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(54) Title: RECOMBINANT CANINE HERPESVIRUSES		
(57) Abstract The present invention includes novel recombinant canine herpesvirus (CHV) and novel recombinant CHV genomes, and particularly to those CHV and CHV genomes that contain heterologous nucleic acid molecules. The present invention also relates to the use of such genomes and viruses in a variety of applications, including therapeutic compositions to protect animals from disease. The present invention also relates to novel isolated CHV nucleic acid molecules, to CHV proteins encoded by such nucleic acid molecules, and to antibodies raised against such CHV proteins as well as to the use of such CHV nucleic acid molecules, proteins and antibodies as therapeutic compositions to protect an animal from CHV. The present invention also includes constructs comprising CHV nucleic acid molecules that include heterologous nucleic acid molecules, to recombinant vectors including such constructs, and to the use of such constructs and vectors in the production of recombinant CHV and recombinant CHV genomes.		

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RECOMBINANT CANINE HERPESVIRUSES

FIELD OF THE INVENTION

The present invention relates to canine herpesvirus (CHV), and particularly to novel recombinant CHV and recombinant CHV
5 genomes, including those that contain heterologous nucleic acid molecules. The present invention also relates to the use of such genomes and viruses in a variety of applications, including as therapeutic compositions to protect animals from disease. The present invention also relates to novel isolated
10 CHV nucleic acid molecules, to proteins encoded by such nucleic acid molecules, and to use of such CHV nucleic acid molecules to insert heterologous nucleic acid molecules into CHV genomes.

BACKGROUND OF THE INVENTION

Dogs and other canids are affected by a number of diseases
15 against which it would be desirable to develop protective vaccines. Live vaccines, and particularly live viral vector vaccines, are attractive vaccine vector candidates as they appear to be associated with longer-lasting immunity than inactivated virus vaccines or subunit vaccines. One
20 disadvantage of live vaccines, however, has been that attenuated virus strains often revert to virulence. Another disadvantage has been the host range of a number of viral vaccines. In an attempt to deliver genes to an animal, several viral and bacterial systems, such as poxviruses, adenoviruses,
25 *Salmonella*, and BCG (*Bacillus Calmette-Guerin*), have been

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genetically manipulated to generate vectors containing heterologous antigen genes in order to immunize a host with a vaccine in which the antigens are presented in a "live" configuration. See, for example, the following two review
5 articles: Esposito et al., pp. 195-247, 1989, *Advances in Veterinary Science and Comparative Medicine*, Vol. 33; Dougan et al., pp. 271-300, 1989, *Advances in Veterinary Science and Comparative Medicine*, Vol. 33.

Several herpes virus vaccines, such as those based on
10 bovine herpes virus (BHV), cytomegalovirus (CMV), Epstein Barr virus (EBV), equine herpes virus (EHV), feline herpes virus (FHV), herpes simplex virus (HSV), Marek's disease virus (MDV), pseudorabies virus (PRV), turkey herpes virus (HVT), and varicella zoster virus (VZV) have been developed and several
15 have shown at least some efficacy as vaccines against the virus per se or as vectors carrying other genes in certain indications. The listed herpes viruses, however, also have the drawback that even if attenuated, they are subject to reversion.

20 Canine herpes virus (CHV) infection is a relatively benign infection except in newborn puppies. A few vaccines to protect against CHV infection have been reported including a small-plaque variant CHV vaccine disclosed in U.S. Patent No. 4,213,965, by Carmichael, issued July 22, 1980. The nucleotide
25 sequences of CHV genes encoding gB, gC, gD and UL45 homologs have been reported by Limbach et al., 1994, *J. Gen. Virol.* 75,

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2029-2039, but these proteins, while proposed as vaccine candidates against CHV, were not tested as such by Limbach et al., *ibid.* In addition, the complete nucleotide sequence of the CHV thymidine kinase (tk) gene was reported by Remond et al., 1995, *Virus Res.*, 39, 341-354. More recently, a restriction map of the CHV genome, as well as a number of small, incomplete sequences in from the ends of various restriction fragments were reported by Remond, et al., 1996, *J. Gen. Virol.*, 77, 37-48. These small sequences were used to infer the placement of certain genes within the CHV genome.

The inventors are not aware of any reports which describe the use of CHV as a vaccine vector, either with respect to inactivating genes in the CHV genome using recombinant DNA techniques, and/or to delivering protective compounds to a canid, in spite of the need to develop safe and efficacious delivery systems to protect canids, and especially dogs, from disease. Two U.S. patents (i.e., U.S. Patent No. 5,266,489, by Rey-Senelongue et al., issued November 30, 1993; and U.S. Patent No. 5,223,424, by Cochran et al., issued June 29, 1993) at best speculate on the insertion of genes into certain CHV loci, but neither claims CHV vectors or vaccines, nor provides data supporting such speculations. US 5,266,489, *ibid.*, claimed HVT having a foreign gene inserted into the ribonucleotide reductase (RR) small subunit gene of the HVT genome, but also disclosed without support the insertion of foreign genes into the RR small subunit genes of BHV, CHV, CMV, duck herpes virus,

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EBV, EHV, FHV, HSV, PRV and VZV. The inventors, however, have demonstrated the inaccuracy of this disclosure in that the inventors have found, and disclosed in the present application, that the CHV genome lacks the RR small subunit gene. That is, 5 the CHV RR small subunit gene does not exist to provide a target for the insertion of foreign genes. This result was similarly verified by Remond, et al., 1996, *ibid.*

US 5,223,424, *ibid.*, claimed specific hybrid PRV constructs having deletions in the TK, repeat, or and/or gX 10 regions and heterologous sequences inserted into the repeat and/or gX regions, but also proposed without data the ability to insert foreign genes into the repeat region of the CHV genome, even though that genome had not yet been mapped. Also disclosed were certain BHV and HVT constructs and proposals, 15 without data, to delete and insert genes in other herpesviruses, such as EHV and FHV, HSV and MDV. It is also of note that a patent application (now U.S. 5,273,876, by Hock et al., issued December 28, 1993) that was filed significantly later than US 5,223,424, *ibid.*, and shares two co-inventors 20 with US 5,223,424, *ibid.*, states in column 2, lines 57-61, "Among the herpesviruses, only four herpesviruses (herpes simplex of humans, herpes saimiri of monkeys, pseudorabies virus and varicella-zoster virus) have been engineered to contain foreign DNA sequences previous to this disclosure," 25 thereby indicating the lack of CHV, or a number of other, herpes virus vectors.

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Thus, there remains a need for new and improved methods to vaccinate canids to protect them from diseases, such as those caused by genetic or metabolic disorders as well as those caused by infectious agents such as protozoan parasites, 5 helminth parasites, ectoparasites, fungi, bacteria, and viruses.

SUMMARY OF THE INVENTION

The present invention relates to a new method to protect animals from disease using a recombinant virus or virus genome. 10 When a recombinant CHV of the present invention is administered to an animal, the virus is able to infect cells within the animal. Infected cells are able to express nucleic acid sequences present on the recombinant CHV genome to produce protective compounds, such as proteins and RNAs, capable of 15 protecting the animal from a variety of diseases. Using methods taught in the present invention, vaccines can be generated that are capable of protecting an animal from any disease for which a protective compound can be produced. As such, the present invention is of extremely broad scope and 20 includes a wide variety of vaccines that have a variety of applications.

The present invention includes a recombinant CHV that comprises a recombinant CHV genome. The invention also includes recombinant CHV genomes. In one embodiment, a 25 recombinant CHV has an inactive gene within its genome, with a preferred recombinant CHV in this embodiment being a CdUTPase

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negative CHV, a CgC negative CHV, a CgE negative CHV, a CgG negative CHV, a CgI negative CHV, a CPK negative CHV, a CTK negative CHV, a CIR6 negative CHV, a CUS2 negative CHV, a CUS9 negative CHV, a CUL49 negative CHV, a CUL51 negative CHV, a
5 CUL45 negative CHV, a CgD negative CHV, a CgB negative CHV, a CUL48 negative CHV, a CUL52 negative CHV, a CgL negative CHV, a CUL49.5 negative CHV, a CICP0 negative CHV, a CICP4 negative CHV, and/or a CUS8.5 negative CHV. In the case of the CUS8.5 negative CHV, a CUS8.5 negative CHV refers to a CHV in which
10 the CUS8.5 open reading frame is disrupted.

The present invention also includes a recombinant CHV genome that comprises a heterologous nucleic acid molecule, which preferably encodes a protective compound that protects a canid from disease. Such a heterologous nucleic acid molecule
15 can be located in an essential gene, a nonessential gene, and/or in an intergenic region. Insertion of a heterologous nucleic acid into a CHV genome can, but need not, inactivate a gene within that genome. Also included in the present invention are methods to produce a recombinant CHV and a
20 recombinant CHV genome, as well as a canine cell line that complements a defect in a gene essential to CHV reproduction *in vitro*.

One embodiment of the present invention is a method to increase recombinant CHV plaque forming efficiency. Such a
25 method can include the steps of introducing a recombinant CHV genome into a canine cell expressing CHV alpha trans-inducing

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factor and culturing the cell to produce recombinant CHV. In another embodiment, the method includes the steps of co-introducing a recombinant CHV genome and a CHV alpha trans-inducing factor gene into a canine cell and culturing the cell
5 to produce recombinant CHV. The present invention also includes a canine cell line comprising a CHV alpha trans-inducing factor gene.

One embodiment of the present invention is a therapeutic composition that includes a recombinant CHV, a recombinant CHV
10 genome, or a mixture thereof. The present invention also includes a method to protect an animal from disease by administering such a therapeutic composition to the animal.

The present invention also includes an isolated CHV nucleic acid molecule that hybridizes under stringent
15 hybridization conditions with at least one of the following nucleic acid regions: a CdUTPase gene, a CgE gene, a CgG gene, a CgI gene, a CPK gene, a CTK gene, a CIR6 gene, a CUS2 gene, a CUS9 gene, a CUL49 gene, a CUL51 gene, a CUL48 gene, a CUL52 gene, a CgL gene, a CUL49.5 gene, a CICIP4 gene, a CUS8.5 open
20 reading frame, and/or a region of the CHV genome spanning from about the 3' end of the coding region of the CUL41 gene through about the 3' end of the coding region of the CUL38 gene. Also included are recombinant molecules, recombinant viruses, recombinant vectors, and recombinant cells that include such
25 CHV nucleic acid molecules. The present invention also includes CHV proteins encoded by such CHV nucleic acid

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molecules and antibodies that selectively bind to such CHV proteins, as well as methods to produce such CHV nucleic acid molecules, recombinant molecules, recombinant viruses, recombinant vectors, recombinant cells, CHV proteins and 5 antibodies. Also included in the present invention are therapeutic compositions including such CHV nucleic acid molecules, CHV proteins and antibodies, as well as methods to use such compositions to protect an animal from disease.

BRIEF DESCRIPTION OF THE FIGURES

10 Fig. 1 depicts a schematic map of two contiguous *Hind*III fragments that include at least portions of CHV UL48 UL49, dUTPase, UL51 and UL52 genes.

Fig. 2 depicts a schematic map of the *Asc*I fragment that includes the unique short region of CHV.

15 Fig. 3 depicts a schematic map of the *Asc*I/blunt fragment that includes the terminal inverted repeat region of CHV.

Fig. 4 depicts a schematic map of a region of the CHV genome spanning at least from the CUS9 gene through the CIR6 20 gene.

Fig. 5 depicts a schematic map of a region of the CHV genome spanning at least from a portion of the CUL52 gene through at least a portion of the CUL48 gene.

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DETAILED DESCRIPTION OF THE INVENTION

The present invention relates to canine herpesviruses (CHV), and particularly to recombinant CHV and recombinant CHV genomes as well as to methods to produce and use such
5 viruses and genomes. The present invention also includes identification of regions of the CHV genome that are preferred targets for deletion and/or for insertion of heterologous nucleic acid molecules. As used herein, the term "canine" refers to "of the family Canidae" and, as such,
10 includes reference to dogs (including wild and domesticated dogs), foxes, wolves, jackals, coyotes, and other members of the family Canidae. Similarly, a "canid" is any member of the family Canidae. As used herein, the term CHV refers to any herpesvirus endogenous to the family Canidae. A
15 particularly preferred CHV of the present invention is a recombinant CHV that infects dogs.

One embodiment of the present invention is the use of a recombinant CHV, and particularly of a CHV having a recombinant CHV genome that includes a (i.e., one or more
20 than one) heterologous nucleic acid molecule, as a live CHV-based therapeutic composition, or vaccine, to protect an animal from a disease against which the heterologous nucleic acid molecule is targeted. Live vaccines are advantageous because they are believed to confer more vigorous and longer-
25 lasting immunity than subunit or killed vaccines. While not being bound by theory, it is believed that such advantages

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are due to the ability of the genetic information carried by the virus to enter cells of the treated animal, replicate itself, and direct the expression of a protective compound, such as a protective protein or a protective RNA, for
5 extended periods of time. Thus, the therapeutic composition need not be administered frequently and, at least in some embodiments, the virus vaccine can function as a self-booster.

CHV is particularly useful as a delivery vehicle for a
10 heterologous nucleic acid molecule to protect canids from a disease for a variety of reasons, including, but not limited to, CHV's limited host range and pathogenicity. CHV, to the inventors' knowledge, has the most limited host range of any herpesvirus, including FHV, in that CHV's host range appears
15 to be substantially limited to canine cells. As far as the inventors are aware, the only report of CHV infection of a cell type other than canine cells is limited infection of mink lung cells; see, for example, Peterson et al., 1988, *Comp. Immunol. Microbiol. Infect. Diseases* 11, 93-98. This
20 limited host range illustrates the safety of CHV in that the virus apparently cannot be transmitted to a variety of species unrelated to canids.

Furthermore, CHV exhibits only limited pathogenicity. Although the virus has been shown to cause a fatal
25 hemorrhagic disease in hypothermic neonatal pups (i.e., essentially all pups experimentally infected with CHV and

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maintained at room temperature (i.e., from about 25°C to 27°C) within a week of birth die from the infection), CHV causes insignificant respiratory infection in adult dogs; see, for example, Carmichael, 1970, *J. Am. Vet. Med. Assn.* 156, 1714-1721. Moreover, prolonged survival or recovery of experimentally infected neonatal pups maintained at 38.4°C to 39.5°C was observed. Adult dogs exposed to CHV do, however, become infected since virus shedding has been shown to occur for at least two weeks post-inoculation; and latency is postulated to occur, since CHV has been isolated from primary cultured cells of normal healthy dogs; see, for example, Carmichael, *ibid.* Furthermore, maternal antibody, or passive transfer of antibody from seropositive dogs has been shown to protect puppies from an otherwise fatal CHV challenge; see, for example, Carmichael, *ibid.* Due to its limited pathogenicity, CHV apparently need not be attenuated to the extent required for other viruses used as live vaccine vectors. In addition, vaccination of a dam with CHV can lead to passive protection in her pups.

Another advantage of CHV is its limited temperature range. CHV grows well at temperatures ranging from about 34°C to about 36°C, with optimal growth occurring at about 35°C. CHV, however, does not grow well at temperatures less than or equal to about 33°C or at temperatures greater than or equal to about 37°C. As such CHV is significantly more temperature sensitive than any other known wild type

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herpesvirus, including FHV.

Yet another advantage of CHV is its potential for use as a single, multivalent therapeutic composition against a variety of canine pathogens. That is, the CHV genome can be
5 manipulated to incorporate multiple heterologous nucleic acid molecules without disrupting the ability of the genome to be packaged (i.e., assembled) into a live virus. Examples of multivalent therapeutic compositions are described below.

As far as the inventors are aware, this application is
10 the first report of the genetic engineering of a CHV genome, particularly for the development of efficacious canid vaccines, in spite of a long felt need for efficacious vaccines against canine pathogens. The inventors have developed methods to identify CHV genes and intergenic
15 regions, particularly those having utility as targets for the insertion of heterologous nucleic acid molecules, despite the difficulty of using known herpesvirus sequences to identify such regions due to the AT-rich nature of the CHV genome. The CHV genome contains about 70% adenosine and thymidine
20 residues, compared to other known herpesvirus genomes which, on the average, contain from about 30% to about 58% adenosine and thymidine residues (e.g., HSV, BHV, and PRV contain about 30%, EHV about 54%, and FHV about 58%, adenosine and thymidine residues). As such, it is very difficult to design
25 primers or probes using known herpesvirus sequences to identify CHV analogs.

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One embodiment of the present invention is a recombinant CHV. As used herein, a recombinant CHV is a CHV that comprises (i.e., has or includes) a genome that has been genetically engineered (i.e., subjected to recombinant
5 nucleic acid (i.e., DNA or RNA) techniques, such as those disclosed in Sambrook et al., 1989, *Molecular Cloning: A Laboratory Manual*, Cold Spring Harbor Labs Press; Sambrook et al., *ibid.*, is incorporated by reference herein in its entirety) to differ from the genome of a natural CHV isolate
10 (i.e., a herpesvirus endogenous to the family Canidae). Such a genetically engineered genome is referred to herein as a recombinant CHV genome and is described in more detail below.

A recombinant CHV of the present invention includes not only a recombinant CHV genome but also an envelope and capsid
15 in which the genome is packaged. The viral envelope and capsid are preferably a CHV envelope and a CHV capsid, encoded at least in part by CHV genes, thereby imparting to the recombinant CHV the host range of a natural CHV isolate. It is to be noted, however, that the present invention also
20 includes recombinant CHV having envelopes and/or capsids that have been modified to, for example, alter (e.g., broaden, narrow, or completely change) the host range of the recombinant CHV genome. Such modifications can be accomplished by one skilled in the art by, for example,
25 modifying CHV envelope and/or capsid genes and/or replacing such genes with those of another virus. Altered genes can be

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located on the CHV genome itself and/or in the genome of the cell in which the recombinant virus is produced.

A recombinant CHV genome of the present invention is a CHV genome in which nucleotides have been deleted, inserted, substituted or inverted using recombinant techniques known to those skilled in the art such that the recombinant CHV genome is no longer the same as a natural CHV genome. A recombinant CHV genome of the present invention is capable of effecting expression (e.g., transcription, translation) of coding regions that are operatively linked to regulatory sequences within the genome. As used herein, a coding region is a stretch of nucleotides that encodes an RNA molecule and/or a protein. Coding regions can be endogenous to CHV or can be heterologous nucleic acid molecules of the present invention, which are described in more detail below. The phrase operatively linked refers to the positioning of a coding region in the CHV genome such that the coding region is able to be expressed when the genome is inside a cell. Regulatory sequences include transcription control sequences, translation control sequences, and other regulatory sequences that control the expression of coding regions. Transcription control sequences are sequences which control the initiation, elongation, and termination of transcription. Particularly important transcription control sequences are those which control transcription initiation, such as promoter, enhancer, operator and repressor sequences. Suitable regulatory

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sequences include any regulatory sequence that can function in the present invention. Preferred regulatory sequences are disclosed herein.

A recombinant CHV genome of the present invention can
5 include a gene that has been inactivated. As used herein, a gene includes a coding region as well as the regulatory sequences involved in expression of that coding region. An inactive gene refers to a gene that no longer exhibits the function of its natural counterpart. Methods to inactivate a
10 gene include, but are not limited to, deletion of one or more nucleotides within the gene, insertion of one or more nucleotides into the gene, replacement of one or more nucleotides within the gene by other nucleotides (i.e., nucleotide substitution), and/or inversion of nucleotides
15 within the gene such that the resulting gene no longer has the function of the corresponding natural gene. Such alterations can be effected anywhere within the gene, such as within the coding region, within the regulatory sequences and/or in regions surrounding the coding region or regulatory
20 sequences such that the alteration(s) cause gene inactivation. In one embodiment, an entire gene or the coding region and/or regulatory sequences thereof can be deleted or replaced.

One embodiment of the present invention is an attenuated
25 recombinant CHV. As used herein, an attenuated CHV is a CHV that does not cause 100% mortality if used to infect canid

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neonates less than 1 week old that are maintained in room temperature. A preferred attenuated CHV of the present invention causes less than about 90% and preferably less than about 70% mortality when used to infect canid neonates less than 1 week of age maintained at room temperature.

An attenuated recombinant CHV can be produced by inactivating a CHV gene that, due to that gene's inactivation, results in an attenuated virus. Methods to inactivate a gene are disclosed above. An attenuated CHV can be identified by exposing pups less than 1 week old to the recombinant virus to be tested and determining the percentage of exposed pups that die; such an exposure method is disclosed, for example, in Carmichael, *ibid*. If less than 100% percent of the pups die, the virus being tested is attenuated in accordance with the present invention.

Suitable CHV genes to inactivate in order to produce an attenuated CHV include any gene that when inactivated leads to an attenuated virus, as determined using an assay as disclosed above. A preferred attenuated recombinant CHV of the present invention is a CHV having a recombinant genome in which a heterologous nucleic acid molecule is inserted into a gene, the insertion resulting in an attenuated virus. An attenuated recombinant CHV has utility, for example, as a therapeutic composition to protect an animal from CHV infection and/or as a live CHV-based vaccine carrying a heterologous nucleic acid molecule. It is to be noted,

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however, that, as disclosed above, it is believed that CHV need not be attenuated for use as a live vaccine vector due to the low pathogenicity of natural CHV, particularly as compared to that of other herpesviruses.

5 One embodiment of the present invention is a recombinant CHV that can reproduce (i.e., grow) in tissue culture; that is, the virus is a reproduction competent CHV. A reproduction competent CHV is a CHV that upon *in vitro* infection of an appropriate host cell is able to use host
10 cell machinery, as well as its own regulatory control regions and/or encoded enzymes, to effect self-reproduction, i.e., to form infectious virus.

Reproduction competent recombinant CHV genomes can have gene alterations in one or more genes non-essential for
15 growth *in vitro*. Suitable gene targets (i.e., genes to alter) include any non-essential CHV gene. A non-essential CHV gene can be identified by altering a CHV gene within a CHV genome (e.g., by genetic engineering or classical mutagenesis) and demonstrating that the altered genome is
20 capable of effecting self-reproduction in tissue culture.

Preferred non-essential CHV genes to target include, but are not limited to, a CHV deoxyuridine triphosphate pyrophosphatase (CdUTPase) gene, a CHV glycoprotein C (CgC) gene, a CHV glycoprotein E (CgE) gene, a CHV glycoprotein G
25 (CgG) gene, a CHV glycoprotein I (CgI) gene, a CHV serine-threonine protein kinase US3 (CPK) gene, a CHV thymidine

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kinase (CTK) gene, a CHV IR6 (CIR6) gene, a CHV US2 (CUS2) gene, a CHV tegument phosphoprotein US9 (CUS9) gene, a CHV membrane protein UL49 (CUL49) gene, a CHV membrane protein CHV UL49.5 (CUL49.5) gene, a CHV regulatory protein ICP0
5 (cICP0) gene, a CHV membrane protein UL51 (CUL51) gene, and a CHV membrane protein UL45 (CUL45) gene. Particularly preferred non-essential genes to target include a CdUTPase gene, a CgC gene, a CgE gene, a CgG gene, a CgI gene, a CIR6 gene, a CUS2 gene and a CUS9 gene. It is to be noted that
10 CHV regions and genes disclosed herein are named in accordance with herpesvirus nomenclature in that the names include "C" for canine and the rest of the name indicating the corresponding herpes simplex virus type-1 (HSV-1) homolog, when one exists (e.g., "dUTPase"). For example,
15 the CHV unique short region (CUS) is the shorter region of the CHV genome that has unique sequences, analogous to the US region of HSV-1; and the CHV unique long region (CUL) is the longer region of CHV that has unique sequences, analogous to the UL region of HSV-1. While the CHV inverted repeat
20 regions (CIRs) are analogous to the HSV-1 IR regions, they appear to be most analogous to the equine herpesvirus type-1 (EHV-1) IR regions. CUS genes are CHV genes that are homologs of (i.e., genes that share some degree of similarity with) HSV-1 genes located in the US region of the HSV-1
25 genome. CUL genes are CHV genes that are homologs of HSV-1 genes located in the UL region of the HSV genome. CIR genes

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are CHV genes that are homologs of HSV-1 or EHV-1 genes located in the IR regions of the HSV-1 or EHV-1 genome. It is also to be noted that although the UL, US, and IR designations refer to the respective genes' locations in the HSV-1 or EHV-1 genome, they do not necessarily refer to the respective genes' locations in the CHV genome. For example, while CUS2 is partially in the IR region of CHV, HSV US2 is entirely in the US region of HSV.

Another embodiment of the present invention is a recombinant CHV that is defective for reproduction in tissue culture. A reproduction defective CHV is a CHV that when inserted into an appropriate host cell is unable to form infectious virus. Such a defective CHV has at least one inactive gene that encodes a protein essential for reproduction, including, but not limited to proteins essential for viral entry, immediate early or early gene expression, DNA replication, capsid assembly, and viral egress. Suitable gene targets include any essential CHV gene, with preferred targets being genes encoding proteins involved in viral entry and/or egress. CHV defective in viral entry and/or egress are easy to complement and are advantageous over most other reproduction defective mutants in that such virus are able to undergo one round of viral replication. An essential CHV gene can be identified by altering a CHV gene within a CHV genome and demonstrating (a) that the altered genome is not capable of effecting self-

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reproduction in tissue culture under wild type conditions or, if a temperature sensitive mutant, at a non-permissive temperature; and (b) that the altered genome can reproduce in a complementing cell line that expresses an active protein

5 corresponding to the essential gene defect on the CHV genome (assuming the defect can be complemented in trans), or at a permissive temperature. Preferred essential CHV genes to target include, but are not limited to, a CHV glycoprotein D (CgD) gene, a CHV glycoprotein B (CgB) gene, a CHV alpha

10 trans-inducing factor UL48 (CUL48) gene, a CHV helicase/primase UL52 (CUL52) gene, a CHV glycoprotein L (CgL) gene and a CHV ICP4 (cICP4) gene. Particularly preferred essential genes to target include a CgD gene and a CgB gene.

15 The present invention also includes cell lines that complement replication defective CHVs and use of such cell lines to produce replication defective viruses. As such, the present invention includes canine cell lines that complement, or supplement, a CHV defect in a gene encoding CgD, CgB,

20 CUL48, or CUL52, and/or CgL. Such cell lines can be produced by a variety of means known to those skilled in the art. For example, a cell capable of complementing a CgD negative, or CgD-, CHV (i.e., a virus with a CHV genome having an inactive CgD gene), can be produced by stable integration of an active

25 CgD gene into the cellular genome or by co-transfection of the CgD- CHV with a nucleic acid molecule capable of

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complementing the defective CgD gene. Such a nucleic acid molecule can be a nucleic acid containing an active CgD gene operatively linked to regulatory sequences to enable expression of the CgD gene in the transfected cell. In
5 another embodiment, such a nucleic acid molecule can be incorporated into a virus that is co-infected with the CgD-CHV. Such methods can also be used to produce cell lines complementing other replication defective CHVs of the present invention. Any canine cell line that CHV can infect and that
10 expresses the complementary active protein can be used in the production of reproduction-defective CHV. Examples include, but are not limited to, the following cell lines available from American Type Culture Collection (ATCC), Rockville, MD: ATCC CRL-1542 A-72 (Tumor, canine), ATCC CRL-1430 Cf2Th
15 (Thymus, canine, *Canis familiaris*), ATCC CRL-10389 DH82 (Monocyte-macrophage, canine), ATCC CRL-8468 D17 (Osteogenic sarcoma, canine), ATCC CCL-183 D-17 (Primary osteogenic sarcoma, canine, *Canis familiaris*), ATCC CCL-34.1 DoCl1 (S+L-) (Kidney, canine, *Canis familiaris*), ATCC CCL-34 MDCK
20 (NBL-2) (Kidney, canine, *Canis familiaris*), and ATCC CCL-34.2 MDCK/SF (Kidney, canine, *Canis familiaris*), such cell lines expressing, preferably in a stable manner, the desired essential gene(s) for complementation. Particularly preferred complementing cell lines include MDCK cells that
25 stably express CgD, CgB, CUL48, CUL52 and/or CgL.

An additional preferred CHV open reading frame to

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inactivate, or disrupt, includes a CUS8.5 open reading frame.

While not being bound by theory, it is believed that a reproductive defective virus-based vaccine may be safer than a reproduction competent virus-based vaccine. On the other
5 hand, a reproduction competent virus-based vaccine may be more efficacious than a reproduction defective virus-based vaccine. Since CHV, as disclosed above, exhibits low pathogenicity, a reproduction competent recombinant CHV is a preferred embodiment of the present invention.

10 As heretofore disclosed, one embodiment of the present invention is a recombinant CHV having one or more inactive genes. Preferred recombinant CHV of the present invention include genomes in which one or more of the following CHV genes have been inactivated, preferably using recombinant
15 techniques: a CdUTPase gene, a CgC gene, a CgE gene, a CgG gene, a CgI gene, a CPK gene, a CTK gene, a CIR6 gene, a CUS2 gene, a CUS9 gene, a CUL49 gene, a CUL51 gene, a CUL45 gene, a CgD gene, a CgB gene, a CUL48 gene, and a CUL52 gene, a CgL gene, a CUL49.5 gene, a CICP0 gene, a CICP4 gene, and a
20 CUS8.5 open reading frame. Other than the genes encoding CgD, CgB, CUL48, CUL52, CgL and CICP4, the preferred genes to inactivate are nonessential genes. Each of the preferred genes to inactivate is a preferred target for the insertion of heterologous nucleic acid molecules; such insertion is a
25 preferred method to inactivate these genes. More preferred recombinant CHV include genomes in which one or more of the

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following CHV genes have been inactivated, preferably using recombinant techniques: a CdUTPase gene, a CgC gene, a CgE gene, a CgG gene, a CgI gene, a CUS2 gene, a CUS9 gene, a CgD gene, and/or a CgB gene being more preferred. Also preferred
5 are the corresponding recombinant CHV genomes.

Particularly preferred recombinant CHV of this embodiment include a CdUTPase negative CHV, a CgC negative CHV, a CgE negative CHV, a CgG negative CHV, a CgI negative CHV, a CPK negative CHV, a CTK negative CHV, a CIR6 negative
10 CHV, a CUS2 negative CHV, a CUS9 negative CHV, a CUL49 negative CHV, a CUL51 negative CHV, a CUL45 negative CHV, a CgD negative CHV, a CgB negative CHV, a CUL48 negative CHV, a CUL52 negative CHV, a CgL negative CHV, a CUL49.5 negative CHV, a CICIP0 negative CHV, a CICIP4 negative CHV, and a CUS8.5
15 negative CHV. Particularly preferred recombinant CHV include a CdUTPase negative CHV, a CgC negative CHV, a CgE negative CHV, a CgG negative CHV, a CgI negative CHV, a CUS2 negative CHV, a CUS9 negative CHV, a CgD negative CHV, and a CgB negative CHV. Also preferred are the corresponding
20 recombinant CHV genomes, as well as recombinant CHV and CHV genomes having more than one of these preferred genes inactivated. Examples of such CHV include, but are not limited to: a CUS2 negative, CdUTPase negative CHV; a CUS2 negative, CdUTPase negative, CgG negative CHV; and a CUS2
25 negative, CdUTPase negative, CgG negative, CgC negative CHV, a CUL49.5, CdUTPase negative CHV.

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One embodiment of the present invention includes a recombinant CHV comprising a recombinant CHV genome comprising a heterologous nucleic acid molecule; i.e., the recombinant CHV genome includes one or more heterologous nucleic acid molecule(s) located, or positioned, in the CHV genome. The present invention also includes a recombinant CHV genome having a heterologous nucleic acid molecule in the genome. Also included is the use of such a CHV and/or CHV genome as a therapeutic composition as well as in the production of a compound encoded by the heterologous nucleic acid molecule(s).

As used herein, a heterologous nucleic acid molecule is a nucleic acid molecule that is not derived from CHV; that is, a heterologous nucleic acid molecule is isolated from a source other than CHV. An isolated nucleic acid molecule of the present invention can be obtained from its natural source, can be produced using recombinant DNA technology (e.g., by amplification, such as by polymerase chain reaction (PCR) amplification and/or cloning) or can be produced by chemical synthesis.

In accordance with the present invention, a heterologous nucleic acid molecule can be inserted into a CHV genome simply to inactivate a CHV gene. A heterologous nucleic acid molecule can also be inserted into a CHV genome to serve as a target for the insertion of a second heterologous nucleic acid molecule, such as to introduce a restriction enzyme site

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or a recombination site otherwise not present in the CHV genome. For example, CHV strain D 004 (available from ATCC), which does not contain a *Sse83871*, *I-Sce-I*, or *NotI* restriction enzyme site, can be genetically engineered to include one or more sites by inserting into the genome a heterologous nucleic acid molecule containing a *Sse83871*, *I-Sce-I*, and/or *NotI* site(s). Such a heterologous nucleic acid molecule is a good target for the insertion of another heterologous nucleic acid molecule. Other restriction enzyme sites lacking in CHV can be identified using techniques known to those skilled in the art. Without being bound by theory, it is believed that CHV is more likely to lack GC-rich restriction enzyme sites than AT-rich sites, since the CHV genome is AT-rich, as disclosed above.

Another example of a heterologous nucleic acid molecule to insert into a CHV genome is a gene encoding a selectable marker, such as, but not limited to, an *E. coli lacZ* gene, a green fluorescent protein gene, a chloramphenicol transacetylase gene, a xanthine-guanine phosphoribosyl transferase gene, a β -glucuronidase gene, a neomycin resistance gene, an *E. coli hygromycin* resistance gene, and a heterologous thymidine kinase gene (e.g., HSV, FHV; assuming the CHV genome is a CTK negative genome). The presence of such a gene in a CHV genome allows for the selection of recombinant CHV having such a marker gene, and includes the ability to distinguish recombinant CHV from natural CHV

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isolates. In addition, a second heterologous nucleic acid molecule can be inserted into such a selectable marker gene, thereby inactivating the protein encoded by the marker gene, allowing for yet another method to select for CHV having a
5 desirable heterologous nucleic acid molecule. Methods to select CHV having selectable marker genes, as well as for the inactivation of such markers, is known to those skilled in the art.

A preferred embodiment of the present invention is a
10 recombinant CHV genome, and corresponding virus, in which the genome contains a heterologous nucleic acid molecule operatively linked to a transcription control sequence. As such, the heterologous nucleic acid molecule can be transcribed when transfected into a cell. A heterologous
15 nucleic acid molecule can be joined to CHV transcription control sequences, can be joined to its own or other homologous transcription control sequences, and/or can be joined to transcription control sequences heterologous to both the heterologous nucleic acid molecule and CHV. The
20 heterologous nucleic acid molecule can also be operatively linked to other regulatory sequences. Suitable regulatory sequences include any regulatory sequence that can function in the present invention. Preferred transcription control sequences include those sequences that can function in canine
25 cells, including, but not limited to: mammalian, preferably canine; viral; or natural (i.e., endogenous to the

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heterologous nucleic acid molecule) transcription control sequences. Examples of transcription control sequences include antibiotic resistance gene, baculovirus, *Heliothis zea* insect virus, vaccinia virus, herpesvirus, poxvirus, 5 adenovirus, simian virus 40, retrovirus, actin, Rous sarcoma virus, heat shock, and mammalian hormone transcription control sequences. Additional suitable transcription control sequences include tissue-specific promoters and enhancers as well as lymphokine-inducible promoters (e.g., promoters 10 inducible by interferons or interleukins). In one embodiment, expression of a heterologous nucleic acid molecule inserted into a CHV genome is mediated, at least in part, by a human cytomegalovirus (CMV) immediate early promoter and a bovine growth hormone polyadenylation site.

15 A heterologous nucleic acid molecule of the present invention can be located in any region of the CHV genome (i.e., in the UL, US, and/or IR regions), including, but not limited to, in an essential gene, in a non-essential gene, or in an intergenic region. As such, a heterologous nucleic 20 acid molecule can be located in a coding region, a regulatory region, an intron, an untranslated region, or a non-transcribed region of a gene. A heterologous nucleic acid molecule can also be located in a direct or inverted repeat, including direct and/or inverted repeats within the IR, US or 25 UL regions of CHV. For example, a heterologous nucleic acid molecule can be located in one or more CHV origins of

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replication (Cori), such as in CoriS.

In one embodiment, a heterologous nucleic acid molecule is located in a CHV genome such that a gene is inactivated. Suitable and preferred gene targets are as disclosed above,
5 with non-essential gene targets being preferred.

In another embodiment, a heterologous nucleic acid molecule is located in a region of the CHV genome spanning from about the 3' end of the coding region of the CUL41 gene through about the 3' end of the coding region of the CUL38
10 gene. CUL41 gene refers to the CHV homolog of the HSV virion host shutoff protein UL41 gene. CUL38 gene refers to the CHV homolog of the HSV capsid protein VP19C UL38 gene. In most herpesviruses analyzed by cloning and sequencing techniques to date, the region between UL41 and UL38 contains genes
15 encoding the large and small subunits of ribonucleotide reductase. The inventors have found, however, that the ribonucleotide reductase genes appear to be at least partially deleted in CHV in such a manner that there is an intergenic target in that region for heterologous nucleic
20 acid molecule insertion.

A preferred recombinant CHV genome of the present invention comprises a heterologous nucleic acid molecule located in a region of the genome such that the heterologous nucleic acid molecule-containing CHV genome can be easily
25 distinguished from a CHV genome not containing the heterologous nucleic acid molecule; that is, the heterologous

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nucleic acid molecule is inserted into a selectable region of the genome. Suitable selectable regions include any region of the CHV genome that, upon introduction of a heterologous nucleic acid molecule, leads to a detectable (e.g., growth-
5 related, biochemical, or molecular) change in the CHV genome or CHV containing the genome. Examples of such selectable regions include, but are not limited to, a CTK gene and a CdUTPase gene. CHV genomes in which a heterologous nucleic acid molecule is inserted into a CTK gene or a CdUTPase gene
10 can be selected using methods known to those skilled in the art; see for example, Kit et al., 1983, *Virology* 130, 381-389; and Holliday et al., 1991, *Antiviral Research* 16, 197-203.

Additional examples of selectable regions include
15 restriction endonuclease sites, such as the *HindIII* site or *XbaI* site in the CdUTPase gene and the *AscI* site in the CUS2 gene. This diploid *AscI* site is particularly preferred as there are no other *AscI* sites in the CHV genome. As such, a particularly preferred CHV of the present invention is a
20 recombinant CHV having a CHV genome including a heterologous nucleic acid molecule in a naturally occurring *AscI* site in the CHV genome. The term "naturally occurring" denotes an *AscI* restriction site that is present in the wild-type CHV genome. Even more preferred is recombinant CHV strain D 004
25 having a heterologous nucleic acid molecule in a naturally occurring *AscI* site in the CHV genome. Also preferred are

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the corresponding genomes. Examples of methods to insert a heterologous nucleic acid molecule into a genome, including into restriction endonuclease site(s) in the genome, are disclosed herein. Such methods are known to those skilled in the art.

One embodiment of the present invention is a recombinant CHV genome having a heterologous nucleic acid molecule in one of the following regions of the CHV genome: a region spanning the 9,300 nucleotide *AscI* restriction endonuclease fragment, denoted herein as nCAsc₉₃₀₀, that apparently includes the entire US region; a region spanning the 10,000 nucleotide fragment from *AscI* to the end of the genome, denoted herein as nCAsc₁₀₀₀₀, that apparently essentially comprises an IR region, including the CIR6 gene; a region spanning the 3,000 nucleotide *HindIII* fragment, denoted herein as nChin₃₀₀₀, that spans from a portion of CUL48 through a portion of the CdUTPase gene; a region spanning the 1,900 nucleotide *HindIII* fragment, denoted herein as nChin₁₉₀₀, that includes the remainder of the CdUTPase gene through a portion of CUL52; a region spanning the 5,500 nucleotide *HindIII* fragment, denoted herein as nChin₅₅₀₀, that includes at least a portion of CgL, CICP0, and CICP4; and/or a region spanning the 8,500 nucleotide *HindIII* fragment, denoted herein as nChin₈₅₀₀, that includes a portion of CUL48, CUL45 and CgC. Details regarding the production of these and certain other nucleic acid molecules of the present invention

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are provided in the Examples section.

Also included in the present invention is a recombinant CHV genome having a heterologous nucleic acid molecule in a region of the genome spanning at least one of the following:

- 5 a CHV US region comprising nCUS₅₄₉₅, a CHV UL region comprising nCgC/CUL45₂₁₀₀, a CgE gene comprising nCgE₇₅₀, a CgI gene comprising nCgI₁₆₁, a CUS9 gene comprising nCUS9₅₇₉, a CHV UL region comprising nCdUTP/CUL51₇₄₃, a CTK gene comprising nCTK₂₈₀, a CUL48 gene comprising nCUL48₂₉₄, a CUL49 gene
- 10 included in nChin₃₀₀₀, a CUL52 gene comprising nCUL52₁₄₆, a CHV UL region comprising nCUL₁₈₂₃, a CHV UL region comprising nCUL49/CUL48₂₀₄₄, a CHV IR region comprising nCICP4₆₂₆, a CHV UL region comprising nCgI₆₅₅, a CHV UL region comprising nCUL52₇₄₉, a CHV UL region comprising nCdUTP₃₂₀₀, as well as
- 15 allelic variants of such (i.e., said, any of these) regions. As such, the present invention also includes a recombinant CHV genome having a heterologous nucleic acid molecule in a region of the genome spanning at least one of the following: a CIR6 gene including nCIR6₅₅₂, a CUS2 gene including
- 20 nCUS2₁₁₇₆, a CPK gene including nCPK₁₂₀₃, a CgG gene including nCgG₁₂₄₈, a CgD gene including nCgD₃₅₇, a CdUTPase gene including nCdUTP₄₅₉, a CUL51 gene including nCUL51₂₆₁, a CgD gene including nCgD₁₀₃₈, a CgI gene including nCgI₁₀₉₅, a CgE gene including nCgE₁₅₆₉, a CUS8.5 open reading frame including
- 25 nCUS8.5₂₃₇, a CUS9 gene including nCUS9₃₆₀, a CUL49 gene including nCUL49₄₂₀, a CUL48 gene including nCUL48₁₂₆₉, a CICP4

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gene including nCICP4₆₂₆, a CgL gene including nCgL₆₅₅, a CdUTPase gene including nCdUTP₉₁₈, a CUL49 gene including nCUL49₂₅₅, a CUL49.5 gene including nCUL49.5₂₆₁, and a CUL52 gene including nCUL52₇₄₉, as well as allelic variants of such regions.

As used herein, an allelic variant of a nucleic acid molecule, or region, for which nucleic acid sequence is provided herein is a nucleic acid molecule, or region, that occurs at essentially the same locus in another CHV genome as the nucleic acid molecule in CHV strain D 004, and that, due to natural variation caused by, for example, mutation or recombination, has a similar but not identical nucleic acid sequence. A coding region allelic variant typically encodes a protein having similar activity to that of the protein encoded by the gene to which it is being compared. An allelic variant can also comprise an alteration in the 5' or 3' untranslated regions of the gene, such as in regulatory control regions. Allelic variants are well known to those skilled in the art and would be expected to be found among the family of canine herpesviruses.

The present invention also includes a recombinant CHV genome having a heterologous nucleic acid molecule in a region of the genome spanning at least one of the following nucleic acid molecules: nCUS₅₄₉₅ (and, as such, nCIR6₅₅₂, nCUS2₁₁₇₆, nCPK₁₂₀₃, nCgG₁₂₄₈, and/or nCgD₃₅₇), nCgC/CUL45₂₁₀₀, nCgE₇₅₀, nCgI₁₆₁, nCUS9₅₇₉, nCdUTP/CUL51₇₄₃ (and, as such,

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nCdUTP₄₅₉ and nCUL51₂₆₁), nCTK₂₈₀, nCUL48₂₉₄, nCUL52₁₄₆, nCUS₁₀₅₉₂, nCgD₁₀₃₈, nCgI₁₀₉₅, nCgE₁₅₆₉, nCUS8.5₂₃₇, nCUS9₃₆₀, nCUL49/CUL48₂₀₄₄, nCUL49₄₂₀, nCUL48₁₂₆₉, nCICP4₆₂₆, nCgL₆₅₅, nCUL₁₈₂₃, nCdUTP₉₁₈, nCUL49.5₂₆₁, nCUL49₂₅₅, nCUL52₇₄₉, and/or nCdUTP₃₂₀₀, as well as
 5 allelic variants of such regions.

A particularly preferred CHV genome of the present invention includes a heterologous nucleic acid molecule located in a region of the CHV genome comprising (e.g., including, represented by, or identified by) at least one of
 10 the following nucleic acid sequences: SEQ ID NO:1, SEQ ID NO:2, SEQ ID NO:3, SEQ ID NO:5, SEQ ID NO:7, SEQ ID NO:9, SEQ ID NO:11, SEQ ID NO:13, SEQ ID NO:14, SEQ ID NO:15, SEQ ID NO:17, SEQ ID NO:19, SEQ ID NO:20, SEQ ID NO:21, SEQ ID NO:23, SEQ ID NO:24, SEQ ID NO:25, SEQ ID NO:27, SEQ ID
 15 NO:28, SEQ ID NO:29, SEQ ID NO:31, SEQ ID NO:32, SEQ ID NO:33, SEQ ID NO:35, SEQ ID NO:37, SEQ ID NO:38, SEQ ID NO:51, SEQ ID NO:52, SEQ ID NO:53, SEQ ID NO:55, SEQ ID NO:57, SEQ ID NO:59, SEQ ID NO:61, SEQ ID NO:63, SEQ ID NO:64, SEQ ID NO:65, SEQ ID NO:67, SEQ ID NO:69, SEQ ID
 20 NO:70, SEQ ID NO:71, SEQ ID NO:73, SEQ ID NO:74, SEQ ID NO:75, SEQ ID NO:77, SEQ ID NO:78, SEQ ID NO:79, SEQ ID NO:81, SEQ ID NO:83, SEQ ID NO:85, SEQ ID NO:86, and/or SEQ ID NO:87, as well as complements of such regions and allelic variants of such regions. The relationships between certain
 25 nucleic acid molecules and nucleic acid sequences of the present invention are detailed below. It should be noted

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that since nucleic acid sequencing technology is not entirely error-free, the sequences represented by the SEQ ID NOs in the present invention at best represent apparent nucleic acid or amino acid sequences of CHV nucleic acid molecules or
5 proteins of the present invention. It is also to be noted that a double-stranded nucleic acid molecule of the present invention for which a nucleic acid sequence has been determined for one strand that is represented by a SEQ ID NO also comprises a complementary strand having a sequence that
10 is a complement of that SEQ ID NO. As such, nucleic acid molecules of the present invention, which can be either double-stranded or single-stranded, include those nucleic acid molecules that form stable hybrids under stringent hybridization conditions with either a given SEQ ID NO
15 denoted herein and/or with the complement of that SEQ ID NO, which may or may not be denoted herein. Methods to deduce a complementary sequence are known to those skilled in the art.

The present invention includes a recombinant CHV genome that includes a heterologous nucleic acid molecule that
20 encodes a protective compound; the present invention also includes a recombinant CHV containing such a genome. As used herein, a protective compound is a compound that when administered to an animal protects that animal from a disease corresponding to that compound. For example, a compound
25 derived from *Dirofilaria immitis* protects an animal from heartworm and other related infections, whereas a compound

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derived from a virus protects an animal from disease caused by that and related viruses. As used herein, the ability of a compound to protect an animal from a disease refers to the ability of that protective compound to treat, ameliorate
5 and/or prevent the disease.

A protective compound of the present invention includes, but is not limited to, a protective protein and a protective RNA species. Essentially any heterologous nucleic acid molecule that encodes a protective protein or RNA can be used
10 in the present invention. A protective protein of the present invention can be, for example, an immunogen that elicits an immune response which will protect an animal from the corresponding disease or some other compound (e.g., an immunomodulator, a toxin, an enzyme, an antibody, or other
15 binding protein) that neutralizes and/or reduces the disease. A protective RNA of the present invention can be, for example, an RNA-based drug, a ribozyme, a molecule capable of triple helix formation, or an antisense RNA that effectively prevents the expression of a detrimental protein, thereby
20 protecting an animal from disease.

It is within the scope of the present invention to produce therapeutic compositions against a variety of diseases, including infectious diseases, genetic diseases, and other metabolic diseases, including diseases that lead to
25 abnormal cell growth, degenerative processes, and/or immunological defects. Therapeutic compositions of the

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present invention can protect animals from a variety of diseases including, but not limited to, allergies, autoimmune diseases, cancers, cardiovascular diseases, graft rejection, hematopoietic disorders, immunodeficiency diseases, 5 immunoproliferative diseases, immunosuppressive disorders, infectious diseases, inflammatory diseases, jaundice, septic shock, other immunological defects, as well as other genetic or metabolic defects.

One preferred embodiment of the present invention is a 10 recombinant CHV having a heterologous nucleic acid molecule within its genome that encodes a compound that protects a canid, or other animal susceptible to CHV infection, from infectious disease. Such disease can be caused by a variety of infectious agents, including, but not limited to, helminth 15 parasites, protozoan parasites, ectoparasites, fungi (including yeast), bacteria and/or viruses. It should also be noted that although some infectious agents have not been definitively classified into one of these groups, such infectious agents are also included in the present invention. 20 A preferred protective compound is derived from (e.g., obtained from natural source or produced using recombinant or synthetic chemistry techniques) an infectious agent.

Preferred helminth infectious agents to target include nematodes, cestodes and trematodes, with filariid, ascarid, 25 capillarid, strongylid, strongyloides, trichostrongyle, and trichurid, parasitic helminths being more preferred, and

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filariid nematodes being even more preferred. More preferred parasitic helminths to target include the following:

- Aelurostrongylus*, *Ancylostoma*, *Angiostrongylus*, *Ascaris*,
Brugia, *Bunostomum*, *Capillaria*, *Chabertia*, *Cooperia*,
5 *Crenosoma*, *Dictyocaulus*, *Diectophyme*, *Dipetalonema*,
Diphyllbothrium, *Diplydium*, *Dirofilaria* (e.g., *D. immitis*),
Dracunculus, *Echinococcus*, *Enterobius*, *Filaroides*,
Haemonchus, *Loa*, *Mansonella*, *Muellerius*, *Nanophyetus*,
Necator, *Nematodirus*, *Oesophagostomum*, *Onchocerca*,
10 *Opisthorchis*, *Ostertagia*, *Parafilaria*, *Paragonimus*,
Parascaris, *Physaloptera*, *Protostrongylus*, *Setaria*,
Spirometra, *Spirocera*, *Stephanofilaria*, *Strongyloides*,
Strongylus, *Taenia*, *Thelazia*, *Toxascaris*, *Toxocara*,
Trichinella, *Trichostrongylus*, *Trichuris*. *Uncinaria*, and
15 *Wuchereria*. More preferred helminths to target,
particularly with respect to being canine pathogens include
Ancylostoma, *Angiostrongylus*, *Brugia*, *Capillaria*, *Crenosoma*,
Diectophyme, *Dipetalonema*, *Diphyllbothrium*, *Diplydium*,
Dirofilaria, *Echinococcus*, *Filaroides*, *Nanophyetus*,
20 *Opisthorchis*, *Paragonimus*, *Physaloptera*, *Spirometra*,
Spirocera, *Strongyloides*, *Taenia*, *Toxascaris*, *Toxocara*,
Trichinella, *Trichuris*, and *Uncinaria*.

Preferred protozoal infectious agents to target include

- Acetospora*, *Apicomplexa*, *Ciliophora*, *Labyrinthomorphophora*,
25 *Microspora*, *Myxozoa* and *Sarcomastigophora*, with *Babesia*,
Balantidium, *Besnoitia*, *Cryptosporidium*, *Eimeria*,

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Encephalitozoon, Entamoeba, Giardia, Hammondia, Hepatozoon, Isospora, Leishmania, Microsporidia, Neospora, Nosema, Pentatrichomonas, Plasmodium, Pneumocystis, Sarcocystis, Schistosoma, Theileria, Toxoplasma, and Trypanosoma, being
5 *more preferred. More preferred protozoans to target, particularly with respect to being canine pathogens, include Babesia, Balantidium, Besnoitia, Cryptosporidium, Encephalitozoon, Entamoeba, Giardia, Hammondia, Hepatozoon, Isospora, Leishmania, Microsporidia, Neospora,*
10 *Pentatrichomonas, Pneumocystis, Sarcocystis, Schistosoma, Toxoplasma, and Trypanosoma.*

Preferred ectoparasite infectious agents to target include fleas, flies, mosquitoes, ticks, mites, lice, spiders, ants and true bugs, with fleas being more preferred.
15 More preferred are fleas of the genera *Ctenocephalides, Ctopsyllus, Diamanus, Echidnophaga, Nosopsyllus, Pulex, Tunga, and Xenopsylla*, with *Ctenocephalides canis* and *Ctenocephalides felis* fleas being particularly preferred.

Preferred fungal agents include *Absidia, Acremonium,*
20 *Alternaria, Aspergillus, Basidiobolus, Bipolaris, Blastomyces, Candida, Chlamydia, Coccidioides, Conidiobolus, Cryptococcus, Curvalaria, Epidermophyton, Exophiala, Geotrichum, Histoplasma, Madurella, Malassezia, Microsporum, Moniliella, Mortierella, Mucor, Paecilomyces, Penicillium,*
25 *Phialemonium, Phialophora, Prototheca, Pseudallescheria, Pseudomicrodochium, Pythium, Rhinosporidium, Rhizopus,*

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Scolecobasidium, *Sporothrix*, *Stemphylium*, *Trichophyton*, *Trichosporon*, and *Xylohypha*.

Preferred bacterial infectious agents to target include *Actinomyces*, *Bacillus*, *Bacteroides*, *Bordetella*, *Bartonella*
5 (e.g., *B. henselae*), *Borrelia* (e.g., *B. burgdorferi*), *Brucella*, *Campylobacter*, *Capnocytophaga*, *Clostridium*, *Corynebacterium*, *Coxiella*, *Dermatophilus*, *Enterococcus*, *Ehrlichia* (e.g., *E. canis*), *Escherichia*, *Francisella*, *Fusobacterium*, *Haemobartonella*, *Helicobacter*, *Klebsiella*,
10 L-form bacteria, *Leptospira*, *Listeria*, *Mycobacteria*, *Mycoplasma*, *Neorickettsia*, *Nocardia*, *Pasteurella*, *Peptococcus*, *Peptostreptococcus*, *Proteus*, *Pseudomonas*, *Rickettsia*, *Rochalimaea*, *Salmonella*, *Shigella*, *Staphylococcus*, *Streptococcus*, and *Yersinia* (e.g., *Y.*
15 *pestis*).

Preferred virus infectious agents to target include adenoviruses, caliciviruses, coronaviruses, distemper
viruses, hepatitis viruses, herpesviruses, immunodeficiency
viruses, infectious peritonitis viruses, leukemia viruses,
20 oncogenic viruses, panleukopenia viruses, papilloma viruses, parainfluenza viruses, parvoviruses, rabies viruses, and reoviruses, as well as other cancer-causing or cancer-related
viruses.

A preferred recombinant CHV of the present invention
25 includes a recombinant CHV genome having a heterologous nucleic acid molecule encoding a protective compound that

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elicits an immune response. As used herein, a protective compound that elicits an immune response refers to a compound that when administered to an animal in an appropriate manner, known to those skilled in the art, leads to the production of

5 an immune response in that animal against the protective compound. The immune response, which can include humoral and/or cell-mediated components, preferably protects the immunized animal against the disease(s) targeted by the protective compound. As such, preferred protective compounds

10 include, but are not limited to, antigens associated with diseases, as disclosed herein. Particularly preferred protective compounds of the present invention include *Dirofilaria immitis* antigens, *Toxoplasma gondii* antigens, *Sarcocystis* antigens, *Bartonella henselae* antigens, *Yersinia*

15 *pestis* antigens, flea antigens, flea allergens, viral antigens, and cancer antigens. Even more preferred protective compounds are those disclosed in the following patent applications and patent publications, which are incorporated by reference herein in their entireties: U.S.

20 Patent No. 5,356,622, issued October 18, 1994; U.S. Patent No. 5,399,485, issued March 21, 1995; U.S. Patent No. 5,418,137, issued May 23, 1995; PCT Publication No. WO 92/13560, published August 20, 1992; PCT Publication No. WO 93/10225, published May 27, 1993; PCT Publication No. WO

25 93/23077, published November 25, 1993; PCT Publication No. WO 94/15593, published July 21, 1994; PCT Publication No. WO

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- 94/17813, published August 18, 1994; PCT Publication No. WO 94/17824, published August 18, 1994; PCT Publication No. WO 95/24198, published September 14, 1995; PCT Publication No. WO 95/32988, published December 7, 1995; U.S. Serial No.
- 5 08/401,509, filed March 9, 1995; U.S. Serial No. 08/415,365, filed March 30, 1995; U.S. Serial No. 08/450,944, filed May 23, 1995; U.S. Serial No. 08/473,034, filed June 6, 1995; U.S. Serial No. 08/482,304, filed June 7, 1995; U.S. Serial No. 08/485,434, filed June 7, 1995; U.S. Serial No.
- 10 08/486,036, filed June 7, 1995; U.S. Serial No. 08/558,735 filed November 16, 1995; PCT Serial No. PCT/US95/13200, filed October 6, 1995; PCT Serial No. PCT/US95/14442, filed October 18, 1995; U.S. Serial No. 08/630,822, filed April 10, 1996; U.S. Serial No. 08/602,262, filed February 15, 1996; PCT
- 15 Serial No.: PCT/US96/03133, filed March filed April 24, 1996; PCT Serial No. PCT/US96/07709, filed May 23, 1996; and PCT Serial No. PCT/US96/09848, filed June 7, 1996, and related filings.

Another preferred protective compound of the present

20 invention is an immunomodulator. Suitable immunomodulators include compounds that enhance the immune response as well as compounds that suppress the immune response. Compounds that enhance the immune response include compounds that preferentially enhance humoral immunity as well as compounds

25 that preferentially enhance cell-mediated immunity. Suitable compounds can be selected depending on the disease being

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targeted. Suitable immunomodulators include, but are not limited to, cytokines, chemokines, superantigens, and other immunomodulators as well as compounds that induce the production of cytokines, chemokines and other

- 5 immunomodulators. Examples of such protective compounds include, but are not limited to, granulocyte macrophage colony stimulating factor (GM-CSF), granulocyte colony stimulating factor (G-CSF), macrophage colony stimulating factor (M-CSF), colony stimulating factor (CSF),
- 10 erythropoietin (EPO), interleukin 2 (IL-2), interleukin-3 (IL-3), interleukin 4 (IL-4), interleukin 5 (IL-5), interleukin 6 (IL-6), interleukin 7 (IL-7), interleukin 8 (IL-8), interleukin 10 (IL-10), interleukin 12 (IL-12), interferon gamma, interferon gamma inducing factor I (IGIF),
- 15 transforming growth factor beta (TGF- β), RANTES (regulated upon activation, normal T-cell expressed and presumably secreted), macrophage inflammatory proteins (e.g., MIP-1 alpha and MIP-1 beta), and Leishmania elongation initiating factor (LEIF).
- 20 One preferred embodiment of the present invention is a recombinant CHV having more than one heterologous nucleic acid molecule included in the CHV genome. Such a CHV can include two or more heterologous nucleic acid molecules encoding two or more protective compounds to protect an
- 25 animal from a given disease (e.g., two or more heartworm antigens), or can include two or more heterologous nucleic
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acid molecules encoding protective compounds each targeted against a different disease (e.g., a compound to protect an animal against heartworm and a compound to protect an animal against a viral infection). A preferred multivalent CHV can
5 also include an heterologous nucleic acid molecule encoding a protective compound that elicits an immune response as well as an heterologous nucleic acid molecule encoding an immunomodulator to enhance the desired immune response. Also included in the present invention are protective compounds
10 that are fusion, or multivalent, proteins comprising more than one functional domain.

The present invention also includes recombinant CHV genomes. As such, the invention includes any CHV genome disclosed herein, including those included in recombinant CHV
15 of the present invention. Also included in the present invention are cells comprising recombinant CHV genomes of the present invention. As used herein, a cell comprising a recombinant CHV genome is a cell into which a recombinant CHV genome has been introduced. Such introduction can be
20 accomplished by any method by which a nucleic acid molecule can be inserted into a cell. Such methods, known to those skilled in the art, include, but are not limited to, infection (i.e., with a virus comprising the genome), transfection, transformation, electroporation,
25 microinjection, lipofection, adsorption, and protoplast fusion. A preferred cell comprises a recombinant CHV having

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a heterologous nucleic acid molecule, which preferably is operatively linked to a transcription control sequence. Cells containing CHV genomes are useful in the production of recombinant CHV. Methods to produce recombinant CHV are disclosed herein.

The present invention also includes isolated CHV nucleic acid molecules. As used herein, a CHV nucleic acid molecule is a nucleic acid molecule that is derived from CHV. As such, the nucleic acid molecule can be produced, for example, by recovery of such a nucleic acid molecule directly from a CHV genome, by recombinant DNA techniques, or by chemical synthesis. That the CHV nucleic acid molecule is isolated indicates that the molecule is removed from its natural milieu. An isolated CHV nucleic acid molecule can include DNA, RNA, or derivatives of either DNA or RNA.

A preferred CHV nucleic acid molecule of the present invention is a CHV nucleic acid molecule that hybridizes under stringent hybridization conditions with at least one of the following: with a CdUTPase gene, a CgC gene, a CgE gene, a CgG gene, a CgI gene, a CPK gene, a CTK gene, a CIR6 gene, a CUS2 gene, a CUS9 gene, a CUL49 gene, a CUL51 gene, a CUL45 gene, a CgD gene, a CUL48 gene, a CgL gene, a CUL49.5 gene, a CICP4 gene, a CUS8.5 open reading frame, and/or a CUL52 gene; with other regions of a CUS; and/or with a region of the CHV genome spanning from about the 3' end of the coding region of the CUL41 gene through about the 3' end of the coding region

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of the CUL38 gene. The identifying characteristics of such regions, including the CHV genes listed, are heretofore described.

As used herein, stringent hybridization conditions refer to standard hybridization conditions under which nucleic acid molecules, including oligonucleotides, are used to identify molecules having similar nucleic acid sequences. Stringent hybridization conditions typically permit isolation of nucleic acid molecules having at least about 70% nucleic acid sequence identity with the nucleic acid molecule being used as a probe in the hybridization reaction. Formulae to calculate the appropriate hybridization and wash conditions to achieve hybridization permitting 30% or less mis-match between two nucleic acid molecules are disclosed, for example, in Meinkoth et al., 1984, *Anal. Biochem* 138, 267-284; Meinkoth et al., *ibid*, is incorporated by reference herein in its entirety. An example of such conditions includes, but is not limited to, the following:

Oligonucleotide probes of about 18-25 nucleotides in length with T_m 's ranging from about 50°C to about 65°C, for example, can be hybridized to nucleic acid molecules typically immobilized on a filter (e.g., nitrocellulose filter) in a solution containing 2X SSPE, 1% Sarkosyl, 5X Denhardt's and 0.1 mg/ml denatured salmon sperm DNA at a temperature as calculated using the formulae of Meinkoth et al., *ibid*. for about 2 to about 12 hours. The filters are then washed 3

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times in a wash solution containing 2X SSPE, 1% Sarkosyl at about 55°C for about 15 minutes each. The filters can be further washed in a wash solution containing 2X SSPE, 1% Sarkosyl at about 55°C for about 15 minutes per wash.

5 A CHV nucleic acid molecule of the present invention can include an isolated natural CHV gene or a homolog thereof, the latter of which is described in more detail below. A CHV nucleic acid molecule of the present invention can include one or more regulatory regions, full-length or partial coding
10 regions, or combinations thereof. The minimal size of a CHV nucleic acid molecule of the present invention is the minimal size that can form a stable hybrid with one of the aforementioned CHV genes and other regions under stringent hybridization conditions.

15 Isolated CHV nucleic acid molecules include natural nucleic acid molecules and homologs thereof, including, but not limited to, natural allelic variants and modified nucleic acid molecules in which nucleotides have been inserted, deleted, substituted, and/or inverted in such a manner that
20 such modifications do not substantially interfere with the nucleic acid molecule's ability to encode a CHV protein of the present invention or to form stable hybrids under stringent conditions with natural gene isolates.

A CHV nucleic acid molecule homolog can be produced
25 using a number of methods known to those skilled in the art (see, for example, Sambrook et al., *ibid.*). CHV nucleic acid

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molecule homologs can be selected from a mixture of modified nucleic acids by screening for the function of the protein encoded by the nucleic acid molecule and/or by hybridization with a CHV region as defined above.

5 An isolated CHV nucleic acid molecule of the present invention can include a nucleic acid sequence that encodes at least one CHV protein of the present invention; such proteins are discussed in further detail below. Although the phrase "nucleic acid molecule" primarily refers to the physical
10 nucleic acid molecule and the phrase "nucleic acid sequence" primarily refers to the sequence of nucleotides on the nucleic acid molecule, the two phrases can be used interchangeably, especially with respect to a nucleic acid molecule, or a nucleic acid sequence, being capable of
15 encoding a CHV protein.

One embodiment of the present invention is a CHV nucleic acid molecule that, when administered to an animal, is capable of protecting that animal from CHV infection. Such a CHV nucleic acid molecule can be, or encode, an antisense
20 RNA, a molecule capable of triple helix formation, a ribozyme, or other nucleic acid-based drug compound. In an additional embodiment, a CHV nucleic acid molecule of the present invention can encode a protective protein, the nucleic acid molecule being delivered to the animal by direct
25 injection (i.e., as a naked nucleic acid) or in a vehicle such as a recombinant virus vaccine or a recombinant cell vaccine.

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One embodiment of the present invention is a CHV nucleic acid molecule that hybridizes under stringent hybridization conditions with nCUS₅₄₉₅, nCgC/CUL45₂₁₀₀, nCgE₇₅₀, nCgI₁₆₁, nCUS₉₅₇₉, nCdUTP/CUL51₇₄₃, nCTK₂₈₀, nCUL48₂₉₄, a nCUL49 included

5 in nChin₃₀₀₀, nCUL52₁₄₆, nCgI₁₀₉₅, nCgE₁₅₆₉, nCUS8.5₂₃₇, nCUS₉₃₆₀, nCUL49/CUL48₂₀₄₄, nCUL49₄₂₀, nCUL48₁₂₆₉, nCICP4₆₂₆, nCgL₆₅₅, nCUL₁₈₂₃, nCdUTP₉₁₈, nCUL49.5₂₆₁, nCUL49₂₅₅, and/or nCUL52₇₄₉.

Such a CHV nucleic acid molecule can also hybridize under stringent hybridization conditions with nCAsc₉₃₀₀, nCAsc₁₀₀₀₀,

10 nChin₃₀₀₀, nChin₁₉₀₀, nChin₅₅₀₀, nChin₈₅₀₀, nCIR6₅₅₂, nCUS2₁₁₇₆, nCPK₁₂₀₃, nCgG₁₂₄₈, nCgD₃₅₇, nCdUTP₄₅₉, nCTK₂₇₉, nCUS₉₄₅₀, nCUL48₂₉₁, nCUL51₂₆₁, nCUL52₁₄₆, nCgI₁₅₉, nCUS₁₀₅₉₂, nCICP4₆₂₄, nCgL₅₁₆, nCUL52₇₄₇, nCdUTP₈₅₈, and/or nCdUTP₃₂₀₀. At least some of such CHV nucleic acid molecules can hybridize under stringent

15 hybridization conditions with a nucleic acid molecule having nucleic acid sequence SEQ ID NO:1, SEQ ID NO:2, SEQ ID NO:13, SEQ ID NO:14, SEQ ID NO:17, SEQ ID NO:19, SEQ ID NO:21, SEQ ID NO:23, SEQ ID NO:25, SEQ ID NO:27, SEQ ID NO:29, SEQ ID NO:31, SEQ ID NO:35, SEQ ID NO:37, SEQ ID NO:51, SEQ ID

20 NO:52, SEQ ID NO:63, SEQ ID NO:64, SEQ ID NO:69, SEQ ID NO:70, SEQ ID NO:71, SEQ ID NO:73, SEQ ID NO:74, SEQ ID NO:77, SEQ ID NO:78, SEQ ID NO:85, SEQ ID NO:86, and/or SEQ ID NO:87, as well as complements of such sequences.

SEQ ID NO:1 and SEQ ID NO:2 represent the deduced

25 nucleic acid sequences of the two complementary strands of nCUS₅₄₉₅. Translation of SEQ ID NO:1 and SEQ ID NO:2

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indicates that nucleic acid molecule nCUS₅₄₉₅ encodes CIR6, CUS2, CPK and CgG proteins as well as a portion of a CgD protein. Specifically, SEQ ID NO:2 includes: a coding region for a CIR6 protein of about 183 amino acids, denoted herein
5 as nCIR6₅₅₂ and represented by SEQ ID NO:3, assuming a start codon spanning about nucleotides 4566-4568 and a stop codon spanning about nucleotides 5115-5117 of SEQ ID NO:2; and a coding region for a CUS2 protein of about 391 amino acids, denoted herein as nCUS2₁₁₇₆ and represented by SEQ ID NO:5,
10 assuming a start codon spanning about nucleotides 3232-3234 and a stop codon spanning about nucleotides 4405-4407 of SEQ ID NO:2. The amino acid sequences of the respective encoded proteins PCIR6₁₈₃ and PCUS2₃₉₁ are represented by SEQ ID NO:4 and SEQ ID NO:6. SEQ ID NO:1 includes: a coding region for a
15 CPK protein of about 400 amino acids, denoted herein as nCPK₁₂₀₃ and represented by SEQ ID NO:7, assuming a start codon spanning about nucleotides 2384-2386 and a stop codon spanning about nucleotides 3584-3586 of SEQ ID NO:1; a coding region for a CgG protein of about 415 amino acids, denoted
20 herein as nCgG₁₂₄₈ and represented by SEQ ID NO:9, assuming a start codon spanning about nucleotides 3698-3700 and a stop codon spanning about nucleotides 4943-4945 of SEQ ID NO:1; and a partial coding region for a CgD protein of about 119 amino acids, denoted herein as nCgD₃₅₇ and represented by SEQ
25 ID NO:11, assuming a start codon spanning about nucleotides 5137-5139. The amino acid sequences of the respective

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encoded proteins PCPK₄₀₀, PCgG₄₁₅, and PCgD₁₁₉ are represented by SEQ ID NO:8, SEQ ID NO:10 and SEQ ID NO:12.

SEQ ID NO:13 and SEQ ID NO:14 represent the deduced nucleic acid sequences of the two complementary strands of 5 nCdUTP/CUL51₇₄₃. SEQ ID NO:13 includes a partial coding region for a CdUTPase protein of about 152 amino acids, denoted herein as nCdUTP₄₅₉ and represented by SEQ ID NO:15, assuming a first in-frame codon spanning about nucleotides 3-5, and a stop codon spanning about nucleotides 459-461 of SEQ 10 ID NO:13. The amino acid sequence of the encoded protein PCdUTP₁₅₂ is represented by SEQ ID NO:16. SEQ ID NO:14 includes a partial coding region for a CUL51 protein of about 86 amino acids, denoted herein as nCUL51₂₆₁ and represented by SEQ ID NO:33, assuming a first in-frame codon spanning about 15 nucleotides 1-3, and a stop codon spanning about nucleotides 259-261 of SEQ ID NO:14. The amino acid sequence of the encoded protein PCUL51₈₆ is represented by SEQ ID NO:34.

SEQ ID NO:17 and SEQ ID NO:19 represent the deduced nucleic acid sequences of the two complementary strands of 20 nCUS9₅₇₉. SEQ ID NO:17 includes a coding region for a CUS9 protein of about 149 amino acids, denoted herein as nCUS9₄₅₀ and represented by SEQ ID NO:20, assuming a start codon spanning about nucleotides 54-56 and a stop codon spanning about nucleotides 501-503 of SEQ ID NO:17. The amino acid 25 sequence of the encoded protein PCUS9₁₄₉ is represented by SEQ ID NO:18.

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SEQ ID NO:21 and SEQ ID NO:23 represent the deduced nucleic acid sequences of the two complementary strands of nCUL48₂₉₄. SEQ ID NO:21 includes a partial coding region for a CUL48 protein of about 97 amino acids, denoted herein as
5 nCUL48₂₉₁ and represented by SEQ ID NO:24, assuming a first in-frame codon spanning about nucleotides 3-5 of SEQ ID NO:21. The amino acid sequence of the encoded protein PCUL48₉₇ is represented by SEQ ID NO:22.

SEQ ID NO:25 and SEQ ID NO:27 represent the deduced
10 nucleic acid sequences of the two complementary strands of nCUL52₁₄₆. SEQ ID NO:25 includes a partial coding region for a CUL52 protein of about 48 amino acids, denoted herein as nCUL52₁₄₄ and represented by SEQ ID NO:28, assuming a first in-frame codon spanning about nucleotides 1-3 of SEQ ID
15 NO:25. The amino acid sequence of the encoded protein PCUL52₄₈ is represented by SEQ ID NO:26.

SEQ ID NO:29 and SEQ ID NO:31 represent the deduced nucleic acid sequences of the two complementary strands of nCgI₁₆₁. SEQ ID NO:29 includes a partial coding region for a
20 CgI protein of about 53 amino acids, denoted herein as nCgI₁₅₉ and represented by SEQ ID NO:32, assuming a first in-frame codon spanning about nucleotides 3-5 of SEQ ID NO:29. The amino acid sequence of the encoded protein PCgI₅₃ is represented by SEQ ID NO:30.

25 SEQ ID NO:35 and SEQ ID NO:37 represent the deduced nucleic acid sequences of the two complementary strands of

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nCTK₂₈₀. SEQ ID NO:35 includes a partial coding region for a CTK protein of about 93 amino acids, denoted herein as nCTK₂₇₉ and represented by SEQ ID NO:38, assuming a first in-frame codon spanning about nucleotides 2-4 of SEQ ID NO:35. The
5 amino acid sequence of the encoded protein PCTK₉₃ is represented by SEQ ID NO:36.

The identities of additional nucleic acid molecules, nucleic acid sequences, proteins, and amino acid sequences are presented in the Examples.

10 Comparison of the CHV nucleic acid sequences SEQ ID NO:1, SEQ ID NO:2, SEQ ID NO:3, SEQ ID NO:5, SEQ ID NO:7, SEQ ID NO:9, SEQ ID NO:13, SEQ ID NO:14, SEQ ID NO:15, SEQ ID NO:17, SEQ ID NO:19, SEQ ID NO:20, SEQ ID NO:21, SEQ ID NO:23, SEQ ID NO:24, SEQ ID NO:25, SEQ ID NO:27, SEQ ID
15 NO:28, SEQ ID NO:29, SEQ ID NO:31, SEQ ID NO:32, SEQ ID NO:33, SEQ ID NO:35, SEQ ID NO:37, SEQ ID NO:38, SEQ ID NO:51, SEQ ID NO:52, SEQ ID NO:55, SEQ ID NO:57, SEQ ID NO:59, SEQ ID NO:61, SEQ ID NO:63, SEQ ID NO:64, SEQ ID NO:65, SEQ ID NO:67, SEQ ID NO:69, SEQ ID NO:70, SEQ ID
20 NO:71, SEQ ID NO:73, SEQ ID NO:74, SEQ ID NO:75, SEQ ID NO:77, SEQ ID NO:78, SEQ ID NO:79, SEQ ID NO:81, SEQ ID NO:83, SEQ ID NO:85, SEQ ID NO:86, and SEQ ID NO:87 with known sequences indicates that none of these CHV nucleic acid
sequences share more than about 70% identity (many, if not
25 all, sharing significantly less identity) with a known nucleic acid sequence. As such, a preferred CHV nucleic acid

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molecule has a nucleic acid sequence that is at least about 80%, preferably at least about 85%, more preferably at least about 90%, even more preferably at least about 95%, and even more preferably at least about 99% identical to nucleic acid

5 sequence SEQ ID NO:1, SEQ ID NO:2, SEQ ID NO:3, SEQ ID NO:5, SEQ ID NO:7, SEQ ID NO:9, SEQ ID NO:13, SEQ ID NO:14, SEQ ID NO:15, SEQ ID NO:17, SEQ ID NO:19, SEQ ID NO:20, SEQ ID NO:21, SEQ ID NO:23, SEQ ID NO:24, SEQ ID NO:25, SEQ ID NO:27, SEQ ID NO:28, SEQ ID NO:29, SEQ ID NO:31, SEQ ID

10 NO:32, SEQ ID NO:33, SEQ ID NO:35, SEQ ID NO:37, SEQ ID NO:38, SEQ ID NO:51, SEQ ID NO:52, SEQ ID NO:55, SEQ ID NO:57, SEQ ID NO:59, SEQ ID NO:61, SEQ ID NO:63, SEQ ID NO:64, SEQ ID NO:65, SEQ ID NO:67, SEQ ID NO:69, SEQ ID NO:70, SEQ ID NO:71, SEQ ID NO:73, SEQ ID NO:74, SEQ ID

15 NO:75, SEQ ID NO:77, SEQ ID NO:78, SEQ ID NO:79, SEQ ID NO:81, SEQ ID NO:83, SEQ ID NO:85, SEQ ID NO:86, and/or SEQ ID NO:87, as well as complements of such sequences.

A more preferred CHV nucleic acid molecule of the present invention includes at least a portion of CHV nucleic

20 acid molecule nCAsc₉₃₀₀, nCAsc₁₀₀₀₀, nChin₃₀₀₀, nChin₁₉₀₀, nChin₅₅₀₀, nChin₈₅₀₀, nCUS₅₄₉₅, nCIR₆₅₅₂, nCUS₂₁₁₇₆, nCPK₁₂₀₃, nCgG₁₂₄₈, nCdUTP/CUL₅₁₇₄₃, nCdUTP₄₅₉, nCUS₉₅₇₉, nCUS₉₄₅₀, nCUL₄₈₂₉₄, nCUL₄₈₂₉₁, nCUL₅₂₁₄₆, nCUL₅₂₁₄₄, nCgI₁₆₁, nCgI₁₅₉, nCgE₇₅₀, nCTK₂₈₀, nCTK₂₇₉, nCUL₅₁₂₆₁, nCUS₁₀₅₉₂, nCgI₁₀₉₅, nCgE₁₅₆₉, nCUS_{8.5237},

25 nCUS₉₃₆₀, nCUL_{49/CUL482044}, nCUL₄₉₄₂₀, nCUL₄₈₁₂₆₉, nCICP₄₆₂₆, nCICP₄₆₂₄, nCgL₆₅₅, nCgL₅₁₆, nCUL₁₈₂₃, nCdUTP₉₁₈, nCUL_{49.5261},

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nCUL49₂₅₅, nCUL52₇₄₉, nCUL52₇₄₇, nCdUTP₈₅₈, and/or nCdUTP₃₂₀₀, as well as allelic variants of those CHV nucleic acid molecules. Such CHV nucleic acid molecules can include nucleotides in addition to those included in the defined fragments; examples

5 of such CHV nucleic acid molecules include full-length genes, full-length coding regions, or nucleic acid molecules encoding multivalent proteins. Particularly preferred CHV nucleic acid molecules are nCAsc₉₃₀₀, nCAsc₁₀₀₀₀, nCHin₃₀₀₀, nCHin₁₉₀₀, nCHin₅₅₀₀, nCHin₈₅₀₀, nCUS₅₄₉₅, nCIR₆₅₅₂, nCUS₂₁₁₇₆,

10 nCPK₁₂₀₃, nCgG₁₂₄₈, nCdUTP/CUL51₇₄₃, nCdUTP₄₅₉, nCUS₉₅₇₉, nCUS₉₄₅₀, nCUL48₂₉₄, nCUL48₂₉₁, nCUL52₁₄₆, nCUL52₁₄₄, nCgI₁₆₁, nCgI₁₅₉, nCgE₇₅₀, nCTK₂₈₀, nCTK₂₇₉, nCUL51₂₆₁, nCUS₁₀₅₉₂, nCgI₁₀₉₅, nCgE₁₅₆₉, nCUS_{8.5237}, nCUS₉₃₆₀, nCUL49/CUL48₂₀₄₄, nCUL49₄₂₀, nCUL48₁₂₆₉, nCICP4₆₂₆, nCICP4₆₂₄, nCgI₆₅₅, nCgI₅₁₆, nCUL₁₈₂₃, nCdUTP₉₁₈,

15 nCUL49.5₂₆₁, nCUL49₂₅₅, nCUL52₇₄₉, nCUL52₇₄₇, nCdUTP₈₅₈, and/or nCdUTP₃₂₀₀,

Similarly, a preferred CHV nucleic acid molecule of the present invention includes at least a portion of nucleic acid sequence SEQ ID NO:1, SEQ ID NO:2, SEQ ID NO:3, SEQ ID NO:5,

20 SEQ ID NO:7, SEQ ID NO:9, SEQ ID NO:13, SEQ ID NO:14, SEQ ID NO:15, SEQ ID NO:17, SEQ ID NO:19, SEQ ID NO:20, SEQ ID NO:21, SEQ ID NO:23, SEQ ID NO:24, SEQ ID NO:25, SEQ ID NO:27, SEQ ID NO:28, SEQ ID NO:29, SEQ ID NO:31, SEQ ID NO:32, SEQ ID NO:33, SEQ ID NO:35, SEQ ID NO:37, SEQ ID

25 NO:38, SEQ ID NO:51, SEQ ID NO:52, SEQ ID NO:55, SEQ ID NO:57, SEQ ID NO:59, SEQ ID NO:61, SEQ ID NO:63, SEQ ID

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NO:64, SEQ ID NO:65, SEQ ID NO:67, SEQ ID NO:69, SEQ ID
NO:70, SEQ ID NO:71, SEQ ID NO:73, SEQ ID NO:74, SEQ ID
NO:75, SEQ ID NO:77, SEQ ID NO:78, SEQ ID NO:79, SEQ ID
NO:81, SEQ ID NO:83, SEQ ID NO:85, SEQ ID NO:86, and/or SEQ
5 ID NO:87; or a complement of SEQ ID NO:3, SEQ ID NO:5, SEQ ID
NO:7, SEQ ID NO:9, SEQ ID NO:15, SEQ ID NO:20, SEQ ID NO:24,
SEQ ID NO:28, SEQ ID NO:32, SEQ ID NO:33, SEQ ID NO:38, SEQ
ID NO:55, SEQ ID NO:57, SEQ ID NO:59, SEQ ID NO:61, SEQ ID
NO:65, SEQ ID NO:67, SEQ ID NO:71, SEQ ID NO:75, SEQ ID
10 NO:79, SEQ ID NO:81, SEQ ID NO:83, and/or SEQ ID NO:87; as
well as allelic variants of such nucleic acid molecules.
More preferred is a nucleic acid molecule that includes at
least one of the following nucleic acid sequences: SEQ ID
NO:1, SEQ ID NO:2, SEQ ID NO:3, SEQ ID NO:5, SEQ ID NO:7, SEQ
15 ID NO:9, SEQ ID NO:13, SEQ ID NO:14, SEQ ID NO:15, SEQ ID
NO:17, SEQ ID NO:19, SEQ ID NO:20, SEQ ID NO:21, SEQ ID
NO:23, SEQ ID NO:24, SEQ ID NO:25, SEQ ID NO:27, SEQ ID
NO:28, SEQ ID NO:29, SEQ ID NO:31, SEQ ID NO:32, SEQ ID
NO:33, SEQ ID NO:35, SEQ ID NO:37, SEQ ID NO:38, SEQ ID
20 NO:51, SEQ ID NO:52, SEQ ID NO:55, SEQ ID NO:57, SEQ ID
NO:59, SEQ ID NO:61, SEQ ID NO:63, SEQ ID NO:64, SEQ ID
NO:65, SEQ ID NO:67, SEQ ID NO:69, SEQ ID NO:70, SEQ ID
NO:71, SEQ ID NO:73, SEQ ID NO:74, SEQ ID NO:75, SEQ ID
NO:77, SEQ ID NO:78, SEQ ID NO:79, SEQ ID NO:81, SEQ ID
25 NO:83, SEQ ID NO:85, SEQ ID NO:86, and/or SEQ ID NO:87; or a
complement SEQ ID NO:5, SEQ ID NO:7, SEQ ID NO:9, SEQ ID

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NO:15, SEQ ID NO:20, SEQ ID NO:24, SEQ ID NO:28, SEQ ID
NO:32, SEQ ID NO:33, SEQ ID NO:38, SEQ ID NO:55, SEQ ID
NO:57, SEQ ID NO:59, SEQ ID NO:61, SEQ ID NO:65, SEQ ID
NO:67, SEQ ID NO:71, SEQ ID NO:75, SEQ ID NO:79, SEQ ID
5 NO:81, SEQ ID NO:83, and/or SEQ ID NO:87; also included are
nucleic acid molecules that are allelic variants of nucleic
acid molecules having those nucleic acid sequences. Such
nucleic acid molecules can include nucleotides in addition to
those included in the SEQ ID NOs.

10 The present invention also includes CHV nucleic acid
molecules encoding a protein, including nucleic acid
molecules that have been modified to accommodate codon usage
properties of the cells in which such nucleic acid molecules
are to be expressed. CHV proteins of the present invention
15 are described in more detail below. Particularly preferred
nucleic acid molecules are those that encode a protein having
at least one of the following amino acid sequences: SEQ ID
NO:4, SEQ ID NO:6, SEQ ID NO:8, SEQ ID NO:10, SEQ ID NO:16,
SEQ ID NO:18, SEQ ID NO:22, SEQ ID NO:26, SEQ ID NO:30, SEQ
20 ID NO:34, SEQ ID NO:36, SEQ ID NO:56, SEQ ID NO:58, SEQ ID
NO:60, SEQ ID NO:62, SEQ ID NO:66, SEQ ID NO:68, SEQ ID
NO:72, SEQ ID NO:76, SEQ ID NO:80, SEQ ID NO:82, SEQ ID
NO:84, and/or SEQ ID NO:88.

The present invention also includes CHV nucleic acid
25 molecules that are oligonucleotides capable of hybridizing,
under stringent hybridization conditions, with complementary

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regions of other, preferably longer, CHV nucleic acid molecules of the present invention. Oligonucleotides of the present invention can be RNA, DNA, or derivatives of either. The minimal size of such oligonucleotides is the size
5 required to form a stable hybrid between a given oligonucleotide and the complementary sequence on another nucleic acid molecule of the present invention. Minimal size characteristics are disclosed herein. The size of the oligonucleotide must also be sufficient for the use of the
10 oligonucleotide in accordance with the present invention. Oligonucleotides of the present invention can be used in a variety of applications including, but not limited to, as probes to identify additional nucleic acid molecules, as primers to amplify or extend nucleic acid molecules or in
15 therapeutic applications to inhibit CHV infection as disclosed herein.

The present invention also includes an isolated CHV protein encoded by a CHV nucleic acid molecule of the present invention. As such, the present invention includes a CHV
20 protein encoded by a CHV nucleic acid molecule that hybridizes under stringent hybridization conditions with at least one of the following: a CdUTPase gene, a CgC gene, a CgE gene, a CgG gene, a CgI gene, a CPK gene, a CTK gene, a CIR6 gene, a CUS2 gene, a CUS9 gene, a CUL49 gene, a CUL51
25 gene, a CUL45 gene, a CgD gene, a CUL48 gene, and/or a CUL52 gene; and/or with other portions of a CUS region; and/or with

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a CgI gene, a CUL49.5 gene, a CICP4 gene, and/or a CUS8.5 open reading frame.

According to the present invention, an isolated, or biologically pure, protein, is a protein that has been
5 removed from its natural milieu. As such, "isolated" and "biologically pure" do not necessarily reflect the extent to which the protein has been purified. An isolated protein of the present invention can be obtained from its natural source, can be produced using recombinant DNA technology or
10 can be produced by chemical synthesis. As used herein, a CHV protein can be a full-length protein or any homolog of such a protein. Examples of CHV homologs include CHV proteins in which amino acids have been deleted (e.g., a truncated version of the protein, such as a peptide), inserted,
15 inverted, substituted and/or derivatized (e.g., by glycosylation, phosphorylation, acetylation, myristoylation, prenylation, palmitoylation, amidation and/or addition of glycerophosphatidyl inositol) such that the homolog retains a desired activity of the natural protein, such as, but not
20 limited to, enzymatic activity, activity important for viral growth, and/or ability to elicit an immune response. These activities can be measured using techniques known to those skilled in the art.

CHV protein homologs can be the result of natural
25 allelic variation or natural mutation. CHV protein homologs of the present invention can also be produced using

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techniques known in the art including, but not limited to, direct modifications to the protein or modifications to the gene encoding the protein using, for example, classic or recombinant DNA techniques to effect random or targeted
5 mutagenesis.

The minimal size of a CHV protein homolog of the present invention is a size sufficient to be encoded by a nucleic acid molecule capable of forming a stable hybrid (i.e., hybridize under stringent hybridization conditions) with the
10 complementary sequence of a nucleic acid molecule encoding the corresponding natural protein. As such, the size of the nucleic acid molecule encoding such a protein homolog is dependent on nucleic acid composition and percent homology between the nucleic acid molecule and complementary sequence.
15 It should also be noted that the extent of homology required to form a stable hybrid can vary depending on whether the homologous sequences are interspersed throughout the nucleic acid molecules or are clustered (i.e., localized) in distinct regions on the nucleic acid molecules. The minimal size of
20 such nucleic acid molecules is typically at least about 12 to about 15 nucleotides in length if the nucleic acid molecules are GC-rich and at least about 15 to about 17 bases in length if they are AT-rich. As such, the minimal size of a nucleic acid molecule used to encode a CHV protein homolog of the
25 present invention is from about 12 to about 18 nucleotides in length. There is no limit, other than a practical limit, on

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the maximal size of such a nucleic acid molecule in that the nucleic acid molecule can include a portion of a gene, an entire gene, or multiple genes, or portions thereof.

Similarly, the minimal size of a CHV protein homolog of the
5 present invention is from about 4 to about 6 amino acids in length, with preferred sizes depending on whether full-length, fusion, or other functional portions of such proteins are desired.

One embodiment of the present invention is a CHV protein
10 that can protect an animal from disease, preferably by eliciting an immune response against CHV, and/or can detect CHV infection in an animal. The minimum size of such a protein is a minimum size sufficient to form an epitope, a size that typically is at least from about 5 to about 9 amino
15 acids. As is appreciated by those skilled in the art, an epitope can include amino acids that naturally are contiguous to each other as well as amino acids that, due to the tertiary structure of the natural protein, are in sufficiently close proximity to form an epitope.

20 The present invention also includes mimetopes of CHV proteins that can be used in accordance with methods as disclosed for CHV proteins of the present invention. As used herein, a mimetope of a CHV protein of the present invention refers to any compound that is able to mimic the activity of
25 such a CHV protein, often because the mimetope has a structure that mimics the CHV protein. Mimetopes can be, but

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are not limited to: peptides that have been modified to decrease their susceptibility to degradation; anti-idiotypic and/or catalytic antibodies, or fragments thereof; non-proteinaceous immunogenic portions of an isolated protein
5 (e.g., carbohydrate structures); and synthetic or natural organic molecules, including nucleic acids. Such mimetopes can be designed using computer-generated structures of proteins of the present invention. Mimetopes can also be obtained by generating random samples of molecules, such as
10 oligonucleotides, peptides or other organic molecules, and screening such samples by affinity chromatography techniques using the corresponding binding partner.

One embodiment of the present invention is a fusion, or multivalent, protein that includes a CHV protein-containing
15 domain attached to another functional domain. Such a domain can be an entire protein, or function portion thereof. Examples of such domains include not only protective compounds as disclosed above, but also domains that enhance a protein's stability (e.g., during production, storage and/or
20 use) or that aid in protein purification.

A preferred isolated protein of the present invention is a protein encoded by a nucleic acid molecule that hybridizes under stringent hybridization conditions with nCIR₆₅₅₂,
nCUS₂₁₁₇₆, nCPK₁₂₀₃, nCgG₁₂₄₈, nCgD₃₅₇, nCgC/CUL45₂₁₀₀, nCdUTP₄₅₉,
25 nCUS₉₄₅₀, nCUL48₂₉₁, nCUL52₁₄₄, nCgI₁₅₉, nCgE₇₅₀, nCTK₂₇₉, nCUL51₂₆₁,
nCgI₁₀₉₅, nCgE₁₅₆₉, nCUS8.5₂₃₇, nCUS₉₃₆₀, nCUL49/CUL48₂₀₄₄,

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nCUL49₄₂₀, nCUL48₁₂₆₉, nCICP4₆₂₆, nCgL₆₅₅, nCUL₁₈₂₃, nCdUTP₉₁₈, nCUL49.5₂₆₁, nCUL49₂₅₅, and/or nCUL52₇₄₉. Also included is a protein that hybridizes under stringent hybridization conditions with nCAsc₉₃₀₀, nCAsc₁₀₀₀₀, nCHin₃₀₀₀, nCHin₁₉₀₀, 5 nCHin₅₅₀₀, and/or nCHin₈₅₀₀. A further preferred isolated protein is encoded by a nucleic acid molecule that hybridizes under stringent hybridization conditions with a nucleic acid molecule having the complement of nucleic acid sequence SEQ ID NO:3, SEQ ID NO:5, SEQ ID NO:7, SEQ ID NO:9, SEQ ID NO:11, 10 SEQ ID NO:15, SEQ ID NO:20, SEQ ID NO:24, SEQ ID NO:28, SEQ ID NO:32, SEQ ID NO:33, SEQ ID NO:38, SEQ ID NO:55, SEQ ID NO:57, SEQ ID NO:59, SEQ ID NO:61, SEQ ID NO:65, SEQ ID NO:67, SEQ ID NO:71, SEQ ID NO:75, SEQ ID NO:79, SEQ ID NO:81, SEQ ID NO:83, and/or SEQ ID NO:87, or by an allelic 15 variant of any of such nucleic acid molecules. Proteins encoded by nucleic acid sequences SEQ ID NO:3, SEQ ID NO:5, SEQ ID NO:7, SEQ ID NO:9, SEQ ID NO:11, SEQ ID NO:15, SEQ ID NO:20, SEQ ID NO:24, SEQ ID NO:28, SEQ ID NO:32, SEQ ID NO:33, SEQ ID NO:38, SEQ ID NO:55, SEQ ID NO:57, SEQ ID 20 NO:59, SEQ ID NO:61, SEQ ID NO:65, SEQ ID NO:67, SEQ ID NO:71, SEQ ID NO:75, SEQ ID NO:79, SEQ ID NO:81, SEQ ID NO:83, and SEQ ID NO:87 have amino acid sequences SEQ ID NO:4, SEQ ID NO:6, SEQ ID NO:8, SEQ ID NO:10, SEQ ID NO:12, SEQ ID NO:16, SEQ ID NO:18, SEQ ID NO:22, SEQ ID NO:26, SEQ 25 ID NO:30, SEQ ID NO:34, SEQ ID NO:36, SEQ ID NO:88, respectively.

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Comparison of the CHV amino acid sequences SEQ ID NO:4, SEQ ID NO:6, SEQ ID NO:8, SEQ ID NO:10, SEQ ID NO:16, SEQ ID NO:18, SEQ ID NO:22, SEQ ID NO:26, SEQ ID NO:30, SEQ ID NO:34, SEQ ID NO:36, SEQ ID NO:56, SEQ ID NO:58, SEQ ID NO:60, SEQ ID NO:62, SEQ ID NO:66, SEQ ID NO:68, SEQ ID NO:72, SEQ ID NO:76, SEQ ID NO:80, SEQ ID NO:82, SEQ ID NO:84, and SEQ ID NO:88 with known sequences indicates that none of these CHV amino acid sequences share more than about 75% identity (many, if not all, sharing significantly less identity) with a known amino acid sequence.

A preferred CHV protein has an amino acid sequence that is at least about 80%, preferably at least about 85%, more preferably at least about 90%, even more preferably at least about 95%, and even more preferably at least about 99% identical to amino acid sequence SEQ ID NO:4, SEQ ID NO:6, SEQ ID NO:8, SEQ ID NO:10, SEQ ID NO:16, SEQ ID NO:18, SEQ ID NO:22, SEQ ID NO:26, SEQ ID NO:30, SEQ ID NO:34, SEQ ID NO:36, SEQ ID NO:56, SEQ ID NO:58, SEQ ID NO:60, SEQ ID NO:62, SEQ ID NO:66, SEQ ID NO:68, SEQ ID NO:72, SEQ ID NO:76, SEQ ID NO:80, SEQ ID NO:82, SEQ ID NO:84, and/or SEQ ID NO:88.

A more preferred CHV protein includes at least a portion of PCIR₆₁₈₃, PCUS₂₃₉₁, PCPK₄₀₀, PCgG₄₁₅, PCdUTP₁₅₂, PCUS₉₁₄₉, PCUL₄₈₉₇, PCUL₅₂₄₈, PCUL₅₁₈₆, PCgI₅₃, PCTK₉₃, PCgI₃₆₄, PCgE₅₂₂, PCUS_{8.578}, PCUS₉₁₁₉, PCUL₄₉₁₃₉, PCUL₄₈₄₂₂, PCICP₄₂₀₈, PCgL₁₇₁, PCdUTP₃₀₅, PCUL_{49.586}, PCUL₄₉₈₅, and/or PCUL₅₂₂₄₉, as well as

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proteins encoded by allelic variants of the nucleic acid molecules encoding such proteins. Also preferred are proteins including at least a portion of CgE and/or CUL49 proteins. A particularly preferred CHV protein includes

5 PCIR6₁₈₃, PCUS2₃₉₁, PCPK₄₀₀, PCgG₄₁₅, PCdUTP₁₅₂, PCUS9₁₄₉, PCUL48₉₇, PCUL52₄₈, PCUL51₈₆, PCgI₅₃, PCTK₉₃, PCgI₃₆₄, PCgE₅₂₂, PCUS8.5₇₈, PCUS9₁₁₉, PCUL49₁₃₉, PCUL48₄₂₂, PCICP4₂₀₈, PCgL₁₇₁, PCdUTP₃₀₅, PCUL49.5₈₆, PCUL49₈₅, and/or PCUL52₂₄₉ (including, but not limited to the encoded proteins, full-length proteins,

10 processed proteins, multivalent proteins).

Similarly, a preferred CHV protein of the present invention includes at least a portion of SEQ ID NO:4, SEQ ID NO:6, SEQ ID NO:8, SEQ ID NO:10, SEQ ID NO:16, SEQ ID NO:18, SEQ ID NO:22, SEQ ID NO:26, SEQ ID NO:30, SEQ ID NO:34, SEQ

15 ID NO:36, SEQ ID NO:56, SEQ ID NO:58, SEQ ID NO:60, SEQ ID NO:62, SEQ ID NO:66, SEQ ID NO:68, SEQ ID NO:72, SEQ ID NO:76, SEQ ID NO:80, SEQ ID NO:82, SEQ ID NO:84, and/or SEQ ID NO:88. A particularly preferred CHV protein includes SEQ ID NO:4, SEQ ID NO:6, SEQ ID NO:8, SEQ ID NO:10, SEQ ID

20 NO:16, SEQ ID NO:18, SEQ ID NO:22, SEQ ID NO:26, SEQ ID NO:30, SEQ ID NO:34, SEQ ID NO:36, SEQ ID NO:56, SEQ ID NO:58, SEQ ID NO:60, SEQ ID NO:62, SEQ ID NO:66, SEQ ID NO:68, SEQ ID NO:72, SEQ ID NO:76, SEQ ID NO:80, SEQ ID NO:82, SEQ ID NO:84, and/or SEQ ID NO:88. Also included are

25 proteins encoded by allelic variants of the nucleic acid molecules encoding such proteins.

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The present invention also includes a recombinant vector, which includes at least one isolated CHV nucleic acid molecule inserted into any vector capable of delivering the CHV nucleic acid molecule into a host cell. The vector can
5 be either RNA or DNA, either prokaryotic or eukaryotic, and typically is a virus or a plasmid. Recombinant vectors can be used in the cloning, sequencing, and/or otherwise manipulating of CHV nucleic acid molecules of the present invention. Suitable and preferred CHV nucleic acid molecules
10 to include in a recombinant vector are disclosed herein.

One embodiment of the present invention is a recombinant vector comprising an inactive CHV gene. Such a recombinant vector, also referred to as a transfer vector, can be used to produce a CHV comprising a CHV genome having an inactive gene
15 by, for example, co-transfecting such a transfer vector with a CHV genome into a host cell and selecting for a CHV comprising a recombinant CHV genome having an inactive gene. Such a recombinant CHV genome is produced in the host cell by homologous recombination between the inactive gene on the
20 transfer vector and the corresponding active gene on the transfected CHV genome. Transfection, culturing and purification methods to obtain recombinant CHV and CHV genomes are known to the art; see, for example, Graham et al., 1973, *Virology* 52:456-467; Graham et al., *ibid.* is
25 incorporated by reference herein in its entirety.

Another embodiment of the present invention is a

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recombinant vector comprising a CHV nucleic acid molecule that includes a heterologous nucleic acid molecule (i.e., a heterologous nucleic acid molecule is located within a CHV nucleic acid molecule). Suitable and preferred heterologous
5 nucleic acid molecules are disclosed herein. Such a heterologous nucleic acid molecule can be operatively linked to a transcription control sequence, as disclosed above. A recombinant vector comprising a CHV nucleic acid molecule into which a heterologous nucleic acid molecule is inserted
10 is also a transfer vector. Such a transfer vector can be co-transfected with a CHV genome into a host cell to produce a recombinant CHV having a CHV genome including a heterologous nucleic acid molecule, using methods as described above. Recombinant CHV can be selected by identifying those CHV that
15 have the heterologous nucleic acid molecule. If the recombinant vector comprises a selectable marker into which the heterologous nucleic acid molecule is inserted, selection methods as disclosed herein can also be used to identify recombinant CHV. A preferred embodiment is a recombinant
20 vector comprising a CHV nucleic acid molecule having a heterologous nucleic acid molecule in which a majority of the CHV nucleic acid molecule is deleted; a sufficient size of the CHV nucleic acid molecule is retained to allow homologous recombination to occur with the corresponding target gene on
25 the CHV genome. Examples of insertion of a heterologous nucleic acid molecule into a CHV genomic restriction site and

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into a CHV gene, as well as use of a selectable marker are provided in the Examples section.

Transfer vectors of the present invention are preferably able to replicate in bacterial, and particularly *E. coli*,
5 hosts, thereby enabling easy manipulation of the CHV nucleic acid molecules, and, if included, heterologous nucleic acid molecules, prior to insertion of such CHV nucleic acid molecules into a CHV genome. Such manipulations, including culturing of *E. coli* comprising such vectors, is described,
10 for example, in Sambrook et al., *ibid*.

In one embodiment, recombinant CHV are produced by co-transfection of a set of overlapping cosmid clones comprising the entire viral CHV genome, at least one of the cosmid clones having been genetically engineered to, for example,
15 contain an inactive CHV gene and/or a heterologous nucleic acid molecule. Details of such a method are presented in the Examples.

Any canid host cell is suitable for recombinant CHV production. Examples of suitable and preferred host cells
20 are provided herein. After transfection, transfected cells are cultured in an effective medium, using techniques such as those described in Graham et al., *ibid*. As used herein, an effective medium refers to any medium in which the transfected cells can produce recombinant CHV. An effective
25 medium is typically an aqueous medium comprising assimilable carbohydrate, nitrogen and phosphate sources, as well as

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appropriate salts, minerals, metals and other nutrients, such as vitamins, growth factors and hormones. Culturing is carried out at a temperature, pH and oxygen content appropriate for the transfected cell. Such culturing
5 conditions are well within the expertise of one of ordinary skill in the art.

Recombinant CHV can be recovered from the cultured transfected cells using a combination of standard techniques such as, but not limited to, freeze/thaw cycles, sonication,
10 sucrose gradient centrifugation, and/or high speed centrifugation. Recombinant CHV genomes can be recovered from the cultured transfected cells using a combination of standard techniques such as, but not limited to, those described by Walboomers et al., 1976, *Virology* 74, 256-258.

15 Preferably, a recombinant CHV or recombinant CHV genome of the present invention is recovered in "substantially pure" form. As used herein, "substantially pure" refers to a purity that allows for the effective use of the recombinant CHV or CHV genome as a vaccine without substantial negative
20 side effects.

The present invention also includes a method to increase recombinant CHV plaque forming efficiency, thereby facilitating the production of recombinant CHV and CHV genomes. The phrase to increase recombinant CHV plaque
25 forming efficiency refers to the ability to increase, or enhance, the production of CHV above the frequency of plaque

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forming units produced when a CHV genome is transfected into a cell in the absence of additional factors. The method includes the step of expressing the CHV alpha trans-inducing factor gene (i.e., CUL48 gene, also called the CHV alpha-tif gene) when a CHV genome is introduced into a canine cell.

Herpesviruses studied to date carry into infected cells a transcriptional activator called alpha trans-inducing factor (also called VP16 or Vmw65); see, for example, Batterson et al., 1983, *J. Virol.*, 46:371-377. This transactivator protein interacts, along with cellular proteins, with a cis-acting sequence element present in the upstream regulatory regions of herpesvirus immediate early genes. Since purified herpesvirus DNA is infectious in the absence of alpha-tif, it is not absolutely required for expression of immediate early genes, but its presence in stably transfected cell lines has been shown to enhance infectivity of herpes simplex virus type-1 viral DNA; see, for example, Werstuck et al., 1990, *J. Virol.*, 64:984-991.

Expression of the CHV alpha-tif gene can be accomplished in a variety of ways, including, but not limited to, the following. In one embodiment, a recombinant CHV genome is introduced into a canine cell expressing CHV alpha trans-inducing factor and the cells are cultured to produce recombinant CHV. A canine cell expressing CHV alpha-tif is a canine cell that has been genetically engineered to produce CHV alpha-tif in either a stable or transient manner. Such a

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canine cell can be produced by introducing a CUL48 nucleic acid molecule of the present invention into a canine cell line in such a manner that the CUL48 nucleic acid molecule can direct the expression of active alpha-tif. An example of
5 a useful CUL48 nucleic acid molecule is such nCUL48₁₂₆₉.

Details regarding the production of an alpha-tif-expressing canine cell and the use such a cell in the production of recombinant CHV and CHV genomes is present in the Examples.

In another embodiment, recombinant CHV plaque forming
10 efficiency is increased by co-introducing a recombinant CHV genome and a CHV alpha trans-inducing factor gene into a canine cell and culturing the cell to produce recombinant CHV. The CHV alpha trans-inducing factor gene can be introduced as part of a recombinant molecule of the present
15 invention. Details regarding this method are also presented in the Examples.

The present invention also includes canine cell lines that include a CHV alpha-tif gene; such cell lines are able to express alpha-tif, thereby facilitating CHV production.

20 One example of such a cell line is a canine cell line transfected with CHV nucleic acid molecule nCUL48₁₂₆₉.

One embodiment of the present invention is a recombinant molecule that includes a CHV nucleic acid molecule operatively linked to a transcription control sequence. Such
25 a recombinant molecule, when introduced into a host cell, can direct the expression of the CHV nucleic acid molecule(s),

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thereby leading to the production of one or more CHV protein of the present invention. Such a recombinant molecule preferably is replication competent. Suitable and preferred CHV nucleic acid molecules to include in such a recombinant molecule are as disclosed herein for suitable and preferred CHV nucleic acid molecules per se.

Isolated CHV proteins of the present invention can be produced in a variety of ways, including production and recovery of natural proteins, production and recovery of recombinant proteins, and chemical synthesis of the proteins. In one embodiment, an isolated protein of the present invention is produced by culturing a cell capable of expressing the protein under conditions effective to produce the protein, and recovering the protein. A preferred cell to culture is a recombinant cell that is capable of expressing one or more CHV proteins, the recombinant cell being produced by transforming a host cell with one or more nucleic acid molecules of the present invention. Transformation of a nucleic acid molecule into a cell can be accomplished by any method by which a nucleic acid molecule can be inserted into the cell. Transformation techniques include, but are not limited to, transfection, electroporation, microinjection, lipofection, adsorption, and protoplast fusion. A recombinant cell may remain unicellular or may grow into a tissue, organ or a multicellular organism. Transformed nucleic acid molecules of the present invention can remain

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extrachromosomal or can integrate into one or more sites within a chromosome of the transformed (i.e., recombinant) cell in such a manner that their ability to be expressed is retained. Suitable and preferred CHV nucleic acid molecules
5 with which to transform a cell are as disclosed herein for suitable and preferred CHV nucleic acid molecules per se.

Suitable host cells to transform include any cell that can be transformed with a CHV nucleic acid molecule of the present invention. Host cells can be either untransformed
10 cells or cells that are already transformed with at least one nucleic acid molecule. Host cells of the present invention either can be endogenously (i.e., naturally) capable of producing CHV proteins of the present invention or can be capable of producing such proteins after being transformed
15 with at least one CHV nucleic acid molecule of the present invention. Host cells of the present invention can be any cell capable of producing at least one protein of the present invention, and include bacterial, fungal (including yeast), parasite (including helminth, protozoa and ectoparasite),
20 insect, other animal and plant cells. Preferred host cells include bacterial, yeast, insect and mammalian cells.

Suitable transcription control sequences include any transcription control sequence that can function in at least one of the recombinant cells of the present invention. A
25 variety of such transcription control sequences are known to those skilled in the art. Preferred transcription control

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sequences include those which function in bacterial, yeast, insect and mammalian cells, such as, but not limited to, *tac*, *lac*, *trp*, *trc*, *oxy-pro*, *omp/lpp*, *rrnB*, bacteriophage lambda (such as lambda p_L and lambda p_R and fusions that include
5 such promoters), bacteriophage T7, T7lac, bacteriophage T3, bacteriophage SP6, bacteriophage SP01, metallothionein, alpha-mating factor, *Pichia* alcohol oxidase, alphavirus, phosphate-regulated and nitrate-regulated transcription control sequences as well as other sequences capable of
10 controlling gene expression in prokaryotic or eukaryotic cells, including those disclosed herein for expression of heterologous nucleic acid molecules, including endogenous CHV transcription control regions.

Recombinant cells of the present invention can be used
15 to produce one or more proteins by culturing such cells under conditions effective to produce such a protein, and recovering the protein. Effective conditions to produce a protein include, but are not limited to, appropriate media, bioreactor, temperature, pH and oxygen conditions that permit
20 protein production. Such culturing conditions are well within the expertise of one of ordinary skill in the art.

Depending on the vector and host system used for production, resultant CHV proteins may either remain within the recombinant cell; be secreted into the fermentation
25 medium; be secreted into a space between two cellular membranes, such as the periplasmic space in *E. coli*; or be

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retained on the outer surface of a cell or viral membrane.

The phrase "recovering the protein" refers simply to collecting the whole fermentation medium containing the protein and need not imply additional steps of separation or
5 purification. Proteins of the present invention can be purified using a variety of standard protein purification techniques, such as, but not limited to, affinity chromatography, ion exchange chromatography, filtration, electrophoresis, hydrophobic interaction chromatography, gel
10 filtration chromatography, reverse phase chromatography, concanavalin A chromatography, chromatofocusing and differential solubilization. Proteins of the present invention are preferably retrieved in "substantially pure" form. As used herein, "substantially pure" refers to a
15 purity that allows for the effective use of the protein as a therapeutic composition or diagnostic. A therapeutic composition for animals, for example, should exhibit no substantial toxicity and should be capable of stimulating the production of antibodies in a treated animal.

20 The present invention also includes isolated antibodies capable of selectively binding to a CHV protein of the present invention or to a mimetope thereof. Such antibodies are also referred to herein as anti-CHV antibodies. Isolated antibodies are antibodies that have been removed from their
25 natural milieu. The term "isolated" does not refer to the state of purity of such antibodies. As such, isolated

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antibodies can include anti-sera containing such antibodies, or antibodies that have been purified to varying degrees.

As used herein, the term "selectively binds to" refers to the ability of antibodies of the present invention to
5 preferentially bind to specified proteins and mimetopes thereof of the present invention. Binding can be measured using a variety of methods known to those skilled in the art.

Antibodies of the present invention can be either polyclonal or monoclonal antibodies. Antibodies of the
10 present invention include functional equivalents such as antibody fragments and genetically-engineered antibodies, including single chain antibodies, that are capable of selectively binding to at least one of the epitopes of the protein or mimetope used to obtain the antibodies.
15 Antibodies of the present invention also include chimeric antibodies that can bind to more than one epitope. Preferred antibodies are raised in response to proteins, or mimetopes thereof, that are encoded, at least in part, by a nucleic acid molecule of the present invention.

20 A preferred method to produce antibodies of the present invention includes (a) administering to an animal an effective amount of a protein or mimetope thereof of the present invention to produce the antibodies and (b) recovering the antibodies. In another method, antibodies of
25 the present invention are produced recombinantly using techniques as heretofore disclosed to produce CHV proteins of

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the present invention. Antibodies raised against defined proteins or mimetopes can be advantageous because such antibodies are not substantially contaminated with antibodies against other substances that might otherwise cause
5 interference in a diagnostic assay or an assay to monitor recombinant CHV administration, or side effects if used in a therapeutic composition.

Antibodies of the present invention have a variety of potential uses that are within the scope of the present
10 invention. For example, such antibodies can be used (a) as compounds to monitor recombinant CHV or recombinant CHV genome administration, (b) as therapeutic compounds to passively immunize an animal in order to protect the animal from CHV infection, and/or (c) as reagents in assays to
15 detect CHV infection.

One embodiment of the present invention is a therapeutic composition that includes a recombinant CHV, a recombinant CHV genome, or a mixture (i.e., combination) of one or more recombinant CHVs and/or recombinant CHV genomes. As used
20 herein, a therapeutic composition, or vaccine, is a formulation that, when administered to an animal in an effective manner, is capable of protecting that animal from a disease against which the therapeutic composition is targeted. Some therapeutic compositions of the present
25 invention can modulate (i.e., either elicit or suppress) an immune response to protect an animal from disease, whereas

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other therapeutic compositions can protect an animal in other ways, as disclosed herein. A therapeutic composition of the present invention can be used to prevent and/or treat a disease depending on whether the composition is administered
5 as a prophylactic or after the animal has the disease.

A therapeutic composition of the present invention, when administered to an animal in an effective manner, can infect the cells of the animal (in a manner essentially harmless to the animal) and direct the production of a protective
10 compound able to protect the animal from a disease targeted by the therapeutic composition. If a recombinant CHV includes a protective compound in its envelope and/or capsid, the CHV can function as an immunogen per se.

As disclosed herein, therapeutic compositions can be
15 designed to target a variety of diseases, depending on the nature of the heterologous nucleic acid molecule(s) included in such recombinant CHV and recombinant CHV genomes.

Examples of such diseases, and the nature of the corresponding heterologous nucleic acid molecules, are
20 disclosed herein. Furthermore, therapeutic compositions of the present invention can comprise multivalent vaccines. For example, a CHV genome can encode a variety of protective compounds, and/or more than one recombinant CHV genome and/or recombinant CHV can be administered. The present invention
25 also includes the use of a recombinant CHV or recombinant CHV genome to protect an animal against CHV infection. Such a

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therapeutic composition can, but need not, include a heterologous nucleic acid molecule.

A therapeutic composition of the present invention is preferably administered to a canid, due to the host range
5 specificity of CHV. Suitable canids include dogs (including domesticated and wild dogs), foxes, wolves, jackals, coyotes, and other members of the family Canidae. Particularly preferred canids to treat include domesticated dogs.

It is, however, also within the scope of the present
10 invention to administer therapeutic compositions to other animals. Recombinant CHV can be administered to any animal susceptible to such therapy. Without being bound by theory, it is believed that sufficiently high doses of a recombinant CHV composition of the present invention may be infectious in
15 other animals, particularly other mammals. Mink and other mink-like mammals (e.g., those of the family Mustelidae, such as ermines, ferrets, fishers, martens, otters, and weasels), in particular, may be susceptible to CHV infection, as suggested by the ability of CHV to infect mink lung cells.
20 The host range of recombinant CHV of the present invention can also be altered, as disclosed herein, to infect other animal cells. It is also to be noted that CHV genomes of the present invention can be administered as naked DNA vaccines or in association with other carriers (e.g., liposomes). In
25 accordance with these embodiments, any animal, including, but not limited to, mammals, birds, amphibians, and arthropods

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(including arachnids and insects) can be administered a therapeutic composition of the present invention. Preferred animals to treat include dogs, cats, humans, ferrets, prairie dogs, other rodents, horses, cattle, sheep, pigs, and
5 poultry, as well as other pets, work animals, economic food animals and zoo animals.

Therapeutic compositions of the present invention can be formulated in an excipient that the animal to be treated can tolerate. Examples of such excipients include water, saline,
10 Ringer's solution, dextrose solution, Hank's solution, and other aqueous physiologically balanced salt solutions. Other useful formulations include suspensions containing viscosity enhancing agents, such as sodium carboxymethylcellulose, sorbitol, or dextran. Excipients can also contain minor
15 amounts of additives, such as substances that enhance isotonicity and chemical stability. Examples of buffers include phosphate buffer, bicarbonate buffer and Tris buffer. Standard formulations can either be liquid injectables or solids which can be taken up in a suitable liquid as a
20 suspension or solution for injection. Thus, in a non-liquid formulation, the excipient can comprise dextrose, human serum albumin, preservatives, etc., to which sterile water or saline can be added prior to administration.

In one embodiment of the present invention, the vaccine
25 can also include an adjuvant and/or a carrier. One advantage of live virus-based vaccines, such as the recombinant CHVs of

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the present invention, is that adjuvants and carriers are not required to produce an efficacious vaccine, and in some cases, the advantages of recombinant CHV vaccines of the present invention would be precluded by the use of some
5 adjuvants. However, it should be noted that use of adjuvants or carriers is not precluded by the present invention. Adjuvants are typically substances that generally enhance the immune response of an animal to a specific antigen. Suitable adjuvants include, but are not limited to, other bacterial
10 cell wall components; aluminum-based salts; calcium-based salts; silica; polynucleotides; toxoids; serum proteins; other viral coat proteins; other bacterial-derived preparations; block copolymer adjuvants, such as Hunter's Titermax™ adjuvant (Vaxcel™, Inc. Norcross, GA); Ribi
15 adjuvants (available from Ribi ImmunoChem Research, Inc., Hamilton, MT); and saponins and their derivatives, such as Quil A (available from Superfos Biosector A/S, Denmark). Carriers are typically compounds that increase the half-life of a therapeutic composition in the treated animal. Suitable
20 carriers include, but are not limited to, polymeric controlled release formulations, biodegradable implants, liposomes, bacteria, viruses, oils, esters, and glycols.

In one embodiment, a therapeutic composition of the present invention is administered to an animal in an
25 effective manner to enable the animal to produce sufficient protective compound(s) and/or to directly mount a sufficient

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immune response to protect the animal from disease.

Acceptable protocols to administer therapeutic compositions in an effective manner include enumeration of individual dose size, number of doses, frequency of dose administration, and
5 mode of administration. Determination of such protocols can be accomplished by those skilled in the art. A suitable single dose is a dose that is capable of protecting an animal from disease when administered one or more times over a suitable time period.

- 10 A preferred single dose of a recombinant CHV of the present invention is from about 1×10^4 to about 1×10^7 virus plaque forming units (pfu) per kilogram body weight of the animal. Booster vaccinations can be administered from about 2 weeks to several years after the original
15 vaccination. Booster vaccinations preferably are administered when the immune response of the animal becomes insufficient to protect the animal from disease. A preferred administration schedule is one in which from about 1×10^4 to about 1×10^7 virus plaque forming units per kilogram (kg)
20 body weight of the animal are administered from about 1 to about 2 times over a time period of from about 12 to about 18 months. Modes of administration can include, but are not limited to, subcutaneous, intradermal, intravenous, intranasal, oral, transdermal and intramuscular routes.
25 A recombinant CHV genome can be administered in a variety of ways, with intramuscular, subcutaneous,
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intradermal, transdermal, intranasal and oral routes of administration being preferred. A preferred single dose of a recombinant CHV genome ranges from about 1 nanogram (ng) to about 100 micrograms (μ g), depending on the route of

5 administration and/or method of delivery, as can be determined by those skilled in the art; see, for example, Wolff et al., 1990, *Science* 247, 1465-1468. Suitable delivery methods include, for example, injection, as drops, aerosolized and/or topical administration. Suitable

10 excipients include, for example, physiologically acceptable aqueous solutions (e.g., phosphate buffered saline as well as others disclosed above), liposomes (including neutral or cationic liposomes), and other lipid membrane-based vehicles (e.g., micelles or cellular membranes).

15 In one embodiment, a therapeutic composition of the present invention is administered to a dam to protect her offspring from disease. In this method, the dam is administered the therapeutic composition at such a time as to be able to develop an immune response such that she can

20 passively transfer antibodies produced against a protective compound of the present invention to her offspring. Such a method can also be used to protect offspring from CHV infection and is particularly useful since neonates are most affected by CHV infection.

25 The efficacy of a therapeutic composition of the present invention to protect an animal from disease can be tested in

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a variety of ways including, but not limited to, detection of protective protein or RNA within the treated animal, detection of protective antibodies within the treated animal, detection of cellular immunity within the treated animal, or
5 challenge of the treated animal with an appropriate infectious agent, or other disease component, to determine whether the animal is now protected from the disease caused by such an agent or other component. Such techniques are known to those skilled in the art. In one embodiment, anti-
10 CHV antibodies of the present invention are used to monitor recombinant CHV infection and can be used to distinguish wild type infections from infections using recombinant CHV of the present invention (i.e., by using antibodies that specifically recognize either recombinant CHV of the present
15 invention or wild type virus).

In one embodiment, the efficacy of a therapeutic composition of the present invention may be improved by co-administering (a) a recombinant CHV or recombinant CHV genome and (b) a protective compound (e.g., subunit vaccine) encoded
20 by a CHV nucleic acid molecule or heterologous nucleic acid molecule present in the CHV genome. While not being bound by theory, it is believed that administration of a protective compound in conjunction with the recombinant CHV or CHV genome can boost the immune response, particularly the
25 antibody titer. The protective compound can be administered prior to, concomitant with, and/or following administration

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of the recombinant CHV or CHV genome. The protective compound can be either produced naturally, recombinantly, or synthetically. The protective compound should be sufficiently pure to allow for effective use of the compound
5 as a vaccine; i.e., it should not cause substantial side effects. The protective compound can be joined (i.e., conjugated) to a carrier or other material that enhances the immunogenicity of the compound.

The present invention also includes the use of CHV
10 nucleic acid molecules, CHV proteins, and anti-CHV antibodies as therapeutic compositions to protect animals from CHV infection. Methods to administer such compositions to canids are known to those skilled in the art. For example, a preferred single dose of a protein, mimetope or antibody
15 therapeutic composition is from about 1 microgram (μg) to about 10 milligrams (mg) of the therapeutic composition per kilogram body weight of the animal. Booster vaccinations can be administered from about 2 weeks to several years after the original administration. Booster vaccinations preferably are
20 administered when the immune response of the animal becomes insufficient to protect the animal from disease. A preferred administration schedule is one in which from about 10 μg to about 1 mg of the therapeutic composition per kg body weight of the animal is administered from about one to about two
25 times over a time period of from about 2 weeks to about 12 months. Modes of administration can include, but are not

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limited to, subcutaneous, intradermal, intravenous, intranasal, oral, transdermal and intramuscular routes. A CHV nucleic acid molecule, including recombinant molecules, can be administered as described herein for administration of
5 CHV genomes or CHV of the present invention. Recombinant molecules including heterologous nucleic acid molecules can also be used as therapeutic compositions to protect an animal from disease, using methods as disclosed herein.

It is also within the scope of the present invention to
10 use isolated CHV proteins, mimetopes, CHV nucleic acid molecules and anti-CHV antibodies of the present invention as diagnostic reagents to detect CHV infection. Methods to use such diagnostic reagents to diagnose infection are well known to those skilled in the art.

15 The following examples are provided for the purposes of illustration and are not intended to limit the scope of the present invention.

EXAMPLES

It is to be noted that the Examples include a number of
20 molecular biology, virology, microbiology, immunology and biochemistry techniques considered to be known to those skilled in the art. Disclosure of such techniques can be found, for example, in Sambrook et al., *ibid.*; Ausubel et al., 1993, *Current Protocols in Molecular Biology*,
25 Greene/Wiley Interscience, New York, NY; Graham et al., *ibid.*; and related references. Ausubel et al., *ibid.* is

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incorporated by reference herein in its entirety. Nucleic acid and amino acid sequences of the present invention were compared to known sequences using BLAST (NCBI) and DNAsis (Hitachi Software, San Bruno, CA).

5

Example 1

This Example demonstrates the isolation of certain CHV nucleic acid molecules of the present invention.

The disclosed CHV nucleic acid molecules were amplified from a CHV genome by PCR amplification using a variety of
10 primers designed in view of published herpesvirus sequences. The following PCR conditions were used: 0.2 millimolar (mM) dNTPs, 1 μ M of each primer, 1X PCR buffer (available from Perkin Elmer Cetus, Emeryville, CA), 50 ng of CHV DNA (isolated from CHV strain D 004 as described in Example 2)
15 and 0.5 μ l of a thermostable DNA polymerase, all in an about 100 μ l total volume. The PCR reactions included an initial denaturation for 3 minutes at 95°C, five cycles of 1 minute each at 95°C, 35°C for 1 minute, 72°C for 1 minute, 35 cycles of 1 minute each at 95°C, 37°C for 1 minute, 72°C for 1
20 minute, and finally 10 minutes at 72°C. The resultant PCR products were directly cloned into the pCRII TA cloning vector (available from Invitrogen Corp., San Diego, CA) according to the manufacturer's specifications. Primers which were successful in amplifying fragments from a CHV
25 genome, which was determined to be very AT-rich compared to other herpesvirus genomes, are described below.

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A. Isolation of a nucleic acid molecule including a partial CHV dUTPase gene and a partial CHV UL51 gene

The following primers were designed using dUTPase protein sequence derived from HSV-1 (McGeoch et al., 1988, *J. Gen. Virol.* 69, 1531-1574), EHV-4 (Riggio et al., 1993, *Arch. Virol.* 133, 171-178), BHV-1 (Liang et al., 1993, *Virology* 195, 42-50), and EBV (Lees et al., 1993, *Virology* 195, 578-586: Primer 212S (dUTPase forward) having nucleic acid sequence 5' GG CGA ATT CCI AAR MGI GAI GAR GAY G 3', denoted
5 herein as SEQ ID NO:39; and Primer 365A (dUTPase reverse) having nucleic acid sequence 5' C GCG GAT CCI GTI SWI CCY AAI CC 3', denoted herein as SEQ ID NO:40. These primers led to the amplification of an about 743 nucleotide fragment, which was significantly larger than expected. Nucleic acid
15 sequence analysis, described in Example 3, indicated that the 743 nucleotide fragment contained part of the CUL51 gene as well as part of the CdUTPase gene; as such, the fragment was denoted nCdUTP/CUL51₇₄₃. Nucleic acid sequence analysis also indicated that the dUTPase reverse primer actually hybridized
20 to a region of the CHV DNA genome within the CUL51 gene rather than within the CdUTPase gene. It is believed that the mispriming was due to nucleotide position 19 of SEQ ID NO:40 being a Y instead of an R; the latter sequence would have matched more closely to the targeted priming region,
25 about 290 nucleotides upstream from the 3' end of nucleic acid molecule nCdUTP/CUL51₇₄₃. This result demonstrates the

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sensitivity of PCR amplification to primer design.

B. Isolation of a CHV gE nucleic acid molecule

The following primers were designed using gE protein sequence derived from FHV-1 (Spatz et al., 1994, *J. Gen. Virol.* 75, 1235-1244), EHV-1 (Elton et al., 1991, *Gene* 101, 203-208), and BHV-1 (Leung-Tack et al., 1994, *Virology* 199, 409-421): Primer 197S (gE forward) having nucleic acid sequence 5' GGC GAA TTC TAY CAY WSI CAY GTI TA 3', denoted herein as SEQ ID NO:41; and Primer 441A (gE reverse) having nucleic acid sequence 5' CGC GGA TCC RTC RTT ISW IGG DAI ISW IGT 3', denoted herein as SEQ ID NO:42. These primers led to the amplification of an about 750 nucleotide fragment, referred to herein as nCgE₇₅₀.

C. Isolation of a CHV TK nucleic acid molecule

The following primers were designed using TK protein sequence derived from HSV-1 (McGeoch et al., 1988, *ibid.*), HSV-2 (Kit et al., 1987, *Antimicrob. Agents Chemother.* 31, 1483-1490), BHV-1 (Kit et al., U.S. Patent No. 4703011, issued October 27, 1987), FHV-1 (Nunberg et al., 1989, *J. Virol.* 63, 3240-3249), EHV-1 (Robertson et al., 1988, *Nuc. Acids Res.* 16, 11303-11317), and PRV (Prieto et al., 1991, *J. Gen. Virol.* 72, 1435-1439): Primer EJH 002 (TK forward) having nucleic acid sequence 5' GGC GAA TTC GGI AAR WSI ACI RC 3', denoted herein as SEQ ID NO:43; and Primer EJH004 (TK reverse) having nucleic acid sequence 5' GGC GGA TCC GGT TGI CKR TC 3', denoted herein as SEQ ID NO:44. These primers led

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to the amplification of an about 280 nucleotide fragment, referred to herein as nCTK₂₈₀.

D. Isolation of a nucleic acid molecule including CHV gC and CHV UL45 genes

5 The following primers were designed using gC and UL45 sequences derived from Limbach et al., *ibid.*: Primer gC sense, having nucleic acid sequence 5' CGCGGATCCAAGGTAATAAGTCAAAATGAG 3', denoted herein as SEQ ID NO:45; and Primer gC ant, having nucleic acid sequence 5' 10 CGCGGATCCGACAAAAACAAAAGTAATG 3', denoted herein as SEQ ID NO:46. These primers led to the amplification of an about 2100 nucleotide fragment, referred to herein as nCgC/CUL45₂₁₀₀.

E. Attempt to isolate a CHV ribonucleotide reductase 15 gene

The following primers were designed using ribonucleotide subunit small subunit protein sequence derived from HSV-1 (McGeoch et al., 1988, *ibid.*), PRV (Dewind et al., 1993, *J. Gen. Virol.* 74, 351-359), EHV-1 (Telford et al., 1992, 20 *Virology* 189, 04-316) and BHV-1 (Simard et al., 1992, *Virology* 190, 689-701): Primer EJH 021 (RR forward) having nucleic acid sequence 5' CCG AAT TCY TIA TGA THY TIA THG ARG G 3', denoted herein as SEQ ID NO:47; and Primer EJH022 (RR reverse) having nucleic acid sequence 5' CCG GAT CCY TCR AAR 25 AAR TTI GTR TGY TT 3', denoted herein as SEQ ID NO:48. These primers did not lead to the amplification of a fragment under

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a variety of magnesium and amplification conditions, suggesting the lack of a coding region for a ribonucleotide reductase small subunit in CHV. As a control, these primers were shown to be able to easily amplify a ribonucleotide reductase small subunit fragment from an FHV genome.

Example 2

This Example describes the production of CHV genomic libraries.

Canine herpesvirus strain D 004 (Binn, et al., 1967, *Proc. Soc. Exp. Biol. Med.* 126, 140) was obtained from ATCC. Virus were propagated on Madin-Darby Canine Kidney (MDCK) cells according to standard virological procedures. Viral DNA was prepared from CHV-infected MDCK cells by previously described methods; see, for example, Walboomers et al., *ibid.*

The viral DNA was digested with restriction endonucleases *HindIII*, *PstI*, *EcoRI* or *XbaI*, and the resultant digests were cloned into either vector pSP72 (available from Promega Corp., Madison, WI), or pLitmus 28 or 38 (available from New England Biolabs, Beverly, MA). DNA was prepared from the resultant recombinant plasmids and the inserts were sorted according to size.

Example 3

This Example describes the isolation of genomic *HindIII* restriction fragment nucleic acid molecules containing CdUTPase nucleic acid sequences and the nucleic acid sequencing of at least regions of these nucleic acid

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molecules.

Nucleic acid molecule nCdUTP/CUL51₇₄₃, produced as described in Example 1, was labelled with either ³²P or digoxigenin (available from Boehringer Mannheim Biochemicals (BMB), Indianapolis, IN) and used to screen the CHV *Hind*III fragment-containing library, either by colony hybridization or Southern blotting. Two clones hybridized with nCdUTP/CUL51₇₄₃, one containing a *Hind*III fragment of about 3000 nucleotides, referred to herein as nChin₃₀₀₀, and another containing a *Hind*III fragment of about 1,900 nucleotides, referred to herein as nChin₁₉₀₀. The *Hind*III fragments were further characterized by restriction mapping, as shown in Fig. 1. Also shown is the relative location of nCdUTP/CUL51₇₄₃ (referred to therein as nCdUTP₇₄₃) with respect to the *Hind*III fragments.

Nucleic acid molecules nCdUTP/CUL51₇₄₃, nChin₃₀₀₀, and nChin₁₉₀₀ were submitted to DNA sequence analysis, using a sequencing strategy as depicted in Fig. 1. Among sequences obtained were SEQ ID NO:13 and SEQ ID NO:14, which include SEQ ID NO:15 and SEQ ID NO:33, as well as SEQ ID NO:21, SEQ ID NO:23, SEQ ID NO:25 and SEQ ID NO:27. The relative locations of genes included in these sequences (i.e., the CUL52, CUL51, CdUTPase and CUL48 genes) are shown in Fig. 1. Also shown is the apparent location of the CUL49 gene.

SEQ ID NO:13 and SEQ ID NO:14 represent the deduced nucleic acid sequences of the two complementary strands of

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nCdUTP/CUL51₇₄₃. SEQ ID NO:13 includes a partial coding region for a CdUTPase protein of about 152 amino acids, denoted herein as nCdUTP₄₅₉ and represented by SEQ ID NO:15, assuming a first in-frame codon spanning about nucleotides 3-5, and a stop codon spanning about nucleotides 459-461 of SEQ ID NO:13. The amino acid sequence of the encoded protein PCdUTP₁₅₂ is represented by SEQ ID NO:16. SEQ ID NO:14 includes a partial coding region for a CUL51 protein of about 86 amino acids, denoted herein as nCUL51₂₆₁ and represented by SEQ ID NO:33, assuming a first in-frame codon spanning about nucleotides 1-3, and a stop codon spanning about nucleotides 259-261 of SEQ ID NO:14. The amino acid sequence of the encoded protein PCUL51₈₆ is represented by SEQ ID NO:34.

SEQ ID NO:21 and SEQ ID NO:23 represent the deduced nucleic acid sequences of the two complementary strands of nCUL48₂₉₄. SEQ ID NO:21 includes a partial coding region for a CUL48 protein of about 97 amino acids, denoted herein as nCUL48₂₉₁ and represented by SEQ ID NO:24, assuming a first in-frame codon spanning about nucleotides 3-5 of SEQ ID NO:21. The amino acid sequence of the encoded protein PCUL48₉₇ is represented by SEQ ID NO:22.

SEQ ID NO:25 and SEQ ID NO:27 represent the deduced nucleic acid sequences of the two complementary strands of nCUL52₁₄₆. SEQ ID NO:25 includes a partial coding region for a CUL52 protein of about 48 amino acids, denoted herein as nCUL52₁₄₄ and represented by SEQ ID NO:28, assuming a first

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in-frame codon spanning about nucleotides 1-3 of SEQ ID NO:25. The amino acid sequence of the encoded protein PCUL52₄₈ is represented by SEQ ID NO:26.

Example 4

5 This Example describes a method to identify restriction enzymes that effect limited cleavage of the CHV genome. Also described is the isolation and sequencing of an *AscI* fragment containing the entire US region of CHV.

CHV DNA was evaluated for recognition sites for several
10 restriction enzymes with 8-base, or larger, recognition sites. No sites were found for enzymes *Sse8387I*, *I-Sce-I*, or *NotI*. Two *AscI* sites were found, which were mapped to sites within the inverted repeats surrounding the US region, specifically within CHV gene US2 (see Fig. 2). The *AscI*
15 fragments, of 9.3, 10.0 and approximately 100-120 kilobases (kb), were cloned into pLitmus 38 and submitted to restriction enzyme mapping analysis. The restriction map of the 9.3-kb *AscI* fragment, denoted herein as nCAsc9300 is shown in Fig. 2; this fragment apparently contains the entire
20 CUS region, as well as small portions of the internal and terminal IR regions. The 10.0-kb *AscI*-blunt fragment, denoted herein as nCAsc10000, contains most of the terminal IR region and is shown in Fig. 3. The about 100-120-kb *AscI*-blunt fragment contains the remainder of the CHV genome.
25 Both *AscI* sites are located just 5' of the diploid copies of the CHV homolog of the EHV-1 IR6 gene (Breedon et al., 1992,

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Virology 191, 649-660), and the orf1 of BHV-1 (Leung-Tack et al., *ibid.*). The AscI sites appear to be located within an open reading frame that is the homolog of the EHV US1 gene (Breedon et al *ibid.*) and the HSV-1 US2 gene (McGeoch et al., 5 1985, *J. Mol. Biol* 181, 1-13), although the size is somewhat different from these other genes. No function has been ascribed to the HSV-1 US2 gene product, but it has been shown to be dispensable for growth in tissue culture and to attenuate the virus (Meignier et al., 1988, *Virology* 162, 10 251-254).

Nucleic acid molecules nCAsc₉₃₀₀ and nCAsc₁₀₀₀₀ were submitted to DNA sequence analysis using a strategy as depicted in Fig. 2 and Fig. 3. Among sequences obtained were SEQ ID NO:1, SEQ ID NO:2, SEQ ID NO:17, SEQ ID NO:19, SEQ ID 15 NO:29, and SEQ ID NO:31. The relative locations of genes included in these sequences (i.e., the CUS9, CgI, CgD, CgG, CPK, CUS2, and CIR6 genes) are shown in Fig. 2 and Fig. 3. Also shown is the putative location of the CgE gene.

SEQ ID NO:1 and SEQ ID NO:2 represent the deduced 20 nucleic acid sequences of the two complementary strands of nCUS₅₄₉₅. Translation of SEQ ID NO:1 and SEQ ID NO:2 indicates that nucleic acid molecule nCUS₅₄₉₅ encodes CIR6, CUS2, CPK and CgG proteins as well as a portion of a CgD protein. Specifically, SEQ ID NO:2 includes: a coding region 25 for a CIR6 protein of about 183 amino acids, denoted herein as nCIR6₅₅₂ and represented by SEQ ID NO:3, assuming a start

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codon spanning about nucleotides 4566-4568 and a stop codon spanning about nucleotides 5115-5117 of SEQ ID NO:2; and a coding region for a CUS2 protein of about 391 amino acids, denoted herein as nCUS2₁₁₇₆ and represented by SEQ ID NO:5, 5 assuming a start codon spanning about nucleotides 3232-3234 and a stop codon spanning about nucleotides 4405-4407 of SEQ ID NO:2. The amino acid sequences of the respective encoded proteins PCIR6₁₈₃ and PCUS2₃₉₁ are represented by SEQ ID NO:4 and SEQ ID NO:6. A portion of SEQ ID NO:3, from about 10 nucleotide 232 through about nucleotide 548, was found to be similar to GenBank Accession No. X90423, as disclosed by Remond, et al., 1996, *ibid*. The published partial sequence, however, appears to contain sequencing errors, in that a G-C inversion and two frame-shifts were found in this sequence 15 relative to SEQ ID NO:3. SEQ ID NO:1 includes: a coding region for a CPK protein of about 400 amino acids, denoted herein as nCPK₁₂₀₃ and represented by SEQ ID NO:7, assuming a start codon spanning about nucleotides 2384-2386 and a stop codon spanning about nucleotides 3584-3586 of SEQ ID NO:1; a 20 coding region for a CgG protein of about 415 amino acids, denoted herein as nCgG₁₂₄₈ and represented by SEQ ID NO:9, assuming a start codon spanning about nucleotides 3698-3700 and a stop codon spanning about nucleotides 4943-4945 of SEQ ID NO:1; and a partial coding region for a CgD protein of 25 about 119 amino acids, denoted herein as nCgD₃₅₇ and represented by SEQ ID NO:11, assuming a start codon spanning

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about nucleotides 5137-5139. The amino acid sequences of the respective encoded proteins PCPK₄₀₀, PCgG₄₁₅, and PCgD₁₁₉ are represented by SEQ ID NO:8, SEQ ID NO:10 and SEQ ID NO:12.

SEQ ID NO:17 and SEQ ID NO:19 represent the deduced
5 nucleic acid sequences of the two complementary strands of nCUS₅₇₉. SEQ ID NO:17 includes a coding region for a CUS9 protein of about 149 amino acids, denoted herein as nCUS₄₅₀ and represented by SEQ ID NO:20, assuming a start codon spanning about nucleotides 54-56 and a stop codon spanning
10 about nucleotides 501-503 of SEQ ID NO:17. The amino acid sequence of the encoded protein PCUS₁₄₉ is represented by SEQ ID NO:18.

SEQ ID NO:29 and SEQ ID NO:31 represent the deduced nucleic acid sequences of the two complementary strands of
15 nCgI₁₆₁. SEQ ID NO:29 includes a partial coding region for a CgI protein of about 53 amino acids, denoted herein as nCgI₁₅₉ and represented by SEQ ID NO:32, assuming a first in-frame codon spanning about nucleotides 3-5 of SEQ ID NO:29. The amino acid sequence of the encoded protein PCgI₅₃ is
20 represented by SEQ ID NO:30.

Example 5

This Example describes the nucleic acid sequencing of additional nucleic acid molecules of the present invention.

Nucleic acid molecule nCTK₂₈₀, produced as described in
25 Example 1, was submitted to DNA sequence analysis to obtain the following sequences. SEQ ID NO:35 and SEQ ID NO:37

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represent the deduced nucleic acid sequences of the two complementary strands of nCTK₂₈₀. SEQ ID NO:35 includes a partial coding region for a CTK protein of about 93 amino acids, denoted herein as nCTK₂₇₉ and represented by SEQ ID NO:38, assuming a first in-frame codon spanning about nucleotides 2-4 of SEQ ID NO:35. The amino acid sequence of the encoded protein PCTK₉₃ is represented by SEQ ID NO:36.

Example 6

This Example discloses the production of a recombinant CHV genome and recombinant CHV of the present invention.

A cassette including the human CMV immediate early promoter and the poly-adenylation signal from bovine growth hormone separated by a polylinker was PCR amplified from plasmid pcDNA3 (available from Invitrogen) using forward primer EJH058 having nucleic acid sequence 5' TCCCCCGGGGGCGCGCCTTGACATTGATTATTGAC 3', denoted SEQ ID NO:49, and reverse primer EJH059 having nucleic acid sequence 5' GCCCTTAAGGGGCGCGCCAATGCGATGCAATTTCC 3', denoted SEQ ID NO:50. EJH058 has *Sma*I and *Asc*I sites attached to the 5' end of pcDNA3 homologous sequences, and EJH059 has *Afl*III and *Asc*I sites attached to the 5' end of pcDNA3 homologous sequences. The resultant PCR amplified fragment of about 930 nucleotides was digested with *Sma*I and *Afl*III and ligated into the *Sna*BI and *Afl*III sites of plasmid pLitmus 38. This cloning procedure eliminated the entire polylinker region of pLitmus38. The resulting recombinant plasmid, denoted herein

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as pAscCMV/BGH, contains the CMV promoter - BGH polyadenylation signal cassette, with its original polylinker, in a plasmid such that the entire cassette can be excised with enzyme AscI. This cassette plasmid can also be
5 prepared with other rare-cutting enzyme sites flanking the cassette.

Plasmid pAscCMV/BGH allows for the insertion of heterologous nucleic acid molecules between the CMV promoter and the BGH polyadenylation signal. The resulting
10 heterologous nucleic acid molecule-containing cassette was excised from the plasmid for insertion into a CHV genome. For example, a heterologous nucleic acid molecule containing a lacZ gene was inserted into the polylinker region of pAscCMV/BGH such that the lacZ gene is expressed by the CMV
15 promoter in a eukaryotic system. The cassette containing the lacZ gene, referred to herein as AscCMV/lacZ/BGH is then excised from the plasmid by AscI digestion and gel purified by standard methods.

About 5-10 μ g of CHV DNA is digested with AscI,
20 resulting in three fragments as disclosed herein. The DNA fragments are dephosphorylated with calf intestine alkaline phosphatase (available from BMB) for 10 minutes at 37°C; the enzyme is then inactivated for by incubation for 10 minutes at 65°C. The phosphatase-treated digested CHV DNA is then
25 subjected to extraction with phenol and phenol/chloroform and precipitated with ethanol.

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The phosphatase-treated digested CHV genomic DNA is mixed with the gel-purified AscCMV/lacZ/BGH cassette at a molar ratio of approximately 1:2 under standard ligation conditions. Since the viral DNA is dephosphorylated, it should not be able to self ligate; thus all resultant ligated viral molecules should contain two copies of the inserted cassette. The ligated DNA is then subjected to phenol extraction and ethanol precipitated.

The precipitated ligated DNA is resuspended in hepes-buffered saline and submitted to standard viral transfection conditions, such as that described by Graham et al., *ibid.*, along with appropriate controls (e.g., undigested viral DNA, digested and dephosphorylated viral DNA that was self-ligated, and no DNA). Resultant viral plaques are screened under an X-gal overlay for expression of β -galactosidase.

Example 7

This Example discloses the production of another recombinant CHV genome and recombinant CHV of the present invention.

A recombinant, or transfer, vector to be used in the production of a recombinant CHV having a heterologous nucleic acid molecule in a TK gene of the CHV genome is constructed as follows. A CHV TK nucleic acid molecule of the present invention (e.g., nCTK₂₈₀) is ligated into a pLitmus plasmid to produce a pCTK-Litmus plasmid. An expression cassette

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including a heterologous nucleic acid molecule (e.g., a *lacZ* gene or a nucleic acid molecule encoding an antigen isolated from a pathogenic organism) ligated to a CMV immediate early promoter and a BHV polyadenylation site in such a manner that
5 the heterologous nucleic acid molecule is expressed in a eukaryotic cell is inserted into the CTK nucleic acid molecule within pCTK-Litmus such that there are CTK flanking sequences on either side of the expression cassette (e.g., into a restriction site internal to nCTK₂₈₀).

10 A recombinant CHV is produced by co-transfecting the recombinant vector and CHV DNA into canine MDCK cells using previously described methods; see, for example, Graham et al., *ibid.* Recombinant TK negative CHV are selected for by passage in bromodeoxyuridine; see, for example, Kit et al.,
15 1983, *Virology* 130, 381-389. If the heterologous nucleic acid molecule is the *lacZ* gene, such recombinant CHV can also be selected as described in Example 6.

Example 8

This Example discloses the production of another
20 recombinant CHV genome and recombinant CHV of the present invention.

A recombinant, or transfer, vector to be used in the production of a recombinant CHV having a heterologous nucleic acid molecule in a dUTPase gene of the CHV genome is
25 constructed as follows. A CHV dUTPase nucleic acid molecule of the present invention (e.g., nCdUTP₄₅₉) is ligated into a

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pLitmus plasmid to produce a pCdUTP-Litmus plasmid. An expression cassette including a heterologous nucleic acid molecule (e.g., a *lacZ* gene or a nucleic acid molecule encoding an antigen isolated from a pathogenic organism) 5 ligated to a CMV immediate early promoter and a BHV polyadenylation site in such a manner that the heterologous nucleic acid molecule is expressed in a eukaryotic cell is inserted into the CdUTP nucleic acid molecule within pCdUTP-Litmus such that there are CdUTPase flanking sequences on 10 either side of the expression cassette (e.g., into a restriction site internal to nCdUTP₄₅₉).

A recombinant CHV is produced by co-transfecting the recombinant vector and CHV DNA into canine MDCK cells as described in Example 7. Recombinant dUTPase negative CHV are 15 selected for by passage in mercurithio analogs of deoxyuridine; see, for example, Holliday et al., 1991, *Antiviral Research* 16, 197-203. If the heterologous nucleic acid molecule is the *lacZ* gene, such recombinant CHV can also be selected as described in Example 6. Recombinant virus 20 carrying the foreign DNA of interest can also be selected by either by plaque hybridizations, or by dot-blot hybridizations of infected cell cultures. Verification of the proper insert within the CHV genome is conducted by Southern hybridization analysis.

25

Example 9

This Example discloses the production of a recombinant

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CHV by co-transfection of a set of overlapping cosmid clones comprising the entire viral CHV genome.

A library of CHV cosmid clones is created in the cosmid vector SuperCos (available from Stratagene Cloning Systems, La Jolla, CA) according to manufacturer's specifications, except that the vector is modified to contain one or more restriction sites not present in CHV genomic DNA (e.g., Sse83871, I-Sce-I, or NotI) so that the cosmid inserts can be excised prior to cotransfection. A heterologous nucleic acid molecule in an expression cassette, such as one of those described in Examples 6-8, is inserted into a cosmid clone using standard procedures. A recombinant CHV is produced by co-transfection of a set of overlapping cosmid clones comprising the entire viral CHV genome, including the cosmid comprising a heterologous nucleic acid molecule, using techniques as described in van Zihl et al., 1988, *J. Virol.* 62, 2191-2195.

Example 10

This Example describes the nucleic acid sequencing of additional nucleic acid molecules of the present invention.

Nucleic acid molecules nCAsc₉₃₀₀ and nCAsc₁₀₀₀₀, produced as described in Example 4, were submitted to additional DNA sequence analysis. The resultant nucleic acid sequences were compiled to produce SEQ ID NO:51 and SEQ ID NO:52. SEQ ID NO:51 and SEQ ID NO:52 represent the deduced nucleic acid sequences of the two complementary strands of a nucleic acid

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molecule referred to herein as nCUS₁₀₅₉₂. Nucleic acid molecule nCUS₁₀₅₉₂ includes the entire US region of CHV plus terminal repeat and internal repeat sequences. Analysis of SEQ ID NO:51 indicates that the US region spans from 5 nucleotides about 2047 through about 9724 of SEQ ID NO:51, whereas the terminal repeat sequences and inverted repeat sequences span from nucleotides about 1 through about 2046 and from nucleotides about 9725 through about 10592, respectively, of SEQ ID NO:51.

10 Translation of SEQ ID NO:51 and SEQ ID NO:52 indicates that nucleic acid molecule nCUS₁₀₅₉₂ contains at least the following open reading frames: CIR6, CUS2, CPK, CgG, CgD, CgI, CgE, CUS8.5 and CUS9. The relative locations of these open reading frames is shown in Fig. 4.

15 Specifically, SEQ ID NO:52 includes: the coding strand of nCIR6₅₅₂ (having SEQ ID NO:3) which encodes a CIR6 protein of about 183 amino acids, assuming a start codon spanning about nucleotides 9672-9674 and a stop codon spanning about nucleotides 10221-10223 of SEQ ID NO:52; and the coding 20 strand of nCUS2₁₁₇₆ (having SEQ ID NO:5) which encodes a CUS2 protein of about 391 amino acids, assuming a start codon spanning about nucleotides 8338-8340 and a stop codon spanning about nucleotides 9511-9513 of SEQ ID NO:52.

Nucleic acid molecules nCIR6₅₅₂ and nCUS2₁₁₇₆ are also 25 described in Example 4 in relation to nCUS₅₄₉₅, as are the corresponding nucleic acid sequences and amino acid sequences

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they encode.

SEQ ID NO:51 includes: the coding strand of nCPK₁₂₀₃ (having SEQ ID NO:7) which encodes a CPK protein of about 400 amino acids, assuming a start codon spanning about
5 nucleotides 2375-2377 and a stop codon spanning about nucleotides 3575-3577 of SEQ ID NO:51; the coding strand of nCgG₁₂₄₈ (having SEQ ID NO:9) which encodes a CgG protein of about 415 amino acids, assuming a start codon spanning about nucleotides 3689-3691 and a stop codon spanning about
10 nucleotides 4934-4936 of SEQ ID NO:51; the coding strand of nCgD₁₀₃₈ (having SEQ ID NO:53, and including SEQ ID NO:11) which encodes a CgD protein of about 345 amino acids, assuming a start codon spanning about nucleotides 5128-5130 and a stop codon spanning about nucleotides 6163-6165 of SEQ
15 ID NO:51; the coding strand of nCgI₁₀₉₅ (having SEQ ID NO:55, and including SEQ ID NO:29) which encodes a CgI protein of about 364 amino acids, assuming a start codon spanning about nucleotides 6225-6227 and a stop codon spanning about nucleotides 7317-7319 of SEQ ID NO:51; the coding strand of
20 nCgE₁₅₆₉ (having SEQ ID NO:57) which encodes a CgE protein of about 522 amino acids, assuming a start codon spanning about nucleotides 7467-7469 and a stop codon spanning about nucleotides 9033-9035 of SEQ ID NO:51; the coding strand of nCUS8.5₂₃₇ (having SEQ ID NO:59) which encodes a CUS8.5
25 protein of about 78 amino acids, assuming a start codon spanning about nucleotides 9028-9030 and a stop codon

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spanning about nucleotides 9262-9264 of SEQ ID NO:51; and the coding strand of nCUS9₃₆₀ (having SEQ ID NO:61) which encodes a CUS9 protein of about 119 amino acids, assuming a start codon spanning about nucleotides 9376-9378 and a stop codon spanning about nucleotides 9733-9735 of SEQ ID NO:51. SEQ ID NO:61 differs from the coding region reported for CUS9 in Example 4 (e.g., SEQ ID NO:20), in that additional sequence analysis indicated that SEQ ID NO:17 included a sequencing error resulting in a frameshift, leading to a longer deduced open reading frame. Nucleic acid molecules nCPK₁₂₀₃ and nCgG₁₂₄₈ are also described in Example 4 in relation to nCUS₅₄₉₅, as are the corresponding nucleic acid sequences and amino acid sequences they encode. The amino acid sequences of the respective encoded proteins PCgD₃₄₅, PCgI₃₆₄, PCgE₅₂₂, PCUS8.5₇₈, and PCUS9₁₁₉ are represented by SEQ ID NO:54, SEQ ID NO:56, SEQ ID NO:58, SEQ ID NO:60 and SEQ ID NO:62, respectively.

Example 11

This Example describes the nucleic acid sequencing of additional nucleic acid molecules of the present invention.

Nucleic acid molecules nChin₃₀₀₀, and nChin₁₉₀₀, produced as described in Example 3, were submitted to additional DNA sequence analysis. Also submitted to additional nucleic acid sequence analysis was nucleic acid molecule nChin₈₅₀₀, a HindIII fragment shown to include the 3' end of CUL48 as well as CgC and CUL45. The resultant nucleic acid sequences were

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compiled to produce SEQ ID NO:63, SEQ ID NO:64, SEQ ID NO:77, SEQ ID NO:78, SEQ ID NO:85, and SEQ ID NO:86. SEQ ID NO:63 and SEQ ID NO:63 represent the deduced nucleic acid sequences of the two complementary strands of a nucleic acid molecule referred to herein as nCUL49/CUL48₂₀₄₄. Translation of SEQ ID NO:63 and SEQ ID NO:64 indicates that nucleic acid molecule nCUL49/CUL48₂₀₄₄ contains at least the following open reading frames: CUL48 and the 3' end of CUL49. SEQ ID NO:77 and SEQ ID NO:78 represent the deduced nucleic acid sequences of the two complementary strands of a nucleic acid molecule referred to herein as nCUL₁₈₂₃. Translation of SEQ ID NO:77 and SEQ ID NO:78 indicates that nucleic acid molecule nCUL₁₈₂₃ contains at least the following open reading frames: CUL51, CdUTPase, CUL49.5, and the 5' end of CUL49. SEQ ID NO:85 and SEQ ID NO:86 represent the deduced nucleic acid sequences of the two complementary strands of a nucleic acid molecule referred to herein as nCUL52₇₄₉. Translation of SEQ ID NO:85 and SEQ ID NO:86 indicates that nucleic acid molecule nCUL52₇₄₉ contains a partial open reading frame for CUL52, the 3' end of which is included in SEQ ID NO:28. A portion of SEQ ID NO:86, from about nucleotide 539 through about nucleotide 749, was found to be identical to GenBank Accession No. X90456, as disclosed by Remond, et al., 1996, *ibid*. The relative location of each of these open reading frames is shown in Fig. 5.

Specifically, SEQ ID NO:63 includes: the coding strand of nCUL49₄₂₀ (having SEQ ID NO:65) which encodes a non-full

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length CUL49 protein of about 139 amino acids, assuming a stop codon spanning about nucleotides 419-421 of SEQ ID NO:63; and the coding strand of nCUL48₁₂₆₉ (having SEQ ID NO:67, and including SEQ ID NO:24) which encodes an

5 apparently full-length CUL48 protein of about 422 amino acids, assuming a start codon spanning about nucleotides 541-543 and a stop codon spanning about nucleotides 1807-1809 of SEQ ID NO:63. A portion of SEQ ID NO:63, from about nucleotide 1252 through about nucleotide 1647, was found to

10 be about 98% identical to GenBank Accession No. X89373, as disclosed by Remond, et al., 1996, *ibid*. Although this published sequence is contained within the coding region for the CUL48 protein, it does not disclose a full-length coding region. The amino acid sequences of the respective encoded

15 proteins PCUL49₁₃₉ and PCUL48₄₂₂ are represented by SEQ ID NO:66 and SEQ ID NO:68, respectively.

SEQ ID NO:77 includes the coding strand of nCdUTP₉₁₈ (having SEQ ID NO:79 and including SEQ ID NO:15) which encodes a CdUTPase protein of about 305 amino acids, assuming

20 a start codon spanning about nucleotides 624-626 and a stop codon spanning about nucleotides 1539-1541 of SEQ ID NO:77. The amino acid sequence of the respective encoded protein PCdUTP₃₀₅ is represented by SEQ ID NO:80.

SEQ ID NO:78 includes: the coding strand of nCUL51₂₆₁

25 (having SEQ ID NO:33) which encodes a non-full length CUL51 protein of about 86 amino acids, assuming translation begins

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at about nucleotide 1 and a stop codon spanning about nucleotides 259-261 of SEQ ID NO:78; the coding strand of nCUL49.5₂₆₁ (having SEQ ID NO:81) which encodes a CUL49.5 protein of about 86 amino acids, assuming a start codon
5 spanning about nucleotides 1175-1177 and a stop codon spanning about nucleotides 1433-1435 of SEQ ID NO:78; and the coding strand of nCUL49₂₅₅ (having SEQ ID NO:83) which encodes a non-full length CUL49 protein of about 85 amino acids, assuming a start codon spanning about nucleotides 1586-1588
10 of SEQ ID NO:78. The amino acid sequence of the respective encoded proteins PCUL51₈₆, PCUL49.5₈₆, and PCUL49₈₅ are represented by SEQ ID NO:34, SEQ ID NO:82 and SEQ ID NO:84, respectively.

SEQ ID NO:85 includes the coding strand of nCUL52₇₄₇
15 (having SEQ ID NO:87) which encodes a non-full length CUL52 protein of about 249 amino acids, assuming translation begins at about nucleotide 1 of SEQ ID NO:85. The amino acid sequence of the respective encoded protein PCUL52₂₄₉ is represented by SEQ ID NO:88.

20

Example 12

This Example discloses the production of another recombinant CHV genome and recombinant CHV of the present invention.

A 3.2 kb fragment containing the entire CdUTPase
25 sequence was amplified from CHV genomic DNA using forward primer RSF009 having nucleic acid sequence 5'

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GCCGGTACCAGGCTTTGGACGAGATTTAGG 3', denoted SEQ ID NO:89, and reverse primer RSF008 having nucleic acid sequence 5' GCCGAATTCAATATAATTAATAAACTCTC3', denoted SEQ ID NO:90. RSF009 has an *Asp*718 site attached to the 5' end of CHV homologous sequences, and RSF008 has an *Eco*RI site attached to the 5' end of CHV homologous sequences. The resultant PCR-amplified fragment of about 3.2 kb, referred to herein as nCdUTP₃₂₀₀, was digested with *Asp*718 and *Eco*RI and ligated into plitmus28 (available from New England Biolabs). The resultant recombinant plasmid, denoted herein as p28CdUTP₃₂₀₀, was verified by end-sequencing and restriction mapping. Plasmid p28CdUTP₃₂₀₀ was then digested with *Hind*III and *Xba*I, releasing an 858 base-pair fragment, referred to herein as nCdUTP₈₅₈, containing all of the dUTPase open reading frame except 108 bp at the 3' end. The *Xba*I site was found to be 49 nucleotides upstream of the start codon of the dUTPase ORF (open reading frame), and is also 70 nucleotides into the UL49.5 ORF on the opposite strand, which overlaps the dUTPase ORF. Previous studies have shown that the UL49.5 ORF in other herpesviruses encodes a membrane protein, and is nonessential for growth in tissue culture (e.g., Liang et al., *ibid.*).

The cohesive ends on the remaining 2.3 kb fragment of p28CdUTP₃₂₀₀, minus the 858 bp *Hind*III/*Xba*I fragment, were filled in using Klenow fragment and dNTPs according to standard methods. The resulting blunt-ended fragment was gel

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purified by standard methods. A heterologous nucleic acid sequence operatively linked to transcription control regions, in this case an AscCMV/lacZ/BGH cassette described in Example 6, was isolated from its plasmid by digestion with *AscI*, and the cohesive ends were filled in by Klenow fragment and dNTPs. This cassette was ligated to the *HindIII* and *XbaI*-digested p28CdUTP₃₂₀₀ fragment described above by standard methods resulting in a plasmid containing flanking regions to the CHV dUTPase gene and with the *lacZ* gene, operatively linked to transcription control regions, inserted into a deletion of the dUTPase gene, herein denoted as pdUTP/*lacZ*.

A recombinant CHV is produced by co-transfecting the plasmid with the deleted dUTPase gene and the inserted heterologous nucleic acid molecule, in this case pdUTP/*lacZ*, and CHV DNA into canine cells using previously described methods; see, for example, Graham et al., *ibid.*). Alternatively, a recombinant CHV is produced by transfecting canine cells with the aforementioned plasmid as described, and then infecting the cells with CHV. Recombinant dUTPase-negative CHV are selected for by passage in mercurithio analogs of deoxyuridine as described in Example 8. If the heterologous nucleic acid molecule is the *lacZ* gene, such a recombinant CHV can be selected as described in Example 6.

Example 13

This example discloses a method for obtaining higher plaque forming efficiencies to facilitate the production of

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recombinant CHV genomes and recombinant CHV of the present invention. The method involves the expression of the CHV alpha-tif gene in the presence of CHV genomes introduced into canine cells during CHV production.

- 5 The alpha-tif gene of CHV (denoted herein as nCUL48₁₂₆₉) was identified to lie on two CHV clones described herein: namely, nCHin₃₀₀₀ and nCHin₈₅₀₀. Nucleotide sequencing from the ends of these two fragments using universal primers and internal primers designed based on previous sequences was
- 10 used to determine the entire sequence. A single fragment including the complete alpha-tif gene was PCR amplified from CHV viral DNA using forward primer RSF014 having nucleic acid sequence 5' CCGGAATTCGCTTAGTGAGAGTATAAAC 3', denoted SEQ ID NO 91, and reverse primer RSF016 having nucleic acid sequence
- 15 5' CCGGAATTCCTCATATTATATACTAAC 3', denoted SEQ ID NO:92. Both primers have *EcoRI* sites attached to the 5' end of the CHV homologous sequences. The resultant PCR amplified fragment of about 1351 base pairs was digested with *EcoRI* and ligated into *EcoRI*-digested pCDNA3 (available from
- 20 Invitrogen, described in Example 6). This plasmid contains a neomycin-resistance gene for selection of stably transformed cell lines by techniques well known to those skilled in the art. Resulting plasmids were checked for the proper orientation by digestion with *HindIII*. A plasmid consisting
- 25 of pCDNA3 with the alpha-tif gene inserted in the proper orientation for expression was found, and is designated
-

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herein as pATIF₁₃₅₁. Expression of CHV alpha-tif from pATIF₁₃₅₁ was verified by cell-free transcription/translation using T7 RNA polymerase and a rabbit reticulocyte lysate system. These techniques are readily apparent to those skilled in the art, and are available in kit form, for example, from Amersham. Improved CHV DNA infectivity is then achieved by cotransfection of pATIF₁₃₅₁ with from about 1 to about 5 μ g of CHV DNA by methods such as described in Examples 6-9 and Example 12.

10 Alternatively, cell lines that stably express CHV alpha-tif are derived. Three canine cell lines, A72, D17 and CF2Th (all available from ATCC) were transfected with pATIF₁₃₅₁ by standard methods, see, for example, Graham et al., *ibid*. The cells are then subjected to selection using varying amounts
15 of the antibiotic G418 (available from BMB), determined empirically for each cell line. Cloned G418-resistant cell lines are then derived by standard dilution methods. Cell lines stably expressing CHV alpha-tif are then used for standard CHV DNA transfections or co-transfections such as
20 those described in Examples 6-9 and Example 12.

Example 14

This Example describes the identification and sequencing of additional CHV nucleic acid molecules of the present invention.

25 CHV nucleic acid molecule nCHIn₅₅₀₀, a CHV *Hind*III fragment derived as described in Example 2, was submitted to

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nucleic acid sequence analysis. Sequences derived from the sequence analysis include SEQ ID NO:69, SEQ ID NO:70, SEQ ID NO:73 and SEQ ID NO:74. Translation of these sequences indicated that nChin₅₅₀₀ includes at least a portion of the
5 CgL and CICIP4 coding regions. The nucleic acid molecule also apparently contains the CICIP0 coding region.

SEQ ID NO:69 and SEQ ID NO:70 represent the deduced nucleic acid sequences of the two complementary strands of a CHV ICP4 nucleic acid molecule referred to herein as
10 nCICP4₆₂₆. Translation of SEQ ID NO:69 indicates that nCICP4₆₂₆ encodes a non-full length CICIP4 protein of about 208 amino acids, denoted herein as PCICP4₂₀₈, having an amino acid sequence represented by SEQ ID NO:72. The coding region for PCICP4₂₀₈ is denoted herein as nCICP4₆₂₄, having nucleic acid
15 sequence SEQ ID NO:71. A portion of SEQ ID NO:69, from about nucleotide 1 through about nucleotide 307, was found to be identical to GenBank Accession No. X90422, as disclosed by Remond, et al., 1996, *ibid*.

SEQ ID NO:73 and SEQ ID NO:74 represent the deduced
20 nucleic acid sequences of the two complementary strands of a CHV gL nucleic acid molecule referred to herein as nCgL₆₅₅. Translation of SEQ ID NO:74 indicates that nCgL₆₅₅ encodes a non-full length CgL protein of about 171 amino acids, denoted herein as PCgL₁₇₁, having an amino acid sequence represented
25 by SEQ ID NO:76. The coding region for PCgL₁₇₁ is denoted herein as nCgL₅₁₆, having nucleic acid sequence SEQ ID NO:75,

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assuming that the open reading frame spans about nucleotides 1 through 516 of SEQ ID NO:74, with a stop codon spanning about nucleotides 514-516.

Example 15

5 This example describes the mapping of messenger RNA molecules transcribed from nucleic acid molecules of the present invention. These transcripts are useful for verifying expression (or lack of expression) of various genes.

10 Total RNA was prepared from CHV-infected cells using a phenol/guanidine extraction method familiar to those skilled in the art. See, for example, Chomczynski et al., 1987, *Anal. Biochem.* 162, 156-159. Multiple samples of RNA were separated on formaldehyde/agarose gels and transferred to
15 nitrocellulose by standard methods. Based on the sequences of nCUS₁₀₅₉₂, designated SEQ ID NO:51 and SEQ ID NO:52, nucleic acid fragments were isolated for use as probes, such that they would hybridize to sequences homologous to the open reading frames nCPK₁₂₀₃ (SEQ ID NO:7), nCgG₁₂₄₈ (SEQ ID NO:9),
20 nCgD₁₀₃₈ (SEQ ID NO:53), nCgI₁₀₉₅ (SEQ ID NO:55), nCgE₁₅₆₉ (SEQ ID NO:57), nCUS8.5237 (SEQ ID NO:59), nCUS9₃₆₀ (SEQ ID NO:61), nCIR6₅₅₂ (SEQ ID NO:3), and nCUS2₁₁₇₆ (SEQ ID NO:5). The probes were as follows: to hybridize with an nCIR6₅₅₂ (SEQ ID NO:3) transcript, a *Pst*I-*Hind*III restriction fragment
25 extending from about nucleotide 1 to about nucleotide 685 in nCUS₁₀₅₉₂ herein denoted as probe A; to hybridize with an

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nCUS_{2,1176} (SEQ ID NO:5) transcript, a PCR -amplified fragment extending from about nucleotide 2056 to about nucleotide 2273 in nCUS₁₀₅₉₂ herein denoted as probe B; to hybridize with an nCPK₁₂₀₃ (SEQ ID NO:7) transcript, a *Pst*I-*Dra*I restriction fragment extending from about nucleotide 2326 to about nucleotide 2788 in nCUS₁₀₅₉₂ herein denoted as probe C; to hybridize with an nCgG₁₂₄₈ (SEQ ID NO:9) transcript, a *Bam*HI-*Pst*I restriction fragment extending from about nucleotide 3766 to about nucleotide 4494 in nCUS₁₀₅₉₂ herein denoted as probe D; to hybridize with an nCgD₁₀₃₈ (SEQ ID NO:53) transcript, either a *Bgl*III-*Bgl*III restriction fragment extending from about nucleotide 5728 to about nucleotide 6561 in nCUS₁₀₅₉₂ (this piece slightly overlaps nCgI₁₀₉₅) herein denoted as probe E, or a PCR-amplified fragment that will extend from about nucleotide 5295 to about nucleotide 5885 in nCUS₁₀₅₉₂ herein denoted as probe F; to hybridize with an nCgI₁₀₉₅ (SEQ ID NO:55) transcript, a *Bgl*III-*Bgl*III restriction fragment extending from about nucleotide 6561 to about nucleotide 7263 in nCUS₁₀₅₉₂ herein denoted as probe G; to hybridize with an nCgE₁₅₆₉ (SEQ ID NO:57) transcript, a deletion subclone extending from about nucleotide 7667 to about nucleotide 8425 in nCUS₁₀₅₉₂ herein denoted as probe H; to hybridize with a putative ncus85237 (SEQ ID NO:59) transcript, a PCR-amplified fragment extending from about nucleotide 9023 to about nucleotide 9242 in nCUS₁₀₅₉₂ herein denoted as probe I; to hybridize to an nCUS_{9,360} (SEQ ID NO:61)

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transcript, a PCR-amplified fragment extending from about nucleotide 9447 to about nucleotide 9715 in nCUS₁₀₅₉₂ herein denoted as probe J. These probes are shown graphically in Fig 4. The probes were labelled with ³²P dATP using random priming, a technique well known to those skilled in the art. Hybridization of the probes to the RNA samples on nitrocellulose and washing at stringent temperatures were done according to well known methods.

The main transcript sizes that hybridized to the various probes were as follows: probe A hybridized strongly to a transcript of about 0.7 kb, but also hybridized weakly to transcripts of about 1.7, 2.2 and 2.6 kb; probe B hybridized with a transcript of about 2.2 kb; probe C hybridized to a transcript of about 2.6 kb; probe D hybridized to two transcripts of about 1.9 kb and 2.6 kb; probe E hybridized to two transcripts of about 4.2 kb and 3.2 kb; probe G hybridized to two transcripts of about 4.2 kb and 3.2 kb; probe H hybridized to three transcripts of about 1.9 kb, 3.2 kb, and 4.2 kb; probe I hybridized to the same three transcripts as probe H; probe J hybridized to a transcript of about 2.1 kb. These data suggest that the transcripts of US2, US9, and IR6, although starting at different points, terminated in a common general area in the inverted repeats, since probe A hybridized to transcripts that were generally the same size as the US2 and US9 transcripts. Furthermore, these data suggest that the PK and gG transcripts overlapped,

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probably terminating at a common 3' terminus, since probe C hybridized to only a 2.6 kb transcript but probe D hybridized with both the 2.6 kb transcript and the 1.4 kb transcript. This result was even more likely because only one

5 polyadenylation consensus sequence (AATAAA) was found downstream of the gG ORF, but before the gD ORF. This polyadenylation signal was found from nucleotide 4935-4940 of nCUS₁₀₅₉₂. Similarly, these data indicate the gI and gE transcripts overlapped, probably terminating at a common 3'

10 terminus since probe G hybridized to a transcript of 2.6 kb, while probe H hybridized both to the 2.6 kb transcript and the 1.9 kb transcript. Probes E, G, and H also all hybridized to a 4.2 kb transcript, suggesting that the gD transcript also overlapped the gI and gE transcripts,

15 probably terminating at a common 3' terminus. Verification of this result is if probe F hybridizes only to the 4.2 kb transcript. Probe I hybridized to only the 4.2, 2.6 and 2.9 kb transcripts suggesting two things; first, that these three transcripts probably terminated at polyadenylation signals at

20 about 9186-9181, 9256-9261 or 9260-9265 of nCUS₁₀₅₉₂, also that the putative US8.5 open reading frame is not transcribed to levels detectable by Northern analysis.

Example 16

This example discloses the production of recombinant

25 canine cell lines that stably express the CHV alpha-trans-

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inducing factor (α -TIF), and demonstrates that such recombinant cell lines have greatly improved plaque forming efficiencies upon transfection with CHV DNA.

Six recombinant canine cell lines that stably express the CHV α -TIF gene were produced as follows. D17 canine tumor cells (available from ATCC) were plated at 4×10^6 cells per 100 mm petri dish. The cells were transfected with 2 μ g of pATIF₁₃₅₁ plasmid DNA, produced as described in Example 13, using the transfection reagent Lipofectamine[™] (available from Life Technologies, Inc., (LTI) Gaithersburg, MD) according to the manufacturer's instructions. Twenty-four hours following the transfection, the antibiotic G418 (Geneticin[™], available from BMB) was added to the media at a concentration of 350 μ g/ml, to select for cells expressing the neomycin resistance gene contained on plasmid pATIF₁₃₅₁. Forty-eight hours later, the cells were diluted to 10 cells per well in a 96-well tissue culture plate. Thirteen G418-resistant cell colonies were cloned out and expanded under antibiotic selection by standard methods well-known to those skilled in the art.

Six of these cloned cell lines, denoted herein as D17:pATIF₁₃₅₁-A through D17:pATIF₁₃₅₁-F, were tested for their ability to support improved plaque-forming efficiency upon transfection with CHV DNA, as follows. The six cell lines, as well as wild-type D17 canine tumor cells, were each plated, in duplicate, at 4×10^6 cells per 100mm petri dish

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just prior to transfection. Each cell line was transfected with 1 μ g of CHV DNA using the CaPO_4 method of Graham, et al., *ibid.* Six hours post-transfection, the cells were treated for one minute with 20% glycerol in PBS as a

5 hypertonic shock, washed with PBS, and grown at 35°C in DMEM containing G418 at 350 μ g/ml. Seventy-two hours post-transfection the medium was removed and replaced with medium containing 0.7% agarose, the total number of virus plaques from each transfection were counted, and the duplicate

10 transfections for each cell line were averaged. The results of these transfections, shown in Table 1, indicate that at least four of the recombinant canine cell lines, D17:pATIF₁₃₅₁-B, D17:pATIF₁₃₅₁-C, D17:pATIF₁₃₅₁-D, and D17:pATIF₁₃₅₁-F, promoted significantly higher plaque forming

15 efficiency upon transfection with CHV DNA than did wild-type D17 cells.

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TABLE 1

Transfection Efficiencies of Recombinant Cell Lines

	Cell Line	Average Number of Plaques (PFU)
	D17:pATIF ₁₃₅₁ -A	5
5	D17:pATIF ₁₃₅₁ -B	29
	D17:pATIF ₁₃₅₁ -C	30
	D17:pATIF ₁₃₅₁ -D	166
	D17:pATIF ₁₃₅₁ -E	0
	D17:pATIF ₁₃₅₁ -F	275
10	Wild-Type D17	0

Example 17

This example discloses the production of another recombinant CHV genome and recombinant CHV of the present invention.

15 A specific deletion in a plasmid containing the CdUTPase open reading frame was produced as follows. Plasmid p28CdUTP₃₂₀₀, produced as described in Example 12, was digested with *HindIII* and *XmnI*, releasing a 727-bp fragment, referred to herein as nCdUTP₇₂₇. This fragment includes most
20 of the CdUTPase ORF, extending from about nucleotide 84 to

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about nucleotide 810 of SEQ ID NO:79. Release of this
XmnI/HindIII fragment does not delete any of the CUL49.5 ORF
contained on the opposite strand of p28CdUTP₃₂₀₀, as did
XbaI/HindIII digestion as disclosed in Example 12, but *XmnI*
5 digestion could delete a portion of the CUL49.5 transcription
control region, since the restriction site is only about 58
nucleotides upstream of the start codon for the CUL49.5 ORF,
i.e., at about nucleotide 1117 of SEQ ID NO:78. Following
XmnI/HindIII digestion of p28CdUTP₃₂₀₀, the cohesive *HindIII*
10 end on the about 4.9-kb fragment (the remaining CHV insert of
about 2.5 kb, plus the 2.4-kb pLitmus28 vector) was filled in
using Klenow enzyme and dNTPs according to standard methods.

A recombinant transfer vector containing a reporter gene
encoding green fluorescent protein (GFP) operatively linked
15 to transcription control regions, inserted into a deletion in
the CHV dUTPase gene, was constructed as follows. The pGreen
Lantern™-1 vector (available from LTI) was digested with *NotI*
to release a 750-bp fragment containing the coding region of
a genetically engineered GFP gene. This 750-bp fragment was
20 cloned into plasmid vector pASCCMV/BGH, prepared as described
in Example 6, which had been digested with *NotI* and
dephosphorylated with calf intestinal alkaline phosphatase.
The proper orientation of the insert was verified by a
diagnostic restriction digest. The resulting recombinant
25 plasmid, denoted herein as pASCCMV/GFP/BGH, contained a
genetically engineered GFP gene operatively linked to the CMV

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immediate-early promoter and the BGH polyadenylation signal, such that the entire transcriptional unit can be excised from the plasmid by digestion with *AscI*. Plasmid pAscCMV/GFP/BGH was digested with *AscI*, releasing a 1.8-kB transcription unit. The cohesive ends of the fragment were filled in with Klenow enzyme and dNTPs and the fragment was gel purified by standard methods. The 1.8-kB transcription unit containing the GFP gene was then ligated into the 4.9-kb p28CdUTP₃₂₀₀ *XmnI*/*HindIII* restriction fragment, produced as described in the previous paragraph, using T4 DNA ligase. Resulting recombinant plasmids were analyzed and verified by restriction digestion and end-sequencing. The resulting recombinant plasmid, containing flanking regions to the CHV dUTPase gene into which had been inserted a genetically-engineered GFP gene operatively linked to transcription control regions, is denoted herein as pdUTP/GFP.

A recombinant CHV genome and a recombinant dUTPase-negative CHV expressing green fluorescent protein was produced as follows. Recombinant cell line D17:pATIF_{1351(F)}, produced as described in Example 16, was plated at 4×10^6 cells/100mm petri dish just prior to transfection. The cells were transfected with 0.5 μ g of CHV DNA, produced as described in Example 2, and 0.5 μ g of pdUTP/GFP DNA, produced as described in the preceding paragraph, by the CaPO₄ method of Graham et al., *ibid*. Six hours post-transfection, the cells were treated for one minute with 20% glycerol in PBS as

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a hypertonic shock, washed with PBS, and grown at 35°C. in DMEM containing G418 at 350 µg/ml. Seventy-two hours post-transfection the medium was removed and replaced with medium containing 0.7% agarose. Resulting virus plaques were

5 screened for expression of GFP by fluorescent microscopy using a standard fluorescein filter on an inverted fluorescent microscope, for example an Olympus 1X70 microscope, available from Olympus Optical Company, Japan. Out of forty-two plaques screened, four were positive for

10 expression of GFP, indicating that the GFP gene contained on pdUTP/GFP had recombined into the dUTPase locus of the CHV genome. One of these recombinant CHV, denoted herein as CHVΔdUTP:GFP-1, is isolated and expanded for further analysis.

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SEQUENCE LISTING

The following Sequence Listing is submitted pursuant to 37 CFR §1.821. A copy in computer readable form is also submitted herewith.

5 Applicants assert pursuant to 37 CFR §1.821(f) that the content of the paper and computer readable copies of SEQ ID NO:1 through SEQ ID NO:92 submitted herewith are the same.

(1) GENERAL INFORMATION:

- 10 (i) APPLICANT: Haanes, Elizabeth J.
Frank, Rexann S.
- (ii) TITLE OF INVENTION: RECOMBINANT CANINE HERPESVIRUSES
- (iii) NUMBER OF SEQUENCES: 92
- 15 (iv) CORRESPONDENCE ADDRESS:
(A) ADDRESSEE: Sheridan Ross
(B) STREET: 1700 Lincoln Street, Suite 3500
(C) CITY: Denver
20 (D) STATE: Colorado
(E) COUNTRY: U.S.A.
(F) ZIP: 80203
- (v) COMPUTER READABLE FORM:
(A) MEDIUM TYPE: Floppy disk
(B) COMPUTER: IBM PC compatible
25 (C) OPERATING SYSTEM: PC-DOS/MS-DOS
(D) SOFTWARE: PatentIn Release #1.0, Version #1.30
- (vi) CURRENT APPLICATION DATA:
(A) APPLICATION NUMBER:
(B) FILING DATE:
(C) CLASSIFICATION:
- 30 (viii) ATTORNEY/AGENT INFORMATION:
(A) NAME: Connell, Gary J.
(B) REGISTRATION NUMBER: 32,020
(C) REFERENCE/DOCKET NUMBER: 2618-46-PCT
- 35 (ix) TELECOMMUNICATION INFORMATION:
(A) TELEPHONE: (303) 863-9700
(B) TELEFAX: (303) 863-0223
- (2) INFORMATION FOR SEQ ID NO:1:
- 40 (i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 5495 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

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(ii) MOLECULE TYPE: DNA (genomic)

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:1:

CTGCAGTGTA TTTAAAAAAT AAAATCTATG AATGAAATCT ATGAATGAAA TCTATGAATG	60
AAATCTATGA ATGAAATCTA TGAATGAAAT CTATGAATGA AATCTATGAA TGAAATCTAT	120
5 GAATGAAATC TATGAATGAA ATCTATGAAT GAAATCTATG AATGAAATCT ATGAATGAAA	180
TCTATGAATG AAATCTATGA ATGAAATCTA TGAATGAAAT CTATGAATGA AATCTATGAA	240
TGAAATCTAT GAATGAAATC TATGAATGAA ATCTATGAAT GAAATCTATG AATGAAATCT	300
ATGAGACAAG TATTTTAAAA ATATTTTAAA TTTATAAGGT TAAGTACAGT AGGCGGTTGG	360
GTAACATTTT TTAGTTTTTC AAGTTTTTTC TTTTCTGGT ATCCTACCCA ACACAAATGC	420
10 ATCTTCGGAT ACATTTATTT TAAGAGAGTA ATCACTTTTT AGAATATATC TTATTGGTGG	480
TACATTTATA AATTTTGGAC CATCCCAATA ACACTTCGAT TCCACAAGCG AAGAAGGTAC	540
TTCCATAAGC TGAGAAGCGT TTAATTGATT GTAGGGAGAA CTGGCGTTT CAAAATCCTT	600
TAGAACGTAT AGTCTGCAAT ACATAGGTTT AATATCATCT TCATACCTCT CATCAGGATA	660
TGAAATGGA AGTTTCACAA AGGTTCATC ACGAAGCTTT TTGAAGAATC GTACATCCGT	720
15 AGGTGGTGTA GGAACAATAG TGAAGGCGTG CGGTTACCCC TGGTTTTTCA CACGTGCAAG	780
CGCTGGTGTC GTTTTAGGGC GAACTGGAAA ATAACCAGGC GGAAGTTGTG CGTAGAATCC	840
TTCAATTAAGT TCTCCACGAC AGCGTCTGAA GTATGATGGC ATATTAGCTT GATCGGAGTT	900
GTTATCAAAAT AGAGCAAATG AAGCACTCAT TTTAAACTT TTTAGTTAAG CTTTAAAAAC	960
AAGTGAAGAT TTAATAATGT AGGATAAAAT GCCAGTTTAT ATACAGTAAG AATATGGGAG	1020
20 TGGTTCACAT AAAAAACCAG AATTCAGGT TTACATCTAC TGTATTATCA CAACAAATAT	1080
AAACAACTT AGTTTCACA TAAACATGAA CTAAATAGAG ATGAACGTTG AGCGTTGGTA	1140
GGTTGTGTAG AAGACATACC ATCGTTTTCA TTTTGGTTA TTGTTTGGC GCGCCTTGAA	1200
AATAATCGTT TAAAAATATT TGGTTTGGAT AGCCTTTTCA TAGGTTTCAC CCCATGCAAG	1260
TCATCCTCTT CTGGTTCAGG AATTCTTCA TAACCATTAT GGGATATTAT TGCACACATA	1320
25 AATGATTCTA TTACCGGGGG GGCAGAACGT GTCTCATTTA TATAAAGAGA ATCACATACA	1380
TCGCTTATAG AACATGTAGA ACTGTCAGAA TCCTCTTTAA AACTATTTTT AATTCACAA	1440
TTAGTTTCTT CTAGTTCATT ATCCACCATC GCATTAGCGT ATTTCCAAAT ATCATTTCTCT	1500
GAGGAATAAT GAGATGCAGA GCATGAAGAA GAGGATGAGG AGGAGGAGGA TGAAGATGAG	1560
GATATAGAGG GACATCTTGG AGAGCTTTCA AAGTTGAATG GAGTATTAAA TGTGTACCA	1620
30 TAAAAAATGT CACTTAACAT AGGGGGTACT TTAAAGGAGG ACAGAAAGGT GTCTAATACA	1680
GGTACCCATA TAAACGAGGG GCAATAAACA CTCCAGAAAT CATCGATATG TTTTACATTA	1740

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	TTTTTGAAA TCTCAAGACA CTCAGGTTTC CAGGATGGTT CCGGCCATTC ACATGATACA	1800
	TATGCATAAA TTAGTCGCTT TGGTCCTGGG ATATTAGAAA TGACTGGCTC ACATAAATCC	1860
	GCTGCACCGA AAACCCATAG ATTAAGAGGA TAGTTTCCAA ATATACCAGA GTTTAGATAG	1920
	TTATACCCCG AAACAGCCGA TTTCCATTCG ATGCTAGCCC CAGGTTTATC CTCATAAAAT	1980
5	AAAAAGTCCT CCTCCTCCCC CTCCGTTGGT TTTAAAAATT TACTATTAGA GGTGTGATGT	2040
	CTTACTATAG GCCTTGAAAC TCTAGGTAGA TGTTTTATAG AGTCCATAAA ATAACATAAG	2100
	TTTGCAGATC GTAATATTAT AGGCATAGCC AATCGTGTGA GAGAAAGGAT ATAGCATTGT	2160
	CTAGCCATAA AACACCAAAG ATCAGGATGA ACATCTTGGG AGTTTCCTGG TAACGCCCCA	2220
	TTTTTGTCAA TAAACGTAAC AATATTAACT TCAACCACAC CCATAATTAA ATTTTATGTA	2280
10	TGAATCCAAT AAAGGTTAAT ACACACCTAA TTTATGTTAT AATTTTAGAA GAAGCTGCAG	2340
	TTGATGAGTT GATATTAAAC TAACAATTC ACAATTACCT GATATGGCAA AGTGTACCAC	2400
	CGAAAAGTTT TGTGTATCA GCGTGAATAG AGAATCTTCT GTCGATCCAG AAGACTTCTA	2460
	TAAACCGGTT CCTCTAACTT CAGATTGAT TGAAGAGGAT AACCTACATC AAGACAAAAT	2520
	AATGGATGAG GATTTATACT CGGATTTTAG TGATGATGAC TTTATGGATT ATACAAAAAA	2580
15	TCCAACTGAA AGTGAAAATG AAAGAGAAAG TGACGAAGAA GTTGAAGAAA GTTATGAAAG	2640
	TGATGAAGAT AAAAAAGTT TATCTCCTAC TAAAAGCGAA GGAATTGAAG CGGCTGAAGC	2700
	GCTAAAGTTT TCTGTTGTTA AATCGTTAAC GCCTGGGTCA GAAGGAAGAG TTTTATTGTC	2760
	TCTTAAAAAA GATAAAGATA CAAGCTATAA GGTAAATTTA AAAATTGGAC AAAGGGGAAA	2820
	CACGCTTGTC GAATCGTTAA TTTTGAGAAA TATTAGTCAC CAATCTATAA TTAACTTCA	2880
20	AGACACTCTT TTTTATAAAG AGTTAACATG TTTGGTGTTA CCGTATTATA AATATGATCT	2940
	ATATAATTTT TTAATGGATC ATGGGAAATC TCTGTCTTTT GAATCTGTAA TTAAATTTGA	3000
	AAAACAAATA TTAATGGAC TTCAATATAT TCATGGAAAA AAAATTATTC ATCGAGATAT	3060
	AAAAACTGAA AATATTTTCT TGGATAATGA CTCTAATGTT TGTATAGGTG ATTTTGGGGC	3120
	TTCTCAATTT CCTGTTTCCT CACCAGATTA TTTGGGAATT GCGGGGACTA TTGAAACTAA	3180
25	TGCTCCTGAA GTTCTATCAA AGGATGCGTA CAACTGTAA GCTGATATTT GGAGTGCTGG	3240
	TATAATTTTA TTTGAAATGC TTGCATATCC TAATGTTTTG TTTGAGGAGG AAGAAAGAGA	3300
	TAGTAGCGAT TTAATAAACA ATTGTAATCT TCATCTTATA AAAATTATAT CAACTCTGAA	3360
	GATTAACCCA AATGAATTC CATCTGATTT GGAATCTAAT CTAGTAAAC ATTTTATAAA	3420
	ATATGCTAAT AATGATAGAC CTCCATTTAC ACGATATAAT CGTCTAAATA ACCTTAAATT	3480
30	ACATCTCGAT GGTGAATTTT TAATTCATAA AATGCTAACA TTTGATGCAT CTCTACGACC	3540
	AAGTGCGGAA GAACTATTAT CCTATCAGAT TTTTAGTAAA CAATAAATTT CATAAAAAATG	3600

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	GGCGTGGAAT	TTTTTATTGT	TTTATATAAA	ACGGGTGTTT	GAAAGCTCTT	TTTTATTAAT	3660
	TTTTTTTTTA	CATCCTAGCT	ACAATATTAT	AGTTATCATG	TTGTATACGC	TGTTTTTTGT	3720
	TTTTTATTTT	AAGGTAGTTT	TATCTCGCAT	AGCTCCGCTA	GAGTTGTGTT	ATGCGGATCC	3780
	TAAAGAAAAT	ACAACTGAAC	CTACACAAC	TCCTACAGGG	GAACAATCTA	AGACTCTTAT	3840
5	TCCCGTGGTA	ACAAACGGAT	ATGTTGAATA	CTCTAAAGGA	TGTGAAC	TACGATTAGA	3900
	TACATATGTA	AATGTATCTT	CACGACCAGA	AAAAAAGGTT	AATGCTACAA	TTGGATGGTC	3960
	ATTTGATCTT	GGTTGTCAAA	TTCCTTTAAT	TTATAGAGAA	TATTATAATT	GTACTGGTAA	4020
	TATAATACCA	TCACCAGAAA	CTTGTGATGG	TTATTCCTTA	ACTTTGGTAA	AATCTGAAAG	4080
	TATATCATCT	TATGCACTTG	TTAATGTTAG	TTTGCTTATT	CAACCAGGAA	TTTTTGATTG	4140
10	TGGTAGATAT	TTATACTCAC	TTGTTTTTGG	AAACGATAGT	TATAACGGAA	GAATTGAAGT	4200
	TCGAGTGGAT	AATGAGACAG	ACTATCCATG	TTTTATGATG	CATGGATTGA	CTGTAAAAAA	4260
	GGGTGATAAA	CTTCATATTC	CTTATAAACC	ATCCACAAAT	CCTAATCATA	AACGATATAG	4320
	AGGTTGTTTT	CCAAATATCAA	ATACTGAGCT	ATGGAATAAT	ATTAGTGATG	AAAGTGTGG	4380
	TAGATATTCA	TATGATGAAG	AATATGAAGA	ATATGAAGAA	GAAAACGAAG	ATTTTGAAGA	4440
15	TCTACAATCA	AAAGATTGCC	GCAAATCCAA	TCTTTTGTAT	ATGAAGAAGA	CTTTTAATTT	4500
	GGCTGCAGGT	TCTCAAAGTT	TATTGATTGC	TAGTTTGGGT	AAATCAATTT	CAGAACAACC	4560
	GTGGTCATTT	AAAATTAATG	AAAGTTATGA	ACTTTTTAAT	AATTTGTCTA	TCACCCTTCA	4620
	ATCGGAAGAA	GATTCTAATA	TACTGAATCC	TGAAATTGTA	ACGTTTACCA	CACCACCACC	4680
	TACTGAAAT	ACACATATGT	TTATGTCAAA	TAATGAAACT	ATGTATGAAG	AAGAAAGTGT	4740
20	TTTAAGCATT	ATTCAATTGT	TTAACAATGG	TTATAATAAT	TGTAATACCC	ATATAAAGGT	4800
	AATTGGATTT	GGAACAATTA	TCTTTATTAT	TTTATTTTTT	GTTGCTGTGT	TTTTTTGTGG	4860
	ATATACTTGT	GTATTAACT	CTCGTATTAA	AATGATTAA	CATGCTTATA	TACAACCCCA	4920
	GAAATTAAAT	TTTTATGATA	TTTAATAAAA	CTATTATGAA	ACTTCTTATA	ACTTATTGT	4980
	TTTTATTAAA	TGGGTGGGT	TGGTTTTAAA	ATTACATACG	TGTATTAGA	ATTAACATCA	5040
25	TAAAGGACAC	ACCCATGAAA	AACATTTAAA	TTCTATTAA	TTGAACGGAT	TAAACATTTT	5100
	CTCATTTTAA	GAGTGTCTAC	GACTTTTGAT	AGTAAATGA	TTAACTTCT	ATTTATCTTA	5160
	TTTTATTTTA	ACCCAATAAC	TGGATATAAA	TGGGTAGACC	CTCCTCGTAG	GTATAATTAC	5220
	ACCGTTTAA	GAATGATTCC	AGATATTCCA	AATCCAATGG	ATCCTTCTAA	AAACGCTGAA	5280
	GTTCCGTATG	TAACTTCTAC	TGACCCATGT	GATATGGTTG	CTTTGATTTC	TAATCCAAAT	5340
30	ATAGAATCTA	CAATTAAAC	GATTCAATTT	GTGCAAAAGA	AAAAATTTTA	CAATGCATCT	5400
	CTTAGTTGGT	TTAAAGTTGG	AGATGATTGT	ACATATCCAA	TATATTTAAT	TCAATATTTT	5460

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GATTGTGATC CTCAAAGAGA ATTTGGCATA TGTTT

5495

(2) INFORMATION FOR SEQ ID NO:2:

(i) SEQUENCE CHARACTERISTICS:

- 5 (A) LENGTH: 5495 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:2:

10 AAACATATGC CAAATTCTCT TTGAGGATCA CAATCAAAAT ATTGAATTAA ATATATTGGA 60
TATGTACAAT CATCTCCAAC TTAAACCAA CTAAGAGATG CATTGTAAAA TTTTCTCTTT 120
TGCACAAATT GAATCGTTT AATTGTAGAT TCTATATTTG GATTAGAAAT CAAAGCAACC 180
ATATCACATG GGTCACTAGA AGTTACATAC CGAACTTCAG CGTTTTTAGA AGGATCCATT 240
GGATTGGAA TATCTGGAAT CATTCTTAAA ACGGTGTAAT TATACCTACG AGGAGGGTCT 300
15 ACCCATTAT ATCCAGTTAT TGGGTAAAA TAAATAAGA TAAATAGAAG TTAATCATT 360
TTACTATCAA AAGTCGTAGC AACTCTTAAA ATGAGAAAAAT GTTAATCCG TTCAAATTAA 420
TAGAATTAA ATGTTTTTCA TGGGTGTGTC CTTTATGATG TTAATTCTTA ATACACGTAT 480
GTAATTTTAA AACCAACCCA ACCCATTTAA TAAAAACAA TAAGTTATAA GAAGTTTCAT 540
AATAGTTTAA TTAATATCA TAAAAATTTA ATTTCTGGGG TTGTATATAA GCATGGTTAA 600
20 TCATTTTAA ATCGAGAGTTT AATACACAAG TATATCCACA AAAAAACACA GCAACAAAAA 660
ATAAATAAT AAAGATAATT GTTCCAAATC CAATTACCTT TATATGGGTA TTACAATTAT 720
TATAACCATT GTTAAACAAT TGAATAATGC TTAACAACT TTCTTCTTCA TACATAGTTT 780
CATTATTGTA CATAAACATA TGTGTATTTT CAGTAGGTGG TGGTGTGGTA AACGTTACAA 840
TTTCAGGATT CAGTATATTA GAATCTTCTT CCGATTGAAG GGTGATAGAC AAATTATTAA 900
25 AAAGTTCATA ACTTTCATTA ATTTTAAATG ACCACGGTTG TTCTGAAATT GATTTACCCA 960
AACTAGCAAT CAATAAATTT TGAGAACCTG CAGCCAAATT AAAAGTCTTC TTCATATCAA 1020
AAAGATTGGA TTTGCGGCAA TCTTTTGATT GTAGATCTTC AAAATCTTCG TTTTCTTCTT 1080
CATATTCTTC ATATTCTTCA TCATATGAAT ATCTACCAAC ACTTTCATCA CTAATATTAT 1140
TCCATAGCTC AGTATTGAT ATTGGAAAAC AACCTCTATA TCGTTTATGA TTAGGATTTG 1200
30 TGGATGGTTT ATAAGGAATA TGAAGTTTAT CACCCTTTTT TACAGTCAAT CCATGCATCA 1260
TAAACATGG ATAGTCGTG TCATTATCCA CTCGAACCTC AATTCTTCG TTATAACTAT 1320
CGTTTCCAAA AACAAGTGAG TATAAATATC TACCAGAATC AAAAATTCCT GGTGAATAA 1380

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	GCAAACTAAC ATTAACAAGT GCATAAGATG ATATACTTTC AGATTTTACC AAAGTTAAAG	1440
	AATAACCATC ACAAGTTTCT GGTGATGGTA TTATATTACC AGTACAATTA TAATATTCTC	1500
	TATAAATTAA AGGAATTTGA CAACCAAGAT CAAATGACCA TCCAATTGTA GCATTAACTT	1560
	TTTTTCTGG TCGTGAAGAT ACATTTACAT ATGTATCTAG TAATCGTAGT TCACATCCTT	1620
5	TAGAGTATTC AACATATCCG TTTGTTACCA CGGGAATAAG AGTCTTAGAT TGTTCCTCG	1680
	TAGGAAGTTG TGTAGGTTCA GTTGATTTT CTTTAGGATC CGCATAACAC AACTCTAGCG	1740
	GAGCTATGCG AGATAAACT ACCTTAAAT AAAAAACAA AAACAGCGTA TACAACATGA	1800
	TAACATAAT ATTGTAGCTA GGATGTAAA ATAAAATTAA TAAAAAGAG CTTTCAAACA	1860
	CCCGTTTAT ATAAACAAT AAAAAATTC ACGCCCATTT TTATGAAAT TATTGTTTAC	1920
10	TAAAAATCTG ATAGGATAAT AGTTCCTCG CACTTGGTCG TAGAGATGCA TCAATGTTA	1980
	GCATTTTATG AATTAAAAAT TCACCATCGA GATGTAATTT AAGGTTATTT AGACGATTAT	2040
	ATCGTGTAAT TGGAGGTCTA TCATTATTAG CATATTTTAT AAAATGTTTT ACTAGATTAG	2100
	ATTCCAAATC AGATGGAAAT TCATTGGGT TAATCTTCAG AGTTGATATA ATTTTATAA	2160
	GATGAAGATT ACAATTGTTT ATTAATCGC TACTATCTCT TTCTTCTCC TCAACAAAA	2220
15	CATTAGGATA TGCAAGCATT TCAATAAAA TTATACCAGC ACTCCAAATA TCAGCTTTAC	2280
	AGTTGTACGC ATCCTTTGAT AGAACTTCAG GAGCATTAGT TTCAATAGTC CCGCAATTC	2340
	CCAAATAATC TGGTGAGGAA ACAGGAAAT GAGAAGCCCC AAAATCACCT ATACAAACAT	2400
	TAGAGTCATT ATCCAAGAAA ATATTTTCAG TTTTATATC TCGATGAATA ATTTTATTC	2460
	CATGAATATA TTGAAGTCCA GTTAATATTT GTTTTCAAT TTTAATTACA GATTCAAAAG	2520
20	ACAGAGATTT CCCATGATCC ATTAATAAAT TATATAGATC ATATTATATA TACGGTAACA	2580
	CCAAACATGT TAACTCTTTA TAAAAAGAG TGTCTTGAAG TTTAATTATA GATTGGTGAC	2640
	TAATATTTCT CAAAATTAAC GATTCCACAA GCGTGTTTCC CCTTGTCCA ATTTTAAAA	2700
	TTACCTTATA GCTTGATCT TTATCTTTT TAAGAGCAAT AAAACTCTT CCTTCTGACC	2760
	CAGGCGTTAA CGATTTAACA ACAGAAAAT TTAGCGCTTC AGCCGCTTCA ATTCCTTCGC	2820
25	TTTGTAGTAGG AGATAAACTT TTTTATCTT CATCACTTTC ATAACCTTCT TCAACTTCTT	2880
	CGTCACTTC TCTTTCATTT TCACCTTCAG TTGGATTTTT TGTATAATCC ATAAAGTCAT	2940
	CATCACTAAA ATCCGAGTAT AAATCCTCAT CCATTATTT GTCTTGATGT AGGTTATCCT	3000
	CTTCAATCAA ATCTGAAGTT AGAGGAACCG GTTTATAGAA GTCTTCTGGA TCGACAGAAG	3060
	ATTCTCTATT CACGCTGATA CAACAAAAT TTTGGGTGGT AACTTTGCC ATATCAGGTA	3120
30	ATTGTGAAAT TGTATGTTA ATATCAATC ATCAACTGCA GCTTCTTCTA AAATTATAAC	3180
	ATAAATTAGG TGTGTATTAA CCTTATTGG ATTCATACAT AAAATTTAAT TATGGGTGTG	3240

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	GTTGAAGTTA ATATTGTTAC GTTTATTGAC AAAAATGGGG CGTTACCAGG AAACCTCCCAA	3300
	GATGTTTCATC CTGATCTTTG GTGTTTATG GCTAGACAAT GCTATATCCT TTCTCTCACA	3360
	CGATTGGCTA TGCCTATAAT ATTACGATCT GCAAACCTTAT GTTATTTTAT GGACTCTATA	3420
	AAACATCTAC CTAGAGTTTC AAGGCCTATA GTAAGAACAT CAACCTCTAA TAGTAAATTT	3480
5	TTAAAACCAA CGGAGGGGGA GGAGGAGGAC TTTTATTTT ATGAGGATAA ACCTGGGGCT	3540
	AGCATCGAAT GGAAATCGGC TGTTCGGGG TATAACTATC TAAACTCTGG TATATTGGGA	3600
	AACTATCCTC TTAATCTATG GGTTCGGT GCAGCGGATT TATGTGAGCC AGTCATTCT	3660
	AATATCCAG GACCAAAGCG ACTAATTTAT GCATATGTAT CATGTGAATG GCOGGAACCA	3720
	TCCTGGAAC CTGAGTGTCT TGAGATTTC AAAAATAATG TAAACATAT CGATGATTCT	3780
10	GGGAGTGTTC ATTGCCCTC GTTATATGG GTACCTGTAT TAGACACCTT TCTGTCTCC	3840
	TTTAAAGTAC CCCCTATGTT AAGTGACATT TTTTATGGTA CAACATTTAA TACTCCATT	3900
	AACTTTGAAA GCTCTCCAAG ATGTCCCTCT ATATCCTCAT CTCATCCTC CTCCTCTCA	3960
	TCCTCTCTT CATGCTCTGC ATCTCATTAT TCCTCAGAGA ATGATATTG GAAATACGCT	4020
	AATGCGATGG TGGATAATGA ACTAGAAGAA ACTAATTGTG AAATTAAAA TAGTTTTAA	4080
15	GAGGATTCTG ACAGTTCTAC ATGTTCTATA AGCGATGTAT GTGATTCTCT TTATATAAAT	4140
	GAGACACGTT CTGCCCCCCC GGAATCGAA TCATTTATGT GTGCAATAAT ATCCCATAT	4200
	GGTTATGAAG AAATTCCTGA ACCAGAAGAG GATGACTTGC ATGGGGTGAA ACCTATGAAA	4260
	AGGCTATCCA AACCAATAT TTTTAAACGA TTATTTTCAA GCGCGCCCAA AACATAACC	4320
	AAAAATGAAA ACGATGGTAT GTCTTCTACA CAACCTACCA ACGCTCAACG TTCATCTCTA	4380
20	TTTAGTTCAT GTTATGTGG AACTAAGTT TGTTTATATT TGTGTGAAT AAACAGTAGA	4440
	TGTAAACCTG AAATTCTGGT TTTTATGTG AACCCTCCC ATATTCTTAC TGTATATAAA	4500
	CTGGCATTTC ATCCTACATT TTTAAATCTT CACTTGTTTT TAAAGCTTAA CTAAAAAGTT	4560
	TTAAAATGAG TGCTTCATTT GCTCTATTG ATAACAACCTC CGATCAAGCT AATATGCCAT	4620
	CATACTTCAG ACGCTGTCGT GGAGAACTTA ATGAAGGATT CTACGCACAA GTTCCGCCTG	4680
25	GTTATTTTCC AGTTCGCCCT AAAACCACAC CAGCGCTTGC ACGTGTGAAA AACAGGGTG	4740
	AACCGCACGC CTTCACTATT GTTCTACAC CACCTACGGA TGTACGATTC TTCAAAAAGC	4800
	TTCTGTATGG AACCTTGTG AACTTCCAT TTTCATATCC TGATGAGAGG TATGAAGATG	4860
	ATATTGAACC TATGTATTGC AGACTATACG TTCTAAAGGA TTTTGAAACG CCAAGTTCTC	4920
	CCTACAATCA AGTAAACGCT TCTCAGCTTA TGAAGTACC TTCTTCGCTT GTGGAATCGA	4980
30	AGTGTATTG GGATGGTCCA AAATTTATAA ATGTACCACC AATAAGATAT ATTCTAAAA	5040
	GTGATTACTC TCTTAAAAA AATGTATCCG AAGATGCATT TGTGTTGGGT AGGATACCAG	5100

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AAAACTAAA AACTGAAAA ACTAAAAATG TTTACCCAAC CGCCTACTGT ACTTAACCTT 5160
 ATAAATTAA AATATTTTAA AAATACTTGT CTCATAGATT TCATTCATAG ATTTCATTCA 5220
 TAGATTTTAT TCATAGATTT CATTATAGATA TTTCATTCAT AGATTTTCATT CATAGATTTT 5280
 ATTCATAGAT TTCATTCATA GATTTTCATTC ATAGATTTCA TTCATAGATT TCATTCATAG 5340
 5 ATTTCATTCA TAGATTTTAT TCATAGATTT CATTATAGATA TTTCATTCAT AGATTTTCATT 5400
 CATAGATTTT ATTTCATAGAT TTCATTCATA GATTTTCATTC ATAGATTTCA TTCATAGATT 5460
 TCATTCATAG ATTTTATTTT TTAAATACAC TGCAG 5495

(2) INFORMATION FOR SEQ ID NO:3:

- (i) SEQUENCE CHARACTERISTICS:
 10 (A) LENGTH: 552 base pairs
 (B) TYPE: nucleic acid
 (C) STRANDEDNESS: single
 (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: cDNA

- (ix) FEATURE:
 15 (A) NAME/KEY: CDS
 (B) LOCATION: 1..552

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:3:

ATG AGT GCT TCA TTT GCT CTA TTT GAT AAC AAC TCC GAT CAA GCT AAT 48
 20 Met Ser Ala Ser Phe Ala Leu Phe Asp Asn Ser Asp Gln Ala Asn
 1 5 10 15
 ATG CCA TCA TAC TTC AGA CGC TGT CGT GGA GAA CTT AAT GAA GGA TTC 96
 Met Pro Ser Tyr Phe Arg Arg Cys Arg Gly Glu Leu Asn Glu Gly Phe
 20 25 30
 TAC GCA CAA GTT CCG CCT GGT TAT TTT CCA GTT CGC CCT AAA ACC ACA 144
 Tyr Ala Gln Val Pro Pro Gly Tyr Phe Pro Val Arg Pro Lys Thr Thr
 35 40 45
 CCA GCG CTT GCA CGT GTG AAA AAC CAG GGT GAA CCG CAC GCC TTC ACT 192
 30 Pro Ala Leu Ala Arg Val Lys Asn Gln Gly Glu Pro His Ala Phe Thr
 50 55 60
 ATT GTT CCT ACA CCA CCT ACG GAT GTA CGA TTC TTC AAA AAG CTT CGT 240
 Ile Val Pro Thr Pro Pro Thr Asp Val Arg Phe Phe Lys Lys Leu Arg
 65 70 75 80
 GAT GGA ACC TTT GTG AAA CTT CCA TTT TCA TAT CCT GAT GAG AGG TAT 288
 35 Asp Gly Thr Phe Val Lys Leu Pro Phe Ser Tyr Pro Asp Glu Arg Tyr
 85 90 95
 GAA GAT GAT ATT GAA CCT ATG TAT TGC AGA CTA TAC GTT CTA AAG GAT 336
 Glu Asp Asp Ile Glu Pro Met Tyr Cys Arg Leu Tyr Val Leu Lys Asp
 100 105 110

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	TTT GAA ACG CCA AGT TCT CCC TAC AAT CAA GTA AAC GCT TCT CAG CTT	384
	Phe Glu Thr Pro Ser Ser Pro Tyr Asn Gln Val Asn Ala Ser Gln Leu	
	115 120 125	
5	ATG GAA GTA CCT TCT TCG CTT GTG GAA TCG AAG TGT TAT TGG GAT GGT	432
	Met Glu Val Pro Ser Ser Leu Val Glu Ser Lys Cys Tyr Trp Asp Gly	
	130 135 140	
	CCA AAA TTT ATA AAT GTA CCA CCA ATA AGA TAT ATT CTA AAA AGT GAT	480
	Pro Lys Phe Ile Asn Val Pro Pro Ile Arg Tyr Ile Leu Lys Ser Asp	
	145 150 155 160	
10	TAC TCT CTT AAA ATA AAT GTA TCC GAA GAT GCA TTT GTG TTG GGT AGG	528
	Tyr Ser Leu Lys Ile Asn Val Ser Glu Asp Ala Phe Val Leu Gly Arg	
	165 170 175	
	ATA CCA GAA AAA CTA AAA ACT TGA	
15	Ile Pro Glu Lys Leu Lys Thr *	552
	180	

(2) INFORMATION FOR SEQ ID NO:4:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 184 amino acids
(B) TYPE: amino acid
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:4:

	Met Ser Ala Ser Phe Ala Leu Phe Asp Asn Asn Ser Asp Gln Ala Asn	
	1 5 10 15	
25	Met Pro Ser Tyr Phe Arg Arg Cys Arg Gly Glu Leu Asn Glu Gly Phe	
	20 25 30	
	Tyr Ala Gln Val Pro Pro Gly Tyr Phe Pro Val Arg Pro Lys Thr Thr	
	35 40 45	
30	Pro Ala Leu Ala Arg Val Lys Asn Gln Gly Glu Pro His Ala Phe Thr	
	50 55 60	
	Ile Val Pro Thr Pro Pro Thr Asp Val Arg Phe Phe Lys Lys Leu Arg	
	65 70 75 80	
	Asp Gly Thr Phe Val Lys Leu Pro Phe Ser Tyr Pro Asp Glu Arg Tyr	
	85 90 95	
35	Glu Asp Asp Ile Glu Pro Met Tyr Cys Arg Leu Tyr Val Leu Lys Asp	
	100 105 110	
	Phe Glu Thr Pro Ser Ser Pro Tyr Asn Gln Val Asn Ala Ser Gln Leu	
	115 120 125	
40	Met Glu Val Pro Ser Ser Leu Val Glu Ser Lys Cys Tyr Trp Asp Gly	
	130 135 140	
	Pro Lys Phe Ile Asn Val Pro Pro Ile Arg Tyr Ile Leu Lys Ser Asp	
	145 150 155 160	

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Tyr Ser Leu Lys Ile Asn Val Ser Glu Asp Ala Phe Val Leu Gly Arg
 165 170 175

Ile Pro Glu Lys Leu Lys Thr *
 180

5 (2) INFORMATION FOR SEQ ID NO:5:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 1176 base pairs
 (B) TYPE: nucleic acid
 (C) STRANDEDNESS: single
 (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: cDNA

(ix) FEATURE:

- (A) NAME/KEY: CDS
 (B) LOCATION: 1..1176

15 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:5:

ATG GGT GTG GTT GAA GTT AAT ATT GTT ACG TTT ATT GAC AAA AAT GGG	48
Met Gly Val Val Glu Val Asn Ile Val Thr Phe Ile Asp Lys Asn Gly	
1 5 10 15	
CGC TTA CCA GGA AAC TCC CAA GAT GTT CAT CCT GAT CTT TGG TGT TTT	96
Ala Leu Pro Gly Asn Ser Gln Asp Val His Pro Asp Leu Trp Cys Phe	
20 25 30	
ATG GCT AGA CAA TGC TAT ATC CTT TCT CTC ACA CGA TTG GCT ATG CCT	144
Met Ala Arg Gln Cys Tyr Ile Leu Ser Leu Thr Arg Leu Ala Met Pro	
35 40 45	
ATA ATA TTA CGA TCT GCA AAC TTA TGT TAT TTT ATG GAC TCT ATA AAA	192
Ile Ile Leu Arg Ser Ala Asn Leu Cys Tyr Phe Met Asp Ser Ile Lys	
50 55 60	
CAT CTA CCT AGA GTT TCA AGG CCT ATA GTA AGA ACA TCA ACC TCT AAT	240
His Leu Pro Arg Val Ser Arg Pro Ile Val Arg Thr Ser Thr Ser Asn	
30 65 70 75 80	
AGT AAA TTT TTA AAA CCA ACG GAG GGG GAG GAG GAG GAC TTT TTA TTT	288
Ser Lys Phe Leu Lys Pro Thr Glu Gly Glu Glu Asp Phe Leu Phe	
85 90 95	
TAT GAG GAT AAA CCT GGG GCT AGC ATC GAA TGG AAA TCG GCT GTT TCG	336
Tyr Glu Asp Lys Pro Gly Ala Ser Ile Glu Trp Lys Ser Ala Val Ser	
100 105 110	
GGG TAT AAC TAT CTA AAC TCT GGT ATA TTT GGA AAC TAT CCT CTT AAT	384
Gly Tyr Asn Tyr Leu Asn Ser Gly Ile Phe Gly Asn Tyr Pro Leu Asn	
115 120 125	
CTA TGG GTT TTC GGT GCA GCG GAT TTA TGT GAG CCA GTC ATT TCT AAT	432
Leu Trp Val Phe Gly Ala Ala Asp Leu Cys Glu Pro Val Ile Ser Asn	
130 135 140	

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	ATC CCA GGA CCA AAG CGA CTA ATT TAT GCA TAT GTA TCA TGT GAA TGG	480
	Ile Pro Gly Pro Lys Arg Leu Ile Tyr Ala Tyr Val Ser Cys Glu Trp	
	145 150 155 160	
5	CCG GAA CCA TCC TGG AAA CCT GAG TGT CTT GAG ATT TCC AAA AAT AAT	528
	Pro Glu Pro Ser Trp Lys Pro Glu Cys Leu Glu Ile Ser Lys Asn Asn	
	165 170 175	
	GTA AAA CAT ATC GAT GAT TCT GGG AGT GTT TAT TGC CCC TCG TTT ATA	576
	Val. Lys His Ile Asp Asp Ser Gly Ser Val Tyr Cys Pro Ser Phe Ile	
	180 185 190	
10	TGG GTA CCT GTA TTA GAC ACC TTT CTG TCC TCC TTT AAA GTA CCC CCT	624
	Trp Val Pro Val Leu Asp Thr Phe Leu Ser Ser Phe Lys Val Pro Pro	
	195 200 205	
	ATG TTA AGT GAC ATT TTT TAT GGT ACA ACA TTT AAT ACT CCA TTC AAC	672
15	Met Leu Ser Asp Ile Phe Tyr Gly Thr Thr Phe Asn Thr Pro Phe Asn	
	210 215 220	
	TTT GAA AGC TCT CCA AGA TGT CCC TCT ATA TCC TCA TCT TCA TCC TCC	720
	Phe Glu Ser Ser Pro Arg Cys Pro Ser Ile Ser Ser Ser Ser Ser	
	225 230 235 240	
20	TCC TCC TCA TCC TCT TCT TCA TGC TCT GCA TCT CAT TAT TCC TCA GAG	768
	Ser Ser Ser Ser Ser Ser Ser Cys Ser Ala Ser His Tyr Ser Ser Glu	
	245 250 255	
	AAT GAT ATT TGG AAA TAC GCT AAT GCG ATG GTG GAT AAT GAA CTA GAA	816
	Asn Asp Ile Trp Lys Tyr Ala Asn Ala Met Val Asp Asn Glu Leu Glu	
	260 265 270	
25	GAA ACT AAT TGT GAA ATT AAA AAT AGT TTT AAA GAG GAT TCT GAC AGT	864
	Glu Thr Asn Cys Glu Ile Lys Asn Ser Phe Lys Glu Asp Ser Asp Ser	
	275 280 285	
	TCT ACA TGT TCT ATA AGC GAT GTA TGT GAT TCT CTT TAT ATA AAT GAG	912
30	Ser Thr Cys Ser Ile Ser Asp Val Cys Asp Ser Leu Tyr Ile Asn Glu	
	290 295 300	
	ACA CGT TCT GCC CCC CCG GTA ATC GAA TCA TTT ATG TGT GCA ATA ATA	960
	Thr Arg Ser Ala Pro Pro Val Ile Glu Ser Phe Met Cys Ala Ile Ile	
	305 310 315 320	
35	TCC CAT AAT GGT TAT GAA GAA ATT CCT GAA CCA GAA GAG GAT GAC TTG	1008
	Ser His Asn Gly Tyr Glu Glu Ile Pro Glu Pro Glu Glu Asp Asp Leu	
	325 330 335	
	CAT GGG GTG AAA CCT ATG AAA AGG CTA TCC AAA CCA AAT ATT TTT AAA	1056
	His Gly Val Lys Pro Met Lys Arg Leu Ser Lys Pro Asn Ile Phe Lys	
	340 345 350	
40	CGA TTA TTT TCA AGG CGC GCC AAA ACA ATA ACC AAA AAT GAA AAC GAT	1104
	Arg Leu Phe Ser Arg Arg Ala Lys Thr Ile Thr Lys Asn Glu Asn Asp	
	355 360 365	
45	GGT ATG TCT TCT ACA CAA CCT ACC AAC GCT CAA CGT TCA TCT CTA TTT	1152
	Gly Met Ser Ser Thr Gln Pro Thr Asn Ala Gln Arg Ser Ser Leu Phe	
	370 375 380	

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AGT TCA TGT TTA TGT GGA AAC TAA
 Ser Ser Cys Leu Cys Gly Asn *
 385 390

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(2) INFORMATION FOR SEQ ID NO:6:

- 5 (i) SEQUENCE CHARACTERISTICS:
 (A) LENGTH: 392 amino acids
 (B) TYPE: amino acid
 (D) TOPOLOGY: linear
- (ii) MOLECULE TYPE: protein

10 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:6:

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

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Ser Ser Ser Ser Ser Ser Ser Cys Ser Ala Ser His Tyr Ser Ser Glu
245 250 255

Asn Asp Ile Trp Lys Tyr Ala Asn Ala Met Val Asp Asn Glu Leu Glu
260 265 270

5 Glu Thr Asn Cys Glu Ile Lys Asn Ser Phe Lys Glu Asp Ser Asp Ser
275 280 285

Ser Thr Cys Ser Ile Ser Asp Val Cys Asp Ser Leu Tyr Ile Asn Glu
290 295 300

10 Thr Arg Ser Ala Pro Pro Val Ile Glu Ser Phe Met Cys Ala Ile Ile
305 310 315 320

Ser His Asn Gly Tyr Glu Glu Ile Pro Glu Pro Glu Glu Asp Asp Leu
325 330 335

His Gly Val Lys Pro Met Lys Arg Leu Ser Lys Pro Asn Ile Phe Lys
340 345 350

15 Arg Leu Phe Ser Arg Arg Ala Lys Thr Ile Thr Lys Asn Glu Asn Asp
355 360 365

Gly Met Ser Ser Thr Gln Pro Thr Asn Ala Gln Arg Ser Ser Leu Phe
370 375 380

20 Ser Ser Cys Leu Cys Gly Asn *
385 390

(2) INFORMATION FOR SEQ ID NO:7:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 1203 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: cDNA

(ix) FEATURE:
(A) NAME/KEY: CDS
(B) LOCATION: 1..1203

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:7:

ATG GCA AAG TGT ACC ACC GAA AAG TTT TGT TGT ATC AGC GTG AAT AGA	48
Met Ala Lys Cys Thr Thr Glu Lys Phe Cys Cys Ile Ser Val Asn Arg	
1 5 10 15	
35 GAA TCT TCT GTC GAT CCA GAA GAC TTC TAT AAA CCG GTT CCT CTA ACT	96
Glu Ser Ser Val Asp Pro Glu Asp Phe Tyr Lys Pro Val Pro Leu Thr	
20 25 30	
40 TCA GAT TTG ATT GAA GAG GAT AAC CTA CAT CAA GAC AAA ATA ATG GAT	144
Ser Asp Leu Ile Glu Glu Asp Asn Leu His Gln Asp Lys Ile Met Asp	
35 40 45	

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	GAG GAT TTA TAC TCG GAT TTT AGT GAT GAT GAC TTT ATG GAT TAT ACA	192
	Glu Asp Leu Tyr Ser Asp Phe Ser Asp Asp Phe Met Asp Tyr Thr	
	50 55 60	
5	AAA AAT CCA ACT GAA AGT GAA AAT GAA AGA GAA AGT GAC GAA GAA GTT	240
	Lys Asn Pro Thr Glu Ser Glu Asn Glu Arg Glu Ser Asp Glu Glu Val	
	65 70 75 80	
	GAA GAA AGT TAT GAA AGT GAT GAA GAT AAA AAA AGT TTA TCT CCT ACT	288
	Glu Glu Ser Tyr Glu Ser Asp Glu Asp Lys Lys Ser Leu Ser Pro Thr	
	85 90 95	
10	AAA AGC GAA GGA ATT GAA GCG GCT GAA GCG CTA AAG TTT TCT GTT GTT	336
	Lys Ser Glu Gly Ile Glu Ala Ala Glu Leu Lys Phe Ser Val Val	
	100 105 110	
	AAA TCG TTA ACG CCT GGG TCA GAA GGA AGA GTT TTT ATT GCT CTT AAA	384
15	Lys Ser Leu Thr Pro Gly Ser Glu Gly Arg Val Phe Ile Ala Leu Lys	
	115 120 125	
	AAA GAT AAA GAT ACA AGC TAT AAG GTA ATT TTA AAA ATT GGA CAA AGG	432
	Lys Asp Lys Asp Thr Ser Tyr Lys Val Ile Leu Lys Ile Gly Gln Arg	
	130 135 140	
20	GGA AAC ACG CTT GTG GAA TCG TTA ATT TTG AGA AAT ATT AGT CAC CAA	480
	Gly Asn Thr Leu Val Glu Ser Leu Ile Leu Arg Asn Ile Ser His Gln	
	145 150 155 160	
	TCT ATA ATT AAA CTT CAA GAC ACT CTT TTT TAT AAA GAG TTA ACA TGT	528
	Ser Ile Ile Lys Leu Gln Asp Thr Leu Phe Tyr Lys Glu Leu Thr Cys	
	165 170 175	
25	TTG GTG TTA CCG TAT TAT AAA TAT GAT CTA TAT AAT TTT TTA ATG GAT	576
	Leu Val Leu Pro Tyr Tyr Lys Tyr Asp Leu Tyr Asn Phe Leu Met Asp	
	180 185 190	
	CAT GGG AAA TCT CTG TCT TTT GAA TCT GTA ATT AAA ATT GAA AAA CAA	624
30	His Gly Lys Ser Leu Ser Phe Glu Ser Val Ile Lys Ile Glu Lys Gln	
	195 200 205	
	ATA TTA ACT GGA CTT CAA TAT ATT CAT GGA AAA AAA ATT ATT CAT CGA	672
	Ile Leu Thr Gly Leu Gln Tyr Ile His Gly Lys Lys Ile Ile His Arg	
	210 215 220	
35	GAT ATA AAA ACT GAA AAT ATT TTC TTG GAT AAT GAC TCT AAT GTT TGT	720
	Asp Ile Lys Thr Glu Asn Ile Phe Leu Asp Asn Asp Ser Asn Val Cys	
	225 230 235 240	
	ATA GGT GAT TTT GGG GCT TCT CAA TTT CCT GTT TCC TCA CCA GAT TAT	768
	Ile Gly Asp Phe Gly Ala Ser Gln Phe Pro Val Ser Ser Pro Asp Tyr	
	245 250 255	
40	TTG GGA ATT GCG GGG ACT ATT GAA ACT AAT GCT CCT GAA GTT CTA TCA	816
	Leu Gly Ile Ala Gly Thr Ile Glu Thr Asn Ala Pro Glu Val Leu Ser	
	260 265 270	
45	AAG GAT GCG TAC AAC TGT AAA GCT GAT ATT TGG AGT GCT GGT ATA ATT	864
	Lys Asp Ala Tyr Asn Cys Lys Ala Asp Ile Trp Ser Ala Gly Ile Ile	
	275 280 285	

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TTA TTT GAA ATG CTT GCA TAT CCT AAT GTT TTG TTT GAG GAG GAA GAA 912
 Leu Phe Glu Met Leu Ala Tyr Pro Asn Val Leu Phe Glu Glu Glu Glu
 290 295 300

AGA GAT AGT AGC GAT TTA ATA AAC AAT TGT AAT CTT CAT CTT ATA AAA 960
 5 Arg Asp Ser Ser Asp Leu Ile Asn Asn Cys Asn Leu His Leu Ile Lys
 305 310 315 320

ATT ATA TCA ACT CTG AAG ATT AAC CCA AAT GAA TTT CCA TCT GAT TTG 1008
 Ile Ile Ser Thr Leu Lys Ile Asn Pro Asn Glu Phe Pro Ser Asp Leu
 325 330 335

10 GAA TCT AAT CTA GTA AAA CAT TTT ATA AAA TAT GCT AAT AAT GAT AGA 1056
 Glu Ser Asn Leu Val Lys His Phe Ile Lys Tyr Ala Asn Asn Asp Arg
 340 345 350

CCT CCA TTT ACA CGA TAT AAT CGT CTA AAT AAC CTT AAA TTA CAT CTC 1104
 15 Pro Pro Phe Thr Arg Tyr Asn Arg Leu Asn Asn Leu Lys Leu His Leu
 355 360 365

GAT GGT GAA TTT TTA ATT CAT AAA ATG CTA ACA TTT GAT GCA TCT CTA 1152
 Asp Gly Glu Phe Leu Ile His Lys Met Leu Thr Phe Asp Ala Ser Leu
 370 375 380

CGA CCA AGT GCG GAA GAA CTA TTA TCC TAT CAG ATT TTT AGT AAA CAA 1200
 20 Arg Pro Ser Ala Glu Glu Leu Leu Ser Tyr Gln Ile Phe Ser Lys Gln
 385 390 395 400

TAA 1203
 *

25 (2) INFORMATION FOR SEQ ID NO:8:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 401 amino acids
 (B) TYPE: amino acid
 (D) TOPOLOGY: linear

30 (ii) MOLECULE TYPE: protein

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:8:

Met Ala Lys Cys Thr Thr Glu Lys Phe Cys Cys Ile Ser Val Asn Arg
 1 5 10 15

Glu Ser Ser Val Asp Pro Glu Asp Phe Tyr Lys Pro Val Pro Leu Thr
 20 25 30

Ser Asp Leu Ile Glu Glu Asp Asn Leu His Gln Asp Lys Ile Met Asp
 35 40 45

Glu Asp Leu Tyr Ser Asp Phe Ser Asp Asp Asp Phe Met Asp Tyr Thr
 50 55 60

40 Lys Asn Pro Thr Glu Ser Glu Asn Glu Arg Glu Ser Asp Glu Glu Val
 65 70 75 80

Glu Glu Ser Tyr Glu Ser Asp Glu Asp Lys Lys Ser Leu Ser Pro Thr
 85 90 95

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

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(2) INFORMATION FOR SEQ ID NO:9:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 1248 base pairs
 (B) TYPE: nucleic acid
 (C) STRANDEDNESS: single
 (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: cDNA

(ix) FEATURE:

- (A) NAME/KEY: CDS
 (B) LOCATION: 1..1248

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:9:

	ATG TTG TAT ACG CTG TTT TTT GTT TTT TAT TTT AAG GTA GTT TTA TCT	48
	Met Leu Tyr Thr Leu Phe Phe Val Phe Tyr Phe Lys Val Val Leu Ser	
	1 5 10 15	
15	CGC ATA GCT CCG CTA GAG TTG TGT TAT GCG GAT CCT AAA GAA AAT ACA	96
	Arg Ile Ala Pro Leu Glu Leu Cys Tyr Ala Asp Pro Lys Glu Asn Thr	
	20 25 30	
	ACT GAA CCT ACA CAA CTT CCT ACA GGG GAA CAA TCT AAG ACT CTT ATT	144
	Thr Glu Pro Thr Gln Leu Pro Thr Gly Glu Gln Ser Lys Thr Leu Ile	
	35 40 45	
	CCC GTG GTA ACA AAC GGA TAT GTT GAA TAC TCT AAA GGA TGT GAA CTA	192
	Pro Val Val Thr Asn Gly Tyr Val Glu Tyr Ser Lys Gly Cys Glu Leu	
	50 55 60	
	CGA TTA CTA GAT ACA TAT GTA AAT GTA TCT TCA CGA CCA GAA AAA AAG	240
	Arg Leu Leu Asp Thr Tyr Val Asn Val Ser Ser Arg Pro Glu Lys Lys	
	65 70 75 80	
	GTT AAT GCT ACA ATT GGA TGG TCA TTT GAT CTT GGT TGT CAA ATT CCT	288
	Val Asn Ala Thr Ile Gly Trp Ser Phe Asp Leu Gly Cys Gln Ile Pro	
	85 90 95	
	TTA ATT TAT AGA GAA TAT TAT AAT TGT ACT GGT AAT ATA ATA CCA TCA	336
	Leu Ile Tyr Arg Glu Tyr Tyr Asn Cys Thr Gly Asn Ile Ile Pro Ser	
	100 105 110	
	CCA GAA ACT TGT GAT GGT TAT TCT TTA ACT TTG GTA AAA TCT GAA AGT	384
	Pro Glu Thr Cys Asp Gly Tyr Ser Leu Thr Leu Val Lys Ser Glu Ser	
	115 120 125	
	ATA TCA TCT TAT GCA CTT GTT AAT GTT AGT TTG CTT ATT CAA CCA GGA	432
	Ile Ser Ser Tyr Ala Leu Val Asn Val Ser Leu Leu Ile Gln Pro Gly	
	130 135 140	
	ATT TTT GAT TCT GGT AGA TAT TTA TAC TCA CTT GTT TTT GGA AAC GAT	480
	Ile Phe Asp Ser Gly Arg Tyr Leu Tyr Ser Leu Val Phe Gly Asn Asp	
	145 150 155 160	
	AGT TAT AAC GGA AGA ATT GAA GTT CGA GTG GAT AAT GAG ACA GAC TAT	528
	Ser Tyr Asn Gly Arg Ile Glu Val Arg Val Asp Asn Glu Thr Asp Tyr	
	165 170 175	

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	CCA TGT TTT ATG ATG CAT GGA TTG ACT GTA AAA AAG GGT GAT AAA CTT	576
	Pro Cys Phe Met Met His Gly Leu Thr Val Lys Lys Gly Asp Lys Leu	
	180 185 190	
5	CAT ATT CCT TAT AAA CCA TCC ACA AAT CCT AAT CAT AAA CGA TAT AGA	624
	His Ile Pro Tyr Lys Pro Ser Thr Asn Pro Asn His Lys Arg Tyr Arg	
	195 200 205	
	GGT TGT TTT CCA ATA TCA AAT ACT GAG CTA TGG AAT AAT ATT AGT GAT	672
	Gly Cys Phe Pro Ile Ser Asn Thr Glu Leu Trp Asn Asn Ile Ser Asp	
	210 215 220	
10	GAA AGT GTT GGT AGA TAT TCA TAT GAT GAA GAA TAT GAA GAA TAT GAA	720
	Glu Ser Val Gly Arg Tyr Ser Thr Asp Glu Glu Tyr Glu Glu Tyr Glu	
	225 230 235 240	
15	GAA GAA AAC GAA GAT TTT GAA GAT CTA CAA TCA AAA GAT TGC CGC AAA	768
	Glu Glu Asn Glu Asp Phe Glu Asp Leu Gln Ser Lys Asp Cys Arg Lys	
	245 250 255	
	TCC AAT CTT TTT GAT ATG AAG AAG ACT TTT AAT TTG GCT GCA GGT TCT	816
	Ser Asn Leu Phe Asp Met Lys Lys Thr Phe Asn Leu Ala Ala Gly Ser	
	260 265 270	
20	CAA AGT TTA TTG ATT GCT AGT TTG GGT AAA TCA ATT TCA GAA CAA CCG	864
	Gln Ser Leu Leu Ile Ala Ser Leu Gly Lys Ser Ile Ser Glu Gln Pro	
	275 280 285	
	TGG TCA TTT AAA ATT AAT GAA AGT TAT GAA CTT TTT AAT AAT TTG TCT	912
	Trp Ser Phe Lys Ile Asn Glu Ser Tyr Glu Leu Phe Asn Asn Leu Ser	
	290 295 300	
25	ATC ACC CTT CAA TCG GAA GAA GAT TCT AAT ATA CTG AAT CCT GAA ATT	960
	Ile Thr Leu Gln Ser Glu Glu Asp Ser Asn Ile Leu Asn Pro Glu Ile	
	305 310 315 320	
30	GTA ACG TTT ACC ACA CCA CCA CCT ACT GAA AAT ACA CAT ATG TTT ATG	1008
	Val Thr Phe Thr Thr Pro Pro Pro Thr Glu Asn Thr His Met Phe Met	
	325 330 335	
	TCA AAT AAT GAA ACT ATG TAT GAA GAA GAA AGT GTT TTA AGC ATT ATT	1056
	Ser Asn Asn Glu Thr Met Tyr Glu Glu Glu Ser Val Leu Ser Ile Ile	
	340 345 350	
35	CAA TTG TTT AAC AAT GGT TAT AAT AAT TGT AAT ACC CAT ATA AAG GTA	1104
	Gln Leu Phe Asn Asn Gly Tyr Asn Asn Cys Asn Thr His Ile Lys Val	
	355 360 365	
	ATT GGA TTT GGA ACA ATT ATC TTT ATT ATT TTA TTT TTT GTT GCT GTG	1152
	Ile Gly Phe Gly Thr Ile Ile Phe Ile Ile Leu Phe Phe Val Ala Val	
	370 375 380	
40	TTT TTT TGT GGA TAT ACT TGT GTA TTA AAC TCT CGT ATT AAA ATG ATT	1200
	Phe Phe Cys Gly Tyr Thr Cys Val Leu Asn Ser Arg Ile Lys Met Ile	
	385 390 395 400	
45	AAC CAT GCT TAT ATA CAA CCC CAG AAA TTA AAT TTT TAT GAT ATT TAA	1248
	Asn His Ala Tyr Ile Gln Pro Gln Lys Leu Asn Phe Tyr Asp Ile *	
	405 410 415	

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(2) INFORMATION FOR SEQ ID NO:10:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 416 amino acids
 (B) TYPE: amino acid
 (D) TOPOLOGY: linear

5

(ii) MOLECULE TYPE: protein

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:10:

```

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

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Gln Ser Leu Leu Ile Ala Ser Leu Gly Lys Ser Ile Ser Glu Gln Pro
 275 280 285
 Trp Ser Phe Lys Ile Asn Glu Ser Tyr Glu Leu Phe Asn Asn Leu Ser
 290 295 300
 5 Ile Thr Leu Gln Ser Glu Glu Asp Ser Asn Ile Leu Asn Pro Glu Ile
 305 310 315 320
 Val Thr Phe Thr Thr Pro Pro Pro Thr Glu Asn Thr His Met Phe Met
 325 330 335
 10 Ser Asn Asn Glu Thr Met Tyr Glu Glu Glu Ser Val Leu Ser Ile Ile
 340 345 350
 Gln Leu Phe Asn Asn Gly Tyr Asn Asn Cys Asn Thr His Ile Lys Val
 355 360 365
 Ile Gly Phe Gly Thr Ile Ile Phe Ile Ile Leu Phe Phe Val Ala Val
 370 375 380
 15 Phe Phe Cys Gly Tyr Thr Cys Val Leu Asn Ser Arg Ile Lys Met Ile
 385 390 395 400
 Asn His Ala Tyr Ile Gln Pro Gln Lys Leu Asn Phe Tyr Asp Ile *
 405 410 415

(2) INFORMATION FOR SEQ ID NO:11:

- 20 (i) SEQUENCE CHARACTERISTICS:
 (A) LENGTH: 357 base pairs
 (B) TYPE: nucleic acid
 (C) STRANDEDNESS: single
 (D) TOPOLOGY: linear
- 25 (ii) MOLECULE TYPE: cDNA
- (ix) FEATURE:
 (A) NAME/KEY: CDS
 (B) LOCATION: 1..357

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:11:

30 ATG ATT AAA CTT CTA TTT ATC TTA TTT TAT TTT AAC CCA ATA ACT GGA 48
 Met Ile Lys Leu Leu Phe Ile Leu Phe Tyr Phe Asn Pro Ile Thr Gly
 1 5 10 15

TAT AAA TGG GTA GAC CCT CCT CGT AGG TAT AAT TAC ACC GTT TTA AGA 96
 Tyr Lys Trp Val Asp Pro Pro Arg Arg Tyr Asn Tyr Thr Val Leu Arg
 35 20 25 30

ATG ATT CCA GAT ATT CCA AAT CCA ATG GAT CCT TCT AAA AAC GCT GAA 144
 Met Ile Pro Asp Ile Pro Asn Pro Met Asp Pro Ser Lys Asn Ala Glu
 35 40 45

40 GTT CGG TAT GTA ACT TCT ACT GAC CCA TGT GAT ATG GTT GCT TTG ATT 192
 Val Arg Tyr Val Thr Ser Thr Asp Pro Cys Asp Met Val Ala Leu Ile
 50 55 60

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	TCT AAT CCA AAT ATA GAA TCT ACA ATT AAA ACG ATT CAA TTT GTG CAA	240
	Ser Asn Pro Asn Ile Glu Ser Thr Ile Lys Thr Ile Gln Phe Val Gln	
	65 70 75 80	
5	AAG AAA AAA TTT TAC AAT GCA TCT CTT AGT TGG TTT AAA GTT GGA GAT	288
	Lys Lys Lys Phe Tyr Asn Ala Ser Leu Ser Trp Phe Lys Val Gly Asp	
	85 90 95	
	GAT TGT ACA TAT CCA ATA TAT TTA ATT CAA TAT TTT GAT TGT GAT CCT	336
	Asp Cys Thr Tyr Pro Ile Tyr Leu Ile Gln Tyr Phe Asp Cys Asp Pro	
	100 105 110	
10	CAA AGA GAA TTT GGC ATA TGT	357
	Gln Arg Glu Phe Gly Ile Cys	
	115	

(2) INFORMATION FOR SEQ ID NO:12:

(i) SEQUENCE CHARACTERISTICS:

15 (A) LENGTH: 119 amino acids
(B) TYPE: amino acid
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:12:

20	Met Ile Lys Leu Leu Phe Ile Leu Phe Tyr Phe Asn Pro Ile Thr Gly	
	1 5 10 15	
	Tyr Lys Trp Val Asp Pro Pro Arg Arg Tyr Asn Tyr Thr Val Leu Arg	
	20 25 30	
25	Met Ile Pro Asp Ile Pro Asn Pro Met Asp Pro Ser Lys Asn Ala Glu	
	35 40 45	
	Val Arg Tyr Val Thr Ser Thr Asp Pro Cys Asp Met Val Ala Leu Ile	
	50 55 60	
	Ser Asn Pro Asn Ile Glu Ser Thr Ile Lys Thr Ile Gln Phe Val Gln	
	65 70 75 80	
30	Lys Lys Lys Phe Tyr Asn Ala Ser Leu Ser Trp Phe Lys Val Gly Asp	
	85 90 95	
	Asp Cys Thr Tyr Pro Ile Tyr Leu Ile Gln Tyr Phe Asp Cys Asp Pro	
	100 105 110	
35	Gln Arg Glu Phe Gly Ile Cys	
	115	

(2) INFORMATION FOR SEQ ID NO:13:

(i) SEQUENCE CHARACTERISTICS:

40 (A) LENGTH: 743 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

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(ii) MOLECULE TYPE: DNA (genomic)

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:13:

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CGAAGCGGGA GGAGGATGCT GGTATGATA TACCATCTCC AAATTTAGTT CAAATAAAAC      60
CGGGATATAG TTACCTTTTT TGTCTTCCTA TTTTCAATT AGAAATGAAA AACCCACCAA      120
5  TCGCTTGAT TTTTGGTAGA TCATCCTTAA ATCAAGCGG AATAATTGTT CTCCAACTA      180
TATGGAAACC AAAACAATT TGTCAATTTT TTATTAATAA TATATCCTCT AAAACTGTAA      240
CTATAGAAAA AGGTCAGAGA ATAGCTCAGT TAGTTCCTTT AAAAACAAT CAACCACTAT      300
GGTTACAACC ACAAATTAAT TGTCACTCTT TATTCCAAA GTCAAATAT TTAAGCTTAT      360
CAAATCGAGA ATGTGATATG TGGAAGTTA CAGAAGATCT GAATTTTGAA GCACCGAAAA      420
10 GTTTACGAGG AATAAATGGA TTGGATCCA CGGATTGTA AAATTCGTTA ATAAAGTTAT      480
ATTTAAAGTG CCAAACTTTC ACGTGTCAAT TTTTGGGAC CGTTCTTTT TTGTTTAGTC      540
GATAAAATAT TTTCAGTTTC CATAGAACTT ATTAGAGGTT CTGTATCTAG TATATCTGTA      600
GAATTATTTT CATCATATTT AACGGTTTGA AGAGATAAGG GTTTGTGTG ATTAGAATCT      660
ATACCAAGGG TTTTCTCTAA AACCGCTACA TCTGCCATAA CAATATTATT TTCTGAAGTC      720
15 ATTTTATGG CTTGGGCACC ACC                                          743

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(2) INFORMATION FOR SEQ ID NO:14:

(i) SEQUENCE CHARACTERISTICS:

- 20 (A) LENGTH: 743 base pairs
 (B) TYPE: nucleic acid
 (C) STRANDEDNESS: single
 (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:14:

```

GGTGGTGCCC AAGCCATAAA AATGACTTCA GAAATAATA TTGTTATGGC AGATGTAGCG      60
25 GTTTTAGAAA AAACCCTTGG TATAGATTCT AATACAACAA AACCCCTATC TCTTCAAACC      120
GTTAAATATG ATGAAAATAA TTCTACAGAT ATACTAGATA CAGAACCTCT AATAAGTTCT      180
ATGGAACTG AAAATATTTT ATCGACTTAA CAAAAAGAA ACGGTCCCAA AAAAATGACA      240
CGTGAAAGTT TGGCACTTTA AATATAACTT TATTAACGAA TTTTACAATC CCGTGGATCC      300
AAATCCATTT ATTCTCGTA AACTTTTCGG TGCTTCAAAA TTCAGATCTT CTGTAAACTT      360
30 CCACATATCA CATTCTCGAT TTGATAAGCT TAAATAGTTT GACTTTGGAA ATAAAGAATG      420
ACAATTAATT TGTGGTTGTA ACCATAGTGG TTGATTGTTT TTTAAAGAA CTAAGTGAGC      480
TATTCTCTGA CCTTTTCTA TAGTTACAGT TTTAGAGGAT ATATTTTAA TAAAAAATTG      540

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ACAAATTGTT TTTGGTTTCC ATATAGTTGG AAGAACAATT ATTCCGCTTG AATTTAAGGA 600
 TGATCTACCA AAAATACAAG CGATTGGTGG GTTTTTCATT TCTAATTGAA AAATAGGAAG 660
 ACAAAAAAGG TAACTATATC CCGGTTTAT TTGAATAAA TTTGGAGATG GTATATCATA 720
 ACCAGCATCC TCCTCCCGCT TCG 743

5 (2) INFORMATION FOR SEQ ID NO:15:

- (i) SEQUENCE CHARACTERISTICS:
 (A) LENGTH: 459 base pairs
 (B) TYPE: nucleic acid
 (C) STRANDEDNESS: single
 (D) TOPOLOGY: linear

10 (ii) MOLECULE TYPE: cDNA

- (ix) FEATURE:
 (A) NAME/KEY: CDS
 (B) LOCATION: 1..459

15 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:15:

AAG CGG GAG GAG GAT GCT GGT TAT GAT ATA CCA TCT CCA AAT TTA GTT 48
 Lys Arg Glu Glu Asp Ala Gly Tyr Asp Ile Pro Ser Pro Asn Leu Val
 1 5 10 15

CAA ATA AAA CCG GGA TAT AGT TAC CTT TTT TGT CTT CCT ATT TTT CAA 96
 Gln Ile Lys Pro Gly Tyr Ser Tyr Leu Phe Cys Leu Pro Ile Phe Gln
 20 20 25 30

TTA GAA ATG AAA AAC CCA CCA ATC GCT TGT ATT TTT GGT AGA TCA TCC 144
 Leu Glu Met Lys Asn Pro Pro Ile Ala Cys Ile Phe Gly Arg Ser Ser
 35 40 45

TTA AAT TCA AGC GGA ATA ATT GTT CTT CCA ACT ATA TGG AAA CCA AAA 192
 Leu Asn Ser Ser Gly Ile Ile Val Leu Pro Thr Ile Trp Lys Pro Lys
 50 55 60

ACA ATT TGT CAA TTT TTT ATT AAA AAT ATA TCC TCT AAA ACT GTA ACT 240
 Thr Ile Cys Gln Phe Phe Ile Lys Asn Ile Ser Ser Lys Thr Val Thr
 30 65 70 75 80

ATA GAA AAA GGT CAG AGA ATA GCT CAG TTA GTT CTT TTA AAA AAC AAT 288
 Ile Glu Lys Gly Gln Arg Ile Ala Gln Leu Val Leu Leu Lys Asn Asn
 85 90 95

CAA CCA CTA TGG TTA CAA CCA CAA ATT AAT TGT CAT TCT TTA TTT CCA 336
 Gln Pro Leu Trp Leu Gln Pro Gln Ile Asn Cys His Ser Leu Phe Pro
 100 105 110

AAG TCA AAC TAT TTA AGC TTA TCA AAT CGA GAA TGT GAT ATG TGG AAG 384
 Lys Ser Asn Tyr Leu Ser Leu Ser Asn Arg Glu Cys Asp Met Trp Lys
 115 120 125

TTT ACA GAA GAT CTG AAT TTT GAA GCA CCG AAA AGT TTA CGA GGA ATA 432
 Phe Thr Glu Asp Leu Asn Phe Glu Ala Pro Lys Ser Leu Arg Gly Ile
 130 135 140

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AAT GGA TTT GGA TCC ACG GGA TTG TAA
 Asn Gly Phe Gly Ser Thr Gly Leu *
 145 150

459

(2) INFORMATION FOR SEQ ID NO:16:

- 5 (i) SEQUENCE CHARACTERISTICS:
 (A) LENGTH: 153 amino acids
 (B) TYPE: amino acid
 (D) TOPOLOGY: linear
 (ii) MOLECULE TYPE: protein

10 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:16:

Lys Arg Glu Glu Asp Ala Gly Tyr Asp Ile Pro Ser Pro Asn Leu Val
 1 5 10 15
 Gln Ile Lys Pro Gly Tyr Ser Tyr Leu Phe Cys Leu Pro Ile Phe Gln
 20 25 30
 15 Leu Glu Met Lys Asn Pro Pro Ile Ala Cys Ile Phe Gly Arg Ser Ser
 35 40 45
 Leu Asn Ser Ser Gly Ile Ile Val Leu Pro Thr Ile Trp Lys Pro Lys
 50 55 60
 20 Thr Ile Cys Gln Phe Phe Ile Lys Asn Ile Ser Ser Lys Thr Val Thr
 65 70 75 80
 Ile Glu Lys Gly Gln Arg Ile Ala Gln Leu Val Leu Lys Asn Asn
 85 90 95
 Gln Pro Leu Trp Leu Gln Pro Gln Ile Asn Cys His Ser Leu Phe Pro
 100 105 110
 25 Lys Ser Asn Tyr Leu Ser Leu Ser Asn Arg Glu Cys Asp Met Trp Lys
 115 120 125
 Phe Thr Glu Asp Leu Asn Phe Glu Ala Pro Lys Ser Leu Arg Gly Ile
 130 135 140
 30 Asn Gly Phe Gly Ser Thr Gly Leu *
 145 150

(2) INFORMATION FOR SEQ ID NO:17:

- 35 (i) SEQUENCE CHARACTERISTICS:
 (A) LENGTH: 579 base pairs
 (B) TYPE: nucleic acid
 (C) STRANDEDNESS: single
 (D) TOPOLOGY: linear
 (ii) MOLECULE TYPE: cDNA
 (ix) FEATURE:
 (A) NAME/KEY: CDS
 40 (B) LOCATION: 54..503

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(xi) SEQUENCE DESCRIPTION: SEQ ID NO:17:

	AATTATTACT CTAAATCTCA CTTTCATTATA CTTATATAAT AATATAAAAC CTT ATG	56
	Met	
	1	
5	TTT GTC ATT ATT AAC TTA ACA CTA GAT GGT ACT ATA AAG CTA ACT TAC	104
	Phe Val Ile Ile Asn Leu Thr Leu Asp Gly Thr Ile Lys Leu Thr Tyr	
	5 10 15	
	AAT ATA AAT AGT AAG ATT AGT TTA TAT AAA TTA CAT TTA ATG GCT TTA	152
	Asn Ile Asn Ser Lys Ile Ser Leu Tyr Lys Leu His Leu Met Ala Leu	
10	20 25 30	
	CCA GAT AAC GTT TTT AGT ATT ATT AAT GAA AAT TAT ATC GAT GGA ATT	200
	Pro Asp Asn Val Phe Ser Ile Ile Asn Glu Asn Tyr Ile Asp Gly Ile	
	35 40 45	
15	TTA ACT ATG AAA ATG GGT GAA GAA ATA GAA AGC TCA TCA CCA TTA AAT	248
	Leu Thr Met Lys Met Gly Glu Glu Ile Glu Ser Ser Ser Pro Leu Asn	
	50 55 60 65	
	GAA ACA AAT GTT AAT ATA GAT CAA CAT ACA ATA GAT ATT TTT GAT TAC	296
	Glu Thr Asn Val Asn Ile Asp Gln His Thr Ile Asp Ile Phe Asp Tyr	
	70 75 80	
20	GAT TCA GAT AAT GGA TGT TAT TAT AGT GAA AGA GAT AAT GAA ACC GCA	344
	Asp Ser Asp Asn Gly Cys Tyr Tyr Ser Glu Arg Asp Asn Glu Thr Ala	
	85 90 95	
	ACT CTT TTT TTA AAA CGT GTT GGT TAT AGA GAA ACC TCA AAA AAG CGT	392
	Thr Leu Phe Leu Lys Arg Val Gly Tyr Arg Glu Thr Ser Lys Lys Arg	
25	100 105 110	
	AAA CGG ATT TGT GGA TTT ATT GTT TTA GCA ATT TTT ATG GTT ATT ATA	440
	Lys Arg Ile Cys Gly Phe Ile Val Leu Ala Ile Phe Met Val Ile Ile	
	115 120 125	
30	TTA TGT TTT TTA TCA ATA ATT TTG GGA GTT TTT ATA GCG CCT CAT ATT	488
	Leu Cys Phe Leu Ser Ile Ile Leu Gly Val Phe Ile Ala Pro-His Ile	
	130 135 140 145	
	TAT AAA GGC CTA TAG TAAGAACATC AACCTCTAAT AGGTAAATTT TTAAACCAA	543
	Tyr Lys Gly Leu *	
	150	
35	CGGAGGGGGA GGAGGAGGAC TTTTATTATTT ATGAGA	579

(2) INFORMATION FOR SEQ ID NO:18:

(i) SEQUENCE CHARACTERISTICS:

- 40 (A) LENGTH: 150 amino acids
(B) TYPE: amino acid
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein

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(xi) SEQUENCE DESCRIPTION: SEQ ID NO:18:

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Met Phe Val Ile Ile Asn Leu Thr Leu Asp Gly Thr Ile Lys Leu Thr
 1           5           10           15
5 Tyr Asn Ile Asn Ser Lys Ile Ser Leu Tyr Lys Leu His Leu Met Ala
 20           25           30
Leu Pro Asp Asn Val Phe Ser Ile Ile Asn Glu Asn Tyr Ile Asp Gly
 35           40           45
Ile Leu Thr Met Lys Met Gly Glu Glu Ile Glu Ser Ser Ser Pro Leu
 50           55           60
10 Asn Glu Thr Asn Val Asn Ile Asp Gln His Thr Ile Asp Ile Phe Asp
 65           70           75           80
Tyr Asp Ser Asp Asn Gly Cys Tyr Tyr Ser Glu Arg Asp Asn Glu Thr
 85           90           95
15 Ala Thr Leu Phe Leu Lys Arg Val Gly Tyr Arg Glu Thr Ser Lys Lys
 100          105          110
Arg Lys Arg Ile Cys Gly Phe Ile Val Leu Ala Ile Phe Met Val Ile
 115          120          125
Ile Leu Cys Phe Leu Ser Ile Ile Leu Gly Val Phe Ile Ala Pro His
 130          135          140
20 Ile Tyr Lys Gly Leu *
 145          150

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(2) INFORMATION FOR SEQ ID NO:19:

(i) SEQUENCE CHARACTERISTICS:

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25 (A) LENGTH: 579 base pairs
    (B) TYPE: nucleic acid
    (C) STRANDEDNESS: single
    (D) TOPOLOGY: linear

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(ii) MOLECULE TYPE: DNA (genomic)

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:19:

```

30 TCTCATAAAA TAAAAAGTCC TCCTCCTCCC CCTCCGTTGG TTTTAAAAAT TTACCTATTA      60
   GAGGTTGATG TTCTTACTAT AGGCCTTTAT AAATATGAGG CGCTATAAAA ACTCCCAAAA      120
   TTATTGATAA AAAACATAAT ATAATAACCA TAAAAATTGC TAAACAATA AATCCACAAA      180
   TCCGTTTACG CTTTTTTCAG GTTCTCTAT AACCAACACG TTTTAAAAAA AGAGTTGCGG      240
   TTTCATTATC TCTTCACTA TAATAACATC CATTATCTGA ATCGTAATCA AAAATATCTA      300
35 TTGTATGTTG ATCTATATTA ACATTTGTTT CATTTAATGG TGATGAGCTT TCTATTCTTT      360
   CACCCATTTT CATAGTTAAA ATTCCATCGA TATAATTTTC ATTAATAATA CTA AAAACGT      420
   TATCTGGTAA AGCCATTAAA TGTAATTTAT ATAACTAAT CTTACTATTT ATATTGTAAG      480

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TTAGCTTTAT AGTACCATCT AGTGTTAAGT TAATAATGAC AACATAAGG TTTTATATTA 540
 TTATATAAGT ATAATGAAGT GAGATTTAGA GTAATAATT 579

(2) INFORMATION FOR SEQ ID NO:20:

- 5 (i) SEQUENCE CHARACTERISTICS:
 (A) LENGTH: 450 base pairs
 (B) TYPE: nucleic acid
 (C) STRANDEDNESS: single
 (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

10 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:20:

ATGTTTGTC TATTAACTT AACACTAGAT GGTACTATAA AGCTAACTTA CAATATAAAT 60
 AGTAAGATTA GTTTATATAA ATTACATTTA ATGGCTTTAC CAGATAACGT TTTTAGTATT 120
 ATTAATGAAA ATTATATCGA TGGAATTTTA ACTATGAAAA TGGGTGAAGA AATAGAAAGC 180
 TCATCACCAT TAAATGAAAC AAATGTTAAT ATAGATCAAC ATACAATAGA TATTTTGTAT 240
 15 TACGATTCAG ATAATGGATG TTATTATAGT GAAAGAGATA ATGAAACCGC AACTCTTTTT 300
 TTAAACGTG TTGGTTATAG AGAAACCTCA AAAAAGCGTA AACGGATTG TGGATTTATT 360
 GTTTTAGCAA TTTTATGGT TATTATATTA TGTTTTTTAT CAATAATTTT GGGAGTTTTT 420
 ATAGCGCCTC ATATTATATA AGGCCTATAG 450

(2) INFORMATION FOR SEQ ID NO:21:

- 20 (i) SEQUENCE CHARACTERISTICS:
 (A) LENGTH: 294 base pairs
 (B) TYPE: nucleic acid
 (C) STRANDEDNESS: single
 (D) TOPOLOGY: linear

25 (ii) MOLECULE TYPE: cDNA

- (ix) FEATURE:
 (A) NAME/KEY: CDS
 (B) LOCATION: 3..293

- 30 (ix) FEATURE:
 (A) NAME/KEY: R = A or G
 (B) LOCATION: 49

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:21:

35 TC CAA AGT GTT TTT GTT TCA TTG TCT TAT TCT TGG AGC CAC CGA CGA 47
 Gln Ser Val Phe Val Ser Leu Ser Tyr Ser Trp Ser His Arg Arg
 1 5 10 15
 CRG TTT GAG TGT ATA TTT CAT CCA ATT TTA TTT AAT CAT GGT ATT GTG 95
 Xaa Phe Glu Cys Ile Phe His Pro Ile Leu Phe Asn His Gly Ile Val
 20 25 30

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AAT TTG GAA AAT AAC CCT TTG ACA TTT AAG GAA CTA CAA AAA ATA AAT 143
 Asn Leu Glu Asn Asn Pro Leu Thr Phe Lys Glu Leu Gln Lys Ile Asn
 35 40 45
 5 TAT AGA CGT CAT ATT CTT GGT TTA CCA TTG ATT AGA GCT GGA TTG GTA 191
 Tyr Arg Arg His Ile Leu Gly Leu Pro Leu Ile Arg Ala Gly Leu Val
 50 55 60
 GAA GAA GAT AAT CAA CCT TTA ATG ATA CCT CCA GAG TTT TCC AGT AAA 239
 Glu Glu Asp Asn Gln Pro Leu Met Ile Pro Pro Glu Phe Ser Ser Lys
 65 70 75
 10 CTA CCT CGA ACA ATA GGA TTT TTA ACT CAA CAA ATT AGA GCC AAA ATG 287
 Leu Pro Arg Thr Ile Gly Phe Leu Thr Gln Gln Ile Arg Ala Lys Met
 80 85 90 95
 GAA GCT T
 Glu Ala 294
 15

(2) INFORMATION FOR SEQ ID NO:22:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 97 amino acids
 (B) TYPE: amino acid
 (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein

(ix) NAME/KEY: Xaa = Arg or Gln
 LOCATION: 16

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:22:

25 Gln Ser Val Phe Val Ser Leu Ser Tyr Ser Trp Ser His Arg Arg Xaa
 1 5 10 15
 Phe Glu Cys Ile Phe His Pro Ile Leu Phe Asn His Gly Ile Val Asn
 20 25 30
 30 Leu Glu Asn Asn Pro Leu Thr Phe Lys Glu Leu Gln Lys Ile Asn Tyr
 35 40 45
 Arg Arg His Ile Leu Gly Leu Pro Leu Ile Arg Ala Gly Leu Val Glu
 50 55 60
 Glu Asp Asn Gln Pro Leu Met Ile Pro Pro Glu Phe Ser Ser Lys Leu
 65 70 75 80
 35 Pro Arg Thr Ile Gly Phe Leu Thr Gln Gln Ile Arg Ala Lys Met Glu
 85 90 95
 Ala

(2) INFORMATION FOR SEQ ID NO:23:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 294 base pairs
 (B) TYPE: nucleic acid

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(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:23:

```

5  AAGCTTCCAT TTTGGCTCTA ATTTGTTGAG TTAAAAATCC TATTGTTCGA GGTAGTTTAC      60
   TGGAAACTC TGGAGGTATC ATTAAGGTT GATTATCTTC TTCTACCAAT CCAGCTCTAA      120
   TCAATGGTAA ACCAAGAATA TGACGTCTAT AATTTATTTT TTGTAGTTCC TTAAATGTCA      180
   AAGGTTTATT TTCCAAATC ACAATACCAT GATTAAATAA AATTGGATGA AATATACACT      240
   CAAACYGTCG TCGGTGGCTC CAAGAATAAG ACAATGAAAC AAAAACACTT TGGA      294

```

10 (2) INFORMATION FOR SEQ ID NO:24:

(i) SEQUENCE CHARACTERISTICS:
 (A) LENGTH: 291 base pairs
 (B) TYPE: nucleic acid
 (C) STRANDEDNESS: single
 (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:24:

```

   CAAAGTGTTC TTGTTTCATT GTCTTATTCT TGGAGCCACC GACGACRGT TGAGTGTATA      60
   TTTCATCCAA TTTTATTTAA TCATGGTATT GTGAATTTGG AAAATAACCC TTGACATTT      120
20  AAGGAACTAC AAAAATAAAA TTATAGACGT CATATTCTTG GTTTACCATT GATTAGAGCT      180
   GGATTGGTAG AAGAAGATAA TCAACCTTTA ATGATACCTC CAGAGTTTTC CAGTAAACTA      240
   CCTCGAACAA TAGGATTTTT AACTCAACAA ATTAGAGCCA AAATGGAAGC T      291

```

(2) INFORMATION FOR SEQ ID NO:25:

25 (i) SEQUENCE CHARACTERISTICS:
 (A) LENGTH: 146 base pairs
 (B) TYPE: nucleic acid
 (C) STRANDEDNESS: single
 (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: cDNA

30 (ix) FEATURE:
 (A) NAME/KEY: CDS
 (B) LOCATION: 1..146

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:25:

```

35  CTA GAA GAT TAT ATA ACA CAT CGA ATT AAT GCC GAT ATT TCA GAG GTT      48
   Leu Glu Asp Tyr Ile Thr His Arg Ile Asn Ala Asp Ile Ser Glu Val
   1           5           10           15

```

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GGT GTA TTG AGA AAT TAT ATT TCT GCT GAT AGA CAG AGT TTA AAA GTT 96
 Gly Val Leu Arg Asn Tyr Ile Ser Ala Asp Arg Gln Ser Leu Lys Val
 20 25 30

5 TCT GAT AGA GAG TTT ATT AAT TAT ATT TAC TTG GCA CAT TTT GAA AGC TT
 146
 Ser Asp Arg Glu Phe Ile Asn Tyr Ile Tyr Leu Ala His Phe Glu Ser
 35 40 45

(2) INFORMATION FOR SEQ ID NO:26:

10 (i) SEQUENCE CHARACTERISTICS:
 (A) LENGTH: 48 amino acids
 (B) TYPE: amino acid
 (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:26:

15 Leu Glu Asp Tyr Ile Thr His Arg Ile Asn Ala Asp Ile Ser Glu Val
 1 5 10 15
 Gly Val Leu Arg Asn Tyr Ile Ser Ala Asp Arg Gln Ser Leu Lys Val
 20 25 30
 20 Ser Asp Arg Glu Phe Ile Asn Tyr Ile Tyr Leu Ala His Phe Glu Ser
 35 40 45

(2) INFORMATION FOR SEQ ID NO:27:

25 (i) SEQUENCE CHARACTERISTICS:
 (A) LENGTH: 146 base pairs
 (B) TYPE: nucleic acid
 (C) STRANDEDNESS: single
 (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:27:

AAGCTTTCAA AATGTGCCAA GTAAATATAA TTAATAAACT CTCTATCAGA AACTTTTAAA 60
 30 CTCTGTCTAT CAGCAGAAAT ATAATTTCTC AATACACCAA CCTCTGAAAT ATCGGCATTA 120
 ATTCGATGTG TTATATAATC TTCTAG 146

(2) INFORMATION FOR SEQ ID NO:28:

35 (i) SEQUENCE CHARACTERISTICS:
 (A) LENGTH: 144 base pairs
 (B) TYPE: nucleic acid
 (C) STRANDEDNESS: single
 (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

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(xi) SEQUENCE DESCRIPTION: SEQ ID NO:28:

CTAGAAGATT ATATAACACA TCGAATTAAT GCCGATATTT CAGAGGTTGG TGTATTGAGA 60
 AATTATATTT CTGCTGATAG ACAGAGTTTA AAAGTTTCTG ATAGAGAGTT TATTAATTAT 120
 ATTTACTTGG CACATTTTGA AAGC 144

5 (2) INFORMATION FOR SEQ ID NO:29:

- (i) SEQUENCE CHARACTERISTICS:
 (A) LENGTH: 161 base pairs
 (B) TYPE: nucleic acid
 (C) STRANDEDNESS: single
 10 (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

- (ix) FEATURE:
 (A) NAME/KEY: CDS
 (B) LOCATION: 3..161

15 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:29:

TT ATG TCA GTG GAC GTT ATA TTT CTC GAT GAC CAA CAT CTG TCA GTA 47
 Met Ser Val Asp Val Ile Phe Leu Asp Asp Gln His Leu Ser Val 15
 1 5 10 15
 AAT AAT TAT AGC GGA ACT ATT GAG TTT ATT CAT TTT AAT AAC TCT TGT 95
 20 Asn Asn Tyr Ser Gly Thr Ile Glu Phe Ile His Phe Asn Asn Ser Cys 25 30
 TAT ACC GTT TAT CAA ACT ATT GAA TAT TTT TCT TGT CCT CGC ATT TTT 143
 Tyr Thr Val Tyr Gln Thr Ile Glu Tyr Phe Ser Cys Pro Arg Ile Phe 35 40 45
 25 AAT AAT GCT TTT AGA TCT 161
 Asn Asn Ala Phe Arg Ser 50

(2) INFORMATION FOR SEQ ID NO:30:

- (i) SEQUENCE CHARACTERISTICS:
 (A) LENGTH: 53 amino acids
 (B) TYPE: amino acid
 30 (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:30:

35 Met Ser Val Asp Val Ile Phe Leu Asp Asp Gln His Leu Ser Val Asn 15
 1 5 10 15
 Asn Tyr Ser Gly Thr Ile Glu Phe Ile His Phe Asn Asn Ser Cys Tyr 20 25 30

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Thr Val Tyr Gln Thr Ile Glu Tyr Phe Ser Cys Pro Arg Ile Phe Asn
35 40 45

Asn Ala Phe Arg Ser
50

5 (2) INFORMATION FOR SEQ ID NO:31:

- (i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 161 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
10 (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:31:

AGATCTAAAA GCATTATTAA AAATGCGAGG ACAAGAAAAA TATTCAATAG TTGATAAAC 60
GGTATAACAA GAGTTATTAA AATGAATAAA CTCAATAGTT CCGCTATAAT TATTTACTGA 120
15 CAGATGTTGG TCATCGAGAA ATATAACGTC CACTGACATA A 161

(2) INFORMATION FOR SEQ ID NO:32:

- (i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 159 base pairs
(B) TYPE: nucleic acid
20 (C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:32:

ATGTCAGTGG ACGTTATATT TCTCGATGAC CAACATCTGT CAGTAAATAA TTATAGCGGA 60
25 ACTATTGAGT TTATTCATTT TAATAACTCT TGTATACCG TTTATCAAAC TATTGAATAT 120
TTTCTTGTC CTCGCATTTT TAATAATGCT TTTAGATCT 159

(2) INFORMATION FOR SEQ ID NO:33:

- (i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 261 base pairs
(B) TYPE: nucleic acid
30 (C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: cDNA

(ix) FEATURE:

- 35 (A) NAME/KEY: CDS
(B) LOCATION: 1..261

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(xi) SEQUENCE DESCRIPTION: SEQ ID NO:33:

```

GGT GGT GCC CAA GCC ATA AAA ATG ACT TCA GAA AAT AAT ATT GTT ATG      48
Gly Gly Ala Gln Ala Ile Lys Met Thr Ser Glu Asn Asn Ile Val Met
 1           5           10           15
5  GCA GAT GTA GCG GTT TTA GAA AAA ACC CTT GGT ATA GAT TCT AAT ACA      96
Ala Asp Val Ala Val Leu Glu Lys Thr Leu Gly Ile Asp Ser Asn Thr
          20           25           30
10 ACA AAA CCC TTA TCT CTT CAA ACC GTT AAA TAT GAT GAA AAT AAT TCT     144
Thr Lys Pro Leu Ser Leu Gln Thr Val Lys Tyr Asp Glu Asn Asn Ser
          35           40           45
ACA GAT ATA CTA GAT ACA GAA CCT CTA ATA AGT TCT ATG GAA ACT GAA      192
Thr Asp Ile Leu Asp Thr Glu Pro Leu Ile Ser Ser Met Glu Thr Glu
          50           55           60
15 AAT ATT TTA TCG ACT AAA CAA AAA AGA AAC GGT CCC AAA AAA ATG ACA      240
Asn Ile Leu Ser Thr Lys Gln Lys Arg Asn Gly Pro Lys Lys Met Thr
          65           70           75           80
CGT GAA AGT TTG GCA CTT TAA
Arg Glu Ser Leu Ala Leu *
          85

```

20 (2) INFORMATION FOR SEQ ID NO:34:

- (i) SEQUENCE CHARACTERISTICS:
 (A) LENGTH: 87 amino acids
 (B) TYPE: amino acid
 (D) TOPOLOGY: linear

25 (ii) MOLECULE TYPE: protein

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:34:

```

Gly Gly Ala Gln Ala Ile Lys Met Thr Ser Glu Asn Asn Ile Val Met
 1           5           10           15
30 Ala Asp Val Ala Val Leu Glu Lys Thr Leu Gly Ile Asp Ser Asn Thr
          20           25           30
Thr Lys Pro Leu Ser Leu Gln Thr Val Lys Tyr Asp Glu Asn Asn Ser
          35           40           45
Thr Asp Ile Leu Asp Thr Glu Pro Leu Ile Ser Ser Met Glu Thr Glu
          50           55           60
35 Asn Ile Leu Ser Thr Lys Gln Lys Arg Asn Gly Pro Lys Lys Met Thr
          65           70           75           80
Arg Glu Ser Leu Ala Leu *
          85

```

(2) INFORMATION FOR SEQ ID NO:35:

- 40 (i) SEQUENCE CHARACTERISTICS:
 (A) LENGTH: 280 base pairs

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(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: cDNA

5 (ix) FEATURE:
(A) NAME/KEY: CDS
(B) LOCATION: 2..280

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:35:

10	T GCA TTA AAT TTT ATT AAA TTA GAA AAA AAT AAT CCA GTA TAT TAT Ala Leu Asn Phe Ile Lys Leu Glu Lys Asn Asn Pro Val Tyr Tyr	46
	1 5 10 15	
	TTT CCG GAA CCT ATG GCA TTC TGG CGT ATC ATC CTA GAA ACA GAT ATT Phe Pro Glu Pro Met Ala Phe Trp Arg Ile Ile Leu Glu Thr Asp Ile	94
	20 25 30	
15	GTG CAA GGT ATA TAC TCA GTA CAA GAC CGG AAG CTG CGT GGT GAA TTA Val Gln Gly Ile Tyr Ser Val Gln Asp Arg Lys Leu Arg Gly Glu Leu	142
	35 40 45	
20	AGC CTA AAT GAT GCG TCA TTA ATT ACA GCT CAA CTT CAA ACT AAA TTT Ser Leu Asn Asp Ala Ser Leu Ile Thr Ala Gln Leu Gln Thr Lys Phe	190
	50 55 60	
	TCT ACG CCA TAT ATT TTA CTT CAT TCC AAT GTA TCC AAA TTT TTT GGA Ser Thr Pro Tyr Ile Leu Leu His Ser Asn Val Ser Lys Phe Phe Gly	238
	65 70 75	
25	GAA AAT GTA ACA TTT GGA ATT CCG GAA GTA ATA TTT ATT TTT Glu Asn Val Thr Phe Gly Ile Pro Glu Val Ile Phe Ile Phe	280
	80 85 90	

(2) INFORMATION FOR SEQ ID NO:36:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 93 amino acids
(B) TYPE: amino acid
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:36:

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

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Thr Pro Tyr Ile Leu Leu His Ser Asn Val Ser Lys Phe Phe Gly Glu
65 70 75 80
Asn Val Thr Phe Gly Ile Pro Glu Val Ile Phe Ile Phe
85 90

5 (2) INFORMATION FOR SEQ ID NO:37:

- (i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 280 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
10 (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:37:

AAAAATAAAT ATTACTTCCG GAATTCCTAAA TGTTACATTT TCTCCAAAAA ATTTGGATAC 60
ATTGGAATGA AGTAAATAT ATGGCGTAGA AAATTTAGTT TGAAGTTGAG CTGTAATTAA 120
15 TGACGCATCA TTTAGGCTTA ATTCACCACG CAGCTCCCG TCTTGTACTG AGTATATACC 180
TTGCACAATA TCTGTTTCTA GGATGATACG CCAGAATGCC ATAGGTTCCG GAAAATAATA 240
TACTGGATTA TTTTCTTCTA ATTTAATAAA ATTTAATGCA 280

(2) INFORMATION FOR SEQ ID NO:38:

- (i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 279 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
20 (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

25 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:38:

GCATTAAATT TTATTAAATT AGAAAAAAT AATCCAGTAT ATTATTTTCC GGAACCTATG 60
GCATTCTGGC GTATCATCCT AGAACAGAT ATTGTGCAAG GTATATACTC AGTACAAGAC 120
CGGAAGCTGC GTGGTGAATT AAGCCTAAAT GATGCGTCAT TAATTACAGC TCAACTTCAA 180
ACTAAATTTT CTACGCCATA TATTTTACTT CATTCCAATG TATCCAAATT TTTTGGAGAA 240
30 AATGTAACAT TTGGAATTCC GGAAGTAATA TTTATTTT 279

(2) INFORMATION FOR SEQ ID NO:39:

- (i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 27 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
35 (D) TOPOLOGY: linear

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(ii) MOLECULE TYPE: DNA (genomic)

(ix) FEATURE:
(A) NAME/KEY: misc feature
(B) LOCATION: 1..27
5 (D) OTHER INFORMATION: /label= primer

(ix) FEATURE:
(A) NAME/KEY: N = Inosine
(B) LOCATION: 11

(ix) FEATURE:
10 (A) NAME/KEY: N = Inosine
(B) LOCATION: 17

(ix) FEATURE:
(A) NAME/KEY: N = Inosine
(B) LOCATION: 20

15 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:39:
GGCGAATTCC NAARMNGAN GARGAYG 27

(2) INFORMATION FOR SEQ ID NO:40:

(i) SEQUENCE CHARACTERISTICS:
20 (A) LENGTH: 24 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(ix) FEATURE:
25 (A) NAME/KEY: misc feature
(B) LOCATION: 1..24
(D) OTHER INFORMATION: /label= primer

(ix) FEATURE:
30 (A) NAME/KEY: N = Inosine
(B) LOCATION: 11

(ix) FEATURE:
(A) NAME/KEY: N = Inosine
(B) LOCATION: 16

(ix) FEATURE:
35 (A) NAME/KEY: N = Inosine
(B) LOCATION: 22

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:40:
CGCGGATCCG NTNSWNCCYA ANCC 24

(2) INFORMATION FOR SEQ ID NO:41:

(i) SEQUENCE CHARACTERISTICS:
40 (A) LENGTH: 26 base pairs
(B) TYPE: nucleic acid

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(C) STRANDEDNESS: single
(D) TOPOLOGY: linear
(ii) MOLECULE TYPE: DNA (genomic)
(ix) FEATURE:
5 (A) NAME/KEY: misc_feature
(B) LOCATION: 1..26
(D) OTHER INFORMATION: /label= primer
(ix) FEATURE:
10 (A) NAME/KEY: N = Inosine
(B) LOCATION: 18
(ix) FEATURE:
(A) NAME/KEY: N = Inosine
(B) LOCATION: 24
(xi) SEQUENCE DESCRIPTION: SEQ ID NO:41:
15 GGCGAATTCT AYCAYWSNCA YGTNTA

26

(2) INFORMATION FOR SEQ ID NO:42:
(i) SEQUENCE CHARACTERISTICS:
20 (A) LENGTH: 30 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear
(ii) MOLECULE TYPE: DNA (genomic)
(ix) FEATURE:
25 (A) NAME/KEY: misc_feature
(B) LOCATION: 1..30
(D) OTHER INFORMATION: /label= primer
(ix) FEATURE:
(A) NAME/KEY: N = Inosine
(B) LOCATION: 16
30 (ix) FEATURE:
(A) NAME/KEY: N = Inosine
(B) LOCATION: 19
(ix) FEATURE:
35 (A) NAME/KEY: N = Inosine
(B) LOCATION: 24
(ix) FEATURE:
(A) NAME/KEY: N = Inosine
(B) LOCATION: 25
(ix) FEATURE:
40 (A) NAME/KEY: N = Inosine
(B) LOCATION: 28
(xi) SEQUENCE DESCRIPTION: SEQ ID NO:42:
CGCGGATCCR TCRTTNSWNG GDANNSWNGT

30

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(2) INFORMATION FOR SEQ ID NO:43:

- (i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 23 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear
- (ii) MOLECULE TYPE: DNA (genomic)
- (ix) FEATURE:
(A) NAME/KEY: misc_feature
(B) LOCATION: 1..20
(D) OTHER INFORMATION: /label= primer
- (ix) FEATURE:
(A) NAME/KEY: N = Inosine
(B) LOCATION: 12
- (ix) FEATURE:
(A) NAME/KEY: N = Inosine
(B) LOCATION: 18
- (ix) FEATURE:
(A) NAME/KEY: N = Inosine
(B) LOCATION: 21

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:43:

GGCGAATTCG GNAARWSNAC NRC

23

(2) INFORMATION FOR SEQ ID NO:44:

- (i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 20 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear
- (ii) MOLECULE TYPE: DNA (genomic)
- (ix) FEATURE:
(A) NAME/KEY: misc_feature
(B) LOCATION: 1..20
(D) OTHER INFORMATION: /label= primer
- (ix) FEATURE:
(A) NAME/KEY: N = Inosine
(B) LOCATION: 15

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:44:

GGCGGATCCG GTTGNCCKRTC

20

(2) INFORMATION FOR SEQ ID NO:45:

- (i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 30 base pairs

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(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

5 (ix) FEATURE:
(A) NAME/KEY: misc feature
(B) LOCATION: 1..30
(D) OTHER INFORMATION: /label= label

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:45:

10 CGCGGATCCA AGGTAATAAG TCAAAATGAG 30

(2) INFORMATION FOR SEQ ID NO:46:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 29 base pairs
(B) TYPE: nucleic acid
15 (C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(ix) FEATURE:
(A) NAME/KEY: misc feature
20 (B) LOCATION: 1..29
(D) OTHER INFORMATION: /label= primer

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:46:

CGCGGATCCG ACAAAAACAA AAAGTAATG 29

(2) INFORMATION FOR SEQ ID NO:47:

25 (i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 28 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

30 (ii) MOLECULE TYPE: DNA (genomic)

(ix) FEATURE:
(A) NAME/KEY: misc feature
(B) LOCATION: 1..28
(D) OTHER INFORMATION: /label= primer

35 (ix) FEATURE:
(A) NAME/KEY: N = Inosine
(B) LOCATION: 11

(ix) FEATURE:
40 (A) NAME/KEY: N = Inosine
(B) LOCATION: 20

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(xi) SEQUENCE DESCRIPTION: SEQ ID NO:47:

CCGAATTCYT NATGATHYTN ATHGARGG

28

(2) INFORMATION FOR SEQ ID NO:48:

(i) SEQUENCE CHARACTERISTICS:

- 5 (A) LENGTH: 29 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(ix) FEATURE:

- 10 (A) NAME/KEY: misc feature
(B) LOCATION: 1..29
(D) OTHER INFORMATION: /label= primer

(ix) FEATURE:

- 15 (A) NAME/KEY: N = Inosine
(B) LOCATION: 21

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:48:

CCGGATCCYT CRAARAARTT NGTRTGYTT

29

(2) INFORMATION FOR SEQ ID NO:49:

(i) SEQUENCE CHARACTERISTICS:

- 20 (A) LENGTH: 35 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(ix) FEATURE:

- (A) NAME/KEY: misc feature
(B) LOCATION: 1..35
(D) OTHER INFORMATION: /label= primer

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:49:

TCCCCCGGGG GCGCGCCTTG ACATTGATTA TTGAC

35

(2) INFORMATION FOR SEQ ID NO:50:

(i) SEQUENCE CHARACTERISTICS:

- 35 (A) LENGTH: 35 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

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(ix) FEATURE:

- (A) NAME/KEY: misc feature
(B) LOCATION: 1..35
(D) OTHER INFORMATION: /label= primer

5 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:50:

GCCCTTAAGG GGCGCGCCAA TCGATGCAA TTCC

35

(2) INFORMATION FOR SEQ ID NO:51:

(i) SEQUENCE CHARACTERISTICS:

- 10 (A) LENGTH: 10592 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:51:

15 CTGCAGTGTA TTTAAAAAT AAAAATCTAT GAATGAAATC TATGAATGAA ATCTATGAAT 60
GAAATCTATG AATGAAATCT ATGAATGAAA TCTATGAATG AAATCTATGA ATGAAATCTA 120
TGAATGAAAT CTATGAATGA AATCTATGAA TGAATCTAT GAATGAAATC TATGAATGAA 180
ATCTATGAAT GAAATCTATG AATGAAATCT ATGAATGAAA TCTATGAATG AAATCTATGA 240
ATGAAATCTA TGAATGAAAT CTATGAATGA AATCTATGAA TGAATCTAT GAGACAAAGT 300
20 AATTTTAA AATATTTTAA ATTTTATTAA GAGTATAGGT TACAAGGTTT AATGCGTTGG 360
GTAAACATTT TAGTTTTCAA GTTTTAGTTT TCTGGTATCT ACCAACACAA ATGCATCTTC 420
GGATACATTA TTTAGAGAGT AATCACTTTT TAGAATATAT CTTATTGGTG GTACATTTAT 480
AAATTTTGA CCATCCCAAT AACACTTCGA TTCCACAAGC GAAGAAGGTA CTTCATAAG 540
CTGAGAAGCG TTTACTTGAT TGTAGGGAGA ACTTGGCGTT TCAAAATCCT TTAGAACGTA 600
25 TAGTCTGCAA TACATAGGTT CAATATCATC TTCATACCTC TCATCAGGAT ATGAAATGG 660
AAGTTTCACA AAGGTTCCAT CACGAAGCTT TTTGAAGAAT CGTACATCCG TAGGTGGTGT 720
AGGAACAATA GTGAAGGCGT GCGGTTCCACC CTGGTTTTTC ACACGTGCAA GCGCTGGTGT 780
GGTTTTAGGG CGAACTGGAA AATAACCAGG OGGAACCTGT GCGTAGAATC CTTCAATTAAG 840
TTCTCCACGA CAGCGTCTGA AGTATGATGG CATATTAGCT TGATCGGAGT TGTATCAAA 900
30 TAGAGCAAAT GAAGCACTCA TTTTAAACT TTTTAGTTAA GCTTTAAAAA CAAGTGAAGA 960
TTTAAAAATG TAGGATAAAA TGCCAGTTTA TATACAGTAA GAATATGGGA GTGGTTCACA 1020
TAAAAAACCA GAATTTTCAGG TTTACATCTA CTGTTTATTC ACAACAAATA TAAACAAACT 1080
TAGTTTCCAC ATAAACATGA ACTAAATAGA GATGAACGTT GAGCGTTGGT AGGTTGTGTA 1140
GAAGACATAC CATCGTTTTT ATTTTGGTT ATTGTTTTGG CGCGCCTTGA AAATAATCGT 1200

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	TTAAAAATAT TTGGTTTGA TAGCCTTTTC ATAGGTTTCA CCCCATGCAA GTCATCCTCT	1260
	TCTGGTTCAG GAATTTCTTC ATAACCATT TGGGATATTA TTGCACACAT AAATGATTCG	1320
	ATTACCGGG GGGCAGAACG TGTCTCATTT ATATAAAGAG AATCACATAC ATCGCTTATA	1380
	GAACATGTAG AACTGTCAGA ATCCTCTTTA AAACATTTT TAATTTTACA ATTAGTTTCT	1440
5	TCTAGTTCAT TATCCACCAT CGCATTAGCG TATTTCCAAA TATCATTCTC TGAGGAATAA	1500
	TGAGATGCAG AGCATGAAGA AGAGGATGAG GAGGAGGAGG ATGAAGATGA GGATATAGAG	1560
	GGACATCTTG GAGAGCTTTC AAAGTTGAAT GGAGTATTAA ATGTTGTACC ATAAAAAATG	1620
	TCACCTAACA TAGGGGTAC TTTAAAGGAG GACAGAAAGG TGTCTAATAC AGGTACCCAT	1680
	ATAACGAGG GGCAATAAAC ACTCCCAGAA TCATCGATAT GTTTTACATT ATTTTGGAA	1740
10	ATCTCAAGAC ACTCAGGTTT CCAGGATGCT TCCGGCCATT CACATGATAC ATATGCATAA	1800
	ATTAGTCGCT TTGGTCCTGG GATATTAGAA ATGACTGGCT CACATAAATC CGCTGCACCG	1860
	AAAACCCATA GATTAAGAGG ATAGTTTCCA AATATACCAG AGTTTAGATA GTTATACCCC	1920
	GAAACAGCCG ATTTCCATTC GATGCTAGCC CCAGGTTTAT CCTCATAAA TAAAAAGTCC	1980
	TCCTCCTCCC CCTCCGTTGG TTTTAAAAAT TTACTATTAG AGGTTGATGT TCTTACTATA	2040
15	GGCCTTGAAA CTCTAGGTAG ATGTTTATA GAGTCCATAA AATAACATAA GTTTCAGAT	2100
	CGTAATATTA TAGGCATAGC CAATCGTGTG AGAGAAAGGA TATAGCATTG TCTAGCCATA	2160
	AAACACCAA GATCAGGATG AACATCTTG GAGTTTCCTG GTAACGCCCC ATTTTGTCA	2220
	ATAACGTAA CAATATTAAC TTCRAACCACA CCCATAATTA AATTTTATGT ATGAATCCAA	2280
	TAAAGGTAA TACACACCTA ATTTATGTTA TAATTTTAGA AGAAGCTGCA GTTGATGAGT	2340
20	TGATATTAAC ATAACAATTT CACAATTACC TGATATGGCA AAGTGATCCA CCGAAAAGTT	2400
	TTGTTGTATC AGCGTGAATA GAGAATCTTC TGTCGATCCA GAAGACTTCT ATAAACCGGT	2460
	TCCTCTAACT TCAGATTTGA TTGAAGAGGA TAACCTACAT CAAGACAAA TAATGGATGA	2520
	GGATTTATAC TCGGATTTTA GTGATGATGA CTTTATGGAT TATACAAAA ATCCAATGA	2580
	AAGTGAATAA GAAAGAGAAA GTGACGAAGA AGTTGAAGAA AGTTATGAAA GTGATGAAGA	2640
25	TAAAAAAGT TTATCTCCTA CTAAAAGCGA AGGAATTGAA GCGGCTGAAG CGCTAAAGTT	2700
	TTCTGTTGTT AAATCGTTAA CGCCTGGGTC AGAAGGAAGA GTTTTATATG CTCTTAAAA	2760
	AGATAAAGAT ACAAGCTATA AGGTAATTTT AAAAATTGGA CAAAGGGGAA ACACGCTTGT	2820
	GGAATCGTTA ATTTTGAGAA ATATTAGTCA CCAATCTATA ATTAACTTC AAGACACTCT	2880
	TTTTTATAAA GAGTTAACAT GTTTGGTGTT ACCGTATTAT AAATATGATC TATATAATTT	2940
30	TTTAATGGAT CATGGGAAAT CTCTGTCTTT TGAATCTGTA ATTAAATTTG AAAACCAAAT	3000
	ATTAACCTGA CTTCAATATA TTCATGGAAA AAAAATTATT CATCGAGATA TAAAACTGA	3060

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	AAATATTTTC TTGGATAATG ACTCTAATGT TTGTATAGGT GATTTTGGGG CTTCTCAATT	3120
	TCCTGTTTCC TCACCAGATT ATTTGGGAAT TGCGGGGACT ATTGAAACTA ATGCTCCTGA	3180
	AGTTCTATCA AAGGATGCGT ACAACTGTAA AGCTGATATT TGGAGTGCTG GTATAATTTT	3240
	ATTTGAAATG CTTGCATATC CTAATGTTTT GTTTGAGGAG GAAGAAAGAG ATAGTAGCGA	3300
5	TTTAATAAAC AATTGTAATC TTCATCTTAT AAAAATTATA TCAACTCTGA AGATTAACCC	3360
	AAATGAATTT CCATCTGATT TGGAACTAA TCTAGTAAA CATTTTATAA AATATGCTAA	3420
	TAATGATAGA CCTCCATTTA CACGATATAA TCGTCTAAAT AACCTTAAAT TACATCTCGA	3480
	TGGTGAATTT TTAATTCATA AAATGCTAAC ATTTGATGCA TCTCTACGAC CAAGTGCGGA	3540
	AGAACTATTA TCCTATCAGA TTTTGTAGTAA ACAATAAATT TCATAAAAT GGGCGTGGAA	3600
10	TTTTTTATTG TTTTATATAA AACGGGTGTT TGAAAGCTCT TTTTATTAA TTTTATTTT	3660
	ACATCCTAGC TACAATATTA TAGTTATCAT GTTGATACG CTGTTTTTTG TTTTATTTT	3720
	TAAGGTAGTT TTATCTCGCA TAGCTCCGCT AGAGTTGTGT TATGCGGATC CTAAGAAAA	3780
	TACAACTGAA CCTACACAAC TTCCTACAGG GGAACAATCT AAGACTCTTA TTCCCGTGGT	3840
	AACAAACGGA TATGTTGAAT ACTCTAAAGG ATGTGAACTA CGATTACTAG ATACATATGT	3900
15	AAATGTATCT TCACGACCAG AAAAAAGGT TAATGCTACA ATTGGATGGT CATTTGATCT	3960
	TGGTGTCAA ATTCCTTTAA TTTATAGAGA ATATTATAAT TGTACTGGTA ATATAATACC	4020
	ATCACCAGAA ACTTGTGATG GTTATTCTTT AACTTTGGTA AAATCTGAAA GTATATCATC	4080
	TTATGCACTT GTTAATGTTA GTTTGCTTAT TCAACCAGGA ATTTTGTATT CTGGTAGATA	4140
	TTTATACTCA CTTGTTTTTG GAAACGATAG TTATAACGGA AGAATTGAAG TTCGAGTGG	4200
20	TAATGAGACA GACTATCCAT GTTTTATGAT GCATGGATTG ACTGTAAAAA AGGGTGATAA	4260
	ACTTCATATT CCTTATAAAC CATCCACAAA TCCTAATCAT AAACGATATA GAGGTGTTT	4320
	TCCAATATCA AATACTGAGC TATGGAATAA TATTAGTGAT GAAAGTGTG GTAGATATT	4380
	ATATGATGAA GAATATGAAG AATATGAAGA AGAAAACGAA GATTTTGAAG ATCTACAATC	4440
	AAAAGATTGC CGCAAATCCA ATCTTTTGA TATGAAGAAG ACTTTTAATT TGGCTGCAGG	4500
25	TTCTCAAAGT TTATTGATTG CTAGTTTGGG TAAATCAATT TCAGAACAAAC CGTGGTCATT	4560
	TAAAATTAAT GAAAGTTATG AACTTTTAA TAATTGTCT ATCACCCTTC AATCGGAAGA	4620
	AGATTCTAAT ATACTGAATC CTGAAATTGT AACGTTTACC ACACCACCAC CTACTGAAAA	4680
	TACACATATG TTTATGTCAA ATAATGAAAC TATGTATGAA GAAGAAAGTG TTTTAAGCAT	4740
	TATTCAATTG TTTAACAATG GTTATAATAA TTGTAATACC CATATAAAGG TAATTGGATT	4800
30	TGGAACAATT ATCTTTATTA TTTTATTTT TGTGCTGTG TTTTGTGTG GATATACTTG	4860
	TGTATTAAAC TCTCGTATTA AATGATTAA CCATGCTTAT ATACAACCCC AGAAATTAA	4920

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	TTTTTATGAT	ATTTAATAAA	ACTATTATGA	AACCTTCTTAT	AACCTTATTTG	TTTTTATTAA	4980
	ATGGGTTGGG	TTGGTTTTAA	AATTACATAC	GTGTATTAAG	AATTAACATC	ATAAAGGACA	5040
	CACCCATGAA	AAACATTTAA	ATTCTATTAA	TTTGAACGGA	TTAAACATTT	TCTCATTTTA	5100
	AGAGTTGCTA	CGACTTTTGA	TAGTAAAATG	ATTAACTTC	TATTTATCTT	ATTTTATTTT	5160
5	AACCCAAATA	CTGGATATAA	ATGGGTAGAC	CCTCCTCGTA	GGTATAATTA	CACCGTTTTA	5220
	AGAATGATTC	CAGATATTCC	AAATCCAATG	GATCCTTCTA	AAAACGCTGA	AGTTCGGTAT	5280
	GTAACCTCTA	CTGACCCATG	TGATATGGTT	GCTTTGATTT	CTAATCCAAA	TATAGAATCT	5340
	ACAATTAAAA	CGATTCAATT	TGTGCAAAAG	AAAAAATTTT	ACAATGCATC	TCTTAGTTGG	5400
	TTTAAAGTTG	GAGATGATTG	TACATATCCA	ATATATTTAA	TTCAATATTT	TGATTGTGAT	5460
10	CCTCAAAGAG	AATTTGGCAT	ATGTTTAAAA	AGATCTCCAG	ATTTTGGAA	ACCATCGTTA	5520
	GTTGGTTACA	CATTTTAAAC	TGATGATGAA	TTGGGATTAG	TTTTAGCTGC	CCCCGCTCCA	5580
	TTTAATCAAG	GTCAATATAG	ACGGGTTATT	CAAATTGAAA	ATGAAGTTTT	TTATACTGAT	5640
	TTTATGGTTC	AATTACCACG	AGAACTTGT	TATTTTCTA	AAGAAGATAA	ATTGAACCA	5700
	ACTTTTATGG	AATGGTGTA	GGAATCTAGA	TCTGTAGGAG	CATCAAAAGT	TGACGATGAA	5760
15	CTTTTTTATC	TAAATAGAGC	TGGTCCCCAA	ACCCTGCTTA	AATATTATGT	TATTAAGAT	5820
	TTTTATAGAC	TTAACGGTAG	AGAACCTCCA	ATAAAATTTA	AAGAAGCTCT	TAGATACGAT	5880
	ATACCATATA	AAGTGAATGA	TAAATTTGAT	GATGAATTAC	CATCGAGGCC	ACATATTAGT	5940
	AATACTATTA	ATAAACTAT	TAAAGAAATT	GTAAATCTTG	AAGATTATTT	TAAAAATACA	6000
	AATGTTATAG	ATACTACTAC	CCCAACACCA	ATAAATAATA	CCCCAAAAA	TATAACCGTG	6060
20	GGAATTGTTA	TAATTATATT	AATAATACTA	TTTATAATTG	GATTTTTTGT	TTATAAAGA	6120
	CAAAAAATAT	ATAATAATTA	TAAAAAATTA	ACAACAAATG	TTAGCCTTT	ATAAATTAAT	6180
	TTACAGAATA	AACAACTGGG	CGGTCTTTTG	TTAATAAAAA	ATTCATGTAC	CTACAACTTT	6240
	TATTCACITG	CAAGAGGGTT	GAGACCAGAT	TACTTATAAC	TATGTTTCTA	CCTATTTTAT	6300
	TTCTTTTTTT	ATATGGTGTA	AATGGATTG	TTTACAAAGG	TACGTATATA	AGTATGTTTT	6360
25	TAAATACTAG	TTCTGGCTTT	TCTATTTTTC	CCGATGATAA	ATTTATTGTC	AGTGGACGTT	6420
	TATTATTTCT	CGATGACCAA	CATCTGTCAG	TAAATAATTA	TAGCGGAAC	ATTGAGTTTA	6480
	TTCATTTTAA	TAACTCTTGT	TATACCGTTT	ATCAAACTAT	TGAATATTTT	TCTTGTCTC	6540
	GCATTTTAA	TAATGCTTTT	AGATCTTGTT	TAAAAAAGGT	ATCAAAACAT	CATGAAAGTC	6600
	AAC TTCGAT	AAATTCATCT	ATAGAAAACG	GTGTTTGT	GGAAATTACA	AATCCTAAAC	6660
30	CAAATGATTC	AGGTGTTTAT	TTTATACGAG	TTCAATTGGA	AAATAATAAA	ACAGATGTGT	6720
	TTGGAATACC	TGCATTTTAT	TATTCCTTTA	ATATGTCAAA	CGAAGTAAAT	AAATCAAAC	6780

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	TCGATGATGT TACTACATCT TTATATACCT CATCACACCC TTCTTCCCAA ACTATTACAC	6840
	CTATCTATTT AAATGAAAAA CACGAACCGA TATGTCATAC TGTAAGAAAG GATGAAAATG	6900
	TGTATGAACT TTTACTAGGT TTGCATGGAA ATATAACTGA TGATATTTTT CTCGATGAGG	6960
	ATTCTGAATT GCTTAAAAGA GTAAATATAC CTACAACGAC AAATAATTAT ATATTTAAGC	7020
5	CTTACCTAGA CCAACGTAAT AGAAAATTTT TAATTATTGT AATTTGATT TCGATAATTT	7080
	TACTTATTCT TTTGGTATTA ATTGGATCAA TTATTAACAA TATTATTCTG AGACACTTTT	7140
	CTTCTCTAG GCGTATTAT CGTCCTAAG GTAACCTCGA ATCTGAAAAT ATAGAAGTGA	7200
	CATGTGGGA AACTCAGTA AACAAAAATA ATCCATTACC AAAAAACCT AACCGCCAAA	7260
	AAAGATCTTC AACTATTCAA AGGGAGACAT CTCTGAAAC TATTAAGGAA GAAGTATAAT	7320
10	TTTAAAAATA TTTACCTACG TAGGTTGATG ACGACTTGTA TGACTAAAAA TTAGAATTTA	7380
	AATGATGAAA ATTTTAA AATAATATAG TATCCAAAG AGCCTTTTAG GAAATCATC	7440
	AAGTCTCCAT TTCTCCAATC TTTACGATGT TCGTTTATT TTTTAAATC GCGTCTACAT	7500
	TATGTTCCGT AAGATTTGGT TTTCAACAA TCGTAATGT TATTGTTCT GAAAAATCTG	7560
	GATTTGTAAT TGATGTTAT AGTACTAACC CACCATTAA TGAGACTAAA AAATTTACTA	7620
15	GAGGATGGGT ATTTTACAA ACCCCCCCTT CTTATTGTAA AGATGGGATA TCAATATCTA	7680
	ATATATGCAT TGAACGTAAT ATTGTGAAG AAGATATTTT TTTGAATAAA CGATGTACAA	7740
	TTAAACTAT TAATTATCCC TTAGCTGTAG CAGATTTTGA GATTAGTAAT AATACTATTA	7800
	AAAAAATAAA TGATGTTAT TTTGTTAATG ATAGTGTTTT TCCAATAATA ACTACAAATA	7860
	AAAGTGGTAT CCATATCACA AATGTGACTA TAAATAATC TGGAAATTTT ACATTGTATG	7920
20	AAAATAATGA TAAGTGGAGT CATCAATCAA AAATCTTGGT AACTATAAAG AAAAAAGAAA	7980
	CAGTAATTAC TAAACCTAAA GTATATATAA AAAACATGG TGGATTTTTT CATGTAAAAA	8040
	ATTATCACTC TCATGTATTT GTACCAAATG ATTCATTAA AATTGAACCT AATCTTGAAT	8100
	CGGAAATTTA TGATTCTGAA TTTTCAGCAA GTATTGATTG GTATTATATG AAAACTAGCT	8160
	CGGAATGTTT AGTGTTTCAT ATATATGAAA CTGTATATT TCACCCCTCAT GCAAACTCTT	8220
25	GTTTGAATCC AATAAACCCA TTGTGTAGTT TTACTCCCC TTTGAGGGCA ACATCACTAA	8280
	TTAATAGATT TTATTTTAGA TGTAACCTG AAGGTAAAAA CTGGACAACT GATTGTATAA	8340
	ACACCTTTTC TATTAATGCA GATAACATA TTAAACAGCA TTCAAATAAT GTAGATTGTA	8400
	TTTTTTTAAA TACTCCAACT AATGCATCTG GTTGTATGT TTTTATCTT AAGTATAATG	8460
	GTATCCAGA GGCTTGGACA TATACTTTGG TTTCAACGGT TAAAAATTT ATGAATGTAA	8520
30	TTAAGGATAT GACACGCCCC CTTTGTCAA ATAATAAAT GAAAAACCT GAGCATTCTA	8580
	CTCAACCACC AACCATAACC AACATAACAC CTGGCTTTAA ATCTAAAAAT TGGGTAGATA	8640

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	AATATATAAT TTCAGTAGCG GTGGTTTCTT GTATTACTAT TGTATATTG ATTGTGGTAA	8700
	TAACCTTTTG TGTTCATCAA TGTATCGGTT TAAATCGTAA ACCATATGAA ATTATAAACC	8760
	CATTTAATAC AGCTTATAAA AGTATACCTA CAAATGAAAA AAATATTCTT CATTTTGCTG	8820
	AAGTAACAGA ATCTGATTAT TCCTCCGACG AATCCTTCGA CAGTGACTCA GAAGAGCTAA	8880
5	ATCAACGAGG TGAACAATA CAACAAGGGA AAAAGGAACA ATCTGGATAT ACTATTGGT	8940
	TTAATGAAGA TTTAGAAGAA TCCGTCTCCA AAAAAGTTAA CCAACCAAC TATTCAAAAA	9000
	TAATTAATAG CTTAAATCA ATCCAGAATG AATAAATCTA AACTCTCATT TAAAGAAAAA	9060
	AACGCTATAT ATGAATTAA AAATATTTTA TCAACACTT CATGTCAAC TTTTCTGTA	9120
	TTATCGTTTA ATGAGGAGCC AAAATCCAGA TTTTTTAAAA TGTTTAAAAA TATTTTACTG	9180
10	GAAAAAATAA AAAAACTTC AATGGATTAT TTAATTTATT GTACTCTAAA AATCTCACTT	9240
	TCATTTATAC TTTATAATAA ATAAAATTAT TAAAAAACT TTATTGTTT GTCATTATTA	9300
	ACTTTAACAC TAGATGGTAC TATAAGCTA ACTTACAATA TAAATAGTAA GATTAGTTTA	9360
	TATAAATTAC ATTTAATGGC TTTACCAGAT AACGTTTTTA GTATTATTAA TGAAAATTAT	9420
	ATCGATGGAA TTTTAACTAT GAAAATGGGT GAAGAAATAG AAAGCTCATC ACCATTAAAT	9480
15	GAAACAAATG TTAATATAGA TCAACATACA ATAGATATTT TTGATTACGA TTCAGATAAT	9540
	GGATGTTATT ATAGTAAAG AGATAATGAA ACCGCAACTC TTTTTTTAAA ACGTGTGGT	9600
	TATAGAGAAA CCTCAAAAAA GCGTAAACGG ATTGTGGAT TTATTGTTT AGCAATTTTT	9660
	ATGGTTATTA TATTATGTTT TTTATCAATA ATTTTGGAG TTTTATAGC GCCTCATATT	9720
	TATAAAGGCC TATAGTAAGA ACATCAACCT CTAATAGTAA ATTTTAAAA CCAACGGAGG	9780
20	GGGAGGAGGA GGACTTTTTA TTTTATGAGG ATAAACCTGG GGCTAGCATC GAATGGAAAT	9840
	CGGCTGTTTC GGGGTATAAC TATCTAACT CTGGTATATT TGGAAGCTAT CCTCTTAATC	9900
	TATGGGTTTT CGGTGCAGCG GATTTATGTG AGCCAGTCAT TTCTAATATC CCAGGACCAA	9960
	AGCGACTAAT TTATGCATAT GTATCATGTG AATGGCCGGA ACCATCCTGG AAACCTGAGT	10020
	GTCTTGAGAT TTCCAAAAAT AATGTAAAAC ATATCGATGA TTCTGGGAGT GTTTATTGCC	10080
25	CCTCGTTTAT ATGGGTACCT GTATTAGACA CCTTCTGTG CTCCTTTAAA GTACCCCTTA	10140
	TGTTAAGTGA CATTTTTTAT GGTACAACAT TTAATACTCC ATTCACTTT GAAAGCTCTC	10200
	CAAGATGTCC CTCTATATCC TCATCTTCAT CCTCCTCCTC CTCATCCTCT TCTTCATGCT	10260
	CTGCATCTCA TTATTCCTCA GAGAATGATA TTTGGAAATA CGCTAATGCG ATGGTGGATA	10320
	ATGAAGTAGA AGAACTAAT TGTGAATTA AAAATAGTTT TAAAGAGGAT TCTGACAGTT	10380
30	CTACATGTTC TATAAGCGAT GTATGTGATT CTCTTTATAT AAATGAGACA CGTTCTGCCC	10440
	CCCCGGTAAT CGAATCATTT ATGTGTGCAA TAATATCCCA TAATGGTTAT GAAGAAATTC	10500

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CTGAACCAGA AGAGGATGAC TTGCATGGGG TGAAACCTAT GAAAAGGCTA TCCAAACCAA 10560
ATATTTTAA ACGATTATTT TCAAGGCGCG CC 10592

(2) INFORMATION FOR SEQ ID NO:52:

5 (i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 10592 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

10 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:52:

GGCGCGCCTT GAAATAATC GTTTAAAAAT ATTTGGTTTG GATAGCCTTT TCATAGGTTT 60
CACCCCATGC AAGTCATCCT CTTCTGGTTC AGGAATTTCT TCATAACCAT TATGGGATAT 120
TATTGCACAC ATAAATGATT CGATTACCGG GGGGGCAGAA CGTGTCTCAT TTATATAAAG 180
AGAATCACAT ACATCGCTTA TAGAACATGT AGAACTGTCA GAATCCTCTT TAAACTATT 240
15 TTTAATTCA CAATTAGTTT CTTCTAGTTC ATTATCCACC ATCGCATTAG CGTATTTCCA 300
AATATCATTG TCTGAGGAAT AATGAGATGC AGAGCATGAA GAAGAGGATG AGGAGGAGGA 360
GGATGAAGAT GAGGATATAG AGGGACATCT TGGAGAGCTT TCAAAGTTGA ATGGAGTATT 420
AAATGTTGTA CCATAAAAAA TGTCACCTTA CATAGGGGGT ACTTTAAAGG AGGACAGAAA 480
GGTGTCTAAT ACAGGTACCC ATATAACGA GGGGCAATAA ACACTCCCAG AATCATCGAT 540
20 ATGTTTTTACA TTATTTTGG AAATCTCAAG AACTCAGGT TTCCAGGATG GTTCCGGCCA 600
TTCACATGAT ACATATGCAT AAATTAGTCG CTTTGGTCCT GGGATATTAG AAATGACTGG 660
CTCACATAAA TCCGCTGCAC CGAAAACCCA TAGATTAAGA GGATAGTTTC EAAATATACC 720
AGAGTTTGA TAGTTATACC CCGAAACAGC CGATTTCAT TCGATGCTAG CCCCAGGTTT 780
ATCCTCATAA AATAAAAAGT CCTCCTCCTC CCCCTCCGTT GGTTTTAAAA ATTTACTATT 840
25 AGAGGTTGAT GTTCTTACTA TAGGCCTTTA TAAATATGAG GCGCTATAAA AACTCCCAAA 900
ATTATGATA AAAACATAA TATAATAACC ATAAAAATTG CTAACAACAT AAATCCACAA 960
ATCCGTTTAC GCTTTTTTGA GGTTCCTCTA TAACCAACAC GTTTTAAAAA AAGAGTTGCG 1020
GTTTCATTAT CTCTTCACT ATAATAACAT CCATTATCTG AATCGTAATC AAAAATATCT 1080
ATTGTATGTT GATCTATATT AACATTTGTT TCATTTAATG GTGATGAGCT TTCTATTCTT 1140
30 TCACCCATTT TCATAGTTAA AATTCATCG ATATAATTTT CATTATAAT ACTAAAAACG 1200
TTATCTGGTA AAGCCATTAA ATGTAATTA TATAAACTAA TCTTACTATT TATATTGTAA 1260
GTTAGCTTTA TAGTACCATC TAGTGTTAAA GTTAATAATG ACAAACAAT AAAGTTTTTT 1320

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	TAATAATTTT ATTTATTATA AAGTATAAAT GAAAGTGAGA TTTTGTAGAGT ACAATAAATT	1380
	AAATAATCCA TTGAAGTTTT TTTTATTTTT TCCAGTAAAA TATTTTAAAA CATTTTAAAA	1440
	AATCTGGATT TTGGCTCCTC ATTAACGAT AATACAGGAA AAGTTGACAA TGAAGTGTTT	1500
	GATAAATAT TTTTAAATTC ATATATAGCG TTTTTTCTT TAAATGAGAG TTTAGATTTA	1560
5	TTCAATCTGG ATTGATTTTA AGCTATTAAT TATTTTGTAA TAGTTTGGTT GGTAAAGTTT	1620
	TTTGAGAGCG GATTCTTCTA AATCTTCATT AAACCAAATA GTATATCCAG ATTGTTCTCT	1680
	TTTCCCTTGT TGTATTGTTT CACCTCGTTG ATTTAGCTCT TCTGAGTCAC TGTCGAAGGA	1740
	TTCGTCGGAG GAATAATCAG ATTCTGTAC TTCAGCAAAA TGAAGAATAT TTTTTCATT	1800
	TGTAGGTATA CTTTATAAG CTGTATTAAA TGGGTTTATA ATTTTCATATG GTTTACGATT	1860
10	TAAACCGATA CATTGATGAA CACAAAAGGT TATTACCACA ATCAATATAA CAATAGTAAT	1920
	ACAAGAAACC ACCGCTACTG AAATTATATA TTTATCTACC CAATTTTTAG ATTTAAAGCC	1980
	AGGTGTTATG TTGGTTATGG TTGGTGGTTG AGTAGAATGC TCAGGTTTTT TCATTTTATT	2040
	ATTTGACAAA AGGGGGCGTG TCATATCCTT AATTACATTC ATAAAATTTT TAACCGTTGA	2100
	AAACCAAGTA TATGTCCAAG CCTCTGGATG ACCATTATAC TTAAGAATAA AAACATACAA	2160
15	ACCAGATGCA TTAGTTGGAG TATTTAAAAA AATCAAATCT ACATTATTTG AATGCTGTTT	2220
	AATATGTTTA TCTGCATTAA TAGAAAAGGT GTTTATACAA TCAGTTGTCC AGTTTTTACC	2280
	TTCAGGTTTA CATCTAAAAA AAAATCTATT AATTAGTGAT GTTGCCCTCA AAGGGGAAGT	2340
	AAACTACAC AATGGGTTTA TTGGATTCAA ACAAGAGTTT GCATGAGGGT GAAATATACA	2400
	AGTTTCATAT ATATGAAACA CTGAACATTC CGAGCTAGTT TTCATATAAT ACCAATCAAT	2460
20	ACTTGCTGAA AATTCAGAAT CATAAATTC CGATTCAAGA TTAAGTTCAA TTTTAAATGA	2520
	ATCATTGGT ACAAAATACAT GAGAGTGATA ATTTTATACA TGAAAAATC CACCATGTTT	2580
	TTTTATATAT ACTTTAGGTT TAGTAATTAC TGTTTCTTTT TTCTTTATAG TTACCAAGAT	2640
	TTTGATTGA TGAATCCACT TATCATTATT TTCATACAA GTATAAATTC CAGAATTATT	2700
	TATAGTCACA TTTGTGATAT GGATACCACT TTTATTTGTA GTTATTATTG GAAAAACACT	2760
25	ATCATTAACA AAATAACAT CATTTATTTT TTTAATAGTA TTATTACTAA TCTCAAAATC	2820
	TGCTACAGCT AAGGGATAAT TAATAGTTTT AATTGTACAT CGTTTATTCA AAAAAATATC	2880
	TTCTTCACAA ATATTACGTT CAATGCATAT ATTAGATATT GATATCCCAT CTTTACAATA	2940
	AGAAGGGGGG GTTTGTAAAA ATACCCATCC TCTAGTAAAT TTTTGTAGCT CATTAAATGG	3000
	TGGGTTAGTA CTATAACCAT CAATTACAAA TCCAGATTTT TCAGAAACAA TAACATTACG	3060
30	AATTGTTGAA AAACCAAATC TTACCGAACA TAATGTAGAC GCGATTAAAA AAAATAAACG	3120
	AAACATCGTA AAGATTGGAG AAATGGAGAC TTGATGATTT TCCTAAAAGG CTCTTTGGAA	3180

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TACTATATTA TTTTAAAAA ATTTTCATCA TTAAATTCT AATTTTAGT CATACAAGTC 3240
GTCATCAACC TACGTAGGTA AATATTTTAA AAATTATACT TCTTCCTTAA TAGTTTCAAG 3300
AGATGTCTCC CTTGAATAG TTGAAGATCT TTTTGGCGG TTAGGTTTTT TTGGTAATGG 3360
ATTATTTTGG TTTACTGAGT TTTCCCCACA TGTCAGTTCT ATATTTTCAG ATTCCGAGTT 3420
5 ACCTTTAGGA CGATAAATAC GCCTAGAAGA AGAAAAGTGT CTACGAATAA TATTGTTAAT 3480
AATTGATCCA ATTAATACCA AAAGAATAAG TAAAATTATC GAAATCGAAA TTACAATAAT 3540
TAAAAATTTT CTATTACGTT GGTCTAGGTA AGGCTTAAAT ATATAATTAT TTGTCGTTGT 3600
AGGTATATTT ACTCTTTTAA GCAATTCAGA ATCCTCATCG AGAAAAATAT CATCAGTTAT 3660
ATTTCCATGC AAACCTAGTA AAAGTTCATA CACATTTTCA TCCTTTTTTA CAGTATGACA 3720
10 TATCGGTTCTG TGTTTTTTCT TTAATAGAT AGGTGTAATA GTTGGGAAG AAGGGTGTGA 3780
TGAGGTATAT AAAGATGTAG TAACATCATC GAAGTTTGAT TTATTTACTT CGTTTGACAT 3840
ATTAAAGGAA TAAATAAATG CAGGTATTCC AAACACATCT GTTTTATTAT TTTCCAATTG 3900
AACTCGTATA AAATAACAC CTGAATCATT TGTTTTAGGA TTTGTAATTT CCAACAAAAC 3960
ACCGTTTTCT ATAGATGAAT TTATCCGAAG TTGACTTTCA TGATGTTTTG ATACCTTTTT 4020
15 TAAACAAGAT CTAAAAGCAT TATTAATAAT GCGAGGACAA GAAAAATATT CAATAGTTTG 4080
ATAAACGGTA TAACAAGAGT TATTAATAATG AATAAATCTA ATAGTTCCGC TATAATTATT 4140
TACTGACAGA TGTGTCATC CGAGAAATAA TAAACGTCCA CTGACAATAA ATTTATCATC 4200
GGGAAAAATA GAAAGCCAG AACTAGTATT TAAAAACATA CTTATATACG TACCTTTGTA 4260
AACAAATCCA TTTACACCAT ATAAAAAAG AAATAAATA GGTAGAAACA TAGTTATAAG 4320
20 TAATCTGGTC TCAACCTCTT TGCAAGTGAA TAAAAGTTGT AGGTACATGA ATTTTATTA 4380
AACAAAAGAC CGCCAGTTG TTTATCTGT AAATTAATTT ATAAAGGCTA AACATTTGTT 4440
GTTAATTTT TATAATTATT ATATATTTT TGTCTTTTAT AAACAAAAA TCCAATTATA 4500
AATAGTATTA TTAATATAAT TATAACAATT CCCACGGTTA TATTTTTTGG GGTATTATT 4560
ATTGGTGTG GGGTAGTAGT ATCTATAACA TTTGTATTTT TAAATAATC TTCAAGATT 4620
25 ACAATTTCTT TAATAGTTT ATTAATAGTA TTAATAATAT GTGGCTCGA TGGTAATTCA 4680
TCATCAAATT TATCATTAC TTTATATGGT ATATCGTATC TAAGAGCTTC TTTAAATTT 4740
ATTGGAGGTT CTCTACCGT AAGTCTATAA AAATCTTTAA TAACATAATA TTTAAGCAGG 4800
GTTGGGGAC CAGCTCTATT TAGATAAAAA AGTTCATCGT CAACTTTGA TGCTCCTACA 4860
GATCTAGATT CCTTACACCA TTCCATAAAA GTTGGTTCAA ATTTATCTTC TTTAGAAAA 4920
30 TAACAAGTTT CTCGTGGTAA TTGAACCATA AAATCAGTAT AAAAACTTC ATTTCAATT 4980
TGAATAACCC GTCTATATTG ACCTTGATTA AATGGAGCGG GGGCAGCTAA AACTAATCCC 5040

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	AATTCATCAT	CAGTTAAAA	TGTGTAACCA	ACTAACGATG	GTTTCCAAAA	ATCTGGAGAT	5100
	CTTTTAAAC	ATATGCCAAA	TTCTCTTTGA	GGATCACAAT	CAAAATATTG	AATTAAATAT	5160
	ATTGGATATG	TACRATCATC	TCCAACTTTA	AACCAACTAA	GAGATGCATT	GTAAAAATTT	5220
	TTCTTTTGCA	CAAATTGAAT	CGTTTAAAT	GTAGATTCTA	TATTTGGATT	AGAAATCAAA	5280
5	GCAACCATAT	CACATGGGTC	AGTAGAAGTT	ACATACCGAA	CTTCAGCGTT	TTTAGAAGGA	5340
	TCCATTGGAT	TTGGAATATC	TGGAATCATT	CTTAAACGG	TGTAATTATA	CCTACGAGGA	5400
	GGGTCTACCC	ATTTATATCC	AGTTATTGGG	TTAAAAATAA	ATAAGATAAA	TAGAAGTTTA	5460
	ATCATTTTAC	TATCAAAAGT	CGTAGCAACT	CTTAAATGA	GAAATGTTT	AATCCGTTCA	5520
	AATTAATAGA	ATTTAAATGT	TTTTCATGGG	TGTGTCCTTT	ATGATGTTAA	TTCTTAATAC	5580
10	ACGTATGTAA	TTTTAAACC	AACCCAACCC	ATTTAATAAA	AACAAATAAG	TTATAAGAAG	5640
	TTTCATAATA	GTTTTATTAA	ATATCATAAA	AATTTAATTT	CTGGGGTTGT	ATATAAGCAT	5700
	GGTTAATCAT	TTTAATACGA	GAGTTTAATA	CACAAGTATA	TCCACAAAAA	AACACAGCAA	5760
	CAAAAAATAA	AATAATAAAG	ATAATTGTTC	CAATCCAAT	TACCTTTATA	TGGGTATTAC	5820
	AATTATTATA	ACCATTGTTA	AACAATTGAA	TAATGCTTAA	AACACTTTCT	TCTTCATACA	5880
15	TAGTTTCATT	ATTGACATA	AACATATGTG	TATTTTCAGT	AGGTGGTGGT	GTGGTAAACG	5940
	TTACAATTC	AGGATTCAGT	ATATTAGAAT	CTTCTCCGA	TTGAAGGGTG	ATAGACAAAT	6000
	TATTAATAAG	TTCAATACTT	TCATTAATTT	TAAATGACCA	CGGTGTTCT	GAAATTGATT	6060
	TACCCAACT	AGCAATCAAT	AACTTTGAG	AACCTGCAGC	CAATTAATAA	GTCTTCTTCA	6120
	TATCAATAAG	ATTGGATTG	CGGCAATCTT	TTGATTGTAG	ATCTTCAAAA	TCTTCGTTTT	6180
20	CTTCTTCATA	TTCTTCATAT	TCTTCATCAT	ATGAATATCT	ACCAACACTT	TCATCACTAA	6240
	TATTATTCCA	TAGCTCAGTA	TTGATATTG	GAAAACAACC	TCTATATCGT	TTATGATTAG	6300
	GATTTGTGGA	TGGTTTATAA	GGAATATGAA	GTTTATCACC	CTTTTTTACA	GTCAATCCAT	6360
	GCATCATAAA	ACATGGATAG	TCTGTCTCAT	TATCCACTCG	AACTTCAATT	CTTCGGTTAT	6420
	AACTATCGTT	TCCAAAAACA	AGTGAGTATA	AATATCTACC	AGAATCAAAA	ATTCCTGGTT	6480
25	GAATAAGCAA	ACTAACATTA	ACAAGTGCAT	AAGATGATAT	ACTTTCAGAT	TTTACCAAG	6540
	TTAAAGAATA	ACCATCACAA	GTTTCTGGTG	ATGGTATTAT	ATTACCAGTA	CAATTATAAT	6600
	ATTCTCTATA	AATTAAAGGA	ATTGACAAC	CAAGATCAAA	TGACCATCCA	ATTGTAGCAT	6660
	TAACCTTTTT	TTCTGGTCGT	GAAGATACAT	TTACATATGT	ATCTAGTAAT	CGTAGTTTAC	6720
	ATCCTTTAGA	GTATTCAACA	TATCCGTTTG	TTACCACGGG	AATAAGAGTC	TTAGATTGTT	6780
30	CCCCTGTAGG	AAGTTGTGTA	GGTTCAGTTG	TATTTTCTTT	AGGATCCGCA	TAACACAAC	6840
	CTAGCGGAGC	TATGCGAGAT	AAAACCTACCT	TAAAATAAAA	AACAAAAAAC	AGCGTATACA	6900

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	ACATGATAAC TATAATATTG TAGCTAGGAT GTAAAAATAA AATTAATAAA AAAGAGCTTT	6960
	CAAACACCCG TTTTATATAA AACAAATAAA AATTCACGCG CCATTTTAT GAAATTTATT	7020
	GTTTACTAAA AATCTGATAG GATAATAGTT CTTCCGCACT TGGTCGTAGA GATGCATCAA	7080
	ATGTTAGCAT TTTATGAATT AAAAATTCAC CATCGAGATG TAATTTAAGG TTATTTAGAC	7140
5	GATTATATCG TGTAAATGGA GGTCTATCAT TATTAGCATA TTTTATAAAA TGTTTACTA	7200
	GATTAGATTC CAAATCAGAT GGAAATTCAT TTGGGTTAAT CTTCAGAGTT GATATAATTT	7260
	TTATAAGATG AAGATTACAA TTGTTTATTA AATCGCTACT ATCTCTTTCT TCCTCCTCAA	7320
	ACAAAACATT AGGATATGCA AGCATTTCBA ATAAAATTAT ACCAGCACTC CAAATATCAG	7380
	CTTTACAGTT GTACGCATCC TTTGATAGAA CTTCAGGAGC ATTAGTTTCA ATAGTCCCGG	7440
10	CAATTCCCAA ATAATCTGGT GAGGAAACAG GAAATTGAGA AGCCCCAAAA TCACCTATAC	7500
	AAACATTAGA GTCATTATCC AAGAAAATAT TTTCAGTTTT TATATCTCGA TGAATAATTT	7560
	TTTTTCCATG AATATATTGA AGTCCAGTTA ATATTTGTTT TTCAATTTTA ATTACAGATT	7620
	CAAAAGACAG AGATTTCCTA TGATCCATTA AAAAATTATA TAGATCATAT TTATAATACG	7680
	GTAACACCAA ACATGTTAAC TCTTTATAAA AAAGAGTGTC TTGAAGTTTA ATTATAGATT	7740
15	GGTGACTAAT ATTTCTCAA ATTAACGATT CCACAAGCGT GTTCCCTT TGTCCTAATT	7800
	TTAAAATTAC CTTATAGCTT GTATCTTTAT CTTTTTTAAG AGCAATAAAA ACTCTTCTT	7860
	CTGACCCAGG CGTTAACGAT TTAACAACAG AAAACTTTAG CGCTTCAGCC GCTTCAATTC	7920
	CTTCGCTTTT AGTAGGAGAT AAACTTTTT TATCTTCATC ACTTTCATAA CTTTCTCAA	7980
	CTTCTTCGTC ACTTTCTCTT TCATTTTCAC TTTCAGTTGG ATTTTTTGTA TAATCCATAA	8040
20	AGTCATCATC ACTAAAATCC GAGTATAAAT CCTCATCCAT TATTTTGTCT TGATGTAGGT	8100
	TATCCTCTTC AATCAAATCT GAAGTTAGAG GAACCGGTTT ATAGAAGTCT TCTGGATCGA	8160
	CAGAGATTTC TCTATTCACG CTGATACAA AAAACTTTTC GGTGGTACAC TTTGCCATAT	8220
	CAGGTAATTG TGAAATTGTT ATGTTAATAT CAACTCATCA ACTGCAGCTT CTTCTAAAAT	8280
	TATAACATAA ATTAGGTGTG TATTAACCTT TATTGGATTG ATACATAAAA TTTAATTATG	8340
25	GGTGTGGTTG AAGTTAATAT TGTTACGTTT ATTGACAAAA ATGGGGCGTT ACCAGGAAAC	8400
	TCCCAAGATG TTCATCCTGA TCTTTGGTGT TTTATGGCTA GACAATGCTA TATCCTTTCT	8460
	CTCACACGAT TGGCTATGCC TATAATATTA CGATCTGCAA ACTTATGTTA TTTTATGGAC	8520
	TCTATAAAAC ATCTACCTAG AGTTTCAAGG CCTATAGTAA GAACATCAAC CTCTAATAGT	8580
	AAATTTTAA AACCAACGGA GGGGAGGAG GAGGACTTTT TATTTTATGA GGATAAACCT	8640
30	GGGGCTAGCA TCGAATGGAA ATCGGCTGTT TCGGGGTATA ACTATCTAAA CTCTGGTATA	8700
	TTTGGAACCT ATCCTCTTAA TCTATGGGTT TTCGGTGCAG CGGATTTATG TGAGCCAGTC	8760

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	ATTCTAATA	TCCCAGGACC	AAAGCGACTA	ATTTATGCAT	ATGTATCATG	TGAATGGCCG	8820
	GAACCATCCT	GGAAACCTGA	GTGTCTTGAG	ATTTCCAAAA	ATAATGTAAA	ACATATCGAT	8880
	GATCTGGGA	GTGTTTATTG	CCCCTCGTTT	ATATGGGTAC	CTGTATTAGA	CACCTTTCTG	8940
	TCCTCCTTTA	AAGTACCCCC	TATGTTAAGT	GACATTTTTT	ATGGTACAAC	ATTTAATACT	9000
5	CCATTCAACT	TTGAAAGCTC	TCCAAGATGT	CCCTCTATAT	CCTCATCTTC	ATCCTCCTCC	9060
	TCCTCATCCT	CTTCTTCATG	CTCTGCATCT	CATTATTCCT	CAGAGAATGA	TATTTGGAAA	9120
	TACGCTAATG	CGATGGTGGA	TAATGAACCTA	GAAGAACTA	ATTGTGAAAT	TAAAAATAGT	9180
	TTTAAAGAGG	ATTCTGCAG	TTCTACATGT	TCTATAAGCG	ATGTATGTGA	TTCTCTTTAT	9240
	ATAAATGAGA	CACGTTCTGC	CCCCCGGTA	ATCGAATCAT	TTATGTGTGC	AATAATATCC	9300
10	CATAATGGTT	ATGAAGAAAT	TCCTGAACCA	GAAGAGGATG	ACTTGCATGG	GGTGAAACCT	9360
	ATGAAAAGGC	TATCCAAACC	AAATATTTTT	AAACGATTAT	TTTCAAGGCG	CGCCAAAACA	9420
	ATAACCAAAA	ATGAAAACGA	TGGTATGTCT	TCTACACAAC	CTACCAACGC	TCAACGTTCA	9480
	TCTCTATTTA	GTTTCATGTT	ATGTGGAAC	TAAGTTTGTT	TATATTTGTT	GTGAATAAAC	9540
	AGTAGATGTA	AACCTGAAAT	TCTGGTTTTT	TATGTGAACC	ACTCCCATAT	TCTTACTGTA	9600
15	TATAAATGCG	CATTTTATCC	TACATTTTAA	AATCTTCACT	TGTTTTTAAA	GCTTAACTAA	9660
	AAAGTTTTAA	AATGAGTGCT	TCATTTGCTC	TATTTGATAA	CAACTCCGAT	CAAGCTAATA	9720
	TGCCATCATA	CTTCAGACGC	TGTCGTGGAG	AACTTAATGA	AGGATTCTAC	GCACAAGTTC	9780
	CGCCTGGTTA	TTTTCCAGTT	CGCCCTAAAA	CCACACCAGC	GCTTGCACGT	GTGAAAAACC	9840
	AGGGTGAACC	GCACGCCTTC	ACTATTGTTC	CTACACCACC	TACGGATGTA	CGATTCTTCA	9900
20	AAAAGCTTCG	TGATGGAACC	TTTGTGAAAC	TTCCATTTTC	ATATCCTGAT	GAGAGGTATG	9960
	AAGATGATAT	TGAACCTATG	TATTGCAGAC	TATACGTTCT	AAAGGATTTT	GAAACGCCAA	10020
	GTTCTCCCTA	CAATCAAGTA	AACGCTTCTC	AGCTTATGGA	AGTACCTTCT	TCGCTTGTGG	10080
	AATCGAAGTG	TTATTGGGAT	GGTCCAAAAT	TTATAAATGT	ACCACCAATA	AGATATATTC	10140
	TAAAAAGTGA	TTACTCTCTA	AATAATGTAT	CCGAAGATGC	ATTTGTGTTG	GATAGATACCA	10200
25	GAAAACTAAA	ACTTGAAAAC	TAAAATGTTT	ACCCAACGCA	TTAAACCTTG	TAACTATATC	10260
	TCTTAATAAA	ATTTAAATA	TTTTTAAAAA	TTACTTTGTC	TCATAGATTT	CATTATAGTA	10320
	TTTCATTCAT	AGATTTTCAT	CATAGATTTC	ATTCATAGAT	TTCATTCATA	GATTTTCATC	10380
	ATAGATTTC	TTATAGATT	TCATTCATAG	ATTTTCATTCA	TAGATTTTCAT	TCATAGATTT	10440
	CATTCATAGA	TTTCATTCAT	AGATTTTCAT	CATAGATTTC	ATTCATAGAT	TTCATTCATA	10500
30	GATTTTCATC	ATAGATTTC	TTATAGATT	TCATTCATAG	ATTTTCATTCA	TAGATTTTCAT	10560
	TCATAGATTT	TTATTTTTTA	AATACACTGC	AG			10592

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(2) INFORMATION FOR SEQ ID NO:53:

(i) SEQUENCE CHARACTERISTICS:

- 5 (A) LENGTH: 1038 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: cDNA

(ix) FEATURE:

- 10 (A) NAME/KEY: CDS
(B) LOCATION: 1..1035

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:53:

	ATG ATT AAA CTT CTA TTT ATC TTA TTT TAT TTT AAC CCA ATA ACT GGA	48
	Met Ile Lys Leu Leu Phe Ile Leu Phe Tyr Phe Asn Pro Ile Thr Gly	
	1 5 10 15	
15	TAT AAA TGG GTA GAC CCT CCT CGT AGG TAT AAT TAC ACC GTT TTA AGA	96
	Tyr Lys Trp Val Asp Pro Pro Arg Arg Tyr Asn Tyr Thr Val Leu Arg	
	20 25 30	
20	ATG ATT CCA GAT ATT CCA AAT CCA ATG GAT CCT TCT AAA AAC GCT GAA	144
	Met Ile Pro Asp Ile Pro Asn Pro Met Asp Pro Ser Lys Asn Ala Glu	
	35 40 45	
	GTT CGG TAT GTA ACT TCT ACT GAC CCA TGT GAT ATG GTT GCT TTG ATT	192
	Val Arg Tyr Val Thr Ser Thr Asp Pro Cys Asp Met Val Ala Leu Ile	
	50 55 60	
25	TCT AAT CCA AAT ATA GAA TCT ACA ATT AAA ACG ATT CAA TTT GTG CAA	240
	Ser Asn Pro Asn Ile Glu Ser Thr Ile Lys Thr Ile Gln Phe Val Gln	
	65 70 75 80	
	AAG AAA AAA TTT TAC AAT GCA TCT CTT AGT TGG TTT AAA GTT GGA GAT	288
	Lys Lys Lys Phe Tyr Asn Ala Ser Leu Ser Trp Phe Lys Val Gly Asp	
	85 90 95	
30	GAT TGT ACA TAT CCA ATA TAT TTA ATT CAA TAT TTT GAT TGT GAT CCT	336
	Asp Cys Thr Tyr Pro Ile Tyr Leu Ile Gln Tyr Phe Asp Cys Asp Pro	
	100 105 110	
35	CAA AGA GAA TTT GGC ATA TGT TTA AAA AGA TCT CCA GAT TTT TGG AAA	384
	Gln Arg Glu Phe Gly Ile Cys Leu Lys Arg Ser Pro Asp Phe Trp Lys	
	115 120 125	
	CCA TCG TTA GTT GGT TAC ACA TTT TTA ACT GAT GAT GAA TTG GGA TTA	432
	Pro Ser Leu Val Gly Tyr Thr Phe Leu Thr Asp Asp Glu Leu Gly Leu	
	130 135 140	
40	GTT TTA GCT GCC CCC GCT CCA TTT AAT CAA GGT CAA TAT AGA CGG GTT	480
	Val Leu Ala Ala Pro Ala Pro Phe Asn Gln Gly Gln Tyr Arg Arg Val	
	145 150 155 160	
	ATT CAA ATT GAA AAT GAA GTT TTT TAT ACT GAT TTT ATG GTT CAA TTA	528
	Ile Gln Ile Glu Asn Glu Val Phe Tyr Thr Asp Phe Met Val Gln Leu	
	165 170 175	

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	CCA CGA GAA ACT TGT TAT TTT TCT AAA GAA GAT AAA TTT GAA CCA ACT	576
	Pro Arg Glu Thr Cys Tyr Phe Ser Lys Glu Asp Lys Phe Glu Pro Thr	
	180 185 190	
5	TTT ATG GAA TGG TGT AAG GAA TCT AGA TCT GTA GGA GCA TCA AAA GTT	624
	Phe Met Glu Trp Cys Lys Glu Ser Arg Ser Val Gly Ala Ser Lys Val	
	195 200 205	
	GAC GAT GAA CTT TTT TAT CTA AAT AGA GCT GGT CCC CAA ACC CTG CTT	672
	Asp Asp Glu Leu Phe Tyr Leu Asn Arg Ala Gly Pro Gln Thr Leu Leu	
	210 215 220	
10	AAA TAT TAT GTT ATT AAA GAT TTT TAT AGA CTT AAC GGT AGA GAA CCT	720
	Lys Tyr Tyr Val Ile Lys Asp Phe Tyr Arg Leu Asn Gly Arg Glu Pro	
	225 230 235 240	
15	CCA ATA AAA TTT AAA GAA GCT CTT AGA TAC GAT ATA CCA TAT AAA GTG	768
	Pro Ile Lys Phe Lys Glu Ala Leu Arg Tyr Asp Ile Pro Tyr Lys Val	
	245 250 255	
	AAT GAT AAA TTT GAT GAT GAA TTA CCA TCG AGG CCA CAT ATT AGT AAT	816
	Asn Asp Lys Phe Asp Asp Glu Leu Pro Ser Arg Pro His Ile Ser Asn	
	260 265 270	
20	ACT ATT AAT AAA ACT ATT AAA GAA ATT GTA AAT CTT GAA GAT TAT TTT	864
	Thr Ile Asn Lys Thr Ile Lys Glu Ile Val Asn Leu Glu Asp Tyr Phe	
	275 280 285	
	AAA AAT ACA AAT GTT ATA GAT ACT ACT ACC CCA ACA CCA ATA AAT AAT	912
	Lys Asn Thr Asn Val Ile Asp Thr Thr Thr Pro Thr Pro Ile Asn Asn	
	290 295 300	
25	ACC CCA AAA AAT ATA ACC GTG GGA ATT GTT ATA ATT ATA TTA ATA ATA	960
	Thr Pro Lys Asn Ile Thr Val Gly Ile Val Ile Ile Ile Leu Ile Ile	
	305 310 315 320	
30	CTA TTT ATA ATT GGA TTT TTT GTT TAT AAA AGA CAA AAA ATA TAT AAT	1008
	Leu Phe Ile Ile Gly Phe Phe Val Tyr Lys Arg Gln Lys Ile Tyr Asn	
	325 330 335	
	AAT TAT AAA AAA TTA ACA ACA AAT GTT TAG	1038
	Asn Tyr Lys Lys Leu Thr Thr Asn Val	
	340 345	

(2) INFORMATION FOR SEQ ID NO:54:

- 35 (i) SEQUENCE CHARACTERISTICS:
 (A) LENGTH: 345 amino acids
 (B) TYPE: amino acid
 (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein

- 40 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:54:

Met Ile Lys Leu Leu Phe Ile Leu Phe Tyr Phe Asn Pro Ile Thr Gly
 1 5 10 15
 Tyr Lys Trp Val Asp Pro Pro Arg Arg Tyr Asn Tyr Thr Val Leu Arg
 20 25 30

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Met Ile Pro Asp Ile Pro Asn Pro Met Asp Pro Ser Lys Asn Ala Glu
35 40 45

Val Arg Tyr Val Thr Ser Thr Asp Pro Cys Asp Met Val Ala Leu Ile
50 55 60

5 Ser Asn Pro Asn Ile Glu Ser Thr Ile Lys Thr Ile Gln Phe Val Gln
65 70 75 80

Lys Lys Lys Phe Tyr Asn Ala Ser Leu Ser Trp Phe Lys Val Gly Asp
85 90 95

10 Asp Cys Thr Tyr Pro Ile Tyr Leu Ile Gln Tyr Phe Asp Cys Asp Pro
100 105 110

Gln Arg Glu Phe Gly Ile Cys Leu Lys Arg Ser Pro Asp Phe Trp Lys
115 120 125

Pro Ser Leu Val Gly Tyr Thr Phe Leu Thr Asp Asp Glu Leu Gly Leu
130 135 140

15 Val Leu Ala Ala Pro Ala Pro Phe Asn Gln Gly Gln Tyr Arg Arg Val
145 150 155 160

Ile Gln Ile Glu Asn Glu Val Phe Tyr Thr Asp Phe Met Val Gln Leu
165 170 175

20 Pro Arg Glu Thr Cys Tyr Phe Ser Lys Glu Asp Lys Phe Glu Pro Thr
180 185 190

Phe Met Glu Trp Cys Lys Glu Ser Arg Ser Val Gly Ala Ser Lys Val
195 200 205

Asp Asp Glu Leu Phe Tyr Leu Asn Arg Ala Gly Pro Gln Thr Leu Leu
210 215 220

25 Lys Tyr Tyr Val Ile Lys Asp Phe Tyr Arg Leu Asn Gly Arg Glu Pro
225 230 235 240

Pro Ile Lys Phe Lys Glu Ala Leu Arg Tyr Asp Ile Pro Tyr Lys Val
245 250 255

30 Asn Asp Lys Phe Asp Asp Glu Leu Pro Ser Arg Pro His Ile Ser Asn
260 265 270

Thr Ile Asn Lys Thr Ile Lys Glu Ile Val Asn Leu Glu Asp Tyr Phe
275 280 285

Lys Asn Thr Asn Val Ile Asp Thr Thr Thr Pro Thr Pro Ile Asn Asn
290 295 300

35 Thr Pro Lys Asn Ile Thr Val Gly Ile Val Ile Ile Ile Leu Ile Ile
305 310 315 320

Leu Phe Ile Ile Gly Phe Phe Val Tyr Lys Arg Gln Lys Ile Tyr Asn
325 330 335

40 Asn Tyr Lys Lys Leu Thr Thr Asn Val
340 345

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(2) INFORMATION FOR SEQ ID NO:55:

(i) SEQUENCE CHARACTERISTICS:

- 5 (A) LENGTH: 1095 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: cDNA

(ix) FEATURE:

- 10 (A) NAME/KEY: CDS
(B) LOCATION: 1..1092

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:55:

	ATG TAC CTA CAA CTT TTA TTC ACT TGC AAG AGG GTT GAG ACC AGA TTA	48
	Met Tyr Leu Gln Leu Phe Thr Cys Lys Arg Val Glu Thr Arg Leu	
	1 5 10 15	
15	CTT ATA ACT ATG TTT CTA CCT ATT TTA TTT CTT TTT TTA TAT GGT GTA	96
	Leu Ile Thr Met Phe Leu Pro Ile Leu Phe Leu Phe Leu Tyr Gly Val	
	20 25 30	
	AAT GGA TTT GTT TAC AAA GGT ACG TAT ATA AGT ATG TTT TTA AAT ACT	144
20	Asn Gly Phe Val Tyr Lys Gly Thr Tyr Ile Ser Met Phe Leu Asn Thr	
	35 40 45	
	AGT TCT GGC TTT TCT ATT TTT CCC GAT GAT AAA TTT ATT GTC ACT GGA	192
	Ser Ser Gly Phe Ser Ile Phe Pro Asp Asp Lys Phe Ile Val Ser Gly	
	50 55 60	
25	CGT TTA TTA TTT CTC GAT GAC CAA CAT CTG TCA GTA AAT AAT TAT AGC	240
	Arg Leu Leu Phe Leu Asp Gln His Leu Ser Val Asn Asn Tyr Ser	
	65 70 75 80	
	GGA ACT ATT GAG TTT ATT CAT TTT AAT AAC TCT TGT TAT ACC GTT TAT	288
	Gly Thr Ile Glu Phe Ile His Phe Asn Asn Ser Cys Tyr Thr Val Tyr	
	85 90 95	
30	CAA ACT ATT GAA TAT TTT TCT TGT CCT CGC ATT TTT AAT AAT GCT TTT	336
	Gln Thr Ile Glu Tyr Phe Ser Cys Pro Arg Ile Phe Asn Asn Ala Phe	
	100 105 110	
	AGA TCT TGT TTA AAA AAG GTA TCA AAA CAT CAT GAA AGT CAA CTT CGG	384
35	Arg Ser Cys Leu Lys Lys Val Ser Lys His His Glu Ser Gln Leu Arg	
	115 120 125	
	ATA AAT TCA TCT ATA GAA AAC GGT GTT TTG TTG GAA ATT ACA AAT CCT	432
	Ile Asn Ser Ser Ile Glu Asn Gly Val Leu Leu Glu Ile Thr Asn Pro	
	130 135 140	
40	AAA CCA AAT GAT TCA GGT GTT TAT TTT ATA CGA GTT CAA TTG GAA AAT	480
	Lys Pro Asn Asp Ser Gly Val Tyr Phe Ile Arg Val Gln Leu Glu Asn	
	145 150 155 160	
	AAT AAA ACA GAT GTG TTT GGA ATA CCT GCA TTT ATT TAT TCC TTT AAT	528
	Asn Lys Thr Asp Val Phe Gly Ile Pro Ala Phe Ile Tyr Ser Phe Asn	
	165 170 175	

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	ATG TCA AAC GAA GTA AAT AAA TCA AAC TTC GAT GAT GTT ACT ACA TCT	576
	Met Ser Asn Glu Val Asn Lys Ser Asn Phe Asp Asp Val Thr Thr Ser	
	180 185 190	
5	TTA TAT ACC TCA TCA CAC CCT TCT TCC CAA ACT ATT ACA CCT ATC TAT	624
	Leu Tyr Thr Ser Ser His Pro Ser Ser Gln Thr Ile Thr Pro Ile Tyr	
	195 200 205	
	TTA AAT GAA AAA CAC GAA CCG ATA TGT CAT ACT GTA AAA AAG GAT GAA	672
	Leu Asn Glu Lys His Glu Pro Ile Cys His Thr Val Lys Lys Asp Glu	
	210 215 220	
10	AAT GTG TAT GAA CTT TTA CTA GGT TTG CAT GGA AAT ATA ACT GAT GAT	720
	Asn Val Tyr Glu Leu Leu Leu Gly Leu His Gly Asn Ile Thr Asp Asp	
	225 230 235 240	
	ATT TTT CTC GAT GAG GAT TCT GAA TTG CTT AAA AGA GTA AAT ATA CCT	768
	Ile Phe Leu Asp Glu Asp Ser Glu Leu Leu Lys Arg Val Asn Ile Pro	
	245 250 255	
15	ACA ACG ACA AAT AAT TAT ATA TTT AAG CCT TAC CTA GAC CAA CGT AAT	816
	Thr Thr Thr Asn Asn Tyr Ile Phe Lys Pro Tyr Leu Asp Gln Arg Asn	
	260 265 270	
20	AGA AAA TTT TTA ATT ATT GTA ATT TCG ATT TCG ATA ATT TTA CTT ATT	864
	Arg Lys Phe Leu Ile Ile Val Ile Ser Ile Ser Ile Ile Leu Leu Ile	
	275 280 285	
	CTT TTG GTA TTA ATT GGA TCA ATT ATT AAC AAT ATT ATT CGT AGA CAC	912
	Leu Leu Val Leu Ile Gly Ser Ile Ile Asn Asn Ile Ile Arg Arg His	
	290 295 300	
25	TTT TCT TCT TCT AGG CGT ATT TAT CGT CCT AAA GGT AAC TCG GAA TCT	960
	Phe Ser Ser Ser Arg Arg Ile Tyr Arg Pro Lys Gly Asn Ser Glu Ser	
	305 310 315 320	
	GAA AAT ATA GAA CTG ACA TGT GGG GAA AAC TCA GTA AAC AAA AAT AAT	1008
	Glu Asn Ile Glu Leu Thr Cys Gly Glu Asn Ser Val Asn Lys Asn Asn	
	325 330 335	
30	CCA TTA CCA AAA AAA CCT AAC CGC CAA AAA AGA TCT TCA ACT ATT CAA	1056
	Pro Leu Pro Lys Lys Pro Asn Arg Gln Lys Arg Ser Ser Thr Ile Gln	
	340 345 350	
35	AGG GAG ACA TCT CTT GAA ACT ATT AAG GAA GAA GTA TAA	1095
	Arg Glu Thr Ser Leu Glu Thr Ile Lys Glu Glu Val	
	355 360	

(2) INFORMATION FOR SEQ ID NO:56:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 364 amino acids

(B) TYPE: amino acid

(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein

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(xi) SEQUENCE DESCRIPTION: SEQ ID NO:56:

Met Tyr Leu Gln Leu Leu Phe Thr Cys Lys Arg Val Glu Thr Arg Leu
 1 5 10 15
 5 Leu Ile Thr Met Phe Leu Pro Ile Leu Phe Leu Phe Leu Tyr Gly Val
 20 25 30
 Asn Gly Phe Val Tyr Lys Gly Thr Tyr Ile Ser Met Phe Leu Asn Thr
 35 40 45
 Ser Ser Gly Phe Ser Ile Phe Pro Asp Asp Lys Phe Ile Val Ser Gly
 50 55 60
 10 Arg Leu Leu Phe Leu Asp Asp Gln His Leu Ser Val Asn Asn Tyr Ser
 65 70 75 80
 Gly Thr Ile Glu Phe Ile His Phe Asn Asn Ser Cys Tyr Thr Val Tyr
 85 90 95
 15 Gln Thr Ile Glu Tyr Phe Ser Cys Pro Arg Ile Phe Asn Asn Ala Phe
 100 105 110
 Arg Ser Cys Leu Lys Lys Val Ser Lys His His Glu Ser Gln Leu Arg
 115 120 125
 Ile Asn Ser Ser Ile Glu Asn Gly Val Leu Leu Glu Ile Thr Asn Pro
 130 135 140
 20 Lys Pro Asn Asp Ser Gly Val Tyr Phe Ile Arg Val Gln Leu Glu Asn
 145 150 155 160
 Asn Lys Thr Asp Val Phe Gly Ile Pro Ala Phe Ile Tyr Ser Phe Asn
 165 170 175
 25 Met Ser Asn Glu Val Asn Lys Ser Asn Phe Asp Asp Val Thr Thr Ser
 180 185 190
 Leu Tyr Thr Ser Ser His Pro Ser Ser Gln Thr Ile Thr Pro Ile Tyr
 195 200 205
 Leu Asn Glu Lys His Glu Pro Ile Cys His Thr Val Lys Lys Asp Glu
 210 215 220
 30 Asn Val Tyr Glu Leu Leu Leu Gly Leu His Gly Asn Ile Thr Asp Asp
 225 230 235 240
 Ile Phe Leu Asp Glu Asp Ser Glu Leu Leu Lys Arg Val Asn Ile Pro
 245 250 255
 35 Thr Thr Thr Asn Asn Tyr Ile Phe Lys Pro Tyr Leu Asp Gln Arg Asn
 260 265 270
 Arg Lys Phe Leu Ile Ile Val Ile Ser Ile Ser Ile Ile Leu Leu Ile
 275 280 285
 Leu Leu Val Leu Ile Gly Ser Ile Ile Asn Asn Ile Ile Arg Arg His
 290 295 300
 40 Phe Ser Ser Ser Arg Arg Ile Tyr Arg Pro Lys Gly Asn Ser Glu Ser
 305 310 315 320

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Glu Asn Ile Glu Leu Thr Cys Gly Glu Asn Ser Val Asn Lys Asn Asn
 325 330 335
 Pro Leu Pro Lys Lys Pro Asn Arg Gln Lys Arg Ser Ser Thr Ile Gln
 340 345 350
 5 Arg Glu Thr Ser Leu Glu Thr Ile Lys Glu Glu Val
 355 360

(2) INFORMATION FOR SEQ ID NO:57:

(i) SEQUENCE CHARACTERISTICS:
 (A) LENGTH: 1569 base pairs
 (B) TYPE: nucleic acid
 (C) STRANDEDNESS: single
 (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: cDNA

(ix) FEATURE:
 (A) NAME/KEY: CDS
 (B) LOCATION: 1..1566

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:57:

20	ATG TTT CGT TTA TTT TTT TTA ATC GCG TCT ACA TTA TGT TCG GTA AGA Met Phe Arg Leu Phe Phe Leu Ile Ala Ser Thr Leu Cys Ser Val Arg 1 5 10 15	48
	TTT GGT TTT TCA ACA ATT CGT AAT GTT ATT GTT TCT GAA AAA TCT GGA Phe Gly Phe Ser Thr Ile Arg Asn Val Ile Val Ser Glu Lys Ser Gly 20 25 30	96
25	TTT GTA ATT GAT GGT TAT AGT ACT AAC CCA CCA TTT AAT GAG ACT AAA Phe Val Ile Asp Gly Tyr Ser Thr Asn Pro Pro Phe Asn Glu Thr Lys 35 40 45	144
	AAA TTT ACT AGA GGA TGG GTA TTT TTA CAA ACC CCC CCT TCT TAT TGT Lys Phe Thr Arg Gly Trp Val Phe Leu Gln Thr Pro Pro Ser Tyr Cys 50 55 60	192
30	AAA GAT GGG ATA TCA ATA TCT AAT ATA TGC ATT GAA CGT AAT ATT TGT Lys Asp Gly Ile Ser Ile Ser Asn Ile Cys Ile Glu Arg Asn Ile Cys 65 70 75 80	240
35	GAA GAA GAT ATT TTT TTG AAT AAA CGA TGT ACA ATT AAA ACT ATT AAT Glu Glu Asp Ile Phe Leu Asn Lys Arg Cys Thr Ile Lys Thr Ile Asn 85 90 95	288
	TAT CCC TTA GCT GTA GCA GAT TTT GAG ATT AGT AAT AAT ACT ATT AAA Tyr Pro Leu Ala Val Ala Asp Phe Glu Ile Ser Asn Asn Thr Ile Lys 100 105 110	336
40	AAA ATA AAT GAT GTT TAT TTT GTT AAT GAT AGT GTT TTT CCA ATA ATA Lys Ile Asn Asp Val Tyr Phe Val Asn Asp Ser Val Phe Pro Ile Ile 115 120 125	384
	ACT ACA AAT AAA AGT GGT ATC CAT ATC ACA AAT GTG ACT ATA AAT AAT Thr Thr Asn Lys Ser Gly Ile His Ile Thr Asn Val Thr Ile Asn Asn 130 135 140	432

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	TCT GGA ATT TAT ACA TTG TAT GAA AAT AAT GAT AAG TGG AGT CAT CAA Ser Gly Ile Tyr Thr Leu Tyr Glu Asn Asn Asp Lys Trp Ser His Gln 145 150 155 160	480
5	TCA AAA ATC TTG GTA ACT ATA AAG AAA AAA GAA ACA GTA ATT ACT AAA Ser Lys Ile Leu Val Thr Ile Lys Lys Lys Glu Thr Val Ile Thr Lys 165 170 175	528
	CCT AAA GTA TAT ATA AAA AAA CAT GGT GGA TTT TTT CAT GTA AAA AAT Pro Lys Val Tyr Ile Lys Lys His Gly Gly Phe Phe His Val Lys Asn 180 185 190	576
10	TAT CAC TCT CAT GTA TTT GTA CCA AAT GAT TCA TTT AAA ATT GAA CTT Tyr His Ser His Val Phe Val Pro Asn Asp Ser Phe Lys Ile Glu Leu 195 200 205	624
15	AAT CTT GAA TCG GAA ATT TAT GAT TCT GAA TTT TCA GCA AGT ATT GAT Asn Leu Glu Ser Glu Ile Tyr Asp Ser Glu Phe Ser Ala Ser Ile Asp 210 215 220	672
	TGG TAT TAT ATG AAA ACT AGC TCG GAA TGT TCA GTG TTT CAT ATA TAT Trp Tyr Tyr Met Lys Thr Ser Ser Glu Cys Ser Val Phe His Ile Tyr 225 230 235 240	720
20	GAA ACT TGT ATA TTT CAC CCT CAT GCA AAC TCT TGT TTG AAT CCA ATA Glu Thr Cys Ile Phe His Pro His Ala Asn Ser Cys Leu Asn Pro Ile 245 250 255	768
	AAC CCA TTG TGT AGT TTT ACT TCC CCT TTG AGG GCA ACA TCA CTA ATT Asn Pro Leu Cys Ser Phe Thr Ser Pro Leu Arg Ala Thr Ser Leu Ile 260 265 270	816
25	AAT AGA TTT TAT TTT AGA TGT AAA CCT GAA GGT AAA AAC TGG ACA ACT Asn Arg Phe Tyr Phe Arg Cys Lys Pro Glu Gly Lys Asn Trp Thr Thr 275 280 285	864
30	GAT TGT ATA AAC ACC TTT TCT ATT AAT GCA GAT AAA CAT ATT AAA CAG Asp Cys Ile Asn Thr Phe Ser Ile Asn Ala Asp Lys His Ile Lys Gln 290 295 300	912
	CAT TCA AAT AAT GTA GAT TTG ATT TTT TTA AAT ACT CCA ACT AAT GCA His Ser Asn Asn Val Asp Leu Ile Phe Leu Asn Thr Pro Thr Asn Ala 305 310 315 320	960
35	TCT GGT TTG TAT GTT TTT ATT CTT AAG TAT AAT GGT CAT CCA GAG GCT Ser Gly Leu Tyr Val Phe Ile Leu Lys Tyr Asn Gly His Pro Glu Ala 325 330 335	1008
	TGG ACA TAT ACT TTG GTT TCA ACG GTT AAA AAT TTT ATG AAT GTA ATT Trp Thr Tyr Thr Leu Val Ser Thr Val Lys Asn Phe Met Asn Val Ile 340 345 350	1056
40	AAG GAT ATG ACA CGC CCC CTT TTG TCA AAT AAT AAA ATG AAA AAA CCT Lys Asp Met Thr Arg Pro Leu Leu Ser Asn Asn Lys Met Lys Lys Pro 355 360 365	1104
45	GAG CAT TCT ACT CAA CCA CCA ACC ATA ACC AAC ATA ACA CCT GGC TTT Glu His Ser Thr Gln Pro Pro Thr Ile Thr Asn Ile Thr Pro Gly Phe 370 375 380	1152

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	AAA TCT AAA AAT TGG GTA GAT AAA TAT ATA ATT TCA GTA GCG GTG GTT	1200
	Lys Ser Lys Asn Trp Val Asp Lys Tyr Ile Ile Ser Val Ala Val Val	
	385 390 395 400	
5	TCT TGT ATT ACT ATT GTT ATA TTG ATT GTG GTA ATA ACC TTT TGT GTT	1248
	Ser Cys Ile Thr Ile Val Ile Leu Ile Val Val Ile Thr Phe Cys Val	
	405 410 415	
	CAT CAA TGT ATC GGT TTA AAT CGT AAA CCA TAT GAA ATT ATA AAC CCA	1296
	His Gln Cys Ile Gly Leu Asn Arg Lys Pro Tyr Glu Ile Ile Asn Pro	
	420 425 430	
10	TTT AAT ACA GCT TAT AAA AGT ATA CCT ACA AAT GAA AAA AAT ATT CTT	1344
	Phe Asn Thr Ala Tyr Lys Ser Ile Pro Thr Asn Glu Lys Asn Ile Leu	
	435 440 445	
	CAT TTT GCT GAA GTA ACA GAA TCT GAT TAT TCC TCC GAC GAA TCC TTC	1392
15	His Phe Ala Glu Val Thr Glu Ser Asp Tyr Ser Ser Asp Glu Ser Phe	
	450 455 460	
	GAC AGT GAC TCA GAA GAG CTA AAT CAA CGA GGT GAA ACA ATA CAA CAA	1440
	Asp Ser Asp Ser Glu Glu Leu Asn Gln Arg Gly Glu Thr Ile Gln Gln	
	465 470 475 480	
20	GGG AAA AAG GAA CAA TCT GGA TAT ACT ATT TGG TTT AAT GAA GAT TTA	1488
	Gly Lys Lys Glu Gln Ser Gly Tyr Thr Ile Trp Phe Asn Glu Asp Leu	
	485 490 495	
	GAA GAA TCC GTC TCC AAA AAA CTT AAC CAA CCA AAC TAT TCA AAA ATA	1536
	Glu Glu Ser Val Ser Lys Lys Leu Asn Gln Pro Asn Tyr Ser Lys Ile	
	500 505 510	
25	ATT AAT AGC TTA AAA TCA ATC CAG AAT GAA TAA	1569
	Ile Asn Ser Leu Lys Ser Ile Gln Asn Glu	
	515 520	

(2) INFORMATION FOR SEQ ID NO:58:

- (i) SEQUENCE CHARACTERISTICS:
- 30 (A) LENGTH: 522 amino acids
- (B) TYPE: amino acid
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:58:

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

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

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Lys Ser Lys Asn Trp Val Asp Lys Tyr Ile Ile Ser Val Ala Val Val
 385 390 395 400
 Ser Cys Ile Thr Ile Val Ile Leu Ile Val Val Ile Thr Phe Cys Val
 405 410 415
 5 His Gln Cys Ile Gly Leu Asn Arg Lys Pro Tyr Glu Ile Ile Asn Pro
 420 425 430
 Phe Asn Thr Ala Tyr Lys Ser Ile Pro Thr Asn Glu Lys Asn Ile Leu
 435 440 445
 10 His Phe Ala Glu Val Thr Glu Ser Asp Tyr Ser Ser Asp Glu Ser Phe
 450 455 460
 Asp Ser Asp Ser Glu Glu Leu Asn Gln Arg Gly Glu Thr Ile Gln Gln
 465 470 475 480
 Gly Lys Lys Glu Gln Ser Gly Tyr Thr Ile Trp Phe Asn Glu Asp Leu
 485 490 495
 15 Glu Glu Ser Val Ser Lys Lys Leu Asn Gln Pro Asn Tyr Ser Lys Ile
 500 505 510
 Ile Asn Ser Leu Lys Ser Ile Gln Asn Glu
 515 520

(2) INFORMATION FOR SEQ ID NO:59:

- 20 (i) SEQUENCE CHARACTERISTICS:
 (A) LENGTH: 237 base pairs
 (B) TYPE: nucleic acid
 (C) STRANDEDNESS: single
 (D) TOPOLOGY: linear
 25 (ii) MOLECULE TYPE: cDNA
 (ix) FEATURE:
 (A) NAME/KEY: CDS
 (B) LOCATION: 1..234
 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:59:
 30 ATG AAT AAA TCT AAA CTC TCA TTT AAA GAA AAA AAC GCT ATA TAT GAA 48
 Met Asn Lys Ser Lys Leu Ser Phe Lys Glu Lys Asn Ala Ile Tyr Glu
 1 5 10 15
 TTT AAA AAT ATT TTA TCA AAC ACT TCA TTG TCA ACT TTT CCT GTA TTA 96
 Phe Lys Asn Ile Leu Ser Asn Thr Ser Leu Ser Thr Phe Pro Val Leu
 35 20 25 30
 TCG TTT AAT GAG GAG CCA AAA TCC AGA TTT TTT AAA ATG TTT AAA AAT 144
 Ser Phe Asn Glu Glu Pro Lys Ser Arg Phe Phe Lys Met Phe Lys Asn
 35 40 45
 ATT TTA CTG GAA AAA ATA AAA AAA ACT TCA ATG GAT TAT TTA ATT TAT 192
 Ile Leu Leu Glu Lys Ile Lys Lys Thr Ser Met Asp Tyr Leu Ile Tyr
 50 55 60

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TGT ACT CTA AAA ATC TCA CTT TCA TTT ATA CTT TAT AAT AAA 234
 Cys Thr Leu Lys Ile Ser Leu Ser Phe Ile Leu Tyr Asn Lys
 65 70 75
 TAA 237

5 (2) INFORMATION FOR SEQ ID NO:60:

- (i) SEQUENCE CHARACTERISTICS:
 (A) LENGTH: 78 amino acids
 (B) TYPE: amino acid
 (D) TOPOLOGY: linear

10 (ii) MOLECULE TYPE: protein

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:60:

Met Asn Lys Ser Lys Leu Ser Phe Lys Glu Lys Asn Ala Ile Tyr Glu
 1 5 10 15
 Phe Lys Asn Ile Leu Ser Asn Thr Ser Leu Ser Thr Phe Pro Val Leu
 15 20 25 30
 Ser Phe Asn Glu Glu Pro Lys Ser Arg Phe Phe Lys Met Phe Lys Asn
 35 40 45
 Ile Leu Leu Glu Lys Ile Lys Lys Thr Ser Met Asp Tyr Leu Ile Tyr
 50 55 60
 20 Cys Thr Leu Lys Ile Ser Leu Ser Phe Ile Leu Tyr Asn Lys
 65 70 75

(2) INFORMATION FOR SEQ ID NO:61:

- (i) SEQUENCE CHARACTERISTICS:
 (A) LENGTH: 360 base pairs
 (B) TYPE: nucleic acid
 (C) STRANDEDNESS: single
 (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: cDNA

(ix) FEATURE:

- (A) NAME/KEY: CDS
 (B) LOCATION: 1..357

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:61:

ATG GCT TTA CCA GAT AAC GTT TTT AGT ATT ATT AAT GAA AAT TAT ATC 48
 35 Met Ala Leu Pro Asp Asn Val Phe Ser Ile Ile Asn Glu Asn Tyr Ile
 1 5 10 15
 GAT GGA ATT TTA ACT ATG AAA ATG GGT GAA GAA ATA GAA AGC TCA TCA 96
 Asp Gly Ile Leu Thr Met Lys Met Gly Glu Glu Ile Glu Ser Ser Ser
 20 25 30
 CCA TTA AAT GAA ACA AAT GTT AAT ATA GAT CAA CAT ACA ATA GAT ATT 144
 40 Pro Leu Asn Glu Thr Asn Val Asn Ile Asp Gln His Thr Ile Asp Ile
 35 40 45

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TTT GAT TAC GAT TCA GAT AAT GGA TGT TAT TAT AGT GAA AGA GAT AAT 192
Phe Asp Tyr Asp Ser Asp Asn Gly Cys Tyr Tyr Ser Glu Arg Asp Asn
50 55 60

GAA ACC GCA ACT CTT TTT TTA AAA CGT GTT GGT TAT AGA GAA ACC TCA 240
5 Glu Thr Ala Thr Leu Phe Leu Lys Arg Val Gly Tyr Arg Glu Thr Ser
65 70 75 80

AAA AAG CGT AAA CGG ATT TGT GGA TTT ATT GTT TTA GCA ATT TTT ATG 288
Lys Lys Arg Lys Arg Ile Cys Gly Phe Ile Val Leu Ala Ile Phe Met
85 90 95

10 GTT ATT ATA TTA TGT TTT TTA TCA ATA ATT TTG GGA GTT TTT ATA GCG 336
Val Ile Ile Leu Cys Phe Leu Ser Ile Ile Leu Gly Val Phe Ile Ala
100 105 110

CCT CAT ATT TAT AAA GGC CTA TAG 360
15 Pro His Ile Tyr Lys Gly Leu
115

(2) INFORMATION FOR SEQ ID NO:62:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 119 amino acids
(B) TYPE: amino acid
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:62:

Met Ala Leu Pro Asp Asn Val Phe Ser Ile Ile Asn Glu Asn Tyr Ile
1 5 10 15

25 Asp Gly Ile Leu Thr Met Lys Met Gly Glu Glu Ile Glu Ser Ser Ser
20 25 30

Pro Leu Asn Glu Thr Asn Val Asn Ile Asp Gln His Thr Ile Asp Ile
35 40 45

30 Phe Asp Tyr Asp Ser Asp Asn Gly Cys Tyr Tyr Ser Glu Arg Asp Asn
50 55 60

Glu Thr Ala Thr Leu Phe Leu Lys Arg Val Gly Tyr Arg Glu Thr Ser
65 70 75 80

Lys Lys Arg Lys Arg Ile Cys Gly Phe Ile Val Leu Ala Ile Phe Met
85 90 95

35 Val Ile Ile Leu Cys Phe Leu Ser Ile Ile Leu Gly Val Phe Ile Ala
100 105 110

Pro His Ile Tyr Lys Gly Leu
115

(2) INFORMATION FOR SEQ ID NO:63:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 2044 base pairs

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(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

5 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:63:

AAATTTACTA	GAACAGAACC	TGGATCTGGT	GTTATTTTTT	CCAGTAAGCC	TATATCCCTT	60
CAGTAATACC	CCAAAAACAC	CAAAATTTCC	ATGGTATGGA	GCCACTCATT	TGTATAACAA	120
AAATGTTTTT	TGTGAAGCTG	TACGTCGATG	TGCTTCTAAA	CATGCTATAG	AAGCCGCATC	180
ATCTATTTGG	GATTTAAATC	CACCACAGTC	AAATGAAGAA	TTGGAAAAGT	TTCTAACTAA	240
10 AGCGGTTATT	CGCATAACCA	TATCTGAGGG	ACTAGGTATT	TTAAAACTG	CAAATACCCC	300
ATTTAGCTGT	GGTCAAAAAA	CTGCTGATGA	TGTTAAATTT	AAGTCTCACT	CCTCACGTAG	360
GAGTAAGAGT	CAGTCAAGAA	GTAGACACAG	TCGGGGTGAT	TTGACGACA	GTAGTGATTA	420
AAGTTTGTTA	CACCCACTAA	TTAAATAAAA	TAAAAAATTT	ATATTTAAAG	CTATTTGTCT	480
GTCTTTTTTT	GTTATATATA	TTCTTGCTTA	GTGAGAGTAT	AAACTATTTT	GTTTTTAAAA	540
15 ATGGAATTTA	ACATAGAAGA	CTTTGATGAA	TCGTTGCTAG	GGGCTGTGG	ATACTCTAAT	600
AATTTTAAAG	GTAAGCAAAG	CCTTCCGATT	AAGGCTTCTA	GTCCATCATC	GTTAATTTAA	660
AATCTTTTAG	ATGAATTAAA	TTTCCCGGAA	GGTCCTAGTT	TATTATCTTC	TATGGAAAAA	720
TGGAATGAGG	ATTTATTTTC	CTGCATCCCA	AGATTTTGG	AAATCTACAT	TGAAAATTCT	780
ATTTTATCAA	CATCTGTCGA	TGAGGTTATT	AAAAATTTGG	ATAATCTTTT	AAATTATGAT	840
20 GATGTAATCG	ATTTTCAGGT	CCATGGACCT	GAAACATTTT	CAAAAACCCC	ATTATTGGAA	900
GAGGAATTGG	AAAATTATGT	AACATCTGTT	CAAAAGTATT	TTTTATCTGA	ACTTAAAGCT	960
AGAGAAGTTA	CATATTCATT	TCTACTCACT	AAATATTGTA	AAGCGCTTTT	GTTATATCTT	1020
CGCTATAATA	CAAAATCATC	GATTAAGGGT	AATAAGGACA	TAAATGCATT	TCACCAAAAA	1080
TTTAAACAAA	ATGTGCGGGA	ACGTTATTAT	AGAGAGGTTG	CAAATATAGC	ACGATTGTTA	1140
25 TATTTACATC	TGTATTTATC	AGTAACTAGG	GAAGTGTCTT	GGAACTACA	TGCCGATCAA	1200
GTATTACTCC	AAAGTGTTTT	TGTTTCATTG	TCTTATTCTT	GGAGCCACCG	ACGACAGTTT	1260
GAGTGTATAT	TTTATCCAAT	TTTATTTAAT	CATGGTATTG	TGAATTGGA	AAATAACCCCT	1320
TTGACATTTA	AGGAACTACA	AAAAATAAAT	TATAGACGTC	ATATTCTTGG	TTTACCATTG	1380
ATTAGAGCTG	GATTGGTAGA	AGAAGATAAT	CAACCTTTAA	TGATACCTCC	AGAGTTTTTCC	1440
30 AGTAAACTAC	CTCGAACAAT	AGGATTTTTA	ACTCAACAAA	TTAGAGCCAA	AATGGAAGCT	1500
TATTCAGACA	ACCATCCTGT	AACACCAAAA	TTTCTCTGTA	TTGAACATTC	ATATGCTAAA	1560
CCTATAGATC	CTATTAACCT	TGGAACCTACA	ATAGAAGCTA	TGATGGACCC	ACCATCACCA	1620

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AGCGCTATTT TACCAGGAGA TCCAAATCCT GAAATTAATG TTAAGGTAA AAGCACTGTT 1680
TCATCCTTTC AAATTCACC TAATATTACC TTGGAAGAAC TGGAGTCAGG TGAATATAAT 1740
TTATTTACAG ATGGTGTAC CTACAATGAT ATACCTGAAA ATGAGTTAAA TAAAATGTTT 1800
CAATTATAAT TTTTTTTTAA TTTTTCCTT TTAACCGTT AGTATATAAT ATGAGTTAT 1860
5 ATTAATCAAT AACACCAATA TATTGGGGAA TTGCCACTAA GATACACGTG AGTGGTACTT 1920
TTGTAGTTAG TGGGTATAAA TAAGGTGGGG TAAGGTGGGG TTCAATCAT TTTTATTAC 1980
TCAGTGTGTTG CTTAAGAAAT TATATATTTA ATATATTTAC TATGGAAAGA GACCATGTT 2040
TTGC 2044

(2) INFORMATION FOR SEQ ID NO:64:

- 10 (i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 2044 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

- 15 (ii) MOLECULE TYPE: DNA (genomic)

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:64:

GCAAAACCAT GGTCTCTTTC CATAGTAAAT ATATTAAATA TATAATTCT TAAGCAAACA 60
CTGAGTAATA AAAAATGATT TGAACCCAC CTTACCCAC CTTATTTATA CCCACTAAT 120
ACAAAAGTAC CACTCAGTG TATCTTAGTG GCAATCCCC AATATATTGG TGTATTGAT 180
20 TAATATAACC TCATATTATA TACTAACGTT TTAATGGAA AAAATTAAA AAAATTATA 240
ATTGAAACAT TTTATTTAAC TCATTTTCAG GTATATCATT GTAGGTAACA CCATCTGTAA 300
ATAAATTATA TTCACCTGAC TCCAGTTCTT CCAAGGTAAT ATTAGGTGGA -ATTGAAAGG 360
ATGAAACAGT GCTTTTAACC TTAACATTAA TTTCAGGATT TGGATCTCCT GGTAAATAG 420
CGCTTGGTGA TGGTGGGTCC ATCATAGCTT CTATTGTAGT TCCATAGTTA ATAGGATCTA 480
25 TAGGTTTAGC ATATGAATGT TCAATACGAG GAAATTTTGG TGTACAGGA TGGTGTCTG 540
AATAAGCTTC CATTTTGGCT CTAATTTGTT GAGTTAAAA TCCTATTGTT CGAGGTAGTT 600
TACTGGAAAA CTCTGGAGGT ATCATTAAG GTTGATTATC TTCTTCTACC AATCCAGCTC 660
TAATCAATGG TAAACCAAGA ATATGACGTC TATAATTTAT TTTTGTAGT TCCTAAATG 720
TCAAAGGGTT ATTTCCAAA TTCACAATAC CATGATTAAA TAAATTGGA TGAATATAC 780
30 ACTCAAACTG TCGTCGGTGG CTCCAAGAAT AAGACAATGA AACAAAAACA CTTGGAGTA 840
ATACTGTATC GGCATGTAGT TTCCAAGACA CTTCCCTAGT TACTGATAAA TACAGATGTA 900
AATATAACAA TCGTGCTATA TTTGCAACCT CTCTATAATA ACGTTCCCGC ACATTTTGT 960

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TAAATTTTGT GTGAAATGCA TTTATGTCCT TATTACCCCTT AATCGATGAT TTTGTATTAT 1020
 AGCGAAGATA TAACAAAAGC GCTTTACAAT ATTTAGTGAG TAGAAATGAA TATGTAACCTT 1080
 CTCTAGCTTT AAGTTCAGAT AAAAAATACT TTTGAACAGA TGTACATAA TTTTCCAATT 1140
 CCTCTTCCAA TAATGGGGTT TTTGGAAATG TTTCAGGTCC ATGGACCTGA AAATCGATTA 1200
 5 CATCATCATA ATTTAAAGAA TTATCCAAAT TTTTAATAAC CTCATCGACA GATGTTGATA 1260
 AAATAGAATT TTCAATGTAG ATTTCCAAAA ATCTTGGGAT GCAGGAAAAAT AAATCCTCAT 1320
 TCCATTTTTC CATAGAAGAT AATAAAGTAG GACCTTCCGG AAAATTTAAT TCATCTAAAA 1380
 GATTTTAAAT TAACGATGAT GGACTAGAAG CCTTAATCGG AAGGCTTTGC TTACCTTTAA 1440
 AATTATTAGA GTATCCAACA GCCCCTAGCA ACGATTCATC AAAGTCTTCT ATGTTAAATT 1500
 10 CCATTTTAA AAACAAAATA GTTTATACTC TCACCTAAGCA AGAATATATA TAACAAAAAA 1560
 AGACAGACAA ATAGCTTTAA ATATAAATTT TTTATTTATT TAAATTAGTG GGTGTAACAA 1620
 ACTTTAATCA CTACTGTCGT CGAAATCACC CCGACTGTGT CTACTTCTTG ACTGACTCTT 1680
 ACTCCTACGT GAGGAGTGAG ACTTAAATTT AACATCATCA GCAGTTTTTT GACCACAGCT 1740
 AAATGGGGTA TTTGCAGTTT TTAATAATACC TAGTCCCTCA GATATGGTTA TGCGAATAAC 1800
 15 CGCTTTAGTT AGAAACTTTT CCAATTCTTC ATTGACTGT GGTGGATTTA AATCCCAAAT 1860
 AGATGATGCG GCTTCTATAG CATGTTTGA AGCACATCGA CGTACAGCTT CACAAAAAAC 1920
 ATTTTGTGTA TACAAATGAG TGGCTCCATA CCATGGAAAT TTTGGTGTGTT TTGGGGTATT 1980
 ACTGAAGGGA TATAGGCTTA CTGGAAAAAA TAACACCAGA TCCAGGTCT GTTCTAGTAA 2040
 ATTT 2044

20 (2) INFORMATION FOR SEQ ID NO:65:

- (i) SEQUENCE CHARACTERISTICS:
 (A) LENGTH: 420 base pairs
 (B) TYPE: nucleic acid
 (C) STRANDEDNESS: single
 25 (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: cDNA

(ix) FEATURE:

- (A) NAME/KEY: CDS
 (B) LOCATION: 1..417

30 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:65:

AAT TTA CTA GAA CAG AAC CTG GAT CTG GTG TTA TTT TTT CCA GTA AGC 48
 Asn Leu Leu Glu Gln Asn Leu Asp Leu Val Leu Phe Phe Pro Val Ser
 1 5 10 15

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CTA TAT CCC TTC AGT AAT ACC CCA AAA ACA CCA AAA TTT CCA TGG TAT 96
 Leu Tyr Pro Phe Ser Asn Thr Pro Lys Thr Pro Lys Phe Pro Trp Tyr
 20 25 30

5 GGA GCC ACT CAT TTG TAT AAC AAA AAT GTT TTT TGT GAA GCT GTA CGT 144
 Gly Ala Thr His Leu Tyr Asn Lys Asn Val Phe Cys Glu Ala Val Arg
 35 40 45

CGA TGT GCT TCT AAA CAT GCT ATA GAA GCC GCA TCA TCT ATT TGG GAT 192
 Arg Cys Ala Ser Lys His Ala Ile Glu Ala Ala Ser Ser Ile Trp Asp
 50 55 60

10 TTA AAT CCA CCA CAG TCA AAT GAA GAA TTG GAA AAG TTT CTA ACT AAA 240
 Leu Asn Pro Pro Gln Ser Asn Glu Glu Leu Glu Lys Phe Leu Thr Lys
 65 70 75 80

15 GCG GTT ATT CGC ATA ACC ATA TCT GAG GGA CTA GGT ATT TTA AAA ACT 288
 Ala Val Ile Arg Ile Thr Ile Ser Glu Gly Leu Gly Ile Leu Lys Thr
 85 90 95

GCA AAT ACC CCA TTT AGC TGT GGT CAA AAA ACT GCT GAT GAT GTT AAA 336
 Ala Asn Thr Pro Phe Ser Cys Gly Gln Lys Thr Ala Asp Asp Val Lys
 100 105 110

20 TTT AAG TCT CAC TCC TCA CGT AGG AGT AAG AGT CAG TCA AGA AGT AGA 384
 Phe Lys Ser His Ser Ser Arg Arg Ser Lys Ser Gln Ser Arg Ser Arg
 115 120 125

CAC AGT CGG GGT GAT TTC GAC GAC AGT AGT GAT TAA 420
 His Ser Arg Gly Asp Phe Asp Asp Ser Ser Asp
 130 135

25 (2) INFORMATION FOR SEQ ID NO:66:

- (i) SEQUENCE CHARACTERISTICS:
 (A) LENGTH: 139 amino acids
 (B) TYPE: amino acid
 (D) TOPOLOGY: linear

30 (ii) MOLECULE TYPE: protein

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:66:

Asn Leu Leu Glu Gln Asn Leu Asp Leu Val Leu Phe Phe Pro Val Ser
 1 5 10 15

35 Leu Tyr Pro Phe Ser Asn Thr Pro Lys Thr Pro Lys Phe Pro Trp Tyr
 20 25 30

Gly Ala Thr His Leu Tyr Asn Lys Asn Val Phe Cys Glu Ala Val Arg
 35 40 45

Arg Cys Ala Ser Lys His Ala Ile Glu Ala Ala Ser Ser Ile Trp Asp
 50 55 60

40 Leu Asn Pro Pro Gln Ser Asn Glu Glu Leu Glu Lys Phe Leu Thr Lys
 65 70 75 80

Ala Val Ile Arg Ile Thr Ile Ser Glu Gly Leu Gly Ile Leu Lys Thr
 85 90 95

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Ala Asn Thr Pro Phe Ser Cys Gly Gln Lys Thr Ala Asp Asp Val Lys
 100 105 110
 Phe Lys Ser His Ser Ser Arg Arg Ser Lys Ser Gln Ser Arg Ser Arg
 115 120 125
 5 His Ser Arg Gly Asp Phe Asp Asp Ser Ser Asp
 130 135

(2) INFORMATION FOR SEQ ID NO:67:

(i) SEQUENCE CHARACTERISTICS:

- 10 (A) LENGTH: 1269 base pairs
 (B) TYPE: nucleic acid
 (C) STRANDEDNESS: single
 (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: cDNA

(ix) FEATURE:

- 15 (A) NAME/KEY: CDS
 (B) LOCATION: 1..1266

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:67:

ATG GAA TTT AAC ATA GAA GAC TTT GAT GAA TCG TTG CTA GGG GCT GTT 48
 Met Glu Phe Asn Ile Glu Asp Phe Asp Glu Ser Leu Leu Gly Ala Val
 20 1 5 10 15
 GGA TAC TCT AAT AAT TTT AAA GGT AAG CAA AGC CTT CCG ATT AAG GCT 96
 Gly Tyr Ser Asn Asn Phe Lys Gly Lys Gln Ser Leu Pro Ile Lys Ala
 20 25 30
 TCT AGT CCA TCA TCG TTA ATT AAA AAT CTT TTA GAT GAA TTA AAT TTT 144
 Ser Ser Pro Ser Ser Leu Ile Lys Asn Leu Leu Asp Glu Leu Asn Phe
 25 35 40 45
 CCG GAA GGT CCT AGT TTA TTA TCT TCT ATG GAA AAA TGG AAT GAG GAT 192
 Pro Glu Gly Pro Ser Leu Leu Ser Ser Met Glu Lys Trp Asn Glu Asp
 50 55 60
 TTA TTT TCC TGC ATC CCA AGA TTT TTG GAA ATC TAC ATT GAA AAT TCT 240
 Leu Phe Ser Cys Ile Pro Arg Phe Leu Glu Ile Tyr Ile Glu Asn Ser
 30 65 70 75 80
 ATT TTA TCA ACA TCT GTC GAT GAG GTT ATT AAA AAT TTG GAT AAT TCT 288
 Ile Leu Ser Thr Ser Val Asp Glu Val Ile Lys Asn Leu Asp Asn Ser
 35 85 90 95
 TTA AAT TAT GAT GAT GTA ATC GAT TTT CAG GTC CAT GGA CCT GAA ACA 336
 Leu Asn Tyr Asp Asp Val Ile Asp Phe Gln Val His Gly Pro Glu Thr
 100 105 110
 TTT CCA AAA ACC CCA TTA TTG GAA GAG GAA TTG GAA AAT TAT GTA ACA 384
 Phe Pro Lys Thr Pro Leu Leu Glu Glu Leu Glu Asn Tyr Val Thr
 40 115 120 125

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	TCT GTT CAA AAG TAT TTT TTA TCT GAA CTT AAA GCT AGA GAA GTT ACA Ser Val Gln Lys Tyr Phe Leu Ser Glu Leu Lys Ala Arg Glu Val Thr 130 135 140	432
5	TAT TCA TTT CTA CTC ACT AAA TAT TGT AAA GCG CTT TTG TTA TAT CTT Tyr Ser Phe Leu Leu Thr Lys Tyr Cys Lys Ala Leu Leu Leu Tyr Leu 145 150 155 160	480
	CGC TAT AAT ACA AAA TCA TCG ATT AAG GGT AAT AAG GAC ATA AAT GCA Arg Tyr Asn Thr Lys Ser Ser Ile Lys gly Asn Lys Asp Ile Asn Ala 165 170 175	528
10	TTT CAC CAA AAA TTT AAA CAA AAT GTG CGG GAA CGT TAT TAT AGA GAG Phe His Gln Lys Phe Lys Gln Asn Val Arg Glu Arg Tyr Arg Glu 180 185 190	576
15	GTT GCA AAT ATA GCA CGA TTG TTA TAT TTA CAT CTG TAT TTA TCA GTA Val Ala Asn Ile Ala Arg Leu Leu Tyr Leu His Leu Tyr Leu Ser Val 195 200 205	624
	ACT AGG GAA GTG TCT TGG AAA CTA CAT GCC GAT CAA GTA TTA CTC CAA Thr Arg Glu Val Ser Trp Lys Leu His Ala Asp Gln Val Leu Leu Gln 210 215 220	672
20	AGT GTT TTT GTT TCA TTG TCT TAT TCT TGG AGC CAC CGA CGA CAG TTT Ser Val Phe Val Ser Leu Ser Tyr Ser Trp Ser His Arg Arg Gln Phe 225 230 235 240	720
	GAG TGT ATA TTT CAT CCA ATT TTA TTT AAT CAT GGT ATT GTG AAT TTG Glu Cys Ile Phe His Pro Ile Leu Phe Asn His Gly Ile Val Asn Leu 245 250 255	768
25	GAA AAT AAC CCT TTG ACA TTT AAG GAA CTA CAA AAA ATA AAT TAT AGA Glu Asn Asn Pro Leu Thr Phe Lys Glu Leu Gln Lys Ile Asn Tyr Arg 260 265 270	816
30	CGT CAT ATT CTT GGT TTA CCA TTG ATT AGA GCT GGA TTG GTA GAA GAA Arg His Ile Leu Gly Leu Pro Leu Ile Arg Ala Gly Leu Val Glu Glu 275 280 285	864
	GAT AAT CAA CCT TTA ATG ATA CCT CCA GAG TTT TCC AGT AAA CTA CCT Asp Asn Gln Pro Leu Met Ile Pro Pro Glu Phe Ser Ser Lys Leu Pro 290 295 300	912
35	CGA ACA ATA GGA TTT TTA ACT CAA CAA ATT AGA GCC AAA ATG GAA GCT Arg Thr Ile Gly Phe Leu Thr Gln Gln Ile Arg Ala Lys Met Glu Ala 305 310 315 320	960
	TAT TCA GAC AAC CAT CCT GTA ACA CCA AAA TTT CCT CGT ATT GAA CAT Tyr Ser Asp Asn His Pro Val Thr Pro Lys Phe Pro Arg Ile Glu His 325 330 335	1008
40	TCA TAT GCT AAA CCT ATA GAT CCT ATT AAC TAT GGA ACT ACA ATA GAA Ser Tyr Ala Lys Pro Ile Asp Pro Ile Asn Tyr Gly Thr Thr Ile Glu 340 345 350	1056
45	GCT ATG ATG GAC CCA CCA TCA CCA AGC GCT ATT TTA CCA GGA GAT CCA Ala Met Met Asp Pro Pro Ser Pro Ser Ala Ile Leu Pro Gly Asp Pro 355 360 365	1104

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	AAT CCT GAA ATT AAT GTT AAG GTT AAA AGC ACT GTT TCA TCC TTT CAA	1152
	Asn Pro Glu Ile Asn Val Lys Val Lys Ser Thr Val Ser Ser Phe Gln	
	370 375 380	
5	ATT CCA CCT AAT ATT ACC TTG GAA GAA CTG GAG TCA GGT GAA TAT AAT	1200
	Ile Pro Pro Asn Ile Thr Leu Glu Glu Leu Glu Ser Gly Glu Tyr Asn	
	385 390 395 400	
	TTA TTT ACA GAT GGT GTT ACC TAC AAT GAT ATA CCT GAA AAT GAG TTA	1248
	Leu Phe Thr Asp Gly Val Thr Tyr Asn Asp Ile Pro Glu Asn Glu Leu	
	405 410 415	
10	AAT AAA ATG TTT CAA TTA TAA	1269
	Asn Lys Met Phe Gln Leu	
	420	

(2) INFORMATION FOR SEQ ID NO:68:

(i) SEQUENCE CHARACTERISTICS:

15 (A) LENGTH: 422 amino acids

(B) TYPE: amino acid

(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:68:

20	Met Glu Phe Asn Ile Glu Asp Phe Asp Glu Ser Leu Leu Gly Ala Val	
	1 5 10 15	
	Gly Tyr Ser Asn Asn Phe Lys Gly Lys Gln Ser Leu Pro Ile Lys Ala	
	20 25 30	
25	Ser Ser Pro Ser Ser Leu Ile Lys Asn Leu Leu Asp Glu Leu Asn Phe	
	35 40 45	
	Pro Glu Gly Pro Ser Leu Leu Ser Ser Met Glu Lys Trp Asn Glu Asp	
	50 55 60	
	Leu Phe Ser Cys Ile Pro Arg Phe Leu Glu Ile Tyr Ile Glu Asn Ser	
	65 70 75 80	
30	Ile Leu Ser Thr Ser Val Asp Glu Val Ile Lys Asn Leu Asp Asn Ser	
	85 90 95	
	Leu Asn Tyr Asp Asp Val Ile Asp Phe Gln Val His Gly Pro Glu Thr	
	100 105 110	
35	Phe Pro Lys Thr Pro Leu Leu Glu Glu Glu Leu Glu Asn Tyr Val Thr	
	115 120 125	
	Ser Val Gln Lys Tyr Phe Leu Ser Glu Leu Lys Ala Arg Glu Val Thr	
	130 135 140	
	Tyr Ser Phe Leu Leu Thr Lys Tyr Cys Lys Ala Leu Leu Leu Tyr Leu	
	145 150 155 160	
40	Arg Tyr Asn Thr Lys Ser Ser Ile Lys Gly Asn Lys Asp Ile Asn Ala	
	165 170 175	

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Phe His Gln Lys Phe Lys Gln Asn Val Arg Glu Arg Tyr Tyr Arg Glu
 180 185 190
 Val Ala Asn Ile Ala Arg Leu Leu Tyr Leu His Leu Tyr Leu Ser Val
 195 200 205
 5 Thr Arg Glu Val Ser Trp Lys Leu His Ala Asp Gln Val Leu Leu Gln
 210 215 220
 Ser Val Phe Val Ser Leu Ser Tyr Ser Trp Ser His Arg Arg Gln Phe
 225 230 235 240
 10 Glu Cys Ile Phe His Pro Ile Leu Phe Asn His Gly Ile Val Asn Leu
 245 250 255
 Glu Asn Asn Pro Leu Thr Phe Lys Glu Leu Gln Lys Ile Asn Tyr Arg
 260 265 270
 Arg His Ile Leu Gly Leu Pro Leu Ile Arg Ala Gly Leu Val Glu Glu
 275 280 285
 15 Asp Asn Gln Pro Leu Met Ile Pro Pro Glu Phe Ser Ser Lys Leu Pro
 290 295 300
 Arg Thr Ile Gly Phe Leu Thr Gln Gln Ile Arg Ala Lys Met Glu Ala
 305 310 315 320
 20 Tyr Ser Asp Asn His Pro Val Thr Pro Lys Phe Pro Arg Ile Glu His
 325 330 335
 Ser Tyr Ala Lys Pro Ile Asp Pro Ile Asn Tyr Gly Thr Thr Ile Glu
 340 345 350
 Ala Met Met Asp Pro Pro Ser Pro Ser Ala Ile Leu Pro Gly Asp Pro
 355 360 365
 25 Asn Pro Glu Ile Asn Val Lys Val Lys Ser Thr Val Ser Ser Phe Gln
 370 375 380
 Ile Pro Pro Asn Ile Thr Leu Glu Glu Leu Glu Ser Gly Glu Tyr Asn
 385 390 395 400
 30 Leu Phe Thr Asp Gly Val Thr Tyr Asn Asp Ile Pro Glu Asn Glu Leu
 405 410 415
 Asn Lys Met Phe Gln Leu
 420

(2) INFORMATION FOR SEQ ID NO:69:

- 35 (i) SEQUENCE CHARACTERISTICS:
 (A) LENGTH: 626 base pairs
 (B) TYPE: nucleic acid
 (C) STRANDEDNESS: single
 (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

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(xi) SEQUENCE DESCRIPTION: SEQ ID NO:69:

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AAGCTTATTG TCCGTGCTTT GCTGATGGTT TCTGGAAC TG TCCCCCTAT TTTAAGATAC      60
AATATAGAAG GAGTAAATG TAAACTAAGT TCATGGAACC TTACAACCGC TGCCTTTTCT      120
ACCCCATCTA CTGTTAATGA AAAAATTAAT GATGTGGTTG AAACAAC TTC AAACCCCTTG      180
5 AGTAAACTAA AAAAGAATTG TAATAGAGAA AAGGAAC TTT CAAATCAAA AAGTATAGTT      240
TCAGGAGGTG TTAGTGTTCA TGGATTAGAA CAAAGCTGTA GCTCTCATAC CTCCAATTTT      300
CAGAAATGCC CAGATAAAAC CAAGTCATCA AATAAAATG ATGCAACAA ACGTGAGTCA      360
AGGGGAAAAA GAAAGTCTGA ACCAATAGTA AATAGTTTGG GAGTCGCAA AGTTTCATCC      420
AACCCACCGC CATCAAAAA GAGAGCATCA TCACAATCTA CCGGACCACT TGGACCAATG      480
10 CCAGAAGAAG GACCGACCCC CAAGGGTGGT TTAGAAGAA TACCTTCTGG GGATTGTCAT      540
ACCCAGTTC CAAGGACAT TGTAATCT ATCTACTGTT CACCAGAGAC TGTGAAAGAA      600
TTACAGATC ATCCATTGTT TCCTGA                                         626

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(2) INFORMATION FOR SEQ ID NO:70:

- (i) SEQUENCE CHARACTERISTICS:
- (A) LENGTH: 626 base pairs
 - (B) TYPE: nucleic acid
 - (C) STRANDEDNESS: single
 - (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

20 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:70:

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TCAGGAACA ATGGATGATC TGTTAATTCT TTCACAGTCT CTGGTGAACA GTAGATAGAT      60
TTTACAATGT CCCTTGGAAC TGGGGTATGA CAATCCCCAG AAGGTATTCT TCTAAAACCA      120
CCCTTGGGGG TCGGTCCTTC TTCTGGCATT GGTCCAAGTG GTCCGGTAGA TTGTGATGAT      180
GCTCTCTTTT TTGATGGCGG TGGGTGGAT GAAACTTTTG CGACTCCAAA ACTATTACT      240
25 ATTGGTTCAG ACTTCTTTT TCCCCTTGAC TCACGTTTGT TTGCATCATT TTTATTTGAT      300
GACTTGGTTT TATCTGGGCA TTTCTGAAAA TTGGAGGTAT GAGAGCTACA GCTTTGTTCT      360
AATCCATGAA CACTAACACC TCCTGAAACT ATACTTTTGG ATTTTGAAAG TTCCTTTTCT      420
CTATTACAAT TCTTTTITAG TTTACTCAA GGGTTTGAAG TTGTTTCAAC CACATCATT      480
ATTTTTTCAT TAACAGTAGA TGGGGTAGAA AAGGCAGCGG TTGTAAGGTT CCATGAACCT      540
30 AGTTTACATT TTAATCCTTC TATATTGTAT CTAAAATAG GGGAGACAGT TCCAGAAACC      600
ATCAGCAAAG CACGGACAAT AAGCTT                                         626

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(2) INFORMATION FOR SEQ ID NO:71:

(i) SEQUENCE CHARACTERISTICS:

- 5 (A) LENGTH: 624 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: cDNA

(ix) FEATURE:

- 10 (A) NAME/KEY: CDS
(B) LOCATION: 1..624

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:71:

	AAG CTT ATT GTC CGT GCT TTG CTG ATG GTT TCT GGA ACT GTC TCC OCT	48
	Lys Leu Ile Val Arg Ala Leu Leu Met Val Ser Gly Thr Val Ser Pro	
	1 5 10 15	
15	ATT TTA AGA TAC AAT ATA GAA GGA GTA AAA TGT AAA CTA AGT TCA TGG	96
	Ile Leu Arg Tyr Asn Ile Glu Gly Val Lys Cys Lys Leu Ser Ser Trp	
	20 25 30	
20	AAC CTT ACA ACC GCT GCC TTT TCT ACC CCA TCT ACT GTT AAT GAA AAA	144
	Asn Leu Thr Thr Ala Ala Phe Ser Thr Pro Ser Thr Val Asn Glu Lys	
	35 40 45	
	ATT AAT GAT GTG GTT GAA ACA ACT TCA AAC CCT TTG AGT AAA CTA AAA	192
	Ile Asn Asp Val Val Glu Thr Thr Ser Asn Pro Leu Ser Lys Leu Lys	
	50 55 60	
25	AAG AAT TGT AAT AGA GAA AAG GAA CTT TCA AAA TCA AAA AGT ATA GTT	240
	Lys Asn Cys Asn Arg Glu Lys Glu Leu Ser Lys Ser Lys Ser Ile Val	
	65 70 75 80	
	TCA GGA GGT GTT AGT GTT CAT GGA TTA GAA CAA AGC TGT AGC TCT CAT	288
	Ser Gly Gly Val Ser Val His Gly Leu Glu Gln Ser Cys Ser Ser His	
	85 90 95	
30	ACC TCC AAT TTT CAG AAA TGC CCA GAT AAA ACC AAG TCA TCA AAT AAA	336
	Thr Ser Asn Phe Gln Lys Cys Pro Asp Lys Thr Lys Ser Ser Asn Lys	
	100 105 110	
35	AAT GAT GCA AAC AAA CGT GAG TCA AGG GGA AAA AGA AAG TCT GAA CCA	384
	Asn Asp Ala Asn Lys Arg Glu Ser Arg Gly Lys Arg Lys Ser Glu Pro	
	115 120 125	
	ATA GTA AAT AGT TTT GGA GTC GCA AAA GTT TCA TCC AAC CCA CCG CCA	432
	Ile Val Asn Ser Phe Gly Val Ala Lys Val Ser Ser Asn Pro Pro Pro	
	130 135 140	
40	TCA AAA AAG AGA GCA TCA TCA CAA TCT ACC GGA CCA CTT GGA CCA ATG	480
	Ser Lys Lys Arg Ala Ser Ser Gln Ser Thr Gly Pro Leu Gly Pro Met	
	145 150 155 160	
	CCA GAA GAA GGA CCG ACC CCC AAG GGT GGT TTT AGA AGA ATA CCT TCT	528
	Pro Glu Glu Gly Pro Thr Pro Lys Gly Gly Phe Arg Arg Ile Pro Ser	
	165 170 175	

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GGG GAT TGT CAT ACC CCA GTT CCA AGG GAC ATT GTA AAA TCT ATC TAC 576
 Gly Asp Cys His Thr Pro Val Pro Arg Asp Ile Val Lys Ser Ile Tyr
 180 185 190

TGT TCA CCA GAG ACT GTG AAA GAA TTA ACA GAT CAT CCA TTG TTT CCT 624
 5 Cys Ser Pro Glu Thr Val Lys Glu Leu Thr Asp His Pro Leu Phe Pro
 195 200 205

(2) INFORMATION FOR SEQ ID NO:72:

(i) SEQUENCE CHARACTERISTICS:
 (A) LENGTH: 208 amino acids
 (B) TYPE: amino acid
 (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:72: -

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

20 Ile Asn Asp Val Val Glu Thr Thr Ser Asn Pro Leu Ser Lys Leu Lys
 50 55 60
 Lys Asn Cys Asn Arg Glu Lys Glu Leu Ser Lys Ser Lys Ser Ile Val
 65 70 75 80

25 Ser Gly Gly Val Ser Val His Gly Leu Glu Gln Ser Cys Ser Ser His
 85 90 95
 Thr Ser Asn Phe Gln Lys Cys Pro Asp Lys Thr Lys Ser Ser Asn Lys
 100 105 110

Asn Asp Ala Asn Lys Arg Glu Ser Arg Gly Lys Arg Lys Ser Glu Pro
 115 120 125

30 Ile Val Asn Ser Phe Gly Val Ala Lys Val Ser Ser Asn Pro Pro Pro
 130 135 140
 Ser Lys Lys Arg Ala Ser Ser Gln Ser Thr Gly Pro Leu Gly Pro Met
 145 150 155 160

35 Pro Glu Glu Gly Pro Thr Pro Lys Gly Gly Phe Arg Arg Ile Pro Ser
 165 170 175
 Gly Asp Cys His Thr Pro Val Pro Arg Asp Ile Val Lys Ser Ile Tyr
 180 185 190

Cys Ser Pro Glu Thr Val Lys Glu Leu Thr Asp His Pro Leu Phe Pro
 195 200 205

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(2) INFORMATION FOR SEQ ID NO:73:

(i) SEQUENCE CHARACTERISTICS:

- 5 (A) LENGTH: 655 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:73:

AAGCTTGACT TGTGATTAA AGTTAAAGAA TTGTTTAAACA AATTAACATT CTTAGGTCTT 60
10 CCTCTAGGTC GTTTAATAAC AGGCTCATTT TTGTTGTCTG TAGAGTCATA CCTGTTTTTCG 120
AGTTTGTGTT TAGAAGTCAT CATAACAAG AAGTAGTTTC AGTCAAACCG GTTTTTTGAG 180
ATATACAACC AAGTGGTGGT GGAGGTAATA TAGGAGCTTC TGGTGAAGC TGTGATGGAT 240
AAAATAATCT GTCTATTATA TCAAAAAATT TGGTTTTTAA ACCTTTGGGT GTATTTATTT 300
TCATAATATC ATCAGCCAAT CCCC GGAGAG CTATAAATGG ATTAACCCAA AATACATCAT 360
15 TCGTTGATTT GAACCATAAA ATGATTCTTA TTGGGTTACA ATCCGTTCTT ATTATAATTC 420
CAGAAAGGTT TTTTATATCT TTATTTATTT TTTTATATAT ATTTTTTCTT ATTTGATGAT 480
TACGGCATGG TCCTGAAGT AGTATATTAA TGTGTTTATA TTGATTTTAA CTCGACGGAA 540
GCATGGTTAA AATATCTTTT ATATACGAAG AAACAATTAG AATTATTAAT GAATTTATTA 600
AACCCCATCT TCTAAAATTG TGGAGAATAT GAAAAATAT CCGTTTTATA TACAA 655

20 (2) INFORMATION FOR SEQ ID NO:74:

(i) SEQUENCE CHARACTERISTICS:

- 25 (A) LENGTH: 655 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:74:

TTGTATATAA AACGGAATAT TTTTCATATT CTCCACAATT TTAGAAGATG GGGTTTAATA 60
AATTCATTAA TAATTCTAAT TGTTTCTTCG TATATAAAG ATATTTTAAC CATGCTTCCG 120
30 TCGAGTAAAA ATCAATATAA CAACATTAAT ATACTACTTC AAGGACCATG CCGTAATCAT 180
CAAATAGAAA AAAATATATA TAAAAAATA AATAAAGATA TAAAAACCT TTCTGGAATT 240
ATAATAAGAA CGGATTGTAA CCAATAGAA ATCATTTTAT GGTTCAAATC AACGAATGAT 300
GTATTTTGGG TTAATCCATT TATAGCTCTC CGGGGATTGG CTGATGATAT TATGAAAATA 360
AATACACCCA AAGGTTTAA AACCAAATTT TTTGATATAA TAGACAGATT ATTTTATCCA 420

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TCACAGCTTT CACCAGAAGC TCCTATATTA CCTCCACCAC CACTTGGTTG TATATCTCAA 480
 AAAACCGGTT TGA CTGAAC TACTTCTTGT TTATGATGAC TTCTAACAC AAACCTCGAAA 540
 ACAGGTATGA CTCTACAGAC AACAAAAATG AGCCTGTTAT TAAACGACCT AGAGGAAGAC 600
 CTAAGAATGT TAATTTGTTA AACAACTCTT TAACTTTAAT CAACAAGTCA AGCTT 655

5 (2) INFORMATION FOR SEQ ID NO:75:

- (i) SEQUENCE CHARACTERISTICS:
 (A) LENGTH: 516 base pairs
 (B) TYPE: nucleic acid
 (C) STRANDEDNESS: single
 (D) TOPOLOGY: linear

10

(ii) MOLECULE TYPE: cDNA

(ix) FEATURE:

- (A) NAME/KEY: CDS
 (B) LOCATION: 1..513

15 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:75:

TTG TAT ATA AAA CGG AAT ATT TTT CAT ATT CTC CAC AAT TTT AGA AGA 48
 Leu Tyr Ile Lys Arg Asn Ile Phe His Ile Leu His Asn Phe Arg Arg
 1 5 10 15

TGG GGT TTA ATA AAT TCA TTA ATA ATT CTA ATT GTT TCT TCG TAT ATA 96
 Trp Gly Leu Ile Asn Ser Leu Ile Ile Leu Ile Val Ser Ser Tyr Ile
 20 20 25 30

AAA GAT ATT TTA ACC ATG CTT CCG TCG AGT AAA AAT CAA TAT AAC AAC 144
 Lys Asp Ile Leu Thr Met Leu Pro Ser Ser Lys Asn Gln Tyr Asn Asn
 35 40 45

ATT AAT ATA CTA CTT CAA GGA CCA TGC CGT AAT CAT CAA ATA GAA AAA 192
 Ile Asn Ile Leu Leu Gln Gly Pro Cys Arg Asn His Gln Ile-Glu Lys
 50 55 60

AAT ATA TAT AAA AAA ATA AAT AAA GAT ATA AAA AAC CTT TCT GGA ATT 240
 Asn Ile Tyr Lys Lys Ile Asn Lys Asp Ile Lys Asn Leu Ser Gly Ile
 30 65 70 75 80

ATA ATA AGA ACG GAT TGT AAC CCA ATA GAA ATC ATT TTA TGG TTC AAA 288
 Ile Ile Arg Thr Asp Cys Asn Pro Ile Glu Ile Ile Leu Trp Phe Lys
 85 90 95

TCA ACG AAT GAT GTA TTT TGG GTT AAT CCA TTT ATA GCT CTC CGG GGA 336
 Ser Thr Asn Asp Val Phe Trp Val Asn Pro Phe Ile Ala Leu Arg Gly
 35 100 105 110

TTG GCT GAT GAT ATT ATG AAA ATA AAT ACA CCC AAA GGT TTA AAA ACC 384
 Leu Ala Asp Asp Ile Met Lys Ile Asn Thr Pro Lys Gly Leu Lys Thr
 115 120 125

AAA TTT TTT GAT ATA ATA GAC AGA TTA TTT TAT CCA TCA CAG CTT TCA 432
 Lys Phe Phe Asp Ile Ile Asp Arg Leu Phe Tyr Pro Ser Gln Leu Ser
 130 135 140

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CCA GAA GCT CCT ATA TTA CCT CCA CCA CCA CTT GGT TGT ATA TCT CAA 480
 Pro Glu Ala Pro Ile Leu Pro Pro Pro Pro Leu Gly Cys Ile Ser Gln
 145 150 155 160

AAA ACC GGT TTG ACT GAA ACT ACT TCT TGT TTA TGA 516
 5 Lys Thr Gly Leu Thr Glu Thr Thr Ser Cys Leu
 165 170

(2). INFORMATION FOR SEQ ID NO:76:

(i) SEQUENCE CHARACTERISTICS:
 (A) LENGTH: 171 amino acids
 (B) TYPE: amino acid
 (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:76:

15 Leu Tyr Ile Lys Arg Asn Ile Phe His Ile Leu His Asn Phe Arg Arg
 1 5 10 15
 Trp Gly Leu Ile Asn Ser Leu Ile Ile Leu Ile Val Ser Ser Tyr Ile
 20 25 30
 Lys Asp Ile Leu Thr Met Leu Pro Ser Ser Lys Asn Gln Tyr Asn Asn
 35 40 45
 20 Ile Asn Ile Leu Leu Gln Gly Pro Cys Arg Asn His Gln Ile Glu Lys
 50 55 60
 Asn Ile Tyr Lys Lys Ile Asn Lys Asp Ile Lys Asn Leu Ser Gly Ile
 65 70 75 80
 25 Ile Ile Arg Thr Asp Cys Asn Pro Ile Glu Ile Ile Leu Trp Phe Lys
 85 90 95
 Ser Thr Asn Asp Val Phe Trp Val Asn Pro Phe Ile Ala Leu Arg Gly
 100 105 110
 Leu Ala Asp Asp Ile Met Lys Ile Asn Thr Pro Lys Gly Leu Lys Thr
 115 120 125
 30 Lys Phe Phe Asp Ile Ile Asp Arg Leu Phe Tyr Pro Ser Gln Leu Ser
 130 135 140
 Pro Glu Ala Pro Ile Leu Pro Pro Pro Pro Leu Gly Cys Ile Ser Gln
 145 150 155 160
 35 Lys Thr Gly Leu Thr Glu Thr Thr Ser Cys Leu
 165 170

(2) INFORMATION FOR SEQ ID NO:77:

(i) SEQUENCE CHARACTERISTICS:
 (A) LENGTH: 1823 base pairs
 (B) TYPE: nucleic acid
 (C) STRANDEDNESS: single
 (D) TOPOLOGY: linear

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(ii). MOLECULE TYPE: DNA (genomic)

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:77:

	GCTTTGGACG AGATTTAGGC TGGGAAATTG TTAGTTGAGC ATATTGATTT TCGCATAGTT	60
	CATAAATATG GTCTTCGTCA TCATCATCAC AAACCTGATC ATACACATTT TTATACTCAA	120
5	AAGTTGGAAT AGTTCGTTCG TAAATAGGAT TTCCCTTTC AATTCGTTGA GATGACTTTC	180
	TTCTTACACC GTTTGTCTC TTAATAGTAG CATATATCGG TTCATCTTCA TATGATGAAA	240
	TACGACGGCT GGCCATAATT CTATAAATAA GAGAAGGTTA AAAATAAGTT GCTTAACTGG	300
	TTTAGGCAAC TAATAAATA TCTCTAAAC ATACCCCTT TTATATAAAT CTGTGGATTA	360
	GTTTCGGATT TCGAAACCCA CCTTCTTATT AGTGTTCAT CTGACGAAGT TCCCGACTAA	420
10	CCATTCTCAA ACAGGTCTA TAAGAATAAC AAAATATCGC AACCCTACT GTTACCAGGG	480
	ATATATAAAA CAAATAGCG GAAGTTGAAG GCGTATTAAT ATTGATACCC CTAGCTGAAC	540
	AACTAGAGCT CCAAACTGT CTCCTAGCTT CAGCTCTAGA ATAATCTAAA CGATCATCGT	600
	CGAAGCATA AACTGAAAA ATAATGGATA GTAAAAATAC TATCTCCATT GCTTTGATTG	660
	AAAAACAAA ACCTTTTAAT TGGACTATCA ACAAATAAA TGAAAGCCTT CTGATGACCA	720
15	ACAACGAAGA AATAAAGTTG ACTGAAAATT TTAAAAATAC GGGCACCTTT TATAGCAAGA	780
	TAATTGACCT TGAATCCGA ACTGCTACAT CTAGTCAATA TGCAGTCTTT GTTACACAAA	840
	TGTGTCTGA TGACGAAAAT ATGAATAATA CAAATATTTT TGTATTAAAT GGTGTTATTG	900
	ATTCTGGATA TAGAGGAATA GTTAAAGCGT TAGTTTATTA CCATCCAACT GTAGAAAAAT	960
	TAAATCCATA CGATCTTAAA ATTAACTTC CACTAATAGA ACTTAGTAAA GATTTAATAC	1020
20	CACTATCACC TAGTTTACAT AGTTATAGTG AATTATATAA TTTTTTAAT GTCTTTAATA	1080
	AAAAACGTGA TGAAGATGCT GGTATGATA TACCATCTCC AAATTTAGTT CAAATAAAAC	1140
	CGGGATATAG TTACCTTTTT TGTCTTCCTA TTTTTCRAAT AGAAATGAAA AACCACCAA	1200
	TCGCTTGAT TTTTGGTAGA TCATCCTTAA ATTCAAGCGG AATAATTGTT CTTCCAACCTA	1260
	TATGGAAACC AAAACAATT TGTCAATTTT TTATTAATAA TATATCCTCT AAACTGTAA	1320
25	CTATAGAAAA AGGTCAGAGA ATAGCTCAGT TAGTTCTTTT AAAAAACAAT CAACCACTAT	1380
	GGTTACAACC ACAAATTAAT TGTCAATCTT TATTCCAAA GTCAACTAT TTAAGCTTAT	1440
	CAATCGAGA ATGTGATATG TGGAGTTTA CAGAAGATCT GAATTTTGAA GCACCGAAAA	1500
	GTTTACGAGG AATAAATGGA TTTGGATCCA CGGGATTGTA AAATTCGTTA ATAAAGTTAT	1560
	ATTTAAAGTG CCAAACTTTC ACGTGTCATT TTTTGGGAC CGTTTCTTTT TTGTTTAGTC	1620
30	GATAAATAT TTTCAGTTTC CATAGAAGTT ATTAGAGGTT CTGTATCTAG TATATCTGTA	1680
	GAATTATTTT CATCATATTT AACGGTTTGA AGAGATAAGG GTTTGTGTT ATTAGAATCT	1740

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ATACCAAGGG TTTTCTCTAA AACCGCTACA TCTGCCATAA CAATATTATT TTCTGAAGTC 1800
ATTTTATGG CTTGGGCACC ACC 1823

(2) INFORMATION FOR SEQ ID NO:78:

- 5 (i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 1823 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

- 10 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:78:

GGTGGTGCCC AAGCCATAAA AATGACTTCA GAAAATAATA TTGTTATGGC AGATGTAGCG 60
GTTTGTAGAAA AAACCCCTGG TATAGATTCT AATACAACAA AACCCCTTATC TCTTCAAACC 120
GTTAAATATG ATGAAAATAA TTCTACAGAT ATACTAGATA CAGAACCTCT AATAAGTTCT 180
ATGGAAACTG AAAATATTTT ATCGACTAAA CAAAAAGAA ACGGTCCCAA AAAAATGACA 240
15 CGTGAAAGTT TGGCACTTTA AATATAACTT TATTAACGAA TTTTACAATC CCGTGGATCC 300
AAATCCATTT ATTCTCGTA AACTTTTCGG TGCTTCAAAA TTCAGATCTT CTGTAAACTT 360
CCACATATCA CATTCTCGAT TTGATAAGCT TAAATAGTTT GACTTTGGAA ATAAAGAATG 420
ACAATTAATT TGTGGTTGTA ACCATAGTGG TTGATTGTTT TTTAAAAGAA CTAAGTGGC 480
TATTCTCTGA CCTTTTCTA TAGTTACAGT TTTAGAGGAT ATATTTTAA TAAAAATTG 540
20 ACAAATTGTT TTTGGTTTCC ATATAGTTGG AAGAACAATT ATTCCGCTTG AATTAAGGA 600
TGATCTACCA AAAATACAAG CGATTGGTGG GTTTTTCATT TCTAATTGAA AATAGGAAG 660
ACAAAAAGG TAACTATATC CCGGTTTAT TTGAACATAA TTTGGAGATG -GTATATCATA 720
ACCAGCATCT TCATCAGT TTTTATTAAA GACATTAAAA AATTATATA ATTCACTATA 780
ACTATGTAAA CTAGGTGATA GTGGTATTAA ATCTTTACTA AGTTCTATTA GTGGAAGTTT 840
25 AATTTTAAGA TCGTATGGAT TTAATTTTTC TACAGTTGGA TGGTAATAAA CTAACGCTTT 900
AACTATTCCT CTATATCCAG AATCAATAAC ACCATTAATA AAAAAATAT TTGTATTATT 960
CATATTTTCG TCATCAGAAC ACATTGTGT AACAAGACT GCATATTGAC TAGATGTAGC 1020
AGTTCGGATT TCAAGGTCAA TTATCTGCT ATAAAAGGTG CCCGTATTTT TAAAAATTTT 1080
AGTCAAGTTT ATTTCTTCGT TGTGGTCAT CAGAAGGCTT TCATTTATTT TGTGATAGT 1140
30 CCAATTAAAA GTTTTTGT TTTCAATCAA AGCAATGGAG ATAGTATTTT TACTATCCAT 1200
TATTTTTC GTTTATGCCT TCGACGATGA TCGTTTAGAT TATTCTAGAG CTGAAGCTAG 1260
GAGACAGTTT TGGAGCTCTA GTTGTTCAGC TAGGGGTATC AATATTAATA CGCCTTCAAC 1320

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TTCCGCTATT TTGTTTTATA TATCCCTGGT AACAGTAGGG GTTGCGATAT TTTGTTATTC 1380
 TTATAGAACC TGTTTGAGAA TGTTAGTCG GGAACCTCGT CAGATGCAAC ACTAATAAGA 1440
 AGGTGGGTTT CGAAATCCGA AACTAATCCA CAGATTTATA TAAAGGGGG TATGTTTATG 1500
 AGATATTTTA TTAGTTCCT AAACCAGTTA AGCAACTTAT TTTAACCTT CTCTTATTTA 1560
 5 TAGAATTATG GCCAGCCGTC GTATTCATC ATATGAAGAT GAACCGATAT ATGCTACTAT 1620
 TAAGAGACAA AACGGTGTA GAAGAAAGTC ATCTCAACGA ATTGAAAGGG AAAATCCTAT 1680
 TTACGAACGA ACTATCCAA CTTTGAGTA TAAAAATGTG TATGATCAAG TTTGTGATGA 1740
 TGATGACGAA GACCATATTT ATGAACATG CGAAAATCAA TATGCTCAAC TAACAATTTC 1800
 CCAGCCTAAA TCTCGTCCAA AGC 1823

10 (2) INFORMATION FOR SEQ ID NO:79:

- (i) SEQUENCE CHARACTERISTICS:
 (A) LENGTH: 918 base pairs
 (B) TYPE: nucleic acid
 (C) STRANDEDNESS: single
 15 (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: cDNA

- (ix) FEATURE:
 (A) NAME/KEY: CDS
 (B) LOCATION: 1..915

20 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:79:

ATG GAT AGT AAA AAT ACT ATC TCC ATT GCT TTG ATT GAA AAA CAA AAA 48
 Met Asp Ser Lys Asn Thr Ile Ser Ile Ala Leu Ile Glu Lys Gln Lys
 1 5 10 15
 CCT TTT AAT TGG ACT ATC AAC AAA ATA AAT GAA AGC CTT CTG ATG ACC 96
 25 Pro Phe Asn Trp Thr Ile Asn Lys Ile Asn Glu Ser Leu Leu Met Thr
 20 25 30
 AAC AAC GAA GAA ATA AAC TTG ACT GAA AAT TTT AAA AAT ACG GGC ACC 144
 Asn Asn Glu Glu Ile Asn Leu Thr Glu Asn Phe Lys Asn Thr Gly Thr
 35 40 45
 30 TTT TAT AGC AAG ATA ATT GAC CTT GAA ATC CGA ACT GCT ACA TCT AGT 192
 Phe Tyr Ser Lys Ile Ile Asp Leu Glu Ile Arg Thr Ala Thr Ser Ser
 50 55 60
 CAA TAT GCA GTC TTT GTT ACA CAA ATG TGT TCT GAT GAC GAA AAT ATG 240
 35 Gln Tyr Ala Val Phe Val Thr Gln Met Cys Ser Asp Asp Glu Asn Met
 65 70 75 80
 AAT AAT ACA AAT ATT TTT GTT ATT AAT GGT GTT ATT GAT TCT GGA TAT 288
 Asn Asn Thr Asn Ile Phe Val Ile Asn Gly Val Ile Asp Ser Gly Tyr
 85 90 95

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	AGA GGA ATA GTT AAA GCG TTA GTT TAT TAC CAT CCA ACT GTA GAA AAA Arg Gly Ile Val Lys Ala Leu Val Tyr Tyr His Pro Thr Val Glu Lys 100 105 110	336
5	TTA AAT CCA TAC GAT CTT AAA ATT AAA CTT CCA CTA ATA GAA CTT AGT Leu Asn Pro Tyr Asp Leu Lys Ile Lys Leu Pro Leu Ile Glu Leu Ser 115 120 125	384
	AAA GAT TTA ATA CCA CTA TCA CCT AGT TTA CAT AGT TAT AGT GAA TTA Lys Asp Leu Ile Pro Leu Ser Pro Ser Leu His Ser Tyr Ser Glu Leu 130 135 140	432
10	TAT AAT TTT TTT AAT GTC TTT AAT AAA AAA CGT GAT GAA GAT GCT GGT Tyr Asn Phe Phe Asn Val Phe Asn Lys Lys Arg Asp Glu Asp Ala Gly 145 150 155 160	480
15	TAT GAT ATA CCA TCT CCA AAT TTA GTT CAA ATA AAA CCG GGA TAT AGT Tyr Asp Ile Pro Ser Pro Asn Leu Val Gln Ile Lys Pro Gly Tyr Ser 165 170 175	528
	TAC CTT TTT TGT CTT CCT ATT TTT CAA TTA GAA ATG AAA AAC CCA CCA Tyr Leu Phe Cys Leu Pro Ile Phe Gln Leu Glu Met Lys Asn Pro Pro 180 185 190	576
20	ATC GCT TGT ATT TTT GGT AGA TCA TCC TTA AAT TCA AGC GGA ATA ATT Ile Ala Cys Ile Phe Gly Arg Ser Ser Leu Asn Ser Ser Gly Ile Ile 195 200 205	624
	GTT CTT CCA ACT ATA TGG AAA CCA AAA ACA ATT TGT CAA TTT TTT ATT Val Leu Pro Thr Ile Trp Lys Pro Lys Thr Ile Cys Gln Phe Phe Ile 210 215 220	672
25	AAA AAT ATA TCC TCT AAA ACT GTA ACT ATA GAA AAA GGT CAG AGA ATA Lys Asn Ile Ser Ser Lys Thr Val Thr Ile Glu Lys Gly Gln Arg Ile 225 230 235 240	720
30	GCT CAG TTA GTT CTT TTA AAA AAC AAT CAA CCA CTA TGG TTA CAA CCA Ala Gln Leu Val Leu Leu Lys Asn Asn Gln Pro Leu Trp Leu Gln Pro 245 250 255	768
	CAA ATT AAT TGT CAT TCT TTA TTT CCA AAG TCA AAC TAT TTA AGC TTA Gln Ile Asn Cys His Ser Leu Phe Pro Lys Ser Asn Tyr Leu Ser Leu 260 265 270	816
35	TCA AAT CGA GAA TGT GAT ATG TGG AAG TTT ACA GAA GAT CTG AAT TTT Ser Asn Arg Glu Cys Asp Met Trp Lys Phe Thr Glu Asp Leu Asn Phe 275 280 285	864
	GAA GCA CCG AAA AGT TTA CGA GGA ATA AAT GGA TTT GGA TCC ACG GGA Glu Ala Pro Lys Ser Leu Arg Gly Ile Asn Gly Phe Gly Ser Thr Gly 290 295 300	912
40	TTG TAA Leu 305	918

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(2) INFORMATION FOR SEQ ID NO:80:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 305 amino acids

(B) TYPE: amino acid

(D) TOPOLOGY: linear

5

(ii) MOLECULE TYPE: protein

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:80:

```

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

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Ser Asn Arg Glu Cys Asp Met Trp Lys Phe Thr Glu Asp Leu Asn Phe
 275 280 285
 Glu Ala Pro Lys Ser Leu Arg Gly Ile Asn Gly Phe Gly Ser Thr Gly
 290 295 300

5 Leu
 305

(2) INFORMATION FOR SEQ ID NO:81:

(i) SEQUENCE CHARACTERISTICS:

- 10 (A) LENGTH: 261 base pairs
 (B) TYPE: nucleic acid
 (C) STRANDEDNESS: single
 (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: cDNA

(ix) FEATURE:

- 15 (A) NAME/KEY: CDS
 (B) LOCATION: 1..258

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:81:

20	ATG GAG ATA GTA TTT TTA CTA TCC ATT ATT TTT TCA GTT TAT GCC TTC	48
	Met Glu Ile Val Phe Leu Leu Ser Ile Ile Phe Ser Val Tyr Ala Phe	
	1 5 10 15	
	GAC GAT GAT CGT TTA GAT TAT TCT AGA GCT GAA GCT AGG AGA CAG TTT	96
	Asp Asp Asp Arg Leu Asp Tyr Ser Arg Ala Glu Ala Arg Arg Gln Phe	
	20 25 30	
25	TGG AGC TCT AGT TGT TCA GCT AGG GGT ATC AAT ATT AAT ACG CCT TCA	144
	Trp Ser Ser Ser Cys Ser Ala Arg Gly Ile Asn Ile Asn Thr Pro Ser	
	35 40 45	
	ACT TCC GCT ATT TTG TTT TAT ATA TCC CTG GTA ACA GTA GGG GTT GCG	192
	Thr Ser Ala Ile Leu Phe Tyr Ile Ser Leu Val Thr Val Gly Val Ala	
	50 55 60	
30	ATA TTT TGT TAT TCT TAT AGA ACC TGT TTG AGA ATG GTT AGT CGG GAA	240
	Ile Phe Cys Tyr Ser Tyr Arg Thr Cys Leu Arg Met Val Ser Arg Glu	
	65 70 75 80	
	CTT CGT CAG ATG CAA CAC TAA	261
35	Leu Arg Gln Met Gln His	
	85	

(2) INFORMATION FOR SEQ ID NO:82:

(i) SEQUENCE CHARACTERISTICS:

- 40 (A) LENGTH: 86 amino acids
 (B) TYPE: amino acid
 (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein

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(xi) SEQUENCE DESCRIPTION: SEQ ID NO:82:

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Met Glu Ile Val Phe Leu Leu Ser Ile Ile Phe Ser Val Tyr Ala Phe
 1           5           10           15
5 Asp Asp Asp Arg Leu Asp Tyr Ser Arg Ala Glu Ala Arg Arg Gln Phe
 20           25           30
Trp Ser Ser Ser Cys Ser Ala Arg Gly Ile Asn Ile Asn Thr Pro Ser
 35           40           45
Thr Ser Ala Ile Leu Phe Tyr Ile Ser Leu Val Thr Val Gly Val Ala
 50           55           60
10 Ile Phe Cys Tyr Ser Tyr Arg Thr Cys Leu Arg Met Val Ser Arg Glu
 65           70           75           80
Leu Arg Gln Met Gln His
                        85

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(2) INFORMATION FOR SEQ ID NO:83:

- 15 (i) SEQUENCE CHARACTERISTICS:
 (A) LENGTH: 255 base pairs
 (B) TYPE: nucleic acid
 (C) STRANDEDNESS: single
 (D) TOPOLOGY: linear
- 20 (ii) MOLECULE TYPE: cDNA
- (ix) FEATURE:
 (A) NAME/KEY: CDS
 (B) LOCATION: 1..255

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:83:

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25 ATG GCC AGC CGT CGT ATT TCA TCA TAT GAA GAT GAA CCG ATA TAT GCT      48
   Met Ala Ser Arg Arg Ile Ser Ser Tyr Glu Asp Glu Pro Ile-Tyr Ala
    1           5           10           15

   ACT ATT AAG AGA CAA AAC GGT GTA AGA AGA AAG TCA TCT CAA CGA ATT      96
   Thr Ile Lys Arg Gln Asn Gly Val Arg Arg Lys Ser Ser Gln Arg Ile
  30           20           25           30

   GAA AGG GAA AAT CCT ATT TAC GAA CGA ACT ATT CCA ACT TTT GAG TAT      144
   Glu Arg Glu Asn Pro Ile Tyr Glu Arg Thr Ile Pro Thr Phe Glu Tyr
           35           40           45

  35 AAA AAT GTG TAT GAT CAA GTT TGT GAT GAT GAT GAC GAA GAC CAT ATT      192
     Lys Asn Val Tyr Asp Gln Val Cys Asp Asp Asp Glu Asp His Ile
        50           55           60

   TAT GAA CTA TGC GAA AAT CAA TAT GCT CAA CTA ACA ATT TCC CAG CCT      240
   Tyr Glu Leu Cys Glu Asn Gln Tyr Ala Gln Leu Thr Ile Ser Gln Pro
        65           70           75           80

  40 AAA TCT CGT CCA AAG
     Lys Ser Arg Pro Lys
        85

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(2) INFORMATION FOR SEQ ID NO:84:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 85 amino acids
 (B) TYPE: amino acid
 (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:84:

Met Ala Ser Arg Arg Ile Ser Ser Tyr Glu Asp Glu Pro Ile Tyr Ala
 1 5 10 15
 10 Thr Ile Lys Arg Gln Asn Gly Val Arg Arg Lys Ser Ser Gln Arg Ile
 20 25 30
 Glu Arg Glu Asn Pro Ile Tyr Glu Arg Thr Ile Pro Thr Phe Glu Tyr
 35 40 45
 15 Lys Asn Val Tyr Asp Gln Val Cys Asp Asp Asp Asp Glu Asp His Ile
 50 55 60
 Tyr Glu Leu Cys Glu Asn Gln Tyr Ala Gln Leu Thr Ile Ser Gln Pro
 65 70 75 80
 Lys Ser Arg Pro Lys
 85

20 (2) INFORMATION FOR SEQ ID NO:85:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 749 base pairs
 (B) TYPE: nucleic acid
 (C) STRANDEDNESS: single
 (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:85:

AAGCTTTCAA AATGTGCCAA GTAAATATAA TTAATAAACT CTCTATCAGA AACTTTTAAA 60
 CTCTGTCTAT CAGCAGAAAT ATAATTCTC AATACACCAA CCTCTGAAAT ATCGGCATTA 120
 30 ATTCGATGTG TTATATAATC TTCTAGTTTA ACAGCAATCT TTCCTGTAGC ATACCCACTT 180
 TGACAACAAA ATTTTGATAA CAAAGAAAAT GATATTAAAT CTATACATT AAGATTAGTT 240
 TTGTTTTGTT GTACAGGTAT TTTATATGTT TCGATAAAAT CTTTATAGC TTGTAGGTCA 300
 TAGGTATGAA AAGGCTTTAA ACTGTTTGTA GCTTGAAATA GATAAAATCT TGTGCTAAA 360
 ACTAAAGTTT TTTCTTCAGG ACCAAATTTT GAAGTAAACC AAAACGGTGT AGGATTGTT 420
 35 CCATATATTC GTCTAAAGGC TGCAAGTATT TGTTGTTTCT GATGAATATA TAATAATGTT 480
 AACCCATGGC GTCCTTTATT ACATTCGAT AAGCATGTTT TTATAGATAA TGTAGGGTCA 540

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TATTTAGCAG ATTCTAAAGT TCTTCCAGAT TTAGGAGTTA GACGCTCTGT CGTTATAGAT 600
AATATAGTTA TTAAATCATC ATGAATATTA AACGTATGCT GATCATCAAT ACAAGAAAGT 660
ATTAATTTTG TAGAGATTGG GTTTCATAT AATAAAGATT TAGCTATAAC AGACGCTTCA 720
TAATTATTTT TAATTGAACA TATAACAT 749

5 (2) INFORMATION FOR SEQ ID NO:86:

- (i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 749 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
10 (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:86:

ATGTTTATAT GTTCAATTAA AAATAATTAT GAAGCGTCTG TTATAGCTAA ATCTTTATTA 60
TATGGAACCC CAATCTCTAC AAAATTAATA CTTTCTTGTA TTGATGATCA GCATACGTTT 120
15 AATATTCATG ATGATTTAAT AACTATATTA TCTATAACGA CAGAGCGTCT AACTCCTAAA 180
TCTGGAAGAA CTTTAGAATC TGCTAAATAT GACCCTACAT TATCTATAAA AACATGCTTA 240
TCGAAATGTA ATAAAGGACG CCATGGGTTA ACATTATTAT ATATTCATCA CGAACAACAA 300
ATACTTGCAG CCTTTAGACG AATATATGGA ACAAATCCTA CACCGTTTGT GTTTACTTCA 360
AAATTTGGTC CTGAAGAAAA AACTTTAGTT TTAGCAACAA GATTTTATCT ATTTCAAGCT 420
20 ACAAACAGTT TAAAGCCTTT TCATACCTAT GACCTACAAG CTATAAAGA TTTTATCGAA 480
ACATATAAAA TACCTGTACA ACAAACAAA ACTAATCTTA AATGTATAGA TTTAATATCA 540
TTTTCTTTGT TATCAAAATT TTGTTGTCAA AGTGGGTATG CTACAGGAAA GATTGCTGTT 600
AAACTAGAAG ATTATATAAC ACATCGAATT AATGCCGATA TTTCAGAGGT TGGTGTATTG 660
AGAAATTATA TTTCTGCTGA TAGACAGAGT TTAAAAGTTT CTGATAGAGA GTTTATTAAT 720
25 TATATTTACT TGGCACATTT TGAAAGCTT 749

(2) INFORMATION FOR SEQ ID NO:87:

- (i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 747 base pairs
(B) TYPE: nucleic acid
30 (C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: cDNA

(ix) FEATURE:

- (A) NAME/KEY: CDS
35 (B) LOCATION: 1..747

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(xi) SEQUENCE DESCRIPTION: SEQ ID NO:87:

	ATG TTT ATA TGT TCA ATT AAA AAT AAT TAT GAA GCG TCT GTT ATA GCT	48
	Met Phe Ile Cys Ser Ile Lys Asn Asn Tyr Glu Ala Ser Val Ile Ala	
	1 5 10 15	
5	AAA TCT TTA TTA TAT GGA AAC CCA ATC TCT ACA AAA TTA ATA CTT TCT	96
	Lys Ser Leu Leu Tyr Gly Asn Pro Ile Ser Thr Lys Leu Ile Leu Ser	
	20 25 30	
10	TGT ATT GAT GAT CAG CAT ACG TTT AAT ATT CAT GAT GAT TTA ATA ACT	144
	Cys Ile Asp Asp Gln His Thr Phe Asn Ile His Asp Asp Leu Ile Thr	
	35 40 45	
	ATA TTA TCT ATA ACG ACA GAG CGT CTA ACT CCT AAA TCT GGA AGA ACT	192
	Ile Leu Ser Ile Thr Thr Glu Arg Leu Thr Pro Lys Ser Gly Arg Thr	
	50 55 60	
15	TTA GAA TCT GCT AAA TAT GAC CCT ACA TTA TCT ATA AAA ACA TGC TTA	240
	Leu Glu Ser Ala Lys Tyr Asp Pro Thr Leu Ser Ile Lys Thr Cys Leu	
	65 70 75 80	
	TCG AAA TGT AAT AAA GGA CGC CAT GGG TTA ACA TTA TTA TAT ATT CAT	288
	Ser Lys Cys Asn Lys Gly Arg His Gly Leu Thr Leu Leu Tyr Ile His	
	85 90 95	
20	CAC GAA CAA CAA ATA CTT GCA GCC TTT AGA CGA ATA TAT GGA ACA AAT	336
	His Glu Gln Gln Ile Leu Ala Ala Phe Arg Arg Ile Tyr Gly Thr Asn	
	100 105 110	
25	CCT ACA CCG TTT TGG TTT ACT TCA AAA TTT GGT CCT GAA GAA AAA ACT	384
	Pro Thr Pro Phe Trp Phe Thr Ser Lys Phe Gly Pro Glu Glu Lys Thr	
	115 120 125	
	TTA GTT TTA GCA ACA AGA TTT TAT CTA TTT CAA GCT ACA AAC AGT TTA	432
	Leu Val Leu Ala Thr Arg Phe Tyr Leu Phe Gln Ala Thr Asn Ser Leu	
	130 135 140	
30	AAG CCT TTT CAT ACC TAT GAC CTA CAA GCT ATA AAA GAT TTT ATC GAA	480
	Lys Pro Phe His Thr Tyr Asp Leu Gln Ala Ile Lys Asp Phe Ile Glu	
	145 150 155 160	
	ACA TAT AAA ATA CCT GTA CAA CAA AAC AAA ACT AAT CTT AAA TGT ATA	528
	Thr Tyr Lys Ile Pro Val Gln Gln Asn Lys Thr Asn Leu Lys Cys Ile	
	165 170 175	
35	GAT TTA ATA TCA TTT TCT TTG TTA TCA AAA TTT TGT TGT CAA AGT GGG	576
	Asp Leu Ile Ser Phe Ser Leu Leu Ser Lys Phe Cys Cys Gln Ser Gly	
	180 185 190	
40	TAT GCT ACA GGA AAG ATT GCT GTT AAA CTA GAA GAT TAT ATA ACA CAT	624
	Tyr Ala Thr Gly Lys Ile Ala Val Lys Leu Glu Asp Tyr Ile Thr His	
	195 200 205	
	CGA ATT AAT GCC GAT ATT TCA GAG GTT GGT GTA TTG AGA AAT TAT ATT	672
	Arg Ile Asn Ala Asp Ile Ser Glu Val Gly Val Leu Arg Asn Tyr Ile	
	210 215 220	
45	TCT GCT GAT AGA CAG AGT TTA AAA GTT TCT GAT AGA GAG TTT ATT AAT	720
	Ser Ala Asp Arg Gln Ser Leu Lys Val Ser Asp Arg Glu Phe Ile Asn	

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225 230 235 240
 TAT ATT TAC TTG GCA CAT TTT GAA AGC
 Tyr Ile Tyr Leu Ala His Phe Glu Ser
 245

747

5 (2) INFORMATION FOR SEQ ID NO:88:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 249 amino acids
 (B) TYPE: amino acid
 (D) TOPOLOGY: linear

10 (ii) MOLECULE TYPE: protein

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:88:

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

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Ser Ala Asp Arg Gln Ser Leu Lys Val Ser Asp Arg Glu Phe Ile Asn
225 230 235 240
Tyr Ile Tyr Leu Ala His Phe Glu Ser
245

5 (2) INFORMATION FOR SEQ ID NO:89:

- (i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 30 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
10 (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(ix) FEATURE:
(A) NAME/KEY: misc feature
(B) LOCATION: 1..30
15 (D) OTHER INFORMATION: /label= primer

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:89:

GCCGGTACCA GGCTTTGGAC GAGATTAGG

30

(2) INFORMATION FOR SEQ ID NO:90:

- (i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 29 base pairs
20 (B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(ix) FEATURE:
(A) NAME/KEY: misc feature
(B) LOCATION: 1..29
25 (D) OTHER INFORMATION: /label= primer

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:90:

30 GCCGAATTCA ATATAATTAA TAAACTCTC

29

(2) INFORMATION FOR SEQ ID NO:91:

- (i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 28 base pairs
35 (B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

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- (ix) FEATURE:
 (A) NAME/KEY: misc feature
 (B) LOCATION: 1..28
 (D) OTHER INFORMATION: /label= primer
- 5 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:91:
 CCGGAATTCG CTTAGTGAGA GTATAAAC 28
- (2) INFORMATION FOR SEQ ID NO:92:
- (i) SEQUENCE CHARACTERISTICS:
 (A) LENGTH: 28 base pairs
 (B) TYPE: nucleic acid
 (C) STRANDEDNESS: single
 (D) TOPOLOGY: linear
- 10 (ii) MOLECULE TYPE: DNA (genomic)
- (ix) FEATURE:
 (A) NAME/KEY: misc feature
 (B) LOCATION: 1..28
 (D) OTHER INFORMATION: /label= primer
- 15 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:92:
 CCGGAATTCC CTCATATTAT ATACTAAC 28
- 20 While various embodiments of the present invention have
 been described in detail, it is apparent that modifications
 and adaptations of those embodiments will occur to those
 skilled in the art. It is to be expressly understood,
 however, that such modifications and adaptations are within
25 the scope of the present invention, as set forth in the
 following claims.

THE CLAIMS DEFINING THE INVENTION ARE AS FOLLOWS:

1. An isolated canine herpesvirus (CHV) nucleic acid molecule that hybridizes under stringent hybridization conditions with a CHV nucleic acid region selected from the group consisting of a CdUTPase gene, a CgE gene, a CgG gene, a Cgl gene, a CPK gene, a CTK gene, a CIR6 gene, aCUS2 gene, a CUS9 gene, a CUL49 gene, a CUL51 gene, a CUL48 gene, a CUL52 gene, a CgL gene, a CUL49.5 gene, a CICIP4 gene, a CUS8.5 open reading frame, and a region of the CHV genome spanning from the 3' end of the coding region of the CUL41 gene through the 3' end of the coding region of the CUL38 gene.
2. A therapeutic composition comprising the isolated CHV nucleic acid molecule of claim 1.
3. A method to protect a canid from disease, said method comprising administering to said canid a therapeutic composition comprising the isolated CHV nucleic acid molecule of claim 1.
4. The isolated CHV nucleic acid molecule of claim 1, wherein said CHV nucleic acid molecule comprises a recombinant CHV genome.
5. The isolated CHV nucleic acid molecule of claim 1, wherein said CHV nucleic acid molecule comprises a recombinant CHV genome having an inactive gene.
6. The isolated CHV nucleic acid molecule of claim 5, wherein said gene is inactive due to a deletion in said gene.
7. The isolated CHV nucleic acid molecule of claim 5, wherein said gene is inactive due to an insertion into said gene.

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8. The isolated CHV nucleic acid molecule of claim 4 wherein said recombinant CHV genome is attenuated.

9. The isolated CHV nucleic acid molecule of claim 4, wherein said CHV genome is selected from the group consisting of a CdUTPase negative CHV genome, a CgC negative CHV genome, a CgE negative CHV genome, a CgG negative CHV genome, a CgI negative CHV genome, a CPK negative CHV genome, a CTK negative CHV genome, a CIR6 negative CHV genome, a CUS2 negative CHV genome, a CUS9 negative CHV genome, a CUL49 negative CHV genome, a CUL51 negative CHV genome, a CUL45 negative CHV genome, a CgD negative CHV genome, a CgB negative CHV genome, a CUL48 negative CHV genome, a CUL52 negative CHV genome, a CgL negative CHV genome, a CUL49.5 negative CHV genome, a CICIP0 negative CHV genome, a CICIP4 negative CHV genome, and a CUS8.5 negative CHV genome.

10. The isolated CHV nucleic acid molecule of claim 4, wherein said CHV genome comprises a heterologous nucleic acid molecule.

11. The isolated CHV nucleic acid molecule of claim 10, wherein said heterologous nucleic acid molecule is operatively linked to a transcription control region.

12. The isolated CHV nucleic acid molecule of claim 4, wherein said CHV genome comprises a heterologous nucleic acid molecule in a region of said genome selected from the group consisting of an essential gene of said genome, a non-essential gene of said genome, an intergenic region, and combinations thereof.

13. The isolated CHV nucleic acid molecule of claim 4, wherein said CHV genome comprises a heterologous nucleic acid molecule in a CHV gene of said genome, wherein said CHV gene is selected from the group consisting of a CdUTPase gene, a CgC gene, a CgE gene, a CgG gene, a CgI gene, a CPK



gene, a CTK gene, a CIR6 gene, a CUS2 gene, a CUS9 gene, a CUL49 gene, a CUL51 gene, a CUL45 gene, a CgD gene, a CgB gene, a CUL48 gene, a CUL52 gene, a CgL gene, a CUL49.5 gene, a CICIP0 gene, a CICIP4 gene, and a CUS8.5 open reading frame.

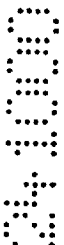
14. The isolated CHV nucleic acid molecule of claim 4, wherein said CHV genome comprises a heterologous nucleic acid molecule in a naturally occurring *Ascl* restriction endonuclease site within said genome.

15. The isolated CHV nucleic acid molecule of claim 4, wherein said CHV genome comprises a heterologous nucleic acid molecule in the US region of said genome.

16. The isolated CHV nucleic acid molecule of claim 4, wherein said CHV genome comprises a heterologous nucleic acid molecule in a region of said genome selected from the group consisting of an internal inverted repeat region and a terminal inverted repeat region.

17. The isolated CHV nucleic acid molecule of claim 4, wherein said CHV genome comprises a heterologous nucleic acid molecule in a region of said genome selected from the group consisting of: a region of said genome selected from the group consisting of nCAsc₉₃₀₀, nCAsc₁₀₀₀₀, nCHin₃₀₀₀, nCHin₁₉₀₀, nCHin₅₅₀₀, and nCHin₈₅₀₀; and an allelic variant of a region of said genome selected from the group consisting of nCAsc₉₃₀₀, nCAsc₁₀₀₀₀, nCHin₃₀₀₀, nCHin₁₉₀₀, nCHin₅₅₀₀, and nCHin₈₅₀₀.

18. The isolated CHV nucleic acid molecule of claim 4, wherein said CHV genome comprises a heterologous nucleic acid molecule in a region of said CHV genome selected from the group consisting of: a region of said CHV genome selected from the group consisting of a CHV US region comprising nCUS₅₄₉₅, a CHV UL region comprising nCgC/CUL45₂₁₀₀, a CgE gene comprising nCgE₇₅₀, a Cgl gene comprising nCgl₁₆₁, a CUS9 gene comprising nCUS9₅₇₉, a CHV UL region comprising nCdUTP/CUL51₇₄₃, a CTK gene



comprising nCTK₂₈₀, a CUL48 gene comprising nCUL48₂₉₄, a CUL49 gene included in nCHin₃₀₀₀, and a CUL52 gene comprising nCUL52₁₄₆; and an allelic variant of a region of said CHV genome selected from the group consisting of a CHV US region comprising nCUS₅₄₉₅, a CHV UL region comprising nCgC/CUL45₂₁₀₀, a CgE gene comprising nCgE₇₅₀, a Cgl gene comprising nCgl₁₆₁, a CUS9 gene comprising nCUS9₅₇₉, a CHV UL region comprising nCdUTP/CUL51₇₄₃, a CTK gene comprising nCTK₂₈₀, a CUL48 gene comprising nCUL48₂₉₄, a CUL49 gene included in nCHin₃₀₀₀, and a CUL52 gene comprising nCUL52₁₄₆.

19. The isolated CHV nucleic acid molecule of claim 4, wherein said CHV genome comprises a heterologous nucleic acid molecule in a region of said genome selected from the group consisting of: a region of said genome selected from the group consisting of a CHV region comprising nCUS₁₀₅₉₂, a CHV UL region comprising nCUL₁₈₂₃, a CHV UL region comprising nCUL49/CUL48₂₀₄₄, a CHV IR region comprising nCICP4₆₂₆, a CHV UL region comprising nCgl₆₅₅, a CHV UL region comprising nCUL52₇₄₉, and a CHV UL region comprising nCdUTP₃₂₀₀; and an allelic variant of a region of said genome selected from the group consisting of a CHV region comprising nCUS₁₀₅₉₂, a CHV UL region comprising nCUL₁₈₂₃, a CHV UL region comprising nCUL49/CUL48₂₀₄₄, a CHV IR region comprising nCICP4₆₂₆, a CHV UL region comprising nCgl₆₅₅, a CHV UL region comprising nCUL52₇₄₉, and a CHV UL region comprising nCdUTP₃₂₀₀.

20. The isolated CHV nucleic acid molecule of claim 4, wherein said CHV genome comprises a heterologous nucleic acid molecule in a region of said genome selected from the group consisting of: a region of said genome selected from the group consisting of nCUS₅₄₉₅, nCgC/CUL45₂₁₀₀, nCgE₇₅₀, nCgl₁₆₁, nCUS9₅₇₉, nCdUTP/CUL51₇₄₃, nCTK₂₈₀, nCUL48₂₉₄, nCUL52₁₄₆, nCUS₁₀₅₉₂, nCgD₁₀₃₈, nCgl₁₀₉₅, nCgE₁₅₆₉, nCUS8.5₂₃₇, nCUS9₃₆₀, nCUL49/CUL48₂₀₄₄, nCUL49₄₂₀, nCUL48₁₂₆₉, nCICP4₆₂₆, nCgl₆₅₅, nCUL₁₈₂₃, nCdUTP₉₁₈, nCUL49.5₂₆₁, nCUL49₂₅₅, nCUL52₇₄₉, and nCdUTP₃₂₀₀, and an allelic variant of a region of said genome selected from the group consisting of



nCUS₅₄₉₅, nCgC/CUL45₂₁₀₀, nCgE₇₅₀, nCgl₁₆₁, nCUS₉₅₇₉, nCdUTP/CUL51₇₄₃,
 nCTK₂₈₀, nCUL48₂₉₄, nCUL52₁₄₆, nCUS₁₀₅₉₂, nCgD₁₀₃₈, nCgl₁₀₉₅, nCgE₁₅₆₉,
 nCUS8.5₂₃₇, nCUS₉₃₆₀, nCUL49/CUL48₂₀₄₄, nCUL49₄₂₀, nCUL48₁₂₆₉,
 nCICP4₆₂₆, nCgL₆₅₅, nCUL₁₈₂₃, nCdUTP₉₁₈, nCUL49.5₂₆₁, nCUL49₂₅₅,
 nCUL52₇₄₉, and nCdUTP₃₂₀₀.

21. The isolated CHV nucleic acid molecule of claim 4, wherein said CHV genome comprises a heterologous nucleic acid molecule in a region of said CHV genome selected from the group consisting of: a nucleic acid molecule comprising a nucleic acid sequence selected from the group consisting of SEQ ID NO: 1, SEQ ID NO: 2, SEQ ID NO: 3, SEQ ID NO: 5, SEQ ID NO: 7, SEQ ID NO: 9, SEQ ID NO: 11, SEQ ID NO: 13, SEQ ID NO: 14, SEQ ID NO: 15, SEQ ID NO: 17, SEQ ID NO: 19, SEQ ID NO: 20, SEQ ID NO: 21, SEQ ID NO: 23, SEQ ID NO: 24, SEQ ID NO: 25, SEQ ID NO: 27, SEQ ID NO: 28, SEQ ID NO: 29, SEQ ID NO: 31, SEQ ID NO: 32, SEQ ID NO: 33, SEQ ID NO: 35, SEQ ID NO: 37, SEQ ID NO: 38, SEQ ID NO: 51, SEQ ID NO: 52, SEQ ID NO: 53, SEQ ID NO: 55, SEQ ID NO: 57, SEQ ID NO: 59, SEQ ID NO: 61, SEQ ID NO: 63, SEQ ID NO: 64, SEQ ID NO: 65, SEQ ID NO: 67, SEQ ID NO: 69, SEQ ID NO: 70, SEQ ID NO: 71, SEQ ID NO: 73, SEQ ID NO: 74, SEQ ID NO: 75, SEQ ID NO: 77, SEQ ID NO: 78, SEQ ID NO: 79, SEQ ID NO: 81, SEQ ID NO: 83, SEQ ID NO: 85, SEQ ID NO: 86, SEQ ID NO: 87, and complements of said nucleic acid sequences; and an allelic variant of a nucleic acid molecule comprising a nucleic acid sequence selected from the group consisting of SEQ ID NO: 1, SEQ ID NO: 2, SEQ ID NO: 3, SEQ ID NO: 5, SEQ ID NO: 7, SEQ ID NO: 9, SEQ ID NO: 11, SEQ ID NO: 13, SEQ ID NO: 14, SEQ ID NO: 15, SEQ ID NO: 17, SEQ ID NO: 19, SEQ ID NO: 20, SEQ ID NO: 21, SEQ ID NO: 23, SEQ ID NO: 24, SEQ ID NO: 25, SEQ ID NO: 27, SEQ ID NO: 28, SEQ ID NO: 29, SEQ ID NO: 31, SEQ ID NO: 32, SEQ ID NO: 33, SEQ ID NO: 35, SEQ ID NO: 37, SEQ ID NO: 38, SEQ ID NO: 51, SEQ ID NO: 52, SEQ ID NO: 53, SEQ ID NO: 55, SEQ ID NO: 57, SEQ ID NO: 59, SEQ ID NO: 61, SEQ ID NO: 63, SEQ ID NO: 64, SEQ ID NO: 65, SEQ ID NO: 67, SEQ ID NO: 69, SEQ ID NO: 70, SEQ ID NO: 71, SEQ ID NO: 73, SEQ ID NO: 74, SEQ ID NO: 75, SEQ ID NO: 77, SEQ ID NO: 78, SEQ ID NO: 79, SEQ ID NO: 81, SEQ ID



NO: 83, SEQ ID NO: 85, SEQ ID NO: 86, SEQ ID NO: 87, and complements of said nucleic acid sequences.

22. The isolated CHV nucleic acid molecule of claim 10, wherein said heterologous nucleic acid molecule encodes a protective compound selected from the group consisting of protective proteins and protective RNA species.

23. The isolated CHV nucleic acid molecule of claim 22, wherein said protective compound protects a canid from a disease selected from the group consisting of infectious, metabolic, and genetic diseases.

24. The isolated CHV nucleic acid molecule of claim 22, wherein said protective compound is derived from an infectious agent selected from the group consisting of protozoan parasites, helminth parasites, ectoparasites, fungi, bacteria, and viruses.

25. The isolated CHV nucleic acid molecule of claim 10, wherein said heterologous nucleic acid molecule comprises a nucleic acid molecule encoding an immunomodulator.

26. The isolated CHV nucleic acid molecule of claim 22, wherein said protective compound elicits an immune response.

27. A transfected cell comprising a recombinant CHV genome as set forth in claim 4.

28. The isolated CHV nucleic acid molecule of claim 4, wherein said CHV genome comprises a recombinant dog herpesvirus genome.

29. The composition of claim 2, wherein said composition further comprises an excipient.



30. The method of claim 3, wherein said therapeutic composition is administered to a dam to protect offspring of said dam from disease.
31. A canine cell line that complements a CHV genome as set forth in claim 4 having a defect in a gene essential to CHV reproduction *in vitro*.
32. The cell line of claim 31, wherein said essential gene is selected from the group consisting of a CgD gene, a CgB gene, a CUL48 gene, a CUL52 gene, a CgL gene and a CICIP4 gene.
33. The isolated CHV nucleic acid molecule of claim 1, wherein said nucleic acid molecule hybridizes under stringent hybridization conditions with a nucleic acid region selected from the group consisting of a CdUTPase gene, a CgE gene, a CgG gene, a CgI gene, a CPK gene, a CUS2 gene, a CUS9 gene, a CUL49 gene, a CUL51 gene, a CgL gene, a CUL49.5 gene, and a CUS8.5 open reading frame.
34. An isolated CHV protein, wherein said protein is encoded by the isolated CHV nucleic acid molecule of claim 1.
35. The isolated CHV protein of claim 34, wherein said protein is selected from the group consisting of a CdUTPase protein, a CgE protein, a CgG protein, a CgI protein, a CPK protein, a CUS2 protein, a CUS9 protein, a CUL49 protein, a CUL51 protein, a CgL protein, and a CUL49.5 protein.
36. The isolated CHV nucleic acid molecule of claim 1, wherein said CHV nucleic acid molecule comprises a nucleic acid sequence that is at least 80% identical to a nucleic acid sequence selected from the group consisting of SEQ ID NO: 1, SEQ ID NO: 2, SEQ ID NO: 3, SEQ ID NO: 51, SEQ ID NO: 52, SEQ ID NO: 63, SEQ ID NO: 64, SEQ ID NO: 67, SEQ ID NO: 69, SEQ ID NO: 70, SEQ ID NO: 71, SEQ ID NO: 85, SEQ ID NO: 86, and SEQ ID NO: 87.



37. The isolated CHV protein of claim 34, wherein said CHV protein is at least 80% identical to a CHV protein having an amino acid sequence selected from the group consisting of SEQ ID NO: 4, SEQ ID NO: 68, SEQ ID NO: 72, and SEQ ID NO: 88.

38. An isolated antibody that selectively binds to a CHV protein of claim 34.

39. A therapeutic composition selected from the group consisting of: an isolated CHV nucleic acid molecule of claim 1; an isolated CHV nucleic acid molecule of claim 36; an isolated CHV protein of claim 34; an isolated CHV protein of claim 37; an isolated antibody that selectively binds to any one of said CHV proteins; and a mixture thereof.

40. A method to protect a canid from CHV comprising administering to said canid the therapeutic composition of claim 39.

41. The composition of claim 39, wherein said composition further comprises a component selected from the group consisting of an excipient, an adjuvant, a carrier, and a mixture thereof.

42. The isolated CHV nucleic acid molecule of claim 1, wherein said CdUTPase gene comprises nCdUTP₉₁₈, wherein said CgE gene comprises nCgE₁₅₆₉, wherein said CgG gene comprises nCgG₁₂₄₈, wherein said CgI gene comprises nCgI₁₀₉₅, wherein said CPK gene comprises nCPK₁₂₀₃, wherein said CUS2 gene comprises nCUS2₁₁₇₆, wherein said CUS9 gene comprises nCUS9₃₆₀, wherein said CUL49 gene comprises nCUL49₄₂₀, wherein said CUL51 gene comprises nCUL51₂₆₁, wherein said CgL gene comprises nCgL₆₅₅, wherein said CUS8.5 open reading frame comprises nCUS8.5₂₃₇, wherein said CUL49.5 gene comprises nCUL49.5₂₆₁, and wherein said CUL49 gene comprises nCUL49₂₅₅.

43. The isolated CHV nucleic acid molecule of claim 1, wherein said CHV nucleic acid molecule comprises a nucleic acid sequence that is at least 80%



identical to a nucleic acid sequence selected from the group consisting of SEQ ID NO: 5, SEQ ID NO: 7, SEQ ID NO: 9, SEQ ID NO: 13, SEQ ID NO: 14, SEQ ID NO: 15, SEQ ID NO: 17, SEQ ID NO: 19, SEQ ID NO: 20, SEQ ID NO: 29, SEQ ID NO: 31, SEQ ID NO: 32, SEQ ID NO: 33, SEQ ID NO: 55, SEQ ID NO: 57, SEQ ID NO: 59, SEQ ID NO: 61, SEQ ID NO: 65, SEQ ID NO: 73, SEQ ID NO: 74, SEQ ID NO: 75, SEQ ID NO: 77, SEQ ID NO: 78, SEQ ID NO: 79, SEQ ID NO: 81, SEQ ID NO: 83, and complements of said nucleic acid sequences.

44. The isolated CHV nucleic acid molecule of claim 1, wherein said CHV nucleic acid molecule hybridizes under stringent hybridization conditions with a nucleic acid molecule selected from the group consisting of nCUS2₁₁₇₆, nCPK₁₂₀₃, nCgG₁₂₄₈, nCgl₁₆₁, nCgE₇₅₀, nCUS9₅₇₉, nCdUTP/CUL51₇₄₃, nCgl₁₀₉₅, nCgE₁₅₆₉, nCUS8.5₂₃₇, nCUS9₃₆₀, nCUL49₄₂₀, nCgL₆₅₅, nCUL₁₈₂₃, nCdUTP₉₁₈, nCUL49.5₂₆₁, and nCUL49₂₅₅.

45. The isolated CHV nucleic acid molecule of claim 1, wherein said CHV nucleic acid molecule comprises a CHV nucleic acid molecule selected from the group consisting of: a CHV nucleic acid molecule selected from the group consisting of nCUS2₁₁₇₆, nCPK₁₂₀₃, nCgG₁₂₄₈, nCdUTP/CUL51₇₄₃, nCdUTP₄₅₉, nCUS9₅₇₉, nCUS9₄₅₀, nCgl₁₆₁, nCgl₁₅₉, nCgE₇₅₀, nCUL51₂₆₁, nCgl₁₀₉₅, nCgE₁₅₆₉, nCUS8.5₂₃₇, nCUS9₃₆₀, nCUL49₄₂₀, nCgL₆₅₅, nCgL₅₁₆, nCUL₁₈₂₃, nCdUTP₉₁₈, nCUL49.5₂₆₁, nCUL49₂₅₅, nCdUTP₈₅₈, nCdUTP₃₂₀₀, nCAsc₉₃₀₀, nCAsc₁₀₀₀₀, nCHin₃₀₀₀, nCHin₁₉₀₀, nCHin₅₅₀₀, nCHin₈₅₀₀, nCUS₅₄₉₅, nCIR6₅₅₂, nCUS₁₀₅₉₂, nCUL49/CUL48₂₀₄₄, nCUL48₁₂₆₉, nCICP4₆₂₆, nCICP4₆₂₄, nCUL52₇₄₉, and nCUL52₇₄₇; and an allelic variant of a CHV nucleic acid molecule selected from the group consisting of nCUS2₁₁₇₆, nCPK₁₂₀₃, nCgG₁₂₄₈, nCdUTP/CUL51₇₄₃, nCdUTP₄₅₉, nCUS9₅₇₉, nCUS9₄₅₀, nCgl₁₆₁, nCgl₁₅₉, nCgE₇₅₀, nCUL51₂₆₁, nCgl₁₀₉₅, nCgE₁₅₆₉, nCUS8.5₂₃₇, nCUS₃₆₀, nCUL49₄₂₀, nCgL₆₅₅, nCgL₅₁₆, nCUL₁₈₂₃, nCdUTP₉₁₈, nCUL49.5₂₆₁, nCUL49₂₅₅, nCdUTP₈₅₈, nCdUTP₃₂₀₀, nCAsc₉₃₀₀, nCAsc₁₀₀₀₀, nCHin₃₀₀₀, nCHin₁₉₀₀, nCHin₅₅₀₀, nCHin₈₅₀₀, nCUS₅₄₉₅, nCIR6₅₅₂, nCUS₁₀₅₉₂, nCUL49/CUL48₂₀₄₄, nCUL48₁₂₆₉, nCICP4₆₂₆, nCICP4₆₂₄, nCUL52₇₄₉, and nCUL52₇₄₇.



46. The isolated CHV nucleic acid molecule of claim 1, wherein said CHV nucleic acid molecule is selected from the group consisting of: a CHV nucleic acid molecule comprising a nucleic acid sequence selected from the group consisting of SEQ ID NO: 5, SEQ ID NO: 7, SEQ ID NO: 9, SEQ ID NO: 13, SEQ ID NO: 14, SEQ ID NO: 15, SEQ ID NO: 17, SEQ ID NO: 19, SEQ ID NO: 20, SEQ ID NO: 29, SEQ ID NO: 31, SEQ ID NO: 32, SEQ ID NO: 33, SEQ ID NO: 55, SEQ ID NO: 57, SEQ ID NO: 59, SEQ ID NO: 61, SEQ ID NO: 65, SEQ ID NO: 73, SEQ ID NO: 74, SEQ ID NO: 75, SEQ ID NO: 77, SEQ ID NO: 78, SEQ ID NO: 79, SEQ ID NO: 81, SEQ ID NO: 83, SEQ ID NO: 1, SEQ ID NO: 2, SEQ ID NO: 3, SEQ ID NO: 51, SEQ ID NO: 52, SEQ ID NO: 63, SEQ ID NO: 64, SEQ ID NO: 67, SEQ ID NO: 69, SEQ ID NO: 70, SEQ ID NO: 71, SEQ ID NO: 85, SEQ ID NO: 86, SEQ ID NO: 87, and complements of said nucleic acid sequences; and an allelic variant of a CHV nucleic acid molecule comprising a nucleic acid sequence selected from the group consisting of SEQ ID NO: 5, SEQ ID NO: 7, SEQ ID NO: 9, SEQ ID NO: 13, SEQ ID NO: 14, SEQ ID NO: 15, SEQ ID NO: 17, SEQ ID NO: 19, SEQ ID NO: 20, SEQ ID NO: 29, SEQ ID NO: 31, SEQ ID NO: 32, SEQ ID NO: 33, SEQ ID NO: 55, SEQ ID NO: 57, SEQ ID NO: 59, SEQ ID NO: 61, SEQ ID NO: 65, SEQ ID NO: 73, SEQ ID NO: 74, SEQ ID NO: 75, SEQ ID NO: 77, SEQ ID NO: 78, SEQ ID NO: 79, SEQ ID NO: 81, SEQ ID NO: 83, SEQ ID NO: 1, SEQ ID NO: 2, SEQ ID NO: 3, SEQ ID NO: 51, SEQ ID NO: 52, SEQ ID NO: 63, SEQ ID NO: 64, SEQ ID NO: 67, SEQ ID NO: 69, SEQ ID NO: 70, SEQ ID NO: 71, SEQ ID NO: 85, SEQ ID NO: 86, SEQ ID NO: 87, and complements of said nucleic acid sequences.

47. The isolated CHV nucleic acid molecule of claim 1, wherein said CHV nucleic acid molecule encodes a protein comprising an amino acid sequence selected from the group consisting of: a protein comprising an amino acid sequence selected from the group consisting of SEQ ID NO: 6, SEQ ID NO: 8, SEQ ID NO: 10, SEQ ID NO: 16, SEQ ID NO: 18, SEQ ID NO: 30, SEQ ID NO: 34, SEQ ID NO: 56, SEQ ID NO: 58, SEQ ID NO: 60, SEQ ID NO: 62, SEQ ID NO: 66, SEQ ID NO: 76, SEQ ID NO: 80, SEQ ID NO: 82, SEQ ID NO: 84, SEQ ID NO: 4, SEQ ID NO: 68, SEQ ID NO: 72, and SEQ ID NO: 88; and a



protein encoded by an allelic variant of a CHV nucleic acid molecule encoding a protein comprising an amino acid sequence selected from the group consisting of SEQ ID NO: 6, SEQ ID NO: 8, SEQ ID NO: 10, SEQ ID NO: 16, SEQ ID NO: 18, SEQ ID NO: 30, SEQ ID NO: 34, SEQ ID NO: 56, SEQ ID NO: 58, SEQ ID NO: 60, SEQ ID NO: 62, SEQ ID NO: 66, SEQ ID NO: 76, SEQ ID NO: 80, SEQ ID NO: 82, SEQ ID NO: 84, SEQ ID NO: 4, SEQ ID NO: 68, SEQ ID NO: 72, and SEQ ID NO: 88.

48. A recombinant molecule comprising a CHV nucleic acid molecule as set forth in claim 1, operatively linked to a transcription control sequence.

49. A recombinant virus comprising a CHV nucleic acid molecule as set forth in claim 1.

50. A recombinant cell comprising a CHV nucleic acid molecule as set forth in claim 1.

51. A recombinant vector comprising a CHV nucleic acid molecule as set forth in claim 1.

52. A recombinant vector comprising a CHV nucleic acid molecule as set forth in claim 1, said CHV nucleic acid molecule having a heterologous nucleic acid molecule in said CHV nucleic acid molecule.

53. The recombinant vector of claim 52, wherein said heterologous nucleic acid molecule is operatively linked to a transcription control sequence.

54. A cell comprising said recombinant vector of claim 51.

55. The isolated protein of claim 34, wherein said protein comprises an amino acid sequence that is at least 80% identical to an amino acid sequence selected from the group consisting of SEQ ID NO: 4, SEQ ID NO: 6, SEQ ID NO: 8, SEQ ID NO: 10, SEQ ID NO: 16, SEQ ID NO: 18, SEQ ID NO: 30, SEQ



ID NO: 34, SEQ ID NO: 56, SEQ ID NO: 58, SEQ ID NO: 60, SEQ ID NO: 62, SEQ ID NO: 66, SEQ ID NO: 68, SEQ ID NO: 72, SEQ ID NO: 76, SEQ ID NO: 80, SEQ ID NO: 82, SEQ ID NO: 84, and SEQ ID NO: 88.

56. The isolated protein of claim 34, wherein said CHV protein is selected from the group consisting of: a CHV protein comprising an amino acid sequence selected from the group consisting of SEQ ID NO: 4, SEQ ID NO: 6, SEQ ID NO: 8, SEQ ID NO: 10, SEQ ID NO: 16, SEQ ID NO: 18, SEQ ID NO: 30, SEQ ID NO: 34, SEQ ID NO: 56, SEQ ID NO: 58, SEQ ID NO: 60, SEQ ID NO: 62, SEQ ID NO: 66, SEQ ID NO: 68, SEQ ID NO: 72, SEQ ID NO: 76, SEQ ID NO: 80, SEQ ID NO: 82, SEQ ID NO: 84, and SEQ ID NO: 88; and a CHV protein encoded by an allelic variant of a CHV nucleic acid molecule encoding a CHV protein comprising an amino acid sequence selected from the group consisting of SEQ ID NO: 4, SEQ ID NO: 6, SEQ ID NO: 8, SEQ ID NO: 10, SEQ ID NO: 16, SEQ ID NO: 18, SEQ ID NO: 30, SEQ ID NO: 34, SEQ ID NO: 56, SEQ ID NO: 58, SEQ ID NO: 60, SEQ ID NO: 62, SEQ ID NO: 66, SEQ ID NO: 68, SEQ ID NO: 72, SEQ ID NO: 76, SEQ ID NO: 80, SEQ ID NO: 82, SEQ ID NO: 84, and SEQ ID NO: 88.

57. The isolated CHV nucleic acid molecule of claim 1, wherein said nucleic acid molecule comprises a transcript.

58. A method to increase recombinant CHV plaque forming efficiency comprising a process selected from the group of: (a) introducing a recombinant CHV genome as set forth in claim 4 into a canine cell expressing CHV alpha trans-inducing factor and culturing said cell to produce a recombinant CHV; and (b) co-introducing a recombinant CHV genome as set forth in claim 4 and a CHV alpha trans-inducing factor gene into a canine cell and culturing said cell to produce a recombinant CHV.

59. The method of claim 58, wherein said canine cell line expressing CHV alpha trans-inducing factor is selected from the group consisting of D17:pATIF₁₃₅₁D and D17:pATIF₁₃₅₁F.



60. A canine cell line comprising a nucleic acid molecule encoding a CHV alpha trans-inducing factor.
61. The cell line of claim 60, wherein said nucleic acid molecule comprises nucleic acid molecule nCUL48₁₂₆₉.
62. The canine cell line of claim 60, wherein said cell line is selected from the group consisting of D17:pATIF₁₃₅₁B, D17:pATIF₁₃₅₁C, D17:pATIF₁₃₅₁D, and D17:pATIF₁₃₅₁F.
63. The isolated CHV nucleic acid molecule of claim 4, wherein said CHV genome comprises a heterologous nucleic acid molecule encoding green fluorescent protein operatively linked to a transcription control region, said heterologous nucleic acid molecule being inserted into a CdUTPase gene of said CHV genome.
64. A recombinant canine herpes virus (CHV) comprising a CHV nucleic acid molecule as set forth in claim 1.
65. A recombinant canine herpes virus (CHV) comprising a recombinant CHV genome as set forth in claim 4.
66. The recombinant canine herpes virus (CHV) of claim 65 wherein said recombinant CHV infects dogs.

Dated this 23rd day of October, 2000

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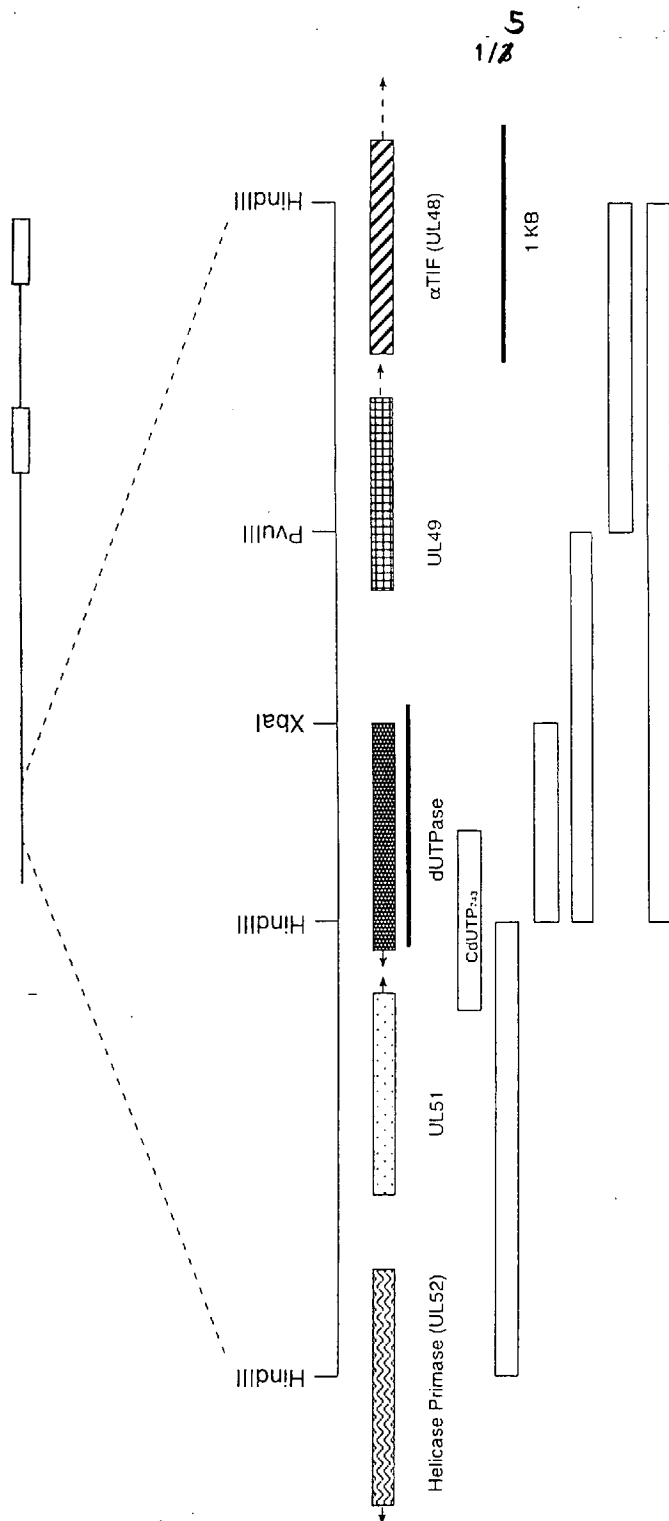


Fig. 1

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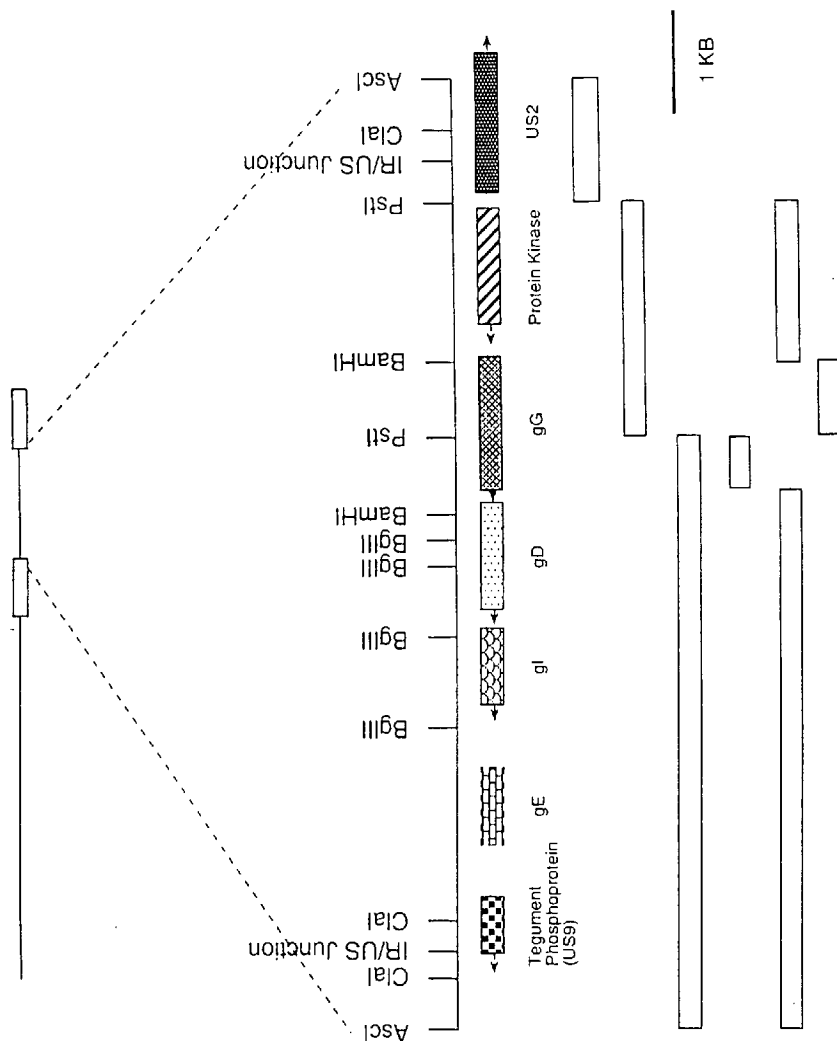


Fig. 2

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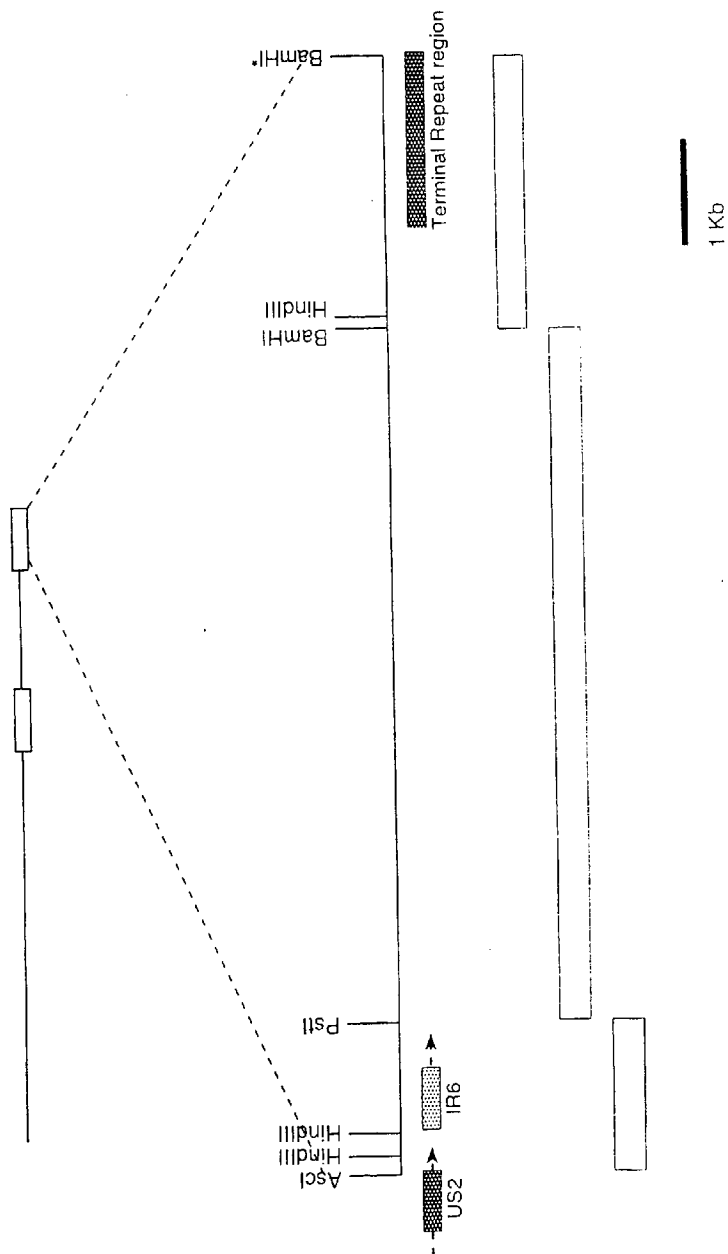


Fig. 3

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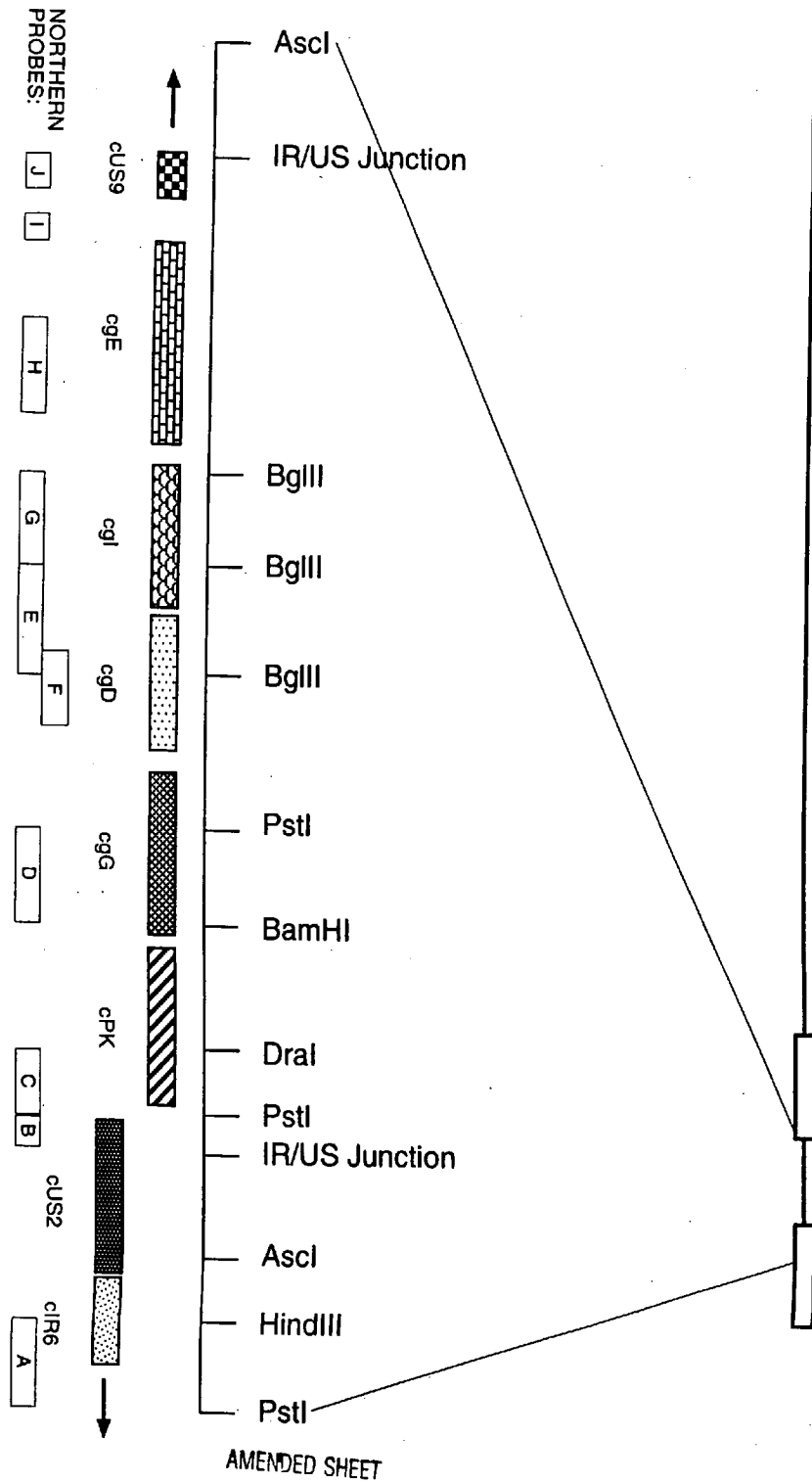


Fig. 4

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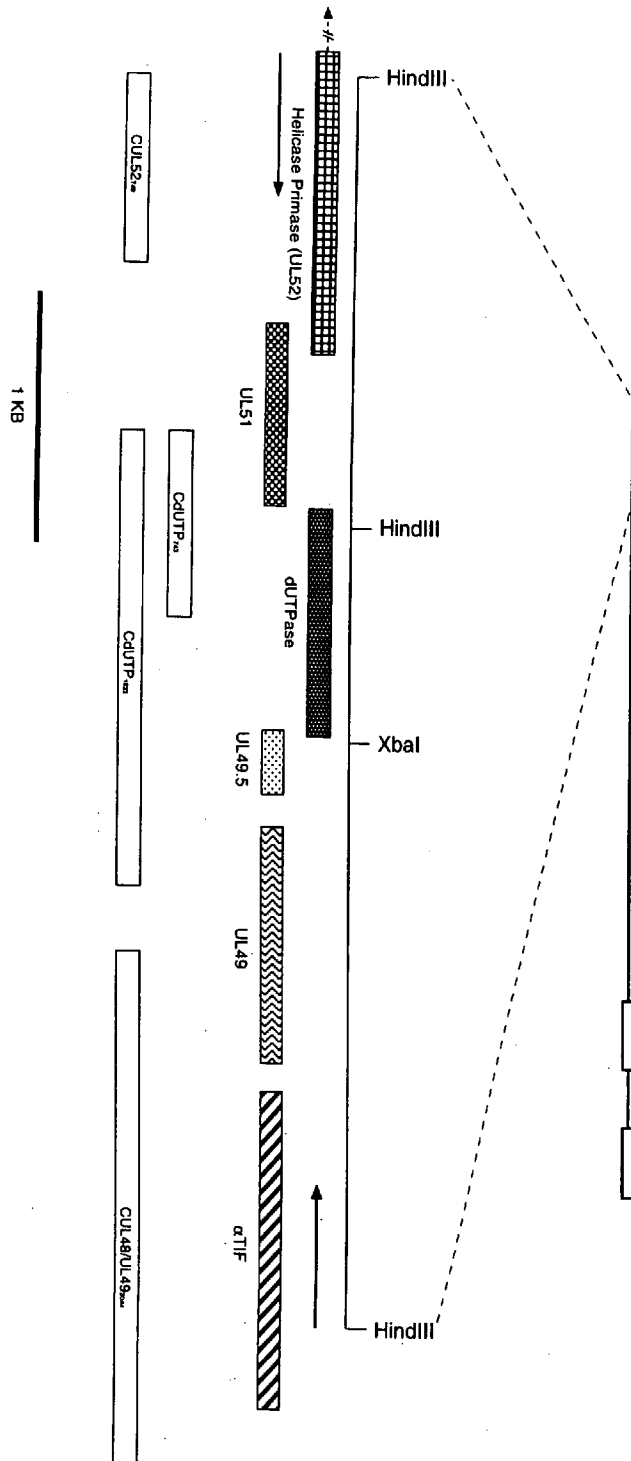


Fig. 5

AMENDED SHEET