SEQUENCE LISTING

<110> Caribou Biosciences, Inc.

<120> ENGINEERED CRISPR-CAS9 COMPOSITIONS AND METHODS OF USE

<130> CBI017.30

<150> 62/202,715
<151> 2015-08-07

<150> 62/209,334
<151> 2015-08-24

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<170> PatentIn version 3.5

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<223> Cas9-associated sgRNA

<400> 101
auacacccaa aguaucagga guuuuuguac ucgaaagaag cuacaaagau aaggcuucau 60

gccgaaauca acacccuguc auuuuauggc aggguguuu 99

<210> 102
<211> 99
<212> RNA
<213> Artificial Sequence

<220>
<223> Cas9-associated sgRNA

<400> 102
gcggucgggg aauaagguau guuuuuguac ucgaaagaag cuacaaagau aaggcuucau 60

gccgaaauca acacccuguc auuuuauggc aggguguuu 99

<210> 103
<211> 58
<212> RNA
<213> Artificial Sequence

<220>
<223> Split-nexus Cas9-associated RNA

<400> 103
uguaagucca ggaugaacua guuuuuguac ucgaaagaag cuacaaagau aaggcuuc 58

<210> 104
<211> 54
<212> RNA
<213> Artificial Sequence

<220>
<223> Split-nexus Cas9-associated RNA

<400> 104
uguucaacuu uagaacgaau guuuuuguac ucgaaagaag cuacaaagau aagg 54

<210> 105
<211> 58
<212> RNA
<213> Artificial Sequence

<220>
<223> Split-nexus Cas9-associated RNA

<400> 105
aggguggggc aggaaggaag guuuuuguac ucgaaagaag cuacaaagau aaggcuuc 58

<210> 106
<211> 58
<212> RNA
<213> Artificial Sequence

<220>
<223> Split-nexus Cas9-associated RNA

<400> 106
cucccucagg gucuguaaga guuuuuguac ucgaaagaag cuacaaagau aaggcuuc 58

<210> 107
<211> 58
<212> RNA
<213> Artificial Sequence

<220>
<223> Split-nexus Cas9-associated RNA

<400> 107
auacacccaa aguaucagga guuuuuguac ucgaaagaag cuacaaagau aaggcuuc 58

<210> 108
<211> 54
<212> RNA
<213> Artificial Sequence

<220>
<223> Split-nexus Cas9-associated RNA

<400> 108
gcggucgggg aauaagguau guuuuuguac ucgaaagaag cuacaaagau aagg 54

<210> 109
<211> 41
<212> RNA
<213> Artificial Sequence

<220>
<223> Split-nexus Cas9-associated RNA

<400> 109
augccgaaau caacacccug ucauuuuaug gcaggguguu u 41

<210> 110
<211> 23
<212> DNA
<213> Artificial Sequence

<220>
<223> Oligonucleotide Primer

<400> 110
tgtaaggaag ctgcagcacc agg 23

<210> 111
<211> 22
<212> DNA
<213> Artificial Sequence

<220>
<223> Oligonucleotide Primer

<400> 111
tctttgcctg gacaccccgt tc 22

<210> 112
<211> 118
<212> RNA
<213> Artificial Sequence

<220>
<223> Cas9-associated sgRNA

<400> 112
agacccaaua ucaggagacu gucucagagc uaugcugucc uggaaacagg acagcauagc 60

aaguugagau gaggcuaguc cguuaucaac uugaaaaagu ggcaccgagu cggugcuu 118

<210> 113
<211> 118
<212> RNA
<213> Artificial Sequence

<220>
<223> Cas9-associated sgRNA

<400> 113
uguccccuagu ggccccacug gucucagagc uaugcugucc uggaaacagg acagcauagc 60

aaguugagau gaggcuaguc cguuaucaac uugaaaaagu ggcaccgagu cggugcuu 118

<210> 114
<211> 118
<212> RNA
<213> Artificial Sequence

<220>
<223> Cas9-associated sgRNA

<400> 114
cggggacaca ggaucccugg gucucagagc uaugcugucc uggaaacagg acagcauagc 60

aaguugagau gaggcuaguc cguuaucaac uugaaaaagu ggcaccgagu cggugcuu 118

<210> 115
<211> 73
<212> RNA
<213> Artificial Sequence

<220>
<223> Split-nexus Cas9-associated RNA

<400> 115
agacccaaua ucaggagacu gucucagagc uaugcugucc uggaaacagg acagcauagc 60

aaguugagau aag 73

<210> 116
<211> 73
<212> RNA
<213> Artificial Sequence

<220>
<223> Split-nexus Cas9-associated RNA

<400> 116
uguccccuagu ggccccacug gucucagagc uaugcugucc uggaaacagg acagcauagc 60

aaguugagau aag 73

<210> 117
<211> 73
<212> RNA
<213> Artificial Sequence

<220>
<223> Split-nexus Cas9-associated RNA

<400> 117
cggggacaca ggaucccugg gucucagagc uaugcugucc uggaaacagg acagcauagc 60

aaguugagau aag 73

<210> 118
<211> 45
<212> RNA
<213> Artificial Sequence

<220>
<223> Split-nexus Cas9-associated RNA

<400> 118
gcuaguccgu uaucaacuug aaaaaguggc accgagucgg ugcuu 45

<210> 119
<211> 76
<212> RNA
<213> Artificial Sequence

<220>
<223> Split-nexus Cas9-associated RNA

<400> 119
agacccaaua ucaggagacu gucucagagc uaugcugucc uggaaacagg acagcauagc 60

aaguugagau aaggcu 76

<210> 120
<211> 76
<212> RNA
<213> Artificial Sequence

<220>
<223> Split-nexus Cas9-associated RNA

<400> 120
uguccc uagu ggccccacug gucucagagc uaugcugucc uggaaacagg acagcauagc 60

aaguugagau aaggcu 76

<210> 121
<211> 76
<212> RNA
<213> Artificial Sequence

<220>
<223> Split-nexus Cas9-associated RNA

<400> 121
cggggacaca ggaucccugg gucucagagc uaugcugucc uggaaacagg acagcauagc 60

aaguugagau aaggcu 76

<210> 122
<211> 43
<212> RNA
<213> Artificial Sequence

<220>
<223> Split-nexus Cas9-associated RNA

<400> 122
gaguccguua ucaacuugaa aaaguggcac cgagucggug cuu 43

<210> 123
<211> 78
<212> RNA
<213> Artificial Sequence

<220>
<223> Split-nexus Cas9-associated RNA

<400> 123
agacccaaua ucaggagacu gucucagagc uaugcugucc uggaaacagg acagcauagc 60

aaguugagau aaggcuag 78

<210> 124
<211> 78
<212> RNA
<213> Artificial Sequence

<220>
<223> Split-nexus Cas9-associated RNA

<400> 124
uguccc uagu ggccccacug gucucagagc uaugcugucc uggaaacagg acagcauagc 60

aaguugagau aaggcuag 78

<210> 125
<211> 78
<212> RNA
<213> Artificial Sequence

<220>
<223> Split-nexus Cas9-associated RNA

<400> 125
cggggacaca ggaucccugg gucucagagc uaugcugucc uggaaacagg acagcauagc 60

aaguugagau aaggcuag 78

<210> 126
<211> 41
<212> RNA
<213> Artificial Sequence

<220>
<223> Split-nexus Cas9-associated RNA

<400> 126
guccguuauc aacuugaaaa aguggcaccg agucggugcu u 41

<210> 127
<211> 1387
<212> PRT
<213> Streptococcus pyogenes

<400> 127

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

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

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

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

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

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

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

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

His Glu Lys Tyr Pro Thr Ile Tyr His Leu Arg Lys Lys Leu Val Asp

```
    130                 135                 140

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

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

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

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

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

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

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

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

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

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

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

Met Ile Lys Arg Tyr Asp Glu His His Gln Asp Leu Thr Leu Leu Lys
```

325 330 335

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

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

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

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

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

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

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

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

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

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

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

Leu Leu Tyr Glu Tyr Phe Thr Val Tyr Asn Glu Leu Thr Lys Val Lys

```
        515                 520                 525

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

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

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

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

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

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

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

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

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

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

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

Lys Glu Asp Ile Gln Lys Ala Gln Val Ser Gly Gln Gly Asp Ser Leu
```

705 710 715 720

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

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

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

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

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

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

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

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

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

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

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

Phe Asp Asn Leu Thr Lys Ala Glu Arg Gly Gly Leu Ser Glu Leu Asp

900 905 910

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

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

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

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

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

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

Val Tyr Gly Asp Tyr Lys Val Tyr Asp Val Arg Lys Met Ile Ala
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

Gly Ser Pro Lys Lys Lys Arg Lys Val Glu Asp Pro Lys Lys Lys
1370 1375 1380

Arg Lys Val Asp
1385

<210> 128
<211> 1168
<212> PRT
<213> Streptococcus thermophilus

<400> 128

Met Pro Lys Lys Lys Arg Lys Val Asp Gly Ser Asp Leu Val Leu Gly
1 5 10 15

Leu Asp Ile Gly Ile Gly Ser Val Gly Val Gly Ile Leu Asn Lys Val
20 25 30

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Thr Gly Glu Ile Ile His Lys Asn Ser Arg Ile Phe Pro Ala Ala Gln
        35                  40                  45

Ala Glu Asn Asn Leu Val Arg Arg Thr Asn Arg Gln Gly Arg Arg Leu
    50                  55                  60

Thr Arg Arg Lys Lys His Arg Arg Val Arg Leu Asn Arg Leu Phe Glu
65                  70                  75                  80

Glu Ser Gly Leu Ile Thr Asp Phe Thr Lys Ile Ser Ile Asn Leu Asn
                85                  90                  95

Pro Tyr Gln Leu Arg Val Lys Gly Leu Thr Asp Glu Leu Ser Asn Glu
            100                 105                 110

Glu Leu Phe Ile Ala Leu Lys Asn Met Val Lys His Arg Gly Ile Ser
        115                 120                 125

Tyr Leu Asp Asp Ala Ser Asp Asp Gly Asn Ser Ser Val Gly Asp Tyr
    130                 135                 140

Ala Gln Ile Val Lys Glu Asn Ser Lys Gln Leu Glu Thr Lys Thr Pro
145                 150                 155                 160

Gly Gln Ile Gln Leu Glu Arg Tyr Gln Thr Tyr Gly Gln Leu Arg Gly
                165                 170                 175

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

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

Gln Gln Glu Phe Asn Pro Gln Ile Thr Asp Glu Phe Ile Asn Arg Tyr
    210                 215                 220
```

```
Leu Glu Ile Leu Thr Gly Lys Arg Lys Tyr Tyr His Gly Pro Gly Asn
225                 230                 235                 240

Glu Lys Ser Arg Thr Asp Tyr Gly Arg Tyr Arg Thr Ser Gly Glu Thr
                245                 250                 255

Leu Asp Asn Ile Phe Gly Ile Leu Ile Gly Lys Cys Thr Phe Tyr Pro
            260                 265                 270

Asp Glu Phe Arg Ala Ala Lys Ala Ser Tyr Thr Ala Gln Glu Phe Asn
        275                 280                 285

Leu Leu Asn Asp Leu Asn Asn Leu Thr Val Pro Thr Glu Thr Lys Lys
    290                 295                 300

Leu Ser Lys Glu Gln Lys Asn Gln Ile Ile Asn Tyr Val Lys Asn Glu
305                 310                 315                 320

Lys Ala Met Gly Pro Ala Lys Leu Phe Lys Tyr Ile Ala Lys Leu Leu
                325                 330                 335

Ser Cys Asp Val Ala Asp Ile Lys Gly Tyr Arg Ile Asp Lys Ser Gly
            340                 345                 350

Lys Ala Glu Ile His Thr Phe Glu Ala Tyr Arg Lys Met Lys Thr Leu
        355                 360                 365

Glu Thr Leu Asp Ile Glu Gln Met Asp Arg Glu Thr Leu Asp Lys Leu
    370                 375                 380

Ala Tyr Val Leu Thr Leu Asn Thr Glu Arg Glu Gly Ile Gln Glu Ala
385                 390                 395                 400

Leu Glu His Glu Phe Ala Asp Gly Ser Phe Ser Gln Lys Gln Val Asp
                405                 410                 415
```

```
Glu Leu Val Gln Phe Arg Lys Ala Asn Ser Ser Ile Phe Gly Lys Gly
            420                 425                 430

Trp His Asn Phe Ser Val Lys Leu Met Met Glu Leu Ile Pro Glu Leu
        435                 440                 445

Tyr Glu Thr Ser Glu Glu Gln Met Thr Ile Leu Thr Arg Leu Gly Lys
    450                 455                 460

Gln Lys Thr Thr Ser Ser Ser Asn Lys Thr Lys Tyr Ile Asp Glu Lys
465                 470                 475                 480

Leu Leu Thr Glu Glu Ile Tyr Asn Pro Val Val Ala Lys Ser Val Arg
                485                 490                 495

Gln Ala Ile Lys Ile Val Asn Ala Ala Ile Lys Glu Tyr Gly Asp Phe
            500                 505                 510

Asp Asn Ile Val Ile Glu Met Ala Arg Glu Thr Asn Glu Asp Asp Glu
        515                 520                 525

Lys Lys Ala Ile Gln Lys Ile Gln Lys Ala Asn Lys Asp Glu Lys Asp
    530                 535                 540

Ala Ala Met Leu Lys Ala Ala Asn Gln Tyr Asn Gly Lys Ala Glu Leu
545                 550                 555                 560

Pro His Ser Val Phe His Gly His Lys Gln Leu Ala Thr Lys Ile Arg
                565                 570                 575

Leu Trp His Gln Gln Gly Glu Arg Cys Leu Tyr Thr Gly Lys Thr Ile
            580                 585                 590

Ser Ile His Asp Leu Ile Asn Asn Ser Asn Gln Phe Glu Val Asp His
        595                 600                 605
```

```
Ile Leu Pro Leu Ser Ile Thr Phe Asp Asp Ser Leu Ala Asn Lys Val
    610                 615                 620

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

Gln Ala Leu Asp Ser Met Asp Asp Ala Trp Ser Phe Arg Glu Leu Lys
                645                 650                 655

Ala Phe Val Arg Glu Ser Lys Thr Leu Ser Asn Lys Lys Lys Glu Tyr
            660                 665                 670

Leu Leu Thr Glu Glu Asp Ile Ser Lys Phe Asp Val Arg Lys Lys Phe
        675                 680                 685

Ile Glu Arg Asn Leu Val Asp Thr Arg Tyr Ala Ser Arg Val Val Leu
    690                 695                 700

Asn Ala Leu Gln Glu His Phe Arg Ala His Lys Ile Asp Thr Lys Val
705                 710                 715                 720

Ser Val Val Arg Gly Gln Phe Thr Ser Gln Leu Arg Arg His Trp Gly
                725                 730                 735

Ile Glu Lys Thr Arg Asp Thr Tyr His His His Ala Val Asp Ala Leu
            740                 745                 750

Ile Ile Ala Ala Ser Ser Gln Leu Asn Leu Trp Lys Lys Gln Lys Asn
        755                 760                 765

Thr Leu Val Ser Tyr Ser Glu Asp Gln Leu Leu Asp Ile Glu Thr Gly
    770                 775                 780

Glu Leu Ile Ser Asp Asp Glu Tyr Lys Glu Ser Val Phe Lys Ala Pro
785                 790                 795                 800
```

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

Ile Leu Phe Ser Tyr Gln Val Asp Ser Lys Phe Asn Arg Lys Ile Ser
            820                 825                 830

Asp Ala Thr Ile Tyr Ala Thr Arg Gln Ala Lys Val Gly Lys Asp Lys
        835                 840                 845

Ala Asp Glu Thr Tyr Val Leu Gly Lys Ile Lys Asp Ile Tyr Thr Gln
    850                 855                 860

Asp Gly Tyr Asp Ala Phe Met Lys Ile Tyr Lys Lys Asp Lys Ser Lys
865                 870                 875                 880

Phe Leu Met Tyr Arg His Asp Pro Gln Thr Phe Glu Lys Val Ile Glu
                885                 890                 895

Pro Ile Leu Glu Asn Tyr Pro Asn Lys Gln Ile Asn Glu Lys Gly Lys
            900                 905                 910

Glu Val Pro Cys Asn Pro Phe Leu Lys Tyr Lys Glu Glu His Gly Tyr
        915                 920                 925

Ile Arg Lys Tyr Ser Lys Lys Gly Asn Gly Pro Glu Ile Lys Ser Leu
    930                 935                 940

Lys Tyr Tyr Asp Ser Lys Leu Gly Asn His Ile Asp Ile Thr Pro Lys
945                 950                 955                 960

Asp Ser Asn Asn Lys Val Val Leu Gln Ser Val Ser Pro Trp Arg Ala
                965                 970                 975

Asp Val Tyr Phe Asn Lys Thr Thr Gly Lys Tyr Glu Ile Leu Gly Leu
            980                 985                 990
```

```
Lys Tyr Ala Asp Leu Gln Phe Glu  Lys Gly Thr Gly Thr  Tyr Lys Ile
        995                 1000                1005

Ser Gln  Glu Lys Tyr Asn Asp  Ile Lys Lys Lys Glu  Gly Val Asp
    1010                1015                1020

Ser Asp  Ser Glu Phe Lys Phe  Thr Leu Tyr Lys Asn  Asp Leu Leu
    1025                1030                1035

Leu Val  Lys Asp Thr Glu Thr  Lys Glu Gln Gln Leu  Phe Arg Phe
    1040                1045                1050

Leu Ser  Arg Thr Met Pro Lys  Gln Lys His Tyr Val  Glu Leu Lys
    1055                1060                1065

Pro Tyr  Asp Lys Gln Lys Phe  Glu Gly Gly Glu Ala  Leu Ile Lys
    1070                1075                1080

Val Leu  Gly Asn Val Ala Asn  Ser Gly Gln Cys Lys  Lys Gly Leu
    1085                1090                1095

Gly Lys  Ser Asn Ile Ser Ile  Tyr Lys Val Arg Thr  Asp Val Leu
    1100                1105                1110

Gly Asn  Gln His Ile Ile Lys  Asn Glu Gly Asp Lys  Pro Lys Leu
    1115                1120                1125

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

Leu Gly  Ser Gly Ser Pro Lys  Lys Lys Arg Lys Val  Asp Gly Ser
    1145                1150                1155

Pro Lys  Lys Lys Arg Lys Val  Asp Ser Gly
    1160                1165
```