

DESCRIPTION

A method for screening a salty taste modulating substance

Technical Field

The present invention relates to a method for screening a salty taste modulating substance including a substance that alternatively shows a salty taste, or modifies a salty taste. A salt alternative or a salty taste modulating substance are useful in the field of food industry and so forth.

Background Art

Taste is important for detection of nutritional components or harmful components in foodstuffs. Taste perception of mammals is attained with the taste receptor cells contained in the taste buds present in the oral cavity. The received signals are transmitted from the taste receptor cells to taste nerves entering into the taste buds, and to the central nerve system. Tastes sensed by mammals are generally divided into five kinds of fundamental quality of tastes, that is, sweet taste, bitter taste, acid taste, salty taste, and umami taste, and these are called five basic tastes.

The receptors for these five basic tastes are being elucidated in accordance with the progress of researches in recent years (Non-patent documents 1 and 2). Identification and isolation of novel taste receptors enable novel methods of modulating taste perception. For example, search of highly affinitive agonists or antagonists using taste receptors enables screening for taste modulating substances. Such taste modulating substances may provide improvement or refinement of quality of tastes in various consumer products.

Salty taste, one of the five basic tastes, is involved in detection of sodium ions or other inorganic cations, and is very important for maintenance of internal

homeostasis. It is considered that, as salty taste perception pathways, there are the amiloride-sensitive pathway which is inhibited by diuretic amiloride, and the amiloride-insensitive pathway which is not affected by amiloride (Non-patent document 3). Molecules involved in both the salty taste perception pathways exist and function in the taste receptor cells in the taste buds (Non-patent document 2).

It is considered that the amiloride-sensitive pathway is mediated by the epithelial sodium channel (ENaC). ENaC is composed of four kinds of subunits, α , β , γ , and δ , and functions as a hetero-multimer consisting of a combination of α , β and γ , or δ , β and γ (Non-patent document 13). However, although marked inhibition of the salty taste perception by amiloride is observed in rodents, such inhibition is observed in only a part of humans, and presence of a different receptor in the human salty taste perception mechanism is suggested. As described above, a significant part of the salty taste perception mechanism including receptors still remains unknown.

Excessive intake of salt from foodstuffs is considered as one of the risk factors of hypertension or cardiovascular system diseases, and there is movement of restricting salt consumption worldwide, including Japan (World Health Organization, Non-patent document 4).

There have been conventional techniques for decreasing intake of salt, for example, low-salt seasonings and low-salt food using potassium chloride as a substitute for sodium chloride. However, potassium chloride has a problem that it has a bitter taste and an irritating taste. Therefore, taste of food using potassium chloride is markedly inferior. In order to improve this drawback, there have been developed a seasoning composition in addition to potassium chloride, such as a mixture of ammonium chloride, calcium lactate, sodium L-aspartate, an L-glutamic acid salt and/or a nucleic acid type taste substance at a specific ratio

(Patent document 1), a low sodium salty taste seasoning containing ascorbic acid (Patent document 2), a bitterness suppressing method using carrageenan (Patent document 3), and so forth. However, salt reduction techniques do not reach such a level that unpleasant tastes other than salty taste are eliminated, and salty taste intensity equivalent to that of sodium chloride is provided at the same time.

Furthermore, there are salt reduction methods using a salty taste enhancing substance, which does not reduce salty taste intensity even if sodium chloride is reduced. For example, it is known that a basic amino acid, especially L-arginine, has an effect of enhancing salty taste (Non-patent documents 5 and 6). As techniques applying the above knowledge, there have been developed a combination of L-arginine, L-aspartic acid and sodium chloride (Patent document 4), a taste improving agent using neutralized salts of a basic amino acid and citric acid (Patent document 5), and so forth. However, any technique that can sufficiently compensate insufficiency by reduction of sodium chloride has not been developed yet, in view of salt reduction effect, flavor, salty taste intensity and so forth.

Meanwhile, the Kv3 family is known as a family of potassium channel that is originally considered to function in a nerve cell that shows stimulation at high frequency, and release potassium ions when cell membrane potential is depolarized to -20 mV or higher to show outward current (Non-patent document 7). However, for these, only the function as a voltage-dependent potassium channel is known (Non-patent documents 8 to 11), and a function as a cation channel depending on extracellular sodium concentration around the resting membrane potential (about -60 to -80 mV) is not known at all.

In connection with taste, expression of Kv3.1 and Kv3.2 genes confirmed by PCR in taste cells isolated from rat fungiform papillae has been reported (Non-patent document 12). However, functions thereof in the taste

cells are not known at all.

Prior Art References

Patent documents

Patent document 1: Japanese Patent Laid-open (KOKAI) No. 11-187841

Patent document 2: Japanese Patent Laid-open No. 1-281054

Patent document 3: Japanese Patent Laid-open No. 4-262758

Patent document 4: U.S. Patent No. 5,145,707

Patent document 5: Japanese Patent Laid-open No. 2003-0144088

Non-patent documents

Non-patent document 1: Chandrashekar, J. et al., Nature, 444:288-294 (2006)

Non-patent document 2: Bachmanov, A.A. et al., Ann. Rev. Nutr., 27:387-412 (2007)

Non-patent document 3: DeSimone, J.A. et al., Am. J. Physiol. Regulatory Integrative Comp. Physiol., 249: 52-61 (1985)

Non-patent document 4: Reducing salt intake in populations - Report a WHO Forum and Technical Meeting, [online], [searched on September 20, 2009], Internet URL: <http://www.who.int/dietphysicalactivity/reducingsalt/en/>

Non-patent document 5: Riha, W. et al., Chem. Senses, 22:778 (1997)

Non-patent document 6: Estrella, N.L. et al., Chem. Senses, 34:A117-8 (2009)

Non-patent document 7: Rudy, B. et al., Trends in Neuroscience, 24:517-526 (2001)

Non-patent document 8: Gutman, G.A. et al., Pharmacological Reviews 57:473-508 (2005)

Non-patent document 9: McCormack, T. et al., Proc. Natl. Acad. Sci. USA., 87:5227-5231 (1990)

Non-patent document 10: HERNANDEZ-PINEDA, R. et al.,

J. Neurophysiol., 82:1512-1528 (1999)

Non-patent document 11: Madeja, M. et al.,
Neuropharmacology, 39:202-210 (2000)

Non-patent document 12: Liu, L. et al., Am. J.
Physiol. Cell Physiol., 289:868-880 (2005)

Non-patent document 13: Stahler, F. et al.,
Chemosensory Perception, 1:78-90 (2008)

Summary of the Invention

Object to be Achieved by the Invention

An object of the present invention is to identify a salty taste receptor protein and a gene encoding the protein, and provide a screening system for searching a compound that enhances or inhibits salty taste perception or a salt alternative substance.

Means for Achieving the Object

The inventors of the present invention conceived that if a salty taste receptor or a molecule controlling such a receptor was used, it became possible to efficiently search and identify a compound that could enhance or inhibit salty taste perception or a salt alternative substance, which can result in development of effective salt reduction method that did not alter tastes, and as a result, enable production of foodstuffs having a low salt concentration with maintaining tastes. Then, they conducted various researches, as a result, succeeded in identifying molecules involved in salty taste perception, and thus accomplished the present invention.

The present invention is as follows.

- (1) A method for screening a salty taste modulating substance, which comprises the step of contacting a test substance with a cell that expresses a Kv3.2 protein, and comparing observed cation influx into the cell with cation influx into the cell observed when the test substance is not contacted with the cell.
- (2) The method according to (1), wherein the cation influx

is measured by measuring cell membrane current of the cell in the presence of sodium ions.

(3) The method according to (1), wherein the cation influx is measured by measuring cell membrane current of the cell in the absence of sodium ion.

(4) The method according to (1) or (2) described above, wherein the salty taste modulating substance is a salty taste enhancing substance or a salty taste inhibiting substance.

(5) The method according to (1) or (3) described above, wherein the salty taste modulating substance is a salt alternative substance.

(6) The method as described above, wherein the Kv3.2 protein has the amino acid sequence of SEQ ID NO: 2, 4, 6, 8, 10, 12, 14, 16, 18, 40, 47, 49, 51 or 53.

(7) The method as described above, wherein the Kv3.2 protein shows a sequence identity of at least 78% or more to the sequence of SEQ ID NO: 2, 4, 6, 8, 10, 12, 14, 16, 18, 40, 47, 49, 51 or 53, and is able to constitute a cation channel of which activity changes according to change of extracellular sodium ion concentration.

(8) The method as described above, wherein the Kv3.2 protein has the amino acid sequence of SEQ ID NO: 2, 4, 6, 8, 10, 12, 14, 16, 18, 40, 47, 49, 51 or 53 including substitutions, deletions, insertions and/or additions of one or more amino acid residues, and is able to constitute a cation channel of which activity changes according to change of extracellular sodium ion concentration.

(9) The method as described above, wherein the Kv3.2 protein is encoded by a DNA shown in the following (a) or (b):

(a) a DNA having the nucleotide sequence of SEQ ID NO: 1, 3, 5, 7, 9, 11, 13, 15, 17, 39, 46, 48, 50 or 52;

(b) a DNA which is able to hybridize with the nucleotide sequence complementary to the nucleotide sequence of SEQ ID NO: 1, 3, 5, 7, 9, 11, 13, 15, 17, 39, 46, 48, 50 or 52, or a probe which can be prepared from

the nucleotide sequence under stringent conditions, and codes for a protein that can constitute a cation channel of which activity changes according to change of extracellular sodium ion concentration.

(10) The method as described above, wherein the Kv3.2 protein is selected from Kv3.2 protein homologues derived from human, mouse, rat, frog of the genus *Xenopus*, dog, horse, chimpanzee, rhesus monkey, fowl, opossum, swine or bovine, and a mutant thereof, a fragment thereof, and a chimera protein thereof.

(11) The method as described above, wherein the cell is an oocyte into which a polynucleotide encoding a Kv3.2 protein is introduced in an expressible form.

(12) The method as described above, wherein the cell expresses a Kv3.2 gene isolated from a tissue selected from taste cell, tongue epithelium, adrenal gland, pineal body, thyroid, melanocyte and kidney.

(13) A Kv3.2 protein variant, which is a protein shown in any of the following (a) to (c):

(a) a protein having the sequence of SEQ ID NO: 47, 49, 51 or 53;

(b) a protein showing a sequence identity of at least 78% or more to the sequence of SEQ ID NO: 47, 49, 51 or 53, and being able to constitute a cation channel of which activity changes according to change of extracellular sodium ion concentration;

(c) a protein which has the amino acid sequence of SEQ ID NO: 47, 49, 51 or 53 including substitutions, deletions, insertions and/or additions of one or more amino acid residues, and is able to constitute a cation channel of which activity changes according to change of extracellular sodium ion concentration.

(14) A DNA encoding a Kv3.2 protein variant, which is a DNA shown in the following (a) or (b):

(a) a DNA having the nucleotide sequence of SEQ ID NO: 46, 48, 50 or 52;

(b) a DNA which is able to hybridize with the

nucleotide sequence complementary to the nucleotide sequence of SEQ ID NO: 46, 48, 50 or 52, or a probe which can be prepared from the nucleotide sequence under stringent conditions, and codes for a protein that can constitute a cation channel of which activity changes according to change of extracellular sodium ion concentration.

(15) A method for searching a protein having a function of positively or negatively regulating the Kv3.2 activity or a protein that constitutes a salty taste receptor, which comprises identifying a gene showing an expression profile similar to that of the Kv3.2 gene or a gene of which expression is suppressed in a Kv3.2 gene-expressing cell among genes expressed in the Kv3.2 gene-expressing cell.

(16) A method for searching a salty taste modulating substance by identifying a compound that acts on a Kv3.2 protein or a cell expressing the protein.

(17) A method for searching a taste substance or a flavor substance, which comprises identifying a compound that acts on a channel or complex constituted by a Kv3.2 protein and a protein specifically expressed in a taste cell.

(18) An isolated oocyte or taste cell into which a polynucleotide encoding a Kv3.2 protein is introduced in an expressible form.

Effect of the Invention

A salty taste receptor protein identified according to the present invention constitutes a salty taste receptor ion channel expressed in a taste cell. A substance that activates this receptor is useful as a candidate substance of salty taste modulating substance, i.e., salt alternative, salty taste enhancer, or salty taste inhibitor. Moreover, if a cell that expresses the receptor on the cell surface is used, a convenient screening system for salt alternative, salty taste enhancer, or salty taste inhibitor can be provided.

Furthermore, a foodstuff containing a salt alternative substance or a salty taste enhancing substance is effective for suppressing excessive intake of salt, and thus prevention of hypertension or circulatory system diseases.

Brief Description of the Drawings

Fig. 1 shows results of RT-PCR indicating expressions of the Kv3.1, Kv3.2, Kv3.3 and Kv3.4 genes in various mouse tissues (electrophoresis photograph): Lane 1: tip of tongue (including fungiform papillae), Lane 2: vallate papillae region, Lane 3: both side portions of tongue (including foliate papillae), Lane 4: tongue epithelium not including taste buds, Lane 5: without reverse transcriptase, Lane 6: kidney.

Fig. 2 shows change of cell membrane current observed for *Xenopus laevis* oocyte expressing a Kv3.2 protein (human) when extracellular sodium ion concentration was changed. KCNC2 indicates injection of Kv3.2 cRNA.

Fig. 3 shows difference of cell membrane current observed for *Xenopus laevis* oocyte expressing a Kv3.2 protein (human) when extracellular sodium ion concentration was changed from 0 mM to 96 mM.

Fig. 4 shows results of in situ hybridization indicating a Kv3.2 gene expression site in mouse tongue epithelium (microphotography).

Fig. 5 shows cell membrane current observed for *Xenopus laevis* oocyte expressing a Kv3.2 protein (human), which was contacted with the low molecular organic compound A. KCNC2 indicates injection of Kv3.2 cRNA.

Fig. 6 shows cell membrane current observed for *Xenopus laevis* oocyte expressing a Kv3.2 protein (*Xenopus laevis*) when extracellular sodium ion concentration was changed. XlKv3.2 indicates injection of *Xenopus laevis* Kv3.2 cRNA.

Embodiments for Carrying out the Invention

Hereafter, the present invention will be explained in detail.

The inventors of the present invention confirmed expression of genes encoding the ion channels Kv3.1, Kv3.2, Kv3.3 and Kv3.4 belonging to the Kv3 family (Rudy et al., Trends in Neuroscience, 24:517-526 (2001)) in a mouse tongue epithelial tissue containing taste buds, which ion channels are potassium channels originally considered to function in a nerve cell that shows stimulation at high frequency, and shows current when cell membrane potential is depolarized to -20 mV or higher, and found that expression of a human Kv 3.2 gene in a *Xenopus laevis* oocyte could be involved in the salty taste perception in the form of change of cell membrane current according to change of extracellular sodium ion concentration. On the basis of this finding, they found that Kv3.2 functioned as a salty taste receptor ion channel, and could be used for screening a novel salty taste modulating substance. Moreover, they confirmed that a Kv3.2 gene is expressed in the taste buds, found that, in two kinds of mice of which salty taste response sensitivities were different, there was difference of expression level of the Kv3.2 gene according to the sensitivity, and further confirmed that Kv3.2 is a salty taste receptor. Moreover, the inventors of the present invention newly found splice variants of the Kv3.2 protein in the taste buds.

The method of the present invention comprises the step of contacting a test substance with a cell that expresses a Kv3.2 protein, and comparing observed cation influx into the cell with cation influx into the cell observed when the test substance is not contacted with the cell.

The Kv3.2 protein constitutes a potassium channel, which is a member of the Kv3 family, and it was found by the inventors of the present invention for the first time that the Kv3.2 protein has a cation channel activity,

which changes according to change of extracellular sodium ion concentration. The Kv3.2 protein is a polypeptide encoded by the *Kcnc2* gene (also written as KCNC2).

In the present invention, examples of the Kv3.2 protein include a protein having the amino acid sequence of SEQ ID NO: 2, 4, 6, 8, 10, 12, 14, 16, 18, 40, 47, 49, 51 or 53.

As polynucleotides encoding human Kv3.2 proteins, four kinds of nucleotide sequences are registered at gene databases (National Center for Biotechnology Information, <http://www.ncbi.nlm.nih.gov/> or Ensembl project, <http://www.ensembl.org/index.html>, NM_139136, NM_139137, NM_153748, AY243473). The nucleotide sequences of SEQ ID NOS: 1, 3, 5 and 7 correspond to the above nucleotide sequences. The amino acid sequences encoded by the nucleotide sequences are shown in SEQ ID NOS: 2, 4, 6 and 8. These amino acid sequences have a common sequence except for the C terminal region (portion corresponding to the positions 1 to 538 in SEQ ID NO: 2), and they are considered to be splice variants.

Moreover, in a similar database, one kind of polynucleotide encoding a mouse Kv3.2 protein is registered (NM_001025581, SEQ ID NO: 9). The amino acid sequence encoded by the nucleotide sequence of SEQ ID NO: 9 is shown in SEQ ID NO: 10. Moreover, four kinds of nucleotide sequences are registered as polynucleotides encoding rat Kv3.2 proteins (NM_139216, NM_139217, ENSRNOT00000049943, X62839). These nucleotide sequences are shown in SEQ ID NOS: 11, 13, 15 and 17. The amino acid sequences encoded by these nucleotide sequences are shown in SEQ ID NOS: 12, 14, 16 and 18. These amino acid sequences also have a common sequence except for the C terminal region (portion corresponding to the positions 1 to 593 in SEQ ID NO: 12), and they are considered to be splice variants.

Moreover, as shown in the Examples described later, a Kv3.2 protein gene of *Xenopus laevis* was isolated, and

it was demonstrated that this protein had a cation channel activity which changed according to change of extracellular sodium ion concentration. The nucleotide sequence of this gene is shown in SEQ ID NO: 39, and the amino acid sequence of the Kv3.2 protein encoded by this gene is shown in SEQ ID NO: 40.

Furthermore, as shown in the Examples described later, four kinds of splice variants of mouse Kv3.2 gene were isolated from a mouse tongue epithelial tissue containing the taste buds. The nucleotide sequences of these splice variants are shown in SEQ ID NOS: 46, 48, 50 and 52. The amino acid sequences encoded by these nucleotide sequences are shown in SEQ ID NOS: 47, 49, 51 and 53, respectively. The amino acid sequences of SEQ ID NOS: 10, 47, 49, 51 and 53 have a common sequence except for the C terminus regions (portion corresponding to the positions 1 to 597 in SEQ ID NO: 10).

The Kv3.2 protein used for the method of the present invention includes interspecific homologues, and it may be, for example, a Kv3.2 protein derived from dog, horse, chimpanzee, fowl, opossum, swine or bovine, in addition to proteins having the sequences derived from human, mouse, rat and *Xenopus laevis* as described above. The sequence information of the genes encoding these proteins are registered with the following numbers, respectively: dog: XM_538289, horse: XM_001488185, chimpanzee: XR_020952, fowl: XM_001235254, opossum: XM_001363374, XM_001363455, swine: XM_001926426, XM_001924780, and bovine: XM_590276. Moreover, as for rhesus monkey, anole lizard, marmoset, guinea pig, sloth, armadillo, kangaroo rat, *Echinops telfairi*, hedgehog, three-spined stickleback, gorilla, elephant, wallaby, lemur, microbat, pika, rabbit, galago, orangutan, hyrax, fruit bat, shrew, squirrel, zebra finch, *Takifugu oblongus*, tarsier, tree shrew and dolphin, the sequence information on the genes encoding the Kv3.2 protein of them are registered with the following numbers, respectively: rhesus monkey: ENSMUG00000012362, anole

lizard: ENSACAG000000007691, marmoset: ENSCJAG000000001261,
 guinea pig: ENSCPOG000000003474, sloth: ENSCHOG000000007167,
 armadillo: ENSDNOG000000013383, kangaroo rat:
 ENSDORG000000000056, *Echinops telfairi*: ENSETEG000000010484,
 hedgehog: ENSEEUG000000002220, three-spined stickleback:
 ENSGACG000000019441, gorilla: ENSGGOG000000003896, elephant:
 ENSLAFG000000031982, wallaby: ENSMEUG000000007789, lemur:
 ENSMICG000000017734, microbat: ENSMLUG000000010813, pika:
 ENSOPRG000000017272, rabbit: ENSOCUG000000004467, galago:
 ENSOGAG000000000768, orangutan: ENSPPYG000000004780, hyrax:
 ENSPCAG000000015808, fruit bat: ENSPVAG000000010964, shrew:
 ENSSARG000000006415, squirrel: ENSSTOG000000004842, zebra
 finch: ENSTGUG000000007354, *Takifugu oblongus*:
 ENSTRUG000000003532, tarsier: ENSTSYG000000010689, tree
 shrew: ENSTBEG000000001105, and dolphin: ENSTTRG000000013226.

The gene encoding Kv3.2 is not limited to a gene having the aforementioned gene information or a gene having a known sequence, a gene having a conservative mutation, such as a homologue or an artificially modified version of such a gene as described above can also be used, so long as the Kv3.2 protein encoded by the chosen gene can constitute a cation channel of which activity changes according to change of extracellular sodium ion concentration. That is, it may be a gene encoding a protein having an amino acid sequence of a known protein including substitutions, deletions, insertions, and/or additions of one or more amino acid residues at one or more positions, or the like. The expression that the Kv3.2 protein "can constitute a cation channel of which activity changes according to change of extracellular sodium ion concentration" means that it has an activity of increasing cell membrane potential induced by influx of cations into the cell when the cell expressing the protein is contacted with sodium ions. Examples of the cation include sodium ion, calcium ion, magnesium ion, lithium ion, ammonium ion, and so forth, and sodium ion is preferred.

Although the number of the "one or more" amino acid residues referred to herein may differ depending on the position in the three-dimensional structure of the protein or the types of amino acid residues, specifically, it may be preferably 1 to 20, more preferably 1 to 10, still more preferably 1 to 5, particularly preferably 1 to 3. A typical example of the conservative mutation is conservative substitution. The conservative substitution is a mutation wherein substitution takes place mutually among Phe, Trp, and Tyr, if the substitution site is an aromatic amino acid; among Leu, Ile and Val, if it is a hydrophobic amino acid; between Gln and Asn, if it is a polar amino acid; among Lys, Arg and His, if it is a basic amino acid; between Asp and Glu, if it is an acidic amino acid; and between Ser and Thr, if it is an amino acid having a hydroxyl group. Substitutions considered conservative substitutions include, specifically, substitution of Ser or Thr for Ala, substitution of Gln, His or Lys for Arg, substitution of Glu, Gln, Lys, His or Asp for Asn, substitution of Asn, Glu or Gln for Asp, substitution of Ser or Ala for Cys, substitution of Asn, Glu, Lys, His, Asp or Arg for Gln, substitution of Gly, Asn, Gln, Lys or Asp for Glu, substitution of Pro for Gly, substitution of Asn, Lys, Gln, Arg or Tyr for His, substitution of Leu, Met, Val or Phe for Ile, substitution of Ile, Met, Val or Phe for Leu, substitution of Asn, Glu, Gln, His or Arg for Lys, substitution of Ile, Leu, Val or Phe for Met, substitution of Trp, Tyr, Met, Ile or Leu for Phe, substitution of Thr or Ala for Ser, substitution of Ser or Ala for Thr, substitution of Phe or Tyr for Trp, substitution of His, Phe or Trp for Tyr, and substitution of Met, Ile or Leu for Val. The aforementioned amino acid substitutions, deletions, insertions, additions, inversions or the like may be a result of a naturally-occurring mutation or a variation due to an individual difference or difference of species of a microorganism from which the genes are derived (mutant or variant).

Such genes can be obtained by, for example, modifying a known nucleotide sequence of a gene by site-specific mutagenesis so that the amino acid residues at the specific sites of the encoded protein include substitutions, deletions, insertions, or additions of amino acid residues.

Furthermore, such genes having a conservative mutations as described above may be a gene encoding a protein having a homology of 78% or more, preferably 80% or more, more preferably 90% or more, still more preferably 95% or more, further preferably 97% or more, particularly preferably 99% or more, to the entire encoded amino acid sequence and having a function equivalent to that of the wild-type Kv3.2 protein. In this specification, the term "homology" may mean "identity".

Moreover, codons in the gene sequences may be replaced with other codons which are easily used in the host into which the genes are introduced.

The gene having a conservative mutation may be a gene obtained by a method usually used for mutation treatment, such as treatment with a mutagen. Furthermore, the Kv3.2 gene may contain one or more introns, so long as the Kv3.2 protein can be expressed when the gene is introduced into a host cell.

Examples of the DNA encoding Kv3.2 (henceforth also referred to as "Kv3.2 gene") include a polynucleotide that is able to hybridize with a nucleotide sequence complementary to a known gene sequence, or a probe which can be prepared from the complementary sequence under stringent conditions, and codes for a protein having a function equivalent to that of a known Kv3.2 protein.

The "stringent conditions" are conditions under which a so-called specific hybrid is formed, and a non-specific hybrid is not formed. Although it is difficult to definitely define the conditions with numerals, examples of the stringent conditions include those under which highly homologous polynucleotides hybridize to each

other, for example, polynucleotides not less than 78% homologous, preferably not less than 80% homologous, more preferably not less than 90% homologous, still more preferably not less than 95% homologous, particularly preferably not less than 97% homologous, hybridize to each other, and polynucleotides less homologous than the above do not hybridize to each other, or conditions of washing once, preferably 2 or 3 times, at a salt concentration and temperature corresponding to washing of typical Southern hybridization, i.e., 1 x SSC, 0.1% SDS at 60°C, preferably 0.1 x SSC, 0.1% SDS at 60°C, more preferably 0.1 x SSC, 0.1% SDS at 68°C.

As the probe, a part of the sequence which is complementary to the gene can also be used. Such a probe can be prepared by PCR using oligonucleotides prepared on the basis of a known gene sequence as primers and a DNA fragment containing the nucleotide sequence as a template. For example, when a DNA fragment having a length of about 300 bp is used as the probe, the washing conditions of hybridization may be 50°C, 2 x SSC and 0.1% SDS.

When various Kv3 family proteins were compared for homology, the Kv3.2 protein homologues of the aforementioned various animals showed a homology (identity) of 78% or more, but when the Kv3.2 protein and other Kv3 family proteins were compared, the highest homology was 74%.

A Kv3.2 gene can be obtained by designing appropriate primers or probe on the basis of information on nucleotide sequence of a known Kv3.2 gene or a novel Kv3.2 gene disclosed in this specification, such as a polynucleotide encoding a polypeptide having the amino acid sequence shown in SEQ ID NO: 2, 4, 6, 8, 10, 12, 14, 16, 18, 40, 47, 49, 51 or 53, and performing polymerase chain reaction (PCR), Southern hybridization, or Northern hybridization by using the primers or probe and a sample (for example, total RNA, mRNA fraction, cDNA library) derived from an objective organism, for example, a mammal

(e.g., human, mouse, rat, dog, horse, chimpanzee, rhesus monkey, fowl, opossum, swine, bovine, etc.).

The Kv3.2 gene may be a fragment or may be a gene encoding a chimera protein of the Kv3.2 protein or a fragment thereof and other protein, so long as the gene codes for a protein that can constitute a cation channel of which activity changes according to change of extracellular sodium ion concentration.

For example, there are splice variants of the Kv3.2 protein as described above, and it is highly possible that the regions on the C-terminal side of the common portions (for example, the positions 1 to 538 of SEQ ID NO: 2) may be deleted or replaced with another sequence.

By introducing a polynucleotide encoding a Kv3.2 protein into an appropriate host cell in an expressible form, and allowing expression of the Kv3.2 protein, a cell having a salty taste receptor ion channel can be obtained. For example, by introducing a linear DNA encoding a Kv3.2 protein or a vector containing a sequence encoding a Kv3.2 protein into a host cell, a Kv3.2 protein can be expressed. Examples of the sequence in an expressible form include a sequence prepared on the basis of the DNA information and comprising a sequence encoding a Kv3.2 protein and sequences required for transcription and translation upstream of the sequence encoding a Kv3.2 protein, so that the Kv3.2 protein can be produced. Furthermore, by injecting a cRNA encoding a Kv3.2 protein into a host cell, a cell having a salty taste receptor ion channel can also be obtained. In this case, the cRNA contains a sequence required for translation on the 5' end side of the cRNA. Examples of the sequence required for transcription include expression control sequences such as promoter and enhancer. Furthermore, it may contain a transcription terminator sequence. Examples of the sequence required for translation include a ribosome-binding site. Furthermore, it may contain, for example, a processing information site, such as RNA splice site, a

polyadenylation site, and so forth, as required. Examples of the promoter include promoters derived from immunoglobulin gene, SV40, adenovirus, bovine papilloma virus, cytomegalovirus, and so forth.

As the cell into which the polynucleotide encoding a Kv3.2 protein is introduced, an animal cell, an insect cell, or yeast are preferred, and an animal cell is particularly preferred. For example, a fraction in which taste cells are concentrated, an isolated taste cell, a tissue isolated from a tissue selected from tongue epithelium, adrenal gland, pineal body, thyroid, melanocyte, and kidney, and so forth may be used. Specific examples of cell, which is considered to enable temporary functional expression, when a recombinant vector that expresses a polynucleotide encoding a Kv3.2 protein is introduced, include *Xenopus laevis* oocyte, Chinese hamster ovary cell (CHO), human embryonic kidney (HEK) cell, Sf-9 insect cell, and so forth. The present invention provides a cell introduced with such a polynucleotide encoding a Kv3.2 protein in an expressible form. As the cell, an oocyte or a taste cell is preferred, and a taste cell is especially preferred for use in screening a salty taste modulating substance.

As the method for introducing a polynucleotide encoding a Kv3.2 protein into such cells, a known method can be used. Techniques required for the operations such as introduction of a polynucleotide into a cell are described in Sambrook, J., Fritsch, E.F. and Maniatis, T., "Molecular Cloning A Laboratory Manual and Second Edition", Cold Spring Harbor Laboratory Press (1989), etc.

As shown in the Examples, a cell that expresses the Kv3.2 protein has a cation channel activity which changes according to change of extracellular sodium ion concentration. Therefore, the Kv3.2 protein expressed in a cell can constitute a cation channel of which activity changes according to change of extracellular sodium ion concentration. Although it is presumed that the Kv3.2

protein constitutes a cation channel of which activity changes according to change of extracellular sodium ion concentration as a multimer, the Kv3.2 protein may be monomer or multimer, so long as the cell that expresses the Kv3.2 protein has the cation channel activity which changes according to change of extracellular sodium ion concentration. The "cation channel" means a channel that allows flow of cations such as sodium ion, calcium ion, and potassium ion into or out of cells.

Furthermore, as shown in the Examples, the gene encoding the Kv3.2 protein is expressed in the taste buds of the tongue, which are taste receptors, and since the expression level thereof is higher in a mouse strain showing higher salty taste perception sensitivity as compared with a mouse strain showing lower salty taste perception sensitivity, it is supported that the Kv3.2 protein is a salty taste receptor protein that controls salty taste perception sensitivity.

Therefore, by identifying a compound that acts on a Kv3.2 protein or a cell expressing it, a salty taste modulating substance can be searched for.

Identification of such a compound can be attained by, in addition to the aforementioned methods, for example, measuring binding between a purified Kv3.2 protein and a test substance. In addition, a compound that acts on the Kv3.2 protein can be efficiently searched by estimating stereostructure thereof with a computer with reference to stereostructure information on related proteins (for example, Kv1.2, Chen et al., Proc. Natl. Acad. Sci. USA, 107:11352-11357 (2010)), and choosing a compound showing affinity to a site that may affect the ion channel activity with a computer.

By contacting a test substance with a cell expressing a Kv3.2 protein obtained as described above, and comparing observed cation influx into the cell with cation influx into the cell observed when the test substance is not contacted with the cell, a salty taste

modulating substance can be screened for.

If the cation influx observed when a test substance is contacted with a cell that expresses the Kv3.2 protein is larger than cation influx into the cell observed when the test substance is not contacted with the cell, it is judged that the test substance activates the salty taste receptor channel, and if the cation influx observed when a test substance is contacted with a cell that expresses the Kv3.2 protein is smaller than cation influx into the cell observed when the test substance is not contacted with the cell, it is judged that the test substance inactivates the salty taste receptor channel.

Furthermore, by identifying a gene showing an expression profile similar to that of the Kv3.2 gene or a gene of which expression is suppressed in a Kv3.2 gene-expressing cell among genes expressed in the Kv3.2 gene-expressing cell, a protein having a function of positively or negatively regulating the Kv3.2 activity or a protein constituting a salty taste receptor can also be searched for.

The Kv3.2 activity means a function of the Kv3.2 protein for constituting a cation channel which changes in a cell that expresses it according to change of extracellular sodium ion concentration. Moreover, the Kv3.2 activity is also an activity of the Kv3.2 protein as a salty taste receptor protein.

The gene showing an expression profile similar to that of the Kv3.2 gene refers to a gene of which tissue specificity of gene expression is similar to tissue specificity of Kv3.2 gene expression. As one of the methods for identifying a gene showing a similar expression profile, a comprehensive gene expression analysis method such as a DNA microarray method can be exemplified. Specifically, such a gene can be identified by extracting RNAs from various tissues and searching them for a gene showing tissue specificity for gene expression similar to that of the Kv3.2 gene using a comprehensive

gene expression analysis method such as a DNA microarray method.

The gene of which expression is suppressed in a Kv3.2 gene-expressing cell refers to a gene of which expression is suppressed in a cell in which Kv3.2 gene is expressed, and of which expression can be confirmed in a cell in which Kv3.2 gene is not expressed. As one of the methods for identifying such a gene of which expression is suppressed, a comprehensive gene expression analysis method such as a DNA microarray method can be exemplified. Specifically, such a gene can be identified by extracting RNAs from various tissues and searching them for a gene of which expression is not observed in a Kv3.2 gene-expressing tissue using a comprehensive gene expression analysis method such as a DNA microarray method.

Such a gene as identified as described above is a gene encoding a protein having a function of controlling the Kv3.2 activity or a protein that constitutes a salty taste receptor, and it is estimated that such a protein constitutes a channel or complex together with the Kv3.2 protein, and is involved in taste perception.

Furthermore, by identifying a compound that acts on a channel or complex constituted by the Kv3.2 protein as a taste receptor and a protein specifically expressed in a taste cell, a taste substance or a flavor substance can also be searched for. The flavor substance is a substance that modifies tastes, and it can be used for foodstuffs as a flavor additive. As the taste substance or flavor substance, specifically, a salty taste modulating substance can be exemplified.

It is known that a substance that activates a taste receptor promotes excitation of a taste receptor cell, and thereby shows a taste or enhances a taste. Therefore, by using a cell in which a salty taste receptor channel is expressed on the cell membrane, a substance that activates or inactivates a salty taste receptor channel, i.e., a salty taste modulating substance, can be screened for.

That is, a substance that activates a salty taste receptor channel can be expected to promote excitation of a salty taste receptor cell in which a salty taste receptor ion channel is originally expressed and thereby enhance salty taste perception. Therefore, a substance that activates a salty taste receptor channel in the absence of sodium ion is useful as a candidate substance of a salt alternative substance, and a substance that activates a salty taste receptor channel in the presence of sodium ions is useful as a candidate substance of a salty taste enhancing substance. Therefore, a cell that expresses the Kv3.2 protein itself can be used for screening for a salt alternative or salty taste enhancing substance. Moreover, a substance that inactivates a salty taste receptor channel is useful as a candidate of a salty taste inhibiting substance.

Cation influx into a cell that expresses the Kv3.2 protein can be measured by suspending the cell in a solution containing cations, and directly or indirectly measuring amount of cations flowing into the cell.

Cation influx into a cell can be measured by, for example, measuring electrophysiological characteristics of the cell, for example, cell current, in the presence of extracellular cations. For example, by contacting a cell expressing the Kv3.2 protein with a test substance in the presence of sodium ions, and detecting change in cell membrane potential or membrane current, or intracellular cation concentration, a salty taste modulating substance such as a salty taste enhancing substance or a salty taste inhibiting substance can be screened for. Moreover, by contacting a cell expressing the Kv3.2 protein with a test substance in the absence of sodium ion, and detecting change in cell membrane potential or membrane current, or intracellular cation concentration, a salt alternative substance can be screened for.

Specific methods for screening for a salty taste modulating substance using a cell expressing the Kv3.2

protein are exemplified below.

(1) A *Xenopus laevis* oocyte is allowed to express cRNA encoding the Kv3.2 protein, and a ligand that acts on a salty taste receptor ion channel is searched for on the basis of increase or decrease of the salty taste receptor ion channel current according to the two electrode voltage clamp method. For example, if inward current increases when a test compound is added to an extracellular fluid of a cell of which membrane voltage is clamped at a holding potential of -60 to 80 mV, as compared with the case where the test compound is not added, it can be judged that the test compound is a substance that activates the polypeptide of the present invention. Alternatively, the extracellular sodium ion concentration may be changed stepwise or continuously, and inward current may be measured.

(2) With a cell where a salty taste receptor ion channel is expressed on the cell surface, a ligand that acts on a salty taste receptor ion channel is searched for on the basis of increase or decrease of the salty taste receptor ion channel current with a membrane potential clamped according to the voltage clamp method, especially the whole cell membrane voltage clamp method. For example, if inward current increases when a test compound is added to an extracellular fluid of a cell of which membrane voltage is clamped at a holding potential of -80 mV in the presence of sodium ions, as compared with the case where the test compound is not added, it can be judged that the test compound is a substance that activates the polypeptide of the present invention, i.e., a salty taste enhancing substance.

(3) A cell where a salty taste receptor ion channel is expressed on the cell surface is allowed to incorporate a membrane potential sensitive dye beforehand, then change

of fluorescence intensity of the dye in the cell is analyzed (namely, measured or detected) when a test compound is added in the presence of sodium ions, and thereby whether the Kv3.2 protein is activated or not is analyzed. This method uses a property of the membrane potential sensitive dye that it enables optical detection of change of the membrane potential in connection with the opening of the ion channel. More specifically, as the membrane potential sensitive dye, DiBAC [bis-(1,3-dibutylbarbituric acid)trimethineoxonol, Molecular Probes] or a derivative thereof, Membrane Potential Assay Kit (Molecular Devices) etc. can be used.

(4) A cell where a salty taste receptor ion channel is expressed on the cell surface is allowed to incorporate a cation sensitive dye (for example, SBFI, CoroNa Green, Sodium Green (Molecular Probes), etc.) beforehand, and a salty taste enhancing or inhibiting substance is searched for on the basis of change of fluorescence intensity ratio (intracellular cation concentration) at the time of contacting a ligand candidate compound and a salty taste receptor ion channel expressing cell for a certain period in the presence of sodium ions.

(5) By performing the methods of (2) to (4) described above in the absence of sodium ion, a salt alternative substance can be searched for.

Examples

Hereafter, the present invention will be specifically explained with reference to examples. However, the examples do not limit the scope of the present invention. Unless otherwise indicated, the procedures of the examples were carried out by known methods (Maniatis, T. et al., "Molecular Cloning - A Laboratory Manual", Cold Spring Harbor Laboratory, NY, 1-1982; and Hille, B., Ionic Channels of Excitable Membranes,

2nd Ed., Sinauer Associates Inc., MA, 1992).

Example 1: Expression analysis of mouse Kv3 family channel genes

Expression distribution of the Kv3 family channel gene encoding a protein having the amino acid sequence shown in SEQ ID NO: 10 in the tongue epithelium was analyzed by RT-PCR according to the following procedures using a mouse tongue epithelial tissue.

The epithelium was isolated from the tongue of mouse, and a tongue tip portion containing fungiform papillae, a region containing vallate papillae (center rear portion of the tongue), both side portions of the tongue containing foliate papillae, and the epithelium not containing taste buds were further excised, respectively. Separately, the kidney was excised and pulverized.

RNA was extracted from each tissue using an RNA extraction kit (Absolutely RNA Microprep Kit, Stratagene). The extracted RNA was reverse transcribed using SuperScript III First Strand Synthesis System for RT-PCR (Invitrogen) to synthesize a first strand cDNA. By using the obtained first strand cDNA as a template, PCR was performed with the combinations of primers shown in Table 1 to amplify cDNAs of the genes of the Kv3.1, Kv3.2, Kv3.3, and Kv3.4 proteins.

Table 1

Gene	Forward primer SEQ ID NO:	Reverse primer SEQ ID NO:
Kv3.1	21	22
Kv3.2	23	24
Kv3.3	25	26
Kv3.4	27	28

PCR was performed by the hot start method using FastStart Taq DNA polymerase (Roche Applied Science). The

nucleotide sequences of the aforementioned primers are specific to a mouse Kv3.1 gene (NM_001112739), mouse Kv3.2 gene (NM_001025581, SEQ ID NO: 9), mouse Kv3.3 gene (NM_008422) and mouse Kv3.4 gene (NM_145922), and allow amplification of the DNA fragments of Kv3.1 (241 bp), Kv3.2 (574 bp), Kv3.3 (204 bp), and Kv3.4 (287 bp), respectively. The GenBank accession numbers are indicated in the parentheses following the gene names.

RT-PCR analysis was performed for mRNAs derived from the tongue tip portion containing fungiform papillae, the region containing vallate papillae (center rear portion of the tongue), the both side portions of the tongue containing foliate papillae, and the epithelium not containing taste buds, and mRNA derived from the kidney. As controls, the same reaction was performed without adding a reverse transcriptase for mRNAs derived from those tissues.

As a result, in the tongue tip portion containing fungiform papillae, the region containing vallate papillae, and the both side portions of the tongue containing foliate papillae, which were epithelial tissues including the taste buds, DNA fragments of expected sizes were amplified for all the proteins, Kv3.1, Kv3.2, Kv3.3 and Kv3.4 (Fig. 1). These results revealed that expression of mRNAs of the ion channel proteins of the Kv3 family was observed in portions containing the taste buds in the tongue epithelium. In particular, it was clarified that the Kv3.2 gene localized only in portions containing taste buds, i.e., the tongue tip portion containing fungiform papillae, the region containing vallate papillae, and the both side portions of the tongue containing foliate papillae, in the tongue epithelium. At the same time, DNA fragments of expected sizes were also amplified for Kv3.1, Kv3.2 and Kv3.3 for the kidney. As for Kv3.4, a DNA fragment of a size different from the expected size was amplified, and there was suggested a possibility of the existence of a splice variant.

Example 2: Isolation of polynucleotide encoding human Kv3.2 protein and construction of expression vector therefor

Although the full length cDNA encoding a human salty taste receptor protein can be cloned from, for example, human mRNA, it can also be purchased as a corresponding full length cDNA among those included in The Mammalian Gene Collection (<http://mgc.nci.nih.gov/>) (MGC: 120670, IMAGE: 7939480, catalog number: MHS1010-98052225, Open Biosystems). By using this commercially available plasmid as a template, an oligonucleotide consisting of the nucleotide sequence shown in SEQ ID NO: 19 (*Kpn*I recognition sequence was added to the 5' end) as a forward primer, and an oligonucleotide consisting of the nucleotide sequence shown in SEQ ID NO: 20 (*Xho*I recognition sequence was added to the 5' end) as a reverse primer, PCR was performed. The obtained DNA fragment was digested with the restriction enzymes *Kpn*I and *Xho*I, and then cloned into the plasmid pcDNA3.1(+). The obtained clone was designated pcDNA3.1-KCNC2. The plasmid pcDNA3.1(+) has a promoter sequence derived from cytomegalovirus, and can be used for expression of a polypeptide encoded by a cloning fragment in an animal cell.

The nucleotide sequence of the obtained clone pcDNA3.1-KCNC2 was analyzed using a DNA sequencer (3130xl Genetic Analyzer, Applied Biosystems) according to the dideoxy terminator method, and the nucleotide sequence shown in SEQ ID NO: 5 was obtained. The nucleotide sequence shown in SEQ ID NO: 5 has an open reading frame consisting of 1677 base pairs. The amino acid sequence predicted from the open reading frame consists of 558 amino acid residues (SEQ ID NO: 6).

Example 3: Expression of Kv3.2 protein in *Xenopus laevis* oocyte

In order to detect the cation channel activity of a protein having the amino acid sequence shown in SEQ ID NO: 5, which activity changes according to the change of extracellular sodium ion concentration, cRNA was synthesized by using the expression vector pcDNA3.1-KCNC2 obtained in Example 2 described above as a template, and injected into a *Xenopus laevis* oocyte, so that the protein was expressed. The aforementioned expression vector pcDNA3.1-KCNC2 was digested with the restriction enzyme *XhoI* at one site and thereby made linear, and then cRNA encoding the Kv3.2 protein was synthesized by using a commercially available cRNA synthesis kit, Megascript High Yield Transcription Kit (Ambion). The synthesized cRNA was injected into a *Xenopus laevis* oocyte prepared in a conventional manner using a glass capillary and a microinjector (World Precision Instruments), so that the Kv3.2 protein was expressed. Furthermore, as a control cell, an oocyte into which water was injected was also prepared in the same manner. The obtained these oocytes were stored in a standard oocyte culture medium such as the ND96+ solution (96 mM NaCl, 2 mM KCl, 1 mM MgCl₂, 1.8 mM CaCl₂, 5 mM HEPES, 2 mM sodium pyruvate, 1/100 penicillin/streptomycin mixture (15140-122, Invitrogen), adjusted to pH 7.4 with NaOH) at 18°C for two to four days, and then used in Examples 4 described below.

Example 4: Detection of cation channel activity of Kv3.2 protein, which activity changes according to change of extracellular sodium ion concentration

The total cell current was measured for each of the oocytes obtained in Example 3, of which membrane potential was clamped by the two electrode voltage clamp method. For this measurement, the ND96 solution (96 mmol/L NaCl, 2 mmol/L KCl, 1 mmol/L MgCl₂, 1.8 mmol/L CaCl₂, and 5 mmol/L HEPES (pH 7.5)) was used.

In the *Xenopus laevis* oocyte injected with cRNA prepared using the plasmid pcDNA3.1-KCNC2 as the template,

an inward current higher than 100 nA was measured at a holding potential of -80 mV, when the NaCl concentration in the extracellular fluid was set to be 96 mM. Increase of this current with increase of the extracellular sodium ion concentration was observed, when the NaCl concentration in the extracellular fluid was changed between 0 to 96 mM by replacing NaCl in the aforementioned ND96 solution with N-methyl-D-glucamine hydrochloride (Fig. 2). On the other hand, in the control oocyte injected with water, such a significant inward current was not observed at a holding potential of -80 mV, when the NaCl concentration in the extracellular fluid was set to be 96 mM, and change of the current was not also observed, even when the sodium ion concentration in the extracellular fluid was changed.

Example 5: Confirmation of presence or absence of cation channel activity that changes according to change of extracellular sodium ion concentration for Kv3 family proteins

Expression vectors were constructed for the channels Kv3.1, Kv3.3 and Kv3.4 belonging to the Kv3 family, like Kv3.2, in the same manner as that of Example 2. Full length cDNAs encoding the corresponding proteins were purchased (Kv3.1: catalog number ORK11519, Promega, Kv3.3: catalog number OHS4559-99848374, Open Biosystems, Kv3.4: catalog number MHS1010-98052650, Open Biosystems). By using each of these full length cDNAs as a template and a combination of the primers shown in Table 2, PCR was performed to prepare gene DNA fragments encoding the proteins of Kv3.1, Kv3.3, and Kv3.4, respectively. Both the 5' and 3' ends of each obtained DNA fragment was digested with restriction enzymes (Kv3.1: *Xba*I and *Xho*I, Kv3.3: *Nhe*I and *Eco*RI, Kv3.4: *Nhe*I and *Xho*I), then the digestion product was cloned into the plasmid pcDNA3.1(+). The obtained clones were designated pcDNA3.1-KCNC1 (Kv3.1), pcDNA3.1-KCNC3 (Kv3.3) and pcDNA3.1-KCNC4 (Kv3.4),

respectively.

Table 2

Gene	Forward primer SEQ ID NO:	Reverse primer SEQ ID NO:
Kv3.1	29	30
Kv3.3	31	32
Kv3.4	33	34

cRNAs were synthesized using these plasmids as templates, and injected into *Xenopus laevis* oocytes in the same manner as that of Example 2, so that the proteins were expressed. The aforementioned expression vectors pcDNA3.1-KCNC1, pcDNA3.1-KCNC3 and pcDNA3.1-KCNC4 were digested with a restriction enzyme (Kv3.1: *Xho*I, Kv3.3: *Eco*RI, Kv3.4: *Xho*I) at one site and thereby made linear, and then cRNAs encoding the Kv3.1, Kv3.3 and Kv3.4 proteins were synthesized respectively using a commercially available cRNA synthesis kit, Megascript High Yield Transcription Kit (Ambion). The synthesized cRNAs were each injected into *Xenopus laevis* oocytes prepared in a conventional manner by using a glass capillary and a microinjector (World Precision Instruments), so that the proteins encoded by the cRNAs were expressed. As control cells, an oocyte injected with Kv3.2 in the same manner as that of Example 2 so that the protein was expressed, and an oocyte into which water was injected were also prepared. The obtained oocytes were stored in a standard oocyte culture medium such as the ND96+ solution (96 mM NaCl, 2 mM KCl, 1 mM MgCl₂, 1.8 mM CaCl₂, 5 mM HEPES, 2 mM sodium pyruvate, 1/100 penicillin/streptomycin mixture (15140-122, Invitrogen), adjusted to pH 7.4 with NaOH) at 18°C for two to four days, and then the total cell current was measured for each of the oocytes, of which membrane potential was clamped by the dual electrode voltage clamp method. For this measurement, the ND96 solution (96 mmol/L NaCl, 2 mmol/L KCl, 1 mmol/L MgCl₂, 1.8 mmol/L CaCl₂, and 5 mmol/L

HEPES (pH 7.5)) was used.

For the case where the NaCl concentration in the extracellular fluid was set to be 96 mM using ND960, and the case where the NaCl concentration in the extracellular fluid was set to be 0 mM by substitution of N-methyl-D-glucamine hydrochloride for NaCl in the ND96 solution, the difference of current amounts at a holding potential of -80 mV was measured for each oocyte. As a result, only when the cRNA encoding the Kv3.2 protein was injected, a current amount difference of about 80 nA or larger in average was measured (Fig. 3). On the other hand, such current amount difference could not be observed for the control oocyte injected with water. For the oocytes injected with each of cRNAs encoding Kv3.1, Kv3.3 and Kv3.4 proteins, which are the other channels of the Kv3 family, only a current smaller than 15 nA was measured, and significant difference was not observed with respect to the control oocyte injected with water. On the basis of these measurement results, it was confirmed that, among the quite similar Kv3 family channels, only the Kv3.2 showed increase in the current amount in connection with the increase of the extracellular sodium ion concentration.

The above results revealed that the Kv3.2 protein could constitute a cation channel of which activity changes according to change of extracellular sodium ion concentration.

Example 6: Comparison of expression levels of Kv3.2 gene in strains showing difference in salty taste perception sensitivity

A method for measuring mouse salty threshold value by using behavioral procedures has been reported (Ishiwatari, Y. and Bachmanov, A.A., *Chemical Senses*, 34:277-293 (2009)). Moreover, it has also been reported that there is difference in salty taste perception sensitivity among mouse strains (Ishiwatari, Y., and Bachmanov, A.A., *Chemical Senses*, 32:A26 (2007)). By

using the aforementioned behavioral method, difference of salty threshold values was measured for two strains showing difference in salty taste perception sensitivity, C57BL/6J (strain showing high salty taste perception sensitivity), and A/J (strain showing low salty taste perception sensitivity). As a result, it was confirmed that there was difference in the threshold value of about 5 times between the both (Table 3). Then, expression amount of the gene encoding the Kv3.2 protein in the tongue epithelium of both the strains were quantified and compared.

Table 3

Strain	Salty threshold value (mM)
C57BL/6J	8.6
A/J	43.3

The epithelia were isolated from the tongues of mice of the two strains (C57BL/6J, A/J), and a tongue tip portion containing the fungiform papillae and epithelium not containing taste buds were excised, respectively, from each of them. RNA was extracted from each tissue using an RNA extraction kit (Absolutely RNA Microprep Kit, Stratagene). The extracted RNA was reverse-transcribed using SuperScript III First Strand Synthesis System for RT-PCR (Invitrogen) to synthesize a first strand cDNA. By using the obtained first strand cDNA as a template, quantitative RT-PCR analysis was conducted with TaqMan Gene Expression Assays (Life Technologies) and StepOnePlus Real-time PCR System (Life Technologies). The quantification results were corrected by expression amount of β -actin gene (actb) in each site, and then the expression levels of the strains were compared. Two kinds of assays (Probe 1: Mm01234233_m1, Probe 2: Mm01234232_m1) were performed for the Kv3.2 gene, and as a result, difference was observed between expression levels in the tongue tip portions of both the strains, A/J and C57BL/6J.

The expression level of the strain C57BL/6J was 3 to 5 times higher than the expression level of the strain A/J, and it is considered that this difference in the expression levels affects the difference of the salty taste perception sensitivity (Table 4). On the other hand, no expression was detected in the epithelia not containing the taste buds of both the strains.

Table 4

Site	B6/A (actb normalized) *	
	Probe 1	Probe 2
Tongue tip portion (containing fungiform papillae)	3.43	5.21

* Ratio of expression amounts of B6 (C57BL/6J) and A (A/J) standardized with actb gene expression amount

On the basis of the above results, it was confirmed that the Kv3.2 gene coded for a protein contributing to salty taste perception.

Example 7: Confirmation of expression of mouse Kv3.2 gene in taste buds by in situ hybridization method

A cDNA encoding the full length of the mouse salty taste receptor protein can be cloned by designing a primer set with reference to SEQ ID NO: 9 and a similar sequence registered at a gene database (GenBank accession number: BY281762), and performing PCR with it. By using an oligonucleotide consisting of the nucleotide sequence shown in SEQ ID NO: 35 as a forward primer, an oligonucleotide consisting of the nucleotide sequence shown in SEQ ID NO: 36 as a reverse primer, and the first strand cDNA obtained in Example 6, which was prepared from the tongue tip portion containing the fungiform papillae, as a template, PCR was performed. The obtained DNA fragment was cloned in the plasmid pGEM-T Easy (Promega). The obtained clone was designated pGEM-T-mKcnc2. The nucleotide sequence of the obtained clone was analyzed

using a DNA sequencer (3130xl Genetic Analyzer, Applied Biosystems) according to the dideoxy terminator method, and it was confirmed that the same nucleotide sequence as that of SEQ ID NO: 9 was obtained. Furthermore, the plasmid pGEM-T-mKcnc2 was digested with the restriction enzyme *Sph*I at one site and thereby made linear, and an antisense RNA of the mouse Kv3.2 gene labeled with digoxigenin was synthesized by using DIG RNA Labeling Kit (Roche Diagnostics).

From a portion of mouse tongue containing taste buds immersed in a frozen tissue embedding agent and cryopreserved at -80°C , sections were prepared using a cryostat. After a fixation treatment (immersion in 4% paraformaldehyde solution for 10 minutes), the sections were subjected to an acylation treatment for 10 minutes, washed 3 times with PBS for 10 minutes, and then immersed in a hybridization buffer (5 x SSC, 50% formamide, 1 x Denhardt's solution, 1 mg/ml of salmon sperm DNA, 1 mg/ml of tRNA). A cRNA probe was prepared using T7 RNA polymerase in the presence of UTP labeled with digoxigenin. Hybridization was performed at 72°C in a 5 x SSC, 50% formamide solution. For signal detection, a color reaction was performed using an alkaline phosphatase-bound anti-digoxigenin antibody (Roche Diagnostics) and NBT/BCIP as the substrate, and then the sections were observed under a light microscope (BX61, Olympus). As a result of hybridization using the antisense RNA of the mouse Kv3.2 gene labeled with digoxigenin as a probe, signals were detected in the taste buds in a region containing the vallate papillae of the mouse tongue epithelium (Fig. 4). Therefore, it became clear that the Kv3.2 gene was expressed in the taste buds.

From the above results, it was confirmed that the Kv3.2 protein is present in the taste buds. Taking into consideration that the Kv3.2 protein contributes to the salty taste perception sensitivity, and constitutes a cation channel of which activity changes according to

change of extracellular sodium ion concentration, it is concluded that the Kv3.2 protein constitutes a salty taste receptor ion channel. The Kv3.2 protein can be used for screening for a novel salty taste modulating substance.

Example 8: Screening for channel activity modulating compound using Kv3.2

cRNA of the human Kv3.2 channel was injected into a matured oocyte taken out from *Xenopus laevis* (female), and the oocyte was stored in a standard oocyte culture medium such as the ND96+ solution (96 mM NaCl, 2 mM KCl, 1 mM MgCl₂, 1.8 mM CaCl₂, 5 mM HEPES, 2 mM sodium pyruvate, 1/100 penicillin/streptomycin mixture (15140-122, Invitrogen), adjusted to pH 7.4 with NaOH) at 18°C. Two to four days after the injection, the oocyte was set on a parallel clamp system for *Xenopus laevis* oocytes, OpusXpress 6000A (Molecular Devices Japan). The oocyte was perfused with an assay buffer (66 mM N-methyl-D-glucamine hydrochloride, 30 mM NaCl, 2 mM KCl, 1 mM MgCl₂, 1.8 mM CaCl₂, 5 mM HEPES, adjusted to pH 7.4 with KOH), and the membrane potential was maintained at -80 mV. The cell membrane current was measured in this state, and screening was performed on the basis of detection of change of the current at the time of adding a test substance solution. It is considered that when an inward current is observed for the electric current, the Kv3.2 channel is activated with a compound, and when an outward current is observed, the Kv3.2 channel activity is suppressed. Moreover, in order to distinguish from nonspecific change of electric current due to influence of a test substance on the oocyte itself, the test substance solution was also added to the oocyte injected with water instead of cRNA to confirm that there was no change in the current. For example, a low molecular organic compound A retrieved by the screening increased the current in a concentration dependent manner in the oocyte expressing the human Kv3.2 when the compound was added, but such

change of the current was not confirmed in the oocyte injected with water (Fig. 5).

Example 9: Salty taste enhancing effect of obtained activity modulating compound

Influence on salty taste of the compound for which Kv3.2 channel activity modulating action was found was confirmed by performing a quantitative sensory evaluation test for the compound.

The quantitative sensory evaluation test was performed as follows. The compound A as a sample was mixed in an amount of 0.0001 to 0.002 g/dl with distilled water containing sodium chloride (0.5 g/dl), and intensity of salty taste enhancing activity of the compound was measured. Distilled water containing 0.55 g/dl, 0.60 g/dl or 0.65 g/dl of sodium chloride was used as objects of comparison. A method according to the linear scale method was used, wherein the panelists marked positions corresponding to their grading on a straight line on which positions of sodium chloride concentrations corresponding to 1.0 time (0.50 g/dl), 1.1 times (0.55 g/dl), 1.2 times (0.60 g/dl), and 1.3 times (0.65 g/dl) the concentration of the mixture were indicated. Test scores were obtained by averaging the positions marked by the panelists and indicated as a salty taste enhancing ratio (times). The test was performed with $n = 6$. The panelists consisted of persons who experienced development of flavoring of foodstuffs for one year or more in total, and could distinguish sodium chloride solutions having different concentrations of 0.50 g/dl, 0.55 g/dl and 0.60 g/dl (this ability was periodically confirmed). As the "initial taste", intensity of salty taste within 2 seconds after holding in the mouth was evaluated, and the "middle and after tastes" means the total of middle taste and after taste, and evaluated as intensity of salty taste after 2 seconds from holding in the mouth. The results for typical concentrations are shown in Table 5. As shown by

the results, it was found that addition of the compound A enhanced salty taste intensity in a concentration dependent manner.

Table 5

Sample	Concentration (g/dl)	Salty taste enhancing ratio (times)		Evaluation comment
		Initial taste	Middle and after tastes	
No additive	-	1	1	-
Compound A	0.0001	1.01	1.01	Almost no effect of addition
	0.001	1.04	1.04	Salty taste was slightly enhanced, after taste included bitter taste
	0.002	1.05	1.07	Salty taste was enhanced in middle and after tastes, after taste included bitter taste

Example 10: Cloning of *Xenopus laevis* Kv3.2 gene

There has been no information on cDNA encoding the Kv3.2 channel protein of *Xenopus laevis*. However, in the gene database of the closely related species, *Xenopus tropicalis* (<http://genome.jgi-psf.org/Xentr4/Xentr4.home.html>), a nucleotide sequence predicted to code for Kv3.2 (C_scaffold_541000003) is registered. With reference to this sequence as well as the gene sequence information on the human, mouse and rat Kv3.2 genes, PCR was performed using an oligonucleotide consisting of the nucleotide sequence shown in SEQ ID NO:

37 as a forward primer, an oligonucleotide consisting of the nucleotide sequence shown in SEQ ID NO: 38 as a reverse primer, and cDNA of *Xenopus laevis* brain as a template. The obtained DNA fragment was cloned into the plasmid pGEM-T Easy. The obtained clone was designated pGEM-T-xlKcnc2. The nucleotide sequence of the obtained clone was analyzed by using a DNA sequencer (3130xl Genetic Analyzer, Applied Biosystems) according to the dideoxy terminator method, and it was confirmed that the nucleotide sequence as shown in SEQ ID NO: 31 was obtained. The nucleotide sequence shown in SEQ ID NO: 39 has an open reading frame consisting of 1716 base pairs. The amino acid sequence predicted from the open reading frame consists of 571 amino acid residues (SEQ ID NO: 40).

Example 11: Expression of *Xenopus laevis* Kv3.2 protein in *Xenopus laevis* oocyte

In order to detect the cation channel activity of a protein having the amino acid sequence shown in SEQ ID NO: 40, which activity changes according to the change of extracellular sodium ion concentration, cRNA was synthesized by using the clone obtained in Example 10 described above as a template, and injected into a *Xenopus laevis* oocyte, so that the protein was expressed. PCR was performed using the aforementioned plasmid pGEM-T-xlKcnc2 as a template, an oligonucleotide consisting of the nucleotide sequence shown in SEQ ID NO: 41 as a forward primer, and an oligonucleotide consisting of the nucleotide sequence shown in SEQ ID NO: 42 as a reverse primer. The obtained DNA fragment was digested with the restriction enzymes *NheI* and *XhoI*, and then cloned into the plasmid pcDNA3.1(+) (Invitrogen). The obtained clone was designated pcDNA3.1-xlKcnc2. The obtained plasmid was digested with the restriction enzyme *XhoI* at one site and thereby made linear, and then cRNA encoding the Kv3.2 protein was synthesized using a commercially available cRNA synthesis kit, Megascript High Yield Transcription

Kit (Ambion). The synthesized cRNA was injected into a *Xenopus laevis* oocyte prepared in a conventional manner using a glass capillary and a microinjector (World Precision Instruments), so that the Kv3.2 protein was expressed. Furthermore, as a control cell, an oocyte into which water was injected was also prepared in the same manner. The obtained these oocytes were stored in a standard oocyte culture medium such as the ND96+ solution (96 mM NaCl, 2 mM KCl, 1 mM MgCl₂, 1.8 mM CaCl₂, 5 mM HEPES, 2 mM sodium pyruvate, 1/100 penicillin/streptomycin mixture (15140-122, Invitrogen), adjusted to pH 7.4 with NaOH) at 18°C for two to four days, and then used in Examples 12 described below.

Example 12: Detection of cation channel activity of *Xenopus laevis* Kv3.2 protein, which changes according to change of extracellular sodium ion concentration

The total cell current was measured for each of the oocytes obtained in Example 11, of which membrane potential was clamped by the dual electrode voltage clamp method. For this measurement, the ND96 solution (96 mmol/L NaCl, 2 mmol/L KCl, 1 mmol/L MgCl₂, 1.8 mmol/L CaCl₂, and 5 mmol/L HEPES (pH 7.5)) was used. In the *Xenopus laevis* oocyte injected with cRNA prepared using the plasmid pcDNA3.1-*xlKcnc2* as the template, an inward current higher than 100 nA was measured at a holding potential of -80 mV, when the NaCl concentration in the extracellular fluid was set to be 96 mM. When the NaCl concentration in the extracellular fluid was 0 mM, this current was not observed, and decrease in the current amount was observed with decrease of the extracellular sodium concentration (Fig. 6). On the other hand, in the control oocyte injected with water, such a significant inward current as described above was not observed at a holding potential of -80 mV, when the NaCl concentration in the extracellular fluid was set to be 96 mM, and change of the current amount was not also observed, even when the

sodium ion concentration in the extracellular fluid was changed to 0 mM.

The above results demonstrated that the *Xenopus laevis* Kv3.2 protein could constitute a cation channel of which activity changes according to change of extracellular sodium ion concentration.

Example 13: Cloning of mouse Kv3.2 gene expressed in taste buds

One kind of mouse Kv3.2 gene has been registered (SEQ ID NO: 9). As for human, four kinds of genes considered to be splice variants are registered at a gene database (SEQ ID NOS: 1, 3, 5 and 7) as Kv3.2 genes, and a plurality of splice variants may similarly exist for mouse. Therefore, for the purpose of obtaining Kv3.2 genes that were expressed and functioned in the mouse taste buds, mouse Kv3.2 genes were cloned from the tongue epithelium containing the taste buds. First, the epithelium was isolated from the tongue of mouse, a portion containing the taste buds was excised, and RNA was extracted using an RNA extraction kit (Absolutely RNA Microprep Kit, Stratagene). The extracted RNA was reverse-transcribed by using SuperScript III First Strand Synthesis System for RT-PCR (Invitrogen) to synthesize a first strand cDNA. By using the obtained first strand cDNA as a template, cDNA was amplified by PCR. As a forward primer, an oligonucleotide consisting of the nucleotide sequence shown in SEQ ID NO: 35 was used, and as a reverse primer, an oligonucleotide consisting of the nucleotide sequence shown in SEQ ID NO: 36, and oligonucleotides consisting of the nucleotide sequences shown in SEQ ID NOS: 43, 44 and 45, respectively, were used. The oligonucleotides consisting of the nucleotide sequences shown in SEQ ID NOS: 43, 44 and 45 were designed as reverse primers corresponding to mouse Kv3.2 splice variants expected from comparison of human Kv3.2 gene sequences (SEQ ID NOS: 1, 3, 5 and 7) and the mouse genomic DNA sequence containing the

mouse Kv3.2 gene (GenBank accession number: NC_000076). For PCR, Phusion Hot Start High-Fidelity DNA Polymerase (New England Biolabs) was used.

Example 14: Splice variants of mouse Kv3.2 gene isolated from taste buds

The obtained DNA fragments were cloned into the plasmid pGEM-T Easy. The nucleotide sequences of the obtained 30 clones were analyzed using a DNA sequencer (3130xl Genetic Analyzer, Applied Biosystems) according to the dideoxy terminator method, and they were roughly classified into 5 groups of similar kinds of nucleotide sequences. The five groups consisted of sequences having the same nucleotide sequence as that of SEQ ID NO: 9, which is uniquely registered at the gene database as the mouse Kv3.2 gene, and sequences having open reading frames shown in SEQ ID NOS: 46, 48, 50 and 52, respectively. The lengths of the nucleotide sequences and the lengths of the amino acid sequences predicted from the open reading frames (SEQ ID NOS: 47, 49, 51 and 53) are as shown in Table 6. These amino acid sequences have a common sequence except for the C terminal regions (part corresponding to the positions 1 to 597 of SEQ ID NO: 10), and they are considered as splice variants. These splice variants of the mouse Kv3.2 gene cloned from the taste buds may form a salty taste receptor channel by themselves or as a complex with another variant.

Table 6

	Nucleotide sequence		Amino acid sequence	
	SEQ ID NO:	Sequence length	SEQ ID NO:	Sequence length
Mouse Kv3.2	9	1920	10	639
Splice variant 1	46	1929	47	642
Splice variant 2	48	1854	49	617
Splice variant 3	50	1845	51	614
Splice variant 4	52	1968	53	655

Claims

1. A method for screening a salty taste modulating substance, which comprises the step of contacting a test substance with a cell that expresses a Kv3.2 protein, and comparing observed cation influx into the cell with cation influx into the cell observed when the test substance is not contacted with the cell.

2. The method according to claim 1, wherein the cation influx is measured by measuring cell membrane current of the cell in the presence of sodium ions.

3. The method according to claim 1, wherein the cation influx is measured by measuring cell membrane current of the cell in the absence of sodium ion.

4. The method according to claim 1 or 2, wherein the salty taste modulating substance is a salty taste enhancing substance or a salty taste inhibiting substance.

5. The method according to claim 1 or 3, wherein the salty taste modulating substance is a salt alternative substance.

6. The method according to any one of claims 1 to 5, wherein the Kv3.2 protein has the amino acid sequence of SEQ ID NO: 2, 4, 6, 8, 10, 12, 14, 16, 18, 40, 47, 49, 51 or 53.

7. The method according to any one of claims 1 to 5, wherein the Kv3.2 protein shows a sequence identity of at least 78% or more to the sequence of SEQ ID NO: 2, 4, 6, 8, 10, 12, 14, 16, 18, 40, 47, 49, 51 or 53, and is able to constitute a cation channel of which activity changes according to change of extracellular sodium ion concentration.

8. The method according to any one of claims 1 to 5, wherein the Kv3.2 protein is has the amino acid sequence of SEQ ID NO: 2, 4, 6, 8, 10, 12, 14, 16, 18, 40, 47, 49, 51 or 53 including substitutions, deletions, insertions and/or additions of one or more amino acid residues, and is able to constitute a cation channel of which activity changes according to change of extracellular sodium ion concentration.

9. The method according to any one of claims 1 to 5, wherein the Kv3.2 protein is encoded by a DNA shown in the following (a) or (b):

(a) a DNA having the nucleotide sequence of SEQ ID NO: 1, 3, 5, 7, 9, 11, 13, 15, 17, 39, 46, 48, 50 or 52;

(b) a DNA which is able to hybridize with the nucleotide sequence complementary to the nucleotide sequence of SEQ ID NO: 1, 3, 5, 7, 9, 11, 13, 15, 17, 39, 46, 48, 50 or 52, or a probe which can be prepared from the nucleotide sequence under stringent conditions, and codes for a protein that can constitute a cation channel of which activity changes according to change of extracellular sodium ion concentration.

10. The method according to any one of claims 1 to 5, wherein the Kv3.2 protein is selected from Kv3.2 protein homologues derived from human, mouse, rat, frog of the genus *Xenopus*, dog, horse, chimpanzee, rhesus monkey, fowl, opossum, swine or bovine, a mutant thereof, a fragment thereof, and a chimera protein thereof.

11. The method according to any one of claims 1 to 10, wherein the cell is an oocyte into which a polynucleotide encoding a Kv3.2 protein is introduced in an expressible form.

12. The method according to any one of claims 1 to 10, wherein the cell expresses a Kv3.2 gene isolated from

a tissue selected from taste cell, tongue epithelium, adrenal gland, pineal body, thyroid, melanocyte and kidney.

13. A Kv3.2 protein variant, which is a protein shown in any of the following (a) to (c):

(a) a protein having the sequence of SEQ ID NO: 47, 49, 51 or 53;

(b) a protein showing a sequence identity of at least 78% or more to the sequence of SEQ ID NO: 47, 49, 51 or 53, and being able to constitute a cation channel of which activity changes according to change of extracellular sodium ion concentration;

(c) a protein which has the amino acid sequence of SEQ ID NO: 47, 49, 51 or 53 including substitutions, deletions, insertions and/or additions of one or more amino acid residues, and is able to constitute a cation channel of which activity changes according to change of extracellular sodium ion concentration.

14. A DNA encoding a Kv3.2 protein variant, which is a DNA shown in the following (a) or (b):

(a) a DNA having the nucleotide sequence of SEQ ID NO: 46, 48, 50 or 52;

(b) a DNA which is able to hybridize with the nucleotide sequence complementary to the nucleotide sequence of SEQ ID NO: 46, 48, 50 or 52, or a probe which can be prepared from the nucleotide sequence under stringent conditions, and codes for a protein that can constitute a cation channel of which activity changes according to change of extracellular sodium ion concentration.

15. A method for searching a protein having a function of positively or negatively regulating the Kv3.2 activity or a protein that constitutes a salty taste receptor, which comprises identifying a gene showing an expression profile similar to that of the Kv3.2 gene, or a

gene of which expression is suppressed in a Kv3.2 gene-expressing cell among genes expressed in the Kv3.2 gene-expressing cell.

16. A method for searching a salty taste modulating substance, which comprises identifying a compound that acts on a Kv3.2 protein, or a cell expressing the protein.

17. A method for searching a taste substance or a flavor substance, which comprises identifying a compound that acts on a channel or complex which is constituted by a Kv3.2 protein and a protein specifically expressed in a taste cell.

18. An isolated taste cell into which a polynucleotide encoding a Kv3.2 protein is introduced in an expressible form.

SEQUENCE LISTING

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Gly	Ala	Gly	Asn	Cys	Ser	Ser	Arg	Gly	Gly	Arg	Ala	Ser	Asp	His	Pro		
			85					90					95				
ggt	ggc	ggc	cgc	gag	ttc	ttc	ttc	gac	cgg	cac	ccg	ggc	gtc	ttc	gcc	336	
Gly	Gly	Gly	Arg	Glu	Phe	Phe	Phe	Asp	Arg	His	Pro	Gly	Val	Phe	Ala		
			100					105					110				
tat	gtg	ctc	aat	tac	tac	cgc	acc	ggc	aag	ctg	cac	tgc	ccc	gca	gac	384	
Tyr	Val	Leu	Asn	Tyr	Tyr	Arg	Thr	Gly	Lys	Leu	His	Cys	Pro	Ala	Asp		
			115					120					125				
gtg	tgc	ggg	ccg	ctc	ttc	gag	gag	gag	ctg	gcc	ttc	tgg	ggc	atc	gac	432	
Val	Cys	Gly	Pro	Leu	Phe	Glu	Glu	Glu	Leu	Ala	Phe	Trp	Gly	Ile	Asp		
		130				135				140							
gag	acc	gac	gtg	gag	ccc	tgc	tgc	tgg	atg	acc	tac	cgg	cag	cac	cgc	480	
Glu	Thr	Asp	Val	Glu	Pro	Cys	Cys	Trp	Met	Thr	Tyr	Arg	Gln	His	Arg		
145					150					155				160			
gac	gcc	gag	gag	gcg	ctg	gac	atc	ttc	gag	acc	ccc	gac	ctc	att	ggc	528	
Asp	Ala	Glu	Glu	Ala	Leu	Asp	Ile	Phe	Glu	Thr	Pro	Asp	Leu	Ile	Gly		
			165					170					175				
ggc	gac	ccc	ggc	gac	gac	gag	gac	ctg	gcg	gcc	aag	agg	ctg	ggc	atc	576	
Gly	Asp	Pro	Gly	Asp	Asp	Glu	Asp	Leu	Ala	Ala	Lys	Arg	Leu	Gly	Ile		
			180					185					190				
gag	gac	gcg	gcg	ggg	ctc	ggg	ggc	ccc	gac	ggc	aaa	tct	ggc	cgc	tgg	624	
Glu	Asp	Ala	Ala	Gly	Leu	Gly	Gly	Pro	Asp	Gly	Lys	Ser	Gly	Arg	Trp		
		195				200				205							
agg	agg	ctg	cag	ccc	cgc	atg	tgg	gcc	ctc	ttc	gaa	gac	ccc	tac	tcg	672	
Arg	Arg	Leu	Gln	Pro	Arg	Met	Trp	Ala	Leu	Phe	Glu	Asp	Pro	Tyr	Ser		
		210				215				220							
tcc	aga	gcc	gcc	agg	ttt	att	gct	ttt	gct	tct	tta	ttc	ttc	atc	ctg	720	
Ser	Arg	Ala	Ala	Arg	Phe	Ile	Ala	Phe	Ala	Ser	Leu	Phe	Phe	Ile	Leu		
225					230					235				240			
ggt	tca	att	aca	act	ttt	tgc	ctg	gaa	aca	cat	gaa	gct	ttc	aat	att	768	
Val	Ser	Ile	Thr	Thr	Phe	Cys	Leu	Glu	Thr	His	Glu	Ala	Phe	Asn	Ile		
			245					250					255				
ggt	aaa	aac	aag	aca	gaa	cca	gtc	atc	aat	ggc	aca	agt	ggt	ggt	cta	816	
Val	Lys	Asn	Lys	Thr	Glu	Pro	Val	Ile	Asn	Gly	Thr	Ser	Val	Val	Leu		
			260					265					270				
cag	tat	gaa	att	gaa	acg	gat	cct	gcc	ttg	acg	tat	gta	gaa	gga	gtg	864	
Gln	Tyr	Glu	Ile	Glu	Thr	Asp	Pro	Ala	Leu	Thr	Tyr	Val	Glu	Gly	Val		

275	280	285	
tgt gtg gtg tgg ttt act ttt gaa ttt tta gtc cgt att gtt ttt tca			912
Cys Val Val Trp Phe Thr Phe Glu Phe Leu Val Arg Ile Val Phe Ser			
290	295	300	
ccc aat aaa ctt gaa ttc atc aaa aat ctc ttg aat atc att gac ttt			960
Pro Asn Lys Leu Glu Phe Ile Lys Asn Leu Leu Asn Ile Ile Asp Phe			
305	310	315	320
gtg gcc atc cta cct ttc tac tta gag gtg gga ctc agt ggg ctg tca			1008
Val Ala Ile Leu Pro Phe Tyr Leu Glu Val Gly Leu Ser Gly Leu Ser			
325	330	335	
tcc aaa gct gct aaa gat gtg ctt ggc ttc ctc agg gtg gta agg ttt			1056
Ser Lys Ala Ala Lys Asp Val Leu Gly Phe Leu Arg Val Val Arg Phe			
340	345	350	
gtg agg atc ctg aga att ttc aag ctc acc cgc cat ttt gta ggt ctg			1104
Val Arg Ile Leu Arg Ile Phe Lys Leu Thr Arg His Phe Val Gly Leu			
355	360	365	
agg gtg ctt gga cat act ctt cga gct agt act aat gaa ttt ttg ctg			1152
Arg Val Leu Gly His Thr Leu Arg Ala Ser Thr Asn Glu Phe Leu Leu			
370	375	380	
ctg ata att ttc ctg gct cta gga gtt ttg ata ttt gct acc atg atc			1200
Leu Ile Ile Phe Leu Ala Leu Gly Val Leu Ile Phe Ala Thr Met Ile			
385	390	395	400
tac tat gcc gag aga gtg gga gct caa cct aac gac cct tca gct agt			1248
Tyr Tyr Ala Glu Arg Val Gly Ala Gln Pro Asn Asp Pro Ser Ala Ser			
405	410	415	
gag cac aca cag ttc aaa aac att ccc att ggg ttc tgg tgg gct gta			1296
Glu His Thr Gln Phe Lys Asn Ile Pro Ile Gly Phe Trp Trp Ala Val			
420	425	430	
gtg acc atg act acc ctg ggt tat ggg gat atg tac ccc caa aca tgg			1344
Val Thr Met Thr Thr Leu Gly Tyr Gly Asp Met Tyr Pro Gln Thr Trp			
435	440	445	
tca ggc atg ctg gtg gga gcc ctg tgt gct ctg gct gga gtg ctg aca			1392
Ser Gly Met Leu Val Gly Ala Leu Cys Ala Leu Ala Gly Val Leu Thr			
450	455	460	
ata gcc atg cca gtg cct gtc att gtc aat aat ttt gga atg tac tac			1440
Ile Ala Met Pro Val Pro Val Ile Val Asn Asn Phe Gly Met Tyr Tyr			
465	470	475	480
tcc ttg gca atg gca aag cag aaa ctt cca agg aaa aga aag aag cac			1488
Ser Leu Ala Met Ala Lys Gln Lys Leu Pro Arg Lys Arg Lys Lys His			
485	490	495	
atc cct cct gct cct cag gca agc tca cct act ttt tgc aag aca gaa			1536
Ile Pro Pro Ala Pro Gln Ala Ser Ser Pro Thr Phe Cys Lys Thr Glu			
500	505	510	
tta aat atg gcc tgc aat agt aca cag agt gac aca tgt ctg ggc aaa			1584
Leu Asn Met Ala Cys Asn Ser Thr Gln Ser Asp Thr Cys Leu Gly Lys			
515	520	525	
gac aat cga ctt ctg gaa cat aac aga tca gtg tta tca ggt gac gac			1632
Asp Asn Arg Leu Leu Glu His Asn Arg Ser Val Leu Ser Gly Asp Asp			
530	535	540	

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agt aca gga agt gag ccg cca cta tca ccc cca gaa agg ctc ccc atc      1680
Ser Thr Gly Ser Glu Pro Pro Leu Ser Pro Pro Glu Arg Leu Pro Ile
545                      550                      555                      560
aga cgc tct agt acc aga gac aaa aac aga aga ggg gaa aca tgt ttc      1728
Arg Arg Ser Ser Thr Arg Asp Lys Asn Arg Arg Gly Glu Thr Cys Phe
                      565                      570                      575
cta ctg acg aca ggt gat tac acg tgt gct tct gat gga ggg atc agg      1776
Leu Leu Thr Thr Gly Asp Tyr Thr Cys Ala Ser Asp Gly Gly Ile Arg
                      580                      585                      590
aaa gga tat gaa aaa tcc cga agc tta aac aac ata gcg ggc ttg gca      1824
Lys Gly Tyr Glu Lys Ser Arg Ser Leu Asn Asn Ile Ala Gly Leu Ala
                      595                      600                      605
ggc aat gct ctg agg ctc tct cca gta aca tca ccc tac aac tct cct      1872
Gly Asn Ala Leu Arg Leu Ser Pro Val Thr Ser Pro Tyr Asn Ser Pro
                      610                      615                      620
tgt cct ctg agg cgc tct cga tct ccc atc cca tct atc ttg taa      1917
Cys Pro Leu Arg Arg Ser Arg Ser Pro Ile Pro Ser Ile Leu
625                      630                      635

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<210> 4
<211> 638
<212> PRT
<213> Homo sapiens

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

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	180		185		190	
Glu Asp Ala Ala Gly Leu Gly Gly	Pro Asp Gly Lys Ser Gly Arg Trp					
195	200	205				
Arg Arg Leu Gln Pro Arg Met Trp	Ala Leu Phe Glu Asp Pro Tyr Ser					
210	215	220				
Ser Arg Ala Ala Arg Phe Ile Ala Phe	Ala Ser Leu Phe Phe Ile Leu					
225	230	235				240
Val Ser Ile Thr Thr Phe Cys Leu Glu	Thr His Glu Ala Phe Asn Ile					
	245	250				255
Val Lys Asn Lys Thr Glu Pro Val Ile	Asn Gly Thr Ser Val Val Leu					
	260	265				270
Gln Tyr Glu Ile Glu Thr Asp Pro Ala	Leu Thr Tyr Val Glu Gly Val					
	275	280				285
Cys Val Val Trp Phe Thr Phe Glu Phe	Leu Val Arg Ile Val Phe Ser					
	290	295				300
Pro Asn Lys Leu Glu Phe Ile Lys Asn	Leu Leu Asn Ile Ile Asp Phe					
305	310	315				320
Val Ala Ile Leu Pro Phe Tyr Leu Glu	Val Gly Leu Ser Gly Leu Ser					
	325	330				335
Ser Lys Ala Ala Lys Asp Val Leu Gly	Phe Leu Arg Val Val Arg Phe					
	340	345				350
Val Arg Ile Leu Arg Ile Phe Lys Leu	Thr Arg His Phe Val Gly Leu					
	355	360				365
Arg Val Leu Gly His Thr Leu Arg Ala	Ser Thr Asn Glu Phe Leu Leu					
	370	375				380
Leu Ile Ile Phe Leu Ala Leu Gly Val	Leu Ile Phe Ala Thr Met Ile					
	385	390				395
400						
Tyr Tyr Ala Glu Arg Val Gly Ala Gln	Pro Asn Asp Pro Ser Ala Ser					
	405	410				415
Glu His Thr Gln Phe Lys Asn Ile Pro	Ile Gly Phe Trp Trp Ala Val					
	420	425				430
Val Thr Met Thr Thr Leu Gly Tyr Gly	Asp Met Tyr Pro Gln Thr Trp					
	435	440				445
Ser Gly Met Leu Val Gly Ala Leu Cys	Ala Leu Ala Gly Val Leu Thr					
	450	455				460
Ile Ala Met Pro Val Pro Val Ile Val	Asn Asn Phe Gly Met Tyr Tyr					
	465	470				475
480						
Ser Leu Ala Met Ala Lys Gln Lys Leu	Pro Arg Lys Arg Lys Lys His					
	485	490				495
Ile Pro Pro Ala Pro Gln Ala Ser Ser	Pro Thr Phe Cys Lys Thr Glu					
	500	505				510
Leu Asn Met Ala Cys Asn Ser Thr Gln	Ser Asp Thr Cys Leu Gly Lys					
	515	520				525
Asp Asn Arg Leu Leu Glu His Asn Arg	Ser Val Leu Ser Gly Asp Asp					
	530	535				540
Ser Thr Gly Ser Glu Pro Pro Leu Ser	Pro Pro Glu Arg Leu Pro Ile					
	545	550				555
560						
Arg Arg Ser Ser Thr Arg Asp Lys Asn	Arg Arg Gly Glu Thr Cys Phe					
	565	570				575

Leu Leu Thr Thr Gly Asp Tyr Thr Cys Ala Ser Asp Gly Gly Ile Arg
 580 585 590
 Lys Gly Tyr Glu Lys Ser Arg Ser Leu Asn Asn Ile Ala Gly Leu Ala
 595 600 605
 Gly Asn Ala Leu Arg Leu Ser Pro Val Thr Ser Pro Tyr Asn Ser Pro
 610 615 620
 Cys Pro Leu Arg Arg Ser Arg Ser Pro Ile Pro Ser Ile Leu
 625 630 635

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 <211> 1677
 <212> DNA
 <213> Homo sapiens

<220>
 <221> CDS
 <222> (1)..(1677)

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 Met Gly Lys Ile Glu Asn Asn Glu Arg Val Ile Leu Asn Val Gly Gly
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 acc cgg cac gaa acc tac cgc agc acc ctc aag acc ctg cct gga aca 96
 Thr Arg His Glu Thr Tyr Arg Ser Thr Leu Lys Thr Leu Pro Gly Thr
 20 25 30
 cgc ctg gcc ctt ctt gcc tcc tcc gag ccc cca ggc gac tgc ttg acc 144
 Arg Leu Ala Leu Leu Ala Ser Ser Glu Pro Pro Gly Asp Cys Leu Thr
 35 40 45
 acg gcg ggc gac aag ctg cag ccg tcg ccg cct cca ctg tcg ccg ccg 192
 Thr Ala Gly Asp Lys Leu Gln Pro Ser Pro Pro Pro Leu Ser Pro Pro
 50 55 60
 ccg aga gcg ccc ccg ctg tcc ccc ggg cca ggc ggc tgc ttc gag ggc 240
 Pro Arg Ala Pro Pro Leu Ser Pro Gly Pro Gly Gly Cys Phe Glu Gly
 65 70 75 80
 ggc gcg ggc aac tgc agt tcc cgc ggc ggc agg gcc agc gac cat ccc 288
 Gly Ala Gly Asn Cys Ser Ser Arg Gly Gly Arg Ala Ser Asp His Pro
 85 90 95
 ggt ggc ggc cgc gag ttc ttc ttc gac cgg cac ccg ggc gtc ttc gcc 336
 Gly Gly Gly Arg Glu Phe Phe Phe Asp Arg His Pro Gly Val Phe Ala
 100 105 110
 tat gtg ctc aat tac tac cgc acc ggc aag ctg cac tgc ccc gca gac 384
 Tyr Val Leu Asn Tyr Tyr Arg Thr Gly Lys Leu His Cys Pro Ala Asp
 115 120 125
 gtg tgc ggg ccg ctc ttc gag gag gag ctg gcc ttc tgg ggc atc gac 432
 Val Cys Gly Pro Leu Phe Glu Glu Glu Leu Ala Phe Trp Gly Ile Asp
 130 135 140
 gag acc gac gtg gag ccc tgc tgc tgg atg acc tac ccg cag cac cgc 480
 Glu Thr Asp Val Glu Pro Cys Cys Trp Met Thr Tyr Arg Gln His Arg

145	150	155	160	
gac gcc gag gag ggc ctg gac atc ttc gag acc ccc gac ctc att ggc				528
Asp Ala Glu Glu Ala Leu Asp Ile Phe Glu Thr Pro Asp Leu Ile Gly				
	165	170	175	
ggc gac ccc ggc gac gac gag gac ctg ggc gcc aag agg ctg ggc atc				576
Gly Asp Pro Gly Asp Asp Glu Asp Leu Ala Ala Lys Arg Leu Gly Ile				
	180	185	190	
gag gac ggc ggc ggg ctc ggg ggc ccc gac ggc aaa tct ggc cgc tgg				624
Glu Asp Ala Ala Gly Leu Gly Gly Pro Asp Gly Lys Ser Gly Arg Trp				
	195	200	205	
agg agg ctg cag ccc cgc atg tgg gcc ctc ttc gaa gac ccc tac tcg				672
Arg Arg Leu Gln Pro Arg Met Trp Ala Leu Phe Glu Asp Pro Tyr Ser				
	210	215	220	
tcc aga gcc gcc agg ttt att gct ttt gct tct tta ttc ttc atc ctg				720
Ser Arg Ala Ala Arg Phe Ile Ala Phe Ala Ser Leu Phe Phe Ile Leu				
	225	230	235	240
gtt tca att aca act ttt tgc ctg gaa aca cat gaa gct ttc aat att				768
Val Ser Ile Thr Thr Phe Cys Leu Glu Thr His Glu Ala Phe Asn Ile				
	245	250	255	
gtt aaa aac aag aca gaa cca gtc atc aat ggc aca agt gtt gtt cta				816
Val Lys Asn Lys Thr Glu Pro Val Ile Asn Gly Thr Ser Val Val Leu				
	260	265	270	
cag tat gaa att gaa acg gat cct gcc ttg acg tat gta gaa gga gtg				864
Gln Tyr Glu Ile Glu Thr Asp Pro Ala Leu Thr Tyr Val Glu Gly Val				
	275	280	285	
tgt gtg gtg tgg ttt act ttt gaa ttt tta gtc cgt att gtt ttt tca				912
Cys Val Val Trp Phe Thr Phe Glu Phe Leu Val Arg Ile Val Phe Ser				
	290	295	300	
ccc aat aaa ctt gaa ttc atc aaa aat ctc ttg aat atc att gac ttt				960
Pro Asn Lys Leu Glu Phe Ile Lys Asn Leu Leu Asn Ile Ile Asp Phe				
	305	310	315	320
gtg gcc atc cta cct ttc tac tta gag gtg gga ctc agt ggg ctg tca				1008
Val Ala Ile Leu Pro Phe Tyr Leu Glu Val Gly Leu Ser Gly Leu Ser				
	325	330	335	
tcc aaa gct gct aaa gat gtg ctt ggc ttc ctc agg gtg gta agg ttt				1056
Ser Lys Ala Ala Lys Asp Val Leu Gly Phe Leu Arg Val Val Arg Phe				
	340	345	350	
gtg agg atc ctg aga att ttc aag ctc acc cgc cat ttt gta ggt ctg				1104
Val Arg Ile Leu Arg Ile Phe Lys Leu Thr Arg His Phe Val Gly Leu				
	355	360	365	
agg gtg ctt gga cat act ctt cga gct agt act aat gaa ttt ttg ctg				1152
Arg Val Leu Gly His Thr Leu Arg Ala Ser Thr Asn Glu Phe Leu Leu				
	370	375	380	
ctg ata att ttc ctg gct cta gga gtt ttg ata ttt gct acc atg atc				1200
Leu Ile Ile Phe Leu Ala Leu Gly Val Leu Ile Phe Ala Thr Met Ile				
	385	390	395	400
tac tat gcc gag aga gtg gga gct caa cct aac gac cct tca gct agt				1248
Tyr Tyr Ala Glu Arg Val Gly Ala Gln Pro Asn Asp Pro Ser Ala Ser				
	405	410	415	

gag cac aca cag ttc aaa aac att ccc att ggg ttc tgg tgg gct gta 1296
 Glu His Thr Gln Phe Lys Asn Ile Pro Ile Gly Phe Trp Trp Ala Val
 420 425 430
 gtg acc atg act acc ctg ggt tat ggg gat atg tac ccc caa aca tgg 1344
 Val Thr Met Thr Thr Leu Gly Tyr Gly Asp Met Tyr Pro Gln Thr Trp
 435 440 445
 tca ggc atg ctg gtg gga gcc ctg tgt gct ctg gct gga gtg ctg aca 1392
 Ser Gly Met Leu Val Gly Ala Leu Cys Ala Leu Ala Gly Val Leu Thr
 450 455 460
 ata gcc atg cca gtg cct gtc att gtc aat aat ttt gga atg tac tac 1440
 Ile Ala Met Pro Val Pro Val Ile Val Asn Asn Phe Gly Met Tyr Tyr
 465 470 475 480
 tcc ttg gca atg gca aag cag aaa ctt cca agg aaa aga aag aag cac 1488
 Ser Leu Ala Met Ala Lys Gln Lys Leu Pro Arg Lys Arg Lys Lys His
 485 490 495
 atc cct cct gct cct cag gca agc tca cct act ttt tgc aag aca gaa 1536
 Ile Pro Pro Ala Pro Gln Ala Ser Ser Pro Thr Phe Cys Lys Thr Glu
 500 505 510
 tta aat atg gcc tgc aat agt aca cag agt gac aca tgt ctg ggc aaa 1584
 Leu Asn Met Ala Cys Asn Ser Thr Gln Ser Asp Thr Cys Leu Gly Lys
 515 520 525
 gac aat cga ctt ctg gaa cat aac aga tca gat aac tgc aaa gag gtt 1632
 Asp Asn Arg Leu Leu Glu His Asn Arg Ser Asp Asn Cys Lys Glu Val
 530 535 540
 gtc att act ggt tac acg caa gcc gag gcc aga tct ctt act taa 1677
 Val Ile Thr Gly Tyr Thr Gln Ala Glu Ala Arg Ser Leu Thr
 545 550 555

<210> 6
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 <212> PRT
 <213> Homo sapiens

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 Arg Leu Ala Leu Leu Ala Ser Ser Glu Pro Pro Gly Asp Cys Leu Thr
 35 40 45
 Thr Ala Gly Asp Lys Leu Gln Pro Ser Pro Pro Pro Leu Ser Pro Pro
 50 55 60
 Pro Arg Ala Pro Pro Leu Ser Pro Gly Pro Gly Gly Cys Phe Glu Gly
 65 70 75 80
 Gly Ala Gly Asn Cys Ser Ser Arg Gly Gly Arg Ala Ser Asp His Pro
 85 90 95
 Gly Gly Gly Arg Glu Phe Phe Phe Asp Arg His Pro Gly Val Phe Ala
 100 105 110

Tyr Val Leu Asn Tyr Tyr Arg Thr Gly Lys Leu His Cys Pro Ala Asp
 115 120 125
 Val Cys Gly Pro Leu Phe Glu Glu Glu Leu Ala Phe Trp Gly Ile Asp
 130 135 140
 Glu Thr Asp Val Glu Pro Cys Cys Trp Met Thr Tyr Arg Gln His Arg
 145 150 155 160
 Asp Ala Glu Glu Ala Leu Asp Ile Phe Glu Thr Pro Asp Leu Ile Gly
 165 170 175
 Gly Asp Pro Gly Asp Asp Glu Asp Leu Ala Ala Lys Arg Leu Gly Ile
 180 185 190
 Glu Asp Ala Ala Gly Leu Gly Gly Pro Asp Gly Lys Ser Gly Arg Trp
 195 200 205
 Arg Arg Leu Gln Pro Arg Met Trp Ala Leu Phe Glu Asp Pro Tyr Ser
 210 215 220
 Ser Arg Ala Ala Arg Phe Ile Ala Phe Ala Ser Leu Phe Phe Ile Leu
 225 230 235 240
 Val Ser Ile Thr Thr Phe Cys Leu Glu Thr His Glu Ala Phe Asn Ile
 245 250 255
 Val Lys Asn Lys Thr Glu Pro Val Ile Asn Gly Thr Ser Val Val Leu
 260 265 270
 Gln Tyr Glu Ile Glu Thr Asp Pro Ala Leu Thr Tyr Val Glu Gly Val
 275 280 285
 Cys Val Val Trp Phe Thr Phe Glu Phe Leu Val Arg Ile Val Phe Ser
 290 295 300
 Pro Asn Lys Leu Glu Phe Ile Lys Asn Leu Leu Asn Ile Ile Asp Phe
 305 310 315 320
 Val Ala Ile Leu Pro Phe Tyr Leu Glu Val Gly Leu Ser Gly Leu Ser
 325 330 335
 Ser Lys Ala Ala Lys Asp Val Leu Gly Phe Leu Arg Val Val Arg Phe
 340 345 350
 Val Arg Ile Leu Arg Ile Phe Lys Leu Thr Arg His Phe Val Gly Leu
 355 360 365
 Arg Val Leu Gly His Thr Leu Arg Ala Ser Thr Asn Glu Phe Leu Leu
 370 375 380
 Leu Ile Ile Phe Leu Ala Leu Gly Val Leu Ile Phe Ala Thr Met Ile
 385 390 395 400
 Tyr Tyr Ala Glu Arg Val Gly Ala Gln Pro Asn Asp Pro Ser Ala Ser
 405 410 415
 Glu His Thr Gln Phe Lys Asn Ile Pro Ile Gly Phe Trp Trp Ala Val
 420 425 430
 Val Thr Met Thr Thr Leu Gly Tyr Gly Asp Met Tyr Pro Gln Thr Trp
 435 440 445
 Ser Gly Met Leu Val Gly Ala Leu Cys Ala Leu Ala Gly Val Leu Thr
 450 455 460
 Ile Ala Met Pro Val Pro Val Ile Val Asn Asn Phe Gly Met Tyr Tyr
 465 470 475 480
 Ser Leu Ala Met Ala Lys Gln Lys Leu Pro Arg Lys Arg Lys Lys His
 485 490 495
 Ile Pro Pro Ala Pro Gln Ala Ser Ser Pro Thr Phe Cys Lys Thr Glu

	500		505		510
Leu	Asn Met	Ala Cys	Asn Ser	Thr Gln	Ser Asp
	515		520		525
Asp	Asn Arg	Leu Leu	Glu His	Asn Arg	Ser Asp
	530		535		540
Val	Ile Thr	Gly Tyr	Thr Gln	Ala Glu	Ala Arg
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<210> 7
 <211> 1890
 <212> DNA
 <213> Homo sapiens

<220>
 <221> CDS
 <222> (1)..(1890)

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acc cgg cac gaa acc tac cgc agc acc ctc aag acc ctg cct gga aca	96
Thr Arg His Glu Thr Tyr Arg Ser Thr Leu Lys Thr Leu Pro Gly Thr	
20 25 30	
cgc ctg gcc ctt ctt gcc tcc tcc gag ccc cca ggc gac tgc ttg acc	144
Arg Leu Ala Leu Leu Ala Ser Ser Glu Pro Pro Gly Asp Cys Leu Thr	
35 40 45	
acg gcg ggc gac aag ctg cag ccg tcg ccg cct cca ctg tcg ccg ccg	192
Thr Ala Gly Asp Lys Leu Gln Pro Ser Pro Pro Pro Leu Ser Pro Pro	
50 55 60	
ccg aga gcg ccc ccg ctg tcc ccc ggg cca ggc ggc tgc ttc gag ggc	240
Pro Arg Ala Pro Pro Leu Ser Pro Gly Pro Gly Gly Cys Phe Glu Gly	
65 70 75 80	
ggc gcg ggc aac tgc agt tcc cgc ggc ggc agg gcc agc gac cat ccc	288
Gly Ala Gly Asn Cys Ser Ser Arg Gly Gly Arg Ala Ser Asp His Pro	
85 90 95	
ggt ggc ggc cgc gag ttc ttc ttc gac cgg cac ccg ggc gtc ttc gcc	336
Gly Gly Gly Arg Glu Phe Phe Phe Asp Arg His Pro Gly Val Phe Ala	
100 105 110	
tat gtg ctc aat tac tac cgc acc ggc aag ctg cac tgc ccc gca gac	384
Tyr Val Leu Asn Tyr Tyr Arg Thr Gly Lys Leu His Cys Pro Ala Asp	
115 120 125	
gtg tgc ggg ccg ctc ttc gag gag gag ctg gcc ttc tgg ggc atc gac	432
Val Cys Gly Pro Leu Phe Glu Glu Glu Leu Ala Phe Trp Gly Ile Asp	
130 135 140	
gag acc gac gtg gag ccc tgc tgc tgg atg acc tac cgg cag cac cgc	480
Glu Thr Asp Val Glu Pro Cys Cys Trp Met Thr Tyr Arg Gln His Arg	
145 150 155 160	

gac gcc gag gag gcg ctg gac atc ttc gag acc ccc gac ctc att ggc	528
Asp Ala Glu Glu Ala Leu Asp Ile Phe Glu Thr Pro Asp Leu Ile Gly	
165 170 175	
ggc gac ccc ggc gac gac gag gac ctg gcg gcc aag agg ctg ggc atc	576
Gly Asp Pro Gly Asp Asp Glu Asp Leu Ala Ala Lys Arg Leu Gly Ile	
180 185 190	
gag gac gcg gcg ggg ctc ggg ggc ccc gac ggc aaa tct ggc cgc tgg	624
Glu Asp Ala Ala Gly Leu Gly Gly Pro Asp Gly Lys Ser Gly Arg Trp	
195 200 205	
agg agg ctg cag ccc cgc atg tgg gcc ctc ttc gaa gac ccc tac tcg	672
Arg Arg Leu Gln Pro Arg Met Trp Ala Leu Phe Glu Asp Pro Tyr Ser	
210 215 220	
tcc aga gcc gcc agg ttt att gct ttt gct tct tta ttc ttc atc ctg	720
Ser Arg Ala Ala Arg Phe Ile Ala Phe Ala Ser Leu Phe Phe Ile Leu	
225 230 235 240	
gtt tca att aca act ttt tgc ctg gaa aca cat gaa gct ttc aat att	768
Val Ser Ile Thr Thr Phe Cys Leu Glu Thr His Glu Ala Phe Asn Ile	
245 250 255	
gtt aaa aac aag aca gaa cca gtc atc aat ggc aca agt gtt gtt cta	816
Val Lys Asn Lys Thr Glu Pro Val Ile Asn Gly Thr Ser Val Val Leu	
260 265 270	
cag tat gaa att gaa acg gat cct gcc ttg acg tat gta gaa gga gtg	864
Gln Tyr Glu Ile Glu Thr Asp Pro Ala Leu Thr Tyr Val Glu Gly Val	
275 280 285	
tgt gtg gtg tgg ttt act ttt gaa ttt tta gtc cgt att gtt ttt tca	912
Cys Val Val Trp Phe Thr Phe Glu Phe Leu Val Arg Ile Val Phe Ser	
290 295 300	
ccc aat aaa ctt gaa ttc atc aaa aat ctc ttg aat atc att gac ttt	960
Pro Asn Lys Leu Glu Phe Ile Lys Asn Leu Leu Asn Ile Ile Asp Phe	
305 310 315 320	
gtg gcc atc cta cct ttc tac tta gag gtg gga ctc agt ggg ctg tca	1008
Val Ala Ile Leu Pro Phe Tyr Leu Glu Val Gly Leu Ser Gly Leu Ser	
325 330 335	
tcc aaa gct gct aaa gat gtg ctt ggc ttc ctc agg gtg gta agg ttt	1056
Ser Lys Ala Ala Lys Asp Val Leu Gly Phe Leu Arg Val Val Arg Phe	
340 345 350	
gtg agg atc ctg aga att ttc aag ctc acc cgc cat ttt gta ggt ctg	1104
Val Arg Ile Leu Arg Ile Phe Lys Leu Thr Arg His Phe Val Gly Leu	
355 360 365	
agg gtg ctt gga cat act ctt cga gct agt act aat gaa ttt ttg ctg	1152
Arg Val Leu Gly His Thr Leu Arg Ala Ser Thr Asn Glu Phe Leu Leu	
370 375 380	
ctg ata att ttc ctg gct cta gga gtt ttg ata ttt gct acc atg atc	1200
Leu Ile Ile Phe Leu Ala Leu Gly Val Leu Ile Phe Ala Thr Met Ile	
385 390 395 400	
tac tat gcc gag aga gtg gga gct caa cct aac gac cct tca gct agt	1248
Tyr Tyr Ala Glu Arg Val Gly Ala Gln Pro Asn Asp Pro Ser Ala Ser	
405 410 415	
gag cac aca cag ttc aaa aac att ccc att ggg ttc tgg tgg gct gta	1296

Glu His Thr Gln Phe Lys Asn Ile Pro Ile Gly Phe Trp Trp Ala Val	
420 425 430	
gtg acc atg act acc ctg ggt tat ggg gat atg tac ccc caa aca tgg	1344
Val Thr Met Thr Thr Leu Gly Tyr Gly Asp Met Tyr Pro Gln Thr Trp	
435 440 445	
tca ggc atg ctg gtg gga gcc ctg tgt gct ctg gct gga gtg ctg aca	1392
Ser Gly Met Leu Val Gly Ala Leu Cys Ala Leu Ala Gly Val Leu Thr	
450 455 460	
ata gcc atg cca gtg cct gtc att gtc aat aat ttt gga atg tac tac	1440
Ile Ala Met Pro Val Pro Val Ile Val Asn Asn Phe Gly Met Tyr Tyr	
465 470 475 480	
tcc ttg gca atg gca aag cag aaa ctt cca agg aaa aga aag aag cac	1488
Ser Leu Ala Met Ala Lys Gln Lys Leu Pro Arg Lys Arg Lys Lys His	
485 490 495	
atc cct cct got cct cag gca agc tca cct act ttt tgc aag aca gaa	1536
Ile Pro Pro Ala Pro Gln Ala Ser Ser Pro Thr Phe Cys Lys Thr Glu	
500 505 510	
tta aat atg gcc tgc aat agt aca cag agt gac aca tgt ctg ggc aaa	1584
Leu Asn Met Ala Cys Asn Ser Thr Gln Ser Asp Thr Cys Leu Gly Lys	
515 520 525	
gac aat cga ctt ctg gaa cat aac aga tca gtg tta tca ggt gac gac	1632
Asp Asn Arg Leu Leu Glu His Asn Arg Ser Val Leu Ser Gly Asp Asp	
530 535 540	
agt aca gga agt gag ccg cca cta tca ccc cca gaa agg ctc ccc atc	1680
Ser Thr Gly Ser Glu Pro Pro Leu Ser Pro Pro Glu Arg Leu Pro Ile	
545 550 555 560	
aga cgc tct agt acc aga gac aaa aac aga aga ggg gaa aca tgt ttc	1728
Arg Arg Ser Ser Thr Arg Asp Lys Asn Arg Arg Gly Glu Thr Cys Phe	
565 570 575	
cta ctg acg aca ggt gat tac acg tgt gct tct gat gga ggg atc agg	1776
Leu Leu Thr Thr Gly Asp Tyr Thr Cys Ala Ser Asp Gly Gly Ile Arg	
580 585 590	
aaa gtg ttg tac aga att tat cat gga tta ttg act gct gag aaa ggg	1824
Lys Val Leu Tyr Arg Ile Tyr His Gly Leu Leu Thr Ala Glu Lys Gly	
595 600 605	
aca gtg gaa ttt agc cat acc aag gac tat act gga aac aga ctt ctg	1872
Thr Val Glu Phe Ser His Thr Lys Asp Tyr Thr Gly Asn Arg Leu Leu	
610 615 620	
ctg ctg aat gtg ccc tga	1890
Leu Leu Asn Val Pro	
625	

<210> 8
 <211> 629
 <212> PRT
 <213> Homo sapiens

<400> 8

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Arg	Leu	Ala	Leu	Leu	Ala	Ser	Ser	Glu	Pro	Pro	Gly	Asp	Cys	Leu	Thr	35	40	45	
Thr	Ala	Gly	Asp	Lys	Leu	Gln	Pro	Ser	Pro	Pro	Pro	Leu	Ser	Pro	Pro	50	55	60	
Pro	Arg	Ala	Pro	Pro	Leu	Ser	Pro	Gly	Pro	Gly	Gly	Cys	Phe	Glu	Gly	65	70	75	80
Gly	Ala	Gly	Asn	Cys	Ser	Ser	Arg	Gly	Gly	Arg	Ala	Ser	Asp	His	Pro	85	90	95	
Gly	Gly	Gly	Arg	Glu	Phe	Phe	Phe	Asp	Arg	His	Pro	Gly	Val	Phe	Ala	100	105	110	
Tyr	Val	Leu	Asn	Tyr	Tyr	Arg	Thr	Gly	Lys	Leu	His	Cys	Pro	Ala	Asp	115	120	125	
Val	Cys	Gly	Pro	Leu	Phe	Glu	Glu	Glu	Leu	Ala	Phe	Trp	Gly	Ile	Asp	130	135	140	
Glu	Thr	Asp	Val	Glu	Pro	Cys	Cys	Trp	Met	Thr	Tyr	Arg	Gln	His	Arg	145	150	155	160
Asp	Ala	Glu	Glu	Ala	Leu	Asp	Ile	Phe	Glu	Thr	Pro	Asp	Leu	Ile	Gly	165	170	175	
Gly	Asp	Pro	Gly	Asp	Asp	Glu	Asp	Leu	Ala	Ala	Lys	Arg	Leu	Gly	Ile	180	185	190	
Glu	Asp	Ala	Ala	Gly	Leu	Gly	Gly	Pro	Asp	Gly	Lys	Ser	Gly	Arg	Trp	195	200	205	
Arg	Arg	Leu	Gln	Pro	Arg	Met	Trp	Ala	Leu	Phe	Glu	Asp	Pro	Tyr	Ser	210	215	220	
Ser	Arg	Ala	Ala	Arg	Phe	Ile	Ala	Phe	Ala	Ser	Leu	Phe	Phe	Ile	Leu	225	230	235	240
Val	Ser	Ile	Thr	Thr	Phe	Cys	Leu	Glu	Thr	His	Glu	Ala	Phe	Asn	Ile	245	250	255	
Val	Lys	Asn	Lys	Thr	Glu	Pro	Val	Ile	Asn	Gly	Thr	Ser	Val	Val	Leu	260	265	270	
Gln	Tyr	Glu	Ile	Glu	Thr	Asp	Pro	Ala	Leu	Thr	Tyr	Val	Glu	Gly	Val	275	280	285	
Cys	Val	Val	Trp	Phe	Thr	Phe	Glu	Phe	Leu	Val	Arg	Ile	Val	Phe	Ser	290	295	300	
Pro	Asn	Lys	Leu	Glu	Phe	Ile	Lys	Asn	Leu	Leu	Asn	Ile	Ile	Asp	Phe	305	310	315	320
Val	Ala	Ile	Leu	Pro	Phe	Tyr	Leu	Glu	Val	Gly	Leu	Ser	Gly	Leu	Ser	325	330	335	
Ser	Lys	Ala	Ala	Lys	Asp	Val	Leu	Gly	Phe	Leu	Arg	Val	Val	Arg	Phe	340	345	350	
Val	Arg	Ile	Leu	Arg	Ile	Phe	Lys	Leu	Thr	Arg	His	Phe	Val	Gly	Leu	355	360	365	
Arg	Val	Leu	Gly	His	Thr	Leu	Arg	Ala	Ser	Thr	Asn	Glu	Phe	Leu	Leu	370	375	380	
Leu	Ile	Ile	Phe	Leu	Ala	Leu	Gly	Val	Leu	Ile	Phe	Ala	Thr	Met	Ile				

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385          390          395          400
Tyr Tyr Ala Glu Arg Val Gly Ala Gln Pro Asn Asp Pro Ser Ala Ser
          405          410          415
Glu His Thr Gln Phe Lys Asn Ile Pro Ile Gly Phe Trp Trp Ala Val
          420          425          430
Val Thr Met Thr Thr Leu Gly Tyr Gly Asp Met Tyr Pro Gln Thr Trp
          435          440          445
Ser Gly Met Leu Val Gly Ala Leu Cys Ala Leu Ala Gly Val Leu Thr
          450          455          460
Ile Ala Met Pro Val Pro Val Ile Val Asn Asn Phe Gly Met Tyr Tyr
465          470          475          480
Ser Leu Ala Met Ala Lys Gln Lys Leu Pro Arg Lys Arg Lys Lys His
          485          490          495
Ile Pro Pro Ala Pro Gln Ala Ser Ser Pro Thr Phe Cys Lys Thr Glu
          500          505          510
Leu Asn Met Ala Cys Asn Ser Thr Gln Ser Asp Thr Cys Leu Gly Lys
          515          520          525
Asp Asn Arg Leu Leu Glu His Asn Arg Ser Val Leu Ser Gly Asp Asp
          530          535          540
Ser Thr Gly Ser Glu Pro Pro Leu Ser Pro Pro Glu Arg Leu Pro Ile
545          550          555          560
Arg Arg Ser Ser Thr Arg Asp Lys Asn Arg Arg Gly Glu Thr Cys Phe
          565          570          575
Leu Leu Thr Thr Gly Asp Tyr Thr Cys Ala Ser Asp Gly Gly Ile Arg
          580          585          590
Lys Val Leu Tyr Arg Ile Tyr His Gly Leu Leu Thr Ala Glu Lys Gly
          595          600          605
Thr Val Glu Phe Ser His Thr Lys Asp Tyr Thr Gly Asn Arg Leu Leu
          610          615          620
Leu Leu Asn Val Pro
625

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<210> 9
<211> 1920
<212> DNA
<213> Mus musculus

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<220>
<221> CDS
<222> (1)..(1920)

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1          5          10          15
acc agg cac gaa acc tac cgc agc acc ctc aag acc ctg oct gga act      96
Thr Arg His Glu Thr Tyr Arg Ser Thr Leu Lys Thr Leu Pro Gly Thr
          20          25          30

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cg	ct	gc	ctt	ctt	gcc	tcc	tct	gaa	cct	cag	ggc	gac	tgc	ctg	act	144
Arg	Leu	Ala	Leu	Leu	Ala	Ser	Ser	Glu	Pro	Gln	Gly	Asp	Cys	Leu	Thr	
		35						40					45			
gc	gc	gg	gac	aag	ctg	caa	ccg	ctg	ccc	cct	ccg	ctg	tct	ccg	ccg	192
Ala	Ala	Gly	Asp	Lys	Leu	Gln	Pro	Leu	Pro	Pro	Pro	Leu	Ser	Pro	Pro	
		50				55					60					
cca	cga	ccg	cct	ccc	ttg	tcc	cct	gtc	ccc	agc	ggc	tgc	ttc	gag	ggc	240
Pro	Arg	Pro	Pro	Pro	Leu	Ser	Pro	Val	Pro	Ser	Gly	Cys	Phe	Glu	Gly	
65					70				75					80		
ggc	gca	ggc	aac	tgc	agt	tcg	cac	ggt	ggc	aac	ggc	ggc	aac	ggc	ggc	288
Gly	Ala	Gly	Asn	Cys	Ser	Ser	His	Gly	Gly	Asn	Gly	Gly	Asn	Gly	Gly	
			85					90					95			
agc	gac	cac	cct	ggg	gga	ggc	cgc	gaa	ttc	ttc	ttc	gat	cgc	cac	cca	336
Ser	Asp	His	Pro	Gly	Gly	Gly	Arg	Glu	Phe	Phe	Phe	Asp	Arg	His	Pro	
			100					105					110			
gga	gta	ttc	gcc	tat	gtg	ctc	aat	tac	tac	cgc	acg	ggc	aag	ctg	cac	384
Gly	Val	Phe	Ala	Tyr	Val	Leu	Asn	Tyr	Tyr	Arg	Thr	Gly	Lys	Leu	His	
		115				120						125				
tgc	ccc	gcc	gac	gtg	tgc	ggg	ccg	ctc	ttc	gag	gaa	gag	ctg	gct	ttc	432
Cys	Pro	Ala	Asp	Val	Cys	Gly	Pro	Leu	Phe	Glu	Glu	Glu	Leu	Ala	Phe	
		130				135						140				
tgg	ggc	atc	gat	gag	acc	gac	gtg	gag	ccc	tgc	tgc	tgg	atg	acc	tac	480
Trp	Gly	Ile	Asp	Glu	Thr	Asp	Val	Glu	Pro	Cys	Cys	Trp	Met	Thr	Tyr	
145					150				155					160		
agg	cag	cac	cgg	gac	gcg	gag	gag	gcc	ctg	gac	atc	ttt	gag	aca	ccc	528
Arg	Gln	His	Arg	Asp	Ala	Glu	Glu	Ala	Leu	Asp	Ile	Phe	Glu	Thr	Pro	
			165					170					175			
gac	ctc	atc	ggg	ggc	gac	cct	ggt	gat	gat	gag	gac	cta	gcg	gcc	aag	576
Asp	Leu	Ile	Gly	Gly	Asp	Pro	Gly	Asp	Asp	Glu	Asp	Leu	Ala	Ala	Lys	
			180					185				190				
aga	ttg	ggc	att	gag	gat	gct	gcg	ggg	ctg	gga	gga	ccc	gat	ggc	aag	624
Arg	Leu	Gly	Ile	Glu	Asp	Ala	Ala	Gly	Leu	Gly	Gly	Pro	Asp	Gly	Lys	
		195				200						205				
tca	ggc	cgc	tgg	agg	aag	ctg	cag	cct	cgc	atg	tgg	gct	ctt	ttt	gag	672
Ser	Gly	Arg	Trp	Arg	Lys	Leu	Gln	Pro	Arg	Met	Trp	Ala	Leu	Phe	Glu	
		210				215					220					
gac	ccc	tac	tca	tct	aga	gcc	gct	agg	ttt	att	gct	ttt	gct	tct	ttg	720
Asp	Pro	Tyr	Ser	Ser	Arg	Ala	Ala	Arg	Phe	Ile	Ala	Phe	Ala	Ser	Leu	
225					230				235				240			
ttc	ttc	att	ttg	gtt	tcc	atc	aca	acc	ttt	tgc	ctg	gag	aca	cat	gaa	768
Phe	Phe	Ile	Leu	Val	Ser	Ile	Thr	Thr	Phe	Cys	Leu	Glu	Thr	His	Glu	
			245					250				255				
gct	ttc	aat	att	gtt	aaa	aac	aag	acg	gag	ccc	gtc	atc	aat	ggc	acc	816
Ala	Phe	Asn	Ile	Val	Lys	Asn	Lys	Thr	Glu	Pro	Val	Ile	Asn	Gly	Thr	
		260				265					270					
agc	ccg	gtc	ctc	cag	tac	gaa	atc	gaa	acg	gat	ccc	gcc	ctg	acg	tac	864
Ser	Pro	Val	Leu	Gln	Tyr	Glu	Ile	Glu	Thr	Asp	Pro	Ala	Leu	Thr	Tyr	
		275				280					285					
gtg	gaa	gga	gta	tgt	gtg	gtg	tgg	ttt	acg	ttt	gaa	ttt	tta	gtc	cga	912

Val Glu Gly Val Cys Val Val Trp Phe Thr Phe Glu Phe Leu Val Arg	
290 295 300	
att gtt ttc tca ccc aat aaa ctt gaa ttc atc aaa aat ctc ttg aac	960
Ile Val Phe Ser Pro Asn Lys Leu Glu Phe Ile Lys Asn Leu Leu Asn	
305 310 315 320	
atc att gac ttt gtg gcc atc ctc ccc ttc tac cta gag gtg gga ctc	1008
Ile Ile Asp Phe Val Ala Ile Leu Pro Phe Tyr Leu Glu Val Gly Leu	
325 330 335	
agc ggg ctg tcc tcc aaa gcg gcc aaa gat gtg ctc ggc ttt ctc agg	1056
Ser Gly Leu Ser Ser Lys Ala Ala Lys Asp Val Leu Gly Phe Leu Arg	
340 345 350	
gtg gtt agg ttt gtg agg atc ctg aga atc ttc aag ctc acc cgc cat	1104
Val Val Arg Phe Val Arg Ile Leu Arg Ile Phe Lys Leu Thr Arg His	
355 360 365	
ttc gta ggt ctg agg gtg ctc gga cat act ctt cgg gcg agc acc aac	1152
Phe Val Gly Leu Arg Val Leu Gly His Thr Leu Arg Ala Ser Thr Asn	
370 375 380	
gaa ttt ttg ttg ctg atc atc ttc ctg gcg ctg gga gtt ttg ata ttc	1200
Glu Phe Leu Leu Leu Ile Ile Phe Leu Ala Leu Gly Val Leu Ile Phe	
385 390 395 400	
gct acg atg atc tac tac gct gag aga gta ggg gct cag ccc aat gac	1248
Ala Thr Met Ile Tyr Tyr Ala Glu Arg Val Gly Ala Gln Pro Asn Asp	
405 410 415	
cct tca gct agt gag cac acg cag ttc aaa aac atc ccc att ggt ttc	1296
Pro Ser Ala Ser Glu His Thr Gln Phe Lys Asn Ile Pro Ile Gly Phe	
420 425 430	
tgg tgg gcc gta gtg acc atg act acc tta ggt tac ggg gat atg tac	1344
Trp Trp Ala Val Val Thr Met Thr Thr Leu Gly Tyr Gly Asp Met Tyr	
435 440 445	
ccc caa aca tgg tca ggg atg ttg gtg ggg gcc ttg tgt gcc ctg gcc	1392
Pro Gln Thr Trp Ser Gly Met Leu Val Gly Ala Leu Cys Ala Leu Ala	
450 455 460	
gga gtg ctg aca ata gcc atg cct gtg cct gtc att gtc aac aat ttt	1440
Gly Val Leu Thr Ile Ala Met Pro Val Pro Val Ile Val Asn Asn Phe	
465 470 475 480	
gga atg tac tac tcc ttg gca atg gcg aag cag aaa ctt cca aga aag	1488
Gly Met Tyr Tyr Ser Leu Ala Met Ala Lys Gln Lys Leu Pro Arg Lys	
485 490 495	
aga aag aag cat att cct cct gcc cct ctg gca agc tcg cct aca ttt	1536
Arg Lys Lys His Ile Pro Pro Ala Pro Leu Ala Ser Ser Pro Thr Phe	
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tgc aag aca gaa ttg aac atg gct tgc aac agt acc cag agt gac aca	1584
Cys Lys Thr Glu Leu Asn Met Ala Cys Asn Ser Thr Gln Ser Asp Thr	
515 520 525	
tgt ctg ggc aaa gaa aac cgg ctt ctg gaa cat aac aga tca gtg tta	1632
Cys Leu Gly Lys Glu Asn Arg Leu Leu Glu His Asn Arg Ser Val Leu	
530 535 540	
tca ggt gac gac agt aca gga agt gag ccg cca tta tca cct cca gaa	1680
Ser Gly Asp Asp Ser Thr Gly Ser Glu Pro Pro Leu Ser Pro Pro Glu	

545	550	555	560	
agg ctc cct atc aga cgc tct agt acc aga gac aaa aac aga aga ggg				1728
Arg Leu Pro Ile Arg Arg Ser Ser Thr Arg Asp Lys Asn Arg Arg Gly				
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gaa acg tgt ttc ctg ttg acg aca ggt gat tac acg tgc gct tct gat				1776
Glu Thr Cys Phe Leu Leu Thr Thr Gly Asp Tyr Thr Cys Ala Ser Asp				
	580	585	590	
gga gga atc agg aaa gca agc aca cta gag ccc atg gag agt act gca				1824
Gly Gly Ile Arg Lys Ala Ser Thr Leu Glu Pro Met Glu Ser Thr Ala				
	595	600	605	
cag act aaa gga gac aca aga cca gaa gct cat tgg aat tgt gcg cac				1872
Gln Thr Lys Gly Asp Thr Arg Pro Glu Ala His Trp Asn Cys Ala His				
	610	615	620	
tta ctc aat ttt ggg tgt cct aca gga agt tca ttt ccc acc ctc taa				1920
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625	630	635		

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 <212> PRT
 <213> Mus musculus

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

195	200	205
Ser Gly Arg Trp Arg Lys Leu Gln Pro Arg Met Trp Ala Leu Phe Glu		
210	215	220
Asp Pro Tyr Ser Ser Arg Ala Ala Arg Phe Ile Ala Phe Ala Ser Leu		
225	230	235
Phe Phe Ile Leu Val Ser Ile Thr Thr Phe Cys Leu Glu Thr His Glu		
245	250	255
Ala Phe Asn Ile Val Lys Asn Lys Thr Glu Pro Val Ile Asn Gly Thr		
260	265	270
Ser Pro Val Leu Gln Tyr Glu Ile Glu Thr Asp Pro Ala Leu Thr Tyr		
275	280	285
Val Glu Gly Val Cys Val Val Trp Phe Thr Phe Glu Phe Leu Val Arg		
290	295	300
Ile Val Phe Ser Pro Asn Lys Leu Glu Phe Ile Lys Asn Leu Leu Asn		
305	310	315
Ile Ile Asp Phe Val Ala Ile Leu Pro Phe Tyr Leu Glu Val Gly Leu		
325	330	335
Ser Gly Leu Ser Ser Lys Ala Ala Lys Asp Val Leu Gly Phe Leu Arg		
340	345	350
Val Val Arg Phe Val Arg Ile Leu Arg Ile Phe Lys Leu Thr Arg His		
355	360	365
Phe Val Gly Leu Arg Val Leu Gly His Thr Leu Arg Ala Ser Thr Asn		
370	375	380
Glu Phe Leu Leu Leu Ile Ile Phe Leu Ala Leu Gly Val Leu Ile Phe		
385	390	395
Ala Thr Met Ile Tyr Tyr Ala Glu Arg Val Gly Ala Gln Pro Asn Asp		
405	410	415
Pro Ser Ala Ser Glu His Thr Gln Phe Lys Asn Ile Pro Ile Gly Phe		
420	425	430
Trp Trp Ala Val Val Thr Met Thr Thr Leu Gly Tyr Gly Asp Met Tyr		
435	440	445
Pro Gln Thr Trp Ser Gly Met Leu Val Gly Ala Leu Cys Ala Leu Ala		
450	455	460
Gly Val Leu Thr Ile Ala Met Pro Val Pro Val Ile Val Asn Asn Phe		
465	470	475
Gly Met Tyr Tyr Ser Leu Ala Met Ala Lys Gln Lys Leu Pro Arg Lys		
485	490	495
Arg Lys Lys His Ile Pro Pro Ala Pro Leu Ala Ser Ser Pro Thr Phe		
500	505	510
Cys Lys Thr Glu Leu Asn Met Ala Cys Asn Ser Thr Gln Ser Asp Thr		
515	520	525
Cys Leu Gly Lys Glu Asn Arg Leu Leu Glu His Asn Arg Ser Val Leu		
530	535	540
Ser Gly Asp Asp Ser Thr Gly Ser Glu Pro Pro Leu Ser Pro Pro Glu		
545	550	555
Arg Leu Pro Ile Arg Arg Ser Ser Thr Arg Asp Lys Asn Arg Arg Gly		
565	570	575
Glu Thr Cys Phe Leu Leu Thr Thr Gly Asp Tyr Thr Cys Ala Ser Asp		
580	585	590

Gly Gly Ile Arg Lys Ala Ser Thr Leu Glu Pro Met Glu Ser Thr Ala
 595 600 605
 Gln Thr Lys Gly Asp Thr Arg Pro Glu Ala His Trp Asn Cys Ala His
 610 615 620
 Leu Leu Asn Phe Gly Cys Pro Thr Gly Ser Ser Phe Pro Thr Leu
 625 630 635

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 <212> DNA
 <213> Rattus norvegicus

<220>
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 <222> (1)..(1842)

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 acc agg cac gaa acc tac cgc agc act ctc aag acc ctt cct gga act 96
 Thr Arg His Glu Thr Tyr Arg Ser Thr Leu Lys Thr Leu Pro Gly Thr
 20 25 30
 cgc ctg gcc ctt ctc gcc tcc tct gaa cct cag ggc gac tgc ctg act 144
 Arg Leu Ala Leu Leu Ala Ser Ser Glu Pro Gln Gly Asp Cys Leu Thr
 35 40 45
 gct gcg ggt gac aag ctg cag ccg ctg ccc cct ccg ctg tct cca ccg 192
 Ala Ala Gly Asp Lys Leu Gln Pro Leu Pro Pro Pro Leu Ser Pro Pro
 50 55 60
 ccg cga ccg cct ccc ttg tcc cct gtc ccc agc ggc tgc ttc gag ggc 240
 Pro Arg Pro Pro Pro Leu Ser Pro Val Pro Ser Gly Cys Phe Glu Gly
 65 70 75 80
 ggc gca ggc aac tgc agt tcg cac ggt ggc aat ggc agc gac cac cct 288
 Gly Ala Gly Asn Cys Ser Ser His Gly Gly Asn Gly Ser Asp His Pro
 85 90 95
 ggg gga ggc cgc gaa ttc ttc ttc gat cgc cac cca gga gtc ttc gcc 336
 Gly Gly Gly Arg Glu Phe Phe Phe Asp Arg His Pro Gly Val Phe Ala
 100 105 110
 tat gtg ctc aac tac tac cgc acg ggc aag ctg cac tgc ccc gcc gac 384
 Tyr Val Leu Asn Tyr Tyr Arg Thr Gly Lys Leu His Cys Pro Ala Asp
 115 120 125
 gtg tgt gga ccg ctc ttc gag gaa gag ctg gca ttc tgg ggc atc gat 432
 Val Cys Gly Pro Leu Phe Glu Glu Glu Leu Ala Phe Trp Gly Ile Asp
 130 135 140
 gag acc gac gtg gag ccc tgc tgc tgg atg acc tac agg cag cac ccg 480
 Glu Thr Asp Val Glu Pro Cys Cys Trp Met Thr Tyr Arg Gln His Arg
 145 150 155 160
 gac gcg gag gag gcc ctg gat atc ttc gag aca ccc gac ctc atc gga 528

Asp Ala Glu Glu Ala Leu Asp Ile Phe Glu Thr Pro Asp Leu Ile Gly	
165 170 175	
ggc gac cct ggt gat gat gag gac cta ggg ggc aag aga ctg ggc att	576
Gly Asp Pro Gly Asp Asp Glu Asp Leu Gly Gly Lys Arg Leu Gly Ile	
180 185 190	
gag gat gct gcg ggg ctg gga gga ccc gat ggc aag tct ggc cgc tgg	624
Glu Asp Ala Ala Gly Leu Gly Gly Pro Asp Gly Lys Ser Gly Arg Trp	
195 200 205	
agg aag ctg cag cct cgc atg tgg gct ctc ttt gag gac ccc tat tca	672
Arg Lys Leu Gln Pro Arg Met Trp Ala Leu Phe Glu Asp Pro Tyr Ser	
210 215 220	
tcc aga gcc gct agg ttt att gct ttt gct tct ctg ttc ttc att ttg	720
Ser Arg Ala Ala Arg Phe Ile Ala Phe Ala Ser Leu Phe Phe Ile Leu	
225 230 235 240	
gtt tcc atc aca acc ttt tgc ctg gag aca cac gaa gct ttc aat att	768
Val Ser Ile Thr Thr Phe Cys Leu Glu Thr His Glu Ala Phe Asn Ile	
245 250 255	
gtt aaa aac aag aca gag cca gtc atc aac ggc acc agc gct gtt ctc	816
Val Lys Asn Lys Thr Glu Pro Val Ile Asn Gly Thr Ser Ala Val Leu	
260 265 270	
cag tat gaa atc gaa acg gat cct gcc ttg aca tat gtg gaa gga gtg	864
Gln Tyr Glu Ile Glu Thr Asp Pro Ala Leu Thr Tyr Val Glu Gly Val	
275 280 285	
tgt gtg gtg tgg ttt act ttt gaa ttt tta gtc cgt att gtt ttc tcg	912
Cys Val Val Trp Phe Thr Phe Glu Phe Leu Val Arg Ile Val Phe Ser	
290 295 300	
ccc aat aaa ctt gag ttc atc aaa aat cta ttg aac atc att gac ttt	960
Pro Asn Lys Leu Glu Phe Ile Lys Asn Leu Leu Asn Ile Ile Asp Phe	
305 310 315 320	
gtg gcc atc ctc ccc ttc tac tta gag gtg gga ctc agc ggg ctg tct	1008
Val Ala Ile Leu Pro Phe Tyr Leu Glu Val Gly Leu Ser Gly Leu Ser	
325 330 335	
tcc aaa gcg gct aaa gat gtg ctc ggc ttt ctc agg gtg gtt agg ttt	1056
Ser Lys Ala Ala Lys Asp Val Leu Gly Phe Leu Arg Val Val Arg Phe	
340 345 350	
gtg agg atc ctg aga atc ttc aag ctt acc cgc cat ttc gta ggt ctg	1104
Val Arg Ile Leu Arg Ile Phe Lys Leu Thr Arg His Phe Val Gly Leu	
355 360 365	
aga gtg ctc gga cac act ctt cgt gcg agc acc aat gaa ttt ttg ttg	1152
Arg Val Leu Gly His Thr Leu Arg Ala Ser Thr Asn Glu Phe Leu Leu	
370 375 380	
ctg atc atc ttt ctg gct ctg gga gtt ttg ata ttc gct acg atg atc	1200
Leu Ile Ile Phe Leu Ala Leu Gly Val Leu Ile Phe Ala Thr Met Ile	
385 390 395 400	
tac tac gct gag cga gta ggg gct caa cct aat gat ccc tca gcg agt	1248
Tyr Tyr Ala Glu Arg Val Gly Ala Gln Pro Asn Asp Pro Ser Ala Ser	
405 410 415	
gag cac aca cag ttc aaa aac atc ccc att ggt ttc tgg tgg gct gtg	1296
Glu His Thr Gln Phe Lys Asn Ile Pro Ile Gly Phe Trp Trp Ala Val	

420	425	430	
gtg acc atg act acc tta ggc tat ggg gat atg tac ccc caa aca tgg			1344
Val Thr Met Thr Thr Leu Gly Tyr Gly Asp Met Tyr Pro Gln Thr Trp			
435	440	445	
tca ggg atg ttg gtg ggg gcc ttg tgt gct ctg gct gga gtg ctg acc			1392
Ser Gly Met Leu Val Gly Ala Leu Cys Ala Leu Ala Gly Val Leu Thr			
450	455	460	
ata gct atg cct gtg ccc gtc att gtc aac aat ttt ggg atg tac tac			1440
Ile Ala Met Pro Val Pro Val Ile Val Asn Asn Phe Gly Met Tyr Tyr			
465	470	475	480
tcc ttg gca atg gcg aag cag aaa ctt cca aga aaa aga aag aag cac			1488
Ser Leu Ala Met Ala Lys Gln Lys Leu Pro Arg Lys Arg Lys Lys His			
485	490	495	
att cct cct gcc cct ctg gca agc tca cct aca ttt tgc aag aca gaa			1536
Ile Pro Pro Ala Pro Leu Ala Ser Ser Pro Thr Phe Cys Lys Thr Glu			
500	505	510	
tta aac atg gct tgt aac agt acc cag agt gac aca tgt ctg ggc aaa			1584
Leu Asn Met Ala Cys Asn Ser Thr Gln Ser Asp Thr Cys Leu Gly Lys			
515	520	525	
gaa aac cgg ctt ctg gaa cat aac aga tca gtg tta tca ggt gac gac			1632
Glu Asn Arg Leu Leu Glu His Asn Arg Ser Val Leu Ser Gly Asp Asp			
530	535	540	
agt aca gga agt gag ccg cca tta tca cct ccg gaa agg ctc ccc atc			1680
Ser Thr Gly Ser Glu Pro Pro Leu Ser Pro Pro Glu Arg Leu Pro Ile			
545	550	555	560
aga cgc tct agt acc aga gac aaa aac aga aga ggg gaa aca tgt ttc			1728
Arg Arg Ser Ser Thr Arg Asp Lys Asn Arg Arg Gly Glu Thr Cys Phe			
565	570	575	
ctg ttg acg aca ggt gat tac acg tgc gct tct gat gga gga atc agg			1776
Leu Leu Thr Thr Gly Asp Tyr Thr Cys Ala Ser Asp Gly Gly Ile Arg			
580	585	590	
aaa gat aac tgc aaa gat gtt gtc att act ggt tac acg caa gcc gag			1824
Lys Asp Asn Cys Lys Asp Val Val Ile Thr Gly Tyr Thr Gln Ala Glu			
595	600	605	
gcc aga tct ctt act taa			1842
Ala Arg Ser Leu Thr			
610			

<210> 12
 <211> 613
 <212> PRT
 <213> Rattus norvegicus

<400> 12
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 1 5 10 15
 Thr Arg His Glu Thr Tyr Arg Ser Thr Leu Lys Thr Leu Pro Gly Thr
 20 25 30

Arg Leu Ala Leu Leu Ala Ser Ser Glu Pro Gln Gly Asp Cys Leu Thr
 35 40 45
 Ala Ala Gly Asp Lys Leu Gln Pro Leu Pro Pro Pro Leu Ser Pro Pro
 50 55 60
 Pro Arg Pro Pro Pro Leu Ser Pro Val Pro Ser Gly Cys Phe Glu Gly
 65 70 75 80
 Gly Ala Gly Asn Cys Ser Ser His Gly Gly Asn Gly Ser Asp His Pro
 85 90 95
 Gly Gly Gly Arg Glu Phe Phe Phe Asp Arg His Pro Gly Val Phe Ala
 100 105 110
 Tyr Val Leu Asn Tyr Tyr Arg Thr Gly Lys Leu His Cys Pro Ala Asp
 115 120 125
 Val Cys Gly Pro Leu Phe Glu Glu Glu Leu Ala Phe Trp Gly Ile Asp
 130 135 140
 Glu Thr Asp Val Glu Pro Cys Cys Trp Met Thr Tyr Arg Gln His Arg
 145 150 155 160
 Asp Ala Glu Glu Ala Leu Asp Ile Phe Glu Thr Pro Asp Leu Ile Gly
 165 170 175
 Gly Asp Pro Gly Asp Asp Glu Asp Leu Gly Gly Lys Arg Leu Gly Ile
 180 185 190
 Glu Asp Ala Ala Gly Leu Gly Gly Pro Asp Gly Lys Ser Gly Arg Trp
 195 200 205
 Arg Lys Leu Gln Pro Arg Met Trp Ala Leu Phe Glu Asp Pro Tyr Ser
 210 215 220
 Ser Arg Ala Ala Arg Phe Ile Ala Phe Ala Ser Leu Phe Phe Ile Leu
 225 230 235 240
 Val Ser Ile Thr Thr Phe Cys Leu Glu Thr His Glu Ala Phe Asn Ile
 245 250 255
 Val Lys Asn Lys Thr Glu Pro Val Ile Asn Gly Thr Ser Ala Val Leu
 260 265 270
 Gln Tyr Glu Ile Glu Thr Asp Pro Ala Leu Thr Tyr Val Glu Gly Val
 275 280 285
 Cys Val Val Trp Phe Thr Phe Glu Phe Leu Val Arg Ile Val Phe Ser
 290 295 300
 Pro Asn Lys Leu Glu Phe Ile Lys Asn Leu Leu Asn Ile Ile Asp Phe
 305 310 315 320
 Val Ala Ile Leu Pro Phe Tyr Leu Glu Val Gly Leu Ser Gly Leu Ser
 325 330 335
 Ser Lys Ala Ala Lys Asp Val Leu Gly Phe Leu Arg Val Val Arg Phe
 340 345 350
 Val Arg Ile Leu Arg Ile Phe Lys Leu Thr Arg His Phe Val Gly Leu
 355 360 365
 Arg Val Leu Gly His Thr Leu Arg Ala Ser Thr Asn Glu Phe Leu Leu
 370 375 380
 Leu Ile Ile Phe Leu Ala Leu Gly Val Leu Ile Phe Ala Thr Met Ile
 385 390 395 400
 Tyr Tyr Ala Glu Arg Val Gly Ala Gln Pro Asn Asp Pro Ser Ala Ser
 405 410 415
 Glu His Thr Gln Phe Lys Asn Ile Pro Ile Gly Phe Trp Trp Ala Val

420	425	430
Val Thr Met Thr Thr Leu Gly Tyr Gly Asp Met Tyr Pro Gln Thr Trp		
435	440	445
Ser Gly Met Leu Val Gly Ala Leu Cys Ala Leu Ala Gly Val Leu Thr		
450	455	460
Ile Ala Met Pro Val Pro Val Ile Val Asn Asn Phe Gly Met Tyr Tyr		
465	470	475
Ser Leu Ala Met Ala Lys Gln Lys Leu Pro Arg Lys Arg Lys Lys His		
485	490	495
Ile Pro Pro Ala Pro Leu Ala Ser Ser Pro Thr Phe Cys Lys Thr Glu		
500	505	510
Leu Asn Met Ala Cys Asn Ser Thr Gln Ser Asp Thr Cys Leu Gly Lys		
515	520	525
Glu Asn Arg Leu Leu Glu His Asn Arg Ser Val Leu Ser Gly Asp Asp		
530	535	540
Ser Thr Gly Ser Glu Pro Pro Leu Ser Pro Pro Glu Arg Leu Pro Ile		
545	550	555
Arg Arg Ser Ser Thr Arg Asp Lys Asn Arg Arg Gly Glu Thr Cys Phe		
565	570	575
Leu Leu Thr Thr Gly Asp Tyr Thr Cys Ala Ser Asp Gly Gly Ile Arg		
580	585	590
Lys Asp Asn Cys Lys Asp Val Val Ile Thr Gly Tyr Thr Gln Ala Glu		
595	600	605
Ala Arg Ser Leu Thr		
610		

<210> 13
 <211> 1917
 <212> DNA
 <213> Rattus norvegicus

<220>
 <221> CDS
 <222> (1)..(1917)

<400> 13	
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Met Gly Lys Ile Glu Asn Asn Glu Arg Val Ile Leu Asn Val Gly Gly	
1 5 10 15	
acc agg cac gaa acc tac cgc agc act ctc aag acc ctt cct gga act	96
Thr Arg His Glu Thr Tyr Arg Ser Thr Leu Lys Thr Leu Pro Gly Thr	
20 25 30	
cgc ctg gcc ctt ctc gcc tcc tct gaa cct cag ggc gac tgc ctg act	144
Arg Leu Ala Leu Leu Ala Ser Ser Glu Pro Gln Gly Asp Cys Leu Thr	
35 40 45	
gct gcg ggt gac aag ctg cag ccg ctg ccc cct ccg ctg tct cca ccg	192
Ala Ala Gly Asp Lys Leu Gln Pro Leu Pro Pro Pro Leu Ser Pro Pro	
50 55 60	

ccg cga ccg cct ccc ttg tcc cct gtc ccc agc ggc tgc ttc gag ggc	240
Pro Arg Pro Pro Pro Leu Ser Pro Val Pro Ser Gly Cys Phe Glu Gly	
65 70 75 80	
ggc gca ggc aac tgc agt tcg cac ggt ggc aat ggc agc gac cac cct	288
Gly Ala Gly Asn Cys Ser Ser His Gly Gly Asn Gly Ser Asp His Pro	
85 90 95	
ggg gga ggc cgc gaa ttc ttc ttc gat cgc cac cca gga gtc ttc gcc	336
Gly Gly Gly Arg Glu Phe Phe Phe Asp Arg His Pro Gly Val Phe Ala	
100 105 110	
tat gtg ctc aac tac tac cgc acg ggc aag ctg cac tgc ccc gcc gac	384
Tyr Val Leu Asn Tyr Tyr Arg Thr Gly Lys Leu His Cys Pro Ala Asp	
115 120 125	
gtg tgt gga ccg ctc ttc gag gaa gag ctg gca ttc tgg ggc atc gat	432
Val Cys Gly Pro Leu Phe Glu Glu Glu Leu Ala Phe Trp Gly Ile Asp	
130 135 140	
gag acc gac gtg gag ccc tgc tgc tgg atg acc tac agg cag cac cgg	480
Glu Thr Asp Val Glu Pro Cys Cys Trp Met Thr Tyr Arg Gln His Arg	
145 150 155 160	
gac gcg gag gag gcc ctg gat atc ttc gag aca ccc gac ctc atc gga	528
Asp Ala Glu Glu Ala Leu Asp Ile Phe Glu Thr Pro Asp Leu Ile Gly	
165 170 175	
ggc gac cct ggt gat gat gag gac cta ggg ggc aag aga ctg ggc att	576
Gly Asp Pro Gly Asp Asp Glu Asp Leu Gly Gly Lys Arg Leu Gly Ile	
180 185 190	
gag gat gct gcg ggg ctg gga gga ccc gat ggc aag tct ggc cgc tgg	624
Glu Asp Ala Ala Gly Leu Gly Gly Pro Asp Gly Lys Ser Gly Arg Trp	
195 200 205	
agg aag ctg cag cct cgc atg tgg gct ctc ttt gag gac ccc tat tca	672
Arg Lys Leu Gln Pro Arg Met Trp Ala Leu Phe Glu Asp Pro Tyr Ser	
210 215 220	
tcc aga gcc gct agg ttt att gct ttt gct tct ctg ttc ttc att ttg	720
Ser Arg Ala Ala Arg Phe Ile Ala Phe Ala Ser Leu Phe Phe Ile Leu	
225 230 235 240	
gtt tcc atc aca acc ttt tgc ctg gag aca cac gaa gct ttc aat att	768
Val Ser Ile Thr Thr Phe Cys Leu Glu Thr His Glu Ala Phe Asn Ile	
245 250 255	
gtt aaa aac aag aca gag cca gtc atc aac ggc acc agc gct gtt ctc	816
Val Lys Asn Lys Thr Glu Pro Val Ile Asn Gly Thr Ser Ala Val Leu	
260 265 270	
cag tat gaa atc gaa acg gat cct gcc ttg aca tat gtg gaa gga gtg	864
Gln Tyr Glu Ile Glu Thr Asp Pro Ala Leu Thr Tyr Val Glu Gly Val	
275 280 285	
tgt gtg gtg tgg ttt act ttt gaa ttt tta gtc cgt att gtt ttc tcg	912
Cys Val Val Trp Phe Thr Phe Glu Phe Leu Val Arg Ile Val Phe Ser	
290 295 300	
ccc aat aaa ctt gag ttc atc aaa aat cta ttg aac atc att gac ttt	960
Pro Asn Lys Leu Glu Phe Ile Lys Asn Leu Leu Asn Ile Ile Asp Phe	
305 310 315 320	
gtg gcc atc ctc ccc ttc tac tta gag gtg gga ctc agc ggg ctg tct	1008

Val Ala Ile Leu Pro Phe Tyr Leu Glu Val Gly Leu Ser Gly Leu Ser	
325 330 335	
tcc aaa gcg gct aaa gat gtg ctc ggc ttt ctc agg gtg gtt agg ttt	1056
Ser Lys Ala Ala Lys Asp Val Leu Gly Phe Leu Arg Val Val Arg Phe	
340 345 350	
gtg agg atc ctg aga atc ttc aag ctt acc cgc cat ttc gta ggt ctg	1104
Val Arg Ile Leu Arg Ile Phe Lys Leu Thr Arg His Phe Val Gly Leu	
355 360 365	
aga gtg ctc gga cac act ctt cgt gcg agc acc aat gaa ttt ttg ttg	1152
Arg Val Leu Gly His Thr Leu Arg Ala Ser Thr Asn Glu Phe Leu Leu	
370 375 380	
ctg atc atc ttt ctg gct ctg gga gtt ttg ata ttc gct acg atg atc	1200
Leu Ile Ile Phe Leu Ala Leu Gly Val Leu Ile Phe Ala Thr Met Ile	
385 390 395 400	
tac tac gct gag cga gta ggg gct caa cct aat gat ccc tca gcg agt	1248
Tyr Tyr Ala Glu Arg Val Gly Ala Gln Pro Asn Asp Pro Ser Ala Ser	
405 410 415	
gag cac aca cag ttc aaa aac atc ccc att ggt ttc tgg tgg gct gtg	1296
Glu His Thr Gln Phe Lys Asn Ile Pro Ile Gly Phe Trp Trp Ala Val	
420 425 430	
gtg acc atg act acc tta ggc tat ggg gat atg tac ccc caa aca tgg	1344
Val Thr Met Thr Thr Leu Gly Tyr Gly Asp Met Tyr Pro Gln Thr Trp	
435 440 445	
tca ggg atg ttg gtg ggg gcc ttg tgt gct ctg gct gga gtg ctg acc	1392
Ser Gly Met Leu Val Gly Ala Leu Cys Ala Leu Ala Gly Val Leu Thr	
450 455 460	
ata gct atg cct gtg ccc gtc att gtc aac aat ttt ggg atg tac tac	1440
Ile Ala Met Pro Val Pro Val Ile Val Asn Asn Phe Gly Met Tyr Tyr	
465 470 475 480	
tcc ttg gca atg gcg aag cag aaa ctt cca aga aaa aga aag aag cac	1488
Ser Leu Ala Met Ala Lys Gln Lys Leu Pro Arg Lys Arg Lys Lys His	
485 490 495	
att cct cct gcc cct ctg gca agc tca cct aca ttt tgc aag aca gaa	1536
Ile Pro Pro Ala Pro Leu Ala Ser Ser Pro Thr Phe Cys Lys Thr Glu	
500 505 510	
tta aac atg gct tgt aac agt acc cag agt gac aca tgt ctg ggc aaa	1584
Leu Asn Met Ala Cys Asn Ser Thr Gln Ser Asp Thr Cys Leu Gly Lys	
515 520 525	
gaa aac cgg ctt ctg gaa cat aac aga tca gtg tta tca ggt gac gac	1632
Glu Asn Arg Leu Leu Glu His Asn Arg Ser Val Leu Ser Gly Asp Asp	
530 535 540	
agt aca gga agt gag ccg cca tta tca cct ccg gaa agg ctc ccc atc	1680
Ser Thr Gly Ser Glu Pro Pro Leu Ser Pro Pro Glu Arg Leu Pro Ile	
545 550 555 560	
aga cgc tct agt acc aga gac aaa aac aga aga ggg gaa aca tgt ttc	1728
Arg Arg Ser Ser Thr Arg Asp Lys Asn Arg Arg Gly Glu Thr Cys Phe	
565 570 575	
ctg ttg acg aca ggt gat tac acg tgc gct tct gat gga gga atc agg	1776
Leu Leu Thr Thr Gly Asp Tyr Thr Cys Ala Ser Asp Gly Gly Ile Arg	

580	585	590	
aaa gga tat gaa aaa tcc cga agc tta aac aac ata gcg ggc ttg gca			1824
Lys Gly Tyr Glu Lys Ser Arg Ser Leu Asn Asn Ile Ala Gly Leu Ala			
595	600	605	
ggc aat gct ctg aga ctc tct cca gta aca tcc ccc tac aac tct ccg			1872
Gly Asn Ala Leu Arg Leu Ser Pro Val Thr Ser Pro Tyr Asn Ser Pro			
610	615	620	
tgt cct ctg agg cgc tct cgg tct ccc atc cca tct atc ttg taa			1917
Cys Pro Leu Arg Arg Ser Arg Ser Pro Ile Pro Ser Ile Leu			
625	630	635	

<210> 14
 <211> 638
 <212> PRT
 <213> Rattus norvegicus

<400> 14
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 20 25 30
 Arg Leu Ala Leu Leu Ala Ser Ser Glu Pro Gln Gly Asp Cys Leu Thr
 35 40 45
 Ala Ala Gly Asp Lys Leu Gln Pro Leu Pro Pro Pro Leu Ser Pro Pro
 50 55 60
 Pro Arg Pro Pro Pro Leu Ser Pro Val Pro Ser Gly Cys Phe Glu Gly
 65 70 75 80
 Gly Ala Gly Asn Cys Ser Ser His Gly Gly Asn Gly Ser Asp His Pro
 85 90 95
 Gly Gly Gly Arg Glu Phe Phe Phe Asp Arg His Pro Gly Val Phe Ala
 100 105 110
 Tyr Val Leu Asn Tyr Tyr Arg Thr Gly Lys Leu His Cys Pro Ala Asp
 115 120 125
 Val Cys Gly Pro Leu Phe Glu Glu Glu Leu Ala Phe Trp Gly Ile Asp
 130 135 140
 Glu Thr Asp Val Glu Pro Cys Cys Trp Met Thr Tyr Arg Gln His Arg
 145 150 155 160
 Asp Ala Glu Glu Ala Leu Asp Ile Phe Glu Thr Pro Asp Leu Ile Gly
 165 170 175
 Gly Asp Pro Gly Asp Asp Glu Asp Leu Gly Gly Lys Arg Leu Gly Ile
 180 185 190
 Glu Asp Ala Ala Gly Leu Gly Gly Pro Asp Gly Lys Ser Gly Arg Trp
 195 200 205
 Arg Lys Leu Gln Pro Arg Met Trp Ala Leu Phe Glu Asp Pro Tyr Ser
 210 215 220
 Ser Arg Ala Ala Arg Phe Ile Ala Phe Ala Ser Leu Phe Phe Ile Leu
 225 230 235 240
 Val Ser Ile Thr Thr Phe Cys Leu Glu Thr His Glu Ala Phe Asn Ile

245										250					255				
Val	Lys	Asn	Lys	Thr	Glu	Pro	Val	Ile	Asn	Gly	Thr	Ser	Ala	Val	Leu				
260								265				270							
Gln	Tyr	Glu	Ile	Glu	Thr	Asp	Pro	Ala	Leu	Thr	Tyr	Val	Glu	Gly	Val				
275								280				285							
Cys	Val	Val	Trp	Phe	Thr	Phe	Glu	Phe	Leu	Val	Arg	Ile	Val	Phe	Ser				
290								295				300							
Pro	Asn	Lys	Leu	Glu	Phe	Ile	Lys	Asn	Leu	Leu	Asn	Ile	Ile	Asp	Phe				
305								310				315							
Val	Ala	Ile	Leu	Pro	Phe	Tyr	Leu	Glu	Val	Gly	Leu	Ser	Gly	Leu	Ser				
				325				330				335							
Ser	Lys	Ala	Ala	Lys	Asp	Val	Leu	Gly	Phe	Leu	Arg	Val	Val	Arg	Phe				
				340				345				350							
Val	Arg	Ile	Leu	Arg	Ile	Phe	Lys	Leu	Thr	Arg	His	Phe	Val	Gly	Leu				
				355				360				365							
Arg	Val	Leu	Gly	His	Thr	Leu	Arg	Ala	Ser	Thr	Asn	Glu	Phe	Leu	Leu				
370								375				380							
Leu	Ile	Ile	Phe	Leu	Ala	Leu	Gly	Val	Leu	Ile	Phe	Ala	Thr	Met	Ile				
385								390				395							
Tyr	Tyr	Ala	Glu	Arg	Val	Gly	Ala	Gln	Pro	Asn	Asp	Pro	Ser	Ala	Ser				
				405				410				415							
Glu	His	Thr	Gln	Phe	Lys	Asn	Ile	Pro	Ile	Gly	Phe	Trp	Trp	Ala	Val				
				420				425				430							
Val	Thr	Met	Thr	Thr	Leu	Gly	Tyr	Gly	Asp	Met	Tyr	Pro	Gln	Thr	Trp				
435								440				445							
Ser	Gly	Met	Leu	Val	Gly	Ala	Leu	Cys	Ala	Leu	Ala	Gly	Val	Leu	Thr				
450								455				460							
Ile	Ala	Met	Pro	Val	Pro	Val	Ile	Val	Asn	Asn	Phe	Gly	Met	Tyr	Tyr				
465								470				475							
Ser	Leu	Ala	Met	Ala	Lys	Gln	Lys	Leu	Pro	Arg	Lys	Arg	Lys	Lys	His				
				485				490				495							
Ile	Pro	Pro	Ala	Pro	Leu	Ala	Ser	Ser	Pro	Thr	Phe	Cys	Lys	Thr	Glu				
				500				505				510							
Leu	Asn	Met	Ala	Cys	Asn	Ser	Thr	Gln	Ser	Asp	Thr	Cys	Leu	Gly	Lys				
				515				520				525							
Glu	Asn	Arg	Leu	Leu	Glu	His	Asn	Arg	Ser	Val	Leu	Ser	Gly	Asp	Asp				
530								535				540							
Ser	Thr	Gly	Ser	Glu	Pro	Pro	Leu	Ser	Pro	Pro	Glu	Arg	Leu	Pro	Ile				
545								550				555							
Arg	Arg	Ser	Ser	Thr	Arg	Asp	Lys	Asn	Arg	Arg	Gly	Glu	Thr	Cys	Phe				
				565				570				575							
Leu	Leu	Thr	Thr	Gly	Asp	Tyr	Thr	Cys	Ala	Ser	Asp	Gly	Gly	Ile	Arg				
				580				585				590							
Lys	Gly	Tyr	Glu	Lys	Ser	Arg	Ser	Leu	Asn	Asn	Ile	Ala	Gly	Leu	Ala				
595								600				605							
Gly	Asn	Ala	Leu	Arg	Leu	Ser	Pro	Val	Thr	Ser	Pro	Tyr	Asn	Ser	Pro				
610								615				620							
Cys	Pro	Leu	Arg	Arg	Ser	Arg	Ser	Pro	Ile	Pro	Ser	Ile	Leu						
625								630				635							

<210> 15
 <211> 1908
 <212> DNA
 <213> Rattus norvegicus

<220>
 <221> CDS
 <222> (1)..(1908)

<400> 15
 atg ggc aag atc gag aac aac gag agg gtg atc ctc aat gtc gga ggc 48
 Met Gly Lys Ile Glu Asn Asn Glu Arg Val Ile Leu Asn Val Gly Gly
 1 5 10 15
 acc agg cac gaa acc tac cgc agc act ctc aag acc ctt cct gga act 96
 Thr Arg His Glu Thr Tyr Arg Ser Thr Leu Lys Thr Leu Pro Gly Thr
 20 25 30
 cgc ctg gcc ctt ctc gcc tcc tct gaa cct cag ggc gac tgc ctg act 144
 Arg Leu Ala Leu Leu Ala Ser Ser Glu Pro Gln Gly Asp Cys Leu Thr
 35 40 45
 gct gcg ggt gac aag ctg cag ccg ctg ccc cct ccg ctg tct cca ccg 192
 Ala Ala Gly Asp Lys Leu Gln Pro Leu Pro Pro Pro Leu Ser Pro Pro
 50 55 60
 ccg cga ccg cct ccc ttg tcc cct gtc ccc agc ggc tgc ttc gag ggc 240
 Pro Arg Pro Pro Pro Leu Ser Pro Val Pro Ser Gly Cys Phe Glu Gly
 65 70 75 80
 ggc gca ggc aac tgc agt tcg cac ggt ggc aat ggc agc gac cac cct 288
 Gly Ala Gly Asn Cys Ser Ser His Gly Gly Asn Gly Ser Asp His Pro
 85 90 95
 ggg gga ggc cgc gaa ttc ttc ttc gat cgc cac cca gga gtc ttc gcc 336
 Gly Gly Gly Arg Glu Phe Phe Phe Asp Arg His Pro Gly Val Phe Ala
 100 105 110
 tat gtg ctc aac tac tac cgc acg ggc aag ctg cac tgc ccc gcc gac 384
 Tyr Val Leu Asn Tyr Tyr Arg Thr Gly Lys Leu His Cys Pro Ala Asp
 115 120 125
 gtg tgt gga ccg ctc ttc gag gaa gag ctg gca ttc tgg ggc atc gat 432
 Val Cys Gly Pro Leu Phe Glu Glu Glu Leu Ala Phe Trp Gly Ile Asp
 130 135 140
 gag acc gac gtg gag ccc tgc tgc tgg atg acc tac agg cag cac ccg 480
 Glu Thr Asp Val Glu Pro Cys Cys Trp Met Thr Tyr Arg Gln His Arg
 145 150 155 160
 gac gcg gag gag gcc ctg gat atc ttc gag aca ccc gac ctc atc gga 528
 Asp Ala Glu Glu Ala Leu Asp Ile Phe Glu Thr Pro Asp Leu Ile Gly
 165 170 175
 ggc gac cct ggt gat gat gag gac cta ggg ggc aag aga ctg ggc att 576
 Gly Asp Pro Gly Asp Asp Glu Asp Leu Gly Gly Lys Arg Leu Gly Ile
 180 185 190
 gag gat gct gcg ggg ctg gga gga ccc gat ggc aag tct ggc cgc tgg 624

Glu Asp Ala Ala Gly Leu Gly Gly Pro Asp Gly Lys Ser Gly Arg Trp	
195	200
agg aag ctg cag cct cgc atg tgg gct ctc ttt gag gac ccc tat tca	672
Arg Lys Leu Gln Pro Arg Met Trp Ala Leu Phe Glu Asp Pro Tyr Ser	
210	215
220	
tcc aga gcc gct agg ttt att gct ttt gct tct ctg ttc ttc att ttg	720
Ser Arg Ala Ala Arg Phe Ile Ala Phe Ala Ser Leu Phe Phe Ile Leu	
225	230
235	240
gtt tcc atc aca acc ttt tgc ctg gag aca cac gaa gct ttc aat att	768
Val Ser Ile Thr Thr Phe Cys Leu Glu Thr His Glu Ala Phe Asn Ile	
245	250
255	
gtt aaa aac aag aca gag cca gtc atc aac ggc acc agc gct gtt ctc	816
Val Lys Asn Lys Thr Glu Pro Val Ile Asn Gly Thr Ser Ala Val Leu	
260	265
270	
cag tat gaa atc gaa acg gat cct gcc ttg aca tat gtg gaa gga gtg	864
Gln Tyr Glu Ile Glu Thr Asp Pro Ala Leu Thr Tyr Val Glu Gly Val	
275	280
285	
tgt gtg gtg tgg ttt act ttt gaa ttt tta gtc cgt att gtt ttc tcg	912
Cys Val Val Trp Phe Thr Phe Glu Phe Leu Val Arg Ile Val Phe Ser	
290	295
300	
ccc aat aaa ctt gag ttc atc aaa aat cta ttg aac atc att gac ttt	960
Pro Asn Lys Leu Glu Phe Ile Lys Asn Leu Leu Asn Ile Ile Asp Phe	
305	310
315	320
gtg gcc atc ctc ccc ttc tac tta gag gtg gga ctc agc ggg ctg tct	1008
Val Ala Ile Leu Pro Phe Tyr Leu Glu Val Gly Leu Ser Gly Leu Ser	
325	330
335	
tcc aaa gcg gct aaa gat gtg ctc ggc ttt ctc agg gtg gtt agg ttt	1056
Ser Lys Ala Ala Lys Asp Val Leu Gly Phe Leu Arg Val Val Arg Phe	
340	345
350	
gtg agg atc ctg aga atc ttc aag ctt acc cgc cat ttc gta ggt ctg	1104
Val Arg Ile Leu Arg Ile Phe Lys Leu Thr Arg His Phe Val Gly Leu	
355	360
365	
aga gtg ctc gga cac act ctt cgt gcg agc acc aat gaa ttt ttg ttg	1152
Arg Val Leu Gly His Thr Leu Arg Ala Ser Thr Asn Glu Phe Leu Leu	
370	375
380	
ctg atc atc ttt ctg gct ctg gga gtt ttg ata ttc gct acg atg atc	1200
Leu Ile Ile Phe Leu Ala Leu Gly Val Leu Ile Phe Ala Thr Met Ile	
385	390
395	400
tac tac gct gag cga gta ggg gct caa cct aat gat ccc tca gcg agt	1248
Tyr Tyr Ala Glu Arg Val Gly Ala Gln Pro Asn Asp Pro Ser Ala Ser	
405	410
415	
gag cac aca cag ttc aaa aac atc ccc att ggt ttc tgg tgg gct gtg	1296
Glu His Thr Gln Phe Lys Asn Ile Pro Ile Gly Phe Trp Trp Ala Val	
420	425
430	
gtg acc atg act acc tta ggc tat ggg gat atg tac ccc caa aca tgg	1344
Val Thr Met Thr Thr Leu Gly Tyr Gly Asp Met Tyr Pro Gln Thr Trp	
435	440
445	
tca ggg atg ttg gtg ggg gcc ttg tgt gct ctg gct gga gtg ctg acc	1392
Ser Gly Met Leu Val Gly Ala Leu Cys Ala Leu Ala Gly Val Leu Thr	

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      450              455              460
ata gct atg cct gtg ccc gtc att gtc aac aat ttt ggg atg tac tac      1440
Ile Ala Met Pro Val Pro Val Ile Val Asn Asn Phe Gly Met Tyr Tyr
465              470              475              480
tcc ttg gca atg gcg aag cag aaa ctt cca aga aaa aga aag aag cac      1488
Ser Leu Ala Met Ala Lys Gln Lys Leu Pro Arg Lys Arg Lys Lys His
      485              490              495
att cct cct gcc cct ctg gca agc tca cct aca ttt tgc aag aca gaa      1536
Ile Pro Pro Ala Pro Leu Ala Ser Ser Pro Thr Phe Cys Lys Thr Glu
      500              505              510
tta aac atg gct tgt aac agt acc cag agt gac aca tgt ctg ggc aaa      1584
Leu Asn Met Ala Cys Asn Ser Thr Gln Ser Asp Thr Cys Leu Gly Lys
      515              520              525
gaa aac cgg ctt ctg gaa cat aac aga tca gtg tta tca ggt gac gac      1632
Glu Asn Arg Leu Leu Glu His Asn Arg Ser Val Leu Ser Gly Asp Asp
      530              535              540
agt aca gga agt gag ccg cca tta tca cct ccg gaa agg ctc ccc atc      1680
Ser Thr Gly Ser Glu Pro Pro Leu Ser Pro Pro Glu Arg Leu Pro Ile
545              550              555              560
aga cgc tct agt acc aga gac aaa aac aga aga ggg gaa aca tgt ttc      1728
Arg Arg Ser Ser Thr Arg Asp Lys Asn Arg Arg Gly Glu Thr Cys Phe
      565              570              575
ctg ttg acg aca ggt gat tac acg tgc gct tct gat gga gga atc agg      1776
Leu Leu Thr Thr Gly Asp Tyr Thr Cys Ala Ser Asp Gly Gly Ile Arg
      580              585              590
aaa gca agc aca cta gag ccc atg gag agt act tca cag act aaa gga      1824
Lys Ala Ser Thr Leu Glu Pro Met Glu Ser Thr Ser Gln Thr Lys Gly
      595              600              605
gac acg aga cca gaa gct cac tgg aat tgt gcg cat tta ctc aat ttt      1872
Asp Thr Arg Pro Glu Ala His Trp Asn Cys Ala His Leu Leu Asn Phe
      610              615              620
ggc tgt cct acg gga agt tca ttt ccc acc ctc taa      1908
Gly Cys Pro Thr Gly Ser Ser Phe Pro Thr Leu
625              630              635

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<210> 16
<211> 635
<212> PRT
<213> Rattus norvegicus

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<400> 16
Met Gly Lys Ile Glu Asn Asn Glu Arg Val Ile Leu Asn Val Gly Gly
1              5              10              15
Thr Arg His Glu Thr Tyr Arg Ser Thr Leu Lys Thr Leu Pro Gly Thr
      20              25              30
Arg Leu Ala Leu Leu Ala Ser Ser Glu Pro Gln Gly Asp Cys Leu Thr
      35              40              45
Ala Ala Gly Asp Lys Leu Gln Pro Leu Pro Pro Pro Leu Ser Pro Pro

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50	55	60
Pro Arg Pro Pro Pro Leu Ser Pro Val Pro Ser Gly Cys Phe Glu Gly		
65	70	75
Gly Ala Gly Asn Cys Ser Ser His Gly Gly Asn Gly Ser Asp His Pro		80
	85	90
Gly Gly Gly Arg Glu Phe Phe Phe Asp Arg His Pro Gly Val Phe Ala		95
	100	105
Tyr Val Leu Asn Tyr Tyr Arg Thr Gly Lys Leu His Cys Pro Ala Asp		110
	115	120
Val Cys Gly Pro Leu Phe Glu Glu Glu Leu Ala Phe Trp Gly Ile Asp		125
	130	135
Glu Thr Asp Val Glu Pro Cys Cys Trp Met Thr Tyr Arg Gln His Arg		140
145	150	155
Asp Ala Glu Glu Ala Leu Asp Ile Phe Glu Thr Pro Asp Leu Ile Gly		160
	165	170
Gly Asp Pro Gly Asp Asp Glu Asp Leu Gly Gly Lys Arg Leu Gly Ile		175
	180	185
Glu Asp Ala Ala Gly Leu Gly Gly Pro Asp Gly Lys Ser Gly Arg Trp		190
	195	200
Arg Lys Leu Gln Pro Arg Met Trp Ala Leu Phe Glu Asp Pro Tyr Ser		205
	210	215
Ser Arg Ala Ala Arg Phe Ile Ala Phe Ala Ser Leu Phe Phe Ile Leu		220
225	230	235
Val Ser Ile Thr Thr Phe Cys Leu Glu Thr His Glu Ala Phe Asn Ile		240
	245	250
Val Lys Asn Lys Thr Glu Pro Val Ile Asn Gly Thr Ser Ala Val Leu		255
	260	265
Gln Tyr Glu Ile Glu Thr Asp Pro Ala Leu Thr Tyr Val Glu Gly Val		270
	275	280
Cys Val Val Trp Phe Thr Phe Glu Phe Leu Val Arg Ile Val Phe Ser		285
	290	295
Pro Asn Lys Leu Glu Phe Ile Lys Asn Leu Leu Asn Ile Ile Asp Phe		300
305	310	315
Val Ala Ile Leu Pro Phe Tyr Leu Glu Val Gly Leu Ser Gly Leu Ser		320
	325	330
Ser Lys Ala Ala Lys Asp Val Leu Gly Phe Leu Arg Val Val Arg Phe		335
	340	345
Val Arg Ile Leu Arg Ile Phe Lys Leu Thr Arg His Phe Val Gly Leu		350
	355	360
Arg Val Leu Gly His Thr Leu Arg Ala Ser Thr Asn Glu Phe Leu Leu		365
	370	375
Leu Ile Ile Phe Leu Ala Leu Gly Val Leu Ile Phe Ala Thr Met Ile		380
385	390	395
Tyr Tyr Ala Glu Arg Val Gly Ala Gln Pro Asn Asp Pro Ser Ala Ser		400
	405	410
Glu His Thr Gln Phe Lys Asn Ile Pro Ile Gly Phe Trp Trp Ala Val		415
	420	425
Val Thr Met Thr Thr Leu Gly Tyr Gly Asp Met Tyr Pro Gln Thr Trp		430
	435	440
		445

Ser Gly Met Leu Val Gly Ala Leu Cys Ala Leu Ala Gly Val Leu Thr
 450 455 460
 Ile Ala Met Pro Val Pro Val Ile Val Asn Asn Phe Gly Met Tyr Tyr
 465 470 475 480
 Ser Leu Ala Met Ala Lys Gln Lys Leu Pro Arg Lys Arg Lys Lys His
 485 490 495
 Ile Pro Pro Ala Pro Leu Ala Ser Ser Pro Thr Phe Cys Lys Thr Glu
 500 505 510
 Leu Asn Met Ala Cys Asn Ser Thr Gln Ser Asp Thr Cys Leu Gly Lys
 515 520 525
 Glu Asn Arg Leu Leu Glu His Asn Arg Ser Val Leu Ser Gly Asp Asp
 530 535 540
 Ser Thr Gly Ser Glu Pro Pro Leu Ser Pro Pro Glu Arg Leu Pro Ile
 545 550 555 560
 Arg Arg Ser Ser Thr Arg Asp Lys Asn Arg Arg Gly Glu Thr Cys Phe
 565 570 575
 Leu Leu Thr Thr Gly Asp Tyr Thr Cys Ala Ser Asp Gly Gly Ile Arg
 580 585 590
 Lys Ala Ser Thr Leu Glu Pro Met Glu Ser Thr Ser Gln Thr Lys Gly
 595 600 605
 Asp Thr Arg Pro Glu Ala His Trp Asn Cys Ala His Leu Leu Asn Phe
 610 615 620
 Gly Cys Pro Thr Gly Ser Ser Phe Pro Thr Leu
 625 630 635

<210> 17
 <211> 1875
 <212> DNA
 <213> Rattus norvegicus

<220>
 <221> CDS
 <222> (1)..(1875)

<400> 17
 atg ggc aag atc gag aac aac gag agg gtg atc ctc aat gtc gga ggc 48
 Met Gly Lys Ile Glu Asn Asn Glu Arg Val Ile Leu Asn Val Gly Gly
 1 5 10 15
 acc agg cac gaa acc tac cgc agc act ctc aag acc ctt cct gga act 96
 Thr Arg His Glu Thr Tyr Arg Ser Thr Leu Lys Thr Leu Pro Gly Thr
 20 25 30
 cgc ctg gcc ctt ctc gcc tcc tct gaa cct cag ggc gac tgc ctg act 144
 Arg Leu Ala Leu Leu Ala Ser Ser Glu Pro Gln Gly Asp Cys Leu Thr
 35 40 45
 gct gcg ggt gac aag ctg cag ccg ctg ccc cct ccg ctg tct cca ccg 192
 Ala Ala Gly Asp Lys Leu Gln Pro Leu Pro Pro Pro Leu Ser Pro Pro
 50 55 60
 ccg cga ccg cct ccc ttg tcc cct gtc ccc agc ggc tgc ttc gag ggc 240

Pro	Arg	Pro	Pro	Pro	Leu	Ser	Pro	Val	Pro	Ser	Gly	Cys	Phe	Glu	Gly	
65					70					75					80	
ggc	gca	ggc	aac	tgc	agt	tcg	cac	ggt	ggc	aat	ggc	agc	gac	cac	cct	288
Gly	Ala	Gly	Asn	Cys	Ser	Ser	His	Gly	Gly	Asn	Gly	Ser	Asp	His	Pro	
				85					90					95		
ggg	gga	ggc	cgc	gaa	ttc	ttc	ttc	gat	cgc	cac	cca	gga	gtc	ttc	gcc	336
Gly	Gly	Gly	Arg	Glu	Phe	Phe	Phe	Asp	Arg	His	Pro	Gly	Val	Phe	Ala	
				100					105					110		
tat	gtg	ctc	aac	tac	tac	cgc	acg	ggc	aag	ctg	cac	tgc	ccc	gcc	gac	384
Tyr	Val	Leu	Asn	Tyr	Tyr	Arg	Thr	Gly	Lys	Leu	His	Cys	Pro	Ala	Asp	
			115						120					125		
gtg	tgt	gga	ccg	ctc	ttc	gag	gaa	gag	ctg	gca	ttc	tgg	ggc	atc	gat	432
Val	Cys	Gly	Pro	Leu	Phe	Glu	Glu	Glu	Leu	Ala	Phe	Trp	Gly	Ile	Asp	
			130						135					140		
gag	acc	gac	gtg	gag	ccc	tgc	tgc	tgg	atg	acc	tac	agg	cag	cac	cgg	480
Glu	Thr	Asp	Val	Glu	Pro	Cys	Cys	Trp	Met	Thr	Tyr	Arg	Gln	His	Arg	
145					150					155					160	
gac	gcg	gag	gag	gcc	ctg	gat	atc	ttc	gag	aca	ccc	gac	ctc	atc	gga	528
Asp	Ala	Glu	Glu	Ala	Leu	Asp	Ile	Phe	Glu	Thr	Pro	Asp	Leu	Ile	Gly	
				165					170					175		
ggc	gac	cct	ggt	gat	gat	gag	gac	cta	ggg	ggc	aag	aga	ctg	ggc	att	576
Gly	Asp	Pro	Gly	Asp	Asp	Glu	Asp	Leu	Gly	Gly	Lys	Arg	Leu	Gly	Ile	
			180						185					190		
gag	gat	gct	gcg	ggg	ctg	gga	gga	ccc	gat	ggc	aag	tct	ggc	cgc	tgg	624
Glu	Asp	Ala	Ala	Gly	Leu	Gly	Gly	Pro	Asp	Gly	Lys	Ser	Gly	Arg	Trp	
			195					200					205			
agg	aag	ctg	cag	cct	cgc	atg	tgg	gct	ctc	ttt	gag	gac	ccc	tat	tca	672
Arg	Lys	Leu	Gln	Pro	Arg	Met	Trp	Ala	Leu	Phe	Glu	Asp	Pro	Tyr	Ser	
			210				215					220				
tcc	aga	gcc	gct	agg	ttt	att	gct	ttt	gct	tct	ctg	ttc	ttc	att	ttg	720
Ser	Arg	Ala	Ala	Arg	Phe	Ile	Ala	Phe	Ala	Ser	Leu	Phe	Phe	Ile	Leu	
225					230				235						240	
gtt	tcc	atc	aca	acc	ttt	tgc	ctg	gag	aca	cac	gaa	gct	ttc	aat	att	768
Val	Ser	Ile	Thr	Thr	Phe	Cys	Leu	Glu	Thr	His	Glu	Ala	Phe	Asn	Ile	
				245					250					255		
gtt	aaa	aac	aag	aca	gag	cca	gtc	atc	aac	ggc	acc	agc	gct	gtt	ctc	816
Val	Lys	Asn	Lys	Thr	Glu	Pro	Val	Ile	Asn	Gly	Thr	Ser	Ala	Val	Leu	
			260					265					270			
cag	tat	gaa	atc	gaa	acg	gat	cct	gcc	ttg	aca	tat	gtg	gaa	gga	gtg	864
Gln	Tyr	Glu	Ile	Glu	Thr	Asp	Pro	Ala	Leu	Thr						

325	330	335	
tcc aaa gcg gct aaa gat gtg ctc ggc ttt ctc agg gtg gtt agg ttt			1056
Ser Lys Ala Ala Lys Asp Val Leu Gly Phe Leu Arg Val Val Arg Phe			
340	345	350	
gtg agg atc ctg aga atc ttc aag ctt acc cgc cat ttc gta ggt ctg			1104
Val Arg Ile Leu Arg Ile Phe Lys Leu Thr Arg His Phe Val Gly Leu			
355	360	365	
aga gtg ctc gga cac act ctt cgt gcg agc acc aat gaa ttt ttg ttg			1152
Arg Val Leu Gly His Thr Leu Arg Ala Ser Thr Asn Glu Phe Leu Leu			
370	375	380	
ctg atc atc ttt ctg gct ctg gga gtt ttg ata ttc gct acg atg atc			1200
Leu Ile Ile Phe Leu Ala Leu Gly Val Leu Ile Phe Ala Thr Met Ile			
385	390	395	400
tac tac gct gag cga gta ggg gct caa cct aat gat ccc tca gcg agt			1248
Tyr Tyr Ala Glu Arg Val Gly Ala Gln Pro Asn Asp Pro Ser Ala Ser			
405	410	415	
gag cac aca cag ttc aaa aac atc ccc att ggt ttc tgg tgg gct gtg			1296
Glu His Thr Gln Phe Lys Asn Ile Pro Ile Gly Phe Trp Trp Ala Val			
420	425	430	
gtg acc atg act acc tta ggc tat ggg gat atg tac ccc caa aca tgg			1344
Val Thr Met Thr Thr Leu Gly Tyr Gly Asp Met Tyr Pro Gln Thr Trp			
435	440	445	
tca ggg atg ttg gtg ggg gcc ttg tgt gct ctg gct gga gtg ctg acc			1392
Ser Gly Met Leu Val Gly Ala Leu Cys Ala Leu Ala Gly Val Leu Thr			
450	455	460	
ata gct atg cct gtg ccc gtc att gtc aac aat ttt ggg atg tac tac			1440
Ile Ala Met Pro Val Pro Val Ile Val Asn Asn Phe Gly Met Tyr Tyr			
465	470	475	480
tcc ttg gca atg gcg aag cag aaa ctt cca aga aaa aga aag aag cac			1488
Ser Leu Ala Met Ala Lys Gln Lys Leu Pro Arg Lys Arg Lys Lys His			
485	490	495	
att cct cct gcc cct ctg gca agc tca cct aca ttt tgc aag aca gaa			1536
Ile Pro Pro Ala Pro Leu Ala Ser Ser Pro Thr Phe Cys Lys Thr Glu			
500	505	510	
tta aac atg gct tgt aac agt acc cag agt gac aca tgt ctg ggc aaa			1584
Leu Asn Met Ala Cys Asn Ser Thr Gln Ser Asp Thr Cys Leu Gly Lys			
515	520	525	
gaa aac cgg ctt ctg gaa cat aac aga tca gtg tta tca ggt gac gac			1632
Glu Asn Arg Leu Leu Glu His Asn Arg Ser Val Leu Ser Gly Asp Asp			
530	535	540	
agt aca gga agt gag ccg cca tta tca cct ccg gaa agg ctc ccc atc			1680
Ser Thr Gly Ser Glu Pro Pro Leu Ser Pro Pro Glu Arg Leu Pro Ile			
545	550	555	560
aga cgc tct agt acc aga gac aaa aac aga aga ggg gaa aca tgt ttc			1728
Arg Arg Ser Ser Thr Arg Asp Lys Asn Arg Arg Gly Glu Thr Cys Phe			
565	570	575	
ctg ttg acg aca ggt gat tac acg tgc gct tct gat gga gga atc agg			1776
Leu Leu Thr Thr Gly Asp Tyr Thr Cys Ala Ser Asp Gly Gly Ile Arg			
580	585	590	

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aaa gtg ttg tac aga att tat cat gga ttt ttg cct gct gaa aat ggg      1824
Lys Val Leu Tyr Arg Ile Tyr His Gly Phe Leu Pro Ala Glu Asn Gly
      595                      600                      605
aca ttg aga ttt agc cat tcc aag gat tgt act gga aac ttc tgc tac      1872
Thr Leu Arg Phe Ser His Ser Lys Asp Cys Thr Gly Asn Phe Cys Tyr
      610                      615                      620
tga                                                                    1875

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<210> 18
<211> 624
<212> PRT
<213> Rattus norvegicus

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<400> 18
Met Gly Lys Ile Glu Asn Asn Glu Arg Val Ile Leu Asn Val Gly Gly
1          5          10          15
Thr Arg His Glu Thr Tyr Arg Ser Thr Leu Lys Thr Leu Pro Gly Thr
      20          25          30
Arg Leu Ala Leu Leu Ala Ser Ser Glu Pro Gln Gly Asp Cys Leu Thr
      35          40          45
Ala Ala Gly Asp Lys Leu Gln Pro Leu Pro Pro Pro Leu Ser Pro Pro
      50          55          60
Pro Arg Pro Pro Pro Leu Ser Pro Val Pro Ser Gly Cys Phe Glu Gly
65          70          75          80
Gly Ala Gly Asn Cys Ser Ser His Gly Gly Asn Gly Ser Asp His Pro
      85          90          95
Gly Gly Gly Arg Glu Phe Phe Phe Asp Arg His Pro Gly Val Phe Ala
      100          105          110
Tyr Val Leu Asn Tyr Tyr Arg Thr Gly Lys Leu His Cys Pro Ala Asp
      115          120          125
Val Cys Gly Pro Leu Phe Glu Glu Glu Leu Ala Phe Trp Gly Ile Asp
      130          135          140
Glu Thr Asp Val Glu Pro Cys Cys Trp Met Thr Tyr Arg Gln His Arg
145          150          155          160
Asp Ala Glu Glu Ala Leu Asp Ile Phe Glu Thr Pro Asp Leu Ile Gly
      165          170          175
Gly Asp Pro Gly Asp Asp Glu Asp Leu Gly Gly Lys Arg Leu Gly Ile
      180          185          190
Glu Asp Ala Ala Gly Leu Gly Gly Pro Asp Gly Lys Ser Gly Arg Trp
      195          200          205
Arg Lys Leu Gln Pro Arg Met Trp Ala Leu Phe Glu Asp Pro Tyr Ser
210          215          220
Ser Arg Ala Ala Arg Phe Ile Ala Phe Ala Ser Leu Phe Phe Ile Leu
225          230          235          240
Val Ser Ile Thr Thr Phe Cys Leu Glu Thr His Glu Ala Phe Asn Ile
      245          250          255
Val Lys Asn Lys Thr Glu Pro Val Ile Asn Gly Thr Ser Ala Val Leu
260          265          270

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Gln Tyr Glu Ile Glu Thr Asp Pro Ala Leu Thr Tyr Val Glu Gly Val
 275 280 285
 Cys Val Val Trp Phe Thr Phe Glu Phe Leu Val Arg Ile Val Phe Ser
 290 295 300
 Pro Asn Lys Leu Glu Phe Ile Lys Asn Leu Leu Asn Ile Ile Asp Phe
 305 310 315 320
 Val Ala Ile Leu Pro Phe Tyr Leu Glu Val Gly Leu Ser Gly Leu Ser
 325 330 335
 Ser Lys Ala Ala Lys Asp Val Leu Gly Phe Leu Arg Val Val Arg Phe
 340 345 350
 Val Arg Ile Leu Arg Ile Phe Lys Leu Thr Arg His Phe Val Gly Leu
 355 360 365
 Arg Val Leu Gly His Thr Leu Arg Ala Ser Thr Asn Glu Phe Leu Leu
 370 375 380
 Leu Ile Ile Phe Leu Ala Leu Gly Val Leu Ile Phe Ala Thr Met Ile
 385 390 395 400
 Tyr Tyr Ala Glu Arg Val Gly Ala Gln Pro Asn Asp Pro Ser Ala Ser
 405 410 415
 Glu His Thr Gln Phe Lys Asn Ile Pro Ile Gly Phe Trp Trp Ala Val
 420 425 430
 Val Thr Met Thr Thr Leu Gly Tyr Gly Asp Met Tyr Pro Gln Thr Trp
 435 440 445
 Ser Gly Met Leu Val Gly Ala Leu Cys Ala Leu Ala Gly Val Leu Thr
 450 455 460
 Ile Ala Met Pro Val Pro Val Ile Val Asn Asn Phe Gly Met Tyr Tyr
 465 470 475 480
 Ser Leu Ala Met Ala Lys Gln Lys Leu Pro Arg Lys Arg Lys Lys His
 485 490 495
 Ile Pro Pro Ala Pro Leu Ala Ser Ser Pro Thr Phe Cys Lys Thr Glu
 500 505 510
 Leu Asn Met Ala Cys Asn Ser Thr Gln Ser Asp Thr Cys Leu Gly Lys
 515 520 525
 Glu Asn Arg Leu Leu Glu His Asn Arg Ser Val Leu Ser Gly Asp Asp
 530 535 540
 Ser Thr Gly Ser Glu Pro Pro Leu Ser Pro Pro Glu Arg Leu Pro Ile
 545 550 555 560
 Arg Arg Ser Ser Thr Arg Asp Lys Asn Arg Arg Gly Glu Thr Cys Phe
 565 570 575
 Leu Leu Thr Thr Gly Asp Tyr Thr Cys Ala Ser Asp Gly Gly Ile Arg
 580 585 590
 Lys Val Leu Tyr Arg Ile Tyr His Gly Phe Leu Pro Ala Glu Asn Gly
 595 600 605
 Thr Leu Arg Phe Ser His Ser Lys Asp Cys Thr Gly Asn Phe Cys Tyr
 610 615 620

<210> 19
 <211> 34
 <212> DNA

<213> Artificial Sequence

<220>

<223> primer

<400> 19

aaggtaccac catgggcaag atcgagaaca acga

34

<210> 20

<211> 31

<212> DNA

<213> Artificial Sequence

<220>

<223> primer

<400> 20

aactcgagca tgttttgtgc cttccccaag t

31

<210> 21

<211> 24

<212> DNA

<213> Artificial Sequence

<220>

<223> primer

<400> 21

gctggcccag gaagaaattt taga

24

<210> 22

<211> 24

<212> DNA

<213> Artificial Sequence

<220>

<223> primer

<400> 22

agaggaagca ggggccgtat ctct

24

<210> 23

<211> 23

<212> DNA

<213> Artificial Sequence

<220>

<223> primer

<400> 23

gaacatggct tgcaacagta ccc

23

<210> 24

<211> 23

<212> DNA

<213> Artificial Sequence

<220>

<223> primer

<400> 24

acttcagtca ggaccccatc ctc

23

<210> 25

<211> 24

<212> DNA

<213> Artificial Sequence

<220>

<223> primer

<400> 25

ccattggctc aagaagaggt gatt

24

<210> 26

<211> 24

<212> DNA

<213> Artificial Sequence

<220>

<223> primer

<400> 26

ggcatagtct gtgacaagga agca

24

<210> 27

<211> 24

<212> DNA

<213> Artificial Sequence

<220>

<223> primer

<400> 27

aagaggggtgt ggtcgagagg aaac

24

<210> 28

<211> 24

<212> DNA

<213> Artificial Sequence

<220>

<223> primer

<400> 28

aagagcacag gtgtgagaca ctgg

24

<210> 29

<211> 36

<212> DNA

<213> Artificial Sequence

<220>

<223> primer

<400> 29

aatctagagc cgccatgggc caaggggacg agagcg

36

<210> 30

<211> 32

<212> DNA

<213> Artificial Sequence

<220>

<223> primer

<400> 30

aactcgagac tggatctgga atcatcgcta ca

32

<210> 31

<211> 42

<212> DNA

<213> Artificial Sequence

<220>

<223> primer

<400> 31
 aagctagcca ccatgctgag ctcagtctgc gtctcgctct tc 42

<210> 32
 <211> 35
 <212> DNA
 <213> Artificial Sequence

<220>
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<400> 32
 aagaattcag ggggatatcc aggccgcggc gttgg 35

<210> 33
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 <213> Artificial Sequence

<220>
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<400> 33
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<210> 34
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<220>
 <223> primer

<400> 34
 aactcgagcc tcaaacacttt gccctcataa ag 32

<210> 35
 <211> 24
 <212> DNA
 <213> Artificial Sequence

<220>
 <223> primer

<400> 35

ggagacccaa gcagatccac ttta

24

<210> 36

<211> 24

<212> DNA

<213> Artificial Sequence

<220>

<223> primer

<400> 36

ggagagcaag acacgtgaat gaaa

24

<210> 37

<211> 24

<212> DNA

<213> Artificial Sequence

<220>

<223> primer

<400> 37

ctgttcgoga catgtogcat acag

24

<210> 38

<211> 25

<212> DNA

<213> Artificial Sequence

<220>

<223> primer

<400> 38

cacatgtatt gtgccttccc aagcc

25

<210> 39

<211> 1716

<212> DNA

<213> Xenopus laevis

<220>

<221> CDS

<222> (1)..(1716)

<400> 39

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48

Met	gly	Lys	Ile	asp	glu	asn	glu	Lys	Ile	Ile	Leu	asn	Val	gly	gly	
1				5					10					15		
acg	aga	cac	gag	act	tac	cga	agc	acc	tta	aag	aca	gtg	ccc	ggg	act	96
thr	arg	His	glu	thr	tyr	arg	Ser	thr	Leu	Lys	thr	Val	Pro	gly	thr	
			20					25						30		
cgc	ttg	gct	cta	ctt	gcc	tgt	gat	gct	ccc	agt	gac	cag	agg	ctg	gac	144
arg	Leu	ala	Leu	Leu	ala	cys	asp	ala	Pro	Ser	asp	gln	arg	Leu	asp	
			35					40						45		
cag	cag	aca	gtg	tcg	ggc	tcc	ttc	aac	atc	acc	tcc	aga	ggc	aat	gaa	192
gln	gln	thr	Val	Ser	gly	Ser	Phe	asn	Ile	thr	Ser	arg	gly	asn	glu	
			50				55				60					
ttc	ttc	ttc	gac	aga	cac	ccc	gga	gta	ttt	gcc	tat	gta	ctc	aac	tac	240
Phe	Phe	Phe	asp	arg	His	Pro	gly	Val	Phe	ala	tyr	Val	Leu	asn	tyr	
65					70						75				80	
tac	cgc	acc	ggc	aag	ctg	cac	tgc	ccc	gct	gat	gtg	tgc	ggg	ccc	ctc	288
tyr	arg	thr	gly	Lys	Leu	His	cys	Pro	ala	asp	Val	cys	gly	Pro	Leu	
				85					90					95		
ttt	gaa	gag	gag	ttg	gca	ttt	tgg	ggc	att	gat	gag	acg	gac	gtg	gag	336
Phe	glu	glu	glu	Leu	ala	Phe	trp	gly	Ile	asp	glu	thr	asp	Val	glu	
			100					105					110			
ccc	tgt	tgc	tgg	atg	acc	tat	cgc	caa	cac	cgg	gat	gca	gaa	gaa	gct	384
Pro	cys	cys	trp	Met	thr	tyr	arg	gln	His	arg	asp	ala	glu	glu	ala	
			115					120					125			
ttg	gac	agc	ttt	gaa	aat	ccc	gac	ctg	atc	aca	ggg	gaa	cct	cta	gat	432
Leu	asp	Ser	Phe	glu	asn	Pro	asp	Leu	Ile	thr	gly	glu	Pro	Leu	asp	
			130				135					140				
gaa	tat	gag	gag	gag	ttg	ggg	aag	aga	ctg	gca	att	gag	gac	gtg	gtg	480
glu	tyr	glu	glu	glu	Leu	gly	Lys	arg	Leu	ala	Ile	glu	asp	Val	Val	
145					150						155				160	
tgt	ccc	gat	ggc	aag	gtt	ggg	cgt	tgg	aga	aga	cta	agg	cct	cgc	ata	528
cys	Pro	asp	gly	Lys	Val	gly	arg	trp	arg	arg	Leu	arg	Pro	arg	Ile	
				165				170						175		
tgg	gct	tta	ttt	gaa	gat	ccc	tat	tct	tcc	aga	gcc	gcc	cgg	ttc	atc	576
trp	ala	Leu	Phe	glu	asp	Pro	tyr	Ser	Ser	arg	ala	ala	arg	Phe	Ile	
			180					185					190			
gcc	ttt	gct	tcc	ctg	ttc	ttc	att	ctg	gta	tct	ata	aca	acc	ttt	tgc	624
ala	Phe	ala	Ser	Leu	Phe	Phe	Ile	Leu	Val	Ser	Ile	thr	thr	Phe	cys	
			195				200					205				
ttg	gag	act	cat	gaa	gca	ttt	aat	acc	atc	att	aac	aaa	acg	gaa	act	672
Leu	glu	thr	His	glu	ala	Phe	asn	thr	Ile	Ile	asn	Lys	thr	glu	thr	

260	265	270	
aga aat ctt tta aat ata ata gat ttt gtg gca att ctg ccc ttt tat			864
arg asn Leu Leu asn Ile Ile asp Phe Val ala Ile Leu Pro Phe tyr			
275	280	285	
ttg gaa gtt gga cta agt ggg ctt tcc tcc aaa gct gct aag gat gtt			912
Leu glu Val gly Leu Ser gly Leu Ser Ser Lys ala ala Lys asp Val			
290	295	300	
ctc ggg ttc ctc agg gtt gta aga ttt gtt cgc atc ctt cga att ttt			960
Leu gly Phe Leu arg Val Val arg Phe Val arg Ile Leu arg Ile Phe			
305	310	315	320
aaa ctg acc cgc cat ttt gta gga ctt aga gtg ctg ggg cac aca ctt			1008
Lys Leu thr arg His Phe Val gly Leu arg Val Leu gly His thr Leu			
325	330	335	
cgt gcg agc act aat gaa ttt ttg ctc ctt att att ttt ttg gct ctg			1056
arg ala Ser thr asn glu Phe Leu Leu Ile Ile Phe Leu ala Leu			
340	345	350	
gga gtc ttg ata ttt gcc aca atg atc tat tac gct gaa aga ata ggt			1104
gly Val Leu Ile Phe ala thr Met Ile tyr tyr ala glu arg Ile gly			
355	360	365	
gcc agt cca agt gat cca tcg gca agt aaa cat aca caa ttc aaa aac			1152
ala Ser Pro Ser asp Pro Ser ala Ser Lys His thr gln Phe Lys asn			
370	375	380	
att cca att gga ttc tgg tgg gct gtg gta act atg act acc ctg gga			1200
Ile Pro Ile gly Phe trp trp ala Val Val thr Met thr thr Leu gly			
385	390	395	400
tat ggg gat atg tac cct cag act tgg tca ggg atg ttg gta gga gca			1248
tyr gly asp Met tyr Pro gln thr trp Ser gly Met Leu Val gly ala			
405	410	415	
tta tgt gct ttg gct ggt gta ctt aca ata gca atg cct gtc cca gtc			1296
Leu cys ala Leu ala gly Val Leu thr Ile ala Met Pro Val Pro Val			
420	425	430	
att gtt aac aac ttt gga atg tat tac tca ctt gct atg gca aaa cag			1344
Ile Val asn asn Phe gly Met tyr tyr Ser Leu ala Met ala Lys gln			
435	440	445	
aag ctt cca agg aaa aga aag aaa tac att cct cat gct cct cag gct			1392
Lys Leu Pro arg Lys arg Lys Lys tyr Ile Pro His ala Pro gln ala			
450	455	460	
gga tcc cct act ttc tgc aag atg gac cta agt att gga tgc aat agc			1440
gly Ser Pro thr Phe cys Lys Met asp Leu Ser Ile gly cys asn Ser			
465	470	475	480
aca cag gta gac aca tgt ctt gga aaa gac aac aga ctg atg gaa cac			1488
thr gln Val asp thr cys Leu gly Lys asp asn arg Leu Met glu His			
485	490	495	
aac atg tca ggt gaa gac agt tca gga agt gac cag cca ctt tcc cct			1536
asn Met Ser gly glu asp Ser Ser gly Ser asp gln Pro Leu Ser Pro			
500	505	510	
ggt gaa aga tat cct ata aga cgt tct agt acc cgc gat aaa aac aga			1584
gly glu arg tyr Pro Ile arg arg Ser Ser thr arg asp Lys asn arg			
515	520	525	

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agg acg gga act tgt ttc cta ctg acc aca ggt gaa tac acg tgc aat      1632
arg thr gly thr cys Phe Leu Leu thr thr gly glu tyr thr cys asn
    530                      535                      540
aca gat gga ggt ata cgg aaa gat aac tgc aaa gag gtt gtc att act      1680
thr asp gly gly Ile arg Lys asp asn cys Lys glu Val Val Ile thr
545                      550                      555                      560
ggt tac acg caa gca gag gcc aga tct ctt tca taa                      1716
gly tyr thr gln ala glu ala arg Ser Leu Ser
                      565                      570

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<210> 40
<211> 571
<212> PRT
<213> Xenopus laevis

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<400> 40
Met gly Lys Ile asp glu asn glu Lys Ile Ile Leu asn Val gly gly
1          5          10          15
thr arg His glu thr tyr arg Ser thr Leu Lys thr Val Pro gly thr
          20          25          30
arg Leu ala Leu Leu ala cys asp ala Pro Ser asp gln arg Leu asp
          35          40          45
gln gln thr Val Ser gly Ser Phe asn Ile thr Ser arg gly asn glu
          50          55          60
Phe Phe Phe asp arg His Pro gly Val Phe ala tyr Val Leu asn tyr
65          70          75          80
tyr arg thr gly Lys Leu His cys Pro ala asp Val cys gly Pro Leu
          85          90          95
Phe glu glu glu Leu ala Phe trp gly Ile asp glu thr asp Val glu
          100         105         110
Pro cys cys trp Met thr tyr arg gln His arg asp ala glu glu ala
          115         120         125
Leu asp Ser Phe glu asn Pro asp Leu Ile thr gly glu Pro Leu asp
          130         135         140
glu tyr glu glu glu Leu gly Lys arg Leu ala Ile glu asp Val Val
145         150         155         160
cys Pro asp gly Lys Val gly arg trp arg arg Leu arg Pro arg Ile
          165         170         175
trp ala Leu Phe glu asp Pro tyr Ser Ser arg ala ala arg Phe Ile
          180         185         190
ala Phe ala Ser Leu Phe Phe Ile Leu Val Ser Ile thr thr Phe cys
          195         200         205
Leu glu thr His glu ala Phe asn thr Ile Ile asn Lys thr glu thr
          210         215         220
Val asn asn gly thr glu Leu Ile Ser Leu Ile glu Ile glu thr asp
225         230         235         240
Pro ala Leu thr tyr Val glu gly Val cys Val Val trp Phe thr Phe
          245         250         255

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glu Phe Leu Val arg Val Ile Phe cys Pro asp Lys Leu glu Phe Ile
      260              265              270
arg asn Leu Leu asn Ile Ile asp Phe Val ala Ile Leu Pro Phe tyr
      275              280              285
Leu glu Val gly Leu Ser gly Leu Ser Ser Lys ala ala Lys asp Val
      290              295              300
Leu gly Phe Leu arg Val Val arg Phe Val arg Ile Leu arg Ile Phe
305              310              315              320
Lys Leu thr arg His Phe Val gly Leu arg Val Leu gly His thr Leu
      325              330              335
arg ala Ser thr asn glu Phe Leu Leu Leu Ile Ile Phe Leu ala Leu
      340              345              350
gly Val Leu Ile Phe ala thr Met Ile tyr tyr ala glu arg Ile gly
      355              360              365
ala Ser Pro Ser asp Pro Ser ala Ser Lys His thr gln Phe Lys asn
      370              375              380
Ile Pro Ile gly Phe trp trp ala Val Val thr Met thr thr Leu gly
385              390              395              400
tyr gly asp Met tyr Pro gln thr trp Ser gly Met Leu Val gly ala
      405              410              415
Leu cys ala Leu ala gly Val Leu thr Ile ala Met Pro Val Pro Val
      420              425              430
Ile Val asn asn Phe gly Met tyr tyr Ser Leu ala Met ala Lys gln
      435              440              445
Lys Leu Pro arg Lys arg Lys Lys tyr Ile Pro His ala Pro gln ala
      450              455              460
gly Ser Pro thr Phe cys Lys Met asp Leu Ser Ile gly cys asn Ser
465              470              475              480
thr gln Val asp thr cys Leu gly Lys asp asn arg Leu Met glu His
      485              490              495
asn Met Ser gly glu asp Ser Ser gly Ser asp gln Pro Leu Ser Pro
      500              505              510
gly glu arg tyr Pro Ile arg arg Ser Ser thr arg asp Lys asn arg
      515              520              525
arg thr gly thr cys Phe Leu Leu thr thr gly glu tyr thr cys asn
      530              535              540
thr asp gly gly Ile arg Lys asp asn cys Lys glu Val Val Ile thr
545              550              555              560
gly tyr thr gln ala glu ala arg Ser Leu Ser
      565              570

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<210> 41
<211> 36
<212> DNA
<213> Artificial Sequence

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<220>
<223> primer

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<400> 41
aaagctagcc gccatgggta agatcgacga gaacga 36

<210> 42
<211> 37
<212> DNA
<213> Artificial Sequence

<220>
<223> primer

<400> 42
aaactcgagc acatgtattg tgccttccca agccatt 37

<210> 43
<211> 25
<212> DNA
<213> Artificial Sequence

<220>
<223> primer

<400> 43
atgcattagt gcactggcca atatc 25

<210> 44
<211> 24
<212> DNA
<213> Artificial Sequence

<220>
<223> primer

<400> 44
ggctctagta ccaagcagcg attc 24

<210> 45
<211> 23
<212> DNA
<213> Artificial Sequence

<220>
<223> primer

<400> 45

cacagacgct gaccatgaat gtg

23

<210> 46

<211> 1929

<212> DNA

<213> Mus musculus

<220>

<221> CDS

<222> (1)..(1929)

<400> 46

atg ggc aag atc gag agc aac gag agg gtg atc ctc aat gtc ggg ggt	48
Met Gly Lys Ile Glu Ser Asn Glu Arg Val Ile Leu Asn Val Gly Gly	
1 5 10 15	
acc agg cac gaa acc tac cgc agc acc ctc aag acc ctg cct gga act	96
Thr Arg His Glu Thr Tyr Arg Ser Thr Leu Lys Thr Leu Pro Gly Thr	
20 25 30	
cgc ctg gcc ctt ctt gcc tcc tct gaa cct cag ggc gac tgc ctg act	144
Arg Leu Ala Leu Leu Ala Ser Ser Glu Pro Gln Gly Asp Cys Leu Thr	
35 40 45	
gcg gcc ggg gac aag ctg caa ccg ctg ccc cct ccg ctg tct ccg ccg	192
Ala Ala Gly Asp Lys Leu Gln Pro Leu Pro Pro Pro Leu Ser Pro Pro	
50 55 60	
cca cga ccg cct ccc ttg tcc cct gtc ccc agc ggc tgc ttc gag ggc	240
Pro Arg Pro Pro Pro Leu Ser Pro Val Pro Ser Gly Cys Phe Glu Gly	
65 70 75 80	
ggc gca ggc aac tgc agt tcg cac ggt ggc aac ggc ggc aac ggc ggc	288
Gly Ala Gly Asn Cys Ser Ser His Gly Gly Asn Gly Gly Asn Gly Gly	
85 90 95	
agc gac cac cct ggg gga ggc cgc gaa ttc ttc ttc gat cgc cac cca	336
Ser Asp His Pro Gly Gly Gly Arg Glu Phe Phe Phe Asp Arg His Pro	
100 105 110	
gga gta ttc gcc tat gtg ctc aat tac tac cgc acg ggc aag ctg cac	384
Gly Val Phe Ala Tyr Val Leu Asn Tyr Tyr Arg Thr Gly Lys Leu His	
115 120 125	
tgc ccc gcc gac gtg tgc ggg ccg ctc ttc gag gaa gag ctg gct ttc	432
Cys Pro Ala Asp Val Cys Gly Pro Leu Phe Glu Glu Glu Leu Ala Phe	
130 135 140	
tgg ggc atc gat gag acc gac gtg gag ccc tgc tgc tgg atg acc tac	480
Trp Gly Ile Asp Glu Thr Asp Val Glu Pro Cys Cys Trp Met Thr Tyr	
145 150 155 160	
agg cag cac cgg gac gcg gag gag gcc ctg gac atc ttt gag aca ccc	528
Arg Gln His Arg Asp Ala Glu Glu Ala Leu Asp Ile Phe Glu Thr Pro	
165 170 175	
gac ctc atc ggg ggc gac cct ggt gat gat gag gac cta gcg gcc aag	576
Asp Leu Ile Gly Gly Asp Pro Gly Asp Asp Glu Asp Leu Ala Ala Lys	

180	185	190	
aga ttg ggc att gag gat gct gcg ggg ctg gga gga ccc gat ggc aag			624
Arg Leu Gly Ile Glu Asp Ala Ala Gly Leu Gly Gly Pro Asp Gly Lys			
195	200	205	
tca ggc cgc tgg agg aag ctg cag cct cgc atg tgg gct ctt ttt gag			672
Ser Gly Arg Trp Arg Lys Leu Gln Pro Arg Met Trp Ala Leu Phe Glu			
210	215	220	
gac ccc tac tca tct aga gcc gct agg ttt att gct ttt gct tct ttg			720
Asp Pro Tyr Ser Ser Arg Ala Ala Arg Phe Ile Ala Phe Ala Ser Leu			
225	230	235	240
ttc ttc att ttg gtt tcc atc aca acc ttt tgc ctg gag aca cat gaa			768
Phe Phe Ile Leu Val Ser Ile Thr Thr Phe Cys Leu Glu Thr His Glu			
245	250	255	
gct ttc aat att gtt aaa aac aag acg gag ccc gtc atc aat ggc acc			816
Ala Phe Asn Ile Val Lys Asn Lys Thr Glu Pro Val Ile Asn Gly Thr			
260	265	270	
agc ccg gtc ctc cag tac gaa atc gaa acg gat ccc gcc ctg acg tac			864
Ser Pro Val Leu Gln Tyr Glu Ile Glu Thr Asp Pro Ala Leu Thr Tyr			
275	280	285	
gtg gaa gga gta tgt gtg gtg tgg ttt acg ttt gaa ttt tta gtc cga			912
Val Glu Gly Val Cys Val Val Trp Phe Thr Phe Glu Phe Leu Val Arg			
290	295	300	
att gtt ttc tca ccc aat aaa ctt gaa ttc atc aaa aat ctc ttg aac			960
Ile Val Phe Ser Pro Asn Lys Leu Glu Phe Ile Lys Asn Leu Leu Asn			
305	310	315	320
atc att gac ttt gtg gcc atc ctc ccc ttc tac cta gag gtg gga ctc			1008
Ile Ile Asp Phe Val Ala Ile Leu Pro Phe Tyr Leu Glu Val Gly Leu			
325	330	335	
agc ggg ctg tcc tcc aaa gcg gcc aaa gat gtg ctc ggc ttt ctc agg			1056
Ser Gly Leu Ser Ser Lys Ala Ala Lys Asp Val Leu Gly Phe Leu Arg			
340	345	350	
gtg gtt agg ttt gtg agg atc ctg aga atc ttc aag ctc acc cgc cat			1104
Val Val Arg Phe Val Arg Ile Leu Arg Ile Phe Lys Leu Thr Arg His			
355	360	365	
ttc gta ggt ctg agg gtg ctc gga cat act ctt cgg gcg agc acc aac			1152
Phe Val Gly Leu Arg Val Leu Gly His Thr Leu Arg Ala Ser Thr Asn			
370	375	380	
gaa ttt ttg ttg ctg atc atc ttc ctg gcg ctg gga gtt ttg ata ttc			1200
Glu Phe Leu Leu Leu Ile Ile Phe Leu Ala Leu Gly Val Leu Ile Phe			
385	390	395	400
gct acg atg atc tac tac gct gag aga gta ggg gct cag ccc aat gac			1248
Ala Thr Met Ile Tyr Tyr Ala Glu Arg Val Gly Ala Gln Pro Asn Asp			
405	410	415	
cct tca gct agt gag cac acg cag ttc aaa aac atc ccc att ggt ttc			1296
Pro Ser Ala Ser Glu His Thr Gln Phe Lys Asn Ile Pro Ile Gly Phe			
420	425	430	
tgg tgg gcc gta gtg acc atg act acc tta ggt tac ggg gat atg tac			1344
Trp Trp Ala Val Val Thr Met Thr Thr Leu Gly Tyr Gly Asp Met Tyr			
435	440	445	

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ccc caa aca tgg tca ggg atg ttg gtg ggg gcc ttg tgt gcc ctg gcc      1392
Pro Gln Thr Trp Ser Gly Met Leu Val Gly Ala Leu Cys Ala Leu Ala
    450                      455                      460
gga gtg ctg aca ata gcc atg cct gtg cct gtc att gtc aac aat ttt      1440
Gly Val Leu Thr Ile Ala Met Pro Val Pro Val Ile Val Asn Asn Phe
465                      470                      475                      480
gga atg tac tac tcc ttg gca atg gcg aag cag aaa ctt cca aga aag      1488
Gly Met Tyr Tyr Ser Leu Ala Met Ala Lys Gln Lys Leu Pro Arg Lys
    485                      490                      495
aga aag aag cat att cct cct gcc cct ctg gca agc tcg cct aca ttt      1536
Arg Lys Lys His Ile Pro Pro Ala Pro Leu Ala Ser Ser Pro Thr Phe
    500                      505                      510
tgc aag aca gaa ttg aac atg gct tgc aac agt acc cag agt gac aca      1584
Cys Lys Thr Glu Leu Asn Met Ala Cys Asn Ser Thr Gln Ser Asp Thr
    515                      520                      525
tgt ctg ggc aaa gaa aac cgg ctt ctg gaa cat aac aga tca gtg tta      1632
Cys Leu Gly Lys Glu Asn Arg Leu Leu Glu His Asn Arg Ser Val Leu
    530                      535                      540
tca ggt gac gac agt aca gga agt gag ccg cca tta tca cct cca gaa      1680
Ser Gly Asp Asp Ser Thr Gly Ser Glu Pro Pro Leu Ser Pro Pro Glu
545                      550                      555                      560
agg ctc cct atc aga cgc tct agt acc aga gac aaa aac aga aga ggg      1728
Arg Leu Pro Ile Arg Arg Ser Ser Thr Arg Asp Lys Asn Arg Arg Gly
    565                      570                      575
gaa acg tgt ttc ctg ttg acg aca ggt gat tac acg tgc gct tct gat      1776
Glu Thr Cys Phe Leu Leu Thr Thr Gly Asp Tyr Thr Cys Ala Ser Asp
    580                      585                      590
gga gga atc agg aaa gga tat gaa aaa tcc cga agc tta aac aac ata      1824
Gly Gly Ile Arg Lys Gly Tyr Glu Lys Ser Arg Ser Leu Asn Asn Ile
    595                      600                      605
gcg ggc ttg gca ggc aat gct ctg aga ctc tct cca gta acg tcc ccc      1872
Ala Gly Leu Ala Gly Asn Ala Leu Arg Leu Ser Pro Val Thr Ser Pro
    610                      615                      620
tac aac tct ccg tgt cct ctg agg cgc tct cgg tct ccc atc cca tct      1920
Tyr Asn Ser Pro Cys Pro Leu Arg Arg Ser Arg Ser Pro Ile Pro Ser
625                      630                      635                      640
atc ttg taa
Ile Leu
1929

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<210> 47
<211> 642
<212> PRT
<213> Mus musculus

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<400> 47
Met Gly Lys Ile Glu Ser Asn Glu Arg Val Ile Leu Asn Val Gly Gly
1          5          10          15

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Thr Arg His Glu Thr Tyr Arg Ser Thr Leu Lys Thr Leu Pro Gly Thr
 20 25 30
 Arg Leu Ala Leu Leu Ala Ser Ser Glu Pro Gln Gly Asp Cys Leu Thr
 35 40 45
 Ala Ala Gly Asp Lys Leu Gln Pro Leu Pro Pro Pro Leu Ser Pro Pro
 50 55 60
 Pro Arg Pro Pro Pro Leu Ser Pro Val Pro Ser Gly Cys Phe Glu Gly
 65 70 75 80
 Gly Ala Gly Asn Cys Ser Ser His Gly Gly Asn Gly Gly Asn Gly Gly
 85 90 95
 Ser Asp His Pro Gly Gly Gly Arg Glu Phe Phe Phe Asp Arg His Pro
 100 105 110
 Gly Val Phe Ala Tyr Val Leu Asn Tyr Tyr Arg Thr Gly Lys Leu His
 115 120 125
 Cys Pro Ala Asp Val Cys Gly Pro Leu Phe Glu Glu Glu Leu Ala Phe
 130 135 140
 Trp Gly Ile Asp Glu Thr Asp Val Glu Pro Cys Cys Trp Met Thr Tyr
 145 150 155 160
 Arg Gln His Arg Asp Ala Glu Glu Ala Leu Asp Ile Phe Glu Thr Pro
 165 170 175
 Asp Leu Ile Gly Gly Asp Pro Gly Asp Asp Glu Asp Leu Ala Ala Lys
 180 185 190
 Arg Leu Gly Ile Glu Asp Ala Ala Gly Leu Gly Gly Pro Asp Gly Lys
 195 200 205
 Ser Gly Arg Trp Arg Lys Leu Gln Pro Arg Met Trp Ala Leu Phe Glu
 210 215 220
 Asp Pro Tyr Ser Ser Arg Ala Ala Arg Phe Ile Ala Phe Ala Ser Leu
 225 230 235 240
 Phe Phe Ile Leu Val Ser Ile Thr Thr Phe Cys Leu Glu Thr His Glu
 245 250 255
 Ala Phe Asn Ile Val Lys Asn Lys Thr Glu Pro Val Ile Asn Gly Thr
 260 265 270
 Ser Pro Val Leu Gln Tyr Glu Ile Glu Thr Asp Pro Ala Leu Thr Tyr
 275 280 285
 Val Glu Gly Val Cys Val Val Trp Phe Thr Phe Glu Phe Leu Val Arg
 290 295 300
 Ile Val Phe Ser Pro Asn Lys Leu Glu Phe Ile Lys Asn Leu Leu Asn
 305 310 315 320
 Ile Ile Asp Phe Val Ala Ile Leu Pro Phe Tyr Leu Glu Val Gly Leu
 325 330 335
 Ser Gly Leu Ser Ser Lys Ala Ala Lys Asp Val Leu Gly Phe Leu Arg
 340 345 350
 Val Val Arg Phe Val Arg Ile Leu Arg Ile Phe Lys Leu Thr Arg His
 355 360 365
 Phe Val Gly Leu Arg Val Leu Gly His Thr Leu Arg Ala Ser Thr Asn
 370 375 380
 Glu Phe Leu Leu Leu Ile Ile Phe Leu Ala Leu Gly Val Leu Ile Phe
 385 390 395 400
 Ala Thr Met Ile Tyr Tyr Ala Glu Arg Val Gly Ala Gln Pro Asn Asp

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              405              410              415
Pro Ser Ala Ser Glu His Thr Gln Phe Lys Asn Ile Pro Ile Gly Phe
              420              425              430
Trp Trp Ala Val Val Thr Met Thr Thr Leu Gly Tyr Gly Asp Met Tyr
              435              440              445
Pro Gln Thr Trp Ser Gly Met Leu Val Gly Ala Leu Cys Ala Leu Ala
              450              455              460
Gly Val Leu Thr Ile Ala Met Pro Val Pro Val Ile Val Asn Asn Phe
465              470              475              480
Gly Met Tyr Tyr Ser Leu Ala Met Ala Lys Gln Lys Leu Pro Arg Lys
              485              490              495
Arg Lys Lys His Ile Pro Pro Ala Pro Leu Ala Ser Ser Pro Thr Phe
              500              505              510
Cys Lys Thr Glu Leu Asn Met Ala Cys Asn Ser Thr Gln Ser Asp Thr
              515              520              525
Cys Leu Gly Lys Glu Asn Arg Leu Leu Glu His Asn Arg Ser Val Leu
              530              535              540
Ser Gly Asp Asp Ser Thr Gly Ser Glu Pro Pro Leu Ser Pro Pro Glu
545              550              555              560
Arg Leu Pro Ile Arg Arg Ser Ser Thr Arg Asp Lys Asn Arg Arg Gly
              565              570              575
Glu Thr Cys Phe Leu Leu Thr Thr Gly Asp Tyr Thr Cys Ala Ser Asp
              580              585              590
Gly Gly Ile Arg Lys Gly Tyr Glu Lys Ser Arg Ser Leu Asn Asn Ile
              595              600              605
Ala Gly Leu Ala Gly Asn Ala Leu Arg Leu Ser Pro Val Thr Ser Pro
              610              615              620
Tyr Asn Ser Pro Cys Pro Leu Arg Arg Ser Arg Ser Pro Ile Pro Ser
625              630              635              640
Ile Leu

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<210> 48
<211> 1854
<212> DNA
<213> Mus musculus

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<220>
<221> CDS
<222> (1)..(1854)

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Met Gly Lys Ile Glu Ser Asn Glu Arg Val Ile Leu Asn Val Gly Gly
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acc agg cac gaa acc tac cgc agc acc ctc aag acc ctg cct gga act      96
Thr Arg His Glu Thr Tyr Arg Ser Thr Leu Lys Thr Leu Pro Gly Thr
              20              25              30
cgc ctg gcc ctt ctt gcc tcc tct gaa cct cag ggc gac tgc ctg act      144

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Arg	Leu	Ala	Leu	Leu	Ala	Ser	Ser	Glu	Pro	Gln	Gly	Asp	Cys	Leu	Thr		
	35						40					45					
gcg	gcc	ggg	gac	aag	ctg	caa	ccg	ctg	ccc	cct	ccg	ctg	tct	ccg	ccg	192	
Ala	Ala	Gly	Asp	Lys	Leu	Gln	Pro	Leu	Pro	Pro	Pro	Leu	Ser	Pro	Pro		
	50					55					60						
cca	cga	ccg	cct	ccc	ttg	tcc	cct	gtc	ccc	agc	ggc	tgc	ttc	gag	ggc	240	
Pro	Arg	Pro	Pro	Pro	Leu	Ser	Pro	Val	Pro	Ser	Gly	Cys	Phe	Glu	Gly		
65					70				75					80			
ggc	gca	ggc	aac	tgc	agt	tcg	cac	ggt	ggc	aac	ggc	ggc	aac	ggc	ggc	288	
Gly	Ala	Gly	Asn	Cys	Ser	Ser	His	Gly	Gly	Asn	Gly	Gly	Asn	Gly	Gly		
			85					90					95				
agc	gac	cac	cct	ggg	gga	ggc	cgc	gaa	ttc	ttc	ttc	gat	cgc	cac	cca	336	
Ser	Asp	His	Pro	Gly	Gly	Gly	Arg	Glu	Phe	Phe	Phe	Asp	Arg	His	Pro		
			100					105					110				
gga	gta	ttc	gcc	tat	gtg	ctc	aat	tac	tac	cgc	acg	ggc	aag	ctg	cac	384	
Gly	Val	Phe	Ala	Tyr	Val	Leu	Asn	Tyr	Tyr	Arg	Thr	Gly	Lys	Leu	His		
		115				120						125					
tgc	ccc	gcc	gac	gtg	tgc	ggg	ccg	ctc	ttc	gag	gaa	gag	ctg	gct	ttc	432	
Cys	Pro	Ala	Asp	Val	Cys	Gly	Pro	Leu	Phe	Glu	Glu	Glu	Leu	Ala	Phe		
		130				135						140					
tgg	ggc	atc	gat	gag	acc	gac	gtg	gag	ccc	tgc	tgc	tgg	atg	acc	tac	480	
Trp	Gly	Ile	Asp	Glu	Thr	Asp	Val	Glu	Pro	Cys	Cys	Trp	Met	Thr	Tyr		
145					150				155					160			
agg	cag	cac	cgg	gac	gcg	gag	gag	gcc	ctg	gac	atc	ttt	gag	aca	ccc	528	
Arg	Gln	His	Arg	Asp	Ala	Glu	Glu	Ala	Leu	Asp	Ile	Phe	Glu	Thr	Pro		
				165				170				175					
gac	ctc	atc	ggg	ggc	gac	cct	ggt	gat	gat	gag	gac	cta	gcg	gcc	aag	576	
Asp	Leu	Ile	Gly	Gly	Asp	Pro	Gly	Asp	Asp	Glu	Asp	Leu	Ala	Ala	Lys		
			180					185				190					
aga	ttg	ggc	att	gag	gat	gct	gcg	ggg	ctg	gga	gga	ccc	gat	ggc	aag	624	
Arg	Leu	Gly	Ile	Glu	Asp	Ala	Ala	Gly	Leu	Gly	Gly	Pro	Asp	Gly	Lys		
		195				200						205					
tca	ggc	cgc	tgg	agg	aag	ctg	cag	cct	cgc	atg	tgg	gct	ctt	ttt	gag	672	
Ser	Gly	Arg	Trp	Arg	Lys	Leu	Gln	Pro	Arg	Met	Trp	Ala	Leu	Phe	Glu		
		210				215						220					
gac	ccc	tac	tca	tct	aga	gcc	gct	agg	ttt	att	gct	ttt	gct	tct	ttg	720	
Asp	Pro	Tyr	Ser	Ser	Arg	Ala	Ala	Arg	Phe	Ile	Ala	Phe	Ala	Ser	Leu		
225					230				235					240			
ttc	ttc	att	ttg	gtt	tcc	atc	aca	acc	ttt	tgc	ctg	gag	aca	cat	gaa	768	
Phe	Phe	Ile	Leu	Val	Ser	Ile	Thr	Thr	Phe	Cys	Leu	Glu	Thr	His	Glu		
				245					250					255			
gct	ttc	aat	att	gtt	aaa	aac	aag	acg	gag	ccc	gtc	atc	aat	ggc	acc	816	
Ala	Phe	Asn	Ile	Val	Lys	Asn	Lys	Thr	Glu	Pro	Val	Ile	Asn	Gly	Thr		
		260						265					270				
agc	ccg	gtc	ctc	cag	tac	gaa	atc	gaa	acg	gat	ccc	gcc	ctg	acg	tac	864	
Ser	Pro	Val	Leu	Gln	Tyr	Glu	Ile	Glu	Thr	Asp	Pro	Ala	Leu	Thr	Tyr		
		275						280					285				
gtg	gaa	gga	gta	tgt	gtg	gtg	tgg	ttt	acg	ttt	gaa	ttt	tta	gtc	cga	912	
Val	Glu	Gly	Val	Cys	Val	Val	Trp	Phe	Thr	Phe	Glu	Phe	Leu	Val	Arg		

290	295	300	
att gtt ttc tca ccc aat aaa ctt gaa ttc atc aaa aat ctc ttg aac			960
Ile Val Phe Ser Pro Asn Lys Leu Glu Phe Ile Lys Asn Leu Leu Asn			
305	310	315	320
atc att gac ttt gtg gcc atc ctc ccc ttc tac cta gag gtg gga ctc			1008
Ile Ile Asp Phe Val Ala Ile Leu Pro Phe Tyr Leu Glu Val Gly Leu			
	325	330	335
agc ggg ctg tcc tcc aaa gcg gcc aaa gat gtg ctc ggc ttt ctc agg			1056
Ser Gly Leu Ser Ser Lys Ala Ala Lys Asp Val Leu Gly Phe Leu Arg			
	340	345	350
gtg gtt agg ttt gtg agg atc ctg aga atc ttc aag ctc acc cgc cat			1104
Val Val Arg Phe Val Arg Ile Leu Arg Ile Phe Lys Leu Thr Arg His			
	355	360	365
ttc gta ggt ctg agg gtg ctc gga cat act ctt cgg gcg agc acc aac			1152
Phe Val Gly Leu Arg Val Leu Gly His Thr Leu Arg Ala Ser Thr Asn			
	370	375	380
gaa ttt ttg ttg ctg atc atc ttc ctg gcg ctg gga gtt ttg ata ttc			1200
Glu Phe Leu Leu Leu Ile Ile Phe Leu Ala Leu Gly Val Leu Ile Phe			
	385	390	395
gct acg atg atc tac tac gct gag aga gta ggg gct cag ccc aat gac			1248
Ala Thr Met Ile Tyr Tyr Ala Glu Arg Val Gly Ala Gln Pro Asn Asp			
	405	410	415
cct tca gct agt gag cac acg cag ttc aaa aac atc ccc att ggt ttc			1296
Pro Ser Ala Ser Glu His Thr Gln Phe Lys Asn Ile Pro Ile Gly Phe			
	420	425	430
tgg tgg gcc gta gtg acc atg act acc tta ggt tac ggg gat atg tac			1344
Trp Trp Ala Val Val Thr Met Thr Thr Leu Gly Tyr Gly Asp Met Tyr			
	435	440	445
ccc caa aca tgg tca ggg atg ttg gtg ggg gcc ttg tgt gcc ctg gcc			1392
Pro Gln Thr Trp Ser Gly Met Leu Val Gly Ala Leu Cys Ala Leu Ala			
	450	455	460
gga gtg ctg aca ata gcc atg cct gtg cct gtc att gtc aac aat ttt			1440
Gly Val Leu Thr Ile Ala Met Pro Val Pro Val Ile Val Asn Asn Phe			
	465	470	475
gga atg tac tac tcc ttg gca atg gcg aag cag aaa ctt cca aga aag			1488
Gly Met Tyr Tyr Ser Leu Ala Met Ala Lys Gln Lys Leu Pro Arg Lys			
	485	490	495
aga aag aag cat att cct cct gcc cct ctg gca agc tcg cct aca ttt			1536
Arg Lys Lys His Ile Pro Pro Ala Pro Leu Ala Ser Ser Pro Thr Phe			
	500	505	510
tgc aag aca gaa ttg aac atg gct tgc aac agt acc cag agt gac aca			1584
Cys Lys Thr Glu Leu Asn Met Ala Cys Asn Ser Thr Gln Ser Asp Thr			
	515	520	525
tgt ctg ggc aaa gaa aac cgg ctt ctg gaa cat aac aga tca gtg tta			1632
Cys Leu Gly Lys Glu Asn Arg Leu Leu Glu His Asn Arg Ser Val Leu			
	530	535	540
tca ggt gac gac agt aca gga agt gag ccg cca tta tca cct cca gaa			1680
Ser Gly Asp Asp Ser Thr Gly Ser Glu Pro Pro Leu Ser Pro Pro Glu			
	545	550	555
			560

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agg ctc cct atc aga cgc tct agt acc aga gac aaa aac aga aga ggg      1728
Arg Leu Pro Ile Arg Arg Ser Ser Thr Arg Asp Lys Asn Arg Arg Gly
                    565                    570                    575
gaa acg tgt ttc ctg ttg acg aca ggt gat tac acg tgc gct tct gat      1776
Glu Thr Cys Phe Leu Leu Thr Thr Gly Asp Tyr Thr Cys Ala Ser Asp
                    580                    585                    590
gga gga atc agg aaa gat aac tgc aaa gag gtt gtc att act ggt tac      1824
Gly Gly Ile Arg Lys Asp Asn Cys Lys Glu Val Val Ile Thr Gly Tyr
                    595                    600                    605
acg caa gcc gag gcc aga tct ctt act taa      1854
Thr Gln Ala Glu Ala Arg Ser Leu Thr
        610                    615

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<210> 49
<211> 617
<212> PRT
<213> Mus musculus

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<400> 49
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Thr Arg His Glu Thr Tyr Arg Ser Thr Leu Lys Thr Leu Pro Gly Thr
                20                    25                    30
Arg Leu Ala Leu Leu Ala Ser Ser Glu Pro Gln Gly Asp Cys Leu Thr
                35                    40                    45
Ala Ala Gly Asp Lys Leu Gln Pro Leu Pro Pro Pro Leu Ser Pro Pro
                50                    55                    60
Pro Arg Pro Pro Pro Leu Ser Pro Val Pro Ser Gly Cys Phe Glu Gly
65                    70                    75                    80
Gly Ala Gly Asn Cys Ser Ser His Gly Gly Asn Gly Gly Asn Gly Gly
                85                    90                    95
Ser Asp His Pro Gly Gly Gly Arg Glu Phe Phe Phe Asp Arg His Pro
                100                    105                    110
Gly Val Phe Ala Tyr Val Leu Asn Tyr Tyr Arg Thr Gly Lys Leu His
                115                    120                    125
Cys Pro Ala Asp Val Cys Gly Pro Leu Phe Glu Glu Glu Leu Ala Phe
                130                    135                    140
Trp Gly Ile Asp Glu Thr Asp Val Glu Pro Cys Cys Trp Met Thr Tyr
145                    150                    155                    160
Arg Gln His Arg Asp Ala Glu Glu Ala Leu Asp Ile Phe Glu Thr Pro
                165                    170                    175
Asp Leu Ile Gly Gly Asp Pro Gly Asp Asp Glu Asp Leu Ala Ala Lys
                180                    185                    190
Arg Leu Gly Ile Glu Asp Ala Ala Gly Leu Gly Gly Pro Asp Gly Lys
                195                    200                    205
Ser Gly Arg Trp Arg Lys Leu Gln Pro Arg Met Trp Ala Leu Phe Glu
                210                    215                    220
Asp Pro Tyr Ser Ser Arg Ala Ala Arg Phe Ile Ala Phe Ala Ser Leu

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225		230		235		240
Phe Phe Ile Leu Val Ser Ile Thr Thr Phe Cys Leu Glu Thr His Glu						
	245		250		255	
Ala Phe Asn Ile Val Lys Asn Lys Thr Glu Pro Val Ile Asn Gly Thr						
	260		265		270	
Ser Pro Val Leu Gln Tyr Glu Ile Glu Thr Asp Pro Ala Leu Thr Tyr						
	275		280		285	
Val Glu Gly Val Cys Val Val Trp Phe Thr Phe Glu Phe Leu Val Arg						
	290		295		300	
Ile Val Phe Ser Pro Asn Lys Leu Glu Phe Ile Lys Asn Leu Leu Asn						
305		310		315		320
Ile Ile Asp Phe Val Ala Ile Leu Pro Phe Tyr Leu Glu Val Gly Leu						
	325		330		335	
Ser Gly Leu Ser Ser Lys Ala Ala Lys Asp Val Leu Gly Phe Leu Arg						
	340		345		350	
Val Val Arg Phe Val Arg Ile Leu Arg Ile Phe Lys Leu Thr Arg His						
	355		360		365	
Phe Val Gly Leu Arg Val Leu Gly His Thr Leu Arg Ala Ser Thr Asn						
	370		375		380	
Glu Phe Leu Leu Leu Ile Ile Phe Leu Ala Leu Gly Val Leu Ile Phe						
385		390		395		400
Ala Thr Met Ile Tyr Tyr Ala Glu Arg Val Gly Ala Gln Pro Asn Asp						
	405		410		415	
Pro Ser Ala Ser Glu His Thr Gln Phe Lys Asn Ile Pro Ile Gly Phe						
	420		425		430	
Trp Trp Ala Val Val Thr Met Thr Thr Leu Gly Tyr Gly Asp Met Tyr						
	435		440		445	
Pro Gln Thr Trp Ser Gly Met Leu Val Gly Ala Leu Cys Ala Leu Ala						
	450		455		460	
Gly Val Leu Thr Ile Ala Met Pro Val Pro Val Ile Val Asn Asn Phe						
465		470		475		480
Gly Met Tyr Tyr Ser Leu Ala Met Ala Lys Gln Lys Leu Pro Arg Lys						
	485		490		495	
Arg Lys Lys His Ile Pro Pro Ala Pro Leu Ala Ser Ser Pro Thr Phe						
	500		505		510	
Cys Lys Thr Glu Leu Asn Met Ala Cys Asn Ser Thr Gln Ser Asp Thr						
	515		520		525	
Cys Leu Gly Lys Glu Asn Arg Leu Leu Glu His Asn Arg Ser Val Leu						
	530		535		540	
Ser Gly Asp Asp Ser Thr Gly Ser Glu Pro Pro Leu Ser Pro Pro Glu						
545		550		555		560
Arg Leu Pro Ile Arg Arg Ser Ser Thr Arg Asp Lys Asn Arg Arg Gly						
	565		570		575	
Glu Thr Cys Phe Leu Leu Thr Thr Gly Asp Tyr Thr Cys Ala Ser Asp						
	580		585		590	
Gly Gly Ile Arg Lys Asp Asn Cys Lys Glu Val Val Ile Thr Gly Tyr						
	595		600		605	
Thr Gln Ala Glu Ala Arg Ser Leu Thr						
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<210> 50
 <211> 1845
 <212> DNA
 <213> Mus musculus

<220>
 <221> CDS
 <222> (1)..(1845)

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 acc agg cac gaa acc tac cgc agc acc ctc aag acc ctg cct gga act 96
 Thr Arg His Glu Thr Tyr Arg Ser Thr Leu Lys Thr Leu Pro Gly Thr
 20 25 30
 cgc ctg gcc ctt ctt gcc tcc tct gaa cct cag ggc gac tgc ctg act 144
 Arg Leu Ala Leu Leu Ala Ser Ser Glu Pro Gln Gly Asp Cys Leu Thr
 35 40 45
 gcg gcc ggg gac aag ctg caa ccg ctg ccc cct ccg ctg tct ccg ccg 192
 Ala Ala Gly Asp Lys Leu Gln Pro Leu Pro Pro Pro Leu Ser Pro Pro
 50 55 60
 cca cga ccg cct ccc ttg tcc cct gtc ccc agc ggc tgc ttc gag ggc 240
 Pro Arg Pro Pro Pro Leu Ser Pro Val Pro Ser Gly Cys Phe Glu Gly
 65 70 75 80
 ggc gca ggc aac tgc agt tcg cac ggt ggc aac ggc ggc aac ggc ggc 288
 Gly Ala Gly Asn Cys Ser Ser His Gly Gly Asn Gly Gly Asn Gly Gly
 85 90 95
 agc gac cac cct ggg gga ggc cgc gaa ttc ttc ttc gat cgc cac cca 336
 Ser Asp His Pro Gly Gly Gly Arg Glu Phe Phe Phe Asp Arg His Pro
 100 105 110
 gga gta ttc gcc tat gtg ctc aat tac tac cgc acg ggc aag ctg cac 384
 Gly Val Phe Ala Tyr Val Leu Asn Tyr Tyr Arg Thr Gly Lys Leu His
 115 120 125
 tgc ccc gcc gac gtg tgc ggg ccg ctc ttc gag gaa gag ctg gct ttc 432
 Cys Pro Ala Asp Val Cys Gly Pro Leu Phe Glu Glu Glu Leu Ala Phe
 130 135 140
 tgg ggc atc gat gag acc gac gtg gag ccc tgc tgc tgg atg acc tac 480
 Trp Gly Ile Asp Glu Thr Asp Val Glu Pro Cys Cys Trp Met Thr Tyr
 145 150 155 160
 agg cag cac cgg gac gcg gag gag gcc ctg gac atc ttt gag aca ccc 528
 Arg Gln His Arg Asp Ala Glu Glu Ala Leu Asp Ile Phe Glu Thr Pro
 165 170 175
 gac ctc atc ggg ggc gac cct ggt gat gat gag gac cta gcg gcc aag 576
 Asp Leu Ile Gly Gly Asp Pro Gly Asp Asp Glu Asp Leu Ala Ala Lys
 180 185 190
 aga ttg ggc att gag gat gct gcg ggg ctg gga gga ccc gat ggc aag 624

Arg	Leu	Gly	Ile	Glu	Asp	Ala	Ala	Gly	Leu	Gly	Gly	Pro	Asp	Gly	Lys		
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tca	ggc	cgc	tgg	agg	aag	ctg	cag	cct	cgc	atg	tgg	gct	ctt	ttt	gag	672	
Ser	Gly	Arg	Trp	Arg	Lys	Leu	Gln	Pro	Arg	Met	Trp	Ala	Leu	Phe	Glu		
		210					215				220						
gac	ccc	tac	tca	tct	aga	gcc	gct	agg	ttt	att	gct	ttt	gct	tct	ttg	720	
Asp	Pro	Tyr	Ser	Ser	Arg	Ala	Ala	Arg	Phe	Ile	Ala	Phe	Ala	Ser	Leu		
		225					230				235				240		
ttc	ttc	att	ttg	gtt	tcc	atc	aca	acc	ttt	tgc	ctg	gag	aca	cat	gaa	768	
Phe	Phe	Ile	Leu	Val	Ser	Ile	Thr	Thr	Phe	Cys	Leu	Glu	Thr	His	Glu		
							245				250				255		
gct	ttc	aat	att	gtt	aaa	aac	aag	acg	gag	ccc	gtc	atc	aat	ggc	acc	816	
Ala	Phe	Asn	Ile	Val	Lys	Asn	Lys	Thr	Glu	Pro	Val	Ile	Asn	Gly	Thr		
							260				265				270		
agc	ccg	gtc	ctc	cag	tac	gaa	atc	gaa	acg	gat	ccc	gcc	ctg	acg	tac	864	
Ser	Pro	Val	Leu	Gln	Tyr	Glu	Ile	Glu	Thr	Asp	Pro	Ala	Leu	Thr	Tyr		
							275				280				285		
gtg	gaa	gga	gta	tgt	gtg	gtg	tgg	ttt	acg	ttt	gaa	ttt	tta	gtc	cga	912	
Val	Glu	Gly	Val	Cys	Val	Val	Trp	Phe	Thr	Phe	Glu	Phe	Leu	Val	Arg		
							290				295				300		
att	gtt	ttc	tca	ccc	aat	aaa	ctt	gaa	ttc	atc	aaa	aat	ctc	ttg	aac	960	
Ile	Val	Phe	Ser	Pro	Asn	Lys	Leu	Glu	Phe	Ile	Lys	Asn	Leu	Leu	Asn		
							305				310				315		
atc	att	gac	ttt	gtg	gcc	atc	ctc	ccc	ttc	tac	cta	gag	gtg	gga	ctc	1008	
Ile	Ile	Asp	Phe	Val	Ala	Ile	Leu	Pro	Phe	Tyr	Leu	Glu	Val	Gly	Leu		
							325				330				335		
agc	ggg	ctg	tcc	tcc	aaa	gcg	gcc	aaa	gat	gtg	ctc	ggc	ttt	ctc	agg	1056	
Ser	Gly	Leu	Ser	Ser	Lys	Ala	Ala	Lys	Asp	Val	Leu	Gly	Phe	Leu	Arg		
							340				345				350		
gtg	gtt	agg	ttt	gtg	agg	atc	ctg	aga	atc	ttc	aag	ctc	acc	cgc	cat	1104	
Val	Val	Arg	Phe	Val	Arg	Ile	Leu	Arg	Ile	Phe	Lys	Leu	Thr	Arg	His		
							355				360				365		
ttc	gta	ggt	ctg	agg	gtg	ctc	gga	cat	act	ctt	cgg	gcg	agc	acc	aac	1152	
Phe	Val	Gly	Leu	Arg	Val	Leu	Gly	His	Thr	Leu	Arg	Ala	Ser	Thr	Asn		
							370				375				380		
gaa	ttt	ttg	ttg	ctg	atc	atc	ttc	ctg	gcg	ctg	gga	gtt	ttg	ata	ttc	1200	
Glu	Phe	Leu	Leu	Leu	Ile	Ile	Phe	Leu	Ala	Leu	Gly	Val	Leu	Ile	Phe		
							385				390				395		
gct	acg	atg	atc	tac	tac	gct	gag	aga	gta	ggg	gct	cag	ccc	aat	gac	1248	
Ala	Thr	Met	Ile	Tyr	Tyr	Ala	Glu	Arg	Val	Gly	Ala	Gln	Pro	Asn	Asp		
							405				410				415		
cct	tca	gct	agt	gag	cac	acg	cag	ttc	aaa	aac	atc	ccc	att	ggg	ttc	1296	
Pro	Ser	Ala	Ser	Glu	His	Thr	Gln	Phe	Lys	Asn	Ile	Pro	Ile	Gly	Phe		
							420				425				430		
tgg	tgg	gcc	gta	gtg	acc	atg	act	acc	tta	ggg	tac	ggg	gat	atg	tac	1344	
Trp	Trp	Ala	Val	Val	Thr	Met	Thr	Thr	Leu	Gly	Tyr	Gly	Asp	Met	Tyr		
							435				440				445		
ccc	caa	aca	tgg	tca	ggg	atg	ttg	gtg	ggg	gcc	ttg	tgt	gcc	ctg	gcc	1392	
Pro	Gln	Thr	Trp	Ser	Gly	Met	Leu	Val	Gly	Ala	Leu	Cys	Ala	Leu	Ala		

450	455	460	
gga gtg ctg aca ata gcc atg cct gtg cct gtc att gtc aac aat ttt			1440
Gly Val Leu Thr Ile Ala Met Pro Val Pro Val Ile Val Asn Asn Phe			
465	470	475	480
gga atg tac tac tcc ttg gca atg gcg aag cag aaa ctt cca aga aag			1488
Gly Met Tyr Tyr Ser Leu Ala Met Ala Lys Gln Lys Leu Pro Arg Lys			
	485	490	495
aga aag aag cat att cct cct gcc cct ctg gca agc tcg cct aca ttt			1536
Arg Lys Lys His Ile Pro Pro Ala Pro Leu Ala Ser Ser Pro Thr Phe			
	500	505	510
tgc aag aca gaa ttg aac atg gct tgc aac agt acc cag agt gac aca			1584
Cys Lys Thr Glu Leu Asn Met Ala Cys Asn Ser Thr Gln Ser Asp Thr			
	515	520	525
tgt ctg ggc aaa gaa aac cgg ctt ctg gaa cat aac aga tca gtg tta			1632
Cys Leu Gly Lys Glu Asn Arg Leu Leu Glu His Asn Arg Ser Val Leu			
	530	535	540
tca ggt gac gac agt aca gga agt gag ccg cca tta tca cct cca gaa			1680
Ser Gly Asp Asp Ser Thr Gly Ser Glu Pro Pro Leu Ser Pro Pro Glu			
545	550	555	560
agg ctc cct atc aga cgc tct agt acc aga gac aaa aac aga aga ggg			1728
Arg Leu Pro Ile Arg Arg Ser Ser Thr Arg Asp Lys Asn Arg Arg Gly			
	565	570	575
gaa acg tgt ttc ctg ttg acg aca ggt gat tac acg tgc gct tct gat			1776
Glu Thr Cys Phe Leu Leu Thr Thr Gly Asp Tyr Thr Cys Ala Ser Asp			
	580	585	590
gga gga atc agg aaa gtg ttg tac aga att tat cat gga ttt ttg act			1824
Gly Gly Ile Arg Lys Val Leu Tyr Arg Ile Tyr His Gly Phe Leu Thr			
	595	600	605
gct gaa aaa aaa gga cat tga			1845
Ala Glu Lys Lys Gly His			
610			

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 <212> PRT
 <213> Mus musculus

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 Met Gly Lys Ile Glu Ser Asn Glu Arg Val Ile Leu Asn Val Gly Gly
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 Thr Arg His Glu Thr Tyr Arg Ser Thr Leu Lys Thr Leu Pro Gly Thr
 20 25 30
 Arg Leu Ala Leu Leu Ala Ser Ser Glu Pro Gln Gly Asp Cys Leu Thr
 35 40 45
 Ala Ala Gly Asp Lys Leu Gln Pro Leu Pro Pro Pro Leu Ser Pro Pro
 50 55 60
 Pro Arg Pro Pro Pro Leu Ser Pro Val Pro Ser Gly Cys Phe Glu Gly
 65 70 75 80

Gly	Ala	Gly	Asn	Cys	Ser	Ser	His	Gly	Gly	Asn	Gly	Gly	Asn	Gly	Gly	85	90	95
Ser	Asp	His	Pro	Gly	Gly	Gly	Arg	Glu	Phe	Phe	Phe	Asp	Arg	His	Pro	100	105	110
Gly	Val	Phe	Ala	Tyr	Val	Leu	Asn	Tyr	Tyr	Arg	Thr	Gly	Lys	Leu	His	115	120	125
Cys	Pro	Ala	Asp	Val	Cys	Gly	Pro	Leu	Phe	Glu	Glu	Glu	Leu	Ala	Phe	130	135	140
Trp	Gly	Ile	Asp	Glu	Thr	Asp	Val	Glu	Pro	Cys	Cys	Trp	Met	Thr	Tyr	145	150	155
Arg	Gln	His	Arg	Asp	Ala	Glu	Glu	Ala	Leu	Asp	Ile	Phe	Glu	Thr	Pro	165	170	175
Asp	Leu	Ile	Gly	Gly	Asp	Pro	Gly	Asp	Asp	Glu	Asp	Leu	Ala	Ala	Lys	180	185	190
Arg	Leu	Gly	Ile	Glu	Asp	Ala	Ala	Gly	Leu	Gly	Gly	Pro	Asp	Gly	Lys	195	200	205
Ser	Gly	Arg	Trp	Arg	Lys	Leu	Gln	Pro	Arg	Met	Trp	Ala	Leu	Phe	Glu	210	215	220
Asp	Pro	Tyr	Ser	Ser	Arg	Ala	Ala	Arg	Phe	Ile	Ala	Phe	Ala	Ser	Leu	225	230	235
Phe	Phe	Ile	Leu	Val	Ser	Ile	Thr	Thr	Phe	Cys	Leu	Glu	Thr	His	Glu	245	250	255
Ala	Phe	Asn	Ile	Val	Lys	Asn	Lys	Thr	Glu	Pro	Val	Ile	Asn	Gly	Thr	260	265	270
Ser	Pro	Val	Leu	Gln	Tyr	Glu	Ile	Glu	Thr	Asp	Pro	Ala	Leu	Thr	Tyr	275	280	285
Val	Glu	Gly	Val	Cys	Val	Val	Trp	Phe	Thr	Phe	Glu	Phe	Leu	Val	Arg	290	295	300
Ile	Val	Phe	Ser	Pro	Asn	Lys	Leu	Glu	Phe	Ile	Lys	Asn	Leu	Leu	Asn	305	310	315
Ile	Ile	Asp	Phe	Val	Ala	Ile	Leu	Pro	Phe	Tyr	Leu	Glu	Val	Gly	Leu	325	330	335
Ser	Gly	Leu	Ser	Ser	Lys	Ala	Ala	Lys	Asp	Val	Leu	Gly	Phe	Leu	Arg	340	345	350
Val	Val	Arg	Phe	Val	Arg	Ile	Leu	Arg	Ile	Phe	Lys	Leu	Thr	Arg	His	355	360	365
Phe	Val	Gly	Leu	Arg	Val	Leu	Gly	His	Thr	Leu	Arg	Ala	Ser	Thr	Asn	370	375	380
Glu	Phe	Leu	Leu	Leu	Ile	Ile	Phe	Leu	Ala	Leu	Gly	Val	Leu	Ile	Phe	385	390	395
Ala	Thr	Met	Ile	Tyr	Tyr	Ala	Glu	Arg	Val	Gly	Ala	Gln	Pro	Asn	Asp	405	410	415
Pro	Ser	Ala	Ser	Glu	His	Thr	Gln	Phe	Lys	Asn	Ile	Pro	Ile	Gly	Phe	420	425	430
Trp	Trp	Ala	Val	Val	Thr	Met	Thr	Thr	Leu	Gly	Tyr	Gly	Asp	Met	Tyr	435	440	445
Pro	Gln	Thr	Trp	Ser	Gly	Met	Leu	Val	Gly	Ala	Leu	Cys	Ala	Leu	Ala	450	455	460
Gly	Val	Leu	Thr	Ile	Ala	Met	Pro	Val	Pro	Val	Ile	Val	Asn	Asn	Phe			

465 470 475 480
 Gly Met Tyr Tyr Ser Leu Ala Met Ala Lys Gln Lys Leu Pro Arg Lys
 485 490 495
 Arg Lys Lys His Ile Pro Pro Ala Pro Leu Ala Ser Ser Pro Thr Phe
 500 505 510
 Cys Lys Thr Glu Leu Asn Met Ala Cys Asn Ser Thr Gln Ser Asp Thr
 515 520 525
 Cys Leu Gly Lys Glu Asn Arg Leu Leu Glu His Asn Arg Ser Val Leu
 530 535 540
 Ser Gly Asp Asp Ser Thr Gly Ser Glu Pro Pro Leu Ser Pro Pro Glu
 545 550 555 560
 Arg Leu Pro Ile Arg Arg Ser Ser Thr Arg Asp Lys Asn Arg Arg Gly
 565 570 575
 Glu Thr Cys Phe Leu Leu Thr Thr Gly Asp Tyr Thr Cys Ala Ser Asp
 580 585 590
 Gly Gly Ile Arg Lys Val Leu Tyr Arg Ile Tyr His Gly Phe Leu Thr
 595 600 605
 Ala Glu Lys Lys Gly His
 610

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 Met Gly Lys Ile Glu Ser Asn Glu Arg Val Ile Leu Asn Val Gly Gly
 1 5 10 15
 acc agg cac gaa acc tac cgc agc acc ctc aag acc ctg cct gga act 96
 Thr Arg His Glu Thr Tyr Arg Ser Thr Leu Lys Thr Leu Pro Gly Thr
 20 25 30
 cgc ctg gcc ctt ctt gcc tcc tct gaa cct cag ggc gac tgc ctg act 144
 Arg Leu Ala Leu Leu Ala Ser Ser Glu Pro Gln Gly Asp Cys Leu Thr
 35 40 45
 gcg gcc ggg gac aag ctg caa ccg ctg ccc cct ccg ctg tct ccg ccg 192
 Ala Ala Gly Asp Lys Leu Gln Pro Leu Pro Pro Pro Leu Ser Pro Pro
 50 55 60
 cca cga ccg cct ccc ttg tcc cct gtc ccc agc ggc tgc ttc gag ggc 240
 Pro Arg Pro Pro Pro Leu Ser Pro Val Pro Ser Gly Cys Phe Glu Gly
 65 70 75 80
 ggc gca ggc aac tgc agt tcg cac ggt ggc aac ggc ggc aac ggc ggc 288
 Gly Ala Gly Asn Cys Ser Ser His Gly Gly Asn Gly Gly Asn Gly Gly
 85 90 95

agc gac cac cct ggg gga ggc cgc gaa ttc ttc ttc gat cgc cac cca	336
Ser Asp His Pro Gly Gly Gly Arg Glu Phe Phe Phe Asp Arg His Pro	
100 105 110	
gga gta ttc gcc tat gtg ctc aat tac tac cgc acg ggc aag ctg cac	384
Gly Val Phe Ala Tyr Val Leu Asn Tyr Tyr Arg Thr Gly Lys Leu His	
115 120 125	
tgc ccc gcc gac gtg tgc ggg ccg ctc ttc gag gaa gag ctg gct ttc	432
Cys Pro Ala Asp Val Cys Gly Pro Leu Phe Glu Glu Glu Leu Ala Phe	
130 135 140	
tgg ggc atc gat gag acc gac gtg gag ccc tgc tgc tgg atg acc tac	480
Trp Gly Ile Asp Glu Thr Asp Val Glu Pro Cys Cys Trp Met Thr Tyr	
145 150 155 160	
agg cag cac cgg gac gcg gag gag gcc ctg gac atc ttt gag aca ccc	528
Arg Gln His Arg Asp Ala Glu Glu Ala Leu Asp Ile Phe Glu Thr Pro	
165 170 175	
gac ctc atc ggg ggc gac cct ggt gat gat gag gac cta gcg gcc aag	576
Asp Leu Ile Gly Gly Asp Pro Gly Asp Asp Glu Asp Leu Ala Ala Lys	
180 185 190	
aga ttg ggc att gag gat gct gcg ggg ctg gga gga ccc gat ggc aag	624
Arg Leu Gly Ile Glu Asp Ala Ala Gly Leu Gly Gly Pro Asp Gly Lys	
195 200 205	
tca ggc cgc tgg agg aag ctg cag cct cgc atg tgg gct ctt ttt gag	672
Ser Gly Arg Trp Arg Lys Leu Gln Pro Arg Met Trp Ala Leu Phe Glu	
210 215 220	
gac ccc tac tca tct aga gcc gct agg ttt att gct ttt gct tct ttg	720
Asp Pro Tyr Ser Ser Arg Ala Ala Arg Phe Ile Ala Phe Ala Ser Leu	
225 230 235 240	
ttc ttc att ttg gtt tcc atc aca acc ttt tgc ctg gag aca cat gaa	768
Phe Phe Ile Leu Val Ser Ile Thr Thr Phe Cys Leu Glu Thr His Glu	
245 250 255	
gct ttc aat att gtt aaa aac aag acg gag ccc gtc atc aat ggc acc	816
Ala Phe Asn Ile Val Lys Asn Lys Thr Glu Pro Val Ile Asn Gly Thr	
260 265 270	
agc ccg gtc ctc cag tac gaa atc gaa acg gat ccc gcc ctg acg tac	864
Ser Pro Val Leu Gln Tyr Glu Ile Glu Thr Asp Pro Ala Leu Thr Tyr	
275 280 285	
gtg gaa gga gta tgt gtg gtg tgg ttt acg ttt gaa ttt tta gtc cga	912
Val Glu Gly Val Cys Val Val Trp Phe Thr Phe Glu Phe Leu Val Arg	
290 295 300	
att gtt ttc tca ccc aat aaa ctt gaa ttc atc aaa aat ctc ttg aac	960
Ile Val Phe Ser Pro Asn Lys Leu Glu Phe Ile Lys Asn Leu Leu Asn	
305 310 315 320	
atc att gac ttt gtg gcc atc ctc ccc ttc tac cta gag gtg gga ctc	1008
Ile Ile Asp Phe Val Ala Ile Leu Pro Phe Tyr Leu Glu Val Gly Leu	
325 330 335	
agc ggg ctg tcc tcc aaa gcg gcc aaa gat gtg ctc ggc ttt ctc agg	1056
Ser Gly Leu Ser Ser Lys Ala Ala Lys Asp Val Leu Gly Phe Leu Arg	
340 345 350	
gtg gtt agg ttt gtg agg atc ctg aga atc ttc aag ctc acc cgc cat	1104

Val Val Arg Phe Val Arg Ile Leu Arg Ile Phe Lys Leu Thr Arg His	
355 360 365	
ttc gta ggt ctg agg gtg ctc gga cat act ctt cgg gcg agc acc aac	1152
Phe Val Gly Leu Arg Val Leu Gly His Thr Leu Arg Ala Ser Thr Asn	
370 375 380	
gaa ttt ttg ttg ctg atc atc ttc ctg gcg ctg gga gtt ttg ata ttc	1200
Glu Phe Leu Leu Leu Ile Ile Phe Leu Ala Leu Gly Val Leu Ile Phe	
385 390 395 400	
gct acg atg atc tac tac gct gag aga gta ggg gct cag ccc aat gac	1248
Ala Thr Met Ile Tyr Tyr Ala Glu Arg Val Gly Ala Gln Pro Asn Asp	
405 410 415	
cct tca gct agt gag cac acg cag ttc aaa aac atc ccc att ggt ttc	1296
Pro Ser Ala Ser Glu His Thr Gln Phe Lys Asn Ile Pro Ile Gly Phe	
420 425 430	
tgg tgg gcc gta gtg acc atg act acc tta ggt tac ggg gat atg tac	1344
Trp Trp Ala Val Val Thr Met Thr Thr Leu Gly Tyr Gly Asp Met Tyr	
435 440 445	
ccc caa aca tgg tca ggg atg ttg gtg ggg gcc ttg tgt gcc ctg gcc	1392
Pro Gln Thr Trp Ser Gly Met Leu Val Gly Ala Leu Cys Ala Leu Ala	
450 455 460	
gga gtg ctg aca ata gcc atg cct gtg cct gtc att gtc aac aat ttt	1440
Gly Val Leu Thr Ile Ala Met Pro Val Pro Val Ile Val Asn Asn Phe	
465 470 475 480	
gga atg tac tac tcc ttg gca atg gcg aag cag aaa ctt cca aga aag	1488
Gly Met Tyr Tyr Ser Leu Ala Met Ala Lys Gln Lys Leu Pro Arg Lys	
485 490 495	
aga aag aag cat att cct cct gcc cct ctg gca agc tcg cct aca ttt	1536
Arg Lys Lys His Ile Pro Pro Ala Pro Leu Ala Ser Ser Pro Thr Phe	
500 505 510	
tgc aag aca gaa ttg aac atg gct tgc aac agt acc cag agt gac aca	1584
Cys Lys Thr Glu Leu Asn Met Ala Cys Asn Ser Thr Gln Ser Asp Thr	
515 520 525	
tgt ctg ggc aaa gaa aac cgg ctt ctg gaa cat aac aga tca gtg tta	1632
Cys Leu Gly Lys Glu Asn Arg Leu Leu Glu His Asn Arg Ser Val Leu	
530 535 540	
tca ggt gac gac agt aca gga agt gag ccg cca tta tca cct cca gaa	1680
Ser Gly Asp Asp Ser Thr Gly Ser Glu Pro Pro Leu Ser Pro Pro Glu	
545 550 555 560	
agg ctc cct atc aga cgc tct agt acc aga gac aaa aac aga aga ggg	1728
Arg Leu Pro Ile Arg Arg Ser Ser Thr Arg Asp Lys Asn Arg Arg Gly	
565 570 575	
gaa acg tgt ttc ctg ttg acg aca ggt gat tac acg tgc gct tct gat	1776
Glu Thr Cys Phe Leu Leu Thr Thr Gly Asp Tyr Thr Cys Ala Ser Asp	
580 585 590	
gga gga atc agg aaa gaa gag gtc ccg cat ctt atg agg cat tta aag	1824
Gly Gly Ile Arg Lys Glu Glu Val Pro His Leu Met Arg His Leu Lys	
595 600 605	
ctt ata aaa ggg act gtg gct gga act gag atg gtg ctc gcc atg gga	1872
Leu Ile Lys Gly Thr Val Ala Gly Thr Glu Met Val Leu Ala Met Gly	

610	615	620	
ata ttc tgc ttg tgc aca gac ctg agt cca cgg aac agc tgt aaa tac			1920
Ile Phe Cys Leu Ser Thr Asp Leu Ser Pro Arg Asn Ser Cys Lys Tyr			
625	630	635	640
caa ccg tgt gca tgg acc tgc cca ctc tca ccg tct cat aga cag tga			1968
Gln Pro Cys Ala Trp Thr Cys Pro Leu Ser Pro Ser His Arg Gln			
645	650	655	

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

<400> 53

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

Ser Pro Val Leu Gln Tyr Glu Ile Glu Thr Asp Pro Ala Leu Thr Tyr
 275 280 285
 Val Glu Gly Val Cys Val Val Trp Phe Thr Phe Glu Phe Leu Val Arg
 290 295 300
 Ile Val Phe Ser Pro Asn Lys Leu Glu Phe Ile Lys Asn Leu Leu Asn
 305 310 315 320
 Ile Ile Asp Phe Val Ala Ile Leu Pro Phe Tyr Leu Glu Val Gly Leu
 325 330 335
 Ser Gly Leu Ser Ser Lys Ala Ala Lys Asp Val Leu Gly Phe Leu Arg
 340 345 350
 Val Val Arg Phe Val Arg Ile Leu Arg Ile Phe Lys Leu Thr Arg His
 355 360 365
 Phe Val Gly Leu Arg Val Leu Gly His Thr Leu Arg Ala Ser Thr Asn
 370 375 380
 Glu Phe Leu Leu Leu Ile Ile Phe Leu Ala Leu Gly Val Leu Ile Phe
 385 390 395 400
 Ala Thr Met Ile Tyr Tyr Ala Glu Arg Val Gly Ala Gln Pro Asn Asp
 405 410 415
 Pro Ser Ala Ser Glu His Thr Gln Phe Lys Asn Ile Pro Ile Gly Phe
 420 425 430
 Trp Trp Ala Val Val Thr Met Thr Thr Leu Gly Tyr Gly Asp Met Tyr
 435 440 445
 Pro Gln Thr Trp Ser Gly Met Leu Val Gly Ala Leu Cys Ala Leu Ala
 450 455 460
 Gly Val Leu Thr Ile Ala Met Pro Val Pro Val Ile Val Asn Asn Phe
 465 470 475 480
 Gly Met Tyr Tyr Ser Leu Ala Met Ala Lys Gln Lys Leu Pro Arg Lys
 485 490 495
 Arg Lys Lys His Ile Pro Pro Ala Pro Leu Ala Ser Ser Pro Thr Phe
 500 505 510
 Cys Lys Thr Glu Leu Asn Met Ala Cys Asn Ser Thr Gln Ser Asp Thr
 515 520 525
 Cys Leu Gly Lys Glu Asn Arg Leu Leu Glu His Asn Arg Ser Val Leu
 530 535 540
 Ser Gly Asp Asp Ser Thr Gly Ser Glu Pro Pro Leu Ser Pro Pro Glu
 545 550 555 560
 Arg Leu Pro Ile Arg Arg Ser Ser Thr Arg Asp Lys Asn Arg Arg Gly
 565 570 575
 Glu Thr Cys Phe Leu Leu Thr Thr Gly Asp Tyr Thr Cys Ala Ser Asp
 580 585 590
 Gly Gly Ile Arg Lys Glu Glu Val Pro His Leu Met Arg His Leu Lys
 595 600 605
 Leu Ile Lys Gly Thr Val Ala Gly Thr Glu Met Val Leu Ala Met Gly
 610 615 620
 Ile Phe Cys Leu Ser Thr Asp Leu Ser Pro Arg Asn Ser Cys Lys Tyr
 625 630 635 640
 Gln Pro Cys Ala Trp Thr Cys Pro Leu Ser Pro Ser His Arg Gln
 645 650 655