SEQUENCE LISTING

<110> NATIONAL UNIVERSITY CORPORATION KOBE UNIVERSITY

<120> Stable genome editing complex having few side effects and nuclei acid encoding the same

<130> 092815

<150> JP 2017-225221
<151> 2017-11-22

<160> 330

<170> PatentIn version 3.5

<210> 1
<211> 4104
<212> DNA
<213> Streptococcus pyogenes

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<221> CDS
<222> (1)..(4104)
<223> dCas9 (D10A and H840A)

<220>
<221> mutation
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atg gat aag aaa tac tca ata ggc tta gct atc ggc aca aat agc gtc         48
Met Asp Lys Lys Tyr Ser Ile Gly Leu Ala Ile Gly Thr Asn Ser Val
1               5                   10                  15

gga tgg gcg gtg atc act gat gaa tat aag gtt ccg tct aaa aag ttc         96
Gly Trp Ala Val Ile Thr Asp Glu Tyr Lys Val Pro Ser Lys Lys Phe
            20                  25                  30

aag gtt ctg gga aat aca gac cgc cac agt atc aaa aaa aat ctt ata        144
Lys Val Leu Gly Asn Thr Asp Arg His Ser Ile Lys Lys Asn Leu Ile
        35                  40                  45

ggg gct ctt tta ttt gac agt gga gag aca gcg gaa gcg act cgt ctc        192
Gly Ala Leu Leu Phe Asp Ser Gly Glu Thr Ala Glu Ala Thr Arg Leu
    50                  55                  60

aaa cgg aca gct cgt aga agg tat aca cgt cgg aag aat cgt att tgt        240
Lys Arg Thr Ala Arg Arg Arg Tyr Thr Arg Arg Lys Asn Arg Ile Cys
65                  70                  75                  80

tat cta cag gag att ttt tca aat gag atg gcg aaa gta gat gat agt        288
Tyr Leu Gln Glu Ile Phe Ser Asn Glu Met Ala Lys Val Asp Asp Ser
                85                  90                  95

ttc ttt cat cga ctt gaa gag tct ttt ttg gtg gaa gaa gac aag aag        336
Phe Phe His Arg Leu Glu Glu Ser Phe Leu Val Glu Glu Asp Lys Lys
            100                 105                 110
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cat gaa cgt cat cct att ttt gga aat ata gta gat gaa gtt gct tat        384
His Glu Arg His Pro Ile Phe Gly Asn Ile Val Asp Glu Val Ala Tyr
        115                 120                 125

cat gag aaa tat cca act atc tat cat ctg cga aaa aaa ttg gta gat        432
His Glu Lys Tyr Pro Thr Ile Tyr His Leu Arg Lys Lys Leu Val Asp
    130                 135                 140

tct act gat aaa gcg gat ttg cgc tta atc tat ttg gcc tta gcg cat        480
Ser Thr Asp Lys Ala Asp Leu Arg Leu Ile Tyr Leu Ala Leu Ala His
145                 150                 155                 160

atg att aag ttt cgt ggt cat ttt ttg att gag gga gat tta aat cct        528
Met Ile Lys Phe Arg Gly His Phe Leu Ile Glu Gly Asp Leu Asn Pro
                165                 170                 175

gat aat agt gat gtg gac aaa cta ttt atc cag ttg gta caa acc tac        576
Asp Asn Ser Asp Val Asp Lys Leu Phe Ile Gln Leu Val Gln Thr Tyr
            180                 185                 190

aat caa tta ttt gaa gaa aac cct att aac gca agt gga gta gat gct        624
Asn Gln Leu Phe Glu Glu Asn Pro Ile Asn Ala Ser Gly Val Asp Ala
        195                 200                 205

aaa gcg att ctt tct gca cga ttg agt aaa tca aga cga tta gaa aat        672
Lys Ala Ile Leu Ser Ala Arg Leu Ser Lys Ser Arg Arg Leu Glu Asn
    210                 215                 220

ctc att gct cag ctc ccc ggt gag aag aaa aat ggc tta ttt ggg aat        720
Leu Ile Ala Gln Leu Pro Gly Glu Lys Lys Asn Gly Leu Phe Gly Asn
225                 230                 235                 240

ctc att gct ttg tca ttg ggt ttg acc cct aat ttt aaa tca aat ttt        768
Leu Ile Ala Leu Ser Leu Gly Leu Thr Pro Asn Phe Lys Ser Asn Phe
                245                 250                 255

gat ttg gca gaa gat gct aaa tta cag ctt tca aaa gat act tac gat        816
Asp Leu Ala Glu Asp Ala Lys Leu Gln Leu Ser Lys Asp Thr Tyr Asp
            260                 265                 270

gat gat tta gat aat tta ttg gcg caa att gga gat caa tat gct gat        864
Asp Asp Leu Asp Asn Leu Leu Ala Gln Ile Gly Asp Gln Tyr Ala Asp
        275                 280                 285

ttg ttt ttg gca gct aag aat tta tca gat gct att tta ctt tca gat        912
Leu Phe Leu Ala Ala Lys Asn Leu Ser Asp Ala Ile Leu Leu Ser Asp
    290                 295                 300

atc cta aga gta aat act gaa ata act aag gct ccc cta tca gct tca        960
Ile Leu Arg Val Asn Thr Glu Ile Thr Lys Ala Pro Leu Ser Ala Ser
305                 310                 315                 320

atg att aaa cgc tac gat gaa cat cat caa gac ttg act ctt tta aaa       1008
Met Ile Lys Arg Tyr Asp Glu His His Gln Asp Leu Thr Leu Leu Lys
                325                 330                 335

gct tta gtt cga caa caa ctt cca gaa aag tat aaa gaa atc ttt ttt       1056
Ala Leu Val Arg Gln Gln Leu Pro Glu Lys Tyr Lys Glu Ile Phe Phe
            340                 345                 350

gat caa tca aaa aac gga tat gca ggt tat att gat ggg gga gct agc       1104
Asp Gln Ser Lys Asn Gly Tyr Ala Gly Tyr Ile Asp Gly Gly Ala Ser
        355                 360                 365
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caa gaa gaa ttt tat aaa ttt atc aaa cca att tta gaa aaa atg gat       1152
Gln Glu Glu Phe Tyr Lys Phe Ile Lys Pro Ile Leu Glu Lys Met Asp
    370                 375                 380

ggt act gag gaa tta ttg gtg aaa cta aat cgt gaa gat ttg ctg cgc       1200
Gly Thr Glu Glu Leu Leu Val Lys Leu Asn Arg Glu Asp Leu Leu Arg
385                 390                 395                 400

aag caa cgg acc ttt gac aac ggc tct att ccc cat caa att cac ttg       1248
Lys Gln Arg Thr Phe Asp Asn Gly Ser Ile Pro His Gln Ile His Leu
                405                 410                 415

ggt gag ctg cat gct att ttg aga aga caa gaa gac ttt tat cca ttt       1296
Gly Glu Leu His Ala Ile Leu Arg Arg Gln Glu Asp Phe Tyr Pro Phe
            420                 425                 430

tta aaa gac aat cgt gag aag att gaa aaa atc ttg act ttt cga att       1344
Leu Lys Asp Asn Arg Glu Lys Ile Glu Lys Ile Leu Thr Phe Arg Ile
        435                 440                 445

cct tat tat gtt ggt cca ttg gcg cgt ggc aat agt cgt ttt gca tgg       1392
Pro Tyr Tyr Val Gly Pro Leu Ala Arg Gly Asn Ser Arg Phe Ala Trp
    450                 455                 460

atg act cgg aag tct gaa gaa aca att acc cca tgg aat ttt gaa gaa       1440
Met Thr Arg Lys Ser Glu Glu Thr Ile Thr Pro Trp Asn Phe Glu Glu
465                 470                 475                 480

gtt gtc gat aaa ggt gct tca gct caa tca ttt att gaa cgc atg aca       1488
Val Val Asp Lys Gly Ala Ser Ala Gln Ser Phe Ile Glu Arg Met Thr
                485                 490                 495

aac ttt gat aaa aat ctt cca aat gaa aaa gta cta cca aaa cat agt       1536
Asn Phe Asp Lys Asn Leu Pro Asn Glu Lys Val Leu Pro Lys His Ser
            500                 505                 510

ttg ctt tat gag tat ttt acg gtt tat aac gaa ttg aca aag gtc aaa       1584
Leu Leu Tyr Glu Tyr Phe Thr Val Tyr Asn Glu Leu Thr Lys Val Lys
        515                 520                 525

tat gtt act gaa gga atg cga aaa cca gca ttt ctt tca ggt gaa cag       1632
Tyr Val Thr Glu Gly Met Arg Lys Pro Ala Phe Leu Ser Gly Glu Gln
    530                 535                 540

aag aaa gcc att gtt gat tta ctc ttc aaa aca aat cga aaa gta acc       1680
Lys Lys Ala Ile Val Asp Leu Leu Phe Lys Thr Asn Arg Lys Val Thr
545                 550                 555                 560

gtt aag caa tta aaa gaa gat tat ttc aaa aaa ata gaa tgt ttt gat       1728
Val Lys Gln Leu Lys Glu Asp Tyr Phe Lys Lys Ile Glu Cys Phe Asp
                565                 570                 575

agt gtt gaa att tca gga gtt gaa gat aga ttt aat gct tca tta ggt       1776
Ser Val Glu Ile Ser Gly Val Glu Asp Arg Phe Asn Ala Ser Leu Gly
            580                 585                 590

acc tac cat gat ttg cta aaa att att aaa gat aaa gat ttt ttg gat       1824
Thr Tyr His Asp Leu Leu Lys Ile Ile Lys Asp Lys Asp Phe Leu Asp
        595                 600                 605

aat gaa gaa aat gaa gat atc tta gag gat att gtt tta aca ttg acc       1872
Asn Glu Glu Asn Glu Asp Ile Leu Glu Asp Ile Val Leu Thr Leu Thr
    610                 615                 620
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tta ttt gaa gat agg gag atg att gag gaa aga ctt aaa aca tat gct       1920
Leu Phe Glu Asp Arg Glu Met Ile Glu Glu Arg Leu Lys Thr Tyr Ala
625                 630                 635                 640

cac ctc ttt gat gat aag gtg atg aaa cag ctt aaa cgt cgc cgt tat       1968
His Leu Phe Asp Asp Lys Val Met Lys Gln Leu Lys Arg Arg Arg Tyr
                645                 650                 655

act ggt tgg gga cgt ttg tct cga aaa ttg att aat ggt att agg gat       2016
Thr Gly Trp Gly Arg Leu Ser Arg Lys Leu Ile Asn Gly Ile Arg Asp
            660                 665                 670

aag caa tct ggc aaa aca ata tta gat ttt ttg aaa tca gat ggt ttt       2064
Lys Gln Ser Gly Lys Thr Ile Leu Asp Phe Leu Lys Ser Asp Gly Phe
        675                 680                 685

gcc aat cgc aat ttt atg cag ctg atc cat gat gat agt ttg aca ttt       2112
Ala Asn Arg Asn Phe Met Gln Leu Ile His Asp Asp Ser Leu Thr Phe
    690                 695                 700

aaa gaa gac att caa aaa gca caa gtg tct gga caa ggc gat agt tta       2160
Lys Glu Asp Ile Gln Lys Ala Gln Val Ser Gly Gln Gly Asp Ser Leu
705                 710                 715                 720

cat gaa cat att gca aat tta gct ggt agc cct gct att aaa aaa ggt       2208
His Glu His Ile Ala Asn Leu Ala Gly Ser Pro Ala Ile Lys Lys Gly
                725                 730                 735

att tta cag act gta aaa gtt gtt gat gaa ttg gtc aaa gta atg ggg       2256
Ile Leu Gln Thr Val Lys Val Val Asp Glu Leu Val Lys Val Met Gly
            740                 745                 750

cgg cat aag cca gaa aat atc gtt att gaa atg gca cgt gaa aat cag       2304
Arg His Lys Pro Glu Asn Ile Val Ile Glu Met Ala Arg Glu Asn Gln
        755                 760                 765

aca act caa aag ggc cag aaa aat tcg cga gag cgt atg aaa cga atc       2352
Thr Thr Gln Lys Gly Gln Lys Asn Ser Arg Glu Arg Met Lys Arg Ile
    770                 775                 780

gaa gaa ggt atc aaa gaa tta gga agt cag att ctt aaa gag cat cct       2400
Glu Glu Gly Ile Lys Glu Leu Gly Ser Gln Ile Leu Lys Glu His Pro
785                 790                 795                 800

gtt gaa aat act caa ttg caa aat gaa aag ctc tat ctc tat tat ctc       2448
Val Glu Asn Thr Gln Leu Gln Asn Glu Lys Leu Tyr Leu Tyr Tyr Leu
                805                 810                 815

caa aat gga aga gac atg tat gtg gac caa gaa tta gat att aat cgt       2496
Gln Asn Gly Arg Asp Met Tyr Val Asp Gln Glu Leu Asp Ile Asn Arg
            820                 825                 830

tta agt gat tat gat gtc gat gcc att gtt cca caa agt ttc ctt aaa       2544
Leu Ser Asp Tyr Asp Val Asp Ala Ile Val Pro Gln Ser Phe Leu Lys
        835                 840                 845

gac gat tca ata gac aat aag gtc tta acg cgt tct gat aaa aat cgt       2592
Asp Asp Ser Ile Asp Asn Lys Val Leu Thr Arg Ser Asp Lys Asn Arg
    850                 855                 860

ggt aaa tcg gat aac gtt cca agt gaa gaa gta gtc aaa aag atg aaa       2640
Gly Lys Ser Asp Asn Val Pro Ser Glu Glu Val Val Lys Lys Met Lys
865                 870                 875                 880
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aac tat tgg aga caa ctt cta aac gcc aag tta atc act caa cgt aag       2688
Asn Tyr Trp Arg Gln Leu Leu Asn Ala Lys Leu Ile Thr Gln Arg Lys
                885                 890                 895

ttt gat aat tta acg aaa gct gaa cgt gga ggt ttg agt gaa ctt gat       2736
Phe Asp Asn Leu Thr Lys Ala Glu Arg Gly Gly Leu Ser Glu Leu Asp
            900                 905                 910

aaa gct ggt ttt atc aaa cgc caa ttg gtt gaa act cgc caa atc act       2784
Lys Ala Gly Phe Ile Lys Arg Gln Leu Val Glu Thr Arg Gln Ile Thr
        915                 920                 925

aag cat gtg gca caa att ttg gat agt cgc atg aat act aaa tac gat       2832
Lys His Val Ala Gln Ile Leu Asp Ser Arg Met Asn Thr Lys Tyr Asp
    930                 935                 940

gaa aat gat aaa ctt att cga gag gtt aaa gtg att acc tta aaa tct       2880
Glu Asn Asp Lys Leu Ile Arg Glu Val Lys Val Ile Thr Leu Lys Ser
945                 950                 955                 960

aaa tta gtt tct gac ttc cga aaa gat ttc caa ttc tat aaa gta cgt       2928
Lys Leu Val Ser Asp Phe Arg Lys Asp Phe Gln Phe Tyr Lys Val Arg
                965                 970                 975

gag att aac aat tac cat cat gcc cat gat gcg tat cta aat gcc gtc       2976
Glu Ile Asn Asn Tyr His His Ala His Asp Ala Tyr Leu Asn Ala Val
            980                 985                 990

gtt gga act gct ttg att aag aaa  tat cca aaa ctt gaa  tcg gag ttt     3024
Val Gly Thr Ala Leu Ile Lys Lys  Tyr Pro Lys Leu Glu  Ser Glu Phe
        995                 1000                1005

gtc tat  ggt gat tat aaa gtt  tat gat gtt cgt aaa  atg att gct       3069
Val Tyr  Gly Asp Tyr Lys Val  Tyr Asp Val Arg Lys  Met Ile Ala
    1010                1015                1020

aag tct  gag caa gaa ata ggc  aaa gca acc gca aaa  tat ttc ttt       3114
Lys Ser  Glu Gln Glu Ile Gly  Lys Ala Thr Ala Lys  Tyr Phe Phe
    1025                1030                1035

tac tct  aat atc atg aac ttc  ttc aaa aca gaa att  aca ctt gca       3159
Tyr Ser  Asn Ile Met Asn Phe  Phe Lys Thr Glu Ile  Thr Leu Ala
    1040                1045                1050

aat gga  gag att cgc aaa cgc  cct cta atc gaa act  aat ggg gaa       3204
Asn Gly  Glu Ile Arg Lys Arg  Pro Leu Ile Glu Thr  Asn Gly Glu
    1055                1060                1065

act gga  gaa att gtc tgg gat  aaa ggg cga gat ttt  gcc aca gtg       3249
Thr Gly  Glu Ile Val Trp Asp  Lys Gly Arg Asp Phe  Ala Thr Val
    1070                1075                1080

cgc aaa  gta ttg tcc atg ccc  caa gtc aat att gtc  aag aaa aca       3294
Arg Lys  Val Leu Ser Met Pro  Gln Val Asn Ile Val  Lys Lys Thr
    1085                1090                1095

gaa gta  cag aca ggc gga ttc  tcc aag gag tca att  tta cca aaa       3339
Glu Val  Gln Thr Gly Gly Phe  Ser Lys Glu Ser Ile  Leu Pro Lys
    1100                1105                1110

aga aat  tcg gac aag ctt att  gct cgt aaa aaa gac  tgg gat cca       3384
Arg Asn  Ser Asp Lys Leu Ile  Ala Arg Lys Lys Asp  Trp Asp Pro
    1115                1120                1125
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aaa aaa  tat ggt ggt ttt gat  agt cca acg gta gct  tat tca gtc        3429
Lys Lys  Tyr Gly Gly Phe Asp  Ser Pro Thr Val Ala  Tyr Ser Val
    1130                 1135                 1140

cta gtg  gtt gct aag gtg gaa  aaa ggg aaa tcg aag  aag tta aaa        3474
Leu Val  Val Ala Lys Val Glu  Lys Gly Lys Ser Lys  Lys Leu Lys
    1145                 1150                 1155

tcc gtt  aaa gag tta cta ggg  atc aca att atg gaa  aga agt tcc        3519
Ser Val  Lys Glu Leu Leu Gly  Ile Thr Ile Met Glu  Arg Ser Ser
    1160                 1165                 1170

ttt gaa  aaa aat ccg att gac  ttt tta gaa gct aaa  gga tat aag        3564
Phe Glu  Lys Asn Pro Ile Asp  Phe Leu Glu Ala Lys  Gly Tyr Lys
    1175                 1180                 1185

gaa gtt  aaa aaa gac tta atc  att aaa cta cct aaa  tat agt ctt        3609
Glu Val  Lys Lys Asp Leu Ile  Ile Lys Leu Pro Lys  Tyr Ser Leu
    1190                 1195                 1200

ttt gag  tta gaa aac ggt cgt  aaa cgg atg ctg gct  agt gcc gga        3654
Phe Glu  Leu Glu Asn Gly Arg  Lys Arg Met Leu Ala  Ser Ala Gly
    1205                 1210                 1215

gaa tta  caa aaa gga aat gag  ctg gct ctg cca agc  aaa tat gtg        3699
Glu Leu  Gln Lys Gly Asn Glu  Leu Ala Leu Pro Ser  Lys Tyr Val
    1220                 1225                 1230

aat ttt  tta tat tta gct agt  cat tat gaa aag ttg  aag ggt agt        3744
Asn Phe  Leu Tyr Leu Ala Ser  His Tyr Glu Lys Leu  Lys Gly Ser
    1235                 1240                 1245

cca gaa  gat aac gaa caa aaa  caa ttg ttt gtg gag  cag cat aag        3789
Pro Glu  Asp Asn Glu Gln Lys  Gln Leu Phe Val Glu  Gln His Lys
    1250                 1255                 1260

cat tat  tta gat gag att att  gag caa atc agt gaa  ttt tct aag        3834
His Tyr  Leu Asp Glu Ile Ile  Glu Gln Ile Ser Glu  Phe Ser Lys
    1265                 1270                 1275

cgt gtt  att tta gca gat gcc  aat tta gat aaa gtt  ctt agt gca        3879
Arg Val  Ile Leu Ala Asp Ala  Asn Leu Asp Lys Val  Leu Ser Ala
    1280                 1285                 1290

tat aac  aaa cat aga gac aaa  cca ata cgt gaa caa  gca gaa aat        3924
Tyr Asn  Lys His Arg Asp Lys  Pro Ile Arg Glu Gln  Ala Glu Asn
    1295                 1300                 1305

att att  cat tta ttt acg ttg  acg aat ctt gga gct  ccc gct gct        3969
Ile Ile  His Leu Phe Thr Leu  Thr Asn Leu Gly Ala  Pro Ala Ala
    1310                 1315                 1320

ttt aaa  tat ttt gat aca aca  att gat cgt aaa cga  tat acg tct        4014
Phe Lys  Tyr Phe Asp Thr Thr  Ile Asp Arg Lys Arg  Tyr Thr Ser
    1325                 1330                 1335

aca aaa  gaa gtt tta gat gcc  act ctt atc cat caa  tcc atc act        4059
Thr Lys  Glu Val Leu Asp Ala  Thr Leu Ile His Gln  Ser Ile Thr
    1340                 1345                 1350

ggt ctt  tat gaa aca cgc att  gat ttg agt cag cta  gga ggt gac        4104
Gly Leu  Tyr Glu Thr Arg Ile  Asp Leu Ser Gln Leu  Gly Gly Asp
    1355                 1360                 1365
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Met Asp Lys Lys Tyr Ser Ile Gly Leu Ala 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
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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
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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
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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 Ala 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
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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
    1010                1015                1020

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

Tyr Ser  Asn Ile Met Asn Phe  Phe Lys Thr Glu Ile  Thr Leu Ala
    1040                1045                1050

Asn Gly  Glu Ile Arg Lys Arg  Pro Leu Ile Glu Thr  Asn Gly Glu
    1055                1060                1065

Thr Gly  Glu Ile Val Trp Asp  Lys Gly Arg Asp Phe  Ala Thr Val
    1070                1075                1080

Arg Lys  Val Leu Ser Met Pro  Gln Val Asn Ile Val  Lys Lys Thr
    1085                1090                1095

Glu Val  Gln Thr Gly Gly Phe  Ser Lys Glu Ser Ile  Leu Pro Lys
    1100                1105                1110

Arg Asn  Ser Asp Lys Leu Ile  Ala Arg Lys Lys Asp  Trp Asp Pro
    1115                1120                1125

Lys Lys  Tyr Gly Gly Phe Asp  Ser Pro Thr Val Ala  Tyr Ser Val
    1130                1135                1140

Leu Val  Val Ala Lys Val Glu  Lys Gly Lys Ser Lys  Lys Leu Lys
    1145                1150                1155

Ser Val  Lys Glu Leu Leu Gly  Ile Thr Ile Met Glu  Arg Ser Ser
    1160                1165                1170

Phe Glu  Lys Asn Pro Ile Asp  Phe Leu Glu Ala Lys  Gly Tyr Lys
    1175                1180                1185

Glu Val  Lys Lys Asp Leu Ile  Ile Lys Leu Pro Lys  Tyr Ser Leu
    1190                1195                1200

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

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

```
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
    1250                1255                1260

His Tyr  Leu Asp Glu Ile Ile  Glu Gln Ile Ser Glu  Phe Ser Lys
    1265                1270                1275

Arg Val  Ile Leu Ala Asp Ala  Asn Leu Asp Lys Val  Leu Ser Ala
    1280                1285                1290

Tyr Asn  Lys His Arg Asp Lys  Pro Ile Arg Glu Gln  Ala Glu Asn
    1295                1300                1305

Ile Ile  His Leu Phe Thr Leu  Thr Asn Leu Gly Ala  Pro Ala Ala
    1310                1315                1320

Phe Lys  Tyr Phe Asp Thr Thr  Ile Asp Arg Lys Arg  Tyr Thr Ser
    1325                1330                1335

Thr Lys  Glu Val Leu Asp Ala  Thr Leu Ile His Gln  Ser Ile Thr
    1340                1345                1350

Gly Leu  Tyr Glu Thr Arg Ile  Asp Leu Ser Gln Leu  Gly Gly Asp
    1355                1360                1365
```

<210> 3
<211> 624
<212> DNA
<213> Perkinsus marinus

<220>
<221> CDS
<222> (1)..(624)
<223> PmCDA1

<400> 3

```
atg acc gac gct gag tac gtg aga atc cat gag aag ttg gac atc tac         48
Met Thr Asp Ala Glu Tyr Val Arg Ile His Glu Lys Leu Asp Ile Tyr
1               5                  10                  15

acg ttt aag aaa cag ttt ttc aac aac aaa aaa tcc gtg tcg cat aga         96
Thr Phe Lys Lys Gln Phe Phe Asn Asn Lys Lys Ser Val Ser His Arg
            20                  25                  30

tgc tac gtt ctc ttt gaa tta aaa cga cgg ggt gaa cgt aga gcg tgt        144
Cys Tyr Val Leu Phe Glu Leu Lys Arg Arg Gly Glu Arg Arg Ala Cys
        35                  40                  45

ttt tgg ggc tat gct gtg aat aaa cca cag agc ggg aca gaa cgt ggc        192
Phe Trp Gly Tyr Ala Val Asn Lys Pro Gln Ser Gly Thr Glu Arg Gly
    50                  55                  60
```

```
att cac gcc gaa atc ttt agc att aga aaa gtc gaa gaa tac ctg cgc        240
Ile His Ala Glu Ile Phe Ser Ile Arg Lys Val Glu Glu Tyr Leu Arg
65                  70                  75                  80

gac aac ccc gga caa ttc acg ata aat tgg tac tca tcc tgg agt cct        288
Asp Asn Pro Gly Gln Phe Thr Ile Asn Trp Tyr Ser Ser Trp Ser Pro
                85                  90                  95

tgt gca gat tgc gct gaa aag atc tta gaa tgg tat aac cag gag ctg        336
Cys Ala Asp Cys Ala Glu Lys Ile Leu Glu Trp Tyr Asn Gln Glu Leu
            100                 105                 110

cgg ggg aac ggc cac act ttg aaa atc tgg gct tgc aaa ctc tat tac        384
Arg Gly Asn Gly His Thr Leu Lys Ile Trp Ala Cys Lys Leu Tyr Tyr
        115                 120                 125

gag aaa aat gcg agg aat caa att ggg ctg tgg aat ctc aga gat aac        432
Glu Lys Asn Ala Arg Asn Gln Ile Gly Leu Trp Asn Leu Arg Asp Asn
    130                 135                 140

ggg gtt ggg ttg aat gta atg gta agt gaa cac tac caa tgt tgc agg        480
Gly Val Gly Leu Asn Val Met Val Ser Glu His Tyr Gln Cys Cys Arg
145                 150                 155                 160

aaa ata ttc atc caa tcg tcg cac aat caa ttg aat gag aat aga tgg        528
Lys Ile Phe Ile Gln Ser Ser His Asn Gln Leu Asn Glu Asn Arg Trp
                165                 170                 175

ctt gag aag act ttg aag cga gct gaa aaa cga cgg agc gag ttg tcc        576
Leu Glu Lys Thr Leu Lys Arg Ala Glu Lys Arg Arg Ser Glu Leu Ser
            180                 185                 190

att atg att cag gta aaa ata ctc cac acc act aag agt cct gct gtt        624
Ile Met Ile Gln Val Lys Ile Leu His Thr Thr Lys Ser Pro Ala Val
        195                 200                 205
```

<210> 4
<211> 208
<212> PRT
<213> Perkinsus marinus

<400> 4

```
Met Thr Asp Ala Glu Tyr Val Arg Ile His Glu Lys Leu Asp Ile Tyr
1               5                   10                  15

Thr Phe Lys Lys Gln Phe Phe Asn Asn Lys Lys Ser Val Ser His Arg
            20                  25                  30

Cys Tyr Val Leu Phe Glu Leu Lys Arg Arg Gly Glu Arg Arg Ala Cys
        35                  40                  45

Phe Trp Gly Tyr Ala Val Asn Lys Pro Gln Ser Gly Thr Glu Arg Gly
    50                  55                  60

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

```
Asp Asn Pro Gly Gln Phe Thr Ile Asn Trp Tyr Ser Ser Trp Ser Pro
                85                  90                  95

Cys Ala Asp Cys Ala Glu Lys Ile Leu Glu Trp Tyr Asn Gln Glu Leu
            100                 105                 110

Arg Gly Asn Gly His Thr Leu Lys Ile Trp Ala Cys Lys Leu Tyr Tyr
        115                 120                 125

Glu Lys Asn Ala Arg Asn Gln Ile Gly Leu Trp Asn Leu Arg Asp Asn
    130                 135                 140

Gly Val Gly Leu Asn Val Met Val Ser Glu His Tyr Gln Cys Cys Arg
145                 150                 155                 160

Lys Ile Phe Ile Gln Ser Ser His Asn Gln Leu Asn Glu Asn Arg Trp
                165                 170                 175

Leu Glu Lys Thr Leu Lys Arg Ala Glu Lys Arg Arg Ser Glu Leu Ser
            180                 185                 190

Ile Met Ile Gln Val Lys Ile Leu His Thr Thr Lys Ser Pro Ala Val
        195                 200                 205
```

<210> 5
<211> 363
<212> DNA
<213> Artificial Sequence

<220>
<223> linker region

<220>
<221> CDS
<222> (1)..(363)

<220>
<221> misc_feature
<222> (31)..(201)
<223> SH3 domain

<220>
<221> misc_feature
<222> (208)..(273)
<223> 3xFLAG tag

<220>
<221> misc_feature
<222> (292)..(357)
<223> 3xFLAG tag

<400> 5

```
ggt gga gga ggt tct gga ggt gga ggt tct gct gag tat gtg cga gcc        48
Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Ala Glu Tyr Val Arg Ala
1               5                   10                  15
```

```
ctc ttt gac ttt aat ggg aat gat gaa gag gat ctt ccc ttt aag aaa         96
Leu Phe Asp Phe Asn Gly Asn Asp Glu Glu Asp Leu Pro Phe Lys Lys
            20                  25                  30

gga gac atc ctg aga atc cgg gat aag cct gag gag cag tgg tgg aat        144
Gly Asp Ile Leu Arg Ile Arg Asp Lys Pro Glu Glu Gln Trp Trp Asn
        35                  40                  45

gca gag gac agc gaa gga aag agg ggg atg att cct gtc cct tac gtg        192
Ala Glu Asp Ser Glu Gly Lys Arg Gly Met Ile Pro Val Pro Tyr Val
    50                  55                  60

gag aag tat tcc gga gac tat aag gac cac gac gga gac tac aag gat        240
Glu Lys Tyr Ser Gly Asp Tyr Lys Asp His Asp Gly Asp Tyr Lys Asp
65                  70                  75                  80

cat gat att gat tac aaa gac gat gac gat aag tct agg ctc gag tcc        288
His Asp Ile Asp Tyr Lys Asp Asp Asp Asp Lys Ser Arg Leu Glu Ser
                85                  90                  95

gga gac tat aag gac cac gac gga gac tac aag gat cat gat att gat        336
Gly Asp Tyr Lys Asp His Asp Gly Asp Tyr Lys Asp His Asp Ile Asp
            100                 105                 110

tac aaa gac gat gac gat aag tct agg                                    363
Tyr Lys Asp Asp Asp Asp Lys Ser Arg
        115                 120
```

<210> 6
<211> 121
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic Construct

<400> 6

```
Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Ala Glu Tyr Val Arg Ala
1               5                   10                  15


Leu Phe Asp Phe Asn Gly Asn Asp Glu Glu Asp Leu Pro Phe Lys Lys
            20                  25                  30


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


Ala Glu Asp Ser Glu Gly Lys Arg Gly Met Ile Pro Val Pro Tyr Val
    50                  55                  60


Glu Lys Tyr Ser Gly Asp Tyr Lys Asp His Asp Gly Asp Tyr Lys Asp
65                  70                  75                  80


His Asp Ile Asp Tyr Lys Asp Asp Asp Asp Lys Ser Arg Leu Glu Ser
                85                  90                  95
```

```
Gly Asp Tyr Lys Asp His Asp Gly Asp Tyr Lys Asp His Asp Ile Asp
            100                 105                 110


Tyr Lys Asp Asp Asp Asp Lys Ser Arg
        115                 120


<210>  7
<211>  171
<212>  DNA
<213>  Artificial Sequence

<220>
<223>  SH3 domain


<220>
<221>  CDS
<222>  (1)..(171)

<400>  7
gct gag tat gtg cga gcc ctc ttt gac ttt aat ggg aat gat gaa gag         48
Ala Glu Tyr Val Arg Ala Leu Phe Asp Phe Asn Gly Asn Asp Glu Glu
1               5                   10                  15

gat ctt ccc ttt aag aaa gga gac atc ctg aga atc cgg gat aag cct         96
Asp Leu Pro Phe Lys Lys Gly Asp Ile Leu Arg Ile Arg Asp Lys Pro
            20                  25                  30

gag gag cag tgg tgg aat gca gag gac agc gaa gga aag agg ggg atg        144
Glu Glu Gln Trp Trp Asn Ala Glu Asp Ser Glu Gly Lys Arg Gly Met
        35                  40                  45

att cct gtc cct tac gtg gag aag tat                                    171
Ile Pro Val Pro Tyr Val Glu Lys Tyr
    50                  55


<210>  8
<211>  57
<212>  PRT
<213>  Artificial Sequence

<220>
<223>  Synthetic Construct

<400>  8

Ala Glu Tyr Val Arg Ala Leu Phe Asp Phe Asn Gly Asn Asp Glu Glu
1               5                   10                  15


Asp Leu Pro Phe Lys Lys Gly Asp Ile Leu Arg Ile Arg Asp Lys Pro
            20                  25                  30


Glu Glu Gln Trp Trp Asn Ala Glu Asp Ser Glu Gly Lys Arg Gly Met
        35                  40                  45


Ile Pro Val Pro Tyr Val Glu Lys Tyr
    50                  55
```

<210> 9
<211> 66
<212> DNA
<213> Artificial Sequence

<220>
<223> 3xFLAG tag

<220>
<221> CDS
<222> (1)..(66)

<400> 9
gac tat aag gac cac gac gga gac tac aag gat cat gat att gat tac 48
Asp Tyr Lys Asp His Asp Gly Asp Tyr Lys Asp His Asp Ile Asp Tyr
1 5 10 15

aaa gac gat gac gat aag 66
Lys Asp Asp Asp Asp Lys
20

<210> 10
<211> 22
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic Construct

<400> 10

Asp Tyr Lys Asp His Asp Gly Asp Tyr Lys Asp His Asp Ile Asp Tyr
1 5 10 15

Lys Asp Asp Asp Asp Lys
20

<210> 11
<211> 24
<212> DNA
<213> Artificial Sequence

<220>
<223> FLAG tag

<220>
<221> CDS
<222> (1)..(24)

<400> 11
gat tac aaa gac gat gac gat aag 24
Asp Tyr Lys Asp Asp Asp Asp Lys
1 5

<210> 12
<211> 8
<212> PRT

<213> Artificial Sequence

<220>
<223> Synthetic Construct

<400> 12

Asp Tyr Lys Asp Asp Asp Asp Lys
1 5

<210> 13
<211> 252
<212> DNA
<213> Myocastor coypus

<220>
<221> CDS
<222> (1)..(252)
<223> PBS2-derived UGI

<400> 13
atg acc aac ctt tcc gac atc ata gag aag gaa aca ggc aaa cag ttg 48
Met Thr Asn Leu Ser Asp Ile Ile Glu Lys Glu Thr Gly Lys Gln Leu
1 5 10 15

gtc atc caa gag tcg ata ctc atg ctt cct gaa gaa gtt gag gag gtc 96
Val Ile Gln Glu Ser Ile Leu Met Leu Pro Glu Glu Val Glu Glu Val
20 25 30

att ggg aat aag ccg gaa agt gac att ctc gta cac act gcg tat gat 144
Ile Gly Asn Lys Pro Glu Ser Asp Ile Leu Val His Thr Ala Tyr Asp
35 40 45

gag agc acc gat gag aac gtg atg ctg ctc acg tca gat gcc cca gag 192
Glu Ser Thr Asp Glu Asn Val Met Leu Leu Thr Ser Asp Ala Pro Glu
50 55 60

tac aaa ccc tgg gct ctg gtg att cag gac tct aat gga gag aac aag 240
Tyr Lys Pro Trp Ala Leu Val Ile Gln Asp Ser Asn Gly Glu Asn Lys
65 70 75 80

atc aag atg cta 252
Ile Lys Met Leu

<210> 14
<211> 84
<212> PRT
<213> Myocastor coypus

<400> 14

Met Thr Asn Leu Ser Asp Ile Ile Glu Lys Glu Thr Gly Lys Gln Leu
1 5 10 15

Val Ile Gln Glu Ser Ile Leu Met Leu Pro Glu Glu Val Glu Glu Val
20 25 30

Ile Gly Asn Lys Pro Glu Ser Asp Ile Leu Val His Thr Ala Tyr Asp

35 40 45

Glu Ser Thr Asp Glu Asn Val Met Leu Leu Thr Ser Asp Ala Pro Glu
50 55 60

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

Ile Lys Met Leu

<210> 15
<211> 484
<212> DNA
<213> Artificial Sequence

<220>
<223> synthetic oligonucleotide: J23119-sgRNA-units

<220>
<221> promoter
<222> (59)..(93)
<223> J23119 promoter

<220>
<221> misc_structure
<222> (94)..(113)
<223> minimal CRISPR array

<220>
<221> misc_structure
<222> (114)..(196)
<223> gRNA scaffold

<220>
<221> promoter
<222> (269)..(303)
<223> J23119 promoter

<220>
<221> misc_structure
<222> (304)..(323)
<223> minimal CRISPR array

<220>
<221> misc_structure
<222> (324)..(406)
<223> gRNA scaffold

<400> 15
gataacaatt gagcaagaat cttcatcgat gcatcagaaa attattttaa atttcctctt 60

gacagctagc tcagtcctag gtataatgct agcagagacc cgggatggtc tcagttttag 120

agctagaaat agcaagttaa aataaggcta gtccgttatc aacttgaaaa agtggcaccg 180

agtcggtgct ttttttccga aaaaaaaacc ccgcccctga cagggcgggg ttttttttaa 240

ttaacagaaa attattttaa atttcctctt gacagctagc tcagtcctag gtataatgct 300

agcagaagag ccggcgctct tcagttttag agctagaaat agcaagttaa aataaggcta 360

gtccgttatc aacttgaaaa agtggcaccg agtcggtgct ttttttccga aaaaaaaacc 420

ccgcccctga cagggcgggg ttttttttttc tagaccgcaa aaatcagcgc gcaaatacgc 480

atac 484

<210> 16
<211> 35
<212> DNA
<213> Artificial Sequence

<220>
<223> J23119 promoter

<400> 16
ttgacagcta gctcagtcct aggtataatg ctagc 35

<210> 17
<211> 20
<212> DNA
<213> Streptococcus pyogenes

<220>
<221> misc_feature
<222> (1)..(20)
<223> minimal CRISPR array

<400> 17
agagacccgg gatggtctca 20

<210> 18
<211> 83
<212> DNA
<213> Streptococcus pyogenes

<220>
<221> misc_structure
<222> (1)..(83)
<223> gRNA scaffold

<400> 18
gttttagagc tagaaatagc aagttaaaat aaggctagtc cgttatcaac ttgaaaaagt 60

ggcaccgagt cggtgctttt ttt 83

<210> 19
<211> 19
<212> RNA
<213> Streptococcus pyogenes

<220>
<221> misc_structure
<222> (1)..(19)
<223> crRNA direct repeat sequence.

<400> 19
aauuucuacu guuguagau 19

<210> 20
<211> 74
<212> DNA
<213> Artificial Sequence

<220>
<223> PCR Primer

<400> 20
gctactctag aaaaaaaaac cccgccctgt caggggcggg gttttttttt cggggtttag 60

caagatggca gcgc 74

<210> 21
<211> 91
<212> DNA
<213> Artificial Sequence

<220>
<223> PCR Primer

<400> 21
gcctgatcga tgcatcagaa aattatttta aatttcctct tgacagctag ctcagtccta 60

ggtataatgc tagcagagac ccgggatggt c 91

<210> 22
<211> 52
<212> DNA
<213> Artificial Sequence

<220>
<223> PCR Primer

<400> 22
gatccttttt gataatctcg tcgacataac aattgagcaa gaatcttcat cg 52

<210> 23
<211> 51
<212> DNA
<213> Artificial Sequence

<220>
<223> PCR Primer

<400> 23
ctcacgttaa gggattttgg tcatctgcag tgtatgcgta tttgcgcgct g 51

<210> 24
<211> 57
<212> DNA
<213> Artificial Sequence

<220>
<223> PCR Primer

<400> 24
gaagattctt gctcaattgt tatgtcgacg agattatcaa aaaggatctt cacctag 57

<210> 25
<211> 51
<212> DNA
<213> Artificial Sequence

<220>
<223> PCR Primer

<400> 25
cagcgcgcaa atacgcatac actgcagatg accaaaatcc cttaacgtga g 51

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

<220>
<223> PCR Primer

<400> 26
ctgcacgcgc acttttatcc 20

<210> 27
<211> 21
<212> DNA
<213> Artificial Sequence

<220>
<223> PCR Primer

<400> 27
ctctgtttgc caacgcattt g 21

<210> 28
<211> 20
<212> DNA
<213> Artificial Sequence

<220>
<223> PCR Primer

<400> 28
caatggtgac atcacgcagg 20

<210> 29
<211> 21
<212> DNA
<213> Artificial Sequence

<220>
<223> PCR Primer

<400> 29
cctgggcgat aacgtagttg c 21

<210> 30
<211> 20
<212> DNA
<213> Artificial Sequence

<220>
<223> PCR Primer

<400> 30
cctcggcaac cgtcgtatcc 20

<210> 31
<211> 20
<212> DNA
<213> Artificial Sequence

<220>
<223> PCR Primer

<400> 31
ccggttatcg gtagcgatac 20

<210> 32
<211> 20
<212> DNA
<213> Artificial Sequence

<220>
<223> PCR Primer

<400> 32
gcctggggat tattgtgtgg 20

<210> 33
<211> 19
<212> DNA
<213> Artificial Sequence

<220>
<223> PCR Primer

<400> 33
gcggctccag gttacttcc 19

<210> 34
<211> 17
<212> DNA
<213> Artificial Sequence

<220>
<223> PCR Primer

<400> 34
gccatcactt ccagcgc 17

<210> 35
<211> 18
<212> DNA

<213> Artificial Sequence

<220>
<223> PCR Primer

<400> 35
gccaaatcgg cggtaacg 18

<210> 36
<211> 20
<212> DNA
<213> Artificial Sequence

<220>
<223> PCR Primer

<400> 36
ccatttcgta accgccagtc 20

<210> 37
<211> 20
<212> DNA
<213> Artificial Sequence

<220>
<223> PCR Primer

<400> 37
ctctcgtatt cgagcagatg 20

<210> 38
<211> 17
<212> DNA
<213> Artificial Sequence

<220>
<223> PCR Primer

<400> 38
ccgcccatag caaccag 17

<210> 39
<211> 16
<212> DNA
<213> Artificial Sequence

<220>
<223> PCR Primer

<400> 39
ggggcggcca tcttcc 16

<210> 40
<211> 18
<212> DNA
<213> Artificial Sequence

<220>
<223> PCR Primer

<400> 40
cagccgagga aattcagg 18

<210> 41
<211> 49
<212> DNA
<213> Artificial Sequence

<220>
<223> PCR Primer

<400> 41
tctttcccta cacgacgctc ttccgatctc cgcagaacag gcagcagag 49

<210> 42
<211> 54
<212> DNA
<213> Artificial Sequence

<220>
<223> PCR Primer

<400> 42
gtgactggag ttcagacgtg tgctcttccg atctgacaat gggcgcatcg aggg 54

<210> 43
<211> 49
<212> DNA
<213> Artificial Sequence

<220>
<223> PCR Primer

<400> 43
tctttcccta cacgacgctc ttccgatctc acaccgacta caacgacgg 49

<210> 44
<211> 54
<212> DNA
<213> Artificial Sequence

<220>
<223> PCR Primer

<400> 44
gtgactggag ttcagacgtg tgctcttccg atctgctgct gcaatacggt tccg 54

<210> 45
<211> 49
<212> DNA
<213> Artificial Sequence

<220>
<223> PCR Primer

<400> 45
tctttcccta cacgacgctc ttccgatctc ttcggcggcg tggacatgg 49

<210> 46
<211> 55
<212> DNA
<213> Artificial Sequence

<220>
<223> PCR Primer

<400> 46
gtgactggag ttcagacgtg tgctcttccg atctacgaca gccacacctt tgggc 55

<210> 47
<211> 52
<212> DNA
<213> Artificial Sequence

<220>
<223> PCR Primer

<400> 47
tctttcccta cacgacgctc ttccgatctg gcggtggaaa cgggtaccgt cg 52

<210> 48
<211> 54
<212> DNA
<213> Artificial Sequence

<220>
<223> PCR Primer

<400> 48
gtgactggag ttcagacgtg tgctcttccg atctcgccca ccagcgatag cgtt 54

<210> 49
<211> 49
<212> DNA
<213> Artificial Sequence

<220>
<223> PCR Primer

<400> 49
tctttcccta cacgacgctc ttccgatctg gcgctcttga ttttcgccg 49

<210> 50
<211> 54
<212> DNA
<213> Artificial Sequence

<220>
<223> PCR Primer

<400> 50
gtgactggag ttcagacgtg tgctcttccg atctggatgg cacgctggca atgc 54

<210> 51
<211> 49
<212> DNA

<213> Artificial Sequence

<220>
<223> PCR Primer

<400> 51
tctttcccta cacgacgctc ttccgatctg cctccctgtg ctgttttgc 49

<210> 52
<211> 54
<212> DNA
<213> Artificial Sequence

<220>
<223> PCR Primer

<400> 52
gtgactggag ttcagacgtg tgctcttccg atctgctcaa cacccacgtt cgcc 54

<210> 53
<211> 20
<212> DNA
<213> Artificial Sequence

<220>
<223> PCR Primer

<400> 53
gctcattatt tgcccgcttg 20

<210> 54
<211> 19
<212> DNA
<213> Artificial Sequence

<220>
<223> PCR Primer

<400> 54
tgccggttgc cagatagtc 19

<210> 55
<211> 19
<212> DNA
<213> Artificial Sequence

<220>
<223> PCR Primer

<400> 55
ggtcttcagg aaatcaccg 19

<210> 56
<211> 20
<212> DNA
<213> Artificial Sequence

<220>
<223> PCR Primer

<400> 56
cgttcaacca cttcagtgtc 20

<210> 57
<211> 20
<212> DNA
<213> Artificial Sequence

<220>
<223> PCR Primer

<400> 57
cacaaagctg taaatcagcg 20

<210> 58
<211> 20
<212> DNA
<213> Artificial Sequence

<220>
<223> PCR Primer

<400> 58
gtcaatgcaa caccccttc 20

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atggctggcc gctgtatgaa tcccgcctga 90

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gcggcggaca aggataagca cgcgtcagca 90

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gcatgaaggc ccacattggt gtcgatgcca 90

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ctg agg ttc aag gcc atc cct gtg ggc aag acc cag gag aac atc gac         96
Leu Arg Phe Lys Ala Ile Pro Val Gly Lys Thr Gln Glu Asn Ile Asp
            20                  25                  30

aat aag cgg ctg ctg gtg gag gac gag aag aga gcc gag gat tat aag        144
Asn Lys Arg Leu Leu Val Glu Asp Glu Lys Arg Ala Glu Asp Tyr Lys
        35                  40                  45

ggc gtg aag aag ctg ctg gat cgc tac tat ctg tct ttt atc aac gac        192
Gly Val Lys Lys Leu Leu Asp Arg Tyr Tyr Leu Ser Phe Ile Asn Asp
    50                  55                  60

gtg ctg cac agc atc aag ctg aag aat ctg aac aat tac atc agc ctg        240
Val Leu His Ser Ile Lys Leu Lys Asn Leu Asn Asn Tyr Ile Ser Leu
65                  70                  75                  80

ttc cgg aag aaa acc aga acc gag aag gag aat aag gag ctg gag aac        288
Phe Arg Lys Lys Thr Arg Thr Glu Lys Glu Asn Lys Glu Leu Glu Asn
                85                  90                  95

ctg gag atc aat ctg cgg aag gag atc gcc aag gcc ttc aag ggc aac        336
Leu Glu Ile Asn Leu Arg Lys Glu Ile Ala Lys Ala Phe Lys Gly Asn
            100                 105                 110

gag ggc tac aag tcc ctg ttt aag aag gat atc atc gag aca atc ctg        384
Glu Gly Tyr Lys Ser Leu Phe Lys Lys Asp Ile Ile Glu Thr Ile Leu
        115                 120                 125

cca gag ttc ctg gac gat aag gac gag atc gcc ctg gtg aac agc ttc        432
Pro Glu Phe Leu Asp Asp Lys Asp Glu Ile Ala Leu Val Asn Ser Phe
    130                 135                 140

aat ggc ttt acc aca gcc ttc acc ggc ttc ttt gat aac aga gag aat        480
Asn Gly Phe Thr Thr Ala Phe Thr Gly Phe Phe Asp Asn Arg Glu Asn
145                 150                 155                 160

atg ttt tcc gag gag gcc aag agc aca tcc atc gcc ttc agg tgt atc        528
Met Phe Ser Glu Glu Ala Lys Ser Thr Ser Ile Ala Phe Arg Cys Ile
                165                 170                 175

aac gag aat ctg acc cgc tac atc tct aat atg gac atc ttc gag aag        576
Asn Glu Asn Leu Thr Arg Tyr Ile Ser Asn Met Asp Ile Phe Glu Lys
            180                 185                 190
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gtg gac gcc atc ttt gat aag cac gag gtg cag gag atc aag gag aag        624
Val Asp Ala Ile Phe Asp Lys His Glu Val Gln Glu Ile Lys Glu Lys
        195                 200                 205

atc ctg aac agc gac tat gat gtg gag gat ttc ttt gag ggc gag ttc        672
Ile Leu Asn Ser Asp Tyr Asp Val Glu Asp Phe Phe Glu Gly Glu Phe
    210                 215                 220

ttt aac ttt gtg ctg aca cag gag ggc atc gac gtg tat aac gcc atc        720
Phe Asn Phe Val Leu Thr Gln Glu Gly Ile Asp Val Tyr Asn Ala Ile
225                 230                 235                 240

atc ggc ggc ttc gtg acc gag agc ggc gag aag atc aag ggc ctg aac        768
Ile Gly Gly Phe Val Thr Glu Ser Gly Glu Lys Ile Lys Gly Leu Asn
                245                 250                 255

gag tac atc aac ctg tat aat cag aaa acc aag cag aag ctg cct aag        816
Glu Tyr Ile Asn Leu Tyr Asn Gln Lys Thr Lys Gln Lys Leu Pro Lys
            260                 265                 270

ttt aag cca ctg tat aag cag gtg ctg agc gat cgg gag tct ctg agc        864
Phe Lys Pro Leu Tyr Lys Gln Val Leu Ser Asp Arg Glu Ser Leu Ser
        275                 280                 285

ttc tac ggc gag ggc tat aca tcc gat gag gag gtg ctg gag gtg ttt        912
Phe Tyr Gly Glu Gly Tyr Thr Ser Asp Glu Glu Val Leu Glu Val Phe
    290                 295                 300

aga aac acc ctg aac aag aac agc gag atc ttc agc tcc atc aag aag        960
Arg Asn Thr Leu Asn Lys Asn Ser Glu Ile Phe Ser Ser Ile Lys Lys
305                 310                 315                 320

ctg gag aag ctg ttc aag aat ttt gac gag tac tct agc gcc ggc atc       1008
Leu Glu Lys Leu Phe Lys Asn Phe Asp Glu Tyr Ser Ser Ala Gly Ile
                325                 330                 335

ttt gtg aag aac ggc ccc gcc atc agc aca atc tcc aag gat atc ttc       1056
Phe Val Lys Asn Gly Pro Ala Ile Ser Thr Ile Ser Lys Asp Ile Phe
            340                 345                 350

ggc gag tgg aac gtg atc cgg gac aag tgg aat gcc gag tat gac gat       1104
Gly Glu Trp Asn Val Ile Arg Asp Lys Trp Asn Ala Glu Tyr Asp Asp
        355                 360                 365

atc cac ctg aag aag aag gcc gtc gtg acc gag aag tac gag gac gat       1152
Ile His Leu Lys Lys Lys Ala Val Val Thr Glu Lys Tyr Glu Asp Asp
    370                 375                 380

cgg aga aag tcc ttc aag aag atc ggc tcc ttt tct ctg gag cag ctg       1200
Arg Arg Lys Ser Phe Lys Lys Ile Gly Ser Phe Ser Leu Glu Gln Leu
385                 390                 395                 400

cag gag tac gcc gac gcc gat ctg tct gtg gtg gag aag ctg aag gag       1248
Gln Glu Tyr Ala Asp Ala Asp Leu Ser Val Val Glu Lys Leu Lys Glu
                405                 410                 415

atc atc atc cag aag gtg gat gag atc tac aag gtg tat ggc tcc tct       1296
Ile Ile Ile Gln Lys Val Asp Glu Ile Tyr Lys Val Tyr Gly Ser Ser
            420                 425                 430

gag aag ctg ttc gac gcc gat ttt gtg ctg gag aag tct ctg aag aag       1344
Glu Lys Leu Phe Asp Ala Asp Phe Val Leu Glu Lys Ser Leu Lys Lys
        435                 440                 445
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aac gac gcc gtg gtg gcc att atg aag gac ctg ctg gat tct gtg aag       1392
Asn Asp Ala Val Val Ala Ile Met Lys Asp Leu Leu Asp Ser Val Lys
    450                 455                 460

tct ttc gag aat tac atc aag gcc ttc ttt ggc gag ggc aag gag aca       1440
Ser Phe Glu Asn Tyr Ile Lys Ala Phe Phe Gly Glu Gly Lys Glu Thr
465                 470                 475                 480

aac agg gac gag tcc ttc tat ggc gat ttt gtg ctg gcc tac gac atc       1488
Asn Arg Asp Glu Ser Phe Tyr Gly Asp Phe Val Leu Ala Tyr Asp Ile
                485                 490                 495

ctg ctg aag gtg gac cac atc tac gat gcc atc cgc aat tat gtg acc       1536
Leu Leu Lys Val Asp His Ile Tyr Asp Ala Ile Arg Asn Tyr Val Thr
            500                 505                 510

cag aag ccc tac tct aag gat aag ttc aag ctg tat ttt cag aac cct       1584
Gln Lys Pro Tyr Ser Lys Asp Lys Phe Lys Leu Tyr Phe Gln Asn Pro
        515                 520                 525

cag ttc atg ggc ggc tgg gac aag gat aag gag aca gac tat cgg gcc       1632
Gln Phe Met Gly Gly Trp Asp Lys Asp Lys Glu Thr Asp Tyr Arg Ala
    530                 535                 540

acc atc ctg aga tac ggc tcc aag tac tat ctg gcc atc atg gat aag       1680
Thr Ile Leu Arg Tyr Gly Ser Lys Tyr Tyr Leu Ala Ile Met Asp Lys
545                 550                 555                 560

aag tac gcc aag tgc ctg cag aag atc gac aag gac gat gtg aac ggc       1728
Lys Tyr Ala Lys Cys Leu Gln Lys Ile Asp Lys Asp Asp Val Asn Gly
                565                 570                 575

aat tac gag aag atc aac tat aag ctg ctg ccc ggc cct aat aag atg       1776
Asn Tyr Glu Lys Ile Asn Tyr Lys Leu Leu Pro Gly Pro Asn Lys Met
            580                 585                 590

ctg cca aag gtg ttc ttt tct aag aag tgg atg gcc tac tat aac ccc       1824
Leu Pro Lys Val Phe Phe Ser Lys Lys Trp Met Ala Tyr Tyr Asn Pro
        595                 600                 605

agc gag gac atc cag aag atc tac aag aat ggt acc ttc aag aag ggc       1872
Ser Glu Asp Ile Gln Lys Ile Tyr Lys Asn Gly Thr Phe Lys Lys Gly
    610                 615                 620

gat atg ttt aac ctg aat gac tgt cac aag ctg atc gac ttc ttt aag       1920
Asp Met Phe Asn Leu Asn Asp Cys His Lys Leu Ile Asp Phe Phe Lys
625                 630                 635                 640

gat agc atc tcc cgg tat cca aag tgg tcc aat gcc tac gat ttc aac       1968
Asp Ser Ile Ser Arg Tyr Pro Lys Trp Ser Asn Ala Tyr Asp Phe Asn
                645                 650                 655

ttt tct gag aca gag aag tat aag gac atc gcc ggc ttt tac aga gag       2016
Phe Ser Glu Thr Glu Lys Tyr Lys Asp Ile Ala Gly Phe Tyr Arg Glu
            660                 665                 670

gtg gag gag cag ggc tat aag gtg agc ttc gag tct gcc agc aag aag       2064
Val Glu Glu Gln Gly Tyr Lys Val Ser Phe Glu Ser Ala Ser Lys Lys
        675                 680                 685

gag gtg gat aag ctg gtg gag gag ggc aag ctg tat atg ttc cag atc       2112
Glu Val Asp Lys Leu Val Glu Glu Gly Lys Leu Tyr Met Phe Gln Ile
    690                 695                 700
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tat aac aag gac ttt tcc gat aag tct cac ggc aca ccc aat ctg cac       2160
Tyr Asn Lys Asp Phe Ser Asp Lys Ser His Gly Thr Pro Asn Leu His
705                 710                 715                 720

acc atg tac ttc aag ctg ctg ttt gac gag aac aat cac gga cag atc       2208
Thr Met Tyr Phe Lys Leu Leu Phe Asp Glu Asn Asn His Gly Gln Ile
                725                 730                 735

agg ctg agc gga gga gca gag ctg ttc atg agg cgc gct tcc ctg aag       2256
Arg Leu Ser Gly Gly Ala Glu Leu Phe Met Arg Arg Ala Ser Leu Lys
            740                 745                 750

aag gag gag ctg gtg gtg cac cca gcc aac tcc cct atc gcc aac aag       2304
Lys Glu Glu Leu Val Val His Pro Ala Asn Ser Pro Ile Ala Asn Lys
        755                 760                 765

aat cca gat aat ccc aag aaa acc aca acc ctg tcc tac gac gtg tat       2352
Asn Pro Asp Asn Pro Lys Lys Thr Thr Thr Leu Ser Tyr Asp Val Tyr
    770                 775                 780

aag gat aag agg ttt tct gag gac cag tac gag ctg cac atc cca atc       2400
Lys Asp Lys Arg Phe Ser Glu Asp Gln Tyr Glu Leu His Ile Pro Ile
785                 790                 795                 800

gcc atc aat aag tgc ccc aag aac atc ttc aag atc aat aca gag gtg       2448
Ala Ile Asn Lys Cys Pro Lys Asn Ile Phe Lys Ile Asn Thr Glu Val
                805                 810                 815

cgc gtg ctg ctg aag cac gac gat aac ccc tat gtg atc ggc atc gat       2496
Arg Val Leu Leu Lys His Asp Asp Asn Pro Tyr Val Ile Gly Ile Asp
            820                 825                 830

agg ggc gag cgc aat ctg ctg tat atc gtg gtg gtg gac ggc aag ggc       2544
Arg Gly Glu Arg Asn Leu Leu Tyr Ile Val Val Val Asp Gly Lys Gly
        835                 840                 845

aac atc gtg gag cag tat tcc ctg aac gag atc atc aac aac ttc aac       2592
Asn Ile Val Glu Gln Tyr Ser Leu Asn Glu Ile Ile Asn Asn Phe Asn
    850                 855                 860

ggc atc agg atc aag aca gat tac cac tct ctg ctg gac aag aag gag       2640
Gly Ile Arg Ile Lys Thr Asp Tyr His Ser Leu Leu Asp Lys Lys Glu
865                 870                 875                 880

aag gag agg ttc gag gcc cgc cag aac tgg acc tcc atc gag aat atc       2688
Lys Glu Arg Phe Glu Ala Arg Gln Asn Trp Thr Ser Ile Glu Asn Ile
                885                 890                 895

aag gag ctg aag gcc ggc tat atc tct cag gtg gtg cac aag atc tgc       2736
Lys Glu Leu Lys Ala Gly Tyr Ile Ser Gln Val Val His Lys Ile Cys
            900                 905                 910

gag ctg gtg gag aag tac gat gcc gtg atc gcc ctg gag gac ctg aac       2784
Glu Leu Val Glu Lys Tyr Asp Ala Val Ile Ala Leu Glu Asp Leu Asn
        915                 920                 925

tct ggc ttt aag aat agc cgc gtg aag gtg gag aag cag gtg tat cag       2832
Ser Gly Phe Lys Asn Ser Arg Val Lys Val Glu Lys Gln Val Tyr Gln
    930                 935                 940

aag ttc gag aag atg ctg atc gat aag ctg aac tac atg gtg gac aag       2880
Lys Phe Glu Lys Met Leu Ile Asp Lys Leu Asn Tyr Met Val Asp Lys
945                 950                 955                 960
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aag tct aat cct tgt gca aca ggc ggc gcc ctg aag ggc tat cag atc       2928
Lys Ser Asn Pro Cys Ala Thr Gly Gly Ala Leu Lys Gly Tyr Gln Ile
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acc aat aag ttc gag agc ttt aag tcc atg tct acc cag aac ggc ttc       2976
Thr Asn Lys Phe Glu Ser Phe Lys Ser Met Ser Thr Gln Asn Gly Phe
           980                 985                 990

atc ttt tac atc cct gcc tgg ctg  aca tcc aag atc gat  cca tct acc     3024
Ile Phe Tyr Ile Pro Ala Trp Leu  Thr Ser Lys Ile Asp  Pro Ser Thr
       995                 1000                1005

ggc ttt  gtg aac ctg ctg aaa  acc aag tat acc agc  atc gcc gat        3069
Gly Phe  Val Asn Leu Leu Lys  Thr Lys Tyr Thr Ser  Ile Ala Asp
    1010                1015                1020

tcc aag  aag ttc atc agc tcc  ttt gac agg atc atg  tac gtg ccc        3114
Ser Lys  Lys Phe Ile Ser Ser  Phe Asp Arg Ile Met  Tyr Val Pro
    1025                1030                1035

gag gag  gat ctg ttc gag ttt  gcc ctg gac tat aag  aac ttc tct        3159
Glu Glu  Asp Leu Phe Glu Phe  Ala Leu Asp Tyr Lys  Asn Phe Ser
    1040                1045                1050

cgc aca  gac gcc gat tac atc  aag aag tgg aag ctg  tac tcc tac        3204
Arg Thr  Asp Ala Asp Tyr Ile  Lys Lys Trp Lys Leu  Tyr Ser Tyr
    1055                1060                1065

ggc aac  cgg atc aga atc ttc  cgg aat cct aag aag  aac aac gtg        3249
Gly Asn  Arg Ile Arg Ile Phe  Arg Asn Pro Lys Lys  Asn Asn Val
    1070                1075                1080

ttc gac  tgg gag gag gtg tgc  ctg acc agc gcc tat  aag gag ctg        3294
Phe Asp  Trp Glu Glu Val Cys  Leu Thr Ser Ala Tyr  Lys Glu Leu
    1085                1090                1095

ttc aac  aag tac ggc atc aat  tat cag cag ggc gat  atc aga gcc        3339
Phe Asn  Lys Tyr Gly Ile Asn  Tyr Gln Gln Gly Asp  Ile Arg Ala
    1100                1105                1110

ctg ctg  tgc gag cag tcc gac  aag gcc ttc tac tct  agc ttt atg        3384
Leu Leu  Cys Glu Gln Ser Asp  Lys Ala Phe Tyr Ser  Ser Phe Met
    1115                1120                1125

gcc ctg  atg agc ctg atg ctg  cag atg cgg aac agc  atc aca ggc        3429
Ala Leu  Met Ser Leu Met Leu  Gln Met Arg Asn Ser  Ile Thr Gly
    1130                1135                1140

cgc acc  gac gtg gat ttt ctg  atc agc cct gtg aag  aac tcc gac        3474
Arg Thr  Asp Val Asp Phe Leu  Ile Ser Pro Val Lys  Asn Ser Asp
    1145                1150                1155

ggc atc  ttc tac gat agc cgg  aac tat gag gcc cag  gag aat gcc        3519
Gly Ile  Phe Tyr Asp Ser Arg  Asn Tyr Glu Ala Gln  Glu Asn Ala
    1160                1165                1170

atc ctg  cca aag aac gcc gac  gcc aat ggc gcc tat  aac atc gcc        3564
Ile Leu  Pro Lys Asn Ala Asp  Ala Asn Gly Ala Tyr  Asn Ile Ala
    1175                1180                1185

aga aag  gtg ctg tgg gcc atc  ggc cag ttc aag aag  gcc gag gac        3609
Arg Lys  Val Leu Trp Ala Ile  Gly Gln Phe Lys Lys  Ala Glu Asp
    1190                1195                1200
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gag aag  ctg gat aag gtg aag  atc gcc atc tct aac  aag gag tgg        3654
Glu Lys  Leu Asp Lys Val Lys  Ile Ala Ile Ser Asn  Lys Glu Trp
    1205                 1210                 1215

ctg gag  tac gcc cag acc agc  gtg aag cac                            3684
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Asn Lys Arg Leu Leu Val Glu Asp Glu Lys Arg Ala Glu Asp Tyr Lys
        35                  40                  45

Gly Val Lys Lys Leu Leu Asp Arg Tyr Tyr Leu Ser Phe Ile Asn Asp
    50                  55                  60

Val Leu His Ser Ile Lys Leu Lys Asn Leu Asn Asn Tyr Ile Ser Leu
65                  70                  75                  80

Phe Arg Lys Lys Thr Arg Thr Glu Lys Glu Asn Lys Glu Leu Glu Asn
                85                  90                  95

Leu Glu Ile Asn Leu Arg Lys Glu Ile Ala Lys Ala Phe Lys Gly Asn
            100                 105                 110

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

Pro Glu Phe Leu Asp Asp Lys Asp Glu Ile Ala Leu Val Asn Ser Phe
    130                 135                 140

Asn Gly Phe Thr Thr Ala Phe Thr Gly Phe Phe Asp Asn Arg Glu Asn
145                 150                 155                 160

Met Phe Ser Glu Glu Ala Lys Ser Thr Ser Ile Ala Phe Arg Cys Ile
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Asn Glu Asn Leu Thr Arg Tyr Ile Ser Asn Met Asp Ile Phe Glu Lys
            180                 185                 190
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Val Asp Ala Ile Phe Asp Lys His Glu Val Gln Glu Ile Lys Glu Lys
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Ile Leu Asn Ser Asp Tyr Asp Val Glu Asp Phe Phe Glu Gly Glu Phe
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Phe Asn Phe Val Leu Thr Gln Glu Gly Ile Asp Val Tyr Asn Ala Ile
225                 230                 235                 240

Ile Gly Gly Phe Val Thr Glu Ser Gly Glu Lys Ile Lys Gly Leu Asn
                245                 250                 255

Glu Tyr Ile Asn Leu Tyr Asn Gln Lys Thr Lys Gln Lys Leu Pro Lys
            260                 265                 270

Phe Lys Pro Leu Tyr Lys Gln Val Leu Ser Asp Arg Glu Ser Leu Ser
        275                 280                 285

Phe Tyr Gly Glu Gly Tyr Thr Ser Asp Glu Glu Val Leu Glu Val Phe
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Arg Asn Thr Leu Asn Lys Asn Ser Glu Ile Phe Ser Ser Ile Lys Lys
305                 310                 315                 320

Leu Glu Lys Leu Phe Lys Asn Phe Asp Glu Tyr Ser Ser Ala Gly Ile
                325                 330                 335

Phe Val Lys Asn Gly Pro Ala Ile Ser Thr Ile Ser Lys Asp Ile Phe
            340                 345                 350

Gly Glu Trp Asn Val Ile Arg Asp Lys Trp Asn Ala Glu Tyr Asp Asp
        355                 360                 365

Ile His Leu Lys Lys Lys Ala Val Val Thr Glu Lys Tyr Glu Asp Asp
    370                 375                 380

Arg Arg Lys Ser Phe Lys Lys Ile Gly Ser Phe Ser Leu Glu Gln Leu
385                 390                 395                 400

Gln Glu Tyr Ala Asp Ala Asp Leu Ser Val Val Glu Lys Leu Lys Glu
                405                 410                 415

Ile Ile Ile Gln Lys Val Asp Glu Ile Tyr Lys Val Tyr Gly Ser Ser
            420                 425                 430

Glu Lys Leu Phe Asp Ala Asp Phe Val Leu Glu Lys Ser Leu Lys Lys
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Asn Asp Ala Val Val Ala Ile Met Lys Asp Leu Leu Asp Ser Val Lys
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Ser Phe Glu Asn Tyr Ile Lys Ala Phe Phe Gly Glu Gly Lys Glu Thr
465                 470                 475                 480

Asn Arg Asp Glu Ser Phe Tyr Gly Asp Phe Val Leu Ala Tyr Asp Ile
                485                 490                 495

Leu Leu Lys Val Asp His Ile Tyr Asp Ala Ile Arg Asn Tyr Val Thr
            500                 505                 510

Gln Lys Pro Tyr Ser Lys Asp Lys Phe Lys Leu Tyr Phe Gln Asn Pro
        515                 520                 525

Gln Phe Met Gly Gly Trp Asp Lys Asp Lys Glu Thr Asp Tyr Arg Ala
    530                 535                 540

Thr Ile Leu Arg Tyr Gly Ser Lys Tyr Tyr Leu Ala Ile Met Asp Lys
545                 550                 555                 560

Lys Tyr Ala Lys Cys Leu Gln Lys Ile Asp Lys Asp Asp Val Asn Gly
                565                 570                 575

Asn Tyr Glu Lys Ile Asn Tyr Lys Leu Leu Pro Gly Pro Asn Lys Met
            580                 585                 590

Leu Pro Lys Val Phe Phe Ser Lys Lys Trp Met Ala Tyr Tyr Asn Pro
        595                 600                 605

Ser Glu Asp Ile Gln Lys Ile Tyr Lys Asn Gly Thr Phe Lys Lys Gly
    610                 615                 620

Asp Met Phe Asn Leu Asn Asp Cys His Lys Leu Ile Asp Phe Phe Lys
625                 630                 635                 640

Asp Ser Ile Ser Arg Tyr Pro Lys Trp Ser Asn Ala Tyr Asp Phe Asn
                645                 650                 655

Phe Ser Glu Thr Glu Lys Tyr Lys Asp Ile Ala Gly Phe Tyr Arg Glu
            660                 665                 670

Val Glu Glu Gln Gly Tyr Lys Val Ser Phe Glu Ser Ala Ser Lys Lys
        675                 680                 685

Glu Val Asp Lys Leu Val Glu Glu Gly Lys Leu Tyr Met Phe Gln Ile
    690                 695                 700
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Tyr Asn Lys Asp Phe Ser Asp Lys Ser His Gly Thr Pro Asn Leu His
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Thr Met Tyr Phe Lys Leu Leu Phe Asp Glu Asn Asn His Gly Gln Ile
                725                 730                 735

Arg Leu Ser Gly Gly Ala Glu Leu Phe Met Arg Arg Ala Ser Leu Lys
            740                 745                 750

Lys Glu Glu Leu Val Val His Pro Ala Asn Ser Pro Ile Ala Asn Lys
        755                 760                 765

Asn Pro Asp Asn Pro Lys Lys Thr Thr Thr Leu Ser Tyr Asp Val Tyr
    770                 775                 780

Lys Asp Lys Arg Phe Ser Glu Asp Gln Tyr Glu Leu His Ile Pro Ile
785                 790                 795                 800

Ala Ile Asn Lys Cys Pro Lys Asn Ile Phe Lys Ile Asn Thr Glu Val
                805                 810                 815

Arg Val Leu Leu Lys His Asp Asp Asn Pro Tyr Val Ile Gly Ile Asp
            820                 825                 830

Arg Gly Glu Arg Asn Leu Leu Tyr Ile Val Val Val Asp Gly Lys Gly
        835                 840                 845

Asn Ile Val Glu Gln Tyr Ser Leu Asn Glu Ile Ile Asn Asn Phe Asn
    850                 855                 860

Gly Ile Arg Ile Lys Thr Asp Tyr His Ser Leu Leu Asp Lys Lys Glu
865                 870                 875                 880

Lys Glu Arg Phe Glu Ala Arg Gln Asn Trp Thr Ser Ile Glu Asn Ile
                885                 890                 895

Lys Glu Leu Lys Ala Gly Tyr Ile Ser Gln Val Val His Lys Ile Cys
            900                 905                 910

Glu Leu Val Glu Lys Tyr Asp Ala Val Ile Ala Leu Glu Asp Leu Asn
        915                 920                 925

Ser Gly Phe Lys Asn Ser Arg Val Lys Val Glu Lys Gln Val Tyr Gln
    930                 935                 940

Lys Phe Glu Lys Met Leu Ile Asp Lys Leu Asn Tyr Met Val Asp Lys
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Lys Ser Asn Pro Cys Ala Thr Gly Gly Ala Leu Lys Gly Tyr Gln Ile
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Thr Asn Lys Phe Glu Ser Phe Lys Ser Met Ser Thr Gln Asn Gly Phe
           980                 985                 990

Ile Phe Tyr Ile Pro Ala Trp Leu  Thr Ser Lys Ile Asp  Pro Ser Thr
        995                 1000                1005

Gly Phe  Val Asn Leu Leu Lys  Thr Lys Tyr Thr Ser  Ile Ala Asp
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Ser Lys  Lys Phe Ile Ser Ser  Phe Asp Arg Ile Met  Tyr Val Pro
    1025                1030                1035

Glu Glu  Asp Leu Phe Glu Phe  Ala Leu Asp Tyr Lys  Asn Phe Ser
    1040                1045                1050

Arg Thr  Asp Ala Asp Tyr Ile  Lys Lys Trp Lys Leu  Tyr Ser Tyr
    1055                1060                1065

Gly Asn  Arg Ile Arg Ile Phe  Arg Asn Pro Lys Lys  Asn Asn Val
    1070                1075                1080

Phe Asp  Trp Glu Glu Val Cys  Leu Thr Ser Ala Tyr  Lys Glu Leu
    1085                1090                1095

Phe Asn  Lys Tyr Gly Ile Asn  Tyr Gln Gln Gly Asp  Ile Arg Ala
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Leu Leu  Cys Glu Gln Ser Asp  Lys Ala Phe Tyr Ser  Ser Phe Met
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Ala Leu  Met Ser Leu Met Leu  Gln Met Arg Asn Ser  Ile Thr Gly
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Arg Thr  Asp Val Asp Phe Leu  Ile Ser Pro Val Lys  Asn Ser Asp
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Gly Ile  Phe Tyr Asp Ser Arg  Asn Tyr Glu Ala Gln  Glu Asn Ala
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Ile Leu  Pro Lys Asn Ala Asp  Ala Asn Gly Ala Tyr  Asn Ile Ala
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Arg Lys  Val Leu Trp Ala Ile  Gly Gln Phe Lys Lys  Ala Glu Asp
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