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<120> Humanized Antibody

<130> 089667-0155

<141> 2008-10-03

<150> US 60/960,616

<151> 2007-10-05

<160> 32

<170> PatentIn version 3.3

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<400> 1

Gly Phe Thr Phe Ser Ser Tyr Gly Met Ser
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Arg Ser Ser Gln Ser Leu Val Tyr Ser Asn Gly Asp Thr Tyr Leu His
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<400> 6

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<223> Aβ epitope, region 2

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<210> 8
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His Gln Lys Leu Val
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<400> 10

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<400> 11

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<210> 12
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<213> Artificial sequence

<220>
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<400> 12

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Glu Pro Ala Ser Ile Ser Cys Arg Ser Ser Gln Ser Leu Val Tyr Ser
20 25 30

Asn Gly Asp Thr Tyr Leu His Trp Tyr Leu Gln Lys Pro Gly Gln Ser
35 40 45

Pro Gln Leu Leu Ile Tyr Lys Val Ser Asn Arg Phe Ser Gly Val Pro
50 55 60

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

Ser Arg Val Glu Ala Glu Asp Val Gly Val Tyr Tyr Cys Ser Gln Ser
85 90 95

Thr His Val Pro Trp Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys
100 105 110

<210> 13
<211> 219
<212> PRT
<213> artificial sequence

<220>

<223> artificial humanized C2 light chain

<400> 13

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            20                  25                  30

Asn Gly Asp Thr Tyr Leu His Trp Tyr Leu Gln Lys Pro Gly Gln Ser
        35                  40                  45

Pro Gln Leu Leu Ile Tyr Lys Val Ser Asn Arg Phe Ser Gly Val Pro
    50                  55                  60

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

Ser Arg Val Glu Ala Glu Asp Val Gly Val Tyr Tyr Cys Ser Gln Ser
                85                  90                  95

Thr His Val Pro Trp Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys
            100                 105                 110

Arg Thr Val Ala Ala Pro Ser Val Phe Ile Phe Pro Pro Ser Asp Glu
        115                 120                 125

Gln Leu Lys Ser Gly Thr Ala Ser Val Val Cys Leu Leu Asn Asn Phe
    130                 135                 140

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

Ser Gly Asn Ser Gln Glu Ser Val Thr Glu Gln Asp Ser Lys Asp Ser
                165                 170                 175

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

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

Pro Val Thr Lys Ser Phe Asn Arg Gly Glu Cys
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210 215

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<212> PRT
<213> artificial sequence

<220>
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<400> 14

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> 15
<211> 112
<212> PRT
<213> artificial sequence

<220>
<223> artificial humanized C2 HuVH AF 4 variable heavy chain

<400> 15

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

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

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

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Ser 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 Ser Gly Asp Tyr Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser
            100                 105                 110
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<213> artificial sequence

<220>
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<400> 16

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

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

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

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Ser 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 Ser Gly Asp Tyr Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser
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100 105 110

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

Ser Thr Ser Glu Ser Thr Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr
130 135 140

Phe Pro Glu Pro Val Thr Val Ser Trp Asn Ser Gly Ala Leu Thr Ser
145 150 155 160

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

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

Tyr Thr Cys Asn Val Asp His Lys Pro Ser Asn Thr Lys Val Asp Lys
195 200 205

Arg Val Glu Ser Lys Tyr Gly Pro Pro Cys Pro Pro Cys Pro Ala Pro
210 215 220

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

Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val
245 250 255

Asp Val Ser Gln Glu Asp Pro Glu Val Gln Phe Asn Trp Tyr Val Asp
260 265 270

Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Phe
275 280 285

Asn Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp
290 295 300

Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Gly Leu
305 310 315 320

Pro Ser Ser Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg
325 330 335

Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Gln Glu Glu Met Thr Lys
340 345 350

Asn Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp
355 360 365

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

Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser
385 390 395 400

Arg Leu Thr Val Asp Lys Ser Arg Trp Gln Glu Gly Asn Val Phe Ser
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Cys Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser
420 425 430

Leu Ser Leu Ser Leu Gly Lys
435

<210> 17
<211> 326
<212> PRT
<213> Homo sapiens

<220>
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<400> 17

Ala Ser Thr Lys Gly Pro Ser Val Phe Pro Leu Ala Pro Cys Ser Arg
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Ser Thr Ser Glu Ser 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 Lys Thr

65 70 75
80

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

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

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

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

Asp Val Ser Gln Glu Asp Pro Glu Val Gln Phe Asn Trp Tyr Val Asp
145 150 155 160

Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Phe
165 170 175

Asn Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp
180 185 190

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

Pro Ser Ser Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg
210 215 220

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

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

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

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

Arg Leu Thr Val Asp Lys Ser Arg Trp Gln Glu Gly Asn Val Phe Ser

290 295 300

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

Leu Ser Leu Ser Leu Gly
325

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<211> 51
<212> DNA
<213> Mus musculus

<220>
<223> C2 HuVH AF 4 humanised heavy chain variable region (CDR2)

<400> 18
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51

<210> 19
<211> 9
<212> DNA
<213> Mus musculus

<220>
<223> C2 HuVH AF 4 humanised heavy chain variable region (CDR3)

<400> 19
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9

<210> 20
<211> 49
<212> DNA
<213> Mus musculus

<220>
<223> C2 HuVK 1 humanised light chain variable region (CDR1)

<400> 20
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49

<210> 21
<211> 635
<212> DNA
<213> artificial sequence

<220>

<223> artificial humanized C2 Hu VK 1 variable light chain

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atctcttgca gatctagtca gagccttgta tatagtaatg gagacaccta tttacattgg
120

tacctgcaga agccaggcca gtctccacag ctcctgatct acaaagtttc caaccgattt
180

tctggggtcc cagacaggtt cagtggcagt ggatcaggga cagatttcac actcaagatc
240

agcagagtgg aggctgagga tgtgggagtt tattactgct ctcaaagtac acatgttcct
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tggacgttcg gccaaggcac caaggtggaa atcaaa
336

<210> 22
<211> 657
<212> DNA
<213> artificial sequence

<220>
<223> artificial humanized C2 light chain

<400> 22
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atctcttgca gatctagtca gagccttgta tatagtaatg gagacaccta tttacattgg
120

tacctgcaga agccaggcca gtctccacag ctcctgatct acaaagtttc caaccgattt
180

tctggggtcc cagacaggtt cagtggcagt ggatcaggga cagatttcac actcaagatc
240

agcagagtgg aggctgagga tgtgggagtt tattactgct ctcaaagtac acatgttcct
300

tggacgttcg gccaaggcac caaggtggaa atcaaaagga ctgtggctgc accatctgtc
360

ttcatcttcc cgccatctga tgagcagttg aaatctggaa ctgcctctgt tgtgtgcctg
420

ctgaataact tctatcccag agaggccaaa gtacagtgga aggtggataa cgccctccaa
480

tcgggtaact cccaggagag tgtcacagag caggacagca aggacagcac ctacagcctc
540

agcagcaccc tgacgctgag caaagcagac tacgagaaac acaaagtcta cgcctgcgaa
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<210> 23
<211> 321
<212> DNA
<213> Homo sapiens

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ggaactgcct ctgttgtgtg cctgctgaat aacttctatc ccagagaggc caaagtacag
120

tggaaggtgg ataacgccct ccaatcgggt aactcccagg agagtgtcac agagcaggac
180

agcaaggaca gcacctacag cctcagcagc accctgacgc tgagcaaagc agactacgag
240

aaacacaaag tctacgcctg cgaagtcacc catcagggcc tgagctcgcc cgtcacaaag
300

agcttcaaca ggggagagtg t
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<210> 24
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<212> DNA
<213> artificial sequence

<220>
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tcctgtgcag cctctggatt cactttcagt agctatggca tgtcttgggt tcgccaggct
120

ccaggcaagg gtctcgaatt ggtcgcaagc atcaatagta atggtggtag cacctattat
180

ccagacagtg tgaagggccg attcaccatc tccagagaca atgccaagaa ctccctgtac
240

ctgcaaatga acagtctgag agctgaggac accgccgtgt attactgtgc aagtggtgac
300

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<210> 25
<211> 1317
<212> DNA
<213> artificial sequence

<220>
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120

ccaggcaagg gtctcgaatt ggtcgcaagc atcaatagta atggtggtag cacctattat
180

ccagacagtg tgaagggccg attcaccatc tccagagaca atgccaagaa ctccctgtac
240

ctgcaaatga acagtctgag agctgaggac accgccgtgt attactgtgc aagtggtgac
300

tactggggcc aaggcaccac tgtcacagtc tcctcagctt ccaccaaggg cccatccgtc
360

ttccccctgg cgccctgctc cagatcgacc tccgagagca cagccgccct gggctgcctg
420

gtcaaggact acttccccga accggtgacg gtgtcgtgga actcaggcgc cctgaccagc
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ggcgtgcaca ccttcccggc tgtcctacag tcctcaggac tctactccct cagcagcgtg
540

gtgaccgtgc cctccagcag cttgggcacg aagacctaca cctgcaacgt agatcacaag
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660

tgcccagcac ctgagttcct gggggggacca tcagtcttcc tgttcccccc aaaacccaag
720

gacactctca tgatctcccg gacccctgag gtcacgtgcg tggtggtgga cgtgagccag
780

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acaaagccgc gggaggagca gttcaacagc acgtaccgtg tggtcagcgt cctcaccgtc
900

ctgcaccagg actggctgaa cggcaaggag tacaagtgca aggtctccaa caaaggcctc
960

ccgtcctcca tcgagaaaac catctccaaa gccaaagggc agccccgaga gccacaggtg
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1080

gtcaaaggct tctaccccag cgacatcgcc gtggagtggg agagcaatgg gcagccggag
1140

aacaactaca agaccacgcc tcccgtcctc gattccgacg gctccttctt cctctacagc
1200

aggctaaccg tggacaagag caggtggcag gaggggaatg tcttctcatg ctccgtgatg
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1317

<210> 26
<211> 981
<212> DNA
<213> Homo sapiens

<220>
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120

tggaactcag gcgccctgac cagcggcgtg cacaccttcc cggctgtcct acagtcctca
180

ggactctact ccctcagcag cgtggtgacc gtgccctcca gcagcttggg cacgaagacc
240

tacacctgca acgtagatca caagcccagc aacaccaagg tggacaagag agttgagtcc
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aaatatggtc ccccgtgtcc cccatgccca gcacctgagt tcctgggggg accatcagtc
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ttcctgttcc ccccaaaacc caaggacact ctcatgatct cccggacccc tgaggtcacg
420

tgcgtggtgg tggacgtgag ccaggaagac cccgaggtcc agttcaactg gtacgtggat
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ggcgtggagg tgcataatgc caagacaaag ccgcgggagg agcagttcaa cagcacgtac
540

cgtgtggtca gcgtcctcac cgtcctgcac caggactggc tgaacggcaa ggagtacaag
600

tgcaaggtct ccaacaaagg cctcccgtcc tccatcgaga aaaccatctc caaagccaaa
660

gggcagcccc gagagccaca ggtgtacacc ctgccccccat cccaggagga gatgaccaag
720

aaccaggtca gcctgacctg cctggtcaaa ggcttctacc ccagcgacat cgccgtggag
780

tgggagagca atgggcagcc ggagaacaac tacaagacca cgcctcccgt cctcgattcc
840

gacggctcct tcttcctcta cagcaggcta accgtggaca agagcaggtg gcaggagggg
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960

ctctccctgt ctctgggtaa a
981

<210> 27
<211> 112
<212> PRT
<213> Mus musculus

<400> 27

Asp Val Val Met Thr Gln Thr Pro Leu Ser Leu Pro Val Ser Leu Gly
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Asp Gln Ala Ser Ile Ser Cys Arg Ser Ser Gln Ser Leu Val Tyr Ser
20 25 30

Asn Gly Asp Thr Tyr Leu His Trp Tyr Leu Gln Lys Pro Gly Gln Ser
35 40 45

Pro Lys Leu Leu Ile Tyr Lys Val Ser Asn Arg Phe Ser Gly Val Pro
50 55 60

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

Ser Arg Val Glu Ala Glu Asp Leu Gly Val Tyr Phe Cys Ser Gln Ser
                85                  90                  95

Thr His Val Pro Trp Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys
            100                 105                 110
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<210> 28
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<212> PRT
<213> Mus musculus

<400> 28

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            20                  25                  30

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

Ala Ser Ile Asn Ser Asn Gly Gly Ser Thr Tyr 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 Lys Ser Glu Asp Thr Ala Met Tyr Tyr Cys
                85                  90                  95

Ala Ser Gly Asp Tyr Trp Gly Gln Gly Ser Thr Leu Thr Val Ser Ser
            100                 105                 110
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<210> 29
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<212> DNA
<213> Mus musculus

<400> 29

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120

tacctgcaga agccaggcca gtctccaaag ctcctgatct acaaagtttc caaccgattt
180

tctggggtcc cagacaggtt cagtggcagt ggatcaggga cagatttcac actcaagatc
240

agcagagtgg aggctgagga tctgggagtt tatttctgct ctcaaagtac acatgttcct
300

tggacgttcg gtggaggcac caagctagaa atcaaa
336

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

<400> 30
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gttgtgatga cccaaactcc actctccctg cctgtcagtc ttggagatca agcctccatc
120

tcttgcagat ctagtcagag ccttgtatat agtaatggag acacctattt acattggtac
180

ctgcagaagc caggccagtc tccaaagctc ctgatctaca aagtttccaa ccgattttct
240

ggggtcccag acaggttcag tggcagtgga tcagggacag atttcacact caagatcagc
300

agagtggagg ctgaggatct gggagtttat ttctgctctc aaagtacaca tgttccttgg
360

acgttcggtg gaggcaccaa gctagaaatc aaacgggctg atgctgcacc aactgta
417

<210> 31
<211> 336
<212> DNA
<213> Mus musculus

<400> 31
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