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<120> Tau-binding antibodies

<130> PF0032-WO

<160> 57

<170> PatentIn version 3.5

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<400> 2

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<223> Xaa can be Ser, Ala, Thr

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<400>  6

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<400>  7

Asp Ile Val Met Thr Gln Thr Pro Val Ser Leu Ser Val Thr Leu Gly
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Asp Gln Ala Ser Ile Ser Cys Arg Ser Ser Gln Ser Leu Glu Tyr Ser
            20                  25                  30


Asp Gly Tyr Thr Tyr Leu Glu Trp Tyr Leu Gln Lys Pro Gly Gln Ser
        35                  40                  45


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


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


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


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


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<400>  8

Glu Val Lys Leu Glu Glu Ser Gly Pro Gly Leu Met Gln Pro Ser Glu
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Thr Leu Ser Leu Thr Cys Thr Val Ser Gly Phe Ser Leu Thr Ser Asn
            20                  25                  30


Asp Ile Ala Trp Val Arg Gln Pro Leu Gly Lys Gly Leu Val Trp Met
        35                  40                  45
```

```
Gly Thr Ile Trp Thr Asp Gly Ser Thr Asn Tyr Asn Ser Ala Val Gln
    50                  55                  60

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

Lys Met Asn Ser Leu Gln Pro Glu Asp Thr Gly Thr Tyr Tyr Cys Ala
                85                  90                  95

Arg His Arg Leu Tyr Tyr Gly Ala Phe Asp Tyr Trp Gly Gln Gly Thr
            100                 105                 110

Met Val Thr Val Ser
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<400>  9

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

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

Asp Gly Tyr Thr Tyr Leu Glu Trp Tyr Leu Gln Lys Pro Gly Gln Ser
        35                  40                  45

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

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

Ser Arg Val Glu Ala Glu Asp Val Gly Val Tyr Tyr Cys Phe Gln Ala
                85                  90                  95

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


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<223> Xaa can be Ile and Met

<220>
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<222> (61)..(61)
<223> Xaa can be Ser, Ala, Thr

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


Thr Leu Ser Leu Thr Cys Thr Val Ser Gly Phe Ser Leu Thr Ser Asn
            20                  25                  30


Asp Ile Ala Trp Ile Arg Gln Pro Pro Gly Lys Gly Leu Glu Trp Xaa
        35                  40                  45


Gly Thr Ile Trp Thr Asp Gly Ser Thr Asn Tyr Asn Xaa Ala Val Gln
    50                  55                  60


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


Lys Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr Cys Ala
                85                  90                  95


Arg His Arg Leu Tyr Tyr Gly Ala Phe Asp Tyr Trp Gly Gln Gly Thr
            100                 105                 110


Met Val Thr Val Ser Ser
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Thr Leu Ser Leu Thr Cys Thr Val Ser Gly Phe Ser Leu Thr Ser Asn
            20                  25                  30


Asp Ile Ala Trp Ile Arg Gln Pro Pro Gly Lys Gly Leu Glu Trp Met
        35                  40                  45


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

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

Lys Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr Cys Ala
85 90 95

Arg His Arg Leu Tyr Tyr Gly Ala Phe Asp Tyr Trp Gly Gln Gly Thr
100 105 110

Met Val Thr Val Ser Ser
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Glu Val Gln Leu Gln Glu Ser Gly Pro Gly Leu Val Lys Pro Ser Glu
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Thr Leu Ser Leu Thr Cys Thr Val Ser Gly Phe Ser Leu Thr Ser Asn
20 25 30

Asp Ile Ala Trp Ile Arg Gln Pro Pro Gly Lys Gly Leu Glu Trp Met
35 40 45

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

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

Lys Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr Cys Ala
85 90 95

Arg His Arg Leu Tyr Tyr Gly Ala Phe Asp Tyr Trp Gly Gln Gly Thr
100 105 110

Met Val Thr Val Ser Ser
115

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

Thr Leu Ser Leu Thr Cys Thr Val Ser Gly Phe Ser Leu Thr Ser Asn
20 25 30

Asp Ile Ala Trp Ile Arg Gln Pro Pro Gly Lys Gly Leu Glu Trp Met
35 40 45

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

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

Lys Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr Cys Ala
85 90 95

Arg His Arg Leu Tyr Tyr Gly Ala Phe Asp Tyr Trp Gly Gln Gly Thr
100 105 110

Met Val Thr Val Ser Ser
115

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

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

Asp Gly Tyr Thr Tyr Leu Glu Trp Tyr Leu Gln Lys Pro Gly Gln Ser
35 40 45

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

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

Ser Arg Val Glu Ala Glu Asp Val Gly Val Tyr Tyr Cys Phe Gln Ala
85 90 95

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

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

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

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

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

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

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

Pro Val Thr Lys Ser Phe Asn Arg Gly Glu Cys
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<223>  Xaa can be Ile or Met

<220>
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<223>  Xaa can be Ser Ala or Thr

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

Thr Leu Ser Leu Thr Cys Thr Val Ser Gly Phe Ser Leu Thr Ser Asn
            20                  25                  30

Asp Ile Ala Trp Ile Arg Gln Pro Pro Gly Lys Gly Leu Glu Trp Xaa
        35                  40                  45

Gly Thr Ile Trp Thr Asp Gly Ser Thr Asn Tyr Asn Xaa Ala Val Gln
    50                  55                  60
```

```
Ser Arg Val Thr Ile Ser Val Asp Thr Ser Lys Asn Gln Phe Ser Leu
65                  70                  75                  80

Lys Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr Cys Ala
                85                  90                  95

Arg His Arg Leu Tyr Tyr Gly Ala Phe Asp Tyr 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 Lys
        435                 440                 445


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<400>  16

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

Thr Leu Ser Leu Thr Cys Thr Val Ser Gly Phe Ser Leu Thr Ser Asn
            20                  25                  30

Asp Ile Ala Trp Ile Arg Gln Pro Pro Gly Lys Gly Leu Glu Trp Met
        35                  40                  45

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

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

Lys Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr Cys Ala
                85                  90                  95

Arg His Arg Leu Tyr Tyr Gly Ala Phe Asp Tyr 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 Lys
        435                 440                 445


<210>  17
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<212>  PRT
<213>  Artificial Sequence

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<223>  humanized

<400>  17

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

Thr Leu Ser Leu Thr Cys Thr Val Ser Gly Phe Ser Leu Thr Ser Asn
            20                  25                  30

Asp Ile Ala Trp Ile Arg Gln Pro Pro Gly Lys Gly Leu Glu Trp Met
        35                  40                  45

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

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

Lys Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr Cys Ala
                85                  90                  95

Arg His Arg Leu Tyr Tyr Gly Ala Phe Asp Tyr 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 Lys
        435                 440                 445
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<213> Artificial Sequence

<220>
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Glu Val Gln Leu Gln Glu Ser Gly Pro Gly Leu Val Lys Pro Ser Glu
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Thr Leu Ser Leu Thr Cys Thr Val Ser Gly Phe Ser Leu Thr Ser Asn
            20                  25                  30

Asp Ile Ala Trp Ile Arg Gln Pro Pro Gly Lys Gly Leu Glu Trp Met
        35                  40                  45

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

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

Lys Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr Cys Ala
                85                  90                  95

Arg His Arg Leu Tyr Tyr Gly Ala Phe Asp Tyr 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
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```
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 Lys
        435                 440                 445


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tacctacaga agccaggcca gtctcctcag ctcctcatct atgaagtttc caaccgattt      180
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agcagagtag agcctgagga cttgggagtt tattactgct tccaagctac acataatccg 300

tacacgtttg gagctgggac caagctggaa ataaaa 336

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<213> Rattus norvegicus

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ctaggaaagg gtttggtgtg gatgggaaca atatggactg atggaagtac aaattataat 180

tcagctgtcc aatcccgact gagcatcagc agggacacct ccaagagcca atttttctta 240

aaaatgaaca gtctgcaacc tgaagacaca ggcacttact actgtgccag acatcgccta 300

tactacgggg cctttgatta ctggggccaa ggaaccatgg tcaccgtctc gagt 354

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<213> Artificial Sequence

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atctcgtgta ggagctccca atccctcgaa tactcggacg gctatactta cctggagtgg 120

tacttgcaga agcccggaca gagcccgcag cttctgatct acgaagtgtc caacagattc 180

tccggcgtgc ctgaccgctt ttcggggtcg ggctccggta ctgatttcac cctgaaaatc 240

tcccgggtgg aagccgagga cgtgggagtc tactactgct tccaagccac ccacaaccct 300

tacaccttcg gacaggggac caagctggag atcaag 336

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<212> DNA
<213> Artificial Sequence

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<223> humanized

<400> 22
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acatgcactg tgtccgggtt ctccctgacc tctaacgaca tcgcctggat tcggcagccg 120

ccaggaaagg gactggagtg gatgggcacc atttggaccg acgggtcaac caactacaat 180

gccgcggtgc aatccagagt gaccatcagc gtggacacgt ccaagaacca gttctcgctg 240

aaattgagct ccgtgactgc cgctgatact gccgtgtatt actgtgcccg gcaccgcctt 300

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ccaggaaagg gactggagtg gatgggcacc atttggaccg acgggtcaac caactacaat 180

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aaattgagct ccgtgactgc cgctgatact gccgtgtatt actgtgcccg gcaccgcctt 300

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<212> DNA
<213> Artificial Sequence

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<400> 24
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tacttgcaga agcccggaca gagcccgcag cttctgatct acgaagtgtc caacagattc 180

tccggcgtgc ctgaccgctt ttcggggtcg ggctccggta ctgatttcac cctgaaaatc 240

tcccgggtgg aagccgagga cgtgggagtc tactactgct tccaagccac ccacaaccct 300

tacaccttcg gacaggggac caagctggag atcaagcgga ccgtggccgc tccctccgtg 360

ttcatcttcc caccctccga cgagcagctt aagtccggca ccgcctccgt cgtgtgcctg 420

ctgaacaact tctacccccg cgaggccaag gtgcagtgga aggtggacaa cgccctgcag 480

tccggcaact cccaggaatc cgtcaccgag caggactcca aggacagcac ctactccctg 540

tcctccaccc tgaccctgtc caaggccgac tacgagaagc acaaggtgta cgcctgcgaa 600

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<210> 25
<211> 1335
<212> DNA
<213> Artificial Sequence

<220>
<223> humanized

<400> 25
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ccaggaaagg gactggagtg gatgggcacc atttggaccg acgggtcaac caactacaat 180

gccgcggtgc aatccagagt gaccatcagc gtggacacgt ccaagaacca gttctcgctg 240

aaattgagct ccgtgactgc cgctgatact gccgtgtatt actgtgcccg gcaccgcctt 300

tactacggcg catttgacta ctggggacag ggaaccatgg tcactgtctc gagtgcctcc 360

accaagggcc cctccgtgtt ccctctggcc ccttgctccc ggtccacctc cgagtctacc 420

gccgctctgg gctgcctggt caaggactac ttccccgagc ccgtgacagt gtcctggaac 480

tctggcgccc tgacctccgg cgtgcacacc ttccctgccg tgctgcagtc ctccggcctg 540

tactccctgt cctccgtcgt gaccgtgccc tcctccagcc tgggcaccaa gacctacacc 600

tgtaacgtgg accacaagcc ctccaacacc aaggtggaca agcgggtgga atctaagtac 660

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<210> 26
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<212> DNA
<213> Artificial Sequence

<220>
<223> humanized

<400> 26
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<210> 27
<211> 134
<212> PRT
<213> Rattus norvegicus

<220>
<221> MISC_FEATURE
<222> (1)..(22)
<223> leader sequence

<400> 27

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Phe Pro Gly Thr Arg Cys Asp Ile Val Met Thr Gln Thr Pro Val Ser
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Leu Ser Val Thr Leu Gly Asp Gln Ala Ser Ile Ser Cys Arg Ser Ser
35 40 45

Gln Ser Leu Glu Tyr Ser Asp Gly Tyr Thr Tyr Leu Glu Trp Tyr Leu
50 55 60

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

Arg Phe Ser Gly Val Pro Asp Arg Phe Ile Gly Ser Gly Ser Gly Thr
85 90 95

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

Tyr Tyr Cys Phe Gln Ala Thr His Asn Pro Tyr Thr Phe Gly Ala Gly
115 120 125

Thr Lys Leu Glu Ile Lys
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<210> 28
<211> 136
<212> PRT
<213> Rattus norvegicus

<400> 28

Met Glu Trp Ser Trp Val Phe Leu Phe Phe Leu Ser Val Thr Thr Gly
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Val His Ser Glu Val Lys Leu Glu Glu Ser Gly Pro Gly Leu Met Gln
20 25 30

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

Thr Ser Asn Asp Ile Ala Trp Val Arg Gln Pro Leu Gly Lys Gly Leu
50 55 60

Val Trp Met Gly Thr Ile Trp Thr Asp Gly Ser Thr Asn Tyr Asn Ser
65 70 75 80

Ala Val Gln Ser Arg Leu Ser Ile Ser Arg Asp Thr Ser Lys Ser Gln
85 90 95

Phe Phe Leu Lys Met Asn Ser Leu Gln Pro Glu Asp Thr Gly Thr Tyr
100 105 110

Tyr Cys Ala Arg His Arg Leu Tyr Tyr Gly Ala Phe Asp Tyr Trp Gly
115 120 125

Gln Gly Thr Met Val Thr Val Ser
130 135

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<211> 402
<212> DNA
<213> Rattus norvegicus

<220>
<221> misc_feature
<222> (1)..(66)
<223> leader sequence

<400> 29

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gcttctatat cttgcaggtc tagtcagagc ctggaatata gtgatggcta cacttatttg 180

gaatggtacc tacagaagcc aggccagtct cctcagctcc tcatctatga agtttccaac 240

cgattttctg gggtcccaga caggttcatt ggcagtgggt cagggacaga tttcaccctc 300

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aatccgtaca cgtttggagc tgggaccaag ctggaaataa aa 402

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<212> DNA
<213> Rattus norvegicus

<220>
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<222> (1)..(57)
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ggaaagggtt tggtgtggat gggaacaata tggactgatg gaagtacaaa ttataattca 240

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<211> 112
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<213> Homo sapiens

<400> 31

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1 5 10 15

Gln Pro Ala Ser Ile Ser Cys Lys Ser Ser Gln Ser Leu Leu His Ser
20 25 30

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

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

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

Ser Arg Val Glu Ala Glu Asp Val Gly Val Tyr Tyr Cys Met Gln Gly
85 90 95

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

<210> 32
<211> 113
<212> PRT
<213> Homo sapiens

<400> 32

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

Thr Leu Ser Leu Thr Cys Thr Val Ser Gly Gly Ser Ile Ser Ser Tyr
20 25 30

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

Gly Tyr Ile Tyr Tyr Ser Gly Ser Thr Asn Tyr Asn Pro Ser Leu Lys
50 55 60

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

Lys Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr Cys Ala
85 90 95

Arg Asp Ala Phe Asp Val Trp Gly Gln Gly Thr Met Val Thr Val Ser
100 105 110

Ser

<210> 33
<211> 336
<212> DNA
<213> Homo sapiens

<400> 33
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tacacttttg gccaggggac caagctggag atcaaa 336

<210> 34

<211> 339
<212> DNA
<213> Homo sapiens

<400> 34
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<210> 35
<211> 441
<212> PRT
<213> Homo sapiens

<400> 35

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Thr Tyr Gly Leu Gly Asp Arg Lys Asp Gln Gly Gly Tyr Thr Met His
20 25 30

Gln Asp Gln Glu Gly Asp Thr Asp Ala Gly Leu Lys Glu Ser Pro Leu
35 40 45

Gln Thr Pro Thr Glu Asp Gly Ser Glu Glu Pro Gly Ser Glu Thr Ser
50 55 60

Asp Ala Lys Ser Thr Pro Thr Ala Glu Asp Val Thr Ala Pro Leu Val
65 70 75 80

Asp Glu Gly Ala Pro Gly Lys Gln Ala Ala Ala Gln Pro His Thr Glu
85 90 95

Ile Pro Glu Gly Thr Thr Ala Glu Glu Ala Gly Ile Gly Asp Thr Pro
100 105 110

Ser Leu Glu Asp Glu Ala Ala Gly His Val Thr Gln Ala Arg Met Val
115 120 125

Ser Lys Ser Lys Asp Gly Thr Gly Ser Asp Asp Lys Lys Ala Lys Gly
130 135 140

Ala Asp Gly Lys Thr Lys Ile Ala Thr Pro Arg Gly Ala Ala Pro Pro
145 150 155 160

Gly Gln Lys Gly Gln Ala Asn Ala Thr Arg Ile Pro Ala Lys Thr Pro
165 170 175

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Pro Ala Pro Lys Thr Pro Pro Ser Ser Gly Glu Pro Pro Lys Ser Gly
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Asp Arg Ser Gly Tyr Ser Ser Pro Gly Ser Pro Gly Thr Pro Gly Ser
        195                 200                 205

Arg Ser Arg Thr Pro Ser Leu Pro Thr Pro Pro Thr Arg Glu Pro Lys
    210                 215                 220

Lys Val Ala Val Val Arg Thr Pro Pro Lys Ser Pro Ser Ser Ala Lys
225                 230                 235                 240

Ser Arg Leu Gln Thr Ala Pro Val Pro Met Pro Asp Leu Lys Asn Val
                245                 250                 255

Lys Ser Lys Ile Gly Ser Thr Glu Asn Leu Lys His Gln Pro Gly Gly
            260                 265                 270

Gly Lys Val Gln Ile Ile Asn Lys Lys Leu Asp Leu Ser Asn Val Gln
        275                 280                 285

Ser Lys Cys Gly Ser Lys Asp Asn Ile Lys His Val Pro Gly Gly Gly
    290                 295                 300

Ser Val Gln Ile Val Tyr Lys Pro Val Asp Leu Ser Lys Val Thr Ser
305                 310                 315                 320

Lys Cys Gly Ser Leu Gly Asn Ile His His Lys Pro Gly Gly Gly Gln
                325                 330                 335

Val Glu Val Lys Ser Glu Lys Leu Asp Phe Lys Asp Arg Val Gln Ser
            340                 345                 350

Lys Ile Gly Ser Leu Asp Asn Ile Thr His Val Pro Gly Gly Gly Asn
        355                 360                 365

Lys Lys Ile Glu Thr His Lys Leu Thr Phe Arg Glu Asn Ala Lys Ala
    370                 375                 380

Lys Thr Asp His Gly Ala Glu Ile Val Tyr Lys Ser Pro Val Val Ser
385                 390                 395                 400

Gly Asp Thr Ser Pro Arg His Leu Ser Asn Val Ser Ser Thr Gly Ser
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Ile Asp Met Val Asp Ser Pro Gln Leu Ala Thr Leu Ala Asp Glu Val
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Ser Ala Ser Leu Ala Lys Gln Gly Leu
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<210> 36
<211> 16
<212> PRT
<213> Rattus norvegicus

<400> 36

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<210> 37
<211> 16
<212> PRT
<213> Rattus norvegicus

<400> 37

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

<210> 38
<211> 16
<212> PRT
<213> Rattus norvegicus

<400> 38

Thr Ile Trp Thr Asp Gly Ser Thr Asn Tyr Asn Thr Ala Val Gln Ser
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<210> 39
<211> 6757
<212> DNA
<213> Artificial Sequence

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<211> 461

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<400> 40

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Asp His Ala Gly Thr Tyr Gly Leu Gly Asp Arg Lys Asp Gln Gly Gly
        35                  40                  45

Tyr Thr Met His Gln Asp Gln Glu Gly Asp Thr Asp Ala Gly Leu Lys
    50                  55                  60

Glu Ser Pro Leu Gln Thr Pro Thr Glu Asp Gly Ser Glu Glu Pro Gly
65                  70                  75                  80

Ser Glu Thr Ser Asp Ala Lys Ser Thr Pro Thr Ala Glu Asp Val Thr
                85                  90                  95

Ala Pro Leu Val Asp Glu Gly Ala Pro Gly Lys Gln Ala Ala Ala Gln
            100                 105                 110

Pro His Thr Glu Ile Pro Glu Gly Thr Thr Ala Glu Glu Ala Gly Ile
        115                 120                 125

Gly Asp Thr Pro Ser Leu Glu Asp Glu Ala Ala Gly His Val Thr Gln
    130                 135                 140

Ala Arg Met Val Ser Lys Ser Lys Asp Gly Thr Gly Ser Asp Asp Lys
145                 150                 155                 160

Lys Ala Lys Gly Ala Asp Gly Lys Thr Lys Ile Ala Thr Pro Arg Gly
                165                 170                 175

Ala Ala Pro Pro Gly Gln Lys Gly Gln Ala Asn Ala Thr Arg Ile Pro
            180                 185                 190

Ala Lys Thr Pro Pro Ala Pro Lys Thr Pro Pro Ser Ser Gly Glu Pro
        195                 200                 205

Pro Lys Ser Gly Asp Arg Ser Gly Tyr Ser Ser Pro Gly Ser Pro Gly
    210                 215                 220

Thr Pro Gly Ser Arg Ser Arg Thr Pro Ser Leu Pro Thr Pro Pro Thr
225                 230                 235                 240
```

Arg Glu Pro Lys Lys Val Ala Val Val Arg Thr Pro Pro Lys Ser Pro
245 250 255

Ser Ser Ala Lys Ser Arg Leu Gln Thr Ala Pro Val Pro Met Pro Asp
260 265 270

Leu Lys Asn Val Lys Ser Lys Ile Gly Ser Thr Glu Asn Leu Lys His
275 280 285

Gln Pro Gly Gly Gly Lys Val Gln Ile Ile Asn Lys Lys Leu Asp Leu
290 295 300

Ser Asn Val Gln Ser Lys Cys Gly Ser Lys Asp Asn Ile Lys His Val
305 310 315 320

Pro Gly Gly Gly Ser Val Gln Ile Val Tyr Lys Pro Val Asp Leu Ser
325 330 335

Lys Val Thr Ser Lys Cys Gly Ser Leu Gly Asn Ile His His Lys Pro
340 345 350

Gly Gly Gly Gln Val Glu Val Lys Ser Glu Lys Leu Asp Phe Lys Asp
355 360 365

Arg Val Gln Ser Lys Ile Gly Ser Leu Asp Asn Ile Thr His Val Pro
370 375 380

Gly Gly Gly Asn Lys Lys Ile Glu Thr His Lys Leu Thr Phe Arg Glu
385 390 395 400

Asn Ala Lys Ala Lys Thr Asp His Gly Ala Glu Ile Val Tyr Lys Ser
405 410 415

Pro Val Val Ser Gly Asp Thr Ser Pro Arg His Leu Ser Asn Val Ser
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Ser Thr Gly Ser Ile Asp Met Val Asp Ser Pro Gln Leu Ala Thr Leu
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Ala Asp Glu Val Ser Ala Ser Leu Ala Lys Gln Gly Leu
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His Gln Asp Gln Glu Gly Asp Thr Asp Ala Gly Leu Lys Glu Ser Pro
        35                  40                  45

Leu Gln Thr Pro Thr Glu Asp Gly Ser Glu Glu Pro Gly Ser Glu Thr
    50                  55                  60

Ser Asp Ala Lys Ser Thr Pro Thr Ala Glu Asp Val Thr Ala Pro Leu
65                  70                  75                  80

Val Asp Glu Gly Ala Pro Gly Lys Gln Ala Ala Ala Gln Pro His Thr
                85                  90                  95

Glu Ile Pro Glu Gly Thr Thr Ala Glu Glu Ala Gly Ile Gly Asp Thr
            100                 105                 110

Pro Ser Leu Glu Asp Glu Ala Ala Gly His Val Thr Gln Ala Arg Met
        115                 120                 125

Val Ser Lys Ser Lys Asp Gly Thr Gly Ser Asp Asp Lys Lys Ala Lys
    130                 135                 140

Gly Ala Asp Gly Lys Thr Lys Ile Ala Thr Pro Arg Gly Ala Ala Pro
145                 150                 155                 160

Pro Gly Gln Lys Gly Gln Ala Asn Ala Thr Arg Ile Pro Ala Lys Thr
                165                 170                 175

Pro Pro Ala Pro Lys Thr Pro Pro Ser Ser Gly Glu Pro Pro Lys Ser
            180                 185                 190

Gly Asp Arg Ser Gly Tyr Ser Ser Pro Gly Ser Pro Gly Thr Pro Gly
        195                 200                 205

Ser Arg Ser Arg Thr Pro Ser Leu Pro Thr Pro Pro Thr Arg Glu Pro
    210                 215                 220

Lys Lys Val Ala Val Val Arg Thr Pro Pro Lys Ser Pro Ser Ser Ala
225                 230                 235                 240

Lys Ser Arg Leu Gln Thr Ala Pro Val Pro Met Pro Asp Leu Lys Asn
                245                 250                 255

Val Lys Ser Lys Ile Gly Ser Thr Glu Asn Leu Lys His Gln Pro Gly
            260                 265                 270

Gly Gly Lys Val Gln Ile Ile Asn Lys Lys Leu Asp Leu Ser Asn Val
        275                 280                 285
```

```
Gln Ser Lys Cys Gly Ser Lys Asp Asn Ile Lys His Val Pro Gly Gly
    290                 295                 300

Gly Ser Val Gln Ile Val Tyr Lys Pro Val Asp Leu Ser Lys Val Thr
305                 310                 315                 320

Ser Lys Cys Gly Ser Leu Gly Asn Ile His His Lys Pro Gly Gly Gly
                325                 330                 335

Gln Val Glu Val Lys Ser Glu Lys Leu Asp Phe Lys Asp Arg Val Gln
            340                 345                 350

Ser Lys Ile Gly Ser Leu Asp Asn Ile Thr His Val Pro Gly Gly Gly
        355                 360                 365

Asn Lys Lys Ile Glu Thr His Lys Leu Thr Phe Arg Glu Asn Ala Lys
    370                 375                 380

Ala Lys Thr Asp His Gly Ala Glu Ile Val Tyr Lys Ser Pro Val Val
385                 390                 395                 400

Ser Gly Asp Thr Ser Pro Arg His Leu Ser Asn Val Ser Ser Thr Gly
                405                 410                 415

Ser Ile Asp Met Val Asp Ser Pro Gln Leu Ala Thr Leu Ala Asp Glu
            420                 425                 430

Val Ser Ala Ser Leu Ala Lys Gln Gly Leu
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ctttctcgcc acgttcgccg gctttccccg tcaagctcta aatcgggggc tccctttagg      180

gttccgattt agtgctttac ggcacctcga ccccaaaaaa cttgattagg gtgatggttc      240

acgtagtggg ccatcgccct gatagacggt ttttcgccct ttgacgttgg agtccacgtt      300

ctttaatagt ggactcttgt tccaaactgg aacaacactc aaccctatct cggtctattc      360

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acaaaaattt aacgcgaatt ttaacaaaat attaacgttt acaatttcag gtggcacttt      480

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<210> 43
<211> 403
<212> PRT
<213> Artificial Sequence

<220>
<223> synthetic

<400> 43

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            20                  25                  30

Asp His Ala Gly Thr Tyr Gly Leu Gly Asp Arg Lys Asp Gln Gly Gly
        35                  40                  45

Tyr Thr Met His Gln Asp Gln Glu Gly Asp Thr Asp Ala Gly Leu Lys
    50                  55                  60

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

Ala Gly His Val Thr Gln Ala Arg Met Val Ser Lys Ser Lys Asp Gly
                85                  90                  95

Thr Gly Ser Asp Asp Lys Lys Ala Lys Gly Ala Asp Gly Lys Thr Lys
            100                 105                 110

Ile Ala Thr Pro Arg Gly Ala Ala Pro Pro Gly Gln Lys Gly Gln Ala
        115                 120                 125

Asn Ala Thr Arg Ile Pro Ala Lys Thr Pro Pro Ala Pro Lys Thr Pro
    130                 135                 140

Pro Ser Ser Gly Glu Pro Pro Lys Ser Gly Asp Arg Ser Gly Tyr Ser
145                 150                 155                 160

Ser Pro Gly Ser Pro Gly Thr Pro Gly Ser Arg Ser Arg Thr Pro Ser
                165                 170                 175

Leu Pro Thr Pro Pro Thr Arg Glu Pro Lys Lys Val Ala Val Val Arg
            180                 185                 190

Thr Pro Pro Lys Ser Pro Ser Ser Ala Lys Ser Arg Leu Gln Thr Ala
        195                 200                 205

Pro Val Pro Met Pro Asp Leu Lys Asn Val Lys Ser Lys Ile Gly Ser
    210                 215                 220

Thr Glu Asn Leu Lys His Gln Pro Gly Gly Gly Lys Val Gln Ile Ile
225                 230                 235                 240
```

```
Asn Lys Lys Leu Asp Leu Ser Asn Val Gln Ser Lys Cys Gly Ser Lys
                245                 250                 255

Asp Asn Ile Lys His Val Pro Gly Gly Gly Ser Val Gln Ile Val Tyr
            260                 265                 270

Lys Pro Val Asp Leu Ser Lys Val Thr Ser Lys Cys Gly Ser Leu Gly
        275                 280                 285

Asn Ile His His Lys Pro Gly Gly Gly Gln Val Glu Val Lys Ser Glu
    290                 295                 300

Lys Leu Asp Phe Lys Asp Arg Val Gln Ser Lys Ile Gly Ser Leu Asp
305                 310                 315                 320

Asn Ile Thr His Val Pro Gly Gly Gly Asn Lys Lys Ile Glu Thr His
                325                 330                 335

Lys Leu Thr Phe Arg Glu Asn Ala Lys Ala Lys Thr Asp His Gly Ala
            340                 345                 350

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

His Leu Ser Asn Val Ser Ser Thr Gly Ser Ile Asp Met Val Asp Ser
    370                 375                 380

Pro Gln Leu Ala Thr Leu Ala Asp Glu Val Ser Ala Ser Leu Ala Lys
385                 390                 395                 400

Gln Gly Leu
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<210> 44
<211> 384
<212> PRT
<213> Artificial Sequence

<220>
<223> synthetic

<400> 44

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Gly Thr Tyr Gly Leu Gly Asp Arg Lys Asp Gln Gly Gly Tyr Thr Met
            20                  25                  30

His Gln Asp Gln Glu Gly Asp Thr Asp Ala Gly Leu Lys Ala Glu Glu
        35                  40                  45
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Ala Gly Ile Gly Asp Thr Pro Ser Leu Glu Asp Glu Ala Ala Gly His
    50                  55                  60

Val Thr Gln Ala Arg Met Val Ser Lys Ser Lys Asp Gly Thr Gly Ser
65                  70                  75                  80

Asp Asp Lys Lys Ala Lys Gly Ala Asp Gly Lys Thr Lys Ile Ala Thr
                85                  90                  95

Pro Arg Gly Ala Ala Pro Pro Gly Gln Lys Gly Gln Ala Asn Ala Thr
            100                 105                 110

Arg Ile Pro Ala Lys Thr Pro Pro Ala Pro Lys Thr Pro Pro Ser Ser
        115                 120                 125

Gly Glu Pro Pro Lys Ser Gly Asp Arg Ser Gly Tyr Ser Ser Pro Gly
    130                 135                 140

Ser Pro Gly Thr Pro Gly Ser Arg Ser Arg Thr Pro Ser Leu Pro Thr
145                 150                 155                 160

Pro Pro Thr Arg Glu Pro Lys Lys Val Ala Val Val Arg Thr Pro Pro
                165                 170                 175

Lys Ser Pro Ser Ser Ala Lys Ser Arg Leu Gln Thr Ala Pro Val Pro
            180                 185                 190

Met Pro Asp Leu Lys Asn Val Lys Ser Lys Ile Gly Ser Thr Glu Asn
        195                 200                 205

Leu Lys His Gln Pro Gly Gly Gly Lys Val Gln Ile Ile Asn Lys Lys
    210                 215                 220

Leu Asp Leu Ser Asn Val Gln Ser Lys Cys Gly Ser Lys Asp Asn Ile
225                 230                 235                 240

Lys His Val Pro Gly Gly Gly Ser Val Gln Ile Val Tyr Lys Pro Val
                245                 250                 255

Asp Leu Ser Lys Val Thr Ser Lys Cys Gly Ser Leu Gly Asn Ile His
            260                 265                 270

His Lys Pro Gly Gly Gly Gln Val Glu Val Lys Ser Glu Lys Leu Asp
        275                 280                 285

Phe Lys Asp Arg Val Gln Ser Lys Ile Gly Ser Leu Asp Asn Ile Thr
    290                 295                 300

His Val Pro Gly Gly Gly Asn Lys Lys Ile Glu Thr His Lys Leu Thr
305                 310                 315                 320
```

Phe Arg Glu Asn Ala Lys Ala Lys Thr Asp His Gly Ala Glu Ile Val
325 330 335

Tyr Lys Ser Pro Val Val Ser Gly Asp Thr Ser Pro Arg His Leu Ser
340 345 350

Asn Val Ser Ser Thr Gly Ser Ile Asp Met Val Asp Ser Pro Gln Leu
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Ala Thr Leu Ala Asp Glu Val Ser Ala Ser Leu Ala Lys Gln Gly Leu
370 375 380

<210> 45
<211> 6490
<212> DNA
<213> Artificial Sequence

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<212> PRT
<213> Artificial Sequence

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<400> 46

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35 40 45

Tyr Thr Met His Gln Asp Gln Glu Gly Asp Thr Asp Ala Gly Leu Lys
50 55 60

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

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Ala Gly His Val Thr Gln Ala Arg Met Val Ser Lys Ser Lys Asp Gly
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Thr Gly Ser Asp Asp Lys Lys Ala Lys Gly Ala Asp Gly Lys Thr Lys
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Ile Ala Thr Pro Arg Gly Ala Ala Pro Pro Gly Gln Lys Gly Gln Ala
        115                 120                 125

Asn Ala Thr Arg Ile Pro Ala Lys Thr Pro Pro Ala Pro Lys Thr Pro
    130                 135                 140

Pro Ser Ser Gly Glu Pro Pro Lys Ser Gly Asp Arg Ser Gly Tyr Ser
145                 150                 155                 160

Ser Pro Gly Ser Pro Gly Thr Pro Gly Ser Arg Ser Arg Thr Pro Ser
                165                 170                 175

Leu Pro Thr Pro Pro Thr Arg Glu Pro Lys Lys Val Ala Val Val Arg
            180                 185                 190

Thr Pro Pro Lys Ser Pro Ser Ser Ala Lys Ser Arg Leu Gln Thr Ala
        195                 200                 205

Pro Val Pro Met Pro Asp Leu Lys Asn Val Lys Ser Lys Ile Gly Ser
    210                 215                 220

Thr Glu Asn Leu Lys His Gln Pro Gly Gly Gly Lys Val Gln Ile Val
225                 230                 235                 240

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

Gly Asn Ile His His Lys Pro Gly Gly Gly Gln Val Glu Val Lys Ser
            260                 265                 270

Glu Lys Leu Asp Phe Lys Asp Arg Val Gln Ser Lys Ile Gly Ser Leu
        275                 280                 285

Asp Asn Ile Thr His Val Pro Gly Gly Gly Asn Lys Lys Ile Glu Thr
    290                 295                 300

His Lys Leu Thr Phe Arg Glu Asn Ala Lys Ala Lys Thr Asp His Gly
305                 310                 315                 320

Ala Glu Ile Val Tyr Lys Ser Pro Val Val Ser Gly Asp Thr Ser Pro
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Arg His Leu Ser Asn Val Ser Ser Thr Gly Ser Ile Asp Met Val Asp
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Lys Gln Gly Leu
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<212>  PRT
<213>  Artificial Sequence

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<400>  47

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His Gln Asp Gln Glu Gly Asp Thr Asp Ala Gly Leu Lys Ala Glu Glu
        35                  40                  45


Ala Gly Ile Gly Asp Thr Pro Ser Leu Glu Asp Glu Ala Ala Gly His
    50                  55                  60


Val Thr Gln Ala Arg Met Val Ser Lys Ser Lys Asp Gly Thr Gly Ser
65                  70                  75                  80


Asp Asp Lys Lys Ala Lys Gly Ala Asp Gly Lys Thr Lys Ile Ala Thr
                85                  90                  95


Pro Arg Gly Ala Ala Pro Pro Gly Gln Lys Gly Gln Ala Asn Ala Thr
            100                 105                 110


Arg Ile Pro Ala Lys Thr Pro Pro Ala Pro Lys Thr Pro Pro Ser Ser
        115                 120                 125


Gly Glu Pro Pro Lys Ser Gly Asp Arg Ser Gly Tyr Ser Ser Pro Gly
    130                 135                 140


Ser Pro Gly Thr Pro Gly Ser Arg Ser Arg Thr Pro Ser Leu Pro Thr
145                 150                 155                 160


Pro Pro Thr Arg Glu Pro Lys Lys Val Ala Val Val Arg Thr Pro Pro
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Lys Ser Pro Ser Ser Ala Lys Ser Arg Leu Gln Thr Ala Pro Val Pro
            180                 185                 190
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Met Pro Asp Leu Lys Asn Val Lys Ser Lys Ile Gly Ser Thr Glu Asn
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Leu Lys His Gln Pro Gly Gly Gly Lys Val Gln Ile Val Tyr Lys Pro
    210                 215                 220

Val Asp Leu Ser Lys Val Thr Ser Lys Cys Gly Ser Leu Gly Asn Ile
225                 230                 235                 240

His His Lys Pro Gly Gly Gly Gln Val Glu Val Lys Ser Glu Lys Leu
                245                 250                 255

Asp Phe Lys Asp Arg Val Gln Ser Lys Ile Gly Ser Leu Asp Asn Ile
            260                 265                 270

Thr His Val Pro Gly Gly Gly Asn Lys Lys Ile Glu Thr His Lys Leu
        275                 280                 285

Thr Phe Arg Glu Asn Ala Lys Ala Lys Thr Asp His Gly Ala Glu Ile
    290                 295                 300

Val Tyr Lys Ser Pro Val Val Ser Gly Asp Thr Ser Pro Arg His Leu
305                 310                 315                 320

Ser Asn Val Ser Ser Thr Gly Ser Ile Asp Met Val Asp Ser Pro Gln
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Leu Ala Thr Leu Ala Asp Glu Val Ser Ala Ser Leu Ala Lys Gln Gly
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Leu
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<213> Artificial Sequence

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<400> 48

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gacggcgcgt gcagggccag actggaggtg gcaacgccaa tcagcaacga ctgtttgccc     4560
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<212> PRT
<213> Artificial Sequence

<220>
<223> synthetic

<400> 49

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Tyr Phe Gln Gly Ser Ala Glu Pro Arg Gln Glu Phe Glu Val Met Glu
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Asp His Ala Gly Thr Tyr Gly Leu Gly Asp Arg Lys Asp Gln Gly Gly
35 40 45

Tyr Thr Met His Gln Asp Gln Glu Gly Asp Thr Asp Ala Gly Leu Lys
50 55 60

Glu Ser Pro Leu Gln Thr Pro Thr Glu Asp Gly Ser Glu Glu Pro Gly
65 70 75 80

Ser Glu Thr Ser Asp Ala Lys Ser Thr Pro Thr Ala Glu Ala Glu Glu
85 90 95

Ala Gly Ile Gly Asp Thr Pro Ser Leu Glu Asp Glu Ala Ala Gly His
100 105 110

Val Thr Gln Ala Arg Met Val Ser Lys Ser Lys Asp Gly Thr Gly Ser
115 120 125

Asp Asp Lys Lys Ala Lys Gly Ala Asp Gly Lys Thr Lys Ile Ala Thr
130 135 140

Pro Arg Gly Ala Ala Pro Pro Gly Gln Lys Gly Gln Ala Asn Ala Thr
145 150 155 160

Arg Ile Pro Ala Lys Thr Pro Pro Ala Pro Lys Thr Pro Pro Ser Ser
165 170 175

Gly Glu Pro Pro Lys Ser Gly Asp Arg Ser Gly Tyr Ser Ser Pro Gly
180 185 190

Ser Pro Gly Thr Pro Gly Ser Arg Ser Arg Thr Pro Ser Leu Pro Thr
195 200 205

```
Pro Pro Thr Arg Glu Pro Lys Lys Val Ala Val Val Arg Thr Pro Pro
    210                 215                 220

Lys Ser Pro Ser Ser Ala Lys Ser Arg Leu Gln Thr Ala Pro Val Pro
225                 230                 235                 240

Met Pro Asp Leu Lys Asn Val Lys Ser Lys Ile Gly Ser Thr Glu Asn
                245                 250                 255

Leu Lys His Gln Pro Gly Gly Gly Lys Val Gln Ile Ile Asn Lys Lys
            260                 265                 270

Leu Asp Leu Ser Asn Val Gln Ser Lys Cys Gly Ser Lys Asp Asn Ile
        275                 280                 285

Lys His Val Pro Gly Gly Gly Ser Val Gln Ile Val Tyr Lys Pro Val
    290                 295                 300

Asp Leu Ser Lys Val Thr Ser Lys Cys Gly Ser Leu Gly Asn Ile His
305                 310                 315                 320

His Lys Pro Gly Gly Gly Gln Val Glu Val Lys Ser Glu Lys Leu Asp
                325                 330                 335

Phe Lys Asp Arg Val Gln Ser Lys Ile Gly Ser Leu Asp Asn Ile Thr
            340                 345                 350

His Val Pro Gly Gly Gly Asn Lys Lys Ile Glu Thr His Lys Leu Thr
        355                 360                 365

Phe Arg Glu Asn Ala Lys Ala Lys Thr Asp His Gly Ala Glu Ile Val
    370                 375                 380

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

Asn Val Ser Ser Thr Gly Ser Ile Asp Met Val Asp Ser Pro Gln Leu
                405                 410                 415

Ala Thr Leu Ala Asp Glu Val Ser Ala Ser Leu Ala Lys Gln Gly Leu
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<212>  PRT
<213>  Artificial Sequence

<220>
<223>  synthetic

<400>  50

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            20                  25                  30

His Gln Asp Gln Glu Gly Asp Thr Asp Ala Gly Leu Lys Glu Ser Pro
        35                  40                  45

Leu Gln Thr Pro Thr Glu Asp Gly Ser Glu Glu Pro Gly Ser Glu Thr
    50                  55                  60

Ser Asp Ala Lys Ser Thr Pro Thr Ala Glu Ala Glu Glu Ala Gly Ile
65                  70                  75                  80

Gly Asp Thr Pro Ser Leu Glu Asp Glu Ala Ala Gly His Val Thr Gln
                85                  90                  95

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

Lys Ala Lys Gly Ala Asp Gly Lys Thr Lys Ile Ala Thr Pro Arg Gly
        115                 120                 125

Ala Ala Pro Pro Gly Gln Lys Gly Gln Ala Asn Ala Thr Arg Ile Pro
    130                 135                 140

Ala Lys Thr Pro Pro Ala Pro Lys Thr Pro Pro Ser Ser Gly Glu Pro
145                 150                 155                 160

Pro Lys Ser Gly Asp Arg Ser Gly Tyr Ser Ser Pro Gly Ser Pro Gly
                165                 170                 175

Thr Pro Gly Ser Arg Ser Arg Thr Pro Ser Leu Pro Thr Pro Pro Thr
            180                 185                 190

Arg Glu Pro Lys Lys Val Ala Val Val Arg Thr Pro Pro Lys Ser Pro
        195                 200                 205

Ser Ser Ala Lys Ser Arg Leu Gln Thr Ala Pro Val Pro Met Pro Asp
    210                 215                 220

Leu Lys Asn Val Lys Ser Lys Ile Gly Ser Thr Glu Asn Leu Lys His
225                 230                 235                 240

Gln Pro Gly Gly Gly Lys Val Gln Ile Ile Asn Lys Lys Leu Asp Leu
                245                 250                 255

Ser Asn Val Gln Ser Lys Cys Gly Ser Lys Asp Asn Ile Lys His Val
            260                 265                 270

Pro Gly Gly Gly Ser Val Gln Ile Val Tyr Lys Pro Val Asp Leu Ser
        275                 280                 285
```

```
Lys Val Thr Ser Lys Cys Gly Ser Leu Gly Asn Ile His His Lys Pro
    290                 295                 300

Gly Gly Gly Gln Val Glu Val Lys Ser Glu Lys Leu Asp Phe Lys Asp
305                 310                 315                 320

Arg Val Gln Ser Lys Ile Gly Ser Leu Asp Asn Ile Thr His Val Pro
                325                 330                 335

Gly Gly Gly Asn Lys Lys Ile Glu Thr His Lys Leu Thr Phe Arg Glu
            340                 345                 350

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

Pro Val Val Ser Gly Asp Thr Ser Pro Arg His Leu Ser Asn Val Ser
    370                 375                 380

Ser Thr Gly Ser Ile Asp Met Val Asp Ser Pro Gln Leu Ala Thr Leu
385                 390                 395                 400

Ala Asp Glu Val Ser Ala Ser Leu Ala Lys Gln Gly Leu
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<210> 51
<211> 6016
<212> DNA
<213> Artificial Sequence

<220>
<223> synthetic

<400> 51

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ggccgccgat atttgaaaat atggcatatt gaaaatgtcg ccgatgtgag tttctgtgta      180

actgacatcg ccatttttcc aaaagtgatt tttgggcata cgcggtatct ggcgatagcg      240

cttatatcgt ttacggggga tggcgataga cgactttggt gacttgggcg attctgtgtg      300

tcgcaaatat cgcagtttcg atataggtga cagacgatat gaggctatat cgccgataga      360

ggcgacatca agctggcaca tggccaatgc atatcgatct atacattgaa tcaatattgg      420

ccattagcca tattattcat tggttatata gcataaatca atattggcta ttggccattg      480

catacgttgt atccatatca taatatgtac atttatattg gctcatgtcc aacattaccg      540

ccatgttgac attgattatt gactagttat taatagtaat caattacggg gtcattagtt      600

catagcccat atatggagtt ccgcgttaca taacttacgg taaatggccc gcctggctga      660

ccgcccaacg acccccgccc attgacgtca ataatgacgt atgttcccat agtaacgcca      720

atagggactt tccattgacg tcaatgggtg gagtatttac ggtaaactgc ccacttggca      780
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<210> 52
<211> 465
<212> PRT
<213> Artificial Sequence

<220>
<223> synthetic

<400> 52

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Gly Glu Asn Leu Tyr Phe Gln Gly Ser Ala Glu Pro Arg Gln Glu Phe
20 25 30

Glu Val Met Glu Asp His Ala Gly Thr Tyr Gly Leu Gly Asp Arg Lys
35 40 45

Asp Gln Gly Gly Tyr Thr Met His Gln Asp Gln Glu Gly Asp Thr Asp
50 55 60

```
Ala Gly Leu Lys Glu Ser Pro Leu Gln Thr Pro Thr Glu Asp Gly Ser
65                  70                  75                  80

Glu Glu Pro Gly Ser Glu Thr Ser Asp Ala Lys Ser Thr Pro Thr Ala
                85                  90                  95

Glu Asp Val Thr Ala Pro Leu Val Asp Glu Gly Ala Pro Gly Lys Gln
            100                 105                 110

Ala Ala Ala Gln Pro His Thr Glu Ile Pro Glu Gly Thr Thr Ala Glu
        115                 120                 125

Glu Ala Gly Ile Gly Asp Thr Pro Ser Leu Glu Asp Glu Ala Ala Gly
    130                 135                 140

His Val Thr Gln Ala Arg Met Val Ser Lys Ser Lys Asp Gly Thr Gly
145                 150                 155                 160

Ser Asp Asp Lys Lys Ala Lys Gly Ala Asp Gly Lys Thr Lys Ile Ala
                165                 170                 175

Thr Pro Arg Gly Ala Ala Pro Pro Gly Gln Lys Gly Gln Ala Asn Ala
            180                 185                 190

Thr Arg Ile Pro Ala Lys Thr Pro Pro Ala Pro Lys Thr Pro Pro Ser
        195                 200                 205

Ser Gly Glu Pro Pro Lys Ser Gly Asp Arg Ser Gly Tyr Ser Ser Pro
    210                 215                 220

Gly Ser Pro Gly Thr Pro Gly Ser Arg Ser Arg Thr Pro Ser Leu Pro
225                 230                 235                 240

Thr Pro Pro Thr Arg Glu Pro Lys Lys Val Ala Val Val Arg Thr Pro
                245                 250                 255

Pro Lys Ser Pro Ser Ser Ala Lys Ser Arg Leu Gln Thr Ala Pro Val
            260                 265                 270

Pro Met Pro Asp Leu Lys Asn Val Lys Ser Lys Ile Gly Ser Thr Glu
        275                 280                 285

Asn Leu Lys His Gln Pro Gly Gly Gly Lys Val Gln Ile Ile Asn Lys
    290                 295                 300

Lys Leu Asp Leu Ser Asn Val Gln Ser Lys Cys Gly Ser Lys Asp Asn
305                 310                 315                 320

Ile Lys His Val Pro Gly Gly Gly Ser Val Gln Ile Val Tyr Lys Pro
                325                 330                 335
```

Val Asp Leu Ser Lys Val Thr Ser Lys Cys Gly Ser Leu Gly Asn Ile
340 345 350

His His Lys Pro Gly Gly Gly Gln Val Glu Val Lys Ser Glu Lys Leu
355 360 365

Asp Phe Lys Asp Arg Val Gln Ser Lys Ile Gly Ser Leu Asp Asn Ile
370 375 380

Thr His Val Pro Gly Gly Gly Asn Lys Lys Ile Glu Thr His Lys Leu
385 390 395 400

Thr Phe Arg Glu Asn Ala Lys Ala Lys Thr Asp His Gly Ala Glu Ile
405 410 415

Val Tyr Lys Ser Pro Val Val Ser Gly Asp Thr Ser Pro Arg His Leu
420 425 430

Ser Asn Val Ser Ser Thr Gly Ser Ile Asp Met Val Asp Ser Pro Gln
435 440 445

Leu Ala Thr Leu Ala Asp Glu Val Ser Ala Ser Leu Ala Lys Gln Gly
450 455 460

Leu
465

<210> 53
<211> 442
<212> PRT
<213> Artificial Sequence

<220>
<223> synthetic

<400> 53

Gly Ser Ala Glu Pro Arg Gln Glu Phe Glu Val Met Glu Asp His Ala
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Gly Thr Tyr Gly Leu Gly Asp Arg Lys Asp Gln Gly Gly Tyr Thr Met
20 25 30

His Gln Asp Gln Glu Gly Asp Thr Asp Ala Gly Leu Lys Glu Ser Pro
35 40 45

Leu Gln Thr Pro Thr Glu Asp Gly Ser Glu Glu Pro Gly Ser Glu Thr
50 55 60

Ser Asp Ala Lys Ser Thr Pro Thr Ala Glu Asp Val Thr Ala Pro Leu
65 70 75 80

Val Asp Glu Gly Ala Pro Gly Lys Gln Ala Ala Ala Gln Pro His Thr
85 90 95

```
Glu Ile Pro Glu Gly Thr Thr Ala Glu Glu Ala Gly Ile Gly Asp Thr
            100                 105                 110

Pro Ser Leu Glu Asp Glu Ala Ala Gly His Val Thr Gln Ala Arg Met
        115                 120                 125

Val Ser Lys Ser Lys Asp Gly Thr Gly Ser Asp Asp Lys Lys Ala Lys
    130                 135                 140

Gly Ala Asp Gly Lys Thr Lys Ile Ala Thr Pro Arg Gly Ala Ala Pro
145                 150                 155                 160

Pro Gly Gln Lys Gly Gln Ala Asn Ala Thr Arg Ile Pro Ala Lys Thr
                165                 170                 175

Pro Pro Ala Pro Lys Thr Pro Pro Ser Ser Gly Glu Pro Pro Lys Ser
            180                 185                 190

Gly Asp Arg Ser Gly Tyr Ser Ser Pro Gly Ser Pro Gly Thr Pro Gly
        195                 200                 205

Ser Arg Ser Arg Thr Pro Ser Leu Pro Thr Pro Pro Thr Arg Glu Pro
    210                 215                 220

Lys Lys Val Ala Val Val Arg Thr Pro Pro Lys Ser Pro Ser Ser Ala
225                 230                 235                 240

Lys Ser Arg Leu Gln Thr Ala Pro Val Pro Met Pro Asp Leu Lys Asn
                245                 250                 255

Val Lys Ser Lys Ile Gly Ser Thr Glu Asn Leu Lys His Gln Pro Gly
            260                 265                 270

Gly Gly Lys Val Gln Ile Ile Asn Lys Lys Leu Asp Leu Ser Asn Val
        275                 280                 285

Gln Ser Lys Cys Gly Ser Lys Asp Asn Ile Lys His Val Pro Gly Gly
    290                 295                 300

Gly Ser Val Gln Ile Val Tyr Lys Pro Val Asp Leu Ser Lys Val Thr
305                 310                 315                 320

Ser Lys Cys Gly Ser Leu Gly Asn Ile His His Lys Pro Gly Gly Gly
                325                 330                 335

Gln Val Glu Val Lys Ser Glu Lys Leu Asp Phe Lys Asp Arg Val Gln
            340                 345                 350

Ser Lys Ile Gly Ser Leu Asp Asn Ile Thr His Val Pro Gly Gly Gly
        355                 360                 365
```

```
Asn Lys Lys Ile Glu Thr His Lys Leu Thr Phe Arg Glu Asn Ala Lys
    370                 375                 380

Ala Lys Thr Asp His Gly Ala Glu Ile Val Tyr Lys Ser Pro Val Val
385                 390                 395                 400

Ser Gly Asp Thr Ser Pro Arg His Leu Ser Asn Val Ser Ser Thr Gly
                405                 410                 415

Ser Ile Asp Met Val Asp Ser Pro Gln Leu Ala Thr Leu Ala Asp Glu
            420                 425                 430

Val Ser Ala Ser Leu Ala Lys Gln Gly Leu
        435                 440


<210>  54
<211>  448
<212>  PRT
<213>  Artificial Sequence

<220>
<223>  humanized

<400>  54

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

Thr Leu Ser Leu Thr Cys Thr Val Ser Gly Phe Ser Leu Thr Ser Asn
            20                  25                  30

Asp Ile Ala Trp Ile Arg Gln Pro Pro Gly Lys Gly Leu Glu Trp Met
        35                  40                  45

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

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

Lys Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr Cys Ala
                85                  90                  95

Arg His Arg Leu Tyr Tyr Gly Ala Phe Asp Tyr 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 Asn 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 Lys 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 Asp Glu Leu 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
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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 Lys
435 440 445

<210> 55
<211> 448
<212> PRT
<213> Artificial Sequence

<220>
<223> humanized

<400> 55

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

Thr Leu Ser Leu Thr Cys Thr Val Ser Gly Phe Ser Leu Thr Ser Asn
20 25 30

Asp Ile Ala Trp Ile Arg Gln Pro Pro Gly Lys Gly Leu Glu Trp Met
35 40 45

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

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

Lys Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr Cys Ala
85 90 95

Arg His Arg Leu Tyr Tyr Gly Ala Phe Asp Tyr 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 Asn 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 Lys 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 Asp Glu Leu 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 Lys
        435                 440                 445
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<211> 1344
<212> DNA
<213> Artificial Sequence

<220>

<223> humanized

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ccaggaaagg gactggagtg gatgggcacc atttggaccg acgggtcaac caactacaat 180

gccgcggtgc aatccagagt gaccatcagc gtggacacgt ccaagaacca gttctcgctg 240

aaattgagct ccgtgactgc cgctgatact gccgtgtatt actgtgcccg gcaccgcctt 300

tactacggcg catttgacta ctggggacag ggaaccatgg tcactgtctc gagtgcctcc 360

accaagggcc cctccgtgtt cccgctcgct ccatcatcga agtctaccag cggaggcact 420

gcggctctcg gttgcctcgt gaaggactac ttcccggagc cggtgaccgt gtcgtggaac 480

agcggagccc tgaccagcgg ggtgcacacc tttccggccg tcttgcagtc aagcggcctt 540

tactccctgt catcagtggt gactgtcccg tccagctcat tgggaaccca aacctacatc 600

tgcaatgtga atcacaaacc tagcaacacc aaggttgaca agaaagtcga gcccaaatcg 660

tgtgacaaga ctcacacttg tccgccgtgc ccggcacccg aactgctggg aggtcccagc 720

gtctttctgt tccctccaaa gccgaaagac acgctgatga tctcccgcac cccggaggtc 780

acttgcgtgg tcgtggacgt gtcacatgag gacccagagg tgaagttcaa ttggtacgtg 840

gatggcgtcg aagtccacaa tgccaaaact aagcccagag aagaacagta caattcgacc 900

taccgcgtcg tgtccgtgct cacggtgttg catcaggatt ggctgaacgg gaaggaatac 960

aagtgcaaag tgtccaacaa ggcgctgccg gcaccgatcg agaaaactat ctccaaagcg 1020

aagggacagc ctagggaacc tcaagtctac acgctgccac catcacggga tgaactgact 1080

aagaatcaag tctcactgac ttgtctggtg aaggggtttt accctagcga cattgccgtg 1140

gagtgggaat ccaacggcca gccagagaac aactacaaga ctacccctcc agtgctcgac 1200

tcggatggat cgttcttcct ttactcgaag ctcaccgtgg ataagtcccg gtggcagcag 1260

ggaaacgtgt tctcctgctc ggtgatgcat gaagccctcc ataaccacta tacccaaaag 1320

tcgctgtccc tgtcgccggg aaag 1344

<210> 57
<211> 1344
<212> DNA
<213> Artificial Sequence

<220>
<223> humanized

<400> 57

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acatgcactg tgtccgggtt ctccctgacc tctaacgaca tcgcctggat tcggcagccg 120

ccaggaaagg gactggagtg gatgggcacc atttggaccg acgggtcaac caactacaat 180

accgcggtgc aatccagagt gaccatcagc gtggacacgt ccaagaacca gttctcgctg 240

aaattgagct ccgtgactgc cgctgatact gccgtgtatt actgtgcccg gcaccgcctt 300

tactacggcg catttgacta ctggggacag ggaaccatgg tcactgtctc gagtgcctcc 360

accaagggcc cctccgtgtt cccgctcgct ccatcatcga agtctaccag cggaggcact 420

gcggctctcg gttgcctcgt gaaggactac ttcccggagc cggtgaccgt gtcgtggaac 480

agcggagccc tgaccagcgg ggtgcacacc tttccggccg tcttgcagtc aagcggcctt 540

tactccctgt catcagtggt gactgtcccg tccagctcat tgggaaccca aacctacatc 600

tgcaatgtga atcacaaacc tagcaacacc aaggttgaca agaaagtcga gcccaaatcg 660

tgtgacaaga ctcacacttg tccgccgtgc ccggcacccg aactgctggg aggtcccagc 720

gtctttctgt tccctccaaa gccgaaagac acgctgatga tctcccgcac cccggaggtc 780

acttgcgtgg tcgtggacgt gtcacatgag gacccagagg tgaagttcaa ttggtacgtg 840

gatggcgtcg aagtccacaa tgccaaaact aagcccagag aagaacagta caattcgacc 900

taccgcgtcg tgtccgtgct cacggtgttg catcaggatt ggctgaacgg gaaggaatac 960

aagtgcaaag tgtccaacaa ggcgctgccg gcaccgatcg agaaaactat ctccaaagcg 1020

aagggacagc ctagggaacc tcaagtctac acgctgccac catcacggga tgaactgact 1080

aagaatcaag tctcactgac ttgtctggtg aaggggtttt accctagcga cattgccgtg 1140

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ggaaacgtgt tctcctgctc ggtgatgcat gaagccctcc ataaccacta tacccaaaag 1320

tcgctgtccc tgtcgccggg aaag 1344