

Page 1
SEQUENCE LISTING

<110> AP Biosciences, Inc.
<120> BIFUNCTIONAL PROTEINS COMBINING CHECKPOINT BLOCKADE FOR TARGETED THERAPY
<130> 9022-1900530
<140> PCT/US2019/019786
<141> 2019-02-27
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<160> 27
<170> PatentIn version 3.5
<210> 1
<211> 732
<212> PRT
<213> Homo sapiens
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Ser Lys Leu Lys Asp Pro Glu Leu Ser Leu Lys Gly Thr Gln His Ile
1 5 10 15

Met Gln Ala Gly Gln Thr Leu His Leu Gln Cys Arg Gly Glu Ala Ala
20 25 30

His Lys Trp Ser Leu Pro Glu Met Val Ser Lys Glu Ser Glu Arg Leu
35 40 45

Ser Ile Thr Lys Ser Ala Cys Gly Arg Asn Gly Lys Gln Phe Cys Ser
50 55 60

Thr Leu Thr Leu Asn Thr Ala Gln Ala Asn His Thr Gly Phe Tyr Ser
65 70 75 80

Cys Lys Tyr Leu Ala Val Pro Thr Ser Lys Lys Lys Glu Thr Glu Ser
85 90 95

Ala Ile Tyr Ile Phe Ile Ser Asp Thr Gly Arg Pro Phe Val Glu Met
100 105 110

Tyr Ser Glu Ile Pro Glu Ile Ile His Met Thr Glu Gly Arg Glu Leu
115 120 125

Val Ile Pro Cys Arg Val Thr Ser Pro Asn Ile Thr Val Thr Leu Lys
130 135 140

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

Asp Ser Arg Lys Gly Phe Ile Ile Ser Asn Ala Thr Tyr Lys Glu Ile
165 170 175

Gly Leu Leu Thr Cys Glu Ala Thr Val Asn Gly His Leu Tyr Lys Thr
180 185 190

Asn Tyr Leu Thr His Arg Gln Thr Asn Thr Ile Ile Asp Val Gln Ile
195 200 205

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

Asn Cys Thr Ala Thr Thr Pro Leu Asn Thr Arg Val Gln Met Thr Trp
225 230 235 240

Ser Tyr Pro Asp Glu Lys Asn Lys Arg Ala Ser Val Arg Arg Arg Ile
245 250 255

Asp Gln Ser Asn Ser His Ala Asn Ile Phe Tyr Ser Val Leu Thr Ile
260 265 270

Asp Lys Met Gln Asn Lys Asp Lys Gly Leu Tyr Thr Cys Arg Val Arg
275 280 285

Ser Gly Pro Ser Phe Lys Ser Val Asn Thr Ser Val His Ile Tyr Asp
290 295 300

Lys Ala Phe Ile Thr Val Lys His Arg Lys Gln Gln Val Leu Glu Thr
305 310 315 320

Val Ala Gly Lys Arg Ser Tyr Arg Leu Ser Met Lys Val Lys Ala Phe
 325 330 335

Pro Ser Pro Glu Val Val Trp Leu Lys Asp Gly Leu Pro Ala Thr Glu
 340 345 350

Lys Ser Ala Arg Tyr Leu Thr Arg Gly Tyr Ser Leu Ile Ile Lys Asp
 355 360 365

Val Thr Glu Glu Asp Ala Gly Asn Tyr Thr Ile Leu Leu Ser Ile Lys
 370 375 380

Gln Ser Asn Val Phe Lys Asn Leu Thr Ala Thr Leu Ile Val Asn Val
 385 390 395 400

Lys Pro Gln Ile Tyr Glu Lys Ala Val Ser Ser Phe Pro Asp Pro Ala
 405 410 415

Leu Tyr Pro Leu Gly Ser Arg Gln Ile Leu Thr Cys Thr Ala Tyr Gly
 420 425 430

Ile Pro Gln Pro Thr Ile Lys Trp Phe Trp His Pro Cys Asn His Asn
 435 440 445

His Ser Glu Ala Arg Cys Asp Phe Cys Ser Asn Asn Glu Glu Ser Phe
 450 455 460

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

Gln Arg Met Ala Ile Ile Glu Gly Lys Asn Lys Met Ala Ser Thr Leu
 485 490 495

Val Val Ala Asp Ser Arg Ile Ser Gly Ile Tyr Ile Cys Ile Ala Ser
 500 505 510

Asn Lys Val Gly Thr Val Gly Arg Asn Ile Ser Phe Tyr Ile Thr Asp
 515 520 525

Val Pro Asn Gly Phe His Val Asn Leu Glu Lys Met Pro Thr Glu Gly

530

535

540

Glu Asp Leu Lys Leu Ser Cys Thr Val Asn Lys Phe Leu Tyr Arg Asp
 545 550 555 560

Val Thr Trp Ile Leu Leu Arg Thr Val Asn Asn Arg Thr Met His Tyr
 565 570 575

Ser Ile Ser Lys Gln Lys Met Ala Ile Thr Lys Glu His Ser Ile Thr
 580 585 590

Leu Asn Leu Thr Ile Met Asn Val Ser Leu Gln Asp Ser Gly Thr Tyr
 595 600 605

Ala Cys Arg Ala Arg Asn Val Tyr Thr Gly Glu Glu Ile Leu Gln Lys
 610 615 620

Lys Glu Ile Thr Ile Arg Asp Gln Glu Ala Pro Tyr Leu Leu Arg Asn
 625 630 635 640

Leu Ser Asp His Thr Val Ala Ile Ser Ser Ser Thr Thr Leu Asp Cys
 645 650 655

His Ala Asn Gly Val Pro Glu Pro Gln Ile Thr Trp Phe Lys Asn Asn
 660 665 670

His Lys Ile Gln Gln Glu Pro Gly Ile Ile Leu Gly Pro Gly Ser Ser
 675 680 685

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

Cys Lys Ala Thr Asn Gln Lys Gly Ser Val Glu Ser Ser Ala Tyr Leu
 705 710 715 720

Thr Val Gln Gly Thr Ser Asp Lys Ser Asn Leu Glu
 725 730

<210> 2

<211> 745

<212> PRT

<213> Homo sapiens

<400> 2

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

Ile Gln Lys Asp Ile Leu Thr Ile Lys Ala Asn Thr Thr Leu Gln Ile
 20 25 30

Thr Cys Arg Gly Gln Arg Asp Leu Asp Trp Leu Trp Pro Asn Asn Gln
 35 40 45

Ser Gly Ser Glu Gln Arg Val Glu Val Thr Glu Cys Ser Asp Gly Leu
 50 55 60

Phe Cys Lys Thr Leu Thr Ile Pro Lys Val Ile Gly Asn Asp Thr Gly
 65 70 75 80

Ala Tyr Lys Cys Phe Tyr Arg Glu Thr Asp Leu Ala Ser Val Ile Tyr
 85 90 95

Val Tyr Val Gln Asp Tyr Arg Ser Pro Phe Ile Ala Ser Val Ser Asp
 100 105 110

Gln His Gly Val Val Tyr Ile Thr Glu Asn Lys Asn Lys Thr Val Val
 115 120 125

Ile Pro Cys Leu Gly Ser Ile Ser Asn Leu Asn Val Ser Leu Cys Ala
 130 135 140

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

Asp Ser Lys Lys Gly Phe Thr Ile Pro Ser Tyr Met Ile Ser Tyr Ala
 165 170 175

Gly Met Val Phe Cys Glu Ala Lys Ile Asn Asp Glu Ser Tyr Gln Ser
 180 185 190

Ile Met Tyr Ile Val Val Val Val Gly Tyr Arg Ile Tyr Asp Val Val
 195 200 205

Leu Ser Pro Ser His Gly Ile Glu Leu Ser Val Gly Glu Lys Leu Val
 210 215 220

Leu Asn Cys Thr Ala Arg Thr Glu Leu Asn Val Gly Ile Asp Phe Asn
 225 230 235 240

Trp Glu Tyr Pro Ser Ser Lys His Gln His Lys Lys Leu Val Asn Arg
 245 250 255

Asp Leu Lys Thr Gln Ser Gly Ser Glu Met Lys Lys Phe Leu Ser Thr
 260 265 270

Leu Thr Ile Asp Gly Val Thr Arg Ser Asp Gln Gly Leu Tyr Thr Cys
 275 280 285

Ala Ala Ser Ser Gly Leu Met Thr Lys Lys Asn Ser Thr Phe Val Arg
 290 295 300

Val His Glu Lys Pro Phe Val Ala Phe Gly Ser Gly Met Glu Ser Leu
 305 310 315 320

Val Glu Ala Thr Val Gly Glu Arg Val Arg Ile Pro Ala Lys Tyr Leu
 325 330 335

Gly Tyr Pro Pro Pro Glu Ile Lys Trp Tyr Lys Asn Gly Ile Pro Leu
 340 345 350

Glu Ser Asn His Thr Ile Lys Ala Gly His Val Leu Thr Ile Met Glu
 355 360 365

Val Ser Glu Arg Asp Thr Gly Asn Tyr Thr Val Ile Leu Thr Asn Pro
 370 375 380

Ile Ser Lys Glu Lys Gln Ser His Val Val Ser Leu Val Val Tyr Val
 385 390 395 400

Pro Pro Gln Ile Gly Glu Lys Ser Leu Ile Ser Pro Val Asp Ser Tyr

405

410

415

Gln Tyr Gly Thr Thr Gln Thr Leu Thr Cys Thr Val Tyr Ala Ile Pro
 420 425 430

Pro Pro His His Ile His Trp Tyr Trp Gln Leu Glu Glu Glu Cys Ala
 435 440 445

Asn Glu Pro Ser Gln Ala Val Ser Val Thr Asn Pro Tyr Pro Cys Glu
 450 455 460

Glu Trp Arg Ser Val Glu Asp Phe Gln Gly Gly Asn Lys Ile Glu Val
 465 470 475 480

Asn Lys Asn Gln Phe Ala Leu Ile Glu Gly Lys Asn Lys Thr Val Ser
 485 490 495

Thr Leu Val Ile Gln Ala Ala Asn Val Ser Ala Leu Tyr Lys Cys Glu
 500 505 510

Ala Val Asn Lys Val Gly Arg Gly Glu Arg Val Ile Ser Phe His Val
 515 520 525

Thr Arg Gly Pro Glu Ile Thr Leu Gln Pro Asp Met Gln Pro Thr Glu
 530 535 540

Gln Glu Ser Val Ser Leu Trp Cys Thr Ala Asp Arg Ser Thr Phe Glu
 545 550 555 560

Asn Leu Thr Trp Tyr Lys Leu Gly Pro Gln Pro Leu Pro Ile His Val
 565 570 575

Gly Glu Leu Pro Thr Pro Val Cys Lys Asn Leu Asp Thr Leu Trp Lys
 580 585 590

Leu Asn Ala Thr Met Phe Ser Asn Ser Thr Asn Asp Ile Leu Ile Met
 595 600 605

Glu Leu Lys Asn Ala Ser Leu Gln Asp Gln Gly Asp Tyr Val Cys Leu
 610 615 620

Ala Gln Asp Arg Lys Thr Lys Lys Arg His Cys Val Val Arg Gln Leu
625 630 635 640

Thr Val Leu Glu Arg Val Ala Pro Thr Ile Thr Gly Asn Leu Glu Asn
645 650 655

Gln Thr Thr Ser Ile Gly Glu Ser Ile Glu Val Ser Cys Thr Ala Ser
660 665 670

Gly Asn Pro Pro Pro Gln Ile Met Trp Phe Lys Asp Asn Glu Thr Leu
675 680 685

Val Glu Asp Ser Gly Ile Val Leu Lys Asp Gly Asn Arg Asn Leu Thr
690 695 700

Ile Arg Arg Val Arg Lys Glu Asp Glu Gly Leu Tyr Thr Cys Gln Ala
705 710 715 720

Cys Ser Val Leu Gly Cys Ala Lys Val Glu Ala Phe Phe Ile Ile Glu
725 730 735

Gly Ala Gln Glu Lys Thr Asn Leu Glu
740 745

<210> 3
<211> 217
<212> PRT
<213> Homo sapiens

<400> 3

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

Arg Val Thr Ile Ser Cys Ser Gly Ser Ser Ser Asn Ile Gly Ser Asn
20 25 30

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

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

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

Ser Glu Asp Glu Ala Asp Tyr Tyr Cys Ala Thr Trp Asp Asp Ser Leu
 85 90 95

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

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

Glu Leu Gln Ala Asn Lys Ala Thr Leu Val Cys Leu Ile Ser Asp Phe
 130 135 140

Tyr Pro Gly Ala Val Thr Val Ala Trp Lys Ala Asp Ser Ser Pro Val
 145 150 155 160

Lys Ala Gly Val Glu Thr Thr Thr Pro Ser Lys Gln Ser Asn Asn Lys
 165 170 175

Tyr Ala Ala Ser Ser Tyr Leu Ser Leu Thr Pro Glu Gln Trp Lys Ser
 180 185 190

His Arg Ser Tyr Ser Cys Gln Val Thr His Glu Gly Ser Thr Val Glu
 195 200 205

Lys Thr Val Ala Pro Thr Glu Cys Ser
 210 215

<210> 4
 <211> 118
 <212> PRT
 <213> Homo sapiens

<400> 4

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 Gly Thr Phe Arg Arg Tyr
20 25 30

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

Gly Gly Ile Ile Pro Val Phe Gly Ala Ala Lys Tyr Ala Gln Lys Phe
50 55 60

Gln Gly Arg Val Thr Ile Thr Ala Asp Glu Phe Thr Ser Thr Ala Tyr
65 70 75 80

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

Ala Leu Ser Gly Asp Ser Asp Ala Phe Asp Ile Trp Gly Gln Gly Thr
100 105 110

Met Val Thr Val Ser Ser
115

<210> 5
<211> 216
<212> PRT
<213> Homo sapiens

<400> 5

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

Ser Ile Thr Ile Ser Cys Thr Gly Thr Ser Asn Asp Val Gly Ser Tyr
20 25 30

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

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

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

Gln Ala Glu Asp Glu Ala Asp Tyr Tyr Cys Ser Ser Tyr Thr Ser Ser
85 90 95

Ser Thr Leu Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu Gly Gln
100 105 110

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

Leu Gln Ala Asn Lys Ala Thr Leu Val Cys Leu Ile Ser Asp Phe Tyr
130 135 140

Pro Gly Ala Val Thr Val Ala Trp Lys Ala Asp Ser Ser Pro Val Lys
145 150 155 160

Ala Gly Val Glu Thr Thr Thr Pro Ser Lys Gln Ser Asn Asn Lys Tyr
165 170 175

Ala Ala Ser Ser Tyr Leu Ser Leu Thr Pro Glu Gln Trp Lys Ser His
180 185 190

Arg Ser Tyr Ser Cys Gln Val Thr His Glu Gly Ser Thr Val Glu Lys
195 200 205

Thr Val Ala Pro Thr Glu Cys Ser
210 215

<210> 6
<211> 121
<212> PRT
<213> Homo sapiens

<400> 6

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

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

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

Gly Arg Ile Ile Pro Ile Leu Gly Ile Ala Asn Tyr Ala Gln Lys Phe
50 55 60

Gln Gly Arg Val Thr Ile Thr Ala Asp Lys 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 Arg Val Val Pro Gly Tyr Ser Tyr Gly Pro Phe Asp Tyr Trp Gly
100 105 110

Gln Gly Thr Thr Val Thr Val Ser Ser
115 120

<210> 7
<211> 328
<212> PRT
<213> Homo sapiens

<400> 7

Ala Ser Thr Lys Gly Pro Ser Val Phe Pro Leu Ala Pro Cys Ser Arg
1 5 10 15

Ser Thr Ser Glu Ser Thr Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr
20 25 30

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

Gly Val His Thr Phe Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser
50 55 60

Leu Ser Ser Val Val Thr Val Pro Ser Ser Ser Leu Gly Thr Lys Thr
65 70 75 80

Tyr Thr Cys Asn Val Asp His Lys Pro Ser Asn Thr Lys Val Asp Lys
85 90 95

Arg Val Glu Ser Lys Tyr Gly Pro Pro Cys Pro Pro Cys Pro Ala Pro
100 105 110

Glu Phe Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys
115 120 125

Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val
130 135 140

Asp Val Ser Gln Glu Asp Pro Glu Val Gln Phe Asn Trp Tyr Val Asp
145 150 155 160

Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Phe
165 170 175

Asn Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp
180 185 190

Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Gly Leu
195 200 205

Pro Ser Ser Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg
210 215 220

Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Gln Glu Glu Met Thr Lys
225 230 235 240

Asn Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp
245 250 255

Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys
260 265 270

Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser
275 280 285

Arg Leu Thr Val Asp Lys Ser Arg Trp Gln Glu Gly Asn Val Phe Ser

290

295

300

Cys Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser
 305 310 315 320

Leu Ser Leu Ser Leu Gly Gly Gly
 325

<210> 8

<211> 329

<212> PRT

<213> Artificial Sequence

<220>

<223> constant domain in heavy chain of engineered IgG1 (eIgG1)

<400> 8

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

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

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

Gly Val His Thr Phe Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser
 50 55 60

Leu Ser Ser Val Val Thr Val Pro Ser Ser Ser Leu Gly Thr Gln Thr
 65 70 75 80

Tyr Ile Cys Asn Val Asn His Lys Pro Ser Asn Thr Lys Val Asp Lys
 85 90 95

Lys Val Glu Pro Lys Ser Cys Asp Lys Thr His Thr Cys Pro Pro Cys
 100 105 110

Pro Ala Pro Glu Leu Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro
 115 120 125

Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys
 130 135 140

Val Val Val Asp Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp
 145 150 155 160

Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu
 165 170 175

Glu Gln Tyr Ala Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu
 180 185 190

His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Ala Val Ser Asn
 195 200 205

Lys Ala Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly
 210 215 220

Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Glu Glu
 225 230 235 240

Met Thr Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr
 245 250 255

Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn
 260 265 270

Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe
 275 280 285

Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn
 290 295 300

Val Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn His Tyr Thr
 305 310 315 320

Gln Lys Ser Leu Ser Leu Ser Pro Gly
 325

<211> 205
 <212> PRT
 <213> Homo sapiens

<400> 9

Gly Asp Thr Gly Arg Pro Phe Val Glu Met Tyr Ser Glu Ile Pro Glu
 1 5 10 15

Ile Ile His Met Thr Glu Gly Arg Glu Leu Val Ile Pro Cys Arg Val
 20 25 30

Thr Ser Pro Asn Ile Thr Val Thr Leu Lys Lys Phe Pro Leu Asp Thr
 35 40 45

Leu Ile Pro Asp Gly Lys Arg Ile Ile Trp Asp Ser Arg Lys Gly Phe
 50 55 60

Ile Ile Ser Asn Ala Thr Tyr Lys Glu Ile Gly Leu Leu Thr Cys Glu
 65 70 75 80

Ala Thr Val Asn Gly His Leu Tyr Lys Thr Asn Tyr Leu Thr His Arg
 85 90 95

Gln Thr Asn Thr Ile Ile Asp Val Val Leu Ser Pro Ser His Gly Ile
 100 105 110

Glu Leu Ser Val Gly Glu Lys Leu Val Leu Asn Cys Thr Ala Arg Thr
 115 120 125

Glu Leu Asn Val Gly Ile Asp Phe Asn Trp Glu Tyr Pro Ser Ser Lys
 130 135 140

His Gln His Lys Lys Leu Val Asn Arg Asp Leu Lys Thr Gln Ser Gly
 145 150 155 160

Ser Glu Met Lys Lys Phe Leu Ser Thr Leu Thr Ile Asp Gly Val Thr
 165 170 175

Arg Ser Asp Gln Gly Leu Tyr Thr Cys Ala Ala Ser Ser Gly Leu Met
 180 185 190

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

<210> 10
 <211> 15
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> peptide linker

<400> 10

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

<210> 11
 <211> 20
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> signal peptide

<400> 11

Met Glu Thr Asp Thr Leu Leu Leu Trp Val Leu Leu Leu Trp Val Pro
 1 5 10 15

Gly Ser Thr Gly
 20

<210> 12
 <211> 666
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Anti-PD-L1-clone 6 Heavy Chain -VID/IgG4 bispecific antibody

<400> 12

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 Gly Thr Phe Arg Arg Tyr
 20 25 30

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

Gly Gly Ile Ile Pro Val Phe Gly Ala Ala Lys Tyr Ala Gln Lys Phe
50 55 60

Gln Gly Arg Val Thr Ile Thr Ala Asp Glu Phe Thr Ser Thr Ala Tyr
65 70 75 80

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

Ala Leu Ser Gly Asp Ser Asp Ala Phe Asp Ile Trp Gly Gln Gly Thr
100 105 110

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

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

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

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

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

Ser Leu Gly Thr Lys Thr Tyr Thr Cys Asn Val Asp His Lys Pro Ser
195 200 205

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

Pro Pro Cys Pro Ala Pro Glu Phe Leu 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 Gln Glu Asp Pro Glu Val Gln
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 Phe 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 Gly Leu Pro Ser Ser 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

Gln Glu Glu Met 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 Arg Leu Thr Val Asp Lys Ser Arg Trp Gln
405 410 415

Glu 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 Leu Gly Gly Gly Gly Gly
435 440 445

Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Asp Thr
 450 455 460

Gly Arg Pro Phe Val Glu Met Tyr Ser Glu Ile Pro Glu Ile Ile His
 465 470 475 480

Met Thr Glu Gly Arg Glu Leu Val Ile Pro Cys Arg Val Thr Ser Pro
 485 490 495

Asn Ile Thr Val Thr Leu Lys Lys Phe Pro Leu Asp Thr Leu Ile Pro
 500 505 510

Asp Gly Lys Arg Ile Ile Trp Asp Ser Arg Lys Gly Phe Ile Ile Ser
 515 520 525

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

Asn Gly His Leu Tyr Lys Thr Asn Tyr Leu Thr His Arg Gln Thr Asn
 545 550 555 560

Thr Ile Ile Asp Val Val Leu Ser Pro Ser His Gly Ile Glu Leu Ser
 565 570 575

Val Gly Glu Lys Leu Val Leu Asn Cys Thr Ala Arg Thr Glu Leu Asn
 580 585 590

Val Gly Ile Asp Phe Asn Trp Glu Tyr Pro Ser Ser Lys His Gln His
 595 600 605

Lys Lys Leu Val Asn Arg Asp Leu Lys Thr Gln Ser Gly Ser Glu Met
 610 615 620

Lys Lys Phe Leu Ser Thr Leu Thr Ile Asp Gly Val Thr Arg Ser Asp
 625 630 635 640

Gln Gly Leu Tyr Thr Cys Ala Ala Ser Ser Gly Leu Met Thr Lys Lys
 645 650 655

Asn Ser Thr Phe Val Arg Val His Glu Lys

660

665

<210> 13
 <211> 669
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Anti-PD-L1-clone 6 Heavy Chain -VID/eIgG1 bispecific antibody

<400> 13

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 Gly Thr Phe Arg Arg Tyr
 20 25 30

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

Gly Gly Ile Ile Pro Val Phe Gly Ala Ala Lys Tyr Ala Gln Lys Phe
 50 55 60

Gln Gly Arg Val Thr Ile Thr Ala Asp Glu Phe Thr Ser Thr Ala Tyr
 65 70 75 80

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

Ala Leu Ser Gly Asp Ser Asp Ala Phe Asp Ile Trp Gly Gln Gly Thr
 100 105 110

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

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

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

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

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

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

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

His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly Gly Pro Ser
 225 230 235 240

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

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

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

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

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

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

Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu
 340 345 350

Pro Pro Ser Arg Glu Glu Met Thr Lys Asn Gln Val Ser Leu Thr Cys
 355 360 365

Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser

370

375

380

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

Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser
 405 410 415

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

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

Gly Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser
 450 455 460

Gly Asp Thr Gly Arg Pro Phe Val Glu Met Tyr Ser Glu Ile Pro Glu
 465 470 475 480

Ile Ile His Met Thr Glu Gly Arg Glu Leu Val Ile Pro Cys Arg Val
 485 490 495

Thr Ser Pro Asn Ile Thr Val Thr Leu Lys Lys Phe Pro Leu Asp Thr
 500 505 510

Leu Ile Pro Asp Gly Lys Arg Ile Ile Trp Asp Ser Arg Lys Gly Phe
 515 520 525

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

Ala Thr Val Asn Gly His Leu Tyr Lys Thr Asn Tyr Leu Thr His Arg
 545 550 555 560

Gln Thr Asn Thr Ile Ile Asp Val Val Leu Ser Pro Ser His Gly Ile
 565 570 575

Glu Leu Ser Val Gly Glu Lys Leu Val Leu Asn Cys Thr Ala Arg Thr
 580 585 590

Glu Leu Asn Val Gly Ile Asp Phe Asn Trp Glu Tyr Pro Ser Ser Lys
595 600 605

His Gln His Lys Lys Leu Val Asn Arg Asp Leu Lys Thr Gln Ser Gly
610 615 620

Ser Glu Met Lys Lys Phe Leu Ser Thr Leu Thr Ile Asp Gly Val Thr
625 630 635 640

Arg Ser Asp Gln Gly Leu Tyr Thr Cys Ala Ala Ser Ser Gly Leu Met
645 650 655

Thr Lys Lys Asn Ser Thr Phe Val Arg Val His Glu Lys
660 665

<210> 14
<211> 49
<212> PRT
<213> Homo sapiens

<400> 14

Pro Glu Leu Ser Leu Lys Gly Thr Gln His Ile Met Gln Ala Gly Gln
1 5 10 15

Thr Leu His Leu Gln Cys Arg Gly Glu Ala Ala His Lys Trp Ser Leu
20 25 30

Pro Glu Met Val Ser Lys Glu Ser Glu Arg Leu Ser Ile Thr Lys Ser
35 40 45

Ala

<210> 15
<211> 64
<212> PRT
<213> Homo sapiens

<400> 15

Gly Arg Glu Leu Val Ile Pro Cys Arg Val Thr Ser Pro Asn Ile Thr

1

5

10

15

Val Thr Leu Lys Lys Phe Pro Leu Asp Thr Leu Ile Pro Asp Gly Lys
 20 25 30

Arg Ile Ile Trp Asp Ser Arg Lys Gly Phe Ile Ile Ser Asn Ala Thr
 35 40 45

Tyr Lys Glu Ile Gly Leu Leu Thr Cys Glu Ala Thr Val Asn Gly His
 50 55 60

<210> 16

<211> 98

<212> PRT

<213> Homo sapiens

<400> 16

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

His Thr Leu Val Leu Asn Cys Thr Ala Thr Thr Pro Leu Asn Thr Arg
 20 25 30

Val Gln Met Thr Trp Ser Tyr Pro Asp Glu Lys Asn Lys Arg Ala Ser
 35 40 45

Val Arg Arg Arg Ile Asp Gln Ser Asn Ser His Ala Asn Ile Phe Tyr
 50 55 60

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

Thr Cys Arg Val Arg Ser Gly Pro Ser Phe Lys Ser Val Asn Thr Ser
 85 90 95

Val His

<210> 17

<211> 87

<212> PRT

<213> Homo sapiens

<400> 17

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

Arg Ser Tyr Arg Leu Ser Met Lys Val Lys Ala Phe Pro Ser Pro Glu
 20 25 30

Val Val Trp Leu Lys Asp Gly Leu Pro Ala Thr Glu Lys Ser Ala Arg
 35 40 45

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

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

Phe Lys Asn Leu Thr Ala Thr
 85

<210> 18

<211> 126

<212> PRT

<213> Homo sapiens

<400> 18

Pro Gln Ile Tyr Glu Lys Ala Val Ser Ser Phe Pro Asp Pro Ala Leu
 1 5 10 15

Tyr Pro Leu Gly Ser Arg Gln Ile Leu Thr Cys Thr Ala Tyr Gly Ile
 20 25 30

Pro Gln Pro Thr Ile Lys Trp Phe Trp His Pro Cys Asn His Asn His
 35 40 45

Ser Glu Ala Arg Cys Asp Phe Cys Ser Asn Asn Glu Glu Ser Phe Ile
 50 55 60

Leu Asp Ala Asp Ser Asn Met Gly Asn Arg Ile Glu Ser Ile Thr Gln
 65 70 75 80

Arg Met Ala Ile Ile Glu Gly Lys Asn Lys Met Ala Ser Thr Leu Val
85 90 95

Val Ala Asp Ser Arg Ile Ser Gly Ile Tyr Ile Cys Ile Ala Ser Asn
100 105 110

Lys Val Gly Thr Val Gly Arg Asn Ile Ser Phe Tyr Ile Thr
115 120 125

<210> 19
<211> 94
<212> PRT
<213> Homo sapiens

<400> 19

Pro Asn Gly Phe His Val Asn Leu Glu Lys Met Pro Thr Glu Gly Glu
1 5 10 15

Asp Leu Lys Leu Ser Cys Thr Val Asn Lys Phe Leu Tyr Arg Asp Val
20 25 30

Thr Trp Ile Leu Leu Arg Thr Val Asn Asn Arg Thr Met His Tyr Ser
35 40 45

Ile Ser Lys Gln Lys Met Ala Ile Thr Lys Glu His Ser Ile Thr Leu
50 55 60

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

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

<210> 20
<211> 87
<212> PRT
<213> Homo sapiens

<400> 20

Pro Tyr Leu Leu Arg Asn Leu Ser Asp His Thr Val Ala Ile Ser Ser

1

5

10

15

Ser Thr Thr Leu Asp Cys His Ala Asn Gly Val Pro Glu Pro Gln Ile
 20 25 30

Thr Trp Phe Lys Asn Asn His Lys Ile Gln Gln Glu Pro Gly Ile Ile
 35 40 45

Leu Gly Pro Gly Ser Ser Thr Leu Phe Ile Glu Arg Val Thr Glu Glu
 50 55 60

Asp Glu Gly Val Tyr His Cys Lys Ala Thr Asn Gln Lys Gly Ser Val
 65 70 75 80

Glu Ser Ser Ala Tyr Leu Thr
 85

<210> 21
 <211> 65
 <212> PRT
 <213> Homo sapiens

<400> 21

Asn Thr Thr Leu Gln Ile Thr Cys Arg Gly Gln Arg Asp Leu Asp Trp
 1 5 10 15

Leu Trp Pro Asn Asn Gln Ser Gly Ser Glu Gln Arg Val Glu Val Thr
 20 25 30

Glu Cys Ser Asp Gly Leu Phe Cys Lys Thr Leu Thr Ile Pro Lys Val
 35 40 45

Ile Gly Asn Asp Thr Gly Ala Tyr Lys Cys Phe Tyr Arg Glu Thr Asp
 50 55 60

Leu
 65

<210> 22
 <211> 67
 <212> PRT

<213> Homo sapiens

<400> 22

Asn Lys Asn Lys Thr Val Val Ile Pro Cys Leu Gly Ser Ile Ser Asn
 1 5 10 15

Leu Asn Val Ser Leu Cys Ala Arg Tyr Pro Glu Lys Arg Phe Val Pro
 20 25 30

Asp Gly Asn Arg Ile Ser Trp Asp Ser Lys Lys Gly Phe Thr Ile Pro
 35 40 45

Ser Tyr Met Ile Ser Tyr Ala Gly Met Val Phe Cys Glu Ala Lys Ile
 50 55 60

Asn Asp Glu
 65

<210> 23

<211> 97

<212> PRT

<213> Homo sapiens

<400> 23

Tyr Asp Val Val Leu Ser Pro Ser His Gly Ile Glu Leu Ser Val Gly
 1 5 10 15

Glu Lys Leu Val Leu Asn Cys Thr Ala Arg Thr Glu Leu Asn Val Gly
 20 25 30

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

Leu Val Asn Arg Asp Leu Lys Thr Gln Ser Gly Ser Glu Met Lys Lys
 50 55 60

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

Leu Tyr Thr Cys Ala Ala Ser Ser Gly Leu Met Thr Lys Lys Asn Ser
 85 90 95

Thr

<210> 24
 <211> 86
 <212> PRT
 <213> Homo sapiens

<400> 24

Phe Val Ala Phe Gly Ser Gly Met Glu Ser Leu Val Glu Ala Thr Val
 1 5 10 15

Gly Glu Arg Val Arg Ile Pro Ala Lys Tyr Leu Gly Tyr Pro Pro Pro
 20 25 30

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

Ile Lys Ala Gly His Val Leu Thr Ile Met Glu Val Ser Glu Arg Asp
 50 55 60

Thr Gly Asn Tyr Thr Val Ile Leu Thr Asn Pro Ile Ser Lys Glu Lys
 65 70 75 80

Gln Ser His Val Val Ser
 85

<210> 25
 <211> 128
 <212> PRT
 <213> Homo sapiens

<400> 25

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

Tyr Gly Thr Thr Gln Thr Leu Thr Cys Thr Val Tyr Ala Ile Pro Pro
 20 25 30

Pro His His Ile His Trp Tyr Trp Gln Leu Glu Glu Glu Cys Ala Asn

35

40

45

Glu Pro Ser Gln Ala Val Ser Val Thr Asn Pro Tyr Pro Cys Glu Glu
 50 55 60

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

Lys Asn Gln Phe Ala Leu Ile Glu Gly Lys Asn Lys Thr Val Ser Thr
 85 90 95

Leu Val Ile Gln Ala Ala Asn Val Ser Ala Leu Tyr Lys Cys Glu Ala
 100 105 110

Val Asn Lys Val Gly Arg Gly Glu Arg Val Ile Ser Phe His Val Thr
 115 120 125

<210> 26
 <211> 110
 <212> PRT
 <213> Homo sapiens

<400> 26

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

Val Ser Leu Trp Cys Thr Ala Asp Arg Ser Thr Phe Glu Asn Leu Thr
 20 25 30

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

Pro Thr Pro Val Cys Lys Asn Leu Asp Thr Leu Trp Lys Leu Asn Ala
 50 55 60

Thr Met Phe Ser Asn Ser Thr Asn Asp Ile Leu Ile Met Glu Leu Lys
 65 70 75 80

Asn Ala Ser Leu Gln Asp Gln Gly Asp Tyr Val Cys Leu Ala Gln Asp
 85 90 95

Arg Lys Thr Lys Lys Arg His Cys Val Val Arg Gln Leu Thr
 100 105 110

<210> 27
 <211> 87
 <212> PRT
 <213> Homo sapiens

<400> 27

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

Ser Ile Glu Val Ser Cys Thr Ala Ser Gly Asn Pro Pro Pro Gln Ile
 20 25 30

Met Trp Phe Lys Asp Asn Glu Thr Leu Val Glu Asp Ser Gly Ile Val
 35 40 45

Leu Lys Asp Gly Asn Arg Asn Leu Thr Ile Arg Arg Val Arg Lys Glu
 50 55 60

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

Lys Val Glu Ala Phe Phe Ile
 85