Chemistry of PEGylation Reaction

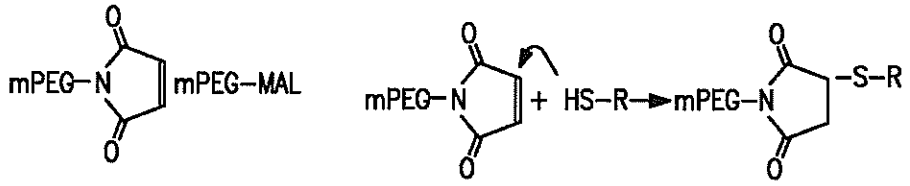


FIG. 1

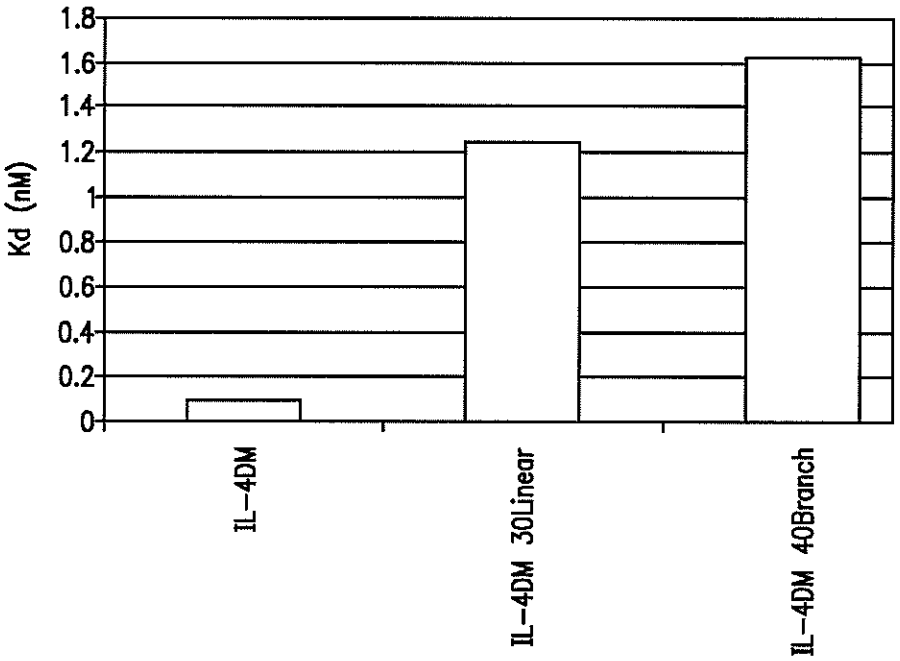
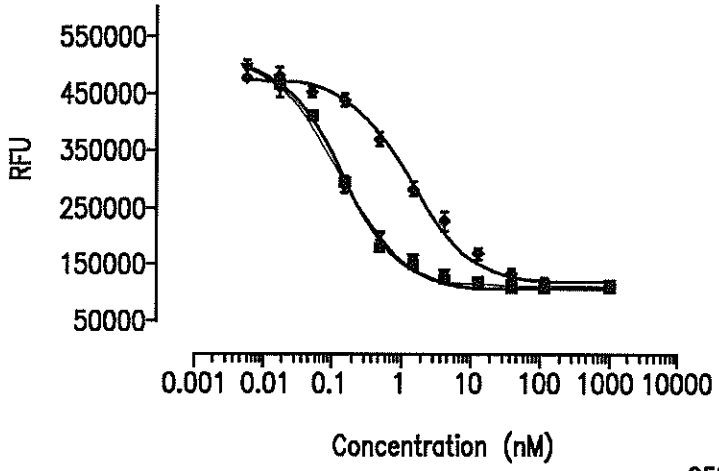


FIG. 2



95% confidence intervals

	EC50
IL-4DM	0.1116 to 0.1605
IL-4TM 40Branch	0.1209 to 0.1639
IL-4DM 40Branch	1.132 to 1.740

FIG. 3

SEQUENCE LISTING

<110> AEROVANCE, INC.
BOISVERT, David
BURMEISTER-GETZ, Elise
DELARIA, Kathy
LONGPHRE, Malinda
TOMKINSON, Adrian
WONG, Teresa Mo-Fun

<120> MODIFIED IL-4 MUTEIN RECEPTOR ANTAGONISTS

<130> AERO1210-4WO

<140> PCT/US2008/083589
<141> 2008-11-14

<150> US 11/940,217
<151> 2007-11-14

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<170> PatentIn version 3.4

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actgagaagg aaaccttctg cagggctgcg actgtgctcc ggcagttcta cagccaccat 180

gagaaggaca ctcgctgcct gggtgcgact gcacagcagt tccacaggca caagcagctg 240

atccgattcc tgaaacggct cgacaggaac ctctggggcc tggcgggctt gaattcctgt 300

cctgtgaagg aagccaacca gagtacgttg gaaaacttct tggaaaggct aaagacgatc 360

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actgagaagg aaaccttctg cagggctgcg actgtgctcc ggcagttcta cagccaccat 180

gagaaggaca ctcgctgcct gggtgcgact gcacagcagt tccacaggca caagcagctg 240

atccgattcc tgaaacggct cgacaggaac ctctggggcc tggcgggctt gaattcctgt 300

cctgtgaagg aagccaacca gagtacgttg gaaaacttct tggaaaggct aaagacgatc 360

atggacgaga aagactcaaa gtgttcgagc taataa 396

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actgagaagg aaaccttctg cagggctgcg actgtgctcc ggcagttcta cagccaccat 180

gagaaggaca ctcgctgcct gggtgcgact gcacagcagt tccacaggca caagcagctg 240

atccgattcc tgaaacggct cgacaggaac ctctggggcc tggcgggctt gaattcctgt 300

cctgtgaagg aagccaacca gagtacgttg gaaaacttct tggaaaggct aaagacgatc 360

atggacgaga aagactcaaa gtgttcgagc taataa 396

<210> 4
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actgagaagg aaaccttctg cagggctgcg actgtgctcc ggcagttcta cagccaccat 180

gagaaggaca ctcgctgcct gggtgcgact gcacagcagt tccacaggca caagcagctg 240

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gagaaggaca ctcgctgcct gggtgcgact gcacagcagt tccacaggca caagcagctg 240

atccgattcc tgaaacggct cgacaggaac ctctggggcc tggcgggctt gaattcctgt 300

cctgtgaagg aagccaacca gagtacgttg gaaaacttct tggaaaggct aaagacgatc 360

atggacgaga aagactcaaa gtgttcgagc taataa 396

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actgagaagg aaaccttctg cagggctgcg actgtgctcc ggcagttcta cagccaccat 180

gagaaggaca ctcgctgcct gggtgcgact gcacagcagt tccacaggca caagcagctg 240

atccgattcc tgaaacggct cgacaggaac ctctggggcc tggcgggctt gaattcctgt 300

cctgtgaagg aatgcaacca gagtacgttg gaaaacttct tggaaaggct aaagacgatc 360

atggacgaga aagactcaaa gtgttcgagc taataa 396

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cagaagactc tgtgcaccga gttgaccgta acagacatct ttgctgcctc caagaacaca 120

actgagaagg aaaccttctg cagggctgcg actgtgctcc ggcagttcta cagccaccat 180

gagaaggaca ctcgctgcct gggtgcgact gcacagcagt tccacaggca caagcagctg 240

atccgattcc tgaaacggct cgacaggaac ctctggggcc tggcgggctt gaattcctgt 300

cctgtgaagg aagcctgcca gagtacgttg gaaaacttct tggaaaggct aaagacgatc 360

atggacgaga aagactcaaa gtgttcgagc taataa 396

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actgagaagg aaaccttctg cagggctgcg actgtgctcc ggcagttcta cagccaccat 180

gagaaggaca ctcgctgcct gggtgcgact gcacagcagt tccacaggca caagcagctg 240

atccgattcc tgaaacggct cgacaggaac ctctggggcc tggcgggctt gaattcctgt 300

cctgtgaagg aagccaactg cagtacgttg gaaaacttct tggaaaggct aaagacgatc 360

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<211> 130
<212> PRT
<213> Artificial sequence

<220>
<223> Modified human sequence

<400> 9

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1 5 10 15

Ser Leu Thr Glu Gln Lys Thr Leu Cys Thr Glu Leu Thr Val Thr Asp
20 25 30

Ile Phe Ala Ala Ser Lys Asn Thr Thr Glu Lys Glu Thr Phe Cys Arg
35 40 45

Ala Ala Thr Val Leu Arg Gln Phe Tyr Ser His His Glu Lys Asp Thr
50 55 60

Arg Cys Leu Gly Ala Thr Ala Gln Gln Phe His Arg His Lys Gln Leu
65 70 75 80

```
Ile Arg Phe Leu Lys Arg Leu Asp Arg Asn Leu Trp Gly Leu Ala Gly
                85                  90                  95

Leu Asn Ser Cys Pro Val Lys Glu Ala Asn Gln Ser Thr Leu Glu Asn
            100                 105                 110

Phe Leu Glu Arg Leu Lys Thr Ile Met Asp Glu Lys Asp Ser Lys Cys
        115                 120                 125

Ser Ser
    130
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<210> 10
<211> 130
<212> PRT
<213> Artificial sequence

<220>
<223> Modified human sequence

<400> 10

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Met His Lys Cys Asp Ile Thr Leu Gln Glu Ile Ile Lys Thr Leu Asn
1               5                   10                  15

Ser Leu Thr Glu Gln Lys Thr Leu Cys Thr Glu Leu Cys Val Thr Asp
            20                  25                  30

Ile Phe Ala Ala Ser Lys Asn Thr Thr Glu Lys Glu Thr Phe Cys Arg
        35                  40                  45

Ala Ala Thr Val Leu Arg Gln Phe Tyr Ser His His Glu Lys Asp Thr
    50                  55                  60

Arg Cys Leu Gly Ala Thr Ala Gln Gln Phe His Arg His Lys Gln Leu
65                  70                  75                  80

Ile Arg Phe Leu Lys Arg Leu Asp Arg Asn Leu Trp Gly Leu Ala Gly
                85                  90                  95

Leu Asn Ser Cys Pro Val Lys Glu Ala Asn Gln Ser Thr Leu Glu Asn
            100                 105                 110

Phe Leu Glu Arg Leu Lys Thr Ile Met Asp Glu Lys Asp Ser Lys Cys
        115                 120                 125

Ser Ser
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130

<210> 11
<211> 130
<212> PRT
<213> Artificial sequence

<220>
<223> Modified human sequence

<400> 11

Met His Lys Cys Asp Ile Thr Leu Gln Glu Ile Ile Lys Thr Leu Asn
1 5 10 15

Ser Leu Thr Glu Gln Lys Thr Leu Cys Thr Glu Leu Thr Val Thr Asp
20 25 30

Ile Phe Ala Ala Cys Lys Asn Thr Thr Glu Lys Glu Thr Phe Cys Arg
35 40 45

Ala Ala Thr Val Leu Arg Gln Phe Tyr Ser His His Glu Lys Asp Thr
50 55 60

Arg Cys Leu Gly Ala Thr Ala Gln Gln Phe His Arg His Lys Gln Leu
65 70 75 80

Ile Arg Phe Leu Lys Arg Leu Asp Arg Asn Leu Trp Gly Leu Ala Gly
85 90 95

Leu Asn Ser Cys Pro Val Lys Glu Ala Asn Gln Ser Thr Leu Glu Asn
100 105 110

Phe Leu Glu Arg Leu Lys Thr Ile Met Asp Glu Lys Asp Ser Lys Cys
115 120 125

Ser Ser
130

<210> 12
<211> 130
<212> PRT
<213> Artificial sequence

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<223> Modified human sequence

<400> 12

Met His Lys Cys Asp Ile Thr Leu Gln Glu Ile Ile Lys Thr Leu Asn
1 5 10 15

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Ser Leu Thr Glu Gln Lys Thr Leu Cys Thr Glu Leu Thr Val Thr Asp
            20                  25                  30

Ile Phe Ala Ala Ser Cys Asn Thr Thr Glu Lys Glu Thr Phe Cys Arg
        35                  40                  45

Ala Ala Thr Val Leu Arg Gln Phe Tyr Ser His His Glu Lys Asp Thr
    50                  55                  60

Arg Cys Leu Gly Ala Thr Ala Gln Gln Phe His Arg His Lys Gln Leu
65                  70                  75                  80

Ile Arg Phe Leu Lys Arg Leu Asp Arg Asn Leu Trp Gly Leu Ala Gly
                85                  90                  95

Leu Asn Ser Cys Pro Val Lys Glu Ala Asn Gln Ser Thr Leu Glu Asn
            100                 105                 110

Phe Leu Glu Arg Leu Lys Thr Ile Met Asp Glu Lys Asp Ser Lys Cys
        115                 120                 125

Ser Ser
    130
```

<210> 13
<211> 130
<212> PRT
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<220>
<223> Modified human sequence

<400> 13

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Met His Lys Cys Asp Ile Thr Leu Gln Glu Ile Ile Lys Thr Leu Asn
1               5                   10                  15

Ser Leu Thr Glu Gln Lys Thr Leu Cys Thr Glu Leu Thr Val Thr Asp
            20                  25                  30

Ile Phe Ala Ala Ser Lys Cys Thr Thr Glu Lys Glu Thr Phe Cys Arg
        35                  40                  45

Ala Ala Thr Val Leu Arg Gln Phe Tyr Ser His His Glu Lys Asp Thr
    50                  55                  60

Arg Cys Leu Gly Ala Thr Ala Gln Gln Phe His Arg His Lys Gln Leu
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65 70 75 80

Ile Arg Phe Leu Lys Arg Leu Asp Arg Asn Leu Trp Gly Leu Ala Gly
85 90 95

Leu Asn Ser Cys Pro Val Lys Glu Ala Asn Gln Ser Thr Leu Glu Asn
100 105 110

Phe Leu Glu Arg Leu Lys Thr Ile Met Asp Glu Lys Asp Ser Lys Cys
115 120 125

Ser Ser
130

<210> 14
<211> 130
<212> PRT
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<223> Modified human sequence

<400> 14

Met His Lys Cys Asp Ile Thr Leu Gln Glu Ile Ile Lys Thr Leu Asn
1 5 10 15

Ser Leu Thr Glu Gln Lys Thr Leu Cys Thr Glu Leu Thr Val Thr Asp
20 25 30

Ile Phe Ala Ala Ser Lys Asn Thr Thr Glu Lys Glu Thr Phe Cys Arg
35 40 45

Ala Ala Thr Val Leu Arg Gln Phe Tyr Ser His His Glu Lys Asp Thr
50 55 60

Arg Cys Leu Gly Ala Thr Ala Gln Gln Phe His Arg His Lys Gln Leu
65 70 75 80

Ile Arg Phe Leu Lys Arg Leu Asp Arg Asn Leu Trp Gly Leu Ala Gly
85 90 95

Leu Asn Ser Cys Pro Val Lys Glu Cys Asn Gln Ser Thr Leu Glu Asn
100 105 110

Phe Leu Glu Arg Leu Lys Thr Ile Met Asp Glu Lys Asp Ser Lys Cys
115 120 125

Ser Ser
130

<210> 15
<211> 130
<212> PRT
<213> Artificial sequence

<220>
<223> Modified human sequence

<400> 15

Met His Lys Cys Asp Ile Thr Leu Gln Glu Ile Ile Lys Thr Leu Asn
1 5 10 15

Ser Leu Thr Glu Gln Lys Thr Leu Cys Thr Glu Leu Thr Val Thr Asp
20 25 30

Ile Phe Ala Ala Ser Lys Asn Thr Thr Glu Lys Glu Thr Phe Cys Arg
35 40 45

Ala Ala Thr Val Leu Arg Gln Phe Tyr Ser His His Glu Lys Asp Thr
50 55 60

Arg Cys Leu Gly Ala Thr Ala Gln Gln Phe His Arg His Lys Gln Leu
65 70 75 80

Ile Arg Phe Leu Lys Arg Leu Asp Arg Asn Leu Trp Gly Leu Ala Gly
85 90 95

Leu Asn Ser Cys Pro Val Lys Glu Ala Cys Gln Ser Thr Leu Glu Asn
100 105 110

Phe Leu Glu Arg Leu Lys Thr Ile Met Asp Glu Lys Asp Ser Lys Cys
115 120 125

Ser Ser
130

<210> 16
<211> 130
<212> PRT
<213> Artificial sequence

<220>
<223> Modified human sequence

<400> 16

Met His Lys Cys Asp Ile Thr Leu Gln Glu Ile Ile Lys Thr Leu Asn

1 5 10 15

Ser Leu Thr Glu Gln Lys Thr Leu Cys Thr Glu Leu Thr Val Thr Asp
20 25 30

Ile Phe Ala Ala Ser Lys Asn Thr Thr Glu Lys Glu Thr Phe Cys Arg
35 40 45

Ala Ala Thr Val Leu Arg Gln Phe Tyr Ser His His Glu Lys Asp Thr
50 55 60

Arg Cys Leu Gly Ala Thr Ala Gln Gln Phe His Arg His Lys Gln Leu
65 70 75 80

Ile Arg Phe Leu Lys Arg Leu Asp Arg Asn Leu Trp Gly Leu Ala Gly
85 90 95

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

Phe Leu Glu Arg Leu Lys Thr Ile Met Asp Glu Lys Asp Ser Lys Cys
115 120 125

Ser Ser
130

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<210> 18
<211> 42
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<220>
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<400> 18
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<210> 19
<211> 39

<212> DNA
<213> Artificial sequence

<220>
<223> Amplification primer

<400> 19
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<210> 20
<211> 39
<212> DNA
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<220>
<223> Amplification primer

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<220>
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<211> 45
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<220>
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<210> 23
<211> 42
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<223> Amplification primer

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<210> 24
<211> 42
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<220>
<223> Amplification primer

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<211> 41
<212> DNA
<213> Artificial sequence

<220>
<223> Amplification primer

<400> 26
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<210> 27
<211> 39
<212> DNA
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<211> 39
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<220>
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<211> 44
<212> DNA
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<223> Amplification primer

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<210> 30
<211> 44
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<210> 31
<211> 390
<212> DNA
<213> Artificial sequence

<220>
<223> Modified human sequence

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accgaaaaag aaaccttctg ccgtgctgct accgttctgc gtcagttcta ctctcaccac 180

gaaaaagaca cccgttgcct gggtgctacc gctcagcagt tccaccgtca caaacagctg 240

atccgtttcc tgaaacgtct ggaccgtaac ctgtggggtc tggctggtct gaacagctgc 300

ccggttaaag aagctaacca gtctaccctg gaaaacttcc tggaacgtct gaaaaccatc 360

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<210> 32
<211> 130
<212> PRT
<213> Artificial sequence

<220>
<223> Modified human sequence

<400> 32

Met His Lys Cys Asp Ile Thr Leu Gln Glu Ile Ile Lys Asp Leu Asn
1 5 10 15

Ser Leu Thr Glu Gln Lys Thr Leu Cys Thr Glu Leu Thr Val Thr Asp
20 25 30

```
Ile Phe Ala Ala Ser Lys Asn Thr Thr Glu Lys Glu Thr Phe Cys Arg
        35                  40                  45

Ala Ala Thr Val Leu Arg Gln Phe Tyr Ser His His Glu Lys Asp Thr
    50                  55                  60

Arg Cys Leu Gly Ala Thr Ala Gln Gln Phe His Arg His Lys Gln Leu
65                  70                  75                  80

Ile Arg Phe Leu Lys Arg Leu Asp Arg Asn Leu Trp Gly Leu Ala Gly
                85                  90                  95

Leu Asn Ser Cys Pro Val Lys Glu Ala Asn Gln Ser Thr Leu Glu Asn
            100                 105                 110

Phe Leu Glu Arg Leu Lys Thr Ile Met Asp Glu Lys Asp Ser Lys Cys
        115                 120                 125

Ser Ser
    130
```

<210> 33
<211> 130
<212> PRT
<213> Artificial sequence

<220>
<223> Modified human sequence

<400> 33

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Met His Lys Cys Asp Ile Thr Leu Gln Glu Ile Ile Lys Asp Leu Asn
1               5                   10                  15

Ser Leu Thr Glu Gln Lys Thr Leu Cys Thr Glu Leu Thr Val Thr Asp
            20                  25                  30

Ile Phe Ala Ala Ser Lys Cys Thr Thr Glu Lys Glu Thr Phe Cys Arg
        35                  40                  45

Ala Ala Thr Val Leu Arg Gln Phe Tyr Ser His His Glu Lys Asp Thr
    50                  55                  60

Arg Cys Leu Gly Ala Thr Ala Gln Gln Phe His Arg His Lys Gln Leu
65                  70                  75                  80

Ile Arg Phe Leu Lys Arg Leu Asp Arg Asn Leu Trp Gly Leu Ala Gly
                85                  90                  95
```

Leu Asn Ser Cys Pro Val Lys Glu Ala Asn Gln Ser Thr Leu Glu Asn
100 105 110

Phe Leu Glu Arg Leu Lys Thr Ile Met Asp Glu Lys Asp Ser Lys Cys
115 120 125

Ser Ser
130

<210> 34
<211> 396
<212> DNA
<213> Artificial sequence

<220>
<223> Modified E.coli sequence

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accgaaaaag aaaccttctg ccgtgctgct accgttctgc gtcagttcta ctctcaccac 180

gaaaaagaca cccgttgcct gggtgctacc gctcagcagt tccaccgtca caaacagctg 240

atccgtttcc tgaaacgtct ggaccgtaac ctgtggggtc tggctggtct gaacagctgc 300

ccggttaaag aatgcaacca gtctaccctg gaaaacttcc tggaacgtct gaaaaccatc 360

atggacgaaa aagactctaa atgctcttct taataa 396

<210> 35
<211> 396
<212> DNA
<213> Artificial sequence

<220>
<223> Modified E.coli sequence

<400> 35
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cagaaaaccc tgtgcaccga actgaccgtt accgacatct tcgctgcttc gaaatgcacc 120

accgaaaaag aaaccttctg ccgtgctgct accgttctgc gtcagttcta ctctcaccac 180

gaaaaagaca cccgttgcct gggtgctacc gctcagcagt tccaccgtca caaacagctg 240

atccgtttcc tgaaacgtct ggaccgtaac ctgtggggtc tggctggtct gaacagctgc 300

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atggacgaaa aagactctaa atgctcttct taataa 396

<210> 36
<211> 390
<212> DNA
<213> Artificial sequence

<220>
<223> Modified E.coli sequence

<400> 36
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cagaaaaccc tgtgcaccga actgaccgtt accgacatct tcgctgcttc gaaatgcacc 120

accgaaaaag aaaccttctg ccgtgctgct accgttctgc gtcagttcta ctctcaccac 180

gaaaaagaca cccgttgcct gggtgctacc gctcagcagt tccaccgtca caaacagctg 240

atccgtttcc tgaaacgtct ggaccgtaac ctgtggggtc tggctggtct gaacagctgc 300

ccggttaaag aagctaacca gtctaccctg gaaaacttcc tggaacgtct gaaaaccatc 360

atggacgaaa aagactctaa atgctcttct 390

<210> 37
<211> 4257
<212> DNA
<213> Artificial sequence

<220>
<223> Modified E.coli sequence

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tgctgccacc gctgagcaat aactagcata acccccttggg gcctctaaac gggtcttgag 120

gggttttttg ctgaaaggag gaactatatc cggataattc ttagaaaaac tcatcgagca 180

tcaaatgaaa ctgcaattta ttcatatcag gattatcaat accatatttt tgaaaaagcc 240

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