Dis Sci. 2007 Feb;52(2):536-42), pancreatic cancer and colorectal cancer (Su *et al.*, *Mod Pathol.* 2008 Nov;21(11):1379-86) and hepatocellular carcinoma (Wong *et al.*, *Biochem Biophys Res Commun.* 2003 Nov 21;311(3):618-24). International Patent Application WO2008/026008 discloses Cadherin-17 as a marker for colorectal cancer and as a biological target for therapeutic antibodies and other pharmaceutical agents.

SUMMARY OF THE INVENTION

[005] Described herein are~~The present invention provides~~ antibodies directed against Cadherin-17, nucleic acids encoding such antibodies and therapeutic proteins, methods for preparing anti-Cadherin-17 monoclonal antibodies and other therapeutic proteins, and methods for the treatment of diseases, such as Cadherin-17 mediated disorders, e.g., human cancers, including colorectal cancer.

[005a] In a first aspect, the present invention refers to an isolated anti-Cadherin-17 antibody comprising:

a heavy chain variable region CDR 1 comprising SEQ ID NO: 4;

a heavy chain variable region CDR2 comprising SEQ ID NO: 8;

a heavy chain variable region CDR3 comprising SEQ ID NO: 17;

a light chain variable region CDR1 comprising SEQ ID NO: 24;

a light chain variable region CDR2 comprising SEQ ID NO: 30; and

a light chain variable region CDR3 comprising SEQ ID NO: 34;

optionally wherein any of the above SEQ ID NOs independently comprise one, two or three amino acid substiutions, additions or deletions.

[005b] In a second aspect, the present invention refers to an isolated anti-Cadherin-17 antibody comprising:

(a) the heavy chain variable region amino acid sequence set forth in SEQ ID NO:38 or an amino acid sequence at least 90% homologous thereto, and

(b) the light chain variable region amino acid sequence set forth in SEQ ID NO:49 or an amino acid sequence at least 90% homologous thereto.

[005c] In a third aspect, the present invention refers to the use of an anti-Cadherin-17 antibody of the present invention or an immunoconjugate of the present invention in the manufacture of a medicament for treating or preventing cancer associated with target cells expressing Cadherin-17.

[006] Thus, further described herein are~~the present invention provides~~ isolated monoclonal antibodies, in particular murine, chimeric, humanized, and fully-human monoclonal antibodies, that bind to Cadherin-17 and that exhibit one or more desirable functional property. Such properties include, for example, high affinity specific binding to human Cadherin-17. Also provided are methods for treating a variety of Cadherin-17-mediated diseases using the antibodies, proteins, and compositions described herein~~of the present invention~~.

[007] Described herein is~~The present invention provides~~ an isolated monoclonal antibody, or an antigen-binding portion thereof, an antibody fragment, or an antibody mimetic which binds an epitope on human Cadherin-17 recognized by an antibody comprising a heavy chain variable region comprising an amino acid sequence set forth in a SEQ ID NO: selected from the group consisting of 38, 35, 36, 37, 39, 40, 41, 42, 43, 44, 45 and 46 and a light chain variable region comprising an amino acid sequence set forth in a SEQ ID NO: selected from the group consisting of 49, 47, 48, 50, 51, 52, 53, 54, 55, 56, 57 and 58. In some ~~embodiments~~examples the isolated antibody is a full-length antibody of an IgG1, IgG2, IgG3, or IgG4 isotype.

[008] In some ~~embodiments~~examples, the antibody described herein~~of the present invention~~ is selected from the group consisting of: a whole antibody, an antibody fragment, a humanized antibody, a single chain antibody, an immunoconjugate, a defucosylated antibody, and a bispecific antibody. The antibody fragment may be selected from the group consisting of: a UniBody, a domain antibody, and a Nanobody. In some ~~embodiments~~examples, the immunoconjugates described herein~~of the invention~~ comprise a therapeutic agent. In another example~~aspect of the invention~~, the therapeutic agent is a cytotoxin or a radioactive isotope.

[009] In some ~~embodiments~~examples, the antibody described herein~~of the present invention~~ is selected from the group consisting of: an Affibody, a DARPin, an Anticalin, an Avimer, a Versabody, and a Duocalin.

[010] In alternative ~~embodiments~~examples, compositions ~~of the present invention~~described herein comprise an isolated antibody or antigen-binding portion and a pharmaceutically acceptable carrier.

[011] In other ~~aspects~~examples, the antibody ~~of the present invention~~described herein is a composition comprising the isolated antibody or antigen-binding portion as described herein~~according to the invention~~ and a pharmaceutically acceptable carrier.

[012] In some ~~embodiments~~examples, it is described~~the invention comprises~~ an isolated nucleic acid molecule encoding the heavy or light chain of the isolated antibody or antigen-binding portion which binds an epitope on human Cadherin-17. Other examples~~aspects of the invention~~ comprise expression vectors comprising such nucleic acid molecules, and host cells comprising such expression vectors.

[013] In some ~~embodiments~~examples, it is described~~the present invention provides~~ a method for preparing an anti-Cadherin-17 antibody, said method comprising the steps of: obtaining a host cell that contains one or more nucleic acid molecules encoding the antibody described herein~~of the invention~~; growing the host cell in a host cell culture; providing host cell culture conditions wherein the one or more nucleic acid molecules are expressed; and recovering the antibody from the host cell or from the host cell culture.

[014] In other ~~embodiments~~examples, described herein are~~the invention is directed to~~ methods for treating or preventing a disease associated with target cells expressing Cadherin-17, said method comprising the step of administering to a subject an anti-Cadherin-17 antibody, or antigen-binding portion thereof, in an amount effective to treat or prevent the disease. In some ~~aspects~~examples, the disease treated or prevented by the antibodies or antigen-binding portion thereof as described herein~~of the invention~~, is human cancer. In some ~~embodiments~~examples, the disease treated or prevented by the antibodies ~~of the present invention~~described herein is colorectal cancer.

[015] In other ~~embodiments~~examples, described herein~~the invention is directed to~~ an anti-Cadherin-17 antibody, or antigen-binding portion thereof, for use in treating or preventing a disease associated with target cells expressing Cadherin-17. In some ~~aspects~~examples, the disease treated or prevented by the antibodies or antigen-binding portion thereof as described herein~~of the invention~~, is human cancer. In some ~~embodiments~~examples, the disease treated or prevented by the antibodies ~~of the present invention~~as described herein is colorectal cancer.

[016] In other ~~embodiments~~examples, it is described~~the invention is directed to~~ the use of an anti-Cadherin-17 antibody, or antigen-binding portion thereof, for the manufacture of a medicament for use in

treating or preventing a disease associated with target cells expressing Cadherin-17. In some ~~aspects~~examples, the disease treated or prevented by the medicament ~~of the invention~~described herein, is human cancer. In some ~~embodiments~~examples, the disease treated or prevented by the medicament described herein~~of the present invention~~ is colorectal cancer.

[017] In other ~~embodiments~~examples, described herein~~the present invention~~ is an isolated monoclonal antibody or an antigen binding portion thereof, an antibody fragment, or an antibody mimetic which binds an epitope on human Cadherin-17 recognized by an antibody comprising a heavy chain variable region and a light chain variable region selected from the group consisting of the heavy chain variable region amino acid sequence set forth in SEQ ID NO:35 and the light chain variable region amino acid sequence set forth in SEQ ID NO:47; the heavy chain variable region amino acid sequence set forth in SEQ ID NO:36 and the light chain variable region amino acid sequence set forth in SEQ ID NO:48; the heavy chain variable region amino acid sequence set forth in SEQ ID NO:37 and the light chain variable region amino acid sequence set forth in SEQ ID NO:48; the heavy chain variable region amino acid sequence set forth in SEQ ID NO:38 and the light chain variable region amino acid sequence set forth in SEQ ID NO:49; the heavy chain variable region amino acid sequence set forth in SEQ ID NO:39 and the light chain variable region amino acid sequence set forth in SEQ ID NO:50; the heavy chain variable region amino acid sequence set forth in SEQ ID NO:40 and the light chain variable region amino acid sequence set forth in SEQ ID NO:51; the heavy chain variable region amino acid sequence set forth in SEQ ID NO:40 and the light chain variable region amino acid sequence set forth in SEQ ID NO:54; the heavy chain variable region amino acid sequence set forth in SEQ ID NO:40 and the light chain variable region amino acid sequence set forth in SEQ ID NO:55; the heavy chain variable region amino acid sequence set forth in SEQ ID NO:41 and the light chain variable region amino acid sequence set forth in SEQ ID NO:52; the heavy chain variable region amino acid sequence set forth in SEQ ID NO:42 and the light chain variable region amino acid sequence set forth in SEQ ID NO:53; the heavy chain variable region amino acid sequence set forth in SEQ ID NO:43 and the light chain variable region amino acid sequence set forth in SEQ ID NO:56; the heavy chain variable region amino acid sequence set forth in SEQ ID NO:44 and the light chain variable region amino acid sequence set forth in SEQ ID NO:55; the heavy chain variable region amino acid sequence set forth in SEQ ID NO:45 and the light chain variable region amino acid sequence set forth in SEQ ID NO:57; and the heavy chain variable region amino acid sequence set forth in SEQ ID NO:46 and the light chain variable region amino acid sequence set forth in SEQ ID NO:58. In further ~~aspects~~examples, the antibody is selected from the

group consisting of: a whole antibody, an antibody fragment, a humanized antibody, a single chain antibody, an immunoconjugate, a defucosylated antibody, and a bispecific antibody. In further examples~~aspects of the invention~~, the antibody fragment is selected from the group consisting of: a UniBody, a domain antibody, and a Nanobody. In some ~~embodiments~~examples, the antibody mimetic is selected from the group consisting of: an Affibody, a DARPin, an Anticalin, an Avimer, a Versabody, and a Duocalin. In further ~~embodiments~~examples, the composition comprises the isolated antibody or antigen binding portion thereof and a pharmaceutically acceptable carrier.

[018] In some ~~embodiments~~examples, described herein~~the present invention~~ is an isolated nucleic acid molecule encoding the heavy or light chain of the isolated antibody or antigen binding portion thereof of antibody ~~of the invention~~as described herein, and in further ~~aspects~~examples may include an expression vector comprising such nucleic acids, and host cells comprising such expression vectors.

[019] Another example~~embodiment of the present invention~~ is a hybridoma expressing the antibody or antigen binding portion thereof of any one of antibodies ~~of the invention~~described herein.

[020] Other examples~~aspects of the invention~~ are directed to methods of making the antibodies ~~of the invention~~as described herein, comprising the steps of:

immunizing an animal with a Cadherin-17 peptide;

recovering mRNA from the B cells of said animal;

converting said mRNA to cDNA;

expressing said cDNA in phages such that anti-Cadherin-17 antibodies encoded by said cDNA are presented on the surface of said phages;

selecting phages that present anti-Cadherin-17 antibodies;

recovering nucleic acid molecules from said selected phages that encode said anti-Cadherin-17 immunoglobulins;

expressing said recovered nucleic acid molecules in a host cell; and

recovering antibodies from said host cell that bind Cadherin-17.

[021] In some examples~~aspects of the invention~~, the isolated monoclonal antibody, or an antigen binding portion thereof, binds an epitope on the Cadherin-17 polypeptide having an amino acid sequence of SEQ ID NOS: 136 or 137 recognized by an antibody comprising a heavy chain variable region comprising an amino acid sequence set forth in a SEQ ID NO: selected from the group consisting of 38, 35, 36, 37, 39, 40, 41, 42, 43, 44, 45, or 46 and a light chain variable region comprising an amino acid sequence set forth in a SEQ ID NO: selected from the group consisiting of 49, 47, 48, 50, 51, 52, 53, 54, 55, 56, 57, or 58.

~~WHAT IS CLAIMED:~~

1. An isolated anti-Cadherin-17 antibody comprising:

a heavy chain variable region CDR 1 comprising SEQ ID NO: 4;

a heavy chain variable region CDR2 comprising SEQ ID NO: 8;

a heavy chain variable region CDR3 comprising SEQ ID NO: 17;

a light chain variable region CDR1 comprising SEQ ID NO: 24;

a light chain variable region CDR2 comprising SEQ ID NO: 30; and

a light chain variable region CDR3 comprising SEQ ID NO: 34;

optionally wherein any of the above SEQ ID NOs independently comprise one, two or three amino acid substiutions, additions or deletions.

2. An isolated anti-Cadherin-17 antibody comprising:

(a) the heavy chain variable region amino acid sequence set forth in SEQ ID NO:38 or an amino acid sequence at least 90% homologous thereto, and

(b) the light chain variable region amino acid sequence set forth in SEQ ID NO:49 or an amino acid sequence at least 90% homologous thereto.

~~3. The antibody of claim 1 or 2, wherein said antibody is a full-length antibody of an IgG1,~~ IgG2, IgG3, or IgG4 isotype.

4. The antibody of any one of the preceding claims, wherein said antibody is selected from the group consisting of: a whole antibody, a monoclonal antibody, an antibody fragment, a humanized antibody, a single chain antibody, a defucosylated antibody, an antibody mimetic and a bispecific antibody.

5. The antibody of claim 4, wherein said fragment is selected from the group consisting of: a UniBody, a domain antibody, and a Nanobody.

6. The antibody of claim 4, wherein the mimetic is selected from the group consisting of: an Affibody, a DARPin, an Anticalin, an Avimer, a Versabody, and a Duocalin.

7. An immunoconjugate comprising an antibody according to any one of the preceding claims conjugated to a therapeutic agent.

8. The immunoconjugate of claim 7 wherein the therapeutic agent is a cytotoxin or a radioactive isotope.

9. A composition comprising the isolated antibody or antigen-binding portion thereof of any one of claims 1 to 8 and a pharmaceutically acceptable carrier.

10. An isolated nucleic acid molecule encoding the heavy or light chain of the antibody or antigen-binding portion thereof of any one of claims 1 to 8.

11. An expression vector comprising the nucleic acid molecule of claim 10.

12. A host cell comprising the expression vector of claim 11.

13. A method for preparing an anti-Cadherin-17 antibody, said method comprising the steps of: obtaining a host cell that contains one or more nucleic acid molecules encoding the antibody of any one of claims 1 to 8;

growing the host cell in a host cell culture;

providing host cell culture conditions wherein the one or more nucleic acid molecules are expressed; and

recovering the antibody from the host cell or from the host cell culture.

14. A method of making anti-Cadherin-17 antibodies, comprising the steps of:

recovering mRNA from the B cells of an animal which has been immunized with a Cadherin-17 peptide;

converting said mRNA to cDNA;

expressing said cDNA in phages such that anti-Cadherin-17 antibodies encoded by said cDNA are presented on the surface of said phages;

selecting phages that present anti-Cadherin-17 antibodies;

recovering nucleic acid molecules from said selected phages that encode said anti-Cadherin-17 immunoglobulins;

expressing said recovered nucleic acid molecules in a host cell; and

recovering antibodies as defined in claim 1 or claim 2 from said host cell that bind Cadherin-17.

15. Use of an anti-Cadherin-17 antibody or antigen binding portion thereof in the manufacture of a medicament for treating or preventing cancer associated with target cells expressing Cadherin-17.

16. The use of claim 15, wherein said disease is a human cancer.

17. The use of claim 16, wherein said human cancer is colorectal cancer.

WHAT IS CLAIMED:

1. An isolated anti-Cadherin-17 antibody comprising:
a heavy chain variable region CDR 1 comprising SEQ ID NO: 4;
a heavy chain variable region CDR2 comprising SEQ ID NO: 8;
a heavy chain variable region CDR3 comprising SEQ ID NO: 17;
a light chain variable region CDR1 comprising SEQ ID NO: 24;
a light chain variable region CDR2 comprising SEQ ID NO: 30; and
a light chain variable region CDR3 comprising SEQ ID NO: 34;
optionally wherein any of the above SEQ ID NOs independently comprise one, two or three amino acid substiutions, additions or deletions.

2. An isolated anti-Cadherin-17 antibody comprising:
(a) the heavy chain variable region amino acid sequence set forth in SEQ ID NO:38 or an amino acid sequence at least 90% homologous thereto, and
(b) the light chain variable region amino acid sequence set forth in SEQ ID NO:49 or an amino acid sequence at least 90% homologous thereto.

3. The antibody of claim 1 or 2, wherein said antibody is a full-length antibody of an IgG1, IgG2, IgG3, or IgG4 isotype.

4. The antibody of any one of the preceding claims, wherein said antibody is selected from the group consisting of: a whole antibody, a monoclonal antibody, an antibody fragment, a humanized antibody, a single chain antibody, a defucosylated antibody, an antibody mimetic and a bispecific antibody.

5. The antibody of claim 4, wherein said fragment is selected from the group consisting of: a UniBody, a domain antibody, and a Nanobody.

6. The antibody of claim 4, wherein the mimetic is selected from the group consisting of: an Affibody, a DARPin, an Anticalin, an Avimer, a Versabody, and a Duocalin.

7. An immunoconjugate comprising an antibody according to any one of the preceding claims conjugated to a therapeutic agent.

8. The immunoconjugate of claim 7 wherein the therapeutic agent is a cytotoxin or a radioactive isotope.

9. A composition comprising the isolated antibody or antigen-binding portion thereof of any one of claims 1 to 8 and a pharmaceutically acceptable carrier.

10. An isolated nucleic acid molecule encoding the heavy or light chain of the antibody or antigen-binding portion thereof of any one of claims 1 to 8.

11. An expression vector comprising the nucleic acid molecule of claim 10.

12. A host cell comprising the expression vector of claim 11.

13. A method for preparing an anti-Cadherin-17 antibody, said method comprising the steps of: obtaining a host cell that contains one or more nucleic acid molecules encoding the antibody of any one of claims 1 to 8;

growing the host cell in a host cell culture;

providing host cell culture conditions wherein the one or more nucleic acid molecules are expressed; and

recovering the antibody from the host cell or from the host cell culture.

14. A method of making anti-Cadherin-17 antibodies, comprising the steps of:

recovering mRNA from the B cells of an animal which has been immunized with a Cadherin-17 peptide;

converting said mRNA to cDNA;

expressing said cDNA in phages such that anti-Cadherin-17 antibodies encoded by said cDNA are presented on the surface of said phages;

selecting phages that present anti-Cadherin-17 antibodies;

recovering nucleic acid molecules from said selected phages that encode said anti-Cadherin-17 immunoglobulins;

expressing said recovered nucleic acid molecules in a host cell; and

recovering antibodies as defined in claim 1 or claim 2 from said host cell that bind Cadherin-17.

15. Use of an anti-Cadherin-17 antibody of any one of claims 1 to 6 or an immunoconjugate of claim 7 or 8 in the manufacture of a medicament for treating or preventing cancer associated with target cells expressing Cadherin-17.

16. The use of claim 15, wherein said disease is a human cancer.

17. The use of claim 16, wherein said human cancer is colorectal cancer.

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165 170 175

Ser Met Val Thr Leu Gly Cys Leu Val Lys Gly Tyr Phe Pro Glu Pro
180 185 190

Val Thr Val Thr Trp Asn Ser Gly Ser Leu Ser Ser Gly Val His Thr
195 200 205

Phe Pro Ala Val Leu Gln Ser Asp Leu Tyr Thr Leu Ser Ser Ser Val
210 215 220

Thr Val Pro Ser Ser Thr Trp Pro Ser Glu Thr Val Thr Cys Asn Val
225 230 235 240

Ala His Pro Ala Ser Ser Thr Lys Val Asp Lys Lys Ile Val Pro Arg
245 250 255

Asp Cys

<210> 38
<211> 262
<212> PRT
<213> Mus musculus

<400> 38

Leu Gly Lys Pro Trp Arg Tyr Pro Arg Phe Val His Gly Glu Asn Lys
1 5 10 15

Val Lys Gln Ser Thr Ile Ala Leu Ala Leu Leu Pro Leu Leu Phe Thr
20 25 30

Pro Val Ala Lys Ala Glu Val Gln Leu Gln Gln Ser Val Ala Glu Leu
35 40 45

Val Lys Pro Gly Ala Ser Val Lys Met Ser Cys Lys Val Ser Gly Tyr
50 55 60

Thr Leu Thr Asp His Thr Ile His Trp Met Lys Gln Arg Pro Glu Gln
65 70 75 80

Gly Leu Glu Trp Ile Gly Tyr Ile Tyr Pro Arg Asp Gly Ile Thr Gly
85 90 95

```
Tyr Asn Glu Lys Phe Lys Gly Lys Ala Thr Leu Thr Ala Asp Thr Ser
            100                 105                 110

Ser Ser Thr Ala Tyr Met Gln Leu Asn Ser Leu Thr Ser Glu Asp Ser
        115                 120                 125

Ala Val Tyr Phe Cys Ala Arg Trp Gly Tyr Ser Tyr Arg Asn Tyr Ala
    130                 135                 140

Tyr Tyr Tyr Asp Tyr Trp Gly Gln Gly Thr Thr Leu Thr Val Ser Ser
145                 150                 155                 160

Ala Lys Thr Thr Pro Pro Ser Val Tyr Pro Leu Ala Pro Gly Ser Ala
                165                 170                 175

Ala Gln Thr Asn Ser Met Val Thr Leu Gly Cys Leu Val Lys Gly Tyr
            180                 185                 190

Phe Pro Glu Pro Val Thr Val Thr Trp Asn Ser Gly Ser Leu Ser Ser
        195                 200                 205

Gly Val His Thr Phe Pro Ala Val Leu Gln Ser Asp Leu Tyr Thr Leu
    210                 215                 220

Ser Ser Ser Val Thr Val Pro Ser Ser Thr Trp Pro Ser Glu Thr Val
225                 230                 235                 240

Thr Cys Asn Val Ala His Pro Ala Ser Ser Thr Lys Val Asp Lys Lys
                245                 250                 255

Ile Val Pro Arg Asp Cys
            260


<210>  39
<211>  258
<212>  PRT
<213>  Mus musculus

<400>  39

Leu Gly Lys Pro Trp Arg Tyr Pro Arg Phe Val His Gly Glu Asn Lys
1               5                   10                  15

Val Lys Gln Ser Thr Ile Ala Leu Ala Leu Leu Pro Leu Leu Phe Thr
            20                  25                  30

Pro Val Ala Lys Ala Gln Val Gln Leu Gln Gln Ser Asp Ala Asp Leu
        35                  40                  45

Val Lys Pro Gly Ala Ser Val Lys Ile Ser Cys Lys Ala Ser Gly Tyr
    50                  55                  60
```

```
Thr Phe Thr Asp His Ala Ile His Trp Val Lys Gln Arg Pro Glu Gln
65                  70                  75                  80

Gly Leu Glu Trp Ile Gly Tyr Ile Tyr Pro Glu His Gly Thr Ile Lys
                85                  90                  95

Tyr Asn Glu Lys Phe Lys Gly Lys Ala Thr Leu Thr Ala Asp Lys Ser
            100                 105                 110

Ser Ser Thr Ala Tyr Met Gln Leu Asn Ser Leu Thr Ser Glu Asp Ser
        115                 120                 125

Ala Val Tyr Phe Cys Ala Arg Leu Arg Asn Tyr Leu Tyr Ile Met Asp
    130                 135                 140

Tyr Trp Gly Gln Gly Thr Ser Val Thr Val Ser Ser Ala Lys Thr Thr
145                 150                 155                 160

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

Ser Met Val Thr Leu Gly Cys Leu Val Lys Gly Tyr Phe Pro Glu Pro
            180                 185                 190

Val Thr Val Thr Trp Asn Ser Gly Ser Leu Ser Ser Gly Val His Thr
        195                 200                 205

Phe Pro Ala Val Leu Gln Ser Asp Leu Tyr Thr Leu Ser Ser Ser Val
    210                 215                 220

Thr Val Pro Ser Ser Thr Trp Pro Ser Glu Thr Val Thr Cys Asn Val
225                 230                 235                 240

Ala His Pro Ala Ser Ser Thr Lys Val Asp Lys Lys Ile Val Pro Arg
                245                 250                 255

Asp Cys
```

<210> 40
<211> 258
<212> PRT
<213> Mus musculus

<400> 40

```
Leu Gly Lys Pro Trp Arg Tyr Pro Arg Phe Val His Gly Glu Asn Lys
1               5                   10                  15

Val Lys Gln Ser Thr Ile Ala Leu Ala Leu Leu Pro Leu Leu Phe Thr
            20                  25                  30
```

```
Pro Val Ala Lys Ala Gln Val Gln Leu Gln Gln Ser Asp Ala Glu Leu
        35                  40                  45

Val Lys Pro Gly Ala Ser Val Lys Ile Ser Cys Lys Ala Ser Gly Tyr
    50                  55                  60

Thr Phe Thr Asp His Ala Ile His Trp Val Lys Gln Arg Pro Glu Gln
65                  70                  75                  80

Gly Leu Glu Trp Ile Gly Tyr Ile Tyr Pro Glu His Gly Thr Ile Lys
                85                  90                  95

Tyr Asn Glu Lys Phe Lys Gly Lys Ala Thr Leu Thr Ala Asp Lys Ser
            100                 105                 110

Ser Ser Thr Ala Tyr Met Gln Leu Asn Ser Leu Thr Ser Glu Asp Ser
        115                 120                 125

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

Tyr Trp Gly Gln Gly Thr Ser Val Thr Val Ser Ser Ala Lys Thr Thr
145                 150                 155                 160

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

Ser Met Val Thr Leu Gly Cys Leu Val Lys Gly Tyr Phe Pro Glu Pro
            180                 185                 190

Val Thr Val Thr Trp Asn Ser Gly Ser Leu Ser Ser Gly Val His Thr
        195                 200                 205

Phe Pro Ala Val Leu Gln Ser Asp Leu Tyr Thr Leu Ser Ser Ser Val
    210                 215                 220

Thr Val Pro Ser Ser Thr Trp Pro Ser Glu Thr Val Thr Cys Asn Val
225                 230                 235                 240

Ala His Pro Ala Ser Ser Thr Lys Val Asp Lys Lys Ile Val Pro Arg
                245                 250                 255

Asp Cys
```

<210> 41
<211> 258
<212> PRT
<213> Mus musculus

<400> 41

```
Leu Gly Lys Pro Trp Arg Tyr Pro Arg Phe Val His Gly Glu Asn Lys
```

```
1               5                   10                  15

Val Lys Gln Ser Thr Ile Ala Leu Ala Leu Leu Pro Leu Leu Phe Thr
            20                  25                  30

Pro Val Ala Lys Ala Gln Val Gln Leu Gln Gln Ser Asp Ala Glu Leu
        35                  40                  45

Val Lys Pro Gly Ala Ser Val Lys Ile Ser Cys Lys Val Ser Gly Tyr
    50                  55                  60

Thr Phe Thr Asp His Ala Ile His Trp Met Lys Gln Arg Pro Glu Gln
65                  70                  75                  80

Gly Leu Glu Trp Ile Gly Tyr Ile Tyr Pro Arg Asp Gly Phe Thr Lys
                85                  90                  95

Tyr Asn Glu Lys Phe Lys Gly Lys Ala Thr Leu Thr Ala Asp Thr Ser
            100                 105                 110

Ser Ser Thr Ala Tyr Met Gln Leu Asn Ser Leu Thr Ser Glu Asp Ser
        115                 120                 125

Thr Val Tyr Phe Cys Ala Arg Met Thr Asn Tyr Phe Tyr Thr Met Asp
    130                 135                 140

Tyr Trp Gly Gln Gly Thr Ser Val Thr Val Ser Ser Ala Lys Thr Thr
145                 150                 155                 160

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

Ser Met Val Thr Leu Gly Cys Leu Val Lys Gly Tyr Phe Pro Glu Pro
            180                 185                 190

Val Thr Val Thr Trp Asn Ser Gly Ser Leu Ser Ser Gly Val His Thr
        195                 200                 205

Phe Pro Ala Val Leu Gln Ser Asp Leu Tyr Thr Leu Ser Ser Ser Val
    210                 215                 220

Thr Val Pro Ser Ser Thr Trp Pro Ser Glu Thr Val Thr Cys Asn Val
225                 230                 235                 240

Ala His Pro Ala Ser Ser Thr Lys Val Asp Lys Lys Ile Val Pro Arg
                245                 250                 255

Asp Cys
```

<210> 42

<211> 258
<212> PRT
<213> Mus musculus

<400> 42

```
Leu Gly Lys Pro Trp Arg Tyr Pro Arg Phe Val His Gly Glu Asn Lys
1               5                  10                  15

Val Lys Gln Ser Thr Ile Ala Leu Ala Leu Leu Pro Leu Leu Phe Thr
            20                  25                  30

Pro Val Ala Lys Ala Gln Val Gln Leu Gln Gln Ser Asp Ala Asp Leu
        35                  40                  45

Val Lys Pro Gly Ala Ser Val Lys Ile Ser Cys Lys Ala Ser Gly Tyr
    50                  55                  60

Thr Phe Thr Asp His Ala Ile His Trp Val Lys Gln Arg Pro Glu Gln
65                  70                  75                  80

Gly Leu Glu Trp Ile Gly Tyr Ile Tyr Pro Glu His Gly Thr Ile Lys
                85                  90                  95

Tyr Asn Glu Lys Phe Lys Gly Lys Ala Thr Leu Thr Ala Asp Lys Ser
            100                 105                 110

Ser Ser Thr Ala Tyr Met Gln Leu Asn Ser Leu Thr Ser Glu Asp Ser
        115                 120                 125

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

Tyr Trp Gly Gln Gly Thr Ser Val Thr Val Ser Ser Ala Lys Thr Thr
145                 150                 155                 160

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

Ser Met Val Thr Leu Gly Cys Leu Val Lys Gly Tyr Phe Pro Glu Pro
            180                 185                 190

Val Thr Val Thr Trp Asn Ser Gly Ser Leu Ser Ser Gly Val His Thr
        195                 200                 205

Phe Pro Ala Val Leu Gln Ser Asp Leu Tyr Thr Leu Ser Ser Ser Val
    210                 215                 220

Thr Val Pro Ser Ser Thr Trp Pro Ser Glu Thr Val Thr Cys Asn Val
225                 230                 235                 240

Ala His Pro Ala Ser Ser Thr Lys Val Asp Lys Lys Ile Val Pro Arg
                245                 250                 255
```

Asp Cys

<210> 43
<211> 258
<212> PRT
<213> Mus musculus

<400> 43

```
Leu Gly Lys Pro Trp Arg Tyr Pro Arg Phe Val His Gly Glu Asn Lys
1               5                  10                  15

Val Lys Gln Ser Thr Ile Ala Leu Ala Leu Leu Pro Leu Leu Phe Thr
            20                  25                  30

Pro Val Ala Lys Ala Gln Val Gln Leu Gln Gln Ser Asp Ala Glu Leu
        35                  40                  45

Val Lys Pro Gly Ala Ser Val Lys Ile Ser Cys Lys Ala Ser Gly Tyr
    50                  55                  60

Thr Phe Thr Asp His Ala Ile His Trp Val Lys Gln Arg Pro Glu Gln
65                  70                  75                  80

Gly Leu Glu Trp Ile Gly Tyr Ile Tyr Pro Glu His Gly Ser Ile Thr
                85                  90                  95

Tyr Asn Glu Lys Phe Lys Gly Lys Ala Thr Leu Thr Ala Asp Lys Ser
            100                 105                 110

Ser Ser Thr Val Tyr Met His Leu Asn Ser Leu Thr Ser Glu Asp Ser
        115                 120                 125

Ala Val Tyr Phe Cys Ala Arg Leu Arg Asn Tyr Leu Tyr Val Met Asp
    130                 135                 140

Tyr Trp Gly Gln Gly Thr Ser Val Thr Val Ser Ser Ala Lys Thr Thr
145                 150                 155                 160

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

Ser Met Val Thr Leu Gly Cys Leu Val Lys Gly Tyr Phe Pro Glu Pro
            180                 185                 190

Val Thr Val Thr Trp Asn Ser Gly Ser Leu Ser Ser Gly Val His Thr
        195                 200                 205

Phe Pro Ala Val Leu Gln Ser Asp Leu Tyr Thr Leu Ser Ser Ser Val
    210                 215                 220
```

```
Thr Val Pro Ser Ser Thr Trp Pro Ser Glu Thr Val Thr Cys Asn Val
225                 230                 235                 240

Ala His Pro Ala Ser Ser Thr Lys Val Asp Lys Lys Ile Val Pro Arg
                245                 250                 255

Asp Cys
```

<210> 44
<211> 258
<212> PRT
<213> Mus musculus

<400> 44

```
Leu Gly Lys Pro Trp Arg Tyr Pro Arg Phe Val His Gly Glu Asn Lys
1               5                   10                  15

Val Lys Gln Ser Thr Ile Ala Leu Ala Leu Leu Pro Leu Leu Phe Thr
            20                  25                  30

Pro Val Ala Lys Ala Gln Val Gln Leu Gln Gln Ser Glu Ala Glu Leu
        35                  40                  45

Val Lys Pro Gly Ala Ser Val Lys Leu Ser Cys Lys Ala Ser Gly Tyr
    50                  55                  60

Thr Phe Thr Asp His Ala Ile His Trp Met Lys Gln Arg Pro Glu Gln
65                  70                  75                  80

Gly Leu Glu Trp Ile Gly Tyr Ile Tyr Pro Arg Asp Asp Phe Ala Lys
                85                  90                  95

Val Asn Glu Lys Phe Lys Gly Lys Ala Thr Leu Thr Ala Asp Thr Ser
            100                 105                 110

Ser Ser Thr Ala Tyr Met Gln Leu Asn Ser Leu Thr Ser Glu Asp Ser
        115                 120                 125

Ala Val Tyr Phe Cys Ala Arg Met Thr Asn Tyr Leu Tyr Ile Met Asp
    130                 135                 140

Tyr Trp Gly Gln Gly Thr Ser Val Thr Val Ser Ser Ala Lys Thr Thr
145                 150                 155                 160

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

Ser Met Val Thr Leu Gly Cys Leu Val Lys Gly Tyr Phe Pro Glu Pro
            180                 185                 190
```

```
Val Thr Val Thr Trp Asn Ser Gly Ser Leu Ser Ser Gly Val His Thr
        195                 200                 205

Phe Pro Ala Val Leu Gln Ser Asp Leu Tyr Thr Leu Ser Ser Ser Val
    210                 215                 220

Thr Val Pro Ser Ser Thr Trp Pro Ser Glu Thr Val Thr Cys Asn Val
225                 230                 235                 240

Ala His Pro Ala Ser Ser Thr Lys Val Asp Lys Lys Ile Val Pro Arg
                245                 250                 255

Asp Cys
```

<210> 45
<211> 258
<212> PRT
<213> Mus musculus

<400> 45

```
Leu Gly Lys Pro Trp Arg Tyr Pro Arg Phe Val His Gly Glu Asn Lys
1               5                   10                  15

Val Lys Gln Ser Thr Ile Ala Leu Ala Leu Leu Pro Leu Leu Phe Thr
            20                  25                  30

Pro Val Ala Lys Ala Gln Val Gln Leu Gln Gln Ser Asp Ala Glu Leu
        35                  40                  45

Val Lys Pro Gly Ala Ser Val Lys Ile Ser Cys Lys Ala Ser Gly Tyr
    50                  55                  60

Thr Phe Thr Asp His Ala Ile His Trp Val Lys Gln Arg Pro Glu Gln
65                  70                  75                  80

Gly Leu Glu Trp Ile Gly Tyr Ile Tyr Pro Glu His Gly Thr Ile Thr
                85                  90                  95

Tyr Asn Glu Lys Phe Lys Gly Lys Ala Thr Leu Thr Ala Asp Lys Ser
            100                 105                 110

Ser Ser Thr Val Tyr Met His Leu Asn Ser Leu Thr Ser Glu Asp Ser
        115                 120                 125

Ala Val Tyr Phe Cys Ala Arg Leu Arg Asn Tyr Leu Tyr Ile Met Asp
    130                 135                 140

Tyr Trp Gly Gln Gly Thr Ser Val Thr Val Ser Ser Ala Lys Thr Thr
145                 150                 155                 160

Pro Pro Ser Val Tyr Pro Leu Ala Pro Gly Ser Ala Ala Gln Thr Asn
```

165 170 175

Ser Met Val Thr Leu Gly Cys Leu Val Lys Gly Tyr Phe Pro Glu Pro
180 185 190

Val Thr Val Thr Trp Asn Ser Gly Ser Leu Ser Ser Gly Val His Thr
195 200 205

Phe Pro Ala Val Leu Gln Ser Asp Leu Tyr Thr Leu Ser Ser Ser Val
210 215 220

Thr Val Pro Ser Ser Thr Trp Pro Ser Glu Thr Val Thr Cys Asn Val
225 230 235 240

Ala His Pro Ala Ser Ser Thr Lys Val Asp Lys Lys Ile Val Pro Arg
245 250 255

Asp Cys

<210> 46
<211> 258
<212> PRT
<213> Mus musculus

<400> 46

Leu Gly Lys Pro Trp Arg Tyr Pro Arg Phe Val His Gly Glu Asn Lys
1 5 10 15

Val Lys Gln Ser Thr Ile Ala Leu Ala Leu Leu Pro Leu Leu Phe Thr
20 25 30

Pro Val Ala Lys Ala Gln Val Gln Leu Gln Gln Ser Asp Ala Ala Leu
35 40 45

Val Lys Pro Gly Ala Ser Val Lys Ile Ser Cys Lys Val Ser Gly Tyr
50 55 60

Thr Phe Ser Asp His Ala Ile His Trp Met Lys Gln Arg Pro Glu Gln
65 70 75 80

Gly Leu Glu Trp Ile Gly Tyr Ile Phe Pro Arg Asp Ala Phe Ser Leu
85 90 95

Asn Asn Glu Lys Phe Lys Gly Lys Ala Thr Leu Ser Ala Asp Thr Ser
100 105 110

Ser Ser Thr Ala Tyr Met Glu Leu Thr Ser Leu Thr Phe Glu Asp Ser
115 120 125

Ala Val Tyr Phe Cys Ala Arg Met Arg Asn Tyr Phe Tyr Val Met Asp
130 135 140

```
Tyr Trp Gly Gln Gly Thr Ser Val Thr Val Ser Ser Ala Lys Thr Thr
145                 150                 155                 160

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

Ser Met Val Thr Leu Gly Cys Leu Val Lys Gly Tyr Phe Pro Glu Pro
            180                 185                 190

Val Thr Val Thr Trp Asn Ser Gly Ser Leu Ser Ser Gly Val His Thr
        195                 200                 205

Phe Pro Ala Val Leu Gln Ser Asp Leu Tyr Thr Leu Ser Ser Ser Val
    210                 215                 220

Thr Val Pro Ser Ser Thr Trp Pro Ser Glu Thr Val Thr Cys Asn Val
225                 230                 235                 240

Ala His Pro Ala Ser Ser Thr Lys Val Asp Lys Lys Ile Val Pro Arg
                245                 250                 255

Asp Cys
```

<210> 47
<211> 275
<212> PRT
<213> Mus musculus

<400> 47

```
Arg Ile Leu Pro Asp Ala Phe Tyr Arg Asn Ser Leu Leu Phe Leu His
1               5                   10                  15

Thr Arg Phe Phe Gly Trp Ser Glu Thr Met Lys Tyr Leu Leu Pro Thr
            20                  25                  30

Ala Ala Ala Gly Leu Leu Leu Leu Ala Ala Gln Pro Ala Met Ala Asp
        35                  40                  45

Val Val Leu Thr Gln Thr Pro Leu Ser Leu Pro Val Thr Leu Gly Asp
    50                  55                  60

Gln Ala Ser Ile Ser Cys Arg Ser Ser Gln Ser Leu Leu His Ser Asn
65                  70                  75                  80

Gly Asn Thr Tyr Leu His Trp Tyr Leu Leu Lys Pro Gly Gln Ser Pro
                85                  90                  95

Lys Leu Leu Ile Tyr Lys Val Ser Asn Arg Phe Ser Gly Val Pro Asp
            100                 105                 110
```

```
Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile Thr
        115                 120                 125

Arg Val Glu Ala Glu Asp Leu Gly Val Tyr Phe Cys Ser Gln Ser Thr
    130                 135                 140

His Val Leu Thr Phe Gly Ala Gly Thr Lys Leu Glu Leu Lys Arg Ala
145                 150                 155                 160

Asp Ala Ala Pro Thr Val Ser Ile Phe Pro Pro Ser Ser Glu Gln Leu
                165                 170                 175

Thr Ser Gly Gly Ala Ser Val Val Cys Phe Leu Asn Asn Phe Tyr Pro
            180                 185                 190

Lys Asp Ile Asn Val Lys Trp Lys Ile Asp Gly Ser Glu Arg Gln Asn
        195                 200                 205

Gly Val Leu Asn Ser Trp Thr Asp Gln Asp Ser Lys Asp Ser Thr Tyr
    210                 215                 220

Ser Met Ser Ser Thr Leu Thr Leu Thr Lys Asp Glu Tyr Glu Arg His
225                 230                 235                 240

Asn Ser Tyr Thr Cys Glu Ala Thr His Lys Thr Ser Thr Ser Pro Ile
                245                 250                 255

Val Lys Ser Phe Asn Arg Asn Glu Ser Tyr Pro Tyr Asp Val Pro Asp
            260                 265                 270

Tyr Ala Ser
        275
```

<210> 48
<211> 276
<212> PRT
<213> Mus musculus

<400> 48

```
Arg Ile Leu Pro Asp Ala Phe Tyr Arg Asn Ser Leu Leu Phe Leu His
1               5                   10                  15

Thr Arg Phe Phe Gly Trp Ser Glu Thr Met Lys Tyr Leu Leu Pro Thr
            20                  25                  30

Ala Ala Ala Gly Leu Leu Leu Leu Ala Ala Gln Pro Ala Met Ala Asp
        35                  40                  45

Ile Val Met Thr Gln Ala Ala Pro Ser Val Pro Val Thr Pro Gly Glu
    50                  55                  60
```

Ser Val Ser Ile Ser Cys Thr Ser Ser Lys Ser Leu Leu Arg Ser Asn
65 70 75 80

Gly Asn Thr Tyr Leu Tyr Trp Phe Leu Gln Arg Pro Gly Gln Ser Pro
85 90 95

Gln Leu Leu Ile Tyr Arg Met Ser Asn Leu Ala Ser Gly Val Pro Asp
100 105 110

Arg Phe Ser Gly Ser Gly Ser Gly Thr Ala Phe Thr Leu Arg Ile Ser
115 120 125

Arg Val Glu Ala Glu Asp Val Gly Val Tyr Tyr Cys Met Gln His Leu
130 135 140

Glu Tyr Pro Phe Thr Phe Gly Ser Gly Thr Lys Leu Glu Ile Lys Arg
145 150 155 160

Ala Asp Ala Ala Pro Thr Val Ser Ile Phe Pro Pro Ser Ser Glu Gln
165 170 175

Leu Thr Ser Gly Gly Ala Ser Val Val Cys Phe Leu Asn Asn Phe Tyr
180 185 190

Pro Lys Asp Ile Asn Val Lys Trp Lys Ile Asp Gly Ser Glu Arg Gln
195 200 205

Asn Gly Val Leu Asn Ser Trp Thr Asp Gln Asp Ser Lys Asp Ser Thr
210 215 220

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

His Asn Ser Tyr Thr Cys Glu Ala Thr His Lys Thr Ser Thr Ser Pro
245 250 255

Ile Val Lys Ser Phe Asn Arg Asn Glu Ser Tyr Pro Tyr Asp Val Pro
260 265 270

Asp Tyr Ala Ser
275

<210> 49
<211> 277
<212> PRT
<213> Mus musculus

<400> 49

Arg Ile Leu Pro Asp Ala Phe Tyr Arg Asn Ser Leu Leu Phe Leu His
1 5 10 15

Thr Arg Phe Phe Gly Trp Ser Glu Thr Met Lys Tyr Leu Leu Pro Thr

20 25 30

Ala Ala Ala Gly Leu Leu Leu Leu Ala Ala Gln Pro Ala Met Ala Asp
35 40 45

Ile Val Met Ser Gln Ser Pro Ser Ser Leu Ala Val Ser Val Gly Glu
50 55 60

Lys Val Thr Met Ser Cys Lys Ser Ser Gln Ser Leu Leu His Ser Ser
65 70 75 80

Asn Gln Lys Asn Tyr Leu Ala Trp Tyr Gln Gln Lys Pro Gly Gln Ser
85 90 95

Pro Lys Val Leu Ile Tyr Trp Ala Ser Thr Arg Glu Ser Gly Val Pro
100 105 110

Asp Arg Phe Thr Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile
115 120 125

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

Tyr Ser Tyr Pro Trp Thr Phe Gly Gly Gly Thr Arg Leu Glu Ile Lys
145 150 155 160

Arg Ala Asp Ala Ala Pro Thr Val Ser Ile Phe Pro Pro Ser Ser Glu
165 170 175

Gln Leu Thr Ser Gly Gly Ala Ser Val Val Cys Phe Leu Asn Asn Phe
180 185 190

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

Gln Asn Gly Val Leu Asn Ser Trp Thr Asp Gln Asp Ser Lys Asp Ser
210 215 220

Thr Tyr Ser Met Ser Ser Thr Leu Thr Leu Thr Lys Asp Glu Tyr Glu
225 230 235 240

Arg His Asn Ser Tyr Thr Cys Glu Ala Thr His Lys Thr Ser Thr Ser
245 250 255

Pro Ile Val Lys Ser Phe Asn Arg Asn Glu Ser Tyr Pro Tyr Asp Val
260 265 270

Pro Asp Tyr Ala Ser
275

<210> 50

<211> 276
<212> PRT
<213> Mus musculus

<400> 50

```
Arg Ile Leu Pro Asp Ala Phe Tyr Arg Asn Ser Leu Leu Phe Leu His
1               5                  10                  15

Thr Arg Phe Phe Gly Trp Ser Glu Thr Met Lys Tyr Leu Leu Pro Thr
            20                  25                  30

Ala Ala Ala Gly Leu Leu Leu Leu Ala Ala Gln Pro Ala Met Ala Asp
        35                  40                  45

Ile Val Met Thr Gln Ala Ala Pro Ser Val Pro Val Thr Pro Gly Glu
    50                  55                  60

Ser Val Ser Ile Ser Cys Arg Ser Ser Lys Ser Leu Leu Arg Ser Asn
65                  70                  75                  80

Gly Asn Thr Tyr Leu Tyr Trp Phe Leu Gln Arg Pro Gly Gln Ser Pro
                85                  90                  95

Gln Leu Leu Ile Tyr Arg Leu Ser Asn Leu Ala Ser Gly Val Pro Asp
            100                 105                 110

Arg Phe Ser Gly Ser Gly Ser Gly Thr Ala Phe Thr Leu Arg Ile Ser
        115                 120                 125

Arg Val Glu Ala Glu Asp Val Gly Val Tyr Tyr Cys Met Gln His Leu
    130                 135                 140

Glu Tyr Pro Phe Thr Phe Gly Ser Gly Thr Lys Leu Glu Ile Lys Arg
145                 150                 155                 160

Ala Asp Ala Ala Pro Thr Val Ser Ile Phe Pro Pro Ser Ser Glu Gln
                165                 170                 175

Leu Thr Ser Gly Gly Ala Ser Val Val Cys Phe Leu Asn Asn Phe Tyr
            180                 185                 190

Pro Lys Asp Ile Asn Val Lys Trp Lys Ile Asp Gly Ser Glu Arg Gln
        195                 200                 205

Asn Gly Val Leu Asn Ser Trp Thr Asp Gln Asp Ser Lys Asp Ser Thr
    210                 215                 220

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

His Asn Ser Tyr Thr Cys Glu Ala Thr His Lys Thr Ser Thr Ser Pro
                245                 250                 255
```

```
Ile Val Lys Ser Phe Asn Arg Asn Glu Ser Tyr Pro Tyr Asp Val Pro
            260                 265                 270

Asp Tyr Ala Ser
        275
```

<210> 51
<211> 276
<212> PRT
<213> Mus musculus

<400> 51

```
Arg Ile Leu Pro Asp Ala Phe Tyr Arg Asn Ser Leu Leu Phe Leu His
1               5                   10                  15

Thr Arg Phe Phe Gly Trp Ser Glu Thr Ile Lys Tyr Leu Leu Pro Thr
            20                  25                  30

Ala Ala Ala Gly Leu Leu Leu Leu Ala Ala Gln Pro Ala Met Ala Asp
        35                  40                  45

Ile Val Met Thr Gln Ala Ala Pro Ser Val Pro Val Thr Pro Gly Glu
    50                  55                  60

Ser Val Ser Ile Ser Cys Thr Ser Ser Lys Ser Leu Leu Arg Ser Asn
65                  70                  75                  80

Gly Asn Thr Tyr Leu Tyr Trp Phe Leu Gln Arg Pro Gly Gln Ser Pro
                85                  90                  95

Gln Leu Leu Ile Tyr Arg Met Ser Asn Leu Ala Ser Gly Val Pro Asp
            100                 105                 110

Arg Phe Ser Gly Ser Gly Ser Gly Thr Ala Phe Thr Leu Arg Ile Ser
        115                 120                 125

Arg Val Glu Ala Glu Asp Val Gly Val Tyr Tyr Cys Met Gln His Leu
    130                 135                 140

Glu Tyr Pro Phe Thr Phe Gly Ser Gly Thr Lys Leu Glu Ile Lys Arg
145                 150                 155                 160

Ala Asp Ala Ala Pro Thr Val Ser Ile Leu Pro Pro Ser Ser Glu Gln
                165                 170                 175

Leu Thr Ser Gly Gly Ala Ser Val Val Cys Phe Leu Asn Asn Phe Tyr
            180                 185                 190

Pro Lys Asp Ile Asn Val Lys Trp Lys Ile Asp Gly Ser Glu Arg Gln
        195                 200                 205
```

Asn Gly Val Leu Asn Ser Trp Thr Asp Gln Asp Ser Lys Asp Ser Thr
210 215 220

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

His Asn Ser Tyr Thr Cys Glu Ala Thr His Lys Thr Ser Thr Ser Pro
245 250 255

Ile Val Lys Ser Phe Asn Arg Asn Glu Ser Tyr Pro Tyr Asp Val Pro
260 265 270

Asp Tyr Ala Ser
275

<210> 52
<211> 276
<212> PRT
<213> Mus musculus

<400> 52

Arg Ile Leu Pro Asp Ala Phe Tyr Arg Asn Ser Leu Leu Phe Leu His
1 5 10 15

Thr Arg Phe Phe Gly Trp Ser Glu Thr Met Lys Tyr Leu Leu Pro Thr
20 25 30

Ala Ala Ala Gly Leu Leu Leu Leu Ala Ala Gln Pro Ala Met Ala Asp
35 40 45

Ile Val Met Thr Gln Ala Ala Pro Ser Val Pro Val Thr Pro Gly Glu
50 55 60

Ser Val Ser Ile Ser Cys Arg Ser Ser Lys Ser Leu Leu Arg Thr Asn
65 70 75 80

Gly Asn Thr Tyr Leu His Trp Phe Leu Gln Arg Pro Gly Gln Ser Pro
85 90 95

Gln Leu Leu Ile Tyr Arg Met Ser Asn Leu Ala Ser Gly Val Pro Asp
100 105 110

Arg Phe Ser Gly Ser Gly Ser Gly Thr Val Phe Thr Leu Arg Ile Ser
115 120 125

Arg Val Glu Ala Glu Asp Val Gly Val Tyr Tyr Cys Met Gln His Leu
130 135 140

Glu Tyr Pro Phe Thr Phe Gly Ser Gly Thr Lys Leu Glu Ile Lys Arg
145 150 155 160

```
Ala Asp Ala Ala Pro Thr Val Ser Ile Phe Pro Pro Ser Ser Glu Gln
                165                 170                 175

Leu Thr Ser Gly Gly Ala Ser Val Val Cys Phe Leu Asn Asn Phe Tyr
            180                 185                 190

Pro Lys Asp Ile Asn Val Lys Trp Lys Ile Asp Gly Ser Glu Arg Gln
        195                 200                 205

Asn Gly Val Leu Asn Ser Trp Thr Asp Gln Asp Ser Lys Asp Ser Thr
    210                 215                 220

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

His Asn Ser Tyr Thr Cys Glu Ala Thr His Lys Thr Ser Thr Ser Pro
                245                 250                 255

Ile Val Lys Ser Phe Asn Arg Asn Glu Ser Tyr Pro Tyr Asp Val Pro
            260                 265                 270

Asp Tyr Ala Ser
        275
```

<210> 53
<211> 276
<212> PRT
<213> Mus musculus

<400> 53

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Thr Arg Phe Phe Gly Trp Ser Glu Thr Met Lys Tyr Leu Leu Pro Thr
            20                  25                  30

Ala Ala Ala Gly Leu Leu Leu Leu Ala Ala Gln Pro Ala Met Ala Asp
        35                  40                  45

Ile Val Met Thr Gln Ala Ala Pro Ser Val Pro Val Thr Pro Gly Glu
    50                  55                  60

Ser Val Ser Ile Ser Cys Arg Ser Ser Lys Ser Leu Leu Arg Ser Asn
65                  70                  75                  80

Gly Asn Thr Tyr Leu Tyr Trp Phe Leu Gln Arg Pro Gly Gln Ser Pro
                85                  90                  95

Gln Leu Leu Ile Tyr Arg Leu Ser Asn Leu Ala Ser Gly Val Pro Asp
            100                 105                 110

Arg Phe Ser Gly Ser Gly Ser Gly Thr Ala Phe Thr Leu Arg Ile Ser
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115 120 125

Arg Val Glu Ala Glu Asp Val Gly Val Tyr Tyr Cys Met Gln His Leu
130 135 140

Glu Tyr Pro Phe Thr Phe Gly Ser Gly Thr Lys Leu Glu Ile Lys Arg
145 150 155 160

Ala Asp Ala Ala Pro Thr Val Ser Ile Phe Pro Pro Ser Ser Glu Gln
165 170 175

Leu Thr Ser Gly Gly Ala Ser Val Val Cys Phe Leu Asn Asn Phe Tyr
180 185 190

Pro Lys Asp Ile Asn Val Lys Trp Lys Ile Asp Gly Ser Glu Arg Gln
195 200 205

Asn Gly Val Leu Asn Ser Trp Thr Asp Gln Asp Ser Lys Asp Ser Thr
210 215 220

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

His Asn Ser Tyr Thr Cys Glu Ala Thr His Lys Thr Ser Thr Ser Pro
245 250 255

Ile Val Lys Ser Phe Asn Arg Asn Glu Ser Tyr Pro Tyr Asp Val Pro
260 265 270

Asp Tyr Ala Ser
275

<210> 54
<211> 276
<212> PRT
<213> Mus musculus

<400> 54

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

Ala Ala Ala Gly Leu Leu Leu Leu Ala Ala Gln Pro Ala Met Ala Asp
35 40 45

Ile Val Met Thr Gln Ala Ala Pro Ser Val Pro Val Thr Pro Gly Glu
50 55 60

Ser Val Ser Ile Ser Cys Thr Ser Ser Lys Ser Leu Leu Arg Ser Asn
65 70 75 80

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Gly Asn Thr Tyr Leu Tyr Trp Phe Leu Gln Arg Pro Gly Gln Ser Pro
                85                  90                  95

Gln Leu Leu Ile Tyr Arg Met Ser Asn Leu Ala Ser Gly Val Pro Asp
            100                 105                 110

Arg Phe Ser Gly Ser Gly Ser Gly Thr Ala Phe Thr Leu Arg Ile Ser
        115                 120                 125

Arg Val Glu Ala Glu Asp Val Gly Val Tyr Tyr Cys Met Gln His Leu
    130                 135                 140

Glu Tyr Pro Phe Thr Phe Gly Ser Gly Thr Lys Leu Glu Ile Lys Arg
145                 150                 155                 160

Ala Asp Ala Ala Pro Thr Val Ser Ile Ser Pro Pro Ser Ser Glu Gln
                165                 170                 175

Leu Thr Ser Gly Gly Ala Ser Val Val Cys Phe Leu Asn Asn Phe Tyr
            180                 185                 190

Pro Lys Asp Ile Asn Val Lys Trp Lys Ile Asp Gly Ser Glu Arg Gln
        195                 200                 205

Asn Gly Val Leu Asn Ser Trp Thr Asp Gln Asp Ser Lys Asp Ser Thr
    210                 215                 220

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

His Asn Ser Tyr Thr Cys Glu Ala Thr His Lys Thr Ser Thr Ser Pro
                245                 250                 255

Ile Val Lys Ser Phe Asn Arg Asn Glu Ser Tyr Pro Tyr Asp Val Pro
            260                 265                 270

Asp Tyr Ala Ser
        275
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<210> 55
<211> 276
<212> PRT
<213> Mus musculus

<400> 55

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Arg Ile Leu Pro Asp Ala Phe Tyr Arg Asn Ser Leu Leu Phe Leu His
1               5                   10                  15

Thr Arg Phe Phe Gly Trp Ser Glu Thr Met Lys Tyr Leu Leu Pro Thr
            20                  25                  30
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Ala Ala Ala Gly Leu Leu Leu Leu Ala Ala Gln Pro Ala Met Ala Asp
35 40 45

Ile Val Met Thr Gln Ala Ala Pro Ser Val Pro Val Thr Pro Gly Glu
50 55 60

Ser Val Ser Ile Ser Cys Arg Ser Ser Lys Ser Leu Leu Arg Ser Asn
65 70 75 80

Gly Asn Thr Tyr Leu Tyr Trp Phe Leu Gln Arg Pro Gly Gln Ser Pro
85 90 95

Gln Leu Leu Ile Tyr Arg Met Ser Asn Leu Ala Ser Gly Val Pro Asp
100 105 110

Arg Phe Ser Gly Ser Gly Ser Gly Thr Ala Phe Thr Leu Arg Ile Ser
115 120 125

Arg Val Glu Ala Glu Asp Val Gly Val Tyr Tyr Cys Met Gln His Leu
130 135 140

Glu Tyr Pro Phe Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys Arg
145 150 155 160

Ala Asp Ala Ala Pro Thr Val Ser Ile Phe Pro Pro Ser Ser Glu Gln
165 170 175

Leu Thr Ser Gly Gly Ala Ser Val Val Cys Phe Leu Asn Asn Phe Tyr
180 185 190

Pro Lys Asp Ile Asn Val Lys Trp Lys Ile Asp Gly Ser Glu Arg Gln
195 200 205

Asn Gly Val Leu Asn Ser Trp Thr Asp Gln Asp Ser Lys Asp Ser Thr
210 215 220

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

His Asn Ser Tyr Thr Cys Glu Ala Thr His Lys Thr Ser Thr Ser Pro
245 250 255

Ile Val Lys Ser Phe Asn Arg Asn Glu Ser Tyr Pro Tyr Asp Val Pro
260 265 270

Asp Tyr Ala Ser
275

<210> 56
<211> 276
<212> PRT

<213> Mus musculus

<400> 56

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

Ala Ala Ala Gly Leu Leu Leu Leu Ala Ala Gln Pro Ala Met Ala Asp
        35                  40                  45

Ile Val Met Thr Gln Ala Ala Pro Ser Val Ser Val Thr Pro Gly Glu
    50                  55                  60

Ser Val Ser Ile Ser Cys Arg Ser Thr Lys Ser Leu Leu Arg Ser Asn
65                  70                  75                  80

Gly Asn Thr Tyr Leu Tyr Trp Phe Leu Gln Arg Pro Gly Gln Ser Pro
                85                  90                  95

Gln Leu Leu Ile Tyr Arg Met Ser Asn Leu Ala Ser Gly Val Pro Asp
            100                 105                 110

Arg Phe Ser Gly Ser Gly Ser Gly Thr Ala Phe Thr Leu Arg Ile Ser
        115                 120                 125

Arg Val Glu Ala Glu Asp Val Gly Val Tyr Tyr Cys Met Gln His Leu
    130                 135                 140

Glu Tyr Pro Phe Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys Arg
145                 150                 155                 160

Ala Asp Ala Ala Pro Thr Val Ser Ile Phe Pro Pro Ser Ser Glu Gln
                165                 170                 175

Leu Thr Ser Gly Gly Ala Ser Val Val Cys Phe Leu Asn Asn Phe Tyr
            180                 185                 190

Pro Lys Asp Ile Asn Val Lys Trp Lys Ile Asp Gly Ser Glu Arg Gln
        195                 200                 205

Asn Gly Val Leu Asn Ser Trp Thr Asp Gln Asp Ser Lys Asp Ser Thr
    210                 215                 220

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

His Asn Ser Tyr Thr Cys Glu Ala Thr His Lys Thr Ser Thr Ser Pro
                245                 250                 255
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Ile Val Lys Ser Phe Asn Arg Asn Glu Ser Tyr Pro Tyr Asp Val Pro
260 265 270

Asp Tyr Ala Ser
275

<210> 57
<211> 276
<212> PRT
<213> Mus musculus

<400> 57

Arg Ile Leu Pro Asp Ala Phe Tyr Arg Asn Ser Leu Leu Phe Leu His
1 5 10 15

Thr Arg Phe Phe Gly Trp Ser Glu Thr Met Lys Tyr Leu Leu Pro Thr
20 25 30

Ala Ala Ala Gly Leu Leu Leu Leu Ala Ala Gln Pro Ala Met Ala Asp
35 40 45

Ile Val Met Thr Gln Ala Ala Pro Ser Val Pro Val Thr Pro Gly Glu
50 55 60

Ser Val Ser Ile Ser Cys Arg Ser Ser Lys Ser Leu Leu Arg Ser Asn
65 70 75 80

Gly Asn Thr Tyr Leu Tyr Trp Phe Leu Gln Arg Pro Gly Gln Ser Pro
85 90 95

Gln Leu Leu Ile Tyr Arg Leu Ser Asn Leu Ala Ser Gly Val Pro Asp
100 105 110

Arg Phe Ser Gly Ser Gly Ser Gly Thr Ala Phe Thr Leu Arg Ile Ser
115 120 125

Arg Val Glu Ala Glu Asp Val Gly Val Tyr Tyr Cys Met Gln His Leu
130 135 140

Glu Tyr Pro Phe Thr Phe Gly Ser Gly Thr Lys Leu Glu Ile Lys Arg
145 150 155 160

Ala Asp Ala Ala Pro Thr Val Ser Ile Phe Pro Gln Tyr Ser Glu Gln
165 170 175

Leu Thr Thr Gly Gly Ala Ser Val Val Cys Phe Leu Asn Asn Phe Tyr
180 185 190

Pro Lys Asp Ile Asn Val Lys Trp Lys Ile Asp Gly Ser Glu Arg Gln
195 200 205

Asn Gly Val Leu Asn Ser Trp Thr Asp Gln Asp Ser Lys Asp Ser Thr

210 215 220

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

His Asn Ser Tyr Thr Cys Glu Ala Thr His Lys Thr Ser Thr Ser Pro
245 250 255

Ile Val Lys Ser Phe Asn Arg Asn Glu Ser Tyr Pro Tyr Asp Val Pro
260 265 270

Asp Tyr Ala Ser
275

<210> 58
<211> 199
<212> PRT
<213> Mus musculus

<400> 58

Arg Ile Leu Pro Asp Ala Phe Tyr Arg Asn Ser Leu Leu Phe Leu His
1 5 10 15

Thr Arg Phe Phe Gly Trp Ser Glu Thr Met Lys Tyr Leu Leu Pro Thr
20 25 30

Ala Ala Ala Gly Leu Leu Leu Leu Ala Ala Gln Pro Ala Met Ala Asp
35 40 45

Ile Val Met Thr Gln Ala Ala Pro Ser Val Pro Val Thr Pro Gly Glu
50 55 60

Ser Val Ser Ile Ser Cys Thr Ser Ser Lys Ser Leu Leu Arg Ser Asn
65 70 75 80

Gly Asn Thr Tyr Leu Tyr Trp Phe Leu Gln Arg Pro Gly Gln Ser Pro
85 90 95

Gln Leu Leu Ile Tyr Arg Met Ser Asn Leu Ala Ser Gly Val Pro Asp
100 105 110

Arg Phe Ser Gly Ser Gly Ser Gly Thr Ala Phe Thr Leu Arg Ile Ser
115 120 125

Arg Val Glu Ala Glu Asp Val Gly Val Tyr Tyr Cys Met Gln His Leu
130 135 140

Glu Tyr Pro Phe Thr Phe Gly Ser Gly Thr Asn Leu Glu Ile Lys Arg
145 150 155 160

Ala Asp Ala Ala Pro Thr Val Ser Ile Phe Thr Thr Ser Arg Glu Gln
165 170 175

Leu Thr Ser Gly Gly Ala Ser Val Val Cys Phe Leu Asn Asn Phe Tyr
180 185 190

Pro Lys Asp Ile Asn Val Lys
195

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<211> 783
<212> DNA
<213> Mus musculus

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cagctgttgg agactggggg aggcgtagtg aagcccggag ggtcccttaa actctcctgt 180

gcagcctctg gattcacttt cagtaactat ggcatgtctt gggttcgcca gactccggag 240

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<212> DNA
<213> Mus musculus

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cagctgcaac agtctgacgc tgagttggtg aaacctggag cttcagtgaa gatatcctgc 180

aaggtttctg gctacacctt cagtgaccat gctattcact ggatgagtca gagacctgga 240

cagggcctga aatggattgg atatatttat cctagacatg ggactactaa ctacaatgag 300

aacttcaagg gcaaggccac actgactgca gacacatcct ccagcacagc ctacatgcag 360

ctcaacagcc tgacatctga agattctgcc gtctatttct gtgcaagaat gagaaactac 420

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<212> DNA
<213> Mus musculus

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ttctatgtta tggagtattg gggtcaagga acctcagtca ccgtctcctc agccaaaacg 480

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<212> DNA
<213> Mus musculus

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cagggcctgg aatggattgg atatatttat cctgaacatg gaactattaa gtataatgag 300

aagttcaagg gcaaggccac attgactgca gataaatcct ccagcactgc ctatatgcag 360

ctcaacagcc tgacatctga ggattcagca gtgtatttct gtgcaagact caggaactat 420

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<213> Mus musculus

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ctcaatagcc tgacatctga ggattcagca gtgtatttct gtgcaagact caggaactac 420

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cagggcctgg aatggattgg atatatctac cccagagatg attttgctaa ggtgaatgag 300

aagttcaagg gcaaggccac actgacagca gacacatcct ccagcacagc ctacatgcag 360

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<211> 777
<212> DNA
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<213> Mus musculus

<400> 70
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<212> DNA
<213> Mus musculus

<400> 71
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gacagcaaag acagcaccta cagcatgagc agcaccctca cgttgaccaa ggacgagtat 720

gaacgacata acagctatac ctgtgaggcc actcacaaga catcaacttc acccattgtc 780

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<210> 72
<211> 840
<212> DNA
<213> Mus musculus

<400> 72
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<211> 843
<212> DNA
<213> Mus musculus

<400> 73
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gagtatgaac gacataacag ctatacctgt gaggccactc acaagacatc aacttcaccc 780

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<213> Mus musculus

<400> 74
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<210> 75
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<212> DNA
<213> Mus musculus

<400> 75
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<211> 840
<212> DNA
<213> Mus musculus

<400> 76
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tatgaacgac ataacagcta tacctgtgag gccactcaca agacatcaac ttcacccatt 780

gtcaagagct tcaacaggaa tgagtcttat ccatatgatg tgccagatta tgcgagctaa 840

<210> 77
<211> 840
<212> DNA
<213> Mus musculus

<400> 77
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<213> Mus musculus

<400> 78
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gtcaagagct tcaacaggaa tgagtcttat ccatatgatg tgccagatta tgcgagctaa 840

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<213> Mus musculus

<400> 80
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<212> DNA
<213> Mus musculus

<400> 81
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<212> DNA
<213> Mus musculus

<400> 82
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<212> DNA
<213> Mus musculus

<400> 83
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<400> 84
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<210> 86
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<210> 89
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<400> 89
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<400> 90
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<210> 91
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<400> 91
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<400> 92
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<210> 95
<211> 51
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Tyr Glu Gly Gln Glu Pro Ser Gln Ile Ile Phe Gln Phe Lys Ala Asn
20 25 30

Pro Pro Ala Val Thr Phe Glu Leu Thr Gly Glu Thr Asp Asn Ile Phe
35 40 45

Val Ile Glu Arg Glu Gly Leu Leu Tyr Tyr Asn Arg Ala Leu Asp Arg
50 55 60

Glu Thr Arg Ser Thr His Asn Leu Gln Val Ala Ala Leu Asp Ala Asn
65 70 75 80

Gly Ile Ile Val Glu Gly Pro Val Pro Ile Thr Ile Lys Val Lys Asp
85 90 95

Ile Asn Asp Asn Arg Pro Thr Phe Leu Gln Ser Lys Tyr Glu Gly Ser
100 105 110

Val Arg Gln Asn Ser Arg Pro Gly Lys Pro Phe Leu Tyr Val Asn Ala
115 120 125

Thr Asp Leu Asp Asp Pro Ala Thr Pro Asn Gly Gln Leu Tyr Tyr Gln
130 135 140

Ile Val Ile Gln Leu Pro Met Ile Asn Asn Val Met Tyr Phe Gln Ile
145 150 155 160

Asn Asn Lys Thr Gly Ala Ile Ser Leu Thr Arg Glu Gly Ser Gln Glu
165 170 175

Leu Asn Pro Ala Lys Asn Pro Ser Tyr Asn Leu Val Ile Ser Val Lys
180 185 190

Asp Met Gly Gly Gln Ser Glu Asn Ser Phe Ser Asp Thr Thr Ser Val
195 200 205

Asp Ile Ile Val Thr Glu Asn Ile Trp Lys Ala Pro Lys Pro
210 215 220

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Gln Glu Gly Lys Phe Ser Gly Pro Leu Lys Pro Met Thr Phe Ser Ile
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Tyr Glu Gly Gln Glu Pro Ser Gln Ile Ile Phe Gln Phe Lys Ala Asn
20 25 30

Pro Pro Ala Val Thr Phe Glu Leu Thr Gly Glu Thr Asp Asn Ile Phe
35 40 45

Val Ile Glu Arg Glu Gly Leu Leu Tyr Tyr Asn Arg Ala Leu Asp Arg
50 55 60

Glu Thr Arg Ser Thr His Asn Leu Gln Val Ala Ala Leu Asp Ala Asn
65 70 75 80

Gly Ile Ile Val Glu Gly Pro Val Pro Ile Thr Ile Lys Val Lys Asp
85 90 95

Ile Asn Asp Asn Arg Pro Thr Phe Leu Gln Ser Lys Tyr Glu Gly Ser
100 105 110

Val Arg Gln Asn Ser Arg Pro Gly Lys Pro Phe Leu Tyr Val Asn Ala
115 120 125

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Thr Asp Leu Asp Asp Pro Ala Thr Pro Asn Gly Gln Leu Tyr Tyr Gln
    130                 135                 140

Ile Val Ile Gln Leu Pro Met Ile Asn Asn Val Met Tyr Phe Gln Ile
145                 150                 155                 160

Asn Asn Lys Thr Gly Ala Ile Ser Leu Thr Arg Glu Gly Ser Gln Glu
                165                 170                 175

Leu Asn Pro Ala Lys Asn Pro Ser Tyr Asn Leu Val Ile Ser Val Lys
            180                 185                 190

Asp Met Gly Gly Gln Ser Glu Asn Ser Phe Ser Asp Thr Thr Ser Val
        195                 200                 205

Asp Ile Ile Val Thr Glu Asn Ile Trp Lys Ala Pro Lys Pro Val Glu
    210                 215                 220

Met Val Glu Asn Ser Thr Asp Pro His Pro Ile Lys Ile Thr Gln Val
225                 230                 235                 240

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

Leu Pro Arg Phe Pro Phe Ser Ile Asp Gln Glu Gly Asp Ile Tyr Val
            260                 265                 270

Thr Gln Pro Leu Asp Arg Glu Glu Lys Asp Ala Tyr Val Phe Tyr Ala
        275                 280                 285

Val Ala Lys Asp Glu Tyr Gly Lys Pro Leu Ser Tyr Pro Leu Glu Ile
    290                 295                 300

His Val Lys Val Lys Asp Ile Asn Asp Asn Pro Pro Thr Cys Pro Ser
305                 310                 315                 320

Pro Val Thr Val Phe Glu Val Gln Glu Asn Glu Arg Leu Gly Asn Ser
                325                 330                 335

Ile Gly Thr Leu Thr Ala His Asp Arg Asp Glu Glu Asn Thr Ala Asn
            340                 345                 350

Ser Phe Leu Asn Tyr Arg Ile Val Glu Gln Thr Pro Lys Leu Pro Met
        355                 360                 365

Asp Gly Leu Phe Leu Ile Gln Thr Tyr Ala Gly Met Leu Gln Leu Ala
    370                 375                 380

Lys Gln Ser Leu Lys Lys Gln Asp Thr Pro Gln Tyr Asn Leu Thr Ile
385                 390                 395                 400
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Glu Val Ser Asp Lys Asp Phe Lys Thr Leu Cys Phe Val Gln Ile Asn
405 410 415

Val Ile Asp Ile Asn Asp Gln Ile Pro Ile Phe Glu Lys Ser Asp Tyr
420 425 430

Gly Asn Leu Thr Leu Ala Glu Asp Thr Asn Ile Gly Ser Thr Ile Leu
435 440 445

Thr Ile Gln Ala Thr Asp Ala Asp Glu Pro Phe Thr Gly Ser Ser Lys
450 455 460

Ile Leu Tyr His Ile Ile Lys Gly Asp Ser Glu Gly Arg Leu Gly Val
465 470 475 480

Asp Thr Asp Pro His Thr Asn Thr Gly Tyr Val Ile Ile Lys Lys Pro
485 490 495

Leu Asp Phe Glu Thr Ala Ala Val Ser Asn Ile Val Phe Lys Ala Glu
500 505 510

Asn Pro Glu Pro Leu Val Phe Gly Val Lys Tyr Asn Ala Ser Ser Phe
515 520 525

Ala Lys Phe Thr Leu Ile Val Thr Asp Val Asn Glu Ala Pro Gln Phe
530 535 540

Ser Gln His Val Phe Gln Ala Lys Val Ser Glu Asp Val Ala Ile Gly
545 550 555 560

Thr Lys Val Gly Asn Val Thr Ala Lys Asp Pro Glu Gly Leu Asp Ile
565 570 575

Ser Tyr Ser Leu Arg Gly Asp Thr Arg Gly Trp Leu Lys Ile Asp His
580 585 590

Val Thr Gly Glu Ile Phe Ser Val Ala Pro Leu Asp Arg Glu Ala Gly
595 600 605

Ser Pro Tyr Arg Val Gln Val Val Ala Thr Glu Val Gly Gly Ser Ser
610 615 620

Leu Ser Ser Val Ser Glu Phe His Leu Ile Leu Met Asp Val Asn Asp
625 630 635 640

Asn Pro Pro Arg Leu Ala Lys Asp Tyr Thr Gly Leu Phe Phe Cys His
645 650 655

Pro Leu Ser Ala Pro Gly Ser Leu Ile Phe Glu Ala Thr Asp Asp Asp
660 665 670

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Gln His Leu Phe Arg Gly Pro His Phe Thr Phe Ser Leu Gly Ser Gly
        675                 680                 685

Ser Leu Gln Asn Asp Trp Glu Val Ser Lys Ile Asn Gly Thr His Ala
    690                 695                 700

Arg Leu Ser Thr Arg His Thr Asp Phe Glu Glu Arg Glu Tyr Val Val
705                 710                 715                 720

Leu Ile Arg Ile Asn Asp Gly Gly Arg Pro Pro Leu Glu Gly Ile Val
                725                 730                 735

Ser Leu Pro Val Thr Phe Cys Ser Cys Val Glu Gly Ser Cys Phe Arg
            740                 745                 750

Pro Ala Gly His Gln Thr Gly Ile Pro Thr Val Gly Met
        755                 760                 765
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