<110> ToolGen Incorporated

<120> Target Specific CRISPR mutant

<130> OPP17-026-PCT-SG

<150> US 62/529601
<151> 2017-07-07

<150> US 62/608722
<151> 2017-12-21

<160> 37

<170> KoPatentIn 3.0

<210> 1
<211> 1368
<212> PRT
<213> Streptococcus pyogenes

<400> 1
Met Asp Lys Lys Tyr Ser Ile Gly Leu Asp Ile Gly Thr Asn Ser Val
1 5 10 15

Gly Trp Ala Val Ile Thr Asp Glu Tyr Lys Val Pro Ser Lys Lys Phe
20 25 30

Lys Val Leu Gly Asn Thr Asp Arg His Ser Ile Lys Lys Asn Leu Ile
35 40 45

Gly Ala Leu Leu Phe Asp Ser Gly Glu Thr Ala Glu Ala Thr Arg Leu
50 55 60

Lys Arg Thr Ala Arg Arg Arg Tyr Thr Arg Arg Lys Asn Arg Ile Cys
65 70 75 80

Tyr Leu Gln Glu Ile Phe Ser Asn Glu Met Ala Lys Val Asp Asp Ser
85 90 95

Phe Phe His Arg Leu Glu Glu Ser Phe Leu Val Glu Glu Asp Lys Lys
100 105 110

His Glu Arg His Pro Ile Phe Gly Asn Ile Val Asp Glu Val Ala Tyr
115 120 125

His Glu Lys Tyr Pro Thr Ile Tyr His Leu Arg Lys Lys Leu Val Asp
130 135 140

Ser Thr Asp Lys Ala Asp Leu Arg Leu Ile Tyr Leu Ala Leu Ala His
145 150 155 160

```
Met Ile Lys Phe Arg Gly His Phe Leu Ile Glu Gly Asp Leu Asn Pro
            165                 170                 175

Asp Asn Ser Asp Val Asp Lys Leu Phe Ile Gln Leu Val Gln Thr Tyr
        180                 185                 190

Asn Gln Leu Phe Glu Glu Asn Pro Ile Asn Ala Ser Gly Val Asp Ala
    195                 200                 205

Lys Ala Ile Leu Ser Ala Arg Leu Ser Lys Ser Arg Arg Leu Glu Asn
210                 215                 220

Leu Ile Ala Gln Leu Pro Gly Glu Lys Lys Asn Gly Leu Phe Gly Asn
225                 230                 235                 240

Leu Ile Ala Leu Ser Leu Gly Leu Thr Pro Asn Phe Lys Ser Asn Phe
            245                 250                 255

Asp Leu Ala Glu Asp Ala Lys Leu Gln Leu Ser Lys Asp Thr Tyr Asp
        260                 265                 270

Asp Asp Leu Asp Asn Leu Leu Ala Gln Ile Gly Asp Gln Tyr Ala Asp
    275                 280                 285

Leu Phe Leu Ala Ala Lys Asn Leu Ser Asp Ala Ile Leu Leu Ser Asp
290                 295                 300

Ile Leu Arg Val Asn Thr Glu Ile Thr Lys Ala Pro Leu Ser Ala Ser
305                 310                 315                 320

Met Ile Lys Arg Tyr Asp Glu His His Gln Asp Leu Thr Leu Leu Lys
            325                 330                 335

Ala Leu Val Arg Gln Gln Leu Pro Glu Lys Tyr Lys Glu Ile Phe Phe
        340                 345                 350

Asp Gln Ser Lys Asn Gly Tyr Ala Gly Tyr Ile Asp Gly Gly Ala Ser
    355                 360                 365

Gln Glu Glu Phe Tyr Lys Phe Ile Lys Pro Ile Leu Glu Lys Met Asp
370                 375                 380

Gly Thr Glu Glu Leu Leu Val Lys Leu Asn Arg Glu Asp Leu Leu Arg
385                 390                 395                 400

Lys Gln Arg Thr Phe Asp Asn Gly Ser Ile Pro His Gln Ile His Leu
            405                 410                 415

Gly Glu Leu His Ala Ile Leu Arg Arg Gln Glu Asp Phe Tyr Pro Phe
        420                 425                 430
```

Leu Lys Asp Asn Arg Glu Lys Ile Glu Lys Ile Leu Thr Phe Arg Ile
435 440 445

Pro Tyr Tyr Val Gly Pro Leu Ala Arg Gly Asn Ser Arg Phe Ala Trp
450 455 460

Met Thr Arg Lys Ser Glu Glu Thr Ile Thr Pro Trp Asn Phe Glu Glu
465 470 475 480

Val Val Asp Lys Gly Ala Ser Ala Gln Ser Phe Ile Glu Arg Met Thr
485 490 495

Asn Phe Asp Lys Asn Leu Pro Asn Glu Lys Val Leu Pro Lys His Ser
500 505 510

Leu Leu Tyr Glu Tyr Phe Thr Val Tyr Asn Glu Leu Thr Lys Val Lys
515 520 525

Tyr Val Thr Glu Gly Met Arg Lys Pro Ala Phe Leu Ser Gly Glu Gln
530 535 540

Lys Lys Ala Ile Val Asp Leu Leu Phe Lys Thr Asn Arg Lys Val Thr
545 550 555 560

Val Lys Gln Leu Lys Glu Asp Tyr Phe Lys Lys Ile Glu Cys Phe Asp
565 570 575

Ser Val Glu Ile Ser Gly Val Glu Asp Arg Phe Asn Ala Ser Leu Gly
580 585 590

Thr Tyr His Asp Leu Leu Lys Ile Ile Lys Asp Lys Asp Phe Leu Asp
595 600 605

Asn Glu Glu Asn Glu Asp Ile Leu Glu Asp Ile Val Leu Thr Leu Thr
610 615 620

Leu Phe Glu Asp Arg Glu Met Ile Glu Glu Arg Leu Lys Thr Tyr Ala
625 630 635 640

His Leu Phe Asp Asp Lys Val Met Lys Gln Leu Lys Arg Arg Arg Tyr
645 650 655

Thr Gly Trp Gly Arg Leu Ser Arg Lys Leu Ile Asn Gly Ile Arg Asp
660 665 670

Lys Gln Ser Gly Lys Thr Ile Leu Asp Phe Leu Lys Ser Asp Gly Phe
675 680 685

Ala Asn Arg Asn Phe Met Gln Leu Ile His Asp Asp Ser Leu Thr Phe
690 695 700

```
Lys Glu Asp Ile Gln Lys Ala Gln Val Ser Gly Gln Gly Asp Ser Leu
705             710             715             720

His Glu His Ile Ala Asn Leu Ala Gly Ser Pro Ala Ile Lys Lys Gly
            725             730             735

Ile Leu Gln Thr Val Lys Val Val Asp Glu Leu Val Lys Val Met Gly
        740             745             750

Arg His Lys Pro Glu Asn Ile Val Ile Glu Met Ala Arg Glu Asn Gln
    755             760             765

Thr Thr Gln Lys Gly Gln Lys Asn Ser Arg Glu Arg Met Lys Arg Ile
770             775             780

Glu Glu Gly Ile Lys Glu Leu Gly Ser Gln Ile Leu Lys Glu His Pro
785             790             795             800

Val Glu Asn Thr Gln Leu Gln Asn Glu Lys Leu Tyr Leu Tyr Tyr Leu
            805             810             815

Gln Asn Gly Arg Asp Met Tyr Val Asp Gln Glu Leu Asp Ile Asn Arg
        820             825             830

Leu Ser Asp Tyr Asp Val Asp His Ile Val Pro Gln Ser Phe Leu Lys
    835             840             845

Asp Asp Ser Ile Asp Asn Lys Val Leu Thr Arg Ser Asp Lys Asn Arg
850             855             860

Gly Lys Ser Asp Asn Val Pro Ser Glu Glu Val Val Lys Lys Met Lys
865             870             875             880

Asn Tyr Trp Arg Gln Leu Leu Asn Ala Lys Leu Ile Thr Gln Arg Lys
            885             890             895

Phe Asp Asn Leu Thr Lys Ala Glu Arg Gly Gly Leu Ser Glu Leu Asp
        900             905             910

Lys Ala Gly Phe Ile Lys Arg Gln Leu Val Glu Thr Arg Gln Ile Thr
    915             920             925

Lys His Val Ala Gln Ile Leu Asp Ser Arg Met Asn Thr Lys Tyr Asp
930             935             940

Glu Asn Asp Lys Leu Ile Arg Glu Val Lys Val Ile Thr Leu Lys Ser
945             950             955             960

Lys Leu Val Ser Asp Phe Arg Lys Asp Phe Gln Phe Tyr Lys Val Arg
            965             970             975
```

Glu Ile Asn Asn Tyr His His Ala His Asp Ala Tyr Leu Asn Ala Val
980 985 990

Val Gly Thr Ala Leu Ile Lys Lys Tyr Pro Lys Leu Glu Ser Glu Phe
995 1000 1005

Val Tyr Gly Asp Tyr Lys Val Tyr Asp Val Arg Lys Met Ile Ala Lys
1010 1015 1020

Ser Glu Gln Glu Ile Gly Lys Ala Thr Ala Lys Tyr Phe Phe Tyr Ser
1025 1030 1035 1040

Asn Ile Met Asn Phe Phe Lys Thr Glu Ile Thr Leu Ala Asn Gly Glu
1045 1050 1055

Ile Arg Lys Arg Pro Leu Ile Glu Thr Asn Gly Glu Thr Gly Glu Ile
1060 1065 1070

Val Trp Asp Lys Gly Arg Asp Phe Ala Thr Val Arg Lys Val Leu Ser
1075 1080 1085

Met Pro Gln Val Asn Ile Val Lys Lys Thr Glu Val Gln Thr Gly Gly
1090 1095 1100

Phe Ser Lys Glu Ser Ile Leu Pro Lys Arg Asn Ser Asp Lys Leu Ile
1105 1110 1115 1120

Ala Arg Lys Lys Asp Trp Asp Pro Lys Lys Tyr Gly Gly Phe Asp Ser
1125 1130 1135

Pro Thr Val Ala Tyr Ser Val Leu Val Val Ala Lys Val Glu Lys Gly
1140 1145 1150

Lys Ser Lys Lys Leu Lys Ser Val Lys Glu Leu Leu Gly Ile Thr Ile
1155 1160 1165

Met Glu Arg Ser Ser Phe Glu Lys Asn Pro Ile Asp Phe Leu Glu Ala
1170 1175 1180

Lys Gly Tyr Lys Glu Val Lys Lys Asp Leu Ile Ile Lys Leu Pro Lys
1185 1190 1195 1200

Tyr Ser Leu Phe Glu Leu Glu Asn Gly Arg Lys Arg Met Leu Ala Ser
1205 1210 1215

Ala Gly Glu Leu Gln Lys Gly Asn Glu Leu Ala Leu Pro Ser Lys Tyr
1220 1225 1230

Val Asn Phe Leu Tyr Leu Ala Ser His Tyr Glu Lys Leu Lys Gly Ser
1235 1240 1245

```
Pro Glu Asp Asn Glu Gln Lys Gln Leu Phe Val Glu Gln His Lys His
  1250             1255             1260

Tyr Leu Asp Glu Ile Ile Glu Gln Ile Ser Glu Phe Ser Lys Arg Val
1265             1270             1275             1280

Ile Leu Ala Asp Ala Asn Leu Asp Lys Val Leu Ser Ala Tyr Asn Lys
            1285             1290             1295

His Arg Asp Lys Pro Ile Arg Glu Gln Ala Glu Asn Ile Ile His Leu
         1300             1305             1310

Phe Thr Leu Thr Asn Leu Gly Ala Pro Ala Ala Phe Lys Tyr Phe Asp
      1315             1320             1325

Thr Thr Ile Asp Arg Lys Arg Tyr Thr Ser Thr Lys Glu Val Leu Asp
  1330             1335             1340

Ala Thr Leu Ile His Gln Ser Ile Thr Gly Leu Tyr Glu Thr Arg Ile
1345             1350             1355             1360

Asp Leu Ser Gln Leu Gly Gly Asp
            1365
```

<210> 2
<211> 87
<212> PRT
<213> Streptococcus pyogenes

<400> 2

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Phe Glu Glu Asn Pro Ile Asn Ala Ser Gly Val Asp Ala Lys Ala Ile
 1               5                  10                  15

Leu Ser Ala Arg Leu Ser Lys Ser Arg Arg Leu Glu Asn Leu Ile Ala
           20                  25                  30

Gln Leu Pro Gly Glu Lys Lys Asn Gly Leu Phe Gly Asn Leu Ile Ala
        35                  40                  45

Leu Ser Leu Gly Leu Thr Pro Asn Phe Lys Ser Asn Phe Asp Leu Ala
    50                  55                  60

Glu Asp Ala Lys Leu Gln Leu Ser Lys Asp Thr Tyr Asp Asp Asp Leu
 65                  70                  75                  80

Asp Asn Leu Leu Ala Gln Ile
                85
```

<210> 3
<211> 79
<212> PRT
<213> Streptococcus pyogenes

<400> 3
Pro Leu Ser Ala Ser Met Ile Lys Arg Tyr Asp Glu His His Gln Asp
1 5 10 15

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

Lys Glu Ile Phe Phe Asp Gln Ser Lys Asn Gly Tyr Ala Gly Tyr Ile
35 40 45

Asp Gly Gly Ala Ser Gln Glu Glu Phe Tyr Lys Phe Ile Lys Pro Ile
50 55 60

Leu Glu Lys Met Asp Gly Thr Glu Glu Leu Leu Val Lys Leu Asn
65 70 75

<210> 4
<211> 103
<212> PRT
<213> Streptococcus pyogenes

<400> 4
Lys His Ser Leu Leu Tyr Glu Tyr Phe Thr Val Tyr Asn Glu Leu Thr
1 5 10 15

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

Gly Glu Gln Lys Lys Ala Ile Val Asp Leu Leu Phe Lys Thr Asn Arg
35 40 45

Lys Val Thr Val Lys Gln Leu Lys Glu Asp Tyr Phe Lys Lys Ile Glu
50 55 60

Cys Phe Asp Ser Val Glu Ile Ser Gly Val Glu Asp Arg Phe Asn Ala
65 70 75 80

Ser Leu Gly Thr Tyr His Asp Leu Leu Lys Ile Ile Lys Asp Lys Asp
85 90 95

Phe Leu Asp Asn Glu Glu Asn
100

<210> 5

<211> 21
<212> PRT
<213> Streptococcus pyogenes

<400> 5
Thr Ile Leu Asp Phe Leu Lys Ser Asp Gly Phe Ala Asn Arg Asn Phe
1 5 10 15

Met Gln Leu Ile His
20

<210> 6
<211> 22
<212> PRT
<213> Streptococcus pyogenes

<400> 6
Met Asp Lys Lys Tyr Ser Ile Gly Leu Asp Ile Gly Thr Asn Ser Val
1 5 10 15

Gly Trp Ala Val Ile Thr
20

<210> 7
<211> 40
<212> PRT
<213> Streptococcus pyogenes

<400> 7
Pro Ala Ile Lys Lys Gly Ile Leu Gln Thr Val Lys Val Val Asp Glu
1 5 10 15

Leu Val Lys Val Met Gly Arg His Lys Pro Glu Asn Ile Val Ile Glu
20 25 30

Met Ala Arg Glu Asn Gln Thr Thr
35 40

<210> 8
<211> 115
<212> PRT
<213> Streptococcus pyogenes

<400> 8
Gln Ile Thr Lys His Val Ala Gln Ile Leu Asp Ser Arg Met Asn Thr
1 5 10 15

Lys Tyr Asp Glu Asn Asp Lys Leu Ile Arg Glu Val Lys Val Ile Thr

```
          20                  25                  30

Leu Lys Ser Lys Leu Val Ser Asp Phe Arg Lys Asp Phe Gln Phe Tyr
       35                  40                  45

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

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

Ser Glu Phe Val Tyr Gly Asp Tyr Lys Val Tyr Asp Val Arg Lys Met
                85                  90                  95

Ile Ala Lys Ser Glu Gln Glu Ile Gly Lys Ala Thr Ala Lys Tyr Phe
          100                 105                 110

Phe Tyr Ser
       115


<210>   9
<211>   126
<212>   PRT
<213>   Streptococcus pyogenes

<400>   9
Lys Asn Ser Arg Glu Arg Met Lys Arg Ile Glu Glu Gly Ile Lys Glu
  1               5                  10                  15

Leu Gly Ser Gln Ile Leu Lys Glu His Pro Val Glu Asn Thr Gln Leu
           20                  25                  30

Gln Asn Glu Lys Leu Tyr Leu Tyr Tyr Leu Gln Asn Gly Arg Asp Met
       35                  40                  45

Tyr Val Asp Gln Glu Leu Asp Ile Asn Arg Leu Ser Asp Tyr Asp Val
    50                  55                  60

Asp His Ile Val Pro Gln Ser Phe Leu Lys Asp Asp Ser Ile Asp Asn
 65                  70                  75                  80

Lys Val Leu Thr Arg Ser Asp Lys Asn Arg Gly Lys Ser Asp Asn Val
                85                  90                  95

Pro Ser Glu Glu Val Val Lys Lys Met Lys Asn Tyr Trp Arg Gln Leu
          100                 105                 110

Leu Asn Ala Lys Leu Ile Thr Gln Arg Lys Phe Asp Asn Leu
       115                 120                 125
```

<210> 10
<211> 41
<212> PRT
<213> Streptococcus pyogenes

<400> 10
Glu Val Gln Thr Gly Gly Phe Ser Lys Glu Ser Ile Leu Pro Lys Arg
1 5 10 15

Asn Ser Asp Lys Leu Ile Ala Arg Lys Lys Asp Trp Asp Pro Lys Lys
20 25 30

Tyr Gly Gly Phe Asp Ser Pro Thr Val
35 40

<210> 11
<211> 1368
<212> PRT
<213> Artificial Sequence

<220>
<223> Streptococcus pyogenes Cas9 variant

<400> 11
Met Asp Lys Lys Tyr Ser Ile Gly Leu Asp Ile Gly Thr Asn Ser Val
1 5 10 15

Gly Trp Ala Val Ile Thr Asp Glu Tyr Lys Val Pro Ser Lys Lys Phe
20 25 30

Lys Val Leu Gly Asn Thr Asp Arg His Ser Ile Lys Lys Asn Leu Ile
35 40 45

Gly Ala Leu Leu Phe Asp Ser Gly Glu Thr Ala Glu Ala Thr Arg Leu
50 55 60

Lys Arg Thr Ala Arg Arg Arg Tyr Thr Arg Arg Lys Asn Arg Ile Cys
65 70 75 80

Tyr Leu Gln Glu Ile Phe Ser Asn Glu Met Ala Lys Val Asp Asp Ser
85 90 95

Phe Phe His Arg Leu Glu Glu Ser Phe Leu Val Glu Glu Asp Lys Lys
100 105 110

His Glu Arg His Pro Ile Phe Gly Asn Ile Val Asp Glu Val Ala Tyr
115 120 125

```
His Glu Lys Tyr Pro Thr Ile Tyr His Leu Arg Lys Lys Leu Val Asp
   130             135             140

Ser Thr Asp Lys Ala Asp Leu Arg Leu Ile Tyr Leu Ala Leu Ala His
145             150             155             160

Met Ile Lys Phe Arg Gly His Phe Leu Ile Glu Gly Asp Leu Asn Pro
            165             170             175

Asp Asn Ser Asp Val Asp Lys Leu Phe Ile Gln Leu Val Gln Thr Tyr
         180             185             190

Asn Gln Leu Phe Glu Glu Asn Pro Ile Asn Ala Ser Gly Val Asp Ala
      195             200             205

Lys Ala Ile Leu Ser Ala Arg Leu Ser Lys Ser Arg Arg Leu Glu Asn
   210             215             220

Leu Ile Ala Gln Leu Pro Gly Glu Lys Lys Asn Gly Leu Phe Gly Asn
225             230             235             240

Leu Ile Ala Leu Ser Leu Gly Leu Thr Pro Asn Phe Lys Ser Asn Phe
            245             250             255

Asp Leu Ala Glu Asp Ala Lys Leu Gln Leu Ser Lys Asp Thr Tyr Asp
         260             265             270

Asp Asp Leu Asp Asn Leu Leu Ala Gln Ile Gly Asp Gln Tyr Ala Asp
      275             280             285

Leu Phe Leu Ala Ala Lys Asn Leu Ser Asp Ala Ile Leu Leu Ser Asp
   290             295             300

Ile Leu Arg Val Asn Thr Glu Ile Thr Lys Ala Pro Leu Ser Ala Ser
305             310             315             320

Met Ile Lys Arg Tyr Asp Glu His His Gln Asp Leu Thr Leu Leu Lys
            325             330             335

Ala Leu Val Arg Gln Gln Leu Pro Glu Lys Tyr Lys Glu Ile Phe Phe
         340             345             350

Asp Gln Ser Lys Asn Gly Tyr Ala Gly Tyr Ile Asp Gly Gly Ala Ser
      355             360             365

Gln Glu Glu Phe Tyr Lys Phe Ile Lys Pro Ile Leu Glu Lys Met Asp
   370             375             380

Gly Thr Glu Glu Leu Leu Val Lys Leu Asn Arg Glu Asp Leu Leu Arg
385             390             395             400
```

Lys Gln Arg Thr Phe Asp Asn Gly Ser Ile Pro His Gln Ile His Leu
405 410 415

Gly Glu Leu His Ala Ile Leu Arg Arg Gln Glu Asp Phe Tyr Pro Phe
420 425 430

Leu Lys Asp Asn Arg Glu Lys Ile Glu Lys Ile Leu Thr Phe Arg Ile
435 440 445

Pro Tyr Tyr Val Gly Pro Leu Ala Arg Gly Asn Ser Arg Phe Ala Trp
450 455 460

Met Thr Arg Lys Ser Glu Glu Thr Ile Thr Pro Trp Asn Phe Glu Glu
465 470 475 480

Val Val Asp Lys Gly Ala Ser Ala Gln Ser Phe Ile Glu Arg Met Thr
485 490 495

Asn Phe Asp Lys Asn Leu Pro Asn Glu Lys Val Leu Pro Lys His Ser
500 505 510

Leu Leu Tyr Glu Tyr Phe Thr Val Tyr Asn Glu Leu Thr Lys Val Lys
515 520 525

Tyr Val Thr Glu Gly Met Arg Lys Pro Ala Ser Leu Ser Gly Glu Gln
530 535 540

Lys Lys Ala Ile Val Asp Leu Leu Phe Lys Thr Asn Arg Lys Val Thr
545 550 555 560

Val Lys Gln Leu Lys Glu Asp Tyr Phe Lys Lys Ile Glu Cys Phe Asp
565 570 575

Ser Val Glu Ile Ser Gly Val Glu Asp Arg Phe Asn Ala Ser Leu Gly
580 585 590

Thr Tyr His Asp Leu Leu Lys Ile Ile Lys Asp Lys Asp Phe Leu Asp
595 600 605

Asn Glu Glu Asn Glu Asp Ile Leu Glu Asp Ile Val Leu Thr Leu Thr
610 615 620

Leu Phe Glu Asp Arg Glu Met Ile Glu Glu Arg Leu Lys Thr Tyr Ala
625 630 635 640

His Leu Phe Asp Asp Lys Val Met Lys Gln Leu Lys Arg Arg Arg Tyr
645 650 655

Thr Gly Trp Gly Arg Leu Ser Arg Lys Leu Ile Asn Gly Ile Arg Asp
660 665 670

Lys Gln Ser Gly Lys Thr Ile Leu Asp Phe Leu Lys Ser Asp Gly Phe
675 680 685

Ala Asn Arg Asn Phe Met Gln Leu Ile His Asp Asp Ser Leu Thr Phe
690 695 700

Lys Glu Asp Ile Gln Lys Ala Gln Val Ser Gly Gln Gly Asp Ser Leu
705 710 715 720

His Glu His Ile Ala Asn Leu Ala Gly Ser Pro Ala Ile Lys Lys Gly
725 730 735

Ile Leu Gln Thr Val Lys Val Val Asp Glu Leu Val Lys Val Met Gly
740 745 750

Arg His Lys Pro Glu Asn Ile Val Ile Glu Ile Ala Arg Glu Asn Gln
755 760 765

Thr Thr Gln Lys Gly Gln Lys Asn Ser Arg Glu Arg Met Lys Arg Ile
770 775 780

Glu Glu Gly Ile Lys Glu Leu Gly Ser Gln Ile Leu Lys Glu His Pro
785 790 795 800

Val Glu Asn Thr Gln Leu Gln Asn Glu Lys Leu Tyr Leu Tyr Tyr Leu
805 810 815

Gln Asn Gly Arg Asp Met Tyr Val Asp Gln Glu Leu Asp Ile Asn Arg
820 825 830

Leu Ser Asp Tyr Asp Val Asp His Ile Val Pro Gln Ser Phe Leu Lys
835 840 845

Asp Asp Ser Ile Asp Asn Lys Val Leu Thr Arg Ser Asp Lys Asn Arg
850 855 860

Gly Lys Ser Asp Asn Val Pro Ser Glu Glu Val Val Lys Lys Met Lys
865 870 875 880

Asn Tyr Trp Arg Gln Leu Leu Asn Ala Asn Leu Ile Thr Gln Arg Lys
885 890 895

Phe Asp Asn Leu Thr Lys Ala Glu Arg Gly Gly Leu Ser Glu Leu Asp
900 905 910

Lys Ala Gly Phe Ile Lys Arg Gln Leu Val Glu Thr Arg Gln Ile Thr
915 920 925

Lys His Val Ala Gln Ile Leu Asp Ser Arg Met Asn Thr Lys Tyr Asp
930 935 940

Glu Asn Asp Lys Leu Ile Arg Glu Val Lys Val Ile Thr Leu Lys Ser
945 950 955 960

Lys Leu Val Ser Asp Phe Arg Lys Asp Phe Gln Phe Tyr Lys Val Arg
965 970 975

Glu Ile Asn Asn Tyr His His Ala His Asp Ala Tyr Leu Asn Ala Val
980 985 990

Val Gly Thr Ala Leu Ile Lys Lys Tyr Pro Lys Leu Glu Ser Glu Phe
995 1000 1005

Val Tyr Gly Asp Tyr Lys Val Tyr Asp Val Arg Lys Met Ile Ala Lys
1010 1015 1020

Ser Glu Gln Glu Ile Gly Lys Ala Thr Ala Lys Tyr Phe Phe Tyr Ser
1025 1030 1035 1040

Asn Ile Met Asn Phe Phe Lys Thr Glu Ile Thr Leu Ala Asn Gly Glu
1045 1050 1055

Ile Arg Lys Arg Pro Leu Ile Glu Thr Asn Gly Glu Thr Gly Glu Ile
1060 1065 1070

Val Trp Asp Lys Gly Arg Asp Phe Ala Thr Val Arg Lys Val Leu Ser
1075 1080 1085

Met Pro Gln Val Asn Ile Val Lys Lys Thr Glu Val Gln Thr Gly Gly
1090 1095 1100

Phe Ser Lys Glu Ser Ile Leu Pro Lys Arg Asn Ser Asp Lys Leu Ile
1105 1110 1115 1120

Ala Arg Lys Lys Asp Trp Asp Pro Lys Lys Tyr Gly Gly Phe Asp Ser
1125 1130 1135

Pro Thr Val Ala Tyr Ser Val Leu Val Val Ala Lys Val Glu Lys Gly
1140 1145 1150

Lys Ser Lys Lys Leu Lys Ser Val Lys Glu Leu Leu Gly Ile Thr Ile
1155 1160 1165

Met Glu Arg Ser Ser Phe Glu Lys Asn Pro Ile Asp Phe Leu Glu Ala
1170 1175 1180

Lys Gly Tyr Lys Glu Val Lys Lys Asp Leu Ile Ile Lys Leu Pro Lys
1185 1190 1195 1200

Tyr Ser Leu Phe Glu Leu Glu Asn Gly Arg Lys Arg Met Leu Ala Ser
1205 1210 1215

```
Ala Gly Glu Leu Gln Lys Gly Asn Glu Leu Ala Leu Pro Ser Lys Tyr
         1220             1225             1230

Val Asn Phe Leu Tyr Leu Ala Ser His Tyr Glu Lys Leu Lys Gly Ser
      1235             1240             1245

Pro Glu Asp Asn Glu Gln Lys Gln Leu Phe Val Glu Gln His Lys His
   1250             1255             1260

Tyr Leu Asp Glu Ile Ile Glu Gln Ile Ser Glu Phe Ser Lys Arg Val
1265             1270             1275             1280

Ile Leu Ala Asp Ala Asn Leu Asp Lys Val Leu Ser Ala Tyr Asn Lys
            1285             1290             1295

His Arg Asp Lys Pro Ile Arg Glu Gln Ala Glu Asn Ile Ile His Leu
         1300             1305             1310

Phe Thr Leu Thr Asn Leu Gly Ala Pro Ala Ala Phe Lys Tyr Phe Asp
      1315             1320             1325

Thr Thr Ile Asp Arg Lys Arg Tyr Thr Ser Thr Lys Glu Val Leu Asp
   1330             1335             1340

Ala Thr Leu Ile His Gln Ser Ile Thr Gly Leu Tyr Glu Thr Arg Ile
1345             1350             1355             1360

Asp Leu Ser Gln Leu Gly Gly Asp
            1365
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<210> 12
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<223> nuclear localization sequence

<400> 12
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Pro Lys Lys Lys Arg Lys Val
  1               5
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<210> 13
<211> 16
<212> PRT
<213> Artificial Sequence

<220>
<223> nuclear localization sequence

<400> 13
Lys Arg Pro Ala Ala Thr Lys Lys Ala Gly Gln Ala Lys Lys Lys Lys
 1   5   10   15

<210> 14
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> nuclear localization sequence

<400> 14
Pro Ala Ala Lys Arg Val Lys Leu Asp
 1   5

<210> 15
<211> 11
<212> PRT
<213> Artificial Sequence

<220>
<223> nuclear localization sequence

<400> 15
Arg Gln Arg Arg Asn Glu Leu Lys Arg Ser Pro
 1   5   10

<210> 16
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
<223> nuclear localization sequence

<400> 16
Asn Gln Ser Ser Asn Phe Gly Pro Met Lys Gly Gly Asn Phe Gly Gly
 1   5   10   15

Arg Ser Ser Gly Pro Tyr Gly Gly Gly Gly Gln Tyr Phe Ala Lys Pro
20 25 30

Arg Asn Gln Gly Gly Tyr
35

<210> 17
<211> 42
<212> PRT
<213> Artificial Sequence

<220>
<223> nuclear localization sequence

<400> 17
Arg Met Arg Ile Glx Phe Lys Asn Lys Gly Lys Asp Thr Ala Glu Leu
1 5 10 15

Arg Arg Arg Arg Val Glu Val Ser Val Glu Leu Arg Lys Ala Lys Lys
20 25 30

Asp Glu Gln Ile Leu Lys Arg Arg Asn Val
35 40

<210> 18
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<223> nuclear localization sequence

<400> 18
Val Ser Arg Lys Arg Pro Arg Pro
1 5

<210> 19
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<223> nuclear localization sequence

<400> 19

Pro Pro Lys Lys Ala Arg Glu Asp
1 5

<210> 20
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<223> nuclear localization sequence

<400> 20
Pro Gln Pro Lys Lys Lys Pro Leu
1 5

<210> 21
<211> 12
<212> PRT
<213> Artificial Sequence

<220>
<223> nuclear localization sequence

<400> 21
Ser Ala Leu Ile Lys Lys Lys Lys Lys Met Ala Pro
1 5 10

<210> 22
<211> 5
<212> PRT
<213> Artificial Sequence

<220>
<223> nuclear localization sequence

<400> 22
Asp Arg Leu Arg Arg
1 5

<210> 23
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<223> nuclear localization sequence

<400> 23
Pro Lys Gln Lys Lys Arg Lys
 1   5

<210> 24
<211> 10
<212> PRT
<213> Artificial Sequence

<220>
<223> nuclear localization sequence

<400> 24
Arg Lys Leu Lys Lys Lys Ile Lys Lys Leu
 1   5   10

<210> 25
<211> 10
<212> PRT
<213> Artificial Sequence

<220>
<223> nuclear localization sequence

<400> 25
Arg Glu Lys Lys Lys Phe Leu Lys Arg Arg
 1   5   10

<210> 26
<211> 20
<212> PRT
<213> Artificial Sequence

<220>
<223> nuclear localization sequence

<400> 26
Lys Arg Lys Gly Asp Glu Val Asp Gly Val Asp Glu Val Ala Lys Lys
 1   5   10   15

Lys Ser Lys Lys

20

<210> 27
<211> 17
<212> PRT
<213> Artificial Sequence

<220>
<223> nuclear localization sequence

<400> 27
Arg Lys Cys Leu Gln Ala Gly Met Asn Leu Glu Ala Arg Lys Thr Lys
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