

```
        115                 120                 125

Val Phe Pro Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala
    130                 135                 140

Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val
145                 150                 155                 160

Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala
                165                 170                 175

Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val
            180                 185                 190

Pro Ser Ser Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His
        195                 200                 205

Lys Pro Ser Asn Thr Lys Val Asp Lys Lys Val Glu Pro Lys Ser Cys
    210                 215                 220

Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Ala Ala Gly
225                 230                 235                 240

Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met
                245                 250                 255

Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His
            260                 265                 270

Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val
        275                 280                 285

His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr
    290                 295                 300

Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly
305                 310                 315                 320

Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Gly Ala Pro Ile
                325                 330                 335

Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val
            340                 345                 350

Tyr Thr Leu Pro Pro Cys Arg Asp Glu Leu Thr Lys Asn Gln Val Ser
        355                 360                 365
```

```
Leu Trp Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu
    370                 375                 380

Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro
385                 390                 395                 400

Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val
                405                 410                 415

Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met
            420                 425                 430

His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser
        435                 440                 445

Pro Gly Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Arg Glu Gly Pro
    450                 455                 460

Glu Leu Ser Pro Asp Asp Pro Ala Gly Leu Leu Asp Leu Arg Gln Gly
465                 470                 475                 480

Met Phe Ala Gln Leu Val Ala Gln Asn Val Leu Leu Ile Asp Gly Pro
                485                 490                 495

Leu Ser Trp Tyr Ser Asp Pro Gly Leu Ala Gly Val Ser Leu Thr Gly
            500                 505                 510

Gly Leu Ser Tyr Lys Glu Asp Thr Lys Glu Leu Val Val Ala Lys Ala
        515                 520                 525

Gly Val Tyr Tyr Val Phe Phe Gln Leu Glu Leu Arg Arg Val Val Ala
    530                 535                 540

Gly Glu Gly Ser Gly Ser Val Ser Leu Ala Leu His Leu Gln Pro Leu
545                 550                 555                 560

Arg Ser Ala Ala Gly Ala Ala Ala Leu Ala Leu Thr Val Asp Leu Pro
                565                 570                 575

Pro Ala Ser Ser Glu Ala Arg Asn Ser Ala Phe Gly Phe Gln Gly Arg
            580                 585                 590

Leu Leu His Leu Ser Ala Gly Gln Arg Leu Gly Val His Leu His Thr
        595                 600                 605

Glu Ala Arg Ala Arg His Ala Trp Gln Leu Thr Gln Gly Ala Thr Val
    610                 615                 620
```

Leu Gly Leu Phe Arg Val Thr Pro Glu Ile Pro Ala Gly Leu Pro Ser
625 630 635 640

Pro Arg Ser Glu

+ADw-210+AD4- 351
+ADw-211+AD4- 1287
+ADw-212+AD4- ADN
+ADw-213+AD4- Secuencia artificial

+ADw-220+AD4-
+ADw-223+AD4- ADN de hu NA3B3A2-avi His

+ADw-400+AD4- 351

cagctgacca ccgagtccat gcccttcaac gtggccgagg gcaaagaggt gctgctgctg 60

gtccacaacc tgccccagca gctgttcggc tacagctggt acaagggcga gcgggtggac 120

ggcaaccggc agatcgtggg ctacgccatc ggcacccagc aggccacacc cggccctgcc 180

aatagcggca gagagacaat ctaccccaac gccagcctgc tgatccagaa cgtgacccag 240

aacgacaccg gcttctacac actccaagtc atcaagagcg acctggtcaa cgaggaagcc 300

accggccagt tccacgtgta ccccgagctg cccaagccca gcatcagcag caacaacagc 360

aagcccgtgg aagataagga cgccgtggcc tttacctgcg agcccgaggc ccagaacacc 420

acctacctgt ggtgggtcaa cggccagagc ctgcccgtgt cccccagact ccagctgagc 480

aacggcaaca gaaccctgac cctgttcaac gtgacccgga atgacgccag agcctacgtg 540

tgcggcatcc agaacagcgt gtccgccaac cgcagcgacc ccgtgaccct ggatgtgctg 600

tacggccccg acaccccccat catcagcccc cctgacagca gctacctgag cggcgccaac 660

ctgaacctga gctgccacag cgccagcaac cccagccctc agtacagctg gcggatcaac 720

ggcatccccc agcagcacac ccaggtgctg tttatcgcca agatcacccc caacaacaac 780

ggcacctacg cctgcttcgt gtccaacctg gccaccggcc ggaacaacag catcgtgaag 840

tccatcaccg tgtccgcctc cctgagcccc gtggtggcca agcctcagat caaggccagc 900

aagaccaccg tgaccggcga caaggacagc gtgaacctga cctgctccac caacgatacc 960

ggcatcagca tccggtggtt cttcaagaat cagtccctgc ccagcagcga gcggatgaag 1020

ctgagccagg gcaacatcac cctgtccatc aaccccgtga aaagagagga cgccggcacc 1080

tattggtgcg aggtgttcaa ccccatcagc aagaaccaga gcgaccccat catgctgaac 1140

gtgaactaca acgccctgcc ccaagaaaac ctgatcaatg ttgatctgga agtgctgttc 1200

cagggcccag gcagcggcct gaacgacatc ttcgaagccc agaaaatcga gtggcacgag 1260

gccagagccc accaccacca tcaccac 1287

+ADw-210+AD4- 352
+ADw-211+AD4- 429
+ADw-212+AD4- PRT
+ADw-213+AD4- Secuencia artificial

+ADw-220+AD4-
+ADw-223+AD4- hu NA3B3A2-avi-His

+ADw-400+AD4- 352

```
Gln Leu Thr Thr Glu Ser Met Pro Phe Asn Val Ala Glu Gly Lys Glu
1               5                  10                  15

Val Leu Leu Leu Val His Asn Leu Pro Gln Gln Leu Phe Gly Tyr Ser
            20                  25                  30

Trp Tyr Lys Gly Glu Arg Val Asp Gly Asn Arg Gln Ile Val Gly Tyr
        35                  40                  45

Ala Ile Gly Thr Gln Gln Ala Thr Pro Gly Pro Ala Asn Ser Gly Arg
    50                  55                  60

Glu Thr Ile Tyr Pro Asn Ala Ser Leu Leu Ile Gln Asn Val Thr Gln
65                  70                  75                  80

Asn Asp Thr Gly Phe Tyr Thr Leu Gln Val Ile Lys Ser Asp Leu Val
                85                  90                  95

Asn Glu Glu Ala Thr Gly Gln Phe His Val Tyr Pro Glu Leu Pro Lys
            100                 105                 110

Pro Ser Ile Ser Ser Asn Asn Ser Lys Pro Val Glu Asp Lys Asp Ala
        115                 120                 125

Val Ala Phe Thr Cys Glu Pro Glu Ala Gln Asn Thr Thr Tyr Leu Trp
    130                 135                 140

Trp Val Asn Gly Gln Ser Leu Pro Val Ser Pro Arg Leu Gln Leu Ser
145                 150                 155                 160

Asn Gly Asn Arg Thr Leu Thr Leu Phe Asn Val Thr Arg Asn Asp Ala
                165                 170                 175

Arg Ala Tyr Val Cys Gly Ile Gln Asn Ser Val Ser Ala Asn Arg Ser
            180                 185                 190

Asp Pro Val Thr Leu Asp Val Leu Tyr Gly Pro Asp Thr Pro Ile Ile
        195                 200                 205

Ser Pro Pro Asp Ser Ser Tyr Leu Ser Gly Ala Asn Leu Asn Leu Ser
```

210 215 220

Cys His Ser Ala Ser Asn Pro Ser Pro Gln Tyr Ser Trp Arg Ile Asn
225 230 235 240

Gly Ile Pro Gln Gln His Thr Gln Val Leu Phe Ile Ala Lys Ile Thr
245 250 255

Pro Asn Asn Asn Gly Thr Tyr Ala Cys Phe Val Ser Asn Leu Ala Thr
260 265 270

Gly Arg Asn Asn Ser Ile Val Lys Ser Ile Thr Val Ser Ala Ser Leu
275 280 285

Ser Pro Val Val Ala Lys Pro Gln Ile Lys Ala Ser Lys Thr Thr Val
290 295 300

Thr Gly Asp Lys Asp Ser Val Asn Leu Thr Cys Ser Thr Asn Asp Thr
305 310 315 320

Gly Ile Ser Ile Arg Trp Phe Phe Lys Asn Gln Ser Leu Pro Ser Ser
325 330 335

Glu Arg Met Lys Leu Ser Gln Gly Asn Ile Thr Leu Ser Ile Asn Pro
340 345 350

Val Lys Arg Glu Asp Ala Gly Thr Tyr Trp Cys Glu Val Phe Asn Pro
355 360 365

Ile Ser Lys Asn Gln Ser Asp Pro Ile Met Leu Asn Val Asn Tyr Asn
370 375 380

Ala Leu Pro Gln Glu Asn Leu Ile Asn Val Asp Leu Glu Val Leu Phe
385 390 395 400

Gln Gly Pro Gly Ser Gly Leu Asn Asp Ile Phe Glu Ala Gln Lys Ile
405 410 415

Glu Trp His Glu Ala Arg Ala His His His His His His
420 425

+ADw-210+AD4- 353
+ADw-211+AD4- 1860
+ADw-212+AD4- ADN
+ADw-213+AD4- Secuencia artificial

+ADw-220+AD4-
+ADw-223+AD4- ADN de hu OX40L dim+AOk-rico (51-183) - CL+ACo- cadena de Fc pomo

+ADw-400+AD4- 353

caggtgtccc acagataccc cagaatccag agcatcaagg tgcagttcac cgagtacaag 60

aaagagaagg gcttcatcct gaccagccag aaagaggacg agatcatgaa ggtgcaggac 120

aacagcgtga tcatcaactg cgacggcttc tacctgatca gcctgaaggg ctacttcagc 180

caggaagtgg acatcagcct gcactaccag aaggacgagg aacccctgtt ccagctgaag 240

aaagtgcgga gcgtgaacag cctgatggtg gccagcctga cctacaagga caaggtgtac 300

ctgaacgtga ccaccgacaa caccagcctg gacgacttcc acgtgaacgg cggcgagctg 360

atcctgattc accagaaccc cggcgagttc tgcgtgctgg gaggcggagg atctggcgga 420

ggcggatctc aggtgtcaca ccgctacccc cggattcagt ccattaaggt gcagtttaca 480

gagtataaga aagaaaaagg ctttattctg acttcccaga aagaagatga gattatgaag 540

gtgcaggata attctgtgat catcaattgt gacggcttct acctgatcag cctgaagggc 600

tacttcagcc aggaagtgga catcagcctg cactaccaga aggacgagga acccctgttc 660

cagctgaaga aagtgcggag cgtgaacagc ctgatggtgg ccagcctgac ctacaaggac 720

aaggtgtacc tgaacgtgac caccgacaac accagcctgg acgacttcca cgtgaacggc 780

ggcgagctga tcctgatcca ccagaaccct ggcgagttct gcgtgctggg aggcggaggc 840

tccggagggg gaggatctcg tacggtggct gcaccatctg tctttatctt cccacccagc 900

gaccggaagc tgaagtctgg cacagccagc gtcgtgtgcc tgctgaataa cttctacccc 960

cgcgaggcca aggtgcagtg gaaggtggac aatgccctgc agagcggcaa cagccaggaa 1020

agcgtgaccg agcaggacag caaggactcc acctacagcc tgagcagcac cctgaccctg 1080

agcaaggccg actacgagaa gcacaaggtg tacgcctgcg aagtgaccca ccagggcctg 1140

tctagccccg tgaccaagag cttcaaccgg ggcgagtgcg acaagaccca cacctgtcct 1200

ccatgccctg cccctgaagc tgctggcggc cctagcgtgt tcctgttccc cccaaagccc 1260

aaggacaccc tgatgatcag ccggacccct gaagtgacct gcgtggtggt ggatgtgtcc 1320

cacgaggacc ctgaagtgaa gttcaattgg tacgtggacg gcgtggaagt gcacaatgcc 1380

aagaccaagc cgcgggagga gcagtacaac agcacgtacc gtgtggtcag cgtcctcacc 1440

gtcctgcacc aggactggct gaatggcaag gagtacaagt gcaaggtctc caacaaagcc 1500

ctcggcgccc ccatcgagaa aaccatctcc aaagccaaag ggcagccccg agaaccacag 1560

gtgtacaccc tgcccccatg ccgggatgag ctgaccaaga accaggtcag cctgtggtgc 1620

ctggtcaaag gcttctatcc cagcgacatc gccgtggagt gggagagcaa tgggcagccg 1680

gagaacaact acaagaccac gcctcccgtg ctggactccg acggctcctt cttcctctac 1740

agcaagctca ccgtggacaa gagcaggtgg cagcagggga acgtcttctc atgctccgtg 1800

atgcatgagg ctctgcacaa ccactacacg cagaagagcc tctccctgtc tccgggtaaa 1860

+ADw-210+AD4- 354
+ADw-211+AD4- 738
+ADw-212+AD4- ADN
+ADw-213+AD4- Secuencia artificial

+ADw-220+AD4-
+ADw-223+AD4- ADN de hu OX40L monom+AOk-rico (51-183) - CH1+ACo-

+ADw-400+AD4- 354

caggtgtccc acagataccc cagaatccag agcatcaagg tgcagttcac cgagtacaag 60

aaagagaagg gcttcatcct gaccagccag aaagaggacg agatcatgaa ggtgcaggac 120

aacagcgtga tcatcaactg cgacggcttc tacctgatca gcctgaaggg ctacttcagc 180

caggaagtgg acatcagcct gcactaccag aaggacgagg aacccctgtt ccagctgaag 240

aaagtgcgga gcgtgaacag cctgatggtg gccagcctga cctacaagga caaggtgtac 300

ctgaacgtga ccaccgacaa caccagcctg gacgacttcc acgtgaacgg cggcgagctg 360

atcctgattc accagaaccc cggcgagttc tgcgtgctgg gaggcggagg ttccggaggc 420

ggaggatctg ctagcacaaa gggccccagc gtgttccctc tggccctag cagcaagagc 480

acatctggcg gaacagccgc cctgggctgc ctggtggaag attacttccc cgagcccgtg 540

accgtgtcct ggaattctgg cgccctgaca agcggcgtgc acacctttcc agccgtgctg 600

cagagcagcg gcctgtactc tctgagcagc gtcgtgacag tgcccagcag ctctctgggc 660

acccagacct acatctgcaa cgtgaaccac aagcccagca acaccaaggt ggacgagaag 720

gtggaaccca agtcctgc 738

+ADw-210+AD4- 355
+ADw-211+AD4- 620
+ADw-212+AD4- PRT
+ADw-213+AD4- Secuencia artificial

+ADw-220+AD4-
+ADw-223+AD4- hu OX40L dim+AOk-rico (51-183) - CL+ACo- cadena de Fc pomo

+ADw-400+AD4- 355

Gln Val Ser His Arg Tyr Pro Arg Ile Gln Ser Ile Lys Val Gln Phe
1   5   10   15

Thr Glu Tyr Lys Lys Glu Lys Gly Phe Ile Leu Thr Ser Gln Lys Glu
            20   25   30

Asp Glu Ile Met Lys Val Gln Asp Asn Ser Val Ile Ile Asn Cys Asp
        35   40   45

Gly Phe Tyr Leu Ile Ser Leu Lys Gly Tyr Phe Ser Gln Glu Val Asp
    50   55   60

```
Ile Ser Leu His Tyr Gln Lys Asp Glu Glu Pro Leu Phe Gln Leu Lys
65                  70                  75                  80

Lys Val Arg Ser Val Asn Ser Leu Met Val Ala Ser Leu Thr Tyr Lys
                85                  90                  95

Asp Lys Val Tyr Leu Asn Val Thr Thr Asp Asn Thr Ser Leu Asp Asp
            100                 105                 110

Phe His Val Asn Gly Gly Glu Leu Ile Leu Ile His Gln Asn Pro Gly
        115                 120                 125

Glu Phe Cys Val Leu Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gln
    130                 135                 140

Val Ser His Arg Tyr Pro Arg Ile Gln Ser Ile Lys Val Gln Phe Thr
145                 150                 155                 160

Glu Tyr Lys Lys Glu Lys Gly Phe Ile Leu Thr Ser Gln Lys Glu Asp
                165                 170                 175

Glu Ile Met Lys Val Gln Asp Asn Ser Val Ile Ile Asn Cys Asp Gly
            180                 185                 190

Phe Tyr Leu Ile Ser Leu Lys Gly Tyr Phe Ser Gln Glu Val Asp Ile
        195                 200                 205

Ser Leu His Tyr Gln Lys Asp Glu Glu Pro Leu Phe Gln Leu Lys Lys
    210                 215                 220

Val Arg Ser Val Asn Ser Leu Met Val Ala Ser Leu Thr Tyr Lys Asp
225                 230                 235                 240

Lys Val Tyr Leu Asn Val Thr Thr Asp Asn Thr Ser Leu Asp Asp Phe
                245                 250                 255

His Val Asn Gly Gly Glu Leu Ile Leu Ile His Gln Asn Pro Gly Glu
            260                 265                 270

Phe Cys Val Leu Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Arg Thr
        275                 280                 285

Val Ala Ala Pro Ser Val Phe Ile Phe Pro Pro Ser Asp Arg Lys Leu
    290                 295                 300

Lys Ser Gly Thr Ala Ser Val Val Cys Leu Leu Asn Asn Phe Tyr Pro
305                 310                 315                 320
```

```
Arg Glu Ala Lys Val Gln Trp Lys Val Asp Asn Ala Leu Gln Ser Gly
                325                 330                 335

Asn Ser Gln Glu Ser Val Thr Glu Gln Asp Ser Lys Asp Ser Thr Tyr
            340                 345                 350

Ser Leu Ser Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu Lys His
        355                 360                 365

Lys Val Tyr Ala Cys Glu Val Thr His Gln Gly Leu Ser Ser Pro Val
    370                 375                 380

Thr Lys Ser Phe Asn Arg Gly Glu Cys Asp Lys Thr His Thr Cys Pro
385                 390                 395                 400

Pro Cys Pro Ala Pro Glu Ala Ala Gly Gly Pro Ser Val Phe Leu Phe
                405                 410                 415

Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val
            420                 425                 430

Thr Cys Val Val Val Asp Val Ser His Glu Asp Pro Glu Val Lys Phe
        435                 440                 445

Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys Pro
    450                 455                 460

Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg Val Val Ser Val Leu Thr
465                 470                 475                 480

Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val
                485                 490                 495

Ser Asn Lys Ala Leu Gly Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala
            500                 505                 510

Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Cys Arg
        515                 520                 525

Asp Glu Leu Thr Lys Asn Gln Val Ser Leu Trp Cys Leu Val Lys Gly
    530                 535                 540

Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro
545                 550                 555                 560

Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser
                565                 570                 575
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Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln Gln
            580                 585                 590


Gly Asn Val Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn His
        595                 600                 605


Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly Lys
    610                 615                 620


+ADw-210+AD4-  356
+ADw-211+AD4-  246
+ADw-212+AD4-  PRT
+ADw-213+AD4-  Secuencia artificial

+ADw-220+AD4-
+ADw-223+AD4-  hu OX40L monom+AOk-rico (51-183) - CH1+ACo-

+ADw-400+AD4-  356

Gln Val Ser His Arg Tyr Pro Arg Ile Gln Ser Ile Lys Val Gln Phe
1               5                   10                  15


Thr Glu Tyr Lys Lys Glu Lys Gly Phe Ile Leu Thr Ser Gln Lys Glu
            20                  25                  30


Asp Glu Ile Met Lys Val Gln Asp Asn Ser Val Ile Ile Asn Cys Asp
        35                  40                  45


Gly Phe Tyr Leu Ile Ser Leu Lys Gly Tyr Phe Ser Gln Glu Val Asp
    50                  55                  60


Ile Ser Leu His Tyr Gln Lys Asp Glu Glu Pro Leu Phe Gln Leu Lys
65                  70                  75                  80


Lys Val Arg Ser Val Asn Ser Leu Met Val Ala Ser Leu Thr Tyr Lys
                85                  90                  95


Asp Lys Val Tyr Leu Asn Val Thr Thr Asp Asn Thr Ser Leu Asp Asp
            100                 105                 110


Phe His Val Asn Gly Gly Glu Leu Ile Leu Ile His Gln Asn Pro Gly
        115                 120                 125


Glu Phe Cys Val Leu Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Ala
    130                 135                 140


Ser Thr Lys Gly Pro Ser Val Phe Pro Leu Ala Pro Ser Ser Lys Ser
145                 150                 155                 160
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Thr Ser Gly Gly Thr Ala Ala Leu Gly Cys Leu Val Glu Asp Tyr Phe
                165                 170                 175

Pro Glu Pro Val Thr Val Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly
            180                 185                 190

Val His Thr Phe Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu
        195                 200                 205

Ser Ser Val Val Thr Val Pro Ser Ser Ser Leu Gly Thr Gln Thr Tyr
    210                 215                 220

Ile Cys Asn Val Asn His Lys Pro Ser Asn Thr Lys Val Asp Glu Lys
225                 230                 235                 240

Val Glu Pro Lys Ser Cys
                245


+ADw-210+AD4-  357
+ADw-211+AD4-  121
+ADw-212+AD4-  PRT
+ADw-213+AD4-  Secuencia artificial

+ADw-220+AD4-
+ADw-223+AD4-  CD19 (8B8-2B11) VH

+ADw-400+AD4-  357

Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1               5                   10                  15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Asp Tyr
            20                  25                  30

Ile Met His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
        35                  40                  45

Gly Tyr Ile Asn Pro Tyr Asn Asp Gly Ser Lys Tyr Thr Glu Lys Phe
    50                  55                  60

Gln Gly Arg Val Thr Met Thr Ser Asp Thr Ser Ile Ser Thr Ala Tyr
65                  70                  75                  80

Met Glu Leu Ser Arg Leu Arg Ser Asp Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95

Ala Arg Gly Thr Tyr Tyr Tyr Gly Pro Gln Leu Phe Asp Tyr Trp Gly
            100                 105                 110
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Gln Gly Thr Thr Val Thr Val Ser Ser
        115   120

+ADw-210+AD4- 358
+ADw-211+AD4- 112
+ADw-212+AD4- PRT
+ADw-213+AD4- Secuencia artificial

+ADw-220+AD4-
+ADw-223+AD4- CD19 (8B8-2B11) VL

+ADw-400+AD4- 358

Asp Ile Val Met Thr Gln Thr Pro Leu Ser Leu Ser Val Thr Pro Gly
1   5   10   15

Gln Pro Ala Ser Ile Ser Cys Lys Ser Ser Gln Ser Leu Glu Thr Ser
            20   25   30

Thr Gly Thr Thr Tyr Leu Asn Trp Tyr Leu Gln Lys Pro Gly Gln Ser
        35   40   45

Pro Gln Leu Leu Ile Tyr Arg Val Ser Lys Arg Phe Ser Gly Val Pro
    50   55   60

Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile
65   70   75   80

Ser Arg Val Glu Ala Glu Asp Val Gly Val Tyr Tyr Cys Leu Gln Leu
                85   90   95

Leu Glu Asp Pro Tyr Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys
            100   105   110

+ADw-210+AD4- 359
+ADw-211+AD4- 121
+ADw-212+AD4- PRT
+ADw-213+AD4- Secuencia artificial

+ADw-220+AD4-
+ADw-223+AD4- CD19 (8B8-7H07) VH

+ADw-400+AD4- 359

Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1   5   10   15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Asp Tyr
            20   25   30

Ile Met His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
        35   40   45

Gly Tyr Ile Asn Pro Tyr Asn Asp Gly Ser Lys Tyr Thr Glu Lys Phe
    50   55   60

Gln Gly Arg Val Thr Met Thr Ser Asp Thr Ser Ile Ser Thr Ala Tyr
65   70   75   80

Met Glu Leu Ser Arg Leu Arg Ser Asp Asp Thr Ala Val Tyr Tyr Cys
                85   90   95

Ala Arg Gly Thr Tyr Tyr Tyr Gly Ser Glu Leu Phe Asp Tyr Trp Gly
            100   105   110

Gln Gly Thr Thr Val Thr Val Ser Ser
        115   120

+ADw-210+AD4- 360
+ADw-211+AD4- 112
+ADw-212+AD4- PRT
+ADw-213+AD4- Secuencia artificial

+ADw-220+AD4-
+ADw-223+AD4- CD19 (8B8-7H07) VL

+ADw-400+AD4- 360

Asp Ile Val Met Thr Gln Thr Pro Leu Ser Leu Ser Val Thr Pro Gly
1   5   10   15

Gln Pro Ala Ser Ile Ser Cys Lys Ser Ser Gln Ser Leu Glu Thr Ser
            20   25   30

Thr Gly Asn Thr Tyr Leu Asn Trp Tyr Leu Gln Lys Pro Gly Gln Ser
        35   40   45

Pro Gln Leu Leu Ile Tyr Arg Val Ser Lys Arg Phe Ser Gly Val Pro
    50   55   60

Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile
65   70   75   80

Ser Arg Val Glu Ala Glu Asp Val Gly Val Tyr Tyr Cys Leu Gln Ala
                85   90   95

Thr His Ile Pro Tyr Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys
            100   105   110

+ADw-210+AD4- 361
+ADw-211+AD4- 121
+ADw-212+AD4- PRT
+ADw-213+AD4- Secuencia artificial

+ADw-220+AD4-
+ADw-223+AD4- CD19 (8B8-2B03) VH

+ADw-400+AD4- 361

Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Asp Tyr
20 25 30

Ile Thr His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
35 40 45

Gly Tyr Ile Asn Pro Tyr Asn Asp Gly Ser Lys Tyr Thr Glu Lys Phe
50 55 60

Gln Gly Arg Val Thr Met Thr Ser Asp Thr Ser Ile Ser Thr Ala Tyr
65 70 75 80

Met Glu Leu Ser Arg Leu Arg Ser Asp Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Gly Thr Tyr Tyr Tyr Gly Pro Asp Leu Phe Asp Tyr Trp Gly
100 105 110

Gln Gly Thr Thr Val Thr Val Ser Ser
115 120

+ADw-210+AD4- 362
+ADw-211+AD4- 112
+ADw-212+AD4- PRT
+ADw-213+AD4- Secuencia artificial

+ADw-220+AD4-
+ADw-223+AD4- CD19 (8B8-2B03) VL

+ADw-220+AD4-
+ADw-221+AD4- misc+AF8-feature
+ADw-222+AD4- (107)..(107)
+ADw-223+AD4- Xaa puede ser cualquier amino+AOE-cido de origen natural

+ADw-400+AD4- 362

Asp Ile Val Met Thr Gln Thr Pro Leu Ser Leu Ser Val Thr Pro Gly
1 5 10 15

Gln Pro Ala Ser Ile Ser Cys Lys Ser Ser Gln Ser Leu Glu Thr Ser
20 25 30

Thr Gly Asn Thr Tyr Leu Asn Trp Tyr Leu Gln Lys Pro Gly Gln Ser

35 40 45

Pro Gln Leu Leu Ile Tyr Arg Val Ser Lys Arg Phe Ser Gly Val Pro
50 55 60

Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile
65 70 75 80

Ser Arg Val Glu Ala Glu Asp Val Gly Val Tyr Tyr Cys Leu Gln Leu
85 90 95

Thr His Val Pro Tyr Thr Phe Gly Gln Gly Xaa Lys Leu Glu Ile Lys
100 105 110

+ADw-210+AD4- 363
+ADw-211+AD4- 121
+ADw-212+AD4- PRT
+ADw-213+AD4- Secuencia artificial

+ADw-220+AD4-
+ADw-223+AD4- CD19 (8B8-5A07) VH

+ADw-400+AD4- 363

Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Asp Tyr
20 25 30

Ile Met His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
35 40 45

Gly Tyr Ile Asn Pro Tyr Asn Asp Gly Ser Lys Tyr Thr Glu Lys Phe
50 55 60

Gln Gly Arg Val Thr Met Thr Ser Asp Thr Ser Ile Ser Thr Ala Tyr
65 70 75 80

Met Glu Leu Ser Arg Leu Arg Ser Asp Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Gly Thr Tyr Tyr Tyr Gly Ser Ala Leu Phe Asp Tyr Trp Gly
100 105 110

Gln Gly Thr Thr Val Thr Val Ser Ser
115 120

+ADw-210+AD4- 364
+ADw-211+AD4- 112

+ADw-212+AD4- PRT
+ADw-213+AD4- Secuencia artificial

+ADw-220+AD4-
+ADw-223+AD4- CD19 (8B8-5A07) VL

+ADw-400+AD4- 364

Asp Ile Val Met Thr Gln Thr Pro Leu Ser Leu Ser Val Thr Pro Gly
1 5 10 15

Gln Pro Ala Ser Ile Ser Cys Lys Ser Ser Gln Ser Leu Glu Thr Ser
20 25 30

Thr Gly Asn Thr Tyr Leu Asn Trp Tyr Leu Gln Lys Pro Gly Gln Ser
35 40 45

Pro Gln Leu Leu Ile Tyr Arg Val Ser Lys Arg Phe Ser Gly Val Pro
50 55 60

Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile
65 70 75 80

Ser Arg Val Glu Ala Glu Asp Val Gly Val Tyr Tyr Cys Leu Gln Pro
85 90 95

Gly His Tyr Pro Gly Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys
100 105 110

+ADw-210+AD4- 365
+ADw-211+AD4- 121
+ADw-212+AD4- PRT
+ADw-213+AD4- Secuencia artificial

+ADw-220+AD4-
+ADw-223+AD4- CD19 (8B8-5D08) VH

+ADw-400+AD4- 365

Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Asp Tyr
20 25 30

Ile Met His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
35 40 45

Gly Tyr Ile Asn Pro Tyr Asn Asp Gly Ser Lys Tyr Thr Glu Lys Phe
50 55 60

Gln Gly Arg Val Thr Met Thr Ser Asp Thr Ser Ile Ser Thr Ala Tyr

65 70 75 80

Met Glu Leu Ser Arg Leu Arg Ser Asp Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Gly Thr Tyr Tyr Tyr Gly Ser Glu Leu Phe Asp Tyr Trp Gly
100 105 110

Gln Gly Thr Thr Val Thr Val Ser Ser
115 120

+ADw-210+AD4- 366
+ADw-211+AD4- 112
+ADw-212+AD4- PRT
+ADw-213+AD4- Secuencia artificial

+ADw-220+AD4-
+ADw-223+AD4- CD19 (8B8-5D08) VL

+ADw-400+AD4- 366

Asp Ile Val Met Thr Gln Thr Pro Leu Ser Leu Ser Val Thr Pro Gly
1 5 10 15

Gln Pro Ala Ser Ile Ser Cys Lys Ser Ser Gln Ser Leu Glu Thr Ser
20 25 30

Thr Gly Asn Thr Tyr Leu Asn Trp Tyr Leu Gln Lys Pro Gly Gln Ser
35 40 45

Pro Gln Leu Leu Ile Tyr Arg Val Ser Lys Arg Phe Ser Gly Val Pro
50 55 60

Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile
65 70 75 80

Ser Arg Val Glu Ala Glu Asp Val Gly Val Tyr Tyr Cys Leu Gln Leu
85 90 95

Thr His Glu Pro Tyr Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys
100 105 110

+ADw-210+AD4- 367
+ADw-211+AD4- 121
+ADw-212+AD4- PRT
+ADw-213+AD4- Secuencia artificial

+ADw-220+AD4-
+ADw-223+AD4- CD19 (8B8-5B08) VH

+ADw-400+AD4- 367

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Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1               5                   10                  15


Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Asp Tyr
            20                  25                  30


Ile Met His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
        35                  40                  45


Gly Tyr Ile Asn Pro Tyr Asn Asp Gly Ser Lys Tyr Thr Glu Lys Phe
    50                  55                  60


Gln Gly Arg Val Thr Met Thr Ser Asp Thr Ser Ile Ser Thr Ala Tyr
65                  70                  75                  80


Met Glu Leu Ser Arg Leu Arg Ser Asp Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95


Ala Arg Gly Thr Tyr Tyr Tyr Gly Pro Gln Leu Phe Asp Tyr Trp Gly
            100                 105                 110


Gln Gly Thr Thr Val Thr Val Ser Ser
        115                 120


+ADw-210+AD4-  368
+ADw-211+AD4-  112
+ADw-212+AD4-  PRT
+ADw-213+AD4-  Secuencia artificial

+ADw-220+AD4-
+ADw-223+AD4-  CD19 (8B8-5B08) VL

+ADw-400+AD4-  368

Asp Ile Val Met Thr Gln Thr Pro Leu Ser Leu Ser Val Thr Pro Gly
1               5                   10                  15


Gln Pro Ala Ser Ile Ser Cys Lys Ser Ser Gln Ser Leu Glu Thr Ser
            20                  25                  30


Thr Gly Asn Thr Tyr Leu Asn Trp Tyr Leu Gln Lys Pro Gly Gln Ser
        35                  40                  45


Pro Gln Leu Leu Ile Tyr Arg Val Ser Lys Arg Phe Ser Gly Val Pro
    50                  55                  60


Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile
65                  70                  75                  80


Ser Arg Val Glu Ala Glu Asp Val Gly Val Tyr Tyr Cys Leu Gln Leu
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85 90 95

Asp Ser Tyr Pro Asn Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys
100 105 110

+ADw-210+AD4- 369
+ADw-211+AD4- 121
+ADw-212+AD4- PRT
+ADw-213+AD4- Secuencia artificial

+ADw-220+AD4-
+ADw-223+AD4- CD19 (8B8-5H09) VH

+ADw-400+AD4- 369

Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Asp Tyr
20 25 30

Ile Met His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
35 40 45

Gly Tyr Ile Asn Pro Tyr Asn Asp Gly Ser Lys Tyr Thr Glu Lys Phe
50 55 60

Gln Gly Arg Val Thr Met Thr Ser Asp Thr Ser Ile Ser Thr Ala Tyr
65 70 75 80

Met Glu Leu Ser Arg Leu Arg Ser Asp Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Gly Thr Tyr Tyr Tyr Gly Ser Ala Leu Phe Asp Tyr Trp Gly
100 105 110

Gln Gly Thr Thr Val Thr Val Ser Ser
115 120

+ADw-210+AD4- 370
+ADw-211+AD4- 112
+ADw-212+AD4- PRT
+ADw-213+AD4- Secuencia artificial

+ADw-220+AD4-
+ADw-223+AD4- CD19 (8B8-5H09) VL

+ADw-400+AD4- 370

Asp Ile Val Met Thr Gln Thr Pro Leu Ser Leu Ser Val Thr Pro Gly
1 5 10 15

Gln Pro Ala Ser Ile Ser Cys Lys Ser Ser Gln Ser Leu Glu Ser Ser
20 25 30

Thr Gly Asn Thr Tyr Leu Asn Trp Tyr Leu Gln Lys Pro Gly Gln Ser
35 40 45

Pro Gln Leu Leu Ile Tyr Arg Val Ser Lys Arg Phe Ser Gly Val Pro
50 55 60

Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile
65 70 75 80

Ser Arg Val Glu Ala Glu Asp Val Gly Val Tyr Tyr Cys Leu Gln Leu
85 90 95

Ile Asp Tyr Pro Val Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys
100 105 110

+ADw-210+AD4- 371
+ADw-211+AD4- 276
+ADw-212+AD4- PRT
+ADw-213+AD4- Secuencia artificial

+ADw-220+AD4-
+ADw-223+AD4- hu OX40L dim+AOk-rico (51-183) conectado mediante el enlazador (G4S)2

+ADw-400+AD4- 371

Gln Val Ser His Arg Tyr Pro Arg Ile Gln Ser Ile Lys Val Gln Phe
1 5 10 15

Thr Glu Tyr Lys Lys Glu Lys Gly Phe Ile Leu Thr Ser Gln Lys Glu
20 25 30

Asp Glu Ile Met Lys Val Gln Asn Asn Ser Val Ile Ile Asn Cys Asp
35 40 45

Gly Phe Tyr Leu Ile Ser Leu Lys Gly Tyr Phe Ser Gln Glu Val Asn
50 55 60

Ile Ser Leu His Tyr Gln Lys Asp Glu Glu Pro Leu Phe Gln Leu Lys
65 70 75 80

Lys Val Arg Ser Val Asn Ser Leu Met Val Ala Ser Leu Thr Tyr Lys
85 90 95

Asp Lys Val Tyr Leu Asn Val Thr Thr Asp Asn Thr Ser Leu Asp Asp
100 105 110

```
Phe His Val Asn Gly Gly Glu Leu Ile Leu Ile His Gln Asn Pro Gly
        115                 120                 125

Glu Phe Cys Val Leu Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gln
    130                 135                 140

Val Ser His Arg Tyr Pro Arg Ile Gln Ser Ile Lys Val Gln Phe Thr
145                 150                 155                 160

Glu Tyr Lys Lys Glu Lys Gly Phe Ile Leu Thr Ser Gln Lys Glu Asp
                165                 170                 175

Glu Ile Met Lys Val Gln Asn Asn Ser Val Ile Ile Asn Cys Asp Gly
            180                 185                 190

Phe Tyr Leu Ile Ser Leu Lys Gly Tyr Phe Ser Gln Glu Val Asn Ile
        195                 200                 205

Ser Leu His Tyr Gln Lys Asp Glu Glu Pro Leu Phe Gln Leu Lys Lys
    210                 215                 220

Val Arg Ser Val Asn Ser Leu Met Val Ala Ser Leu Thr Tyr Lys Asp
225                 230                 235                 240

Lys Val Tyr Leu Asn Val Thr Thr Asp Asn Thr Ser Leu Asp Asp Phe
                245                 250                 255

His Val Asn Gly Gly Glu Leu Ile Leu Ile His Gln Asn Pro Gly Glu
            260                 265                 270

Phe Cys Val Leu
        275


+ADw-210+AD4-  372
+ADw-211+AD4-  274
+ADw-212+AD4-  PRT
+ADw-213+AD4-  Secuencia artificial

+ADw-220+AD4-
+ADw-223+AD4-  hu OX40L dim+AOk-rico (52-183) conectado mediante el enlazador
(G4S)2

+ADw-400+AD4-  372

Val Ser His Arg Tyr Pro Arg Ile Gln Ser Ile Lys Val Gln Phe Thr
1               5                   10                  15

Glu Tyr Lys Lys Glu Lys Gly Phe Ile Leu Thr Ser Gln Lys Glu Asp
            20                  25                  30
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```
Glu Ile Met Lys Val Gln Asn Asn Ser Val Ile Ile Asn Cys Asp Gly
        35                  40                  45

Phe Tyr Leu Ile Ser Leu Lys Gly Tyr Phe Ser Gln Glu Val Asn Ile
    50                  55                  60

Ser Leu His Tyr Gln Lys Asp Glu Glu Pro Leu Phe Gln Leu Lys Lys
65                  70                  75                  80

Val Arg Ser Val Asn Ser Leu Met Val Ala Ser Leu Thr Tyr Lys Asp
                85                  90                  95

Lys Val Tyr Leu Asn Val Thr Thr Asp Asn Thr Ser Leu Asp Asp Phe
            100                 105                 110

His Val Asn Gly Gly Glu Leu Ile Leu Ile His Gln Asn Pro Gly Glu
        115                 120                 125

Phe Cys Val Leu Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Val Ser
    130                 135                 140

His Arg Tyr Pro Arg Ile Gln Ser Ile Lys Val Gln Phe Thr Glu Tyr
145                 150                 155                 160

Lys Lys Glu Lys Gly Phe Ile Leu Thr Ser Gln Lys Glu Asp Glu Ile
                165                 170                 175

Met Lys Val Gln Asn Asn Ser Val Ile Ile Asn Cys Asp Gly Phe Tyr
            180                 185                 190

Leu Ile Ser Leu Lys Gly Tyr Phe Ser Gln Glu Val Asn Ile Ser Leu
        195                 200                 205

His Tyr Gln Lys Asp Glu Glu Pro Leu Phe Gln Leu Lys Lys Val Arg
    210                 215                 220

Ser Val Asn Ser Leu Met Val Ala Ser Leu Thr Tyr Lys Asp Lys Val
225                 230                 235                 240

Tyr Leu Asn Val Thr Thr Asp Asn Thr Ser Leu Asp Asp Phe His Val
                245                 250                 255

Asn Gly Gly Glu Leu Ile Leu Ile His Gln Asn Pro Gly Glu Phe Cys
            260                 265                 270

Val Leu
```

+ADw-210+AD4- 373
+ADw-211+AD4- 164
+ADw-212+AD4- PRT
+ADw-213+AD4- Secuencia artificial

+ADw-220+AD4-
+ADw-223+AD4- hu 4-1BBL (85-248)

+ADw-400+AD4- 373

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Leu Asp Leu Arg Gln Gly Met Phe Ala Gln Leu Val Ala Gln Asn Val
1               5                  10                  15

Leu Leu Ile Asp Gly Pro Leu Ser Trp Tyr Ser Asp Pro Gly Leu Ala
            20                  25                  30

Gly Val Ser Leu Thr Gly Gly Leu Ser Tyr Lys Glu Asp Thr Lys Glu
        35                  40                  45

Leu Val Val Ala Lys Ala Gly Val Tyr Tyr Val Phe Phe Gln Leu Glu
    50                  55                  60

Leu Arg Arg Val Val Ala Gly Glu Gly Ser Gly Ser Val Ser Leu Ala
65                  70                  75                  80

Leu His Leu Gln Pro Leu Arg Ser Ala Ala Gly Ala Ala Ala Leu Ala
                85                  90                  95

Leu Thr Val Asp Leu Pro Pro Ala Ser Ser Glu Ala Arg Asn Ser Ala
            100                 105                 110

Phe Gly Phe Gln Gly Arg Leu Leu His Leu Ser Ala Gly Gln Arg Leu
        115                 120                 125

Gly Val His Leu His Thr Glu Ala Arg Ala Arg His Ala Trp Gln Leu
    130                 135                 140

Thr Gln Gly Ala Thr Val Leu Gly Leu Phe Arg Val Thr Pro Glu Ile
145                 150                 155                 160

Pro Ala Gly Leu
```

+ADw-210+AD4- 374
+ADw-211+AD4- 169
+ADw-212+AD4- PRT
+ADw-213+AD4- Secuencia artificial

+ADw-220+AD4-
+ADw-223+AD4- hu 4-1BBL (80-248)

+ADw-400+AD4- 374

Asp Pro Ala Gly Leu Leu Asp Leu Arg Gln Gly Met Phe Ala Gln Leu
1   5   10   15

Val Ala Gln Asn Val Leu Leu Ile Asp Gly Pro Leu Ser Trp Tyr Ser
            20   25   30

Asp Pro Gly Leu Ala Gly Val Ser Leu Thr Gly Gly Leu Ser Tyr Lys
        35   40   45

Glu Asp Thr Lys Glu Leu Val Val Ala Lys Ala Gly Val Tyr Tyr Val
    50   55   60

Phe Phe Gln Leu Glu Leu Arg Arg Val Val Ala Gly Glu Gly Ser Gly
65   70   75   80

Ser Val Ser Leu Ala Leu His Leu Gln Pro Leu Arg Ser Ala Ala Gly
                85   90   95

Ala Ala Ala Leu Ala Leu Thr Val Asp Leu Pro Pro Ala Ser Ser Glu
            100   105   110

Ala Arg Asn Ser Ala Phe Gly Phe Gln Gly Arg Leu Leu His Leu Ser
        115   120   125

Ala Gly Gln Arg Leu Gly Val His Leu His Thr Glu Ala Arg Ala Arg
    130   135   140

His Ala Trp Gln Leu Thr Gln Gly Ala Thr Val Leu Gly Leu Phe Arg
145   150   155   160

Val Thr Pro Glu Ile Pro Ala Gly Leu
                165

+ADw-210+AD4- 375
+ADw-211+AD4- 197
+ADw-212+AD4- PRT
+ADw-213+AD4- Secuencia artificial

+ADw-220+AD4-
+ADw-223+AD4- hu 4-1BBL (52-248)

+ADw-400+AD4- 375

Pro Trp Ala Val Ser Gly Ala Arg Ala Ser Pro Gly Ser Ala Ala Ser
1   5   10   15

Pro Arg Leu Arg Glu Gly Pro Glu Leu Ser Pro Asp Asp Pro Ala Gly
            20   25   30

```
Leu Leu Asp Leu Arg Gln Gly Met Phe Ala Gln Leu Val Ala Gln Asn
        35                  40                  45

Val Leu Leu Ile Asp Gly Pro Leu Ser Trp Tyr Ser Asp Pro Gly Leu
    50                  55                  60

Ala Gly Val Ser Leu Thr Gly Gly Leu Ser Tyr Lys Glu Asp Thr Lys
65                  70                  75                  80

Glu Leu Val Val Ala Lys Ala Gly Val Tyr Tyr Val Phe Phe Gln Leu
                85                  90                  95

Glu Leu Arg Arg Val Val Ala Gly Glu Gly Ser Gly Ser Val Ser Leu
            100                 105                 110

Ala Leu His Leu Gln Pro Leu Arg Ser Ala Ala Gly Ala Ala Ala Leu
        115                 120                 125

Ala Leu Thr Val Asp Leu Pro Pro Ala Ser Ser Glu Ala Arg Asn Ser
    130                 135                 140

Ala Phe Gly Phe Gln Gly Arg Leu Leu His Leu Ser Ala Gly Gln Arg
145                 150                 155                 160

Leu Gly Val His Leu His Thr Glu Ala Arg Ala Arg His Ala Trp Gln
                165                 170                 175

Leu Thr Gln Gly Ala Thr Val Leu Gly Leu Phe Arg Val Thr Pro Glu
            180                 185                 190

Ile Pro Ala Gly Leu
        195
```

Señor
SUPERINTENDENTE DE INDUSTRIA Y COMERCIO
DIVISION DE NUEVAS CREACIONES
E. S. D.

Trámite: 11
Evento: 378
Actuación: 851

Re: PI.-**F. HOFFMANN-LA ROCHE AG**.-Solicitud de Patente de Invención en Fase Nacional PCT para **"MOLÉCULAS DE UNIÓN A ANTÍGENO QUE COMPRENDEN UN TRÍMERO DE LIGANDO DE LA FAMILIA DE TNF"**.-Clase **C07K 14/705**.-Expediente NC2017/0003212.-Div.-

1. Me refiero al auto dictado por ese Despacho mediante notificación en línea de Mayo 05 de 2017 mediante el Oficio N 6377.

2. **PRESENTACIÓN DE SOLICITUD DIVISIONAL.**

Inicialmente, con el fin de dar respuesta a las objeciones de la examinadora, y dado que la Resolución No. 3719 de 2016 establece que "*Una solicitud divisional podrá presentarse como resultado del requerimiento efectuado por la Dirección de Nuevas Creaciones, en aquellos casos en que se determina que la solicitud inicial carece de unidad de invención.* ***La Dirección de nuevas Creaciones señalará la manera en que deberá presentarse la o las solicitudes fraccionarias***" (énfasis añadido), me permito manifestar que es deseo del solicitante dividir la presente solicitud de patente en dos (2) solicitudes **siguiendo los grupos inventivos planteados por la examinadora**, a saber:

i. Una solicitud **original** compuesta por un capítulo reivindicatorio de **22 reivindicaciones**, las cuales se encuentran en el memorial como parte de la respuesta al requerimiento elevado por la SIC mediante **Oficio N° 6377**; y

ii. Una **solicitud divisional** que comprende **22 reivindicaciones** que encuentran pleno sustento en el capítulo reivindicatorio de la solicitud original y en la memoria descriptiva presentada a este Despacho con la presente solicitud divisional.

En conexión con lo anterior, me permito resaltar que la anterior división de materia **responde a los grupos inventivos planteados por la examinadora** en su objeción a la unidad de invención de la presente solicitud,

A continuación especifico, de manera detallada, la división de materia en cada una de las solicitudes anteriormente mencionadas:

a) ***Capítulo reivindicatorio de la solicitud original*** **N° NC2017/0003212: "MOLÉCULAS DE UNIÓN A ANTÍGENO QUE COMPREDEN UN TRÍMERO DE LIGANDO DE LA FAMILIA TNF" presentado ante su Despacho como parte de la respuesta al requerimiento elevado por la SIC mediante Oficio N° 6377.**

Con base en lo anteriormente mencionado, la solicitud original ahora cuenta con un **capítulo reivindicatorio modificado** compuesto por **22 reivindicaciones**, las cuales comprenden el Grupo I planteado por la examinadora, a saber:

Grupo I (planteado por la examinadora): Molécula de unión a antígeno que contiene trímero de ligando de la familia de TNF, donde dicho miembro es 4-1BBL y donde la molécula comprende: i) un sitio de unión a FAP que contiene una primera cadena pesada con un dominio VH que comprenden la SEQ ID NO: 16 y una primera cadena ligera con un dominio VL que comprende la SEQ ID NO: 17, o una primera cadena pesada con un dominio VH que comprende la SEQ ID NO: 106 y una primera cadena ligera con un dominio VL que comprende la SEQ ID NO: 107, (ii) una segunda cadena pesada que comprende la secuencia de aminoácidos seleccionada entre el grupo que consiste en SEQ ID NO: 5, SEQ ID NO: 97, SEQ ID NO: 98, SEQ ID NO: 99, SEQ ID NO: 14, SEQ ID NO: 108, SEQ ID NO: 111, SEQ ID NO: 113, SEQ ID NO: 115, SEQ ID NO: 117, SEQ ID NO: 119 y SEQ ID NO: 173, y (iii) una segunda cadena ligera que comprende la secuencia de aminoácidos seleccionada entre el grupo que consiste en SEQ ID NO: 1, SEQ ID NO: 96, SEQ ID NO: 3, SEQ ID NO: 4, SEQ ID NO: 15, SEQ ID NO: 109, SEQ ID NO: 110, SEQ ID NO: 112, SEQ ID NO: 114, SEQ ID NO: 116, SEQ ID NO: 118, SEQ ID NO: 120 y SEQ ID NO: 174. Así mismo, hace parte de este grupo inventivo la molécula de unión de la reivindicación 31.

b) ***Capítulo reivindicatorio de la solicitud divisional: "MOLÉCULAS DE UNIÓN A ANTÍGENO QUE COMPREDEN UN TRÍMERO DE LIGANDO DE LA FAMILIA TNF".***

La **solicitud divisional** cuenta con un **capítulo reivindicatorio** compuesto por **22 reivindicaciones**, las cuales comprenden el Grupo II planteado por la examinadora, a saber:

Grupo II (planteado por la examinadora): Molécula de unión a antígeno que contiene trímero de ligando de la familia de TNF, donde dicho miembro es 4-1BBL y donde la molécula comprende: i) un sitio de unión a CD19 que contiene una primera

cadena pesada con un dominio VH que comprenden la SEQ ID NO: 201 y una primera cadena ligera con un dominio VL que comprende la SEQ ID NO: 202, o una primera cadena pesada con un dominio VH que comprende la SEQ ID NO: 357 y una primera cadena ligera con un dominio VL que comprende la SEQ ID NO: 358, (ii) una segunda cadena pesada que comprende la secuencia de aminoácidos seleccionada entre el grupo que consiste en SEQ ID NO: 14, SEQ ID NO: 108, SEQ ID NO: 111, SEQ ID NO: 113, SEQ ID NO:115, SEQ ID NO: 117, SEQ ID NO: 119 y SEQ ID NO: 173, y (iii) una segunda cadena ligera que comprende la secuencia de aminoácidos seleccionada entre el grupo que consiste en SEQ ID NO: 15, SEQ ID NO: 109, SEQ ID NO: 110, SEQ ID NO: 112, SEQ ID NO: 114, SEQ ID NO: 116, SEQ ID NO: 118, SEQ ID NO: 120 y SEQ ID NO: 174. Así mismo, hace parte de este grupo inventivo la molécula de unión de la reivindicación 37.

De acuerdo con lo anterior, el capítulo reivindicatorio actualmente presentado de la solicitud parental NC2017/0003212 fue dividido **de acuerdo con los grupos inventivos planteados por la examinadora.** Tal división atiende a cabalidad de objeción plantada en el **Oficio N° 6377**, y por consiguiente, el capítulo presentado para la presente divisional cumple a cabalidad con los requerimientos establecidos en el Capítulo Primero, Título X de la Circular Única respecto a la división de solicitudes de patentes.

2.1. De conformidad con todo lo anterior, a continuación especifico los documentos anexos al presente memorial y que se relacionan con la solicitud divisional resultante del presente fraccionamiento:

***Solicitud divisional*: "MOLÉCULAS DE UNIÓN A ANTÍGENO QUE COMPREDEN UN TRÍMERO DE LIGANDO DE LA FAMILIA TNF".**

(a) Me permito mencionar que los respectivos pagos por **i)** los derechos que causa el presente fraccionamiento, **ii)** el pago de Examen de Patentabilidad y **iii)** Pago de las reivindicaciones adicionales **11 a 22,** se efectuaron a través de la plataforma SIPI.

(b) Nuevo Resumen-Objeto y Finalidad de la Invención (formato digital);

(c) Páginas **1 a 506** del texto de la descripción de la solicitud divisional (formato digital);

(d) Páginas **507 a 513** que corresponden al nuevo capítulo reivindicatorio compuesto por **22 reivindicaciones** que, como se comentó previamente, encuentran pleno sustento en la descripción de la presente invención (formato digital);

(e) Copia del documento que acredita a la suscrita ALICIA LLOREDA, y/o a la doctor GUSTAVO TAMAYO, y/o al doctor IGNACIO SANTAMARIA y/o al doctor ENRIQUE ALVAREZ, en los términos del Párrafo 1º del Artículo 543 del Decreto-Ley 410 de 1971, como Representantes Legales en Bogotá para todos los asuntos relacionados con la Propiedad Industrial de la sociedad **F. HOFFMANN-LA ROCHE AG.,** domiciliada en Basilea, Suiza. (formato digital);

(f) Listado de secuencias (formato digital);

(g) Figuras (formato digital); y

(h) Formato Único de Conversión, División y Fusión de Solicitudes.

2.2. En cuanto a la reivindicación de la prioridad respecto de la solicitud divisional, es la misma invocada en la solicitud original, la cual fue reivindicada oportunamente en Fase Internacional de las solicitudes número: EP 14193260.8 del 14 de noviembre de 2014, EP 15183736.6 del 3 de septiembre de 2015 y EP 15188142.2 del 2 de octubre de 2015.

2.3. Ratifico a usted que la sociedad titular de la solicitud fraccionada en cuestión es **F. HOFFMANN–LA ROCHE AG.,** domiciliada en domiciliada en Basilea, Suiza.

2.4. De conformidad con lo establecido por el Artículo 36 de la Decisión 486 de 2000, solicito a ese Despacho se sirva aceptar y estudiar la solicitud divisional presentada y conceder el privilegio de patente solicitado.

Señor Superintendente,

ALICIA LLOREDA RICAURTE

T.P. 53.215

Industria y Comercio
SUPERINTENDENCIA

Trámite: 11
Evento: 378
Actuación: 851

DIRECCIÓN DE NUEVAS CREACIONES
CONVERSIÓN, DIVISIÓN Y FUSIÓN DE SOLICITUDES

1. Identificación del Tramite

[ ] Conversión [X] División [ ] Fusión

[X] Patente de Invención
[ ] Patente de Modelo de Utilidad

2. Datos del solicitante

[ ] Persona Natural [X] Persona Juridica

F. HOFFMANN-LA ROCHE AG
Nombre o denominación / Nombre o razón social

ALICIA LLOREDA RICAURTE
Nombre del representante legal

Tipo de empresa [ ] Micro [ ] Pequeña [ ] Mediana [X] Otra

Documento de Identificación [X] C.C. [ ] C.E. [ ] NIT [ ] Otro Número **C.C. 39.690.713**

Nacionalidad/País de constitución	Dirección del titular	Ciudad
Suiza	Grenzacherstrasse 124, CH-4070 Basilea, Suiza.	Basilea
Dirección electrónica	**No. Fax**	**Número telefónico**
notificacionespatentes@lloredacamacho.com	6069701	3264270

[X] **Autorizo expresamente a la Superintendencia de Industria y Comercio para que todas las comunicaciones sean enviadas a través de la dirección de correo electrónico**

3. Datos del apoderado:

LLOREDA RICAURTE ALICIA	**C.C. 39.690.713**	**53.215**
Apellidos y Nombre	Documento de identificación	Tarjeta profesional

Dirección y domicilio	Dirección del titular	Ciudad
Calle 72 No. 5-83 Piso 5º		Bogotá D.C.
Dirección electrónica	**No. Fax**	**Número telefónico**
notificacionespatentes@lloredacamacho.com	6069701	3264270

En caso de haber presentado poder general para asuntos que se adelanten ante la Delegatura de Propiedad Industrial, sírvase indicar el número de su radicación o protocolo de poder general _____

4. Datos del trámite:

CONVERSION	DIVISION	FUSION
Expediente No.	Expediente No. **NC2017/0003212**	Expediente No.
De:	No. de divisionales **1**	Expediente No.
A:		

5. Comprobante de Pago No El pago se realizó por medio de la plataforma SIPI **(05-09-2017).** **Fecha** **5** **9** **2017**

6. Anexos

X	Comprobante de pago de la tasa para la presentación de la corrección y/o modificación
X	Poder, si fuere el caso con el que se acredita la representación
	Número de documento que ordena la comisión o fusión o división
X	Documento que contiene la conversión, división o fusión de la solicitud
	Copia de la solicitud y sus anexos en formato magnético

7. Firma

ALICIA LLOREDA RICAURTE
Nombre y apellidos

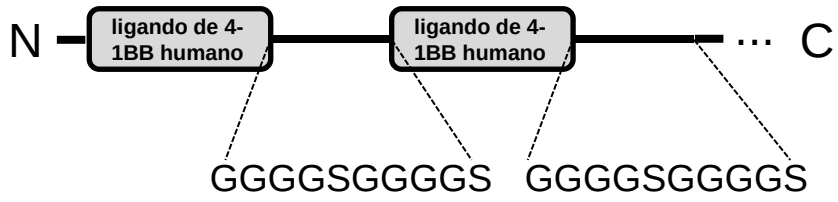
Firma

C.C. 39.690.713 de Usaquén
C.C.

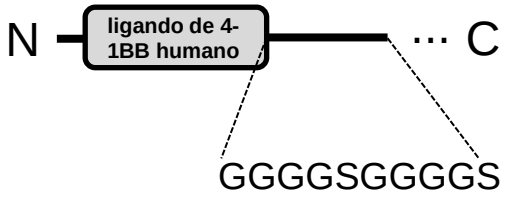
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Tarjeta Profesional

Fig. 1

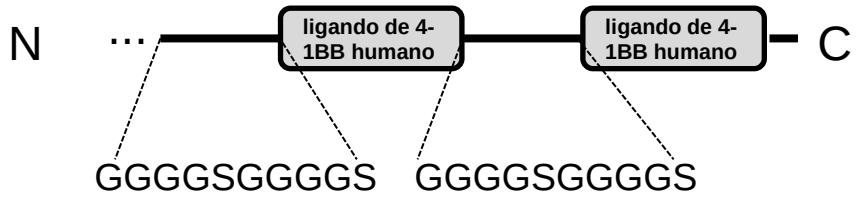
(1A)



(1 B)



(1C)



(1D)

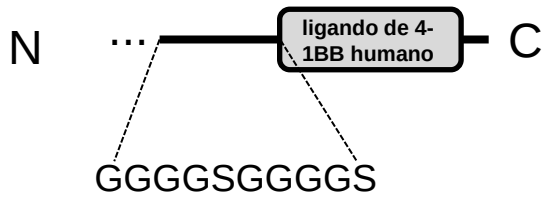
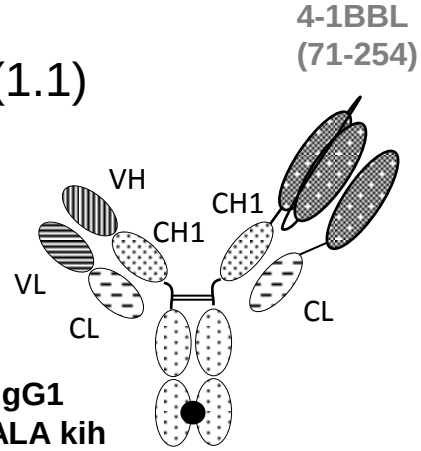
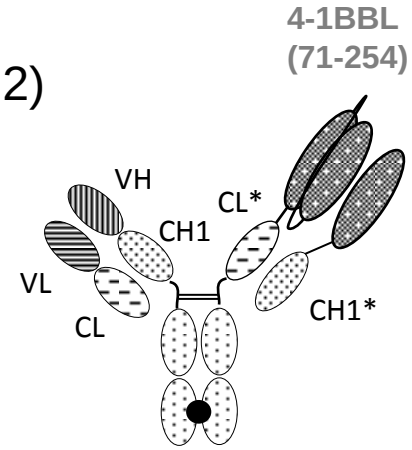


Fig. 2

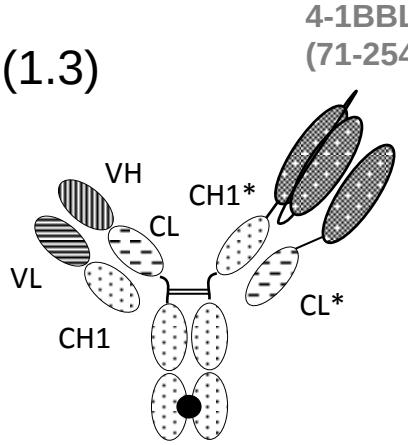
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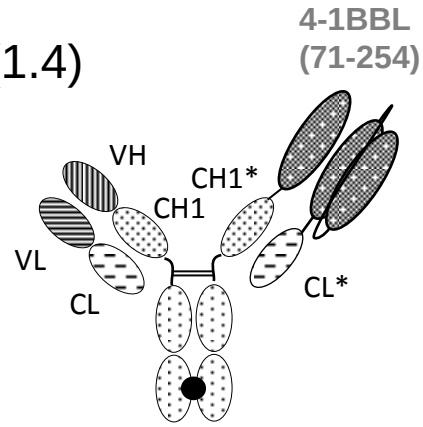
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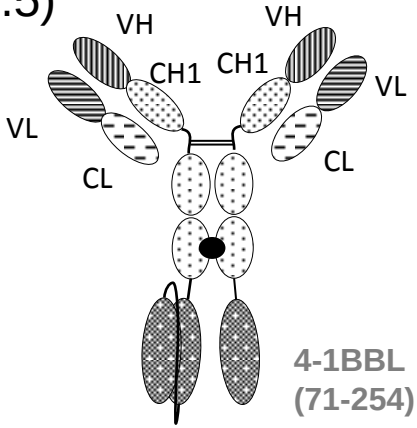
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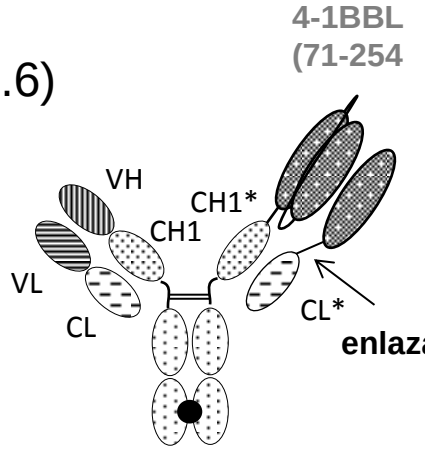
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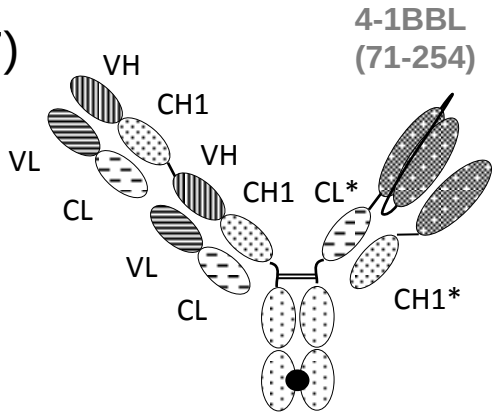
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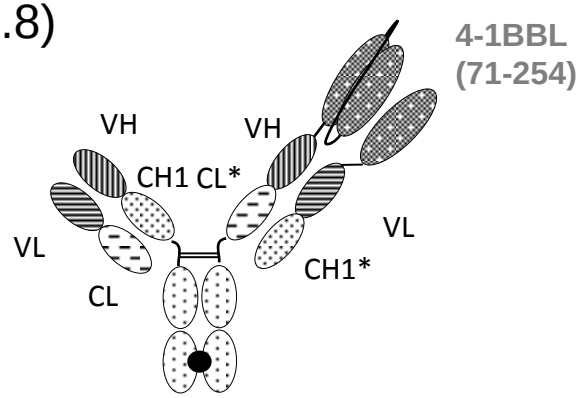
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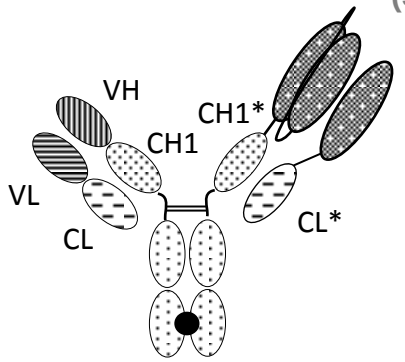
(1.7)



(1.8)



(1.9)



(1.10)

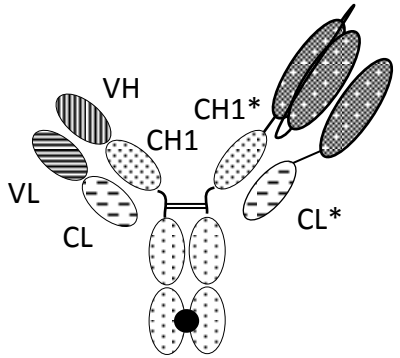


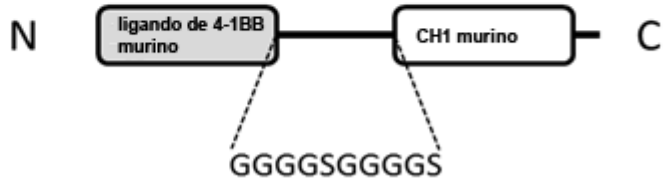
Fig. 2

Fig. 3

(3 A)


N
ligando de 4-1BB murino
ligando de 4-1BB murino
CL murino
C
GGGGSGGGGS
GGGGSGGGGS

(3 B)


N
ligando de 4-1BB murino
CH1 murino
C
GGGGSGGGGS

(3C)

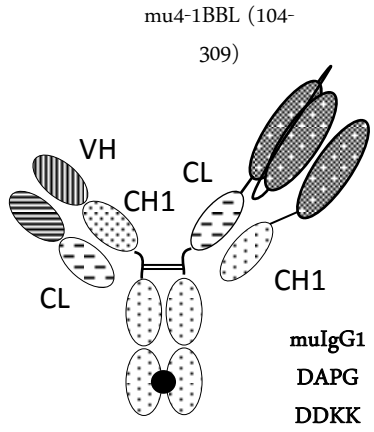
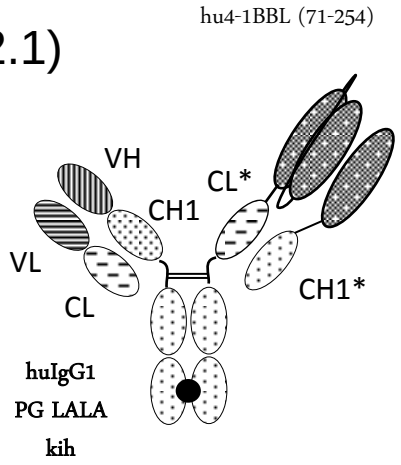
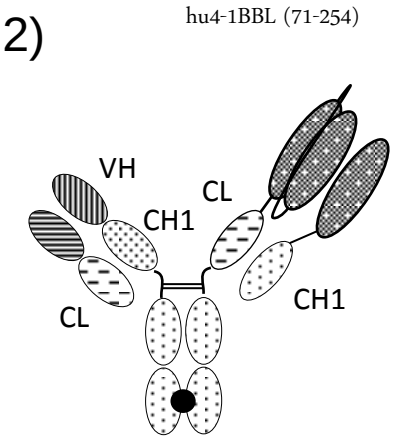

mu4-1BBL (104-309)
VH
CL
CH1
CL
CH1
muIgG1
DAPG
DDKK

Fig. 4

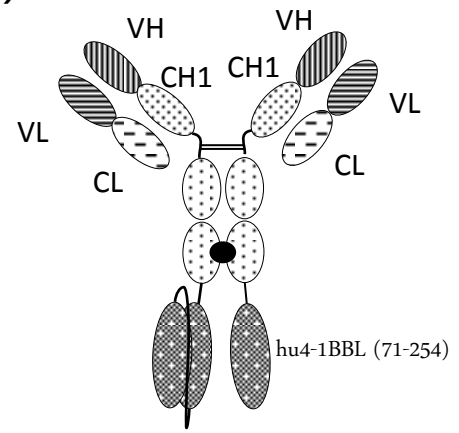
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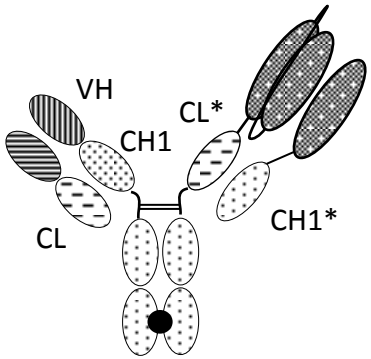
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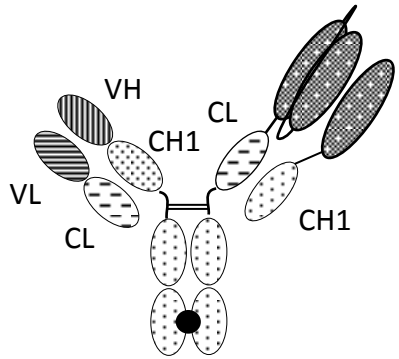
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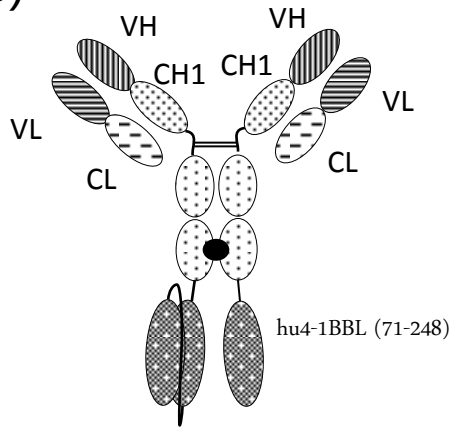
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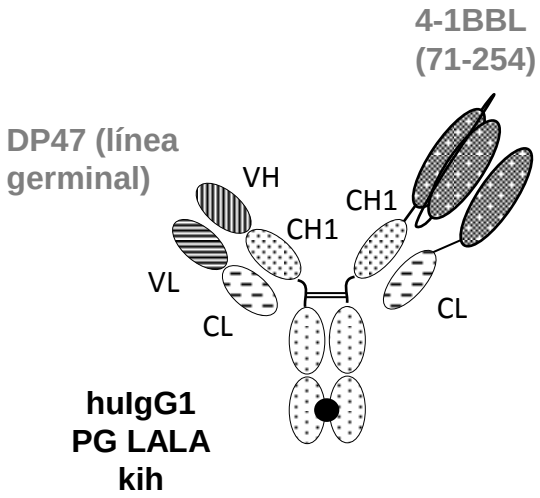
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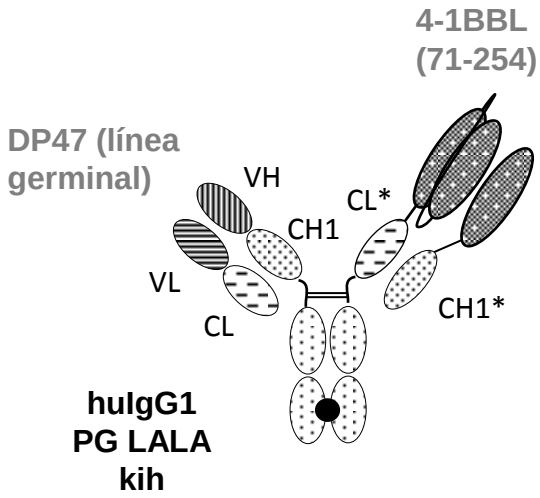
(2.6)



(5 A)


4-1BBL
(71-254)
DP47 (línea germinal)
VH
CH1
CH1
VL
CL
CL
huIgG1
PG LALA
kih

(5 B)


4-1BBL
(71-254)
DP47 (línea germinal)
VH
CL*
CH1
VL
CH1*
CL
huIgG1
PG LALA
kih

(5C)

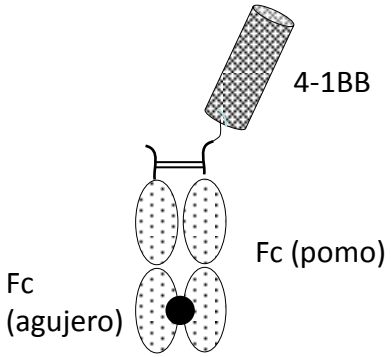
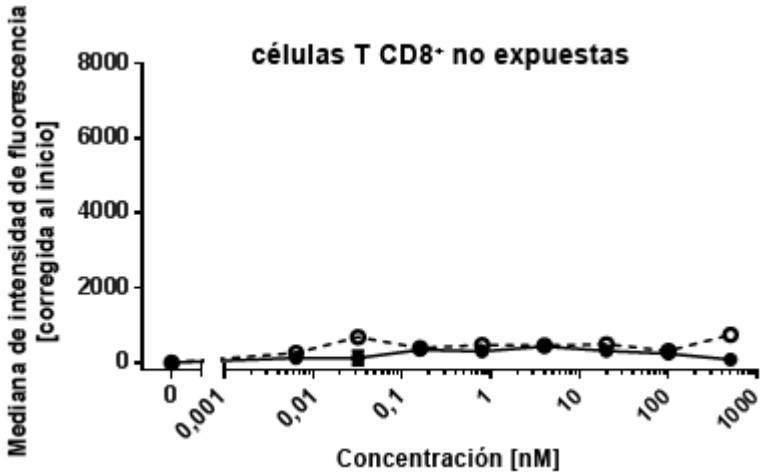
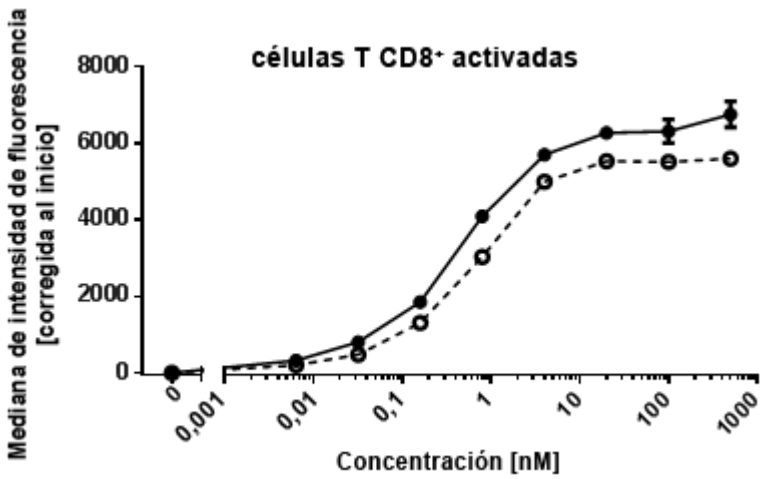

4-1BB
Fc (pomo)
Fc
(agujero)

Fig. 5

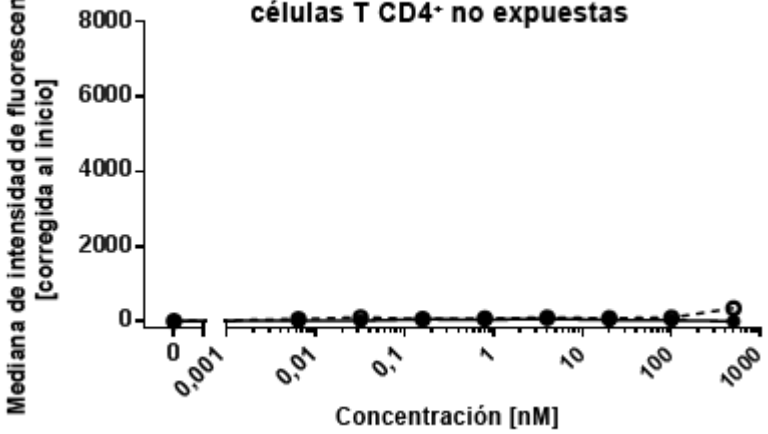
Fig. 6

(6 A)


células T CD8+ no expuestas
Mediana de intensidad de fluorescencia [corregida al inicio]
8000
6000
4000
2000
0
0
0,001
0,01
0,1
1
10
100
1000
Concentración [nM]


células T CD8+ activadas
Mediana de intensidad de fluorescencia [corregida al inicio]
8000
6000
4000
2000
0
0
0,001
0,01
0,1
1
10
100
1000
Concentración [nM]

(6 B)


células T CD4+ no expuestas
Mediana de intensidad de fluorescencia [corregida al inicio]
8000
6000
4000
2000
0
0
0,001
0,01
0,1
1
10
100
1000
Concentración [nM]

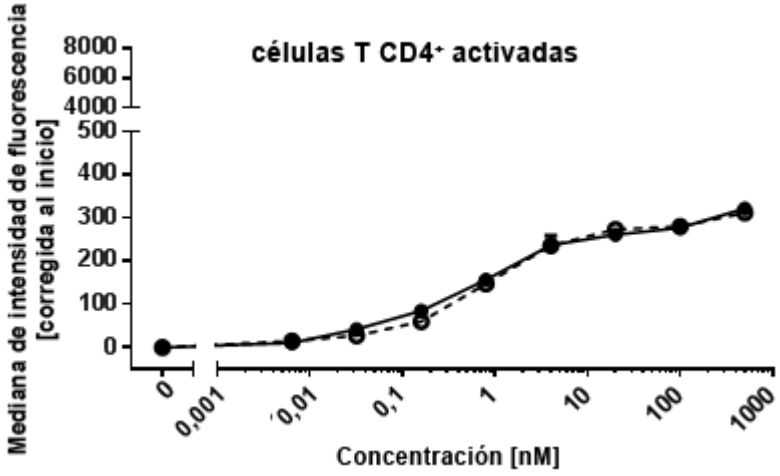

células T CD4+ activadas
Mediana de intensidad de fluorescencia [corregida al inicio]
8000
6000
4000
500
400
300
200
100
0
0
0,001
0,01
0,1
1
10
100
1000
Concentración [nM]

Fig. 6

(6C)

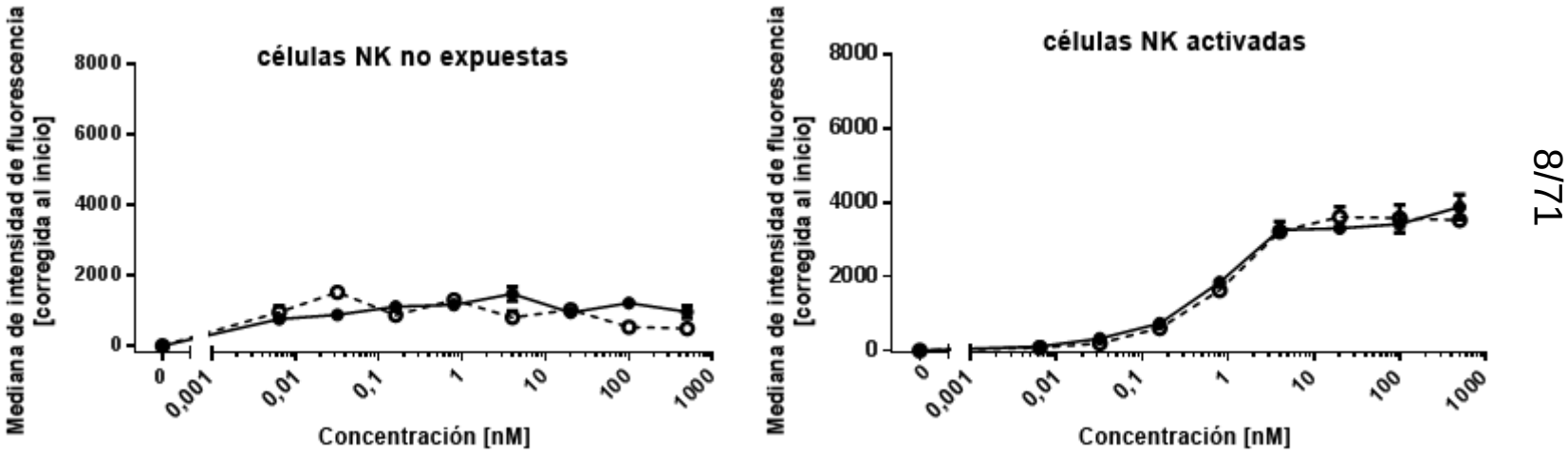

células NK no expuestas
Mediana de intensidad de fluorescencia [corregida al inicio]
8000
6000
4000
2000
0
0
0,001
0,01
0,1
1
10
100
1000
Concentración [nM]
células NK activadas
Mediana de intensidad de fluorescencia [corregida al inicio]
8000
6000
4000
2000
0
0
0,001
0,01
0,1
1
10
100
1000
Concentración [nM]

Fig. 7 A

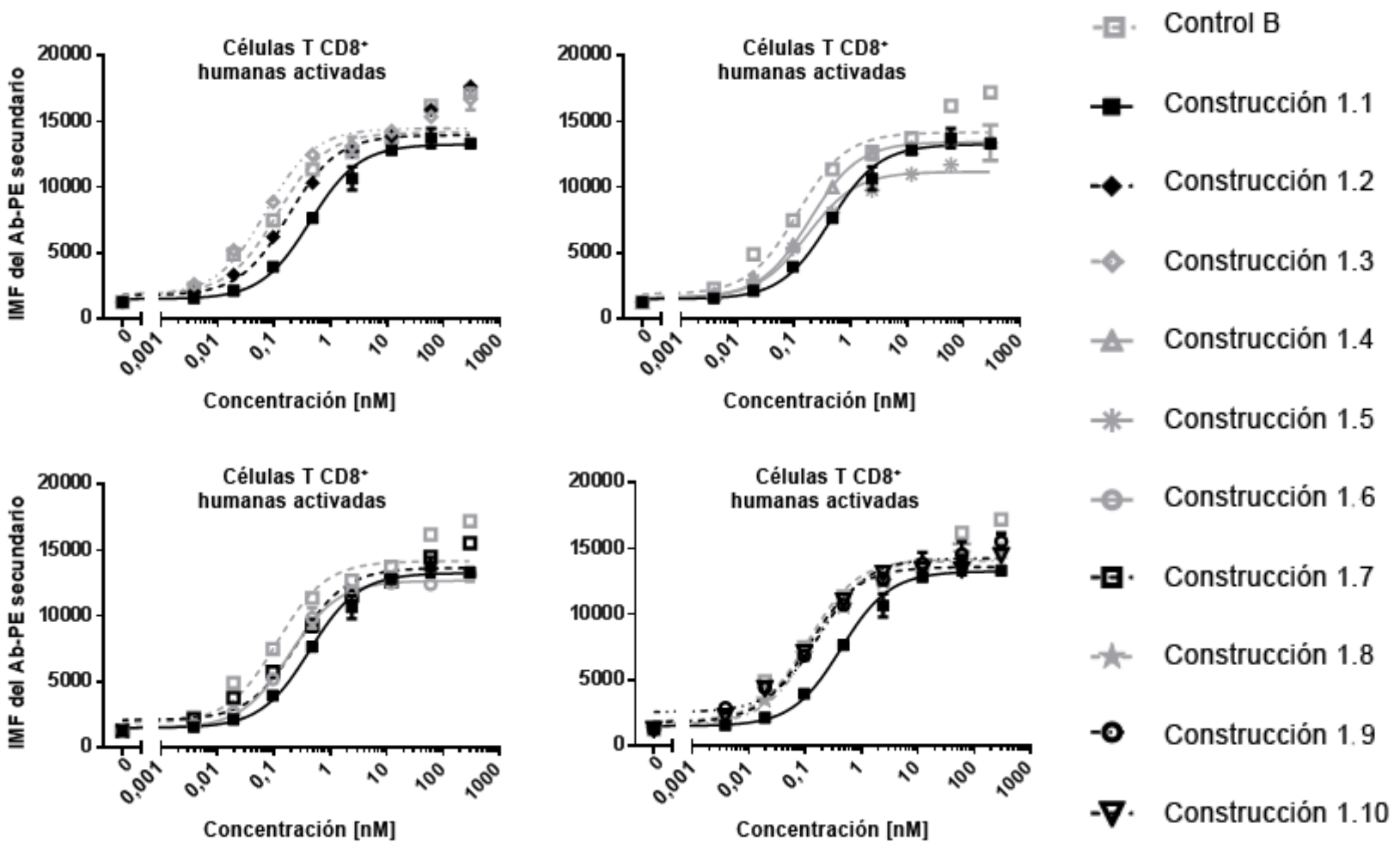

Células T CD8+ humanas activadas
IMF del Ab-PE secundario
Concentración [nM]
Control B
Construcción 1.1
Construcción 1.2
Construcción 1.3
Construcción 1.4
Construcción 1.5
Construcción 1.6
Construcción 1.7
Construcción 1.8
Construcción 1.9
Construcción 1.10

Fig. 7 B

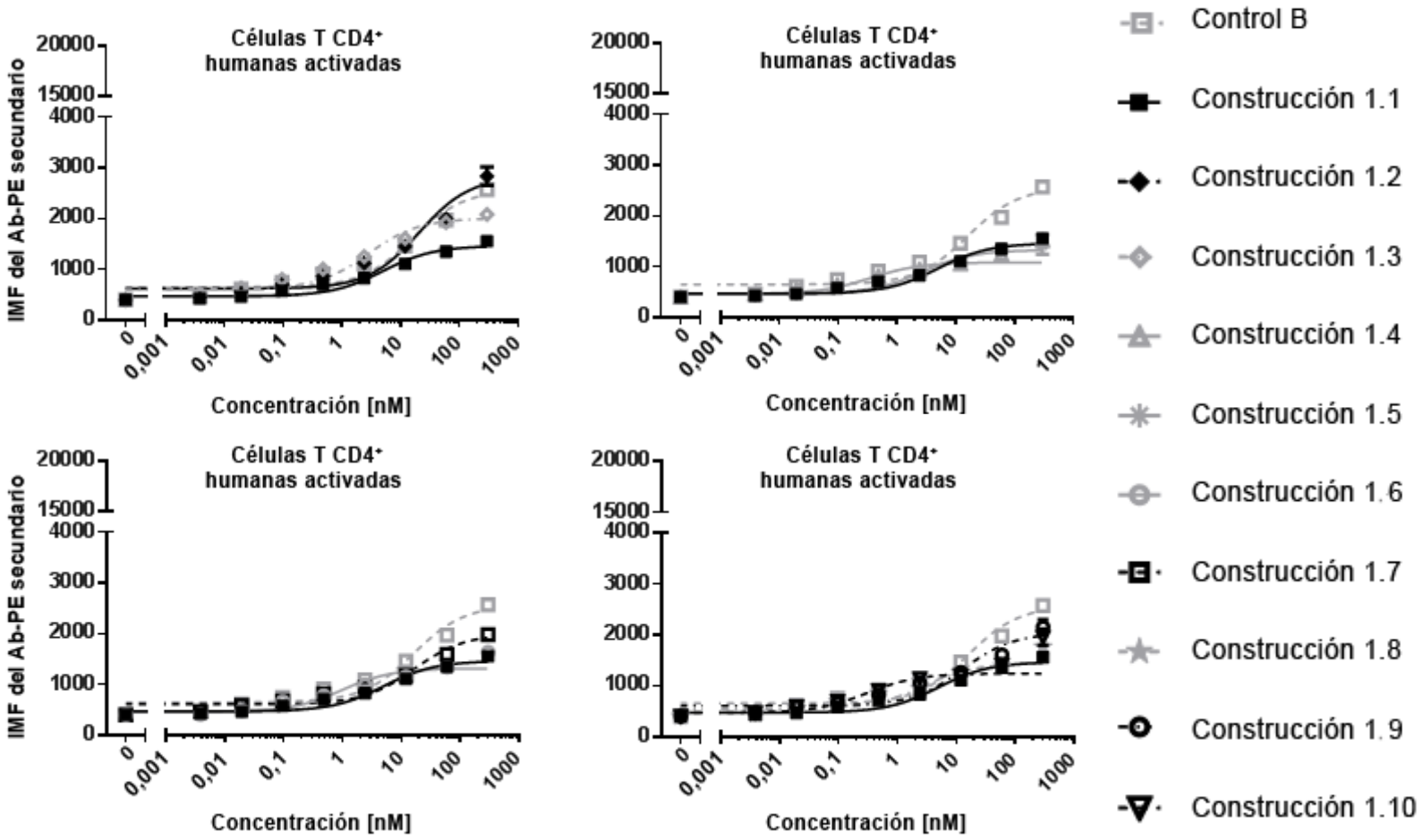

Células T CD4+ humanas activadas
IMF del Ab-PE secundario
Concentración [nM]
Control B
Construcción 1.1
Construcción 1.2
Construcción 1.3
Construcción 1.4
Construcción 1.5
Construcción 1.6
Construcción 1.7
Construcción 1.8
Construcción 1.9
Construcción 1.10

Fig. 8A

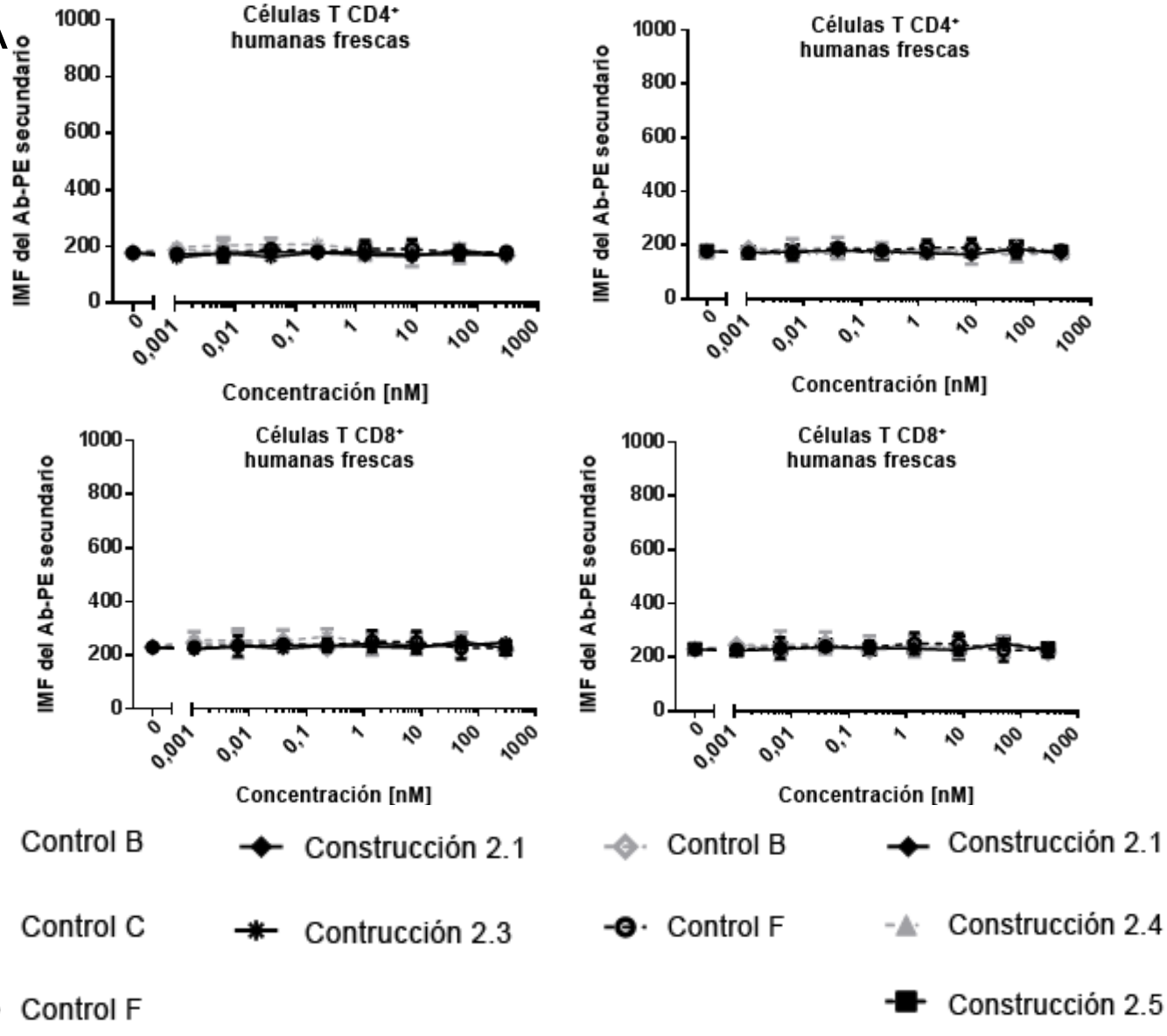

Células T CD4+ humanas frescas
IMF del Ab-PE secundario
1000
800
600
400
200
0
0
0,001
0,01
0,1
1
10
100
1000
Concentración [nM]
Células T CD4+ humanas frescas
IMF del Ab-PE secundario
Concentración [nM]
Células T CD8+ humanas frescas
IMF del Ab-PE secundario
Concentración [nM]
Células T CD8+ humanas frescas
IMF del Ab-PE secundario
Concentración [nM]
Control B
Construcción 2.1
Control C
Contrucción 2.3
Control F
Control B
Construcción 2.1
Control F
Construcción 2.4
Construcción 2.5

Fig. 8 B

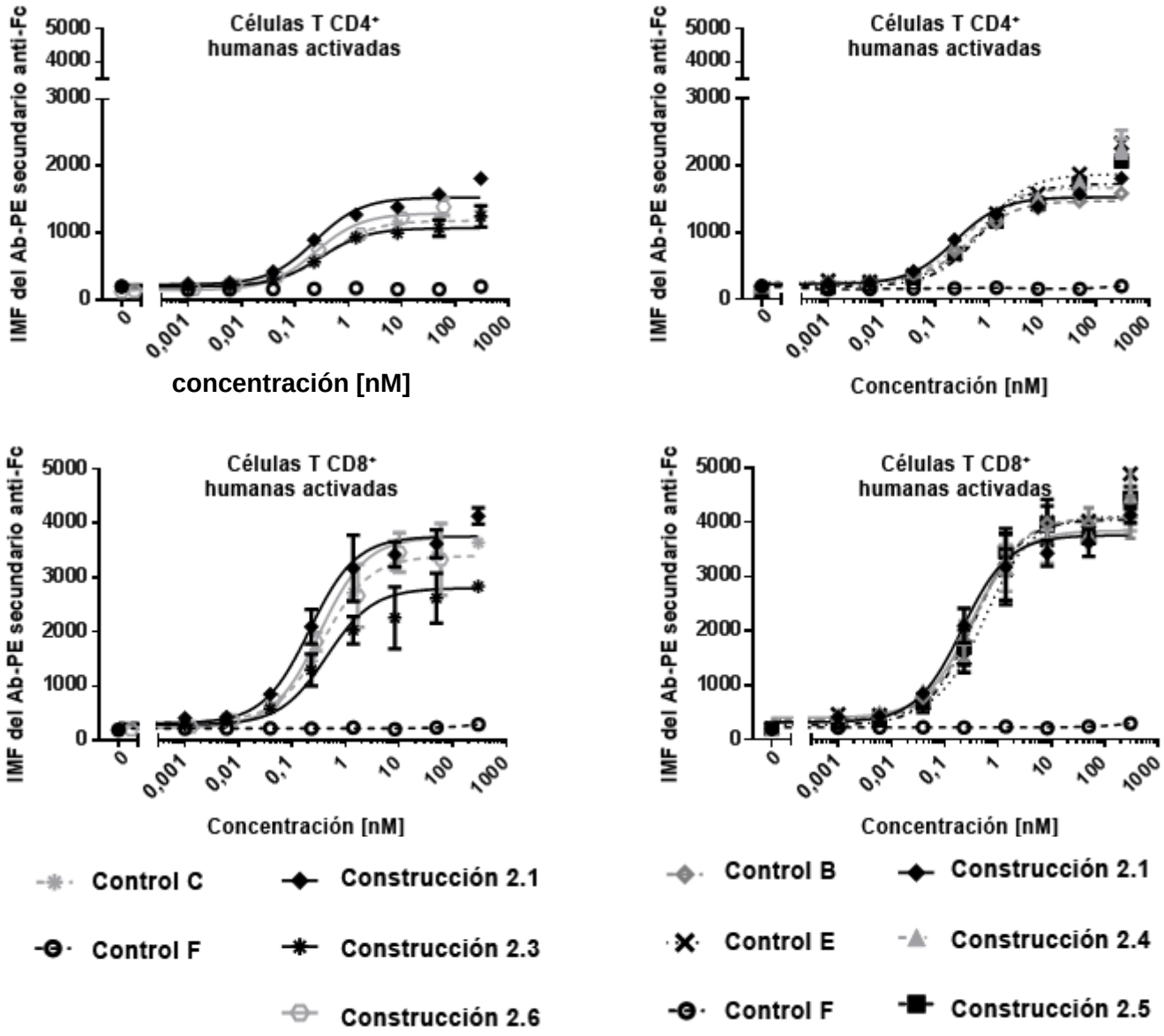
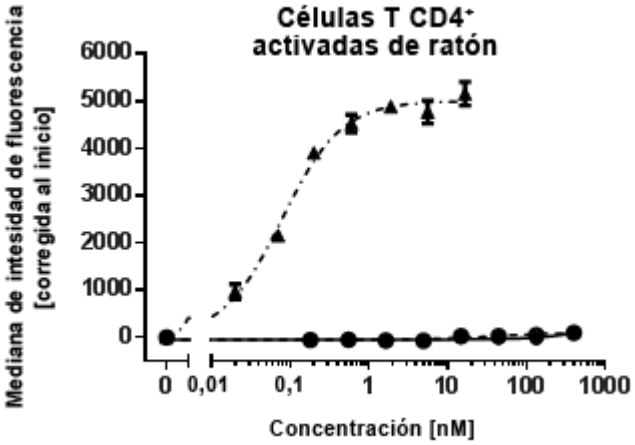

Células T CD4+ humanas activadas
IMF del Ab-PE secundario anti-Fc
5000
4000
3000
2000
1000
0
0
0,001
0,01
0,1
1
10
100
1000
concentración [nM]
Células T CD4+ humanas activadas
IMF del Ab-PE secundario anti-Fc
Concentración [nM]
Células T CD8+ humanas activadas
IMF del Ab-PE secundario anti-Fc
Concentración [nM]
Células T CD8+ humanas activadas
IMF del Ab-PE secundario anti-Fc
Concentración [nM]
Control C
Construcción 2.1
Control F
Construcción 2.3
Construcción 2.6
Control B
Construcción 2.1
Control E
Construcción 2.4
Control F
Construcción 2.5

Fig. 9

(9 A)


Células T CD4+ activadas de ratón
Mediana de intesidad de fluorescencia [corregida al inicio]
6000
5000
4000
3000
2000
1000
0
0
0,01
0,1
1
10
100
1000
Concentración [nM]

(9 B)

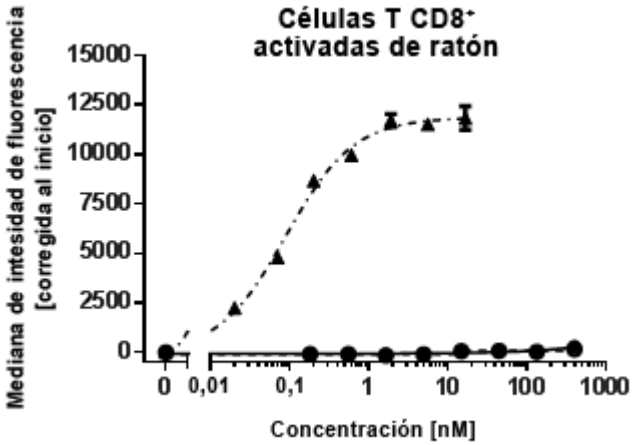
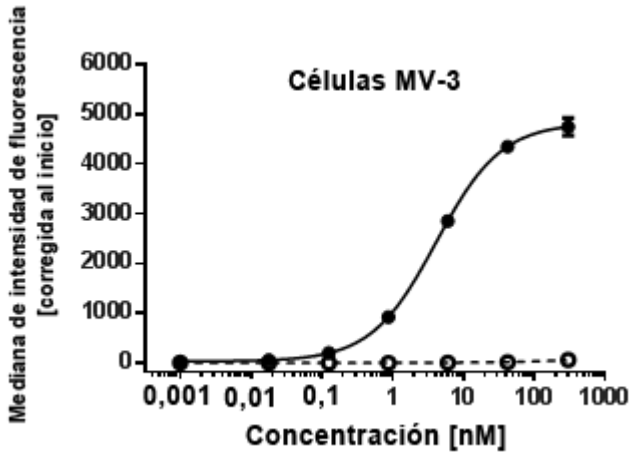

Células T CD8+ activadas de ratón
Mediana de intesidad de fluorescencia [corregida al inicio]
15000
12500
10000
7500
5000
2500
0
0
0,01
0,1
1
10
100
1000
Concentración [nM]

Fig. 10

(10 A)



(10 B)

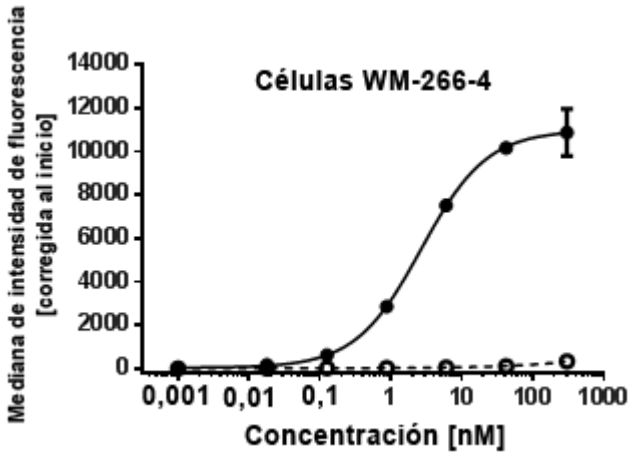


Fig. 11 A

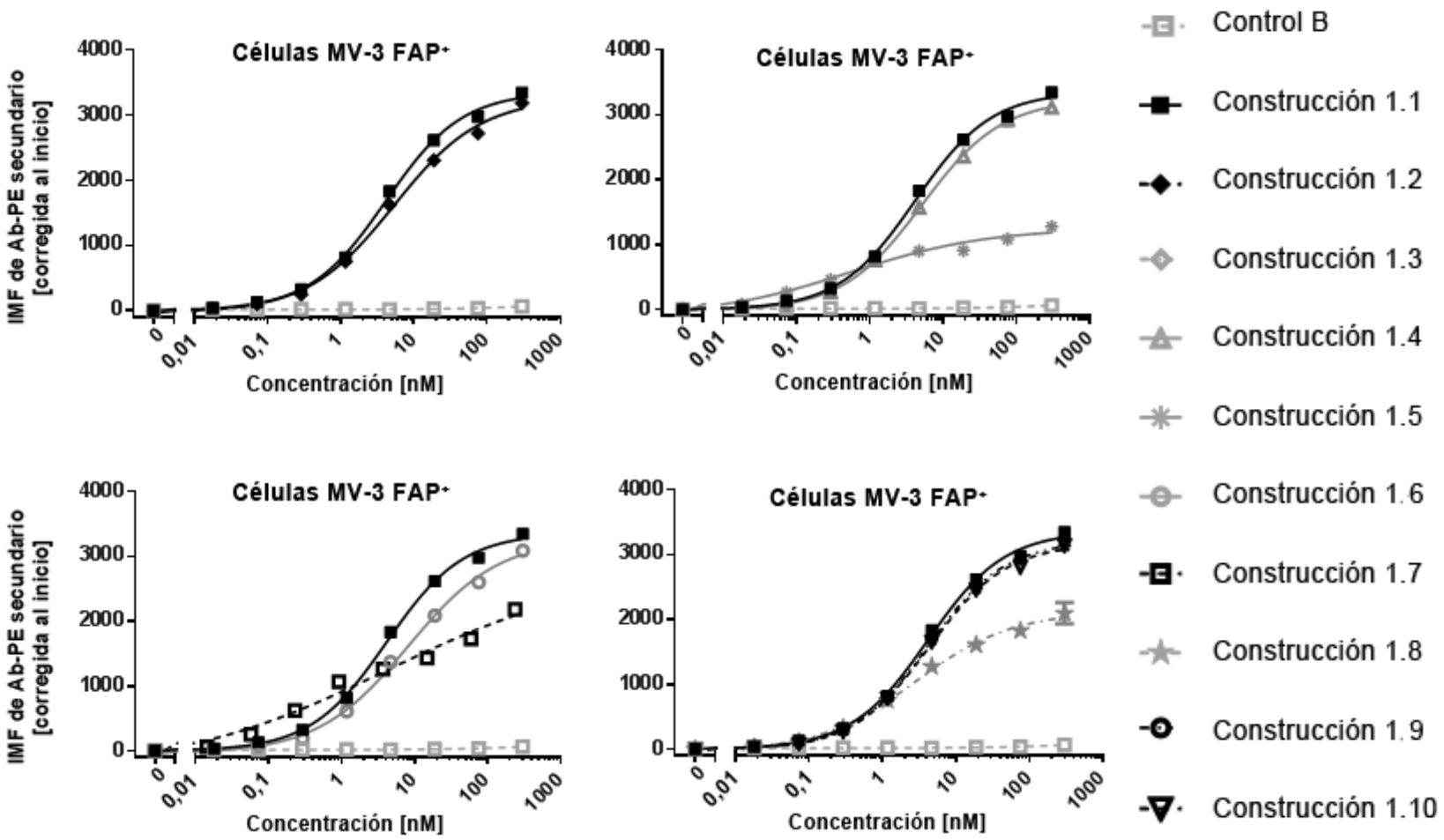

Células MV-3 FAP+
IMF de Ab-PE secundario [corregida al inicio]
Concentración [nM]
0
0,01
0,1
1
10
100
1000
4000
3000
2000
1000
Control B
Construcción 1.1
Construcción 1.2
Construcción 1.3
Construcción 1.4
Construcción 1.5
Construcción 1.6
Construcción 1.7
Construcción 1.8
Construcción 1.9
Construcción 1.10

Fig. 11 B

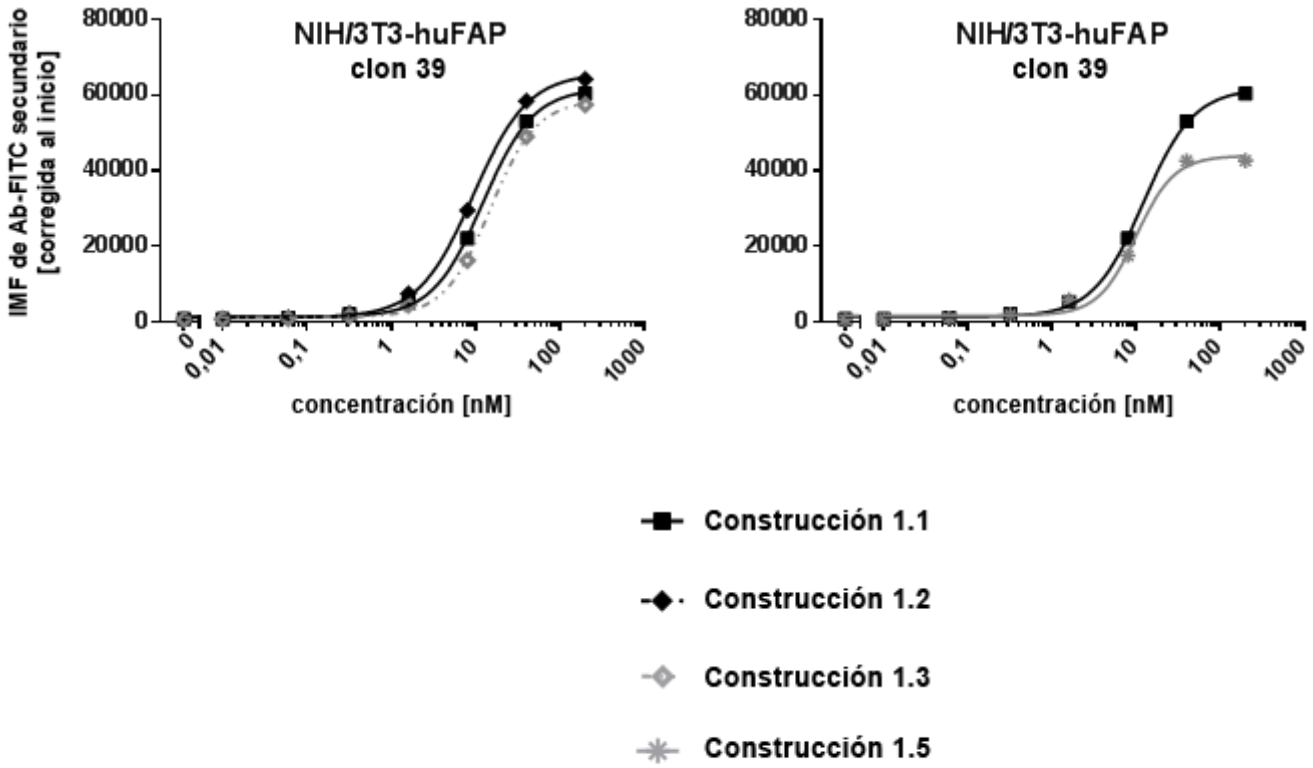

IMF de Ab-FITC secundario [corregida al inicio]
80000
60000
40000
20000
0
NIH/3T3-huFAP clon 39
0
0,01
0,1
1
10
100
1000
concentración [nM]
NIH/3T3-huFAP clon 39
concentración [nM]
Construcción 1.1
Construcción 1.2
Construcción 1.3
Construcción 1.5

Fig. 12 A

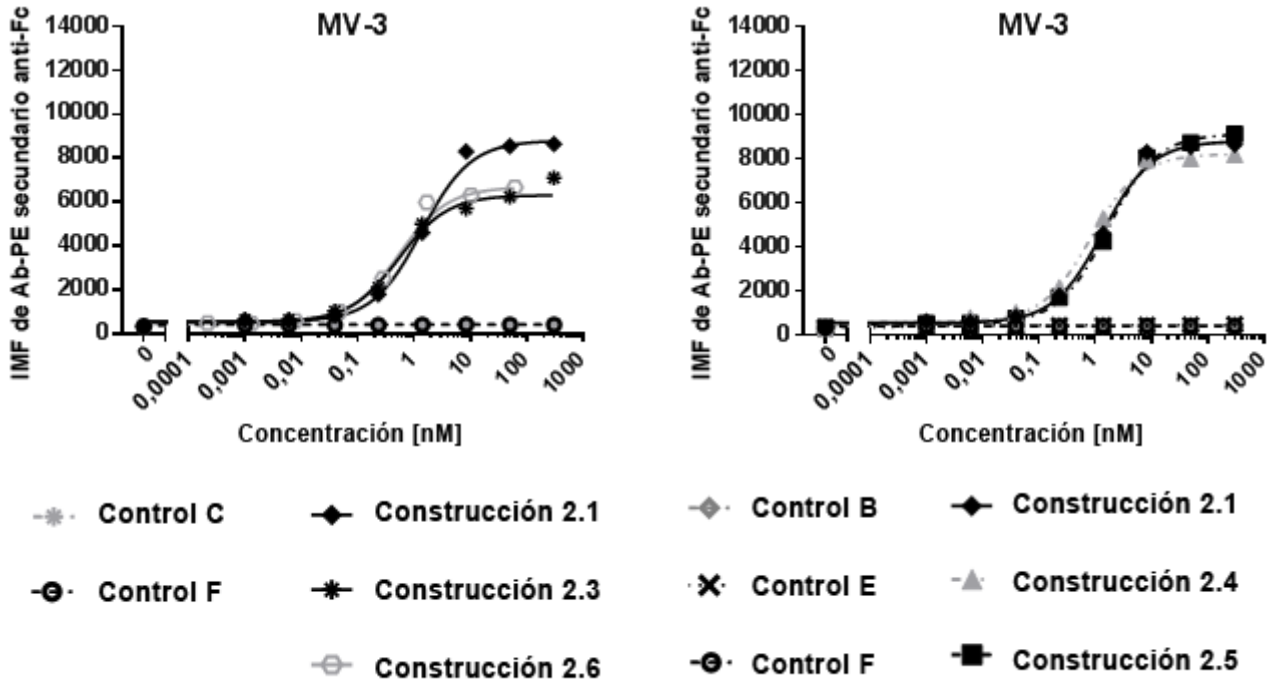
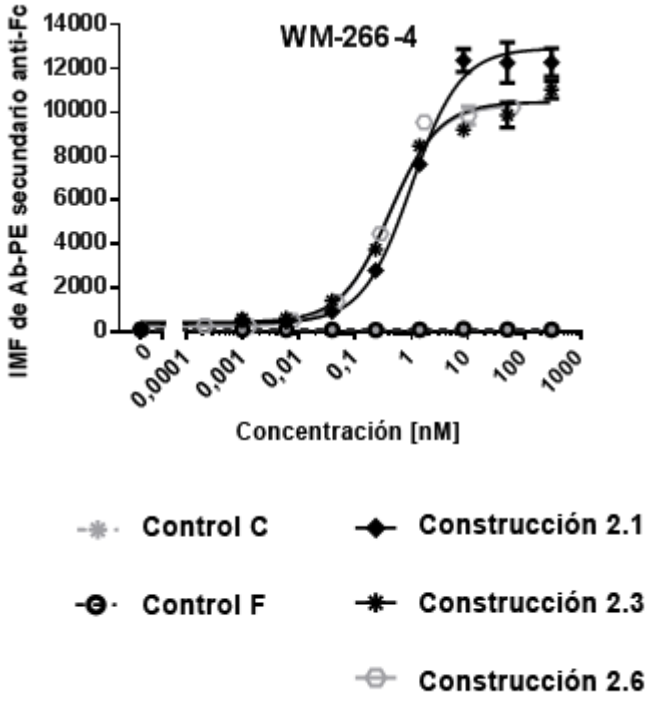

MV-3
IMF de Ab-PE secundario anti-Fc
14000
12000
10000
8000
6000
4000
2000
0
0
0,0001
0,001
0,01
0,1
1
10
100
1000
Concentración [nM]
Control C
Construcción 2.1
Control F
Construcción 2.3
Construcción 2.6
MV-3
IMF de Ab-PE secundario anti-Fc
Concentración [nM]
Control B
Construcción 2.1
Control E
Construcción 2.4
Control F
Construcción 2.5

Fig. 12 B


WM-266-4
IMF de Ab-PE secundario anti-Fc
14000
12000
10000
8000
6000
4000
2000
0
0
0,0001
0,001
0,01
0,1
1
10
100
1000
Concentración [nM]
Control C
Construcción 2.1
Control F
Construcción 2.3
Construcción 2.6

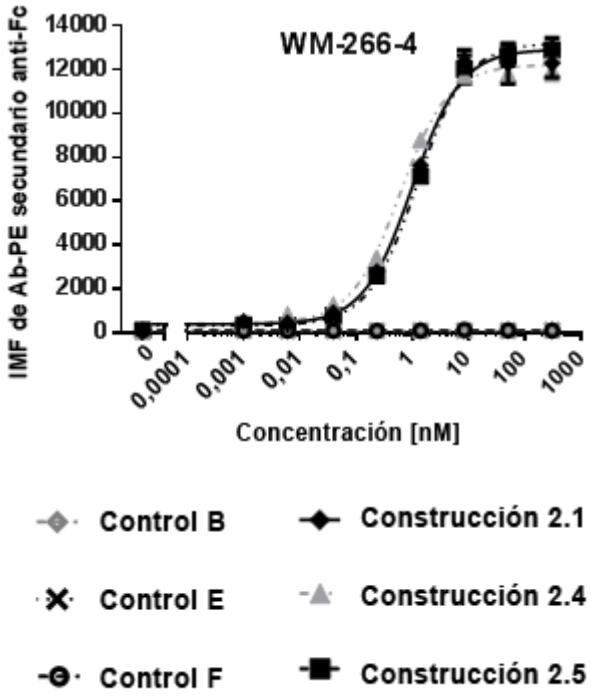
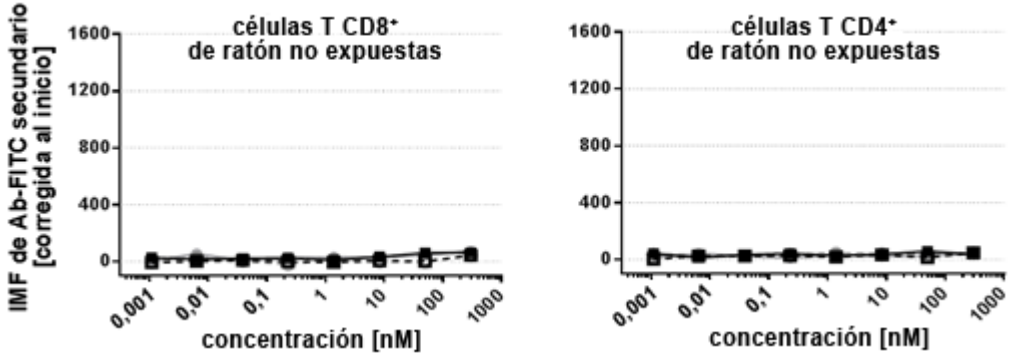

WM-266-4
IMF de Ab-PE secundario anti-Fc
14000
12000
10000
8000
6000
4000
2000
0
0
0,0001
0,001
0,01
0,1
1
10
100
1000
Concentración [nM]
Control B
Construcción 2.1
Control E
Construcción 2.4
Control F
Construcción 2.5

Fig. 13

(13 A)



(13 B)

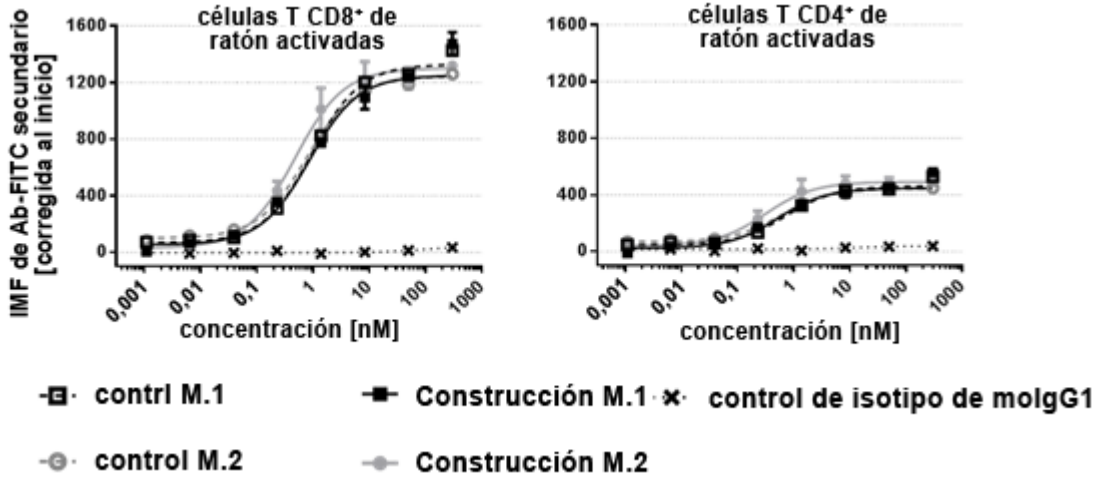
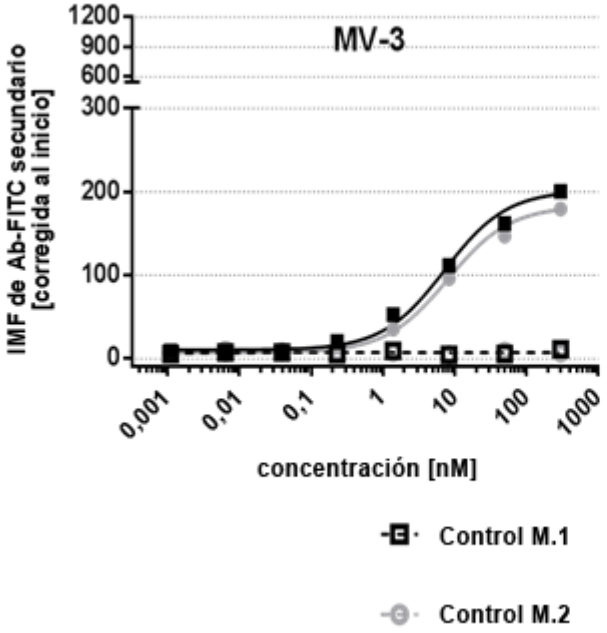
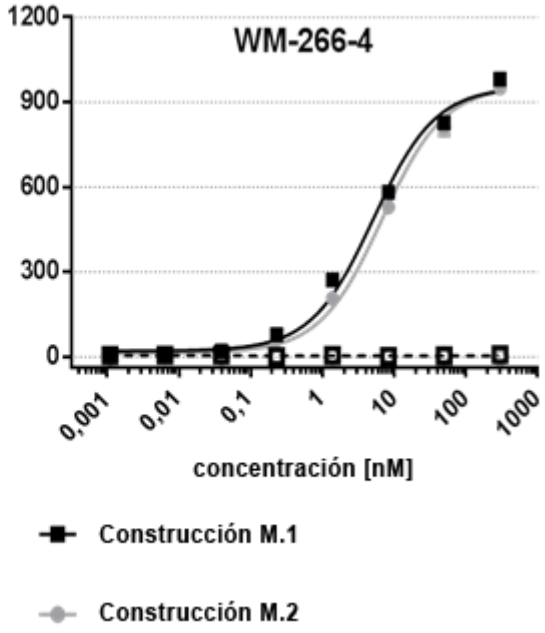


Fig. 14

(14 A)



(14 B)



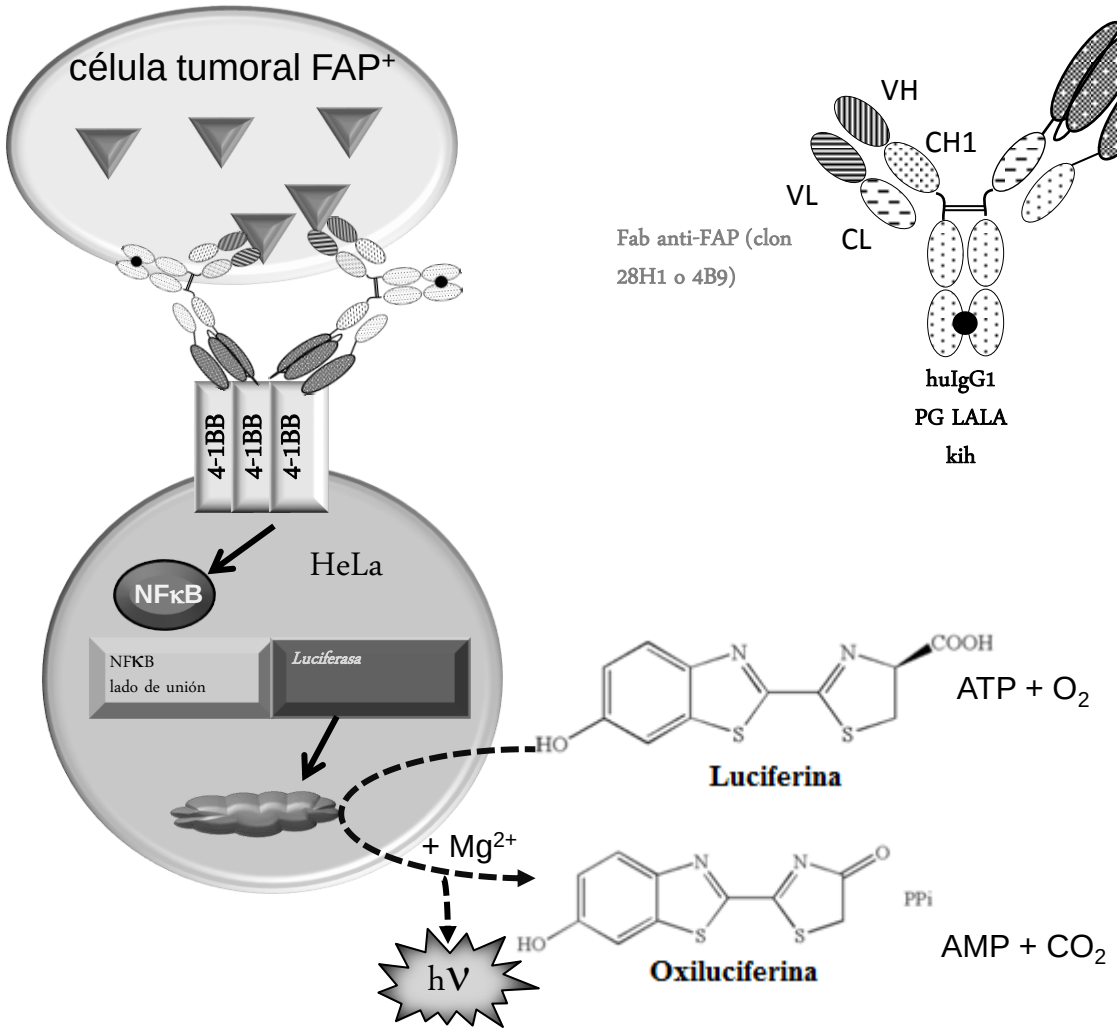
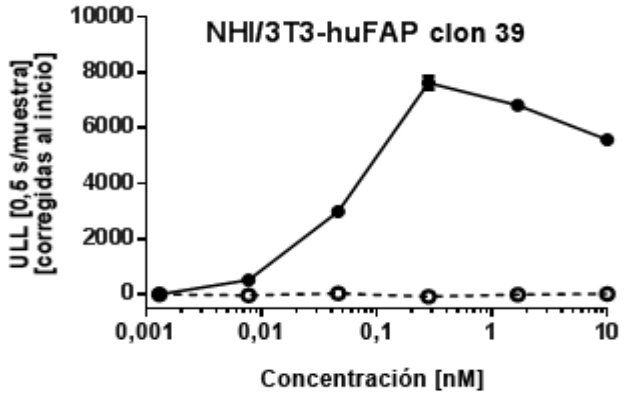
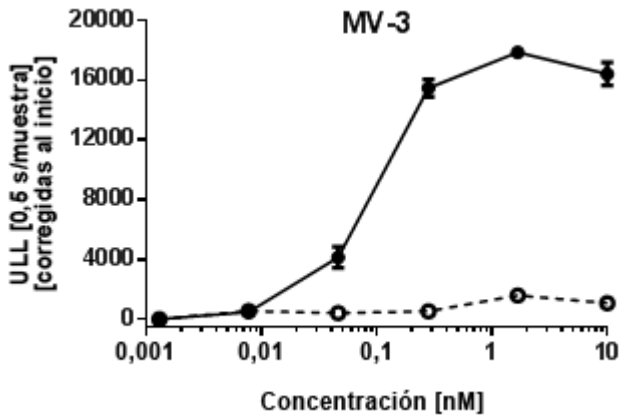

célula tumoral FAP+
4-1BB
4-1BB
4-1BB
HeLa
NFκB
NFKB
lado de unión
Luciferasa
+ Mg2+
hν
VH
CH1
VL
CL
Fab anti-FAP (clon 28H1 o 4B9)
huIgG1
PG LALA
kih
COOH
N
N
S
S
HO
Luciferina
ATP + O2
O
PPi
Oxiluciferina
AMP + CO2

Fig. 15

(16 A)



(16 B)



(16C)

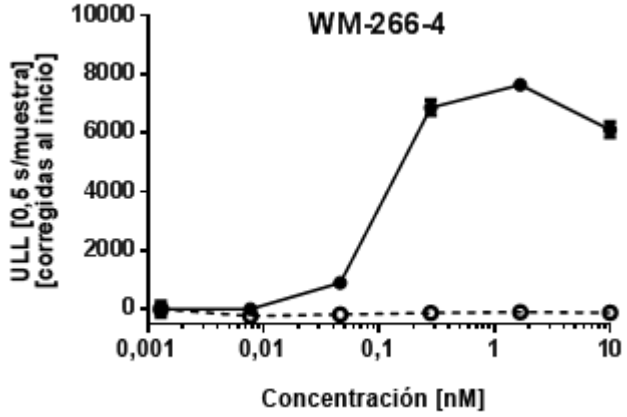


Fig. 16

Fig. 17 A

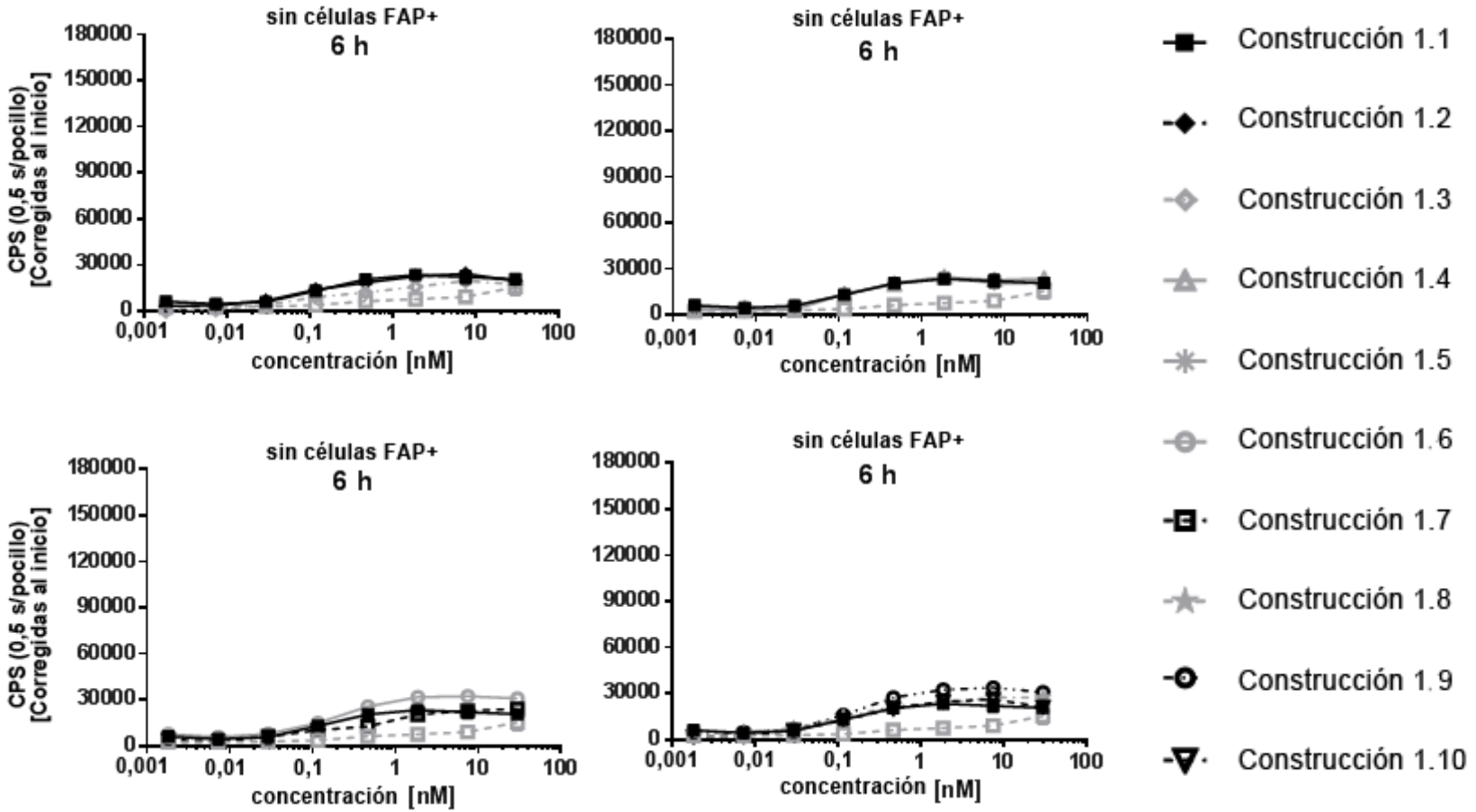

sin células FAP+
6 h
CPS (0,5 s/pocillo) [Corregidas al inicio]
180000
150000
120000
90000
60000
30000
0
0,001
0,01
0,1
1
10
100
concentración [nM]
Control B
Construcción 1.1
Construcción 1.2
Construcción 1.3
Construcción 1.4
Construcción 1.5
Construcción 1.6
Construcción 1.7
Construcción 1.8
Construcción 1.9
Construcción 1.10

Fig. 17 B

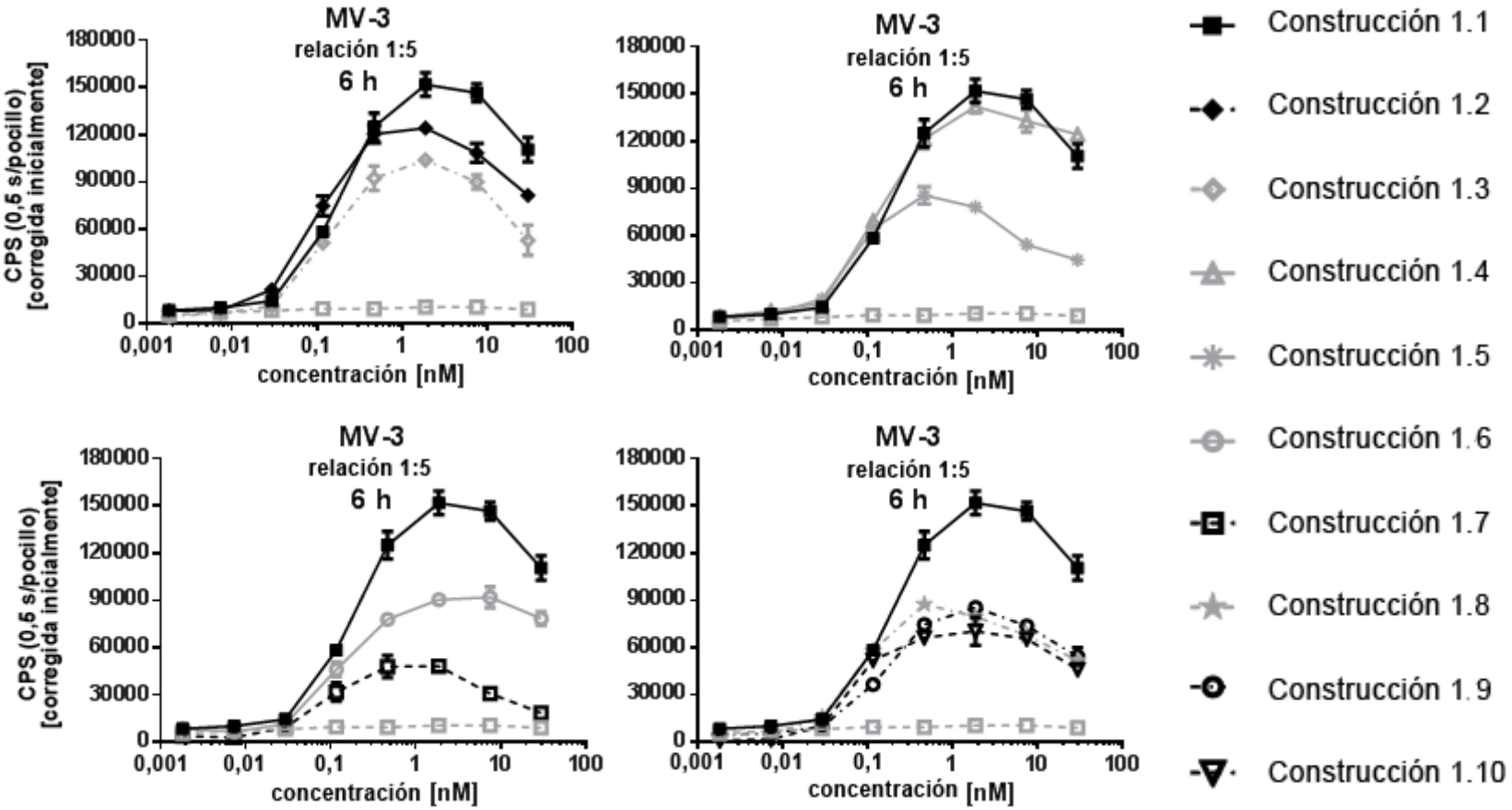

MV-3
relación 1:5
6 h
CPS (0,5 s/pocillo) [corregida inicialmente]
concentración [nM]
Control B
Construcción 1.1
Construcción 1.2
Construcción 1.3
Construcción 1.4
Construcción 1.5
Construcción 1.6
Construcción 1.7
Construcción 1.8
Construcción 1.9
Construcción 1.10

Fig. 17C

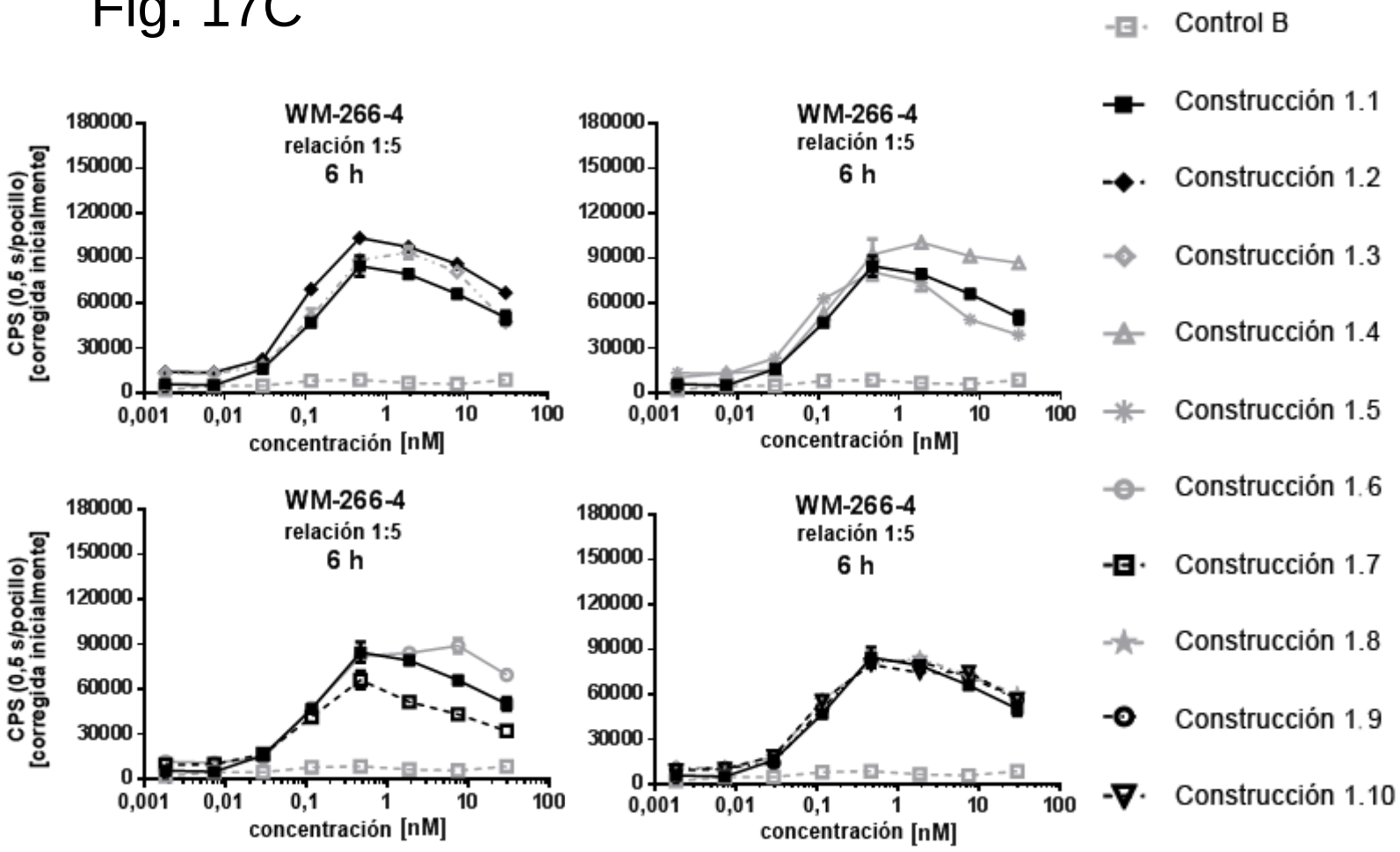

WM-266-4
relación 1:5
6 h
CPS (0,5 s/pocillo)
[corregida inicialmente]
concentración [nM]
Control B
Construcción 1.1
Construcción 1.2
Construcción 1.3
Construcción 1.4
Construcción 1.5
Construcción 1.6
Construcción 1.7
Construcción 1.8
Construcción 1.9
Construcción 1.10

Fig. 18

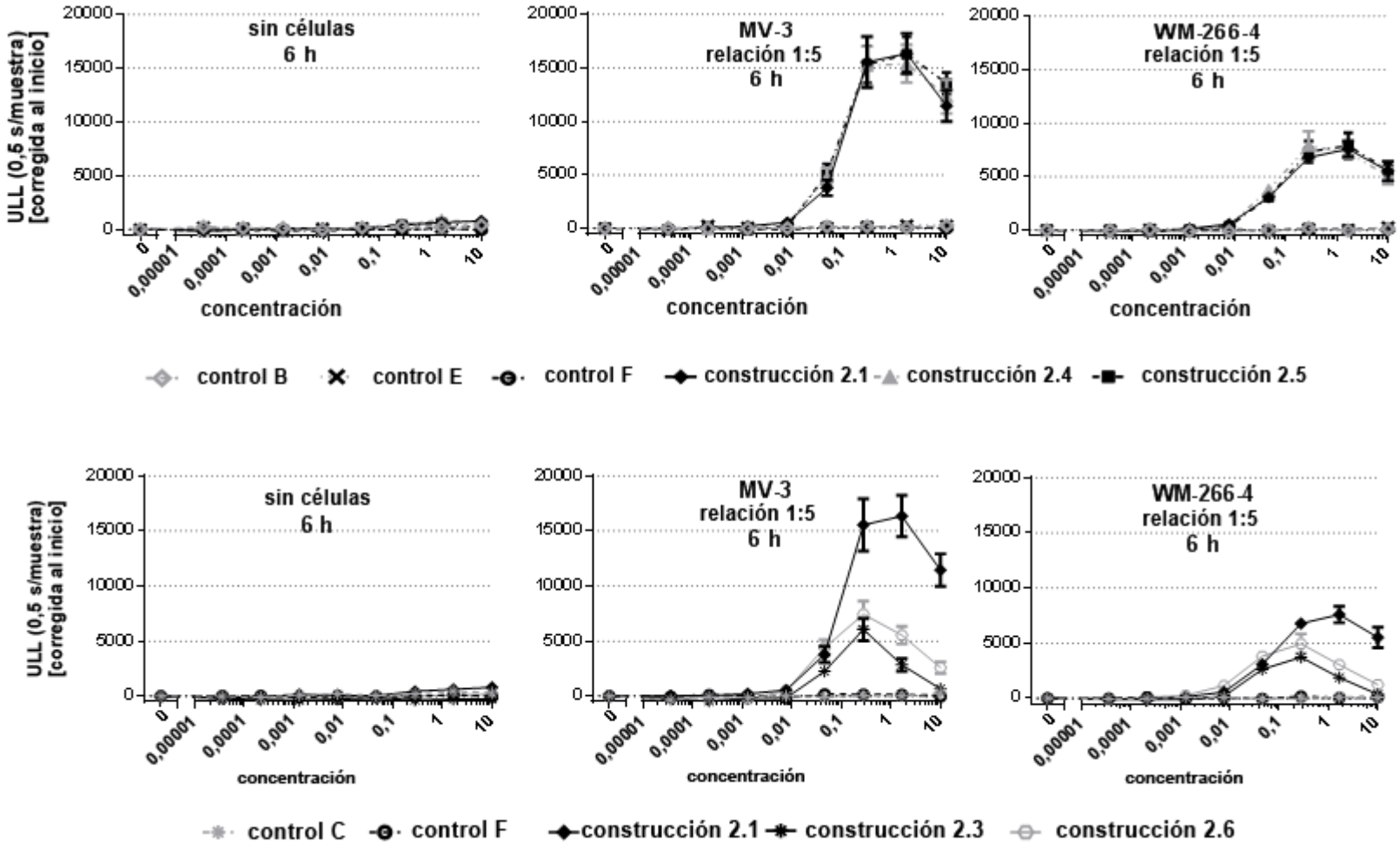

sin células
6 h
MV-3
relación 1:5
6 h
WM-266-4
relación 1:5
6 h
ULL (0,5 s/muestra)
[corregida al inicio]
20000
15000
10000
5000
0
0
0,00001
0,0001
0,001
0,01
0,1
1
10
concentración
control B
control E
control F
construcción 2.1
construcción 2.4
construcción 2.5
sin células
6 h
MV-3
relación 1:5
6 h
WM-266-4
relación 1:5
6 h
ULL (0,5 s/muestra)
[corregida al inicio]
concentración
control C
control F
construcción 2.1
construcción 2.3
construcción 2.6

Fig. 19

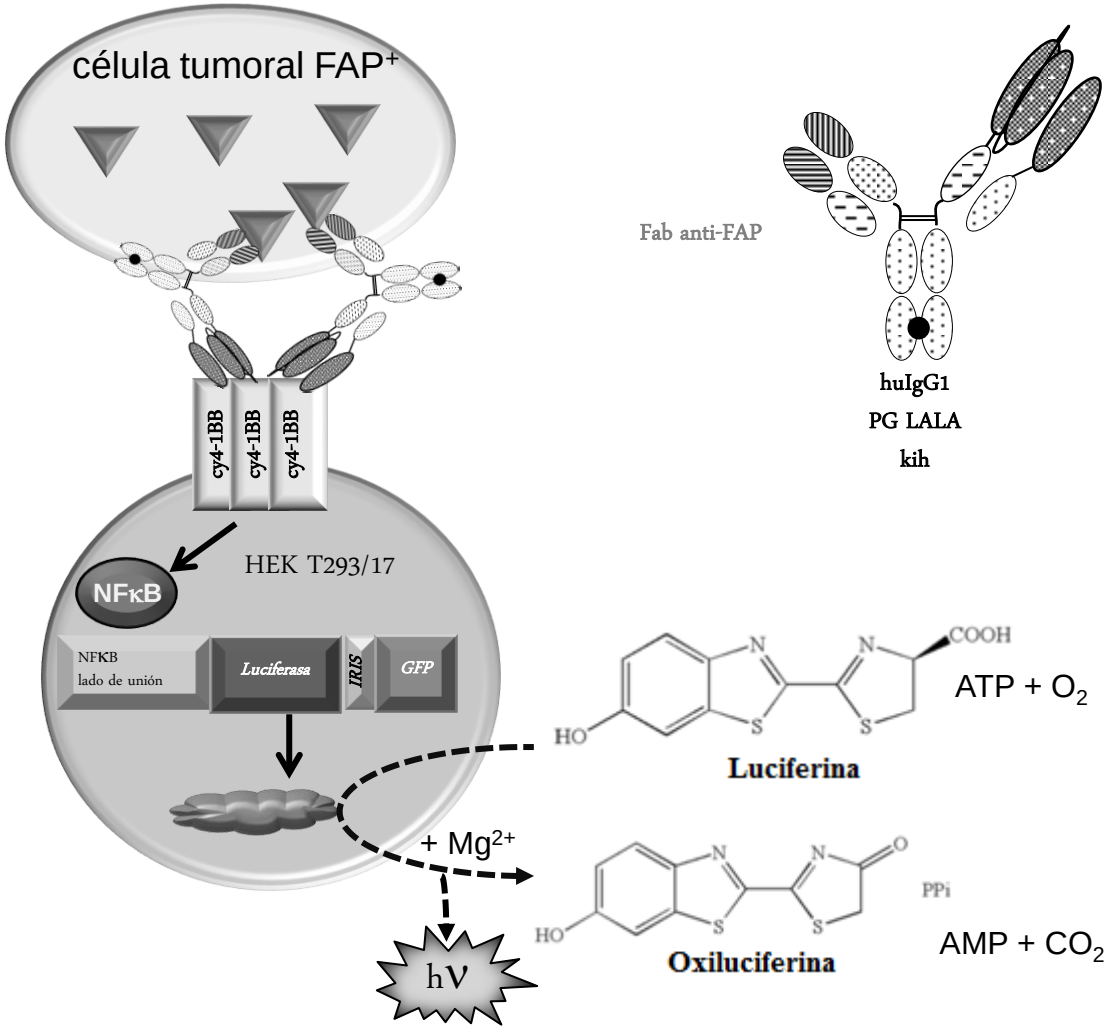
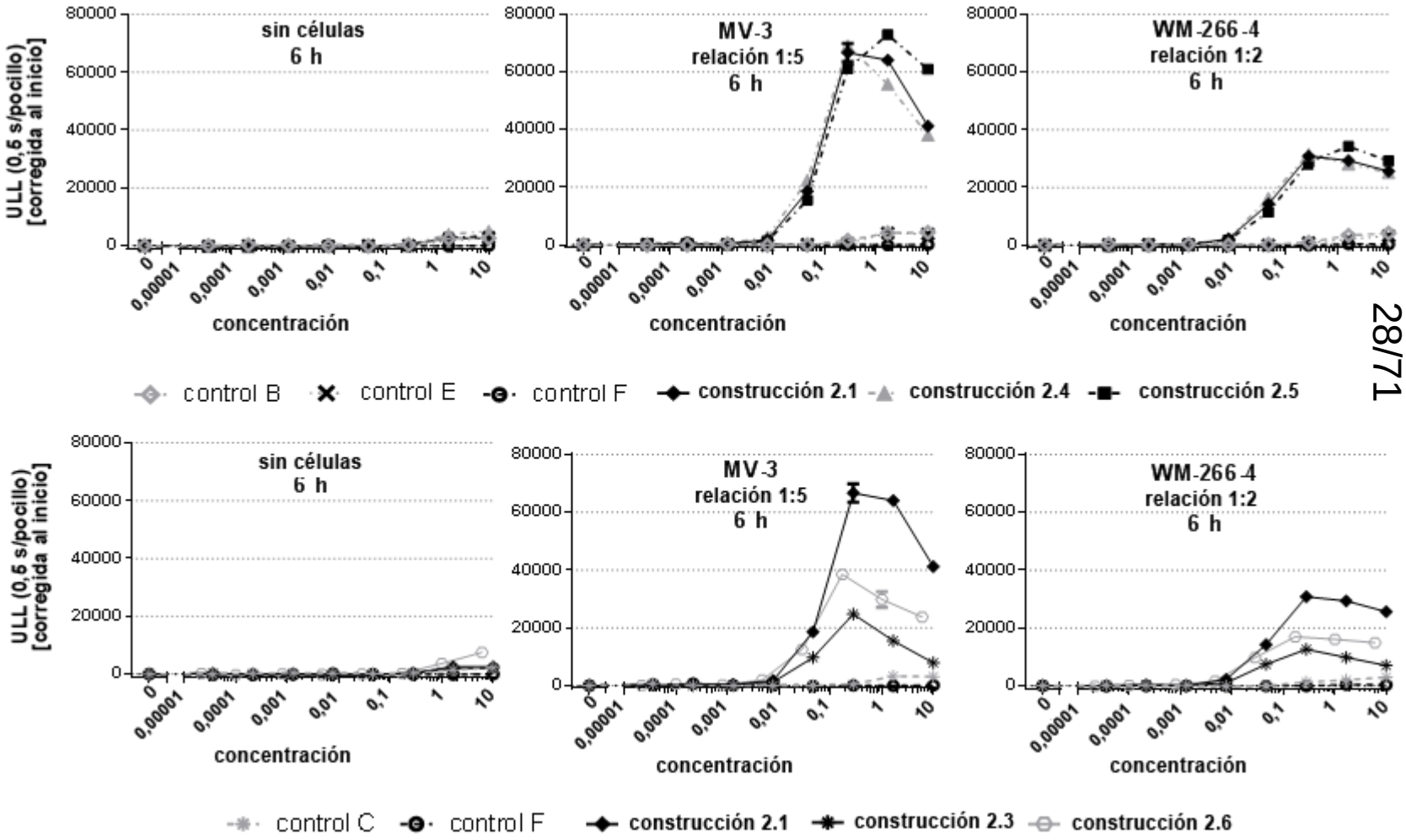

célula tumoral FAP+
cy4-1BB
cy4-1BB
cy4-1BB
HEK T293/17
NFκB
NFKB
lado de unión
Luciferasa
IRES
GFP
+ Mg2+
hν
Fab anti-FAP
huIgG1
PG LALA
kih
COOH
HO
Luciferina
ATP + O2
PPi
Oxiluciferina
AMP + CO2

Fig. 20


ULL (0,5 s/pocillo) [corregida al inicio]
sin células
6 h
MV-3
relación 1:5
6 h
WM-266-4
relación 1:2
6 h
concentración
0
0,00001
0,0001
0,001
0,01
0,1
1
10
control B
control E
control F
construcción 2.1
construcción 2.4
construcción 2.5
control C
control F
construcción 2.1
construcción 2.3
construcción 2.6

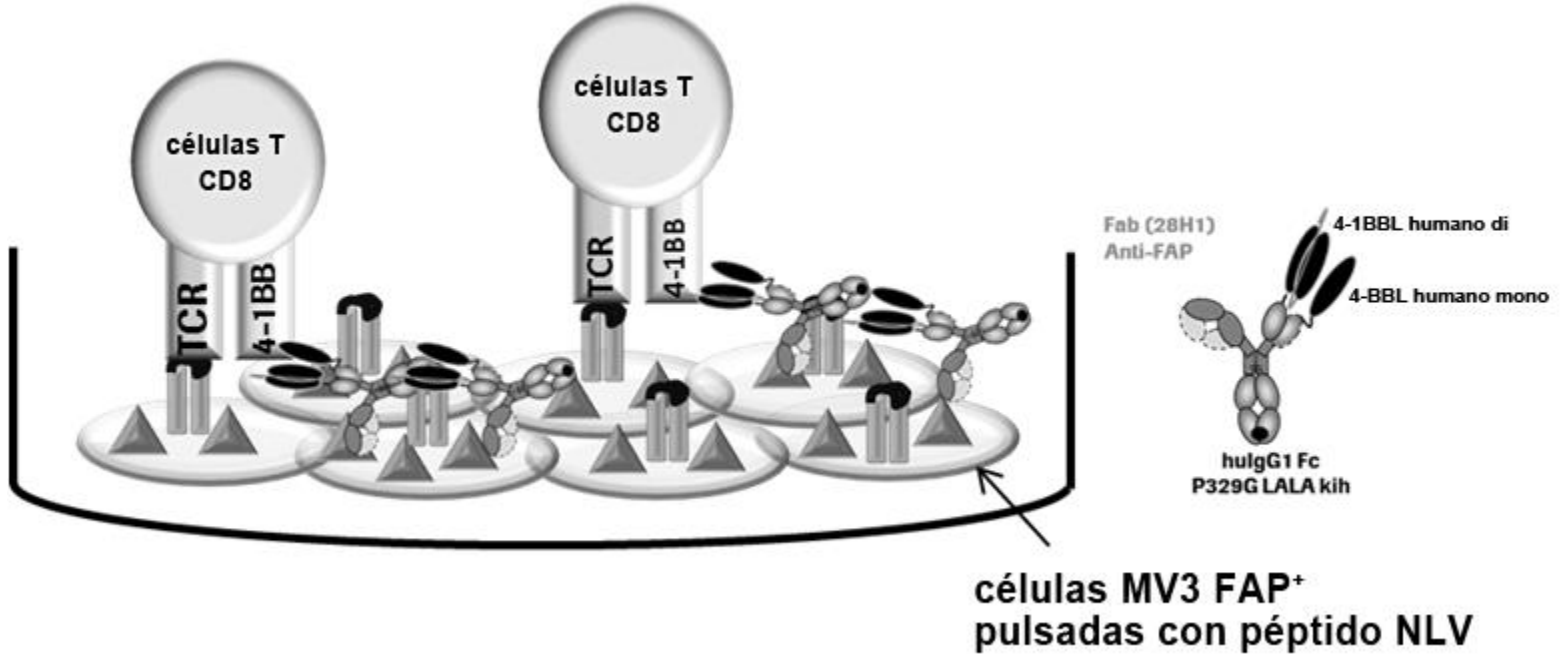
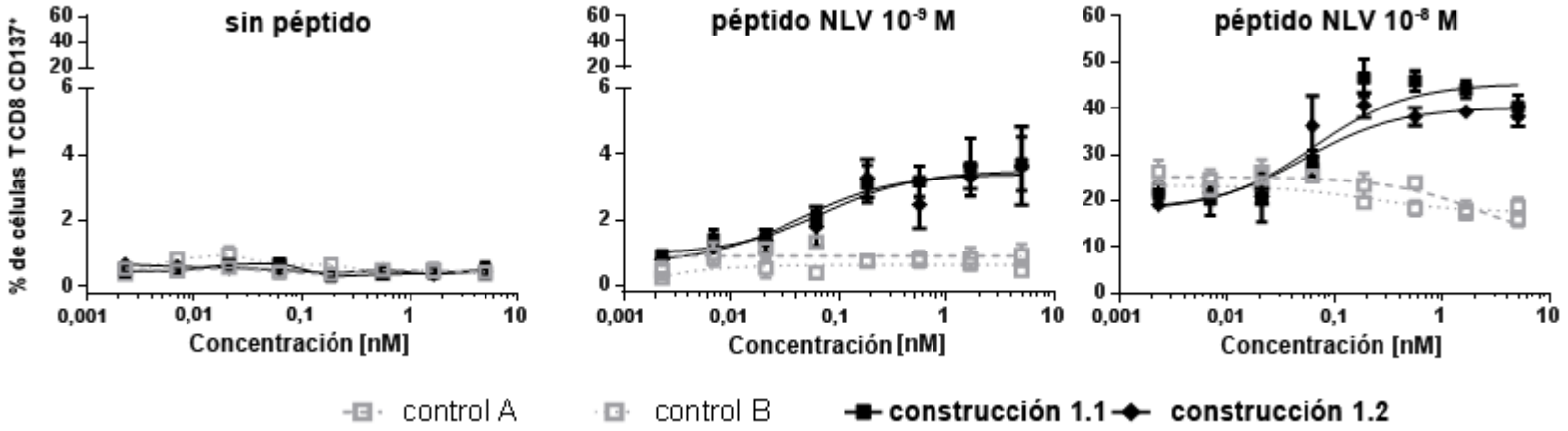

células T
CD8
TCR
4-1BB
células T
CD8
TCR
4-1BB
Fab (28H1)
Anti-FAP
4-1BBL humano di
4-BBL humano mono
huIgG1 Fc
P329G LALA kih
células MV3 FAP+
pulsadas con péptido NLV

Fig. 21

Fig. 22

(22 A)



(22 B)

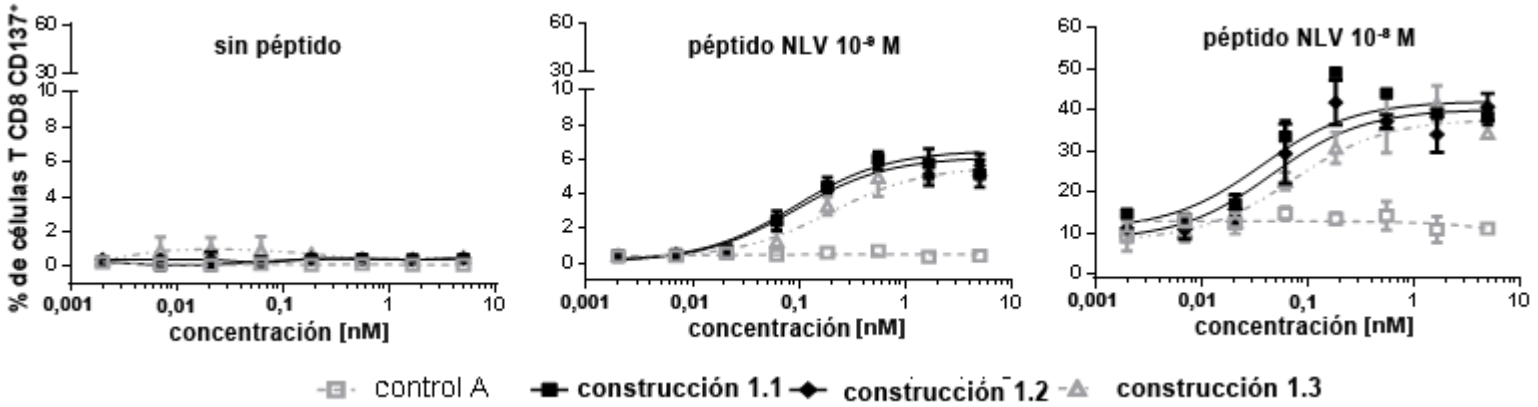
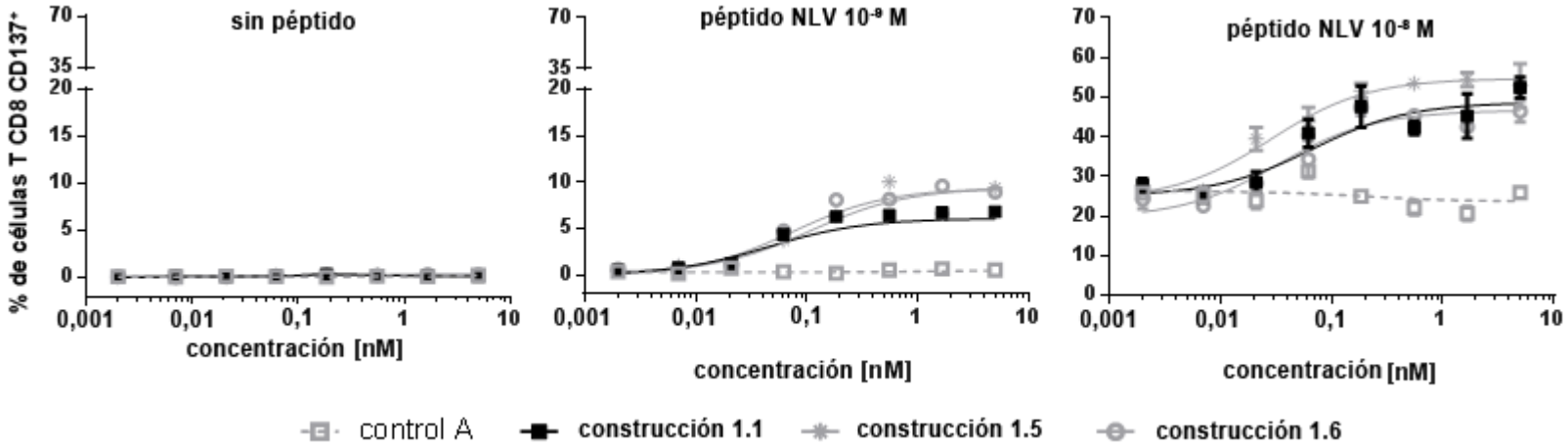


Fig. 22

(22C)



(22D)

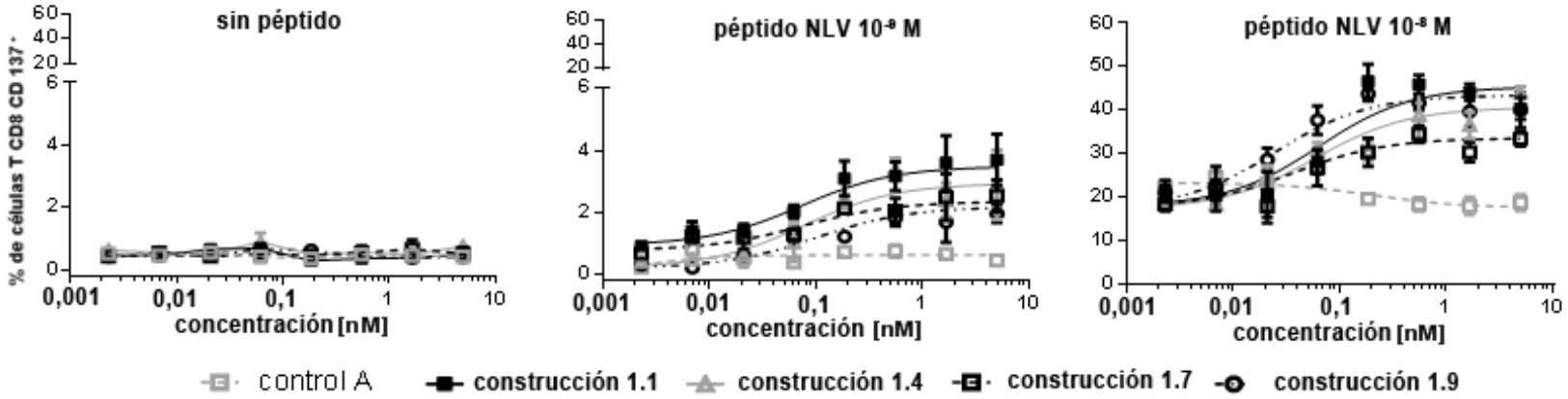


Fig. 22

(22E)

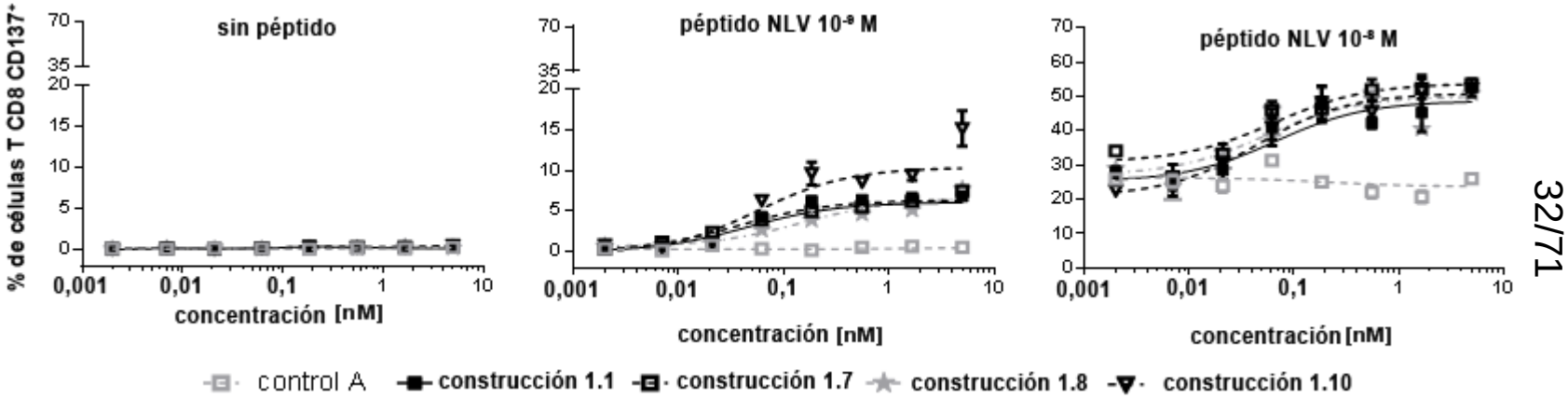
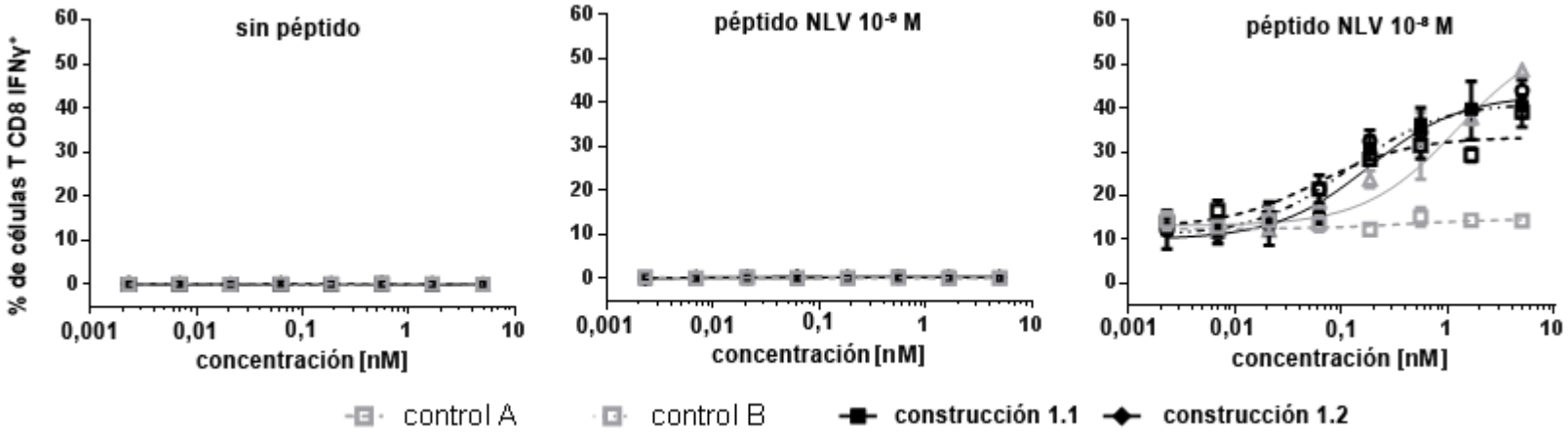

% de células T CD8 CD137+
sin péptido
péptido NLV 10-8 M
péptido NLV 10-8 M
concentración [nM]
concentración [nM]
concentración [nM]
control A
construcción 1.1
construcción 1.7
construcción 1.8
construcción 1.10

Fig. 23

(23 A)



(23 B)

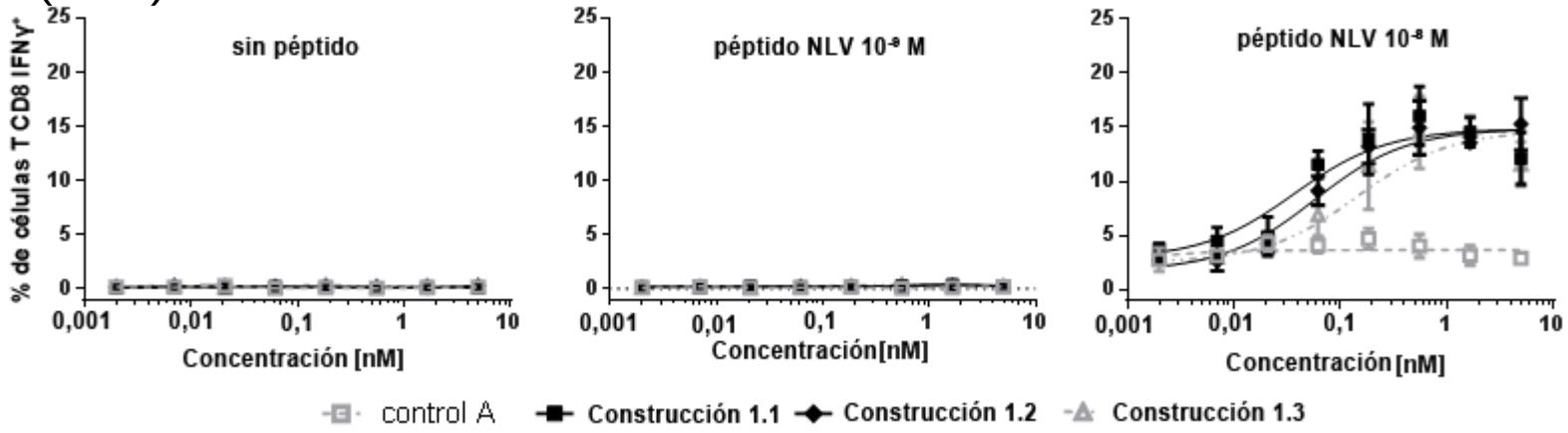
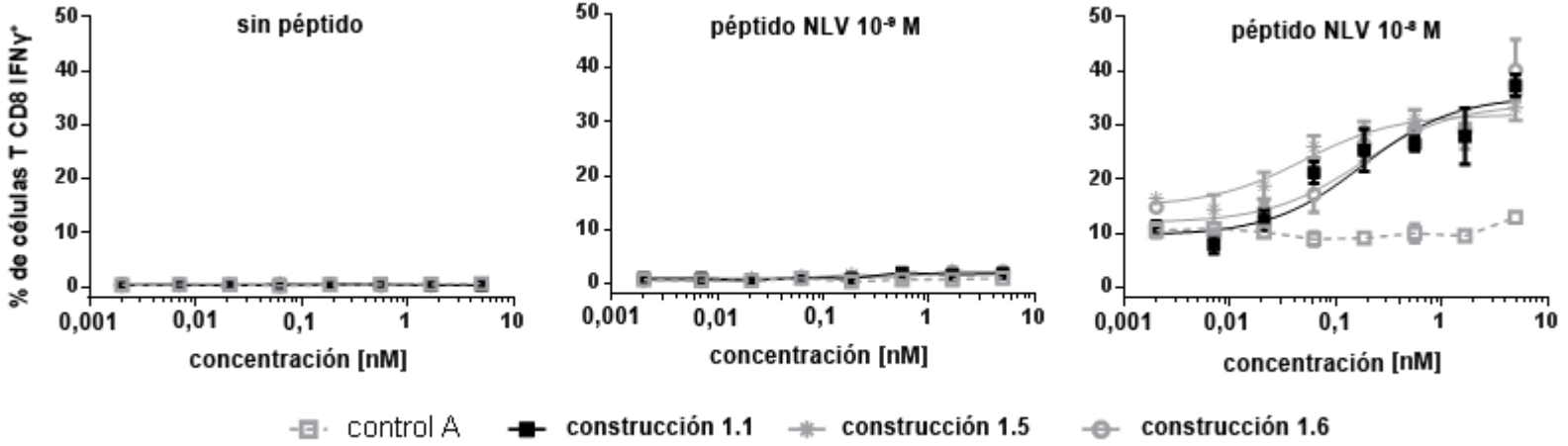


Fig. 23

(23C)



(23D)

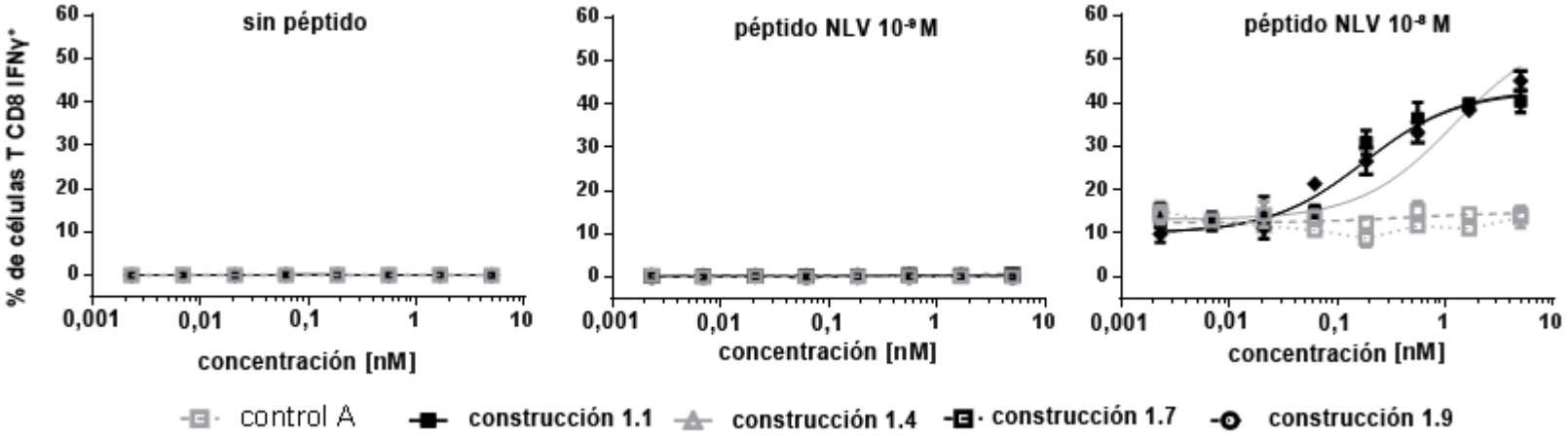


Fig. 23

(23E)

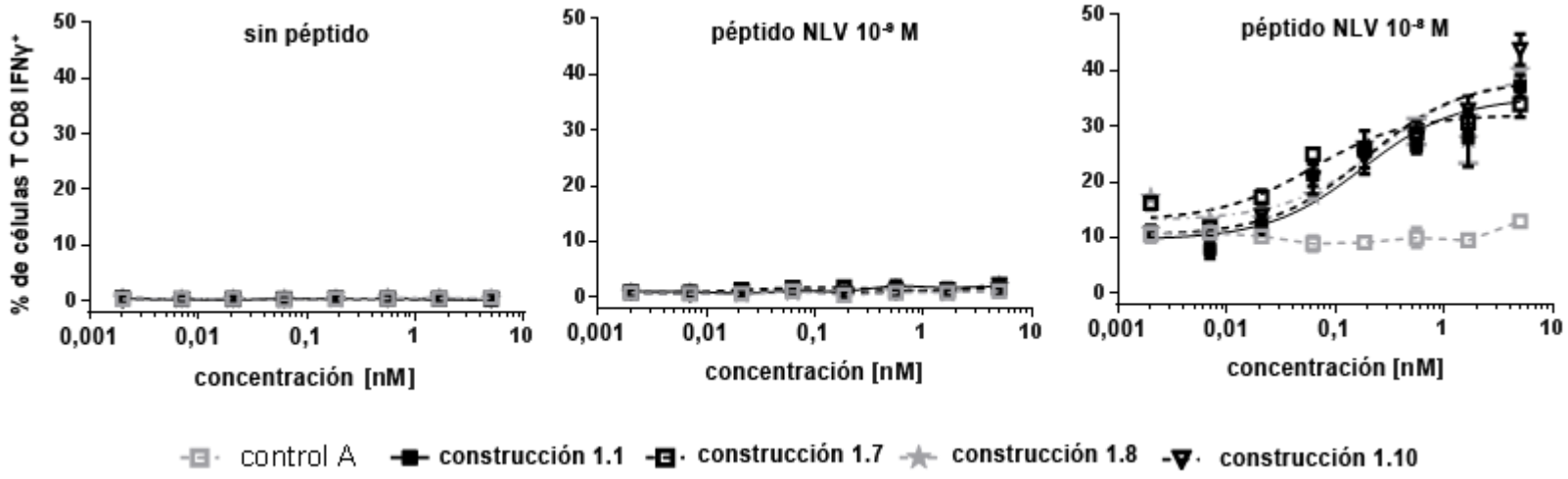
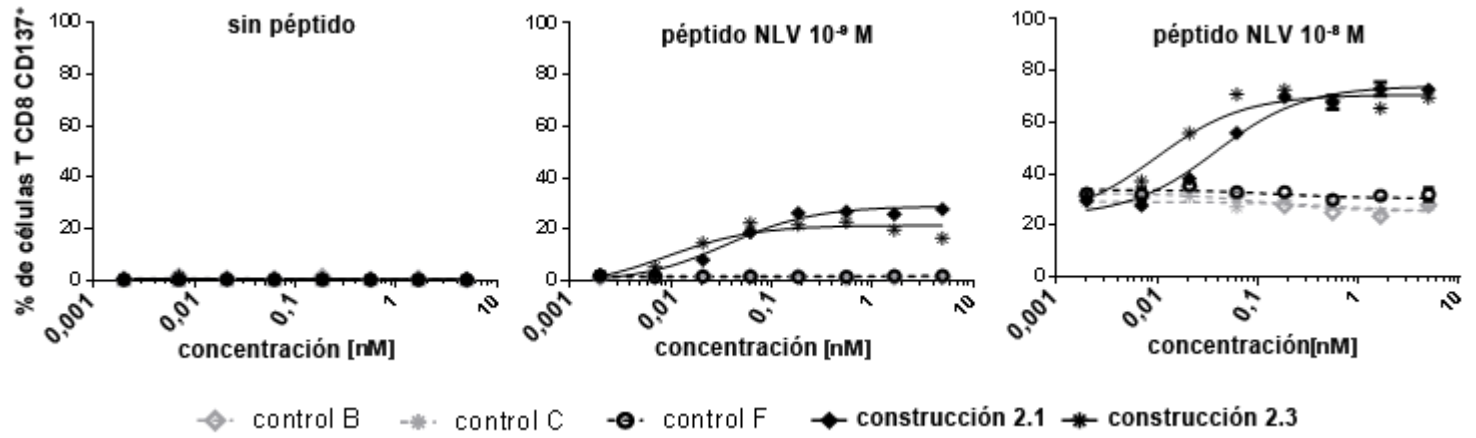

sin péptido
péptido NLV 10⁻⁹ M
péptido NLV 10⁻⁸ M
% de células T CD8 IFNγ⁺
concentración [nM]
0,001
0,01
0,1
1
10
0
10
20
30
40
50
control A
construcción 1.1
construcción 1.7
construcción 1.8
construcción 1.10

Fig. 24

(24 A)



(24 B)

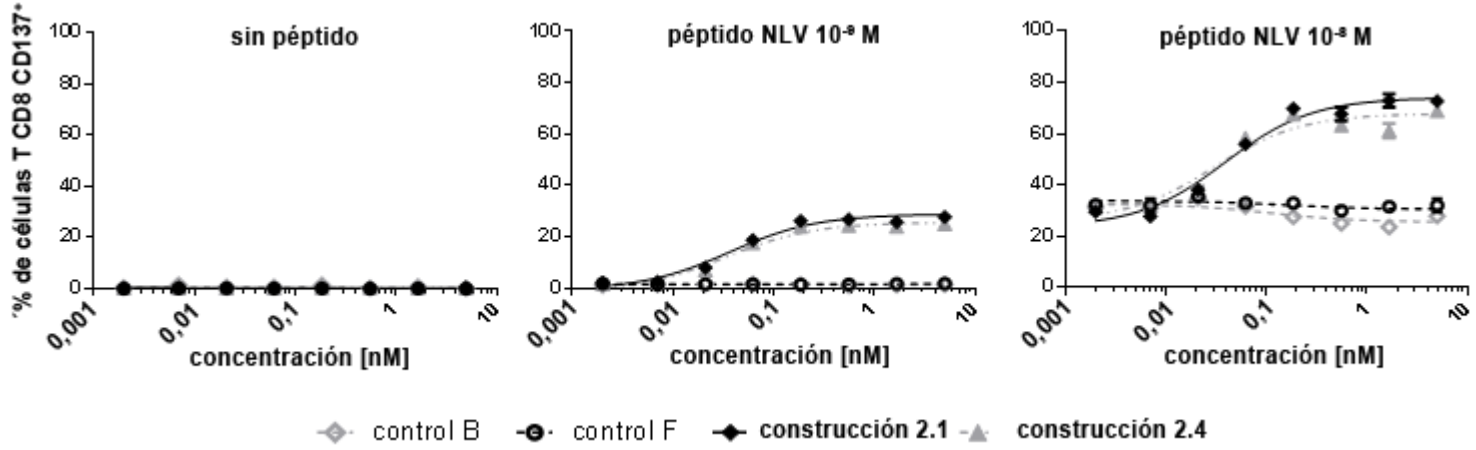
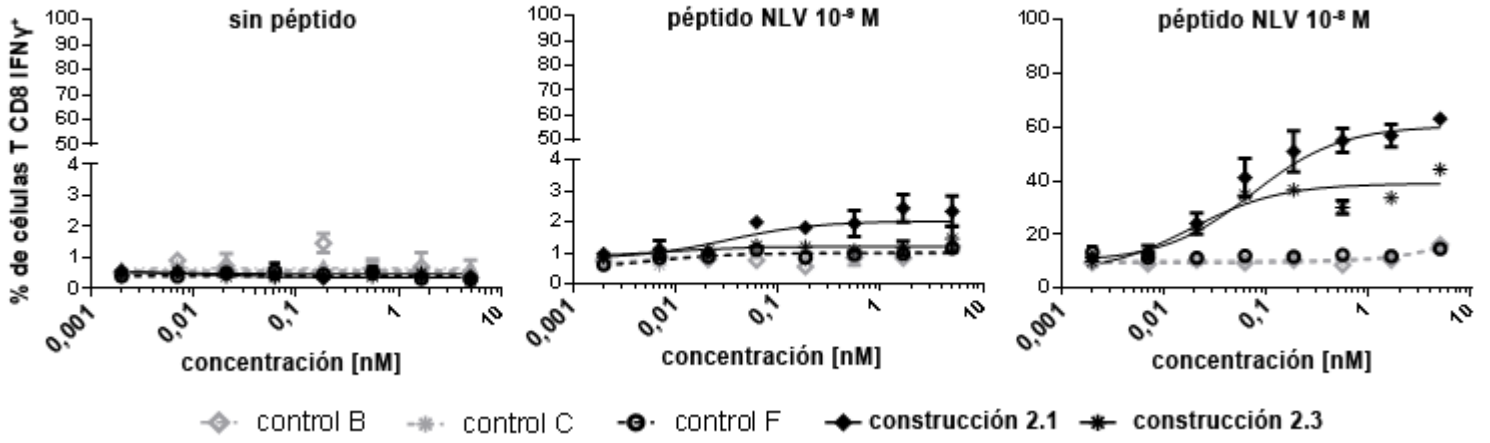
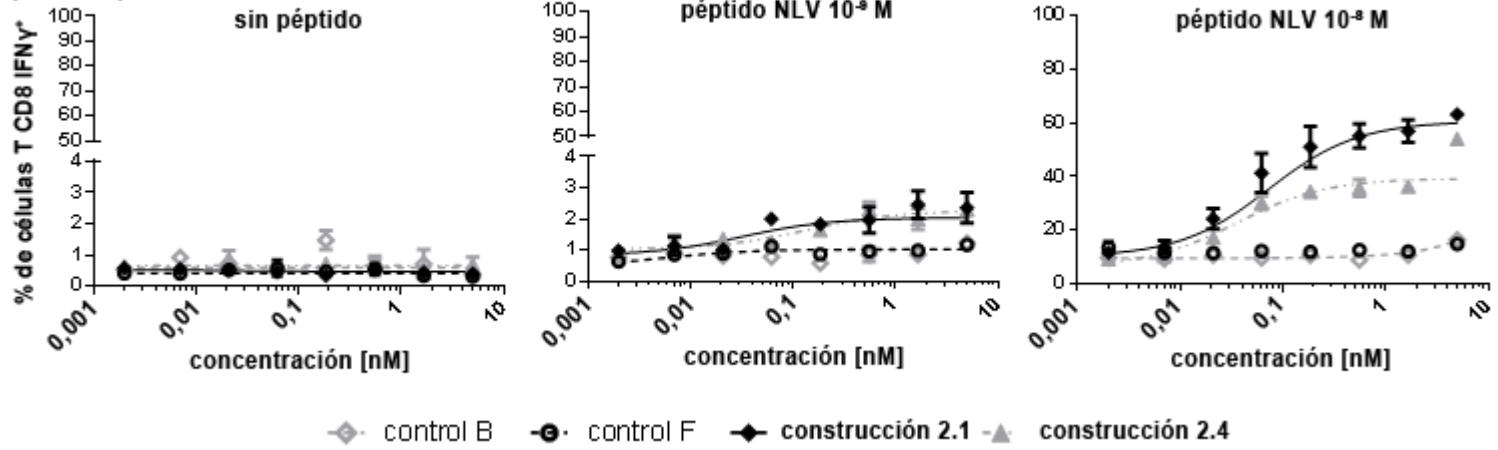


Fig. 25

(25 A)



(25 B)



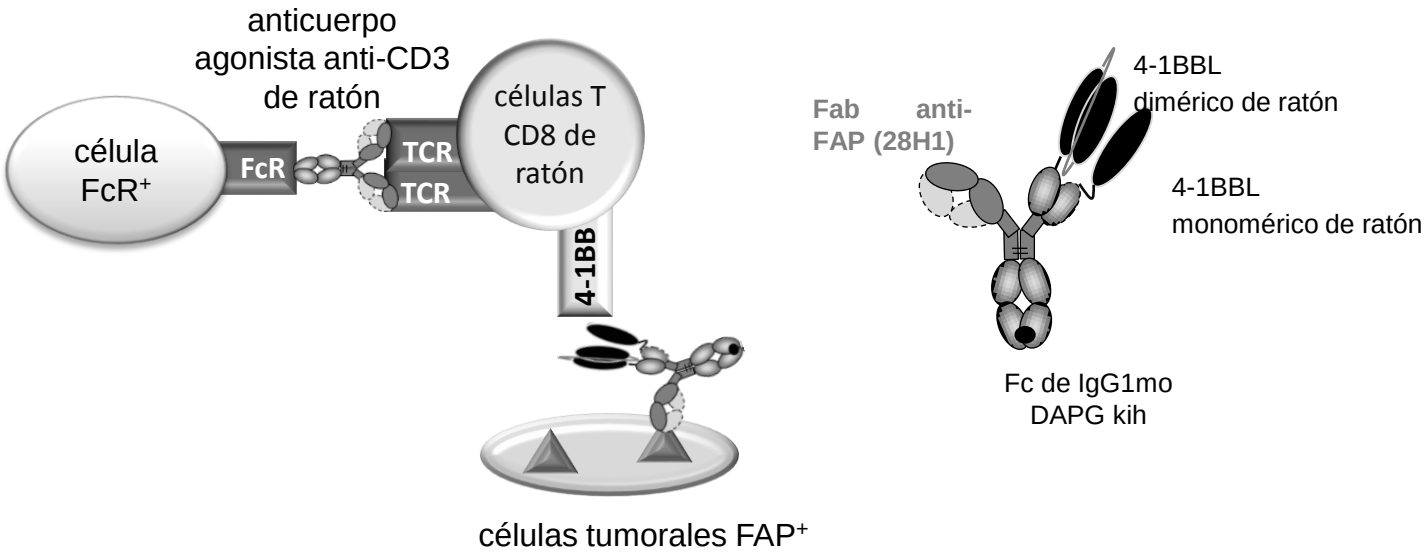

anticuerpo
agonista anti-CD3
de ratón
célula
FcR+
FcR
TCR
TCR
células T
CD8 de
ratón
4-1BB
células tumorales FAP+
Fab anti-
FAP (28H1)
4-1BBL
dimérico de ratón
4-1BBL
monomérico de ratón
Fc de IgG1mo
DAPG kih

Fig. 26

Fig. 27

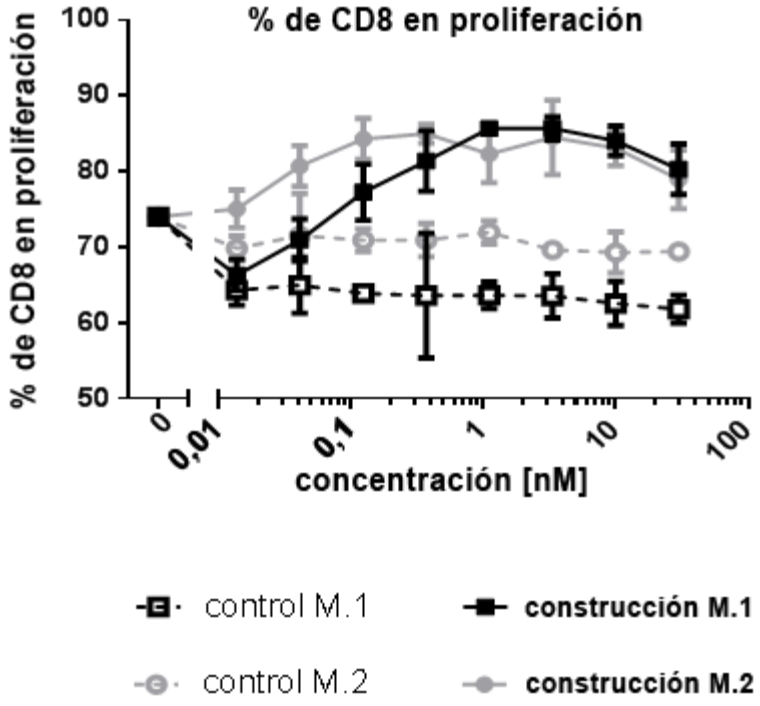

% de CD8 en proliferación
% de CD8 en proliferación
100
90
80
70
60
50
0
0,01
0,1
1
10
100
concentración [nM]
control M.1
construcción M.1
control M.2
construcción M.2

Fig. 28 A

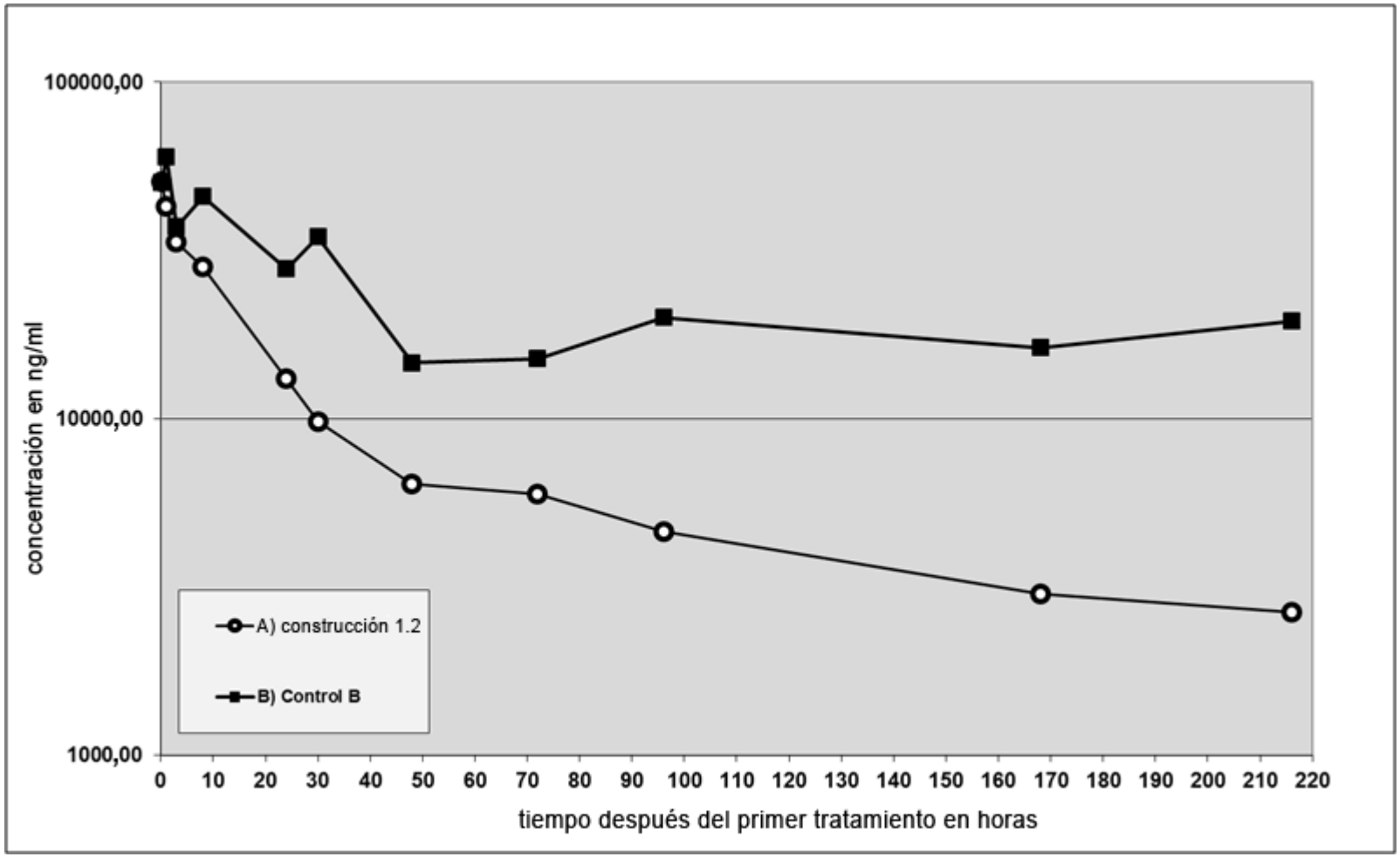

100000,00
10000,00
1000,00
concentración en ng/ml
0 10 20 30 40 50 60 70 80 90 100 110 120 130 140 150 160 170 180 190 200 210 220
tiempo después del primer tratamiento en horas
A) construcción 1.2
B) Control B

Fig. 28 B

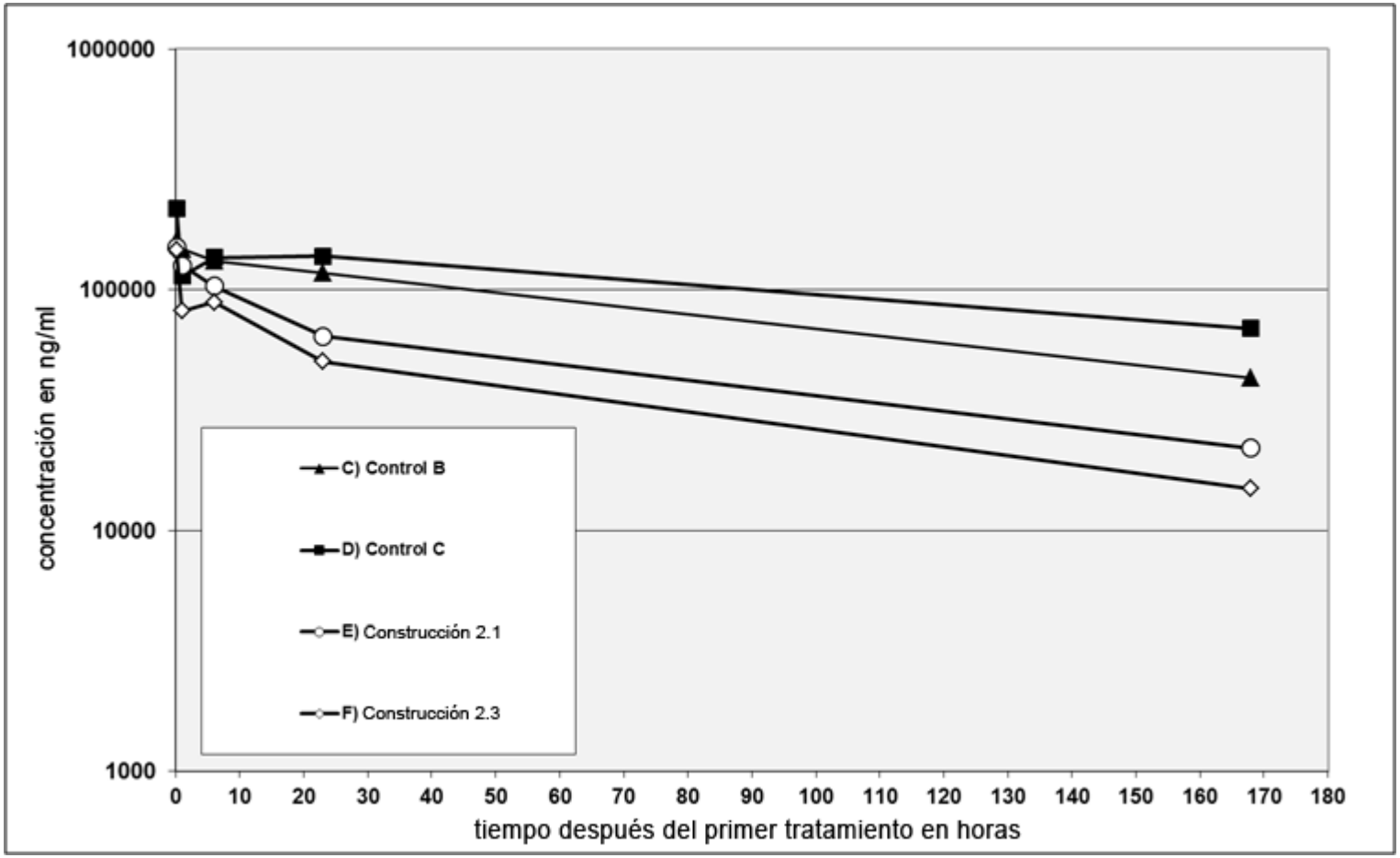

1000000
100000
10000
1000
concentración en ng/ml
C) Control B
D) Control C
E) Construcción 2.1
F) Construcción 2.3
0
10
20
30
40
50
60
70
80
90
100
110
120
130
140
150
160
170
180
tiempo después del primer tratamiento en horas

Fig. 28C

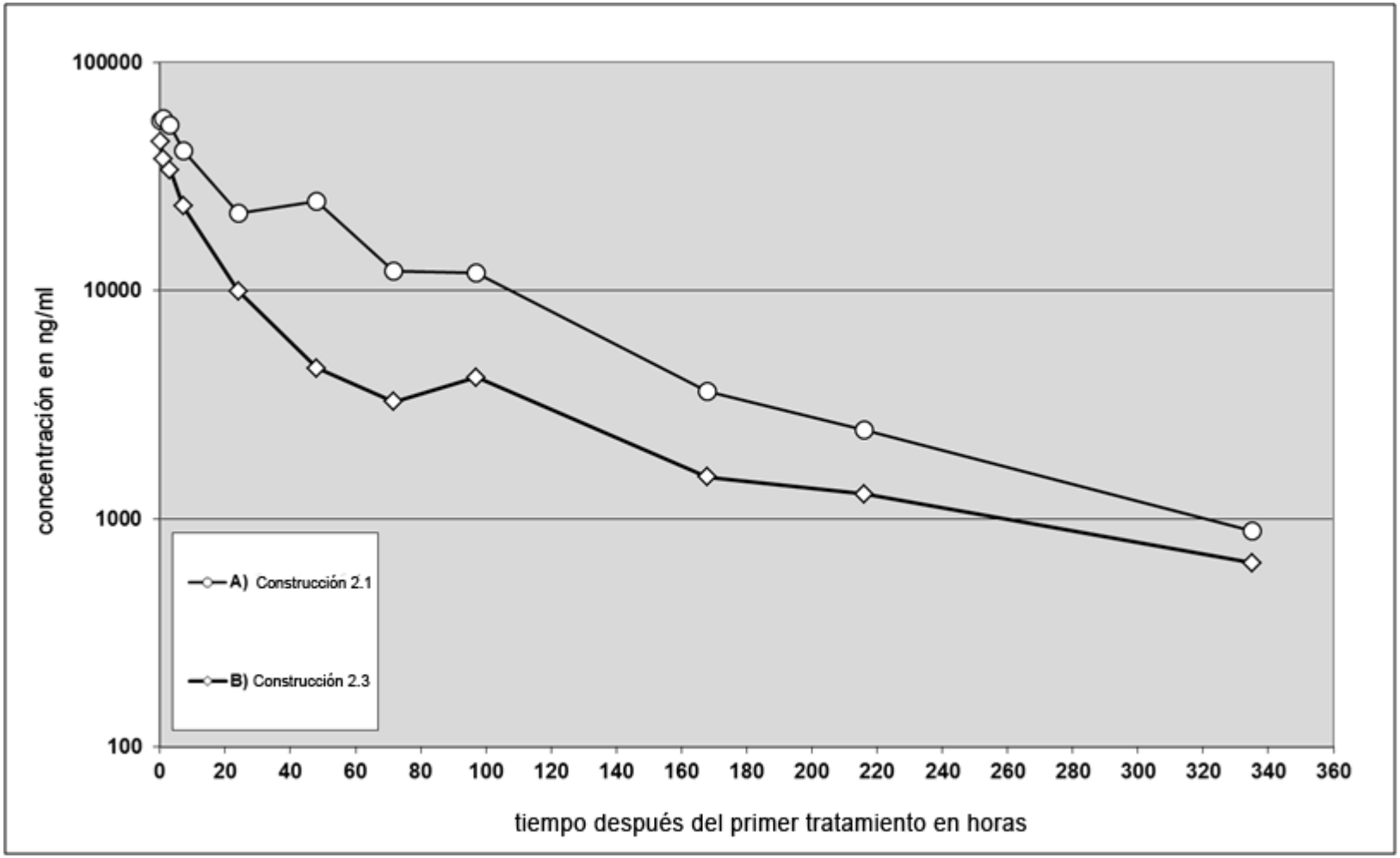

100000
10000
1000
100
concentración en ng/ml
A) Construcción 2.1
B) Construcción 2.3
0
20
40
60
80
100
120
140
160
180
200
220
240
260
280
300
320
340
360
tiempo después del primer tratamiento en horas

Fig. 29

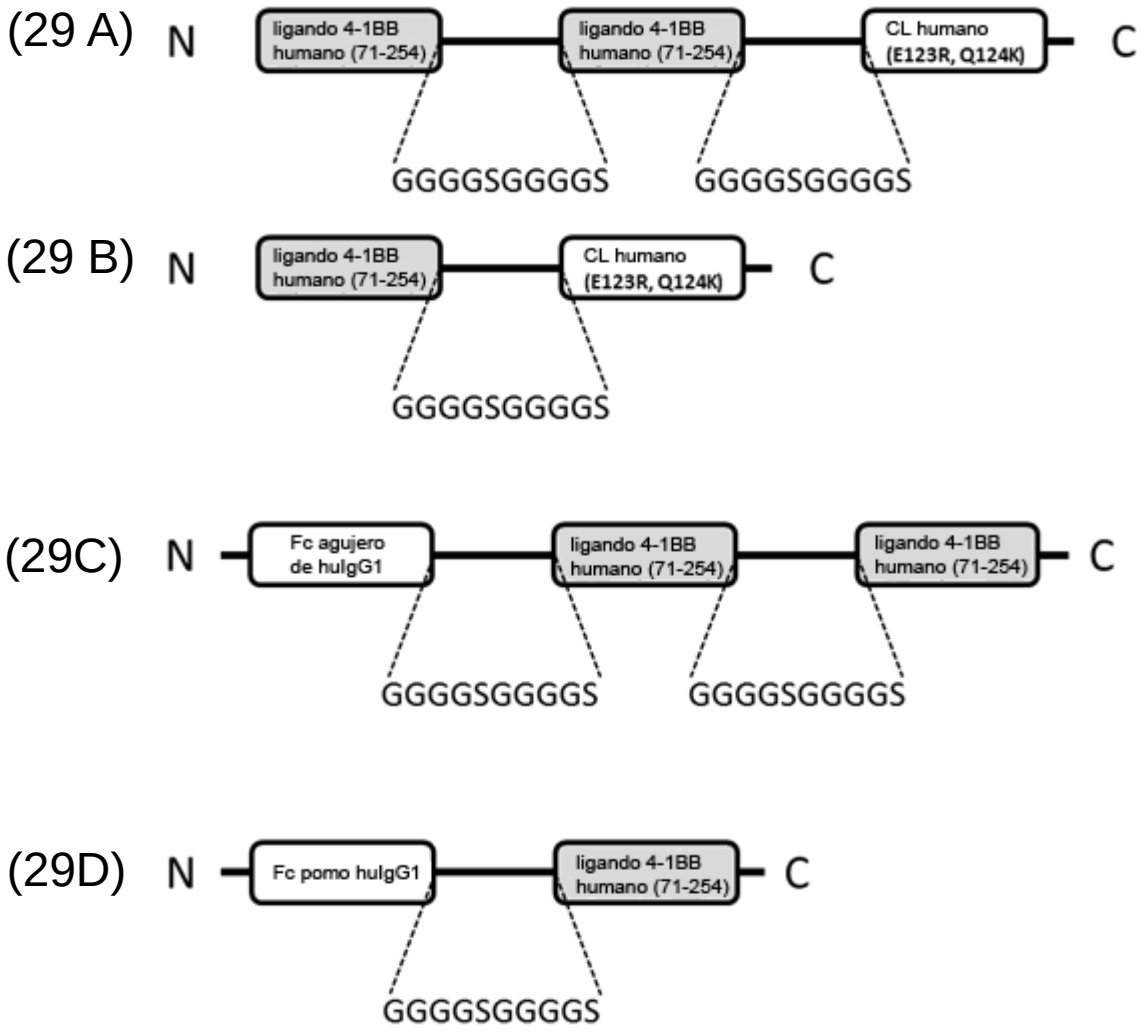
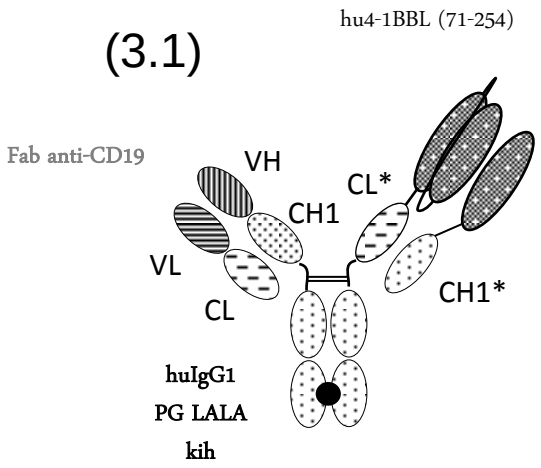
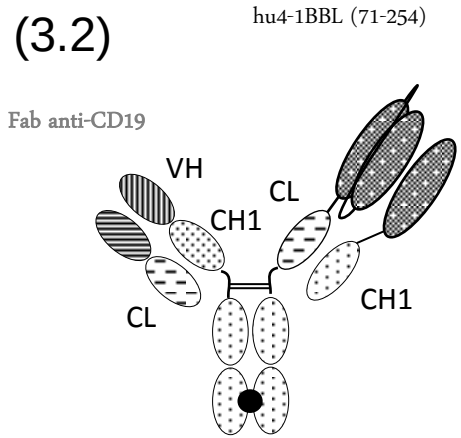

(29 A)
N
ligando 4-1BB humano (71-254)
ligando 4-1BB humano (71-254)
CL humano (E123R, Q124K)
C
GGGGSGGGGS
GGGGSGGGGS
(29 B)
N
ligando 4-1BB humano (71-254)
CL humano (E123R, Q124K)
C
GGGGSGGGGS
(29C)
N
Fc agujero de hulgG1
ligando 4-1BB humano (71-254)
ligando 4-1BB humano (71-254)
C
GGGGSGGGGS
GGGGSGGGGS
(29D)
N
Fc pomo hulgG1
ligando 4-1BB humano (71-254)
C
GGGGSGGGGS

Fig. 30

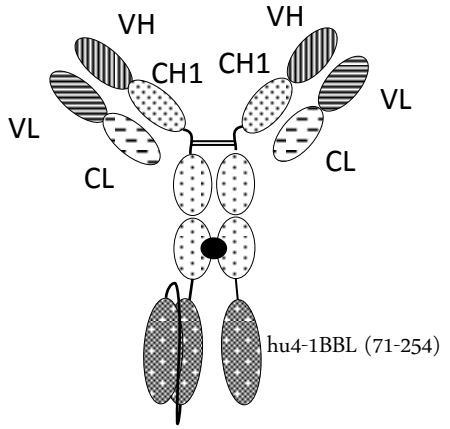
(3.1)



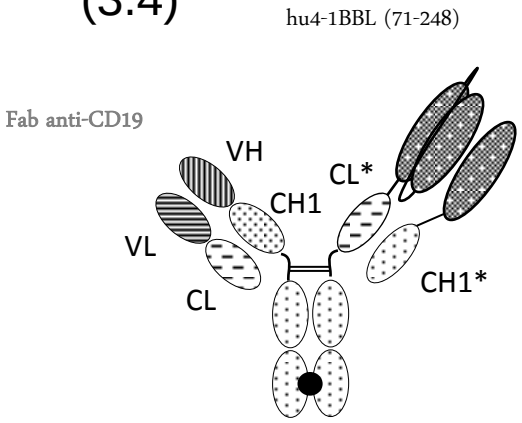
(3.2)



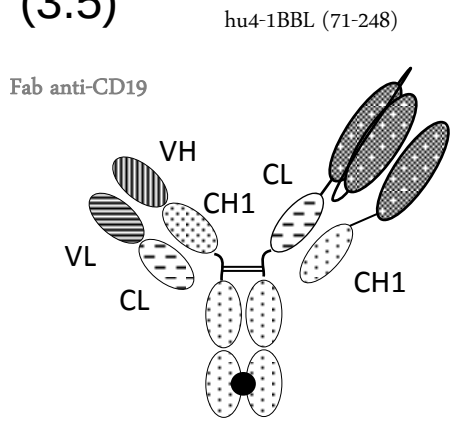
(3.3)



(3.4)



(3.5)



(3.6)

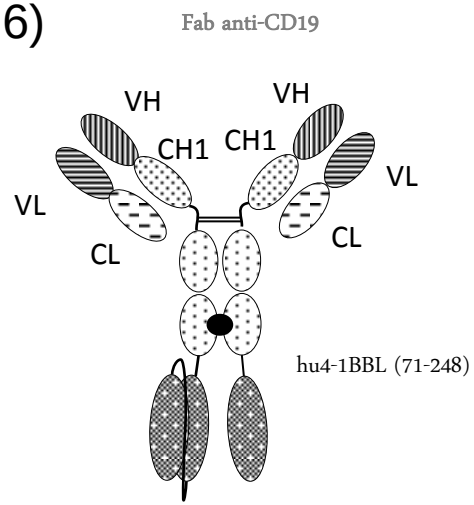
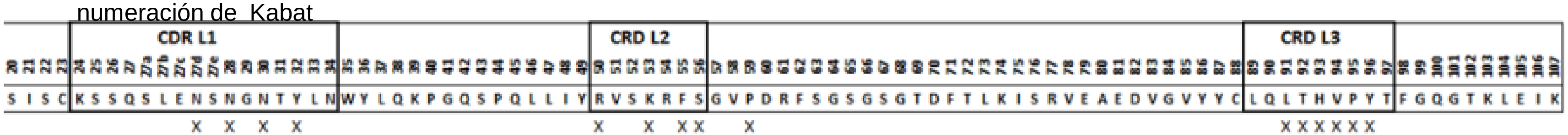


Fig. 31 A

CDRs de acuerdo con la

numeración de Kabat



secuencia de VL de 8B8



secuencia de VH de 8B8

X = posiciones aleatorizadas

Fig. 31 B

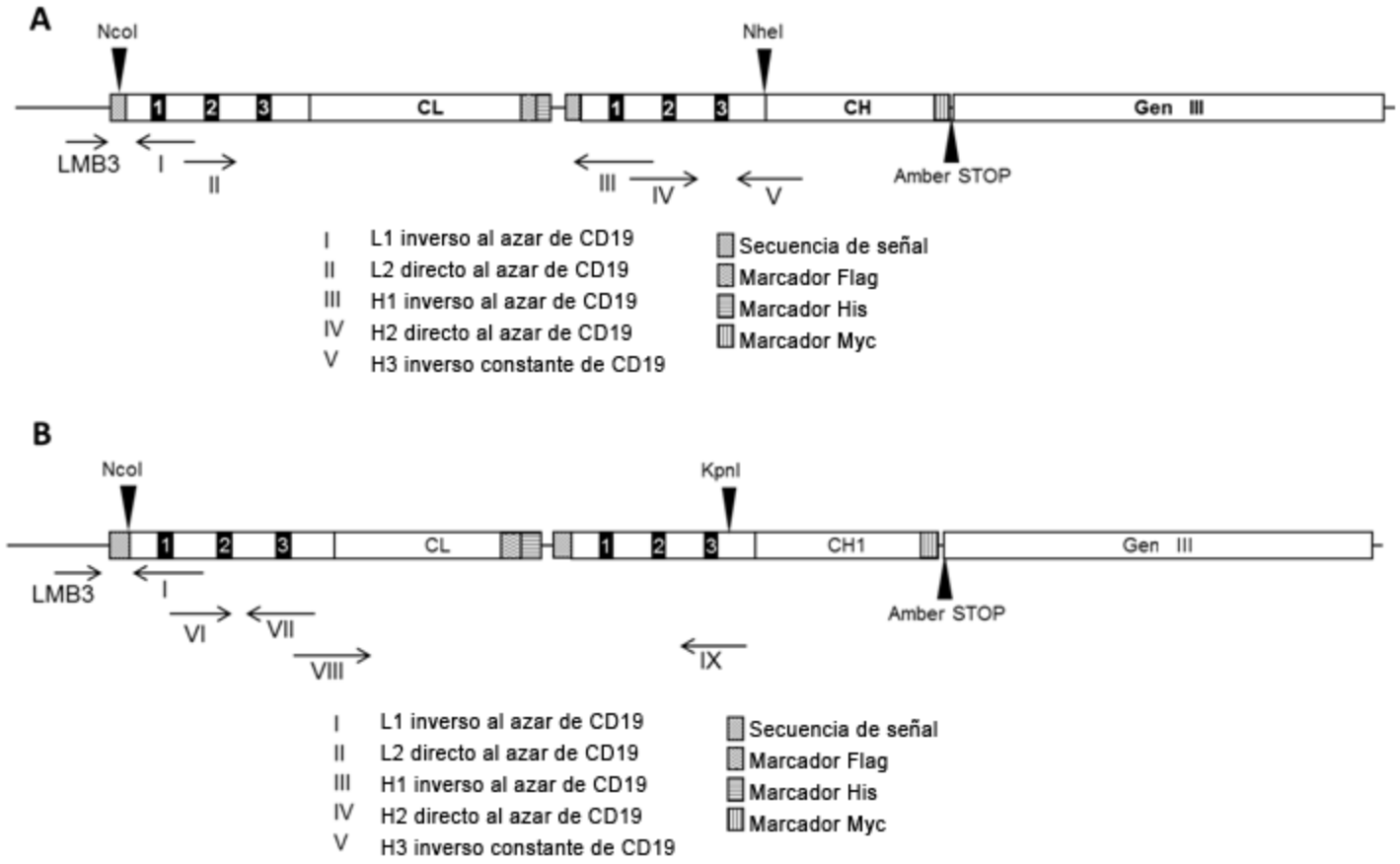

A
NcoI
NheI
1
2
3
CL
1
2
3
CH
Gen III
LMB3
I
II
III
IV
V
Amber STOP
I L1 inverso al azar de CD19
II L2 directo al azar de CD19
III H1 inverso al azar de CD19
IV H2 directo al azar de CD19
V H3 inverso constante de CD19
Secuencia de señal
Marcador Flag
Marcador His
Marcador Myc
B
NcoI
KpnI
1
2
3
CL
1
2
3
CH1
Gen III
LMB3
I
VI
VII
VIII
IX
Amber STOP
I L1 inverso al azar de CD19
II L2 directo al azar de CD19
III H1 inverso al azar de CD19
IV H2 directo al azar de CD19
V H3 inverso constante de CD19
Secuencia de señal
Marcador Flag
Marcador His
Marcador Myc

Fig. 32

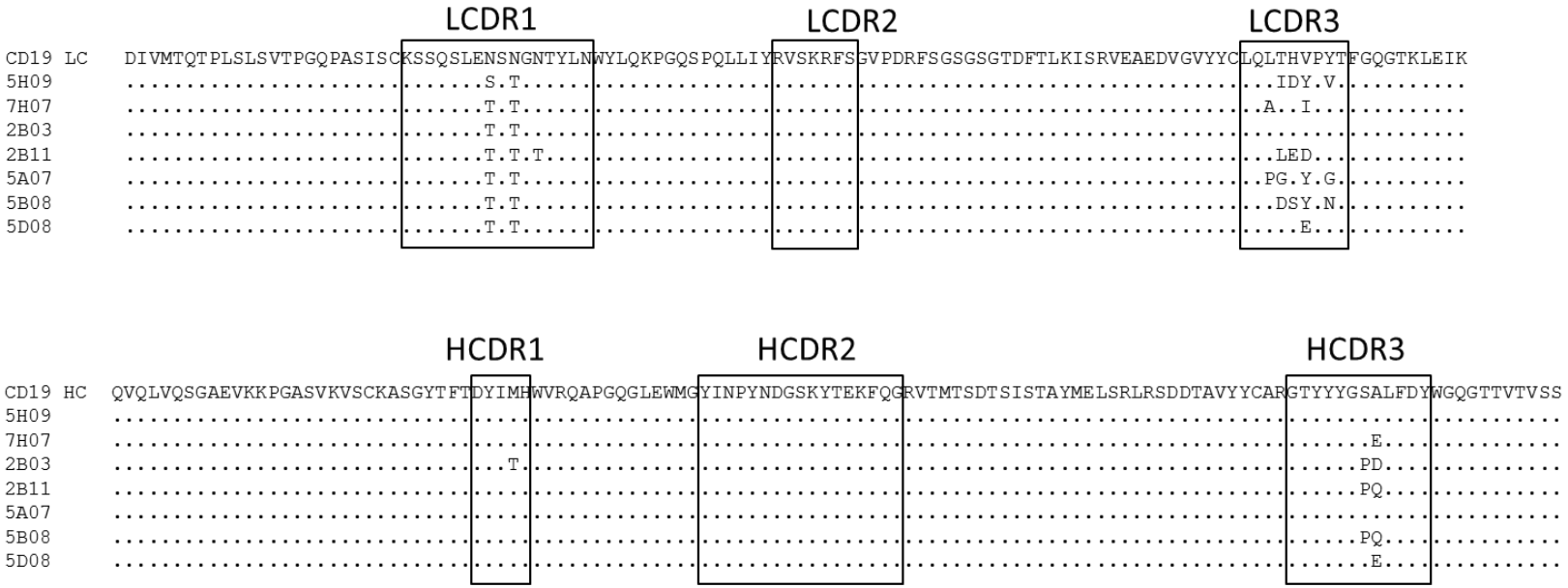

LCDR1
LCDR2
LCDR3
CD19 LC DIVMTQTPLSLSVTPGQPASISCKSSQSLENSNGNTYLNWYLQKPGQSPQLLIYRVSKRFSGVPDRFSGSGSGTDFTLKISRVEAEDVGVYYCLQLTHVPYTFGQGTKLEIK
5H09 .....S.T.....IDY.V.....
7H07 .....T.T.....A..I.....
2B03 .....T.T.....
2B11 .....T.T.T.....LED.....
5A07 .....T.T.....PG.Y.G.....
5B08 .....T.T.....DSY.N.....
5D08 .....T.T.....E.....
HCDR1
HCDR2
HCDR3
CD19 HC QVQLVQSGAEVKKPGASVKVSCKASGYTFTDYIMHWVRQAPGQGLEWMGYINPYNDGSKYTEKFQGRVTMTSDTSISTAYMELSRLRSDDTAVYYCARGTYYYGSALFDYWGQGTTVTVSS
5H09 .....
7H07 .....E.....
2B03 ...T.....PD.....
2B11 .....PQ.....
5A07 .....
5B08 .....PQ.....
5D08 .....E.....

Fig. 33

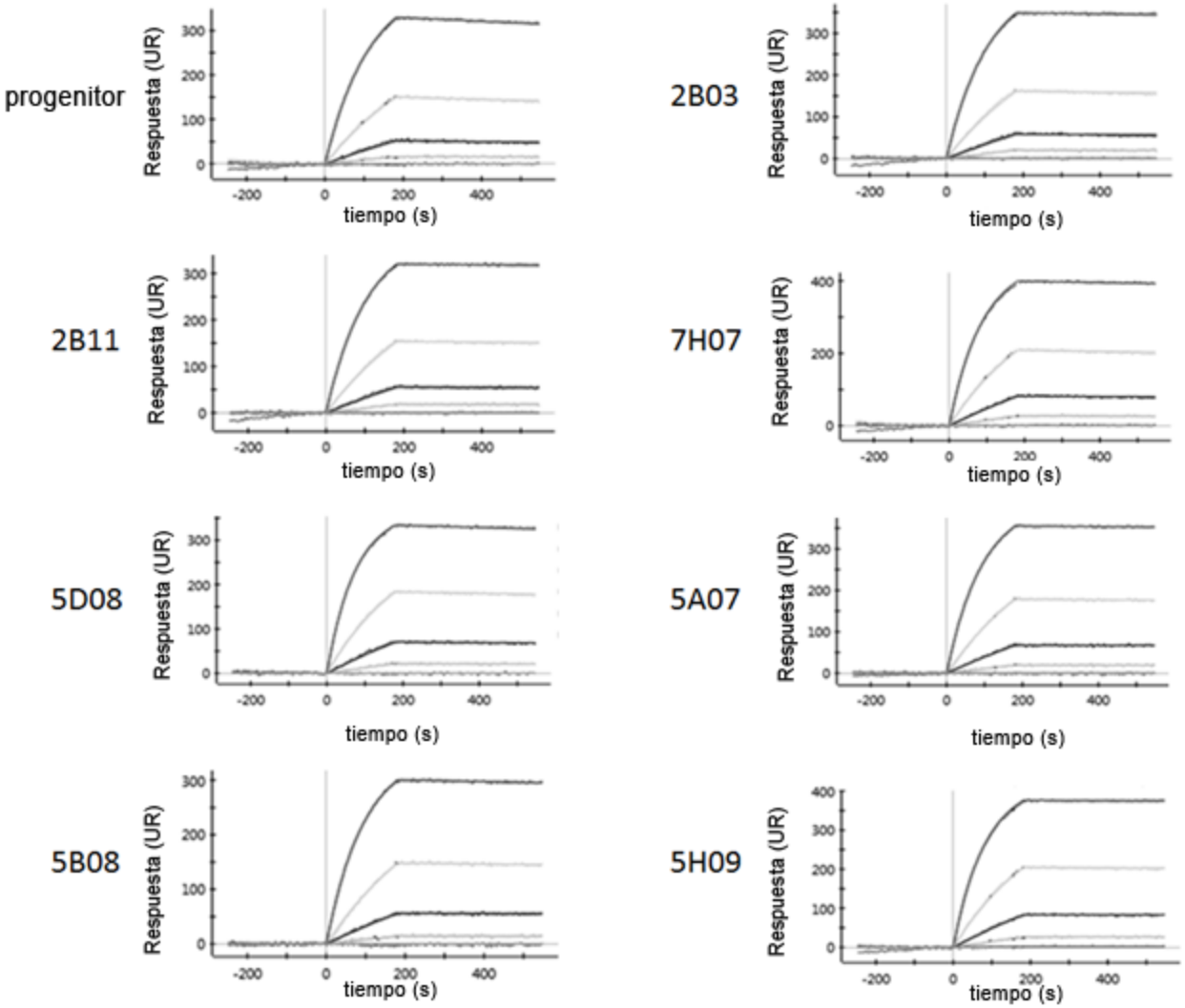

progenitor
Respuesta (UR)
tiempo (s)
2B03
2B11
7H07
5D08
5A07
5B08
5H09

Fig. 34

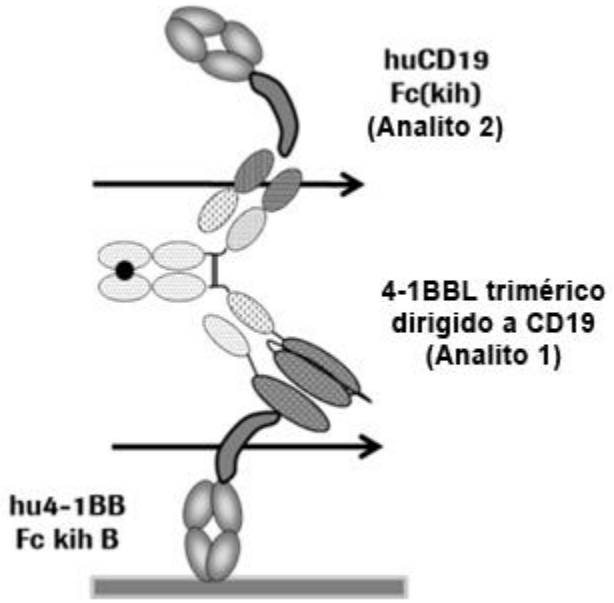
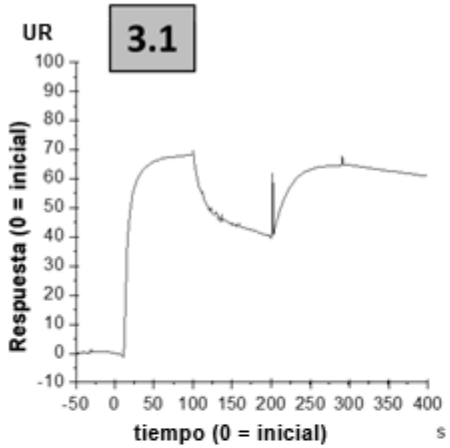
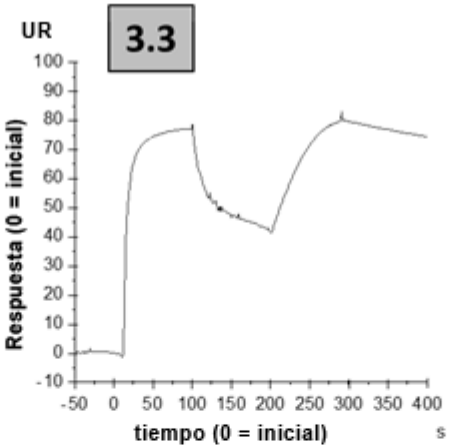
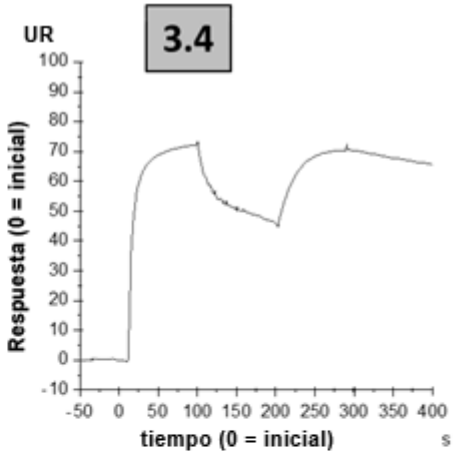
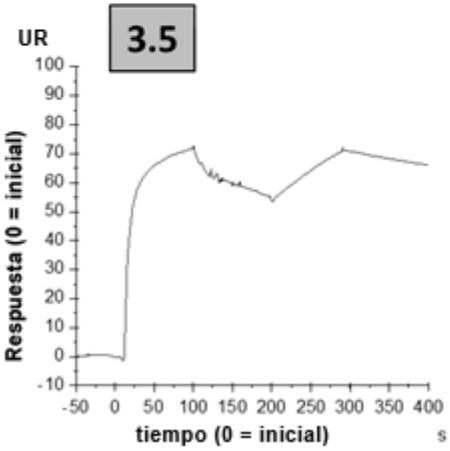

huCD19
Fc(kih)
(Analito 2)
4-1BBL trimérico
dirigido a CD19
(Analito 1)
hu4-1BB
Fc kih B

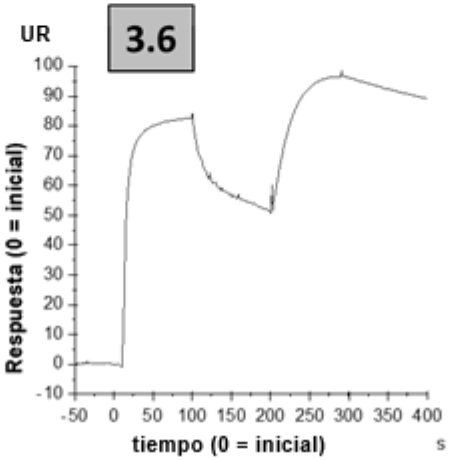
Fig. 35


3.1
UR
Respuesta (0 = inicial)
tiempo (0 = inicial)
s


3.3
UR
Respuesta (0 = inicial)
tiempo (0 = inicial)
s


3.4
UR
Respuesta (0 = inicial)
tiempo (0 = inicial)
s


3.5
UR
Respuesta (0 = inicial)
tiempo (0 = inicial)
s


3.6
UR
Respuesta (0 = inicial)
tiempo (0 = inicial)
s

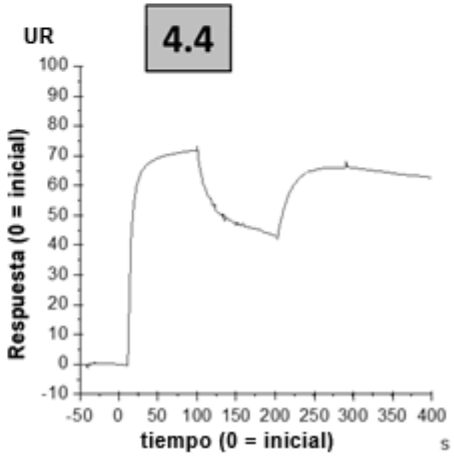

4.4
UR
Respuesta (0 = inicial)
tiempo (0 = inicial)
s

Fig. 36 A

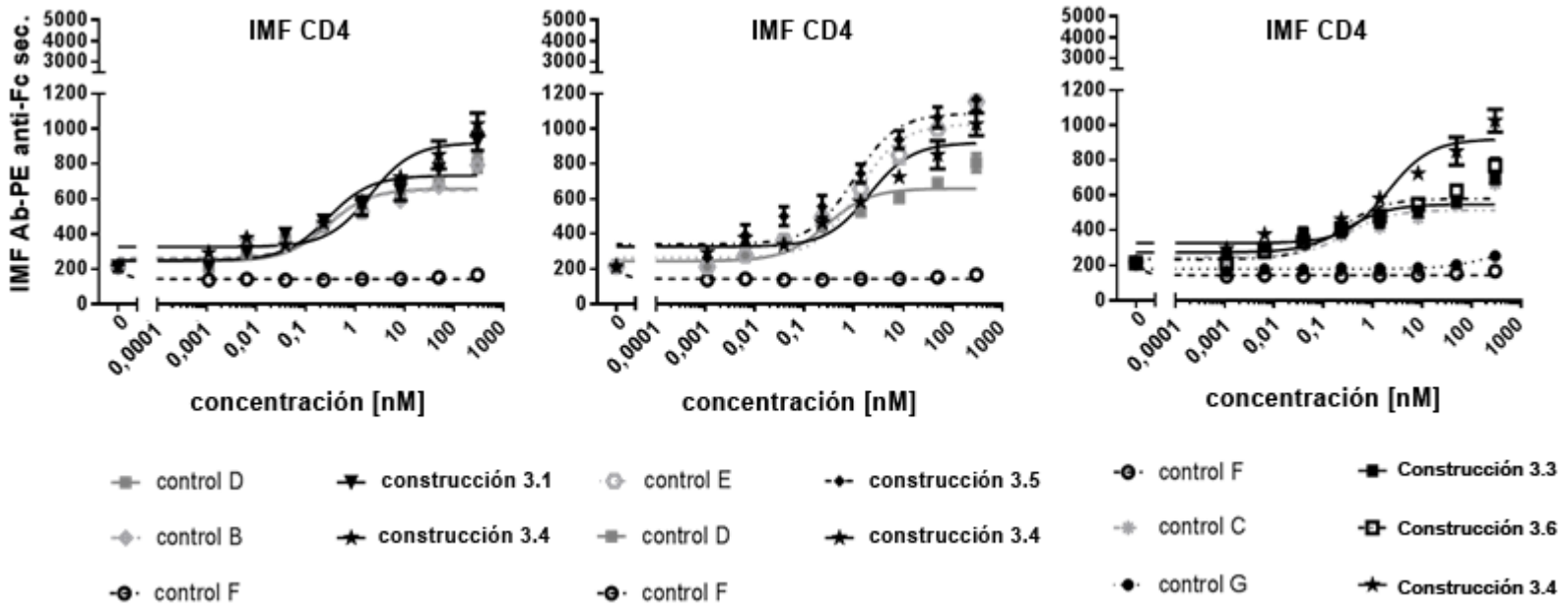

IMF CD4
IMF Ab-PE anti-Fc sec.
5000
4000
3000
1200
1000
800
600
400
200
0
0
0,0001
0,001
0,01
0,1
1
10
100
1000
concentración [nM]
control D
construcción 3.1
control B
construcción 3.4
control F
IMF CD4
concentración [nM]
control E
construcción 3.5
control D
construcción 3.4
control F
IMF CD4
concentración [nM]
control F
Construcción 3.3
control C
Construcción 3.6
control G
Construcción 3.4

Fig. 36B

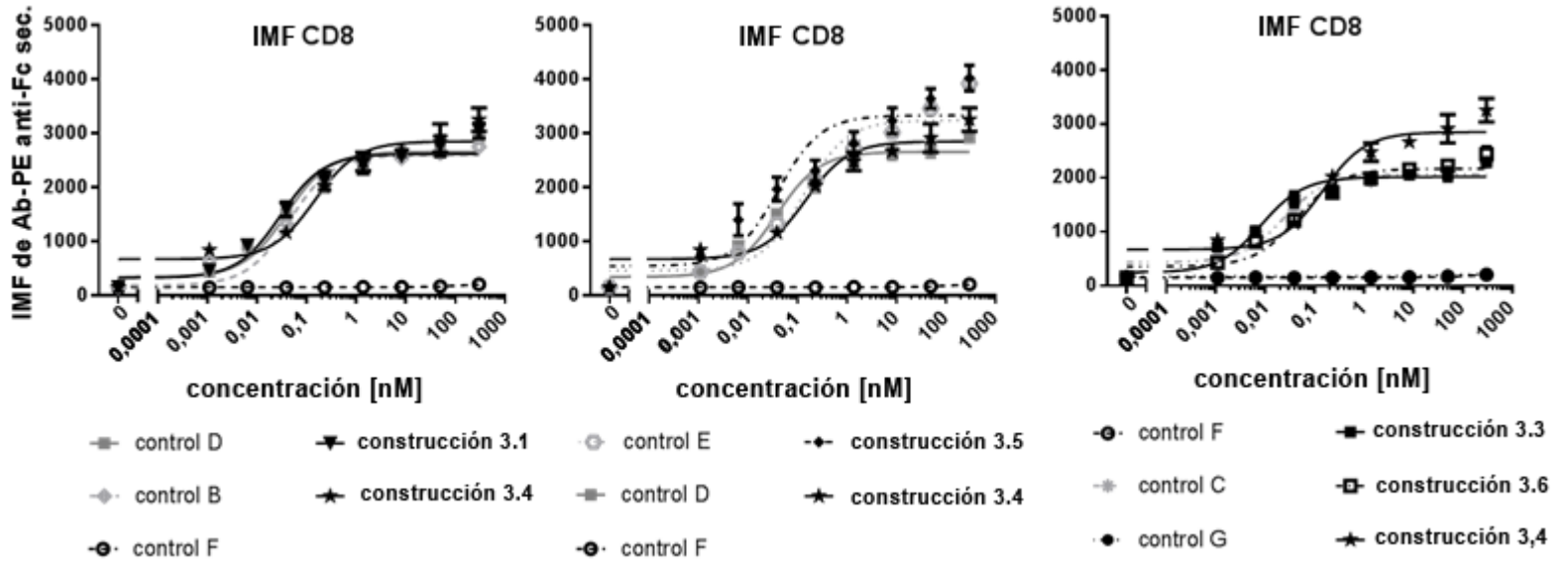

IMF de Ab-PE anti-Fc sec.
IMF CD8
concentración [nM]
control D
construcción 3.1
control B
construcción 3.4
control F
IMF CD8
concentración [nM]
control E
construcción 3.5
control D
construcción 3.4
control F
IMF CD8
concentración [nM]
control F
construcción 3.3
control C
construcción 3.6
control G
construcción 3,4

Fig. 37A

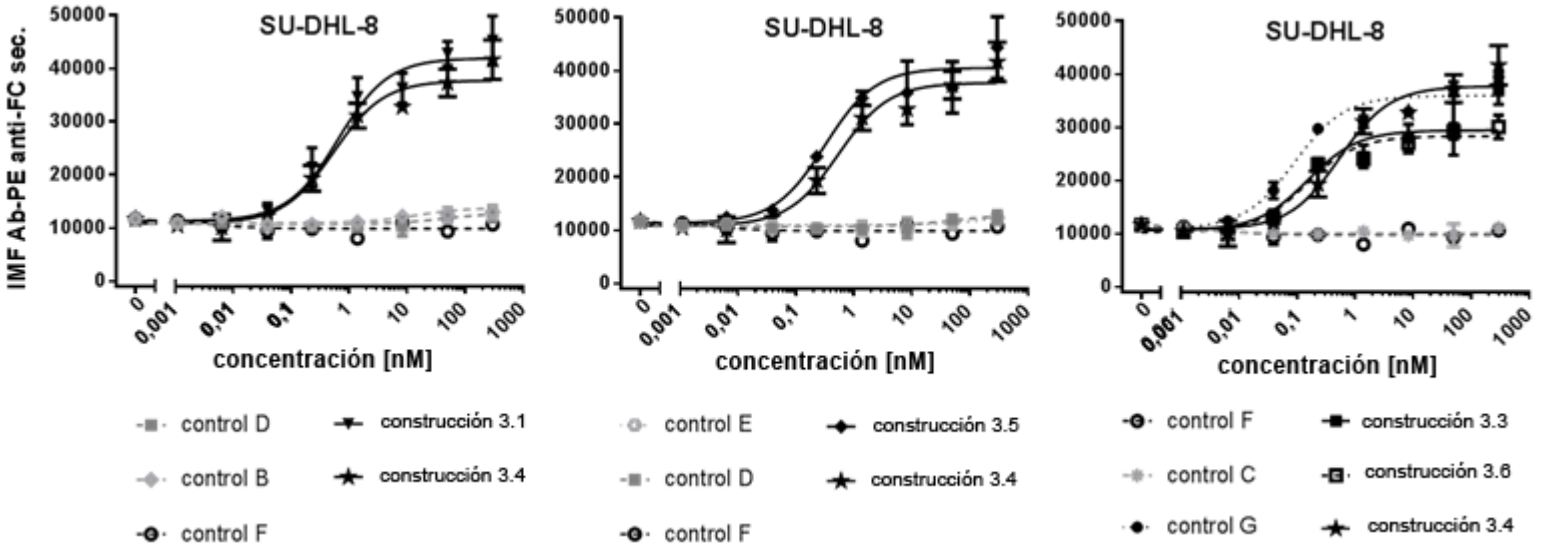

SU-DHL-8
IMF Ab-PE anti-FC sec.
50000
40000
30000
20000
10000
0
0
0,001
0,01
0,1
1
10
100
1000
concentración [nM]
control D
control B
control F
construcción 3.1
construcción 3.4
SU-DHL-8
concentración [nM]
control E
control D
control F
construcción 3.5
construcción 3.4
SU-DHL-8
concentración [nM]
control F
control C
control G
construcción 3.3
construcción 3.6
construcción 3.4

Fig. 37 B

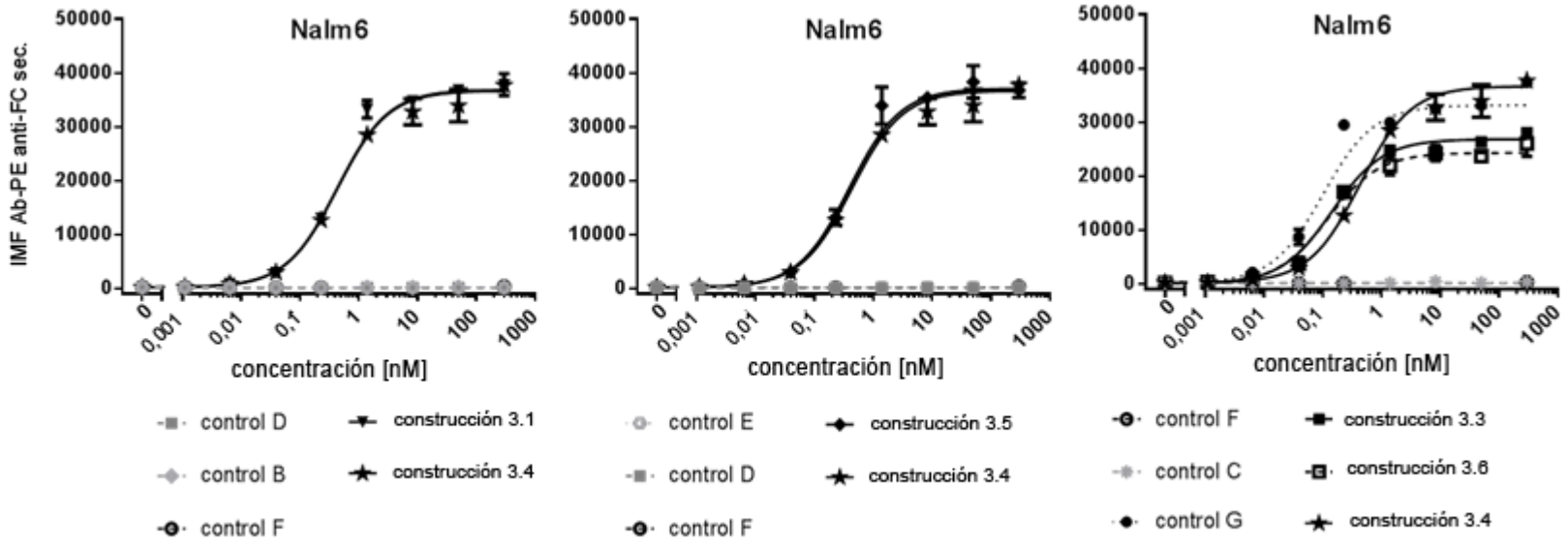

Nalm6
IMF Ab-PE anti-FC sec.
50000
40000
30000
20000
10000
0
0
0,001
0,01
0,1
1
10
100
1000
concentración [nM]
control D
construcción 3.1
control B
construcción 3.4
control F
Nalm6
concentración [nM]
control E
construcción 3.5
control D
construcción 3.4
control F
Nalm6
concentración [nM]
control F
construcción 3.3
control C
construcción 3.6
control G
construcción 3.4

Fig. 37C

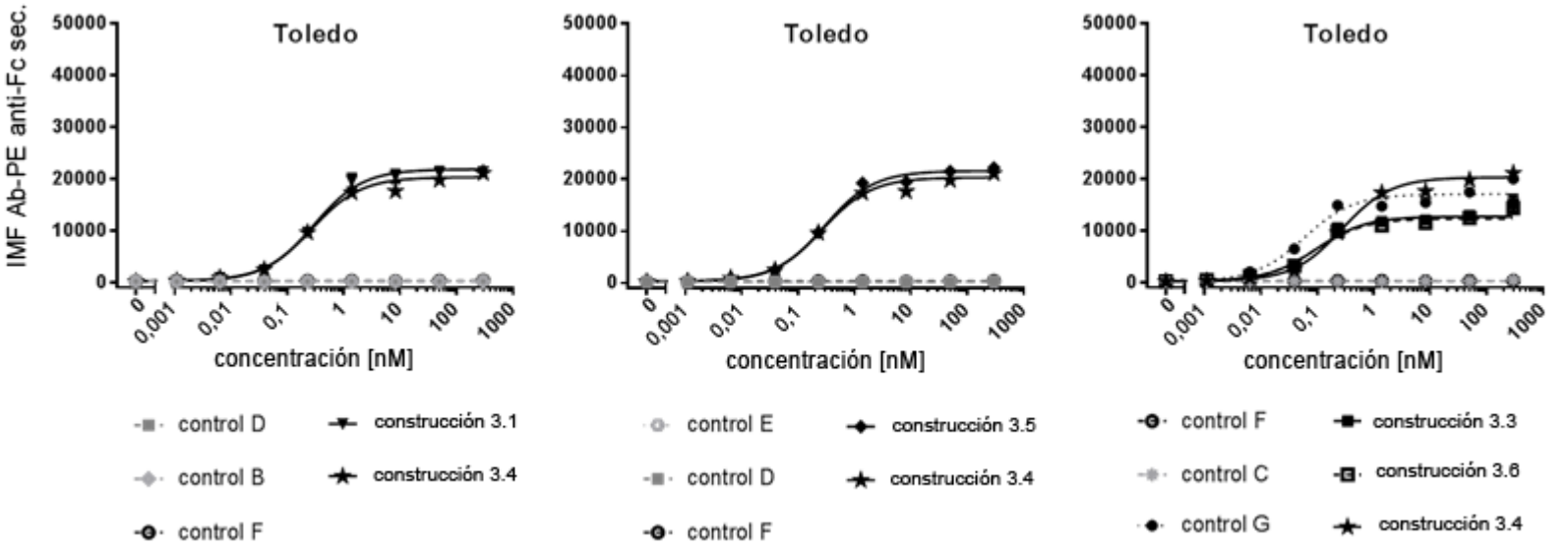

IMF Ab-PE anti-Fc sec.
Toledo
50000
40000
30000
20000
10000
0
0
0,001
0,01
0,1
1
10
100
1000
concentración [nM]
control D
construcción 3.1
control B
construcción 3.4
control F
Toledo
concentración [nM]
control E
construcción 3.5
control D
construcción 3.4
control F
Toledo
concentración [nM]
control F
construcción 3.3
control C
construcción 3.6
control G
construcción 3.4

Fig. 37D

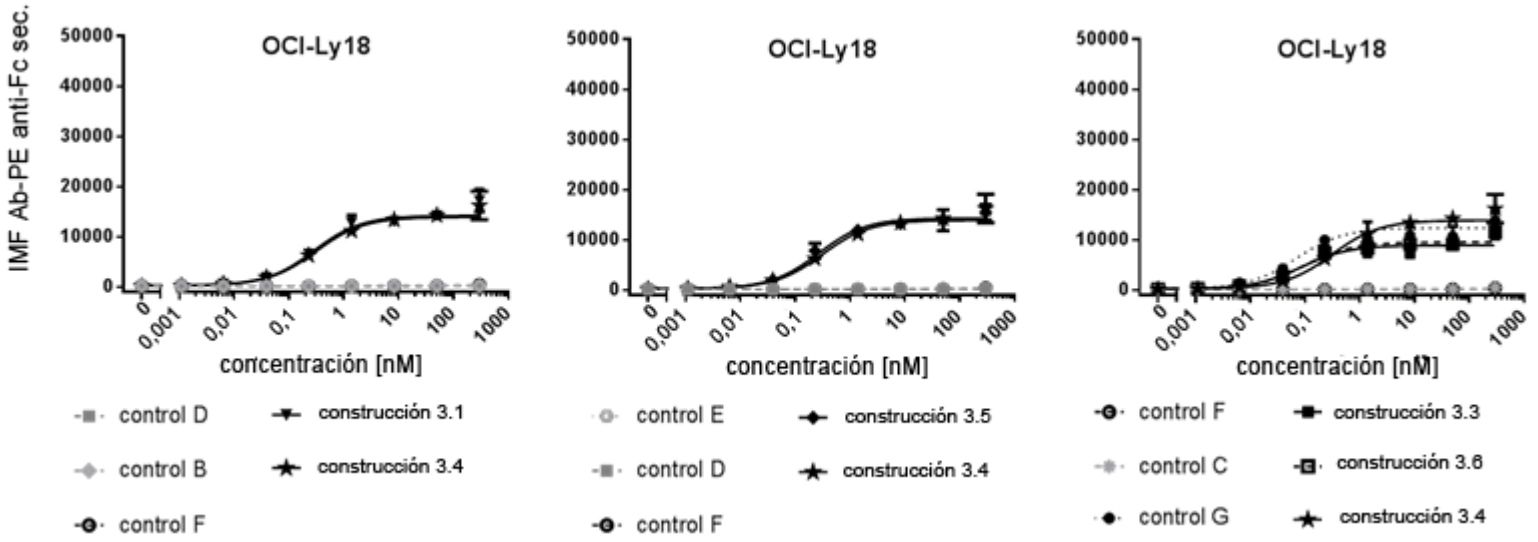

IMF Ab-PE anti-Fc sec.
OCI-Ly18
50000
40000
30000
20000
10000
0
0
0,001
0,01
0,1
1
10
100
1000
concentración [nM]
control D
construcción 3.1
control B
construcción 3.4
control F
OCI-Ly18
concentración [nM]
control E
construcción 3.5
control D
construcción 3.4
control F
OCI-Ly18
concentración [nM]
control F
construcción 3.3
control C
construcción 3.6
control G
construcción 3.4

Fig. 38

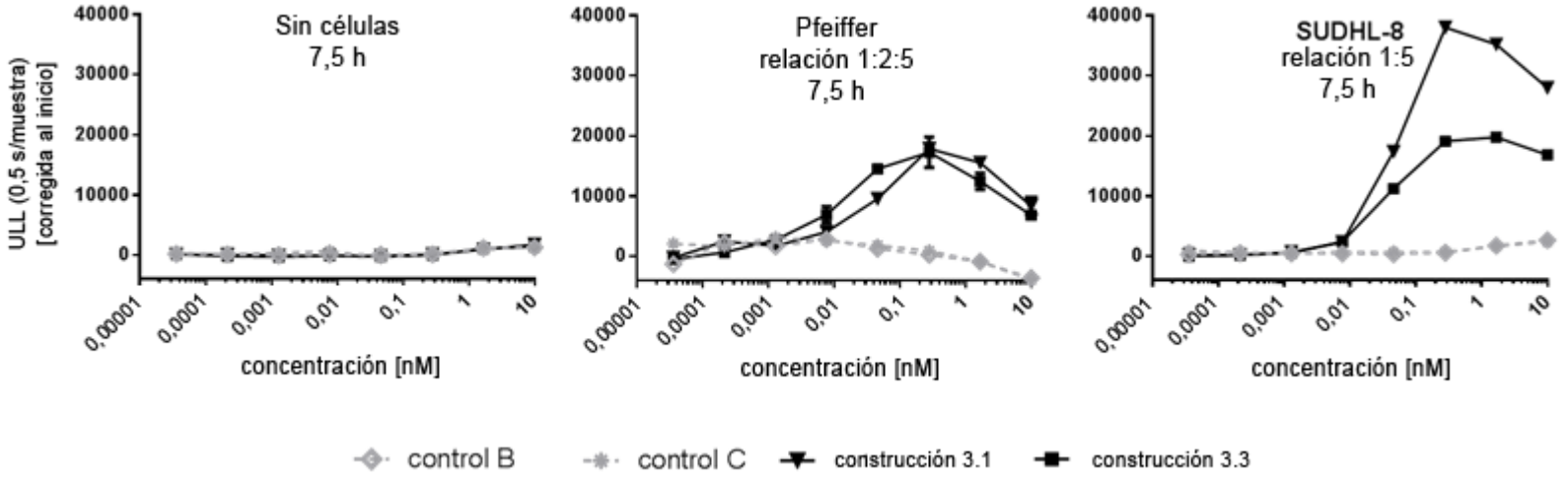

Sin células
7,5 h
Pfeiffer
relación 1:2:5
7,5 h
SUDHL-8
relación 1:5
7,5 h
ULL (0,5 s/muestra)
[corregida al inicio]
40000
30000
20000
10000
0
0,00001
0,0001
0,001
0,01
0,1
1
10
concentración [nM]
control B
control C
construcción 3.1
construcción 3.3

Fig. 39

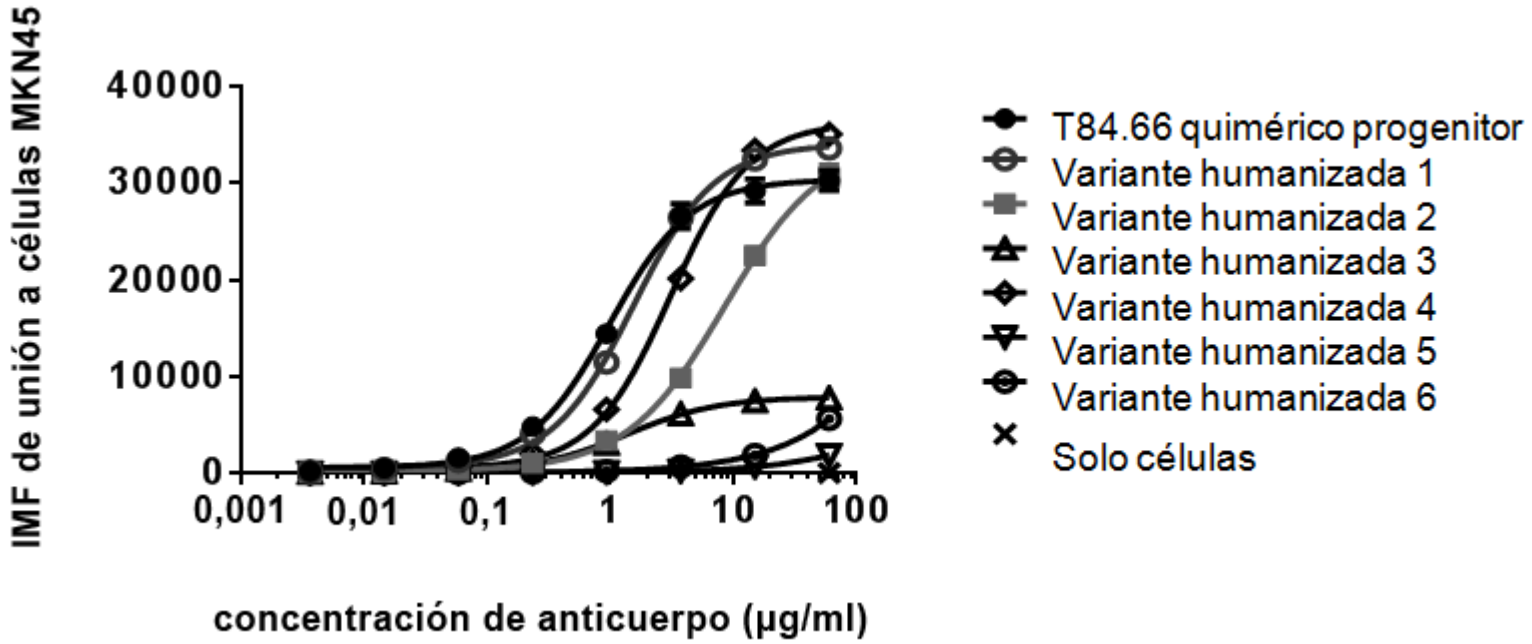
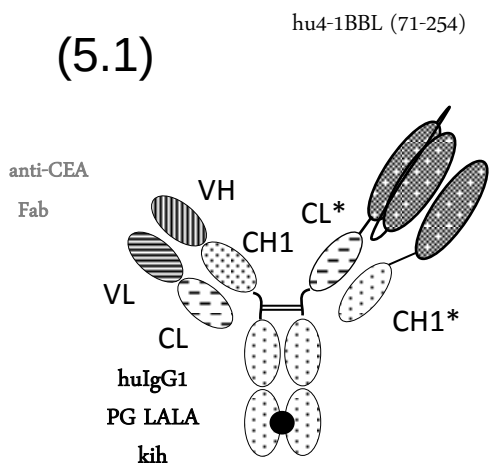
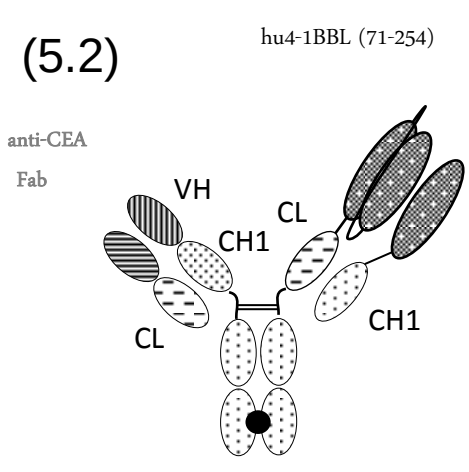

IMF de unión a células MKN45
40000
30000
20000
10000
0
0,001
0,01
0,1
1
10
100
concentración de anticuerpo (µg/ml)
T84.66 quimérico progenitor
Variante humanizada 1
Variante humanizada 2
Variante humanizada 3
Variante humanizada 4
Variante humanizada 5
Variante humanizada 6
Solo células

Fig. 40

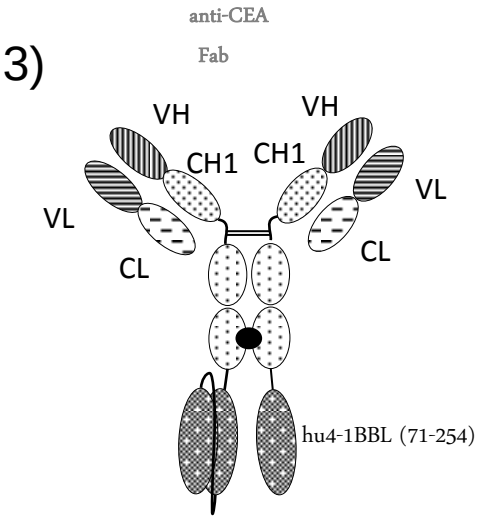
(5.1)



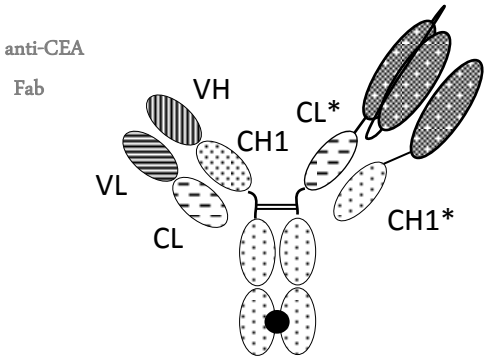
(5.2)



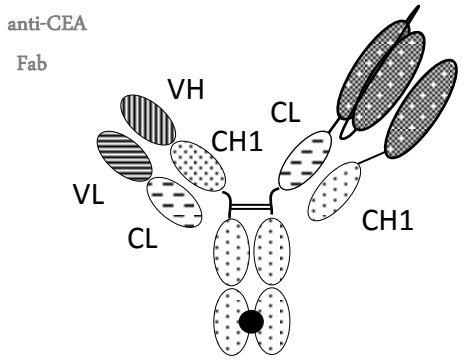
(5.3)



(5.4)



(5.5)



(5.6)

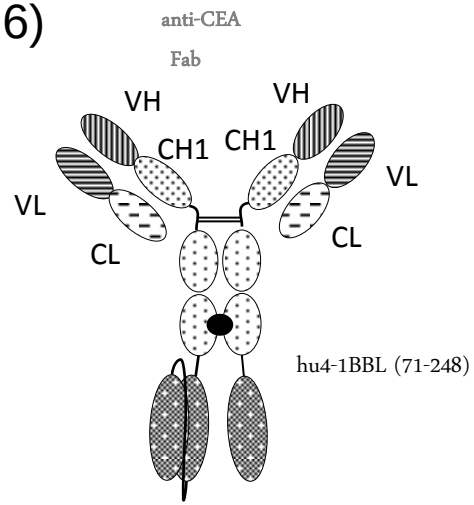
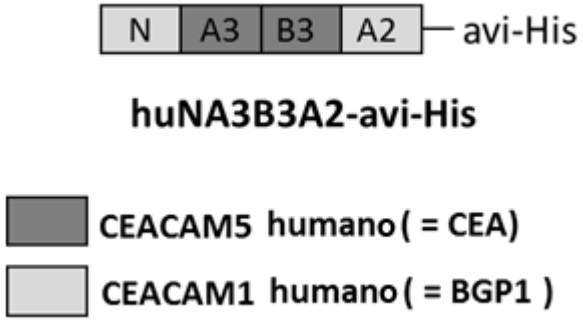


Fig. 41

(41 A)



(41 B)

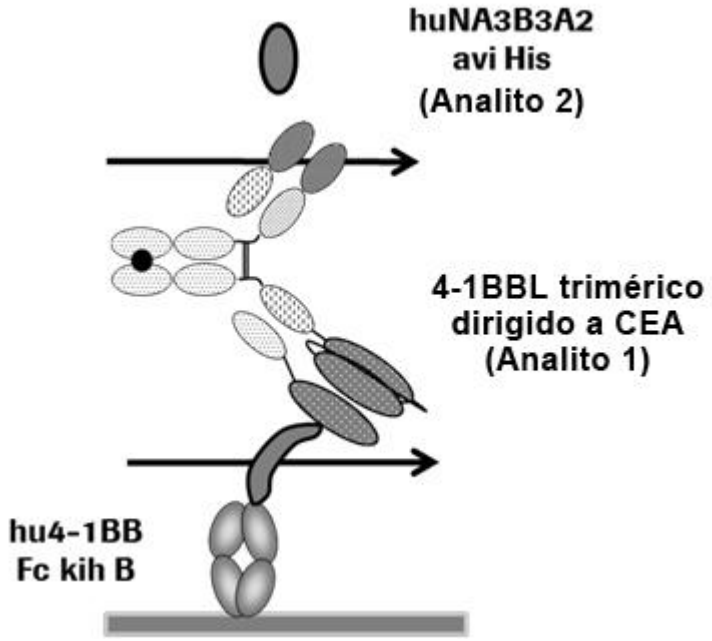
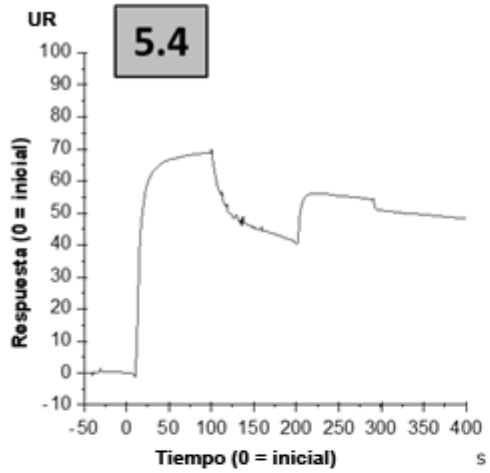
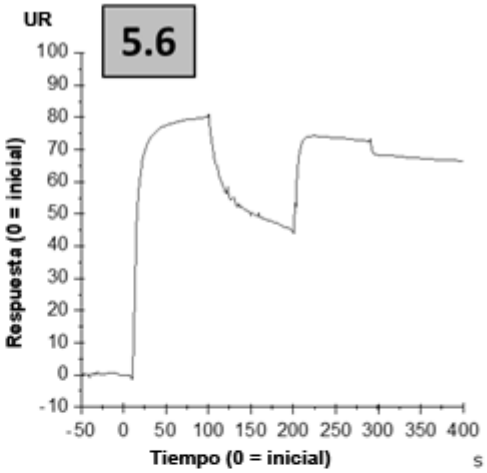
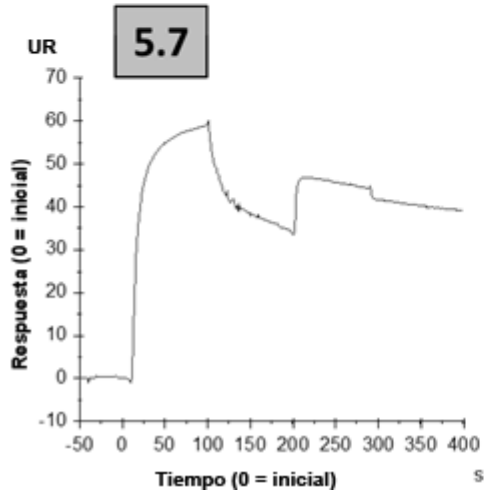


Fig. 42


5.4
UR
Respuesta (0 = inicial)
Tiempo (0 = inicial)
s


5.6
UR
Respuesta (0 = inicial)
Tiempo (0 = inicial)
s


5.7
UR
Respuesta (0 = inicial)
Tiempo (0 = inicial)
s

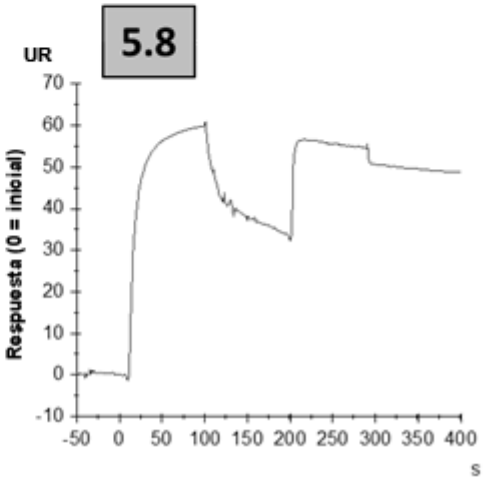

5.8
UR
Respuesta (0 = inicial)
s

Fig. 43

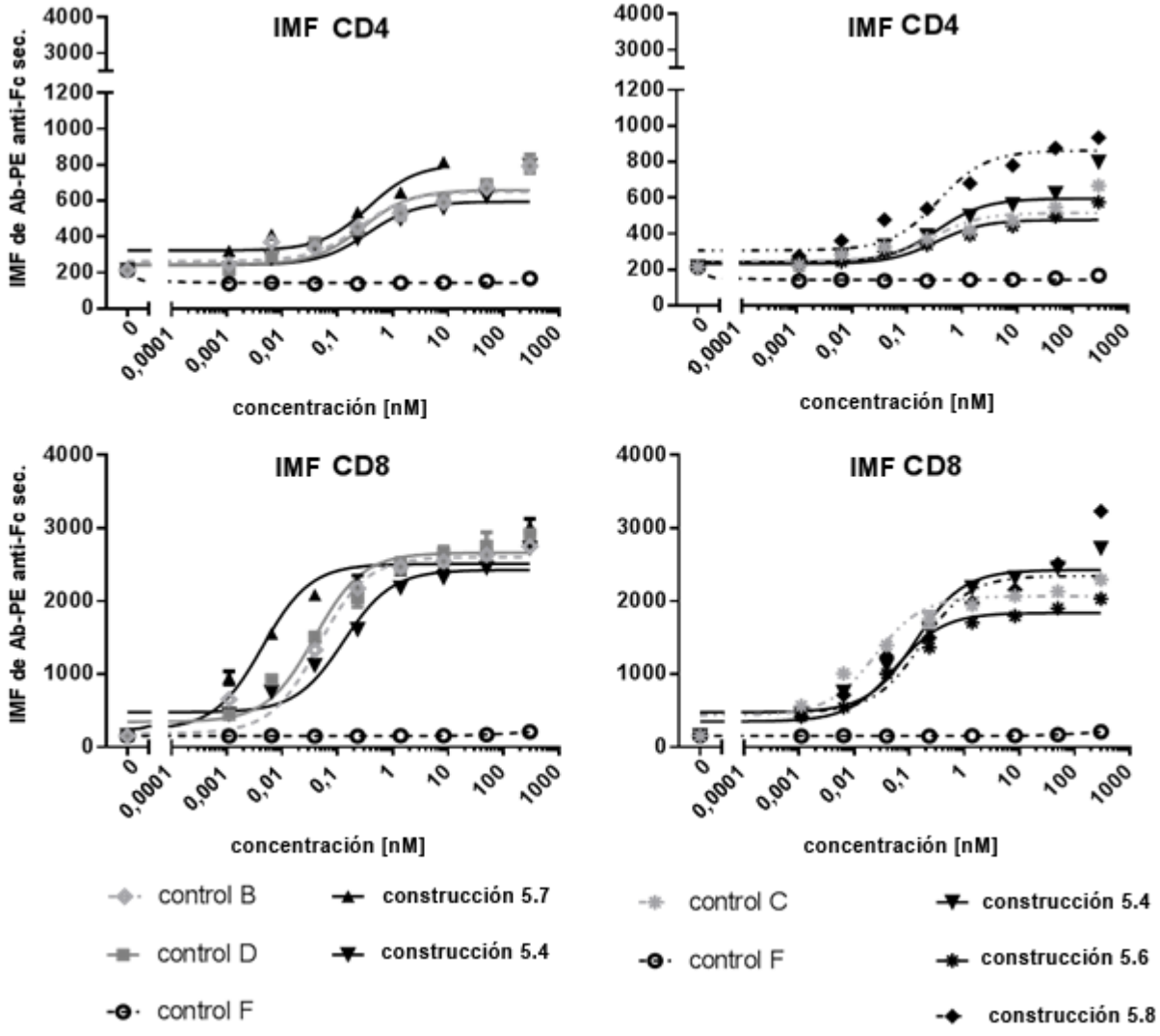

IMF CD4
IMF de Ab-PE anti-Fc sec.
concentración [nM]
IMF CD4
concentración [nM]
IMF CD8
IMF de Ab-PE anti-Fc sec.
concentración [nM]
IMF CD8
concentración [nM]
control B
control D
control F
construcción 5.7
construcción 5.4
control C
control F
construcción 5.4
construcción 5.6
construcción 5.8

Fig. 44

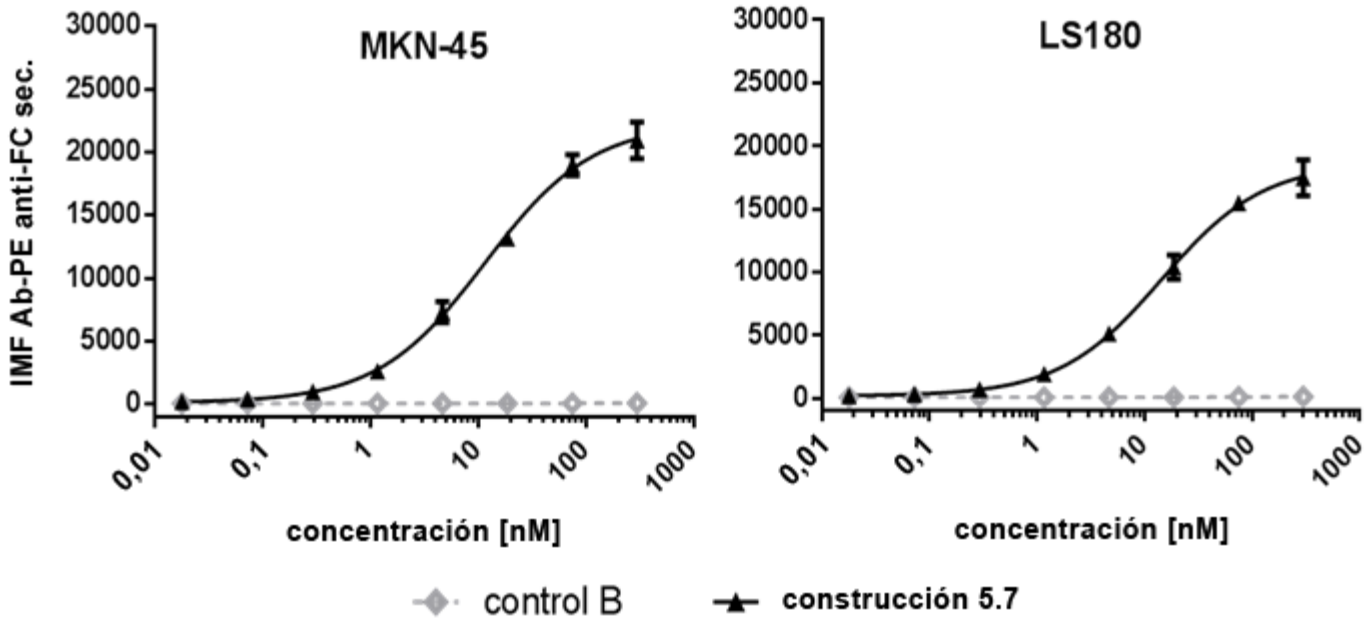

MKN-45
LS180
IMF Ab-PE anti-FC sec.
30000
25000
20000
15000
10000
5000
0
0,01
0,1
1
10
100
1000
concentración [nM]
control B
construcción 5.7

Fig. 45

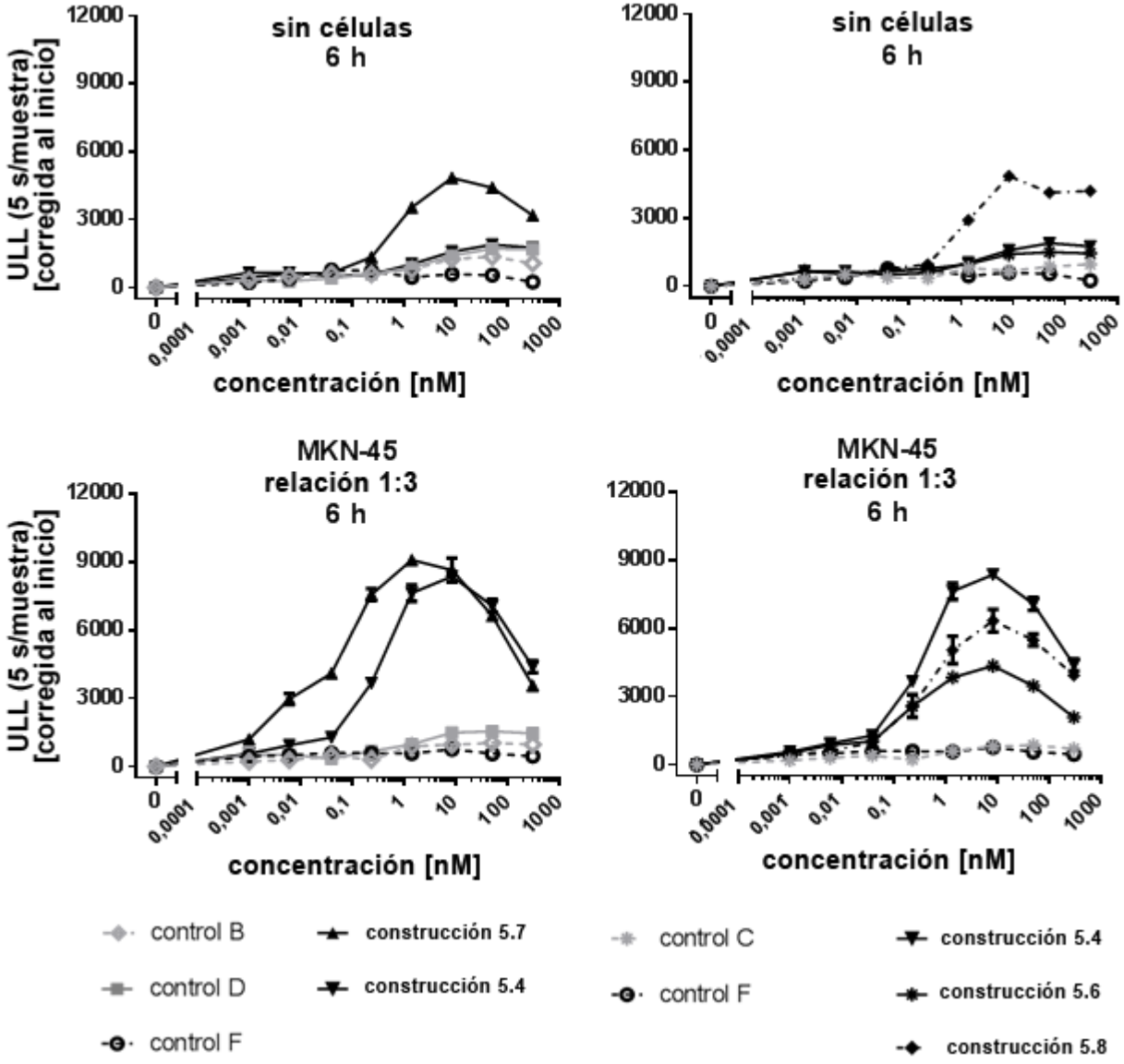
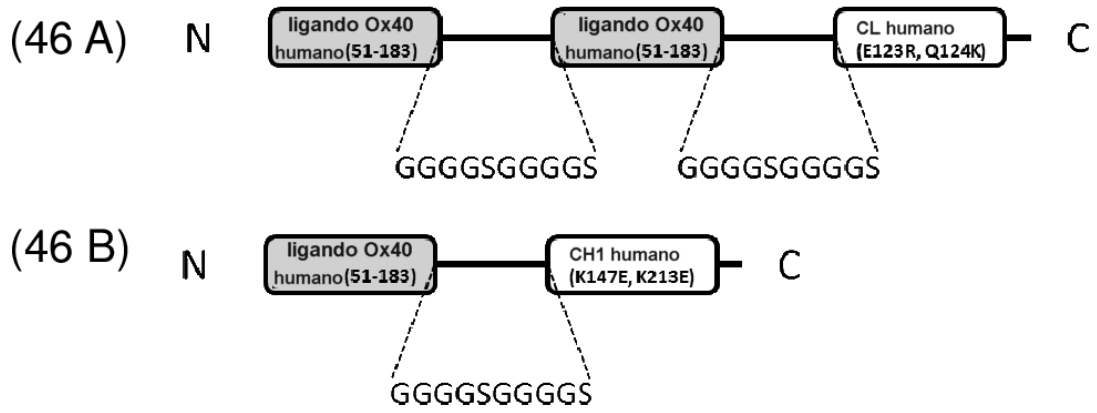
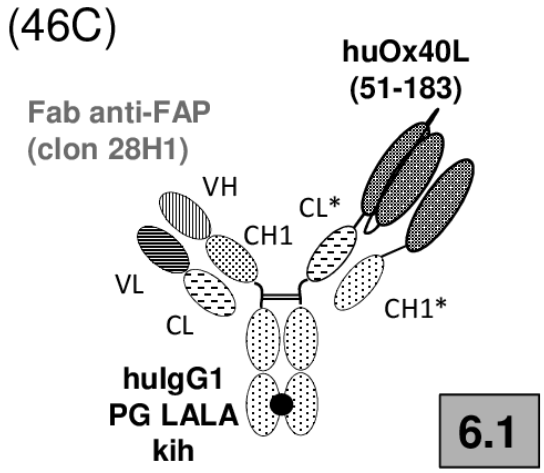

sin células
6 h
ULL (5 s/muestra) [corregida al inicio]
12000
9000
6000
3000
0
0
0,0001
0,001
0,01
0,1
1
10
100
1000
concentración [nM]
sin células
6 h
concentración [nM]
MKN-45
relación 1:3
6 h
ULL (5 s/muestra) [corregida al inicio]
concentración [nM]
MKN-45
relación 1:3
6 h
concentración [nM]
control B
construcción 5.7
control D
construcción 5.4
control F
control C
construcción 5.4
control F
construcción 5.6
construcción 5.8

Fig. 46


(46 A)
N
ligando Ox40 humano(51-183)
ligando Ox40 humano(51-183)
CL humano (E123R, Q124K)
C
GGGGSGGGGS
GGGGSGGGGS
(46 B)
N
ligando Ox40 humano(51-183)
CH1 humano (K147E, K213E)
C
GGGGSGGGGS


(46C)
huOx40L (51-183)
Fab anti-FAP (clon 28H1)
VH
CH1
CL*
VL
CL
CH1*
huIgG1 PG LALA kih
6.1

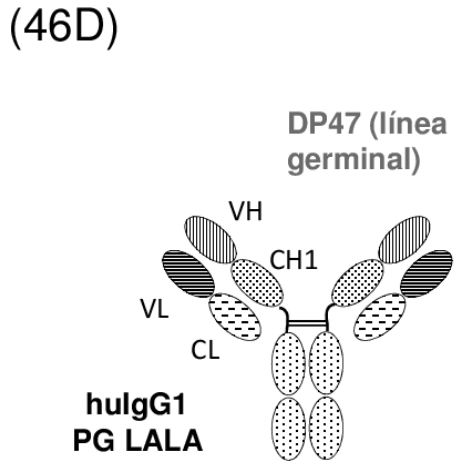
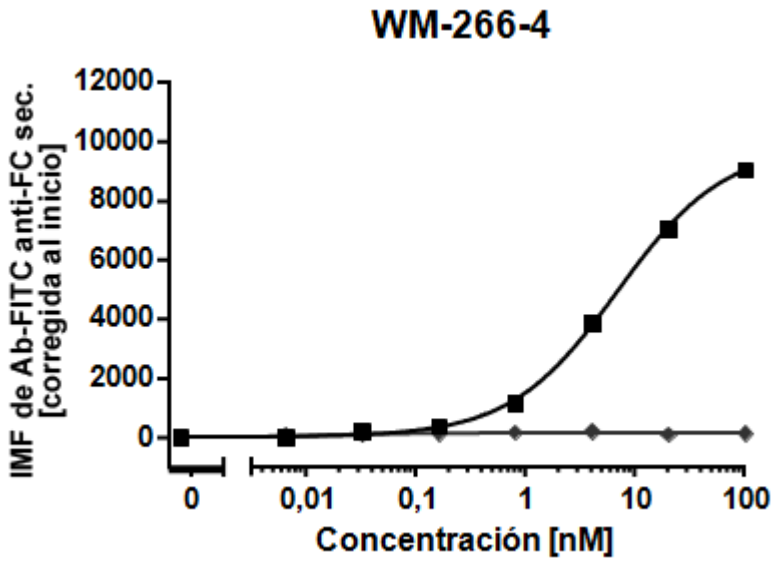
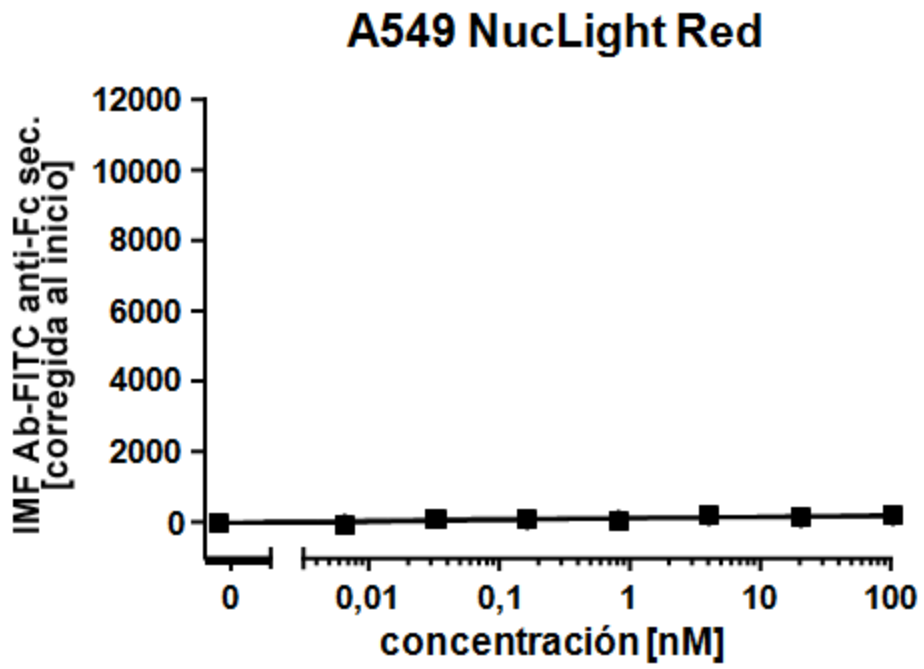

(46D)
DP47 (línea germinal)
VH
CH1
VL
CL
huIgG1 PG LALA

Fig. 47 A



Fusión de Fc (kih) de ligando Ox40 trimérico separado dirigido a FAP (28H1) monovalente
Control F

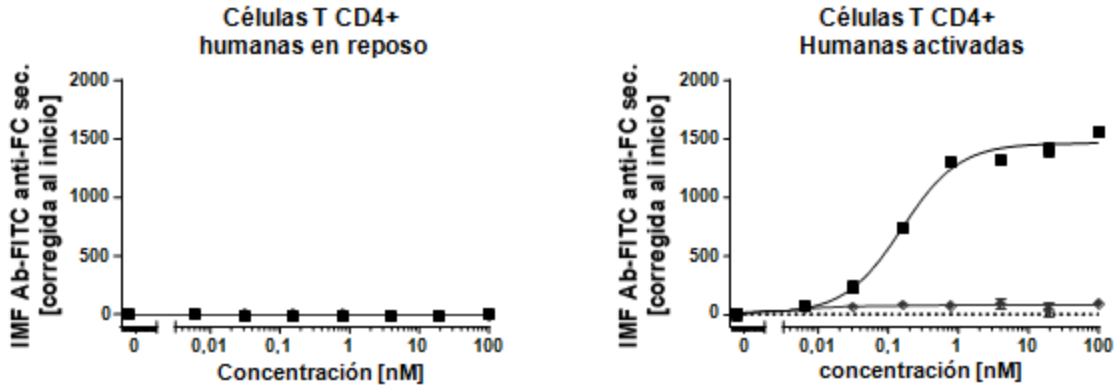
Fig. 47 B



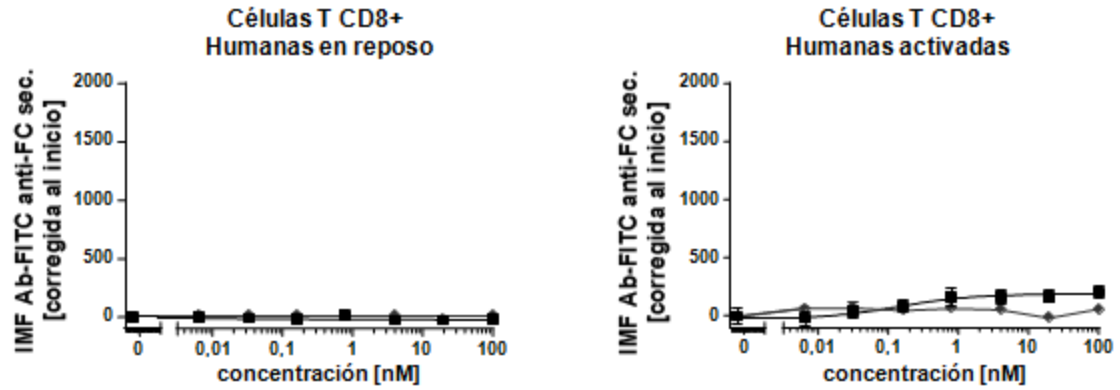
Fusión de Fc (kih) de ligando Ox40 trimérico separado dirigido a FAP (28H1) monovalente
Control F

Fig. 48

(48 A)



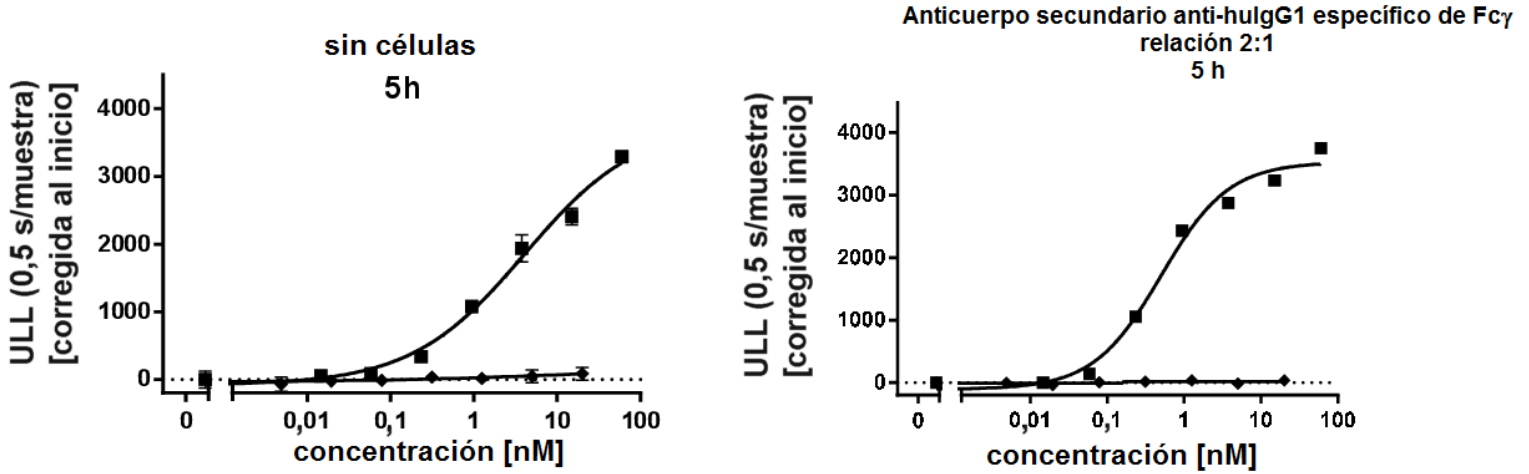
(48 B)



Fusión de Fc (kih) de ligando Ox40 trimérico separado dirigido a FAP (28H1) monovalente

Control F

Fig. 49

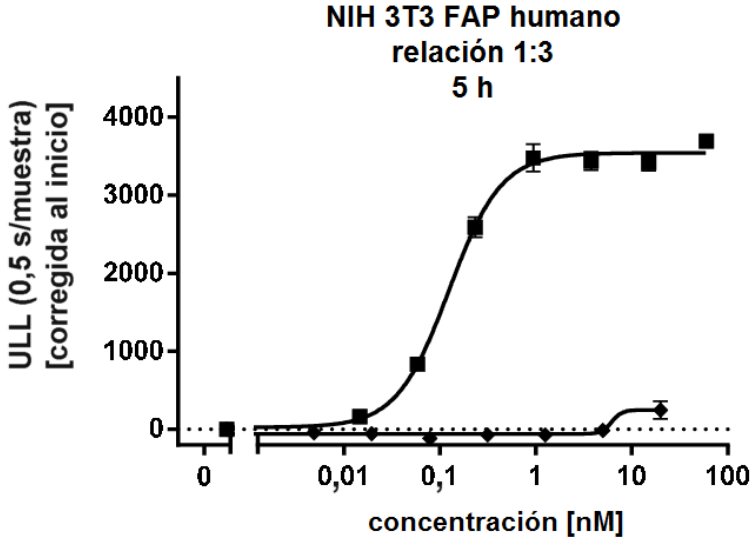


Fusión de Fc (kih) de ligando Ox40 trimérico separado dirigido a FAP (28H1) monovalente

Control F

Fig. 50

(50 A)



(50 B)

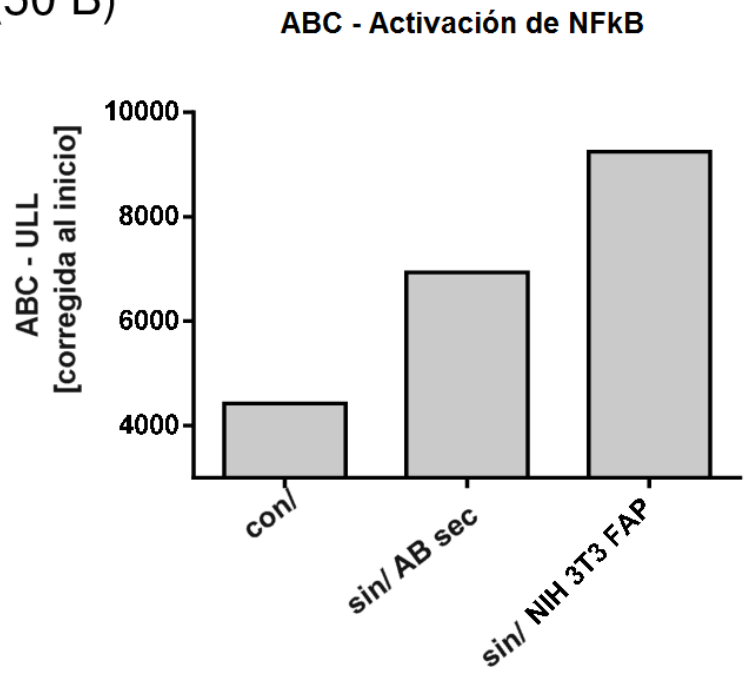
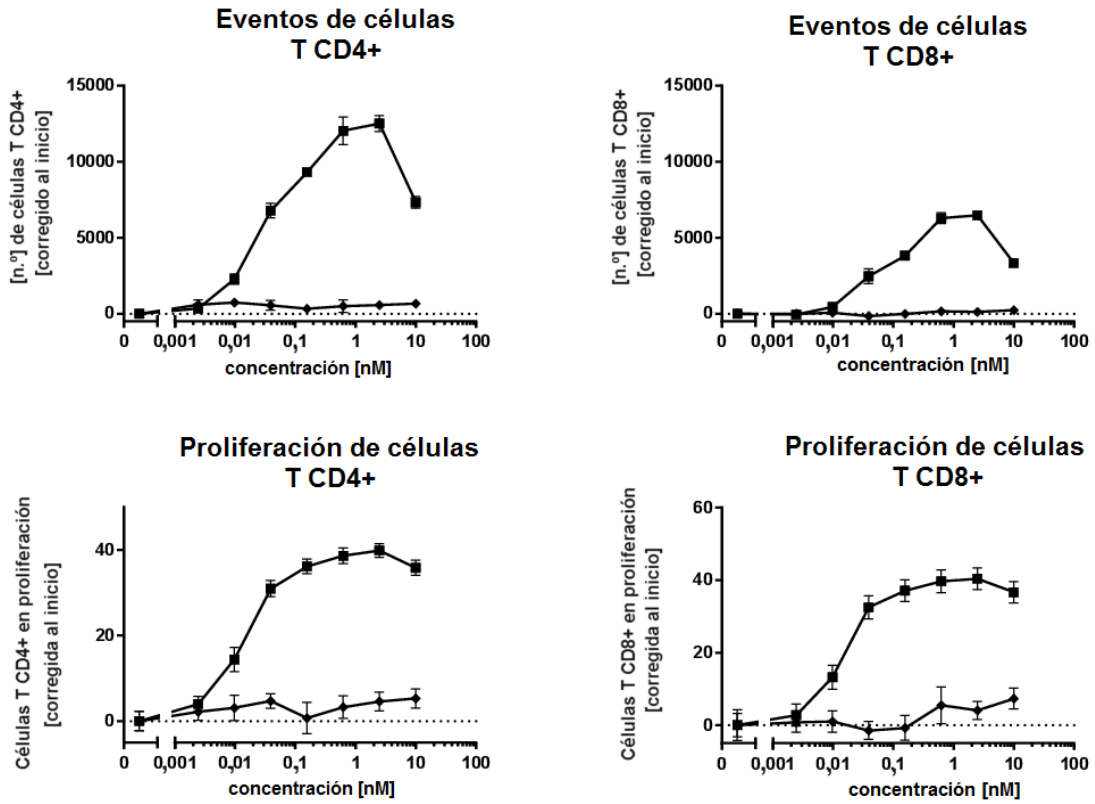


Fig. 51



Fusión de Fc (kih) de ligando Ox40 trimérico separado dirigido a FAP (28H1) monovalente

Control F