

## LISTADO DE SECUENCIAS

<110> MacroGenics, Inc.  
 Johnson, Leslie  
 Bonvini, Ezio  
 Lam, Chia-Ying Kao  
 Moore, Paul  
 Liu, Liqin  
 Koenig, Scott

<120> Diacuerpos Monovalentes Biespecíficos que son Capaces  
 de Unir CD19 y CD3, y Usos de los Mismos

<130> 1301.0116PCT

<150> US 62/0255,695  
 <151> 2014-09-26

<160> 48

<170> PatentIn versión 3.5

<210> 1  
 <211> 8  
 <212> PRT  
 <213> Secuencia Artificial

<220>  
 <223> Péptido Espaciador de Intervención (Enlazador 1)

<400> 1

Gly Gly Gly Ser Gly Gly Gly Gly  
 1 5

<210> 2  
 <211> 5  
 <212> PRT  
 <213> Secuencia Artificial

<220>  
 <223> Enlazador 2

<400> 2

Ala Ser Thr Lys Gly  
 1 5

<210> 3  
 <211> 6  
 <212> PRT  
 <213> Secuencia Artificial

<220>  
 <223> Enlazador que contiene Cisteína

<400> 3

Gly Gly Cys Gly Gly Gly  
1 5

<210> 4  
<211> 10  
<212> PRT  
<213> Homo sapiens

<220>  
<221> MISC\_CARACTERÍSTICA  
<222> (1)..(10)  
<223> Dominio de bisagra de IgG1

<400> 4

Asp Lys Thr His Thr Cys Pro Pro Cys Pro  
1 5 10

<210> 5  
<211> 13  
<212> PRT  
<213> Secuencia Artificial

<220>  
<223> Espaciador-Enlazador 3

<400> 5

Gly Gly Gly Asp Lys Thr His Thr Cys Pro Pro Cys Pro  
1 5 10

<210> 6  
<211> 7  
<212> PRT  
<213> Secuencia Artificial

<220>  
<223> Dominio que Promueve Heterodímero

<400> 6

Gly Val Glu Pro Lys Ser Cys  
1 5

<210> 7  
<211> 6  
<212> PRT  
<213> Secuencia Artificial

<220>

<223> Dominio que Promueve Heterodímero

<400> 7

Val Glu Pro Lys Ser Cys  
1 5

<210> 8

<211> 7

<212> PRT

<213> Secuencia Artificial

<220>

<223> Dominio que Promueve Heterodímero

<400> 8

Gly Phe Asn Arg Gly Glu Cys  
1 5

<210> 9

<211> 6

<212> PRT

<213> Secuencia Artificial

<220>

<223> Dominio que Promueve Heterodímero

<400> 9

Phe Asn Arg Gly Glu Cys  
1 5

<210> 10

<211> 28

<212> PRT

<213> Secuencia Artificial

<220>

<223> Dominio que Promueve Heterodímero de E-coil

<400> 10

Glu Val Ala Ala Leu Glu Lys Glu Val Ala Ala Leu Glu Lys Glu Val  
1 5 10 15

Ala Ala Leu Glu Lys Glu Val Ala Ala Leu Glu Lys  
20 25

<210> 11

<211> 28

<212> PRT

<213> Secuencia Artificial

&lt;220&gt;

&lt;223&gt; Dominio que Promueve Heterodímero de K-coil

&lt;400&gt; 11

|     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| Lys | Val | Ala | Ala | Leu | Lys | Glu | Lys | Val | Ala | Ala | Leu | Lys | Glu | Lys | Val |
| 1   |     |     |     | 5   |     |     |     | 10  |     |     |     |     |     | 15  |     |

|     |     |     |     |     |     |     |     |     |     |     |     |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| Ala | Ala | Leu | Lys | Glu | Lys | Val | Ala | Ala | Leu | Lys | Glu |
|     |     |     | 20  |     |     |     | 25  |     |     |     |     |

&lt;210&gt; 12

&lt;211&gt; 28

&lt;212&gt; PRT

&lt;213&gt; Secuencia Artificial

&lt;220&gt;

&lt;223&gt; Dominio que Promueve Heterodímero que contiene Cisteína de E-coil

&lt;400&gt; 12

|     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| Glu | Val | Ala | Ala | Cys | Glu | Lys | Glu | Val | Ala | Ala | Leu | Glu | Lys | Glu | Val |
| 1   |     |     |     | 5   |     |     |     | 10  |     |     |     |     |     | 15  |     |

|     |     |     |     |     |     |     |     |     |     |     |     |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| Ala | Ala | Leu | Glu | Lys | Glu | Val | Ala | Ala | Leu | Glu | Lys |
|     |     |     | 20  |     |     |     | 25  |     |     |     |     |

&lt;210&gt; 13

&lt;211&gt; 28

&lt;212&gt; PRT

&lt;213&gt; Secuencia Artificial

&lt;220&gt;

&lt;223&gt; Dominio que Promueve Heterodímero que contiene Cisteína de K-coil

&lt;400&gt; 13

|     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| Lys | Val | Ala | Ala | Cys | Lys | Glu | Lys | Val | Ala | Ala | Leu | Lys | Glu | Lys | Val |
| 1   |     |     |     | 5   |     |     |     | 10  |     |     |     |     |     | 15  |     |

|     |     |     |     |     |     |     |     |     |     |     |     |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| Ala | Ala | Leu | Lys | Glu | Lys | Val | Ala | Ala | Leu | Lys | Glu |
|     |     |     | 20  |     |     |     | 25  |     |     |     |     |

&lt;210&gt; 14

&lt;211&gt; 217

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; MISC\_CARACTERÍSTICA

&lt;222&gt; (1)..(217)

&lt;223&gt; Dominio CH2-CH3 de IgG1 Humano

&lt;400&gt; 14

|     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| Ala | Pro | Glu | Leu | Leu | Gly | Gly | Pro | Ser | Val | Phe | Leu | Phe | Pro | Pro | Lys |
| 1   |     |     |     | 5   |     |     |     |     | 10  |     |     |     |     | 15  |     |

|     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| Pro | Lys | Asp | Thr | Leu | Met | Ile | Ser | Arg | Thr | Pro | Glu | Val | Thr | Cys | Val |
|     |     |     | 20  |     |     |     |     | 25  |     |     |     |     | 30  |     |     |

|     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| Val | Val | Asp | Val | Ser | His | Glu | Asp | Pro | Glu | Val | Lys | Phe | Asn | Trp | Tyr |
|     |     | 35  |     |     |     |     | 40  |     |     |     |     | 45  |     |     |     |

|     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| Val | Asp | Gly | Val | Glu | Val | His | Asn | Ala | Lys | Thr | Lys | Pro | Arg | Glu | Glu |
|     | 50  |     |     |     |     | 55  |     |     |     |     | 60  |     |     |     |     |

|     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| Gln | Tyr | Asn | Ser | Thr | Tyr | Arg | Val | Val | Ser | Val | Leu | Thr | Val | Leu | His |
| 65  |     |     |     |     | 70  |     |     |     |     | 75  |     |     |     |     | 80  |

|     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| Gln | Asp | Trp | Leu | Asn | Gly | Lys | Glu | Tyr | Lys | Cys | Lys | Val | Ser | Asn | Lys |
|     |     |     | 85  |     |     |     |     |     | 90  |     |     |     |     | 95  |     |

|     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| Ala | Leu | Pro | Ala | Pro | Ile | Glu | Lys | Thr | Ile | Ser | Lys | Ala | Lys | Gly | Gln |
|     |     |     | 100 |     |     |     |     | 105 |     |     |     |     | 110 |     |     |

|     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| Pro | Arg | Glu | Pro | Gln | Val | Tyr | Thr | Leu | Pro | Pro | Ser | Arg | Glu | Glu | Met |
|     |     | 115 |     |     |     |     | 120 |     |     |     |     | 125 |     |     |     |

|     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| Thr | Lys | Asn | Gln | Val | Ser | Leu | Thr | Cys | Leu | Val | Lys | Gly | Phe | Tyr | Pro |
|     | 130 |     |     |     |     | 135 |     |     |     |     | 140 |     |     |     |     |

|     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| Ser | Asp | Ile | Ala | Val | Glu | Trp | Glu | Ser | Asn | Gly | Gln | Pro | Glu | Asn | Asn |
| 145 |     |     |     |     | 150 |     |     |     |     | 155 |     |     |     |     | 160 |

|     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| Tyr | Lys | Thr | Thr | Pro | Pro | Val | Leu | Asp | Ser | Asp | Gly | Ser | Phe | Phe | Leu |
|     |     |     |     | 165 |     |     |     |     | 170 |     |     |     |     | 175 |     |

|     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| Tyr | Ser | Lys | Leu | Thr | Val | Asp | Lys | Ser | Arg | Trp | Gln | Gln | Gly | Asn | Val |
|     |     |     | 180 |     |     |     |     | 185 |     |     |     |     | 190 |     |     |

|     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| Phe | Ser | Cys | Ser | Val | Met | His | Glu | Ala | Leu | His | Asn | His | Tyr | Thr | Gln |
|     |     | 195 |     |     |     |     | 200 |     |     |     |     | 205 |     |     |     |

|     |     |     |     |     |     |     |     |     |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| Lys | Ser | Leu | Ser | Leu | Ser | Pro | Gly | Lys |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|

210

215

<210> 15  
 <211> 217  
 <212> PRT  
 <213> Secuencia Artificial

<220>  
 <223> "Knob-Bearing" Dominio CH2-CH3

<400> 15

Ala Pro Glu Ala Ala Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys  
 1 5 10 15

Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val  
 20 25 30

Val Val Asp Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr  
 35 40 45

Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu  
 50 55 60

Gln Tyr Asn Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His  
 65 70 75 80

Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys  
 85 90 95

Ala Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln  
 100 105 110

Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Glu Glu Met  
 115 120 125

Thr Lys Asn Gln Val Ser Leu Trp Cys Leu Val Lys Gly Phe Tyr Pro  
 130 135 140

Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn  
 145 150 155 160

Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu  
 165 170 175

Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val

|                                                                 |     |         |
|-----------------------------------------------------------------|-----|---------|
| 180                                                             | 185 | 190     |
| Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln |     |         |
| 195                                                             | 200 | 205     |
| Lys Ser Leu Ser Leu Ser Pro Gly Lys                             |     |         |
| 210                                                             | 215 |         |
| <210> 16                                                        |     |         |
| <211> 217                                                       |     |         |
| <212> PRT                                                       |     |         |
| <213> Secuencia Artificial                                      |     |         |
| <220>                                                           |     |         |
| <223> "Hole-Bearing" Dominio CH2-CH3                            |     |         |
| <400> 16                                                        |     |         |
| Ala Pro Glu Ala Ala Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys |     |         |
| 1                                                               | 5   | 10 15   |
| Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val |     |         |
|                                                                 | 20  | 25 30   |
| Val Val Asp Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr |     |         |
|                                                                 | 35  | 40 45   |
| Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu |     |         |
|                                                                 | 50  | 55 60   |
| Gln Tyr Asn Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His |     |         |
| 65                                                              | 70  | 75 80   |
| Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys |     |         |
|                                                                 | 85  | 90 95   |
| Ala Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln |     |         |
|                                                                 | 100 | 105 110 |
| Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Glu Glu Met |     |         |
|                                                                 | 115 | 120 125 |
| Thr Lys Asn Gln Val Ser Leu Ser Cys Ala Val Lys Gly Phe Tyr Pro |     |         |
|                                                                 | 130 | 135 140 |
| Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn |     |         |



<211> 10  
 <212> PRT  
 <213> Secuencia Artificial

<220>  
 <223> CDR1 de la Cadena Ligera Variable del Anticuerpo Anti-CD19

<400> 18

Arg Ala Ser Gln Ser Val Ser Tyr Met His  
 1 5 10

<210> 19  
 <211> 7  
 <212> PRT  
 <213> Secuencia Artificial

<220>  
 <223> CDR2 de la Cadena Ligera Variable del Anticuerpo Anti-CD19

<400> 19

Asp Ala Ser Asn Arg Ala Ser  
 1 5

<210> 20  
 <211> 9  
 <212> PRT  
 <213> Secuencia Artificial

<220>  
 <223> CDR3 de la Cadena Ligera Variable del Anticuerpo Anti-CD19

<400> 20

Phe Gln Gly Ser Val Tyr Pro Phe Thr  
 1 5

<210> 21  
 <211> 120  
 <212> PRT  
 <213> Secuencia Artificial

<220>  
 <223> Cadena Pesada Variable del Anticuerpo Anti-CD19

<400> 21

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

Thr Leu Thr Leu Thr Cys Thr Phe Ser Gly Phe Ser Leu Ser Thr Ser  
 20 25 30

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

Trp Leu Ala His Ile Trp Trp Asp Asp Asp Lys Arg Tyr Asn Pro Ala  
       50                                  55                                  60

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

Phe Leu Thr Met Thr Asn Met Asp Pro Val Asp Thr Ala Thr Tyr Tyr  
                                   85                                  90                                  95

Cys Ala Arg Met Glu Leu Trp Ser Tyr Tyr Phe Asp Tyr Trp Gly Gln  
                   100                                  105                                  110

Gly Thr Thr Val Thr Val Ser Ser  
       115                                  120

<210> 22

<211> 7

<212> PRT

<213> Secuencia Artificial

<220>

<223> CDR1 de la Cadena Pesada Variable del Anticuerpo Anti-CD19

<400> 22

Thr Ser Gly Met Gly Val Gly  
   1                                  5

<210> 23

<211> 16

<212> PRT

<213> Secuencia Artificial

<220>

<223> CDR2 de la Cadena Pesada Variable del Anticuerpo Anti-CD19

<400> 23

His Ile Trp Trp Asp Asp Asp Lys Arg Tyr Asn Pro Ala Leu Lys Ser  
   1                                  5                                  10                                  15

<210> 24

<211> 10

<212> PRT

<213> Secuencia Artificial

&lt;220&gt;

&lt;223&gt; CDR3 de la Cadena Pesada Variable del Anticuerpo Anti-CD19

&lt;400&gt; 24

Met Glu Leu Trp Ser Tyr Tyr Phe Asp Tyr  
 1 5 10

&lt;210&gt; 25

&lt;211&gt; 110

&lt;212&gt; PRT

&lt;213&gt; Secuencia Artificial

&lt;220&gt;

&lt;223&gt; Cadena Ligera Variable del Anticuerpo Anti-CD3

&lt;400&gt; 25

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

Thr Val Thr Leu Thr Cys Arg Ser Ser Thr Gly Ala Val Thr Thr Ser  
 20 25 30

Asn Tyr Ala Asn Trp Val Gln Gln Lys Pro Gly Gln Ala Pro Arg Gly  
 35 40 45

Leu Ile Gly Gly Thr Asn Lys Arg Ala Pro Trp Thr Pro Ala Arg Phe  
 50 55 60

Ser Gly Ser Leu Leu Gly Gly Lys Ala Ala Leu Thr Ile Thr Gly Ala  
 65 70 75 80

Gln Ala Glu Asp Glu Ala Asp Tyr Tyr Cys Ala Leu Trp Tyr Ser Asn  
 85 90 95

Leu Trp Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu Gly  
 100 105 110

&lt;210&gt; 26

&lt;211&gt; 14

&lt;212&gt; PRT

&lt;213&gt; Secuencia Artificial

&lt;220&gt;

&lt;223&gt; CDR1 de la Cadena Ligera Variable del Anticuerpo Anti-CD3

&lt;400&gt; 26

Arg Ser Ser Thr Gly Ala Val Thr Thr Ser Asn Tyr Ala Asn



65

70

75

80

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

Tyr Cys Val Arg His Gly Asn Phe Gly Asn Ser Tyr Val Ser Trp Phe  
                                     100                                    105                                    110

Ala Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser  
                                     115                                    120                                    125

&lt;210&gt; 30

&lt;211&gt; 5

&lt;212&gt; PRT

&lt;213&gt; Secuencia Artificial

&lt;220&gt;

&lt;223&gt; CDR1 de la Cadena Pesada Variable del Anticuerpo Anti-CD3

&lt;400&gt; 30

Thr Tyr Ala Met Asn  
 1                                    5

&lt;210&gt; 31

&lt;211&gt; 19

&lt;212&gt; PRT

&lt;213&gt; Secuencia Artificial

&lt;220&gt;

&lt;223&gt; CDR2 de la Cadena Pesada Variable del Anticuerpo Anti-CD3

&lt;400&gt; 31

Arg Ile Arg Ser Lys Tyr Asn Asn Tyr Ala Thr Tyr Tyr Ala Asp Ser  
 1                                    5                                    10                                    15

Val Lys Gly

&lt;210&gt; 32

&lt;211&gt; 14

&lt;212&gt; PRT

&lt;213&gt; Secuencia Artificial

&lt;220&gt;

&lt;223&gt; CDR3 de la Cadena Pesada Variable del Anticuerpo Anti-CD3

&lt;400&gt; 32

His Gly Asn Phe Gly Asn Ser Tyr Val Ser Trp Phe Ala Tyr

<400> 33

<400> 34

Gly Val Lys Ala Leu Ile Asp Glu Ile Leu Ala Ala Leu Pro  
35 40 45

<400> 35

His Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Arg Leu Leu Ile Tyr

|            |                                                                    |         |
|------------|--------------------------------------------------------------------|---------|
| 35         | 40                                                                 | 45      |
| Asp<br>50  | Ala Ser Asn Arg Ala Ser Gly Val Pro Ser Arg Phe Ser Gly Ser<br>55  | 60      |
| Gly<br>65  | Ser Gly Thr Asp His Thr Leu Thr Ile Ser Ser Leu Glu Ala Glu<br>70  | 75 80   |
| Asp<br>85  | Ala Ala Thr Tyr Tyr Cys Phe Gln Gly Ser Val Tyr Pro Phe Thr<br>90  | 95      |
| Phe<br>100 | Gly Gln Gly Thr Lys Leu Glu Ile Lys Gly Gly Gly Ser Gly Gly<br>105 | 110     |
| Gly<br>115 | Gly Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro<br>120 | 125     |
| Gly<br>130 | Gly Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser<br>135 | 140     |
| Thr<br>145 | Tyr Ala Met Asn Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu<br>150 | 155 160 |
| Trp<br>165 | Val Gly Arg Ile Arg Ser Lys Tyr Asn Asn Tyr Ala Thr Tyr Tyr<br>170 | 175     |
| Ala<br>180 | Asp Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asp Ser Lys<br>185 | 190     |
| Asn<br>195 | Ser Leu Tyr Leu Gln Met Asn Ser Leu Lys Thr Glu Asp Thr Ala<br>200 | 205     |
| Val<br>210 | Tyr Tyr Cys Val Arg His Gly Asn Phe Gly Asn Ser Tyr Val Ser<br>215 | 220     |
| Trp<br>225 | Phe Ala Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Ala<br>230 | 235 240 |
| Ser<br>245 | Thr Lys Gly Glu Val Ala Ala Cys Glu Lys Glu Val Ala Ala Leu<br>250 | 255     |
| Glu<br>260 | Lys Glu Val Ala Ala Leu Glu Lys Glu Val Ala Ala Leu Glu Lys<br>265 | 270     |

Gly Gly Gly Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu  
275 280 285

Ala Ala Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp  
290 295 300

Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp  
305 310 315 320

Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly  
325 330 335

Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn  
340 345 350

Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp  
355 360 365

Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro  
370 375 380

Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu  
385 390 395 400

Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn  
405 410 415

Gln Val Ser Leu Trp Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile  
420 425 430

Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr  
435 440 445

Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys  
450 455 460

Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys  
465 470 475 480

Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu  
485 490 495

Ser Leu Ser Pro Gly Lys

500

<210> 36  
 <211> 1506  
 <212> ADN  
 <213> Secuencia Artificial

<220>  
 <223> Polinucleótido que Codifica DART-A (SEQ ID NO:35)

<400> 36  
 gagaatgtgc tcacacagtc ccctgcaact ctgagcgtaa ctccaggga gaaggccacc 60  
 atcacgtgta gagcctccca gagtgtgagc tacatgcact ggtatcagca gaaacctgga 120  
 caagctccca ggttgctgat ctatgacgag agcaaccggg ctagtggcgt tccatcccg 180  
 ttttctggct caggatctgg cactgaccac accctcacca tatccagcct tgaagccgaa 240  
 gatgccgcaa cctactactg ctttcagggg agtgtgtatc ctttcacatt cggtcagggt 300  
 acaaagctgg agattaaggg tggaggatcc ggcggcggag gcgagggtgca gctgggtggag 360  
 tctgggggag gcttggtcca gcctggaggg tccctgagac tctcctgtgc agcctctgga 420  
 ttcaccttca gcacatacgc tatgaattgg gtccgccagg ctccaggga ggggctggag 480  
 tgggttgga ggatcaggtc caagtacaac aattatgcaa cctactatgc cgactctgtg 540  
 aagggtagat tcaccatctc aagagatgat tcaaagaact cactgtatct gcaaatgaac 600  
 agcctgaaaa ccgaggacac ggccgtgtat tactgtgtga gacacggtaa cttcggcaat 660  
 tcttacgtgt cttggtttgc ttattgggga caggggacac tggtgactgt gtcttccgcc 720  
 tccaccaagg gcgaagtggc cgcatgtgag aaagagggtg ctgctttgga gaaggaggtc 780  
 gctgcacttg aaaaggaggt cgagccctg gagaaaggcg gcggggacaa aactcacaca 840  
 tgcccaccgt gccagcacc tgaagccgag gggggaccgt cagtcttctt cttccccca 900  
 aaacccaagg acaccctcat gatctcccg acccctgagg tcacatgcgt ggtggtggac 960  
 gtgagccacg aagaccctga ggtcaagttc aactggtacg tggacggcgt ggagggtgcat 1020  
 aatgccaaga caaagccgag ggaggagcag tacaacagca cgtaccgtgt ggtcagcgtc 1080  
 ctcaccgtcc tgcaccagga ctggctgaat ggcaaggagt acaagtgcaa ggtctccaac 1140  
 aaagccctcc cagccccat cgagaaaacc atctccaaag ccaaagggca gccccgagaa 1200  
 ccacaggtgt acaccctgcc ccatcccg gagagatga ccaagaacca ggtcagcgtg 1260  
 tgggtgcctg tcaaaggctt ctatcccagc gacatcgccg tggagtggga gagcaatggg 1320  
 cagccggaga acaactacaa gaccacgcct cccgtgctgg actccgacgg ctccttcttc 1380

```

ctctacagca agctcaccgt ggacaagagc aggtggcagc aggggaacgt cttctcatgc      1440
tccgtgatgc atgaggctct gcacaaccac tacacgcaga agagcctctc cctgtctccg      1500
ggtaaa                                           1506

```

```

<210> 37
<211> 271
<212> PRT
<213> Secuencia Artificial

```

```

<220>
<223> Segunda Cadena de Polipéptido de DART-A

```

```

<400> 37

```

```

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

```

```

Thr Val Thr Leu Thr Cys Arg Ser Ser Thr Gly Ala Val Thr Thr Ser
              20              25              30

```

```

Asn Tyr Ala Asn Trp Val Gln Gln Lys Pro Gly Gln Ala Pro Arg Gly
35              40              45

```

```

Leu Ile Gly Gly Thr Asn Lys Arg Ala Pro Trp Thr Pro Ala Arg Phe
50              55              60

```

```

Ser Gly Ser Leu Leu Gly Gly Lys Ala Ala Leu Thr Ile Thr Gly Ala
65              70              75              80

```

```

Gln Ala Glu Asp Glu Ala Asp Tyr Tyr Cys Ala Leu Trp Tyr Ser Asn
85              90              95

```

```

Leu Trp Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu Gly Gly Gly
100             105             110

```

```

Gly Ser Gly Gly Gly Gly Gln Val Thr Leu Arg Glu Ser Gly Pro Ala
115             120             125

```

```

Leu Val Lys Pro Thr Gln Thr Leu Thr Leu Thr Cys Thr Phe Ser Gly
130             135             140

```

```

Phe Ser Leu Ser Thr Ser Gly Met Gly Val Gly Trp Ile Arg Gln Pro
145             150             155             160

```

```

Pro Gly Lys Ala Leu Glu Trp Leu Ala His Ile Trp Trp Asp Asp Asp

```

|                                                                                             | 165 | 170 | 175 |     |
|---------------------------------------------------------------------------------------------|-----|-----|-----|-----|
| Lys Arg Tyr Asn Pro Ala Leu Lys Ser Arg Leu Thr Ile Ser Lys Asp                             |     |     |     |     |
|                                                                                             | 180 | 185 | 190 |     |
| Thr Ser Lys Asn Gln Val Phe Leu Thr Met Thr Asn Met Asp Pro Val                             |     |     |     |     |
|                                                                                             | 195 | 200 | 205 |     |
| Asp Thr Ala Thr Tyr Tyr Cys Ala Arg Met Glu Leu Trp Ser Tyr Tyr                             |     |     |     |     |
|                                                                                             | 210 | 215 | 220 |     |
| Phe Asp Tyr Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser Ala Ser                             |     |     |     |     |
|                                                                                             | 225 | 230 | 235 | 240 |
| Thr Lys Gly Lys Val Ala Ala Cys Lys Glu Lys Val Ala Ala Leu Lys                             |     |     |     |     |
|                                                                                             | 245 | 250 | 255 |     |
| Glu Lys Val Ala Ala Leu Lys Glu Lys Val Ala Ala Leu Lys Glu                                 |     |     |     |     |
|                                                                                             | 260 | 265 | 270 |     |
| <210> 38                                                                                    |     |     |     |     |
| <211> 813                                                                                   |     |     |     |     |
| <212> ADN                                                                                   |     |     |     |     |
| <213> Secuencia Artificial                                                                  |     |     |     |     |
| <220>                                                                                       |     |     |     |     |
| <223> Polinucleótido que Codifica la Segunda Cadena de Polipéptido de DART-A (SEQ ID NO:37) |     |     |     |     |
| <400> 38                                                                                    |     |     |     |     |
| caggctgtgg tgactcagga gccttcactg accgtgtccc caggcggaac tgtgaccctg                           |     |     |     | 60  |
| acatgcagat ccagcacagg cgcagtgacc acatctaact acgccaattg ggtgcagcag                           |     |     |     | 120 |
| aagccaggac aggcaccaag gggcctgata ggggtacaa aaaaaagggc tccctggacc                            |     |     |     | 180 |
| cctgcacggt tttctggaag tctgctgggc ggaaaggccg ctctgactat taccggggca                           |     |     |     | 240 |
| caggccgagg acgaagccga ttactattgt gctctgtggt atagcaatct gtgggtgttc                           |     |     |     | 300 |
| gggggtggca caaaactgac tgtgctggga ggggtggat ccggcgagg tggacaggtg                             |     |     |     | 360 |
| acactgaggg aatctggtcc agctctggtg aaaccactc agacgctcac tctcacttgc                            |     |     |     | 420 |
| accttttagtg ggttctcact gtccacatct ggcatgggag taggctggat tcgacagcca                          |     |     |     | 480 |
| cctgggaaaag ccttggagtg gcttgccac atctgggtggg atgacgacaa gcggtataat                          |     |     |     | 540 |
| cccgactga agagcagact gaccatcagc aaggatacat ccaagaacca ggtgtttctg                            |     |     |     | 600 |
| accatgacca acatggaccc tgtcgataca gccacctact attgtgctcg catggagttg                           |     |     |     | 660 |

```

tggtcctact acttcgacta ttggggacaa ggcacaaccg tgactgtctc atccgcctcc      720
accaagggca aagtggccgc atgtaaggag aaagttgctg ctttgaaaga gaaggtcgcc      780
gcacttaagg aaaaggtcgc agccctgaaa gag                                  813

```

```

<210> 39
<211> 227
<212> PRT
<213> Secuencia Artificial

```

```

<220>
<223> Tercera Cadena de Polipéptido de DART-A

```

```

<400> 39

```

```

Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Ala Ala 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

```

```

Tyr Thr Leu Pro Pro Ser Arg Glu Glu Met 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 Arg Tyr Thr Gln Lys Ser Leu Ser Leu Ser  
 210 215 220

Pro Gly Lys  
 225

<210> 40  
 <211> 681  
 <212> ADN  
 <213> Secuencia Artificial

<220>  
 <223> Polinucleótido que Codifica la Tercera Cadena de Polipéptido  
 de DART-A

<400> 40  
 gacaaaactc acacatgccc accgtgcca gcacctgaag ccgcgggggg accgtcagtc 60  
 ttctcttcc ccccaaaacc caaggacacc ctcatgatct cccggacccc tgaggtcaca 120  
 tgcgtagtg tggacgtgag ccacgaagac cctgagggtca agttcaactg gtacgtggag 180  
 ggcgtaggag tgcataatgc caagacaaaag ccgcggggagg agcagtacaa cagcacgtac 240  
 cgtgtgggtca gcgtcctcac cgtcctgcac caggactggc tgaatggcaa ggagtacaag 300  
 tgcaaggtct ccaacaaagc cctcccagcc cccatcgaga aaaccatctc caaagccaaa 360  
 gggcagcccc gagaaccaca ggtgtacacc ctgcccccat cccgggagga gatgaccaag 420  
 aaccagggtca gcctgagttg cgcagtcaaa ggcttctatc ccagcgacat cgccgtggag 480  
 tgggagagca atgggcagcc ggagaacaac tacaagacca cgcctcccgt gctggactcc 540  
 gacggctcct tcttctcgt cagcaagctc accgtggaca agagcagggtg gcagcagggg 600  
 aacgtcttct catgctccgt gatgcatgag gctctgcaca accgctacac gcagaagagc 660  
 ctctccctgt ctccgggtaa a 681

<210> 41  
 <211> 112  
 <212> PRT

<213> Secuencia Artificial

<220>

<223> Dominio Variable de Cadena Ligera del Anticuerpo Anti-Fluoresceína 4-4-20

<400> 41

Asp Val Val Met Thr Gln Thr Pro Phe Ser Leu Pro Val Ser Leu Gly  
1 5 10 15

Asp Gln Ala Ser Ile Ser Cys Arg Ser Ser Gln Ser Leu Val His Ser  
20 25 30

Asn Gly Asn Thr Tyr Leu Arg Trp Tyr Leu Gln Lys Pro Gly Gln Ser  
35 40 45

Pro Lys Val Leu Ile Tyr Lys Val Ser Asn 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 Leu Gly Val Tyr Phe Cys Ser Gln Ser  
85 90 95

Thr His Val Pro Trp Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys  
100 105 110

<210> 42

<211> 118

<212> PRT

<213> Secuencia Artificial

<220>

<223> Dominio Variable de Cadena Pesada del Anticuerpo Anti-Fluoresceína 4-4-20

<400> 42

Glu Val Lys Leu Asp Glu Thr Gly Gly Gly Leu Val Gln Pro Gly Arg  
1 5 10 15

Pro Met Lys Leu Ser Cys Val Ala Ser Gly Phe Thr Phe Ser Asp Tyr  
20 25 30

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

Ala Gln Ile Arg Asn Lys Pro Tyr Asn Tyr Glu Thr Tyr Tyr Ser Asp  
 50 55 60

Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asp Ser Lys Ser Ser  
 65 70 75 80

Val Tyr Leu Gln Met Asn Asn Leu Arg Val Glu Asp Met Gly Ile Tyr  
 85 90 95

Tyr Cys Thr Gly Ser Tyr Tyr Gly Met Asp Tyr Trp Gly Gln Gly Thr  
 100 105 110

Ser Val Thr Val Ser Ser  
 115

<210> 43  
 <211> 508  
 <212> PRT  
 <213> Secuencia Artificial

<220>  
 <223> Primera Cadena de Polipéptido del Control DART 1

<400> 43

Asp Val Val Met Thr Gln Thr Pro Phe Ser Leu Pro Val Ser Leu Gly  
 1 5 10 15

Asp Gln Ala Ser Ile Ser Cys Arg Ser Ser Gln Ser Leu Val His Ser  
 20 25 30

Asn Gly Asn Thr Tyr Leu Arg Trp Tyr Leu Gln Lys Pro Gly Gln Ser  
 35 40 45

Pro Lys Val Leu Ile Tyr Lys Val Ser Asn 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 Leu Gly Val Tyr Phe Cys Ser Gln Ser  
 85 90 95

Thr His Val Pro Trp Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys  
 100 105 110

Gly Gly Gly Ser Gly Gly Gly Gly Glu Val Gln Leu Val Glu Ser Gly  
 115 120 125

Gly Gly Leu Val Gln Pro Gly Gly Ser Leu Arg Leu Ser Cys Ala Ala  
 130 135 140

Ser Gly Phe Thr Phe Ser Thr Tyr Ala Met Asn Trp Val Arg Gln Ala  
 145 150 155 160

Pro Gly Lys Gly Leu Glu Trp Val Gly Arg Ile Arg Ser Lys Tyr Asn  
 165 170 175

Asn Tyr Ala Thr Tyr Tyr Ala Asp Ser Val Lys Gly Arg Phe Thr Ile  
 180 185 190

Ser Arg Asp Asp Ser Lys Asn Ser Leu Tyr Leu Gln Met Asn Ser Leu  
 195 200 205

Lys Thr Glu Asp Thr Ala Val Tyr Tyr Cys Val Arg His Gly Asn Phe  
 210 215 220

Gly Asn Ser Tyr Val Ser Trp Phe Ala Tyr Trp Gly Gln Gly Thr Leu  
 225 230 235 240

Val Thr Val Ser Ser Ala Ser Thr Lys Gly Glu Val Ala Ala Cys Glu  
 245 250 255

Lys Glu Val Ala Ala Leu Glu Lys Glu Val Ala Ala Leu Glu Lys Glu  
 260 265 270

Val Ala Ala Leu Glu Lys Gly Gly Gly Asp Lys Thr His Thr Cys Pro  
 275 280 285

Pro Cys Pro Ala Pro Glu Ala Ala Gly Gly Pro Ser Val Phe Leu Phe  
 290 295 300

Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val  
 305 310 315 320

Thr Cys Val Val Val Asp Val Ser His Glu Asp Pro Glu Val Lys Phe  
 325 330 335

Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys Pro



| 20  |     |     |     |     | 25  |     |     |     |     | 30  |     |     |     |     |     |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| Asn | Tyr | Ala | Asn | Trp | Val | Gln | Gln | Lys | Pro | Gly | Gln | Ala | Pro | Arg | Gly |
|     |     | 35  |     |     |     |     | 40  |     |     |     |     | 45  |     |     |     |
| Leu | Ile | Gly | Gly | Thr | Asn | Lys | Arg | Ala | Pro | Trp | Thr | Pro | Ala | Arg | Phe |
|     | 50  |     |     |     |     | 55  |     |     |     |     | 60  |     |     |     |     |
| Ser | Gly | Ser | Leu | Leu | Gly | Gly | Lys | Ala | Ala | Leu | Thr | Ile | Thr | Gly | Ala |
| 65  |     |     |     |     |     | 70  |     |     |     |     | 75  |     |     |     | 80  |
| Gln | Ala | Glu | Asp | Glu | Ala | Asp | Tyr | Tyr | Cys | Ala | Leu | Trp | Tyr | Ser | Asn |
|     |     |     |     | 85  |     |     |     |     | 90  |     |     |     |     | 95  |     |
| Leu | Trp | Val | Phe | Gly | Gly | Gly | Thr | Lys | Leu | Thr | Val | Leu | Gly | Gly | Gly |
|     |     |     | 100 |     |     |     |     | 105 |     |     |     |     | 110 |     |     |
| Gly | Ser | Gly | Gly | Gly | Gly | Glu | Val | Lys | Leu | Asp | Glu | Thr | Gly | Gly | Gly |
|     |     | 115 |     |     |     |     | 120 |     |     |     |     | 125 |     |     |     |
| Leu | Val | Gln | Pro | Gly | Arg | Pro | Met | Lys | Leu | Ser | Cys | Val | Ala | Ser | Gly |
|     | 130 |     |     |     |     | 135 |     |     |     |     | 140 |     |     |     |     |
| Phe | Thr | Phe | Ser | Asp | Tyr | Trp | Met | Asn | Trp | Val | Arg | Gln | Ser | Pro | Glu |
| 145 |     |     |     |     |     | 150 |     |     |     |     | 155 |     |     |     | 160 |
| Lys | Gly | Leu | Glu | Trp | Val | Ala | Gln | Ile | Arg | Asn | Lys | Pro | Tyr | Asn | Tyr |
|     |     |     |     | 165 |     |     |     |     | 170 |     |     |     |     | 175 |     |
| Glu | Thr | Tyr | Tyr | Ser | Asp | Ser | Val | Lys | Gly | Arg | Phe | Thr | Ile | Ser | Arg |
|     |     |     | 180 |     |     |     |     | 185 |     |     |     |     | 190 |     |     |
| Asp | Asp | Ser | Lys | Ser | Ser | Val | Tyr | Leu | Gln | Met | Asn | Asn | Leu | Arg | Val |
|     |     | 195 |     |     |     |     | 200 |     |     |     |     | 205 |     |     |     |
| Glu | Asp | Met | Gly | Ile | Tyr | Tyr | Cys | Thr | Gly | Ser | Tyr | Tyr | Gly | Met | Asp |
|     | 210 |     |     |     |     | 215 |     |     |     |     | 220 |     |     |     |     |
| Tyr | Trp | Gly | Gln | Gly | Thr | Ser | Val | Thr | Val | Ser | Ser | Ala | Ser | Thr | Lys |
| 225 |     |     |     |     |     | 230 |     |     |     |     | 235 |     |     |     | 240 |
| Gly | Lys | Val | Ala | Ala | Cys | Lys | Glu | Lys | Val | Ala | Ala | Leu | Lys | Glu | Lys |
|     |     |     | 245 |     |     |     |     | 250 |     |     |     |     |     | 255 |     |

Val Ala Ala Leu Lys Glu Lys Val Ala Ala Leu Lys Glu  
 260 265

<210> 45  
 <211> 495  
 <212> PRT  
 <213> Secuencia Artificial

<220>  
 <223> Primera Cadena de Polipéptido del Control DART 2

<400> 45

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

Glu Lys Ala Thr Ile Thr Cys Arg Ala Ser Gln Ser Val Ser Tyr Met  
 20 25 30

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

Asp Ala Ser Asn Arg Ala Ser Gly Val Pro Ser Arg Phe Ser Gly Ser  
 50 55 60

Gly Ser Gly Thr Asp His Thr Leu Thr Ile Ser Ser Leu Glu Ala Glu  
 65 70 75 80

Asp Ala Ala Thr Tyr Tyr Cys Phe Gln Gly Ser Val Tyr Pro Phe Thr  
 85 90 95

Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys Gly Gly Gly Ser Gly Gly  
 100 105 110

Gly Gly Glu Val Lys Leu Asp Glu Thr Gly Gly Gly Leu Val Gln Pro  
 115 120 125

Gly Arg Pro Met Lys Leu Ser Cys Val Ala Ser Gly Phe Thr Phe Ser  
 130 135 140

Asp Tyr Trp Met Asn Trp Val Arg Gln Ser Pro Glu Lys Gly Leu Glu  
 145 150 155 160

Trp Val Ala Gln Ile Arg Asn Lys Pro Tyr Asn Tyr Glu Thr Tyr Tyr  
 165 170 175

Ser Asp Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asp Ser Lys  
 180 185 190

Ser Ser Val Tyr Leu Gln Met Asn Asn Leu Arg Val Glu Asp Met Gly  
 195 200 205

Ile Tyr Tyr Cys Thr Gly Ser Tyr Tyr Gly Met Asp Tyr Trp Gly Gln  
 210 215 220

Gly Thr Ser Val Thr Val Ser Ser Ala Ser Thr Lys Gly Glu Val Ala  
 225 230 235 240

Ala Cys Glu Lys Glu Val Ala Ala Leu Glu Lys Glu Val Ala Ala Leu  
 245 250 255

Glu Lys Glu Val Ala Ala Leu Glu Lys Gly Gly Gly Asp Lys Thr His  
 260 265 270

Thr Cys Pro Pro Cys Pro Ala Pro Glu Ala Ala Gly Gly Pro Ser Val  
 275 280 285

Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr  
 290 295 300

Pro Glu Val Thr Cys Val Val Val Asp Val Ser His Glu Asp Pro Glu  
 305 310 315 320

Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala Lys  
 325 330 335

Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg Val Val Ser  
 340 345 350

Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys  
 355 360 365

Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu Lys Thr Ile  
 370 375 380

Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro  
 385 390 395 400

Pro Ser Arg Glu Glu Met Thr Lys Asn Gln Val Ser Leu Trp Cys Leu

405

410

415

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

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

Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg  
 450 455 460

Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His Glu Ala Leu  
 465 470 475 480

His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly Lys  
 485 490 495

&lt;210&gt; 46

&lt;211&gt; 269

&lt;212&gt; PRT

&lt;213&gt; Secuencia Artificial

&lt;220&gt;

&lt;223&gt; Segunda Cadena de Polipéptido del Control DART 2

&lt;400&gt; 46

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

Thr Val Thr Leu Thr Cys Arg Ser Ser Thr Gly Ala Val Thr Thr Ser  
 20 25 30

Asn Tyr Ala Asn Trp Val Gln Gln Lys Pro Gly Gln Ala Pro Arg Gly  
 35 40 45

Leu Ile Gly Gly Thr Asn Lys Arg Ala Pro Trp Thr Pro Ala Arg Phe  
 50 55 60

Ser Gly Ser Leu Leu Gly Gly Lys Ala Ala Leu Thr Ile Thr Gly Ala  
 65 70 75 80

Gln Ala Glu Asp Glu Ala Asp Tyr Tyr Cys Ala Leu Trp Tyr Ser Asn  
 85 90 95

Leu Trp Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu Gly Gly Gly

|     |     |     |     |     |     |
|-----|-----|-----|-----|-----|-----|
|     | 100 |     | 105 |     | 110 |
| Gly | Ser | Gly | Gly | Gly | Gly |
|     | 115 |     |     | Glu | Val |
|     |     |     |     | 120 |     |
|     |     |     |     | Lys | Leu |
|     |     |     |     | Asp | Glu |
|     |     |     |     | Thr | Gly |
|     |     |     |     | 125 | Gly |
|     |     |     |     |     | Gly |
|     |     |     |     |     | Gly |
| Leu | Val | Gln | Pro | Gly | Arg |
|     | 130 |     |     | 135 |     |
|     |     |     |     | Met | Lys |
|     |     |     |     | Leu | Ser |
|     |     |     |     | Cys | Val |
|     |     |     |     | 140 | Ala |
|     |     |     |     |     | Ser |
|     |     |     |     |     | Gly |
| Phe | Thr | Phe | Ser | Asp | Tyr |
|     |     |     |     | 150 | Trp |
|     |     |     |     | Met | Asn |
|     |     |     |     | Trp | Val |
|     |     |     |     | 155 | Arg |
|     |     |     |     |     | Gln |
|     |     |     |     |     | Ser |
|     |     |     |     |     | Pro |
|     |     |     |     |     | Glu |
|     |     |     |     |     | 160 |
| Lys | Gly | Leu | Glu | Trp | Val |
|     |     |     |     | 165 | Ala |
|     |     |     |     | Gln | Ile |
|     |     |     |     | Arg | Asn |
|     |     |     |     | 170 | Lys |
|     |     |     |     |     | Pro |
|     |     |     |     |     | Tyr |
|     |     |     |     |     | Asn |
|     |     |     |     |     | Tyr |
|     |     |     |     |     | 175 |
| Glu | Thr | Tyr | Tyr | Ser | Asp |
|     |     |     |     | 180 | Ser |
|     |     |     |     | Val | Lys |
|     |     |     |     | 185 | Gly |
|     |     |     |     | Arg | Phe |
|     |     |     |     | Thr | Ile |
|     |     |     |     |     | Ser |
|     |     |     |     |     | Arg |
|     |     |     |     |     | 190 |
| Asp | Asp | Ser | Lys | Ser | Ser |
|     |     | 195 |     | Val | Tyr |
|     |     |     |     | 200 | Leu |
|     |     |     |     | Gln | Met |
|     |     |     |     | Asn | Asn |
|     |     |     |     | 205 | Leu |
|     |     |     |     |     | Arg |
|     |     |     |     |     | Val |
| Glu | Asp | Met | Gly | Ile | Tyr |
|     | 210 |     |     | 215 | Tyr |
|     |     |     |     | Cys | Thr |
|     |     |     |     | Gly | Ser |
|     |     |     |     | 220 | Tyr |
|     |     |     |     | Tyr | Gly |
|     |     |     |     | Met | Asp |
|     |     |     |     |     |     |
| Tyr | Trp | Gly | Gln | Gly | Thr |
|     | 225 |     |     | 230 | Ser |
|     |     |     |     | Val | Thr |
|     |     |     |     | 235 | Ser |
|     |     |     |     | Ala | Ser |
|     |     |     |     | Leu | Lys |
|     |     |     |     | Glu | Lys |
|     |     |     |     | 255 |     |
| Gly | Lys | Val | Ala | Ala | Cys |
|     |     |     | 245 | Lys | Glu |
|     |     |     |     | Lys | Val |
|     |     |     |     | 250 | Ala |
|     |     |     |     | Ala | Leu |
|     |     |     |     | Lys | Glu |
|     |     |     |     |     | Lys |
|     |     |     |     |     |     |
| Val | Ala | Ala | Leu | Lys | Glu |
|     |     |     | 260 | Val | Ala |
|     |     |     |     | 265 | Ala |
|     |     |     |     | Leu | Lys |
|     |     |     |     | Glu |     |

&lt;210&gt; 47

&lt;211&gt; 5

&lt;212&gt; PRT

&lt;213&gt; Secuencia Artificial

&lt;220&gt;

&lt;223&gt; Péptido Espaciador de Intervención (Enlazador 4)

&lt;400&gt; 47

|     |     |     |     |     |
|-----|-----|-----|-----|-----|
| Ala | Pro | Ser | Ser | Ser |
| 1   |     |     |     | 5   |

&lt;210&gt; 48

<211> 8  
<212> PRT  
<213> Secuencia Artificial

<220>  
<223> Péptido Espaciador de Intervención (Enlazador 4)

<400> 48

Ala Pro Ser Ser Ser Pro Met Glu  
1 5