

<110> CJ CheilJedang Corporation

<120> NOVEL O-SUCCINYL HOMOSERINE TRANSFERASE MUTANT AND METHOD FOR PRODUCING O-SUCCINYL HOMOSERINE USING SAME

<130> OPA18186

<150> KR 10-2017-0083439

<151> 2017-06-30

<160> 98

<170> KoPatentIn 3.0

<210> 1

<211> 377

<212> PRT

<213> Corynebacterium glutamicum

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<221> PEPTIDE

<222> (1)..(377)

<223> metX

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Leu  Gly  Ala  Ala  Arg  Arg  Ile  Ala  His  Leu  Thr  Tyr  Arg  Gly  Glu  Leu
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6430426_1

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 Tyr Val Leu Leu Thr Asp Ala Leu Asn Arg His Asp Ile Gly Arg Asp
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 Arg Gly Gly Leu Asn Lys Ala Leu Glu Ser Ile Lys Val Pro Val Leu
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 Val Ala Gly Val Asp Thr Asp Ile Leu Tyr Pro Tyr His Gln Gln Glu
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 His Leu Ser Arg Asn Leu Gly Asn Leu Leu Ala Met Ala Lys Ile Val
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Ser Cys Ile Gly Pro Gly Lys Pro Ile Asp Thr Arg Lys Phe Phe Val
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Val Ala Leu Asn Asn Leu Gly Gly Cys Asn Gly Ser Ser Gly Pro Ala
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 Ser Lys₂₁₀ Ile Leu Val Leu Arg₂₁₅ Ser Val Glu Tyr Ala₂₂₀ Arg Ala Phe Asn
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 Ser Asp Lys₂₇₅ Pro Gly Glu Ala₂₈₀ Ala Lys Val Phe Arg Ala₂₈₅ Leu Ala Asp
 Ala Glu₂₉₀ Ile Asn Ile Asp Met₂₉₅ Val Leu Gln Asn Val₃₀₀ Ser Ser Val Glu
 Asp₃₀₅ Gly Thr Thr Asp₃₁₀ Ile Thr Phe Thr Cys₃₁₅ Pro Arg Ser Asp Gly Arg₃₂₀
 Arg Ala Met Glu₃₂₅ Ile Leu Lys Lys Leu Gln₃₃₀ Val Gln Gly Asn Trp₃₃₅ Thr
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 Gly Met Lys₃₅₅ Ser His Pro Gly₃₆₀ Val Thr Ala Glu Phe Met₃₆₅ Glu Ala Leu
 Arg Asp₃₇₀ Val Asn Val Asn₃₇₅ Ile Glu Leu Ile Ser Thr₃₈₀ Ser Glu Ile Arg
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tcttctgtag	aagacggcac	caccgacatc	atcttcacct	gccctcgttc	cgacggccgc		960
cgcgcgatgg	agatcttgaa	gaagcttcag	gttcagggca	actggacca	tgtgctttac		1020
gacgaccagg	tcggcaaagt	ctccctcgtg	ggtgctggca	tgaagtctca	cccagggtgtt		1080
accgcagagt	tcatggaagc	tctgcgcgat	gtcaacgtga	acatcgaatt	gatttccacc		1140
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cqctaa							1266

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<220>
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<210> 28
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 <212> DNA
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<220>
 <223> Reverse primer for Q176F,L313R

<400> 28
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<210> 29
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 <212> DNA
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<220>
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<400> 29
 acgcgccagc gcctgggtcta tcggcattca atccg 35

<210> 30
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<220>
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<400> 30
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<210> 31
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<220>
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<400> 31
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<220>
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<210> 33
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<220>
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<400> 33
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<210> 34
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<220>
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<210> 35
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<400> 35
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<220>
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<400> 36
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<400> 37

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<210> 38
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<400> 38
cggattgaat gccgatgtgc caggcgctgg cgcgt 35

<210> 39
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<212> DNA
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<220>
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<400> 39
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<210> 40
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<220>
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<220>
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<400> 41
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<210> 42
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<220>
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<400> 42
cggattgaat gccgataatc caggcgctgg cgcgt 35

<210> 43
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 <220>
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 <210> 44
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 <210> 45
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 <400> 45
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 <210> 46
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 <220>
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 <400> 46
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 <210> 47
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 <220>
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 <400> 47
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<213> Artificial Sequence

<220>

<223> Reverse primer for Q176K,L313R

<400> 48

cggattgaat gccgattttc caggcgctgg cgcgt

35

<210> 49

<211> 35

<212> DNA

<213> Artificial Sequence

<220>

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<400> 49

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<210> 50

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<212> DNA

<213> Artificial Sequence

<220>

<223> Reverse primer for Q176V,L313R

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<210> 51

<211> 35

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<213> Artificial Sequence

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<223> Forward primer for Q176A,L313R

<400> 51

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<210> 52

<211> 35

<212> DNA

<213> Artificial Sequence

<220>

<223> Reverse primer for Q176A,L313R

<400> 52

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<210> 53

<211> 35

<212> DNA

<213> Artificial Sequence

<220>

<223> Forward primer for Q176D,L313R

<400> 53
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<210> 54
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<212> DNA
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<220>
<223> Reverse primer for Q176D,L313R

<400> 54
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<210> 55
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<220>
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<400> 55
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<400> 56
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<210> 57
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<220>
<223> Forward primer for Q176G,L313R

<400> 57
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<210> 58
<211> 35
<212> DNA
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<220>
<223> Reverse primer for Q176G,L313R

<400> 58
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<210> 59
<211> 35
<212> DNA
<213> Artificial Sequence

<220>
<223> Forward primer for Q176W,L313R

<400> 59
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<210> 60
<211> 35
<212> DNA
<213> Artificial Sequence

<220>
<223> Reverse primer for Q176W,L313R

<400> 60
cggtatgaat gccgatccac caggcgctgg cgcgt 35

<210> 61
<211> 377
<212> PRT
<213> Artificial Sequence

<220>
<223> metX L313R

<400> 61
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Asp Val Ser Thr Glu Ala Gly Ala Ile Ile Thr Asn Ala Glu Ile Ala
20 25 30
Tyr His Arg Trp Gly Glu Tyr Arg Val Asp Lys Glu Gly Arg Ser Asn
35 40 45
Val Val Leu Ile Glu His Ala Leu Thr Gly Asp Ser Asn Ala Ala Asp
50 55 60
Trp Trp Ala Asp Leu Leu Gly Pro Gly Lys Ala Ile Asn Thr Asp Ile
65 70 75 80
Tyr Cys Val Ile Cys Thr Asn Val Ile Gly Gly Cys Asn Gly Ser Thr
85 90 95
Gly Pro Gly Ser Met His Pro Asp Gly Asn Phe Trp Gly Asn Arg Phe
100 105 110
Pro Ala Thr Ser Ile Arg Asp Gln Val Asn Ala Glu Lys Gln Phe Leu
115 120 125
Asp Ala Leu Gly Ile Thr Thr Val Ala Ala Val Leu Gly Gly Ser Met
130 135 140
Gly Gly Ala Arg Thr Leu Glu Trp Ala Ala Met Tyr Pro Glu Thr Val

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145 150 155 160
 Gly Ala Ala Ala Val₁₆₅ Leu Ala Val Ser Ala₁₇₀ Arg Ala Ser Ala Trp₁₇₅ Gln
 Ile Gly Ile Gln₁₈₀ Ser Ala Gln Ile Lys₁₈₅ Ala Ile Glu Asn Asp₁₉₀ His His
 Trp His Glu₁₉₅ Gly Asn Tyr Tyr Glu₂₀₀ Ser Gly Cys Asn Pro₂₀₅ Ala Thr Gly
 Leu Gly₂₁₀ Ala Ala Arg Arg Ile₂₁₅ Ala His Leu Thr Tyr₂₂₀ Arg Gly Glu Leu
 Glu₂₂₅ Ile Asp Glu Arg Phe₂₃₀ Gly Thr Lys Ala Gln₂₃₅ Lys Asn Glu Asn Pro₂₄₀
 Leu Gly Pro Tyr Arg₂₄₅ Lys Pro Asp Gln Arg₂₅₀ Phe Ala Val Glu Ser₂₅₅ Tyr
 Leu Asp Tyr Gln₂₆₀ Ala Asp Lys Leu Val₂₆₅ Gln Arg Phe Asp Ala₂₇₀ Gly Ser
 Tyr Val Leu₂₇₅ Leu Thr Asp Ala Leu₂₈₀ Asn Arg His Asp Ile₂₈₅ Gly Arg Asp
 Arg Gly₂₉₀ Gly Leu Asn Lys Ala₂₉₅ Leu Glu Ser Ile Lys₃₀₀ Val Pro Val Leu
 Val₃₀₅ Ala Gly Val Asp Thr₃₁₀ Asp Ile Arg Tyr Pro₃₁₅ Tyr His Gln Gln Glu₃₂₀
 His Leu Ser Arg Asn₃₂₅ Leu Gly Asn Leu Leu₃₃₀ Ala Met Ala Lys Ile₃₃₅ Val
 Ser Pro Val Gly₃₄₀ His Asp Ala Phe Leu₃₄₅ Thr Glu Ser Arg Gln₃₅₀ Met Asp
 Arg Ile Val₃₅₅ Arg Asn Phe Phe Ser₃₆₀ Leu Ile Ser Pro Asp₃₆₅ Glu Asp Asn
 Pro Ser₃₇₀ Thr Tyr Ile Glu Phe₃₇₅ Tyr Ile

<210> 62
 <211> 1134
 <212> DNA
 <213> Artificial Sequence

<220>
 <223> metX L313R

<400> 62
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 gtagataaag aaggacgcag caatgtcggt ctcacgaac acgccctcac tggagattcc 180
 aacgcagccg attggtgggc tgacttgctc ggtcccggca aagccatcaa cactgatatt 240
 tactgctga tctgtaccaa cgtcatcggt gggtgcaacg gttccaccgg acctggctcc 300
 atgcatccag atggaaattt ctggggtaat cgcttccccg ccacgtccat tcgtgatcag 360
 gtaaacgccg aaaaacaatt cctcgacgca ctcggcatca ccacggtcgc cgcagtactt 420

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ggtggttcca tgggtggtgc ccgcacccta gagtgggccc caatgtaccc agaaactggt      480
ggcgagctg ctgttcttgc agtttctgca cgcgccagcg cctggcaaat cggcattcaa      540
tccgccccaaa ttaaggcgat tgaaaacgac caccactggc acgaaggcaa ctactacgaa      600
tccggctgca acccagccac cggactcggc gccgcccgac gcatcgccca cctcacctac      660
cgtggcgaac tagaaatcga cgaacgcttc ggcaccaaag cccaaaagaa cgaaaaccca      720
ctcggtcctt accgcaagcc cgaccagcgc ttcgccgtgg aatcctactt ggactaccaa      780
gcagacaagc tagtacagcg tttcgacgcc ggctcctacg tcttgctcac cgacgccctc      840
aaccgccacg acattgggtc cgaccgcgga ggcctcaaca aggcactcga atccatcaaa      900
gttccagtcc ttgtcgcagg cgtagatacc gatattcggg acccctacca ccagcaagaa      960
cacctctcca gaaacctggg aaatctactg gcaatggcaa aaatcgtatc ccctgtcggc     1020
cacgatgctt tcctcaccga aagccgccaa atggatcgca tcgtgaggaa cttcttcagc     1080
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<210>      63
<211>      377
<212>      PRT
<213>      Artificial Sequence

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<220>
<223>      metX Q176N_L313R

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Asp Val Ser Thr Glu Ala Gly Ala Ile Ile Thr Asn Ala Glu Ile Ala
          20          25          30
Tyr His Arg Trp Gly Glu Tyr Arg Val Asp Lys Glu Gly Arg Ser Asn
          35          40          45
Val Val Leu Ile Glu His Ala Leu Thr Gly Asp Ser Asn Ala Ala Asp
          50          55          60
Trp Trp Ala Asp Leu Leu Gly Pro Gly Lys Ala Ile Asn Thr Asp Ile
          65          70          75          80
Tyr Cys Val Ile Cys Thr Asn Val Ile Gly Gly Cys Asn Gly Ser Thr
          85          90          95
Gly Pro Gly Ser Met His Pro Asp Gly Asn Phe Trp Gly Asn Arg Phe
          100          105          110
Pro Ala Thr Ser Ile Arg Asp Gln Val Asn Ala Glu Lys Gln Phe Leu
          115          120          125
Asp Ala Leu Gly Ile Thr Thr Val Ala Ala Val Leu Gly Gly Ser Met
          130          135          140
Gly Gly Ala Arg Thr Leu Glu Trp Ala Ala Met Tyr Pro Glu Thr Val
          145          150          155          160
Gly Ala Ala Ala Val Leu Ala Val Ser Ala Arg Ala Ser Ala Trp Asn
          165          170          175

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Ile Gly Ile Gln Ser Ala Gln Ile Lys Ala Ile Glu Asn Asp His His
180 185 190
Trp His Glu Gly Asn Tyr Tyr Glu Ser Gly Cys Asn Pro Ala Thr Gly
195 200 205
Leu Gly Ala Ala Arg Arg Ile Ala His Leu Thr Tyr Arg Gly Glu Leu
210 215 220
Glu Ile Asp Glu Arg Phe Gly Thr Lys Ala Gln Lys Asn Glu Asn Pro
225 230 235 240
Leu Gly Pro Tyr Arg Lys Pro Asp Gln Arg Phe Ala Val Glu Ser Tyr
245 250 255
Leu Asp Tyr Gln Ala Asp Lys Leu Val Gln Arg Phe Asp Ala Gly Ser
260 265 270
Tyr Val Leu Leu Thr Asp Ala Leu Asn Arg His Asp Ile Gly Arg Asp
275 280 285
Arg Gly Gly Leu Asn Lys Ala Leu Glu Ser Ile Lys Val Pro Val Leu
290 295 300
Val Ala Gly Val Asp Thr Asp Ile Arg Tyr Pro Tyr His Gln Gln Glu
305 310 315 320
His Leu Ser Arg Asn Leu Gly Asn Leu Leu Ala Met Ala Lys Ile Val
325 330 335
Ser Pro Val Gly His Asp Ala Phe Leu Thr Glu Ser Arg Gln Met Asp
340 345 350
Arg Ile Val Arg Asn Phe Phe Ser Leu Ile Ser Pro Asp Glu Asp Asn
355 360 365
Pro Ser Thr Tyr Ile Glu Phe Tyr Ile
370 375

<210> 64
<211> 1134
<212> DNA
<213> Artificial Sequence

<220>
<223> metX Q176N_L313R

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gtagataaag aaggacgcag caatgtcggt ctcatcgaac acgccctcac tggagattcc 180
aacgcagccg attggtgggc tgacttgctc ggtcccggca aagccatcaa cactgatatt 240
tactgctga tctgtaccaa cgtcatcggg ggttgcaacg gttccaccgg acctggctcc 300
atgcatccag atggaaattt ctggggtaat cgcttccccg ccacgtccat tcgtgatcag 360
gtaaacgccg aaaaacaatt cctcgacgca ctcggcacat ccacggctgc cgcagtactt 420
ggtggttcca tgggtggtgc cgcacccta gagtgggccg caatgtaccc agaaactggt 480
ggcgcagctg ctgttcttgc agtttctgca cgcgccagcg cctggaacat cggcattcaa 540

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 cgtggcgaa tagaaatcga cgaacgcttc ggcaccaaag cccaaaagaa cgaaaaccca 720
 ctcggtccct accgcaagcc cgaccagcgc ttcgccgtgg aatcctactt ggactaccaa 780
 gcagacaagc tagtacagcg tttcgacgcc ggctcctacg tcttgctcac cgacgccctc 840
 aaccgccacg acattggctc cgaccgcgga ggcctcaaca aggcactcga atccatcaaa 900
 gttccagtcc ttgtcgcagg cgtagatacc gatattcggg acccctacca ccagcaagaa 960
 cacctctcca gaaacctggg aaatctactg gcaatggcaa aaatcgtatc ccctgtcggc 1020
 cacgatgctt tcctcaccga aagccgcaa atggatcgca tcgtgaggaa cttcttcagc 1080
 ctcatctccc cagacgaaga caacccttcg acctacatcg agttctacat ctaa 1134

<210> 65
 <211> 377
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Q176F,L313R

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 Asp Val Ser Thr Glu Ala Gly Ala Ile Ile Thr Asn Ala Glu Ile Ala
 20 25 30
 Tyr His Arg Trp Gly Glu Tyr Arg Val Asp Lys Glu Gly Arg Ser Asn
 35 40 45
 Val Val Leu Ile Glu His Ala Leu Thr Gly Asp Ser Asn Ala Ala Asp
 50 55 60
 Trp Trp Ala Asp Leu Leu Gly Pro Gly Lys Ala Ile Asn Thr Asp Ile
 65 70 75 80
 Tyr Cys Val Ile Cys Thr Asn Val Ile Gly Gly Cys Asn Gly Ser Thr
 85 90 95
 Gly Pro Gly Ser Met His Pro Asp Gly Asn Phe Trp Gly Asn Arg Phe
 100 105 110
 Pro Ala Thr Ser Ile Arg Asp Gln Val Asn Ala Glu Lys Gln Phe Leu
 115 120 125
 Asp Ala Leu Gly Ile Thr Thr Val Ala Ala Val Leu Gly Gly Ser Met
 130 135 140
 Gly Gly Ala Arg Thr Leu Glu Trp Ala Ala Met Tyr Pro Glu Thr Val
 145 150 155 160
 Gly Ala Ala Ala Val Leu Ala Val Ser Ala Arg Ala Ser Ala Trp Phe
 165 170 175
 Ile Gly Ile Gln Ser Ala Gln Ile Lys Ala Ile Glu Asn Asp His His
 180 185 190

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Trp His Glu Gly Asn Tyr Tyr Glu Ser Gly Cys Asn Pro Ala Thr Gly
 195 200 205
 Leu Gly Ala Ala Arg Arg Ile Ala His Leu Thr Tyr Arg Gly Glu Leu
 210 215 220
 Glu Ile Asp Glu Arg Phe Gly Thr Lys Ala Gln Lys Asn Glu Asn Pro
 225 230 235 240
 Leu Gly Pro Tyr Arg Lys Pro Asp Gln Arg Phe Ala Val Glu Ser Tyr
 245 250 255
 Leu Asp Tyr Gln Ala Asp Lys Leu Val Gln Arg Phe Asp Ala Gly Ser
 260 265 270
 Tyr Val Leu Leu Thr Asp Ala Leu Asn Arg His Asp Ile Gly Arg Asp
 275 280 285
 Arg Gly Gly Leu Asn Lys Ala Leu Glu Ser Ile Lys Val Pro Val Leu
 290 295 300
 Val Ala Gly Val Asp Thr Asp Ile Arg Tyr Pro Tyr His Gln Gln Glu
 305 310 315 320
 His Leu Ser Arg Asn Leu Gly Asn Leu Leu Ala Met Ala Lys Ile Val
 325 330 335
 Ser Pro Val Gly His Asp Ala Phe Leu Thr Glu Ser Arg Gln Met Asp
 340 345 350
 Arg Ile Val Arg Asn Phe Phe Ser Leu Ile Ser Pro Asp Glu Asp Asn
 355 360 365
 Pro Ser Thr Tyr Ile Glu Phe Tyr Ile
 370 375

<210> 66
 <211> 1134
 <212> DNA
 <213> Artificial Sequence

<220>
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 gtagataaag aaggacgcag caatgtcggt ctcatcgaac acgccctcac tggagattcc 180
 aacgcagccg attggtgggc tgacttgctc ggtcccggca aagccatcaa cactgatatt 240
 tactgctgta tctgtaccaa cgtcatcggt gggtgcaacg gttccaccgg acctggctcc 300
 atgcatccag atggaaattt ctggggtaat cgcttccccg ccacgtccat tcgtgatcag 360
 gtaaacgccg aaaaacaatt cctcgacgca ctcgcatca ccacggtcgc cgcagtactt 420
 ggtggttcca tgggtggtgc ccgcacccta gagtggggccg caatgtaccc agaaactggt 480
 ggcgcagctg ctgttcttgc agtttctgca cgcgccagcg cctggtttat cggcattcaa 540
 tccgccc aaa ttaaggcgat tgaaaacgac caccactggc acgaaggcaa ctactacgaa 600
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gcagacaagc tagtacagcg tttcgacgcc ggctcctacg tcttgctcac cgacgccttc      840
aaccgccacg acattggtcg cgaccgcgga ggcctcaaca aggcactcga atccatcaaa      900
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cacctctcca gaaacctggg aaatctactg gcaatggcaa aaatcgatc ccctgtcggc     1020
cacgatgctt tcctaccga aagccgcaa atggatcgca tcgtgaggaa cttcttcagc     1080
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<210>      67
<211>      377
<212>      PRT
<213>      Artificial Sequence

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<220>
<223>      Q176S,L313R

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  1          5          10          15
Asp Val Ser Thr Glu Ala Gly Ala Ile Ile Thr Asn Ala Glu Ile Ala
          20          25          30
Tyr His Arg Trp Gly Glu Tyr Arg Val Asp Lys Glu Gly Arg Ser Asn
          35          40          45
Val Val Leu Ile Glu His Ala Leu Thr Gly Asp Ser Asn Ala Ala Asp
          50          55          60
Trp Trp Ala Asp Leu Leu Gly Pro Gly Lys Ala Ile Asn Thr Asp Ile
          65          70          75          80
Tyr Cys Val Ile Cys Thr Asn Val Ile Gly Gly Cys Asn Gly Ser Thr
          85          90          95
Gly Pro Gly Ser Met His Pro Asp Gly Asn Phe Trp Gly Asn Arg Phe
          100          105          110
Pro Ala Thr Ser Ile Arg Asp Gln Val Asn Ala Glu Lys Gln Phe Leu
          115          120          125
Asp Ala Leu Gly Ile Thr Thr Val Ala Ala Val Leu Gly Gly Ser Met
          130          135          140
Gly Gly Ala Arg Thr Leu Glu Trp Ala Ala Met Tyr Pro Glu Thr Val
          145          150          155          160
Gly Ala Ala Ala Val Leu Ala Val Ser Ala Arg Ala Ser Ala Trp Ser
          165          170          175
Ile Gly Ile Gln Ser Ala Gln Ile Lys Ala Ile Glu Asn Asp His His
          180          185          190
Trp His Glu Gly Asn Tyr Tyr Glu Ser Gly Cys Asn Pro Ala Thr Gly
          195          200          205
Leu Gly Ala Ala Arg Arg Ile Ala His Leu Thr Tyr Arg Gly Glu Leu

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220

210 215 220
 Glu Ile Asp Glu Arg Phe Gly Thr Lys Ala Gln Lys Asn Glu Asn Pro
 225 230 235 240
 Leu Gly Pro Tyr Arg Lys Pro Asp Gln Arg Phe Ala Val Glu Ser Tyr
 245 250 255
 Leu Asp Tyr Gln Ala Asp Lys Leu Val Gln Arg Phe Asp Ala Gly Ser
 260 265 270
 Tyr Val Leu Leu Thr Asp Ala Leu Asn Arg His Asp Ile Gly Arg Asp
 275 280 285
 Arg Gly Gly Leu Asn Lys Ala Leu Glu Ser Ile Lys Val Pro Val Leu
 290 295 300
 Val Ala Gly Val Asp Thr Asp Ile Arg Tyr Pro Tyr His Gln Gln Glu
 305 310 315 320
 His Leu Ser Arg Asn Leu Gly Asn Leu Leu Ala Met Ala Lys Ile Val
 325 330 335
 Ser Pro Val Gly His Asp Ala Phe Leu Thr Glu Ser Arg Gln Met Asp
 340 345 350
 Arg Ile Val Arg Asn Phe Phe Ser Leu Ile Ser Pro Asp Glu Asp Asn
 355 360 365
 Pro Ser Thr Tyr Ile Glu Phe Tyr Ile
 370 375

<210> 68
 <211> 1134
 <212> DNA
 <213> Artificial Sequence

<220>
 <223> Q176S,L313R

<400> 68
 atgccacc tcgcgcttc aggtcaactt gaaatccaag cgatcggtga tgtctccacc 60
 gaagccggag caatcattac aaacgctgaa atcgcttatc accgctgggg tgaataccgc 120
 gtagataaag aaggacgcag caatgtcggt ctcacgaac acgccctcac tggagattcc 180
 aacgcagccg attggtgggc tgacttgctc ggtcccggca aagccatcaa cactgatatt 240
 tactgcgtga tctgtacaa cgatcatcggg ggttgcaac gttccaccgg acctggctcc 300
 atgcatccag atggaaattt ctggggtaat cgcttccccg ccacgtccat tcgtgatcag 360
 gtaaacgccg aaaaacaatt cctcgacgca ctcggcatca ccacggtcgc cgcagtactt 420
 ggtggttcca tgggtggtgc cgcacccta gagtgggccg caatgtaccc agaaactggt 480
 ggcgcagctg ctgttcttgc agtttctgca cgcgccagcg cctggtctat cggcattcaa 540
 tccgccc aaa ttaaggcgat tgaaaacgac caccactggc acgaaggcaa ctactacgaa 600
 tccggctgca acccagccac cggactcggc gccgcccgc gcatcgcca cctcacctac 660
 cgtggcgaac tagaaatcga cgaacgctt cggcacc aaag cccaaaagaa cgaaaacca 720
 ctcggtccct accgcaagcc cgaccagcgc ttcgccgtgg aatcctactt ggactacaa 780

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gcagacaagc tagtacagcg tttcgacgcc ggctcctacg tcttgctcac cgacgccctc 840
aaccgccacg acattgggtcg cgaccgcgga ggcctcaaca aggcactcga atccatcaaa 900
gttccagtcc ttgtcgcagg cgtagatacc gatattcggt acccctacca ccagcaagaa 960
cacctctcca gaaacctggg aaatctactg gcaatggcaa aaatcgtatc ccctgtcggc 1020
cacgatgctt tcctcaccga aagccgcaa atggatcgca tcgtgaggaa cttcttcagc 1080
ctcatctccc cagacgaaga caacccttcg acctacatcg agttctacat ctaa 1134

<210> 69
<211> 377
<212> PRT
<213> Artificial Sequence

<220>
<223> Q176Y,L313R

<400> 69
Met Pro Thr Leu Ala₅ Pro Ser Gly Gln Leu₁₀ Glu Ile Gln Ala Ile₁₅ Gly
1
Asp Val Ser Thr₂₀ Glu Ala Gly Ala Ile₂₅ Ile Thr Asn Ala Glu₃₀ Ile Ala
Tyr His Arg₃₅ Trp Gly Glu Tyr Arg₄₀ Val Asp Lys Glu Gly₄₅ Arg Ser Asn
Val Val₅₀ Leu Ile Glu His Ala₅₅ Leu Thr Gly Asp Ser₆₀ Asn Ala Ala Asp
Trp Trp Ala Asp Leu₇₀ Gly Pro Gly Lys Ala₇₅ Ile Asn Thr Asp Ile₈₀
Tyr Cys Val Ile Cys₈₅ Thr Asn Val Ile Gly₉₀ Gly Cys Asn Gly Ser₉₅ Thr
Gly Pro Gly Ser₁₀₀ Met His Pro Asp Gly₁₀₅ Asn Phe Trp Gly Asn Arg Phe
Pro Ala Thr₁₁₅ Ser Ile Arg Asp Gln Val Asn Ala Glu Lys₁₂₅ Gln Phe Leu
Asp Ala₁₃₀ Leu Gly Ile Thr Thr₁₃₅ Val Ala Ala Val Leu₁₄₀ Gly Gly Ser Met
Gly Gly Ala Arg Thr Leu₁₅₀ Glu Trp Ala Ala Met₁₅₅ Tyr Pro Glu Thr Val₁₆₀
Gly Ala Ala Ala Val₁₆₅ Leu Ala Val Ser Ala₁₇₀ Arg Ala Ser Ala Trp Tyr₁₇₅
Ile Gly Ile Gln₁₈₀ Ser Ala Gln Ile Lys₁₈₅ Ala Ile Glu Asn Asp₁₉₀ His His
Trp His Glu₁₉₅ Gly Asn Tyr Tyr Glu₂₀₀ Ser Gly Cys Asn Pro₂₀₅ Ala Thr Gly
Leu Gly₂₁₀ Ala Ala Arg Arg Ile₂₁₅ Ala His Leu Thr Tyr₂₂₀ Arg Gly Glu Leu
Glu Ile Asp Glu Arg Phe₂₃₀ Gly Thr Lys Ala Gln₂₃₅ Lys Asn Glu Asn Pro₂₄₀
225

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Leu Gly Pro Tyr Arg Lys Pro Asp Gln Arg Phe Ala Val Glu Ser Tyr
 245 250 255
 Leu Asp Tyr Gln Ala Asp Lys Leu Val Gln Arg Phe Asp Ala Gly Ser
 260 265 270
 Tyr Val Leu Leu Thr Asp Ala Leu Asn Arg His Asp Ile Gly Arg Asp
 275 280 285
 Arg Gly Gly Leu Asn Lys Ala Leu Glu Ser Ile Lys Val Pro Val Leu
 290 295 300
 Val Ala Gly Val Asp Thr Asp Ile Arg Tyr Pro Tyr His Gln Gln Glu
 305 310 315 320
 His Leu Ser Arg Asn Leu Gly Asn Leu Leu Ala Met Ala Lys Ile Val
 325 330 335
 Ser Pro Val Gly His Asp Ala Phe Leu Thr Glu Ser Arg Gln Met Asp
 340 345 350
 Arg Ile Val Arg Asn Phe Phe Ser Leu Ile Ser Pro Asp Glu Asp Asn
 355 360 365
 Pro Ser Thr Tyr Ile Glu Phe Tyr Ile
 370 375

<210> 70
 <211> 1134
 <212> DNA
 <213> Artificial Sequence

<220>
 <223> Q176Y,L313R

<400> 70
 atgccaccc tcgcgccttc aggtcaactt gaaatccaag cgatcggtga tgtctccacc 60
 gaagccggag caatcattac aaacgctgaa atcgctatc accgctgggg tgaataaccgc 120
 gtagataaag aaggacgcag caatgtcggt ctcatcgaac acgccctcac tggagattcc 180
 aacgcagccg attggtgggc tgacttgctc ggtcccggca aagccatcaa cactgatatt 240
 tactgctga tctgtaccaa cgtcatcggg ggttgcaacg gttccaccgg acctggctcc 300
 atgcatccag atggaaattt ctggggtaat cgcttccccg ccacgtccat tcgtgatcag 360
 gtaaacgccg aaaaacaatt cctcgacgca ctcggcacga ccacggtcgc cgcagtactt 420
 ggtggttcca tgggtggtgc ccgcacccta gagtgggccc caatgtaccc agaaactggt 480
 ggcgcagctg ctgttcttgc agtttctgca cgcgccagcg cctgggtatat cggcattcaa 540
 tccgccc aaa ttaaggcgat tgaaaacgac caccactggc acgaaggcaa ctactacgaa 600
 tccggctgca acccagccac cggactcggc gccgccgac gcatcgcca cctcacctac 660
 cgtggcgaac tagaaatcga cgaacgcttc ggcaccaaag cccaaaagaa cgaaaaccca 720
 ctcggtccct accgcaagcc cgaccagcgc ttcgccgtgg aatcctactt ggactaccaa 780
 gcagacaagc tagtacagcg tttcgacgcc ggctcctacg tcttgctcac cgacgccctc 840
 aaccgccacg acattggtcg cgaccgcgga ggcctcaaca aggcactcga atccatcaaa 900

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gttcagtc tttgtcgcagg cgtagatacc gatattcggg acccctacca ccagcaagaa 960
cacctctcca gaaacctggg aaatctactg gcaatggcaa aaatcgtatc ccctgtcggc 1020
cacgatgctt tcctcaccga aagccgcaa atggatcgca tcgtgaggaa cttcttcagc 1080
ctcatctccc cagacgaaga caacccttcg acctacatcg agttctacat ctaa 1134

<210> 71
<211> 377
<212> PRT
<213> Artificial Sequence

<220>
<223> Q176C,L313R

<400> 71
Met Pro Thr Leu Ala Pro Ser Gly Gln Leu Glu Ile Gln Ala Ile Gly
1 5 10 15
Asp Val Ser Thr Glu Ala Gly Ala Ile Ile Thr Asn Ala Glu Ile Ala
20 25 30
Tyr His Arg Trp Gly Glu Tyr Arg Val Asp Lys Glu Gly Arg Ser Asn
35 40 45
Val Val Leu Ile Glu His Ala Leu Thr Gly Asp Ser Asn Ala Ala Asp
50 55 60
Trp Trp Ala Asp Leu Leu Gly Pro Gly Lys Ala Ile Asn Thr Asp Ile
65 70 75 80
Tyr Cys Val Ile Cys Thr Asn Val Ile Gly Gly Cys Asn Gly Ser Thr
85 90 95
Gly Pro Gly Ser Met His Pro Asp Gly Asn Phe Trp Gly Asn Arg Phe
100 105 110
Pro Ala Thr Ser Ile Arg Asp Gln Val Asn Ala Glu Lys Gln Phe Leu
115 120 125
Asp Ala Leu Gly Ile Thr Thr Val Ala Ala Val Leu Gly Gly Ser Met
130 135 140
Gly Gly Ala Arg Thr Leu Glu Trp Ala Ala Met Tyr Pro Glu Thr Val
145 150 155 160
Gly Ala Ala Ala Val Leu Ala Val Ser Ala Arg Ala Ser Ala Trp Cys
165 170 175
Ile Gly Ile Gln Ser Ala Gln Ile Lys Ala Ile Glu Asn Asp His His
180 185 190
Trp His Glu Gly Asn Tyr Tyr Glu Ser Gly Cys Asn Pro Ala Thr Gly
195 200 205
Leu Gly Ala Ala Arg Arg Ile Ala His Leu Thr Tyr Arg Gly Glu Leu
210 215 220
Glu Ile Asp Glu Arg Phe Gly Thr Lys Ala Gln Lys Asn Glu Asn Pro
225 230 235 240
Leu Gly Pro Tyr Arg Lys Pro Asp Gln Arg Phe Ala Val Glu Ser Tyr
245 250 255

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Leu Asp Tyr Gln Ala Asp Lys Leu Val Gln Arg Phe Asp Ala Gly Ser
 260 265 270
 Tyr Val Leu Leu Thr Asp Ala Leu Asn Arg His Asp Ile Gly Arg Asp
 275 280 285
 Arg Gly Gly Leu Asn Lys Ala Leu Glu Ser Ile Lys Val Pro Val Leu
 290 295 300
 Val Ala Gly Val Asp Thr Asp Ile Arg Tyr Pro Tyr His Gln Gln Glu
 305 310 315 320
 His Leu Ser Arg Asn Leu Gly Asn Leu Leu Ala Met Ala Lys Ile Val
 325 330 335
 Ser Pro Val Gly His Asp Ala Phe Leu Thr Glu Ser Arg Gln Met Asp
 340 345 350
 Arg Ile Val Arg Asn Phe Phe Ser Leu Ile Ser Pro Asp Glu Asp Asn
 355 360 365
 Pro Ser Thr Tyr Ile Glu Phe Tyr Ile
 370 375

<210> 72
 <211> 1134
 <212> DNA
 <213> Artificial Sequence

<220>
 <223> Q176C,L313R

<400> 72
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 gaagccggag caatcattac aaacgctgaa atcgctatc accgctgggg tgaataccgc 120
 gtagataaag aaggacgcag caatgtcggt ctcatcgaac acgccctcac tggagattcc 180
 aacgcagccg attggtgggc tgacttgctc ggtcccggca aagccatcaa cactgatatt 240
 tactgctga tctgtaccaa cgtcatcggg ggttgcaacg gttccaccgg acctgggtcc 300
 atgcatccag atggaaattt ctggggtaat cgcttccccg ccacgtccat tcgtgatcag 360
 gtaaagccg aaaaacaatt cctcgacgca ctcggcata ccacggtcgc cgcagtactt 420
 ggtggttcca tgggtggtgc ccgcacccta gagtgggccc caatgtaccc agaaactggt 480
 ggcgcagctg ctgttcttgc agtttctgca cgcgccagcg cctgggtgtat cggcattcaa 540
 tccgccccaa ttaaggcgat tgaaaacgac caccactggc acgaaggcaa ctactacgaa 600
 tccggctgca acccagccac cggactcggc gccgccgac gcacgcccc cctcacctac 660
 cgtggcgaac tagaaatcga cgaacgctt gccaccaaag cccaaaagaa cgaaaaccca 720
 ctcggtccct accgcaagcc cgaccagcgc ttgccgtgg aatcctactt ggactaccaa 780
 gcagacaagc tagtacagcg tttcgacgcc ggctcctacg tcttgctcac cgacgccctc 840
 aaccgccacg acattggtcg cgaccgcgga ggcctcaaca aggcactcga atccatcaaa 900
 gttccagtcc ttgtcgcagg cgtagatacc gatattcggg acccctacca ccagcaagaa 960
 cacctctcca gaaacctggg aaatctactg gcaatggcaa aaatcgatc ccctgtcggc 1020

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cacgatgctt tcctcaccga aagccgccaa atggatcgca tcgtgaggaa cttcttcagc 1080
ctcatctccc cagacgaaga caacccttcg acctacatcg agttctacat ctaa 1134

<210> 73
<211> 377
<212> PRT
<213> Artificial Sequence

<220>
<223> Q176P,L313R

<400> 73
Met Pro Thr Leu Ala Pro Ser Gly Gln Leu Glu Ile Gln Ala Ile Gly
1 5 10 15
Asp Val Ser Thr Glu Ala Gly Ala Ile Ile Thr Asn Ala Glu Ile Ala
20 25 30
Tyr His Arg Trp Gly Glu Tyr Arg Val Asp Lys Glu Gly Arg Ser Asn
35 40 45
Val Val Leu Ile Glu His Ala Leu Thr Gly Asp Ser Asn Ala Ala Asp
50 55 60
Trp Trp Ala Asp Leu Leu Gly Pro Gly Lys Ala Ile Asn Thr Asp Ile
65 70 75 80
Tyr Cys Val Ile Cys Thr Asn Val Ile Gly Gly Cys Asn Gly Ser Thr
85 90 95
Gly Pro Gly Ser Met His Pro Asp Gly Asn Phe Trp Gly Asn Arg Phe
100 105 110
Pro Ala Thr Ser Ile Arg Asp Gln Val Asn Ala Glu Lys Gln Phe Leu
115 120 125
Asp Ala Leu Gly Ile Thr Thr Val Ala Ala Val Leu Gly Gly Ser Met
130 135 140
Gly Gly Ala Arg Thr Leu Glu Trp Ala Ala Met Tyr Pro Glu Thr Val
145 150 155 160
Gly Ala Ala Ala Val Leu Ala Val Ser Ala Arg Ala Ser Ala Trp Pro
165 170 175
Ile Gly Ile Gln Ser Ala Gln Ile Lys Ala Ile Glu Asn Asp His His
180 185 190
Trp His Glu Gly Asn Tyr Tyr Glu Ser Gly Cys Asn Pro Ala Thr Gly
195 200 205
Leu Gly Ala Ala Arg Arg Ile Ala His Leu Thr Tyr Arg Gly Glu Leu
210 215 220
Glu Ile Asp Glu Arg Phe Gly Thr Lys Ala Gln Lys Asn Glu Asn Pro
225 230 235 240
Leu Gly Pro Tyr Arg Lys Pro Asp Gln Arg Phe Ala Val Glu Ser Tyr
245 250 255
Leu Asp Tyr Gln Ala Asp Lys Leu Val Gln Arg Phe Asp Ala Gly Ser
260 265 270
Tyr Val Leu Leu Thr Asp Ala Leu Asn Arg His Asp Ile Gly Arg Asp

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275 280 285
 Arg Gly Gly Leu Asn Lys Ala Leu Glu Ser Ile Lys Val Pro Val Leu
 290 295 300
 Val Ala Gly Val Asp Thr Asp Ile Arg Tyr Pro Tyr His Gln Gln Glu
 305 310 315 320
 His Leu Ser Arg Asn Leu Gly Asn Leu Leu Ala Met Ala Lys Ile Val
 325 330 335
 Ser Pro Val Gly His Asp Ala Phe Leu Thr Glu Ser Arg Gln Met Asp
 340 345 350
 Arg Ile Val Arg Asn Phe Phe Ser Leu Ile Ser Pro Asp Glu Asp Asn
 355 360 365
 Pro Ser Thr Tyr Ile Glu Phe Tyr Ile
 370 375

<210> 74
 <211> 1134
 <212> DNA
 <213> Artificial Sequence
 <220>
 <223> Q176P,L313R

<400> 74
 atgccaccc tcgcgccctc aggtcaactt gaaatccaag cgatcggtga tgtctccacc 60
 gaagccggag caatcattac aaacgctgaa atcgccctatc accgctgggg tgaataccgc 120
 gtagataaag aaggacgcag caatgtcggt ctcacgaac acgccctcac tggagattcc 180
 aacgcagccg attggtgggc tgacttgctc ggtcccggca aagccatcaa cactgatatt 240
 tactgctgta tctgtaccaa cgtcatcggt gggtgcaac gttccaccgg acctggctcc 300
 atgcatccag atggaaattt ctggggtaat cgcttccccg ccacgtccat tcgtgatcag 360
 gtaaagccg aaaaacaatt cctcgacgca ctcggcatca ccacggtcgc cgcagtactt 420
 ggtggttcca tgggtggtgc ccgcacccta gagtgggccc caatgtaccc agaaactggt 480
 ggcgcagctg ctgttcttgc agtttctgca cgcgccagcg cctggccaat cggcattcaa 540
 tccgccc aaa ttaaggcgat tgaaaacgac caccactggc acgaaggcaa ctactacgaa 600
 tccggctgca acccagccac cggactcggc gccgcccgc gcacgccc cctcacctac 660
 cgtggcgaac tagaaatcga cgaacgctt cggcacc aaag cccaaaagaa cgaaaaccca 720
 ctcggtccct accgcaagcc cgaccagcgc ttcgccgtgg aatcctactt ggactaccaa 780
 gcagacaagc tagtacagcg tttcgacgcc ggctcctacg tcttgctcac cgacgccctc 840
 aaccgccacg acattggtcg cgaccgcgga ggcctcaaca aggcactcga atccatcaaa 900
 gttccagtcc ttgtcgcagg cgtagatacc gatattcggt acccctacca ccagcaagaa 960
 cacctctcca gaaacctggg aaatctactg gcaatggcaa aaatcgatc ccctgtcggc 1020
 cacgatgctt tcctcaccga aagccgcaa atggatcgca tcgtgaggaa cttcttcagc 1080
 ctcactctcc cagacgaaga caacccttcg acctacatcg agttctacat ctaa 1134

<210> 75
 <211> 377
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Q176H,L313R

<400> 75
 Met Pro Thr Leu Ala₅ Pro Ser Gly Gln Leu₁₀ Glu Ile Gln Ala Ile₁₅ Gly
 1
 Asp Val Ser Thr₂₀ Glu Ala Gly Ala Ile₂₅ Ile Thr Asn Ala Glu₃₀ Ile Ala
 Tyr His Arg₃₅ Trp Gly Glu Tyr Arg₄₀ Val Asp Lys Glu Gly₄₅ Arg Ser Asn
 Val Val₅₀ Leu Ile Glu His Ala₅₅ Leu Thr Gly Asp Ser₆₀ Asn Ala Ala Asp
 Trp Trp Ala Asp Leu₇₀ Gly Pro Gly Lys Ala₇₅ Ile Asn Thr Asp Ile₈₀
 Tyr Cys Val Ile Cys₈₅ Thr Asn Val Ile Gly₉₀ Gly Cys Asn Gly Ser₉₅ Thr
 Gly Pro Gly Ser₁₀₀ Met His Pro Asp Gly₁₀₅ Asn Phe Trp Gly Asn₁₁₀ Arg Phe
 Pro Ala Thr₁₁₅ Ser Ile Arg Asp Gln Val Asn Ala Glu Lys₁₂₅ Gln Phe Leu
 Asp Ala₁₃₀ Leu Gly Ile Thr Thr₁₃₅ Val Ala Ala Val Leu₁₄₀ Gly Gly Ser Met
 Gly₁₄₅ Gly Ala Arg Thr Leu₁₅₀ Glu Trp Ala Ala Met₁₅₅ Tyr Pro Glu Thr Val₁₆₀
 Gly Ala Ala Ala Val₁₆₅ Leu Ala Val Ser Ala₁₇₀ Arg Ala Ser Ala Trp₁₇₅ His
 Ile Gly Ile Gln₁₈₀ Ser Ala Gln Ile Lys₁₈₅ Ala Ile Glu Asn Asp₁₉₀ His His
 Trp His Glu₁₉₅ Gly Asn Tyr Tyr Glu₂₀₀ Ser Gly Cys Asn Pro₂₀₅ Ala Thr Gly
 Leu Gly₂₁₀ Ala Ala Arg Arg Ile₂₁₅ Ala His Leu Thr Tyr₂₂₀ Arg Gly Glu Leu
 Glu Ile Asp Glu Arg Phe₂₃₀ Gly Thr Lys Ala Gln₂₃₅ Lys Asn Glu Asn Pro₂₄₀
 Leu Gly Pro Tyr Arg₂₄₅ Lys Pro Asp Gln Arg₂₅₀ Phe Ala Val Glu Ser₂₅₅ Tyr
 Leu Asp Tyr Gln₂₆₀ Ala Asp Lys Leu Val₂₆₅ Gln Arg Phe Asp Ala₂₇₀ Gly Ser
 Tyr Val Leu₂₇₅ Leu Thr Asp Ala Leu₂₈₀ Asn Arg His Asp Ile₂₈₅ Gly Arg Asp
 Arg Gly₂₉₀ Gly Leu Asn Lys Ala₂₉₅ Leu Glu Ser Ile Lys₃₀₀ Val Pro Val Leu

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Val Ala Gly Val Asp Thr Asp Ile Arg Tyr Pro Tyr His Gln Gln Glu
 305 310 315 320
 His Leu Ser Arg Asn Leu Gly Asn Leu Leu Ala Met Ala Lys Ile Val
 325 330 335
 Ser Pro Val Gly His Asp Ala Phe Leu Thr Glu Ser Arg Gln Met Asp
 340 345 350
 Arg Ile Val Arg Asn Phe Phe Ser Leu Ile Ser Pro Asp Glu Asp Asn
 355 360 365
 Pro Ser Thr Tyr Ile Glu Phe Tyr Ile
 370 375

<210> 76
 <211> 1134
 <212> DNA
 <213> Artificial Sequence

<220>
 <223> Q176H,L313R

<400> 76
 atgccaccc tcgcgcttc aggtcaactt gaaatccaag cgatcggtga tgtctccacc 60
 gaagccggag caatcattac aaacgctgaa atcgctatc accgctggg tgaataccgc 120
 gtagataaag aaggacgcag caatgtcggt ctcatcgaac acgccctcac tggagattcc 180
 aacgcagccg attggtgggc tgacttgctc ggtcccggca aagccatcaa cactgatatt 240
 tactgctga tctgtaccaa cgtcatcggg ggttgcaacg gttccaccgg acctggctcc 300
 atgcatccag atggaaattt ctggggtaat cgcttccccg ccacgtccat tcgtgatcag 360
 gtaaagccg aaaaacaatt cctcgacgca ctcggcata ccacggtcgc cgcagtactt 420
 ggtggttcca tgggtggtgc ccgcacccta gagtgggccc caatgtaccc agaaactggt 480
 ggcgcagctg ctgttcttgc agtttctgca cgcgccagcg cctggcacat cggcattcaa 540
 tccgccc aaa ttaaggcgat tgaaaacgac caccactggc acgaaggcaa ctactacgaa 600
 tccggctgca acccagccac cggactcggc gccgcccgc gcatcgcca cctcacctac 660
 cgtggcgaac tagaaatcga cgaacgcttc ggcaccaaag cccaaaagaa cgaaaaccca 720
 ctcggtccct accgcaagcc cgaccagcgc ttcgccgtgg aatcctactt ggactaccaa 780
 gcagacaagc tagtacagcg tttcgacgcc ggctcctacg tcttgctcac cgacgccctc 840
 aaccgccacg acattggtcg cgaccgcgga ggcctcaaca aggcactcga atccatcaaa 900
 gttccagtcc ttgtcgcagg cgtagatacc gatattcggg acccctacca ccagcaagaa 960
 cacctctcca gaaacctggg aaatctactg gcaatggcaa aaatcgtatc ccctgtcggc 1020
 cacgatgctt tcctcaccga aagccgcaa atggatcgca tcgtgaggaa cttcttcagc 1080
 ctcatctccc cagacgaaga caacccttcg acctacatcg agttctacat ctaa 1134

<210> 77
 <211> 377

<212> PRT
 <213> Artificial Sequence

<220>
 <223> Q176L,L313R

<400> 77
 Met Pro Thr Leu Ala Pro Ser Gly Gln Leu Glu Ile Gln Ala Ile Gly
 1 5 10 15
 Asp Val Ser Thr Glu Ala Gly Ala Ile Ile Thr Asn Ala Glu Ile Ala
 20 25 30
 Tyr His Arg Trp Gly Glu Tyr Arg Val Asp Lys Glu Gly Arg Ser Asn
 35 40 45
 Val Val Leu Ile Glu His Ala Leu Thr Gly Asp Ser Asn Ala Ala Asp
 50 55 60
 Trp Trp Ala Asp Leu Leu Gly Pro Gly Lys Ala Ile Asn Thr Asp Ile
 65 70 75 80
 Tyr Cys Val Ile Cys Thr Asn Val Ile Gly Gly Cys Asn Gly Ser Thr
 85 90 95
 Gly Pro Gly Ser Met His Pro Asp Gly Asn Phe Trp Gly Asn Arg Phe
 100 105 110
 Pro Ala Thr Ser Ile Arg Asp Gln Val Asn Ala Glu Lys Gln Phe Leu
 115 120 125
 Asp Ala Leu Gly Ile Thr Thr Val Ala Ala Val Leu Gly Gly Ser Met
 130 135 140
 Gly Gly Ala Arg Thr Leu Glu Trp Ala Ala Met Tyr Pro Glu Thr Val
 145 150 155 160
 Gly Ala Ala Ala Val Leu Ala Val Ser Ala Arg Ala Ser Ala Trp Leu
 165 170 175
 Ile Gly Ile Gln Ser Ala Gln Ile Lys Ala Ile Glu Asn Asp His His
 180 185 190
 Trp His Glu Gly Asn Tyr Tyr Glu Ser Gly Cys Asn Pro Ala Thr Gly
 195 200 205
 Leu Gly Ala Ala Arg Arg Ile Ala His Leu Thr Tyr Arg Gly Glu Leu
 210 215 220
 Glu Ile Asp Glu Arg Phe Gly Thr Lys Ala Gln Lys Asn Glu Asn Pro
 225 230 235 240
 Leu Gly Pro Tyr Arg Lys Pro Asp Gln Arg Phe Ala Val Glu Ser Tyr
 245 250 255
 Leu Asp Tyr Gln Ala Asp Lys Leu Val Gln Arg Phe Asp Ala Gly Ser
 260 265 270
 Tyr Val Leu Leu Thr Asp Ala Leu Asn Arg His Asp Ile Gly Arg Asp
 275 280 285
 Arg Gly Gly Leu Asn Lys Ala Leu Glu Ser Ile Lys Val Pro Val Leu
 290 295 300
 Val Ala Gly Val Asp Thr Asp Ile Arg Tyr Pro Tyr His Gln Gln Glu
 305 310 315 320

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His Leu Ser Arg Asn Leu Gly Asn Leu Leu Ala Met Ala Lys Ile Val
 325 330 335
 Ser Pro Val Gly His Asp Ala Phe Leu Thr Glu Ser Arg Gln Met Asp
 340 345 350
 Arg Ile Val Arg Asn Phe Phe Ser Leu Ile Ser Pro Asp Glu Asp Asn
 355 360 365
 Pro Ser Thr Tyr Ile Glu Phe Tyr Ile
 370 375

<210> 78
 <211> 1134
 <212> DNA
 <213> Artificial Sequence

<220>
 <223> Q176L,L313R

<400> 78
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 gaagccggag caatcattac aaacgctgaa atcgccctatc accgctgggg tgaataccgc 120
 gtagataaag aaggacgcag caatgtcgtt ctcatcgaac acgccctcac tggagattcc 180
 aacgcagccg attggtgggc tgacttgctc ggtcccggca aagccatcaa cactgatatt 240
 tactgctga tctgtaccaa cgtcatcggg ggttgcaacg gttccaccgg acctggctcc 300
 atgcatccag atggaaattt ctggggtaat cgcttccccg ccacgtccat tcgtgatcag 360
 gtaaacgccg aaaaacaatt cctcgacgca ctcggcata caacggtcgc cgcagtactt 420
 ggtggttcca tgggtggtgc ccgcacccta gagtggggccg caatgtaccc agaaactggt 480
 ggcgcagctg ctgttcttgc agtttctgca cgcgccagcg cctgggtcat cggcattcaa 540
 tccgccc aaa ttaaggcgat tgaaaacgac caccactggc acgaaggcaa ctactacgaa 600
 tccggctgca acccagccac cggactcggc gccgcccagc gcacgcccac cctcacctac 660
 cgtggcgaac tagaaatcga cgaacgcttc ggcaccaaag cccaaaagaa cgaaaaccca 720
 ctcggtccct accgcaagcc cgaccagcgc ttccgctggg aatcctactt ggactaccaa 780
 gcagacaagc tagtacagcg tttcgacgcc ggctcctacg tcttgctcac cgacgccctc 840
 aaccgccacg acattggtcg cgaccgcgga ggcctcaaca aggcactcga atccatcaaa 900
 gttccagtcc ttgtcgcagg cgtagatacc gatattcggg acccctacca ccagcaagaa 960
 caccttcca gaaacctggg aaatctactg gcaatggcaa aaatcgtatc ccctgtcggc 1020
 cacgatgctt tcctcaccga aagccgcaa atggatcgca tcgtgaggaa cttcttcagc 1080
 ctcatctccc cagacgaaga caacccttcg acctacatcg agttctacat ctaa 1134

<210> 79
 <211> 377
 <212> PRT
 <213> Artificial Sequence

<220>

<223> Q176I,L313R

<400> 79

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 20 25 30
 Tyr His Arg Trp Gly Glu Tyr Arg Val Asp Lys Glu Gly Arg Ser Asn
 35 40 45
 Val Val Leu Ile Glu His Ala Leu Thr Gly Asp Ser Asn Ala Ala Asp
 50 55 60
 Trp Trp Ala Asp Leu Leu Gly Pro Gly Lys Ala Ile Asn Thr Asp Ile
 65 70 75 80
 Tyr Cys Val Ile Cys Thr Asn Val Ile Gly Gly Cys Asn Gly Ser Thr
 85 90 95
 Gly Pro Gly Ser Met His Pro Asp Gly Asn Phe Trp Gly Asn Arg Phe
 100 105 110
 Pro Ala Thr Ser Ile Arg Asp Gln Val Asn Ala Glu Lys Gln Phe Leu
 115 120 125
 Asp Ala Leu Gly Ile Thr Thr Val Ala Ala Val Leu Gly Gly Ser Met
 130 135 140
 Gly Gly Ala Arg Thr Leu Glu Trp Ala Ala Met Tyr Pro Glu Thr Val
 145 150 155 160
 Gly Ala Ala Ala Val Leu Ala Val Ser Ala Arg Ala Ser Ala Trp Ile
 165 170 175
 Ile Gly Ile Gln Ser Ala Gln Ile Lys Ala Ile Glu Asn Asp His His
 180 185 190
 Trp His Glu Gly Asn Tyr Tyr Glu Ser Gly Cys Asn Pro Ala Thr Gly
 195 200 205
 Leu Gly Ala Ala Arg Arg Ile Ala His Leu Thr Tyr Arg Gly Glu Leu
 210 215 220
 Glu Ile Asp Glu Arg Phe Gly Thr Lys Ala Gln Lys Asn Glu Asn Pro
 225 230 235 240
 Leu Gly Pro Tyr Arg Lys Pro Asp Gln Arg Phe Ala Val Glu Ser Tyr
 245 250 255
 Leu Asp Tyr Gln Ala Asp Lys Leu Val Gln Arg Phe Asp Ala Gly Ser
 260 265 270
 Tyr Val Leu Leu Thr Asp Ala Leu Asn Arg His Asp Ile Gly Arg Asp
 275 280 285
 Arg Gly Gly Leu Asn Lys Ala Leu Glu Ser Ile Lys Val Pro Val Leu
 290 295 300
 Val Ala Gly Val Asp Thr Asp Ile Arg Tyr Pro Tyr His Gln Gln Glu
 305 310 315 320
 His Leu Ser Arg Asn Leu Gly Asn Leu Leu Ala Met Ala Lys Ile Val
 325 330 335
 Ser Pro Val Gly His Asp Ala Phe Leu Thr Glu Ser Arg Gln Met Asp

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340

345

350

Arg Ile Val Arg Asn Phe Phe Ser Leu Ile Ser Pro Asp Glu Asp Asn
 355 360 365

Pro Ser Thr Tyr Ile Glu Phe Tyr Ile
 370 375

<210> 80
 <211> 1134
 <212> DNA
 <213> Artificial Sequence

<220>
 <223> Q176I,L313R

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 aacgcagccg attggtgggc tgacttgctc ggtcccggca aagccatcaa cactgatatt 240
 tactgctga tctgtacaa cgtcatcggt ggttgcaac gttccaccgg acctggctcc 300
 atgcatccag atggaaattt ctggggtaat cgcttccccg ccacgtccat tcgtgatcag 360
 gtaaacgccg aaaaacaatt cctcgacgca ctcggcatca ccacggtcgc cgcagtactt 420
 ggtggttcca tgggtggtgc ccgcacccta gagtgggccg caatgtaccc agaaactggt 480
 ggcgcagctg ctgttcttgc agtttctgca cgcgccagcg cctggattat cggcattcaa 540
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 tccggctgca acccagccac cggactcggc gccgcccgc gcacgcacca cctcacctac 660
 cgtggcgaac tagaaatcga cgaacgctt gccaccaaag cccaaaagaa cgaaaaccca 720
 ctcggtccct accgcaagcc cgaccagcgc ttcgccgtgg aatcctactt ggactaccaa 780
 gcagacaagc tagtacagcg tttcgacgcc ggctcctacg tcttgctcac cgacgccctc 840
 aaccgccacg acattggtcg cgaccgcgga ggcctcaaca aggcactcga atccatcaaa 900
 gttccagtcc ttgtcgcagg cgtagatacc gatattcggt acccctacca ccagcaagaa 960
 cacctctcca gaaacctggg aaatctactg gcaatggcaa aaatcgatc ccctgtcggc 1020
 cacgatgctt tcctcaccga aagccgcaa atggatcgca tcgtgaggaa cttcttcagc 1080
 ctcactctcc cagacgaaga caacccttcg acctacatcg agttctacat ctaa 1134

<210> 81
 <211> 377
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Q176T,L313R

<400> 81

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 Asp Val Ser Thr₂₀ Glu Ala Gly Ala Ile₂₅ Ile Thr Asn Ala Glu₃₀ Ile Ala
 Tyr His Arg₃₅ Trp Gly Glu Tyr Arg₄₀ Val Asp Lys Glu₄₅ Gly Arg Ser Asn
 Val Val₅₀ Leu Ile Glu His Ala₅₅ Leu Thr Gly Asp Ser₆₀ Asn Ala Ala Asp
 Trp₆₅ Trp Ala Asp Leu₇₀ Leu Gly Pro Gly Lys Ala₇₅ Ile Asn Thr Asp Ile₈₀
 Tyr Cys Val Ile Cys₈₅ Thr Asn Val Ile Gly₉₀ Gly Cys Asn Gly Ser₉₅ Thr
 Gly Pro Gly Ser₁₀₀ Met His Pro Asp Gly₁₀₅ Asn Phe Trp Gly Asn₁₁₀ Arg Phe
 Pro Ala Thr₁₁₅ Ser Ile Arg Asp Gln₁₂₀ Val Asn Ala Glu Lys₁₂₅ Gln Phe Leu
 Asp Ala₁₃₀ Leu Gly Ile Thr Thr₁₃₅ Val Ala Ala Val Leu₁₄₀ Gly Gly Ser Met
 Gly₁₄₅ Gly Ala Arg Thr Leu₁₅₀ Glu Trp Ala Ala Met₁₅₅ Tyr Pro Glu Thr Val₁₆₀
 Gly Ala Ala Ala Val₁₆₅ Leu Ala Val Ser Ala₁₇₀ Arg Ala Ser Ala Trp₁₇₅ Thr
 Ile Gly Ile Gln₁₈₀ Ser Ala Gln Ile Lys₁₈₅ Ala Ile Glu Asn Asp₁₉₀ His His
 Trp His Glu₁₉₅ Gly Asn Tyr Tyr Glu₂₀₀ Ser Gly Cys Asn Pro₂₀₅ Ala Thr Gly
 Leu Gly₂₁₀ Ala Ala Arg Arg Ile₂₁₅ Ala His Leu Thr Tyr₂₂₀ Arg Gly Glu Leu
 Glu₂₂₅ Ile Asp Glu Arg Phe₂₃₀ Gly Thr Lys Ala Gln₂₃₅ Lys Asn Glu Asn Pro₂₄₀
 Leu Gly Pro Tyr Arg₂₄₅ Lys Pro Asp Gln Arg₂₅₀ Phe Ala Val Glu Ser₂₅₅ Tyr
 Leu Asp Tyr Gln₂₆₀ Ala Asp Lys Leu Val₂₆₅ Gln Arg Phe Asp Ala₂₇₀ Gly Ser
 Tyr Val Leu₂₇₅ Leu Thr Asp Ala Leu₂₈₀ Asn Arg His Asp Ile₂₈₅ Gly Arg Asp
 Arg Gly₂₉₀ Gly Leu Asn Lys Ala₂₉₅ Leu Glu Ser Ile Lys₃₀₀ Val Pro Val Leu
 Val₃₀₅ Ala Gly Val Asp Thr₃₁₀ Asp Ile Arg Tyr Pro₃₁₅ Tyr His Gln Gln Glu₃₂₀
 His Leu Ser Arg Asn₃₂₅ Leu Gly Asn Leu Leu₃₃₀ Ala Met Ala Lys Ile₃₃₅ Val
 Ser Pro Val Gly₃₄₀ His Asp Ala Phe Leu₃₄₅ Thr Glu Ser Arg Gln₃₅₀ Met Asp
 Arg Ile Val₃₅₅ Arg Asn Phe Phe Ser₃₆₀ Leu Ile Ser Pro Asp₃₆₅ Glu Asp Asn

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Pro Ser Thr Tyr Ile Glu Phe Tyr Ile
370 375

<210> 82
<211> 1134
<212> DNA
<213> Artificial Sequence

<220>
<223> Q176T,L313R

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gtagataaag aaggacgcag caatgtcggt ctcatcgaac acgccctcac tggagattcc 180
aacgcagccg attggtgggc tgacttgctc ggtcccggca aagccatcaa cactgatatt 240
tactgctgta tctgtaccaa cgtcatcggg ggttgcaacg gttccaccgg acctgggtcc 300
atgcatccag atggaaattt ctggggtaat cgcttccccg ccacgtccat tcgtgatcag 360
gtaaacgccg aaaaacaatt cctcgacgca ctcgggcatca ccacggctgc cgcagtactt 420
ggtggttcca tgggtggtgc ccgcacccta gagtggggccg caatgtaccc agaaactggt 480
ggcgcagctg ctgttcttgc agtttctgca cgcgccagcg cctggactat cggcattcaa 540
tccgccc aaa ttaaggcgat tga aaacgac caccactggc acgaaggcaa ctactacgaa 600
tccggctgca acccagccac cggactcggc gccgccgac gcatcgcca cctcacctac 660
cgtggcgaac tagaaatcga cgaacgctt gccaccaaag cccaaaagaa cgaaaaccca 720
ctcggctcct accgcaagcc cgaccagcgc ttcgccgtgg aatcctactt ggactaccaa 780
gcagacaagc tagtacagcg tttcgacgcc ggctcctacg tcttgctcac cgacgccctc 840
aaccgccacg acattggtcg cgaccgcgga ggcctcaaca aggcactcga atccatcaaa 900
gttccagtcc ttgtcgcagg cgtagatacc gatattcggg acccctacca ccagcaagaa 960
cacctctcca gaaacctggg aaatctactg gcaatggcaa aaatcgtatc ccctgtcggc 1020
cacgatgctt tcctcaccga aagccgcaa atggatcgca tcgtgaggaa cttcttcagc 1080
ctcatctccc cagacgaaga caacccttcg acctacatcg agttctacat ctaa 1134

<210> 83
<211> 377
<212> PRT
<213> Artificial Sequence

<220>
<223> Q176R,L313R

<400> 83
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1 5 10 15

Asp Val Ser Thr Glu Ala Gly Ala Ile Ile Thr Asn Ala Glu Ile Ala

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20					25					30					
Tyr	His	Arg ₃₅	Trp	Gly	Glu	Tyr	Arg ₄₀	Val	Asp	Lys	Glu	Gly ₄₅	Arg	Ser	Asn
Val	Val ₅₀	Leu	Ile	Glu	His	Ala ₅₅	Leu	Thr	Gly	Asp	Ser ₆₀	Asn	Ala	Ala	Asp
Trp ₆₅	Trp	Ala	Asp	Leu	Leu ₇₀	Gly	Pro	Gly	Lys	Ala ₇₅	Ile	Asn	Thr	Asp	Ile ₈₀
Tyr	Cys	Val	Ile	Cys ₈₅	Thr	Asn	Val	Ile	Gly ₉₀	Gly	Cys	Asn	Gly	Ser ₉₅	Thr
Gly	Pro	Gly	Ser ₁₀₀	Met	His	Pro	Asp	Gly ₁₀₅	Asn	Phe	Trp	Gly	Asn ₁₁₀	Arg	Phe
Pro	Ala	Thr ₁₁₅	Ser	Ile	Arg	Asp	Gln ₁₂₀	Val	Asn	Ala	Glu	Lys ₁₂₅	Gln	Phe	Leu
Asp	Ala ₁₃₀	Leu	Gly	Ile	Thr	Thr ₁₃₅	Val	Ala	Ala	Val	Leu ₁₄₀	Gly	Gly	Ser	Met
Gly ₁₄₅	Gly	Ala	Arg	Thr	Leu ₁₅₀	Glu	Trp	Ala	Ala	Met ₁₅₅	Tyr	Pro	Glu	Thr	Val ₁₆₀
Gly	Ala	Ala	Ala	Val ₁₆₅	Leu	Ala	Val	Ser	Ala ₁₇₀	Arg	Ala	Ser	Ala	Trp ₁₇₅	Arg
Ile	Gly	Ile	Gln ₁₈₀	Ser	Ala	Gln	Ile	Lys ₁₈₅	Ala	Ile	Glu	Asn	Asp ₁₉₀	His	His
Trp	His	Glu ₁₉₅	Gly	Asn	Tyr	Tyr	Glu ₂₀₀	Ser	Gly	Cys	Asn	Pro ₂₀₅	Ala	Thr	Gly
Leu	Gly ₂₁₀	Ala	Ala	Arg	Arg	Ile ₂₁₅	Ala	His	Leu	Thr	Tyr ₂₂₀	Arg	Gly	Glu	Leu
Glu ₂₂₅	Ile	Asp	Glu	Arg	Phe ₂₃₀	Gly	Thr	Lys	Ala	Gln ₂₃₅	Lys	Asn	Glu	Asn	Pro ₂₄₀
Leu	Gly	Pro	Tyr	Arg ₂₄₅	Lys	Pro	Asp	Gln	Arg ₂₅₀	Phe	Ala	Val	Glu	Ser ₂₅₅	Tyr
Leu	Asp	Tyr	Gln ₂₆₀	Ala	Asp	Lys	Leu	Val ₂₆₅	Gln	Arg	Phe	Asp	Ala ₂₇₀	Gly	Ser
Tyr	Val ₂₇₅	Leu	Leu	Thr	Asp	Ala	Leu ₂₈₀	Asn	Arg	His	Asp	Ile ₂₈₅	Gly	Arg	Asp
Arg	Gly ₂₉₀	Gly	Leu	Asn	Lys	Ala ₂₉₅	Leu	Glu	Ser	Ile	Lys ₃₀₀	Val	Pro	Val	Leu
Val ₃₀₅	Ala	Gly	Val	Asp	Thr ₃₁₀	Asp	Ile	Arg	Tyr	Pro ₃₁₅	Tyr	His	Gln	Gln	Glu ₃₂₀
His	Leu	Ser	Arg	Asn ₃₂₅	Leu	Gly	Asn	Leu	Leu ₃₃₀	Ala	Met	Ala	Lys	Ile ₃₃₅	Val
Ser	Pro	Val	Gly ₃₄₀	His	Asp	Ala	Phe	Leu ₃₄₅	Thr	Glu	Ser	Arg	Gln ₃₅₀	Met	Asp
Arg	Ile	Val ₃₅₅	Arg	Asn	Phe	Phe	Ser ₃₆₀	Leu	Ile	Ser	Pro	Asp ₃₆₅	Glu	Asp	Asn
Pro	Ser	Thr	Tyr	Ile	Glu	Phe ₃₇₅	Tyr	Ile							

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<210> 84
 <211> 1134
 <212> DNA
 <213> Artificial Sequence

<220>
 <223> Q176R,L313R

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 gtagataaag aaggacgcag caatgtcggt ctcatcgaac acgccctcac tggagattcc 180
 aacgcagccg attggtgggc tgacttgctc ggtcccggca aagccatcaa cactgatatt 240
 tactgctga tctgtaccaa cgtcatcggt ggttgcaacg gttccaccgg acctggctcc 300
 atgcatccag atggaaattt ctggggtaat cgcttccccg ccacgtccat tcgtgatcag 360
 gtaaacgccg aaaaacaatt cctcgacgca ctcggcata caacggctgc cgcagtactt 420
 ggtggttcca tgggtggtgc ccgcacccta gagtgggccg caatgtaccc agaaactggt 480
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 tccgccc aaa ttaaggcgat tgaaaacgac caccactggc acgaaggcaa ctactacgaa 600
 tccggctgca acccagccac cggactcggc gccgcccgac gcatcgccca cctcacctac 660
 cgtggcgaa tagaaatcga cgaacgctt ggacacaaag ccaaaaagaa cgaaaaccca 720
 ctcggtccct accgcaagcc cgaccagcgc ttcgccgtgg aatcctactt ggactaccaa 780
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 aaccgccacg acattggtcg cgaccgcgga ggcctcaaca aggcactcga atccatcaaa 900
 gttccagtcc ttgtcgcagg cgtagatacc gatattcggg acccctacca ccagcaagaa 960
 cacctctcca gaaacctggg aaatctactg gcaatggcaa aaatcgtatc ccctgtcggc 1020
 cacgatgctt tcctcaccga aagccgcaa atggatcgca tcgtgaggaa cttcttcagc 1080
 ctcatctccc cagacgaaga caacccttcg acctacatcg agttctacat ctaa 1134

<210> 85
 <211> 377
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Q176K,L313R

<400> 85
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 20 25 30
 Tyr His Arg Trp Gly Glu Tyr Arg Val Asp Lys Glu Gly Arg Ser Asn
 35 40 45

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Val Val Leu Ile Glu His Ala Leu Thr Gly Asp Ser Asn Ala Ala Asp
 50 55 60
 Trp Trp Ala Asp Leu Leu Gly Pro Gly Lys Ala Ile Asn Thr Asp Ile
 65 70 75 80
 Tyr Cys Val Ile Cys Thr Asn Val Ile Gly Gly Cys Asn Gly Ser Thr
 85 90 95
 Gly Pro Gly Ser Met His Pro Asp Gly Asn Phe Trp Gly Asn Arg Phe
 100 105 110
 Pro Ala Thr Ser Ile Arg Asp Gln Val Asn Ala Glu Lys Gln Phe Leu
 115 120 125
 Asp Ala Leu Gly Ile Thr Thr Val Ala Ala Val Leu Gly Gly Ser Met
 130 135 140
 Gly Gly Ala Arg Thr Leu Glu Trp Ala Ala Met Tyr Pro Glu Thr Val
 145 150 155 160
 Gly Ala Ala Ala Val Leu Ala Val Ser Ala Arg Ala Ser Ala Trp Lys
 165 170 175
 Ile Gly Ile Gln Ser Ala Gln Ile Lys Ala Ile Glu Asn Asp His His
 180 185 190
 Trp His Glu Gly Asn Tyr Tyr Glu Ser Gly Cys Asn Pro Ala Thr Gly
 195 200 205
 Leu Gly Ala Ala Arg Arg Ile Ala His Leu Thr Tyr Arg Gly Glu Leu
 210 215 220
 Glu Ile Asp Glu Arg Phe Gly Thr Lys Ala Gln Lys Asn Glu Asn Pro
 225 230 235 240
 Leu Gly Pro Tyr Arg Lys Pro Asp Gln Arg Phe Ala Val Glu Ser Tyr
 245 250 255
 Leu Asp Tyr Gln Ala Asp Lys Leu Val Gln Arg Phe Asp Ala Gly Ser
 260 265 270
 Tyr Val Leu Leu Thr Asp Ala Leu Asn Arg His Asp Ile Gly Arg Asp
 275 280 285
 Arg Gly Gly Leu Asn Lys Ala Leu Glu Ser Ile Lys Val Pro Val Leu
 290 295 300
 Val Ala Gly Val Asp Thr Asp Ile Arg Tyr Pro Tyr His Gln Gln Glu
 305 310 315 320
 His Leu Ser Arg Asn Leu Gly Asn Leu Leu Ala Met Ala Lys Ile Val
 325 330 335
 Ser Pro Val Gly His Asp Ala Phe Leu Thr Glu Ser Arg Gln Met Asp
 340 345 350
 Arg Ile Val Arg Asn Phe Phe Ser Leu Ile Ser Pro Asp Glu Asp Asn
 355 360 365
 Pro Ser Thr Tyr Ile Glu Phe Tyr Ile
 370 375

<210> 86
 <211> 1134
 <212> DNA

<213> Artificial Sequence

<220>

<223> Q176K,L313R

<400> 86

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gtagataaag aaggacgcag caatgtcggt ctcatcgaac acgccctcac tggagattcc      180
aacgcagccg attggtgggc tgacttgctc ggtcccggca aagccatcaa cactgatatt      240
tactgctgta tctgtaccaa cgtcatcggg ggttgcaacg gttccaccgg acctggctcc      300
atgcatccag atggaaatct ctggggtaat cgcttccccg ccacgtccat tcgtgatcag      360
gtaaacgccg aaaaacaatt cctcgacgca ctcggcatac ccacggtcgc cgcagtactt      420
ggtggttcca tgggtggtgc ccgcacccta gagtggggccg caatgtaccc agaaactggt      480
ggcgcagctg ctgttcttgc agtttctgca cgcgccagcg cctggaaaat cggcattcaa      540
tccgccc aaa ttaaggcgat tgaaaacgac caccactggc acgaaggcaa ctactacgaa      600
tccggctgca acccagccac cggactcggc gccgccgcac gcacgccc cctcacctac      660
cgtggcgaac tagaaatcga cgaacgcttc ggcaccaaag cccaaaagaa cgaaaaccca      720
ctcgttcctt accgcaagcc cgaccagcgc ttcgccgtgg aatcctactt ggactaccaa      780
gcagacaagc tagtacagcg tttcgacgcc ggctcctacg tcttgctcac cgacgccctc      840
aaccgccacg acattggtcg cgaccgcgga ggcctcaaca aggcactcga atccatcaaa      900
gttccagtcc ttgtcgcagg cgtagatacc gatattcggg acccctacca ccagcaagaa      960
caccttcca gaaacctggg aaatctactg gcaatggcaa aaatcgtatc ccctgtcggc     1020
cacgatgctt tcctcaccga aagccgcaa atggatcgca tcgtgaggaa cttcttcagc     1080
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<210> 87

<211> 377

<212> PRT

<213> Artificial Sequence

<220>

<223> Q176V,L313R

<400> 87

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          20          25          30
Tyr His Arg Trp Gly Glu Tyr Arg Val Asp Lys Glu Gly Arg Ser Asn
          35          40          45
Val Val Leu Ile Glu His Ala Leu Thr Gly Asp Ser Asn Ala Ala Asp
          50          55          60

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Trp Trp Ala Asp Leu Leu Gly Pro Gly Lys Ala Ile Asn Thr Asp Ile
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Tyr Cys Val Ile Cys Thr Asn Val Ile Gly Gly Cys Asn Gly Ser Thr
85 90 95

Gly Pro Gly Ser Met His Pro Asp Gly Asn Phe Trp Gly Asn Arg Phe
100 105 110

Pro Ala Thr Ser Ile Arg Asp Gln Val Asn Ala Glu Lys Gln Phe Leu
115 120 125

Asp Ala Leu Gly Ile Thr Thr Val Ala Ala Val Leu Gly Gly Ser Met
130 135 140

Gly Gly Ala Arg Thr Leu Glu Trp Ala Ala Met Tyr Pro Glu Thr Val
145 150 155 160

Gly Ala Ala Ala Val Leu Ala Val Ser Ala Arg Ala Ser Ala Trp Val
165 170 175

Ile Gly Ile Gln Ser Ala Gln Ile Lys Ala Ile Glu Asn Asp His His
180 185 190

Trp His Glu Gly Asn Tyr Tyr Glu Ser Gly Cys Asn Pro Ala Thr Gly
195 200 205

Leu Gly Ala Ala Arg Arg Ile Ala His Leu Thr Tyr Arg Gly Glu Leu
210 215 220

Glu Ile Asp Glu Arg Phe Gly Thr Lys Ala Gln Lys Asn Glu Asn Pro
225 230 235 240

Leu Gly Pro Tyr Arg Lys Pro Asp Gln Arg Phe Ala Val Glu Ser Tyr
245 250 255

Leu Asp Tyr Gln Ala Asp Lys Leu Val Gln Arg Phe Asp Ala Gly Ser
260 265 270

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

Arg Gly Gly Leu Asn Lys Ala Leu Glu Ser Ile Lys Val Pro Val Leu
290 295 300

Val Ala Gly Val Asp Thr Asp Ile Arg Tyr Pro Tyr His Gln Gln Glu
305 310 315 320

His Leu Ser Arg Asn Leu Gly Asn Leu Leu Ala Met Ala Lys Ile Val
325 330 335

Ser Pro Val Gly His Asp Ala Phe Leu Thr Glu Ser Arg Gln Met Asp
340 345 350

Arg Ile Val Arg Asn Phe Phe Ser Leu Ile Ser Pro Asp Glu Asp Asn
355 360 365

Pro Ser Thr Tyr Ile Glu Phe Tyr Ile
370 375

<210> 88
<211> 1134
<212> DNA
<213> Artificial Sequence

<220>
<223> Q176V,L313R

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gtagataaag aaggacgcag caatgtcggt ctcacgaac acgccctcac tggagattcc      180
aacgcagccg attggtgggc tgacttgctc ggtcccggca aagccatcaa cactgatatt      240
tactgctgta tctgtaccaa cgtcatcggt ggttgcaacg gttccaccgg acctgggtcc      300
atgcatccag atggaaattt ctggggtaat cgcttccccg ccacgtccat tcgtgatcag      360
gtaaacgccg aaaaacaatt cctcgacgca ctcggcatca ccacggtcgc cgcagtactt      420
ggtggttcca tgggtggtgc ccgcacccta gagtgggccc caatgtaccc agaaactggt      480
ggcgcagctg ctgttcttgc agtttctgca cgcgccagcg cctgggttat cggcattcaa      540
tccgccccaa ttaaggcgat tgaaaacgac caccactggc acgaaggcaa ctactacgaa      600
tccggctgca acccagccac cggactcggc gccgcccgcac gcatcgccca cctcacctac      660
cgtggcgaac tagaaatcga cgaacgcttc ggcaccaaag cccaaaagaa cgaaaaccca      720
ctcggtcctt accgcaagcc cgaccagcgc ttcgccgtgg aatcctactt ggactaccaa      780
gcagacaagc tagtacagcg tttcgacgcc ggctcctacg tcttgctcac cgacgccctc      840
aaccgccacg acattggtcg cgaccgcgga ggcctcaaca aggcactcga atccatcaaa      900
gttccagtcc ttgtcgcagg cgtagatacc gatattcggt acccctacca ccagcaagaa      960
cacctctcca gaaacctggg aaatctactg gcaatggcaa aaatcgtatc ccctgtcggc     1020
cacgatgctt tcctcaccga aagccgcaa atggatcgca tcgtgaggaa cttcttcagc     1080
ctcatctccc cagacgaaga caacccttcg acctacatcg agttctacat ctaa      1134

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<210>      89
<211>      377
<212>      PRT
<213>      Artificial Sequence

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<220>
<223>      Q176A,L313R

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<400>      89
Met Pro Thr Leu Ala Pro Ser Gly Gln Leu Glu Ile Gln Ala Ile Gly
  1           5           10          15
Asp Val Ser Thr Glu Ala Gly Ala Ile Ile Thr Asn Ala Glu Ile Ala
          20          25          30
Tyr His Arg Trp Gly Glu Tyr Arg Val Asp Lys Glu Gly Arg Ser Asn
          35          40          45
Val Val Leu Ile Glu His Ala Leu Thr Gly Asp Ser Asn Ala Ala Asp
          50          55          60
Trp Trp Ala Asp Leu Leu Gly Pro Gly Lys Ala Ile Asn Thr Asp Ile
          65          70          75          80
Tyr Cys Val Ile Cys Thr Asn Val Ile Gly Gly Cys Asn Gly Ser Thr

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85										90					95				
Gly	Pro	Gly	Ser	Met	His	Pro	Asp	Gly	Asn	Phe	Trp	Gly	Asn	Arg	Phe				
			100					105					110						
Pro	Ala	Thr	Ser	Ile	Arg	Asp	Gln	Val	Asn	Ala	Glu	Lys	Gln	Phe	Leu				
		115					120					125							
Asp	Ala	Leu	Gly	Ile	Thr	Thr	Val	Ala	Ala	Val	Leu	Gly	Gly	Ser	Met				
	130					135					140								
Gly	Gly	Ala	Arg	Thr	Leu	Glu	Trp	Ala	Ala	Met	Tyr	Pro	Glu	Thr	Val				
145					150					155					160				
Gly	Ala	Ala	Ala	Val	Leu	Ala	Val	Ser	Ala	Arg	Ala	Ser	Ala	Trp	Ala				
				165					170					175					
Ile	Gly	Ile	Gln	Ser	Ala	Gln	Ile	Lys	Ala	Ile	Glu	Asn	Asp	His	His				
			180					185					190						
Trp	His	Glu	Gly	Asn	Tyr	Tyr	Glu	Ser	Gly	Cys	Asn	Pro	Ala	Thr	Gly				
		195					200					205							
Leu	Gly	Ala	Ala	Arg	Arg	Ile	Ala	His	Leu	Thr	Tyr	Arg	Gly	Glu	Leu				
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Glu	Ile	Asp	Glu	Arg	Phe	Gly	Thr	Lys	Ala	Gln	Lys	Asn	Glu	Asn	Pro				
225					230					235					240				
Leu	Gly	Pro	Tyr	Arg	Lys	Pro	Asp	Gln	Arg	Phe	Ala	Val	Glu	Ser	Tyr				
				245					250					255					
Leu	Asp	Tyr	Gln	Ala	Asp	Lys	Leu	Val	Gln	Arg	Phe	Asp	Ala	Gly	Ser				
			260					265					270						
Tyr	Val	Leu	Leu	Thr	Asp	Ala	Leu	Asn	Arg	His	Asp	Ile	Gly	Arg	Asp				
		275					280					285							
Arg	Gly	Gly	Leu	Asn	Lys	Ala	Leu	Glu	Ser	Ile	Lys	Val	Pro	Val	Leu				
	290					295					300								
Val	Ala	Gly	Val	Asp	Thr	Asp	Ile	Arg	Tyr	Pro	Tyr	His	Gln	Gln	Glu				
305					310					315					320				
His	Leu	Ser	Arg	Asn	Leu	Gly	Asn	Leu	Leu	Ala	Met	Ala	Lys	Ile	Val				
				325					330					335					
Ser	Pro	Val	Gly	His	Asp	Ala	Phe	Leu	Thr	Glu	Ser	Arg	Gln	Met	Asp				
			340					345					350						
Arg	Ile	Val	Arg	Asn	Phe	Phe	Ser	Leu	Ile	Ser	Pro	Asp	Glu	Asp	Asn				
		355					360					365							
Pro	Ser	Thr	Tyr	Ile	Glu	Phe	Tyr	Ile											
	370					375													

<210> 90
 <211> 1134
 <212> DNA
 <213> Artificial Sequence

<220>
 <223> Q176A,L313R

<400> 90
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gaagccggag caatcattac aaacgctgaa atcgctatc accgctgggg tgaataaccgc      120
gtagataaag aaggacgcag caatgtcggt ctcatcgaac acgccctcac tggagattcc      180
aacgcagccg attggtgggc tgacttgctc ggtcccggca aagccatcaa cactgatatt      240
tactgctga tctgtaccaa cgtcatcggt gggtgcaacg gttccaccgg acctggctcc      300
atgcatccag atggaaatct ctggggtaat cgcttccccg ccacgtccat tcgtgatcag      360
gtaaacgccg aaaaacaatt cctcgacgca ctcggcatca ccacggtcgc cgcagtactt      420
gggtggtcca tgggtggtgc ccgcacccta gagtggggccg caatgtaccc agaaactggt      480
ggcgcagctg ctgttcttgc agtttctgca cgcgccagcg cctgggcaat cggcattcaa      540
tccgccc aaa ttaaggcgat tgaaaacgac caccactggc acgaaggcaa ctactacgaa      600
tccggctgca acccagccac cggactcggc gccgcccgac gcatcgccca cctcacctac      660
cgtggcgaac tagaaatcga cgaacgcttc ggcaccaaag cccaaaagaa cgaaaaccca      720
ctcggtcctt accgcaagcc cgaccagcgc ttcgccgtgg aatcctactt ggactaccaa      780
gcagacaagc tagtacagcg tttcgacgcc ggctcctacg tcttgctcac cgacgccctc      840
aaccgccacg acattggtcg cgaccgcgga ggcctcaaca aggcactcga atccatcaaa      900
gttccagtcc ttgtcgcagg cgtagatacc gatattcggg acccctacca ccagcaagaa      960
cacctctcca gaaacctggg aaatctactg gcaatggcaa aaatcgatc ccctgtcggc     1020
cacgatgctt tcctcaccga aagccgcaa atggatcgca tcgtgaggaa cttcttcagc     1080
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<210>      91
<211>      377
<212>      PRT
<213>      Artificial Sequence

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<220>
<223>      Q176D,L313R

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<400>      91
Met Pro Thr Leu Ala Pro Ser Gly Gln Leu Glu Ile Gln Ala Ile Gly
 1          5          10          15
Asp Val Ser Thr Glu Ala Gly Ala Ile Ile Thr Asn Ala Glu Ile Ala
          20          25          30
Tyr His Arg Trp Gly Glu Tyr Arg Val Asp Lys Glu Gly Arg Ser Asn
          35          40          45
Val Val Leu Ile Glu His Ala Leu Thr Gly Asp Ser Asn Ala Ala Asp
          50          55          60
Trp Trp Ala Asp Leu Leu Gly Pro Gly Lys Ala Ile Asn Thr Asp Ile
          65          70          75          80
Tyr Cys Val Ile Cys Thr Asn Val Ile Gly Gly Cys Asn Gly Ser Thr
          85          90          95
Gly Pro Gly Ser Met His Pro Asp Gly Asn Phe Trp Gly Asn Arg Phe
          100          105          110

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Pro Ala Thr Ser Ile Arg Asp Gln Val Asn Ala Glu Lys Gln Phe Leu
115 120 125
Asp Ala Leu Gly Ile Thr Thr Val Ala Ala Val Leu Gly Gly Ser Met
130 135 140
Gly Gly Ala Arg Thr Leu Glu Trp Ala Ala Met Tyr Pro Glu Thr Val
145 150 155 160
Gly Ala Ala Ala Val Leu Ala Val Ser Ala Arg Ala Ser Ala Trp Asp
165 170 175
Ile Gly Ile Gln Ser Ala Gln Ile Lys Ala Ile Glu Asn Asp His His
180 185 190
Trp His Glu Gly Asn Tyr Tyr Glu Ser Gly Cys Asn Pro Ala Thr Gly
195 200 205
Leu Gly Ala Ala Arg Arg Ile Ala His Leu Thr Tyr Arg Gly Glu Leu
210 215 220
Glu Ile Asp Glu Arg Phe Gly Thr Lys Ala Gln Lys Asn Glu Asn Pro
225 230 235 240
Leu Gly Pro Tyr Arg Lys Pro Asp Gln Arg Phe Ala Val Glu Ser Tyr
245 250 255
Leu Asp Tyr Gln Ala Asp Lys Leu Val Gln Arg Phe Asp Ala Gly Ser
260 265 270
Tyr Val Leu Leu Thr Asp Ala Leu Asn Arg His Asp Ile Gly Arg Asp
275 280 285
Arg Gly Gly Leu Asn Lys Ala Leu Glu Ser Ile Lys Val Pro Val Leu
290 295 300
Val Ala Gly Val Asp Thr Asp Ile Arg Tyr Pro Tyr His Gln Gln Glu
305 310 315 320
His Leu Ser Arg Asn Leu Gly Asn Leu Leu Ala Met Ala Lys Ile Val
325 330 335
Ser Pro Val Gly His Asp Ala Phe Leu Thr Glu Ser Arg Gln Met Asp
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355 360 365
Pro Ser Thr Tyr Ile Glu Phe Tyr Ile
370 375

<210> 92
<211> 1134
<212> DNA
<213> Artificial Sequence

<220>
<223> Q176D,L313R

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gaagccggag caatcattac aaacgctgaa atcgctatc accgctgggg tgaataccgc 120
gtagataaag aaggacgcag caatgtcggt ctcacgaac acgcctcac tggagattcc 180

6430426_1

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aacgcagccg attggtgggc tgacttgctc ggtcccggca aagccatcaa cactgatatt      240
tactgctga tctgtaccaa cgtcatcggg ggttgcaacg gttccaccgg acctggctcc      300
atgcatccag atggaaatct ctggggtaat cgcttccccg ccacgtccat tcgtgatcag      360
gtaaacgccg aaaaacaatt cctcgacgca ctcggcatca ccacggtcgc cgcagtactt      420
ggtgggtcca tgggtggtgc ccgcacccta gagtggggccg caatgtaccc agaaactggt      480
ggcgcagctg ctgttcttgc agtttctgca cgcgccagcg cctgggacat cggcattcaa      540
tccgccc aaa ttaaggcgat tgaaaacgac caccactggc acgaaggcaa ctactacgaa      600
tccggctgca acccagccac cggactcggc gccgcccgac gcatcgcca cctcacctac      660
cgtggcgaac tagaaatcga cgaacgcttc ggcaccaaag cccaaaagaa cgaaaaccca      720
ctcggtcctt accgcaagcc cgaccagcgc ttcgccgtgg aatcctactt ggactaccaa      780
gcagacaagc tagtacagcg tttcgacgcc ggctcctacg tcttgctcac cgacgccctc      840
aaccgccacg acattggtcg cgaccgcgga ggcctcaaca aggcactcga atccatcaaa      900
gttccagtcc ttgtcgcagg cgtagatacc gatattcggg acccctacca ccagcaagaa      960
cacctctcca gaaacctggg aaatctactg gcaatggcaa aaatcgtatc cctgtcggc     1020
cacgatgctt tcctcaccga aagccgcaa atggatcgca tcgtgaggaa cttcttcagc     1080
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<210>      93
<211>      377
<212>      PRT
<213>      Artificial Sequence

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<220>
<223>      Q176E,L313R

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<400>      93
Met  Pro  Thr  Leu  Ala  Pro  Ser  Gly  Gln  Leu  Glu  Ile  Gln  Ala  Ile  Gly
 1          5          10          15
Asp  Val  Ser  Thr  Glu  Ala  Gly  Ala  Ile  Ile  Thr  Asn  Ala  Glu  Ile  Ala
          20          25          30
Tyr  His  Arg  Trp  Gly  Glu  Tyr  Arg  Val  Asp  Lys  Glu  Gly  Arg  Ser  Asn
          35          40          45
Val  Val  Leu  Ile  Glu  His  Ala  Leu  Thr  Gly  Asp  Ser  Asn  Ala  Ala  Asp
          50          55          60
Trp  Trp  Ala  Asp  Leu  Leu  Gly  Pro  Gly  Lys  Ala  Ile  Asn  Thr  Asp  Ile
          65          70          75          80
Tyr  Cys  Val  Ile  Cys  Thr  Asn  Val  Ile  Gly  Gly  Cys  Asn  Gly  Ser  Thr
          85          90          95
Gly  Pro  Gly  Ser  Met  His  Pro  Asp  Gly  Asn  Phe  Trp  Gly  Asn  Arg  Phe
          100          105          110
Pro  Ala  Thr  Ser  Ile  Arg  Asp  Gln  Val  Asn  Ala  Glu  Lys  Gln  Phe  Leu
          115          120          125

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6430426_1

Asp Ala Leu Gly Ile Thr Thr Val Ala Ala Val Leu Gly Gly Ser Met
 130 135 140
 Gly Gly Ala Arg Thr Leu Glu Trp Ala Ala Met Tyr Pro Glu Thr Val
 145 150 155 160
 Gly Ala Ala Ala Val Leu Ala Val Ser Ala Arg Ala Ser Ala Trp Glu
 165 170 175
 Ile Gly Ile Gln Ser Ala Gln Ile Lys Ala Ile Glu Asn Asp His His
 180 185 190
 Trp His Glu Gly Asn Tyr Tyr Glu Ser Gly Cys Asn Pro Ala Thr Gly
 195 200 205
 Leu Gly Ala Ala Arg Arg Ile Ala His Leu Thr Tyr Arg Gly Glu Leu
 210 215 220
 Glu Ile Asp Glu Arg Phe Gly Thr Lys Ala Gln Lys Asn Glu Asn Pro
 225 230 235 240
 Leu Gly Pro Tyr Arg Lys Pro Asp Gln Arg Phe Ala Val Glu Ser Tyr
 245 250 255
 Leu Asp Tyr Gln Ala Asp Lys Leu Val Gln Arg Phe Asp Ala Gly Ser
 260 265 270
 Tyr Val Leu Leu Thr Asp Ala Leu Asn Arg His Asp Ile Gly Arg Asp
 275 280 285
 Arg Gly Gly Leu Asn Lys Ala Leu Glu Ser Ile Lys Val Pro Val Leu
 290 295 300
 Val Ala Gly Val Asp Thr Asp Ile Arg Tyr Pro Tyr His Gln Gln Glu
 305 310 315 320
 His Leu Ser Arg Asn Leu Gly Asn Leu Leu Ala Met Ala Lys Ile Val
 325 330 335
 Ser Pro Val Gly His Asp Ala Phe Leu Thr Glu Ser Arg Gln Met Asp
 340 345 350
 Arg Ile Val Arg Asn Phe Phe Ser Leu Ile Ser Pro Asp Glu Asp Asn
 355 360 365
 Pro Ser Thr Tyr Ile Glu Phe Tyr Ile
 370 375

<210> 94
 <211> 1134
 <212> DNA
 <213> Artificial Sequence

<220>
 <223> Q176E,L313R

<400> 94
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 gtagataaag aaggacgcag caatgtcggt ctcatcgaac acgccctcac tggagattcc 180
 aacgcagccg attggtgggc tgacttgctc ggtcccggca aagccatcaa cactgatatt 240
 tactgcgtga tctgtaccaa cgtcatcggt ggttgcaacg gttccaccgg acctggctcc 300

6430426_1

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atgcatccag atggaaattt ctggggtaat cgcttccccg ccacgtccat tcgtgatcag      360
gtaaacgccg aaaaacaatt cctcgacgca ctcggcatca ccacggtcgc cgcagtactt      420
ggtggttcca tgggtggtgc cgcacccta gagtgggccc caatgtaccc agaaactggt      480
ggcgcagctg ctgttcttgc agtttctgca cgcgccagcg cctgggagat cggcattcaa      540
tccgccccaa ttaaggcgat tgaaaacgac caccactggc acgaaggcaa ctactacgaa      600
tccgggtgca acccagccac cggactcggc gccgcccgcac gcatcgccca cctcacctac      660
cgtggcgaac tagaaatcga cgaacgcttc ggcaccaaag cccaaaagaa cgaaaaccca      720
ctcggtcctt accgcaagcc cgaccagcgc ttcgccgtgg aatcctactt ggactaccaa      780
gcagacaagc tagtacagcg tttcgacgcc ggctcctacg tcttgctcac cgacgccctc      840
aaccgccacg acattggtcg cgaccgcgga ggcctcaaca aggcactcga atccatcaaa      900
gttccagtcc ttgtcgcagg cgtagatacc gatattcggg acccctacca ccagcaagaa      960
cacctctcca gaaacctggg aaatctactg gcaatggcaa aaatcgtatc ccctgtcggc     1020
cacgatgctt tcctaccga aagccgcaa atggatcgca tcgtgaggaa cttcttcagc     1080
ctcatctccc cagacgaaga caacccttcg acctacatcg agttctacat ctaa         1134

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<210>      95
<211>      377
<212>      PRT
<213>      Artificial Sequence

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<220>
<223>      Q176G,L313R

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<400>      95
Met Pro Thr Leu Ala Pro Ser Gly Gln Leu Glu Ile Gln Ala Ile Gly
  1           5           10           15
Asp Val Ser Thr Glu Ala Gly Ala Ile Ile Thr Asn Ala Glu Ile Ala
           20           25           30
Tyr His Arg Trp Gly Glu Tyr Arg Val Asp Lys Glu Gly Arg Ser Asn
           35           40           45
Val Val Leu Ile Glu His Ala Leu Thr Gly Asp Ser Asn Ala Ala Asp
           50           55           60
Trp Trp Ala Asp Leu Leu Gly Pro Gly Lys Ala Ile Asn Thr Asp Ile
           65           70           75           80
Tyr Cys Val Ile Cys Thr Asn Val Ile Gly Gly Cys Asn Gly Ser Thr
           85           90           95
Gly Pro Gly Ser Met His Pro Asp Gly Asn Phe Trp Gly Asn Arg Phe
           100          105          110
Pro Ala Thr Ser Ile Arg Asp Gln Val Asn Ala Glu Lys Gln Phe Leu
           115          120          125
Asp Ala Leu Gly Ile Thr Thr Val Ala Ala Val Leu Gly Gly Ser Met
           130          135          140
Gly Gly Ala Arg Thr Leu Glu Trp Ala Ala Met Tyr Pro Glu Thr Val

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145 150 155 160
 Gly Ala Ala Ala Val₁₆₅ Leu Ala Val Ser Ala₁₇₀ Arg Ala Ser Ala Trp₁₇₅ Gly
 Ile Gly Ile Gln₁₈₀ Ser Ala Gln Ile Lys₁₈₅ Ala Ile Glu Asn Asp₁₉₀ His His
 Trp His Glu₁₉₅ Gly Asn Tyr Tyr Glu₂₀₀ Ser Gly Cys Asn Pro₂₀₅ Ala Thr Gly
 Leu Gly₂₁₀ Ala Ala Arg Arg Ile₂₁₅ Ala His Leu Thr Tyr₂₂₀ Arg Gly Glu Leu
 Glu₂₂₅ Ile Asp Glu Arg Phe₂₃₀ Gly Thr Lys Ala Gln₂₃₅ Lys Asn Glu Asn Pro₂₄₀
 Leu Gly Pro Tyr Arg₂₄₅ Lys Pro Asp Gln Arg₂₅₀ Phe Ala Val Glu Ser₂₅₅ Tyr
 Leu Asp Tyr Gln₂₆₀ Ala Asp Lys Leu Val₂₆₅ Gln Arg Phe Asp Ala₂₇₀ Gly Ser
 Tyr Val Leu₂₇₅ Leu Thr Asp Ala Leu₂₈₀ Asn Arg His Asp Ile₂₈₅ Gly Arg Asp
 Arg Gly₂₉₀ Gly Leu Asn Lys Ala₂₉₅ Leu Glu Ser Ile Lys₃₀₀ Val Pro Val Leu
 Val₃₀₅ Ala Gly Val Asp Thr₃₁₀ Asp Ile Arg Tyr Pro₃₁₅ Tyr His Gln Gln Glu₃₂₀
 His Leu Ser Arg Asn₃₂₅ Leu Gly Asn Leu Leu₃₃₀ Ala Met Ala Lys Ile₃₃₅ Val
 Ser Pro Val Gly₃₄₀ His Asp Ala Phe Leu₃₄₅ Thr Glu Ser Arg Gln₃₅₀ Met Asp
 Arg Ile Val₃₅₅ Arg Asn Phe Phe Ser₃₆₀ Leu Ile Ser Pro Asp₃₆₅ Glu Asp Asn
 Pro Ser₃₇₀ Thr Tyr Ile Glu Phe₃₇₅ Tyr Ile

<210> 96
 <211> 1134
 <212> DNA
 <213> Artificial Sequence

<220>
 <223> Q176G,L313R

<400> 96
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 gtagataaag aaggacgcag caatgtcggt ctcacgaac acgccctcac tggagattcc 180
 aacgcagccg attggtgggc tgacttgctc ggtcccggca aagccatcaa cactgatatt 240
 tactgctga tctgtaccaa cgtcatcggt ggttgcaacg gttccaccgg acctggctcc 300
 atgcatccag atggaaattt ctggggtaat cgcttccccg ccacgtccat tcgtgatcag 360
 gtaaacgccg aaaaacaatt cctcgacgca ctcggcatca ccacggtcgc cgcagtactt 420

6430426_1

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ggtggttcca tgggtggtgc ccgcacccta gagggtggccg caatgtaccc agaaactggt      480
ggcgagctg ctgttcttgc agtttctgca cgcgccagcg cctggggcat cggcattcaa      540
tccgccccaaa ttaaggcgat tgaaaacgac caccactggc acgaaggcaa ctactacgaa      600
tccgggtgca acccagccac cggactcggc gccgcccgc gcatcgccca cctcacctac      660
cgtggcgaac tagaaatcga cgaacgcttc ggcaccaaag cccaaaagaa cgaaaaccca      720
ctcgggtccct accgcaagcc cgaccagcgc ttcgccgtgg aatcctactt ggactaccaa      780
gcagacaagc tagtacagcg tttcgacgcc ggctcctacg tcttgctcac cgacgccctc      840
aaccgccacg acattgggtc cgaccgcgga ggcctcaaca aggcactcga atccatcaaa      900
gttccagtcc ttgtcgcagg cgtagatacc gatattcggg acccctacca ccagcaagaa      960
cacctctcca gaaacctggg aaatctactg gcaatggcaa aaatcgtatc ccctgtcggc     1020
cacgatgctt tcctaccga aagccgcaa atggatcgca tcgtgaggaa cttcttcagc     1080
ctcatctccc cagacgaaga caacccttcg acctacatcg agttctacat ctaa         1134

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<210>      97
<211>      377
<212>      PRT
<213>      Artificial Sequence

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<220>
<223>      Q176W,L313R

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<400>      97
Met Pro Thr Leu Ala Pro Ser Gly Gln Leu Glu Ile Gln Ala Ile Gly
 1          5          10          15
Asp Val Ser Thr Glu Ala Gly Ala Ile Ile Thr Asn Ala Glu Ile Ala
          20          25          30
Tyr His Arg Trp Gly Glu Tyr Arg Val Asp Lys Glu Gly Arg Ser Asn
          35          40          45
Val Val Leu Ile Glu His Ala Leu Thr Gly Asp Ser Asn Ala Ala Asp
          50          55          60
Trp Trp Ala Asp Leu Leu Gly Pro Gly Lys Ala Ile Asn Thr Asp Ile
          65          70          75          80
Tyr Cys Val Ile Cys Thr Asn Val Ile Gly Gly Cys Asn Gly Ser Thr
          85          90          95
Gly Pro Gly Ser Met His Pro Asp Gly Asn Phe Trp Gly Asn Arg Phe
          100          105          110
Pro Ala Thr Ser Ile Arg Asp Gln Val Asn Ala Glu Lys Gln Phe Leu
          115          120          125
Asp Ala Leu Gly Ile Thr Thr Val Ala Ala Val Leu Gly Gly Ser Met
          130          135          140
Gly Gly Ala Arg Thr Leu Glu Trp Ala Ala Met Tyr Pro Glu Thr Val
          145          150          155          160
Gly Ala Ala Ala Val Leu Ala Val Ser Ala Arg Ala Ser Ala Trp Trp
          165          170          175

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6430426_1

Ile Gly Ile Gln Ser Ala Gln Ile Lys Ala Ile Glu Asn Asp His His
 180 185 190
 Trp His Glu Gly Asn Tyr Tyr Glu Ser Gly Cys Asn Pro Ala Thr Gly
 195 200 205
 Leu Gly Ala Ala Arg Arg Ile Ala His Leu Thr Tyr Arg Gly Glu Leu
 210 215
 Glu Ile Asp Glu Arg Phe Gly Thr Lys Ala Gln Lys Asn Glu Asn Pro
 225 230 235 240
 Leu Gly Pro Tyr Arg Lys Pro Asp Gln Arg Phe Ala Val Glu Ser Tyr
 245 250 255
 Leu Asp Tyr Gln Ala Asp Lys Leu Val Gln Arg Phe Asp Ala Gly Ser
 260 265 270
 Tyr Val Leu Leu Thr Asp Ala Leu Asn Arg His Asp Ile Gly Arg Asp
 275 280 285
 Arg Gly Gly Leu Asn Lys Ala Leu Glu Ser Ile Lys Val Pro Val Leu
 290 295 300
 Val Ala Gly Val Asp Thr Asp Ile Arg Tyr Pro Tyr His Gln Gln Glu
 305 310 315 320
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 Ser Pro Val Gly His Asp Ala Phe Leu Thr Glu Ser Arg Gln Met Asp
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