SEQUENCE LISTING

<110> Pfizer Inc.
Mader, Michelle M.
Parris, Kevin D.
Apgar, James R.

<120> IMPROVED ANTAGONIST ANTIBODIES AGAINST GDF-8 AND USES THEREFOR

<130> PC071914

<150> 61/660,232
<151> 2012-06-15

<160> 73

<170> PatentIn version 3.5

<210> 1
<211> 109
<212> PRT
<213> Homo sapiens

<400> 1

Asp Phe Gly Leu Asp Cys Asp Glu His Ser Thr Glu Ser Arg Cys Cys
1 5 10 15

Arg Tyr Pro Leu Thr Val Asp Phe Glu Ala Phe Gly Trp Asp Trp Ile
20 25 30

Ile Ala Pro Lys Arg Tyr Lys Ala Asn Tyr Cys Ser Gly Glu Cys Glu
35 40 45

Phe Val Phe Leu Gln Lys Tyr Pro His Thr His Leu Val His Gln Ala
50 55 60

Asn Pro Arg Gly Ser Ala Gly Pro Cys Cys Thr Pro Thr Lys Met Ser
65 70 75 80

Pro Ile Asn Met Leu Tyr Phe Asn Gly Lys Glu Gln Ile Ile Tyr Gly
85 90 95

Lys Ile Pro Ala Met Val Val Asp Arg Cys Gly Cys Ser
100 105

<210> 2
<211> 348
<212> DNA
<213> Mus musculus

<400> 2
gaagtgcagc tggtggagtc tgggggaggc ttagtgaagc ctggagggtc cctgaaactc 60

tcctgtgcag cctctggatt cactttcagt agctatgcca tgtcttgggt tcgccagact 120

ccggagaaga ggctggagtg ggtcgcaacc attagtagtg gtggtagtta cacctcctat 180

ccagacagtg tgaagggtcg attcaccatc tccagagaca atgccaagaa caccctgtac 240

ctgcaaatga gcagtctgag gtctgaggac acggccatgt attactgtgc aagacaagac 300

tatgctatga actactgggg tcaaggaacc tcagtcaccg tctcctca 348

<210> 3
<211> 116
<212> PRT
<213> Mus musculus

<400> 3

Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Lys Pro Gly Gly
1 5 10 15

Ser Leu Lys Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Ser Tyr
20 25 30

Ala Met Ser Trp Val Arg Gln Thr Pro Glu Lys Arg Leu Glu Trp Val
35 40 45

Ala Thr Ile Ser Ser Gly Gly Ser Tyr Thr Ser Tyr Pro Asp Ser Val
50 55 60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Thr Leu Tyr
65 70 75 80

Leu Gln Met Ser Ser Leu Arg Ser Glu Asp Thr Ala Met Tyr Tyr Cys
85 90 95

Ala Arg Gln Asp Tyr Ala Met Asn Tyr Trp Gly Gln Gly Thr Ser Val
100 105 110

Thr Val Ser Ser
115

<210> 4
<211> 321
<212> DNA
<213> Mus musculus

<400> 4
gacattgaga tgacccagtc tcacaaattc atgtccacat cagtaggaga cagggtcagc 60

atcacctgca aggccagtca ggatgtgagt actgctgtag cctggtatca acagaaacca 120

ggacaatctc ctaaactact gctttactcg gcatcctacc ggtacactgg agtccctgat 180

cggttcactg gcagtggatc tgggacggat ttcactttca ccatcagcag tgtgcaggct 240

gaagacctgg cagtttatta ctgtcagcaa cattatagta ctccgtggac gttcggtgga 300

ggcaccaagc tggaaatcaa a 321

<210> 5
<211> 107
<212> PRT
<213> Mus musculus

<400> 5

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Asp Ile Glu Met Thr Gln Ser His Lys Phe Met Ser Thr Ser Val Gly
1               5                   10                  15

Asp Arg Val Ser Ile Thr Cys Lys Ala Ser Gln Asp Val Ser Thr Ala
            20                  25                  30

Val Ala Trp Tyr Gln Gln Lys Pro Gly Gln Ser Pro Lys Leu Leu Leu
        35                  40                  45

Tyr Ser Ala Ser Tyr Arg Tyr Thr Gly Val Pro Asp Arg Phe Thr Gly
    50                  55                  60

Ser Gly Ser Gly Thr Asp Phe Thr Phe Thr Ile Ser Ser Val Gln Ala
65                  70                  75                  80

Glu Asp Leu Ala Val Tyr Tyr Cys Gln Gln His Tyr Ser Thr Pro Trp
                85                  90                  95

Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys
            100                 105
```

<210> 6
<211> 348
<212> DNA
<213> Artificial Sequence

<220>
<223> Mouse CDRs and human VH & J segment

<400> 6

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agttgcgctg cgtcgggatt cacctttca agttacgcaa tgtcatgggt tcgtcaggca      120

ccggggaaag gcttagagtg ggtgtcaact attagctctg gcggtagcta tacgtcgtat      180

cctgactctg tgaagggacg atttacaata agccgggaca attctaaaaa cactttgtac      240

ctacagatga attccttgag agccgaagat accgccgtct actattgtgc gaagcaagat      300

tacgctatga actattgggg tcaagggaca atggtaacgg tatcctcc                  348
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<210> 7
<211> 116
<212> PRT
<213> Artificial Sequence

<220>
<223> Mouse CDRs and human VH & J segment

<400> 7

```
Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1               5                   10                  15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Ser Tyr
            20                  25                  30
```

```
Ala Met Ser Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
        35                  40                  45

Ser Thr Ile Ser Ser Gly Gly Ser Tyr Thr Ser Tyr Pro Asp Ser Val
    50                  55                  60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65                  70                  75                  80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95

Ala Lys Gln Asp Tyr Ala Met Asn Tyr Trp Gly Gln Gly Thr Met Val
            100                 105                 110

Thr Val Ser Ser
        115
```

<210> 8
<211> 321
<212> DNA
<213> Artificial Sequence

<220>
<223> Mouse CDRs and human VH & J segment

<400> 8

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ataacgtgta aagcgagcca agatgtgagt actgcagtag cgtggtatca gcaaaagcca      120

gggaaggctc cgaaactatt gatttactcc gcctcttaca gatatacggg cgttcctgat      180

aggtttagtg gaagtgggtc gggtacggac tttaccctga ctatatcgtc acttcagcca      240

gaggattttg ctacctacta ttgccaacag cattattcaa caccgtggac attcggccag      300

ggaactaagg tcgaaataaa a                                                321
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<210> 9
<211> 107
<212> PRT
<213> Artificial Sequence

<220>
<223> Mouse CDRs and human VH & J segment

<400> 9

```
Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1               5                   10                  15

Asp Arg Val Thr Ile Thr Cys Lys Ala Ser Gln Asp Val Ser Thr Ala
            20                  25                  30

Val Ala Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
        35                  40                  45
```

```
Tyr Ser Ala Ser Tyr Arg Tyr Thr Gly Val Pro Ser Arg Phe Ser Gly
    50                  55                  60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65                  70                  75                  80

Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln His Tyr Ser Thr Pro Trp
                85                  90                  95

Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys
            100                 105
```

<210> 10
<211> 5
<212> PRT
<213> Mus musculus

<400> 10

```
Ser Tyr Ala Met Ser
1               5
```

<210> 11
<211> 17
<212> PRT
<213> Mus musculus

<400> 11

```
Thr Ile Ser Ser Gly Gly Ser Tyr Thr Ser Tyr Pro Asp Ser Val Lys
1               5                   10                  15

Gly
```

<210> 12
<211> 7
<212> PRT
<213> Mus musculus

<400> 12

```
Gln Asp Tyr Ala Met Asn Tyr
1               5
```

<210> 13
<211> 11
<212> PRT
<213> Mus musculus

<400> 13

```
Lys Ala Ser Gln Asp Val Ser Thr Ala Val Ala
1               5                   10
```

<210> 14
<211> 7
<212> PRT

<213> Mus musculus

<400> 14

Ser Ala Ser Tyr Arg Tyr Thr
1 5

<210> 15
<211> 9
<212> PRT
<213> Mus musculus

<400> 15

Gln Gln His Tyr Ser Thr Pro Trp Thr
1 5

<210> 16
<211> 321
<212> DNA
<213> Homo sapiens

<400> 16
cgaaccgtag cggcaccgtc agtattcata ttccctccat cggacgagca attgaaaagt 60

gggacagctt cggtcgtgtg tctcttgaat aacttttacc ccagagaagc taaggtccag 120

tggaaagttg acaatgcgtt acagagcgga aattctcaag aatccgttac tgaacaggat 180

agtaaggatt ctacgtattc acttagcagt actctgaccc tatcaaaggc agattatgaa 240

aaacacaagg tatacgcctg cgaggtgacg catcaaggct tatccagccc agttacaaaa 300

tcttttaaca ggggtgagtg t 321

<210> 17
<211> 107
<212> PRT
<213> Homo sapiens

<400> 17

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

Gln Leu Lys Ser Gly Thr Ala Ser Val Val Cys Leu Leu Asn Asn Phe
20 25 30

Tyr Pro Arg Glu Ala Lys Val Gln Trp Lys Val Asp Asn Ala Leu Gln
35 40 45

Ser Gly Asn Ser Gln Glu Ser Val Thr Glu Gln Asp Ser Lys Asp Ser
50 55 60

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

Lys His Lys Val Tyr Ala Cys Glu Val Thr His Gln Gly Leu Ser Ser
85 90 95

Pro Val Thr Lys Ser Phe Asn Arg Gly Glu Cys
100 105

<210> 18
<211> 990
<212> DNA
<213> Artificial Sequence

<220>
<223> Human sequence with substitution mutations

<400> 18
gcctccacaa aaggaccatc tgtttttccc ttggcgccat caagtaaatc tacttccgga 60

ggtaccgctg cgcttggctg cctcgtgaaa gactatttcc cagaacctgt cacagtctcg 120

tggaatagtg gtgctttaac ctcgggcgta catacttttc ctgctgtact tcaatcaagc 180

ggactgtact cattatcgtc tgtagtcacg gtcccgagtt cttcactcgg aacacagact 240

tatatatgca acgttaatca taagcctagc aacaccaagg ttgacaaaaa ggtggaacca 300

aaatcgtgcg ataagacgca cacatgtcca ccctgtcctg caccagaagc tctgggcgcg 360

ccatcggttt tcttgttccc acccaaacct aaggacacgt taatgataag tcgaacgcca 420

gaggtgacat gtgttgtagt ggatgtgagc cacgaagatc cggaagtaaa attcaattgg 480

tatgtagatg gtgttgaagt ccataacgca aaaactaagc cgagggaaga gcagtacaac 540

tctacttata gggtagtctc cgtactaact gtcttgcacc aagattggct aaatgggaag 600

gaatataaat gtaaggtttc aaataaggca ctaccagccc cgatagagaa gacaataagc 660

aaagcgaagg ggcaaccaag agagccccaa gtgtacacct tgcctccgag cagagaggaa 720

atgacaaaaa atcaagtatc ccttacgtgt ctggtaaagg gattttatcc aagtgacata 780

gcagtggagt gggagagtaa cggccagcca gaaaacaatt acaaaaccac tcccccggtt 840

ttagatagcg atgggagttt ctttttgtac tcaaagttga ccgttgacaa gtcacgatgg 900

cagcaaggta atgtatttag ttgttctgtt atgcatgagg ccttacataa tcactacacg 960

cagaaatctc tctccttaag ccccgggaaa 990

<210> 19
<211> 330
<212> PRT
<213> Artificial Sequence

<220>
<223> Human CH region with substitution mutations

<400> 19

Ala Ser Thr Lys Gly Pro Ser Val Phe Pro Leu Ala Pro Ser Ser Lys
1 5 10 15

Ser Thr Ser Gly Gly Thr Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr
20 25 30

Phe Pro Glu Pro Val Thr Val Ser Trp Asn Ser Gly Ala Leu Thr Ser

```
        35                  40                  45

Gly Val His Thr Phe Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser
    50                  55                  60

Leu Ser Ser Val Val Thr Val Pro Ser Ser Ser Leu Gly Thr Gln Thr
65                  70                  75                  80

Tyr Ile Cys Asn Val Asn His Lys Pro Ser Asn Thr Lys Val Asp Lys
                85                  90                  95

Lys Val Glu Pro Lys Ser Cys Asp Lys Thr His Thr Cys Pro Pro Cys
            100                 105                 110

Pro Ala Pro Glu Ala Leu Gly Ala Pro Ser Val Phe Leu Phe Pro Pro
        115                 120                 125

Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys
    130                 135                 140

Val Val Val Asp Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp
145                 150                 155                 160

Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu
                165                 170                 175

Glu Gln Tyr Asn Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu
            180                 185                 190

His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn
        195                 200                 205

Lys Ala Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly
    210                 215                 220

Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Glu Glu
225                 230                 235                 240

Met Thr Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr
                245                 250                 255

Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn
            260                 265                 270

Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe
        275                 280                 285

Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn
    290                 295                 300

Val Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn His Tyr Thr
```

305 310 315 320

Gln Lys Ser Leu Ser Leu Ser Pro Gly Lys
325 330

<210> 20
<211> 10
<212> PRT
<213> Mus musculus

<400> 20

Gly Phe Thr Phe Ser Ser Tyr Ala Met Ser
1 5 10

<210> 21
<211> 10
<212> PRT
<213> Mus musculus

<400> 21

Thr Ile Ser Ser Gly Gly Ser Tyr Thr Ser
1 5 10

<210> 22
<211> 7
<212> PRT
<213> Mus musculus

<400> 22

Gln Asp Tyr Ala Met Asn Tyr
1 5

<210> 23
<211> 11
<212> PRT
<213> Mus musculus

<400> 23

Lys Ala Ser Gln Asp Val Ser Thr Ala Val Ala
1 5 10

<210> 24
<211> 7
<212> PRT
<213> Mus musculus

<400> 24

Ser Ala Ser Tyr Arg Tyr Thr
1 5

<210> 25
<211> 9
<212> PRT
<213> Mus musculus

<400> 25

Gln Gln His Tyr Ser Thr Pro Trp Thr
1 5

<210> 26
<211> 116
<212> PRT
<213> Artificial Sequence

<220>
<223> Human VH, murine CDRs

<400> 26

Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Ser Tyr
20 25 30

Ala Met Ser Trp Val Arg Gln Ala Pro Glu Lys Arg Leu Glu Trp Val
35 40 45

Ala Thr Ile Ser Ser Gly Gly Ser Tyr Thr Ser Tyr Pro Asp Ser Val
50 55 60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65 70 75 80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Met Tyr Tyr Cys
85 90 95

Ala Lys Gln Asp Tyr Ala Met Asn Tyr Trp Gly Gln Gly Thr Met Val
100 105 110

Thr Val Ser Ser
115

<210> 27
<211> 107
<212> PRT
<213> Artificial Sequence

<220>
<223> Human VL, murine CDRs

<400> 27

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

Asp Arg Val Thr Ile Thr Cys Lys Ala Ser Gln Asp Val Ser Thr Ala
20 25 30

Val Ala Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
35 40 45

```
Tyr Ser Ala Ser Tyr Arg Tyr Thr Gly Val Pro Asp Arg Phe Ser Gly
    50                  55                  60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Ala
65                  70                  75                  80

Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln His Tyr Ser Thr Pro Trp
                85                  90                  95

Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys
            100                 105
```

<210> 28
<211> 405
<212> DNA
<213> Mus musculus

<400> 28

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atgaactttg tgctcagctt gattttcctt gccctcattt taaaaggtgt ccagtgtgaa       60

gtgcagctgg tggagtctgg gggaggctta gtgaagcctg gagggtccct gaaactctcc      120

tgtgcagcct ctggattcac tttcagtagc tatgccatgt cttgggttcg ccagactccg      180

gagaagaggc tggagtgggt cgcaaccatt agtagtggtg gtagttacac ctcctatcca      240

gacagtgtga agggtcgatt caccatctcc agagacaatg ccaagaacac cctgtacctg      300

caaatgagca gtctgaggtc tgaggacacg gccatgtatt actgtgcaag acaagactat      360

gctatgaact actggggtca aggaacctca gtcaccgtct cctca                      405
```

<210> 29
<211> 135
<212> PRT
<213> Mus musculus

<400> 29

```
Met Asn Phe Val Leu Ser Leu Ile Phe Leu Ala Leu Ile Leu Lys Gly
1               5                   10                  15

Val Gln Cys Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Lys
            20                  25                  30

Pro Gly Gly Ser Leu Lys Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe
        35                  40                  45

Ser Ser Tyr Ala Met Ser Trp Val Arg Gln Thr Pro Glu Lys Arg Leu
    50                  55                  60

Glu Trp Val Ala Thr Ile Ser Ser Gly Gly Ser Tyr Thr Ser Tyr Pro
65                  70                  75                  80

Asp Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn
                85                  90                  95
```

```
Thr Leu Tyr Leu Gln Met Ser Ser Leu Arg Ser Glu Asp Thr Ala Met
            100                 105                 110

Tyr Tyr Cys Ala Arg Gln Asp Tyr Ala Met Asn Tyr Trp Gly Gln Gly
        115                 120                 125

Thr Ser Val Thr Val Ser Ser
    130                 135
```

<210> 30
<211> 381
<212> DNA
<213> Mus musculus

<400> 30

```
atggagtcac agattcaggt ctttgtattc gtgtttctct ggttgtctgg tgttgacgga       60

gacattgaga tgacccagtc tcacaaattc atgtccacat cagtaggaga cagggtcagc      120

atcacctgca aggccagtca ggatgtgagt actgctgtag cctggtatca acagaaacca      180

ggacaatctc ctaaactact gctttactcg gcatcctacc ggtacactgg agtccctgat      240

cggttcactg gcagtggatc tgggacggat ttcactttca ccatcagcag tgtgcaggct      300

gaagacctgg cagtttatta ctgtcagcaa cattatagta ctccgtggac gttcggtgga      360

ggcaccaagc tggaaatcaa a                                                381
```

<210> 31
<211> 127
<212> PRT
<213> Mus musculus

<400> 31

```
Met Glu Ser Gln Ile Gln Val Phe Val Phe Val Phe Leu Trp Leu Ser
1               5                   10                  15

Gly Val Asp Gly Asp Ile Glu Met Thr Gln Ser His Lys Phe Met Ser
            20                  25                  30

Thr Ser Val Gly Asp Arg Val Ser Ile Thr Cys Lys Ala Ser Gln Asp
        35                  40                  45

Val Ser Thr Ala Val Ala Trp Tyr Gln Gln Lys Pro Gly Gln Ser Pro
    50                  55                  60

Lys Leu Leu Leu Tyr Ser Ala Ser Tyr Arg Tyr Thr Gly Val Pro Asp
65                  70                  75                  80

Arg Phe Thr Gly Ser Gly Ser Gly Thr Asp Phe Thr Phe Thr Ile Ser
                85                  90                  95

Ser Val Gln Ala Glu Asp Leu Ala Val Tyr Tyr Cys Gln Gln His Tyr
            100                 105                 110
```

Ser Thr Pro Trp Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys
115 120 125

<210> 32
<211> 95
<212> PRT
<213> Homo sapiens

<400> 32

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

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Ser Ile Ser Ser Tyr
20 25 30

Leu Asn Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
35 40 45

Tyr Ala Ala Ser Ser Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly
50 55 60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65 70 75 80

Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Ser Tyr Ser Thr Pro
85 90 95

<210> 33
<211> 98
<212> PRT
<213> Homo sapiens

<400> 33

Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Ser Tyr
20 25 30

Ala Met Ser Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Ser Ala Ile Ser Gly Ser Gly Gly Ser Thr Tyr Tyr Ala Asp Ser Val
50 55 60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65 70 75 80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Lys

<210> 34
<211> 15
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic protein sequence

<400> 34

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

<210> 35
<211> 45
<212> DNA
<213> Homo sapiens

<400> 35
gcttttgata tctggggcca agggacaatg gtcaccgtct cttca 45

<210> 36
<211> 15
<212> PRT
<213> Homo sapiens

<400> 36

Ala Phe Asp Ile Trp Gly Gln Gly Thr Met Val Thr Val Ser Ser
1 5 10 15

<210> 37
<211> 46
<212> DNA
<213> Homo sapiens

<400> 37
tactttgact actggggcca aggaaccctg gtcaccgtct cctcag 46

<210> 38
<211> 15
<212> PRT
<213> Homo sapiens

<400> 38

Tyr Phe Asp Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser
1 5 10 15

<210> 39
<211> 37
<212> DNA
<213> Homo sapiens

<400> 39
tggacgttcg gccaagggac caaggtggaa atcaaac 37

<210> 40
<211> 12

<212> PRT
<213> Homo sapiens

<400> 40

Trp Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys
1 5 10

<210> 41
<211> 37
<212> DNA
<213> Homo sapiens

<400> 41
ctcactttcg gcggagggac caaggtggag atcaaac 37

<210> 42
<211> 12
<212> PRT
<213> Homo sapiens

<400> 42

Leu Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys
1 5 10

<210> 43
<211> 348
<212> DNA
<213> Artificial Sequence

<220>
<223> Human VH, murine CDRs

<400> 43
gaggtgcagc tgttggagtc tgggggaggc ttggtacagc ctgggggtc cctgagactc 60

tcctgtgcag cctctggatt cacctttagc agctatgcca tgagctgggt ccgccaggct 120

ccagggaagg ggctggagtg ggtctcaacc attagtagtg gtggtagtta cacctcctat 180

ccagacagtg tgaagggtcg gttcaccatc tccagagaca attccaagaa cacgctgtat 240

ctgcaaatga acagcctgag agccgaggac acggccgtat attactgtgc gaaacaagac 300

tatgctatga actactgggg ccagggcacc ctggtcaccg tgtcctcc 348

<210> 44
<211> 116
<212> PRT
<213> Artificial Sequence

<220>
<223> Mouse CDRs and human VH & J segment

<400> 44

Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Ser Tyr
20 25 30

```
Ala Met Ser Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
        35                  40                  45

Ser Thr Ile Ser Ser Gly Gly Ser Tyr Thr Ser Tyr Pro Asp Ser Val
    50                  55                  60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65                  70                  75                  80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95

Ala Lys Gln Asp Tyr Ala Met Asn Tyr Trp Gly Gln Gly Thr Leu Val
            100                 105                 110

Thr Val Ser Ser
        115
```

<210> 45
<211> 321
<212> DNA
<213> Artificial Sequence

<220>
<223> Human VL, murine CDRs

<400> 45

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gacatccaga tgacccagtc cccctcctcc ctgtccgcct ccgtgggcga cagagtgacc       60

atcacctgca aggccagtca ggatgtgagt actgctgtgg cctggtatca gcagaagcct      120

ggcaaggccc ctaagctgct gatctactcc gcatcctacc ggtacactgg cgtgccttcc      180

cggttctccg gctccggctc tggcaccgac ttcaccctga ccatctcctc cctgcagcct      240

gaggacttcg ccacctacta ctgccagcaa cattatagta ctccatggac ctttggcggt      300

ggaacaaagg tggaaatcaa a                                                 321
```

<210> 46
<211> 107
<212> PRT
<213> Artificial Sequence

<220>
<223> Mouse CDRs and human VH & J segment

<400> 46

```
Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1               5                   10                  15

Asp Arg Val Thr Ile Thr Cys Lys Ala Ser Gln Asp Val Ser Thr Ala
            20                  25                  30

Val Ala Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
        35                  40                  45
```

Tyr Ser Ala Ser Tyr Arg Tyr Thr Gly Val Pro Ser Arg Phe Ser Gly
50 55 60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65 70 75 80

Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln His Tyr Ser Thr Pro Trp
85 90 95

Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys
100 105

<210> 47
<211> 348
<212> DNA
<213> Artificial Sequence

<220>
<223> Human VH, murine CDRs

<400> 47
gaggtgcagc tgttggagtc tgggggaggc ttggtacagc ctgggggtc cctgagactc 60

tcctgtgcag cctctggatt cacctttagc agctatgcca tgagctgggt ccgccaggct 120

ccagggaagg ggctggagtg ggtctcaacc attagtagtg gtggtagtta cacctcctat 180

ccagacagtg tgaagggtcg gttcaccatc tccagagaca attccaagaa cacgctgtat 240

ctgcaaatga acagcctgag agccgaggac acggccgtat attactgtgc gaaacaagac 300

tatgctatga actactgggg ccagggcacc atggtcaccg tgtcctcc 348

<210> 48
<211> 321
<212> DNA
<213> Artificial Sequence

<220>
<223> Human VL, murine CDRs

<400> 48
gacatccaga tgacccagtc cccctcctcc ctgtccgcct ccgtgggcga cagagtgacc 60

atcacctgca aggccagtca ggatgtgagt actgctgtgg cctggtatca gcagaagcct 120

ggcaaggccc ctaagctgct gatctactcc gcatcctacc ggtacactgg cgtgccttcc 180

cggttctccg gctccggctc tggcaccgac ttcaccctga ccatctcctc cctgcagcct 240

gaggacttcg ccacctacta ctgccagcaa cattatagta ctccatggac ctttggccaa 300

ggaacaaagg tggaaatcaa a 321

<210> 49
<211> 405
<212> DNA
<213> Artificial Sequence

<220>
<223> Human VH, murine CDRs

<400> 49
atgggatgga gctgtatcat cctcttcttg gtagcaacag ctacaggcgc gcactccgag 60

gtgcagctgt tggagtctgg gggaggcttg gtacagcctg gggggtccct gagactctcc 120

tgtgcagcct ctggattcac ctttagcagc tatgccatga gctgggtccg ccaggctcca 180

gggaaggggc tggagtgggt ctcaaccatt agtagtggtg gtagttacac ctcctatcca 240

gacagtgtga agggtcggtt caccatctcc agagacaatt ccaagaacac gctgtatctg 300

caaatgaaca gcctgagagc cgaggacacg gccgtatatt actgtgcgaa acaagactat 360

gctatgaact actggggcca gggcaccctg gtcaccgtgt cctcc 405

<210> 50
<211> 135
<212> PRT
<213> Artificial Sequence

<220>
<223> Human VH, murine CDRs

<400> 50

Met Gly Trp Ser Cys Ile Ile Leu Phe Leu Val Ala Thr Ala Thr Gly
1 5 10 15

Ala His Ser Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Val Gln
20 25 30

Pro Gly Gly Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe
35 40 45

Ser Ser Tyr Ala Met Ser Trp Val Arg Gln Ala Pro Gly Lys Gly Leu
50 55 60

Glu Trp Val Ser Thr Ile Ser Ser Gly Gly Ser Tyr Thr Ser Tyr Pro
65 70 75 80

Asp Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn
85 90 95

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

Tyr Tyr Cys Ala Lys Gln Asp Tyr Ala Met Asn Tyr Trp Gly Gln Gly
115 120 125

Thr Leu Val Thr Val Ser Ser
130 135

<210> 51
<211> 378
<212> DNA
<213> Artificial Sequence

<220>
<223> Human VL, murine CDRs

<400> 51
atgggatgga gctgtatcat cctcttcttg gtagcaacag ctacaggcgc gcactccgac 60

atccagatga cccagtcccc ctcctccctg tccgcctccg tgggcgacag agtgaccatc 120

acctgcaagg ccagtcagga tgtgagtact gctgtggcct ggtatcagca gaagcctggc 180

aaggccccta agctgctgat ctactccgca tcctaccggt acactggcgt gccttcccgg 240

ttctccggct ccggctctgg caccgacttc accctgacca tctcctccct gcagcctgag 300

gacttcgcca cctactactg ccagcaacat tatagtactc catggacctt tggcggtgga 360

acaaaggtgg aaatcaaa 378

<210> 52
<211> 126
<212> PRT
<213> Artificial Sequence

<220>
<223> Human VL, murine CDRs

<400> 52

Met Gly Trp Ser Cys Ile Ile Leu Phe Leu Val Ala Thr Ala Thr Gly
1 5 10 15

Ala His Ser Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala
20 25 30

Ser Val Gly Asp Arg Val Thr Ile Thr Cys Lys Ala Ser Gln Asp Val
35 40 45

Ser Thr Ala Val Ala Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys
50 55 60

Leu Leu Ile Tyr Ser Ala Ser Tyr Arg Tyr Thr Gly Val Pro Ser Arg
65 70 75 80

Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser
85 90 95

Leu Gln Pro Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln His Tyr Ser
100 105 110

Thr Pro Trp Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys
115 120 125

<210> 53
<211> 405
<212> DNA
<213> Artificial Sequence

<220>
<223> Human VH, murine CDRs

<400> 53
atgggatgga gctgtatcat cctcttcttg gtagcaacag ctacaggcgc gcactccgag 60

gtgcagctgt tggagtctgg gggaggcttg gtacagcctg gggggtccct gagactctcc 120

tgtgcagcct ctggattcac ctttagcagc tatgccatga gctgggtccg ccaggctcca 180

gggaaggggc tggagtgggt ctcaaccatt agtagtggtg gtagttacac ctcctatcca 240

gacagtgtga agggtcggtt caccatctcc agagacaatt ccaagaacac gctgtatctg 300

caaatgaaca gcctgagagc cgaggacacg gccgtatatt actgtgcgaa acaagactat 360

gctatgaact actggggcca gggcaccatg gtcaccgtgt cctcc 405

<210> 54
<211> 135
<212> PRT
<213> Artificial Sequence

<220>
<223> Human VH, murine CDRs

<400> 54

Met Gly Trp Ser Cys Ile Ile Leu Phe Leu Val Ala Thr Ala Thr Gly
1 5 10 15

Ala His Ser Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Val Gln
20 25 30

Pro Gly Gly Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe
35 40 45

Ser Ser Tyr Ala Met Ser Trp Val Arg Gln Ala Pro Gly Lys Gly Leu
50 55 60

Glu Trp Val Ser Thr Ile Ser Ser Gly Gly Ser Tyr Thr Ser Tyr Pro
65 70 75 80

Asp Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn
85 90 95

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

Tyr Tyr Cys Ala Lys Gln Asp Tyr Ala Met Asn Tyr Trp Gly Gln Gly
115 120 125

Thr Met Val Thr Val Ser Ser
130 135

<210> 55
<211> 378
<212> DNA
<213> Artificial Sequence

<220>
<223> Human VL, murine CDRs

<400> 55
atgggatgga gctgtatcat cctcttcttg gtagcaacag ctacaggcgc gcactccgac 60

atccagatga cccagtcccc ctcctccctg tccgcctccg tgggcgacag agtgaccatc 120

acctgcaagg ccagtcagga tgtgagtact gctgtggcct ggtatcagca gaagcctggc 180

aaggccccta agctgctgat ctactccgca tcctaccggt acactggcgt gccttcccgg 240

ttctccggct ccggctctgg caccgacttc accctgacca tctcctccct gcagcctgag 300

gacttcgcca cctactactg ccagcaacat tatagtactc catggacctt tggccaagga 360

acaaaggtgg aaatcaaa 378

<210> 56
<211> 126
<212> PRT
<213> Artificial Sequence

<220>
<223> Human VL, murine CDRs

<400> 56

Met Gly Trp Ser Cys Ile Ile Leu Phe Leu Val Ala Thr Ala Thr Gly
1 5 10 15

Ala His Ser Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala
20 25 30

Ser Val Gly Asp Arg Val Thr Ile Thr Cys Lys Ala Ser Gln Asp Val
35 40 45

Ser Thr Ala Val Ala Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys
50 55 60

Leu Leu Ile Tyr Ser Ala Ser Tyr Arg Tyr Thr Gly Val Pro Ser Arg
65 70 75 80

Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser
85 90 95

Leu Gln Pro Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln His Tyr Ser
100 105 110

Thr Pro Trp Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys
115 120 125

<210> 57
<211> 330
<212> PRT
<213> Artificial Sequence

<220>
<223> Human CH region with substitution mutations

<400> 57

```
Ala Ser Thr Lys Gly Pro Ser Val Phe Pro Leu Ala Pro Ser Ser Lys
1               5                  10                  15

Ser Thr Ser Gly Gly Thr Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr
            20                  25                  30

Phe Pro Glu Pro Val Thr Val Ser Trp Asn Ser Gly Ala Leu Thr Ser
        35                  40                  45

Gly Val His Thr Phe Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser
    50                  55                  60

Leu Ser Ser Val Val Thr Val Pro Ser Ser Ser Leu Gly Thr Gln Thr
65                  70                  75                  80

Tyr Ile Cys Asn Val Asn His Lys Pro Ser Asn Thr Lys Val Asp Lys
                85                  90                  95

Lys Val Glu Pro Lys Ser Cys Asp Lys Thr His Thr Cys Pro Pro Cys
            100                 105                 110

Pro Ala Pro Glu Ala Ala Gly Ala Pro Ser Val Phe Leu Phe Pro Pro
        115                 120                 125

Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys
    130                 135                 140

Val Val Val Asp Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp
145                 150                 155                 160

Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu
                165                 170                 175

Glu Gln Tyr Asn Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu
            180                 185                 190

His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn
        195                 200                 205

Lys Ala Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly
    210                 215                 220

Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Glu Glu
225                 230                 235                 240

Met Thr Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr
                245                 250                 255

Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn
```

260 265 270

Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe
275 280 285

Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn
290 295 300

Val Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn His Tyr Thr
305 310 315 320

Gln Lys Ser Leu Ser Leu Ser Pro Gly Lys
325 330

<210> 58
<211> 446
<212> PRT
<213> Artificial Sequence

<220>
<223> Mouse CDRs and human VH & J segment; Human CH region with substitution mutations

<400> 58

Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Ser Tyr
20 25 30

Ala Met Ser Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Ser Thr Ile Ser Ser Gly Gly Ser Tyr Thr Ser Tyr Pro Asp Ser Val
50 55 60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65 70 75 80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Lys Gln Asp Tyr Ala Met Asn Tyr Trp Gly Gln Gly Thr Leu Val
100 105 110

Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser Val Phe Pro Leu Ala
115 120 125

Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu Gly Cys Leu
130 135 140

Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser Trp Asn Ser Gly
145 150 155 160

```
Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala Val Leu Gln Ser Ser
                165                 170                 175

Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser Ser Ser Leu
            180                 185                 190

Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys Pro Ser Asn Thr
        195                 200                 205

Lys Val Asp Lys Lys Val Glu Pro Lys Ser Cys Asp Lys Thr His Thr
    210                 215                 220

Cys Pro Pro Cys Pro Ala Pro Glu Ala Ala Gly Ala Pro Ser Val Phe
225                 230                 235                 240

Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro
                245                 250                 255

Glu Val Thr Cys Val Val Val Asp Val Ser His Glu Asp Pro Glu Val
            260                 265                 270

Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr
        275                 280                 285

Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg Val Val Ser Val
    290                 295                 300

Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys
305                 310                 315                 320

Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser
                325                 330                 335

Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro
            340                 345                 350

Ser Arg Glu Glu Met Thr Lys Asn Gln Val Ser Leu Thr Cys Leu Val
        355                 360                 365

Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly
    370                 375                 380

Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp
385                 390                 395                 400

Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp
                405                 410                 415

Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His Glu Ala Leu His
            420                 425                 430
```

```
Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly Lys
        435                 440                 445


<210>  59
<211>  214
<212>  PRT
<213>  Artificial Sequence

<220>
<223>  Mouse CDRs and human VH, J segment and CH

<400>  59

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


Asp Arg Val Thr Ile Thr Cys Lys Ala Ser Gln Asp Val Ser Thr Ala
            20                  25                  30


Val Ala Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
        35                  40                  45


Tyr Ser Ala Ser Tyr Arg Tyr Thr Gly Val Pro Ser Arg Phe Ser Gly
    50                  55                  60


Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65                  70                  75                  80


Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln His Tyr Ser Thr Pro Trp
                85                  90                  95


Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys Arg Thr Val Ala Ala
            100                 105                 110


Pro Ser Val Phe Ile Phe Pro Pro Ser Asp Glu Gln Leu Lys Ser Gly
        115                 120                 125


Thr Ala Ser Val Val Cys Leu Leu Asn Asn Phe Tyr Pro Arg Glu Ala
    130                 135                 140


Lys Val Gln Trp Lys Val Asp Asn Ala Leu Gln Ser Gly Asn Ser Gln
145                 150                 155                 160


Glu Ser Val Thr Glu Gln Asp Ser Lys Asp Ser Thr Tyr Ser Leu Ser
                165                 170                 175


Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu Lys His Lys Val Tyr
            180                 185                 190


Ala Cys Glu Val Thr His Gln Gly Leu Ser Ser Pro Val Thr Lys Ser
        195                 200                 205
```

eolf-seq1

Phe Asn Arg Gly Glu Cys
210

<210> 60
<211> 1476
<212> DNA
<213> Artificial Sequence

<220>
<223> scFv

<400> 60
atgggatgga gctgtatcat cctcttcttg gtagcaacag ctacaggcgc gcactccgac 60

attgagatga cccagtctca caaattcatg tccacatcag taggagacag ggtcagcatc 120

acctgcaagg ccagtcagga tgtgagtact gctgtagcct ggtatcaaca gaaaccagga 180

caatctccta aactactgct ttactcggca tcctaccggt acactggagt ccctgatcgg 240

ttcactggca gtggatctgg gacggatttc actttcacca tcagcagtgt gcaggctgaa 300

gacctggcag tttattactg tcagcaacat tatagtactc cgtggacgtt tggcggtgga 360

acaaaggtgg aaatcaaagg aggcggcggt tcaggcggag gtggctctgg cggtggcgga 420

<220>
<223> scFv

<400> 61

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Met Gly Trp Ser Cys Ile Ile Leu Phe Leu Val Ala Thr Ala Thr Gly
1               5                  10                  15

Ala His Ser Asp Ile Glu Met Thr Gln Ser His Lys Phe Met Ser Thr
            20                  25                  30

Ser Val Gly Asp Arg Val Ser Ile Thr Cys Lys Ala Ser Gln Asp Val
        35                  40                  45

Ser Thr Ala Val Ala Trp Tyr Gln Gln Lys Pro Gly Gln Ser Pro Lys
    50                  55                  60

Leu Leu Leu Tyr Ser Ala Ser Tyr Arg Tyr Thr Gly Val Pro Asp Arg
65                  70                  75                  80

Phe Thr Gly Ser Gly Ser Gly Thr Asp Phe Thr Phe Thr Ile Ser Ser
                85                  90                  95

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

Thr Pro Trp Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys Gly Gly
        115                 120                 125

Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Ser Glu Val
    130                 135                 140

Gln Leu Val Glu Ser Gly Gly Gly Leu Val Lys Pro Gly Gly Ser Leu
145                 150                 155                 160

Lys Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Ser Tyr Ala Met
                165                 170                 175

Ser Trp Val Arg Gln Thr Pro Glu Lys Arg Leu Glu Trp Val Ala Thr
            180                 185                 190

Ile Ser Ser Gly Gly Ser Tyr Thr Ser Tyr Pro Asp Ser Val Lys Gly
        195                 200                 205

Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Thr Leu Tyr Leu Gln
    210                 215                 220

Met Ser Ser Leu Arg Ser Glu Asp Thr Ala Met Tyr Tyr Cys Ala Arg
225                 230                 235                 240

Gln Asp Tyr Ala Met Asn Tyr Trp Gly Gln Gly Thr Leu Val Thr Val
                245                 250                 255
```

```
Ser Ser Asp Gln Glu Pro Lys Ser Ser Asp Lys Thr His Thr Cys Pro
            260                 265                 270

Pro Cys Pro Ala Pro Glu Ala Ala Gly Ala Pro Ser Val Phe Leu Phe
        275                 280                 285

Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val
    290                 295                 300

Thr Cys Val Val Val Asp Val Ser His Glu Asp Pro Glu Val Lys Phe
305                 310                 315                 320

Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys Pro
                325                 330                 335

Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg Val Val Ser Val Leu Thr
            340                 345                 350

Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val
        355                 360                 365

Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala
    370                 375                 380

Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg
385                 390                 395                 400

Glu Glu Met Thr Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys Gly
                405                 410                 415

Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro
            420                 425                 430

Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser
        435                 440                 445

Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln Gln
    450                 455                 460

Gly Asn Val Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn His
465                 470                 475                 480

Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly Lys
                485                 490
```

<210> 62
<211> 1476
<212> DNA
<213> Artificial Sequence

<220>

eolf-seq1

<223> scFv

<400> 62

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gtgcagctgt tggagtctgg gggaggcttg gtacagcctg gggggtccct gagactctcc 120

tgtgcagcct ctggattcac ctttagcagc tatgccatga gctgggtccg ccaggctcca 180

gggaaggggc tggagtgggt ctcaaccatt agtagtggtg gtagttacac ctcctatcca 240

gacagtgtga agggtcggtt caccatctcc agagacaatt ccaagaacac gctgtatctg 300

caaatgaaca gcctgagagc cgaggacacg gccgtatatt actgtgcgaa acaagactat 360

gctatgaact actggggcca gggcaccctg gtcaccgtgt cctctggagg cggcggttca 420

ggcggaggtg gctctggcgg tggcggaagc tccgacatcc agatgaccca gtcccctcc 480

tccctgtccg cctccgtggg cgacagagtg accatcacct gcaaggccag tcaggatgtg 540

agtactgctg tggcctggta tcagcagaag cctggcaagg cccctaagct gctgatctac 600

tccgcatcct accggtacac tggcgtgcct tcccggttct ccggctccgg ctctggcacc 660

gacttcaccc tgaccatctc ctccctgcag cctgaggact tcgccaccta ctactgccag 720

```
Ala His Ser Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Val Gln
            20                  25                  30

Pro Gly Gly Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe
        35                  40                  45

Ser Ser Tyr Ala Met Ser Trp Val Arg Gln Ala Pro Gly Lys Gly Leu
    50                  55                  60

Glu Trp Val Ser Thr Ile Ser Ser Gly Gly Ser Tyr Thr Ser Tyr Pro
65                  70                  75                  80

Asp Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn
                85                  90                  95

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

Tyr Tyr Cys Ala Lys Gln Asp Tyr Ala Met Asn Tyr Trp Gly Gln Gly
        115                 120                 125

Thr Leu Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly
    130                 135                 140

Ser Gly Gly Gly Gly Ser Ser Asp Ile Gln Met Thr Gln Ser Pro Ser
145                 150                 155                 160

Ser Leu Ser Ala Ser Val Gly Asp Arg Val Thr Ile Thr Cys Lys Ala
                165                 170                 175

Ser Gln Asp Val Ser Thr Ala Val Ala Trp Tyr Gln Gln Lys Pro Gly
            180                 185                 190

Lys Ala Pro Lys Leu Leu Ile Tyr Ser Ala Ser Tyr Arg Tyr Thr Gly
        195                 200                 205

Val Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu
    210                 215                 220

Thr Ile Ser Ser Leu Gln Pro Glu Asp Phe Ala Thr Tyr Tyr Cys Gln
225                 230                 235                 240

Gln His Tyr Ser Thr Pro Trp Thr Phe Gly Gly Gly Thr Lys Val Glu
                245                 250                 255

Ile Lys Asp Gln Glu Pro Lys Ser Ser Asp Lys Thr His Thr Cys Pro
            260                 265                 270

Pro Cys Pro Ala Pro Glu Ala Ala Gly Ala Pro Ser Val Phe Leu Phe
        275                 280                 285
```

eolf-seql

Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val
290 295 300

Thr Cys Val Val Val Asp Val Ser His Glu Asp Pro Glu Val Lys Phe
305 310 315 320

Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys Pro
325 330 335

Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg Val Val Ser Val Leu Thr
340 345 350

Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val
355 360 365

Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala
370 375 380

Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg
385 390 395 400

Glu Glu Met Thr Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys Gly
405 410 415

Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro
420 425 430

Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser
435 440 445

Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln Gln
450 455 460

Gly Asn Val Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn His
465 470 475 480

Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly Lys
485 490

<210> 64
<211> 1476
<212> DNA
<213> Artificial Sequence

<220>
<223> scFv

<400> 64
atgggatgga gctgtatcat cctcttcttg gtagcaacag ctacaggcgc gcactccgac 60

atccagatga cccagtcccc ctcctccctg tccgcctccg tgggcgacag agtgaccatc 120

acctgcaagg ccagtcagga tgtgagtact gctgtggcct ggtatcagca gaagcctggc 180

aaggccccta agctgctgat ctactccgca tcctaccggt acactggcgt gccttcccgg 240

eolf-seq1

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ttctccggct ccggctctgg caccgacttc accctgacca tctcctccct gcagcctgag      300
gacttcgcca cctactactg ccagcaacat tatagtactc catggacctt tggcggtgga      360
acaaaggtgg aaatcaaagg aggcggcggt tcaggcggag gtggctctgg cggtggcgga      420
agctccgagg tgcagctgtt ggagtctggg ggaggcttgg tacagcctgg ggggtccctg      480
agactctcct gtgcagcctc tggattcacc tttagcagct atgccatgag ctgggtccgc      540
caggctccag ggaaggggct ggagtgggtc tcaaccatta gtagtggtgg tagttacacc      600
tcctatccag acagtgtgaa gggtcggttc accatctcca gagacaattc caagaacacg      660
ctgtatctgc aaatgaacag cctgagagcc gaggacacgg ccgtatatta ctgtgcgaaa      720
caagactatg ctatgaacta ctggggccag ggcaccctgg tcaccgtgtc ctctgatcag      780
gagcccaaat cttctgacaa aactcacaca tgcccaccgt gcccagcacc tgaagccgct      840
ggggcaccgt cagtcttcct cttccccccа aaacccaagg acaccctcat gatctcccgg      900
acccctgagg tcacatgcgt ggtggtggac gtgagccacg aagaccctga ggtcaagttc      960
aactggtacg tggacggcgt ggaggtgcat aatgccaaga caaagccgcg ggaggagcag     1020
tacaacagca cgtaccgtgt ggtcagcgtc ctcaccgtcc tgcaccagga ctggctgaat     1080
```

```
Leu Leu Ile Tyr Ser Ala Ser Tyr Arg Tyr Thr Gly Val Pro Ser Arg
65                  70                  75                  80

Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser
                85                  90                  95

Leu Gln Pro Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln His Tyr Ser
            100                 105                 110

Thr Pro Trp Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys Gly Gly
        115                 120                 125

Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Ser Glu Val
    130                 135                 140

Gln Leu Leu Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly Ser Leu
145                 150                 155                 160

Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Ser Tyr Ala Met
                165                 170                 175

Ser Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val Ser Thr
            180                 185                 190

Ile Ser Ser Gly Gly Ser Tyr Thr Ser Tyr Pro Asp Ser Val Lys Gly
        195                 200                 205

Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr Leu Gln
    210                 215                 220

Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys Ala Lys
225                 230                 235                 240

Gln Asp Tyr Ala Met Asn Tyr Trp Gly Gln Gly Thr Leu Val Thr Val
                245                 250                 255

Ser Ser Asp Gln Glu Pro Lys Ser Ser Asp Lys Thr His Thr Cys Pro
            260                 265                 270

Pro Cys Pro Ala Pro Glu Ala Ala Gly Ala Pro Ser Val Phe Leu Phe
        275                 280                 285

Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val
    290                 295                 300

Thr Cys Val Val Val Asp Val Ser His Glu Asp Pro Glu Val Lys Phe
305                 310                 315                 320

Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys Pro
                325                 330                 335
```

```
Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg Val Val Ser Val Leu Thr
            340                 345                 350

Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val
        355                 360                 365

Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala
    370                 375                 380

Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg
385                 390                 395                 400

Glu Glu Met Thr Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys Gly
                405                 410                 415

Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro
            420                 425                 430

Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser
        435                 440                 445

Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln Gln
    450                 455                 460

Gly Asn Val Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn His
465                 470                 475                 480

Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly Lys
                485                 490
```

<210> 66
<211> 116
<212> PRT
<213> Artificial Sequence

<220>
<223> Human with mouse CDRs.

<400> 66

```
Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1               5                   10                  15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Ser Tyr
            20                  25                  30

Ala Met Ser Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
        35                  40                  45

Ser Ala Ile Ser Gly Ser Gly Gly Ser Thr Tyr Tyr Ala Asp Ser Val
    50                  55                  60
```

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Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65 70 75 80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Lys Gln Asp Tyr Ala Met Asn Tyr Trp Gly Gln Gly Thr Leu Val
100 105 110

Thr Val Ser Ser
115

<210> 67
<211> 107
<212> PRT
<213> Artificial Sequence

<220>
<223> Human with mouse CDRs.

<400> 67

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

Asp Arg Val Thr Ile Thr Cys Lys Ala Ser Gln Asp Val Ser Thr Ala
20 25 30

Val Ala Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
35 40 45

Tyr Ala Ala Ser Ser Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly
50 55 60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65 70 75 80

Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln His Tyr Ser Thr Pro Trp
85 90 95

Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys
100 105

<210> 68
<211> 116
<212> PRT
<213> Artificial Sequence

<220>
<223> Human with mouse CDRs.

<400> 68

Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Ser Tyr
20 25 30

Ala Met Ser Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Ser Ala Ile Ser Ser Ser Gly Gly Tyr Thr Tyr Tyr Ala Asp Ser Val
50 55 60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65 70 75 80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Lys Gln Asp Tyr Ala Met Asn Tyr Trp Gly Gln Gly Thr Leu Val
100 105 110

Thr Val Ser Ser
115

<210> 69
<211> 107
<212> PRT
<213> Artificial Sequence

<220>
<223> Human with mouse CDRs.

<400> 69

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

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Ser Ile Ser Thr Ala
20 25 30

Leu Asn Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
35 40 45

Tyr Ser Ala Ser Ser Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly
50 55 60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65 70 75 80

Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Ser Tyr Ser Thr Pro Trp
85 90 95

Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys
100 105

<210> 70
<211> 116

<212> PRT
<213> Artificial Sequence

<220>
<223> Human with mouse CDRs.

<400> 70

Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Ser Tyr
20 25 30

Ala Met Ser Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Ser Thr Ile Ser Ser Gly Gly Ser Tyr Thr Ser Tyr Pro Asp Ser Val
50 55 60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65 70 75 80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Lys Gln Asp Tyr Ala Phe Asp Tyr Trp Gly Gln Gly Thr Leu Val
100 105 110

Thr Val Ser Ser
115

<210> 71
<211> 107
<212> PRT
<213> Artificial Sequence

<220>
<223> Human with mouse CDRs.

<400> 71

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

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Ser Ile Ser Thr Ala
20 25 30

Leu Asn Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
35 40 45

Tyr Ala Ala Ser Ser Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly
50 55 60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65 70 75 80

Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Ser Tyr Ser Thr Pro Trp
85 90 95

Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys
100 105

<210> 72
<211> 116
<212> PRT
<213> Artificial Sequence

<220>
<223> Human with mouse CDRs.

<400> 72

Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Ser Tyr
20 25 30

Ala Met Ser Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Ser Thr Ile Ser Ser Ser Gly Ser Tyr Thr Ser Tyr Pro Asp Ser Val
50 55 60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65 70 75 80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Lys Gln Asp Tyr Ala Met Asn Tyr Trp Gly Gln Gly Thr Leu Val
100 105 110

Thr Val Ser Ser
115

<210> 73
<211> 107
<212> PRT
<213> Artificial Sequence

<220>
<223> Human with mouse CDRs.

<400> 73

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

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Ser Ile Ser Thr Ala
20 25 30

```
Leu Asn Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
        35                  40                  45

Tyr Ser Ala Ser Ser Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly
    50                  55                  60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65                  70                  75                  80

Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Ser Tyr Ser Thr Pro Leu
                85                  90                  95

Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys
            100                 105
```