SEQUENCE LISTING

<110> Wageningen Universiteit

<120> MODIFIED CASCADE RIBONUCLEOPROTEINS AND USES THEREOF

<130> P200547WO

<150> GB1122458.1
<151> 2011-12-30

<160> 47

<170> PatentIn version 3.5

<210> 1
<211> 502
<212> PRT
<213> Escherichia coli

<400> 1

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Gly Lys Val Gln Ile Ile Asn Leu Gln Ser Leu Tyr Cys Ser Arg Asp
            20                  25                  30

Gln Trp Arg Leu Ser Leu Pro Arg Asp Asp Met Glu Leu Ala Ala Leu
        35                  40                  45

Ala Leu Leu Val Cys Ile Gly Gln Ile Ile Ala Pro Ala Lys Asp Asp
    50                  55                  60

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

Gln Gln Leu Ile Ala Pro Trp Ile Asp Met Phe Tyr Leu Asn His Ala
                85                  90                  95

Glu His Pro Phe Met Gln Thr Lys Gly Val Lys Ala Asn Asp Val Thr
            100                 105                 110

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

Phe Val Asn Gln Pro Gly Gln Gly Glu Ala Leu Cys Gly Gly Cys Thr
    130                 135                 140

Ala Ile Ala Leu Phe Asn Gln Ala Asn Gln Ala Pro Gly Phe Gly Gly
145                 150                 155                 160

Gly Phe Lys Ser Gly Leu Arg Gly Gly Thr Pro Val Thr Thr Phe Val
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                165                 170                 175

Arg Gly Ile Asp Leu Arg Ser Thr Val Leu Leu Asn Val Leu Thr Leu
            180                 185                 190

Pro Arg Leu Gln Lys Gln Phe Pro Asn Glu Ser His Thr Glu Asn Gln
        195                 200                 205

Pro Thr Trp Ile Lys Pro Ile Lys Ser Asn Glu Ser Ile Pro Ala Ser
    210                 215                 220

Ser Ile Gly Phe Val Arg Gly Leu Phe Trp Gln Pro Ala His Ile Glu
225                 230                 235                 240

Leu Cys Asp Pro Ile Gly Ile Gly Lys Cys Ser Cys Cys Gly Gln Glu
                245                 250                 255

Ser Asn Leu Arg Tyr Thr Gly Phe Leu Lys Glu Lys Phe Thr Phe Thr
            260                 265                 270

Val Asn Gly Leu Trp Pro His Pro His Ser Pro Cys Leu Val Thr Val
        275                 280                 285

Lys Lys Gly Glu Val Glu Glu Lys Phe Leu Ala Phe Thr Thr Ser Ala
    290                 295                 300

Pro Ser Trp Thr Gln Ile Ser Arg Val Val Val Asp Lys Ile Ile Gln
305                 310                 315                 320

Asn Glu Asn Gly Asn Arg Val Ala Ala Val Val Asn Gln Phe Arg Asn
                325                 330                 335

Ile Ala Pro Gln Ser Pro Leu Glu Leu Ile Met Gly Gly Tyr Arg Asn
            340                 345                 350

Asn Gln Ala Ser Ile Leu Glu Arg Arg His Asp Val Leu Met Phe Asn
        355                 360                 365

Gln Gly Trp Gln Gln Tyr Gly Asn Val Ile Asn Glu Ile Val Thr Val
    370                 375                 380

Gly Leu Gly Tyr Lys Thr Ala Leu Arg Lys Ala Leu Tyr Thr Phe Ala
385                 390                 395                 400

Glu Gly Phe Lys Asn Lys Asp Phe Lys Gly Ala Gly Val Ser Val His
                405                 410                 415
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Glu Thr Ala Glu Arg His Phe Tyr Arg Gln Ser Glu Leu Leu Ile Pro
            420                 425                 430

Asp Val Leu Ala Asn Val Asn Phe Ser Gln Ala Asp Glu Val Ile Ala
        435                 440                 445

Asp Leu Arg Asp Lys Leu His Gln Leu Cys Glu Met Leu Phe Asn Gln
    450                 455                 460

Ser Val Ala Pro Tyr Ala His His Pro Lys Leu Ile Ser Thr Leu Ala
465                 470                 475                 480

Leu Ala Arg Ala Thr Leu Tyr Lys His Leu Arg Glu Leu Lys Pro Gln
                485                 490                 495

Gly Gly Pro Ser Asn Gly
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<213> Escherichia coli

<400> 2

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

Glu Leu Arg Asp Ile Pro Ala Phe Tyr Arg Leu Val Gln Pro Phe Gly
        35                  40                  45

Trp Glu Asn Pro Arg His Gln Gln Ala Leu Leu Arg Met Val Phe Cys
    50                  55                  60

Leu Ser Ala Gly Lys Asn Val Ile Arg His Gln Asp Lys Lys Ser Glu
65                  70                  75                  80

Gln Thr Thr Gly Ile Ser Leu Gly Arg Ala Leu Ala Asn Ser Gly Arg
                85                  90                  95

Ile Asn Glu Arg Arg Ile Phe Gln Leu Ile Arg Ala Asp Arg Thr Ala
            100                 105                 110

Asp Met Val Gln Leu Arg Arg Leu Leu Thr His Ala Glu Pro Val Leu
        115                 120                 125
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Asp Trp Pro Leu Met Ala Arg Met Leu Thr Trp Trp Gly Lys Arg Glu
130 135 140

Arg Gln Gln Leu Leu Glu Asp Phe Val Leu Thr Thr Asn Lys Asn Ala
145 150 155 160

<210> 3
<211> 363
<212> PRT
<213> Escherichia coli

<400> 3

Met Ser Asn Phe Ile Asn Ile His Val Leu Ile Ser His Ser Pro Ser
1 5 10 15

Cys Leu Asn Arg Asp Asp Met Asn Met Gln Lys Asp Ala Ile Phe Gly
20 25 30

Gly Lys Arg Arg Val Arg Ile Ser Ser Gln Ser Leu Lys Arg Ala Met
35 40 45

Arg Lys Ser Gly Tyr Tyr Ala Gln Asn Ile Gly Glu Ser Ser Leu Arg
50 55 60

Thr Ile His Leu Ala Gln Leu Arg Asp Val Leu Arg Gln Lys Leu Gly
65 70 75 80

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

Gly Lys Ser Val Asp Glu Ala Glu Lys Ile Ser Ala Asp Ala Val Thr
100 105 110

Pro Trp Val Val Gly Glu Ile Ala Trp Phe Cys Glu Gln Val Ala Lys
115 120 125

Ala Glu Ala Asp Asn Leu Asp Asp Lys Lys Leu Leu Lys Val Leu Lys
130 135 140

Glu Asp Ile Ala Ala Ile Arg Val Asn Leu Gln Gln Gly Val Asp Ile
145 150 155 160

Ala Leu Ser Gly Arg Met Ala Thr Ser Gly Met Met Thr Glu Leu Gly
165 170 175

Lys Val Asp Gly Ala Met Ser Ile Ala His Ala Ile Thr Thr His Gln
180 185 190

```
Val Asp Ser Asp Ile Asp Trp Phe Thr Ala Val Asp Asp Leu Gln Glu
        195                 200                 205

Gln Gly Ser Ala His Leu Gly Thr Gln Glu Phe Ser Ser Gly Val Phe
    210                 215                 220

Tyr Arg Tyr Ala Asn Ile Asn Leu Ala Gln Leu Gln Glu Asn Leu Gly
225                 230                 235                 240

Gly Ala Ser Arg Glu Gln Ala Leu Glu Ile Ala Thr His Val Val His
                245                 250                 255

Met Leu Ala Thr Glu Val Pro Gly Ala Lys Gln Arg Thr Tyr Ala Ala
            260                 265                 270

Phe Asn Pro Ala Asp Met Val Met Val Asn Phe Ser Asp Met Pro Leu
        275                 280                 285

Ser Met Ala Asn Ala Phe Glu Lys Ala Val Lys Ala Lys Asp Gly Phe
    290                 295                 300

Leu Gln Pro Ser Ile Gln Ala Phe Asn Gln Tyr Trp Asp Arg Val Ala
305                 310                 315                 320

Asn Gly Tyr Gly Leu Asn Gly Ala Ala Ala Gln Phe Ser Leu Ser Asp
                325                 330                 335

Val Asp Pro Ile Thr Ala Gln Val Lys Gln Met Pro Thr Leu Glu Gln
            340                 345                 350

Leu Lys Ser Trp Val Arg Asn Asn Gly Glu Ala
        355                 360


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<212>  PRT
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<400>  4

Met Arg Ser Tyr Leu Ile Leu Arg Leu Ala Gly Pro Met Gln Ala Trp
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Gly Gln Pro Thr Phe Glu Gly Thr Arg Pro Thr Gly Arg Phe Pro Thr
            20                  25                  30

Arg Ser Gly Leu Leu Gly Leu Leu Gly Ala Cys Leu Gly Ile Gln Arg
        35                  40                  45
```

eolf-seql

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

Val Arg Cys Asp Glu Leu Ile Leu Asp Asp Arg Arg Val Ser Val Thr
65                  70                  75                  80

Gly Leu Arg Asp Tyr His Thr Val Leu Gly Ala Arg Glu Asp Tyr Arg
                85                  90                  95

Gly Leu Lys Ser His Glu Thr Ile Gln Thr Trp Arg Glu Tyr Leu Cys
            100                 105                 110

Asp Ala Ser Phe Thr Val Ala Leu Trp Leu Thr Pro His Ala Thr Met
        115                 120                 125

Val Ile Ser Glu Leu Glu Lys Ala Val Leu Lys Pro Arg Tyr Thr Pro
    130                 135                 140

Tyr Leu Gly Arg Arg Ser Cys Pro Leu Thr His Pro Leu Phe Leu Gly
145                 150                 155                 160

Thr Cys Gln Ala Ser Asp Pro Gln Lys Ala Leu Leu Asn Tyr Glu Pro
                165                 170                 175

Val Gly Gly Asp Ile Tyr Ser Glu Glu Ser Val Thr Gly His His Leu
            180                 185                 190

Lys Phe Thr Ala Arg Asp Glu Pro Met Ile Thr Leu Pro Arg Gln Phe
        195                 200                 205

Ala Ser Arg Glu Trp Tyr Val Ile Lys Gly Gly Met Asp Val Ser Gln
    210                 215                 220
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<210> 5
<211> 199
<212> PRT
<213> Escherichia coli

<400> 5

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Met Tyr Leu Ser Lys Val Ile Ile Ala Arg Ala Trp Ser Arg Asp Leu
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Tyr Gln Leu His Gln Gly Leu Trp His Leu Phe Pro Asn Arg Pro Asp
            20                  25                  30

Ala Ala Arg Asp Phe Leu Phe His Val Glu Lys Arg Asn Thr Pro Glu
        35                  40                  45
```

eolf-seql

Gly Cys His Val Leu Leu Gln Ser Ala Gln Met Pro Val Ser Thr Ala
50 55 60

Val Ala Thr Val Ile Lys Thr Lys Gln Val Glu Phe Gln Leu Gln Val
65 70 75 80

Gly Val Pro Leu Tyr Phe Arg Leu Arg Ala Asn Pro Ile Lys Thr Ile
85 90 95

Leu Asp Asn Gln Lys Arg Leu Asp Ser Lys Gly Asn Ile Lys Arg Cys
100 105 110

Arg Val Pro Leu Ile Lys Glu Ala Glu Gln Ile Ala Trp Leu Gln Arg
115 120 125

Lys Leu Gly Asn Ala Ala Arg Val Glu Asp Val His Pro Ile Ser Glu
130 135 140

Arg Pro Gln Tyr Phe Ser Gly Asp Gly Lys Ser Gly Lys Ile Gln Thr
145 150 155 160

Val Cys Phe Glu Gly Val Leu Thr Ile Asn Asp Ala Pro Ala Leu Ile
165 170 175

Asp Leu Val Gln Gln Gly Ile Gly Pro Ala Lys Ser Met Gly Cys Gly
180 185 190

Leu Leu Ser Leu Ala Pro Leu
195

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<213> Artificial Sequence

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ggcggcagcg gcggcggcag cgacaagcag aagaacggca tcaaggcgaa cttcaagatc 120

cgccacaaca tcgaggacgg cggcgtgcag ctcgccgacc actaccagca gaacaccccc 180

atcggcgacg gccccgtgct gctgcccgac aaccactacc tgagctacca gtccgccctg 240

agcaaagacc ccaacgagaa gcgcgatcac atggtcctgc tggagttcgt gaccgccgcc 300

gggatcactc tcggcatgga cgagctgtac aagtaagcgg ccgcggcgcg cctaggcctt 360

gacggccttc cttcaattcg ccctatagtg ag 392

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<211> 603
<212> DNA
<213> Artificial Sequence

<220>
<223> GA1070941

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cccatcctgg tcgagctgga cggcgacgta aacggccaca agttcagcgt gtccggcgag 180

ggcgagggcg atgccaccta cggcaagctg accctgaagc tcatctgcac caccggcaag 240

ctgcccgtgc cctggcccac cctcgtgacc accctcggct acggcctgca gtgcttcgcc 300

cgctaccccg accacatgaa gcagcacgac ttcttcaagt ccgccatgcc cgaaggctac 360

gtccaggagc gcaccatctt cttcaaggac gacggcaact acaagacccg cgccgaggtg 420

aagttcgagg gcgacaccct ggtgaaccgc atcgagctga agggcatcga cttcaaggag 480

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<212> DNA
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gaaaaaatgc tttaagaaca aatgtatact tttagagagt tccccgcgcc agcggggata 180

aaccgggccg attgaaggtc cggtggatgg cttaaaagag ttccccgcgc cagcggggat 240

aaaccgccgc aggtacagca ggtagcgcag atcatcaaga gttccccgcg ccagcgggga 300

taaaccgact tctctccgaa aagtcaggac gctgtggcag agttccccgc gccagcgggg 360

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gataaaccgg tgtggccatg cacgccttta acggtgaact ggagttcccc gcgccagcgg 480

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ctcactgccc gctttccag 679

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<212> DNA
<213> Artificial Sequence

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<223> GA1047360

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caacacaagc taccgcgaat gctatgctta cgagaatgga agcgagcgcg agccacttat 180

tttcatcccc aaatcttatt cttgctcatg gcaattcacg gtttaaccac ctctttcaat 240

caataaaatc acgcgcgatt actgaacagg ggcaagaaga agcgtgggtt cagtgttgtc 300

agtggttgtc acaaagcaat aagaaagtgt ttcttgggca aatcggcgtt tgcacgattg 360

atcaggtgtt gatttcggta ttgccagtta aacaccgctt tatccgtggt ttgggaattg 420

gtagatctgt tttaattgtt aatgaagttc atgcttacga cacctatatg aacggcttgc 480

tcgaggcagt gctcaaggct caggctgatg tgggagggag tgttattctt ctttccgcaa 540

ccctaccaat gaaacaaaaa cagaagcttc tggatactta tggtctgcat acagatccag 600

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ttgatctgct agcggatccg gtacc 685

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<211> 37
<212> DNA
<213> Artificial Sequence

<220>
<223> Primer BG3186

<400> 10
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<210> 11
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<210> 12

<211> 43
<212> DNA
<213> Artificial Sequence

<220>
<223> Primer BG3303

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<210> 13
<211> 44
<212> DNA
<213> Artificial Sequence

<220>
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<210> 14
<211> 45
<212> DNA
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<220>
<223> Primer BG3076

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<211> 23
<212> DNA
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<400> 15
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<210> 16
<211> 24
<212> DNA
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<220>
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<400> 16
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<210> 17
<211> 199
<212> PRT
<213> Escherichia coli

<400> 17

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Tyr Gln Leu His Gln Gly Leu Trp His Leu Phe Pro Asn Arg Pro Asp
            20                  25                  30

Ala Ala Arg Asp Phe Leu Phe His Val Glu Lys Arg Asn Thr Pro Glu
        35                  40                  45

Gly Cys His Val Leu Leu Gln Ser Ala Gln Met Pro Val Ser Thr Ala
    50                  55                  60

Val Ala Thr Val Ile Lys Thr Lys Gln Val Glu Phe Gln Leu Gln Val
65                  70                  75                  80

Gly Val Pro Leu Tyr Phe Arg Leu Arg Ala Asn Pro Ile Lys Thr Ile
                85                  90                  95

Leu Asp Asn Gln Lys Arg Leu Asp Ser Lys Gly Asn Ile Lys Arg Cys
            100                 105                 110

Arg Val Pro Leu Ile Lys Glu Ala Glu Gln Ile Ala Trp Leu Gln Arg
        115                 120                 125

Lys Leu Gly Asn Ala Ala Arg Val Glu Asp Val His Pro Ile Ser Glu
    130                 135                 140

Arg Pro Gln Tyr Phe Ser Gly Asp Gly Lys Ser Gly Lys Ile Gln Thr
145                 150                 155                 160

Val Cys Phe Glu Gly Val Leu Thr Ile Asn Asp Ala Pro Ala Leu Ile
                165                 170                 175

Asp Leu Val Gln Gln Gly Ile Gly Pro Ala Lys Ser Met Gly Cys Gly
            180                 185                 190

Leu Leu Ser Leu Ala Pro Leu
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<210> 18
<211> 2154
<212> DNA
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cgtattctgg aaatgaaagt gatggaattt tttatgaaag tgtacggcta tcgcggtgaa 180

catctgggtg gtagccgtaa accggatggt gcaatttata ccgttggtag cccgattgat 240

tatggtgtta ttgttgatac caaagcctat agcggtggtt ataatctgcc gattggtcag 300

gcagatgaaa tggaacgtta tgtggaagaa aatcagaccc gtgataaaca tctgaatccg 360

aatgaatggt ggaaagttta tccgagcagc gttaccgagt ttaaattcct gtttgttagc 420

ggtcacttca aaggcaacta taaagcacag ctgacccgtc tgaatcatat taccaattgt 480

aatggtgcag ttctgagcgt tgaagaactg ctgattggtg gtgaaatgat taaagcaggc 540

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gtaacagtca agaaagggga ggttgaggaa aaatttcttg ctttcaccac ctccgcacca 1560

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aaagacttca aaggggccgg agtctctgtt catgagactg cagaaaggca tttctatcga 1920

cagagtgaat tattaattcc cgatgtactg gcgaatgtta atttttccca ggctgatgag 1980

gtaatagctg atttacgaga caaacttcat caattgtgtg aaatgctatt taatcaatct 2040

gtagctccct atgcacatca tcctaaatta ataagcacat tagcgcttgc ccgcgccacg 2100

ctatacaaac atttacggga gttaaaaccg caaggagggc catcaaatgg ctga 2154

<210> 19
<211> 717
<212> PRT
<213> Artificial Sequence

<220>
<223> Fusion protein

<400> 19

Met Ala Gln Leu Val Lys Ser Glu Leu Glu Glu Lys Lys Ser Glu Leu
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Arg His Lys Leu Lys Tyr Val Pro His Glu Tyr Ile Glu Leu Ile Glu
20 25 30

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

Glu Phe Phe Met Lys Val Tyr Gly Tyr Arg Gly Glu His Leu Gly Gly
50 55 60

Ser Arg Lys Pro Asp Gly Ala Ile Tyr Thr Val Gly Ser Pro Ile Asp
65 70 75 80

Tyr Gly Val Ile Val Asp Thr Lys Ala Tyr Ser Gly Gly Tyr Asn Leu
85 90 95

Pro Ile Gly Gln Ala Asp Glu Met Glu Arg Tyr Val Glu Glu Asn Gln
100 105 110

Thr Arg Asp Lys His Leu Asn Pro Asn Glu Trp Trp Lys Val Tyr Pro
115 120 125

Ser Ser Val Thr Glu Phe Lys Phe Leu Phe Val Ser Gly His Phe Lys
130 135 140

Gly Asn Tyr Lys Ala Gln Leu Thr Arg Leu Asn His Ile Thr Asn Cys
145 150 155 160

Asn Gly Ala Val Leu Ser Val Glu Glu Leu Leu Ile Gly Gly Glu Met
165 170 175

```
Ile Lys Ala Gly Thr Leu Thr Leu Glu Glu Val Arg Arg Lys Phe Asn
            180                 185                 190

Asn Gly Glu Ile Asn Phe Ala Asp Pro Thr Asn Arg Ala Lys Gly Leu
        195                 200                 205

Glu Ala Val Ser Val Ala Ser Met Asn Leu Leu Ile Asp Asn Trp Ile
    210                 215                 220

Pro Val Arg Pro Arg Asn Gly Gly Lys Val Gln Ile Ile Asn Leu Gln
225                 230                 235                 240

Ser Leu Tyr Cys Ser Arg Asp Gln Trp Arg Leu Ser Leu Pro Arg Asp
                245                 250                 255

Asp Met Glu Leu Ala Ala Leu Ala Leu Leu Val Cys Ile Gly Gln Ile
            260                 265                 270

Ile Ala Pro Ala Lys Asp Asp Val Glu Phe Arg His Arg Ile Met Asn
        275                 280                 285

Pro Leu Thr Glu Asp Glu Phe Gln Gln Leu Ile Ala Pro Trp Ile Asp
    290                 295                 300

Met Phe Tyr Leu Asn His Ala Glu His Pro Phe Met Gln Thr Lys Gly
305                 310                 315                 320

Val Lys Ala Asn Asp Val Thr Pro Met Glu Lys Leu Leu Ala Gly Val
                325                 330                 335

Ser Gly Ala Thr Asn Cys Ala Phe Val Asn Gln Pro Gly Gln Gly Glu
            340                 345                 350

Ala Leu Cys Gly Gly Cys Thr Ala Ile Ala Leu Phe Asn Gln Ala Asn
        355                 360                 365

Gln Ala Pro Gly Phe Gly Gly Gly Phe Lys Ser Gly Leu Arg Gly Gly
    370                 375                 380

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

Leu Leu Asn Val Leu Thr Leu Pro Arg Leu Gln Lys Gln Phe Pro Asn
                405                 410                 415

Glu Ser His Thr Glu Asn Gln Pro Thr Trp Ile Lys Pro Ile Lys Ser
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            420                 425                 430

Asn Glu Ser Ile Pro Ala Ser Ser Ile Gly Phe Val Arg Gly Leu Phe
        435                 440                 445

Trp Gln Pro Ala His Ile Glu Leu Cys Asp Pro Ile Gly Ile Gly Lys
    450                 455                 460

Cys Ser Cys Cys Gly Gln Glu Ser Asn Leu Arg Tyr Thr Gly Phe Leu
465                 470                 475                 480

Lys Glu Lys Phe Thr Phe Thr Val Asn Gly Leu Trp Pro His Pro His
                485                 490                 495

Ser Pro Cys Leu Val Thr Val Lys Lys Gly Glu Val Glu Glu Lys Phe
            500                 505                 510

Leu Ala Phe Thr Thr Ser Ala Pro Ser Trp Thr Gln Ile Ser Arg Val
        515                 520                 525

Val Val Asp Lys Ile Ile Gln Asn Glu Asn Gly Asn Arg Val Ala Ala
    530                 535                 540

Val Val Asn Gln Phe Arg Asn Ile Ala Pro Gln Ser Pro Leu Glu Leu
545                 550                 555                 560

Ile Met Gly Gly Tyr Arg Asn Asn Gln Ala Ser Ile Leu Glu Arg Arg
                565                 570                 575

His Asp Val Leu Met Phe Asn Gln Gly Trp Gln Gln Tyr Gly Asn Val
            580                 585                 590

Ile Asn Glu Ile Val Thr Val Gly Leu Gly Tyr Lys Thr Ala Leu Arg
        595                 600                 605

Lys Ala Leu Tyr Thr Phe Ala Glu Gly Phe Lys Asn Lys Asp Phe Lys
    610                 615                 620

Gly Ala Gly Val Ser Val His Glu Thr Ala Glu Arg His Phe Tyr Arg
625                 630                 635                 640

Gln Ser Glu Leu Leu Ile Pro Asp Val Leu Ala Asn Val Asn Phe Ser
                645                 650                 655

Gln Ala Asp Glu Val Ile Ala Asp Leu Arg Asp Lys Leu His Gln Leu
            660                 665                 670
```

eolf-seql

Cys Glu Met Leu Phe Asn Gln Ser Val Ala Pro Tyr Ala His His Pro
675 680 685

Lys Leu Ile Ser Thr Leu Ala Leu Ala Arg Ala Thr Leu Tyr Lys His
690 695 700

Leu Arg Glu Leu Lys Pro Gln Gly Gly Pro Ser Asn Gly
705 710 715

<210> 20
<211> 2154
<212> DNA
<213> Artificial Sequence

<220>
<223> Fusion protein

<400> 20
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cgtattctgg aaatgaaagt gatggaattt tttatgaaag tgtacggcta tcgcggtgaa 180

catctgggtg gtagccgtaa accggatggt gcaatttata ccgttggtag cccgattgat 240

tatggtgtta ttgttgatac caaagcctat agcggtggtt ataatctgcc gattggtcag 300

gcagatgaaa tgcagcgtta tgtgaaagaa aatcagaccc gcaacaaaca tattaacccg 360

aatgaatggt ggaaagttta tccgagcagc gttaccgagt ttaaattcct gtttgttagc 420

ggtcacttca aaggcaacta taaagcacag ctgacccgtc tgaatcgtaa aaccaattgt 480

aatggtgcag ttctgagcgt tgaagaactg ctgattggtg gtgaaatgat taaagcaggc 540

accctgaccc tggaagaagt tcgtcgcaaa tttaacaatg gcgaaatcaa ctttgcggat 600

cccaccaacc gcgcgaaagg cctggaagcg gtgagcgtgg cgagcatgaa tttgcttatt 660

gataactgga ttcctgtacg cccgcgaaac ggggggaaag tccaaatcat aaatctgcaa 720

tcgctatact gcagtagaga tcagtggcga ttaagtttgc cccgtgacga tatggaactg 780

gccgctttag cactgctggt ttgcattggg caaattatcg ccccggcaaa agatgacgtt 840

gaatttcgac atcgcataat gaatccgctc actgaagatg agtttcaaca actcatcgcg 900

ccgtggatag atatgttcta ccttaatcac gcagaacatc cctttatgca gaccaaaggt 960

gtcaaagcaa atgatgtgac tccaatggaa aaactgttgg ctggggtaag cggcgcgacg 1020

aattgtgcat ttgtcaatca accggggcag ggtgaagcat tatgtggtgg atgcactgcg 1080

attgcgttat tcaaccaggc gaatcaggca ccaggttttg gtggtggttt taaaagcggt 1140

ttacgtggag gaacacctgt aacaacgttc gtacgtggga tcgatcttcg ttcaacggtg 1200

ttactcaatg tcctcacatt acctcgtctt caaaaacaat ttcctaatga atcacatacg 1260

gaaaaccaac ctacctggat taaacctatc aagtccaatg agtctatacc tgcttcgtca 1320

attgggtttg tccgtggtct attctggcaa ccagcgcata ttgaattatg cgatcccatt 1380

gggattggta aatgttcttg ctgtggacag gaaagcaatt tgcgttatac cggttttctt 1440

aaggaaaaat ttacctttac agttaatggg ctatggcccc atccgcattc cccttgtctg 1500

gtaacagtca agaaagggga ggttgaggaa aaatttcttg ctttcaccac ctccgcacca 1560

tcatggacac aaatcagccg agttgtggta gataagatta ttcaaaatga aaatggaaat 1620

cgcgtggcgg cggttgtgaa tcaattcaga aatattgcgc cgcaaagtcc tcttgaattg 1680

attatggggg gatatcgtaa taatcaagca tctattcttg aacggcgtca tgatgtgttg 1740

atgtttaatc aggggtggca acaatacggc aatgtgataa acgaaatagt gactgttggt 1800

ttgggatata aaacagcctt acgcaaggcg ttatatacct ttgcagaagg gtttaaaaat 1860

aaagacttca aaggggccgg agtctctgtt catgagactg cagaaaggca tttctatcga 1920

cagagtgaat tattaattcc cgatgtactg gcgaatgtta atttttccca ggctgatgag 1980

gtaatagctg atttacgaga caaacttcat caattgtgtg aaatgctatt taatcaatct 2040

gtagctccct atgcacatca tcctaaatta ataagcacat tagcgcttgc ccgcgccacg 2100

ctatacaaac atttacggga gttaaaaccg caaggagggc catcaaatgg ctga 2154

<210> 21
<211> 717
<212> PRT
<213> Artificial Sequence

<220>
<223> Fusion protein

<400> 21

Met Ala Gln Leu Val Lys Ser Glu Leu Glu Glu Lys Lys Ser Glu Leu
1 5 10 15

Arg His Lys Leu Lys Tyr Val Pro His Glu Tyr Ile Glu Leu Ile Glu
20 25 30

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

Glu Phe Phe Met Lys Val Tyr Gly Tyr Arg Gly Glu His Leu Gly Gly
50 55 60

Ser Arg Lys Pro Asp Gly Ala Ile Tyr Thr Val Gly Ser Pro Ile Asp
65 70 75 80

Tyr Gly Val Ile Val Asp Thr Lys Ala Tyr Ser Gly Gly Tyr Asn Leu
85 90 95

```
Pro Ile Gly Gln Ala Asp Glu Met Gln Arg Tyr Val Lys Glu Asn Gln
            100                 105                 110

Thr Arg Asn Lys His Ile Asn Pro Asn Glu Trp Trp Lys Val Tyr Pro
        115                 120                 125

Ser Ser Val Thr Glu Phe Lys Phe Leu Phe Val Ser Gly His Phe Lys
    130                 135                 140

Gly Asn Tyr Lys Ala Gln Leu Thr Arg Leu Asn Arg Lys Thr Asn Cys
145                 150                 155                 160

Asn Gly Ala Val Leu Ser Val Glu Glu Leu Leu Ile Gly Gly Glu Met
                165                 170                 175

Ile Lys Ala Gly Thr Leu Thr Leu Glu Glu Val Arg Arg Lys Phe Asn
            180                 185                 190

Asn Gly Glu Ile Asn Phe Ala Asp Pro Thr Asn Arg Ala Lys Gly Leu
        195                 200                 205

Glu Ala Val Ser Val Ala Ser Met Asn Leu Leu Ile Asp Asn Trp Ile
    210                 215                 220

Pro Val Arg Pro Arg Asn Gly Gly Lys Val Gln Ile Ile Asn Leu Gln
225                 230                 235                 240

Ser Leu Tyr Cys Ser Arg Asp Gln Trp Arg Leu Ser Leu Pro Arg Asp
                245                 250                 255

Asp Met Glu Leu Ala Ala Leu Ala Leu Leu Val Cys Ile Gly Gln Ile
            260                 265                 270

Ile Ala Pro Ala Lys Asp Asp Val Glu Phe Arg His Arg Ile Met Asn
        275                 280                 285

Pro Leu Thr Glu Asp Glu Phe Gln Gln Leu Ile Ala Pro Trp Ile Asp
    290                 295                 300

Met Phe Tyr Leu Asn His Ala Glu His Pro Phe Met Gln Thr Lys Gly
305                 310                 315                 320

Val Lys Ala Asn Asp Val Thr Pro Met Glu Lys Leu Leu Ala Gly Val
                325                 330                 335

Ser Gly Ala Thr Asn Cys Ala Phe Val Asn Gln Pro Gly Gln Gly Glu
```

```
            340                 345                 350

Ala Leu Cys Gly Gly Cys Thr Ala Ile Ala Leu Phe Asn Gln Ala Asn
        355                 360                 365

Gln Ala Pro Gly Phe Gly Gly Gly Phe Lys Ser Gly Leu Arg Gly Gly
    370                 375                 380

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

Leu Leu Asn Val Leu Thr Leu Pro Arg Leu Gln Lys Gln Phe Pro Asn
                405                 410                 415

Glu Ser His Thr Glu Asn Gln Pro Thr Trp Ile Lys Pro Ile Lys Ser
            420                 425                 430

Asn Glu Ser Ile Pro Ala Ser Ser Ile Gly Phe Val Arg Gly Leu Phe
        435                 440                 445

Trp Gln Pro Ala His Ile Glu Leu Cys Asp Pro Ile Gly Ile Gly Lys
    450                 455                 460

Cys Ser Cys Cys Gly Gln Glu Ser Asn Leu Arg Tyr Thr Gly Phe Leu
465                 470                 475                 480

Lys Glu Lys Phe Thr Phe Thr Val Asn Gly Leu Trp Pro His Pro His
                485                 490                 495

Ser Pro Cys Leu Val Thr Val Lys Lys Gly Glu Val Glu Glu Lys Phe
            500                 505                 510

Leu Ala Phe Thr Thr Ser Ala Pro Ser Trp Thr Gln Ile Ser Arg Val
        515                 520                 525

Val Val Asp Lys Ile Ile Gln Asn Glu Asn Gly Asn Arg Val Ala Ala
    530                 535                 540

Val Val Asn Gln Phe Arg Asn Ile Ala Pro Gln Ser Pro Leu Glu Leu
545                 550                 555                 560

Ile Met Gly Gly Tyr Arg Asn Asn Gln Ala Ser Ile Leu Glu Arg Arg
                565                 570                 575

His Asp Val Leu Met Phe Asn Gln Gly Trp Gln Gln Tyr Gly Asn Val
            580                 585                 590
```

eolf-seql

Ile Asn Glu Ile Val Thr Val Gly Leu Gly Tyr Lys Thr Ala Leu Arg
595 600 605

Lys Ala Leu Tyr Thr Phe Ala Glu Gly Phe Lys Asn Lys Asp Phe Lys
610 615 620

Gly Ala Gly Val Ser Val His Glu Thr Ala Glu Arg His Phe Tyr Arg
625 630 635 640

Gln Ser Glu Leu Leu Ile Pro Asp Val Leu Ala Asn Val Asn Phe Ser
645 650 655

Gln Ala Asp Glu Val Ile Ala Asp Leu Arg Asp Lys Leu His Gln Leu
660 665 670

Cys Glu Met Leu Phe Asn Gln Ser Val Ala Pro Tyr Ala His His Pro
675 680 685

Lys Leu Ile Ser Thr Leu Ala Leu Ala Arg Ala Thr Leu Tyr Lys His
690 695 700

Leu Arg Glu Leu Lys Pro Gln Gly Gly Pro Ser Asn Gly
705 710 715

<210> 22
<211> 2235
<212> DNA
<213> Artificial Sequence

<220>
<223> Fusion protein

<400> 22
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aaagttgaag atccgaaaga catggctcaa ctggttaaaa gcgaactgga agagaaaaaa 120

agtgaactgc gccacaaact gaaatatgtg ccgcatgaat atatcgagct gattgaaatt 180

gcacgtaatc cgacccagga tcgtattctg gaaatgaaag tgatggaatt ttttatgaaa 240

gtgtacggct atcgcggtga acatctgggt ggtagccgta aaccggatgg tgcaatttat 300

accgttggta gcccgattga ttatggtgtt attgttgata ccaaagccta tagcggtggt 360

tataatctgc cgattggtca ggcagatgaa atgcagcgtt atgtgaaaga aaatcagacc 420

cgcaacaaac atattaaccc gaatgaatgg tggaaagttt atccgagcag cgttaccgag 480

tttaaattcc tgtttgttag cggtcacttc aaaggcaact ataaagcaca gctgacccgt 540

ctgaatcgta aaaccaattg taatggtgca gttctgagcg ttgaagaact gctgattggt 600

ggtgaaatga ttaaagcagg caccctgacc ctggaagaag ttcgtcgcaa atttaacaat 660

ggcgaaatca actttgcgga tcccaccaac cgcgcgaaag gcctggaagc ggtgagcgtg 720

gcgagcatga atttgcttat tgataactgg attcctgtac gcccgcgaaa cgggggggaaa 780

gtccaaatca taaatctgca atcgctatac tgcagtagag atcagtggcg attaagtttg 840

ccccgtgacg atatggaact ggccgcttta gcactgctgg tttgcattgg gcaaattatc 900

gccccggcaa aagatgacgt tgaatttcga catcgcataa tgaatccgct cactgaagat 960

gagtttcaac aactcatcgc gccgtggata gatatgttct accttaatca cgcagaacat 1020

ccctttatgc agaccaaagg tgtcaaagca aatgatgtga ctccaatgga aaaactgttg 1080

gctggggtaa gcggcgcgac gaattgtgca tttgtcaatc aaccggggca gggtgaagca 1140

ttatgtggtg gatgcactgc gattgcgtta ttcaaccagg cgaatcaggc accaggtttt 1200

ggtggtggtt ttaaaagcgg tttacgtgga ggaacacctg taacaacgtt cgtacgtggg 1260

atcgatcttc gttcaacggt gttactcaat gtcctcacat tacctcgtct tcaaaaacaa 1320

tttcctaatg aatcacatac ggaaaaccaa cctacctgga ttaaacctat caagtccaat 1380

gagtctatac ctgcttcgtc aattgggttt gtccgtggtc tattctggca accagcgcat 1440

attgaattat gcgatcccat tgggattggt aaatgttctt gctgtggaca ggaaagcaat 1500

ttgcgttata ccggttttct taaggaaaaa tttaccttta cagttaatgg gctatggccc 1560

catccgcatt ccccttgtct ggtaacagtc aagaaagggg aggttgagga aaaatttctt 1620

gctttcacca cctccgcacc atcatggaca caaatcagcc gagttgtggt agataagatt 1680

attcaaaatg aaaatggaaa tcgcgtggcg gcggttgtga atcaattcag aaatattgcg 1740

ccgcaaagtc ctcttgaatt gattatgggg ggatatcgta ataatcaagc atctattctt 1800

gaacggcgtc atgatgtgtt gatgtttaat caggggtggc aacaatacgg caatgtgata 1860

aacgaaatag tgactgttgg tttgggatat aaaacagcct tacgcaaggc gttatatacc 1920

tttgcagaag ggtttaaaaa taaagacttc aaaggggccg gagtctctgt tcatgagact 1980

gcagaaaggc atttctatcg acagagtgaa ttattaattc ccgatgtact ggcgaatgtt 2040

aatttttccc aggctgatga ggtaatagct gatttacgag acaaacttca tcaattgtgt 2100

gaaatgctat ttaatcaatc tgtagctccc tatgcacatc atcctaaatt aataagcaca 2160

ttagcgcttg cccgcgccac gctatacaaa catttacggg agttaaaacc gcaaggaggg 2220

ccatcaaatg gctga 2235

<210> 23
<211> 744
<212> PRT
<213> Artificial Sequence

<220>
<223> Fusion protein

<400> 23

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Met His His His His His His Pro Lys Lys Lys Arg Lys Val Asp Pro
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Lys Lys Lys Arg Lys Val Glu Asp Pro Lys Asp Met Ala Gln Leu Val
            20                  25                  30

Lys Ser Glu Leu Glu Glu Lys Lys Ser Glu Leu Arg His Lys Leu Lys
        35                  40                  45

Tyr Val Pro His Glu Tyr Ile Glu Leu Ile Glu Ile Ala Arg Asn Pro
    50                  55                  60

Thr Gln Asp Arg Ile Leu Glu Met Lys Val Met Glu Phe Phe Met Lys
65                  70                  75                  80

Val Tyr Gly Tyr Arg Gly Glu His Leu Gly Gly Ser Arg Lys Pro Asp
                85                  90                  95

Gly Ala Ile Tyr Thr Val Gly Ser Pro Ile Asp Tyr Gly Val Ile Val
            100                 105                 110

Asp Thr Lys Ala Tyr Ser Gly Gly Tyr Asn Leu Pro Ile Gly Gln Ala
        115                 120                 125

Asp Glu Met Gln Arg Tyr Val Lys Glu Asn Gln Thr Arg Asn Lys His
    130                 135                 140

Ile Asn Pro Asn Glu Trp Trp Lys Val Tyr Pro Ser Ser Val Thr Glu
145                 150                 155                 160

Phe Lys Phe Leu Phe Val Ser Gly His Phe Lys Gly Asn Tyr Lys Ala
                165                 170                 175

Gln Leu Thr Arg Leu Asn Arg Lys Thr Asn Cys Asn Gly Ala Val Leu
            180                 185                 190

Ser Val Glu Glu Leu Leu Ile Gly Gly Glu Met Ile Lys Ala Gly Thr
        195                 200                 205

Leu Thr Leu Glu Glu Val Arg Arg Lys Phe Asn Asn Gly Glu Ile Asn
    210                 215                 220

Phe Ala Asp Pro Thr Asn Arg Ala Lys Gly Leu Glu Ala Val Ser Val
225                 230                 235                 240

Ala Ser Met Asn Leu Leu Ile Asp Asn Trp Ile Pro Val Arg Pro Arg
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                245                 250                 255

Asn Gly Gly Lys Val Gln Ile Ile Asn Leu Gln Ser Leu Tyr Cys Ser
            260                 265                 270

Arg Asp Gln Trp Arg Leu Ser Leu Pro Arg Asp Asp Met Glu Leu Ala
        275                 280                 285

Ala Leu Ala Leu Leu Val Cys Ile Gly Gln Ile Ile Ala Pro Ala Lys
    290                 295                 300

Asp Asp Val Glu Phe Arg His Arg Ile Met Asn Pro Leu Thr Glu Asp
305                 310                 315                 320

Glu Phe Gln Gln Leu Ile Ala Pro Trp Ile Asp Met Phe Tyr Leu Asn
                325                 330                 335

His Ala Glu His Pro Phe Met Gln Thr Lys Gly Val Lys Ala Asn Asp
            340                 345                 350

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

Cys Ala Phe Val Asn Gln Pro Gly Gln Gly Glu Ala Leu Cys Gly Gly
    370                 375                 380

Cys Thr Ala Ile Ala Leu Phe Asn Gln Ala Asn Gln Ala Pro Gly Phe
385                 390                 395                 400

Gly Gly Gly Phe Lys Ser Gly Leu Arg Gly Gly Thr Pro Val Thr Thr
                405                 410                 415

Phe Val Arg Gly Ile Asp Leu Arg Ser Thr Val Leu Leu Asn Val Leu
            420                 425                 430

Thr Leu Pro Arg Leu Gln Lys Gln Phe Pro Asn Glu Ser His Thr Glu
        435                 440                 445

Asn Gln Pro Thr Trp Ile Lys Pro Ile Lys Ser Asn Glu Ser Ile Pro
    450                 455                 460

Ala Ser Ser Ile Gly Phe Val Arg Gly Leu Phe Trp Gln Pro Ala His
465                 470                 475                 480

Ile Glu Leu Cys Asp Pro Ile Gly Ile Gly Lys Cys Ser Cys Cys Gly
                485                 490                 495
```

```
Gln Glu Ser Asn Leu Arg Tyr Thr Gly Phe Leu Lys Glu Lys Phe Thr
            500                 505                 510

Phe Thr Val Asn Gly Leu Trp Pro His Pro His Ser Pro Cys Leu Val
        515                 520                 525

Thr Val Lys Lys Gly Glu Val Glu Glu Lys Phe Leu Ala Phe Thr Thr
    530                 535                 540

Ser Ala Pro Ser Trp Thr Gln Ile Ser Arg Val Val Val Asp Lys Ile
545                 550                 555                 560

Ile Gln Asn Glu Asn Gly Asn Arg Val Ala Ala Val Val Asn Gln Phe
                565                 570                 575

Arg Asn Ile Ala Pro Gln Ser Pro Leu Glu Leu Ile Met Gly Gly Tyr
            580                 585                 590

Arg Asn Asn Gln Ala Ser Ile Leu Glu Arg Arg His Asp Val Leu Met
        595                 600                 605

Phe Asn Gln Gly Trp Gln Gln Tyr Gly Asn Val Ile Asn Glu Ile Val
    610                 615                 620

Thr Val Gly Leu Gly Tyr Lys Thr Ala Leu Arg Lys Ala Leu Tyr Thr
625                 630                 635                 640

Phe Ala Glu Gly Phe Lys Asn Lys Asp Phe Lys Gly Ala Gly Val Ser
                645                 650                 655

Val His Glu Thr Ala Glu Arg His Phe Tyr Arg Gln Ser Glu Leu Leu
            660                 665                 670

Ile Pro Asp Val Leu Ala Asn Val Asn Phe Ser Gln Ala Asp Glu Val
        675                 680                 685

Ile Ala Asp Leu Arg Asp Lys Leu His Gln Leu Cys Glu Met Leu Phe
    690                 695                 700

Asn Gln Ser Val Ala Pro Tyr Ala His His Pro Lys Leu Ile Ser Thr
705                 710                 715                 720

Leu Ala Leu Ala Arg Ala Thr Leu Tyr Lys His Leu Arg Glu Leu Lys
                725                 730                 735

Pro Gln Gly Gly Pro Ser Asn Gly
            740
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<210> 24
<211> 2235
<212> DNA
<213> Artificial Sequence

<220>
<223> Fusion protein

<400> 24
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aaagttgaag atccgaaaga catggctcaa ctggttaaaa gcgaactgga agagaaaaaa 120

agtgaactgc gccacaaact gaaatatgtg ccgcatgaat atatcgagct gattgaaatt 180

gcacgtaatc cgacccagga tcgtattctg gaaatgaaag tgatggaatt ttttatgaaa 240

gtgtacggct atcgcggtga acatctgggt ggtagccgta aaccggatgg tgcaatttat 300

accgttggta gcccgattga ttatggtgtt attgttgata ccaaagccta tagcggtggt 360

tataatctgc cgattggtca ggcagatgaa atggaacgtt atgtggaaga aaatcagacc 420

cgtgataaac atctgaatcc gaatgaatgg tggaaagttt atccgagcag cgttaccgag 480

tttaaattcc tgtttgttag cggtcacttc aaaggcaact ataaagcaca gctgacccgt 540

ctgaatcata ttaccaattg taatggtgca gttctgagcg ttgaagaact gctgattggt 600

ggtgaaatga ttaaagcagg caccctgacc ctggaagaag ttcgtcgcaa atttaacaat 660

ggcgaaatca actttgcgga tcccaccaac cgcgcgaaag gcctggaagc ggtgagcgtg 720

gcgagcatga atttgcttat tgataactgg attcctgtac gcccgcgaaa cgggggggaaa 780

gtccaaatca taaatctgca atcgctatac tgcagtagag atcagtggcg attaagtttg 840

ccccgtgacg atatggaact ggccgcttta gcactgctgg tttgcattgg gcaaattatc 900

gccccggcaa aagatgacgt tgaatttcga catcgcataa tgaatccgct cactgaagat 960

gagtttcaac aactcatcgc gccgtggata gatatgttct accttaatca cgcagaacat 1020

ccctttatgc agaccaaagg tgtcaaagca aatgatgtga ctccaatgga aaaactgttg 1080

gctggggtaa gcggcgcgac gaattgtgca tttgtcaatc aaccggggca gggtgaagca 1140

ttatgtggtg gatgcactgc gattgcgtta ttcaaccagg cgaatcaggc accaggtttt 1200

ggtggtggtt ttaaaagcgg tttacgtgga ggaacacctg taacaacgtt cgtacgtggg 1260

atcgatcttc gttcaacggt gttactcaat gtcctcacat tacctcgtct tcaaaaacaa 1320

tttcctaatg aatcacatac ggaaaaccaa cctacctgga ttaaacctat caagtccaat 1380

gagtctatac ctgcttcgtc aattgggttt gtccgtggtc tattctggca accagcgcat 1440

attgaattat gcgatcccat tgggattggt aaatgttctt gctgtggaca ggaaagcaat 1500

ttgcgttata ccggttttct taaggaaaaa tttaccttta cagttaatgg gctatggccc 1560

catccgcatt ccccttgtct ggtaacagtc aagaaagggg aggttgagga aaaatttctt 1620

gctttcacca cctccgcacc atcatggaca caaatcagcc gagttgtggt agataagatt 1680

attcaaaatg aaaatggaaa tcgcgtggcg gcggttgtga atcaattcag aaatattgcg 1740

ccgcaaagtc ctcttgaatt gattatgggg ggatatcgta ataatcaagc atctattctt 1800

gaacggcgtc atgatgtgtt gatgtttaat caggggtggc aacaatacgg caatgtgata 1860

aacgaaatag tgactgttgg tttgggatat aaaacagcct tacgcaaggc gttatatacc 1920

tttgcagaag ggtttaaaaa taaagacttc aaaggggccg gagtctctgt tcatgagact 1980

gcagaaaggc atttctatcg acagagtgaa ttattaattc ccgatgtact ggcgaatgtt 2040

aatttttccc aggctgatga ggtaatagct gatttacgag acaaacttca tcaattgtgt 2100

gaaatgctat ttaatcaatc tgtagctccc tatgcacatc atcctaaatt aataagcaca 2160

ttagcgcttg cccgcgccac gctatacaaa catttacggg agttaaaacc gcaaggaggg 2220

ccatcaaatg gctga 2235

<210> 25
<211> 744
<212> PRT
<213> Artificial Sequence

<220>
<223> Fusion protein

<400> 25

Met His His His His His His Pro Lys Lys Lys Arg Lys Val Asp Pro
1 5 10 15

Lys Lys Lys Arg Lys Val Glu Asp Pro Lys Asp Met Ala Gln Leu Val
20 25 30

Lys Ser Glu Leu Glu Glu Lys Lys Ser Glu Leu Arg His Lys Leu Lys
35 40 45

Tyr Val Pro His Glu Tyr Ile Glu Leu Ile Glu Ile Ala Arg Asn Pro
50 55 60

Thr Gln Asp Arg Ile Leu Glu Met Lys Val Met Glu Phe Phe Met Lys
65 70 75 80

Val Tyr Gly Tyr Arg Gly Glu His Leu Gly Gly Ser Arg Lys Pro Asp
85 90 95

Gly Ala Ile Tyr Thr Val Gly Ser Pro Ile Asp Tyr Gly Val Ile Val
100 105 110

Asp Thr Lys Ala Tyr Ser Gly Gly Tyr Asn Leu Pro Ile Gly Gln Ala

```
        115                 120                 125

Asp Glu Met Glu Arg Tyr Val Glu Glu Asn Gln Thr Arg Asp Lys His
    130                 135                 140

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

Phe Lys Phe Leu Phe Val Ser Gly His Phe Lys Gly Asn Tyr Lys Ala
                165                 170                 175

Gln Leu Thr Arg Leu Asn His Ile Thr Asn Cys Asn Gly Ala Val Leu
            180                 185                 190

Ser Val Glu Glu Leu Leu Ile Gly Gly Glu Met Ile Lys Ala Gly Thr
        195                 200                 205

Leu Thr Leu Glu Glu Val Arg Arg Lys Phe Asn Asn Gly Glu Ile Asn
    210                 215                 220

Phe Ala Asp Pro Thr Asn Arg Ala Lys Gly Leu Glu Ala Val Ser Val
225                 230                 235                 240

Ala Ser Met Asn Leu Leu Ile Asp Asn Trp Ile Pro Val Arg Pro Arg
                245                 250                 255

Asn Gly Gly Lys Val Gln Ile Ile Asn Leu Gln Ser Leu Tyr Cys Ser
            260                 265                 270

Arg Asp Gln Trp Arg Leu Ser Leu Pro Arg Asp Asp Met Glu Leu Ala
        275                 280                 285

Ala Leu Ala Leu Leu Val Cys Ile Gly Gln Ile Ile Ala Pro Ala Lys
    290                 295                 300

Asp Asp Val Glu Phe Arg His Arg Ile Met Asn Pro Leu Thr Glu Asp
305                 310                 315                 320

Glu Phe Gln Gln Leu Ile Ala Pro Trp Ile Asp Met Phe Tyr Leu Asn
                325                 330                 335

His Ala Glu His Pro Phe Met Gln Thr Lys Gly Val Lys Ala Asn Asp
            340                 345                 350

Val Thr Pro Met Glu Lys Leu Leu Ala Gly Val Ser Gly Ala Thr Asn
        355                 360                 365
```

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Cys Ala Phe Val Asn Gln Pro Gly Gln Gly Glu Ala Leu Cys Gly Gly
    370                 375                 380

Cys Thr Ala Ile Ala Leu Phe Asn Gln Ala Asn Gln Ala Pro Gly Phe
385                 390                 395                 400

Gly Gly Gly Phe Lys Ser Gly Leu Arg Gly Gly Thr Pro Val Thr Thr
                405                 410                 415

Phe Val Arg Gly Ile Asp Leu Arg Ser Thr Val Leu Leu Asn Val Leu
            420                 425                 430

Thr Leu Pro Arg Leu Gln Lys Gln Phe Pro Asn Glu Ser His Thr Glu
        435                 440                 445

Asn Gln Pro Thr Trp Ile Lys Pro Ile Lys Ser Asn Glu Ser Ile Pro
    450                 455                 460

Ala Ser Ser Ile Gly Phe Val Arg Gly Leu Phe Trp Gln Pro Ala His
465                 470                 475                 480

Ile Glu Leu Cys Asp Pro Ile Gly Ile Gly Lys Cys Ser Cys Cys Gly
                485                 490                 495

Gln Glu Ser Asn Leu Arg Tyr Thr Gly Phe Leu Lys Glu Lys Phe Thr
            500                 505                 510

Phe Thr Val Asn Gly Leu Trp Pro His Pro His Ser Pro Cys Leu Val
        515                 520                 525

Thr Val Lys Lys Gly Glu Val Glu Glu Lys Phe Leu Ala Phe Thr Thr
    530                 535                 540

Ser Ala Pro Ser Trp Thr Gln Ile Ser Arg Val Val Val Asp Lys Ile
545                 550                 555                 560

Ile Gln Asn Glu Asn Gly Asn Arg Val Ala Ala Val Val Asn Gln Phe
                565                 570                 575

Arg Asn Ile Ala Pro Gln Ser Pro Leu Glu Leu Ile Met Gly Gly Tyr
            580                 585                 590

Arg Asn Asn Gln Ala Ser Ile Leu Glu Arg Arg His Asp Val Leu Met
        595                 600                 605

Phe Asn Gln Gly Trp Gln Gln Tyr Gly Asn Val Ile Asn Glu Ile Val
    610                 615                 620
```

Thr Val Gly Leu Gly Tyr Lys Thr Ala Leu Arg Lys Ala Leu Tyr Thr
625 630 635 640

Phe Ala Glu Gly Phe Lys Asn Lys Asp Phe Lys Gly Ala Gly Val Ser
645 650 655

Val His Glu Thr Ala Glu Arg His Phe Tyr Arg Gln Ser Glu Leu Leu
660 665 670

Ile Pro Asp Val Leu Ala Asn Val Asn Phe Ser Gln Ala Asp Glu Val
675 680 685

Ile Ala Asp Leu Arg Asp Lys Leu His Gln Leu Cys Glu Met Leu Phe
690 695 700

Asn Gln Ser Val Ala Pro Tyr Ala His His Pro Lys Leu Ile Ser Thr
705 710 715 720

Leu Ala Leu Ala Arg Ala Thr Leu Tyr Lys His Leu Arg Glu Leu Lys
725 730 735

Pro Gln Gly Gly Pro Ser Asn Gly
740

<210> 26
<211> 168
<212> DNA
<213> Artificial Sequence

<220>
<223> Target plasmid

<400> 26
gaattcacaa cggtgagcaa gtcactgttg gcaagccagg atctgaacaa taccgtcttg 60

ctttcgagcg ctagctctag aactagtcct cagcctaggc ctcgttccga agctgtcttt 120

cgctgctgag ggtgacgatc ccgcataggc ggcctttaac tcggatcc 168

<210> 27
<211> 163
<212> DNA
<213> Artificial Sequence

<220>
<223> Target plasmid

<400> 27
gaattcacaa cggtgagcaa gtcactgttg gcaagccagg atctgaacaa taccgtcttt 60

tcgagcgcta gctctagaac tagtcctcag cctaggcctc gttcaagctg tctttcgctg 120

ctgagggtga cgatcccgca taggcggcct ttaactcgga tcc 163

<210> 28
<211> 158
<212> DNA
<213> Artificial Sequence

<220>
<223> Target plasmid

<400> 28
gaattcacaa cggtgagcaa gtcactgttg gcaagccagg atctgaacaa taccgtcttc 60

gagcgctagc tctagaacta gtcctcagcc taggcctcga agctgtcttt cgctgctgag 120

ggtgacgatc ccgcataggc ggcctttaac tcggatcc 158

<210> 29
<211> 153
<212> DNA
<213> Artificial Sequence

<220>
<223> Target plasmid

<400> 29
gaattcacaa cggtgagcaa gtcactgttg gcaagccagg atctgaacaa taccgtcttg 60

cgctagctct agaactagtc ctcagcctag gcctaagctg tctttcgctg ctgagggtga 120

cgatcccgca taggcggcct ttaactcgga tcc 153

<210> 30
<211> 148
<212> DNA
<213> Artificial Sequence

<220>
<223> Target plasmid

<400> 30
gaattcacaa cggtgagcaa gtcactgttg gcaagccagg atctgaacaa taccgtcttg 60

ctagctctag aactagtcct cagcctagga agctgtcttt cgctgctgag ggtgacgatc 120

ccgcataggc ggcctttaac tcggatcc 148

<210> 31
<211> 143
<212> DNA
<213> Artificial Sequence

<220>
<223> Target plasmid

<400> 31
gaattcacaa cggtgagcaa gtcactgttg gcaagccagg atctgaacaa taccgtcttc 60

tctagaacta gtcctcagcc taggaagctg tctttcgctg ctgagggtga cgatcccgca 120

taggcggcct ttaactcgga tcc 143

<210> 32
<211> 41
<212> DNA
<213> Artificial Sequence

<220>
<223> Cleavage product

<400> 32
cttgcgctag ctctagaact agtcctcagc ctaggcctaa g 41

<210> 33
<211> 41
<212> DNA
<213> Artificial Sequence

<220>
<223> Cleavage product

<400> 33
cttaggccta ggctgaggac tagttctaga gctagcgcaa g 41

<210> 34
<211> 45
<212> DNA
<213> Artificial Sequence

<220>
<223> Fill-in ligation

<400> 34
cttgcgctag ctctagaact agctagtcct cagcctaggc ctaag 45

<210> 35
<211> 45
<212> DNA
<213> Artificial Sequence

<220>
<223> Fill-in ligation

<400> 35
cttaggccta ggctgaggac tagctagttc tagagctagc gcaag 45

<210> 36
<211> 1100
<212> DNA
<213> Homo sapiens

<400> 36
ggtggaacaa gatggattat caagtgtcaa gtccaatcta tgacatcaat tattatacat 60

cggagccctg ccaaaaaatc aatgtgaagc aaatcgcagc ccgcctcctg cctccgctct 120

actcactggt gttcatcttt ggttttgtgg gcaacatgct ggtcatcctc atcctgataa 180

actgcaaaag gctgaagagc atgactgaca tctacctgct caacctggcc atctctgacc 240

tgtttttcct tcttactgtc cccttctggg ctcactatgc tgccgcccag tgggactttg 300

gaaatacaat gtgtcaactc ttgacagggc tctattttat aggcttcttc tctggaatct 360

tcttcatcat cctcctgaca atcgataggt acctggctgt cgtccatgct gtgtttgctt 420

taaaagccag gacggtcacc tttggggtgg tgacaagtgt gatcacttgg gtggtggctg 480

tgtttgcgtc tctcccagga atcatcttta ccagatctca aaaagaaggt cttcattaca 540

cctgcagctc tcattttcca tacagtcagt atcaattctg gaagaatttc cagacattaa 600

agatagtcat cttggggctg gtcctgccgc tgcttgtcat ggtcatctgc tactcgggaa 660

tcctaaaaac tctgcttcgg tgtcgaaatg agaagaagag gcacagggct gtgaggctta 720

tcttcaccat catgattgtt tattttctct tctgggctcc ctacaacatt gtccttctcc 780

tgaacacctt ccaggaattc tttggcctga ataattgcag tagctctaac aggttggacc 840

aagctatgca ggtgacagag actcttggga tgacgcactg ctgcatcaac cccatcatct 900

atgcctttgt cggggagaag ttcagaaact acctcttagt cttcttccaa aagcacattg 960

ccaaacgctt ctgcaaatgc tgttctattt tccagcaaga ggctcccgag cgagcaagct 1020

cagtttacac ccgatccact ggggagcagg aaatatctgt gggcttgtga cacggactca 1080

agtgggctgg tgacccagtc 1100

<210> 37
<211> 424
<212> DNA
<213> Artificial Sequence

<220>
<223> CRISPR array red1

<400> 37
ccatggtaat acgactcact atagggagaa ttagctgatc tttaataata aggaaatgtt 60

acattaaggt tggtgggttg tttttatggg aaaaaatgct ttaagaacaa atgtatactt 120

ttagagagtt ccccgcgcca gcggggataa accgcaaaca cagcatggac gacagccagg 180

tacctagagt tccccgcgcc agcggggata aaccgcaaac acagcatgga cgacagccag 240

gtacctagag ttccccgcgc cagcggggat aaaccgcaaa cacagcatgg acgacagcca 300

ggtacctaga gttccccgcg ccagcgggga taaaccgaaa acaaaaggct cagtcggaag 360

actgggcctt ttgttttaac cccttggggc ctctaaacgg gtcttgaggg gttttttggg 420

tacc 424

<210> 38
<211> 424
<212> DNA
<213> Artificial Sequence

<220>
<223> CRISPR array red2

<400> 38
ccatggtaat acgactcact atagggagaa ttagctgatc tttaataata aggaaatgtt 60

acattaaggt tggtgggttg tttttatggg aaaaaatgct ttaagaacaa atgtatactt 120

ttagagagtt ccccgcgcca gcggggataa accgtgtgat cacttgggtg gtggctgtgt 180

ttgcgtgagt tccccgcgcc agcggggata aaccgtgtga tcacttgggt ggtggctgtg 240

tttgcgtgag ttccccgcgc cagcggggat aaaccgtgtg atcacttggg tggtggctgt 300

gtttgcgtga gttccccgcg ccagcgggga taaaccgaaa acaaaaggct cagtcggaag 360

actgggcctt ttgttttaac cccttggggc ctctaaacgg gtcttgaggg gttttttggg 420

tacc 424

<210> 39
<211> 43
<212> DNA
<213> Artificial Sequence

<220>
<223> plasmid

<400> 39
aaggatgcca gtgataagtg gaatgccatg tgggctgtca aaa 43

<210> 40
<211> 43
<212> DNA
<213> Artificial Sequence

<220>
<223> plasmid mutant 1

<400> 40
aaggatgcga gtgataagtg gaatgccatg tgggctgtca aaa 43

<210> 41
<211> 19
<212> DNA
<213> Artificial Sequence

<220>
<223> plasmid mutant 2

<400> 41
gccatgtggg ctgtcaaaa 19

<210> 42
<211> 23
<212> DNA
<213> Artificial Sequence

<220>
<223> plasmid mutant 3

<400> 42
gaatgccatg tgggctgtca aaa 23

<210> 43
<211> 1604
<212> PRT
<213> Streptomyces sp. SPB78

<400> 43

Met Pro Asp Gln Leu Asn Ala Pro Thr Pro Leu Gly Asp Arg Leu Thr
1 5 10 15

Gly Ala Val Arg Thr Val Trp Ala Lys His Asp Arg Asp Thr Gly Lys
20 25 30

Trp Leu Pro Leu Trp Arg His Met Thr Asp Ser Ala Ala Val Ala Gly
35 40 45

Leu Leu Trp Asp His Trp Leu Pro Arg Asn Ile Lys Asp Leu Ile Ala
50 55 60

Glu Pro Leu Pro Gly Gly Val Ala Asp Ala Arg Ser Leu Cys Val Trp
65 70 75 80

Leu Ala Gly Thr His Asp Ile Gly Lys Ala Thr Pro Ala Phe Ala Cys
85 90 95

Gln Val Asp Glu Leu Ala Gly Val Met Thr Ala Ala Gly Leu Asp Met
100 105 110

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

Leu Ala Gly Gln Val Leu Leu Gln Glu Trp Leu Glu Glu Arg Arg Gly
130 135 140

Trp Thr His Arg Ala Ser Ala Gln Phe Ala Val Val Ala Gly Gly His
145 150 155 160

His Gly Val Pro Pro Asp His Met Gln Leu His Asn Leu Asp Ala His
165 170 175

Pro Glu Leu Leu Arg Thr Gln Gly Leu Ala Glu Ala Gln Trp Arg Ala
180 185 190

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

```
        195                 200                 205

Glu Arg Leu Asp Ala Trp Arg Thr Val Lys Leu Pro Gln Thr Val Gln
    210                 215                 220

Val Leu Leu Thr Ala Thr Val Ile Val Ser Asp Trp Ile Ala Ser Asn
225                 230                 235                 240

Pro Asp Leu Phe Pro Tyr Phe Pro Glu Glu His Pro Arg Glu Glu Ala
                245                 250                 255

Glu Arg Val Ala Ala Ala Trp Gln Gly Leu Leu Leu Pro Ala Pro Trp
            260                 265                 270

Glu Pro Glu Glu Pro Ser Ala Pro Ala Ala Glu Phe Tyr Ala Ser Arg
        275                 280                 285

Phe Ala Leu Pro Pro Gly Ala Val Val Arg Pro Val Gln Glu Gln Ala
    290                 295                 300

Leu Ala Met Ala Arg Asp Met Glu Arg Pro Gly Met Leu Ile Ile Glu
305                 310                 315                 320

Ala Pro Met Gly Glu Gly Lys Thr Glu Ala Ala Leu Ala Val Ala Glu
                325                 330                 335

Val Phe Ala Ala Arg Ser Gly Ala Gly Gly Cys Tyr Val Ala Leu Pro
            340                 345                 350

Thr Met Ala Thr Ser Asn Ala Met Phe Pro Arg Leu Leu Arg Trp Leu
        355                 360                 365

Asp Arg Leu Pro Arg Ala Asp Val Ser Gly Gly Arg Asp His Glu Gln
    370                 375                 380

Arg Ser Val Leu Leu Ala His Ala Lys Ser Ala Leu Gln Glu Asp Tyr
385                 390                 395                 400

Ala Thr Leu Met Arg Glu Ser His Arg Thr Ile Ala Ala Val Asp Ala
                405                 410                 415

Tyr Gly Asp Asp Ser Arg Pro Arg Lys Gly Arg Pro Ala Ala Asp Gly
            420                 425                 430

Val Arg Arg Lys Ala Pro Ala Glu Leu Val Ala His Gln Trp Leu Arg
        435                 440                 445
```

```
Gly Arg Lys Lys Gly Leu Leu Ala Ser Phe Ala Val Gly Thr Ile Asp
    450                 455                 460

Gln Leu Leu Met Ala Gly Leu Lys Ser Arg His Leu Ala Leu Arg His
465                 470                 475                 480

Leu Ala Met Ala Gly Lys Val Val Val Ile Asp Glu Val His Ala Tyr
                485                 490                 495

Asp Thr Tyr Met Asn Ala Tyr Leu Asp Arg Val Leu Ala Trp Leu Gly
            500                 505                 510

Glu Tyr Arg Val Pro Val Val Val Leu Ser Ala Thr Leu Pro Ala Arg
        515                 520                 525

Arg Arg Gly Glu Leu Ala Ala Ala Tyr Thr Gly Glu Asp Ala Gln Ala
    530                 535                 540

Leu Thr Glu Ala Thr Gly Tyr Pro Leu Leu Thr Ala Val Val Pro Gly
545                 550                 555                 560

Arg Glu Ala Val Gln Phe Val Ala Ala Ala Ser Gly Arg Gly Ser Asp
                565                 570                 575

Val Leu Leu Glu Lys Leu Asp Asp Asp Asp Glu Ala Leu Ala Asp Arg
            580                 585                 590

Leu Asp Thr Asp Leu Ala Asp Gly Gly Cys Ala Leu Val Val Arg Asn
        595                 600                 605

Thr Val Asp Arg Val Met Asp Thr Ala Ser Val Leu Arg Glu Arg Phe
    610                 615                 620

Gly Ala Asp His Val Thr Val Ala His Ala Arg Phe Val Asp Leu Asp
625                 630                 635                 640

Arg Ala Arg Lys Asp Ser Glu Leu Leu Ala Arg Phe Gly Pro Pro Asp
                645                 650                 655

Pro Asp Gly Gly Ser Pro Gln Arg Pro Arg Asn Ala His Ile Val Val
            660                 665                 670

Ala Ser Gln Val Ala Glu Gln Ser Leu Asp Val Asp Phe Asp Leu Leu
        675                 680                 685

Val Ser Asp Leu Cys Pro Val Asp Leu Leu Leu Gln Arg Met Gly Arg
    690                 695                 700
```

```
Leu His Arg His Pro Arg Gly Arg Asp Gln Glu Arg Arg Pro Ala Arg
705                 710                 715                 720

Leu Arg Gln Ala Arg Cys Leu Val Thr Gly Val Gly Trp Asp Thr Ser
                725                 730                 735

Pro Ala Pro Glu Ala Asp Glu Gly Ser Arg Ala Ile Tyr Gly Ala Tyr
            740                 745                 750

Ser Leu Leu Arg Ser Leu Ala Val Leu Ala Pro His Leu Gly Thr Ala
        755                 760                 765

Gly Ala Ala Gly His Pro Leu Arg Leu Pro Glu Asp Ile Ser Pro Leu
    770                 775                 780

Val Arg Arg Ala Tyr Gly Glu Glu Asp Pro Cys Pro Pro Glu Trp Glu
785                 790                 795                 800

Pro Val Leu Ala Pro Ala Arg Asp Lys Tyr Arg Thr Ala Arg Glu Arg
                805                 810                 815

Gln Ser Gln Lys Ala Glu Val Phe Arg Leu Asp Glu Val Arg Lys Ala
            820                 825                 830

Gly Arg Pro Leu Ile Gly Trp Ile Asp Ala Gly Val Gly Asp Ala Asp
        835                 840                 845

Asp Thr Pro Val Gly Arg Ala Gln Val Arg Asp Thr Lys Glu Gly Leu
    850                 855                 860

Glu Val Leu Val Val Arg Arg Arg Ala Asp Gly Ser Leu Cys Thr Leu
865                 870                 875                 880

Pro Trp Leu Asp Lys Gly Arg Gly Gly Leu Glu Leu Pro Val Asp Ala
                885                 890                 895

Val Pro Ser Ala Leu Ala Ala Arg Ala Val Ala Ala Ser Gly Leu Arg
            900                 905                 910

Leu Pro Tyr His Phe Thr Ser Ser Pro Gln Thr Leu Asp Arg Thr Leu
        915                 920                 925

Ala Glu Leu Glu Glu Leu Tyr Val Pro Ala Trp Gln Glu Lys Glu Ser
    930                 935                 940

His Trp Ile Ala Gly Glu Leu Ile Leu Ala Leu Asp Glu Glu Gly Arg
945                 950                 955                 960
```

```
Ala Ala Leu Ala Gly Gln Gln Leu Val Tyr Asn Pro Glu Glu Gly Leu
               965                 970                 975

Leu Val Ala Ser Ala Asp Ala Asn Thr Glu Ala Thr Ser Gly Arg Val
           980                 985                 990

Met Asp Gly Lys Pro Ser Ser Ala  Gly Asp Gly Lys Pro  Gly His Ala
       995                 1000                1005

Ala Asp  Gly Asn Arg Ala Arg  Thr Thr Val Gly Gln  Ser Pro Ala
    1010                1015                1020

Asp Arg  Gln Thr His Gln Pro  Pro Glu Gly Glu Arg  His Pro Val
    1025                1030                1035

Pro Pro  Ser Ala Ala Pro Pro  Pro Ala Arg Pro Ser  Phe Asp Leu
    1040                1045                1050

Thr Ser  Arg Pro Trp Leu Pro  Val Leu Leu Lys Asp  Gly Ser Glu
    1055                1060                1065

Arg Glu  Leu Ser Leu Pro Glu  Val Phe Asp Gln Ala  Arg Asp Ile
    1070                1075                1080

Arg Arg  Leu Val Gly Asp Leu  Pro Thr Gln Asp Phe  Ala Leu Thr
    1085                1090                1095

Arg Met  Leu Leu Ala Leu Leu  Tyr Asp Ala Leu Ser  Glu Pro Gly
    1100                1105                1110

Gly Asp  Met Ala Pro Ala Asp  Thr Asp Ala Trp Glu  Glu Leu Trp
    1115                1120                1125

Leu Ser  Gln Ser Ala Tyr Ala  Ala Pro Val Ala Ala  Tyr Leu His
    1130                1135                1140

Arg Tyr  Arg Glu Arg Phe Asp  Leu Leu His Pro Glu  Ser Pro Phe
    1145                1150                1155

Phe Gln  Thr Pro Gly Leu Arg  Thr Ala Lys Asn Glu  Val Phe Ser
    1160                1165                1170

Leu Asn  Arg Leu Val Ala Asp  Val Pro Asn Gly Asp  Pro Phe Phe
    1175                1180                1185

Ser Met  Arg Arg Pro Gly Val  Asp Arg Leu Gly Phe  Ala Glu Ala
```

```
    1190                1195                1200

Ala Arg  Trp Leu Val His Ala  Gln Ala Tyr Asp Thr  Ser Gly Ile
    1205                1210                1215

Lys Thr  Gly Ala Val Gly Asp  Pro Arg Val Lys Ala  Gly Lys Gly
    1220                1225                1230

Tyr Pro  Gln Gly Pro Ala Trp  Ala Gly Asn Leu Gly  Gly Val Leu
    1235                1240                1245

Leu Glu  Gly Asp Asn Leu His  Glu Thr Leu Leu Leu  Asn Leu Ile
    1250                1255                1260

Ala Gly  Asp Thr Pro Gly Val  His Ala Ala Glu Val  Asp Arg Pro
    1265                1270                1275

Ala Trp  Arg Ala Glu Pro Ser  Gly Pro Ala Pro Ala  Pro Asp Leu
    1280                1285                1290

Gly Leu  Arg Pro Tyr Gly Leu  Arg Asp Leu Tyr Thr  Trp Gln Ser
    1295                1300                1305

Arg Arg  Ile Arg Leu His His  Asp Ala Asp Gly Val  His Gly Val
    1310                1315                1320

Val Leu  Ala Tyr Gly Asp Ser  Leu Glu Pro His Asn  Arg His Gly
    1325                1330                1335

His Glu  Pro Met Thr Ser Trp  Arg Arg Ser Pro Thr  Gln Glu Lys
    1340                1345                1350

Lys Arg  Gln Glu Asn Leu Val  Tyr Leu Pro Arg Glu  His Asp Pro
    1355                1360                1365

Ser Arg  Leu Ala Trp Arg Gly  Met Asp Gly Leu Leu  Ala Gly Arg
    1370                1375                1380

Glu Thr  Gly Ser Ala Gln Gly  Pro Asp Gly Ala Asp  Arg Leu Ala
    1385                1390                1395

Pro Lys  Val Val Gln Trp Ala  Ala Gln Leu Thr Thr  Glu Gly Leu
    1400                1405                1410

Leu Pro  Arg Gly Tyr Leu Ile  Arg Thr Arg Val Ile  Gly Ala Arg
    1415                1420                1425
```

```
Tyr Gly  Thr Gln Gln Ser Val  Ile Asp Glu Val Val  Asp Asp Gly
    1430                1435                1440

Val Leu  Met Pro Ala Val Leu  Leu His Glu Ala Asp  Arg Arg Tyr
    1445                1450                1455

Gly Asp  Lys Ala Val Asp Ala  Leu His Asp Ala Glu  Lys Ala Val
    1460                1465                1470

Gly Ala  Leu Ala Gln Leu Ala  Ala Asp Leu Ala Leu  Ala Val Gly
    1475                1480                1485

Thr Asp  Pro Glu Pro Gly Arg  Asn Thr Ala Arg Asp  Leu Gly Phe
    1490                1495                1500

Gly Thr  Leu Asp Thr His Tyr  Arg Arg Trp Leu Arg  Glu Leu Gly
    1505                1510                1515

Gly Thr  Ser Asp Pro Glu Glu  His Arg Asp Arg Trp  Lys Gln Glu
    1520                1525                1530

Val Arg  Arg Leu Val Ala Glu  Leu Gly Glu Arg Leu  Leu Asp Gly
    1535                1540                1545

Ala Gly  Pro Ala Ala Trp Glu  Gly Arg Leu Val Glu  Thr Gly Lys
    1550                1555                1560

Gly Thr  Arg Trp Leu Asn Asp  Ala Ala Ala Glu Leu  Arg Phe Arg
    1565                1570                1575

Thr Arg  Leu Arg Glu Phe Leu  Thr Thr Ala Pro Asp  Thr Pro Thr
    1580                1585                1590

Ser Pro  Arg Pro Ala Pro Val  Glu Ser Pro Ala
    1595                1600
```

<210> 44
<211> 1559
<212> PRT
<213> Streptomyces griseus

<400> 44

```
Met Ser Asn Thr Pro Met Ser Arg Asp His Pro Glu Ser Leu Ser Ala
1               5                  10                  15

Tyr Ala Arg Leu Ser Pro Val Ser Arg Thr Ala Trp Gly Lys His Asp
            20                  25                  30
```

```
Arg Gln Thr Glu Gln Trp Leu Pro Leu Trp Arg His Met Ala Asp Ser
        35                  40                  45

Ala Ala Val Ala Glu Arg Leu Trp Asp Gln Trp Val Pro Asp Asn Val
    50                  55                  60

Lys Ala Leu Ile Ala Asp Ala Phe Pro Gln Gly Ala Gln Asp Ala Arg
65                  70                  75                  80

Arg Val Ala Val Phe Leu Ala Cys Val His Asp Ile Gly Lys Ala Thr
                85                  90                  95

Pro Ala Phe Ala Cys Gln Val Asp Gly Leu Ala Asp Arg Met Arg Ala
            100                 105                 110

Ala Gly Leu Ser Met Pro Tyr Leu Lys Gln Phe Gly Leu Asp Arg Arg
        115                 120                 125

Met Ala Pro His Gly Leu Ala Gly Gln Leu Leu Leu Gln Glu Trp Leu
    130                 135                 140

Ala Glu Arg Phe Gly Trp Ser Glu Arg Ala Ser Gly Gln Phe Ala Val
145                 150                 155                 160

Val Ala Gly Gly His His Gly Thr Pro Pro Asp His Gln His Ile His
                165                 170                 175

Asp Leu Gly Leu Arg Pro His Leu Leu Arg Thr Ala Gly Glu Ser Gln
            180                 185                 190

Asp Thr Trp Arg Ser Val Gln Asp Glu Leu Met Asp Ala Cys Ala Val
        195                 200                 205

Arg Ala Gly Val Gly Gly Arg Phe Gly Ala Trp Arg Ser Val Arg Leu
    210                 215                 220

Pro Gln Pro Val Gln Val Val Leu Thr Ala Ile Val Ile Val Ser Asp
225                 230                 235                 240

Trp Ile Ala Ser Ser Ser Glu Leu Phe Pro Tyr Asp Pro Ala Ser Trp
                245                 250                 255

Ser Pro Val Gly Pro Glu Gly Glu Gly Arg Arg Leu Thr Ala Ala Trp
            260                 265                 270

Gly Gly Leu Asp Leu Pro Gly Pro Trp Arg Ala Asp Gln Pro Asp Cys
        275                 280                 285
```

```
Thr Ala Ala Glu Leu Phe Gly Lys Arg Phe Asp Leu Pro Glu Gly Ala
    290                 295                 300

Gly Val Arg Pro Val Gln Glu Glu Ala Val Arg Val Ala Gln Glu Leu
305                 310                 315                 320

Pro Gly Pro Gly Leu Leu Ile Ile Glu Ala Pro Met Gly Glu Gly Lys
                325                 330                 335

Thr Glu Ala Ala Phe Ala Ala Ala Glu Ile Leu Ala Ala Arg Thr Gly
            340                 345                 350

Ala Gly Gly Cys Leu Val Ala Leu Pro Thr Arg Ala Thr Gly Asp Ala
        355                 360                 365

Met Phe Pro Arg Leu Leu Arg Trp Leu Glu Arg Leu Pro Ser Asp Gly
    370                 375                 380

Pro Arg Ser Val Val Leu Ala His Ala Lys Ala Ala Leu Asn Glu Val
385                 390                 395                 400

Trp Ala Gly Met Thr Lys Ala Asp Arg Arg Lys Ile Thr Ala Val Asp
                405                 410                 415

Leu Asp Ser Gln Val Glu Asp Val Ser Ser Ala Gly Gly Ala Arg Arg
            420                 425                 430

Ala Asn Pro Ala Ser Leu His Ala His Gln Trp Leu Arg Gly Arg Lys
        435                 440                 445

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

Phe Ala Gly Leu Lys Ser Arg His Leu Ala Leu Arg His Leu Ala Val
465                 470                 475                 480

Ala Gly Lys Val Val Ile Val Asp Glu Val His Ala Tyr Asp Ala Tyr
                485                 490                 495

Met Ser Ala Tyr Leu Asp Arg Val Leu Glu Trp Leu Ala Ala Tyr Arg
            500                 505                 510

Val Pro Val Val Met Leu Ser Ala Thr Leu Pro Ala His Arg Arg Arg
        515                 520                 525

Glu Leu Ala Ala Ala Tyr Ala Gly Glu Glu Thr Pro Glu Leu Ala Asp
    530                 535                 540
```

```
Ala Leu Ala Leu Pro Asp Asp Ala Tyr Pro Leu Ile Thr Ala Val Ala
545                 550                 555                 560

Pro Gly Gly Leu Val Leu Thr Ala Arg Pro Glu Pro Ala Ser Gly Arg
                565                 570                 575

Arg Thr Glu Val Val Leu Glu Arg Leu Gly Asp Gly Pro Ala Leu Leu
            580                 585                 590

Ala Ala Arg Leu Asp Glu Glu Leu Arg Asp Gly Gly Cys Ala Leu Val
        595                 600                 605

Val Arg Asn Thr Val Asp Arg Val Leu Glu Ala Ala Glu His Leu Arg
    610                 615                 620

Ala His Phe Gly Ala Glu Ala Val Thr Val Ala His Ser Arg Phe Val
625                 630                 635                 640

Ala Ala Asp Arg Ala Arg Asn Asp Thr Val Leu Arg Glu Arg Phe Gly
                645                 650                 655

Pro Gly Gly Asp Arg Pro Ala Gly Pro His Ile Val Val Ala Ser Gln
            660                 665                 670

Val Val Glu Gln Ser Leu Asp Ile Asp Phe Asp Leu Leu Val Thr Asp
        675                 680                 685

Leu Ala Pro Val Asp Leu Val Leu Gln Arg Met Gly Arg Leu His Arg
    690                 695                 700

His Pro Arg Thr Arg Pro Pro Arg Leu Ser Arg Ala Arg Cys Leu Ile
705                 710                 715                 720

Thr Gly Val Glu Asp Trp His Ala Glu Arg Pro Val Pro Val Arg Gly
                725                 730                 735

Ser Leu Ala Val Tyr Gln Gly Pro His Thr Leu Leu Arg Ala Leu Ala
            740                 745                 750

Val Leu Gly Pro His Leu Asp Gly Val Pro Leu Val Leu Pro Asp His
        755                 760                 765

Ile Ser Pro Leu Val Gln Ala Ala Tyr Asp Glu Arg Pro Val Gly Pro
    770                 775                 780

Ala His Trp Ala Pro Val Leu Asp Glu Ala Arg Arg Gln Tyr Leu Thr
```

785 790 795 800

Arg Leu Ala Glu Lys Arg Glu Arg Ala Asp Val Phe Arg Leu Gly Pro
805 810 815

Val Arg Arg Pro Gly Arg Pro Leu Phe Gly Trp Leu Asp Gly Asn Ala
820 825 830

Gly Asp Ala Asp Asp Ser Arg Thr Gly Arg Ala Gln Val Arg Asp Ser
835 840 845

Glu Glu Ser Leu Glu Val Leu Val Val Gln Arg Arg Ala Asp Gly Arg
850 855 860

Leu Thr Thr Val Ser Trp Leu Asp Gly Gly Arg Gly Gly Leu Asp Leu
865 870 875 880

Pro Glu His Ala Pro Pro Pro Pro Arg Ala Ala Glu Val Val Ala Ala
885 890 895

Cys Ala Leu Thr Leu Pro Arg Ser Leu Thr His Pro Gly Val Ile Asp
900 905 910

Arg Thr Ile Ala Glu Leu Glu Arg Phe Val Val Pro Ala Trp Gln Val
915 920 925

Lys Glu Cys Pro Trp Leu Ala Gly Glu Leu Leu Leu Val Leu Asp Glu
930 935 940

Asp Cys Gln Thr Arg Leu Ser Gly Leu Glu Val His Tyr Ser Thr Asp
945 950 955 960

Gln Gly Leu Arg Val Gly Ser Val Gly Thr Arg Ser Thr Asn Arg Ala
965 970 975

Lys Gly Leu Glu Ala Val Ser Val Ala Ser Phe Asp Leu Val Ser Arg
980 985 990

Pro Trp Leu Pro Val Gln Tyr Glu Asp Gly Ala Thr Gly Glu Leu Ser
995 1000 1005

Leu Arg Glu Val Phe Ala Arg Ala Gly Glu Val Arg Arg Leu Val
1010 1015 1020

Gly Asp Leu Pro Thr Gln Glu Leu Ala Leu Leu Arg Leu Leu Leu
1025 1030 1035

```
Ala Ile  Leu Tyr Asp Ala Tyr  Asp Glu Ala Pro Gly  Arg Ser Gly
    1040                1045                1050

Gly Ala  Pro Ala Gln Leu Glu  Asp Trp Glu Ala Leu  Trp Asp Glu
    1055                1060                1065

Pro Asp  Ser Phe Ala Val Val  Ala Gly Tyr Leu Asp  Arg His Arg
    1070                1075                1080

Asp Arg  Phe Asp Leu Leu His  Pro Glu Arg Pro Phe  Phe Gln Val
    1085                1090                1095

Ala Gly  Leu His Thr Gln Lys  His Glu Val Ala Ser  Leu Asn Arg
    1100                1105                1110

Ile Val  Ala Asp Val Pro Asn  Gly Glu Ala Phe Phe  Ser Met Arg
    1115                1120                1125

Arg Pro  Gly Val His Arg Leu  Gly Leu Ala Glu Ala  Ala Arg Trp
    1130                1135                1140

Leu Val  His Thr His Ala Tyr  Asp Ala Ser Gly Ile  Lys Ser Gly
    1145                1150                1155

Met Glu  Gly Asp Ala Arg Val  Lys Gly Gly Lys Val  Tyr Pro Gln
    1160                1165                1170

Gly Val  Gly Trp Val Gly Gly  Leu Gly Gly Val Phe  Ala Glu Gly
    1175                1180                1185

Ala Ser  Leu Arg Glu Thr Leu  Leu Leu Asn Leu Ile  Pro Thr Asp
    1190                1195                1200

Glu Asp  Ile Leu Thr Ser Glu  Pro Lys Ala Asp Leu  Pro Val Trp
    1205                1210                1215

Arg Arg  Glu Thr Pro Pro Gly  Pro Gly Val Val Glu  Gly Asp Pro
    1220                1225                1230

Ser Ala  Pro Arg Pro Ala Gly  Pro Arg Asp Leu Tyr  Thr Trp Gln
    1235                1240                1245

Ser Arg  Arg Leu Leu Leu His  Thr Glu Gly Ser Asp  Ala Ile Gly
    1250                1255                1260

Val Val  Leu Gly Tyr Gly Asp  Pro Leu Ser Pro Ala  Asn Arg Gln
    1265                1270                1275
```

```
Lys Thr  Glu Pro Met Thr Gly  Trp Arg Arg Ser Pro  Ala Gln Glu
    1280                1285                1290

Lys Lys  Leu Gly Arg Pro Leu  Val Tyr Leu Pro Arg  Gln His Asp
    1295                1300                1305

Pro Gly  Arg Ala Ala Trp Arg  Gly Leu Ala Ser Leu  Leu Tyr Pro
    1310                1315                1320

Gln Gly  Glu Asp Gly Asp Thr  Thr Gly Arg Gly Thr  Asp Arg Ser
    1325                1330                1335

Arg Pro  Ala Gly Ile Val Arg  Trp Leu Ala Leu Leu  Ser Thr Glu
    1340                1345                1350

Gly Val  Leu Pro Lys Gly Ser  Leu Ile Arg Thr Arg  Leu Val Gly
    1355                1360                1365

Ala Val  Tyr Gly Thr Gln Gln  Ser Val Val Asp Asp  Val Val Asp
    1370                1375                1380

Asp Ser  Ile Ala Leu Pro Val  Val Leu Leu His Gln  Asp Arg Arg
    1385                1390                1395

Leu His  Gly Ala Val Ala Val  Asp Ala Val Ala Asp  Ala Glu Arg
    1400                1405                1410

Ala Val  Ser Ala Leu Gly His  Leu Ala Gly Asn Leu  Ala Arg Ala
    1415                1420                1425

Ser Gly  Ser Glu Ala Gly Pro  Ala Thr Ala Thr Ala  Arg Asp Gln
    1430                1435                1440

Gly Phe  Gly Ala Leu Asp Gly  Pro Tyr Arg Arg Trp  Leu Val Asp
    1445                1450                1455

Leu Ala  Glu Asp Thr Asp Leu  Glu Arg Ala Arg Ala  Ala Trp Arg
    1460                1465                1470

Asp Thr  Val Arg Leu Val Val  Leu Gly Ile Gly Arg  Glu Leu Leu
    1475                1480                1485

Asp Ala  Ala Gly Arg Ala Ala  Ala Glu Gly Arg Val  Ile Glu Leu
    1490                1495                1500

Pro Gly  Val Gly Lys Arg Trp  Ile Asp Ser Ser Arg  Ala Asp Leu
    1505                1510                1515
```

Trp Phe Arg Thr Arg Ile Asn Arg Val Leu Pro Arg Pro Leu Pro
1520 1525 1530

Glu Ala His Ala Pro Thr Ala Asp Ile His Ala Gly His Ala Val
1535 1540 1545

Arg Ala Asp Glu Ala Leu Ser Glu Glu Thr Val
1550 1555

<210> 45
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<212> PRT
<213> Catenulispora acidiphila

<400> 45

Met Phe Asn Val Gly Ser Thr Arg Cys Trp Gly Asp Gly Gly Leu Arg
1 5 10 15

Asn Ala Ala Glu Asp Leu Ser Ala Ala Thr Arg Ser Ala Trp Ala Lys
20 25 30

Ser Asp Pro Asp Ser Gly Gln Ser Leu Ser Leu Ile Arg His Leu Ala
35 40 45

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

His Val Lys Ser Leu Ile Ala Glu Gly Leu Pro Glu Gly Leu Val Asp
65 70 75 80

Gly Arg Thr Leu Ala Val Trp Leu Ala Gly Thr His Asp Ile Gly Lys
85 90 95

Leu Thr Pro Ala Phe Ala Cys Gln Cys Glu Pro Leu Ala Gln Ala Met
100 105 110

Arg Glu Cys Gly Leu Asp Met Pro Thr Arg Thr Gln Phe Gly Asp Asp
115 120 125

Arg Arg Val Ala Pro His Gly Leu Ala Gly Gln Val Leu Leu Arg Glu
130 135 140

Trp Leu Met Glu Arg His Gly Trp Ser Gly Arg Ser Ala Asp Ala Phe
145 150 155 160

Thr Val Ile Ala Gly Gly His His Gly Val Pro Pro Ser Tyr Ser Gln
165 170 175

```
Leu His Asp Leu Asp Ala Tyr Pro Glu Leu Leu Arg Thr Pro Gly Ala
            180                 185                 190

Ser Glu Gly Ile Trp Lys Ser Ser Gln His Glu Leu Leu Asp Ala Cys
        195                 200                 205

Ala Val Met Thr Gly Ala Ser Ser Arg Leu Ala His Trp Arg Gly Leu
    210                 215                 220

Arg Leu Ser Gln Gln Ala Gln Val Leu Leu Thr Gly Leu Val Ile Val
225                 230                 235                 240

Ala Asp Trp Ile Ala Ser Asn Thr Asp Leu Phe Pro Tyr Pro Ala Leu
                245                 250                 255

Gly Thr Gly Glu Ala Ala Ile Asp Pro Gly Lys Arg Val Glu Leu Ala
            260                 265                 270

Trp Arg Gly Leu Glu Leu Pro Ala Pro Trp Ala Pro Lys Tyr Leu Met
        275                 280                 285

Pro Gly Met Gln Gly Leu Leu Ala Ser Arg Phe Gly Leu Pro Ala Asp
    290                 295                 300

Ala Gln Leu Arg Pro Val Gln Gln Met Ala Val Gln Leu Ala Ser Ala
305                 310                 315                 320

Asn Ala Ala Pro Gly Leu Leu Val Ile Glu Ala Pro Met Gly Glu Gly
                325                 330                 335

Lys Thr Glu Ala Ala Leu Leu Ala Ala Glu Ile Leu Ala Ala Arg Ser
            340                 345                 350

Gly Ala Gly Gly Val Phe Leu Ala Leu Pro Thr Gln Ala Thr Ser Asn
        355                 360                 365

Ala Met Phe Ala Arg Val Val Asn Trp Leu Arg Gln Val Pro Arg Glu
    370                 375                 380

Gly Val Ala Ser Val His Leu Ala His Gly Lys Ala Ala Leu Asp Asp
385                 390                 395                 400

Ala Phe Ala Ser Phe Leu Arg Ala Ala Pro Arg Leu Thr Ser Ile Asp
                405                 410                 415

Ala Asp Gly Tyr Ala Gly Glu Ala Asn Val Arg Arg Asp Arg Arg Ala
```

```
            420                 425                 430

Gly Ser Ala Asp Met Val Ala His Gln Trp Leu Arg Gly Arg Lys Lys
        435                 440                 445

Gly Ile Leu Ser Pro Phe Val Val Gly Thr Ile Asp Gln Leu Leu Phe
    450                 455                 460

Thr Gly Leu Lys Ser Arg His Leu Ala Leu Arg His Leu Ala Val Ala
465                 470                 475                 480

Gly Lys Val Val Val Ile Asp Glu Val His Ala Tyr Asp Ala Tyr Met
                485                 490                 495

Ser Val Tyr Leu Glu Arg Val Leu Ser Trp Leu Gly Ala Tyr Arg Val
            500                 505                 510

Pro Val Val Leu Leu Ser Ala Thr Leu Pro Ala Asp Arg Arg Gln Ala
        515                 520                 525

Leu Val Glu Ala Tyr Gly Gly Ile Thr Ser Glu Ala Leu Arg Asp Ala
    530                 535                 540

Arg Glu Ala Tyr Pro Val Leu Thr Ala Val Thr Ile Gly Ala Pro Ala
545                 550                 555                 560

Gln Ala Val Gly Thr Glu Pro Ala Glu Gly Arg Arg Val Asp Val Asn
                565                 570                 575

Val Glu Ala Phe Asp Asp Asp Leu Gly Arg Leu Ala Asp Arg Leu Glu
            580                 585                 590

Ala Glu Leu Val Asp Gly Gly Cys Ala Leu Ile Ile Arg Asn Thr Val
        595                 600                 605

Gly Arg Val Leu Gln Thr Ala Gln Gln Leu Arg Glu Arg Phe Gly Ala
    610                 615                 620

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

Arg Lys Asp Ala Asp Leu Leu Ala Arg Phe Gly His Asp Gly Ala Arg
                645                 650                 655

Pro Arg Arg His Ile Val Val Ala Ser Gln Val Ala Glu Gln Ser Leu
            660                 665                 670
```

```
Asp Ile Asp Phe Asp Leu Leu Val Thr Asp Leu Ala Pro Ile Asp Leu
        675                 680                 685

Val Leu Gln Arg Met Gly Arg Val His Arg His His Arg Gly Gly Pro
    690                 695                 700

Glu Gln Ser Glu Arg Pro Pro Ser Leu Arg Thr Ala Arg Cys Leu Val
705                 710                 715                 720

Thr Gly Val Asp Trp Ala Gly Ile Pro Ser Ala Pro Ile Ala Gly Ser
                725                 730                 735

Val Ala Val Tyr Gly Leu His Pro Leu Leu Arg Ser Leu Ala Val Leu
            740                 745                 750

Gln Pro Tyr Leu Thr Gly Ser Ala Leu Thr Leu Pro Gly Asp Ile Asn
        755                 760                 765

Pro Leu Val Gln Cys Ala Tyr Ala Gln Ser Phe Val Ala Pro Thr Gly
    770                 775                 780

Trp Gly Glu Ala Met Asp Ala Ala Gln Ala Glu His Met Ala His Ile
785                 790                 795                 800

Val Gln Gln Arg Glu Gly Ala Met Ala Phe Cys Leu Asp Glu Val Arg
                805                 810                 815

Gly Pro Gly Arg Ser Leu Ile Gly Trp Ile Asp Gly Gly Val Gly Asp
            820                 825                 830

Ala Asp Asp Thr Arg Ala Gly Arg Ala Gln Val Arg Asp Ser Pro Glu
        835                 840                 845

Thr Ile Glu Val Leu Val Val Gln Arg Gly Ser Asp Gly Val Leu Arg
    850                 855                 860

Thr Leu Pro Trp Leu Asp Arg Gly Arg Gly Gly Leu Glu Leu Pro Thr
865                 870                 875                 880

Glu Ala Val Pro Pro Pro Arg Ala Ala Arg Ala Ala Ala Ala Ser Ala
                885                 890                 895

Leu Arg Leu Pro Gly Leu Phe Ala Lys Pro Trp Met Phe Asp Arg Val
            900                 905                 910

Leu Arg Glu Leu Glu Arg Glu Tyr His Glu Ala Trp Gln Ala Lys Glu
        915                 920                 925
```

```
Ser Ser Trp Leu Gln Gly Glu Leu Leu Leu Val Leu Asp Glu Glu Cys
    930                 935                 940

Arg Thr Val Leu Ala Gly Tyr Glu Leu Ser Tyr Asn Pro Asp Asp Gly
945                 950                 955                 960

Leu Glu Met Val Met Pro Gly Glu Pro His Ala Ala Val Val Arg Asp
                965                 970                 975

Lys Glu Ala Ser Asp Asp Lys Thr Ala Ser Phe Asp Leu Thr Ser Ala
            980                 985                 990

Pro Trp Leu Pro Val Leu Tyr Ala  Asp Gly Met Gln Gly  Val Leu Ser
        995                 1000                1005

Leu Arg  Asp Val Phe Ala Gln  Ser Asn Leu Ile Arg  Arg Leu Val
    1010                1015                1020

Gly Asp  Leu Pro Thr Gln Asp  Phe Ala Leu Leu Arg  Leu Leu Leu
    1025                1030                1035

Ala Val  Leu Tyr Asp Ala Val  Asp Gly Pro Arg Asp  Gly Gln Asp
    1040                1045                1050

Trp Glu  Asp Leu Trp Thr Ser  Asp Asp Pro Phe Ala  Ala Val Pro
    1055                1060                1065

Ala Tyr  Leu Asp Ser His Arg  Glu Arg Phe Asp Leu  Leu His Pro
    1070                1075                1080

Ala Thr  Pro Phe Tyr Gln Val  Pro Gly Leu Gln Thr  Ala Lys Gly
    1085                1090                1095

Glu Val  Gly Pro Leu Asn Lys  Ile Val Ala Asp Val  Pro Asp Gly
    1100                1105                1110

Asp Pro  Phe Leu Thr Met Arg  Met Pro Gly Val Glu  Gln Leu Ser
    1115                1120                1125

Phe Ala  Glu Ala Ala Arg Trp  Leu Val His Thr Gln  Ala Phe Asp
    1130                1135                1140

Thr Ser  Gly Ile Lys Ser Gly  Val Val Gly Asp Pro  Lys Ala Val
    1145                1150                1155

Asn Gly  Lys Arg Tyr Pro Gln  Gly Val Ala Trp Leu  Gly Asn Leu
    1160                1165                1170
```

```
Gly Gly  Val Phe Ala Glu Gly  Asp Thr Leu Arg Gln  Thr Leu Leu
    1175                1180                1185

Leu Asn  Leu Ile Pro Ala Asp  Thr Thr Asn Leu Gln  Val Thr Ser
    1190                1195                1200

Ala Gln  Asp Val Pro Ala Trp  Arg Gly Thr Asn Gly  Arg Ala Gly
    1205                1210                1215

Ser Asp  His Ala Asp Ala Glu  Pro Arg Val Pro Ala  Gly Leu Arg
    1220                1225                1230

Asp Leu  Tyr Thr Trp Gln Ser  Arg Arg Ile Arg Leu  Glu Tyr Asp
    1235                1240                1245

Thr Arg  Gly Val Thr Gly Ala  Val Leu Thr Tyr Gly  Asp Glu Leu
    1250                1255                1260

Thr Ala  His Asn Lys His Gly  Val Glu Pro Met Thr  Gly Trp Arg
    1265                1270                1275

Arg Ser  Lys Pro Gln Glu Lys  Lys Leu Gly Leu Ser  Thr Val Tyr
    1280                1285                1290

Met Pro  Gln Gln His Asp Pro  Thr Arg Ala Ala Trp  Arg Gly Ile
    1295                1300                1305

Glu Ser  Leu Leu Ala Gly Ser  Ala Gly Ser Gly Ser  Ser Gln Thr
    1310                1315                1320

Gly Glu  Pro Ala Ser His Tyr  Arg Pro Lys Ile Val  Asp Trp Leu
    1325                1330                1335

Gly Glu  Leu Ala His His Gly  Asn Leu Pro Ser Arg  Gly Leu Ile
    1340                1345                1350

Arg Val  Arg Thr Ser Gly Ala  Val Tyr Gly Thr Gln  Gln Ser Ile
    1355                1360                1365

Ile Asp  Glu Val Val Ser Asp  Glu Leu Thr Met Ala  Val Val Leu
    1370                1375                1380

Leu His  Glu Asp Asp Pro Arg  Phe Gly Lys Ala Ala  Val Thr Ala
    1385                1390                1395

Val Lys  Asp Ala Asp Ser Ala  Val Ala Ala Leu Gly  Asp Leu Ala
```

1400 1405 1410

Ser Asp Leu Ala Arg Ala Ala Gly Leu Asp Pro Glu Pro Glu Arg
1415 1420 1425

Val Thr Ala Arg Asp Arg Ala Phe Gly Ala Leu Asp Gly Pro Tyr
1430 1435 1440

Arg Arg Trp Leu Leu Asp Leu Gly Asn Ser Thr Asp Pro Ala Ala
1445 1450 1455

Met Arg Ala Val Trp Gln Gly Arg Val Tyr Asp Ile Ile Ala Val
1460 1465 1470

Gln Gly Gln Met Leu Leu Asp Ser Ala Gly Ser Ala Ala Ala Gln
1475 1480 1485

Gly Arg Met Val Lys Thr Thr Arg Gly Glu Arg Trp Met Asp Asp
1490 1495 1500

Ser Leu Ala Asp Leu Tyr Phe Lys Gly Arg Ile Ala Lys Ala Leu
1505 1510 1515

Ser Ser Arg Leu Gly Lys Lys Pro Thr Asp Pro Gly Glu Pro Val
1520 1525 1530

Gly Ile Gln Glu Asp Pro Ala
1535 1540

<210> 46
<211> 1407
<212> PRT
<213> Artificial Sequence

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<223> Fusion Cas3-Cse1

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Met Glu Pro Phe Lys Tyr Ile Cys His Tyr Trp Gly Lys Ser Ser Lys
1 5 10 15

Ser Leu Thr Lys Gly Asn Asp Ile His Leu Leu Ile Tyr His Cys Leu
20 25 30

Asp Val Ala Ala Val Ala Asp Cys Trp Trp Asp Gln Ser Val Val Leu
35 40 45

Gln Asn Thr Phe Cys Arg Asn Glu Met Leu Ser Lys Gln Arg Val Lys
50 55 60

```
Ala Trp Leu Leu Phe Phe Ile Ala Leu His Asp Ile Gly Lys Phe Asp
65                  70                  75                  80

Ile Arg Phe Gln Tyr Lys Ser Ala Glu Ser Trp Leu Lys Leu Asn Pro
                85                  90                  95

Ala Thr Pro Ser Leu Asn Gly Pro Ser Thr Gln Met Cys Arg Lys Phe
            100                 105                 110

Asn His Gly Ala Ala Gly Leu Tyr Trp Phe Asn Gln Asp Ser Leu Ser
        115                 120                 125

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

Pro Tyr Glu Ser Trp Phe Pro Trp Val Glu Ala Val Thr Gly His His
145                 150                 155                 160

Gly Phe Ile Leu His Ser Gln Asp Gln Asp Lys Ser Arg Trp Glu Met
                165                 170                 175

Pro Ala Ser Leu Ala Ser Tyr Ala Ala Gln Asp Lys Gln Ala Arg Glu
            180                 185                 190

Glu Trp Ile Ser Val Leu Glu Ala Leu Phe Leu Thr Pro Ala Gly Leu
        195                 200                 205

Ser Ile Asn Asp Ile Pro Pro Asp Cys Ser Ser Leu Leu Ala Gly Phe
    210                 215                 220

Cys Ser Leu Ala Asp Trp Leu Gly Ser Trp Thr Thr Thr Asn Thr Phe
225                 230                 235                 240

Leu Phe Asn Glu Asp Ala Pro Ser Asp Ile Asn Ala Leu Arg Thr Tyr
                245                 250                 255

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

Leu Val Ser Asn Lys Arg Cys Tyr Glu Gly Val His Ala Leu Leu Asp
        275                 280                 285

Asn Gly Tyr Gln Pro Arg Gln Leu Gln Val Leu Val Asp Ala Leu Pro
    290                 295                 300

Val Ala Pro Gly Leu Thr Val Ile Glu Ala Pro Thr Gly Ser Gly Lys
```

```
305                 310                 315                 320

Thr Glu Thr Ala Leu Ala Tyr Ala Trp Lys Leu Ile Asp Gln Gln Ile
                325                 330                 335

Ala Asp Ser Val Ile Phe Ala Leu Pro Thr Gln Ala Thr Ala Asn Ala
            340                 345                 350

Met Leu Thr Arg Met Glu Ala Ser Ala Ser His Leu Phe Ser Ser Pro
        355                 360                 365

Asn Leu Ile Leu Ala His Gly Asn Ser Arg Phe Asn His Leu Phe Gln
    370                 375                 380

Ser Ile Lys Ser Arg Ala Ile Thr Glu Gln Gly Gln Glu Glu Ala Trp
385                 390                 395                 400

Val Gln Cys Cys Gln Trp Leu Ser Gln Ser Asn Lys Lys Val Phe Leu
                405                 410                 415

Gly Gln Ile Gly Val Cys Thr Ile Asp Gln Val Leu Ile Ser Val Leu
            420                 425                 430

Pro Val Lys His Arg Phe Ile Arg Gly Leu Gly Ile Gly Arg Ser Val
        435                 440                 445

Leu Ile Val Asp Glu Val His Ala Tyr Asp Thr Tyr Met Asn Gly Leu
    450                 455                 460

Leu Glu Ala Val Leu Lys Ala Gln Ala Asp Val Gly Gly Ser Val Ile
465                 470                 475                 480

Leu Leu Ser Ala Thr Leu Pro Met Lys Gln Lys Gln Lys Leu Leu Asp
                485                 490                 495

Thr Tyr Gly Leu His Thr Asp Pro Val Glu Asn Asn Ser Ala Tyr Pro
            500                 505                 510

Leu Ile Asn Trp Arg Gly Val Asn Gly Ala Gln Arg Phe Asp Leu Leu
        515                 520                 525

Ala His Pro Glu Gln Leu Pro Pro Arg Phe Ser Ile Gln Pro Glu Pro
    530                 535                 540

Ile Cys Leu Ala Asp Met Leu Pro Asp Leu Thr Met Leu Glu Arg Met
545                 550                 555                 560
```

```
Ile Ala Ala Ala Asn Ala Gly Ala Gln Val Cys Leu Ile Cys Asn Leu
                565                 570                 575

Val Asp Val Ala Gln Val Cys Tyr Gln Arg Leu Lys Glu Leu Asn Asn
            580                 585                 590

Thr Gln Val Asp Ile Asp Leu Phe His Ala Arg Phe Thr Leu Asn Asp
        595                 600                 605

Arg Arg Glu Lys Glu Asn Arg Val Ile Ser Asn Phe Gly Lys Asn Gly
    610                 615                 620

Lys Arg Asn Val Gly Arg Ile Leu Val Ala Thr Gln Val Val Glu Gln
625                 630                 635                 640

Ser Leu Asp Val Asp Phe Asp Trp Leu Ile Thr Gln His Cys Pro Ala
                645                 650                 655

Asp Leu Leu Phe Gln Arg Leu Gly Arg Leu His Arg His His Arg Lys
            660                 665                 670

Tyr Arg Pro Ala Gly Phe Glu Ile Pro Val Ala Thr Ile Leu Leu Pro
        675                 680                 685

Asp Gly Glu Gly Tyr Gly Arg His Glu His Ile Tyr Ser Asn Val Arg
    690                 695                 700

Val Met Trp Arg Thr Gln Gln His Ile Glu Glu Leu Asn Gly Ala Ser
705                 710                 715                 720

Leu Phe Phe Pro Asp Ala Tyr Arg Gln Trp Leu Asp Ser Ile Tyr Asp
                725                 730                 735

Asp Ala Glu Met Asp Glu Pro Glu Trp Val Gly Asn Gly Met Asp Lys
            740                 745                 750

Phe Glu Ser Ala Glu Cys Glu Lys Arg Phe Lys Ala Arg Lys Val Leu
        755                 760                 765

Gln Trp Ala Glu Glu Tyr Ser Leu Gln Asp Asn Asp Glu Thr Ile Leu
    770                 775                 780

Ala Val Thr Arg Asp Gly Glu Met Ser Leu Pro Leu Leu Pro Tyr Val
785                 790                 795                 800

Gln Thr Ser Ser Gly Lys Gln Leu Leu Asp Gly Gln Val Tyr Glu Asp
                805                 810                 815
```

```
Leu Ser His Glu Gln Gln Tyr Glu Ala Leu Ala Leu Asn Arg Val Asn
            820                 825                 830

Val Pro Phe Thr Trp Lys Arg Ser Phe Ser Glu Val Val Asp Glu Asp
        835                 840                 845

Gly Leu Leu Trp Leu Glu Gly Lys Gln Asn Leu Asp Gly Trp Val Trp
    850                 855                 860

Gln Gly Asn Ser Ile Val Ile Thr Tyr Thr Gly Asp Glu Gly Met Thr
865                 870                 875                 880

Arg Val Ile Pro Ala Asn Pro Lys Gly Asp Pro Thr Asn Arg Ala Lys
                885                 890                 895

Gly Leu Glu Ala Val Ser Val Ala Ser Met Asn Leu Leu Ile Asp Asn
            900                 905                 910

Trp Ile Pro Val Arg Pro Arg Asn Gly Gly Lys Val Gln Ile Ile Asn
        915                 920                 925

Leu Gln Ser Leu Tyr Cys Ser Arg Asp Gln Trp Arg Leu Ser Leu Pro
    930                 935                 940

Arg Asp Asp Met Glu Leu Ala Ala Leu Ala Leu Leu Val Cys Ile Gly
945                 950                 955                 960

Gln Ile Ile Ala Pro Ala Lys Asp Asp Val Glu Phe Arg His Arg Ile
                965                 970                 975

Met Asn Pro Leu Thr Glu Asp Glu Phe Gln Gln Leu Ile Ala Pro Trp
            980                 985                 990

Ile Asp Met Phe Tyr Leu Asn His  Ala Glu His Pro Phe  Met Gln Thr
        995                 1000                1005

Lys Gly  Val Lys Ala Asn Asp  Val Thr Pro Met Glu  Lys Leu Leu
    1010                1015                1020

Ala Gly  Val Ser Gly Ala Thr  Asn Cys Ala Phe Val  Asn Gln Pro
    1025                1030                1035

Gly Gln  Gly Glu Ala Leu Cys  Gly Gly Cys Thr Ala  Ile Ala Leu
    1040                1045                1050

Phe Asn  Gln Ala Asn Gln Ala  Pro Gly Phe Gly Gly  Gly Phe Lys
    1055                1060                1065
```

```
Ser Gly  Leu Arg Gly Gly Thr  Pro Val Thr Thr Phe  Val Arg Gly
    1070                 1075                 1080

Ile Asp  Leu Arg Ser Thr Val  Leu Leu Asn Val Leu  Thr Leu Pro
    1085                 1090                 1095

Arg Leu  Gln Lys Gln Phe Pro  Asn Glu Ser His Thr  Glu Asn Gln
    1100                 1105                 1110

Pro Thr  Trp Ile Lys Pro Ile  Lys Ser Asn Glu Ser  Ile Pro Ala
    1115                 1120                 1125

Ser Ser  Ile Gly Phe Val Arg  Gly Leu Phe Trp Gln  Pro Ala His
    1130                 1135                 1140

Ile Glu  Leu Cys Asp Pro Ile  Gly Ile Gly Lys Cys  Ser Cys Cys
    1145                 1150                 1155

Gly Gln  Glu Ser Asn Leu Arg  Tyr Thr Gly Phe Leu  Lys Glu Lys
    1160                 1165                 1170

Phe Thr  Phe Thr Val Asn Gly  Leu Trp Pro His Pro  His Ser Pro
    1175                 1180                 1185

Cys Leu  Val Thr Val Lys Lys  Gly Glu Val Glu Glu  Lys Phe Leu
    1190                 1195                 1200

Ala Phe  Thr Thr Ser Ala Pro  Ser Trp Thr Gln Ile  Ser Arg Val
    1205                 1210                 1215

Val Val  Asp Lys Ile Ile Gln  Asn Glu Asn Gly Asn  Arg Val Ala
    1220                 1225                 1230

Ala Val  Val Asn Gln Phe Arg  Asn Ile Ala Pro Gln  Ser Pro Leu
    1235                 1240                 1245

Glu Leu  Ile Met Gly Gly Tyr  Arg Asn Asn Gln Ala  Ser Ile Leu
    1250                 1255                 1260

Glu Arg  Arg His Asp Val Leu  Met Phe Asn Gln Gly  Trp Gln Gln
    1265                 1270                 1275

Tyr Gly  Asn Val Ile Asn Glu  Ile Val Thr Val Gly  Leu Gly Tyr
    1280                 1285                 1290

Lys Thr  Ala Leu Arg Lys Ala  Leu Tyr Thr Phe Ala  Glu Gly Phe
```

1295 1300 1305

Lys Asn Lys Asp Phe Lys Gly Ala Gly Val Ser Val His Glu Thr
1310 1315 1320

Ala Glu Arg His Phe Tyr Arg Gln Ser Glu Leu Leu Ile Pro Asp
1325 1330 1335

Val Leu Ala Asn Val Asn Phe Ser Gln Ala Asp Glu Val Ile Ala
1340 1345 1350

Asp Leu Arg Asp Lys Leu His Gln Leu Cys Glu Met Leu Phe Asn
1355 1360 1365

Gln Ser Val Ala Pro Tyr Ala His His Pro Lys Leu Ile Ser Thr
1370 1375 1380

Leu Ala Leu Ala Arg Ala Thr Leu Tyr Lys His Leu Arg Glu Leu
1385 1390 1395

Lys Pro Gln Gly Gly Pro Ser Asn Gly
1400 1405

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<211> 49
<212> DNA
<213> Artificial Sequence

<220>
<223> CASCADE sequence cleavage

<400> 47
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