SEQUENCE LISTING

<110> Belouski, Edward J.
Ellison, Murielle M.
Hamburger, Agnes E.
Hecht, Randy I.
Li, Yue-Sheng
Michaels, Mark L.
Sun, Jeonghoon
Xu, Jing

<120> FGF21 Mutants and Uses Thereof

<130> A-1429-WO-PCT

<140> PCT/US2009/046113
<141> 2009-06-03

<160> 41

<170> PatentIn version 3.5

<210> 1
<211> 630
<212> DNA
<213> Homo sapiens

<400> 1
atggactcgg acgagaccgg gttcgagcac tcaggactgt gggtttctgt gctggctggt 60

cttctgctgg gagcctgcca ggcacacccc atccctgact ccagtcctct cctgcaattc 120

gggggccaag tccggcagcg gtacctctac acagatgatg cccagcagac agaagcccac 180

ctggagatca gggaggatgg gacggtgggg ggcgctgctg accagagccc cgaaagtctc 240

ctgcagctga aagccttgaa gccgggagtt attcaaatct tgggagtcaa gacatccagg 300

ttcctgtgcc agcggccaga tggggccctg tatggatcgc tccactttga ccctgaggcc 360

tgcagcttcc gggagctgct tcttgaggac ggatacaatg tttaccagtc cgaagcccac 420

ggcctcccgc tgcacctgcc agggaacaag tccccacacc gggaccctgc accccgagga 480

ccagctcgct tcctgccact accaggcctg ccccccgcac ccccggagcc acccggaatc 540

ctggcccccc agcccccga tgtgggctcc tcggaccctc tgagcatggt gggaccttcc 600

cagggccgaa gccccagcta cgcttcctga 630

<210> 2
<211> 209
<212> PRT
<213> Homo sapiens

<400> 2

Met Asp Ser Asp Glu Thr Gly Phe Glu His Ser Gly Leu Trp Val Ser
1 5 10 15

Val Leu Ala Gly Leu Leu Leu Gly Ala Cys Gln Ala His Pro Ile Pro
20 25 30

Asp Ser Ser Pro Leu Leu Gln Phe Gly Gly Gln Val Arg Gln Arg Tyr
35 40 45

```
Leu Tyr Thr Asp Asp Ala Gln Gln Thr Glu Ala His Leu Glu Ile Arg
     50                  55                  60

Glu Asp Gly Thr Val Gly Gly Ala Ala Asp Gln Ser Pro Glu Ser Leu
65                  70                  75                  80

Leu Gln Leu Lys Ala Leu Lys Pro Gly Val Ile Gln Ile Leu Gly Val
                85                  90                  95

Lys Thr Ser Arg Phe Leu Cys Gln Arg Pro Asp Gly Ala Leu Tyr Gly
            100                 105                 110

Ser Leu His Phe Asp Pro Glu Ala Cys Ser Phe Arg Glu Leu Leu Leu
        115                 120                 125

Glu Asp Gly Tyr Asn Val Tyr Gln Ser Glu Ala His Gly Leu Pro Leu
    130                 135                 140

His Leu Pro Gly Asn Lys Ser Pro His Arg Asp Pro Ala Pro Arg Gly
145                 150                 155                 160

Pro Ala Arg Phe Leu Pro Leu Pro Gly Leu Pro Pro Ala Pro Pro Glu
                165                 170                 175

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

Pro Leu Ser Met Val Gly Pro Ser Gln Gly Arg Ser Pro Ser Tyr Ala
        195                 200                 205

Ser
```

<210> 3
<211> 546
<212> DNA
<213> Homo sapiens

<400> 3
caccccatcc ctgactccag tcctctcctg caattcgggg gtcaagtccg gcagcggtac 60

ctctacacag atgatgccca gcagacagaa gcccacctgg agatcaggga ggatgggacg 120

gtgggggcg ctgctgacca gagccccgaa agtctcctgc agctgaaagc cttgaagccg 180

ggagttattc aaatcttggg agtcaagaca tccaggttcc tgtgccagcg gccagatggg 240

gccctgtatg gatcgctcca ctttgaccct gaggcctgca gcttccggga gctgcttctt 300

gaggacggat acaatgttta ccagtccgaa gcccacggcc tcccgctgca cctgccaggg 360

aacaagtccc cacaccggga ccctgcaccc cgaggaccag ctcgcttcct gccactacca 420

ggcctgcccc ccgcaccccc ggagccaccc ggaatcctgg ccccccagcc ccccgatgtg 480

ggctcctcgg accctctgag catggtggga ccttcccagg gccgaagccc cagctacgct 540

tcctga 546

<210> 4
<211> 181
<212> PRT
<213> Homo sapiens

<400> 4

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

Arg Gln Arg Tyr Leu Tyr Thr Asp Asp Ala Gln Gln Thr Glu Ala His
20 25 30

Leu Glu Ile Arg Glu Asp Gly Thr Val Gly Gly Ala Ala Asp Gln Ser
35 40 45

Pro Glu Ser Leu Leu Gln Leu Lys Ala Leu Lys Pro Gly Val Ile Gln
50 55 60

Ile Leu Gly Val Lys Thr Ser Arg Phe Leu Cys Gln Arg Pro Asp Gly
65 70 75 80

Ala Leu Tyr Gly Ser Leu His Phe Asp Pro Glu Ala Cys Ser Phe Arg
85 90 95

Glu Leu Leu Leu Glu Asp Gly Tyr Asn Val Tyr Gln Ser Glu Ala His
100 105 110

Gly Leu Pro Leu His Leu Pro Gly Asn Lys Ser Pro His Arg Asp Pro
115 120 125

Ala Pro Arg Gly Pro Ala Arg Phe Leu Pro Leu Pro Gly Leu Pro Pro
130 135 140

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

Gly Ser Ser Asp Pro Leu Ser Met Val Gly Pro Ser Gln Gly Arg Ser
165 170 175

Pro Ser Tyr Ala Ser
180

<210> 5
<211> 40
<212> DNA
<213> Artificial Sequence

<220>
<223> PCR primer

<400> 5
aggaggaata acatatgcat ccaattccag attcttctcc 40

<210> 6
<211> 33
<212> DNA
<213> Artificial Sequence

<220>
<223> PCR primer

<400> 6
tagtgagctc gaattcttag gaagcgtagc tgg 33

<210> 7
<211> 41
<212> DNA
<213> Artificial Sequence

<220>
<223> PCR primer

<400> 7
ggagatatac atatgccaat tccagattct tctccattat t 41

<210> 8
<211> 34
<212> DNA
<213> Artificial Sequence

<220>
<223> PCR primer

<400> 8
catatgtata tctccttctt aaagttaaac aaaa 34

<210> 9
<211> 34
<212> DNA
<213> Artificial

<220>
<223> PCR primer

<400> 9
aaaacaaatt gaaattcttc ctctatatgt atac 34

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

<220>
<223> portion of a mature human FGF21 polypeptide

<400> 10

Met His Pro Ile Pro Asp Ser Ser Pro Leu
1 5 10

<210> 11
<211> 63

<212> DNA
<213> Artificial Sequence

<220>
<223> sense strand from a portion of an FGF21 expression construct

<400> 11
ttttgtttaa ctttaagaag gagatataca tatgcatcca attccagatt cttctccatt 60

att 63

<210> 12
<211> 63
<212> DNA
<213> Artificial

<220>
<223> antisense strand from a portion of an FGF21 expression construct

<400> 12
aaaacaaatt gaaattcttc ctctatatgt atacgtaggt taaggtctaa gaagaggtaa 60

taa 63

<210> 13
<211> 227
<212> PRT
<213> Homo sapiens

<400> 13

Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly
1 5 10 15

Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met
20 25 30

Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His
35 40 45

Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val
50 55 60

His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr
65 70 75 80

Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly
85 90 95

Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile
100 105 110

Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val
115 120 125

Tyr Thr Leu Pro Pro Ser Arg Asp Glu Leu Thr Lys Asn Gln Val Ser
130 135 140

Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu
145 150 155 160

Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro
165 170 175

Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val
180 185 190

Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met
195 200 205

His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser
210 215 220

Pro Gly Lys
225

<210> 14
<211> 34
<212> DNA
<213> Artificial Sequence

<220>
<223> PCR primer

<400> 14
aggaggaata acatatggac aaaactcaca catg 34

<210> 15
<211> 23
<212> DNA
<213> Artificial Sequence

<220>
<223> PCR primer

<400> 15
ggatccacca ccaccgctac cac 23

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

<220>
<223> PCR primer

<400> 16
ggtggtggtg gatcccatcc aattccagat tcttctcca 39

<210> 17
<211> 33
<212> DNA
<213> Artificial Sequence

<220>
<223> PCR primer

<400> 17
tagtgagctc gaattcttag gaagcgtagc tgg 33

<210> 18
<211> 27
<212> DNA
<213> Artificial Sequence

<220>
<223> PCR primer

<400> 18
atggtggaac cttcccaggg ccgaagc 27

<210> 19
<211> 30
<212> DNA
<213> Artificial Sequence

<220>
<223> PCR primer

<400> 19
ggaaggttcc accatgctca gagggtccga 30

<210> 20
<211> 50
<212> DNA
<213> Artificial Sequence

<220>
<223> sense strand from a portion of an FGF21 expression construct

<400> 20
ctcctcggac cctctgagca tggtgggacc ttcccagggc cgaagcccca 50

<210> 21
<211> 30
<212> DNA
<213> Artificial

<220>
<223> PCR primer

<400> 21
agcctgggag actcgtacca ccttggaagg 30

<210> 22
<211> 50
<212> DNA
<213> artificial

<220>
<223> antisense strand from a portion of an FGF21 expression construct

<400> 22
gaggagcctg ggagactcgt accaccctgg aagggtcccg gcttcggggt 50

<210> 23
<211> 15
<212> PRT

<213> Artificial Sequence

<220>
<223> linker sequence

<400> 23

Gly Gly Gly Gly Gly Ser Gly Gly Gly Ser Gly Gly Gly Gly Ser
1 5 10 15

<210> 24
<211> 424
<212> PRT
<213> Artificial

<220>
<223> Fc-(G4S)3-FGF21

<400> 24

Met Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu
1 5 10 15

Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu
20 25 30

Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser
35 40 45

His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu
50 55 60

Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr
65 70 75 80

Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn
85 90 95

Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro
100 105 110

Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln
115 120 125

Val Tyr Thr Leu Pro Pro Ser Arg Asp Glu Leu Thr Lys Asn Gln Val
130 135 140

Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val
145 150 155 160

Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro
165 170 175

Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr
180 185 190

```
Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val
        195                 200                 205

Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu
    210                 215                 220

Ser Pro Gly Lys Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly
225                 230                 235                 240

Gly Gly Ser His Pro Ile Pro Asp Ser Ser Pro Leu Leu Gln Phe Gly
                245                 250                 255

Gly Gln Val Arg Gln Arg Tyr Leu Tyr Thr Asp Asp Ala Gln Gln Thr
            260                 265                 270

Glu Ala His Leu Glu Ile Arg Glu Asp Gly Thr Val Gly Gly Ala Ala
        275                 280                 285

Asp Gln Ser Pro Glu Ser Leu Leu Gln Leu Lys Ala Leu Lys Pro Gly
    290                 295                 300

Val Ile Gln Ile Leu Gly Val Lys Thr Ser Arg Phe Leu Cys Gln Arg
305                 310                 315                 320

Pro Asp Gly Ala Leu Tyr Gly Ser Leu His Phe Asp Pro Glu Ala Cys
                325                 330                 335

Ser Phe Arg Glu Leu Leu Leu Glu Asp Gly Tyr Asn Val Tyr Gln Ser
            340                 345                 350

Glu Ala His Gly Leu Pro Leu His Leu Pro Gly Asn Lys Ser Pro His
        355                 360                 365

Arg Asp Pro Ala Pro Arg Gly Pro Ala Arg Phe Leu Pro Leu Pro Gly
    370                 375                 380

Leu Pro Pro Ala Pro Pro Glu Pro Pro Gly Ile Leu Ala Pro Gln Pro
385                 390                 395                 400

Pro Asp Val Gly Ser Ser Asp Pro Leu Ser Met Val Gly Pro Ser Gln
                405                 410                 415

Gly Arg Ser Pro Ser Tyr Ala Ser
            420
```

<210> 25
<211> 424
<212> PRT
<213> Artificial

<220>
<223> FGF21(15)-Fc

<400> 25

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

Val Arg Gln Arg Tyr Leu Tyr Thr Asp Asp Ala Gln Gln Thr Glu Ala
20 25 30

His Leu Glu Ile Arg Glu Asp Gly Thr Val Gly Gly Ala Ala Asp Gln
35 40 45

Ser Pro Glu Ser Leu Leu Gln Leu Lys Ala Leu Lys Pro Gly Val Ile
50 55 60

Gln Ile Leu Gly Val Lys Thr Ser Arg Phe Leu Cys Gln Arg Pro Asp
65 70 75 80

Gly Ala Leu Tyr Gly Ser Leu His Phe Asp Pro Glu Ala Cys Ser Phe
85 90 95

Arg Glu Leu Leu Leu Glu Asp Gly Tyr Asn Val Tyr Gln Ser Glu Ala
100 105 110

His Gly Leu Pro Leu His Leu Pro Gly Asn Lys Ser Pro His Arg Asp
115 120 125

Pro Ala Pro Arg Gly Pro Ala Arg Phe Leu Pro Leu Pro Gly Leu Pro
130 135 140

Pro Ala Pro Pro Glu Pro Pro Gly Ile Leu Ala Pro Gln Pro Pro Asp
145 150 155 160

Val Gly Ser Ser Asp Pro Leu Ser Met Val Gly Pro Ser Gln Gly Arg
165 170 175

Ser Pro Ser Tyr Ala Ser Gly Gly Gly Gly Gly Ser Gly Gly Gly Ser
180 185 190

Gly Gly Gly Gly Ser Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala
195 200 205

Pro Glu Leu Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro
210 215 220

Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val
225 230 235 240

Val Asp Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val
245 250 255

Asp Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln

260 265 270

Tyr Asn Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln
275 280 285

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

Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro
305 310 315 320

Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Asp Glu Leu Thr
325 330 335

Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser
340 345 350

Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr
355 360 365

Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr
370 375 380

Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe
385 390 395 400

Ser Cys Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys
405 410 415

Ser Leu Ser Leu Ser Pro Gly Lys
420

<210> 26
<211> 424
<212> PRT
<213> Artificial

<220>
<223> Fc-(G4S)3-FGF21 G170E

<400> 26

Met Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu
1 5 10 15

Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu
20 25 30

Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser
35 40 45

His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu
50 55 60

Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr
65 70 75 80

Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn
85 90 95

Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro
100 105 110

Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln
115 120 125

Val Tyr Thr Leu Pro Pro Ser Arg Asp Glu Leu Thr Lys Asn Gln Val
130 135 140

Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val
145 150 155 160

Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro
165 170 175

Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr
180 185 190

Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val
195 200 205

Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu
210 215 220

Ser Pro Gly Lys Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly
225 230 235 240

Gly Gly Ser His Pro Ile Pro Asp Ser Ser Pro Leu Leu Gln Phe Gly
245 250 255

Gly Gln Val Arg Gln Arg Tyr Leu Tyr Thr Asp Asp Ala Gln Gln Thr
260 265 270

Glu Ala His Leu Glu Ile Arg Glu Asp Gly Thr Val Gly Gly Ala Ala
275 280 285

Asp Gln Ser Pro Glu Ser Leu Leu Gln Leu Lys Ala Leu Lys Pro Gly
290 295 300

Val Ile Gln Ile Leu Gly Val Lys Thr Ser Arg Phe Leu Cys Gln Arg
305 310 315 320

Pro Asp Gly Ala Leu Tyr Gly Ser Leu His Phe Asp Pro Glu Ala Cys
325 330 335

```
Ser Phe Arg Glu Leu Leu Leu Glu Asp Gly Tyr Asn Val Tyr Gln Ser
            340                 345                 350

Glu Ala His Gly Leu Pro Leu His Leu Pro Gly Asn Lys Ser Pro His
        355                 360                 365

Arg Asp Pro Ala Pro Arg Gly Pro Ala Arg Phe Leu Pro Leu Pro Gly
    370                 375                 380

Leu Pro Pro Ala Pro Pro Glu Pro Pro Gly Ile Leu Ala Pro Gln Pro
385                 390                 395                 400

Pro Asp Val Gly Ser Ser Asp Pro Leu Ser Met Val Glu Pro Ser Gln
                405                 410                 415

Gly Arg Ser Pro Ser Tyr Ala Ser
            420
```

<210> 27
<211> 424
<212> PRT
<213> Artificial

<220>
<223> Fc-(G4S)3-FGF21 P171A

<400> 27

```
Met Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu
1               5                   10                  15

Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu
            20                  25                  30

Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser
        35                  40                  45

His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu
    50                  55                  60

Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr
65                  70                  75                  80

Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn
                85                  90                  95

Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro
            100                 105                 110

Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln
        115                 120                 125

Val Tyr Thr Leu Pro Pro Ser Arg Asp Glu Leu Thr Lys Asn Gln Val
```

130 135 140

Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val
145 150 155 160

Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro
165 170 175

Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr
180 185 190

Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val
195 200 205

Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu
210 215 220

Ser Pro Gly Lys Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly
225 230 235 240

Gly Gly Ser His Pro Ile Pro Asp Ser Ser Pro Leu Leu Gln Phe Gly
245 250 255

Gly Gln Val Arg Gln Arg Tyr Leu Tyr Thr Asp Asp Ala Gln Gln Thr
260 265 270

Glu Ala His Leu Glu Ile Arg Glu Asp Gly Thr Val Gly Gly Ala Ala
275 280 285

Asp Gln Ser Pro Glu Ser Leu Leu Gln Leu Lys Ala Leu Lys Pro Gly
290 295 300

Val Ile Gln Ile Leu Gly Val Lys Thr Ser Arg Phe Leu Cys Gln Arg
305 310 315 320

Pro Asp Gly Ala Leu Tyr Gly Ser Leu His Phe Asp Pro Glu Ala Cys
325 330 335

Ser Phe Arg Glu Leu Leu Leu Glu Asp Gly Tyr Asn Val Tyr Gln Ser
340 345 350

Glu Ala His Gly Leu Pro Leu His Leu Pro Gly Asn Lys Ser Pro His
355 360 365

Arg Asp Pro Ala Pro Arg Gly Pro Ala Arg Phe Leu Pro Leu Pro Gly
370 375 380

Leu Pro Pro Ala Pro Pro Glu Pro Pro Gly Ile Leu Ala Pro Gln Pro
385 390 395 400

Pro Asp Val Gly Ser Ser Asp Pro Leu Ser Met Val Gly Ala Ser Gln

405 410 415

Gly Arg Ser Pro Ser Tyr Ala Ser
420

<210> 28
<211> 424
<212> PRT
<213> Artificial

<220>
<223> Fc-(G4S)3-FGF21 S172L

<400> 28

Met Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu
1 5 10 15

Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu
20 25 30

Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser
35 40 45

His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu
50 55 60

Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr
65 70 75 80

Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn
85 90 95

Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro
100 105 110

Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln
115 120 125

Val Tyr Thr Leu Pro Pro Ser Arg Asp Glu Leu Thr Lys Asn Gln Val
130 135 140

Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val
145 150 155 160

Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro
165 170 175

Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr
180 185 190

Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val
195 200 205

```
Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu
    210                 215                 220

Ser Pro Gly Lys Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly
225                 230                 235                 240

Gly Gly Ser His Pro Ile Pro Asp Ser Ser Pro Leu Leu Gln Phe Gly
                245                 250                 255

Gly Gln Val Arg Gln Arg Tyr Leu Tyr Thr Asp Asp Ala Gln Gln Thr
            260                 265                 270

Glu Ala His Leu Glu Ile Arg Glu Asp Gly Thr Val Gly Gly Ala Ala
        275                 280                 285

Asp Gln Ser Pro Glu Ser Leu Leu Gln Leu Lys Ala Leu Lys Pro Gly
    290                 295                 300

Val Ile Gln Ile Leu Gly Val Lys Thr Ser Arg Phe Leu Cys Gln Arg
305                 310                 315                 320

Pro Asp Gly Ala Leu Tyr Gly Ser Leu His Phe Asp Pro Glu Ala Cys
                325                 330                 335

Ser Phe Arg Glu Leu Leu Leu Glu Asp Gly Tyr Asn Val Tyr Gln Ser
            340                 345                 350

Glu Ala His Gly Leu Pro Leu His Leu Pro Gly Asn Lys Ser Pro His
        355                 360                 365

Arg Asp Pro Ala Pro Arg Gly Pro Ala Arg Phe Leu Pro Leu Pro Gly
    370                 375                 380

Leu Pro Pro Ala Pro Pro Glu Pro Pro Gly Ile Leu Ala Pro Gln Pro
385                 390                 395                 400

Pro Asp Val Gly Ser Ser Asp Pro Leu Ser Met Val Gly Pro Leu Gln
                405                 410                 415

Gly Arg Ser Pro Ser Tyr Ala Ser
            420
```

<210> 29
<211> 4
<212> PRT
<213> Artificial

<220>
<223> linker

<400> 29

```
Gly Gly Gly Gly
```

1

<210> 30
<211> 5
<212> PRT
<213> Artificial

<220>
<223> linker

<400> 30

Gly Gly Gly Gly Gly
1 5

<210> 31
<211> 15
<212> PRT
<213> Artificial

<220>
<223> linker

<400> 31

Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser
1 5 10 15

<210> 32
<211> 8
<212> PRT
<213> Artificial

<220>
<223> linker

<400> 32

Gly Gly Gly Lys Gly Gly Gly Gly
1 5

<210> 33
<211> 8
<212> PRT
<213> Artificial

<220>
<223> linker

<400> 33

Gly Gly Gly Asn Gly Ser Gly Gly
1 5

<210> 34
<211> 8
<212> PRT
<213> Artificial

<220>
<223> linker

<400> 34

Gly Gly Gly Cys Gly Gly Gly Gly
1 5

<210> 35
<211> 5
<212> PRT
<213> Artificial

<220>
<223> linker

<400> 35

Gly Pro Asn Gly Gly
1 5

<210> 36
<211> 424
<212> PRT
<213> Artificial

<220>
<223> Fc-(G4S)3-FGF21 L98R, P171G

<400> 36

Met Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu
1 5 10 15

Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu
20 25 30

Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser
35 40 45

His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu
50 55 60

Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr
65 70 75 80

Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn
85 90 95

Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro
100 105 110

Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln
115 120 125

Val Tyr Thr Leu Pro Pro Ser Arg Asp Glu Leu Thr Lys Asn Gln Val
130 135 140

Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val
145 150 155 160

```
Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro
                165                 170                 175

Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr
            180                 185                 190

Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val
        195                 200                 205

Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu
    210                 215                 220

Ser Pro Gly Lys Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly
225                 230                 235                 240

Gly Gly Ser His Pro Ile Pro Asp Ser Ser Pro Leu Leu Gln Phe Gly
                245                 250                 255

Gly Gln Val Arg Gln Arg Tyr Leu Tyr Thr Asp Asp Ala Gln Gln Thr
            260                 265                 270

Glu Ala His Leu Glu Ile Arg Glu Asp Gly Thr Val Gly Gly Ala Ala
        275                 280                 285

Asp Gln Ser Pro Glu Ser Leu Leu Gln Leu Lys Ala Leu Lys Pro Gly
    290                 295                 300

Val Ile Gln Ile Leu Gly Val Lys Thr Ser Arg Phe Leu Cys Gln Arg
305                 310                 315                 320

Pro Asp Gly Ala Leu Tyr Gly Ser Leu His Phe Asp Pro Glu Ala Cys
                325                 330                 335

Ser Phe Arg Glu Arg Leu Leu Glu Asp Gly Tyr Asn Val Tyr Gln Ser
            340                 345                 350

Glu Ala His Gly Leu Pro Leu His Leu Pro Gly Asn Lys Ser Pro His
        355                 360                 365

Arg Asp Pro Ala Pro Arg Gly Pro Ala Arg Phe Leu Pro Leu Pro Gly
    370                 375                 380

Leu Pro Pro Ala Pro Pro Glu Pro Pro Gly Ile Leu Ala Pro Gln Pro
385                 390                 395                 400

Pro Asp Val Gly Ser Ser Asp Pro Leu Ser Met Val Gly Gly Ser Gln
                405                 410                 415

Gly Arg Ser Pro Ser Tyr Ala Ser
            420
```

<210> 37
<211> 1274
<212> DNA
<213> Artificial

<220>
<223> Fc(15)FGF21 L98R, P171G

<400> 37
atggacaaaa ctcacacatg tccaccttgt ccagctccgg aactcctggg gggaccgtca 60

gtcttcctct tccccccaaa acccaaggac accctcatga tctcccgtac ccctgaggtc 120

acatgcgtgg tggtggacgt gagccacgaa gaccctgagg tcaagttcaa ctggtacgtg 180

gacggcgtgg aggtgcataa tgccaagaca aagccgcgtg aggagcagta caacagcacg 240

taccgtgtgg tcagcgtcct caccgtcctg caccaggact ggctgaatgg caaggagtac 300

aagtgcaagg tctccaacaa agccctccca gccccatcg agaaaaccat ctccaaagcc 360

aaagggcagc cccgagaacc acaggtgtac accctgcccc catcccgtga tgagctgacc 420

aagaaccagg tcagcctgac ctgcctggtc aaaggcttct atcccagcga catcgccgtg 480

gagtgggaga gcaatgggca gccggagaac aactacaaga ccacgcctcc cgtgctggac 540

tccgacggct ccttcttcct ctacagcaag ctcaccgtgg acaagagccg ttggcagcag 600

gggaacgtct tctcatgctc cgtgatgcat gaggctctgc acaaccacta cacgcagaag 660

agcctctccc tgtctccggg taaaggtgga ggtggtggtt ctggtggtgg tagcggtggt 720

ggtggatccc atccaattcc agattcttct ccattattac aattcggggg ccaagtccgg 780

cagcggtacc tctacacaga tgatgcccag cagacagaag cccacctgga gatcagggag 840

gatgggacgg tgggggcgc tgctgaccag agccccgaaa gtctcctgca gctgaaagcc 900

ttgaagccgg gagttattca aatcttggga gtcaagacat ccaggttcct gtgccagcgg 960

ccagatgggg ccctgtatgg atcgctccac tttgaccctg aggcctgcag cttccgggag 1020

cgtcttcttg aggacggata caatgtttac cagtccgaag cccacggcct cccgctgcac 1080

ctgccaggga acaagtcccc acaccgggac cctgcacccc gaggaccagc tcgcttcctg 1140

ccactaccag gcctgccccc cgcacccccg gagccacccg gaatcctggc cccccagccc 1200

cccgatgtgg gctcctcgga ccctctgagc atggtgggag gttcccaggg ccgaagcccc 1260

agctacgctt ccta 1274

<210> 38
<211> 424
<212> PRT
<213> Artificial

<220>
<223> Fc(15)FGF21

<400> 38

Met Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu
1 5 10 15

```
Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu
            20                  25                  30

Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser
        35                  40                  45

His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu
    50                  55                  60

Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr
65                  70                  75                  80

Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn
                85                  90                  95

Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro
            100                 105                 110

Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln
        115                 120                 125

Val Tyr Thr Leu Pro Pro Ser Arg Asp Glu Leu Thr Lys Asn Gln Val
    130                 135                 140

Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val
145                 150                 155                 160

Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro
                165                 170                 175

Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr
            180                 185                 190

Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val
        195                 200                 205

Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu
    210                 215                 220

Ser Pro Gly Lys Gly Gly Gly Gly Gly Ser Gly Gly Gly Ser Gly Gly
225                 230                 235                 240

Gly Gly Ser His Pro Ile Pro Asp Ser Ser Pro Leu Leu Gln Phe Gly
                245                 250                 255

Gly Gln Val Arg Gln Arg Tyr Leu Tyr Thr Asp Asp Ala Gln Gln Thr
            260                 265                 270

Glu Ala His Leu Glu Ile Arg Glu Asp Gly Thr Val Gly Gly Ala Ala
        275                 280                 285
```

Asp Gln Ser Pro Glu Ser Leu Leu Gln Leu Lys Ala Leu Lys Pro Gly
290 295 300

Val Ile Gln Ile Leu Gly Val Lys Thr Ser Arg Phe Leu Cys Gln Arg
305 310 315 320

Pro Asp Gly Ala Leu Tyr Gly Ser Leu His Phe Asp Pro Glu Ala Cys
325 330 335

Ser Phe Arg Glu Leu Leu Leu Glu Asp Gly Tyr Asn Val Tyr Gln Ser
340 345 350

Glu Ala His Gly Leu Pro Leu His Leu Pro Gly Asn Lys Ser Pro His
355 360 365

Arg Asp Pro Ala Pro Arg Gly Pro Ala Arg Phe Leu Pro Leu Pro Gly
370 375 380

Leu Pro Pro Ala Pro Pro Glu Pro Pro Gly Ile Leu Ala Pro Gln Pro
385 390 395 400

Pro Asp Val Gly Ser Ser Asp Pro Leu Ser Met Val Gly Pro Ser Gln
405 410 415

Gly Arg Ser Pro Ser Tyr Ala Ser
420

<210> 39
<211> 424
<212> PRT
<213> Artificial

<220>
<223> Fc(15)FGF21 G170E

<400> 39

Met Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu
1 5 10 15

Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu
20 25 30

Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser
35 40 45

His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu
50 55 60

Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr
65 70 75 80

Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn

85 90 95

Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro
100 105 110

Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln
115 120 125

Val Tyr Thr Leu Pro Pro Ser Arg Asp Glu Leu Thr Lys Asn Gln Val
130 135 140

Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val
145 150 155 160

Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro
165 170 175

Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr
180 185 190

Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val
195 200 205

Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu
210 215 220

Ser Pro Gly Lys Gly Gly Gly Gly Gly Ser Gly Gly Gly Ser Gly Gly
225 230 235 240

Gly Gly Ser His Pro Ile Pro Asp Ser Ser Pro Leu Leu Gln Phe Gly
245 250 255

Gly Gln Val Arg Gln Arg Tyr Leu Tyr Thr Asp Asp Ala Gln Gln Thr
260 265 270

Glu Ala His Leu Glu Ile Arg Glu Asp Gly Thr Val Gly Gly Ala Ala
275 280 285

Asp Gln Ser Pro Glu Ser Leu Leu Gln Leu Lys Ala Leu Lys Pro Gly
290 295 300

Val Ile Gln Ile Leu Gly Val Lys Thr Ser Arg Phe Leu Cys Gln Arg
305 310 315 320

Pro Asp Gly Ala Leu Tyr Gly Ser Leu His Phe Asp Pro Glu Ala Cys
325 330 335

Ser Phe Arg Glu Leu Leu Leu Glu Asp Gly Tyr Asn Val Tyr Gln Ser
340 345 350

Glu Ala His Gly Leu Pro Leu His Leu Pro Gly Asn Lys Ser Pro His

355 360 365

Arg Asp Pro Ala Pro Arg Gly Pro Ala Arg Phe Leu Pro Leu Pro Gly
370 375 380

Leu Pro Pro Ala Pro Pro Glu Pro Pro Gly Ile Leu Ala Pro Gln Pro
385 390 395 400

Pro Asp Val Gly Ser Ser Asp Pro Leu Ser Met Val Glu Pro Ser Gln
405 410 415

Gly Arg Ser Pro Ser Tyr Ala Ser
420

<210> 40
<211> 424
<212> PRT
<213> Artificial

<220>
<223> Fc(15)FGF21 P171A

<400> 40

Met Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu
1 5 10 15

Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu
20 25 30

Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser
35 40 45

His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu
50 55 60

Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr
65 70 75 80

Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn
85 90 95

Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro
100 105 110

Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln
115 120 125

Val Tyr Thr Leu Pro Pro Ser Arg Asp Glu Leu Thr Lys Asn Gln Val
130 135 140

Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val
145 150 155 160

```
Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro
                165                 170                 175

Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr
            180                 185                 190

Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val
        195                 200                 205

Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu
    210                 215                 220

Ser Pro Gly Lys Gly Gly Gly Gly Gly Ser Gly Gly Gly Ser Gly Gly
225                 230                 235                 240

Gly Gly Ser His Pro Ile Pro Asp Ser Ser Pro Leu Leu Gln Phe Gly
                245                 250                 255

Gly Gln Val Arg Gln Arg Tyr Leu Tyr Thr Asp Asp Ala Gln Gln Thr
            260                 265                 270

Glu Ala His Leu Glu Ile Arg Glu Asp Gly Thr Val Gly Gly Ala Ala
        275                 280                 285

Asp Gln Ser Pro Glu Ser Leu Leu Gln Leu Lys Ala Leu Lys Pro Gly
    290                 295                 300

Val Ile Gln Ile Leu Gly Val Lys Thr Ser Arg Phe Leu Cys Gln Arg
305                 310                 315                 320

Pro Asp Gly Ala Leu Tyr Gly Ser Leu His Phe Asp Pro Glu Ala Cys
                325                 330                 335

Ser Phe Arg Glu Leu Leu Leu Glu Asp Gly Tyr Asn Val Tyr Gln Ser
            340                 345                 350

Glu Ala His Gly Leu Pro Leu His Leu Pro Gly Asn Lys Ser Pro His
        355                 360                 365

Arg Asp Pro Ala Pro Arg Gly Pro Ala Arg Phe Leu Pro Leu Pro Gly
    370                 375                 380

Leu Pro Pro Ala Pro Pro Glu Pro Pro Gly Ile Leu Ala Pro Gln Pro
385                 390                 395                 400

Pro Asp Val Gly Ser Ser Asp Pro Leu Ser Met Val Gly Ala Ser Gln
                405                 410                 415

Gly Arg Ser Pro Ser Tyr Ala Ser
            420
```

<210> 41
<211> 424
<212> PRT
<213> Artificial

<220>
<223> Fc(15)FGF21 S172L

<400> 41

Met Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu
1 5 10 15

Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu
20 25 30

Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser
35 40 45

His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu
50 55 60

Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr
65 70 75 80

Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn
85 90 95

Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro
100 105 110

Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln
115 120 125

Val Tyr Thr Leu Pro Pro Ser Arg Asp Glu Leu Thr Lys Asn Gln Val
130 135 140

Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val
145 150 155 160

Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro
165 170 175

Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr
180 185 190

Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val
195 200 205

Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu
210 215 220

Ser Pro Gly Lys Gly Gly Gly Gly Gly Ser Gly Gly Gly Ser Gly Gly

225 230 235 240

Gly Gly Ser His Pro Ile Pro Asp Ser Ser Pro Leu Leu Gln Phe Gly
245 250 255

Gly Gln Val Arg Gln Arg Tyr Leu Tyr Thr Asp Asp Ala Gln Gln Thr
260 265 270

Glu Ala His Leu Glu Ile Arg Glu Asp Gly Thr Val Gly Gly Ala Ala
275 280 285

Asp Gln Ser Pro Glu Ser Leu Leu Gln Leu Lys Ala Leu Lys Pro Gly
290 295 300

Val Ile Gln Ile Leu Gly Val Lys Thr Ser Arg Phe Leu Cys Gln Arg
305 310 315 320

Pro Asp Gly Ala Leu Tyr Gly Ser Leu His Phe Asp Pro Glu Ala Cys
325 330 335

Ser Phe Arg Glu Leu Leu Leu Glu Asp Gly Tyr Asn Val Tyr Gln Ser
340 345 350

Glu Ala His Gly Leu Pro Leu His Leu Pro Gly Asn Lys Ser Pro His
355 360 365

Arg Asp Pro Ala Pro Arg Gly Pro Ala Arg Phe Leu Pro Leu Pro Gly
370 375 380

Leu Pro Pro Ala Pro Pro Glu Pro Pro Gly Ile Leu Ala Pro Gln Pro
385 390 395 400

Pro Asp Val Gly Ser Ser Asp Pro Leu Ser Met Val Gly Pro Leu Gln
405 410 415

Gly Arg Ser Pro Ser Tyr Ala Ser
420