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<120> VARIANTS OF TISSUE INHIBITOR OF METALLOPROTEINASE TYPE THREE (TIMP-3), COMPOSITIONS AND METHODS

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Lys Gln Met Lys Met Tyr Arg Gly Phe Thr Lys Met Pro His Val Gln

65 70 75 80

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

Val Asn Lys Tyr Gln Tyr Leu Leu Thr Gly Arg Val Tyr Asp Gly Lys
100 105 110

Met Tyr Thr Gly Leu Cys Asn Phe Val Glu Arg Trp Asp Gln Leu Thr
115 120 125

Leu Ser Gln Arg Lys Gly Leu Asn Tyr Arg Tyr His Leu Gly Cys Asn
130 135 140

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

Asn Glu Cys Leu Trp Thr Asp Met Leu Ser Asn Phe Gly Tyr Pro Gly
165 170 175

Tyr Gln Ser Lys His Tyr Ala Cys Ile Arg Gln Lys Gly Gly Tyr Cys
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Ser Trp Tyr Arg Gly Trp Ala Pro Pro Asp Lys Ser Ile Ile Asn Ala
195 200 205

Thr Asp Pro
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Xaa Xaa Xaa Xaa Xaa Xaa Xaa Cys Thr Cys Ser Pro Ser His Pro Gln
            20                  25                  30

Asp Ala Phe Cys Asn Ser Asp Ile Val Ile Arg Ala Glu Val Val Gly
        35                  40                  45

Lys Lys Leu Val Lys Glu Gly Pro Phe Gly Thr Leu Val Tyr Glu Ile
    50                  55                  60

Lys Gln Met Lys Met Tyr Arg Gly Phe Thr Lys Met Pro His Val Gln
65                  70                  75                  80

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

Val Asn Lys Tyr Gln Tyr Leu Leu Thr Gly Arg Val Tyr Asp Gly Lys
            100                 105                 110

Met Tyr Thr Gly Leu Cys Asn Phe Val Glu Arg Trp Asp Gln Leu Thr
        115                 120                 125

Leu Ser Gln Arg Lys Gly Leu Asn Tyr Arg Tyr His Leu Gly Cys Asn
    130                 135                 140

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

Asn Glu Cys Leu Trp Thr Asp Met Leu Ser Asn Phe Gly Tyr Pro Gly
                165                 170                 175
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Tyr Gln Ser Lys His Tyr Ala Cys Ile Arg Gln Lys Gly Gly Tyr Cys
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Ser Trp Tyr Arg Gly Trp Ala Pro Pro Asp Lys Ser Ile Ile Asn Ala
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Thr Asp Pro
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Xaa Xaa Xaa Xaa Xaa Xaa Xaa Cys Thr Cys Ser Pro Ser His Pro Gln
20 25 30

Asp Ala Phe Cys Asn Ser Asp Ile Val Ile Arg Ala Glu Val Val Gly
35 40 45

Lys Lys Leu Val Lys Glu Gly Pro Phe Gly Thr Leu Val Tyr Thr Ile
50 55 60

Lys Gln Met Lys Met Tyr Arg Gly Phe Thr Lys Met Pro His Val Glu
65 70 75 80

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

Val Asn Lys Tyr Gln Tyr Leu Leu Thr Gly Arg Val Tyr Asp Gly Lys
100 105 110

Met Tyr Thr Gly Leu Cys Asn Phe Val Glu Arg Trp Asp Gln Leu Thr
115 120 125

Leu Ser Gln Arg Lys Gly Leu Asn Tyr Arg Tyr His Leu Gly Cys Asn
130 135 140

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

Asn Glu Cys Leu Trp Thr Asp Met Leu Ser Asn Phe Gly Tyr Pro Gly
165 170 175

Tyr Gln Ser Lys His Tyr Ala Cys Ile Arg Gln Lys Gly Gly Tyr Cys
180 185 190

Ser Trp Tyr Arg Gly Trp Ala Pro Pro Asp Lys Ser Ile Ile Asn Ala
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Thr Asp Pro
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            20   25   30

Asp Ala Phe Cys Asn Ser Asp Ile Val Ile Arg Ala Lys Val Val Gly
        35   40   45

Lys Lys Leu Val Lys Glu Gly Pro Phe Gly Thr Leu Val Tyr Glu Ile
    50   55   60

Lys Gln Met Lys Met Tyr Arg Gly Phe Thr Lys Met Pro Glu Val Gln
65   70   75   80

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

Val Asn Lys Tyr Gln Tyr Leu Leu Thr Gly Arg Val Tyr Asp Gly Lys
            100   105   110

Met Tyr Thr Gly Leu Cys Asn Phe Val Glu Arg Trp Asp Gln Leu Thr
        115   120   125

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Leu Ser Gln Arg Lys Gly Leu Asn Tyr Arg Tyr His Leu Gly Cys Asn
    130                 135                 140

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

Asn Glu Cys Leu Trp Thr Asp Met Leu Ser Asn Phe Gly Tyr Pro Gly
                165                 170                 175

Tyr Gln Ser Lys His Tyr Ala Cys Ile Arg Gln Lys Gly Gly Tyr Cys
            180                 185                 190

Ser Trp Tyr Arg Gly Trp Ala Pro Pro Asp Lys Ser Ile Ile Asn Ala
        195                 200                 205

Thr Asp Pro
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Asp Ala Phe Cys Asn Ser Asp Ile Val Ile Arg Ala Glu Val Val Gly
35 40 45

Lys Lys Leu Val Lys Glu Gly Pro Phe Gly Thr Leu Val Tyr Glu Ile
50 55 60

Lys Gln Met Lys Met Tyr Arg Gly Phe Thr Lys Met Pro Glu Val Gln
65 70 75 80

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

Val Asn Lys Tyr Gln Tyr Leu Leu Thr Gly Arg Val Tyr Asp Gly Lys
100 105 110

Met Tyr Thr Gly Leu Cys Asn Phe Val Glu Arg Trp Asp Gln Leu Thr
115 120 125

Leu Ser Gln Arg Lys Gly Leu Asn Tyr Arg Tyr His Leu Gly Cys Asn
130 135 140

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

Asn Glu Cys Leu Trp Thr Asp Met Leu Ser Asn Phe Gly Tyr Pro Gly
165 170 175

Tyr Gln Ser Lys His Tyr Ala Cys Ile Arg Gln Lys Gly Gly Tyr Cys
180 185 190

Ser Trp Tyr Arg Gly Trp Ala Pro Pro Asp Lys Ser Ile Ile Asn Ala
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Thr Asp Pro
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Asp Ala Phe Cys Asn Ser Asp Ile Val Ile Arg Ala Lys Val Val Gly
        35   40   45

Lys Lys Leu Val Lys Glu Gly Pro Phe Gly Thr Leu Val Tyr Glu Ile
    50   55   60

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Lys Gln Met Lys Met Tyr Arg Gly Phe Thr Lys Met Pro Glu Val Glu
65                  70                  75                  80

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

Val Asn Lys Tyr Gln Tyr Leu Leu Thr Gly Arg Val Tyr Asp Gly Lys
            100                 105                 110

Met Tyr Thr Gly Leu Cys Asn Phe Val Glu Arg Trp Asp Gln Leu Thr
        115                 120                 125

Leu Ser Gln Arg Lys Gly Leu Asn Tyr Arg Tyr His Leu Gly Cys Asn
    130                 135                 140

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

Asn Glu Cys Leu Trp Thr Asp Met Leu Ser Asn Phe Gly Tyr Pro Gly
                165                 170                 175

Tyr Gln Ser Lys His Tyr Ala Cys Ile Arg Gln Lys Gly Gly Tyr Cys
            180                 185                 190

Ser Trp Tyr Arg Gly Trp Ala Pro Pro Asp Lys Ser Ile Ile Asn Ala
        195                 200                 205

Thr Asp Pro
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Asp Ala Phe Cys Asn Ser Asp Ile Val Ile Arg Ala Glu Val Val Gly
35 40 45

Lys Lys Leu Val Lys Glu Gly Pro Phe Gly Thr Leu Val Tyr Glu Ile
50 55 60

Lys Gln Met Lys Met Tyr Arg Gly Phe Thr Lys Met Pro Glu Val Glu
65 70 75 80

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

Val Asn Lys Tyr Gln Tyr Leu Leu Thr Gly Arg Val Tyr Asp Gly Lys
100 105 110

Met Tyr Thr Gly Leu Cys Asn Phe Val Glu Arg Trp Asp Gln Leu Thr
115 120 125

Leu Ser Gln Arg Lys Gly Leu Asn Tyr Arg Tyr His Leu Gly Cys Asn
130 135 140

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

Asn Glu Cys Leu Trp Thr Asp Met Leu Ser Asn Phe Gly Tyr Pro Gly
165 170 175

Tyr Gln Ser Lys His Tyr Ala Cys Ile Arg Gln Lys Gly Gly Tyr Cys
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Ser Trp Tyr Arg Gly Trp Ala Pro Pro Asp Lys Ser Ile Ile Asn Ala
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Thr Asp Pro
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Asp Ala Phe Cys Asn Ser Asp Ile Val Ile Arg Ala Lys Val Val Gly
        35                  40                  45

Lys Lys Leu Val Lys Glu Gly Pro Phe Gly Thr Leu Val Tyr Glu Ile
    50                  55                  60

Lys Gln Met Lys Met Tyr Arg Gly Phe Glu Lys Met Pro Glu Val Gln
65                  70                  75                  80

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

Val Asn Lys Tyr Gln Tyr Leu Leu Thr Gly Arg Val Tyr Asp Gly Lys
            100                 105                 110

Met Tyr Thr Gly Leu Cys Asn Phe Val Glu Arg Trp Asp Gln Leu Thr
        115                 120                 125

Leu Ser Gln Arg Lys Gly Leu Asn Tyr Arg Tyr His Leu Gly Cys Asn
    130                 135                 140

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

Asn Glu Cys Leu Trp Thr Asp Met Leu Ser Asn Phe Gly Tyr Pro Gly
                165                 170                 175

Tyr Gln Ser Lys His Tyr Ala Cys Ile Arg Gln Lys Gly Gly Tyr Cys
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Ser Trp Tyr Arg Gly Trp Ala Pro Pro Asp Lys Ser Ile Ile Asn Ala
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Thr Asp Pro
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            20   25   30

Asp Ala Phe Cys Asn Ser Asp Ile Val Ile Arg Ala Lys Val Val Gly
        35   40   45

Lys Lys Leu Val Lys Glu Gly Pro Phe Gly Thr Leu Val Tyr Glu Ile
    50   55   60

Lys Gln Met Lys Met Tyr Arg Gly Phe Glu Lys Met Pro Asp Val Gln
65   70   75   80

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

Val Asn Lys Tyr Gln Tyr Leu Leu Thr Gly Arg Val Tyr Asp Gly Lys
            100   105   110

Met Tyr Thr Gly Leu Cys Asn Phe Val Glu Arg Trp Asp Gln Leu Thr

115 120 125

Leu Ser Gln Arg Lys Gly Leu Asn Tyr Arg Tyr His Leu Gly Cys Asn
130 135 140

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

Asn Glu Cys Leu Trp Thr Asp Met Leu Ser Asn Phe Gly Tyr Pro Gly
165 170 175

Tyr Gln Ser Lys His Tyr Ala Cys Ile Arg Gln Lys Gly Gly Tyr Cys
180 185 190

Ser Trp Tyr Arg Gly Trp Ala Pro Pro Asp Lys Ser Ile Ile Asn Ala
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20 25 30

Asp Ala Phe Cys Asn Ser Asp Ile Val Ile Arg Ala Lys Val Val Gly
35 40 45

Lys Lys Thr Val Lys Glu Gly Pro Phe Gly Thr Leu Val Tyr Thr Ile
50 55 60

Lys Gln Met Lys Met Tyr Arg Gly Phe Glu Lys Met Pro Asp Val Gln
65 70 75 80

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

Val Asn Lys Tyr Gln Tyr Leu Leu Thr Gly Arg Val Tyr Asp Gly Lys
100 105 110

Met Tyr Thr Gly Leu Cys Asn Phe Val Glu Arg Trp Asp Gln Leu Thr
115 120 125

Leu Ser Gln Arg Lys Gly Leu Asn Tyr Arg Tyr His Leu Gly Cys Asn
130 135 140

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

Asn Glu Cys Leu Trp Thr Asp Met Leu Ser Asn Phe Gly Tyr Pro Gly
165 170 175

Tyr Gln Ser Lys His Tyr Ala Cys Ile Arg Gln Lys Gly Gly Tyr Cys
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Ser Trp Tyr Arg Gly Trp Ala Pro Pro Asp Lys Ser Ile Ile Asn Ala
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Thr Asp Pro
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Asp Ala Phe Cys Asn Ser Asp Ile Val Ile Arg Ala Lys Val Val Gly
        35   40   45

Lys Lys Leu Val Lys Glu Gly Pro Phe Gly Thr Leu Val Tyr Thr Ile
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Lys Gln Met Lys Met Tyr Arg Gly Phe Glu Lys Met Pro Glu Val Glu
65 70 75 80

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

Val Asn Lys Tyr Gln Tyr Leu Leu Thr Gly Arg Val Tyr Asp Gly Lys
100 105 110

Met Tyr Thr Gly Leu Cys Asn Phe Val Glu Arg Trp Asp Gln Leu Thr
115 120 125

Leu Ser Gln Arg Lys Gly Leu Asn Tyr Arg Tyr His Leu Gly Cys Asn
130 135 140

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

Asn Glu Cys Leu Trp Thr Asp Met Leu Ser Asn Phe Gly Tyr Pro Gly
165 170 175

Tyr Gln Ser Lys His Tyr Ala Cys Ile Arg Gln Lys Gly Gly Tyr Cys
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Thr Asp Pro
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Asp Ala Phe Cys Asn Ser Asp Ile Val Ile Arg Ala Lys Val Val Gly
35 40 45

Lys Lys Leu Val Lys Glu Gly Pro Phe Gly Thr Leu Val Tyr Thr Ile
50 55 60

Lys Gln Met Lys Met Tyr Arg Gly Phe Glu Lys Met Pro Asp Val Glu
65 70 75 80

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

Val Asn Lys Tyr Gln Tyr Leu Leu Thr Gly Arg Val Tyr Asp Gly Lys
100 105 110

Met Tyr Thr Gly Leu Cys Asn Phe Val Glu Arg Trp Asp Gln Leu Thr
115 120 125

Leu Ser Gln Arg Lys Gly Leu Asn Tyr Arg Tyr His Leu Gly Cys Asn
130 135 140

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

Asn Glu Cys Leu Trp Thr Asp Met Leu Ser Asn Phe Gly Tyr Pro Gly
165 170 175

Tyr Gln Ser Lys His Tyr Ala Cys Ile Arg Gln Lys Gly Gly Tyr Cys
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Ser Trp Tyr Arg Gly Trp Ala Pro Pro Asp Lys Ser Ile Ile Asn Ala
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Thr Asp Pro
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Asp Ala Phe Cys Asn Ser Asp Ile Val Ile Arg Ala Asn Val Thr Gly
35 40 45

Lys Lys Leu Val Lys Glu Gly Pro Phe Gly Thr Leu Val Tyr Glu Ile
50 55 60

Lys Gln Met Lys Met Tyr Arg Gly Phe Glu Lys Met Pro Glu Val Gln
65 70 75 80

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

Val Asn Lys Tyr Gln Tyr Leu Leu Thr Gly Arg Val Tyr Asp Gly Lys
100 105 110

Met Tyr Thr Gly Leu Cys Asn Phe Val Glu Arg Trp Asp Gln Leu Thr
115 120 125

Leu Ser Gln Arg Lys Gly Leu Asn Tyr Arg Tyr His Leu Gly Cys Asn
130 135 140

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

Asn Glu Cys Leu Trp Thr Asp Met Leu Ser Asn Phe Gly Tyr Pro Gly
165 170 175

Tyr Gln Ser Lys His Tyr Ala Cys Ile Arg Gln Lys Gly Gly Tyr Cys
180 185 190

Ser Trp Tyr Arg Gly Trp Ala Pro Pro Asp Lys Ser Ile Ile Asn Ala
195 200 205

Thr Asp Pro
210

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Xaa Xaa Xaa Xaa Xaa Xaa Xaa Cys Thr Cys Ser Pro Ser His Pro Gln
20 25 30

Asp Ala Phe Cys Asn Ser Asp Ile Val Ile Arg Ala Lys Val Val Gly
35 40 45

Asn Lys Thr Val Lys Glu Gly Pro Phe Gly Thr Leu Val Tyr Glu Ile
50 55 60

Lys Gln Met Lys Met Tyr Arg Gly Phe Glu Lys Met Pro Glu Val Gln
65 70 75 80

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

Val Asn Lys Tyr Gln Tyr Leu Leu Thr Gly Arg Val Tyr Asp Gly Lys
100 105 110

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Met Tyr Thr Gly Leu Cys Asn Phe Val Glu Arg Trp Asp Gln Leu Thr
        115                 120                 125

Leu Ser Gln Arg Lys Gly Leu Asn Tyr Arg Tyr His Leu Gly Cys Asn
    130                 135                 140

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

Asn Glu Cys Leu Trp Thr Asp Met Leu Ser Asn Phe Gly Tyr Pro Gly
                165                 170                 175

Tyr Gln Ser Lys His Tyr Ala Cys Ile Arg Gln Lys Gly Gly Tyr Cys
            180                 185                 190

Ser Trp Tyr Arg Gly Trp Ala Pro Pro Asp Lys Ser Ile Ile Asn Ala
        195                 200                 205

Thr Asp Pro
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            20   25   30

Asp Ala Phe Cys Asn Ser Asp Ile Val Ile Arg Ala Glu Val Val Gly
        35   40   45

Asn Lys Thr Val Lys Glu Gly Pro Phe Gly Thr Leu Val Tyr Glu Ile
    50   55   60

Lys Gln Met Lys Met Tyr Arg Gly Phe Thr Lys Met Pro His Val Gln
65   70   75   80

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

Val Asn Lys Tyr Gln Tyr Leu Leu Thr Gly Arg Val Tyr Asp Gly Lys
            100   105   110

Met Tyr Thr Gly Leu Cys Asn Phe Val Glu Arg Trp Asp Gln Leu Thr
        115   120   125

Leu Ser Gln Arg Lys Gly Leu Asn Tyr Arg Tyr His Leu Gly Cys Asn
    130   135   140

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

Asn Glu Cys Leu Trp Thr Asp Met Leu Ser Asn Phe Gly Tyr Pro Gly
                165   170   175

Tyr Gln Ser Lys His Tyr Ala Cys Ile Arg Gln Lys Gly Gly Tyr Cys
            180   185   190

Ser Trp Tyr Arg Gly Trp Ala Pro Pro Asp Lys Ser Ile Ile Asn Ala
        195   200   205

Thr Asp Pro
    210

<210> 21
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            20   25   30

Asp Ala Phe Cys Asn Ser Asp Ile Val Ile Arg Ala Lys Val Val Gly
        35   40   45

Asn Lys Thr Val Lys Glu Gly Pro Phe Gly Thr Leu Val Tyr Thr Ile
    50   55   60

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Lys Gln Met Lys Met Tyr Arg Gly Phe Glu Lys Met Pro Glu Val Gln
65                  70                  75                  80

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

Val Asn Lys Tyr Gln Tyr Leu Leu Thr Gly Arg Val Tyr Asp Gly Lys
            100                 105                 110

Met Tyr Thr Gly Leu Cys Asn Phe Val Glu Arg Trp Asp Gln Leu Thr
        115                 120                 125

Leu Ser Gln Arg Lys Gly Leu Asn Tyr Arg Tyr His Leu Gly Cys Asn
    130                 135                 140

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

Asn Glu Cys Leu Trp Thr Asp Met Leu Ser Asn Phe Gly Tyr Pro Gly
                165                 170                 175

Tyr Gln Ser Lys His Tyr Ala Cys Ile Arg Gln Lys Gly Gly Tyr Cys
            180                 185                 190

Ser Trp Tyr Arg Gly Trp Ala Pro Pro Asp Lys Ser Ile Ile Asn Ala
        195                 200                 205

Thr Asp Pro
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20 25 30

Asp Ala Phe Cys Asn Ser Asp Ile Val Ile Arg Ala Ser Val Val Gly
35 40 45

Lys Lys Leu Val Lys Glu Gly Pro Phe Gly Thr Leu Val Tyr Thr Ile
50 55 60

Lys Gln Met Lys Met Tyr Arg Gly Phe Thr Lys Met Pro His Val Gln
65 70 75 80

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

Val Asn Lys Tyr Gln Tyr Leu Leu Thr Gly Arg Val Tyr Asp Gly Lys
100 105 110

Met Tyr Thr Gly Leu Cys Asn Phe Val Glu Arg Trp Asp Gln Leu Thr
115 120 125

Leu Ser Gln Arg Lys Gly Leu Asn Tyr Arg Tyr His Leu Gly Cys Asn
130 135 140

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

Asn Glu Cys Leu Trp Thr Asp Met Leu Ser Asn Phe Gly Tyr Pro Gly

165 170 175

Tyr Gln Ser Lys His Tyr Ala Cys Ile Arg Gln Lys Gly Gly Tyr Cys
180 185 190

Ser Trp Tyr Arg Gly Trp Ala Pro Pro Asp Lys Ser Ile Ile Asn Ala
195 200 205

Thr Asp Pro
210

<210> 23
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20 25 30

Asp Ala Phe Cys Asn Ser Asp Ile Val Ile Arg Ala Ser Val Val Gly
35 40 45

Lys Lys Leu Val Lys Glu Gly Pro Asn Gly Thr Leu Val Tyr Thr Ile
50 55 60

Lys Gln Met Lys Met Tyr Arg Gly Phe Thr Lys Met Pro His Val Gln
65 70 75 80

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

Val Asn Lys Tyr Gln Tyr Leu Leu Thr Gly Arg Val Tyr Asp Gly Lys
100 105 110

Met Tyr Thr Gly Leu Cys Asn Phe Val Glu Arg Trp Asp Gln Leu Thr
115 120 125

Leu Ser Gln Arg Lys Gly Leu Asn Tyr Arg Tyr His Leu Gly Cys Asn
130 135 140

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

Asn Glu Cys Leu Trp Thr Asp Met Leu Ser Asn Phe Gly Tyr Pro Gly
165 170 175

Tyr Gln Ser Lys His Tyr Ala Cys Ile Arg Gln Lys Gly Gly Tyr Cys
180 185 190

Ser Trp Tyr Arg Gly Trp Ala Pro Pro Asp Lys Ser Ile Ile Asn Ala
195 200 205

Thr Asp Pro
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            20   25   30

Asp Ala Phe Cys Asn Ser Asp Ile Val Ile Arg Ala Ser Val Val Gly
        35   40   45

Lys Lys Leu Val Lys Glu Gly Pro Asn Gly Thr Leu Val Tyr Thr Ile
    50   55   60

Lys Gln Met Lys Met Tyr Arg Gly Phe Thr Lys Met Pro His Val Gln
65   70   75   80

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

Val Asn Lys Tyr Gln Tyr Leu Leu Thr Gly Arg Val Tyr Asp Gly Lys
            100   105   110

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Met Tyr Thr Gly Leu Cys Asn Phe Val Glu Arg Trp Asp Gln Leu Thr
        115                 120                 125

Leu Ser Gln Arg Ser Gly Leu Asn Tyr Arg Tyr His Leu Gly Cys Asn
    130                 135                 140

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

Asn Glu Cys Leu Trp Thr Asp Met Leu Ser Asn Phe Gly Tyr Pro Gly
                165                 170                 175

Tyr Gln Ser Lys His Tyr Ala Cys Ile Arg Gln Lys Gly Gly Tyr Cys
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Thr Asp Pro
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        35                  40                  45

Lys Lys Leu Val Lys Glu Gly Pro Phe Gly Thr Leu Val Tyr Thr Ile
    50                  55                  60

Lys Gln Met Lys Met Tyr Arg Gly Phe Glu Lys Met Pro Asp Val Glu
65                  70                  75                  80

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

Val Asn Lys Tyr Gln Tyr Leu Leu Thr Gly Arg Val Tyr Asp Gly Lys
            100                 105                 110

Met Tyr Thr Gly Leu Cys Asn Phe Val Glu Arg Trp Asp Gln Leu Thr
        115                 120                 125

Leu Ser Gln Arg Lys Gly Leu Asn Tyr Arg Tyr His Leu Gly Cys Asn
    130                 135                 140

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

Asn Glu Cys Leu Trp Thr Asp Met Leu Ser Asn Phe Gly Tyr Pro Gly
                165                 170                 175

Tyr Gln Ser Lys His Tyr Ala Cys Ile Arg Gln Lys Gly Gly Tyr Cys
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Thr Asp Pro
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20 25 30

Asp Ala Phe Cys Asn Ser Asp Ile Val Ile Arg Ala Asn Val Thr Gly
35 40 45

Lys Lys Leu Val Lys Glu Gly Pro Phe Gly Thr Leu Val Tyr Thr Ile

50 55 60

Lys Gln Met Lys Met Tyr Arg Gly Phe Thr Lys Met Pro His Val Gln
65 70 75 80

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

Val Asn Lys Tyr Gln Tyr Leu Leu Thr Gly Arg Val Tyr Asp Gly Lys
100 105 110

Met Tyr Thr Gly Leu Cys Asn Phe Val Glu Arg Trp Asp Gln Leu Thr
115 120 125

Leu Ser Gln Arg Lys Gly Leu Asn Tyr Arg Tyr His Leu Gly Cys Asn
130 135 140

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

Asn Glu Cys Leu Trp Thr Asp Met Leu Ser Asn Phe Gly Tyr Pro Gly
165 170 175

Tyr Gln Ser Lys His Tyr Ala Cys Ile Arg Gln Lys Gly Gly Tyr Cys
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Asp Ala Phe Cys Asn Ser Asp Ile Val Ile Arg Ala Lys Val Val Gly
        35   40   45

Asn Lys Thr Val Lys Glu Gly Pro Phe Gly Thr Leu Val Tyr Thr Ile
    50   55   60

Lys Gln Met Lys Met Tyr Arg Gly Phe Thr Lys Met Pro His Val Gln
65   70   75   80

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

Val Asn Lys Tyr Gln Tyr Leu Leu Thr Gly Arg Val Tyr Asp Gly Lys
            100   105   110

Met Tyr Thr Gly Leu Cys Asn Phe Val Glu Arg Trp Asp Gln Leu Thr
        115   120   125

Leu Ser Gln Arg Lys Gly Leu Asn Tyr Arg Tyr His Leu Gly Cys Asn
    130   135   140

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

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Asn Glu Cys Leu Trp Thr Asp Met Leu Ser Asn Phe Gly Tyr Pro Gly
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Tyr Gln Ser Lys His Tyr Ala Cys Ile Arg Gln Lys Gly Gly Tyr Cys
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Thr Asp Pro
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Asp Ala Phe Cys Asn Ser Asp Ile Val Ile Arg Ala Lys Val Val Gly
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Ser Lys Leu Val Lys Glu Gly Pro Asn Gly Thr Leu Val Tyr Thr Ile
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Lys Gln Met Lys Met Tyr Arg Gly Phe Thr Lys Met Pro His Val Gln
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Tyr Ile His Thr Glu Ala Ser Glu Ser Leu Cys Gly Leu Lys Leu Glu
85 90 95

Val Asn Lys Tyr Gln Tyr Leu Leu Thr Gly Arg Val Tyr Asp Gly Lys
100 105 110

Met Tyr Thr Gly Leu Cys Asn Phe Val Glu Arg Trp Asp Gln Leu Thr
115 120 125

Leu Ser Gln Arg Lys Gly Leu Asn Tyr Arg Tyr His Leu Gly Cys Asn
130 135 140

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

Asn Glu Cys Leu Trp Thr Asp Met Leu Ser Asn Phe Gly Tyr Pro Gly
165 170 175

Tyr Gln Ser Lys His Tyr Ala Cys Ile Arg Gln Lys Gly Gly Tyr Cys
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        35   40   45

Ser Lys Leu Val Lys Glu Gly Pro Asn Gly Thr Leu Val Tyr Thr Ile
    50   55   60

Lys Gln Met Ser Met Tyr Arg Gly Phe Thr Lys Met Pro His Val Gln
65   70   75   80

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

Val Asn Lys Tyr Gln Tyr Leu Leu Thr Gly Arg Val Tyr Asp Gly Lys
            100   105   110

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Met Tyr Thr Gly Leu Cys Asn Phe Val Glu Arg Trp Asp Gln Leu Thr
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Cys Lys Ile Lys Ser Cys Tyr Tyr Leu Pro Cys Phe Val Thr Ser Lys
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Asn Glu Cys Leu Trp Thr Asp Met Leu Ser Asn Phe Gly Tyr Pro Gly
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Tyr Gln Ser Lys His Tyr Ala Cys Ile Arg Gln Lys Gly Gly Tyr Cys
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Ser Trp Tyr Arg Gly Trp Ala Pro Pro Asp Lys Ser Ile Ile Asn Ala
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Thr Asp Pro
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Tyr Ile His Thr Glu Ala Ser Glu Ser Leu Cys Gly Leu Lys Leu Glu
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Leu Ser Gln Arg Lys Gly Leu Asn Tyr Arg Tyr His Leu Gly Cys Asn
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Cys Lys Ile Lys Ser Cys Tyr Tyr Leu Pro Cys Phe Val Thr Ser Lys
145                 150                 155                 160

Asn Glu Cys Leu Trp Thr Asp Met Leu Ser Asn Phe Gly Tyr Pro Gly
                165                 170                 175

Tyr Gln Ser Lys His Tyr Ala Cys Ile Arg Gln Lys Gly Gly Tyr Cys
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Ser Trp Tyr Arg Gly Trp Ala Pro Pro Asp Lys Ser Ile Ile Asn Ala
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Thr Asp Pro
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Asp Ala Phe Cys Asn Ser Asp Ile Val Ile Arg Ala Lys Val Val Gly
        35   40   45

Lys Lys Leu Val Lys Glu Gly Asn Phe Thr Thr Leu Val Tyr Thr Ile
50 55 60

Lys Gln Met Lys Met Tyr Arg Gly Phe Thr Lys Met Pro His Val Gln
65 70 75 80

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

Val Asn Lys Tyr Gln Tyr Leu Leu Thr Gly Arg Val Tyr Asp Gly Lys
100 105 110

Met Tyr Thr Gly Leu Cys Asn Phe Val Glu Arg Trp Asp Gln Leu Thr
115 120 125

Leu Ser Gln Arg Lys Gly Leu Asn Tyr Arg Tyr His Leu Gly Cys Asn
130 135 140

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

Asn Glu Cys Leu Trp Thr Asp Met Leu Ser Asn Phe Gly Tyr Pro Gly
165 170 175

Tyr Gln Ser Lys His Tyr Ala Cys Ile Arg Gln Lys Gly Gly Tyr Cys
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20 25 30

Asp Ala Phe Cys Asn Ser Asp Ile Val Ile Arg Ala Lys Val Val Gly
35 40 45

Lys Lys Leu Val Lys Glu Gly Asn Phe Thr Thr Leu Val Tyr Asn Ile
50 55 60

Thr Gln Met Lys Met Tyr Arg Gly Phe Thr Lys Met Pro His Val Gln
65 70 75 80

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

Val Asn Lys Tyr Gln Tyr Leu Leu Thr Gly Arg Val Tyr Asp Gly Lys
100 105 110

Met Tyr Thr Gly Leu Cys Asn Phe Val Glu Arg Trp Asp Gln Leu Thr
115 120 125

Leu Ser Gln Arg Lys Gly Leu Asn Tyr Arg Tyr His Leu Gly Cys Asn
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Cys Lys Ile Lys Ser Cys Tyr Tyr Leu Pro Cys Phe Val Thr Ser Lys
145 150 155 160

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Asn Glu Cys Leu Trp Thr Asp Met Leu Ser Asn Phe Gly Tyr Pro Gly
                165                 170                 175

Tyr Gln Ser Lys His Tyr Ala Cys Ile Arg Gln Lys Gly Gly Tyr Cys
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Ser Trp Tyr Arg Gly Trp Ala Pro Pro Asp Lys Ser Ile Ile Asn Ala
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Thr Asp Pro
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Asp Ala Phe Cys Asn Ser Asp Ile Val Ile Arg Ala Lys Val Val Gly
35 40 45

Lys Lys Leu Val Lys Glu Gly Pro Asn Gly Thr Leu Val Tyr Thr Ile
50 55 60

Lys Gln Met Lys Met Tyr Arg Gly Phe Thr Lys Met Pro His Val Gln
65 70 75 80

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

Val Asn Lys Tyr Gln Tyr Leu Leu Thr Gly Arg Val Tyr Asp Gly Lys
100 105 110

Met Tyr Thr Gly Leu Cys Asn Phe Val Glu Arg Trp Asp Gln Leu Thr
115 120 125

Leu Ser Gln Arg Lys Gly Leu Asn Tyr Arg Tyr His Leu Gly Cys Asn
130 135 140

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

Asn Glu Cys Leu Trp Thr Asp Met Leu Ser Asn Phe Gly Tyr Pro Gly
165 170 175

Tyr Gln Ser Lys His Tyr Ala Cys Ile Arg Gln Lys Gly Gly Tyr Cys
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Asp Ala Phe Cys Asn Ser Asp Ile Val Ile Arg Ala Lys Val Val Gly
        35   40   45

Lys Lys Leu Val Lys Glu Gly Pro Asn Gly Thr Leu Val Tyr Thr Ile
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Lys Gln Met Ser Met Tyr Arg Gly Phe Thr Lys Met Pro His Val Gln
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Tyr Ile His Thr Glu Ala Ser Glu Ser Leu Cys Gly Leu Lys Leu Glu
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Val Asn Lys Tyr Gln Tyr Leu Leu Thr Gly Arg Val Tyr Asp Gly Lys

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Met Tyr Thr Gly Leu Cys Asn Phe Val Glu Arg Trp Asp Gln Leu Thr
115 120 125

Leu Ser Gln Arg Lys Gly Leu Asn Tyr Arg Tyr His Leu Gly Cys Asn
130 135 140

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

Asn Glu Cys Leu Trp Thr Asp Met Leu Ser Asn Phe Gly Tyr Pro Gly
165 170 175

Tyr Gln Ser Lys His Tyr Ala Cys Ile Arg Gln Lys Gly Gly Tyr Cys
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Asp Ala Phe Cys Asn Ser Asp Ile Val Ile Arg Ala Lys Val Val Gly
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Lys Gln Met Lys Met Tyr Arg Gly Phe Thr Lys Met Pro His Val Gln
65 70 75 80

Tyr Ile His Thr Glu Ala Ser Glu Ser Leu Cys Gly Leu Lys Leu Glu
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Val Asn Lys Tyr Gln Tyr Leu Leu Thr Gly Arg Val Tyr Asp Gly Lys
100 105 110

Met Tyr Thr Gly Leu Cys Asn Phe Val Glu Arg Trp Asp Gln Leu Thr
115 120 125

Leu Ser Gln Arg Ser Gly Leu Asn Tyr Arg Tyr His Leu Gly Cys Asn
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Cys Lys Ile Lys Ser Cys Tyr Tyr Leu Pro Cys Phe Val Thr Ser Lys
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Asn Glu Cys Leu Trp Thr Asp Met Leu Ser Asn Phe Gly Tyr Pro Gly
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Tyr Gln Ser Lys His Tyr Ala Cys Ile Arg Gln Lys Gly Gly Tyr Cys
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Asp Ala Phe Cys Asn Ser Asp Ile Val Ile Arg Ala Lys Val Val Gly
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Thr Gln Met Lys Met Tyr Arg Gly Phe Thr Lys Met Pro His Val Gln
65                  70                  75                  80

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

Val Asn Lys Tyr Gln Tyr Leu Leu Thr Gly Arg Val Tyr Asp Gly Lys
            100                 105                 110

Met Tyr Thr Gly Leu Cys Asn Phe Val Glu Arg Trp Asp Gln Leu Thr
        115                 120                 125

Leu Ser Gln Arg Lys Gly Leu Asn Tyr Arg Tyr His Leu Gly Cys Asn
    130                 135                 140

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

Asn Glu Cys Leu Trp Thr Asp Met Leu Ser Asn Phe Gly Tyr Pro Gly
                165                 170                 175

Tyr Gln Ser Lys His Tyr Ala Cys Ile Arg Gln Lys Gly Gly Tyr Cys
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Ser Trp Tyr Arg Gly Trp Ala Pro Pro Asp Lys Ser Ile Ile Asn Ala
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Thr Asp Pro
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Asp Ala Phe Cys Asn Ser Asp Ile Val Ile Arg Ala Lys Val Val Gly
35 40 45

Lys Lys Leu Val Lys Glu Gly Pro Phe Gly Thr Leu Val Tyr Thr Ile
50 55 60

Asn Gln Thr Lys Met Tyr Arg Gly Phe Thr Lys Met Pro His Val Gln
65 70 75 80

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

Val Asn Lys Tyr Gln Tyr Leu Leu Thr Gly Arg Val Tyr Asp Gly Lys
100 105 110

Met Tyr Thr Gly Leu Cys Asn Phe Val Glu Arg Trp Asp Gln Leu Thr
115 120 125

Leu Ser Gln Arg Lys Gly Leu Asn Tyr Arg Tyr His Leu Gly Cys Asn
130 135 140

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

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Asn Glu Cys Leu Trp Thr Asp Met Leu Ser Asn Phe Gly Tyr Pro Gly
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Tyr Gln Ser Lys His Tyr Ala Cys Ile Arg Gln Lys Gly Gly Tyr Cys
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Thr Asp Pro
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Xaa Xaa Xaa Xaa Xaa Xaa Xaa Cys Thr Cys Ser Pro Ser His Pro Gln
20 25 30

Asp Ala Phe Cys Asn Ser Asp Ile Val Ile Arg Ala Lys Val Val Gly
35 40 45

Lys Lys Leu Val Lys Glu Gly Pro Phe Gly Thr Leu Val Tyr Thr Ile
50 55 60

Lys Gln Met Lys Met Tyr Arg Gly Phe Thr Asn Met Thr His Val Gln
65 70 75 80

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

Val Asn Lys Tyr Gln Tyr Leu Leu Thr Gly Arg Val Tyr Asp Gly Lys
100 105 110

Met Tyr Thr Gly Leu Cys Asn Phe Val Glu Arg Trp Asp Gln Leu Thr
115 120 125

Leu Ser Gln Arg Lys Gly Leu Asn Tyr Arg Tyr His Leu Gly Cys Asn
130 135 140

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

Asn Glu Cys Leu Trp Thr Asp Met Leu Ser Asn Phe Gly Tyr Pro Gly
165 170 175

Tyr Gln Ser Lys His Tyr Ala Cys Ile Arg Gln Lys Gly Gly Tyr Cys
180 185 190

Ser Trp Tyr Arg Gly Trp Ala Pro Pro Asp Lys Ser Ile Ile Asn Ala
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Thr Asp Pro
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            20   25   30

Asp Ala Phe Cys Asn Ser Asp Ile Val Ile Arg Ala Lys Val Val Gly
        35   40   45

Lys Lys Leu Val Lys Glu Gly Pro Phe Gly Thr Leu Val Tyr Thr Ile
    50   55   60

Lys Gln Met Lys Met Tyr Arg Gly Phe Thr Lys Met Pro Asn Val Thr
65   70   75   80

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

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Val Asn Lys Tyr Gln Tyr Leu Leu Thr Gly Arg Val Tyr Asp Gly Lys
            100                 105                 110

Met Tyr Thr Gly Leu Cys Asn Phe Val Glu Arg Trp Asp Gln Leu Thr
        115                 120                 125

Leu Ser Gln Arg Lys Gly Leu Asn Tyr Arg Tyr His Leu Gly Cys Asn
    130                 135                 140

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

Asn Glu Cys Leu Trp Thr Asp Met Leu Ser Asn Phe Gly Tyr Pro Gly
                165                 170                 175

Tyr Gln Ser Lys His Tyr Ala Cys Ile Arg Gln Lys Gly Gly Tyr Cys
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Ser Trp Tyr Arg Gly Trp Ala Pro Pro Asp Lys Ser Ile Ile Asn Ala
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Thr Asp Pro
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Asp Ala Phe Cys Asn Ser Asp Ile Val Ile Arg Ala Lys Val Val Gly
35 40 45

Lys Lys Leu Val Lys Glu Gly Pro Phe Gly Thr Leu Val Tyr Thr Ile
50 55 60

Lys Gln Met Lys Met Tyr Arg Gly Phe Thr Lys Met Pro His Val Gln
65 70 75 80

Tyr Ile His Thr Glu Ala Ser Glu Ser Leu Cys Gly Leu Asn Leu Thr
85 90 95

Val Asn Lys Tyr Gln Tyr Leu Leu Thr Gly Arg Val Tyr Asp Gly Lys
100 105 110

Met Tyr Thr Gly Leu Cys Asn Phe Val Glu Arg Trp Asp Gln Leu Thr
115 120 125

Leu Ser Gln Arg Lys Gly Leu Asn Tyr Arg Tyr His Leu Gly Cys Asn
130 135 140

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

Asn Glu Cys Leu Trp Thr Asp Met Leu Ser Asn Phe Gly Tyr Pro Gly
165 170 175

Tyr Gln Ser Lys His Tyr Ala Cys Ile Arg Gln Lys Gly Gly Tyr Cys
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Ser Trp Tyr Arg Gly Trp Ala Pro Pro Asp Lys Ser Ile Ile Asn Ala
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Thr Asp Pro
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Asp Ala Phe Cys Asn Ser Asp Ile Val Ile Arg Ala Lys Val Val Gly
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Lys Lys Leu Val Lys Glu Gly Pro Phe Gly Thr Leu Val Tyr Thr Ile
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Lys Gln Met Lys Met Tyr Arg Gly Phe Thr Lys Met Pro His Val Gln
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Tyr Ile His Thr Glu Ala Ser Glu Ser Leu Cys Gly Leu Lys Leu Asn
                85                  90                  95

Val Thr Lys Tyr Gln Tyr Leu Leu Thr Gly Arg Val Tyr Asp Gly Lys
            100                 105                 110

Met Tyr Thr Gly Leu Cys Asn Phe Val Glu Arg Trp Asp Gln Leu Thr
        115                 120                 125

Leu Ser Gln Arg Lys Gly Leu Asn Tyr Arg Tyr His Leu Gly Cys Asn
    130                 135                 140

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

Asn Glu Cys Leu Trp Thr Asp Met Leu Ser Asn Phe Gly Tyr Pro Gly
                165                 170                 175

Tyr Gln Ser Lys His Tyr Ala Cys Ile Arg Gln Lys Gly Gly Tyr Cys
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Thr Asp Pro
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Asp Ala Phe Cys Asn Ser Asp Ile Val Ile Arg Ala Lys Val Val Gly
35 40 45

Lys Lys Leu Val Lys Glu Gly Pro Phe Gly Thr Leu Val Tyr Thr Ile
50 55 60

Lys Gln Met Lys Met Tyr Arg Gly Phe Thr Lys Met Pro His Val Gln
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Tyr Ile His Thr Glu Ala Ser Glu Ser Leu Cys Gly Leu Lys Leu Glu
85 90 95

Asn Asn Thr Tyr Gln Tyr Leu Leu Thr Gly Arg Val Tyr Asp Gly Lys
100 105 110

Met Tyr Thr Gly Leu Cys Asn Phe Val Glu Arg Trp Asp Gln Leu Thr
115 120 125

Leu Ser Gln Arg Lys Gly Leu Asn Tyr Arg Tyr His Leu Gly Cys Asn
130 135 140

Cys Lys Ile Lys Ser Cys Tyr Tyr Leu Pro Cys Phe Val Thr Ser Lys

145 150 155 160

Asn Glu Cys Leu Trp Thr Asp Met Leu Ser Asn Phe Gly Tyr Pro Gly
165 170 175

Tyr Gln Ser Lys His Tyr Ala Cys Ile Arg Gln Lys Gly Gly Tyr Cys
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Ser Trp Tyr Arg Gly Trp Ala Pro Pro Asp Lys Ser Ile Ile Asn Ala
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Thr Asp Pro
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20 25 30

Asp Ala Phe Cys Asn Ser Asp Ile Val Ile Arg Ala Lys Val Val Gly
35 40 45

Lys Lys Leu Val Lys Glu Gly Pro Phe Gly Thr Leu Val Tyr Thr Ile
50 55 60

Lys Gln Met Lys Met Tyr Arg Gly Phe Thr Lys Met Pro His Val Gln
65 70 75 80

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

Val Asn Lys Tyr Gln Tyr Leu Leu Thr Gly Arg Val Tyr Asn Gly Thr
100 105 110

Met Tyr Thr Gly Leu Cys Asn Phe Val Glu Arg Trp Asp Gln Leu Thr
115 120 125

Leu Ser Gln Arg Lys Gly Leu Asn Tyr Arg Tyr His Leu Gly Cys Asn
130 135 140

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

Asn Glu Cys Leu Trp Thr Asp Met Leu Ser Asn Phe Gly Tyr Pro Gly
165 170 175

Tyr Gln Ser Lys His Tyr Ala Cys Ile Arg Gln Lys Gly Gly Tyr Cys
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Ser Trp Tyr Arg Gly Trp Ala Pro Pro Asp Lys Ser Ile Ile Asn Ala
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Thr Asp Pro
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20 25 30

Asp Ala Phe Cys Asn Ser Asp Ile Val Ile Arg Ala Lys Val Val Gly
35 40 45

Lys Lys Leu Val Lys Glu Gly Pro Phe Gly Thr Leu Val Tyr Thr Ile
50 55 60

Lys Gln Met Lys Met Tyr Arg Gly Phe Thr Lys Met Pro His Val Gln
65 70 75 80

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

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Val Asn Lys Tyr Gln Tyr Leu Leu Thr Gly Arg Val Tyr Asp Gly Lys
            100                 105                 110

Met Tyr Thr Gly Leu Cys Asn Phe Val Glu Arg Trp Asp Asn Leu Thr
        115                 120                 125

Leu Ser Gln Arg Lys Gly Leu Asn Tyr Arg Tyr His Leu Gly Cys Asn
    130                 135                 140

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

Asn Glu Cys Leu Trp Thr Asp Met Leu Ser Asn Phe Gly Tyr Pro Gly
                165                 170                 175

Tyr Gln Ser Lys His Tyr Ala Cys Ile Arg Gln Lys Gly Gly Tyr Cys
            180                 185                 190

Ser Trp Tyr Arg Gly Trp Ala Pro Pro Asp Lys Ser Ile Ile Asn Ala
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Thr Asp Pro
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Xaa Xaa Xaa Xaa Xaa Xaa Xaa Cys Thr Cys Ser Pro Ser His Pro Gln
20 25 30

Asp Ala Phe Cys Asn Ser Asp Ile Val Ile Arg Ala Lys Val Val Gly
35 40 45

Lys Lys Leu Val Lys Glu Gly Pro Phe Gly Thr Leu Val Tyr Thr Ile
50 55 60

Lys Gln Met Lys Met Tyr Arg Gly Phe Thr Lys Met Pro His Val Gln
65 70 75 80

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

Val Asn Lys Tyr Gln Tyr Leu Leu Thr Gly Arg Val Tyr Asp Gly Lys
100 105 110

Met Tyr Thr Gly Leu Cys Asn Phe Val Glu Arg Trp Asp Gln Leu Thr
115 120 125

Leu Ser Gln Arg Lys Gly Leu Asn Tyr Thr Tyr His Leu Gly Cys Asn
130 135 140

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

Asn Glu Cys Leu Trp Thr Asp Met Leu Ser Asn Phe Gly Tyr Pro Gly
165 170 175

Tyr Gln Ser Lys His Tyr Ala Cys Ile Arg Gln Lys Gly Gly Tyr Cys
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Ser Trp Tyr Arg Gly Trp Ala Pro Pro Asp Lys Ser Ile Ile Asn Ala
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Thr Asp Pro
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            20   25   30

Asp Ala Phe Cys Asn Ser Asp Ile Val Ile Arg Ala Lys Val Val Gly

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        35                  40                  45

Lys Lys Leu Val Lys Glu Gly Pro Phe Gly Thr Leu Val Tyr Thr Ile
    50                  55                  60

Lys Gln Met Lys Met Tyr Arg Gly Phe Thr Lys Met Pro His Val Gln
65                  70                  75                  80

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

Val Asn Lys Tyr Gln Tyr Leu Leu Thr Gly Arg Val Tyr Asp Gly Lys
            100                 105                 110

Met Tyr Thr Gly Leu Cys Asn Phe Val Glu Arg Trp Asp Gln Leu Thr
        115                 120                 125

Leu Ser Gln Arg Lys Gly Leu Asn Tyr Asn Tyr Thr Leu Gly Cys Asn
    130                 135                 140

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

Asn Glu Cys Leu Trp Thr Asp Met Leu Ser Asn Phe Gly Tyr Pro Gly
                165                 170                 175

Tyr Gln Ser Lys His Tyr Ala Cys Ile Arg Gln Lys Gly Gly Tyr Cys
            180                 185                 190

Ser Trp Tyr Arg Gly Trp Ala Pro Pro Asp Lys Ser Ile Ile Asn Ala
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Thr Asp Pro
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            20   25   30

Asp Ala Phe Cys Asn Ser Asp Ile Val Ile Arg Ala Lys Val Val Gly
        35   40   45

Lys Lys Leu Val Lys Glu Gly Pro Phe Gly Thr Leu Val Tyr Thr Ile
    50   55   60

Lys Gln Met Lys Met Tyr Arg Gly Phe Thr Lys Met Pro His Val Gln
65   70   75   80

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

Val Asn Lys Tyr Gln Tyr Leu Leu Thr Gly Arg Val Tyr Asp Gly Lys
            100   105   110

Met Tyr Thr Gly Leu Cys Asn Phe Val Glu Arg Trp Asp Gln Leu Thr
        115   120   125

Leu Ser Gln Arg Lys Gly Leu Asn Tyr Arg Tyr His Leu Gly Cys Asn
    130   135   140

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Cys Lys Ile Lys Ser Cys Tyr Tyr Leu Pro Cys Phe Val Asn Ser Thr
145                 150                 155                 160

Asn Glu Cys Leu Trp Thr Asp Met Leu Ser Asn Phe Gly Tyr Pro Gly
                165                 170                 175

Tyr Gln Ser Lys His Tyr Ala Cys Ile Arg Gln Lys Gly Gly Tyr Cys
            180                 185                 190

Ser Trp Tyr Arg Gly Trp Ala Pro Pro Asp Lys Ser Ile Ile Asn Ala
        195                 200                 205

Thr Asp Pro
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Xaa Xaa Xaa Xaa Xaa Xaa Xaa Cys Thr Cys Ser Pro Ser His Pro Gln
            20                  25                  30

Asp Ala Phe Cys Asn Ser Asp Ile Val Ile Arg Ala Lys Val Val Gly
        35                  40                  45

Lys Lys Leu Val Lys Glu Gly Pro Phe Gly Thr Leu Val Tyr Thr Ile
    50                  55                  60

Lys Gln Met Lys Met Tyr Arg Gly Phe Thr Lys Met Pro His Val Gln
65                  70                  75                  80

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

Val Asn Lys Tyr Gln Tyr Leu Leu Thr Gly Arg Val Tyr Asp Gly Lys
            100                 105                 110

Met Tyr Thr Gly Leu Cys Asn Phe Val Glu Arg Trp Asp Gln Leu Thr
        115                 120                 125

Leu Ser Gln Arg Lys Gly Leu Asn Tyr Arg Tyr His Leu Gly Cys Asn
    130                 135                 140

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

Asn Glu Cys Leu Trp Asn Asp Thr Leu Ser Asn Phe Gly Tyr Pro Gly
                165                 170                 175

Tyr Gln Ser Lys His Tyr Ala Cys Ile Arg Gln Lys Gly Gly Tyr Cys
            180                 185                 190

Ser Trp Tyr Arg Gly Trp Ala Pro Pro Asp Lys Ser Ile Ile Asn Ala
        195                 200                 205

Thr Asp Pro
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            20   25   30

Asp Ala Phe Cys Asn Ser Asp Ile Val Ile Arg Ala Lys Val Val Gly
        35   40   45

Lys Lys Leu Val Lys Glu Gly Pro Phe Gly Thr Leu Val Tyr Thr Ile
    50   55   60

Lys Gln Met Lys Met Tyr Arg Gly Phe Thr Lys Met Pro His Val Gln
65   70   75   80

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

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Val Asn Lys Tyr Gln Tyr Leu Leu Thr Gly Arg Val Tyr Asp Gly Lys
            100                 105                 110

Met Tyr Thr Gly Leu Cys Asn Phe Val Glu Arg Trp Asp Gln Leu Thr
        115                 120                 125

Leu Ser Gln Arg Lys Gly Leu Asn Tyr Arg Tyr His Leu Gly Cys Asn
    130                 135                 140

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

Asn Glu Cys Leu Trp Thr Asp Met Leu Ser Asn Phe Thr Tyr Pro Gly
                165                 170                 175

Tyr Gln Ser Lys His Tyr Ala Cys Ile Arg Gln Lys Gly Gly Tyr Cys
            180                 185                 190

Ser Trp Tyr Arg Gly Trp Ala Pro Pro Asp Lys Ser Ile Ile Asn Ala
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Thr Asp Pro
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Xaa Xaa Xaa Xaa Xaa Xaa Xaa Cys Thr Cys Ser Pro Ser His Pro Gln
20 25 30

Asp Ala Phe Cys Asn Ser Asp Ile Val Ile Arg Ala Lys Val Val Gly
35 40 45

Lys Lys Leu Val Lys Glu Gly Pro Phe Gly Thr Leu Val Tyr Thr Ile
50 55 60

Lys Gln Met Lys Met Tyr Arg Gly Phe Thr Lys Met Pro His Val Gln
65 70 75 80

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

Val Asn Lys Tyr Gln Tyr Leu Leu Thr Gly Arg Val Tyr Asp Gly Lys
100 105 110

Met Tyr Thr Gly Leu Cys Asn Phe Val Glu Arg Trp Asp Gln Leu Thr
115 120 125

Leu Ser Gln Arg Lys Gly Leu Asn Tyr Arg Tyr His Leu Gly Cys Asn
130 135 140

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

Asn Glu Cys Leu Trp Thr Asp Met Leu Ser Asn Phe Gly Tyr Pro Gly
165 170 175

Tyr Gln Ser Lys Asn Tyr Thr Cys Ile Arg Gln Lys Gly Gly Tyr Cys
180 185 190

Ser Trp Tyr Arg Gly Trp Ala Pro Pro Asp Lys Ser Ile Ile Asn Ala

195 200 205

Thr Asp Pro
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            20   25   30

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Asp Ala Phe Cys Asn Ser Asp Ile Val Ile Arg Ala Lys Val Val Gly
        35                  40                  45

Lys Lys Leu Val Lys Glu Gly Pro Phe Gly Thr Leu Val Tyr Thr Ile
    50                  55                  60

Lys Gln Met Lys Met Tyr Arg Gly Phe Thr Lys Met Pro His Val Gln
65                  70                  75                  80

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

Val Asn Lys Tyr Gln Tyr Leu Leu Thr Gly Arg Val Tyr Asp Gly Lys
            100                 105                 110

Met Tyr Thr Gly Leu Cys Asn Phe Val Glu Arg Trp Asp Gln Leu Thr
        115                 120                 125

Leu Ser Gln Arg Lys Gly Leu Asn Tyr Arg Tyr His Leu Gly Cys Asn
    130                 135                 140

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

Asn Glu Cys Leu Trp Thr Asp Met Leu Ser Asn Phe Gly Tyr Pro Gly
                165                 170                 175

Tyr Gln Ser Lys His Tyr Ala Cys Ile Asn Gln Thr Gly Gly Tyr Cys
            180                 185                 190

Ser Trp Tyr Arg Gly Trp Ala Pro Pro Asp Lys Ser Ile Ile Asn Ala
        195                 200                 205

Thr Asp Pro
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            20   25   30

Asp Ala Phe Cys Asn Ser Asp Ile Val Ile Arg Ala Lys Val Val Gly
        35   40   45

Lys Lys Leu Val Lys Glu Gly Pro Phe Gly Thr Leu Val Tyr Thr Ile
    50   55   60

Lys Gln Met Lys Met Tyr Arg Gly Phe Thr Lys Met Pro His Val Gln
65   70   75   80

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

Val Asn Lys Tyr Gln Tyr Leu Leu Thr Gly Arg Val Tyr Asp Gly Lys
            100   105   110

Met Tyr Thr Gly Leu Cys Asn Phe Val Glu Arg Trp Asp Gln Leu Thr
        115   120   125

Leu Ser Gln Arg Lys Gly Leu Asn Tyr Arg Tyr His Leu Gly Cys Asn
    130   135   140

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

Asn Glu Cys Leu Trp Thr Asp Met Leu Ser Asn Phe Gly Tyr Pro Gly
                165                 170                 175

Tyr Gln Ser Lys His Tyr Ala Cys Ile Arg Gln Lys Gly Gly Tyr Cys
            180                 185                 190

Ser Trp Tyr Arg Gly Trp Ala Pro Asn Asp Thr Ser Ile Ile Asn Ala
        195                 200                 205

Thr Asp Pro
    210
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20 25 30

Asp Ala Phe Cys Asn Ser Asp Ile Val Ile Arg Ala Lys Val Val Gly
35 40 45

Lys Lys Thr Val Lys Glu Gly Pro Phe Gly Thr Leu Val Tyr Thr Ile
50 55 60

Lys Gln Met Lys Met Tyr Arg Gly Phe Glu Lys Met Pro Asp Val Gln
65 70 75 80

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

Val Asn Lys Tyr Gln Tyr Leu Leu Thr Gly Arg Val Tyr Asp Gly Lys
100 105 110

Met Tyr Thr Gly Leu Cys Asn Phe Val Glu Arg Trp Asp Gln Leu Thr
115 120 125

Leu Ser Gln Arg Lys Gly Leu Asn Tyr Arg Tyr His Leu Gly Cys Asn
130 135 140

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

Asn Glu Cys Leu Trp Thr Asp Met Leu Ser Asn Phe Gly Tyr Pro Gly
165 170 175

Tyr Gln Ser Lys His Tyr Ala Cys Ile Arg Gln Lys Gly Gly Tyr Cys
180 185 190

Ser Trp Tyr Arg Gly Trp Ala Pro Pro Asp Lys Ser Ile Ile Asn Ala
195 200 205

Thr Asp Pro
210

<210> 54
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Xaa Xaa Xaa Xaa Xaa Xaa Xaa Cys Thr Cys Ser Pro Ser His Pro Gln
            20   25   30

Asp Ala Phe Cys Asn Ser Asp Ile Val Ile Arg Ala Lys Val Val Gly
        35   40   45

Lys Lys Asn Val Thr Glu Gly Pro Phe Gly Thr Leu Val Tyr Thr Ile
    50   55   60

Lys Gln Met Lys Met Tyr Arg Gly Phe Thr Lys Met Pro His Val Gln
65   70   75   80

Tyr Ile His Thr Glu Ala Ser Glu Ser Leu Cys Gly Leu Lys Leu Glu

85 90 95

Val Asn Lys Tyr Gln Tyr Leu Leu Thr Gly Arg Val Tyr Asp Gly Lys
100 105 110

Met Tyr Thr Gly Leu Cys Asn Phe Val Glu Arg Trp Asp Gln Leu Thr
115 120 125

Leu Ser Gln Arg Lys Gly Leu Asn Tyr Arg Tyr His Leu Gly Cys Asn
130 135 140

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

Asn Glu Cys Leu Trp Thr Asp Met Leu Ser Asn Phe Gly Tyr Pro Gly
165 170 175

Tyr Gln Ser Lys His Tyr Ala Cys Ile Arg Gln Lys Gly Gly Tyr Cys
180 185 190

Ser Trp Tyr Arg Gly Trp Ala Pro Pro Asp Lys Ser Ile Ile Asn Ala
195 200 205

Thr Asp Pro
210

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<213> Artificial Sequence

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<223> Pro or any amino acid from a heterologous signal peptide

<220>
<221> MOD_RES
<222> (4)..(4)
<223> Trp or any amino acid from a heterologous signal peptide

<220>
<221> MOD_RES
<222> (5)..(5)

<223> Leu or any amino acid from a heterologous signal peptide

<220>
<221> MOD_RES
<222> (6)..(6)
<223> Gly or any amino acid from a heterologous signal peptide

<220>
<221> MOD_RES
<222> (7)..(7)
<223> Leu or any amino acid from a heterologous signal peptide

<220>
<221> MOD_RES
<222> (8)..(8)
<223> Ile or any amino acid from a heterologous signal peptide

<220>
<221> MOD_RES
<222> (9)..(9)
<223> Val or any amino acid from a heterologous signal peptide

<220>
<221> MOD_RES
<222> (10)..(11)
<223> Leu or any amino acid from a heterologous signal peptide

<220>
<221> MOD_RES
<222> (12)..(12)
<223> Gly or any amino acid from a heterologous signal peptide

<220>
<221> MOD_RES
<222> (13)..(13)
<223> Ser or any amino acid from a heterologous signal peptide

<220>
<221> MOD_RES
<222> (14)..(14)
<223> Trp or any amino acid from a heterologous signal peptide

<220>
<221> MOD_RES
<222> (15)..(15)
<223> Ser or any amino acid from a heterologous signal peptide

<220>
<221> MOD_RES
<222> (16)..(16)
<223> Leu or any amino acid from a heterologous signal peptide

<220>
<221> MOD_RES
<222> (17)..(17)
<223> Gly or any amino acid from a heterologous signal peptide

<220>
<221> MOD_RES
<222> (18)..(18)
<223> Asp or any amino acid from a heterologous signal peptide

<220>
<221> MOD_RES
<222> (19)..(19)
<223> Trp or any amino acid from a heterologous signal peptide

<220>

<221> MOD_RES
<222> (20)..(20)
<223> Gly or any amino acid from a heterologous signal peptide

<220>
<221> MOD_RES
<222> (21)..(21)
<223> Ala or any amino acid from a heterologous signal peptide

<220>
<221> MOD_RES
<222> (22)..(22)
<223> Glu or any amino acid from a heterologous signal peptide

<220>
<221> MOD_RES
<222> (23)..(23)
<223> Ala or any amino acid from a heterologous signal peptide

<400> 55

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Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa
1               5                  10                  15

Xaa Xaa Xaa Xaa Xaa Xaa Xaa Cys Thr Cys Ser Pro Ser His Pro Gln
            20                  25                  30

Asp Ala Phe Cys Asn Ser Asp Ile Val Ile Arg Ala Lys Val Val Gly
        35                  40                  45

Lys Lys Leu Val Lys Glu Gly Pro Phe Gly Thr Leu Val Tyr Thr Ile
    50                  55                  60

Lys Gln Met Lys Met Tyr Arg Gly Phe Thr Lys Met Pro His Val Gln
65                  70                  75                  80

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

Val Asn Lys Tyr Gln Tyr Leu Leu Thr Gly Arg Val Tyr Asp Gly Lys
            100                 105                 110

Met Tyr Thr Gly Leu Cys Asn Phe Val Glu Arg Trp Asp Gln Leu Thr
        115                 120                 125

Leu Ser Gln Arg Lys Gly Leu Asn Tyr Arg Tyr His Leu Gly Cys Asn
    130                 135                 140

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

Asn Glu Cys Leu Trp Thr Asp Met Leu Ser Asn Phe Gly Tyr Pro Gly
                165                 170                 175

Tyr Gln Ser Lys His Tyr Ala Cys Ile Arg Gln Lys Gly Gly Tyr Cys
            180                 185                 190
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Ser Trp Tyr Arg Gly Trp Ala Pro Pro Asp Lys Ser Ile Ile Asn Tyr
195 200 205

Thr Asp Pro
210

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

<220>
<223> Description of Artificial Sequence: Synthetic polypeptide

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<222> (1)..(1)
<223> Met or any amino acid from a heterologous signal peptide

<220>
<221> MOD_RES
<222> (2)..(2)
<223> Thr or any amino acid from a heterologous signal peptide

<220>
<221> MOD_RES
<222> (3)..(3)
<223> Pro or any amino acid from a heterologous signal peptide

<220>
<221> MOD_RES
<222> (4)..(4)
<223> Trp or any amino acid from a heterologous signal peptide

<220>
<221> MOD_RES
<222> (5)..(5)
<223> Leu or any amino acid from a heterologous signal peptide

<220>
<221> MOD_RES
<222> (6)..(6)
<223> Gly or any amino acid from a heterologous signal peptide

<220>
<221> MOD_RES
<222> (7)..(7)
<223> Leu or any amino acid from a heterologous signal peptide

<220>
<221> MOD_RES
<222> (8)..(8)
<223> Ile or any amino acid from a heterologous signal peptide

<220>
<221> MOD_RES
<222> (9)..(9)
<223> Val or any amino acid from a heterologous signal peptide

<220>
<221> MOD_RES
<222> (10)..(11)
<223> Leu or any amino acid from a heterologous signal peptide

<220>
<221> MOD_RES
<222> (12)..(12)
<223> Gly or any amino acid from a heterologous signal peptide

<220>
<221> MOD_RES
<222> (13)..(13)
<223> Ser or any amino acid from a heterologous signal peptide

<220>
<221> MOD_RES
<222> (14)..(14)
<223> Trp or any amino acid from a heterologous signal peptide

<220>
<221> MOD_RES
<222> (15)..(15)
<223> Ser or any amino acid from a heterologous signal peptide

<220>
<221> MOD_RES
<222> (16)..(16)
<223> Leu or any amino acid from a heterologous signal peptide

<220>
<221> MOD_RES
<222> (17)..(17)
<223> Gly or any amino acid from a heterologous signal peptide

<220>
<221> MOD_RES
<222> (18)..(18)
<223> Asp or any amino acid from a heterologous signal peptide

<220>
<221> MOD_RES
<222> (19)..(19)
<223> Trp or any amino acid from a heterologous signal peptide

<220>
<221> MOD_RES
<222> (20)..(20)
<223> Gly or any amino acid from a heterologous signal peptide

<220>
<221> MOD_RES
<222> (21)..(21)
<223> Ala or any amino acid from a heterologous signal peptide

<220>
<221> MOD_RES
<222> (22)..(22)
<223> Glu or any amino acid from a heterologous signal peptide

<220>
<221> MOD_RES
<222> (23)..(23)
<223> Ala or any amino acid from a heterologous signal peptide

<400> 56
Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa
1   5   10   15

Xaa Xaa Xaa Xaa Xaa Xaa Xaa Cys Thr Cys Ser Pro Ser His Pro Gln
            20   25   30

```
Asp Ala Phe Cys Asn Ser Asp Ile Val Ile Arg Ala Lys Val Val Gly
        35                  40                  45

Lys Lys Leu Val Lys Glu Gly Pro Phe Gly Thr Leu Val Tyr Thr Ile
    50                  55                  60

Lys Gln Met Lys Met Tyr Arg Gly Phe Thr Lys Met Pro His Val Gln
65                  70                  75                  80

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

Val Asn Lys Tyr Gln Tyr Leu Leu Thr Gly Arg Val Tyr Asp Gly Lys
            100                 105                 110

Met Tyr Thr Gly Leu Cys Asn Phe Val Glu Arg Trp Asp Gln Leu Thr
        115                 120                 125

Leu Ser Gln Arg Lys Gly Leu Asn Tyr Arg Tyr His Leu Gly Cys Asn
    130                 135                 140

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

Asn Glu Cys Leu Trp Thr Asp Met Leu Ser Asn Phe Gly Tyr Pro Gly
                165                 170                 175

Tyr Gln Ser Lys His Tyr Ala Cys Ile Arg Gln Lys Gly Gly Tyr Cys
            180                 185                 190

Ser Trp Tyr Arg Gly Trp Ala Pro Pro Asp Lys Ser Ile Ile Asn Val
        195                 200                 205

Thr Asp Pro
    210
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<210> 57
<211> 188
<212> PRT
<213> Homo sapiens

<220>
<223> huTIMP3(K45S, F57N, I205F, A208G)

<400> 57

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Cys Thr Cys Ser Pro Ser His Pro Gln Asp Ala Phe Cys Asn Ser Asp
1               5                   10                  15

Ile Val Ile Arg Ala Ser Val Val Gly Lys Lys Leu Val Lys Glu Gly
            20                  25                  30

Pro Asn Gly Thr Leu Val Tyr Thr Ile Lys Gln Met Lys Met Tyr Arg
```

35 40 45

Gly Phe Thr Lys Met Pro His Val Gln Tyr Ile His Thr Glu Ala Ser
50 55 60

Glu Ser Leu Cys Gly Leu Lys Leu Glu Val Asn Lys Tyr Gln Tyr Leu
65 70 75 80

Leu Thr Gly Arg Val Tyr Asp Gly Lys Met Tyr Thr Gly Leu Cys Asn
85 90 95

Phe Val Glu Arg Trp Asp Gln Leu Thr Leu Ser Gln Arg Lys Gly Leu
100 105 110

Asn Tyr Arg Tyr His Leu Gly Cys Asn Cys Lys Ile Lys Ser Cys Tyr
115 120 125

Tyr Leu Pro Cys Phe Val Thr Ser Lys Asn Glu Cys Leu Trp Thr Asp
130 135 140

Met Leu Ser Asn Phe Gly Tyr Pro Gly Tyr Gln Ser Lys His Tyr Ala
145 150 155 160

Cys Ile Arg Gln Lys Gly Gly Tyr Cys Ser Trp Tyr Arg Gly Trp Ala
165 170 175

Pro Pro Asp Lys Ser Phe Ile Asn Gly Thr Asp Pro
180 185

<210> 58
<211> 188
<212> PRT
<213> Homo sapiens

<220>
<223> huTIMP3(K45S, F57N, A208G)

<400> 58
Cys Thr Cys Ser Pro Ser His Pro Gln Asp Ala Phe Cys Asn Ser Asp
1 5 10 15

Ile Val Ile Arg Ala Ser Val Val Gly Lys Lys Leu Val Lys Glu Gly
20 25 30

Pro Asn Gly Thr Leu Val Tyr Thr Ile Lys Gln Met Lys Met Tyr Arg
35 40 45

Gly Phe Thr Lys Met Pro His Val Gln Tyr Ile His Thr Glu Ala Ser
50 55 60

Glu Ser Leu Cys Gly Leu Lys Leu Glu Val Asn Lys Tyr Gln Tyr Leu
65 70 75 80

```
Leu Thr Gly Arg Val Tyr Asp Gly Lys Met Tyr Thr Gly Leu Cys Asn
                85                  90                  95

Phe Val Glu Arg Trp Asp Gln Leu Thr Leu Ser Gln Arg Lys Gly Leu
            100                 105                 110

Asn Tyr Arg Tyr His Leu Gly Cys Asn Cys Lys Ile Lys Ser Cys Tyr
        115                 120                 125

Tyr Leu Pro Cys Phe Val Thr Ser Lys Asn Glu Cys Leu Trp Thr Asp
    130                 135                 140

Met Leu Ser Asn Phe Gly Tyr Pro Gly Tyr Gln Ser Lys His Tyr Ala
145                 150                 155                 160

Cys Ile Arg Gln Lys Gly Gly Tyr Cys Ser Trp Tyr Arg Gly Trp Ala
                165                 170                 175

Pro Pro Asp Lys Ser Ile Ile Asn Gly Thr Asp Pro
            180                 185
```

<210> 59
<211> 188
<212> PRT
<213> Homo sapiens

<220>
<223> huTIMP3(K45S, F57N, I205Y)

<400> 59

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Cys Thr Cys Ser Pro Ser His Pro Gln Asp Ala Phe Cys Asn Ser Asp
1               5                   10                  15

Ile Val Ile Arg Ala Ser Val Val Gly Lys Lys Leu Val Lys Glu Gly
            20                  25                  30

Pro Asn Gly Thr Leu Val Tyr Thr Ile Lys Gln Met Lys Met Tyr Arg
        35                  40                  45

Gly Phe Thr Lys Met Pro His Val Gln Tyr Ile His Thr Glu Ala Ser
    50                  55                  60

Glu Ser Leu Cys Gly Leu Lys Leu Glu Val Asn Lys Tyr Gln Tyr Leu
65                  70                  75                  80

Leu Thr Gly Arg Val Tyr Asp Gly Lys Met Tyr Thr Gly Leu Cys Asn
                85                  90                  95

Phe Val Glu Arg Trp Asp Gln Leu Thr Leu Ser Gln Arg Lys Gly Leu
            100                 105                 110

Asn Tyr Arg Tyr His Leu Gly Cys Asn Cys Lys Ile Lys Ser Cys Tyr
```

```
        115                 120                 125

Tyr Leu Pro Cys Phe Val Thr Ser Lys Asn Glu Cys Leu Trp Thr Asp
    130                 135                 140

Met Leu Ser Asn Phe Gly Tyr Pro Gly Tyr Gln Ser Lys His Tyr Ala
145                 150                 155                 160

Cys Ile Arg Gln Lys Gly Gly Tyr Cys Ser Trp Tyr Arg Gly Trp Ala
                165                 170                 175

Pro Pro Asp Lys Ser Tyr Ile Asn Ala Thr Asp Pro
            180                 185

<210> 60
<211> 188
<212> PRT
<213> Homo sapiens

<220>
<223> huTIMP3(K45S, F57N, I205Y, A208G)

<400> 60
Cys Thr Cys Ser Pro Ser His Pro Gln Asp Ala Phe Cys Asn Ser Asp
1               5                   10                  15

Ile Val Ile Arg Ala Ser Val Val Gly Lys Lys Leu Val Lys Glu Gly
            20                  25                  30

Pro Asn Gly Thr Leu Val Tyr Thr Ile Lys Gln Met Lys Met Tyr Arg
        35                  40                  45

Gly Phe Thr Lys Met Pro His Val Gln Tyr Ile His Thr Glu Ala Ser
    50                  55                  60

Glu Ser Leu Cys Gly Leu Lys Leu Glu Val Asn Lys Tyr Gln Tyr Leu
65                  70                  75                  80

Leu Thr Gly Arg Val Tyr Asp Gly Lys Met Tyr Thr Gly Leu Cys Asn
                85                  90                  95

Phe Val Glu Arg Trp Asp Gln Leu Thr Leu Ser Gln Arg Lys Gly Leu
            100                 105                 110

Asn Tyr Arg Tyr His Leu Gly Cys Asn Cys Lys Ile Lys Ser Cys Tyr
        115                 120                 125

Tyr Leu Pro Cys Phe Val Thr Ser Lys Asn Glu Cys Leu Trp Thr Asp
    130                 135                 140

Met Leu Ser Asn Phe Gly Tyr Pro Gly Tyr Gln Ser Lys His Tyr Ala
145                 150                 155                 160
```

```
Cys Ile Arg Gln Lys Gly Gly Tyr Cys Ser Trp Tyr Arg Gly Trp Ala
                165                 170                 175

Pro Pro Asp Lys Ser Tyr Ile Asn Gly Thr Asp Pro
            180                 185

<210> 61
<211> 188
<212> PRT
<213> Homo sapiens

<220>
<223> huTIMP3(K45N,V47T,F57N,K75N,P77T,K94N,E96T,R138T,G173T)

<400> 61
Cys Thr Cys Ser Pro Ser His Pro Gln Asp Ala Phe Cys Asn Ser Asp
1               5                   10                  15

Ile Val Ile Arg Ala Asn Val Thr Gly Lys Lys Leu Val Lys Glu Gly
            20                  25                  30

Pro Asn Gly Thr Leu Val Tyr Thr Ile Lys Gln Met Lys Met Tyr Arg
        35                  40                  45

Gly Phe Thr Asn Met Thr His Val Gln Tyr Ile His Thr Glu Ala Ser
    50                  55                  60

Glu Ser Leu Cys Gly Leu Asn Leu Thr Val Asn Lys Tyr Gln Tyr Leu
65                  70                  75                  80

Leu Thr Gly Arg Val Tyr Asp Gly Lys Met Tyr Thr Gly Leu Cys Asn
                85                  90                  95

Phe Val Glu Arg Trp Asp Gln Leu Thr Leu Ser Gln Arg Lys Gly Leu
            100                 105                 110

Asn Tyr Thr Tyr His Leu Gly Cys Asn Cys Lys Ile Lys Ser Cys Tyr
        115                 120                 125

Tyr Leu Pro Cys Phe Val Thr Ser Lys Asn Glu Cys Leu Trp Thr Asp
    130                 135                 140

Met Leu Ser Asn Phe Thr Tyr Pro Gly Tyr Gln Ser Lys His Tyr Ala
145                 150                 155                 160

Cys Ile Arg Gln Lys Gly Gly Tyr Cys Ser Trp Tyr Arg Gly Trp Ala
                165                 170                 175

Pro Pro Asp Lys Ser Ile Ile Asn Ala Thr Asp Pro
            180                 185

<210> 62
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<211> 188
<212> PRT
<213> Homo sapiens

<220>
<223> huTIMP3(K45N,V47T,F57N,K94N,E96T,R138T,G173T)

<400> 62
Cys Thr Cys Ser Pro Ser His Pro Gln Asp Ala Phe Cys Asn Ser Asp
1 5 10 15

Ile Val Ile Arg Ala Asn Val Thr Gly Lys Lys Leu Val Lys Glu Gly
20 25 30

Pro Asn Gly Thr Leu Val Tyr Thr Ile Lys Gln Met Lys Met Tyr Arg
35 40 45

Gly Phe Thr Lys Met Pro His Val Gln Tyr Ile His Thr Glu Ala Ser
50 55 60

Glu Ser Leu Cys Gly Leu Asn Leu Thr Val Asn Lys Tyr Gln Tyr Leu
65 70 75 80

Leu Thr Gly Arg Val Tyr Asp Gly Lys Met Tyr Thr Gly Leu Cys Asn
85 90 95

Phe Val Glu Arg Trp Asp Gln Leu Thr Leu Ser Gln Arg Lys Gly Leu
100 105 110

Asn Tyr Thr Tyr His Leu Gly Cys Asn Cys Lys Ile Lys Ser Cys Tyr
115 120 125

Tyr Leu Pro Cys Phe Val Thr Ser Lys Asn Glu Cys Leu Trp Thr Asp
130 135 140

Met Leu Ser Asn Phe Thr Tyr Pro Gly Tyr Gln Ser Lys His Tyr Ala
145 150 155 160

Cys Ile Arg Gln Lys Gly Gly Tyr Cys Ser Trp Tyr Arg Gly Trp Ala
165 170 175

Pro Pro Asp Lys Ser Ile Ile Asn Ala Thr Asp Pro
180 185

<210> 63
<211> 188
<212> PRT
<213> Homo sapiens

<220>
<223> huTIMP3(K45N,V47T,K50N,V52T,F57N,V97N,K99T)

<400> 63
Cys Thr Cys Ser Pro Ser His Pro Gln Asp Ala Phe Cys Asn Ser Asp

1 5 10 15

Ile Val Ile Arg Ala Asn Val Thr Gly Lys Asn Leu Thr Lys Glu Gly
20 25 30

Pro Asn Gly Thr Leu Val Tyr Thr Ile Lys Gln Met Lys Met Tyr Arg
35 40 45

Gly Phe Thr Lys Met Pro His Val Gln Tyr Ile His Thr Glu Ala Ser
50 55 60

Glu Ser Leu Cys Gly Leu Lys Leu Glu Asn Asn Thr Tyr Gln Tyr Leu
65 70 75 80

Leu Thr Gly Arg Val Tyr Asp Gly Lys Met Tyr Thr Gly Leu Cys Asn
85 90 95

Phe Val Glu Arg Trp Asp Gln Leu Thr Leu Ser Gln Arg Lys Gly Leu
100 105 110

Asn Tyr Arg Tyr His Leu Gly Cys Asn Cys Lys Ile Lys Ser Cys Tyr
115 120 125

Tyr Leu Pro Cys Phe Val Thr Ser Lys Asn Glu Cys Leu Trp Thr Asp
130 135 140

Met Leu Ser Asn Phe Gly Tyr Pro Gly Tyr Gln Ser Lys His Tyr Ala
145 150 155 160

Cys Ile Arg Gln Lys Gly Gly Tyr Cys Ser Trp Tyr Arg Gly Trp Ala
165 170 175

Pro Pro Asp Lys Ser Ile Ile Asn Ala Thr Asp Pro
180 185

<210> 64
<211> 188
<212> PRT
<213> Homo sapiens

<220>
<223> huTIMP3(K45S,K50N,V52T,F57N,V97N,K99T,R186N,K188T)

<400> 64
Cys Thr Cys Ser Pro Ser His Pro Gln Asp Ala Phe Cys Asn Ser Asp
1 5 10 15

Ile Val Ile Arg Ala Ser Val Val Gly Lys Asn Leu Thr Lys Glu Gly
20 25 30

Pro Asn Gly Thr Leu Val Tyr Thr Ile Lys Gln Met Lys Met Tyr Arg
35 40 45

```
Gly Phe Thr Lys Met Pro His Val Gln Tyr Ile His Thr Glu Ala Ser
    50                  55                  60

Glu Ser Leu Cys Gly Leu Lys Leu Glu Asn Asn Thr Tyr Gln Tyr Leu
65                  70                  75                  80

Leu Thr Gly Arg Val Tyr Asp Gly Lys Met Tyr Thr Gly Leu Cys Asn
                85                  90                  95

Phe Val Glu Arg Trp Asp Gln Leu Thr Leu Ser Gln Arg Lys Gly Leu
            100                 105                 110

Asn Tyr Arg Tyr His Leu Gly Cys Asn Cys Lys Ile Lys Ser Cys Tyr
        115                 120                 125

Tyr Leu Pro Cys Phe Val Thr Ser Lys Asn Glu Cys Leu Trp Thr Asp
    130                 135                 140

Met Leu Ser Asn Phe Gly Tyr Pro Gly Tyr Gln Ser Lys His Tyr Ala
145                 150                 155                 160

Cys Ile Asn Gln Thr Gly Gly Tyr Cys Ser Trp Tyr Arg Gly Trp Ala
                165                 170                 175

Pro Pro Asp Lys Ser Ile Ile Asn Ala Thr Asp Pro
            180                 185
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<210> 65
<211> 188
<212> PRT
<213> Homo sapiens

<220>
<223> huTIMP3(K45S,F57N,K94N,E96T,D110N,K112T,R138T,G173T)

<400> 65

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Cys Thr Cys Ser Pro Ser His Pro Gln Asp Ala Phe Cys Asn Ser Asp
1               5                   10                  15

Ile Val Ile Arg Ala Ser Val Val Gly Lys Lys Leu Val Lys Glu Gly
            20                  25                  30

Pro Asn Gly Thr Leu Val Tyr Thr Ile Lys Gln Met Lys Met Tyr Arg
        35                  40                  45

Gly Phe Thr Lys Met Pro His Val Gln Tyr Ile His Thr Glu Ala Ser
    50                  55                  60

Glu Ser Leu Cys Gly Leu Asn Leu Thr Val Asn Lys Tyr Gln Tyr Leu
65                  70                  75                  80

Leu Thr Gly Arg Val Tyr Asn Gly Thr Met Tyr Thr Gly Leu Cys Asn
```

85 90 95

Phe Val Glu Arg Trp Asp Gln Leu Thr Leu Ser Gln Arg Lys Gly Leu
100 105 110

Asn Tyr Thr Tyr His Leu Gly Cys Asn Cys Lys Ile Lys Ser Cys Tyr
115 120 125

Tyr Leu Pro Cys Phe Val Thr Ser Lys Asn Glu Cys Leu Trp Thr Asp
130 135 140

Met Leu Ser Asn Phe Thr Tyr Pro Gly Tyr Gln Ser Lys His Tyr Ala
145 150 155 160

Cys Ile Arg Gln Lys Gly Gly Tyr Cys Ser Trp Tyr Arg Gly Trp Ala
165 170 175

Pro Pro Asp Lys Ser Ile Ile Asn Ala Thr Asp Pro
180 185

<210> 66
<211> 188
<212> PRT
<213> Homo sapiens

<220>
<223> huTIMP3(K45S,F57N,T63N,K65T,K94N,E96T,G173T)

<400> 66
Cys Thr Cys Ser Pro Ser His Pro Gln Asp Ala Phe Cys Asn Ser Asp
1 5 10 15

Ile Val Ile Arg Ala Ser Val Val Gly Lys Lys Leu Val Lys Glu Gly
20 25 30

Pro Asn Gly Thr Leu Val Tyr Asn Ile Thr Gln Met Lys Met Tyr Arg
35 40 45

Gly Phe Thr Lys Met Pro His Val Gln Tyr Ile His Thr Glu Ala Ser
50 55 60

Glu Ser Leu Cys Gly Leu Asn Leu Thr Val Asn Lys Tyr Gln Tyr Leu
65 70 75 80

Leu Thr Gly Arg Val Tyr Asp Gly Lys Met Tyr Thr Gly Leu Cys Asn
85 90 95

Phe Val Glu Arg Trp Asp Gln Leu Thr Leu Ser Gln Arg Lys Gly Leu
100 105 110

Asn Tyr Arg Tyr His Leu Gly Cys Asn Cys Lys Ile Lys Ser Cys Tyr
115 120 125

```
Tyr Leu Pro Cys Phe Val Thr Ser Lys Asn Glu Cys Leu Trp Thr Asp
    130                 135                 140

Met Leu Ser Asn Phe Thr Tyr Pro Gly Tyr Gln Ser Lys His Tyr Ala
145                 150                 155                 160

Cys Ile Arg Gln Lys Gly Gly Tyr Cys Ser Trp Tyr Arg Gly Trp Ala
                165                 170                 175

Pro Pro Asp Lys Ser Ile Ile Asn Ala Thr Asp Pro
            180                 185

<210> 67
<211> 188
<212> PRT
<213> Homo sapiens

<220>
<223> huTIMP3(K45N,V47T,K50N,V52T,F57N,V97N,K99T,R138T,R186N,K188T)

<400> 67
Cys Thr Cys Ser Pro Ser His Pro Gln Asp Ala Phe Cys Asn Ser Asp
1               5                   10                  15

Ile Val Ile Arg Ala Asn Val Thr Gly Lys Asn Leu Thr Lys Glu Gly
            20                  25                  30

Pro Asn Gly Thr Leu Val Tyr Thr Ile Lys Gln Met Lys Met Tyr Arg
        35                  40                  45

Gly Phe Thr Lys Met Pro His Val Gln Tyr Ile His Thr Glu Ala Ser
    50                  55                  60

Glu Ser Leu Cys Gly Leu Lys Leu Glu Asn Asn Thr Tyr Gln Tyr Leu
65                  70                  75                  80

Leu Thr Gly Arg Val Tyr Asp Gly Lys Met Tyr Thr Gly Leu Cys Asn
                85                  90                  95

Phe Val Glu Arg Trp Asp Gln Leu Thr Leu Ser Gln Arg Lys Gly Leu
            100                 105                 110

Asn Tyr Thr Tyr His Leu Gly Cys Asn Cys Lys Ile Lys Ser Cys Tyr
        115                 120                 125

Tyr Leu Pro Cys Phe Val Thr Ser Lys Asn Glu Cys Leu Trp Thr Asp
    130                 135                 140

Met Leu Ser Asn Phe Gly Tyr Pro Gly Tyr Gln Ser Lys His Tyr Ala
145                 150                 155                 160

Cys Ile Asn Gln Thr Gly Gly Tyr Cys Ser Trp Tyr Arg Gly Trp Ala
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165 170 175

Pro Pro Asp Lys Ser Ile Ile Asn Ala Thr Asp Pro
180 185

<210> 68
<211> 188
<212> PRT
<213> Homo sapiens

<220>
<223> huTIMP3(K45S,F57N,T63N,K65T,K94N,E96T,Q126N,R138T)

<400> 68
Cys Thr Cys Ser Pro Ser His Pro Gln Asp Ala Phe Cys Asn Ser Asp
1 5 10 15

Ile Val Ile Arg Ala Ser Val Val Gly Lys Lys Leu Val Lys Glu Gly
20 25 30

Pro Asn Gly Thr Leu Val Tyr Asn Ile Thr Gln Met Lys Met Tyr Arg
35 40 45

Gly Phe Thr Lys Met Pro His Val Gln Tyr Ile His Thr Glu Ala Ser
50 55 60

Glu Ser Leu Cys Gly Leu Asn Leu Thr Val Asn Lys Tyr Gln Tyr Leu
65 70 75 80

Leu Thr Gly Arg Val Tyr Asp Gly Lys Met Tyr Thr Gly Leu Cys Asn
85 90 95

Phe Val Glu Arg Trp Asp Asn Leu Thr Leu Ser Gln Arg Lys Gly Leu
100 105 110

Asn Tyr Thr Tyr His Leu Gly Cys Asn Cys Lys Ile Lys Ser Cys Tyr
115 120 125

Tyr Leu Pro Cys Phe Val Thr Ser Lys Asn Glu Cys Leu Trp Thr Asp
130 135 140

Met Leu Ser Asn Phe Gly Tyr Pro Gly Tyr Gln Ser Lys His Tyr Ala
145 150 155 160

Cys Ile Arg Gln Lys Gly Gly Tyr Cys Ser Trp Tyr Arg Gly Trp Ala
165 170 175

Pro Pro Asp Lys Ser Ile Ile Asn Ala Thr Asp Pro
180 185

<210> 69
<211> 188
<212> PRT

<213> Homo sapiens

<220>
<223> huTIMP3(K45N,V47T,K50N,V52T,F57N,V97N,K99T,R186N,K188T)

<400> 69
Cys Thr Cys Ser Pro Ser His Pro Gln Asp Ala Phe Cys Asn Ser Asp
1 5 10 15

Ile Val Ile Arg Ala Asn Val Thr Gly Lys Asn Leu Thr Lys Glu Gly
20 25 30

Pro Asn Gly Thr Leu Val Tyr Thr Ile Lys Gln Met Lys Met Tyr Arg
35 40 45

Gly Phe Thr Lys Met Pro His Val Gln Tyr Ile His Thr Glu Ala Ser
50 55 60

Glu Ser Leu Cys Gly Leu Lys Leu Glu Asn Asn Thr Tyr Gln Tyr Leu
65 70 75 80

Leu Thr Gly Arg Val Tyr Asp Gly Lys Met Tyr Thr Gly Leu Cys Asn
85 90 95

Phe Val Glu Arg Trp Asp Gln Leu Thr Leu Ser Gln Arg Lys Gly Leu
100 105 110

Asn Tyr Arg Tyr His Leu Gly Cys Asn Cys Lys Ile Lys Ser Cys Tyr
115 120 125

Tyr Leu Pro Cys Phe Val Thr Ser Lys Asn Glu Cys Leu Trp Thr Asp
130 135 140

Met Leu Ser Asn Phe Gly Tyr Pro Gly Tyr Gln Ser Lys His Tyr Ala
145 150 155 160

Cys Ile Asn Gln Thr Gly Gly Tyr Cys Ser Trp Tyr Arg Gly Trp Ala
165 170 175

Pro Pro Asp Lys Ser Ile Ile Asn Ala Thr Asp Pro
180 185

<210> 70
<211> 188
<212> PRT
<213> Homo sapiens

<220>
<223> huTIMP3(K45N,V47T,K50N,V52T,V97N,K99T,R138T,R186N,K188T)

<400> 70
Cys Thr Cys Ser Pro Ser His Pro Gln Asp Ala Phe Cys Asn Ser Asp
1 5 10 15

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Ile Val Ile Arg Ala Asn Val Thr Gly Lys Asn Leu Thr Lys Glu Gly
            20                  25                  30

Pro Phe Gly Thr Leu Val Tyr Thr Ile Lys Gln Met Lys Met Tyr Arg
        35                  40                  45

Gly Phe Thr Lys Met Pro His Val Gln Tyr Ile His Thr Glu Ala Ser
    50                  55                  60

Glu Ser Leu Cys Gly Leu Lys Leu Glu Asn Asn Thr Tyr Gln Tyr Leu
65                  70                  75                  80

Leu Thr Gly Arg Val Tyr Asp Gly Lys Met Tyr Thr Gly Leu Cys Asn
                85                  90                  95

Phe Val Glu Arg Trp Asp Gln Leu Thr Leu Ser Gln Arg Lys Gly Leu
            100                 105                 110

Asn Tyr Thr Tyr His Leu Gly Cys Asn Cys Lys Ile Lys Ser Cys Tyr
        115                 120                 125

Tyr Leu Pro Cys Phe Val Thr Ser Lys Asn Glu Cys Leu Trp Thr Asp
    130                 135                 140

Met Leu Ser Asn Phe Gly Tyr Pro Gly Tyr Gln Ser Lys His Tyr Ala
145                 150                 155                 160

Cys Ile Asn Gln Thr Gly Gly Tyr Cys Ser Trp Tyr Arg Gly Trp Ala
                165                 170                 175

Pro Pro Asp Lys Ser Ile Ile Asn Ala Thr Asp Pro
            180                 185


<210> 71
<211> 188
<212> PRT
<213> Homo sapiens


<220>
<223> huTIMP3(K45S,F57N,H78N,Q80T,K94N,E96T,R138T,G173T)

<400> 71
Cys Thr Cys Ser Pro Ser His Pro Gln Asp Ala Phe Cys Asn Ser Asp
1               5                   10                  15

Ile Val Ile Arg Ala Ser Val Val Gly Lys Lys Leu Val Lys Glu Gly
            20                  25                  30

Pro Asn Gly Thr Leu Val Tyr Thr Ile Lys Gln Met Lys Met Tyr Arg
        35                  40                  45

Gly Phe Thr Lys Met Pro Asn Val Thr Tyr Ile His Thr Glu Ala Ser
```

50 55 60

Glu Ser Leu Cys Gly Leu Asn Leu Thr Val Asn Lys Tyr Gln Tyr Leu
65 70 75 80

Leu Thr Gly Arg Val Tyr Asp Gly Lys Met Tyr Thr Gly Leu Cys Asn
85 90 95

Phe Val Glu Arg Trp Asp Gln Leu Thr Leu Ser Gln Arg Lys Gly Leu
100 105 110

Asn Tyr Thr Tyr His Leu Gly Cys Asn Cys Lys Ile Lys Ser Cys Tyr
115 120 125

Tyr Leu Pro Cys Phe Val Thr Ser Lys Asn Glu Cys Leu Trp Thr Asp
130 135 140

Met Leu Ser Asn Phe Thr Tyr Pro Gly Tyr Gln Ser Lys His Tyr Ala
145 150 155 160

Cys Ile Arg Gln Lys Gly Gly Tyr Cys Ser Trp Tyr Arg Gly Trp Ala
165 170 175

Pro Pro Asp Lys Ser Ile Ile Asn Ala Thr Asp Pro
180 185

<210> 72
<211> 188
<212> PRT
<213> Homo sapiens

<220>
<223> huTIMP3(K45S,F57N,K75N,P77T,K94N,E96T,R138T,G173T)

<400> 72
Cys Thr Cys Ser Pro Ser His Pro Gln Asp Ala Phe Cys Asn Ser Asp
1 5 10 15

Ile Val Ile Arg Ala Ser Val Val Gly Lys Lys Leu Val Lys Glu Gly
20 25 30

Pro Asn Gly Thr Leu Val Tyr Thr Ile Lys Gln Met Lys Met Tyr Arg
35 40 45

Gly Phe Thr Asn Met Thr His Val Gln Tyr Ile His Thr Glu Ala Ser
50 55 60

Glu Ser Leu Cys Gly Leu Asn Leu Thr Val Asn Lys Tyr Gln Tyr Leu
65 70 75 80

Leu Thr Gly Arg Val Tyr Asp Gly Lys Met Tyr Thr Gly Leu Cys Asn
85 90 95

```
Phe Val Glu Arg Trp Asp Gln Leu Thr Leu Ser Gln Arg Lys Gly Leu
            100                 105                 110

Asn Tyr Thr Tyr His Leu Gly Cys Asn Cys Lys Ile Lys Ser Cys Tyr
        115                 120                 125

Tyr Leu Pro Cys Phe Val Thr Ser Lys Asn Glu Cys Leu Trp Thr Asp
    130                 135                 140

Met Leu Ser Asn Phe Thr Tyr Pro Gly Tyr Gln Ser Lys His Tyr Ala
145                 150                 155                 160

Cys Ile Arg Gln Lys Gly Gly Tyr Cys Ser Trp Tyr Arg Gly Trp Ala
                165                 170                 175

Pro Pro Asp Lys Ser Ile Ile Asn Ala Thr Asp Pro
            180                 185

<210> 73
<211> 188
<212> PRT
<213> Homo sapiens

<220>
<223> huTIMP3(K45N,V47T,K50N,V52T,V97N,K99T,G173T,R186N,K188T)

<400> 73
Cys Thr Cys Ser Pro Ser His Pro Gln Asp Ala Phe Cys Asn Ser Asp
1               5                   10                  15

Ile Val Ile Arg Ala Asn Val Thr Gly Lys Asn Leu Thr Lys Glu Gly
            20                  25                  30

Pro Phe Gly Thr Leu Val Tyr Thr Ile Lys Gln Met Lys Met Tyr Arg
        35                  40                  45

Gly Phe Thr Lys Met Pro His Val Gln Tyr Ile His Thr Glu Ala Ser
    50                  55                  60

Glu Ser Leu Cys Gly Leu Lys Leu Glu Asn Asn Thr Tyr Gln Tyr Leu
65                  70                  75                  80

Leu Thr Gly Arg Val Tyr Asp Gly Lys Met Tyr Thr Gly Leu Cys Asn
                85                  90                  95

Phe Val Glu Arg Trp Asp Gln Leu Thr Leu Ser Gln Arg Lys Gly Leu
            100                 105                 110

Asn Tyr Arg Tyr His Leu Gly Cys Asn Cys Lys Ile Lys Ser Cys Tyr
        115                 120                 125

Tyr Leu Pro Cys Phe Val Thr Ser Lys Asn Glu Cys Leu Trp Thr Asp
```

130 135 140

Met Leu Ser Asn Phe Thr Tyr Pro Gly Tyr Gln Ser Lys His Tyr Ala
145 150 155 160

Cys Ile Asn Gln Thr Gly Gly Tyr Cys Ser Trp Tyr Arg Gly Trp Ala
165 170 175

Pro Pro Asp Lys Ser Ile Ile Asn Ala Thr Asp Pro
180 185

<210> 74
<211> 188
<212> PRT
<213> Homo sapiens

<220>
<223> huTIMP3(K45E,F57N,Q126N,R138T,G173T)

<400> 74
Cys Thr Cys Ser Pro Ser His Pro Gln Asp Ala Phe Cys Asn Ser Asp
1 5 10 15

Ile Val Ile Arg Ala Glu Val Val Gly Lys Lys Leu Val Lys Glu Gly
20 25 30

Pro Asn Gly Thr Leu Val Tyr Thr Ile Lys Gln Met Lys Met Tyr Arg
35 40 45

Gly Phe Thr Lys Met Pro His Val Gln Tyr Ile His Thr Glu Ala Ser
50 55 60

Glu Ser Leu Cys Gly Leu Lys Leu Glu Val Asn Lys Tyr Gln Tyr Leu
65 70 75 80

Leu Thr Gly Arg Val Tyr Asp Gly Lys Met Tyr Thr Gly Leu Cys Asn
85 90 95

Phe Val Glu Arg Trp Asp Asn Leu Thr Leu Ser Gln Arg Lys Gly Leu
100 105 110

Asn Tyr Thr Tyr His Leu Gly Cys Asn Cys Lys Ile Lys Ser Cys Tyr
115 120 125

Tyr Leu Pro Cys Phe Val Thr Ser Lys Asn Glu Cys Leu Trp Thr Asp
130 135 140

Met Leu Ser Asn Phe Thr Tyr Pro Gly Tyr Gln Ser Lys His Tyr Ala
145 150 155 160

Cys Ile Arg Gln Lys Gly Gly Tyr Cys Ser Trp Tyr Arg Gly Trp Ala
165 170 175

Pro Pro Asp Lys Ser Ile Ile Asn Ala Thr Asp Pro
180 185

<210> 75
<211> 188
<212> PRT
<213> Homo sapiens

<220>
<223> huTIMP3(K45S,F57N,T63N,K65T,K94N,E96T,R138T,G173T)

<400> 75
Cys Thr Cys Ser Pro Ser His Pro Gln Asp Ala Phe Cys Asn Ser Asp
1 5 10 15

Ile Val Ile Arg Ala Ser Val Val Gly Lys Lys Leu Val Lys Glu Gly
20 25 30

Pro Asn Gly Thr Leu Val Tyr Asn Ile Thr Gln Met Lys Met Tyr Arg
35 40 45

Gly Phe Thr Lys Met Pro His Val Gln Tyr Ile His Thr Glu Ala Ser
50 55 60

Glu Ser Leu Cys Gly Leu Asn Leu Thr Val Asn Lys Tyr Gln Tyr Leu
65 70 75 80

Leu Thr Gly Arg Val Tyr Asp Gly Lys Met Tyr Thr Gly Leu Cys Asn
85 90 95

Phe Val Glu Arg Trp Asp Gln Leu Thr Leu Ser Gln Arg Lys Gly Leu
100 105 110

Asn Tyr Thr Tyr His Leu Gly Cys Asn Cys Lys Ile Lys Ser Cys Tyr
115 120 125

Tyr Leu Pro Cys Phe Val Thr Ser Lys Asn Glu Cys Leu Trp Thr Asp
130 135 140

Met Leu Ser Asn Phe Thr Tyr Pro Gly Tyr Gln Ser Lys His Tyr Ala
145 150 155 160

Cys Ile Arg Gln Lys Gly Gly Tyr Cys Ser Trp Tyr Arg Gly Trp Ala
165 170 175

Pro Pro Asp Lys Ser Ile Ile Asn Ala Thr Asp Pro
180 185

<210> 76
<211> 188
<212> PRT
<213> Homo sapiens

<220>
<223> huTIMP3(K45S,K50N,V52T,F57N,V97N,K99T,R138T,R186N,K188T)

<400> 76
Cys Thr Cys Ser Pro Ser His Pro Gln Asp Ala Phe Cys Asn Ser Asp
1 5 10 15

Ile Val Ile Arg Ala Ser Val Val Gly Lys Asn Leu Thr Lys Glu Gly
            20 25 30

Pro Asn Gly Thr Leu Val Tyr Thr Ile Lys Gln Met Lys Met Tyr Arg
        35 40 45

Gly Phe Thr Lys Met Pro His Val Gln Tyr Ile His Thr Glu Ala Ser
    50 55 60

Glu Ser Leu Cys Gly Leu Lys Leu Glu Asn Asn Thr Tyr Gln Tyr Leu
65 70 75 80

Leu Thr Gly Arg Val Tyr Asp Gly Lys Met Tyr Thr Gly Leu Cys Asn
                85 90 95

Phe Val Glu Arg Trp Asp Gln Leu Thr Leu Ser Gln Arg Lys Gly Leu
            100 105 110

Asn Tyr Thr Tyr His Leu Gly Cys Asn Cys Lys Ile Lys Ser Cys Tyr
        115 120 125

Tyr Leu Pro Cys Phe Val Thr Ser Lys Asn Glu Cys Leu Trp Thr Asp
    130 135 140

Met Leu Ser Asn Phe Gly Tyr Pro Gly Tyr Gln Ser Lys His Tyr Ala
145 150 155 160

Cys Ile Asn Gln Thr Gly Gly Tyr Cys Ser Trp Tyr Arg Gly Trp Ala
                165 170 175

Pro Pro Asp Lys Ser Ile Ile Asn Ala Thr Asp Pro
            180 185

<210> 77
<211> 188
<212> PRT
<213> Homo sapiens

<220>
<223> huTIMP3(K45S.K50N,V52T,F57N,V97N,K99T,G173T,R186N,K188T)

<400> 77
Cys Thr Cys Ser Pro Ser His Pro Gln Asp Ala Phe Cys Asn Ser Asp
1 5 10 15

Ile Val Ile Arg Ala Ser Val Val Gly Lys Asn Leu Thr Lys Glu Gly

```
            20                  25                  30

Pro Asn Gly Thr Leu Val Tyr Thr Ile Lys Gln Met Lys Met Tyr Arg
        35                  40                  45

Gly Phe Thr Lys Met Pro His Val Gln Tyr Ile His Thr Glu Ala Ser
    50                  55                  60

Glu Ser Leu Cys Gly Leu Lys Leu Glu Asn Asn Thr Tyr Gln Tyr Leu
65                  70                  75                  80

Leu Thr Gly Arg Val Tyr Asp Gly Lys Met Tyr Thr Gly Leu Cys Asn
                85                  90                  95

Phe Val Glu Arg Trp Asp Gln Leu Thr Leu Ser Gln Arg Lys Gly Leu
            100                 105                 110

Asn Tyr Arg Tyr His Leu Gly Cys Asn Cys Lys Ile Lys Ser Cys Tyr
        115                 120                 125

Tyr Leu Pro Cys Phe Val Thr Ser Lys Asn Glu Cys Leu Trp Thr Asp
    130                 135                 140

Met Leu Ser Asn Phe Thr Tyr Pro Gly Tyr Gln Ser Lys His Tyr Ala
145                 150                 155                 160

Cys Ile Asn Gln Thr Gly Gly Tyr Cys Ser Trp Tyr Arg Gly Trp Ala
                165                 170                 175

Pro Pro Asp Lys Ser Ile Ile Asn Ala Thr Asp Pro
            180                 185


<210> 78
<211> 188
<212> PRT
<213> Homo sapiens


<220>
<223> huTIMP3(K45N,V47T, F57N, K94N,E96T, G173T, R186N,K188T)

<400> 78
Cys Thr Cys Ser Pro Ser His Pro Gln Asp Ala Phe Cys Asn Ser Asp
1               5                   10                  15

Ile Val Ile Arg Ala Asn Val Thr Gly Lys Lys Leu Val Lys Glu Gly
            20                  25                  30

Pro Asn Gly Thr Leu Val Tyr Thr Ile Lys Gln Met Lys Met Tyr Arg
        35                  40                  45

Gly Phe Thr Lys Met Pro His Val Gln Tyr Ile His Thr Glu Ala Ser
    50                  55                  60
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Glu Ser Leu Cys Gly Leu Asn Leu Thr Val Asn Lys Tyr Gln Tyr Leu
65                  70                  75                  80

Leu Thr Gly Arg Val Tyr Asp Gly Lys Met Tyr Thr Gly Leu Cys Asn
                85                  90                  95

Phe Val Glu Arg Trp Asp Gln Leu Thr Leu Ser Gln Arg Lys Gly Leu
            100                 105                 110

Asn Tyr Arg Tyr His Leu Gly Cys Asn Cys Lys Ile Lys Ser Cys Tyr
        115                 120                 125

Tyr Leu Pro Cys Phe Val Thr Ser Lys Asn Glu Cys Leu Trp Thr Asp
    130                 135                 140

Met Leu Ser Asn Phe Thr Tyr Pro Gly Tyr Gln Ser Lys His Tyr Ala
145                 150                 155                 160

Cys Ile Asn Gln Thr Gly Gly Tyr Cys Ser Trp Tyr Arg Gly Trp Ala
                165                 170                 175

Pro Pro Asp Lys Ser Ile Ile Asn Ala Thr Asp Pro
            180                 185

<210> 79
<211> 188
<212> PRT
<213> Homo sapiens

<220>
<223> huTIMP3(K45N,V47T, F57N, K94N,E96T, D110N,K112T, R186N,K188T)

<400> 79
Cys Thr Cys Ser Pro Ser His Pro Gln Asp Ala Phe Cys Asn Ser Asp
1               5                   10                  15

Ile Val Ile Arg Ala Asn Val Thr Gly Lys Lys Leu Val Lys Glu Gly
            20                  25                  30

Pro Asn Gly Thr Leu Val Tyr Thr Ile Lys Gln Met Lys Met Tyr Arg
        35                  40                  45

Gly Phe Thr Lys Met Pro His Val Gln Tyr Ile His Thr Glu Ala Ser
    50                  55                  60

Glu Ser Leu Cys Gly Leu Asn Leu Thr Val Asn Lys Tyr Gln Tyr Leu
65                  70                  75                  80

Leu Thr Gly Arg Val Tyr Asn Gly Thr Met Tyr Thr Gly Leu Cys Asn
                85                  90                  95

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

100 105 110

Asn Tyr Arg Tyr His Leu Gly Cys Asn Cys Lys Ile Lys Ser Cys Tyr
115 120 125

Tyr Leu Pro Cys Phe Val Thr Ser Lys Asn Glu Cys Leu Trp Thr Asp
130 135 140

Met Leu Ser Asn Phe Gly Tyr Pro Gly Tyr Gln Ser Lys His Tyr Ala
145 150 155 160

Cys Ile Asn Gln Thr Gly Gly Tyr Cys Ser Trp Tyr Arg Gly Trp Ala
165 170 175

Pro Pro Asp Lys Ser Ile Ile Asn Ala Thr Asp Pro
180 185

<210> 80
<211> 188
<212> PRT
<213> Homo sapiens

<220>
<223> huTIMP3(K45N,V47T, F57N, V97N,K99T, R138T, G173T)

<400> 80
Cys Thr Cys Ser Pro Ser His Pro Gln Asp Ala Phe Cys Asn Ser Asp
1 5 10 15

Ile Val Ile Arg Ala Asn Val Thr Gly Lys Lys Leu Val Lys Glu Gly
20 25 30

Pro Asn Gly Thr Leu Val Tyr Thr Ile Lys Gln Met Lys Met Tyr Arg
35 40 45

Gly Phe Thr Lys Met Pro His Val Gln Tyr Ile His Thr Glu Ala Ser
50 55 60

Glu Ser Leu Cys Gly Leu Lys Leu Glu Asn Asn Thr Tyr Gln Tyr Leu
65 70 75 80

Leu Thr Gly Arg Val Tyr Asp Gly Lys Met Tyr Thr Gly Leu Cys Asn
85 90 95

Phe Val Glu Arg Trp Asp Gln Leu Thr Leu Ser Gln Arg Lys Gly Leu
100 105 110

Asn Tyr Thr Tyr His Leu Gly Cys Asn Cys Lys Ile Lys Ser Cys Tyr
115 120 125

Tyr Leu Pro Cys Phe Val Thr Ser Lys Asn Glu Cys Leu Trp Thr Asp
130 135 140

```
Met Leu Ser Asn Phe Thr Tyr Pro Gly Tyr Gln Ser Lys His Tyr Ala
145                 150                 155                 160

Cys Ile Arg Gln Lys Gly Gly Tyr Cys Ser Trp Tyr Arg Gly Trp Ala
                165                 170                 175

Pro Pro Asp Lys Ser Ile Ile Asn Ala Thr Asp Pro
            180                 185

<210> 81
<211> 188
<212> PRT
<213> Homo sapiens

<220>
<223> huTIMP3(K45N,V47T, F57N, K99E G173T, R186N,K188T)

<400> 81
Cys Thr Cys Ser Pro Ser His Pro Gln Asp Ala Phe Cys Asn Ser Asp
1               5                   10                  15

Ile Val Ile Arg Ala Asn Val Thr Gly Lys Lys Leu Val Lys Glu Gly
            20                  25                  30

Pro Asn Gly Thr Leu Val Tyr Thr Ile Lys Gln Met Lys Met Tyr Arg
        35                  40                  45

Gly Phe Thr Lys Met Pro His Val Gln Tyr Ile His Thr Glu Ala Ser
    50                  55                  60

Glu Ser Leu Cys Gly Leu Lys Leu Glu Val Asn Glu Tyr Gln Tyr Leu
65                  70                  75                  80

Leu Thr Gly Arg Val Tyr Asp Gly Lys Met Tyr Thr Gly Leu Cys Asn
                85                  90                  95

Phe Val Glu Arg Trp Asp Gln Leu Thr Leu Ser Gln Arg Lys Gly Leu
            100                 105                 110

Asn Tyr Arg Tyr His Leu Gly Cys Asn Cys Lys Ile Lys Ser Cys Tyr
        115                 120                 125

Tyr Leu Pro Cys Phe Val Thr Ser Lys Asn Glu Cys Leu Trp Thr Asp
    130                 135                 140

Met Leu Ser Asn Phe Thr Tyr Pro Gly Tyr Gln Ser Lys His Tyr Ala
145                 150                 155                 160

Cys Ile Asn Gln Thr Gly Gly Tyr Cys Ser Trp Tyr Arg Gly Trp Ala
                165                 170                 175

Pro Pro Asp Lys Ser Ile Ile Asn Ala Thr Asp Pro
```

180 185

<210> 82
<211> 188
<212> PRT
<213> Homo sapiens

<220>
<223> huTIMP3(K45E, K49E, F57N, K94N,E96T, D110N,K112T, G173T, R186N,K188T)

<400> 82
Cys Thr Cys Ser Pro Ser His Pro Gln Asp Ala Phe Cys Asn Ser Asp
1 5 10 15

Ile Val Ile Arg Ala Glu Val Val Gly Glu Lys Leu Val Lys Glu Gly
20 25 30

Pro Asn Gly Thr Leu Val Tyr Thr Ile Lys Gln Met Lys Met Tyr Arg
35 40 45

Gly Phe Thr Lys Met Pro His Val Gln Tyr Ile His Thr Glu Ala Ser
50 55 60

Glu Ser Leu Cys Gly Leu Asn Leu Thr Val Asn Lys Tyr Gln Tyr Leu
65 70 75 80

Leu Thr Gly Arg Val Tyr Asn Gly Thr Met Tyr Thr Gly Leu Cys Asn
85 90 95

Phe Val Glu Arg Trp Asp Gln Leu Thr Leu Ser Gln Arg Lys Gly Leu
100 105 110

Asn Tyr Arg Tyr His Leu Gly Cys Asn Cys Lys Ile Lys Ser Cys Tyr
115 120 125

Tyr Leu Pro Cys Phe Val Thr Ser Lys Asn Glu Cys Leu Trp Thr Asp
130 135 140

Met Leu Ser Asn Phe Thr Tyr Pro Gly Tyr Gln Ser Lys His Tyr Ala
145 150 155 160

Cys Ile Asn Gln Thr Gly Gly Tyr Cys Ser Trp Tyr Arg Gly Trp Ala
165 170 175

Pro Pro Asp Lys Ser Ile Ile Asn Ala Thr Asp Pro
180 185

<210> 83
<211> 188
<212> PRT
<213> Homo sapiens

<220>

<223> huTIMP3(K50N,V52T, K94N,E96T, R138T, G173T)

<400> 83
Cys Thr Cys Ser Pro Ser His Pro Gln Asp Ala Phe Cys Asn Ser Asp
1 5 10 15

Ile Val Ile Arg Ala Lys Val Val Gly Lys Asn Leu Thr Lys Glu Gly
20 25 30

Pro Phe Gly Thr Leu Val Tyr Thr Ile Lys Gln Met Lys Met Tyr Arg
35 40 45

Gly Phe Thr Lys Met Pro His Val Gln Tyr Ile His Thr Glu Ala Ser
50 55 60

Glu Ser Leu Cys Gly Leu Asn Leu Thr Val Asn Lys Tyr Gln Tyr Leu
65 70 75 80

Leu Thr Gly Arg Val Tyr Asp Gly Lys Met Tyr Thr Gly Leu Cys Asn
85 90 95

Phe Val Glu Arg Trp Asp Gln Leu Thr Leu Ser Gln Arg Lys Gly Leu
100 105 110

Asn Tyr Thr Tyr His Leu Gly Cys Asn Cys Lys Ile Lys Ser Cys Tyr
115 120 125

Tyr Leu Pro Cys Phe Val Thr Ser Lys Asn Glu Cys Leu Trp Thr Asp
130 135 140

Met Leu Ser Asn Phe Thr Tyr Pro Gly Tyr Gln Ser Lys His Tyr Ala
145 150 155 160

Cys Ile Arg Gln Lys Gly Gly Tyr Cys Ser Trp Tyr Arg Gly Trp Ala
165 170 175

Pro Pro Asp Lys Ser Ile Ile Asn Ala Thr Asp Pro
180 185

<210> 84
<211> 188
<212> PRT
<213> Homo sapiens

<220>
<223> huTIMP3(K45E, K50N,V52T, K94N,E96T, D110N,K112T, R138T, G173T)

<400> 84
Cys Thr Cys Ser Pro Ser His Pro Gln Asp Ala Phe Cys Asn Ser Asp
1 5 10 15

Ile Val Ile Arg Ala Glu Val Val Gly Lys Asn Leu Thr Lys Glu Gly
20 25 30

```
Pro Phe Gly Thr Leu Val Tyr Thr Ile Lys Gln Met Lys Met Tyr Arg
        35                  40                  45

Gly Phe Thr Lys Met Pro His Val Gln Tyr Ile His Thr Glu Ala Ser
    50                  55                  60

Glu Ser Leu Cys Gly Leu Asn Leu Thr Val Asn Lys Tyr Gln Tyr Leu
65                  70                  75                  80

Leu Thr Gly Arg Val Tyr Asn Gly Thr Met Tyr Thr Gly Leu Cys Asn
                85                  90                  95

Phe Val Glu Arg Trp Asp Gln Leu Thr Leu Ser Gln Arg Lys Gly Leu
            100                 105                 110

Asn Tyr Thr Tyr His Leu Gly Cys Asn Cys Lys Ile Lys Ser Cys Tyr
        115                 120                 125

Tyr Leu Pro Cys Phe Val Thr Ser Lys Asn Glu Cys Leu Trp Thr Asp
    130                 135                 140

Met Leu Ser Asn Phe Thr Tyr Pro Gly Tyr Gln Ser Lys His Tyr Ala
145                 150                 155                 160

Cys Ile Arg Gln Lys Gly Gly Tyr Cys Ser Trp Tyr Arg Gly Trp Ala
                165                 170                 175

Pro Pro Asp Lys Ser Ile Ile Asn Ala Thr Asp Pro
            180                 185


<210> 85
<211> 188
<212> PRT
<213> Homo sapiens


<220>
<223> huTIMP3(K50N,V52T, K94N,E96T, R138T, G173T, R186N,K188T)

<400> 85
Cys Thr Cys Ser Pro Ser His Pro Gln Asp Ala Phe Cys Asn Ser Asp
1               5                   10                  15

Ile Val Ile Arg Ala Lys Val Val Gly Lys Asn Leu Thr Lys Glu Gly
            20                  25                  30

Pro Phe Gly Thr Leu Val Tyr Thr Ile Lys Gln Met Lys Met Tyr Arg
        35                  40                  45

Gly Phe Thr Lys Met Pro His Val Gln Tyr Ile His Thr Glu Ala Ser
    50                  55                  60

Glu Ser Leu Cys Gly Leu Asn Leu Thr Val Asn Lys Tyr Gln Tyr Leu
```

65 70 75 80

Leu Thr Gly Arg Val Tyr Asp Gly Lys Met Tyr Thr Gly Leu Cys Asn
85 90 95

Phe Val Glu Arg Trp Asp Gln Leu Thr Leu Ser Gln Arg Lys Gly Leu
100 105 110

Asn Tyr Thr Tyr His Leu Gly Cys Asn Cys Lys Ile Lys Ser Cys Tyr
115 120 125

Tyr Leu Pro Cys Phe Val Thr Ser Lys Asn Glu Cys Leu Trp Thr Asp
130 135 140

Met Leu Ser Asn Phe Thr Tyr Pro Gly Tyr Gln Ser Lys His Tyr Ala
145 150 155 160

Cys Ile Asn Gln Thr Gly Gly Tyr Cys Ser Trp Tyr Arg Gly Trp Ala
165 170 175

Pro Pro Asp Lys Ser Ile Ile Asn Ala Thr Asp Pro
180 185

<210> 86
<211> 188
<212> PRT
<213> Homo sapiens

<220>
<223> huTIMP3(K45E, F57N ,T63N,K65T, K94N,E96T ,G173T, R186N,K188T)

<400> 86
Cys Thr Cys Ser Pro Ser His Pro Gln Asp Ala Phe Cys Asn Ser Asp
1 5 10 15

Ile Val Ile Arg Ala Glu Val Val Gly Lys Lys Leu Val Lys Glu Gly
20 25 30

Pro Asn Gly Thr Leu Val Tyr Asn Ile Thr Gln Met Lys Met Tyr Arg
35 40 45

Gly Phe Thr Lys Met Pro His Val Gln Tyr Ile His Thr Glu Ala Ser
50 55 60

Glu Ser Leu Cys Gly Leu Asn Leu Thr Val Asn Lys Tyr Gln Tyr Leu
65 70 75 80

Leu Thr Gly Arg Val Tyr Asp Gly Lys Met Tyr Thr Gly Leu Cys Asn
85 90 95

Phe Val Glu Arg Trp Asp Gln Leu Thr Leu Ser Gln Arg Lys Gly Leu
100 105 110

```
Asn Tyr Arg Tyr His Leu Gly Cys Asn Cys Lys Ile Lys Ser Cys Tyr
        115                 120                 125

Tyr Leu Pro Cys Phe Val Thr Ser Lys Asn Glu Cys Leu Trp Thr Asp
    130                 135                 140

Met Leu Ser Asn Phe Thr Tyr Pro Gly Tyr Gln Ser Lys His Tyr Ala
145                 150                 155                 160

Cys Ile Asn Gln Thr Gly Gly Tyr Cys Ser Trp Tyr Arg Gly Trp Ala
                165                 170                 175

Pro Pro Asp Lys Ser Ile Ile Asn Ala Thr Asp Pro
            180                 185


<210> 87
<211> 188
<212> PRT
<213> Homo sapiens


<220>
<223> huTIMP3(K45N,V47T, F57N, K94N,E96T, D110N,K112T, G173T, R186Q,K188Q)

<400> 87
Cys Thr Cys Ser Pro Ser His Pro Gln Asp Ala Phe Cys Asn Ser Asp
1               5                   10                  15

Ile Val Ile Arg Ala Asn Val Thr Gly Lys Lys Leu Val Lys Glu Gly
            20                  25                  30

Pro Asn Gly Thr Leu Val Tyr Thr Ile Lys Gln Met Lys Met Tyr Arg
        35                  40                  45

Gly Phe Thr Lys Met Pro His Val Gln Tyr Ile His Thr Glu Ala Ser
    50                  55                  60

Glu Ser Leu Cys Gly Leu Asn Leu Thr Val Asn Lys Tyr Gln Tyr Leu
65                  70                  75                  80

Leu Thr Gly Arg Val Tyr Asn Gly Thr Met Tyr Thr Gly Leu Cys Asn
                85                  90                  95

Phe Val Glu Arg Trp Asp Gln Leu Thr Leu Ser Gln Arg Lys Gly Leu
            100                 105                 110

Asn Tyr Arg Tyr His Leu Gly Cys Asn Cys Lys Ile Lys Ser Cys Tyr
        115                 120                 125

Tyr Leu Pro Cys Phe Val Thr Ser Lys Asn Glu Cys Leu Trp Thr Asp
    130                 135                 140

Met Leu Ser Asn Phe Thr Tyr Pro Gly Tyr Gln Ser Lys His Tyr Ala
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145 150 155 160

Cys Ile Gln Gln Gln Gly Gly Tyr Cys Ser Trp Tyr Arg Gly Trp Ala
165 170 175

Pro Pro Asp Lys Ser Ile Ile Asn Ala Thr Asp Pro
180 185

<210> 88
<211> 188
<212> PRT
<213> Homo sapiens

<220>
<223> HuTIMP3(K45S, F57N, K94N, E96T, R138T, G173T)

<400> 88
Cys Thr Cys Ser Pro Ser His Pro Gln Asp Ala Phe Cys Asn Ser Asp
1 5 10 15

Ile Val Ile Arg Ala Ser Val Val Gly Lys Lys Leu Val Lys Glu Gly
20 25 30

Pro Asn Gly Thr Leu Val Tyr Thr Ile Lys Gln Met Lys Met Tyr Arg
35 40 45

Gly Phe Thr Lys Met Pro His Val Gln Tyr Ile His Thr Glu Ala Ser
50 55 60

Glu Ser Leu Cys Gly Leu Asn Leu Thr Val Asn Lys Tyr Gln Tyr Leu
65 70 75 80

Leu Thr Gly Arg Val Tyr Asp Gly Lys Met Tyr Thr Gly Leu Cys Asn
85 90 95

Phe Val Glu Arg Trp Asp Gln Leu Thr Leu Ser Gln Arg Lys Gly Leu
100 105 110

Asn Tyr Thr Tyr His Leu Gly Cys Asn Cys Lys Ile Lys Ser Cys Tyr
115 120 125

Tyr Leu Pro Cys Phe Val Thr Ser Lys Asn Glu Cys Leu Trp Thr Asp
130 135 140

Met Leu Ser Asn Phe Thr Tyr Pro Gly Tyr Gln Ser Lys His Tyr Ala
145 150 155 160

Cys Ile Arg Gln Lys Gly Gly Tyr Cys Ser Trp Tyr Arg Gly Trp Ala
165 170 175

Pro Pro Asp Lys Ser Ile Ile Asn Ala Thr Asp Pro
180 185

<210> 89
<211> 188
<212> PRT
<213> Homo sapiens

<220>
<223> HuTIMP3(K45E, F57N, K94N, E96T, R138T, G173T)

<400> 89
Cys Thr Cys Ser Pro Ser His Pro Gln Asp Ala Phe Cys Asn Ser Asp
1 5 10 15

Ile Val Ile Arg Ala Glu Val Val Gly Lys Lys Leu Val Lys Glu Gly
20 25 30

Pro Asn Gly Thr Leu Val Tyr Thr Ile Lys Gln Met Lys Met Tyr Arg
35 40 45

Gly Phe Thr Lys Met Pro His Val Gln Tyr Ile His Thr Glu Ala Ser
50 55 60

Glu Ser Leu Cys Gly Leu Asn Leu Thr Val Asn Lys Tyr Gln Tyr Leu
65 70 75 80

Leu Thr Gly Arg Val Tyr Asp Gly Lys Met Tyr Thr Gly Leu Cys Asn
85 90 95

Phe Val Glu Arg Trp Asp Gln Leu Thr Leu Ser Gln Arg Lys Gly Leu
100 105 110

Asn Tyr Thr Tyr His Leu Gly Cys Asn Cys Lys Ile Lys Ser Cys Tyr
115 120 125

Tyr Leu Pro Cys Phe Val Thr Ser Lys Asn Glu Cys Leu Trp Thr Asp
130 135 140

Met Leu Ser Asn Phe Thr Tyr Pro Gly Tyr Gln Ser Lys His Tyr Ala
145 150 155 160

Cys Ile Arg Gln Lys Gly Gly Tyr Cys Ser Trp Tyr Arg Gly Trp Ala
165 170 175

Pro Pro Asp Lys Ser Ile Ile Asn Ala Thr Asp Pro
180 185

<210> 90
<211> 188
<212> PRT
<213> Homo sapiens

<220>
<223> HuTIMP3(K45E, F57N, K94N, E96T, D110N, K112T, R138T, G173T)

<400> 90
Cys Thr Cys Ser Pro Ser His Pro Gln Asp Ala Phe Cys Asn Ser Asp
1 5 10 15

Ile Val Ile Arg Ala Glu Val Val Gly Lys Lys Leu Val Lys Glu Gly
20 25 30

Pro Asn Gly Thr Leu Val Tyr Thr Ile Lys Gln Met Lys Met Tyr Arg
35 40 45

Gly Phe Thr Lys Met Pro His Val Gln Tyr Ile His Thr Glu Ala Ser
50 55 60

Glu Ser Leu Cys Gly Leu Asn Leu Thr Val Asn Lys Tyr Gln Tyr Leu
65 70 75 80

Leu Thr Gly Arg Val Tyr Asn Gly Thr Met Tyr Thr Gly Leu Cys Asn
85 90 95

Phe Val Glu Arg Trp Asp Gln Leu Thr Leu Ser Gln Arg Lys Gly Leu
100 105 110

Asn Tyr Thr Tyr His Leu Gly Cys Asn Cys Lys Ile Lys Ser Cys Tyr
115 120 125

Tyr Leu Pro Cys Phe Val Thr Ser Lys Asn Glu Cys Leu Trp Thr Asp
130 135 140

Met Leu Ser Asn Phe Thr Tyr Pro Gly Tyr Gln Ser Lys His Tyr Ala
145 150 155 160

Cys Ile Arg Gln Lys Gly Gly Tyr Cys Ser Trp Tyr Arg Gly Trp Ala
165 170 175

Pro Pro Asp Lys Ser Ile Ile Asn Ala Thr Asp Pro
180 185

<210> 91
<211> 188
<212> PRT
<213> Homo sapiens

<220>
<223> HuTIMP3(K45E, F57N, K94N, E96T, R138T, G173T, R186Q, K188Q)

<400> 91
Cys Thr Cys Ser Pro Ser His Pro Gln Asp Ala Phe Cys Asn Ser Asp
1 5 10 15

Ile Val Ile Arg Ala Glu Val Val Gly Lys Lys Leu Val Lys Glu Gly
20 25 30

Pro Asn Gly Thr Leu Val Tyr Thr Ile Lys Gln Met Lys Met Tyr Arg

35 40 45

Gly Phe Thr Lys Met Pro His Val Gln Tyr Ile His Thr Glu Ala Ser
50 55 60

Glu Ser Leu Cys Gly Leu Asn Leu Thr Val Asn Lys Tyr Gln Tyr Leu
65 70 75 80

Leu Thr Gly Arg Val Tyr Asp Gly Lys Met Tyr Thr Gly Leu Cys Asn
85 90 95

Phe Val Glu Arg Trp Asp Gln Leu Thr Leu Ser Gln Arg Lys Gly Leu
100 105 110

Asn Tyr Thr Tyr His Leu Gly Cys Asn Cys Lys Ile Lys Ser Cys Tyr
115 120 125

Tyr Leu Pro Cys Phe Val Thr Ser Lys Asn Glu Cys Leu Trp Thr Asp
130 135 140

Met Leu Ser Asn Phe Thr Tyr Pro Gly Tyr Gln Ser Lys His Tyr Ala
145 150 155 160

Cys Ile Gln Gln Gln Gly Gly Tyr Cys Ser Trp Tyr Arg Gly Trp Ala
165 170 175

Pro Pro Asp Lys Ser Ile Ile Asn Ala Thr Asp Pro
180 185

<210> 92
<211> 188
<212> PRT
<213> Homo sapiens

<220>
<223> HuTIMP3(K45E, F57N, K94N, E96T, R138T, G173T, R186E)

<400> 92
Cys Thr Cys Ser Pro Ser His Pro Gln Asp Ala Phe Cys Asn Ser Asp
1 5 10 15

Ile Val Ile Arg Ala Glu Val Val Gly Lys Lys Leu Val Lys Glu Gly
20 25 30

Pro Asn Gly Thr Leu Val Tyr Thr Ile Lys Gln Met Lys Met Tyr Arg
35 40 45

Gly Phe Thr Lys Met Pro His Val Gln Tyr Ile His Thr Glu Ala Ser
50 55 60

Glu Ser Leu Cys Gly Leu Asn Leu Thr Val Asn Lys Tyr Gln Tyr Leu
65 70 75 80

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Leu Thr Gly Arg Val Tyr Asp Gly Lys Met Tyr Thr Gly Leu Cys Asn
                85                  90                  95

Phe Val Glu Arg Trp Asp Gln Leu Thr Leu Ser Gln Arg Lys Gly Leu
            100                 105                 110

Asn Tyr Thr Tyr His Leu Gly Cys Asn Cys Lys Ile Lys Ser Cys Tyr
        115                 120                 125

Tyr Leu Pro Cys Phe Val Thr Ser Lys Asn Glu Cys Leu Trp Thr Asp
    130                 135                 140

Met Leu Ser Asn Phe Thr Tyr Pro Gly Tyr Gln Ser Lys His Tyr Ala
145                 150                 155                 160

Cys Ile Glu Gln Lys Gly Gly Tyr Cys Ser Trp Tyr Arg Gly Trp Ala
                165                 170                 175

Pro Pro Asp Lys Ser Ile Ile Asn Ala Thr Asp Pro
            180                 185
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<210> 93
<211> 188
<212> PRT
<213> Homo sapiens

<220>
<223> HuTIMP3(K45E, F57N, K94N, E96T, R138T, G173T, K188E)

<400> 93

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Cys Thr Cys Ser Pro Ser His Pro Gln Asp Ala Phe Cys Asn Ser Asp
1               5                   10                  15

Ile Val Ile Arg Ala Glu Val Val Gly Lys Lys Leu Val Lys Glu Gly
            20                  25                  30

Pro Asn Gly Thr Leu Val Tyr Thr Ile Lys Gln Met Lys Met Tyr Arg
        35                  40                  45

Gly Phe Thr Lys Met Pro His Val Gln Tyr Ile His Thr Glu Ala Ser
    50                  55                  60

Glu Ser Leu Cys Gly Leu Asn Leu Thr Val Asn Lys Tyr Gln Tyr Leu
65                  70                  75                  80

Leu Thr Gly Arg Val Tyr Asp Gly Lys Met Tyr Thr Gly Leu Cys Asn
                85                  90                  95

Phe Val Glu Arg Trp Asp Gln Leu Thr Leu Ser Gln Arg Lys Gly Leu
            100                 105                 110

Asn Tyr Thr Tyr His Leu Gly Cys Asn Cys Lys Ile Lys Ser Cys Tyr
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        115                 120                 125

Tyr Leu Pro Cys Phe Val Thr Ser Lys Asn Glu Cys Leu Trp Thr Asp
    130                 135                 140

Met Leu Ser Asn Phe Thr Tyr Pro Gly Tyr Gln Ser Lys His Tyr Ala
145                 150                 155                 160

Cys Ile Arg Gln Glu Gly Gly Tyr Cys Ser Trp Tyr Arg Gly Trp Ala
                165                 170                 175

Pro Pro Asp Lys Ser Ile Ile Asn Ala Thr Asp Pro
            180                 185

<210> 94
<211> 188
<212> PRT
<213> Homo sapiens

<220>
<223> HuTIMP3(K45E, F57N, K94N, E96T, R138T, G173T, R186N, K188T)

<400> 94
Cys Thr Cys Ser Pro Ser His Pro Gln Asp Ala Phe Cys Asn Ser Asp
1               5                   10                  15

Ile Val Ile Arg Ala Glu Val Val Gly Lys Lys Leu Val Lys Glu Gly
            20                  25                  30

Pro Asn Gly Thr Leu Val Tyr Thr Ile Lys Gln Met Lys Met Tyr Arg
        35                  40                  45

Gly Phe Thr Lys Met Pro His Val Gln Tyr Ile His Thr Glu Ala Ser
    50                  55                  60

Glu Ser Leu Cys Gly Leu Asn Leu Thr Val Asn Lys Tyr Gln Tyr Leu
65                  70                  75                  80

Leu Thr Gly Arg Val Tyr Asp Gly Lys Met Tyr Thr Gly Leu Cys Asn
                85                  90                  95

Phe Val Glu Arg Trp Asp Gln Leu Thr Leu Ser Gln Arg Lys Gly Leu
            100                 105                 110

Asn Tyr Thr Tyr His Leu Gly Cys Asn Cys Lys Ile Lys Ser Cys Tyr
        115                 120                 125

Tyr Leu Pro Cys Phe Val Thr Ser Lys Asn Glu Cys Leu Trp Thr Asp
    130                 135                 140

Met Leu Ser Asn Phe Thr Tyr Pro Gly Tyr Gln Ser Lys His Tyr Ala
145                 150                 155                 160
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Cys Ile Asn Gln Thr Gly Gly Tyr Cys Ser Trp Tyr Arg Gly Trp Ala
                165                 170                 175

Pro Pro Asp Lys Ser Ile Ile Asn Ala Thr Asp Pro
            180                 185

<210> 95
<211> 188
<212> PRT
<213> Homo sapiens

<220>
<223> HuTIMP3(K45E, K50N, V52T, K94N, E96T, D110N, K112T, R138T, G173T)

<400> 95
Cys Thr Cys Ser Pro Ser His Pro Gln Asp Ala Phe Cys Asn Ser Asp
1               5                   10                  15

Ile Val Ile Arg Ala Glu Val Val Gly Lys Asn Leu Thr Lys Glu Gly
            20                  25                  30

Pro Phe Gly Thr Leu Val Tyr Thr Ile Lys Gln Met Lys Met Tyr Arg
        35                  40                  45

Gly Phe Thr Lys Met Pro His Val Gln Tyr Ile His Thr Glu Ala Ser
    50                  55                  60

Glu Ser Leu Cys Gly Leu Asn Leu Thr Val Asn Lys Tyr Gln Tyr Leu
65                  70                  75                  80

Leu Thr Gly Arg Val Tyr Asn Gly Thr Met Tyr Thr Gly Leu Cys Asn
                85                  90                  95

Phe Val Glu Arg Trp Asp Gln Leu Thr Leu Ser Gln Arg Lys Gly Leu
            100                 105                 110

Asn Tyr Thr Tyr His Leu Gly Cys Asn Cys Lys Ile Lys Ser Cys Tyr
        115                 120                 125

Tyr Leu Pro Cys Phe Val Thr Ser Lys Asn Glu Cys Leu Trp Thr Asp
    130                 135                 140

Met Leu Ser Asn Phe Thr Tyr Pro Gly Tyr Gln Ser Lys His Tyr Ala
145                 150                 155                 160

Cys Ile Arg Gln Lys Gly Gly Tyr Cys Ser Trp Tyr Arg Gly Trp Ala
                165                 170                 175

Pro Pro Asp Lys Ser Ile Ile Asn Ala Thr Asp Pro
            180                 185

<210> 96
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<211> 188
<212> PRT
<213> Homo sapiens

<220>
<223> HuTIMP3(K45E, K50N, V52T, K94N, E96T, R138T, G173T, K188E)

<400> 96
Cys Thr Cys Ser Pro Ser His Pro Gln Asp Ala Phe Cys Asn Ser Asp
1 5 10 15

Ile Val Ile Arg Ala Glu Val Val Gly Lys Asn Leu Thr Lys Glu Gly
20 25 30

Pro Phe Gly Thr Leu Val Tyr Thr Ile Lys Gln Met Lys Met Tyr Arg
35 40 45

Gly Phe Thr Lys Met Pro His Val Gln Tyr Ile His Thr Glu Ala Ser
50 55 60

Glu Ser Leu Cys Gly Leu Asn Leu Thr Val Asn Lys Tyr Gln Tyr Leu
65 70 75 80

Leu Thr Gly Arg Val Tyr Asp Gly Lys Met Tyr Thr Gly Leu Cys Asn
85 90 95

Phe Val Glu Arg Trp Asp Gln Leu Thr Leu Ser Gln Arg Lys Gly Leu
100 105 110

Asn Tyr Thr Tyr His Leu Gly Cys Asn Cys Lys Ile Lys Ser Cys Tyr
115 120 125

Tyr Leu Pro Cys Phe Val Thr Ser Lys Asn Glu Cys Leu Trp Thr Asp
130 135 140

Met Leu Ser Asn Phe Thr Tyr Pro Gly Tyr Gln Ser Lys His Tyr Ala
145 150 155 160

Cys Ile Arg Gln Glu Gly Gly Tyr Cys Ser Trp Tyr Arg Gly Trp Ala
165 170 175

Pro Pro Asp Lys Ser Ile Ile Asn Ala Thr Asp Pro
180 185

<210> 97
<211> 188
<212> PRT
<213> Homo sapiens

<220>
<223> HuTIMP3(K50N, V52T, F57N, K94N, E96T, R138T, G173T)

<400> 97
Cys Thr Cys Ser Pro Ser His Pro Gln Asp Ala Phe Cys Asn Ser Asp

1 5 10 15

Ile Val Ile Arg Ala Lys Val Val Gly Lys Asn Leu Thr Lys Glu Gly
20 25 30

Pro Asn Gly Thr Leu Val Tyr Thr Ile Lys Gln Met Lys Met Tyr Arg
35 40 45

Gly Phe Thr Lys Met Pro His Val Gln Tyr Ile His Thr Glu Ala Ser
50 55 60

Glu Ser Leu Cys Gly Leu Asn Leu Thr Val Asn Lys Tyr Gln Tyr Leu
65 70 75 80

Leu Thr Gly Arg Val Tyr Asp Gly Lys Met Tyr Thr Gly Leu Cys Asn
85 90 95

Phe Val Glu Arg Trp Asp Gln Leu Thr Leu Ser Gln Arg Lys Gly Leu
100 105 110

Asn Tyr Thr Tyr His Leu Gly Cys Asn Cys Lys Ile Lys Ser Cys Tyr
115 120 125

Tyr Leu Pro Cys Phe Val Thr Ser Lys Asn Glu Cys Leu Trp Thr Asp
130 135 140

Met Leu Ser Asn Phe Thr Tyr Pro Gly Tyr Gln Ser Lys His Tyr Ala
145 150 155 160

Cys Ile Arg Gln Lys Gly Gly Tyr Cys Ser Trp Tyr Arg Gly Trp Ala
165 170 175

Pro Pro Asp Lys Ser Ile Ile Asn Ala Thr Asp Pro
180 185

<210> 98
<211> 188
<212> PRT
<213> Homo sapiens

<220>
<223> HuTIMP3(K50N, V52T, F57N, K94N, E96T, D110N, K112T, R138T)

<400> 98
Cys Thr Cys Ser Pro Ser His Pro Gln Asp Ala Phe Cys Asn Ser Asp
1 5 10 15

Ile Val Ile Arg Ala Lys Val Val Gly Lys Asn Leu Thr Lys Glu Gly
20 25 30

Pro Asn Gly Thr Leu Val Tyr Thr Ile Lys Gln Met Lys Met Tyr Arg
35 40 45

```
Gly Phe Thr Lys Met Pro His Val Gln Tyr Ile His Thr Glu Ala Ser
    50                  55                  60

Glu Ser Leu Cys Gly Leu Asn Leu Thr Val Asn Lys Tyr Gln Tyr Leu
65                  70                  75                  80

Leu Thr Gly Arg Val Tyr Asn Gly Thr Met Tyr Thr Gly Leu Cys Asn
                85                  90                  95

Phe Val Glu Arg Trp Asp Gln Leu Thr Leu Ser Gln Arg Lys Gly Leu
            100                 105                 110

Asn Tyr Thr Tyr His Leu Gly Cys Asn Cys Lys Ile Lys Ser Cys Tyr
        115                 120                 125

Tyr Leu Pro Cys Phe Val Thr Ser Lys Asn Glu Cys Leu Trp Thr Asp
    130                 135                 140

Met Leu Ser Asn Phe Gly Tyr Pro Gly Tyr Gln Ser Lys His Tyr Ala
145                 150                 155                 160

Cys Ile Arg Gln Lys Gly Gly Tyr Cys Ser Trp Tyr Arg Gly Trp Ala
                165                 170                 175

Pro Pro Asp Lys Ser Ile Ile Asn Ala Thr Asp Pro
            180                 185
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<210> 99
<211> 188
<212> PRT
<213> Homo sapiens

<220>
<223> HuTIMP3(K45E, F57N, K94N, E96T, D110N, K112T, R138T)

<400> 99

```
Cys Thr Cys Ser Pro Ser His Pro Gln Asp Ala Phe Cys Asn Ser Asp
1               5                   10                  15

Ile Val Ile Arg Ala Glu Val Val Gly Lys Lys Leu Val Lys Glu Gly
            20                  25                  30

Pro Asn Gly Thr Leu Val Tyr Thr Ile Lys Gln Met Lys Met Tyr Arg
        35                  40                  45

Gly Phe Thr Lys Met Pro His Val Gln Tyr Ile His Thr Glu Ala Ser
    50                  55                  60

Glu Ser Leu Cys Gly Leu Asn Leu Thr Val Asn Lys Tyr Gln Tyr Leu
65                  70                  75                  80

Leu Thr Gly Arg Val Tyr Asn Gly Thr Met Tyr Thr Gly Leu Cys Asn
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```
                85                  90                  95

Phe Val Glu Arg Trp Asp Gln Leu Thr Leu Ser Gln Arg Lys Gly Leu
            100                 105                 110

Asn Tyr Thr Tyr His Leu Gly Cys Asn Cys Lys Ile Lys Ser Cys Tyr
        115                 120                 125

Tyr Leu Pro Cys Phe Val Thr Ser Lys Asn Glu Cys Leu Trp Thr Asp
    130                 135                 140

Met Leu Ser Asn Phe Gly Tyr Pro Gly Tyr Gln Ser Lys His Tyr Ala
145                 150                 155                 160

Cys Ile Arg Gln Lys Gly Gly Tyr Cys Ser Trp Tyr Arg Gly Trp Ala
                165                 170                 175

Pro Pro Asp Lys Ser Ile Ile Asn Ala Thr Asp Pro
            180                 185
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