<110> GENENTECH, INC., et al.

<120> Immunoglobulin Variants and Uses Thereof

<130> P4182R1 WO

<150> US 61/105,086
<151> 2008-10-14

<150> US 61/152,131
<151> 2009-02-12

<150> US 61/171,768
<151> 2009-04-22

<150> US 61/220,514
<151> 2009-06-25

<160> 17

<210> 1
<211> 123
<212> PRT
<213> Artificial sequence

<220>
<223> sequence is synthesized

<400> 1

Glu	Val	Gln	Leu	Val	Glu	Ser	Gly	Gly	Gly	Leu	Val	Gln	Pro	Gly	
1				5				10						15	
Gly	Ser	Leu	Arg	Leu	Ser	Cys	Ala	Ala	Ser	Gly	Tyr	Thr	Phe	Thr	
				20				25						30	
Asn	Tyr	Gly	Met	Asn	Trp	Val	Arg	Gln	Ala	Pro	Gly	Lys	Gly	Leu	
				35				40						45	
Glu	Trp	Val	Gly	Trp	Ile	Asn	Thr	Tyr	Thr	Gly	Glu	Pro	Thr	Tyr	
				50				55						60	
Ala	Ala	Asp	Phe	Lys	Arg	Arg	Phe	Thr	Phe	Ser	Leu	Asp	Thr	Ser	
				65				70						75	
Lys	Ser	Thr	Ala	Tyr	Leu	Gln	Met	Asn	Ser	Leu	Arg	Ala	Glu	Asp	
				80				85						90	
Thr	Ala	Val	Tyr	Tyr	Cys	Ala	Lys	Tyr	Pro	His	Tyr	Tyr	Gly	Ser	
				95				100						105	
Ser	His	Trp	Tyr	Phe	Asp	Val	Trp	Gly	Gln	Gly	Thr	Leu	Val	Thr	
				110				115						120	
Val	Ser	Ser													

<210> 2
<211> 108
<212> PRT
<213> Artificial sequence

<220>
<223> sequence is synthesized

<400> 2

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

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

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

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

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

Ser Ser Leu Gln Pro Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln
                80                  85                  90

Tyr Ser Thr Val Pro Trp Thr Phe Gly Gln Gly Thr Lys Val Glu
                95                 100                 105

Ile Lys Arg
```

<210> 3
<211> 118
<212> PRT
<213> Artificial Sequence

<220>
<223> sequence is synthesized

<400> 3

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

Gly Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Tyr Asp Phe Thr
                20                  25                  30

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

Glu Trp Val Gly Trp Ile Asn Thr Tyr Thr Gly Glu Pro Thr Tyr
                50                  55                  60

Ala Ala Asp Phe Lys Arg Arg Phe Thr Phe Ser Leu Asp Thr Ser
                65                  70                  75

Lys Ser Thr Ala Tyr Leu Gln Met Asn Ser Leu Arg Ala Glu Asp
                80                  85                  90

Thr Ala Val Tyr Tyr Cys Ala Lys Tyr Pro Tyr Tyr Tyr Gly Thr
                95                 100                 105

Ser His Trp Tyr Phe Asp Val Trp Gly Gln Gly Thr Leu
               110                 115
```

<210> 4
<211> 110
<212> PRT
<213> Artificial Sequence

<220>
<223> sequence is synthesized

<400> 4

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

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

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

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

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

Ser Ser Leu Gln Pro Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln
                80                  85                  90

Tyr Ser Thr Val Pro Trp Thr Phe Gly Gln Gly Thr Lys Val Glu
            95                  100                 105

Ile Lys Arg Thr Val
        110
```

<210> 5
<211> 118
<212> PRT
<213> Artificial sequence

<220>
<223> sequence is synthesized

<400> 5

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

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

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

Glu Trp Met Gly Glu Ile Tyr Pro Gly Ser Gly Ser Ser Tyr Tyr
    50                  55                  60

Asn Glu Lys Phe Lys Gly Arg Val Thr Met Thr Arg Asp Thr Ser
65                  70                  75

Thr Ser Thr Val Tyr Met Glu Leu Ser Ser Leu Arg Ser Glu Asp
            80                  85                  90

Thr Ala Val Tyr Tyr Cys Ala Arg Ser Gly Asp Gly Ser Arg Phe
        95                  100                 105

Val Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser
    110                 115
```

<210> 6
<211> 111
<212> PRT
<213> Artificial sequence

<220>
<223> sequence is synthesized

<400> 6

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

Gly Glu Arg Ala Thr Ile Asn Cys Lys Ala Ser Gln Ser Val Asp
```

20 25 30

Tyr Asp Gly Asp Ser Tyr Met Asn Trp Tyr Gln Gln Lys Pro Gly
35 40 45

Gln Pro Pro Lys Leu Leu Ile Tyr Val Ala Ser Asn Leu Glu Ser
50 55 60

Gly Val Pro Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe
65 70 75

Thr Leu Thr Ile Ser Ser Leu Gln Ala Glu Asp Val Ala Val Tyr
80 85 90

Tyr Cys Gln Gln Ser Leu Gln Asp Pro Pro Thr Phe Gly Gly Gly
95 100 105

Thr Lys Val Glu Ile Lys
110

<210> 7
<211> 449
<212> PRT
<213> Artificial sequence

<220>
<223> sequence is synthesized

<400> 7
Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly
1 5 10 15

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

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

Glu Trp Val Ala Arg Ile Tyr Pro Thr Asn Gly Tyr Thr Arg Tyr
50 55 60

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

Lys Asn Thr Ala Tyr Leu Gln Met Asn Ser Leu Arg Ala Glu Asp
80 85 90

Thr Ala Val Tyr Tyr Cys Ser Arg Trp Gly Gly Asp Gly Phe Tyr
95 100 105

Ala Met Asp Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser
110 115 120

Ala Ser Thr Lys Gly Pro Ser Val Phe Pro Leu Ala Pro Ser Ser
125 130 135

Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu Gly Cys Leu Val Lys
140 145 150

Asp Tyr Phe Pro Glu Pro Val Thr Val Ser Trp Asn Ser Gly Ala
155 160 165

Leu Thr Ser Gly Val His Thr Phe Pro Ala Val Leu Gln Ser Ser
170 175 180

Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser Ser Ser
185 190 195

Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys Pro Ser
200 205 210

Asn Thr Lys Val Asp Lys Lys Val Glu Pro Lys Ser Cys Asp Lys
215 220 225

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

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

Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser
260 265 270

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

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

Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp
305 310 315

Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala
320 325 330

Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln
335 340 345

Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Glu Glu
350 355 360

Met Thr Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe
365 370 375

Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro
380 385 390

Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly
395 400 405

Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp
410 415 420

Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His Glu Ala Leu
425 430 435

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

<210> 8
<211> 214
<212> PRT
<213> Artificial sequence

<220>
<223> sequence is synthesized

<400> 8
Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val
1 5 10 15

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

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

Leu Leu Ile Tyr Ser Ala Ser Phe Leu Tyr Ser Gly Val Pro Ser
50 55 60

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

Ser Ser Leu Gln Pro Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln
80 85 90

His Tyr Thr Thr Pro Pro Thr Phe Gly Gln Gly Thr Lys Val Glu
95 100 105

Ile Lys Arg Thr Val Ala Ala Pro Ser Val Phe Ile Phe Pro Pro
110 115 120

Ser Asp Glu Gln Leu Lys Ser Gly Thr Ala Ser Val Val Cys Leu
125 130 135

Leu Asn Asn Phe Tyr Pro Arg Glu Ala Lys Val Gln Trp Lys Val
140 145 150

Asp Asn Ala Leu Gln Ser Gly Asn Ser Gln Glu Ser Val Thr Glu
155 160 165

Gln Asp Ser Lys Asp Ser Thr Tyr Ser Leu Ser Ser Thr Leu Thr
170 175 180

Leu Ser Lys Ala Asp Tyr Glu Lys His Lys Val Tyr Ala Cys Glu
185 190 195

Val Thr His Gln Gly Leu Ser Ser Pro Val Thr Lys Ser Phe Asn
200 205 210

Arg Gly Glu Cys

<210> 9
<211> 360
<212> DNA
<213> Artificial sequence

<220>
<223> sequence is synthesized

<400> 9
tcctgtgcag cctctggatt caccttcagt aacgcctgga tgagctgggt 50

ccgccaggct ccagggaagg ggctggagtg ggtctccgct attagtggta 100

gtggtaacac atactatgca gactccgtga agggccggtt caccatctcc 150

agagacaatt ccaagaacac gctgtatctg caaatgaaca gcctgagagc 200

cgaggacact gccgtgtatt actgtgcgag agcctcccac cgtatattag 250

gttatgcttt tgatatctgg ggccagggta cactggtcac cgtgagctca 300

gaggtgcagc tgttggagtc tgggggaggc ttggtacagc ctgggggtc 350

cctgagactc 360

<210> 10
<211> 327
<212> DNA
<213> Artificial sequence

<220>

<223> sequence is synthesized

<400> 10
tcttgttctg gaagccgctc caacatcggg agaaatgctg ttagttggta 50

tcagcagctc ccaggaacgg cccccaaact cctcatctat gctaacagca 100

atcggccctc aggggtccct gaccgattct ctggctccaa gtctggcacc 150

tcagcctccc tggccatcag tgggctccgg tccgaggatg aggctgatta 200

ttactgtgca gcatgggatg gcagcctgaa tggttgggtg ttcggcggag 250

gaaccaagct gacggtccca gtctgtgctg actcagccac cctcagcgtc 300

tgggaccccc gggcagaggg tcaccat 327

<210> 11
<211> 227
<212> PRT
<213> Artificial sequence

<220>
<223> sequence is synthesized

<400> 11

Asp	Lys	Thr	His	Thr	Cys	Pro	Pro	Cys	Pro	Ala	Pro	Glu	Leu	Leu
1				5					10					15
Gly	Gly	Pro	Ser	Val	Phe	Leu	Phe	Pro	Pro	Lys	Pro	Lys	Asp	Thr
				20					25					30
Leu	Met	Ile	Ser	Arg	Thr	Pro	Glu	Val	Thr	Cys	Val	Val	Val	Asp
				35					40					45
Val	Ser	His	Glu	Asp	Pro	Glu	Val	Lys	Phe	Asn	Trp	Tyr	Val	Asp
				50					55					60
Gly	Val	Glu	Val	His	Asn	Ala	Lys	Thr	Lys	Pro	Arg	Glu	Glu	Gln
				65					70					75
Tyr	Asn	Ser	Thr	Tyr	Arg	Val	Val	Ser	Val	Leu	Thr	Val	Leu	His
				80					85					90
Gln	Asp	Trp	Leu	Asn	Gly	Lys	Glu	Tyr	Lys	Cys	Lys	Val	Ser	Asn
				95					100					105
Lys	Ala	Leu	Pro	Ala	Pro	Ile	Glu	Lys	Thr	Ile	Ser	Lys	Ala	Lys
				110					115					120
Gly	Gln	Pro	Arg	Glu	Pro	Gln	Val	Tyr	Thr	Leu	Pro	Pro	Ser	Arg
				125					130					135
Asp	Glu	Leu	Thr	Lys	Asn	Gln	Val	Ser	Leu	Thr	Cys	Leu	Val	Lys
				140					145					150
Gly	Phe	Tyr	Pro	Ser	Asp	Ile	Ala	Val	Glu	Trp	Glu	Ser	Asn	Gly
				155					160					165
Gln	Pro	Glu	Asn	Asn	Tyr	Lys	Thr	Thr	Pro	Pro	Val	Leu	Asp	Ser
				170					175					180
Asp	Gly	Ser	Phe	Phe	Leu	Tyr	Ser	Lys	Leu	Thr	Val	Asp	Lys	Ser
				185					190					195
Arg	Trp	Gln	Gln	Gly	Asn	Val	Phe	Ser	Cys	Ser	Val	Met	His	Glu
				200					205					210

Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro
215 220 225

Gly Lys

<210> 12
<211> 227
<212> PRT
<213> Artificial sequence

<220>
<223> sequence is synthesized

<400> 12
Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu
1 5 10 15

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

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

Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp
50 55 60

Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln
65 70 75

Tyr Asn Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His
80 85 90

Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn
95 100 105

Lys Ala Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys
110 115 120

Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg
125 130 135

Glu Glu Met Thr Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys
140 145 150

Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly
155 160 165

Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser
170 175 180

Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser
185 190 195

Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His Glu
200 205 210

Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro
215 220 225

Gly Lys

<210> 13
<211> 226
<212> PRT
<213> Artificial sequence

<220>
<223> sequence is synthesized

<400> 13
Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu
1 5 10 15

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

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

Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp
50 55 60

Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln
65 70 75

Tyr Asn Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His
80 85 90

Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn
95 100 105

Lys Ala Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys
110 115 120

Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg
125 130 135

Asp Glu Leu Thr Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys
140 145 150

Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly
155 160 165

Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser
170 175 180

Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser
185 190 195

Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His Glu
200 205 210

Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro
215 220 225

Gly

<210> 14
<211> 226
<212> PRT
<213> Artificial sequence

<220>
<223> sequence is synthesized

<400> 14
Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu
1 5 10 15

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

Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp

35 40 45

Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp
50 55 60

Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln
65 70 75

Tyr Asn Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His
80 85 90

Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn
95 100 105

Lys Ala Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys
110 115 120

Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg
125 130 135

Glu Glu Met Thr Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys
140 145 150

Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly
155 160 165

Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser
170 175 180

Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser
185 190 195

Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His Glu
200 205 210

Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro
215 220 225

Gly

<210> 15
<211> 225
<212> PRT
<213> Artificial sequence

<220>
<223> sequence is synthesized

<400> 15
Cys Cys Val Glu Cys Pro Pro Cys Pro Ala Pro Pro Val Ala Gly
1 5 10 15

Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met
20 25 30

Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser
35 40 45

His Glu Asp Pro Glu Val Gln Phe Asn Trp Tyr Val Asp Gly Val
50 55 60

Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Phe Asn
65 70 75

Ser Thr Phe Arg Val Val Ser Val Leu Thr Val Val His Gln Asp
80 85 90

Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Gly
95 100 105

Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys Thr Lys Gly Gln
110 115 120

Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Glu Glu
125 130 135

Met Thr Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe
140 145 150

Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro
155 160 165

Glu Asn Asn Tyr Lys Thr Thr Pro Pro Met Leu Asp Ser Asp Gly
170 175 180

Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp
185 190 195

Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His Glu Ala Leu
200 205 210

His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly Lys
215 220 225

<210> 16
<211> 274
<212> PRT
<213> Artificial sequence

<220>
<223> sequence is synthesized

<400> 16
Leu Gly Asp Thr Thr His Thr Cys Pro Arg Cys Pro Glu Pro Lys
1 5 10 15

Ser Cys Asp Thr Pro Pro Pro Cys Pro Arg Cys Pro Glu Pro Lys
20 25 30

Ser Cys Asp Thr Pro Pro Pro Cys Pro Arg Cys Pro Glu Pro Lys
35 40 45

Ser Cys Asp Thr Pro Pro Pro Cys Pro Arg Cys Pro Ala Pro Glu
50 55 60

Leu Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys
65 70 75

Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val
80 85 90

Val Asp Val Ser His Glu Asp Pro Glu Val Gln Phe Lys Trp Tyr
95 100 105

Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu
110 115 120

Glu Gln Tyr Asn Ser Thr Phe Arg Val Val Ser Val Leu Thr Val
125 130 135

Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val
140 145 150

Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys
155 160 165

```
Thr Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro
                170                 175                 180

Ser Arg Glu Glu Met Thr Lys Asn Gln Val Ser Leu Thr Cys Leu
                185                 190                 195

Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser
                200                 205                 210

Ser Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Met Leu
                215                 220                 225

Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp
                230                 235                 240

Lys Ser Arg Trp Gln Gln Gly Asn Ile Phe Ser Cys Ser Val Met
                245                 250                 255

His Glu Ala Leu His Asn Arg Phe Thr Gln Lys Ser Leu Ser Leu
                260                 265                 270

Ser Pro Gly Lys
```

<210> 17
<211> 224
<212> PRT
<213> Artificial sequence

<220>
<223> sequence is synthesized

<400> 17

```
 Pro Pro Cys Pro Ser Cys Pro Ala Pro Glu Phe Leu Gly Gly Pro
   1               5                  10                  15

 Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile
                20                  25                  30

 Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser Gln
                35                  40                  45

 Glu Asp Pro Glu Val Gln Phe Asn Trp Tyr Val Asp Gly Val Glu
                50                  55                  60

 Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Phe Asn Ser
                65                  70                  75

 Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp
                80                  85                  90

 Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Gly Leu
                95                 100                 105

 Pro Ser Ser Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro
               110                 115                 120

 Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Gln Glu Glu Met
               125                 130                 135

 Thr Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr
               140                 145                 150

 Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu
               155                 160                 165

 Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser
```

```
                170                 175                 180

Phe Phe Leu Tyr Ser Arg Leu Thr Val Asp Lys Ser Arg Trp Gln
                185                 190                 195

Glu Gly Asn Val Phe Ser Cys Ser Val Met His Glu Ala Leu His
                200                 205                 210

Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Leu Gly Lys
                215                 220
```