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Jayaram, Hari
Selleck, William Jr.

<120> Evaluation of Cas9 molecule/guide RNA molecule complexes

<130> 118945.8008.WO00 (EM050PCT)

<150> US 62/152,473
<151> 2015-04-24

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

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

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

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Tyr Leu Gln Glu Ile Phe Ser Glu Glu Met Gly Lys Val Asp Asp Ser
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Phe Phe His Arg Leu Glu Asp Ser Phe Leu Val Thr Glu Asp Lys Arg
            100                 105                 110

Gly Glu Arg His Pro Ile Phe Gly Asn Leu Glu Glu Glu Val Lys Tyr
        115                 120                 125

His Glu Asn Phe Pro Thr Ile Tyr His Leu Arg Gln Tyr Leu Ala Asp
    130                 135                 140

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

Ile Ile Lys Phe Arg Gly His Phe Leu Ile Glu Gly Lys Phe Asp Thr
                165                 170                 175

Arg Asn Asn Asp Val Gln Arg Leu Phe Gln Glu Phe Leu Ala Val Tyr
            180                 185                 190

Asp Asn Thr Phe Glu Asn Ser Ser Leu Gln Glu Gln Asn Val Gln Val
        195                 200                 205

Glu Glu Ile Leu Thr Asp Lys Ile Ser Lys Ser Ala Lys Lys Asp Arg
    210                 215                 220

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

Phe Leu Lys Leu Ile Val Gly Asn Gln Ala Asp Phe Lys Lys His Phe
                245                 250                 255

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

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

Leu Phe Leu Ser Ala Lys Lys Leu Tyr Asp Ser Ile Leu Leu Ser Gly
    290                 295                 300

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

Met Ile Gln Arg Tyr Asn Glu His Gln Met Asp Leu Ala Gln Leu Lys
                325                 330                 335
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Gln Phe Ile Arg Gln Lys Leu Ser Asp Lys Tyr Asn Glu Val Phe Ser
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Asp Val Ser Lys Asp Gly Tyr Ala Gly Tyr Ile Asp Gly Lys Thr Asn
        355                 360                 365

Gln Glu Ala Phe Tyr Lys Tyr Leu Lys Gly Leu Leu Asn Lys Ile Glu
    370                 375                 380

Gly Ser Gly Tyr Phe Leu Asp Lys Ile Glu Arg Glu Asp Phe 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

Gln Glu Met Arg Ala Ile Ile Arg Arg Gln Ala Glu Phe Tyr Pro Phe
            420                 425                 430

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

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

Leu Ser Arg Lys Ser Ala Asp Lys Ile Thr Pro Trp Asn Phe Asp Glu
465                 470                 475                 480

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

Asn Tyr Asp Leu Tyr Leu Pro Asn Gln Lys Val Leu Pro Lys His Ser
            500                 505                 510

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

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

Gln Glu Ile Phe Asp Gly Val Phe Lys Val Tyr Arg Lys Val Thr Lys
545                 550                 555                 560

Asp Lys Leu Met Asp Phe Leu Glu Lys Glu Phe Asp Glu Phe Arg Ile
                565                 570                 575

Val Asp Leu Thr Gly Leu Asp Lys Glu Asn Lys Val Phe Asn Ala Ser
            580                 585                 590
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Tyr Gly Thr Tyr His Asp Leu Cys Lys Ile Leu Asp Lys Asp Phe Leu
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Asp Asn Ser Lys Asn Glu Lys Ile Leu Glu Asp Ile Val Leu Thr Leu
    610                 615                 620

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

Ser Asp Leu Leu Thr Lys Glu Gln Val Lys Lys Leu Glu Arg Arg His
                645                 650                 655

Tyr Thr Gly Trp Gly Arg Leu Ser Ala Glu Leu Ile His Gly Ile Arg
            660                 665                 670

Asn Lys Glu Ser Arg Lys Thr Ile Leu Asp Tyr Leu Ile Asp Asp Gly
        675                 680                 685

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

Phe Lys Glu Glu Ile Ala Lys Ala Gln Val Ile Gly Glu Thr Asp Asn
705                 710                 715                 720

Leu Asn Gln Val Val Ser Asp Ile Ala Gly Ser Pro Ala Ile Lys Lys
                725                 730                 735

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

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

Phe Thr Asn Gln Gly Arg Arg Asn Ser Gln Gln Arg Leu Lys Gly Leu
    770                 775                 780

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

Val Glu Asn Ser Gln Leu Gln Asn Asp Arg Leu Phe Leu Tyr Tyr Leu
                805                 810                 815

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

Leu Ser Gln Tyr Asp Ile Asp His Ile Ile Pro Gln Ala Phe Ile Lys
        835                 840                 845
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Asp Asn Ser Ile Asp Asn Arg Val Leu Thr Ser Ser Lys Glu Asn Arg
    850                 855                 860

Gly Lys Ser Asp Asp Val Pro Ser Lys Asp Val Val Arg Lys Met Lys
865                 870                 875                 880

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

Phe Asp Asn Leu Thr Lys Ala Glu Arg Gly Gly Leu Thr Asp Asp 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 Arg Ile Leu Asp Glu Arg Phe Asn Thr Glu Thr Asp
    930                 935                 940

Glu Asn Asn Lys Lys Ile Arg Gln Val Lys Ile Val Thr Leu Lys Ser
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Asn Leu Val Ser Asn Phe Arg Lys Glu Phe Glu Leu Tyr Lys Val Arg
                965                 970                 975

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

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

Val Tyr  Gly Asp Tyr Pro His  Phe His Gly His Lys  Glu Asn Lys
    1010                1015                1020

Ala Thr  Ala Lys Lys Phe Phe  Tyr Ser Asn Ile Met  Asn Phe Phe
    1025                1030                1035

Lys Lys  Asp Asp Val Arg Thr  Asp Lys Asn Gly Glu  Ile Ile Trp
    1040                1045                1050

Lys Lys  Asp Glu His Ile Ser  Asn Ile Lys Lys Val  Leu Ser Tyr
    1055                1060                1065

Pro Gln  Val Asn Ile Val Lys  Lys Val Glu Glu Gln  Thr Gly Gly
    1070                1075                1080

Phe Ser  Lys Glu Ser Ile Leu  Pro Lys Gly Asn Ser  Asp Lys Leu
    1085                1090                1095
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Ile Pro  Arg Lys Thr Lys Lys  Phe Tyr Trp Asp Thr  Lys Lys Tyr
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Gly Gly  Phe Asp Ser Pro Ile  Val Ala Tyr Ser Ile  Leu Val Ile
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Ala Asp  Ile Glu Lys Gly Lys  Ser Lys Lys Leu Lys  Thr Val Lys
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Ala Leu  Val Gly Val Thr Ile  Met Glu Lys Met Thr  Phe Glu Arg
    1145                1150                1155

Asp Pro  Val Ala Phe Leu Glu  Arg Lys Gly Tyr Arg  Asn Val Gln
    1160                1165                1170

Glu Glu  Asn Ile Ile Lys Leu  Pro Lys Tyr Ser Leu  Phe Lys Leu
    1175                1180                1185

Glu Asn  Gly Arg Lys Arg Leu  Leu Ala Ser Ala Arg  Glu Leu Gln
    1190                1195                1200

Lys Gly  Asn Glu Ile Val Leu  Pro Asn His Leu Gly  Thr Leu Leu
    1205                1210                1215

Tyr His  Ala Lys Asn Ile His  Lys Val Asp Glu Pro  Lys His Leu
    1220                1225                1230

Asp Tyr  Val Asp Lys His Lys  Asp Glu Phe Lys Glu  Leu Leu Asp
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Val Val  Ser Asn Phe Ser Lys  Lys Tyr Thr Leu Ala  Glu Gly Asn
    1250                1255                1260

Leu Glu  Lys Ile Lys Glu Leu  Tyr Ala Gln Asn Asn  Gly Glu Asp
    1265                1270                1275

Leu Lys  Glu Leu Ala Ser Ser  Phe Ile Asn Leu Leu  Thr Phe Thr
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Ala Ile  Gly Ala Pro Ala Thr  Phe Lys Phe Phe Asp  Lys Asn Ile
    1295                1300                1305

Asp Arg  Lys Arg Tyr Thr Ser  Thr Thr Glu Ile Leu  Asn Ala Thr
    1310                1315                1320

Leu Ile  His Gln Ser Ile Thr  Gly Leu Tyr Glu Thr  Arg Ile Asp
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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
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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
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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
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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
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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
    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
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Leu Val  Val Ala Lys Val Glu  Lys Gly Lys Ser Lys  Lys Leu Lys
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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
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Glu Leu  Gln Lys Gly Asn Glu  Leu Ala Leu Pro Ser  Lys Tyr Val
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Asn Phe  Leu Tyr Leu Ala Ser  His Tyr Glu Lys Leu  Lys Gly Ser
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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
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Gly Leu  Tyr Glu Thr Arg Ile  Asp Leu Ser Gln Leu  Gly Gly Asp
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ccccttatag agacaaatgg tgaaacaggt gaaatcgtct gggataaggg cagggatttc 3240

gctactgtga ggaaggtgct gagtatgcca caggtaaata tcgtgaaaaa aaccgaagta 3300

cagaccggag gattttccaa ggaaagcatt ttgcctaaaa gaaactcaga caagctcatc 3360

gcccgcaaga aagattggga ccctaagaaa tacgggggat ttgactcacc caccgtagcc 3420

tattctgtgc tggtggtagc taaggtggaa aaaggaaagt ctaagaagct gaagtccgtg 3480

aaggaactct tgggaatcac tatcatggaa agatcatcct ttgaaaagaa ccctatcgat 3540

ttcctggagg ctaagggtta caaggaggtc aagaaagacc tcatcattaa actgccaaaa 3600

tactctctct tcgagctgga aaatggcagg aagagaatgt tggccagcgc cggagagctg 3660

caaaagggaa acgagcttgc tctgccctcc aaatatgtta attttctcta tctcgcttcc 3720

cactatgaaa agctgaaagg gtctcccgaa gataacgagc agaagcagct gttcgtcgaa 3780

cagcacaagc actatctgga tgaaataatc gaacaaataa gcgagttcag caaaagggtt 3840

atcctggcgg atgctaattt ggacaaagta ctgtctgctt ataacaagca ccgggataag 3900

cctattaggg aacaagccga gaatataatt cacctcttta cactcacgaa tctcggagcc 3960

cccgccgcct tcaaatactt tgatacgact atcgaccgga aacggtatac cagtaccaaa 4020

gaggtcctcg atgccaccct catccaccag tcaattactg gcctgtacga aacacggatc 4080

gacctctctc aactgggcgg cgactag 4107

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Met Thr Lys Pro Tyr Ser Ile Gly Leu Asp Ile Gly Thr Asn Ser Val
1 5 10 15

Gly Trp Ala Val Thr Thr Asp Asn Tyr Lys Val Pro Ser Lys Lys Met
20 25 30

Lys Val Leu Gly Asn Thr Ser Lys Lys Tyr Ile Lys Lys Asn Leu Leu
35 40 45

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

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

Tyr Leu Gln Glu Ile Phe Ser Thr Glu Met Ala Thr Leu Asp Asp Ala
85 90 95

```
Phe Phe Gln Arg Leu Asp Asp Ser Phe Leu Val Pro Asp Asp Lys Arg
            100                 105                 110

Asp Ser Lys Tyr Pro Ile Phe Gly Asn Leu Val Glu Glu Lys Ala Tyr
        115                 120                 125

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

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

Met Ile Lys Tyr Arg Gly His Phe Leu Ile Glu Gly Glu Phe Asn Ser
                165                 170                 175

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

Asn Ala Ile Phe Glu Ser Asp Leu Ser Leu Glu Asn Ser Lys Gln Leu
        195                 200                 205

Glu Glu Ile Val Lys Asp Lys Ile Ser Lys Leu Glu Lys Lys Asp Arg
    210                 215                 220

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

Phe Leu Lys Leu Ile Val Gly Asn Gln Ala Asp Phe Arg Lys Cys Phe
                245                 250                 255

Asn Leu Asp Glu Lys Ala Ser Leu His Phe Ser Lys Glu Ser Tyr Asp
            260                 265                 270

Glu Asp Leu Glu Thr Leu Leu Gly Tyr Ile Gly Asp Asp Tyr Ser Asp
        275                 280                 285

Val Phe Leu Lys Ala Lys Lys Leu Tyr Asp Ala Ile Leu Leu Ser Gly
    290                 295                 300

Phe Leu Thr Val Thr Asp Asn Glu Thr Glu Ala Pro Leu Ser Ser Ala
305                 310                 315                 320

Met Ile Lys Arg Tyr Asn Glu His Lys Glu Asp Leu Ala Leu Leu Lys
                325                 330                 335

Glu Tyr Ile Arg Asn Ile Ser Leu Lys Thr Tyr Asn Glu Val Phe Lys
            340                 345                 350
```

```
Asp Asp Thr Lys Asn Gly Tyr Ala Gly Tyr Ile Asp Gly Lys Thr Asn
        355                 360                 365

Gln Glu Asp Phe Tyr Val Tyr Leu Lys Lys Leu Leu Ala Glu Phe Glu
    370                 375                 380

Gly Ala Asp Tyr Phe Leu Glu Lys Ile Asp Arg Glu Asp Phe Leu Arg
385                 390                 395                 400

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

Gln Glu Met Arg Ala Ile Leu Asp Lys Gln Ala Lys Phe Tyr Pro Phe
            420                 425                 430

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

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

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

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

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

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

Phe Ile Ala Glu Ser Met Arg Asp Tyr Gln Phe Leu Asp Ser Lys Gln
    530                 535                 540

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

Asp Lys Asp Ile Ile Glu Tyr Leu His Ala Ile Tyr Gly Tyr Asp Gly
                565                 570                 575

Ile Glu Leu Lys Gly Ile Glu Lys Gln Phe Asn Ser Ser Leu Ser Thr
            580                 585                 590

Tyr His Asp Leu Leu Asn Ile Ile Asn Asp Lys Glu Phe Leu Asp Asp
        595                 600                 605
```

```
Ser Ser Asn Glu Ala Ile Ile Glu Glu Ile Ile His Thr Leu Thr Ile
    610                 615                 620

Phe Glu Asp Arg Glu Met Ile Lys Gln Arg Leu Ser Lys Phe Glu Asn
625                 630                 635                 640

Ile Phe Asp Lys Ser Val Leu Lys Lys Leu Ser Arg Arg His Tyr Thr
                645                 650                 655

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

Lys Ser Gly Asn Thr Ile Leu Asp Tyr Leu Ile Asp Asp Gly Ile Ser
        675                 680                 685

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

Lys Lys Ile Gln Lys Ala Gln Ile Ile Gly Asp Glu Asp Lys Gly Asn
705                 710                 715                 720

Ile Lys Glu Val Val Lys Ser Leu Pro Gly Ser Pro Ala Ile Lys Lys
                725                 730                 735

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

Gly Gly Arg Lys Pro Glu Ser Ile Val Val Glu Met Ala Arg Glu Asn
        755                 760                 765

Gln Tyr Thr Asn Gln Gly Lys Ser Asn Ser Gln Gln Arg Leu Lys Arg
    770                 775                 780

Leu Glu Lys Ser Leu Lys Glu Leu Gly Ser Lys Ile Leu Lys Glu Asn
785                 790                 795                 800

Ile Pro Ala Lys Leu Ser Lys Ile Asp Asn Asn Ala Leu Gln Asn Asp
                805                 810                 815

Arg Leu Tyr Leu Tyr Tyr Leu Gln Asn Gly Lys Asp Met Tyr Thr Gly
            820                 825                 830

Asp Asp Leu Asp Ile Asp Arg Leu Ser Asn Tyr Asp Ile Asp His Ile
        835                 840                 845

Ile Pro Gln Ala Phe Leu Lys Asp Asn Ser Ile Asp Asn Lys Val Leu
    850                 855                 860
```

```
Val Ser Ser Ala Ser Asn Arg Gly Lys Ser Asp Asp Val Pro Ser Leu
865                 870                 875                 880

Glu Val Val Lys Lys Arg Lys Thr Phe Trp Tyr Gln Leu Leu Lys Ser
                885                 890                 895

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

Gly Gly Leu Ser Pro Glu Asp Lys Ala Gly Phe Ile Gln Arg Gln Leu
        915                 920                 925

Val Glu Thr Arg Gln Ile Thr Lys His Val Ala Arg Leu Leu Asp Glu
    930                 935                 940

Lys Phe Asn Asn Lys Lys Asp Glu Asn Asn Arg Ala Val Arg Thr Val
945                 950                 955                 960

Lys Ile Ile Thr Leu Lys Ser Thr Leu Val Ser Gln Phe Arg Lys Asp
                965                 970                 975

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

Asp Ala Tyr Leu Asn Ala Val Val  Ala Ser Ala Leu Leu  Lys Lys Tyr
        995                 1000                1005

Pro Lys  Leu Glu Pro Glu Phe  Val Tyr Gly Asp Tyr  Pro Lys Tyr
    1010                1015                1020

Asn Ser  Phe Arg Glu Arg Lys  Ser Ala Thr Glu Lys  Val Tyr Phe
    1025                1030                1035

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

Asp Gly  Arg Val Ile Glu Arg  Pro Leu Ile Glu Val  Asn Glu Glu
    1055                1060                1065

Thr Gly  Glu Ser Val Trp Asn  Lys Glu Ser Asp Leu  Ala Thr Val
    1070                1075                1080

Arg Arg  Val Leu Ser Tyr Pro  Gln Val Asn Val Val  Lys Lys Val
    1085                1090                1095

Glu Glu  Gln Asn His Gly Leu  Asp Arg Gly Lys Pro  Lys Gly Leu
    1100                1105                1110
```

```
Phe Asn  Ala Asn Leu Ser Ser  Lys Pro Lys Pro Asn  Ser Asn Glu
    1115                 1120                 1125

Asn Leu  Val Gly Ala Lys Glu  Tyr Leu Asp Pro Lys  Lys Tyr Gly
    1130                 1135                 1140

Gly Tyr  Ala Gly Ile Ser Asn  Ser Phe Thr Val Leu  Val Lys Gly
    1145                 1150                 1155

Thr Ile  Glu Lys Gly Ala Lys  Lys Lys Ile Thr Asn  Val Leu Glu
    1160                 1165                 1170

Phe Gln  Gly Ile Ser Ile Leu  Asp Arg Ile Asn Tyr  Arg Lys Asp
    1175                 1180                 1185

Lys Leu  Asn Phe Leu Leu Glu  Lys Gly Tyr Lys Asp  Ile Glu Leu
    1190                 1195                 1200

Ile Ile  Glu Leu Pro Lys Tyr  Ser Leu Phe Glu Leu  Ser Asp Gly
    1205                 1210                 1215

Ser Arg  Arg Met Leu Ala Ser  Ile Leu Ser Thr Asn  Asn Lys Arg
    1220                 1225                 1230

Gly Glu  Ile His Lys Gly Asn  Gln Ile Phe Leu Ser  Gln Lys Phe
    1235                 1240                 1245

Val Lys  Leu Leu Tyr His Ala  Lys Arg Ile Ser Asn  Thr Ile Asn
    1250                 1255                 1260

Glu Asn  His Arg Lys Tyr Val  Glu Asn His Lys Lys  Glu Phe Glu
    1265                 1270                 1275

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

Ala Lys  Lys Asn Gly Lys Leu  Leu Asn Ser Ala Phe  Gln Ser Trp
    1295                 1300                 1305

Gln Asn  His Ser Ile Asp Glu  Leu Cys Ser Ser Phe  Ile Gly Pro
    1310                 1315                 1320

Thr Gly  Ser Glu Arg Lys Gly  Leu Phe Glu Leu Thr  Ser Arg Gly
    1325                 1330                 1335

Ser Ala  Ala Asp Phe Glu Phe  Leu Gly Val Lys Ile  Pro Arg Tyr
    1340                 1345                 1350
```

```
Arg Asp  Tyr Thr Pro Ser Ser  Leu Leu Lys Asp Ala  Thr Leu Ile
    1355                1360                1365


His Gln  Ser Val Thr Gly Leu  Tyr Glu Thr Arg Ile  Asp Leu Ala
    1370                1375                1380


Lys Leu  Gly Glu Gly
    1385


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<222>  (985)..(992)
<223>  RuvC-like domain

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Met Lys Lys Pro Tyr Thr Ile Gly Leu Asp Ile Gly Thr Asn Ser Val
1               5                   10                  15


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


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


Gly Val Arg Leu Phe Asp Glu Gly Gln Thr Ala Ala Asp Arg Arg Met
    50                  55                  60


Ala Arg Thr Ala Arg Arg Arg Ile Glu Arg Arg Arg Asn Arg Ile Ser
65                  70                  75                  80


Tyr Leu Gln Gly Ile Phe Ala Glu Glu Met Ser Lys Thr Asp Ala Asn
                85                  90                  95
```

```
Phe Phe Cys Arg Leu Ser Asp Ser Phe Tyr Val Asp Asn Glu Lys Arg
            100                 105                 110

Asn Ser Arg His Pro Phe Phe Ala Thr Ile Glu Glu Glu Val Glu Tyr
        115                 120                 125

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

Ser Ser Glu Lys Ala Asp Leu Arg Leu Val Tyr Leu Ala Leu Ala His
145                 150                 155                 160

Ile Ile Lys Tyr Arg Gly Asn Phe Leu Ile Glu Gly Ala Leu Asp Thr
                165                 170                 175

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

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

Glu Asp Asn Lys Asp Val Ala Lys Ile Leu Val Glu Lys Val Thr Arg
    210                 215                 220

Lys Glu Lys Leu Glu Arg Ile Leu Lys Leu Tyr Pro Gly Glu Lys Ser
225                 230                 235                 240

Ala Gly Met Phe Ala Gln Phe Ile Ser Leu Ile Val Gly Ser Lys Gly
                245                 250                 255

Asn Phe Gln Lys Pro Phe Asp Leu Ile Glu Lys Ser Asp Ile Glu Cys
            260                 265                 270

Ala Lys Asp Ser Tyr Glu Glu Asp Leu Glu Ser Leu Leu Ala Leu Ile
        275                 280                 285

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

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

Ala Lys Leu Ser Ala Ser Met Ile Glu Arg Phe Asp Thr His Glu Glu
                325                 330                 335

Asp Leu Gly Glu Leu Lys Ala Phe Ile Lys Leu His Leu Pro Lys His
            340                 345                 350
```

```
Tyr Glu Glu Ile Phe Ser Asn Thr Glu Lys His Gly Tyr Ala Gly Tyr
        355                 360                 365

Ile Asp Gly Lys Thr Lys Gln Ala Asp Phe Tyr Lys Tyr Met Lys Met
    370                 375                 380

Thr Leu Glu Asn Ile Glu Gly Ala Asp Tyr Phe Ile Ala Lys Ile Glu
385                 390                 395                 400

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

Pro His Gln Leu His Leu Glu Glu Leu Glu Ala Ile Leu His Gln Gln
            420                 425                 430

Ala Lys Tyr Tyr Pro Phe Leu Lys Glu Asn Tyr Asp Lys Ile Lys Ser
        435                 440                 445

Leu Val Thr Phe Arg Ile Pro Tyr Phe Val Gly Pro Leu Ala Asn Gly
    450                 455                 460

Gln Ser Glu Phe Ala Trp Leu Thr Arg Lys Ala Asp Gly Glu Ile Arg
465                 470                 475                 480

Pro Trp Asn Ile Glu Glu Lys Val Asp Phe Gly Lys Ser Ala Val Asp
                485                 490                 495

Phe Ile Glu Lys Met Thr Asn Lys Asp Thr Tyr Leu Pro Lys Glu Asn
            500                 505                 510

Val Leu Pro Lys His Ser Leu Cys Tyr Gln Lys Tyr Leu Val Tyr Asn
        515                 520                 525

Glu Leu Thr Lys Val Arg Tyr Ile Asn Asp Gln Gly Lys Thr Ser Tyr
    530                 535                 540

Phe Ser Gly Gln Glu Lys Glu Gln Ile Phe Asn Asp Leu Phe Lys Gln
545                 550                 555                 560

Lys Arg Lys Val Lys Lys Lys Asp Leu Glu Leu Phe Leu Arg Asn Met
                565                 570                 575

Ser His Val Glu Ser Pro Thr Ile Glu Gly Leu Glu Asp Ser Phe Asn
            580                 585                 590

Ser Ser Tyr Ser Thr Tyr His Asp Leu Leu Lys Val Gly Ile Lys Gln
        595                 600                 605
```

```
Glu Ile Leu Asp Asn Pro Val Asn Thr Glu Met Leu Glu Asn Ile Val
    610                 615                 620

Lys Ile Leu Thr Val Phe Glu Asp Lys Arg Met Ile Lys Glu Gln Leu
625                 630                 635                 640

Gln Gln Phe Ser Asp Val Leu Asp Gly Val Val Leu Lys Lys Leu Glu
                645                 650                 655

Arg Arg His Tyr Thr Gly Trp Gly Arg Leu Ser Ala Lys Leu Leu Met
            660                 665                 670

Gly Ile Arg Asp Lys Gln Ser His Leu Thr Ile Leu Asp Tyr Leu Met
        675                 680                 685

Asn Asp Asp Gly Leu Asn Arg Asn Leu Met Gln Leu Ile Asn Asp Ser
    690                 695                 700

Asn Leu Ser Phe Lys Ser Ile Ile Glu Lys Glu Gln Val Thr Thr Ala
705                 710                 715                 720

Asp Lys Asp Ile Gln Ser Ile Val Ala Asp Leu Ala Gly Ser Pro Ala
                725                 730                 735

Ile Lys Lys Gly Ile Leu Gln Ser Leu Lys Ile Val Asp Glu Leu Val
            740                 745                 750

Ser Val Met Gly Tyr Pro Pro Gln Thr Ile Val Val Glu Met Ala Arg
        755                 760                 765

Glu Asn Gln Thr Thr Gly Lys Gly Lys Asn Asn Ser Arg Pro Arg Tyr
    770                 775                 780

Lys Ser Leu Glu Lys Ala Ile Lys Glu Phe Gly Ser Gln Ile Leu Lys
785                 790                 795                 800

Glu His Pro Thr Asp Asn Gln Glu Leu Arg Asn Asn Arg Leu Tyr Leu
                805                 810                 815

Tyr Tyr Leu Gln Asn Gly Lys Asp Met Tyr Thr Gly Gln Asp Leu Asp
            820                 825                 830

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

Phe Ile Thr Asp Asn Ser Ile Asp Asn Leu Val Leu Thr Ser Ser Ala
    850                 855                 860
```

```
Gly Asn Arg Glu Lys Gly Asp Asp Val Pro Pro Leu Glu Ile Val Arg
865                 870                 875                 880

Lys Arg Lys Val Phe Trp Glu Lys Leu Tyr Gln Gly Asn Leu Met Ser
                885                 890                 895

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

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

Gln Ile Thr Lys Asn Val Ala Asn Ile Leu His Gln Arg Phe Asn Tyr
    930                 935                 940

Glu Lys Asp Asp His Gly Asn Thr Met Lys Gln Val Arg Ile Val Thr
945                 950                 955                 960

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

Lys Val Arg Asp Val Asn Asp Tyr His His Ala His Asp Ala Tyr Leu
            980                 985                 990

Asn Gly Val Val Ala Asn Thr Leu  Leu Lys Val Tyr Pro  Gln Leu Glu
        995                 1000                1005

Pro Glu  Phe Val Tyr Gly Asp  Tyr His Gln Phe Asp  Trp Phe Lys
    1010                1015                1020

Ala Asn  Lys Ala Thr Ala Lys  Lys Gln Phe Tyr Thr  Asn Ile Met
    1025                1030                1035

Leu Phe  Phe Ala Gln Lys Asp  Arg Ile Ile Asp Glu  Asn Gly Glu
    1040                1045                1050

Ile Leu  Trp Asp Lys Lys Tyr  Leu Asp Thr Val Lys  Lys Val Met
    1055                1060                1065

Ser Tyr  Arg Gln Met Asn Ile  Val Lys Lys Thr Glu  Ile Gln Lys
    1070                1075                1080

Gly Glu  Phe Ser Lys Ala Thr  Ile Lys Pro Lys Gly  Asn Ser Ser
    1085                1090                1095

Lys Leu  Ile Pro Arg Lys Thr  Asn Trp Asp Pro Met  Lys Tyr Gly
    1100                1105                1110
```

```
Gly Leu  Asp Ser Pro Asn Met  Ala Tyr Ala Val Val  Ile Glu Tyr
    1115                 1120                 1125

Ala Lys  Gly Lys Asn Lys Leu  Val Phe Glu Lys Lys  Ile Ile Arg
    1130                 1135                 1140

Val Thr  Ile Met Glu Arg Lys  Ala Phe Glu Lys Asp  Glu Lys Ala
    1145                 1150                 1155

Phe Leu  Glu Glu Gln Gly Tyr  Arg Gln Pro Lys Val  Leu Ala Lys
    1160                 1165                 1170

Leu Pro  Lys Tyr Thr Leu Tyr  Glu Cys Glu Glu Gly  Arg Arg Arg
    1175                 1180                 1185

Met Leu  Ala Ser Ala Asn Glu  Ala Gln Lys Gly Asn  Gln Gln Val
    1190                 1195                 1200

Leu Pro  Asn His Leu Val Thr  Leu Leu His His Ala  Ala Asn Cys
    1205                 1210                 1215

Glu Val  Ser Asp Gly Lys Ser  Leu Asp Tyr Ile Glu  Ser Asn Arg
    1220                 1225                 1230

Glu Met  Phe Ala Glu Leu Leu  Ala His Val Ser Glu  Phe Ala Lys
    1235                 1240                 1245

Arg Tyr  Thr Leu Ala Glu Ala  Asn Leu Asn Lys Ile  Asn Gln Leu
    1250                 1255                 1260

Phe Glu  Gln Asn Lys Glu Gly  Asp Ile Lys Ala Ile  Ala Gln Ser
    1265                 1270                 1275

Phe Val  Asp Leu Met Ala Phe  Asn Ala Met Gly Ala  Pro Ala Ser
    1280                 1285                 1290

Phe Lys  Phe Phe Glu Thr Thr  Ile Glu Arg Lys Arg  Tyr Asn Asn
    1295                 1300                 1305

Leu Lys  Glu Leu Leu Asn Ser  Thr Ile Ile Tyr Gln  Ser Ile Thr
    1310                 1315                 1320

Gly Leu  Tyr Glu Ser Arg Lys  Arg Leu Asp Asp
    1325                 1330
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<211> 1053

<212> PRT
<213> Staphylococcus aureus

<400> 6

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Met Lys Arg Asn Tyr Ile Leu Gly Leu Asp Ile Gly Ile Thr Ser Val
1               5                  10                  15

Gly Tyr Gly Ile Ile Asp Tyr Glu Thr Arg Asp Val Ile Asp Ala Gly
            20                  25                  30

Val Arg Leu Phe Lys Glu Ala Asn Val Glu Asn Asn Glu Gly Arg Arg
        35                  40                  45

Ser Lys Arg Gly Ala Arg Arg Leu Lys Arg Arg Arg Arg His Arg Ile
    50                  55                  60

Gln Arg Val Lys Lys Leu Leu Phe Asp Tyr Asn Leu Leu Thr Asp His
65                  70                  75                  80

Ser Glu Leu Ser Gly Ile Asn Pro Tyr Glu Ala Arg Val Lys Gly Leu
                85                  90                  95

Ser Gln Lys Leu Ser Glu Glu Glu Phe Ser Ala Ala Leu Leu His Leu
            100                 105                 110

Ala Lys Arg Arg Gly Val His Asn Val Asn Glu Val Glu Glu Asp Thr
        115                 120                 125

Gly Asn Glu Leu Ser Thr Lys Glu Gln Ile Ser Arg Asn Ser Lys Ala
    130                 135                 140

Leu Glu Glu Lys Tyr Val Ala Glu Leu Gln Leu Glu Arg Leu Lys Lys
145                 150                 155                 160

Asp Gly Glu Val Arg Gly Ser Ile Asn Arg Phe Lys Thr Ser Asp Tyr
                165                 170                 175

Val Lys Glu Ala Lys Gln Leu Leu Lys Val Gln Lys Ala Tyr His Gln
            180                 185                 190

Leu Asp Gln Ser Phe Ile Asp Thr Tyr Ile Asp Leu Leu Glu Thr Arg
        195                 200                 205

Arg Thr Tyr Tyr Glu Gly Pro Gly Glu Gly Ser Pro Phe Gly Trp Lys
    210                 215                 220

Asp Ile Lys Glu Trp Tyr Glu Met Leu Met Gly His Cys Thr Tyr Phe
225                 230                 235                 240
```

```
Pro Glu Glu Leu Arg Ser Val Lys Tyr Ala Tyr Asn Ala Asp Leu Tyr
                245                 250                 255

Asn Ala Leu Asn Asp Leu Asn Asn Leu Val Ile Thr Arg Asp Glu Asn
            260                 265                 270

Glu Lys Leu Glu Tyr Tyr Glu Lys Phe Gln Ile Ile Glu Asn Val Phe
        275                 280                 285

Lys Gln Lys Lys Lys Pro Thr Leu Lys Gln Ile Ala Lys Glu Ile Leu
    290                 295                 300

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

Pro Glu Phe Thr Asn Leu Lys Val Tyr His Asp Ile Lys Asp Ile Thr
                325                 330                 335

Ala Arg Lys Glu Ile Ile Glu Asn Ala Glu Leu Leu Asp Gln Ile Ala
            340                 345                 350

Lys Ile Leu Thr Ile Tyr Gln Ser Ser Glu Asp Ile Gln Glu Glu Leu
        355                 360                 365

Thr Asn Leu Asn Ser Glu Leu Thr Gln Glu Glu Ile Glu Gln Ile Ser
    370                 375                 380

Asn Leu Lys Gly Tyr Thr Gly Thr His Asn Leu Ser Leu Lys Ala Ile
385                 390                 395                 400

Asn Leu Ile Leu Asp Glu Leu Trp His Thr Asn Asp Asn Gln Ile Ala
                405                 410                 415

Ile Phe Asn Arg Leu Lys Leu Val Pro Lys Lys Val Asp Leu Ser Gln
            420                 425                 430

Gln Lys Glu Ile Pro Thr Thr Leu Val Asp Asp Phe Ile Leu Ser Pro
        435                 440                 445

Val Val Lys Arg Ser Phe Ile Gln Ser Ile Lys Val Ile Asn Ala Ile
    450                 455                 460

Ile Lys Lys Tyr Gly Leu Pro Asn Asp Ile Ile Ile Glu Leu Ala Arg
465                 470                 475                 480

Glu Lys Asn Ser Lys Asp Ala Gln Lys Met Ile Asn Glu Met Gln Lys
                485                 490                 495
```

```
Arg Asn Arg Gln Thr Asn Glu Arg Ile Glu Glu Ile Ile Arg Thr Thr
            500                 505                 510

Gly Lys Glu Asn Ala Lys Tyr Leu Ile Glu Lys Ile Lys Leu His Asp
        515                 520                 525

Met Gln Glu Gly Lys Cys Leu Tyr Ser Leu Glu Ala Ile Pro Leu Glu
    530                 535                 540

Asp Leu Leu Asn Asn Pro Phe Asn Tyr Glu Val Asp His Ile Ile Pro
545                 550                 555                 560

Arg Ser Val Ser Phe Asp Asn Ser Phe Asn Asn Lys Val Leu Val Lys
                565                 570                 575

Gln Glu Glu Asn Ser Lys Lys Gly Asn Arg Thr Pro Phe Gln Tyr Leu
            580                 585                 590

Ser Ser Ser Asp Ser Lys Ile Ser Tyr Glu Thr Phe Lys Lys His Ile
        595                 600                 605

Leu Asn Leu Ala Lys Gly Lys Gly Arg Ile Ser Lys Thr Lys Lys Glu
    610                 615                 620

Tyr Leu Leu Glu Glu Arg Asp Ile Asn Arg Phe Ser Val Gln Lys Asp
625                 630                 635                 640

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

Met Asn Leu Leu Arg Ser Tyr Phe Arg Val Asn Asn Leu Asp Val Lys
            660                 665                 670

Val Lys Ser Ile Asn Gly Gly Phe Thr Ser Phe Leu Arg Arg Lys Trp
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Lys Phe Lys Lys Glu Arg Asn Lys Gly Tyr Lys His His Ala Glu Asp
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Ala Leu Ile Ile Ala Asn Ala Asp Phe Ile Phe Lys Glu Trp Lys Lys
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Leu Asp Lys Ala Lys Lys Val Met Glu Asn Gln Met Phe Glu Glu Lys
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Gln Ala Glu Ser Met Pro Glu Ile Glu Thr Glu Gln Glu Tyr Lys Glu
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Tyr Lys Tyr Ser His Arg Val Asp Lys Lys Pro Asn Arg Glu Leu Ile
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Asn Asp Thr Leu Tyr Ser Thr Arg Lys Asp Asp Lys Gly Asn Thr Leu
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Ile Val Asn Asn Leu Asn Gly Leu Tyr Asp Lys Asp Asn Asp Lys Leu
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Lys Lys Leu Ile Asn Lys Ser Pro Glu Lys Leu Leu Met Tyr His His
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Asp Pro Gln Thr Tyr Gln Lys Leu Lys Leu Ile Met Glu Gln Tyr Gly
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Asp Glu Lys Asn Pro Leu Tyr Lys Tyr Tyr Glu Glu Thr Gly Asn Tyr
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Leu Thr Lys Tyr Ser Lys Lys Asp Asn Gly Pro Val Ile Lys Lys Ile
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Lys Tyr Tyr Gly Asn Lys Leu Asn Ala His Leu Asp Ile Thr Asp Asp
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Tyr Pro Asn Ser Arg Asn Lys Val Val Lys Leu Ser Leu Lys Pro Tyr
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Arg Phe Asp Val Tyr Leu Asp Asn Gly Val Tyr Lys Phe Val Thr Val
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Lys Asn Leu Asp Val Ile Lys Lys Glu Asn Tyr Tyr Glu Val Asn Ser
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Glu Phe Ile Ala Ser Phe Tyr Asn Asn Asp Leu Ile Lys Ile Asn Gly
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Glu Leu Tyr Arg Val Ile Gly Val Asn Asn Asp Leu Leu Asn Arg Ile
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Ala Arg Ser Val Arg Arg Leu Thr Arg Arg Arg Ala His Arg Leu Leu
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Phe Asp Glu Asn Gly Leu Ile Lys Ser Leu Pro Asn Thr Pro Trp Gln
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Leu Arg Ala Ala Ala Leu Asp Arg Lys Leu Thr Pro Leu Glu Trp Ser
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Lys Asn Glu Gly Glu Thr Ala Asp Lys Glu Leu Gly Ala Leu Leu Lys
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Gly Val Ala Asp Asn Ala His Ala Leu Gln Thr Gly Asp Phe Arg Thr
165 170 175

Pro Ala Glu Leu Ala Leu Asn Lys Phe Glu Lys Glu Ser Gly His Ile
180 185 190

Arg Asn Gln Arg Gly Asp Tyr Ser His Thr Phe Ser Arg Lys Asp Leu
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Gln Ala Glu Leu Ile Leu Leu Phe Glu Lys Gln Lys Glu Phe Gly Asn
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Leu Met Asp Glu Pro Tyr Arg Lys Ser Lys Leu Thr Tyr Ala Gln Ala
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Arg Lys Leu Leu Gly Leu Glu Asp Thr Ala Phe Phe Lys Gly Leu Arg
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Tyr Gly Lys Asp Asn Ala Glu Ala Ser Thr Leu Met Glu Met Lys Ala
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Tyr His Ala Ile Ser Arg Ala Leu Glu Lys Glu Gly Leu Lys Asp Lys
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Lys Ser Pro Leu Asn Leu Ser Pro Glu Leu Gln Asp Glu Ile Gly Thr
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Asp Arg Ile Gln Pro Glu Ile Leu Glu Ala Leu Leu Lys His Ile Ser
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Phe Asp Lys Phe Val Gln Ile Ser Leu Lys Ala Leu Arg Arg Ile Val
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Asp Arg Glu Lys Ala Ala Ala Lys Phe Arg Glu Tyr Phe Pro Asn Phe
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Val Gly Glu Pro Lys Ser Lys Asp Ile Leu Lys Leu Arg Leu Tyr Glu
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Gln Gln His Gly Lys Cys Leu Tyr Ser Gly Lys Glu Ile Asn Leu Gly
                565                 570                 575

Arg Leu Asn Glu Lys Gly Tyr Val Glu Ile Asp His Ala Leu Pro Phe
            580                 585                 590

Ser Arg Thr Trp Asp Asp Ser Phe Asn Asn Lys Val Leu Val Leu Gly
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Ser Glu Asn Gln Asn Lys Gly Asn Gln Thr Pro Tyr Glu Tyr Phe Asn
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Gly Lys Asp Asn Ser Arg Glu Trp Gln Glu Phe Lys Ala Arg Val Glu
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Thr Ser Arg Phe Pro Arg Ser Lys Lys Gln Arg Ile Leu Leu Gln Lys
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Phe Asp Glu Asp Gly Phe Lys Glu Arg Asn Leu Asn Asp Thr Arg Tyr
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Val Asn Arg Phe Leu Cys Gln Phe Val Ala Asp Arg Met Arg Leu Thr
        675                 680                 685

Gly Lys Gly Lys Lys Arg Val Phe Ala Ser Asn Gly Gln Ile Thr Asn
    690                 695                 700

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Arg His His Ala Leu Asp Ala Val Val Val Ala Cys Ser Thr Val Ala
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Ile Arg Val Phe Gly Lys Pro Asp Gly Lys Pro Glu Phe Glu Glu Ala
785                 790                 795                 800

Asp Thr Pro Glu Lys Leu Arg Thr Leu Leu Ala Glu Lys Leu Ser Ser
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Arg Pro Glu Ala Val His Glu Tyr Val Thr Pro Leu Phe Val Ser Arg
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Ala Pro Asn Arg Lys Met Ser Gly Gln Gly His Met Glu Thr Val Lys
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Ser Ala Lys Arg Leu Asp Glu Gly Val Ser Val Leu Arg Val Pro Leu
    850                 855                 860

Thr Gln Leu Lys Leu Lys Asp Leu Glu Lys Met Val Asn Arg Glu Arg
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Glu Pro Lys Leu Tyr Glu Ala Leu Lys Ala Arg Leu Glu Ala His Lys
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Asp Asp Pro Ala Lys Ala Phe Ala Glu Pro Phe Tyr Lys Tyr Asp Lys
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Gln Lys Thr Gly Val Trp Val Arg Asn His Asn Gly Ile Ala Asp Asn
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Pro Xaa Phe Xaa Xaa Glu Tyr His Xaa Xaa Pro Thr Ile Tyr His Leu
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Arg Xaa Leu Xaa Lys Asp Leu Arg Leu Xaa Tyr Leu Ala Leu Ala His
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Xaa Ile Lys Xaa Arg Gly Asn Phe Leu Ile Glu Gly Xaa Xaa Asn Xaa
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Xaa Xaa Phe Xaa Ala Asn Xaa Xaa Xaa Xaa Xaa Leu Xaa Xaa Gly Xaa
            820                 825                 830

Ala Phe Xaa Xaa Xaa Ile Arg Arg Tyr Xaa Xaa Xaa Thr Xaa Ile Xaa
        835                 840                 845

Gln Ser Xaa Thr Gly Leu Tyr Glu Xaa Arg Leu
    850                 855
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<220>
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<220>
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<223> Xaa is Val or His

<220>
<221> VARIANT

<222> (3)..(3)
<223> Xaa is Ile, Leu, or Val

<220>
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<222> (5)..(5)
<223> Xaa is Met or Thr

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Ile Xaa Xaa Glu Xaa Ala Arg Glu
1   5

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<223> Xaa is Ile, Leu, or Val

<400> 16

Ile Val Xaa Glu Met Ala Arg Glu
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<223> Xaa is Arg or Val

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<223> Xaa is Glu or Val

<400> 17

His His Ala Xaa Asp Ala Xaa Xaa
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<220>
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<400> 18

His His Ala His Asp Ala Tyr Leu
1 5

<210> 19
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<222> (4)..(4)
<223> Xaa is Val, Leu, Ile, or Phe

<220>
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<223> Xaa is Gly, Ala, or Ser

<220>
<221> VARIANT
<222> (6)..(6)
<223> Xaa is Leu, Ile, Val, or Phe

<220>
<221> MOD_RES
<222> (7)..(26)
<223> N-terminal RuvC-like domain, each Xaa can be any amino acid or absent, region may encompass 5-20 residues

<220>
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<222> (29)..(29)
<223> Xaa is Asp, Glu, Asn, or Gln

<400> 19

Lys Xaa Tyr Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa
1 5 10 15

Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Thr Asp Xaa Tyr
20 25 30

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<223> Xaa is Ile, Val, Met, Leu, or Thr

<220>
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<222> (4)..(4)
<223> Xaa is Thr, Ile, Val, Ser, Asn, Tyr, Glu, or Leu

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<222> (5)..(5)
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<220>
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<223> Xaa is Ser, Tyr, Asn, or Phe

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<223> Xaa is Val, Ile, Leu, Cys, Thr, or Phe

<220>
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<223> Xaa is Trp, Phe, Val, Tyr, Ser, or Leu

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<222> (10)..(10)
<223> Xaa is Ala, Ser, Cys, Val, or Gly

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<222> (11)..(11)
<223> Xaa is Val, Ile, Leu, Ala, Met, or His

<220>
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<223> Any amino acid or absent

<400> 20

Asp Xaa Gly Xaa Xaa Xaa Xaa Gly Xaa Xaa Xaa Xaa
1 5 10

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<220>
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<223> Xaa is Thr, Ile, Val, Ser, Asn, Tyr, Glu, or Leu

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<223> Xaa is Trp, Phe, Val, Tyr, Ser, or Leu

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<223> Xaa is Ala, Ser, Cys, Val, or Gly

<220>
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<222> (11)..(11)
<223> Xaa is Val, Ile, Leu, Ala, Met, or His

<220>
<221> VARIANT
<222> (12)..(12)
<223> Any amino acid or absent

<400> 21

Asp Xaa Gly Xaa Xaa Ser Xaa Gly Xaa Xaa Xaa Xaa
1   5   10

<210> 22
<211> 12
<212> PRT
<213> Artificial Sequence

<220>
<223> N-terminal RuvC-like domain

<220>
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<220>
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<223> Xaa is Asn, Ser, Gly, Ala, Asp, Thr, Arg, Met, or Phe

<220>
<221> VARIANT
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<223> Xaa is Val, Ile, Leu, Ala, Met, or His

<220>
<221> VARIANT
<222> (12)..(12)
<223> Any amino acid or absent

<400> 22

Asp Ile Gly Xaa Xaa Ser Val Gly Trp Ala Xaa Xaa
1 5 10

<210> 23
<211> 12
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<220>
<223> N-terminal RuvC-like domain

<220>
<221> MOD_RES
<222> (12)..(12)
<223> Any non-polar alkyl amino acid or a hydroxyl amino acid

<400> 23

Asp Ile Gly Thr Asn Ser Val Gly Trp Ala Val Xaa
1 5 10

<210> 24
<211> 73
<212> PRT
<213> Artificial Sequence

<220>
<223> HNH-like domain

<220>
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<222> (8)..(8)
<223> Xaa is Lys or Arg

<220>
<221> VARIANT
<222> (12)..(12)
<223> Xaa is Val or Thr

<220>
<221> VARIANT
<222> (13)..(13)

<223> Xaa is Gly or Asp

<220>
<221> VARIANT
<222> (14)..(14)
<223> Xaa is Glu, Gln, or Asp

<220>
<221> VARIANT
<222> (15)..(15)
<223> Xaa is Glu or Asp

<220>
<221> VARIANT
<222> (19)..(19)
<223> Xaa is Asp, Asn, or His

<220>
<221> VARIANT
<222> (20)..(20)
<223> Xaa is Tyr, Arg, or Asn

<220>
<221> VARIANT
<222> (23)..(23)
<223> Xaa is Gln, Asp, or Asn

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       may encompass 15-40 residues

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<223> Xaa is Gly or Glu

<220>
<221> VARIANT
<222> (69)..(69)
<223> Xaa is Ser or Gly

<220>
<221> VARIANT
<222> (71)..(71)
<223> Xaa is Asp or Asn

<400> 24

Leu Tyr Tyr Leu Gln Asn Gly Xaa Asp Met Tyr Xaa Xaa Xaa Xaa Leu
1   5   10   15

Asp Ile Xaa Xaa Leu Ser Xaa Tyr Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa
            20   25   30

Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa
        35   40   45

Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa
    50   55   60

Asn Arg Xaa Lys Xaa Asp Xaa Val Pro
65 70

<210> 25
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<220>
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<223> Xaa is Leu, Ile, Arg, Gln, Val, Met, or Lys

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<223> Xaa is Asp or Glu

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<223> Xaa is Ile, Val, Thr, Ala, or Leu

<220>
<221> VARIANT
<222> (6)..(6)
<223> Xaa is Val, Tyr, Ile, Leu, Phe, or Trp

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<223> Xaa is Ser, Ala, Asp, Thr, or Lys

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<223> Xaa is Leu, Ile, Val, or Ala

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Arg, or Tyr

<220>
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<223> Xaa is Lys, Val, Ala, Glu, Tyr, Ile, Cys, Leu, Ser, Thr, Gly, Lys, Met, Asp, or Phe

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Xaa Xaa Xaa His Xaa Xaa Pro Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa
1 5 10 15

Xaa Asn Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Asn
20 25

<210> 26
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<223> Xaa is Asp or Glu

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<223> Xaa is Ile, Val, Thr, Ala, or Leu

<220>
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<223> Xaa is Val, Tyr, Ile, Leu, Phe, or Trp

<220>
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<223> Xaa is Lys, Val, Ala, Glu, Tyr, Ile, Cys, Leu, Ser, Thr, Gly, Lys, Met, Asp, or Phe

<400> 26

Xaa Xaa Xaa His Xaa Xaa Pro Xaa Ser Xaa Xaa Xaa Asp Asp Ser Xaa
1 5 10 15

Xaa Asn Lys Val Leu Xaa Xaa Xaa Xaa Xaa Asn
20 25

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<220>
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<223> Xaa is Gln, His, Arg, Lys, Tyr, Ile, Leu, or Trp

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<223> Xaa is Phe, Leu, Val, Lys, Tyr, Met, Ile, Arg, Ala, Glu, Asp, or Gln

<220>
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<220>
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<220>
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<220>
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<220>
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<223> Xaa is Lys, Val, Ala, Glu, Tyr, Ile, Cys, Leu, Ser, Thr, Gly,
Lys, Met, Asp, or Phe

<400> 27

Xaa Val Xaa His Ile Val Pro Xaa Ser Xaa Xaa Xaa Asp Asp Ser Xaa
1 5 10 15

Xaa Asn Lys Val Leu Thr Xaa Xaa Xaa Xaa Asn
20 25

<210> 28
<211> 27
<212> PRT
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<220>
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<220>
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<223> Xaa is Ala or Ser

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<223> Xaa is Asp or Asn

<220>
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<223> Xaa is Thr or Val

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<223> Xaa is Ser or Arg

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<223> Xaa is Lys, Asp, or Ala

<220>
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<223> Xaa is Glu, Lys, Gly, or Asn

<400> 28

Asp Xaa Asp His Ile Xaa Pro Gln Xaa Phe Xaa Xaa Asp Xaa Ser Ile
1 5 10 15

Asp Asn Xaa Val Leu Xaa Xaa Ser Xaa Xaa Asn
20 25

<210> 29
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<220>
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<220>
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<220>
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<222> (21)..(42)
<223> first complementarity domain

<220>
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<222> (43)..(46)
<223> linking domain

<220>
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<222> (47)..(70)
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<400> 29
nnnnnnnnnn nnnnnnnnnn guuuuagagc uaugcuguuu uggaaacaaa acagcauagc 60

aaguuaaaau aaggcuaguc cguuaucaac uugaaaaagu ggcaccgagu cggugc 116

<210> 30
<211> 116
<212> RNA
<213> Artificial Sequence

<220>
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<220>
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<223> a, c, u, g, unknown or other

<220>
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<220>
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<223> first complementarity domain

<220>
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<223> linking domain

<220>
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<222> (47)..(70)
<223> second complementarity domain

<400> 30
nnnnnnnnnn nnnnnnnnnn guauuagagc uaugcuguau uggaaacaau acagcauagc 60

aaguuaauau aaggcuaguc cguuaucaac uugaaaaagu ggcaccgagu cggugc 116

<210> 31
<211> 96
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<220>
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<222> (21)..(32)

<223> first complementarity domain

<220>
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<222> (33)..(36)
<223> linking domain

<220>
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<222> (37)..(50)
<223> second complementarity domain

<220>
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<222> (51)..(62)
<223> proximal domain

<400> 31
nnnnnnnnnn nnnnnnnnnn guuuaagagc uagaaauagc aaguuuaaau aaggcuaguc 60

cguuaucaac uugaaaaagu ggcaccgagu cggugc 96

<210> 32
<211> 47
<212> RNA
<213> Artificial Sequence

<220>
<223> gRNA proximal and tail domains derived from S. pyogenes

<400> 32
aaggcuaguc cguuaucaac uugaaaaagu ggcaccgagu cggugcu 47

<210> 33
<211> 49
<212> RNA
<213> Artificial Sequence

<220>
<223> gRNA proximal and tail domains

<400> 33
aaggcuaguc cguuaucaac uugaaaaagu ggcaccgagu cgguggugc 49

<210> 34
<211> 51
<212> RNA
<213> Artificial Sequence

<220>
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<400> 34
aaggcuaguc cguuaucaac uugaaaaagu ggcaccgagu cggugcggau c 51

<210> 35
<211> 31
<212> RNA
<213> Artificial Sequence

<220>
<223> gRNA proximal and tail domains

<400> 35
aaggcuaguc cguuaucaac uugaaaaagu g 31

<210> 36
<211> 18
<212> RNA
<213> Artificial Sequence

<220>
<223> gRNA proximal and tail domains

<400> 36
aaggcuaguc cguuauca 18

<210> 37
<211> 12
<212> RNA
<213> Artificial Sequence

<220>
<223> gRNA proximal and tail domains

<400> 37
aaggcuaguc cg 12

<210> 38
<211> 102
<212> RNA
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<220>
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<223> n is a, c, g, or u

<220>
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<222> (1)..(20)
<223> Targeting domain

<400> 38
nnnnnnnnnn nnnnnnnnnn guuuuaguac ucuggaaaca gaaucuacua aaacaaggca 60

aaaugccgug uuuaucucgu caacuuguug gcgagauuuu uu 102

<210> 39
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<212> RNA
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<220>
<223> Modular gRNA derived from S. pyogenes

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<223> a, c, u, g, unknown or other

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<223> Targeting domain

<220>
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<222> (21)..(42)
<223> First complementarity domain

<400> 39
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aaguuaaaau aaggcuaguc cguuauc 87

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caccgauucg guguuuuu 78

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guggcaccga gucggugcuu uuuuu 85

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cguuaucaac uugaaaaagu ggcaccgagu cggugc 96

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ggcuaguccg uuaucaacuu gaaaaagugg caccgagucg gugc 104

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aaggcuaguc cguuaucaac uugaaaaagu ggcaccgagu cggugc 106

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1 5 10

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<210> 58
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<213> Bacteroides fragilis, NCTC 9343

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<210> 67
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<210> 68
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<210> 74
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<210> 82
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<210> 83
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<210> 84
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<213> Eubacterium dolichum DSM 3991

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<210> 85
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<210> 86
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<210> 87
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<210> 88
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<210> 91
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<213> Staphylococcus pseudintermedius ED99

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<210> 94
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<213> Prevotella denticola

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1 5 10

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<213> Methylophilus sp. OH31

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1 5 10

<210> 103
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<210> 104
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<213> Clostridium perfringens

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<210> 105
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<210> 108
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1 5 10

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1 5 10

<210> 120
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1 5 10

<210> 121
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1 5 10

<210> 122
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1 5 10

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<213> Solobacterium moorei F0204

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1 5 10

<210> 124
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<213> Treponema denticola

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<213> Coprococcus catus GD-7

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            20   25

<210> 126
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<213> Peptoniphilus duerdenii

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Glu Asn Arg Val Leu Val Lys Lys Asn Leu Asn
            20   25

<210> 127
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<212> PRT
<213> Catenibacterium mitsuokai DSM 15897

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Asp Asn Arg Val Leu Val Val Pro Ser Glu Asn
            20   25

<210> 128
<211> 27
<212> PRT
<213> S. mutans

<400> 128

Asp Ile Asp His Ile Ile Pro Gln Ala Phe Ile Lys Asp Asn Ser Ile
1   5   10   15

Asp Asn Arg Val Leu Thr Ser Ser Lys Glu Asn
            20   25

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<210> 130
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<213> Oenococcus kitaharae DSM 17330

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1 5 10 15

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<210> 131
<211> 27
<212> PRT
<213> L. inocua

<400> 131

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1 5 10 15

Asp Asn Leu Val Leu Thr Ser Ser Ala Gly Asn
20 25

<210> 132
<211> 27
<212> PRT
<213> S. pyogenes

<400> 132

Asp Val Asp His Ile Val Pro Gln Ser Phe Leu Lys Asp Asp Ser Ile
1 5 10 15

Asp Asn Lys Val Leu Thr Arg Ser Asp Lys Asn
20 25

<210> 133
<211> 27
<212> PRT
<213> Acidaminococcus sp. D21

<400> 133

Asn Ile Asp His Ile Tyr Pro Gln Ser Met Val Lys Asp Asp Ser Leu
1 5 10 15

Asp Asn Lys Val Leu Val Gln Ser Glu Ile Asn
20 25

<210> 134
<211> 27
<212> PRT
<213> Lactobacillus rhamnosus GG

<400> 134

Asp Ile Asp His Ile Leu Pro Gln Ser Leu Ile Lys Asp Asp Ser Leu
1 5 10 15

Asp Asn Arg Val Leu Val Asn Ala Thr Ile Asn
20 25

<210> 135
<211> 27
<212> PRT
<213> Lactobacillus gasseri

<400> 135

Asp Ile Asp His Ile Leu Pro Gln Ser Phe Ile Lys Asp Asp Ser Leu
1 5 10 15

Glu Asn Arg Val Leu Val Lys Lys Ala Val Asn
20 25

<210> 136
<211> 27
<212> PRT
<213> Staphylococcus pseudintermedius ED99

<400> 136

Glu Val Asp His Ile Phe Pro Arg Ser Phe Ile Lys Asp Asp Ser Ile
1 5 10 15

Asp Asn Lys Val Leu Val Ile Lys Lys Met Asn
20 25

<210> 137
<211> 27
<212> PRT
<213> Olsenella uli

<400> 137

Glu Val Asp His Ile Ile Pro Arg Ser Tyr Ile Lys Asp Asp Ser Phe

1 5 10 15

Glu Asn Lys Val Leu Val Tyr Arg Glu Glu Asn
20 25

<210> 138
<211> 27
<212> PRT
<213> Bifidobacterium bifidum S17

<400> 138

Asp Ile Asp His Ile Ile Pro Gln Ala Val Thr Gln Asn Asp Ser Ile
1 5 10 15

Asp Asn Arg Val Leu Val Ala Arg Ala Glu Asn
20 25

<210> 139
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<212> PRT
<213> Mycoplasma gallisepticum str. F

<400> 139

Glu Ile Asp His Ile Ile Pro Tyr Ser Ile Ser Phe Asp Asp Ser Ser
1 5 10 15

Ser Asn Lys Leu Leu Val Leu Ala Glu Ser Asn
20 25

<210> 140
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<212> PRT
<213> Mycoplasma canis PG 14

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1 5 10 15

Ala Asn Lys Val Leu Val His Lys Gln Ser Asn
20 25

<210> 141
<211> 27
<212> PRT
<213> Ilyobacter polytropus DSM 2926

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1 5 10 15

Ser Asn Lys Val Leu Val Leu Ser Gly Glu Asn

20 25

<210> 142
<211> 27
<212> PRT
<213> Uncultured Termite group 1 bacterium

<400> 142

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1 5 10 15

Asn Asn Lys Val Leu Cys Leu Ala Glu Glu Asn
20 25

<210> 143
<211> 27
<212> PRT
<213> Campylobacter jejuni

<400> 143

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1 5 10 15

Met Asn Lys Val Leu Val Phe Thr Lys Gln Asn
20 25

<210> 144
<211> 27
<212> PRT
<213> Clostridium cellulolyticum H10

<400> 144

Gln Ile Asp His Ile Tyr Pro Tyr Ser Arg Ser Met Asp Asp Ser Tyr
1 5 10 15

Met Asn Lys Val Leu Val Leu Thr Asp Glu Asn
20 25

<210> 145
<211> 27
<212> PRT
<213> Clostridium perfringens

<400> 145

Glu Ile Asp His Ile Ile Pro Phe Ser Arg Ser Phe Asp Asp Ser Leu
1 5 10 15

Ser Asn Lys Ile Leu Val Leu Gly Ser Glu Asn
20 25

<210> 146

<211> 27
<212> PRT
<213> N. meningitides

<400> 146

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20 25

<210> 147
<211> 27
<212> PRT
<213> Pasteurella multocida str. Pm70

<400> 147

Glu Ile Asp His Ala Leu Pro Phe Ser Arg Thr Trp Asp Asp Ser Phe
1 5 10 15

Asn Asn Lys Val Leu Val Leu Ala Ser Glu Asn
20 25

<210> 148
<211> 27
<212> PRT
<213> Enterococcus faecalis TX0012

<400> 148

Glu Ile Asp His Ile Ile Pro Ile Ser Ile Ser Leu Asp Asp Ser Ile
1 5 10 15

Asn Asn Lys Val Leu Val Leu Ser Lys Ala Asn
20 25

<210> 149
<211> 27
<212> PRT
<213> Eubacterium dolichum DSM 3991

<400> 149

Glu Val Asp His Ile Ile Pro Ile Ser Ile Ser Leu Asp Asp Ser Ile
1 5 10 15

Thr Asn Lys Val Leu Val Thr His Arg Glu Asn
20 25

<210> 150
<211> 27
<212> PRT
<213> Acidovorax ebreus

<400> 150

Gln Val Asp His Ala Leu Pro Tyr Ser Arg Ser Tyr Asp Asp Ser Lys
1 5 10 15

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20 25

<210> 151
<211> 27
<212> PRT
<213> Streptococcus thermophilus LMD-9

<400> 151

Glu Val Asp His Ile Leu Pro Leu Ser Ile Thr Phe Asp Asp Ser Leu
1 5 10 15

Ala Asn Lys Val Leu Val Tyr Ala Thr Ala Asn
20 25

<210> 152
<211> 27
<212> PRT
<213> Eubacterium rectale

<400> 152

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Ser Asn Lys Val Leu Val Tyr Arg Ser Glu Asn
20 25

<210> 153
<211> 27
<212> PRT
<213> Staphylococcus lugdunensis M23590

<400> 153

Glu Val Asp His Ile Ile Pro Arg Ser Val Ser Phe Asp Asn Ser Tyr
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His Asn Lys Val Leu Val Lys Gln Ser Glu Asn
20 25

<210> 154
<211> 27
<212> PRT
<213> Roseburia intestinalis

<400> 154

Asp Ile Asp His Ile Leu Pro Tyr Ser Ile Thr Phe Asp Asp Ser Phe
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Arg Asn Lys Val Leu Val Thr Ser Gln Glu Asn
            20   25

<210> 155
<211> 27
<212> PRT
<213> Wolinella succinogenes DSM 1740

<400> 155

Glu Ile Asp His Ile Leu Pro Arg Ser Arg Ser Ala Asp Asp Ser Phe
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Ala Asn Lys Val Leu Cys Leu Ala Arg Ala Asn
            20   25

<210> 156
<211> 27
<212> PRT
<213> Cand. Puniceispirillum marinum

<400> 156

Glu Ile Glu His Leu Leu Pro Phe Ser Leu Thr Leu Asp Asp Ser Met
1   5   10   15

Ala Asn Lys Thr Val Cys Phe Arg Gln Ala Asn
            20   25

<210> 157
<211> 27
<212> PRT
<213> Azospirillum sp. B510

<400> 157

Asp Ile Asp His Ile Leu Pro Phe Ser Val Ser Leu Asp Asp Ser Ala
1   5   10   15

Ala Asn Lys Val Val Cys Leu Arg Glu Ala Asn
            20   25

<210> 158
<211> 27
<212> PRT
<213> Bradyrhizobium sp. BTAi1

<400> 158

Asp Ile Asp His Leu Ile Pro Phe Ser Ile Ser Trp Asp Asp Ser Ala
1   5   10   15

Ala Asn Lys Val Val Cys Met Arg Tyr Ala Asn
            20   25

<210> 159
<211> 27
<212> PRT
<213> Nitrobacter hamburgensis X14

<400> 159

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

Ala Asn Lys Ile Ile Cys Met Arg Tyr Ala Asn
20 25

<210> 160
<211> 27
<212> PRT
<213> Dinoroseobacter shibae

<400> 160

Asp Val Asp His Ile Leu Pro Tyr Ser Arg Thr Leu Asp Asp Ser Phe
1 5 10 15

Pro Asn Arg Thr Leu Cys Leu Arg Glu Ala Asn
20 25

<210> 161
<211> 27
<212> PRT
<213> Verminephrobacter eiseniae

<400> 161

Glu Ile Glu His Ile Leu Pro Phe Ser Arg Thr Leu Asp Asp Ser Leu
1 5 10 15

Asn Asn Arg Thr Val Ala Met Arg Arg Ala Asn
20 25

<210> 162
<211> 27
<212> PRT
<213> Lactobacillus coryniformis KCTC 3535

<400> 162

Glu Val Asp His Ile Ile Pro Tyr Ser Ile Ser Trp Asp Asp Ser Tyr
1 5 10 15

Thr Asn Lys Val Leu Thr Ser Ala Lys Cys Asn
20 25

<210> 163
<211> 27

<212> PRT
<213> Rhodopseudomonas palustris

<400> 163

Gln Val Asp His Ile Leu Pro Trp Ser Arg Phe Gly Asp Asp Ser Tyr
1 5 10 15

Leu Asn Lys Thr Leu Cys Thr Ala Arg Ser Asn
20 25

<210> 164
<211> 27
<212> PRT
<213> Ralstonia syzygii R24

<400> 164

Gln Val Asp His Ile Leu Pro Phe Ser Lys Thr Leu Asp Asp Ser Phe
1 5 10 15

Ala Asn Lys Val Leu Ala Gln His Asp Ala Asn
20 25

<210> 165
<211> 27
<212> PRT
<213> Helicobacter mustelae 12198

<400> 165

Gln Ile Asp His Ala Phe Pro Leu Ser Arg Ser Leu Asp Asp Ser Gln
1 5 10 15

Ser Asn Lys Val Leu Cys Leu Thr Ser Ser Asn
20 25

<210> 166
<211> 27
<212> PRT
<213> Mycoplasma mobile 163K

<400> 166

Asp Ile Asp His Ile Val Pro Arg Ser Ile Ser Phe Asp Asp Ser Phe
1 5 10 15

Ser Asn Leu Val Ile Val Asn Lys Leu Asp Asn
20 25

<210> 167
<211> 27
<212> PRT
<213> Mycoplasma ovipneumoniae SC01

<400> 167

Glu Ile Glu His Ile Ile Pro Tyr Ser Met Ser Tyr Asp Asn Ser Gln
1   5   10   15

Ala Asn Lys Ile Leu Thr Glu Lys Ala Glu Asn
            20   25

<210> 168
<211> 27
<212> PRT
<213> Mycoplasma synoviae 53

<400> 168

Glu Ile Asp His Val Ile Pro Tyr Ser Lys Ser Ala Asp Asp Ser Trp
1   5   10   15

Phe Asn Lys Leu Leu Val Lys Lys Ser Thr Asn
            20   25

<210> 169
<211> 27
<212> PRT
<213> Aminomonas paucivorans DSM 12260

<400> 169

Glu Met Asp His Ile Leu Pro Tyr Ser Arg Ser Leu Asp Asn Gly Trp
1   5   10   15

His Asn Arg Val Leu Val His Gly Lys Asp Asn
            20   25

<210> 170
<211> 27
<212> PRT
<213> Ruminococcus albus 8

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Glu Val Asp His Ile Val Pro Tyr Ser Leu Ile Leu Asp Asn Thr Ile
1   5   10   15

Asn Asn Lys Ala Leu Val Tyr Ala Glu Glu Asn
            20   25

<210> 171
<211> 27
<212> PRT
<213> Fibrobacter succinogenes

<400> 171

Glu Ile Glu His Val Ile Pro Gln Ser Leu Tyr Phe Asp Asp Ser Phe
1   5   10   15

Ser Asn Lys Val Ile Cys Glu Ala Glu Val Asn
            20   25

<210> 172
<211> 27
<212> PRT
<213> Bacteroides fragilis, NCTC 9343

<400> 172

Asp Ile Glu His Ile Ile Pro Gln Ala Arg Leu Phe Asp Asp Ser Phe
1   5   10   15

Ser Asn Lys Thr Leu Glu Ala Arg Ser Val Asn
            20   25

<210> 173
<211> 27
<212> PRT
<213> Capnocytophaga sputigena

<400> 173

Glu Ile Glu His Ile Val Pro Lys Ala Arg Val Phe Asp Asp Ser Phe
1   5   10   15

Ser Asn Lys Thr Leu Thr Phe His Arg Ile Asn
            20   25

<210> 174
<211> 28
<212> PRT
<213> Finegoldia magna

<400> 174

Asp Lys Asp His Ile Ile Pro Gln Ser Met Lys Lys Asp Asp Ser Ile
1   5   10   15

Ile Asn Asn Leu Val Leu Val Asn Lys Asn Ala Asn
            20   25

<210> 175
<211> 27
<212> PRT
<213> Parvibaculum lavamentivorans DS-1

<400> 175

Glu Val Glu His Ile Trp Pro Arg Ser Arg Ser Phe Asp Asn Ser Pro
1   5   10   15

Arg Asn Lys Thr Leu Cys Arg Lys Asp Val Asn
            20   25

<210> 176
<211> 27
<212> PRT
<213> Bacillus cereus

<400> 176

Ile Val Asn His Ile Ile Pro Tyr Asn Arg Ser Phe Asp Asp Thr Tyr
1 5 10 15

His Asn Arg Val Leu Thr Leu Thr Glu Thr Lys
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<210> 177
<211> 27
<212> PRT
<213> Prevotella micans

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Asp Met Glu His Thr Ile Pro Lys Ser Ile Ser Phe Asp Asn Ser Asp
1 5 10 15

Gln Asn Leu Thr Leu Cys Glu Ser Tyr Tyr Asn
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<210> 178
<211> 27
<212> PRT
<213> Prevotella ruminicola

<400> 178

Asp Ile Glu His Thr Ile Pro Arg Ser Ala Gly Gly Asp Ser Thr Lys
1 5 10 15

Met Asn Leu Thr Leu Cys Ser Ser Arg Phe Asn
20 25

<210> 179
<211> 27
<212> PRT
<213> Flavobacterium columnare

<400> 179

Asp Ile Glu His Thr Ile Pro Arg Ser Ile Ser Gln Asp Asn Ser Gln
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Met Asn Lys Thr Leu Cys Ser Leu Lys Phe Asn
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<210> 180
<211> 27
<212> PRT

<213> Rhodospirillum rubrum

<400> 180

Asp Ile Asp His Val Ile Pro Leu Ala Arg Gly Gly Arg Asp Ser Leu
1 5 10 15

Asp Asn Met Val Leu Cys Gln Ser Asp Ala Asn
20 25

<210> 181
<211> 27
<212> PRT
<213> Elusimicrobium minutum Pei191

<400> 181

Asp Ile Glu His Leu Phe Pro Ile Ala Glu Ser Glu Asp Asn Gly Arg
1 5 10 15

Asn Asn Leu Val Ile Ser His Ser Ala Cys Asn
20 25

<210> 182
<211> 27
<212> PRT
<213> Sphaerochaeta globus str. Buddy

<400> 182

Asp Val Asp His Ile Phe Pro Arg Asp Asp Thr Ala Asp Asn Ser Tyr
1 5 10 15

Gly Asn Lys Val Val Ala His Arg Gln Cys Asn
20 25

<210> 183
<211> 27
<212> PRT
<213> Nitratifractor salsuginis DSM 16511

<400> 183

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

Tyr Asn Thr Ile Val Thr Leu Lys Ser Val Asn
20 25

<210> 184
<211> 27
<212> PRT
<213> Acidothermus cellulolyticus 11B

<400> 184

Glu Leu Asp His Ile Val Pro Arg Thr Asp Gly Gly Ser Asn Arg His
1   5   10   15

Glu Asn Leu Ala Ile Thr Cys Gly Ala Cys Asn
            20   25

<210> 185
<211> 28
<212> PRT
<213> Bifidobacterium longum DJO10A

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Glu Met Asp His Ile Val Pro Arg Lys Gly Val Gly Ser Thr Asn Thr
1   5   10   15

Arg Thr Asn Phe Ala Ala Val Cys Ala Glu Cys Asn
            20   25

<210> 186
<211> 28
<212> PRT
<213> Bifidobacterium dentium

<400> 186

Glu Met Asp His Ile Val Pro Arg Lys Gly Val Gly Ser Thr Asn Thr
1   5   10   15

Arg Val Asn Leu Ala Ala Ala Cys Ala Ala Cys Asn
            20   25

<210> 187
<211> 28
<212> PRT
<213> Corynebacterium diphtheria

<400> 187

Glu Met Asp His Ile Val Pro Arg Ala Gly Gln Gly Ser Thr Asn Thr
1   5   10   15

Arg Glu Asn Leu Val Ala Val Cys His Arg Cys Asn
            20   25

<210> 188
<211> 33
<212> PRT
<213> Sutterella wadsworthensis

<400> 188

Glu Ile Asp His Ile Leu Pro Arg Ser Leu Ile Lys Asp Ala Arg Gly
1   5   10   15

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Asn
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<210> 189
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<213> Gamma proteobacterium HTCC5015

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Thr Val Phe Asn Ser Glu Ala Asn Leu Ile Tyr Cys Ser Ser Lys Gly
            20                  25                  30

Asn
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<210> 190
<211> 33
<212> PRT
<213> Parasutterella excrementihominis

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1               5                   10                  15

Ser Ile Tyr Asn Ser Glu Val Asn Leu Ile Phe Val Ser Ala Gln Gly
            20                  25                  30

Asn
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<210> 191
<211> 33
<212> PRT
<213> Legionella pneumophila str. Paris

<400> 191

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1               5                   10                  15

Val Ile Phe Asn Ser Glu Val Asn Leu Ile Tyr Cys Ser Ser Gln Gly
            20                  25                  30

Asn
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<210> 192
<211> 33
<212> PRT
<213> Wolinella succinogenes DSM 1740

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Thr Val Phe Asn Pro Glu Gly Asn Leu Ile Tyr Val His Gln Lys Cys
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Asn

<210> 193
<211> 30
<212> PRT
<213> Francisella tularensis

<400> 193

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1 5 10 15

Asn Asp Glu Ala Asn Leu Ile Cys Val Thr Arg Gly Asp Asn
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<210> 194
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<212> PRT
<213> Akkermansia muciniphila

<400> 194

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Ser Ser Leu Val Leu Thr Trp Pro Gly Val Asn
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<210> 195
<211> 27
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Asp Ile Asp His Ile Tyr Pro Arg Ser Lys Ile Lys Asp Asp Ser Ile
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Thr Asn Arg Val Leu Val Glu Lys Asp Ile Asn
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<210> 196
<211> 28
<212> PRT
<213> Veillonella atypica ACS-134-V-Col7a

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Tyr Asp Ile Asp His Ile Tyr Pro Arg Ser Leu Thr Lys Asp Asp Ser
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Phe Asp Asn Leu Val Leu Cys Glu Arg Thr Ala Asn
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<210> 197
<211> 28
<212> PRT
<213> Fusobacterium nucleatum

<400> 197

Asp Ile Asp His Ile Tyr Pro Arg Ser Lys Val Ile Lys Asp Asp Ser
1 5 10 15

Phe Asp Asn Leu Val Leu Val Leu Lys Asn Glu Asn
20 25

<210> 198
<211> 27
<212> PRT
<213> Filifactor alocis

<400> 198

Asp Arg Asp His Ile Tyr Pro Gln Ser Lys Ile Lys Asp Asp Ser Ile
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20 25

<210> 199
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<212> DNA
<213> Streptococcus thermophilus

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ccguuaucaa cuugaaaaag uggcaccgag ucggugcuuu u 101

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uccguuauca acuugaaaaa guggcaccga gucggugcuu uu 102