

SEQUENCE LISTING

<110> Inserm

<120> METHODS AND PHARMACEUTICAL COMPOSITIONS FOR ENHANCING CD8+ T
CELL-DEPENDENT IMMUNE RESPONSES IN SUBJECTS SUFFERING FROM CANCER

<130> BI01634102 HERMINE / MC

<160> 18

<170> PatentIn version 3.3

<210> 1

<211> 923

<212> PRT

<213> Homo sapiens

<400> 1

Met	Glu	Arg	Gly	Leu	Pro	Leu	Leu	Cys	Ala	Val	Leu	Ala	Leu	Val	Leu
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Ala	Pro	Ala	Gly	Ala	Phe	Arg	Asn	Asp	Lys	Cys	Gly	Asp	Thr	Ile	Lys
			20					25					30		

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

His	Pro	Ser	Glu	Lys	Cys	Glu	Trp	Leu	Ile	Gln	Ala	Pro	Asp	Pro	Tyr
	50					55					60				

Gln	Arg	Ile	Met	Ile	Asn	Phe	Asn	Pro	His	Phe	Asp	Leu	Glu	Asp	Arg
65					70					75					80

Asp	Cys	Lys	Tyr	Asp	Tyr	Val	Glu	Val	Phe	Asp	Gly	Glu	Asn	Glu	Asn
				85					90					95	

Gly	His	Phe	Arg	Gly	Lys	Phe	Cys	Gly	Lys	Ile	Ala	Pro	Pro	Pro	Val
			100					105					110		

Val	Ser	Ser	Gly	Pro	Phe	Leu	Phe	Ile	Lys	Phe	Val	Ser	Asp	Tyr	Glu
			115				120						125		

Thr His Gly Ala Gly Phe Ser Ile Arg Tyr Glu Ile Phe Lys Arg Gly
130 135 140

Pro Glu Cys Ser Gln Asn Tyr Thr Thr Pro Ser Gly Val Ile Lys Ser
145 150 155 160

Pro Gly Phe Pro Glu Lys Tyr Pro Asn Ser Leu Glu Cys Thr Tyr Ile
165 170 175

Val Phe Ala Pro Lys Met Ser Glu Ile Ile Leu Glu Phe Glu Ser Phe
180 185 190

Asp Leu Glu Pro Asp Ser Asn Pro Pro Gly Gly Met Phe Cys Arg Tyr
195 200 205

Asp Arg Leu Glu Ile Trp Asp Gly Phe Pro Asp Val Gly Pro His Ile
210 215 220

Gly Arg Tyr Cys Gly Gln Lys Thr Pro Gly Arg Ile Arg Ser Ser Ser
225 230 235 240

Gly Ile Leu Ser Met Val Phe Tyr Thr Asp Ser Ala Ile Ala Lys Glu
245 250 255

Gly Phe Ser Ala Asn Tyr Ser Val Leu Gln Ser Ser Val Ser Glu Asp
260 265 270

Phe Lys Cys Met Glu Ala Leu Gly Met Glu Ser Gly Glu Ile His Ser
275 280 285

Asp Gln Ile Thr Ala Ser Ser Gln Tyr Ser Thr Asn Trp Ser Ala Glu
290 295 300

Arg Ser Arg Leu Asn Tyr Pro Glu Asn Gly Trp Thr Pro Gly Glu Asp
305 310 315 320

Ser Tyr Arg Glu Trp Ile Gln Val Asp Leu Gly Leu Leu Arg Phe Val
325 330 335

Thr Ala Val Gly Thr Gln Gly Ala Ile Ser Lys Glu Thr Lys Lys Lys
340 345 350

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

Trp Ile Thr Ile Lys Glu Gly Asn Lys Pro Val Leu Phe Gln Gly Asn
370 375 380

Thr Asn Pro Thr Asp Val Val Val Ala Val Phe Pro Lys Pro Leu Ile
385 390 395 400

Thr Arg Phe Val Arg Ile Lys Pro Ala Thr Trp Glu Thr Gly Ile Ser
405 410 415

Met Arg Phe Glu Val Tyr Gly Cys Lys Ile Thr Asp Tyr Pro Cys Ser
420 425 430

Gly Met Leu Gly Met Val Ser Gly Leu Ile Ser Asp Ser Gln Ile Thr
435 440 445

Ser Ser Asn Gln Gly Asp Arg Asn Trp Met Pro Glu Asn Ile Arg Leu
450 455 460

Val Thr Ser Arg Ser Gly Trp Ala Leu Pro Pro Ala Pro His Ser Tyr
465 470 475 480

Ile Asn Glu Trp Leu Gln Ile Asp Leu Gly Glu Glu Lys Ile Val Arg
485 490 495

Gly Ile Ile Ile Gln Gly Gly Lys His Arg Glu Asn Lys Val Phe Met
500 505 510

Arg Lys Phe Lys Ile Gly Tyr Ser Asn Asn Gly Ser Asp Trp Lys Met
515 520 525

Ile Met Asp Asp Ser Lys Arg Lys Ala Lys Ser Phe Glu Gly Asn Asn
530 535 540

Asn Tyr Asp Thr Pro Glu Leu Arg Thr Phe Pro Ala Leu Ser Thr Arg
545 550 555 560

Phe Ile Arg Ile Tyr Pro Glu Arg Ala Thr His Gly Gly Leu Gly Leu
565 570 575

Arg Met Glu Leu Leu Gly Cys Glu Val Glu Ala Pro Thr Ala Gly Pro
580 585 590

Thr Thr Pro Asn Gly Asn Leu Val Asp Glu Cys Asp Asp Asp Gln Ala
595 600 605

Asn Cys His Ser Gly Thr Gly Asp Asp Phe Gln Leu Thr Gly Gly Thr
610 615 620

Thr Val Leu Ala Thr Glu Lys Pro Thr Val Ile Asp Ser Thr Ile Gln
625 630 635 640

Ser Glu Phe Pro Thr Tyr Gly Phe Asn Cys Glu Phe Gly Trp Gly Ser
645 650 655

His Lys Thr Phe Cys His Trp Glu His Asp Asn His Val Gln Leu Lys
660 665 670

Trp Ser Val Leu Thr Ser Lys Thr Gly Pro Ile Gln Asp His Thr Gly
675 680 685

Asp Gly Asn Phe Ile Tyr Ser Gln Ala Asp Glu Asn Gln Lys Gly Lys
690 695 700

Val Ala Arg Leu Val Ser Pro Val Val Tyr Ser Gln Asn Ser Ala His
705 710 715 720

Cys Met Thr Phe Trp Tyr His Met Ser Gly Ser His Val Gly Thr Leu
725 730 735

Arg Val Lys Leu Arg Tyr Gln Lys Pro Glu Glu Tyr Asp Gln Leu Val
740 745 750

Trp Met Ala Ile Gly His Gln Gly Asp His Trp Lys Glu Gly Arg Val
755 760 765

Leu Leu His Lys Ser Leu Lys Leu Tyr Gln Val Ile Phe Glu Gly Glu
770 775 780

Ile Gly Lys Gly Asn Leu Gly Gly Ile Ala Val Asp Asp Ile Ser Ile
785 790 795 800

Asn Asn His Ile Ser Gln Glu Asp Cys Ala Lys Pro Ala Asp Leu Asp
805 810 815

Lys Lys Asn Pro Glu Ile Lys Ile Asp Glu Thr Gly Ser Thr Pro Gly
820 825 830

Tyr Glu Gly Glu Gly Glu Gly Asp Lys Asn Ile Ser Arg Lys Pro Gly
835 840 845

Asn Val Leu Lys Thr Leu Asp Pro Ile Leu Ile Thr Ile Ile Ala Met
850 855 860

Ser Ala Leu Gly Val Leu Leu Gly Ala Val Cys Gly Val Val Leu Tyr
865 870 875 880

Cys Ala Cys Trp His Asn Gly Met Ser Glu Arg Asn Leu Ser Ala Leu
885 890 895

Glu Asn Tyr Asn Phe Glu Leu Val Asp Gly Val Lys Leu Lys Lys Asp
900 905 910

Lys Leu Asn Thr Gln Ser Thr Tyr Ser Glu Ala
915 920

<210> 2
<211> 771
<212> PRT
<213> Homo sapiens

<400> 2

Met Gly Trp Leu Thr Arg Ile Val Cys Leu Phe Trp Gly Val Leu Leu
1 5 10 15

Thr Ala Arg Ala Asn Tyr Gln Asn Gly Lys Asn Asn Val Pro Arg Leu
20 25 30

Lys Leu Ser Tyr Lys Glu Met Leu Glu Ser Asn Asn Val Ile Thr Phe
35 40 45

Asn Gly Leu Ala Asn Ser Ser Ser Tyr His Thr Phe Leu Leu Asp Glu
50 55 60

Glu Arg Ser Arg Leu Tyr Val Gly Ala Lys Asp His Ile Phe Ser Phe
65 70 75 80

Asp Leu Val Asn Ile Lys Asp Phe Gln Lys Ile Val Trp Pro Val Ser
85 90 95

Tyr Thr Arg Arg Asp Glu Cys Lys Trp Ala Gly Lys Asp Ile Leu Lys
100 105 110

Glu Cys Ala Asn Phe Ile Lys Val Leu Lys Ala Tyr Asn Gln Thr His
115 120 125

Leu Tyr Ala Cys Gly Thr Gly Ala Phe His Pro Ile Cys Thr Tyr Ile
130 135 140

Glu Ile Gly His His Pro Glu Asp Asn Ile Phe Lys Leu Glu Asn Ser
145 150 155 160

His Phe Glu Asn Gly Arg Gly Lys Ser Pro Tyr Asp Pro Lys Leu Leu

165

170

175

Thr Ala Ser Leu Leu Ile Asp Gly Glu Leu Tyr Ser Gly Thr Ala Ala
 180 185 190

Asp Phe Met Gly Arg Asp Phe Ala Ile Phe Arg Thr Leu Gly His His
 195 200 205

His Pro Ile Arg Thr Glu Gln His Asp Ser Arg Trp Leu Asn Asp Pro
 210 215 220

Lys Phe Ile Ser Ala His Leu Ile Ser Glu Ser Asp Asn Pro Glu Asp
 225 230 235 240

Asp Lys Val Tyr Phe Phe Phe Arg Glu Asn Ala Ile Asp Gly Glu His
 245 250 255

Ser Gly Lys Ala Thr His Ala Arg Ile Gly Gln Ile Cys Lys Asn Asp
 260 265 270

Phe Gly Gly His Arg Ser Leu Val Asn Lys Trp Thr Thr Phe Leu Lys
 275 280 285

Ala Arg Leu Ile Cys Ser Val Pro Gly Pro Asn Gly Ile Asp Thr His
 290 295 300

Phe Asp Glu Leu Gln Asp Val Phe Leu Met Asn Phe Lys Asp Pro Lys
 305 310 315 320

Asn Pro Val Val Tyr Gly Val Phe Thr Thr Ser Ser Asn Ile Phe Lys
 325 330 335

Gly Ser Ala Val Cys Met Tyr Ser Met Ser Asp Val Arg Arg Val Phe
 340 345 350

Leu Gly Pro Tyr Ala His Arg Asp Gly Pro Asn Tyr Gln Trp Val Pro
 355 360 365

Tyr Gln Gly Arg Val Pro Tyr Pro Arg Pro Gly Thr Cys Pro Ser Lys
370 375 380

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

Thr Phe Ala Arg Ser His Pro Ala Met Tyr Asn Pro Val Phe Pro Met
405 410 415

Asn Asn Arg Pro Ile Val Ile Lys Thr Asp Val Asn Tyr Gln Phe Thr
420 425 430

Gln Ile Val Val Asp Arg Val Asp Ala Glu Asp Gly Gln Tyr Asp Val
435 440 445

Met Phe Ile Gly Thr Asp Val Gly Thr Val Leu Lys Val Val Ser Ile
450 455 460

Pro Lys Glu Thr Trp Tyr Asp Leu Glu Glu Val Leu Leu Glu Glu Met
465 470 475 480

Thr Val Phe Arg Glu Pro Thr Ala Ile Ser Ala Met Glu Leu Ser Thr
485 490 495

Lys Gln Gln Gln Leu Tyr Ile Gly Ser Thr Ala Gly Val Ala Gln Leu
500 505 510

Pro Leu His Arg Cys Asp Ile Tyr Gly Lys Ala Cys Ala Glu Cys Cys
515 520 525

Leu Ala Arg Asp Pro Tyr Cys Ala Trp Asp Gly Ser Ala Cys Ser Arg
530 535 540

Tyr Phe Pro Thr Ala Lys Arg Arg Thr Arg Arg Gln Asp Ile Arg Asn
545 550 555 560

Gly Asp Pro Leu Thr His Cys Ser Asp Leu His His Asp Asn His His

565

570

575

Gly His Ser Pro Glu Glu Arg Ile Ile Tyr Gly Val Glu Asn Ser Ser
 580 585 590

Thr Phe Leu Glu Cys Ser Pro Lys Ser Gln Arg Ala Leu Val Tyr Trp
 595 600 605

Gln Phe Gln Arg Arg Asn Glu Glu Arg Lys Glu Glu Ile Arg Val Asp
 610 615 620

Asp His Ile Ile Arg Thr Asp Gln Gly Leu Leu Leu Arg Ser Leu Gln
 625 630 635 640

Gln Lys Asp Ser Gly Asn Tyr Leu Cys His Ala Val Glu His Gly Phe
 645 650 655

Ile Gln Thr Leu Leu Lys Val Thr Leu Glu Val Ile Asp Thr Glu His
 660 665 670

Leu Glu Glu Leu Leu His Lys Asp Asp Asp Gly Asp Gly Ser Lys Thr
 675 680 685

Lys Glu Met Ser Asn Ser Met Thr Pro Ser Gln Lys Val Trp Tyr Arg
 690 695 700

Asp Phe Met Gln Leu Ile Asn His Pro Asn Leu Asn Thr Met Asp Glu
 705 710 715 720

Phe Cys Glu Gln Val Trp Lys Arg Asp Arg Lys Gln Arg Arg Gln Arg
 725 730 735

Pro Gly His Thr Pro Gly Asn Ser Asn Lys Trp Lys His Leu Gln Glu
 740 745 750

Asn Lys Lys Gly Arg Asn Arg Arg Thr His Glu Phe Glu Arg Ala Pro
 755 760 765

Arg Ser Val
770

<210> 3
<211> 11
<212> PRT
<213> Artificial

<220>
<223> VL-CDR1

<400> 3

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

<210> 4
<211> 7
<212> PRT
<213> Artificial

<220>
<223> VL-CDR2

<400> 4

Gly Ala Ser Ser Arg Ala Ser
1 5

<210> 5
<211> 9
<212> PRT
<213> Artificial

<220>
<223> VL-CDR3

<400> 5

Gln Gln Tyr Met Ser Val Pro Ile Thr
1 5

<210> 6
<211> 10
<212> PRT

<213> Artificial

<220>

<223> VH-CDR1

<400> 6

Gly	Phe	Ser	Phe	Ser	Ser	Glu	Pro	Ile	Ser
1				5					10

<210> 7

<211> 17

<212> PRT

<213> Artificial

<220>

<223> VH-CDR2

<400> 7

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

Lys

<210> 8

<211> 10

<212> PRT

<213> Artificial

<220>

<223> VH-CDR3

<400> 8

Trp	Gly	Lys	Lys	Val	Tyr	Gly	Met	Asp	Val
1				5					10

<210> 9

<211> 108

<212> PRT

<213> Artificial

<220>

<223> VL domain

<400> 9

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

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Ser Ile Ser Ser Tyr
20 25 30

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

Tyr Gly Ala Ser Ser Arg Ala Ser Gly Val Pro Ser Arg Phe Ser Gly
50 55 60

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

Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Tyr Met Ser Val Pro Ile
85 90 95

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

<210> 10

<211> 119

<212> PRT

<213> Artificial

<220>

<223> VH domain

<400> 10

Glu Val Gln Leu Val 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 Ser Phe Ser Ser Glu
20 25 30

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

35

40

45

Ser Ser Ile Thr Gly Lys Asn Gly Tyr Thr Tyr Tyr Ala Asp Ser Val
 50 55 60

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

Thr Leu Val Thr Val Ser Ser
 115

<210> 11
 <211> 120
 <212> PRT
 <213> Artificial

<220>
 <223> VH domain pembrolizumab

<400> 11

Gln Val Gln Leu Val Gln Ser Gly Val 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 Asn Tyr
 20 25 30

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

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

Lys Asn Arg Val Thr Leu Thr Thr Asp Ser Ser Thr Thr Thr Ala Tyr

65		70		75		80									
Met	Glu	Leu	Lys	Ser	Leu	Gln	Phe	Asp	Asp	Thr	Ala	Val	Tyr	Tyr	Cys
				85					90					95	

Ala	Arg	Arg	Asp	Tyr	Arg	Phe	Asp	Met	Gly	Phe	Asp	Tyr	Trp	Gly	Gln
			100					105					110		

Gly	Thr	Thr	Val	Thr	Val	Ser	Ser
		115				120	

<210> 12
 <211> 111
 <212> PRT
 <213> Artificial

<220>
 <223> VL domain of pembrolizumab

<400> 12

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

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

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

Arg	Leu	Leu	Ile	Tyr	Leu	Ala	Ser	Tyr	Leu	Glu	Ser	Gly	Val	Pro	Ala
	50					55					60				

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

Ser	Leu	Glu	Pro	Glu	Asp	Phe	Ala	Val	Tyr	Tyr	Cys	Gln	His	Ser	Arg
				85					90					95	

Asp	Leu	Pro	Leu	Thr	Phe	Gly	Gly	Gly	Thr	Lys	Val	Glu	Ile	Lys
-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----

100

105

110

<210> 13
<211> 440
<212> PRT
<213> Artificial

<220>
<223> heavy chain of pembrolizumab

<400> 13

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

Ser Leu Arg Leu Asp Cys Lys Ala Ser Gly Ile Thr Phe Ser Asn Ser
20 25 30

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

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

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

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

Ala Thr Asn Asp Asp Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser
100 105 110

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

Arg Ser Thr Ser Glu Ser Thr Ala Ala Leu Gly Cys Leu Val Lys Asp
130 135 140

Tyr Phe Pro Glu Pro Val Thr Val Ser Trp Asn Ser Gly Ala Leu Thr

145					150					155					160	
Ser	Gly	Val	His	Thr	Phe	Pro	Ala	Val	Leu	Gln	Ser	Ser	Gly	Leu	Tyr	
				165					170					175		
Ser	Leu	Ser	Ser	Val	Val	Thr	Val	Pro	Ser	Ser	Ser	Leu	Gly	Thr	Lys	
				180					185					190		
Thr	Tyr	Thr	Cys	Asn	Val	Asp	His	Lys	Pro	Ser	Asn	Thr	Lys	Val	Asp	
				195					200					205		
Lys	Arg	Val	Glu	Ser	Lys	Tyr	Gly	Pro	Pro	Cys	Pro	Pro	Cys	Pro	Ala	
				210					215					220		
Pro	Glu	Phe	Leu	Gly	Gly	Pro	Ser	Val	Phe	Leu	Phe	Pro	Pro	Lys	Pro	
				225					230					235		
Lys	Asp	Thr	Leu	Met	Ile	Ser	Arg	Thr	Pro	Glu	Val	Thr	Cys	Val	Val	
				245					250					255		
Val	Asp	Val	Ser	Gln	Glu	Asp	Pro	Glu	Val	Gln	Phe	Asn	Trp	Tyr	Val	
				260					265					270		
Asp	Gly	Val	Glu	Val	His	Asn	Ala	Lys	Thr	Lys	Pro	Arg	Glu	Glu	Gln	
				275					280					285		
Phe	Asn	Ser	Thr	Tyr	Arg	Val	Val	Ser	Val	Leu	Thr	Val	Leu	His	Gln	
				290					295					300		
Asp	Trp	Leu	Asn	Gly	Lys	Glu	Tyr	Lys	Cys	Lys	Val	Ser	Asn	Lys	Gly	
				310					315					320		
Leu	Pro	Ser	Ser	Ile	Glu	Lys	Thr	Ile	Ser	Lys	Ala	Lys	Gly	Gln	Pro	
				325					330					335		
Arg	Glu	Pro	Gln	Val	Tyr	Thr	Leu	Pro	Pro	Ser	Gln	Glu	Glu	Met	Thr	
				340					345					350		

Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser
355 360 365

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

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

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

Ser Cys Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys
420 425 430

Ser Leu Ser Leu Ser Leu Gly Lys
435 440

<210> 14
<211> 218
<212> PRT
<213> Artificial

<220>
<223> light chain of pembrolizumab

<400> 14

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

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

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

Arg Leu Leu Ile Tyr Leu Ala Ser Tyr Leu Glu Ser Gly Val Pro Ala
50 55 60

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

Ser Leu Glu Pro Glu Asp Phe Ala Val Tyr Tyr Cys Gln His Ser Arg
85 90 95

Asp Leu Pro Leu Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys Arg
100 105 110

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

Leu Lys Ser Gly Thr Ala Ser Val Val Cys Leu Leu Asn Asn Phe Tyr
130 135 140

Pro Arg Glu Ala Lys Val Gln Trp Lys Val Asp Asn Ala Leu Gln Ser
145 150 155 160

Gly Asn Ser Gln Glu Ser Val Thr Glu Gln Asp Ser Lys Asp Ser Thr
165 170 175

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

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

Val Thr Lys Ser Phe Asn Arg Gly Glu Cys
210 215

<210> 15
<211> 113
<212> PRT
<213> Artificial

<220>
<223> VH domain of nivolumab

<400> 15

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

Ser Leu Arg Leu Asp Cys Lys Ala Ser Gly Ile Thr Phe Ser Asn Ser
20 25 30

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

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

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

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

Ala Thr Asn Asp Asp Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser
100 105 110

Ser

<210> 16
<211> 107
<212> PRT
<213> Artificial

<220>
<223> VL domain of nivolumab

<400> 16

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

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

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

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

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

Glu Asp Phe Ala Val Tyr Tyr Cys Gln Gln Ser Ser Asn Trp Pro Arg
85 90 95

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

<210> 17
<211> 447
<212> PRT
<213> Artificial

<220>
<223> heavy chain of nivolumab

<400> 17

Gln Val Gln Leu Val Gln Ser Gly Val 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 Asn Tyr
20 25 30

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

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

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

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

Ala Arg Arg Asp Tyr Arg Phe Asp Met Gly Phe Asp Tyr Trp Gly Gln
100 105 110

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

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

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

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

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

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

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

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

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

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

Val Gln Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala Lys

275

280

285

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

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

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

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

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

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

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

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

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

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

<210> 18

<211> 214

<212> PRT

<213> Artificial

<220>

<223> light chain of nivolumab

<400> 18

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

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

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

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

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

Glu Asp Phe Ala Val Tyr Tyr Cys Gln Gln Ser Ser Asn Trp Pro Arg
85 90 95

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

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

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

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

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

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

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

Phe Asn Arg Gly Glu Cys
210