

RECOMBINANT VITELLOGENIN ENRICHED FEED

CROSS REFERENCE TO RELATED APPLICATIONS

[0001] This application claims the benefit of United States Provisional Application Serial No. 60/425,263 filed November 12, 2002, the contents of which is hereby incorporated by reference.

FIELD OF INVENTION

[0002] The invention relates to feed technology and to recombinant technology and in particular relates to feed enriched with recombinant vitellogenin. Embodied in this invention is the use of live recombinants to enrich live intermediate live feed and the development of microdiets for larvae.

BACKGROUND OF INVENTION

[0003] Vitellogenesis, the formation of yolk proteins, has been extensively studied. Yolk proteins are derived from a large lipophosphoglycoprotein precursor, vitellogenin (Vtg). Vtg is synthesized in the liver under estrogen influence, extensively modified post-translationally, secreted into the bloodstream and sequestered by the oocytes via specific Vtg receptors (Lim et al., 1991; Li et al., 2003). After internalization, Vtg is cleaved into subunits of yolk proteins, lipovitellin I (LVI), phosvitin, and lipovitellin II (LVII). Vtg serves to provide a pool of amino acids for the embryos, and also functions as a carrier protein for phosphates, lipids, carbohydrates, ions (eg. Ca^{2+} , Mg^{2+} , Zn^{2+}), vitamins and possibly, hormones (Sappington and Raikhel, 1998). These essential nutrients amassed in the yolk provide exclusive nourishment to the developing embryos of all oviparous animals. For most fish, the newly-hatched larvae continue to derive nutrients from the yolk sac until first feeding. Hence, proper formation and deposition of the yolk proteins in the oocyte and the ability of the embryos to utilize the yolk reserves are crucial for reproductive success.

[0004] Broodstock nutrition is a crucial factor influencing larval quality and survival. In

particular, lipids have been shown to affect the spawning and the egg quality of many fish species (Sivaloganathan et al., 1998). Deficiency of n-3 polyunsaturated fatty acids (PUFA), in broodstock has been linked to reduced fecundity, and lower rates of fertilization and hatching in many species. Thorough evaluation of lipids as a source of energy at the embryonic and larval stages in relation to proteins and carbohydrates indicates that lipids play a significant role in the early life stages of marine larvae (Rainuzzo et al., 1997).

[0005] Considerable research has been conducted on the nutritional requirements of commercially produced animals. One important problem the aquaculture industry encounters is high mortality at the early stage of larval development presumably due to poor egg quality, small size and simple digestive systems at the start of feeding. One of the keys to enhancement of biological performance is through feed technology. To maximize feed utilization, diets targeted for specific developmental stages of aquaculture species, and high protein live feed including yeast, rotifer, and brine shrimp have been formulated and tested (Fitzsimmons et al., 1999; Lochmann, 2001; Su et al., 1997). However, rotifers for instance, showed batch inconsistencies in nutritional value depending on their primary feed (Su et al., 1994). With new bioreactor technology, yeast enriched by recombinant technology has become a cost-effective protein for energy source (Chen et al., 2000).

[0006] There remains however a need for improved feed for oviparous larvae and broodstock, in particular to increase the survival rate of larvae.

SUMMARY OF THE INVENTION

[0007] Yolk proteins represent the major nutrient constituent in the yolk. The present invention is based in part on the recognition that oviparous larval mortality and oviparous broodstock egg quality may be improved by providing a feed enriched with yolk proteins. Since yeast is a low-cost micronutrient, we set out to construct a yeast strain for synthesis of single cell protein, actively producing the precursor of yolk proteins. Without being limited to any particular theory, it is believed that such transgenic host expressing recombinant vitellogenin proteins may partially mimic the natural yolk formation process and thereby

provide an exogenous source of nutrients for larvae and broodstock particularly beneficial for optimal oviparous larval survival rates and/or oviparous broodstock egg quality.

[0008] In accordance with one aspect of the present invention, there is provided a recombinant expression vector wherein the expression vector comprises a vitellogenin gene operably linked to a promoter, wherein the promoter is functional in a eukaryotic host suitable for use as a feed or a feed additive.

[0009] In accordance with another aspect of the present invention, there is provided a transgenic eukaryotic host suitable for use as a feed or feed additive, such as, for example, yeast wherein the eukaryotic host comprises an expression vector according to various embodiments of the invention.

[0010] In a specific embodiment, the transgenic yeast according to the invention intracellularly expresses a recombinant vitellogenin.

[0011] In accordance with yet another aspect of the invention, there is provided a method for increasing the level of polyunsaturated fatty acids in a transgenic host according to the invention, including a transgenic yeast, comprising culturing the transgenic host in media comprising fish oil.

[0012] In accordance with yet another aspect of the invention, there is provided a method for increasing the survival rates of oviparous larvae, and a method for increasing broodstock egg quality of an oviparous animal comprising the step of feeding to the larvae or to the broodstock a transgenic host, or an intermediate live feed that has been fed a transgenic host, including a transgenic yeast according to different embodiments of the invention.

[0013] In accordance with yet another aspect of the invention, there is provided a method for enriching an intermediate live feed comprising the step of feeding to the intermediate live feed a transgenic host, such as a transgenic yeast according to various embodiments of the invention.

[0014] In a specific embodiment, the intermediate live feed is *Artemia* nauplii.

[0015] In another aspect of the invention, there is provided use of recombinant vitellogenin for delivery of a therapeutic material such as hormones, vitamins, minerals, ions and nucleic acid to the maternal oocytes of an oviparous animal.

[0016] Other aspects and features of the present invention will become apparent to those of ordinary skill in the art upon review of the following description of specific embodiments of the invention in conjunction with the accompanying figures.

BRIEF DESCRIPTION OF THE DRAWINGS

[0017] FIG. 1 is a schematic representation of the rVtg expression vectors: Vtg(-SS)/pGAPZA, Vtg(VtgSS)/pGAPZA and Vtg(α SS)/pGAPZA.

[0018] FIG 2A shows a Southern blot of genomic DNA of the transgenic *P. pastoris* clones indicated using a DIG-labeled *O. aureus* Vtg fragment. The hybridization signal for HIS4 is to control for differences in loading amounts. The numbers below the blot indicate the copy number of the Vtg expression cassettes based on the ratio of the densitometric intensity of the Vtg-bands to those of the *His4*.

[0019] FIG 2B is a Western blot of vitellogenin with an apparent molecular weight of 194 kD from the lysate and membrane fractions of transgenic yeast clones indicated.

[0020] FIG 3 depicts the effects of media composition on the expression of the recombinant vitellogenin protein.

[0021] FIG 4 is a graph depicting recombinant vitellogenin expression as a function of culture conditions.

[0022] FIG 5A is a graph depicting the increase in total amino acid content for two transgenic *P. pastoris* clones grown in shake flasks relative to a native *P. pastoris* control. The inset of this figure shows the increase in total amino acid content for transgenic clone # 6 grown in different culture conditions. FIG 5B is a graph showing the amino acid content of the listed amino acids of transgenic *P. pastoris* clone # 6 relative to a native *P. pastoris* control.

[0023] FIG. 6 is a graph depicting the relative amount of the indicated fatty acids for transgenic *P. pastoris* clone # 6, grown in the presence and absence of fish oil, relative to a native *P. pastoris* control. The inset to the graph depicts the increase in total lipid content for transgenic *P. pastoris* clones # 6 and #52, relative to native *P. pastoris* (SMD1186H).

[0024] Figure 7 shows the levels of 18:3 (n-3), 20:5 (n-3) and 22:6 (n-3) in total lipids from *Artemia* larvae fed 48 hr with baker's yeast SC (*Saccromyces crevisiae*), SMD (*Pichia pastoris*), recombinant yeast clone #6 (#6) or recombinant yeast clone #6 cultured in 5% cod liver oil (#6 5% oil). Data are mean $\pm$ SE of triplicate sample.

[0025] Figure 8 shows the length, weight and survival of *O. mossambicus* larvae fed different types or combinations of yeast for 20 days. (A) Length of larvae fed 20 days with different types or combinations of yeast. (B). Weight of larvae fed 20 days with different types or combinations of yeast. (C) Survival of larvae fed 20 days with different types or combinations of yeast. Data are mean $\pm$ SE of triplicate sample.

[0026] Figure 9 shows the length, weight and survival of *O. mossambicus* larvae fed 10 days with different types or combinations of yeast and another 10 days with *Artemia* (wild type). (A) Length of larvae fed 10 days with different types or combinations of yeast and another 10 days with *Artemia* (wild type). (B) Weight of larvae fed 10 days with different types or combinations of yeast and another 10 days with *Artemia* (wild type). (C) Survival of larvae fed 10 days with different types or combinations of yeast and another 10 days with *Artemia* (wild type). Data are mean $\pm$ SE of triplicate sample.

[0027] Figure 10 shows the length, weight and survival of *O. mossambicus* larvae fed 10 days with different types of yeast and another 10 days with enriched *Artemia*. (A) Length of larvae fed 10 days with different types of yeast and another 10 days with enriched *Artemia*. (B) Weight of larvae fed 10 days with different types of yeast and another 10 days with enriched *Artemia*. (C) Survival of larvae fed 10 days with different types of yeast and another 10 days with enriched *Artemia*. Data are mean $\pm$ SE of triplicate sample.

DETAILED DESCRIPTION OF EMBODIMENTS OF THE INVENTION

[0028] Developing larvae require three macronutrients: proteins, fats, and carbohydrates, along with many elements classified as micronutrients. Some are indispensable during fertilization as well as larval growth. Vitellogenin is one of the most crucial factors for the reproductive success and survival of oviparous embryos.

[0029] We present here a novel strategy for genetically engineering a eukaryotic host that produces recombinant Vtg (rVtg), for application as an enriched feed. In an illustrative embodiment, the host is *Pichia pastoris*. *Pichia pastoris* has been employed as a high protein feed for some domestic animals (Chen et al., 2000) and may advantageously be used to express foreign proteins as it: (1) has the ability to grow to high cell densities using inexpensive simple, defined media; (2) has the capacity to express high levels of recombinant proteins when multiple copies of the expression cassette are integrated; and (3) is competent in carrying out eukaryotic post-translational modifications (Clare et al., 1991a; 1991b; Cregg et al., 1993; Romanos, 1995).

[0030] In various aspects, the invention therefore relates to transgenic eukaryotic hosts suitable for use as a feed or feed additive that express recombinant Vtg (rVtg). The transgenic hosts in some embodiments are suitable as a feed or feed additive for an oviparous animal, and may be fed to an oviparous animal, preferably to an oviparous larvae, thereby providing an exogenous source of vitellogenin. Owing to the high nutritional value of vitellogenin, a phospholipoglycoprotein, suitable eukaryotic hosts expressing a recombinant vitellogenin may also be used as a high quality feed additive for non-oviparous animals, including domesticated animals.

[0031] In one aspect, the invention provides an expression vector that comprises a vitellogenin gene operably linked to a promoter functional in such hosts. As will be understood by those skilled in the art, the expression vector may be linear or circular. The expression vector may be single stranded or preferably double stranded. Preferably, the expression vector is a plasmid. The expression vector may integrate into a host cell chromosome or may contain an appropriate origin of replication, allowing for extra-chromosomal replication and propagation. The expression vector will often contain, in addition to a vitellogenin gene and a eukaryotic promoter, other sequences to facilitate vector

propagation and selection in other host cells, such as *E. coli*. For example, the vector may include sequences conferring resistance to antibiotics, for example, Zeocin. In addition, the vectors of the present invention may comprise a sequence of nucleotides for one or more restriction endonuclease recognition sites.

[0032] The term "vitellogenin gene" refers to any nucleotide sequence that encodes a vitellogenin protein or a functional equivalent thereof. As used herein, "vitellogenin gene" includes DNA sequences encoding for either a mature vitellogenin protein or a precursor, for example, a sequence that also encodes a secretion signal sequence (SS). Vitellogenin gene and protein sequences are known and publicly available, for example from GenBank database and include the sequences shown in SEQ ID NOS: 1 to 20. The term "functional equivalent" is used to describe structurally and functionally related amino acids sequence that may differ from the parent amino acid by one or more deletions, substitutions, modifications or additions that do not affect the normal biological function of vitellogenin. In one embodiment, the functional equivalent will be substantially homologous, meaning that there is a substantial correspondence between the amino acid sequence of the equivalent and the parent amino acid sequence. In specific embodiments, the functional equivalent will be at least about 50%, 75%, 90% and 95% homologous.

[0033] Homology is measured using sequence analysis software such as Sequence Analysis Software Package of the Genetics Computer Group, University of Wisconsin Biotechnology Center, 1710 University Avenue, Madison, WI 53705. Amino acid sequences are aligned to maximize identity. Gaps may be artificially introduced into the sequence to attain proper alignment. Once the optimal alignment has been set up, the degree of homology is established by recording all of the positions in which the amino acids of both sequences are identical, relative to the total number of positions.

[0034] In one embodiment, the functional equivalent differs by one or more conservative amino acid substitutions. Conservative amino acid substitutions are substitutions among amino acids of the same class. These classes include, for example, amino acids having uncharged polar side chains, such as asparagine, glutamine, serine, threonine, and tyrosine; amino acids having basic side chains, such as lysine, arginine, and histidine; amino acids

having acidic side chains, such as aspartic acid and glutamic acid; and amino acids having nonpolar side chains, such as glycine, alanine, valine, leucine, isoleucine, proline, phenylalanine, methionine, tryptophan, and cysteine. Generally, the functional equivalent will include one or more deletions, substitutions, modifications or additions in non-conserved sequences. Homology among sequences from different species may be analyzed to determine conserved sequences using, as an example, the BLAST homology searching algorithm of Altschul *et al.*, Nucleic Acids Res.; 25:3389-3402 (1997). Vitellogenin genes from various organisms are functionally and structurally conserved and an alignment of a number of vitellogenin sequences have identified five well-aligned subdomains (Lim et al, 2001). One skilled in the art therefore can identify DNA sequences encoding functional polypeptide variants of naturally occurring vitellogenins by alignment to one or more of these subdomains.

[0035] The term "promoter" as will be understood by those skilled in the art refers to a nucleic acid sequence capable of driving the transcription of a gene to which the promoter is operably linked and a promoter is functional in a host if it is so capable in the host. In the expression vector, the vitellogenin gene is operably linked to a promoter, meaning the promoter drives the transcription of the vitellogenin gene in a host in which the promoter is functional.

[0036] The promoter may be an inducible promoter, or preferably a constitutive promoter. The term "constitutive promoter" refers to a sequence that directs transcription of the operably linked gene under most normal cellular conditions. Preferably the promoter is a strong constitutive promoter, in that it directs high levels of expression of the transgenic vitellogenin gene in the selected host cell. A number of appropriate promoters would be known to a person skilled in the art, and include the algal chloroplast *atpA* or *rbcl* promoters the yeast 3-phosphoglycerate kinase, glyceraldehyde-3-phosphate dehydrogenase (GAP), or alcohol dehydrogenase promoters or alcohol oxidase (AOX) promoter

[0037] The expression vector of the present invention may be constructed by standard techniques known to someone skilled in the art and described, for example in Sambrook et al. in Molecular Cloning: A Laboratory Manual 3rd Edition, Cold Spring Harbour, Laboratory

Press and other laboratory manuals. Nucleic acid molecules may be chemically synthesized using techniques such as disclosed, for example in Itakura et al US Pat No. 4,598,049; Caruthers et al US Pat No 4,458,066; and Itakura et al US Patents Nos. 4,401,796 and 4,373,071.

[0038] Nucleic acids molecules may also be isolated and combined. By isolated it is meant that the isolated substance has been substantially separated or purified away from other components, such as biological components, with which it would otherwise be associated, for example in vivo, so that the isolated substance may itself be manipulated or processed. The term isolated therefore includes substances purified by standard purification methods, as well as substance purified by recombinant expression in a host, as well as chemically synthesized substances. A variety of strategies are available for combining and ligating individual nucleic acid molecules, and depending on the nature or the termini of the nucleic acids to be ligated, a suitable strategy will readily be apparent to one skilled in the art. As will be apparent to a person skilled in the art of molecular biology, the DNA fragments must be ligated in the proper frame to ensure that the resulting gene encodes for the desired amino acid sequence.

[0039] An expression vector of the present invention may be introduced into a host cell, which may include a cell capable of transcribing and translating the gene of the expression vector. Accordingly, the invention also provides host cells containing an expression vector of the invention and recombinant vitellogenin expressed by such host cells, which recombinant protein may be isolated and purified using well-known techniques. The term "host cell" refers not only to the particular subject cell but to the progeny or potential progeny of such a cell. Because certain modifications may occur in succeeding generations due to either cellular differentiation, mutation or environmental influences, such progeny may not, in fact, be identical to the parent cell, but are still included within the scope of the term as used herein.

[0040] Vector DNA can be introduced into cells by conventional transformation or transfection techniques. The terms "transformation" and "transfection" refer to techniques for introducing foreign nucleic acid into a host cell, including calcium phosphate or calcium chloride co-precipitation, DEAE-dextran-mediated transfection, lipofection, electroporation, microinjection and viral-mediated transfection. Suitable methods for transforming or

transfecting host cells are well known in the art and can for example be found in Sambrook et al. (Molecular Cloning: A Laboratory Manual, 3rd Edition, Cold Spring Harbor Laboratory press (2001)), and other laboratory manuals.

[0041] A cell, tissue, organ, or organism into which has been introduced a foreign nucleic acid, is considered "transformed", "transfected", or "transgenic". A transgenic or transformed cell or organism also includes progeny of the cell or organism and progeny produced from a breeding program employing a transgenic organism as a parent and exhibiting an altered phenotype resulting from the presence of a recombinant nucleic acid. A transgenic organism is therefore an organism that has been transformed with a heterologous nucleic acid, or the progeny of such an organism that includes the transgene.

[0042] A eukaryotic host cell suitable for use as a feed or feed additive for an oviparous animal such as fish, into which has been introduced the expression vector according to the invention is one important aspect of this invention. Preferably, the host contains an expression vector that is stably maintained within the host cell either by autonomous replication within the host cell or by integrating into the host cell's genome. If the expression vector is an integrative vector, the vector may integrate into a random chromosomal location or, preferably, may be targeted to a specific chromosomal locus through the process of homologous recombination. In one embodiment, multiple copies of the expression vectors have integrated into the genome of the host.

[0043] The vitellogenin protein is preferably expressed intracellularly in the host. Intracellular expression as that term is used herein is intended to broadly describe the expressed vitellogenin associated with the host cell for example where the expressed protein is localized within the cell or associated with the cell membrane. In contrast, vitellogenin that is secreted into the culture media is not expressed intracellularly.

[0044] In one embodiment, the transgenic eukaryotic host according to the invention is capable of effecting post-translational modification of a eukaryotic protein such as Vtg. In one embodiment, the eukaryotic cell may be cultured to a significant cell density. Ideally, the eukaryotic host will have a genetic code compatible with the expression of higher eukaryotic

DNA sequences, however, as would be appreciated by one skilled in the art, a lower eukaryote with a non-standard genetic code, for example ciliates, may be used provided the vitellogenin gene sequence is appropriately modified to allow expression under this alternate genetic code.

[0045] The eukaryotic host according to various embodiments of the invention may be used as a direct feed or as an indirect feed that is used to enrich the nutrient quality of other organisms in the food chain.

[0046] In a specific embodiment, the transgenic eukaryotic cell is a yeast cell, for example *S. cerevisiae* or *P. pastoris*. *P. pastoris* is particularly preferred since, as indicated above, this host has (1) the ability to grow to high cell densities using inexpensive simple, defined media; (2) the capacity to express high levels of recombinant proteins when multiple copies of an expression cassette are chromosomally integrated; and (3) known to carrying out eukaryotic post-translational modifications (Clare et al, 1991a; 1991b; Cregg et al. 1993; Romanos 1995. In another specific embodiment, the transgenic yeast cell is protease deficient, for example *P. pastoris* strain SMD1168H.

[0047] A specific embodiment of the invention relates to a transgenic SMD1168H strain of *Pichia pastoris* expressing vitellogenin protein, wherein the expression of rVtg, is driven by a glyceraldehyde-3-phosphate dehydrogenase (GAP) promoter (Waterham et al., 1997). The GAP promoter offers an attractive alternative to the alcohol oxidase 1(AOX1) promoter for the heterologous expression of some recombinant proteins. In the presence of glucose, expression under the control of GAP promoter is significantly higher than under the commonly used AOX1 promoter (Waterham et al., 1997). The constitutive GAP promoter allows a simplified fermentation regime and avoids the use of methanol, which is potentially toxic for subsequent applications. In one embodiment, the vitellogenin gene is from *O. aureus*.

[0048] The transgenic host according to the invention, including transgenic yeast described herein may be used as a feed alone, or co-fed with another food source. The specific transgenic host should be capable of being digested by the animal to which it is fed,

and preferably is a natural feed source for the intended animal. For example, if the feed is intended for fish, the transgenic host may be algae or yeast, both of which have been used as feed in aquaculture. Alternatively, transgenic algae or yeast may be used to enrich another food source for fish such as rotifers or artemia (intermediate live feed as they are known in the art). High protein yeast feed has also been used for other domestic animals (Chen et al., 2000). In a specific embodiment, the methylotrophic yeast *Pichia pastoris* transformed according to the invention is used as a live feed or in dry form. In another specific embodiment, the *Pichia pastoris* strain is protease deficient, such as *P. pastoris* SMD1168H.

[0049] Nutritional analyses show that transgenic yeast clones according to the invention expressing rVtg contain increased levels (meaning a detectable increase when compared to a control native yeast strain) of essential amino acids and fatty acids, and these recombinant clones may therefore be advantageously used in aquaculture either as a direct probiotic feed, a feed additive for formulated diets or as primary feed for live intermediate feed hosts such as rotifers or artemia. In one aspect of the invention, the transgenic yeast and other hosts according to various embodiments of the invention are used to enrich an intermediate live feed such as *Artemia* nauplii and in one embodiment, the polyunsaturated lipid content of artemia is increased.

[0050] The level of important n-3 polyunsaturated fatty acids (PUFA) can be drastically elevated by culturing the yeast clones in the presence of fish oil. As PUFA's are important components of cellular and structural function, such transgenic yeast may be particularly advantageous as a feed or feed additive. Another aspect of the invention therefore relates to a method of increasing polyunsaturated fatty acid content in the transgenic eukaryotic host according to the invention comprising culturing the host in a media comprising fish oil. The fish oil may be pure cod liver oil containing approximately 8% (w/v) eicosapentaenoic acid and 7% (w/v) docosahexanoic acid, or other similar fish liver oils. In a specific embodiment, the culture media includes about 2-5 % of fish oil.

[0051] In another aspect, the invention relates to a method for increasing the survival rates of oviparous larvae comprising the step of feeding the larvae with a transgenic yeast or other host or an intermediate live feed that has been fed with a transgenic yeast or other host

according to various embodiments of the invention. In various embodiments the method relates to increasing the survival rates of the larvae of aquatic or marine oviparous animal, such as fish, for example tilapia. The amount of transgenic yeast administered in the method will depend on the nature of the larvae to be fed. For example, the transgenic yeast may be administered to tilapia larvae in an amount corresponding to about 1.0 to 1.6 mg of dried yeast per tilapia larvae per day. In another specific embodiment of the invention, the transgenic yeast may be co-fed with another food source such as rotifers or artemia. The amount of the other food source will depend on the nature of the oviparous larvae being fed. For example, where tilapia larvae are co-fed with rotifers, the rotifers may be fed to the tilapia larvae at a density of 5 individuals per milliliter of the volume of the vessel containing the tilapia larvae. For other larvae, a person skilled in the art would know the appropriate amount of the other food source.

[0052] In yet another aspect, the invention relates to a method of enriching an intermediate live feed, for example artemia or rotifers, comprising the step of feeding to the intermediate live feed a transgenic yeast or other host according to various embodiments of the invention. In a specific embodiment, the total lipid content of *Artemia nauplii* is increased by feeding about 0.5 μ g of the transgenic yeast according to various embodiments of the invention per *Artemia* per day.

[0053] In another aspect, the invention relates to a method for increasing broodstock egg quality of an oviparous animal comprising the step of feeding the broodstock a transgenic yeast or other host or an intermediate live feed that has been fed a transgenic yeast or other host according to various embodiments of the invention. In a specific embodiment, the broodstock are aquatic or marine oviparous animal, for example fish, such as tilapia. The amount of transgenic yeast administered will depend on the nature of the broodstock being fed and whether the transgenic yeast of the invention are employed alone or co-fed with another food source.

[0054] In another aspect, the invention relates to use of recombinant vitellogenin for delivery of a therapeutic material to the maternal oocytes of an oviparous animal. A therapeutic material as used in this context describes any material that enhances the survival

and growth of broodstock and includes hormones, vitamins, minerals, ions, and nucleic acid. For example, if the oocytes of a broodstock animal contains a suboptimal amount of any number of nutrients capable of being bound by vitellogenin, such as minerals, ions, or vitamins, these nutrients may be selectively delivered to oocytes by mixing such materials with purified vitellogenin and subsequently administering the resulting vitellogenin complex to the desired broodstock, for example by injection into the bloodstream of the maternal broodstock animal, where the vitellogenin complex is subsequently taken up by oocytes by Vtg receptor mediated-endocytosis.

[0055] As can be understood by one skilled in the art, many modifications to the exemplary embodiments described herein are possible. The invention is intended to encompass all such modifications within its scope, as defined by the claims.

[0056] The documents referred to herein are fully incorporated by reference.

EXAMPLES

[0057] Bacto yeast extract, bacto-peptone, yeast nitrogen base, bacto-agar, and skimmed milk were obtained from Difco, USA. Zeocin was from Invitrogen, USA and zymolyase was from Seikagaku Corp., Japan. DIG-labelling kit was obtained from Roche, GmbH. Goat anti-rabbit HRP-conjugated antibody was a product of Dako, Denmark, and supersignal chemiluminiscent substrate was purchased from Pierce, USA. Protein A agarose and ³H-leucine were from Zymed (USA) and Amersham (UK), respectively. Fish oil, containing pure cod liver oil with 8.28 % (w/v) eicosapentaenoic acid (EPA) and 7.36 % (w/v) docosahexaenoic acid (DHA) was from Seven Seas, UK.

[0058] EXAMPLE 1 Construction of the expression Vectors & Transformation of *Pichia pastoris*

[0059] *P. pastoris* vectors, pGAPZA and pGAPZαC, were from Invitrogen (USA). The plasmids harbour a dominant selectable shuttle marker, Zeocin, which allows selection of both *E. coli* and *P. pastoris* transformants. While pGAPZA contains no secretion signal, pGAPZαC carries *S. cerevisiae* α-factor secretion signal sequence downstream of GAP

promoter. The constitutive *GAP* promoter allows a simplified fermentation regime over the methanol-inducible *AOXI* promoter by avoiding the use of methanol, which is flammable and is potentially toxic for subsequent applications.

[0060] The tilapia, *O. aureus*, Vtg cDNA (GenBank pOAVtg1 sequence AF017250) was inserted in the sense orientation, downstream of the *GAP* promoter of pGAPZA and pGAPZαC to create three constitutive Vtg expression vectors. Prior to subcloning into the *GAP* vectors, the native TAA stop codon of the Vtg gene was altered to introduce an *ApaI* restriction site to enable subsequent in-frame fusion with the myc-His C-terminal tags in the *GAP* vectors. PCR-based mutations of the cDNA were manipulated in pBlueScript (pBSIISK) vector using the QuikChange™ Site-Directed Mutagenesis kit (Stratagene, USA). The two primers used were the T7 forward primer and 5'-C CAT GGG CCC AGC ACA CTG AGG AGT GCA GC-3', where the *ApaI* site is underlined (SEQ ID NO: 21). The PCR product was sequenced to confirm the change of TAA and TCT codons to GGG and CCC, respectively.

[0061] Vtg(-SS)/pGAPZA is the plasmid for constitutive intracellular expression. Prior to insertion into pGAPZA, the 5' region of the cDNA where the native VtgSS ends was mutated to create an *SpeI* site preceding a new internal start codon. Primers used were 5'-T CTT GCT GTG GCT CTA CTA **GTG ATG** GAC CAG TCC AAC TTG GCC-3' (SEQ ID NO: 22) and 5'-C CAA GTT GGA CTG GTC **CAT CAC** TAG TAG AGC CAC AGC AAG AGC-3' (SEQ ID NO: 23). The *SpeI* restriction sites are underlined and the new ATG codons are bold. In the SEQ ID NO: 22 primer, the codons for the 12th and 13th residue from the translation start site were both changed, from CTC (Leu) and GCA (Ala) to CTA, to create the *SpeI* site. An intentional codon change of the last residue of the VtgSS from GGG (gly) to ATG (met) was made to create a new internal start codon. By digesting the mutated pOAVtg1 with *SpeI*, the fragment flanked by two *SpeI* sites, one from the mutated *SpeI* and the other from the multicloning region of pBSIISK, was lost together with the VtgSS, and the plasmid was religated. Finally, the pOAVtg1 with mutations at both 5' and 3' ends was digested with *NotI* and *ApaI* and the resulting 5.3 kb fragment was inserted between the *NotI* and *ApaI* sites of pGAPZA to create Vtg(-SS)/pGAPZA. A schematic representation of the

Vtg(-SS)/pGAPZA plasmid is depicted in FIG 1A.

[0062] Vtg(VtgSS)/pGAPZA was intended for constitutive expression and secretion of rVtg using native VtgSS. In this vector, a *Oa*Vtg cDNA of 5.4 kb with an intact 5' VtgSS but a mutated 3' TAA codon was inserted between the *Not*I and *Apa*I sites downstream of the GAP promoter in pGAPZA. A schematic representation of the Vtg(VtgSS)/pGAPZA plasmid is depicted in FIG 1B.

[0063] Vtg(α SS)/pGAPZaC was intended for constitutive expression and secretion of rVtg using the *S. cerevisiae* α -factor secretion signal (α SS). To construct this, the *Not*I-AgeI DNA fragment from (A) was inserted in the similar way into the pGAPZaC vector. A schematic representation of the Vtg(α SS)/pGAPZaC plasmid is depicted in FIG 1C.

[0064] All plasmids were prepared by alkaline lysis method and further purified through a CsCl/ethidium bromide gradient-ultracentrifugation. To direct integration of the Vtg expression cassettes, *Bln*I-linearised plasmids (10 μ g each) were added to 80 μ l of competent *P. pastoris* (Higgins and Cregg, 1998). Transformation was effected by electroporation in a 0.2 cm electroporation cuvette, using the BioRad Gene Pulser at 1500 V, 25 μ F and 200 Ω . Transformed colonies were selected on YPD agar plates (1% yeast extract, 2% each of peptone, dextrose, 1 M sorbitol and 2% agar) containing 100, 500 or 1000 μ g/ml Zeocin and incubated at 30 °C for 4 days.

[0065] Preliminary results showed that none of the clones harbouring secretion signal (VtgSS or α SS) secreted rVtg. Regardless of the SS, the rVtg remained within the yeast, in cell lysate and membrane-bound fractions. Nevertheless, this may be advantageous for its application as a recombinant feed. Since Vtg(α SS)/pGAPZaC constructs yielded only minimal number of clones with poor viability, further experiments were carried out with the Vtg(-SS)/pGAPZA and Vtg(VtgSS)/pGAPZA clones.

[0066] EXAMPLE 2 Southern and Western analyses of Vtg gene copy number and expression levels

[0067] It has been reported that the expression levels of a recombinant protein in *Pichia*

can be enhanced dramatically with multicopy transformants (Vassileva et al., 2001). Thus, we investigated the effect of gene copy number on the expression efficiency of the GAP-regulated rVtg constructs. The putative recombinant clones harboring multiple copies of the expression cassette were isolated by selection with increasing concentrations of Zeocin.

[0068] Yeast transformants were spheroplasted using zymolyase, and lysed using 1 % sodium dodecyl sulfate (SDS). Genomic DNA was isolated by ethanol precipitation and resuspended in TE buffer, pH 7.5. The *AvrII*-digested genomic DNA samples (10 µg each) were electrophoresed on a 0.6 % agarose gel and transferred onto 0.45 µm nylon membrane (Pall Biodyne, USA). The Southern blot was hybridised with a DIG-labelled *O. aureus* Vtg *XhoI-XbaI* fragment of 926 bp, excised from *pOaVtg1* (Lim et al., 2001). For normalization, the blot was simultaneously probed with a *histidinol dehydrogenase 4 (HIS4)* gene fragment (612 bp) from the pPIC9 vector (Invitrogen), to detect the presence of the single-copy chromosomal *HIS4* gene. To determine the copy number of the OaVtg cDNA integrated in the yeast host genome, the ratio of the intensity of the Vtg specific band and that of the *HIS4* specific band was obtained by densitometric scan using Image-Master VDS software (Pharmacia Biotech). For normalization of the ratio of intensity, DNA from the untransformed host was also included in the analysis.

[0069] The total protein in culture supernatant, cell lysate and membrane bound fractions were quantified by Bradford assay (Bradford, 1976). The rVtg protein in each fraction was analyzed by SDS-PAGE and immunoblotting (Burnette, 1981) with some modifications. Fixed amount of 35µg of total protein from the lysate and membrane fractions prepared from shake flask cultures of rVtg clones was loaded on a 10 % SDS-polyacrylamide gel. The proteins were transferred by electroblotting. To detect rVtg, rabbit anti-Vtg antibody (1:10000) was used as primary antibody, with goat-anti-rabbit-HRP (1:20000) as secondary antibody, in the presence of 5 % skimmed milk. The chemiluminiscent substrate, Supersignal West Pico was used to develop the signal.

[0070] Southern blots of genomic DNA to determine the copy number of Vtg expression cassettes in Vtg(VtgSS) and Vtg(-SS) clones are shown in FIG 2A. *P. pastoris* genomic DNA isolated from clones that survived selection with increasing zeocin concentrations (100, 500,

and 1000 µg/ml) was digested and probed as described above. The numbers below the blot indicate the copy number of the Vtg expression cassettes based on the ratio of the densitometric intensity of the Vtg bands to those of the *His4*.

[0071] There is an apparent correlation between the increasing Zeocin tolerance (from 100 to 500 to 1000 µg/ml) and the copy number of Vtg expression cassettes (Fig. 2A). Thus, the clones with high copy numbers were named according to their levels of Zeocin Resistance (ZR): (a) clones harbouring Vtg(-SS)/pGAPZA were #1, #2 (1000ZR); #6, #7, #8, #9 (500ZR). (b) clones harbouring Vtg(VtgSS)/pGAPZA were #1, #2 (1000ZR), #50, #52 (500ZR).

[0072] Western analyses of the cell lysate and membrane fractions from the selected ZR clones, detected an rVtg band of 194 kDa (FIG. 2B). The combined levels of rVtg in these two fractions give the total intracellularly expressed rVtg. Amongst these clones, the highest integrants, represented by clones #6 and #52, harbored up to 31 and 21 copies respectively, of Vtg expression cassettes, and they expressed the highest combined (lysate and membrane-bound) levels of rVtg (Fig. 2B). The intensity of the bands compares closely with the copy number of the expression cassettes in the corresponding clone. Henceforth, we focused on investigating clones #6 and #52. Since clone #6 grows most robustly, biochemical analyses were performed on this clone.

[0073] EXAMPLE 3 Effects of media composition on the expression level and integrity of rVtg

[0074] The expression levels of rVtg in cultures of clone # 6 containing the Vtg(-SS)/pGAPZA plasmid were determined in three different YPD-based media: (a) YPD containing 1 % yeast extract, 2 % peptone and 2 % dextrose, pH 6.0; (b) buffered YPD (BYPD) containing YPD supplemented with 100 mM phosphate buffer, pH 6.0; and (c) BYPDN containing BYPD, 1.34 % yeast nitrogen base and 4×10^{-5} % biotin, pH 6.0. Single colonies of the yeast were pre-cultured in 10 ml of each of the 3 media until OD_{600nm} of ~7.0. One ml of this starter culture was inoculated into 200 ml fresh media in a 1 L shake flask for overnight incubation at 23 °C, with continuous shaking at 260 rpm. The optimal time for the

growth of clones was also monitored at 25 °C, 28 °C and 30 °C. From this culture, aliquots of 30 ml were harvested at 16, 19, 22 and 25 hr time points. The cells were pelleted at 5000 g for 5 min. The culture supernatant was set aside for analysis of secreted rVtg. The cell pellet was washed in breaking buffer (50 mM sodium phosphate, pH 7.4, 1 mM PMSF, 1 mM EDTA and 5 % glycerol) and resuspended in 7.5 ml of breaking buffer. The cells were lysed either by glass beads (0.45 µm, Sigma) or French Press (Basic Z 0.75KW Benchtop Cell Disruptor, UK) operated at 30 kpsi. After 1 h centrifugation at 14000 g at 4 °C, the cell lysate and debris were separately stored at -80 °C for further analyses. The debris was solubilised with 1 % SDS to obtain the membrane bound fraction. The Western blot analysis of the cell lysate and membrane fractions were as described above and the position of the 194 kDa vitellogenin band in each of the panels is indicated by the arrow (←). In all three media, it appears that the majority of rVtg is localised to the membrane fractions. The buffered media, BYPD and BYPDN, supported optimal growth of the recombinant yeast and conferred maximal yield of total cell protein. Considering the combined intensity of rVtg in the cell lysate and membrane-bound fractions, higher expression levels were sustained in BYPD (Fig. 3B) and BYPDN (Fig. 3C) than YPD (Fig. 3A). However, degraded bands of rVtg are more prominent in the YPD and BYPDN media. Since culture in BYPD maintained rVtg with highest integrity, further studies employed this medium.

[0075] EXAMPLE 4:rVtg expression in single and multiple shake flasks, and fed-batch fermentation culture of clone #6

[0076] For the single shake flask experiments, Clone #6 was grown at 23 °C in a single 1 L baffled shake flask containing 200 ml of BYPD medium with shaking at 260 rpm. When tested over 23, 25, 28 and 30 °C, the multicopy clones expressed optimally at 23 °C. This is in agreement with the report of Li et al. (2001). At each time point, 30 ml cells were harvested with concurrent top-up of 30 ml of fresh BYPD after each sampling.

[0077] For the multiple shake flask experiments, seven replicates (one for each time point) of 1 L baffled shake flasks, each containing 200 ml of BYPD, were simultaneously inoculated with clone #6. The cultures were grown under the same conditions as the single shake flask culture. At each time point, 30 ml culture was sampled from one of the flasks.

[0078] For the fed-batch fermentation experiments, a single colony of yeast was inoculated into 10 ml BYPD medium and grown overnight at 23 °C in a shaker incubator at 260 rpm, to achieve OD₆₀₀ ~ 7.0. The culture was inoculated into 100 ml of BYPD in a 1 L shake flask and grown to same density before inoculation into 1 L BYPD contained in a 2 L fermentor flask (BioSTAT, B. Braun). The dissolved oxygen level was maintained above 20 % by air saturation at a rate of 2:1 (v/v) of air to fermentor per minute. The pO₂ cascade was maintained at consistent level with appropriate stirring speed. At various time intervals, 30 ml of culture was sampled for analysis and an equal volume of fresh medium was introduced to maintain the original culture volume.

[0079] The rate and peak of expression of rVtg were monitored for each culture condition as shown in FIG 4, where the pH (•), OD 600_{nm} (○) and total protein (▲) of Clone # 6 cultured under the different conditions are shown as a function of time. The Western blot presented below each growth curve in FIG. 4 shows that rVtg was detected in the cell lysate and membrane fractions. Comparison of the three Western blots revealed an apparent forward shift in the time of maximal rVtg protein accumulation from 22h for the single flask, to 18h for the multiple flasks and the fastest time of 16 h for the fed-batch fermentation cultures. Maintaining the pH near 6 appears to be important for prolonging exponential cell growth (refer to FIG. 4C).

[0080] As shown above, the recombinant yeast clones are amenable to continuous fermentor culture, permitting in principle, indefinite rVtg expression. Theoretically, the expression level can be maintained constant in the fermentation culture due to the constitutive property of the GAP promoter. However, rVtg level in fed-batch fermentation culture was maximum at 16 h, achieving peak concentration earlier than the shake flask cultures, but diminished thereafter. This is despite the maintenance in fermentor culture of constant pO₂ and pH. It is unlikely that the Vtg gene was lost after the peak of expression, since further inoculations of the fermentor clones into fresh BYPD again showed similar profiles of rVtg expression, thus, indicating that the integrated Vtg gene was still intact and expression competent. Furthermore, the clones were found to be stable and continuously and constitutively express rVtg over 2-3 years of culture since its existence. A plausible

explanation may be depletion of the carbon source, and low saturation of the culture medium could have occurred after expression. It would be of interest in future, to monitor the levels of Vtg mRNA in the clones over these time intervals and beyond, to determine the point at which the Vtg expression was ceased, viz., the transcriptional or translational levels. This will help to address any potential concerns over the transcriptional and/or translational stress, where the Vtg mRNA stability and Vtg protein integrity, respectively, may become questionable. While this experiment indicates that variations in the culture conditions can drastically affect the expression level of rVtg in *P. pastoris*, a person skilled in the art can take necessary steps to ensure desired level of rVtg expression.

[0081] Immunoprecipitation of ^3H -protein to determine the level of rVtg was performed as follows. Overnight cultures in BYPD were pelleted and washed twice with breaking buffer, resuspended in 50 ml BYPD containing 10 μCi ^3H -leucine (specific activity 5 mCi/ml) and incubated with shaking at 260 rpm at 23 °C for 22 h. The cells pelleted from 15 ml of the culture were lysed using glass beads and centrifuged for 10 min at 9000 g. The supernatant contains the cell lysate. The pellet was solubilised with 0.1 % SDS at 4 °C for 2 h and centrifuged. The resulting supernatant represented the solubilised membrane fraction.

[0082] Subsequently, 100 μl of cell lysate and membrane fraction were preincubated separately with 20 μl preimmune serum for 60 min at 4 °C, following which 20 μl of protein A-agarose was added and allowed to react for 60 min at 4 °C. The samples were centrifuged at 12000 g for 5 min. To the supernatant, 100 μl of anti-Vtg antibody (1:100) was added followed by overnight incubation at 4 °C. After addition of 30 μl of protein A-agarose, the mixtures were centrifuged at 12000 g for 5 min. The immunoprecipitate was washed thrice with immunoprecipitation buffer containing 50 mM Tris, pH 7.5, 50 mM EDTA, 150 mM NaCl, and 1 % NP-40. The resulting immunoprecipitate was treated with TCA (Melo et al., 2000). An aliquot of 50 μl of the radiolabelled cell lysate and membrane fractions were spotted on a 3MM Whatman filter paper and dried at room temperature. The filter papers were washed once with cold 10 % TCA for 25 min and twice with 5 % TCA followed by ethanol:ether (1:1) and finally with ether for 15 min. After drying, the radioactivity of ^3H -labelled Vtg was counted in Aquasol using Wallac 1414 Liquid Scintillation counter

(Beckman).

[0083] Radiolabelling of total protein in clone #6 showed 46.2 % protein in the cell lysate and 53.8 % in the membrane fraction. Immunoprecipitation of the radiolabelled rVtg by Vtg-specific antibodies showed that rVtg represents 1.16 % of total protein (Table 1). The rVtg partitioned into the soluble cell lysate (0.44 %) and membrane fractions (0.72 %).

[0084] EXAMPLE 5 Amino acid analyses of clones #6 and #52

[0085] Unless otherwise stated, the growth and harvest of all *P. pastoris* cultures were performed according to the respective optimal conditions determined for the single shake flask, multiple shake flasks and fed-batch fermentation methodology (refer to Fig. 4). Shake flask cultures of clones #6 and #52 and the control SMD 1168H were harvested, washed and freeze-dried. One mg of freeze-dried yeast cells from the respective time points of different cultures was digested for 22 h with 6 N HCl at 110 °C under vacuum. HCl was evaporated from the sample by passing through nitrogen gas. The dried samples were resuspended in 2 ml of 0.2 M sodium citrate, pH 2.2 and filtered through a 0.22 µm filter. Amino acid analysis was carried out using Shimadzu Amino Acid Analyzer, LC-6A.

[0086] The amino acids values were expressed as nmol/mg dry yeast. All results were normalized against the native *P. pastoris*, SMD1168H. The percentage increase of total amino acid content in clones #6 and #52 is depicted in FIG 5A. Compared to the host SMD1168H, clone #6 shows a 33 % rise in total amino acid content, in contrast to the modest 6 % increase in clone #52. The inset of FIG 5A compares the profiles of percentage increases of total amino acid content amongst cultures of clone #6 in single shake flask (SSF; 19 % increase), multiple shake flasks (MSF; 33 % increase) and fed-batch fermentor (FERM; 15.3 % increase). The percentage increase of individual amino acids in clones #6 cultured in multiple shake flasks is depicted in FIG 5B.

[0087] Examination of the amino acid profiles showed that amongst the 16 amino acids analyzed, the content of 10 amino acids (glu, pro, gly, ala, lys, val, met, ile, his and arg) were higher in clone #6 compared to the control host SMD1168H (Fig. 5B). The latter 6 amino acids are generally considered as essential amino acids for most fish (Cowey and Cho, 1993,

De Silva and Anderson, 1995). Amongst the individual amino acid analyzed in clone #6, arginine and methionine were most significantly enriched (Fig. 5B). Most noteworthy is the 98 % increase in the methionine content. Considering that most formulated diets tend to be methionine-deficient, clone #6 appears to have great potential as a diet supplement.

[0088] EXAMPLE 6: Fatty acid analysis of clones #6 and # 52

[0089] Lipids were extracted from the *Pichia* clones (Folch et al., 1957) using 2:1 v/v chloroform : methanol containing an anti-oxidant (made up with 1 g each of butylated hydroxyanisole and butylated hydroxytoluene in 100 ml chloroform:methanol mixture). Fatty acid methyl esters were prepared using boron trifluoride (AOAC, 1980). Separation of the methyl esters was carried out by gas-liquid chromatography on a Shimadzu GC-9A with a Thermon 3000A (Shimadzu) capillary column (2.5 m x 0.25 mm i.d.). The temperature gradient was programmed at 4 °C/min, over 160 - 220 °C and the flow rate of carrier gas, helium, was 0.63 ml/min. For the identification of fatty acids, a mixture of known fatty acids was used as standard (T. Watanabe, Tokyo University of Fisheries and Sigma).

[0090] In a separate experiment, clone #6 and the native host, SMD1168H, were grown in BYPD supplemented with sterile-filtered 2 % cod liver oil, with a view to improving the fatty acid composition of the rVtg clone (Guo and Ota, 2000). The cells were washed thoroughly with 0.9 % NaCl to remove any trace of adherent fish oil before lipid analysis.

[0091] Comparison of the total lipid content in clones #6 and #52 over native SMD1168H (inset) shows that clone #6 exhibited 47.5 % boost in total lipid content, outperforming the 13 % rise in clone #52. The bar chart in the main figure shows the comparison of the fatty acid composition between clone #6 and control SMD1168H, grown in BYPD with or without fish oil. The first and second numbers below the bar chart represent the numbers of carbon atoms and double bonds in the fatty acid chain and the pharmaceutically important omega 3 fatty acids (n-3) are denoted. Native SMD1168H contains much higher level of lauric acid (12:0) than clone #6. The levels of the myristic acid (C14:0), palmitic acid (16:0), palmitoleic acid (16:1) and the C18 PUFAs are comparable between clone #6 and the control. With the exception of C20:3 (n-6), the levels of C20 and

C22 PUFAs are found in clone #6, but they are low or undetectable in the control. Interestingly, when clone #6 was supplemented with 2 % fish oil as carbon source, the content of the C20 and C22 PUFAs was drastically enhanced. Therefore, the capability of clone #6 in incorporating PUFAs further promotes the application of the rVtg clone as a high quality broodstock diet supplement.

[0092] The level of important PUFAs could be drastically elevated by culturing the yeast clone in the presence of fish oil. Although information on the genome of SMD1168H is lacking, BLAST search using *O. aureus* Vtg gene against the *S. cerevisiae* genome identified a stretch of 100 amino acid residues within the *O. aureus* LVI that shows some similarity to the ABC family long-chain fatty acid transporter, Pxa1p, in *S. cerevisiae*. It is therefore tempting to speculate that this putative fatty acid binding site in the *O. aureus* LV1 that is integrated into the *P. pastoris* clone #6 is functional, thus contributing to the facilitated incorporation of long-chain PUFAs, especially docosahexaenoic acid (DHA, 22:6, n-3). These PUFAs have attracted considerable interest as pharmaceutical and nutraceutical compounds, and are important components of cellular structure and function. They are known to be required by rapidly growing fish larvae (Owen et al., 1975; Sargent et al., 1989; Watanabe, 1982). Owing to its ability to incorporate PUFAs, clone #6 is an excellent candidate for development into a high quality broodstock diet supplement. Therefore, careful considerations must be given to the culture condition, to attain the optimal expression rate, and nutrient value of this novel live recombinant yeast feed-package.

[0093] Although the specific amount of rVtg expressed was not high, the amino acid and lipid analyses showed significant increase in amino acids (33 %) (see EXAMPLE 4) and lipids (47.5 %), indicating the subtle nutrient potentials that clone #6 harbours as a direct single cell protein feed or as a primary feed for enriching rotifers to be used as a live feed for the developing fish larvae (De Silva and Anderson, 1995). The nutrient value is in agreement with other yeast products, which have been used as feed attractants (Sanderson and Jolly, 1994).

[0094] EXAMPLE 7 Feeding trials using clone #6 as novel nutrient package

[0095] The rotifer, *Brachionus plicatilis*, was cultured in seawater (salinity 36 ppt) at 26-30°C in 400 L fiber plastic tanks, for at least 3 months prior to testing. The rotifers were fed twice daily with 0.5 mg of commercial baker's yeast (DCL Yeast Ltd, UK) per million rotifers. The rotifers were filtered and inoculated to 20 L conical cylinder glass tanks to ensure no contamination over two weeks prior to feeding trial with clone #6.

[0096] Wild type *Pichia pastoris*, SMD1168H (SMD) and recombinant yeast clone #6 were cultured as the negative control and test cultures, respectively, in BYPD as previously described. In separate cultures, 2% and 5% pure cod liver oil (SEVEN SEAS, UK) - containing BYPD medium was used to culture the clones for further nutrient enrichment. Cells were freeze-dried and the powder yeasts were sealed and kept at 4 °C. All the cultures were tested by Western-blot to confirm rVtg expression.

[0097] Fertilized eggs from within the mouth of the tilapia fish (*Oreochromis aureus*) were taken periodically to allow artificial hatching in a tank, at a density up to 500 eggs/liter with gentle aeration. Dechlorinated water was used for the culture and the temperature was within 26-30 °C. The water was renewed every day to avoid fungal contamination and to increase the hatching rate. Approximately 3 days after hatching, the larvae were counted to assess the hatching rate, and at the same time, they were randomly distributed into 3 L glass cylinder tanks containing 2.5 L water at a density of 10-20 individuals/L, with gentle constant aeration at 26-33 °C.

[0098] The co-feeding experiments were performed as follows. 50 fish larvae were placed in the tank, and co-fed with rotifer (at a density of 5 individuals/ml) and yeast (either baker's yeast or SMD or #6). Either the commercial baker's yeast or the lab cultured yeasts, all in dried powders were fed at a ratio of 1mg/larvae/day. The survival rate, length and weight of the fish were taken. Six experimental groups were set up:

- (1) feeding with rotifer alone (control);
- (2) feeding with 100 % baker's yeast (control);
- (3) co-feeding with rotifer and yeasts (75% baker's yeast + 25% #6);

(4) co-feeding with rotifer and yeasts (50% baker's yeast + 50% #6);

(5) feeding with the yeasts alone (25% baker's yeast + 75% # 6);

(6) co-feeding with 100% #6 alone (control).

[0099] The results of the co-feeding experiments after 15 days of feeding post hatching are reported in Table 2, where S.c. denotes Baker's yeast (*S. cerevisiae*); ind is an abbreviation for individual and #6 denotes transgenic *P. pastoris* clone # 6.

TABLE 2

	Groups (16 days)	Survival No.	Total Wet Wt. (mg)	Survival Rate (%)	Wet Wt. (mg/ind)	Length (mm)
1	Rotifer	7/50	19.6	14	2.80	10
2	Rotifer + 100% S.c	32/50	148.5	64	4.64	11.1
3	Rotifer + 75% S.c/25%#6.	30/50	82.5	60	2.75	11.4
4	Rotifer + 50% S.c/50% #6	38/50	137.5	76	3.62	10.75
5	Rotifer + 25% S.c/75%#6	41/50	179.0	82	4.37	10.8
6	Rotifer + 100% #6	36/50	176.6	72	4.90	10.8

[00100] The direct yeast feeding experiments were performed as follows. 38 fish larvae were inoculated into the 2.5 L water in the 3 L tanks. Yeasts were offered at the ratio of 1.6 mg yeast / larvae/day. Three groups were set up:

(1) 100% baker's yeast;

(2) 100% SMD1168H

(3) 100% of #6.

[00101] Results of the direct feeding experiment after 48 days of feeding are reported in

Table 3.

Table 3

Group (49 days)	Survival No.	Survival rate (%)	Wet Wt (mg)	Wet Wt (mg/ind)	Mean Length (cm)
S.c	4/38	10.53	139.20	34.80	1.43
SMD	8/38	21.05	220.20	27.53	1.33
#6	17/38	44.74	568.40	33.44	1.42

[00102] The oil-enriched yeast feeding experiments were performed as follows. 32 fish larvae were randomly distributed into 2 of the 3 L tanks with 2.5 L water. Two groups were set up and fed at ratio of 1.6 mg yeast /larvae/day:

(1) 100% of #6 cultured with 2% oil in BYPD

(2) 100% of #6 cultured with 5% oil in BYPD

[00103] Results for the oil-enriched yeast feeding after a 35 day feeding are reported in Table 4.

Table 4

Group	Survival No.	Survival rate (%)	Wet wt (mg)	Wet wt (mg/ind)	Mean Length (mm)
#6 (2% oil)	13/32	40.63	164	12.62	10.89
#6 (5% oil)	24/32	75.00	242	10.08	10.55

[00104] EXAMPLE 8: Live intermediate feed hosts

[00105] Materials

[00106] *Artemia* (*Artemia salina*) cyst was obtained from Biomarine, USA.

[00107] *Pichia pastoris*, SMD1168H (SMD), is the wild type yeast used as the negative control. *FL(-ss)pGAPzA in SMD1168H/500ZR # 6* is the optimal yeast Vtg expression (intracellular) clone tested. The yeasts were cultured as described previously. Recombinant yeast clone #6 was cultured in BYPD medium containing 5 % pure cod liver oil. This culture is henceforth referred to as #6 5% fish oil. With clone #6 grown in fish oil, repeated washings were needed to remove the unconsumed oil. The cells were freeze-dried using a FLEX1-DRY™ (FTS, USA) freeze drier and sealed and kept at 4°C. For comparison, commercially available baker's yeast (*Saccharomyces cerevisiae*, DCL, UK) in lyophilized form was used.

[00108] Summary: The potential of using recombinant vitellogenin in the yeast *Pichia pastoris* as a direct probiotic feed, or for *Artemia* enrichment as nutrient feed to fish larvae has been evaluated. The amount of total lipids of *Artemia* nauplii enriched with recombinant yeast vitellogenin clone #6 (or clone #6 cultured in 5% cod liver oil) increased by 2-fold from 34.23 to 68.27 mg/g compared to the wild type *Artemia* nauplii. Feeding *Artemia* with either clone #6 or clone #6 in 5% oil increased the level of highly unsaturated fatty acids especially eicosapentaenoate (20:5 n-3; EPA) and docosahexaenoate (22:6 n-3; DHA). The level of EPA increased from 3.46 ± 0.46 to $5.57 \pm 0.39\%$ when compared to *Artemia* nauplii fed with wild type *Pichia pastoris* and *Saccharomyces cerevisiae*. The concentration of DHA in *Artemia* nauplii enriched with clone #6 or clone #6 in 5% oil was 0.28 ± 0.14 and 1.02 ± 0.28 , respectively, but the DHA was undetectable in the *Artemia* nauplii fed with *P. pastoris* and *S. cerevisiae*. The maximum length (10.8 ± 0.7 mm) and weight (16.3 ± 2.5 mg) were achieved with tilapia larvae fed with clone #6 or #6 5% oil. The percentage survival ($85.3 \pm 1.5\%$) of the tilapia larvae was significantly ($P < 0.05$) higher when fed with clone #6 or #6 in 5% oil compared to larvae fed with either *S. cerevisiae* or *P. pastoris*, although larval growth (length and weight) did not differ significantly. Co-feeding with wild type *Artemia* nauplii resulted in

improvement of the larval growth and survival rate. Larvae fed 10 days with *S. cerevisiae* and another 10 days with enriched *Artemia* showed no significant difference in growth and survival. However, larvae fed 10 days with clone #6 and another 10 days with clone #6 or clone #6 in 5% oil-enriched *Artemia* achieved maximum length (18.2 ± 0.5 mm), weight (89.6 ± 8.3 mg) and survival (89.0 ± 2.3). Thus, clone #6 and clone #6 in 5% cod liver oil could be used either directly as a high quality live-nutrient feed or indirectly via enrichment through *Artemia* nauplii, which is subsequently fed to the larvae, resulting in significant improvements in growth and survival.

Intermediate live food culture – *Artemia*

[00109] *Artemia* cysts (*Artemia salina*) were hatched in a 15 L conical glass container filled with 10 L of filtered seawater. Strong aeration was provided and the cysts were incubated at room temperature (26-30 °C) for 36 h. *Artemia* nauplii were separated from the empty cysts and debris, and were transferred to clean filtered seawater with aeration. The *Artemia* at second instar stage were sampled and counted for estimation of density.

Enrichment of *Artemia* nauplii with yeasts (wild type and rVtg clones)

[00110] The *Artemia* was enriched by feeding for 48 h with different yeast preparations: (1) baker's yeast; (2) SMD1168H; (3) clone #6 and (4) clone #6 in 5 % fish oil. Each experiment was conducted in triplicate. The yeast was offered at a rate of 0.5 µg per *Artemia* per day. All freeze-dried yeasts were first mixed to homogeneity in a small amount of water. A quantity sufficient for 3-5 day feeding was prepared each time and was kept at -30 °C. Samples of wild type and enriched *Artemia* nauplii were obtained for lipid analysis by collecting 50,000 *Artemia* per triplicate feed on a nylon mesh. The *Artemia* were rinsed using distilled water, blotted on absorbent tissue, transferred to a cryovial, and stored in -30 °C.

Tilapia fish larviculture

[00111] Tilapia *Oreochromis mosambicus* broodstock were collected from the culture tanks. Fertilized eggs within the mother's mouth were taken and were pooled to obtain the required quantity. They were then placed in a 3 L glass cylinder tank with gentle aeration. The water was changed every day to avoid fungal contamination and to increase the hatching rate. Hatched larvae were transferred to 3 L flat-bottomed glass cylinder tanks at a density of 30 larvae/L with gentle and constant aeration. Larvae were reared at 26-30 °C with continuous light.

Feeding trials of tilapia larvae with yeasts with/without *Artemia* nauplii

[00112] Five different feeding experiments were carried out to evaluate the effects of the feed on growth and survival rates of *Oreochromis mosambicus* larvae. All experiments used 3-day posthatched fish larvae at a density of 30/L. The first experiment involved feeding with four different yeasts: (i) *S. cerevisiae*; (ii) SMD1168H; (iii) clone #6 and (iv) clone #6 in 5 % oil. In the second experiment, the larvae were fed with three different combinations of yeasts: (i) 50 % *S. cerevisiae* + 50 % SMD1168H; (ii) 50 % *S. cerevisiae* + 50 % clone #6; and (iii) 50 % *S. cerevisiae* + 50 % of clone #6 in 5 % oil. The third experiment involved feeding for the first 10 days with (i) *S. cerevisiae*; or (ii) SMD1168H; or (iii) clone #6 or (iv) clone #6 in 5 % oil, followed by co-feeding with wild type *Artemia* nauplii (5 individuals/ml) for another 10 days. The fourth experiment involved feeding the larvae for 10 days with three different combinations of yeasts: (i) 50 % *S. cerevisiae* + 50 % SMD1168H; (ii) 50 % *S. cerevisiae* + 50 % of clone #6; (iii) 50 % *S. cerevisiae* + 50 % clone #6 in 5 % oil. After 10 days, the larvae were co-fed for another 10 days with wild type *Artemia* nauplii (5 individuals/ml). The fifth feeding regime was for first 10 days with: (i) *S. cerevisiae*; (ii) clone #6, followed by another 10 days co-feeding with *Artemia* nauplii (5 individuals/ml) which had been enriched previously with either *S. cerevisiae*, SMD1168H, clone #6 or clone #6 in 5 % oil.

Growth and survival assessments of the tilapia larvae

[00113] At the end of the feeding regimes, the larvae were sampled and anesthetized by placing in beakers that were kept in ice. The standard length was defined as the length in millimeters from the tip of the head to the end of the tail. After morphometric measurements, the larvae were placed on paper towels to dry, and weighed. The survival was determined by counting the larvae after the end of feeding experiment.

Lipid and fatty acid analyses

[00114] Total lipids from *Artemia* fed with wild type yeasts and *Artemia* enriched with Vtg yeast recombinant clones were extracted in chloroform/methanol according to Floch *et al.* (1957). Briefly, lipids were extracted from the *Artemia* using 2:1 (v/v) chloroform/methanol containing an antioxidant (made up with 1 g each of butylated hydroxyanisole and butylated hydroxytoluene in 100 ml chloroform: methanol mixture). The fatty acids were converted to methyl esters by the Boron trifluoride (BF₃) method. The methyl esters of fatty acids were further separated by Gas-Liquid Chromatography on a Shimadzu GC-9A with a Thermon 3000A capillary column (2.5 m x 0.25 mm i.d.). The temperature gradient was programmed at 4 °C/min over 160-220 °C and the flow rate of the carrier gas helium, was 0.63 mL/min. For the identification of fatty acids, a mixture of known fatty acids was used as standard (T. Watanabe, Tokyo University of Fisheries and Sigma Co).

Statistical analysis

[00115] Diet-related differences in growth and survival profiles between treatments were analyzed using one-way ANOVA. Differences between means were compared using Newman-Keuls multiple comparisons test. A significance level of 95% ($P < 0.05$) was used throughout.

Results

Artemia nauplii fed with rVtg yeast clone #6 exhibits increased total lipids

[00116] The total lipids in *Artemia* nauplii that has been starved for 48 h decreased by 38% from 34.23 to 21.15 mg/g (see Table 5). This indicates that, *Artemia* enrichment with any of the yeasts should always be applied since lipid contents in *Artemia* gradually decreases after hatching (Watanabe *et al.* 1982). The amount of total lipids of *Artemia* nauplii enriched with clone #6 or clone #6 in 5% fish oil increased from 34.23 to 68.27 mg/g compared to that of wild type *Artemia*.

The fatty acid composition of the cultured *Artemia* nauplii

[00117] The fatty acid composition of *Artemia* nauplii (wild type) and *Artemia* nauplii fed for 48 h with baker's yeast (*S. cerevisiae*, SC), *P. pastoris* (wild type SMD1168H), rVtg clone #6 or clone #6 in 5 % oil, are presented in Table 6. The amount of fatty acid 18:3 in *Artemia* starved for 48 h decreased from $16.5 \pm 0.3\%$ to $9.9 \pm 0.8\%$. In contrast, the amount of fatty acid 20:5 increased from $3.5 \pm 0.6\%$ to $4.7 \pm 0.3\%$ (Fig. 7). Fresh *Artemia* nauplii contained $3.53 \pm 0.55\%$ EPA but lacked DHA. Similarly, *Artemia* fed with SC & SMD1168H contained 3.46 ± 0.46 and $3.85 \pm 0.02\%$ EPA, respectively but lacked DHA. Interestingly, the levels of 20:5 (EPA) and 22:6 (DHA) were found to be higher in *Artemia* fed with clone #6 and clone #6 in 5 % oil, but they were low or undetectable in the *Artemia* fed with control wild type yeasts (Fig 7). The concentration of eicosapentaenoic acid (20.5 n-3) and docosahexaenoate (22.6 n-3) in *artemia* nauplii enriched with clone #6 and #6 in 5% oil were 4.77 ± 0.14 , 5.57 ± 0.39 and 0.28 ± 0.14 , 1.02 ± 0.28 , respectively.

Larvae fed with clone #6 and #6 in 5% oil exhibited higher growth and survival.

[00118] The maximum length, weight and survival were obtained with larvae fed with clone #6 or clone #6 in 5% oil for 20 days are shown in Fig. 8 A & B. The survival of fish larvae fed with SC, SMD, #6 or #6 in 5%oil were 26.6 ± 8.4 , 45.3 ± 6.7 , 82.6 ± 6.7 and 85.3

$\pm 1.5\%$, respectively. The means survival for #6 and #6 in 5% oil fed larvae were statistically significant ($p < 0.05$) than SC and SMD fed larvae. But there was no significant differences between SC and SMD fed larvae. The length and weight of fish larvae fed with SC, SMD, #6 or #6 in 5% oil were not statistically different from each other. On the other hand, supplementing with 50% *S. cerevisiae* results a 15% decrease in larval growth (length and weight). However, the survival rate increased by 5% (Fig. 8 C).

Larvae co-feeding with clone #6 and wild type or #6 enriched *Artemia* exhibited higher growth and survival.

[00119] The co-feeding experiment clearly shows that the larvae fed for 10 days with clone #6 or #6 in 5% oil and subsequently for 10 days with *Artemia* (wild type) showed maximum length (19.6 ± 0.1 and weight (112.2 ± 2.9) when compared to other feeding regimes (Fig. 9 A & B). The survival was also 21% ($p < 0.05$) higher when compared between the larvae were fed 10 days with SC and clone #6 or #6 in 5% oil and subsequently 10 days with wild type *Artemia* (Fig. 9 C). Co-feeding with wild type *Artemia* resulted in improvement of the larval survival rate with SC and SMD yeast fed fish larvae. If we compare larvae fed 10 days with wild type yeast *S. cerevisiae* followed by another 10 days with enriched *Artemia*, there was no significant difference in length and weight between *Artemia* enriched with SC or with clone #6 (Fig. 10 A & B). However, larvae fed for 10 days with clone #6 and another 10 days with enriched *Artemia* achieved maximum length (18.2 ± 0.5) and weight (89.6 ± 8.3) with *Artemia* enriched with #6 (Fig. 10 A & B). Interestingly the highest survival was obtained with larvae fed for 10 days with clone #6 and another 10 days with *Artemia* enriched with clone #6 or #6 in 5% oil (Fig. 10 C).

[00120] Table 5. Total amount of lipids, % of total lipids and % increase in total lipids in fresh, 48 hr starved and 48 hr fed with Baker's yeast SC (*Saccromyces crevisiae*) SMD (*Pichia pastoris*), recombinant yeast clone #6 or recombinant yeast clone #6 cultured in 5% cod liver oil (#6 5% oil). Data are mean $\pm$ SE of triplicate sample.

	Total lipids (mg/g)	Total lipids (%)	% increase in total lipids
Freshly hatched <i>Artemia</i> nauplii	34.23 ± 1.14	3.42 ± 0.11	-
48 hr Starved <i>Artemia</i> nauplii	21.00 ± 1.28	2.10 ± 0.12	- 38.6 ± 1.6
SC fed <i>Artemia</i> nauplii	48.76 ± 2.29	4.88 ± 0.23	43.7 ± 11.5
SMD fed <i>Artemia</i> nauplii	53.10 ± 3.49	5.31 ± 0.35	55.8 ± 15.6
#6 fed <i>Artemia</i> nauplii	65.03 ± 2.30	6.50 ± 0.29	90.3 ± 10.6
#6 in 5% fish oil-fed <i>Artemia</i> nauplii	68.27 ± 2.29	6.82 ± 0.23	99.5 ± 5.6

[00121] Table 6: Comparison of major fatty acid (% mean ± SE) of newly hatched *Artemia* nauplii and *Artemia* nauplii enriched by feeding 48 hr with baker's yeast SC (*Saccharomyces cerevisiae*), SMD (*Pichia pastoris*), recombinant yeast clone #6 (#6) or recombinant yeast clone #6 cultured in 5% cod liver oil (#6 5% oil). Data are mean ± SEM of triplicate sample.

Fatty acid	ARTEMIA (WILD)	SC	SMD	#6	#6 5% Oil
C14:0	1.02 ± 0.40	0.48 ± 0.29	0.62 ± 0.10	0.60 ± 0.09	0.84 ± 0.28
C16:0	9.68 ± 0.99	8.46 ± 0.22	9.32 ± 0.14	8.98 ± 0.41	8.89 ± 1.14
C17:0	1.53 ± 0.05	2.14 ± 0.87	1.94 ± 0.39	1.97 ± 0.30	1.64 ± 0.21
C18:0	3.91 ± 0.40	5.19 ± 0.73	5.44 ± 0.30	4.98 ± 0.52	5.37 ± 0.89
ΣSFA	19.34 ± 0.15	20.15 ± 0.13	20.41 ± 0.16	19.24 ± 0.07	21.74 ± 0.19
C16:1	5.43 ± 0.20	14.59 ± 0.09	4.99 ± 0.31	4.35 ± 0.48	4.11 ± 0.19
C18:1	36.08 ± 1.12	35.93 ± 2.94	34.27 ± 0.95	35.93 ± 0.01	35.40 ± 0.31
C20:1	1.26 ± 0.15	1.15 ± 0.47	0.78 ± 0.20	0.73 ± 0.15	1.16 ± 0.47
C22:1	0.83 ± 0.25	0.81 ± 0.33	0.53 ± 0.45	1.02 ± 0.29	0.87 ± 0.06

Σ MUFA	45.9 ± 0.23	57.35 ± 0.53	42.48 ± 0.17	42.96 ± 0.10	42.57 ± 0.08
C18:2	3.57 ± 0.52	3.14 ± 0.89	4.90 ± 1.59	6.81 ± 1.59	6.72 ± 0.36
C18:3	16.51 ± 0.28	10.02 ± 1.53	11.52 ± 0.41	10.72 ± 0.15	11.41 ± 0.20
C18:4	2.42 ± 0.27	1.64 ± 0.40	1.53 ± 0.27	1.33 ± 0.40	1.64 ± 0.22
C20:4	1.40 ± 0.34	2.19 ± 0.05	2.51 ± 0.40	2.62 ± 0.19	2.36 ± 0.14
C20:5	3.53 ± 0.55	3.46 ± 0.46	3.85 ± 0.02	4.77 ± 0.14	5.57 ± 0.39
C22:6				0.28 ± 0.14	1.02 ± 0.28
Σ PUFA	29.39 ± 0.06	22.45 ± 0.25	27.0 ± 0.27	29.14 ± 0.23	30.41 ± 0.03

[00122] Discussion: One of the greatest obstacles to the mass production of very small, rapidly developing and highly vulnerable fish larvae is the high mortality that occurs in the first two weeks at the early stage of larval development during the transition from endogenous to exogenous food supply. A particular aspect of the problem is that the high growth and developmental rates of the larvae place a premium on providing optimal nutrition so that larval growth and development and, therefore, survival is maximum. Vitellogenin (Vtg) is a principal precursor of yolk proteins crucial for successful embryonic development and rapid growth of the larvae (Owen et al., 1975; Watanabe 1982; Sargent et al., 1989). Furthermore, the fish larvae require some form of live feed, like *Artemia* and rotifer during the earliest growth phases.

[00123] The small size and poorly developed digestive function of fish larvae (Segner et al., 1994) renders pelleted diets unsuitable for first feeding. The only viable alternative involves live-prey species such as *Artemia nauplii* or rotifers. Brine shrimp nauplii (*Artemia* spp.) are widely recognized to be an excellent starter feed for freshwater and marine fish species (Leger et al., 1986). Its nutritional value is strictly dependent on the nutrient quality of its food source, particularly the content of highly unsaturated fatty acids (HUFA), like docosahexaenoic acid (DHA, 22:6) and eicosapentaenoic acid (EPA, 20:5) (Scott and Middleton, 1979; Watanabe et al., 1983; Caric et al., 1993). It has been suggested that such HUFAs function as essential components of biomembranes (Koven et al., 1990), and their levels in the tissue phospholipid fraction are associated with larval growth. Sorgeloos et al.

(1988) reported a strong correlation between the dietary EPA content and survival, and between DHA and growth of the Asian sea bass larvae. Watanabe (1993) concluded that DHA and EPA increased survival and growth of several marine fish larvae. However, these organisms are naturally low in long-chain polyunsaturated fatty acids (PUFA), especially DHA (Navarro et al., 1993; Copeman *et al.*, 2002). Therefore, live feeds enriched with PUFA is highly desired. Lipids are particularly important in fish nutrition, not only for supplying caloric energy but also for providing the essential PUFAs required for normal cell membrane function (Sargent et al., 1995).

[00124] Several enrichment techniques have been developed, including microalgae, oil-based emulsions and microencapsulated preparations (Leger et al., 1986; Southgate and Lou 1995; Barclay and Zeller 1996; McEvou et al., 1996). Oil emulsions have been widely used for enrichment of live feeds in aquaculture (Dhert et al., 1990; Ostrowski and Divakaran 1990; Clawson and Lovell 1992; Stottrup and Attramadal 1992). Emulsion-type preparations have major advantages over dried enrichment diets as they have very high lipid and HUFA content. However, oil emulsions can be difficult to remove from *Artemia* following enrichment and this can result in transfer of oil, leading to water quality problems within larval rearing tanks (Rodgers and Barlow 1987; Rimmer and Reed 1990), and difficulties with swim bladder inflation in larval fish (Foscarini 1988).

[00125] Live nauplii of the brine shrimp (*Artemia* spp.) have been used as vectors for delivering compounds of diverse nutritional (Dhert *et al.*, 1990; Tackaert *et al.*, 1991) and/or therapeutic (Leger *et al.*, 1987; Chair *et al.*, 1991; Touraki *et al.*, 1991; Cappellaro *et al.*, 1993) values, which are otherwise difficult to administer to larval stages of aquatic animals, a process known as bioencapsulation. Bioencapsulated lactic acid bacteria have been successfully introduced into turbot larvae with significant improvements in survival (Garcia et al., 1992). This route has also been used to vaccinate sea bass fry (Chair et al., 1994), and juvenile carp (Joosten et al., 1995).

[00126] Before exogenous feeding, oviparous species of fish larvae are entirely dependent on their yolk supply for nourishment. Presumably, the lipids contained therein represent the optimum balance of fatty acids and other nutrients for the early stages of larval growth. The

present study was designed to evaluate the nutritional value of the yeast recombinant Vtg (rVtg) as a direct probiotic feed, or for *Artemia*-enrichment as nutrient feed. We present data to demonstrate that the tilapia larvae fed with this novel yeast rVtg-enriched *Artemia* nauplii exhibit increased growth and survival.

[00127] Previous examples showed that the recombinant *O. aureus* Vtg yeast clone #6 exhibits significant increase in essential amino acids and long chain polyunsaturated fatty acids, for example, 20:5 n-3 and 22:6 n-3 (Ding et al., 2003). This study has shown that the engineered *P. pastoris* strain (#6) used as a direct feed or for HUFA enrichment of *Artemia* nauplii is an effective nutrient feed. The *Artemia* nauplii enriched with clone #6 supports greater growth of the tilapia larvae than wild type *Artemia* nauplii, which has significantly lower HUFA content.

[00128] The fatty acid composition of *Artemia* is probably the most studied biochemical component of this organism (Bengtson et al., 1991). In this study, the six fatty acids, 16:0; 16:1; 18:1; 18:2; 18:3; and 20:5 make up about 80 % of the total fatty acids in all *Artemia* samples. A large database of published fatty acid profiles reveals that the above six fatty acids, normally make up about 80 % of the total fatty acids in an *Artemia* sample (Leger et al., 1986). The saturated and monoene fatty acids of that group, 16:0, 16:1, and 18:1, typically comprise 40 to 60 % of the total fatty acids. However, the n-3 series of fatty acids, linolenic acid 18:3 (n-3) is essential for fresh water organisms and 20:5 (n-3), is essential for marine organisms. The content of 20:5 (n-3) and 22:6 (n-3) of freshly hatched *Artemia* nauplii is low or even absent.

[00129] *Artemia* feeds on any particulate diet when its particle size is below 50 μm (Dobbeleir et al., 1980). Taking advantage of its continuous nonselective feeding behavior, *Artemia* nauplii fed for 48 h with #6 and #6 5% fish oil showed increase in the fatty acid content of 20:5 (n-3) and 22:6 (n-3). Pre-feeding with SC or SMD1168H lacking 20:5 (n-3) and 22:6 (n-3) did not increase the level of either of these fatty acids in the *Artemia*. When tilapia larvae were fed with #6-enriched *Artemia* or #6 in 5% oil-enriched *Artemia*, the impact of the nutritional value was significantly ($p < 0.05$) reflected in increase in the growth of the larvae compared to those larvae fed with newly hatched wild type *Artemia*. Pre-

feeding with wild type SC or SMD1168H did not enhance the nutritional quality of *Artemia* nauplii. A similar enhancement of the nutritional value of *Artemia* nauplii for marine fish larvae (red seabream) was demonstrated by Watanabe et al. (1980) using algae and yeasts containing EFA (DHA/EPA). From our experiments, it is apparent that the nutritional value of *Artemia* is governed by its content of EFA, especially 20:5 (n-3) and 22:6 (n-3), and that the nutritional value of *Artemia* can be enhanced by enriching the *Artemia* nauplii through pre-feeding with EFA-rich yeast rVtg clone #6 or #6 in 5% oil diets. While similarly, in this study high levels of HUFA are present in recombinant yeast clone #6 in 5% oil microcapsule containing cod liver oil, a major advantage of microcapsulated diet is that the enriching oil is not in direct contact with culture water. This reduces the potential of water quality degradation and bacterial proliferation.

[00130] Some authors have concluded that DHA is superior to EPA as an essential fatty acid for fish larvae. Watanabe (1993) studied the larviculture of five marine fish (red sea bream, yellowtail, striped knifejaw, Japanese flounder and trout) and found that DHA was necessary in greater quantities than EPA, and that its presence in adequate quantities increased survival and growth. Similarly, Rodriguez et al. (1997) reported that gilthead sea bream larvae achieved best growth rate a DHA:EPA ratio of about 1:3. Ibeas et al. (1997) obtained maximal growth of gilthead sea bream larvae with a ratio of 2, while in the juvenile stage the best ratio was found to be 0.5. The highest DHA:EPA ratio found in the present study was 0.25 (*Artemia* fed with #6 5 % fish oil).

[00131] In the larvae feeding experiments, #6 and #6 5 % fish oil proved to be an excellent nutrient supplement, in terms of growth and survival. In contrast, the survival rate was poorest (at 26%) when the larvae were fed exclusively on baker's yeast *S. cerevisiae*. Similarly, by replacing 50 % of #6 with *S. cerevisiae* in the fish diet, only small differences were observed in growth and survival of the tilapia larvae. The wild type baker's yeast and *P. pastoris* have low dietary EFA levels (20:5 n-3 and 22:6 n-3). Low dietary EFA levels can lead to lower growth and higher mortality in fish larviculture (Scott and Middleton, 1979; Watanabe et al., 1983; Caric et al., 1993).

[00132] Several studies have shown the beneficial effect of feeding (n-3) HUFA-enriched

Artemia nauplii to several species of marine fish and crustaceans (Leger et al. 1986). However, no study has clearly indicated the requirements for (n-3) HUFA for one species or another. Furthermore, the n-3 HUFA requirements of larval fish are highly variable. Such differences could be explained by species-specific nutritional requirements, culture period or quality of larvae. The latter can be influenced by both the nutritional conditions during gonad formation (Lavens and Sorgelos, 1991) and the process used for spawning induction of broodstock (Lam 1991). Some investigators have proposed that the presence of (n-3) HUFA may not be important for young (newly hatched) larvae. Kraul (1993) reported that the first stage survival (0-9 days) of mahimahi larvae was not affected by the content of fatty acids in the feed and suggested that this is probably due to high levels of endogenous EPA and DHA stored in the larval yolk sac. Mourente et al. (1993) suggested that the presence of DHA in the diet of larval gilthead sea bream might not be necessary, because they could retain DHA from yolk. A high mortality of gilthead sea bream larvae was observed during the first 2-3 days of external feeding (Rodriguez et al., 1998). The high mortality obtained just after yolk adsorption was probably due to the transition from endogenous to exogenous feeding. Thus, a major advantage of the rVtg yeast clone is its constitutive production of the precursor yolk proteins, hence partially mimicking the natural yolk, which may be useful in buffering sudden switch of feed for the post-yolk absorption larvae.

[00133] In conclusion, the genetically-engineered *Pichia pastoris* rVtg yeast clone #6 used in this investigation promotes good growth and excellent survival in tilapia larvae. They are relatively simple, rapid and economical to prepare using readily available laboratory chemicals and equipment. The clone is robust, can be cultured over long term with neither loss in Vtg gene nor its ability to constitutively express the Vtg protein. The clone can be freeze-dried for prolonged storage. Therefore, large-scale production of yeast biomass represents a potential high quality substitute for fish-based nutrients in aquaculture feeds. Specifically, clone #6 enriched with cod liver oil could be a superior source for DHA and EPA enrichment for a wide variety of oviparous animals. We have demonstrated that the yeast clone could be used either directly as a high quality live-nutrient feed for fish larvae or indirectly via enrichment through *Artemia* nauplii, which is subsequently fed to the larvae, resulting in significant improvements in growth and survival. The subtle source of high

PUFA and HUFA in clone #6 renders it a uniquely enriched nutrient package.

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WHAT IS CLAIMED IS:

1. An expression vector comprising a vitellogenin gene operably linked to a promoter, wherein the promoter is functional in a eukaryotic host suitable for use as a feed or feed additive.
2. The expression vector according to claim 1 wherein the promoter is functional in yeast.
3. The expression vector according to claim 2 wherein the promoter is a constitutive promoter.
4. The expression vector according to claim 3 wherein the promoter is a yeast glyceraldehyde-3-phosphate dehydrogenase (GAP) promoter.
5. The expression vector according to claim 4 comprising SEQ ID NO:1.
6. The expression vector according to claim 5 which is Vtg (-SS)/pGAPZA, Vtg (Vtg SS)/pGAPZA or Vtg (α SS)/pGAPZ α C.
7. A transgenic eukaryotic host suitable for use as a feed or feed additive comprising the expression vector according to claim 1.
8. A transgenic yeast comprising an expression vector wherein the expression vector comprises a vitellogenin gene operably linked to a promoter functional in yeast.
9. The transgenic yeast according to claim 8 wherein multiple copies of the expression vector has integrated into the yeast genome.
10. The transgenic yeast according to claim 8 or 9 wherein the promoter is yeast GAP promoter.
11. The transgenic yeast according to claim 10 comprising SEQ ID NO: 1.
12. The transgenic yeast according to claim 11 wherein the yeast is *Pichia pastoris*.

13. The transgenic yeast according to claim 12 wherein vitellogenin protein is expressed intracellularly.
14. The transgenic yeast according to claim 13 wherein yeast is protease deficient.
15. The transgenic yeast according to claim 14 wherein the amino acid and lipid contents are increased.
16. The transgenic yeast according to claim 15 wherein the level of polyunsaturated fatty acids is increased.
17. A method of increasing the level of polyunsaturated fatty acids in a transgenic yeast according to any one of claims 8 to 15 comprising culturing the transgenic yeast in media comprising fish oil.
18. The method according to claim 17 wherein the concentration of the fish oil in the media is between about 2% and 5%.
19. A method for increasing the survival rates of oviparous larvae comprising the step of feeding the larvae transgenic yeast according to any one of claims 8 to 16 or an intermediate live feed that has been fed transgenic yeast according to any one of claims 8 to 16.
20. The method according to claim 19 wherein the larvae are aquatic or marine larvae.
21. The method according to claim 20 wherein the aquatic or marine larvae are tilapia larvae.
22. The method according to claim 21 wherein the tilapia larvae is fed about 1.0 to 1.6mg of transgenic yeast per tilapia larvae per day.
23. The method according to claim 21 wherein the intermediate live feed is rotifer or artemia.
24. The method according to claim 22 wherein the step of feeding the larvae

transgenic yeast further comprises co-feeding with an intermediate live feed.

25. The method according to claim 24 wherein the intermediate live feed is a rotifer or artemia.

26. The method according to claim 25 wherein the rotifer or artemia is co-fed at a density of 5 individuals per milliliter.

27. A method of increasing broodstock egg quality of an oviparous animal comprising the step of feeding the broodstock the transgenic yeast according to any one of claims 8 to 16 or an intermediate live feed that has been fed transgenic yeast according to any one of claims 8 to 16.

28. The method according to claim 27 wherein the oviparous animal is an aquatic or marine oviparous animal.

29. The method according to claim 28 wherein the aquatic or marine oviparous animal is a fish.

30. The method according to claim 28 wherein the fish is tilapia.

31. A method of enriching an intermediate live feed comprising the step of feeding the intermediate live feed the transgenic yeast according to any one of claims 8 to 16.

32. The method according to claim 31 wherein the intermediate live feed is a rotifer or an artemia.

33. The method according to claim 32 wherein the artemia is an *Artemia* *napulii*.

34. The method according to claim 33 wherein the fatty acid content of the artemia is increased.

35. The method according to claim 34 wherein the fatty acid is a polyunsaturated fatty acid.

36. The method according to claim 35 wherein the polyunsaturated fatty acid is

eicosapentaenoic acid or docosahexanoic acid.

SEQUENCE LISTING

<110> Jeak Ling, Ding
 Toong Jin, Lam
 Eng Hwa, Lim

<120> Recombinant Vitellogenin Enriched Feed

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<150> US 60/425,263
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 275 280 285
 Glu Val Tyr Ser His Val His Met Glu Leu Ile Ser Val Asp Gln Asp
 290 295 300
 Ser Gly Ala Glu Trp Pro Arg Ala Gly Ala Met Arg Pro Ala Gln Ser
 305 310 315 320
 Ile Leu Tyr Ser Leu Ser Thr Lys Gln Met Thr Lys His Tyr Glu Ser
 325 330 335
 Ser Ser Ser Ser Ser Ser Ser Glu Ser His Glu Phe Asn Phe Pro Glu
 340 345 350
 Gln His Glu His Pro His Gln Ser Asn Gln Arg Ser Arg Arg Ser Tyr
 355 360 365
 Met Arg Ser Lys Leu Val Thr Val His Lys Val Leu Lys Lys Arg Asn
 370 375 380
 Ser Glu Ser Ser Ser Gly Ser Ser Ser Ser Ser Ala Asp Ser Ser Ser
 385 390 395 400
 Thr Tyr Ile Asn Asp Asp Ile Pro Asp Ile Asp Glu Pro Ala Tyr Ala
 405 410 415
 Ala Leu Tyr Met Ser Pro Gln Pro His Ala Asp Lys Lys Gln Asn Ala
 420 425 430
 Met Asn Ala Gln Lys Ile Leu Gln Asp Ile Ala Gln Gln Leu Gln Asn
 435 440 445
 Pro Asn Asn Met Pro Lys Ser Asp Phe Leu Ser Lys Phe Asn Ile Leu
 450 455 460
 Val Arg Leu Ile Ala Ser Met Ser Thr Glu Gln Leu Ser Gln Thr Ser
 465 470 475 480
 Arg Ser Ile Glu Thr Ala Lys Thr Ser Asn Asn Ile Ile Lys Ser Asp
 485 490 495
 Met Trp Met Ile Phe Arg Asp Gly Val Thr Gln Ala Gly Thr Leu Pro
 500 505 510
 Ala Phe Lys Gln Ile Gln Ser Trp Ile Glu Asn Lys Lys Ile Gln Glu
 515 520 525
 Glu Glu Ala Ala Gln Val Val Val Ala Leu Pro Arg Thr Leu Arg Tyr
 530 535 540

Pro Thr Lys Gln Ile Met Thr Gln Phe Phe Asn Phe Ala Arg Ser Pro
545 550 555 560

Ala Val Lys Asp Gln Met Phe Leu Asn Ser Ser Ala Leu Met Ala Ala
565 570 575

Thr Lys Leu Ile Asn Leu Gly Gln Val Asn Asn Tyr Thr Ala His Ser
580 585 590

Tyr Tyr Pro Thr His Met Tyr Gly Arg Leu Thr His Lys His Asp Ala
595 600 605

Phe Val Leu Glu Glu Ile Leu Pro Thr Leu Ala Ala Asp Leu Lys Ala
610 615 620

Thr Val Glu Tyr Lys Asp Ser Thr Lys Ala Gln Val Tyr Ile Gln Ala
625 630 635 640

Ile Gly Asn Leu Gly His Arg Glu Ile Leu Lys Val Phe Ala Pro Tyr
645 650 655

Leu Glu Gly Lys Val Glu Ile Ser Thr Tyr Leu Arg Thr His Ile Val
660 665 670

Lys Asn Leu Lys Thr Leu Ala Lys Leu Arg Asp Arg His Val Arg Ala
675 680 685

Val Leu Phe Ser Ile Leu Arg Asn Thr Ala Glu Pro Tyr Pro Val Arg
690 695 700

Val Ala Ala Ile Gln Ser Ile Phe Ile Ser His Pro Thr Gly Glu Met
705 710 715 720

Met Gln Ala Met Ala Glu Met Thr His Asn Asp Pro Ser Val Glu Val
725 730 735

Arg Ala Val Leu Lys Ser Ala Ile Leu Ser Ala Ala Glu Leu Gln His
740 745 750

Pro Arg Asn Phe Tyr Leu Ser Arg Thr Ala Gln Ala Ala Arg Tyr Leu
755 760 765

Val Thr Asn Glu Glu Phe Gly Tyr Gln His Ser Phe Lys Phe Ile Asp
770 775 780

Asp Ser Tyr Asp Glu Asp Asn Asp Ile Gly Thr Phe Val Ile Ser His
785 790 795 800

Ile Gly Ser Glu Asp Ser Leu Leu Pro Lys Asp Phe Lys Ile Val Thr
805 810 815

Asn Ser Lys Gly Gly Ala Trp Glu Arg Asn Thr Ile Glu Ala Ser Phe
820 825 830

Ser Ser Ala Glu Arg Phe Leu Asp Tyr Leu Arg Asp Ser Val Phe Ala
 835 840 845
 Pro His Pro Lys Phe Asp Arg Ala His Lys Tyr Ser Ala Glu Lys Ile
 850 855 860
 Ala Lys Leu Leu Asn Ile Lys Asn Asp Glu Glu Glu Pro Leu Glu Ala
 865 870 875 880
 Ser Phe Tyr Val Asp Phe Met Asn Asn Gln Arg Leu Phe Ser Phe Ser
 885 890 895
 Glu Ser Asp Leu Gln Gln Leu Ser Gln Tyr Ile Ser Glu Tyr Met Lys
 900 905 910
 Lys Val Glu Ser Gly Ala Glu Lys His Tyr Thr Lys Val Tyr Asn Gln
 915 920 925
 Asp Gln Val Ser Ile Met Phe Pro Val Ala Ser Gly Met Pro Phe Ile
 930 935 940
 Phe Lys Tyr Lys Glu Pro Ala Val Ile His Phe Gln Ser Lys Leu Lys
 945 950 955 960
 Gly Lys Phe Ser Phe Pro Ser Lys Asp Asn Lys Tyr Tyr Glu Ala Asn
 965 970 975
 Met Ile Lys Asp Val Gln Phe Thr Tyr Ala Ile Asn Ile Asp Gly Asn
 980 985 990
 Val Gly Phe Met Asp Thr Leu Ser Asn Gln Tyr Ser Ser Val Gly Val
 995 1000 1005
 Val Asn Lys Leu Gln Phe Asn Ile Pro Phe Lys Phe Gly Ile Glu
 1010 1015 1020
 Ile Lys Ser Gly Leu Ile Lys Phe Arg Val Glu Pro Leu His Pro
 1025 1030 1035
 Asp Gln Asp Gln Thr Leu Val His Tyr Ser Val Trp Pro Tyr Ser
 1040 1045 1050
 Ala Ser Gln Lys Lys Asp Ser Leu Val Ala Ile Ser Gln Asp Pro
 1055 1060 1065
 Ala Thr Lys Ile Val Glu Arg Arg Ser Lys Val Phe Ser Val Asp
 1070 1075 1080
 Ser Lys Tyr Gly Gln Ser Thr His Ala Val Ile Tyr Ala Gln Gly
 1085 1090 1095

Tyr Thr Tyr Ser Ser Asp Trp Arg Asn Phe Gly Ala Lys Phe Thr
 1100 1105 1110
 Ser Arg Asp Tyr Phe Thr Asn Leu Ala Ser Leu Leu Thr Gln Glu
 1115 1120 1125
 Asp Ile Ala Leu Thr His Phe Asn Leu Lys His Leu Cys Lys Gln
 1130 1135 1140
 Ser Gln Ser Lys Ala Leu Thr Ile Thr Ala Tyr Tyr Asp Glu Tyr
 1145 1150 1155
 Tyr Asn Gln Gln Asn Ser Gly Ile Leu Thr Asp Ala Thr Asp Arg
 1160 1165 1170
 Asn Asp Leu Ser Pro Asn Ser Glu Thr Arg Arg Ala Glu Met Val
 1175 1180 1185
 Lys Leu Val Ser Ala Gly Ile Asn Lys Ala Arg Val Arg Val Val
 1190 1195 1200
 Asp Leu Ser Ala Ser Phe Glu Gly Ser Gln Asp Gln Asn Tyr Val
 1205 1210 1215
 Leu Thr Gly Thr Trp Gly Asp Ser Pro Val Asp Ser Lys Val Gln
 1220 1225 1230
 Gly Met Leu Phe Ala Gly Thr Lys Ser Ala Thr Gln Gly Asn Gln
 1235 1240 1245
 Gln Ile Asn Ala Val Phe Ala Thr Thr Lys Pro Glu Ile His Ser
 1250 1255 1260
 Leu Ser Phe Ser Lys Pro Leu Gln Ser Asp Leu Arg Ala Pro Phe
 1265 1270 1275
 Gly Met His Phe Lys Tyr Gly Gln Ser Gly Glu Ile Arg Val Ser
 1280 1285 1290
 Gly Ser Phe Asp Arg Thr Lys Lys Tyr Thr Thr Glu Leu Glu Asn
 1295 1300 1305
 His Pro Leu Ala Lys Gln Cys Ser Gln Gln Thr Thr Leu Asn Asn
 1310 1315 1320
 Phe Tyr Gln Asp Ser Cys His Lys Ala Ile Val Met Ala His Ala
 1325 1330 1335
 Pro Asp His Val Glu Phe Ser Val Ser Phe Gln Asp Met Ser Pro
 1340 1345 1350
 Gln Tyr Arg Asn Phe Ser Tyr His Thr Tyr Arg Leu Tyr Glu Tyr
 1355 1360 1365

Leu Gly Tyr Trp Tyr Thr Glu Ala Asn Pro Leu Lys Leu Thr Gln
 1370 1375 1380
 Asn Gly Lys Met Asp Phe Lys Ile Asp Phe Ser Tyr Phe Asp Arg
 1385 1390 1395
 Thr Tyr Thr Val Asp Ile Ala Ser Pro Ser Gly Glu Ala Arg Met
 1400 1405 1410
 Arg Asp Met Pro Ile Ala Thr Met Ala Pro Gly Ala Leu Ser Phe
 1415 1420 1425
 Tyr Gln Pro Leu Lys Ala Tyr Glu Leu Val Ala Asn Tyr Phe Thr
 1430 1435 1440
 Gly His Gln Tyr Gln Pro Tyr Cys Ser Ile Asp Gly Thr Arg Ile
 1445 1450 1455
 His Thr Phe Ser Asn Arg Ser Tyr Glu Tyr Pro Leu Ser Arg Ser
 1460 1465 1470
 Trp His Val Val Met Gln Asp Glu Ser Thr Gln Arg Gly Asn Trp
 1475 1480 1485
 His Glu Leu Ala Ile Leu Ser Arg Arg Gln Gln Arg Asp Gln Gln
 1490 1495 1500
 Glu Ile Tyr Ile Ser Tyr Lys Ser Glu Ser Gly Gln Asp Leu Glu
 1505 1510 1515
 Ile Glu Ile Gln Pro Ala Ser Gly Asp Ser Ala Tyr Gln Val Lys
 1520 1525 1530
 Val Thr Thr Asn Thr Lys Lys Ile Thr Asp Asp Asp Leu Thr Met
 1535 1540 1545
 Tyr Trp Asp Asp Val Lys Glu Gln Pro Phe Leu Gln Tyr His Thr
 1550 1555 1560
 His Lys Asp Gly Val Leu Val Ile Asn Ile Glu Asp Asp Arg Ile
 1565 1570 1575
 Arg Ala Ile Tyr Asp Gly Gln Arg Phe Val Val Phe Thr Gln Asp
 1580 1585 1590
 Tyr Arg Asn Ser Thr Arg Gly Ile Cys Gly Arg Met Ser Gly Glu
 1595 1600 1605
 Gln Arg Asp Asp Tyr Leu Thr Pro Glu Gly Leu Val Asp Lys Pro
 1610 1615 1620

Glu Leu Tyr Ala Ala Ala Tyr Ser Leu Asn Glu Glu Asn Ser Asp
1625 1630 1635

Pro Lys Thr Gln Glu Leu Lys Ala Leu Ala Thr Gln Gln Ala Tyr
1640 1645 1650

Tyr Pro Glu Tyr Lys Tyr Thr Ser Ile Leu Arg Ser Asp Pro Thr
1655 1660 1665

Trp Gln Glu Glu Ser Gln Ser Cys Gly Glu Asp Gln Trp Gln Ser
1670 1675 1680

Glu Thr Val Tyr Lys Ser Arg Ser Tyr Asp Lys His Lys Gly Ala
1685 1690 1695

Cys Glu Val Arg Gln Gln Val Gln Phe Tyr Glu Asn His Gly Asp
1700 1705 1710

Ile Cys Ile Thr Thr Ser Arg Val Pro Ser Cys Gln Ser His Cys
1715 1720 1725

Arg Ala Gly Asp Tyr Lys Ile Gln His Val Gln Val Thr Cys Lys
1730 1735 1740

Ser Lys Leu Asp His Asp Phe Arg Met Tyr Lys Glu Gln Ile Lys
1745 1750 1755

Lys Gly Gln Asn Pro Glu Val Ser Gly Ile Pro Ser Val Lys Gln
1760 1765 1770

Phe Lys Val Pro Val Thr Cys Gln Pro
1775 1780

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<212> PRT
<213> Lymantria dispar

<400> 4

Met Arg Leu Leu Leu Ile Ser Ala Phe Ile Ala Val Val Ser Ser Ser
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Pro Leu Thr Glu Pro Gln Pro Val His Gln Gln Ser Pro Trp Gln Asn
20 25 30

Gly Lys Gln Tyr Leu Tyr Glu Val Asn Ser His Thr Leu Ser His Phe
35 40 45

Tyr Glu Gly Thr Ser Ser Gly Asn Ala Phe Lys Ala Asn Phe Ile Ile
50 55 60

Arg Val Thr Ala Gln Gly Leu Leu Gln Ala Lys Leu Glu Glu Pro Arg
65 70 75 80

Arg Ala Gln Phe His Gln Lys Leu Asp Asn Lys Met Gln Ile Pro Ala
 85 90 95

Asp Leu Lys Tyr Thr Asn Val Val Asn Leu Asp Gln Pro Phe Glu Ile
 100 105 110

Ser Phe Asp Gly Gly Arg Ile Leu Ser Leu Arg Leu Pro Glu Val Leu
 115 120 125

Ser Val Ala Asn Glu Asn Leu Leu Lys Gly Leu Ile Ser Thr Leu Gln
 130 135 140

Val Asp Leu Thr Asn Tyr Arg Leu Val Asn Arg Ser Gln Asp Ser Tyr
 145 150 155 160

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

Thr Gly Asp Cys Glu Thr Val Tyr Ser Val Ser Pro Val Asn Ala Glu
 180 185 190

Trp Arg Arg Glu Val Pro His Phe Ala Ser Asp Ser Ala Pro Ile Gln
 195 200 205

Ile Thr Lys Ser Lys Asn Tyr Asn Arg Cys His Gln Cys Ile Ile Tyr
 210 215 220

Asn Phe Gly Val Pro Arg Gly Ala Leu Trp Thr Gly Ile Ala His Gly
 225 230 235 240

Asn Thr Glu Lys Gln Phe Ile Ser His Thr Thr Val Ser Arg Ile Leu
 245 250 255

Val Gly His Gln Gly Ile Tyr Asn Thr Glu Thr Thr Ser Ser Val Asn
 260 265 270

Val His Pro His Ile His Gly Arg Gln Lys Ala Glu Val His Ser Tyr
 275 280 285

Ile Gln Met Arg Leu Lys Ser Ile Glu Glu Asn Pro Gly Thr Asn Trp
 290 295 300

Gln Lys Pro Glu Ala Thr Arg His Val Lys Ser Leu Leu His Ser Met
 305 310 315 320

Leu Thr Lys Gln Val Gln Asn Ser Tyr Gln Ala Ser Ser Glu Ser Asn
 325 330 335

Glu Glu Thr Glu Gly Ser Thr Tyr Thr Ala Gln Gln Pro Tyr Glu Ala
 340 345 350

Tyr Asp Gly Cys Tyr Tyr Glu Ser Ser Ser Tyr Leu Asp Ser Ser Asn

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

Ala Leu Lys Pro Leu Ala Glu Gln Lys Asp Arg Tyr Val Arg Ser Ala
 645 650 655
 Leu Phe Ser Ile Leu Met Asn Thr Ala Glu Pro Tyr Glu Val Arg Val
 660 665 670
 Ala Ala Ala Met Ile Leu Phe Leu Asn Glu Pro Thr Thr Asp Met Leu
 675 680 685
 Arg Val Met Ala Gln Leu Thr Asn Asp Asp Pro Ser Ile His Val Arg
 690 695 700
 Ala Val Leu Lys Ser Ser Ile Glu Thr Ala Ala Thr Leu Glu Gly Pro
 705 710 715 720
 Lys Tyr Trp His Leu Ala Lys Ala Ala Gln Ser Val Lys Glu Leu Val
 725 730 735
 Thr Ser Glu Asp Phe Gly Tyr Ala Tyr Ser Ala Ala Trp Phe Phe Ala
 740 745 750
 Lys Asn Phe Asp Ser Glu Glu Val Thr Arg Tyr Arg Leu Ala Asn Tyr
 755 760 765
 Ile Gly Ser Asp Gly Ser Leu Ile Pro Asn Leu Phe Ser Leu Thr Trp
 770 775 780
 Asn Asn Arg Phe Tyr Gly Arg Gly Ala Glu Asn Thr Val Gly Phe Thr
 785 790 795 800
 Ser Ser Asn Val Gln Asp Ile Phe Asp Tyr Ile Lys Gln Leu Ile Leu
 805 810 815
 Gln Pro Arg Lys Ser Thr Thr Glu His Gln Phe Ser Ala Asp Lys Ile
 820 825 830
 Ala Lys Leu Leu Asn Ile Lys Gln Asp Pro Leu Gln Pro Ile Glu Ser
 835 840 845
 Ser Ile Tyr Tyr Lys Ile Phe Asp Lys Glu Phe Phe Trp Pro Leu Asp
 850 855 860
 Gln Pro Asn Ile Lys Gln Leu Val Asn Asp Val Phe Gly Phe Val Lys
 865 870 875 880
 Glu Leu Glu Asn Gly Val Gln Ser His Tyr Thr Lys Val Phe Tyr Ser
 885 890 895
 Lys Gln Val Ser Val Ile Phe Pro Ile Ala Thr Gly Glu Pro Phe Val
 900 905 910
 Phe Glu Tyr Lys Glu Pro Val Val Val His Leu Gln Thr Lys Leu Ser

915	920	925
Gly Lys Ile Asn Tyr Pro	Pro Thr Ser Lys Asp	Ile Ser Ser Asn Ile
930	935	940
Gln Thr Glu Ile Gln Phe Thr Phe Ala Arg	Asn Met Glu Gly Ser	Val
945	950	955 960
Gly Phe Ile Asp Thr Asn Thr Asn Gln Leu Ala Asn Ile Gly Val Val		
	965 970	975
Lys Lys Tyr Gln Ile Asn Leu Pro Val Lys Ile Asn Val Ile Gly Gln		
	980 985	990
Ser Gly Lys Phe Gln Val Lys Leu Glu Pro Leu His Thr Asp Gln Asp		
	995 1000	1005
Leu Ile Leu Leu His His Ser Val Trp Pro Tyr Ser Ala Tyr Gln		
	1010 1015	1020
Gln Thr Asn Thr Thr Thr Thr Pro Ser His Asp Leu Lys Thr Lys		
	1025 1030	1035
Leu Ile Lys Arg Leu Lys Lys Val Ala Glu Met Asn Lys Glu Leu		
	1040 1045	1050
Gly Gln Gln Phe Asn Leu Leu Phe Lys Tyr His Gly Phe Ser Ser		
	1055 1060	1065
Ser Asn Thr Tyr Arg Asn Ala Gly Asp Phe Val Gln Asp Ala Leu		
	1070 1075	1080
Asp Phe Ser Asp Phe Met Ser Leu Asn Asp Leu Ala Glu Thr His		
	1085 1090	1095
Tyr Glu Phe Thr Tyr Ser Gly Lys Gln Ser Lys Thr Lys Ala Val		
	1100 1105	1110
Thr Phe Thr Ala Ala Tyr Asp Val Ser His Asn Leu Asn Ser Thr		
	1115 1120	1125
Gly Lys Phe Gly Glu Ala His Arg Phe Ser Asp Val Thr Pro Asn		
	1130 1135	1140
Ser Ala Pro Arg Arg Glu Glu Ile Val Lys Arg Val Ser Ser Gly		
	1145 1150	1155
Ile Lys Thr Ala Thr Ala Arg Val Ile Asp Phe Ser Ala Ser Phe		
	1160 1165	1170
Glu Gly Leu Gln Lys Leu Glu Tyr Ala Val Thr Ala Ala Val Ala		
	1175 1180	1185

Gly Ser Met Val Asp Leu Lys Thr Gln Phe Ala Val Phe Met Gly
 1190 1195 1200
 Ser Gln Ser Asp Asn Gly Gln Ile Asn Ala Val Phe Lys Leu Gln
 1205 1210 1215
 Lys Pro Gln Met Ala Pro Leu Asp Phe His Lys Ala Leu Asn Ser
 1220 1225 1230
 Ala Val Lys Tyr Leu Ile Glu Ala Asp Val Thr Tyr Gly Glu Asn
 1235 1240 1245
 Ser Asn Ile Asn Phe Lys Gly His Thr Glu Arg Ser Gln Glu Tyr
 1250 1255 1260
 Ala Glu Gln Leu Lys Asn Ser Leu Trp Ala Asn Gln Cys Ala Gln
 1265 1270 1275
 Glu Asn Ala Gln Gln Asn Lys Phe Gln Leu Gly Cys His Asn Val
 1280 1285 1290
 Leu Ile Glu Ser His Ala Pro Asp Arg Phe Lys Ala Ser Ile Thr
 1295 1300 1305
 Tyr Lys His Ile Pro Ala Ala His Thr Ala Leu Leu Asp Ser Tyr
 1310 1315 1320
 Ile Gln Gly Leu Trp Ser Lys Gly Phe Glu Tyr Asn Pro Ser Lys
 1325 1330 1335
 Arg Leu Pro Val Gly Gln Ile Glu Leu Glu Ala Asn Ala Ser Tyr
 1340 1345 1350
 Val Asp Gln Thr Ala Asn Val Ala Trp Thr Trp Trp Asn Gly Gln
 1355 1360 1365
 Val Arg Phe Asn Asn Leu Pro Asn Thr Tyr Ile Thr Pro Ala Leu
 1370 1375 1380
 Thr Thr Ala Tyr Gln Pro Ile Gly Ile Glu Asp Ser Trp Thr His
 1385 1390 1395
 Phe Ala Asn Ser Tyr Ser Tyr His Gln Tyr Glu Pro Phe Cys Thr
 1400 1405 1410
 Val Asp Gly Thr Lys Val Lys Thr Phe Ser Asn Arg Asp Tyr Asn
 1415 1420 1425
 Val Thr Leu Pro Glu Ile Trp Thr Val Leu Met His Ala Gln Thr
 1430 1435 1440
 Asn Trp Glu Glu Leu Val Val Leu Ala Lys Arg Pro Asn Glu Ala

1445		1450		1455
Lys Ala 1460	Lys Arg Glu Ile	Gly 1465	Lys Ile Gly Lys	Leu Asp Leu Tyr 1470
Ile Ser 1475	His Lys Thr Ala	Thr 1480	Gly Lys His Leu	Glu Val Asn Ile 1485
Pro Tyr 1490	Ser Ala Ala Asn	Asn 1495	Lys Ala Asn Val	Lys Val Glu Thr 1500
Asn Ala 1505	Gln Leu Val Ala	Asp 1510	Gly Asp Leu Thr	Thr Tyr Trp Asp 1515
Asp Val 1520	Ala Glu Thr Pro	Leu 1525	Leu Gln Tyr Ser	Asn His Pro Asp 1530
Arg Val 1535	Leu Leu Leu His	Leu 1540	Ser Asp Gly Leu	His Leu Leu Phe 1545
Asp Gly 1550	Lys Arg Gly Ile	Phe 1555	Thr Thr Ser Gln	Tyr Arg Asn Ile 1560
Thr Arg 1565	Gly Ile Cys Gly	Gln 1570	Asn Ser Gly Asp	Pro Leu Asp Asp 1575
Tyr Lys 1580	Thr Pro Leu Gly	Ile 1585	Val Asp His Ser	Gln His Phe Gly 1590
Ala Ala 1595	Phe Thr Leu Asp	Leu 1600	Glu Lys Thr Asn	Ser Gln Ile Gln 1605
Gln Trp 1610	Lys Lys Ile Ala	Gln 1615	Glu Thr Ala Tyr	Gln Pro Lys Leu 1620
Thr His 1625	Thr Val Ile Leu	Arg 1630	Phe Asp Glu Glu	Trp Lys Ile Ala 1635
Gly Glu 1640	Gln Lys Gly Leu	Glu 1645	Trp Gly Ser Gln	Lys Val Tyr Arg 1650
Ser Arg 1655	Ser Tyr Gln Lys	Gln 1660	Arg Gly Pro Cys	Gln Val Gln Asn 1665
Gln Val 1670	Gln Tyr His Glu	Asn 1675	His Gly Glu Ile	Cys Ile Thr Thr 1680
Thr Pro 1685	Ile Ser Ala Cys	Gln 1690	Ser His Cys His	Ser Ser Asn Tyr 1695
Gln Val 1700	Gln Ala Val Gln	Ala 1705	Val Cys Lys Gly	Lys Lys Asp Pro 1710

Glu Phe Arg Met Tyr Lys Asp Gln Ile His Gln Gly Gln Asn Pro
 1715 1720 1725

Gln Val Thr Gly Val Pro Lys Val Glu Gln Tyr Arg Val Pro Thr
 1730 1735 1740

Thr Cys Thr Glu
 1745

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 <212> PRT
 <213> *Athalia rosae*

<400> 5

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

Gly Arg Thr Leu Ala Ala Leu His Gln Val Ala Asp Gln Tyr Thr Gly
 35 40 45

Ile Ala Leu Lys Ala Gln Leu Lys Cys Gln Pro Lys Gly Ser Asp Ala
 50 55 60

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

Leu Pro Gly Gly Trp Asp Ser Pro Leu Pro Glu Lys Lys Thr Asn Tyr
 85 90 95

Gln Lys Phe Glu Leu Ser Glu Lys Pro Phe Glu Ile Lys Phe Lys Asn
 100 105 110

Gly Val Ile Asp Asp Leu Val Val Glu Lys Ser Leu Pro Thr Trp Gln
 115 120 125

Val Asn Ile Ile Lys Ser Ile Ala Ser Gln Leu Gln Val Asp Thr Gln
 130 135 140

Gly Glu Asn Ala Met Lys Ser Arg Tyr Asn Gln Glu Pro Glu Gly Asp
 145 150 155 160

Gln Ala Tyr Ala Thr Tyr Lys Ala Met Glu Asp Thr Val Thr Gly Glu
 165 170 175

Cys Glu Val Leu Tyr Asp Ile Ser Pro Leu Pro Glu Tyr Val Leu Gln
 180 185 190

Thr Lys Pro Glu Leu Ala Pro Val Pro Gln Leu Lys Gly Ser Gly Gln
 195 200 205

Ile Ile Asp Ile Val Lys Thr Ser Asn Phe Ser Asn Cys Glu Gln Arg
 210 215 220
 Met Gly Tyr His Phe Gly Ile Thr Gly Glu Thr Asp Trp Glu Ala Gly
 225 230 235 240
 Ser Asn Ser Met Gly Asp Phe Leu Ala Lys Ser Ser Val Ser Arg Val
 245 250 255
 Val Ile Ser Gly Ser Leu Asp Arg Tyr Thr Ile Gln Ser Ser Val Thr
 260 265 270
 Thr Asn Lys Ile Val Val Ser Pro Asn Leu Lys Tyr Ser Gln Lys Gly
 275 280 285
 Met Val Val Ser Arg Leu Asn Ile Thr Leu Asp Ser Val Asn Ala Ala
 290 295 300
 Ser Gly Ser Pro Arg Ser Pro Ser Glu Pro Glu Ser Thr Gly Asn Leu
 305 310 315 320
 Val Tyr Ser Tyr Asn Ser Pro Phe Glu Ala Asn Asn Lys Arg Arg Pro
 325 330 335
 His Asn Asn Asn Asp Asp Asp Ser Ser Ser Ser Ser Ser Ser Ser Ser
 340 345 350
 Ser Ser Ser Ser Ser Ser Ser Ser Ser Ser Ser Ser Ser Ser Ser Glu
 355 360 365
 Glu Asp Gln Gln Arg Gly Asn Ser Glu Asn Lys Asn Asn Asn Gln His
 370 375 380
 Gly His Arg Gln Ala Arg Ala Ala Asn Gln Arg Gly Gln Gly Asn Gln
 385 390 395 400
 Asp Ser Asp Ser Ser Ser Ser Ser Ser Ser Ser Ser Ser Ser Ser Ser
 405 410 415
 Ser Ser Asp Ser Ser Ser Ser Ser Ser Ser Glu Ser Asp Ser Leu Ser
 420 425 430
 Ser Ser Glu Glu Tyr Trp Gln Ser Arg Pro Thr Leu Thr Asp Ala Pro
 435 440 445
 Glu Ala Pro Met Leu Pro Leu Phe Ile Gly Tyr Lys Gly Ser Ala Ala
 450 455 460
 Gln Gln Ser Ser Gln Val Asn Pro Val Ser Val Ala Lys Lys Leu Ala
 465 470 475 480

Ser Gln Ile Gly Glu Glu Leu Gln Lys Pro Ser Asn Ile Pro Lys Gln
 485 490 495
 Asn Thr Leu Glu Lys Phe Ser His Leu Ala Ala Leu Leu Arg Thr Met
 500 505 510
 Ser Ala Lys Gln Ile Glu Gln Ala Ala His Asp Met Tyr Ala Pro Ala
 515 520 525
 Lys Glu Asn Ala Ser Lys Ser Glu Ser Ala Lys Asn Ala Ala Trp Lys
 530 535 540
 Ala Phe Arg Asp Ala Val Ala Gln Ala Gly Thr Gly Pro Ala Phe Ser
 545 550 555 560
 Val Ile Lys Asn Trp Ile Gln Thr Asn Lys Ile Arg Asn Asn Gln Ala
 565 570 575
 Ala Asp Leu Ile Ala Val Leu Pro Ser Thr Thr Arg Tyr Pro Thr Ala
 580 585 590
 Glu Tyr Met Asp Ala Phe Phe Glu Leu Ala Thr Ser Pro Glu Val Thr
 595 600 605
 Lys Gln Ala Pro Leu Asn Asn Thr Ala Ile Leu Ala Phe Ala Asp Leu
 610 615 620
 Val Arg Glu Ser Gln Val Asn Asn Ala Ser Ala His Gly Arg Tyr Pro
 625 630 635 640
 Val His Ser Phe Gly Arg Leu Ser Pro Lys Asn Asn Pro Ala Val Gln
 645 650 655
 Gly Gln Trp Ile Pro Tyr Ile Ala Lys Gln Leu Lys Ser Ala Ile Arg
 660 665 670
 Ala Ala Asp Ser Gln Lys Ile Gln Val Tyr Ile Arg Ala Leu Gly Asn
 675 680 685
 Val Gly His Pro Lys Met Leu Ser Val Phe Glu Pro Tyr Leu Glu Gly
 690 695 700
 Gln Glu Asp Ser Ser Asp Phe Gln Arg Leu Ser Met Val Leu Ser Met
 705 710 715 720
 Gly Asn Leu Ala Arg Leu Tyr Pro Lys Gln Ala Arg Ala Val Leu Tyr
 725 730 735
 Lys Ile Tyr Gln Asn Thr Gly Glu Ala Tyr Gln Val Arg Thr Ala Ala
 740 745 750
 Val Phe Gln Leu Met Arg Thr Asn Pro Pro Pro Ser Met Leu Gln Arg
 755 760 765

Met Ala Glu Phe Thr Asn Gln Asp Thr Ser Lys Gln Val Asn Ala Ala
770 775 780

Val Lys Ser Ile Ile Glu Thr Ala Ala Lys Leu Asp Asp Ala Glu Leu
785 790 795 800

Ala His Asn Ala Arg Ala Ala Arg Asp Leu Leu Ser Thr Lys Asn Met
805 810 815

Gly Leu Gln Tyr Ser Arg Gly Trp Leu His Asp Tyr Thr Ser Glu Ala
820 825 830

Met Ser Ser Gly Tyr Gln Leu Asn Ser Tyr Trp Ile Gly Ser Glu Asp
835 840 845

Ala Ile Ala Pro Gln Ala Val Phe Ala Thr Ala Ala Phe Asn Lys Gly
850 855 860

Gly Phe Gln Ser Pro Ala Ser Ile Tyr Gly Ala Met Val Ser Ser Val
865 870 875 880

Asp Asp Leu Leu Asp Val Leu Tyr Asp Gln Phe Glu Asp Asn Asp Glu
885 890 895

Ala Asn Gln Lys Lys Asn Ser Lys Ser Ser Lys Phe Ser Pro Glu Asn
900 905 910

Ile Leu Asn Ala Leu Asn Ile Gln Ser Asn Asp Ala Glu Gln Leu Glu
915 920 925

Gly Ser Phe Leu Phe Pro Ala Leu Gln Gly Asn Arg Phe Tyr Ala Phe
930 935 940

Asp Asn Asn Thr Ile Glu Gln Leu Pro Lys Val Val Lys Gln Ala Ala
945 950 955 960

Ala Ala Leu Lys His Gly Gln Ser Phe Asn Tyr Thr Lys Leu Tyr Ser
965 970 975

Asn Glu Glu Leu Thr Val Ser Phe Pro Thr Ala Met Gly Leu Pro Phe
980 985 990

Val Tyr Thr Met Arg Thr Pro Ser Leu Val Gln Val Gly Gly Glu Ile
995 1000 1005

Gln Ala Arg Thr Tyr Pro Glu Gln Tyr Ser Gly Ser Asn Glu Glu
1010 1015 1020

Ile Ser Ile Pro Glu Ala Val Asn Ala Ser Leu Asp Ile His Ala
1025 1030 1035

Val Tyr Ser Ser Lys Val Ile Ala Arg Ile Gly Phe Val Asn Pro
 1040 1045 1050
 Ala Asn His Gln His His Met Ala Gly Tyr Asp Lys Asn Phe Gln
 1055 1060 1065
 Val Asn Leu Pro Leu Ser Ala Glu Met Asp Ile Asp Leu Glu Asn
 1070 1075 1080
 Ser His Val Arg Val Lys Leu Glu Pro Ile Gln Gln Asn Lys Glu
 1085 1090 1095
 Tyr Asn Leu Phe His Tyr Ser Ser Trp Pro Tyr Thr Ala Gln Lys
 1100 1105 1110
 Asp Ile Leu Ser Glu Lys Pro Val Ser Gln Gln Lys Gly Tyr Ala
 1115 1120 1125
 Leu Ile Ser Glu Arg Gly Ser Glu Gln Asn Glu Trp Ala Phe Gly
 1130 1135 1140
 Gln Lys Ser Thr Gly Leu Ala Leu Arg Phe Thr Ser Glu Gly Glu
 1145 1150 1155
 Gln Thr Glu His Gln Leu Arg Asn Trp Ala Trp Glu Met Leu Gln
 1160 1165 1170
 Ser Glu Asp Pro Leu Ala Ile Ala Phe Ser Leu Asp Asp Glu Ile
 1175 1180 1185
 Gln His Ser Asn Tyr Asn Leu Trp Leu Asp Gly Gln His Ser Ser
 1190 1195 1200
 Asn Glu Ala Val Val Leu Thr Ala Ser Tyr Ala Asn Tyr Thr Lys
 1205 1210 1215
 Gly Met Gly Gly Asp Ser Asp Ser Gln Ser Gly Tyr Gln His Pro
 1220 1225 1230
 Ala Gly Arg Lys Asn Ser Gly Gly Glu Asp Asn Gln Ser Ser Ser
 1235 1240 1245
 Thr Phe Val Pro Ala Phe Gln Pro Ser Ser Gln Lys Pro Asp Ser
 1250 1255 1260
 Glu Ser Arg Gln Gln Glu Leu Leu Gln Lys Ala Ala Ser Gly Ile
 1265 1270 1275
 Lys Asp Ala Tyr Ser Gln Ser Ile Asp Phe Gly Ala Val Phe Gln
 1280 1285 1290
 Gly Lys Asn Lys Ala Glu Tyr Ala Ala Thr Phe Ala Met Ala Asn
 1295 1300 1305

Ser Pro Val Asp Pro Lys Ser Arg Val Val Phe Tyr Tyr Gly Ser
 1310 1315 1320
 Asn Pro Ala Gln Gln Lys Asn Tyr Gln Ile Cys Leu Ser Ala Gln
 1325 1330 1335
 Ser Ser Arg Pro Lys Val Pro Val Met Asp Phe Ile Lys Ala Leu
 1340 1345 1350
 Lys Ala Asp Pro Thr Thr Lys Phe Ala Ala Asp Leu Lys Phe Gly
 1355 1360 1365
 Glu Gln Cys Gln Ser Gly Ala Gln Val Gln Ile Gln Gly Gln Leu
 1370 1375 1380
 Glu Gln Thr Glu Gly Arg Arg Glu Tyr Leu Arg Arg Thr Pro Thr
 1385 1390 1395
 Gly Gln Gln Cys Ala Gln Gln Met Gln Glu Gly Asn Lys Ile Leu
 1400 1405 1410
 Pro Ala Cys Arg Asn Val Thr Ala Arg Ala Asn Phe Leu Asn Glu
 1415 1420 1425
 Gly Ser Leu Thr Val Lys Phe Ser His Val Thr Asp Tyr Met Lys
 1430 1435 1440
 Asn Val Ser Ala Arg Ala Tyr Gly Leu Ala Arg Tyr Phe Gly Tyr
 1445 1450 1455
 His Ser Ala Tyr Glu Asn Ile Val Asn Pro Gly Asn Gln Lys Asn
 1460 1465 1470
 Gly Gln Ile Asp Phe Gly Tyr Glu Ile Ser Pro Asp Phe Gln Arg
 1475 1480 1485
 Leu Asn Val Ser Met Ser Ala Pro Gly Leu Asp Ala Asn Ile Thr
 1490 1495 1500
 Asp Leu Glu Ile His Pro Trp Ala Arg Ser Ile Val Ala Val Asp
 1505 1510 1515
 Pro Val Gln Ser Gly Ala Arg Arg Phe Ala Arg Glu Ala Leu Ala
 1520 1525 1530
 Gly Gln Tyr Asn Pro Thr Cys Val Ile Asp Asn Asn Gln Ala Ser
 1535 1540 1545
 Thr Phe Asp Asn Lys Thr Tyr Pro Ile Glu Leu Gly Asn Cys Trp
 1550 1555 1560

His Val Val Met Thr Thr Ile Pro Asp Asp Glu Gln Asn Gly Asp
 1565 1570 1575
 Asp Glu Ile Pro Glu Asp Met Arg Val Ser Val Val Cys Arg Asp
 1580 1585 1590
 Ile Asn Glu His Gln Arg Glu Cys Arg Leu Val Leu Gly Glu Ala
 1595 1600 1605
 Glu Ile Glu Met Tyr Pro Asn Asn Asp Gln Ala Ala Ile Lys Val
 1610 1615 1620
 Asn Gly Arg Ala Val Gln Leu Ser Gln Glu Glu Thr Tyr Arg Tyr
 1625 1630 1635
 Thr Ser Gln Asn Gly Glu Ile Gln Phe Glu Ala Tyr Leu Lys Pro
 1640 1645 1650
 Ser Gly Val Val Tyr Ile His Ser Glu Glu Tyr Gly Val Arg Ala
 1655 1660 1665
 Leu Tyr Asp Gly Glu Arg Ile Lys Leu Ile Leu Asn Asn Glu Tyr
 1670 1675 1680
 Arg Asp Gln Ile Arg Gly Leu Cys Gly Thr Phe Asn Gly Glu Pro
 1685 1690 1695
 Ala Thr Asp Phe Thr Ala Pro Gln Asn Cys Ile Leu Lys Asn Pro
 1700 1705 1710
 Glu His Phe Ala Ala Ser Tyr Ala Leu Thr Lys Asp Gln Cys Glu
 1715 1720 1725
 Gly Pro Ala Lys Glu Asn Ala Arg Arg Ala Gln Gln Ala His Cys
 1730 1735 1740
 Tyr Arg Glu Ala Val Leu Phe Gly Asn Val Val Ser Asp Gln Asp
 1745 1750 1755
 Ala Gly Arg Ser Lys Asn Lys Asp Ser Lys Trp Glu Asn Asn Lys
 1760 1765 1770
 Ser Arg Lys Ser Gly Ser Gly Gly Lys Lys Ser Gly Ser Cys Thr
 1775 1780 1785
 Lys Phe Ala Thr Ala Thr Ile Glu Glu Asn Gly Lys Thr Cys Phe
 1790 1795 1800
 Ser Leu Arg Pro Val Ala Thr Cys Ala Ala Gly Cys Lys Ala Thr
 1805 1810 1815
 Arg Lys Gln Glu Thr Thr Val Lys Met His Cys Val Gln Ser Ser
 1820 1825 1830

Ser Ser Ser Gln Gln Leu Val His Arg Ile Lys Gln Gly Ala Asn
1835 1840 1845

Pro Asp Phe Ser Gln Lys Ser His Asp Lys Ser Ser Arg Ile Glu
1850 1855 1860

Val Pro Glu Ser Cys Val Ala Gln Gln
1865 1870

<210> 6
<211> 1807
<212> PRT
<213> *Pimpla nipponica*

<400> 6

Met Trp Cys Pro Leu Phe Leu Val Leu Leu Ala Gly Ala Ala Thr Ala
1 5 10 15

Glu His Leu Gln Ala Trp Lys Thr Asp Thr Glu Tyr Gln Tyr Ala Val
20 25 30

Arg Gly Arg Thr Leu Ser Ala Leu His Asp Val Ala Asp Gln Tyr Ser
35 40 45

Gly Ile Ile Met Arg Ala Leu Leu Thr Ile Gln Pro Lys Ser Asp Gly
50 55 60

Thr Leu Glu Ala Lys Val Thr Lys Ala Arg Tyr Ala Gln Ile His Thr
65 70 75 80

Lys Leu Pro Gly Gly Trp Asn Ser Glu Ile Pro Asp His Lys Leu Glu
85 90 95

Met Lys Gln Phe Pro Met Ser Glu Lys Val Phe Glu Ile Lys Met Lys
100 105 110

His Gly Val Val Arg Asp Leu Ile Val Asp Lys Asp Val Pro Thr Trp
115 120 125

Glu Val Asn Val Leu Lys Ser Ile Val Ser Gln Leu Gln Val Asp Thr
130 135 140

Gln Gly Glu Asn Leu Met Ala Ser Lys Tyr Asn Gln Glu Pro Glu Asp
145 150 155 160

Glu Gly Val Thr Ala Met Phe Lys Thr Met Glu Asp Thr Val Gly Gly
165 170 175

Arg Cys Glu Val Leu Tyr Asp Ile Asn Pro Leu Pro Glu Phe Val Leu
180 185 190

Gln Lys Arg Pro Glu Leu Val Pro Met Pro Asp Ile Arg Gly Asp Gly

33

Ser Asn Asn Glu Ile Asp Pro His Asp Glu Ser Gln Ser Val Arg Arg
 485 490 495

Gly Thr Trp Ala Ala Phe Arg Asp Ala Val Ala Gln Ala Gly Thr Ala
 500 505 510

Pro Ala Leu Val Thr Ile Thr Leu Trp Ile Lys Gln Lys Lys Ile Arg
 515 520 525

Gly Val Glu Ala Ala Ser Val Val Gly Val Leu Ala Lys Thr Ala Arg
 530 535 540

Thr Pro Thr Arg Glu Tyr Ile Asp Val Phe Phe Glu Leu Ala Thr Met
 545 550 555 560

Pro Glu Thr Ile His Glu Pro Phe Leu Asn Thr Thr Ala Leu Phe Thr
 565 570 575

Phe Ser Glu Leu Val Arg Tyr Ser Gln Met Asp Asn Pro Ser Ser His
 580 585 590

Thr Arg Tyr Pro Val His Thr Phe Gly Arg Phe Ser Asp Lys Ile Asn
 595 600 605

Pro Glu Val Phe Arg Met Tyr Val Pro Tyr Leu Ala Glu Lys Leu Lys
 610 615 620

Thr Ser Ile Glu Lys Asn Glu Asn Ala Lys Ala His Thr Tyr Ile Val
 625 630 635 640

Ser Leu Gly Asn Ile Ala His Pro Lys Ile Leu Ala Val Phe Glu Pro
 645 650 655

Tyr Leu Glu Gly Lys Met Pro Ala Ser Thr Phe Gln Arg Leu Leu Met
 660 665 670

Val Ile Ser Leu Asn Lys Leu Ala Thr Leu Lys Pro Lys Leu Ala Arg
 675 680 685

Gly Val Phe Tyr Arg Ile Tyr Lys Asn Thr Gly Glu Ala His Gln Leu
 690 695 700

Arg Cys Ala Ala Val Thr Ala Leu Met Ser Thr Asn Pro Pro Ala Ser
 705 710 715 720

Met Leu Gln Arg Met Ala Glu Phe Thr Asn Glu Asp His Ser Lys His
 725 730 735

Val Asn Ala Ala Val Lys Ser Ala Ile Glu Ser Ala Ser Glu Leu Glu
 740 745 750

Thr Pro Gln Trp Gln Glu Leu Ala Glu Asn Ala Arg Asn Ala Lys Pro

755 760 765
 Leu Leu Asn Lys Glu Ser Tyr Gly Phe Glu Tyr Ser Lys Leu Tyr Leu
 770 775 780
 Thr Asp Phe Ile Glu Arg Glu Met Asn Val Ala Tyr Gln Ala Gln Ala
 785 790 795 800
 Ser Phe Ile Ser Ser Asp Asp Ser Tyr Val Pro Glu Ala Leu Phe Val
 805 810 815
 Lys Ala Arg Ala Ile Phe Gly Gly Phe Thr Phe Pro Arg Thr Ser Ala
 820 825 830
 Gly Ala Met Val Ser Ser Ala Lys Asp Leu Leu Ser Ala Phe Glu Asp
 835 840 845
 Ala Phe Lys Gly Glu Lys Thr Ser His Lys His Ser His Val Glu Phe
 850 855 860
 Ser Pro Glu Asn Val Ala Lys Leu Leu Lys Ile Lys Ser Glu Pro Asn
 865 870 875 880
 Glu Asp Val Glu Gly Ala Phe Met Leu Gln Ser Ala Tyr Asn Asn Lys
 885 890 895
 Phe Met Ser Leu Asp Lys Asn Thr Leu Lys Asn Leu Pro Glu Leu Ser
 900 905 910
 Ser Lys Ala Leu Lys Ala Leu Lys Asp Gly His His Phe Asn Thr Ala
 915 920 925
 Arg Ile Glu Ser Tyr Glu Met Thr Met Ser Phe Pro Met Glu Ser Gly
 930 935 940
 Phe Pro Phe Val Tyr Thr Met Lys Val Pro Ser Met Leu Lys Leu Ala
 945 950 955 960
 Gly Ser Val Lys Gly Asp Ser Asn Glu Asp Ser Leu Asp Gly His Val
 965 970 975
 His Leu Arg Ala Val Tyr Ser Val Gln Phe Gln Ser Lys Leu Gly Phe
 980 985 990
 Val Thr Pro Phe Glu His Gln His Tyr Met Ala Gly Ile Asn Lys Asn
 995 1000 1005
 Tyr Gln Ala Tyr Val Pro Leu Arg Val Asn Val Asn Tyr Glu Asp
 1010 1015 1020
 Ser Asp Lys Arg Val Thr Leu Lys Ile Gln Pro Ile Glu Gln Asn
 1025 1030 1035

Glu Lys Phe Lys Leu Trp His His Ser Val Val Pro Phe Thr Ser
 1040 1045 1050
 Arg His Asp Ile Leu Lys Met Ser Pro Val Leu Lys Asp Lys Glu
 1055 1060 1065
 Thr Gln Lys Ile Ile Thr Glu Glu Val Ser Lys Asn Glu Tyr Asn
 1070 1075 1080
 Phe Gly Ser Asp Lys His Gly Val Lys Phe Thr Val Leu Ala Glu
 1085 1090 1095
 Ala Asp Asn Asp Asn Ser Pro Leu Asn Phe Glu Asp Ala Lys Trp
 1100 1105 1110
 Glu Arg Asn Pro Leu Thr Gln Leu Phe His Leu Phe Val Glu Gln
 1115 1120 1125
 Pro Val Tyr His Lys Val Asp Ile Phe Met Gln Pro Ser Lys Ser
 1130 1135 1140
 Ser Glu Gln Ser Ile Ile Leu Ser Thr Ala Phe Glu Thr Leu Gln
 1145 1150 1155
 Asp Asp Thr Thr Lys Tyr Asp Glu Asp Arg Ser Lys His Ile Lys
 1160 1165 1170
 Ala Glu Ala Pro Lys Val Glu Asn Lys Lys Leu Asn Asp Pro Gln
 1175 1180 1185
 Arg Arg Arg Lys Leu Leu Lys Glu Ala Ala Lys Gly Ile Ala Ala
 1190 1195 1200
 Ala Asp Ala Phe Ala Val Asp Ile Gly Leu Glu Tyr Pro Gly Gln
 1205 1210 1215
 Ala Pro Val Gln Ala Phe Ala Thr Leu Ala Phe Ala Ser Ser Glu
 1220 1225 1230
 Val Asp Glu Lys Ser Arg Gly Leu Val Tyr Trp Arg Leu Thr Asp
 1235 1240 1245
 Ala Gly Asn Asp Phe Glu Phe Glu Ser Cys Thr Ser Leu Glu Ala
 1250 1255 1260
 Arg Ser Pro Arg Thr Ser Asp Phe Gly Lys Asp Met Leu Asp Gln
 1265 1270 1275
 Pro Glu Phe Arg Ser Arg Lys Phe Asp Ile Asp Leu Arg Tyr Gly
 1280 1285 1290
 Gln Thr Cys Glu Lys Gly Tyr Lys Val Glu Ile Gln Gly Ser Gln

1295		1300		1305
Glu Gln Thr Glu Lys Tyr Arg Asp Thr Ile Lys Arg Leu Pro Thr				
1310		1315		1320
Ala Ile Glu Cys Ile Arg Ala Ala Lys Lys Gly Met Lys Ser Leu				
1325		1330		1335
Pro Ala Cys His Asp Val Ser Val Lys Met Thr Met Leu Asp Lys				
1340		1345		1350
Thr Arg Ile Thr Ile Lys Tyr Asp Lys Asp Ser Arg Glu Met Tyr				
1355		1360		1365
Gln Leu Phe Asp Asp Tyr Leu Asp Ser Met Ser Asp Ala Asp Asp				
1370		1375		1380
Asp Leu Lys Ser Ser Lys Lys Arg Leu Asn Ala Val Lys Asp Asp				
1385		1390		1395
Asp Lys Ala Tyr Asp Asp Thr Val Lys Ile Ala Val Asp Leu Ser				
1400		1405		1410
Pro Asn Asp Asn Asn Gly Arg Phe Ser Tyr Glu Ser Asp Phe Val				
1415		1420		1425
Lys Leu Glu Ala Arg Asp Val Pro Ile Asn Gly Ile Gly Pro Leu				
1430		1435		1440
Val Asn Val His Pro Asp Leu Glu Thr Ala Glu Arg Leu Asp Met				
1445		1450		1455
Asp Met Ser Asp Glu Pro Val Arg Gln Arg Ile Cys Val Leu Asp				
1460		1465		1470
Ser His Ser Ala Thr Thr Phe Asp Glu Ser Thr Tyr Pro Ile Asn				
1475		1480		1485
Leu Gly Lys Cys Trp His Val Val Met Thr Thr Phe Pro Lys Thr				
1490		1495		1500
Asn Lys Asn Ser Gly Ser Ala Glu Pro Ile Asp Glu Asp Met Ala				
1505		1510		1515
Leu Ser Ile Leu Val Arg Asp Ala Gly Asp Lys Lys Lys Asp Ile				
1520		1525		1530
Lys Val Thr Leu Gly Asp Lys Glu Leu Gln Phe Ser His Ala Asp				
1535		1540		1545
Ser Lys Asn Lys Val Thr Leu Asp Gly Lys Lys Val Asp Leu Ser				
1550		1555		1560

Glu Lys Arg Ser Tyr Arg His Lys Asn Gly Lys Asp Ile Asp Phe
 1565 1570 1575
 Glu Val Leu Gln Arg Pro Asp Gly Thr Leu Gly Leu Val Ser Ser
 1580 1585 1590
 Lys Tyr Asp Ile Asp Ala Trp Tyr Asp Gly Gln Arg Val Gln Ile
 1595 1600 1605
 Lys Ala Ser Gly Lys Tyr Arg Ser Asp Ile Arg Gly Leu Cys Gly
 1610 1615 1620
 Asn Phe Asp Gly Glu Pro Asp Asn Asp Phe Thr Ser Pro Lys Asp
 1625 1630 1635
 Cys Val Leu Leu Lys Pro Glu Glu Phe Ala Ala Ser Tyr Ala Leu
 1640 1645 1650
 Thr Thr Lys Asp Cys His Gly Ser Ala Leu Glu His Ala Arg Lys
 1655 1660 1665
 Ala Ser Gln Ala Val Cys Ser Gln Lys Ser Pro Arg Pro Gly Asn
 1670 1675 1680
 Val Val Ser Asp Arg Asp Ala Gly Arg Lys Tyr Ser Glu Asn Ser
 1685 1690 1695
 Asn Trp Gly Tyr His Ser Arg Gln Asn Ser Asp Asp Glu Gln Gly
 1700 1705 1710
 Lys Asn Asp Ser Ser Asp His Lys Arg Cys Asn Thr Leu Arg Thr
 1715 1720 1725
 Lys Val Ile Glu Glu Glu Asp Gln Ile Cys Phe Ser Leu Arg Pro
 1730 1735 1740
 Leu Pro Thr Cys Ala Glu Gly Cys Thr Ala Asn Arg Thr Lys Pro
 1745 1750 1755
 Lys Val Met Pro Met His Cys Met Pro Lys Asn Ile Ala Ala Glu
 1760 1765 1770
 Arg Met Ala Asp Arg Ile Lys Gln Gly Ala Asn Pro Asp Phe Ser
 1775 1780 1785
 Gln Lys Ser Tyr Thr Lys Lys Asn Gly Phe Asp Ile Pro Val Gly
 1790 1795 1800
 Cys His Ala Ala
 1805

<210> 7

<211> 1876
 <212> PRT
 <213> Riptortus clavatus

<400> 7

Met Trp Ser Pro Val Ile Ile Cys Leu Leu Val Gly Leu Ala Ser Ala
 1 5 10 15

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

Arg Thr Leu Thr Gly Leu His Gln Val Ala Asp Gln Tyr Thr Gly Val
 35 40 45

Met Ile Gln Gly Gln Leu Thr Val Arg Ala Glu Ser Asp Asn Lys Ala
 50 55 60

Thr Ala Val Ile Glu Asn Ala Lys Tyr Ala Asp Leu Gln Ala Asn Leu
 65 70 75 80

Ser Arg Gly Trp Asp Ser Glu Ile Gln Glu Asn Glu Leu Gln Tyr Asn
 85 90 95

Glu Leu Pro Ile Ser Lys Asp Pro Phe Glu Ile His Phe Arg Asn Gly
 100 105 110

Val Ile Glu Lys Met Val Val Asn Lys Asp Ile Pro Gln Trp Gln Leu
 115 120 125

Asn Phe Tyr Lys Ser Ile Ala Ser Gln Phe Gln Val Asp Thr Gln Gly
 130 135 140

Lys Asn Leu Lys Asp Ser Lys Ile Asn Leu Val Pro Ser Gly Gln Ser
 145 150 155 160

Gly Glu Pro Met Gly Val Tyr Lys Thr Met Glu Asp Ser Val Asn Gly
 165 170 175

Ile Tyr Glu Thr Leu Tyr Asp Ile Ser Val Leu Pro Glu Tyr Ile Leu
 180 185 190

Gln Ala Arg Pro Glu Leu Ala Pro Leu Pro His Leu Lys Gly Asp Gly
 195 200 205

Glu Phe Ile Glu Val Val Lys Thr Arg Asn Phe Ser Asn Ser Asn Gln
 210 215 220

His Val Ile Tyr Arg Phe Gly Ser Ser Gly His Glu Gly Trp Glu Ala
 225 230 235 240

Gly Thr Asn Gln Met Gly Asp Phe Leu Ser Arg Ser Ser Gln Ser Arg
 245 250 255

Val Ile Leu Ser Gly Lys Leu Asn Arg Tyr Thr Ile Gln Ser Ala Val
 260 265 270
 Thr Thr Glu Lys Val Leu Val Ala Pro His Val Tyr Asn Asn Gln Lys
 275 280 285
 Gly Ile Val Val Ser Ser Met Asn Ile Thr Leu Gln Gln Ala Thr Gly
 290 295 300
 Ser Gln Gly Ser Pro Gln Ser Val Ser Asn Pro Arg Glu Val Lys Ser
 305 310 315 320
 Leu Val Tyr Glu Tyr Glu Ser Gln Gly Asn Ser Glu Asn Leu Gln Ser
 325 330 335
 Ser Gln Gln Ser Ser Gln Gln Ser Ser Ser Glu Glu Ser Ser Ser Ser
 340 345 350
 Ser Ser Ser Ser Ser Ser Ser Ser Ser Glu Glu Asn Met Asn Ser Met
 355 360 365
 Lys Thr Asn Gln Gln Met Lys Glu Asp Arg Ala Lys Arg Ile Arg Arg
 370 375 380
 Ser Leu Glu Glu Gln Gln Ser Ser Ile Asn Arg Lys Gly Lys Asn Ala
 385 390 395 400
 Arg Ser Gln Ala Asp Ser Ser Ser Ser Ser Ser Ser Ser Ser Ser Ser
 405 410 415
 Ser Ser Ser Ser Ser Ser Ser Ser Ser Asp Ser Ser Ser Ser Val Ser
 420 425 430
 Ser Ser Glu Glu Asn Leu Pro Arg Gln Pro Arg Ser Ile Glu Gln Ala
 435 440 445
 Pro Gly Ser Glu Leu Gln Ala Gly Tyr Tyr Met Gly Ser Met Gly Gln
 450 455 460
 Gln Lys Gln Asn Val Pro Glu Gln Ile Lys Ser Leu Ala Lys Lys Val
 465 470 475 480
 Gly Gln Trp Val Gln Asn Pro Gly Gln Ile Pro Glu Glu Asn Arg Leu
 485 490 495
 Pro Leu Phe Ser Met Leu Thr Arg Met Val Gln Asn Ala Asn Ser Gln
 500 505 510
 Gln Leu Glu Gln Val Thr Gln Ser Leu Tyr His Gln Gln Ser Lys Asn
 515 520 525
 Gln Gln Gln Ser Asp Ala Glu Arg Gln Gln Tyr Gln Ser Trp Ala Ala
 530 535 540

Phe Arg Asp Ala Val Ala Gln Ala Gly Thr Gly Pro Ala Leu Val Thr
 545 550 555 560
 Ile Lys Gln Trp Ile Gln Ser Lys Lys Val Gln Gly Glu Glu Ala Ala
 565 570 575
 Gln Leu Leu Ala Val Leu Pro Tyr Thr Ala Arg Tyr Pro Asn Thr Glu
 580 585 590
 Tyr Met Asn Tyr Phe Phe Asp Met Val Thr Ser Glu Glu Ile Gln Arg
 595 600 605
 Gln Arg Ser Leu Asn Thr Thr Ala Leu Phe Ala Phe Thr Glu Leu Ser
 610 615 620
 Arg Lys Ser Gln Val Asp Tyr Asp Val Ala His Asn Arg Tyr Pro Val
 625 630 635 640
 His Leu His Ala Lys Asn Ser Gln Glu His Arg Gln Ala Val Pro Gln
 645 650 655
 Lys Tyr Ile Pro Trp Leu Gln Glu Arg Leu Glu Arg Ala Val Ser Arg
 660 665 670
 Gly Asp Ser Ile Lys Ala Gln Val Tyr Ile Arg Ala Leu Gly Asn Thr
 675 680 685
 Ala His Pro Lys Ile Leu Ala Val Phe Glu Pro Tyr Leu Glu Gly Lys
 690 695 700
 Ser Gln Ile Ser Glu Phe Gln Arg Leu Ser Ile Ile Ala Ser Leu Asp
 705 710 715 720
 Glu Met Thr Arg Thr His Pro Asn Leu Ala Arg Asp Val Leu Tyr Arg
 725 730 735
 Ile Tyr Gln Asn Thr Ala Glu Lys Ser Glu Ile Arg Ala Ala Ala Val
 740 745 750
 Arg Gln Leu Met Arg Thr Asn Pro Pro Ala Gln Met Leu Gln Arg Met
 755 760 765
 Ala Asp Phe Thr Asn Tyr Asp His Ser His Gln Val Asn Ala Ala Val
 770 775 780
 Lys Ser Ala Ile Glu Ser Ala Ala Ala Cys Thr Asp Ser Ser Val Asp
 785 790 795 800
 Gln Gln Leu Val Asn Asn Ala Arg Ala Ala Ala Asn Tyr Leu Thr Pro
 805 810 815

Lys Asn Tyr Gly Val Gln Tyr Ser Lys Thr His Leu Lys Ser His Asn
 820 825 830
 Val Glu Gly Gln Asn Leu Gln Tyr Gln Gln His Cys Ser Ser Ile Gln
 835 840 845
 Ser Gln Asp Ser Ser Leu Pro Ser Ser Leu Met Tyr Glu Val Gln Gln
 850 855 860
 Ser Val Gly Gly Tyr His Arg Asp Pro His Lys Phe Tyr Phe Met Thr
 865 870 875 880
 Ser Ser Ser Glu Gln Ala Ile Asn Leu Met Arg Gln Thr Ile Ala Gln
 885 890 895
 Gln Ser Gly Ser Tyr Arg Lys Arg Trp Ser Arg Asn Gln His Gly Ser
 900 905 910
 Glu Gln Ser Tyr Glu Asn Ile Leu Arg Ser Ile His Leu His Thr Asp
 915 920 925
 Glu Pro Val Gln Val Glu Gly Asn Ile Leu Val Ser Gly Leu Gly Gly
 930 935 940
 Lys Glu Phe Phe Thr Phe Asp Asn His Thr Ile Glu Gln Ile Pro Gln
 945 950 955 960
 Phe Phe Ser Asn Ile Asn Glu Lys Leu Gln Asp Lys Ser Tyr Val Gln
 965 970 975
 His Thr Lys Tyr Tyr Asn Gln Tyr Ser Leu Glu Ile Gly Phe Pro Ser
 980 985 990
 Ala Met Gly Leu Pro Phe Val Tyr His Leu Asp Val Pro Thr Leu Ala
 995 1000 1005
 Ser Val Ser Gly Lys Trp Ser Gly Gln Val Glu Leu Gln Gln His
 1010 1015 1020
 Gln Lys Glu Gln Asn Glu Lys Tyr Ser Ile Pro Val Lys Gly Gln
 1025 1030 1035
 Val His Gly Asp Phe Glu Phe Val Tyr Ser Ala Gln Lys Ser Gly
 1040 1045 1050
 Leu Met Gly Phe Val Ala Pro Phe Ser Gln Asn Arg Tyr Ile Ala
 1055 1060 1065
 Gly Leu Glu Lys Asn Ile His Ala Tyr Val Pro Val Gln Ala Lys
 1070 1075 1080
 Val Glu Tyr Asn Pro Glu Glu Asn Lys Val Gln Ala Ser Leu Gln
 1085 1090 1095

Pro Leu Ala Gln Gln Lys Gln Glu Glu Gln Gln Val Phe Gln Tyr
 1100 1105 1110
 Ser Ser Asn Ala Tyr Thr Thr Tyr Gln Lys Ser Ser Asp Leu Thr
 1115 1120 1125
 Pro Tyr Leu Gln Gly Glu Asn Thr Gln Ala Val Tyr Ala Lys Ala
 1130 1135 1140
 Pro Arg Trp Tyr His Asn Thr Tyr Gly Gln Ala Ala Thr Gly Tyr
 1145 1150 1155
 Ala Phe Asp Leu Ser Tyr Lys Thr Glu His Asn Ser His Ser Trp
 1160 1165 1170
 Ala Ser Ile Tyr Asn Ala Leu Gln Cys His Asp Tyr Ile Ser Ala
 1175 1180 1185
 Phe Leu Tyr Tyr Asp Thr Pro Gly Thr Ile Gln Asn Asp Tyr Ile
 1190 1195 1200
 Ser Ile Lys Tyr Asn Pro Gln Lys Ser Ser Pro Gln Glu Val Asn
 1205 1210 1215
 Val Ala Leu Ser Phe Ile Ser Asn Glu Tyr Gly Asn Lys Gly Ala
 1220 1225 1230
 Arg Met Thr Ser Lys Phe Lys Lys Ala Asn Ile Arg Asp Arg Ser
 1235 1240 1245
 Ala Ser Ser Ala Arg Asp Asn Leu Ala Val Pro Ser Ser Glu Gln
 1250 1255 1260
 Gln Arg Glu Gln Glu Leu Leu Arg Asn Val Glu Ala Glu Ile Gln
 1265 1270 1275
 Asp Ala Lys Ser His Leu Leu Asp Ala Ser Val Thr Phe Gly Gly
 1280 1285 1290
 Lys Asn Asn Asn Ala Gly Tyr Ser Phe Thr Leu Ala His Ala Asn
 1295 1300 1305
 Ser Pro Val Ser Glu Lys Ser Arg Val Leu Phe Tyr Tyr Asn Ala
 1310 1315 1320
 Gln Pro Val Ser Ser Ser Glu Asn Thr Lys Pro Phe Gln Ala Ala
 1325 1330 1335
 Phe Gln Leu Asp Ile Lys Asp Pro Gln Leu Pro Ala Phe Asn Tyr
 1340 1345 1350

Gln Asp Ala Leu Asn Ala Asp Ser Thr Ser Gln Val Gln Gly Lys
 1355 1360 1365
 Ile Asn Met Gly Glu Gln Leu Glu Ser Gln Ile Thr Phe Lys Gly
 1370 1375 1380
 Lys Leu Glu Arg Thr Gln Glu Arg Lys Glu Tyr Leu Gln Gln His
 1385 1390 1395
 Pro Leu Ala Arg Ala Cys Glu Ser Gln Met Gln Arg Arg Asn Tyr
 1400 1405 1410
 Ile Gln Pro Ala Cys Leu Asn Ala Thr Leu Gln Ala Asn Phe His
 1415 1420 1425
 Asn Arg Tyr Gln Phe Val Phe Asn Tyr Gln Asn Val Pro Ala Gly
 1430 1435 1440
 Val Arg Arg Ala Phe His Ser Ala Tyr Ser Met Gly Arg Tyr Ala
 1445 1450 1455
 Leu Tyr Gln Asn Asn Glu Glu Asn Ile Asn Thr Glu Gln Asn Gln
 1460 1465 1470
 Glu Gly Gln Ile Gln Ile Gly Val Gln Phe Glu Glu Asn Leu Arg
 1475 1480 1485
 Ser Val Asn Leu Ser Ile Ala Ala Pro Gly Leu Ser Ser Asn Phe
 1490 1495 1500
 Ser Asn Val Arg Val Pro Gly Met Ala Val Pro Phe Val Val Tyr
 1505 1510 1515
 His Pro Arg Tyr Asn Thr Tyr Gln Leu Leu Lys Ser Lys Leu Tyr
 1520 1525 1530
 Gln Thr Glu Gln Pro Gln Ala Thr Ala Val Ile Asp Gly Asn Lys
 1535 1540 1545
 Ala Thr Thr Phe Ser Asn Arg Thr Tyr Pro Ile Asp Leu Gly Asn
 1550 1555 1560
 Cys Tyr His Val Phe Ala Met Tyr Ala Pro Gln Gly Gln Gly Glu
 1565 1570 1575
 Asn Arg Gln His Glu Ser Ser Ile Ser Asn Ile Gln Gln Gly Tyr
 1580 1585 1590
 Ala Val Leu Val Lys Glu Thr Asp Ser Glu His Lys Glu Val Lys
 1595 1600 1605
 Val Ile Leu Gly Ser Asp Val Ile Glu Leu Lys Ser Lys Ser Ser
 1610 1615 1620

Gly Leu Ser Ile Gln Ala Asn Gly Gln Asn Ile His Ala Ser Glu
 1625 1630 1635
 Lys Gln Leu Thr Lys Trp Ser Asn Asn Asn Asn Tyr Leu Glu Ala
 1640 1645 1650
 Tyr Ala Arg Pro Asp Ala Val Val Leu Ser Leu Pro Gln Gln Gly
 1655 1660 1665
 Ile Glu Leu Thr Tyr Asp Gly Ala Arg Val Gln Leu Ser Ala Ser
 1670 1675 1680
 Ser Ser Tyr Lys Gly Asn Val Arg Gly Leu Ala Gly Thr Phe Asp
 1685 1690 1695
 Gly Gln Glu Ala Asn Asp Phe Thr Thr Pro Asn Asn Arg Val Leu
 1700 1705 1710
 Arg Asn Pro Leu Gln Phe Ala Ala Thr Tyr Ala Leu Leu Asp Ser
 1715 1720 1725
 Glu Cys Gln Gly Pro Ala Val Gln Arg Gln Gln Gln Ala Gln Gln
 1730 1735 1740
 Ser Pro Ser Tyr Glu Arg Arg Val Ile Leu Gly Asp Val Val Asn
 1745 1750 1755
 Glu Leu Glu Ala Gly Arg Gln Gln Gln Gln Asn Asn Lys Ser Lys
 1760 1765 1770
 Lys Asn Lys Ala Asn Gly Ser Glu Glu Arg Met Lys Val Gln Gly
 1775 1780 1785
 Ser Ser Cys Ser Lys Leu Met Thr Gln Ile Val Glu Glu Asn Asp
 1790 1795 1800
 Lys Ser Cys Phe Ser Thr Thr Pro Gln Pro Ala Cys Ala Ser His
 1805 1810 1815
 Cys Arg Pro Thr Gly Lys Ile Gln Lys Ile Val Asp Phe His Cys
 1820 1825 1830
 Val Gln Ala Ser Ser Ser Ser Arg Asn Trp Ala Gln Met Ile Lys
 1835 1840 1845
 Asn Gly Ala Asn Pro Asp Phe Ser Ala Lys Glu Lys His Arg Gln
 1850 1855 1860
 Ile Leu Leu Gln Leu Pro Thr Gly Cys Val Pro Lys Ala
 1865 1870 1875

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Tyr Gln Tyr Glu Asn Ser Phe Lys Gly Tyr Asn Pro Gly Tyr Lys Gly
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Tyr Asp Ala Gly Tyr Lys Gly Tyr Gly Tyr Asp Ala Gly Tyr Lys Tyr
 35 40 45

Asn Asn Gln Gly Tyr Ser Tyr Lys Asn Gly Phe Glu Tyr Gly Tyr Gln
 50 55 60

Asn Ala Tyr Gln Ala Ala Phe Tyr Lys His Arg Pro Asn Val Thr Glu
 65 70 75 80

Phe Glu Phe Ser Ser Trp Met Pro Asn Tyr Glu Tyr Val Tyr Asn Val
 85 90 95

Thr Ser Lys Thr Met Thr Ala Leu Ala Glu Leu Asp Asp Gln Trp Thr
 100 105 110

Gly Val Phe Thr Arg Ala Tyr Leu Val Ile Arg Pro Lys Ser Arg Asp
 115 120 125

Tyr Val Val Ala Tyr Val Lys Gln Pro Glu Tyr Ala Val Phe Asn Glu
 130 135 140

Arg Leu Pro His Gly Tyr Ala Thr Lys Phe Tyr His Asp Met Phe Lys
 145 150 155 160

Phe Gln Pro Met Pro Met Ser Ser Lys Pro Phe Gly Ile Arg Tyr His
 165 170 175

Lys Gly Ala Ile Lys Gly Leu Tyr Val Glu Lys Thr Ile Pro Asn Asn
 180 185 190

Glu Val Asn Ile Leu Lys Ala Trp Ile Ser Gln Leu Gln Val Asp Thr
 195 200 205

Arg Gly Ala Asn Leu Met His Ser Ser Lys Pro Ile His Pro Ser Lys
 210 215 220

Asn Glu Trp Asn Gly His Tyr Lys Val Met Glu Pro Leu Val Thr Gly
 225 230 235 240

Glu Cys Glu Thr His Tyr Asp Val Asn Leu Ile Pro Ala Tyr Met Ile
 245 250 255

Gln Ala His Lys Gln Trp Val Pro Gln Gly Gln Leu Arg Gly Glu Asp
 260 265 270

Asp Gln Phe Ile Gln Val Thr Lys Thr Gln Asn Phe Asp Arg Cys Asp
 275 280 285

Gln Arg Met Gly Tyr His Phe Gly Phe Thr Gly Tyr Ser Asp Phe Arg
 290 295 300

Pro Asn Thr Asn Gln Met Gly Asn Val Ala Ser Lys Ser Leu Val Ser
 305 310 315 320

Tyr Met Tyr Leu Thr Gly Asn Trp Tyr Asn Phe Thr Ile Gln Ser Ser
 325 330 335

Ser Met Ile Asn Lys Val Ala Ile Ala Pro Ser Leu Val Asn Lys Glu
 340 345 350

Pro Ala Leu Val Tyr Ala Gln Val Asn Met Thr Leu Asn Asp Val His
 355 360 365

Pro Tyr Asp Lys Val Pro Met Gly Pro Ala Glu Asp Leu Lys Val Phe
 370 375 380

Val Asp Leu Val Tyr Ser Tyr Asn Met Pro Ser Asp Lys Lys Asn Tyr
 385 390 395 400

Val Arg Pro Gly Asn Glu Thr Ser Ser Ser Ser Ser Ser Ser Ser
 405 410 415

Ser Ser Ser Ser Ser Ser Glu Ser Ser Ser Ser Ser Ser Glu Ser Val
 420 425 430

Glu Asn Pro Lys Ile Ser Pro Val Glu Gln Tyr Lys Pro Leu Leu Asp
 435 440 445

Lys Val Glu Lys Arg Gly Asn Arg Tyr Arg Arg Asp Leu Asn Ala Ile
 450 455 460

Lys Glu Lys Lys Tyr Tyr Glu Ala Tyr Lys Met Asp Gln Tyr Arg Leu
 465 470 475 480

His Arg Leu Asn Asp Thr Ser Ser Asp Ser Ser Ser Ser Asp Ser Ser
 485 490 495

Ser Ser Ser Ser Ser Glu Ser Lys Glu His Arg Asn Gly Thr Ser Ser
 500 505 510

Tyr Ser Ser Ser Ser Ser Ser Ser Ser Ser Ser Ser Ser Ser Glu Ser
 515 520 525

Ser Ser Tyr Ser Ser Ser Ser Ser Ser Ser Ser Glu Ser Tyr Ser Ile

530 535 540
 Ser Ser Glu Glu Tyr Tyr Tyr Gln Pro Thr Pro Ala Asn Phe Ser Tyr
 545 550 555 560
 Ala Pro Glu Ala Pro Phe Leu Pro Phe Phe Thr Gly Tyr Lys Gly Tyr
 565 570 575
 Asn Ile Phe Tyr Ala Arg Asn Val Asp Ala Ile Arg Ser Val Gly Lys
 580 585 590
 Leu Val Glu Glu Ile Ala Ser Asp Leu Glu Asn Pro Ser Asn Leu Pro
 595 600 605
 Lys Ala Asn Thr Met Ser Lys Phe Asn Ile Leu Thr Arg Ala Ile Arg
 610 615 620
 Ala Met Gly Tyr Glu Asp Ile Tyr Glu Leu Ala Gln Lys Tyr Phe Val
 625 630 635 640
 Ser Gln Lys Glu Arg Gln Val Ala Gln Phe Ser Asp Lys Lys Phe Ser
 645 650 655
 Lys Arg Val Asp Ala Trp Val Thr Leu Arg Asp Ala Val Ala Glu Ala
 660 665 670
 Gly Thr Pro Ser Ala Phe Lys Leu Ile Phe Asp Phe Ile Lys Glu Lys
 675 680 685
 Lys Leu Arg Gly Tyr Glu Ala Ala Thr Val Ile Ala Ser Leu Ala Gln
 690 695 700
 Ser Ile Arg Tyr Pro Thr Glu His Leu Leu His Glu Phe Phe Leu Leu
 705 710 715 720
 Val Thr Ser Asp Val Val Leu His Gln Glu Tyr Leu Asn Ala Thr Ala
 725 730 735
 Leu Phe Ala Tyr Ser Asn Phe Val Asn Gln Ala His Val Ser Asn Arg
 740 745 750
 Ser Ala Tyr Asn Tyr Tyr Pro Val Phe Ser Phe Gly Arg Leu Ala Asp
 755 760 765
 Ala Asp Tyr Lys Ile Ile Glu His Lys Ile Val Pro Trp Phe Ala His
 770 775 780
 Gln Leu Arg Glu Ala Val Asn Glu Gly Asp Ser Val Lys Ile Gln Val
 785 790 795 800
 Tyr Ile Arg Ser Leu Gly Asn Leu Gly His Pro Gln Ile Leu Ser Val
 805 810 815

Phe Glu Pro Tyr Leu Glu Gly Thr Ile Gln Ile Thr Asp Phe Gln Arg
 820 825 830

Leu Ala Ile Met Val Ala Leu Asp Asn Leu Val Ile Tyr Tyr Pro Ser
 835 840 845

Leu Ala Arg Ser Val Leu Tyr Arg Ala Tyr Gln Asn Thr Ala Asp Val
 850 855 860

His Glu Val Arg Cys Ala Ala Val His Leu Leu Met Arg Thr Asp Pro
 865 870 875 880

Pro Ala Asp Met Leu Gln Arg Met Ala Glu Phe Thr His His Asp Pro
 885 890 895

Ser Leu Tyr Val Arg Ala Ala Val Lys Ser Ala Ile Glu Thr Ala Ala
 900 905 910

Leu Ala Asp Asp Tyr Asp Glu Asp Ser Lys Leu Ala Leu Asn Ala Lys
 915 920 925

Ala Ala Ile Asn Phe Leu Asn Pro Glu Asp Val Ser Ile Gln Tyr Ser
 930 935 940

Phe Asn His Ile Arg Asp Tyr Ala Leu Glu Asn Leu Glu Leu Ser Tyr
 945 950 955 960

Arg Leu His Tyr Gly Glu Ile Ala Ser Asn Asp His Arg Tyr Pro Ser
 965 970 975

Gly Leu Phe Tyr His Leu Arg Gln Asn Phe Gly Gly Phe Lys Lys Tyr
 980 985 990

Thr Ser Phe Tyr Tyr Leu Val Ser Ser Met Glu Ala Phe Phe Asp Ile
 995 1000 1005

Phe Lys Lys Gln Tyr Asn Thr Lys Tyr Phe Ala Asp Tyr Tyr Lys
 1010 1015 1020

Ser Ala Asp Tyr Ser Thr Asn Tyr Tyr Asn Phe Asp Lys Tyr Ser
 1025 1030 1035

Lys Tyr Tyr Lys Gln Tyr Tyr Tyr Ser Lys Asp Ser Glu Tyr Tyr
 1040 1045 1050

Gln Lys Phe Tyr Gly Gln Lys Lys Asp Tyr Tyr Asn Asp Lys Glu
 1055 1060 1065

Pro Phe Lys Phe Thr Ala Pro Arg Ile Ala Lys Leu Leu Asn Ile
 1070 1075 1080

Asp Ala Gln Glu Ala Glu Gln Leu Glu Gly Gln Leu Leu Phe Lys

1085		1090		1095
Leu Phe Asn Gly Tyr Phe Phe Thr Ala Phe Asp Asn Gln Thr Ile	1100	1105		1110
Glu Asn Leu Pro His Lys Met Arg His Leu Phe Glu Asn Leu Glu	1115	1120		1125
Asp Gly Tyr Ala Phe Asp Val Thr Lys Phe Tyr Gln Gln Gln Asp	1130	1135		1140
Val Val Leu Ala Trp Pro Leu Ala Thr Gly Phe Pro Phe Ile Tyr	1145	1150		1155
Thr Leu Lys Ala Pro Thr Val Phe Lys Phe Glu Val Asp Ala Ser	1160	1165		1170
Ala Lys Thr His Pro Gln Val Tyr Lys Met Pro Ala Gly His Pro	1175	1180		1185
Glu Thr Glu Asn Asp Asp Phe Phe Tyr Met Pro Gln Ser Ile Asn	1190	1195		1200
Gly Ser Val Asp Val Asn Leu Leu Tyr His Arg Met Val Asp Ala	1205	1210		1215
Lys Val Gly Phe Val Thr Pro Phe Asp His Gln Arg Tyr Ile Ala	1220	1225		1230
Gly Tyr Gln Lys Lys Leu His Gly Tyr Leu Pro Phe Asn Val Glu	1235	1240		1245
Leu Gly Leu Asp Phe Val Lys Asp Glu Tyr Glu Phe Glu Phe Lys	1250	1255		1260
Phe Leu Glu Pro Lys Asp Asp His Leu Leu Phe His Met Ser Ser	1265	1270		1275
Trp Pro Tyr Thr Gly Tyr Lys Asp Ile Thr Asp Met Arg Pro Ile	1280	1285		1290
Ala Glu Asn Pro Asn Ala Lys Ile Val His Asp Asp Asn Gln Ser	1295	1300		1305
Thr Lys Thr Met Glu His Thr Phe Gly Gln Asp Met Thr Gly Val	1310	1315		1320
Ala Leu Arg Phe His Ala Lys Tyr Asp Phe Asp Leu Ile Asn Phe	1325	1330		1335
Gln Gln Phe Trp Ser Leu Ile Gln Lys Asn Asp Phe Val Ser Ala	1340	1345		1350

Val Asn Tyr Pro Phe Ala Tyr Gln Pro Tyr Glu Tyr His Gln Phe
 1355 1360 1365
 Asn Leu Phe Tyr Asp Ser Gln Arg Thr His Ala Lys Ser Phe Lys
 1370 1375 1380
 Phe Tyr Ala Tyr Gln Lys Phe Gly Ala Pro Ser Phe Glu Glu Thr
 1385 1390 1395
 Gly Pro Lys His Pro Ala Asn Arg His Ser Tyr Ser Gly Asn Tyr
 1400 1405 1410
 Tyr Glu Ser Asn Tyr Ala Gln Pro Phe Val Tyr Ser Pro Gly Ser
 1415 1420 1425
 Gln Arg Arg Tyr Glu Gln Phe Phe Arg Asn Ala Ala Ser Gly Ile
 1430 1435 1440
 Arg Asn Ser Phe Val Arg Tyr Tyr Asp Phe Gly Phe Glu Phe Tyr
 1445 1450 1455
 Ala Pro Gln Tyr Lys Ser Glu Phe Thr Phe Thr Thr Ala Phe Ala
 1460 1465 1470
 Asp Ser Pro Val Asp Lys Thr Ser Arg Gln Leu Tyr Tyr Phe Tyr
 1475 1480 1485
 Ala Ser Pro Met Phe Pro Ser Gln Ser Tyr Phe Lys Asp Ile Pro
 1490 1495 1500
 Phe Ser Gly Lys Gln Phe Gln Phe Cys Ala Thr Ala Thr Ser Glu
 1505 1510 1515
 Phe Pro Arg Val Pro Tyr Leu Lys Phe Ser Asp Phe Asp Lys Tyr
 1520 1525 1530
 Tyr Gly Asp Ala Ser Gln Tyr Phe Asp Phe Leu Tyr Gly Glu Ser
 1535 1540 1545
 Cys Gln Gly Gly Ala His Ile Ala Val Lys Gly Lys Gln Lys Gln
 1550 1555 1560
 Thr Gly Lys Tyr Arg Glu Tyr Leu Arg Phe Ser Asp Val Ala Lys
 1565 1570 1575
 Ala Cys Lys Glu Gln Met Ala Asn Gly Tyr Tyr Gln Phe Glu Glu
 1580 1585 1590
 Cys Gln Gln Ala Ile Asp Gln Ala Tyr Tyr Tyr Asp Phe Tyr Asp
 1595 1600 1605
 Tyr Ala Ile Glu Tyr Lys Asp Val Gly Ser Val Ala Lys Asn Leu

1610		1615		1620
Thr Asn 1625	Lys Phe Tyr Asn	Tyr 1630	Phe Gln Tyr Ala	Phe Tyr Pro Tyr 1635
Phe Glu 1640	Ser Asn Phe Phe	Tyr 1645	His Gly Lys Ser	Asn Tyr Ile Lys 1650
Ala Glu 1655	Phe Glu Phe Ala	Pro 1660	Tyr Gly Asp Tyr	Tyr Asn Ala Ser 1665
Phe Phe 1670	Gly Pro Ser Tyr	Ala 1675	Phe Gln Val Gln	Asn Tyr Pro Val 1680
Phe Asn 1685	Asp Tyr Ser Thr	Tyr 1690	Phe Pro Tyr Phe	Phe Lys Tyr Thr 1695
Phe Phe 1700	Pro Arg Tyr Gln	Pro 1705	Tyr Tyr Met His	Arg Leu Pro Ser 1710
His Lys 1715	Pro Arg Asn Arg	Pro 1720	Tyr Tyr Glu Leu	Ser Asn Tyr Glu 1725
Gln Phe 1730	Ala Ile Phe Asp	Arg 1735	Lys Pro Gln Tyr	Pro Ser Cys Ser 1740
Phe Ser 1745	Asn Asp Tyr Phe	Tyr 1750	Thr Phe Asp Asn	Lys Lys Tyr Phe 1755
Tyr Asp 1760	Met Gly Glu Cys	Trp 1765	His Ala Val Met	Tyr Thr Val Lys 1770
Pro Asp 1775	Tyr Asp Phe Tyr	Ala 1780	Gln Gln Ser His	Phe Tyr Asn Ser 1785
Asp Phe 1790	Glu Tyr Lys Tyr	Lys 1795	Asn Gly Phe Glu	Glu Tyr Glu Gln 1800
Phe Ala 1805	Ala Leu Ala Arg	Arg 1810	Gly Ser Asp Asn	Gln Leu Tyr Phe 1815
Lys Phe 1820	Leu Phe Gly Asp	Asn 1825	Tyr Ile Glu Val	Phe Pro Asn Asn 1830
Gly Gly 1835	Val Pro Phe Val	Lys 1840	Tyr Asn Gly Arg	Pro Tyr Asp Ile 1845
Ser Lys 1850	Ser Asn Ile Ala	His 1855	Phe Glu Tyr Lys	Glu Gly Tyr Pro 1860
Ser Phe 1865	Pro Phe Phe Tyr	Ala 1870	Phe Ala Tyr Pro	Asn Lys Asp Leu 1875

Glu Val Ser Phe Phe Gly Gly Lys Leu Lys Phe Ala Thr Asp Gly
 1880 1885 1890
 Tyr Arg Ala Arg Phe Phe Ser Asp Tyr Ser Phe Tyr Asn Asn Phe
 1895 1900 1905
 Val Gly Leu Cys Gly Thr Asn Asn Gly Glu Tyr Phe Asp Glu Phe
 1910 1915 1920
 Val Thr Pro Asp Gln Cys Tyr Met Arg Lys Pro Glu Phe Phe Ala
 1925 1930 1935
 Ala Ser Tyr Ala Ile Thr Gly Gln Asn Cys Thr Gly Pro Ala Lys
 1940 1945 1950
 Ala Phe Asn Tyr Ala Tyr Gln Gln Lys Ala Lys Gln Glu Cys Val
 1955 1960 1965
 Lys Arg Glu Val Tyr Tyr Gly Asp Ile Ile Tyr Asn Gln Glu Tyr
 1970 1975 1980
 Tyr His Pro Arg Tyr Arg Tyr Tyr Asn His Asn Val Glu Glu Ser
 1985 1990 1995
 Ser Ser Ser Ser Ser Ser Ser Ser Asp Ser Ser Ser Ser Ser
 2000 2005 2010
 Ser Ser Ser Glu Phe Ser Ser Leu Ser Arg Ser Gly Ser Ser Ser
 2015 2020 2025
 Ser Ser Ser Ser Ser Glu Glu Gln Lys Glu Phe His Pro His Lys
 2030 2035 2040
 Gln Glu His Ser Met Lys Glu Cys Pro Val Gln His Gln His Gln
 2045 2050 2055
 Phe Phe Glu Gln Gly Asp Arg Ile Cys Phe Ser Leu Arg Pro Leu
 2060 2065 2070
 Pro Val Cys His Ser Lys Cys Ala Ala Thr Glu Lys Ile Ser Lys
 2075 2080 2085
 Tyr Phe Asp Val His Cys Phe Glu Lys Asp Ser Thr Gln Ala Lys
 2090 2095 2100
 Lys Tyr Lys Ser Glu Ile Gly Arg Gly Tyr Thr Pro Asp Phe Lys
 2105 2110 2115
 Ser Phe Ala Pro His Lys Thr Tyr Lys Phe Asn Tyr Pro Lys Ser
 2120 2125 2130
 Cys Val Tyr Lys Ala Tyr

2135

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 <212> PRT
 <213> *Anthonomus grandis*

<400> 9

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

Ser Gly Val Phe Leu Glu Ala Lys Leu His Leu Ser Ile Arg Pro Asp
 50 55 60

Gly Lys Leu Gln Gly Arg Ile Ser Glu Pro Lys Phe Ala Gln Ile Leu
 65 70 75 80

Ser Gln Leu Pro Asp Gly Trp Lys Ser Glu Ile Pro Asp Ser Gln Ile
 85 90 95

Ser Tyr Lys Gln Leu Gln Leu Ser Gln Lys Pro Phe Gln Leu Val Leu
 100 105 110

Glu Asn Gly Leu Ile Lys Arg Leu Ile Val Glu Lys Asp Thr Leu Asn
 115 120 125

Trp Glu Ala Asn Ile Ile Lys Ser Ile Val Ser Gln Phe Gln Met Asp
 130 135 140

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

Asn Glu Tyr Met Asp Ala Val Phe Lys Thr Met Glu Glu Thr Val Thr
 165 170 175

Gly Lys Thr Glu Thr Ile Tyr Asp Ile His Arg Leu Pro Glu Tyr Leu
 180 185 190

Val Gln Ser Gln Pro Trp Ile Ala Pro Gln Tyr Lys Leu Lys Gly Glu
 195 200 205

Gly Asp Leu Ile Glu Val Ile Lys Ser Lys Asn Tyr Thr Asn Ala Arg
 210 215 220

Asp Arg Pro Ser Tyr His Tyr Gly Phe Gly Glu Ile Glu Glu Ser Glu
 225 230 235 240

Pro Thr Ala Asn Lys Met Gly Gln Phe Phe Ile Arg Gln Ser Asn Ser
 245 250 255
 Arg Ala Ile Leu Thr Gly Lys Pro Ser Arg Tyr Ile Ile Gln Ser Thr
 260 265 270
 Tyr Thr Val Asn Lys Ile Met Val Asn Pro Ile Leu Lys Asn Lys Glu
 275 280 285
 Met Gly Ser Ile Thr Ser Met Val Asn Val Thr Leu Leu Glu Ile Asn
 290 295 300
 Asn Gln Gln Gln Gln Pro Glu Glu Leu Ser Asn Pro Leu Asp Ile Gly
 305 310 315 320
 Asn Leu Val Tyr Thr Tyr Gly Gln Pro Lys Asn Asn Gln Val His Ser
 325 330 335
 Lys Leu Asn Glu Asn Leu Met Glu Asp Ser Ser Ser Glu Glu Ser Ser
 340 345 350
 Glu Gln Glu Met Thr His Arg Arg Phe Arg Arg Ser Ala Asn Ser Leu
 355 360 365
 Thr Lys Gln Trp Arg Glu Ser Ser Glu Glu Trp Asn Gln Gln Gln Gln
 370 375 380
 Gln Pro Arg Pro Gln Leu Thr Arg Ala Pro His Ser Pro Leu Leu Pro
 385 390 395 400
 Ser Met Val Gly Tyr His Gly Lys Ser Ile Lys Glu Asn Lys Asp Phe
 405 410 415
 Asp Ile Arg Gln Asn Val Glu Asn Leu Val Thr Glu Ile Ser Asp Glu
 420 425 430
 Ile Lys Gln Ser Glu Lys Thr Ile Ser Lys His Thr Leu Asp Lys Tyr
 435 440 445
 Thr Ile Leu Asn Thr Leu Val Arg Leu Met Asp Glu Asp Asp Ile Gln
 450 455 460
 Phe Val Ala Glu Gln Met Tyr Ser Gln Met Lys Asn Gly Gln Gln Arg
 465 470 475 480
 Tyr Thr Trp Ser Ile Phe Arg Asp Ser Val Ala Glu Ala Gly Thr Gly
 485 490 495
 Pro Ala Leu Leu Asn Ile Lys Lys Trp Ile Glu Thr Lys Lys Ile Gln
 500 505 510
 Lys Thr Glu Ala Ala Gln Val Ile Gly Thr Leu Ala Gln Ser Thr Arg
 515 520 525

Phe Pro Thr Glu Glu Tyr Met Arg Lys Phe Phe Glu Leu Ala Thr Glu
 530 535 540
 Thr Gln Val Arg Gln Gln Glu Thr Leu Asn Gln Thr Cys Ile Leu Ser
 545 550 555 560
 Tyr Thr Asn Leu Val His Lys Val Tyr Ile Asn Arg Asn Glu Ser His
 565 570 575
 Asn Gln Phe Pro Val His Ala Phe Gly Ser Phe Tyr Thr Lys Lys Gly
 580 585 590
 Arg Glu Phe Val Lys Thr Thr Val Ile Pro His Leu Lys Gln Glu Leu
 595 600 605
 Glu Lys Ala Ile Ser Asn Ala Asp Asn Asn Lys Ile His Val Met Ile
 610 615 620
 Arg Ala Leu Gly Asn Ile Gly His Lys Ser Ile Leu Asn Val Phe Gln
 625 630 635 640
 Pro Tyr Phe Glu Gly Glu Lys Gln Val Ser Gln Phe Gln Arg Leu Met
 645 650 655
 Met Val Ala Cys Met Asp Arg Leu Ala Asp Cys Tyr Pro His Ile Ala
 660 665 670
 Arg Ser Val Phe Tyr Lys Ile Tyr Gln Asn Thr Ala Glu Leu Pro Glu
 675 680 685
 Ile Arg Val Val Ala Val His Gln Leu Ile Arg Ala Asn Pro Pro Val
 690 695 700
 Glu Met Leu Gln Arg Met Ala Gln Tyr Thr Asn Thr Asp Ser Gln Glu
 705 710 715 720
 Glu Val Asn Ala Ala Val Lys Ser Val Ile Glu Ser Ser Cys Lys Leu
 725 730 735
 Glu Ser Ser Lys His Ala Glu Leu Arg Lys Ala Ala Gln Ser Ala Arg
 740 745 750
 Pro Leu Leu Thr Lys Lys Gln Tyr Gly Met Glu Gln Ser Tyr Ile Asn
 755 760 765
 Leu Arg Asp Tyr Val Ala Glu Gln Met Gly Leu Glu Leu His Val Gln
 770 775 780
 Arg Thr Ser His Ser Ser Ala Glu Ser Ser Phe Pro Lys Ile Met Lys
 785 790 795 800

Phe Gln Leu His Gln His Asn His Gly Met Lys Gln His Ile Leu Ser
 805 810 815
 Thr Gly Gly Met Ile Ser Ser Ile Arg Glu Leu Leu Asn Val Leu Tyr
 820 825 830
 Arg Gln Thr Glu Val Phe Gln Gln Glu Lys Ser Gln Arg Ser Gln Glu
 835 840 845
 Gln Gly Lys Asp Asn Glu Trp Ser Ser Ala Asn Ile Ala Arg Leu Met
 850 855 860
 Asn Tyr Glu Arg Asp Glu Arg Glu Gln Leu Glu Ala Ile Ile Tyr Ala
 865 870 875 880
 Gln Val Glu Asp Val Gln Lys Leu Trp Ser Phe Asp Asn Gln Thr Leu
 885 890 895
 Glu His Leu Pro Glu Val Ile Arg Gln Gln Glu Glu Ile Tyr Arg Gln
 900 905 910
 Gly Lys Asp Phe Ser Tyr Val Lys Leu Lys Gln Leu Asn Glu Met Ala
 915 920 925
 Leu Ser Phe Pro Thr Glu Met Gly Leu Pro Phe Leu Tyr Thr Tyr Asp
 930 935 940
 Val Pro Val Leu Met Lys Val Glu Gly Lys Ile Arg Ala Leu Ala Asn
 945 950 955 960
 Pro Ala Ile Ser Arg Asn Asn Lys Leu Thr Lys Pro Glu Gln Ile Ser
 965 970 975
 Thr Glu Ile Lys Ala Arg Val Thr Cys Thr Gly Lys Thr Gln Ser His
 980 985 990
 Leu Ser Phe Val Thr Pro Phe Asp His Gln Ile Tyr Met Ala Gly Tyr
 995 1000 1005
 Asp Lys Asn Met Tyr Val Ser Ile Pro Val Asn Ala Arg Leu Glu
 1010 1015 1020
 Met Asp Val Lys Ser Lys Glu Ala Lys Ile Glu Phe Glu Val Glu
 1025 1030 1035
 Gln Gln Gln Gln Asp Ser Arg Leu Val His Ile Thr Ser Thr Pro
 1040 1045 1050
 Tyr Thr Ser Arg Ser Asp Val Met Ala Ile Ser Pro Val Ala Leu
 1055 1060 1065
 Arg Pro Asn Thr Tyr Val Ile Lys Ser His Arg Asn Asn His Arg
 1070 1075 1080

Tyr Phe Asp Phe Asn Phe Gly Lys Lys Glu Thr Gly Leu Thr Phe
 1085 1090 1095
 Arg Gly Trp Gly His His Pro Glu Gln Ser Ile Gly Phe Asn Asp
 1100 1105 1110
 Leu Val Ser Met Trp Gln Ser Arg Gly Val Ala Gly Val Trp Glu
 1115 1120 1125
 Gln Leu Trp Asp Lys Cys Ser Thr Glu Tyr Ser Glu Ala Thr Ile
 1130 1135 1140
 Ser Phe Ile Pro Ser Gln Ser Thr Thr Arg Lys Ala Thr Phe Arg
 1145 1150 1155
 Ile Asn Val Asp Gln Lys Tyr Gln Lys Gln Pro Glu Thr Gln Ser
 1160 1165 1170
 Pro Glu Asp Leu Leu Thr Leu Asn Gln Leu Ser Ser Lys Leu Gln
 1175 1180 1185
 Lys Asp Glu Pro Lys Gln Arg Gln Gln Glu Ile Lys Lys His Val
 1190 1195 1200
 Gly Ser Gly Ile Asn Ser Ala Leu Leu Ser Cys Ser Asp Ile Ser
 1205 1210 1215
 Leu Glu Phe Glu Gly Asp Lys Lys Tyr Glu His Val Val Gly Phe
 1220 1225 1230
 Ala Val Ala Lys Ser Asn Ala Asp Pro Lys Ser Arg Val Met Phe
 1235 1240 1245
 Tyr Tyr Lys Asn Lys Asn Glu Asn Lys Gln Gly Ala Leu Glu Ile
 1250 1255 1260
 Arg Ser Glu Ile Pro Asn Thr Asn Gly Leu Asn Leu Asp Asp Ser
 1265 1270 1275
 Leu Asp Thr Glu Pro Ser Thr Lys Tyr Asn Met Arg Leu Gln Tyr
 1280 1285 1290
 Gly Asn Ser Glu Asn Asp Ala Phe Glu Ile Ser Ala Gln Ala Gln
 1295 1300 1305
 Leu Ser Arg Ser Gln Glu Arg Lys Gln Tyr Leu Ile Asn Gln Asp
 1310 1315 1320
 Pro Leu Tyr His Val Cys Lys Glu Gln Met Gln Gln Lys Asn Phe
 1325 1330 1335

Gln Leu Pro Ala Cys Gln Asn Met Thr Ile Lys Ala Asn Phe Leu
 1340 1345 1350
 Asp His Ile Lys Tyr Gln Val Gln Tyr Gln Lys Leu Asn Trp Lys
 1355 1360 1365
 Leu Val Glu Thr Leu Glu Gly Met Phe Lys Gly Leu Arg Val Leu
 1370 1375 1380
 Tyr Tyr Pro Met Thr Glu Ile Lys Ser Ile Ser Ser Val Gly Gln
 1385 1390 1395
 Asn Val Val Glu Gly Glu Val Gln Phe Gln Pro Glu Asp Phe Arg
 1400 1405 1410
 Gln Val Asn Val Thr Val Arg Asn Thr Asp Glu Glu Thr Val Phe
 1415 1420 1425
 Phe Asn Ile Ser Leu Asn Asn Glu Leu Leu Arg Thr Leu Leu Val
 1430 1435 1440
 Pro His Pro Val Phe His Ala Lys Cys Arg Phe Ala Gly Leu Met
 1445 1450 1455
 Gln Gly Gln Gln Asn Tyr Arg Pro Thr Cys Val Ile Asp Gln Thr
 1460 1465 1470
 Thr Ala Gln Thr Phe Ser Asn Lys Thr Tyr Ser Val Asn Leu Asp
 1475 1480 1485
 Lys Glu Pro Thr Val Val Met Gln Tyr Val Pro Lys Asp Ala Arg
 1490 1495 1500
 Val Asn Gly Gln Gln Ser Lys Ser Val Glu Gln Leu Leu Arg Glu
 1505 1510 1515
 Ser Ile Glu Asn Tyr Val Val Leu Val Arg Gln Val Ala Ala Asn
 1520 1525 1530
 Gln Lys Glu Val Ile Ile Asn Leu Asn His Pro Arg Thr Gln Gly
 1535 1540 1545
 Lys Thr Val Lys Ile Glu Met Lys Pro Ser Glu Asp Arg Gln Lys
 1550 1555 1560
 Ser Ala Arg Asn Pro Ala Ala Lys Val Thr Ile Asp Gly Gln Glu
 1565 1570 1575
 Met His Phe Asp Asp Lys Gln Ile Ala Asp Lys Cys Asp Gly Tyr
 1580 1585 1590
 Val Gln Val Tyr Ala Leu Pro Asn Gly Glu Val Lys Leu Glu Val
 1595 1600 1605

Glu Asp Ala Phe Tyr Leu Ile Tyr Asp Gly Gln Arg Val Lys Val
1610 1615 1620

Thr Ala Thr Gly Asn Lys Leu Arg Asp Ser Val Tyr Gly Leu Cys
1625 1630 1635

Gly Arg Phe Ser Gln Asp Lys His Glu Asp Phe Thr Val Pro Ser
1640 1645 1650

Asn Cys Val Thr Arg Asp Thr Arg Lys Phe Val Glu Ser Tyr Gln
1655 1660 1665

Val Glu Lys Gly Gln Gln Trp Arg Asn Ser Pro Ser Glu Gln Cys
1670 1675 1680

Ile Lys Lys Val Leu Pro Leu Tyr Thr Asn Val Ile Ser Asn Gln
1685 1690 1695

Asn Gly Ser Gln Met Arg Thr Lys Leu Ala Ser Gly Thr Val Met
1700 1705 1710

Lys His Arg Tyr Ile Glu Glu Asn Gly Glu Ile Cys Phe Thr Ile
1715 1720 1725

Arg Pro Leu Pro Val Cys Asn Thr Ser Val Lys Gln Val Val Thr
1730 1735 1740

Lys Asn Val Pro Val His Cys Ile Gln Gly Thr Lys Thr Ala Tyr
1745 1750 1755

Tyr Tyr Lys Ser Leu Ile Asp Gln Gly Gly Asn Pro Asp Phe Ser
1760 1765 1770

Arg Lys Ser Glu Thr Arg Thr Ala Arg Met Glu Val Ala Ala Gln
1775 1780 1785

Cys Asn
1790

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<211> 1862
<212> PRT
<213> Blattella germanica

<400> 10

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Ala Ile Thr Pro Gly Trp Leu Pro Ile Asn Ser Gln Leu Asp Tyr His
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Val His Gly Arg Thr Phe Ser Ser Leu Phe Gln Val Ala Asn Gln Tyr

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

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

595	600	605																	
Gln	Glu	Phe	Asp	Asp	Ala	Val	Lys	Glu	Asn	Asn	Ser	Ile	Lys	Ile	Gln				
610						615					620								
Leu	Tyr	Thr	His	Ala	Leu	Gly	Val	Thr	Gly	Asn	Thr	His	Ile	Leu	His				
625					630					635					640				
Tyr	Leu	Arg	Pro	Tyr	Ile	Ile	Gln	Leu	Lys	Thr	Ile	Thr	His	His	Gln				
				645					650					655					
Arg	Leu	Phe	Met	Val	Gln	Ser	Leu	Glu	Arg	Val	Val	Glu	His	Asn	Pro				
			660					665					670						
Arg	Lys	Val	Ile	Asp	Leu	Leu	Leu	Ser	Leu	Tyr	Leu	Asp	Gln	Asn	Glu				
		675					680					685							
His	Ala	Asp	Ile	Arg	Val	Glu	Ala	Leu	Phe	Leu	Leu	Met	Lys	Ala	Asp				
690						695						700							
Pro	Ser	Ile	His	Val	Leu	Lys	Met	Val	Ala	Glu	Leu	Thr	His	Thr	Glu				
705					710					715					720				
Ser	Asn	Asn	Gln	Val	Leu	Ser	Ala	Ser	Gln	Ser	Ala	Ile	Lys	Ser	Ala				
				725					730					735					
Ala	Asn	Val	Glu	Gly	Asp	Ile	Tyr	Ser	Glu	Met	Arg	Arg	Lys	Ala	Lys				
			740					745					750						
Ala	Val	Glu	His	Leu	Leu	Ser	Thr	Arg	Asn	Met	Asp	Val	Ser	Tyr	Ser				
		755					760					765							
Lys	Ser	Tyr	Leu	Tyr	Gly	Tyr	Lys	Ser	Lys	Lys	Ile	Asn	Tyr	Asp	Ser				
		770				775						780							
Leu	Tyr	Asn	Leu	Asn	Tyr	Ile	Gly	Ser	Glu	Asp	Ser	Ile	Tyr	Pro	Lys				
785					790					795					800				
Ser	Met	Leu	Leu	Asn	Ile	Phe	Thr	Asn	Asn	Leu	Gly	Arg	Ile	Asn	Thr				
				805					810					815					
His	Val	Gln	Lys	Gly	Tyr	Met	Val	Ser	Ser	Met	Thr	Asp	Leu	Trp	Glu				
			820					825					830						
Ala	Phe	His	Thr	Ile	Tyr	Lys	Lys	Asp	Asn	Gly	Ser	Pro	Thr	Asp	Pro				
		835					840					845							
Lys	Thr	Leu	Val	Lys	Phe	Val	Glu	Gly	Asn	Leu	Lys	Tyr	Phe	Asn	Met				
		850				855					860								
Gly	Val	Gln	Lys	Phe	Trp	Ala	Phe	Asp	Asn	Thr	Thr	Phe	Ser	Asn	Ala				
865					870					875					880				

Ser Ala Val Ile Gln Glu Phe Leu Lys Thr Tyr Lys Lys Pro Thr Asn
 885 890 895

Phe Asn His Thr Lys Leu Ser Ser Ser Ser Ser Ile Thr Leu Thr Leu
 900 905 910

Pro Cys Ala Met Gly Leu Pro Ala Tyr Phe Lys Met Asn Ser Pro Ser
 915 920 925

Leu Trp Lys Tyr Asn Gly Glu Phe Ser Ile Gln Thr Asp Ala Lys Thr
 930 935 940

Asp Val Pro Met Ser Leu Glu Asn Phe Met Asn Ile Thr Gly Ser Ile
 945 950 955 960

Asn Leu Met Phe Ser Gln Met Tyr His Ala Gln Leu Ala Phe Ser Thr
 965 970 975

Ala Phe Asp Asn Lys Glu Tyr Ile Ser Gly Leu Asp Arg Lys Val Glu
 980 985 990

Val His Val Pro Val Lys Phe Gln Ile Asn Leu Asp Phe Lys Asn His
 995 1000 1005

Asn Gly Phe Ile Arg Ile Ile Pro Leu Phe Thr Asp Arg Asp Tyr
 1010 1015 1020

Asp Val Leu Gln Trp Gln Thr Ile Pro Tyr Thr Thr Ile His Asn
 1025 1030 1035

Val Pro Asp Phe Glu Thr Val Tyr Met Asp Gln Leu Phe Lys Leu
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Ile His Val Arg Lys Thr Ala His Phe Glu Lys Lys Met Gly Glu
 1055 1060 1065

Asn Thr Gly Ile Val Phe Lys Val Lys Tyr Asp Thr Asp Gln Glu
 1070 1075 1080

Phe Leu Asp Thr Lys Trp Phe Leu Asp Glu Phe Lys Val Leu Gln
 1085 1090 1095

Leu Phe Thr Gly Leu Asn Tyr Asp Val Pro Thr Lys Asp Ile Phe
 1100 1105 1110

Tyr Asn Asn Leu Thr Val Tyr Tyr Asp His Glu Asp Thr Lys Asn
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His Ala Val Ser Phe Thr Val Thr Lys Glu Gln Ser Lys Phe Tyr
 1130 1135 1140

Glu Thr Leu Asn Pro Val Val Gln Gln Asn Leu Lys Leu Ser Ser

1145		1150		1155
Gly Lys Lys Gln Lys His Arg Asn Val Lys Ser His Arg Ile Arg				
1160		1165		1170
Arg Glu Tyr Thr Glu Asp Glu Asn Pro Ala Ile Pro Lys Asp Lys				
1175		1180		1185
Gln Pro Asn Ser His Pro Arg Arg Gln Glu Tyr Leu Ser Lys Ser				
1190		1195		1200
Met Ala Leu Thr Gly Asp Ala Thr Ala Val Val Leu Asp Met Thr				
1205		1210		1215
Leu Lys Phe Glu Gly Pro Ala Glu Ser Tyr Phe Thr Thr Thr Val				
1220		1225		1230
Ser His Ala Thr Ser Leu Val Asn Gly Ser Ser Asn Tyr Leu Leu				
1235		1240		1245
Phe Tyr Asp Gln His Tyr Tyr Glu Glu Lys Lys Arg Asn Gln Phe				
1250		1255		1260
Cys Leu Ser Trp Ser Val Tyr Lys Pro Gln Val Pro Ile Met Asn				
1265		1270		1275
Ile Tyr Ser Ala Phe Glu Phe Asp Pro Asn Ser Lys Val His Ala				
1280		1285		1290
Ile Met Asn Ile Gly Lys Glu Cys Glu Asn Gly Gly Ser Ala Val				
1295		1300		1305
Ala Asn Ile Asp Met Leu Arg Leu Ser Glu His Leu Asp Tyr Val				
1310		1315		1320
Lys Asn Leu Thr Val Ser Lys Leu Cys Asp His Glu Met Arg Thr				
1325		1330		1335
Lys Arg Asp His Val Leu Pro Ala Cys Arg Asn Ser Thr Glu Arg				
1340		1345		1350
Ala Ser Asp Leu Asn Arg Val His Val Asp Ile Asn Tyr Asn Leu				
1355		1360		1365
Lys Gln His Glu Thr Phe Lys Arg Arg Val Tyr Lys Val Tyr Asp				
1370		1375		1380
Phe Val Arg Thr His Leu Tyr Pro His Val Ser Glu Asp Val Ile				
1385		1390		1395
Val Asp Asn Pro Ala Gln Phe Ile Ser Ala Asn Phe Thr Leu Lys				
1400		1405		1410

Asp	Asn	Thr	Arg	Ala	Phe	Asn	Val	Ser	Ile	Glu	Thr	Pro	Val	Leu
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Ser	Val	Asn	Ala	Thr	Ser	Val	Arg	Leu	Gln	Ser	Trp	Gln	Ser	Glu
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1445						1450					1455			
Lys	Trp	Ala	Leu	Pro	Leu	Tyr	Tyr	Lys	Pro	Thr	Cys	Val	Val	Asp
1460						1465					1470			
Ser	Ser	Tyr	Ile	Asn	Thr	Phe	Asp	Asn	Phe	Thr	Tyr	Ser	Ala	His
1475						1480					1485			
His	Ile	Val	Gln	Asn	Asp	Ala	Phe	Tyr	Thr	Ile	Leu	Asp	Ile	Pro
1490						1495					1500			
Gln	Lys	Phe	Asn	Met	Glu	Tyr	Phe	Lys	Val	Ala	Phe	Lys	Pro	Thr
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Ser	Pro	Val	Pro	Asn	Met	Gln	Arg	Glu	Val	Leu	Val	Phe	Leu	Arg
1520						1525					1530			
Asn	Ala	Lys	Ile	Glu	Leu	Lys	Pro	Asn	Gln	Gly	Met	Pro	Glu	Val
1535						1540					1545			
Tyr	Val	Glu	Gly	Lys	Arg	Val	Asp	Tyr	Asn	His	His	His	Ser	Thr
1550						1555					1560			
Asp	Leu	Asn	Val	Ser	Gln	Asp	Arg	Ile	Gly	Tyr	Val	Tyr	Ala	Leu
1565						1570					1575			
Pro	Thr	Lys	Ala	Ala	His	Ile	Val	Phe	Pro	Ser	Tyr	Glu	Ile	Glu
1580						1585					1590			
Met	Phe	Tyr	Asp	Gly	Ser	Arg	Ile	Met	Ile	Gln	Ala	Ser	Asn	Met
1595						1600					1605			
Tyr	Arg	Asn	Phe	Thr	Lys	Gly	Leu	Cys	Gly	Asn	Met	Asp	Gly	Glu
1610						1615					1620			
Phe	Val	Asn	Asp	Val	Leu	Thr	Pro	Trp	Gly	Cys	Tyr	Ala	Lys	Asp
1625						1630					1635			
Met	Ala	Leu	Phe	Val	Ala	Ser	Tyr	Ala	Asp	Asn	Ser	Asn	Ser	Glu
1640						1645					1650			
Val	Arg	Lys	Ile	Lys	Ala	Thr	Gln	Asn	Glu	Gln	Thr	Cys	Val	Pro
1655						1660					1665			
Gln	Phe	His	Gln	Pro	Leu	Val	Ser	His	Gln	Met	Arg	Leu	Ser	Gln

1670 1675 1680
 Val Ile Lys Leu Ala Asp Thr Ser Ser Ser Ser Glu Ser Ser Ser
 1685 1690 1695
 Ser Ser Glu Ser His Glu Asn Asn Ser Ser Pro Ser Ser Glu Ser
 1700 1705 1710
 Gln Val Asn Lys Ser Lys Arg Gln Pro Asn Ser Arg Pro Arg Ser
 1715 1720 1725
 Ser Ser Ser Ser Ser Ser Ser Ser Ser Ser Glu Ser Asn Glu Ser
 1730 1735 1740
 Val Leu Ala Lys Lys Ile Ile Asn Asn Gln Ile Gly Pro Lys Pro
 1745 1750 1755
 Thr Leu Ile Pro Ser Gln Ser Pro Met Thr Ser Asp Asp Lys Cys
 1760 1765 1770
 Met Thr Gln Gln Pro Arg His Thr Tyr Tyr Glu Asn Gln Phe Cys
 1775 1780 1785
 Val Ser Glu Lys Pro Leu Asp Thr Cys Met Pro Leu Ile Cys His
 1790 1795 1800
 Ala Thr Glu Ser Tyr Thr Ile Asp Val Asn Phe Tyr Cys Val Pro
 1805 1810 1815
 Leu Gly Pro Ala Ala Asn His Tyr Met Lys Leu Val Lys Lys Gly
 1820 1825 1830
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 Leu Pro Val Glu Ile Pro Ile Gln Cys Glu Pro Val Leu Asn
 1850 1855 1860

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 <211> 2587
 <212> PRT
 <213> Marsupinaeus japonicus

 <400> 11

 Met Thr Thr Ser Ser Leu Leu Phe Val Leu Ala Leu Val Ala Gly Gly
 1 5 10 15

 Leu Ala Ala Pro Trp Gly Ala Asp Leu Pro Arg Cys Ser Thr Glu Cys
 20 25 30

 Pro Ile Ser Gly Ser Pro Lys Leu Ala Tyr Gln Pro Glu Lys Thr Tyr
 35 40 45

Thr Tyr Gln Tyr Ser Gly Lys Ser Arg Val Gln Leu Lys Gly Val Asp
 50 55 60

Asp Gly Val Ser Glu Thr Glu Trp Ala Ala Arg Val Asp Leu Thr Trp
 65 70 75 80

Ile Ser Pro Cys Asp Val Ala Ile Ser Phe Asn Asn Met Lys Met Asp
 85 90 95

Gly Ala Arg Gly Pro Ile Ala Ala Arg Thr Leu Glu Arg His Pro Leu
 100 105 110

Val Val Ala Val Val Asp Gly Arg Val Gln His Val Cys Ala His Pro
 115 120 125

Asp Asp Glu Pro Trp Ala Ile Asn Leu Lys Lys Gly Val Ala Ser Ala
 130 135 140

Phe Gln Asn Ser Ile Pro Ser Leu Ser Thr Val Ser Ser Gly Met Thr
 145 150 155 160

Val Thr Glu Thr Asp Val Val Gly Lys Cys Pro Thr Thr Tyr Gln Ile
 165 170 175

Glu Thr Glu Gly Glu Lys Val Ile Val Val Lys Glu Lys Asn His Arg
 180 185 190

His Cys Gln Gln Arg Tyr Pro Thr Pro Ala Glu Thr Pro Ala Pro Trp
 195 200 205

Leu Lys Ala Pro Leu Pro Ile Glu Glu Ser Lys Ser Glu Cys Lys Gln
 210 215 220

Glu Ile Thr Asn Gly Ile Tyr Thr Ser Ile Met Cys His Asp Lys Asn
 225 230 235 240

Ile Val Arg Pro Ala Ile Gly Ile Tyr Lys Tyr Val Glu Ala Asn Gln
 245 250 255

Glu Ser Thr Leu His Phe Ile Ser Glu Thr Thr Asp Thr Ser Ala Ile
 260 265 270

Thr Ala Ile Pro Arg Gly Glu Met His Ile Glu Ser Leu Leu Tyr Asn
 275 280 285

His Glu Thr Met Lys Asp Pro Glu Leu Ala Pro Glu Leu Asp Gln Leu
 290 295 300

Met Lys Glu Ile Cys Glu Lys Thr Lys Asp Thr Val Glu Ala Glu Ala
 305 310 315 320

Ala Ala Leu Val Ala Lys Ala Leu His Leu Leu Arg Arg Val Pro Glu
 325 330 335

Thr Val Val Val Glu Ile Ala Gln Lys Val Arg Gln Gly His Tyr Cys
 340 345 350
 Ser Asp Ser Ala Lys Leu Glu Ser Ile Phe Leu Asp Ala Val Ala Phe
 355 360 365
 Leu His Glu Ser Gly Ala Val Lys Val Met Val Gln Glu Ile Leu Asn
 370 375 380
 Gly Arg Ala Thr Gly Gly Arg Leu Ala Leu Tyr Thr Ala Ala Leu Tyr
 385 390 395 400
 Leu Thr Pro Arg Pro Asn Ile Glu Ala Val Lys Ala Leu Thr Pro Leu
 405 410 415
 Phe Glu Ser Pro Arg Pro Met Pro Ser Leu Leu Leu Ala Ala Ala Ser
 420 425 430
 Met Val Asn His Tyr Cys Arg His Thr Pro His Cys His Gln Glu Ala
 435 440 445
 Pro Val Glu Arg Ile Ala Glu Ile Leu Ala Ala Lys Val Glu Gly His
 450 455 460
 Cys Ser Pro Ser Ile Gly Val Glu Glu Lys Glu Glu Ala Leu Ala Ile
 465 470 475 480
 Phe Lys Ala Leu Gly Asn Met Gly Val Val Thr Pro Ala Val Thr Arg
 485 490 495
 Ala Ala Ala Gln Cys Ile Glu Lys Glu Gly Leu Glu Thr Ser Ile Arg
 500 505 510
 Val Ala Ala Ala Gln Ala Phe Arg Gln Ala Asn Cys Asp Arg Pro Ala
 515 520 525
 Val Gln Lys Leu Val Asp Ile Ala Thr Arg Pro Thr Phe Glu Thr Glu
 530 535 540
 Val Arg Ile Ala Ser Tyr Leu Ala Ala Ile Arg Cys Ala Glu Lys Glu
 545 550 555 560
 His Leu Glu Gln Ile Ile Glu Lys Ile Ser Glu Glu Glu Asn Thr Gln
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 Val Arg Gly Phe Val Leu Gly His Leu Ile Asn Ile Gln Glu Ser Thr
 580 585 590
 Cys Pro Thr Lys Glu Asn Leu Lys Tyr Leu Leu Thr Asn Val Val Ile
 595 600 605

Pro Thr Asp Phe Glu Lys Asp Phe Arg Lys Phe Ser Arg Asn Val Glu
 610 615 620
 Met Ser Tyr His Ala Pro Ala Phe Gly Met Gly Ala Asp Leu Glu Ser
 625 630 635 640
 Asn Ile Ile Tyr Ala Pro Gly Ser Phe Ile Pro Arg Ala Val Asn Leu
 645 650 655
 Asn Met Lys Ala Ala Val Asp Glu Thr His Met Asp Leu Ala Glu Ile
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 Gly Ala Arg Phe Glu Gly Ile Asp Ser Ile Ile Glu Glu Leu Phe Gly
 675 680 685
 Pro Glu Gly Tyr Leu Arg Lys Ala Thr Phe Gly Lys Ile Met Gln Asp
 690 695 700
 Ile Thr Gly Phe Ala Glu Glu Lys Gly Leu Lys Val Met Glu His Ile
 705 710 715 720
 Lys Gln Thr Leu Arg Thr Lys Arg Ser Ile Asp Ser Ser Val Ile Ser
 725 730 735
 Asp Phe Phe Gly Lys Leu Tyr Gly Glu Gly Arg Ser His Thr His Ala
 740 745 750
 Glu Val Phe Ala Arg Ile Met Gly His Glu Ile Thr Tyr Ala Asp Val
 755 760 765
 Ala Glu Ser Leu Lys Gly Val Thr Ala Asp Thr Leu Ile Glu Thr Phe
 770 775 780
 Phe Ser Phe Phe Glu Glu Ser Leu Glu Gln Met Lys Gly Leu Asn Leu
 785 790 795 800
 Asn Thr Ala Arg Thr Ala Gln Leu Tyr Met Asp Tyr Ser Leu Pro Thr
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 Ile Gln Gly Thr Pro Leu Lys Leu Lys Leu Ala Gly Thr Ala Val Ala
 820 825 830
 Gly Leu Lys Met Glu Gly Asp Phe Asn Ile Ala Gln Ile Leu Ser Asp
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 Pro Gly Asn Leu Gln Thr Gly Ile Lys Leu Phe Pro Ala Leu Ser Val
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 Gln Ala Thr Gly Phe Val Gly Phe Glu Cys Arg Leu Thr Arg Val Gly
 865 870 875 880
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 885 890 895

Ile Arg Thr Thr Glu Asn Lys Lys Ile Gln Met Glu Leu Glu Ile Pro
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 Glu Lys Met Glu Leu Leu Asn Ile Lys Ala Glu Thr Tyr Leu Val Lys
 915 920 925
 Ala Val Gly Lys Lys Leu Thr Lys Ile Thr Pro Pro Thr Val Arg Asp
 930 935 940
 Val Arg Val Thr His Ala Ala Cys Leu Asn Ala Val Glu Pro Val Leu
 945 950 955 960
 Gly Ile Lys Val Cys Tyr Asn Ile Asn Met Pro Asp Val Phe Arg Ala
 965 970 975
 Asn Gly Leu Pro Leu Gly Glu Pro Ala Ile Ala Lys Leu Tyr Ile Glu
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 Lys Ala Asp Pro Ser Met Arg Gly Tyr Leu Met Thr Ala Ala Ile Lys
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 1010 1015 1020
 Gly Ala Thr Thr Pro Arg Arg Ala Glu Met Thr Leu Ser Tyr Thr
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 Lys Glu Glu Gly Ser His Ile Val Ser Ala Lys Leu Asp Ser Ser
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 Ser Ile Ala Ala Gly Val Trp Ala Thr Leu Thr Asn Glu Glu Gly
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 His Lys Ala Met Glu Thr Tyr Val Lys Phe Asp Tyr Gly Gln Ile
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 Ala Ile Ser Arg Gly Ile Lys Leu Asp Met Ile Val Lys Glu Glu
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 Ser Ala Gly Lys Glu Phe Glu Val Asn Val Phe Ser Gly Arg Ser
 1100 1105 1110
 Arg Arg Phe Thr Pro Glu Ser His Ile Val Glu Ala Lys Phe Ile
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 Lys Lys Thr Asn Gly Pro Glu Val Asn Val Asp Val Ile Cys Arg
 1130 1135 1140
 Thr Arg Asn Ala Leu Ala Gln Tyr Phe Asp Leu Asn Ile Glu Val
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Gly Ala Asp Phe Met Glu Phe Ser Pro Glu Gly Val Tyr Pro Ala
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 Arg Tyr Ile Pro Lys Val Ser Ile Leu Leu Pro Val Ala Leu Arg
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 Lys Met Glu Val His Ala Asn Thr Val Ala Trp Lys Leu Ala Ser
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 Tyr Ile Arg Glu Gly Ser Gln Ser Gly Glu Ser Arg Glu Leu Ile
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 Gln Ala Thr His Lys Ile Glu Gly Thr Leu Pro Gln Asn Ile Val
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 Ala Met Tyr Asp Ile Phe Tyr His Pro Glu Lys Met Gly Ala Ser
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 Glu Ala Ile Tyr Glu Asn Thr Gly Glu Lys Tyr Tyr Thr Lys Phe
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 Leu Val Glu Ala Pro Gly Tyr Ile Arg Pro Val Arg Ile Glu Ala
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 Thr Ala Glu Glu Glu Thr Gly Gly Arg Tyr Ala Leu Glu Ser Ala
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 Ile Lys Tyr Gly Glu Arg Thr Val Phe Glu Val Thr Gly Pro Val
 1340 1345 1350
 Met Ala Arg Phe Thr Ser Lys Thr Ala Lys Leu Gln Ala Asn Ile
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 Lys Leu Ser Ala Met Ala Ser Glu Pro Tyr Ile Ile Gly Ala Asn
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 Phe Val Phe Gly Asn Lys Lys Gln Met Ile Ala Met Glu Ile Lys
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 Glu Arg Glu Glu Pro Val Phe Gly Val Glu Trp Lys Met Val Gln
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 Glu Ser Ala Glu Lys Thr Thr Leu Ser Ile Ala Phe Val Leu Pro
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Ala	Leu	Ile	Glu	Asn	Lys	Val	Asp	Ala	Val	Ile	Thr	Glu	Asp	Leu
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Val	His	Val	Ser	Phe	Asn	Asn	Leu	Val	Leu	Pro	Lys	Thr	Ser	Tyr
1445						1450					1455			
Arg	Arg	Arg	Val	Lys	Gly	Phe	Ala	Asp	Val	Asn	Ile	Gly	Glu	Lys
1460						1465					1470			
Arg	Ala	Asn	Val	Glu	Phe	Ser	Trp	Asp	Ala	Asp	Lys	Ser	Pro	Glu
1475						1480					1485			
Lys	Lys	Leu	Val	Val	Asp	Ala	Ser	Leu	Ile	Ser	Ser	Pro	Ser	Asn
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Pro	Gly	His	Ala	Glu	Ile	His	Gly	Asn	Ile	Val	Ile	Ala	Gly	Glu
1505						1510					1515			
Pro	Tyr	His	Met	Lys	Leu	Ile	Leu	Thr	Ala	Thr	Asn	Leu	Leu	Glu
1520						1525					1530			
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1535						1540					1545			
Ser	Gln	Lys	Thr	Ile	Val	Leu	Gly	Ala	Ser	Cys	Asp	Val	Gln	Leu
1550						1555					1560			
Glu	Gly	Thr	Thr	Thr	Lys	Val	Val	Ser	Val	Ile	Glu	Tyr	Lys	Asn
1565						1570					1575			
Met	Glu	Asn	Lys	Glu	Tyr	Lys	Tyr	Thr	Ser	Val	Ile	Ala	Leu	Glu
1580						1585					1590			
Lys	Leu	Gly	Gly	Pro	Tyr	Asn	Tyr	Val	Val	Lys	Ala	Lys	Val	Ile
1595						1600					1605			
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1610						1615					1620			
Lys	His	Gln	Trp	Thr	Pro	Glu	Glu	His	Leu	Val	Ala	Phe	Lys	Val
1625						1630					1635			
Gly	Ala	Lys	Ala	Pro	Val	Leu	Lys	Met	Pro	Leu	Met	Ile	Ala	Phe
1640						1645					1650			
Ser	Ile	His	Asn	Thr	Arg	Gly	Ser	Phe	Val	Gly	Phe	Cys	Lys	Ile
1655						1660					1665			
Glu	Arg	Asn	Thr	Pro	Ser	Asn	Val	Phe	Glu	Trp	Lys	Ile	Gln	Met
1670						1675					1680			

Thr	Pro	Glu	Gly	Gly	Ile	Glu	Val	Val	Glu	Ala	Gly	Leu	Asp	Ile
1685						1690					1695			
Lys	Ala	Ile	Asn	Glu	Val	Leu	Lys	Ile	Val	His	Ala	Val	Val	Thr
1700						1705					1710			
Phe	Glu	Glu	Glu	Gly	Tyr	Gln	Ala	Tyr	Gly	Gln	Glu	Thr	Ala	Lys
1715						1720					1725			
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1730						1735					1740			
Gln	Met	Arg	Thr	Pro	Thr	Arg	Thr	Ile	Glu	Gly	Arg	Ala	Lys	Leu
1745						1750					1755			
Ser	Pro	Arg	Glu	Ser	Gly	Ile	Lys	Phe	Tyr	Pro	Asn	Lys	Gly	Lys
1760						1765					1770			
Ala	Glu	Ala	Lys	Tyr	Glu	Val	Gly	Tyr	Lys	Ala	Asn	His	Gln	Gly
1775						1780					1785			
Ser	Trp	Gly	Gln	His	Ala	Ser	Asn	Ile	Glu	Val	Arg	Met	Asn	His
1790						1795					1800			
Pro	Thr	Leu	Pro	Lys	Pro	Ile	Met	Val	Ala	Ala	His	Tyr	Thr	Ala
1805						1810					1815			
Ile	Gly	Glu	Thr	Ile	Lys	Gly	Thr	Ile	Glu	Leu	Asp	Ile	Phe	Pro
1820						1825					1830			
Glu	Glu	Glu	Asn	Lys	Ile	Thr	Gly	Thr	Leu	Glu	Thr	Gln	Arg	Ile
1835						1840					1845			
Ser	Glu	Asn	Ala	Ile	Arg	Val	Glu	Val	Phe	Leu	Thr	Gly	Lys	Ile
1850						1855					1860			
Leu	Gln	Val	Asn	Pro	Lys	Ala	Ile	Val	Thr	Val	Ala	Tyr	Ala	Pro
1865						1870					1875			
Glu	Thr	Phe	Ala	Leu	Asp	Val	Val	Phe	His	Lys	Thr	Pro	Ser	Thr
1880						1885					1890			
Ala	Pro	Val	Phe	Ala	Leu	Ala	Ala	Lys	Tyr	Asp	Lys	Thr	Ser	Ala
1895						1900					1905			
His	Asn	Ala	Ala	Ala	Thr	Phe	Thr	Val	Glu	Met	Glu	Gln	Arg	Pro
1910						1915					1920			
Val	Phe	Glu	Ile	Thr	Ala	Val	Ala	Glu	Pro	Glu	Glu	Glu	Val	Pro
1925						1930					1935			
Cys	Asn	Gly	Ile	Arg	Ile	Lys	Ala	Ile	Ala	Asn	Ala	Pro	Ala	Phe
1940						1945					1950			

Gly Lys Tyr Asn Ile Phe Ser Lys Met Cys Lys Pro Ala Phe Ile
 1955 1960 1965
 Glu Leu Thr Thr Met Arg His Gly Gly Glu Lys Glu Tyr Thr Ala
 1970 1975 1980
 Arg Leu Gly Leu Arg Tyr Pro Asp Thr Ala Glu Ala Gly Val Tyr
 1985 1990 1995
 Val Ala Ser Gly Arg Ala Glu Glu Ile Arg Gly Val Ala Val Ala
 2000 2005 2010
 Ala Val Lys Leu Ala Ser Pro Thr Met Leu Lys Val Glu Met Ala
 2015 2020 2025
 Tyr Gly Pro Glu Glu Ala Gln Val Leu Met Asn Glu Met Thr Glu
 2030 2035 2040
 Glu Tyr Glu Lys Ala Ala Val Leu Phe Lys Ser Val Val Met Glu
 2045 2050 2055
 Val Val His Phe Leu Glu Glu Glu Ala Ser Ala Lys Gly Ile His
 2060 2065 2070
 Phe Pro Ser Ser Gln Leu Val Thr Leu Leu Gly Val Ala Lys Glu
 2075 2080 2085
 Glu Ile Glu Glu Ile Tyr Arg Asp Ile Leu Ser Asp Ala Arg Ile
 2090 2095 2100
 Phe Asp Thr Glu Ile Ile Arg Asp Ile Leu Ala Ser Pro Val Val
 2105 2110 2115
 Ser Phe Val Pro Arg Val Tyr Phe Gly Val Trp Ser Glu Ile Val
 2120 2125 2130
 Leu Leu Gln His Gln Leu Ser Val Asn Ile Ile Gln Ala Ile Glu
 2135 2140 2145
 Arg Phe Gln Gly Glu Phe Glu Gly Ile Thr Glu Ile Ile Met Glu
 2150 2155 2160
 Ile Val Met Glu Ala Thr Arg Met Ala Glu Thr Gly Glu Val Pro
 2165 2170 2175
 Lys Val Leu Leu Asp Val Leu Glu Gln Ile Arg Ala Ser Lys Val
 2180 2185 2190
 Phe Arg Ile Val Lys Arg Glu Val Tyr Glu Ile Leu Glu Glu Tyr
 2195 2200 2205

Pro Glu Glu Tyr Glu Ala Ile Thr His Val Val Gly Asn Val Met
 2210 2215 2220
 Ala Met Leu Glu Arg Asp Val Glu Ile Val Arg Val Gly Leu Met
 2225 2230 2235
 Lys Met Pro Ala Val Gln Arg Ile Ile Asp Tyr Ile Met Asn His
 2240 2245 2250
 Phe His Ser Lys Gln Val Phe Ala Val Glu Ala Glu Arg Val Val
 2255 2260 2265
 Ser Leu Ile Leu Ser Glu Leu Leu Tyr Val Ser Ile Glu Arg Glu
 2270 2275 2280
 Gly Asn Gly Ile Glu Val Gln Ile Pro Leu His Arg Pro Leu Tyr
 2285 2290 2295
 Ser Leu Thr Gln Val Ala Gln Glu Ala Val Pro Asn Pro Ile Thr
 2300 2305 2310
 Met Leu Glu Asn Leu Ile Phe Ala Tyr Leu Glu Tyr Ile Pro Ile
 2315 2320 2325
 Pro Val Glu His Ala Ile Trp Ala Tyr Tyr Asn Phe Ile Pro Arg
 2330 2335 2340
 Tyr Ile Thr Asp Val Leu Pro Pro Tyr Pro Arg Thr Ala Met Val
 2345 2350 2355
 Val Gly Gly Ser Glu Ile Leu Thr Phe Asp Gly Leu Val Val Arg
 2360 2365 2370
 Ala Pro Arg Ser Pro Cys Lys Val Leu Leu Ala Ala His Gly Ser
 2375 2380 2385
 His Arg Leu Met Met Ser His Pro Gln Pro Ser Ala Pro Pro Gln
 2390 2395 2400
 Leu Glu Leu Asn Thr Pro Ala Ala Ser Val Val Ile Lys Pro Asp
 2405 2410 2415
 Phe Glu Val Leu Val Asn Gly Arg Pro Leu Thr Gly Ser Gln Gln
 2420 2425 2430
 Thr Ile Gly Asn Ile Arg Ile Val Asn Ala Ala Lys His Ile Glu
 2435 2440 2445
 Val Gly Cys Pro Leu Met Lys Val Val Val Ala Lys Thr Gly Gln
 2450 2455 2460
 Val Val Ala Val Glu Ala Ser Gly Trp Thr Tyr Gly Arg Val Ala
 2465 2470 2475

Gly Leu Leu Gly Pro Asn Thr Gly Glu Ile Ala Asp Asp Arg Leu
2480 2485 2490

Met Pro Thr Gly Val Gln Ala Ser Ser Pro Arg Glu Leu Val Ser
2495 2500 2505

Ala Trp Gln Glu Asp Gln Gly Cys Ser Thr Pro Glu Val Pro Arg
2510 2515 2520

Ser Glu Thr Thr Val Ala Arg Leu Ile Gln Cys Gln Thr Leu Leu
2525 2530 2535

Gly Ile Arg Ser Arg Cys Asn Pro Val Val Gln Pro Gln Pro Phe
2540 2545 2550

Ile Asn Met Cys His Ala Ala Arg Asn Ala Cys Asp Ala Ala Gln
2555 2560 2565

Ala Tyr Arg Thr Ile Cys Ala Leu Arg Gly Val Glu Glu Met Arg
2570 2575 2580

Pro Trp Ala Cys
2585

<210> 12
<211> 1603
<212> PRT
<213> Caenorhabditis elegans

<400> 12

Met Lys Ser Ile Ile Ile Ala Ser Leu Val Ala Leu Ala Ile Ala Ala
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Ser Pro Ala Leu Asp Arg Thr Phe Ser Pro Lys Ser Glu Tyr Val Tyr
20 25 30

Lys Phe Asp Gly Leu Leu Leu Ser Gly Leu Pro Thr Arg Ser Ser Asp
35 40 45

Ala Ser Gln Thr Leu Ile Ser Cys Arg Thr Arg Leu Gln Ala Val Asp
50 55 60

Asp Arg Tyr Ile His Leu Gln Leu Thr Asp Ile Gln Tyr Ser Ala Ser
65 70 75 80

His Ile Pro Gln Ser Glu Gln Trp Pro Lys Ile Glu Ser Leu Glu Gln
85 90 95

Arg Glu Leu Ser Asp Glu Phe Lys Glu Leu Leu Glu Leu Pro Phe Arg
100 105 110

Ala Gln Ile Arg Asn Gly Leu Ile Ser Glu Ile Gln Phe Ser Ser Glu

78

Ile Gln His Leu Ile His His Phe Glu Lys Lys Ser Ile Thr Pro Leu
 405 410 415
 Arg Ala Ala Glu Leu Leu Lys Ser Val Gln Glu Thr Leu Tyr Pro Ser
 420 425 430
 Glu His Ile Ala Asp Leu Leu Ile Gln Leu Ala Gln Ser Pro Leu Ser
 435 440 445
 Glu Lys Tyr Glu Pro Leu Arg Gln Ser Ala Trp Leu Ala Ala Gly Ser
 450 455 460
 Val Val Arg Gly Phe Ala Ser Lys Thr Gln Asp Leu Pro Leu Ile Arg
 465 470 475 480
 Pro Ala Ser Arg Gln Thr Lys Glu Lys Tyr Val Arg Val Phe Met Gln
 485 490 495
 His Phe Arg Asn Ala Asp Ser Thr Tyr Glu Lys Val Leu Ala Leu Lys
 500 505 510
 Thr Leu Gly Asn Ala Gly Ile Asp Leu Ser Val Tyr Glu Leu Val Gln
 515 520 525
 Ile Ile Gln Asp Pro Arg Gln Pro Leu Ser Ile Arg Thr Glu Ala Val
 530 535 540
 Asp Ala Leu Arg Leu Leu Lys Asp Val Met Pro Arg Lys Ile Gln Lys
 545 550 555 560
 Val Leu Leu Pro Val Tyr Lys Asn Arg Gln Asn Lys Pro Glu Leu Arg
 565 570 575
 Met Ala Ala Leu Trp Arg Met Met His Thr Ile Pro Glu Glu Pro Val
 580 585 590
 Leu Ala His Ile Val Ser Gln Met Glu Asn Glu Ser Asn Gln His Val
 595 600 605
 Ala Ala Phe Thr Tyr His Val Leu Arg Gln Phe Tyr Lys Ser Thr Asn
 610 615 620
 Pro Cys Tyr Gln Gln Leu Ala Val Arg Cys Ser Lys Ile Leu Leu Phe
 625 630 635 640
 Thr Arg Tyr Gln Pro Gln Glu Gln Met Leu Ser Thr Tyr Ser Gln Leu
 645 650 655
 Pro Leu Phe Asn Ser Glu Trp Leu Ser Gly Val Gln Phe Asp Phe Ala
 660 665 670
 Thr Ile Phe Glu Lys Asn Ala Phe Leu Pro Lys Glu Val Gln Ala Ser

675 680 685
 Leu Glu Thr Val Phe Gly Gly Asn Trp Asn Lys Tyr Phe Ala Gln Val
 690 695 700
 Gly Phe Ser Gln Gln Asn Phe Glu Gln Val Ile Leu Lys Thr Leu Glu
 705 710 715 720
 Lys Leu Ser Leu Tyr Gly Lys Gln Ser Asp Glu Leu Arg Ser Arg Arg
 725 730 735
 Val Gln Ser Gly Ile Gln Met Leu Gln Glu Ile Val Lys Lys Met Asn
 740 745 750
 Ile Arg Pro Arg Val Gln Gln Thr Asp Ser Gln Asn Ala His Ala Val
 755 760 765
 Phe Tyr Leu Arg Tyr Lys Glu Met Asp Tyr Ile Val Leu Pro Ile Asp
 770 775 780
 Met Glu Thr Ile Asp Thr Leu Val Glu Lys Tyr Val Arg Asn Gly Glu
 785 790 795 800
 Phe Asp Ile Lys Ser Leu Leu Thr Phe Leu Thr Asn Asp Ser Lys Phe
 805 810 815
 Glu Leu His Arg Ala Leu Phe Phe Tyr Glu Ala Glu Arg Arg Ile Pro
 820 825 830
 Thr Thr Ile Gly Met Pro Leu Thr Ile Ser Gly Lys Met Pro Thr Ile
 835 840 845
 Leu Ser Ile Asn Gly Lys Val Ser Ile Glu Leu Glu Lys Leu Gly Ala
 850 855 860
 Arg Leu Val Leu Asp Ile Val Pro Thr Val Ala Thr Thr His Val Thr
 865 870 875 880
 Glu Met Pro Leu Leu Tyr Pro Val Ile Glu Gln Gly Val Lys Ser Leu
 885 890 895
 Gln Ser Ala Arg Leu His Thr Pro Leu Arg Phe Glu Ser Thr Val Glu
 900 905 910
 Leu Lys Lys Asn Thr Leu Glu Ile Thr His Lys Phe Val Val Pro Glu
 915 920 925
 Asn Lys Lys Thr Thr Val Ser Val His Thr Arg Pro Val Ala Phe Ile
 930 935 940
 Arg Val Pro Lys Asn Gln Asp Ser Glu Tyr Val Glu Ala Glu Glu Lys
 945 950 955 960

Thr Ile Ser His Ser Gln Tyr Gln Met Ser Thr Glu Glu Ile Asp Arg
 965 970 975

Gln Tyr Glu Thr Phe Gly Leu Arg Ile Asn Ala Gln Gly Asn Val Leu
 980 985 990

Ser Gln Trp Thr Leu Pro Met Val Leu Met Thr Glu Gln Asp Phe Glu
 995 1000 1005

Tyr Thr Leu Glu Asn Lys Asn Arg Pro Val Glu Phe Thr Ala Arg
 1010 1015 1020

Val Thr Ile Gly Asn Leu Glu Lys Thr Asp Leu Ser Glu Ile Lys
 1025 1030 1035

Phe Asp Lys Ile Phe Glu Lys Glu Phe Asp Leu Glu Asn Asn Glu
 1040 1045 1050

Ser Glu Asn Arg Arg Gln Tyr Phe His Lys Met Ile Arg Glu Ile
 1055 1060 1065

Gln Ser Glu Gln Gly Phe Lys Asn Leu Ile Thr Leu Lys Leu Glu
 1070 1075 1080

Ala Pro Gln Gln Met Tyr Trp Asn Thr Glu Leu Arg Thr Val Cys
 1085 1090 1095

Asp Lys Trp Ile Arg Met Cys Lys Val Glu Met Asp Ala Arg Arg
 1100 1105 1110

Ser Pro Met Glu His Glu Asn Lys Glu Trp Thr Leu Arg Thr Glu
 1115 1120 1125

Leu Leu Ala Ala Arg Pro Gln Met Pro Ser Ser Leu Arg Gln Leu
 1130 1135 1140

Arg Glu Gln Pro His Arg Glu Val Gln Leu Ala Phe Asn Ala Lys
 1145 1150 1155

Trp Gly Ser Ser Lys Lys Ser Glu Ile Thr Val Asn Ala Gln Leu
 1160 1165 1170

Glu Gln Ser Thr Glu Gln Lys Lys Phe Ile Arg Asn Ile Glu Arg
 1175 1180 1185

Glu Tyr Lys Gly Ile Pro Glu Tyr Glu Leu Leu Ile Lys Ala Ala
 1190 1195 1200

Arg Leu Asn Gln Val Asn Val Val Ser Glu Tyr Lys Leu Thr Pro
 1205 1210 1215

Gln Ser Glu Tyr Thr Phe Ser Arg Ile Phe Asp Leu Ile Lys Ala

1220	1225	1230
Tyr Asn Phe Trp Thr Val Ser Glu Lys Arg Val Gln Asn Glu Asn 1235 1240 1245		
Arg Arg Val Val Leu Gln Leu Ser Val Glu Pro Leu Ser Arg Gln 1250 1255 1260		
Ser His Glu His Asp His Gln Thr Pro Glu Gln Glu Val Glu Leu 1265 1270 1275		
Lys Asn Ala Arg Ile Pro Arg Val Val Leu Pro Thr Ile Ala Arg 1280 1285 1290		
Ser Ala Met Phe Gln Gln Thr Trp Glu Lys Thr Gly Ala Thr Cys 1295 1300 1305		
Lys Val Asp Gln Ser Glu Val Ser Thr Phe His Asn Val Ile Tyr 1310 1315 1320		
Arg Ala Pro Leu Thr Thr Cys Tyr Ser Leu Val Ala Lys Asp Cys 1325 1330 1335		
Ser Glu Gln Pro Arg Phe Ala Val Leu Ala Lys Lys Ile Asn Lys 1340 1345 1350		
Asn Ser Glu Glu Leu Leu Val Lys Val Val Arg Arg Glu Glu Glu 1355 1360 1365		
Ile Val Val Lys Lys Ser Asp Asp Lys Phe Leu Val Lys Val Asp 1370 1375 1380		
Gly Lys Lys Val Asn Pro Thr Glu Leu Glu Gln Tyr Asn Ile Glu 1385 1390 1395		
Ile Leu Gly Asp Asn Leu Ile Val Ile Arg Leu Pro Gln Gly Glu 1400 1405 1410		
Val Arg Phe Asp Gly Tyr Thr Val Lys Thr Asn Met Pro Ser Val 1415 1420 1425		
Ala Ser Gln Asn Gln Leu Cys Gly Leu Cys Gly Asn Asn Asp Gly 1430 1435 1440		
Glu Arg Asp Asn Glu Phe Met Thr Ala Asp Asn Tyr Glu Thr Glu 1445 1450 1455		
Asp Val Glu Glu Phe His Arg Ser Tyr Leu Leu Lys Asn Glu Glu 1460 1465 1470		
Cys Glu Phe Glu Phe Asp Arg Ile Ser Glu Lys Lys Asn Tyr Arg 1475 1480 1485		

Asn Lys Trp Asn Arg Glu Glu Lys Lys Ser Asp Tyr Glu Ser Ser
1490 1495 1500

Ser Asp Tyr Glu Ser Asn Tyr Asp Glu Lys Glu Thr Glu Glu Glu
1505 1510 1515

Leu Val Lys Lys Thr Leu Ile Lys Glu Phe Ser Asn Arg Val Cys
1520 1525 1530

Phe Ser Ile Glu Pro Val Ser Glu Cys Arg Arg Gly Leu Glu Ser
1535 1540 1545

Glu Lys Thr Ser Asn Lys Lys Ile Arg Phe Thr Cys Met Pro Arg
1550 1555 1560

His Arg Gln Glu Arg Ser Arg Phe Leu Gln Gly Ser Ser Glu Gln
1565 1570 1575

Thr Val Ala Glu Leu Val Asp Phe Pro Val Ser Phe Val Glu Ser
1580 1585 1590

Val Lys Ile Pro Thr Ala Cys Val Ala Tyr
1595 1600

<210> 13
<211> 1660
<212> PRT
<213> Oscheius tipulae

<400> 13

Met Arg Phe Ala Val Leu Leu Ala Leu Phe Gly Leu Ala Leu Ala Ala
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Arg Gln Ser Ser Val Ser Glu Gln Tyr Tyr Arg Ser Gly Arg Glu Tyr
20 25 30

Arg Tyr Gln Phe Asn Gly His Leu Ser Ala Gly Leu Pro Ile Pro Gly
35 40 45

Glu Glu Asn Ser Ala Thr Arg Ile Gln Ser Leu Ile Arg Ile Gln Pro
50 55 60

Glu Asn Gly Asp Phe Met Arg Leu Gln Met Thr Lys Thr Arg Phe Ala
65 70 75 80

Thr Ser Glu Glu Asp Arg Val Leu Ser Phe Glu Asn Met Asn Glu Val
85 90 95

Pro Val Ser Glu Lys Val Glu Lys Val Leu Ser Leu Pro Ile Arg Phe
100 105 110

Ser Tyr Arg His Gly Met Val Gly Glu Ile Glu Phe Ser Thr Glu Glu
115 120 125

Gln Thr Trp Ser Ser Asn Ile Lys Lys Ala Val Val Asn Met Leu Gln
 130 135 140
 Val Asn Leu Val Lys Lys Gly Met Ser Glu Lys Asn Glu Tyr Glu Thr
 145 150 155 160
 Glu His Asp Asn Asp Phe Phe Leu Ser Asn Glu Arg Thr Leu Glu Gly
 165 170 175
 Glu Cys Glu Val Ala Tyr Thr Lys Ile Glu Lys Ser Glu Lys Glu Gln
 180 185 190
 Gln Trp Thr Lys Ser Ile Asn Phe Glu Lys Cys Ser Leu Arg Pro Glu
 195 200 205
 Ile Val Tyr Gly Arg Arg Tyr Ala Glu Glu Cys Asn Glu Cys Arg Glu
 210 215 220
 Arg Asp Glu Lys Phe Ser Ser Thr Val Phe Phe Tyr Asn Ile Thr Gly
 225 230 235 240
 Thr Pro Glu Phe Leu Ile Asn Ser Val Glu Leu Gln Ser Lys His Met
 245 250 255
 Phe Ala Pro Val Thr Glu Gln Lys Gln Leu Ile Thr Ala Arg Ile Thr
 260 265 270
 Asn Arg Leu Glu Leu Val Tyr Ser Gly Glu Gln Lys Glu Gln Ile Glu
 275 280 285
 Ala Val Arg Asn Ser Asp Lys Lys Glu Asn Leu Leu Tyr Asn Pro Glu
 290 295 300
 His Glu Ile Ala Glu Glu Lys Phe Ala Gln Thr Gly Asp Glu Glu Val
 305 310 315 320
 Ser Ser Ser Tyr Ser Gln Leu Arg Arg Ser Gly Arg Asn His Pro Ser
 325 330 335
 Ala Ala Glu Pro Ser Leu Gln Ala Asp Arg Ala Asn Arg Ala Arg Glu
 340 345 350
 Gln Pro Arg Pro Arg Lys Ile Leu Leu Val Asn Tyr Gln Pro Cys Ile
 355 360 365
 Gln Ala Arg Leu Val Lys Ser Leu Arg Phe Ala Thr Glu Asp Asn Leu
 370 375 380
 Ser Ser Ile Arg Ser Leu Val Ser Gln Lys Ser Glu Val Val Gln Ser
 385 390 395 400

Leu Tyr Trp Asp Ala Leu Ala Ile Ala Gly Thr Lys Val Thr Val Ser
 405 410 415
 His Leu Leu Glu Lys Ile Asn Asn Lys Glu Ile Ser Pro Met Lys Ala
 420 425 430
 Ser Gln Leu Met Lys Ile Leu Ala Glu Val Arg Ile Pro Ser Glu Gln
 435 440 445
 Ile Ala Gln Glu Leu His Arg Phe Cys Glu Ser Asp Ile Val Ser Arg
 450 455 460
 Ser Ala Val Leu Arg Gln Ser Cys Trp Leu Ser Tyr Gly Ser Val Leu
 465 470 475 480
 Asn Gly Val Cys Gly Gln Thr Lys Asn Val Tyr Gly Ser Glu Ile Thr
 485 490 495
 Glu Thr Arg Lys Gln Cys Thr Arg Gln Met Lys Glu Lys Tyr Ile Arg
 500 505
 Glu Leu Ile Glu Lys Met Asn Gln Ala Glu Ser Arg Tyr Glu Lys Val
 515 520 525
 Leu Phe Val Lys Ala Ile Ala Asn Ala Gly Ile Asp Thr Ser Val Val
 530 535 540
 Glu Leu Glu Lys Ile Ile Arg Asn Gln Glu Val Glu Lys Thr Val Arg
 545 550 555 560
 Met Gln Ala Ile Asp Ala Leu Arg Arg Leu Arg Leu Ser Met Pro Lys
 565 570 575
 Lys Ile Gln Asn Val Leu Met Pro Val Tyr Arg Asn His Lys Glu Thr
 580 585 590
 Pro Gly Ile Arg Ile Ser Ala Leu His Met Ile Met Gln Thr Gln Pro
 595 600 605
 Thr Ser Gly Val Leu Asp Met Ile Val Arg Gly Leu Glu Lys Glu Arg
 610 615 620
 Ser Gln Gln Val Arg Val Tyr Thr Trp Ser Thr Leu Lys Thr Leu Ser
 625 630 635 640
 Glu Ser Glu Asn Pro Ala Glu Lys Glu Ile Arg Arg Arg Val Ser Gln
 645 650 655
 Ser Leu Ala Ser Ile Pro Val Glu Glu Gln Lys Tyr Leu Glu Ser Lys
 660 665 670
 His Lys Thr Phe Asn Trp Phe Asn Met Gln Ser Gly Ala Thr Leu Asn
 675 680 685

Trp Ala Thr Ile Phe Ser Asn Asp Ser Val Leu Pro Lys Glu Ile Thr
 690 695 700

Ala Ser Leu Glu Thr Val Phe Gly Gly Glu Trp Asn Lys Tyr Leu Ala
 705 710 715 720

Gln Ile Gly Leu Tyr Gln Asn Asn Leu Asp Ser Val Leu Ser Lys Leu
 725 730 735

Leu Gln Lys Val Glu Glu Thr Gly Leu Glu Gln Leu Val Val Arg Gly
 740 745 750

Lys Arg Ser Ser Ser Phe Phe Arg Pro Ala Glu Met Leu Arg Ser Leu
 755 760 765

Val Glu Ser Leu Arg Ile Ser His Arg Gln Val Pro Ala Met Ser Pro
 770 775 780

Ile Ala Met Ile Tyr Leu Arg Tyr Lys Asp Gln Asp Tyr Ala Phe Leu
 785 790 795 800

Pro Ile Asp Ile Asp Thr Leu Pro Glu Met Ile Arg Arg Val Ala Arg
 805 810 815

Asp Gly Gln Leu Asp Leu Ser Glu Ile Glu Lys Val Leu Thr Gln Ala
 820 825 830

Ala Arg Phe Thr Val Ala Gly Ser Ala Phe Phe His Glu Thr Val Arg
 835 840 845

Lys Val Pro Ser Ala Leu Gly Met Pro Gln Val Met Thr Ser Lys Met
 850 855 860

Pro Thr Val Ala Gln Met Asn Gly Glu Val Lys Phe Asp Leu Glu Pro
 865 870 875 880

Leu Asn Ser Asp Lys Phe Thr Gly Leu Arg Leu Arg Val Lys Ala Glu
 885 890 895

Pro His Val Ala Ser Thr His Val Cys Lys Leu Glu Leu Phe Thr Pro
 900 905 910

Ile Gly Gly Gln Gly Ile Lys Leu Leu His Gly Gly Arg Ile Gln Ala
 915 920 925

Pro Ile Asp Ser Glu Ile Glu Ile Asn Trp Glu Lys Lys Leu Ile Val
 930 935 940

Lys Ala Thr Ile Lys Ser Pro Glu Gln Lys Arg His Ile Ala His Phe
 945 950 955 960

Met Thr Arg Pro Val Leu Phe Ser Arg Glu Val Thr Met Asp Lys Gln
965 970 975

Met Arg Gln Tyr Pro Glu Pro Arg Glu Lys Thr Ile Gln Leu Arg Glu
980 985 990

Asn Arg Phe Pro Ile His Ala Phe Glu Arg Gln Tyr Phe Glu Gln Thr
995 1000 1005

Gly Leu Lys Met Thr Val Ser Gly His Tyr Arg Arg Pro Phe Thr
1010 1015 1020

Thr Ala Phe Thr Leu Gly Glu Ser Ile Met Met Ser Ser Ser Ser
1025 1030 1035

Leu Pro Arg Met Leu Ser Leu Lys Glu Val Val Ala Tyr Met Ser
1040 1045 1050

Phe Ser Gly Phe Glu Glu Thr Glu Met Asp Glu Pro Arg Leu Leu
1055 1060 1065

Asn Arg Phe Tyr Glu Lys Glu Thr Glu Leu Phe Glu Thr Glu Lys
1070 1075 1080

Asn Val Glu Tyr Glu Gln Glu Asp Lys Glu Pro Lys Ser Ser Gln
1085 1090 1095

Leu Gln Ser Gln Ile Arg Lys Val Lys Ser Glu Gly Lys Ala Tyr
1100 1105 1110

Lys His Arg Val His Met Lys Ile His Thr Val Gly Gly Pro Lys
1115 1120 1125

Thr Gln Glu Ala Glu Cys Glu Ile Arg Ala Leu Cys Asp Glu Arg
1130 1135 1140

Val Arg Phe Cys Arg Leu Asn Leu Asp Ala Ser Arg Ser Pro Ile
1145 1150 1155

Gln Gly Glu Ser Arg Gln Trp Gln Leu Lys Ser Ser Ala Glu Trp
1160 1165 1170

Leu Tyr Pro Glu Val Pro Ser Thr Met Lys Lys Met Leu Glu Ser
1175 1180 1185

Arg Arg Glu Trp Asn Ala Met Trp Thr Gly Lys Trp Gly Ser Glu
1190 1195 1200

Lys Gln Asn Glu Val Thr Ile Arg Val Gln Gly Glu Gln Ser Ser
1205 1210 1215

Glu Gln Lys Phe Trp Met Lys Lys Ala Glu Arg Glu Gln Ser Pro
1220 1225 1230

Leu Thr Ser Gly Gly Gln Ala Ser Arg Ala Ala Gln Leu Asn Gln
 1235 1240 1245
 Tyr Asn Ile His Ala Thr Tyr Glu Val Thr Pro Glu Thr Glu Phe
 1250 1255 1260
 Trp Met Glu Asn Val Tyr Ser Met Phe Lys Thr Tyr Tyr Phe Phe
 1265 1270 1275
 Ser Ala Glu Val Gln Pro Lys Gln Asn Lys Glu Asn Arg Ile Gln
 1280 1285 1290
 Cys Gln Ile Thr Leu Glu Pro Phe Thr Arg Gln Leu Phe Asn Val
 1295 1300 1305
 Thr Val Met Ser Pro Lys Glu Lys Leu Val Leu Glu Leu Glu Asn
 1310 1315 1320
 Gln Gln Thr Pro Phe Arg Leu Pro Ala Val Asn Ile Gly Arg Glu
 1325 1330 1335
 Phe Gly Arg Val Gln Ser Val Arg His Val Val Lys Ala Val Glu
 1340 1345 1350
 Arg Gln Thr Arg Pro Glu Cys Ile Val Lys Ser Lys Glu Ile Gln
 1355 1360 1365
 Thr Phe Asp Glu Val Phe Tyr Arg Thr Pro Val Met Glu Cys Phe
 1370 1375 1380
 Ser Val Leu Ala Lys Asp Cys Ser Glu Asn Pro Asp Phe Ala Val
 1385 1390 1395
 Leu Met Arg Lys Val Ser Lys Arg Gly Glu Glu Lys Met Trp Lys
 1400 1405 1410
 Val Ile Ser Arg Glu Asn Val Ile Glu Leu Glu Lys Lys Ser Glu
 1415 1420 1425
 Glu Met Ser Val Arg Val Asn Gly Lys Glu Ile Ser Glu Asp Lys
 1430 1435 1440
 Trp Glu Asp Phe Gly Ile Ser Gln Arg Gly Glu Glu Lys Phe Phe
 1445 1450 1455
 Ile Asp Ala Glu Lys Val Thr Val Glu Phe Asp Gly Phe Gln Ala
 1460 1465 1470
 Lys Ile Gln Met Ser Ser Leu Tyr Lys Asn Lys Gln Cys Gly Leu
 1475 1480 1485

Cys Gly His Tyr Asp Gly Glu Lys Thr Asn Glu Phe Arg Arg Ala
 1490 1495 1500
 Asp Asn Glu Glu Thr Asp Asp Ile Glu Glu Phe Ser Arg Ser Tyr
 1505 1510 1515
 Leu Ser Lys Asp Asp Glu Cys Glu Val Asp Glu Gln Glu Met Thr
 1520 1525 1530
 Asn Lys Arg Asn Tyr Lys Val Leu Arg Glu Glu Thr Ser Ser Ser
 1535 1540 1545
 Glu Glu Ile Ser Glu Ser Leu Ile Glu Leu Tyr Ser Glu Ala Phe
 1550 1555 1560
 Gln Ser Arg Glu Ala His His Arg Leu Gly Arg Arg Glu Asp Arg
 1565 1570 1575
 Gln Val Cys Phe Ser Gln Gln Ala Trp Asn Lys Cys Leu Lys Ser
 1580 1585 1590
 Lys Asp Asn Lys Thr Glu Thr Lys Asn Val His Phe Lys Cys Leu
 1595 1600 1605
 Thr Glu Thr Thr Arg Ser Pro Arg Ile Ser Ser Val Phe Ser Gln
 1610 1615 1620
 Ala Asp Ile Ser Glu Asn Leu Ser Asp Val Glu Gly Leu Pro Ser
 1625 1630 1635
 Leu Ala Glu Pro Ser Pro His Ser Arg Phe Leu Pro Cys Val Ile
 1640 1645 1650
 Pro Ser Leu Ser Leu Ser Gln
 1655 1660

<210> 14
 <211> 1687
 <212> PRT
 <213> Fundulus heteroclitus

<400> 14

Met Arg Val Leu Val Leu Ala Leu Thr Val Ala Leu Val Ala Gly Asn
 1 5 10 15
 Gln Val Ser Tyr Ala Pro Glu Phe Ala Pro Gly Lys Thr Tyr Glu Tyr
 20 25 30
 Lys Tyr Glu Gly Tyr Ile Leu Gly Gly Leu Pro Glu Glu Gly Leu Ala
 35 40 45
 Lys Ala Gly Val Lys Ile Gln Ser Lys Val Leu Ile Gly Ala Ala Gly
 50 55 60

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

91

Ser Tyr Arg Tyr Ser Arg Ala Phe His Tyr Asp His Tyr His Asn Pro
 625 630 635 640
 Trp Met Leu Gly Ala Ala Ala Ser Ala Phe Tyr Ile Asn Asp Ala Ala
 645 650 655
 Thr Val Leu Pro Lys Asn Ile Met Ala Lys Ala Arg Val Tyr Leu Ser
 660 665 670
 Gly Val Ser Val Asp Val Leu Glu Phe Gly Ala Arg Ala Glu Gly Val
 675 680 685
 Gln Glu Ala Leu Leu Lys Ala Arg Asp Val Pro Glu Ser Ala Asp Arg
 690 695 700
 Leu Thr Lys Met Lys Gln Ala Leu Lys Ala Leu Thr Glu Trp Arg Ala
 705 710 715 720
 Asn Pro Ser Arg Gln Pro Leu Gly Ser Leu Tyr Val Lys Val Leu Gly
 725 730 735
 Gln Asp Val Ala Phe Ala Asn Ile Asp Lys Glu Met Val Glu Lys Ile
 740 745 750
 Ile Glu Phe Ala Thr Gly Pro Glu Ile Arg Thr Arg Gly Lys Lys Ala
 755 760 765
 Leu Asp Ala Leu Leu Ser Gly Tyr Ser Met Lys Tyr Ser Lys Pro Met
 770 775 780
 Ser Ala Ile Glu Val Arg His Ile Phe Pro Thr Ser Leu Gly Leu Pro
 785 790 795 800
 Met Glu Leu Ser Leu Tyr Thr Ala Ala Val Thr Ala Ala Ser Val Glu
 805 810 815
 Val Gln Ala Thr Ile Ser Pro Pro Leu Pro Glu Asp Phe His Pro Ala
 820 825 830
 His Leu Leu Lys Ser Asp Ile Ser Met Lys Ala Ser Val Thr Pro Ser
 835 840 845
 Val Ser Leu His Thr Tyr Gly Val Met Gly Val Asn Ser Pro Phe Ile
 850 855 860
 Gln Ala Ser Val Leu Ser Arg Ala Lys Asp His Ala Ala Leu Pro Lys
 865 870 875 880
 Lys Met Glu Ala Arg Leu Asp Ile Val Lys Gly Tyr Phe Ser Tyr Gln
 885 890 895
 Phe Leu Pro Val Glu Gly Val Lys Thr Ile Ala Ser Ala Arg Leu Glu

900	905	910
Thr Val Ala Ile Ala Arg Asp Val Glu Gly Leu Ala Ala Ala Lys Val		
915	920	925
Thr Pro Val Val Pro Tyr Glu Pro Ile Val Ser Lys Asn Ala Thr Leu		
930	935	940
Asn Leu Ser Gln Met Ser Tyr Tyr Leu Asn Asp Ser Ile Ser Ala Ser		
945	950	955
Ser Glu Leu Leu Pro Phe Ser Leu Gln Arg Gln Thr Gly Lys Asn Lys		
965	970	975
Ile Pro Lys Pro Ile Val Lys Lys Met Cys Ala Thr Thr Tyr Thr Tyr		
980	985	990
Gly Ile Glu Gly Cys Val Asp Ile Trp Ser Arg Asn Ala Thr Phe Leu		
995	1000	1005
Arg Asn Thr Pro Ile Tyr Ala Ile Ile Gly Asn His Ser Leu Leu		
1010	1015	1020
Val Asn Val Thr Pro Ala Ala Gly Pro Ser Ile Glu Arg Ile Glu		
1025	1030	1035
Ile Glu Val Gln Phe Gly Glu Gln Ala Ala Glu Lys Ile Leu Lys		
1040	1045	1050
Glu Val Tyr Leu Asn Glu Glu Glu Glu Val Leu Glu Asp Lys Asn		
1055	1060	1065
Val Leu Met Lys Leu Lys Lys Ile Leu Ser Pro Gly Leu Lys Asn		
1070	1075	1080
Ser Thr Lys Ala Ser Ser Ser Ser Ser Gly Ser Ser Arg Ser Ser		
1085	1090	1095
Arg Ser Arg Ser Ser Ser Ser Ser Ser Ser Ser Ser Ser Ser Ser		
1100	1105	1110
Ser Ser Arg Ser Ser Ser Ser Ser Ser Arg Ser Ser Ser Ser Leu		
1115	1120	1125
Arg Arg Asn Ser Lys Met Leu Asp Leu Ala Asp Pro Leu Asn Ile		
1130	1135	1140
Thr Ser Lys Arg Ser Ser Ser Ser Ser Ser Ser Ser Ser Ser Ser		
1145	1150	1155
Ser Ser Ser Ser Ser Ser Ser Ser Ser Ser Lys Thr Lys Trp		
1160	1165	1170

Gln Leu His Glu Arg Asn Phe Thr Lys Asp His Ile His Gln His
 1175 1180 1185
 Ser Val Ser Lys Glu Arg Leu Asn Ser Lys Ser Ser Ala Ser Ser
 1190 1195 1200
 Phe Glu Ser Ile Tyr Asn Lys Ile Thr Tyr Leu Ser Asn Ile Val
 1205 1210 1215
 Ser Pro Val Val Thr Val Leu Val Arg Ala Ile Arg Ala Asp His
 1220 1225 1230
 Lys Asn Gln Gly Tyr Gln Ile Ala Val Tyr Tyr Asp Lys Leu Thr
 1235 1240 1245
 Thr Arg Val Gln Ile Ile Val Ala Asn Leu Thr Glu Asp Asp Asn
 1250 1255 1260
 Trp Arg Ile Cys Ser Asp Ser Met Met Leu Ser His His Lys Val
 1265 1270 1275
 Met Thr Arg Val Thr Trp Gly Ile Gly Cys Lys Gln Tyr Asn Thr
 1280 1285 1290
 Thr Ile Val Ala Glu Thr Gly Arg Val Glu Lys Glu Pro Ala Val
 1295 1300 1305
 Arg Val Lys Leu Ala Trp Ala Arg Leu Pro Thr Tyr Ile Arg Asp
 1310 1315 1320
 Tyr Ala Arg Arg Val Ser Arg Tyr Ile Ser Arg Val Ala Glu Asp
 1325 1330 1335
 Asn Gly Val Asn Arg Thr Lys Val Ala Ser Lys Pro Lys Glu Ile
 1340 1345 1350
 Lys Leu Thr Val Ala Val Ala Asn Glu Thr Ser Leu Asn Val Thr
 1355 1360 1365
 Leu Asn Thr Pro Lys Asn Thr Phe Phe Lys Leu Gly Trp Val Leu
 1370 1375 1380
 Pro Phe Tyr Leu Pro Ile Asn Asn Thr Ala Ala Glu Leu Gln Ala
 1385 1390 1395
 Phe Gln Gly Arg Trp Met Asp Gln Val Thr Tyr Met Leu Thr Lys
 1400 1405 1410
 Ser Ala Ala Ala Glu Cys Thr Val Val Glu Asp Thr Val Val Thr
 1415 1420 1425
 Phe Asn Asn Arg Lys Tyr Lys Thr Glu Thr Pro His Ser Cys His

1430		1435		1440
Gln Val 1445	Leu Ala Gln Asp Cys	Thr Ser Glu Ile Lys	Phe Ile Val	
Leu Leu 1460	Lys Arg Asp Gln Thr	Ala Glu Arg Asn Glu	Ile Ser Ile	
Lys Ile 1475	Glu Asn Ile Asp Val	Asp Met Tyr Pro Lys	Asp Asn Ala	
Val Val 1490	Val Lys Val Asn Gly	Val Glu Ile Pro Leu	Thr Asn Leu	
Pro Tyr 1505	Gln His Pro Thr Gly	Asn Ile Gln Ile Arg	Gln Arg Glu	
Glu Gly 1520	Ile Ser Leu His Ala	Pro Ser His Gly Leu	Gln Glu Val	
Phe Leu 1535	Ser Leu Asn Lys Val	Gln Val Lys Val Val	Asp Trp Met	
Arg Gly 1550	Gln Thr Cys Gly Leu	Cys Gly Lys Ala Asp	Gly Glu Val	
Arg Gln 1565	Glu Tyr Ser Thr Pro	Asn Glu Arg Val Ser	Arg Asn Ala	
Thr Ser 1580	Phe Ala His Ser Trp	Val Leu Pro Ala Lys	Ser Cys Arg	
Asp Ala 1595	Ser Glu Cys Tyr Met	Gln Leu Glu Ser Val	Lys Leu Glu	
Lys Gln 1610	Ile Ser Leu Glu Gly	Glu Glu Ser Lys Cys	Tyr Ser Val	
Glu Pro 1625	Val Trp Arg Cys Leu	Pro Gly Cys Ala Pro	Val Arg Thr	
Thr Ser 1640	Val Thr Val Gly Leu	Pro Cys Val Ser Leu	Asp Ser Asn	
Leu Asn 1655	Arg Ser Asp Ser Leu	Ser Ser Ile Tyr Gln	Lys Ser Val	
Asp Val 1670	Ser Glu Thr Ala Glu	Ser His Leu Ala Cys	Arg Cys Thr	
Pro Gln 1685	Cys Ala			

<210> 15
 <211> 1659
 <212> PRT
 <213> *Oncorhynchus mykiss*

<400> 15

Met Arg Ala Val Val Leu Ala Leu Thr Leu Ala Leu Val Ala Ser Gln
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Ser Val Asn Phe Ala Pro Asp Phe Ala Ala Ser Lys Thr Tyr Val Tyr
 20 25 30

Lys Tyr Glu Ala Leu Leu Leu Gly Gly Leu Pro Glu Glu Gly Leu Ala
 35 40 45

Arg Ala Gly Val Lys Val Ile Ser Lys Val Leu Ile Ser Ala Val Ala
 50 55 60

Glu Asn Thr Tyr Leu Leu Lys Leu Val Asn Pro Glu Ile Phe Glu Tyr
 65 70 75 80

Ser Gly Val Trp Pro Lys Asp Pro Phe Val Pro Ala Ala Lys Leu Thr
 85 90 95

Ser Ala Leu Ala Ala Gln Phe Ser Ile Pro Ile Lys Phe Glu Tyr Ala
 100 105 110

Lys Gly Val Val Gly Lys Val Leu Ala Pro Thr Ala Val Ser Glu Thr
 115 120 125

Val Leu Asn Val His Arg Gly Ile Leu Asn Ile Leu Gln Leu Asn Ile
 130 135 140

Lys Lys Thr Gln Asn Val Tyr Glu Leu Gln Glu Ala Gly Ala Gln Gly
 145 150 155 160

Val Cys Lys Thr His Tyr Val Ile Arg Glu Asp Ala Lys Ala Glu Arg
 165 170 175

Ile His Leu Thr Lys Ser Lys Asp Leu Asn Asn Cys Gln Gln Arg Ile
 180 185 190

Met Lys Asp Phe Gly Leu Ala Tyr Thr Glu Lys Cys Val Glu Cys Arg
 195 200 205

Gln Arg Gly Glu Ala Leu Met Gly Ala Ala Thr Tyr Asn Tyr Leu Met
 210 215 220

Lys Pro Ala Asp Asn Gly Ala Leu Ile Leu Glu Ala Thr Val Thr Glu
 225 230 235 240

Leu His Gln Phe Thr Pro Phe Asn Glu Met Ser Gly Ala Ala Gln Met
 245 250 255

Glu Ala Lys Gln Met Leu Thr Phe Val Glu Ile Lys Lys Asp Pro Ile
 260 265 270
 Ile Val Pro Asp Asn Asn Tyr Val His Arg Gly Ser Ile Arg Tyr Glu
 275 280 285
 Phe Ala Thr Glu Ile Leu Gln Met Pro Ile Gln Leu Leu Lys Ile Ser
 290 295 300
 Asn Ala Arg Ala Gln Ala Val Lys Ile Leu Asn His Leu Val Thr Tyr
 305 310 315 320
 Asn Thr Ala Pro Val His Glu Asp Ala Pro Leu Lys Phe Leu Gln Phe
 325 330 335
 Ile Gln Leu Leu Arg Met Ala Ser Ser Glu Thr Ile Asn Ala Ile Trp
 340 345 350
 Ala Glu Phe Lys Ala Lys Pro Ala Tyr Arg His Trp Ile Leu Asp Ala
 355 360 365
 Val Pro Ser Ile Gly Ser Ser Val Ala Val Arg Phe Ile Lys Glu Lys
 370 375 380
 Phe Leu Ala Gly Asp Ile Thr Ile Phe Glu Ala Ala Gln Ala Leu Val
 385 390 395 400
 Ala Ala Val His Met Val Ala Ala Asp Leu Glu Thr Val Lys Leu Val
 405 410 415
 Glu Ser Leu Ala Phe Asn His Lys Ile Gln Thr His Pro Val Leu Arg
 420 425 430
 Glu Leu Thr Met Leu Gly Tyr Gly Thr Met Val Ser Lys Tyr Cys Val
 435 440 445
 Glu His Pro Asn Cys Pro Ala Glu Leu Val Lys Pro Ile His Glu Leu
 450 455 460
 Ala Val Gln Ala Val Ala Asn Ser Lys Phe Glu Glu Leu Ser Met Val
 465 470 475 480
 Leu Lys Ala Leu Gly Asn Ala Gly His Pro Ala Ser Ile Lys Pro Ile
 485 490 495
 Thr Lys Leu Leu Pro Val Phe Gly Thr Ala Ala Ala Ala Leu Pro Leu
 500 505 510
 Arg Val Gln Ala Asp Ala Val Leu Ala Leu Arg Asn Ile Ala Lys Arg
 515 520 525

Glu Pro Arg Met Val Gln Glu Val Ala Val Gln Leu Phe Met Asp Lys
 530 535 540

Ala Leu His Pro Glu Leu Arg Met Leu Ala Cys Ile Val Leu Phe Glu
 545 550 555 560

Thr Lys Pro Pro Met Gly Leu Val Ile Thr Leu Ala Ser Ile Leu Lys
 565 570 575

Thr Glu Lys Asn Met Gln Val Ala Ser Phe Thr Tyr Ser His Met Met
 580 585 590

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

Cys Asn Val Ala Val Lys Met Leu Ser Asn Lys Phe Arg Arg Leu Ser
 610 615 620

Cys His Phe Ser Gln Ala Ile His Leu Asp Ala Tyr Ser Asn Pro Leu
 625 630 635 640

Arg Ile Gly Ala Ala Ala Ser Ala Phe Tyr Ile Asn Asp Ala Ala Thr
 645 650 655

Leu Phe Pro Arg Thr Val Val Ala Lys Ala Arg Thr Tyr Phe Ala Gly
 660 665 670

Ala Ala Ala Asp Val Leu Glu Val Gly Val Arg Thr Glu Gly Ile Gln
 675 680 685

Glu Ala Leu Leu Lys Leu Pro Pro Ala Pro Glu Asn Ala Asp Arg Ile
 690 695 700

Thr Lys Met Arg Arg Val Ile Lys Ala Leu Ser Asp Trp Arg Ser Leu
 705 710 715 720

Ala Thr Ser Lys Pro Leu Ala Ser Ile Tyr Val Lys Phe Phe Gly Gln
 725 730 735

Glu Ile Ala Phe Ala Asn Ile Asp Lys Ser Ile Ile Asp Gln Ala Leu
 740 745 750

Gln Leu Ala Asn Ser Pro Ser Ala His Ala Leu Gly Arg Asn Ala Leu
 755 760 765

Lys Ala Leu Leu Ala Gly Ala Thr Phe Gln Tyr Val Lys Pro Leu Leu
 770 775 780

Ala Ala Glu Val Arg Arg Ile Phe Pro Thr Ala Val Gly Leu Pro Met
 785 790 795 800

Glu Leu Ser Tyr Tyr Thr Ala Ala Val Ala Lys Ala Tyr Val Asn Val
 805 810 815

Arg Ala Thr Leu Thr Pro Ala Leu Pro Glu Thr Phe His Ala Ala Gln
 820 825 830

Leu Leu Lys Thr Asn Ile Glu Leu His Ala Glu Val Arg Pro Ser Ile
 835 840 845

Val Met His Thr Phe Ala Val Met Gly Val Asn Thr Ala Phe Ile Gln
 850 855 860

Ala Ala Ile Met Ala Arg Ala Lys Val Arg Thr Ile Val Pro Ala Lys
 865 870 875 880

Phe Ala Ala Gln Leu Asp Ile Ala Asn Gly Asn Phe Lys Phe Glu Ala
 885 890 895

Phe Pro Val Ser Pro Pro Glu His Ile Ala Ala Ala His Ile Glu Thr
 900 905 910

Phe Ala Val Ala Arg Asn Val Glu Asp Val Pro Ala Glu Arg Ile Thr
 915 920 925

Pro Leu Ile Pro Ala Gln Gly Val Ala Arg Ser Thr Gln Gln Ser Arg
 930 935 940

Asp Lys Leu Thr Ser Met Ile Ala Asp Ser Ala Ala Ser Phe Ala Gly
 945 950 955 960

Ser Leu Ser Arg Ser Ser Glu Ile Leu Tyr Ser Asp Leu Pro Ser Asn
 965 970 975

Phe Lys Pro Ile Ile Lys Ala Ile Val Val His Leu Glu Glu Thr Ile
 980 985 990

Cys Val Glu Arg Leu Gly Val Lys Ala Cys Phe Glu Phe Thr Ser Glu
 995 1000 1005

Ser Ala Ala Phe Ile Arg Asn Thr Leu Phe Tyr Asn Met Ile Gly
 1010 1015 1020

Lys His Ser Val Leu Ile Ser Val Lys Pro Ser Ala Ser Glu Pro
 1025 1030 1035

Ala Ile Glu Arg Leu Glu Phe Glu Val Gln Val Gly Pro Lys Ala
 1040 1045 1050

Ala Glu Lys Ile Ile Lys Val Ile Thr Met Asn Glu Glu Glu Glu
 1055 1060 1065

Ala Pro Glu Gly Lys Thr Val Leu Leu Lys Leu Lys Lys Ile Leu
 1070 1075 1080

Leu	Pro	Asp	Leu	Lys	Asn	Gly	Thr	Arg	Ala	Ser	Ser	Ser	Ser	Ser
1085						1090					1095			
Ser	Ser	Ser	Ser	Ser	Ser	Ser	Arg	Ser	Ser	Ser	Ser	Arg	Ser	Arg
1100						1105					1110			
Ser	Arg	Lys	Ser	Glu	Ser	Ser	Ser	Ser	Ser	Ser	Ser	Ser	Ser	Ser
1115						1120					1125			
Arg	Ile	Ser	Lys	Arg	Asp	Gly	Pro	Asp	Gln	Pro	Tyr	Asn	Pro	Asn
1130						1135					1140			
Asp	Arg	Lys	Phe	Lys	Lys	Asn	His	Lys	Asp	Ser	Gln	Ser	Thr	Ser
1145						1150					1155			
Asn	Val	Ile	Ser	Arg	Ser	Lys	Ser	Ser	Ala	Ser	Ser	Phe	His	Ala
1160						1165					1170			
Ile	Tyr	Lys	Gln	Asp	Lys	Phe	Leu	Gly	Asn	Lys	Leu	Ala	Pro	Met
1175						1180					1185			
Val	Ile	Ile	Leu	Phe	Arg	Leu	Val	Arg	Ala	Asp	His	Lys	Ile	Glu
1190						1195					1200			
Gly	Tyr	Gln	Val	Thr	Ala	Tyr	Leu	Asn	Lys	Ala	Thr	Ser	Arg	Leu
1205						1210					1215			
Gln	Ile	Ile	Met	Ala	Ala	Leu	Asp	Glu	Asn	Asp	Asn	Trp	Lys	Leu
1220						1225					1230			
Cys	Ala	Asp	Gly	Val	Leu	Leu	Ser	Lys	His	Lys	Val	Thr	Ala	Lys
1235						1240					1245			
Ile	Ala	Trp	Gly	Ala	Glu	Cys	Lys	Asp	Tyr	Asn	Thr	Phe	Ile	Thr
1250						1255					1260			
Ala	Glu	Thr	Gly	Leu	Val	Gly	Pro	Ser	Pro	Ala	Val	Arg	Leu	Arg
1265						1270					1275			
Leu	Ser	Trp	Asp	Lys	Leu	Pro	Lys	Val	Pro	Lys	Ala	Val	Trp	Arg
1280						1285					1290			
Tyr	Val	Arg	Ile	Val	Ser	Glu	Phe	Ile	Pro	Gly	Tyr	Ile	Pro	Tyr
1295						1300					1305			
Tyr	Leu	Ala	Asp	Leu	Val	Pro	Met	Gln	Lys	Asp	Lys	Asn	Asn	Glu
1310						1315					1320			
Lys	Gln	Ile	Gln	Phe	Thr	Val	Val	Ala	Thr	Ser	Glu	Arg	Thr	Leu
1325						1330					1335			
Asp	Val	Ile	Leu	Lys	Thr	Pro	Lys	Met	Thr	Leu	Tyr	Lys	Leu	Gly
1340						1345					1350			

Val Asn Leu Pro Cys Ser Leu Pro Phe Glu Ser Met Thr Asp Leu
 1355 1360 1365
 Ser Pro Phe Asp Asp Asn Ile Val Asn Lys Ile His Tyr Leu Phe
 1370 1375 1380
 Ser Glu Val Asn Ala Val Lys Cys Ser Met Val Arg Asp Thr Leu
 1385 1390 1395
 Thr Thr Phe Asn Asn Lys Lys Tyr Lys Ile Asn Met Pro Leu Ser
 1400 1405 1410
 Cys Tyr Gln Val Leu Ala Gln Asp Cys Thr Thr Glu Leu Lys Phe
 1415 1420 1425
 Met Val Leu Leu Lys Lys Asp His Ala Ser Glu Gln Asn His Ile
 1430 1435 1440
 Asn Val Lys Ile Ser Asp Ile Asp Val Asp Leu Tyr Thr Glu Asp
 1445 1450 1455
 His Gly Val Ile Val Lys Val Asn Glu Met Glu Ile Ser Asn Asp
 1460 1465 1470
 Asn Leu Pro Tyr Lys Asp Pro Ser Gly Ser Ile Lys Ile Asp Arg
 1475 1480 1485
 Lys Gly Lys Gly Val Ser Leu Tyr Ala Pro Ser His Gly Leu Gln
 1490 1495 1500
 Glu Val Tyr Phe Asp Lys Tyr Ser Trp Lys Ile Lys Val Val Asp
 1505 1510 1515
 Trp Met Lys Gly Gln Thr Cys Gly Leu Cys Gly Lys Ala Asp Gly
 1520 1525 1530
 Glu Asn Arg Gln Glu Tyr Arg Thr Pro Ser Gly Arg Leu Thr Lys
 1535 1540 1545
 Ser Ser Val Ser Phe Ala His Ser Trp Val Leu Pro Ser Asp Ser
 1550 1555 1560
 Cys Arg Asp Ala Ser Glu Cys Leu Met Lys Leu Glu Ser Val Lys
 1565 1570 1575
 Leu Glu Lys Gln Val Ile Val Asp Asp Arg Glu Ser Lys Cys Tyr
 1580 1585 1590
 Ser Val Glu Pro Val Leu Arg Cys Leu Pro Gly Cys Leu Pro Val
 1595 1600 1605

Arg Thr Thr Pro Ile Thr Ile Gly Phe His Cys Leu Pro Val Asp
1610 1615 1620

Ser Asn Leu Asn Arg Ser Glu Gly Leu Ser Ser Ile Tyr Glu Lys
1625 1630 1635

Ser Val Asp Leu Met Glu Lys Ala Glu Ala His Val Ala Cys Arg
1640 1645 1650

Cys Ser Glu Gln Cys Met
1655

<210> 16
<211> 1704
<212> PRT
<213> Fundulus heteroclitus

<400> 16

Met Lys Ala Val Val Leu Ala Leu Thr Leu Ala Phe Val Ala Gly Gln
1 5 10 15

Asn Phe Ala Pro Glu Phe Ala Ala Gly Lys Thr Tyr Val Tyr Lys Tyr
20 25 30

Glu Ala Leu Ile Leu Gly Gly Leu Pro Glu Glu Gly Leu Ala Arg Ala
35 40 45

Gly Leu Lys Ile Ser Thr Lys Leu Leu Leu Ser Ala Ala Asp Gln Asn
50 55 60

Thr Tyr Met Leu Lys Leu Val Glu Pro Glu Leu Ser Glu Tyr Ser Gly
65 70 75 80

Ile Trp Pro Lys Asp Pro Ala Val Pro Ala Thr Lys Leu Thr Ala Ala
85 90 95

Leu His Leu Ser Ser Gln Phe Pro Ser Ser Leu Asn Thr Pro Met Val
100 105 110

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

Asn Ile Tyr Arg Gly Ile Leu Asn Ile Leu Gln Leu Asn Ile Lys Lys
130 135 140

Thr His Lys Val Tyr Asp Leu Gln Glu Val Gly Thr Gln Gly Val Cys
145 150 155 160

Lys Thr Leu Tyr Ser Ile Ser Glu Asp Ala Arg Ile Glu Asn Ile Leu
165 170 175

Leu Thr Lys Thr Arg Asp Leu Ser Asn Cys Gln Glu Arg Leu Asn Lys
180 185 190

Asp Ile Gly Leu Ala Tyr Thr Glu Lys Cys Asp Lys Cys Gln Glu Glu
 195 200 205
 Thr Lys Asn Leu Arg Gly Thr Thr Thr Leu Ser Tyr Val Leu Lys Pro
 210 215 220
 Val Ala Asp Ala Val Met Ile Leu Lys Ala Tyr Val Asn Glu Leu Ile
 225 230 235 240
 Gln Phe Ser Pro Phe Ser Glu Ala Asn Gly Ala Ala Gln Met Arg Thr
 245 250 255
 Lys Gln Ser Leu Glu Phe Leu Glu Ile Glu Lys Glu Pro Ile Pro Ser
 260 265 270
 Val Lys Ala Glu Tyr Arg His Arg Gly Ser Leu Lys Tyr Glu Phe Ser
 275 280 285
 Asp Glu Leu Leu Gln Thr Pro Leu Gln Leu Ile Lys Ile Ser Asp Ala
 290 295 300
 Pro Ala Gln Val Ala Glu Val Leu Lys His Leu Ala Thr Tyr Asn Ile
 305 310 315 320
 Glu Asp Val His Glu Asn Ala Pro Leu Lys Phe Leu Glu Leu Val Gln
 325 330 335
 Leu Leu Arg Ile Ala Arg Tyr Glu Asp Leu Glu Met Tyr Trp Asn Gln
 340 345 350
 Tyr Lys Lys Met Ser Pro His Arg His Trp Phe Leu Asp Thr Ile Pro
 355 360 365
 Ala Thr Gly Thr Phe Ala Gly Leu Arg Phe Ile Lys Glu Lys Phe Met
 370 375 380
 Ala Glu Glu Ile Thr Ile Ala Glu Ala Ala Gln Ala Phe Ile Thr Ala
 385 390 395 400
 Val His Met Val Thr Ala Asp Pro Glu Val Ile Lys Leu Phe Glu Ser
 405 410 415
 Leu Val Asp Ser Asp Lys Val Val Glu Asn Pro Leu Leu Arg Glu Val
 420 425 430
 Val Phe Leu Gly Tyr Gly Thr Met Val Asn Lys Tyr Cys Asn Lys Thr
 435 440 445
 Val Asp Cys Pro Val Glu Leu Ile Lys Pro Ile Gln Gln Arg Leu Ser
 450 455 460
 Asp Ala Ile Ala Lys Asn Glu Glu Glu Asn Ile Ile Leu Tyr Ile Lys

104

Gly Lys Glu Leu Pro Ile Gln Glu Tyr Gly Arg Glu Ala Leu Lys Ala
 755 760 765

Leu Leu Leu Ser Gly Ile Asn Phe His Tyr Ala Lys Pro Val Leu Ala
 770 775 780

Ala Glu Met Arg Arg Ile Leu Pro Thr Val Ala Gly Ile Pro Met Glu
 785 790 795 800

Leu Ser Leu Tyr Ser Ala Ala Val Ala Ala Ser Val Glu Ile Lys
 805 810 815

Pro Asn Thr Ser Pro Arg Leu Ser Ala Asp Phe Asp Val Lys Thr Leu
 820 825 830

Leu Glu Thr Asp Val Glu Leu Lys Ala Glu Ile Arg Pro Met Val Ala
 835 840 845

Met Asp Thr Tyr Ala Val Met Gly Leu Asn Thr Asp Ile Phe Gln Ala
 850 855 860

Ala Leu Val Ala Arg Ala Lys Leu His Ser Val Val Pro Ala Lys Ile
 865 870 875 880

Ala Ala Arg Leu Asn Ile Lys Glu Gly Asp Phe Lys Leu Glu Ala Leu
 885 890 895

Pro Val Asp Val Pro Glu Asn Ile Thr Ser Met Asn Val Thr Thr Phe
 900 905 910

Ala Val Ala Arg Asn Ile Glu Glu Pro Leu Val Glu Arg Ile Thr Pro
 915 920 925

Leu Leu Pro Thr Lys Val Leu Val Pro Ile Pro Ile Arg Arg His Thr
 930 935 940

Ser Lys Leu Asp Pro Thr Arg Asn Ser Met Leu Asp Ser Ser Glu Leu
 945 950 955 960

Leu Pro Met Glu Glu Glu Asp Val Glu Pro Ile Pro Glu Tyr Lys Phe
 965 970 975

Arg Arg Phe Ala Lys Lys Tyr Cys Ala Lys His Ile Gly Val Gly Leu
 980 985 990

Lys Ala Cys Phe Lys Phe Ala Ser Gln Asn Gly Ala Ser Ile Gln Asp
 995 1000 1005

Ile Val Leu Tyr Lys Leu Ala Gly Ser His Asn Phe Ser Phe Ser
 1010 1015 1020

Val Thr Pro Ile Glu Gly Glu Val Val Glu Arg Leu Glu Met Glu

1025		1030		1035
Val Lys 1040	Val Gly Ala Lys 1045	Ala Glu Lys Leu 1050	Val Lys Arg Ile 1055	
Asn Leu 1055	Ser Glu Asp Glu 1060	Thr Glu Glu Gly 1065	Pro Val Leu 1070	
Val Lys 1070	Leu Asn Lys Ile 1075	Ser Ser Arg Arg 1080	Asn Ser Ser Ser 1085	
Ser Ser 1085	Ser Ser Ser Ser 1090	Ser Ser Ser Glu 1095	Arg Ser Ser 1100	
Arg Ser 1100	Ser Ser Ser Ser 1105	Ser Ser Ser Arg 1110	Ser Arg Lys 1115	
Ile Asp 1115	Leu Ala Ala Arg 1120	Asn Ser Ser Ser 1125	Ser Ser Ser 1130	
Arg Arg 1130	Ser Arg Ser Ser 1135	Ser Ser Ser Ser 1140	Ser Ser Ser 1145	
Ser Ser 1145	Ser Ser Ser Ser 1150	Ser Ser Arg Arg 1155	Ser Ser Ser 1160	
Ser Ser 1160	Ser Ser Ser Ser 1165	Ser Ser Arg Ser 1170	Arg Arg Val 1175	
Asn Ser 1175	Thr Arg Ser Ser 1180	Ser Ser Ser Arg 1185	Thr Ser Ser Ala 1190	
Ser Ser 1190	Leu Ala Ser Phe 1195	Ser Asp Ser Ser 1200	Ser Ser Ser 1205	
Ser Ser 1205	Asp Arg Arg Ser 1210	Lys Glu Val Met Glu 1215	Lys Phe Gln Arg 1220	
Leu His 1220	Lys Lys Met Val 1225	Ser Gly Ser Ser 1230	Ser Ser Val 1235	
Glu Ala 1235	Ile Tyr Lys Glu 1240	Lys Tyr Leu Gly 1245	Glu Glu Ala 1250	
Val Val 1250	Ala Val Ile Leu 1255	Ala Val Lys Ala 1260	Asp Lys Arg Met 1265	
Val Gly 1265	Tyr Gln Leu Gly 1270	Phe Tyr Leu Asp Lys 1275	Pro Asn Ala Arg 1280	
Val Gln 1280	Ile Ile Val Ala 1285	Asn Ile Ser Ser Asp 1290	Ser Asn Trp Arg 1295	

Ile Cys Ala Asp Ala Val Val Leu Ser Lys His Lys Val Thr Thr
 1295 1300 1305
 Lys Ile Ser Trp Gly Glu Gln Cys Arg Lys Tyr Ser Thr Asn Val
 1310 1315 1320
 Thr Gly Glu Thr Gly Ile Val Ser Ser Ser Pro Ala Ala Arg Leu
 1325 1330 1335
 Arg Val Ser Trp Glu Arg Leu Pro Ser Thr Leu Lys Arg Tyr Gly
 1340 1345 1350
 Lys Met Val Asn Lys Tyr Val Pro Val Lys Ile Leu Ser Asp Leu
 1355 1360 1365
 Ile His Thr Lys Arg Glu Asn Ser Thr Arg Asn Ile Ser Val Ile
 1370 1375 1380
 Ala Val Ala Thr Ser Glu Lys Thr Ile Asp Ile Ile Thr Lys Thr
 1385 1390 1395
 Pro Met Ser Ser Val Tyr Asn Val Thr Met His Leu Pro Met Cys
 1400 1405 1410
 Ile Pro Ile Asp Glu Ile Lys Gly Leu Ser Pro Phe Asp Glu Val
 1415 1420 1425
 Ile Asp Lys Ile His Phe Met Val Ser Lys Ala Ala Ala Ala Glu
 1430 1435 1440
 Cys Ser Phe Val Glu Asp Thr Leu Tyr Thr Phe Asn Asn Arg Ser
 1445 1450 1455
 Tyr Lys Asn Lys Met Pro Ser Ser Cys Tyr Gln Val Ala Ala Gln
 1460 1465 1470
 Asp Cys Thr Asp Glu Leu Lys Phe Met Val Leu Leu Arg Lys Asp
 1475 1480 1485
 Ser Ser Glu Gln His His Ile Asn Val Lys Ile Ser Glu Ile Asp
 1490 1495 1500
 Ile Asp Met Phe Pro Lys Asp Asp Asn Val Thr Val Lys Val Asn
 1505 1510 1515
 Glu Met Glu Ile Pro Pro Pro Ala Cys Leu Thr Ala Thr Gln Gln
 1520 1525 1530
 Leu Pro Leu Lys Ile Lys Thr Lys Arg Arg Gly Leu Ala Val Tyr
 1535 1540 1545
 Ala Pro Ser His Gly Leu Gln Glu Val Tyr Phe Asp Arg Lys Thr

1550 1555 1560
 Trp Arg Ile Lys Val Ala Asp Trp Met Lys Gly Lys Thr Cys Gly
 1565 1570 1575
 Leu Cys Gly Lys Ala Asp Gly Glu Ile Arg Gln Glu Tyr His Thr
 1580 1585 1590
 Pro Asn Gly Arg Val Ala Lys Asn Ser Ile Ser Phe Ala His Ser
 1595 1600 1605
 Trp Ile Leu Pro Ala Glu Ser Cys Arg Asp Ala Ser Glu Cys Arg
 1610 1615 1620
 Leu Lys Leu Glu Ser Val Gln Leu Glu Lys Gln Leu Thr Ile His
 1625 1630 1635
 Gly Glu Asp Ser Thr Cys Phe Ser Val Glu Pro Val Pro Arg Cys
 1640 1645 1650
 Leu Pro Gly Cys Leu Pro Val Lys Thr Thr Pro Val Thr Val Gly
 1655 1660 1665
 Phe Ser Cys Leu Ala Ser Asp Pro Gln Thr Ser Val Tyr Asp Arg
 1670 1675 1680
 Ser Val Asp Leu Arg Gln Thr Thr Gln Ala His Leu Ala Cys Ser
 1685 1690 1695
 Cys Asn Thr Lys Cys Ser
 1700
 <210> 17
 <211> 1677
 <212> PRT
 <213> Acipenser transmontanus
 <400> 17
 Leu Thr Ile Ala Leu Val Gly Ser Gln Gln Thr Lys Tyr Glu Pro Ser
 1 5 10 15
 Phe Ser Gly Ser Lys Thr Tyr Gln Tyr Lys Tyr Glu Gly Val Ile Leu
 20 25 30
 Thr Gly Leu Pro Glu Lys Gly Leu Ala Arg Ala Gly Leu Lys Val His
 35 40 45
 Cys Lys Val Glu Ile Ser Glu Val Ala Gln Lys Thr Tyr Leu Leu Lys
 50 55 60
 Ile Leu Asn Pro Glu Ile Gln Glu Tyr Asn Gly Ile Trp Pro Lys Ala
 65 70 75 80

Pro Phe Tyr Pro Ala Ser Lys Leu Thr Gln Ala Leu Ala Ser Gln Leu
 85 90 95

Thr Gln Pro Ile Lys Phe Gln Tyr Arg Asn Gly Gln Val Gly Asp Ile
 100 105 110

Phe Ala Ser Glu Asp Val Ser Asp Thr Val Leu Asn Ile Gln Arg Gly
 115 120 125

Ile Leu Asn Met Leu Gln Leu Thr Ile Lys Thr Thr Gln Asn Val Tyr
 130 135 140

Gly Leu Gln Glu Asn Gly Ile Ala Gly Ile Cys Glu Ala Ser Tyr Val
 145 150 155 160

Ile Gln Glu Asp Arg Lys Ala Asn Lys Ile Ile Val Thr Lys Ser Lys
 165 170 175

Asp Leu Asn Asn Cys Asn Glu Lys Ile Lys Met Asp Ile Gly Met Ala
 180 185 190

Tyr Ser His Thr Cys Ser Asn Cys Arg Lys Ile Arg Lys Asn Thr Arg
 195 200 205

Gly Thr Ala Ala Tyr Thr Tyr Ile Leu Lys Pro Thr Asp Thr Gly Thr
 210 215 220

Leu Ile Thr Gln Ala Thr Ser Gln Glu Val His Gln Leu Thr Pro Phe
 225 230 235 240

Asn Glu Met Thr Gly Ala Ala Ile Thr Glu Ala Arg Gln Lys Leu Val
 245 250 255

Leu Glu Asp Ala Lys Val Ile His Val Thr Val Pro Glu Gln Glu Leu
 260 265 270

Lys Asn Arg Gly Ser Ile Gln Tyr Gln Phe Ala Ser Glu Ile Leu Gln
 275 280 285

Thr Pro Ile Gln Leu Phe Lys Thr Arg Ser Pro Glu Thr Lys Ile Lys
 290 295 300

Glu Val Leu Gln His Leu Val Gln Asn Asn Gln Gln Gln Val Gln Ser
 305 310 315 320

Asp Ala Pro Ser Lys Phe Leu Gln Leu Thr Gln Leu Leu Arg Ala Cys
 325 330 335

Thr His Glu Asn Ile Glu Gly Ile Trp Arg Gln Tyr Glu Lys Thr Gln
 340 345 350

Leu Tyr Arg Arg Trp Ile Leu Asp Ala Leu Pro Ala Ala Ala Thr Pro
 355 360 365

Thr Ala Phe Arg Phe Ile Thr Gln Arg Ile Met Lys Arg Asp Leu Thr
370 375 380

Asp Ala Glu Ala Ile Gln Thr Leu Val Thr Ala Met His Leu Val Gln
385 390 395 400

Thr Asn His Gln Ile Val Gln Met Ala Ala Glu Leu Val Phe Asp Arg
405 410 415

Ala Asn Leu Lys Cys Pro Val Leu Arg Lys His Ala Val Leu Ala Tyr
420 425 430

Gly Ser Met Val Asn Arg Tyr Cys Ala Glu Thr Leu Asn Cys Arg Glu
435 440 445

Glu Ala Leu Lys Pro Leu His Asp Phe Ala Asn Asp Ala Ile Ser Arg
450 455 460

Ala His Glu Glu Glu Thr Val Leu Ala Leu Lys Ala Leu Gly Asn Ala
465 470 475 480

Gly Gln Pro Ser Ser Ile Lys Arg Ile Gln Lys Cys Leu Pro Gly Phe
485 490 495

Ser Ser Gly Ala Ser Gln Leu Pro Val Lys Ile Gln Val Asp Ala Val
500 505 510

Met Ala Leu Arg Asn Ile Ala Lys Lys Glu Pro Gly Lys Val Gln Glu
515 520 525

Leu Thr Met Gln Leu Phe Met Asp His Gln Leu His Ser Glu Val Arg
530 535 540

Met Val Ala Ser Met Val Leu Leu Glu Thr Arg Pro Ser Met Ala Leu
545 550 555 560

Val Ala Thr Leu Ala Glu Ala Leu Leu Lys Glu Thr Ser Leu Gln Val
565 570 575

Ala Ser Phe Thr Tyr Ser His Met Lys Ala Ile Thr Arg Ser Thr Ala
580 585 590

Pro Glu Asn His Ala Leu Ser Ser Ala Cys Asn Val Ala Val Lys Leu
595 600 605

Leu Ser Arg Lys Leu Asp Arg Leu Ser Tyr Arg Tyr Ser Lys Ala Met
610 615 620

His Met Asp Thr Phe Lys Tyr Pro Leu Met Ala Gly Ala Ala Ala Asn
625 630 635 640

Ile His Ile Ile Asn Asn Ala Ala Ser Ile Leu Pro Ser Ala Val Val
 645 650 655

Met Lys Phe Gln Ala Tyr Ile Leu Ser Ala Thr Ala Asp Pro Leu Glu
 660 665 670

Ile Gly Leu His Thr Glu Gly Leu Gln Glu Val Leu Met Gln Asn His
 675 680 685

Glu His Ile Asp Gln Met Pro Ser Ala Gly Lys Ile Gln Gln Ile Met
 690 695 700

Lys Met Leu Ser Gly Trp Lys Ser Val Pro Ser Glu Lys Thr Leu Ala
 705 710 715 720

Ser Ala Tyr Ile Lys Leu Phe Gly Gln Glu Ile Ser Phe Ser Arg Leu
 725 730 735

Asp Lys Lys Thr Ile Gln Glu Ala Leu Gln Ala Val Arg Glu Pro Val
 740 745 750

Glu Arg Gln Thr Val Ile Lys Arg Val Val Asn Gln Leu Glu Arg Gly
 755 760 765

Ala Ala Ala Gln Leu Ser Lys Pro Leu Leu Val Ala Glu Val Arg Arg
 770 775 780

Ile Leu Pro Thr Cys Ile Gly Leu Pro Met Glu Met Ser Leu Tyr Val
 785 790 795 800

Ser Ala Val Thr Thr Ala Asp Ile Asn Val Gln Ala His Ile Thr Pro
 805 810 815

Ser Pro Thr Asn Asp Phe Asn Val Ala Gln Leu Leu Asn Ser Asn Ile
 820 825 830

Val Leu His Thr Asp Val Thr Pro Ser Ile Ala Met His Thr Ile Ala
 835 840 845

Val Met Gly Ile Asn Thr His Val Ile Gln Thr Gly Val Glu Leu His
 850 855 860

Val Lys Ala Arg Thr Thr Val Pro Met Lys Phe Thr Ala Lys Ile Asp
 865 870 875 880

Leu Lys Glu Lys Asn Phe Lys Ile Glu Ser Glu Pro Cys Gln Gln Glu
 885 890 895

Thr Glu Val Leu Ser Leu Ser Ala Gln Ala Phe Ala Ile Ser Arg Asn
 900 905 910

Val Glu Asp Leu Asp Ala Ala Lys Lys Asn Pro Leu Leu Pro Glu Glu
 915 920 925

Ala Val Arg Asn Ile Leu Asn Glu Gln Phe Asn Ser Gly Thr Glu Asp
 930 935 940

Ser Asn Glu Arg Glu Arg Ala Gly Lys Phe Ala Arg Pro Ser Ala Glu
 945 950 955 960

Met Met Ser Gln Glu Leu Met Asn Ser Gly Glu His Gln Asn Arg Lys
 965 970 975

Gly Ala His Ala Thr Arg Ser Ala Cys Ala Lys Ala Lys Asn Phe Gly
 980 985 990

Phe Glu Val Cys Phe Glu Gly Lys Ser Glu Asn Val Ala Phe Leu Arg
 995 1000 1005

Asp Ser Pro Leu Tyr Lys Ile Ile Gly Gln His His Cys Lys Ile
 1010 1015 1020

Ala Leu Lys Pro Ser His Ser Ser Glu Ala Thr Ile Glu Lys Ile
 1025 1030 1035

Gln Leu Glu Leu Gln Thr Gly Asn Lys Ala Ala Ser Lys Ile Ile
 1040 1045 1050

Arg Val Val Ala Met Gln Ser Leu Ala Glu Ala Asp Glu Met Lys
 1055 1060 1065

Gly Asn Ile Leu Lys Lys Leu Asn Lys Leu Leu Thr Val Asp Gly
 1070 1075 1080

Glu Thr Gln Asp Ser Thr Leu Arg Gly Phe Lys Arg Arg Ser Ser
 1085 1090 1095

Ser Ser Ser Ser Ser Ser Ser Ser Ser Ser Ser Ser Ser Ser
 1100 1105 1110

Ser Ser Ser Ser Ser Ser Gln Gln Ser Arg Met Glu Lys Arg Met
 1115 1120 1125

Glu Gln Asp Lys Leu Thr Glu Asn Leu Glu Arg Asp Arg Asp His
 1130 1135 1140

Met Arg Gly Lys Gln Ser Lys Asn Lys Lys Gln Glu Trp Lys Asn
 1145 1150 1155

Lys Gln Lys Lys His His Lys Gln Leu Pro Ser Ser Ser Ser Ser
 1160 1165 1170

Ser Ser Ser Ser Ser Ser Gly Ser Asn Ser Ser Ser Ser Ser Ser
 1175 1180 1185

Ser Ser Ser Ser Ser Ser Arg Ser His Asn His Arg Asn Asn
 1190 1195 1200
 Thr Arg Thr Leu Ser Lys Ser Lys Arg Tyr Gln Asn Asn Asn Asn
 1205 1210 1215
 Ser Ser Ser Ser Ser Gly Ser Ser Ser Ser Ser Glu Glu Ile Gln
 1220 1225 1230
 Lys Asn Pro Glu Ile Phe Ala Tyr Arg Phe Arg Ser His Arg Asp
 1235 1240 1245
 Lys Leu Gly Phe Gln Asn Lys Arg Gly Arg Met Ser Ser Ser Ser
 1250 1255 1260
 Ser Ser Ser Ser Ser Ser Ser Gln Ser Thr Leu Asn Ser Lys
 1265 1270 1275
 Gln Asp Ala Lys Phe Leu Gly Asp Ser Ser Pro Pro Ile Phe Ala
 1280 1285 1290
 Phe Val Ala Arg Ala Val Arg Ser Asp Gly Leu Gln Gln Gly Tyr
 1295 1300 1305
 Gln Val Ala Ala Tyr Thr Asp Asn Arg Val Ser Arg Pro Arg Val
 1310 1315 1320
 Gln Leu Leu Ala Thr Glu Ile Ile Glu Lys Ser Arg Trp Gln Ile
 1325 1330 1335
 Cys Ala Asp Ala Ile Leu Ala Ser Asn Tyr Lys Ala Met Ala Leu
 1340 1345 1350
 Met Arg Trp Gly Glu Glu Cys Gln Asp Tyr Lys Val Ala Val Ser
 1355 1360 1365
 Ala Val Thr Gly Arg Leu Ala Ser His Pro Ser Leu Gln Ile Lys
 1370 1375 1380
 Ala Lys Trp Ser Arg Ile Pro Arg Ala Ala Lys Gln Thr Gln Asn
 1385 1390 1395
 Ile Leu Ala Glu Tyr Val Pro Gly Ala Ala Phe Met Leu Gly Phe
 1400 1405 1410
 Ser Gln Lys Glu Gln Arg Asn Pro Ser Lys Gln Phe Lys Ile Ile
 1415 1420 1425
 Leu Ala Val Thr Ser Pro Asn Thr Ile Asp Thr Leu Ile Lys Ala
 1430 1435 1440
 Pro Lys Ile Thr Leu Phe Lys Gln Ala Val Gln Ile Pro Val Gln
 1445 1450 1455

Ile Pro Met Glu Pro Ser Asp Ala Glu Arg Arg Ser Pro Gly Leu
1460 1465 1470

Ala Ser Ile Met Asn Glu Ile Pro Phe Leu Ile Glu Glu Ala Thr
1475 1480 1485

Lys Ser Lys Cys Val Ala Gln Glu Asn Lys Phe Ile Thr Phe Asp
1490 1495 1500

Gly Val Lys Phe Ser Tyr Gln Met Pro Gly Gly Cys Tyr His Ile
1505 1510 1515

Leu Ala Gln Asp Cys Arg Ser Lys Val Arg Phe Met Val Met Leu
1520 1525 1530

Lys Gln Ala Ser Met Ser Lys Asn Leu Arg Ala Val Asn Ala Lys
1535 1540 1545

Ile Tyr Asn Lys Asp Ile Asp Ile Leu Pro Thr Thr Lys Gly Ser
1550 1555 1560

Val Arg Leu Leu Ile Asn Asn Asn Glu Ile Pro Leu Ser Gln Leu
1565 1570 1575

Pro Phe Thr Asp Ser Ser Gly Asn Ile His Ile Lys Arg Ala Asp
1580 1585 1590

Glu Gly Val Ser Val Ser Ala Gln Gln Tyr Gly Leu Glu Ser Leu
1595 1600 1605

Tyr Phe Asp Gly Lys Thr Val Gln Val Lys Val Thr Ser Glu Met
1610 1615 1620

Arg Gly Lys Thr Cys Gly Leu Cys Gly His Asn Asp Gly Glu Arg
1625 1630 1635

Arg Lys Glu Phe Arg Met Pro Asp Gly Arg Gln Ala Arg Gly Pro
1640 1645 1650

Ser Val Ser Pro Thr Pro Gly Leu Cys Leu Glu Lys Thr Ala Thr
1655 1660 1665

Glu Ala Ala Ser Phe Cys Val Ile Met
1670 1675

<210> 18
<211> 1807
<212> PRT
<213> *Xenopus laevis*

<400> 18

Met Lys Gly Ile Val Leu Ala Leu Leu Leu Ala Leu Ala Gly Ser Glu

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Arg Thr His Ile Glu Pro Val Phe Ser Glu Ser Lys Ile Ser Val Tyr	20	25	30
Asn Tyr Glu Ala Val Ile Leu Asn Gly Phe Pro Glu Ser Gly Leu Ser	35	40	45
Arg Ala Gly Ile Lys Ile Asn Cys Lys Val Glu Ile Ser Ala Tyr Ala	50	55	60
Gln Arg Ser Tyr Phe Leu Lys Ile Gln Ser Pro Glu Ile Lys Glu Tyr	65	70	75
Asn Gly Val Trp Pro Lys Asp Pro Phe Thr Arg Ser Ser Lys Leu Thr	85	90	95
Gln Ala Leu Ala Glu Gln Leu Thr Lys Pro Ala Arg Phe Glu Tyr Ser	100	105	110
Asn Gly Arg Val Gly Asp Ile Phe Val Ala Asp Asp Val Ser Asp Thr	115	120	125
Val Ala Asn Ile Tyr Arg Gly Ile Leu Asn Leu Leu Gln Val Thr Ile	130	135	140
Lys Lys Ser Gln Asp Val Tyr Asp Leu Gln Glu Ser Ser Val Gly Gly	145	150	155
Ile Cys His Thr Arg Tyr Val Ile Gln Glu Asp Lys Arg Gly Asp Gln	165	170	175
Ile Arg Ile Ile Lys Ser Thr Asp Phe Asn Asn Cys Gln Asp Lys Val	180	185	190
Ser Lys Thr Ile Gly Leu Glu Leu Ala Glu Phe Cys His Ser Cys Lys	195	200	205
Gln Leu Asn Arg Val Ile Gln Gly Ala Ala Thr Tyr Thr Tyr Lys Leu	210	215	220
Lys Gly Arg Asp Gln Gly Thr Val Ile Met Glu Val Thr Ala Arg Gln	225	230	235
Val Leu Gln Val Thr Pro Phe Ala Glu Arg His Gly Ala Ala Thr Met	245	250	255
Glu Ser Arg Gln Val Leu Ala Trp Val Gly Ser Lys Ser Gly Gln Leu	260	265	270
Thr Pro Pro Gln Ile Gln Leu Lys Asn Arg Gly Asn Leu His Tyr Gln	275	280	285

Phe Ala Ser Glu Leu His Gln Met Pro Ile His Leu Met Lys Thr Lys
 290 295 300

Ser Pro Glu Ala Gln Ala Val Glu Val Leu Gln His Leu Val Gln Asp
 305 310 315 320

Thr Gln Gln His Ile Arg Glu Asp Ala Pro Ala Lys Phe Leu Gln Leu
 325 330 335

Val Gln Leu Leu Arg Ala Ser Asn Phe Glu Asn Leu Gln Ala Leu Trp
 340 345 350

Lys Gln Phe Ala Gln Arg Thr Gln Tyr Arg Arg Cys Leu Leu Asp Ala
 355 360 365

Leu Pro Met Ala Gly Thr Val Asp Cys Leu Lys Phe Ile Lys Gln Leu
 370 375 380

Ile His Asn Glu Glu Leu Thr Thr Gln Glu Ala Ala Val Leu Ile Thr
 385 390 395 400

Phe Ala Met Arg Ser Ala Arg Pro Gly Gln Arg Asn Phe Gln Ile Ser
 405 410 415

Ala Asp Leu Val Gln Asp Ser Lys Val Gln Lys Tyr Ser Thr Val His
 420 425 430

Lys Ala Ala Ile Leu Ala Tyr Gly Thr Met Val Arg Arg Tyr Cys Asp
 435 440 445

Gln Leu Ser Ser Cys Pro Glu His Ala Leu Glu Pro Leu His Glu Leu
 450 455 460

Ala Ala Glu Ala Ala Asn Lys Gly His Tyr Glu Asp Ile Ala Leu Ala
 465 470 475 480

Leu Lys Ala Leu Gly Asn Ala Gly Gln Pro Glu Ser Ile Lys Arg Ile
 485 490 495

Gln Lys Phe Leu Pro Gly Phe Ser Ser Ser Ala Asp Gln Leu Pro Val
 500 505 510

Arg Ile Gln Thr Asp Ala Val Met Ala Leu Arg Asn Ile Ala Lys Glu
 515 520 525

Asp Pro Arg Lys Val Gln Glu Ile Leu Leu Gln Ile Phe Met Asp Arg
 530 535 540

Asp Val Arg Thr Glu Val Arg Met Met Ala Cys Leu Ala Leu Phe Glu
 545 550 555 560

Thr Arg Pro Gly Leu Ala Thr Val Thr Ala Ile Ala Asn Val Ala Ala

565 570 575
 Arg Glu Ser Lys Thr Asn Leu Gln Leu Ala Ser Phe Thr Phe Ser Gln
 580 585 590
 Met Lys Ala Leu Ser Lys Ser Ser Val Pro His Leu Glu Pro Leu Ala
 595 600 605
 Ala Ala Cys Ser Val Ala Leu Lys Ile Leu Asn Pro Ser Leu Asp Asn
 610 615 620
 Leu Gly Tyr Arg Tyr Ser Lys Val Met Arg Val Asp Thr Phe Lys Tyr
 625 630 635 640
 Asn Leu Met Ala Gly Ala Ala Ala Lys Val Phe Ile Met Asn Ser Ala
 645 650 655
 Asn Thr Met Phe Pro Val Phe Ile Leu Ala Lys Phe Arg Glu Tyr Thr
 660 665 670
 Ser Leu Val Glu Asn Asp Asp Ile Glu Ile Gly Ile Arg Gly Glu Gly
 675 680 685
 Ile Glu Glu Phe Leu Arg Lys Gln Asn Ile Gln Phe Ala Asn Phe Pro
 690 695 700
 Met Arg Lys Lys Ile Ser Gln Ile Val Lys Ser Leu Leu Gly Phe Lys
 705 710 715 720
 Gly Leu Pro Ser Gln Val Pro Leu Ile Ser Gly Tyr Ile Lys Leu Phe
 725 730 735
 Gly Gln Glu Ile Ala Phe Thr Glu Leu Asn Lys Glu Val Ile Gln Asn
 740 745 750
 Thr Ile Gln Ala Leu Asn Gln Pro Ala Glu Arg His Thr Met Ile Arg
 755 760 765
 Asn Val Leu Asn Lys Leu Leu Asn Gly Val Val Gly Gln Tyr Ala Arg
 770 775 780
 Arg Trp Met Thr Trp Glu Tyr Arg His Ile Ile Pro Thr Thr Val Gly
 785 790 795 800
 Leu Pro Ala Glu Leu Ser Leu Tyr Gln Ser Ala Ile Val His Ala Ala
 805 810 815
 Val Asn Ser Asp Val Lys Val Lys Pro Thr Pro Ser Gly Asp Phe Ser
 820 825 830
 Ala Ala Gln Leu Leu Glu Ser Gln Ile Gln Leu Asn Gly Glu Val Lys
 835 840 845

Pro Ser Val Leu Val His Thr Val Ala Thr Met Gly Ile Asn Ser Pro
 850 855 860

Leu Phe Gln Ala Gly Ile Glu Phe His Gly Lys Val His Ala His Leu
 865 870 875 880

Pro Ala Lys Phe Thr Ala Phe Leu Asp Met Lys Asp Arg Asn Phe Lys
 885 890 895

Ile Glu Thr Pro Pro Phe Gln Gln Glu Asn His Leu Val Glu Ile Arg
 900 905 910

Ala Gln Thr Phe Ala Phe Thr Arg Asn Ile Ala Asp Leu Asp Ser Ala
 915 920 925

Arg Lys Thr Leu Val Val Pro Arg Asn Asn Glu Gln Asn Ile Leu Lys
 930 935 940

Lys His Phe Glu Thr Thr Gly Arg Thr Ser Ala Glu Gly Ala Ser Met
 945 950 955 960

Met Glu Asp Ser Ser Glu Met Gly Pro Lys Lys Tyr Ser Ala Glu Pro
 965 970 975

Gly His His Gln Tyr Ala Pro Asn Ile Asn Ser Tyr Asp Ala Cys Thr
 980 985 990

Lys Phe Ser Lys Ala Gly Val His Leu Cys Ile Gln Cys Lys Thr His
 995 1000 1005

Asn Ala Ala Ser Arg Arg Asn Thr Ile Phe Tyr Gln Ala Val Gly
 1010 1015 1020

Glu His Asp Phe Lys Leu Thr Met Lys Pro Ala His Thr Glu Gly
 1025 1030 1035

Ala Ile Glu Lys Leu Gln Leu Glu Ile Thr Ala Gly Pro Lys Ala
 1040 1045 1050

Ala Ser Lys Ile Met Gly Leu Val Glu Val Glu Gly Thr Glu Gly
 1055 1060 1065

Glu Pro Met Asp Glu Thr Ala Val Thr Lys Arg Leu Lys Met Ile
 1070 1075 1080

Leu Gly Ile Asp Glu Ser Arg Lys Asp Thr Asn Glu Thr Ala Leu
 1085 1090 1095

Tyr Arg Ser Lys Gln Lys Lys Lys Asn Lys Ile His Asn Arg Arg
 1100 1105 1110

Leu Asp Ala Glu Val Val Glu Ala Arg Lys Gln Gln Ser Ser Leu

1115		1120		1125
Ser Ser Ser Ser Ser Ser Ser Ser Ser Ser Ser Ser Ser Ser Ser	1130	1135	1140	
Ser Ser Ser Ser Ser Ser Ser Ser Ser Ser Pro Ser Ser Ser Ser	1145	1150	1155	
Ser Ser Ser Tyr Ser Lys Arg Ser Lys Arg Arg Glu His Asn Pro	1160	1165	1170	
His His Gln Arg Glu Ser Ser Ser Ser Ser Ser Gln Glu Gln Asn	1175	1180	1185	
Lys Lys Arg Asn Leu Gln Glu Asn Arg Lys His Gly Gln Lys Gly	1190	1195	1200	
Met Ser Ser Ser Ser Ser Ser Ser Ser Ser Ser Ser Ser Ser Ser	1205	1210	1215	
Ser Ser Ser Ser Ser Ser Ser Ser Ser Ser Ser Ser Ser Ser Ser	1220	1225	1230	
Glu Asn Arg Pro His Lys Asn Arg Gln His Asp Asn Lys Gln Ala	1235	1240	1245	
Lys Met Gln Ser Asn Gln His Gln Gln Lys Lys Asn Lys Phe Ser	1250	1255	1260	
Glu Ser Ser Ser Ser Ser Ser Ser Ser Ser Ser Ser Ser Ser Ser	1265	1270	1275	
Asn Lys Lys Lys His His Arg Asn Phe Tyr Asp Leu Asn Phe Arg	1280	1285	1290	
Arg Thr Ala Arg Thr Lys Gly Thr Glu His Arg Gly Ser Arg Leu	1295	1300	1305	
Ser Ser Ser Ser Glu Ser Ser Ser Ser Ser Ser Ser Ser Ser Ser	1310	1315	1320	
Arg His Lys Ala Lys Phe Leu Gly Asp Lys Glu Pro Pro Val Leu	1325	1330	1335	
Val Val Thr Phe Lys Ala Val Arg Asn Asp Asn Thr Lys Gln Gly	1340	1345	1350	
Tyr Gln Met Val Val Tyr Gln Glu Tyr His Ser Ser Lys Gln Gln	1355	1360	1365	
Ile Gln Ala Tyr Val Met Asp Ile Ser Lys Thr Arg Trp Ala Ala	1370	1375	1380	

Cys Phe Asp Ala Val Val Val Asn Pro His Glu Ala Gln Ala Ser
 1385 1390 1395
 Leu Lys Trp Gly Gln Asn Cys Gln Asp Tyr Lys Ile Asn Met Lys
 1400 1405 1410
 Ala Glu Thr Gly Asn Phe Gly Asn Gln Pro Ala Leu Arg Val Thr
 1415 1420 1425
 Ala Asn Trp Pro Lys Ile Pro Ser Lys Trp Lys Ser Thr Gly Lys
 1430 1435 1440
 Val Val Gly Glu Tyr Val Pro Gly Ala Met Tyr Met Met Gly Phe
 1445 1450 1455
 Gln Gly Glu Tyr Lys Arg Asn Ser Gln Arg Gln Val Lys Leu Val
 1460 1465 1470
 Phe Ala Leu Ser Ser Pro Arg Thr Cys Asp Val Val Ile Arg Ile
 1475 1480 1485
 Pro Arg Leu Thr Val Tyr Tyr Arg Ala Leu Arg Leu Pro Val Pro
 1490 1495 1500
 Ile Pro Val Gly His His Ala Lys Glu Asn Val Leu Gln Thr Pro
 1505 1510 1515
 Thr Trp Asn Ile Phe Ala Glu Ala Pro Lys Leu Ile Met Asp Ser
 1520 1525 1530
 Ile Gln Gly Glu Cys Lys Val Ala Gln Asp Gln Ile Thr Thr Phe
 1535 1540 1545
 Asn Gly Val Asp Leu Ala Ser Ala Leu Pro Glu Asn Cys Tyr Asn
 1550 1555 1560
 Val Leu Ala Gln Asp Cys Ser Pro Glu Met Lys Phe Met Val Leu
 1565 1570 1575
 Met Arg Asn Ser Lys Glu Ser Pro Asn His Lys Asp Ile Asn Val
 1580 1585 1590
 Lys Leu Gly Glu Tyr Asp Ile Asp Met Tyr Tyr Ser Ala Asp Ala
 1595 1600 1605
 Phe Lys Met Lys Ile Asn Asn Leu Glu Val Ser Glu Glu His Leu
 1610 1615 1620
 Pro Tyr Lys Ser Phe Asn Tyr Pro Thr Val Glu Ile Lys Lys Lys
 1625 1630 1635
 Gly Asn Gly Val Ser Leu Ser Ala Ser Glu Tyr Gly Ile Asp Ser

1640 1645 1650
 Leu Asp Tyr Asp Gly Leu Thr Phe Lys Phe Arg Pro Thr Ile Trp
 1655 1660 1665
 Met Lys Gly Lys Thr Cys Gly Ile Cys Gly His Asn Asp Asp Glu
 1670 1675 1680
 Ser Glu Lys Glu Leu Gln Met Pro Asp Gly Ser Val Ala Lys Asp
 1685 1690 1695
 Gln Met Arg Phe Ile His Ser Trp Ile Leu Pro Ala Glu Ser Cys
 1700 1705 1710
 Ser Glu Gly Cys Asn Leu Lys His Thr Leu Val Lys Leu Glu Lys
 1715 1720 1725
 Ala Ile Ala Thr Asp Gly Ala Lys Ala Lys Cys Tyr Ser Val Gln
 1730 1735 1740
 Pro Val Leu Arg Cys Ala Lys Gly Cys Ser Pro Val Lys Thr Val
 1745 1750 1755
 Glu Val Ser Thr Gly Phe His Cys Leu Pro Ser Asp Val Ser Leu
 1760 1765 1770
 Asp Leu Pro Glu Gly Gln Ile Arg Leu Glu Lys Ser Glu Asp Phe
 1775 1780 1785
 Ser Glu Lys Val Glu Ala His Thr Ala Cys Ser Cys Glu Thr Ser
 1790 1795 1800
 Pro Cys Ala Ala
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 <210> 19
 <211> 1852
 <212> PRT
 <213> Gallus gallus
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 Lys Phe Asp Ile Asp Pro Gly Phe Asn Ser Arg Arg Ser Tyr Leu Tyr
 20 25 30
 Asn Tyr Glu Gly Ser Met Leu Asn Gly Leu Gln Asp Arg Ser Leu Gly
 35 40 45
 Lys Ala Gly Val Arg Leu Ser Ser Lys Leu Glu Ile Ser Gly Leu Pro
 50 55 60

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

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

Met Ser Tyr Arg Tyr Ser Lys Val Ile Arg Ala Asp Thr Tyr Phe Asp
 625 630 635 640
 Asn Tyr Arg Val Gly Ala Thr Gly Glu Ile Phe Val Val Asn Ser Pro
 645 650 655
 Arg Thr Met Phe Pro Ser Ala Ile Ile Ser Lys Leu Met Ala Asn Ser
 660 665 670
 Ala Gly Ser Val Ala Asp Leu Val Glu Val Gly Ile Arg Val Glu Gly
 675 680 685
 Leu Ala Asp Val Ile Met Lys Arg Asn Ile Pro Phe Ala Glu Tyr Pro
 690 695 700
 Thr Tyr Lys Gln Ile Lys Glu Leu Gly Lys Ala Leu Gln Gly Trp Lys
 705 710 715 720
 Glu Leu Pro Thr Glu Thr Pro Leu Val Ser Ala Tyr Leu Lys Ile Leu
 725 730 735
 Gly Gln Glu Val Ala Phe Ile Asn Ile Asn Lys Glu Leu Leu Gln Gln
 740 745 750
 Val Met Lys Thr Val Val Glu Pro Ala Asp Arg Asn Ala Ala Ile Lys
 755 760 765
 Arg Ile Ala Asn Gln Ile Leu Asn Ser Ile Ala Gly Gln Trp Thr Gln
 770 775 780
 Pro Val Trp Met Gly Glu Leu Arg Tyr Val Val Pro Ser Cys Leu Gly
 785 790 795 800
 Leu Pro Leu Glu Tyr Gly Ser Tyr Thr Thr Ala Leu Ala Arg Ala Ala
 805 810 815
 Val Ser Val Glu Gly Lys Met Thr Pro Pro Leu Thr Gly Asp Phe Arg
 820 825 830
 Leu Ser Gln Leu Leu Glu Ser Thr Met Gln Ile Arg Ser Asp Leu Lys
 835 840 845
 Pro Ser Leu Tyr Val His Thr Val Ala Thr Met Gly Val Asn Thr Glu
 850 855 860
 Tyr Phe Gln His Ala Val Glu Ile Gln Gly Glu Val Gln Thr Arg Met
 865 870 875 880
 Pro Met Lys Phe Asp Ala Lys Ile Asp Val Lys Leu Lys Asn Leu Lys
 885 890 895
 Ile Glu Thr Asn Pro Cys Arg Glu Glu Thr Glu Ile Val Val Gly Arg
 900 905 910

His Lys Ala Phe Ala Val Ser Arg Asn Ile Gly Glu Leu Gly Val Glu
 915 920 925

Lys Arg Thr Ser Ile Leu Pro Glu Asp Ala Pro Leu Asp Val Thr Glu
 930 935 940

Glu Pro Phe Gln Thr Ser Glu Arg Ala Ser Arg Glu His Phe Ala Met
 945 950 955 960

Gln Gly Pro Asp Ser Met Pro Arg Lys Gln Ser His Ser Ser Arg Glu
 965 970 975

Asp Leu Arg Arg Ser Thr Gly Lys Arg Ala His Lys Arg Asp Ile Cys
 980 985 990

Leu Lys Met His His Ile Gly Cys Gln Leu Cys Phe Ser Arg Arg Ser
 995 1000 1005

Arg Asp Ala Ser Phe Ile Gln Asn Thr Tyr Leu His Lys Leu Ile
 1010 1015 1020

Gly Glu His Glu Ala Lys Ile Val Leu Met Pro Val His Thr Asp
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Ala Asp Ile Asp Lys Ile Gln Leu Glu Ile Gln Ala Gly Ser Arg
 1040 1045 1050

Ala Ala Ala Arg Ile Ile Thr Glu Val Asn Pro Glu Ser Glu Glu
 1055 1060 1065

Glu Asp Glu Ser Ser Pro Tyr Glu Asp Ile Gln Ala Lys Leu Lys
 1070 1075 1080

Arg Ile Leu Gly Ile Asp Ser Met Phe Lys Val Ala Asn Lys Thr
 1085 1090 1095

Arg His Pro Lys Asn Arg Pro Ser Lys Lys Gly Asn Thr Val Leu
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Ala Glu Phe Gly Thr Glu Pro Asp Ala Lys Thr Ser Ser Ser Ser
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Ser Ser Ala Ser Ser Thr Ala Thr Ser Ser Ala Ser Ser Ser Ala
 1130 1135 1140

Ser Ser Pro Asn Arg Lys Lys Pro Met Asp Glu Glu Glu Asn Asp
 1145 1150 1155

Gln Val Lys Gln Ala Arg Asn Lys Asp Ala Ser Ser Ser Ser Arg
 1160 1165 1170

Ser Ser Lys Ser Ser Asn Ser Ser Lys Arg Ser Ser Ser Lys Ser
 1175 1180 1185
 Ser Asn Ser Ser Lys Arg Ser Ser Ser Ser Ser Ser Ser Ser Ser
 1190 1195 1200
 Ser Ser Ser Arg Ser Ser Ser Ser Ser Ser Ser Ser Ser Ser Asn
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 Ser Lys Ser Ser Ser Ser Ser Lys Ser Ser Ser Ser Ser Ser Ser
 1220 1225 1230
 Arg Ser Arg Ser Ser Ser Lys Ser Ser Ser Ser Ser Ser Ser Ser
 1235 1240 1245
 Ser Ser Ser Ser Ser Lys Ser Ser Ser Ser Arg Ser Ser Ser
 1250 1255 1260
 Ser Ser Ser Lys Ser Ser Ser His His Ser His Ser His His Ser
 1265 1270 1275
 Gly His Leu Asn Gly Ser Ser Ser Ser Ser Ser Ser Arg Ser
 1280 1285 1290
 Val Ser His His Ser His Glu His His Ser Gly His Leu Glu Asp
 1295 1300 1305
 Asp Ser Ser Ser Ser Ser Ser Ser Ser Val Leu Ser Lys Ile Trp
 1310 1315 1320
 Gly Arg His Glu Ile Tyr Gln Tyr Arg Phe Arg Ser Ala His Arg
 1325 1330 1335
 Gln Glu Phe Pro Lys Arg Lys Leu Pro Gly Asp Arg Ala Thr Ser
 1340 1345 1350
 Arg Tyr Ser Ser Thr Arg Ser Ser His Asp Thr Ser Arg Ala Ala
 1355 1360 1365
 Ser Trp Pro Lys Phe Leu Gly Asp Ile Lys Thr Pro Val Leu Ala
 1370 1375 1380
 Ala Phe Leu His Gly Ile Ser Asn Asn Lys Lys Thr Gly Gly Leu
 1385 1390 1395
 Gln Leu Val Val Tyr Ala Asp Thr Asp Ser Val Arg Pro Arg Val
 1400 1405 1410
 Gln Val Phe Val Thr Asn Leu Thr Asp Ser Ser Lys Trp Lys Leu
 1415 1420 1425
 Cys Ala Asp Ala Ser Val Arg Asn Ala Pro Gln Ala Val Ala Tyr
 1430 1435 1440

Val	Lys	Trp	Gly	Trp	Asp	Cys	Arg	Asp	Tyr	Lys	Val	Ser	Thr	Glu
	1445					1450					1455			
Leu	Val	Thr	Gly	Arg	Phe	Ala	Gly	His	Pro	Ala	Ala	Gln	Val	Lys
	1460					1465					1470			
Leu	Glu	Trp	Pro	Lys	Val	Pro	Ser	Asn	Val	Arg	Ser	Val	Val	Glu
	1475					1480					1485			
Trp	Phe	Tyr	Glu	Phe	Val	Pro	Gly	Ala	Ala	Phe	Met	Leu	Gly	Phe
	1490					1495					1500			
Ser	Glu	Arg	Met	Asp	Lys	Asn	Pro	Ser	Arg	Gln	Ala	Arg	Met	Val
	1505					1510					1515			
Val	Ala	Leu	Thr	Ser	Pro	Arg	Thr	Cys	Asp	Val	Val	Val	Lys	Leu
	1520					1525					1530			
Pro	Asp	Ile	Ile	Leu	Tyr	Gln	Lys	Ala	Val	Arg	Leu	Pro	Leu	Ser
	1535					1540					1545			
Leu	Pro	Val	Gly	Pro	Arg	Ile	Pro	Ala	Ser	Glu	Leu	Gln	Pro	Pro
	1550					1555					1560			
Ile	Trp	Asn	Val	Phe	Ala	Glu	Ala	Pro	Ser	Ala	Val	Leu	Glu	Asn
	1565					1570					1575			
Leu	Lys	Ala	Arg	Cys	Ser	Val	Ser	Tyr	Asn	Lys	Ile	Lys	Thr	Phe
	1580					1585					1590			
Asn	Glu	Val	Lys	Phe	Asn	Tyr	Ser	Met	Pro	Ala	Asn	Cys	Tyr	His
	1595					1600					1605			
Ile	Leu	Val	Gln	Asp	Cys	Ser	Ser	Glu	Leu	Lys	Phe	Leu	Val	Met
	1610					1615					1620			
Met	Lys	Ser	Ala	Gly	Glu	Ala	Thr	Asn	Leu	Lys	Ala	Ile	Asn	Ile
	1625					1630					1635			
Lys	Ile	Gly	Ser	His	Glu	Ile	Asp	Met	His	Pro	Val	Asn	Gly	Gln
	1640					1645					1650			
Val	Lys	Leu	Leu	Val	Asp	Gly	Ala	Glu	Ser	Pro	Thr	Ala	Asn	Ile
	1655					1660					1665			
Ser	Leu	Ile	Ser	Ala	Gly	Ala	Ser	Leu	Trp	Ile	His	Asn	Glu	Asn
	1670					1675					1680			
Gln	Gly	Phe	Ala	Leu	Ala	Ala	Pro	Gly	His	Gly	Ile	Asp	Lys	Leu
	1685					1690					1695			

Tyr Phe Asp Gly Lys Thr Ile Thr Ile Gln Val Pro Leu Trp Met
1700 1705 1710

Ala Gly Lys Thr Cys Gly Ile Cys Gly Lys Tyr Asp Ala Glu Cys
1715 1720 1725

Glu Gln Glu Tyr Arg Met Pro Asn Gly Tyr Leu Ala Lys Asn Ala
1730 1735 1740

Val Ser Phe Gly His Ser Trp Ile Leu Glu Glu Ala Pro Cys Arg
1745 1750 1755

Gly Ala Cys Lys Leu His Arg Ser Phe Val Lys Leu Glu Lys Thr
1760 1765 1770

Val Gln Leu Ala Gly Val Asp Ser Lys Cys Tyr Ser Thr Glu Pro
1775 1780 1785

Val Leu Arg Cys Ala Lys Gly Cys Ser Ala Thr Lys Thr Thr Pro
1790 1795 1800

Val Thr Val Gly Phe His Cys Leu Pro Ala Asp Ser Ala Asn Ser
1805 1810 1815

Leu Thr Asp Lys Gln Met Lys Tyr Asp Gln Lys Ser Glu Asp Met
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Gln Asp Thr Val Asp Ala His Thr Thr Cys Ser Cys Glu Asn Glu
1835 1840 1845

Glu Cys Ser Thr
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Gln Phe Gln Pro Gly Lys Val Tyr Arg Tyr Ser Tyr Asp Ala Phe Ser
20 25 30

Ile Ser Gly Leu Pro Glu Pro Gly Val Asn Arg Ala Gly Leu Ser Gly
35 40 45

Glu Met Lys Ile Glu Ile His Gly His Thr His Asn Gln Ala Thr Leu
50 55 60

Lys Ile Thr Gln Val Asn Leu Lys Tyr Phe Leu Gly Pro Trp Pro Ser
65 70 75 80

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

355 360 365
 Ala Thr Ser Glu Ala Leu Leu Phe Leu Lys Arg Thr Leu Ala Ser Glu
 370 375 380
 Gln Leu Thr Ser Ala Glu Ala Thr Gln Ile Val Tyr Ser Thr Leu Ser
 385 390 395 400
 Asn Gln Gln Ala Thr Arg Glu Ser Leu Ser Tyr Ala Arg Glu Leu Leu
 405 410 415
 His Thr Ser Phe Ile Arg Asn Arg Pro Ile Leu Arg Lys Thr Ala Val
 420 425 430
 Leu Gly Tyr Gly Ser Leu Val Phe Arg Tyr Cys Ala Asn Thr Val Ser
 435 440 445
 Cys Pro Asp Glu Leu Leu Gln Pro Leu His Asp Leu Leu Ser Gln Ser
 450 455 460
 Ser Asp Arg Ala Asp Glu Glu Glu Ile Val Leu Ala Leu Lys Ala Leu
 465 470 475 480
 Gly Asn Ala Gly Gln Pro Asn Ser Ile Lys Lys Ile Gln Arg Phe Leu
 485 490 495
 Pro Gly Gln Gly Lys Ser Leu Asp Glu Tyr Ser Thr Arg Val Gln Ala
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 Glu Ala Ile Met Ala Leu Arg Asn Ile Ala Lys Arg Asp Pro Arg Lys
 515 520 525
 Val Gln Glu Ile Val Leu Pro Ile Phe Leu Asn Val Ala Ile Lys Ser
 530 535 540
 Glu Leu Arg Ile Arg Ser Cys Ile Val Phe Phe Glu Ser Lys Pro Ser
 545 550 555 560
 Val Ala Leu Val Ser Met Val Ala Val Arg Leu Arg Arg Glu Pro Asn
 565 570 575
 Leu Gln Val Ala Ser Phe Val Tyr Ser Gln Met Arg Ser Leu Ser Arg
 580 585 590
 Ser Ser Asn Pro Glu Phe Arg Asp Val Ala Ala Ala Cys Ser Val Ala
 595 600 605
 Ile Lys Met Leu Gly Ser Lys Leu Asp Arg Leu Gly Cys Arg Tyr Ser
 610 615 620
 Lys Ala Val His Val Asp Thr Phe Asn Ala Arg Thr Met Ala Gly Val
 625 630 635 640

Ser Ala Asp Tyr Phe Arg Ile Asn Ser Pro Ser Gly Pro Leu Pro Arg
645 650 655

Ala Val Ala Ala Lys Ile Arg Gly Gln Gly Met Gly Tyr Ala Ser Asp
660 665 670

Ile Val Glu Phe Gly Leu Arg Ala Glu Gly Leu Gln Glu Leu Leu Tyr
675 680 685

Arg Gly Ser Gln Glu Gln Asp Ala Tyr Gly Thr Ala Leu Asp Arg Gln
690 695 700

Thr Leu Leu Arg Ser Gly Gln Ala Arg Ser His Val Ser Ser Ile His
705 710 715 720

Asp Thr Leu Arg Lys Leu Ser Asp Trp Lys Ser Val Pro Glu Glu Arg
725 730 735

Pro Leu Ala Ser Gly Tyr Val Lys Val His Gly Gln Glu Val Val Phe
740 745 750

Ala Glu Leu Asp Lys Lys Met Met Gln Arg Ile Ser Gln Leu Trp His
755 760 765

Ser Ala Arg Ser His His Ala Ala Ala Gln Glu Gln Ile Arg Ala Val
770 775 780

Val Ser Lys Leu Glu Gln Gly Met Asp Val Leu Leu Thr Lys Gly Tyr
785 790 795 800

Val Val Ser Glu Val Arg Tyr Met Gln Pro Val Cys Ile Gly Ile Pro
805 810 815

Met Asp Leu Asn Leu Leu Val Ser Gly Val Thr Thr Asn Arg Ala Asn
820 825 830

Leu His Ala Ser Phe Ser Gln Ser Leu Pro Ala Asp Met Lys Leu Ala
835 840 845

Asp Leu Leu Ala Thr Asn Ile Glu Leu Arg Val Ala Ala Thr Thr Ser
850 855 860

Met Ser Gln His Ala Val Ala Ile Met Gly Leu Thr Thr Asp Leu Ala
865 870 875 880

Lys Ala Gly Met Gln Thr His Tyr Lys Thr Ser Ala Gly Leu Gly Val
885 890 895

Asn Gly Lys Ile Glu Met Asn Ala Arg Glu Ser Asn Phe Lys Ala Ser
900 905 910

Leu Lys Pro Phe Gln Gln Lys Thr Val Val Val Leu Ser Thr Met Glu

915	920	925
Ser Ile Val Phe Val Arg Asp Pro Ser Gly Ser Arg Ile Leu Pro Val 930 935 940		
Leu Pro Pro Lys Met Thr Leu Asp Lys Gly Leu Ile Ser Gln Gln Gln 945 950 955 960		
Gln Gln Pro His His Gln Gln Gln Pro His Gln His Gly Gln Asp Gln 965 970 975		
Ala Arg Ala Ala Tyr Gln Arg Pro Trp Ala Ser His Glu Phe Ser Pro 980 985 990		
Ala Glu Gln Lys Gln Ile His Asp Ile Met Thr Ala Arg Pro Val Met 995 1000 1005		
Arg Arg Lys Gln His Cys Ser Lys Ser Ala Ala Leu Ser Ser Lys 1010 1015 1020		
Val Cys Phe Ser Ala Arg Leu Arg Asn Ala Ala Phe Ile Arg Asn 1025 1030 1035		
Ala Leu Leu Tyr Lys Ile Thr Gly Asp Tyr Val Ser Lys Val Tyr 1040 1045 1050		
Val Gln Pro Thr Ser Ser Lys Ala Gln Ile Gln Lys Val Glu Leu 1055 1060 1065		
Glu Leu Gln Ala Gly Pro Gln Ala Ala Glu Lys Val Ile Arg Met 1070 1075 1080		
Val Glu Leu Val Ala Lys Ala Ser Lys Lys Ser Lys Lys Asn Ser 1085 1090 1095		
Thr Ile Thr Glu Glu Gly Val Gly Glu Thr Ile Ile Ser Gln Leu 1100 1105 1110		
Lys Lys Ile Leu Ser Ser Asp Lys Asp Lys Asp Ala Lys Lys Pro 1115 1120 1125		
Pro Gly Ser Ser Ser Ser Ser Ser Ser Ser Ser Ser Ser Ser Ser 1130 1135 1140		
Ser Ser Ser Ser Ser Asp Lys Ser Gly Lys Lys Thr Pro Arg Gln 1145 1150 1155		
Gly Ser Thr Val Asn Leu Ala Ala Lys Arg Ala Ser Lys Lys Gln 1160 1165 1170		
Arg Gly Lys Asp Ser Ser Ser Ser Ser Ser Ser Ser Ser Ser Ser 1175 1180 1185		

Ser Asp Ser Ser Lys Ser Pro His Lys His Gly Gly Ala Lys Arg
 1190 1195 1200
 Gln His Ala Gly His Gly Ala Pro His Leu Gly Pro Gln Ser His
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 Ser Ser Ser Ser Ser Ser Ser Ser Ser Ser Ser Ser Ser Ala
 1220 1225 1230
 Ser Lys Ser Phe Ser Thr Val Lys Pro Pro Met Thr Arg Lys Pro
 1235 1240 1245
 Arg Pro Ala Arg Ser Ser Ser Ser Ser Ser Ser Asp Ser Ser
 1250 1255 1260
 Ser Ser Ser Ser Ser Ser Ser Ser Ser Ser Ser Ser Ser Ser
 1265 1270 1275
 Ser Ser Ser Ser Ser Ser Glu Ser Lys Ser Leu Glu Trp Leu Ala
 1280 1285 1290
 Val Lys Asp Val Asn Gln Ser Ala Phe Tyr Asn Phe Lys Tyr Val
 1295 1300 1305
 Pro Gln Arg Lys Pro Gln Thr Ser Arg Arg His Thr Pro Ala Ser
 1310 1315 1320
 Ser Ser Ser Ser Ser Ser Ser Ser Ser Ser Ser Ser Ser Ser
 1325 1330 1335
 Ser Ser Ser Asp Ser Asp Met Thr Val Ser Ala Glu Ser Phe Glu
 1340 1345 1350
 Lys His Ser Lys Pro Lys Val Val Ile Val Leu Arg Ala Val Arg
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 Ala Asp Gly Lys Gln Gln Gly Leu Gln Thr Thr Leu Tyr Tyr Gly
 1370 1375 1380
 Leu Thr Ser Asn Gly Leu Pro Lys Ala Lys Ile Val Ala Val Glu
 1385 1390 1395
 Leu Ser Asp Leu Ser Val Trp Lys Leu Cys Ala Lys Phe Arg Leu
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 Ser Ala His Met Lys Ala Lys Ala Ala Ile Gly Trp Gly Lys Asn
 1415 1420 1425
 Cys Gln Gln Tyr Arg Ala Met Leu Glu Ala Ser Thr Gly Asn Leu
 1430 1435 1440
 Gln Ser His Pro Ala Ala Arg Val Asp Ile Lys Trp Gly Arg Leu

1445		1450		1455
Pro Ser Ser Leu Gln Arg Ala Lys Asn Ala Leu Leu Glu Asn Lys	1460	1465	1470	
Ala Pro Val Ile Ala Ser Lys Leu Glu Met Glu Ile Met Pro Lys	1475	1480	1485	
Lys Asn Gln Lys His Gln Val Ser Val Ile Leu Ala Ala Met Thr	1490	1495	1500	
Pro Arg Arg Met Asn Ile Ile Val Lys Leu Pro Lys Val Thr Tyr	1505	1510	1515	
Phe Gln Gln Gly Ile Leu Leu Pro Phe Thr Phe Pro Ser Pro Arg	1520	1525	1530	
Phe Trp Asp Arg Pro Glu Gly Ser Gln Ser Asp Ser Leu Pro Ala	1535	1540	1545	
Gln Ile Ala Ser Ala Phe Ser Gly Ile Val Gln Asp Pro Val Ala	1550	1555	1560	
Ser Ala Cys Glu Leu Asn Glu Gln Ser Leu Thr Thr Phe Asn Gly	1565	1570	1575	
Ala Phe Phe Asn Tyr Asp Met Pro Glu Ser Cys Tyr His Val Leu	1580	1585	1590	
Ala Gln Glu Cys Ser Ser Arg Pro Pro Phe Ile Val Leu Ile Lys	1595	1600	1605	
Leu Asp Ser Glu Arg Arg Ile Ser Leu Glu Leu Gln Leu Asp Asp	1610	1615	1620	
Lys Lys Val Lys Ile Val Ser Arg Asn Asp Ile Arg Val Asp Gly	1625	1630	1635	
Glu Lys Val Pro Leu Arg Arg Leu Ser Gln Lys Asn Gln Tyr Gly	1640	1645	1650	
Phe Leu Val Leu Asp Ala Gly Val His Leu Leu Leu Lys Tyr Lys	1655	1660	1665	
Asp Leu Arg Val Ser Phe Asn Ser Ser Ser Val Gln Val Trp Val	1670	1675	1680	
Pro Ser Ser Leu Lys Gly Gln Thr Cys Gly Leu Cys Gly Arg Asn	1685	1690	1695	
Asp Asp Glu Leu Val Thr Glu Met Arg Met Pro Asn Leu Glu Val	1700	1705	1710	

Ala Lys Asp Phe Thr Ser Phe Ala His Ser Trp Ile Ala Pro Asp
1715 1720 1725

Glu Thr Cys Gly Gly Ala Cys Ala Leu Ser Arg Gln Thr Val His
1730 1735 1740

Lys Glu Ser Thr Ser Val Ile Ser Gly Ser Arg Glu Asn Cys Tyr
1745 1750 1755

Ser Thr Glu Pro Ile Met Arg Cys Pro Ala Thr Cys Ser Ala Ser
1760 1765 1770

Arg Ser Val Pro Val Ser Val Ala Met His Cys Leu Pro Ala Glu
1775 1780 1785

Ser Glu Ala Ile Ser Leu Ala Met Ser Glu Gly Arg Pro Phe Ser
1790 1795 1800

Leu Ser Gly Lys Ser Glu Asp Leu Val Thr Glu Met Glu Ala His
1805 1810 1815

Val Ser Cys Val Ala
1820

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