

LISTADO DE SECUENCIAS

<110> Autolus Limited

<120> DOMINIO DE UNIÓN A ANTÍGENO

<130> P112494PCT

<150> GB 1709203.2

<151> 2017-06-09

<160> 36

<170> PatentIn version 3.5

<210> 1

<211> 7

<212> PRT

<213> Secuencia artificial

<220>

<223> región determinante de la complementariedad de la cadena pesada variable (VH)

(CDR)1, VH CDR1

<400> 1

Gly Tyr Thr Phe Thr Gly Tyr

1

5

<210> 2

<211> 6

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<213> Secuencia artificial

<220>

<223> CDR2 de la VH

<400> 2

Asn Pro Tyr Asn Asp Asp

1

5

<210> 3

<211> 15

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<213> Secuencia artificial

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<223> CDR3 de la VH

<400> 3

Gly Ala Gly Tyr Asn Phe Asp Gly Ala Tyr Arg Phe Phe Asp Phe
 1 5 10 15

<210> 4
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<220>
 <223> CDR1 de la cadena ligera variable (VL)

<400> 4

Arg Ser Ser Gln Arg Leu Val His Ser Asn Gly Asn Thr Tyr Leu His
 1 5 10 15

<210> 5
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 <213> Secuencia artificial

<220>
 <223> VL CDR2

<400> 5

Arg Val Ser Asn Arg Phe Pro
 1 5

<210> 6
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<220>
 <223> CDR3 de la VL

<400> 6

Ser Gln Ser Thr His Val Pro Tyr Thr
 1 5

<210> 7
 <211> 124
 <212> PRT
 <213> Mus musculus

<400> 7

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

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

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

Gly Phe Ile Asn Pro Tyr Asn Asp Asp Ile Gln Ser Asn Glu Arg Phe
 50 55 60

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

Phe Trp Gly Gln Gly Thr Thr Leu Thr Val Ser Ser
 115 120

<210> 8
 <211> 113
 <212> PRT
 <213> Mus musculus

<400> 8

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

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

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

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

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

Arg

<210> 9
 <211> 124
 <212> PRT
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<220>

<223> marco H-AF062256 Jovi-1 humanizado

<400> 9

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 Gly Tyr
20 25 30

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

Gly Phe Ile Asn Pro Tyr Asn Asp Asp Ile Gln Ser Asn Glu Arg Phe
50 55 60

Arg Gly Arg Val Thr Met Thr Arg 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 Ala Gly Tyr Asn Phe Asp Gly Ala Tyr Arg Phe Phe Asp
100 105 110

Phe Trp Gly Gln Gly Thr Met Val Thr Val Ser Ser
115 120

<210> 10

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<212> PRT

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<223> marco H-EF177999 Jovi-1 humanizado

<400> 10

Glu Val Gln Leu Val Glu 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 Gly Tyr
20 25 30

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

Gly Phe Ile Asn Pro Tyr Asn Asp Asp Ile Gln Ser Asn Glu Arg Phe
50 55 60

Arg Gly Arg Val Thr Met Thr Arg Asp Thr Ser Thr Ser Thr Val 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 Arg Gly Ala Gly Tyr Asn Phe Asp Gly Ala Tyr Arg Phe Phe Asp
100 105 110

Phe Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser
115 120

<210> 11

<211> 124

<212> PRT

<213> Secuencia artificial

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<223> marco H-KF688165 Jovi-1 humanizado

<400> 11

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 Glu Tyr Ser Phe Thr Gly Tyr
20 25 30

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

Gly Phe Ile Asn Pro Tyr Asn Asp Asp Ile Gln Ser Asn Glu Arg Phe
50 55 60

Arg Gly Arg Val Thr Met Thr Arg Asp Thr Ser Ile Ser Thr Ala Tyr
65 70 75 80

Met Glu Val Ser Ser Leu Thr Ser Asp Asp Ala Ala Ile Tyr Tyr Cys
85 90 95

Ala Arg Gly Ala Gly Tyr Asn Phe Asp Gly Ala Tyr Arg Phe Phe Asp
100 105 110

Phe Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser
115 120

<210> 12

<211> 124

<212> PRT

<213> Secuencia artificial

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<223> secuencia de cadena pesada variable (VH) con mutación revertida,
mutación K73

<400> 12

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	Gly	Tyr	
			20					25					30			
Val	Met	His	Trp	Val	Arg	Gln	Ala	Pro	Gly	Gln	Gly	Leu	Glu	Trp	Met	
		35					40					45				
Gly	Phe	Ile	Asn	Pro	Tyr	Asn	Asp	Asp	Ile	Gln	Ser	Asn	Glu	Arg	Phe	
	50					55					60					
Arg	Gly	Arg	Val	Thr	Met	Thr	Arg	Asp	Lys	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	Ala	Gly	Tyr	Asn	Phe	Asp	Gly	Ala	Tyr	Arg	Phe	Phe	Asp	
			100					105					110			
Phe	Trp	Gly	Gln	Gly	Thr	Met	Val	Thr	Val	Ser	Ser					
		115					120									

<210> 13

<211> 124

<212> PRT

<213> Secuencia artificial

<220>

<223> secuencia VH con mutación revertida, mutación S71

<400> 13

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	Gly	Tyr	
			20					25					30			
Val	Met	His	Trp	Val	Arg	Gln	Ala	Pro	Gly	Gln	Gly	Leu	Glu	Trp	Met	
		35					40					45				
Gly	Phe	Ile	Asn	Pro	Tyr	Asn	Asp	Asp	Ile	Gln	Ser	Asn	Glu	Arg	Phe	
	50					55					60					
Arg	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	Ala	Gly	Tyr	Asn	Phe	Asp	Gly	Ala	Tyr	Arg	Phe	Phe	Asp	
			100					105					110			

Phe Trp Gly Gln Gly Thr Met Val Thr Val Ser Ser
 115 120

<210> 14

<211> 124

<212> PRT

<213> Secuencia artificial

<220>

<223> secuencia VH con mutación revertida, mutaciones S71, K73

<400> 14

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 Gly Tyr
 20 25 30

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

Gly Phe Ile Asn Pro Tyr Asn Asp Asp Ile Gln Ser Asn Glu Arg Phe
 50 55 60

Arg Gly Arg Val Thr Met Thr Ser Asp Lys 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 Ala Gly Tyr Asn Phe Asp Gly Ala Tyr Arg Phe Phe Asp
 100 105 110

Phe Trp Gly Gln Gly Thr Met Val Thr Val Ser Ser
 115 120

<210> 15

<211> 124

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<213> Secuencia artificial

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<223> secuencia VH con mutación revertida, mutación I48

<400> 15

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 Gly Tyr
 20 25 30

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

Gly Phe Ile Asn Pro Tyr Asn Asp Asp Ile Gln Ser Asn Glu Arg Phe
50 55 60

Arg Gly Arg Val Thr Met Thr Arg 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 Ala Gly Tyr Asn Phe Asp Gly Ala Tyr Arg Phe Phe Asp
100 105 110

Phe Trp Gly Gln Gly Thr Met Val Thr Val Ser Ser
115 120

<210> 16

<211> 124

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<220>

<223> secuencia VH con mutación revertida, mutaciones I48, K73

<400> 16

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 Gly Tyr
20 25 30

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

Gly Phe Ile Asn Pro Tyr Asn Asp Asp Ile Gln Ser Asn Glu Arg Phe
50 55 60

Arg Gly Arg Val Thr Met Thr Arg Asp Lys 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 Ala Gly Tyr Asn Phe Asp Gly Ala Tyr Arg Phe Phe Asp
100 105 110

Phe Trp Gly Gln Gly Thr Met Val Thr Val Ser Ser
115 120

<210> 17

<211> 124

<212> PRT

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<220>

<223> secuencia VH con mutación revertida, mutaciones M20, S71, K73

<400> 17

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

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

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

Gly Phe Ile Asn Pro Tyr Asn Asp Asp Ile Gln Ser Asn Glu Arg Phe
50 55 60

Arg Gly Arg Val Thr Met Thr Ser Asp Lys 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 Ala Gly Tyr Asn Phe Asp Gly Ala Tyr Arg Phe Phe Asp
100 105 110

Phe Trp Gly Gln Gly Thr Met Val Thr Val Ser Ser
115 120

<210> 18

<211> 124

<212> PRT

<213> Secuencia artificial

<220>

<223> secuencia VH con mutación revertida, mutaciones M20, I48

<400> 18

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

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

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

Gly Phe Ile Asn Pro Tyr Asn Asp Asp Ile Gln Ser Asn Glu Arg Phe
50 55 60

Arg Gly Arg Val Thr Met Thr Arg 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 Ala Gly Tyr Asn Phe Asp Gly Ala Tyr Arg Phe Phe Asp
100 105 110

Phe Trp Gly Gln Gly Thr Met Val Thr Val Ser Ser
115 120

<210> 19

<211> 112

<212> PRT

<213> Secuencia artificial

<220>

<223> CDR de VL JOVI-1 con marco humano 3aaz

<400> 19

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

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

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

Pro Arg Leu Leu Ile Tyr Arg Val Ser Asn Arg Phe Pro 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 Ser Gln Ser
85 90 95

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

<210> 20

<211> 112

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<213> Secuencia artificial

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<223> secuencia de cadena ligera variable (VL) con mutaciones revertidas

<400> 20

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

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

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

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

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

<210> 21

<211> 112

<212> PRT

<213> Secuencia artificial

<220>

<223> secuencia VL con mutaciones revertidas

<400> 21

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

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

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

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

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

<210> 22

<211> 112

<212> PRT
 <213> Secuencia artificial

<220>
 <223> secuencia VL con mutaciones revertidas

<400> 22

Asp	Ile	Val	Met	Thr	Gln	Ser	Pro	Leu	Ser	Leu	Pro	Val	Thr	Leu	Gly
1				5					10					15	
Glu	Gln	Ala	Ser	Ile	Ser	Cys	Arg	Ser	Ser	Gln	Arg	Leu	Val	His	Ser
			20					25					30		
Asn	Gly	Asn	Thr	Tyr	Leu	His	Trp	Tyr	Leu	Gln	Lys	Pro	Gly	Gln	Ser
		35					40					45			
Pro	Arg	Leu	Leu	Ile	Tyr	Arg	Val	Ser	Asn	Arg	Phe	Pro	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	Ser	Gln	Ser
				85				90						95	
Thr	His	Val	Pro	Tyr	Thr	Phe	Gly	Gly	Gly	Thr	Lys	Leu	Glu	Ile	Lys
			100					105					110		

<210> 23
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 <212> PRT
 <213> Secuencia artificial

<220>
 <223> secuencia VL con mutaciones revertidas

<400> 23

Asp	Ile	Val	Met	Thr	Gln	Ser	Pro	Leu	Ser	Leu	Pro	Val	Thr	Leu	Gly
1				5					10					15	
Glu	Gln	Ala	Ser	Ile	Ser	Cys	Arg	Ser	Ser	Gln	Arg	Leu	Val	His	Ser
			20					25					30		
Asn	Gly	Asn	Thr	Tyr	Leu	His	Trp	Tyr	Leu	Gln	Lys	Pro	Gly	Gln	Ser
		35					40					45			
Pro	Arg	Leu	Leu	Ile	Tyr	Arg	Val	Ser	Asn	Arg	Phe	Pro	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 Ser Gln Ser
85 90 95

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

<210> 24

<211> 112

<212> PRT

<213> Secuencia artificial

<220>

<223> secuencia VL con mutaciones revertidas

<400> 24

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

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

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

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

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

<210> 25

<211> 112

<212> PRT

<213> Secuencia artificial

<220>

<223> secuencia VL con mutaciones revertidas

<400> 25

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

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

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

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

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

<210> 26

<211> 112

<212> PRT

<213> Secuencia artificial

<220>

<223> secuencia VL con mutaciones revertidas

<400> 26

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

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

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

Pro Arg Leu Leu Ile Tyr Arg Val Ser Asn Arg Phe Pro 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 Ser Gln Ser
 85 90 95

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

<210> 27

<211> 112

<212> PRT

<213> Secuencia artificial

<220>

<223> secuencia VL con mutaciones revertidas

<400> 27

Asp	Ile	Val	Met	Thr	Gln	Ser	Pro	Leu	Ser	Leu	Pro	Val	Thr	Leu	Gly
1				5					10					15	
Glu	Pro	Ala	Ser	Ile	Ser	Cys	Arg	Ser	Ser	Gln	Arg	Leu	Val	His	Ser
			20					25					30		
Asn	Gly	Asn	Thr	Tyr	Leu	His	Trp	Tyr	Leu	Gln	Lys	Pro	Gly	Gln	Ser
		35					40					45			
Pro	Arg	Leu	Leu	Ile	Tyr	Arg	Val	Ser	Asn	Arg	Phe	Pro	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	Ser	Gln	Ser
				85					90					95	
Thr	His	Val	Pro	Tyr	Thr	Phe	Gly	Gln	Gly	Thr	Lys	Leu	Glu	Ile	Lys
			100					105					110		

<210> 28

<211> 112

<212> PRT

<213> Secuencia artificial

<220>

<223> secuencia VL con mutaciones revertidas

<400> 28

Asp	Ile	Val	Met	Thr	Gln	Ser	Pro	Leu	Ser	Leu	Pro	Val	Thr	Pro	Gly
1				5					10					15	
Glu	Gln	Ala	Ser	Ile	Ser	Cys	Arg	Ser	Ser	Gln	Arg	Leu	Val	His	Ser
			20					25					30		
Asn	Gly	Asn	Thr	Tyr	Leu	His	Trp	Tyr	Leu	Gln	Lys	Pro	Gly	Gln	Ser
		35					40					45			
Pro	Arg	Leu	Leu	Ile	Tyr	Arg	Val	Ser	Asn	Arg	Phe	Pro	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	Phe	Cys	Ser	Gln	Ser
				85					90					95	

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

<210> 29

<211> 112

<212> PRT

<213> Secuencia artificial

<220>

<223> secuencia VL con mutaciones revertidas

<400> 29

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

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

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

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

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

<210> 30

<211> 112

<212> PRT

<213> Secuencia artificial

<220>

<223> secuencia VL con mutaciones revertidas

<400> 30

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

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

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

Pro Arg Leu Leu Ile Tyr Arg Val Ser Asn Arg Phe Pro 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 Ser Gln Ser
85 90 95

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

<210> 31

<211> 112

<212> PRT

<213> Secuencia artificial

<220>

<223> secuencia VL con mutaciones revertidas

<400> 31

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

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

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

Pro Arg Leu Leu Ile Tyr Arg Val Ser Asn Arg Phe Pro 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 Ser Gln Ser
85 90 95

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

<210> 32

<211> 112

<212> PRT

<213> Secuencia artificial

<220>

<223> secuencia VL con mutaciones revertidas

<400> 32

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

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

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

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

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

<210> 33

<211> 112

<212> PRT

<213> Secuencia artificial

<220>

<223> secuencia VL con mutaciones revertidas

<400> 33

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

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

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

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

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

<210> 34

<211> 112

<212> PRT

<213> Secuencia artificial

<220>

<223> secuencia VL con mutaciones revertidas

<400> 34

Asp	Ile	Val	Met	Thr	Gln	Ser	Pro	Leu	Ser	Leu	Pro	Val	Thr	Pro	Gly	1	5	10	15
Glu	Pro	Ala	Ser	Ile	Ser	Cys	Arg	Ser	Ser	Gln	Arg	Leu	Val	His	Ser	20	25	30	
Asn	Gly	Asn	Thr	Tyr	Leu	His	Trp	Tyr	Leu	Gln	Lys	Pro	Gly	Gln	Ser	35	40	45	
Pro	Arg	Leu	Leu	Ile	Tyr	Arg	Val	Ser	Asn	Arg	Phe	Pro	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	Ser	Gln	Ser	85	90	95	
Thr	His	Val	Pro	Tyr	Thr	Phe	Gly	Gly	Gly	Thr	Lys	Leu	Glu	Ile	Lys	100	105	110	

<210> 35

<211> 175

<212> PRT

<213> Homo sapiens

<400> 35

Asp	Leu	Asn	Lys	Val	Phe	Pro	Pro	Glu	Val	Ala	Val	Phe	Glu	Pro	Ser	1	5	10	15
Glu	Ala	Glu	Ile	Ser	His	Thr	Gln	Lys	Ala	Thr	Leu	Val	Cys	Leu	Ala	20	25	30	
Thr	Gly	Phe	Phe	Pro	Asp	His	Val	Glu	Leu	Ser	Trp	Trp	Val	Asn	Gly	35	40	45	
Lys	Glu	Val	His	Ser	Gly	Val	Ser	Thr	Asp	Pro	Gln	Pro	Leu	Lys	Glu	50	55	60	
Gln	Pro	Ala	Leu	Asn	Asp	Ser	Arg	Tyr	Cys	Leu	Ser	Ser	Arg	Leu	Arg	65	70	75	80
Val	Ser	Ala	Thr	Phe	Trp	Gln	Asn	Pro	Arg	Asn	His	Phe	Arg	Cys	Gln	85	90	95	

Val Gln Phe Tyr Gly Leu Ser Glu Asn Asp Glu Trp Thr Gln Asp Arg
100 105 110

Ala Lys Pro Val Thr Gln Ile Val Ser Ala Glu Ala Trp Gly Arg Ala
115 120 125

Asp Cys Gly Phe Thr Ser Val Ser Tyr Gln Gln Gly Val Leu Ser Ala
130 135 140

Thr Ile Leu Tyr Glu Ile Leu Leu Gly Lys Ala Thr Leu Tyr Ala Val
145 150 155 160

Leu Val Ser Ala Leu Val Leu Met Ala Met Val Lys Arg Lys Asp
165 170 175

<210> 36

<211> 175

<212> PRT

<213> Homo sapiens

<400> 36

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

Glu Ala Glu Ile Ser His Thr Gln Lys Ala Thr Leu Val Cys Leu Ala
20 25 30

Thr Gly Phe Tyr Pro Asp His Val Glu Leu Ser Trp Trp Val Asn Gly
35 40 45

Lys Glu Val His Ser Gly Val Ser Thr Asp Pro Gln Pro Leu Lys Glu
50 55 60

Gln Pro Ala Leu Asn Asp Ser Arg Tyr Cys Leu Ser Ser Arg Leu Arg
65 70 75 80

Val Ser Ala Thr Phe Trp Gln Asn Pro Arg Asn His Phe Arg Cys Gln
85 90 95

Val Gln Phe Tyr Gly Leu Ser Glu Asn Asp Glu Trp Thr Gln Asp Arg
100 105 110

Ala Lys Pro Val Thr Gln Ile Val Ser Ala Glu Ala Trp Gly Arg Ala
115 120 125

Asp Cys Gly Phe Thr Ser Glu Ser Tyr Gln Gln Gly Val Leu Ser Ala
130 135 140

Thr Ile Leu Tyr Glu Ile Leu Leu Gly Lys Ala Thr Leu Tyr Ala Val
145 150 155 160

Leu Val Ser Ala Leu Val Leu Met Ala Met Val Lys Arg Lys Asp
165 170 175