

SEQUENCE LISTING

<110> Philogen S.p.A.

<120> IL-12 antagonists with optimized linkers

<130> PD 43256

<160> 36

<170> PatentIn version 3.5

<210> 1

<211> 306

<212> PRT

<213> Homo sapiens

<400> 1

Ile	Trp	Glu	Leu	Lys	Lys	Asp	Val	Tyr	Val	Val	Glu	Leu	Asp	Trp	Tyr
1				5					10					15	

Pro	Asp	Ala	Pro	Gly	Glu	Met	Val	Val	Leu	Thr	Cys	Asp	Thr	Pro	Glu
			20					25					30		

Glu	Asp	Gly	Ile	Thr	Trp	Thr	Leu	Asp	Gln	Ser	Ser	Glu	Val	Leu	Gly
		35					40					45			

Ser	Gly	Lys	Thr	Leu	Thr	Ile	Gln	Val	Lys	Glu	Phe	Gly	Asp	Ala	Gly
	50					55					60				

Gln	Tyr	Thr	Cys	His	Lys	Gly	Gly	Glu	Val	Leu	Ser	His	Ser	Leu	Leu
65					70					75				80	

Leu	Leu	His	Lys	Lys	Glu	Asp	Gly	Ile	Trp	Ser	Thr	Asp	Ile	Leu	Lys
			85						90					95	

Asp	Gln	Lys	Glu	Pro	Lys	Asn	Lys	Thr	Phe	Leu	Arg	Cys	Glu	Ala	Lys
			100					105					110		

Asn	Tyr	Ser	Gly	Arg	Phe	Thr	Cys	Trp	Trp	Leu	Thr	Thr	Ile	Ser	Thr
		115					120					125			

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

Gly Val Thr Cys Gly Ala Ala Thr Leu Ser Ala Glu Arg Val Arg Gly
145 150 155 160

Asp Asn Lys Glu Tyr Glu Tyr Ser Val Glu Cys Gln Glu Asp Ser Ala
165 170 175

Cys Pro Ala Ala Glu Glu Ser Leu Pro Ile Glu Val Met Val Asp Ala
180 185 190

Val His Lys Leu Lys Tyr Glu Asn Tyr Thr Ser Ser Phe Phe Ile Arg
195 200 205

Asp Ile Ile Lys Pro Asp Pro Pro Lys Asn Leu Gln Leu Lys Pro Leu
210 215 220

Lys Asn Ser Arg Gln Val Glu Val Ser Trp Glu Tyr Pro Asp Thr Trp
225 230 235 240

Ser Thr Pro His Ser Tyr Phe Ser Leu Thr Phe Cys Val Gln Val Gln
245 250 255

Gly Lys Ser Lys Arg Glu Lys Lys Asp Arg Val Phe Thr Asp Lys Thr
260 265 270

Ser Ala Thr Val Ile Cys Arg Lys Asn Ala Ser Ile Ser Val Arg Ala
275 280 285

Gln Asp Arg Tyr Tyr Ser Ser Ser Trp Ser Glu Trp Ala Ser Val Pro
290 295 300

Cys Ser
305

<210> 2
<211> 15
<212> PRT
<213> artificial sequence

<220>
<223> linker

<400> 2

Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser
1 5 10 15

<210> 3
<211> 197
<212> PRT
<213> Homo sapiens

<400> 3

Arg Asn Leu Pro Val Ala Thr Pro Asp Pro Gly Met Phe Pro Cys Leu
1 5 10 15

His His Ser Gln Asn Leu Leu Arg Ala Val Ser Asn Met Leu Gln Lys
20 25 30

Ala Arg Gln Thr Leu Glu Phe Tyr Pro Cys Thr Ser Glu Glu Ile Asp
35 40 45

His Glu Asp Ile Thr Lys Asp Lys Thr Ser Thr Val Glu Ala Cys Leu
50 55 60

Pro Leu Glu Leu Thr Lys Asn Glu Ser Cys Leu Asn Ser Arg Glu Thr
65 70 75 80

Ser Phe Ile Thr Asn Gly Ser Cys Leu Ala Ser Arg Lys Thr Ser Phe
85 90 95

Met Met Ala Leu Cys Leu Ser Ser Ile Tyr Glu Asp Leu Lys Met Tyr
100 105 110

Gln Val Glu Phe Lys Thr Met Asn Ala Lys Leu Leu Met Asp Pro Lys
115 120 125

Arg Gln Ile Phe Leu Asp Gln Asn Met Leu Ala Val Ile Asp Glu Leu
130 135 140

Met Gln Ala Leu Asn Phe Asn Ser Glu Thr Val Pro Gln Lys Ser Ser
145 150 155 160

Leu Glu Glu Pro Asp Phe Tyr Lys Thr Lys Ile Lys Leu Cys Ile Leu
165 170 175

Leu His Ala Phe Arg Ile Arg Ala Val Thr Ile Asp Arg Val Met Ser
180 185 190

Tyr Leu Asn Ala Ser
195

<210> 4
<211> 15
<212> PRT
<213> artificial sequence

<220>
<223> linker

<400> 4

Gly Ser Ala Asp Gly Gly Ser Ser Ala Gly Gly Ser Asp Ala Gly
1 5 10 15

<210> 5
<211> 108
<212> PRT
<213> artificial sequence

<220>
<223> antibody sequence (variable domain)

<400> 5

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

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

Ile Tyr Tyr 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 Thr Gly Arg Ile Pro
85 90 95

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

<210> 6
<211> 5
<212> PRT
<213> artificial sequence

<220>
<223> linker

<400> 6

Gly Ser Ser Gly Gly
1 5

<210> 7
<211> 116
<212> PRT
<213> artificial sequence

<220>
<223> antibody sequence (variable domain)

<400> 7

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 Phe
20 25 30

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

Ser Ser Ile Ser Gly Ser Ser Gly Thr 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 Pro Phe Pro Tyr Phe Asp Tyr Trp Gly Gln Gly Thr Leu Val
100 105 110

Thr Val Ser Ser
115

<210> 8
<211> 15
<212> PRT
<213> artificial sequence

<220>
<223> linker

<400> 8

Ser Ser Ser Ser Gly Ser Ser Ser Ser Gly Ser Ser Ser Ser Gly
1 5 10 15

<210> 9
<211> 15
<212> PRT
<213> artificial sequence

<220>
<223> linker

<400> 9

Gly Gly Gly Ala Lys Gly Gly Gly Gly Lys Ala Gly Gly Gly Ser
1 5 10 15

<210> 10
<211> 15
<212> PRT
<213> artificial sequence

<220>
<223> linker

<400> 10

Gly Gly Gly Gly Asp Gly Gly Gly Gly Asp Gly Gly Gly Gly Ser
1 5 10 15

<210> 11
<211> 15

<212> PRT
<213> artificial sequence

<220>
<223> linker

<400> 11

Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser
1 5 10 15

<210> 12
<211> 15
<212> PRT
<213> artificial sequence

<220>
<223> linker

<400> 12

Gly Gly Gly Gly Ser Gly Gly Gly Gly Glu Gly Gly Gly Gly Ser
1 5 10 15

<210> 13
<211> 17
<212> PRT
<213> artificial sequence

<220>
<223> linker

<400> 13

Ala Glu Ala Ala Ala Lys Glu Ala Ala Ala Lys Glu Ala Ala Ala Lys
1 5 10 15

Ala

<210> 14
<211> 12
<212> PRT
<213> artificial sequence

<220>
<223> linker

<400> 14

Ala Pro Ala Pro Ala Pro Ala Pro Ala Pro Ala Pro
1 5 10

<210> 15
<211> 14
<212> PRT
<213> artificial sequence

<220>
<223> linker

<400> 15

Ala Pro Ala Pro Ala Pro Ala Pro Ala Pro Ala Pro Ala Pro
1 5 10

<210> 16
<211> 1006
<212> PRT
<213> artificial sequence

<220>
<223> Immunoconjugate sequence

<400> 16

Ile Trp Glu Leu Lys Lys Asp Val Tyr Val Val Glu Leu Asp Trp Tyr
1 5 10 15

Pro Asp Ala Pro Gly Glu Met Val Val Leu Thr Cys Asp Thr Pro Glu
20 25 30

Glu Asp Gly Ile Thr Trp Thr Leu Asp Gln Ser Ser Glu Val Leu Gly
35 40 45

Ser Gly Lys Thr Leu Thr Ile Gln Val Lys Glu Phe Gly Asp Ala Gly
50 55 60

Gln Tyr Thr Cys His Lys Gly Gly Glu Val Leu Ser His Ser Leu Leu
65 70 75 80

Leu Leu His Lys Lys Glu Asp Gly Ile Trp Ser Thr Asp Ile Leu Lys
85 90 95

Asp Gln Lys Glu Pro Lys Asn Lys Thr Phe Leu Arg Cys Glu Ala Lys
100 105 110

Asn Tyr Ser Gly Arg Phe Thr Cys Trp Trp Leu Thr Thr Ile Ser Thr
115 120 125

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

Gly Val Thr Cys Gly Ala Ala Thr Leu Ser Ala Glu Arg Val Arg Gly
145 150 155 160

Asp Asn Lys Glu Tyr Glu Tyr Ser Val Glu Cys Gln Glu Asp Ser Ala
165 170 175

Cys Pro Ala Ala Glu Glu Ser Leu Pro Ile Glu Val Met Val Asp Ala
180 185 190

Val His Lys Leu Lys Tyr Glu Asn Tyr Thr Ser Ser Phe Phe Ile Arg
195 200 205

Asp Ile Ile Lys Pro Asp Pro Pro Lys Asn Leu Gln Leu Lys Pro Leu
210 215 220

Lys Asn Ser Arg Gln Val Glu Val Ser Trp Glu Tyr Pro Asp Thr Trp
225 230 235 240

Ser Thr Pro His Ser Tyr Phe Ser Leu Thr Phe Cys Val Gln Val Gln
245 250 255

Gly Lys Ser Lys Arg Glu Lys Lys Asp Arg Val Phe Thr Asp Lys Thr
260 265 270

Ser Ala Thr Val Ile Cys Arg Lys Asn Ala Ser Ile Ser Val Arg Ala
275 280 285

Gln Asp Arg Tyr Tyr Ser Ser Ser Trp Ser Glu Trp Ala Ser Val Pro
290 295 300

Cys Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly
305 310 315 320

Ser Arg Asn Leu Pro Val Ala Thr Pro Asp Pro Gly Met Phe Pro Cys
325 330 335

Leu His His Ser Gln Asn Leu Leu Arg Ala Val Ser Asn Met Leu Gln
340 345 350

Lys Ala Arg Gln Thr Leu Glu Phe Tyr Pro Cys Thr Ser Glu Glu Ile
355 360 365

Asp His Glu Asp Ile Thr Lys Asp Lys Thr Ser Thr Val Glu Ala Cys
370 375 380

Leu Pro Leu Glu Leu Thr Lys Asn Glu Ser Cys Leu Asn Ser Arg Glu
385 390 395 400

Thr Ser Phe Ile Thr Asn Gly Ser Cys Leu Ala Ser Arg Lys Thr Ser
405 410 415

Phe Met Met Ala Leu Cys Leu Ser Ser Ile Tyr Glu Asp Leu Lys Met
420 425 430

Tyr Gln Val Glu Phe Lys Thr Met Asn Ala Lys Leu Leu Met Asp Pro
435 440 445

Lys Arg Gln Ile Phe Leu Asp Gln Asn Met Leu Ala Val Ile Asp Glu
450 455 460

Leu Met Gln Ala Leu Asn Phe Asn Ser Glu Thr Val Pro Gln Lys Ser
465 470 475 480

Ser Leu Glu Glu Pro Asp Phe Tyr Lys Thr Lys Ile Lys Leu Cys Ile
485 490 495

Leu Leu His Ala Phe Arg Ile Arg Ala Val Thr Ile Asp Arg Val Met
500 505 510

Ser Tyr Leu Asn Ala Ser Gly Ser Ala Asp Gly Gly Ser Ser Ala Gly
515 520 525

Gly Ser Asp Ala Gly Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu
530 535 540

Val Gln Pro Gly Gly Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe
545 550 555 560

Thr Phe Ser Ser Phe Ser Met Ser Trp Val Arg Gln Ala Pro Gly Lys
565 570 575

Gly Leu Glu Trp Val Ser Ser Ile Ser Gly Ser Ser Gly Thr Thr Tyr
580 585 590

Tyr Ala Asp Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser
595 600 605

Lys Asn Thr Leu Tyr Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr
610 615 620

Ala Val Tyr Tyr Cys Ala Lys Pro Phe Pro Tyr Phe Asp Tyr Trp Gly
625 630 635 640

Gln Gly Thr Leu Val Thr Val Ser Ser Gly Ser Ser Gly Gly Glu Ile
645 650 655

Val Leu Thr Gln Ser Pro Gly Thr Leu Ser Leu Ser Pro Gly Glu Arg
660 665 670

Ala Thr Leu Ser Cys Arg Ala Ser Gln Ser Val Ser Ser Ser Phe Leu
675 680 685

Ala Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Arg Leu Leu Ile Tyr
690 695 700

Tyr Ala Ser Ser Arg Ala Thr Gly Ile Pro Asp Arg Phe Ser Gly Ser
705 710 715 720

Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Arg Leu Glu Pro Glu
725 730 735

Asp Phe Ala Val Tyr Tyr Cys Gln Gln Thr Gly Arg Ile Pro Pro Thr
740 745 750

Phe Gly Gln Gly Thr Lys Val Glu Ile Lys Ser Ser Ser Ser Gly Ser
755 760 765

Ser Ser Ser Gly Ser Ser Ser Ser Gly Glu Val Gln Leu Leu Glu Ser
770 775 780

Gly Gly Gly Leu Val Gln Pro Gly Gly Ser Leu Arg Leu Ser Cys Ala
785 790 795 800

Ala Ser Gly Phe Thr Phe Ser Ser Phe Ser Met Ser Trp Val Arg Gln
805 810 815

Ala Pro Gly Lys Gly Leu Glu Trp Val Ser Ser Ile Ser Gly Ser Ser
820 825 830

Gly Thr Thr Tyr Tyr Ala Asp Ser Val Lys Gly Arg Phe Thr Ile Ser
835 840 845

Arg Asp Asn Ser Lys Asn Thr Leu Tyr Leu Gln Met Asn Ser Leu Arg
850 855 860

Ala Glu Asp Thr Ala Val Tyr Tyr Cys Ala Lys Pro Phe Pro Tyr Phe
865 870 875 880

Asp Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Gly Ser Ser
885 890 895

Gly Gly Glu Ile Val Leu Thr Gln Ser Pro Gly Thr Leu Ser Leu Ser
900 905 910

Pro Gly Glu Arg Ala Thr Leu Ser Cys Arg Ala Ser Gln Ser Val Ser
915 920 925

Ser Ser Phe Leu Ala Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Arg
930 935 940

Leu Leu Ile Tyr Tyr Ala Ser Ser Arg Ala Thr Gly Ile Pro Asp Arg
945 950 955 960

Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Arg
965 970 975

Leu Glu Pro Glu Asp Phe Ala Val Tyr Tyr Cys Gln Gln Thr Gly Arg
980 985 990

Ile Pro Pro Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys
995 1000 1005

<210> 17

<211> 999

<212> PRT

<213> artificial sequence

<220>

<223> Immunoconjugate sequence

<400> 17

Met Trp Glu Leu Glu Lys Asp Val Tyr Val Val Glu Val Asp Trp Thr
1 5 10 15

Pro Asp Ala Pro Gly Glu Thr Val Asn Leu Thr Cys Asp Thr Pro Glu
20 25 30

Glu Asp Asp Ile Thr Trp Thr Ser Asp Gln Arg His Gly Val Ile Gly
35 40 45

Ser Gly Lys Thr Leu Thr Ile Thr Val Lys Glu Phe Leu Asp Ala Gly
50 55 60

Gln Tyr Thr Cys His Lys Gly Gly Glu Thr Leu Ser His Ser His Leu
65 70 75 80

Leu Leu His Lys Lys Glu Asn Gly Ile Trp Ser Thr Glu Ile Leu Lys
85 90 95

Asn Phe Lys Asn Lys Thr Phe Leu Lys Cys Glu Ala Pro Asn Tyr Ser
100 105 110

Gly Arg Phe Thr Cys Ser Trp Leu Val Gln Arg Asn Met Asp Leu Lys
115 120 125

Phe Asn Ile Lys Ser Ser Ser Ser Pro Asp Ser Arg Ala Val Thr
130 135 140

Cys Gly Met Ala Ser Leu Ser Ala Glu Lys Val Thr Leu Asp Gln Arg
145 150 155 160

Asp Tyr Glu Lys Tyr Ser Val Ser Cys Gln Glu Asp Val Thr Cys Pro
165 170 175

Thr Ala Glu Glu Thr Leu Pro Ile Glu Leu Ala Leu Glu Ala Arg Gln
180 185 190

Gln Asn Lys Tyr Glu Asn Tyr Ser Thr Ser Phe Phe Ile Arg Asp Ile
195 200 205

Ile Lys Pro Asp Pro Pro Lys Asn Leu Gln Met Arg Pro Leu Lys Asn
210 215 220

Ser Gln Val Glu Val Ser Trp Glu Tyr Pro Asp Ser Trp Ser Thr Pro
225 230 235 240

His Ser Tyr Phe Ser Leu Lys Phe Phe Val Arg Ile Gln Arg Lys Lys
245 250 255

Glu Lys Met Lys Glu Thr Glu Glu Gly Cys Asn Gln Lys Gly Ala Phe
260 265 270

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

Cys Val Gln Ala Gln Asp Arg Tyr Tyr Asn Ser Ser Cys Ser Lys Trp
290 295 300

Ala Cys Val Pro Cys Arg Val Arg Ser Gly Gly Gly Gly Ser Gly Gly
305 310 315 320

Gly Gly Ser Gly Gly Gly Gly Ser Arg Val Ile Pro Val Ser Gly Pro
325 330 335

Ala Arg Cys Leu Ser Gln Ser Arg Asn Leu Leu Lys Thr Thr Asp Asp
340 345 350

Met Val Lys Thr Ala Arg Glu Lys Leu Lys His Tyr Ser Cys Thr Ala
355 360 365

Glu Asp Ile Asp His Glu Asp Ile Thr Arg Asp Gln Thr Ser Thr Leu
370 375 380

Lys Thr Cys Leu Pro Leu Glu Leu His Lys Asn Glu Ser Cys Leu Ala
385 390 395 400

Thr Arg Glu Thr Ser Ser Thr Thr Arg Gly Ser Cys Leu Pro Pro Gln
405 410 415

Lys Thr Ser Leu Met Met Thr Leu Cys Leu Gly Ser Ile Tyr Glu Asp
420 425 430

Leu Lys Met Tyr Gln Thr Glu Phe Gln Ala Ile Asn Ala Ala Leu Gln
435 440 445

Asn His Asn His Gln Gln Ile Ile Leu Asp Lys Gly Met Leu Val Ala
450 455 460

Ile Asp Glu Leu Met Gln Ser Leu Asn His Asn Gly Glu Thr Leu Arg
465 470 475 480

Gln Lys Pro Pro Val Gly Glu Ala Asp Pro Tyr Arg Val Lys Met Lys
485 490 495

Leu Cys Ile Leu Leu His Ala Phe Ser Thr Arg Val Val Thr Ile Asn
500 505 510

Arg Val Met Gly Tyr Leu Ser Ser Ala Gly Ser Ala Asp Gly Glu Val
515 520 525

Gln Leu Leu Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly Ser Leu
530 535 540

Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Ser Phe Ser Met
545 550 555 560

Ser Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val Ser Ser
565 570 575

Ile Ser Gly Ser Ser Gly Thr Thr Tyr Tyr Ala Asp Ser Val Lys Gly
580 585 590

Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr Leu Gln
595 600 605

Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys Ala Lys
610 615 620

Pro Phe Pro Tyr Phe Asp Tyr Trp Gly Gln Gly Thr Leu Val Thr Val
625 630 635 640

Ser Ser Gly Ser Ser Gly Gly Glu Ile Val Leu Thr Gln Ser Pro Gly
645 650 655

Thr Leu Ser Leu Ser Pro Gly Glu Arg Ala Thr Leu Ser Cys Arg Ala
660 665 670

Ser Gln Ser Val Ser Ser Ser Phe Leu Ala Trp Tyr Gln Gln Lys Pro
675 680 685

Gly Gln Ala Pro Arg Leu Leu Ile Tyr Tyr Ala Ser Ser Arg Ala Thr
690 695 700

Gly Ile Pro Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr
705 710 715 720

Leu Thr Ile Ser Arg Leu Glu Pro Glu Asp Phe Ala Val Tyr Tyr Cys
725 730 735

Gln Gln Thr Gly Arg Ile Pro Pro Thr Phe Gly Gln Gly Thr Lys Val
740 745 750

Glu Ile Lys Ser Ser Ser Ser Gly Ser Ser Ser Ser Gly Ser Ser Ser
755 760 765

Ser Gly Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Val Gln Pro
770 775 780

Gly Gly Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser
785 790 795 800

Ser Phe Ser Met Ser Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu
805 810 815

Trp Val Ser Ser Ile Ser Gly Ser Ser Gly Thr Thr Tyr Tyr Ala Asp
820 825 830

Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr
835 840 845

Leu Tyr Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr
850 855 860

Tyr Cys Ala Lys Pro Phe Pro Tyr Phe Asp Tyr Trp Gly Gln Gly Thr
865 870 875 880

Leu Val Thr Val Ser Ser Gly Ser Ser Gly Gly Glu Ile Val Leu Thr
885 890 895

Gln Ser Pro Gly Thr Leu Ser Leu Ser Pro Gly Glu Arg Ala Thr Leu
900 905 910

Ser Cys Arg Ala Ser Gln Ser Val Ser Ser Ser Phe Leu Ala Trp Tyr
915 920 925

Gln Gln Lys Pro Gly Gln Ala Pro Arg Leu Leu Ile Tyr Tyr Ala Ser
930 935 940

Ser Arg Ala Thr Gly Ile Pro Asp Arg Phe Ser Gly Ser Gly Ser Gly
945 950 955 960

Thr Asp Phe Thr Leu Thr Ile Ser Arg Leu Glu Pro Glu Asp Phe Ala
965 970 975

Val Tyr Tyr Cys Gln Gln Thr Gly Arg Ile Pro Pro Thr Phe Gly Gln
980 985 990

Gly Thr Lys Val Glu Ile Lys
995

<210> 18
<211> 45
<212> PRT
<213> artificial sequence

<220>
<223> linker

<400> 18

Gly Gly Ala Gly Gly Gly Gly Gly Ala Gly Cys Thr Ala Ala Ala Gly
1 5 10 15

Gly Thr Gly Gly Cys Gly Gly Thr Gly Gly Cys Ala Ala Gly Gly Cys
20 25 30

Ala Gly Gly Gly Gly Gly Ala Gly Gly Gly Ala Gly Thr
35 40 45

<210> 19
<211> 42
<212> DNA
<213> artificial sequence

<220>
<223> linker

<400> 19

gcaccagcac cagcaccagc accagcacca gcaccagcac ca

42

<210> 20
<211> 45
<212> DNA
<213> artificial sequence

<220>
<223> linker

<400> 20

ggaggtgggg gtgatggtgg gggaggtgac ggcggaggtg ggtct

45

<210> 21
<211> 36
<212> DNA
<213> artificial sequence

<220>

<223> linker

<400> 21
gcaccagcac cagcaccagc accagcacca gcacca 36

<210> 22
<211> 45
<212> DNA
<213> artificial sequence

<220>
<223> linker

<400> 22
ggtggaggcg ggtcaggcgg agggggttct ggcggtggcg gatcg 45

<210> 23
<211> 45
<212> DNA
<213> artificial sequence

<220>
<223> linker

<400> 23
ggtgggggtg ggtccggagg cggaggcgaa ggcggaggtg ggtcg 45

<210> 24
<211> 51
<212> DNA
<213> artificial sequence

<220>
<223> linker

<400> 24
gcagaagcag cagcaaaaga agcagcagca aaagaagcag cagcaaaagc a 51

<210> 25
<211> 45
<212> DNA
<213> artificial sequence

<220>
<223> linker

<400> 25
gggtctgcag acggcggatc atcagctggg ggaagtgcg cagga 45

<210> 26
<211> 6
<212> PRT
<213> artificial sequence

<220>
<223> linker

<400> 26

Gly Ser Ala Asp Gly Gly
1 5

<210> 27
<211> 997
<212> PRT
<213> artificial sequence

<220>
<223> Immunoconjugate sequence

<400> 27

Ile Trp Glu Leu Lys Lys Asp Val Tyr Val Val Glu Leu Asp Trp Tyr
1 5 10 15

Pro Asp Ala Pro Gly Glu Met Val Val Leu Thr Cys Asp Thr Pro Glu
20 25 30

Glu Asp Gly Ile Thr Trp Thr Leu Asp Gln Ser Ser Glu Val Leu Gly
35 40 45

Ser Gly Lys Thr Leu Thr Ile Gln Val Lys Glu Phe Gly Asp Ala Gly
50 55 60

Gln Tyr Thr Cys His Lys Gly Gly Glu Val Leu Ser His Ser Leu Leu
65 70 75 80

Leu Leu His Lys Lys Glu Asp Gly Ile Trp Ser Thr Asp Ile Leu Lys
85 90 95

Asp Gln Lys Glu Pro Lys Asn Lys Thr Phe Leu Arg Cys Glu Ala Lys
100 105 110

Asn Tyr Ser Gly Arg Phe Thr Cys Trp Trp Leu Thr Thr Ile Ser Thr
115 120 125

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

Gly Val Thr Cys Gly Ala Ala Thr Leu Ser Ala Glu Arg Val Arg Gly
145 150 155 160

Asp Asn Lys Glu Tyr Glu Tyr Ser Val Glu Cys Gln Glu Asp Ser Ala
165 170 175

Cys Pro Ala Ala Glu Glu Ser Leu Pro Ile Glu Val Met Val Asp Ala
180 185 190

Val His Lys Leu Lys Tyr Glu Asn Tyr Thr Ser Ser Phe Phe Ile Arg
195 200 205

Asp Ile Ile Lys Pro Asp Pro Pro Lys Asn Leu Gln Leu Lys Pro Leu
210 215 220

Lys Asn Ser Arg Gln Val Glu Val Ser Trp Glu Tyr Pro Asp Thr Trp
225 230 235 240

Ser Thr Pro His Ser Tyr Phe Ser Leu Thr Phe Cys Val Gln Val Gln
245 250 255

Gly Lys Ser Lys Arg Glu Lys Lys Asp Arg Val Phe Thr Asp Lys Thr
260 265 270

Ser Ala Thr Val Ile Cys Arg Lys Asn Ala Ser Ile Ser Val Arg Ala
275 280 285

Gln Asp Arg Tyr Tyr Ser Ser Ser Trp Ser Glu Trp Ala Ser Val Pro
290 295 300

Cys Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly
305 310 315 320

Ser Arg Asn Leu Pro Val Ala Thr Pro Asp Pro Gly Met Phe Pro Cys
325 330 335

Leu His His Ser Gln Asn Leu Leu Arg Ala Val Ser Asn Met Leu Gln
340 345 350

Lys Ala Arg Gln Thr Leu Glu Phe Tyr Pro Cys Thr Ser Glu Glu Ile
355 360 365

Asp His Glu Asp Ile Thr Lys Asp Lys Thr Ser Thr Val Glu Ala Cys
370 375 380

Leu Pro Leu Glu Leu Thr Lys Asn Glu Ser Cys Leu Asn Ser Arg Glu
385 390 395 400

Thr Ser Phe Ile Thr Asn Gly Ser Cys Leu Ala Ser Arg Lys Thr Ser
405 410 415

Phe Met Met Ala Leu Cys Leu Ser Ser Ile Tyr Glu Asp Leu Lys Met
420 425 430

Tyr Gln Val Glu Phe Lys Thr Met Asn Ala Lys Leu Leu Met Asp Pro
435 440 445

Lys Arg Gln Ile Phe Leu Asp Gln Asn Met Leu Ala Val Ile Asp Glu
450 455 460

Leu Met Gln Ala Leu Asn Phe Asn Ser Glu Thr Val Pro Gln Lys Ser
465 470 475 480

Ser Leu Glu Glu Pro Asp Phe Tyr Lys Thr Lys Ile Lys Leu Cys Ile
485 490 495

Leu Leu His Ala Phe Arg Ile Arg Ala Val Thr Ile Asp Arg Val Met
500 505 510

Ser Tyr Leu Asn Ala Ser Gly Ser Ala Asp Gly Gly Glu Val Gln Leu
515 520 525

Leu Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly Ser Leu Arg Leu
530 535 540

Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Ser Phe Ser Met Ser Trp
545 550 555 560

Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val Ser Ser Ile Ser
565 570 575

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

Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr Leu Gln Met Asn
595 600 605

Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys Ala Lys Pro Phe
610 615 620

Pro Tyr Phe Asp Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser
625 630 635 640

Gly Ser Ser Gly Gly Glu Ile Val Leu Thr Gln Ser Pro Gly Thr Leu
645 650 655

Ser Leu Ser Pro Gly Glu Arg Ala Thr Leu Ser Cys Arg Ala Ser Gln
660 665 670

Ser Val Ser Ser Ser Phe Leu Ala Trp Tyr Gln Gln Lys Pro Gly Gln
675 680 685

Ala Pro Arg Leu Leu Ile Tyr Tyr Ala Ser Ser Arg Ala Thr Gly Ile
690 695 700

Pro Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr
705 710 715 720

Ile Ser Arg Leu Glu Pro Glu Asp Phe Ala Val Tyr Tyr Cys Gln Gln
725 730 735

Thr Gly Arg Ile Pro Pro Thr Phe Gly Gln Gly Thr Lys Val Glu Ile
740 745 750

Lys Ser Ser Ser Ser Gly Ser Ser Ser Ser Gly Ser Ser Ser Ser Gly
755 760 765

Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
770 775 780

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Ser Phe
785 790 795 800

Ser Met Ser Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
805 810 815

Ser Ser Ile Ser Gly Ser Ser Gly Thr Thr Tyr Tyr Ala Asp Ser Val
820 825 830

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
835 840 845

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
850 855 860

Ala Lys Pro Phe Pro Tyr Phe Asp Tyr Trp Gly Gln Gly Thr Leu Val
865 870 875 880

Thr Val Ser Ser Gly Ser Ser Gly Gly Glu Ile Val Leu Thr Gln Ser
885 890 895

Pro Gly Thr Leu Ser Leu Ser Pro Gly Glu Arg Ala Thr Leu Ser Cys
900 905 910

Arg Ala Ser Gln Ser Val Ser Ser Ser Phe Leu Ala Trp Tyr Gln Gln
915 920 925

Lys Pro Gly Gln Ala Pro Arg Leu Leu Ile Tyr Tyr Ala Ser Ser Arg
930 935 940

Ala Thr Gly Ile Pro Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp
945 950 955 960

Phe Thr Leu Thr Ile Ser Arg Leu Glu Pro Glu Asp Phe Ala Val Tyr
965 970 975

Tyr Cys Gln Gln Thr Gly Arg Ile Pro Pro Thr Phe Gly Gln Gly Thr
980 985 990

Lys Val Glu Ile Lys
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Gly

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Gly Gly Gly Gly Ala
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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 Phe
20 25 30

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

Ser Ser Ile Ser Gly Ser Ser Gly Thr 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 Pro Phe Pro Tyr Phe Asp Tyr Trp Gly Gln Gly Thr Leu Val
100 105 110

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

Pro Gly Thr Leu Ser Leu Ser Pro Gly Glu Arg Ala Thr Leu Ser Cys
130 135 140

Arg Ala Ser Gln Ser Val Ser Ser Ser Phe Leu Ala Trp Tyr Gln Gln
145 150 155 160

Lys Pro Gly Gln Ala Pro Arg Leu Leu Ile Tyr Tyr Ala Ser Ser Arg
165 170 175

Ala Thr Gly Ile Pro Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp
180 185 190

Phe Thr Leu Thr Ile Ser Arg Leu Glu Pro Glu Asp Phe Ala Val Tyr
195 200 205

Tyr Cys Gln Gln Thr Gly Arg Ile Pro Pro Thr Phe Gly Gln Gly Thr
210 215 220

Lys Val Glu Ile Lys
225