THE HIGH BONE MASS GENE OF 11q13.3

FIELD OF THE INVENTION

The present invention relates generally to the field of genetics, genomics and molecular biology. More particularly, the invention relates to methods and materials used to isolate, detect and sequence a high bone mass gene and corresponding wild-type gene, and mutants thereof. The present invention also relates to the high bone mass gene, the corresponding wild-type gene, and mutants thereof. The genes identified in the present invention are implicated in the ontology and physiology of bone development. The invention also provides nucleic acids, proteins, cloning vectors, expression vectors, transformed hosts, methods of developing pharmaceutical compositions, methods of identifying molecules involved in bone development, and methods of diagnosing and treating diseases involved in bone development. In preferred embodiments, the present invention is directed to methods for treating, diagnosing, preventing and screening for normal and abnormal conditions of bone, including metabolic bone diseases such as osteoporosis.

BACKGROUND OF THE INVENTION

Two of the most common types of osteoporosis are postmenopausal and senile osteoporosis. Osteoporosis affects men as well as women, and, taken with other abnormalities of bone, presents an ever-increasing health risk for an aging population. The most common type of osteoporosis is that associated with menopause. Most women lose between 20-60% of the bone mass in the trabecular compartment of the bone within 3-6 years after the cessation of menses. This rapid loss is generally associated with an increase of bone resorption and formation. However, the resorptive cycle is more dominant and the result is a net loss of bone mass. Osteoporosis is a common and serious disease among postmenopausal women. There are an estimated 25 million women in the United States alone who are afflicted with this disease. The results of osteoporosis are both personally

harmful, and also account for a large economic loss due to its chronicity and the need for extensive and long-term support (hospitalization and nursing home care) from the disease sequelae. This is especially true in more elderly patients. Additionally, while osteoporosis is generally not thought of as a life-threatening condition, a 20-30% mortality rate is related to hip fractures in elderly women. A large percentage of this mortality rate can be directly associated with postmenopausal osteoporosis.

The most vulnerable tissue in the bone to the effects of postmenopausal osteoporosis is the trabecular bone. This tissue is often referred to as spongy bone and is particularly concentrated near the ends of the bone near the joints and in the vertebrae of the spine. The trabecular tissue is characterized by small structures which inter-connect with each other as well as the more solid and dense cortical tissue which makes up the outer surface and central shaft of the bone. This criss-cross network of trabeculae gives lateral support to the outer cortical structure and is critical to the biomechanical strength of the overall structure. In postmenopausal osteoporosis, it is primarily the net resorption and loss of the trabeculae which lead to the failure and fracture of the bone. In light of the loss of the trabeculae in postmenopausal women, it is not surprising that the most common fractures are those associated with bones which are highly dependent on trabecular support, e.g., the vertebrae, the neck of the femur, and the forearm. Indeed, hip fracture, Colle's fractures, and vertebral crush fractures are indicative of postmenopausal osteoporosis.

One of the earliest generally accepted methods for treatment of postmenopausal osteoporosis was estrogen replacement therapy. Although this therapy frequently is successful, patient compliance is low, primarily due to the undesirable side-effects of chronic estrogen treatment. Frequently cited side-effects of estrogen replacement therapy include reinitiation of menses, bloating, depression, and fear of breast or uterine cancer. In order to limit the known threat of uterine cancer in those women who have not undergone a hysterectomy, a protocol of

estrogen and progestin cyclic therapy is often employed. This protocol is similar to that which is used in birth control regimens, and often is not tolerated by women because of the side-effects characteristic of progestin. More recently, certain antiestrogens, originally developed for the treatment of breast cancer, have been shown in experimental models of postmenopausal osteoporosis to be efficacious. Among these agents is raloxifene (See, U.S. Patent No. 5,393,763, and Black et al, *J. Clin. Invest.*, 93:63-69 (1994)). In addition, tamoxifene, a widely used clinical agent for the treatment of breast cancer, has been shown to increase bone mineral density in post menopausal women suffering from breast cancer (Love et al, *N. Engl. J. Med.*, 326:852-856 (1992)).

Another therapy for the treatment of postmenopausal osteoporosis is the use of calcitonin. Calcitonin is a naturally occurring peptide which inhibits bone resorption and has been approved for this use in many countries (Overgaard et al, *Br. Med. J.*, 305:556-561 (1992)). The use of calcitonin has been somewhat limited, however. Its effects are very modest in increasing bone mineral density and the treatment is very expensive. Another therapy for the treatment of postmenopausal osteoporosis is the use of bis-phosphonates. These compounds were originally developed for use in Paget's disease and malignant hypercalcemia. They have been shown to inhibit bone resorption. Alendronate, one compound of this class, has been approved for the treatment of postmenopausal osteoporosis. These agents may be helpful in the treatment of osteoporosis, but these agents also have potential liabilities which include osteomalacia, extremely long half-life in bone (greater than 2 years), and possible "frozen bone syndrome," e.g., the cessation of normal bone remodeling.

Senile osteoporosis is similar to postmenopausal osteoporosis in that it is marked by the loss of bone mineral density and resulting increase in fracture rate, morbidity, and associated mortality. Generally, it occurs in later life, i.e., after 70 years of age. Historically, senile osteoporosis has been more common in females, but with the advent of a more elderly male population, this disease is becoming a

major factor in the health of both sexes. It is not clear what, if any, role hormones such as testosterone or estrogen have in this disease, and its etiology remains obscure. Treatment of this disease has not been very satisfactory. Hormone therapy, estrogen in women and testosterone in men, has shown equivocal results; calcitonin and bis-phosphonates may be of some utility.

The peak mass of the skeleton at maturity is largely under genetic control. Twin studies have shown that the variance in bone mass between adult monozygotic twins is smaller than between dizygotic twins (Slemenda et al, *J. Bone Miner. Res.*, 6:561-567 (1991); Young et al, *J. Bone Miner. Res.*, 6:561-567 (1995); Pocock et al, *J. Clin. Invest.*, 80:706-710 (1987); Kelly et al, *J. Bone Miner. Res.*, 8:11-17 (1993)), and it has been estimated that up to 60% or more of the variance in skeletal mass is inherited (Krall et al, *J. Bone Miner. Res.*, 10:S367 (1993)). Peak skeletal mass is the most powerful determinant of bone mass in elderly years (Hui et al, *Ann. Int. Med.*, 111:355-361 (1989)), even though the rate of age-related bone loss in adult and later life is also a strong determinant (Hui et al, *Osteoporosis Int.*, 1:30-34 (1995)). Since bone mass is the principal measurable determinant of fracture risk, the inherited peak skeletal mass achieved at maturity is an important determinant of an individual's risk of fracture later in life. Thus, study of the genetic basis of bone mass is of considerable interest in the etiology of fractures due to osteoporosis.

Recently, a strong interest in the genetic control of peak bone mass has developed in the field of osteoporosis. The interest has focused mainly on candidate genes with suitable polymorphisms to test for association with variation in bone mass within the normal range, or has focused on examination of genes and gene loci associated with low bone mass in the range found in patients with osteoporosis. The vitamin D receptor locus (VDR) (Morrison et al, *Nature*, 367:284-287 (1994)), PTH gene (Howard et al, *J. Clin. Endocrinol. Metab.*, 80:2800-2805 (1995); Johnson et al, *J. Bone Miner. Res.*, 8:11-17 (1995); Gong et al, *J. Bone Miner. Res.*, 10:S462 (1995)) and the estrogen receptor gene (Hosoi et al, *J. Bone Miner. Res.*, 10:S170 (1995); Morrison et al, *Nature*, 367:284-287 (1994)) have figured most prominently

in this work. These studies are difficult because bone mass (the phenotype) is a continuous, quantitative, polygenic trait, and is confounded by environmental factors such as nutrition, co-morbid disease, age, physical activity, and other factors. Also, this type of study design requires large numbers of subjects. In particular, the results of VDR studies to date have been confusing and contradictory (Garnero et al, *J. Bone Miner. Res.*, 10:1283-1288 (1995); Eisman et al, *J. Bone. Miner. Res.*, 10:1289-1293 (1995); Peacock, *J. Bone Miner. Res.*, 10:1294-1297 (1995)). Furthermore, the work thus far has not shed much light on the mechanism(s) whereby the genetic influences might exert their effect on bone mass.

While it is well known that peak bone mass is largely determined by genetic rather than environmental factors, studies to determine the gene loci (and ultimately the genes) linked to variation in bone mass are difficult and expensive. Study designs which utilize the power of linkage analysis, e.g., sib-pair or extended family, are generally more informative than simple association studies, although the latter do have value. However, genetic linkage studies involving bone mass are hampered by two major problems. The first problem is the phenotype, as discussed briefly above. Bone mass is a continuous, quantitative trait, and establishing a discrete phenotype is difficult. Each anatomical site for measurement may be influenced by several genes, many of which may be different from site to site. The second problem is the age component of the phenotype. By the time an individual can be identified as having low bone mass, there is a high probability that their parents or other members of prior generations will be deceased and therefore unavailable for study, and younger generations may not have even reached peak bone mass, making their phenotyping uncertain for genetic analysis.

Regardless, linkage analysis can be used to find the location of a gene causing a hereditary "disorder" and does not require any knowledge of the biochemical nature of the disorder, i.e., a mutated protein that is believed to cause the disorder does not need to be known. Traditional approaches depend on assumptions concerning the disease process that might implicate a known protein as

a candidate to be evaluated. The genetic localization approach using linkage analysis can be used to first find the general chromosomal region in which the defective gene is located and then to gradually reduce the size of the region in order to determine the location of the specific mutated gene as precisely as possible. After the gene itself is discovered within the candidate region, the messenger RNA and the protein are identified and, along with the DNA, are checked for mutations.

The genetic localization approach has practical implications since the location of the disease can be used for prenatal diagnosis even before the altered gene that causes the disease is found. Linkage analysis can enable families, even many of those that do not have a sick child, to know whether they are carriers of a disease gene and to evaluate the condition of an unborn child through molecular diagnosis. The transmission of a disease within families, then, can be used to find the defective gene. As used herein, reference to "high bone mass" (HBM) is analogous to reference to a disease state, although from a practical standpoint high bone mass can actually help a subject avoid the disease known as osteoporosis.

Linkage analysis is possible because of the nature of inheritance of chromosomes from parents to offspring. During meiosis, the two parental homologues pair to guide their proper separation to daughter cells. While they are lined up and paired, the two homologues exchange pieces of the chromosomes, in an event called "crossing over" or "recombination." The resulting chromosomes are chimeric, that is, they contain parts that originate from both parental homologues. The closer together two sequences are on the chromosome, the less likely that a recombination event will occur between them, and the more closely linked they are. In a linkage analysis experiment, two positions on the chromosomes are followed from one generation to the next to determine the frequency of recombination between them. In a study of an inherited disease, one of the chromosomal positions is marked by the disease gene or its normal counterpart, i.e., the inheritance of the chromosomal region can be determined by examining whether the individual displays symptoms of the disorder or not. The other position is marked by a DNA

sequence that shows natural variation in the population such that the two homologues can be distinguished based on the copy of the "marker" sequence that they possess. In every family, the inheritance of the genetic marker sequence is compared to the inheritance of the disease state. If, within a family carrying an autosomal dominant disorder such as high bone mass, every affected individual carries the same form of the marker and all the unaffected individuals carry at least one different form of the marker, there is a great probability that the disease gene and the marker are located close to each other. In this way, chromosomes may be systematically checked with known markers and compared to the disease state. The data obtained from the different families is combined, and analyzed together by a computer using statistical methods. The result is information indicating the probability of linkage between the genetic marker and the disease allowing different distances between them. A positive result can mean that the disease is very close to the marker, while a negative result indicates that it is far away on that chromosome, or on an entirely different chromosome.

Linkage analysis is performed by typing all members of the affected family at a given marker locus and evaluating the co-inheritance of a particular disease state with the marker probe, thereby determining how often the two of them are co-inherited. The recombination frequency can be used as a measure of the genetic distance between two gene loci. A recombination frequency of 1% is equivalent to 1 map unit, or 1 centiMorgan (cM), which is roughly equivalent to 1,000 kb of DNA. This relationship holds up to frequencies of about 20% or 20 cM.

The entire human genome is 3,300 cM long. In order to find an unknown disease gene within 5-10 cM of a marker locus, the whole human genome can be searched with roughly 330 informative marker loci spaced at approximately 10 cM intervals (Botstein et al, *Am. J. Hum. Genet.*, 32:314-331 (1980)). The reliability of linkage results is established by using a number of statistical methods. The method most commonly used for the analysis of linkage in humans is the LOD score method (Morton, *Prog. Clin. Biol. Res.*, 147:245-265 (1984), Morton et al, *Am. J. Hum.*

Genet., 38:868-883 (1986)) which was incorporated into the computer program LIPED by Ott, *Am. J. Hum. Genet.*, 28:528-529 (1976). LOD scores are the logarithm of the ratio of the likelihood that two loci are linked at a given distance to that they are not linked (>50 cM apart). The advantage of using logarithmic values is that they can be summed among families with the same disease. This becomes necessary given the relatively small size of human families.

By convention, a total LOD score greater than + 3.0 (that is, odds of linkage at the specified recombination frequency being 1000 times greater than odds of no linkage) is considered to be significant evidence for linkage at that particular recombination frequency. A total LOD score of less than - 2.0 (that is, odds of no linkage being 100 times greater than odds of linkage at the specified frequency) is considered to be strong evidence that the two loci under consideration are not linked at that particular recombination frequency. Until recently, most linkage analyses have been performed on the basis of two-point data, which is the relationship between the disorder under consideration and a particular genetic marker. However, as a result of the rapid advances in mapping the human genome over the last few years, and concomitant improvements in computer methodology, it has become feasible to carry out linkage analyses using multi-point data. Multi-point analysis provide a simultaneous analysis of linkage between the disease and several linked genetic markers, when the recombination distance among the markers is known.

Multi-point analysis is advantageous for two reasons. First, the informativeness of the pedigree is usually increased. Each pedigree has a certain amount of potential information, dependent on the number of parents heterozygous for the marker loci and the number of affected individuals in the family. However, few markers are sufficiently polymorphic as to be informative in all those individuals. If multiple markers are considered simultaneously, then the probability of an individual being heterozygous for at least one of the markers is greatly increased. Second, an indication of the position of the disease gene among the markers may be determined. This allows identification of flanking markers, and thus

eventually allows isolation of a small region in which the disease gene resides. Lathrop et al, *Proc. Natl. Acad. Sci. USA*, 81:3443-3446 (1984) have written the most widely used computer package, LINKAGE, for multi-point analysis.

There is a need in the art for identifying the gene associated with a high bone mass phenotype. The present invention is directed to this, as well as other, important ends.

SUMMARY OF THE INVENTION

The present invention describes the Zmax1 gene and the HBM gene on chromosome 11q13.3 by genetic linkage and mutation analysis. The use of additional genetic markers linked to the genes has aided this discovery. By using linkage analysis and mutation analysis, persons predisposed to HBM may be readily identified. Cloning methods using Bacterial Artificial Chromosomes have enabled the inventors to focus on the chromosome region of 11q13.3 and to accelerate the sequencing of the autosomal dominant gene. In addition, the invention identifies the Zmax1 gene and the HBM gene, and identifies the guanine-to-thymine polymorphism mutation at position 582 in the Zmax1 gene that produces the HBM gene and the HBM phenotype.

The present invention identifies the Zmax1 gene and the HBM gene, which may be used to determine if people are predisposed to HBM and, therefore, not susceptible to diseases characterized by reduced bone density, including, for example, osteoporosis, or are predisposed and susceptible to diseases characterized by abnormally high bone density, such as, for example, osteoporosis. Older individuals carrying the HBM gene express the HBM protein, and, therefore, do not develop osteoporosis. In other words, the HBM gene may be a suppressor of osteoporosis. This *in vivo* observation is a strong evidence that treatment of normal individuals with the HBM gene or protein, or fragments thereof, may ameliorate osteoporosis.

Moreover, such treatment will be indicated in the treatment of bone lesions, particularly bone fractures, for bone remodeling in the healing of such lesions. For example, persons predisposed to or suffering from stress fractures (i.e., the accumulation of stress-induced microfractures, eventually resulting in a true fracture through the bone cortex) may be identified and/or treated by means of the invention. Moreover, the methods and compositions of the invention will be of use in the treatment of secondary osteoporosis, where the course of therapy involves bone remodeling, such as endocrine conditions accompanying corticosteroid administration, hyperthyroidism, hypogonadism, hematologic malignancies, malabsorption and alcoholism, as well as disorders associated with vitamin D and/or phosphate metabolism, such as osteomalacia and rickets, and diseases characterized by abnormal or disordered bone remodeling, such as Paget's disease, and in neoplasms of bone, which may be benign or malignant.

In various embodiments, the present invention is directed to nucleic acids, proteins, vectors, and transformed hosts of HBM and Zmax1.

Additionally, the present invention is directed to applications of the above embodiments of the invention including, for example, gene therapy, pharmaceutical development, and diagnostic assays for bone development disorders. In preferred embodiments, the present invention is directed to methods for treating, diagnosing, preventing and screening for osteoporosis.

In one aspect of the present invention, there is provided an isolated nucleic acid sequence of SEQ ID NO: 2.

In another aspect of the present invention, there is provided an isolated amino acid sequence of SEQ ID NO: 4.

In another aspect of the present invention, there is provided a nucleic acid sequence encoding the amino acid sequence of SEQ ID NO: 4.

In another aspect of the present invention, there is provided a replicative cloning vector comprising the nucleic acid sequence of SEQ ID NO: 2 and a replicon operative in an isolated host cell.

In another aspect of the present invention, there is provided an isolated host cell transformed with the replicative cloning vector as disclosed above.

In another aspect of the present invention, there is provided an expression vector comprising the nucleic acid sequence of SEQ ID NO: 2 operably linked to a transcription regulatory region.

In another aspect of the present invention, there is provided an isolated host cell transformed with the expression vector as disclosed above.

In another aspect of the present invention, there is provided a method for testing a substance as a therapeutic agent for bone modulation in a host comprising administering the nucleic acid of SEQ ID NO: 2 to the host, and assessing whether bone modulation occurs.

In another aspect of the present invention, there is provided a method of identifying a molecule involved in bone modulation comprising identifying a molecule that bids to, or that inhibits binding of a molecule to, HBM.

In another aspect of the present invention, there is provided a method for identifying a protein involved in bone modulation comprising identifying a protein that has an expression level that is different in a first host comprising the Zmax1 gene when compared to a second host comprising the HBM gene.

In another aspect of the present invention, there is provided a method of identifying a candidate protein involved in bone modulation comprising, identifying a protein in a first individual having the high bone mass phenotype, identifying a protein in a second individual not having the high bone mass phenotype, comparing the protein of the first individual to the protein of the second individual, wherein (i) the protein that is present in the first individual but not the second individual is the candidate protein or (ii) the protein that is present in a higher amount in the first individual than in the second individual is the candidate protein or (iii) the protein that is present in a lower

amount in the first individual than in the second individual than in the second individual is the candidate protein.

In another aspect of the present invention, there is provided a method of identifying a candidate protein involved in bone modulation comprising, identifying a protein in a first individual having the high bone mass phenotype, identifying a protein in a second individual not having the high bone mass phenotype, and comparing the protein of the first individual tot he protein of the second individual, wherein (i) the protein that is present in the second individual but not the first individual is the candidate protein or (ii) the protein that is present in a higher amount in the second individual than in the first individual is the candidate protein or (iii) the protein that is present in a lower amount in the second individual than in the first individual is the candidate protein.

In another aspect of the present invention, there is provided a method of testing for HBM activity comprising immobilizing an HBM protein, binding a protein to the HBM protein, and measuring the extant of binding.

In another aspect of the present invention, there is provided a method for identification of a candidate molecule involved in bone modulation comprising, identifying a molecule that binds to, or that inhibits binding of a molecule to, the nucleic acid sequence of SEQ ID NO: 1, identifying a molecule that binds to, or that inhibits binding of a molecule to, the nucleic acid sequence of SEQ ID NO: 2, and comparing the extent of binding, or the extent of inhibition of binding, of the molecule to each nucleic acid sequence, wherein the molecule that binds, or inhibits binding, more or less to the nucleic acid sequence of SEQ ID NO: 2 or the nucleic acid sequence of SEQ ID NO: 1 is the candidate molecule.

In another aspect of the present invention, there is provided a method of pharmaceutical development for treatment of bone development disorders comprising identifying a molecule that binds to the amino acid sequence of SEQ ID NO: 4.
In another aspect of the present invention, there is provided a method of pharmaceutical development for treatment of bone development disorders comprising constructing a first host that contains the Zmax1 gene or protein, constructing a second host that contains the HBM gene or protein, analyzing a difference between the first host and the second host, identifying a molecule that, when added to the first host, causes the first host to exhibit a characteristic feature of the second host.

In another aspect of the present invention, there is provided use of the nucleic acid sequence of SEQ ID NO: 2 for the manufacture of a medicament for treating a

bone development disorder in an animal wherein the nucleic acid sequence of SEQ ID NO: 2 is capable of being transferred into a somatic cell of an animal suffering from a bone development disorder.

In another aspect of the present invention, there is provided a use of the nucleic acid sequence of SEQ ID NO: 2 for the manufacture of a medicament for treating a bone development disorder in an animal wherein the nucleic acid sequence of SEQ ID NO: 2 is capable of being transferred into a germ-line cell of an animal suffering from a bone development disorder.

In another aspect of the present invention, there is provided a use of the amino acid sequence of SEQ ID NO: 4 for the manufacture of a medicament for altering bone development in a host wherein a somatic cell of the host is capable of receiving the amino acid sequence of SEQ ID NO: 4.

In another aspect of the present invention, there is provided a use of the amino acid sequence of SEQ ID NO: 4 for the manufacture of a medicament for altering bone development in a host wherein a germ-line cell of the host is capable of receiving the amino acid sequence of SEQ ID NO: 4.

In another aspect of the present invention, there is provided a use of the amino acid sequence of SEQ ID NO: 4 for the manufacture of a medicament for treating osteoporosis in a patient.

In another aspect of the present invention, there is provided a use of the extracellular domain of the amino acid sequence of SEQ ID NO: 4 for the manufacture of a medicament for treating osteoporosis in a patient.

In another aspect of the present invention, there is provided a use of intracellular domain of the amino acid sequence of SEQ ID NO: 4 for the manufacture of a medicament for treating osteoporosis in a patient.

In another aspect of the present invention, there is provided a use of a molecule that binds to the nucleic acid sequence of SEQ ID NO: 2 in the manufacture of a medicament for treating bone development disorders in a patient.

In another aspect of the present invention, there is provided a use of an antibody, wherein the antibody is to the amino acid sequence of SEQ ID NO: 4 for the manufacture of a medicament for treating bone development disorders in a patient.

In another aspect of the present invention, there is provided a method for diagnostic screening for a genetic predisposition to a bone development disorder comprising screening a sample from a patient with a nucleotide sequence derived from the genomic or cDNA nucleic acid sequence of HBM or Zmax1.

In another aspect of the present invention, there is provided a diagnostic assay for bone development disorders comprising an antibody to the HBM protein.

In another aspect of the present invention, there is provided a method for identifying a genetic predisposition to bone development disorders comprising performing a haplotype analysis using the nucleic acid sequence of SEQ ID NO: 2 or the nucleic acid of SEQ ID NO: 1.

In another aspect of the present invention, there is provided a method of expressing the HBM protein in bone tissue comprising constructing an expression vector comprising a promoter that directs expression in bone tissue operably linked to the nucleic acid sequence of SEQ ID NO: 2.

In another aspect of the present invention, there is provided a bacterial artifical chromosome having the nucleic acid sequence of SEQ ID NO: 5, 6, 7, 8, 9, 10 or 11.

In another aspect of the present invention, there is provided a method for amplifying a nucleotide polymorphism in the Zmax1 gene comprising using the bacterial artificial chromosome as disclosed above.

In another aspect of the present invention, there is provided a method for amplifying a nucleotide polymorphism in the HBM gene comprising using the bacterial artificial chromosome as disclosed above.

In another aspect of the present invention, there is provided a method for identifying a regulatory element of a HBM gene comprising using the bacterial artificial chromosome as disclosed above.

In another aspect of the present invention, there is provided an isolated nucleic acid sequence comprising at least 15 contiguous nucleotides of SEQ ID NO: 2, wherein said 15 contiguous nucleotides comprise position 582 of SEQ ID NO: 2. In another aspect of the present invention, there is provided a replicative cloning vector comprising said nucleic acid sequence and a replicon operative in a host cell.

In another aspect of the present invention, there is provided an isolated host cell transformed with said replicative cloning vector.

In another aspect of the present invention, there is provided an expression vector comprising a nucleic acid sequence operably linked to a transcription regulatory region, wherein the nucleic acid sequence comprises at least 15 contiguous nucleotides of SEQ ID NO: 2, wherein said 15 contiguous nucleotides comprise position 582 of SEQ ID NO: 2.

In another aspect of the present invention, there is provided an isolated host cell transformed with the expression vector as disclosed above.

In another aspect of the present invention, there is provided an isolated nucleic acid sequence comprising at least 15 contiguous nucleotides of SEQ ID NO: 2, wherein said 15 contiguous nucleotides comprise position 582 of SEQ ID NO: 2, and which encodes for an amino acid sequence including a valine corresponding to valine at postion 171 of SEQ ID NO: 4 and wherein valine substitution is associated with a high bone mass phenotype.

In another aspect of the present invention, there is provided an isolated nucleic acid segment of at least 15 contiguous nucleotides including a polymorphic site from the nucleic acid sequence of SEQ ID NO: 2 in which G at position 582 is replaced by T, and sequences complementary thereto.

In another aspect of the present invention, there is provided an isolated nucleic acid segment of at least 15 contiguous nucleotides including a single nucleotide polymorphic site from an exon sequence selected from the group consisting of:

SEQ ID NO: 9 wherein nucleotide 69169 is replaced by A,

SEQ ID NO: 9 wherein nucleotide 27402 is replaced by G,

SEQ ID NO: 9 wherein nucleotide 27841 is replaced by C,

SEQ ID NO: 9 wherein nucleotide 35600 is replaced by G,

SEQ ID NO: 9 wherein nucleotide 45619 is replaced by A,

SEQ ID NO: 9 wherein nucleotide 46018 is replaced by G,

SEQ ID NO: 9 wherein nucleotide 46093 is replaced by G,

SEQ ID NO: 9 wherein nucleotide 46190 is replaced by G,

SEQ ID NO: 9 wherein nucleotide 50993 is replaced by C,

SEQ ID NO: 9 wherein nucleotide 51124 is replaced by T,

SEQ ID NO: 9 wherein nucleotide 55461 is replaced by T,

SEQ ID NO: 9 wherein nucleotide 63645 is replaced by A,

SEQ ID NO: 9 wherein nucleotide 63646 is replaced by C,

SEQ ID NO: 9 wherein nucleotide 24809 is replaced by G,

SEQ ID NO: 9 wherein nucleotide 27837 is replaced by C,

SEQ ID NO: 9 wherein nucleotide 31485 is replaced by T,

SEQ ID NO: 9 wherein nucleotide 31683 is replaced by G,

SEQ ID NO: 9 wherein nucleotide 24808 is replaced by G,

SEQ ID NO: 8 wherein nucleotide 31340 is replaced by C,

SEQ ID NO: 8 wherein nucleotide 32538 is replaced by G,

SEQ ID NO: 8 wherein nucleotide 13224 is replaced by G,

SEQ ID NO: 8 wherein nucleotide 21119 is replaced by A,

SEQ ID NO: 8 wherein nucleotide 30497 is replaced by A,

SEQ ID NO: 9 wherein nucleotide 24811 is replaced by C,

SEQ ID NO: 9 wherein nucleotide 68280 is replaced by A, and

sequences complementary thereto.

In another aspect of the present invention, there is provided a method of identifying a molecule involved in bone modulation comprising identifying a molecule that binds to or that inhibits binding of a molecule to a protein involved in focal adhesion signaling.

In another aspect of the present invention, there is provided a use of an agent that regulates a nucleic acid or polypeptide encoded thereby involved in focal adhesion signaling for the manufacture of a medicament for modulating bone density in a subject.

In other aspects of the present invention, there are provided a nucleic acid comprising SEQ ID NO: 66, SEQ ID NO: 71, SEQ ID NO: 77 or SEQ ID NO: 79; a replicative cloning vector comprising said nucleic acid and a replicon operative in a host cell; an expression vector comprising said nucleic acid, and an isolated host cell transformed with said expression vector.

In another aspect of the present invention, there is provided a a polypeptide comprising SEQ ID NO:90, SEQ ID NO:93, SEQ ID NO:94, SEQ ID NO:99 or SEQ ID NO:102.

In another aspect of the present invention, there is provided a nucleic acid encoding a polypetide selected from the group consisting of SEQ ID NO:90, SEQ ID NO:93, SEQ ID NO:94, SEQ ID NO:99 or SEQ ID NO:102.

In another aspect of the present invention, there is provided a use of an agent which modulates a nucleic acid or a polypeptide involved in focal adhesion signaling for the manufacture of a medicament for treating bone development disorders.

In another aspect of the present invention, there is provided a method of testing a compound for bone modulation activity of Zmax1 or a Zmax1 mutant comprising:

(a) immobilizing a Zmax1 protein, or a Zmax1 mutant protein, or a portion of a Zmax1 protein or a portion of a Zmax1 mutant protein to a substrate;

(b) exposing a compound to said Zmax1 protein or portion thereof, or to said Zmax1 mutant protein or portion thereof;

(c) determining whether said compound bound to said Zmax1 protein or to said Zmax1 mutant protein; and

(d) administering said compound to a host and determining whether administration of said protein modulates bone mass, if said compound bound to said Zmax1 protein or said Zmax1 mutant protein.

In another aspect of the present invention, there is provided a method for identifying proteins involved in Zmax1 signaling that modulates bone mass comprising:

(a) preparing a bait protein comprising operably linking a nucleic acid encoding Zmax1 or a biologically active portion of Zmax1 to a DNA binding domain of a yeast transcription factor;

(b) preparing a prey protein comprising operably linking a nucleic acid encoding a prey protein to a DNA binding domain of a yeast transcription factor;

(c) expressing said bait protein in a bate yeast and expressing said prey protein in a prey yeast;

(d) mixing said bait yeast and said prey yeast;

(e) determining whether the prey yeast mated to the bait yeast and given yeast mating, analyzing whether modulation of the prey protein modulates bone mass.

In another aspect of the present invention, there is provided an isolated nucleic acid comprising SEQ ID NO:1 or a biologically active fragment of SEQ ID NO:1, wherein a nucleotide of SEQ ID NO:1 which encodes YWTD motif is mutated and said mutation causes an altered bone mass phenotype in a host when SEQ ID NO:1 or said biologically active fragment of SEQ ID NO:1 is expressed in said host.

In another aspect of the present invention, there is provided a replicative cloning vector comprising the nucleic acid disclosed immediately above.

In another aspect of the present invention, there is provided an isolated host cell transformed with the replicative cloning vector disclosed immediately above.

In another aspect of the present invention, there is provided a transgenic animal which expresses a mutated Zmax1, wherein said mutated Zmax1 produces an altered bone mass when expressed in said animal.

In another aspect of the present invention, there is provided a use of a nucleic acid comprising SEQ ID NO:1 in the manufacture of a medicament for treating a bone development disorder in an animal wherein said nucleic acid is capable of being transferred into a somatic cell of an animal suffering from said bone development disorder.

In another aspect of the present invention, there is provided a use of a nucleic acid comprising SEQ ID NO:1 in the manufacture of a medicament for treating a bone

development disorder in an animal wherein said nucleic acid is capable of being transferred into a germ-line cell of an animal suffering from said bone development disorder.

In another aspect of the present invention, there is provided a use of an amino acid sequence comprising SEQ ID NO:3 or a biologically active fragment thereof for the manufacture of a medicament for modulating bone development in a host wherein a somatic cell of a host suffering from a bone development disorder is capable of receiving said amino acid sequence or a biologically active fragment thereof.

In another aspect of the present invention, there is provided an isolated high bone mass (HBM) polynucleotide comprising a nucleic acid selected from the group consisting of:

(a) a nucleic acid having SEQ ID NO: 2;

(b) a nucleic acid encoding a polypeptide of SEQ ID NO: 4;

(c) a nucleic acid amplified from a mammalian library using primers which hybridize to loci within the nucleic acid of SEQ ID NO: 2 or a nucleic acid encoding a polypeptide of SEQ ID NO: 4;

(d) a nucleic acid which hybridizes to the nucleic acid of SEQ ID NO: 2;

(e) a nucleic acid which is complementary to a nucleic acid of (a), (b), (c), and (d);

(f) a nucleic acid comprising at least 15 contiguous nucleotides which comprise position 582 of SEQ ID NO: 2 from a polynucleotide of (a), (b), (c), (d), and (e); and

wherein said isolated HBM polynucleotide encodes a protein or polypeptide, which when administered to a subject modulates bone mass.

In another aspect of the present invention, there is provided a method for testing a substance as a therapeutic agent for bone modulation in a host comprising administering a nucleic acid comprising SEQ ID NO: 1 to said host, and assessing whether bone modulation occurs in said host.

In another aspect of the present invention, there is provided a method for expressing Zmax1 protein in bone tissue comprising constructing an expression vector comprising a promoter that directs expression in bone tissue operably linked a nucleic acid comprising SEQ ID NO: 1 or a nucleic acid encoding a biologically active fragment of SEQ ID NO: 1.

In another aspect of the present invention, there is provided a use of a nucleic acid which is antisense to SEQ ID NO: 1 or to a portion of SEQ ID NO: 1 in an amount

which modulates bone mass for the manufacture of a medicament for modulating bone mass in an animal.

In another aspect of the present invention, there is provided a method of studying bone disorders comprising preparing a transgenic animal which expresses Zmax1; regulating said Zmax1; and determining impact of said Zmax1 regulation on bone development in said mammal.

In another aspect of the present invention, there is provided a transgenic animal which express a mutated Zmax1, wherein said mutated Zmax1 produces an altered bone mass when expressed in said animal.

In another aspect of the present invention, there is provided a method of testing a compound as a bone modulating compound by administering said compound to said transgenic animal and determining whether said compound modulated bone mass in said animal.

In another aspect of the present invention, there is provided an isolated high bone mass (HBM) polynucleotide disclosed above, wherein the nucleic acid is a nucleic acid of (a) or (b) or a nucleic acid complementary thereto.

In another aspect of the present invention, there is provided an isolated nucleic acid sequence comprising at least 15 contiguous nucleotides of SEQ ID NO:2 wherein said 15 contiguous nucleotides comprises positions 581, 582 and 583 of SEQ ID NO: 2.

In another aspect of the present invention, there is provided an isolated nucleic acid sequence comprising at least 15 contiguous nucleotides of SEQ ID NO: 2, wherein said 15 contiguous nucleotides comprise nucleotides which encode for an amino acid substitution at position 171 of SEQ ID NO: 4, which substitution is associated with a high bone mass phenotype.

In another aspect of the present invention, there is provided an isolated high bone mass (HBM) polynucleotide comprising a nucleic acid selected from the group consisting of:

(a) a nucleic acid having SEQ ID NO: 2;

(b) a nucleic acid encoding a polypeptide of SEQ ID NO: 4;

(c) a nucleic acid which is complementary to a nucleic acid of (a), (b); and

(d) a nucleic acid comprising at least 15 contiguous nucleotides which comprise position 582 of SEQ ID NO: 2 from a polynucleotide of (a), (b) and (c).

These and other aspects of the present invention are described in more detail below.

BRIEF DESCRIPTION OF THE FIGURES

Fig. 1A and 1B show the pedigree of the individuals used in the genetic linkage studies. Under each individual is an ID number, the z-score for spinal BMD, and the allele calls for the critical markers on chromosome 11. Solid symbols represent "affected" individuals. Symbols containing "N" are "unaffected"

individuals. DNA from 37 individuals was genotyped. Question marks denote unknown genotypes or individuals who were not genotyped.

Fig. 2A and 2B depict the BAC/STS content physical map of the HBM region in 11q13.3. STS markers derived from genes, ESTs, microsatellites, random sequences, and BAC endsequences are denoted above the long horizontal line. For markers that are present in GDB the same nomenclature has been used. Locus names (D11S####) are listed in parentheses after the primary name if available. STSs derived from BAC endsequences are listed with the BAC name first followed by L or R for the left and right end of the clone, respectively. The two large arrows indicate the genetic markers that define the HBM critical region. The horizontal lines below the STSs indicate BAC clones identified by PCR-based screening of a nine-fold coverage BAC library. Open circles indicate that the marker did not amplify the corresponding BAC library address during library screening. Clone names use the following convention: B for BAC, the plate, row and column address, followed by -H indicating the HBM project (i.e., B36F16-H).

Figs. 3A-3F show the genomic structure of Zmax1 with flanking intron sequences. Translation is initiated by the underlined "ATG" in exon 1. The site of the polymorphism in the HBM gene is in exon 3 and is represented by the underlined "G," whereby this nucleotide is a "T" in the HBM gene. The 3' untranslated region of the mRNA is underlined within exon 23 (exon 1, SEQ ID NO:40; exon 2, SEQ ID NO:41; exon 3, SEQ ID NO:42; exon 4, SEQ ID NO:43; exon 5, SEQ ID NO:44; exon 6, SEQ ID NO:45; exon 7, SEQ ID NO:46; exon 8, SEQ ID NO:47; exon 9, SEQ ID NO:48; exon 10, SEQ ID NO:49; exon 11, SEQ ID NO:50; exon 12, SEQ ID NO:51; exon 13, SEQ ID NO:52; exon 14, SEQ ID NO:53; exon 15, SEQ ID NO:54; exon 16, SEQ ID NO:55; exon 17, SEQ ID NO:56; exon 18, SEQ ID NO:57; exon 19, SEQ ID NO:58; exon 20, SEQ ID NO:59; exon 21, SEQ ID NO:60; exon 22, SEQ ID NO:61; and exon 23; SEQ ID NO:62).

Fig. 4 shows the domain organization of Zmax1, including the YWTD spacers, the extracellular attachment site, the binding site for LDL and calcium, the cysteine-rich growth factor repeats, the transmembrane region, the ideal PEST region with the CK-II phosphorylation site and the internalization domain. **Fig. 4** also shows the site of the glycine to valine change that occurs in the HBM protein. The signal peptide is located at amino acids 1-22, the extracellular domain is located at amino acids 23-1385, the transmembrane segment is located at amino acids 1386-1413, and the cytoplasmic domain is located at amino acids 1414-1615.

Fig. 5 is a schematic illustration of the BAC contigs B527D12 and B200E21 in relation to the HBM gene.

Figs. 6A-6J are the nucleotide and amino acid sequences of the wild-type gene, Zmax1. The location for the base pair substitution at nucleotide 582, a guanine to thymine, is underlined. This allelic variant is the HBM gene. The HBM gene encodes for a protein with an amino acid substitution of glycine to valine at position 171. The 5' untranslated region (UTR) boundaries bases 1 to 70, and the 3' UTR boundaries bases 4916-5120.

Figs. 7A and **7B** are northern blot analyses showing the expression of Zmax1 in various tissues.

Fig. 8 is a PCR product analysis.

Fig. 9 is allele specific oligonucleotide detection of the Zmax1 exon 3 mutation.

Fig. 10 is the cellular localization of mouse Zmax1 by *in situ* hybridization at 100X magnification using sense and antisense probes.

Fig. 11 is the cellular localization of mouse Zmax1 by *in situ* hybridization at 400X magnification using sense and antisense probes.

Fig. 12 is the cellular localization of mouse Zmax1 by *in situ* hybridization of osteoblasts in the endosteum at 400X magnification using sense and antisense probes.

Fig. 13 shows antisense inhibition of Zmax1 expression in MC-3T3 cells.

Fig. 14 shows a Zmax1 Exon3 Allele Specific Oligonucleotide (ASO) assay which illustrates the rarity of the HBM1 allele (right panels; T-specific oligo; 58°C Wash) as compared to the wild-type Zmax1 allele (left panels, G-specific oligo; 55°C Wash). The positive spots appearing in the right panels were positive controls.

Fig. 15 depicts a model representing the potential role of Zmax1 in focal adhesion signaling.

DETAILED DESCRIPTION OF THE INVENTION

To aid in the understanding of the specification and claims, the following definitions are provided.

"Gene" refers to a DNA sequence that encodes through its template or messenger RNA a sequence of amino acids characteristic of a specific peptide. The term "gene" includes intervening, non-coding regions, as well as regulatory regions, and can include 5' and 3' ends.

"Gene sequence" refers to a DNA molecule, including both a DNA molecule which contains a non-transcribed or non-translated sequence. The term is also intended to include any combination of gene(s), gene fragment(s), non-transcribed sequence(s) or non-translated sequence(s) which are present on the same DNA molecule.

The sequences of the present invention may be derived from a variety of sources including DNA, cDNA, synthetic DNA, synthetic RNA or combinations thereof. Such sequences may comprise genomic DNA which may or may not include naturally occurring introns. Moreover, such genomic DNA may be obtained in association with promoter regions or poly (A) sequences. The sequences, genomic DNA or cDNA may be obtained in any of several ways. Genomic DNA can be extracted and purified from suitable cells by means well known in the art. Alternatively, mRNA can be isolated from a cell and used to produce cDNA by reverse transcription or other means.

"cDNA" refers to complementary or copy DNA produced from an RNA template by the action of RNA-dependent DNA polymerase (reverse transcriptase). Thus, a "cDNA clone" means a duplex DNA sequence complementary to an RNA molecule of interest, carried in a cloning vector or PCR amplified. This term includes genes from which the intervening sequences have been removed.

"Recombinant DNA" means a molecule that has been recombined by *in vitro* splicing cDNA or a genomic DNA sequence.

"Cloning" refers to the use of *in vitro* recombination techniques to insert a particular gene or other DNA sequence into a vector molecule. In order to successfully clone a desired gene, it is necessary to use methods for generating DNA fragments, for joining the fragments to vector molecules, for introducing the composite DNA molecule into a host cell in which it can replicate, and for selecting the clone having the target gene from amongst the recipient host cells.

"cDNA library" refers to a collection of recombinant DNA molecules containing cDNA inserts which together comprise the entire genome of an organism. Such a cDNA library can be prepared by methods known to one skilled in the art and described by, for example, Cowell and Austin, "cDNA Library Protocols," Methods in Molecular Biology (1997). Generally, RNA is first isolated from the cells of an organism from whose genome it is desired to clone a particular gene.

"Cloning vehicle" refers to a plasmid or phage DNA or other DNA sequence which is able to replicate in a host cell. The cloning vehicle is characterized by one or more endonuclease recognition sites at which such DNA sequences may be cut in a determinable fashion without loss of an essential biological function of the DNA, which may contain a marker suitable for use in the identification of transformed cells.

"Expression control sequence" refers to a sequence of nucleotides that control or regulate expression of structural genes when operably linked to those genes. These include, for example, the lac systems, the trp system, major operator and promoter regions of the phage lambda, the control region of fd coat protein and

other sequences known to control the expression of genes in prokaryotic or eukaryotic cells. Expression control sequences will vary depending on whether the vector is designed to express the operably linked gene in a prokaryotic or eukaryotic host, and may contain transcriptional elements such as enhancer elements, termination sequences, tissue-specificity elements and/or translational initiation and termination sites.

"Expression vehicle" refers to a vehicle or vector similar to a cloning vehicle but which is capable of expressing a gene which has been cloned into it, after transformation into a host. The cloned gene is usually placed under the control of (i.e., operably linked to) an expression control sequence.

"Operator" refers to a DNA sequence capable of interacting with the specific repressor, thereby controlling the transcription of adjacent gene(s).

"Promoter" refers to a DNA sequence that can be recognized by an RNA polymerase. The presence of such a sequence permits the RNA polymerase to bind and initiate transcription of operably linked gene sequences.

"Promoter region" is intended to include the promoter as well as other gene sequences which may be necessary for the initiation of transcription. The presence of a promoter region is sufficient to cause the expression of an operably linked gene sequence.

"Operably linked" means that the promoter controls the initiation of expression of the gene. A promoter is operably linked to a sequence of proximal DNA if upon introduction into a host cell the promoter determines the transcription of the proximal DNA sequence(s) into one or more species of RNA. A promoter is operably linked to a DNA sequence if the promoter is capable of initiating transcription of that DNA sequence.

"Prokaryote" refers to all organisms without a true nucleus, including bacteria.

"Eukaryote" refers to organisms and cells that have a true nucleus, including mammalian cells.

"Host" includes prokaryotes and eukaryotes, such as yeast and filamentous fungi, as well as plant and animal cells. The term includes an organism or cell that is the recipient of a replicable expression vehicle.

"Fragment" of a gene refers to any variant of the gene that possesses the biological activity of that gene.

"Variant" refers to a gene that is substantially similar in structure and biological activity or immunological characteristics to either the entire gene or to a fragment of the gene. Provided that the two genes possess a similar activity, they are considered variant as that term is used herein even if the sequence of amino acid residues is not identical.

"Amplification of nucleic acids" refers to methods such as polymerase chain reaction (PCR), ligation amplification (or ligase chain reaction, LCR) and amplification methods based on the use of Q-beta replicase. These methods are well known in the art and described, for example, in U.S. Patent Nos. 4,683,195 and 4,683,202. Reagents and hardware for conducting PCR are commercially available. Primers useful for amplifying sequences from the HBM region are preferably complementary to, and hybridize specifically to sequences in the HBM region or in regions that flank a target region therein. HBM sequences generated by amplification may be sequenced directly. Alternatively, the amplified sequence(s) may be cloned prior to sequence analysis.

"Antibodies" may refer to polyclonal and/or monoclonal antibodies and fragments thereof, and immunologic binding equivalents thereof, that can bind to the HBM proteins and fragments thereof or to nucleic acid sequences from the HBM region, particularly from the HBM locus or a portion thereof. The term antibody is used both to refer to a homogeneous molecular entity, or a mixture such as a serum product made up of a plurality of different molecular entities. Proteins may be prepared synthetically in a protein synthesizer and coupled to a carrier molecule and injected over several months into rabbits. Rabbit sera is tested for immunoreactivity to the HBM protein or fragment. Monoclonal antibodies may be made by injecting

mice with the proteins, or fragments thereof. Monoclonal antibodies will be screened by ELISA and tested for specific immunoreactivity with HBM protein or fragments thereof. Harlow et al, *Antibodies: A Laboratory Manual*, Cold Spring Harbor Laboratory, Cold Spring Harbor, NY (1988). These antibodies will be useful in assays as well as pharmaceuticals.

"HBM" refers to high bone mass.

"HBM protein" refers to a protein that is identical to a Zmax1 protein except that it contains an alteration of glycine 171 to valine. An HBM protein is defined for any organism that encodes a Zmax1 true homologue. For example, a mouse HBM protein refers to the mouse Zmax1 protein having the glycine 170 to valine substitution.

"HBM gene" refers to the genomic DNA sequence found in individuals showing the HBM characteristic or phenotype, where the sequence encodes the protein indicated by SEQ ID NO: 4. The HBM gene and the Zmax1 gene are allelic. The protein encoded by the HBM gene has the property of causing elevated bone mass, while the protein encoded by the Zmax1 gene does not. The HBM gene and the Zmax1 gene differ in that the HBM gene has a thymine at position 582, while the Zmax1 gene has a guanine at position 582. The HBM gene comprises the nucleic acid sequence shown as SEQ ID NO: 2. The HBM gene may also be referred to as an "HBM polymorphism."

"Normal," "wild-type," "unaffected" and "Zmax1" all refer to the genomic DNA sequence that encodes the protein indicated by SEQ ID NO: 3. The Zmax1 gene has a guanine at position 582. The Zmax1 gene comprises the nucleic acid sequence shown as SEQ ID NO: 1. "Normal," "wild-type," "unaffected" and "Zmax1" also refer to allelic variants of the genomic sequence that encodes proteins that do not contribute to elevated bone mass. The Zmax1 gene is common in the human population, while the HBM gene is rare.

"5YWT+EGF" refers to a repeat unit found in the Zmax1 protein, consisting of five YWT repeats followed by an EGF repeat.

"Bone development" generally refers to any process involved in the change of bone over time, including, for example, normal development, changes that occur during disease states, and changes that occur during aging. "Bone development disorder" particularly refers to any disorders in bone development including, for example, changes that occur during disease states and changes that occur during aging. Bone development may be progressive or cyclical in nature. Aspects of bone that may change during development include, for example, mineralization, formation of specific anatomical features, and relative or absolute numbers of various cell types.

"Bone modulation" or "modulation of bone formation" refers to the ability to affect any of the physiological processes involved in bone remodeling, as will be appreciated by one skilled in the art, including, for example, bone resorption and appositional bone growth, by, inter alia, osteoclastic and osteoblastic activity, and may comprise some or all of bone formation and development as used herein.

"Normal bone density" refers to a bone density within two standard deviations of a Z score of 0.

A "Zmax1 system" refers to a purified protein, cell extract, cell, animal, human or any other composition of matter in which Zmax1 is present in a normal or mutant form.

A "surrogate marker" refers to a diagnostic indication, symptom, sign or other feature that can be observed in a cell, tissue, human or animal that is correlated with the HBM gene or elevated bone mass or both, but that is easier to measure than bone density. The general concept of a surrogate marker is well accepted in diagnostic medicine.

The present invention encompasses the Zmax1 gene and Zmax1 protein in the forms indicated by SEQ ID NOS: 1 and 3, respectively, and other closely related variants, as well as the adjacent chromosomal regions of Zmax1 necessary for its accurate expression. In a preferred embodiment, the present invention is directed to at least 15 contiguous nucleotides of the nucleic acid sequence of SEQ ID NO: 1.

The present invention also encompasses the HBM gene and HBM protein in the forms indicated by SEQ ID NO: 2 and 4, respectively, and other closely related variants, as well as the adjacent chromosomal regions of the HBM gene necessary for its accurate expression. In a preferred embodiment, the present invention is directed to at least 15 contiguous nucleotides of the nucleic acid sequence of SEQ ID NO: 2. More preferably, the present invention is directed to at least 15 contiguous nucleotides of the nucleic acid sequence of SEQ ID NO: 2, wherein one of the 15 contiguous nucleotides is the thymine at nucleotide 582.

The invention also relates to the nucleotide sequence of the Zmax1 gene region, as well as the nucleotide sequence of the HBM gene region. More particularly, a preferred embodiment are the BAC clones containing segments of the Zmax1 gene region B200E21-H and B527D12-H. A preferred embodiment is the nucleotide sequence of the BAC clones consisting of SEQ ID NOS: 5-11.

The invention also concerns the use of the nucleotide sequence to identify DNA probes for the Zmax1 gene and the HBM gene, PCR primers to amplify the Zmax1 gene and the HBM gene, nucleotide polymorphisms in the Zmax1 gene and the HBM gene, and regulatory elements of the Zmax1 gene and the HBM gene.

This invention describes the further localization of the chromosomal location of the Zmax1 gene and HBM gene on chromosome 11q13.3 between genetic markers D11S987 and SNP_CONTIG033-6, as well as the DNA sequences of the Zmax1 gene and the HBM gene. The chromosomal location was refined by the addition of more genetic markers to the mapping panel used to map the gene, and by the extension of the pedigree to include more individuals. The pedigree extension was critical because the new individuals that have been genotyped harbor critical recombination events that narrow the region. To identify genes in the region on 11q13.3, a set of BAC clones containing this chromosomal region was identified. The BAC clones served as a template for genomic DNA sequencing, and also as a reagent for identifying coding sequences by direct cDNA selection. Genomic sequencing and direct cDNA selection were used to characterize more than 1.5

million base pairs of DNA from 11q13.3. The Zmax1 gene was identified within this region and the HBM gene was then discovered after mutational analysis of affected and unaffected individuals.

When a gene has been genetically localized to a specific chromosomal region, the genes in this region can be characterized at the molecular level by a series of steps that include: cloning of the entire region of DNA in a set of overlapping clones (physical mapping), characterization of genes encoded by these clones by a combination of direct cDNA selection, exon trapping and DNA sequencing (gene identification), and identification of mutations in these genes by comparative DNA sequencing of affected and unaffected members of the HBM kindred (mutation analysis).

Physical mapping is accomplished by screening libraries of human DNA cloned in vectors that are propagated in *E. coli* or *S. cereviseae* using PCR assays designed to amplify unique molecular landmarks in the chromosomal region of interest. To generate a physical map of the HBM candidate region, a library of human DNA cloned in Bacterial Artificial Chromosomes (BACs) was screened with a set of Sequence Tagged Site (STS) markers that had been previously mapped to chromosome 11q12-q13 by the efforts of the Human Genome Project.

STSs are unique molecular landmarks in the human genome that can be assayed by PCR. Through the combined efforts of the Human Genome Project, the location of thousands of STSs on the twenty-two autosomes and two sex chromosomes has been determined. For a positional cloning effort, the physical map is tied to the genetic map because the markers used for genetic mapping can also be used as STSs for physical mapping. By screening a BAC library with a combination of STSs derived from genetic markers, genes, and random DNA fragments, a physical map comprised of overlapping clones representing all of the DNA in a chromosomal region of interest can be assembled.

BACs are cloning vectors for large (80 kilobase to 200 kilobase) segments of human or other DNA that are propagated in *E. coli*. To construct a physical map

using BACs, a library of BAC clones is screened so that individual clones harboring the DNA sequence corresponding to a given STS or set of STSs are identified. Throughout most of the human genome, the STS markers are spaced approximately 20 to 50 kilobases apart, so that an individual BAC clone typically contains at least two STS markers. In addition, the BAC libraries that were screened contain enough cloned DNA to cover the human genome six times over. Therefore, an individual STS typically identifies more than one BAC clone. By screening a six-fold coverage BAC library with a series of STS markers spaced approximately 50 kilobases apart, a physical map consisting of a series of overlapping BAC clones, i.e. BAC contigs, can be assembled for any region of the human genome. This map is closely tied to the genetic map because many of the STS markers used to prepare the physical map are also genetic markers.

When constructing a physical map, it often happens that there are gaps in the STS map of the genome that result in the inability to identify BAC clones that are overlapping in a given location. Typically, the physical map is first constructed from a set of STSs that have been identified through the publicly available literature and World Wide Web resources. The initial map consists of several separate BAC contigs that are separated by gaps of unknown molecular distance. To identify BAC clones that fill these gaps, it is necessary to develop new STS markers from the ends of the clones on either side of the gap. This is done by sequencing the terminal 200 to 300 base pairs of the BACs flanking the gap, and developing a PCR assay to amplify a sequence of 100 or more base pairs. If the terminal sequences are demonstrated to be unique within the human genome, then the new STS can be used to screen the BAC library to identify additional BACs that contain the DNA from the gap in the physical map. To assemble a BAC contig that covers a region the size of the HBM candidate region (2,000,000 or more base pairs), it is often necessary to develop new STS markers from the ends of several clones.

After building a BAC contig, this set of overlapping clones serves as a template for identifying the genes encoded in the chromosomal region. Gene

identification can be accomplished by many methods. Three methods are commonly used: (1) a set of BACs selected from the BAC contig to represent the entire chromosomal region can be sequenced, and computational methods can be used to identify all of the genes, (2) the BACs from the BAC contig can be used as a reagent to clone cDNAs corresponding to the genes encoded in the region by a method termed direct cDNA selection, or (3) the BACs from the BAC contig can be used to identify coding sequences by selecting for specific DNA sequence motifs in a procedure called exon trapping. The present invention includes genes identified by the first two methods.

To sequence the entire BAC contig representing the HBM candidate region, a set of BACs was chosen for subcloning into plasmid vectors and subsequent DNA sequencing of these subclones. Since the DNA cloned in the BACs represents genomic DNA, this sequencing is referred to as genomic sequencing to distinguish it from cDNA sequencing. To initiate the genomic sequencing for a chromosomal region of interest, several non-overlapping BAC clones are chosen. DNA for each BAC clone is prepared, and the clones are sheared into random small fragments which are subsequently cloned into standard plasmid vectors such as pUC18. The plasmid clones are then grown to propagate the smaller fragments, and these are the templates for sequencing. To ensure adequate coverage and sequence quality for the BAC DNA sequence, sufficient plasmid clones are sequenced to yield six-fold coverage of the BAC clone. For example, if the BAC is 100 kilobases long, then phagemids are sequenced to yield 600 kilobases of sequence. Since the BAC DNA was randomly sheared prior to cloning in the phagemid vector, the 600 kilobases of raw DNA sequence can be assembled by computational methods into overlapping DNA sequences termed sequence contigs. For the purposes of initial gene identification by computational methods, six-fold coverage of each BAC is sufficient to yield ten to twenty sequence contigs of 1000 base pairs to 20,000 base pairs.

The sequencing strategy employed in this invention was to initially sequence "seed" BACs from the BAC contig in the HBM candidate region. The sequence of the "seed" BACs was then used to identify minimally overlapping BACs from the contig, and these were subsequently sequenced. In this manner, the entire candidate region was sequenced, with several small sequence gaps left in each BAC. This sequence served as the template for computational gene identification. One method for computational gene identification is to compare the sequence of BAC contig to publicly available databases of cDNA and genomic sequences, e.g. unigene, dbEST, genbank. These comparisons are typically done using the BLAST family of computer algorithms and programs (Altschul et al, *J. Mol. Biol.*, 215:403-410 (1990)). The BAC sequence can also be translated into protein sequence, and the protein sequence can be used to search publicly available protein databases, using a version of BLAST designed to analyze protein sequences (Altschul et al, *Nucl. Acids Res.*, 25:3389-3402 (1997)). Another method is to use computer algorithms such as MZEF (Zhang, *Proc. Natl. Acad. Sci.*, 94:565-568 (1997)) and GRAIL (Uberbacher et al, *Methods Enzymol.*, 266:259-281 (1996)), which predict the location of exons in the sequence based on the presence of specific DNA sequence motifs that are common to all exons, as well as the presence of codon usage typical of human protein encoding sequences.

In addition to identifying genes by computational methods, genes were also identified by direct cDNA selection (Del Mastro et al, *Genome Res.* 5(2):185-194 (1995)). In direct cDNA selection, cDNA pools from tissues of interest are prepared, and the BACs from the candidate region are used in a liquid hybridization assay to capture the cDNAs which base pair to coding regions in the BAC. In the methods described herein, the cDNA pools were created from several different tissues by random priming the first strand cDNA from polyA RNA, synthesizing the second strand cDNA by standard methods, and adding linkers to the ends of the cDNA fragments. The linkers are used to amplify the cDNA pools. The BAC clones are used as a template for *in vitro* DNA synthesis to create a biotin labelled

copy of the BAC DNA. The biotin labelled copy of the BAC DNA is then denatured and incubated with an excess of the PCR amplified, linkered cDNA pools which have also been denatured. The BAC DNA and cDNA are allowed to anneal in solution, and heteroduplexes between the BAC and the cDNA are isolated using streptavidin coated magnetic beads. The cDNAs that are captured by the BAC are then amplified using primers complimentary to the linker sequences, and the hybridization/selection process is repeated for a second round. After two rounds of direct cDNA selection, the cDNA fragments are cloned, and a library of these direct selected fragments is created.

The cDNA clones isolated by direct selection are analyzed by two methods. Since a pool of BACs from the HBM candidate region is used to provide the genomic DNA sequence, the cDNAs must be mapped to individual BACs. This is accomplished by arraying the BACs in microtiter dishes, and replicating their DNA in high density grids. Individual cDNA clones are then hybridized to the grid to confirm that they have sequence identity to an individual BAC from the set used for direct selection, and to determine the specific identity of that BAC. cDNA clones that are confirmed to correspond to individual BACs are sequenced. To determine whether the cDNA clones isolated by direct selection share sequence identity or similarity to previously identified genes, the DNA and protein coding sequences are compared to publicly available databases using the BLAST family of programs.

The combination of genomic DNA sequence and cDNA sequence provided by BAC sequencing and by direct cDNA selection yields an initial list of putative genes in the region. The genes in the region were all candidates for the HBM locus. To further characterize each gene, Northern blots were performed to determine the size of the transcript corresponding to each gene, and to determine which putative exons were transcribed together to make an individual gene. For Northern blot analysis of each gene, probes were prepared from direct selected cDNA clones or by PCR amplifying specific fragments from genomic DNA or from the BAC encoding the putative gene of interest. The Northern blots gave information on the size of the

transcript and the tissues in which it was expressed. For transcripts which were not highly expressed, it was sometimes necessary to perform a reverse transcription PCR assay using RNA from the tissues of interest as a template for the reaction.

Gene identification by computational methods and by direct cDNA selection provides unique information about the genes in a region of a chromosome. When genes are identified, then it is possible to examine different individuals for mutations in each gene.

I. Phenotyping using DXA Measurements

Spinal bone mineral content (BMC) and bone mineral density (BMD) measurements performed at Creighton University (Omaha, Nebraska) were made by DXA using a Norland Instruments densitometer (Norland XR2600 Densitometer, Dual Energy X-ray Absorptiometry, DXA). Spinal BMC and BMD at other locations used the machinery available. There are estimated to be 800 DXA machines currently operating in the U.S. Most larger cities have offices or imaging centers which have DXA capabilities, usually a Lunar or Hologic machine. Each location that provided spine BMC and BMD data included copies of the printouts from their machines to provide verification that the regions of interest for measurement of BMD have been chosen appropriately. Complete clinical histories and skeletal radiographs were obtained.

The HBM phenotype is defined by the following criteria: very high spinal BMD; a clinical history devoid of any known high bone mass syndrome; and skeletal radiographs showing a normal shape of the appendicular skeleton.

II. Genotyping of Microsatellite Markers

To narrow the genetic interval to a region smaller than that originally reported by Johnson et al, *Am. J. Hum. Genet.*, 60:1326-1332 (1997), additional microsatellite markers on chromosome 11q12-13 were typed. The new markers included: D11S4191, D11S1883, D11S1785, D11S4113, D11S4136, D11S4139, (Dib, et al, *Nature*, 380:152-154 (1996), FGF3 (Polymeropolous, et al, *Nucl. Acid Res.*, 18:7468 (1990)), as well as GTC_HBM_Marker_1, GTC_HBM_Marker_2,

GTC_HBM_Marker_3, GTC_HBM_Marker_4, GTC_HBM_Marker_5, GTC_HBM_Marker_6, and GTC_HBM_Marker_7 (*See* **Fig. 2**).

Blood (20 ml) was drawn into lavender cap (EDTA containing) tubes by a certified phlebotomist. The blood was stored refrigerated until DNA extraction. DNA has been extracted from blood stored for up to 7 days in the refrigerator without reduction in the quality or quantity of yield. For those subjects that have blood drawn at distant sites, a shipping protocol was successfully used on more than a dozen occasions. Blood samples were shipped by overnight express in a styrofoam container with freezer packs to provide cooling. Lavender cap tubes were placed on individual plastic shipping tubes and then into "zip-lock" biohazard bags. When the samples arrived the next day, they were immediately processed to extract DNA.

The DNA extraction procedure used a kit purchased from Gentra Systems, Inc. (Minneapolis, Minnesota). Briefly, the procedure involved adding 3 volumes of a red blood cell lysis buffer to the whole blood. After incubations for 10 minutes at room temperature, the solution was centrifuged in a Beckman tabletop centrifuge at 2,000 X g for 10 minutes. The white blood cell pellet was resuspended in Cell Lysis Buffer. Once the pellet was completely resuspended and free of cell clumps, the solution was digested with RNase A for 15 minutes at 37°C. Proteins were precipitated by addition of the provided Protein Precipitation Solution and removed by centrifugation. The DNA was precipitated out of the supernatant by addition of isopropanol. This method was simple and fast, requiring only 1-2 hours, and allowed for the processing of dozens of samples simultaneously. The yield of DNA was routinely >8 mg for a 20 ml sample of whole blood and had a MW of >50 kb. DNA was archived by storing coded 50 µg aliquots at -80°C as an ethanol precipitate.

DNA was genotyped using one fluorescently labeled oligonucleotide primer and one unlabeled oligonucleotide primer. Labeled and unlabeled oligonucleotides were obtained from Integrated DNA Technologies, Inc. (Coralville, Iowa). All other

reagents for microsatellite genotyping were purchased from Perkin Elmer-Applied Biosystems, Inc. ("PE-ABI") (Norwalk, Connecticut). Individual PCR reactions were performed for each marker, as described by PE-ABI using AmpliTag DNA Polymerase. The reactions were added to 3.5 µl of loading buffer containing deionized formamide, blue dextran and TAMRA 350 size standards (PE-ABI). After heating at 95°C for 5 minutes to denature the DNA, the samples were loaded and electrophoresed as described in the operator's manual for the Model 377 DNA Sequencer (PE-ABI, Foster City, California). After gel electrophoresis, the data was analyzed using PE-ABI GENESCAN™ and GENOTYPER™ software. First, within the GENESCAN™ software, the lane tracking was manually optimized prior to the first step of analysis. After the gel lane data was extracted, the standard curve profiles of each lane were examined and verified for linearity and size calling. Lanes, which had problems with either of these parameters, were re-tracked and verified. Once all lanes were tracked and the size standards were correctly identified, the data were imported into GENOTYPER™ for allele identification To expedite allele calling (binning), the program Linkage Designer from the Internet web-site of Dr. Guy Van Camp (http://alt.www.uia.ac.be/u/dnalab/ld.html) was used. This program greatly facilitates the importing of data generated by GENOTYPER™ into the pedigree drawing program Cyrillic (Version 2.0, Cherwell Scientific Publishing Limited, Oxford, Great Britain) and subsequent linkage analysis using the program LINKAGE (Lathrop et al, *Am. J. Hum. Genet.*, 37:482-498 (1985)).

III. Linkage Analysis

Fig. 1 demonstrates the pedigree of the individuals used in the genetic linkage studies for this invention. Specifically, two-point linkage analysis was performed using the MLINK and LINKMAP components of the program LINKAGE (Lathrop et al, *Am. J. Hum. Genet.*, 37:482-498 (1985)). Pedigree/marker data was exported from Cyrillic as a pre-file into the Makeped program and converted into a suitable ped-file for linkage analysis.

The original linkage analysis was performed using three models: (i) an autosomal dominant, fully penetrant model, (ii) an autosomal dominant model with reduced penetrance, and (iii) a quantitative trait model. The HBM locus was mapped to chromosome 11q12-13 by analyzing DNA for linked markers from 22 members of a large, extended kindred. A highly automated technology was used with a panel of 345 fluorescent markers which spanned the 22 autosomes at a spacing interval ranging from 6-22 cM. Only markers from this region of chromosome 11 showed evidence of linkage (LOD score ~3.0). The highest LOD score (5.74) obtained by two-point and multipoint analysis was D11S987 (map position 55 in **Fig. 2**). The 95% confidence interval placed the HBM locus between markers D11S905 and D11S937 (map position 41-71 in **Fig. 2**). Haplotype analysis also places the Zmax1 gene in this same region. Further descriptions of the markers D11S987, D11S905, and D11S937 can be found in Gyapay et al, *Nature Genetics*, Vol. 7, (1994).

In this invention, the inventors report the narrowing of the HBM interval to the region between markers D11S987 and GTC_HBM_Marker_5. These two markers lie between the delimiting markers from the original analysis (D11S11S905 and D11S937) and are approximately 3 cM from one another. The narrowing of the interval was accomplished using genotypic data from the markers D11S4191, D11S1883, D11S1785, D11S4113, D11S4136, D11S4139, (Dib et al, *Nature*, 380:152-154 (1996)), FGF3 (Polymeropolous et al, *Nucl. Acid Res.*, 18:7468 (1990)) (information about the genetic markers can be found at the internet site of the Genome Database, http://gdbwww.gdb.org/), as well as the markers GTC_HBM_Marker_1, GTC_HBM_Marker_2, GTC_HBM_Marker_3, GTC_HBM_Marker_4, GTC_HBM_Marker_5, GTC_HBM_Marker_6, and GTC_HBM_Marker_7.

As shown in **Fig. 1**, haplotype analysis with the above genetic markers identifies recombination events (crossovers) in individuals 9019 and 9020 that significantly refine the interval of chromosome 11 to which the Zmax1 gene is

localized. Individual 9019 is an HBM-affected individual that inherits a portion of chromosome 11 from the maternal chromosome with the HBM gene, and a portion from the chromosome 11 homologue. The portion inherited from the HBM gene-carrying chromosome includes markers D11S935, D11S1313, GTC_HBM_Marker_4, D11S987, D11S1296, GTC_HBM_Marker_6, GTC_HBM_Marker_2, D11S970, GTC_HBM_Marker_3, D11S4113, GTC_HBM_Marker_1, GTC_HBM_Marker_7 and GTC_HBM_Marker_5. The portion from D11S4136 and continuing in the telomeric direction is derived from the non-HBM chromosome. This data places the Zmax1 gene in a location centromeric to the marker GTC_HBM_Marker_5. Individual 9020 is an unaffected individual who also exhibits a critical recombination event. This individual inherits a recombinant paternal chromosome 11 that includes markers D11S935, D11S1313, GTC_HBM_Marker_4, D11S987, D11S1296 and GTC_HBM_Marker_6 from her father's (individual 0115) chromosome 11 homologue that carries the HBM gene, and markers GTC_HBM_Marker_2, D11S970, GTC_HBM_Marker_3, GTC_HBM_Marker_1, GTC_HBM_Marker_7, GTC_HBM_Marker_5, D11S4136, D11S4139, D11S1314, and D11S937 from her father's chromosome 11 that does not carry the HBM gene. Marker D11S4113 is uninformative due to its homozygous nature in individual 0115. This recombination event places the centromeric boundary of the HBM region between markers D11S1296 and D11S987.

Two-point linkage analysis was also used to confirm the location of the Zmax1 gene on chromosome 11. The linkage results for two point linkage analysis under a model of full penetrance are presented in Table 1 below. This table lists the genetic markers in the first column and the recombination fractions across the top of the table. Each cell of the column shows the LOD score for an individual marker tested for linkage to the Zmax1 gene at the recombination fraction shown in the first row. For example, the peak LOD score of 7.66 occurs at marker D11S970, which is within the interval defined by haplotype analysis.

TABLE 1

Marker	0.0	0.05	0.1	0.15	0.2	0.25	0.3	0.35	0.4
D11S935	- infinity	0.39	0.49	0.47	0.41	0.33	0.25	0.17	0.10
D11S1313	- infinity	2.64	2.86	2.80	2.59	2.30	1.93	1.49	1.00
D11S987	- infinity	5.49	5.18	4.70	4.13	3.49	2.79	2.03	1.26
D11S4113	4.35	3.99	3.62	3.24	2.83	2.40	1.94	1.46	0.97
D11S1337	2.29	2.06	1.81	1.55	1.27	0.99	0.70	0.42	0.18
D11S970	7.66	6.99	6.29	5.56	4.79	3.99	3.15	2.30	1.44
D11S4136	6.34	5.79	5.22	4.61	3.98	3.30	2.59	1.85	1.11
D11S4139	6.80	6.28	5.73	5.13	4.50	3.84	3.13	2.38	1.59
FGF3	0.59	3.23	3.15	2.91	2.61	2.25	1.84	1.40	0.92
D11S1314	6.96	6.49	5.94	5.34	4.69	4.01	3.27	2.49	1.67
D11S937	-infinity	4.98	4.86	4.52	4.06	3.51	2.88	2.20	1.47

A single nucleotide polymorphism (SNP) further defines the HBM region. This SNP is termed SNP_Contig033-6 and is located 25 kb centromeric to the genetic marker GTC_HBM_Marker_5. This SNP is telomeric to the genetic marker GTC_HBM_Marker_7. SNP_Contig033-6 is present in HBM-affected individual 0113. However, the HBM-affected individual 9019, who is the son of 0113, does not carry this SNP. Therefore, this indicates that the crossover is centromeric to this SNP. The primer sequence for the genetic markers GTC_HBM_Marker_5 and GTC_HBM_Marker_7 is shown in Table 2 below.

TABLE 2

Marker	Primer (Forward)	Primer (Reverse)
GTC_HBM_ Marker_5	TTTTGGGTACACAATTCAGTCG	AAAACTGTGGGTGCTTCTGG
GTC_HBM_ Marker_7	GTGATTGAGCCAATCCTGAGA	TGAGCCAAATAAACCCCTTCT

The kindred described have several features of great interest, the most important being that their bones, while very dense, have an absolutely normal shape. The outer dimensions of the skeletons of the HBM-affected individuals are normal, and, while medullary cavities are present, there is no interference with hematopoiesis. The HBM-affected members seem to be resistant to fracture, and there are no neurologic symptoms, and no symptoms of impairment of any organ or system function in the members examined. HBM-affected members of the kindred live to advanced age without undue illness or disability. Furthermore, the HBM phenotype matches no other bone disorders such as osteoporosis, osteoporosis pseudoglioma, Engelmann's disease, Ribbing's disease, hyperphosphatasemia, Van Buchem's disease, melorheostosis, osteopetrosis, pycnodysostosis, sclerostenosis, osteopoikilosis, acromegaly, Paget's disease, fibrous dysplasia, tubular stenosis, osteogenesis imperfecta, hypoparathyroidism, pseudohypoparathyroidism, pseudopseudohypoparathyroidism, primary and secondary hyperparathyroidism and associated syndromes, hypercalciuria, medullary carcinoma of the thyroid gland, osteomalacia and other diseases. Clearly, the HBM locus in this family has a very powerful and substantial role in regulating bone density, and its identification is an important step in understanding the pathway(s) that regulate bone density and the pathogenesis of diseases such as osteoporosis.

In addition, older individuals carrying the HBM gene, and therefore expression of the HBM protein, do not show loss of bone mass characteristic of normal individuals. In other words, the HBM gene is a suppressor of osteoporosis. In essence, individuals carrying the HBM gene are dosed with the HBM protein, and, as a result, do not develop osteoporosis. This *in vivo* observation is strong evidence that treatment of normal individuals with the HBM gene or protein, or a fragment thereof, will ameliorate osteoporosis.

IV. Physical Mapping

To provide reagents for the cloning and characterization of the HBM locus, the genetic mapping data described above were used to construct a physical map of

the region containing Zmax1 on chromosome 11q13.3. The physical map consists of an ordered set of molecular landmarks, and a set of BAC clones that contain the Zmax1 gene region from chromosome 11q13.3.

Various publicly available mapping resources were utilized to identify existing STS markers (Olson et al, *Science*, 245:1434-1435 (1989)) in the HBM region. Resources included the GDB, the Whitehead Institute Genome Center, dbSTS and dbEST (NCBI), 11db, the University of Texas Southwestern GESTEC, the Stanford Human Genome Center, and several literature references (Courseaux et al, *Genomics*, 40:13-23 (1997), Courseaux et al, *Genomics*, 37:354-365 (1996), Guru et al, *Genomics*, 42:436-445 (1997), Hosoda et al, *Genes Cells*, 2:345-357 (1997), James et al, *Nat. Genet.*, 8:70-76 (1994), Kitamura et al, *DNA Research*, 4:281-289 (1997), Lemmens et al, *Genomics*, 44:94-100 (1997), Smith et al, *Genome Res.*, 7:835-842 (1997)). Maps were integrated manually to identify markers mapping to the region containing Zmax1.

Primers for existing STSs were obtained from the GDB or literature references are listed in Table 3 below. Thus, Table 3 shows the STS markers used to prepare the physical map of the Zmax1 gene region.

TABLE 3: HBM STS Table

STS Name	Locus Nam	Type	GDB Access.	Size (kb)	Forward Primer	Reverse Primer	Gene Name
AGTN3		Gene	GDB:187568	0.164	CTGGACTACGTGCCTCTC	TTCAGAAGCACTTGGCTGG	Actinin, alpha 3 - skeletal muscle
PC-B/PC-Y		Gene	GDB:197884	0.125	CTCAGTGCCATGAAGATGGA	CAAGATCACTCGAATGTCCAGG	Pyruvate Carboxylase
	D11S2161	Gene		0.322	GTTTCAGGAGACTCAGAGTC	TTGTGCAGGTTGCTGTTGAG	Adenosine Receptor (A2) Gene
ADRBK1		Gene	GDB:1650178	0.117	TTATTGTGATTTCCCGTGGC	GCCCTCTGTCTGACTTCAGG	Beta-adrenergic receptor kinase
PSANK3		GENE		0.258	GAGAAAGAAATAAGGGGACC	TGCTTTGTAAAGCACTGAGA	sim. to Human endogenous retrovirus mRNA long terminal repeat
PP1(1/2)/PP1(2/2)		Gene	GDB:197589	0.206	GAAGTACGGGCAGTTCAGTGGCCT	ATACACAAGGTCCATGTTCCCCGT	Protein phosphatase 1, catalytic subunit, alpha isoform
GSTP1 PCR1		Gene	GDB:270088	0.19	AGCCTGGGCCACAGCGTGAGACTAC	CATGTGCCCACTTCATTCAT	Glutathione S-transferase pi
NDUFV1		Gene		0.21	CAGAAGAGTCAAGGGACTTG	CAAGATTCTGTAGCTCTCTGG	NADH dehydrogenase (ubiquinone) flavoprotein 1 (51kD)
PSANK2		GENE		0.167	CAGAAGAGTCAAGGGACTTG	ATCCTCTCACATCCCCACACT	Aldehyde Dehydrogenase 8 (ALDH8)
PSANK1		EST		0.3	CAAGGCTAAAAGACGAAAAA	TCAGTGAGCATTTCATCTTTT	Human ribosomal protein L37 (PSANK1) pseudogene.
UT8620	D11S1817	NBAT	GDB:314521	0.211	AAGTCGAGGCTCGCAAGGAG	GCCCTGTGTTCCTTTCAGTA	
AFM289ya9	D11S1337	NBAT	GDB:199809	0.287	AAGGTGTAGGATCACTGG	AGCTCATGGGGGCTATT	
GALN		Gene		0.322	GCTTCTCCCAAGTGTATCAAC	ATGGCAGAGGACTTAGAACA	Preprogalanin (GAL1)
PMB51	D11S97	VNTR	GDB:177850	0.205	GATGAGGGAAGTTCCTCTCGGCTC	TCCACATTGAGGACTGTGGGAACG	
BCL1(1)/BCL1(2)		Gene		0.248	GCACAGCTGTAGTGGGGTTGTAGAT	CAGCGGGAAAAGAAGATGCACACGGC	B-cell CLL/lymphoma 1 - Cyclin D1 (PRAD1 gene)
CCND1		Gene	GDB:4590141	0.549	CACCGATGAGTGGACAGTTCAAGGAG	CAGACAGAGATGGTCCACGCCATAC	Cyclin D1
FGF4		Gene	GDB:4590113	0.161	TTTCTGGGTGTGTGTGTAAT	ACACAGTTGCCTCTAAAGGGT	Fibroblast growth factor 4
FGF3, PCR1		Gene	GDB:186827	0.22	CATTGGGAAATCCAGAAGA	TAGGTGTCTTATTTTTGTTGTCTC	Fibroblast growth factor 3
AFM164ZF12	D11S913	NBAT	GDB:189161	0.184	GTGGACAGCCATAGTGAGG	CAACCCATACCAGGGATAAG	Choline Kinase
AFMA190YD5	D11S703	STS	GDB:1952200	0.276	GACATACCATGAACACTATAAGAGG	TGTTCACTCTCTGCCTGCAG	
BHGC-15205	D11S1899	NBAT	GDB:497865	0.183	AGGTGGACTGTGACAGAATG	CAAGAGGCTGGTAGAAGGTG	
AFMb356ya9	D11S887	MBAT	GDB:195002	0.092	GACTCCAGTCTGGGCAATAAAAGC	GGTGGGCAGCATGACTCTAAG	
BHGC-14407	D11S4178	NBAT	GDB:611922	0.237	CAAGCCCAGTGTCTTG	CGTGTCCAGATGAAAGTG	
AFMa272yb5	D11S4113	MBAT	GDB:609116	0.218	ACCTCACGGTGTAATCCC	CTTGAAGCCCATCTTTGC	
BHGC-10945		EST	GDB:4581844	0.18	TATTGCAAAGCTTGAGACTTGT	AATCACTGTGTCTTTGTTGCC	
SGC31023		EST	GDB:4578608	0.128	ACTTTATTGTCAGCGTGGTGC	ACTCCCTCGATGGCTTCC	
WI-7741	D11S4364	GENE	GDB:477602	0.321	GAGCAGCGGGAGAGAAGGC	CCCAACTGGCTGTTTATTG	Transformation-sensitive protein IEF SSP 3521
SGC36223		EST	GDB:4582698	0.13	AGCCACTTTATTGTTATTTTGATGC	AAGAGTGAACAAAAGCAAACATACC	ZNF162 - zinc finger protein 162
WI-16754	D11S4118	EST	GDB:4578377	0.15	GTGGAGTGTGGGATTGGG	TACTGTTCTTGATAAGTATGTCGGC	
WI-16315		EST	GDB:4578604	0.224	ATGCTTTTGCATGATTCTAATTATT	TCCCCCAAAAGAATGTTAAAGG	
WI-16918		EST	GDB:4584065	0.128	CTGGTCTTCCTTGTGTGCTG	ATCACCCAGGGCAGGGAT	Mitogen inducible gene (MIG-2)
SGC30208		EST		-0.128	TCAGAAGCAGAACTGTTTTTAACA	CCTGCTTGAAAGTTGTAGGCC	
WI-17683		EST	GDB:4583346	0.126	CAAGCCGGGTTTTATTGAAA	GATGCCAGGACCATGGAC	
WI-6393		Gene	GDB:1222231	0.199	GCATATAGAAACATTTATTGCCG	CTCTGAAGCAGCGGACCAGAG	Human Int integrative protein (TIP60)
SGC31597		Gene	GDB:4578432	0.207	GTACCACACCACCACCAGGC	CAAGCGAAAGCTGCCTTC	Calcium activated neutral protease large subunit, mu/CANP, calpain
SGC30886		EST	GDB:4584087	0.15	GTTGTCTTGACTTCACGTCTGTC	TTTTCCTTCAACAATCACTACTCC	
SGC31927		EST		0.19	GCGTGGTGGATATAGAGGTCA	TACATGGCCAAGAAGCTAGG	
WI-8871		EST	GDB:1222235	0.18	TAATATATCCCAGTCTAAGGCAT	AGCTTGCAGATCGGACGCCC	
WI-18334		EST	GDB:1222257	0.124	TGGTTTTAAAGCTTTAATGAGAAAA	TGTTGATCTATACCCTGTTTCCG	
WI-18402		EST	GDB:4581874	0.127	TATTATTTAAAAGAAGTAAAGGCA	TGGTGTGAACTTCCTCTGA	
WI-18671		EST	GDB:4581941	0.113	GGTTACAGAAAACATTTAGAGAT	TGAGGTTAGTTCCCTCTCTG	
WI-12855		EST	GDB:4581947	0.131	TGAAAACCATTTATTCACCG	TGTGCCACTGTTGGATTT	Hlark
SGC33787		EST	GDB:4578608	0.209	TTGAAAACCATTTATTCACCG	TGTTCTCTTGTGCCCAGCG	Hlark
AFM343Y8S		MBAT	GDB:4581106	0.16	GTTATTGAAACATTGAGTGCA	TTGTCAATTCCCCCCAAAA	
SGC33744		EST	GDB:1222337	0.181	AAACCACGACCNCCCA	CCGTGAAAGGTTAGAYGGT	
SGC32272		EST	GDB:4578628	0.15	CTTTGGTAGAGACAAGGTCTCA	TATCTGTCTGTAGTGCTTCAAATGT	
SGC34148		EST	GDB:4581692	0.135	GACGAAGGTGATTCAGGGAC	ACTGAAGAAGTCTTGTCGT	
WI-18548		EST	GDB:4583094	0.1	CAGATAAAAGAGTGACTATGGCTCA	CAGTTGTCCACTTTGTCCC	
SGC31103		EST	GDB:4574598	0.133	TTATTGATAAGGATTAGTGAACCCC	TGGCAAGTTAGGCAGAGTCA	Human 1.1 kb mRNA upregulated by retinoic acid treated HL-60 neutrophilic cells
SGC34028		Gene	GDB:4580505	0.1	CTATGCCCAGAGATGAACAGAG	TCCACTTAAGGGCTATGTCGC	
WI-2875		EST	GDB:4577258	0.128	GCCAGCTTTATTGAGTAAAATTTC	CACTGGAGACTACAAGTGGTGG	Human pyruvate carboxylase precursor
SGC36986	D11S4407	STS	GDB:4579546	0.126	CATCCCAACCATCCACTCAGT	GGCGACTAGCTTCACGATTTGA	
GCT16807		Gene	GDB:4577182	0.223	AGACTACATTTGGAACCAGTGG	TGAAAGGATATTTATAGCTGTGA	LAR-interacting protein 1b
WI-6504	D11S4270	STS	GDB:626245	0.137	GAAGGTTTTGTCCCTGGATC	TGAGGGTTGGGAAGATCATA	
SGC31049	D11S3974	EST	GDB:598142	0.174	CCTTCATAGCCACACCCG	CAGCTAAGTGTTGACATGCCA	
		EST	GDB:4580939	0.16	TCTTACTGTGCTTACACTTTGCT	CAACAGTGCAGTGGGTATGG	

TABLE 3: HBM STS Table

TIGR-A002J17		EST	GDB:1222193	0.199	AGATCAGCAAGCAGATAG	CATTCCACATGGATAGAG	NDUFV1
WI-5995	D11S2382	EST	GDB:459883	0.1	CATACCTATGAGGTGTGCTACAGG	GCATTTTCTCATCATCCTTGC	amplaxin (EMS1)
WI-16987		EST	GDB:4575848	0.15	TTACAGCCACCAAGGTTTGC	AGGTGTGTGTGCCAGGTTGA	Nuclear mitotic apparatus protein 1, NUMA
SGC31912		EST	GDB:4567869	0.101	CACTGTTATCTCATTAACTGTGAGG	TTTGATTTTGTGTCTCCCAAA	
WI-13500		EST	GDB:4577893	0.15	CCCCACTCCCACTTTTATTT	CCAGTCACCTTTACTAGTCCTTTG	
CHLC.GAAT1B01.P7933	D11S971	MSAT	GDB:684255	0.103	AGGACACAGCCTGCATCTAG	ACCAGGCATTGCACTAAAAG	
SGC35519		Gene	GDB:4577180	0.134	GATGGGTCACACTAACCTGTCA	AGATTTATATTTGGACATGCAACC	LAR-interacting protein 1a mRNA
WI-11974		EST	GDB:1222265	0.108	AGCATCTTTAATGTGTCAGGCA	ATGTGCTGGGCTGGAAAG	Carnitine palmitoyl transferase I
WI-15244		Gene	GDB:4574740	0.108	TCACATTCAAAAATCGGCAA	CTGCCTGTGTGGTGTCGC	Beta-adrenergic receptor kinase 1, ADRB1
WI-17498		EST	GDB:4583335	0.131	TGTTTTATTTCTCAGTACAAAGCCA	GACCTCCTGTGACACCACG	
WI-9159	D11S4381	EST	GDB:678144	0.111	CCACCAAATTATTTATAGTTCTGCG	GTAAGATTCTCCACTGTTGCACC	FGF4 /
WI-4232		STS	GDB:1222250	0.176	CCTATAATGGGCTGGACCAA	ACTCCTCATGTGAAGTCACCG	
SHGC-4167		EST	GDB:4580789	0.161	CAGTGTGCACGTTTTCATTT	CAGCATCTTCAGCACTTACG	Human DNA helicase gen (SMBP2)
WI-14303		EST	GDB:4576939	0.15	CTGCATTTATTATGAGAATCAACAG	TGGTGGTGGGAGTCAGAGTC	
WI-16597		EST	GDB:4585666	0.13	CAGGGCACTGAGATACACTTACC	AAGGATCAAGCAGGCATTTG	
RC29S1CATTFOR/RC29S1CATT	D11S970	MSAT	GDB:191084	0.15	ACACATCTCTTCTGTGCCCC	TGAACCCTGGAGGCAGAG	
UT978	D11S1296	MSAT	GDB:196625	0.362	CATTCCCCAGTTTGCAGAC	GTGCTGGGATTACAGGTGT	
1281/1282	D11S1959	EST	GDB:335216	0.07	GCAGAGAAGTCCTGTTAGCC	CCATGCTAGAGAAGCACAAG	
D11S466	D11S466	STS		0.096	AGTGTGGGGCAGGACCTGTG	CAGACAGATAGCCGTGGGTTC	
D11S666	D11S666	STS	GDB:179349	0.143	TCCCTCATCCCCTTGTCTGT	AGCCCCCCTGGGGATAATC	
RH18048		Gene	GDB:4572853	0.188	GATGCTTACCTACCACGGG	AGGATTCCTATCTGGGCTATG	Aldehyde dehydrogenase (ALDH8)
IGHMBP2		Gene	GDB:4590087	0.699	TGGCAGACCATGCTCCGCCT	GAGAAGGCCGGGAGGCTCTG	Human DNA helicase gen (SMBP2)
NUMA		Gene	GDB:4590244	0.277	GTCCATCACAACCAGATTTGAGGCT	GGGTGTGAGCTGCTGCTGAAGG	Nuclear mitotic apparatus protein 1, NUMA
KRN1		Gene	GDB:4590232	0.226	AGTGGGAAACCTCAGGTAGCTCCCG	CAGTTTGGGTCAGACATATGGGGGC	High sulphur keratin, KRN
Cda11f06	D11S2302	EST	GDB:445887	0.091	CATTAAGTAGTGGGGGGACAG	CAAAGCGACAGTGAGTTAGGG	
RH10763		Gene	GDB:4583698	0.194	GGAGTAGACCATGATTACTG	CATGGTCTATTTATTCTCG	
EMS1		Gene	GDB:459016	0.64	CGCCCTGGATCCTCACACTACA	GGGCATCAGGGGATGGGTAGA	protein phosphatase 2A , PP2A
SHGC-11095	DXS9735	Gene	GDB:737674	0.137	GCTCCTATCTGTGTTTTGAATGG	CCGTGGCATAAGATAAGTAAACG	Amplaxin
INPPL1		Gene	GDB:4590093	0.362	CTTGGAGCGCTATGAGGAGGGC	ATGGCAACTGACCTTCCGTCGTG	Androgen Receptor
RH19051		EST	GDB:4572659	0.195	TTGGAGTCACAGGGGC	CAGCACTATCCTTGGGG	51C protein, inositol polyphosphate phosphatase-like 1
Cda1cc11	D11S2297	EST	GDB:445869	0.1	AACAAAGCTGCTTAGCACCTG	GATGAGGACCAACTGGTGAG	NDF1
1249/1250	D11S1957	EST	GDB:336210	0.247	TTTTCCAATAATGTGACTTC	CAATCCCAACCGTAACAGGC	
NDUFV1	D11S2245	EST	GDB:445885		CTTGATCTCGCCCAGGAAG	GCTCGCTGAAGGATGAAGAC	NDUFV1
AFMb092zg5	D11S4135	MSAT	GDB:609549	0.19	GAATCGCTTGAACCCAG	CCAGGTGGTCTTAACGG	
AFMa059xg9	D11S4166	MSAT	GDB:614025	0.2	GAACGTTINTTCATGTAGGCGT	TAATGGTCGCTGTCCC	
Cda17c12	D11S2288	EST	GDB:445842	0.155	AGGGAAAATGGTATGTGGGGAG	GCAGTGTGTGAAGGCAGG	
SHGC-1384	D11S951E	EST	GDB:4562766	0.137	AGTGGACAAAATGAGGAAAACAGG	CCAACACAGTTTGCTCACATGCC	
RH17419		EST	GDB:4571597	0.126	TGACATCTTTGCATTATGGC	AGTTATCCCACCTGATACCG	
RH17414		EST	GDB:4571695	0.121	AGCTCTTGCTTCTCAGTCCA	CAAAAGTTGTTTCTGTGTTTGTTC	
RH17775		EST	GDB:4572301	0.267	GCCTCTCAAAGTAGTTGGAACC	TGTGTATGCATAGTGCAAAACAG	
BEA		EST	GDB:4590169	0.13	CTCAAGGCCAGGCATCACT	GGACTCTTCCATGCCAGTG	
RH10889		EST	GDB:4583460	0.107	AATGATGATCTCAACTCTG	ACTGAAGAACTCTTGTCCT	S13 avian erythroblastosis oncogene homolog
TIGR-A006P20		EST	GDB:4587692	0.236	GACATCTGTTAGTGTCATAATTC	GGTAACAGTGTCTTGCTT	
TIGR-A007D15		Gene	GDB:4586398	0.24	CTATGTACAAAACAGGAAGAG	ATCCTAGTTTCCTCTCCTT	Menin gene (MEN1)
TIGR-A008B14		EST	GDB:4588882	0.141	GTAAATGAGAAACAGACAAATGA	CTATTGGATGTGATATGTTATGG	
TIGR-A008K11		EST	GDB:4589094	0.203	AAGTAGAAACAAAATGAGGGAC	CCTACCCCAAGGTAACAG	
TIGR-A008P15		EST	GDB:4589662	0.182	AGTTCCTATAAATGGAGGTGAG	GAGGAGCTTCAAGAGGAA	
TIGR-A008T11		EST	GDB:4589278	0.139	CATACTCCTAGACTCAAGGAATC	GAATGATGTACATGAATTCTTTG	
TIGR-A008U48		EST	GDB:4589354	0.107	GTGTTGAGGAGAAAAGCACT	CTCCCAGTAGTCACATTCC	
TIGR-A008X45		EST	GDB:4589838	0.242	CAAGTTACAAATAACTTAAGCCG	CAAGACCCTATCTCTACAAAAAC	
SHGC-11839	D11S4611	Gene	GDB:740339	0.161	TTATTAGAAGTGACTCTTGGCCC	GACTACCTGCCCTCAGCTTG	Folate receptor 2 (FBP2)
NIB1242	D11S4929	EST	GDB:3888276	0.149	TTCTCATGTACAAAGCGGTC	CCACTGGCTTCTCTCTTTT	cGMP-stimulated 3',5'-cyclic nucleotide phosphodiesterase PDE2A3 (PDE2A)
SHGC-13699	D22S1553	Gene	GDB:737656	0.147	CACCAGAAGGTTGGGGTG	ACTATTACGACATGAACGCGG	Macrophage Migration Inhibitory factor
SHGC-11897	D11S4931	Gene	GDB:674984	0.14	CTCATGCTGGATGACCCC	TTGCCTTTCTTGAAACTTAATTCC	P2U Purinoceptor
SHGC-15349	D12S2124	EST	GDB:740819	0.141	TCACAGCCTTCAGTCAGGG	ACATGCTGTGGCACCATG	
Bda84a05	D11S2235	EST	GDB:445682	0.095	CCTGAGCTACTGCCACAG	CCCTGACTTGGACAGTGTCC	
Bda99d07	D11S2236	EST	GDB:445874	0.09	TCAGACTCACTCGTGCCC	CAAATTCAAGCTCATCCAGACC	
folr1		Gene	GDB:197640	0.3	CGGCATTTCATCCAGGAC	GGTGTAGGAGGTGCGACAAT	Folate receptor2 (FBP2)
NIB1738	D11S4284	EST	GDB:626260	0.173	TTCTCATTTGAGCACCTG	CTTAAGCCACTGTGTTTTGG	
WI-7351	D11S4433	Gene	GDB:679143	0.324	CCTCCTACACCTGCAAAAGC	TGGAAGAACCCCAGAGGAG	Folate receptor3 (FBP3)
WI-14325		EST	GDB:4576507	0.132	AAAGCACAAAAGTAACAGCAACA	GTGTGTGGGCCACAATATTG	
WI-15192		EST	GDB:4576805	0.15	AGAGCACCTTTCCTGAGCAG	AGAATCTCATCACAGGGGCG	

TABLE 3: HBM STS Table

WI-17872		EST	GDB:4577492	0.141	AAAAGGACAGTGTCTAAATTGA	AATTGTTTTGTTGTTTTTGAGT		
BHGC-30732		EST	GDB:4567830	0.105	GATTAGGGAGTACAAGTGCGG	GGGGACAAATATACTTATTCAGG		
slSG4288		EST	GDB:4566057	0.123	CCATCATCATATTGGTGTGACC	TGGCTGCCCAAGAAGAAG		
WI-19314		EST	GDB:4578290	0.15	TTAAGATGCCATTAAACTCATGAC	CCAAGGAGATGACAGAAGTGG		
WI-14122		Gene	GDB:4578114	0.128	CCATGTCTTTTATCAGGTTGG	CTTGTGTCAAGTAGCATCTTACA	(DRES9	
272B2730	D1181057	EST	GDB:4568509	0.118	CGACTGTGTATTTTCACAG	AGAAGCCATATCAATGCAC	Human VEGF related factor isoform VRF186 precursor (VRF)	
SHGC-31329		EST	GDB:4567386	0.16	AGCTTAAAGTAGCAACAACCATGG	GGATGCTTCACTCCACAGAAAG		
BGC33658		EST	GDB:4578600	0.127	TGTTGTTATTTCCACCTTGCC	AGAGTGGCTGCAGGCCAG		
WI-12191		EST	GDB:1222208	0.15	TTTTTTTTTTACAGAATTTGAAG	TGAGGAAGTAAAAACAGGTCATG		
WI-13701		EST	GDB:574882	0.16	ATGAAATGTTAAGGAAATCCCA	CACAGAGTCCCAGGGTGTGT		
WI-14058		EST	GDB:4584372	0.16	AAAGCCTTATTTATCTCTCTG	GCCTCAGAGTGTGGGT		
WI-14272		EST	GDB:4578526	0.126	GCTTCTAAGTCTAGAGTCAGGTGG	AGCCCACAGTCAGCCTACC		
WI-17347		EST	GDB:4578423	0.127	TTGGTTAAATGATGCCCAGA	TGGTGCCACTCATCACTCCC		
slSG1581		EST	GDB:4584115	0.215	ACACAGCATGCAGGGAGAG	ATCCCTGTGTGCTTAGGTGTG		
slSG18336		EST	GDB:4584568	0.137	GATGCAAGTAGCTCCTCTCTGG	GGAAGGCCAGCAAGTACTACC		
slSG2726		EST	GDB:4585137	0.141	CCAGGTGCTTGTGAAAGATG	GAAGTGTCTCTGTTGGGGA		
RH97		EST	GDB:4589910	0.17	TTACAGGCATGAGTGACTACGC	ACCACTCTCACAGCCCTTACA		
slSG4794		EST	GDB:4573113	0.141	CCCTCCCTCCACACACAC	GCTCACTGAACTTCAGGGC		
slSG4987		EST	GDB:4566051	0.171	AGATACGGGCAAAACACTGG	GTTGAATATAGAGCAGCCCC		
slSG4974		EST	GDB:4569063	0.169	TTGTGAGGTCAGGCTGTGCT	AGCTTGCAAATGTGGTGTCA		
slSG8144		EST	GDB:4573127	0.17	ACTCAGTCCCTCCACCC	TGGAGGACTGCTGAGCC		
slSG9275		EST	GDB:4589998	0.19	GTGATCACCGCTCAACCTG	TCCTCTCACTGCTTCCAGA		
BHGC-10837	D1184583	Gene	GDB:740248	0.277	CTGCAGCTGCTCATCAGTTTC	TCAAAAGTCCTGGTGACAGC	4F2 Cell-Surface Antigen Heavy Chain (4F2HC)	
SHGC-11930		Gene	GDB:1231223	0.21	ATTTCCAGAGCCAGGTCAAA	CTTTAATGTTGTGATGACACAAAGC	Human protein kinase (MLK-3)	
SHGC-32788		EST	GDB:4567879	0.126	GATCATGCACTGTTGACCAC	TACATTTGAAACATTTAAAACGTGA	FGF3	
FKBP2		Gene		0.084	AACTGAGTGTACCAGACTGGGA	TGGAACAGTCTGGTCCTGATGG	FK506-Binding Protein Precursor (FKBP-13)	
WI-13116		EST	GDB:4585099	0.202	TTATCCTTTATTGTTCTCCTTTG	TGGTCACCTGTATTTATTGCTATG		
MDU1		Gene	GDB:4580064	0.859	TGTTCAAAGCCTCTGTGCTATACC	GTCATCTCCAACCTGTCTCTAACC	4F2 Cell-Surface Antigen Heavy Chain (4F2HC)	
9453	D1184583	Gene	GDB:196216	0.108	GTGGCTGCAGCTAATGTAAGADAC	CAGCAGACAATGCCTAAGTCC	Human protein kinase (MLK-3)	
ST81-sRL-112911	D1183968	STS	GDB:547651	0.133	CTGATTGAGAACCAGAACAG	TAAAGCCCTATAACTCTCC	FGF3	
ST81-sRL-4483	D1183630	STS	GTC:547606	0.119	TAGTAAGGAGCTTCACCAAG	AGATGTTTGGTATGACTTGG		
ST81-sRL-31b12	D1182438	STS	GDB:4569728	0.123	GATGATTAAAACTCTCCTGGC	GAGACAGCTAAGCACTCATG		
cSRL_f19	D1181197	STS	GDB:197824	0.198	CAGTGTGTGGGCACCTGTA	AGAGGGGAGGAACACACTT		
SHGC-10323	D1184351	Gene	GDB:878135	0.141	GACCAGAGTCTGCCCAGAAG	TCCCCCAGCTCTATCCCAAC	Folate receptor2 (FBP2)	
WI-9218		Gene	GDB:878179	0.1	GGAGGTGATGGACAAGTCTGA	GTCCAGCTCGCTGACTATCC	Collagen binding protein 2, collagen-2 gene (CBP2)	
GTG_ZNF		Gene		0.172	TGAAAAGAGAGTCATCTCCA	GCAAAGGCTTACCATATTG	Retinal outer segment membrane protein 1, ROM1	
AFMa162vh1	D1184087	MSAT	GDB:1653787	0.158	GCTCAGCACCCCCATT	TCCCTGCTCGGGGAAAC	ZNF126	
AFMb331zh5	D1184162	MSAT	GDB:811241	0.289	GTTCTCCAGAGAGACAGCAC	CCTCTGTAGGATGCAGTTGG		
AFMb038yb9	D1184139	MSAT	GDB:809821	0.161	TATAGACTTCAGCCCTGCTGC	GTGAAGCCAGGAAATGTGAG		
AFM212xe3	D1181314	MSAT	GDB:1589282	0.209	TTGCTACGACACTCCTCTACT	CTCCCCCTGGTGCAGTTATT	Serine/threonine kinase	
WI-18613		EST		0.19	ATCCTAGACCAGAGCACCCC	AGCAGATCTGCTCTTGCGAT		
WI-19549		EST		0.283	AACTTCATTTGCCAAGGGA	AAAAGTATGAATGGGATGGAGC		
WI-20164		EST	GDB:2583084	0.26	ACAGTTGTCATCGGTAGGCA	CCCTATATCTCCAGTGTGGTCC	DRES9	
WI-22393		EST	GDB:1223732	0.142	GTGCAGGTGGCGTTATTTT	GAATTCCAGGCTCTTGCTTG	Ultra high-sulphur keratin protein (KRN1)	
WI-7597		EST		0.274	GCTGTAGTGGGAAACCTCAGG	CCAGTACATGGTGGTCACA		
EST-455578		EST		0.273	GATTCGTCTCAAAGGCAAA	GTGCTGTGATGGGAAAAG	Fas-associating death domain-containing protein, FADD	
WI-21134		EST		0.293	GCTGCTTGAATTTCTGTT	GCAGTGGCCTCTTGAAACTC		
WI-21666		EST		0.25	ATTCAAGGTCATCCAGACCG	GCAGTGGCCTCTTGAAACTC		
SHGC-7373	D1184887	STS	GDB:7-40182	0.228	ATATTGACCGTGCACAAATACG	AGACCTGAGAAAAGTGGAGAA		
SHGC-38533		STS		0.126	ATGGCAGTGCAAAATGCTT	TTATTCTTTGTCAACTTGGTGATT		
ARIX		Gene		0.242	tctgtcctttaccagaagc	gaataaagaactcgcctgcgtcgtggaa	Actin homeodomain protein, neuroendocrine specific, bX factor	
CLCLPCR		Gene	GDB:6262813		TGAGGCCTGTGTTGCTGCACTCTG	AGCGATGTAAAGGTACCAGTGACCG	Chloride channel current inducer, ICLN gene	
B186N21-HL		STS			AGGCATGTAAGCTTCTTA	CGGGGAGGAGACTCTAT		
B234C17-HR		STS			TGGTAAGCACAGAAAATGC	AATGGATGGGGGATTATT		
B235G10-HR		STS				CTGCACGTTATGTGCCC		
B247F23-HR		STS			ATCACTCTGAACTGCCACT	AGAGGCCCAGTCACATGAT		
B337H24-HL		STS			CAAGCTTGAAGGAAGAG	CTCCTCTGTTTTCTGTTTT		
B337L5-HL		STS			GCTCTGCAGTGGGTAAA	TAGGAGGTTAAGTGAGGAC		
B382N10-HR		STS			CCCTTTCTGAGCCAAGAT	AGTGTCCAAGAGTGTGCG		
B121-HR		STS			CGCTATGAGTGCCCATCTG	GACCACCTGGGAGAGAAC		
B186D17-HR		STS			TTGAGTAGACGGGGTGAC	GCCAGGACTGAAAGATGA		
B236E5-HR		STS			ACCTGTCTCCCTCTCCTGG	TGGTTTTCTTCTGTGGGA		

TABLE 3: HBM STS Table

B270E22-HR		STS			ATGACCAGCAAGCATTGT	GTACTGGGATTACAGGCG	
B312F21-HR		STS			GCAGAAGGTCCTTTGCAT	TTTGCAGGATTCATGCTT	
B337H24-HR		STS			CGACATTCTTTCTGGAGG	ACCTTTGCATGTTGGTTT	
B358I19-HR		STS			GCACTTTTCCTCCTTCC	TGCTTTGCTTTCTTGG	
B148N16-HL		STS			ACAGCTCCAGAGAAGGA	GCAGTTACTTGAAACCAG	
B172N12-HL		STS			AGGCATCAAGCTTTCCTT	GGTTTAGAGAACCGAGCC	
B172N12-HR		STS			GTGGTGCTGCAAGTTACC	GGAATCCCTTCTTTCCA	
B218J11-HR		STS			GACCATTTGTTACCCAGG	GATGGGTGTGAATGAACAA	
B223E5-HL		STS			CTCAAGCTTCTGTTCATGC	GCTGTGAGTGTCTTGGCT	
B312B3-HR		STS			TACAGAAAACCCCAGGTC	GCCACCAAAGGAAAGATT	
B328J19-HL		STS			AAAAGGAGGGAATCATGG	TCACTTAGCAGGAGGCAG	
B328J19-HR		STS			CTGAGCATCCGATGATGAC	GTGCAAAATGAGCAGCTT	
B32B110-HL		STS			TCTAACCCCTTACTGGGC	TCCTCAAACTGGGAATGA	
B32B110-HR		STS			TTTACACAGGACCAGGGA	ATCTCCCCCACTCACAAAG	
B358G19-HL		STS			GTCCACAGGGCTTTATTCT	TGAGCATAAATTCATTAGCTG	
B359G10-HR		STS			GGAAGAGCAAAATAAATGCA	GGTGCACAGAATTGTTCAT	
B38F18-HL		STS			AGCAGCCTATTTCATGTG	GTAACACCAGCAGGGACA	
B333D17-HL		STS			TCCTGCTGCATTATGGAT	GGGGGTGAGAAGTAGGAA	
B333D17-HR		STS			ATGGGGATTAAATACGTG	AGGTAGCATTTGGGTCTT	
B208I23-HL		STS			CTGAGGAGAAGAGGCTGG	CGCCTACAAGGCAAGTA	
B208I23-HR		STS			AGGATGCTTGCTAGGGTT	CACAAGTGTCTGGAAGGC	
B371E15-HR		STS			GGTCTCAGGAGCCTTTA	ACATGCCACTCTTCTCACTAA	
B312P21-HL		STS			ACTTAACCAAGGATGGGG	CAACCCACGAGCATAAGA	
B333D17-HL		STS			TAAGGCTGCTGAAGTGAG	ACCCACGGAGTCTCTCTG	
B369H18-HL		STS			TGGGGCCAGATAATTCTT	CTACGGGTGTCTCTAGGT	
B369H18-HR		STS			AAGGAAGAGGTCAGCAGG	CTGGTGTTTGGTGGTGTT	
B444M11-HR		STS			TCAATAGGTGATCCAACATTT	CACAATTCCATTTCCCA	
B226K21-HR		STS			GGGTAGGGGGATCTTTTT	AAAGTCCCACAAAGGGTC	
B286L23-HR		STS			GTCCTGGGAAAGATGGAA	TGTGGAACATTCATTGGC	
B334H4-HL		STS			TCTTTCCCTGTACTTGGC	TCGGGAGGTCACAGTGATG	
B334H4-HR		STS			GGACAGTGTATGTTGTGGG	AGGCAGCTGTTTTTGTGA	
B473O3-HR		STS			CTTCTTGAGTCCCGTGTG	CAAGCGAGAATCCTCTAGC	
B186D17-HL		STS			GCTGGGAGAGAATCACAA	GCTTTGACAGAAGAGACCA	
B200E21-HL		STS			ACGCTGTCAGGTCACACT	GGAGGATGCTCAGGTGAT	
B200E21-HR		STS			TAGGGGGATCTTTTTGCA	GAGCAATTTGAAAAGCCA	
B14L15-HR		STS			ATGGTCCAGCTCCTCTGT	ATAGAGCACCCCATCTCC	
B442P6-HR		STS			AACATTGCTGTAGCCCCA	GCAATTGAAACAGCATTC	
B198N21-HR		STS			ATGAGTTGGCAGCTGAAG	AATGAAGGTCTTGCCTCC	Beta-arrestin-1
GTC-ARRB1		Gene		0.067	GAGGAGAAGATGCACAAGGG	TCTCTGGGGCATACTGAACC	
B560A5-HL		STS			CTGAGTTTTTGGCAGTGT	CTGCTAGGTGACAGCAGG	
B38F18-HR		STS			TGTATGAGTCTGGAGGGTGT	ADACCTGGCTGAGGAAAT	
B117N19-HL		STS			GCAGGGCAGGTGATAATA	TTTTGCTTCTCTACATGC	
B14L15-HL		STS			AAAATTGTGAGCACCTCC	TTTATATTTAAAGTGCCTTTGTT	
B211K22-HL		STS			GTGCAAAGCGCACAGTAT	AGGAAAATGCAAGAGCAG	
B211K22-HR		STS			CCACTGAATTGCATACTTTG	TGTGGGTCCAGTGCTGCTA	
B229E5-HL		STS			AGATTTTGGGGAGTCAGG	GCGCTCAAGCAATTGTC	
B270E22-HL		STS			CAAGCGCCAAAGTAGTCA	GAATCATCCAATCCACTA	
B444M11-HL		STS			AGCCTCCAGGTGACTACC	GAAGGACATGGTCAGCAG	
B543O19-HR		STS			ATGGTTCAGCATTTTCG	TGATCCGTGGTAGGGTTA	
B117N18-HR		STS			GTCGGATTGGTTTGACAA	TTTTATGGGAATTTGAGCG	
B543O19-HL		STS			TTTGGAAAGAACAGAAATGT	GGCTAGTCTTTCCTGAACC	
B442P6-HL		STS			CCTTAATGCCCGTGATTG	GCGTTACAAGCTGAGGA	
B3967H4-HR		STS			TCAAGCTTGCTTCTCAA	GTAGCCCACAAGTGTGT	
B250E21-HR		STS			CCTGGCTGGAGATAGGAT	CTTCCCCTCTGCCTATGT	
B250E21-HL		STS			GGCACGTACTTCTCTACCA	GGTGCTTCTTACAGCCAA	
B248C16-HL		STS			ACCCAAGCCTGGTGTGT	ACTGAGTTAATTATCACTGCCCT	
B248C16-HR		STS			GATGCATTTTGCTTCACC	TCTGCTTTTAGAGCTGTTAGC	
B160D8-HR		STS			TCAAGCTTCAAAGAGCAGA	GGAGTACATCCCAGGACC	
B539L7-HR		STS			TGGTGCTTTTAAATCCAGA	CTCCCTTACTTACTTGCATTG	
B473O3-HL		STS			TCTTCTCCCAGGGAATCT	TTTATGTCCCTGAGCAC	
AFM419xb9	D11S4095	STS	GDB:606084	0.193	TTCCTGGCTATCTTGAATC	CTTGACTGGGTCCACG	

TABLE 3: HBM STS Table

ARRB1(2)		STS			CGAGACGCCAGTAGATACCA	CATCCTCCATGCCTTCAGT	
ARRB1(1)		STS			AGTTCCAGAGAACGAGACGC	CTTGTCATCCTCCATGCCTT	
P102F3B		STS	GDB:6054146		GAGCGTGAGAGGTTGAGGAG	AAACAAGTCCAGACGCACC	
N172A		STS	GDB:6054146	0.208	CTGAACCACTACCGTGTATGAGCTG	CTAACTAGTTACTCTCTACAGGgCCC	
N60A		STS	GDB:6054147	0.23	GAAGCATTTCAATACTTTAACTG	CCACTCCAGTGCACCCAATC	
cC(1)1-44A		STS	GDB:6054148	0.239	CTTCTCCTGCCACTCTGAC	GGTTACCTTTGAATCCCAGC	
CN1677-2A	1	STS	GDB:6054149	0.271	TGAGGATGAATGAGCACATAGG	TTTGTGGTCCATTGAGTAGGC	
cC(1)1-524B		STS	GDB:6054150	0.221	AGGGGAAGGAATGTGCTTGG	TTCGGCTGAGCAGGCAGTGT	
R117F3T		STS	GDB:6054151	0.186	ATGAAGGTCCTCCAAAAGAATGCTG	AGAACGTCAACATATGCTTTTGGGGACAC	
ARRB1(3)		Gene			TTGTATTTGAGGACTTTGCTCG	CGGTACCATCTCCTCCTCTTCC	
B216J11-HL		STS		0.122	TTTTTGCCTCATCTATGCCC	GGGTGACAGACAAGACTCC	
B317G1-HR		STS			TTGCTCAAGTTCTCCTGG	ACCTTGTTTTGAGGGGAG	
B317G1-HL		STS			CTTGGCTATTTGGACAGC	GGGCATTTACTCACTTGC	
B292J18-HR		STS			CTTGTGTCAGTTGTCAGGG	TGGAATTGTTGTGTCTTGG	
B10A18-HL		STS			CCAGTTCCACTGGATGTT	ATGGGCTGTGTTTCTCAA	
B10A18-HR		STS			CTGCCTATCCCTGGACTT	AGTTTGTCCCTAGTGCCC	
B527D12-HL		STS			CAACACGTGTGACATCCAT	GGATAGTGCACACCCA	
B372J11-HR		STS			TGGGTGGTACTATTGTTCCCAT	AGTTCCAGCCCCCTTACCAG	
B372J11-HL		STS			GGCCACTATCATCCCTGTGT	TTTCACATGGGAAGAACACG	
B37E17-HR(GS)		STS			ACAGTGACACTAGGGACGGG	TGCCAGGATGGAGATAACAA	
B37E17-HL(GS)		STS			CCTGTGGCACACATATCACC	ACAACCAAGAATGGAGCCAC	
B34F22-HR(GS)		STS			TGCTGTGTAACAAGTCCCCA	TGAACGGAGGAGCTACCAAG	
B34F22-HL(GS)		STS			GCAGGGTCCGACTCACTAAG	GCTGTGAGTTCCCTTACGC	
B648P22-HR1		STS			ACAGTGGGGACAAAGACAGG	TACAGGGCACCTCACAGTAG	
B82A1-HR2		STS			TCTTCTGTTAAGGTTCCCCC	TGTCTCAAACCTCCCTCTGC	
B648P22-HL		STS			AACATATTCCTCCCCAGCC	CAGTCCCAGCCAATGAGAAC	
B82L11-HL (GS)		STS			CTCCTCTGCATGGAGAATC	AGACCTGGGACCAGTCTGTG	
B82J13-HL (GS)		STS			GGGAGACGACGTCACAAGAT	TGATGTTGTGGAAGATGGTGA	
144A24-HL		STS			CAGGCATCTTCTATGTGCCA	GGGAGGCACAAGTTCTTTCA	
B82L11-HR (GS)		STS			ACTTCGTGGCACTGAGTGTG	CCTTTCTTACGGATGAGGCA	
B83J13-HR (GS)		STS			GGCTGCTGAGCTCTTCTGAT	TGGaGTCTCTGTGCCTGACTT	
B82L11-HL2(GS)		STS			TCACCTACTTCCAGCTTCCG	AGACCTGGGACCAGTCTGTG	
B82L11-HL3(GS)		STS			CTCCTCTGCATGGAGAATC	AATTCAGGAGACCTGGGACC	

Novel STSs were developed either from publicly available genomic sequence or from sequence-derived BAC insert ends. Primers were chosen using a script which automatically performs vector and repetitive sequence masking using Cross_match (P. Green, U. of Washington) and subsequent primer picking using Primer3 (Rozen, Skaletsky (1996, 1997). Primer3 is available at www.genome.wi.mit. edu/genome_software/other/primer3.html.

Polymerase chain reaction (PCR) conditions for each primer pair were initially optimized with respect to $MgCl_2$ concentration. The standard buffer was 10 mM Tris-HCl (pH 8.3), 50 mM KCl, $MgCl_2$, 0.2 mM each dNTP, 0.2 μM each primer, 2.7 ng/μl human DNA, 0.25 units of AmpliTaq (Perkin Elmer) and $MgCl_2$ concentrations of 1.0 mM, 1.5 mM, 2.0 mM or 2.4 mM. Cycling conditions included an initial denaturation at 94°C for 2 minutes followed by 40 cycles at 94°C for 15 seconds, 55°C for 25 seconds, and 72°C for 25 seconds followed by a final extension at 72°C for 3 minutes. Depending on the results from the initial round of optimization the conditions were further optimized if necessary. Variables included increasing the annealing temperature to 58°C or 60°C, increasing the cycle number to 42 and the annealing and extension times to 30 seconds, and using AmpliTaqGold (Perkin Elmer).

BAC clones (Kim et al, *Genomics*, 32:213-218 (1996), Shizuya et al, *Proc. Natl. Acad. Sci. USA*, 89:8794-8797 (1992)) containing STS markers of interest were obtained by PCR-based screening of DNA pools from a total human BAC library purchased from Research Genetics. DNA pools derived from library plates 1-596 were used corresponding to nine genomic equivalents of human DNA. The initial screening process involved PCR reactions of individual markers against superpools, i.e., a mixture of DNA derived from all BAC clones from eight 384-well library plates. For each positive superpool, plate (8), row (16) and column (24) pools were screened to identify a unique library address. PCR products were electrophoresed in 2% agarose gels (Sigma) containing 0.5 μg/ml ethidium bromide in 1X TBE at 150 volts for 45 min. The electrophoresis units used were the Model A3-1 systems from Owl Scientific Products. Typically, gels contained 10 tiers of lanes with 50 wells/tier. Molecular weight markers (100 bp ladder, Life Technologies, Bethesda, MD) were loaded at both ends of the gel. Images of the

gels were captured with a Kodak DC40 CCD camera and processed with Kodak 1D software. The gel data were exported as tab delimited text files; names of the files included information about the library screened, the gel image files and the marker screened. These data were automatically imported using a customized Perl script into Filemaker™ PRO (Claris Corp.) databases for data storage and analysis. In cases where incomplete or ambiguous clone address information was obtained, additional experiments were performed to recover a unique, complete library address.

Recovery of clonal BAC cultures from the library involved streaking out a sample from the library well onto LB agar (Maniatis et al, *Molecular Cloning: A Laboratory Manual.*, Cold Spring Harbor Laboratory, Cold Spring Harbor, NY (1982)) containing 12.5 µg/ml chloramphenicol (Sigma). Two individual colonies and a portion of the initial streak quadrant were tested with appropriate STS markers by colony PCR for verification. Positive clones were stored in LB broth containing 12.5 µg/ml chloramphenicol and 15% glycerol at -70°C.

Several different types of DNA preparation methods were used for isolation of BAC DNA. The manual alkaline lysis miniprep protocol listed below (Maniatis et al, *Molecular Cloning: A Laboratory Manual*, Cold Spring Harbor Laboratory, Cold Spring Harbor, NY (1982)) was successfully used for most applications, i.e., restriction mapping, CHEF gel analysis, FISH mapping, but was not successfully reproducible in endsequencing. The Autogen and Qiagen protocols were used specifically for BAC DNA preparation for endsequencing purposes.

Bacteria were grown in 15 ml Terrific Broth containing 12.5 µg/ml chloramphenicol in a 50 ml conical tube at 37°C for 20 hrs with shaking at 300 rpm. The cultures were centrifuged in a Sorvall RT 6000 D at 3000 rpm (~1800 g) at 4°C for 15 min. The supernatant was then aspirated as completely as possible. In some cases cell pellets were frozen at -20°C at this step for up to 2 weeks. The pellet was then vortexed to homogenize the cells and minimize clumping. 250 µl of P1 solution (50 mM glucose, 15 mM Tris-HCl, pH 8, 10 mM EDTA, and 100 µg/ml RNase A) was added and the mixture pipetted up and down to mix. The mixture was then transferred to a 2 ml Eppendorf tube. 350 µl of P2 solution (0.2 N NaOH, 1% SDS) was then added, the mixture mixed gently and incubated for 5 min. at

room temperature. 350 µl of P3 solution (3 M KOAc, pH 5.5) was added and the mixture mixed gently until a white precipitate formed. The solution was incubated on ice for 5 min. and then centrifuged at 4°C in a microfuge for 10 min. The supernatant was transferred carefully (avoiding the white precipitate) to a fresh 2 ml Eppendorf tube, and 0.9 ml of isopropanol was added, the solution mixed and left on ice for 5 min. The samples were centrifuged for 10 min., and the supernatant removed carefully. Pellets were washed in 70% ethanol and air dried for 5 min. Pellets were resuspended in 200 µl of TE8 (10 mM Tris-HCl, pH 8.0, 1.0 mM EDTA), and RNase A (Boehringer Mannheim) added to 100 µg/ml. Samples were incubated at 37°C for 30 min., then precipitated by addition of $C_2H_3O_2Na{\cdot}3H_2O$ to 0.5 M and 2 volumes of ethanol. Samples were centrifuged for 10 min., and the pellets washed with 70% ethanol followed by air drying and dissolving in 50 μl TE8. Typical yields for this DNA prep were 3-5 μg/15 ml bacterial culture. Ten to 15 µl were used for HindIII restriction analysis; 5 µl was used for NotI digestion and clone insert sizing by CHEF gel electrophoresis.

BACs were inoculated into 15 ml of 2X LB Broth containing 12.5 µg/ml chloramphenicol in a 50 ml conical tube. 4 tubes were inoculated for each clone. Cultures were grown overnight (~16 hr) at 37°C with vigorous shaking (>300 rpm). Standard conditions for BAC DNA isolation were followed as recommended by the Autogen 740 manufacturer. 3 ml samples of culture were placed into Autogen tubes for a total of 60 ml or 20 tubes per clone. Samples were dissolved finally in 100 µl TE8 with 15 seconds of shaking as part of the Autogen protocol. After the Autogen protocol was finished DNA solutions were transferred from each individual tube and pooled into a 2 ml Eppendorf tube. Tubes with large amounts of debris (carry over from the pelleting debris step) were avoided. The tubes were then rinsed with 0.5 ml of TE8 successively and this solution added to the pooled material. DNA solutions were stored at 4°C; clumping tended to occur upon freezing at -20°C. This DNA was either used directly for restriction mapping, CHEF gel analysis or FISH mapping or was further purified as described below for use in endsequencing reactions.

The volume of DNA solutions was adjusted to 2 ml with TE8, samples were then mixed gently and heated at 65°C for 10 min. The DNA solutions were then

centrifuged at 4°C for 5 min. and the supernatants transferred to a 15 ml conical tube. The NaCl concentration was then adjusted to 0.75 M (~0.3 ml of 5 M NaCl to the 2 ml sample). The total volume was then adjusted to 6 ml with Qiagen column equilibration buffer (Buffer QBT). The supernatant containing the DNA was then applied to the column and allowed to enter by gravity flow. Columns were washed twice with 10 ml of Qiagen Buffer QC. Bound DNA was then eluted with four separate 1 ml aliquots of Buffer QF kept at 65°C. DNA was precipitated with 0.7 volumes of isopropanol (~2.8 ml). Each sample was then transferred to 4 individual 2.2 ml Eppendorf tubes and incubated at room temperature for 2 hr or overnight. Samples were centrifuged in a microfuge for 10 min. at 4°C. The supernatant was removed carefully and 1 ml of 70% ethanol was added. Samples were centrifuged again and because the DNA pellets were often loose at this stage, the supernatant removed carefully. Samples were centrifuged again to concentrate remaining liquid which was removed with a micropipet tip. DNA pellets were then dried in a desiccator for 10 min. 20 µl of sterile distilled and deionized H_2O was added to each tube which was then placed at 4°C overnight. The four 20 µl samples for each clone were pooled and the tubes rinsed with another 20 µl of sterile distilled and deionized H_2O for a final volume of 100 µl. Samples were then heated at 65°C for 5 min. and then mixed gently. Typical yields were 2-5 µg/60 ml culture as assessed by NotI digestion and comparison with uncut lambda DNA.

3 ml of LB Broth containing 12.5 µg/ml of chloramphenicol was dispensed into autoclaved Autogen tubes. A single tube was used for each clone. For inoculation, glycerol stocks were removed from -70°C storage and placed on dry ice. A small portion of the glycerol stock was removed from the original tube with a sterile toothpick and transferred into the Autogen tube; the toothpick was left in the Autogen tube for at least two minutes before discarding. After inoculation the tubes were covered with tape making sure the seal was tight. When all samples were inoculated, the tube units were transferred into an Autogen rack holder and placed into a rotary shaker at 37°C for 16-17 hours at 250 rpm. Following growth, standard conditions for BAC DNA preparation, as defined by the manufacturer, were used to program the Autogen. Samples were not dissolved in TE8 as part of the program and DNA pellets were left dry. When the program was complete, the

tubes were removed from the output tray and 30 µl of sterile distilled and deionized H_2O was added directly to the bottom of the tube. The tubes were then gently shaken for 2-5 seconds and then covered with parafilm and incubated at room temperature for 1-3 hours. DNA samples were then transferred to an Eppendorf tube and used either directly for sequencing or stored at 4°C for later use.

V. BAC Clone Characterization for Physical Mapping

DNA samples prepared either by manual alkaline lysis or the Autogen protocol were digested with HindIII for analysis of restriction fragment sizes. This data were used to compare the extent of overlap among clones. Typically 1-2 µg were used for each reaction. Reaction mixtures included: 1X Buffer 2 (New England Biolabs), 0.1 mg/ml bovine serum albumin (New England Biolabs), 50 µg/ml RNase A (Boehringer Mannheim), and 20 units of HindIII (New England Biolabs) in a final volume of 25 µl. Digestions were incubated at 37°C for 4-6 hours. BAC DNA was also digested with NotI for estimation of insert size by CHEF gel analysis (see below). Reaction conditions were identical to those for HindIII except that 20 units of NotI were used. Six µl of 6X Ficoll loading buffer containing bromphenol blue and xylene cyanol was added prior to electrophoresis.

HindIII digests were analyzed on 0.6% agarose (Seakem, FMC Bioproducts) in 1X TBE containing 0.5 µg/ml ethidium bromide. Gels (20 cm X 25 cm) were electrophoresed in a Model A4 electrophoresis unit (Owl Scientific) at 50 volts for 20-24 hrs. Molecular weight size markers included undigested lambda DNA, HindIII digested lambda DNA, and HaeIII digested _X174 DNA. Molecular weight markers were heated at 65°C for 2 min. prior to loading the gel. Images were captured with a Kodak DC40 CCD camera and analyzed with Kodak 1D software.

NotI digests were analyzed on a CHEF DRII (BioRad) electrophoresis unit according to the manufacturer's recommendations. Briefly, 1% agarose gels (BioRad pulsed field grade) were prepared in 0.5X TBE, equilibrated for 30 minutes in the electrophoresis unit at 14°C, and electrophoresed at 6 volts/cm for 14 hrs with circulation. Switching times were ramped from 10 sec to 20 sec. Gels were stained after electrophoresis in 0.5 µg/ml ethidium bromide. Molecular weight markers included undigested lambda DNA, HindIII digested lambda DNA, lambda ladder PFG ladder, and low range PFG marker (all from New England Biolabs).

BAC DNA prepared either by the manual alkaline lysis or Autogen protocols were labeled for FISH analysis using a Bioprime labeling kit (BioRad) according to the manufacturer's recommendation with minor modifications. Approximately 200 ng of DNA was used for each 50 µl reaction. 3 µl were analyzed on a 2% agarose gel to determine the extent of labeling. Reactions were purified using a Sephadex G50 spin column prior to *in situ* hybridization. Metaphase FISH was performed as described (Ma et al, *Cytogenet. Cell Genet.*, 74:266-271 (1996)).

VI. BAC Endsequencing

The sequencing of BAC insert ends utilized DNA prepared by either of the two methods described above. The DYEnamic energy transfer primers and Dynamic Direct cycle sequencing kits from Amersham were used for sequencing reactions. Ready made sequencing mix including the M13 -40 forward sequencing primer was used (Catalog # US79730) for the T7 BAC vector terminus; ready made sequencing mix (Catalog # US79530) was mixed with the M13 -28 reverse sequencing primer (Catalog # US79339) for the SP6 BAC vector terminus. The sequencing reaction mixes included one of the four fluorescently labeled dye-primers, one of the four dideoxy termination mixes, dNTPs, reaction buffer, and Thermosequenase. For each BAC DNA sample, 3 µl of the BAC DNA sample was aliquoted to 4 PCR strip tubes. 2 µl of one of the four dye primer/termination mix combinations was then added to each of the four tubes. The tubes were then sealed and centrifuged briefly prior to PCR. Thermocycling conditions involved a 1 minute denaturation at 95°C, 15 second annealing at 45°C, and extension for 1 minute at 70°C for 35 total cycles. After cycling the plates were centrifuged briefly to collect all the liquid to the bottom of the tubes. 5 µl of sterile distilled and deionized H_2O was then added into each tube, the plates sealed and centrifuged briefly again. The four samples for each BAC were then pooled together. DNA was then precipitated by adding 1.5 µl of 7.5 M NH_4OAc and 100 µl of -20°C 100% ethanol to each tube. Samples were mixed by pipetting up and down once. The plates were then sealed and incubated on ice for 10 minutes. Plates were centrifuged in a table top Haraeus centrifuge at 4000 rpm (3,290 g) for 30 minutes at 4°C to recover the DNA. The supernatant was removed and excess liquid blotted onto paper towels. Pellets were washed by adding 100 µl of -20°C 70% ethanol into each

tube and recentrifuging at 4000 rpm (3,290 g) for 10 minutes at 4°C. The supernatant was removed and excess liquid again removed by blotting on a paper towel. Remaining traces of liquid were removed by placing the plates upside down over a paper towel and centrifuging only until the centrifuge reached 800 rpm. Samples were then air dried at room temperature for 30 min. Tubes were capped and stored dry at -20°C until electrophoresis. Immediately prior to electrophoresis the DNA was dissolved in 1.5 µl of Amersham loading dye. Plates were then sealed and centrifuged at 2000 rpm (825 g). The plates were then vortexed on a plate shaker for 1-2 minutes. Samples were then recentrifuged at 2000 rpm (825 g) briefly. Samples were then heated at 65°C for 2 min. and immediately placed on ice. Standard gel electrophoresis was performed on ABI 377 fluorescent sequencers according to the manufacturer's recommendation.

VII. Sub-cloning and Sequencing of HBM BAC DNA

The physical map of the Zmax1 gene region provides a set of BAC clones that contain within them the Zmax1 gene and the HBM gene. DNA sequencing of several of the BACs from the region has been completed. The DNA sequence data is a unique reagent that includes data that one skilled in the art can use to identify the Zmax1 gene and the HBM gene, or to prepare probes to identify the gene(s), or to identify DNA sequence polymorphisms that identify the gene(s).

BAC DNA was isolated according to one of two protocols, either a Qiagen purification of BAC DNA (Qiagen, Inc. as described in the product literature) or a manual purification which is a modification of the standard alkaline lysis/Cesium Chloride preparation of plasmid DNA (see e.g., Ausubel et al, *Current Protocols in Molecular Biology*, John Wiley & Sons (1997)). Briefly for the manual protocol, cells were pelleted, resuspended in GTE (50 mM glucose, 25 mM Tris-Cl (pH 8), 10 mM EDTA) and lysozyme (50 mg/ml solution), followed by NaOH/SDS (1% SDS/0.2 N NaOH) and then an ice-cold solution of 3 M KOAc (pH 4.5-4.8). RnaseA was added to the filtered supernatant, followed by Proteinase K and 20% SDS. The DNA was then precipitated with isopropanol, dried and resuspended in TE (10 mM Tris, 1 mM EDTA (pH 8.0)). The BAC DNA was further purified by Cesium Chloride density gradient centrifugation (Ausubel et al, *Current Protocols in Molecular Biology*, John Wiley & Sons (1997)).

Following isolation, the BAC DNA was sheared hydrodynamically using an HPLC (Hengen, *Trends in Biochem. Sci.*, 22:273-274 (1997)) to an insert size of 2000-3000 bp. After shearing, the DNA was concentrated and separated on a standard 1% agarose gel. A single fraction, corresponding to the approximate size, was excised from the gel and purified by electroelution (Sambrook et al, *Molecular Cloning: A Laboratory Manual*, Cold Spring Harbor Laboratory, Cold Spring, NY (1989)).

The purified DNA fragments were then blunt-ended using T4 DNA polymerase. The blunt-ended DNA was then ligated to unique BstXI-linker adapters (5' GTCTTCACCACGGGG and 5' GTGGTGAAGAC in 100-1000 fold molar excess). These linkers were complimentary to the BstXI-cut pMPX vectors (constructed by the inventors), while the overhang was not self-complimentary. Therefore, the linkers would not concatemerize nor would the cut-vector religate itself easily. The linker-adapted inserts were separated from the unincorporated linkers on a 1% agarose gel and purified using GeneClean (BIO 101, Inc.). The linker-adapted insert was then ligated to a modified pBlueScript vector to construct a "shotgun" subclone library. The vector contained an out-of-frame lacZ gene at the cloning site which became in-frame in the event that an adapter-dimer is cloned, allowing these to be avoided by their blue-color.

All subsequent steps were based on sequencing by ABI377 automated DNA sequencing methods. Only major modifications to the protocols are highlighted. Briefly, the library was then transformed into DH5α competent cells (Life Technologies, Bethesda, MD, DH5α transformation protocol). It was assessed by plating onto antibiotic plates containing ampicillin and IPTG/Xgal. The plates were incubated overnight at 37°C. Successful transformants were then used for plating of clones and picking for sequencing. The cultures were grown overnight at 37°. DNA was purified using a silica bead DNA preparation (Ng et al, *Nucl. Acids Res.*, 24:5045-5047 (1996)) method. In this manner, 25 μg of DNA was obtained per clone.

These purified DNA samples were then sequenced using ABI dye-terminator chemistry. The ABI dye terminator sequence reads were run on ABI377 machines and the data was directly transferred to UNIX machines following lane tracking of

the gels. All reads were assembled using PHRAP (P. Green, Abstracts of DOE Human Genome Program Contractor-Grantee Workshop V, Jan. 1996, p.157) with default parameters and quality scores. The initial assembly was done at 6-fold coverage and yielded an average of 8-15 contigs. Following the initial assembly, missing mates (sequences from clones that only gave one strand reads) were identified and sequenced with ABI technology to allow the identification of additional overlapping contigs. Primers for walking were selected using a Genome Therapeutics program Pick_primer near the ends of the clones to facilitate gap closure. These walks were sequenced using the selected clones and primers. Data were reassembled with PHRAP into sequence contigs.

VIII. Gene Identification by Computational Methods

Following assembly of the BAC sequences into contigs, the contigs were subjected to computational analyses to identify coding regions and regions bearing DNA sequence similarity to known genes. This protocol included the following steps.

1. Degap the contigs: the sequence contigs often contain symbols (denoted by a period symbol) that represent locations where the individual ABI sequence reads have insertions or deletions. Prior to automated computational analysis of the contigs, the periods were removed. The original data was maintained for future reference.

2. BAC vector sequences were "masked" within the sequence by using the program cross match (Phil Green, http:\\chimera.biotech.washington.edu\UWGC). Since the shotgun libraries construction detailed above leaves some BAC vector in the shotgun libraries, this program was used to compare the sequence of the BAC contigs to the BAC vector and to mask any vector sequence prior to subsequent steps. Masked sequences were marked by an "X" in the sequence files, and remained inert during subsequent analyses.

3. *E. coli* sequences contaminating the BAC sequences were masked by comparing the BAC contigs to the entire *E. coli* DNA sequence.

4. Repetitive elements known to be common in the human genome were masked using cross match. In this implementation of crossmatch, the BAC

sequence was compared to a database of human repetitive elements (Jerzy Jerka, Genetic Information Research Institute, Palo Alto, CA). The masked repeats were marked by X and remained inert during subsequent analyses.

5. The location of exons within the sequence was predicted using the MZEF computer program (Zhang, *Proc. Natl. Acad. Sci.*, 94:565-568 (1997)).

6. The sequence was compared to the publicly available unigene database (National Center for Biotechnology Information, National Library of Medicine, 38A, 8N905, 8600 Rockville Pike, Bethesda, MD 20894; www.ncbi.nlm.nih.gov) using the blastn2 algorithm (Altschul et al, *Nucl. Acids Res.*, 25:3389-3402 (1997)). The parameters for this search were: E=0.05, v=50, B=50 (where E is the expected probability score cutoff, V is the number of database entries returned in the reporting of the results, and B is the number of sequence alignments returned in the reporting of the results (Altschul et al, *J. Mol. Biol.*, 215:403-410 (1990)).

7. The sequence was translated into protein for all six reading frames, and the protein sequences were compared to a non-redundant protein database compiled from Genpept Swissprot PIR (National Center for Biotechnology Information, National Library of Medicine, 38A, 8N905, 8600 Rockville Pike, Bethesda, MD 20894; www.ncbi.nlm.nih.gov). The parameters for this search were E=0.05, V=50, B= 50, where E, V, and B are defined as above.

8. The BAC DNA sequence was compared to the database of the cDNA clones derived from direct selection experiments (described below) using blastn2 (Altschul et al, *Nucl. Acids. Res.*, 25:3389-3402 (1997)). The parameters for this search were E=0.05, V=250, B=250, where E, V, and B are defined as above.

9. The BAC sequence was compared to the sequences of all other BACs from the HBM region on chromosome 11q12-13 using blastn2 (Altschul et al, *Nucl. Acids. Res.*, 25:3389-3402 (1997)). The parameters for this search were E=0.05, V=50, B=50, where E, V, and B are defined as above.

10. The BAC sequence was compared to the sequences derived from the ends of BACs from the HBM region on chromosome 11q12-13 using blastn2 (Altschul et al, *Nucl. Acids. Res.*, 25:3389-3402 (1997)). The parameters for this search were E=0.05, V=50, B=50, where E, V, and B are defined as above.

11. The BAC sequence was compared to the Genbank database (National Center for Biotechnology Information, National Library of Medicine, 38A, 8N905, 8600 Rockville Pike, Bethesda, MD 20894; www.ncbi.nlm.nih.gov) using blastn2 (Altschul et al, *Nucl. Acids. Res.*, 25:3389-3402 (1997)). The parameters for this search were E=0.05, V=50, B=50, where E, V, and B are defined as above.

12. The BAC sequence was compared to the STS division of Genbank database (National Center for Biotechnology Information, National Library of Medicine, 38A, 8N905, 8600 Rockville Pike, Bethesda, MD 20894; www.ncbi.nlm.nih.gov) using blastn2 (Altschul et al, 1997). The parameters for this search were E=0.05, V=50, B= 50, where E, V, and B are defined as above.

13. The BAC sequence was compared to the Expressed Sequence (EST) Tag Genbank database (National Center for Biotechnology Information, National Library of Medicine, 38A, 8N905, 8600 Rockville Pike, Bethesda, MD 20894; www.ncbi.nlm.nih.gov) using blastn2 (Altschul et al, *Nucl. Acids. Res.*, 25:3389-3402 (1997)). The parameters for this search were E=0.05, V=250, B=250, where E, V, and B are defined as above.

IX. Gene Identification by Direct cDNA Selection

Primary linkered cDNA pools were prepared from bone marrow, calvarial bone, femoral bone, kidney, skeletal muscle, testis and total brain. Poly (A) + RNA was prepared from calvarial and femoral bone tissue (Chomczynski et al, *Anal. Biochem.*, 162:156-159 (1987); D'Alessio et al, *Focus*, 9:1-4 (1987)) and the remainder of the mRNA was purchased from Clontech (Palo Alto, California). In order to generate oligo(dT) and random primed cDNA pools from the same tissue, 2.5 µg mRNA was mixed with oligo(dT) primer in one reaction and 2.5 µg mRNA was mixed with random hexamers in another reaction, and both were converted to first and second strand cDNA according to manufacturers recommendations (Life Technologies, Bethesda, MD). Paired phosphorylated cDNA linkers (see sequence below) were annealed together by mixing in a 1:1 ratio (10 µg each) incubated at 65°C for five minutes and allowed to cool to room temperature.

Paired linkers oligo1/2

OLIGO 1: 5'CTG AGC GGA ATT CGT GAG ACC3' (SEQ ID NO:12)

OLIGO 2: 5'TTG GTC TCA CGT ATT CCG CTC GA3' (SEQ ID NO:13)

Paired linkers oligo3/4

OLIGO 3: 5'CTC GAG AAT TCT GGA TCC TC3' (SEQ ID NO:14)

OLIGO 4: 5'TTG AGG ATC CAG AAT TCT CGA G3' (SEQ ID NO:15)

Paired linkers oligo5/6

OLIGO 5: 5'TGT ATG CGA ATT CGC TGC GCG3' (SEQ ID NO:16)

OLIGO 6: 5'TTC GCG CAG CGA ATT CGC ATA CA3' (SEQ ID NO:17)

Paired linkers oligo7/8

OLIGO 7: 5'GTC CAC TGA ATT CTC AGT GAG3' (SEQ ID NO:18)

OLIGO 8: 5'TTG TCA CTG AGA ATT CAG TGG AC3' (SEQ ID NO:19)

Paired linkers oligo11/12

OLIGO 11: 5'GAA TCC GAA TTC CTG GTC AGC3' (SEQ ID NO:20)

OLIGO 12: 5'TTG CTG ACC AGG AAT TCG GAT TC3' (SEQ ID NO:21)

Linkers were ligated to all oligo(dT) and random primed cDNA pools (see below) according to manufacturers instructions (Life Technologies, Bethesda, MD).

Oligo 1/2 was ligated to oligo(dT) and random primed cDNA pools prepared from bone marrow. Oligo 3/4 was ligated to oligo(dT) and random primed cDNA pools prepared from calvarial bone. Oligo 5/6 was ligated to oligo(dT) and random primed cDNA pools prepared from brain and skeletal muscle. Oligo 7/8 was ligated to oligo(dT) and random primed cDNA pools prepared from kidney. Oligo 11/12 was ligated to oligo(dT) and random primed cDNA pools prepared from femoral bone.

The cDNA pools were evaluated for length distribution by PCR amplification using 1 µl of a 1:1, 1:10, and 1:100 dilution of the ligation reaction, respectively. PCR reactions were performed in a Perkin Elmer 9600, each 25 µl volume reaction contained 1 µl of DNA, 10 mM Tris-HCl (pH 8.3), 50 mM KCl, 1.5 mM MgCl2, 0.001% gelatin, 200 mM each dNTPs, 10 µM primer and 1 unit Taq DNA polymerase (Perkin Elmer) and was amplified under the following conditions:

30 seconds at 94°C, 30 seconds at 60°C and 2 minutes at 72°C for 30 cycles. The length distribution of the amplified cDNA pools were evaluated by electrophoresis on a 1% agarose gel. The PCR reaction that gave the best representation of the random primed and oligo(dT) primed cDNA pools was scaled up so that ~2-3 µg of each cDNA pool was produced. The starting cDNA for the direct selection reaction comprised of 0.5 µg of random primed cDNAs mixed with 0.5 µg of oligo(dT) primed cDNAs.

The DNA from the 54 BACs that were used in the direct cDNA selection procedure was isolated using Nucleobond AX columns as described by the manufacturer (The Nest Group, Inc.).

The BACs were pooled in equimolar amounts and 1 µg of the isolated genomic DNA was labeled with biotin 16-UTP by nick translation in accordance with the manufacturers instructions (Boehringer Mannheim). The incorporation of the biotin was monitored by methods that could be practiced by one skilled in the art (Del Mastro and Lovett, *Methods in Molecular Biology*, Humana Press Inc., NJ (1996)).

Direct cDNA selection was performed using methods that could be practiced by one skilled in the art (Del Mastro and Lovett, *Methods in Molecular Biology*, Humana Press Inc., NJ (1996)). Briefly, the cDNA pools were multiplexed in two separate reactions: In one reaction cDNA pools from bone marrow, calvarial bone, brain and testis were mixed, and in the other cDNA pools from skeletal muscle, kidney and femoral bone were mixed. Suppression of the repeats, yeast sequences and plasmid in the cDNA pools was performed to a Cot of 20. 100 ng of biotinylated BAC DNA was mixed with the suppressed cDNAs and hybridized in solution to a Cot of 200. The biotinylated DNA and the cognate cDNAs was captured on streptavidin-coated paramagnetic beads. The beads were washed and the primary selected cDNAs were eluted. These cDNAs were PCR amplified and a second round of direct selection was performed. The product of the second round of direct selection is referred to as the secondary selected material. A Galanin cDNA clone, previously shown to map to 11q12-13 (Evans, *Genomics*, 18:473-477 (1993)), was used to monitor enrichment during the two rounds of selection.

The secondary selected material from bone marrow, calvarial bone, femoral bone, kidney, skeletal muscle, testis and total brain was PCR amplified using modified primers of oligos 1, 3, 5, 7 and 11, shown below, and cloned into the UDG vector pAMP10 (Life Technologies, Bethesda, MD), in accordance with the manufacturer's recommendations.

Modified primer sequences:

Oligo1-CUA: 5'CUA CUA CUA CUA CTG AGC GGA ATT CGT GAG ACC3' (SEQ ID NO:22)

Oligo3-CUA: 5'CUA CUA CUA CUA CTC GAG AAT TCT GGA TCC TC3' (SEQ ID NO:23)

Oligo5-CUA: 5'CUA CUA CUA CUA TGT ATG CGA ATT CGC TGC GCG3' (SEQ ID NO:24)

Oligo7-CUA: 5'CUA CUA CUA CUA GTC CAC TGA ATT CTC AGT GAG3' (SEQ ID NO:25)

Oligo11-CUA: 5'CUA CUA CUA CUA GAA TCC GAA TTC CTG GTC AGC3' (SEQ ID NO:26)

The cloned secondary selected material, from each tissue source, was transformed into MAX Efficiency DH5a Competent Cells (Life Technologies, Bethesda, MD) as recommended by the manufacturer. 384 colonies were picked from each transformed source and arrayed into four 96 well microtiter plates.

All secondarily selected cDNA clones were sequenced using M13 dye primer terminator cycle sequencing kit (Applied Biosystems), and the data collected by the ABI 377 automated fluorescence sequencer (Applied Biosystems).

All sequences were analyzed using the BLASTN, BLASTX and FASTA programs (Altschul et al, *J. Mol. Biol.*, 215:403-410 (1990), Altschul et al, *Nucl. Acids. Res.*, 25:3389-3402 (1997)). The cDNA sequences were compared to a database containing sequences derived from human repeats, mitochondrial DNA, ribosomal

RNA, *E. coli* DNA to remove background clones from the dataset using the program cross_match. A further round of comparison was also performed using the program BLASTN2 against known genes (Genbank) and the BAC sequences from the HBM region. Those cDNAs that were >90% homologous to these sequences were filed according to the result and the data stored in a database for further analysis. cDNA sequences that were identified but did not have significant similarity to the BAC sequences from the HBM region or were eliminated by cross_match were hybridized to nylon membranes which contained the BACs from the HBM region, to ascertain whether they hybridized to the target.

Hybridization analysis was used to map the cDNA clones to the BAC target that selected them. The BACs that were identified from the HBM region were arrayed and grown into a 96 well microtiter plate. LB agar containing 25 μg/ml kanamycin was poured into 96 well microtiter plate lids. Once the agar had solidified, pre-cut Hybond N+ nylon membranes (Amersham) were laid on top of the agar and the BACs were stamped onto the membranes in duplicate using a hand held 96 well replica plater (V&P Scientific, Inc.). The plates were incubated overnight at 37°C. The membranes were processed according to the manufacturers recommendations.

The cDNAs that needed to be mapped by hybridization were PCR amplified using the relevant primer (oligos 1, 3, 5, 7 and 11) that would amplify that clone. For this PCR amplification, the primers were modified to contain a linkered digoxigenin molecule at the 5' of the oligonucleotide. The PCR amplification was performed under the same conditions as described in Preparation of cDNA Pools (above). The PCR products were evaluated for quality and quantity by electrophoresis on a 1% agarose gel by loading 5 μl of the PCR reaction. The nylon membranes containing the stamped BACs were individually pre-hybridized in 50 ml conical tubes containing 10 ml of hybridization solution (5x SSPE, 0.5x Blotto, 2.5% SDS and 1 mM EDTA (pH 8.0)). The 50 ml conical tubes were placed in a rotisserie oven (Robbins Scientific) for 2 hours at 65°C. Twenty-five ng of each cDNA probe was denatured and added into individual 50 ml conical tubes containing the nylon membrane and hybridization solution. The hybridization was performed overnight at 65°C. The filters were washed for 20 minutes at 65°C in

each of the following solutions: 3x SSPE, 0.1% SDS; 1x SSPE, 0.1% SDS and 0.1x SSPE, 0.1% SDS.

The membranes were removed from the 50 ml conical tubes and placed in a dish. Acetate sheets were placed between each membrane to prevent them from sticking to each other. The incubation of the membranes with the Anti-DIG-AP and CDP-Star was performed according to manufacturers recommendations (Boehringer Mannheim). The membranes were wrapped in Saran wrap and exposed to Kodak Bio-Max X-ray film for 1 hour.

X. cDNA Cloning and Expression Analysis

To characterize the expression of the genes identified by direct cDNA selection and genomic DNA sequencing in comparison to the publicly available databases, a series of experiments were performed to further characterize the genes in the HBM region. First, oligonucleotide primers were designed for use in the polymerase chain reaction (PCR) so that portions of a cDNA, EST, or genomic DNA could be amplified from a pool of DNA molecules (a cDNA library) or RNA population (RT-PCR and RACE). The PCR primers were used in a reaction containing genomic DNA to verify that they generated a product of the size predicted based on the genomic (BAC) sequence. A number of cDNA libraries were then examined for the presence of the specific cDNA or EST. The presence of a fragment of a transcription unit in a particular cDNA library indicates a high probability that additional portions of the same transcription unit will be present as well.

A critical piece of data that is required when characterizing novel genes is the length, in nucleotides, of the processed transcript or messenger RNA (mRNA). One skilled in the art primarily determines the length of an mRNA by Northern blot hybridization (Sambrook et al, *Molecular Cloning: A Laboratory Manual*, Cold Spring Harbor Laboratory, Cold Spring Harbor NY (1989)). Groups of ESTs and direct-selected cDNA clones that displayed significant sequence similarity to sequenced BACs in the critical region were grouped for convenience into approximately 30 kilobase units. Within each 30 kilobase unit there were from one up to fifty ESTs and direct-selected cDNA clones which comprised one or more independent transcription units. One or more ESTs or direct-selected cDNAs were

used as hybridization probes to determine the length of the mRNA in a variety of tissues, using commercially available reagents (Multiple Tissue Northern blot; Clontech, Palo Alto, California) under conditions recommended by the manufacturer.

Directionally cloned cDNA libraries from femoral bone, and calvarial bone tissue were constructed by methods familiar to one skilled in the art (for example, Soares in *Automated DNA Sequencing and Analysis*, Adams, Fields and Venter, Eds., Academic Press, NY, pages 110-114 (1994)). Bones were initially broken into fragments with a hammer, and the small pieces were frozen in liquid nitrogen and reduced to a powder in a tissue pulverizer (Spectrum Laboratory Products). RNA was extracted from the powdered bone by homogenizing the powdered bone with a standard Acid Guanidinium Thiocyanate-Phenol-Chloroform extraction buffer (e.g. Chomczynski and Sacchi, *Anal. Biochem.*, 162:156-159 (1987)) using a polytron homogenizer (Brinkman Instruments). Additionally, human brain and lung total RNA was purchased from Clontech. PolyA RNA was isolated from total RNA using dynabeads-dT according to the manufacturer's recommendations (Dynal, Inc.).

First strand cDNA synthesis was initiated using an oligonucleotide primer with the sequence: 5'-AACTGGAAGAATTCGCGGCCGCAGGAATTTTTTTTT TTTTTTTTT-3' (SEQ ID NO:27). This primer introduces a NotI restriction site (underlined) at the 3' end of the cDNA. First and second strand synthesis were performed using the "one-tube" cDNA synthesis kit as described by the anufacturer (Life Technologies, Bethesda, MD). Double stranded cDNAs were treated with T4 polynucleotide kinase to ensure that the ends of the molecules were blunt (Soares in *Automated DNA Sequencing and Analysis*, Adams, Fields and Venter, Eds., Academic Press, NY, pages 110-114 (1994)), and the blunt ended cDNAs were then size selected by a Biogel column (Huynh et al in *DNA Cloning*, Vol. 1, Glover, Ed., IRL Press, Oxford, pages 49-78 (1985)) or with a size-sep 400 sepharose column (Pharmacia, catalog # 27-5105-01). Only cDNAs of 400 base pairs or longer were used in subsequent steps. EcoRI adapters (sequence: 5' OH-AATTCGGCACGAG-OH 3' (SEQ ID NO:28), and 5' p-CTCGTGCCG-OH 3' (SEQ ID NO:29)) were then ligated to the double stranded cDNAs by methods familiar to one skilled in the art (Soares, 1994). The EcoRI adapters were then

removed from the 3' end of the cDNA by digestion with NotI (Soares, 1994). The cDNA was then ligated into the plasmid vector pBluescript II KS+ (Stratagene, La Jolla, California), and the ligated material was transformed into *E. coli* host DH10B or DH12S by electroporation methods familiar to one skilled in the art (Soares, 1994). After growth overnight at 37°C, DNA was recovered from the *E. coli* colonies after scraping the plates by processing as directed for the Mega-prep kit (Qiagen, Chatsworth, California). The quality of the cDNA libraries was estimated by counting a portion of the total numbers of primary transformants and determining the average insert size and the percentage of plasmids with no cDNA insert. Additional cDNA libraries (human total brain, heart, kidney, leukocyte, and fetal brain) were purchased from Life Technologies, Bethesda, MD.

cDNA libraries, both oligo (dT) and random hexamer (N_6) primed, were used for isolating cDNA clones transcribed within the HBM region: human bone, human brain, human kidney and human skeletal muscle (all cDNA libraries were made by the inventors, except for skeletal muscle (dT) and kidney (dT) cDNA libraries). Four 10 x 10 arrays of each of the cDNA libraries were prepared as follows: the cDNA libraries were titered to 2.5 x 10^6 using primary transformants. The appropriate volume of frozen stock was used to inoculate 2 L of LB/ampicillin (100 mg/ml). This inoculated liquid culture was aliquotted into 400 tubes of 4 ml each. Each tube contained approximately 5000 cfu. The tubes were incubated at 30°C overnight with gentle agitation. The cultures were grown to an OD of 0.7-0.9. Frozen stocks were prepared for each of the cultures by aliquotting 100 µl of culture and 300 µl of 80% glycerol. Stocks were frozen in a dry ice/ethanol bath and stored at -70°C. The remaining culture was DNA prepared using the Qiagen (Chatsworth, CA) spin miniprep kit according to the manufacturer's instructions. The DNAs from the 400 cultures were pooled to make 80 column and row pools. The cDNA libraries were determined to contain HBM cDNA clones of interest by PCR. Markers were designed to amplify putative exons. Once a standard PCR optimization was performed and specific cDNA libraries were determined to contain cDNA clones of interest, the markers were used to screen the arrayed library. Positive addresses indicating the presence of cDNA clones were confirmed by a second PCR using the same markers.

Once a cDNA library was identified as likely to contain cDNA clones corresponding to a specific transcript of interest from the HBM region, it was manipulated to isolate the clone or clones containing cDNA inserts identical to the EST or direct-selected cDNA of interest. This was accomplished by a modification of the standard "colony screening" method (Sambrook et al, *Molecular Cloning: A Laboratory Manual*, Cold Spring Harbor Laboratory, Cold Spring Harbor NY (1989)). Specifically, twenty 150 mm LB+ampicillin agar plates were spread with 20,000 colony forming units (cfu) of cDNA library and the colonies allowed to grow overnight at 37°C. Colonies were transferred to nylon filters (Hybond from Amersham, or equivalent) and duplicates prepared by pressing two filters together essentially as described (Sambrook et al, *Molecular Cloning: A Laboratory Manual*, Cold Spring Harbor Laboratory, Cold Spring Harbor NY (1989)). The "master" plate was then incubated an additional 6-8 hours to allow the colonies to grow back. The DNA from the bacterial colonies was then affixed to the nylon filters by treating the filters sequentially with denaturing solution (0.5 N NaOH, 1.5 M NaCl) for two minutes, neutralization solution (0.5 M Tris-Cl pH 8.0, 1.5 M NaCl) for two minutes (twice). The bacterial colonies were removed from the filters by washing in a solution of 2X SSC/0.1% SDS for one minute while rubbing with tissue paper. The filters were air dried and baked under vacuum at 80°C for 1-2 hours.

A cDNA hybridization probe was prepared by random hexamer labeling (Fineberg and Vogelstein, *Anal. Biochem.*, 132:6-13 (1983)) or by including gene-specific primers and no random hexamers in the reaction (for small fragments). Specific activity was calculated and was $>5X10^8$ cpm/10^8 µg of cDNA. The colony membranes were then prewashed in 10 mM Tris-Cl pH 8.0, 1 M NaCl, 1 mM EDTA, 0.1% SDS for 30 minutes at 55°C. Following the prewash, the filters were prehybridized in > 2 ml/filter of 6X SSC, 50 % deionized formamide, 2% SDS, 5X Denhardt's solution, and 100 mg/ml denatured salmon sperm DNA, at 42°C for 30 minutes. The filters were then transferred to hybridization solution (6X SSC, 2% SDS, 5X Denhardt's, 100 mg/ml denatured salmon sperm DNA) containing denatured α^{32}P-dCTP-labeled cDNA probe and incubated at 42°C for 16-18 hours.

After the 16-18 hour incubation, the filters were washed under constant agitation in 2X SSC, 2% SDS at room temperature for 20 minutes, followed by two

washes at 65°C for 15 minutes each. A second wash was performed in 0.5 X SSC, 0.5% SDS for 15 minutes at 65°C. Filters were then wrapped in plastic wrap and exposed to radiographic film for several hours to overnight. After film development, individual colonies on plates were aligned with the autoradiograph so that they could be picked into a 1 ml solution of LB Broth containing ampicillin. After shaking at 37°C for 1-2 hours, aliquots of the solution were plated on 150 mm plates for secondary screening. Secondary screening was identical to primary screening (above) except that it was performed on plates containing ~250 colonies so that individual colonies could be clearly identified for picking.

After colony screening with radiolabeled probes yielded cDNA clones, the clones were characterized by restriction endonuclease cleavage, PCR, and direct sequencing to confirm the sequence identity between the original probe and the isolated clone. To obtain the full-length cDNA, the novel sequence from the end of the clone identified was used to probe the library again. This process was repeated until the length of the cDNA cloned matches that estimated to be full-length by the northern blot analysis.

RT-PCR was used as another method to isolate full length clones. The cDNA was synthesized and amplified using a "Superscript One Step RT-PCR" kit (Life Technologies, Gaithersburg, MD). The procedure involved adding 1.5 µg of RNA to the following: 25 µl of reaction mix provided which is a proprietary buffer mix with $MgSO_4$ and dNTP's, 1 µl sense primer (10 µM) and 1 µl anti-sense primer (10 µM), 1 µl reverse transcriptase and Taq DNA polymerase mix provided and autoclaved water to a total reaction mix of 50 µl. The reaction was then placed in a thermocycler for 1 cycle at 50°C for 15 to 30 minutes, then 94°C for 15 seconds, 55-60°C for 30 seconds and 68-72°C for 1 minute per kilobase of anticipated product and finally 1 cycle of 72°C for 5-10 minutes. The sample was analyzed on an agarose gel. The product was excised from the gel and purified from the gel (GeneClean, Bio 101). The purified product was cloned in pCTNR (General Contractor DNA Cloning System, 5 Prime - 3 Prime, Inc.) and sequenced to verify that the clone was specific to the gene of interest.

Rapid Amplification of cDNA ends (RACE) was performed following the manufacturer's instructions using a Marathon cDNA Amplification Kit (Clontech,

Palo Alto, CA) as a method for cloning the 5' and 3' ends of candidate genes. cDNA pools were prepared from total RNA by performing first strand synthesis, where a sample of total RNA sample was mixed with a modified oligo (dT) primer, heated to 70°C, cooled on ice and followed by the addition of: 5x first strand buffer, 10 mM dNTP mix, and AMV Reverse Transcriptase (20 U/µl). The tube was incubated at 42°C for one hour and then the reaction tube was placed on ice. For second strand synthesis, the following components were added directly to the reaction tube: 5x second strand buffer, 10 mM dNTP mix, sterile water, 20x second strand enzyme cocktail and the reaction tube was incubated at 16°C for 1.5 hours. T4 DNA Polymerase was added to the reaction tube and incubated at 16°C for 45 minutes. The second-strand synthesis was terminated with the addition of an EDTA/Glycogen mix. The sample was subjected to a phenol/chloroform extraction and an ammonium acetate precipitation. The cDNA pools were checked for quality by analyzing on an agarose gel for size distribution. Marathon cDNA adapters (Clontech) were then ligated onto the cDNA ends. The specific adapters contained priming sites that allowed for amplification of either 5' or 3' ends, depending on the orientation of the gene specific primer (GSP) that was chosen. An aliquot of the double stranded cDNA was added to the following reagents: 10 µM Marathon cDNA adapter, 5x DNA ligation buffer, T4 DNA ligase. The reaction was incubated at 16°C overnight. The reaction was heat inactivated to terminate the reaction. PCR was performed by the addition of the following to the diluted double stranded cDNA pool: 10x cDNA PCR reaction buffer, 10 µM dNTP mix, 10 µM GSP, 10 µM AP1 primer (kit), 50x Advantage cDNA Polymerase Mix. Thermal Cycling conditions were 94°C for 30 seconds, 5 cycles of 94°C for 5 seconds, 72°C for 4 minutes, 5 cycles of 94°C for 5 seconds, 70°C for 4 minutes, 23 cycles of 94°C for 5 seconds, 68°C for 4 minutes. After the first round of PCR was performed using the GSP to extend to the end of the adapter to create the adapter primer binding site, exponential amplification of the specific cDNA of interest was observed. Usually a second nested PCR is performed to confirm the specific cDNA. The RACE product was analyzed on an agarose gel and then excised and purified from the gel (GeneClean, BIO 101). The RACE product was then cloned into pCTNR (General Contractor

DNA Cloning System, 5' - 3', Inc.) and the DNA sequence determined to verify that the clone is specific to the gene of interest.

XI. Mutation Analysis

Comparative genes were identified using the above procedures and the exons from each gene were subjected to mutation detection analysis. Comparative DNA sequencing was used to identify polymorphisms in HBM candidate genes from chromosome 11q12-13. DNA sequences for candidate genes were amplified from patient lymphoblastoid cell lines.

The inventors developed a method based on analysis of direct DNA sequencing of PCR products amplified from candidate regions to search for the causative polymorphism. The procedure consisted of three stages that used different subsets of HBM family to find segregating polymorphisms and a population panel to assess the frequency of the polymorphisms. The family resources result from a single founder leading to the assumption that all affected individuals will share the same causative polymorphism.

Candidate regions were first screened in a subset of the HBM family consisting of the proband, daughter, and her mother, father and brother. Monochromosomal reference sequences were produced concurrently and used for comparison. The mother and daughter carried the HBM polymorphism in this nuclear family, providing the ability to monitor polymorphism transmission. The net result is that two HBM chromosomes and six non-HBM chromosomes were screened. This allowed exclusion of numerous frequent alleles. Only alleles exclusively present in the affected individuals passed to the next level of analysis.

Polymorphisms that segregated exclusively with the HBM phenotype in this original family were then re-examined in an extended portion of the HBM pedigree consisting of two additional nuclear families. These families consisted of five HBM and three unaffected individuals. The HBM individuals in this group included the two critical crossover individuals, providing the centromeric and telomeric boundaries of the critical region. Tracking the heredity of polymorphisms between these individuals and their affected parents allowed for further refining of the critical region. This group brought the total of HBM chromosomes screened to seven and the total of non-HBM chromosomes to seventeen.

When a given polymorphism continued to segregate exclusively with the HBM phenotype in the extended group, a population panel was then examined. This panel of 84 persons consisted of 42 individuals known to have normal bone mineral density and 42 individuals known to be unrelated but with untyped bone mineral density. Normal bone mineral density is within two standard deviations of BMD Z score 0. The second group was from the widely used CEPH panel of individuals. Any segregating polymorphisms found to be rare in this population were subsequently examined on the entire HBM pedigree and a larger population.

Polymerase chain reaction (PCR) was used to generate sequencing templates from the HBM family's DNA and monochromosomal controls. Enzymatic amplification of genes within the HBM region on 11q12-13 was accomplished using the PCR with oligonucleotides flanking each exon as well as the putative 5' regulatory elements of each gene. The primers were chosen to amplify each exon as well as 15 or more base pairs within each intron on either side of the splice. All PCR primers were made as chimeras to facilitate dye primer sequencing. The M13-21F (5'- GTA A CGA CGG CCA GT -3') (SEQ ID NO:30) and -28REV (5'- AAC AGC TAT GAC CAT G -3') (SEQ ID NO:31) primer binding sites were built on to the 5' end of each forward and reverse PCR primer, respectively, during synthesis. 150 ng of genomic DNA was used in a 50 µl PCR with 2 U AmpliTaq, 500 nM primer and 125 µM dNTP. Buffer and cycling conditions were specific to each primer set. TaqStart antibody (Clontech) was used for hot start PCR to minimize primer dimer formation. 10% of the product was examined on an agarose gel. The appropriate samples were diluted 1:25 with deionized water before sequencing.

Each PCR product was sequenced according to the standard Energy Transfer primer (Amersham) protocol. All reactions took place in 96 well trays. 4 separate reactions, one each for A, C, G and T were performed for each template. Each reaction included 2 µl of the sequencing reaction mix and 3 µl of diluted template. The plates were then heat sealed with foil tape and placed in a thermal cycler and cycled according to the manufacturer's recommendation. After cycling, the 4 reactions were pooled. 3 µl of the pooled product was transferred to a new 96 well plate and 1 µl of the manufacturer's loading dye was added to each well. All 96 well pipetting procedures occurred on a Hydra 96 pipetting station (Robbins Scientific,

USA). 1 µl of pooled material was directly loaded onto a 48 lane gel running on an ABI 377 DNA sequencer for a 10 hour, 2.4 kV run.

Polyphred (University of Washington) was used to assemble sequence sets for viewing with *Consed* (University of Washington). Sequences were assembled in groups representing all relevant family members and controls for a specified target region. This was done separately for each of the three stages. Forward and reverse reads were included for each individual along with reads from the monochromosomal templates and a color annotated reference sequence. *Polyphred* indicated potential polymorphic sites with a purple flag. Two readers independently viewed each assembly and assessed the validity of the purple-flagged sites.

A total of 23 exons present in the mature mRNA and several other portions of the primary transcript were evaluated for heterozygosity in the nuclear family of two HBM-affected and two unaffected individuals. 25 SNPs were identified, as shown in the table below.

TABLE 4: Single Nucleotide Polymorphisms in the Zmax1 Gene and Environs

Exon Name	Location	Base Change
b200e21-h_Contig1_1.nt	69169 (309G)	C/A
b200e21-h_Contig4_12.nt	27402 (309G)	A/G
b200e21-h_Contig4_13.nt	27841 (309G)	T/C
b200e21-h_Contig4_16.nt	35600 (309G)	A/G
b200e21-h_Contig4_21.nt	45619 (309G)	G/A
b200e21-h_Contig4_22.nt-a	46018 (309G)	T/G
b200e21-h_Contig4_22.nt-b	46093 (309G)	T/G
b200e21-h_Contig4_22.nt-c	46190 (309G)	A/G
b200e21-h_Contig4_24.nt-a	50993 (309G)	T/C
b200e21-h_Contig4_24.nt-b	51124 (309G)	C/T
b200e21-h_Contig4_25.nt	55461 (309G)	C/T
b200e21-h_Contig4_33.nt-a	63645 (309G)	C/A
b200e21-h_Contig4_33.nt-b	63646 (309G)	A/C
b200e21-h_Contig4_61.nt	24809 (309G)	T/G
b200e21-h_Contig4_62.nt	27837 (309G)	T/C

Exon Name	Location	Base Change
b200e21-h_Contig4_63.nt-a	31485 (309G)	C/T
b200e21-h_Contig4_63.nt-b	31683 (309G)	A/G
b200e21-h_Contig4_9.nt	24808 (309G)	T/G
b527d12-h_Contig030g_1.nt-a	31340 (308G)	T/C
b527d12-h_Contig030g_1.nt-b	32538 (308G)	A/G
b527d12-h_Contig080C_2.nt	13224 (308G)	A/G
b527d12-h_Contig087C_1.nt	21119 (308G)	C/A
b527d12-h_Contig087C_4.nt	30497 (308G)	G/A
b527d12-h_Contig088C_4.nt	24811 (309G)	A/C
b527d12-h_Contig089_1HP.nt	68280 (309G)	G/A

In addition to the polymorphisms presented in Table 4, two additional polymorphisms can also be present in SEQ ID NO:2. These is a change at position 2002 of SEQ ID NO:2. Either a guanine or an adenine can appear at this position. This polymorphism is silent and is not associated with any change in the amino acid sequence. The second change is at position 4059 of SEQ ID NO:2 corresponding in a cytosine (C) to thymine (T) change. This polymorphism results in a corresponding amino acid change from a valine (V) to an alanine (A). Other polymorphisms were found in the candidate gene exons and adjacent intron sequences. Any one or combination of the polymorphisms listed in Table 4 or the two discussed above could also have a minor effect on bone mass when present in SEQ ID NO:2.

The present invention encompasses the nucleic acid sequences having the nucleic acid sequence of SEQ ID NO: 1 with the above-identified point mutations.

Preferably, the present invention encompasses the nucleic acid of SEQ ID NO: 2. Specifically, a base-pair substitution changing G to T at position 582 in the coding sequence of Zmax1 (the HBM gene) was identified as heterozygous in all HBM individuals, and not found in the unaffected individuals (i.e., b527d12-h_Contig087C_1.nt). Fig. 5 shows the order of the contigs in B527D12. The direction of transcription for the HBM gene is from left to right. The sequence of contig308G of B527D12 is the reverse complement of the coding region to the

HBM gene. Therefore, the relative polymorphism in contig 308G shown in Table 4 as a base change substitution of C to A is the complement to the G to T substitution in the HBM gene. This mutation causes a substitution of glycine 171 with valine (G171V).

The HBM polymorphism was confirmed by examining the DNA sequence of different groups of individuals. In all members of the HBM pedigree (38 individuals), the HBM polymorphism was observed in the heterozygous form in affected (i.e., elevated bone mass) individuals only (N=18). In unaffected relatives (N=20) (BMDZ<2.0) the HBM polymorphism was never observed. To determine whether this polymorphism was ever observed in individuals outside of the HBM pedigree, 297 phenotyped individuals were characterized at the site of the HBM gene. None were heterozygous at the site of the HBM polymorphism. In an unphenotyped control group, none of 64 individuals were observed to be heterozygous at position 582. Taken together, these data prove that the polymorphism observed in the kindred displaying the high bone mass phenotype is strongly correlated with the G→T polymorphism at position 582 of Zmax1. Furthermore, these results coupled with the ASO results described below, establish that the HBM polymorphism genetically segregates with the HBM phenotype, and that both the HBM polymorphism and phenotype are rare in the general population.

XII. Allele Specific Oligonucleotide (ASO) Analysis

The amplicon containing the HBM1 polymorphism was PCR amplified using primers specific for the exon of interest. The appropriate population of individuals was PCR amplified in 96 well microtiter plates as follows. PCR reactions (20 µl) containing 1X Promega PCR buffer (Cat. # M1883 containing 1.5 mM $MgCl_2$), 100mM dNTP, 200 nM PCR primers (1863F: CCAAGTTCTGAGAAGTCC and 1864R: AATACCTGAAACCATACCTG), 1 U Amplitaq, and 20 ng of genomic DNA were prepared and amplified under the following PCR conditions: 94°C, 1 minute, (94°C, 30 sec.; 58°C, 30 sec.; 72°C, 1 min.) X35 cycles), 72°C, 5', 4°C, hold. Loading dye was then added and 10 µl of the products was electrophoresed on 1.5% agarose gels containing 1 µg/ml ethidium bromide at 100-150 V for 5-10 minutes. Gels were treated 20 minutes in denaturing

solution (1.5 M NaCl, 0.5 N NaOH), and rinsed briefly with water. Gels were then neutralized in 1 M Tris-HCl, pH 7.5, 1.5 M NaCl, for 20 minutes and rinsed with water. Gels were soaked in 10 X SSC for 20 minutes and blotted onto nylon transfer membrane (Hybond N+- Amersham) in 10X SSC overnight. Filters were the rinsed in 6X SSC for 10 minutes and UV crosslinked.

The allele specific oligonucleotides (ASO) were designed with the polymorphism approximately in the middle. Oligonucleotides were phosphate free at the 5'end and were purchased from Gibco BRL. Sequences of the oligonucleotides are:

2326 Zmax1.ASO.g: AGACTGGGGTGAGACGC

2327 Zmax1.ASO.t: CAGACTGGGTTGAGACGCC

The polymorphic nucleotides are underlined. To label the oligos, 1.5 µl of 1 µg/µl ASO oligo (2326.Zmax1.ASO.g or 2327.Zmax1.ASO.t), 11 µl ddH_2O, 2 µl 10X kinase forward buffer, 5 µl γ^{32}P-ATP (6000 Ci/mMole), and 1 µl T4 polynucleotide kinase (10 U/µl) were mixed, and the reaction incubated at 37°C for 30-60 minutes. Reactions were then placed at 95°C for 2 minutes and 30 ml H_2O was added. The probes were purified using a G25 microspin column (Pharmacia).

Blots were prehybridized in 10 ml 5X SSPE, 5X Denhardt's, 2% SDS, and 100 µg/ml, denatured, sonicated salmon sperm DNA at 40°C for 2 hr. The entire reaction mix of kinased oligo was then added to 10 ml fresh hybridization buffer (5X SSPE, 5X Denhardt's, 2% SDS) and hybridized at 40°C for at least 4 hours to overnight.

All washes done in 5X SSPE, 0.1 % SDS. The first wash was at 45°C for 15 minutes; the solution was then changed and the filters washed 50°C for 15 minutes. Filters were then exposed to Kodak biomax film with 2 intensifying screens at –70°C for 15 minutes to 1 hr. If necessary the filters were washed at 55°C for 15 minutes and exposed to film again. Filters were stripped by washing in boiling 0.1X SSC, 0.1% SDS for 10 minutes at least 3 times.

The two films that best captured the allele specific assay with the 2 ASOs were converted into digital images by scanning them into Adobe PhotoShop. These

images were overlaid against each other in Graphic Converter and then scored and stored in FileMaker Pro 4.0 (see Fig. 9).

In order to determine the HBM1 allele frequency in ethnically diverse populations, 672 random individuals from various ethnic groups were typed by the allele specific oligonucleotide (ASO) method. This population included 96 CEPH grandparents (primarily Caucasian), 192 Caucasian, 192 African-American, 96 Hispanic, and 96 Asian individuals. No evidence was obtained for the presence of the HBM1 polymorphism in any of these individuals. Overall, a total of 911 individuals were typed either by direct sequencing or ASO hybridization; all were homozygous GG at the site of the HBM polymorphism (Fig. 14). This information illustrates that the HBM1 allele is rare in various ethnic populations.

Thus this invention provides a rapid method of identifying individuals with the HBM1 allele. This method could be used in the area of diagnostics and screening of an individual for susceptibility to osteoporosis or other bone disorder. The assay could also be used to identify additional individuals with the HBM1 allele or the additional polymorphisms described herein.

XIII. Cellular Localization of Zmax1

A. Gene Expression in Rat tibia by non isotopic In Situ Hybridization

In situ hybridization was conducted by Pathology Associates International (PAI), Frederick, MD. This study was undertaken to determine the specific cell types that express the Zmax1 gene in rat bone with particular emphasis on areas of bone growth and remodeling. Zmax1 probes used in this study were generated from both human (HuZmax1) and mouse (MsZmax1) cDNAs, which share an 87% sequence identity. The homology of human and mouse Zmax1 with rat Zmax1 is unknown.

For example, gene expression by non-isotopic *in situ* hybridization was performed as follows, but other methods would be known to the skilled artisan. Tibias were collected from two 6 to 8 week old female Sprague Dawley rats

euthanized by carbon dioxide asphyxiation. Distal ends were removed and proximal tibias were snap frozen in OCT embedding medium with liquid nitrogen immediately following death. Tissues were stored in a –80°C freezer.

Probes for amplifying PCR products from cDNA were prepared as follows. The primers to amplify PCR products from a cDNA clone were chosen using published sequences of both human LRP5 (Genbank Accession No. ABO17498) and mouse LRP5 (Genbank Accession No. AFO64984). In order to minimize cross reactivity with other genes in the LDL receptor family, the PCR products were derived from an intracellular portion of the protein coding region. PCR was performed in a 50 µl reaction volume using cDNA clone as template. PCR reactions contained 1.5 mM $MgCl_2$, 1 unit Amplitaq, 200 µM dNTPs and 2 µM each primer. PCR cycling conditions were 94°C for 1 min., followed by 35 cycles of 94°C for 30 seconds, 55°C for 30 seconds, 72°C for 30 seconds; followed by a 5 minute extension at 72°C. The reactions were then run on a 1.5% agarose Tris-Acetate gel. DNA was eluted from the agarose, ethanol precipitated and resuspended in 10 mM Tris, pH 8.0. Gel purified PCR products were prepared for both mouse and human cDNAs and supplied to Pathology Associates International for *in situ* hybridizations.

The sequence of the human and mouse PCR primers and products were as follows:

Human Zmax 1 sense primer (HBM1253)

CCCGTGTGCTCCGCCGCCCAGTTC

Human Zmax 1 antisense primer (HBM1465)

GGCTCACGGAGCTCATCATGGACTT

Human Zmax1 PCR product

CCCGTGTGCTCCGCCGCCCAGTTCCCCTGCGCGCGGGGTCAGTGTGTGGA

CCTGCGCCTGCGCTGCGACGGCGAGGCAGACTGTCAGGACCGCTCAGAC

GAGGTGGACTGTGACGCCATCTGCCTGCCCAACCAGTTCCGGTGTGCGA
GCGGCCAGTGTGTCCTCATCAAACAGCAGTGCGACTCCTTCCCCGACTGT
ATCGACGGCTCCGACGAGCTCATGTGTGAAATCACCAAGCCGCCCTCAG
ACGACAGCCCGGCCCACAGCAGTGCCATCGGGCCCGTCATTGGCATCAT
CCTCTCTCTCTTCGTCATGGGTGGTGTCTATTTTGTGTGCCAGCGCGTGGT
GTGCCAGCGCTATGCGGGGGCCAACGGGCCCTTCCCGCACGAGTATGTC
AGCGGGACCCCGCACGTGCCCCTCAATTTCATAGCCCCGGGCGGTTCCC
AGCATGGCCCCTTCACAGGCATCGCATGCGGAAAGTCCATGATGAGCTC
CGTGAGCC

Mouse Zmax 1 Sense primer (HBM1655)

AGCGAGGCCACCATCCACAGG

Mouse Zmax 1 antisense primer (HBM1656)

TCGCTGGTCGGCATAATCAAT

Mouse Zmax1 PCR product

AGCAGAGCCACCATCCACAGGATCTCCCTGGAGACTAACAACAACGATG
TGGCTATCCCACTCACGGGTGTCAAAGAGGCCTCTGCACTGGACTTTGAT
GTGTCCAACAATCACATCTACTGGACTGATGTTAGCCTCAAGACGATCA
GCCGAGCCTTCATGAATGGGAGCTCAGTGGAGCACGTGATTGAGTTTGG
CCTCGACTACCCTGAAGGAATGGCTGTGGACTGGATGGGCAAGAACCTC
TATTGGGCGGACACAGGGACCAACAGGATTGAGGTGGCCCGGCTGGATG
GGCAGTTCCGGCAGGTGCTTGTGTGGAGAGACCTTGACAACCCCAGGTC
TCTGGCTCTGGATCCTACTAAAGGCTACATCTACTGGACTGAGTGGGGTG
GCAAGCCAAGGATTGTGCGGGCCTTCATGGATGGGACCAATTGTATGAC
ACTGGTAGACAAGGTGGGCCGGGCCAACGACCTCACCATTGATTATGCC
GACCAGCGA

Riboprobes were synthesized as follows. The PCR products were reamplified with chimeric primers designed to incorporate either a T3 promoter upstream, or a T7 promoter downstream of the reamplification products. The resulting PCR products were used as template to synthesize digoxigenin-labeled riboprobes by *in vitro* transcription (IVT). Antisense and sense riboprobes were synthesized using T7 and T3 RNA polymerases, respectively, in the presence of digoxigenin-11-UTP (Boehringer-Mannheim) using a MAXIscript IVT kit (Ambion) according to the manufacturer. The DNA was then degraded with Dnase-1, and unincorporated digoxigenin was removed by ultrafiltration. Riboprobe integrity was assessed by electrophoresis through a denaturing polyacrylamide gel. Molecular size was compared with the electrophoretic mobility of a 100–1000 base pair (bp) RNA ladder (Ambion). Probe yield and labeling was evaluated by blot immunochemistry. Riboprobes were stored in 5 µl aliquots at –80°C.

The *in situ* hybridization was performed as follows. Frozen rat bone was cut into 5 µM sections on a Jung CM3000 cryostat (Leica) and mounted on adhesive slides (Instrumedics). Sections were kept in the cryostat at –20°C until all the slides were prepared in order to prevent mRNA degradation prior to post-fixation for 15 minutes in 4% paraformaldehyde. Following post-fixation, sections were incubated with 1 ng/µl of either antisense or sense riboprobe in Pathology Associates International (PAI) customized hybridization buffer for approximately 40 hours at 58°C. Following hybridization, slides were subjected to a series of post-hybridization stringency washes to reduce nonspecific probe binding. Hybridization was visualized by immunohistochemistry with an anti-digoxigenin antibody (FAB fragment) conjugated to alkaline phosphatase. Nitroblue tetrazolium chloride/bromochloroindolyl phosphate (Boehringer-Mannheim), a precipitating alkaline phosphatase substrate, was used as the chromogen to stain hybridizing cells

purple to nearly black, depending on the degree of staining. Tissue sections were counter-stained with nuclear fast red. Assay controls included omission of the probe, omission of probe and anti-digoxigenin antibody.

Specific cell types were assessed for demonstration of hybridization with antisense probes by visualizing a purple to black cytoplasmic and/or peri-nuclear staining indicating a positive hybridization signal for mRNA. Each cell type was compared to the replicate sections, which were hybridized with the respective sense probe. Results were considered positive if staining was observed with the antisense probe and no staining or weak background with the sense probe.

The cellular localization of the hybridization signal for each of the study probes is summarized in Table 5. Hybridization for Zmax1 was primarily detected in areas of bone involved in remodeling, including the endosteum and trabecular bone within the metaphysis. Hybridization in selected bone lining cells of the periosteum and epiphysis were also observed. Positive signal was also noted in chondrocytes within the growth plate, particularly in the proliferating chondrocytes. See Figs. 10, 11 and 12 for representative photomicrographs of *in situ* hybridization results.

TABLE 5

Summary of Zmax1 *in situ* hybridization in rat tibia

PROBE	SITE	ISH SIGNAL
Hu Zmax1	Epiphysis	
	Osteoblasts	+
	Osteoclasts	–
	Growth Plate	
	resting chondrocytes	-
	proliferating chondrocytes	+
	hypertrophic chondrocytes	-
	Metaphysis	
	osteoblasts	+
	osteoclasts	+

PROBE	SITE	ISH SIGNAL
	Diaphysis	-
	Endosteum	
	osteoblasts	+
	osteoclasts	+
	Periosteum	-
MsZmax1	Epiphysis	
	Osteoblasts	+
	Osteoclasts	-
	Growth Plate	
	resting chondrocytes	-
	proliferating chondrocytes	+
	hypertrophic chondrocytes	+
	Metaphysis	
	osteoblasts	+
	osteoclasts	+
	Diaphysis	-
	Endosteum	
	osteoblasts	+
	osteoclasts	+
	Periosteum	+

Legend: "+" = hybridization signal detected "-" = no hybridization signal detected "ISH" – *In situ* hybridization

These studies confirm the positional expression of Zmax1 in cells involved in bone remodeling and bone formation. Zmax1 expression in the zone of proliferation and in the osteoblasts and osteoclasts of the proximal metaphysis, suggests that the Zmax1 gene is involved in the process of bone growth and mineralization. The activity and differentiation of osteoblasts and osteoclasts are closely coordinated during development as bone is formed and during growth as well as in adult life as bone undergoes continuous remodeling. The formation of internal bone structures and bone remodeling result from the coupling of bone resorption by activated osteoclasts with subsequent deposition of new material by osteoblasts. Zmax1 is related to the LDL receptor gene, and thus may be a receptor involved in mechanosensation and subsequent signaling in the process of bone

remodeling. Therefore, changes in the level of expression of this gene could impact on the rate of remodeling and degree of mineralization of bone.

XIV. Antisense

Antisense oligonucleotides are short synthetic nucleic acids that contain complementary base sequences to a targeted RNA. Hybridization of the RNA in living cells with the antisense oligonucleotide interferes with RNA function and ultimately blocks protein expression. Therefore, any gene for which the partial sequence is known can be targeted by an antisense oligonucleotide.

Antisense technology is becoming a widely used research tool and will play an increasingly important role in the validation and elucidation of therapeutic targets identified by genomic sequencing efforts.

Antisense technology was developed to inhibit gene expression by utilizing an oligonucleotide complementary to the mRNA that encodes the target gene. There are several possible mechanisms for the inhibitory effects of antisense oligonucleotides. Among them, degradation of mRNA by RNase H is considered to be the major mechanism of inhibition of protein function. This technique was originally used to elucidate the function of a target gene, but may also have therapeutic applications, provided it is designed carefully and properly.

An example of materials and methods for preparing antisense oligonucleotides can be performed as follows. Preliminary studies have been undertaken in collaboration with Sequiter (Natick, MA) using the antisense technology in the osteoblast-like murine cell line, MC3T3. These cells can be triggered to develop along the bone differentiation sequence. An initial proliferation period is characterized by minimal expression of differentiation markers and initial synthesis of collagenous extracellular matrix. Collagen matrix synthesis is required for subsequent induction of differentiation markers. Once the matrix synthesis begins, osteoblast marker genes are activated in a clear temporal sequence: alkaline phosphatase is induced at early times while bone sialoprotien and osteocalcin appear later in the differentiation process. This temporal sequence of gene expression is useful in monitoring the maturation and mineralization process. Matrix mineralization, which does not begin until several days after maturation has started,

involves deposition of mineral on and within collagen fibrils deep within the matrix near the cell layer-culture plate interface. The collagen fibril–associated mineral formed by cultured osteoblasts resembles that found in woven bone in vivo and therefore is used frequently as a study reagent.

MC3T3 cells were transfected with antisense oligonucleotides for the first week of the differentiation, according to the manufacturer's specifications (U.S. Patent No. 5,849,902).

The oligonucleotides designed for Zmax1 are given below:

10875: AGUACAGCUUCUUGCCAACCCAGUC

10876: UCCUCCAGGUCGAUGGUCAGCCCAU

10877: GUCUGAGUCCGAGUUCAAAUCCAGG

Fig. 13 shows the results of antisense inhibition of Zmax1 in MC3T3 cells. The three oligonucleotides shown above were transfected into MC3T3 and RNA was isolated according to standard procedures. Northern analysis clearly shows markedly lower steady state levels of the Zmax1 transcript while the control gene GAPDH remained unchanged. Thus, antisense technology using the primers described above allows for the study of the role of Zmax1 expression on bone biology.

XV. Yeast Two Hybrid

In order to identify the signaling pathway that Zmax1 participates in to modulate bone density, the yeast two hybrid protein interaction technology was utilized. This technique facilitates the identification of proteins that interact with one another by coupling tester proteins to components of a yeast transcription system (Fields and Song, 1989, *Nature* 340: 245-246; U.S. Pat. No. 5,283,173 by Fields and Song; Johnston, 1987, *Microbiol. Rev.* 51: 458-476; Keegan et al, 1986, *Science* 231: 699-704; Durfee et al, 1993, *Genes Dev.* 7: 555-569; Chien et al, 1991, *Proc. Natl. Acad. Sci USA* 88: 9578-9582; Fields et al., 1994, *Trends in Genetics* 10: 286-292; and Gyuris et al., 1993, *Cell* 75: 791-803). First a "bait" protein, the protein for which one seeks interacting proteins, is fused to the DNA binding domain of a yeast transcription factor. Second, a cDNA library is constructed that contains cDNAs fused to the transcriptional activation domain of the same yeast

transcription factor; this is termed the prey library. The bait construct and prey library are transformed into yeast cells and then mated to produce diploid cells. If the bait interacts with a specific prey from the cDNA library, the activation domain is brought into the vicinity of the promoter via this interaction. Transcription is then driven through selectable marker genes and growth on selective media indicates the presence of interacting proteins.

The amino acid sequence used in the yeast two hybrid experiments discussed herein consisted of the entire cytoplasmic domain and a portion of the transmembrane domain and is shown below (amino to carboxy orientation):

RVVCQRYAGA NGPFPHEYVS GTPHVPLNFI APGGSQHGPF TGIACGKSMM SSVSLMGGRG GVPLYDRNHV TGASSSSSSS TKATLYPPIL NPPPSPATDP SLYNMDMFYS SNIPATVRPY RPYIIRGMAP PTTPCSTDVC DSDYSASRWK ASKYYLDLNS DSDPYPPPPT PHSQYLSAED SCPPSPATER SYFHLFPPPP SPCTDSS

The last 6 amino acids of the putative transmembrane domain are indicated in bold. Putative SH3 domains are underlined. Additional amino acid sequences of 50 amino acids or greater in either the proteins encoded by the Zmax1 or HBM alleles can also be used as bait. The upper size of the polypeptide used as bait is limited only by the presence of a complete transmembrane domain (see Fig. 4), which will render the bait to be nonfunctional in a yeast two hybrid system. These additional bait proteins can be used to identify additional proteins which interact with the proteins encoded by HBM or Zmax1 in the focal adhesion signaling pathway or in other pathways in which these HBM or Zmax1 proteins may act. Once identified, methods of identifying agents which regulate the proteins in the focal adhesion signaling pathway or other pathways in which HBM acts can be performed as described herein for the HBM and Zmax1 proteins.

In order to identify cytoplasmic Zmax1 signaling pathways, the cytoplasmic domain of Zmax1 was subcloned into two bait vectors. The first vector was pDBleu, which was used to screen a brain, and Hela prey cDNA library cloned into the vector pPC86 (Clontech). The second bait vector used was pDBtrp, which was used to screen a cDNA prey library derived from the TE85 osteosarcoma cell line in

vector pOP46. Standard techniques known to those skilled in the art were used as described in Fields and Song, 1989, *Nature* 340: 245-246; U.S. Pat. No. 5,283,173 by Fields and Song; Johnston, 1987, *Microbiol. Rev.* 51: 458-476; Keegan et al., 1986, *Science* 231: 699-704; Durfee et al., 1993, *Genes Dev.* 7: 555-569; Chien et al., 1991, *Proc. Natl. Acad. Sci USA* 88: 9578-9582; Fields et al., 1994, *Trends in Genetics* 10: 286-292; and Gyuris et al., 1993, *Cell* 75: 791-803. The bait construct and prey cDNA libraries were transformed into yeast using standard procedures.

To perform the protein interaction screen, an overnight culture of the bait yeast strain was grown in 20 ml SD selective medium with 2% glucose (pDBLeu, SD -Leu medium, pDBtrp, SD –trp medium). The cultures were shaken vigorously at 30°C overnight. The cultures were diluted 1 : 10 with complete medium (YEPD with 2% glucose) and the cultures then incubated with shaking for 2 hrs at 30°C.

The frozen prey library was thawed, and the yeast cells reactivated by growing them in 150 ml YEPD medium with 2% glucose for 2 hrs at 30°C. A filter unit was sterilized with 70% ethanol and washed with sterile water to remove the ethanol. The cell densities of both bait and prey cultures were measured by determining the OD at 600 nm. An appropriate volume of yeast cells that corresponded to a cell number of 1 ml of OD 600 = 4 of each yeast strain, bait and prey (library) was placed in a 50 ml Falcon tube. The mixture was then filtered through the sterilized filter unit. The filter was then transferred onto a prewarmed YEPD agar plate with the cell side up, removing all air bubbles underneath the filter. Plates were then incubated at 30°C for 6 hrs. One filter was transferred into a 50 ml Falcon tube, and 10 ml of SD with 2% Glucose was added; cells were resuspended by vortexing for 10 sec.

The number of primary diploid cells (growth on SD -Leu, -Trp plates) versus the numbers of colony forming units growing on SD -Trp and SD -Leu plates only was then titered. Different dilutions were plated and incubated at 30°C for two days. The number of colony forming units was then counted. The number of diploid colonies (colonies on SD -Leu -Trp plates) permits the calculation of whether or not the whole library of prey constructs was mated to the yeast expressing the bait. This information is important to judge the quality of the screen.

A. Indirect selection

Resuspended cells from 5 filtermatings were then pooled and the cells sedimented by centrifugation in a 50 ml Falcon tube. Cells were then resuspended in 16 ml SD medium with 2% Glc. Two ml of this cell suspension was plated onto 8 square plates each (SD -Leu, -Trp) with sterile glass beads and selected for diploid cells by incubating at 30°C for 18 - 20 hrs.

Cells were then scraped off the square plates, the cells centrifuged and combined into one 50 ml Falcon tube. The cell pellet was then resuspended in 25 ml of SD medium with 2% glucose. The cell number was then determined by counting of an appropriate dilution (usually 1:100 to 1:1000) with a Neugebauer chamber. Approximately 5 x 10^7 diploid cells were plated onto the selective medium. The observations about the growth of the bait strain together with irrelevant prey vectors helps to determine which selective plates will have to be chosen for the library screen. Generally, all screens were plated on one square plate each with SD -Leu, -Trp, -His; SD -Leu, -Trp, His, 5 mM 3AT, and SD -Leu, -Trp, -His, -Ade is recommended.

The yeast cells were then spread homogeneously with sterile glass beads and incubated at 30°C for 4 days. The number of colony forming yeast cells was titered by plating different dilutions of the scraped cell suspension onto SD -Leu, -Trp plates. Usually, plating of 100 µl of a 10^{-3} and 10^{-4} dilution gave 100 - 1000 colonies per plate.

B. Direct selection

Five filters with the mated yeast cells were each transferred into separate 50 ml Falcon tubes and the cells resuspended with 10 ml SD medium with 2% Glc, each, followed by vortexing for 10 sec. The resuspended cells were combined and centrifuged in a Beckman centrifuge at 3000 rpm. The supernatant was discarded and the cells resuspended in 6 ml of SD medium with 2% Glc. Two ml of the suspension was spread onto each selective square plate and incubated at 30°C for 4 - 5 days.

C. Isolation of Single Colonies

Yeast cells from an isolated colony were picked with a sterile tooth pick and transferred into individual wells of a 96 well plate. The cells were resuspended in 50 µl of SD -Leu, -Trp, -His medium and incubated at 30°C for one day. The yeast cells were then stamped onto a SD -Leu, -Trp, -His plate in 96 well format and incubated at 30°C for 2 days. Yeast cells were also stamped onto a Nylon filter covering a YEPD plate and incubated at 30°C for one day. The cells on the Nylon filter were used for the analysis of the ß - Gal reporter activity.

Yeast colonies were scraped from the SD -Leu, -Trp, -His plate with a sterile tooth pick, and reconfigured, if necessary, according to the ß - Gal activity and then resuspended in 20 % glycerol. This served as a master plate for storage at -80°C.

For DNA preparation, yeast cells from the glycerol stock were stamped onto a SD -Trp plate and incubated at 30°C for 2 days. After two days of incubation, the yeast colonies were ready for colony PCR and sequencing. Standard colony PCR conditions were used to amplify inserts from preys recovered from the interaction screen. Sequencing was done using standard sequencing reactions and ABI377 (Perkin Elmer) fluorescent sequencing machines.

D. Verification of bait/prey interaction

Glycerol stocks of the prey of interest were thawed and inoculated in a 10 ml overnight culture of SD with glucose -Trp. After overnight growth, plasmid DNA preparation was performed using the BIO 101 RPM Yeast Plasmid Isolation Kit with 10 ml of culture. The culture was centrifuged and transfered to a 1.5 ml microcentrifuge tube. Yeast Lysis Matrix was then added to the pellet followed by 250 µl of Alkaline Lysis Solution. Samples were then vortexed for 5 minutes. 250 µl Neutralizing Solution was added and the sample mixed briefly. Samples were centrifuged for 2 minutes at room temperature in a microcentrifuge. The supernatant was transferred to a Spin Filter avoiding debris and Lysis Matrix. 250 µl of Glassmilk Spin Buffer was added, and the tubes inverted to mix. Samples were centrifuged for 1 min and the liquid in the Catch Tube was discarded. 500 µl of Wash Solution was added, the samples were centrifuged for 1 min, and the wash solution was discarded. The wash step was repeated once followed by a 1 min dry

centrifugation to drive the remaining liquid out of the Spin Filter. The filter was transferred to a new Catch Tube and 100 µl of sterile H_2O was added; samples were then vortexed briefly to resuspend and centrifuged for 30 seconds to collect the DNA in the bottom of the Catch Tube.

Five µl of DNA was then transformed into DH10B Electromax cells using standard procedures and glycerol stocks prepared. Miniprep DNA was prepared using the Qiagen QIAprep Spin Miniprep Kit. DNA was finally eluted with 30 µl of Qiagen EB buffer. One µl of the plasmid DNA samples was then used to transform yeast cells using standard procedures. After 2 days of growth on SD –trp media, colonies were picked and patched onto fresh media. Similarly, bait colonies were patched onto SD –Leu media. Both were grown overnight at 30°C.

For mating, cells from bait and prey patches were spread together on YAPD media and incubated at 30°C for 12 hr. This plate was then replicaplated onto an SD Agar-Leu-Trp plate and grown for 2 days at 30°C. To test the strength of interaction these plates were replicaplated onto SD Agar-Leu-Trp-His, SD Agar-Leu-Trp-His with 5 mM 3AT and 10 mM 3AT, SD Agar-Leu-Trp-His-Ade, and SD Agar-Leu-Trp-Ura media and grown for 2 days at 30°C.

E. Galacton Star β-Galactosidase Activity Assay

After streaking and replica plating positive interactors on selection plates, colonies were placed in a 96 well dish with 200 µl of SD-medium, leaving wells 1 and 96 blank. Ten microliters from the first 96 well dish was plated into another flat bottom 96 well dish containing 100 µl of SD-medium. Controls consisted of a negative control and a very weak positive control. The cell density was measured at OD_{600} (a value of 1 corresponds to $1x10^7$ cells utilizing a 96 well spectrophotometer). The OD was usually between 0.03 and 0.10. Using microplates specifically for the luminometer, 50 µl of reaction mixture were pipetted into each well. Fifty microliters of culture were then added and mixed by pipetting up and down twice. The reaction was incubated for 30 minutes at room temperature followed by measurement of Relative Light Units using a luminometer.

Table 6 lists the genes identified in the yeast two hybrid screens from the 3 prey libraries tested. Two genes, zyxin and axin, were found to interact with the

cytoplasmic domain of Zmax1 in all three screens. Three genes, alpha-actinin, TCB and S1-5 interacted in two of the three screens.

A variety of proteins found at sites of cell-cell and cell-matrix contact (focal contacts/adesion plaques) were shown to interact with the cytoplasmic domain of Zmax1. These include alpha-actinin, Trio, Pinch-like protein, and Zyxin. PINCH is a LIM domain-containing protein that is known to interact with integrin-linked kinase, an early signaler in integrin and growth factor signaling pathways. The finding of a closely related gene in the yeast two hybrid screen raises the possibility of a novel pathway linked to integrin signaling from extracellular matrix signals. Trio, also known to localize to focal adhesions, is thought to play a key role in coordinating cell-matrix interactions and cytoskeletal rearrangements involved in cell movement. Zyxin, another LIM domain-containing protein, is also localized to adhesion plaques and is thought to be involved in reorganization of the cytoskeleton when triggers are transmitted via integrin signaling pathways. Zyxin also interacts with alpha actinin, which we identified as interacting with Zmax1. Other LIM domain containing proteins identified include the human homologue of mouse ajuba, LIMD1, and a novel LIMD1-like protein.

Axin was also identified from the two hybrid experiments. This protein is involved in inhibition of the Wnt signaling pathway and interacts with the tumor suppressor APC. There is a link here with the focal adhesion signaling described above: one common step in the two pathways involves inhibition of glycogen synthase kinase 3, which in turn results in the activation of ß-catenin/Lef-1 and AP-1 transcription factors. Axin/APC are involved in this as well as integrin linked kinase. The Wnt pathway has a role in determining cell fates during embryogenesis. If inappropriately activated, the Wnt pathway may also lead to cancer. The Wnt pathway also seems to have a role in cytoskeletal rearrangements. A model depicting Zmax1 involvement in focal adhesion signaling is depicted in Fig. 15.

This data coupled with other studies suggest that integrin signaling pathways have a role in cellular responses to mechanical stress and adhesion. This provides an attractive model for the mechanism of action of Zmax1 in bone biology. It is possible that Zmax1 is involved in sensing either mechanical stress directly or

binding a molecule in the extracellular matrix that is related to mechanical sensation. Signaling through subsequent pathways may be involved in bone remodeling due to effects on cell morphology, cell adhesion, migration, proliferation, differentiation, and apoptosis in bone cells.

Table 6: Yeast Two Hybrid Results

Gene Symbol	Gene	Genbank Accession #	NT SEQ ID NO:	AA SEQ ID NO:
ACTN1	alpha-actinin	NM_001102	63	
AES	amino-terminal enhancer of	NM_001130.3	64	
AIP4	atrophin-1 interacting protein	AF038564.1	65	
Novel	Ajuba		66	
AXIN	Wnt signaling	AF009674.1	67	
CDC23	cell division cycle 23, yeast, homolog	NM_004661.1	68	
HSM800944	Similar to TRIO	AL117435.1	69	
HSM800936		AL117427.1	70	
Novel	Similar to LIM domains containing protein 1		71	
DEEPEST	mitotic spindle coiled-coil related protein	NM_006461.1	72	
ECM1	extracellular matrix protein 1	U65932.1	73	
EF1A	elongation factor 1-alpha	X16869.1	74	
FN	fibronectin	X02761.1	75	
HOXB13	homeodomain protein	U81599.1	76	
Novel	Glu-Lys Rich protein		77	
LIMD1	LIM domains containing 1	NM_014240.1	78	
Novel	PINCH-like		79	
RANBPM	centrosomal protein	NM_005493.1	80	
S1-5	extracellular protein	U03877.1	81	
TCB	gene encoding cytosolic thyroid hormone-binding	M26252.1	82	
TID	tumorous imaginal discs	NM_005147.1	83	
ZYX	Zyxin	NM_003461.1	84	
TRIO	GTPase	U42390.1	85	
HUMPITPB	phosphatidylinositol transfer protein	D30037.1	86	
ACTN1	alpha-actinin	NP_001093.1		87

Gene Symbol	Gene	Genbank Accession #	NT SEQ ID NO:	AA SEQ ID NO:
AES	amino-terminal enhancer of	NP_001121.2		88
AIP4	atrophin-1 interacting protein	AAC04845.1		89
Novel	Ajuba			90
AXIN	Wnt signalling	AAC51624.1		91
CDC23	cell division cycle 23, yeast homolog	NP_004652.1		92
Novel	Similar to TRIO CAB55923.1			93
Novel	Similar to LIM domains containing protein 1			94
DEEPEST	mitotic spindle coiled-coil related protein	NP_006452.1		95
ECM1	extracellular matrix protein 1	AAB05933.1		96
EF1A	elongation factor 1-alpha	CAA34756.1		97
FN	fibronectin	CAA26536.1		98
Novel	Glu-Lys rich protein			99
HOXB13	homeodomain protein B13	AAB39863.1		100
LIMD1	LIM domains containing 1	NP_055055.1		101
Novel	PINCH-like			102
RANBPM	centrosomal protein	NP_005484.1		103
S1-5	extracellular protein	AAA65590.1		104
TCB	cytosolic thyroid hormone-binding protein	AAA36672.1		105
TID	tumorous imaginal discs	NP_005138.1		106
ZYX	Zyxin	NP_003452.1		107
TRIO	GTPase	AAC34245.1		108
PTDINSTP	phosphatidylinositol transfer protein beta isoform	P48739		109

In light of the model depicted in Fig. 15 and the results shown in Table 6, another aspect contemplated by the invention would be to regulate bone density and bone mass disorders by the regulating focal adhesion signaling. The regulation can occur by regulating the DNA, mRNA transcript or protein encoded by any of the members involved in the focal adhesion signaling pathway as identified by the yeast two hybrid system.

Also contemplated are the novel nucleic acids and proteins identified by the HBM yeast two hybrid system. These include but are not limited to SEQ ID NO: 66

(Ajuba), SEQ ID NO: 71 (a gene similar to a gene encoding LIM domains containing protein 1), SEQ ID NO: 77 (Glu-Lys Rich protein), SEQ ID NO: 79 (PINCH-like gene), SEQ ID NO: 90 (Ajuba protein), SEQ ID NO: 93 (protein similar to TRIO), SEQ ID NO: 94 (), SEQ ID NO: 99 (Glu-Lys rich protein) and SEQ ID NO: 102 (PINCH-like protein).

XVI. Potential Function

The protein encoded by Zmax1 is related to the Low Density Lipoprotein receptor (LDL receptor). *See*, Goldstein et al, *Ann. Rev. Cell Biology*, 1:1-39 (1985); Brown et al, *Science*, 232:34-47 (1986). The LDL receptor is responsible for uptake of low density lipoprotein, a lipid-protein aggregate that includes cholesterol. Individuals with a defect in the LDL receptor are deficient in cholesterol removal and tend to develop artherosclerosis. In addition, cells with a defective LDL receptor show increased production of cholesterol, in part because of altered feedback regulation of cholesterol synthetic enzymes and in part because of increased transcription of the genes for these enzymes. In some cell types, cholesterol is a precursor for the formation of steroid hormones.

Thus, the LDL receptor may, directly or indirectly, function as a signal transduction protein and may regulate gene expression. Because Zmax1 is related to the LDL receptor, this protein may also be involved in signaling between cells in a way that affects bone remodeling.

The glycine 171 amino acid is likely to be important for the function of Zmax1 because this amino acid is also found in the mouse homologue of Zmax1. The closely related LRP6 protein also contains glycine at the corresponding position (Brown et al, *Biochemical and Biophysical Research Comm.*, 248:879-888 (1988)). Amino acids that are important in a protein's structure or function tend to be conserved between species, because natural selection prevents mutations with altered amino acids at important positions from arising.

In addition, the extracellular domain of Zmax1 contains four repeats consisting of five YWTD motifs followed by an EFG motif. This 5YWTD+EGF repeat is likely to form a distinct folded protein domain, as this repeat is also found in the LDL receptor and other LDL receptor-related proteins. The first three

5YWTD+EGF repeats are very similar in their structure, while the fourth is highly divergent. Glycine 171 occurs in the central YWTD motif of the first 5YWTD+EGF repeat in Zmax1. The other two similar 5YWTD+EGF repeats of Zmax1 also contain glycine at the corresponding position, as does the 5YWTD+EGF repeat in the LDL receptor protein. However, only 17.6% of the amino acids are identical among the first three 5YWTD+EGF repeats in Zmax1 and the single repeat in the LDL receptor. These observations indicate that glycine 171 is essential to the function of this repeat, and mutation of glycine 171 causes a functional alteration of Zmax1. The cDNA and peptide sequences are shown in Figs. 6A-6E. The critical base at nucleotide position 582 is indicated in bold and is underlined.

Northern blot analysis (Figs. 7A-B) reveals that Zmax1 is expressed in human bone tissue as well as numerous other tissues. A multiple-tissue Northern blot (Clontech, Palo Alto, CA) was probed with exons from Zmax1. As shown in Fig. 7A, the 5.5 kb Zmax1 transcript was highly expressed in heart, kidney, lung, liver and pancreas and is expressed at lower levels in skeletal muscle and brain. A second northern blot, shown in Fig. 7B, confirmed the transcript size at 5.5 kb, and indicated that Zmax1 is expressed in bone, bone marrow, calvaria and human osteoblastic cell lines.

Taken together, these results coupled with the yeast two hybrid results indicate that the HBM polymorphism in the Zmax1 gene is responsible for the HBM phenotype, and that the Zmax1 gene is important in bone development. In addition, because mutation of Zmax1 can alter bone mineralization and development, it is likely that molecules that bind to Zmax1 may usefully alter bone development. Such molecules may include, for example, small molecules, proteins, RNA aptamers, peptide aptamers, and the like.

XVII. Preparation of Nucleic Acids, Vectors, Transformations and Host Cells

Large amounts of the nucleic acids of the present invention may be produced by replication in a suitable host cell. Natural or synthetic nucleic acid fragments coding for a desired fragment will be incorporated into recombinant nucleic acid constructs, usually DNA constructs, capable of introduction into and replication in a

prokaryotic or eukaryotic cell. Usually the nucleic acid constructs will be suitable for replication in a unicellular host, such as yeast or bacteria, but may also be intended for introduction to (with and without integration within the genome) cultured mammalian or plant or other eukaryotic cell lines. The purification of nucleic acids produced by the methods of the present invention is described, for example, in Sambrook et al, *Molecular Cloning. A Laboratory Manual*, 2nd Ed. (Cold Spring Harbor Laboratory, Cold Spring Harbor, NY (1989) or Ausubel et al, *Current Protocols in Molecular Biology*, J. Wiley and Sons, NY (1992).

The nucleic acids of the present invention may also be produced by chemical synthesis, e.g., by the phosphoramidite method described by Beaucage et al, *Tetra. Letts.*, 22:1859-1862 (1981) or the triester method according to Matteucci,et al, J. *Am. Chem. Soc.*, 103:3185 (1981), and may be performed on commercial, automated oligonucleotide synthesizers. A double-stranded fragment may be obtained from the single-stranded product of chemical synthesis either by synthesizing the complementary strand and annealing the strands together under appropriate conditions or by adding the complementary strand using DNA polymerase with an appropriate primer sequence.

Nucleic acid constructs prepared for introduction into a prokaryotic or eukaryotic host may comprise a replication system recognized by the host, including the intended nucleic acid fragment encoding the desired protein, and will preferably also include transcription and translational initiation regulatory sequences operably linked to the protein encoding segment. Expression vectors may include, for example, an origin of replication or autonomously replicating sequence (ARS) and expression control sequences, a promoter, an enhancer and necessary processing information sites, such as ribosome-binding sites, RNA splice sites, polyadenylation sites, transcriptional terminator sequences, and mRNA stabilizing sequences. Secretion signals may also be included where appropriate, whether from a native HBM or Zmax1 protein or from other receptors or from secreted proteins of the same or related species, which allow the protein to cross and/or lodge in cell membranes, and thus attain its functional topology, or be secreted from the cell. Such vectors may be prepared by means of standard recombinant techniques well

known in the art and discussed, for example, in Sambrook et al, *Molecular Cloning. A Laboratory Manual*, 2nd Ed. (Cold Spring Harbor Laboratory, Cold Spring Harbor, NY (1989) or Ausubel et al, *Current Protocols in Molecular Biology*, J. Wiley and Sons, NY (1992).

An appropriate promoter and other necessary vector sequences will be selected so as to be functional in the host, and may include, when appropriate, those naturally associated with Zmax1 or HBM genes. Examples of workable combinations of cell lines and expression vectors are described in Sambrook et al, *Molecular Cloning. A Laboratory Manual*, 2nd Ed. (Cold Spring Harbor Laboratory, Cold Spring Harbor, NY (1989) or Ausubel et al, *Current Protocols in Molecular Biology*, J. Wiley and Sons, NY (1992). Many useful vectors are known in the art and may be obtained from such vendors as Stratagene, New England BioLabs, Promega Biotech, and others. Promoters such as the trp, lac and phage promoters, tRNA promoters and glycolytic enzyme promoters may be used in prokaryotic hosts. Useful yeast promoters include promoter regions for metallothionein, 3-phosphoglycerate kinase or other glycolytic enzymes such as enolase or glyceraldehyde-3-phosphate dehydrogenase, enzymes responsible for maltose and galactose utilization, and others. Vectors and promoters suitable for use in yeast expression are further described in EP 73,675A. Appropriate non-native mammalian promoters might include the early and late promoters from SV40 (Fiers et al, *Nature*, 273:113 (1978)) or promoters derived from murine Moloney leukemia virus, mouse tumor virus, avian sarcoma viruses, adenovirus II, bovine papilloma virus or polyoma. In addition, the construct may be joined to an amplifiable gene (e.g., DHFR) so that multiple copies of the gene may be made. For appropriate enhancer and other expression control sequences, see also *Enhancers and Eukaryotic Gene Expression*, Cold Spring Harbor Press, Cold Spring Harbor, NY (1983).

While such expression vectors may replicate autonomously, they may also replicate by being inserted into the genome of the host cell, by methods well known in the art.

Expression and cloning vectors will likely contain a selectable marker, a gene encoding a protein necessary for survival or growth of a host cell transformed with the vector. The presence of this gene ensures growth of only those host cells which express the inserts. Typical selection genes encode proteins that a) confer resistance to antibiotics or other toxic substances, e.g. ampicillin, neomycin, methotrexate, etc.; b) complement auxotrophic deficiencies, or c) supply critical nutrients not available from complex media, e.g., the gene encoding D-alanine racemase for Bacilli. The choice of the proper selectable marker will depend on the host cell, and appropriate markers for different hosts are well known in the art.

The vectors containing the nucleic acids of interest can be transcribed *in vitro*, and the resulting RNA introduced into the host cell by well-known methods, e.g., by injection (see, Kubo et al, *FEBS Letts.* 241:119 (1988)), or the vectors can be introduced directly into host cells by methods well known in the art, which vary depending on the type of cellular host, including electroporation; transfection employing calcium chloride, rubidium chloride, calcium phosphate, DEAE-dextran, or other substances; microprojectile bombardment; lipofection; infection (where the vector is an infectious agent, such as a retroviral genome); and other methods. See generally, Sambrook et al., 1989 and Ausubel et al., 1992. The introduction of the nucleic acids into the host cell by any method known in the art, including those described above, will be referred to herein as "transformation." The cells into which have been introduced nucleic acids described above are meant to also include the progeny of such cells.

Large quantities of the nucleic acids and proteins of the present invention may be prepared by expressing the Zmax1 or HBM nucleic acids or portions thereof in vectors or other expression vehicles in compatible prokaryotic or eukaryotic host cells. The most commonly used prokaryotic hosts are strains of *Escherichia coli*, although other prokaryotes, such as *Bacillus subtilis* or *Pseudomonas* may also be used.

Mammalian or other eukaryotic host cells, such as those of yeast, filamentous fungi, plant, insect, or amphibian or avian species, may also be useful for production of the proteins of the present invention. Propagation of mammalian

cells in culture is per se well known. See, Jakoby and Pastan (eds.), *Cell Culture. Methods in Enzymology*, volume 58, Academic Press, Inc., Harcourt Brace Jovanovich, NY, (1979)). Examples of commonly used mammalian host cell lines are VERO and HeLa cells, Chinese hamster ovary (CHO) cells, and WI38, BHK, and COS cell lines, although it will be appreciated by the skilled practitioner that other cell lines may be appropriate, e.g., to provide higher expression desirable glycosylation patterns, or other features.

Clones are selected by using markers depending on the mode of the vector construction. The marker may be on the same or a different DNA molecule, preferably the same DNA molecule. In prokaryotic hosts, the transformant may be selected, e.g., by resistance to ampicillin, tetracycline or other antibiotics. Production of a particular product based on temperature sensitivity may also serve as an appropriate marker.

Prokaryotic or eukaryotic cells transformed with the nucleic acids of the present invention will be useful not only for the production of the nucleic acids and proteins of the present invention, but also, for example, in studying the characteristics of Zmax1 or HBM proteins.

Antisense nucleic acid sequences are useful in preventing or diminishing the expression of Zmax1 or HBM, as will be appreciated by one skilled in the art. For example, nucleic acid vectors containing all or a portion of the Zmax1 or HBM gene or other sequences from the Zmax1 or HBM region may be placed under the control of a promoter in an antisense orientation and introduced into a cell. Expression of such an antisense construct within a cell will interfere with Zmax1 or HBM transcription and/or translation and/or replication.

The probes and primers based on the Zmax1 and HBM gene sequences disclosed herein are used to identify homologous Zmax1 and HBM gene sequences and proteins in other species. These Zmax1 and HBM gene sequences and proteins are used in the diagnostic/prognostic, therapeutic and drug screening methods described herein for the species from which they have been isolated.

XVIII. Protein Expression and Purification

Expression and purification of the HBM protein of the invention can be performed essentially as outlined below. To facilitate the cloning, expression and purification of membrane and secreted protein from the HBM gene, a gene expression system, such as the pET System (Novagen), for cloning and expression of recombinant proteins in *E. coli* was selected. Also, a DNA sequence encoding a peptide tag, the His-Tap, was fused to the 3' end of DNA sequences of interest to facilitate purification of the recombinant protein products. The 3' end was selected for fusion to avoid alteration of any 5' terminal signal sequence.

Nucleic acids chosen, for example, from the nucleic acids set forth in SEQ ID NOS: 1, 3 and 5-11 for cloning HBM were prepared by polymerase chain reaction (PCR). Synthetic oligonucleotide primers specific for the 5' and 3' ends of the HBM nucleotide sequence were designed and purchased from Life Technologies (Gaithersburg, MD). All forward primers (specific for the 5' end of the sequence) were designed to include an NcoI cloning site at the 5' terminus. These primers were designed to permit initiation of protein translation at the methionine residue encoded within the NcoI site followed by a valine residue and the protein encoded by the HBM DNA sequence. All reverse primers (specific for the 3' end of the sequence) included an EcoRI site at the 5' terminus to permit cloning of the HBM sequence into the reading frame of the pET-28b. The pET-28b vector provided a sequence encoding an additional 20 carboxyl-terminal amino acids including six histidine residues (at the C-terminus), which comprised the histidine affinity tag.

Genomic DNA prepared from the HBM gene was used as the source of template DNA for PCR amplification (Ausubel et al, *Current Protocols in Molecular Biology*, John Wiley & Sons (1994)). To amplify a DNA sequence containing the HBM nucleotide sequence, genomic DNA (50 ng) was introduced into a reaction vial containing 2 mM $MgCl_2$, 1 μM synthetic oligonucleotide primers (forward and reverse primers) complementary to and flanking a defined HBM, 0.2 mM of each of deoxynucleotide triphosphate, dATP, dGTP, dCTP, dTTP and 2.5 units of heat stable DNA polymerase (Amplitaq, Roche Molecular Systems, Inc., Branchburg, NJ) in a final volume of 100 microliters.

Upon completion of thermal cycling reactions, each sample of amplified DNA was purified using the Qiaquick Spin PCR purification kit (Qiagen, Gaithersburg, MD). All amplified DNA samples were subjected to digestion with the restriction endonucleases, e.g., NcoI and EcoRI (New England BioLabs, Beverly, MA) (Ausubel et al, *Current Protocols in Molecular Biology*, John Wiley & Sons, Inc. (1994)). DNA samples were then subjected to electrophoresis on 1.0% NuSeive (FMC BioProducts, Rockland, ME) agarose gels. DNA was visualized by exposure to ethidium bromide and long wave UV irradiation. DNA contained in slices isolated from the agarose gel was purified using the Bio 101 GeneClean Kit protocol (Bio 101, Vista, CA).

The pET-28b vector was prepared for cloning by digestion with restriction endonucleases, e.g., NcoI and EcoRI (New England BioLabs, Beverly, MA) (Ausubel et al, *Current Protocols in Molecular Biology*, John Wiley & Sons, Inc. (1994)). The pET-28a vector, which encodes the histidine affinity tag that can be fused to the 5' end of an inserted gene, was prepared by digestion with appropriate restriction endonucleases.

Following digestion, DNA inserts were cloned (Ausubel et al, *Current Protocols in Molecular Biology*, John Wiley & Sons, Inc. (1994)) into the previously digested pET-28b expression vector. Products of the ligation reaction were then used to transform the BL21 strain of *E. coli* (Ausubel et al, *Current Protocols in Molecular Biology*, John Wiley & Sons, Inc. (1994)) as described below.

Competent bacteria, *E. coli* strain BL21 or *E. coli* strain BL21 (DE3), were transformed with recombinant pET expression plasmids carrying the cloned HBM sequence according to standard methods (Ausubel et al, *Current Protocols in Molecular Biology*, John Wiley & Sons, Inc. (1994)). Briefly, 1 µl of ligation reaction was mixed with 50 µl of electrocompetent cells and subjected to a high voltage pulse, after which samples were incubated in 0.45 ml SOC medium (0.5% yeast extract, 2.0% tryptone, 10 mM NaCl, 2.5 mM KCl, 10 mM $MgCl_2$, 10 mM $MgSO_4$ and 20 mM glucose) at 37°C with shaking for 1 hour. Samples were then spread on LB agar plates containing 25 µg/ml kanamycin sulfate for growth

overnight. Transformed colonies of BL21 were then picked and analyzed to evaluate cloned inserts, as described below.

Individual BL21 clones transformed with recombinant pET-28b HBM nucleotide sequences were analyzed by PCR amplification of the cloned inserts using the same forward and reverse primers specific for the HBM sequences that were used in the original PCR amplification cloning reactions. Successful amplification verifies the integration of the HBM sequence in the expression vector (Ausubel et al, *Current Protocols in Molecular Biology*, John Wiley & Sons, Inc. (1994)).

Individual clones of recombinant pET-28b vectors carrying properly cloned HBM nucleotide sequences were picked and incubated in 5 ml of LB broth plus 25 μg/ml kanamycin sulfate overnight. The following day plasmid DNA was isolated and purified using the Qiagen plasmid purification protocol (Qiagen Inc., Chatsworth, CA).

The pET vector can be propagated in any *E. coli* K-12 strain, e.g., HMS174, HB101, JM109, DH5 and the like, for purposes of cloning or plasmid preparation. Hosts for expression include *E. coli* strains containing a chromosomal copy of the gene for T7 RNA polymerase. These hosts were lysogens of bacteriophage DE3, a lambda derivative that carries the lacI gene, the lacUV5 promoter and the gene for T7 RNA polymerase. T7 RNA polymerase was induced by addition of isopropyl-β-D-thiogalactoside (IPTG), and the T7 RNA polymerase transcribes any target plasmid containing a functional T7 promoter, such as pET-28b, carrying its gene of interest. Strains include, for example, BL21(DE3) (Studier et al, *Meth. Enzymol.*, 185:60-89 (1990)).

To express the recombinant HBM sequence, 50 ng of plasmid DNA are isolated as described above to transform competent BL21(DE3) bacteria as described above (provided by Novagen as part of the pET expression kit). The lacZ gene (β-galactosidase) is expressed in the pET-System as described for the HBM recombinant constructions. Transformed cells were cultured in SOC medium for 1 hour, and the culture was then plated on LB plates containing 25 μg/ml kanamycin sulfate. The following day, the bacterial colonies were pooled and grown in LB

medium containing kanamycin sulfate (25 μg/ml) to an optical density at 600 nM of 0.5 to 1.0 O.D. units, at which point 1 mM IPTG was added to the culture for 3 hours to induce gene expression of the HBM recombinant DNA constructions.

After induction of gene expression with IPTG, bacteria were collected by centrifugation in a Sorvall RC-3B centrifuge at 3500 x g for 15 minutes at 4°C. Pellets were resuspended in 50 ml of cold mM Tris-HCl, pH 8.0, 0.1 M NaCl and 0.1 mM EDTA (STE buffer). Cells were then centrifuged at 2000 x g for 20 minutes at 4°C. Wet pellets were weighed and frozen at -80°C until ready for protein purification.

A variety of methodologies known in the art can be used to purify the isolated proteins (Coligan et al, *Current Protocols in Protein Science,* John Wiley & Sons (1995)). For example, the frozen cells can be thawed, resuspended in buffer and ruptured by several passages through a small volume microfluidizer (Model M-110S, Microfluidics International Corp., Newton, MA). The resultant homogenate is centrifuged to yield a clear supernatant (crude extract) and, following filtration, the crude extract is fractioned over columns. Fractions are monitored by absorbance at OD_{280} nm and peak fractions may be analyzed by SDS-PAGE.

The concentrations of purified protein preparations are quantified spectrophotometrically using absorbance coefficients calculated from amino acid content (Perkins, *Eur. J. Biochem.*, 157:169-180 (1986)). Protein concentrations are also measured by the method of Bradford, *Anal. Biochem.*, 72:248-254 (1976) and Lowry et al, *J. Biol. Chem.*, 193:265-275 (1951) using bovine serum albumin as a standard.

SDS-polyacrylamide gels of various concentrations were purchased from BioRad (Hercules, CA), and stained with Coomassie blue. Molecular weight markers may include rabbit skeletal muscle myosin (200 kDa), *E. coli* β-galactosidase (116 kDa), rabbit muscle phosphorylase B (97.4 kDa), bovine serum albumin (66.2 kDa), ovalbumin (45 kDa), bovine carbonic anyhdrase (31 kDa), soybean trypsin inhibitor (21.5 kDa), egg white lysozyme (14.4 kDa) and bovine aprotinin (6.5 kDa).

Once a sufficient quantity of the desired protein has been obtained, it may be used for various purposes. A typical use is the production of antibodies specific for binding. These antibodies may be either polyclonal or monoclonal, and may be produced by *in vitro* or *in vivo* techniques well known in the art. Monoclonal antibodies to epitopes of any of the peptides identified and isolated as described can be prepared from murine hybridomas (Kohler, *Nature*, 256:495 (1975)). In summary, a mouse is inoculated with a few micrograms of HBM protein over a period of two weeks. The mouse is then sacrificed. The cells that produce antibodies are then removed from the mouse's spleen. The spleen cells are then fused with polyethylene glycol with mouse myeloma cells. The successfully fused cells are diluted in a microtiter plate and growth of the culture is continued. The amount of antibody per well is measured by immunoassay methods such as ELISA (Engvall, *Meth. Enzymol.*, 70:419 (1980)). Clones producing antibody can be expanded and further propagated to produce HBM antibodies. Other suitable techniques involve *in vitro* exposure of lymphocytes to the antigenic polypeptides, or alternatively, to selection of libraries of antibodies in phage or similar vectors. See Huse et al, *Science,* 246:1275-1281 (1989). For additional information on antibody production see Davis et al, *Basic Methods in Molecular Biology*, Elsevier, NY, Section 21-2 (1989).

XIX. Methods of Use: Gene Therapy

In recent years, significant technological advances have been made in the area of gene therapy for both genetic and acquired diseases. (Kay et al, *Proc. Natl. Acad. Sci. USA*, 94:12744-12746 (1997)) Gene therapy can be defined as the deliberate transfer of DNA for therapeutic purposes. Improvement in gene transfer methods has allowed for development of gene therapy protocols for the treatment of diverse types of diseases. Gene therapy has also taken advantage of recent advances in the identification of new therapeutic genes, improvement in both viral and nonviral gene delivery systems, better understanding of gene regulation, and improvement in cell isolation and transplantation.

The preceding experiments identify the HBM gene as a dominant mutation conferring elevated bone mass. The fact that this mutation is dominant indicates that

expression of the HBM protein causes elevated bone mass. Older individuals carrying the HBM gene, and, therefore expressing the HBM protein, do not suffer from osteoporosis. These individuals are equivalent to individuals being treated with the HBM protein. These observations are a strong experimental indication that therapeutic treatment with the HBM protein prevents osteoporosis. The bone mass elevating activity of the HBM gene is termed "HBM function."

Therefore, according to the present invention, a method is also provided of supplying HBM function to mesenchymal stem cells (Onyia et al, *J. Bone Miner. Res.*, 13:20-30 (1998); Ko et al, *Cancer Res.*, 56:4614-4619 (1996)). Supplying such a function provides protection against osteoporosis. The HBM gene or a part of the gene may be introduced into the cell in a vector such that the gene remains extrachromosomal. In such a situation, the gene will be expressed by the cell from the extrachromosomal location.

Vectors for introduction of genes both for recombination and for extrachromosomal maintenance are known in the art, and any suitable vector may be used. Methods for introducing DNA into cells such as electroporation, calcium phosphate co-precipitation, and viral transduction are known in the art, and the choice of method is within the competence of one skilled in the art (Robbins, Ed., *Gene Therapy Protocols*, Human Press, NJ (1997)). Cells transformed with the HBM gene can be used as model systems to study osteoporosis and drug treatments that promote bone growth.

As generally discussed above, the HBM gene or fragment, where applicable, may be used in gene therapy methods in order to increase the amount of the expression products of such genes in mesenchymal stem cells. It may be useful also to increase the level of expression of a given HBM protein, or a fragment thereof, even in those cells in which the wild type gene is expressed normally. Gene therapy would be carried out according to generally accepted methods as described by, for example, Friedman, *Therapy for Genetic Diseases*, Friedman, Ed., Oxford University Press, pages 105-121 (1991).

A virus or plasmid vector containing a copy of the HBM gene linked to expression control elements and capable of replicating inside mesenchymal stem

cells, is prepared. Suitable vectors are known and described, for example, in U.S. Patent No. 5,252,479 and WO 93/07282, the disclosures of which are incorporated by reference herein in their entirety. The vector is then injected into the patient, either locally into the bone marrow or systemically (in order to reach any mesenchymal stem cells located at other sites, i.e., in the blood). If the transfected gene is not permanently incorporated into the genome of each of the targeted cells, the treatment may have to be repeated periodically.

Gene transfer systems known in the art may be useful in the practice of the gene therapy methods of the present invention. These include viral and non-viral transfer methods. A number of viruses have been used as gene transfer vectors, including polyoma, i.e., SV40 (Madzak et al, *J. Gen. Virol.*, 73:1533-1536 (1992)), adenovirus (Berkner, *Curr. Top. Microbiol. Immunol.*, 158:39-61 (1992); Berkner et al, *Bio Techniques*, 6:616-629 (1988); Gorziglia et al, *J. Virol.*, 66:4407-4412 (1992); Quantin et al, *Proc. Natl. Acad. Sci. USA*, 89:2581-2584 (1992); Rosenfeld et al, *Cell*, 68:143-155 (1992); Wilkinson et al, *Nucl. Acids Res.*, 20:2233-2239 (1992); Stratford-Perricaudet et al, *Hum. Gene Ther.*, 1:241-256 (1990)), vaccinia virus (Mackett et al, *Biotechnology*, 24:495-499 (1992)), adeno-associated virus (Muzyczka, *Curr. Top. Microbiol. Immunol.*, 158:91-123 (1992); Ohi et al, *Gene*, 89:279-282 (1990)), herpes viruses including HSV and EBV (Margolskee, *Curr. Top. Microbiol. Immunol.*, 158:67-90 (1992); Johnson et al, *J. Virol.*, 66:2952-2965 (1992); Fink et al, *Hum. Gene Ther.*, 3:11-19 (1992); Breakfield et al, *Mol. Neurobiol.*, 1:337-371 (1987;) Fresse et al, *Biochem. Pharmacol.*, 40:2189-2199 (1990)), and retroviruses of avian (Brandyopadhyay et al, *Mol. Cell Biol.*, 4:749-754 (1984); Petropouplos et al, *J. Virol.*, 66:3391-3397 (1992)), murine (Miller, *Curr. Top. Microbiol. Immunol.*, 158:1-24 (1992); Miller et al, *Mol. Cell Biol.*, 5:431-437 (1985); Sorge et al, *Mol. Cell Biol.*, 4:1730-1737 (1984); Mann et al, *J. Virol.*, 54:401-407 (1985)), and human origin (Page et al, *J. Virol.*, 64:5370-5276 (1990); Buchschalcher et al, *J. Virol.*, 66:2731-2739 (1992)). Most human gene therapy protocols have been based on disabled murine retroviruses.

Non-viral gene transfer methods known in the art include chemical techniques such as calcium phosphate coprecipitation (Graham et al, *Virology*,

52:456-467 (1973); Pellicer et al, *Science*, 209:1414-1422 (1980)), mechanical techniques, for example microinjection (Anderson et al, *Proc. Natl. Acad. Sci. USA*, 77:5399-5403 (1980); Gordon et al, *Proc. Natl. Acad. Sci. USA*, 77:7380-7384 (1980); Brinster et al, *Cell*, 27:223-231 (1981); Constantini et al, *Nature*, 294:92-94 (1981)), membrane fusion-mediated transfer via liposomes (Felgner et al, *Proc. Natl. Acad. Sci. USA*, 84:7413-7417 (1987); Wang et al, *Biochemistry*, 28:9508-9514 (1989); Kaneda et al, *J. Biol. Chem.*, 264:12126-12129 (1989); Stewart et al, *Hum. Gene Ther.*, 3:267-275 (1992); Nabel et al, *Science*, 249:1285-1288 (1990); Lim et al, *Circulation*, 83:2007-2011 (1992)), and direct DNA uptake and receptor-mediated DNA transfer (Wolff et al, *Science*, 247:1465-1468 (1990); Wu et al, *BioTechniques*, 11:474-485 (1991); Zenke et al, *Proc. Natl. Acad. Sci. USA*, 87:3655-3659 (1990); Wu et al, *J. Biol. Chem.*, 264:16985-16987 (1989); Wolff et al, *BioTechniques*, 11:474-485 (1991); Wagner et al, 1990; Wagner et al, *Proc. Natl. Acad. Sci. USA*, 88:4255-4259 (1991); Cotten et al, *Proc. Natl. Acad. Sci. USA*, 87:4033-4037 (1990); Curiel et al, *Proc. Natl. Acad. Sci. USA*, 88:8850-8854 (1991); Curiel et al, *Hum. Gene Ther.*, 3:147-154 (1991)). Viral-mediated gene transfer can be combined with direct *in vivo* vectors to the mesenchymal stem cells and not into the surrounding cells (Romano et al, *In Vivo*, 12(1):59-67 (1998); Gonez et al, *Hum. Mol. Genetics*, 7(12):1913-9 (1998)). Alternatively, the retroviral vector producer cell line can be injected into the bone marrow (Culver et al, *Science*, 256:1550-1552 (1992)). Injection of producer cells would then provide a continuous source of vector particles. This technique has been approved for use in humans with inoperable brain tumors.

In an approach which combines biological and physical gene transfer methods, plasmid DNA of any size is combined with a polylysine-conjugated antibody specific to the adenovirus hexon protein, and the resulting complex is bound to an adenovirus vector. The trimolecular complex is then used to infect cells. The adenovirus vector permits efficient binding, internalization, and degradation of the endosome before the coupled DNA is damaged.

Liposome/DNA complexes have been shown to be capable of mediating direct *in vivo* gene transfer. While in standard liposome preparations the gene

transfer process is non-specific, localized *in vivo* uptake and expression have been reported in tumor deposits, for example, following direct *in situ* administration (Nabel, *Hum. Gene Ther.*, 3:399-410 (1992)).

XX. Methods of Use: Transformed Hosts, Development of Pharmaceuticals and Research Tools

Cells and animals that carry the HBM gene can be used as model systems to study and test for substances that have potential as therapeutic agents (Onyia et al, *J. Bone Miner. Res.*, 13:20-30 (1998); Broder et al, *Bone*, 21:225-235 (1997)). The cells are typically cultured mesenchymal stem cells. These may be isolated from individuals with somatic or germline HBM genes. Alternatively, the cell line can be engineered to carry the HBM gene, as described above. After a test substance is applied to the cells, the transformed phenotype of the cell is determined. Any trait of transformed cells can be assessed, including formation of bone matrix in culture (Broder et al, *Bone*, 21:225-235 (1997)), mechanical properties (Kizer et al, *Proc. Natl. Acad. Sci. USA*, 94:1013-1018 (1997)), and response to application of putative therapeutic agents.

Animals for testing therapeutic agents can be selected after treatment of germline cells or zygotes. Such treatments include insertion of the Zmax1 gene, as well as insertion of the HBM gene and disrupted homologous genes. Alternatively, the inserted Zmax1 gene(s) and/or HBM gene(s) of the animals may be disrupted by insertion or deletion mutation of other genetic alterations using conventional techniques, such as those described by, for example, Capechi, *Science*, 244:1288 (1989); Valancuis et al, *Mol. Cell Biol.*, 11:1402 (1991); Hasty et al, *Nature*, 350:243 (1991); Shinkai et al, *Cell*, 68:855 (1992); Mombaerts et al, *Cell*, 68:869 (1992); Philpott et al, *Science*, 256:1448 (1992); Snouwaert et al, *Science*, 257:1083 (1992); Donehower et al, *Nature*, 356:215 (1992). After test substances have been administered to the animals, the growth of bone must be assessed. If the test substance enhances the growth of bone, then the test substance is a candidate therapeutic agent. These animal models provide an extremely important vehicle for potential therapeutic products.

Individuals carrying the HBM gene have elevated bone mass. The HBM gene causes this phenotype by altering the activities, levels, expression patterns, and modification states of other molecules involved in bone development. Using a variety of established techniques, it is possible to identify molecules, preferably proteins or mRNAs, whose activities, levels, expression patterns, and modification states are different between systems containing the Zmax 1 gene and systems containing the HBM gene. Such systems can be, for example, cell-free extracts, cells, tissues or living organisms, such as mice or humans. For a mutant form of Zmax1, a complete deletion of Zmax1, mutations lacking the extracellular or intracellular portion of the protein, or any other mutation in the Zmax1 gene may be used. It is also possible to use expression of antisense Zmax1 RNA or oligonucleotides to inhibit production of the Zmax1 protein. For a mutant form of HBM, a complete deletion of HBM, mutations lacking the extracellular or intracellular portion of the HBM protein, or any other mutation in the HBM gene may be used. It is also possible to use expression of antisense HBM RNA or oligonucleotides to inhibit production of the HBM protein.

Molecules identified by comparison of Zmax1 systems and HBM systems can be used as surrogate markers in pharmaceutical development or in diagnosis of human or animal bone disease. Alternatively, such molecules may be used in treatment of bone disease. *See*, Schena et al, *Science*, 270:467-470 (1995).

For example, a transgenic mouse carrying the HBM gene in the mouse homologue is constructed. A mouse of the genotype HBM/+ is viable, healthy and has elevated bone mass. To identify surrogate markers for elevated bone mass, HBM/+ (i.e., heterozygous) and isogenic +/+ (i.e., wild-type) mice are sacrificed. Bone tissue mRNA is extracted from each animal, and a "gene chip" corresponding to mRNAs expressed in the +/+ individual is constructed. mRNA from different tissues is isolated from animals of each genotype, reverse-transcribed, fluorescently labeled, and then hybridized to gene fragments affixed to a solid support. The ratio of fluorescent intensity between the two populations is indicative of the relative abundance of the specific mRNAs in the +/+ and HBM/+ animals. Genes encoding

mRNAs over- and under-expressed relative to the wild-type control are candidates for genes coordinately regulated by the HBM gene.

One standard procedure for identification of new proteins that are part of the same signaling cascade as an already-discovered protein is as follows. Cells are treated with radioactive phosphorous, and the already-discovered protein is manipulated to be more ore less active. The phosphorylation state of other proteins in the cell is then monitored by polyacrylamide gel electrophoresis and autoradiography, or similar techniques. Levels of activity of the known protein may be manipulated by many methods, including, for example, comparing wild-type mutant proteins using specific inhibitors such as drugs or antibodies, simply adding or not adding a known extracellular protein, or using antisense inhibition of the expression of the known protein (Tamura et al, *Science*, 280(5369):1614-7 (1998); Meng, *EMBO J.*, 17(15):4391-403 (1998); Cooper et al, *Cell*, 1:263-73 (1982)).

In another example, proteins with different levels of phosphorylation are identified in TE85 osteosarcoma cells expressing either a sense or antisense cDNA for Zmax1. TE85 cells normally express high levels of Zmax1 (Dong et al, *Biochem. & Biophys. Res. Comm.*, 251:784-790 (1998)). Cells containing the sense construct express even higher levels of Zmax1, while cells expressing the antisense construct express lower levels. Cells are grown in the presence of ^{32}P, harvested, lysed, and the lysates run on SDS polyacrylamide gels to separate proteins, and the gels subjected to autoradiography (Ausubel et al, *Current Protocols in Molecular Biology*, John Wiley & Sons (1997)). Bands that differ in intensity between the sense and antisense cell lines represent phosphoproteins whose phosphorylation state or absolute level varies in response to levels of Zmax1. As an alternative to the ^{32}P-labeling, unlabeled proteins may be separated by SDS-PAGE and subjected to immunoblotting, using the commercially available anti-phosphotyrosine antibody as a probe (Thomas et al, *Nature*, 376(6537):267-71 (1995)). As an alternative to the expression of antisense RNA, transfection with chemically modified antisense oligonucleotides can be used (Woolf et al, *Nucleic Acids Res.*, 18(7):1763-9 (1990)).

Many bone disorders, such as osteoporosis, have a slow onset and a slow response to treatment. It is therefore useful to develop surrogate markers for bone

development and mineralization. Such markers can be useful in developing treatments for bone disorders, and for diagnosing patients who may be at risk for later development of bone disorders. Examples of preferred markers are N- and C-terminal telopeptide markers described, for example, in U.S. Patent Nos. 5,455,179, 5,641,837 and 5,652,112, the disclosures of which are incorporated by reference herein in their entirety. In the area of HIV disease, CD4 counts and viral load are useful surrogate markers for disease progression (Vlahov et al, *JAMA*, 279(1):35-40 (1998)). There is a need for analogous surrogate markers in the area of bone disease.

A surrogate marker can be any characteristic that is easily tested and relatively insensitive to non-specific influences. For example, a surrogate marker can be a molecule such as a protein or mRNA in a tissue or in blood serum. Alternatively, a surrogate marker may be a diagnostic sign such as sensitivity to pain, a reflex response or the like.

In yet another example, surrogate markers for elevated bone mass are identified using a pedigree of humans carrying the HBM gene. Blood samples are withdrawn from three individuals that carry the HBM gene, and from three closely related individuals that do not. Proteins in the serum from these individuals are electrophoresed on a two dimensional gel system, in which one dimension separates proteins by size, and another dimension separates proteins by isoelectric point (Epstein et al, *Electrophoresis*, 17(11):1655-70 (1996)). Spots corresponding to proteins are identified. A few spots are expected to be present in different amounts or in slightly different positions for the HBM individuals compared to their normal relatives. These spots correspond to proteins that are candidate surrogate markers. The identities of the proteins are determined by microsequencing, and antibodies to the proteins can be produced by standard methods for use in diagnostic testing procedures. Diagnostic assays for HBM proteins or other candidate surrogate markers include using antibodies described in this invention and a reporter molecule to detect HBM in human body fluids, membranes, bones, cells, tissues or extracts thereof. The antibodies can be labeled by joining them covalently or noncovalently with a substance that provides a detectable signal. In many scientific and patent literature, a variety of reporter molecules or labels are described including

radionuclides, enzymes, fluorescent, chemi-luminescent or chromogenic agents (U.S. Patent Nos. 3,817,837; 3,850,752; 3,939,350; 3,996,345; 4,277,437; 4,275,149; and 4,366,241).

Using these antibodies, the levels of candidate surrogate markers are measured in normal individuals and in patients suffering from a bone disorder, such as osteoporosis, osteoporosis pseudoglioma, Engelmann's disease, Ribbing's disease, hyperphosphatasemia, Van Buchem's disease, melorheostosis, osteopetrosis, pychodysostosis, sclerosteosis, osteopoikilosis, acromegaly, Paget's disease, fibrous dysplasia, tubular stenosis, osteogenesis imperfecta, hypoparathyroidism, pseudohypoparathyroidism, pseudopseudohypoparathyroidism, primary and secondary hyperparathyroidism and associated syndromes, hypercalciuria, medullary carcinoma of the thyroid gland, osteomalacia and other diseases. Techniques for measuring levels of protein in serum in a clinical setting using antibodies are well established. A protein that is consistently present in higher or lower levels in individuals carrying a particular disease or type of disease is a useful surrogate marker.

A surrogate marker can be used in diagnosis of a bone disorder. For example, consider a child that present to a physician with a high frequency of bone fracture. The underlying cause may be child abuse, inappropriate behavior by the child, or a bone disorder. To rapidly test for a bone disorder, the levels of the surrogate marker protein are measured using the antibody described above.

Levels of modification states of surrogate markers can be measured as indicators of the likely effectiveness of a drug that is being developed. It is especially convenient to use surrogate markers in creating treatments for bone disorders, because alterations in bone development or mineralization may require a long time to be observed. For example, a set of bone mRNAs, termed the "HBM-inducible mRNA set" is found to be overexpressed in HBM/+ mice as compared to +/+ mice, as described above. Expression of this set can be used as a surrogate marker. Specifically, if treatment of +/+ mice with a compound results in overexpression of the HBM-inducible mRNA set, then that compound is considered a promising candidate for further development.

This invention is particularly useful for screening compounds by using the Zmax1 or HBM protein or binding fragment thereof in any of a variety of drug screening techniques.

The Zmax1 or HBM protein or fragment employed in such a test may either be free in solution, affixed to a solid support, or borne on a cell surface. One method of drug screening utilizes eukaryotic or prokaryotic host cells which are stably transformed with recombinant nucleic acids expressing the protein or fragment, preferably in competitive binding assays. Such cells, either in viable or fixed form, can be used for standard binding assays. One may measure, for example, for the formation of complexes between a Zmax1 or HBM protein or fragment and the agent being tested, or examine the degree to which the formation of a complex between a Zmax1 or HBM protein or fragment and a known ligand is interfered with by the agent being tested.

Thus, the present invention provides methods of screening for drugs comprising contacting such an agent with a Zmax1 or HBM protein or fragment thereof and assaying (i) for the presence of a complex between the agent and the Zmax1 or HBM protein or fragment, or (ii) for the presence of a complex between the Zmax1 or HBM protein or fragment and a ligand, by methods well known in the art. In such competitive binding assays the Zmax1 or HBM protein or fragment is typically labeled. Free Zmax1 or HBM protein or fragment is separated from that present in a protein:protein complex, and the amount of free (i.e., uncomplexed) label is a measure of the binding of the agent being tested to Zmax1 or HBM or its interference with Zmax1 or HBM: ligand binding, respectively.

Another technique for drug screening provides high throughput screening for compounds having suitable binding affinity to the Zmax1 or HBM proteins and is described in detail in WO 84/03564. Briefly stated, large numbers of different small peptide test compounds are synthesized on a solid substrate, such as plastic pins or some other surface. The peptide test compounds are reacted with Zmax1 or HBM proteins and washed. Bound Zmax1 or HBM protein is then detected by methods well known in the art. Purified Zmax1 or HBM can be coated directly onto plates for use in the aforementioned drug screening techniques. However, non-neutralizing

antibodies to the protein can be used to capture antibodies to immobilize the Zmax1 or HBM protein on the solid phase.

This invention also contemplates the use of competitive drug screening assays in which neutralizing antibodies capable of specifically binding the Zmax1 or HBM protein compete with a test compound for binding to the Zmax1 or HBM protein or fragments thereof. In this manner, the antibodies can be used to detect the presence of any peptide that shares one or more antigenic determinants of the Zmax1 or HBM protein.

A further technique for drug screening involves the use of host eukaryotic cell lines or cells (such as described above) that have a nonfunctional Zmax1 or HBM gene. These host cell lines or cells are defective at the Zmax1 or HBM protein level. The host cell lines or cells are grown in the presence of drug compound. The rate of growth of the host cells is measured to determine if the compound is capable of regulating the growth of Zmax1 or HBM defective cells.

The goal of rational drug design is to produce structural analogs of biologically active proteins of interest or of small molecules with which they interact (e.g., agonists, antagonists, inhibitors) in order to fashion drugs which are, for example, more active or stable forms of the protein, or which, e.g., enhance or interfere with the function of a protein *in vivo*. See, e.g., Hodgson, *Bio/Technology*, 9:19-21 (1991). In one approach, one first determines the three-dimensional structure of a protein of interest (e.g., Zmax1 or HBM protein) or, for example, of the Zmax1- or HBM-receptor or ligand complex, by x-ray crystallography, by computer modeling or most typically, by a combination of approaches. Less often, useful information regarding the structure of a protein may be gained by modeling based on the structure of homologous proteins. An example of rational drug design is the development of HIV protease inhibitors (Erickson et al, *Science*, 249:527-533 (1990)). In addition, peptides (e.g., Zmax1 or HBM protein) are analyzed by an alanine scan (Wells, *Methods in Enzymol.*, 202: 390-411 (1991)). In this technique, an amino acid residue is replaced by Ala, and its effect on the peptide's activity is determined. Each of the amino acid residues of the peptide is analyzed in this manner to determine the important regions of the peptide.

It is also possible to isolate a target-specific antibody, selected by a functional assay, and then to solve its crystal structure. In principle, this approach yields a pharmacore upon which subsequent drug design can be based. It is possible to bypass protein crystallography altogether by generating anti-idiotypic antibodies (anti-ids) to a functional, pharmacologically active antibody. As a mirror image of a mirror image, the binding site of the anti-ids would be expected to be an analog of the original receptor. The anti-id could then be used to identify and isolate peptides from banks of chemically or biologically produced banks of peptides. Selected peptides would then act as the pharmacore.

Thus, one may design drugs which have, e.g., improved Zmax1 or HBM protein activity or stability or which act as inhibitors, agonists, antagonists, etc. of Zmax1 or HBM protein activity. By virtue of the availability of cloned Zmax1 or HBM sequences, sufficient amounts of the Zmax1 or HBM protein may be made available to perform such analytical studies as x-ray crystallography. In addition, the knowledge of the Zmax1 or HBM protein sequence provided herein will guide those employing computer modeling techniques in place of, or in addition to x-ray crystallography.

XXI. Methods of Use: Avian and Mammalian Animal Husbandry

The Zmax1 DNA and Zmax1 protein and/or the HBM DNA and HBM protein can be used for vertebrate and preferably human therapeutic agents and for avian and mammalian veterinary agents, including for livestock breeding. Birds, including, for example, chickens, roosters, hens, turkeys, ostriches, ducks, pheasants and quails, can benefit from the identification of the gene and pathway for high bone mass. In many examples cited in literature (for example, McCoy et al, *Res. Vet. Sci.*, 60(2): 185-186 (1996)), weakened bones due to husbandry conditions cause cage layer fatigue, osteoporosis and high mortality rates. Additional therapeutic agents to treat osteoporosis or other bone disorders in birds can have considerable beneficial effects on avian welfare and the economic conditions of the livestock industry, including, for example, meat and egg production.

XXII. Methods of use: Diagnostic assays using Zmax1-specific oligonucleotides for detection of genetic alterations affecting bone development.

In cases where an alteration or disease of bone development is suspected to involve an alteration of the Zmax1 gene or the HBM gene, specific oligonucleotides may be constructed and used to assess the level of Zmax1 mRNA or HBM mRNA, respectively, in bone tissue or in another tissue that affects bone development.

For example, to test whether a person has the HBM gene, which affects bone density, polymerase chain reaction can be used. Two oligonucleotides are synthesized by standard methods or are obtained from a commercial supplier of custom-made oligonucleotides. The length and base composition are determined by standard criteria using the Oligo 4.0 primer Picking program (Wojchich Rychlik, 1992). One of the oligonucleotides is designed so that it will hybridize only to HBM DNA under the PCR conditions used. The other oligonucleotide is designed to hybridize a segment of Zmax1 genomic DNA such that amplification of DNA using these oligonucleotide primers produces a conveniently identified DNA fragment. For example, the pair of primers CCAAGTTCTGAGAAGTCC (SEQ ID NO:32) and AATACCTGAAACCATACCTG (SEQ ID NO:33) will amplify a 530 base pair DNA fragment from a DNA sample when the following conditions are used: step 1 at 95°C for 120 seconds; step 2 at 95°C for 30 seconds; step 3 at 58°C for 30 seconds; step 4 at 72°C for 120 seconds; where steps 2-4 are repeated 35 times. Tissue samples may be obtained from hair follicles, whole blood, or the buccal cavity.

The fragment generated by the above procedure is sequenced by standard techniques. Individuals heterozygous for the HBM gene will show an equal amount of G and T at the second position in the codon for glycine 171. Normal or homozygous wild-type individuals will show only G at this position.
Other amplification techniques besides PCR may be used as alternatives, such as ligation-mediated PCR or techniques involving Q-beta replicase (Cahill et al, *Clin. Chem.*, 37(9):1482-5 (1991)). For example, the oligonucleotides AGCTGCTCGT AGCTG TCTCTCCCTGGATCACGGGTACATGTACTGGACAGACTGGGT (SEQ ID NO:34) and TGAGACGCCCCGGATTGAGCGGGCAGGGATAGCTTA

TTCCCTGTGCCGCATTACGGC (SEQ ID NO:35) can be hybridized to a denatured human DNA sample, treated with a DNA ligase, and then subjected to PCR amplification using the primer oligonucleotides AGCTGCTCGTAGCTGTCT CTCCCTGGA (SEQ ID NO:36) and GCCGTAATGCGGCACAGGGAATAAGCT (SEQ ID NO:37). In the first two oligonucleotides, the outer 27 bases are random sequence corresponding to primer binding sites, and the inner 30 bases correspond to sequences in the Zmax1 gene. The T at the end of the first oligonucleotide corresponds to the HBM gene. The first two oligonucleotides are ligated only when hybridized to human DNA carrying the HBM gene, which results in the formation of an amplifiable 114 bp DNA fragment.

Products of amplification can be detected by agarose gel electrophoresis, quantitative hybridization, or equivalent techniques for nucleic acid detection known to one skilled in the art of molecular biology (Sambrook et al, *Molecular Cloning: A Laboratory Manual,* Cold Spring Harbor Laboratory, Cold Spring, NY (1989)).

Other alterations in the Zmax1 gene or the HBM gene may be diagnosed by the same type of amplification-detection procedures, by using oligonucleotides designed to identify those alterations. These procedures can be used in animals as well as humans to identify alterations in Zmax1 or HBM that affect bone development.

Expression of Zmax1 or HBM in bone tissue may be accomplished by fusing the cDNA of Zmax1or HBM, respectively, to a bone-specific promoter in the context of a vector for genetically engineering vertebrate cells. DNA constructs are introduced into cells by packaging the DNA into virus capsids, by the use of cationic liposomes, electroporation, or by calcium phosphate transfection. Transfected cells, preferably osteoblasts, may be studied in culture or may be introduced into bone tissue in animals by direct injection into bone or by intravenous injection of osteoblasts, followed by incorporation into bone tissue (Ko et al, *Cancer Research,* 56(20):4614-9 (1996)). For example, the osteocalcin promoter, which is specifically active in osteoblasts, may be used to direct transcription of the Zmax1 gene or the HBM gene. Any of several vectors and transfection methods may be used, such as retroviral vectors, adenovirus vectors, or vectors that are maintained after

transfection using cationic liposomes, or other methods and vectors described herein.

Alteration of the level of functional Zmax1 protein or HBM protein affects the level of bone mineralization. By manipulating levels of functional Zmax1 protein or HBM protein, it is possible to affect bone development and to increase or decrease levels of bone mineralization. For example, it may be useful to increase bone mineralization in patients with osteoporosis. Alternatively, it may be useful to decrease bone mineralization in patients with osteopetrosis or Paget's disease. Alteration of Zmax1 levels or HBM levels can also be used as a research tool. Specifically, it is possible to identify proteins, mRNA and other molecules whose level or modification status is altered in response to changes in functional levels of Zmax1 or HBM. The pathology and pathogenesis of bone disorders is known and described, for example, in Rubin and Farber (Eds.), *Pathology*, 2nd Ed., S.B. Lippincott Co., Philadelphia, PA (1994).

A variety of techniques can be used to alter the levels of functional Zmax1 or HBM. For example, intravenous or intraosseous injection of the extracellular portion of Zmax1 or mutations thereof, or HBM or mutations thereof, will alter the level of Zmax1 activity or HBM activity, respectively, in the body of the treated human, animal or bird. Truncated versions of the Zmax1 protein or HBM protein can also be injected to alter the levels of functional Zmax1 protein or HBM protein, respectively. Certain forms of Zmax1 or HBM enhance the activity of endogenous protein, while other forms are inhibitory.

In a preferred embodiment, the HBM protein is used to treat osteoporosis. In a further preferred embodiment, the extracellular portion of the HBM protein is used. This HBM protein may be optionally modified by the addition of a moiety that causes the protein to adhere to the surface of cells. The protein is prepared in a pharmaceutically acceptable solution and is administered by injection or another method that achieves acceptable pharmacokinetics and distribution.

In a second embodiment of this method, Zmax1 or HBM levels are increased or decreased by gene therapy techniques. To increase Zmax1 or HBM levels, osteoblasts or another useful cell type are genetically engineered to express high

levels of Zmax1 or HBM as described above. Alternatively, to decrease Zmax1 or HBM levels, antisense constructs that specifically reduce the level of translatable Zmax1 or HBM mRNA can be used. In general, a tissue-nonspecific promoter may be used, such as the CMV promoter or another commercially available promoter found in expression vectors (Wu et al, *Toxicol. Appl. Pharmacol.*, 141(1):330-9 (1996)). In a preferred embodiment, a Zmax1 cDNA or its antisense is transcribed by a bone-specific promoter, such as the osteocalcin or another promoter, to achieve specific expression in bone tissue. In this way, if a Zmax1-expressing DNA construct or HBM-expressing construct is introduced into non-bone tissue, it will not be expressed.

In a third embodiment of this method, antibodies against Zmax1 or HBM are used to inhibit its function. Such antibodies are identified herein.

In a fourth embodiment of this method, drugs that inhibit Zmax1 function or HBM function are used. Such drugs are described herein and optimized according to techniques of medicinal chemistry well known to one skilled in the art of pharmaceutical development.

Zmax1 and HBM interact with several proteins, such as ApoE. Molecules that inhibit the interaction between Zmax1 or HBM and ApoE or another binding partner are expected to alter bone development and mineralization. Such inhibitors may be useful as drugs in the treatment of osteoporosis, osteopetrosis, or other diseases of bone mineralization. Such inhibitors may be low molecular weight compounds, proteins or other types of molecules. *See*, Kim et al, *J. Biochem.* (Tokyo), 124(6):1072-1076 (1998).

Inhibitors of the interaction between Zmax1 or HBM and interacting proteins may be isolated by standard drug-screening techniques. For example, Zmax1 protein, (or a fragment thereof) or HBM protein (or a fragment thereof) can be immobilized on a solid support such as the base of microtiter well. A second protein or protein fragment, such as ApoE is derivatized to aid in detection, for example with fluorescein. Iodine, or biotin, then added to the Zmax1 or HBM in the presence of candidate compounds that may specifically inhibit this protein-protein domain of Zmax1 or HBM, respectively, and thus avoid problems associated with its

transmembrane segment. Drug screens of this type are well known to one skilled in the art of pharmaceutical development.

Because Zmax1 and HBM are involved in bone development, proteins that bind to Zmax1 and HBM are also expected to be involved in bone development. Such binding proteins can be identified by standard methods, such as co-immunoprecipitation, co-fractionation, or the two-hybrid screen (Ausubel et al, *Current Protocols in Molecular Biology*, John Wiley & Sons (1997)). For example, to identify Zmax1-interacting proteins or HBM-interacting proteins using the two-hybrid system, the extracellular domain of Zmax1 or HBM is fused to LexA and expressed for the yeast vector pEG202 (the "bait") and expressed in the yeast strain EGY48. The yeast strain is transformed with a "prey" library in the appropriate vector, which encodes a galactose-inducible transcription-activation sequence fused to candidate interacting proteins. The techniques for initially selecting and subsequently verifying interacting proteins by this method are well known to one skilled in the art of molecular biology (Ausubel et al, *Current Protocols in Molecular Biology*, John Wiley & Sons (1997)).

In a preferred embodiment, proteins that interact with HBM, but not Zmax1, are identified using a variation of the above procedure (Xu et al, *Proc. Natl. Acad. Sci. USA*, 94(23):12473-8 (Nov. 1997)). This variation of the two-hybrid system uses two baits, and Zmax1 and HBM are each fused to LexA and TetR, respectively. Alternatively, proteins that interact with the HBM but not Zmax1 are also isolated. These procedures are well known to one skilled in the art of molecular biology, and are a simple variation of standard two-hybrid procedures.

As an alternative method of isolating Zmax1 or HBM interacting proteins, a biochemical approach is used. The Zmax1 protein or a fragment thereof, such as the extracellular domain, or the HBM protein or a fragment thereof, such as the extracellular domain, is chemically coupled to Sepharose beads. The Zmax1- or HBM-coupled beads are poured into a column. An extract of proteins, such as serum proteins, proteins in the supernatant of a bone biopsy, or intracellular proteins from gently lysed TE85 osteoblastic cells, is added to the column. Non-specifically bound proteins are eluted, the column is washed several times with a low-salt buffer,

and then tightly binding proteins are eluted with a high-salt buffer. These are candidate proteins that bind to Zmax1 or HBM, and can be tested for specific binding by standard tests and control experiments. Sepharose beads used for coupling proteins and the methods for performing the coupling are commercially available (Sigma), and the procedures described here are well known to one skilled in the art of protein biochemistry.

As a variation of the above procedure, proteins that are eluted by high salt from the Zmax1- or HBM-Sepharose column are then added to an HBM-Zmax1-sepharose column. Proteins that flow through without sticking are proteins that bind to Zmax1 but not to HBM. Alternatively, proteins that bind to the HBM protein and not to the Zmax1 protein can be isolated by reversing the order in which the columns are used.

XXIII. Method of Use: Transformation-Associated Recombination (TAR) Cloning

Essential for the identification of novel allelic variants of Zmax1 is the ability to examine the sequence of both copies of the gene in an individual. To accomplish this, two "hooks," or regions of significant similarity, are identified within the genomic sequence such that they flank the portion of DNA that is to be cloned. Most preferably, the first of these hooks is derived from sequences 5' to the first exon of interest and the second is derived from sequences 3' to the last exon of interest. These two "hooks" are cloned into a bacterial/yeast shuttle vector such as that described by Larionov et al, *Proc. Natl. Acad. Sci. USA*, 94:7384-7387 (1997). Other similar vector systems may also be used. To recover the entire genomic copy of the Zmax1 gene, the plasmid containing the two "hooks" is linearized with a restriction endonuclease or is produced by another method such as PCR. This linear DNA fragment is introduced into yeast cells along with human genomic DNA. Typically, the yeast *Saccharomyces cerevisiae* is used as a host cell, although Larionov et al (in press) have reported using chicken host cells as well. During and after the process of transformation, the endogenous host cell converts the linear plasmid to a circle by a recombination event whereby the region of the human genomic DNA homologous to the "hooks" is inserted into the plasmid. This

plasmid can be recovered and analyzed by methods well known to one skilled in the art. Obviously, the specificity for this reaction requires the host cell machinery to recognize sequences similar to the "hooks" present in the linear fragment. However, 100% sequence identity is not required, as shown by Kouprina et al, *Genomics*, 53(1):21-28 (October 1998), where the author describes using degenerate repeated sequences common in the human genome to recover fragments of human DNA from a rodent/human hybrid cell line.

In another example, only one "hook" is required, as described by Larionov et al, *Proc. Natl. Acad. Sci. USA*, 95(8):4469-74 (April 1998). For this type of experiment, termed "radial TAR cloning," the other region of sequence similarity to drive the recombination is derived from a repeated sequence from the genome. In this way, regions of DNA adjacent to the Zmax1 gene coding region can be recovered and examined for alterations that may affect function.

XXIV. Methods of Use: Genomic Screening

The use of polymorphic genetic markers linked to the HBM gene or to Zmax1 is very useful in predicting susceptibility to osteoporosis or other bone diseases. Koller et al, *Amer. J. Bone Min. Res.*, 13:1903-1908 (1998) have demonstrated that the use of polymorphic genetic markers is useful for linkage analysis. Similarly, the identification of polymorphic genetic markers within the high bone mass gene will allow the identification of specific allelic variants that are in linkage disequilibrium with other genetic lesions that affect bone development. Using the DNA sequence from the BACs, a dinucleotide CAn repeat was identified and two unique PCR primers that will amplify the genomic DNA containing this repeat were designed, as shown below:

B200E21C16_L: GAGAGGCTATATCCCTGGGC (SEQ ID NO:38)

B200E21C16_R: ACAGCACGTGTTTAAAGGGG (SEQ ID NO:39)

and used in the genetic mapping study.

This method has been used successfully by others skilled in the art (e.g., Sheffield et al, *Genet.*, 4:1837-1844 (1995); LeBlanc-Straceski et al, *Genomics*, 19:341-9 (1994); Chen et al, *Genomics*, 25:1-8 (1995)). Use of these reagents with populations or individuals will predict their risk for osteoporosis. Similarly, single

nucleotide polymorphisms (SNPs), such as those shown in Table 4 above, can be used as well to predict risk for developing bone diseases or resistance to osteoporosis in the case of the HBM gene.

XXV. Methods of Use: Modulators of Tissue Calcification

The calcification of tissues in the human body is well documented. Towler et al, *J. Biol. Chem.*, 273:30427-34 (1998) demonstrated that several proteins known to regulate calcification of the developing skull in a model system are expressed in calcified aorta. The expression of Msx2, a gene transcribed in osteoprogenitor cells, in calcified vascular tissue indicates that genes which are important in bone development are involved in calcification of other tissues. Treatment with HBM protein, agonists or antagonists is likely to ameliorate calcification (such as the vasculature, dentin and bone of the skull visera) due to its demonstrated effect on bone mineral density. In experimental systems where tissue calcification is demonstrated, the over-expression or repression of Zmax1 activity permits the identification of molecules that are directly regulated by the Zmax1 gene. These genes are potential targets for therapeutics aimed at modulating tissue calcification. For example, an animal, such as the LDLR -/-, mouse is fed a high fat diet and is observed to demonstrate expression of markers of tissue calcification, including Zmax1. These animals are then treated with antibodies to Zmax1 or HBM protein, antisense oligonucleotides directed against Zmax1 or HBM cDNA, or with compounds known to bind the Zmax1 or HBM protein or its binding partner or ligand. RNA or proteins are extracted from the vascular tissue and the relative expression levels of the genes expressed in the tissue are determined by methods well known in the art. Genes that are regulated in the tissue are potential therapeutic targets for pharmaceutical development as modulators of tissue calcification.

The nucleic acids, proteins, peptides, amino acids, small molecules or other pharmaceutically useful compounds of the present invention that are to be given to an individual may be administered in the form of a composition with a pharmaceutically acceptable carrier, excipient or diluent, which are well known in the art. The individual may be a mammal or a bird, preferably a human, a rat, a mouse or bird. Such compositions may be administered to an individual in a

pharmaceutically effective amount. The amount administered will vary depending on the condition being treated and the patient being treated. The compositions may be administered alone or in combination with other treatments.

EXAMPLES

The present invention is described by reference to the following Examples, which are offered by way of illustration and are not intended to limit the invention in any manner. Standard techniques well known in the art or the techniques specifically described below were utilized.

Example 1

The propositus was referred by her physicians to the Creighton Osteoporosis Center for evaluation of what appeared to be unusually dense bones. She was 18 years old and came to medical attention two years previous because of back pain, which was precipitated by an auto accident in which the car in which she was riding as a passenger was struck from behind. Her only injury was soft tissue injury to her lower back that was manifested by pain and muscle tenderness. There was no evidence of fracture or subluxation on radiographs. The pain lasted for two years, although she was able to attend school full time. By the time she was seen in the Center, the pain was nearly resolved and she was back to her usual activities as a high school student. Physical exam revealed a normal healthy young woman standing 66 inches and weighing 128 pounds. Radiographs of the entire skeleton revealed dense looking bones with thick cortices. All bones of the skeleton were involved. Most importantly, the shapes of all the bones were entirely normal. The spinal BMC was 94.48 grams in L1-4, and the spinal BMD was 1.667 gm/cm^2 in L1-4. BMD was 5.62 standard deviations (SD) above peak skeletal mass for women. These were measured by DXA using a Hologic 2000~. Her mother was then scanned and a lumbar spinal BMC of 58.05 grams and BMD of 1.500 gm/cm^2 were found. Her mother's values place her 4.12 SD above peak mass and 4.98 SD above her peers. Her mother was 51 years old, stood 65 inches and weighed 140 pounds. Her mother was in excellent health with no history of musculoskeletal or other symptoms. Her father's lumbar BMC was 75.33 grams and his BMD was

1.118 gm/cm^2. These values place him 0.25 SD above peak bone mass for males. He was in good health, stood 72 inches tall, and weighed 187 pounds.

These clinical data suggested that the propositus inherited a trait from her mother, which resulted in very high bone mass, but an otherwise normal skeleton, and attention was focused on the maternal kindred. In U.S. Patent No. 5,691,153, twenty- two of these members had measurement of bone mass by DXA. In one case, the maternal grandfather of the propositus, was deceased, however, medical records, antemortem skeletal radiographs and a gall bladder specimen embedded in paraffin for DNA genotyping were obtained. His radiographs showed obvious extreme density of all of the bones available for examination including the femur and the spine, and he was included among the affected members. In this invention, the pedigree has been expanded to include 37 informative individuals. These additions are a significant improvement over the original kinship (Johnson et al, *Am. J. Hum. Genet.*, 60:1326-1332 (1997)) because, among the fourteen individuals added since the original study, two individuals harbor key crossovers. X-linkage is ruled out by the presence of male-to-male transmission from individual 12 to 14 and 15.

Example 2

The present invention describes DNA sequences derived from two BAC clones from the HBM gene region, as evident in Table 7 below, which is an assembly of these clones. Clone b200e21-h (ATCC No. 98628; SEQ ID NOS : 1011) was deposited at the American Type Culture Collection (ATCC), 10801 University Blvd., Manassas, VA 20110-2209 U. S. A., on December 30, 1997. Clone b527dl2-h (ATCC No. 98907; SEQ ID NOS : 5-9) was deposited at the American Type Culture Collection (ATCC), 10801 University Blvd., Manassas, VA 20110-2209 U. S. A., on October 2, 1998. These sequences are unique reagents that can be used by one skilled in the art to identify DNA probes for the Zmaxl gene, PCR primers to amplify the gene, nucleotide polymorphisms in the Zmaxl gene, or regulatory elements of the Zmaxl gene.

TABLE 7

Contig	ATCC No.	SEQ ID NO.	Length (base pairs)
b527dl2-h_contig302G	98907	5	3096
b527dl2-h_contig306G	98907	6	26928
b527dl2-h_contig307G	98907	7	29430
b527dl2-h_contig308G	98907	8	33769
b527dl2-h_contig309G	98907	9	72049
b200e21-h_contigl	98628	10	8705
b200e21-h_contig4	98628	11	66933

The disclosure of each of the patents, patent applications and publications cited in the specification is hereby incorporated by reference herein in its entirety.

Although the invention has been set forth in detail, one skilled in the art will recognize that numerous changes and modifications can be made, and that such changes and modifications may be made without departing from the spirit and scope of the invention.

This application claims priority to U.S. Application Nos. 09/543,771 and 09/544,398 filed on April 5, 2000, which are a continuation-in-part of Application No. 09/229,319, filed January 13, 1999, which claims benefit of U.S. Provisional Application No. 60/071,449, filed January 13, 1998, and U.S. Provisional Application No. 60/105,511, filed October 23, 1998, all of which are herein incorporated by reference in their entirety.

CLAIMS

What is claimed is:

1. An isolated nucleic acid sequence of SEQ ID NO: 2.

2. The isolated nucleic acid sequence of claim 1, wherein the nucleic acid sequence is DNA.

3. An isolated amino acid sequence of SEQ ID NO: 4.

4. A nucleic acid sequence encoding the amino acid sequence of SEQ ID NO:4.

5. A replicative cloning vector comprising the nucleic acid sequence of claim 1 and a replicon operative in an isolated host cell.

6. An isolated host cell transformed with the replicative cloning vector of claim 5.

7. An expression vector comprising the nucleic acid sequence of claim 1 operably linked to a transcription regulatory region.

8. An isolated host cell transformed with the expression vector of claim 7.

9. A method for testing a substance as a therapeutic agent for bone modulation in a host comprising administering the nucleic acid of claim 1 to the host, and assessing whether bone modulation occurs.

10. The method of claim 9, wherein the host is a cell or an animal.

11. The method of claim 10, wherein the animal is a human, a rodent or a bird.

12. A method of identifying a molecule involved in bone modulation comprising identifying a molecule that binds to, or that inhibits binding of a molecule to, HBM.

13. The method of claim 12, wherein said molecule is a protein.

14. A method for identifying a protein involved in bone modulation comprising identifying a protein that has an expression level that is different in a first host comprising the Zmax1 gene when compared to a second host comprising the HBM gene.

15. The method of claim 14, wherein the host is a cell or an animal.

16. A method of identifying a candidate protein involved in bone modulation comprising

identifying a protein in a first individual having the high bone mass phenotype;

identifying a protein in a second individual not having the high bone mass phenotype;

comparing the protein of the first individual to the protein of the second individual, wherein (i) the protein that is present in the first individual but not the second individual is the candidate protein or (ii) the protein that is present in a higher amount in the first individual than in the second individual is the candidate protein or (iii) the protein that is present in a lower amount in the first individual than in the second individual is the candidate protein.

17. The method of claim 16, further comprising producing an antibody to the candidate protein.

18. A method of identifying a candidate protein involved in bone modulation comprising

identifying a protein in a first individual having the high bone mass phenotype;

identifying a protein in a second individual not having the high bone mass phenotype; and

comparing the protein of the first individual to the protein of the second individual, wherein (i) the protein that is present in the second individual but not the first individual is the candidate protein or (ii) the protein that is present in a higher amount in the second individual than in the first individual is the candidate protein or (iii) the protein that is present in a lower amount in the second individual than in the first individual is the candidate protein.

19. The method of claim 18, further comprising producing an antibody to the candidate protein.

20. A method of testing for HBM activity comprising immobilizing an HBM protein, binding a protein to the HBM protein, and measuring the extent of binding.

21. The method of claim 20, wherein the protein is ApoE.

22. A method for identification of a candidate molecule involved in bone modulation comprising

identifying a molecule that binds to, or that inhibits binding of a molecule to, the nucleic acid sequence of SEQ ID NO: 1;

identifying a molecule that binds to, or that inhibits binding of a molecule to, the nucleic acid sequence of SEQ ID NO: 2; and

comparing the extent of binding, or the extent of inhibition of binding, of the molecule to each nucleic acid sequence, wherein the molecule that binds, or inhibits

binding, more or less to the nucleic acid sequence of SEQ ID NO: 2 or the nucleic acid sequence of SEQ ID NO: 1 is the candidate molecule.

23. The method of claim 22, wherein the candidate molecule is a protein or an mRNA.

24. A method of pharmaceutical development for treatment of bone development disorders comprising identifying a molecule that binds to the amino acid sequence of SEQ ID NO: 4.

25. The method of claim 24, wherein the molecule inhibits or enhances the function of the amino acid.

26. A method of pharmaceutical development for treatment of bone development disorders comprising

constructing a first host that contains the Zmax1 gene or protein;

constructing a second host that contains the HBM gene or protein;

analyzing a difference between the first host and the second host;

identifying a molecule that, when added to the first host, causes the first host to exhibit a characteristic feature of the second host.

27. The method of claim 26, wherein the host is a cell-free extract, a cell or an animal.

28. The method of claim 26, wherein the difference is a surrogate marker.

29. A use of the nucleic acid sequence of claim 1 for the manufacture of a medicament for treating a bone development disorder in an animal wherein the nucleic acid sequence of claim 1 is capable of being transferred into a somatic cell of an animal suffering from a bone development disorder.

30. The use of claim 29, wherein the animal is a human or a bird.

31. A use of the nucleic acid sequence of claim 1 for the manufacture of a medicament for treating a bone development disorder in an animal wherein the nucleic acid sequence of claim 1 is capable of being transferred into a germ-line cell of an animal suffering from a bone development disorder.

32. The use of claim 31, wherein the animal is a human or a bird.

33. A use of the amino acid sequence of claim 3 for the manufacture of a medicament for altering bone development in a host wherein a somatic cell of the host is capable of receiving the amino acid sequence of claim 3.

34. The use of claim 33, wherein the host is a human or a bird.

35. A use of the amino acid sequence of claim 3 for the manufacture of a medicament for altering bone development in a host wherein a germ-line cell of the host is capable of receiving the amino acid sequence of claim 3.

36. The use of claim 35, wherein the animal is a human or a bird.

37. A use of the amino acid sequence of claim 3 for the manufacture of a medicament for treating osteoporosis in a patient.

38. The use of claim 37, wherein the patient is a human or a bird.

39. A use of the extracellular domain of the amino acid sequence of claim 3 for the manufacture of a medicament for treating osteoporosis in a patient.

40. The use of claim 39, wherein the patient is a human or a bird.

41. A use of intracellular domain of the amino acid sequence of claim 3 for the manufacture of a medicament for treating osteoporosis in a patient.

42. The use of claim 41, wherein the patient is a human or a bird.

43. A use of a molecule that binds to the nucleic acid sequence of claim 1 in the manufacture of a medicament for treating bone development disorders in a patient.

44. The use of claim 43, wherein the patient is a human or a bird.

45. A use of an antibody, wherein the antibody is to the amino acid sequence of claim 3 for the manufacture of a medicament for treating bone development disorders in a patient.

46. A method for diagnostic screening for a genetic predisposition to a bone development disorder comprising screening a sample from a patient with a nucleotide sequence derived from the genomic or cDNA nucleic acid sequence of HBM or Zmax1.

47. A diagnostic assay for bone development disorders comprising an antibody to the HBM protein.

48. A method for identifying a genetic predisposition to bone development disorders comprising performing a haplotype analysis using the nucleic acid sequence of claim 1 or the nucleic acid of SEQ ID NO: 1.

49. A method of expressing the HBM protein in bone tissue comprising constructing an expression vector comprising a promoter that directs expression in bone tissue operably linked to the nucleic acid sequence of claim 1.

50. The method of claim 49, wherein the promoter that directs expression in bone is an osteocalcin promoter, a bone sialoprotein promoter or an AML-3 promoter.

51. A bacterial artificial chromosome having the nucleic acid sequence of SEQ ID NO: 5, 6, 7, 8, 9, 10 or 11.

52. A method for amplifying a nucleotide polymorphism in the Zmax1 gene comprising using the bacterial artificial chromosome of claim 51.

53. A method for amplifying a nucleotide polymorphism in the HBM gene comprising using the bacterial artificial chromosome of claim 51.

54. A method for identifying a regulatory element of a HBM gene comprising using the bacterial artificial chromosome of claim 1 or claim 51.

55. An isolated nucleic acid sequence comprising at least 15 contiguous nucleotides of SEQ ID NO: 2, wherein said 15 contiguous nucleotides comprise position 582 of SEQ ID NO: 2.

56. The isolated nucleic acid sequence of claim 55 that is DNA.

57. The isolated nucleic acid sequence of claim 55 that is RNA.

58. A replicative cloning vector comprising the nucleic acid sequence of claim 55 and a replicon operative in a host cell.

59. An isolated host cell transformed with the replicative cloning vector of claim 58.

60. An expression vector comprising the nucleic acid sequence of claim 55 operably linked to a transcription regulatory region.

61. An isolated host cell transformed with the expression vector of claim 60.

62. An isolated nucleic acid sequence comprising at least 15 contiguous nucleotides of SEQ ID NO: 2, wherein said 15 contiguous nucleotides comprise position 582 of SEQ ID NO: 2, and which encodes for an amino acid sequence including a valine corresponding to valine at position 171 of SEQ ID NO: 4 and wherein valine substitution is associated with a high bone mass phenotype.

63. The nucleic acid sequence of claim 62 which is DNA.

64. An isolated nucleic acid segment of at least 15 contiguous nucleotides including a polymorphic site from the nucleic acid sequence of SEQ ID NO: 2 in which G at position 582 is replaced by T, and sequences complementary thereto.

65. The isolated nucleic acid segment of claim 64, wherein said complementary sequence is the reverse complement.

66. The isolated nucleic acid segment of claim 65, wherein said reverse complementary sequence is mRNA.

67. The isolated nucleic acid segment of claim 64 that is DNA.

68. The isolated nucleic acid segment of claim 64 that is cDNA.

69. The isolated nucleic acid segment of claim 65 that is RNA.

70. An isolated nucleic acid segment of at least 15 contiguous nucleotides including a single nucleotide polymorphic site from an exon sequence selected from the group consisting of:

SEQ ID NO: 9 wherein nucleotide 69169 is replaced by A,
SEQ ID NO: 9 wherein nucleotide 27402 is replaced by G,
SEQ ID NO: 9 wherein nucleotide 27841 is replaced by C,
SEQ ID NO: 9 wherein nucleotide 35600 is replaced by G,
SEQ ID NO: 9 wherein nucleotide 45619 is replaced by A,
SEQ ID NO: 9 wherein nucleotide 46018 is replaced by G,
SEQ ID NO: 9 wherein nucleotide 46093 is replaced by G,
SEQ ID NO: 9 wherein nucleotide 46190 is replaced by G,
SEQ ID NO: 9 wherein nucleotide 50993 is replaced by C,
SEQ ID NO: 9 wherein nucleotide 51124 is replaced by T,
SEQ ID NO: 9 wherein nucleotide 55461 is replaced by T,
SEQ ID NO: 9 wherein nucleotide 63645 is replaced by A,
SEQ ID NO: 9 wherein nucleotide 63646 is replaced by C,
SEQ ID NO: 9 wherein nucleotide 24809 is replaced by G,
SEQ ID NO: 9 wherein nucleotide 27837 is replaced by C,
SEQ ID NO: 9 wherein nucleotide 31485 is replaced by T,
SEQ ID NO: 9 wherein nucleotide 31683 is replaced by G,
SEQ ID NO: 9 wherein nucleotide 24808 is replaced by G,
SEQ ID NO: 8 wherein nucleotide 31340 is replaced by C,
SEQ ID NO: 8 wherein nucleotide 32538 is replaced by G,
SEQ ID NO: 8 wherein nucleotide 13224 is replaced by G,
SEQ ID NO: 8 wherein nucleotide 21119 is replaced by A,
SEQ ID NO: 8 wherein nucleotide 30497 is replaced by A,
SEQ ID NO: 9 wherein nucleotide 24811 is replaced by C,
SEQ ID NO: 9 wherein nucleotide 68280 is replaced by A, and

sequences complementary thereto.

71. The isolated nucleic acid segment of claim 70, wherein nucleotide 21119 of said exon sequence of SEQ ID NO: 8 is replaced by A.

72. The isolated nucleic acid segment of claim 70 that is DNA.

73. The isolated nucleic acid segment of claim 70 that is RNA.

74. The isolated nucleic acid segment of claim 64 or claim 70 which is a probe or primer.

75. A method of identifying a molecule involved in bone modulation comprising identifying a molecule that binds to or that inhibits binding of a molecule to a protein involved in focal adhesion signaling.

76. The method of claim 75, wherein the molecule involved in focal adhesion signaling binds to a protein selected from the group consisting of: SEQ ID NO: 87-109.

77. The method of claim 75, wherein the molecule involved in focal adhesion signaling binds to a protein selected from the group consisting of: SEQ ID NO:90, SEQ ID NO:93, SEQ ID NO:94, SEQ ID NO:99 and SEQ ID NO:102.

78. A use of an agent that regulates a nucleic acid or polypeptide encoded thereby involved in focal adhesion signaling for the manufacture of a medicament for modulating bone density in a subject.

79. The use of claim 78, wherein the nucleic acid comprises a nucleic acid selected from the group consisting of: SEQ ID NOS: 63-86.

80. The use of claim 78, wherein the nucleic acid comprises SEQ ID NO: 66, SEQ ID NO: 71, SEQ ID NO: 77 or SEQ ID NO: 79.

81. The use of claim 78, wherein the polypeptide is selected from the group consisting of: SEQ ID NOS: 87-109.

82. The use of claim 78, wherein the polypeptide is SEQ ID NO:90, SEQ ID NO:93, SEQ ID NO:94, SEQ ID NO:99 or SEQ ID NO:102.

83. A nucleic acid comprising SEQ ID NO: 66, SEQ ID NO: 71, SEQ ID NO: 77 or SEQ ID NO: 79.

84. A nucleic acid of claim 83, wherein the nucleic acid is RNA or DNA.

85. A replicative cloning vector comprising a nucleic acid of claim 83 and a replicon operative in a host cell.

86. An isolated host cell transformed with the replicative cloning vector of claim 85.

87. An expression vector comprising the nucleic acid sequence of claim 83.

88. An isolated host cell transformed with the expression vector of claim 87.

89. A polypeptide comprising SEQ ID NO:90, SEQ ID NO:93, SEQ ID NO:94, SEQ ID NO:99 or SEQ ID NO:102.

90. A nucleic acid encoding a polypetide selected from the group consisting of SEQ ID NO:90, SEQ ID NO:93, SEQ ID NO:94, SEQ ID NO:99 or SEQ ID NO:102.

91. A use of an agent which modulates a nucleic acid or a polypeptide involved in focal adhesion signaling for the manufacture of a medicament for treating bone development disorders.

92. The use of claim 91, wherein the nucleic acid modulated by the agent is selected from any one of SEQ ID NOS: 63-86.

93. The use of claim 91, wherein the polypeptide modulated by the agent is selected from any one of SEQ ID NOS: 87-109.

94. A method of testing a compound for bone modulation activity of Zmax1 or a Zmax1 mutant comprising:

(a) immobilizing a Zmax1 protein, or a Zmax1 mutant protein, or a portion of a Zmax1 protein or a portion of a Zmax1 mutant protein to a substrate;

(b) exposing a compound to said Zmax1 protein or portion thereof, or to said Zmax1 mutant protein or portion thereof;

(c) determining whether said compound bound to said Zmax1 protein or to said Zmax1 mutant protein; and

(d) administering said compound to a host and determining whether administration of said protein modulates bone mass, if said compound bound to said Zmax1 protein or said Zmax1 mutant protein.

95. The method of claim 94, wherein the compound is a protein.

96. A method for identifying proteins involved in Zmax1 signaling that modulates bone mass comprising:

(a) preparing a bait protein comprising operably linking a nucleic acid encoding Zmax1 or a biologically active portion of Zmax1 to a DNA binding domain of a yeast transcription factor;

(b) preparing a prey protein comprising operably linking a nucleic acid encoding a pre y protein to a DNA binding domain of a yeast transcription factor;

(c) expressing said bait protein in a bate yeast and expressing said pre y protein in a prey yeast;

(d) mixing said bait yeast and said prey yeast;

(e) determining whether the prey yeast mated to the bait yeast and given yeast mating, analyzing whether modulation of the prey protein modulates bone mass.

97. An isolated nucleic acid comprising SEQ ID NO:1 or a biologically active fragment of SEQ ID NO:1, wherein a nucleotide of SEQ ID NO:1 which encodes YWTD motif is mutated and said mutation causes an altered bone mass phenotype in a host when SEQ ID NO:1 or said biologically active fragment of SEQ ID NO:1 is expressed in said host.

98. A replicative cloning vector comprising the nucleic acid of claim 97.

99. An isolated host cell transformed with the replicative cloning vector of claim 98.

100. A transgenic animal which expresses a mutated Zmax1, wherein said mutated Zmax1 produces an altered bone mass when expressed in said animal.

101. A use of a nucleic acid comprising SEQ ID NO:1 in the manufacture of a medicament for treating a bone development disorder in an animal wherein said nucleic acid is capable of being transferred into a somatic cell of an animal suffering from said bone development disorder.

102. A use of a nucleic acid comprising SEQ ID NO:1in the manufacture of a medicament for treating a bone development disorder in an animal wherein said nucleic acid is capable of being transferred into a germ-line cell of an animal suffering from said bone development disorder.

103. A use of an amino acid sequence comprising SEQ ID NO:3 or a biologically

active fragment thereof for the manufacture of a medicament for modulating bone development in a host wherein a somatic cell of a host suffering from a bone development disorder is capable of receiving said amino acid sequence or a biologically active fragment thereof.

104. An isolated high bone mass (HBM) polynucleotide comprising a nucleic acid selected from the group consisting of:

(a) a nucleic acid having SEQ ID NO: 2;

(b) a nucleic acid encoding a polypeptide of SEQ ID NO: 4;

(c) a nucleic acid amplified from a mammalian library using primers which hybridize to loci within the nucleic acid of SEQ ID NO: 2 or a nucleic acid encoding a polypeptide of SEQ ID NO: 4;

(d) a nucleic acid which hybridizes to the nucleic acid of SEQ ID NO: 2;

(e) a nucleic acid which is complementary to a nucleic acid of (a), (b), (c), and (d);

(f) a nucleic acid comprising at least 15 contiguous nucleotides which comprise position 582 of SEQ ID NO: 2 from a polynucleotide of (a), (b), (c), (d), and (e); and

wherein said isolated HBM polynucleotide encodes a protein or polypeptide, which when administered to a subject modulates bone mass.

105. The polynucleotide of claim 104, wherein the nucleic acid comprises at least 100 contiguous nucleotides from a polynucleotide of (a), (b), (c), (d) or (e).

106. A method for testing a substance as a therapeutic agent for bone modulation in a host comprising administering a nucleic acid comprising SEQ ID NO: 1 to said host, and assessing whether bone modulation occurs in said host.

107. A method for expressing Zmax1 protein in bone tissue comprising constructing an expression vector comprising a promoter that directs expression in bone tissue operably linked a nucleic acid comprising SEQ ID NO: 1 or a nucleic acid encoding a biologically active fragment of SEQ ID NO: 1.

108. The method of claim 107, wherein the promoter is an osteocalcin promoter, a bone sialoprotein promoter of an AML-3 promoter.

109. The method of claim 108, wherein the promoter is the osteocalcin promoter and the bone tissue is osteoblasts.

110. A use of a nucleic acid which is antisense to SEQ ID NO: 1 or to a portion of SEQ ID NO: 1 in an amount which modulates bone mass for the manufacture of a medicament for modulating bone mass in an animal.

111. A method of studying bone disorders comprising preparing a transgenic animal which expresses Zmax1; regulating said Zmax1; and determining impact of said Zmax1 regulation on bone development in said mammal.

112. A transgenic animal which express a mutated Zmax1, wherein said mutated Zmax1 produces an altered bone mass when expressed in said animal.

113. A method of testing a compound as a bone modulating compound by administering said compound to said transgenic animal of claim 112 and determining whether said compound modulated bone mass in said animal.

114. An isolated high bone mass (HBM) polynucleotide of claim 104, wherein the nucleic acid is a nucleic acid of (a) or (b) or a nucleic acid complementary thereto.

115. An isolated nucleic acid sequence of claim 55, wherein said 15 contiguous nucleotides comprises positions 581, 582 and 583 of SEQ ID NO: 2.

116. An isolated nucleic acid sequence comprising at least 15 contiguous nucleotides of SEQ ID NO: 2, wherein said 15 contiguous nucleotides comprise

nucleotides which encode for an amino acid substitution at position 171 of SEQ ID NO: 4; which substitution is associated with a high bone mass phenotype.

117. An isolated high bone mass (HBM) polynucleotide comprising a nucleic acid selected from the group consisting of:

(a) a nucleic acid having SEQ ID NO: 2;

(b) a nucleic acid encoding a polypeptide of SEQ ID NO: 4;

(c) a nucleic acid which is complementary to a nucleic acid of (a), (b);

and (d) a nucleic acid comprising at least 15 contiguous nucleotides which comprise position 582 of SEQ ID NO: 2 from a ~~polynucleotide~~ of (a), (b), and (c).

SEQUENCE LISTING

<110> John P. Carulli et al.

<120> THE HIGH BONE MASS GENE OF 11q13.3

<130> 032796-021

<150> US 09/544,398

<151> 2000-04-05

<150> US 09/543,771

<151> 2000-04-05

<150> US 09/229,319

<151> 1999-01-13

<150> US 60/071,449

<151> 1998-01-13

<150> US 60/105,511

<151> 1998-10-23

<160> 109

<210> 1

<211> 5120

<212> DNA

<213> Homo sapiens

<400> 1

actaaagcgc cgccgccgcg ccatggagcc cgagtgagcg cggcgcgggc ccgtccggcc 60

gccggacaac atg gag gca gcg ccg ccc ggg ccg ccg tgg ccg ctg ctg 109

Met Glu Ala Ala Pro Pro Gly Pro Pro Trp Pro Leu Leu

```
                1               5                  10
ctg ctg ctg ctg ctg ctg ctg gcg ctg tgc ggc tgc ccg gcc ccc gcc      157
Leu Leu Leu Leu Leu Leu Leu Ala Leu Cys Gly Cys Pro Ala Pro Ala
    15                  20                  25
gcg gcc tcg ccg ctc ctg cta ttt gcc aac cgc cgg gac gta cgg ctg      205
Ala Ala Ser Pro Leu Leu Leu Phe Ala Asn Arg Arg Asp Val Arg Leu
30              35                  40                  45
gtg gac gcc ggc gga gtc aag ctg gag tcc acc atc gtg gtc agc ggc      253
Val Asp Ala Gly Gly Val Lys Leu Glu Ser Thr Ile Val Val Ser Gly
                50                  55                  60
ctg gag gat gcg gcc gca gtg gac ttc cag ttt tcc aag gga gcc gtg      301
Leu Glu Asp Ala Ala Ala Val Asp Phe Gln Phe Ser Lys Gly Ala Val
            65                  70                  75
tac tgg aca gac gtg agc gag gag gcc atc aag cag acc tac ctg aac      349
Tyr Trp Thr Asp Val Ser Glu Glu Ala Ile Lys Gln Thr Tyr Leu Asn
        80                  85                  90
cag acg ggg gcc gcc gtg cag aac gtg gtc atc tcc ggc ctg gtc tct      397
Gln Thr Gly Ala Ala Val Gln Asn Val Val Ile Ser Gly Leu Val Ser
    95                  100                 105
ccc gac ggc ctc gcc tgc gac tgg gtg ggc aag aag ctg tac tgg acg      445
Pro Asp Gly Leu Ala Cys Asp Trp Val Gly Lys Lys Leu Tyr Trp Thr
110                 115                 120                 125
gac tca gag acc aac cgc atc gag gtg gcc aac ctc aat ggc aca tcc      493
Asp Ser Glu Thr Asn Arg Ile Glu Val Ala Asn Leu Asn Gly Thr Ser
                130                 135                 140
cgg aag gtg ctc ttc tgg cag gac ctt gac cag ccg agg gcc atc gcc      541
Arg Lys Val Leu Phe Trp Gln Asp Leu Asp Gln Pro Arg Ala Ile Ala
```

```
            145                 150                 155

ttg gac ccc gct cac ggg tac atg tac tgg aca gac tgg ggt gag acg        589
Leu Asp Pro Ala His Gly Tyr Met Tyr Trp Thr Asp Trp Gly Glu Thr

        160                 165                 170

ccc cgg att gag cgg gca ggg atg gat ggc agc acc cgg aag atc att        637
Pro Arg Ile Glu Arg Ala Gly Met Asp Gly Ser Thr Arg Lys Ile Ile

    175                 180                 185

gtg gac tcg gac att tac tgg ccc aat gga ctg acc atc gac ctg gag        685
Val Asp Ser Asp Ile Tyr Trp Pro Asn Gly Leu Thr Ile Asp Leu Glu

190                 195                 200                 205

gag cag aag ctc tac tgg gct gac gcc aag ctc agc ttc atc cac cgt        733
Glu Gln Lys Leu Tyr Trp Ala Asp Ala Lys Leu Ser Phe Ile His Arg

                210                 215                 220

gcc aac ctg gac ggc tcg ttc cgg cag aag gtg gtg gag ggc agc ctg        781
Ala Asn Leu Asp Gly Ser Phe Arg Gln Lys Val Val Glu Gly Ser Leu

            225                 230                 235

acg cac ccc ttc gcc ctg acg ctc tcc ggg gac act ctg tac tgg aca        829
Thr His Pro Phe Ala Leu Thr Leu Ser Gly Asp Thr Leu Tyr Trp Thr

        240                 245                 250

gac tgg cag acc cgc tcc atc cat gcc tgc aac aag cgc act ggg ggg        877
Asp Trp Gln Thr Arg Ser Ile His Ala Cys Asn Lys Arg Thr Gly Gly

    255                 260                 265

aag agg aag gag atc ctg agt gcc ctc tac tca ccc atg gac atc cag        925
Lys Arg Lys Glu Ile Leu Ser Ala Leu Tyr Ser Pro Met Asp Ile Gln

270                 275                 280                 285

gtg ctg agc cag gag cgg cag cct ttc ttc cac act cgc tgt gag gag        973
Val Leu Ser Gln Glu Arg Gln Pro Phe Phe His Thr Arg Cys Glu Glu
```

290 295 300

gac aat ggc ggc tgc tcc cac ctg tgc ctg ctg tcc cca agc gag cct 1021
Asp Asn Gly Gly Cys Ser His Leu Cys Leu Leu Ser Pro Ser Glu Pro

305 310 315

ttc tac aca tgc gcc tgc ccc acg ggt gtg cag ctg cag gac aac ggc 1069
Phe Tyr Thr Cys Ala Cys Pro Thr Gly Val Gln Leu Gln Asp Asn Gly

320 325 330

agg acg tgt aag gca gga gcc gag gag gtg ctg ctg ctg gcc cgg cgg 1117
Arg Thr Cys Lys Ala Gly Ala Glu Glu Val Leu Leu Leu Ala Arg Arg

335 340 345

acg gac cta cgg agg atc tcg ctg gac acg ccg gac ttc acc gac atc 1165
Thr Asp Leu Arg Arg Ile Ser Leu Asp Thr Pro Asp Phe Thr Asp Ile

350 355 360 365

gtg ctg cag gtg gac gac atc cgg cac gcc att gcc atc gac tac gac 1213
Val Leu Gln Val Asp Asp Ile Arg His Ala Ile Ala Ile Asp Tyr Asp

370 375 380

ccg cta gag ggc tat gtc tac tgg aca gat gac gag gtg cgg gcc atc 1261
Pro Leu Glu Gly Tyr Val Tyr Trp Thr Asp Asp Glu Val Arg Ala Ile

385 390 395

cgc agg gcg tac ctg gac ggg tct ggg gcg cag acg ctg gtc aac acc 1309
Arg Arg Ala Tyr Leu Asp Gly Ser Gly Ala Gln Thr Leu Val Asn Thr

400 405 410

gag atc aac gac ccc gat ggc atc gcg gtc gac tgg gtg gcc cga aac 1357
Glu Ile Asn Asp Pro Asp Gly Ile Ala Val Asp Trp Val Ala Arg Asn

415 420 425

ctc tac tgg acc gac acg ggc acg gac cgc atc gag gtg acg cgc ctc 1405
Leu Tyr Trp Thr Asp Thr Gly Thr Asp Arg Ile Glu Val Thr Arg Leu

```
430                 435                 440                 445

aac ggc acc tcc cgc aag atc ctg gtg tcg gag gac ctg gac gag ccc      1453
Asn Gly Thr Ser Arg Lys Ile Leu Val Ser Glu Asp Leu Asp Glu Pro

                450                 455                 460

cga gcc atc gca ctg cac ccc gtg atg ggc ctc atg tac tgg aca gac      1501
Arg Ala Ile Ala Leu His Pro Val Met Gly Leu Met Tyr Trp Thr Asp

            465                 470                 475

tgg gga gag aac cct aaa atc gag tgt gcc aac ttg gat ggg cag gag      1549
Trp Gly Glu Asn Pro Lys Ile Glu Cys Ala Asn Leu Asp Gly Gln Glu

        480                 485                 490

cgg cgt gtg ctg gtc aat gcc tcc ctc ggg tgg ccc aac ggc ctg gcc      1597
Arg Arg Val Leu Val Asn Ala Ser Leu Gly Trp Pro Asn Gly Leu Ala

    495                 500                 505

ctg gac ctg cag gag ggg aag ctc tac tgg gga gac gcc aag aca gac      1645
Leu Asp Leu Gln Glu Gly Lys Leu Tyr Trp Gly Asp Ala Lys Thr Asp

510                 515                 520                 525

aag atc gag gtg atc aat gtt gat ggg acg aag agg cgg acc ctc ctg      1693
Lys Ile Glu Val Ile Asn Val Asp Gly Thr Lys Arg Arg Thr Leu Leu

                530                 535                 540

gag gac aag ctc ccg cac att ttc ggg ttc acg ctg ctg ggg gac ttc      1741
Glu Asp Lys Leu Pro His Ile Phe Gly Phe Thr Leu Leu Gly Asp Phe

            545                 550                 555

atc tac tgg act gac tgg cag cgc cgc agc atc gag cgg gtg cac aag      1789
Ile Tyr Trp Thr Asp Trp Gln Arg Arg Ser Ile Glu Arg Val His Lys

        560                 565                 570

gtc aag gcc agc cgg gac gtc atc att gac cag ctg ccc gac ctg atg      1837
Val Lys Ala Ser Arg Asp Val Ile Ile Asp Gln Leu Pro Asp Leu Met
```

575 580 585

ggg ctc aaa gct gtg aat gtg gcc aag gtc gtc gga acc aac ccg tgt 1885
Gly Leu Lys Ala Val Asn Val Ala Lys Val Val Gly Thr Asn Pro Cys
590 595 600 605

gcg gac agg aac ggg ggg tgc agc cac ctg tgc ttc ttc aca ccc cac 1933
Ala Asp Arg Asn Gly Gly Cys Ser His Leu Cys Phe Phe Thr Pro His
610 615 620

gca acc cgg tgt ggc tgc ccc atc ggc ctg gag ctg ctg agt gac atg 1981
Ala Thr Arg Cys Gly Cys Pro Ile Gly Leu Glu Leu Leu Ser Asp Met
625 630 635

aag acc tgc atc gtg cct gag gcc ttc ttg gtc ttc acc agc aga gcc 2029
Lys Thr Cys Ile Val Pro Glu Ala Phe Leu Val Phe Thr Ser Arg Ala
640 645 650

gcc atc cac agg atc tcc ctc gag acc aat aac aac gac gtg gcc atc 2077
Ala Ile His Arg Ile Ser Leu Glu Thr Asn Asn Asn Asp Val Ala Ile
655 660 665

ccg ctc acg ggc gtc aag gag gcc tca gcc ctg gac ttt gat gtg tcc 2125
Pro Leu Thr Gly Val Lys Glu Ala Ser Ala Leu Asp Phe Asp Val Ser
670 675 680 685

aac aac cac atc tac tgg aca gac gtc agc ctg aag acc atc agc cgc 2173
Asn Asn His Ile Tyr Trp Thr Asp Val Ser Leu Lys Thr Ile Ser Arg
690 695 700

gcc ttc atg aac ggg agc tcg gtg gag cac gtg gtg gag ttt ggc ctt 2221
Ala Phe Met Asn Gly Ser Ser Val Glu His Val Val Glu Phe Gly Leu
705 710 715

gac tac ccc gag ggc atg gcc gtt gac tgg atg ggc aag aac ctc tac 2269
Asp Tyr Pro Glu Gly Met Ala Val Asp Trp Met Gly Lys Asn Leu Tyr

720 725 730

tgg gcc gac act ggg acc aac aga atc gaa gtg gcg cgg ctg gac ggg 2317
Trp Ala Asp Thr Gly Thr Asn Arg Ile Glu Val Ala Arg Leu Asp Gly
735 740 745

cag ttc cgg caa gtc ctc gtg tgg agg gac ttg gac aac ccg agg tcg 2365
Gln Phe Arg Gln Val Leu Val Trp Arg Asp Leu Asp Asn Pro Arg Ser
750 755 760 765

ctg gcc ctg gat ccc acc aag ggc tac atc tac tgg acc gag tgg ggc 2413
Leu Ala Leu Asp Pro Thr Lys Gly Tyr Ile Tyr Trp Thr Glu Trp Gly
770 775 780

ggc aag ccg agg atc gtg cgg gcc ttc atg gac ggg acc aac tgc atg 2461
Gly Lys Pro Arg Ile Val Arg Ala Phe Met Asp Gly Thr Asn Cys Met
785 790 795

acg ctg gtg gac aag gtg ggc cgg gcc aac gac ctc acc att gac tac 2509
Thr Leu Val Asp Lys Val Gly Arg Ala Asn Asp Leu Thr Ile Asp Tyr
800 805 810

gct gac cag cgc ctc tac tgg acc gac ctg gac acc aac atg atc gag 2557
Ala Asp Gln Arg Leu Tyr Trp Thr Asp Leu Asp Thr Asn Met Ile Glu
815 820 825

tcg tcc aac atg ctg ggt cag gag cgg gtc gtg att gcc gac gat ctc 2605
Ser Ser Asn Met Leu Gly Gln Glu Arg Val Val Ile Ala Asp Asp Leu
830 835 840 845

ccg cac ccg ttc ggt ctg acg cag tac agc gat tat atc tac tgg aca 2653
Pro His Pro Phe Gly Leu Thr Gln Tyr Ser Asp Tyr Ile Tyr Trp Thr
850 855 860

gac tgg aat ctg cac agc att gag cgg gcc gac aag act agc ggc cgg 2701
Asp Trp Asn Leu His Ser Ile Glu Arg Ala Asp Lys Thr Ser Gly Arg

865 870 875

aac cgc acc ctc atc cag ggc cac ctg gac ttc gtg atg gac atc ctg 2749
Asn Arg Thr Leu Ile Gln Gly His Leu Asp Phe Val Met Asp Ile Leu

880 885 890

gtg ttc cac tcc tcc cgc cag gat ggc ctc aat gac tgt atg cac aac 2797
Val Phe His Ser Ser Arg Gln Asp Gly Leu Asn Asp Cys Met His Asn

895 900 905

aac ggg cag tgt ggg cag ctg tgc ctt gcc atc ccc ggc ggc cac cgc 2845
Asn Gly Gln Cys Gly Gln Leu Cys Leu Ala Ile Pro Gly Gly His Arg

910 915 920 925

tgc ggc tgc gcc tca cac tac acc ctg gac ccc agc agc cgc aac tgc 2893
Cys Gly Cys Ala Ser His Tyr Thr Leu Asp Pro Ser Ser Arg Asn Cys

930 935 940

agc ccg ccc acc acc ttc ttg ctg ttc agc cag aaa tct gcc atc agt 2941
Ser Pro Pro Thr Thr Phe Leu Leu Phe Ser Gln Lys Ser Ala Ile Ser

945 950 955

cgg atg atc ccg gac gac cag cac agc ccg gat ctc atc ctg ccc ctg 2989
Arg Met Ile Pro Asp Asp Gln His Ser Pro Asp Leu Ile Leu Pro Leu

960 965 970

cat gga ctg agg aac gtc aaa gcc atc gac tat gac cca ctg gac aag 3037
His Gly Leu Arg Asn Val Lys Ala Ile Asp Tyr Asp Pro Leu Asp Lys

975 980 985

ttc atc tac tgg gtg gat ggg cgc cag aac atc aag cga gcc aag gac 3085
Phe Ile Tyr Trp Val Asp Gly Arg Gln Asn Ile Lys Arg Ala Lys Asp

990 995 1000 1005

gac ggg acc cag ccc ttt gtt ttg acc tct ctg agc caa ggc caa aac 3133
Asp Gly Thr Gln Pro Phe Val Leu Thr Ser Leu Ser Gln Gly Gln Asn

1010 1015 1020

cca gac agg cag ccc cac gac ctc agc atc gac atc tac agc cgg aca 3181

Pro Asp Arg Gln Pro His Asp Leu Ser Ile Asp Ile Tyr Ser Arg Thr

1025 1030 1035

ctg ttc tgg acg tgc gag gcc acc aat acc atc aac gtc cac agg ctg 3229

Leu Phe Trp Thr Cys Glu Ala Thr Asn Thr Ile Asn Val His Arg Leu

1040 1045 1050

agc ggg gaa gcc atg ggg gtg gtg ctg cgt ggg gac cgc gac aag ccc 3277

Ser Gly Glu Ala Met Gly Val Val Leu Arg Gly Asp Arg Asp Lys Pro

1055 1060 1065

agg gcc atc gtc gtc aac gcg gag cga ggg tac ctg tac ttc acc aac 3325

Arg Ala Ile Val Val Asn Ala Glu Arg Gly Tyr Leu Tyr Phe Thr Asn

1070 1075 1080 1085

atg cag gac cgg gca gcc aag atc gaa cgc gca gcc ctg gac ggc acc 3373

Met Gln Asp Arg Ala Ala Lys Ile Glu Arg Ala Ala Leu Asp Gly Thr

1090 1095 1100

gag cgc gag gtc ctc ttc acc acc ggc ctc atc cgc cct gtg gcc ctg 3421

Glu Arg Glu Val Leu Phe Thr Thr Gly Leu Ile Arg Pro Val Ala Leu

1105 1110 1115

gtg gtg gac aac aca ctg ggc aag ctg ttc tgg gtg gac gcg gac ctg 3469

Val Val Asp Asn Thr Leu Gly Lys Leu Phe Trp Val Asp Ala Asp Leu

1120 1125 1130

aag cgc att gag agc tgt gac ctg tca ggg gcc aac cgc ctg acc ctg 3517

Lys Arg Ile Glu Ser Cys Asp Leu Ser Gly Ala Asn Arg Leu Thr Leu

1135 1140 1145

gag gac gcc aac atc gtg cag cct ctg ggc ctg acc atc ctt ggc aag 3565

Glu Asp Ala Asn Ile Val Gln Pro Leu Gly Leu Thr Ile Leu Gly Lys

1150 1155 1160 1165

cat ctc tac tgg atc gac cgc cag cag cag atg atc gag cgt gtg gag 3613

His Leu Tyr Trp Ile Asp Arg Gln Gln Gln Met Ile Glu Arg Val Glu

1170 1175 1180

aag acc acc ggg gac aag cgg act cgc atc cag ggc cgt gtc gcc cac 3661

Lys Thr Thr Gly Asp Lys Arg Thr Arg Ile Gln Gly Arg Val Ala His

1185 1190 1195

ctc act ggc atc cat gca gtg gag gaa gtc agc ctg gag gag ttc tca 3709

Leu Thr Gly Ile His Ala Val Glu Glu Val Ser Leu Glu Glu Phe Ser

1200 1205 1210

gcc cac cca tgt gcc cgt gac aat ggt ggc tgc tcc cac atc tgt att 3757

Ala His Pro Cys Ala Arg Asp Asn Gly Gly Cys Ser His Ile Cys Ile

1215 1220 1225

gcc aag ggt gat ggg aca cca cgg tgc tca tgc cca gtc cac ctc gtg 3805

Ala Lys Gly Asp Gly Thr Pro Arg Cys Ser Cys Pro Val His Leu Val

1230 1235 1240 1245

ctc ctg cag aac ctg ctg acc tgt gga gag ccg ccc acc tgc tcc ccg 3853

Leu Leu Gln Asn Leu Leu Thr Cys Gly Glu Pro Pro Thr Cys Ser Pro

1250 1255 1260

gac cag ttt gca tgt gcc aca ggg gag atc gac tgt atc ccc ggg gcc 3901

Asp Gln Phe Ala Cys Ala Thr Gly Glu Ile Asp Cys Ile Pro Gly Ala

1265 1270 1275

tgg cgc tgt gac ggc ttt ccc gag tgc gat gac cag agc gac gag gag 3949

Trp Arg Cys Asp Gly Phe Pro Glu Cys Asp Asp Gln Ser Asp Glu Glu

1280 1285 1290

ggc tgc ccc gtg tgc tcc gcc gcc cag ttc ccc tgc gcg cgg ggt cag 3997

Gly Cys Pro Val Cys Ser Ala Ala Gln Phe Pro Cys Ala Arg Gly Gln

1295 1300 1305

tgt gtg gac ctg cgc ctg cgc tgc gac ggc gag gca gac tgt cag gac 4045
Cys Val Asp Leu Arg Leu Arg Cys Asp Gly Glu Ala Asp Cys Gln Asp

1310 1315 1320 1325

cgc tca gac gag gtg gac tgt gac gcc atc tgc ctg ccc aac cag ttc 4093
Arg Ser Asp Glu Val Asp Cys Asp Ala Ile Cys Leu Pro Asn Gln Phe

1330 1335 1340

cgg tgt gcg agc ggc cag tgt gtc ctc atc aaa cag cag tgc gac tcc 4141
Arg Cys Ala Ser Gly Gln Cys Val Leu Ile Lys Gln Gln Cys Asp Ser

1345 1350 1355

ttc ccc gac tgt atc gac ggc tcc gac gag ctc atg tgt gaa atc acc 4189
Phe Pro Asp Cys Ile Asp Gly Ser Asp Glu Leu Met Cys Glu Ile Thr

1360 1365 1370

aag ccg ccc tca gac gac agc ccg gcc cac agc agt gcc atc ggg ccc 4237
Lys Pro Pro Ser Asp Asp Ser Pro Ala His Ser Ser Ala Ile Gly Pro

1375 1380 1385

gtc att ggc atc atc ctc tct ctc ttc gtc atg ggt ggt gtc tat ttt 4285
Val Ile Gly Ile Ile Leu Ser Leu Phe Val Met Gly Gly Val Tyr Phe

1390 1395 1400 1405

gtg tgc cag cgc gtg gtg tgc cag cgc tat gcg ggg gcc aac ggg ccc 4333
Val Cys Gln Arg Val Val Cys Gln Arg Tyr Ala Gly Ala Asn Gly Pro

1410 1415 1420

ttc ccg cac gag tat gtc agc ggg acc ccg cac gtg ccc ctc aat ttc 4381
Phe Pro His Glu Tyr Val Ser Gly Thr Pro His Val Pro Leu Asn Phe

1425 1430 1435

ata gcc ccg ggc ggt tcc cag cat ggc ccc ttc aca ggc atc gca tgc 4429
Ile Ala Pro Gly Gly Ser Gln His Gly Pro Phe Thr Gly Ile Ala Cys

1440 1445 1450

gga aag tcc atg atg agc tcc gtg agc ctg atg ggg ggc cgg ggc ggg 4477

Gly Lys Ser Met Met Ser Ser Val Ser Leu Met Gly Gly Arg Gly Gly

1455 1460 1465

gtg ccc ctc tac gac cgg aac cac gtc aca ggg gcc tcg tcc agc agc 4525

Val Pro Leu Tyr Asp Arg Asn His Val Thr Gly Ala Ser Ser Ser Ser

1470 1475 1480 1485

tcg tcc agc acg aag gcc acg ctg tac ccg ccg atc ctg aac ccg ccg 4573

Ser Ser Ser Thr Lys Ala Thr Leu Tyr Pro Pro Ile Leu Asn Pro Pro

1490 1495 1500

ccc tcc ccg gcc acg gac ccc tcc ctg tac aac atg gac atg ttc tac 4621

Pro Ser Pro Ala Thr Asp Pro Ser Leu Tyr Asn Met Asp Met Phe Tyr

1505 1510 1515

tct tca aac att ccg gcc act gcg aga ccg tac agg ccc tac atc att 4669

Ser Ser Asn Ile Pro Ala Thr Ala Arg Pro Tyr Arg Pro Tyr Ile Ile

1520 1525 1530

cga gga atg gcg ccc ccg acg acg ccc tgc agc acc gac gtg tgt gac 4717

Arg Gly Met Ala Pro Pro Thr Thr Pro Cys Ser Thr Asp Val Cys Asp

1535 1540 1545

agc gac tac agc gcc agc cgc tgg aag gcc agc aag tac tac ctg gat 4765

Ser Asp Tyr Ser Ala Ser Arg Trp Lys Ala Ser Lys Tyr Tyr Leu Asp

1550 1555 1560 1565

ttg aac tcg gac tca gac ccc tat cca ccc cca ccc acg ccc cac agc 4813

Leu Asn Ser Asp Ser Asp Pro Tyr Pro Pro Pro Pro Thr Pro His Ser

1570 1575 1580

cag tac ctg tcg gcg gag gac agc tgc ccg ccc tcg ccc gcc acc gag 4861

Gln Tyr Leu Ser Ala Glu Asp Ser Cys Pro Pro Ser Pro Ala Thr Glu

1585 1590 1595

agg agc tac ttc cat ctc ttc ccg ccc cct ccg tcc ccc tgc acg gac 4909

Arg Ser Tyr Phe His Leu Phe Pro Pro Pro Ser Pro Cys Thr Asp

1600 1605 1610

tca tcc tgacctcggc cgggccactc tggcttctct gtgcccctgt aaatagtttt 4965

Ser Ser

1615

aaatatgaac aaagaaaaaa atatatttta tgatttaaaa aataaatata attgggattt 5025

taaaaacatg agaaatgtga actgtgatgg ggtgggcagg gctgggagaa ctttgtacag 5085

tggagaaata tttataaact taattttgta aaaca 5120

<210> 2

<211> 5120

<212> DNA

<213> Homo sapiens

<400> 2

actaaagcgc cgccgccgcg ccatggagcc cgagtgagcg cggcgcgggc ccgtccggcc 60

gccggacaac atg gag gca gcg ccg ccc ggg ccg ccg tgg ccg ctg ctg 109

Met Glu Ala Ala Pro Pro Gly Pro Pro Trp Pro Leu Leu

1 5 10

ctg ctg ctg ctg ctg ctg ctg gcg ctg tgc ggc tgc ccg gcc ccc gcc 157

Leu Leu Leu Leu Leu Leu Leu Ala Leu Cys Gly Cys Pro Ala Pro Ala

15 20 25

gcg gcc tcg ccg ctc ctg cta ttt gcc aac cgc cgg gac gta cgg ctg 205

Ala Ala Ser Pro Leu Leu Leu Phe Ala Asn Arg Arg Asp Val Arg Leu

30 35 40 45

gtg gac gcc ggc gga gtc aag ctg gag tcc acc atc gtg gtc agc ggc 253
Val Asp Ala Gly Gly Val Lys Leu Glu Ser Thr Ile Val Val Ser Gly
50 55 60

ctg gag gat gcg gcc gca gtg gac ttc cag ttt tcc aag gga gcc gtg 301
Leu Glu Asp Ala Ala Ala Val Asp Phe Gln Phe Ser Lys Gly Ala Val
65 70 75

tac tgg aca gac gtg agc gag gag gcc atc aag cag acc tac ctg aac 349
Tyr Trp Thr Asp Val Ser Glu Glu Ala Ile Lys Gln Thr Tyr Leu Asn
80 85 90

cag acg ggg gcc gcc gtg cag aac gtg gtc atc tcc ggc ctg gtc tct 397
Gln Thr Gly Ala Ala Val Gln Asn Val Val Ile Ser Gly Leu Val Ser
95 100 105

ccc gac ggc ctc gcc tgc gac tgg gtg ggc aag aag ctg tac tgg acg 445
Pro Asp Gly Leu Ala Cys Asp Trp Val Gly Lys Lys Leu Tyr Trp Thr
110 115 120 125

gac tca gag acc aac cgc atc gag gtg gcc aac ctc aat ggc aca tcc 493
Asp Ser Glu Thr Asn Arg Ile Glu Val Ala Asn Leu Asn Gly Thr Ser
130 135 140

cgg aag gtg ctc ttc tgg cag gac ctt gac cag ccg agg gcc atc gcc 541
Arg Lys Val Leu Phe Trp Gln Asp Leu Asp Gln Pro Arg Ala Ile Ala
145 150 155

ttg gac ccc gct cac ggg tac atg tac tgg aca gac tgg gtt gag acg 589
Leu Asp Pro Ala His Gly Tyr Met Tyr Trp Thr Asp Trp Val Glu Thr
160 165 170

ccc cgg att gag cgg gca ggg atg gat ggc agc acc cgg aag atc att 637
Pro Arg Ile Glu Arg Ala Gly Met Asp Gly Ser Thr Arg Lys Ile Ile
175 180 185

gtg gac tcg gac att tac tgg ccc aat gga ctg acc atc gac ctg gag 685
Val Asp Ser Asp Ile Tyr Trp Pro Asn Gly Leu Thr Ile Asp Leu Glu
190 195 200 205

gag cag aag ctc tac tgg gct gac gcc aag ctc agc ttc atc cac cgt 733
Glu Gln Lys Leu Tyr Trp Ala Asp Ala Lys Leu Ser Phe Ile His Arg
210 215 220

gcc aac ctg gac ggc tcg ttc cgg cag aag gtg gtg gag ggc agc ctg 781
Ala Asn Leu Asp Gly Ser Phe Arg Gln Lys Val Val Glu Gly Ser Leu
225 230 235

acg cac ccc ttc gcc ctg acg ctc tcc ggg gac act ctg tac tgg aca 829
Thr His Pro Phe Ala Leu Thr Leu Ser Gly Asp Thr Leu Tyr Trp Thr
240 245 250

gac tgg cag acc cgc tcc atc cat gcc tgc aac aag cgc act ggg ggg 877
Asp Trp Gln Thr Arg Ser Ile His Ala Cys Asn Lys Arg Thr Gly Gly
255 260 265

aag agg aag gag atc ctg agt gcc ctc tac tca ccc atg gac atc cag 925
Lys Arg Lys Glu Ile Leu Ser Ala Leu Tyr Ser Pro Met Asp Ile Gln
270 275 280 285

gtg ctg agc cag gag cgg cag cct ttc ttc cac act cgc tgt gag gag 973
Val Leu Ser Gln Glu Arg Gln Pro Phe Phe His Thr Arg Cys Glu Glu
290 295 300

gac aat ggc ggc tgc tcc cac ctg tgc ctg ctg tcc cca agc gag cct 1021
Asp Asn Gly Gly Cys Ser His Leu Cys Leu Leu Ser Pro Ser Glu Pro
305 310 315

ttc tac aca tgc gcc tgc ccc acg ggt gtg cag ctg cag gac aac ggc 1069
Phe Tyr Thr Cys Ala Cys Pro Thr Gly Val Gln Leu Gln Asp Asn Gly
320 325 330

```
agg acg tgt aag gca gga gcc gag gag gtg ctg ctg ctg gcc cgg cgg        1117
Arg Thr Cys Lys Ala Gly Ala Glu Glu Val Leu Leu Leu Ala Arg Arg
    335                 340                 345

acg gac cta cgg agg atc tcg ctg gac acg ccg gac ttc acc gac atc        1165
Thr Asp Leu Arg Arg Ile Ser Leu Asp Thr Pro Asp Phe Thr Asp Ile
350                 355                 360                 365

gtg ctg cag gtg gac gac atc cgg cac gcc att gcc atc gac tac gac        1213
Val Leu Gln Val Asp Asp Ile Arg His Ala Ile Ala Ile Asp Tyr Asp
                370                 375                 380

ccg cta gag ggc tat gtc tac tgg aca gat gac gag gtg cgg gcc atc        1261
Pro Leu Glu Gly Tyr Val Tyr Trp Thr Asp Asp Glu Val Arg Ala Ile
            385                 390                 395

cgc agg gcg tac ctg gac ggg tct ggg gcg cag acg ctg gtc aac acc        1309
Arg Arg Ala Tyr Leu Asp Gly Ser Gly Ala Gln Thr Leu Val Asn Thr
        400                 405                 410

gag atc aac gac ccc gat ggc atc gcg gtc gac tgg gtg gcc cga aac        1357
Glu Ile Asn Asp Pro Asp Gly Ile Ala Val Asp Trp Val Ala Arg Asn
    415                 420                 425

ctc tac tgg acc gac acg ggc acg gac cgc atc gag gtg acg cgc ctc        1405
Leu Tyr Trp Thr Asp Thr Gly Thr Asp Arg Ile Glu Val Thr Arg Leu
430                 435                 440                 445

aac ggc acc tcc cgc aag atc ctg gtg tcg gag gac ctg gac gag ccc        1453
Asn Gly Thr Ser Arg Lys Ile Leu Val Ser Glu Asp Leu Asp Glu Pro
                450                 455                 460

cga gcc atc gca ctg cac ccc gtg atg ggc ctc atg tac tgg aca gac        1501
Arg Ala Ile Ala Leu His Pro Val Met Gly Leu Met Tyr Trp Thr Asp
            465                 470                 475
```

tgg gga gag aac cct aaa atc gag tgt gcc aac ttg gat ggg cag gag 1549
Trp Gly Glu Asn Pro Lys Ile Glu Cys Ala Asn Leu Asp Gly Gln Glu
480 485 490

cgg cgt gtg ctg gtc aat gcc tcc ctc ggg tgg ccc aac ggc ctg gcc 1597
Arg Arg Val Leu Val Asn Ala Ser Leu Gly Trp Pro Asn Gly Leu Ala
495 500 505

ctg gac ctg cag gag ggg aag ctc tac tgg gga gac gcc aag aca gac 1645
Leu Asp Leu Gln Glu Gly Lys Leu Tyr Trp Gly Asp Ala Lys Thr Asp
510 515 520 525

aag atc gag gtg atc aat gtt gat ggg acg aag agg cgg acc ctc ctg 1693
Lys Ile Glu Val Ile Asn Val Asp Gly Thr Lys Arg Arg Thr Leu Leu
530 535 540

gag gac aag ctc ccg cac att ttc ggg ttc acg ctg ctg ggg gac ttc 1741
Glu Asp Lys Leu Pro His Ile Phe Gly Phe Thr Leu Leu Gly Asp Phe
545 550 555

atc tac tgg act gac tgg cag cgc cgc agc atc gag cgg gtg cac aag 1789
Ile Tyr Trp Thr Asp Trp Gln Arg Arg Ser Ile Glu Arg Val His Lys
560 565 570

gtc aag gcc agc cgg gac gtc atc att gac cag ctg ccc gac ctg atg 1837
Val Lys Ala Ser Arg Asp Val Ile Ile Asp Gln Leu Pro Asp Leu Met
575 580 585

ggg ctc aaa gct gtg aat gtg gcc aag gtc gtc gga acc aac ccg tgt 1885
Gly Leu Lys Ala Val Asn Val Ala Lys Val Val Gly Thr Asn Pro Cys
590 595 600 605

gcg gac agg aac ggg ggg tgc agc cac ctg tgc ttc ttc aca ccc cac 1933
Ala Asp Arg Asn Gly Gly Cys Ser His Leu Cys Phe Phe Thr Pro His
610 615 620

```
gca acc cgg tgt ggc tgc ccc atc ggc ctg gag ctg ctg agt gac atg        1981
Ala Thr Arg Cys Gly Cys Pro Ile Gly Leu Glu Leu Leu Ser Asp Met
            625                 630                 635

aag acc tgc atc gtg cct gag gcc ttc ttg gtc ttc acc agc aga gcc        2029
Lys Thr Cys Ile Val Pro Glu Ala Phe Leu Val Phe Thr Ser Arg Ala
        640                 645                 650

gcc atc cac agg atc tcc ctc gag acc aat aac aac gac gtg gcc atc        2077
Ala Ile His Arg Ile Ser Leu Glu Thr Asn Asn Asn Asp Val Ala Ile
    655                 660                 665

ccg ctc acg ggc gtc aag gag gcc tca gcc ctg gac ttt gat gtg tcc        2125
Pro Leu Thr Gly Val Lys Glu Ala Ser Ala Leu Asp Phe Asp Val Ser
670                 675                 680                 685

aac aac cac atc tac tgg aca gac gtc agc ctg aag acc atc agc cgc        2173
Asn Asn His Ile Tyr Trp Thr Asp Val Ser Leu Lys Thr Ile Ser Arg
                690                 695                 700

gcc ttc atg aac ggg agc tcg gtg gag cac gtg gtg gag ttt ggc ctt        2221
Ala Phe Met Asn Gly Ser Ser Val Glu His Val Val Glu Phe Gly Leu
            705                 710                 715

gac tac ccc gag ggc atg gcc gtt gac tgg atg ggc aag aac ctc tac        2269
Asp Tyr Pro Glu Gly Met Ala Val Asp Trp Met Gly Lys Asn Leu Tyr
        720                 725                 730

tgg gcc gac act ggg acc aac aga atc gaa gtg gcg cgg ctg gac ggg        2317
Trp Ala Asp Thr Gly Thr Asn Arg Ile Glu Val Ala Arg Leu Asp Gly
    735                 740                 745

cag ttc cgg caa gtc ctc gtg tgg agg gac ttg gac aac ccg agg tcg        2365
Gln Phe Arg Gln Val Leu Val Trp Arg Asp Leu Asp Asn Pro Arg Ser
750                 755                 760                 765
```

```
ctg gcc ctg gat ccc acc aag ggc tac atc tac tgg acc gag tgg ggc        2413
Leu Ala Leu Asp Pro Thr Lys Gly Tyr Ile Tyr Trp Thr Glu Trp Gly
                770                 775                 780

ggc aag ccg agg atc gtg cgg gcc ttc atg gac ggg acc aac tgc atg        2461
Gly Lys Pro Arg Ile Val Arg Ala Phe Met Asp Gly Thr Asn Cys Met
            785                 790                 795

acg ctg gtg gac aag gtg ggc cgg gcc aac gac ctc acc att gac tac        2509
Thr Leu Val Asp Lys Val Gly Arg Ala Asn Asp Leu Thr Ile Asp Tyr
        800                 805                 810

gct gac cag cgc ctc tac tgg acc gac ctg gac acc aac atg atc gag        2557
Ala Asp Gln Arg Leu Tyr Trp Thr Asp Leu Asp Thr Asn Met Ile Glu
    815                 820                 825

tcg tcc aac atg ctg ggt cag gag cgg gtc gtg att gcc gac gat ctc        2605
Ser Ser Asn Met Leu Gly Gln Glu Arg Val Val Ile Ala Asp Asp Leu
830                 835                 840                 845

ccg cac ccg ttc ggt ctg acg cag tac agc gat tat atc tac tgg aca        2653
Pro His Pro Phe Gly Leu Thr Gln Tyr Ser Asp Tyr Ile Tyr Trp Thr
                850                 855                 860

gac tgg aat ctg cac agc att gag cgg gcc gac aag act agc ggc cgg        2701
Asp Trp Asn Leu His Ser Ile Glu Arg Ala Asp Lys Thr Ser Gly Arg
            865                 870                 875

aac cgc acc ctc atc cag ggc cac ctg gac ttc gtg atg gac atc ctg        2749
Asn Arg Thr Leu Ile Gln Gly His Leu Asp Phe Val Met Asp Ile Leu
        880                 885                 890

gtg ttc cac tcc tcc cgc cag gat ggc ctc aat gac tgt atg cac aac        2797
Val Phe His Ser Ser Arg Gln Asp Gly Leu Asn Asp Cys Met His Asn
    895                 900                 905
```

```
aac ggg cag tgt ggg cag ctg tgc ctt gcc atc ccc ggc ggc cac cgc        2845
Asn Gly Gln Cys Gly Gln Leu Cys Leu Ala Ile Pro Gly Gly His Arg
910                 915                 920                 925

tgc ggc tgc gcc tca cac tac acc ctg gac ccc agc agc cgc aac tgc        2893
Cys Gly Cys Ala Ser His Tyr Thr Leu Asp Pro Ser Ser Arg Asn Cys
                930                 935                 940

agc ccg ccc acc acc ttc ttg ctg ttc agc cag aaa tct gcc atc agt        2941
Ser Pro Pro Thr Thr Phe Leu Leu Phe Ser Gln Lys Ser Ala Ile Ser
            945                 950                 955

cgg atg atc ccg gac gac cag cac agc ccg gat ctc atc ctg ccc ctg        2989
Arg Met Ile Pro Asp Asp Gln His Ser Pro Asp Leu Ile Leu Pro Leu
        960                 965                 970

cat gga ctg agg aac gtc aaa gcc atc gac tat gac cca ctg gac aag        3037
His Gly Leu Arg Asn Val Lys Ala Ile Asp Tyr Asp Pro Leu Asp Lys
    975                 980                 985

ttc atc tac tgg gtg gat ggg cgc cag aac atc aag cga gcc aag gac        3085
Phe Ile Tyr Trp Val Asp Gly Arg Gln Asn Ile Lys Arg Ala Lys Asp
990                 995                 1000                1005

gac ggg acc cag ccc ttt gtt ttg acc tct ctg agc caa ggc caa aac        3133
Asp Gly Thr Gln Pro Phe Val Leu Thr Ser Leu Ser Gln Gly Gln Asn
                1010                1015                1020

cca gac agg cag ccc cac gac ctc agc atc gac atc tac agc cgg aca        3181
Pro Asp Arg Gln Pro His Asp Leu Ser Ile Asp Ile Tyr Ser Arg Thr
            1025                1030                1035

ctg ttc tgg acg tgc gag gcc acc aat acc atc aac gtc cac agg ctg        3229
Leu Phe Trp Thr Cys Glu Ala Thr Asn Thr Ile Asn Val His Arg Leu
        1040                1045                1050
```

agc ggg gaa gcc atg ggg gtg gtg ctg cgt ggg gac cgc gac aag ccc 3277
Ser Gly Glu Ala Met Gly Val Val Leu Arg Gly Asp Arg Asp Lys Pro
1055 1060 1065

agg gcc atc gtc gtc aac gcg gag cga ggg tac ctg tac ttc acc aac 3325
Arg Ala Ile Val Val Asn Ala Glu Arg Gly Tyr Leu Tyr Phe Thr Asn
1070 1075 1080 1085

atg cag gac cgg gca gcc aag atc gaa cgc gca gcc ctg gac ggc acc 3373
Met Gln Asp Arg Ala Ala Lys Ile Glu Arg Ala Ala Leu Asp Gly Thr
1090 1095 1100

gag cgc gag gtc ctc ttc acc acc ggc ctc atc cgc cct gtg gcc ctg 3421
Glu Arg Glu Val Leu Phe Thr Thr Gly Leu Ile Arg Pro Val Ala Leu
1105 1110 1115

gtg gtg gac aac aca ctg ggc aag ctg ttc tgg gtg gac gcg gac ctg 3469
Val Val Asp Asn Thr Leu Gly Lys Leu Phe Trp Val Asp Ala Asp Leu
1120 1125 1130

aag cgc att gag agc tgt gac ctg tca ggg gcc aac cgc ctg acc ctg 3517
Lys Arg Ile Glu Ser Cys Asp Leu Ser Gly Ala Asn Arg Leu Thr Leu
1135 1140 1145

gag gac gcc aac atc gtg cag cct ctg ggc ctg acc atc ctt ggc aag 3565
Glu Asp Ala Asn Ile Val Gln Pro Leu Gly Leu Thr Ile Leu Gly Lys
1150 1155 1160 1165

cat ctc tac tgg atc gac cgc cag cag cag atg atc gag cgt gtg gag 3613
His Leu Tyr Trp Ile Asp Arg Gln Gln Gln Met Ile Glu Arg Val Glu
1170 1175 1180

aag acc acc ggg gac aag cgg act cgc atc cag ggc cgt gtc gcc cac 3661
Lys Thr Thr Gly Asp Lys Arg Thr Arg Ile Gln Gly Arg Val Ala His
1185 1190 1195

ctc act ggc atc cat gca gtg gag gaa gtc agc ctg gag gag ttc tca 3709
Leu Thr Gly Ile His Ala Val Glu Glu Val Ser Leu Glu Glu Phe Ser
1200 1205 1210

gcc cac cca tgt gcc cgt gac aat ggt ggc tgc tcc cac atc tgt att 3757
Ala His Pro Cys Ala Arg Asp Asn Gly Gly Cys Ser His Ile Cys Ile
1215 1220 1225

gcc aag ggt gat ggg aca cca cgg tgc tca tgc cca gtc cac ctc gtg 3805
Ala Lys Gly Asp Gly Thr Pro Arg Cys Ser Cys Pro Val His Leu Val
1230 1235 1240 1245

ctc ctg cag aac ctg ctg acc tgt gga gag ccg ccc acc tgc tcc ccg 3853
Leu Leu Gln Asn Leu Leu Thr Cys Gly Glu Pro Pro Thr Cys Ser Pro
1250 1255 1260

gac cag ttt gca tgt gcc aca ggg gag atc gac tgt atc ccc ggg gcc 3901
Asp Gln Phe Ala Cys Ala Thr Gly Glu Ile Asp Cys Ile Pro Gly Ala
1265 1270 1275

tgg cgc tgt gac ggc ttt ccc gag tgc gat gac cag agc gac gag gag 3949
Trp Arg Cys Asp Gly Phe Pro Glu Cys Asp Asp Gln Ser Asp Glu Glu
1280 1285 1290

ggc tgc ccc gtg tgc tcc gcc gcc cag ttc ccc tgc gcg cgg ggt cag 3997
Gly Cys Pro Val Cys Ser Ala Ala Gln Phe Pro Cys Ala Arg Gly Gln
1295 1300 1305

tgt gtg gac ctg cgc ctg cgc tgc gac ggc gag gca gac tgt cag gac 4045
Cys Val Asp Leu Arg Leu Arg Cys Asp Gly Glu Ala Asp Cys Gln Asp
1310 1315 1320 1325

cgc tca gac gag gtg gac tgt gac gcc atc tgc ctg ccc aac cag ttc 4093
Arg Ser Asp Glu Val Asp Cys Asp Ala Ile Cys Leu Pro Asn Gln Phe
1330 1335 1340

cgg tgt gcg agc ggc cag tgt gtc ctc atc aaa cag cag tgc gac tcc 4141
Arg Cys Ala Ser Gly Gln Cys Val Leu Ile Lys Gln Gln Cys Asp Ser
1345 1350 1355

ttc ccc gac tgt atc gac ggc tcc gac gag ctc atg tgt gaa atc acc 4189
Phe Pro Asp Cys Ile Asp Gly Ser Asp Glu Leu Met Cys Glu Ile Thr
1360 1365 1370

aag ccg ccc tca gac gac agc ccg gcc cac agc agt gcc atc ggg ccc 4237
Lys Pro Pro Ser Asp Asp Ser Pro Ala His Ser Ser Ala Ile Gly Pro
1375 1380 1385

gtc att ggc atc atc ctc tct ctc ttc gtc atg ggt ggt gtc tat ttt 4285
Val Ile Gly Ile Ile Leu Ser Leu Phe Val Met Gly Gly Val Tyr Phe
1390 1395 1400 1405

gtg tgc cag cgc gtg gtg tgc cag cgc tat gcg ggg gcc aac ggg ccc 4333
Val Cys Gln Arg Val Val Cys Gln Arg Tyr Ala Gly Ala Asn Gly Pro
1410 1415 1420

ttc ccg cac gag tat gtc agc ggg acc ccg cac gtg ccc ctc aat ttc 4381
Phe Pro His Glu Tyr Val Ser Gly Thr Pro His Val Pro Leu Asn Phe
1425 1430 1435

ata gcc ccg ggc ggt tcc cag cat ggc ccc ttc aca ggc atc gca tgc 4429
Ile Ala Pro Gly Gly Ser Gln His Gly Pro Phe Thr Gly Ile Ala Cys
1440 1445 1450

gga aag tcc atg atg agc tcc gtg agc ctg atg ggg ggc cgg ggc ggg 4477
Gly Lys Ser Met Met Ser Ser Val Ser Leu Met Gly Gly Arg Gly Gly
1455 1460 1465

gtg ccc ctc tac gac cgg aac cac gtc aca ggg gcc tcg tcc agc agc 4525
Val Pro Leu Tyr Asp Arg Asn His Val Thr Gly Ala Ser Ser Ser Ser
1470 1475 1480 1485

tcg tcc agc acg aag gcc acg ctg tac ccg ccg atc ctg aac ccg ccg 4573
Ser Ser Ser Thr Lys Ala Thr Leu Tyr Pro Pro Ile Leu Asn Pro Pro
1490 1495 1500

ccc tcc ccg gcc acg gac ccc tcc ctg tac aac atg gac atg ttc tac 4621
Pro Ser Pro Ala Thr Asp Pro Ser Leu Tyr Asn Met Asp Met Phe Tyr
1505 1510 1515

tct tca aac att ccg gcc act gcg aga ccg tac agg ccc tac atc att 4669
Ser Ser Asn Ile Pro Ala Thr Ala Arg Pro Tyr Arg Pro Tyr Ile Ile
1520 1525 1530

cga gga atg gcg ccc ccg acg acg ccc tgc agc acc gac gtg tgt gac 4717
Arg Gly Met Ala Pro Pro Thr Thr Pro Cys Ser Thr Asp Val Cys Asp
1535 1540 1545

agc gac tac agc gcc agc cgc tgg aag gcc agc aag tac tac ctg gat 4765
Ser Asp Tyr Ser Ala Ser Arg Trp Lys Ala Ser Lys Tyr Tyr Leu Asp
1550 1555 1560 1565

ttg aac tcg gac tca gac ccc tat cca ccc cca ccc acg ccc cac agc 4813
Leu Asn Ser Asp Ser Asp Pro Tyr Pro Pro Pro Pro Thr Pro His Ser
1570 1575 1580

cag tac ctg tcg gcg gag gac agc tgc ccg ccc tcg ccc gcc acc gag 4861
Gln Tyr Leu Ser Ala Glu Asp Ser Cys Pro Pro Ser Pro Ala Thr Glu
1585 1590 1595

agg agc tac ttc cat ctc ttc ccg ccc cct ccg tcc ccc tgc acg gac 4909
Arg Ser Tyr Phe His Leu Phe Pro Pro Pro Pro Ser Pro Cys Thr Asp
1600 1605 1610

tca tcc tgacctcggc cgggccactc tggcttctct gtgcccctgt aaatagtttt 4965
Ser Ser
1615

aaatatgaac aaagaaaaaa atatatttta tgatttaaaa aataaatata attgggattt 5025

taaaaacatg agaaatgtga actgtgatgg ggtgggcagg gctgggagaa ctttgtacag 5085

tggagaaata tttataaact taattttgta aaaca 5120

<210> 3

<211> 1615

<212> PRT

<213> Homo sapiens

<400> 3

Met Glu Ala Ala Pro Pro Gly Pro Pro Trp Pro Leu Leu Leu Leu Leu

1 5 10 15

Leu Leu Leu Leu Ala Leu Cys Gly Cys Pro Ala Pro Ala Ala Ala Ser

20 25 30

Pro Leu Leu Leu Phe Ala Asn Arg Arg Asp Val Arg Leu Val Asp Ala

35 40 45

Gly Gly Val Lys Leu Glu Ser Thr Ile Val Val Ser Gly Leu Glu Asp

50 55 60

Ala Ala Ala Val Asp Phe Gln Phe Ser Lys Gly Ala Val Tyr Trp Thr

65 70 75 80

Asp Val Ser Glu Glu Ala Ile Lys Gln Thr Tyr Leu Asn Gln Thr Gly

85 90 95

Ala Ala Val Gln Asn Val Val Ile Ser Gly Leu Val Ser Pro Asp Gly

100 105 110

Leu Ala Cys Asp Trp Val Gly Lys Lys Leu Tyr Trp Thr Asp Ser Glu

115 120 125

Thr Asn Arg Ile Glu Val Ala Asn Leu Asn Gly Thr Ser Arg Lys Val

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

Arg Arg Ile Ser Leu Asp Thr Pro Asp Phe Thr Asp Ile Val Leu Gln
355 360 365

Val Asp Asp Ile Arg His Ala Ile Ala Ile Asp Tyr Asp Pro Leu Glu
370 375 380

Gly Tyr Val Tyr Trp Thr Asp Asp Glu Val Arg Ala Ile Arg Arg Ala
385 390 395 400

Tyr Leu Asp Gly Ser Gly Ala Gln Thr Leu Val Asn Thr Glu Ile Asn
405 410 415

Asp Pro Asp Gly Ile Ala Val Asp Trp Val Ala Arg Asn Leu Tyr Trp
420 425 430

Thr Asp Thr Gly Thr Asp Arg Ile Glu Val Thr Arg Leu Asn Gly Thr
435 440 445

Ser Arg Lys Ile Leu Val Ser Glu Asp Leu Asp Glu Pro Arg Ala Ile
450 455 460

Ala Leu His Pro Val Met Gly Leu Met Tyr Trp Thr Asp Trp Gly Glu
465 470 475 480

Asn Pro Lys Ile Glu Cys Ala Asn Leu Asp Gly Gln Glu Arg Arg Val
485 490 495

Leu Val Asn Ala Ser Leu Gly Trp Pro Asn Gly Leu Ala Leu Asp Leu
500 505 510

Gln Glu Gly Lys Leu Tyr Trp Gly Asp Ala Lys Thr Asp Lys Ile Glu
515 520 525

Val Ile Asn Val Asp Gly Thr Lys Arg Arg Thr Leu Leu Glu Asp Lys
530 535 540

Leu Pro His Ile Phe Gly Phe Thr Leu Leu Gly Asp Phe Ile Tyr Trp
545 550 555 560

Thr Asp Trp Gln Arg Arg Ser Ile Glu Arg Val His Lys Val Lys Ala

565 570 575

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

580 585 590

Ala Val Asn Val Ala Lys Val Val Gly Thr Asn Pro Cys Ala Asp Arg

595 600 605

Asn Gly Gly Cys Ser His Leu Cys Phe Phe Thr Pro His Ala Thr Arg

610 615 620

Cys Gly Cys Pro Ile Gly Leu Glu Leu Leu Ser Asp Met Lys Thr Cys

625 630 635 640

Ile Val Pro Glu Ala Phe Leu Val Phe Thr Ser Arg Ala Ala Ile His

645 650 655

Arg Ile Ser Leu Glu Thr Asn Asn Asn Asp Val Ala Ile Pro Leu Thr

660 665 670

Gly Val Lys Glu Ala Ser Ala Leu Asp Phe Asp Val Ser Asn Asn His

675 680 685

Ile Tyr Trp Thr Asp Val Ser Leu Lys Asn Ile Ser Arg Ala Phe Met

690 695 700

Asn Gly Ser Ser Val Glu His Val Val Glu Phe Gly Leu Asp Tyr Pro

705 710 715 720

Glu Gly Met Ala Val Asp Trp Met Gly Lys Asn Leu Tyr Trp Ala Asp

725 730 735

Thr Gly Thr Asn Arg Ile Glu Val Ala Arg Leu Asp Gly Gln Phe Arg

740 745 750

Gln Val Leu Val Trp Arg Asp Leu Asp Asn Pro Arg Ser Leu Ala Leu

755 760 765

Asp Pro Thr Lys Gly Tyr Ile Tyr Trp Thr Glu Trp Gly Gly Lys Pro

770 775 780

Arg Ile Val Arg Ala Phe Met Asp Gly Thr Asn Cys Met Thr Leu Val
785 790 795 800

Asp Lys Val Gly Arg Ala Asn Asp Leu Thr Ile Asp Tyr Ala Asp Gln
805 810 815

Arg Leu Tyr Trp Thr Asp Leu Asp Thr Asn Met Ile Glu Ser Ser Asn
820 825 830

Met Leu Gly Gln Glu Arg Val Val Ile Ala Asp Asp Leu Pro His Pro
835 840 845

Phe Gly Leu Thr Gln Tyr Ser Asp Tyr Ile Tyr Trp Thr Asp Trp Asn
850 855 860

Leu His Ser Ile Glu Arg Ala Asp Lys Thr Ser Gly Arg Asn Arg Thr
865 870 875 880

Leu Ile Gln Gly His Leu Asp Phe Val Met Asp Ile Leu Val Phe His
885 890 895

Ser Ser Arg Gln Asp Gly Leu Asn Asp Cys Met His Asn Asn Gly Gln
900 905 910

Cys Gly Gln Leu Cys Leu Ala Ile Pro Gly Gly His Arg Cys Gly Cys
915 920 925

Ala Ser His Tyr Thr Leu Asp Pro Ser Ser Arg Asn Cys Ser Pro Pro
930 935 940

Thr Thr Phe Leu Leu Phe Ser Gln Lys Ser Ala Ile Ser Arg Met Ile
945 950 955 960

Pro Asp Asp Gln His Ser Pro Asp Leu Ile Leu Pro Leu His Gly Leu
965 970 975

Arg Asn Val Lys Ala Ile Asp Tyr Asp Pro Leu Asp Lys Phe Ile Tyr
980 985 990

Trp Val Asp Gly Arg Gln Asn Ile Lys Arg Ala Lys Asp Asp Gly Thr

995 1000 1005

Gln Pro Phe Val Leu Thr Ser Leu Ser Gln Gly Gln Asn Pro Asp Arg

1010 1015 1020

Gln Pro His Asp Leu Ser Ile Asp Ile Tyr Ser Arg Thr Leu Phe Trp

1025 1030 1035 1040

Thr Cys Glu Ala Thr Asn Thr Ile Asn Val His Arg Leu Ser Gly Glu

1045 1050 1055

Ala Met Gly Val Val Leu Arg Gly Asp Arg Asp Lys Pro Arg Ala Ile

1060 1065 1070

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

1075 1080 1085

Arg Ala Ala Lys Ile Glu Arg Ala Ala Leu Asp Gly Thr Glu Arg Glu

1090 1095 1100

Val Leu Phe Thr Thr Gly Leu Ile Arg Pro Val Ala Leu Val Val Asp

1105 1110 1115 1120

Asn Thr Leu Gly Lys Leu Phe Trp Val Asp Ala Asp Leu Lys Arg Ile

1125 1130 1135

Glu Ser Cys Asp Leu Ser Gly Ala Asn Arg Leu Thr Leu Glu Asp Ala

1140 1145 1150

Asn Ile Val Gln Pro Leu Gly Leu Thr Ile Leu Gly Lys His Leu Tyr

1155 1160 1165

Trp Ile Asp Arg Gln Gln Gln Met Ile Glu Arg Val Glu Lys Thr Thr

1170 1175 1180

Gly Asp Lys Arg Thr Arg Ile Gln Gly Arg Val Ala His Leu Thr Gly

1185 1190 1195 1200

Ile His Ala Val Glu Glu Val Ser Leu Glu Glu Phe Ser Ala His Pro

1205 1210 1215

Cys Ala Arg Asp Asn Gly Gly Cys Ser His Ile Cys Ile Ala Lys Gly
1220 1225 1230

Asp Gly Thr Pro Arg Cys Ser Cys Pro Val His Leu Val Leu Leu Gln
1235 1240 1245

Asn Leu Leu Thr Cys Gly Glu Pro Pro Thr Cys Ser Pro Asp Gln Phe
1250 1255 1260

Ala Cys Ala Thr Gly Glu Ile Asp Cys Ile Pro Gly Ala Trp Arg Cys
1265 1270 1275 1280

Asp Gly Phe Pro Glu Cys Asp Asp Gln Ser Asp Glu Glu Gly Cys Pro
1285 1290 1295

Val Cys Ser Ala Ala Gln Phe Pro Cys Ala Arg Gly Gln Cys Val Asp
1300 1305 1310

Leu Arg Leu Arg Cys Asp Gly Glu Ala Asp Cys Gln Asp Arg Ser Asp
1315 1320 1325

Glu Val Asp Cys Asp Ala Ile Cys Leu Pro Asn Gln Phe Arg Cys Ala
1330 1335 1340

Ser Gly Gln Cys Val Leu Ile Lys Gln Gln Cys Asp Ser Phe Pro Asp
1345 1350 1355 1360

Cys Ile Asp Gly Ser Asp Glu Leu Met Cys Glu Ile Thr Lys Pro Pro
1365 1370 1375

Ser Asp Asp Ser Pro Ala His Ser Ser Ala Ile Gly Pro Val Ile Gly
1380 1385 1390

Ile Ile Leu Ser Leu Phe Val Met Gly Gly Val Tyr Phe Val Cys Gln
1395 1400 1405

Arg Val Val Cys Gln Arg Tyr Ala Gly Ala Asn Gly Pro Phe Pro His
1410 1415 1420

Glu Tyr Val Ser Gly Thr Pro His Val Pro Leu Asn Phe Ile Ala Pro

1425 1430 1435 1440

Gly Gly Ser Gln His Gly Pro Phe Thr Gly Ile Ala Cys Gly Lys Ser

1445 1450 1455

Met Met Ser Ser Val Ser Leu Met Gly Gly Arg Gly Gly Val Pro Leu

1460 1465 1470

Tyr Asp Arg Asn His Val Thr Gly Ala Ser Ser Ser Ser Ser Ser Ser

1475 1480 1485

Thr Lys Ala Thr Leu Tyr Pro Pro Ile Leu Asn Pro Pro Pro Ser Pro

1490 1495 1500

Ala Thr Asp Pro Ser Leu Tyr Asn Met Asp Met Phe Tyr Ser Ser Asn

1505 1510 1515 1520

Ile Pro Ala Thr Ala Arg Pro Tyr Arg Pro Tyr Ile Ile Arg Gly Met

1525 1530 1535

Ala Pro Pro Thr Thr Pro Cys Ser Thr Asp Val Cys Asp Ser Asp Tyr

1540 1545 1550

Ser Ala Ser Arg Trp Lys Ala Ser Lys Tyr Tyr Leu Asp Leu Asn Ser

1555 1560 1565

Asp Ser Asp Pro Tyr Pro Pro Pro Pro Thr Pro His Ser Gln Tyr Leu

1570 1575 1580

Ser Ala Glu Asp Ser Cys Pro Pro Ser Pro Ala Thr Glu Arg Ser Tyr

1585 1590 1595 1600

Phe His Leu Phe Pro Pro Pro Pro Ser Pro Cys Thr Asp Ser Ser

1605 1610 1615

<210> 4

<211> 1615

<212> PRT

<213> Homo sapiens

<400> 4

Met Glu Ala Ala Pro Pro Gly Pro Pro Trp Pro Leu Leu Leu Leu Leu
1 5 10 15

Leu Leu Leu Leu Ala Leu Cys Gly Cys Pro Ala Pro Ala Ala Ala Ser
20 25 30

Pro Leu Leu Leu Phe Ala Asn Arg Arg Asp Val Arg Leu Val Asp Ala
35 40 45

Gly Gly Val Lys Leu Glu Ser Thr Ile Val Val Ser Gly Leu Glu Asp
50 55 60

Ala Ala Ala Val Asp Phe Gln Phe Ser Lys Gly Ala Val Tyr Trp Thr
65 70 75 80

Asp Val Ser Glu Glu Ala Ile Lys Gln Thr Tyr Leu Asn Gln Thr Gly
85 90 95

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

Leu Ala Cys Asp Trp Val Gly Lys Lys Leu Tyr Trp Thr Asp Ser Glu
115 120 125

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

Leu Phe Trp Gln Asp Leu Asp Gln Pro Lys Ala Ile Ala Leu Asp Pro
145 150 155 160

Ala His Gly Tyr Met Tyr Trp Thr Asp Trp Val Glu Thr Pro Arg Ile
165 170 175

Glu Arg Ala Gly Met Asp Gly Ser Thr Arg Lys Ile Ile Val Asp Ser

180 185 190

Asp Ile Tyr Trp Pro Asn Gly Leu Thr Ile Asp Leu Glu Glu Gln Lys

195 200 205

Leu Tyr Trp Ala Asp Ala Lys Leu Ser Phe Ile His Arg Ala Asn Leu

210 215 220

Asp Gly Ser Phe Arg Gln Lys Val Val Glu Gly Ser Leu Thr His Pro

225 230 235 240

Phe Ala Leu Thr Leu Ser Gly Asp Thr Leu Tyr Trp Thr Asp Trp Gln

245 250 255

Thr Arg Ser Ile His Ala Cys Asn Lys Arg Thr Gly Gly Lys Arg Lys

260 265 270

Glu Ile Leu Ser Ala Leu Tyr Ser Pro Met Asp Ile Gln Val Leu Ser

275 280 285

Gln Glu Arg Gln Pro Phe Phe His Thr Arg Cys Glu Glu Asp Asn Gly

290 295 300

Gly Trp Ser His Leu Cys Leu Leu Ser Pro Ser Glu Pro Phe Tyr Thr

305 310 315 320

Cys Ala Cys Pro Thr Gly Val Gln Met Gln Asp Asn Gly Arg Thr Cys

325 330 335

Lys Ala Gly Ala Glu Glu Val Leu Leu Leu Ala Arg Arg Thr Asp Leu

340 345 350

Arg Arg Ile Ser Leu Asp Thr Pro Asp Phe Thr Asp Ile Val Leu Gln

355 360 365

Val Asp Asp Ile Arg His Ala Ile Ala Ile Asp Tyr Asp Pro Leu Glu

370 375 380

Gly Tyr Val Tyr Trp Thr Asp Asp Glu Val Arg Ala Ile Arg Arg Ala

385 390 395 400

Tyr Leu Asp Gly Ser Gly Ala Gln Thr Leu Val Asn Thr Glu Ile Asn
405 410 415

Asp Pro Asp Gly Ile Ala Val Asp Trp Val Ala Arg Asn Leu Tyr Trp
420 425 430

Thr Asp Thr Gly Thr Asp Arg Ile Glu Val Thr Arg Leu Asn Gly Thr
435 440 445

Ser Arg Lys Ile Leu Val Ser Glu Asp Leu Asp Glu Pro Arg Ala Ile
450 455 460

Ala Leu His Pro Val Met Gly Leu Met Tyr Trp Thr Asp Trp Gly Glu
465 470 475 480

Asn Pro Lys Ile Glu Cys Ala Asn Leu Asp Gly Gln Glu Arg Arg Val
485 490 495

Leu Val Asn Ala Ser Leu Gly Trp Pro Asn Gly Leu Ala Leu Asp Leu
500 505 510

Gln Glu Gly Lys Leu Tyr Trp Gly Asp Ala Lys Thr Asp Lys Ile Glu
515 520 525

Val Ile Asn Val Asp Gly Thr Lys Arg Arg Thr Leu Leu Glu Asp Lys
530 535 540

Leu Pro His Ile Phe Gly Phe Thr Leu Leu Gly Asp Phe Ile Tyr Trp
545 550 555 560

Thr Asp Trp Gln Arg Arg Ser Ile Glu Arg Val His Lys Val Lys Ala
565 570 575

Ser Arg Asp Val Ile Ile Asp Gln Leu Pro Asp Leu Met Gly Leu Lys
580 585 590

Ala Val Asn Val Ala Lys Val Val Gly Thr Asn Pro Cys Ala Asp Arg
595 600 605

Asn Gly Gly Cys Ser His Leu Cys Phe Phe Thr Pro His Ala Thr Arg

610 615 620

Cys Gly Cys Pro Ile Gly Leu Glu Leu Leu Ser Asp Met Lys Thr Cys

625 630 635 640

Ile Val Pro Glu Ala Phe Leu Val Phe Thr Ser Arg Ala Ala Ile His

645 650 655

Arg Ile Ser Leu Glu Thr Asn Asn Asn Asp Val Ala Ile Pro Leu Thr

660 665 670

Gly Val Lys Glu Ala Ser Ala Leu Asp Phe Asp Val Ser Asn Asn His

675 680 685

Ile Tyr Trp Thr Asp Val Ser Leu Lys Asn Ile Ser Arg Ala Phe Met

690 695 700

Asn Gly Ser Ser Val Glu His Val Val Glu Phe Gly Leu Asp Tyr Pro

705 710 715 720

Glu Gly Met Ala Val Asp Trp Met Gly Lys Asn Leu Tyr Trp Ala Asp

725 730 735

Thr Gly Thr Asn Arg Ile Glu Val Ala Arg Leu Asp Gly Gln Phe Arg

740 745 750

Gln Val Leu Val Trp Arg Asp Leu Asp Asn Pro Arg Ser Leu Ala Leu

755 760 765

Asp Pro Thr Lys Gly Tyr Ile Tyr Trp Thr Glu Trp Gly Gly Lys Pro

770 775 780

Arg Ile Val Arg Ala Phe Met Asp Gly Thr Asn Cys Met Thr Leu Val

785 790 795 800

Asp Lys Val Gly Arg Ala Asn Asp Leu Thr Ile Asp Tyr Ala Asp Gln

805 810 815

Arg Leu Tyr Trp Thr Asp Leu Asp Thr Asn Met Ile Glu Ser Ser Asn

820 825 830

Met Leu Gly Gln Glu Arg Val Val Ile Ala Asp Asp Leu Pro His Pro
835 840 845

Phe Gly Leu Thr Gln Tyr Ser Asp Tyr Ile Tyr Trp Thr Asp Trp Asn
850 855 860

Leu His Ser Ile Glu Arg Ala Asp Lys Thr Ser Gly Arg Asn Arg Thr
865 870 875 880

Leu Ile Gln Gly His Leu Asp Phe Val Met Asp Ile Leu Val Phe His
885 890 895

Ser Ser Arg Gln Asp Gly Leu Asn Asp Cys Met His Asn Asn Gly Gln
900 905 910

Cys Gly Gln Leu Cys Leu Ala Ile Pro Gly Gly His Arg Cys Gly Cys
915 920 925

Ala Ser His Tyr Thr Leu Asp Pro Ser Ser Arg Asn Cys Ser Pro Pro
930 935 940

Thr Thr Phe Leu Leu Phe Ser Gln Lys Ser Ala Ile Ser Arg Met Ile
945 950 955 960

Pro Asp Asp Gln His Ser Pro Asp Leu Ile Leu Pro Leu His Gly Leu
965 970 975

Arg Asn Val Lys Ala Ile Asp Tyr Asp Pro Leu Asp Lys Phe Ile Tyr
980 985 990

Trp Val Asp Gly Arg Gln Asn Ile Lys Arg Ala Lys Asp Asp Gly Thr
995 1000 1005

Gln Pro Phe Val Leu Thr Ser Leu Ser Gln Gly Gln Asn Pro Asp Arg
1010 1015 1020

Gln Pro His Asp Leu Ser Ile Asp Ile Tyr Ser Arg Thr Leu Phe Trp
1025 1030 1035 1040

Thr Cys Glu Ala Thr Asn Thr Ile Asn Val His Arg Leu Ser Gly Glu

1045 1050 1055

Ala Met Gly Val Val Leu Arg Gly Asp Arg Asp Lys Pro Arg Ala Ile

1060 1065 1070

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

1075 1080 1085

Arg Ala Ala Lys Ile Glu Arg Ala Ala Leu Asp Gly Thr Glu Arg Glu

1090 1095 1100

Val Leu Phe Thr Thr Gly Leu Ile Arg Pro Val Ala Leu Val Val Asp

1105 1110 1115 1120

Asn Thr Leu Gly Lys Leu Phe Trp Val Asp Ala Asp Leu Lys Arg Ile

1125 1130 1135

Glu Ser Cys Asp Leu Ser Gly Ala Asn Arg Leu Thr Leu Glu Asp Ala

1140 1145 1150

Asn Ile Val Gln Pro Leu Gly Leu Thr Ile Leu Gly Lys His Leu Tyr

1155 1160 1165

Trp Ile Asp Arg Gln Gln Gln Met Ile Glu Arg Val Glu Lys Thr Thr

1170 1175 1180

Gly Asp Lys Arg Thr Arg Ile Gln Gly Arg Val Ala His Leu Thr Gly

1185 1190 1195 1200

Ile His Ala Val Glu Glu Val Ser Leu Glu Glu Phe Ser Ala His Pro

1205 1210 1215

Cys Ala Arg Asp Asn Gly Gly Cys Ser His Ile Cys Ile Ala Lys Gly

1220 1225 1230

Asp Gly Thr Pro Arg Cys Ser Cys Pro Val His Leu Val Leu Leu Gln

1235 1240 1245

Asn Leu Leu Thr Cys Gly Glu Pro Pro Thr Cys Ser Pro Asp Gln Phe

1250 1255 1260

Ala Cys Ala Thr Gly Glu Ile Asp Cys Ile Pro Gly Ala Trp Arg Cys
1265 1270 1275 1280

Asp Gly Phe Pro Glu Cys Asp Asp Gln Ser Asp Glu Glu Gly Cys Pro
1285 1290 1295

Val Cys Ser Ala Ala Gln Phe Pro Cys Ala Arg Gly Gln Cys Val Asp
1300 1305 1310

Leu Arg Leu Arg Cys Asp Gly Glu Ala Asp Cys Gln Asp Arg Ser Asp
1315 1320 1325

Glu Val Asp Cys Asp Ala Ile Cys Leu Pro Asn Gln Phe Arg Cys Ala
1330 1335 1340

Ser Gly Gln Cys Val Leu Ile Lys Gln Gln Cys Asp Ser Phe Pro Asp
1345 1350 1355 1360

Cys Ile Asp Gly Ser Asp Glu Leu Met Cys Glu Ile Thr Lys Pro Pro
1365 1370 1375

Ser Asp Asp Ser Pro Ala His Ser Ser Ala Ile Gly Pro Val Ile Gly
1380 1385 1390

Ile Ile Leu Ser Leu Phe Val Met Gly Gly Val Tyr Phe Val Cys Gln
1395 1400 1405

Arg Val Val Cys Gln Arg Tyr Ala Gly Ala Asn Gly Pro Phe Pro His
1410 1415 1420

Glu Tyr Val Ser Gly Thr Pro His Val Pro Leu Asn Phe Ile Ala Pro
1425 1430 1435 1440

Gly Gly Ser Gln His Gly Pro Phe Thr Gly Ile Ala Cys Gly Lys Ser
1445 1450 1455

Met Met Ser Ser Val Ser Leu Met Gly Gly Arg Gly Gly Val Pro Leu
1460 1465 1470

Tyr Asp Arg Asn His Val Thr Gly Ala Ser Ser Ser Ser Ser Ser Ser

1475 1480 1485

Thr Lys Ala Thr Leu Tyr Pro Pro Ile Leu Asn Pro Pro Pro Ser Pro

1490 1495 1500

Ala Thr Asp Pro Ser Leu Tyr Asn Met Asp Met Phe Tyr Ser Ser Asn

1505 1510 1515 1520

Ile Pro Ala Thr Ala Arg Pro Tyr Arg Pro Tyr Ile Ile Arg Gly Met

1525 1530 1535

Ala Pro Pro Thr Thr Pro Cys Ser Thr Asp Val Cys Asp Ser Asp Tyr

1540 1545 1550

Ser Ala Ser Arg Trp Lys Ala Ser Lys Tyr Tyr Leu Asp Leu Asn Ser

1555 1560 1565

Asp Ser Asp Pro Tyr Pro Pro Pro Pro Thr Pro His Ser Gln Tyr Leu

1570 1575 1580

Ser Ala Glu Asp Ser Cys Pro Pro Ser Pro Ala Thr Glu Arg Ser Tyr

1585 1590 1595 1600

Phe His Leu Phe Pro Pro Pro Pro Ser Pro Cys Thr Asp Ser Ser

1605 1610 1615

<210> 5

<211> 3096

<212> DNA

<213> Homo sapiens

<400> 5

catcttctca cacgatctct cgcttcgcac tccttccttt gattggtttt caccatttac 60

tcagacgacg gtccttcttc gatctttgca cattcttcta tcatctacta ccttcatacc 120

cagctccgtc ccctaatatt catgcgcgga tggcccattc cgtggtgaaa attcccttct 180

actctgctaa tctgctgttc tctctccctc ccgtcgggtt ctgctcctgc cacgttctcc 240

cctctcccca ccaaaggctg ggttttcttt gtcagggctc ctttcccctt tggaagaagg 300

ggggctgtat ggccttggtg cgaggccctc cagtgacagg atcccccatc acccagagtt 360

ccacaggccc tggtagggag gagggggagc agaagaggag gtgccatctt tgcctgctgg 420

ggaagggcag gggccaccca cacagagctc tcccatttgc tgtggaccct ggggccactg 480

cccagttcct tccaaaggaa agccagctcc ccaggtggtg ggagagtgat atggcttcct 540

cttaaactta gggaattgag tgtgtggttg cttctaagtg ccttagaagc cgggagcggc 600

tcctggaaag agcctgcctg ccacagcggg ccttaccctg gctgtgccca cagatgtccc 660

tggggcctgc cgctcctgcc cggctctcct ggcctccccc ggtgtgggtt gggaaaagca 720

cagcaaatta aaaaacacct ccatctctgg cctttgaaga atgcatctga acagccgaga 780

gtgtaaaccg tggtgaaatg tggtctttcc agtttgggga gaagcagggc agagctgggg 840

cttttgtacc cagggtttcc aagagctcct gcctccctcg gctgggctgg ccagggcccc 900

ccgctgggac ctccagctgt aatagggaag gttttactgg gttgctggcc actgtggact 960

gcccctaagg gcaggtatgc ctgcctttac ccgggttccc ctcctgcctg gaagatacag 1020

cccatgggag gcctgttgtc tgtgggatcc tccagcatca gagacactgg ggccagcgtc 1080

tgcctggtga ggtgcaggcc tggcaggccc ggtcccccac ctgcttgagc acccacggtg 1140

gtgggggctc gctgcctccc gagacaatct atgtcattgt tgtccaagga agctaatttа 1200

gagtagaaag ttccgtgtcc agtcccactc tgtgcgtgtg ttagcagggg actctcgggc 1260

cggagctggg tccaccctgg tagggggact tcatggggcc tgggcgacag cactgtgtat 1320

ttgtgtgtgt gtgtgtttgt gtgtgtgtgt gtctgaggag gtggaccagt ttctcaaaag 1380

gcctgtgacc ccaagaacca aggaatttca gcctgggtgg atcacacctt cactggtgag 1440

tgggacaagc tgggggccct cgccacagga gcagccaggg catggggcac agttggcctc 1500

attcacaaaa tgggagtata agtgatccct gctctggcgg ccaggacgat gagtgggaac 1560

acaccgtgtg ggggctgcct ggcctgggtg tgccgcgggt gtccttgttg gtgatggttc 1620

cacctgcttg tgccaccagt gccctctggg tctcacacac aactctcttc ccagcgaagg 1680

cccctcctgc cctcaggcct cagtgctgct tccgtctcgg aaggccccag gagctcctgc 1740

atcctgggcg tgattcctgt gtgcctgcag acccccctcgc ggctgccatc tcatcctttg 1800

gtgcacctgt tggccagacc tcctggtagc gggtgctgca ctcccctgaa tgtgccgggg 1860

cctgggggca gggacctggg ctcctccctc actgagtgga gggaactcag tgtcttggag 1920

ttggggtgcc tgcaggctgg gtggtgcagg tgaaatgcag acctctcagc tggtgttcca 1980

gagcagctgc cttcccccgc ccgagggact tcacccgcag cccagtcagg ggtggcgcct 2040

gggtgcatcg cccgcaggct gggtaggggt ggagcctggg tggccctgcc tgtgagctgc 2100

atagttgtcg cctttgaccc tgagttttct tcgttatctg tttggacctg tttggggcag 2160

gcaggggatg agatctgaag ataaatgcct tagctgtgac catctccttt tgtgagaggt 2220

caatgtccag ttccgctgca gttataacat cccatttttt gatttctttt tatttttcc 2280

tttttctttt tgagatggag tctcgctctg tcacccaggc tggagtgcaa tggggtgacc 2340

tcagctcact gcaacctcca cttctcgggt tcaagtgatt ctcctgcctc agcctcctga 2400

ctagcagggg ttacaggcgt gagccaccac gcccagctaa tttttgtatt tttagtagag 2460

gcaaggtttc gtcatgttgg ccaggctggt ctcaaactcc tggccttaag tgatctgccc 2520

gcctcggcct cccaaagtgc tgagatgaca ggtgtgagcc accgtgcccg gcccagaact 2580

ctttaattcc cacctgaaac ttgccgcctt aagcaggtcc ccagtctccc tcccctagtc 2640

cctggtccca ccattctgct ttctgtctca atgaatttgc ctaccgtaag tacctcatat 2700

aaattgaatc ataaagtatt tgtctttttа tatctggctt atttcactta gcataacatt 2760

cttaagtttc atccatgttg tagcatgtgt cagaatctct ctctttttt ttttttttt 2820

ttttttttt ttttgcagac agagtctcgc tctgtcatct agactggagt tcagtggcac 2880

gatctcggtt cactgcaaca tctgcctcct gggtccaagc aattctcctg cctcagcctc 2940

cttagcagct ggaactacag gcgcgtgcca ccatgccttg ctaatttttg tatttttatg 3000

tggaggcagg gtttcaccat cttggccagg ctggtctcga attcctggtc ttcaccacgg 3060

gggcccgaag gacccgggca aagcgtggag gggagg 3096

<210> 6

<211> 26928

<212> DNA

<213> Homo sapiens

<220>

<221> unsure

<222> (12044),(12489),(26433),(26434),(26435),(26436),(26439),(26441)

<223> Identity of nucleotide sequences at the above locations are unknown.

<400> 6

gaagaccaag ggcacacagc gaggcagttt cagggcgggc agcctggggc cccacggggc 60

ggccccggac acttgttctc acctgtggag ggcagagaag ggaacaggga gagaagtggc 120

cggctgggag tggaggtggg tttgaggttt tactgtaaac taaatgtgta ccctctacct 180

tagttatgaa ttatgagaca cgaagactgc gaaacagaca cactcctcta aaagtgcctc 240

taggctgaca gggagaaagt cccgccaggc tcccagacgc caccttgag tccttcaaca 300

agcccgccag ggcctcttgc ccaccggtgt cagctcagcc actgaaccct ccaggaagaa 360

gacgtgctgg taggagaaga atctcaccca ggcacagcct ggaaggggca cagaaggggc 420

tccggaacca gcaagcccaa gttggaactc ccagtctgct actttctaga acgactgtgc 480

ccttggcggg tctaagtaga acctctccgc gcactctttc ctcctttgta aagtggggac 540

agcaatggcc accttgcagg ttcagagagg gcttgcagta cctcacagaa ctgagtgccc 600

gtgaacgtgt gtgttcctcc agatttgtga cagctttgcc aggctggagt caggctgaac 660

gcctctgccc tcatggggtt tatattctag gaagaccaac aaaaacaaga agacggaaaa 720

ttaaaacaac aaaagcccca ttgacaggcc gtgaagaatg ccatgaaaaa tgaatggcgt 780

tgtgctgcag tctttgggga aacgggctta cggaaagaag gacacttgag ctgctaccaa 840

tgagcagccg tccggtggga gggcagttca ggaagagcag acatccactg aggaggcgct 900

ggggcagagg gcagcctggt cgctggattc gggggaggaa ccacatcagg ccatgagctg 960

gagctggtgg tagaatgtac aggagaggcc agccagggcc agctcatgtc agacctcaag 1020

cggggaagat gaatcgagaa tgcaccccac gagcaatggg aagccagtct acgatttaag 1080

cagcaaaaat attttccctt cttccaccct gcatccagct ctaccagcac agcctggggt 1140

tctattttca agatagaata gacccagact cccagctctt cttacacttc tactactgcc 1200

acctgtcacc cactcatgcg tccccacttg cagcctcgac ccccttccac ctgatctcat 1260

ggcagccagg gaagctccag ggctcgtgag ggctgccatc tcaggaaaga agcaaaagcc 1320

ttcggcacct gcagggcctg ctccaaccac acttcttcct tgacctctca gcttccttag 1380

ccactccctt cccacatctc accctgctcc agccacagtg gtgtctctgt gggttctcaa 1440

acacaccagg tgcactcctg cctcagggcc tttgtgcttg ctgttctctg ctgggactct 1500

ttttttttt ttttttttg agacagggtc tcactctgtg gcccaggctg gagtgtagtg 1560

gtgtgatcgt agctcattgc aacctcaaac tcctgggctc aagcaatcct cccacctcag 1620

cctctcaagt agttagcttt tgttgttttg ttttgagatg ggatctcact ctgttgccca 1680

ggctggagtg cagtggggca atcttggctc accacaacct ctgcctccca ggctcaagca 1740

attctcctgc ctcagcctcc caagtagctg ggattacagg catgtgccac cacgcccagc 1800

ttatttttgt atttttagta gagacagggt ttcaccatgt tggtctggct ggtcttgaac 1860

tcctggcctc agatgatcca cctgcctcgg cctcccaaag tgctgggatg acaggcatga 1920

gcctgtctct agtagttagg actacagaga ggggccatca tgcctggtga tcctcccacc 1980

ttttctgctc caactctttc accccactta gcctcgtggc tcactctctt acctcttcag 2040

ctcctcagtc aggcctgagg acccctgttg aaaattgcaa accacacccc ccaccaccac 2100

cacccactat tgccagcact ttctactcca tttctctgct ttacttttct cctttgtact 2160

catcaccacc tgactcatta catgtttacg tatctttctt ctctccacta gcatggaagc 2220

tccaggagag cagagagtgt agttttattc cctgatgtgt ttcctgtgcc cgtaccaggg 2280

cctagcacac agtaggtgct cagtaaatgt gtgttggatg aacaaataca gtgaaaggat 2340

ctgatctaca tttataaaga aggcactctg gctgctgagt ggggatgaga ctgtcaggag 2400

gaaagaggcc cctgtggggg cctggccagc aggtgggtac aatggtagca gccaggagag 2460

agggcctctt ggactcaagt ggatggggcc tgctcagggc tccggccaca ggaacaaagg 2520

gaaggggcc caggatggcc tgtcatagag gacacattac aactggccca aagttcaagt 2580

caggtttcta aatttgggaa gggatacaga aaaactaaag actctactgg acagtcagtt 2640

attgaaatga ttacatagaa aatgtaccaa gaattaaaaa aaaaaaaaaa aagcattatg 2700

aaggggccac cagagactcc cagagaggaa agggactatg ggctggatgc ggtgactcac 2760

acctataatc ccagcacttt gggaggccga ggagggtgga tcacgaggtc aggagttcaa 2820

aaccagccta ggcaacatgg taaaaccccc gtttctacta aaaatacaaa aaattagctg 2880

ggcatggcag catgtgcctg taatcccagc tactcgggag gctgaggcag gagagttgct 2940

agaacccagg aggcagaggt tgcagtgagc cgagattgag ccactatgct ccagcttggg 3000

cgacagagca agactccgtc tctaaaaaaa agaaaaaaaa ggccagatga ggtggctcat 3060

gcctgtaatc ccagcacttt gggaggccga ggtgggtgga tcacgaggtc aggagatcga 3120

gaccatcctg gctaacatgg tgaaactcca tctctactta aaatacaaaa aattagccgg 3180

gcgtggtggc gggcacctgt agtcccagct acttgggagg ctgaggcagg agaatggcgt 3240

gaacctggga ggcggagctt gcagtgagcc gagattgcgc cactgcactc catccagcct 3300

gggcgacaga gttagactcc gtctcaaaaa aaaaaaaaaa aaaaaaatta gctgattagt 3360

tgggcttggt ggcgggcgcc tgtaatccca actactcggg aggctgaggc gggagaatca 3420

cttgaacccg ggaggcagag gttgcaatga gccgatatca cgccactaca ctccagcctg 3480

ggcgacagag caagactcca tctcaaaaaa gaaaaaaaaa aagaaagggg ctgtgctgtg 3540

gcctgggacc caaagcacac tactgcaagg tcccagggtg cctgactcca accggagcct 3600

tgagaacatt catttgcaaa gaatgaatta aaattcagca ctattttatt ctgcaggatt 3660

ccagcacccc aaggacagtc atttttagac ccttcagtaa cgtaataagt aaccggagga 3720

tgtgctgagc ttccacttcc ccagacggtt gcctgtcaca gctcatcagg ccaacaaact 3780

tttcttaggc ctcaaatttg gaaatgttca ctctcagttc gttccttaga tgcaagtcca 3840

tcccaatgaa gtaacagggg ctcagcacct gtccaatctc attgcttccg gggacagggg 3900

cccatgagga tgtcgtttca gcccggtgac acttgggcaa agtgcctttt ggtttccctc 3960

ccaggctgga acgtgctggc tctgtgaagt tacgctgggc acaagagccc cccccaaccc 4020

ggcaggactg actgctgtgg tcagaggcgc ccctggggct ttgggagcca cagaatcttc 4080

ctgagggcag cgccggagga ggccccagtg agagtgccca ctgccaggct cattcctcag 4140

gctgccgcag gcctctcccc aaaacaggca atgcttctca gcaacctgcc ccaggagcag 4200

gccagggaag gccgccatcg gcctacagtg ctgggctctg gagggcttgg ttggtaacag 4260

gccatggttt ctatgagcca gctggggtgt gaaggacaca ggctggattc acctctctgg 4320

gcctcagttt ctgcattcaa aaagtgggaa tcatgatatc tgctctattt cttatctctc 4380

agtgctgatg tgaacctcca ataagacttt taaaaatact ctttctacct tacttttatt 4440

tttcatttat tttaagataa tgtctagctg tctcacccag gctggagtgc agtggtgtga 4500

ttacggctca ctacagcctt aacctcccag gctcaagtga tcctcctacc acagcctccc 4560

aagtagctgg aactacaggc atgcaccacc gcacctggat aatttttttct tttgagacaa 4620

ggtttcactc tgttgcccag gctggagtgc agtggtgcac tcttggctca ctgcagcctc 4680

aacctccctg ggcttaggtg atcctcacac ttcagtctcc caagtagctg ggactacagg 4740

tatgtgccag tacacccagc taatattttt gaaggatggg gtttcactat attgcccagg 4800

ctggtcttga actccagggt ttaagcaatc taccttcctc agcctgccaa agtgctagga 4860

ttataggtat gagccacccc ccggcctata atcctaccac tttaaaaaag cctgtaattt 4920

tagcacttta aaaaattttt ctaaattttt tatagagatg ggggacagct gtggtctcac 4980

tgtgttgccc aggctggtct tgaactccta ggatcaagcc atcctcctgg cctggcctcc 5040

caaagtgttg ggattataag cataagcctt accttacctt tttttttga gttgcagttt 5100

tgttcttgtt gctcaggctg gagtgcaatg gcaagatctt ggctcactgc aacctccacc 5160

tcccgggttc aagcaattct cctgcctcag cctcccgagt agctgggatt acaggcatgc 5220

gccaccacac ccagctaatt ttgtattttt agtagagatg gggtttctct atatacctta 5280

attttaaagc actgcattca tgtaaattgt gattaacatg gattcaagag agggagtgag 5340

gatgaatgag ccaggcagtc acctcggctg tcaccctcca cttctctcct ccttctgaca 5400

gtcatcgtcc atccgtttct gcagctgttt gtttgactct cctgatcatt ttgcttgcca 5460

cataacttgc ctcctgggaa agaatgccct gggcaggccc acatgagtag tgaaaaataa 5520

tctgcagtga aaaataaaac taagtagtct ggtccacaga gcagtcttat tttttcactg 5580

cagatgaagg agttgacatt caggcttcat tctcatttat aagtgtttta aagacacata 5640

cagtggattg aacagtggcc ttcaaaaaga tgtatctaca tcctaatccc tgggacctgt 5700

gaatgttaac caagttagga aaagggtctt cccgggtgtc attaagttag agatcttgag 5760

atgaggagct catcgtggat tatccaggtg gaccctgcat ccaaggacaa atggtcctta 5820

gaaaagaaaa gcagaggctg ggcacagtgg ctcaagcctg taatcccagc actttgagag 5880

gccgaggtgg gtggatcacc taaggtcatg agttcgagag cagcctggcc aacatgatga 5940

aatcccatct ctactaaaaa tacaaaaatt agcaaggcat ggtggcgggt gcctataatc 6000

ccagctactc aggaagctga ggcaggagaa tggcttgcac ctgggaggcg gaggttgcag 6060

tgagccaaga tcgcgccact gcactccagc ctgagggaga aaagtgaaac tctgtctcat 6120

aaaagaaaag aaaagcagac agagatctga gacagaagag gagagtgaag gaaaaaaggc 6180

catgtgaaga tgaggcagag gttggagcca tgcagccaca agccaaggaa tacctggagc 6240

cccagaagtt gcaagaggta ggaagaagcc tcccctagag cctccagacg gagcacagcc 6300

ctgccaacac ctccacctca gacttctggc ctccagcact gtgagataat caactgctgt 6360

tgttttaagc caccagattt gtggtaattt gttatggcag ccacaggaaa ctaatacagt 6420

acctaatctt cacaaaccca tcttacagaa aaggaaactg aagtcagaga ggtagtggct 6480

tgtgcagtgt gttaggccat tcttgtatta ctataaagaa atacctgagg ccgggcatgg 6540

tggctcacgc ctgtaatccc agcactttgg gaggccaagg tgagtggatc acttgaggtc 6600

aggagttcaa gaccagcctg gacaacatgg tgaaacccca tttctactga aaatatgaaa 6660

attagccagg catggtggcg tgcatctgta gtcccagcta ctcaggaggc tgaggcagga 6720

gaatcacttg cgcccgggag gaggaggttg tagtgagcca agattgtgcc actgcactcc 6780

agcctgggag acaagagaga aaccctgtct caaaataaat aaaaaacaaa taaacacctg 6840

agactgggta gtttataaag aaaggggtta actggctccc ggttctgcag gctgtacaag 6900

catggtgccg gcatctgctt ggttgctggg aaggcttcag ggagttttac tcatcgtgga 6960

aggcagagcc agagcaggtg catcacacag caaaagcagg agcgagagag agagagagca 7020

gggaggtgtg cacactttta aatgagcaga tctcacgaga actcaccatt gcaaggacag 7080

caccaagcca cgaggggtct gcccccatga cccaaacctc ccactaggcc ccacccccaa 7140

cattgggaat tacagttcaa catgaggttt gggggggacaa atatccaaac tatatcattc 7200

caccccctggc cccccagatc tcatgttctt ctcacattgc aaaatatagt catgccttcc 7260

cagtagcccc ccaaagtctt aactcatccc agcattaact caaaaatccc attcccaagt 7320

ccaacgtctc atctgaagat gagttccttt cacctacaag actgtaaaaa tgaaaacagt 7380

tatttactgc tgagatacaa tgggggcata ggcattaggt aaacattcct gttccaaaag 7440

ggagaaatcg gtcaaaagaa aggggctata ggccccaagc aagtccaaaa cccagcagag 7500

caatcattca atcttaaagc tccaaaataa cctccttaaa ctccatgtcc catagccagg 7560

gcacactggt gcaaggggca ggctcccaag gccttgggca gctctattcc tgcggctttg 7620

cagaattcag tccccatggc tgctcttaca gattggagat gagggcctgc ggcttttcca 7680

ggtgcagggt gcaagctgct ggtgatctac cattctgggg tgtggatggt ggcggccccg 7740

tcccgcagct ccactaggca ttgtcccagt ggggactcta tgtggggcct ccaaccccac 7800

atttcccctc caatgggaag gctctgcccc tgcagcagcc ttcttcctgg gctcccaggc 7860

tttctcatac atcctctgac atctaggtgg atggtgtcaa gcttccttca ctcttgcact 7920

ctgcacacct acaggcttaa caccacatgg aagctgccaa ggtgtatggc tggaaccctc 7980

tgaagcagca gcctgagctg tgactatggc cctttgagcc aaggctggag ctggaacagt 8040

ctagatgcag gcagggagca gtgtcctgag gctgtgcaga gcagcagggc cctgtgcctg 8100

gacaatgaaa ccattctttc ctcctcatcc tctgggcctg tgatgggagg gttgtggaag 8160

atctctgaaa tgcctttgag gccttttgc ctctgaggcc tatttcctat tgtctcagtt 8220

attggcagtc ggctcctttt tagttatgca aatcctctag caagaggtta ctccactgcc 8280

ggcttgaact cctctcctga aaaagctttt tctttctttg tcacatggcc aggctgcaaa 8340

ttttccaaac ttttatgctc tgttttacct ttaaatataa cttctaactt taattcattt 8400

atttgctcct gcatttgagc atagggaatt caaagaagct gggccacatc ttgaatgctt 8460

tgctgcttca aaatttatgg ccacgcttgg tggctcacac ctgtaatccc agcactttgg 8520

gaggcctagg tgggcagatc acgagatcag gagatcgaga ccatcctggt caacatggtg 8580

aaacccatct ctactaaaaa tacaaaaaaa ttagcttggt gtggtggcgc agacctgtag 8640

tcccagctac tggagaggct gaggcaggag aattacttga acctgggagg cagaggttgc 8700

agtgagccca gatcatgcca ctgcactcca gcctggtgac agaataagat ttgatctcga 8760

aaggaaggaa ggaaggagga agggaagaaa tgtcttcccc ccagatgtcc tgggtcatcc 8820

ctcttatgtt caaacttcaa cagatcccta gggcatgaaa ataatacagc caaattattt 8880

gctaaggcat aacgaaagtg acctttgctc cagttcccaa taagttcctc atttccatct 8940

gagactcatc accctggcct tggcttgtcc atatcactgt cagcattttg gtcacaatca 9000

tttaaccagc taatcgggag gctgaggcaa gaggatcact tgaacccagg aggttgaggc 9060

tgcagtgagc tgtgatcaca tcactgcagt ccagcttggg caacagagca agatcctgtc 9120

tcaataaata aataaataaa tacataaata acttaagttt atttaaagct gcatctttgc 9180

caccatggag aaaggccagg ccagctcctt ctctctttct gcacgtgttc ctcccacctc 9240

agctgcctct gctcctcaag gaggaacaga gggagtagga aaggccatcc caggaggccc 9300

agcaccccat gacctggctc tggggccttg tgggtttatg gattcccagt gctgagtcat 9360

ccctcacagg ctcttgtggg caccttggac attggtcaga agcatgtggt ccccgggaac 9420

acacctttc ctgatcatct gggaagggca gcttgtgcca gcgaggccac ctgttcagcg 9480

ccacggcccg ccagacagct gcagccacag ccttgccttt gatcagagca aacaccagac 9540

atgtgtgtca tgcccccaac ccatctccag gggacacatg tcctttcttg ccaggcctga 9600

gatgaacaag agagggacaa gtccccaagc ctctctctcc ttcctgcctc acccactccg 9660

ctgttagatt ctcaaggtgg atggtgggct aactagggca accgaccatc ctggtttacc 9720

tagaactgag ggggcatttt caggaataaa actgcaaaag tctggagcaa acaggagcaa 9780

gttggtcact ctgggggctgg tggagtcagg tttccttctg caggcccccc ccccgcaagc 9840

atgggtggaa cccaggacag gaacacagag caggccccag gaccgggctt gtcacttaca 9900

agtctttttt ttttttttt ttttgagatg gagtcttgct ctgtcatcag ggctggagta 9960

cagtggtgcc atcttagctc actgcaacct ctgccttctg ggttcaagtg atccccctgc 10020

ctcagcctcc tgagtagctg ggactacagg tggcaccacc acgcccagct aatttttttgt 10080

atttctagta gagatgagat ggccaggctg gtcttgaact cctgacctca agtgatctgc 10140

ccgccttggc ctcccaaagt gctgggatta caggtgtgag ccactgtgcc tggccccact 10200

cacaagtctt aaaccatgcc tcagcacatc aatgccattt acaaaaaggt agagggattt 10260

tccaggcaaa aatagatgaa agacatagga tgattgatca tgtcctgctt aaacataggt 10320

ctgatgctat taagaattga gggctgggag cggtggctca cgcctgtaat cccagcactt 10380

tgggaggccg aggcgggcgg atcacgaggt caggagatcg agaccatcct ggctaacacg 10440

gtgaaacccc atctctacta aaaatacaaa aaatggccgc gcgcggtgac tcacgcctgt 10500

aatcccagca ctttgggagg ccaaggcggg cggatcacga ggtcaggaga tcgagaccat 10560

cctggctaac acagtgaagc cccgtctcta ctaaaaaata caaaaaaaat tagccaggca 10620

tggtggcggg cgcctgtagt cccagcaact tgggaggctg aggcaggaga agaatggtgt 10680

gaacctggga ggtggagctt ccagtgagcc gagatcacac cactgcactc cagcctgggc 10740

gacagagtga aactccatct caaaaaaaaa ataaataaat aaataagaat tgttagtatt 10800

ttgcaggtgt gacaaatgat tctgtttctg tggcagaatg ttctcaggag atctcttttg 10860

aactctcatg gaaagcatca tgctgttggc aacatcacat ttatttttat ttatttatta 10920

ttttttagag acagggtctt gctctgttgc ccaggctgga gtgcagtggc acaatcacag 10980

ctcactgcag cctcaacctc ctgggctcaa gcaatcctcc tgcctcagcc tcccaaagta 11040

gctgggacca caggcgtgag ccactgcact cagcccaatg taccttcaat atttacattt 11100

ctggcaaagg tagcaaaacc ttaacaaatt ttgaatctag ataataaaat tatgaggctg 11160

ggtgcagtgg ccctgacagg gatggctcac atctgtaatc tcaacatttt gggaggccaa 11220

ggtaggcgga tcacctgagg ccaggagttt gagaccagcc tggccaacat ggtgtaaccc 11280

tgtctctaac aaaaatacaa aaaaattagc cagacgtggt ggtgcacgtc tgtcatccca 11340

gctactaggg aggctgaggc aggagaattg cttgaacccg agaggcagag gttgtgatga 11400

gccgagatcg cgtcattgca ctccagcctg ggcaaaagca agagcgaaac tctctctcca 11460

aaaaataaaa aaaaaataaa ttaatgaatt aattaaaata aaataaaata atggatagtc 11520

actgtaaaga aaaaataaat gtatatatca gccaacaagt gatggaatag agcaccccat 11580

ctccctggct ggacagatac atcccacaac acctggaagg cggctccatg tagaactttc 11640

tggactgctt gaggtgctgt gctggagcac ggtgacagag gagctggacc atggacctcc 11700

cccggccccc accaagggcg aggtcccccc gtggtgggtc tgagggaggc atccgtatgg 11760

cctctgcggc ttgggcaggg aatttggggt ccaagtactt ggtgcaaagc ctggaaagag 11820

ggtttgggtg ctgagggcat atcccctggg ccacatgggg gcagaagtgg ggcccccctga 11880

agcttggagt cctgggcagg ggcatctatt ttgctgtctg aggccttcag tacttgaagc 11940

aaaatggagg cagaatgtcc caccttaatg cccctgattc ctccaaacca attccagaga 12000

cagcaagggc cagaacaggg atggccctgc ccagggtcat gcancgagga agtggccagg 12060

ctgggatctg aacccaggct aatcccctcc cttgtcctcc tccaggccct caccctgca 12120

tagagccctc cagctcactc atcctcggcc agctccatct cctcagcttg taaacccccc 12180

cgggattttc ctttcttaaa aaacaaaggc ttggccaggc acggtggctc acgcctgtac 12240

tttgggggtg gctcccagca ctttgggagg ccaaggtggg cggatcatga ggtcaagaga 12300

ttgagaccat tctggccagc atggtgaaac cctgtattta ctaaaaaaaa aaaaattaac 12360

tgggcatggt ggctagctac ttaggaggct gaggcaggag aatcgcttga acctgggaga 12420

aagaggttgc agtgagccaa gatcgcgcca ctccacttta acctggcaac agaacaagat 12480

tccgtttcna aaaacaaaca aacaaacaaa taaacaaaaa aaggcggagc gcgatggctc 12540

gcgcctgcaa tcccagcact ttgggaggct gaggcgggcg gatcacttga ggttaggagt 12600

ttgagaccag cttggccaac atggtgaaac cccatttcca ctaaaagtac aaaaatcagc 12660

caggtgtggt ggtgggtgcc tgtaatccca gctactcagg aggctgaggc aggagaatcg 12720

cttgaaccca tgacctggag gctacagtga gctgagattg cgccactgta ctccagcttg 12780

ggcaacaaga tttgtttctc taaaaaaaaa aaaaaaaaga ctggcccttc cccttcagct 12840

cttcctcagg gtccctgagc actctacacc cccgtctaca ctgagcactc caccctgctg 12900

tctacactga gcactccacc ctgccatcta cactgaggac tccaccccac tgtctacact 12960

ggctgcctcc cgccctcacc tcctgctaag gccattcccc gctgcatctg tcttctagat 13020

tctgcagcct tcagcacgct gggcccctcc tttgtcccct tgagccacct ccagcctccc 13080

cctgagctgc tactcctctc ccagcagcct ccacccaagc ccctccagtc cccaagctgt 13140

cccttgcatc cagcactgcc cttccacgtg ccccttcccc ccagcttcac agcagggtgg 13200

ggcctccagg ccctgcccac tgtgcccatc cacaagttgt ggtgggagct ccgaggggag 13260

gcaggggtgt gcatggactt gggacgtcca agtctgggac caggggcagc tggttggtgg 13320

agtgtggagg gggataggga ctttcaggta gagaggctgt aggggcaaga tcgggacggc 13380

ggatgtccct aaggagggct ctgacctggg aaatattgtg cagcttcctc tttgccattc 13440

ctggagctca gacactggcc ggctctcacc ccgcccttcc tgcaggacac agctccatcc 13500

cagtgagttc ctagtgtaga catctccagc agcacggatg ggaaaggaag tcatcaaagg 13560

tgcccaggac cggaggcttt ttctggaggt ggcagaggag ggtgtgggtc tcagggctct 13620

ggctgagggc aagcgtggga ggtcttaggt ctgcaccagc cccgtgaagg cccctcctgc 13680

tccctggtgg agtcctagag ggaacagcag cccctaggct ctagcaggag tgggtagggg 13740

cttttctggc ttcctactgt gccagcagga tagctgggcc tggcactgag cccaaagatc 13800

acatgccggg gcattggcgc agtgaggaac agacccttgc caaagctggc aaagaagacc 13860

ccatggggtg cagctggtga agctgagagc tcaatgtttg ggggagcctg gcaaaagggg 13920

tcctcccctc cctctgcagg ccaggatcgc aggttttccc tacatgttgg taattctcaa 13980

acaatcccat ggccactgga gcaaagatca cagtgggcgg cggcctcggg agcagtggac 14040

agggcacgca gtgcctttga tgccagagcc ctcgccccaa agtcaacaaa ctctgcagcg 14100

gactttgcac ccggactttg ttttcaccat acaaggaaag ggacagatca caggccctct 14160

cgctgccctc gctgagccgg aagctgcagc gtgagctctc tcaagcccca tttctaggtt 14220

ccccaggcgc acccctgagc ccctactcgc ctattaagtt ctcctaatag cccttcaagg 14280

tcttaatgta tgtccattag acagagggga aaactgaggc gagggcaagt gacttgaccg 14340

aggttcctcg gcgagcaggg cgtggagctg agaacctcgt tattactgct ccccacacaa 14400

ccctctggcc gttcttggaa gaaggctgag ccccgggggg gccagagtga cccaaacacc 14460

atgggccgcc tgcggtaaca cgtgcggcca cgaaggggca gcagtttccc gcccggccgg 14520

gctctctccg gcgctcagta tccgtcccag gccaagaaga agaaactcgg ggaggagggc 14580

ggaggggggct gcgtgggagg gcgtggaaga tggacgtggc caggggagtg gcagctgcac 14640

acagtggatg ctgttaagat gaagggaaag aacgtgggct ccgagatcac tggacacggt 14700

tccacctttc ttcccgctca ctgcatggcc ctgggcgggt tgttgaaccc ttggaaacct 14760

gtttttcctt ttttcctttt tttttgagac agggtcttgc tctgtggccc agactggagt 14820

gccgtggcac gatcttggct cactgctgcc tcccaggttc aagtgatcct cccagctcag 14880

cctcctgcgt agctgggacc ccaggtatgt gtcaccacag ccggctaatt tttgtatttt 14940

tttgtagaga cgggatttcg ccgtattgcc caggctggtc tcaaactcct gagttcaccg 15000

gatcttcctg cctcagcctc ccaaagtgct gggattactg gcatgagcca ccgcacccag 15060

cagagacctc agttttctaa cctgtgccag caggaataat gatagctgcc tagcttggct 15120

gtgctgggaa ttaagtaaga tgaccgggta gcaaatatga agtattactg gacacagagg 15180

gccccaggct gggttagcag cggtggtcag ggctgctgct tcctggcctg agctcgaagg 15240

agggccctca ttaccacctg ggtgagtcct cgtccaagcc tggcactgct gcgtgggaat 15300

aacttctgcc acccaagttg gcagattgtg tgcaaagtta agtcctgact ctgtggggtg 15360

gacttcgagg cctcttcatc ggacctgctt ccggtgactg cattcgcacc tcctcctgtt 15420

cctggtttaa cacagcccag ctttcctcct gctgagccct ccctgggcct gctgtcaccc 15480

tcgtgccgct gtgcctcgca gtgccactcc ctgtaccctg aatactttgc cctgcctctc 15540

cacccagctg agagtcaggg cccctgtgag gctctgccca gcccgtcctc cgggtttctg 15600

cctctgctga gcacttccct gcatgattgc ttctgagagt ccccccagcc tgtgagcttc 15660

tcaggactgg gacagcttct caggaccgag gcttcctggt ctgcttgcaa ttttacaggc 15720

gggcacattt tcccttggcc aacatcagag actggacatc tgcagatctg tgctagccac 15780

tgagcaccca ggcaccccag caggtagctc tgtaaccaac ccattctgta aagctgaggc 15840

tcagagaggt gaagcgcctg gcctggggcc acagcctgcg tcagctgcag agccaggagc 15900

tgagatatgc acctgcggct ctgctcacag ggtcctgcac agactgctgc tggagccacc 15960

tatgtagagt caagagagtt catgttaact ccctctcaca tccctcagcc agggtggggg 16020

ctgacgatag acactcaggg atggcctacc ctccccaaca acccccgtca ggtttgccgg 16080

atctccttgg aagaaaagtt ctgggcagaa ttccaccgtt ggcctggcct acactctcct 16140

tagtggctta ggaccctcag cggtggataa gttgtgggca gaagagatgc aatcaggatt 16200

ctcacccact cacccccttgc cagccccaat aagctcaata agctgggctc ggtctgagga 16260

agtgtccagg aaatgtgcaa atggcctggg acagccctgt gttcctttca gtaaggttgc 16320

tgaaggtgag gctgaaagtt ggagaaacag aagccagtgc ttatggtttt aattaagata 16380

atggaatgta tgtatgtatg tatgtatgta tgtatgtatt tatgtattta tctttagaga 16440

tagagtctca ctctgttgcc caggctggaa tgcggtgaca caatcatagc tccttgcagc 16500

ctcgacttcc tatgcccaaa tgatcctcct acctcagcct cctgagtagc tgggactaca 16560

gacacacgcc aactatgcct agctaatttt tatttctatt ttttgtggag actgggttct 16620

cactttgttg cccaggctgg tcttgaaccc ctagcttcaa gcaatcctcc tgcctcagcc 16680

tcccaaagtg gagggattac aggtgtgagc caccacacct ggcctggaat ttatttgtat 16740

tctgcttata aaattaatac attcttattg cagaaaagtt tgaaaataaa agaaaggaca 16800

aagaacaaaa agcgtatata atttcacagc tcagatctca ctgctattaa catttttatt 16860

tactttcagg ctttttctt tctaggtaca tatgcagaga ttattttatt ttatttattt 16920

tattttatat tttatttttat atttttttatt tcattatttt attttatttt attttattat 16980

ttttagagac agggcctcac tctgtcaccc aggctggagt acaatggagt gatcatagct 17040

cactgcagcc tcaaacacct gggctcaagc aatccccccca ctcagccttc tgagtagttg 17100

ggactaaagt gtgagtctgg ctaatttttt ttacttttttg tattgacaga ggtctcacta 17160

tgttgcccag gctgatctca aactcctggg ttcaagcgat cctcccacct tggactccca 17220

aagtgctggg attacaggca tgagccacca tgcctggcct aaaatgccac tttttgtcat 17280

ttactaaaat cccatggaca ctttgacatg tctgtattct atgctattga tctgactgtt 17340

ggcatctaca tcattatggc catctatcat ctatcataat ccattttaac attaaaattg 17400

tgctgctgct tagatttttc tggcctgtct cctatttgta ttcttccaga taaattttag 17460

aatcatttta tcaaattccc cttgcagaaa aagccctatt ggattttggt tgaaaaatac 17520

tgaattttta cattaactta ggaaagggct gggcacggtg gctcacgcct gtaatcccta 17580

cacttttcga ggccaaggca ggtggatcac ttgaggttgg gagtttgaga ccagcctggc 17640

caacatggtg aaactcggtc tttactaaaa atacaaaaat tgccaggcgc attggctcac 17700

ctgtaatccc agcactttgg gaggccgagg tgggtggatc acgaggtcag gagatagaga 17760

ccatcctggc taacacggtg caaccccgtc tctcctaaaa atacaaaaaa ttagccaggc 17820

gtggtggtgg gcgcctgtgg tctcagctac ttaggaggct gaggcaggag aatggtgtga 17880

acccaggagg cggagcttgc agtgagccaa gatcgcgcca ctgcactcca gcctgggcga 17940

cagagtgaga ctccatctca aaaaaaaata ataataataa tacaaaaatt agccgggggt 18000

cgtggcgtgc acctataatc ccagttactt gggaggctga ggcaggagaa tcgcttgaat 18060

ccaggaggtg gaggttgcaa tgagcagaga tcgtgccact gtactccagc ctgggtgaca 18120

gagtgacact ctgtgaaaaa aaaaaaaaaa ttctgaagga ttgagactct tagactctta 18180

ggtcttccta tccaagagca caatatagct tttcatgtat tcaagccttt ttcaatgcat 18240

caacagaatt ttacagtttt tttcatgata tcctgctatt tcttataaaa tgtattccta 18300

gatattctgc atgttttccg gttgtttgtt aataaatatt tttcatttgt cattatttcc 18360

taattggctg ttatttgtat atatgacatc tgttgaattt tttgattact ttgaaaatgg 18420

ccattctttt gtgttttttt ttaactttct attttgagat aattttgact tacagaagat 18480

ttgcaaaaat agtacagaga gttcctgttt ccccccttatg ttaacccagt ttctccttat 18540

gttaacatct tacataacta cagaacaatt gtcaaatcta agaatcaacc tgggcacaat 18600

gctattaact aaactgcaga agctgttcag atctcaccag ttcttctact gctccccttt 18660

tctcttccag tgttcaatcc ggaatcctac attatattta gttgtcattt ctctttggtg 18720

tcttccaatc tgtgacagtt cctcagtctt tctttgtctt tcatgacttt catttttta 18780

tacttttgaa aaatactggc cggttgtttt gtagaacgcc ctcagtttgg gtttgcctga 18840

agtttttttgt gattagatcg aggtcatgca ttattggaga gggtgccacc gcctcgatgt 18900

gcaagctcaa tgcatcatat cagagggttt gtaatgtcag tttataccgc cggagaccct 18960

aacctggagc atttcgtgaa ggtgctgtct gccaggattc tccactagaa agttactatt 19020

tttccctttt taattactga atgtctgagg ggaaatactt tgagactatg caaatatcct 19080

gtttctgctt taacttcggc tcactaagtt tagcattcat ctatggatct cgcttatagc 19140

aagtattact gtggagttct aatggtaatt ttctgtttct ctcattcctt caacctttat 19200

taatatgctt cttcctcact tattcatttt gtttcagttg tttataccaa catggatttg 19260

tggatattgg ttttattctt tgggttgcaa ttgaatccta tcattatttt gttagtcagt 19320

tgttccatcc gaccttggtc attaggagcc cttgaaattt ggctcccatg cctttttttt 19380

ttttttgag accgagtctc actctgtcac ccaggtttga gtgcagtggc atgatcttgg 19440

cttcctgcaa cctccgcctc ccaggttcaa gcaattctcc tgcctcagcc tcctgagtag 19500

ctggtattat aggcgctcca ccaccttgcc cggctaattt tttgtatttt tagtagagat 19560

ggggttttat tatgttggcc aggctggtct caaactcctg acctcaggtg atctgcccgc 19620

ctcggcctcc caaagtgctg ggactacagg cgtgagccac cacacctggc ctcctatgcc 19680

attttaacat gcccgtcttt tctttttctt tcctactttc tgtgactgta agaagctcca 19740

ggatacattt ttgctgccct agacttagcc tcaatcagtt ctcagaaaag ctctggttct 19800

ttttatggga tacttagaaa actagctctg tatggcctgg cgcggtggct cacgcctgta 19860

atcccagtac tttgggaggc cgaggtgggc agatcacaga tcacgaagtc aggagatcaa 19920

gaccatcctg gctaacatgg tgaaactctg tctctactaa acatacaaaa aattagtcca 19980

ggcgcggtgg cgggcgcctg tagtcccagc tactcaggag gctgaggcag gagaacggca 20040

tgaacccggg aggcggagct tgcagtgagc cgagatcggc agccactgca ctccagcctg 20100

ggccacagag cgagactccg tctcaaaaaa aaaaaaagga aaaagaaaaa agaaaactag 20160

ctctgtatgc tagttttttt tttaagacag ggtctctctt gccccagctg gagtgtagca 20220

gcacgatcac agctcactgt agcctcaacc ttctgggctc aagcaatcct cctgcctcag 20280

tctcctaagt agctgggtct acaggcatgc accaccgtac gtggcaattt ttaaaaactg 20340

tttgtagaga tggagtctcc ctatgttgcc tggtctggaa ctcctggcct caagtgatcc 20400

tcctgcctcg gcctcccaaa gtgctgagat tacaggcatg agccactgta cctggcctgg 20460

ccaaggtctg tctttttttа aaagaagttg ttgtatagtt gttttttttt ttatttttt 20520

ttctgagacg gagtctcgct ctgtcgccca ggctggagtg cagtggtgcg atctcggctc 20580

actgcaagct ccgcctccca ggttcacgcc attctcctgc ctcagcctcc cgagtagctg 20640

ggcctacagg cgcccgctac cacgcccggc taatttttg catttttagt agagacgggg 20700

tttcaccgtg ttagccagga tggtctcgat ctcctgacct cgtgatccgc ccgcctcggc 20760

ctcccaaagt gctgggatta caggcgtgag ccaccgcgcc cggcctgttg tatagttttt 20820

atctcgagtt ttctagcgat ttaatcatat tggttacaaa aaaggatgat tttactacct 20880

cctttccaat gtttctacat atttttttcat tttatctaac tgcattttaa aataaacttt 20940

taattttaga atggtttcat atttacagaa aatgtgcaaa gatagtacag agagttcctg 21000

tgtactccac acccggtttc cttattatta tcttaacgtg atacacaatt aataaaccag 21060

taacattatt attcactgaa gtccacactt tctttttttt tttttctgag acggagtcta 21120

cttctgtcac ccaggctgga gtgcagtggc gcaatctcgg ctcactgcaa cctccacctc 21180

ctgggttcag gcaattctgt ggctcagcat cccaagtagc tgggaataca ggtgcccgcc 21240

accacgcccg gctaattttt tgtattttta gtagagatgg ggtttcacca tgttagccag 21300

gatggtcttg aactcctgac ctcgtgatct gcctgcctca gcctcccaaa gtgctgggat 21360

tacaggcgtg agccaccgcg cccggcgtcc atactttctt tagatatcct tccttttttac 21420

ctaacgtcct tcttctggtt caggatccca tccagaaagc aacattaccc ctcgccatca 21480

cgtcttcaca ggctcccctt gacgggaaga gttcctcaga ctttccttgt ttttgttgac 21540

cttgacagtt ttgaggagga ctggtatctt agtctgtttt gtgctgctat cacagactag 21600

ctgagaccga tacatgatac atgaaaaaaa atgtattctt acagttgtgg aggctgggaa 21660

gttcaagacg aagttgctgg ttggtttggt ctctggtttc aagatggcgc cttgctgctg 21720

catcctctgg agaagaagaa tgcggtgtcc tctcactgca gaagatggaa gcgctaaaag 21780

gaatgaactc cctttgccaa gccattttat aatgggcatt aatccacaaa ggatgaaacc 21840

ctgagaaaca tcaagcttta aagcactggt tctcaacctt tttggtctca ggagcccttt 21900

atactcttaa aacgttttga ggatcccaaa aaaaggcttc tacaggttcc atcttttaat 21960

atttaccata tcaaaaatta aactgaaaaa attttaaatt atttattcat ttaaaataac 22020

aaggataaac ccattacatg ctaacataaa tcatgtattt tatgaaaaat agctatattt 22080

atcaaaacaa aaattagtga gaagagtggc atgtataatt ttttttgttt atttttttgtt 22140

tttagatgga atcttattct gtcgcccagg ctggagtgca gtggtgtgat ctcggctcac 22200

tgcaagctct gcctcccagg ttcacaccat tctcctgcct cagcctcctg agtagctggg 22260

actgcaggtg cctgccacca cgcccggcta atttttttgta tttttagtag agatggagtt 22320

tcaccgtgtt agccaggatg gtcttgatct cctgaccttg tgatccaccc gcctcagcct 22380

cccaaagtgc tgggattaca ggcttgagcc actgcgtctg gcctaaattt ttgtgaatgt 22440

ctttaatgcc tgccttctca tatttgtttc tgcattcaag ttattgcaaa atgttgtgtt 22500

ggttgaagtt tgtaaagaaa atgtggcctc atacagttgt gtagttggaa aggcaagagt 22560

attttgattc tctcttcaaa caactatgga caacctgctg ttacaaaacc agaatgcaaa 22620

aagttgtagt aaatacaggt taggtgtagt gtggaatctg aaagcatgtg aatgaacttt 22680

ctgagttttg taacattaaa gtccagttgc gttaagctac tgtgatagca tatagcattg 22740

tcctaatact ggaattagta tcagaagtgg ggtgctactg ttaataaata aaaagaaata 22800

aataaatcat gtgatactgg ctcagaagtc aggcagtagg ctgtgtggaa cctgacatca 22860

cgccatgtaa tacattggca accatttgat ccagctgtct gtcatgatga cttggaaagt 22920

caaccacata cttacagagc ctgtagacat aggggaaaat agtataaaac agaatactaa 22980

cagtggacct tggttcttgc cagttgcatt tagccaaata ttaaacaaaa gagatattct 23040

tgggcagcaa ctggaccatc ttcaagtaaa agtgaaaggt aataaacaga gtccagacat 23100

ttgtgcccat gcgggttaag aaaaatccag ttgcttctag acaccgtata tgaaaacaac 23160

gctgaaaaca agcctttgag tggtaaaggc cgattaacac tcagcgcggt aacaaagacc 23220

aggtgggcta acccgaaatg aaatgagaag cctgtggtga tgaggaggca gagaagtaaa 23280

atcaagtttg agcatttcgt ttaggagagt ttgggctctg attacttgca catgcaaacg 23340

aactggaaac aaacagatca gatgtctacc acttcttcga gggaattgca ttgccaaaga 23400

agtcatgaaa gcagactcta tactgattag gcattaaaac aaaaacaatc tttaggcccc 23460

taaacttgca tgggcaggaa gtgggctgtc aaagctgttc atcctctaag gtggacctag 23520

ttcctagtcc ccagtataca cttcagatgt ggccctggag gacactggac atggaggacc 23580

tcccagagga tgaggctagg gcttcatttc tccaatgacc tcagctgcct ctatttcccc 23640

ttcttcctct ggaagtccta tcatcgttat tattattatt atcatcattt ttattttgag 23700

ataaggtctc gctctgttgc ccaggctgga gtgcagtgac atgatcatgg ctcactgcag 23760

ccctcccagg ctcaagtgat cctcctgcct cagcctcctg agtagctggg agtacaggca 23820

catgccacca tgcttggcta ttttttttt cagtagagat agggctctca ctatgttgcc 23880

agggctgatc tcaacctcct gggttcaaga gatcctccta cctcagctcc tgagtagctg 23940

ggattcgggt gcacaccacc atgccaacta atttttaatt tttttttgta tggacaggat 24000

gtacagtgtt agaaatggat tgcttgcaga ggcaggagga tcacttgagc ccaggagttt 24060

gatcacactg tgaaccatga tcgcacccct gcactccaat ctgggcaaca gagtgagacc 24120

ttgtctcaaa aaaaaaaaaa aagagagaga gagagagact caaagatagg caaaaaagtg 24180

ggaaagcttt atagtggaca aaaaggaacg ctctaagtct gccctattgg catggtgctg 24240

aaggtgggct aactagagat agggggtact atgtggttga ctatgggtgc atctttggct 24300

ttccctgggt gatcctaagt tggaagcagg gacaaaaatt agggaagctg ttagttattc 24360

atcacgttct ggcagtagtg gactggttgt gatagaagtt attgttttgg ccaggtgcgg 24420

tggctcatgc ctgtaatcct agccctttca gagttcaacg tgggtggatc aggaaggagg 24480

gaggatttgg gaggtcagga gttagcctgg ctaacctggc gaaatcccat ctctactaaa 24540

aatacaaaaa ttagctgggc gtggtggtgc atgcctataa tcccagctac tcgggacgct 24600

gaggcaggag aatcagttga acctggggag gcggaggttg cagtgagcca agatcgtgcc 24660

caatttcatc tcaaaaaaaa aaaaaaagtt atcgtttagc ttcctcgatt gttactggac 24720

gtagtaatct ggcttcctgc aagtctaact ttcagcagac tggctacatg ggctgtgtac 24780

tgtagataag gcagtaagta aagcaaaaat tgatagagca tcaaggataa atagaaaatc 24840

cgtaatcaag cagaagattt gaacacttca ctttcagtaa ctgataaaac aagtagacaa 24900

aaaaaatcag taaggatgta gaagatttga acaacgtaat taacaaactt gacttgattt 24960

acacgtctag aaccctgcag aacacacact ttttcaagca tactcagaac atttatataa 25020

agtgaccata tggtggacca taaagcagtt tcaacaaatc tcacaggagt aaaataacag 25080

accgtgtttt ctgaccgtaa gtacagttaa cctagaaatt gaaaacaaaa agctagaaaa 25140

accccatgta tctggaaatt ttaatataca ctttgaaata acaaatggat cagagattaa 25200

ttcaaatagg aatttagaaa taccttgaac tgaaaaataa tgagaatact ataccccaaa 25260

actgtggggt gcagctgaac agtatataga cgaaaagtat actcatatgt gcatacctta 25320

aggagcgggg aggattgaaa gttaatggga ggcaaaagca ggtggatcac ttgaggttag 25380

gagttcaaga tcagcctggc taacagggtg aaaccccatc tctactaaaa atacaaaaaa 25440

ttatccaggc gtagtgaggc tgaggcaaga gaatcgttgg aacccaggag gcagaggttg 25500

cagtgagccg cgattgcgcc actgcacccc agcctgggag acagagcgag actccatctc 25560

aagaaagaaa aaaaaaaaag aaaaggccag gcgcggtggc tcatgcctgt aatcccagca 25620

ttttgggagg ccgaggtggg cggatcacga ggtcaggaga tcgagactat cctggctagc 25680

acggtgaaac cccgcctcta ctaaaaatac aaaaaaatta gccaggcgtg gtggcgggtg 25740

cctgtagtcc cagctactca ggaggctgag gcaggagaat gtcatgaacc caggaggcag 25800

agcttgcagt gagccgagat cgcgccactg tactccagcc tgggcaacag agagagactc 25860

tgtctcaaaa aaaaaaaaaa gttaatggga taaacatcca tctcaagaag ttagaaagga 25920

atgacaaata aaccaaaaaa aaaaaaatca aaagaagaaa atcataaggt caagactata 25980

aagagagtgg ctgggtgcag tggctcaggc ctgtaatctc agcattttgg gaagcagagg 26040

tgggcagatc acttgagccc aggagttcaa gaccagcctg agtaacatag agagacctca 26100

tctttgctga aaataaaaat aaaaaattag ccaggcatgg tggtactgag gtgggaggat 26160

cacttgagcc taggaggttg aggctgcagt aagccatgat tgtgccactg cacttcagcc 26220

tgggtgacag agtgggaccc tgtctctaaa aaactaaaat aaggctgggc gcggtggctc 26280

aaatctgtaa tcccaccact ttgggaggcc aaggctgagg tcagcagttt gagaacagct 26340

tggccaacaa gatgaaacct catctctact aaaaatacaa aaaattagtt gggtgtggtg 26400

gcatgtgcct gtaatcccag ctacttagga ggnnnnctnt ngattatatt ttctccttcc 26460

tacgtcgtta ttggactgaa ttcagaatga tgactctcat tggagctctt cctgtctcct 26520

aactacagtg gcttccgacc ccactctggt tttcacttca cccctctgct gctcatacga 26580

gtagatactt ccttccttct ttctcacttg ttgctcttcc tcaacccccc ccgttggtgt 26640

cccctcctct ttatcttttt ctcgcgacac ctgcgttctc ttgccctctt atcatccctt 26700

tctcgaggcg gtcctttcct ttatccagct taaatacctt ctcctctgtt tatttggggg 26760

ttgggttttt atctctcacc ctccctctaa tttctttcct ctttccgcac ccatcaagcc 26820

tctcgtggtt tctcttcctc tactctcggg tccccccccc ctcccccttct ttttttcttc 26880

acccccccaa gcgctttgcc tttttttttct ttgcccttta ttccccccc 26928

<210> 7

<211> 29430

<212> DNA

<213> Homo sapiens

<220>

<221> unsure

<222> (4336),(4345),(4349),(4392),(4447),(4490)

<223> Identity of nucleotide sequences at the above locations are unknown.

<400> 7

aggggaaggg ccggctccgt agctcacacc tataatccca gcactttccg aggagaggag 60

atcatctcag gccaggagtt caagaccagc ctgggcaaca cagcaagacc gcatctctac 120

aaaaacttct tttaaagctt aaaaaaaaaa aaaaaagcaa agaggacagt tcaggagaaa 180

agcctgtaga ggcagcacac taaggaggag acgcagccca ggcaccagga ggggctggcc 240

atgggcactc actcctccag caggcgagtg cccagcacca gctggcccac ccagacaccc 300

aggacacggc ctgaatggct ccgtattcac gtgggtggta ataaacaagc aatacacata 360

gccaataagg acaccttagt aatgttacat cataaacgct gcagatcagg gaaatggtgc 420

agggtgaagt gggttggggg gctgcatgct acatgagaag tgggtcgggg ggctgcatgc 480

tacctgagac agagcaggcc ttgctgggaa agaaggagcc ggcaggcctg ggcaaaggtc 540

ctggggtggg agcacactgg agcagagtgt gggggtagca tggcgggtgc tggtcctctg 600

ggcgccttcc caccacgtca tgtgcccatg tgcccaaggt ctctcgtttc acagcccccc 660

gaagctcagg ggtcacagct acacagcccc cagatacctt ggcctgcccc aggtcattcc 720

atccagtgat ggacctgctg acctctagcc tgacctctgg gcagcgtaat ttgagaagga 780

ggagaaggga gggcaacaga cctggggcga tgagggatgc acagggtggc agacacctga 840

ggctgcacct tggagcctca gttctgggtg tgggtggggg atggacaggc tgagggctga 900

agcagctggg cccggccacc atcacacccc aggacccacc agatcaccat gaaaaaccga 960

atgtcaactg gcagcccaga gtgcagaaca aacctttcag aaacacggtg gtgactgccg 1020

catcatgaac ataaaataat tacgccctct ccccagggat caccctgca ggagtttgtc 1080

ccaagaaaca ccagaaagaa ggaaaacgtc tgagtcacaa tatttgctga ggccttattt 1140

gtaatagcaa aaaaaaaaaa aaaaaaagaa caatctccag cggcaggggt aactagacta 1200

ttgtctccgt ggaaaggtag caccaattaa ctagtaacaa aatgactgcg gtaacaacaa 1260

aacgttcgac atgtcaacac caaaaaccac acacccagca taaccgtgaa ccatgatttc 1320

tactagaatg aatggcagtt atgagaaagc accagcggag acaaagattg aaaaagtaaa 1380

ggtggcctca ttagggagac aagtctctgg gtaatatatt gtaatactgg taaatatata 1440

gtttttaata tatttttaa ttccaaattc catatatgtt cctatgaagc tatttctgca 1500

aatatttttt tcaggaccgt acatcacaaa ggcaaaaggg ccaggtcagc tctccagctg 1560

agagtgacca cttcagagca gacggcagac tccagggtta gcaagcctgg ctgagacctg 1620

gcccatgaca atcactcaac ccctctgacc tcaacatcct gtctgtgaaa tggggataat 1680

tactgcacct ccacatcaca gagtgcgagg cttaaacagg atgcttcata gaaaagcgct 1740

caagaggtaa cagccgggag ggggtagtgg ttttcattaa ttaaatgttg ccttcatcca 1800

gccctgggcc agctccaaca caaagcacac accatccact cagactcagt tgcctggatt 1860

caaagcccgg cctggcctcc agctgtgaga ttccgggcag gatttcccat ctcccagagc 1920

ctcagtttcc tcattcatga aacaggaagt gatcattcct tttatttta tttttatttt 1980

tattttgaga cggagtttca ctctagttgc ccaggctgga gtatgatggc gcaatctcag 2040

ctcactgcaa cctcggcctc ccagtttcaa gcgattctcc cacctcagtc tcctgagtag 2100

ctgggattac aggcacacgc caccacgccc agctaatttt gtatttttag tagagacggg 2160

gttttgccat gttggtcagg ctggtctcga actcctgacc tcaggtgatc cgcccgcctt 2220

ggcatcccaa agtgctggga ttacaggtgt gagccaccaa gcccagttga caactgcttt 2280

taaagacacc tctggctgct gtggaaaaca gcctggtagt gcctcaaaaa gttacacata 2340

gaatgatcct atgaccagta attccactcc tacatatata cccaaaagaa ctgaacccct 2400

ctactcatgt atgtacacat acaggtacac gcatgttaac agcagtgttc acaaagccaa 2460

aacatggaaa cagctcaaat gtccataacc gatgaacgga taaatgaaac gtagtctatt 2520

caccacctga cggaggtgag aggggccata aaaaggaatg atgcataaaa acgaatatta 2580

tggccaggta tggtggctca cgcctgtaat cccaggactt tgggaggctg aggcgggcgg 2640

atcacgaggt aaggagttcg agaccagcct ggccaacacg gtgaaacccc atctctacta 2700

aaaatacaca aattagctgg gcatggtgga gggcgcctgt aataccagct actccggagg 2760

ctgaggcaag agaatccctt gaacctggga aacagaggtt gcagtgagct gagattgcac 2820

cactgcactc cagcctgggc gacagaccaa aactccgttt cggaaaaaaa agaaaaaatt 2880

agccaggtgt ggtggcgggt gggtccctgt aatcccagct ctacttggga tactgaggca 2940

ggagaaccac ttgaacccgg gaggtggagg tagcggtgag ctgagattgt gccactgcgc 3000

tccagcctgt gtgacagaag gagactctgt ctctaaaaaa caaaaacaaa aaaggcccga 3060

cgcggtgtct tacacctgta atgccaacac tttgggaagc caaggcaggc agatcatctg 3120

aggtcaggag tttgagagca gcctgggcaa cacggtgaaa ccccatctct actaaaaata 3180

cagaaattag ccaggtgtgg tggcacatgc ctgtaatccc agctactcgg gaggctgagg 3240

caggagaatc gcttgaaccc aggaagcgga ggttgcagtg agccgacatt gcaccattat 3300

actccagcct gggtgacaga gtgagattct gtctcaaaaa aaaaaaaaaa aaaaaaaaaa 3360

ctaaacaaaa gcaaaaaaac caatgagtaa tgttgtcaag tgaacttcat cccaatggga 3420

atgcagataa tttgtttaaa aggcaccatg cacactgggc aggctggctt cccctgggaa 3480

cgtcttcttt tgcctggatt cccagttggt ttaatcgggc gtagaacact ttcttcaatc 3540

cgggattcag gcacccctgc tcagcacaaa ctcagtacac cccgcactct gctgtgggtt 3600

cttggcacta ttaggagaat gtgagggggt gattcagatc tatctctagt gggtgcatgt 3660

ctgccactcc caggaacgcc cacttctggc aagtcagtgt cagagaaagg ccagctcgtg 3720

gcccctcctg ccttgagtcc caggacccgt gatcagtcct acccggagca gaatcaggag 3780

tttgaaaacc caagtgccaa caatctcatt ttaacccatg taagcatatc caatatttat 3840

atatagaatt cataacagat gtctgggctt ccattccaat agcctatatt ttacactgtt 3900

tatttacatg gttacaccaa acaagactca attcaaggta acccaatcct ttgctactat 3960

accaaaataa gcaacatttt cagtccatgc cttatatata ttcaccaagc attacactag 4020

gcctccaact gctcatcgga gcaagctgca gcctggacac aagctagaga ttaatcagtc 4080

aggaatgatc ctgcgtccag tgccagcatg atggaagaga cagagaaaca gaagacatca 4140

gggctccaga gtcaaggagc ctgcaggtta gttgggcagg atatacacac atacacacac 4200

acacgcacac acaaaaccac ccaagaagaa aaggtgggat gaatgcatgg acaggtaatg 4260

cctggagcct ggggatggat aagctgactg caggtggccc aggcaggctt cctggaggaa 4320

gaagacctgg ctgtangtgg ggtangcang ctttctaaat ggggaaaatc tggctgtggg 4380

tggagttggc angtttccga aaagaagaaa agctgactat gggtacacct ggctgttggt 4440

ggaacangca ggcttcttgg aagaagaaaa tctggctgtg ggtggatcan gcaagcttct 4500

tggaagaagt aaacctgact atgggtggac caggcaggct tcctagagga agaagaccgg 4560

ctgtgggtga accaggcagg cttcctagac agaggaagat ctggctgcgg ttagagtggg 4620

caggcttcta agaagaggaa gggctgactg tgggtagacc tggctgtggg tagactgggc 4680

aggcttcctg gaggaggaag agctggagca ttgaaaaaca aacatgactt ggtgaatgtt 4740

gagcatgccc aggcctgatc cccagaggca attacgcact caagttactt aattctactc 4800

acaatgcctc acaaacaact tctctgacac ctaacacagc tctgggcacc ttctagcttc 4860

agctcctcaa agcagttatt cacgctacta ccctgcacac ctcctcacac cccaacccca 4920

gggacaggag ttctgccaga tgccaaagct cctgatgcca aagcctgggt ctgcttccgg 4980

gctcctcttg gtctaactgt ccaccccgca tcggcatgat gtgcaaaaac aaggctttgc 5040

aatctgccct gatgcctggc ggagcgagtc cctcccgatt cgtctccttc agaaacacct 5100

gggctgccct ggtcctgtta tacccccaac acattctaca gtcagctccg caagttccac 5160

aaagatcaac gctggcgttt ttatggcatt ttatttacag tttttacaat ataaaaaagg 5220

aaggatgcca cagctcagcc agcaggacag acagagatct atgatgcttc tgctgcacca 5280

ttgtttgtgg tcaagaaagt ctgttttcaa tgatttatta aattgtggtg ggagatggat 5340

ggtggcagtg gttaccagca acatgaatgt tcttaatgcc actgaacttc acacttacaa 5400

atggttacga cgataagtgt tatatgtatt ttaccacaat taaaaacagg taaatgcagg 5460

ccgggcacgg tggctcacga ctgtaatctc agcactttgg gaggccaagg caggcagatc 5520

acctgaggtc aggggttcga gaccagtctc gccaacacgg tgaaactctg tctctattaa 5580

aaatacaaaa attagccaga tgtggtggtg catgcctgta atcccagctt ctcaggaggc 5640

tgaggcagga aaatagcttg aaaccgggag gcagaggttg ccatgagctg agattgtacc 5700

attgcactcc agcctgggtg acaaaagcaa aactctgtct caaaaaaata aaataaaata 5760

aaaataggta aatgcaaaca tatggtatag taatattatg ggctattatg agctacaaaa 5820

aagaatgact tgggactaca gttacagccc tcattcagga atttgtttta aatgtgggtt 5880

ggtcgctaag gcatgtacac aacattttga cgttcaaata ttcctagatt tggacagtga 5940

gcacccctct aagctggctc ttctgtccca gaggtcccca ccagtcctcc agaacttctt 6000

tgctttctta cacaataaga tgccccatgc tcggcttgta cctttccttg ccccagccct 6060

agaaccagct tcttcgtgga caagctctga ctcctttggg tggagaatgg tattcagaaa 6120

cccagacctg ggctctggtg tgctcactgc tacttggggt cattgcttct aggcctctct 6180

gctgatggag gtaggatata cacgtacagt cttccctctt cccagattcc gtacttgagc 6240

tcgcctactt gctaacattt atttatatcc cccaaattaa acctcacagc acttctgcaa 6300

tcactcactg acttgcagag tgtgaaaaaa ctgagtcacc atcacacgtt ccaaactgag 6360

gtcaactgag gccacaacgc cccatcttct tgctccggct gtcgagatgt aagcaagtgt 6420

ccttctctcg gtctagctag tgccatgctt tccacatcac tgtgcttttt gtgggcaatt 6480

ttgctgtata aaatgtcccc tgcacatatg ctgctgtgta gtgctcctag gtgcatgagg 6540

ctgccccacg ccttacagag agaatatgca tgagaggctt tattcaggta tgagttatag 6600

cgtagttggc catgaattca atgttaatga atcaacaata tacagtaaat aaggtgcttt 6660

ttagagacag ggtctcactc tgtcacccag gctttagagt ccagtggtgt gaccttggct 6720

cactgccgcc tcaacctcct gggctcaagt gatcctccca cctcagcctc ccaaactgtt 6780

gggattacag gcgtgagcta ctgcactcag cctaaataag gtgtcttaga aacacacata 6840

agacaaggtt atgggctgag tgcggtggct catgcctgta atcccaacac tttgggaggc 6900

caaggtggga ggttcacttg aggccagaag tttgagacta gcctgggcaa catggcaaga 6960

cctcatctgt atatttttt aaatcagaca ggtgtggtgg tgcatgccta tagtcccagc 7020

tactggagag gctgaggcag gaaaatggcc tgagcccagg aggtcaaggc tgcagtgacc 7080

catgattgta ccactgcatt ccagcctggg gtgacacagc aagacgctgt cttaaaaaaa 7140

aaaaaaaaaa aagccaggtc aggtatcgaa cagttggcaa aaacgttgtg acctgaggct 7200

cacaggaacc tagcccgatg tttcccctag gagcaatggt tcagtattca ataattcagg 7260

gttcccagtg actttatgga gcataacttt caagaataac aagaaccaac tgtacgtgtg 7320

tatgtatact cacactttta ttttatttta ttttatttt tgagacagag tctcactctg 7380

tcacccaggc tggagtaaaa tggcgtgatc tcgactcact gcaacctccg cctcccaggt 7440

tcaagtgatt ctcagcctcc caagtagctg ggattacagg tgtgccccca caaccggcta 7500

atttctgtat ttttagtaga gacggagttt cgccacattg gccacgctgg tctcaaactc 7560

ctaacctcaa gtgatccacc cacctcagcc tcccaaagtg ctggaattac aggcatgagc 7620

tgccgtgcct agcctacata cacttttata cacacatgca tctatgacta tttctctatt 7680

tctgtgcatg tgtgcgtggc agtacctaca gtttcagcta tgtgtctggg tactgtctcg 7740

tccaagtttg taagcacctt ctccaaagtg caaagcctgg cttgtgttac tatccatatg 7800

tttacttatt tgctcaatca atttacttat tagctccata accagcttcc catctgctcc 7860

agtagcctct gctgtcagtc acctctgcac cctaccccac cttgcttccg gatgctggat 7920

gccaatcacc cccgacacct ctacatagca ccaccctcga catgctgctt ctttatttct 7980

tatttatttg tttgagatgg agtcttactc tgttgcccag gctggagtgc agtggcacga 8040

tccaggctca ctgcaacgtc cgcctcctgg gttcaagtga ttctcctgcc tcagcttctc 8100

aaatagctgg gattacaggt gcccaccacc acgcccagct aatttttgta tttttagtag 8160

agatggggtt tcaccatgtt ggccaggctg gtctcgaact cctgacctca agtgatccac 8220

cttggcctct caaagtgctg ggattacagg tgtgagccac cgcgcctggt ctgcttcttt 8280

aaatgccagg caccaacatt tgtgcaatgg ggtgggagga aagaacaggg aggagagcac 8340

actgccggcc cctgcactga atccactgat caatctgggg gcaactgcca tctccatctc 8400

ctgtcttcct atccgtgaac atctactgca gtcctctcca atgtccttct gtaaagttgt 8460

attatgtttt gcatacaggc cttgcatatt agttctcaga tataatccat atactttata 8520

taaaattcaa accacattta aaaaaataaa actagcatga ctataacgga gtctgcaaca 8580

ttctcacaga ctttatgata aaacatgaaa cttcaaagat acttagggtg gggcagggac 8640

aatgtttaag gctgcctgga agcctcccca tccctgagcc agaaagtcct atctcccctt 8700

caaggggaaa tgcttgaaaa agcactgatc aggctaaaat gacagggatc agggagtaat 8760

caaagtacaa gtgagctggt ctcctccatt ctgagcacag caaagttcag tctctccaag 8820

tccaagaatc atacacctgt ttgccaagaa tgaagttcag gtgtctacaa gtggctgaaa 8880

atattcattg ctgggccatt aacaacattc ttggcaaaac cataccttag cttctcgtgg 8940

aaatttctta aggtagaaga aacaggaaac acccaggctc gcttttatgt agacagttcc 9000

atgaagccag ggaccttccc cacatccacg tttcaattac ctgcacgcag ctcacagtgt 9060

attcaacatc tacgcgtctc tcctactggg gtggcggtgg ccactcaaac cctcatgcag 9120

ctacgatgac cgcaattttg gcaacataat ttcatgtttt tccttgggct tttacccaag 9180

tcagtgacac aattctgcag ttgtctaaag attcaaaatg agggacttga catttacaac 9240

aataataaaa tcttgggttt cctttaacca agcacatgtt ctgcctttta gagaaagctc 9300

tgcaaactca agctggagtg ggatacttgc tgacatcttc aagcacccca ggaatagctc 9360

tactccccca tttccacctt ggctgaacca tctatatccc accaattccc ccaacatccc 9420

tccatccgtc catccatcca cccaaggacc tgctaagcca ggaggtctct cccatctacc 9480

ccacagcctg gcctcagccc acaagggctc tctctacatg aatcccaccg caccagagta 9540

gaccaagtct cccgtagact ccaccctgac cacctccatg cctccagcca ttcccacccc 9600

taaaaaccct ccctggtctc tacacccagc tgatgaatac ttggctgaat gtgacctggc 9660

ctcctggacc caggtgaagc ccacgtcctc cgtaagcccg ccagctcacc ctgcctctgc 9720

accttcactg gagagagccc gcacttcacc tcctcagggc aggcatggct gatgccaccc 9780

agtggaatct ggtgcaaagc agggcccggt gcagagcagg gctgcctgca gagcaaggcc 9840

ctggtgctgg ggccgagcac ctccaatgct ggccgtggaa ccatccctcc cattccaggt 9900

gctgtctcca tcaagaatga gcgagctgct gacatttgca tgacaataat gaataaatac 9960

catattttgc ttcaaatcca gaatagatgt ggccagggtt ggcatatgac tgttgggaaa 10020

ggacagtttg cctcttccca aaccaacttg gattataaaa agcttttctt aacgaccaca 10080

agagcggagg agctcagggg cagacaaaag gaaggctggc tgcagaaggc gggagagtgg 10140

ggccttcagg ggcgggtggg gagagagaaa gcctggagct gcacccccaa ggtctgtgta 10200

catcaggtgc tacagaataa caccacctct tccagcttgg cccccacctg ccctctccca 10260

gcccagtcac ccagacagca ccccactccc cacacacacc tcacatctgc ccgcctcaca 10320

ctcaccagct tcggctctca atgcaacctg gaacctgccc ttggcctctc agctcagcca 10380

cccccattcc tgttggcccc tggcccccca tcgaattctc tctaatccta atgcacacac 10440

ttgcacactc aaacacacac acacacacac acacacacag cccagaggaa aaccataatt 10500

gactgaggtc caggcaagtt tcccgagcag ggaccacatt tcaaaggtca gggaagcagg 10560

cgaacaggaa acatacaggg ggcacgtttg ggggtggagc aggaaataag aaatcacttg 10620

caaaagataa aaagaaaatg aggtagctgg tttcagacac ctcggagcac acagaacagg 10680

acaggcgcct ccgggtcttc cctcaacagg gagatgggcc aggcaggtcc ctgctgctcc 10740

accgcagagc tgggggctat ggccctgaca ccaaggccct ggggcaggcg gggaggcagc 10800

tgttctcctg cctgtgctcc cgggcagggc ctggccccac aagggaactg gccgaaggct 10860

ctgcttggct actccggaaa gtcctgggag acaagcaaag gacttgctag gtcactccaa 10920

acggcccaga tgtgacaact gtgaagaagc cacaccaaag caaggtgaca gaacaatgtt 10980

ggtgacgtca ggttatcagc ttacgctcaa ctccacttac ccggactcac ccgtaacctg 11040

ccgtctcttc ccaaccagta aaggatgcct aggtagaggg gcacaaggcc tggagcataa 11100

ttaccatttt aaaggctctg agaagtcctg cggtgaggaa gcctagttca ctttctctcc 11160

cctaggattt cccaactgcg cctgatcaca gaacattttt tcatttccac tcaggaaaca 11220

tattttgaaa aacactggcc tagaggcaga agtgaaatgg aaaacacaaa agtaaaactg 11280

aacaggaggc actgggcaga gaacggtcag aggcgccctg aatcctggac cggtggagat 11340

ccccagcttg gcatgctccc ctccctgggc ccagaccgcc tccccccatt tcctggataa 11400

gaaggctaat gcgcatcagg gtgaagggct tgcctgggct acacccccag gctcgcccca 11460

caccaatcgc gctcctgcga gagccagtga ctttcttgat ttggctactg tggaattgtt 11520

tgcaactaac caccccagat acagatacaa atgacaggat gatcagatgt aaaggaccca 11580

caggtctctg tgatacggct tcatgcagcc agcatggcta gtgccgtgca gaatgagaat 11640

gaccccaggc aagtccttgc ctcccagacc cagaacccca tggagcccac cagggctggt 11700

tcacaagcac tgtctgggtc gggcagagat tccagcaaga ggagggaaca tccatgcacc 11760

ggagccagtt accagaagca aatcgcctct tccaaaaccc aggctattaa tggagtccac 11820

tgttgagtgg agctggggtc tagctatgga atactgcaca gcagagatct tcctgagaga 11880

aagcagtttt ccctgaaagc catgtgtcct ccactaactg tgttttaatt gggcgaacgt 11940

ctgtatctca ttgcagtggc cgcgcatgtg ctgacaaggg gctgggggcg gggtggggag 12000

cagaagctca ggggcctggg agggaaggaa acaggccacc agggctcccc agaaggcatg 12060

tatctctctc acaaacacac gcatgcacac acacgtgcac acatactctg caagccctga 12120

gttagcaact gtggaatgtg accagctcag tgatcccagg acaagctgct agggaatatg 12180

acatttgatt gatgtctgca aatgtgcgtt ttcactaatt agaaggttta gggcagagca 12240

gagaaaaata tgtatttcag agtcccagtt tgacctgcca gaaaccagcc cattactaac 12300

attcttattt tcaacaaaat atagcattct gattacatac catcttggtt ccacgcctcc 12360

tgccttgcca agcccccgga agcggcccaa ggccatggca aatagtgaga gaaacagttc 12420

cagggtggag actgactcag gggtgtcagt cagtggggcg ctgatggccg gtgggaggcc 12480

agcagtcatc accctctcct tgggacagtt gagtagctct cccccagggt catgtggcca 12540

ctcaggttca tatgggaggc gagaggagtg gcagagtcca ggagagtggc tccgaagtca 12600

ctgttccctc caggcctcag tgtcttcatc cattaaatgg gtaggctgag gtctgggatg 12660

acaaggaggg cttgcactta ctgaaaccca tgggaggctg ttcgccgatt tcttttattg 12720

atggaagaaa acactcgtat aattcaagta ccaattaaaa ggcaggcact ggaaccaccg 12780

tctgccaatt cctagttttg cctataccaa atttgagcaa gttaattgac ctctcccagc 12840

ctcagtttct tcgtctgtaa aatgagggta gggatggccc ccagcccaca gggcagctgg 12900

aaggattaaa gaaatcaaac atctcttaga gcccacctgg cacactgtga tacacaacaa 12960

atgttagcta tttttgtcta tgaagtctag attttatatc ttgggtgttc taaagcagga 13020

tacatttatt taaaaacaag gattttcatt aaacacgtac cccacagaca gcaaccccat 13080

ggagactgct cttaattcag gccagtatcg aaacgactct aactacaagc tttatacagg 13140

tctcttggct gtccttcaaa tccaactaag gtggtacttc tgaagcactg tgcacatgtg 13200

tgtgtgcatg cacacgtgtg ggaagggcgg gctcacggat ccctcaggta ccccacccac 13260

gcagtctcaa gtcacaaagc gacagagcag ccgaggaagg tctgtgcccc actggaccct 13320

cgtgaagcca ccaactctac ctctgcgccg tgtcctgcag actgggctac cctttgggtg 13380

gggaccagca tttgatgcaa gaaaggcaga cagaaaagga aaagggcaag ttcgactcca 13440

gataacacag acagtaccaa gccccagggt ccataaatgc cacgcagatg gaagcattta 13500

ctgcgaggcc acacagcaaa cgcacggatc cagggacgga ggtgcagact gcggtgcccc 13560

tgagccatga ccctgcaaat taccaccatg ggaaaggagg ctgccaaacc ccccgacagt 13620

cggctgggct ggcacagact cgtggtttcc atcgaggtgg gaggaggtgg gacgtcccag 13680

cccctccccc atgcccactg cagagggaag cggccgtttc ccctgtgtgg ttacaaaggt 13740

ctcattgttc ttcctcacag ggaggaaact ggaggaccga gctcagaacg cattttagaa 13800

ctggcagaaa agaacatctg gggaaggaaa cacatttcag aaacaaacat acctttgtac 13860

cagcttttat tttctttaag tgttgaaaaa ataataataa taaagacatg ccaaatttat 13920

catcgctcta caaaatccct ttattgagca aaacgtggca gctctacttt caaatgatta 13980

ctgttcctgg aaaattgcag caacgtggat gccaaggccc gaaggccgcc atcagcagcc 14040

aaacaaaaga tgccacctcg ggctccgcga cactgtacca tgccagggaa ctggacagat 14100

ttggggaatg ccacggtttg cctttaaccc cttgcctcct ggtctcctga tgcatctcag 14160

aggctaacat tctttgagga actggcattt cttagttgta aatatgcatg tgggtttggg 14220

agctgcctgc aaagtccagt gttgacgatc agctttgatt tccttggaat caagtttacg 14280

tgtcgagtct ggaagttaag aagaatttgg agaagctgag cactatggtg ttgcaggccc 14340

tgggtgaact cttccaccaa gcattcattg tggactgaca gcgtgcgagg ggctctgcag 14400

gcaggtgcac aggacgaaac acattccgtc cgggggaaac ctgcaggaaa gctccctctt 14460

cttcctaagg tgccgggcct agcttcatgg gtccctaccc tccacgcctg tcacactttc 14520

tgagtctcat gtgggagctg cttctggttc ctgacttcac tcagtcctca taggaggtgg 14580

aactactgtc accccatttt acagatgggg agactgggca caaggggacc aagaaaccaa 14640

tgcaaagtca cacttgtggg atcagtgaca ggggagatca attcccaggt tctttctgca 14700

agagttaaat tgttttcatg ctgcctaagg gggggcaact gaaagaccac tgcatatctt 14760

tgccaaaagg gtcaagcaca ggagccgcag ccagtgggtc agatccgcag aggcgctggg 14820

gtgaccctcc ccatacctgg agggatgctt gtcccctcct ggccttcact gggtcccctc 14880

atgaccgtgg cctcccagga cctcagcaca atcccggtcc tgtgctccag gacaagccct 14940

ccgtccccaa gactgtgagg aaatggaacg aagaggggct cgctgcagcc cagcacccac 15000

actgcccctt ctcaggggca agaaccgtcc tggaggactt ggctttggag ggggagcctg 15060

ggaggccagt aagtcaacaa gcctctactg ctcatgggtg ggatcccacc gcaggccccc 15120

acctgctggg gcgggcaggg acgggcggca cagcttggcc agggcagata acccccacct 15180

tggccagggc gaaggcagga cacgtgggct ccagcctggc cccaccatcc ctgcacaaca 15240

ctgggcaaag tccacgtttt cctcaactgg gtgttgacat ctgcaggaca ggggcatgga 15300

ggtacagagc gctgaagcca cacagcaacc taggagcgag actccatgcc tccccgggga 15360

cccctcccca ccatgaggac catgaaggct tcccatgtgc cgcaaggact ctggtgtgga 15420

gacacacgtc tcctacacag ccaggcctaa cgctcttgta actgggtggt cccacctggg 15480

ctcacagctg gagggccagg agctcaaggc ttcgcagggt ctgctctcat cccagaggcg 15540

atggggagcc acagcaggct gcaggagaga gggtgggccc cctccacttc agaggcccca 15600

tctggcccac agactggaga gcacatctct cagcaaccac ggagcgccaa ctgcgcacag 15660

ggcctggtcg tcagagcggg gcaaaggcac tgaccgtcac ggccagggcg agggaagacg 15720

ggtgggcagg gaccttgggc agaggggggaa gaacctggtg cccaggctgg ccctgccttc 15780

agcagtgaag ctgagtgggg aggcgctgat gcagggggcc agaaagggct gctggtcagc 15840

cgggaggagc cccccacaga ggaagcagcc agcccagacg cagatggcag ggtcccctca 15900

acaatgtcct ctgaaaagga gaggcgggga ctgctctggt gacacctaca aatagatagt 15960

cagccctcag ccccctgcca tacttctgac aaagcagagg cccccagggg aggcgcaccc 16020

gaaggtacct gcacctgtcc cccagactcc tagagcccac ctgaccccat cccaccaggg 16080

ctccagctac aaaataaatg ccgaggccag ctaggcaagg acgcacactc ggtaccgact 16140

gaataggctc cacgttgtca tgagcgcaac ccacaggcca ccaggccaca ctatgcagag 16200

ctgagatggt ttcggccaag cagcctctca gctgagctga acaagtccag agtccccggg 16260

gggtcgtcac tatggagtaa caattgcgat gcgatggtaa ccctaacagc taaccgtcac 16320

tgagccaggc cctgagctag gtacttttca acgctgcctc tctgcagcct caggacgagc 16380

ctgtgggagc ataaagatca ttccctatca cggatgggga aactgagctc tgaagcagtt 16440

aacgtgcttg tcccagaccg cagagctagg agcaggacac aacagcaggt caggcaggaa 16500

cgggtgaggg gggcctgcat gggcttctct ggaggctgcg catacacgca acccccagga 16560

ccccgaccct gcacctgcag ctcgctactg ccccctcagt gactccagca aacctcgggg 16620

taggggaagg aggctgggaa tacctcgggt gtccgaaaca gcagcttctg cttggaggcc 16680

actgctgcat aatggttgct gcccagcaca ccccaagcca cctgtgccac ctgtggtgac 16740

cttccagcat gccttggtga ccaagctggc cttaggtgct gtgggcagcc aagaatagaa 16800

cagggcccac ccctcctctt cacactaaca caaagcaaga ggcgggcact tcgactgagt 16860

gcatccctct agctcaaggg cctcacggat cacaggggtc agggcaagat cccaattctg 16920

cattcccgtc tgcctttcat cctgctctgc caacaacagc cagtgaggct ggggacatcc 16980

ctgaacctgt ttctcacctg aaacacatca taccattgga ccccagccct ccgggagagg 17040

ccctaatccc tgactgtggt gagatcagat cactggttaa gtacccagaa gggccttggt 17100

caggggctcc aggggtgggg ggtgatgggc gtggtggtat cccgctctgg gctatagtcc 17160

accctgatgg aggaggtctg tggtcagaac cgggctgtgc agggcacagg agcccagagg 17220

gacccccaga gctcacctgg tggtctctga gcagggctcc ctcaaccctc agagaaaagc 17280

acagcaagga ggccgcccag agcccagcgc ctagcaccca gtggcgtgcc agacctgcct 17340

ggatcctgga gatctctcat caccctccaa gtcagtcatg cccaacccag ggacccacag 17400

cccacggggc cgtgaaggtg tgctgagtcc aagaaggcct tcgacactgg gaagccaagt 17460

ggcacctcct ggtgtggagc aggcggaatc ccaccagcct ctgctctgcc agtgggcaca 17520

gctggacgat gagcagaagg ggctgttgct taataaacgt catttcctta agaggataaa 17580

acctttcaaa acagatggaa attttttttt aattaaaact ggtggccaaa gagatggaaa 17640

gcaccccttg tgcctcccte ccatcgtgac ccatcctctg cacacctcaa gctgttcgct 17700

gcccaggtgt ctcctgaggc actgggggcg ggtgagaatc cgtgagccct cggccagccg 17760

tggctctctg gagctctgcc ccaggccatc agggcacacg ccgggcaccc tgggggccac 17820

acagggcaga gcccagctgg gtcagcacac agggccacac tgggcacaca agtctctgag 17880

cctcccctgt ggacgcagct ctcactatcc caccccacta ggtcccgggg atctgtccca 17940

cagggtgata tgctgtcaca gaccactacc agagccatgg cctgctgttc cgcccgcagc 18000

caggtagtca cttgctccac agggacaggc aacgccgcac ttgggggctg ctctgcggca 18060

ggactagagc tccagcagct cagccctcct gagaaggaga actccatgct ctaagaggca 18120

gacgcagcgg acggcaccaa agccaccaca agcccacggg gccctgcatg gcaggtcagg 18180

agtccctgac cactcgctct ttgtaaccag agctgcagtg gagtctacga ggcaaggact 18240

gtgggcggca gtggccacag caaatgaatg agtgtcccaa gggagcaggc ggctgcgggg 18300

aggcacagcc gggacccagg agtcctccgg cactgcagca aactccctgg gccccctgag 18360

cagcgaccag gtggcaagtg catgaactcc cgggggcata acctgggagg gtgacactct 18420

cttcgtgttc aaattcttga gaacgcatta aaaatatcac tcagtcacct actctatagt 18480

tttaactcaa aagtaccaaa gtagccaggc gcggtggctc acgcctataa tcccagtact 18540

ttgggaagct gaggcaagag gatcacttaa gcccaggagt tccaaatgaa cctgggcaac 18600

atggagggac cccatttcta caaaaaaagt gttttaaaaa attacctggg cctggtggtg 18660

tgtgcctgta gtcccagcta ctcaggaggc tgaggcggga gaaccacatg aacccagggg 18720

aggtagaggc tgcagtaggc tgtgatggca ccactgcact ccagcctggg taacagagtc 18780

agactctatc tcaaaataaa tttaaaaagc accaagccag gcttggtggc tcacacctgt 18840

aatcccagca ctcagggagg ctgaggcaag tggatcacct gagtcagaag ttcgagacca 18900

gcccagccaa catggtgaaa ctccatctcc actaaaaata caaaaattac ccaggcgtgg 18960

tggcgggtgc ctgtaatccc agctactcag gaagctgagg caggagaact gcttgaaccc 19020

aggaggcaga ggttgcagtg agccaagact gtgctactgc actcaagcct gggagacaga 19080

acgagactcc atctcaaaaa ataaataaat caatcaaaac caccaagact ttttaatata 19140

aacatttatt attccataat tccttttttg catgattaaa aatgtttata taaagtttcc 19200

tgaaaatggt aagaatgcca agtgaaggct gcaaatgccc aagcccccac cgtggcatct 19260

cacggagtct gggccctagg aggctggtgg gtaccacgtg gacccgagac ttcacagtca 19320

agtccctttg gggtacactg ggtttcccac accccagaaa tatgggctct tactgcagga 19380

ccatgggggt cctcacactt ggcccagaag ctgtcacata gccagacagg tgttctacaa 19440

cctaggctag agggagctca tgctccagca gaattcgagc cagaggaggt aaaagatggg 19500

taagatctgc tccctggaca gatgaggcct tggcctcaga acagttactg atcatctacc 19560

agacatcaca ctagaggcag aggggcgcag acgaagacag cccctgtcct caaggccctc 19620

ccaggttggg tggaccatgg aaggttccag acagatctgg caagagaagt gcccacacca 19680

ggggcagaag atgggcaggt ctgctcaggg cggcacggcc tgccaggcca aaaagttcca 19740

acttcagatg ctggagaatg ggcacgactg tctgagaaag ggaaggatgt gatgaaaact 19800

acttggagaa aaattaatct ggccagagca taagataaat gggcaaaggg gaggttccag 19860

aaagcaagga gaccaagtaa aagctgatgt cattggctct gaatctaggc tttcactgaa 19920

tatgcaccgc agggcctgta ggtaaagcct cagagcccag ggagtctgag tggaggagag 19980

ggcaggggac agagctgggg cctgtgtcta cagtgctcag gaggaatagg catggacgtc 20040

agctcggagg ctccagctga agtgaggagg cggccagggc agcacggcca cgcccggatc 20100

cagactcctt ttgggaagca agttcgctct gggggaaagt ttggagaaat ggcctttacc 20160

cgcagaagca agccccagaa catatcttgc tccaaaacta tctcgtacag tgaggacgtt 20220

aagcttcagg tcccctagag gagacagtct gctccttcct ggggcagaac ccaaggtggc 20280

cagagcctgg aaggcaccca gcacccaggc tggtgtgttc cagcccaggc cacacgctca 20340

gatagctatt aatgccccgt tgagcaattt cctgagagct ttgccaggca ggtaccgcct 20400

ccccatctga actaatacag gggtacatcc caaggaagaa atgaaaggtg cccacatttt 20460

gctctgggat taactaggga ggggagtgat aattaactca gtaattatat ttgccatcgg 20520

gctaatgcta aaattagtgt gcattagaat ttctttcctg agcagacacc ggagtgagtt 20580

gggcagcagg agtggctcgg gcaagtcggc acaaagggca cctccagagc cttccacaaa 20640

tgtcagcaaa acccacaaat gtcaaggccg gctccactgc acccagcaga tgaattcact 20700

tccacagcct gagaccgcca gctcatcgga ggccatttaa aatccagccc tctgacacct 20760

gctggatatc accatttacc gtccccagat caagagatca aagggtggaa cctgatagga 20820

cggctctgaa gttcaccaca aaagcataaa cgtgcaagca gagccaatac gtcttttgaa 20880

aaggacaatg aggtgggaat ttacataact gatcttaaaa tatgttctga tgcttcagag 20940

atggagacag cagcattccg gtacacaaag acactcacag gcagtggagc acagtgaagg 21000

gtctggaatc aggacccagg tgtctgtgga cactacacat aaaagagcag catttacaat 21060

gaatggatag gatggaccat cccaccaagg tgttggacaa ctccctattc actggccaga 21120

cccctacctc ataccatata caaaaaaaaa aaaaaaaaaa aaacccagac agaataatgt 21180

ctgaatgtaa aacataaaac agtaacagtc ctggaagaaa ataatggagg atatatttat 21240

aatctggaga tggagtaaca agggatagga aaaaagccat agggaaaaag tagagttatg 21300

attatatgaa gcttcttaat atctttatga taatgtacca ccagaaacaa ggatgaagga 21360

ctagctacag accagcagtg aaacctgaaa caaacagaac aaagaattaa agtccatacc 21420

aaataaagac ctcccacaaa tctataagaa aaagataaac aggctggcac cgtggcttat 21480

gtctgtaatc ccagcacttt gggaggcgga gatgggtagg tcacttgagg tcaggagttc 21540

gagaccagcc tggccaacat ggtgaaaccc tgtctctacc aaaaatacaa aaattagcca 21600

ggcgtggtgg cgcatgcctg tagtcccagc tacttgggag gctgagccag gagaacagct 21660

ggaacccggg aggcagaggt tgcagtgaac caagatggca atcgcgccac tgcactccag 21720

cctggaggac acagcgagac tctgtctcaa aaaaaaaaaa aaaagaagaa gaagaaaaaa 21780

gaaaagaaaa agacaacaga aaaatgggcc aaggataagt gtaggcaatt tgcagaaaag 21840

taaataccaa taaaccagaa atgagggttg tgcaaatcaa aaggtgttat aatttttaac 21900

caaactggac caaagaaaac accaaaaacc aaaatcttgt aattgccagc atcagagagg 21960

atataggaaa gtgtgtgttc tcgtagatgc ttgcaggtat gaactgctac agccttttag 22020

gagttatgta tgtatgtatg cttgtatgta tgtatttgag acagggtctc gctctgttgc 22080

ccaggctaga tctgttgcag tgctgtgatc atggcttact gcagccttga cctcctgagc 22140

tcaatagatt ttcccacctc agcctttcaa gtagctgaga ctacaggagt gtgcaatcat 22200

actcagctaa ttttttaaat tttttgtaga catggggggt ctcccaattt tgcccaggct 22260

ggtctcgaac tcctggactc aagtgatcct cctgcctcaa cctcccaaag tgctgggatt 22320

acctggatga gccactgtgc ccggcctcaa tatctttaaa aacagaaatg gacacactct 22380

ttgactagga atgtatccta taaaaacact tatacacatg cagagacaca cgagcaagca 22440

tgctttgtaa tagcaatgaa ggctggaaaa actcctcaat caggtaaatg ctgtcaagtg 22500

cacctgtgta ctatgaaatg gcacttggct tttaacaaga gcaaagacag aaaagcaaaa 22560

gtacaaagta gggtgtgatg gcacatgcct gcagtcccag ctactcagga ggctgaggca 22620

ggaagatcct ttgagcccag gagttggagg ccaggagctg ggcaatagtg agaaaaaata 22680

aaattaaata ataataataa taaaataggc tgggcacagc ggctcatgcc tgtaatccca 22740

acactttggg aggctgaggt gggaggatcg cttgatccca ggagttcaag gccagcctgg 22800

gcagcaaagc aagacaccca tctcaacgac aaattttaaa aaatcagcca ggcaggctgg 22860

gcatggtggc tcacgcctgt aatcccagca ctttgggagg ccgaggcagg cagatcactt 22920

gaggtcagga gttcgagacc agcctggcca acgtggcaaa accctgtctc tactaaaaat 22980

acaaaaatta gctgggcatg gtggcagatg cctgtagtcc cagctactga ggcacaagaa 23040

tcgcttgaac cagggtggca gaagttacag tgagccgaga tcgtgccacc gcactccatc 23100

ctgggcgtga gtgagactcc tgtctcaaaa aaaaaaaaaa aaaaaaaaca aggagccagg 23160

cacggtgggg tgagggaggg cacagaagca gcgcctcttc tgggggcacc cccaatctct 23220

agcgatccag aggcctcagg atcctgaagg gagaaaaaac gtgaagctcc gtgctagaag 23280

agaccataga gattggaatc agctggttct attttacaaa aaaaggaaac tgaggccctc 23340

agaaggtgag tgcctctcaa tgccccacag ggaggcaggg agagggctct gagccctgca 23400

gggccctgga ttcttgcaat ggggtggagt ggagcctgtg ccgcccccac caggcacctt 23460

ctcaggagag gagccgttgt catatccttg aaggggtcct tgagcccctc aaaaggctaa 23520

aaaccacttt cctccttgag tgaaccttca cctcagttta accacaagaa aaactacatt 23580

aaggcccagc gcagtggctc atgtctgtaa tcccagcact ttgggaggct gaggtgggtg 23640

gatcgcttga gcccaggagt tcaagaccag cctgggcaac atagtgaaac cctgtctcta 23700

caaaaaacaa caaaatcagc tgggcgtggt ggtgcacacc tgaggtccca actacttgcg 23760

ggctgaggtg agaggattgc ttcagcccag gaggtagagg ctgcagtaag cggtgactga 23820

atcactgcac tccagcctca gcaacagagc aagactcaaa aaaaaaaaaa aaagcaggcc 23880

gggtgtggtg gctcacgcct gtaatcccag caccttggga ggccgagcgg gaggatcagg 23940

agatggagac catcctggct aacacggtga aaccccgtct ctactaaaaa tgcaaaaaat 24000

tagccgggcg tggtggcggg tgcctgtagt tccagctact caggaggctg aggcaggaga 24060

aaggcgtgac cctgggaggt ggagcttgca gtgagctgag atcacaccgc tgcactccag 24120

cctgggcgac agagcaagac tccatctcaa aaaaaaaaaa attaaatctc aaaaaaaatt 24180

acattaaggc aaactaaaag atgtttaaaa tatatatatt aaattaaata cactccaata 24240

gagcaaatac gaaaataccc agaaaacaca atccccgcac ccccaggaca acctcccagg 24300

gggtccacag caagagaccc caagcacgag agacagagaa cagtgtccct gtggcggaac 24360

ctctggccca tcaggctcta ttagaaaata aggctcttgc cactgagaga aagaggcaca 24420

gtcgcccagc agccacgggc tctggcacac cacgagtcag gccagcaaag tgtcaactgc 24480

cccctacaag gtgacaaact aggacaaact ggaaaccaga ggctggacct ggagcacagg 24540

gaccaccaca tggggctggg gaatgggcag ggacctcaga gcgccaccca catgcctaag 24600

agcagcgcgt atgcgcatgc ctctgcatgg cttagggaca cagggagctc cccccacccc 24660

caacccagga aggcagcccc cactacccag gtagggaacg gataggacca gcaccccgtt 24720

ctgctcgtaa ctcagggctc caggcccccc cgggggcaac cagcacagag ctcagacccc 24780

aaatatcttc acccacctcc tggtccccat ctggacaagg gtgctgggga ctggctctca 24840

gtcacaccct cggggtactc ttcaaaggac agctggatgc cccagggcag gagcttttgg 24900

cccccagctc cctcacccca gacaccagct cttgggaccc caccagcatg ggcaaggtgg 24960

acaccatcgt cccgattttg cagatgagga aactgaggct gagggctggc acacggctct 25020

ccagagctga agagaatgca gagagcagcc ggagccagcc ggtgggtccc tgaggccggc 25080

tcgtagcaag ccacagctgc ctccgcccat cacacttgga cctcactggc cccaggacag 25140

ccctccaggg cggcctggca cagagcccac accctgctgc ttcctgaaca aataagtgaa 25200

caaggccacc aagccgagga cctggatgta gccccggctc ccgccagggc ctccccaaca 25260

gactccccat ttggagagcg cattaagtgt ttccaaagcc tcacaaacca cagatgtccg 25320

gctgtctcac ggcttctgta acctgaactt ggccctcact ctgccctccc agcactcctc 25380

tcagggccca ggcccctcct ctgagatgcc agcactgact ccccaacttg tccccatcac 25440

ctggctcgtt cctgaacctc ggcaggagag tctcaggcca gatcctccca ccagccacct 25500

ccaccaggat gcaggaggca tgagacctgc tcgtgccggc tgggagatgc aaccaaccaa 25560

gatcaatcca atcagcggat gaactgacaa atataatgtg gtccctccac acaatggaat 25620

attattcagc cacaaaaagg gctgaaatag gccgggcgtg atggctcaca cctgtaatcc 25680

cagcactttg ggaggccgag gccggcagct cacttgaggt caggagttca agaccagcct 25740

ggccaacatg gtgaaatccc gtctctacta aaaatacaaa aattagctgg gcgtggtggc 25800

gggcacctgt aatgcaagct acttgggagc ctgaggcagg agaatcactt aaacccagga 25860

ggcagaagtt gcagtgagcc aagatcgcac caccgcactc caacctgggc aacagagcaa 25920

gactccattt caaaaaaaaa ataaaaggct gaaacaccca tacgtggtac tacttggatg 25980

actcctgaaa acgttacagt aaccaaggaa gtcagccacg aagacgcatt gtaagattcc 26040

cttcatgcaa aatgcccaga acaggcagaa ccacagaggc agaaagtcga ctggtgttca 26100

ccaggggatc cggggagagg gaacgggaag tcaccgtgta atgggtatgg gttttatttt 26160

ggggtgatgg aaatctctta taacttgata gaagagaggg ttgtaaacac tgtgaatgta 26220

ccaaatgcct gccttctata ctttaatatt ttatattata taagtttcac ctcaatttaa 26280

aaaaaaaaca actcgacacc tttcacctag gaaagatctg gctttagctt gcatttcctg 26340

taactcctgc ctaaagcctt ccagaagctt ccgctgcctt gtggatcaca accagactcc 26400

acaccatgat ctggcctcta agggcctctc gcaggacacc ccgagggtga aggagcaccc 26460

gtgggcccac ctctgcatag ctgcaaagct tctttccctg tcctcccctc tacatgggaa 26520

gctctgcccg caggggcggg gccttatctg ccattctatc gcactcaacc ctagcacttc 26580

actcggtagc agacaccaaa gcaaaacagc aacagcatta taccgggcca ggtgcacgtt 26640

aactcactga attcatggta ggaaggattc tattcccatt ttacaggtga gaaaactgag 26700

gcacacaaag gtagcatcag cttcctaagc ctcccagcac aggaagcggc caggctggaa 26760

tcagaccctg ggcgcagggg ctctgtccac agtgctaact aactactcct gcccccgagg 26820

gctgcagcgg tgagtgagtg agtttgtcag tggactggat gtccaaggtc atacaggaaa 26880

aatccagact attgtaataa cagcctctag accggctggg gccagaaaga tcgaggacgc 26940

tgacacacaa ctgcgctcac tgcagctctg ccagggatgg ggctaaaggt ctcacacagg 27000

gcagttaggg ctccccatag cctgggagag gaacggggtg agataacaga aactaggtat 27060

ggtgcccgaa gtcaaacagc cactgagcat gtaaacccag gtgggtctga ccccaaaccc 27120

ctccaccccc atcagccctg caacccgtcg ctgcaaggga gaaagcaact cagaggcctc 27180

acctgcctac atcccccacc cgtgtgtgtg agttctacta aatgcctgag cagtgacaca 27240

gcacggctga aattaaacgg gttccaaaaa cgacaggaag cacgaagtga atctccccag 27300

gaaagtgctg aacaaatgct ggatcgggtt caccggcgaa tttcttggaa ctgaagaggg 27360

gagctaaaca cacggggccc tgctttggag gggactctct cagggtgctc cacacagcac 27420

ttggttaacc ccactcagcc cttctgggct ctcccagagg gcccggcctt ggccttgggc 27480

atctacagga ggaacctcca gggggagagg gggtgcctgg acaggccggc cctggaacaa 27540

gcacttgggc cccgaggaga gaggactagg gcttgggagc tggggaagtt ctcagcactg 27600

ggaccactag aacaaagcca tttccgtgcg ttcacagctt ccaattgcaa caggaagcaa 27660

tcaggaaaaa taattagcgg cccacttact ggcttcgctg aggtccgagg catgtatttc 27720

acacagtaaa accagggata taacatcaaa accgttctgc agaaagattc ctccctttcc 27780

ttccatttta ggcctggatc accacattca ctggggctcc caggccttgc tgcctaatgt 27840

taaaataatc aactctattt ttgcctcaca cacaactgaa ctctacagct ataattcttt 27900

ctcctcaggg gctcgaacca catggacgac aggcatttga ctccagcaac atcaccccaa 27960

aacgtgcaca aaacccaaaa ctgcaatgag gtgaaaggca acgcggtcgg cctagaaacc 28020

ccccctttaa aacaaacagt ttccccaaaa ccccttttgc ctccttgacc caggcatttc 28080

cggaaaaagg agcggcgctg gcctgtactc cccagatact gtcgctgttt tgtcttcacc 28140

ttgttttgct agctccagac aaggccccac aatgtaaaca cgctcctgaa agaggcagat 28200

ttggggtgaa actgtccata gaatctctag gcttgggtca gaggcaggag gacgtgaaac 28260

aaactccaag ctcctcctgt tccccgctgt cccccacacc tccaagcaga ggctgcagcc 28320

tgggggatct gactacaggg ccaccccgct gcaccattca cactggaaat attcagggag 28380

acagctgttt gccttaagga ggcccagaca aaggggcccg aggtcctccc cgctaaactg 28440

ccacaaacag aacaggagcc gcggcgtgca caggcacttg cggccgtgcc acttggccag 28500

ccatactcca gaaaaacaaa acacgcacat ccgaagagaa tgatttaggt agcaagaggc 28560

ttgcttgaaa aaccacatgg caatctccaa attaaaagaa catgtgtagc gtttcacgac 28620

tgcttaagtt tcctgagtcc tcctgacctc aactccaccc cctgggaaac accaaaagtt 28680

ggatgagaaa gttcccccgc cctacctctc cccacgggag tgtacaactg aggcacaagc 28740

ctgcctcccc cactgccccg cgatctggga ccacgtctcc tccgcgtagc cgacccgggg 28800

atggacacta tctggggacc cggcggccac acggggcatt cgggtcgccc gggcacctgg 28860

caggtgtcag tccgcttgga aacccacagc cacgcggctc acaggagcag cgccaccggc 28920

taggccgccc cgcgcccggg ctcagaactt tctcgctgcc acttcagccc gtcctcggag 28980

cacgcggggc ggccgcgcgg ccgctggaaa caggcttgcg aaccggctcc ccgggccagg 29040

cccgcctccg cgccccaagt ccccgctcgg tgcccggccc gggccacacg ggcccagcgc 29100

gggctcggct cggctcccgg cttcccgcgg gctcgggcag gtgaggaccc gcccgcgccg 29160

cacctggcgg agcgggcgcc ctcctcgcca gcccgggacg cagcgtcccc ggggagggcc 29220

cgggtgggga gacaaagggc ccgcgcgtgg cggggacgcc ggggacggca gggggatccc 29280

gggcgcgcgc cccaactcgc tcccaactcg ccaagtcgct tccgagacgg cggcggcgcc 29340

cgcgcacttg gccgcggggc cgcccgggcc attgtccgag caacccgcgg cccgtcttac 29400

acgccgggcg cgggaaggta tcgaatcagg 29430

<210> 8

<211> 33769

<212> DNA

<213> Homo sapiens

<220>

<221> unsure

<222> (33739),(33749),(33758)

<223> Identity of nucleotide sequences at the above locations are unknown.

<400> 8

cttcccctta cactggtcct tcgacccgcc tcggatgaaa actgaatggg tttagcctta 60

gaggctctcg gtctctaagg gaggtgggtc aggatgccgg ggacagggtc ctcttcctgg 120

ggcaacgtgg gggaacgagc cacctacccc tccactgaat tgccctgggg tgtgggtacc 180

gacggctcat tcggtgtcca gggtctgaga tgtgttgaca ggaagaatga aaggggatgg 240

gagggatggg gcgaaagaag ccacctgcag ccccaggaac tatctggcca gcacaccgtc 300

acccagcggc ctgagccacc cctgccagag ccaggaggag accctgccaa tgggtcacca 360

gtgtgcagga actcagaagg tcatcacagt taataccctc catgccccaa tgtgggaaaa 420

caggtttttt cacaacaaac aagataattt ttgttatttt ggcaaaagga ggcagggcag 480

ccccggacac ctccatccca cctcatcacc cagccgcagg gccccggcca tccctgcaga 540

cagagtggat gtcacaacct ccctgcaccg aaccaagtgc agctcccagg ccacaggcca 600

cccaggaaag gtccagtggc ccccggaggc tcccaccgca ggcctcccac cacagccggc 660

accaacccag gatagctgtg ttctcctggc ttcttttcac acgggtagca gaaagctgag 720

atccggggaa agctgagatc cagggaaagc tgagaatcgg cctctgctgc ccggacgccc 780

acccccagct ctgctcccag ctccagggcc tccttctcag gtgcccttac aggaggcaga 840

gggcttgagc cacctcctgg gcctggggca cgcaggatga acggggtcac ggtgcaggcc 900

actgtccact gcgcagatcc caaggccata aacagcctgg ccacagtggc ttcccagctg 960

gcaggcggcc agattatttt tgttgtttag caattgatta agtttctccg ctgcccccag 1020

gggtaagtgg tggggcaaat gccgcaaccg cagcatttga cccgggatcc tgtgccaagt 1080

gaccataggg tcacaaagca caagggaagt ggctgggccc gatgctggct ctgctggaac 1140

ctgaggccgg ccactgtcac ctgcacggtg cctgggacct tccagcaagc acagagaagc 1200

tatggccctc caggagcagc tggcaggcac cttggcctgc agtcaggggc tctgtctgct 1260

cagctctaaa acaggaaagt cgctgctctg cctggggtca gggcagccag agagtgacca 1320

agtcagtgcc ggcctcagga agggacctgc aggcgggtcc cttcctctcc catccctcgg 1380

tgccagccag cccctcctgt ggccccccac tgcctgcctc tgcccccatg ccccaccaca 1440

acctcaggcc catggctgca tggccactcc ccaggcaggc agtggggatg ggatttcacc 1500

atgttggcca ggctggtctc gaactcctga cctcaggtga ggagttccta aagtgctggg 1560

attacaggcg tgagccaccg cgccagccct ccctgtggta ctaaacactc acacccccct 1620

gctggggacc ctggtgaggg aacacagcct cacaagtgaa gtgtggtttt gttgagcaaa 1680

tgacgcctgg gcagccctct catctttgcc taaaactgaa gaatttaggg gcgtggatgt 1740

ataaaacagt tggtgactta aatgaaaaag aaggccacac tccccccttt aggcaggcgg 1800

cctaattctt taaaagccag cacagggtgc ctttctgaac ccaggcacac agtaggtgtt 1860

caatggacag cagcggttac ttgtactgct catgacaccc tgtctgtggc ctctgcagct 1920

ggctccagcc tgacgcatgg ctgcgccccc ccgcaaggcc accccggtat acatggaaac 1980

tctgtggaga aggccttggg ggccggccag gacgccaggc ccagatccca tctgcgccct 2040

tcctccatag acctcagcga gctctcggca ccatgtgcct caggcccatt taagaagtag 2100

ggccggccag gcatggtggc tcatgcctgt aatcccagca ctttgggagg cccaaggtgg 2160

gtggatcacg agatggtcag gagatcgaga ccatcctggc taacacggtg aaaccccatc 2220

tctactaaaa atacaaaaaa taagccgagt gtggtggcgg gtgcctatag tccaagctac 2280

tcgggaggct gaggcaggat aatcgcttga gctcagcagg cagaggttgc agttagcgga 2340

gatcgcgcca ttgcactcca gcctaggtga cagagagaga ctctgtctca attaaaaaaa 2400

aaaaaaataa aaaaaagaag cagggccagc cacggacgac ccctcacaca gctcccagga 2460

cgcgtgcctg ggtatagggc tcaggaccat gaccgctgca gtggcccccа agaaacgtta 2520

cttttgtcac ccaccccgcc tcagtggcag tagccaaaat aacggattag aatggaacca 2580

tgtgacaatg ccactgcccc aactgacaga agatggctat cagcagttca cgcggcccca 2640

cctatcacaa gtgcagggca ctctacaact tatgcatcct tccccagaca ccgtcctttc 2700

gaccctccca ggtcagcaag gcacacaggg cctacatttc acagccacac agcagagggc 2760

tgaggctgga actcggatgc tctgatttcc gttcaatcac atccccagag gtggcacaga 2820

gacggggggc ttctcttgac aaagtcaaga aagtcactgc cagctccact gaagaccaaa 2880

gaacctcagc tctcaaaccc tcttgaaggt gttaccgaac tctcccagcc tgtttcctgg 2940

gtcccgatgt tggtcccgtg ggacacagga agaggaagaa gctccctaga gcagagcctg 3000

gtgcacctgc cacactctca gagggctgcg cacgggcgga ggagccgtgt gcaggagtgg 3060

ggtctggatg gaggggcgct gtggccgggg gcaggggcca ggggaagggt gctccaggtg 3120

gtgggcacag cacgagcagg ggcagggagg tccacactca gatgtgcaca gggagaaaca 3180

aatcgtgcat ttccattgga ataggcggta aaaggtagaa aaacagagtg ggggccagga 3240

agggagtcgg agccttctag tgtctctctg caggtgagcg gcagcccgag gtgtcagctc 3300

agcagacttg gggtccaggg gccgtgtctt ctatcactga ccccagggca cacggaactg 3360

gggagggaga gcagaggcac agggcacggt cagtgaaacg aaacaaggag tcatcaccaa 3420

atgcggaaag ggcaaggagt gcccgcagcc gcacaagggt tctgtctggg caacgtgggc 3480

gtcccaccag gccccgcacc ctgcaagcgc aaagctcgcc actgaagata aagggaagct 3540

gttggagctg cggagctggt ctggggtccg catggagctg ggcttatgct gcagtcacaa 3600

gggggacatg gaagaggctg caggggacaa aaccagtgac cacagtctaa ctctgagcct 3660

gtggaaaggc gcccacagca ttcacccatc ccagagatgc cattcccccc gtgcccccgc 3720

tccacggtga cagcgttctc caggaatatg atgcgccccc ctcctcttgc atcagccctg 3780

acagtgagta ttcaggccaa aaagcagaag agcacagctg cgtggttcca tttccatgta 3840

gttctggaac aggcaacgct aatccaaggt gatagaagtc aggagagtgg tggagggggc 3900

gggggttgag gatggcaaag gggcaccggg aactttccca gtggtagaaa tgttctctgt 3960

ctggaccgtg tggtagttat gcagacatat gcagctgtca aagttaatcc aaatgtacac 4020

gttaaaatgt gtgcgtttta ttgcctgcaa gttatacctc aattaaaaaa ataaagttag 4080

cactcaggct tcttccacaa cttcctgaac cgtgtgagct gattttcttg ctattaaaaa 4140

ttcacggtcc atggctgaga acagcagctg ccttctgttt gcaaagtcaa cgccaatcac 4200

tgcccggccg cggcagactc ggccccacag gacctccttt ctttttccc tttgacctac 4260

ttccctgata agtgacaaga cagccagact ctgggaacaa acgcccgtta ttcggccccg 4320

agctgagcgg gccctgcttc ctgagctaat ccgcccggac agacggaggg acgtgagggg 4380

ctttgccgtc ggctccagct gtcagtctgc ccgtcagact cgacagtggc cccctctgtt 4440

cctcccgctg cccccactcc atccccgact tctttttgtt tcctgtccct gacagacgaa 4500

catctgttaa aactctgtct gggtgagctg tggccagcgg cccacaaatc cccaagccgc 4560

accccagcct catctgggcg ctgccgggag cactgcctgg ccaccctctg gacatagctc 4620

tgagagccac cggccagggc acgtgtggcc cgagtggcat ggtgcacgcc gctaagccca 4680

ctgcccaaag gcccccaagc aggagggatg tgcaggagac aaaagtcaaa agaacagggg 4740

cacgttccac agaggatggg gctggagggg tggcagtgag gaacagcagc ttccgaggat 4800

ggcggtggca actcccaaat aaggcctcac tcctgctgtt tttagctcat tccacataat 4860

tggaaaaaca tggcagaaac cgaagccagc tgctgccttg gtcctggggc tgtgtggagg 4920

gggtggggag gccggaggcc caggctctgc actcgactgc tggggatgag agtgactctg 4980

agctgcagag agcagcatcg cagccgccat ggtcccattg agccccggcc acgctgggcg 5040

gcagaggctc gtgggatata cctgccctgt ctcatggggg tcacttcagg aggggcgggg 5100

gagccaggac acagcccagg gctagcggtc accctgcagc tcaggggcca cgtaaatagt 5160

gccaccttga aggcacacag cagtgcgggg ccccccccgc caccaacgca tccctacctc 5220

taggaggccg cctgtgtgcc cctgggaacg ctgctccctg tcccttgggg tcctggtgtg 5280

accaccctct cagccccttc cttggggaag gcacctgact ccctacaccc agctggcttt 5340

catttgctca aaatcaggaa aaagcagaat tcaagacatc acagaaatgt cttcgcctgt 5400

aactccatga aagataaacg gtcagacacc caggagggag tcccagggac ccttgagtct 5460

cacctgaggc tctggcttca aacctcgaga tgtttccagc catgctagcg ccgccccca 5520

caacctgccc cacacagtcc tcccttggga actcacagat ttggccccca cctgccccgt 5580

ttcttctggt ggagtgggtg cgttgggttg gggtggggct ggggactctg gatgtgtctt 5640

aagagtctga gtgattctga cacagccagg ccctgccccc ctcctgacct tcgccccaca 5700

ggaaagggag ccacacgcct gaagcgccca gcacaccccc ctccgtcctc cccaggtcac 5760

ccgctggccg tgtgagccgt gctccccact gccccttcac ccaccccagc tcctcctggc 5820

agcacccagc cttggaagct acttctgatt acaaccgccg aaggaagact cgctccctcg 5880

gcactgaccc agacagcctg caccatcacg ctgctcagca caacccacac agccttcctc 5940

caaaccccat ggagcgggga gtataatcac ccccttttcta ccaacggaca aactgaagca 6000

cagagaggtt aagtcacttt cctaagctcc caacacgatg acaaaaaata gaaggtcagc 6060

ccgcaagtgg aactaggtgc tccaagtccc cggtctgcct gacactgcac ctcctcgccg 6120

ccacggtccc gggtccgcct gacactgcac ctcctcgccg ccacggtccc gggtccgcct 6180

gacactgcac ctcctcgccg ccacggtccc gggtccgcct gacactgcac ctcctcgccg 6240

ccacggtccc gggtccgcct gacactgcac ctcctcgccg ccacggtccc gggtccgcct 6300

gacactgcac ctcctcgccg ccacggtccc gggtccgcct gacactgcac ctcctcgccg 6360

ccacggtccc gggtctgcct gacactgcac ctcctcaaca ccaccacggt cccgggtctg 6420

cctgacactg cacctcctca ccaccaccac agtcccgggt ctgcctgaca ctgcatttcc 6480

tcatcaccac agtcccgggt ctgcctgaca ctgcatttcc tcatcaccac ggtcccgggt 6540

ctgcctgaca ctgcacctcc tcaccgccac ggtcccgggt ctgcctgaca ctgcactttc 6600

tcaacaccac tccttggccg gctcccaact acaaaccaag ccatgtcttc catcctgaat 6660

cctcttggcc taaacatcac tcacaatgcc tccctcggga acaggcacaa gtcccaccag 6720

cacagcctcc ttcgttacct gcgtttccgc tagcccaggg ccagctccag agccctcacc 6780

acagagcctc tatccttcac ccccggacac tggacctcac caacccatag cctggaggag 6840

atccctgtgt gaccccaggg cctcctctgc ccgactctga atttcactgc ccaacgtgac 6900

acctcggaag gctctctggg cactggcagc cctccatggg caccgctcct tctggccagc 6960

tctgacatcc cggctggtga ggtgccctgc acgaggcctc tgcccactgg gacctcacag 7020

ccgtgctgtc agctgcaaca agcgacagaa tttcacgttt tcttcacgtt gcccctgggt 7080

gagcagctcc aggtagtttt cagtcgaggc gaggcgtccc gtcagcagcc aggcggcaca 7140

gctaattcat gcccgccggg cgcacggccg caataccaat gggcacctgc agcctggaaa 7200

gccacagagg aaccgagaac agcgactgtg ctcaggtgac aggactgtgg tcttttaaca 7260

aaacattttc ctttaacgtg atattttacg gcaaggaatg aaacctggag ggcaggacat 7320

ttggatacta aagccccagg ctgccgcgtg gtctgctttg tgaagtctga agcccgcgcc 7380

ccattctggc cccgctcaca ggtccggctc tgactcacca gcttcaatgc taggccgtgc 7440

ctgtcctcca accagaacat gacttcctta aggacaaagc cgtttctcgc ccatccccat 7500

ctccctctgg attaagaaat atgggaagat cttctagaac cacctcaaat ttgcagagag 7560

ccatcctggt gacaaaccct tgaaatgctt ctaagaagag tttaggtttc ttctcaactc 7620

taaaacctct agaaaactct atttccacac cagctgcccc tggaacactt cagcttcaaa 7680

agggcccagg gcagggagac ggaggagcca gcatccacac cgagcaccag cctgttaatt 7740

aacgggaagc gggtggggcc catctccagg cagctctgag gtcagactgg ggaaccatgc 7800

ttacaaaaaa aagtgaactg aaacgctcac gtcctcatgc aaaaccagac tcccagttgc 7860

atctttctgt ctcattgagg agctttttcc tcccttgac agaacaccct acacacggca 7920

tctggaacca aagcagaaag attcaggctc agagtaaaac agtccccaca ctggctgcat 7980

gtggacgttc ccggcccaga gtctcgccca agcagggcct ataaatgaca caaaatgttt 8040

ttctcctgcg tgccagtcat gctccaactg agttatgtgt aaaagtgcct ctcacggctg 8100

agggcaaaaa cagttcccac aagactagag aaaggtgacc cctgacggct gagtctctag 8160

ggagcgtgga gctgcgtgct cagccctgcg gccctgacgg ctctggaatg gaaaagctat 8220

ccaactggaa gggcagggct cgctgctagt ccagcggtcc aaccccacag gtgtctgtgg 8280

tgtcagctcc atgccacaga gcccagggct ggggccagag ccaccaggcc ccctgccagc 8340

ctgcaggggc ctcctcctct gggtagccta accaccccct gtgagcgcag gcagcctcct 8400

ctaatcacca cagggcctgt ccccccctct cccccgcttg caggaaaatg agccctgagg 8460

actccccagg gctgctctgg gcctggacat ggagactggg aattacattt gcagaaggag 8520

cgcaatgccc ttgaagggct cagccacgag cagccagtcc ccagggctca gaaggcccag 8580

ctgttagaac cctgggagcc agcaaagagc caggggctcc acctaagtct atagcccctg 8640

cctcttctgg ttgggaaaga aatcaacgcc cctttactgg ctcccactga cagcccactc 8700

ccccaggtat gggaggattc tgggacgatg caggcaaacc tggaccctga gtgaacctgc 8760

cccagctctc acgggcctgg caccagccac agcacctaag gcgccggtca tggtgacaac 8820

atgaaggtga taagggcatg gacagtggac atggcagctg gacactgggc acccactgga 8880

tgccaggcac ccagcacggc tccgtcaccc ctggatgagc agtggccctt tgcaagccag 8940

ggtagcctgg gcaagttatt tgggggtctc caagcttgtc cagctgtgcg acttcactga 9000

gccatgagtc tgggatttta tcagggccca cacccgttcc tggaactctg atacgtgagg 9060

gagccacaca gggaccctta acaaaagctc ccagggcaac atgttctctt gcctcagtct 9120

cccaaatagc tgggattaca ggcgcacgac taccgcccgg ctaatttttg tatttttagt 9180

agagacaggg tttcaccatg ttggccaggc tggtcttgaa cccctgacct caaatgatcc 9240

ttccactgtt agggcaaggc acctgacagg cacgactgca cgatctgctt gttgggggct 9300

gtgtccattc cccactcctt cgacaaatgt ccacacccag ccttgctttg acaccccaag 9360

aacagagatg gtgacacctg cttcctacat gcccattgct ctcccaaggc agacatcccc 9420

agcagatgca acacagtgtt taggcagaca tcaccaatcg atggtggcaa cagacaccag 9480

gccctgctcc ctctaactcc agtggccagg ccccaagcca gctctcacct gcccactccc 9540

aacccacagc agcaagactc agaaatggca aaaacacaaa gagaacagaa acgccccata 9600

gcgggaggat gactaaaaga catgtcttga taagatattg ttcaggcata ggccaggcac 9660

agtggctcat gcctgtgatc ctagaacttt aggaggctga ggtaggtgga tcacctgagg 9720

ttaggagttc aagaccagcc tagccaacat ggtgaaaccc catctctact aaacatacaa 9780

aaattagcca gacatagtag cgggcgcctg taatcccagc tgcttgggag gctgaggcag 9840

gagaattgct tgaacctggg aggtggaagc tgctgtgagc cactgtactc caacctggac 9900

aacagagcaa gactctgtct caaaaaaaaa aaaaaaaaaa gatatccttc actaaaactc 9960

atgtctttga tacatattta cctcctgcaa tcgcaaatgc ttctgcagtg cataaagtga 10020

aataaatagc aggaagcctt acggttcgat cacccacaca gacacacagt cacatacagg 10080

aaaaacgcag ggagggctgg ggaacaaaaa aacagaagat aaaatgtgga gacagacaca 10140

ccaagagagt aagagaccac ctccagacct cccttcagct tctcaaacac acgagccggg 10200

cccgttacag aatttgcggg gaccgctgca aaatggaagt gcagacagcc ccttactcaa 10260

aaggtaggaa tttcaggtca acaacagagc tcacctcata tgactacaca ggtcacacag 10320

cccgtgaagt cggtcccaac accagcatgc tcctgcctca aagccgctgc acgtgctgtt 10380

ccttctcgcc tttccctctt ttagtccttc agatctcagg cctcctgaga gagacctctg 10440

acctgccggc tcaggcggcc acacccccag tacaggagtc tccggctcag cccctgctgt 10500

gttccgtacc cgatccaggt ctgtcctatg tccatctgtg tgccggcttg cttcctgaca 10560

tggcccccac cacacgtgtg cctcggggca ggggaacagg cccgtctcat taactgcttt 10620

cttctcagat attttctgga atatttgtgg atattgggca acatatatgc tccacctttt 10680

tcagactagc caggacgagc tgcatttttt ttttttttt tttgagacag ggtctcactc 10740

tgttgcccag gctggagtat agcggcatga tcttggctca gtgcaacctc cgcctcctag 10800

gctcaagcaa ttctcctgcc tcagtctccc aagtagctgg gattacaggc ccgtgccact 10860

actgcccagc taatttttat atttttagta gagatggagt ttcaccatgt tggccaggct 10920

ggtcttgaac tcctgacctc aaatgatcca cctgccttgg actcccaaat tgttgggatt 10980

acaggcgtga gccactgcgc ccggcccgag ctgcctgttt tacacctttg ccatattccg 11040

gtgattctct ctcccctccg tcccccggcc ctgactgtgg tggccactcc ctgccgtcat 11100

gagcccgtat gtcctcactc tttccctttc cgccaggact tcaaccaaca ctgcagagcg 11160

cagggtccag ctccagcact gagttcagcc tcttctcacc aacagacagg caggaaagaa 11220

aacaaactct gagaaggcca aggttcccgg gcagccagca agccaagcat ccttctccgc 11280

tgaggcttgt gcagccgagg caccccctcc tccagggagc aggcagcgtc ctggggcagt 11340

ctgcgaggga gaccagggcc cttgctccac cagggcccca ggtatggggg cagcagcaaa 11400

ctcatggctc tgggagccag accccacctg ctagaaccta ctatgccacc tgctgtgggc 11460

aaccccaggc tggtgacttg ccctggcctc ctctgtaaac aaagggctca tccaacctgg 11520

tcaaaccact cctccccttc aagggtctat aatcctccct taacctgctt ggtccaaacc 11580

cctggtgtcg ccaggtcact caggaggcag ctcatctgga ctccttccct gggtccagtt 11640

tctctctcaa cattgccttt gaggccgagg tgaacggtca acagcgaagg gccccagagg 11700

tgatggagga gcgggtgtcc aagacactca ccctttctaa tgcactgact ccctcgtgga 11760

ctcacttgtg ccgtctcccc cacccaccca gccccagagc ccagagtgcg agcgccagag 11820

gcccgggatt ctgtctgcac cgcggggtcc ccagtgcctc ggagcaatgc cagcacccgg 11880

caagtgttcg acaaatgcct gctgaatgag caaatggatg gatgaacgaa tgaatgagca 11940

agcagatgaa tgaatggggt gctgtccaga gccgtgagga ctaggccgcc caagtcccca 12000

tttctcaaat tctccttctc ccgacttggg aaacaagatg cttggtcggg gaggctctcc 12060

aaccatcccc tgcagcagcc ggcacagcgg acagaccctt tgatgtaaca gccatgtctt 12120

cattaaagat gccctgctct cagaaagaga aagacaaata caaacctgga aaatcctcac 12180

caaacgcagg acccctgcca gggagcagag aaaagaccca cacgccacgg gcgccacgac 12240

cacacacaca ccccagccgc tgcacacaaa cacagaccct agccagcaag aacaggggga 12300

ccaggaaact gttcctaaag tcaggacccc catgtgctca gacagcagtg agagcaagga 12360

cacttctcca tccaccggat gccaggagag tcctttttagg gggccccaca ccgagactct 12420

gcccttagga ctgttcctga gtgtggaagc cagcccactt ggaagccccc tgccctcccg 12480

agtgggacac cggcacagga agcaggccct gtcccccacc actttctgca agctgggccc 12540

catcacgcta cagaaacggg gaggactggt cccagggatg gcgctttcct gacacctctc 12600

gttacccccct cgcttgccag gccccagggt cagccccaga ggccagactg gctatcccag 12660

gcccgggagc atccccgaag gcgagctgca tcctgaacgt gtgtgatttc ccgaagggcc 12720

cgccccgaac cgacacctgg aaagaaagat cctcagccgg tgccccagag gagaagagcc 12780

atgcctcact gcaacacagt cccaggaagc accaagtgcc tgaggaccaa ggcggagagt 12840

aaaaaagtgg aaaatatctg gggcaaaaat aaaacaaaac aaaacaggat tgacctcctg 12900

ggctcaagca atcctcccaa ctcagcttcc cgagtagctg ggaccacaga cttgaatcac 12960

cacacccgcc aagtggatca tttcgaacgg gtttgccgag gttccttctg gggcaccccc 13020

ggcggccgca acccattccc gccaggcccc gccccgcccg cccgccccgt cccgtcccac 13080

cgcctcacct gccttacacg tcctgccgtt gtcctgcagc tgcacacccg tggggcaggc 13140

gcatgtgtag aaaggctcgc ttggggacag caggcacagg tgggagcagc cgccattgtc 13200

ctcctcacag cgagtgtgga ctgagaaaac caggacagac tgagagaagg ttccagaaga 13260

ggaccgtcac ttgtttctga atgagtcaca tcctgcctcg tcccccgtga cagcctccag 13320

tgtgtccctc tgcccaaaca tcggcctcaa gtggcatcag ggacctcccc gcgggcacca 13380

ttccacctgc ctcatcgctg gccccgtcca catggggccc tcagcctggc cagacggcct 13440

gcaatttccc caaaaccagc cgtgaccttc ctggccaccc tcacacccag atgtgacctg 13500

cccatggagt gacatcctcc ccatctgctt cctcccacca agctcctatg actagaacac 13560

cctccccagc tcctcggagc ccccaaagga cacccctctg caaaggctgc cccccacgct 13620

ccaatggccg gggtcaggac ctgcctgtgt ggtagtgacg ggaaccccag agacaatggg 13680

ctcctgggca aaaggcttgt cttgtctttg tgctatgtgt ggacccagca gcttccatag 13740

gaacactgtc cttcttgctg ggatggccaa gcttgtcact ctcccaagcc ctcctatgac 13800

caacagcaat tgaacggaac tcgataaatg cttccagcac ctcattcaaa ccaggggaaa 13860

gctgggtgta gcagccccaa aatacggata taactggaac aacaaactca tcaaaatgaa 13920

cctctccctc cctcatgctg ccccaagtgt agatgggttt tgtgaccacg actttctcac 13980

caggaaacag ctccagagag ccccaccctc ctgtgtcctg ctctgggaac agctggcacc 14040

cctaggcccc acatttcaat tcaaagtcca aaccttccat aatggcctgg ccagaaatct 14100

ccatccctgg tccctgtggg agtgggccac tgtccccaga gccgcagccc cactgtcaca 14160

gaagctggtg catttcccca tcagggacct ctgtcacaac ccagcgtggc ccccaggctg 14220

agaactgctg attctgggca gattattcat tgataaatac gcgacttgca gggccaagca 14280

tggtggctca tacctgtgac cccagcactt tgggaagtca aggtgtgagg atcactggag 14340

cccacgagtt tgagacaagc ctgggcaacg tggcaaaatc tctcatctct attaaaaata 14400

catacacaca cacacacaca cacacacaca cacatatata tgtatatata aataaccata 14460

tatatatata cacacatacg tgtatgtgta tataaataca tatacacaca cacacagaca 14520

acttcttctg ggccttgaaa acgaggcaac cttccttgga aatccccttg ccactgctga 14580

gcctgaaata gcccccatga gctctgcaga ggggtcctct gcaggcccgt gtcccccagc 14640

cagccacaca cctccctcca ttgcagcagg taccccttta gagaggggge cccccagagc 14700

atgggcttct gcagggaggg gtcacctgcc cccccacccc acccacgccc gcgcaccccc 14760

acgcccccgc atcctcccac tcccctgccc cgcgcccccg ctccccccag cccccctcacc 14820

ctctcccccg tgccccaacc ggcactcaca aaaaggctgc cgctcctggc tcagcacctg 14880

gatgtccatg ggtgagtata gggcactcag gatctccttc ctcttccccc cagtgcgctt 14940

gttgcaggca tggatggagc gggtctgcca gtctgtccag tacagagtgt ccccggagag 15000

cgtcagggcg aaggggtgcg tcaggctgcc ctccaccacc ttctgcctgc agtcagggaa 15060

gcggggtgga ggagccatca ggagggtccc ccgacagtca ttgctgctga cccaattaat 15120

ttctttttt ttttttgaga tggagtctcg gtctgtcgcc caggctggag tgcagtgatg 15180

taatctcagc tcactgcaac ctccgcctcc cgggttcaag caattatcct gcctcagcct 15240

cccgagtagc tgggatcact gatgcccacc actacgccca gatgattttt gtatttttag 15300

tagagacagg gtttcatcat gttggcaagg ctggtctcga actcctgacc tcaggtgatc 15360

cacccacctc agcctctcaa agcgctggga ttacaggcgt gcgccaccat gccaggcttc 15420

ccatttgctt tcaaccagac aagtgaggcc aggtcaagag ccccaggagc tggcgccctc 15480

gtacatttct cccggcgtgc acagggcacc tcccaaacac agcctgtgat ggtgacacac 15540

gggctccccc aggtcaagtg gcaaagtctc ccccagggaa gaaaggagga agccatgcct 15600

ggcaaaaagc acacctctcc tgcccaacgc tttaacctct gtatacaaat caggccatgt 15660

gcactcgctc cttcttacaa tgctcataat ttatactttc agagtaaatg aaacttggca 15720

tcaacccgag aaacagctat tcttttctag atgcttacag tgcccagcaa atgaggactc 15780

gggtgtaatg agattatgga cactggaaac aggatcataa tgtgacgtgg tcggtaatgt 15840

gcagttttat ttgcttaatg accctcgccc cgtgacaggc tccctgaggg tgggcctggg 15900

ggcagaggtc cccgccacgt ccccagccct cagcacagtt gccaggagag ggtgacactc 15960

atgaagtggc acagggaaga tgggagctgt gggctctgca gatccaccac ctcttctgtt 16020

catttttgtt gatgctgttt tttaagaaaa ttattgaagt aaaattcaca ggacatacgt 16080

ttacttttt ttttttttt ggagatgggg tctcactctg tcacccaggt tggagtgcag 16140

tggtgtgatc tcagctcact gcaacctctg cctcccaggt tcaagcgatt ctcccacctc 16200

cgcctccaga gtagctggga ccacaggcgt gcaccaccac acccagctaa tttttggggg 16260

gtatcttttt ggtagagaca gggtttcgcc atgttgccca aggctggtct tgaagccctg 16320

agctcaggcg atccacccgc cttggcctct caaagtgctg ggattacagg cataagccac 16380

tgcacccagc ctaaatttac cactttaaag tgaatagtgt tacctagtgc attcgcaagg 16440

cggtgcagcc tccacttctg tctagttcca aagcacttcc attgccccac aggcaaaccc 16500

cacacccggc agcagtcatg ccccagtccc cgcccccagc cccggcaaac acttttgatg 16560

gacttaacta cacacattct caacatctca tataaacgga atcacaatat acagcctctg 16620

atgtctgtct tctttgactt ggcaccatgt tttcgaggtt catccaggct gtagcatgtc 16680

agtgcttcat cccgttttag gggtgaacca tattccagtg tgcagacaga aaccaatctg 16740

tgcatccatt cacccactgg gggacctttg tgtcatttcc accctcggct gttgtgcaca 16800

gtgctgctac ggacattact gtccattcac attttgtgtg aagacctgtt ttcgattctt 16860

aagagtatac agctaggagc ggaattgctg ggtcatacgt aaatcaatgt ttacgtctca 16920

aggaatcaac aaactgtttt ccacaatgtt gtctttttttg tttgttttct gagacagggt 16980

cttgctctgt cacccaggct ggagtgcggt ggtgtgatca tggctcactg cagcctcaat 17040

ctcctaagct caatccatcc tcctgcctca gcctcctgag tagctgggaa cacaggtatg 17100

taccaccatg gccagctaat tttctaattt tatttttttt tgtttttgtt tttttgagac 17160

agagtctcgc tctgtcgccc aggctggagt gcagtggtgc catctcagct cactgcaagc 17220

tctgcctccc gggttcacac cattctcctg cctcagcctc ccgagtggct gggactatag 17280

tcaccggcca ccacgcctgg ctaatttttt tgtattttta gtagagatgg ggtttcaccg 17340

tgttacccag gatggtctcg atctcctaac ttcatgatcc acctgccttg gcctcccaaa 17400

gttctgggat tacaggcgtg agccaccacg cccgacctta cttttaattt tttaatttta 17460

ttatttttatt ttatttttttt ttttttttgag acagagtctc gctctgtagc ccaggctgga 17520

gtgcagtggc gggatctcag ctcactgcaa gctccacctc ccaggttcac gccattctcc 17580

tgcctcagcc tcccgagtag ctgggactac aggtgcccac cacgatgccc ggctaatttt 17640

ttgtattttt agtagagaca gggtttcact gtgttagcca ggatgatctc aatctcctga 17700

cctcgtgatc cgcccgtctc agcctcccaa agtgctggga ttacaggcgt gagccaccgc 17760

gcccagcctt ttttttttttt ttttttttttt ttttgagata gagtcttgct ctgtcgccca 17820

ggctggagtg cagtggcggg atctcagctc actgcaagct ccgcctccca ggttcacgcc 17880

attctcctgc ctcagcctcc cgagtagctg ggactacagg cacccaccac cacacctggc 17940

taatgttttg tatttttagt agagacgagg tttcaccgtg ttagccagga tggtctcgat 18000

ctcctgacct cgtaatccgc ccgcctcggc ctcccaaagt gctgggatta cacgcgtaag 18060

ccatggcgcc cagcccatgt ggccattttt cagtgagaga agccagaggc ccatcactct 18120

cggttgctcc ctgggccatg ctctgcctca gccagaagca ctgagggaag gtcagcctcg 18180

gcccttgccc cagccacagt cacagataaa ggggcctgca caggtctgtg tggctccaga 18240

gctcgtcacc caacacacga cgcttccatg tgaatagccc caggtgcatc atgaagagcg 18300

atggccgctg cagaggcaga agaatcccgc ggggaagcag gtgggagaga ggctgagaac 18360

agaccagacc ctggagctac agaccctatg ttccaaccct ggctgggact agctgtgtgg 18420

ctctgggcaa attcacatgc ttctctgtgc acaggggatc aaaatagcaa acacaggcta 18480

ggcacagtgg ttcacaccta taatcccagt gctttgagag gccgaggtgg acacatggct 18540

taagctcagg agtttgagac cagcctgggc aacatggtga aacctcgtct ctacaaaaaa 18600

aataccaaat aaattagcca ggcgtggtgg tacgtgcctg tggtctcagc tacttggaag 18660

gctgaggcgg gaggaacact tgagcccaag aagtcaaggc tgtggccgcg tgtggtggct 18720

cacgcctgta atcccagcac tttgagaggc tcaggtgggt ggatcacttg tgatcaggag 18780

ttcaagacca gcctggccaa catggtgaaa ccccgtccct actaaaaaaa tacaacaatt 18840

tgccaggcgt ggtggcgggc acctgtaatc ccagctactt gggaggctga ggcaggagaa 18900

tagttagaac ttgggaggtg gaggttgtag ttagccaaga tggtgccgct gcactccagc 18960

caggggggaca gagcaagact ccatcccaaa aaaaaaaaaa acaaacaaac aaacaaaaaa 19020

agaggtcaag gctgcagtga accatgattg tgccaatgca ctccagcctg ggtgacaaag 19080

tgagaccctg cctcaaaaca ataaaaatat aaataaaaat aaaacataat agcaaacgtt 19140

tcatagaggt ggtatgagca ttaaatgaac tgataaacgt ccctggaaaa cagtaagtgc 19200

tatggaagga ttcgctgccg ccaccgccac caccattagc atgtttcaac ctccatcacc 19260

ctcactgtcc cctgtcacca tcctttgacc agggcactcc cagctgcagc ctttctatcc 19320

tcttgtccac ccttcataac tgtaagatca ctcagctccc aagaaccaca gtctacaggg 19380

taaccacatt tccaaatctc aaaccagacc cgctggtctg cacttccagg gacaacagga 19440

tattttcaaa ccagcccaaa agagatgtgt ggctcagcat aagaggaaca ggagaaactg 19500

aggcctcttg ccctgagaat gagcttggaa gtggatgtcc cggcctcact caaaccttca 19560

gatgactgag gcccagccag gagcttgagt gtaccctcag gtcataccct gagccagaag 19620

cacccagcta atccactcct catcactgac tccctcccca taaaaaacct gtttgctgtt 19680

tcaggctgtt aagttgtggg ctgttttgtt acacagcaat ggataactaa cacacgaggc 19740

ctggcaagtg tggagcaaag ctgcccaagc cctcaagtct gttcatgtgg gtgttggcct 19800

gtgtttgcag aaatccagcc actgagtcct cccatgcagt cactactgcc ctctgcacag 19860

acacctgcca catccctgcc tgggccagga gctccactag tgcaggaatg gggtctgccg 19920

tcccaggagg atccctgaca cctagcacag ggctagcagc aggcagcact tggttagtga 19980

ataaactgcc cttcacctgt acacagaagg gatgtttcta taaggggtaa ttaagtacag 20040

agctgggaag ctatgctgac cagaaggctc taaaagcaat taaccaacga ggggaaaacc 20100

cttcctactc attctcggcc cattttattg agcactgacc atgtggaagg ccccctggtg 20160

agactgggga atgcaccaat aactgagaca gcttccggct gttgccctca ggatgcctga 20220

gctgggatag ggccagggtg ggggtggtgc gtgtgacagg gttactgttc acaaccctgc 20280

cgggccataa gccctcccca acaattccaa aatccaaaac gctctgaaga tggaaagctt 20340

ttgttgctca tctggtgaca aaacctcatt tggtgcatgg gccgggtgcg gtggctcacg 20400

cctgtaatcc cagcactctg ggagccgagg ggaaggatcc cttgagctta ggagtttgag 20460

accagcctga gcaacatgtg agaccccgtc tctaccaaaa atacaaaaat tagccaggtg 20520

tggtggcgca ctcctgtagt cccagctact cgggaggctg aggcgggagg atcgcttgag 20580

cctgggaggt gggggctgca gtgagctgag attatgacat tgcactccag cctgggtgaa 20640

agagtgagac tctgtctcaa aaaaacaaag ttaaaaaaaa aaaaactgtg catgggtgtg 20700

ggctacagat agtcttttct gccctactta gaatgaacgt gccacatttg ctatagaaat 20760

attcaagggc tggtggcaaa tgccacacag accctgacgc tgttccaagt tctgagaagt 20820

cctgcattcc tcagggcccc agagtttcag agaagagtct gtaggcctga gttaagaagg 20880

aacgccttca aaagccctgg ggacaaaggg gaaaggggtg ccccaggact gcgtgggtac 20940

ctaccggaac gagccgtcca ggttggcacg gtggatgaag ctgagcttgg cgtcagccca 21000

gtagagcttc tgctcctcca ggtcgatggt cagtccattg ggccagtaaa tgtccgagtc 21060

cacaatgatc ttccgggtgc tgccatccat ccctgcccgc tcaatccggg gcgtctcacc 21120

ccagtctgtc cagtacatgt acctgtgacg ggggcagggc aagagaagca gctaacacag 21180

atctgttttt tgtttttgtc tgcatagatg cagacatgaa acaacagaca gtgaacttgc 21240

cctaaaatct cacccatcgg aaataaccaa caggtatggt ttcaggtatt cctgccttaa 21300

gctgggcaat caaaatatac tatttccaac ttgttctcag ttaacagtaa attctgggca 21360

ccttcccttc ttgtggatag aaagattcct tgttcttttg atgattgcct agtgtactct 21420

gctgtaagtt ttttaaagaa cttcaggtta tttctgattt ttttgctacc atgaaaatgc 21480

tgtaaatgaa cctctaaaag gcaattcaaa acactcagga tggaatatta tttagtggta 21540

taaagaaatg agctatcggc tgggcccagt ggctcacacc tctaatccca gcactttggg 21600

aggccaaggc gggtggatca cgaggtcggg agatcaagac catcctggct aacacagtga 21660

aaccccgtcc ctactaaaaa tacaaaaacat tagccaggcg tggtagtgag cacctgtagt 21720

cccagctact taggaggctg aggcaggaga atcatttgaa cccgggaggg ggaggttgca 21780

gtgagcagaa atcgcaccat tgcactccat cctgggcgac agagcgagac tccatctcaa 21840

aaaaaaaaaa aagaaaagaa aagaaatgat ctatcaagcc atgaaaagac atggaggaaa 21900

cttaaatgca tgttagtagg tgaaagagcc aatctgtatg agtccagttc taaacactct 21960

ggaaaaagca aatacacaga gacagtaaag catcagtggt tgccaggagt tggagaggag 22020

agggatgaat gagtggagca cagaaaatca gggcagtgga actatcctgt atgacatgga 22080

atggtgggtg catgtcctta ctcatctgtc taaaccaaga atgtacaaat caagggcgaa 22140

ccctcgtgta aacgtggatt ttgggtgatg gtgcgtcagc cagctttcat cagttgtaac 22200

aaatgtacca ccctgcacag gatgctgaca gttgggaagg ctgtgtgggt gtgaggacag 22260

ggatgtatag gaactcagta cctgctgctc atcaattttg ctgtgaacct acaactgttt 22320

gaaaaaatta agtctattta aaaacaacaa aacatggcca ggcacgatgg cttgcacctg 22380

taattccagt acttcgggag gctgaggtgg gtgggtcact tgagccaccc tgggcaacat 22440

ggcaaaatcc cacctctaca aaaaataaaa attaaaaaaa agttagctgg gcatggtggc 22500

acactcttgt agtcccagct acttgggagg ctgacgtggg aggatccctt cagccctggg 22560

aggtcgaggc tgcagtgagc tgtgactgta ccactgcact ccagcctgga tgacagagtg 22620

agaccctgcc taaaaaaaaa aaaaaaaagg ctgggtgcgg tggctcatgc ctgtaattcc 22680

agcgctttgg gaggccgaga tgggcggatc acgaggtcag gagatcgaga ccatcctggc 22740

taacacggtg aaaccccgtc tctactaaaa gtacaaaaaa aaaaattagc cgggcatggt 22800

ggcggacacc tgtagtcaca gctactcggg aggctgaggc aggagaatgg cgtgaacccg 22860

ggaggcggag cttgcagtga gccaagatca caccactgca ctctcagcct gggagacagc 22920

aacactccgt ctcaaaaaaa aaagaataaa acccatggct gggatggacc ctgaacctgc 22980

agctgcagct gttcctgggt aggtctgtgg gcgacgtggc tttgcttctc catgttccca 23040

agagacaagc atcacccatc catgagaaac aagcacatcc tcagggcgcc cttacgtgat 23100

ctctggccaa tgaaccaaga caaagtgagc agacaccagg tctgggatgg caggtcccac 23160

ccccaccagt gcccagtgtg ccctgtttgg aggtgaccac agggtgtgtg cccagaggct 23220

gggcgtgact ctcagcggag accagagggg aaccacacca gcttggagga ctcagttccc 23280

atcccagcca gctgggatga gccacaggac acaagggctg gcagacctat tgtgttttgt 23340

ccacccttca cagcagagaa aggggacagt gcccagaatg tcctctgagg agcctcctcc 23400

cactcttggt ccttgtaaaa tggtgctgac tcccttgctc ccttcttcct ggggtgggcg 23460

gcaaacccca ttcccctcag ccttagcaag tgatttagaa acaggcagct cgcccaagcc 23520

aggcatgaga gtgatcccgg gacacaggga gaacaagccc cgctttgccc tctgggggtc 23580

tccattcagc agaagaggca aatgacagac acacagccgc ctcctccccc accatggtgc 23640

tctgcagcct caggagcctc aggtgcacca agggccaccc catccagggg gccatgcttc 23700

cttgagtggt atcgttcctg agcgagtacc atctccacct tccagagggg ctgtgacaag 23760

atcaacaaga atgagggcat aggagcctcg aaccaaacat gccctcttcc ctgcagaggc 23820

tgactgcgcc cagctgctat caccaagccc ctgctcctcc ggccccgtgg ggacagggta 23880

agaggggtgt cacatggaac agctctccaa acagtccctc tcaagctgct gtctcctgtg 23940

catctagtga gaacccaacc aacaaaggga aggtgggaat tgctattccc attaggcaga 24000

tgagaaaact gaggccccga aaggctggcc tgttccaggt tacaggcgct gagcggctgc 24060

tctgggaaca cacttggtgt ctgctgaggg cccgagcccg gccatcatat gactcaccct 24120

tcgccagcaa agcccgggtg tgggtgaact tttcctggca gcctgggact ccaaggtgct 24180

ggcagccagc ccagggaagg ctcccgcgtg cctgcggcag acgccttgct ttacctgcac 24240

gtccccaccc ctaggagcct ggacagagcc cagaccctcc gccacctcct gagaaggtat 24300

caggggcatc agtctggact tgggggggaa tccacacagg ccttccccaa atgctccacc 24360

gtggcccatg gaaaaggctg gaaaacgtgc aggagcagga gcctccgcat ggagcataat 24420

tcacattcct tccccgagtt tcataacaga ggcctgctgg tttccttaaa tggggaattt 24480

gcgagccagt cggtgaccag agactggttg gcgtggacgt gctcttgcag agtctcaaac 24540

gctaccacaa gcccagccaa attccacgga ggaaaatcga cttccgaaga aaagagctgc 24600

agcatggcct tcgtgcagag ccagctgcgg ttgtggttgt gtgttatttt agggaagggc 24660

cattttgcat tttaaagagg gggttgggtt tcaccctggc tttaatttga gacccggggg 24720

ccactgcagc cccttgtcag gctggtacag gccggggact cctcccatgc taagccagtg 24780

tctttctggc cccagatcct caggggccag agggtcatcc ccagagcccg ctctgccacc 24840

cacatgggta ccctgggcct gggagggatg tgccttccct caaccctgcc tggatgtccg 24900

cacggggcca cctgcattgc tgaaactgca acgaagtcga gtctcaggag gggcccccct 24960

ggctgcaggg ctcttgatcc ttttggccac gtgcacactg aggtggacgc tcggacccag 25020

agacccccct catgatgatg gccggggcag gaacccccctc ctctgaggaa ggaccctggt 25080

gggggacagc actgcaggag ggcacaggag atgacggggg ctctagcagg gccgggagga 25140

aggccaagat gctcctcgca accgtgtgcc tgtggccagg acagaggaca aacccaccct 25200

ccactgtccc cactctcagg acagcagtcc tgccccagga ctcagcgccc acacttatgc 25260

ctgaggacca ctattcaagt cagtatttgg cgagcagggg ttgctgccgc gggcgctgtg 25320

acaggctgga atcctctccc tctccctctc cctctccgga gacatggagc ctacagggac 25380

agagtcagca cctcagggta ggaccatggc tggcgtcatc agcatcactg gatctgatga 25440

gtgggagccg gcatctcact gttttcactc tctcattcaa atgactggag caaagggaag 25500

gtgtggggag aggcccagga atcaacacta aggtcaactt tgcccccagg ggcaggggtg 25560

ggagtgaaca gccacaggtg tgatcctggg gagggcttct gggagagaat tcagaggcaa 25620

gcatgtagag gaaccatttc aaatagttaa gaaaagccag agccaaacag ggacagttgg 25680

ctcgcagaga tgatgcaggc aaagccagct cagatctgag catgggaaag actactccca 25740

accaagggcc cagcatctcc caaccaagca ccaagtacct cccaaccaaa tgccaagcac 25800

ctcccaatca aatacctccc aaccaagcac ctagcacctc tcaactggac accaactact 25860

cccaaccagg caccaagtac ctcccaacca agtgccaagc acctcccaac caagtaccaa 25920

ttacctccca accaagcgcc tagcacctcc caactgagca tcatgcacct cccaacagag 25980

catctagcac ctcccaactg atcacctccc aacctagcac cgagcacctc ccaaccaagt 26040

gcagagcacc tcccaaccaa gtgccaagca cctcccaatc aaatacctcc caaccaagca 26100

cctagcacct ctcaactgga caccaacaac tcccaaccaa gcgccaagca cctcctaaca 26160

aagtaccaat caccttccaa ccgagcacct agcacctccc aactgagcat catgcacctc 26220

ccaacaaatc acctagcacc tcccgactga tcacctccca acctagcact gagcacttcc 26280

caaccaacat agcaaaagcc ataaagaagt aaaaagacaa aaccacgtag gcatggagac 26340

tggacttctg gtggcgagga aagggcattt ttattataac gacagctaac atttgttgaa 26400

ctcacaaact gttcttggtg ttttcctcat gacatgcagc atggtcacgc ctctgtacag 26460

acaaggatac tgaggcacag agtggcaccg tgccaacctt gtctcatctt tttatcgaac 26520

ctacatgcag agtgccagca aatccagctg tcttttctct tcagaacaga tcccaaatct 26580

cgccactcct tacccccaca agtgaggtgt ccccgctgct gctttctgtc gccaggatcc 26640

cggtaataac cgtggagagg gctcctgccc ccacgccacc caccccacag ctcactctcg 26700

ctccagccac caggggatgc cttccagcac gagtcagagc tggcacctcc tctgctcgag 26760

acctcatgtg tcctctcctc acaccttggg ccctgtttcc ctacattctg ctacagcccc 26820

tcaaacaggc cccgccccaa accagcccag ggcctttgca ctggctgatc cctctgcctg 26880

gaccgcgctg cccccagaca gccacacggt tctcagcctc atctgcttcc agtctcgact 26940

caaaagtcac caagaggcct tcccagcacc tgagctccga cggaagcccc tcgccacagc 27000

acccaagcac tgctttatcc ccctacgcac acgtcccttt caaatactat tcatttacca 27060

tctcctccca ctcactgaaa gggccagaga ctgggctata cccgctgcgt ggggagcagg 27120

accaggcgca agggctcaca aatgcagtgg atgcctggtt gggaggtgag ggagctgcag 27180

cgacccacgc tgggagggaa cgcaatgaca ggaggagcgc aggtcctggc gacacgatgg 27240

ccatggcagc cgctggtgag caaccgcagg ccggccctgg gagagggctt ctagcaagct 27300

gctatcttca gcctctccga ctactgcaga tgccccctcc tagccagaga cactgctaca 27360

ccagccgacc cttccaaaaa gaaggtcagt aaccccgcga ctcctggagc cacagtgcag 27420

ggggagaggg ctgagagggc aacagttcac caagcggaac agaggctgcc ccggaggtca 27480

gctggctccc cggcagctgc aggggtggct agcccactcg gagggcagcg agggcatacg 27540

aggggctcca gggatgagtg gttgcccagc acagcacccc tgggaggccg ggggcacttc 27600

tcaggtagtg ggggcacgag gctgctctgg cctgacctca gggactcaaa atactttggc 27660

gataaattcc accgtgtccc acccctgctg gtaccccata cttacacaca gactggttca 27720

gatgcagaca ctctcgcgca catactcgct cacacgggca catacacgtg cacacacagt 27780

cacatgcgca cactcataca cacacaaata tccactcaca cgcatgcatg cacacacacg 27840

gacacacaca ggctcacacg tatgcacgca tatgcgtgca cacgcacaca cacacacaca 27900

cgctcacatc ctcccactcc cacactcagt tgctcagaca cacacacgcc tggctctcac 27960

acaaacctgt tgggctctga aaggctccag cccttcccat gctcgtcaga agccagtcaa 28020

tggcttccta agtcaccaca cagatcaaag aggtgaactt ggccacatgg cactctgctt 28080

cctgagctcc caaacaccag ccttggtgag gacagaccct caccccacac cctcattccc 28140

actaccctgg gcaggcccag aggaggggca tctgcaggat ctggcaacca gcccctcccg 28200

cccggctcct gcagccggca ccatgggagt caggggggagg tcactgcaaa gggcaacagc 28260

aagttggtgg ccccaggact agagcccagg ggtcttcagt cctactccag agcttggaca 28320

ctgtcccaca gggcatggcc aagggaaggg cttccagagc cctgacttca gggaggaggg 28380

caggcgggct cctgtggcag gcctggatgc atggccgccc actcctggga ctttctaacc 28440

tagaatatct aggtcaggct gggtgcagtg gctcacgcct gcaatcccaa cactttggga 28500

ggccgaggag ggtggatcac ttgaggttag gagtttgaga ccagcctggc caacatggcg 28560

aaaccctgtg tctactaaaa atacaaaacc tagccaggtg tggtagtgca cgcctgtaat 28620

cacagctact caggaggctg aggcaggaga atcacttgaa ctcgggaggt ggaggttgca 28680

gtgagctgag atcgtgccat tgcgcaaaga agatctaggc cggcccctca accggtgagg 28740

tccaggctgg gagtgctgag agactgtggt gacactgaat gaactaacag gcaaagggct 28800

tccaactgag cctgggggtg gtgggaaatg gctcttgtgt tctagtcaag acctctgcca 28860

accagttctg acactgaccc agcacagaac ctgacaggtc agcaagggcc agggcttagc 28920

acagcccagg taagggtgtg tgtacggccc ccagagtcac tcccaggctg caagaaaagg 28980

gacaaaggag ggacaagggg tggccaagca aactgttccc tctgctcggg agtctggggt 29040

gacctggcct agctggccag tggagctggg ccacctcccc ttaaactctc caccccggac 29100

ttcgactcca aagctttcct gccacccacg ctctccccac ctgggatcac ggccaggccc 29160

tgagccttca agggcccagg tgaactcagc cagactagga gctgaggagg acacagggca 29220

gcttccagaa cggacccgag aaccactccc agcaggttct gcttccagac aaggagctgc 29280

actttttcag ccaatgcaat tagaaagcca ggagaaggtg caaattccac ctgcctgagc 29340

gtccgcactt cccaggccgc ccaccataca cacagcaaag atgtgtttaa ccattcaaac 29400

ccatggccaa ccacatcggt tgcctcagac atgcaagttt taaaaaggaa cataactatg 29460

ggccaggcac ggtggttcac gtctgtaatc ccagcacttt gggaggccga ggtgggtgga 29520

tcacctgagg tcaggagttc gagaccagcc tagacaccat ggtgaaaccc catctgtacc 29580

aaaactacaa aaattagctg ggcgtggtgg tgggcgcctg taatcccagc tacttgggaa 29640

gctgaggcag gagaatcact tgaacccggg aggcgaaggt tgcagtgagc cgagattgtg 29700

ccactgcact ccagcctggg caacaaggga gactccatct caattaaaaa aaaaaaaaaa 29760

aaaaaggaac ataactatgg agtctcaagg ggaagtaatt ccttcaacaa taacaaatct 29820

tgaaagctga gctctttttt ttttttgaga caggatctcc tcactttgtc gcccaggctg 29880

gagtgcagtg gtgggatcac agctcactgc agcctcgatc tcccaggctc aaatgatcct 29940

cctacctcag cctcccaaga agctgggatt acaggtgcat accatcacac ccgattcatt 30000

tttgtatact ttgaagagat ggggtctcac catgttgccc agtgtggtct tgaattcctg 30060

gactcaggtg atctgcccgc cttggcctcc cagagtgctg ggattacagg cctgagccaa 30120

caccccacg ggttcatttt cagagtcgca ccgagtgctg gggttacagg cctgagccaa 30180

ccccccacg ggttcatttt aagagtgaca ccgagtgctg gggttacagg cctgaaccaa 30240

ccccccacg agttcatttt cagagtcgca ccgagtgctg gggttacagg cctgagccaa 30300

ccccccacg ggttcatttt aagagtgaca ccgagtgctg gggttacagg cctgagccaa 30360

caccccacg ggttcatttt cagagtcaca ccgagtgctg gggttacagg cctgagccaa 30420

ccccccacg ggttcatttt cagagtcaca ccctttttct gaaaaacaac ttgggctcat 30480

gcaaattcga gagagagatg gtgacactcc ccgcccctg gacccaggtg gagtcgcagc 30540

agggtttacc cgtgagcggg gtccaaggcg atggccctcg gctggtcaag gtcctgccag 30600

aagagcacct tccgggatgt gccattgagg ttggccacct cgatgcggtt ggtctctgag 30660

tccgtccagt acagcttctt gcccacccag tcgcaggcga ggccgtcggg agagaccagg 30720

ccggagatga ccacgttctg cacggcggcc cccgtctggt tcaggtaggt ctgcttgatg 30780

gcctcctcgc tcacgtctgt ccagtacacg gctcccttgg aaaactggaa gtccactgcg 30840

gccgcatcct ccaggccgct gaccacgatg gtggactcca gcttgactcc gccggcgtcc 30900

accagccgta cgtcccggcg gttggcaaat agcaggagcg gcgaggctgt ggggcagaag 30960

caaaccgtga gggccactgg ctaagccagc aagatacaca gccctgggat ggagcactat 31020

gcccagagca ctcctggtac tgccctgccc atgcccaaga cctccagttc cttcctccca 31080

cccctaaggc gttgtcagga agttgcctgg gcagccccgg cccgcatcat tcagaggctc 31140

ctgcagcgca gcaaacagcc ttcttcccac attcggtgac agcacctgtt tgtttaccaa 31200

ctgttacgtc tgttccccca gatatgggtg acccttcctg ccatgcccaa aacctcccac 31260

atcgtcctcc agaggctaca ggggccctgt cctgttctgc agagaagcca catccccttt 31320

gttggcctga cacaggggat ggggacatgc aggcacagca ctggccatgc tgctcgctac 31380

agacccagcc acagggccac atttttgag gggttcagag cccaggccag acagagcctc 31440

aagattccct tacaagtctt tgaccactgt ccaagctcag gcccgtttcc ttggccgtgg 31500

catcagcttc ccatccaccc ctgtattcca tgtttctccc accctgcttc tggacattcc 31560

tacatttaaa gggtcactct ggaatgccac cccttggctc agacaccttc cacagctccc 31620

tgtgccagtg ccatgcagaa caaggtcaga ccccctagcc tggcctccaa ggccttggcc 31680

tctggcctca cctacacttc tctccaccac cccaccccaa gcattcctga tctgcctgcg 31740

gccaggctgg ctccctcacc tccctgtgca ccgcagccct cagccccttc tgcctgtgca 31800

agaagcctca tctcacagac aacggtctca ttcccacaac gggctcaatg agaaatcagg 31860

agaggccttc agaccatcac cccaccagac acctcagacg tcggaccagg agggtccagc 31920

aacccccaac acagactcag agggactaag aagccacatg aggagtgaac acaagatgtg 31980

gacaggagga ggttaagggc ctccagggag ctccatcagt ccgtgttctg ctgtcagcag 32040

ggttaggctg ggctggccac aaacaccccc aaaaaacatc tgaagccttg gcttgaaaca 32100

gctgacattc ctcatgaaaa ctgcagaccc ctgggtcctc ctgcgcagat gggggagccc 32160

agccaacccc acactcccac cttcaccaag aaagagaaag ccaaaacaaa ctcaactcag 32220

ccaatgacaa tcacagaact gaatcctgta gttagttcag ttggtttcat ttcagcaggg 32280

gaaagatttg cagcctctat gagggtagct gggaacacaa agggccagag catggcccag 32340

gagaccccag cgcagtgggg tagatggttc cgagcacagg cctccctgcc aagacaagca 32400

ctggctcaaa tcctggcccc tcccattccc aggagacatg ctccacagga tgggaggaca 32460

cacagaggac ctgaggccag gaaaatgaca gcggcgcctc cgccgcccca cccgtgctgt 32520

catcatctta ggtctacagt tctttgtggc aacgagggac actgtgaaag tcaaacaaca 32580

ggaaggcata ggccacaaat aaagacaaac gggacttcat gggaagctaa agattttgtg 32640

catcaaaaga cactatcgag agagtaaaaa ggcaacccac agaatgagag aaaatatttc 32700

caaatcatag atctactaag agattaatat ccatgaaata cagagaactc ctaaaactca 32760

acaatgagaa aacaactaag ccaactcaaa aatgggcaaa caacttgaac agacatttct 32820

ccaaagatga catataaatg gccaataaac acatcaaaac aggcttaata tatccctaat 32880

catcagggaa atgcaaatca aaactacaat aagataccat cttgcaccaa ttaggacggc 32940

tactatcaaa aaaacaaaat agcaagtgtt ggtgaggatc tggagcaact ggaacccttg 33000

tgcaccactg gcaaaaatgt gaaatggtgc agctactatg gaaaacagca tggcagttcc 33060

ccaaaaactt aaacacagaa ttaccatatg acccagcaat ttcgctttgg gttatatacc 33120

caaaagaact gaaaacaggg acacaatcag atatgcatac accttggatc acagcagcat 33180

ccttcccaac agctaaaaca tggaggcagc caggcatggt ggctcacgcc tgtaatccca 33240

gcactttggg aggctgaggc gggtggatca cctgaggtca ggagttcgag accagcctgg 33300

ccaacatggt gaaaccccgt ctctactaaa atacaaaaat tagctgggcg tagtgacggg 33360

cacctgtaat cccagctact cacaagtctg aggcaggaga atcacttgaa ccctggaagt 33420

ggacgttgca gtgagccaag attgcgccac tgcattccag cctgggtgac acagcgagac 33480

tctgtctcaa aaaacagcaa aacaaaaaca aaaaaacaaa caaacatgga agcaacccaa 33540

gcgtccctct actgagggat gaatagcggg gcaaaatctg ctccatccac acaatggagt 33600

actattcagt ctcaaaaagg aaaaagattc tggtcaggca cggtggctca tgcctgtaat 33660

cccagcactt ggggaggctg aggcgggtgg atcacctgaa gtcaggaatt caaggcccgc 33720

ctggccaaga ctggcaccna gctacacana aagtatangg ccccggaaa 33769

<210> 9

<211> 72049

<212> DNA

<213> Homo sapiens

<220>

<221> unsure

<222> (8356),(8385),(38585)

<223> Identity of nucleotide sequences at the above locations are unknown.

<400> 9

tataccttgc gcggaccttc ggctcctgtg gtgaagacaa tatgaagaaa atagaaatta 60

cccataattt tgccacacag acttagttgt gtccatgtat cttgtgcacc ttttttctgt 120

ttacggatca aaatcgactt ttagggtcag gcgcggtggc tcacacctgt aatcccaaca 180

ctttgggagg ctggagttgg ggttgggggg tggatcactg aagatcagga gtttgagacc 240

agcctggcca acatggcgaa actccatctc tactaaaaat aaaagattag ccaggcgtgg 300

tggtgggtgc ctctaatccc agctactccg gaggctgagg caggagaatc gcttgaaccc 360

aggagacaga ggttgcagtg agccaggatc acgccactgc actccagcct ggcaacagag 420

cgagactctg tctcaaaaaa aaaaataaaa ataaaataaa taaatacata aattgacttt 480

taggagattg gttcaaacaa tgtgtgtaat gttgtgtctg agtgtttttc atttatcgtt 540

catgcaaatt ccgacatcat tcactcttct ccagagtgtg ctgttttcct gcctgtgtca 600

tcacccgtca ccttgaatgc cctcgtttag gtaaaataag tacatttat tcaaaaatat 660

ttgaggacat ttgggttgtc tccaggttct tggtcttgag ttttgctgtt cttgtggagc 720

catggtggtg tctggttgca ggaacctcca tgcgttccag ctgctgcttc tgcctgtgtt 780

cttagagagg aaatgctggg gtccgcggtt cccgggctgc tgaccaggaa gcctgcggtg 840

ctttacggcc cttccagaag cgggagatgc ccccacttaa gtgtcagaca ggcctttcca 900

cctcactggc agctctgagc ggctcccttc tatttgcaga tgactgagaa gttaccaatt 960

tccacgttta ctgactgctg tttctcctgt taatttgtat ttatagtctt cgctaattta 1020

ttgctagggt tttggtgttg tccctattga cttgtatgcc ttttaatttt ttaaacaaca 1080

ttaatatact tcatttttt agagcagttt taagtttaca ggaaaattaa gggacaagta 1140

cagagagttc cttccacctg ctgtcctcct ctcctcctcc ccaccttccc tccttcccct 1200

attgtaactt tctttctgat attataaaag tcactcatgg ctgggcgtgg tggctcacgc 1260

ctgtaatccc agcacgttgg gaggcagagg caggcagatc acctgaggtc aggagttcca 1320

gaccagcctg gccaacatgg tgaaaccccg tctctactaa aaacacaaaa agttagccag 1380

gcgtggtggc gggcacctgt aatcccagct actcaggagg ctgaggcagg agaatggcgt 1440

gaacctggga ggcagaggtt acagtgagtc gagatcgcgc cactgcactc cagcctgggc 1500

aataagagtg aagcttcgtc tcaaaaacaa agtcacacac gcttcttgta cgagggtcat 1560

ttggccgagg ggccagatgg ctcaccatct agttgggaca ggccatgagc tcggaatgct 1620

ttttacatat ttacatggtt gagaagaaaa tcaggagaat aatgttttgg gacatgggaa 1680

aatgacatgg aatttgcatt ttagtgtcca taaatgaagt tttgtttgct cccagctgtg 1740

ttgactgagg caggctggct tcctacagct gcggcagagc tgaggaggcg ggaaggagac 1800

cgtgcaggcc gcagcaccga aaatatttgc tctctggccc ttcccagagt gcttgccgac 1860

ctctgtccga cagctagaag gaaggatagg acccgtccga cgataaccac tgttgacatt 1920

tgagcgcgtt tccttcccgg cttttgtgtg agagtggcag tctgtttgct tttgtggtcg 1980

ggatctgctg cacgcacggc gggctgtttg catgaggctt cctggaggat agggctgggc 2040

tcggagctgc acgcagtggg gcgtgtcctg catgcagtgg ggcctcagaa gagagctgtg 2100

gtgggcgggg cagtgccaac gctggtgggt gccaggcctc cacgctcaga tcagccccgg 2160

cgacaggttt gggccaccct ctctctggcc tctgtgcagt ggcccaggcc gtctgctctg 2220

cctggcacac ttgcctctgt ccttccactg aagcgctcct cttaccctct gctcccggct 2280

gggtacgttg aattgtgtcc ctcaaggaga tatgctaaag gtctaacccc aggaacctgt 2340

gtatgtgatc taatttggaa acagggtctt ggctgatgta atcaagcgag gatgaggtca 2400

ccctagagta gggggcctat atccacggtg ctggtgtcct catgagagca ggtgagcaga 2460

cactgacact caggggtgaa ggctgcatgg agtcagaaca gggcttagtg cgatggcggc 2520

cacaagccaa ggaactccaa gtatttcctg caacaccaga agctggaaga tgccaggaag 2580

gatcctgccc tggagccttc ggagggagtc tgtccctgca gacgtcttga cttttgattg 2640

cagggatgca tgtcttaggg tgtgtggggg ggtgcatttc tgatgttaga agccacctgg 2700

ttggtggcga tgtgtcacgg gagccctctg caggttctgc gtgtccatgt ggtcggggac 2760

agaggtgggc agggacggac ggtgtcgagc tggacatgtc catgacgtcg gccatccctt 2820

gggatggctt ttttgttttg aggataaggc tgcctgccag gaagctgtgc cctgcctggc 2880

ccttgcccca agcccctggc ctgtgcttgg cctcgcggaa gggatgtcgc ccttctctcc 2940

tgcatgcgtg cagggaggaa ggggagaggt cagcagcccg cctggaggag gctcgggcga 3000

ggggaaggtt tcactttcag gcaatgttgt ggggctgttt aaacaacccc aaagaaaacc 3060

atttggccaa actgttagtt tccaaacatt ttacttcctt ggtgtttaaa taaattccta 3120

ccaagactct gtagctggtc ccagggaagg agttggcctc tcttctttat agcccggcac 3180

agtcagtccc ctgcacctgc ccctcccaac cccaggcctg cttccccgtg gccatggctg 3240

ctgcccggac ctctctacac acagaacctc ctggaggcca gctgtgggca ccagccttgg 3300

cagggctgtg gcggagccca ggctgctggt actctctctg cagctgctcc ctgctggcct 3360

ggctggacag cgtccccacc accactgggg tcacctctgt gctggtcaca gctcactcag 3420

accttcaggc aaatgggttg gatcctgcct ctctcccagg tgtctcagtc tctgcaaaac 3480

tcaaaaacct cagaggcctt gcagcctgag gggtgtcaga gacacctcct tcgaatcagt 3540

aaacacctac agattcaccc cagcagtgaa aggactgctt cgccacagag gtttgattta 3600

ctcctaagta attggaaggg atgccgagaa taggttcctc atggtgggac tagaggccct 3660

ctgctgacct agttaacaga gggctagggc tgggtgtgct cagcccctga aggttctagg 3720

cccatttggg acaccccgcc agaacctgcc acaacctgcc atgtggtgac agctacctaa 3780

atcccagagg ctcttgagct ggagagcaga cctctcaatc tcagcaggcc ccccacacag 3840

accccataac cctagtctgc cttcacagta cagttcgtgg ctatgtgttc acggatggtg 3900

ttgttcacct aaggtctctg ccctgtgacc ccaagggcgt cctgagggca gattccaagt 3960

ctgtttcgtc caccctcct tccctagcag cgggtccagg gcctggcctg aactagcttc 4020

ccacagagat actggtggga tgatgaaggc agccaggcgg caagtgaaaa acgcacttcc 4080

tgcatgtgct ggctcctggg attgaagtgt ttgaggaagc aaagtgaagt gagctttcct 4140

cttgcggctg tgtgtccttg ggccgggagc ctaccctctc tgagcgttgg ggtccttgtc 4200

agtagaatgg ggcatcctca tagctcaagg ggtggtgtgt gaaaattgtg ctattgtgtt 4260

actttaatga ttttttttt ttcgagacaa agtctcaccc caacgcgcag gctggagtgc 4320

agtggcgcga tctcagctca ttgcaacctc tgcctcctgg gttcaagtga ttctcctgcc 4380

tcagcctccc aagtagctgg aattacagga gtgcgccacc aggcccggca tatttttcta 4440

tttttagtag agaggggttt ttaccatgtt ggctaggctg gtcttgaact cctgacctca 4500

ggtgatccac ctgcctcggc ctcccaaagt gctgggatta caagcatgag ccaccgcgcc 4560

cggcctactt tagtgatttc ttaggaggac agagggaacg ggctggcaag acaggcttgg 4620

aatgtgtttt gggatcaagt gccggtttct gtctggcact ggcgttctct gtggggccat 4680

gatggacaca ctgctgaggt caagcgtgat tcgtcttgcg ctgtgcctgg cagtctcatt 4740

ggaaagttct gtagacatcg tgtggatggg gctcttcccg gccaagccct tggggacctt 4800

ccaggactgt gatctcccca cagtggctgt taagcaggga cctttcgtga agtggagtct 4860

ctggtccctt ccaagtcata gctagacagg gactcgggca tcgccaagcc tggctgatta 4920

ttcactggat gaggagacag gcccagagag gggcaggaac ctgcccgagg tcacccagca 4980

ggccccagag gtttcggtct cggattctcc ctgctcatcc ctggatgtag tgctgctgtg 5040

gatgtggttc tgtgctgggg gctgtggaga gcaggggget tgtgccagga ccccagtgag 5100

ggtggcgccc tcgccatgag gccgactgtt ggtatggggc ggccatccac tggggtgtgg 5160

ggaggaacag ctttcctgag gaggaggtgg cgggaggaac agcttccctg aggaggaggt 5220

ggcggtgctg tgtgacctgg gccttgaagg acaggtccat tgtcaacaga acattttggg 5280

agtggagcct agagggagaa aatttgttga aattcagatt cccctccccc taccaataca 5340

caccaaatca gatgcccctg accagatcta aatttggctc tcagagattt ccattgtagc 5400

tgggcacttg gggaaccttc taagtgctgc ctctgcctct ccccagcctg cctgcctcag 5460

tttccccagc cctgggcccg tgtcgctgtt gccatcacgt gggcgccctc tagtggagga 5520

atcagattat gcactccggg gcttggagca ggagtcagga ggggctcctg tctttccttg 5580

aaacgttgga tgccgggatc ctggaacagt ctctgcattc ctcctggcga gaaccagagc 5640

ctgggcacag gggaccatct gttgtttgaa ggctgcagcc tggcagggca ctcaggagat 5700

ctggcagttg gctgcagggc caggtctagg ggccagggca tcagggaggc tctgggctgg 5760

ttcagccccg ggccccttg cagattgtga cctgggcccc tgtgcagggg catggccaca 5820

ggatgctggg aggggtctct gaccctgacc ttcttggctc tgtgcatcct tgagaccaga 5880

aaggtctgga acaaatgagt agacgatgcc ctaacctggg gagggagcca catcctgatc 5940

ccagcaacct cgggaaggat ctgtcaggat tatggggcac cctgggggcc ccaagtctgc 6000

atgggtctcc acttgcaatt tctgtaggaa gctctgataa atccaaactg ggggtcctag 6060

gacacagtca gaaatgctga taccgttgtg tgtggagcct cgggccctgg gggtcaggag 6120

catgtggagg gtgggccacg ggggttcaga agagaatcct gtaacccccc acccccaaa 6180

ctgaagccca cttgagggcc atggctgaaa ggttgggggg tctccgtgcg tcctgtggag 6240

tgggtggtga ggagtccttg ggtttgcacg cctctgggcc tgagcggcgg gaccccgtcc 6300

acagcggatc cctgggccct gttgctcaga tgctctcaga gtgttgctgt ggccacggag 6360

ggagcctgag ttaagcttct cttgtgccgg ttgtacgctg tcaggtcaca ctggtgagtt 6420

aggcagggca cagatgccca gagcagaggg aactttcctt ggggattcaa cacgtgcaag 6480

tcttaggggc tggcaaatcc tgccctcagc tagagagggg gcttttattt gagaccagaa 6540

tcacctgagc atcctcctgt ccccagctgt gtccagcctg tctgcaggga catcctgaga 6600

ggaccaggct ctcccctcat ccacctgcct aagtgccact ctgaaccctg tccacctgtg 6660

ccgtggaggg gcgtgacctc aagctgctca gccagcagca ggcttggccc tgggggggcag 6720

cagagaccca ggtggctgtg gggtgggtgc ttcgtggcgt ggttctgaaa cttcgttgga 6780

agtgtgtgga cagtgccttg cctgttctct gtgggaccct atttagaaac gaggtctgag 6840

ttactggggg tcatcactgt gttctgatgg cccagctgtg tggaggccgc ggtgcagccc 6900

catccaagga gccagggccc tgggtctagc cgtgaccaga atgcatgccc cggaggtgtt 6960

tctcatctcg cacctgtgtt gcctggtgtg tcaagtggtc gtgaaactct gtgttagctc 7020

ttggtgttcc tgaaagtgcc cccgggtctc aggcctcaga accagggttt cccttcatct 7080

cggtggcctg ggagcatctg ggcagttgag caaagagggc gattcacttg aaggatgtgt 7140

ctggccctgc ctaggagccc cccggcacgg tgctggggcc tgaagctgcc ctcgggtggt 7200

ggagaggagg gagcgatgaa gtggcgtcga gctgggcagg aagggtgagc ccctgcaagg 7260

tgggcatgct ggggacgctg agcagcatgg ccagcagctg ggtctgcagc ctggtacccg 7320

gcgggacttg tggttggggc tggtttgtgg ccaggagagg ggctggcagg agacaagggg 7380

gactgtgagg cagctcccac ccagcagctg aagcccaatg gcctggctgt gtggctctca 7440

gctgcgtgca taacctctca gtgcttcagt tctctcattt gtaaaatgag gaaacaaaca 7500

gtgccagcct cccagaggtg tcatgaggat gaacgagtga ccatgtagca tgggctgggt 7560

gcgtgtcacc taacatcacc agcctttgca aggagagccc tgggggcctg gctgagtatt 7620

tcccttgccc ggcccacccc aggcctagac ttgtgcctgc tgcaggccct tgacccctga 7680

ccccattgca cctgtctcca caggagccga ggaggtgctg ctgctggccc ggcggacgga 7740

cctacggagg atctcgctgg acacgccgga cttcaccgac atcgtgctgc aggtggacga 7800

catccggcac gccattgcca tcgactacga cccgctagag ggctatgtct actggacaga 7860

tgacgaggtg cgggccatcc gcagggcgta cctggacggg tctggggcgc agacgctggt 7920

caacaccgag atcaacgacc ccgatggcat cgcggtcgac tgggtggccc gaaacctcta 7980

ctggaccgac acgggcacgg accgcatcga ggtgacgcgc ctcaacggca cctcccgcaa 8040

gatcctggtg tcggaggacc tggacgagcc ccgagccatc gcactgcacc ccgtgatggg 8100

gtaagacggg cgggggctgg ggcctggagc cagggccagg ccaagcacag gcgagaggga 8160

gattgacctg gacctgtcat tctgggacac tgtcttgcat cagaacccgg aggagggctt 8220

gttaaaacac cggcagctgg gccccacccc cagagcggtg attcaggagc tccagggcgg 8280

ggctgaagac ttgggtttct aacaagcacc ccagtggtcc ggtgctgctg ctgggtccat 8340

gcgtagaaag ccctgnaaac tggagggagc cctttgtccc cctgncttca gtttcctcat 8400

ctgtagaatg gaacggtcca tctgggtgat ttccaggatg acagtagtga cagtaagggc 8460

agcctctgtg acactgacca cagtacaggc caggcctctt ttttttcttt ttttttgag 8520

atggagtctc actctgtcgc ccaggctgga gtgcagtggt gtgatctcag ctcactacaa 8580

cctctgcctc ctgggctcaa gtgattctcc tgcctcagcc tcctgagtag ctgggattac 8640

aggtgcctgc cactgtgctt ggctaatgtt tgtatttttg gtagagatgg ggtttcaccg 8700

tcttggccag gctggtcgca aactcctgac ctcaggtgat ccacctgcct cagcctccca 8760

aagtgctggg attacaggca tgagccacca cgcccggtca ggccaggcct cttttgaaca 8820

ctttgcacac catgggtctt ttcatccagg ggggtaggta cagttgtaca gttgaggaca 8880

ctgaagccca gagaggctca gggacttgcc cagggtcaca cagcaggatg tggcaggtgt 8940

ggggctgggc ctggcagcgt ggctccagct ttccagcata gaaatctgtg aaagcagata 9000

gtttgtcggt cggtagggga gactttctga gacccgcccc agcggctcag agggtagtag 9060

ccaggggcct tcctgggggc tcataaccca gaacactgaa tgggaaaacc ctgatggagg 9120

aggcgcagtg gagctgtggg tgccgatggg aagtcccaga ggagctggga ggtcagtagc 9180

ggtgctgccc tctgtggagc acttagtggg caccaggtgt gtttccaggt tcatggccct 9240

gggacctgaa gctcagaagg tgaagtaact tgcccagggc acccgtcggg cagcggcggg 9300

cagaggattt gtgggctgtg gagcctgtgc tcgtggccca gccctggggg ttgtgagtgt 9360

gctggccggg gagcttttcc tgcaagtgga ctggtgtcta ggagccagca tgtcaggcag 9420

caggcagcgg gagtgcagca ggcagcggga gcacagcagg cagagggcgg ggctcgagca 9480

gccatccgtg gaccctgggg cacggaggca tgtgggagag ggctgctcca tggcagtggc 9540

tgaagggctg ggttgtgccc cgaggagggt ggatgagggt aagaagtggg gtccccaggg 9600

gctttagcaa gaggaggccc aggaactggt tgccagctac agtgaaggga acacggccct 9660

gaggtcagga gcttggtcaa gtcactgtct acatgggcct cggtgtcctc atctgtgaaa 9720

aaggaaggga tggggaagct gactccaagg cccctcctag ccctggtttc atgagtctga 9780

ggatcccagg gacatgggct tggcagtctg acctgtgagg tcgtggggtc cagggagggg 9840

caccgagctg gaagcgggag gcagaggggc tggccggctg ggtcagacac agctgaagca 9900

gaggctgtga cttggggcct cagaaccttc acccctgagc tgccacccca ggatctgggt 9960

tccctccttg gggggcccca gggaacaagt cacctgtcct ttgcataggg gagcccttca 10020

gctatgtgca gaaggttctg ctctgccccc tcctccctct aggtgctcag ctcctccagc 10080

ccactagtca gatgtgaggc tgccccagac cctgggcagg gtcatttctg tccactgacc 10140

tttgggatgg gagatgagct cttggcccct gagagtccaa gggctggtgt ggtgaaaccc 10200

gcacagggtg gaagtgggca tccctgtccc aggggagccc ccagggactc tggtcactgg 10260

gcttgccgct ggcatgctca gtcctccagc acttactgac accagcatct actgacacca 10320

acatttacaa acaccgacat tgaccgacac cgacatttac cgacactgac atttaccaac 10380

actgtttacc aacactgaca tctactgaca ctggcatcta ccaacactga catttaccga 10440

cactgacatt taccaacact atttaccaac actgacatct actgacattg gcatctacca 10500

acaccaacat ttaccgacac caacatttac caacactgaa atttaccgac accgacattt 10560

accgacaccg tttaccaaca ccgacgttta ccgacaccga catttaccga cactgatatt 10620

taccaacact gacatctact gacgctggca tctactgaca ccgatgccag catctaccaa 10680

caccgacatt taccaacact gacatttacc aacactgaca tttaccgaca ttgacattta 10740

ctgacactga catctactga cactggcatc tactgacact gacgtttacc gacactagca 10800

tctactgaca ctgacattta ccaacaccag catctaccaa caccgacatt taccaacact 10860

gacatttact gacactgata tctactgaca ctggcatcta ctgacaccaa catttaccaa 10920

caccagcatc taccaacacc gacatttacc aacaccagca tttaccaaca ccgatgttta 10980

ccaacgccga cgtttaccga cgccagcatc taccaacact gacatttacc gacaccgaca 11040

tttaccgaca ctgacattta ctgacactga catctactga tactggcatc taccgacact 11100

gatatttacc aacgccagca tctactgaca ctgatgttta ccaacaccga catttacgag 11160

caccgacatt tactgacacc aatatttact gacatcaaca tttagccatg tgatgggggc 11220

cggcttgggg gcaggccttg ctcttggcac tggggatgct gcagagacca gacagactca 11280

tggggtcatg gacttctgct tcttctccag cctcatgtac tggacagact ggggagagaa 11340

ccctaaaatc gagtgtgcca acttggatgg gcaggagcgg cgtgtgctgg tcaatgcctc 11400

cctcgggtgg cccaacggcc tggccctgga cctgcaggag gggaagctct actggggaga 11460

cgccaagaca gacaagatcg aggtgaggct cctgtggaca tgtttgatcc aggaggccag 11520

gcccagccac cccctgcagc cagatgtacg tattggcgag gcaccgatgg gtgcctgtgc 11580

tctgctattt ggccacatgg aatgcttgag aaaatagtta caatactttc tgacaaaaac 11640

gccttgagag ggtagcgcta tacaacgtcc tgtggttacg taagatgtta tcattcggcc 11700

aggtgcctgt agacacagct acttggagac tgaggtggga ggatcgctgg agtccaagag 11760

tttgaggcca gcccgggcaa aggggacaca ggaatcctct gcactgcttt tgccacttac 11820

tgtgagattt aaattatttc acaatacaaa attaagacaa aaagttaatc acatatccac 11880

tgccctgctt aagacagaaa acatgggtgt tgttgaagcc agaggcagct gctggcctga 11940

gtttggtgat tggttcctaa gcagttgaag gcagttttgt ttttccatag atgtctgttc 12000

tccctttgct gggtgcagcc tcgccctgct gctgtggtcg ggtttcagtg gcctcgtccc 12060

gtggacgcag cctcgccctg ccgctgtggt cgggtttcag tggcctcgtc ccgtggacgc 12120

agcctcgccc tgccgctgtg gtcgggtttc agtggcctcg tcccgtggac gcagcctcgc 12180

cctgccgctg tggtcgggtt tcagtggcct cgtcccgtgg acgcagcctc gccctgccgc 12240

tgtggtcggg tttcagtggc ctcgtcctgt ggacgcagcc tcgccctgcc gctgtggtcg 12300

ggtttcagtg gcctcgtccc atgggcgtgc tttggcagct ttttgctcac ctgtggagcc 12360

tctcttgagc ttttttgttt gttgtttgtt tttgtttgat tttgtttgat tgtttgtttt 12420

tgttgtcgtt gttgttgccc aggctggagt gcagtggcgc gatctcagct cactgaaacc 12480

tctgcctcct tgggttcatg ccattctcct gcctcagcct cccacatagc tgggattaca 12540

agtgcccgcc accacgcctg gctaaatttt gtatttttag tagacagggg gtttcaccat 12600

gttggtcagg ctggtctgga actcctggtc tcacatgatc cacctgcctc ggcctcccaa 12660

agtgttggga ttacaggcgt gagccaccgc gcccagccct ctgttgagca tattttgagg 12720

ttctcttggt gccagtgata tgtacatgtg tccccatcgc accatcgtca cccattgagg 12780

tgacattggt gcctctcctc ggggtggatg cctccctctg tttccagcaa cttctgaagg 12840

attttcctga gctgcatcag tccttgttga cgtcaccatc ggggtcacct ttgctctcct 12900

cagggctccc aggggaggcc cgaatcaggc agcttgcagg gcagggcagg atggagaaca 12960

cgagtgtgtg tctgtgttgc aggatttcag accctgcttc tgagcgggag gagtttcagc 13020

accttcaggg tggggaaccc agggatgggg gaggctgagt ggacgccctt cccacgaaaa 13080

ccctaggagc tgcaggtgtg gccatttcct gctggagctc cttgtaaatg ttttgttttt 13140

ggcaaggccc atgtttgcgg gccgctgagg atgatttgcc ttcacgcatc cccgctaccc 13200

gtgggagcag gtcagggact cgcgtgtctg tggcacacca ggcctgtgac aggcgttgtt 13260

ccatgtactg tctcagcagt ggttttcttg agacagggtc tcgctcgctc acccaggcga 13320

gagtgcagtg gcgcaatcac ggctcgctgt agcctcaatc tccctgggct caggtgatcc 13380

tcctgcctca ccctctgagt agctgggact acagacacat accaccacac ccagctagtt 13440

tttgtgtatt ttttgtgggg ggagatgggg tttcgctgtg gtgcccaagc tgatctcaaa 13500

ctcctgaggc acaagcgatc cacctgcctc ggcctcccaa agtgctggga tgacaggcat 13560

cagccgtcac acgcagctca atgattttat tgtggtaaaa taaacatagc acaaaattga 13620

tgattttaac cattttaaag tgaacagttc aggctgggcg tggtggctta tgcttgtaat 13680

cccagtactt tgagaggctg aggtgggcag atcacctgag gtcaggagtt tgagaccagc 13740

ctggccaaca tgatgaaatc cagtctctac taaaaataca aaaattagcc gggcatggtg 13800

gcaggtgcct gtaatcccag ctactcggga ggctgaggca ggagaatcgc ttgagcccgg 13860

gaggtggagg ttgcagtgat ctgagatcat gccactgcac tccaatctgt gtgacagagc 13920

aagactctgt cttgaaaaat aaataaataa aaaaaatttt aaaaagtgaa caattcaggg 13980

catttagtat gaggacaatg tggtgcaggt atctctgcta ctatctactt ctagaacact 14040

ttcttctgcc ctgaaggaaa ccccatgccc accggcactc acgcccattc tcccctctct 14100

cccagcctct gtcaaccact aatctacttt ctgtctctgg gggttcactt cttctggacg 14160

ttttgtgtga ctggaatcct gcaatatgtg gtccctgcgt gtggcttctt tccatagcat 14220

tgtgttttcc agattcaccc acacattgtc gcacgttatc agaatctcat tcctgactgg 14280

gtgcagtggg ttaggcctgt aatcctaaca ttctgggagg ccaaggcggg acgatcactt 14340

gaggcaggag tttgagacca gcctggccag cctagcaaga ccccagctac caaaaaattt 14400

taaaagttaa ctgaacgtgg tggtggtggg cacttgtggt tcccagctac ctgggaggct 14460

gaggttggag gatcgcttaa gcccaggagg tcaaggctgc agtgagctat gatcgcacca 14520

ctgcactcca gcctggacaa cagagcaaga ccctgtctga aaaaaaaaac aaaaaaaaaa 14580

gttcctttct ttttgtggct ggatgacatc ccattgtatg gccacagcac attttgtttg 14640

tctgtttatc gggtggtggg cagtggtttc cacctttgt ctcctgtgaa taatgctgct 14700

gtgaacattt gaattcaagt ttttgtttga acacctgttg tgaattattt ggatatatgt 14760

gtaggggtag gattgctgag tcctatggta atgttaggtt tgacttactg aggaaccatt 14820

aaactgtttt caacagtggc tgcgccgttc tgcatcccca ccggcagtgt gtgagggttc 14880

tgactttacc tcctcacaaa cgcttctttt ccatttaaaa aaatattcag ccaggtgctc 14940

tggctcacgc ctgtaatccc agcactttgg gaggccgtgg cgggcggatc acctgaggtc 15000

aggagttcga gacgagcctg gccaacatgg tgtaacccca tctctaccaa aaatataaaa 15060

attagccggg tgtggcagcg ggcgcctgta atcccagcta cttgggaggc tgaggcagga 15120

gaatcacttg aacccgggag gcagaggttg cagtgagcca agatcgcgcc actacactcc 15180

agcctgggtg acaagagtga aactccatct aaaataaaac aaaaataaaa ataaataaaa 15240

atttattaaa acattcatca cagccagcct agtgggtgtc ccatgtggct ttgcctcgca 15300

tttccctgat aactaggatg ctgagcgtct tgtcccaggc ttgccacacc tcagcacttt 15360

gagatacgtc gcacagtccc catttgcgaa cgagaaatga ggtttaggga acagcagctg 15420

tgtcatgtca cacagcgagc agggggtctc tgagccgtct gaccccacag ccgaccaagc 15480

tccaatcctt accgcctcct agtgttgtgg atgtagccca gggtgctccc acatttttca 15540

gatgagaaca ccgaagctca aaacaggagc gttttgtcca cattggatac acgatgtctg 15600

tggtttggtc ctgaagtcac tttatatctc agtggtccag actggagtag gacagggggt 15660

tctggggaat ggggaaggtg tctcaggtga aaggaaggaa ttccagattc tccatactgt 15720

ccttgggaag ttagaagact cagagggtct ggcaaagtca gacaaagcaa gagaaatgca 15780

gtcaggagga agcggagctg tccaggaaca ggggggtcgc aggagctcac ccccaggaac 15840

tacacttgct ggggccttcg tgtcacaatg acgtgagcac tgcgtgttga ttacccactt 15900

ttttttttt tttgaggtgg agtctcgctc tcttgcccag tctggagtgc agtggcacga 15960

tctcggctca ctgcaagctc tgcctcccgg gttcatgcca ttctcctgcc tcagcctccc 16020

gcgtagctgg gactacaggc gcctgccacc gcgcccggct aatttttgta ttttagtag 16080

agatgggatt tcactacatt agccaggatg gtctcgatct cctgacctca tgatccgccc 16140

gtctcggcct cccaaagtgc tgggattaca ggcgtgagcc accgcgcccg gcccgatttc 16200

ccactttaag aatctgtctg tacatcctca aagccctata cacagtgctg ggttgctata 16260

gggaatatga ggcttacagg ccatggtgct ggacacacag aagggacgga ggtcaggagg 16320

tagaagggcg gagagaggga acaggcggag gtcacatcct tggctttcaa aatgggccag 16380

ggagagacac cctctgagca tggtaggaca ggaaagcaag attggaacac attgagagca 16440

accgaggtgg ctgggcgtgg tggcttacgc ctgtaatccc aacactttgg aaagctgagg 16500

tgggtggatt gcttgaggcc aggagttcaa gaccagcctg gccaacatgg tgagaccccg 16560

tctctactaa atatacaaaa attagccagg cgtgatggtg catacctgta atcccagctg 16620

cttgggaggc tgaggcagga gaattgctta aacctgggag gcggaggttg cagtgagccg 16680

agatcccgcc actgcactcc agcctgggcc acagagtgag actccatctc aaaaaaaaaa 16740

aaaaaaaaga taaaaagacc aaccgaggaa ttgaagtggg ggggcgtcac agtagcagaa 16800

gggggatcgt ggagcaggcc accctgtggt catgcactgg aagctcatta cctgacgatt 16860

tggagctcat cactgggggc ctaaggagaa tagatactga aggatgagga gtgatggcgc 16920

ggggcacggg tgtctttggt ggccagaact tggggactgc tggggtgcct cactgcaggc 16980

cttctcagcg ccctttatat gcttacacag gctgtttcta agagggggat acattgcata 17040

agcgttttca gactacctca tcatgggtcc ctttctttac cctctgtggc cctggtggcg 17100

cactctctgg gaaggtgcag gtggatgccc agacccgccc tgccatccac ctgcacgtcc 17160

agagctgact tagcctcgag attgctgctg gcacctcctg ccccgggaca cctcggatgt 17220

gcccgtggag atgctggctc tgtgttttct gctggagttt ggtgcgtctt ttcctcctgc 17280

aagtggccac cgctcttggg tatgtcctca ggcttctgcg agtcatggct gcttctcagg 17340

tccttgccca gcgccaggag caaaccctcc tggcactttg ttcaggggtg gatgcgccag 17400

tgttcctgct gtggaccgcc atctcacatg agggtcttgg gcctgcaggc tcgttcagga 17460

aacacccgct gagtatgcag tgtgtgccag ctgtgtccca ggcaatggcg gggacagtgg 17520

ctgctgctgg ggttgtggtg gcttctgggg actctgggga cagctgaggt gcaaggagcc 17580

acggctcctt gaggatgcag ttggactcca ggtggaaggg atggttgggg gaggtataaa 17640

tggggtcagg gaggagacac atttggaaca atgggaacat ttttaagatg ctatgtcggg 17700

aggcaacaag gtggccaacc caggtgctga ggagcccaca ccagccctgg acgtgttttg 17760

ccgctcacct ttgctgggga gtggtgggag agaggattcc gttccacgtg gtggtgtgcg 17820

cagctgggct gtgtggagct gggcgctagg aggaaggtgc tttctgcggg gctagccggg 17880

ctctgccttt gaacacaatc aggctccagg ttttcagcat ccagtgcatg agaggacttc 17940

acgggcagct gtggctgatc ccttgatgaa ttgggagaag aacaaaggtc tatgaaatga 18000

ggtttcatgt agatggcatt agagacgccc acaacagatt tacagagtgg agcggagacg 18060

gcggatgggt ctgggaggcc cctcctgctg gccttgactg tgacagctgt cctgggaatc 18120

agcttccagg ccgccccagc agcctgactg acacacacag gggttttagc cccatcctgc 18180

gaccagctgt tgccatcatc agtgacagct gggagtggcg gtggttccag ccctgggcac 18240

cctccccacc tgctggggcc cacccagggc agtcctgaca cctacaggtt gcttggagcc 18300

gcatccgagt cctgccccac cacgtgtgaa gcccgagtgg tcgtgggctg aggtcccctg 18360

attgcatccc cacttccctt ctgcttcaca tagctgcctc ttctcaccgt ttttccagcc 18420

tcctgggcta ggaattccag tgttgtgctg gctttgcccc aggacacctc cttagccctc 18480

ttcctgagtc tagagccccg ggggttggaa gtcctggccc ctgggacacc tgcagccaca 18540

ctcagcttct cctgtgagcc tccagcatgt cccctcagga ccaagccctc acgttcttgc 18600

ctccccgccc acctgggctc agccagggga aggcctggct gggagcgtct cccctctgcc 18660

ctgcccttct cccctcctac cctgcccttc tctcctctgc cccgccatgg cttttatatc 18720

ctgtgccaca agacatggct gtgtgtgaaa gtggcagggt ctggcatctc tgtgggtctc 18780

tgaggcccac gctccagtgc cactcttccc acccgctggc cgtgccctca tgctggaggg 18840

acagcccagc cctctcccga accccagccc catgtgccca gctgcccccg gccctctccc 18900

ctggaagccg gggtcactcc agccgtatgc catggtgggg acatcctgct tccttggcct 18960

tccagggaag gtcctctttc caaatggcga cacctggtcc ctgcctggag gctggaagct 19020

gtggcccttg tatgcccctc cagggtctgt gcgctcggtt ggcccgagtt cccatcaccg 19080

tcatcatcac catcatcatt gtcatttcgc ttgtctgtga gccggcctgg tctcccagag 19140

cagagaccct ctgaggtcca gcctgagttg gggtctccgt gctgacccct gacggggact 19200

caggacgtac caggtctggg tcaggagtga cccccaaacc tcgtgccctt tgacaggcac 19260

ccctgacttt tgctaagtgg gtggaggtga catcacttac agcgggagtg atgggacagg 19320

gtctgttggc tgcactgtgc tcccagggat ctggggagag gctatatccc tgggctttgg 19380

cactgcagag ctgtgtgtgt ttgtgtgtgt gtgtgtgtgt gtgtgtgtgt gtgtgtgtgt 19440

gtgtgtgttt gcgtgcgcgc acatgtgtat aagatctttt tttattacat gaagcaagat 19500

aactgttgct gtttcctttt gggttttgtg ttcaacagag tggggtactt cttccctcag 19560

acaacagaac tctccccttt aaacacgtgc tgtcagaggg tgggtcttgg gctcatgtct 19620

gtttgcacag ccgagtcaga ggaaacacag ggttcttcat aaaaacactg cacagcaggc 19680

gactgtccag agtcagcctg caggacggca gcagccctgc ccctcagagc acagctaggg 19740

tgggctgctt tgggatctcc cgtcattccc tcccagctgg cagccggcgg ccggcccatt 19800

ccttggtgtg ctggtcaggg gggcgtgcgc ctgctctgct caccctggga atgggacaga 19860

agctggcagc tcggagagga cagggctgga cccttgggtg gcctctggct ggaccatctc 19920

attgtcctca gacacagcct ctcgggtcta gtttcatttc ctgaaaaaca agtgcacaga 19980

actagagcag gagtcgagag ctacggcccc cgggccagat ccagccctgc cacctgtttt 20040

cacaccatgc tcaagctgag tgggttttac atttttaat tacttgaaaa aaaaaaagcc 20100

aaaggaggtt tcatgaccca tgaaaattat atggaattca aaaaaaaaaa attatatgga 20160

attcaaattt cagtgtccat aaataatttc ttgagacagg gtctcgctct gtcacccagg 20220

ctggagtgca gtgctatggc atggctcgct gtaccttga cctcccaggc tcaagcgatc 20280

ctcctgtctc agcctcctga gtagctggga ctacgggtgt gtgccaccaa gcccggctaa 20340

ttttttttta attttagtaa agacagggtc tttctatgtt gcccaggctt ttctggaact 20400

ccatcttggc ctcccaaagt gctgggatta caggctcgag ccacggagcc cagcctgttt 20460

ttgtttttc actgataaag ttttgccggg tgtggtagtg tgtgcctcta gcgatttggg 20520

aggctgaggt gggaggatcg cttaagccca ggagtttgag gctgggctca agtgatcagg 20580

aggtgaacta tgatcatgtc attgcattcc agcctgggtg acagagcaag aacctatctc 20640

ttaaaaatat atatttaaaa agtattgggt gtggtggctc acgcctgtgg tcccagctac 20700

ttaggcatct gaggtgggag gatggcttga gcccaggagt ttgaggttgc agcgagccaa 20760

gatcgtgtca ctacactcta gcctgggtga cagagcccag accctgcctc tttaaaaaaa 20820

aaaaccaaaa aacatgtatt ggaacacagc catgcctgtt cagtcacgtg ctctccatgc 20880

tgctttctgc tccagagacc cttatggcct gaaagctgaa aatattttct atcctttaca 20940

aaaaagtttg ctgacctctg tcctggaaaa ttcatctccc aagttctctt ccggcactgg 21000

cgttcctggg tgtcctaaat ttggcccctg ttatttctga actctgtttt ggctctgttc 21060

cctcccagga gccaggacag gcacgttctc tgcatcttgt cccctgacgc ccagaggctt 21120

ggctcggctc aggcattctt ggaaatatct ggctccagga aaggcagagg cctcctgagt 21180

cggcccagag ggaacctgcc ccaggtctgg gggaggcctg acccagcaga gtggcttttg 21240

ccgatgggtt gggccggtca agatgtgctg aaagttgtcc tcagaaggcc actttgggat 21300

tccttcctcc agtattagag caactgagag ctgctcattg caagcctgat gttttcccag 21360

ttggccgggt ccaccgggtg ccctgggatt ctgggatctg ggtggaaagt agggggcttg 21420

ggggagtgtc ctgggttctg gaatccaggt ggcaagtggt gaggttcagg gagtggcttc 21480

tgagccacca taggggtctc tgtgggaggc tctgcccatc caggagattc cgcaggccct 21540

gccggcccag agccagcgtc ttgcgcttgc cgaggctaca gccagcccca gccgggtgga 21600

acagcccgtc gcctcctctc actttgtttt ggggccacct gggagtgtgg agcaagggta 21660

gagagggagg aagtggctgc cggccgctgc ccagcaccct tgtttgcctt gggccctctg 21720

tgggctcctt tttattgctc ttcaatgaag ccagggaaat ggacttcctt gcctcacttc 21780

agttcaacat gtctggaagt ttggtattaa aattaagaaa gtgtggaaat agagcaagaa 21840

gagaaaaatc tctccaagag ataatagtga cctctgagct gggcgcggtg gctcacgcct 21900

gtaaatccca gtactttggg aggctgaggc gggcagatca cctgaggtcg ggagtttgtg 21960

accggcctga ccaagatgga gaaaccccgt ctctactaaa aataaataaa taaataaata 22020

aataaataca aaattagcca ggcatggtgg cgcctgccta taatcccagc taaggcagga 22080

gaatcgcttg aacctgggag gcaaaggttg cagtgagcca agatcacgcc attgcactct 22140

agtctgggca acaagagtga aactccgtct caaaaaaaat aaataaataa aaaataaaaa 22200

tagtgacctc tggccaggtg tggcagctca tacccgtaat cccagcactt tggaaggaag 22260

gccgagatgg gcagattgct ttagcacagg agtttgagac cagcctggcc aacatggtgg 22320

aaccccatct ctacaaaaat agaataaaat ttaagaggta atagtgacct tttggtagat 22380

cgaaacctgg attgctttct ttttctaaat gctgattctt ttctttgtgg tgtttgtgtt 22440

ctgtgccgat gtcccctccc cagccctgtt attgtgagtg gaagaagggg aaagggttcg 22500

cccgctactg tgagcccctc ctctcacgct gggtgtcctt ggagaagcct gcacttcttc 22560

attgtacgcc agggctgggt ccctccctgg agtggttctg tgctgctggg atggggccaa 22620

cccctcagat gttttctgag tgtcacacac aggtgtgtgc attcatggcc tttgcgtgtc 22680

ttcctgttgt ggaggcaaaa atgtgaagaa ccctagatga ttttgggacc agggctccat 22740

cacctgctgt tcattgcaca ccggagcatc caggcatggg tggagagctc agacttccag 22800

gcacggtcgc aggggctggt ctaaccatgt tcccgcccgc ctgctcgtca gaaccgcctg 22860

ttgggagctg ttatcatgat accatacctg ggccctgggc tatccgattc tgacttaatt 22920

gctccaggtt ggggccaggc cgttgtttgc tgttttgttg tttcttctgt gacgttagcc 22980

actgggctaa tctgagcccc tcagttacag gtggagaaac tgagacccat gggggtgcaa 23040

ggacttgccg aggacccaga gccccttggg ggcagagctg aggcggggcc tggctttggg 23100

tcccagagct tccagtcccc ttcccgctct cctaacagct tttttttttg agacaagatc 23160

tcaccctgtc acccaggctg gagtgcaatg gcatgatctc ggctcactgc aatcttcgct 23220

agctgcgttc cagcgattct cctgcctcag cctcccgagc agctgggatt acaggtgtgt 23280

gccgccatgc ccagctcgtt tttttttgta cttttagtag agatagggtt tcaccatgtt 23340

ggccaggctg atctcgaact cctgacctca aatgatccgc ctgcctcggc ctcccaaagt 23400

gctaggatta caggctggga tcacactgtg cctggcccta gcagctttgt cctgtgccat 23460

ccaacaacag atgaccgaag tctttgtttc ttaacatgca ttccatctgc cttacagttt 23520

tgccacctgc aaaacagagg acttgtcgct tttctggtaa gctggaaatg taatctggta 23580

gcaggaggcc tgtggaagct tgcctttaat ggccttgtgt ctctttcatc ctgtcctgag 23640

agccggagaa cttggatgtt gcacctaact caaccttcct gttaacatac agttctgcag 23700

gctcatggat catcagaacc acgtcctatc tcacgcggct gtatgcttcc gttggttcag 23760

gtgtttttac cttgacagta ttttctcctc ggtggctttt gcggtggttg cttttaatca 23820

gcattgactc ttcaagaaaa atatttagct gctacatctc agaggagaca gggtggaaag 23880

catctgagac ctgcaggctc agacttagaa ccagaagtgc cctcagagtt catccggccc 23940

tgacccagcg ggaaatgagt tcacagagaa gcgggagaac tttgccccag gccctgccgt 24000

tgctcataac tgccccaggt ccttacattt gctccaggtc ctgccccagg ccctgcagtt 24060

gctcataact gccccaggtc cttatatttg ctccaggtcc tgccccaggt cctgcagttg 24120

ctctgtgtgg tgggtgtgat ctggagccct ccgcccattg ctgcacctgg ggcaggcatt 24180

gctaattgat cccaggactc cttcctgcgg agcacgccct ggttctccag gcagccgctg 24240

cctgtcagcc tgcagtggtt cgggagagga cacctgcttg cctggtctgt tccaaatctt 24300

gcttctcatc ccagcacagg taggggtgc tatgggaaag ggatcctcag ttggccctgt 24360

cactgctcta tcagctgggg acgtggcatc ctagtgaaaa catcatggcc gggcgcggtg 24420

gctcacgcct ggaatcccag cactttggga ggctgaggag ggtggatcac ttgaggtcag 24480

aagttcgaga ccagcctggt caacatggtg aaacccatct ctactaaaaa tacaaaaatt 24540

cgccaggtgt ggtggcgggt acctgtaatc cgagctactc gggaggctga ggcaggagaa 24600

tcgcttgaac ctgggaggtg gagcttgcag tgagccgaga tcttgccact gcactccagc 24660

ctgggcaaca gagtgagacg ctgtctcaaa atctcaaaca aacaaacaaa caaaaaacaa 24720

acaaacaaag cgtcatttat ccagcacccc tggggaacca tgctacctgg tgttttatgg 24780

tacctggcaa ggtgcaggtg aagttgctgc tcttgggcat tgaacccgtc ttgtttgggg 24840

cagctcaggc cccaggcagg gtccgggttg gctctcgttg gtgtggccct ggcccatcca 24900

gacctatatt tctgccgtcc tgcaggtgat caatgttgat gggacgaaga ggcggaccct 24960

cctggaggac aagctcccgc acattttcgg gttcacgctg ctgggggact tcatctactg 25020

gactgactgg cagcgccgca gcatcgagcg ggtgcacaag gtcaaggcca gccgggacgt 25080

catcattgac cagctgcccg acctgatggg gctcaaagct gtgaatgtgg ccaaggtcgt 25140

cggtgagtcc ggggggtccc aagccatggc tcagccatgc agacttgcat gaggaggaag 25200

tgacgggtcc atgcctgggc ataagtgttg agctcaggtg ccccgacctg gggaagggca 25260

ggacaggaaa ggtgacagta tctggccaag gacagatggg aagggaccaa gggagctgat 25320

tagggagtgg ttatggacta ggaatgtcgg taacaatggt tagaaagtga ctaacatttg 25380

ttgagcacct gctgtgtgcc cggccctggc cgggagcctt cgtgcccaca gtgaccccgt 25440

ctgcaaatgt agttccttgc cctactcgca ctggggagca ggacgcagag ccgtgcaact 25500

cacaggtgcc aagctcagga ctccctcctg ggtctgcctg ggctgggctg tgcttgttgc 25560

ccctgtggcc cacgcatgtg caccttccac ctgaaagcca ggatcttcag gacgctcccc 25620

gaggaggtcg ttgtctggca caatgatttg tctcttcctg aaaaggtgac agagttacac 25680

tggagagagc agcatccagg tgcggcaggg acaggcctgg ggctcgcggg cagggactct 25740

gtgtcctgcc ggggtcccac actgcacctg cttgtcagag gcactcagtc aatctttgct 25800

gatgaaggat gagaggacag aggacgtgat gcttgctgct gcattgcctg cagtcctggg 25860

tgagatgccc gggttgactc tgctgcccgt cgggtggatg tgatgtcaga tccccggctt 25920

taaaatacga gggagctggg aattgaggga gcaggttggg gcagaaagca cagccccgtg 25980

gaagcctgga gctgaggcag tgtgggcgac ccctggagca gtgagtgctt ccttcatggc 26040

cttcatcgca ccctgcagtc ctcatgtagg ggatgccatc catgaattta gttttcccag 26100

cctcctttaa aaacgcgttc atgctggggc cggggcagtg cagtggctca catctgaaat 26160

cccaccactt tgggaggccg aggcgggtgg atcatgaggt caggagatcg agaccatcct 26220

ggctaacaag gtgaaacccc gtctctacta aaaatacaaa aaattagccg ggtgcggtgg 26280

cgggcgcctg tagtcccagc tactcgggag gctgaggcag gagaatggcg tgaacccggg 26340

aagcggagct tgcagtgagc cgagattgcg ccactgcagt ccgcagtccg gcctgggcga 26400

cagagcgaga ctccgtctca aaaaaaaaaa aaaaagtaca aaaaaaaaaa aattagtctg 26460

ggtgtggtat cacgcgccta taatctcact actcgagagg ctgaggcgga gaattgcttg 26520

aacccaggag gtagaggttg tagtgagccc gtatcgtacc actgccctcc acctgggcaa 26580

tagagcgaga ctctgtctca aaaagaaaaa aaaaaaaaga acatttatgc caggtgtggt 26640

ggctcatgcc tgaaatccca gaactttgga agactgaggc aggaggatca cttgagccca 26700

gaaatttgag agtgtcttcc ctgggcaaca tagagagacc tcatctctac cagaaaaaaa 26760

aaaattagcc cggcatggtg gcatatccct gtggtcccag ctacttaggg ggctgacgtg 26820

gcaggatcac ctgagtctgg aggcagaggt tgaagtgagc tgagatcatg ccactgcact 26880

ccagcctggg tgacagacag agaccctgtc tcaaaaaaaa aaaaaaaaaa aagcatttac 26940

tatccaccat ggaaggtgag actgacctgt gagtgattgt tcaaagaaca aaaaataaac 27000

cccagagata agacaaaagg gtgcctccat gggggtgtga tttaaagctg agaaattggg 27060

cttcttcccc ctcccctctc accccgtggt ttgctaaagg agatgggaaa aaggattctt 27120

tttttggctg aaatatttaa cactaaatta aagccaattt taacagcact ttggttgatg 27180

agtgaaatta acagactggc caaaaataaa cgaacggtct gtactatgtg aaaaagaggc 27240

agctttggcc atgctgggcc aatgtgagtt ttcagggttg ctgggaatgt ctgtgaatcg 27300

gaggaagggc ctagctggga ctctcaggag ccaaggccct gaggggcaac ttgcctggtc 27360

cctgccctga ggcgttcact gctttcttcc tgggccagat cacaggcccg gaggctggac 27420

cactgggctg gcactcttgc cgagctgctc cctgacttcc tgaccatgct cctttcagca 27480

gccttgctgc actttagttt ccttgaatga aaaatgggga tgagaatagc tcctacctcc 27540

aaggtgaatg gagtgagttc ggacaggtga ctccctggga ccagtgcctg gcgcctgaca 27600

aggtccagtc agagcccgca ctgctgttac tgataccctt ggctgtacca ggggagaact 27660

tggttgccat tgccaggtgt tctcccacca cccccactac tgtccctgtt tgatgtgtgg 27720

cgggaataaa gctgtgcaca ttggagcttt tggcacatcc tggctttcag gtgaaaggtg 27780

cgtgtgtgtt tgagggttta gcctggccaa cccagccatg aggtcggacc tgacctgggg 27840

gtgagtcctg agctcggcac ccctgagctg tgtggctcac ggcagcattc attgtgtggc 27900

ttgggccgca ccccttccc tgctgggctg ttgatgttta gactggagcc tctgtgttcg 27960

cttccaggaa ccaacccgtg tgcggacagg aacgggggggt gcagccacct gtgcttctgc 28020

acaccccacg caacccggtg tggctgcccc atcggcctgg agctgctgag tgacatgaag 28080

acctgcatcg tgcctgaggc cttcttggtc ttcaccagca gagccgccat ccacaggatc 28140

tccctcgaga ccaataacaa cgacgtggcc atcccgctca cgggcgtcaa ggaggcctca 28200

gccctggact ttgatgtgtc caacaaccac atctactgga cagacgtcag cctgaaggta 28260

gcgtgggcca gaacgtgcac acaggcagcc tttatgggaa aaccttgcct ctgttcctgc 28320

ctcaaaggct tcagacactt ttcttaaagc actatcgtat ttattgtaac gcagttcaag 28380

ctaatcaaat atgagcaagc ctatttaaaa aaaaaaaaga tgattataat gagcaagtcc 28440

ggtagacaca cataagggct tttgtgaaat gcttgtgtga atgtgaaata tttgttgtcc 28500

gttgagcttg acttcagaca ccccacccac tcccttgtcg gtgcccgttt gctcagcaga 28560

ctctttcttc atttatagtg caaatgtaaa catccaggac aaatacagga agacttttt 28620

ttttttttt tgagacagag tcttactctg ttgcccaggc tggagtaccg tagcgtgagc 28680

tcagctcact gcaacctccg cctcccaggt tcaagcgatt cttctgcctc agcctcctga 28740

gtagctggga ctacagacat gcaccaccac acccagctaa ttttttttat atttttagta 28800

gagacagggt ttcatcatgt tggccaggct ggtcttgaac tcctgacctc aggggaacag 28860

acggggttgg cctcccaaag ggcggaaata acaggggtga gccaccgttc ccggcctagg 28920

aaaacttttt gccttctaaa gaagagttta gcaaactagt ctgtgggctg gccttctgat 28980

tctgtaaaga aagtttgatt ggtggctggg tgcggtggct cacacctgta atcccagcac 29040

tttgggaggc cgaggtgggc agatcacctg aggtcgggag ttcgagacca gcctcaccaa 29100

cgtggagaaa ccccgtctct actaaaaata caaaaaaaaa attaaccggg catggcggcg 29160

cctgcctgta atcgcagcta ctcaggaggc tgaagcagga gaattgcttg aacctgggag 29220

gcggaggttg tggtgagctg agatggcacc attgcactcc agcctgggca acaaaagtga 29280

aactccgtct cagaaaaaaa aaagtttgat tggtgtaacc aaagcgcatt tgtttatgga 29340

ttgtctgtgg cagcttttgt tctgccgaga tgagttgtga cagatctgta tgggctctaa 29400

agcctaaaac atgtgccatc cgccccttta cagaaaaagt gtgctgacct ctgttctaaa 29460

gtattggaca actacaatgt ttgctcattt attattctat gatttgtttt ctgctttttg 29520

ttgttgttgt tgttgttgag atagggtttc cctctgtcac tcaggctgga gtgcagtggt 29580

gtaatttcag ctcactgcag cctcgacctc ctgggctcta gtgatcctct catctcagcc 29640

tccctagtag ctgggactac aggcacacac caccactcct ggctgatttt ttttttttt 29700

ttttttttt gtggagacag ggtttccgca tgttgcccag gctggtttca aactcctagg 29760

ctcaaacacc cacctcagcc tcccaaagtg ctgggattac aggcgtgagc caccatgccc 29820

agcctattct actgtttgta ttacatagct ttaaaagatt ttttatgact ttaagtcaca 29880

agggttcttt gtagaaaaaa atatatatat aggaaagtat aaaaagaaag taaaaattgt 29940

ccataacctc tccagccaga gacgaccgtt gctgacacct cagcatattg cctttaagtc 30000

ttttttctct aagatagcat ttctcttcat cacagtcata tgctacgcag aattctgtat 30060

cctgattttt tcacttgaca ttacaacagg tatttgatgg cgctgtgaca aactctttgg 30120

cacaatcttt taaatgtatg aaatactcca ctgcacagat gtttgctttt aggcttaact 30180

gttcttttat tttgcgtgtg ctggttacag ccgggcacag tggctcatgc ctgtaatcac 30240

aacactttga gagggtgagg caggaggatc acttgagccc agaagtttga gaccggcctg 30300

ggcaacatag tgagacccca tctctacaaa aaacttttt aataagtcgg gcgtagtggt 30360

gcatagctgt agtcccagcc accaaggagg ctgagttggg aggattgctt gagccccagg 30420

aggttgatgc tgcagtgacc tgagattact ccactgtact ccaacctgag cgacagagca 30480

agacttgtct ggggaaaaaa aaaaaaaaaa tatatatata tatatatata tatatacata 30540

tatacataca cgcacacaca cataatataa aaatatatat ttataaatat ataatatata 30600

atataaaaat atatatttat aaataaaatt tataaattat atttataagt aaatatataa 30660

tatataatat aaaaatatat attatataat atataataaa atatataata taaaaatata 30720

tatttataaa taatatataa tacatactta taagtatata tttaaaatat atgtaatgta 30780

tatttttaa tgtatgatat ataatataca tttataaata cacatttata ttattttata 30840

taaaatatat ataaaatctc caagttgctt tttccaaaaa ggtgtcttgc tgcatttcaa 30900

acattcattt aaaaacttga atgctggtga tctggtccag aatgtgttca gtagctgctg 30960

ccagtggcca agcatctcgg gagatgtcta caaaacacgc tggttctggc ctggcgtggt 31020

ggctcacgcc tgtaatctca gcactttggg aggctgaggc aggtggatca actgaggtct 31080

ggatttcgag accagccttg ccagcttggt gaaaccccat ctctactaat aatacaaaaa 31140

aattagccag gcgtggtggc atgtgcctgt aatcccacct acttgggagg ctaaggctgg 31200

agaatcgctt gaacccaggg ggcagaggtt gcagtgagcc gagatcgcac cattgcactc 31260

caggctgggc aagaagagcg aaactccgtc tcaaaaaaaa aaaaaaagat gctggttcct 31320

aaaatgtggc ccttttcctc ctcacctgct gccagaccat cagccgcgcc ttcatgaacg 31380

ggagctcggt ggagcacgtg gtggagtttg gccttgacta ccccgagggc atggccgttg 31440

actggatggg caagaacctc tactgggccg acactgggac caacagaatc gaagtggcgc 31500

ggctggacgg gcagttccgg caagtcctcg tgtggaggga cttggacaac ccgaggtcgc 31560

tggccctgga tcccaccaag gggtaagtgt ttgcctgtcc cgtgcgtcct tgtgttcacc 31620

tcgtatgaga cagtgcgggg gtgccaactg ggcaaggtgg caggctgtcc gtgtggccct 31680

cagtgattag agctgtactg atgtcattag ccttgatggt ggccaggact ggtagggccc 31740

tcagaggtca tggagttcct tcgtggagcg ggtgctgagg ctgtatcagg cacagtgctg 31800

gctgctttca cctgggccgt ctcaccgaag tgtccatgga gcctgcgtag ggtgggtatc 31860

tgtgtcgatt ttacagatgc agaaacaggc tcagagaaac cgagtgactt ccctaaggtc 31920

acatacccag ttagagcaga gctgggccag gaagtgctgt ctcaggctcc tgaccaggtc 31980

tccttgcttt gcactcttgc caaaaccatg atccagaact gactttgagg tccccggacc 32040

tcaggctcct ccgaaatggc ctcttggagg ctgctgagcc acagcttagg acccacctcg 32100

agaggcaaat gtgctttgag ctgccaggcg tcctgggggc cctgccttgg gcacggggtt 32160

cagacaggcc ccagatgtgt ggggcgtctt tctggacttg agttttcttt tctgtgtggt 32220

ggacacagtg ctcacccctt aaagcacctg tgatgtgtgc agcagcccaa tccctgcctg 32280

tcgcctgttc tgctagggaa ggaaggaata cttcaggatg gcaggacaac agaaagaggt 32340

ccaggtttta gagcaagggc aggtcaaact tagaaaattc tggaatgagg atgtgcattt 32400

cctcttctgg atctgctaaa agaagaggga aggaggggct gctgggggag gagcccagag 32460

ccgagtttac atccggatcc cgcaaggcct cccctgccct gaggtcttgt tttgtgatgt 32520

gcttgtgtcc atcctggttt ctgccgtgtc cccaacatcc ggccaagctt aggtggatgt 32580

tccagcacac actcaccctg tctgtgcacc tgtttttgtg tccgtaagtg ggtatttact 32640

caccttacga gtgagccact gtgggaattc agggaggtgg cgcagtgacc acccctggag 32700

ggatatgtgt gtggcagggg tcgagggtct cgcccttccc tgcttcctgc gcgtggcttt 32760

ctccaggacg gggagggctg agctgaagag gtggggacag ttgcgtcccc ccgccaccca 32820

ctgtcctgcg gtgagagcag actcactgag cctgcccttc tcccttgtgc cttccagcta 32880

catctactgg accgagtggg gcggcaagcc gaggatcgtg cgggccttca tggacgggac 32940

caactgcatg acgctggtgg acaaggtggg ccgggccaac gacctcacca ttgactacgc 33000

tgaccagcgc ctctactgga ccgacctgga caccaacatg atcgagtcgt ccaacatgct 33060

gggtgagggc cgggctgggg ccttctggtc atggagggcg gggcagccgg gcgttggcca 33120

cctcccagcc tcgccgcacg taccctgtgg cctgcaagtt ccccaacctg gcaggagctg 33180

tggccacacc cacgactgcc cagcagcctc accctctgct gtgggagttg tccccgtcca 33240

cccctgggtg cctttgctgc agttatgtcg ggagaggctc tggtgacagc tgtttcctgt 33300

gcacctgctg ggcactaggt cccagctaat ccctgtgcca ggactctaat ttcaccctaa 33360

cacacatggt ggttttcatt gctggggaag ctgaggcctg agcacatgac ttgccttagg 33420

tcacatagct ggtgagttca ggatccccca gagataccag ggccagcact cgatccccac 33480

ccagccctga accccaccat gtgctgggat tgtgctggga gtgtccacac gcctgggacc 33540

ccagggctgg tgctctcatc tccttttttcc agatcatgag aatgaggctc agggaagttt 33600

gaaaaaaacc tatcccaagt cacacagcaa caggagcagg atttgaaccc agaaaagggg 33660

accgcacact ctgttctgct agagtagtta gctgtcctgg gtgatatggc aggtgacagg 33720

ggcaactgtg cttaacaaag gaacccccat ccccctgcc aagttgggag actagaaggt 33780

caggggcaga agctctgaag ggccaggtgc agtggctgac acctctaatc ccagcacttt 33840

gtgaggccaa ggcgggcaga tgatttgagc ccaggagttc aagatcagcc tgggtaatgt 33900

agtgagacgc catctctaca aaaaaatttt ttaaaaatta gctgggcatg gtggttcatg 33960

cctgtagtcc aagctacttg ggaggctcag gtgggaggat tgcttgagcc caggaggttg 34020

aggttgtggt gagctgtgat catgccactg cactccagcc tgggcaatag agtgagaccg 34080

tctccaaaaa aaaaaaaaga agaagaaaaa gaagctctga ggctccaagt ccccaggcac 34140

cccttggctt gagggcagac aagggaggag agggtcacct gggcagccct gacttttgtc 34200

ccctggcaaa gggaccttca gtgaccttgg ccctaggaga gcctctgagc acgtcagcca 34260

tgtcgaaccg ctcaggaagg gcagcaagaa tttggcttct gacctctgcc tctcctactc 34320

gccatctgca ctgggtgtgg ttgtgcccat tttacagatg aggaggctgg ggcatcgacc 34380

agctgaatgc cttgtcccag gtactgcgta ggcagagctg gcagttgaac cccgtgtcct 34440

ggttgtcgct gggggtgggc tgcaccctga cttgtgaggc cagtagcaag gtttgcacgt 34500

gacttcgtga ccgtcaccca gctctgcagc acatcccgtg acccagctca tccaggccgc 34560

atgcaaacct gttgccaggc gagaaaccag tcaccgcaca gctgtggttg cctgaaatga 34620

ttaagctcat taatcacccc ggagtgagga cagactcaga tgaaaaccag caaaagccct 34680

ggaaactcat gtgaccctgc caatgagggc ggccatgtgc attgcagcct ggccgtcact 34740

cctcggtacg tgttttggac ttaaacgctc cggatgttta ctgagtgctt gattaataac 34800

atggaaggcc tggtctcatt gctgtgggag tgaaggatgc acagccaggc ctgacatgat 34860

gagaacaaga acctggagtc tcgctgcctg ggtggtaatc ctggccctgc cacttagcaa 34920

ctgtgtgact gtagccaggt cacttaattt tgctagatcc tgcctgcgct tcagtggatc 34980

ttgctggttt tccaaggtgg ccaaacactt taaggcattc atgtggtcgc taggctgcag 35040

ggttgaaccc tggctcaccc cgcagggcgc cgtgtgctct gtggcctggc tgtgcctttg 35100

ctgacaccgt gcccgtgtgt gttcatgcag gtcaggagcg ggtcgtgatt gccgacgatc 35160

tcccgcaccc gttcggtctg acgcagtaca gcgattatat ctactggaca gactggaatc 35220

tgcacagcat tgagcgggcc gacaagacta gcggccggaa ccgcaccctc atccagggcc 35280

acctggactt cgtgatggac atcctggtgt tccactcctc ccgccaggat ggcctcaatg 35340

actgtatgca caacaacggg cagtgtgggc agctgtgcct tgccatcccc ggcggccacc 35400

gctgcggctg cgcctcacac tacaccctgg accccagcag ccgcaactgc agccgtaagt 35460

gcctcatggt cccccgcacc tcactccctc gttagatcag gctggttctg ggagctgacg 35520

ctgaaaggag cttctcatct ggggttcctg ggtgtacata gatggttggg taggttgtgc 35580

actgcacaag ctgcatgatg ctacctgggg gtccaggtcc aggctggatg gacttgttgc 35640

ttcatcagga catagataaa tggccaaaac tcctcagctg gaaggtcctg ggcaggatct 35700

ttgggtgtga aaaccagtca caggggaagg gtgcttgctc atactgccag cacagtgctg 35760

agtgctttcc atagcgctcg tttactcctc aagcctggag ggtggggagt agcatggtcc 35820

catttcacgt acaaggaacc cgatgcacag agaggtgtgg caacccatcc aaggccatac 35880

aactggggtg ggttgagccg gggttgactg tggcaggctg gctcaagagt ccctgctcct 35940

gaacccttgc caggcagcct ggcatcagct cggggaattt ttgccctgac ccttggaagc 36000

aagtgggcct ctttgttctc atgtcagtga tgagaagagt gactttccta tggcccctct 36060

ggagtacagg tgtttcctgt tggcgggctc ttcccccatg acatcagcag cgagctggtt 36120

atgattccct acgcagaact tgatagttta taaagctctt tgtcatccag gccccgttgg 36180

agtctcacgc agacctggtc gcaggcgggg ctggtcttgc ctgtcccagc tgcatggatg 36240

gggaacttga ggcttgcaaa ggttaagggg ctgttcgagg cccacgctgg caggagatgg 36300

gcctgggcca gagtctggga cttcccatgc ctgggctgtc tttggtcctg ttgctcacca 36360

tccctccctg gggccatgac cttagagagc caaatggagg tgcaggtaac ccacggcaag 36420

gaggggttgc catgactcag agtccccgtc ctgtggccgg cagtacctgg tgcaacgact 36480

tggatttcag accagccact gtagcccgct gacggtgcgc tcgaagtgcc acagcttctg 36540

aagccaggca ggactcaggc caggagactc tgttagctgt tgagagggag aggccaacgg 36600

atgttctggt tctgctagag agctggttct tcggatcctg gtaccagtgc actgagagga 36660

ggcccagctt gattctgggg ctgccttgtg gtggcatgtg ctgctcactg acaccctcga 36720

ggagtgtctt ctctcgggct tgttgactgt gcccggtttt ccgcagttca ctggtgcaca 36780

cataggcaca tagcaaaccg cacacacagt cgtgggtatg agtttcacta cattccacca 36840

ccagtgttca ctaccattac ctgccttccg tcttaagtgt tcatcattta aaaataaatt 36900

tattgggctg gacgcggtgg ctcatgactg ttatcccagc actttgggag gctgaggcgg 36960

gcagatcacc tgaggtcagg agttcaagac cagcctggcc aatatggtga aactccatct 37020

ctactaaaaa tacaaaatta gctgggcatg gtggggcatg cctataatcc cagctactca 37080

ggaggctgag gcaggagaat ggcgtgaacc cgagaggcag agcttacagt gagcccagat 37140

agcaccactg cagtccagcg tgggcaacag tgcgagactc catctcaaaa aaaaaataaa 37200

taaataaaag aaaaataaat ttatgatcta tttcaaaaat aacacatgta ctttgaaaca 37260

gcagagacac atatgacacg gagaatgaaa ttccccatag cgcaccccca agagacagcc 37320

ctggtccccc cgtctttccc gtggacctcc agcggggcag atgctgagcc gcctgttgtc 37380

gagtggcatg ctatcccgtc ctccagctcc tctgtggctt acagacaccc acctgcagcc 37440

ctgtctttgc ctcctctagc gcccaccacc ttcttgctgt tcagccagaa atctgccatc 37500

agtcggatga tcccggacga ccagcacagc ccggatctca tcctgcccct gcatggactg 37560

aggaacgtca aagccatcga ctatgaccca ctggacaagt tcatctactg ggtggatggg 37620

cgccagaaca tcaagcgagc caaggacgac gggacccagg caggtgcccc gtgggaaggg 37680

tgcggggtgt gcttcccaag gcgctcctct tgctggtttc caggctgctg cccctgtcct 37740

tagcagaggg aggaaacaga ggatggctct gggtgaatga tgacttgggc ttcgattatg 37800

tagtcacagg gtatgaccct gagatgcgtg gaaccccgag actgtgatta tatgtagaaa 37860

ctgggtttcc ccgttgttta agtagtcatg gtggggtcag accccacagg acttttgtct 37920

tttcaagaaa gaaaatggtc gtgtgtcatg caggggtagt tggtactggt taatccaggt 37980

ttatccttta ttttgtggga actgtacagt catttctgct acaatgctgt atatgctctt 38040

ctgaaagaca cctatgcaaa atcgcacagt aaaaatgaca caactcatag ggaaagcggg 38100

gccagggcac agccctcaaa atctccatca atgacatgta agaaaagaga ggaacctggg 38160

aaatagcaaa gtgccttttg cacattaaat ggttagctat atcccacaat actgtgcatt 38220

cgtaaacgtt aatgctgcaa taaatacggc acttcacctt gggaagatct ggagttggct 38280

tatgagtgtg gaagggtgta gcgcatgagt ttttgtgaaa cactggaagg aggattgtgg 38340

gaaatcaaat ggaaagttct caccccaggc gtggagaaga gtgggtcatg gccccagcag 38400

tgagcccagg gaggtcagag acggaggtgt gtgtgtgggt gtgaccctgc gcagttccct 38460

gccggctgta gttttttgca ttcgcttaat gtttctcgtg gaggaaattg tgcatgagca 38520

aatgtgaaac cgtgctgtgc tcaaattgtc ctaatacatc attgcattgg aacagattgg 38580

ctttnttttt ttttttttt ttttttttt tttgaaatgg agtctcactc tgtcaccagc 38640

ctggagtgca gtggcatgat cttggctcac tgcaaccttt gcctcctatg ttcaagtgat 38700

tttcctgcct cagcctcctg agtaactggg attacagggc atgagccacc gcggccggcc 38760

agatttgcat ttttgaaaca actgctaggc tgggcgcggt ggctcacacc tgtaatccca 38820

gcactgtggg aggccgaggc aggtggatca cctgaggtca ggggttcgag accagcctgg 38880

ccaacatggt gaaaccccgt ctctactgaa tatacaaaaa tcagctgggt gtggtggcgg 38940

gtgcctgtaa tcccagctac tcaggaggct gaggcaggag aattgcttga acccaggagg 39000

cagaggttgc ggtgagccga gatcacacca ttgcactcca gcctgggcaa caagagcaaa 39060

actccatctc aaaaaataaa aaatagaaaa acaagtgctg tagcggaagt gagcactttg 39120

cggagtcagg cttgtgtggc ctgttccaca aatgatgtgc tcacggtggc ctcaggccca 39180

cctggagtct gcagcatggg gcacaacagg ttcattagtg tagaattcca ggacaggcct 39240

ggctcctaag cagccttctt ttacaaaaac tgcagagccc gcctgtatcg tagcactttg 39300

ggaggccgaa gtgggtggat cacgaggtca ggagttcaag accagcctgg ccaacatggt 39360

gaaaccccat ctctactaaa tatacgaaaa ttagctgggt gtggtggcac gcgcctgtag 39420

tcccagctac tcgggaggct gaggcagaat tgcttgaacc tgggaggtgg aggttgcagg 39480

gatctgagac catgtcattg cactccagcc tgggcaacag agcgagacgc catctcaaaa 39540

aaaaaaaacc tacagagcca cacggcctct ttctccaccg agtgttggtg tgggagcttg 39600

tgttattgtg gtgaaatctt ggtactttct tgaggcagag agaggctgag cgcctggaga 39660

gactttcaca tgggtcgcca tgtccgccgt cggtttcgct gttgtgctcc ccatctgaag 39720

gctggtgccg tccagacagg ctggacgccc ctttccacca gatccttcct cccgcagcag 39780

tttctagtta cgttgtactg tgaggtctgt gtccttggtt gatggcaaaa gtcagccgaa 39840

ttgaaattca gagccatgcc tggctccctg gagcttctct cctgggcagc tgtgatcatt 39900

gcctctgctg tggtgtgggt ggtggaaatg gattcctttc atcttgcttg ctacaggtga 39960

ctgtcacgtg gagtcctttg gagagaggga cgtgttaatt gatggatgtg gctcccatgc 40020

tgagaaagct cctgggcgta cattgcctta gagtttcatt ggagctgcgt tcttttatgg 40080

tgtctgctag gcagaagtga tgaagacttg gaagaaaacc cagaaggttt tccacttaat 40140

ttggaaaatg tgcttttccc ctcctgtgtc ttttgctaag gtccagcctc ctgcagcctc 40200

cccgctctgt ggactctggc tttgattctt tattaggagt ccccctgctc ccccaaaaga 40260

tggtgtctaa attatcatcc aattggccga ggttttgttt tctattaatt gtttttattt 40320

tttattgtgg taaatttata taacataaaa tttgccattt taattgtttt gttattgttg 40380

tttttgagac agggtctcac cccagtgccc aggctggagt gcagtggtgc gatcatggct 40440

cactgcagcc tcagcctcca gggctccagt gatcctctca cctcagcctc tctagtagcc 40500

gggactacag gcatacacta ccacatctgg ctgatttttt gtatttttt tttattgtag 40560

agacccgcta tgttgcccag gctggtctca actcctggac tcaagccatc ctcccacctc 40620

accctcccaa agtgctggga ttacaggcat gagccacaac acccagccat tttaattttt 40680

ttttttttt ttgagatgga gtctcactct atcgcccagg ctggagtgca gtggcgtggt 40740

atcaactcac tgcaacctct gcctcccagg ttcaagcgac tctcctgcct cagcctcctc 40800

ccgagtagct gggattacag gtgcccatca ctatgcctgg ctaatttttg tatttttag 40860

cagagacggg gtttcaccat gttggccagg ctggtcttga actcctaacc tggtgatccg 40920

cccgcctcgg cctcccaaaa tgctgagatt acaggtgtga gccaccgtgc ccggcctttt 40980

tttgtttttg agacagggtc ttgccctgtc acccagactg gagtgcaatg gtgggctctt 41040

ggctcactgc agcctccgcc tcccaggctc aagttgtgca cctccacacc tggctaactg 41100

tattttatgt agagacagat ttcaccatgt tgcccaggct gggcttgaaa tggactcaag 41160

cagtccaccc acctcagcct cccaaagtgc tgagattaca ggcgcgagcc accgcaccca 41220

gcccatttta cctattctgc agttgacagt tcagtggcat tcagtcagtt cacgaggtaa 41280

ccatcactgc cattcatctc cagactactt caccttctcg gcagatgtcc gaaactgtcc 41340

gcattgaaca cactcctcat ctccctctga cagccaccat tctactttgt atctctctct 41400

gccttctcta ggtacctcat gtaagtggaa ttataccaat atttgccctt gtgtgactgg 41460

cttctttcat gtgacatggt gtcctcaagg ttcatctgtg ttatagcctg tgtcagaatt 41520

tccttcctta aagcctgaat aataacccgt tgtaaaggct gggcgcggtg gctcacaccc 41580

tctaatccca gcattttggg agtccgaggt gggcagatca cttgaggtca ggagtttgag 41640

accagcctgg ccaacatagt gaaaccctgg ctctactaaa agtacaaaat tagctgggtg 41700

tggtggcgcg cacctgtaat cccagttact caggaggctg aggcaggaga atcgcttgta 41760

cccgggaggc agaggttgca atgaaccaag attgtgcctc tgcagtccag cctgggtaac 41820

agagtgagac ttcctgtctc aaaaaaaaaa aaaatcatcg gatggatgga cggaccactt 41880

cttgttattt atccatccac gggtgctagg tttcttccac ctttggttgt cgtgaataag 41940

gccactatga acatttcctt ccgtggtgaa ggttttgtac tagtgaggaa aaggcgtgtt 42000

tgtggtgttg cataggattc tggtaagaaa gtttgcacta accataagta tttgtactac 42060

attaaaatga aagctcaggg gccgggcgcg gtggctcacg cctgtaatcc cagcactttg 42120

ggaggccagg gcgggcggat catgaggtca ggagatcaag accatcctgg ccaacatggt 42180

gaaaccccgt ctctactaaa aataccaaaa aactagccag gtgtggtggc gggcacctgt 42240

agtcccagct acttgggagg ctgaggcagg agaatggcgt gaacccggga ggcggagctt 42300

gcggtgagcc gagatcgctt cactgcactc gagcctgggc aacagagcaa gactccgtct 42360

cacgcaaaac tctgtctcac gcaagactcc gtctcaaaaa aaaaaagagt tcagggttta 42420

tgaaactggc cagccgcgta aagtttgctg tgttgttttt gtgcccggga ggagtgtggc 42480

cagggtgtca cgtcacacag tacacgtttc tcagatggtg gttctccaga ctgctgtccc 42540

aaagtctgtt tttgcatctg gttcccacag acccaccctc cacggtgagc ctgattttgg 42600

ccagggtagc tggaatcttg cttgtctttc agcccggcag ctgtaccagt ccagggtcca 42660

cagctagtgg cttttaggaa ggaatttgtt cagttggctt tgacacatgg ccccctaggg 42720

tccacagctc tgtagtgatg tggatgttgt tatctacaaa gacacatgat ccttcgtgtc 42780

cagatgaaag tgatgatgtc tttgcagctg cccagcaagg ctgtgtgtgt gtgtgtgtgt 42840

gtgtgtgtgt gtgtgtgtgg tgtgtgtgtg gtgtgtgtgt gtgtatgggg gagggaggca 42900

ccctttccat ctgggggtgt gtgtgtgtgg ggtgtgtgtg tgtgtgtgcg cgtgtgtgtg 42960

gtgtgtggtg tgtgtgtgtg tatgggggag gcaccctttc catctgggtc caagagactg 43020

ggcctgggga agacgcttct ttttatctac ttagagactt tgttttattt gtatttttt 43080

gagacagggt ctcactctgt cacccaggct ggggtatggt gatatgagca tagctcactg 43140

cagcctcggc ctcccaggct gaagcgatcc tcccacctca gccttctgaa tagctgggac 43200

tgtaggcgtg cgtcaccata ctgagctatt gttttttttg tttggttggt ttaatttttt 43260

ttgatacaga tggagtcttg ctatgttgcc cagactagtc tcaaactcct gaactcaagt 43320

gattctccca cctcagtttc ccgacattct gggatcacag gtgtgagcca ctgctgtctc 43380

cctgttttat taactgctga aagacctaga taaagaaagt ctgaaaagac ttactatcag 43440

agcaccatcc taagatgatt ccctctgact caatggagag ggaggggagc ttttccttca 43500

ggcctgggtg gcaggagccc aggtgctcca ggccccattt gccccaggcc aaatcactcg 43560

ggaacttgga tgcagctgtc tttcagggta acccaaagga accagatccc cgcaggcagt 43620

aggcttctgg gctgtcctct cctcctacgt cagctcagta agagcccttc gaagggatgc 43680

tgtgtcggag gccccaaaag cccaggctca tccctgagat gcacagggtg ggctgggctt 43740

aggcagcgct cgagcatctc ctggacggtg accccagaga gtgtggagac ggagagtcct 43800

tgagagtcac tgagagacgt ggctgccctg ccttcccaag aggggctctg agtcattccc 43860

cacactcacc tgcccctacc caccctcacc tggcccccag cctcacctac ccccacatct 43920

gtaccgatcc ctttacccgc accttcccta cccaccctca cctcccctgt accttcacct 43980

cccccactca cccgcccctg caccctcacc tgtcccccac cttcacctaa cccccaccct 44040

cacctgccct cccctcacct ggcctccttc cgttggggaa ggggttgtaa ggggcggccc 44100

ccaaactgtc tgtcctggtg ccctgcagag aaaacagtac gtgagggccg cagtccaaaa 44160

gcttgagtcc tggaaggtgg aggagacagg gatgtgttgg gaagggcccc atggtcttgg 44220

atcccttctc gactgtcaat ggggccttca tgggagcgcc agtctagtga tgcacagctg 44280

ggtgcccggc gggtggctga ggaggcctaa agtccgaggc ggcaagagct cttccagagg 44340

ctgttgtcct aatcgctctg gcatactcag gcgggcacgt agttaggagc tgattggaga 44400

ggagagaccc ccacaccaat actgggattt gactttcagg ctaaacttga gaagtgtggc 44460

ctctgctgtc ctgccagagc tctccagcca gtgcccaggg ctctccagcc agtgcccggg 44520

ggtctccacc agtgcccggg ggtctccgcc agtgccaggg gtctccgcca gtgcccaggg 44580

gtctccgcca gtgctcagga gtcttggttt ctttgtctta cagccctttg ttttgacctc 44640

tctgagccaa ggccaaaacc cagacaggca gccccacgac ctcagcatcg acatctacag 44700

ccggacactg ttctggacgt gcgaggccac caataccatc aacgtccaca ggctgagcgg 44760

ggaagccatg ggggtggtgc tgcgtgggga ccgcgacaag cccagggcca tcgtcgtcaa 44820

cgcggagcga gggtaggagg ccaacgggtg ggtgggggtg ctgcccgtcc aggcgtgccc 44880

gccgtgtctt ctgccgaatg ccagcctctc acaggctggg gagactttcc accctgggga 44940

tccaatgggt ggctttccag ggtcccaaaa gcaaacacag gctctttcac agcccctcca 45000

ggaaagcaga aagccccaag ggctggaagg gaaggggggag ctctgctgag aggttacaag 45060

gcagcgctgg ccgacgggag ttgcagttga taggttttgt atcatccttg ttaaacttga 45120

accctgtgca gaaatcccct ccacggcatg ggggctgcct gttgactcgc tcctgttcca 45180

ccacagggag ctcctgggct tcttcctccc agaggccccc gacgctccca cctgttggtc 45240

gtcagagctt ctggttggtg ggaaggcacc caggaccttg aggtctccag agagaaaagc 45300

cagggaaaga gggagaccga aacccatgtg acatgaaact caggctccaa actgagcacg 45360

ggaacgtttg gggacaggag cgcgatggcc ttcctcagat agctgggggg ctggcatgaa 45420

gacgggagct acagccagca caggtcctgg gccgggagcc cagagattga gccctgactc 45480

tgtcacttac tggccacgtg accttgggcg ggtggcatag cctcttggag actcagtttc 45540

ctcattggta ggagtgacgg ccacagtggt gcggcctctg cagcacacgg ggggctcggt 45600

gggcggaagc cccgggtcta taaggcggct gtgcaggagc cagccgagct ggtctcccaa 45660

cagccagggc tccggggtcc ttagcagctg tgggggggcct gcacctgttt cccatggctg 45720

ctgtcagaaa ttaccagaag ccaggtggct gagagtaatg gacacttgtt ctctcacagt 45780

tcctgagggc tgaagcccga gatcgaggtg tgggcagggc cctgcgccct ctgaaggctc 45840

tgagggaacc tttgggcttc tggtggctcc aggcaccct tgacttgtgg tcctgtcact 45900

ccagtctctc tgtctggctg cacatggcgt ggcctcttct gtaccattga aggacacttc 45960

agttggattt agggcctacc ctcacccatt gtggtcgtat cttgatcctt catgacattt 46020

gtaaagaccc tgcttccaaa taagctcaca ttctgaggtt ctggggtgag cgggaatttg 46080

gagagcattg ttcaactagt atagaatgtg acctgtcagc ctcgggcagc cctgagaggc 46140

aggggctttc cacagcccag ctgggtgccc tgggctccgt gctgtccgag gagacgccat 46200

ccccacaccc gtccttcacc cgccaccctc ccgcaggtac ctgtacttca ccaacatgca 46260

ggaccgggca gccaagatcg aacgcgcagc cctggacggc accgagcgcg aggtcctctt 46320

caccaccggc ctcatccgcc ctgtggccct ggtggtggac aacacactgg gcaagctgtt 46380

ctgggtggac gcggacctga agcgcattga gagctgtgac ctgtcaggta cgcgccccgg 46440

ggcctgccct aaccgcagac acccggcctt cattgtcagt aatggcagca gctgccacat 46500

tgtccgagac ctgccgtgag cccagtgccg cgccaggggc tttgtgtgta gcgtgttttg 46560

tcctcacact gacagctgta ggctggggtt ctgagtgagc cccacagggc agaggcagaa 46620

aatgagtctc agagagggtg agcgagctgc ttggggcccc acagcaggag atggagcagg 46680

actgcagcct agcctctgcc cccagcacct gcgcaagaag ctgctctgct ctggactgtg 46740

ttaggctgcg agggctggag agaaatgaga gttggtgctt agagaggggg cgcaggtccc 46800

catggctttt cctcttatga tgaggtagat gggtgaaggg aggggccatg cttgcagggg 46860

ccagtgaccg aggcccgccg ttggaactga tggccttcat cccgagccca gcccaggtgg 46920

gagcagggct ttccgagggc ttgtcttggg tcggcctgct tccagggact ctgctgcagc 46980

tcccaccccc gtccaaagca tggaatcccc caggctccct ggcagtcctg tcaacctctg 47040

tcctcccaag ctgagtgtgg ggcaagttct ggaggtcagc actgctcagg ggggcccacg 47100

ggctgcttgc aggggccaac cgcctgaccc tggaggacgc caacatcgtg cagcctctgg 47160

gcctgaccat ccttggcaag catctctact ggatcgaccg ccagcagcag atgatcgagc 47220

gtgtggagaa gaccaccggg gacaagcgga ctcgcatcca gggccgtgtc gcccacctca 47280

ctggcatcca tgcagtggag gaagtcagcc tggaggagtt ctgtacgtgg gggctggcag 47340

tggggtgggc agggtggcct ctaaacccga cccctggagg aggctggagg ccagtgcaag 47400

atcctgtgtg gcctcagcca ggcggtggtc tctgccagat gccaactgtt gcccgctggg 47460

gttcagcgac atgtccgaat gtcccgaggc ctctgaggtt gttttctttt gccgcagaac 47520

aaatcaccac gaacagcgtt ttaagacaac accaactctt ttttttttt ttttttttga 47580

gtcaggatct tgctctgttg cccaggctgg ggtgccctgg tgcaaacaca gttcactgca 47640

gcctcgacct ctgggcttaa ttaagtgaac accttgcctc agcctcccag gtagctggga 47700

ctacaggtgg gcaccaccac acctggctaa ttttttttg tagagacggg gtttccccat 47760

gttgcccagg ctggtctgca actcctgggc acaagctatc tgcctgctgt ggcctcccaa 47820

agtgctagga ttataggtgt gagccactgg cctgacaaca cccacggatt gtctctcagt 47880

tctgtaaggc aaagtccagg cacagcgtgg ctcacctggg ttctctgctc agggtctcac 47940

ggggccagaa tcaaggtgtc aggaacgctg ggccctcagc ggaggctctg tggagaaatt 48000

agcttccttg ctcactcagc aggtagcagt tgtgggatcg aggttctgtt ttctctctgg 48060

ttattggtcg gggaccactc tcagctccta gaggccaccc caggtccttg ccccgtggcc 48120

ctctctgcct cagcagtggg ggctccctgc gtcagtccct cccgcacctt gagtctctct 48180

gatttgcttc taaagggccc tgtgattcgg ctcagccacc tttagattag gttagcctcc 48240

cctttgatag actccaagtc ggctgattaa taaccttact cacatctgca gaatcccttc 48300

tgccacataa ggtcatgacg ccgtgctggg gactggggtg ggaaattacg gggtcattta 48360

ggattctgcc tgccactgcc ttgctgtgtc ccagggcttg ggggaggggc ctccacagct 48420

gggaccacag tccttcctcc cctccatggt aaccatctga ggattacttg agaccagcct 48480

gggcaacatg gtgagaaccc atccctacaa aaaatacaaa caaaaaggga ccaggctggg 48540

cttggtggct catgcctata atcccagcac tttgggagac caaggtgggc tgatcacttg 48600

aggttgggag ttcgagacca gcctgcccaa catagtgaaa tcccgtctct actaaaaata 48660

caaaaattag ctgggtgtgg tggcaggcgc ctgtattccc agctactggg gaggctgagg 48720

tgggagaatt acttgaacct gggaggcgga agttgcagtg agccaaaatt acgccactgc 48780

actccagcct aggcaataga gtgagactcc gtctcaaaaa aaaaaaaggg ccaggggtgg 48840

tagtgacaaa gagaccctat cccaaaaaaa ccgaacactg aatccttgag actgagtaag 48900

gacactgtga aatttttctg ggtggggcag ggaacagagc gtcttctgtc atttcttcca 48960

cctgggtgtg gtcagctctc cctccaagct gcctcctctt cttctcattg tccgggtgtt 49020

ggacacattt ggttaactgg atagaataac gcgagttccc agggacttgg tccatttgct 49080

attttatttt attttatttt attttatttt atttatttat ttatttattt atttatttat 49140

tgagatggag tttcgttttt gtcgcccagg ctggagtgca gtggcgcgat ctcggttcac 49200

tgcaacctct gcctcccagg ttcaagtgat tctcctacct cagccttcca agtaactggg 49260

attacaggca cccaccacca taccaggcta atttttttgt atttttagta gagacgggtt 49320

ttcgccattt tgcccaggct ggtcttcaac tcctagcctc aggtgatcca cgcacctcgg 49380

cctcccaaag tgctgggatt acaggcatga gccaccacgc ctggcaccat ttgctatttt 49440

aattcccatg tgtattagtg tcccacggct gctgtaacaa atgaccacaa actggatggc 49500

ttaaagcaac agaaatggat tcccccaatg tgctggagac cagaagcctg cgaccaaact 49560

gttgggaggg ctgtgcttcc tctgggggct ccagggagga tctatttgtt ggcccttcca 49620

gtgctgtggg tgccagcgtt ccacacttgt ggatgcgccg cctcaacctc tgcccatctt 49680

catgtgtcca tctcctttgt gtctgcgtct ttacctcttc ttcttgtctg tgttgcctct 49740

tataaggacg tttgtcattg ggtttagggc ccacccaaat catccgagat gacctcgtct 49800

tgagatcctt aacctgcaaa gacccttttt ccaaaaaaag gttatgctca cagattctag 49860

gccttaagac atgggtgtat ctttctgggg ggcactatcc aaccccttat acaatgaaag 49920

acgggaagag ggccaggtgt ggtagttcac gcctgtaatc tcagcacttt aggaagctga 49980

agcgggagga tcacttgagc ccaggagttt acaagtagct aggcaacatg atgagacccc 50040

atttctacaa aaagtaaaaa aaaaaaaaaa aaaaaaaaag ccaggtgtgg tggctcacac 50100

ctgtaatccc agcactttgg gaggctgagg caggcagatc acgaggtcag gagattgaga 50160

ccatcctggc taacacggtg aaaccccgtc tctactaaaa atacaaaaaa ttatggccgg 50220

gcgcagtggc tcccgcctgt aatcccagca ctttgggagg ccgaggtggg tgaattacaa 50280

ggtcaagaga tcgagaccat cttggctaac acggtgaaac cccatcaaga tcacaaggtc 50340

aagagatgga gaccatcctg gctaacacgg tgaaaccccg tctctactaa aaatacaaaa 50400

aattagccgg gcatggtagc gggcgcctgt agtcccagct gctcgggagg ctgaggcagg 50460

agaatggcgt gaacccggga ggcggagctt gcggtgagcc gagatcgctc catgccattg 50520

cactccagcc tgggtgacag agtgagactc cgtctcaaaa aaaaaaaaaa aaagaaaatt 50580

agccaggcac agtggcaggt gcctattgtc ccagctactt gggaggctaa ggcaggagaa 50640

tggcatgaac ccgggaggtg gagtttgcag tgagccgaga tcatgccact gcgctccagc 50700

ctgggcgata gagcaagact ctgtctcaaa aaaaaaagcc aggcatggtg gtgcatgcct 50760

gtagtcccag ctactcaaga ggctgaggca ggagggttgt tcgacccacg gagatcaagg 50820

ctacagtgag ccatgatcgc accactgccc tccagcctgg gtgacagagt gtgaccctgt 50880

ctcaaagtaa gtaaatagga ggagagacaa gtgggcagtt cagactgatg gtatgggcac 50940

agtagagact ggtgcagaca ggctggcctg tgatgtcaag caacttctgt aactgtttcc 51000

ggcatccatt tgtgtgtcaa tttccgtgtc agtaggaaga ctctgtaggc tgccaagagg 51060

aataagtggg aggatcctcc cagagaggcc gggcctgcag gagggccagt tctcatgagt 51120

tcttatttgg cccctaccct ccaggctgtg gttctgaggt gggagacaga gcctgacctc 51180

tgtttgtctt gttttgtctt tgcagcagcc cacccatgtg cccgtgacaa tggtggctgc 51240

tcccacatct gtattgccaa gggtgatggg acaccacggt gctcatgccc agtccacctc 51300

gtgctcctgc agaacctgct gacctgtgga ggtaggtgtg acctaggtgc tcctttgggg 51360

tgatggacag gtacctgatt ctctgcctgc taggctgctg cctggcatcc ttttaaaatc 51420

acagtccctg tggcatccag tttccaaagc tgattgtgtc ttcctttgcc ctcctttctt 51480

ttctactatg tgcattcggt gctatgaatt ttcctctaag tactgcgttt cctgcatctc 51540

acaaattttg ttacattttc attttcaggt agtttgaata tttttacact tctcctgaga 51600

tgacatcttt ggctcatgtg ttatttagaa gtgttgctta gtttctaaag agttggggct 51660

tttccagctg tctctctgca actgatttct aatttaattc tactgtagtc tgagagctta 51720

ttttatatga tttctgttat tttaaatgtg ttgggtgtgg tgtttttgtt gttattgttt 51780

ttgtgtcttt ttgttttgtt ttgcttcgtt tgttttgttt ttgagacagt gtcttgctct 51840

gtcactcagg ctggagtgca atggcgcgat ctcagctcac cgcaacctct gcctcccggg 51900

ttcaagtgat cctcttgcct cagcctcctg agtagctggg attacaggtg cacgccacca 51960

tacccagcta atttttgtat ttttagtaga gacggggttt caccatgttg gtcaggctgg 52020

tctcgaactc ctgacctcgt gatccgccca cctcggcctc ccaaagtgct gggattatag 52080

gcgtgagcca ctgtgcctgg ccattaggtg tgttttatca cccagcatca tgcagtttat 52140

cttggtgaat gttctgtgta ctcttgaaaa gaatgtggat tctgctgttg ttgggtggag 52200

tgttccagaa acatcaatta gatccagttg gttaatagtg ctcatcaggt tgtctctatc 52260

cttccttcct gactgcctgc ttgagctgtc agttattgac aggggtgtgg agtctccaac 52320

tctaatggtg gatttgttta tttctcctag tagttctatc tttttctctc cttctaccct 52380

tgatcctctt ctccccctag ggcttcctgg tgttggtggt gggagagtgg ggtagtgaag 52440

aacctggact ttagggccaa agaggccagg gttcaaatcc tggctctgtc acttcccagt 52500

tgagtgaccc tggctggtgc ctgaatctct gtgagcctcc acttcctcct ctgtgaaatt 52560

gagagcactt acctggcagg ctgtcatggg catcaagtaa cagggcactc cacctggacc 52620

ctgacacgtg atgcacagga atgccagctg ctatgccatg ggtgtggcag tagtaataaa 52680

gtgaccatct gtatcctcac cacagtgaag cctgtccagg gctttctctc ctatgccccc 52740

atgcctccag gtggccttgg atcctgttgg ttctgtgctc tgctcagcga cctttctccc 52800

gtgggagttc ctgggggttc agcttcatcc tacagacagc agcacacact ggctgtgcac 52860

ccttttttct ttttttttct ttttttttga gatggagtct cgcttttttc gcgcaggctg 52920

aagtgcagtg gtgtgatctt ggctcactgc aacctctacc tcctgggttc aagtgatttt 52980

cctgcctcac cctcccaagt agctgggatt acaggctccc accaccacgc ccggctaatt 53040

tttgtatttt cagtagagat ggtgtttcac catgttggcc aggatggtct tgaactcctg 53100

acctcaggtg atccgcccac ctcagcctcc caaagtgcag ggattacagg cgtgagccac 53160

cacacccgga gtgccggttg tttttagcag tttgtcttgt tcctggagag actggctcct 53220

gcccaggagc tcggggagta gggccgcggg gtgctgcctc acacctcgag tttggccgta 53280

agcagagggg acattttgtg actgtccccc tcctgagctt cccagcagct tttctccaag 53340

ttacagccca aaagctcagg tggatttgca acccaacggt gtctgtgcac ctcccactga 53400

tgcccgaact gccctggcca agaaacgggg ccgtcagaac gctgcactaa ctgcagcctt 53460

gggcctccat gccagaggcc atgcccttcc atccaccacc ccctggcctg ggccctggcc 53520

ctcctggctc gggaactcca ggcccccttcc tcacggatcg agagacgtgt atttaccgca 53580

caggtgcttg tcattctctt gtggcctctt ctccagggag atcacagaag gacagggcct 53640

cactgaggtc tcggacatgg acccctttgat agtggcagga gccaggctgg gcaagaggcg 53700

gccacagtca cctcagcagt gccatcacca ccgccattca gcccttcccc gagccgggcg 53760

cgcccctggc tctggcccca gtgtcccagt tacagctcac aggagcttgt ggtgcccagc 53820

ggctgcttct gattgagagt cgaggtcgga ggctttggga ggctgagagg ctgctcggtt 53880

tcacaactgc tgagggagac ttgggctcca tctcaggtct gccccatgtc gccctcaacc 53940

tccagccacc ggtcctccgt gtcccccatg gccaggcacg gcttgcagac atctgtcgtt 54000

ggctcctctc agccgtcgtg ggctgaccct ggcacgtcct cctgtggctg agcccagtgg 54060

ggacagctgc ttccttttat taccctagaa ctctcgtctt tgatcaggcc ccctccccta 54120

tgccacacag tccctgtcac tcgggtgagc ccagtagtca tggggaaggc ctgcgggttc 54180

caaacatcca aaggcttgcg tgcagcatga cagcttgaaa ccgatgtttt ttaccttgat 54240

cagatttcag cttggcgggg gctttgctca gctttcagtg aggcctgggc cgatttccca 54300

gcatcccctc ctgaggccag cctctgtttc ctgtgatttt ctgcacaaag tgggagggag 54360

gagtcttagg aaatgggggg ccacctcgaa acctaggcct cctctggctt ctctgtgcca 54420

gtgcccccac gctttgtgtc tgtgtcccca gcccatggga ctgtgttatt ccctgagtgc 54480

tgccgcatgc ccagcccgca ctgaggacgt ggagccccga ggggcaggat ggcctccatg 54540

gtcacacgta ggaagtggcc tccaccctcc gatgatcctc tccccccctc cctttcagcg 54600

ccttccccgg gggtgtcatc agccctcctg cctgtgcttt gtcccgtctt ctgcaggcgc 54660

atgggacgtg ctgacaggtc ctctgccggg ttcctgcctt gctatgcgca cgctggtcac 54720

cacagaggcc tggcccttct tctgtagcag tcccacaccc gcaacaggtg tggctgctga 54780

ccacctgctt tctgcccctc tggtcctgag gagggcgcag tgggcactca ggcgtggctg 54840

agcagatgtg tgttgccggg aggaggaagg actgctccag tcagggctga atttcccacc 54900

cggagcattt ctgctgtatt tggtgtagcg cctgctgctt aaagctctga ttcccagttg 54960

gcacccttte ccttctgcat tgaaaaacat acggatgcat gtcttcttgc agtgaatgtg 55020

tattctccca gcctctcttc tgggttgggg ctggaggtgg agcggcacac aggagccgca 55080

gcgatggagg atgtgcgggt gcagcacccc gtacagcagg gatgccaaac ccgcgctgag 55140

tccctctcaa cttctgcttt gaagcccagt cacgccattg cctgggtttt gctgggcggg 55200

gctgcatgtg atgttctcct ctgtccctcc cccagagccg cccacctgct ccccggacca 55260

gtttgcatgt gccacagggg agatcgactg tatccccggg gcctggcgct gtgacggctt 55320

tcccgagtgc gatgaccaga gcgacgagga gggctgcccc gtgtgctccg ccgcccagtt 55380

cccctgcgcg cggggtcagt gtgtggacct gcgcctgcgc tgcgacggcg aggcagactg 55440

tcaggaccgc tcagacgagg tggactgtga cggtgaggcc ctccccgtca aggctctgcc 55500

aagaccctgg ccctgccctc cgggatacga gcttggggct gcctccggcc tcacaggagt 55560

aggggctctg aaaacctttg cttgcaggga gattgccaag tctgtctttt aggcccaaca 55620

aggaaaactc tgcagttcca cccatcctgt cccaccaggt agtgtggctt gaaggcagac 55680

tgtgagggtc tatctcacct tcctgcatta ggtcaggagt ttcacagaaa cctgaggcac 55740

attcaggggt gggctgcaga ggtccatggc tcacaccctg gaaaatccgc ccccaaaaga 55800

cagtgctgtc tccactgacc agtctgtggg atagtgctta agcctgagtg gtttctatca 55860

acatgtagaa tcaggaggta taaagagatt tgctcaggca tcctgggccc tctctgacca 55920

gcaggatctt cctttagatc ttgacagtga aacacatctc ttctgtgccc cctgtgagtt 55980

ttctttcatt cattcattca ttcattcatt cattcattca ttcgagacag agtcttgctc 56040

tgtcacccag gctggagtgc cctggtgtaa tctcggctca ctgcaacctc tgcctccagg 56100

gttcaatcga ttctcctgcc tcagcctccc gagtagctgg gatgacaggt gcgcaccacc 56160

atgcctggct aatttttgta tttttagtag agacagggtt tcaccatgtt ggccaggctg 56220

gtctcgaact cctgacctca ggtgatccgc ccgcctcagc ctcccaaagt gctgggatta 56280

caggcatgag ccaccgcgcc cggcctgagt tttcctttta tgaaggacct gcttggttgg 56340

ttgcctgcca catgttgtca gcaccatggg cccaggactg ctgaggagct gttgatgccc 56400

tcgctctccc agagccaccg gctctgttag ataattcaca tgcagtctgg ccactgtcct 56460

acgtcctcat tcacaaagag cagacatttc gtagaagatg agggcctggg agtaacctcc 56520

ctgcatgttt ttctataaag gcatagtggt taagtccttc cagctcattg accattggag 56580

aattttatgg aggctgtaga ctaggggctg gtaaactaag ggcccagggg ccaaatccag 56640

cctgccacct acttttgtaa ataaagtttt cttggtgcac agccatgccc attcattcat 56700

ttgcacaatg tctgtggctg ctttcatgcc aaaagcagga gaactgagtg gttatgctgg 56760

agacctacgg ccttcaaagc cccagacctc acgtctggcc cttgacagac agagcttccc 56820

cagccctgct gcgcatcctg gcccagcatg tgctgtgtgt gtgatttcag cttgcaggag 56880

ccgtggttag gaattgtccc tgtgttggtc cattttgcat tgctatgaag gagcacctga 56940

ggccgggtag attatgaagg aaagaggtct gtctggctca tggttctgta ggcagcacca 57000

gtatggcacc cgcatctgct cagcttctag tgaggtctca ggaagctttg actcatggtg 57060

gaagtcgaag cgggagcagg tgcatcacat ggtgagagag ggagcaacgg agagagagag 57120

agagagagag agagcgcctc tccctcttgc cctcaccttg agaggagatg ccaggctcct 57180

ttaagtaacc agctcccatg tgaactcaca gtgagagccc atttgctact gcggagaggg 57240

caccaggcat ctgctcccat gacccaaaca ctgcccacca ggccctacct ccaaccttgg 57300

ggtcatattt tattctgttc tatgctatgc tatgctatgc catgccatgc catgccatgc 57360

tattcctatt ctattatttg agacagaatc tcgctctgtt gcccaggctg gagtgcagtg 57420

gcatgatctt ggctcactgc aacctccacc tcccaggttc aagcgattct cctgcctcag 57480

cctcccgagt agctgggatt acaggcacac accaccacac ccgggtaatt tttgtatttt 57540

caatagagat ggggtttcac catgttggcc aggctggtct caaactcctg gcctcaagtg 57600

atccacttac ctcggcctcc caaagtgcca tgattacaga tgtgagtcac tgcgcccagt 57660

gagggtcaca tttccgttga gatttggagg ggcagacgtt ggagccatct gagccccctc 57720

gtcccgctct agcttctcct cccgtgtgcc ccgcggtgct ggtggcaggc ccttacgccg 57780

gttctggctg cacgctctgt tccagaagct ttcttccctg cttggttacc agaaaatcat 57840

cccatccatt acaaggacag ggtcccctta tctcccattc ccagggcagg acaccggggg 57900

cagggcaggt ggggaactga gcaagttctc tgggggcagg cgtggctatg gctccctctg 57960

ggtgggcgtc tggggagggg tggaggcagc cgtcagcgcc ctggcttgct cttcctccct 58020

ggccagagac tgtggccttg tgctgctccc gtgtgggctg cctgcacctc cagtgggttg 58080

tgctccctcc cctcccctcc cctcaagctc tgctgagcac cactgccttc cacagccccc 58140

actctcggga ggcgaggctc ctcgtggcca ttcctgtcct tggcacccac ccccccacca 58200

acctggtaga gccttgggcg gggtctgtta ctccttgcat ggcgtagacc tccccacagt 58260

aggcacctga cacatacctc ctgggggggca ggcaggaggt gcgttgaggt ctcagccctg 58320

gcagtccctc ccctgcgtgg cataggcctc gccacagggt catcgagggt gggtggagac 58380

tgtactagac cactccccgc tggtcctaga aagggtccca tctgtctgct ctctgtttgg 58440

agtccagacc ttggttgctg tgccctgcat ggtgggctgg ggggcaccct ccagcctctc 58500

tgagtgcatg gcctctcctt gcagccatct gcctgcccaa ccagttccgg tgtgcgagcg 58560

gccagtgtgt cctcatcaaa cagcagtgcg actccttccc cgactgtatc gacggctccg 58620

acgagctcat gtgtggtgag ccagcttctg gcacggggaa ggggcgtccg ggctgggttc 58680

ccccaggaac gtggagttta ggggaggaga cgtgcctttc cagcggggct gggggctgtg 58740

tgggagactc aggcggctgg gaggctcctt gcgggaggca gggaagcctt tcccagggca 58800

gcggccagga ggacagactg tgagctgtgg gctcggcggc tacagagtct gcctcagtgg 58860

gcggggctga tggtgtccag gtgcctgcag cacgcaccca cccacgggac cttgctgagc 58920

agcgtctgtc aggcagcaag attacccgag ggctgcagtg gtcctgttcc ctggcagctt 58980

actgtctggc tgaggaggag tgatgttcac atatgcacac atgtcatgtg cacacacatg 59040

tacatgacaa catcccacat gctcctcaaa tagcatgacc tgtacagtca cggatatagg 59100

gcctagggga taggaggcca agacagtcag ggaagacttt ccagaggcag tggctcctga 59160

aaggctgtct gattcaggca ggaagggagc tgagttcaga taggaagtag caatgagtca 59220

ttgtgtctgg ggacatggcc actccttcgc tgcagaggga cctgggctga gagctcctct 59280

cttatggctg cagtcgggag agaagtctgt tgggggggaga agggggcttc ctcaagggac 59340

tccctgtgcc ctttggcacc ttcgtgccag gtcaggcttg aggcctgaag gcagtggtgg 59400

gggccaccaa gggtcgcctc ctctgctggg caagttccca gtctgacggg cctgtgccgt 59460

gggccccagc tgtgggggcg ctgttgatgc gcagccaggc ctcgccgcca gagcccgcac 59520

gcttccattc cgctgacttc atcgacgccc tcaggatcgc tgggccggcc ctgtgggaga 59580

gtgaatgtgg cttttgccaa agttgagtct ggagcctgga aacttcccta tgggcagcct 59640

tgatagtgga gtggcccaag gagcccaccc agccgaccct gcccctcccg tggctggtgg 59700

gcggcaccag gggctgcctg gctttgctcg ttcaccaaca tcacccgggc tggccagggc 59760

gcgctcactt ctgccaccac cgagggccct gggcgaagga gtgaatacca ggctgccttg 59820

gcagggatgt gttgagggct gtggggagtc ggacagcggc gggggtcaga ggaggaggag 59880

ggtgcaccgt gcaggctgaa gggccacgtt accctgaggt tggccaggct ccccaggcct 59940

agcctcccag ctcccccact ttctccccac cctccaccag tggcaaagcc agcccttca 60000

gggcgcacgg tgtctgcccc caaggagggc ccattccgtt ggggttaatg ttggccacct 60060

ctttctgttt gtctctggca gaaatcacca agccgccctc agacgacagc ccggcccaca 60120

gcagtgccat cgggcccgtc attggcatca tcctctctct cttcgtcatg ggtggtgtct 60180

attttgtgtg ccagcgcgtg gtgtgccagc gctatgcggg ggccaacggg cccttcccgc 60240

acgagtatgt cagcgggacc ccgcacgtgc ccctcaattt catagccccg ggcggttccc 60300

agcatggccc cttcacaggt aaggagcctg agatatggaa tgatctggag gaggcaggag 60360

agtagtctgg gcagctttgg ggagtggagc agggatgtgc taccccaggc cctcttgcac 60420

atgtggcaga cattgctaat cgatcacagc attcagcctt tcccactgag cctgtgcttg 60480

gcatcagaat ccttcaacac agaggcctgc atggctgtag caacccaccc tttggcactg 60540

taggtgtgga gaaagctcct tggacttgac cttcatattc tagtaggaca tgtgctgtgt 60600

tgtccacaaa tcctcatgta ccctagaaat gaatgtgggg gcggctgggc tctctccaga 60660

gctgaaggaa tcactctgta ccatacagca gctttgtctt gagtgcagct gggatttgtg 60720

gctgagcagt tacaattcct acgtggccca ggcaccagga acgcaggctg tgtttgtaga 60780

tggctgggca gccgcaccgc agagctgcac catgctggtt tgtatcacat gggtgaccat 60840

ggtatgtcta agaaggtgga gtccctgtga ggtctgcagg tgcccccaca gctccaggcc 60900

accttgagga ttgcctctgc ctgcccagcc ctgagttccc tctcccctgt cctgtcccac 60960

tgtcacccca agccggcctc attgggagcc tgttggatgg cagggtatag atgtaacctg 61020

attctctctg gggagcgggg ttatctggct tctcaagagc tcctaggagc ccacagtggt 61080

ggcaccatca cagtcgcagc agcccccaga gaacgcggcc ctgtctgttc ctggcgtgct 61140

ctgtgctgcc ccgcctgggt tccctgcccc agtcgcaggc cccttggagg aggtaccatg 61200

tgtctcccgt ttcacagatg agccccgggg agctcactct agtagtggcc agagaggcct 61260

gcggctcagg gagcggggca catttccaac aggacacacc gccctggtct gagtctcgtg 61320

ggtagtggga gcagaggaga gcgccctatg tctgtggggc ggcttggctg agcctggaag 61380

ccacctgacc tccccgtcc cttccctgcc aggcatcgca tgcggaaagt ccatgatgag 61440

ctccgtgagc ctgatggggg gccggggcgg ggtgccccтc tacgaccgga accacgtcac 61500

aggggcctcg tccagcagct cgtccagcac gaaggccacg ctgtacccgc cggtgagggg 61560

cggggccggg gaggggcggg gcgggatggg gctgtgggcc cctcccaccg tcagtgctgg 61620

ccaccggagg cttcccgggt tcctgggggc tgtgccaccg cctctgaggc atgcttgctt 61680

tcttcccttt tcaaaccctt ctgcttcctt ctttaatgac attgttgatt gtggataatc 61740

tgaaaactac acaaaaatat aaagagccaa aatctcaccc aaatccacct cctagagtgg 61800

ctgttgggct ccgtcagcat ccaggcggcc gtctgtgttc cgcacggccc agcccatcga 61860

tagccgcctg caccaggcct gtctgccctc tgtgagcctc cccacagggt tccctccaca 61920

aacaccctgt tctcccaccc agggctggct gcttcctgga aaacagctgg atggttttgt 61980

gcatgacaga caaacacagg gtgattttcg tggctaaaat actccctgga gcttttggca 62040

gggtgagggg ctggctccag ctgagccacg ccttgagtga aatgactgtg aggagaataa 62100

actgccgctg ccctccagga tcactggggc tggctgggga gaacccccgt ttctgggagc 62160

acagtcccag gatgccaagg cgagcttggt gccgagatgt gaactcctga gtgtaaacag 62220

cgggggctga cttgacatgc tttgtatgct tttcatttgt tcctgcagct gtatgccccт 62280

aaggtgagtc cagcccccтt ctgcttcctc tggggcctcg ccagtgagcc ccaccttgct 62340

ggggctggtt cctcctgccc ttctgggtat ccctcacatc tggggtcttg tcttcttgtt 62400

ttatttttct ttttttttтg agacggagtt tcacttttgt tgcccaggct tcagtgcaat 62460

ggtgtgatct ctaggctcac cgcaacctct gcctcccagg ttcaagcagt tctcctgcct 62520

cagcctccct agtagctggg attacaggca tgtgccacca cgcccagcta attttgtatt 62580

tttagtagag atggggtttc tccatgttgg tcaggctgat cttgaactcc ctacctcagg 62640

tgatccgccc accttggcct cccaaagtgc tgggattaca ggcgtgagcc accgcacctg 62700

gccttttttct tttcttttct tttcttttttt ctgagacagg gtctcgctct gtcacccagg 62760

ctggagtgca atggtgtcat catggctaac tgcagcctct accttctagg ctcaagcaat 62820

cctcccatct cagcccctaa gtagctagga ctgcacgcat gcatccccat gcccagctaa 62880

tatttacatt ttttgtagag atgaagtttc actatattgc ccaggctggt ctccaactcc 62940

tggactcgag cgatcctcct gcctcggcct ccccaggtgc tgggattaca ggcgtgagcc 63000

accgtgcctg gcctggggta ttgtcttctt atggcacctg actgtggtgg gccctgggaa 63060

ggaagtagca gaagagggtt cttcttggtt tcctggacag taactgagtg ttctggaggc 63120

cccagggcct ggctttgttt agggacaaag ggaactggta accagaagcc gagagtttaa 63180

acacccactg cccttcttcc ctgctcctgc tgctgcaacc cagcttaacc agccaggagt 63240

gctaggaacc caagcagggc ccccgagcac acagcaggca gctcacgaat tctcttttcc 63300

tgttctccct tgggagctgg gaggatctta atcaggcaat aagagatggc actgagcagc 63360

cagctaattt tttaaatcac tttattgttt aaccatatga ctcacccact taaaaaaggg 63420

tacagttcag tgggttttag tgtattcaca gatgtgtgca accctcacca cagttaattt 63480

tagaacattt tcctgccccc aaaagaaact ctgcatgaag ccagctgttt ttaaattagc 63540

aaagttattt tgcatccttt aaatatatgt tcatggtaca aaattcaaaa gatacagaag 63600

agtctgcagt ccaaagagac tccgccccca tgacgccaag caggactccc tgggaggcat 63660

ggcctcctgc agtgtgtttc ttctatgtcc ccccaggggt catctgtaca tatgcaagca 63720

tacaagagcg tggactttgt tttccaagcc agaagataat tgtagattta tgtgcagttg 63780

tgagaaagag cacagaccca tttatcctct gcctggtttc ccccagtgct gcctgccatc 63840

ttgcatgact tccattccta tcataagcaa gacactgata acgattcttt caccttattc 63900

agattgacat aagtgttttt tgtttgttct tgagacaaac ttcctctgtc acccagtggg 63960

agtgcagtgg cacaatcaca gctcactgca gcctcaaact cctgggctca agcgattctc 64020

ctgcctcagt cccctcaagt agctcagatg gcaggtgtgc accatcatgc caggctaatt 64080

tttaaatttt ttgtggaggt gaggcctcac taaatttcct gggctagtct tgaactcctg 64140

agctaaagtg atcctcctgc ctcagcctcc caaagtggta ggattacagg catgagccac 64200

tgcgcctggg ctgacatatg tgttttcgta agcccgaaag atagcatctg aagagtcaac 64260

attgagcctt gccttttgct gctaatgatg tataaaagct gctgttctga gcatttcgga 64320

ggctcccagc tgccgtgtgc accctgccta gagctctacc gtaacccatc tccgggagga 64380

ggtgctattg ttttcctcat tttgcaacaa ggaggctgaa gaactgagca tgaaccactg 64440

gcctgggtcg ttcggttggt aggcagtggg gccaggccat ccaactcaca accaccttct 64500

actctgcttc ccccgcaccc tgaagtttgt tctgttttga ggacacagcc gtcacattct 64560

tggtggctga acagcactcc ttgtcaggtg tggctgggcc cccactggag ggcatcatgg 64620

tcctctctcc tgctgcggtt gaaccttggc tgtttcaacc actcctgcca agtggccctc 64680

tgaaagggac agtccatctt ttctcagcag agggccacac tggcaaaacg gtccctggca 64740

ccctttctct ccacctgtct aatatagagt aaaaatggta tcatgttaag atcttcattt 64800

atatttattt tatcatgaat gatgtaagca tcattttgtg tgtttaagaa cctttgggcc 64860

cagcgtgatg gcttgcagct gtaatctcag cactttagga ggctgagatg agcggatcac 64920

ttgaggccgg gagtttgaga ccagcctggc caacatggag aaaccccgtc tctagtaaaa 64980

atttaaaaat tagccgggta tggtgatccc agctacttgg gagtctgaag catgagaatt 65040

gcttgaacat gggaggcgga ggttgcagtg agccgagatc gcgccattgc actccagcct 65100

gggcgacaga gcgagactct gtctcacaaa aaaaaaaaaa aaagaaaaga aaagaaatta 65160

tcaatctcct cttttatggc atatatatat atatatatat atatatatat ttatttccct 65220

ttcttggtta tgttcataaa ggcctccct gctctgatca taaaaaacaa cttattttca 65280

cactctctct ctttttttt tgagacagag ttttgctcct gttgcccagg ctggagtgca 65340

gtggcgcaat ctcagctcac tgtaacctcc gcctcccggg ttggagtgat tctcctgcct 65400

taccttcccg agtagctggg attataggca tgcaccacca tgcctggcta attttgtact 65460

tttagtagag acgggggttt ctccatgttg gtcaggctgg tctcgaactc gcgacctcag 65520

gtgatccacc cacctcggcc tcccaaagtg ctgggattac agacgtgagc caccatgccc 65580

agcccacact ctctttctta acgtcctcct cctttcgttt tacgttcaca tctttaattc 65640

ttctgggatg taattagatt tgatgagcaa ggtgggcatc cagcttgttt cttggctgat 65700

ggcttatggg tggcgtgaat tagtcggggt ctatcaggag gcagaaactc tatgagaatt 65760

tgaacagaga aagttccgtc tacaggctta ttaccaggga ctggaatagc agaaattgaa 65820

cagtgagatg tacagagaac tctaagaatg caggaatagg ccaggcatgg tggctcacac 65880

ctgtcatccc agcactttgg gagaccaagg cgggtggatc acctgaggtc aggagttcga 65940

gaccagcctg gccaacatag tgaaacccca tctctactaa aaatacaaaa aaattagctg 66000

ggtgtggtgg cgcatgcctg taatcccagc ttctcgggag tctgaggctg gagaatcact 66060

tgaacctggg aggcagaggt tgtagtgagc cgagatcatg ccattgtact ccagcctggg 66120

caacaagagc gagactcagt caaaacaaca acaacgcagg aatagcagat gagccgaggt 66180

ggggcctccc cagcccccac cccccacccc gcaccctggg ccgagatcca gtcctctttg 66240

aatagggcct gggcgtggtt cacgggacat ctgagacatt gccgaggcgc tgcactggtg 66300

gatcttgcca gaagtctgcc cagtgcagat ttgggcagaa tctcaaactg ccttgggatg 66360

taggagagaa accaggcctg gtcaagttca tgggaagagg tggaaacaga ccccataggc 66420

tggggcttgg gcagctgtag gaagccctct ctgctgcctc cctgcctgct ctctgctttg 66480

aagcatcttc cccagtgccc ccagtctcat gccctctcaa cgttggggtc aaatcctgag 66540

gaatacccag actggctctc tgggccaaag aggaccctct ccagaaagag cagggcccag 66600

tgcggcttcc taaagggcag gggaagggcc tggccactcc ccagaggcta ctcaccagcc 66660

atcaggatag ccccaggaag caggccttct cgagcccatt ttattacttt attttattat 66720

tttatttaat tttaaattta ttttttgaga cagagtctca ctctgttgcc caggctggag 66780

tgcagtggtg cgatctcaac ccactgcagc ctctgcctcc agggttcaag ggattctccc 66840

acctcagcct cccaagtagc tgggattaca ggtgcccgcc accacacccg gctaattttc 66900

atatttttag tagagacgag gtttcaccat gttggccagg ctggtctcga actcctgacc 66960

tcaagtgatc cgcccgcctc ggcctcccaa agtgctaggt caagcccatt ttaaagttga 67020

agaaactgag gctgaggtaa attccctccc cagggatcct gctgcagcca gaaggtggta 67080

aaacaggact tcacccgggt ctgtctggcg tgaaaggcag tgttcttgta ccaccctagg 67140

gggcctgaga gaactgagtc cctcgggcat aactgacagt tctgttccca ttattccgca 67200

ggggctcgga tctggctgta tgctttccag gatggccttg gagacccaca taagccctac 67260

acccttgggg aagctgcatg ttgggttggg gtgccgtcag tggcacttgt ggaaggtgca 67320

gacctgtgtg ggtgtgtggg cccagggccc ctggtccctt cctccctttg tagggctggt 67380

tgtgtgctgc ctggacctgg ggggcacgtt cacgtggtga atttgtctat ttactatccc 67440

cgctttgggg ctggtgccag cacaggccct tgtgaagggg gtgcctttgt ctggagtggg 67500

actgtggccc ctccctcagc gtggtgactt ctgtgtcagg gcttcagcag ggacgcagag 67560

ccctgagtg ttcggaacaa gggcgtcatt gcaggagtta gactgtgtgt gatggaggga 67620

ggaggggcag gaggaaaggt cagaaggaga gttcctggga aggtccctga ggagcctggt 67680

gaggtgctaa ctggtgtgga ggacactcag ggcctgtggg gacatctcct actgctgggg 67740

gccagccaca aagggaactg gccgaagtcc tgtccccgcc ttcacagccc agcatctggt 67800

cacaaggcag gtacttggaa gggcgcgggc acctgggcca aaagtgcctg ggttcccttt 67860

gcctttcact gagatgacct tcggggcagg tggctgctgc ctcccctcct gtccccaggt 67920

tttgccaact ggccagagga aggggtcctg ggaagcaggg gggccagaag ccctctctgc 67980

aaggaaagcc cgaggggtgt gggaggaagg aaggaatgcc caggctggcg aggctctaag 68040

tcaccctggc ttggctctcc tcagatcctg aacccgccgc cctccccggc cacggacccc 68100

tccctgtaca acatggacat gttctactct tcaaacattc cggccactgc gagaccgtac 68160

aggtaggaca tcccctgcag ccctccatgg ccattgggtt cccgccagcc cgtggtggag 68220

gggcctaatc cccatgccac tgatgagggg aggtattctg ggtgctagtg ggcaggtgcc 68280

gggcccagcc ctgcctccct ctgctctgcc aaccacacta ggctgcctcc ccagacaagc 68340

tcagcgggca ctgcatgttg ggttcagaaa tcagcagaac tccacgttct gagctgctct 68400

tcaagttgct cctatggggg ttacttttaa gctgggaaat ggctgtggcg tcgaggggcc 68460

gggggcttgg gctccaaact ctgactgtgt gtttgagtcc ggctgtggaa acctagccat 68520

tgagatgccc cctcttggtg gctctgtcct cttaggatgg gacaagtctg tgaaggctgc 68580

tgcagcaccc accgtagacc cctaatcgtg tgacgtcacc aggatggtcc gggctgctca 68640

cttgccacag tggcctgttt gagcccggga agccaacggg gctgctcagc tggacaccag 68700

ccccccgagc tgcccatgtt ggggtcacag gccccacctc cctggttggg gaggggcaac 68760

tgagagtgtg gagaggtggg acccaggtgt gctggtctcc gcaggggctg gatcagagcc 68820

tgggatgggc agggtgagcc tcctgacctt taacccagtg gtgtcaggca acgtggccca 68880

cccgccagcc gcaccaggcc ccacccccgc aggtgaaggg gtgggatagg ctgggcctgg 68940

gccaggacac ctctggacca cgcattcctc attgcttggg tccctggagc agcagggcct 69000

cccgagtgtg gtgccgcctg ccacctagtg gccatttcca cgaactccca ggcctggctg 69060

gggagccgga actgcagcct ccatttccac cccactccgg gtcgggccac ctccctgatg 69120

cctcagtatt atatcaaact gtcacagtct gtcccacagc cttacagacc actgtctcca 69180

gaatggtcac atccacactg ggcagcccag tctcgctagt tcctcgtccc acctcctgcc 69240

tttgctcatg cccgtcctgc tctgggccca ccgcggacac atcttccccc cgcccgccgt 69300

ctgacctcac agcagctggg ccccaagagg agtatcctgt cctgctgcac ttttctcaac 69360

acccggtgtt ggctgcacct tcccacccat tgcaggcccc tctgtgacag gacgggggct 69420

cctaaacaca ccacagttcc gagtctgaac tcacacagtg ggatgcggcg tttctgggcc 69480

acagttgggt gcaggtagcc tctgggagga tgggaggtca ggagccatct tgcgagtcag 69540

gttgcttgaa ctcaggatgg aagtgttccg ggcccattgg ttgctgtatt agcctgttct 69600

cacgctgcta ataaagacat acccaagact gggtaattgt aaaggaaaga ggtttaacgg 69660

actcacagtt ccacctgcct ggggtggcct cacaatcatg gtagaagaca aggaggagca 69720

agtcacatct tacatggctt cagggaacag acagcatgag aaccaagcga aaggggtttc 69780

cccttgtaaa accatcaagt ctagtgagat ttattcacta ccacgagaac agtatggggg 69840

gaaccacccc catgattcaa tcatctccca ctgggtccct cccacagcac gtgggaatta 69900

tgggagtaca attcaagatg agatttgggt ggggacacag ccaaacccta tcggttgcca 69960

acatttacag taacagtgtt aggtgaacag ttgtccagtc tcctgttttg tcggacactg 70020

tttctagcac cttccaggca gaatctcatg tatccttcac tttcgaaatg ggtactattt 70080

catccccact tttatcaatg agaaactaaa gctcgaagag gtcaagtaag ttcctggcca 70140

aggtcagcta gcaggctcta gaggcctcgt tctccttaga ggcagccttg ccagggccca 70200

ggcttggcag gctgcagggc aggtgcgggc atgcccatgg tagaggtggg accattgagg 70260

ctcagagagg gtaagtgatg agccctggcg acacagcggg gtgggtccag agtccggcct 70320

gcatcttctg gagctggcca gtggacaggc ctttcccgtt cacagccccg gggctgctgt 70380

gcccaccagg gcggatgtgc ctaccgaatc ccactcctct gtgtgtgtcc ctttcaggcc 70440

ctacatcatt cgaggaatgg cgcccccgac gacgccctgc agcaccgacg tgtgtgacag 70500

cgactacagc gccagccgct ggaaggccag caagtactac ctggatttga actcggactc 70560

agacccctat ccacccccac ccacgcccca cagccagtac ctgtcggcgg aggacagctg 70620

cccgccctcg cccgccaccg agaggagcta cttccatctc ttcccgcccc ctccgtcccc 70680

ctgcacggac tcatcctgac ctcggccggg ccactctggc ttctctgtgc ccctgtaaat 70740

agttttaaat atgaacaaag aaaaaaatat attttatgat ttaaaaaata aatataattg 70800

ggattttaaa aacatgagaa atgtgaactg tgatggggtg ggcagggctg ggagaacttt 70860

gtacagtgga gaaatattta taaacttaat tttgtaaaac agaactgcca ttcttttgtg 70920

ccctgtgtgc atttgagttg tgtgtccccg tggagggaat gccgaccccc ggaccaccat 70980

gagagtcctc ctgcacccgg gcgtccctct gtccggctcc tgcagggaag ggctggggcc 71040

ttgggcagag gtggatatct cccctgggat gcatccctga gctgcaggcc gggccggctt 71100

tatgtgcgtg tggcctgtgc cgtcagaaag ggccctgggc ttcatcacgc tgttgctgtt 71160

cgtcttcctc agattcttag tctttttttt ttttttttt ttttgagacg gagtctttct 71220

ctgtcatcca ggctggagtg cagtggtaca atctcagctc actgcaagct ccgactccca 71280

ggttcaagtg agtctcctgc ctcagcctcc cgagtagctg ggactacagg tgcgcgccac 71340

cacacccgcc cagctaattt ttgtattttt agtagagatg gggtttcacc atgttggcca 71400

ggatgatctc gatctcttga cctcgtgatc cgcccacctc ggcctcccaa agtgctggga 71460

ttataggcat gagccactgt acccagctga ctcttagtca cttttaagaa ggggactgtg 71520

ccttcatttt tcactgggcc ctgcagaata tatgcctggg ctctgggctc ttctgaacct 71580

gtgttggctt ccatctgacc tctctgtgcc agcccaaggc tgctgctctt cctgagggca 71640

aggagcccca tgactgcgtg ttgactcgct ggatggggct gctgagccca ctctgccaca 71700

ccacgtgccc ctggcaggga gggaatccct gggtcctcac aggaacagtc agcaagccac 71760

acctgacgcc tgctgtgggc ccatccctgc ggtgctggag aagacagaca aggcctggtc 71820

actgcctctg cagggtcccc agtccgtgga aggagacagt aatctaggca ttttcggtgg 71880

ggaagctgag ctgttctcgt gtcctgaagg ccaggcggga acagccgtct tcagagggaa 71940

gggagaaaat gcacatcgca tcagtggaga agggcctgac ttccctcagc atggtggagg 72000

gaggtcagaa aacagtcaag cttgagtatt ctatagtgtc acctaaata 72049

<210> 10

<211> 8705

<212> DNA

<213> Homo sapiens

<400> 10

ggactcaggg gcagcaggga ggtacaccca tggttagtgg gcggaccata gggggtaatg 60

agagggtgaa tcgatggaac ctgggggaca caatcgaagt ggttccagag tcgggctgta 120

ctaattaaag agacggggca gtggacaggc attttcagtt gactgcccag ggagtgttct 180

gcccaacagg gaggatatgc gtacagaatc atactcgatc agcatgagtc caattcagac 240

cgtacatcag tggagatatg ggtcccccga tgactccgtg gaacactgat gtttgtgaca 300

ggggagtaca gcaccagcca tcagcaggcc agtaaatcat accggcctgc gaaattggac 360

tcagacccgg atccaccctg accgacgtcc caagccccca ccccccaccc cccaccatgg 420

gccgagatcc agtcctcttt gaatagggcc tggccgtggt tcacgggaca tctgagacat 480

tgccgaggcg ctgcattggt ggatcttgcc agaagtttgc ccagtgcaga tttgggcaga 540

atctcaaact gccttgggat gtaggagaga aaccaggcct ggtcaagttc atgggaagag 600

gtggaaacag accccatagg ctggggcttg ggcagctgta ggaagccctc tctgctgcct 660

ccctgcctgc tctctgcttt gaagcatctt ccccagtgcc cccagtctca tgccctctca 720

acgttggggt caaatcctga ggaataccca gactggctct ctgggccaaa gaggaccctc 780

tccagaaaga gcagggccca gtgcggcttc ctaaagggca ggggaagggc ctggccactc 840

cccagaggct actcaccagc catcaggata gccccaggaa gcaggccttc tcgagcccat 900

tttattactt tattttatta ttttatttaa ttttaaattt atttttgag acagagtctc 960

actctgttgc ccaggctgga gtgcagtggt gcgatctcaa cccactgcag cctctgcctc 1020

cagggttcaa gggattctcc cacctcagcc tcccaagtag ctgggattac aggtgcccgc 1080

caccacaccc ggctaatttt catattttta gtagagatga ggtttcacca tgttggccag 1140

gctggtctcg aactcctgac ctcaagtgat ccgcccgcct cggcctccca aagtgctagg 1200

tcaagcccat tttaaagttg aagaaactga ggctgaggta aattccctcc ccagggatcc 1260

tgctgcagcc agaaggtggt aaaacaggac ttcacccggg tctgtctggc gtgaaaggca 1320

gtgttcttgt accaccctag ggggcctgag agaactgagt ccctcgggca taactgacag 1380

ttctgttccc attattccgc aggggctcgg atctggctgt atgctttcca ggatggcctt 1440

ggagacccac ataagcccta cacccttttgg gaagctgcat gttgggttgg ggtgccgtca 1500

gtggcacttg tggaaggtgc agacctgtgt gggtgtgtgg gcccagggcc cctggtccct 1560

tcctcccttt gtagggctgg ttgtgtgctg cctggacctg gggggcacgt tcacgtggtg 1620

aatttgtcta tttactatcc ccgctttggg gctggtgcca gcacaggccc ttgtgaaggg 1680

ggtgcctttg tctggagtgg gactgtggcc cctccctcag cgtggtgact tctgtgtcag 1740

ggcttcagca gggacgcaga gcccctgagt gttcggaaca agggcgtcat tgcaggagtt 1800

agactgtgtg tgatggaggg aggaggggca ggaggaaagg tcagaaggag agttcctggg 1860

aaggtccctg aggagcctgg tgaggtgcta actggtgtgg aggacactca gggcctgtgg 1920

ggacatctcc tactgctggg ggccagccac aaagggaact ggccgaagtc ctgtccccgc 1980

cttcacagcc cagcatctgg tcacaaggca ggtacttgga agggcgcggg cacctgggcc 2040

aaaagtgcct gggttccctt tgcctttcac tgagatgacc ttcggggcag gtggctgctg 2100

cctcccctcc tgtccccagg ttttgccaac tggccagagg aaggggtcct gggaagcagg 2160

ggggccagaa gccctctctg caaggaaagc ccgaggggtg tgggaggaag gaaggaatgc 2220

ccaggctggc gaggctctaa gtcaccctgg cttggctctc ctcagatcct gaacccgccg 2280

ccctccccgg ccacggaccc ctccctgtac aacatggaca tgttctactc ttcaaacatt 2340

ccggccactg cgagaccgta caggtaggac atcccctgca gccctccatg gccattgggt 2400

tcccgccagc ccgtggtgga ggggcctaat ccccatgcca ctgatgaggg gaggtattct 2460

gggtgctaat gggcaggtgc cgggcccagc cctgcctccc tctgctctgc caaccacact 2520

aggctgcctc cccagacaag ctcagcgggc actgcatgtt gggttcagaa atcagcagaa 2580

ctccacgttc tgagctgctc ttcaagttgc tcctatgggg gttactttta agctgggaaa 2640

tggctgtggc gtcgaggggc cgggggcttg ggctccagag tctgactgtg tgtttgagtc 2700

cggctgtgga aacctagcca ttgagatgcc ccctcttggt ggctctgtcc tcttaggatg 2760

ggacaagtct gtgaaggctg ctgcagcacc caccgtagac ccctaatcgt gtgacgtcac 2820

caggatggtc cgggctgctc acttgccaca gtggcctgtt tgagcccggg aagccaacgg 2880

ggctgctcag ctggacacca gccccccgag ctgcccatgt tggggtcaca ggccccacct 2940

ccctggttgg ggaggggcaa ctgagagtgt ggagaggtgg gacccaggtg tgctggtctc 3000

cgcaggggct ggatcagagc ctgggatggg cagggtgagc ctcctgacct ttaacccagt 3060

ggtgtcaggc aacgtggccc acccgccagc cgcaccaggc cccacccccg caggtgaagg 3120

ggtgggatag gctgggcctg ggccaggaca cctctggacc acgcattcct cattgcttgg 3180

gtccctggag cagcagggcc tcccgagtgt ggtgccgcct gccacctagt ggccatttcc 3240

acgaactccc aggcctggct ggggagccgg aactgcagcc tccatttcca ccccactccg 3300

ggtcgggcca cctccctgat gcctcagtat tatatcaaac tgtcacagtc tgtcccacag 3360

ccttacagac cactgtctcc agaatggtca catccacact gggcagccca gtctcgctag 3420

ttcctcgtcc cacctcctgc ctttgctcat gcccgtcctg ctctgggccc accgcggaca 3480

catcttcccc ccgcccgccg tctgacctca cagcagctgg gccccaagag gagtatcctg 3540

tcctgctgca cttttctcaa cacccggtgt tggctgcacc ttcccaccca ttgcaggccc 3600

ctctgtgaca ggacgggggc tcctaaacac accacagttc cgagtctgaa ctcacacagt 3660

gggatgcggc gtttctgggc cacagttggg tgcaggtagc ctctgggagg atgggaggtc 3720

aggagccatc ttgcgagtca ggttgcttga actcaggatg gaagtgttcc gggcccattg 3780

gttgctgtat tagcctgttc tcacgctgct aataaagaca tacccaagac tgggtaattg 3840

taaaggaaag aggtttaacg gactcacagt tccacctgcc tggggtggcc tcacaatcat 3900

ggtagaagac aaggaggagc aagtcacatc ttacatggct tcagggaaca gacagcatga 3960

gaaccaagcg aaaggggttt ccccttgtaa aaccatcaag tctagtgaga tttattcact 4020

accacgagaa cagtatgggg ggaaccaccc ccatgattca atcatctccc actgggtccc 4080

tcccacagca cgtgggaatt atgggagtac aattcaagat gagatttggg tggggacaca 4140

gccaaaccct atcggttgcc aacatttaca gtaacagtgt taggtgaaca gttgtccagt 4200

ctcctgtttt gtcggacact gtttctagca ccttccaggc agaatctcat gtatccttca 4260

ctttcgaaat gggtactatt tcatccccac ttttatcaat gagaaactaa agctcgaaga 4320

ggtcaagtaa gttcctggcc aaggtcagct agcaggctct agaggcctcg ttctccttag 4380

aggcagcctt gccagggccc aggcttggca ggctgcaggg caggtgcggg catgcccatg 4440

gtagaggtgg gaccattgag gctcagagag ggtaagtgat gagccctggc gacacagcgg 4500

ggtgggtcca gagtccggcc tgcatcttct ggagctggcc agtggacagg cctttcccgt 4560

tcacagcccc ggggctgctg tgcccaccag ggcggatgtg cctaccgaat cccactcctc 4620

tgtgtgtgtc cctttcaggc cctacatcat tcgaggaatg gcgcccccga cgacgccctg 4680

cagcaccgac gtgtgtgaca gcgactacag cgccagccgc tggaaggcca gcaagtacta 4740

cctggatttg aactcggact cagaccccta tccacccccа cccacgcccc acagccagta 4800

cctgtcggcg gaggacagct gcccgccctc gcccgccacc gagaggagct acttccatct 4860

cttcccgccc cctccgtccc cctgcacgga ctcatcctga cctcggccgg gccactctgg 4920

cttctctgtg cccctgtaaa tagttttaaa tatgaacaaa gaaaaaaata tattttatga 4980

tttaaaaaat aaatataatt gggattttaa aaacatgaga aatgtgaact gtgatggggt 5040

gggcagggct gggagaactt tgtacagtgg agaaatattt ataaacttaa ttttgtaaaa 5100

cagaactgcc attctttcgt gccctgtgtg catttgagtt gtgtgtcccc gtggagggaa 5160

tgccgacccc cggaccacca tgagagtcct cctgcacccg ggcgtccctc tgtccggctc 5220

ctgcagggaa gggctggggc cttgggcaga ggtggatatc tcccctggga tgcatccctg 5280

agctgcaggc cgggccggct ttatgtgcgt gtggcctgtg ccgtcagaaa gggccctggg 5340

cttcatcacg ctgttgctgt tcgtcttcct cagattctta gtctttttt ttttttttt 5400

ttttttgaga cggagtcttt ctctgtcatc caggctggag tgcagtggta caatctcagc 5460

tcactgcaag ctccgactcc caggttcaag tgagtctcct gcctcagcct cccgagtagc 5520

tgggactaca ggtgcgcgcc accacacccg cccagctaat ttttgtattt ttagtagaga 5580

tggggtttca ccatgttggc caggatgatc tcgatctctt gacctcgtga tccgcccacc 5640

tcggcctccc aaagtgctgg gattataggc atgagccact gtacccagct gactcttagt 5700

cacttttaag aaggggactg tgccttcatt tttcactggg ccctgcagaa tatatgcctg 5760

ggctctgggc tcttctgaac ctgtgttggc ttccatctga cctctctgtg ccagcccaag 5820

gctgctgctc ttcctgaggg caaggagccc catgactgcg tgttgactcg ctggatgggg 5880

ctgctgagcc cactctgcca caccacgtgc ccctggcagg gagggaatcc ctgggtcctc 5940

acaggaacag tcagcaagcc acacctgacg cctgctgtgg gcccatccct gcggtgctgg 6000

agaagacaga caaggcctgg tcactgcctc tgcagggtcc ccagtccgtg gaaggagaca 6060

gtaatctagg cattttcggt ggggaagctg agctgttctc gtgtcctgaa ggccaggcgg 6120

gaacagccgt cttcagaggg aagggagaaa atgcacatcg catcagtgga gaagggcctg 6180

acttccctca gcatggtgga gggaggtcag aaaacagtca agcttgttgc tgggtgacag 6240

tgcatttaat aatcaaaata taggctgggt acggtggctc atgcctgtaa tcccagcact 6300

ttgggaggct gaggcaggtg gatcacttga ggccaggagt ttgagaccgg cctggccaac 6360

atggcaaaac ctcaactact aaaatacaaa aactagccgg gcgtggtggt gcacgcctgt 6420

aatcccagct acttgggagg ctgaggcagg agaattgctt gaacctggga ggcggaggct 6480

gcagtgagcc gagattgtgc cactgcactc cagcctgggc aacagagcaa gactctgtct 6540

caaaaaaaaa aaaaaaaaaa gcaatacaaa atacaaatat cactttcact aaaagaaggg 6600

atggaagacc caaaacaaac agaaaacaac aaaatggcag gagtaagtcc ccacttatca 6660

ataataacat tgactgtaaa taggctaagc tctgcaatca aaagagtggg ccaggagcgg 6720

tggctcacgc ctgtaattcc aacgctttgg gaggctgagg cggatggatc atttgatgtc 6780

acgagtttta agaccagcct ggccaacaag gtgaaacccc atctgtacta aaaatacaaa 6840

aattagccag gcggtagtgg cacgcacctg taatcccagc tacttgtgag gctgaggcag 6900

gagaatcact ggaggctggg aagcggaggt tgctgtgagc caagatggag ccactgcact 6960

cccacctggg cgacagagtg agatcctgtc ttaagaaaaa aaagagtgga tgaatggatc 7020

aaaaaacaag acccaaccat ctcttgcata caagaaacac actttaccta taaaaacaca 7080

ctaggccagg tgtggtggct cacacctgta atcccagccc tttgggaggc ctgactggca 7140

gatcacctga ggccaggagt ttcagaccag cttgaccgac atggcaaaac cccatctctc 7200

ctaaaaatac aaaaaaacaa aaaaaagaaa aaggctggaa gtagtgatgt gtgcctgtag 7260

ccccagctac ttgggaggct gaggcaggag aattgcttga atccgggaag tggaggttgc 7320

agtgagccag gatggtgcca ctgcactcca gcctgggtga cagagcgaga ccctgtcata 7380

aaaaaaaaaa gaaaagaaaa gaaaaacgag aaaaacaaac acaaaattag tagaagaaaa 7440

gaaataataa agatcagaac aggccaggct catgggcaca gtggctcaac tcctacctgc 7500

tcaggagttt gagaccagtc tggccaacat ggcaaaaccc catctctcct aaaaatatga 7560

aaaaaaaaaa ataggctgga tgtggtgatg tgtgtgtgcc tgtagcccca gctacttggg 7620

aggctgaggt gggagaatca cttgagccca ggaagtggag gctgcagcga gtcatgaatg 7680

caccctgcac tctagctggg taactggagt gagattctgt ctcaaaaaag caaagaccag 7740

agcagaaata aatgaaatgg aaatgaagga aacaatgcaa aatgatacaa aaagtttttt 7800

cgaaaagata aacaaaatca acaaaccttt agccagatta agaaaaaaag agagaagacc 7860

caaataaata aaatccgaga ttaaaaagga gacattacca ctgataccac agaaattcaa 7920

aggatcatta gaggcaacta tgtgcaacta tatgctaatg aactggaaaa cctagaagaa 7980

ctgggtaaat ttctagacac atacaaccta tcaagattga accatgaaga aatccaaaac 8040

ctgaacaggc cgggcacggt ggcttacgcc tgtaatccca gcactttgga aggcctgaga 8100

tcaggagttc gagaccagcc tggccaacat ggtgaaaccc catctctact gaaaaaatat 8160

aaaaattagc cgggcgtggt ggcgggtgcc tctaatgtca gccactcggg aggctgaggc 8220

aggaaaatca cttgaacctg ggaggcatag gttgcagcga gccgaggttg caccactgca 8280

ctccagcctt ggcgacagag ccagactcca tctcaaaaaa attaaaataa caaaaacctg 8340

aacagaccaa taacaagtaa tgcgatgaaa actgtaataa aatgtttccc aacaaagaaa 8400

gcccaggaac aaatggcttc actgctgaat tttaccaaac attttttttt ttttgagacg 8460

gagtctcgct ctgtcgccca ggctggagtg cagtggtgta acctcggttc gctggtaact 8520

tatgcctctc aggctgcaag tgattttcct gcttcaggcc ccccgagtgg ctggaaatta 8580

gatggtactt gtcaaacaag gcctggctaa atttctatat ttccttcaag tagaagatgt 8640

gcttccaaca aaggttgggt tacggctggc ttctgaaaat cttggatttc aaggctcccc 8700

aaaag 8705

<210> 11

<211> 66933

<212> DNA

<213> Homo sapiens

<400> 11

tataatcaag cgcgttccgt ccagtccggt gggaagattt tcgatatgct tcgtgatctg 60

ctcaagaacg ttgatcttaa agggttcgag cctgatgtac gtattttgct taccaaatac 120

agcaatagta atggctctca gtccccgtgg atggaggagc aaattcggga tgcctgggga 180

agcatggttc taaaaaatgt tgtacgtgaa acggatgaag ttggtaaagg tcagatccgg 240

atgagaactg tttttgaaca ggccattgat caacgctctt caactggtgc ctggagaaat 300

gctctttcta tttgggaacc tgtctgcaat gaaattttcg atcgtctgat taaaccacgc 360

tgggagatta gataatgaag cgtgcgcctg ttattccaaa acatacgctc aatactcaac 420

cggttgaaga tacttcgtta tcgacaccag ctgccccgat ggtggattcg ttaattgcgc 480

gcgtaggagt aatggctcgc ggtaatgcca ttactttgcc tgtatgtggt cgggatgtga 540

agtttactct tgaagtgctc cggggtgata gtgttgagaa gacctctcgg gtatggtcag 600

gtaatgaacg tgaccaggag ctgcttactg aggacgcact ggatgatctc atcccttctt 660

ttctactgac tggtcaacag acaccggcgt tcggtcgaag agtatctggt gtcatagaaa 720

ttgccgatgg gagtcgccgt cgtaaagctg ctgcacttac cgaaagtgat tatcgtgttc 780

tggttggcga gctggatgat gagcagatgg ctgcattatc cagattgggt aacgattatc 840

gcccaacaag tgcttatgaa cgtggtcagc gttatgcaag ccgattgcag aatgaatttg 900

ctggaaatat ttctgcgctg gctgatgcgg aaaatatttc acgtaagatt attacccgct 960

gtatcaacac cgccaaattg cctaaatcag ttgttgctct ttttttctcac cccggtgaac 1020

tatctgcccg gtcaggtgat gcacttcaaa aagcctttac agataaagag gaattactta 1080

agcagcaggc atctaacctt catgagcaga aaaaagctgg ggtgatattt gaagctgaag 1140

aagttatcac tcttttaact tctgtgctta aaacgtcatc tgcatcaaga actagtttaa 1200

gctcacgaca tcagtttgct cctggagcga cagtattgta taagggcgat aaaatggtgc 1260

ttaacctgga caggtctcgt gttccaactg agtgtataga gaaaattgag gccattctta 1320

aggaacttga aaagccagca ccctgatgcg accacgtttt agtctacgtt tatctgtctt 1380

tacttaatgt cctttgttac aggccagaaa gcataactgg cctgaatatt ctctctgggc 1440

ccactgttcc acttgtatcg tcggtctgat aatcagactg ggaccacggt cccactcgta 1500

tcgtcggtct gattattagt ctgggaccac ggtcccactc gtatcgtcgg tctgattatt 1560

agtctgggac cacggtccca ctcgtatcgt cggtctgata atcagactgg gaccacggtc 1620

ccactcgtat cgtcggtctg attattagtc tgggaccatg gtcccactcg tatcgtcggt 1680

ctgattatta gtctgggacc acggtcccac tcgtatcgtc ggtctgatta ttagtctgga 1740

accacggtcc cactcgtatc gtcggtctga ttattagtct gggaccacgg tcccactcgt 1800

atcgtcggtc tgattattag tctgggacca cgatcccact cgtgttgtcg gtctgattat 1860

cggtctggga ccacggtccc acttgtattg tcgatcagac tatcagcgtg agactacgat 1920

tccatcaatg cctgtcaagg gcaagtattg acatgtcgtc gtaacctgta gaacggagta 1980

acctcggtgt gcggttgtat gcctgctgtg gattgctgct gtgtcctgct tatccacaac 2040

attttgcgca cggttatgtg gacaaaatac ctggttaccc aggccgtgcc ggcacgttaa 2100

ccgggctgca tccgatgcaa gtgtgtcgct gtcgacgagc tcgcgagctc ggacatgagg 2160

ttgccccgta ttcagtgtcg ctgatttgta ttgtctgaag ttgtttttac gttaagttga 2220

tgcagatcaa ttaatacgat acctgcgtca taattgatta tttgacgtgg tttgatggcc 2280

tccacgcacg ttgtgatatg tagatgataa tcattatcac tttacgggtc ctttccggtg 2340

atccgacagg ttacggggcg gcgacctcgc gggttttcgc tatttatgaa aattttccgg 2400

tttaaggcgt ttccgttctt cttcgtcata acttaatgtt tttatttaaa ataccctctg 2460

aaaagaaagg aaacgacagg tgctgaaagc gagcttttg gcctctgtcg tttcctttct 2520

ctgtttttgt ccgtggaatg aacaatggaa gtccgagctc atcgctaata acttcgtata 2580

gcatacatta tacgaagtta tattcgatgc ggccgcaagg ggttcgcgtc agcgggtgtt 2640

ggcgggtgtc ggggctggct taactatgcg gcatcagagc agattgtact gagagtgcac 2700

catatgcggt gtgaaatacc gcacagatgc gtaaggagaa aataccgcat caggcgccat 2760

tcgccattca ggctgcgcaa ctgttgggaa gggcgatcgg tgcgggcctc ttcgctatta 2820

cgccagctgg cgaaaggggg atgtgctgca aggcgattaa gttgggtaac gccagggttt 2880

tcccagtcac gacgttgtaa aacgacggcc agtgaattgt aatacgactc actatagggc 2940

gaattcgagc tcggtacccg gggatcctct agagtcgacc tgcaggcatg caagcttctc 3000

ttgtgccggt tgtacgctgt caggtcacac tggtgagtta ggcagggcac agatgcccag 3060

agcagaggga actttccttg gggattcaac acgtgcaagt cttaggggct ggcaaatcct 3120

gccctcagct agagaggggg cttttatttg agaccagaat cacctgagca tcctcctgtc 3180

cccagctgtg tccagcctgt ctgcagggac atcctgagag gaccaggctc tcccctcatc 3240

cacctgccta agtgccactc tgaaccctgt ccacctgtgc cgtggagggg cgtgacctca 3300

agctgctcag ccagcagcag gcttggccct ggggggcagc agagacccag gtggctgtgg 3360

ggtgggtgct tcgtggcgtg gttctgaaac ttcgttggaa gtgtgtggac agtgccttgc 3420

ctgttctctg tgggacccta tttagaaacg aggtctgagt tactgggggt catcactgtg 3480

ttctgatggc ccagctgtgt ggaggccgcg gtgcagcccc atccaaggag ccagggccct 3540

gggtctagcc gtgaccagaa tgcatgcccc ggaggtgttt ctcatctcgc acctgtgttg 3600

cctggtgtgt caagtggtcg tgaaactctg tgttagctct tggtgttcct gaaagtgccc 3660

ccgggtctca ggcctcagaa ccagggtttc ccttcatctc ggtggcctgg gagcatctgg 3720

gcagttgagc aaagagggcg attcacttga aggatgtgtc tggccctgcc taggagcccc 3780

ccggcacggt gctggggcct gaagctgccc tcgggtggtg gagaggaggg agcgatgaag 3840

tggcgtcgag ctgggcagga agggtgagcc cctgcaaggt gggcatgctg gggacgctga 3900

gcagcatggc cagcagctgg gtctgcagcc tggtacccgg cgggacttgt ggttggggct 3960

ggtttgtggc caggagaggg gctggcagga gacaaggggg actgtgaggc agctcccacc 4020

cagcagctga agcccaatgg cctggctgtg tggctctcag ctgcgtgcat aacctctcag 4080

tgcttcagtt ctctcatttg taaaatgagg aaacaaacag tgccagcctc ccagaggtgt 4140

catgaggatg aacgagtgac catgtagcat gggctgggtg cgtgtcacct aacatcacca 4200

gcctttgcaa ggagagccct gggggcctgg ctgagtattt cccttgcccg gcccacccca 4260

ggcctagact tgtgcctgct gcaggccctt gacccctgac cccattgcac ctgtctccac 4320

aggagccgag gaggtgctgc tgctggcccg gcggacggac ctacggagga tctcgctgga 4380

cacgccggac ttcaccgaca tcgtgctgca ggtggacgac atccggcacg ccattgccat 4440

cgactacgac ccgctagagg gctatgtcta ctggacagat gacgaggtgc gggccatccg 4500

cagggcgtac ctggacgggt ctggggcgca gacgctggtc aacaccgaga tcaacgaccc 4560

cgatggcatc gcggtcgact gggtggcccg aaacctctac tggaccgaca cgggcacgga 4620

ccgcatcgag gtgacgcgcc tcaacggcac ctcccgcaag atcctggtgt cggaggacct 4680

ggacgagccc cgagccatcg cactgcaccc cgtgatgggg taagacgggc gggggctggg 4740

gcctggagcc agggccaggc caagcacagg cgagagggag attgacctgg acctgtcatt 4800

ctgggacact gtcttgcatc agaacccgga ggagggcttg ttaaaacacc ggcagctggg 4860

ccccaccccc agagcggtga ttcaggagct ccagggcggg gctgaagact tgggtttcta 4920

acaagcaccc cagtggtccg gtgctgctgc tgggtccatg cgtagaaagc cctggagacc 4980

tggagggagc cctttgttcc cctggcttca gtttcctcat ctgtagaatg gaacggtcca 5040

tctgggtgat ttccaggatg acagtagtga cagtaagggc agcctctgtg acactgacca 5100

cagtacaggc caggcctctt ttttttcttt ttttttttttg agatggagtc tcactctgtc 5160

gcccaggctg gagtgcagtg gtgtgatctc agctcactac aacctctgcc tcctgggctc 5220

aagtgattct cctgcctcag cctcctgagt agctgggatt acaggtgcct gccactgtgc 5280

ttggctaatg tttgtatttt tggtagagat ggggtttcac cgtcttggcc aggctggtcg 5340

caaactcctg acctcaggtg atccacctgc ctcagcctcc caaagtgctg ggattacagg 5400

catgagccac cacgcccggt caggccaggc ctcttttgaa cactttgcac accatgggtc 5460

ttttcatcca ggggggtagg tacagttgta cagttgagga cactgaagcc cagagaggct 5520

cagggacttg cccagggtca cacagcagga tgtggcaggt gtggggctgg gcctggcagc 5580

gtggctccag ctttccagca tagaaatctg tgaaagcaga tagtttgtcg gtcggtaggg 5640

gagactttct gagacccgcc ccagcggctc agagggtagt agccaggggc cttcctgggg 5700

gctcataacc cagaacactg aatgggaaaa ccctgatgga ggaggcgcag tggagctgtg 5760

ggtgccgatg ggaagtccca gaggagctgg gaggtcagta gcggtgctgc cctctgtgga 5820

gcacttagtg ggcaccaggt gtgtttccag gttcatggcc ctgggacctg aagctcagaa 5880

ggtgaagtaa cttgcccagg gcacccgtcg ggcagcggcg ggcagaggat ttgtgggctg 5940

tggagcctgt gctcgtggcc cagccctggg ggttgtgagt gtgctggccg gggagctttt 6000

cctgcaagtg gactggtgtc taggagccag catgtcaggc agcaggcagc gggagtgcag 6060

caggcagcgg gagcacagca ggcagagggc ggggctcgag cagccatccg tggaccctgg 6120

ggcacggagg catgtgggag agggctgctc catggcagtg gctgaagggc tgggttgtgc 6180

cccgaggagg gtggatgagg gtaagaagtg gggtccccag gggctttagc aagaggaggc 6240

ccaggaactg gttgccagct acagtgaagg gaacacggcc ctgaggtcag gagcttggtc 6300

aagtcactgt ctacatgggc ctcggtgtcc tcatctgtga aaaaggaagg gatggggaag 6360

ctgactccaa ggcccctcct agccctggtt tcatgagtct gaggatccca gggacatggg 6420

cttggcagtc tgacctgtga ggtcgtgggg tccagggagg ggcaccgagc tggaagcggg 6480

aggcagaggg gctggccggc tgggtcagac acagctgaag cagaggctgt gacttggggc 6540

ctcagaacct tcacccctga gctgccaccc caggatctgg gttccctcct tgggggccc 6600

cagggaacaa gtcacctgtc ctttgcatag gggagccctt cagctatgtg cagaaggttc 6660

tgctctgccc cttcctccct ctaggtgctc agctcctcca gcccactagt cagatgtgag 6720

gctgccccag accctgggca gggtcatttc tgtccactga cctttgggat gggagatgag 6780

ctcttggccc ctgagagtcc aagggctggt gtggtgaaac ccgcacaggg tggaagtggg 6840

catccctgtc ccaggggagc ccccagggac tctggtcact gggcttgccg ctggcatgct 6900

cagtcctcca gcacttactg acaccagcat ctactgacac caacatttac aaacaccgac 6960

attgaccgac accgacattt accgacactg acatttacca acactgttta ccaacactga 7020

catctactga cactggcatc taccaacact gacatttacc gacactgaca tttaccaaca 7080

ctatttacca acactgacat ctactgacat tggcatctac caacaccaac atttaccgac 7140

accaacattt accaacactg aaatttaccg acaccgacat ttaccgacac cgtttaccaa 7200

caccgacgtt taccgacacc gacatttacc gacactgata tttaccaaca ctgacatcta 7260

ctgacgctgg catctactga caccgatgcc agcatctacc aacaccgaca tttaccaaca 7320

ctgacattta ctgacactga tatctactga cactggcatc tactgacacc aacatttacc 7380

aacaccagca tctaccaaca ccgacattta ccaacaccag catttaccaa caccgatgtt 7440

taccaacgcc gacgtttacc gacgccagca tctaccaaca ctgacattta ccgacaccga 7500

catttaccga cactgacatt tactgacact gacatctact gatactggca tctaccgaca 7560

ctgatattta ccaacgccag catctactga cactgatgtt taccaacacc gacatttacg 7620

agcaccgaca tttactgaca ccaatattta ctgacatcaa catttagcca tgtgatgggg 7680

gccggcttgg gggcaggcct tgctcttggc actggggatg ctgcagagac cagacagact 7740

catggggtca tggacttctg cttcttctcc agcctcatgt actggacaga ctggggagag 7800

aaccctaaaa tcgagtgtgc caacttggat gggcaggagc ggcgtgtgct ggtcaatgcc 7860

tccctcgggt ggcccaacgg cctggccctg gacctgcagg aggggaagct ctactgggga 7920

gacgccaaga cagacaagat cgaggtgagg ctcctgtgga catgtttgat ccaggaggcc 7980

aggcccagcc acccccctgca gccagatgta cgtattggcg aggcaccgat gggtgcctgt 8040

gctctgctat ttggccacat ggaatgcttg agaaaatagt tacaatactt tctgacaaaa 8100

acgccttgag agggtagcgc tatacaacgt cctgtggtta cgtaagatgt tatcattcgg 8160

ccaggtgcct gtagacacag ctacttggag actgaggtgg gaggatcgct ggagtccaag 8220

agtttgaggc cagcccgggc aaaggggaca caggaatcct ctgcactgct tttgccactt 8280

actgtgagat ttaaattatt tcacaataca aaattaagac aaaaagttaa tcacatatcc 8340

actgccctgc ttaagacaga aaacatgggt gttgttgaag ccagaggcag ctgctggcct 8400

gagtttggtg attggttcct aagcagttga aggcagtttt gtttttccat agatgtctgt 8460

tctccctttg ctgggtgcag cctcgccctg ctgctgtggt cgggtttcag tggcctcgtc 8520

ccgtggacgc agcctcgccc tgccgctgtg gtcgggtttc agtggcctcg tcccgtggac 8580

gcagcctcgc cctgctgctg tggtcgggtt tcagtggcct cgtcccgtgg acgcagcctc 8640

gccctgccgc tgtggtcggg tttcagtggc ctcgtcccgt ggacgcagcc tcgccctgcc 8700

gctgtggtcg ggtttcagtg gcctcgtccc atgggcgtgc tttggcagct ttttgctcac 8760

ctgtggagcc tctcttgagc ttttttgttt gttgtttgtt tttgtttgat tttgtttgat 8820

tgtttgtttt tgttgtcgtt gttgttgccc aggctggagt gcagtggcgc gatctcagct 8880

cactgaaacc tctgcctcct tgggttcatg ccattctcct gcctcagcct cccacatagc 8940

tgggattaca agtgcccgcc accacgcctg gctaaatttt gtatttttag tagacagggg 9000

gtttcaccat gttggtcagg ctggtctgga actcctggtc tcacatgatc cacctgcctc 9060

ggcctcccaa agtgttggga ttacaggcgt gagccaccgc gcccagcctc tgttgagcat 9120

attttgaggt tctcttggtg ccagtgatat gtacatgtgt ccccatcgca ccatcgtcac 9180

ccattgaggt gacattggtg cctctcctcg gggtggatgc ctccctctgt ttccagcaac 9240

ttctgaagga ttttcctgag ctgcatcagt ccttgttgac gtcaccatcg gggtcacctt 9300

tgctctcctc agggctccca ggggaggccc gaatcaggca gcttgcaggg cagggcagga 9360

tggagaacac gagtgtgtgt ctgtgttgca ggatttcaga ccctgcttct gagcgggagg 9420

agtctcagca ccttcagggt ggggaaccca gggatggggg aggctgagtg gacgcccttc 9480

ccacgaaaac cctaggagct gcaggtgtgg ccatttcctg ctggagctcc ttgtaaatgt 9540

tttgtttttg gcaaggccca tgtttgcggg ccgctgagga tgatttgcct tcacgcatcc 9600

ccgctacccg tgggagcagg tcagggactc gcgtgtctgt ggcacaccag gcctgtgaca 9660

ggcgttgttc catgtactgt ctcagcagtg gttttcttga gacagggtct cgctcgctca 9720

cccaggcgag agtgcagtgg cgcaatcacg gctcgctgta gcctcaatct ccctgggctc 9780

aggtgatcct cctgcctcac cctctgagta gctgggacta cagacacata ccaccacacc 9840

cagctagttt ttgtgtattt tttgtggggg gagatggggt ttcgctgtgg tgcccaagct 9900

gatctcaaac tcctgaggca caagcgatcc acctgcctcg gcctcccaaa gtgctgggat 9960

gacaggcatc agccgtcaca cgcagctcaa tgattttatt gtggtaaaat aaacatagca 10020

caaaattgat gattttaacc attttaaagt gaacagttca ggctgggcgt ggtggcttat 10080

gcttgtaatc ccagtacttt gagaggctga ggtgggcaga tcacctgagg tcaggagttt 10140

gagaccagcc tggccaacat gatgaaatcc agtctctact aaaaatacaa aaattagccg 10200

ggcatggtgg caggtgcctg taatcccagc tactcgggag gctgaggcag gagaatcgct 10260

tgagcccggg aggtggaggt tgcagtgatc tgagatcatg ccactgcact ccaatctgtg 10320

tgacagagca agactctgtc ttgaaaaata aataaataaa aaaaatttta aaaagtgaac 10380

aattcagggc atttagtatg aggacaatgt ggtgcaggta tctctgctac tatctacttc 10440

tagaacactt tctttctgccc tgaaggaaac cccatgccca ccggcactca cgcccattct 10500

cccctctctc ccagcctctg tcaaccacta atctactttc tgtctctggg ggttcacttc 10560

ttctggacgt tttgtgtgac tggaatcctg caatatgtgg tccctgcgtg tggcttcttt 10620

ccatagcatt gtgttttcca gattcaccca cacattgtcg cacgttatca gaatctcatt 10680

cctgactggg tgcagtgggt taggcctgta atcctaacat tctgggaggc caaggcggga 10740

cgatcacttg aggcaggagt ttgagaccag cctggccagc ctagcaagac cccagctacc 10800

aaaaaatttt aaaagttaac tgaacgtggt ggtggtgggc acttgtggtt cccagctacc 10860

tgggaggctg aggtgggagg atcgcttaag cccaggaggt caaggctgca gtgagctatg 10920

atcgcaccac tgcactccag cctggacaac agagcaagac cctgtctgaa aaaaaaaaca 10980

aaaaaaaaag ttcctttctt tttgtggctg gatgacatcc cattgtatgg ccacagcaca 11040

ttttgtttgt ctgtttatcg ggtggtgggc agtggtttcc acctttgtc tcctgtgaat 11100

aatgctgctg tgaacatttg aattcaagtt tttgtttgaa cacctgttgt gaattatttg 11160

gatatatgtg taggggtagg attgctgagt cctatggtaa tgttaggttt gacttactga 11220

ggaaccatta aactgttttc aacagtggct gcgccgttct gcatccccac cggcagtgtg 11280

tgagggttct gactttacct cctcacaaac gcttcttttc catttaaaaa aatattcagc 11340

caggtgctct ggctcacgcc tgtaatccca gcactttggg aggccgtggc gggcggatca 11400

cctgaggtca ggagttcgag acgagcctgg ccaacatggt gtaaccccat ctctaccaaa 11460

aatataaaaa ttagccgggt gtggcagcgg gcgcctgtaa tcccagctac ttgggaggct 11520

gaggcaggag aatcacttga acccgggagg cagaggttgc agtgagccaa gatcgcgcca 11580

ctacactcca gcctgggtga caagagtgaa actccatcta aaataaaaca aaaataaaaa 11640

taaataaaaa tttattaaaa cattcatcac agccagccta gtgggtgtcc catgtggctt 11700

tgcctcgcat ttccctgata actaggatgc tgagcgtctt gtcccaggct tgccacacct 11760

cagcactttg agatacgtcg cacagtcccc atttgcgaac gagaaatgag gtttagggaa 11820

cagcagctgt gtcatgtcac acagcgagca gggggtctct gagccgtctg accccacagc 11880

cgaccaagct ccaatcctta ccgcctccta gtgttgtgga tgtagcccag ggtgctccca 11940

catttttcag atgagaacac cgaagctcaa aacaggagcg ttttgtccac attggataca 12000

cgatgtctgt ggtttggtcc tgaagtcact ttatatctca gtggtccaga ctggagtagg 12060

acaggggggtt ctggggaatg gggaaggtgt ctcaggtgaa aggaaggaat tccagattct 12120

ccatactgtc cttgggaagt tagaagactc agagggtctg gcaaagtcag acaaagcaag 12180

agaaatgcag tcaggaggaa gcggagctgt ccaggaacag gggggtcgca ggagctcacc 12240

cccaggaact acacttgctg gggccttcgt gtcacaatga cgtgagcact gcgtgttgat 12300

tacccacttt ttttttttt ttgaggtgga gtctcgctct cttgcccagt ctggagtgca 12360

gtggcacgat ctcggctcac tgcaagctct gcctcccggg ttcatgccat tctcctgcct 12420

cagcctcccg cgtagctggg actacaggcg cctgccaccg cgcccggcta atttttgtat 12480

ttttagtaga gatgggattt cactacatta gccaggatgg tctcgatctc ctgacctcat 12540

gatccgcccg tctcggcctc ccaaagtgct gggattacag gcgtgagcca ccgcgcccgg 12600

cccgatttcc cactttaaga atctgtctgt acatcctcaa agccctatac acagtgctgg 12660

gttgctatag ggaatatgag gcttacaggc catggtgctg gacacacaga agggacggag 12720

gtcaggaggt agaagggcgg agagagggaa caggcggagg tcacatcctt ggctttcaaa 12780

atgggccagg gagagacacc ctctgagcat ggtaggacag gaaagcaaga ttggaacaca 12840

ttgagagcaa ccgaggtggc tgggcgtggt ggcttacgcc tgtaatccca acactttgga 12900

aagctgaggt gggtggattg cttgaggcca ggagttcaag accagcctgg ccaacatggt 12960

gagaccccgt ctctactaaa tatacaaaaa ttagccaggc gtgatggtgc atacctgtaa 13020

tcccagctgc ttgggaggct gaggcaggag aattgcttaa acctgggagg cggaggttgc 13080

agtgagccga gatcccgcca ctgcactcca gcctgggcca cagagtgaga ctccatctca 13140

aaaaaaaaaa aaaaaaaaga taaaaagacc aaccgaggaa ttgaagtggg ggggcgtcac 13200

agtagcagaa gggggatcgt ggagcaggcc accctgtggt catgcactgg aagctcatta 13260

cctgacgatt tggagctcat cactgggggc ctaaggagaa tagatactga aggatgagga 13320

gtgatggcgc ggggcacggg tgtctttggt ggccagaact tggggactgc tggggtgcct 13380

cactgcaggc cttctcagcg ccctttatat gcttacacag gctgtttcta agaggggat 13440

acattgcata agcgttttca gactacctca tcatgggtcc ctttctttac cctctgtggc 13500

cctggtggcg cactctctgg gaaggtgcag gtggatgccc agacccgccc tgccatccac 13560

ctgcacgtcc agagctgact tagcctcgag attgctgctg gcacctcctg ccccgggaca 13620

cctcggatgt gcccgtggag atgctggctc tgtgttttct gctggagttt ggtgcgtctt 13680

ttcctcctgc aagtggccac cgctcttggg tatgtcctca ggcttctgcg agtcatggct 13740

gcttctcagg tccttgccca gcgccaggag caaaccctcc tggcactttg ttcaggggtg 13800

gatgcgccag tgttcctgct gtggaccccc atctcacatg agggtcttgg gcctgcaggc 13860

tcgttcagga aacacccgct gagtacgcag tgtgtgccag ctgtgtccca ggcaatggcg 13920

gggacagtgg ctgctgctgg ggttgtggtg gcttctgggg actctgggga cagctgaggt 13980

gcaaggagcc acggctcctt gaggatgcag ttggactcca ggtggaaggg atggttgggg 14040

gaggtataaa tggggtcagg gaggagacac atttggaaca atgggaacat ttttaagatg 14100

ctatgtcggg aggcaacaag gtggccaacc caggtgctga ggagcccaca ccagccctgg 14160

acgtgttttg ccgctcacct ttgctgggga gtggtgggag agaggattcc gttccacgtg 14220

gtggtgtgcg cagctgggct gtgtggagct gggcgctagg aggaaggtgc tttctgcggg 14280

gctagccggg ctctgccttt gaacacaatc aggctccagg ttttcagcat ccagtgcatg 14340

agaggacttc acgggcagct gtggctgatc ccttgatgaa ttgggagaag aacaaaggtc 14400

tatgaaatga ggtttcatgt agatggcatt agagacgccc acaacagatt tacagagtgg 14460

agcggagacg gcggatgggt ctgggaggcc cctcctgctg gccttgactg tgacagctgt 14520

cctgggaatc agcttccagg ccgccccagc agcctgactg acacacacag gggttttagc 14580

cccatcctgc gaccagctgt tgccatcatc agtgacagct gggagtggcg gtggttccag 14640

ccctgggcac cctccccacc tgctggggcc cacccagggc agtcctgaca cctacaggtt 14700

gcttggagcc gcatccgagt cctgccccac cacgtgtgaa gcccgagtgg tcgtgggctg 14760

aggtcccctg attgcatccc cacttccctt ctgcttcaca tagctgcctc ttctcaccgt 14820

ttttccagcc tcctgggcta ggaattccag tgttgtgctg gctttgcccc aggacacctc 14880

cttagccctc ttcctgagtc tagagccccg ggggttggaa gttctggccc ctgggacacc 14940

tgcagccaca ctcagcttct cctgtgagcc tccagcatgt cccctcagga ccaagccctc 15000

acgttcttgc ctccccgccc acctgggctc agccagggga aggcctggct gggagcgtct 15060

ccccctctgcc ctgcccttct cccctctacc ctgcccttct ctcctctgcc ccgccatggc 15120

ttttatatcc tgtgccacaa gacatggctg tgtgtgaaag tggcagggtc tggcatctct 15180

gtgggtctct gaggcccacg ctccagtgcc actcttccca cccgctggcc gtgccctcat 15240

gctggaggga cagcccagcc ctctcccgaa ccccagcccc atgtgcccag ctgccccccgg 15300

ccctctcccc tggaagccgg ggtcactcca gccgtatgcc atggtgggga catcctgctt 15360

ccttggcctt ccagggaagg tcctctttcc aaatggcgac acctggtccc tgcctggagg 15420

ctggaagctg tggcccttgt atgcccctcc agggtctgtg cgctcggttg gcccgagttc 15480

ccatcaccgt catcatcacc atcatcattg tcatttcgct tgtctgtgag ccggcctggt 15540

ctcccagagc agagaccctc tgaggtccag cctgagttgg ggtctccgtg ctgaccctg 15600

acggggactc aggacgtacc aggtctgggt caggagtgac ccccaaacct cgtgcccttt 15660

gacaggcacc cctgactttt gctaagtggg tggaggtgac atcacttaca gcgggagtga 15720

tgggacaggg tctgttggct gcactgtgct cccagggatc tggggagagg ctatatccct 15780

gggctttggc actgcagagc tgtgtgtgtt tgtgtgtgtg tgtgtgtgtg tgtgtgtgtg 15840

tgtgtgtgtg tgtgtgtgtg tttgcgtgcg cgcacatgtg tataagatct ttttttatta 15900

catgaagcaa gataactgtt gctgtttcct tttgggtttt gtgttcaaca gagtggggta 15960

cttcttccct cagacaacag aactctcccc tttaaacacg tgctgtcaga gggtgggtct 16020

tgggctcatg tctgtttgca cagccgagtc agaggaaaca cagggttctt cataaaaaca 16080

ctgcacagca ggcgactgtc cagagtcagc ctgcaggacg gcagcagccc tgcccctcag 16140

agcacagcta gggtgggctg ctttgggatc tcccgtcatt ccctcccagc tggcagccgg 16200

cggccggccc attccttggt gtgctggtca gggggggcgtg cgcctgctct gctcaccctg 16260

ggaatgggac agaagctggc agctcggaga ggacagggct ggacccttgg gtggcctctg 16320

gctggaccat ctcattgtcc tcagacacag cctctcgggt ctagtttcat ttcctgaaaa 16380

acaagtgcac agaactagag caggagtcga gagctacggc ccccgggcca gatccagccc 16440

tgccacctgt tttcacacca tgctcaagct gagtgggttt tacatttttt aattacttga 16500

aaaaaaaaaa gccaaaggag gtttcatgac ccatgaaaat tatatggaat tcaaaaaaaa 16560

aaaattatat ggaattcaaa tttcagtgtc cataaataat ttcttgagac agggtctcgc 16620

tctgtcaccc aggctggagt gcagtgctat ggcatggctc gctgtaccct tgacctccca 16680

ggctcaagcg atcctcctgt ctcagcctcc tgagtagctg ggactacggg tgtgtgccac 16740

caagcccggc taatttttt ttaattttag taaagacagg gtctttctat gttgcccagg 16800

cttttctgga actccatctt ggcctcccaa agtgctggga ttacaggctc gagccacgga 16860

gcccagcctg tttttgtttt ttcactgata aagttttgcc gggtgtggta gtgtgtgcct 16920

ctagcgattt gggaggctga ggtgggagga tcgcttaagc ccaggagttt gaggctgggc 16980

tcaagtgatc aggaggtgaa ctatgatcat gtcattgcat tccagcctgg gtgacagagc 17040

aagaacctat ctcttaaaaa tatatattta aaaagtattg ggtgtggtgg ctcacgcctg 17100

tggtcccagc tacttaggca tctgaggtgg gaggatggct tgagcccagg agtttgaggt 17160

tgcagcgagc caagatcgtg tcactacact ctagcctggg tgacagagcc cagaccctgc 17220

ctctttaaaa aaaaaaacca aaaaacatgt attggaacac agccatgcct gttcagtcac 17280

gtgctctcca tgctgctttc tgctccagag acccttatgg cctgaaagct gaaaatattt 17340

tctatccttt acaaaaaagt ttgctgacct ctgtcctgga aaattcatct cccaagttct 17400

cttccggcac tggcgttcct gggtgtccta aatttggccc ctgttatttc tgaactctgt 17460

tttggctctg ttccctccca ggagccagga caggcacgtt ctctgcatct tgtcccctga 17520

cgcccagagg cttggctcgg ctcaggcatt cttggaaata tctggctcca ggaaaggcag 17580

aggcctcctg agtcagccca gagggaacct gccccaggtc tgggggaggc ctgacccagc 17640

agagtggctt ttgccgatgg gttgggccgg tcaagatgtg ctgaaagttg tcctcagaag 17700

gccactttgg gattccttcc tccagtatta gagcaactga gagctgctca ttgcaagcct 17760

gatgttttcc cagttggccg ggtccaccgg gtgccctggg attctgggat ctgggtggaa 17820

agtaggggggc ttgggggagt gtcctgggtt ctggaatcca ggtggcaagt ggtgaggttc 17880

agggagtggc ttctgagcca ccataggggt ctctgtggga ggctctgccc atccaggaga 17940

ttccgcaggc cctgccggcc cagagccagc gtcttgcgct tgccgaggct acagccagcc 18000

ccagccgggt ggaacagccc gtcgcctcct ctcactttgt tttggggcca cctgggagtg 18060

tggagcaagg gtagagaggg aggaagtggc tgccggccgc tgcccagcac ccttgtttgc 18120

cttgggccct ctgtgggctc ctttttattg ctcttcaatg aagccaggga aatggacttc 18180

cttgcctcac ttcagttcaa catgtctgga agtttggtat taaaattaag aaagtgtgga 18240

aatagagcaa gaagagaaaa atctctccaa gagataatag tgacctctga gctgggcgcg 18300

gtggctcacg cctgtaaatc ccagtacttt gggaggctga ggcgggcaga tcacctgagg 18360

tcgggagttt gtgaccggcc tgaccaagat ggagaaaccc cgtctctact aaaaataaat 18420

aaataaataa ataaataaat acaaaattag ccaggcatgg tggcgcctgc ctataatccc 18480

agctaaggca ggagaatcgc ttgaacctgg gaggcaaagg ttgcagtgag ccaagatcac 18540

gccattgcac tctagtctgg gcaacaagag tgaaactccg tctcaaaaaa aataaataaa 18600

taaaaaataa aaatagtgac ctctggccag gtgtggcagc tcatacccgt aatcccagca 18660

ctttggaagg aaggccgaga tgggcagatt gctttagcac aggagtttga gaccagcctg 18720

gccaacatgg tggaacccca tctctacaaa aatagaataa aatttaagag gtaatagtga 18780

ccttttggta gatcgaaacc tggattgctt tctttttcta aatgctgatt cttttctttg 18840

tggtgtttgt gttctgtgcc gatgtccctc ccccagccct gttattgtga gtggaagaag 18900

gggaaagggt tcgcccgcta ctgtgagccc ctcctctcac gctgggtgtc cttggagaag 18960

cctgcacttc ttcattgtac gccagggctg ggtccctccc tggagtggtt ctgtgctgct 19020

gggatggggc caacccctca gatgttttct gagtgtcaca cacaggtgtg tgcattcatg 19080

gcctttgcgt gtcttcctgt tgtggaggca aaaatgtgaa gaaccctaga tgattttggg 19140

accagggctc catcacctgc tgttcattgc acaccggagc atccaggcat gggtggagag 19200

ctcagacttc caggcacggt cgcaggggct ggtctaacca tgttcccgcc cgcctgctcg 19260

tcagaaccgc ctgttgggag ctgttatcat gataccatac ctgggccctg ggctatccga 19320

ttctgactta attgctccag gttggggcca ggccgttgtt tgctgttttg ttgtttcttc 19380

tgtgacgtta gccactgggc taatctgagc ccctcagtta caggtggaga aactgagacc 19440

catgggggtg caaggacttg ccgaggaccc agagcccctt gggggcagag ctgaggcggg 19500

gcctggcttt gggtcccaga gcttccagtc cccttcccgc tctcctaaca gctttttttt 19560

ttgagacaag atctcaccct gtcacccagg ctggagtgca atggcatgat ctcggctcac 19620

tgcaatcttc gctagctgcg ttccagcgat tctcctgcct cagcctcccg agcagctggg 19680

attacaggtg tgtgccgcca tgcccagctc gttttttttt gtacttttag tagagatagg 19740

gtttcaccat gttggccagg ctgatctcga actcctgacc tcaaatgatc cgcctgcctc 19800

ggcctcccaa agtgctagga ttacaggctg ggatcacact gtgcctggcc ctagcagctt 19860

tgtcctgtgc catccaacaa cagatgaccg aagtctttgt ttcttaacat gcattccatc 19920

tgccttacag ttttgccacc tgcaaaacag aggacttgtc gcttttctgg taagctggaa 19980

atgtaatctg gtagcaggag gcctgtggaa gcttgccttt aatggccttg tgtctctttc 20040

atcctgtcct gagagccgga gaacttggat gttgcaccta actcaacctt cctgttaaca 20100

tacagttctg caggctcatg gatcatcaga accacgtcct atctcacgcg gctgtatgct 20160

tccgttggtt caggtgtttt taccttgaca gtattttctc ctcggtggct tttgcggtgg 20220

ttgcttttaa tcagcattga ctcttcaaga aaaatattta gctgctacat ctcagaggag 20280

acagggtgga aagcatctga gacctgcagg ctcagactta gaaccagaag tgccctcaga 20340

gttcatccgg ccctgaccca gcgggaaatg agttcacaga gaagcgggag aactttgccc 20400

caggccctgc cgttgctcat aactgcccca ggtccttaca tttgctccag gtcctgcccc 20460

aggccctgca gttgctcata actgccccag gtccttatat ttgctccagg tcctgcccca 20520

ggtcctgcag ttgctctgtg tggtgggtgt gatctggagc cctccgccca ttgctgcacc 20580

tggggcaggc attgctaatt gatcccagga ctccttcctg cggagcacgc cctggttctc 20640

caggcagccg ctgcctgtca gcctgcagtg gttcgggaga ggacacctgc ttgcctggtc 20700

tgttccaaat cttgcttctc atcccagcac aggtaggggg tgctatggga aagggatcct 20760

cagttggccc tgtcactgct ctatcagctg gggacgtggc atcctagtga aaacatcatg 20820

gccgggcgcg gtggctcacg cctggaatcc cagcactttg ggaggctgag gagggtggat 20880

cacttgaggt cagaagttcg agaccagcct ggtcaacatg gtgaaaccca tctctactaa 20940

aaatacaaaa attcgccagg tgtggtggcg ggtacctgta atccgagcta ctcgggaggc 21000

tgaggcagga gaatcgcttg aacctgggag gtggagcttg cagtgagccg agatcttgcc 21060

actgcactcc agcctgggca acagagtgag acgctgtctc aaaatctcaa acaaacaaac 21120

aaacaaaaaa caaacaaaca aagcgtcatt tatccagcac ccctggggaa ccatgctacc 21180

tggtgtttta tggtacctgg caaggtgcag gtgaagttgc tgctcttggg cattgaaccc 21240

gtcttgtttg gggcagctca ggccccaggc agggtccggg ttggctctcg ttggtgtggc 21300

cctggcccat ccagacctat atttctgccg tcctgcaggt gatcaatgtt gatgggacga 21360

agaggcggac cctcctggag gacaagctcc cgcacatttt cgggttcacg ctgctggggg 21420

acttcatcta ctggactgac tggcagcgcc gcagcatcga gcgggtgcac aaggtcaagg 21480

ccagccggga cgtcatcatt gaccagctgc ccgacctgat ggggctcaaa gctgtgaatg 21540

tggccaaggt cgtcggtgag tccgggggct cccaagccat ggctcagcca tgcagacttg 21600

catgaggagg aagtgacggg tccatgcctg ggcataagtg ttgagctcag gtgccccgac 21660

ctggggaagg gcaggacagg aaaggtgaca gtatctggcc aaggacagat gggaagggac 21720

caagggagct gattagggag tggttatgga ctaggaatgt cggtaacaat ggttagaaag 21780

tgactaacat ttgttgagca cctgctgtgt gcccggccct ggccgggagc cttcgtgccc 21840

acagtgaccc cgtctgcaaa tgtagttcct tgccctactc gcactgggga gcaggacgca 21900

gagccgtgca tctcacaggt gccaagctca ggactccctc ctgggtctgc ctgggctggg 21960

ctgtgcttgt tgcccctgtg gcccacgcat gtgcaccttc cacctgaaag ccaggatctt 22020

caggacgctc cccgaggagg tcgttgtctg gcacaatgat ttgtctcttc ctgaaaaggt 22080

gacagagtta cactggagag agcagcatcc aggtgcggca gggacaggcc tggggctcgc 22140

gggcagggac tctgtgtcct gccggggtcc cacactgcac ctgcttgtca gaggcactca 22200

gtcaatcttt gctgatgaag gatgagagga cagaggacgt gatgcttgct gctgcattgc 22260

ctgcagtcct gggtgagatg cccgggttga ctctgctgcc cgtcgggtgg atgtgatgtc 22320

agatccccgg ctttaaaata cgagggagct gggaattgag ggagcaggtt ggggcagaaa 22380

gcacagcccc gtggaagcct ggagctgagg cagtgtgggc gacccctgga gcagtgagtg 22440

cttccttcat ggccttcatc gcaccctgca gtcctcatgt aggggatgcc atccatgaat 22500

ttagttttcc cagcctcctt taaaaacgcg ttcatgctgg ggccggggca gtgcagtggc 22560

tcacatctga aatcccacca ctttgggagg ccgaggcggg tggatcatga ggtcaggaga 22620

tcgagaccat cctggctaac aaggtgaaac cccgtctcta ctaaaaatac aaaaaattag 22680

ccgggtgcgg tggcgggcgc ctgtagtccc agctactcgg gaggctgagg caggagaatg 22740

gcgtgaaccc gggaagcgga gcttgcagtg agccgagatt gcgccactgc agtccgcagt 22800

ccggcctggg cgacagagcg agactccgtc tcaaaaaaaa aaaaaaaagt acaaaaaaaa 22860

aaaaattagt ctgggtgtgg tatcacgcgc ctataatctc actactcgag aggctgaggc 22920

ggagaattgc ttgaacccag gaggtagagg ttgtagtgag cccgtatcgt accactgccc 22980

tccacctggg caatagagcg agactctgtc tcaaaaagaa aaaaaaaaaa agaacattta 23040

tgccaggtgt ggtggctcat gcctgaaatc ccagaacttt ggaagactga ggcaggagga 23100

tcacttgagc ccagaaattt gagagtgtct tccctgggca acatagagag acctcatctc 23160

taccagaaaa aaaaaaatta gcccggcatg gtggcatatc cctgtggtcc cagctactta 23220

gggggctgac gtggcaggat cacctgagtc tggaggcaga ggttgaagtg agctgagatc 23280

atgccactgc actccagcct gggtgacaga cagagaccct gtctcaaaaa aaaaaaaaaa 23340

aaaaagcatt tactatccac catggaaggt gagactgacc tgtgagtgat tgttcaaaga 23400

acaaaaaata aaccccagag ataagacaaa agggtgcctc catgggggtg tgatttaaag 23460

ctgagaaatt gggcttcttc cccctcccct ctcaccccgt ggtttgctaa aggagatggg 23520

aaaaaggatt ctttttttgg ctgaaatatt taacactaaa ttaaagccaa ttttaacagc 23580

actttggttg atgagtgaaa ttaacagact ggccaaaaat aaacgaacgg tctgtactat 23640

gtgaaaaaga ggcagctttg gccatgctgg gccaatgtga gttttcaggg ttgctgggaa 23700

tgtctgtgaa tcggaggaag ggcctagctg ggactctcag gagccaaggc cctgaggggc 23760

aacttgcctg gtccctgccc tgaggcgttc actgctttct tcctgggcca gatcacaggc 23820

ccggaggctg gaccactggg ctggcactct tgccgagctg ctccctgact tcctgaccat 23880

gctcctttca gcagccttgc tgcactttag tttccttgaa tgaaaaatgg ggatgagaat 23940

agctcctacc tccaaggtga atggagtgag ttcggacagg tgactccctg ggaccagtgc 24000

ctggcgcctg acaaggtcca gtcagagccc gcactgctgt tactgatacc cttggctgta 24060

ccaggggaga acttggttgc cattgccagg tgttctccca ccacccccac tactgtccct 24120

gtttgatgtg tggcgggaat aaagctgtgc acattggagc ttttggcaca tcctggcttt 24180

caggtgaaag gtgcgtgtgt gtttgagggt ttagcctggc caacccagcc atgaggtcgg 24240

acctgacctg ggggtgagtc ctgagctcgg caccccctgag ctgtgtggct cacggcagca 24300

ttcattgtgt ggcttggccg caccccttтc cctgctgggc tgttgatgtt tagactggag 24360

cctctgtgtt cgcttccagg aaccaacccg tgtgcggaca ggaacggggg gtgcagccac 24420

ctgtgcttct tcacacccca cgcaacccgg tgtggctgcc ccatcggcct ggagctgctg 24480

agtgacatga agacctgcat cgtgcctgag gccttcttgg tcttcaccag cagagccgcc 24540

atccacagga tctccctcga gaccaataac aacgacgtgg ccatcccgct cacgggcgtc 24600

aaggaggcct cagccctgga ctttgatgtg tccaacaacc acatctactg gacagacgtc 24660

agcctgaagg tagcgtgggc cagaacgtgc acacaggcag cctttatggg aaaaccttgc 24720

ctctgttcct gcctcaaagg cttcagacac ttttcttaaa gcactatcgt atttattgta 24780

acgcagttca agctaatcaa atatgagcaa gcctatttaa aaaaaaaaaa gatgattata 24840

atgagcaagt ccggtagaca cacataaggg cttttgtgaa atgcttgtgt gaatgtgaaa 24900

tatttgttgt ccgttgagct tgacttcaga caccccaccc actcccttgt cggtgcccgt 24960

ttgctcagca gactctttct tcatttatag tgcaaatgta aacatccagg acaaatacag 25020

gaagactttt ttttttttt tttgagacag agtcttactc tgttgcccag gctggagtac 25080

cgtagcgtga gctcagctca ctgcaacctc cgcctcccag gttcaagcga ttcttctgcc 25140

tcagcctcct gagtagctgg gactacagac atgcaccacc acacccagct aatttttttt 25200

atatttttag tagagacagg gtttcatcat gttggccagg ctggtcttga actcctgacc 25260

tcaggtgatc tgcccgcctc ggcctcccaa agtgctgaga taacaggtgt gagccaccgt 25320

tcccggcata ggaaaacttt ttgccttcta aagaagagtt tagcaaacta gtctgtgggc 25380

tggccttctg attctgtaaa gaaagtttga ttggtggctg ggtgcggtgg ctcacacctg 25440

taatcccatc actttgggag gccgacgtgg gcatatcacc tgatgtcggg acttcgagac 25500

cagcctcacc aacgtggaga aaccccgtct ctactaaaaa tacaaaaaaa aaattaaccg 25560

ggcatggcgg cgcctgcctg taatcgcagc tactcaggag gctgaagcag gagaattgct 25620

tgaacctggg aggcggaggt tgtggtgagc tgagatggca ccattgcact ccagcctggg 25680

caacaaaagt gaaactccgt ctcagaaaaa aaaaagtttg attggtgtaa ccaaagcgca 25740

tttgtttatg gattgtctgt ggcagctttt gttctgccga gatgagttgt gacagatctg 25800

tatgggctct aaagcctaaa acatgtgcca tccgcccctt tacagaaaaa gtgtgctgac 25860

ctctgttcta aagtattgga caactacaat gtttgctcat ttattattct atgatttgtt 25920

ttctgctttt tgttgttgtt gttgttgttg agatagggtt tccctctgtc actcaggctg 25980

gagtgcagtg gtgtaatctc agctcactgc agcctcgacc tcctgggctc tagtgatcct 26040

ctcatctcag cctccctagt agctgggact acaggcacac accaccactc ctggctgatt 26100

ttttttttt ttttttttt ttgtggagac agggtttccg catgttgccc aggctggttt 26160

caaactccta ggctcaaaca cccacctcag cctcccaaag tgctgggatt acaggcgtga 26220

gccaccatgc ccagcctatt ctactgtttg tattacatag ctttaaaaga ttttttatga 26280

ctttaagtca caagggttct ttgtagaaaa aaatatatat ataggaaagt ataaaaagaa 26340

agtaaaaatt gtccataacc tctccagcca gagacgaccg ttgctgacac ctcagcatat 26400

tgcctttaag tctttttttct ctaagatagc atttctcttc atcacagtca tatgctacgc 26460

agaattctgt atcctgattt tttcacttga cattacaaca ggtatttgat ggcgctgtga 26520

caaactcttt ggcacaatct tttaaatgta tgaaatactc cactgcacag atgtttgctt 26580

ttaggcttaa ctgttctttt attttgcgtg tgctggttac agccgggcac agtggctcat 26640

gcctgtaatc acaacacttt gagagggtga ggcaggagga tcacttgagc ccagaagttt 26700

gagaccggcc tgggcaacat agtgagaccc catctctaca aaaaactttt ttaataagtc 26760

gggcgtagtg gtgcatagct gtagtcccag ccaccaagga ggctgagttg ggaggattgc 26820

ttgagcccca ggaggttgat gctgcagtga cctgagatta ctccactgta ctccaacctg 26880

agcgacagag caagacttgt ctggggaaaa aaaaaaaaaa aatatatata tatatatata 26940

tatatataca tatatacata cacgcacaca cacataatat aaaaatatat atttataaat 27000

atataatata taatataaaa atatatattt ataaataaaa tttataaatt atatttataa 27060

gtaaatatat aatatataat ataaaaatat atattatata atatataata aaatatataa 27120

tataaaaata tatatttata aataatatat aatacatact tataagtata tatttaaaat 27180

atatgtaatg tatatttttt aatgtatgat atataatata catttataaa tacacattta 27240

tattatttta tataaaatat atataaaatc tccaagttgc tttttccaaa aaggtgtctt 27300

gctgcatttc aaacattcat ttaaaaactt gaatgctggt gatctggtcc agaatgtgtt 27360

cagtagctgc tgccagtggc caagcatctc gggagatgtc tacaaaacac gctggttctg 27420

gcctggcgtg gtggctcacg cctgtaatct cagcactttg ggaggctgag gcaggtggat 27480

caactgaggt ctggatttcg agaccagcct tgccagcttg gtgaaacccc atctctacta 27540

agaatacaaa aaaattagcc aggcgtggtg gcatgtgcct gtaatcccac ctacttggga 27600

ggctaaggct ggagaatcgc ttgaacccag ggggcagagg ttgcagtgag ccgagatcgc 27660

accattgcac tccaggctgg gcaagaagag cgaaactccg tctcaaaaaa aaaaaaaaag 27720

atgctggttc ctaaaatgtg gccctttcc tcctcacctg ctgccagacc atcagccgcg 27780

ccttcatgaa cgggagctcg gtggagcacg tggtggagtt tggccttgac taccccgagg 27840

gcatggccgt tgactggatg ggcaagaacc tctactgggc cgacactggg accaacagaa 27900

tcgaagtggc gcggctggac gggcagttcc ggcaagtcct cgtgtggagg gacttggaca 27960

acccgaggtc gctggccctg gatcccacca aggggtaagt gtttgcctgt cccgtgcgtc 28020

cttgtgttca cctcgtatga gacagtgcgg gggtgccaac tgggcaaggt ggcaggctgt 28080

ccgtgtggcc ctcagtgatt agagctgtac tgatgtcatt agccttgatg gtggccagga 28140

ctggtagggc cctcagaggt catggagttc cttcgtggag cgggtgctga ggctgtatca 28200

ggcacagtgc tggctgcttt cacctgggcc gtctcaccga agtgtccatg gagcctgcgt 28260

agggtgggta tctgtgtcga ttttacagat gcagaaacag gctcagagaa accgagtgac 28320

ttccctaagg tcacataccc agttagagca gagctgggcc aggaagtgct gtctcaggct 28380

cctgaccagg tctccttgct ttgcactctt gccaaaacca tgatccagaa ctgactttga 28440

ggtccccgga cctcaggctc ctccgaaatg gcctcttgga ggctgctgag ccacagctta 28500

ggacccacct cgagaggcaa atgtgctttg agctgccagg cgtcctgggg gccctgcctt 28560

gggcacgggg ttcagacagg ccccagatgt gtggggcgtc tttctggact tgagttttct 28620

tttctgtgtg gtggacacag tgctcacccc ttaaagcacc tgtgatgtgt gcagcagccc 28680

aatccctgcc tgtcgcctgt tctgctaggg aaggaaggaa gacttcagga tggcaggaca 28740

acagaaagag gtccaggttt tagagcaagg gcaggtcaaa cttagaaaat tctggaatga 28800

ggatgtgcat ttcctcttct ggatctgcta aaagaagagg gaaggagggg ctgctggggg 28860

aggagcccag agccgagttt acatccggat cccgcaaggc ctcccctgcc ctgaggtctt 28920

gttttgtgat gtgcttgtgt ccatcctggt ttctgccgtg tccccaacat ccggccaagc 28980

ttaggtggat gttccagcac acactcaccc tgtctgtgca cctgtttttg tgtccgtaag 29040

tgggtattta ctcaccttac gagtgagcca ctgtgggaat tcagggaggt ggcgcagtga 29100

ccacccctgg agggatatgt gtgtggcagg ggtcgagggt ctcgcccttc cctgcttcct 29160

gcgcgtggct ttctccagga cggggagggc tgagctgaag aggtggggac agttgcgtcc 29220

ccccgccacc cactgtcctg cggtgagagc agactcactg agcctgccct tctcccttgt 29280

gccttccagc tacatctact ggaccgagtg gggcggcaag ccgaggatcg tgcgggcctt 29340

catggacggg accaactgca tgacgctggt ggacaaggtg ggccgggcca acgacctcac 29400

cattgactac gctgaccagc gcctctactg gaccgacctg gacaccaaca tgatcgagtc 29460

gtccaacatg ctgggtgagg gccgggctgg ggccttctgg tcatggaggg cggggcagcc 29520

gggcgttggc cacctcccag cctcgccgca cgtaccctgt ggcctgcaag ttccccaacc 29580

tggcaggagc tgtggccaca cccacgactg cccagcagcc tcaccctctg ctgtgggagt 29640

tgtccccgtc cacccctggg tgcctttgct gcagttatgt cgggagaggc tctggtgaca 29700

gctgtttcct gtgcacctgc tgggcactag gtcccagcta atccctgtgc caggactcta 29760

atttcaccct aacacacatg gtggttttca ttgctgggga agctgaggcc tgagcacatg 29820

acttgcctta ggtcacatag ctggtgagtt caggatcccc cagagatacc agggccagca 29880

ctcgatcccc acccagccct gaaccccacc atgtgctggg attgtgctgg gagtgtccac 29940

acgcctggga ccccagggct ggtgctctca tctccttttt ccagatcatg agaatgaggc 30000

tcagggaagt ttgaaaaaaa cctatcccaa gtcacacagc aacaggagca ggatttgaac 30060

ccagaaaagg ggaccgcaca ctctgttctg ctagagtagt tagctgtcct gggtgatatg 30120

gcaggtgaca ggggcaactg tgcttaacaa aggaaccccc atccccctg ccaagttggg 30180

agactagaag gtcaggggca gaagctctga agggccaggt gcagtggctg acacctctaa 30240

tcccagcact ttgtgaggcc aaggcgggca gatgatttga gcccaggagt tcaagatcag 30300

cctgggtaat gtagtgagac gccatctcta caaaaaaatt ttttaaaaat tagctgggca 30360

tggtggttca tgcctgtagt ccaagctact tgggaggctc aggtgggagg attgcttgag 30420

cccaggaggt tgaggttgtg gtgagctgtg atcatgccac tgcactccag cctgggcaat 30480

agagtgagac cgtctccaaa aaaaaaaaaa gaagaagaaa aagaagctct gaggctccaa 30540

gtccccaggc acccttggc ttgagggcag acaagggagg agagggtcac ctgggcagcc 30600

ctgacttttg tcccctggca aagggacctt cagtgacctt ggccctagga gagcctctga 30660

gcacgtcagc catgtcgaac cgctcaggaa gggcagcaag aatttggctt ctgacctctg 30720

cctctcctac tcgccatctg cactgggtgt ggttgtgccc attttacaga tgaggaggct 30780

ggggcatcga ccagctgaat gccttgtccc aggtactgcg taggcagagc tggcagttga 30840

accccgtgtc ctggttgtcg ctgggggtgg gctgcaccct gacttgtgag gccagtagca 30900

aggtttgcac gtgacttcgt gaccgtcacc cagctctgca gcacatcccg tgacccagct 30960

catccaggcc gcatgcaaac ctgttgccag gcgagaaacc agtcaccgca cagctgtggt 31020

tgcctgaaat gattaagctc attaatcacc ccggagtgag gacagactca gatgaaaacc 31080

agcaaaagcc ctggaaactc atgtgaccct gccaatgagg gcggccatgt gcattgcagc 31140

ctggccgtca ctcctcggta cgtgttttgg acttaaacgc tccggatgtt tactgagtgc 31200

ttgattaata acatggaagg cctggtctca ttgctgtggg agtgaaggat gcacagccag 31260

gcctgacatg atgagaacaa gaacctggag tctcgctgcc tgggtggtaa tcctggccct 31320

gccacttagc aactgtgtga ctgtagccag gtcacttaat tttgctagat cctgcctgcg 31380

cttcagtgga tcttgctggt tttccaaggt ggccaaacac tttaaggcat tcatgtggtc 31440

gctaggctgc agggttgaac cctggctcac cccgcagggc gccgtgtgct ctgtggcctg 31500

gctgtgcctt tgctgacacc gtgcccgtgt gtgttcatgc aggtcaggag cgggtcgtga 31560

ttgccgacga tctcccgcac ccgttcggtc tgacgcagta cagcgattat atctactgga 31620

cagactggaa tctgcacagc attgagcggg ccgacaagac tagcggccgg aaccgcaccc 31680

tcatccaggg ccacctggac ttcgtgatgg acatcctggt gttccactcc tcccgccagg 31740

atggcctcaa tgactgtatg cacaacaacg ggcagtgtgg gcagctgtgc cttgccatcc 31800

ccggcggcca ccgctgcggc tgcgcctcac actacaccct ggaccccagc agccgcaact 31860

gcagccgtaa gtgcctcatg gtcccccgca cctcactccc tcgttagatc aggctggttc 31920

tgggagctga cgctgaaagg agcttctcat ctggggttcc tgggtgtaca tagatggttg 31980

ggtaggttgt gcactgcaca agctgcatga tgctacctgg gggtccaggt ccaggctgga 32040

tggacttgtt gcttcatcag gacatagata aatggccaaa actcctcagc tggaaggtcc 32100

tgggcaggat ctttgggtgt gaaaaccagt cacaggggaa gggtgcttgc tcatactgcc 32160

agcacagtgc tgagtgcttt ccatagcgct cgtttactcc tcaagcctgg agggtgggga 32220

gtagcatggt cccatttcac gtacaaggaa cccgatgcac agagaggtgt ggcaacccat 32280

ccaaggccat acaactgggg tgggttgagc cggggttgac tgtggcaggc tggctcaaga 32340

gtccctgctc ctgaaccctt gccaggcagc ctggcatcag ctcggggaat ttttgccctg 32400

acccttggaa gcaagtgggc ctctttgttc tcatgtcagt gatgagaaga gtgactttcc 32460

tatggccccc ctggagtaca ggtgtttcct gttggcgggc tcttccccca tgacatcagc 32520

agcgagctgg ttatgattcc ctacgcagaa cttgatagtt tataaagctc tttgtcatcc 32580

aggccccgtt ggagtctcac gcagacctgg tcgcaggcgg ggctggtctt gcctgtccca 32640

gctgcatgga tggggaactt gaggcttgca aaggttaagg ggctgttcga ggcccaggct 32700

ggcaggagat gggcctgggc cagagtctgg gacttcccat gcctgggctg tctttggtcc 32760

tgttgctcac catccctccc tggggccatg accttagaga gccaaatgga ggtgcaggta 32820

acccacggca aggaggggtt gccatgactc agagtccccg tcctgtggcc ggcagtacct 32880

ggtgcaacga cttggatttc agaccagcca ctgtagcccg ctgacggtgc gctcgaagtg 32940

ccacagcttc tgaagccagg caggactcag gccaggagac tctgttagct gttgagaggg 33000

agaggccaac ggatgttctg gttctgctag agagctggtt cttcggatcc tggtaccagt 33060

gcactgagag gaggcccagc ttgattctgg ggctgccttg tggtggcatg tgctgctcac 33120

tgacaccctc gaggagtgtc ttctctcggg cttgttgact gtgcccggtt ttccgcagtt 33180

cactggtgca cacataggca catagcaaac cgcacacaca gtcgtgggta tgagtttcac 33240

tacattccac caccagtgtt cactaccatt acctgccttc cgtcttaagt gttcatcatt 33300

taaaaataaa tttattgggc tggacgcggt ggctcatgac tgttatccca gcactttggg 33360

aggctgaggc gggcagatca cctgaggtca ggagttcaag accagcctgg ccaatatggt 33420

gaaactccat ctctactaaa aatacaaaat tagctgggca tggtggggca tgcctataat 33480

cccagctact caggaggctg aggcaggaga atggcgtgaa cccgagaggc agagcttaca 33540

gtgagcccag atagcaccac tgcagtccag cgtgggcaac agtgcgagac tccatctcaa 33600

aaaaaaaata aataaataaa agaaaaataa atttatgatc tatttcaaaa ataacacatg 33660

tactttgaaa cagcagagac acatatgaca cggagaatga aattccccat agcgcagccc 33720

caagagacag ccctggtccc cccgtctttc ccgtggacct ccagcggggc agatgctgag 33780

ccgcctgttg tcgagtggcg tgctatcccg tcctccagct cctctgtggc ttacagacac 33840

ccacctgcag ccctgtcttt gcctcctcta gcgcccacca ccttcttgct gttcagccag 33900

aaatctgcca tcagtcggat gatcccggac gaccagcaca gcccggatct catcctgccc 33960

ctgcatggac tgaggaacgt caaagccatc gactatgacc cactggacaa gttcatctac 34020

tgggtggatg ggcgccagaa catcaagcga gccaaggacg acgggaccca ggcaggtgcc 34080

ctgtgggaag ggtgcggggt gtgcttccca aggcgctcct cttgctggtt tccaggctgc 34140

tgcccctgtc cttagcagag ggaggaaaca gaggatggct ctgggtgaat gatgacttgg 34200

gcttcgatta tgtagtcaca gggtatgacc ctgagatgcg tggaaccccg agactgtgat 34260

tatatgtaga aactgggttt ccccgttgtt taagtagtca tggtggggtc agaccccaca 34320

ggacttttgt cttttcaaga aagaaaatgg tcgtgtgtca tgcaggggta gttggtactg 34380

gttaatccag gtttatcctt tattttgtgg gaactgtaca gtcatttctg ctacaatgct 34440

gtatatgctc ttctgaaaga cacctatgca aaatcgcaca gtaaaaatga cacaactcat 34500

agggaaagcg gggccagggc acagccctca aaatctccat caatgacatg taagaaaaga 34560

gaggaacctg ggaaatagca aagtgccttt tgcacattaa atggttagct atatcccaca 34620

atactgtgca ttcgtaaacg ttaatgctgc aataaatacg gcacttcacc ttgggaagat 34680

ctggagttgg cttatgagtg tggaagggtg tagcgcatga gtttttgtga aacactggaa 34740

ggaggattgt gggaaatcaa atggaaagtt ctcaccccag gcgtggagaa gagtgggtca 34800

tggccccagc agtgagccca gggaggtcag agacggaggt gtgtgtgtgg gtgtgaccct 34860

gcgcagttcc ctgccggctg tagtttttg cattcgctta atgtttctcg tggaggaaat 34920

tgtgcatgag caaatgtgaa accgtgctgt gctcaaattg tcctaataca tcattgcatt 34980

ggaacagatt ggctttttt ttttttttt ttttttttt tttttgagat ggagtctcac 35040

tctgtcacca gcctggagtg cagtggcatg atcttggctc actgcaacct ttgcctccta 35100

tgttcaagtg attttcctgc ctcagcctcc tgagtaactg ggattacagg catgagccac 35160

cgcggccggc cagatttgca tttttgaaac aactgctagg ctgggcgcgg tggctcacac 35220

ctgtaatccc agcactgtgg gaggccgagg caggtggatc acctgaggtc aggggttcga 35280

gaccagcctg gccaacatgg tgaaaccccg tctctactga atatacaaaa atcagctggg 35340

tgtggtggcg ggtgcctgta atcccagcta ctcaggaggc tgaggcagga gaattgcttg 35400

aacccaggag gcagaggttg cggtgagccg agatcacacc attgcactcc agcctgggca 35460

acaagagcaa aactccatct caaaaaataa aaaatagaaa aacaagtgct gtagcggaag 35520

tgagcacttt gcggagtcag gcttgtgtgg cctgttccac aaatgatgtg ctcacggtgg 35580

cctcaggccc acctggagtc tgcagcatgg ggcacaacag gttcattagt gtagaattcc 35640

aggacaggcc tggctcctaa gcagccttct tttacaaaaa ctgcagagcc cgcctgtatc 35700

ctagcacttt gggaggccga agtgggtgga tcacgaggtc aggagttcaa gaccagcctg 35760

gccaacatgg tgaaacccca tctctactaa atatacgaaa attagctggg tgtggtggca 35820

cgcgcctgta gtcccagcta ctcgggaggc tgaggcagaa ttgcttgaac ctgggaggtg 35880

gaggttgcag ggatctgaga ccatgtcatt gcactccagc ctgggcaaca gagcgagacg 35940

ccatctcaaa aaaaaaaaac ctacagagcc acacggcctc tttctccacc gagtgttggt 36000

gtgggagctt gtgttattgt ggtgaaatct tggtactttc ttgaggcaga gagaggctga 36060

gcgcctggag agactttcac atgggtcgcc atgtccgccg tcggtttcgc tgttgtgctc 36120

cccatctgaa ggctggtgcc gtccagacag gctggacgcc cctttccacc agatccttcc 36180

tcccgcagca gtttctagtt acgttgtact gtgaggtctg tgtccttggt tgatggcaaa 36240

agtcagccga attgaaattc agagccatgc ctggctccct ggagcttctc tcctgggcag 36300

ctgtgatcat tgcctctgct gtggtgtggg tggtggaaat ggattccttt catcttgctt 36360

gctacaggtg actgtcacgt ggagtccttt ggagagaggg acgtgttaat tgatggatgt 36420

ggctcccatg ctgagaaagc tcctgggcgt acattgcctt agagtttcat tggagctgcg 36480

ttcttttatg gtgtctgcta ggcagaagtg atgaagactt ggaagaaaac ccagaaggtt 36540

ttccacttaa tttggaaaat gtgcttttcc cctcctgtgt cttttgctaa ggtccagcct 36600

cctgcagcct ccccgctctg tggactctgg ctttgattct ttattaggag tccccctgct 36660

cccccaaaag atggtgtcta aattatcatc caattggccg aggttttgtt ttctattaat 36720

tgtttttatt ttttattgtg gtaaatttat ataacataaa atttgccatt ttaattgttt 36780

tgttattgtt gtttttgaga cagggtctca ccccagtgcc caggctggag tgcagtggtg 36840

cgatcatggc tcactgcagc ctcagcctcc agggctccag tgatcctctc acctcagcct 36900

ctctagtagc cgggactaca ggcatacact accacatctg gctgattttt tgtatttttt 36960

ttttattgta gagacccgct atgttgccca ggctggtctc aactcctgga ctcaagccat 37020

cctcccacct caccctccca aagtgctggg attacaggca tgagccacaa cacccagcca 37080

ttttaatttt tttttttttt tttgagatgg agtctcactc tatcgcccag gctggagtgc 37140

agtggcgtgg tatcaactca ctgcaacctc tgcctcccag gttcaagcga ctctcctgcc 37200

tcagcctcct cccgagtagc tgggattaca ggtgcccatc actatgcctg gctaattttt 37260

gtatttttta gcagagacgg ggtttcacca tgttggccag gctggtcttg aactcctaac 37320

ctggtgatcc gcccgcctcg gcctcccaaa atgctgagat tacaggtgtg agccaccgtg 37380

cccggccttt ttttgttttt gagacagggt cttgccctgt cacccagact ggagtgcaat 37440

ggtgggctct tggctcactg cagcctccgc ctcccaggct caagttgtgc acctccacac 37500

ctggctaact gtattttatg tagagacaga tttcaccatg ttgcccaggc tgggcttgaa 37560

atggactcaa gcagtccacc cacctcagcc tcccaaagtg ctgagattac aggcgcgagc 37620

caccgcaccc agcccatttt acctattctg cagttgacag ttcagtggca ttcagtcagt 37680

tcacgaggta accatcactg ccattcatct ccagactact tcaccttctc ggcagatgtc 37740

cgaaactgtc cgcattgaac acactcctca tctccctctg acagccacca ttctactttg 37800

tatctctctc tgccttctct aggtacctca tgtaagtgga attataccaa tatttgccct 37860

tgtgtgactg gcttctttca tgtgacatgg tgtcctcaag gttcatctgt gttatagcct 37920

gtgtcagaat ttccttcctt aaagcctgaa taataacccg ttgtaaaggc tgggcgcggt 37980

ggctcacacc ctctaatccc agcattttgg gagtccgagg tgggcagatc acttgaggtc 38040

aggagtttga gaccagcctg gccaacatag tgaaaccctg gctctactaa aagtacaaaa 38100

ttagctgggt gtggtggcgc gcacctgtaa tcccagttac tcaggaggct gaggcaggag 38160

aatcgcttgt acccgggagg cagaggttgc agtgaaccaa gattgtgcct ctgcagtcca 38220

gcctgggtaa cagagtgaga cttcctgtct caaaaaaaaa aaaaatcatc ggatggatgg 38280

acggaccact tcttgttatt tatccatcca cgggtgctag gtttcttcca cctttggttg 38340

tcgtgaataa ggccactatg aacatttcct tccgtggtga aggttttgta ctagtgagga 38400

aaaggcgtgt ttgtggtgtt gcataggatt ctggtaagaa agtttgcact aaccataagt 38460

atttgtacta cattaaaatg aaagctcagg ggccgggcgc ggtggctcac gcctgtaatc 38520

ccagcacttt gggaggccag ggcgggcgga tcatgaggtc aggagatcaa gaccatcctg 38580

gccaacatgg tgaaaccccg tctctactaa aaataccaaa aaactagcca ggtgtggtgg 38640

cgggcacctg tagtcccagc tacttgggag gctgaggcag gagaatggcg tgaacccggg 38700

aggcggagct tgcggtgagc cgagatcgct tcactgcact cgagcctggg caacagagca 38760

agactccgtc tcacgcaaaa ctctgtctca cgcaagactc cgtctcaaaa aaaaaaagag 38820

ttcagggttt atgaaactgg ccagccgcgt aaagtttgct gtgttgtttt tgtgcccggg 38880

aggagtgtgg ccagggtgtc acgtcacaca gtacacgttt ctcagatggt ggttctccag 38940

actgctgtcc caaagtctgt ttttgcatct ggttcccaca gacccaccct ccacggtgag 39000

cctgattttg gccagggtag ctggaatctt gcttgtcttt cagcccggca gctgtaccag 39060

tccagggtcc acagctagtg gcttttagga aggaatttgt tcagttggct ttgacacatg 39120

gccccctagg gtccacagct ctgtagtgat gtggatgttg ttatctacaa agacacatga 39180

tccttcgtgt ccagatgaaa gtgatgatgt ctttgcagct gcccagcaag gctgtgtgtg 39240

tgtgtgtgtg tgtgtgtgtg tgtgtgtgtg tggtgtgtgt gtggtgtgtg tgtgtgtatg 39300

ggggagggag gcaccctttc catctggggg tgtgtgtgtg tggggtgtgt gtgtgtgtgt 39360

gcgcgtgtgt gtggtgtgtg gtgtgtgtgt gtgtatgggg gaggcaccct ttccatctgg 39420

gtccaagaga ctgggcctgg ggaagacgct tctttttatc tacttagaga ctttgtttta 39480

tttgtatttt tttgagacag ggtctcactc tgtcacccag gctggggtat ggtgatatga 39540

gcatagctca ctgcagcctc ggcctcccag gctgaagcga tcctcccacc tcagccttct 39600

gaatagctgg gactgtaggc gtgcgtcacc atactgagct attgtttttt ttgtttggtt 39660

ggtttaattt tttttgatac agatggagtc ttgctatgtt gcccagacta gtctcaaact 39720

cctgaactca agtgattctc ccacctcagt ttcccgacat tctgggatca caggtgtgag 39780

ccactgctgt ctccctgttt tattaactgc tgaaagacct agataaagaa agtctgaaaa 39840

gacttactat cagagcacca tcctaagatg attccctctg actcaatgga gagggagggg 39900

agcttttcct tcaggcctgg gtggcaggag cccaggtgct ccaggcccca tttgccccag 39960

gccaaatcac tcgggaactt ggatgcagct gtctttcagg gtaacccaaa ggaaccagat 40020

ccccgcaggc agtaggcttc tgggctgtcc tctcctccta cgtcagctca gtaagagccc 40080

ttcgaaggga tgctgtgtcg gaggccccaa aagcccaggc tcatccctga gatgcacagg 40140

gtgggctggg cttaggcagc gctcgagcat ctcctggacg gtgaccccag agagtgtgga 40200

gacggagagt ccttgagagt cactgagaga cgtggctgcc ctgccttccc aagaggggct 40260

ctgagtcatt ccccacactc acctgcccct acccaccctc acctggcccc cagcctcacc 40320

taccccaca tctgtaccga tccctttacc cgcaccttcc ctacccaccc tcacctcccc 40380

tgtaccttca cctcccccac tcacccgccc ctgcaccctc acctgtcccc caccttcacc 40440

taacccccac cctcacctgc cctcccctca cctggcctcc ttccgttggg gaaggggttg 40500

taaggggcgg ccccaaact gtctgtcctg gtgccctgca gagaaaacag tacgtgaggg 40560

ccgcagtcca aaagcttgag tcctggaagg tggaggagac agggatgtgt tgggaagggc 40620

cccatggtct tggatccctt ctcgactgtc aatggggcct tcatgggagc gccagtctag 40680

tgatgcacag ctgggtgccc ggcgggtggc tgaggaggcc taaagtccga ggcggcaaga 40740

gctcttccag aggctgttgt cctaatcgct ctggcatact caggcgggca cgtagttagg 40800

agctgattgg agaggagaga cccccacacc aatactggga tttgactttc aggctaaact 40860

tgagaagtgt ggcctctgct gtcctgccag agctctccag ccagtgccca gggctctcca 40920

gccagtgccc ggggtctcc accagtgccc ggggtctcc gccagtgcca ggggtctccg 40980

ccagtgccca ggggtctccg ccagtgctca ggagtcttgg tttctttgtc ttacagccct 41040

ttgttttgac ctctctgagc caaggccaaa acccagacag gcagccccac gacctcagca 41100

tcgacatcta cagccggaca ctgttctgga cgtgcgaggc caccaatacc atcaacgtcc 41160

acaggctgag cggggaagcc atgggggtgg tgctgcgtgg ggaccgcgac aagcccaggg 41220

ccatcgtcgt caacgcggag cgagggtagg aggccaacgg gtgggtgggg gtgctgcccg 41280

tccaggcgtg cccgccgtgt cttatgccga atgccagcct ctcacaggct ggggagactt 41340

tccacctggg gatccaatgg gtggctttcc agggtcccaa aagcaaacac aggtttttca 41400

cagcccgtcc gggaaagcag aaagccccaa ggggctggaa ggggaaaggg ggagctctgc 41460

tgagaggtta caaggcagcg ctggccgacg ggagttgcag ttgataggtt ttgtatcatc 41520

cttgttaaac ttgaaccctg tgcagaaatc ccttccacgg catgggggct gcctgttgac 41580

tcgctcctgt tccaccacag ggagctcctg ggcttcttcc tcccagaggc ccccgacgct 41640

cccacctgtt ggtcgtcaga gcttctggtt ggtgggaagg cacccaggac cttgaggtct 41700

ccagagagaa aagccaggga aagagggaga ccgaaaccca tgtgacatga aactcaggct 41760

ccaaactgag cacgggaacg tttggggaca ggagcgcgat ggccttcctc agatagctgg 41820

ggggctggca tgaagacggg agctacagcc agcacaggtc ctgggccggg agcccagaga 41880

ttgagccctg actctgtcac ttactggcca cgtgaccttg ggcgggtggc atagcctctt 41940

ggagactcag tttcctcatt ggtaggagtg acggccacag tggtgcggcc tctgcagcac 42000

acgggggggct cggtgggcgg aagccccggg tctataaggc ggctgtgcag gagccagccg 42060

agctggtctc ccaacagcca gggctccggg gtccttagca gctgtggggg gcctgcacct 42120

gtttcccatg gctgctgtca gaaattacca gaagccaggt ggctgagagt aatggacact 42180

tgttctctca cagttcctga gggctgaagc ccgagatcga ggtgtgggca gggccctgcg 42240

ccctctgaag gctctgaggg aacctttggg cttctggtgg ctccaggcac cccttgactt 42300

gtggtcctgt cactccagtc tctctgtctg gctgcacatg gcgtggcctc ttctgtacca 42360

ttgaaggaca cttcagttgg atttagggcc taccctcacc cattgtggtc gtatcttgat 42420

ccttcatgac atttgtaaag accctgcttc caaataagct cacattctga ggttctgggg 42480

tgagcgggaa tttggagagc attgttcaac tagtatagaa tgtgacctgt cagcctcggg 42540

cagccctgag aggcaggggc tttccacagc ccagctgggt gccctgggct ccgtgctgtc 42600

cgaggagacg ccatccccac acccgtcctt cacccgccac cctcccgcag gtacctgtac 42660

ttcaccaaca tgcaggaccg ggcagccaag atcgaacgcg cagccctgga cggcaccgag 42720

cgcgaggtcc tcttcaccac cggcctcatc cgccctgtgg ccctggtggt agacaacaca 42780

ctgggcaagc tgttctgggt ggacgcggac ctgaagcgca ttgagagctg tgacctgtca 42840

ggtacgcgcc ccggggcctg ccctaaccgc agacacccgg ccttcattgt cagtaatggc 42900

agcagctgcc acattgtccg agacctgccg tgagcccagt gccgcgccag gggctttgtg 42960

tgtagcgtgt tttgtcctca cactgacagc tgtaggctgg ggttctgagt gagccccaca 43020

gggcagaggc agaaaatgag tctcagagag ggtgagcgag ctgcttgggg ccccacagca 43080

ggagatggag caggactgca gcctagcctc tgcccccagc acctgcgcaa gaagctgctc 43140

tgctctggac tgtgttaggc tgcgagggct ggagagaaat gagagttggt gcttagagag 43200

ggggcgcagg tccccatggc ttttcctctt atgatgaggt agatgggtga agggaggggc 43260

catgcttgca ggggccagtg accgaggccc gccgttggaa ctgatggcct tcatcccgag 43320

cccagcccag gtgggagcag ggctttccga gggcttgtct tgggtcggcc tgcttccagg 43380

gactctgctg cagctcccac ccctgtccaa agcatggaat cccccaggct ccctggcagt 43440

cctgtcaacc tctgtcctcc caagctgagt gtggggcaag ttctggaggt cagcactgct 43500

caggggggcc cacgggctgc ttgcaggggc caaccgcctg accctggagg acgccaacat 43560

cgtgcagcct ctgggcctga ccatccttgg caagcatctc tactggatcg accgccagca 43620

gcagatgatc gagcgtgtgg agaagaccac cggggacaag cggactcgca tccagggccg 43680

tgtcgcccac ctcactggca tccatgcagt ggaggaagtc agcctggagg agttctgtac 43740

gtgggggctg gcagtggggt gggcagggtg gcctctaaac ccgacccctg gaggaggctg 43800

gaggccagtg caagatcctg tgtggcctca gccaggcggt ggtctctgcc agatgccaac 43860

tgttgcccgc tggggttcag cgacatgtcc gaatgtcccg aggcctctga ggttgttttc 43920

ttttgccgca gaacaaatca ccacgaacag cgttttaaga caacaccaac tctttttttt 43980

ttttttttt tgagtcagga tcttgctctg ttgcccaggc tggggtgccc tggtgcaaac 44040

acagttcact gcagcctcga cctctgggct taattaagtg aacaccttgc ctcagcctcc 44100

caggtagctg ggactacagg tgggcaccac cacacctggc taatttttt ttgtagagac 44160

ggggtttccc catgttgccc aggctggtct gcaactcctg ggcacaagct atctgcctgc 44220

tgtggcctcc caaagtgcta ggattatagg tgtgagccac tggcctgaca acacccacgg 44280

attgtctctc agttctgtaa ggcaaagtcc aggcacagcg tggctcacct gggttctctg 44340

ctcagggtct cacggggcca gaatcaaggt gtcaggaacg ctgggccctc agcggaggct 44400

ctgtggagaa attagcttcc ttgctcactc agcaggtagc agttgtggga tcgaggttct 44460

gttttctctc tggttattgg tcggggacca ctctcagctc ctagaggcca ccacaggtcc 44520

ttgccccgtg gccctctctg cctcagcagt gggggctccc tgcgtcagtc cctcccacac 44580

cttgagtctc tctgatttgc ttctaaaggg ccctgtgatt cggctcagcc acctttagat 44640

taggttagcc tccccttga tagactccaa gtcggctgat taataacctt aatcacatct 44700

gcagaatccc ttctgccaca taaggtcatg acgccgtgct ggggactggg gtgggaaatt 44760

acggggtcat ttaggattct gcctgccact gccttgctgt gtcccagggc ttgggggagg 44820

ggcctccaca gctgggacca cagtccttcc tcccctccat ggtaaccatc tgaggattac 44880

ttgagaccag cctgggcaac atggtgagaa cccatcccta caaaaaatac aaacaaaaag 44940

ggaccaggct gggcttggtg gctcatgcct ataatcccag cactttggga gaccaaggtg 45000

ggctgatcac ttgaggttgg gagttcgaga ccagcctgcc caacatagtg aaatccccgtc 45060

tctactaaaa atacaaaaat tagctgggtg tggtggcagg cgcctgtatt cccagctact 45120

ggggaggctg aggtgggaga attacttgaa cctgggaggc ggaagttgca gtgagccaaa 45180

attacgccac tgcactccag cctaggcaat agagtgagac tccgtctcaa aaaaaaaaaa 45240

gggccagggg tggtagtgac aaagagaccc tatcccaaaa aaaccgaaca ctgaatcctt 45300

gagactgagt aaggacactg tgaaattttt ctgggtgggg cagggaacag agcgtcttct 45360

gtcatttctt ccacctgggt gtggtcagct ctccctccaa gctgcctcct cttcttctca 45420

ttgtccgggt gttggacaca tttggttaac tggatagaat aacgcgagtt cccagggact 45480

tggtccattt gctattttat tttattttat tttattttat tttatttatt tatttattta 45540

tttatttatt tattgagatg gagtttcgtt tttgtcgccc aggctggagt gcagtggcgc 45600

gatctcggtt cactgcaacc tctgcctccc aggttcaagt gattctccta cctcagcctt 45660

ccaagtaact gggattacag gcacccacca ccataccagg ctaatttttt tgtatttttа 45720

gtagagacgg gttttcgcca ttttgcccag gctggtcttc aactcctagc ctcaggtgat 45780

ccacgcacct cggcctccca aagtgctggg attacaggca tgagccacca cgcctggcac 45840

catttgctat tttaattccc atgtgtatta gtgtcccacg gctgctgtaa caaatgacca 45900

caaactggat ggcttaaagc aacagaaatg gattccccca atgtgctgga gaccagaagc 45960

ctgcgaccaa actgttggga gggctgtgct tcctctgggg gctccaggga ggatctattt 46020

gttggccctt ccagtgctgt gggtgccagc gttccacact tgtggatgcg ccgcctcaac 46080

ctctgcccat cttcatgtgt ccatctcctt tgtgtctgcg tctttacctc ttcttcttgt 46140

ctgtgttgcc tcttataagg acgtttgtca ttgggtttag ggcccaccca aatcatccga 46200

gatgacctcg tcttgagatc cttaacctgc aaagaccctt tttccaaaaa aaggttatgc 46260

tcacagattc taggccttaa gacatgggtg tatctttctg gggggcacta tccaacccct 46320

tatacaatga aagacgggaa gagggccagg tgtggtagtt cacgcctgta atctcagcac 46380

tttaggaagc tgaagcggga ggatcacttg agcccaggag tttacaagta gctaggcaac 46440

atgatgagac cccatttcta caaaaagtga aaaaaaaaaa aaaaaaaaaa aagccaggtg 46500

tggtggctca cacctgtaat cccagcactt tgggaggctg aggcaggcag atcacgaggt 46560

caggagattg agaccatcct ggctaacacg gtgaaacccc gtctctacta aaaatacaaa 46620

aaattatggc cgggcgcagt ggctcccgcc tgtaatccca gcactttggg aggccgaggt 46680

gggtgaatta caaggtcaag agatcgagac catcttggct aacacggtga aaccccatca 46740

agatcacaag gtcaagagat ggagaccatc ctggctaaca cggtgaaacc ccgtctctac 46800

taaaaataca aaaaattagc cgggcatggt agcgggcgcc tgtagtccca gctgctcggg 46860

aggctgaggc aggagaatgg cgtgaacccg ggaggcggag cttgcggtga gccgagatcg 46920

ctccatgcca ctgcactcca gcctgggtga cagagtgaga ctccgtctca aaaaaaaaaa 46980

aaaaaaaaaa aaaaaaagaa aattagccag gcacagtggc aggtgcctat tgtcccagct 47040

acttgggagg ctaaggcagg agaatggcat gaacccggga ggtggagttt gcagtgagcc 47100

gagatcatgc cactgcgctc cagcctgggc gatagagcaa gactctgtct caaaaaaaaa 47160

agccaggcat ggtggtgcat gcctgtagtc ccagctactc aagaggctga ggcaggaggg 47220

ttgttcgacc cacggagatc aaggctacag tgagccatga tcgcaccact gccctccagc 47280

ctgggtgaca gagtgtgacc ctgtctcaaa gtaagtaaat aggaggagag acaagtgggc 47340

agttcagact gatggtatgg gcacagtaga gactggtgca gacaggctgg cctgtgatgt 47400

caagcaactt ctgtaattgt ttccggcatc catttgtgtg tcaatttccg tgtcagtagg 47460

aagactctgt aggctgccaa gaggaataag tgggaggatc ctcccagaga ggccgggcct 47520

gcaggagggc cagttctcat gagttctcat ttggccccta ccctccaggc tgtggttctg 47580

aggtgggaga cagagcctga cctctgtttg tcttgttttg tctttgcagc agcccaccca 47640

tgtgcccgtg acaatggtgg ctgctcccac atctgtattg ccaagggtga tgggacacca 47700

cggtgctcat gcccagtcca cctcgtgctc ctgcagaacc tgctgacctg tggaggtagg 47760

tgtgacctag gtgctccttt ggggtgatgg acaggtacct gattctctgc ctgctaggct 47820

gctgcctggc atcctttaa aatcacagtc cctgtggcat ccagtttcca aagctgattg 47880

tgtcttcctt tgccctcctt tcttttctac tatgtgcatt cggtgctatg aattttcctc 47940

taagtactgc gtttcctgca tctcacaaat tttgttacat tttcattttc aggtagtttg 48000

aatattttta cacttctcct gagatgacat ctttggctca tgtgttattt agaagtgttg 48060

cttagtttct aaagagttgg ggcttttcca gctgtctctc tgcaactgat ttctaattta 48120

attctactgt agtctgagag cttattttat atgatttctg ttattttaaa tgtgttgggt 48180

gtggtgtttt tgttgttatt gtttttgtgt ctttttgttt tgttttgctt cgtttgtttt 48240

gtttttgaga cagtgtcttg ctctgtcact caggctggag tgcaatggcg cgatctcagc 48300

tcaccgcaac ctctgcctcc cgggttcaag tgatcctctt gcctcagcct cctgagtagc 48360

tgggattaca ggtgcacgcc accataccca gctaattttt gtatttttag tagagacggg 48420

gtttcaccat gttggtcagg ctggtctcga actcctgacc tcgtgatccg cccacctcgg 48480

cctcccaaag tgctgggatt ataggcgtga gccactgtgc ctggccatta ggtgtgtttt 48540

atcacccagc atcatgcagt ttatcttggt gaatgttctg tgtactcttg aaaagaatgt 48600

ggattctgct gttgttgggt ggagtgttcc agaaacatca attagatcca gttggttaat 48660

agtgctcatc aggttgtctc tatccttcct tcctgactgc ctgcttgagc tgtcagttat 48720

tgacaggggt gtggagtctc caactctaat ggtggatttg tttatttctc ctagtagttc 48780

tatctttttc tctccttcta cccttgatcc tcttctcccc ctagggcttc ctggtgttag 48840

tggtgggaga gtggggtagt gaagaacctg gactttaggg ccaaagaggc cagggttcaa 48900

atcctggctc tgtcacttcc cagttgagtg accctggctg gtgcctgaat ctctgtgagc 48960

ctccacttcc tcctctgtga aattgagagc acttacctgg caggctgtca tgggcatcaa 49020

gtaacagggc actccacctg gaccctgaca cgtgatgcac aggaatgcca gctgctatgc 49080

catgggtgtg gcagtagtaa taaagtgacc atctgtatcc tcaccacagt gaagcctgtc 49140

cagggctttc tctcctatgc ccccatgcct ccaggtggcc ttggatcctg ttggttctgt 49200

gctctgctca gcgacctttc tcccgtggga gttcctgggg gttcagcttc atcctacaga 49260

cagcagcaca cactggctgt gcacccttt ttttttttt ttttttttt tgagatggag 49320

tctcgctttt ttcgcgcagg ctgaagtgca gtggtgtgat cttggctcac tgcaacctct 49380

acctcctggg ttcaagtgat tttcctgcct caccctccca agtagctggg attacaggct 49440

cccaccacca cgcccggcta atttttgtat tttcagtaga gatggtgttt caccatgttg 49500

gccaggatgg tcttgaactc ctgacctcag gtgatccgcc cacctcagcc tcccaaagtg 49560

cagggattac aggcgtgagc caccacaccc ggagtgccgg ttgtttttag cagtttgtct 49620

tgttcctgga gagactggct cctgcccagg agctcgggga gtagggccgc ggggtgctgc 49680

ctcacacctc gagtttggcc gtaagcagag gggacatttt gtgactgtcc ccctcctgag 49740

cttcccagca gcttttctcc aagttacagc ccaaaagctc aggtggattt gcaacccaac 49800

ggtgtctgtg cacctcccac tgatgcccga actgccctgg ccaagaaacg gggccgtcag 49860

aacgctgcac taactgcagc cttgggcctc catgccagag gccatgccct tccatccacc 49920

acccccctggc ctgggccctg ggccctcctg gctcgggaac tccaggcccc ttcctcacgg 49980

ctcgagagac gtgtatttac cgcacaggtg cttgtcattc tcttgtggcc tcttctccag 50040

ggagatcaca gaaggacagg gcctcactga ggtctcggac atggaccctt tgatagtggc 50100

aggagccagg ctgggcaaga ggcggccaca gtcacctcag cagtgccatc accaccgcca 50160

ttcagccctt ccctgagccg ggcgcgcccc tggctctggc cccagtgtcc cagttacagc 50220

tcacaggagc ttgtggtgcc cagcggctgc ttctgattga gagtcgaggt cggaggcttt 50280

gggaggctga gaggctgctc ggtttcacaa ctgctgaggg agacttgggc tccatctcag 50340

gtatgcccca tgtcgccctc aacctccagc caccggtcct ccgtgtcccc catggccagg 50400

cacggcttgc agacatctgt cgttggctcc tctcagccgt cgtgggctga ccctggcacg 50460

tcctcctgtg gctgagccca gtggggacag ctgcttcctt ttattaccct agaactctcg 50520

tctttgatca ggccccctcc cctatgccac acagtccctg tcactcgggt gagcccagta 50580

gtcatgggga aggcctgcgg gttccaaaca tccaaaggct tgcgtgcagc atgacagctt 50640

gaaaccgatg ttttttacct tgatcagatt tcagcttggc gggggctttg ctcagctttc 50700

agtgaggcct gggccgattt cccagcatcc cctcctgagg ccagcctctg tttcctgtga 50760

ttttctgcac aaagtgggag ggaggagtcc taggaaatgg ggggccacct cgaagcctag 50820

gcctcctctg gcttctctgt gccagtgccc ccacgctttg tgtctgtgtc cccagcccat 50880

gggactctgc tattccctga gtgctgccgc atgcccagcc cgcactgagg acgtggagcc 50940

ccgaggggca ggatggcctc catggtcaca cgtaggaagt ggcctccacc ctccgatgat 51000

cctctccctc ctcccttca gcgccctccc cgggggtgtc ctcagccctc ctgcctgtgc 51060

tttgtcccgt cttctgcagg cgcctgggac gtgctgacag gtcctctgcc ggctcctgcc 51120

ttgctatgcg cacgctggtc accacagagg cctggccctt cttctgtagc agtcccacac 51180

ccgcaacagg tgtggctgct gaccacctgc tttctgcccc tctggtcctg aggagggcgc 51240

agtgggcact caggcgtggc tgagcagatg tgtgttgccg ggaggaggaa ggactgctcc 51300

agtcagggct gaatttccca cccggagcat ttctgctgta tttggtgtag cgcctgctgc 51360

ttaaagctct gattcccagt tggcaccctt tcccttctgc attgaaaaac atacggatgc 51420

atgtcttctt gcagtgaatg tgtattctcc cagcctctct tctgggttgg ggctggaggt 51480

ggagcggcac acaggagccg cagcgatgga ggatgtgcgg gtgcagcacc ccgtacagca 51540

gggatgccaa acccgcgctg agtccctctc aacttctgct ttgaagccca gtcacgccat 51600

tgcctgggtt ttgctgggcg gggctgcgtg tgatgttctc ctctgtccct cccccagagc 51660

cgcccacctg ctccccggac cagtttgcat gtgccacagg ggagatcgac tgtatccccg 51720

gggcctggcg ctgtgacggc tttcccgagt gcgatgacca gagcgacgag gagggctgcc 51780

ccgtgtgctc cgccgcccag ttcccctgcg cgcggggtca gtgtgtggac ctgcgcctgc 51840

gctgcgacgg cgaggcagac tgtcaggacc gctcagacga ggcggactgt gacggtgagg 51900

ccctccccgt caaggctctg ccaagaccct ggccctgccc tccgggatac gagcttgggg 51960

ctgcctccgg cctcacagga gtaggggctc tgaaaacctt tgcttgcagg gagattgcca 52020

agtctgtctt ttaggcccaa caaggaaaac tctgcagttc cacccatcct gtcccaccag 52080

gtagtgtggc ttgaaggcag actgtgaggg tctatctcac cttcctgcat taggtcagga 52140

gtttcacaga aacctgaggc acattcaggg gtgggctgca gaggtccatg gctcacaccc 52200

tggaaaatcc gcccccaaaa gacagtgctg tctccactga ccagtctgtg ggatagtgct 52260

taagcctgag tggtttctat caacatgtag aatcaggagg tataaagaga tttgctcagg 52320

catcctgggc cctctctgac cagcaggatc ttcctttaga tcttgacagt gaaacacatc 52380

tcttctgtgc cccctgtgag ttttctttca ttcattcatt cattcattca ttcattcatt 52440

cattcattcg agacagagtc ttgctctgtc acccaggctg gagtgccctg gtgtaatctc 52500

ggctcactgc aacctctgcc tccagggttc aatcgattct cctgcctcag cctcccgagt 52560

agctgggatg acaggtgcgc accaccatgc ctggctaatt tttgtatttt tagtagagac 52620

agggtttcac catgttggcc aggctggtct cgaactcctg acctcaggtg atccgcccgc 52680

ctcagcctcc caaagtgctg ggattacagg catgagccac cgcgcccggc ctgagttttc 52740

cttttatgaa ggacctgctt ggttggttgc ctgccacatg ttgtcagcac catgggccca 52800

ggactgctga ggagctgttg atgccctcgc tctcccagag ccaccggctc tgttagataa 52860

ttcacatgca gtctggccac tgtcctacgt cctcattcac aaagagcaga catttcgtag 52920

aagatgaggg cctgggagta acctccctgc atgtttttct ataaaggcat agtggttaag 52980

tccttccagc tcattgacca ttggagaatt ttatggaggc tgtagactag gggctggtaa 53040

actaagggcc caggggccaa atccagcctg ccacctactt ttgtaaataa agttttcttg 53100

gtgcacagcc atgcccattc attcatttgc acaatgtctg tggctgcttt catgccaaaa 53160

gcaagagaac tgagtggtta tgctggagac ctacggcctt caaagcccca gacctcacgt 53220

ctggcccttg acagacagag cttccccagc cctgctgcgc atcctggccc agcatgtgct 53280

gtgtgtgtga tttcagcttg caggagccgt ggttaggaat tgtccctgtg ttggtccatt 53340

ttgcattgct atgaaggagc acctgaggcc gggtagatta tgaaggaaag aggtctgtct 53400

ggctcatggt tctgtaggca gcaccagtat ggcacccgca tctgctcagc ttctagtgag 53460

gtctcaggaa gctttgactc atggtgaaag tcgaagcggg agcaggtgca tcacatggtg 53520

agagagggag caacggagag agagagagag cgcctctccc tcttgccctc accttgagag 53580

gagatgccag gctcctttaa gtaaccagct cccatgtgaa ctcacagtga gagcccattt 53640

gctactgcgg agagggcacc aggcatctgc tcccatgacc caaacactgc ccaccaggcc 53700

ctacctccaa ccttggggtc atattttatt ctgttctatg ctatgctatg ctatgccatg 53760

ccatgccatg ccatgctatt cctattctat tatttgagac agaatctcgc tctgttgccc 53820

aggctggagt gcagtggcat gatcttggct cactgcaacc tccacctccc aggttcaagc 53880

gattctcctg tatcagcctc ccgagtagct gggattacag gcacacacca ccacacccgg 53940

ctaatttttg tattttcaat agagatgggg tttcaccatg ttggccaggc tggtctcaaa 54000

ctcctggcct caagtgatcc acctacctcg gcctcccaaa gtgccatgat tacagatgtg 54060

agtcactgcg cccagtgagg gtcacatttc cgttgagatt tggaggggca gacgttggag 54120

ccatctgagc cccctcgtcc cgctctagct tctcctcccg tgtgccccgc ggtgctggtg 54180

gcaggccctt acgccggttc tggctgcatg ctctgttcca gaagctttct tccctgcttg 54240

gttaccagaa aatcatccca tccattacaa ggacagggtc cccttatctc ccattcccag 54300

ggcaggacac cgggggcagg gcaggtgggg aactgagcaa gttctctggg ggcaggcgtg 54360

gctatggctc cctctgggtg ggcgtctggg gaggggtgga ggcagccgtc agcgccctgg 54420

cttgctcttc ctccctggcc agagactgtg gccttgtgct gctcccgtgt gggctgcctg 54480

cacctccagt gggttgtgct ccctcccctc ccctcccctc aagctctgct gagcaccact 54540

gccttccaca gcccccactc tcgggaggcg aggctcctcg tggccattcc tgtccttggc 54600

acccacccct ccaccaacct ggtagagcct tgggcggggt ctgttactcc ttgcatggcg 54660

tagacctccc cacagtaggc acctgacaca tacctcctgg ggggcaggca ggaggtgcgt 54720

tgaggtctca gccctggcag tccctccccc gcgtggcata ggcctcgcca cagggtcatc 54780

gagggtgggt ggagactgta ctagaccact ccccgctggt cctagaaagg gtcccatctg 54840

tctgctctct gtttggagtc cagaccttgg ttgctgtgcc ctgcatggtg ggctgggggg 54900

caccctccag cctctctgag tgcatggcct ctccttgcag ccatctgcct gcccaaccag 54960

ttccggtgtg cgagcggcca gtgtgtcctc atcaaacagc agtgcgactc cttccccgac 55020

tgtatcgacg gctccgacga gctcatgtgt ggtgagccag cttctggcac ggggaagggg 55080

cgtccgggct gggttccccc aggaacgtgg agtttagggg aggagacgtg cctttccagc 55140

ggggctgggg gctgtgtggg agactcaggc ggctgggagg ctccttgcgg gaggcaggga 55200

agcctttccc agggcagcgg ccaggaggac agactgtgag ctgtgggctc ggcggctaca 55260

gagtctgcct cagtgggcgg ggctgatggt gtccaggtgc ctgcagcacg cacccaccca 55320

cgggaccttg ctgagcagcg tctgtcaggc agcaagatta cccgagggct gcagtggtcc 55380

tgttccctgg cagcttactg tctggctgag gaggagtgat gttcacatat gcacacatgt 55440

catgtgcaca cacatgtaca tgacaacatc ccacatgctc ctcaaatagc atgacctgta 55500

cagtcacgga tatagggcct aggggatagg aggccaagac agtcagggaa gactttccag 55560

aggcagtggc tcctgaaagg ctgtctgatt caggcaggaa gggagctgag ttcagatagg 55620

aagtagcaat gagtcattgt gtctggggac atggccactc cttcgctgca gagggacctg 55680

ggctgagagc tcctctctta tggctgcagt cgggagagaa gtctgttggg gggagaaggg 55740

ggcttcctca agggactccc tgtgcccttt ggcaccttcg tgccaggtca ggcttgaggc 55800

ctgaaggcag tggtgggggc caccaagggt cgcctcctct gctgggcaag ttcccagtct 55860

gacgggcctg tgccgtgggc cccagctgtg ggggcgctgt tgatgcgcag ccaggcctcg 55920

ccgccagagc ccgcacgctt ccattccgct gacttcatcg acgccctcag gatcgctggg 55980

ccggccctgt gggagagtga atgtggcttt tgccaaagtt gagtctggag cctggaaact 56040

tccctatggg cagccttgat agtggagtgg cccaaggagc ccacccagcc gaccctgccc 56100

ctcccgtggc tggtgggcgg caccaggggc tgcctggctt tgctcgttca ccaacatcac 56160

ctgggctggc cagggcgcgc tcacttctgc caccaccgag ggccctgggc gaaggagtga 56220

ataccaggct gccttggcag ggatgtgttg agggctgtgg ggagtcggac agcggcgggg 56280

gtcagaggag gaggagggtg caccgtgcag gctgaagggc cacgttaccc tgaggttggc 56340

caggctcccc aggcctagcc tcccagctcc cccactttct ccccaccctc caccagtggc 56400

aaagccagcc ccttcagggc gcacggtgtc tgcccccaag gagggcccat tccgttgggg 56460

ttaatgttgg ccacctcttt ctgtttgtct ctggcagaaa tcaccaagcc gccctcagac 56520

gacagcccgg cccacagcag tgccatcggg cccgtcattg gcatcatcct ctctctcttc 56580

gtcatgggtg gtgtctattt tgtgtgccag cgcgtggtgt gccagcgcta tgcgggggcc 56640

aacgggccct tcccgcacga gtatgtcagc gggaccccgc acgtgccccc caatttcata 56700

gccccgggcg gttcccagca tggcccccttc acaggtaagg agcctgagat atggaatgat 56760

ctggaggagg caggagagta gtctgggcag ctttggggag tggagcaggg atgtgctacc 56820

ccaggccctc ttgcacatgt ggcagacatt gctaatcgat cacagcattc agcctttccc 56880

actgagcctg tgcttggcat cagaatcctt caacacagag gcctgcatgg ctgtagcaac 56940

ccaccctttg gcactgtagg tgtggagaaa gctccttgga cttgaccttc atattctagt 57000

aggacatgtg ctgtgttgtc cacaaatcct catgtaccct agaaatgaat gtgggggcgg 57060

ctgggctctc tccagagctg aaggaatcac tctgtaccat acagcagctt tgtcttgagt 57120

gcagctggga tttgtggctg agcagttaca attcctacgt ggcccaggca ccaggaacgc 57180

aggctgtgtt tgtagatggc tgggcagccg caccgcagag ctgcaccatg ctggtttgta 57240

tcacatgggt gaccatggta tgtctaagaa ggtggagtcc ctgtgaggtc tgcaggtgcc 57300

cccacagctc caggccacct tgaggattgc ctctgcctgc ccagccctga gttccctctc 57360

ccctgtcctg tcccactgtc accccaagcc ggcctcattg ggagcctgtt ggatggcagg 57420

gtatagatgt aacctgattc tctctgggga gcggggttat ctggcttctc aagagctcct 57480

aggagcccac agtggtggca ccatcacagt cgcagcagcc cccagagaac gcggccctgt 57540

ctgttcctgg cgtgctctgt gctgccccgc ctgggttccc tgccccagtc gcaggccctt 57600

tggaggaggt accatgtgtc tcccgtttca cagatgagcc ccggggagct cactctagta 57660

gtggccagag aggcctgcgg ctcagggagc ggggcacatt tccaacagga cacaccgccc 57720

tggtctgagt ctcgtgggta gtgggagcag aggagagcgc cctatgtctg tggggcggct 57780

tggctgagcc tggaagccac ctgacctccc ccgtcccttc cctgccaggc atcgcatgcg 57840

gaaagtccat gatgagctcc gtgagcctga tgggggggcg gggcggggtg cccctctacg 57900

accggaacca cgtcacaggg gcctcgtcca gcagctcgtc cagcacgaag gccacgctgt 57960

acccgccggt gaggggcggg gccggggagg ggcggggcgg gatggggctg tgggcccctc 58020

ccaccgtcag tgctggccac cggaggcttc ccgggttcct gggggctgtg ccaccgcctc 58080

tgaggcatgc ttgctttctt ccctttttcaa acccttctgc ttccttcttt aatgacattg 58140

ttgattgtgg ataatctgaa aactacacaa aaatataaag agccaaaatc tcacccaaat 58200

ccacctccta gagtggctgt tgggctccgt cagcatccag gcggccgtct gtgttccgca 58260

cggcccagcc catcgatagc cgcctgcacc aggcctgtct gccctctgtg agcctcccca 58320

cagggttccc tccacaaaca ccctgttctc ccacccaggg ctggctgctt cctggaaaac 58380

agctggatgg ttttgtgcat gacagacaaa cacagggtga ttttcgtggc taaaatactc 58440

cctggagctt ttggcagggt gaggggctgg ctccagctga gccacgcctt gagtgaaatg 58500

actgtgagga gaataaactg ccgctgccct ccaggatcac tggggctggc tggggagaac 58560

ccccgtttct gggagcacag tcccaggatg ccaaggcgag cttggtgccg agatgtgaac 58620

tcctgagtgt aaacagcggg ggctgacttg acatgctttg tatgcttttc atttgttcct 58680

gcagctgtat gcccctaagg tgagtccagc ccccttctgc ttcctctggg gcctcgccag 58740

tgagccccac cttgctgggg ctggttcctc ctgcccttct gggtatccct cacatctggg 58800

gtcttgtctt cttgttttct ttttcttttt tttttgagac ggagtttcac ttttgttgcc 58860

caggcttcag tgcaatggtg tgatctctag gctcaccgca acctctgcct cccaggttca 58920

agcagttccc ctgcctcagc ctccctagta gctgggatta caggcatgtg ccaccacgcc 58980

cagctaattt tgtattttta gtagagatgg ggtttctcca tgttggtcag gctgatcttg 59040

aactccctac ctcaggtgat ccgcccacct tggcctccca aagtgctggg attacaggcg 59100

tgagccaccg cacctggcct ttttcttttc ttttcttttc ttttttctga gacagggtct 59160

cgctctgtca cccaggctgg agtgcaatgg tgtcatcatg gctaactgca gcctctacct 59220

tctaggctca agcaatcctc ccatctcagc ccctaagtag ctaggactgc acgcatgcat 59280

ccccatgccc agctaatatt tacatttttt gtagagatga agtttcacta tattgcccag 59340

gctggtctcc aactcctgga ctcgagcgat cctcctgcct cggcctcccc aggtgctggg 59400

attacaggcg tgagccaccg tgcctggcct ggggtattgt cttcttatgg cacctgactg 59460

tggtgggccc tgggaaggaa gtagcagaag agggttcttc ttggtttcct ggacagtaac 59520

tgagtgttct ggaggcccca gggcctggct ttgtttaggg acaaagggaa ctggtaacca 59580

gaagccgaga gtttaaacac ccactgccct tcttccctgc tcctgctgct gcaacccagc 59640

ttaaccagcc aggagtgcta ggaacccaag cagggccccc gagcacacag caggcagctc 59700

acgaattctc ttttcctgtt ctcccttggg agctgggagg atcttaatca ggcaataaga 59760

gatggcactg agcagccagc taatttttta aatcacttta ttgtttaacc atatgactca 59820

cccacttaaa aaagggtaca gttcagtggg ttttagtgta ttcacagatg tgtgcaaccc 59880

tcaccacagt taattttaga acattttcct gcccctaaaa gaaactctgc atgaagccag 59940

ctgtttttaa attagcaaag ttattttgca tcctttaaat atatgttcat ggtacaaaat 60000

tcaaaagata cagaagagtc tgcagtccaa agagactccg cccccatgac gccaagcagg 60060

catccctggg aggcatggcc tcctgcagtg tgtttcttct atgtcccccc aggggtcatc 60120

tgtacatatg caagcataca agagcgtgga ctttgttttc caagccagaa gataattgta 60180

gatttatgtg cagttgtgag aaagagcaca gacccattta tcctctgcct ggtttccccc 60240

agtgctgcct gccatcttgc atgacttcca ttcctatcat aagcaagaca ctgataacga 60300

ttctttcacc ttattcagat tgacataagt gtttttttgtt tgttcttgag acaaacttcc 60360

tctgtcaccc agtgggagtg cagtggcaca atcacagctc actgcagcct caaactcctg 60420

ggctcaagcg attctcctgc ctcagtcccc tcaagtagct cagatggcag gtgtgcacca 60480

tcatgccagg ctaattttta aatttttgt ggaggtgagg cctcactaaa tttcctgggc 60540

tagtcttgaa ctcctgagct aaagtgatcc tcctgcctca gcctcccaaa gtggtaggat 60600

tacaggcatg agccactgcg cctgggctga catatgtgtt ttcgtaagcc cgaaagatag 60660

catctgaaga gtcaacattg agccttgcct tttgctgcta acgatgtata aaagctgctg 60720

ttctgagcat ttcggaggct cccagctgcc gtgtgcaccc tgcctagagc tctaccgtaa 60780

cccatctccg ggaggaggtg ctattgtttt cctcattttg caacaaggag gctgaagaac 60840

tgagcatgaa ccactggcct gggtcgttcg gttggtaggc agtggggcca ggccatccaa 60900

ctcacaacca ccttctactc tgcttccccc gcaccctgaa gtttgttctg ttttgaggac 60960

acagccgtca cattcttggt ggctgaacag cactccttgt caggcgtggc tgggccccca 61020

ctggagggca tcatggtcct ctctcctgct gcggttgaac cttggctgtt tcaaccactc 61080

ctgccaagtg gccctctgaa agggacagtc catcttttct cagcagaggg ccacactggc 61140

aaaacggtcc ctggcaccct ttctctccac ctgtctaata tagagtaaaa atggtatcat 61200

gttaagatct tcatttatat ttatttttatc atgaatgatg taagcatcat tttgtgtgtt 61260

taagaacctt tgggcccagc gtgatggctt gcagctgtaa tctcagcact ttaggaggct 61320

gagatgagcg gatcacttga ggccgggagt ttgagaccag cctggccaac atggagaaac 61380

cccgtctcta gtaaaaattt aaaaattagc cgggtatggt gatcccagct acttgggagt 61440

ctgaagcatg agaattgctt gaacatggga ggcggaggtt gcagtgagcc gagatcgcgc 61500

cattgcactc cagcctgggc gacagagcga gactctgtct caaaaaaaaa aaaaaaaaag 61560

aaaagaaaag aaattatcaa tctcctcttt tatggcatat atatatatat atatatatat 61620

atatatatat atatatattt ttttttttg gttatgttca gaaaggcctt ccctgctctg 61680

atcataaaaa acaacttatt ttcacactct ctctcttttt tttttgagac agagttttgc 61740

tcctgttgcc caggctggag tgcagtggcg caatctcagc tcactgtaac ctccgcctcc 61800

cgggttggag tgattctcct gccttacctt cccgagtagc tgggattata ggcatgcacc 61860

accatgcctg gctaattttg tacttttagt agagacgggg gtttctccat gttggtcagg 61920

ctggtctcga actcgcgacc tcaggtgatc cacccacctc ggcctcccaa agtgctggga 61980

ttacagacgt gagccaccat gcccagccca cactctcttt cttaacgtcc tcctcctttc 62040

gttttacgtt cacatcttta attcttctgg gatgtaatta gatttgatga gcaaggtggg 62100

catccagctt gtttcttggc tgatggctta tgggtggcgt gaattagtcg gggtctatca 62160

ggaggcagaa actctatgag aatttgaaca gagaaagttc cgtctacagg cttattacca 62220

gggactggaa tagcagaaat tgaacagtga gatgtacaga gaactctaag aatgcaggaa 62280

taggccaggc atggtggctc acacctgtca tcccagcact ttgggagacc aaggcgggtg 62340

gatcacctga ggtcaggagt tcgagaccag cctggccaac atagtgaaac cccatctcta 62400

ctaaaaatac aaaaaaatta gctgggtgtg gtggcgcatg cctgtaatcc cagctactcg 62460

ggaggctgag gcaggagaat cacttgaacc tgggaggcag aggttgcagt gagccgagat 62520

catgccactg tactccagcc tgggtggaag agcggaactc tgtctgaaaa aaaaaaaaaa 62580

aacaagaagt tcaacttgaa gggaaaaatg ccgtattgtc tttccctttg ttatgtcacc 62640

agggcacagt ccatcccagg ctggcgctga tccacgggct ggagaggggc tgccccagaa 62700

gaggacatgc caggaagggc ttggctggtg ttcaggagcc caggccaggt caggtcaaga 62760

ggtgttgagg ctggacggga gaggccagct aggggctcat gtaggatatg aggggtcggc 62820

ccatttcaac gtggaaactg agctcttctg cttctctttc ttcttcactg cattaagatt 62880

caataccgct tgggaagcag gtatttccct tcctataaag gatggttggg agcctgagtg 62940

ttgggagaaa gtgtagccgc tgagttacta acaactaggg ctgccgtcaa gcctatgggg 63000

aaagagagaa gaggacattt ggaaggagag agatcaagct gtggcaccct gggagaggac 63060

cacagaaaag aggccagtga gggggttccc cggtggcatc tgaaggtgtg gcccaaccag 63120

gaggtccaga ggctgccagc cgagtggccc aggagaggga acctcacagg ggctgagtgg 63180

gacccaagcc ctatccaccg tcctaaccac ccacatttct cgggaacaag acctcccaca 63240

gtggcctccc cggcagtgga aatagccaaa ctggcaacat ggactttctt caactgcccg 63300

ggcgatgctg cctcagtgcc ccagggcagg caggaagctc ccacacccat tctggaatga 63360

ggggttggag gaaggctgag ctgagcaaag gacccatctc tgctctggtt ggtggggagg 63420

gagcccatta tacaagagac ccctcagggc tcagtgaggg gtgacagaga cttggggagt 63480

agtggctgtc actgcagagg tgagagggtt tggagagaag gtacatgcct ttttggccac 63540

attgagtagc acctggtagc cagttagtaa cgtgtattgg ataaacaaaa gattaaacgg 63600

atgcaaaaaa aaatgttggc tttgcttctt tttacccaaa cctcagttcc ctcaagtaga 63660

ttctgggaac acccccctacc tggctggact gttgtgaagt ttaaataagc caggttaact 63720

tcacctcctc ctttaagaca cagctcagac actgcctcct ccaagaagcc ccctctggct 63780

tcctgtgtga atatgacggc cctctgggct ctagggtatc ttagaacaat gcttccttat 63840

ggctttggaa ccccgctgtc tcctggattg ggagcaaatg caggggagga gccacacctg 63900

actaatctct gggtctccca gcacataagt ggcataaggg cagggctgtg cccgcttcag 63960

gcacttactg aaggatgtac ttggcagagg gtaggcagcc ggcggatgag cccctcactc 64020

tccccagctg actgcgtggg cgggaaaggc gggttcagga gacccagcct ccctgggctg 64080

tcaccacctc tgcacatcca gccccattga tcaagggttc aatttttggg gtcctgttgg 64140

gaggccagga gactctctcc aggcacttct tccaggtctt tgtgttaggg tgtgtgtgtg 64200

tgtgtgtgtg tgtgtgtgtg tgtgttgttt gttttatttt atttatttat ttatttattt 64260

atttatttat ttatttattt tgagacgcag tctcgctctg ttgcccaggt tggagggtgg 64320

tggcatgatc tcggctcact gcaagctccg cctcccgggt tcacgccatt ctcctgcctc 64380

actcttcctg agtagccgga ttacaggcgc acgcaccatg cctggctaat tattttgttt 64440

ttttagtaga gacagggttt cgccacgttg cccaggctgg tcttgaatcc ctggcctcaa 64500

gcgatccgcc cgcctcagcc tcccaaagtg ctgggattac aggcgtgagc caccgtgccc 64560

gcccagccta ggggtacatg aaacttttct ttttttttct ttgagacaga gtttcactct 64620

gtcctcaggc tggagtgcag tggcgtgatc tcggcgtact gcaatctccg cctcccggtt 64680

caagcgattc tcctgcctca gcctcccgag tagctgggat tgcaggcacg cgccaccaca 64740

cccagctaat ttttgtattt ttagtagaga cgggctttca ccatgtggga caggatggtc 64800

tcgatctcct gacctcgtga tccgcccgcc tcagcctccg aaagtgctgg gattacaggc 64860

ctgagccacc gtgcccagcc atgatgtttt gatacaggca tataacgtat aataatcaca 64920

tcagggtaaa tgatgtaacc atcacatcaa gcatttatcc tttgtgttac aaaaaaaaat 64980

ctaattatac tttcctactt attcttttct ttttttttct ttgagacgga gtctccctca 65040

gtcgcccagg ctggagtgca gtggcatgat ctcagttcac tgcaagctct gcctcctagc 65100

tctgcctcct gggttcatgc cattctcctg tctcagcctc gcgagtagct gggactacag 65160

gcgcctgcca ccgtgcccgg ctaatttttt tttttgtatt tttggtagag acagggtttc 65220

accgtgttag ccaggatggt ctcgatctcc tgacctcata atccgcccgt ctcggcctcc 65280

caaagtgctg ggattacagg catgagccac cgcccccagc ctatttattc ttaaatgtac 65340

aataaattat tgttgactcc agtcaccctg ctgtgctacc aaatacggat cttcttcatt 65400

ctatctaact gtatttctgt acctgttaac catctctcct ccacctcacc ccccaaaccc 65460

actacccttc tcagcctctg gtaaccatcc ttctactctc tatctctatg agttcaattg 65520

tattaatttt tagctccccg gccgggcacg gtggctcacg cctgtaatcc cagcacttca 65580

ggaggctgag gcaggtggat cacgaggtca ggagtttgag accagcctgg ccaacatggt 65640

ggaaccccat ctctactaaa aacacaaaaa ttagctgggc gtggtggtgg gcgcttgtag 65700

tcccagctac ttgggaggct gaggcaggag aatcgcttga aactgggagg cagaggttgc 65760

agtgagccaa gattgcgcca ctgcactcca gtctgggtga cagagtaaga ttccatcccg 65820

aaaaaaaaaa agtttagctc ccacaaataa gtgagaacac gtgaagtttc tctttctgtg 65880

cctcgcttgt ttcacttaac ataatgacct ccagttccat ccacgttgtt gctttgttat 65940

aaatgacagg atcttggtca ggcgcagtgg ctcatgcctg taatcccagc actttgggag 66000

gctgaggtgg actgatcatg aggtcaagag atcgagacca tcctggctaa cacagtgaaa 66060

ccccgtctct actaaaaata caagaaatta gccgggcgtg gtggtgggca cccatttccg 66120

ccccttctcg ggacgctgat gcacgacata ttacccatcc ccggaagact aatcctcccc 66180

cactctatat tgtacctctt cctttctcct ccacgcgatt ccccgagtaa cccgtcttcc 66240

ctcctcctc ggattacgct caccttccg cttcaatcac gttgctccgt ccccttcccc 66300

attcgtacca ctcctcactt tcgtcttcct acccccacta tccctttcg tcctctctat 66360

tccttactta ctcctccccc ttctcttcat acttcattcc ctccgctctt cccactcgcg 66420

ctcccacttt cacctagttg ccctcaccta cgttgccatc tcgccccttc ttcagctctc 66480

ggcctctcac ccatctgtcc tctctcttac ctctctcctc atctcgctca gacatctctc 66540

tagactatcc ctcactttac cttctcagtc gtcttcttcc tatccttcgt tctccatgat 66600

cttcacgtcg ccatctcttt tcgccccttt catatgtctc tcttcatgtt ctcactatca 66660

ttctcatgat cactatcgtt ctcactactt atcactcccc tctttcttca tcaattcctc 66720

tccgtcattc tcgtctctct cttacaaccg ccttccttgt gctatctaac tcaaccatgc 66780

ctctcctact ctctctctat cgcccctcca tcgcttatgc atcctcttct attgcacacc 66840

cgcccctcca tcgcttatgc atcctcttct attgcacacc gcccctccat cgcttatgca 66900

tcctcttcta ttgcacatcc tcttctattg cac 66933

<210> 12

<211> 21

<212> DNA

<213> Artificial Sequence

<220>

<223> Artificial sequence is a primer.

<400> 12
ctgagcggaa ttcgtgagac c 21

<210> 13

<211> 23

<212> DNA

<213> Artificial Sequence

<220>

<223> Artificial sequence is a primer.

<400> 13
ttggtctcac gtattccgct cga 23

<210> 14

<211> 20

<212> DNA

<213> Artificial Sequence

<220>

<223> Artificial sequence is a primer.

<400> 14
ctcgagaatt ctggatcctc 20

<210> 15

<211> 22

<212> DNA

<213> Artificial Sequence

<220>

<223> Artificial sequence is a primer.

<400> 15
ttgaggatcc agaattctcg ag 22

<210> 16

<211> 21

<212> DNA

<213> Artificial Sequence

<220>

<223> Artificial sequence is a primer.

<400> 16
tgtatgcgaa ttcgctgcgc g 21

<210> 17

<211> 23

<212> DNA

<213> Artificial Sequence

<220>

<223> Artificial sequence is a primer.

<400> 17
ttcgcgcagc gaattcgcat aca 23

<210> 18

<211> 21

<212> DNA

<213> Artificial Sequence

<220>

<223> Artificial sequence is a primer.

<400> 18
gtccactgaa ttctcagtga g 21

<210> 19

<211> 23

<212> DNA

<213> Artificial Sequence

<220>

<223> Artificial sequence is a primer.

<400> 19
ttgtcactga gaattcagtg gac 23

<210> 20

<211> 21

<212> DNA

<213> Artificial Sequence

<220>

<223> Artificial sequence is a primer.

<400> 20
gaatccgaat tcctggtcag c 21

<210> 21

<211> 23

<212> DNA

<213> Artificial Sequence

<220>

<223> Artificial sequence is a primer.

<400> 21

ttgctgacca ggaattcgga ttc 23

<210> 22

<211> 33

<212> DNA

<213> Artificial Sequence

<220>

<223> Artificial sequence is a primer.

<400> 22
cuacuacuac uactgagcgg aattcgtgag acc 33

<210> 23

<211> 32

<212> DNA

<213> Artificial Sequence

<220>

<223> Artificial sequence is a primer.

<400> 23
cuacuacuac uactcgagaa ttctggatcc tc 32

<210> 24

<211> 33

<212> DNA

<213> Artificial Sequence

<220>

<223> Artificial sequence is a primer.

<400> 24
cuacuacuac uatgtatgcg aattcgctgc gcg 33

<210> 25

<211> 33

<212> DNA

<213> Artificial Sequence

<220>

<223> Artificial sequence is a primer.

<400> 25
cuacuacuac uagtccactg aattctcagt gag 33

<210> 26

<211> 33

<212> DNA

<213> Artificial Sequence

<220>

<223> Artificial sequence is a primer.

<400> 26
cuacuacuac uagaatccga attcctggtc agc 33

<210> 27

<211> 45

<212> DNA

<213> Artificial Sequence

<220>

<223> Artificial sequence is a primer.

<400> 27
aactggaaga attcgcggcc gcaggaattt ttttttttt ttttt 45

<210> 28

<211> 13

<212> DNA

<213> Artificial Sequence

<220>

<223> Artificial sequence is a primer.

<400> 28
aattcggcac gag 13

<210> 29

<211> 9

<212> DNA

<213> Artificial Sequence

<220>

<223> Artificial sequence is a primer.

<400> 29
ctcgtgccg 9

<210> 30

<211> 14

<212> DNA

<213> Artificial Sequence

<220>

<223> Artificial sequence is a primer.

<400> 30
gtacgacggc cagt 14

<210> 31

<211> 16

<212> DNA

<213> Artificial Sequence

<220>

<223> Artificial sequence is a primer.

<400> 31

aacagctatg accatg 16

<210> 32

<211> 18

<212> DNA

<213> Artificial Sequence

<220>

<223> Artificial sequence is a primer.

<400> 32
ccaagttctg agaagtcc 18

<210> 33

<211> 20

<212> DNA

<213> Artificial Sequence

<220>

<223> Artificial sequence is a primer.

<400> 33
aatacctgaa accatacctg 20

<210> 34

<211> 57

<212> DNA

<213> Artificial Sequence

<220>

<223> Artificial sequence is a primer.

<400> 34
agctgctcgt agctgtctct ccctggatca cgggtacatg tactggacag actgggt 57

<210> 35

<211> 56

<212> DNA

<213> Artificial Sequence

<220>

<223> Artificial sequence is a primer.

<400> 35
tgagacgccc ggattgagcg ggcagggata gcttattccc tgtgccgcat tacggc 56

<210> 36

<211> 27

<212> DNA

<213> Artificial Sequence

<220>

<223> Artificial sequence is a primer.

<400> 36
agctgctcgt agctgtctct ccctgga 27

<210> 37

<211> 27

<212> DNA

<213> Artificial Sequence

<220>

<223> Artificial sequence is a primer.

<400> 37
gccgtaatgc ggcacaggga ataagct 27

<210> 38

<211> 20

<212> DNA

<213> Artificial Sequence

<220>

<223> Artificial sequence is a primer.

<400> 38
gagaggctat atccctgggc 20

<210> 39

<211> 20

<212> DNA

<213> Artificial Sequence

<220>

<223> Artificial sequence is a primer.

<400> 39
acagcacgtg tttaaagggg 20

<210> 40

<211> 163

<212> DNA

<213> Homo sapiens

<400> 40
actaaagcgc cgccgccgcg ccatggagcc cgagtgagct cggcgcgggc ccgtccggcc 60
gccggacaac atggaggcag ctccgcccgg gccgccgtgg ccgctgctgc tgctgctgct 120
gctgctgctg gcgctgtgcg gctgcccggc ccccgccgcg gcc 163

<210> 41

<211> 419

<212> DNA

<213> Homo sapiens

<400> 41
gccccacagc ctcgccgctc ctgctatttg ccaaccgccg ggacgtacgg ctggtggacg 60
ccggcggagt caagctggag tccaccatcg tggtcagcgg cctggaggat gcggccgcag 120
tggacttcca gttttccaag ggagccgtgt actggacaga cgtgagcgag gaggccatca 180
agcagaccta cctgaaccag acgggggccg ccgtgcagaa cgtggtcatc tccggcctgg 240
tctctcccga cggcctcgcc tgcgactggg tgggcaagaa gctgtactgg acggactcag 300
agaccaaccg catcgaggtg gccaacctca atggcacatc ccggaaggtg ctcttctggc 360

aggaccttga ccagccgagg gccatcgcct tggaccccgc tcacgggtaa accctgctg 419

<210> 42

<211> 221

<212> DNA

<213> Homo sapiens

<400> 42
ccccgtcaca ggtacatgta ctggacagac tggggtgaga cgccccggat tgagcgggca 60
gggatggatg gcagcacccg gaagatcatt gtggactcgg acatttactg gcccaatgga 120
ctgaccatcg acctggagga gcagaagctc tactgggctg acgccaagct cagcttcatc 180
caccgtgcca acctggacgg ctcgttccgg taggtaccca c 221

<210> 43

<211> 221

<212> DNA

<213> Homo sapiens

<400> 43
tccctgactg caggcagaag gtggtggagg gcagcctgac gcacccttc gccctgacgc 60
tctccgggga cactctgtac tggacagact ggcagacccg ctccatccat gcctgcaaca 120
agcgcactgg ggggaagagg aaggagatcc tgagtgccct atactcaccc atggacatcc 180
aggtgctgag ccaggagcgg cagccttttt gtgagtgccg g 221

<210> 44

<211> 156

<212> DNA

<213> Homo sapiens

<400> 44
tttctcagtc cacactcgct gtgaggagga caatggcggc tggtcccacc tgtgcctgct 60
gtccccaagc gagccttttt acacatgcgc ctgccccacg ggtgtgcaga tgcaggacaa 120
cggcaggacg tgtaaggcag gtgaggcggt gggacg 156

<210> 45

<211> 416

<212> DNA

<213> Homo sapiens

<400> 45
ctccacagga gccgaggagg tgctgctgct ggcccggcgg acggacctac ggaggatctc 60
gctggacacg ccggacttca ccgacatcgt gctgcaggtg gacgacatcc ggcacgccat 120
tgccatcgac tacgacccgc tagagggcta tgtctactgg acagatgacg aggtgcgggc 180
catccgcagg gcgtacctgg acgggtctgg ggcgcagacg ctggtcaaca ccgagatcaa 240
cgaccccgat ggcatcgcgg tcgactgggt ggcccgaaac ctctactgga ccgacacggg 300
cacggaccgc atcgaggtga cgcgcctcaa cggcacctcc cgcaagatcc tggtgtcgga 360
ggacctggac gagccccgag ccatcgcact gcaccccgtg atggggtaag acgggc 416

<210> 46

<211> 198

<212> DNA

<213> Homo sapiens

<400> 46
ttcttctcca gcctcatgta ctggacagac tggggagaga accctaaaat cgagtgtgcc 60
aacttggatg ggcaggagcg gcgtgtgctg gtcaatgcct ccctcgggtg gcccaacggc 120
ctggccctgg acctgcagga ggggaagctc tactggggag acgccaagac agacaagatc 180
gaggtgaggc tcctgtgg 198

<210> 47

<211> 244

<212> DNA

<213> Homo sapiens

<400> 47
ccgtcctgca ggtgatcaat gttgatggga cgaagaggcg gaccctcctg gaggacaagc 60
tcccgcacat tttcgggttc acgctgctgg gggacttcat ctactggact gactggcagc 120
gccgcagcat cgagcgggtg cacaaggtca aggccagccg ggacgtcatc attgaccagc 180
tgcccgacct gatggggctc aaagctgtga atgtggccaa ggtcgtcggt gagtccgggg 240
ggtc 244

<210> 48

<211> 313

<212> DNA

<213> Homo sapiens

<400> 48
gttcgcttcc aggaaccaac ccgtgtgcgg acaggaacgg ggggtgcagc cacctgtgct 60

tctgcacacc ccacgcaacc cggtgtggct gccccatcgg cctggagctg ctgagtgaca 120
tgaagacctg catcgtgcct gaggcctttt tggtcttcac cagcagagcc gccatccaca 180
ggatctccct cgagaccaat aacaacgacg tggccatccc gctcacgggc gtcaaggagg 240
cctcagccct ggactttgat gtgtccaaca accacatcta ctggacagac gtcagcctga 300
aggtagcgtg ggc 313

<210> 49

<211> 255

<212> DNA

<213> Homo sapiens

<400> 49
cctgctgcca gaccatcagc cgcgccttca tgaacgggag ctcggtggag cacgtggtgg 60
agtttggcct tgactacccc gagggcatgg ccgttgactg gatgggcaag aacctctact 120
gggccgacac tgggaccaac agaatcgaag tggcgcggct ggacgggcag ttccggcaag 180
tcctcgtgtg gagggacttg gacaacccga ggtcgctggc cctggatccc accaaggggt 240
aagtgtttgc ctgtc 255

<210> 50

<211> 210

<212> DNA

<213> Homo sapiens

<400> 50
gtgccttcca gctacatcta ctggaccgag tggggcggca agccgaggat cgtgcgggcc 60
ttcatggacg ggaccaactg catgacgctg gtggacaagg tgggccgggc caacgacctc 120
accattgact acgctgacca gcgcctctac tggaccgacc tggacaccaa catgatcgag 180
tcgtccaaca tgctgggtga gggccgggct 210

<210> 51

<211> 352

<212> DNA

<213> Homo sapiens

<400> 51
gtgttcatgc aggtcaggag cgggtcgtga ttgccgacga tctcccgcac ccgttcggtc 60
tgacgcagta cagcgattat atctactgga cagactggaa tctgcacagc attgagcggg 120
ccgacaagac tagcggccgg aaccgcaccc tcatccaggg ccacctggac ttcgtgatgg 180
acatcctggt gttccactcc tcccgccagg atggcctcaa tgactgtatg cacaacaacg 240
ggcagtgtgg gcagctgtgc cttgccatcc ccggcggcca ccgctgcggc tgcgcctcac 300
actacaccct ggaccccagc agccgcaact gcagccgtaa gtgcctcatg gt 352

<210> 52

<211> 225

<212> DNA

<213> Homo sapiens

<400> 52
gcctcctcta cgcccaccac cttcttgctg ttcagccaga aatctgccat cagtcggatg 60
atcccggacg accagcacag cccggatctc atcctgcccc tgcatggact gaggaacgtc 120
aaagccatcg actatgaccc actggacaag ttcatctact gggtggatgg gcgccagaac 180
atcaagcgag ccaaggacga cgggacccag gcaggtgccc tgtgg 225

<210> 53

<211> 235

<212> DNA

<213> Homo sapiens

<400> 53
ctttgtctta cagccctttg ttttgacctc tctgagccaa ggccaaaacc cagacaggca 60
gccccacgac ctcagcatcg acatctacag ccggacactg ttctggacgt gcgaggccac 120
caataccatc aacgtccaca ggctgagcgg ggaagccatg ggggtggtgc tgcgtgggga 180
ccgcgacaag cccagggcca tcgtcgtcaa cgcggagcga gggtaggagg ccaac 235

<210> 54

<211> 218

<212> DNA

<213> Homo sapiens

<400> 54
ccaccctccc gcaggtacct gtacttcacc aacatgcagg accgggcagc caagatcgaa 60
cgcgcagccc tggacggcac cgagcgcgag gtcctcttca ccaccggcct catccgccct 120
gtggccctgg tggtggacaa cacactgggc aagctgttct gggtggacgc ggacctgaag 180
cgcattgaga gctgtgacct gtcaggtacg cgccccgg 218

<210> 55

<211> 234

<212> DNA

<213> Homo sapiens

<400> 55
ggctgcttgc aggggccaac cgcctgaccc tggaggacgc caacatcgtg cagcctctgg 60
gcctgaccat ccttggcaag catctctact ggatcgaccg ccagcagcag atgatcgagc 120
gtgtggagaa gaccaccggg gacaagcgga ctcgcatcca gggccgtgtc gcccacctca 180
ctggcatcca tgcagtggag gaagtcagcc tggaggagtt ctgtacgtgg gggc 234

<210> 56

<211> 157

<212> DNA

<213> Homo sapiens

<400> 56
ttgtctttgc agcagcccac ccatgtgccc gtgacaatgg tggctgctcc cacatctgta 60
ttgccaaggg tgatgggaca ccacggtgct catgcccagt ccacctcgtg ctcctgcaga 120
acctgctgac ctgtggaggt aggtgtgacc taggtgc 157

<210> 57

<211> 272

<212> DNA

<213> Homo sapiens

<400> 57
gttctcctct gtccctcccc cagagccgcc cacctgctcc ccggaccagt ttgcatgtgc 60
cacaggggag atcgactgta tccccggggc ctggcgctgt gacggctttc ccgagtgcga 120
tgaccagagc gacgaggagg gctgccccgt gtgctccgcc gcccagttcc cctgcgcgcg 180
gggtcagtgt gtggacctgc gcctgcgctg cgacggcgag gcagactgtc aggaccgctc 240
agacgaggtg gactgtgacg gtgaggccct cc 272

<210> 58

<211> 134

<212> DNA

<213> Homo sapiens

<400> 58
tctccttgca gccatctgcc tgcccaacca gttccggtgt gcgagcggcc agtgtgtcct 60
catcaaacag cagtgcgact ccttccccga ctgtatcgac ggctccgacg agctcatgtg 120
tggtgagcca gctt 134

<210> 59

<211> 274

<212> DNA

<213> Homo sapiens

<400> 59
gtttgtctct ggcagaaatc accaagccgc cctcagacga cagcccggcc cacagcagtg 60
ccatcgggcc cgtcattggc atcatcctct ctctcttcgt catgggtggt gtctattttg 120
tgtgccagcg cgtggtgtgc cagcgctatg cgggggccaa cgggcccttc ccgcacgagt 180
atgtcagcgg gaccccgcac gtgcccctca atttcatagc cccgggcggt tcccagcatg 240
gccccttcac aggtaaggag cctgagatat ggaa 274

<210> 60

<211> 164

<212> DNA

<213> Homo sapiens

<400> 60
cttccctgcc aggcatcgca tgcggaaagt ccatgatgag ctccgtgagc ctgatggggg 60
gccggggcgg ggtgcccctc tacgaccgga accacgtcac aggggcctcg tccagcagct 120
cgtccagcac gaaggccacg ctgtacccgc cggtgagggg cggg 164

<210> 61

<211> 130

<212> DNA

<213> Homo sapiens

<400> 61
ttggctctcc tcagatcctg aacccgccgc cctccccggc cacggacccc tccctgtaca 60
acatggacat gttctactct tcaaacattc cggccactgc gagaccgtac aggtaggaca 120
tccctgcag 130

<210> 62

<211> 496

<212> DNA

<213> Homo sapiens

<400> 62
tcaaacattc cggccactgc gagaccgtac aggccctaca tcattcgagg aatggcgccc 60
ccgacgacgc cctgcagcac cgacgtgtgt gacagcgact acagcgccag ccgctggaag 120

gccagcaagt actacctgga tttgaactcg gactcagacc cctatccacc cccacccacg 180
ccccacagcc agtacctgtc ggcggaggac agctgcccgc cctcgcccgc caccgagagg 240
agctacttcc atctcttccc gccccctccg tccccctgca cggactcatc ctgacctcgg 300
ccgggccact ctggcttctc tgtgcccctg taaatagttt taaatatgaa caaagaaaaa 360
aatatatttt atgatttaaa aaataaatat aattgggatt ttaaaaacat gagaaatgtg 420
aactgtgatg gggtgggcag ggctgggaga actttgtaca gtggagaaat atttataaac 480
ttaattttgt aaaaca 496

<210> 63
<211> 3081
<212> DNA
<213> Homo sapiens

<400> 63
cccgccagcc cagcccagcc caaccctact ccctccccac gccagggcag cagccgttgc 60
tcagagagaa ggtggaggaa gaaatccaga ccctagcacg cgcgcaccat catggaccat 120
tatgattctc agcaaaccaa cgattacatg cagccagaag aggactggga ccgggacctg 180
ctcctggacc cggcctggga gaagcagcag agaaagacat tcacggcatg gtgtaactcc 240
cacctccgga aggcggggac acagatcgag aacatcgaag aggacttccg ggatggcctg 300
aagctcatgc tgctgctgga ggtcatctca ggtgaacgct tggccaagcc agagcgaggc 360
aagatgagag tgcacaagat ctccaacgtc aacaaggccc tggatttcat agccagcaaa 420
ggcgtcaaac tggtgtccat cggagccgaa gaaatcgtgg atgggaatgt gaagatgacc 480
ctgggcatga tctggaccat catcctgcgc tttgccatcc aggacatctc cgtggaagag 540
acttcagcca aggaagggct gctcctgtgg tgtcagagaa agacagcccc ttacaaaaat 600
gtcaacatcc agaacttcca cataagctgg aaggatggcc tcggcttctg tgctttgatc 660
caccgacacc ggcccgagct gattgactac gggaagctgc ggaaggatga tccactcaca 720
aatctgaata cggcttttga cgtggcagag aagtacctgg acatccccaa gatgctggat 780
gccgaagaca tcgttggaac tgcccgaccg gatgagaaag ccatcatgac ttacgtgtct 840
agcttctacc acgccttctc tggagcccag aaggcggaga cagcagccaa tcgcatctgc 900
aaggtgttgg ccgtcaacca ggagaacgag cagcttatgg aagactacga gaagctggcc 960
agtgatctgt tggagtggat ccgccgcaca atcccgtggc tggagaaccg ggtgcccgag 1020
aacaccatgc atgccatgca acagaagctg gaggacttcc gggactaccg gcgcctgcac 1080
aagccgccca aggtgcagga gaagtgccag ctggagatca acttcaacac gctgcagacc 1140
aagctgcggc tcagcaaccg gcctgccttc atgccctctg agggcaggat ggtctcggac 1200
atcaacaatg cctggggctg cctggagcag gtggagaagg gctatgagga gtggttgctg 1260
aatgagatcc ggaggctgga gcgactggac cacctggcag agaagttccg gcagaaggcc 1320
tccatccacg aggcctggac tgacggcaaa gaggccatgc tgcgacagaa ggactatgag 1380
accgccaccc tctcggagat caaggccttg ctcaagaagc atgaggcctt cgagagtgac 1440
ctggctgccc accaggaccg tgtggagcag attgccgcca tcgcacagga gctcaatgag 1500
ctggactatt atgactcacc cagtgtcaac gcccgttgcc aaaagatctg tgaccagtgg 1560
gacaatctgg gggccctaac tcagaagcga agggaagctc tggagcggac cgagaaactg 1620
ctggagacca ttgaccagct gtacttggag tatgccaagc gggctgcacc cttcaacaac 1680
tggatggagg gggccatgga ggacctgcag gacaccttca ttgtgcacac cattgaggag 1740
atccagggac tgaccacagc ccatgagcag ttcaaggcca ccctccctga tgccgacaag 1800
gagcgcctgg ccatcctggg catccacaat gaggtgtcca agattgtcca gacctaccac 1860
gtcaatatgg cgggcaccaa cccctacaca accatcacgc ctcaggagat caatggcaaa 1920
tgggaccacg tgcggcagct ggtgcctcgg agggaccaag ctctgacgga ggagcatgcc 1980
cgacagcagc acaatgagag gctacgcaag cagtttggag cccaggccaa tgtcatcggg 2040
ccctggatcc agaccaagat ggaggagatc gggaggatct ccattgagat gcatgggacc 2100
ctggaggacc agctcagcca cctgcggcag tatgagaaga gcatcgtcaa ctacaagcca 2160
aagattgatc agctggaggg cgaccaccag ctcatccagg aggcgctcat cttcgacaac 2220
aagcacacca actacaccat ggagcacatc cgtgtgggct gggagcagct gctcaccacc 2280

atcgccagga ccatcaatga ggtagagaac cagatcctga cccgggatgc caagggcatc 2340
agccaggagc agatgaatga gttccgggcc tccttcaacc actttgaccg ggatcactcc 2400
ggcacactgg gtcccgagga gttcaaagcc tgcctcatca gcttgggtta tgatattggc 2460
aacgaccccc agggagaagc agaatttgcc cgcatcatga gcattgtgga ccccaaccgc 2520
ctgggggtag tgacattcca ggccttcatt gacttcatgt cccgcgagac agccgacaca 2580
gatacagcag accaagtcat ggcttccttc aagatcctgg ctggggacaa gaactacatt 2640
accatggacg agctgcgccg cgagctgcca cccgaccagg ctgagtactg catcgcgcgg 2700
atggcccccc acaccggccc cgactccgtg ccaggtgctc tggactacat gtccttctcc 2760
acggcgctgt acggcgagag tgacctctaa tccacccccgc ccggccgccc tcgtcttgtg 2820
cgccgtgccc acagatgtga aatgaatgta atctaataga agcctaatca gcccaccatg 2880
ttctccactg aaaaatcctc tttctttggg gtttttcttt ctttcttttt tgattttgca 2940
ctggacggtg acgtcagcct gtacaggctc ccaggggtgg cgtcaaatgc tattgaaatt 3000
gcgctgaatc gtatgctttt tccttttgat aaataaacaa tgtaaaaatg tttcaaaaac 3060
ctaataaaat aaataaatac g 3081

<210> 64
<211> 1324
<212> DNA
<213> Homo sapiens

<220>
<221> misc_feature
<222> (1)...(1324)
<223> n = A,T,C or G

<400> 64
ggccgcccgg cgcccccagc agnccgagcc ggggcgcaca gncggggcgc agcccgcgcc 60
ccccgccgcg attgacatga tgtttccaca aagcaggcat tcgggctcct cgcacctacc 120
ccagcaactc aaattcacca cctcggactc ctgcgaccgc atcaaagacg aatttcagct 180
actgcaagct cagtaccaca gcctcaagct cgaatgtgac aagttggcca gtgagaagtc 240
agagatgcag cgtcactatg tgatgtacta cgagatgtcc tacggcttga acatcgagat 300
gcacaaacag gctgagatcg tcaaaaggct gaacgggatt tgtgcccagg tcctgcccta 360
cctctcccaa gagcaccagc agcaggtctt gggagccatt gagagggcca agcaggtcac 420
cgctcccgag ctgaactcta tcatccgaca gcagctccaa gcccaccagc tgtcccagct 480
gcaggccctg gccctgccct tgaccccact acccgtgggg ctgcagccgc cttcgctgcc 540
ggcggtcagc gcaggcaccg gcctcctctc gctgtccgcg ctgggttccc aggcccacct 600
ctccaaggaa gacaagaacg ggcacgatgg tgacacccac caggaggatg atggcgagaa 660
gtcggattag caggggccg ggacagggag gttgggaggg gggacagagg ggagacagag 720
gcacggagag aaaggaatgt ttagcacaag acacagcgga gctcgggatt ggctaatctc 780
ccatagtatt tatggtggcg ccggcggggc cccagcccag cttgcaggcc acctctagct 840
ttcttcctac cccattccgg cttccctcct cctcccctgc agcctggtta ggtggatacc 900
tgccctgaca tgtgaggcaa gctaaggcct ggagggtcag atgggagacc aggtcccaag 960
ggagcaagac ctgcgaagcg cagcagcccc ggcccttccc ccgttttgaa catgtgtaac 1020
cgacagtctg ccctgggcca cagccctctc accctggtac tgcatgcacg caatgctagc 1080
tgcccctttc ccgtcctggg caccccgagt ctcccccgac cccgggtccc aggtatgctc 1140
ccacctccac ctgccccact caccacctct gctagttcca gacacctcca cgcccacctg 1200
gtcctctccc atcgcccaca aaaggggggg cacgagggac gagcttagct gagctgggag 1260
gagcagggtg agggtgggcg acccaggatt ccccctcccc ttcccaaata aagatgaggg 1320
tact 1324

<210> 65
<211> 2377
<212> DNA

<213> Homo sapiens

<400> 65

ggtgacaaag agccaacaga gacaatagga gacttgtcaa tttgtcttga tgggctacag 60
ttagagtctg aagttgttac caatggtgaa actacatgtt cagaaagtgc ttctcagaat 120
gatgatggct ccagatccaa ggatgaaaca agagtgagca caaatggatc agatgaccct 180
gaagatgcag gagctggtga aaataggaga gtcagtggga ataattctcc atcactctca 240
aatggtggtt ttaaaccttc tagacctcca agaccttcac gaccaccacc acccacccca 300
cgtagaccag catctgtcaa tggttcacca tctgccactt ctgaaagtga tgggtctagt 360
acaggctctc tgccgccgac aaatacaaat acaaatacat ctgaaggagc aacatctgga 420
ttaataattc ctcttactat atctggaggc tcaggcccta ggccattaaa tcctgtaact 480
caagctccct tgccacctgg ttgggagcag agagtggacc agcacgggcg agtttactat 540
gtagatcatg ttgagaaaag aacaacatgg gatagaccag aacctctacc tcctggctgg 600
gaacggcggg ttgacaacat gggacgtatt tattatgttg accatttcac aagaacaaca 660
acgtggcaga ggccaacact ggaatccgtc cggaactatg aacaatggca gctacagcgt 720
agtcagcttc aaggagcaat gcagcagttt aaccagagat tcatttatgg gaatcaagat 780
ttatttgcta catcacaaag taaagaattt gatcctcttg gtccattgcc acctggatgg 840
gagaagagaa cagacagcaa tggcagagta tatttcgtca accacaacac acgaattaca 900
caatgggaag accccagaag tcaaggtcaa ttaaatgaaa agcccttacc tgaaggttgg 960
gaaatgagat tcacagtgga tggaattcca tattttgtgg accacaatag aagaactacc 1020
acctatatag atccccgcac aggaaaatct gccctagaca atggacctca gatagcctat 1080
gttcgggact tcaaagcaaa ggttcagtat ttccggttct ggtgtcagca actggccatg 1140
ccacagcaca taaagattac agtgacaaga aaaacattgt ttgaggattc ctttcaacag 1200
ataatgagct tcagtcccca agatctgcga agacgtttgt gggtgatttt tccaggagaa 1260
gaaggtttag attatggagg tgtagcaaga gaatggttct ttcttttgtc acatgaagtg 1320
ttgaacccaa tgtattgcct gtttgaatat gcagggaagg ataactactg cttgcagata 1380
aaccccgctt cttacatcaa tccagatcac ctgaaatatt ttcgttttat tggcagattt 1440
attgccatgg ctctgttcca tgggaaattc atagacacgg gtttttcttt accattctat 1500
aagcgtatct tgaacaaacc agttggactc aaggatttag aatctattga tccagaattt 1560
tacaattctc tcatctgggt taaggaaaac aatattgagg aatgtgattt ggaaatgtac 1620
ttctccgttg acaaagaaat tctaggtgaa attaagagtc atgatctgaa acctaatggt 1680
ggcaatattc ttgtaacaga agaaaataaa gaggaataca tcagaatggt agctgagtgg 1740
aggttgtctc gaggtgttga agaacagaca caagctttct ttgaaggctt taatgaaatt 1800
cttccccagc aatatttgca atactttgat gcaaaggaat tagaggtcct tttatgtgga 1860
atgcaagaga ttgatttgaa tgactggcaa agacatgcca tctaccgtca ttatgcaagg 1920
accagcaaac aaatcatgtg gttttggcag tttgttaaag aaattgataa tgagaagaga 1980
atgagacttc tgcagtttgt tactggaacc tgccgattgc cagtaggagg atttgctgat 2040
ctcatgggga gcaatggacc acagaaattc tgcattgaaa aagttgggaa agaaaattgg 2100
ctacccagaa gtcatacctg ttttaatcgc ctggacctgc caccatacaa gagctatgag 2160
caactgaagg aaaagctgtt gtttgccata gaagaaacag aaggatttgg acaagagtaa 2220
cttctgagaa cttgcaccat gaatgggcaa gaacttattt gcaatgtttg tccttctctg 2280
cctgttgcac atcttgtaaa attggacaat ggctctttag agagttatct gagtgtaagt 2340
aaattaatgt tctcatttaa aaaaaaaaaa aaaaaaa 2377

<210> 66
<211> 1295
<212> DNA
<213> Homo sapiens

<400> 66

gggccgccgc ccacccgggc cttgcctcta cctcagtcgt tgccccccga ttttcggctg 60
gagcccacgg ccccggccct cagcccccgc tctagcttcg ccagtagctc ggccagcgac 120
gcgagcaagc cgtccagccc ccgggggcagc ctgctgctgg acggggcggg ggctggcgga 180

gctggaggta gccggccctg cagcaatcgc accagcggca tcagcatggg ctacgaccag 240
cgccacggga gccccttgcc agcggggccg tgcctgtttg gcccaccccc ggccggagca 300
ccggcaggct attctcccgg aggggtcccg tccgcctacc cggagctcca cgccgccctg 360
gaccgattgt acgctcagcg gcccgcgggg ttcggctgcc aggaaagccg ccactcgtat 420
ccccccggccc tgggcagccc tggagctcta gccggggccc gagtgggagc ggcggggccc 480
ttggagagac gggggggcgca acccggacga cactctgtga ccggctacgg ggactgcgcc 540
gtgggcgccc ggtaccagga cgagctaaca gctttgcttc gcctgacggt gggcaccggt 600
gggcgagaag ccggagcccg cggagaaccc tcggggattg agccgtcggg tctggaggag 660
ccaccaggtc ctttcgttcc ggaggccgcc cgggcccgga tgcgggagcc agaggccagg 720
gaggactact tcggcacctg tatcaagtgc aacaaaggca tctatgggca gagcaatgcc 780
tgccaggccc tggacagcct ctaccacacc cagtgctttg tttgctgctc ttgtgggcga 840
actttgcgtt gcaaggcttt ctacagtgtc aatggctctg tgtactgtga ggaagattat 900
ctgttttcag ggtttcagga ggcagctgag aaatgctgtg tctgtggtca cttgattttg 960
gagaagatcc tacaagcaat ggggaagtcc tatcatccag gctgtttccg atgcattgtt 1020
tgcaacaagt gcctggatgg catccccttc acagtggact tctccaacca agtatactgt 1080
gtcaccgact accacaaaaa ttatgctcct aagtgtgcag cctgtggcca acccatcctc 1140
ccctctgagg gctgtgagga catcgtgagg gtgatatcca tggaccggga ttatcacttt 1200
gagtgctacc actgtgagga ctgccggatg cagctgagtg atgaggaagg ctgctgctgt 1260
ttccctctgg atgggcactt gctctgccat ggttg 1295

<210> 67
<211> 3411
<212> DNA
<213> Homo sapiens

<400> 67
gggcccgggg tcccgccacc accgcgcgcg ggacagattg attcactttg gagctgtaag 60
tactgatgta ttagggtgca gcgctcattg ttcattgacg cagagtccca aaatgaatat 120
ccaagagcag ggtttccccct tggacctcgg agcaagtttc accgaagatg ctccccgacc 180
cccagtgcct ggtgaggagg gagaactggt gtccacagac ccgaggcccg ccagctacag 240
tttctgctcc gggaaaggtg ttggcattaa aggtgagact tcgacggcca ctccgaggcg 300
ctcggatctg gacctggggt atgagcctga gggcagtgcc tcccccaccc caccatactt 360
gaagtgggct gagtcactgc attccctgct ggatgaccaa gatgggataa gcctgttcag 420
gactttcctg aagcaggagg gctgtgccga cttgctggac ttctggtttg cctgcactgg 480
cttcaggaag ctggagccct gtgactcgaa cgaggagaag aggctgaagc tggcgagagc 540
catctaccga aagtacattc ttgataacaa tggcatcgtg tcccggcaga ccaagccagc 600
caccaagagc ttcataaagg gctgcatcat gaagcagctg atcgatcctg ccatgtttga 660
ccaggcccag accgaaatcc aggccactat ggaggaaaac acctatccct ccttccttaa 720
gtctgatatt tatttggaat atacgaggac aggctcggag agccccaaag tctgtagtga 780
ccagagctct gggtcaggga cagggaaggg catatctgga tacctgccga ccttaaatga 840
agatgaggaa tggaagtgtg accaggacat ggacgaggac gatggcagag acgctgctcc 900
ccccggaaga ctccctcaga agctgctcct ggagacagct gccccgaggg tctcctccag 960
tagacggtac agcgaaggca gagagttcag gtatggatcc tggcgggagc cagtcaaccc 1020
ctattatgtc aatgccggct atgccctggc cccagccacc agtgccaacg acagcgagca 1080
gcagagcctg tccagcgatg cagacaccct gtccctcacg gacagcagcg tggatgggat 1140
ccccccatac aggatccgta agcagcaccg cagggagatg caggagagcg cgcaggtcaa 1200
tgggcgggtg cccctacctc acattccccg cacgtaccgg gtgccgaagg aggtccgcgt 1260
ggagcctcag aagttcgcgg aggagctcat ccaccgcctg gaggctgtgc agcgcacgcg 1320
ggaggccgag gagaagctgg aggagcggct gaagcgcgtg cgcatggagg aggaaggtga 1380
ggacggcgat ccatcgtcag ggcccccagg gccgtgtcac aagctgcctc ccgccccgc 1440
ttggcaccac ttcccgcccc gcttgtgttg gacatgggct tgtgccgggc tccgggatgc 1500
acacgaggag aaccctgaga gcatcctgga cgagcacgta cagcgtgtgc tgaggacaac 1560
tggccgccag tcgcctgggc ctggccatcg ctccccggac agtgggcacg tggccaagat 1620

gccagtggca ctgggggtg ccgcctcggg gcacgggaag cacgtaccca agtcaggggc 1680
gaagctggac gcggccggcc tgcaccacca ccgacacgtc caccaccacg tccaccacag 1740
cacagcccgg cccaaggagc aggtggaggc cgaggccacc cgcagggccc agagcagctt 1800
cgcctggggc ctggaaccac acagccatgg ggcaaggtcc cgaggctact cagagagtgt 1860
tggcgctgcc cccaacgcca gtgatggcct cgcccacagt gggaaggtgg gcgttgcgtg 1920
caaaagaaat gccaagaagg ctgagtcggg gaagagcgcc agcaccgagg tgccaggtgc 1980
ctcggaggat gcggagaaga accagaaaat catgcagtgg atcattgagg gggaaaagga 2040
gatcagcagg caccgcagga ccggccacgg gtcttcgggg acgaggaagc cacagcccca 2100
tgagaactcc agaccyttgt cccttgagca cccctgggcc ggccctcagc tccggacctc 2160
cgtgcagccc tcccacctct tcatccaaga ccccaccatg ccaccccacc cagctcccaa 2220
ccccctaacc cagctggagg aggcgcgccg acgtctggag gaggaagaaa agagagccag 2280
ccgagcaccc tccaagcaga ggtatgtgca ggaggttatg cggcggggac gcgcctgcgt 2340
caggccagcg tgcgcgccgg tgctgcacgt ggtaccagcc gtgtcggaca tggagctctc 2400
cgagacagag acaagatcgc agaggaaggt gggcggcggg agtgcccagc cgtgtgacag 2460
catcgttgtg gcgtactact tctgcgggga acccatcccc taccgcaccc tggtgagggg 2520
ccgcgctgtc accctgggcc agttcaagga gctgctgacc aaaaagggca gctacagata 2580
ctacttcaag aaagtgagcg acgagtttga ctgtggggtg gtgtttgagg aggttcgaga 2640
ggacgaggcc gtcctgcccg tctttgagga gaagatcatc ggcaaagtgg agaaggtgga 2700
ctgataggct ggtgggctgg ccgctgtgcc aggcgaggcc cttggcgggc acgggtgtca 2760
cggccaggca gatgacctcg tactcaggag cccgatgggg aacagtgttg ggtgtaccac 2820
ccatccctgt ggtctacccg tgtctagagg caggtagggg gtccctccaa gtggtccaca 2880
agcttctgtc ctgcccccaa ggaggcagcc tggaccactc ctcatagcaa tacttggagg 2940
gcccagccca agtgaggcag ccgaggtccc tgctgccagc ttcaggtgac ccccccccat 3000
cccccggcac ctcccttggg cacgtgtgct gggatctact ttccctctgg gatttgccca 3060
cgtacccagg tctggctggg gcccaggccc ggatgcagag gcctgcaggg cctctgtcaa 3120
ttgtacgcgc caccaagtgc cttcaacaca gcttgtctct tgcctgccac tgtgtgaatc 3180
ggcgacggag cactgcacct gcctccagcc gccggctgtg cagtcctggg tcctcctttc 3240
tgagggcccg tgtaaatatg tacatttctc aggctagggc cagcaggggc tgcccgagtc 3300
tgtttttcat gcgatgacac ttgtacaatt atcttttcaa aggtacttgg ataataatga 3360
aataaaactg tttttgaacc tgaataaaaa aaaaaaaaaa aaaaaaaaaa a 3411

<210> 68
<211> 3140
<212> DNA
<213> Homo sapiens

<400> 68
ggctgcgagt acctccatgg tcccggtggc tgtgacggcg gcagtggcgc ctgtcctgtc 60
cataaacagc gatttctcag atttgcggga aattaaaaag caactgctgc ttattgcggg 120
ccttacccgg gagcggggcc tactacacag tagcaaatgg tcggcggagt tggctttctc 180
tctccctgca ttgcctctgg ccgagctgca accgcctccg cctattacag aggaagatgc 240
ccaggatatg gatgcctata ccctggccaa ggcctacttt gacgttaaag agtatgatcg 300
ggcagcacat ttcctgcatg gctgcaatag caagaaagcc tattttctgt atatgtattc 360
cagatatctg tctggagaaa aaaagaagga cgatgaaaca gttgatagct taggcccccc 420
ggaaaaagga caagtgaaaa atgaggcgct tagagaattg agagtggagc tcagcaaaaa 480
acaccaagct cgagaacttg atggatttgg actttatctg tatggtgtgg tgcttcgaaa 540
actggacttg gttaaagagg ccattgatgt gtttgtggaa gctactcatg ttttgccctt 600
gcattgggga gcctggttag aactctgtaa cctgatcaca gacaaagaga tgctgaagtt 660
cctgtctttg ccagacacct ggatgaaaga gtttttttctg gctcatatat acacagagtt 720
gcagttgata gaggaggccc tgcaaaagta tcagaatctc attgatgtgg gcttctctaa 780
gagctcgtat attgtttccc aaattgcagt tgcctatcac aatatcagag atattgacaa 840
agccctctcc atttttaatg agctaaggaa acaagaccct tacaggattg aaaatatgga 900
cacattctcc aaccttcttt atgtcaggag catgaaatcg gagttgagtt atctggctca 960

taacctctgt gagattgata aataccgtgt agaaacgtgc tgtgtaattg gcaattatta 1020
cagtttacgt tctcagcatg agaaagcagc cttatatttc cagagagccc tgaaattaaa 1080
tcctcggtat cttggtgcct ggacactaat gggacatgag tacatggaga tgaagaacac 1140
gtctgctgct atccaggctt atagacatgc cattgaggtc aacaaacggg actacagagc 1200
ttggtatggc ctcgggcaga cctatgaaat ccttaagatg ccattttact gcctttatta 1260
ttatagacgg gcccaccagc ttcgacccaa tgattctcgc atgctggttg ctttaggaga 1320
atgttacgag aaactcaatc aactagtgga agccaaaaag tgttattgga gagcttacgc 1380
cgtgggagat gtggagaaaa tggctctggt gaaactggca aagcttcatg aacagttgac 1440
tgagtcagaa caggctgccc agtgttacat caaatatatc caagatatct attcctgtgg 1500
ggaaatagta gaacacttgg aggaaagcac tgcctttcgc tatctggccc agtactattt 1560
taagtgcaaa ctgtgggatg aagcttcaac ttgtgcacaa aagtgttgtg catttaatga 1620
tacccgggaa gaaggtaagg ccttactccg gcaaatccta cagcttcgga accaaggcga 1680
gactcctacc accgaggtgc ctgctccctt tttcctacct gcttcactct ctgctaacaa 1740
taccccaca cgcagagttt ctccactcaa cttgtcttct gtcacgccat agttggctac 1800
tctcaagcca gcacattgtt agacccatct taattaagcc ttacctccat gtaaagaaca 1860
gcacgtctgt tccaaggacc tcagctcttc ttgtttctac agatggcaac agctccatag 1920
ggacagcttg tataattacc ttcagaggcc aactgacaga atcctggcag gaacagacat 1980
tatcttgcca gttagaagta cttctgtctc acttatgtcc aaagagtggc tatagatctt 2040
ggccttcttc cctgaatgct ttttttttt ggcccccaag aaagtccctt ttatagcact 2100
ttagcacagg caatgctaca ggaacaaagt ttcaatgctg ctgagagtga aagaaaggag 2160
gaaagtctgc cactctaccc tgagctggca gtagggcact gagtaccctt aggaagaagt 2220
cagagcaatg gatacaaatg accttgctct tggatttgct gagcatgatc cctattctga 2280
tgtcagagat taggtttaaa tggaatagag ctatccattt gttcttactc tctagggaga 2340
caatcttcca aaacagtttt gggggggtct tctaaagctt tcaaattgga agtaacttta 2400
ttcaactaga gttgaataaa agaagggcaa aaataatctc acagagcttg gaactgctga 2460
tagcccttac tgagggcaaa agatggctat attgttagct atactcctac caaagcaagc 2520
aaggagatag gattatagat aatttcacgg acatttggaa ataacattgg tgattataca 2580
gacaagaata aactcacttc aagctggtct gttttaataa attttcaacg taattgtcta 2640
ttttttccc tcccatctgc aacagaatac attttttca gcctttatct agatgaggta 2700
aagggaatca ttcttatggt gctcttggag agtttcaggc ctgtgcatgt gtgtacagca 2760
ggaggtaata tgctataatg tctgctgtaa tatatttgca cagtagatgc tatggatcat 2820
tctgagctca gggtccagac tttattctta ttcccagaat tttgtgttac gtttttacct 2880
cctaacatat gacacttcat cttatattaa ggaaggttta gaatatctaa tacgacttga 2940
attcatttgt tactaagcct tctcaggcaa gctgtatact agttactggt ctccactgcc 3000
atgccttttc aaggttccca tggtccagaa tgatgtttga ttcttaattt ttctgtccct 3060
tttataattt gttttaatga ttttgctaca tttggaattc aataaaaaat gtgaacaata 3120
ataaaaaaaa aaaaaaaaaa 3140

<210> 69
<211> 3513
<212> DNA
<213> Homo sapiens

<400> 69
ccgtgtacca ggtgctgcta gtgggaagca cgctgctgaa ggaagtgcct tccgggctgc 60
agctggagca gttgccttct cagagcctgc tgacccacat cccaacggcg gggctgccca 120
cttcgctagg aggaggcctg ccttactgcc accaggcctg gctggatttc cgaaggcggc 180
tggaagctct actacagaac tgccaggcag cttgtgccct gctccagggg gccatcgaaa 240
gtgtgaaggc tgtgccccag cccatggagc ctggggaggt cggtcagctg ctacagcaga 300
cagaggtcct gatgcagcag gtgctagact cgccatggct ggcatggcta caatgccagg 360
ggggccggga gctgacatgg ctgaagcaag aggtcccaga ggtgaccctg agcccagact 420
acaggacggc aatggacaag gctgacgagc tatatgaccg ggtggatgga ttgctgcacc 480
aactgaccct gcagagcaac cagcgaatac aggccctaga gttggtccaa acactggagg 540

cccgggaaag cggactgcac cagattgaag tgtggctgca gcaggtgggc tggccagcac 600
tggaggaggc tggggagccc tcgctggaca tgctgctcca ggcccaaggc tcttttcagg 660
agctgtacca ggttgcccag gagcaggtca ggcaagggga gaagtttctg cagccgctga 720
ctggctggga ggcggctgaa ctggaccccc ctggggcacg ctttctggcc ctgcgagccc 780
agctgactga attctctagg gctttggccc agcggtgcca gcggctggcg gatgctgaga 840
ggctgtttca gctcttcagg gaggccttga cgtgggctga ggaggggcag cgagtgttgg 900
cagagctgga gcaggaacgc ccgggggttg tgttgcagca gctgcagctg cactggacca 960
ggcaccctga cttgcctcct gcccacttcc gaaagatgtg ggctctggcc acggggctgg 1020
gctcagaggc catccgccag gagtgccgct gggcctgggc gcggtgccag gacacctggc 1080
tggccctgga ccaaaagctt gaggcttcac tgaagctacc accggtgggc agcacagcta 1140
gcctgtgtgt cagccaggtc cccgctgcac ctgcccaccc tcccctgagg aaggcctaca 1200
gcttcgatcg gaatctgggg cagagtctca gtgaacctgc ctgccactgc caccatgcgg 1260
ccactattgc tgcctgccgc agaccagagg ctggaggagg tgccctgccc caggcatccc 1320
ctactgtgcc tccaccaggc agctctgacc ccaggagcct caacaggcta cagctggtgc 1380
tggcagagat ggtggccacg gagcgggagt atgtccgggc tctagagtac actatggaga 1440
actatttccc cgagctggat cgccccgatg tgccccaggg cctccgcggt cagcgtgccc 1500
acctctttgg caacctggag aagctgcggg acttccactg ccacttcttc ctgcgtgagc 1560
tggaggcttg cacccggcac ccaccacgag tggcctatgc cttcctgcgc catagggtgc 1620
agtttgggat gtacgcgctc tacagcaaga ataagcctcg ctccgatgcc ctgatgtcaa 1680
gctatgggca caccttcttc aaggacaagc agcaagcact gggggaccac ctggacctgg 1740
cctcctacct gctaaagccc atccagcgca tgggcaagta cgcactgctg ctgcaggagc 1800
tggcacgggc ctgcgggggc cccacgcagg agctcagtgc gctgcgggag gcccagagcc 1860
ttgtgcactt ccagctgcgg cacggaaacg acctgctggc catggacgcc atccagggct 1920
gtgatgttaa cctcaaggaa caggggcagc tggtgcgaca ggatgagttt gtggtgcgca 1980
ctgggcgcca caagtccgtg cgccgcatct tccttttga ggagctgctg ctcttcagca 2040
agcctcgcca tgggcccaca ggggttgaca catttgccta caagcgctcc ttcaagatgg 2100
cagaccttgg tctcactgag tgctgtggga acagcaacct gcgcttcgag atctggttcc 2160
gccgccgcaa ggccagggac accttgtgc tgcaggcctc cagcctggct atcaagcagg 2220
cctggacagc tgacatctcc cacctgcttt ggaggcaggc cgtccacaac aaggaggtgc 2280
gcatggctga gatggtgtcc atgggtgtgg ggaacaaggc cttccgagac attgctccca 2340
gcgaggaagc catcaacgac cgcaccgtca actatgtcct gaagtgccga gaagttcgct 2400
ctcgggcgtc cattgccgta gccccgtttg accatgacag cctctacctg ggggcctcga 2460
actcccttcc tggagaccct gcctcttgct ctgttctggg gtccctcaac ctgcacctgt 2520
acagagaccc agctcttctg ggtctccgct gtcccctgta tcccagcttc ctagaggaag 2580
cagcactgga ggctgaggca gagctgggcg gccagccctc tttgactgct gaggactcag 2640
agatctcgtc ccaatgccca tcagccagtg gctccagtgg ctctgacagc agctgtgtgt 2700
cagggcaggc cctgggtagg ggcctggagg acttaccctg tgtctgagcc cgggactgga 2760
cgagcagtag atccagcagc ctgcagctcc aaggaacatt gcctctctgg atctgctgtg 2820
accagggtgt ggctgacacc tgggctacct ccaacctaca tgtgcaacgc tgttgactac 2880
cctttctgat gtgtgtggcc attggactaa ctggcacggg gcctctctag ggaagtctgg 2940
ttgtagagcc tgaataggct cctggcccca tgaccccttc tcctgtcccc agctcccatc 3000
ccagttgtgg gttaagaata ggctagagca gacattgggt gtttccatgc tgtaggctgg 3060
tgggggacca tgtgcctcta ggcagtgact agggtgcccc caccctcag gaagaacaca 3120
ggtgggctcc tagcagctga tccccaatgc ctggccttaa agccgagctc agttaccata 3180
gggacaggtc cacctctact gggccctcat gcttgccttt cctggccccc aggcccagcc 3240
ccttttact ggggcagttt cgttattttg acttgatgcc ttttgaataa ctttcaatag 3300
aattgtctaa aattatctta ctggttgtta ggcctttggt gtctcagaga aggagtctag 3360
gtctttgatg tgtgatttaa tcttttattt gtttataata aaaaatagac tgatttgtaa 3420
aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa 3480
aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaa 3513

<210> 70
<211> 3597

<212> DNA
<213> Homo sapiens

<400> 70

catgccagtt acttcctcag gaaaatattt tcttgccttc ttctttcagt atggttttaa 60
atttgggaac agtggataac ccaagtgtcc cacaggccaa ggtatattcc aatggcagca 120
tgatccctgc acccaaagcc agcccctaaa gcctacccct tgtgcacccg cagcctggta 180
agtgagcttg gctgcttgtg aggagctaca agtgaaagag aagttatttt aaataaatcc 240
caaagtttga ggcagactgt ccaggactgt tcccaggaag aagcaggagt tacccacagg 300
aaaagtctct gacctggtcc cctcaggccc agctacctgc gcccaccagc agtgaaggtt 360
gatgtactgg cccagcatct ccacctcccc catgcaacca ggtccctggt accgtgtctc 420
ccgttgcatg tctggcttct gcctgtgctc ctcctgccac gagcatcctc cctgtccctc 480
ctcattccac cgtgtctctc ctgcacacat agcctctgtc ccagggcgat ttatccactt 540
gagtacagga gctgctcaga cctctcagcc cagccctctg tgactgcccc agccccatcc 600
taccccaccc aaagctgcct tcctggctgt aggagctccc tcgtctagcc aaggccctat 660
gggtccccat ccgaggatcc acaagcaatg acttcccaaa tgacctccac tgcaagaaga 720
atccttacca ctgtttccag agccgtgaac gatgctgtga tggcccaggt ctcagcacca 780
ccctctgtga cctaaaaaga aaagctcaat ttccatctgt cttctttccc aggaccaagg 840
ggacacagta atgtgaagtc aaatacttaa ccgagcaaag ggccagtgtt gttatcagtc 900
aaggacaaac ctcccacctc acagacagcc aagcagtgag ggaaagacag acagacatag 960
gtaggaaggt gctctgcagg cacaaggccc agagaagccc ctctccggga acttcccctg 1020
ctccttccag gaacagtgag cccagtgagc agtcccagcc agctcttcaa ggccttcaag 1080
gggtctttcc atgactgagt cacctccagg agctcacctg acccccagag aagacctacc 1140
ccaggcagct ccgtgccctg gcttctcccc atgccccaaa tccccccccag ccatccctcc 1200
tggtcctcgt ctacatcaag ggcctcttcc cctcttcctc ccagctctca ggacaggtga 1260
ctgggagacc ttgaaccctc agcctcttcc tttaaaaaaa acaaaacaaa acaaaactgt 1320
gggccattta tttgggattt tggagttgtt tggtttttgt ttttatatct taatagttcg 1380
aaagtaagaa gggagccctg ctatggatgt taagtccaaa ttactcggtt agtgggagca 1440
aaacctatga cttccaaggg gatgaggaga ggttcagagg acaggaggag cctcccccat 1500
tgaaaaaaaa aaaatgggtc aggacattcc ctggatgagg acaatgctag gggtggcatc 1560
tcacatggct gctgctattc ctggtgcttc cccacacttt tgacagatgg agtccttctc 1620
ctaccgcctc ctgccacctc accctacagg cattctctat gtaggaaaca agagccttat 1680
cttatagagt ggggagctga gacacagcct caggtaacac tgacacagct cccgaatgag 1740
gctgggacac tctgcaaacc tctcctcatg gtgctaaggg tggcatgctc ttgacaggaa 1800
acctaaatga ccactcctct catttggaaa gtaatccact gcagtaaaag tttcagacat 1860
gcaagagaga gtttttttct ttttttacta caaatttttg ctcccccata aaattatttt 1920
tttattagag ggagtatcca agttttaaaa gtatatagaa ttttttggtt gtaagagaaa 1980
tacatactca ttaggatccc gattaaattc cttgagtaga ctggtgccta ccagaaagca 2040
aagcaaagtt aaacaaaacg aaacaaaatc cttcatatac aaaaagaact ttctgtttgt 2100
attggcagag gtagtgaggt gattcaggta ggctgaaaat cctgggttgc gggagcctca 2160
ctttattcca ttcccacccg ctttgatgtc tatgcttggc tctctgggct gcccctggta 2220
ctgccgaatc ctacacatct cttatcagct ttcctcaaac tttaaggagg ctctgtgagg 2280
gatgggtcat gggaagaccc aagctttccc tccgccagga ttgcaaaagc aagtagactt 2340
ggtctatgca gctcttcttc caacaatttc tttatttgga attagaactt cctttgttag 2400
tatctttgat cttttgactc aagcacattt tggaagggct cccttacaaa agtagaattt 2460
aaaacagagg atacagttaa agagcaaccc aaaggacgct taagaaaccg agaccacttc 2520
accgaacagg actaaggaac actttcgtgc acagaagtca gccgcaatcc aggcacagga 2580
cgaagatggg atacacgtgc tcatctgtct gtcctccttt cctctccctc cccgacgttc 2640
tagttagctt gttgacttgt taaaccttct gttcttaaaa tgaaaagcta gcttacctca 2700
aagaatcttg tttccattcg gaaaccaacg attttgtgtt ttagaatgga cagccctccc 2760
ctcaccactc cctaccttgg cctggtgtcc ttgagacata cggtctttgc ttagtcgtgt 2820
gttggctgct ttgagcagga acgaggcctc caggccctga ggtgggaagg aaggattgga 2880
tgccactgcc ctcctcccca ctttagcatg taggggccag cccatctctt ccagcagggt 2940

cctgctgagt taccatagca accagcaact ccagggtacc acaacagaca atggctcagc 3000
gagccgacgt gtggggatga tgcaggggtt ttggcccagc cagaggaccc agagttgagc 3060
ttcaaatgct agagaagggg agaaacagga tggaagggtg gtttaaggaa ctggcagggg 3120
tctttgagtc acatagagaa gccgttgaag gaggtagggc aggttatctc tgttccagtc 3180
acccccttcc agccccatcc cacttctgtt tcaaactaaa gctcccacct cgaacattga 3240
ccctttgtta gaacaaagca aagcatatct ttaaacaaca gtgttaaaat gagcctcaaa 3300
tgtatgtgga tgagatctct aagaagaggg tcttctggtt ttgattttta aagaagagta 3360
tcctagtaaa atattaaaaa aaaattaaaa agtttttaaa aaggaaacct atgctattta 3420
aattggagcc cagttgtaac ttggtaaagg caagcttctg taccttttgtt ataattaatt 3480
gtatacctgt gtatgtaaat ataaggcatt cctattttgc agttcagaac aaaaaaaact 3540
tatttgtaat atagaataaa gtttattaaa aaataagaaa aaaaaaaaaa aaaaaaa 3597

<210> 71
<211> 855
<212> DNA
<213> Homo sapiens

<400> 71
cgctcaatta tctactcgag tctagactcg aggcggccgc ccattgtgca ctaaagcagg 60
ggatagcaac ggcgtccctc ctccccgctc agctgcagcc cgcagtcctc acagtggtaa 120
catgccacgt ggtagtctct gtccatggac accacacgga tggttgtctc gcagccctgt 180
gcagggagga taggacgggc acaggaggcg cattttggtg caaaaaccgt gtgatagtct 240
cgcacgcagt agatgttgtt ctccacgtcc acggtgaagg gaaccccgtc caggcactca 300
ttgcacacgg agcaccggaa gcagcctggg tggtaggact tgcccagggc ctgcaggatc 360
atttccatga tgagatgtcc acacacgctg catttgtcgg ccgtctgctg gaacccggag 420
tacaggaagt cctcctggca gtacactttc tcacccacgt tgtagaacgc cttcccacgg 480
agtcgtctcc cacacgagtc gcaggtgaag cagtcagtgt gataaagact ccccattgcc 540
tggcacgcct gctgggctcc gtagatgcca agcccacact tgatgcaaat gccgaagtag 600
tcccgcgccg tgcgcgcctc gagcgcccgc tccagctccc gggtgagcgc ctccagccgc 660
cgctcggccg cgcttgggcc gccctcccgg ccaggggcca gcgggagtgc aggcagcggg 720
aaggggccg gccccgcagg ctccggggag cgagcgggcg cggggcaggc gccgggcggg 780
aggaagtcag cgtaggcttt agtgcacaat gggaattcgg atccggtcga cactagttct 840
aggatctctt ttttt 855

<210> 72
<211> 3791
<212> DNA
<213> Homo sapiens

<400> 72
acagacggcg ggtgaacatg gcgtcctcga cttggtctga gacgtgatag gcctgccttc 60
tggttgaaga tgtggcgagt gaaaaaactg agcctcagcc tgtcgccttc gccccagacg 120
ggaaaaccat ctatgagaac tcctctccgt gaacttaccc tgcagcccgg tgccctcacc 180
acctctggaa aaagatcccc cgcttgctcc tcgctgaccc catcactgtg caagctgggg 240
ctgcaggaag gcagcaacaa ctcgtctcca gtggattttg taaataacaa gaggacagac 300
ttatcttcag aacatttcag tcattcctca aagtggctag aaacttgtca gcatgaatca 360
gatgagcagc ctctagatcc aattccccaa attagctcta ctcctaaaac gtctgaggaa 420
gcagtagacc cactgggcaa ttatatggtt aaaaccatcg tccttgtacc atctccactg 480
gggcagcaac aagacatgat atttgaggcc cgtttagata ccatggcaga gacaaacagc 540
atatctttaa atggaccttt gagaacagac gatctggtga gagaggaggt ggcaccctgc 600
atgggagaca ggttttcaga agttgctgct gtatctgaga aacctatctt tcaggaatct 660
ccgtcccatc tcttagagga gtctccacca aatccctgtt ctgaacaact acattgctcc 720
aaggaaagcc tgagcagtag aactgaggct gtgcgtgagg acttagtacc ttctgaaagt 780

aacgccttct tgccttcctc tgttctctgg ctttcccctt caactgcctt ggcagcagat 840
ttccgtgtca atcatgtgga cccagaggag gaaattgtag agcatggagc tatggaggaa 900
agagaaatga ggtttcccac acatcctaag gagtctgaaa cagaagatca agcacttgtc 960
tcaagtgtgg aagatattct gtccacatgc ctgacaccaa atctagtaga aatggaatcc 1020
caagaagctc caggcccagc agtagaagat gttggtagga ttcttggctc tgatacagag 1080
tcttggatgt ccccactggc ctggctggaa aaaggtgtaa atacctccgt catgctggaa 1140
aatctccgcc aaagcttatc ccttccctcg atgcttcggg atgctgcaat tggcactacc 1200
cctttctcta cttgctcggt ggggacttgg tttactcctt cagcaccaca ggaaaagagt 1260
acaaacacat cccagacagg cctggttggc accaagcaca gtacttctga gacagagcag 1320
ctcctgtgtg gccggcctcc agatctgact gccttgtctc gacatgactt ggaagataac 1380
ctgctgagct ctcttgtcat tgtggagttt ctctcccgcc agcttcggga ctggaagagc 1440
cagctggctg tccctcaccc agaaacccag gacagtagca cacagactga cacatctcac 1500
agtgggataa ctaataaact tcagcatctt aaggagagcc atgagatggg acaggcccta 1560
cagcaggcca gaaatgtcat gcaatcatgg gtgcttatct ctaaagagct gatatccttg 1620
cttcacctat ccctgttgca tttagaagaa gataagacta ctgtgaatca ggagtctcgg 1680
cgtgcagaaa cattggtctg ttgctgtttt gatttgctga agaaattgag ggcaaagctc 1740
cagagcctca aagcagaaag ggaggaggca aggcacagag aggaaatggc tctcagaggc 1800
aaggatgcgg cagagatagt gttggaggct ttctgtgcac acgccagcca gcgcatcagc 1860
cagctggaac aggacctagc atccatgcgg gaattcagag gccttctgaa ggatgcccag 1920
acccaactgg tagggcttca tgccaagcaa gaagagctgg ttcagcagac agtgagtctt 1980
actttctacct tgcaacaaga ctggaggtcc atgcaactgg attatacaac atggacagct 2040
ttgctgagtc ggtcccgaca actcacagag aaactcacag tcaagagcca gcaagccctg 2100
caggaacgtg atgtggcaat tgaggaaaag caggaggttt ctagggtgct ggaacaagtc 2160
tctgcccagt tagaggagtg caaaggccaa acagaacaac tggagttgga aaacattcgt 2220
ctagcaacag atctccgggc tcagttgcag attctggcca acatggacag ccagctaaaa 2280
gagctacaga gtcagcatac ccattgtgcc caggacctgg ctatgaagga tgagttactc 2340
tgccagctta cccagagcaa tgaggagcag gctgctcaat gcgtaaagga agagatggca 2400
ctaaaacaca tgcaggcaga actgcagcag caacaagctg tcctggccaa agaggtgcgg 2460
gacctgaaag agaccttgga gtttgcagac caggagaatc aggttgctca cctggagctg 2520
ggtcaggttg agtgtcaatt gaaaaccaca ctggaagtgc tccgggagcg cagcttgcag 2580
tgtgagaacc tcaaggacac tgtagagaac ctaacggcta aactggccag caccatagca 2640
gataaccagg agcaagatct ggagaaaaca cggcagtact ctcaaaagct agggctgctg 2700
actgagcaac tacagagcct gactctcttt ctacagacaa aactaaagga gaagactgaa 2760
caagagaccc ttctgctgag tacagcctgt cctcccaccc aggaacaccc tctgcctaat 2820
gacaggacct tcctgggaag catcttgaca gcagtggcag atgaagagcc agaatcaact 2880
cctgtgccct tgcttggaag tgacaagagt gctttcaccc gagtagcatc aatggtttcc 2940
cttcagcccg cagagacccc aggcatggag gagagcctgg cagaaatgag tattatgact 3000
actgagcttc agagtctttg ttccctgcta caagagtcta aagaagaagc catcaggact 3060
ctgcagcgaa aaatttgtga gctgcaagct aggctgcagg cccaggaaga acagcatcag 3120
gaagtccaga aggcaaaaga agcagacata gagaagctga accaggcctt gtgcttgcgc 3180
tacaagaatg aaaaggagct ccaggaagtg atacagcaga atgagaagat cctagaacag 3240
atagacaaga gtggcgagct cataagcctt agagaggagg tgacccacct tacccgctca 3300
cttcggcgtg cggagacaga gaccaaagtg ctccaggagg cctggcaggc cagctggact 3360
ccaactgcca gcctatggcc accaattgga tccaggagaa agtgtggctc tctcaggagg 3420
tggacaaact gagagtgatg ttcctggaga tgaaaaatga gaaggaaaac tcctgatcaa 3480
gttccagagc ccatagaaat atcctagagg agaaccttcg gcgctctgac aaggagttag 3540
aaaaactaga tgacattgtt cagcatattt ataagaccct gctctctatt ccagaggtgg 3600
tgaggggatg caaagaacta cagggattgc tggaatttct gagctaagaa actgaaagcc 3660
agaatttgtt tcacctcttt ttacctgcaa taccccctta ccccaatacc aagaccaact 3720
ggcatagagc caactgagat aaatgctatt taaataaagt gtatttaatg aaaaaaaaaa 3780
aaaaaaaaaa a 3791

<210> 73

<211> 1683
<212> DNA
<213> Homo sapiens

<400> 73
ctctgagtgt ccagtggtca gttgccccag gatggggacc acagccagag cagccttggt 60
cttgacctat ttggctgttg cttctgctgc ctctgaggga ggcttcacgg ctacaggaca 120
gaggcagctg aggccagagc actttcaaga agttggctac gcagctcccc cctccccacc 180
cctatcccga agcctcccca tggatcaccc tgactcctct cagcatggcc ctccctttga 240
gggacagagt caagtgcagc cccctcccta tcaggaggcc acccctctcc aacaggaaaa 300
gctgctacct gcccaactcc ctgctgaaaa ggaagtgggt ccccctctcc ctcaggaagc 360
tgtcccccta caaaaagagc tgccctctct ccagcacccc aatgaacaga aggaaggaac 420
gccagctcca tttggggacc agagccatcc agaacctgag tcctggaatg cagcccagca 480
ctgccaacag gaccggtccc aaggggggctg gggccaccgg ctggatggct tcccccctgg 540
gcggccttct ccagacaatc tgaaccaaat ctgccttcct aaccgtcagc atgtggtata 600
tggtccctgg aacctaccac agtccagcta ctcccacctc actcgccagg gtgagaccct 660
caatttcctg gagattggat attcccgctg ctgccactgc cgcagccaca caaaccgcct 720
agagtgtgcc aaacttgtgt gggaggaagc aatgagccga ttctgtgagg ccgagttctc 780
ggtcaagacc cgaccccact ggtgctgcac gcggcagggg gaggctcggt tctcctgctt 840
ccaggaggaa gctccccagc cacactacca gctccgggcc tgccccagcc atcagcctga 900
tatttcctcg ggtcttgagc tgcctttccc tcctggggtg cccacattgg acaatatcaa 960
gaacatctgc cacctgaggc gcttccgctc tgtgccacgc aacctgccag ctactgaccc 1020
cctacaaagg gagctgctgg cactgatcca gctggagagg gagttccagc gctgctgccg 1080
ccaggggaac aatcacacct gtacatggaa ggcctgggag gataccccttg acaaatactg 1140
tgaccgggag tatgctgtga agacccacca ccacttgtgt tgccgccacc ctcccagccc 1200
tactcgggat gagtgctttg cccgtcgggc tccttacccc aactatgacc gggacatctt 1260
gaccattgac atcagtcgag tcacccccaa cctcatgggc cacctctgtg gaaaccaaag 1320
agttctcacc aagcataaac atattcctgg gctgatccac aacatgactg cccgctgctg 1380
tgacctgcca tttccagaac aggcctgctg tgcagaggag gagaaattaa ccttcatcaa 1440
tgatctgtgt ggtccccgac gtaacatctg gcgagaccct gccctctgct gttacctgag 1500
tcctggggat gaacaggtca actgcttcaa catcaattat ctgaggaacg tggctctagt 1560
gtctggagac actgagaacg ccaagggcca gggggagcag ggctcaactg gaggaacaaa 1620
tatcagctcc acctctgagc ccaaggaaga atgagtcacc ccagagccct agagggtcag 1680
atg 1683

<210> 74
<211> 1696
<212> DNA
<213> Homo sapiens

<400> 74
cacctaaaag ccaaaatggg aaaggaaaag actcatatca acattgtcgt cattggacac 60
gtagattcgg gcaagtccac cactactggc catctgatct ataaatgcgg tggcatcgac 120
aaaagaacca ttgaaaaatt tgagaaggag gctgctgaga tgggaaaggg ctccttcaag 180
tatgcctggg tcttggataa actgaaagct gagcgtgaac gtggtatcac cattgatatc 240
tccttgtgga aatttgagac cagcaagtac tatgtgacta tcattgatgc cccaggacac 300
agagacttta tcaaaaacat gattacaggg acatctcagg ctgactgtgc tgtcctgatt 360
gttgctgctg gtgttggtga atttgaagct ggtatctcca agaatgggca gacccgagag 420
catgcccttc tggcttacac actgggtgtg aaacaactaa ttgtcggtgt taacaaaatg 480
gattccactg agccacccta cagccagaag agatatgagg aaattgttaa ggaagtcagc 540
acttacatta agaaaattgg ctacaacccc gacacagtag catttgtgcc aatttctggt 600
tggaatggtg acaacatgct ggagccaagt gctaacatgc cttggttcaa gggatggaaa 660
gtcacccgta aggatggcaa tgccagtgga accacgctgc ttgaggctgt ggactgcatc 720

ctaccaccaa ctcgtccaac tgacaagccc ttgcgcctgc ctctccagga tgtctacaaa 780
attggtggta ttggtactgt tcctgttggc cgagtggaga ctggtgttct caaacccggt 840
atggtggtca cctttgctcc agtcaacgtt acaacggaag taaaatctgt cgaaatgcac 900
catgaagctt tgagtgaagc tcttcctggg gacaatgtgg gcttcaatgt caagaatgtg 960
tctgtcaagg atgttcgtcg tggcaacgtt gctggtgaca gcaaaaatga cccaccaatg 1020
gaagcagctg gcttcactgc tcaggtgatt atcctgaacc atccaggcca aataagcgcc 1080
ggctatgccc ctgtattgga ttgccacacg gctcacattg catgcaagtt tgctgagctg 1140
aaggaaaaga ttgatcgccg ttctggtaaa aagctggaag atggccctaa attcttgaag 1200
tctggtgatg ctgccattgt tgatatggtt cctggcaagc ccatgtgtgt tgagagcttc 1260
tcagactatc caccttttggg tcgctttgct gttcgtgata tgagacagac agttgcggtg 1320
ggtgtcatca aagcagtgga caagaaggct gctggagctg gcaaggtcac caagtctgcc 1380
cagaaagctc agaaggctaa atgaatatta tccctaatac ctgccacccc actcttaatc 1440
agtggtggaa gaacggtctc agaactgttt gtttcaattg gccatttaag tttagtagta 1500
aaagactggt taatgataac aatgcatcgt aaaaccttca gaaggaaagg agaatgtttt 1560
gtggaccact ttggttttct tttttgcgtg tggcagtttt aagttattag tttttaaaat 1620
cagtactttt taatggaaac aacttgacca aaaatttgtc acagaatttt gagacccatt 1680
aaaaaagtta aatgag 1696

<210> 75
<211> 7680
<212> DNA
<213> Homo sapiens

<400> 75
gaagagcaag aggcaggctc agcaaatggt tcagccccag tccccggtgg ctgtcagtca 60
aagcaagccc ggttgttatg acaatggaaa acactatcag ataaatcaac agtgggagcg 120
gacctaccta ggtaatgtgt tggtttgtac ttgttatgga ggaagccgag gttttaactg 180
cgaaagtaaa cctgaagctg aagagacttg ctttgacaag tacactggga acacttaccg 240
agtgggtgac acttatgagc gtcctaaaga ctccatgatc tgggactgta cctgcatcgg 300
ggctgggcga gggagaataa gctgtaccat cgcaaaccgc tgccatgaag ggggtcagtc 360
ctacaagatt ggtgacacct ggaggagacc acatgagact ggtggttaca tgttagagtg 420
tgtgtgtctt ggtaatggaa aaggagaatg gacctgcaag cccatagctg agaagtgttt 480
tgatcatgct gctgggactt cctatgtggt cggagaaacg tgggagaagc cctaccaagg 540
ctggatgatg gtagattgta cttgcctggg agaaggcagc ggacgcatca cttgcacttc 600
tagaaataga tgcaacgatc aggacacaag gacatcctat agaattggag acacctggag 660
caagaaggat aatcgaggaa acctgctcca gtgcatctgc acaggcaacg gccgaggaga 720
gtggaagtgt gagaggcaca cctctgtgca gaccacatcg agcggatctg gccccttcac 780
cgatgttcgt gcagctgttt accaaccgca gcctcacccc cagcctcctc cctatggcca 840
ctgtgtcaca gacagtggtg tggtctactc tgtggggatg cagtggttga agacacaagg 900
aaataagcaa atgctttgca cgtgcctggg caacggagtc agctgccaag agacagctgt 960
aacccagact tacggtggca acttaaatgg agagccatgt gtcttaccat tcacctacaa 1020
tggcaggacg ttctactcct gcaccacgga agggcgacag gacggacatc tttggtgcag 1080
cacaacttcg aattatgagc aggaccagaa atactctttc tgcacagacc acactgtttt 1140
ggttcagact caaggaggaa attccaatgg tgccttgtgc cacttccccc tcctatacaa 1200
caaccacaat tacactgatt gcacttctga gggcagaaga gacaacatga agtggtgtgg 1260
gaccacacag aactatgatg ccgaccagaa gtttgggttc tgccccatgg ctgcccacga 1320
ggaaatctgc acaaccaatg aaggggtcat gtaccgcatt ggagatcagt gggataagca 1380
gcatgacatg ggtcacatga tgaggtgcac gtgtgttggg aatggtcgtg gggaatggac 1440
atgcattgcc tactcgcaac ttcgagatca gtgcattgtt gatgacatca cttacaatgt 1500
gaacgacaca ttccacaagc gtcatgaaga ggggcacatg ctgaactgta catgcttcgg 1560
tcagggtcgg ggcaggtgga agtgtgatcc cgtcgaccaa tgccaggatt cagagactgg 1620
gacgttttat caaattggag attcatggga gaagtatgtg catggtgtca gataccagtg 1680
ctactgctat ggccgtggca ttggggagtg gcattgccaa cctttacaga cctatccaag 1740

ctcaagtggt cctgtcgaag tatttatcac tgagactccg agtcagccca actcccaccc 1800
catccagtgg aatgcaccac agccatctca catttccaag tacattctca ggtggagacc 1860
taaaaattct gtaggccgtt ggaaggaagc taccatacca ggccacttaa actcctacac 1920
catcaaaggc ctgaagcctg gtgtggtata cgagggccag ctcatcagca tccagcagta 1980
cggccaccaa gaagtgactc gctttgactt caccaccacc agcaccagca cacctgtgac 2040
cagcaacacc gtgacaggag agacgactcc cttttctcct cttgtggcca cttctgaatc 2100
tgtgaccgaa atcacagcca gtagctttgt ggtctcctgg gtctcagctt ccgacaccgt 2160
gtcgggattc cgggtggaat atgagctgag tgaggaggga gatgagccac agtacctgga 2220
tcttccaagc acagccactt ctgtgaacat ccctgacctg cttcctggcc gaaaatacat 2280
tgtaaatgtc tatcagatat ctgaggatgg ggagcagagt ttgatcctgt ctacttcaca 2340
aacaacagcg cctgatgccc ctcctgaccc gactgtggac caagttgatg acacctcaat 2400
tgttgttcgc tggagcagac cccaggctcc catcacaggg tacagaatag tctattcgcc 2460
atcagtagaa ggtagcagca cagaactcaa ccttcctgaa actgcaaact ccgtcaccct 2520
cagtgacttg caacctggtg ttcagtataa catcactatc tatgctgtgg aagaaaatca 2580
agaaagtaca cctgttgtca ttcaacaaga aaccactggc accccacgct cagatacagt 2640
gccctctccc agggacctgc agtttgtgga agtgacagac gtgaaggtca ccatcatgtg 2700
gacaccgcct gagagtgcag tgaccggcta ccgtgtggat gtgatccccg tcaacctgcc 2760
tggcgagcac gggcagaggc tgcccatcag caggaacacc tttgcagaag tcaccgggct 2820
gtcccctggg gtcacctatt acttcaaagt ctttgcagtg agccatggga gggagagcaa 2880
gcctctgact gctcaacaga caaccaaact ggatgctccc actaacctcc agtttgtcaa 2940
tgaaactgat tctactgtcc tggtgagatg gactccacct cgggcccaga taacaggata 3000
ccgactgacc gtgggcctta cccgaagagg ccagcccagg cagtacaatg tgggtccctc 3060
tgtctccaag taccccctga ggaatctgca gcctgcatct gagtacaccg tatccctcgt 3120
ggccataaag ggcaaccaag agagccccaa agccactgga gtctttacca cactgcagcc 3180
tgggagctct attccacctt acaacaccga ggtgactgag accaccatcg tgatcacatg 3240
gacgcctgct ccaagaattg gttttaagct gggtgtacga ccaagccagg gaggagaggc 3300
accacgagaa gtgacttcag actcaggaag catcgttgtg tccggcttga ctccaggagt 3360
agaatacgtc tacaccatcc aagtcctgag agatggacag gaaagagatg cgccaattgt 3420
aaacaaagtg gtgacaccat tgtctccacc aacaaacttg catctggagg caaaccctga 3480
cactggagtg ctcacagtct cctgggagag gagcaccacc ccagacatta ctggttatag 3540
aattaccaca acccctacaa acggccagca gggaaattct ttggaagaag tggtccatgc 3600
tgatcagagc tcctgcactt ttgataacct gagtcccggc ctggagtaca atgtcagtgt 3660
ttacactgtc aaggatgaca aggaaagtgt ccctatctct gataccatca tcccagctgt 3720
tcctcctccc actgacctgc gattcaccaa cattggtcca gacaccatgc gtgtcacctg 3780
ggctccaccc ccatccattg atttaaccaa cttcctggtg cgttactcac ctgtgaaaaa 3840
tgaggaagat gttgcagagt tgtcaatttc tccttcagac aatgcagtgg tcttaacaaa 3900
tctcctgcct ggtacagaat atgtagtgag tgtctccagt gtctacgaac aacatgagag 3960
cacacctctt agaggaagac agaaaacagg tcttgattcc ccaactggca ttgacttttc 4020
tgatattact gccaactctt ttactgtgca ctggattgct cctcgagcca ccatcactgg 4080
ctacaggatc cgccatcatc ccgagcactt cagtgggaga cctcgagaag atcgggtgcc 4140
ccactctcgg aattccatca ccctcaccaa cctcactcca ggcacagagt atgtggtcag 4200
catcgttgct cttaatggca gagaggaaag tcccttattg attggccaac aatcaacagt 4260
ttctgatgtt ccgagggacc tggaagttgt tgctgcgacc cccaccagcc tactgatcag 4320
ctgggatgct cctgctgtca cagtgagata ttacaggatc acttacggag aaacaggagg 4380
aaatagccct gtccaggagt tcactgtgcc tgggagcaag tctacagcta ccatcagcgg 4440
ccttaaacct ggagttgatt ataccatcac tgtgtatgct gtcactggcc gtggagacag 4500
ccccgcaagc agcaagccaa tttccattaa ttaccgaaca gaaattgaca aaccatccca 4560
gatgcaagtg accgatgttc aggacaacag cattagtgtc aagtggctgc cttcaagttc 4620
ccctgttact ggttacagag taaccaccac tcccaaaaat ggaccaggac caacaaaaac 4680
taaaactgca ggtccagatc aaacagaaat gactattgaa ggcttgcagc ccacagtgga 4740
gtatgtggtt agtgtctatg ctcagaatcc aagcggagag agtcagcctc tggttcagac 4800
tgcagtaacc aacattgatc gccctaaagg actggcattc actgatgtgg atgtcgattc 4860
catcaaaatt gcttgggaaa gcccacaggg gcaagtttcc aggtacaggg tgacctactc 4920

gagccctgag gatggaatcc atgagctatt ccctgcacct gatggtgaag aagacactgc 4980
agagctgcaa ggcctcagac cgggttctga gtacacagtc agtgtggttg ccttgcacga 5040
tgatatggag agccagcccc tgattggaac ccagtccaca gctattcctg caccaactga 5100
cctgaagttc actcaggtca cacccacaag cctgagcgcc cagtggacac cacccaatgt 5160
tcagctcact ggatatcgag tgcgggtgac ccccaaggag aagaccggac caatgaaaga 5220
aatcaacctt gctcctgaca gctcatccgt ggttgtatca ggacttatgg tggccaccaa 5280
atatgaagtg agtgtctatg ctcttaagga cactttgaca agcagaccag ctcagggtgt 5340
tgtcaccact ctggagaatg tcagcccacc aagaagggct cgtgtgacag atgctactga 5400
gaccaccatc accattagct ggagaaccaa gactgagacg atcactggct tccaagttga 5460
tgccgttcca gccaatggcc agactccaat ccagagaacc atcaagccag atgtcagaag 5520
ctacaccatc acaggtttac aaccaggcac tgactacaag atctacctgt acaccttgaa 5580
tgacaatgct cggagctccc ctgtggtcat cgacgcctcc actgccattg atgcaccatc 5640
caacctgcgt ttcctggcca ccacacccaa ttccttgctg gtatcatggc agccgccacg 5700
tgccaggatt accggctaca tcatcaagta tgagaagcct gggtctcctc ccagagaagt 5760
ggtccctcgg ccccgccctg gtgtcacaga ggctactatt actggcctgg aaccgggaac 5820
cgaatataca atttatgtca ttgccctgaa gaataatcag aagagcgagc ccctgattgg 5880
aaggaaaaag acagacgagc ttccccaact ggtaaccctt ccacacccca atcttcatgg 5940
accagagatc ttggatgttc cttccacagt tcaaaagacc cctttcgtca cccaccctgg 6000
gtatgacact ggaaatggta ttcagcttcc tggcacttct ggtcagcaac ccagtgttgg 6060
gcaacaaatg atctttgagg aacatggttt taggcggacc acaccgccca caacggccac 6120
ccccataagg cataggccaa gaccataccc gccgaatgta ggacaagaag ctctctctca 6180
gacaaccatc tcatgggccc cattccagga cacttctgag tacatcattt catgtcatcc 6240
tgttggcact gatgaagaac ccttacagtt cagggttcct ggaacttcta ccagtgccac 6300
tctgacaggc ctcaccagag gtgccaccta caacatcata gtggaggcac tgaaagacca 6360
gcagaggcat aaggttcggg aagaggttgt taccgtgggc aactctgtca acgaaggctt 6420
gaaccaacct acggatgact cgtgctttga cccctacaca gtttcccatt atgccgttgg 6480
agatgagtgg gaacgaatgt ctgaatcagg ctttaaactg ttgtgccagt gcttaggctt 6540
tggaagtggt catttcagat gtgattcatc tagatggtgc catgacaatg gtgtgaacta 6600
caagattgga gagaagtggg accgtcaggg agaaaatggc cagatgatga gctgcacatg 6660
tcttgggaac ggaaaaggag aattcaagtg tgaccctcat gaggcaacgt gttacgatga 6720
tgggaagaca taccacgtag gagaacagtg gcagaaggaa tatctcggtg ccatttgctc 6780
ctgcacatgc tttggaggcc agcggggctg gcgctgtgac aactgccgca gacctggggg 6840
tgaacccagt cccgaaggca ctactggcca gtcctacaac cagtattctc agagatacca 6900
tcagagaaca aacactaatg ttaattgccc aattgagtgc ttcatgcctt tagatgtaca 6960
ggctgacaga gaagattccc gagagtaaat catctttcca atccagagga acaagcatgt 7020
ctctctgcca agatccatct aaactggagt gatgttagca gacccagctt agagttcttc 7080
tttctttctt aagccctttg ctctggagga agttctccag cttcagctca actcacagct 7140
tctccaagca tcaccctggg agtttcctga gggttttctc ataaatgagg gctgcacatt 7200
gcctgttctg cttcgaagta ttcaataccg ctcagtattt taaatgaagt gattctaaga 7260
tttggtttgg gatcaatagg aaagcatatg cagccaacca agatgcaaat gttttgaaat 7320
gatatgacca aaattttaag taggaaagtc acccaaacac ttctgctttc acttaagtgt 7380
ctggcccgca atactgtagg aacaagcatg atcttgttac tgtgatattt taaatatcca 7440
cagtactcac tttttccaaa tgatcctagt aattgcctag aaatatcttt ctcttacctg 7500
ttatttatca atttttccca gtatttttat acggaaaaaa ttgtattgaa aacacttagt 7560
atgcagttga taagaggaat ttggtataat tatggtgggt gattattttt tatactgtat 7620
gtgccaaagc tttactactg tggaaagaca actgttttaa taaaagattt acattccaca 7680

<210> 76
<211> 1316
<212> DNA
<213> Homo sapiens

<400> 76
tcctaatacg actcactata gggctcgagc ggccgcccgg gcaggtcgaa tgcaggcgac 60
ttgcgagctg ggagcgattt aaaacgcttt ggattccccc ggcctgggtg gggagagcga 120
gctgggtgcc ccctagattc cccgcccccg cacctcatga gccgaccctc ggctccatgg 180
agcccggcaa ttatgccacc ttggatggag ccaaggatat cgaaggcttg ctgggagcgg 240
gaggggggcg gaatctggtc gcccactccc ctctgaccag ccacccagcg gcgcctacgc 300
tgatgcctgc tgtcaactat gcccccttgg atctgccagg ctcggcggag ccgccaaagc 360
aatgccaccc atgccctggg gtgccccagg ggacgtcccc agctcccgtg ccttatggtt 420
actttggagg cgggtactac tcctgccgag tgtcccggag ctcgctgaaa ccctgtgccc 480
aggcagccac cctggccgcg taccccgcgg agactcccac ggccggggaa gagtacccca 540
gtcgccccac tgagtttgcc ttctatccgg gatatccggg aacctaccac gctatggcca 600
gttacctgga cgtgtctgtg gtgcagactc tgggtgctcc tggagaaccg cgacatgact 660
ccctgttgcc tgtggacagt taccagtctt gggctctcgc tggtggctgg aacagccaga 720
tgtgttgcca gggagaacag aacccaccag gtccctttg gaaggcagca tttgcagact 780
ccagcgggca gcaccctcct gacgcctgcg cctttcgtcg cggccgcaag aaacgcattc 840
cgtacagcaa ggggcagttg cgggagctgg agcgggagta tgcggctaac aagttcatca 900
ccaaggacaa gaggcgcaag atctcggcag ccaccagcct ctcggagcgc cagattacca 960
tctggtttca gaaccgccgg gtcaaagaga agaaggttct cgccaaggtg aagaacagcg 1020
ctacccctta agagatctcc ttgcctgggt gggaggagcg aaagtggggg tgtcctgggg 1080
agaccagaaa cctgccaagc ccaggctggg gccaaggact ctgctgagag gcccctagag 1140
acaacaccct tcccaggcca ctggctgctg gactgttcct caggagcggc ctgggtaccc 1200
agtatgtgca gggagacgga accccatgtg acaggcccac tccaccaggg ttcccaaaga 1260
acctggccca gtcataatca ttcatcctca cagtggcaat aatcacgata accagt 1316

<210> 77
<211> 566
<212> DNA
<213> Homo sapiens

<400> 77
cccaccaaac ccataaagag ggtgggtcga cccacgcgtc cgcggacgcg tgggaaatta 60
ttgaattgga aacagaaata gaaaagttta aagctgagaa cgcatcttta gctaaacttc 120
gcattgaacg agaaagtgcc ttggaaaaac tcaggaaaga aattgcagac ttcgaacaac 180
agaaagcaaa agaattagct cgaatagaag agtttaaaaa ggaggagatg aggaagctac 240
aaaaggaacg taaagttttt gaaaagtata ctacagctgc aagaactttt ccagataaaa 300
aggaacgtga agaaatacag actttaaaac agcaaatagc agatttacgg gaagatttga 360
aaagaaagga gaccaaatgg tcaagtacac acagccgtct cagaagccag atacaaatgt 420
tagtcagaga gaacacagac ctccgggaag aaataaaagt gatggaaaga ttccgactgg 480
atgcctggaa gagagcagaa gccatagaga gcagcctcga ggtggagaag aaggacaagc 540
ttgcgaacac atctgttcga tttcaa 566

<210> 78
<211> 5067
<212> DNA
<213> Homo sapiens

<400> 78
gcccggacac ctgtctgcag catggataag tatgacgacc tgggcctgga ggccagtaaa 60
ttcatcgagg acctgaacat gtatgaggcc tctaaggatg ggctcttccg agtggacaag 120
ggtgcaggca acaaccccga gtttgaggaa actcgcaggg tgttcgccac caagatggcc 180
aaaatccacc tccagcagca gcagcagcag ctcctgcagg aggagactct gcccaggggg 240
agtagaggcc ctgtcaatgg agggggccgc ctgggcccac aggcccgttg ggaagttgtg 300
ggcagcaagc tgactgtgga tggtgctgcc aagcctcctc ttgctgcctc gacaggggca 360

cctggggcag tcaccaccct cgctgctggg cagcccccgt acccaccgca ggagcagaga 420
tccaggccat acctgcatgg cacgaggcat ggcagccagg actgtggttc cagggagagc 480
ctggcgactt ctgagatgtc tgctttccac cagccaggcc cctgtgagga tccttcctgc 540
ctcactcatg gagactatta tgacaacctc tccttggcaa gcccaaagtg gggtgacaaa 600
ccaggagtgt cccccagcat cggcctgagt gtagggagtg ggtggcctag ctccccgggg 660
agtgacccac cactgcccaa accctgcggg gaccatcccc taaatcaccg acagctctcc 720
ctgagctcca gcaggtcttc tgagggtagc ctcggtggtc agaatagtgg cattggtggc 780
cgcagcagcg agaagccaac aggcctttgg tccactgcct cctcccagcg ggtgagccct 840
ggcctgcctt ccccaaactt ggagaacgga gcaccagctg tggggcctgt tcagcccagg 900
actccttctg tgtcagcacc cttggccctg agctgcccca ggcaaggagg tcttccaaga 960
tcaaactcgg ggctgggggg tgaggtttca ggtgtgatgt ccaaacccaa tgtggacccc 1020
caaccctggt tccaggatgg gcccaaatct taccttttca gttctgcccc gtcatcctcg 1080
ccagctggcc tggacggttc acagcagggt gcggtccctg ggctggggcc gaagcctggc 1140
tgcacagacc ttggcactgg tcccaagctc agccccacca gtcttgtcca tccagtgatg 1200
tccaccctgc ctgagttatc ttgtaaagag ggtcccctgg gctggtcttc tgatggtagc 1260
ctgggatctg tgctcctgga cagccccagc tcccctaggg taaggctgcc ctgccagccc 1320
ctcgtcccag gtcctgagct gagaccctct gctgctgagt tgaaattaga agccctcacc 1380
caacgtctgg agcgagagat ggatgctcac ccgaaggctg attactttgg agcctgtgtg 1440
aaatgcagca aaggggtgtt tggggctggc caggcctgtc aggccatggg gaacctctac 1500
catgacacat gcttcacctg tgcagcttgc agccggaagc tgagaggaaa agccttttat 1560
tttgtcaacg gcaaagtgtt ttgtgaagaa gacttcctgt actctggttt ccagcagtcg 1620
gctgacaggt gttttctttg tggacatctg atcatggaca tgatcctgca agccctgggg 1680
aagtcctacc accccggctg tttccgctgt gtcatctgta atgagtgttt ggatggggtg 1740
cccttcaccg tggactcaga gaacaagatc tactgtgtcc gagattacca caaggtgctg 1800
gcccccaagt gtgcagcctg tgggcttccc atccttccac ctgagggctc agatgagacc 1860
atccgtgtcg tgtccatgga cagagactac cacgtggagt gttaccactg cgaggactgt 1920
ggtctggagc tcaatgatga agatggccac cgctgttatc cgctggagga ccacctgttc 1980
tgtcactcct gccacgtgaa gaggctggag aagagaccct catctacagc ccttcaccag 2040
caccacttct agccagagcc acttgcagac atcacggcag gggatgagga gccggggttg 2100
ctgctgctgc ttccggtggc ccctggggtg gaagtggggt aggggaagag gaggggcagg 2160
agggagagtt cctgtgagca tgtgggggct gcctttcctt taaccaggga ggtgaacact 2220
acctgcctcc tgcgtgtatt ttccaagtgc ttttctctgt tgccacattt tcctcaggtt 2280
actcaggaaa atgctccagc atgtgcgagc acatgacctg aggttgcatc atagcaccaa 2340
aggaatcctc ctgtcccctc tgggaacatt tcatgcttca gagggagagg tttttattga 2400
gcttgtttca caatatcccc ttgaagggac agctcagctg ccaatacatt caacccttte 2460
tcttccttca ggaaaatacc tatacccaaa tgttccctcc cccgacatat atcatggcat 2520
gacttaaggc ttcttttcac ctgagagctt cagttcttct gcagaatggc tgcaaattta 2580
attgcattaa ggcaagaagg aagctctaat gtgtgctttg tatcctaaga taaatttgct 2640
tagaaaacca gagtcaagat ttgaaatagg tgaggcaggg tttcctcctt agacactgac 2700
agcattctcc gtacccctte aaatccttac tctcctaaag gcagctgagt ccgcgacaga 2760
aatttgccct atgggagtaa aacatacttt gggagaagaa cttggtgcag gcaccaggat 2820
ttttttttte gcccacgtgt ttgcgctgtt tttctctgga gttctcaaga gttggtgact 2880
tggaaggccg cttctgcaag gcaagtctca ggaacccatg caggtacatc gcttgcacct 2940
gtttttagct tatttaatga cgggcttttg ggaagagctg cccgcatact gagagacagc 3000
ttcttataaa caaggagagt ttttgtgtgt gcgagatctc taagccagcg tgggagggag 3060
cgcctcagga taagttatta tattcatttc gttggtttct ctcctgccca attcttggca 3120
caggcattat gtttgaagaa accaggataa ggtacactgc ttttgtctgt ttaatttttt 3180
tagttgtttc ccttcacttt cagtcttcca cacacaaaaa atacctcaca gagcttcacc 3240
aaatcacaga ttcaggagga atttggcttt cacactggac tcagatacct tcttcagtgt 3300
gttggaaatc actggcttca cacaggccca actccaactg gtcagggcag agtgatcgta 3360
actaaaggtc agtggggaat agatccgatt cagtgctttt gccttatgca tttcagcatc 3420
ctggctcccc agggtggcag gagctgagga agggccacac actggcaaga tttcaagacc 3480
actctctgca ctgaagaggt aaaatttgca ctgcaagtca catccctgag gccagaggtc 3540

agtacccttt ggtatttcga ttagaagaag ctgcaaaaga aaggcagccc attttaccat 3600
tgccagccag gccggggaca caggagccgg tgtgtgcact ctgcctccta acattgcacc 3660
cagagcaaga ggactgggtg ctgggctgca gaggccggtc agtggagccc ctagcacgtg 3720
tgaactcagg cttttcattg ggcccggctc cacttctagg ccatgttttg actcatttgg 3780
taaccattgc ctgtaagcag cacagaattg gtgccatgga ttatcttttc catgttgatg 3840
gaattcattc tgttggaatc ctttggccag atgtcacttc agccagggtg tgcatcatca 3900
ttggttcttt ttcacaggct gagcctcctg aaaacccatg aacgctgggg ctggggaagt 3960
gaaccctgag gtggggaccc tctcttccca tcaaatcatc cagctcagtg tggggcgtgg 4020
caggggggta aatgaagcca gccaatgtgt taacctgtct ctgtcaacct aagaatgttg 4080
gccttactga cacacctttg ctccatgttc aagaccagaa gtagctggga tttgtttgca 4140
aattgggtaa ttagtttaaa aatctgtgat tacattttta aatgaaattt tcaaagtggc 4200
ctagattgag gtgattcaga taggtttgcg aatataccat tttatattgt tgagaaagaa 4260
caaaaaggga atttccagat gtcctagaaa tcctagcaac agatttctct ggttgtcagt 4320
ttccctggag aaggcgccag ataggaatct ccaatcagtt gtttttctct tcgcttcagg 4380
cccttacaca aaagccatga agagatgttc acctacccgg tattttaaat gttctgtaaa 4440
ttattagcca aatagaactg taatggggtt gtatttatgg gcgcctagaa agaaaacaca 4500
aggacttggt aggccaggaa gaaaagattt taaaatttag aatgaatagc ccttctgggt 4560
tttctttttg acaattcttg gacttgaggt aaaacaagga ggattgtggc cggatttcag 4620
atcccaaagc cagcctccat cttaggcctt tgcctcattg tgccttttag gttttcttac 4680
ccaccgtctc ctgttttgtc ttttttttct tttctcctac ccctatcttg ggacattcag 4740
aaactgcctg ggtggtttga gaagagacaa cccagtttga tctgcaatac aaggatccat 4800
tcgtaatctc tctctcactg atgttattcc cccatctgcc gtcttggttc atctcaccac 4860
agaagggcat ttagtcctac ccagccatcg gctgcggtat gacagcagga tggcacttcc 4920
catttctctg tggttagtgc tcgagtgaaa acctctttca gctgagtcct ctgaggttct 4980
gctgttgagt cctgggtggc tgatggaatg attgaggagg tctggtcacc ctcaagcgcc 5040
gtcatcgcct tgtttccatg ggcttct 5067

<210> 79
<211> 950
<212> DNA
<213> Homo sapiens

<400> 79
tcgaccggat ccgaattccc attgtgcact aaagcgtctc cctgctccgc ggcccgggct 60
ggcgggcggg cgctcggctg gcggctgcag cagcagaggg agacccgcgg caaccccggc 120
aacccagggc tcggcgtcgc tgccaccatg acgggaagca atatgtcgga cgccttggcc 180
aacgccgtgt gccagcgctg ccaggcccgc ttctcccccg ccgagcgcat tgtcaacagc 240
aatggggagc tgtaccatga gcactgcttc gtgtgtgccc agtgcttccg gcccttcccc 300
gaggggctct tctatgagtt tgaaggccgg aagtactgcg aacacgactt ccaaatgctg 360
tttgctccgt gctgtggatc ctgcggtgag ttcatcattg gccgcgtcat caaggccatg 420
aacaacaact ggcacccggg ctgcttccgc tgcgagctgt gtgatgtgga gctggctgac 480
ctgggctttg tgaagaatgc cggcaggcat ctctgccggc cttgccacaa ccgtgagaag 540
gccaagggcc tgggcaagta catctgccag cggtgccacc tggtcatcga cgagcagccc 600
ctcatgttca ggagcgacgc ctaccaccct gaccacttca actgcaccca ctgtgggaag 660
gagctgacag ccgaggcccg cgagctgaag ggtgagctct actgcctgcc ctgccatgac 720
aagatgggcg ttcccatctg cggggcctgc cgccggccca tcgagggccg agtggtcaac 780
gcgctgggca agcagtggca cgtggagcac tttgtctgtg ccaagtgtga gaagccattc 840
ctggggcacc ggcactatga gaagagggc ctggcctact gcgagcttta gtgcacaatg 900
ggcggccgcc tcgagtctag actcgagtag ataattgagc ggaatttctt 950

<210> 80
<211> 2346
<212> DNA

<213> Homo sapiens

<400> 80

ccgccgtcgc ccccgcctcc ccctgcctca gcggctgccc ccgccagcgg gccgcccgct 60
ccccgggcc ttgcagcggg ccccggcccg gctggagggg ccccgacccc agctctggtg 120
gcgggcagca gcgccgcggc ccccttccct cacggggact cggccctgaa cgagcaggag 180
aaggagttgc agcggcggct gaagcgtctc tacccggccg tggacgaaca agagacgccg 240
ctgcctcggt cctggagccc gaaggacaag ttcagctaca tcggcctctc tcagaacaac 300
ctgcgggtgc actacaaagg tcatggcaaa accccaaaag atgccgcgtc agttcgagcc 360
acgcatccaa taccagcagc ctgtgggatt tattattttg aagtaaaaat tgtcagtaag 420
ggaagagatg gttacatggg aattggtctt tctgctcaag gtgtgaacat gaatagacta 480
ccaggttggg ataagcattc atatggttac catggggatg atggacattc gttttgttct 540
tctggaactg gacaaccttа tggaccaact ttcactactg gtgatgtcat tggctgttgt 600
gttaatctta tcaacaatac ctgcttttac accaagaatg gacatagttt aggtattgct 660
ttcactgacc taccgccaaa tttgtatcct actgtggggc ttcaaacacc aggagaagtg 720
gtcgatgcca attttgggca acatcctttc gtgtttgata tagaagacta tatgcgggag 780
tggagaacca aaatccaggc acagatagat cgatttccta tcggagatcg agaaggagaa 840
tggcagacca tgatacaaaa aatggtttca tcttatttag tccaccatgg gtactgtgcc 900
acagcagagg cctttgccag atctacagac cagaccgttc tagaagaatt agcttccatt 960
aagaatagac aaagaattca gaaattggta ttagcaggaa gaatgggaga agccattgaa 1020
acaacacaac agttatаccc aagtttactt gaaagaaatc ctaatctcct tttcacatta 1080
aaagtgcgtc agtttataga aatggtgaat ggtacagata gtgaagtacg atgtttggga 1140
ggccgaagtc caaagtctca agacagttat cctgttagtc ctcgaccttt tagtagtcca 1200
agtatgagcc ccagccatgg aatgaatatc cacaatttag catcaggcaa aggaagcacc 1260
gcacattttt caggttttga aagttgtagt aatggtgtaa tatcaaataa agcacatcaa 1320
tcatattgcc atagtaataa acaccagtca tccaacttga atgtaccaga actaaacagt 1380
ataaatatgt caagatcaca gcaagttaat aacttcacca gtaatgatgt agacatggaa 1440
acagatcact actccaatgg agttggagaa acttcatcca atggtttcct aaatggtagc 1500
tctaaacatg accacgaaat ggaagattgt gacaccgaaa tggaagttga ttcaagtcag 1560
ttgagacgcc agttgtgtgg aggaagtcag gccgccatag aaagaatgat ccactttgga 1620
cgagagctgc aagcaatgag tgaacagcta aggagagact gtggcaagaa cactgcaaac 1680
aaaaaaatgt tgaaggatgc attcagtcta ctagcatatt cagatccctg gaacagccca 1740
gttggaaatc agcttgaccc gattcagaga gaacctgtgt gctcagctct taacagtgca 1800
atattagaaa cccacaatct gccaaagcaa cctccacttg ccctagcaat gggacaggcc 1860
acacaatgtc taggactgat ggctcgatca ggaattggat cctgcgcatt tgccacagtg 1920
gaagactacc tacattagct atgcatttca agagctcaca cttatattgt ggcatatagt 1980
caacatggaa gtagaccagc tctgctgatt tgaaatttag atttttaaa ttatgtactg 2040
gggacaggtt tttgtcgctt tacattgctt cctagtttac agcatgatgc aaatgatttt 2100
ctaacttagt gttaggagaa attattttcc atctttaacc tcttagttgt ctaagagtta 2160
aatattactg aatttcagac gttcaaattg atcatcacaa atcctttaaa acaattacct 2220
aaaagaaacc aaaaatcctg ccttctttgt gggggagggg ggagagaggg gaaggaaatg 2280
gaacaagttg tgtttgtgtt agcatgtggg tgatgtaaac ttcaaattgg gagatgttcc 2340
gacccc 2346

<210> 81
<211> 2512
<212> DNA
<213> Homo sapiens

<400> 81

caatgcactg acggatatga gtgggatcct gtgagacagc aatgcaaaga tattgatgaa 60
tgtgacattg tcccagacgc ttgtaaaggt ggaatgaagt gtgtcaacca ctatggagga 120
tacctctgcc ttccgaaaac agcccagatt attgtcaata atgaacagcc tcagcaggaa 180

acacaaccag cagaaggaac ctcaggggca accaccgggg ttgtagctgc cagcagcatg 240
gcaaccagtg gagtgttgcc cgggggtggt tttgtggcca gtgctgctgc agtcgcaggc 300
cctgaaatgc agactggccg aaataacttt gtcatccggc ggaacccagc tgaccctcag 360
cgcattccct ccaacccttc ccaccgtatc cagtgtgcag caggctacga gcaaagtgaa 420
cacaacgtgt gccaagacat agacgagtgc actgcaggga cgcacaactg tagagcagac 480
caagtgtgca tcaatttacg gggatccttt gcatgtcagt gccctcctgg atatcagaag 540
cgaggggagc agtgcgtaga catagatgaa tgtaccatcc ctccatattg ccaccaaaga 600
tgcgtgaata caccaggctc attttattgc cagtgcagtc ctgggtttca attggcagca 660
aacaactata cctgcgtaga tataaatgaa tgtgatgcca gcaatcaatg tgctcagcag 720
tgctacaaca ttcttggttc attcatctgt cagtgcaatc aaggatatga gctaagcagt 780
gacaggctca actgtgaaga cattgatgaa tgcagaacct caagctacct gtgtcaatat 840
caatgtgtca atgaacctgg gaaattctca tgtatgtgcc cccagggata ccaagtggtg 900
agaagtagaa catgtcaaga tataaatgag tgtgagacca caaatgaatg ccgggaggat 960
gaaatgtgtt ggaattatca tggcggcttc cgttgttatc cacgaaatcc ttgtcaagat 1020
ccctacattc taacaccaga gaaccgatgt gtttgcccag tctcaaatgc catgtgccga 1080
gaactgcccc agtcaatagt ctacaaatac atgagcatcc gatctgatag gtctgtgcca 1140
tcagacatct tccagataca ggccacaact atttatgcca acaccatcaa tacttttcgg 1200
attaaatctg gaaatgaaaa tggagagttc tacctacgac aaacaagtcc tgtaagtgca 1260
atgcttgtgc tcgtgaagtc attatcagga ccaagagaac atatcgtgga cctggagatg 1320
ctgacagtca gcagtatagg gaccttccgc acaagctctg tgttaagatt gacaataata 1380
gtggggccat tttcatttta gtctttttcta agagtcaacc acaggcattt aagtcagcca 1440
aagaatattg ttaccttaaa gcactatttt atttatagat atatctagtg catctacatc 1500
tctatactgt acactcaccc ataacaaaca attacaccat ggtataaagt gggcatttaa 1560
tatgtaaaga ttcaaagttt gtctttatta ctatatgtaa attagacatt aatccactaa 1620
actggtcttc ttcaagagag ctaagtatac actatctggt gaaacttgga ttctttccta 1680
taaaagtggg accaagcaat gatgatcttc tgtggtgctt aaggaaactt actagagctc 1740
cactaacagt ctcataagga ggcagccatc ataaccattg aatagcatgc aagggtaaga 1800
atgagttttt aactgctttg taagaaaatg gaaaaggtca ataaagatat atttctttag 1860
aaaatgggga tctgccatat ttgtgttggt ttttattttc atatccagcc taaaggtggt 1920
tgtttattat atagtaataa atcattgctg tacaacatgc tggtttctgt agggtatttt 1980
taattttgtc agaaatttta gattgtgaat attttgtaaa aaacagtaag caaaattttc 2040
cagaattccc aaaatgaacc agataccccc tagaaaatta tactattgag aaatctatgg 2100
ggaggatatg agaaaataaa ttccttctaa accacattgg aactgacctg aagaagcaaa 2160
ctcggaaaat ataataacat ccctgaattc aggcattcac aagatgcaga acaaaatgga 2220
taaaaggtat ttcactggag aagttttaat ttctaagtaa aatttaaatc ctaacacttc 2280
actaatttat aactaaaatt tctcatcttc gtacttgatg ctcacagagg aagaaaatga 2340
tgatggtttt tattcctggc atccagagtg acagtgaact taagcaaatt accctcctac 2400
ccaattctat ggaatatttt atacgtctcc ttgtttaaaa tctgactgct ttactttgat 2460
gtatcatatt tttaaataaa aataaatatt cctttagaag atcactctaa aa 2512

<210> 82
<211> 2306
<212> DNA
<213> Homo sapiens

<400> 82
gggcgggagc tgcacgcgcc gtggctccgg atctcttcgt ctttgcagcg tacgcccgag 60
tcggtcagcg ccggaggacc tcagcagcca tgtcgaagcc ccatagtgaa gccgggactg 120
ccttcattca gacccagcag ctgcacgcag ccatggctga cacattcctg gagcacatgt 180
gccgcctgga cattgattca ccacccatca cagcccggaa cactggcatc atctgtacca 240
ttggcccagc ttcccgatca gtggagacgt tgaaggagat gattaagtct ggaatgaatg 300
tggctcgtct gaacttctct catggaactc atgagtacca tgcggagacc atcaagaatg 360
tgcgcacagc cacggaaagc tttgcttctg acccctacct ctaccggccc gttgctgtgg 420

ctctagacac taaaggacct gagatccgaa ctgggctcat caagggcagc ggcactgcag 480
agctggagct gaagaaggga gccactctca aaatcacgct ggataacgcc tacatggaaa 540
agtgtgacga gaacatcctg tggctggact acaagaacat ctgcaaggtg gtggaagtgg 600
gcagcaagat ctacgtggat gatgggctta tttctctcca ggtgaagcag aaaggtgccg 660
acttcctggt gacggaggtg gaaaatggtg gctccttggg cagcaagaag ggtgtgaacc 720
ttcctggggc tgctgtggac ttgcctgctg tgtcggagaa ggacatccag gatctgaagt 780
ttggggtcga gcaggatgtt gatatggtgt ttgcgtcatt catccgcaag gcatctgatg 840
tccatgaagt taggaaggtc ctgggagaga agggaaagaa catcaagatt atcagcaaaa 900
tcgagaatca tgaggggttt cggaggtttg atgaaatcct ggaggccagt gatgggatca 960
tggtggctcg tggtgatcta ggcattgaga ttcctgcaga gaaggtcttc cttgctcaga 1020
agatgatgat tggacggtgc aaccgagctg ggaagcctgt catctgtgct actcagatgc 1080
tggagagcat gatcaagaag ccccgcccca ctcgggctga aggcagtgat gtggccaatg 1140
cagtcctgga tggagccgac tgcatcatgc tgtctggaga aacagccaaa ggggactatc 1200
ctctggaggc tgtgcgcatg cagcacctga ttgcccgtga ggcagaggct gccatctacc 1260
acttgcaatt atttgaggaa ctccgccgcc tggcgcccat taccagcgac cccacagaag 1320
ccaccgccgt gggtgccgtg gaggcctcct tcaagtgctg cagtggggcc ataatcgtcc 1380
tcaccaagtc tggcaggtct gctcaccagg tggccagata ccgcccacgt gcccccatca 1440
ttgctgtgac ccggaatccc cagacagctc gtcaggccca cctgtaccgt ggcatcttcc 1500
ctgtgctgtg caaggaccca gtccaggagg cctgggctga ggacgtggac ctccgggtga 1560
actttgccat gaatgttggc aaggcccgag gcttcttcaa gaagggagat gtggtcattg 1620
tgctgaccgg atggcgccct ggctccggct tcaccaacac catgcgtgtt gttcctgtgc 1680
cgtgatggac cccagagccc ctcctccagc ccctgtccca ccccttccc ccagcccatc 1740
cattaggcca gcaacgcttg tagaactcac tctgggctgt aacgtggcac tggtaggttg 1800
ggacaccagg gaagaagatc aacgcctcac tgaaacatgg ctgtgtttgc agcctgctct 1860
agtgggacag cccagagcct ggctgcccat catgtggccc cacccaatca agggaagaag 1920
gaggaatgct ggactggagg cccctggagc cagatggcaa gagggtgaca gcttcctttc 1980
ctgtgtgtac tctgtccagt tcctttagaa aaaatggatg cccagaggac tcccaaccct 2040
ggcttggggt caagaaacag ccagcaagag ttaggggcct tagggcactg ggctgttgtt 2100
ccattgaagc cgactctggc cctggccctt acttgcttct ctagctctct aggcctctcc 2160
agtttgcacc tgtccccacc ctccactcag ctgtcctgca gcaaacactc caccctccac 2220
cttccatttt cccccactac tgcagcacct ccaggcctgt tgctatagag cctacctgta 2280
tgtcaataaa caacagctga agcacc 2306

<210> 83
<211> 2656
<212> DNA
<213> Homo sapiens

<400> 83
gaattcgcgg ccgcagagtc cccgggccaa gatggctgcg cggtgctcca cacgctggtt 60
gctggtggtt gtggggaccc cgcggctgcc ggctatatcg ggtagagggg cccggccgcc 120
cagggagggc gtggtggggg catggctgag ccgcaagctg agcgtccccg cctttgcgtc 180
ttccctgacc tcttgcggcc cccgagcgct gctgacattg agacctggtg tcagccttac 240
aggaacaaaa cataaccctt tcatttgtac tgcctccttc cacacgagtg ccccttggc 300
caaagaagat tattatcaga tattaggagt gcctcgaaat gccagccaga aagagatcaa 360
gaaagcctat tatcagcttg ccaagaagta tcaccctgac acaaataagg atgatcccaa 420
agccaaggag aagttctccc agctggcaga agcctatgag gttttgagtg atgaggtgaa 480
gaggaagcag tacgatgcct acggctctgc aggcttcgat cctggggcca gcggctccca 540
gcatagctac tggaagggag gccccactgt ggaccccgag gagctgttca ggaagatctt 600
tggcgagttc tcatcctctt catttggaga tttccagacc gtgtttgatc agcctcagga 660
atacttcatg gagttgacat tcaatcaagc tgcaaagggg gtcaacaagg agttcaccgt 720
gaacatcatg gacacgtgtg agcgctgcaa cggcaagggg aacgagcccg gcaccaaggt 780
gcagcattgc cactactgtg gcggctccgg catggaaacc atcaacacag gccctttgt 840

gatgcgttcc acgtgtagga gatgtggtgg ccgcggctcc atcatcatat cgccctgtgt 900
ggtctgcagg ggagcaggac aagccaagca gaaaaagcga gtgatgatcc ctgtgcctgc 960
aggagtcgag gatggccaga ccgtgaggat gcctgtggga aaaagggaaa ttttcattac 1020
gttcagggtg cagaaaagcc ctgtgttccg gagggacggc gcagacatcc actccgacct 1080
ctttatttct atagctcagg ctcttcttgg gggaacagcc agagcccagg gcctgtacga 1140
gacgatcaac gtgacgatcc cccctgggac tcagacagac cagaagattc ggatgggtgg 1200
gaaaggcatc ccccggatta acagctacgg ctacggagac cactacatcc acatcaagat 1260
acgagttcca aagaggctaa cgagccggca gcagagcctg atcctgagct acgccgagga 1320
cgagacagat gtggagggga cggtgaacgg cgtcaccctc accagctctg gtggcagcac 1380
catggatagc tccgcaggaa gcaaggctag gcgtgaggct ggggaggacg aggagggatt 1440
cctttccaaa cttaagaaaa tgtttacctc atgatatccc agccgaggaa aaagatccac 1500
tggaaactag gccgggaagc agcagcccct ccaagggcca gggcacctgg gagacgggag 1560
gattccagaa cagcagcact gagctcccac ccgcagagcc tctggacggc cttggcaaca 1620
gcaaaatcat gggacaacac ctctctccac ggaaaggtca cagtggacag cccgggcagt 1680
aggatgcagc cccagaggct ggtggcagtt tcctgtccat tggtaggtga cggccccctg 1740
gtcagcagag gagaggttag atcttgcagg ctaaaactct aatttggaat tgaatattgt 1800
ggatatctta gttaaaggcc atgcttacag cttagaaatg aagccttaag ctgcatcaag 1860
ttacgaagtg attaatttcc ttctcagcaa acctccggga ggttccagaa tgagttcttc 1920
ctgacaggtt gtcttcactg ggagcgtggg gcccccaggc cccaccagca ccgtcctccc 1980
ctaatgaggg gccctgccga ggcatcagct gctctgctca gttagttttt attcccgggg 2040
taccaagcag ctgcacagtc ggtgcctggg aagcacgtta aaggcccaga gagatcctgg 2100
gggttctgct ctgaccgtgt gggtggtgat ccttgtcagg atgtacagtc cttgctccca 2160
ccccatccgg gatggccgcc tgtccctgac tattgagtcc tgttgttgta agccaggcat 2220
ggagggctcc tgcccttctg ctgagccaca gcccattgca gcactgtgct ggccagactt 2280
cagctgcctt gggaactgaa gccctgccac tgttgctagt caggggcttg gttctcccac 2340
ttacactgtt gacatctatt ttctgaagtg tgtttaaatt attcagtgct aatcattgtt 2400
ttttcctttg taaatgttga ttcagaaaag gaaagcacag gctaagcagt tgaaggttcc 2460
ccaccattca gtgagagcag aacccccatt ccccagcctc tgctggtagc atgtcgcagt 2520
ttccatgtgt ttcaggatct tcgggctgtc gttagacagg ttaatgaaga acacttctca 2580
acagtttcct ttttgttttc ctttataatt cactaaaata aagcatctat tagtgtctga 2640
aaaaaaaaaa aaaaaa 2656

<210> 84
<211> 2217
<212> DNA
<213> Homo sapiens

<400> 84
gcggacccgg cgccgaggcg gccacccgag acgcggcgcg cacgctccgg cctgcgcagc 60
ccggcccggc catggcggcc ccccgcccgt ctcccgcgat ctccgtttcg gtctcggctc 120
cggcttttta cgccccgcag aagaagttcg gccctgtggt ggccccaaag cccaaagtga 180
atcccttccg gcccggggac agcgagcctc ccccggcacc cggggcccag cgcgcacaga 240
tgggccgggt gggcgagatt ccccccgccgc ccccggaaga ctttcccctg cctccacctc 300
cccttgctgg ggatggcgac gatgcagagg gtgctctggg aggtgccttc ccgccgcccc 360
ctccccccgat cgaggaatca tttcccccctg cgcctctgga ggaggagatc ttcccttccc 420
cgccgcctcc tccggaggag gagggagggc ctgaggcccc cataccgccc ccaccacagc 480
ccagggagaa ggtgagcagt attgatttgg agatcgactc tctgtcctca ctgctggatg 540
acatgaccaa gaatgatcct ttcaaagccc gggtgtcatc tggatatgtg cccccaccag 600
tggccactcc attcagttcc aagtccagta ccaagcctgc agccgggggc acagcacccc 660
tgcctccttg gaagtccccct tccagctccc agcctctgcc ccaggttccg gctccggctc 720
agagccagac acagttccat gttcagcccc agccccagcc caagcctcag gtccaactcc 780
atgtccagtc ccagacccag cctgtgtctt tggctaacac ccagccccga gggcccccag 840
cctcatctcc ggctccagcc cctaagtttt ctccagtgac tcctaagttt actcctgtgg 900

cttccaagtt cagtcctgga gccccaggtg gatctgggtc acaaccaaat caaaaattgg 960
ggcaccccga agctctttct gctggcacag gctcccctca acctcccagc ttcacctatg 1020
cccagcagag ggagaagccc cgagtgcagg agaagcagca ccccgtgccc ccaccggctc 1080
agaaccaaaa ccaggtgcgc tcccctgggg ccccagggcc cctgactctg aaggaggtgg 1140
aggagctgga gcagctgacc cagcagctaa tgcaggacat ggagcatcct cagaggcaga 1200
atgtggctgt caacgaactc tgcggccgat gccatcaacc cctggcccgg gcgcagccag 1260
ccgtccgcgc tctagggcag ctgttccaca tcgcctgctt cacctgccac cagtgtgcgc 1320
agcagctcca gggccagcag ttctacagtc tggagggggc gccgtactgc gagggctgtt 1380
acactgacac cctggagaag tgtaacacct gcggggagcc catcactgac cgcatgctga 1440
gggccacggg caaggcctat cacccgcact gcttcacctg tgtggtctgc gcccgccccc 1500
tggagggcac ctccttcatc gtggaccagg ccaaccggcc ccactgtgtc cccgactacc 1560
acaagcagta cgccccgagg tgctccgtct gctctgagcc catcatgcct gagcctggcc 1620
gagatgagac tgtgcgagtg gtcgccctgg acaagaactt ccacatgaag tgttacaagt 1680
gtgaggactg cgggaagccc ctgtcgattg aggcagatga caatggctgc ttcccccctgg 1740
acggtcacgt gctctgtcgg aagtgccaca ctgctagagc ccagacctga gtgaggacag 1800
gccctcttca gaccgcagtc catgccccat tgtggaccac ccacactgag accacctgcc 1860
cccacctcag ttattgtttt gatgtctagc ccctcccatt tccaaccccct ccctagcatc 1920
ccaggtgccc tgacccagga cccaacatgg tctagggatg caggatcccc gccctggggt 1980
ctggtcctcg cccatcctgc agggattgcc caccgtcttc cagacacccc acctgagggg 2040
ggcaccaggt ttagtgctgc tgctttcact gctgcacccg cgccctcggc cggccccccg 2100
agcagccttt gtactctgct tgcggagggc tgggagaccc tccaggacat tcccaccctc 2160
ccccatgctg ccaagttgta gctatagcta caaataaaaa aaaaccttgt tttccag 2217

<210> 85
<211> 8906
<212> DNA
<213> Homo sapiens

<400> 85
gaggcggcca aggacctggc cgacatcgcg gccttcttcc gatccgggtt tcgaaaaaac 60
gatgaaatga aagctatgga tgttttacca attttgaagg aaaaagttgc atacctttca 120
ggtgggagag ataaacgtgg aggtcccatt ttaacgtttc cggcccgcag caatcatgac 180
agaatacgac aggaggatct caggagactc atttcctatc tagcctgtat tcccagcgag 240
gaggtctgca agcgtggctt cacggtgatc gtggacatgc gtgggtccaa gtgggactcc 300
atcaagcccc ttctgaagat cctgcaggag tccttccgct gctgcatcca tgtggccctg 360
atcatcaagc cagacaactt ctggcagaaa cagaggacta attttggcag ttctaaattt 420
gaatttgaga caaatatggt ctctttagaa ggccttacca aagtagttga tccttctcag 480
ctaactcctg agtttgatgg ctgcctggaa tacaaccacg aagaatggat tgaaatcaga 540
gttgcttttg aagactacat tagcaatgcc acccacatgc tgtctcggct ggaggaactt 600
caggacatcc tagctaagaa ggagctgcct caggatttag agggggctcg gaatatgatc 660
gaggaacatt ctcagctgaa gaagaaggtg attaaggccc ccatcgagga cctggatttg 720
gagggacaga agctgcttca gaggatacag agcagtgaaa gctttcccaa aaagaactca 780
ggctcaggca atgcggacct gcagaacctc ttgcccaagg tgtccaccat gctggaccgg 840
ctgcactcga cacggcagca tctgcaccag atgtggcatg tgaggaagct gaagctggac 900
cagtgcttcc agctgaggct gtttgaacag gatgctgaga agatgtttga ctggatcaca 960
cacaacaaag gcctgtttct aaacagctac acagagattg ggaccagcca ccctcatgcc 1020
atggagcttc agacgcagca caatcacttt gccatgaact gtatgaacgt gtatgtaaat 1080
ataaaccgca tcatgtcggt ggccaatcgt ctggtggagt ctggccacta tgcctcgcag 1140
cagatcaggc agatcgcgag tcagctggag caggagtgga aggcgtttgc ggcagccctg 1200
gatgagcgga gcaccttgct ggacatgtcc tccattttcc accagaaggc cgaaaagtat 1260
atgagcaacg tggattcatg gtgtaaagct tgcggtgagg tagaccttcc ctcagagctg 1320
caggacctag aagatgccat tcatcaccac cagggaatat atgaacatat cactcttgct 1380
tattctgagg tcagccaaga tgggaagtcg ctccttgaca agctccagcg gcccttgact 1440

cccggcagct ccgattccct gacagcctct gccaactact ccaaggccgt gcaccatgtc 1500
ctggatgtca tccacgaggt gctgcaccac cagcggcacg tgagaacaat ctggcaacac 1560
cgcaaggtcc ggctgcatca gaggctgcag ctgtgtgttt tccagcagga agttcagcag 1620
gtgctagact ggatcgagaa ccacggagaa gcatttctga gcaaacatac aggtgtgggg 1680
aaatctcttc atcgggccag agcattgcag aaacgtcatg aagattttga agaagtggca 1740
cagaacacat acaccaatgc ggataaatta ctggaagcag cagaacagct ggctcagact 1800
ggggaatgtg accccgaaga gatttatcag gctgcccatc agctggaaga ccggattcaa 1860
gatttcgttc ggcgtgttga gcagcgaaag atcctactgg acatgtcagt gtcctttcac 1920
acccatgtga aagagctgtg gacgtggctg gaggagctgc agaaggagct gctggacgac 1980
gtgtatgccg agtcggtgga ggccgtgcag gacctcatca agcgctttgg ccagcagcag 2040
cagaccaccc tgcaggtgac tgtcaacgtg atcaaggaag gggaggacct catccagcag 2100
ctcagggact ctgccatctc cagtaacaag acccccccaca acagctccat caaccacatt 2160
gagacggtgc tgcagcagct ggacgaggcg cagtcgcaga tggaggagct cttccaggag 2220
cgcaagatca agctggagct cttcctgcac gtgcgcatct tcgagaggga cgccatcgac 2280
attatctcag acctcgagtc ttggaatgat gagctttctc agcaaatgaa tgacttcgac 2340
acagaagatc tcacgattgc agagcagcgc ctccagcacc atgcagacaa agccttgacc 2400
atgaacaact tgacttttga cgtcatccac caagggcaag atcttctgca gtatgtcaat 2460
gaggtccagg cctctggtgt ggagctgctg tgtgatagag atgtagacat ggcaactcgg 2520
gtccaggacc tgctggagtt tcttcatgaa aaacagcagg aattggattt agccgcagag 2580
cagcatcgga aacacctgga gcagtgcgtg cagctgcgcc acctgcaggc agaagtgaaa 2640
caggtgctgg gttggatccg caacggagag tccatgttaa atgccggact tatcacagcc 2700
agctcgttac aagaggcaga gcagctccag cgagagcacg agcagttcca gcatgccatt 2760
gagaaaacac atcagagcgc gctgcaggtg cagcagaagg cagaagccat gctacaggcc 2820
aaccactacg acatggacat gatccgggac tgcgccgaga aggtggcgtc tcactggcaa 2880
cagctcatgc tcaagatgga agatcgcctc aagctcgtca acgcctctgt cgctttctac 2940
aaaacctcag agcaggtctg cagcgtcctc gagagcctgg aacaggagta caagagagaa 3000
gaagactggt gtggcggggc ggataagctg ggcccaaact ctgagacgga ccacgtgacg 3060
cccatgatca gcaagcacct ggagcagaag gaggcattcc tgaaggcttg caccttgct 3120
cggaggaatg cagacgtctt cctgaaatac ctgcacagga acagcgtgaa catgccagga 3180
atggtgacgc acatcaaagc tcctgaacag caagtgaaaa atatcttgaa tgaactcttc 3240
caacgggaga acagggtatt gcattactgg accatgagga agagacggct ggaccagtgt 3300
cagcagtacg tggtctttga gaggagtgcc aagcaggctt tggaatggat ccatgacaat 3360
ggcgagttct acctttccac acacacctcc acgggctcca gtatacagca cacccaggag 3420
ctcctgaaag agcacgagga gttccagata actgcaaagc aaaccaaaga gagagtgaag 3480
ctattgatac agctggctga tggcttttgt gaaaaagggc atgcccatgc ggcagagata 3540
aaaaaatgtg ttactgctgt ggataagagg tacagagatt tctctctgcg gatggagaag 3600
tacaggacct ctttggaaaa agccctgggg atttcttcag attccaacaa atcgagtaaa 3660
agtctccagc tagatatcat tccagccagt atccctggct cagaggtgaa acttcgagat 3720
gctgctcatg aacttaatga agagaagcgg aaatctgccc gcaggaaaga gttcataatg 3780
gctgagctca ttcaaactga aaaggcttat gtaagagacc tccgggaatg tatggatacg 3840
tacctgtggg aaatgaccag tggcgtggaa gagattccac ctggcattgt aaacaaagaa 3900
ctcatcatct tcggaaacat gcaagaaatc tacgaatttc ataataacat attcctaaag 3960
gagctggaaa aatatgaaca gttgccagag gatgttggac attgttttgt tacttgggca 4020
gacaagtttc agatgtatgt cacatattgc aaaaataagc ctgattctac tcagctgata 4080
ttggaacatg cagggtccta ttttgacgag atacagcagc gacatggatt agccaattcc 4140
atttcttcct accttattaa accagttcag cgaataacga aatatcagct ccttttaaaa 4200
gagctgctga cgtgctgtga ggaaggaaag ggagagatta aagatggcct ggaggtgatg 4260
ctcagcgtgc cgaagcgagc caatgacgcc atgcacctca gcatgctgga agggtttgat 4320
gaaaacattg agtctcaggg agaactcatc ctacaggaat ccttccaagt gtgggaccca 4380
aaaaccttaa ttcgaaaggg tcgagaacgg catctcttcc tttttgaaat gtccttagta 4440
tttagtaaag aagtgaaaga ttccagtggg agaagcaagt acctttataa aagcaaattg 4500
tttacctcag agttgggtgt cacagaacat gttgaaggag acccttgcaa atttgcactg 4560
tgggtgggga gaacaccaac ttcagataat aaaattgtcc ttaaggcttc cagcatagag 4620

aacaagcagg actggataaa gcatatccgc gaagtcatcc aggagcggac gatccacctg 4680
aagggagccc tgaaggagcc cattcacatc cctaagaccg ctcccgccac aagacagaag 4740
ggaaggaggg atggagagga tctggacagc caaggagacg gcagcagcca gcctgatacg 4800
atttccatcg cctcacggac gtctcagaac acgctggaca gcgataagct ctctggtggc 4860
tgtgagctga cagtggtgat ccatgacttc accgcttgca acagcaacga gctgaccatc 4920
cgacggggcc agaccgtgga agttctggag cggccgcatg acaagcctga ctggtgtctg 4980
gtgcggacca ctgaccgctc cccagcggca gaaggcctgg tcccctgtgg ttcactgtgc 5040
atcgcccact ccagaagtag catggaaatg gagggcatct tcaaccacaa agactcgctc 5100
tccgtctcca gcaatgacgc cagtccaccc gcatccgtgg cttccctcca gccccacatg 5160
atcggggccc agagctcgcc gggccccaag cggccgggca acaccctgcg caagtggctc 5220
accagccccg tgcggcggct cagcagcggc aaggccgacg ggcacgtgaa gaagctggcg 5280
cacaagcaca agaagagccg cgaggtccgc aagagcgccg acgccggctc gcagaaggac 5340
tccgacgaca gtgcggccac cccgcaggac gagacggtcg aggagagagg ccggaacgag 5400
ggcctgagca gcggtactct ctccaaatcc tcctcctcgg ggatgcagag ctgtggagaa 5460
gaggaaggcg aggagggggc cgacgccgtg cccctgccgc cacccatggc catccagcag 5520
cacagcctcc tccagccaga ctcacaggat gacaaggcct cttctcggtt attagtccgc 5580
cccaccagct ccgaaacacc gagtgcagcc gagctcgtca gtgcaattga ggaactcgtg 5640
aaaagcaaga tggcactgga ggatcgcccc agctcactcc ttgttgacca gggagatagt 5700
agcagccctt ccttcaaccc ttcggataat tcccttctct cttcctcctc gcccattgat 5760
gagatggaag aaaggaaatc cagctcttta aagagaagac actacgtttt gcaagaacta 5820
gtggagacag agcgtgacta tgtgcgggac cttggctatg tggttgaggg ctacatggca 5880
cttatgaaag aagatggtgt tcctgatgac atgaaaggaa aagacaaaat tgtgttcggc 5940
aacatccatc agatttacga ctggcacaga gacttttttt taggagagtt agagaagtgc 6000
cttgaagatc cagaaaaact aggatccctt tttgttaaac acgagagaag gttgcacatg 6060
tacatagctt attgtcaaaa taaaccaaag tctgagcaca ttgtctcaga atacattgat 6120
acctttttg aggacttaaa gcagcgtctt ggccacaggt tacagctcac agatctgttg 6180
atcaaaccag tgcagagaat catgaagtat cagctgttac tgaaggactt cctcaagtat 6240
tccaaaaagg ccagcctgga tacatcagaa ttagagagag ctgtggaagt catgtgcata 6300
gtacccaggc ggtgcaacga catgatgaac gtggggcggc tgcaaggatt cgacgggaaa 6360
atcgttgccc agggtaaact gctcttgcag gacacattct tggtcacaga ccaagatgca 6420
ggacttctgc ctcgctgcag agagaggcgc atcttcctct ttgagcagat cgtcatattc 6480
agcgaaccac ttgataaaaa gaagggcttc tccatgccgg gattcctgtt taagaacagt 6540
atcaaggtga gttgcctttg cctggaggaa aatgtggaaa atgatccctg taaatttgct 6600
ctgacatcga ggacgggtga cgtggtagag accttcattt tgcattcatc tagtccaagt 6660
gtccggcaaa cttggatcca tgaaatcaac caaattttag aaaaccagcg caatttttta 6720
aatgccttga catcgccaat cgagtaccag aggaaccaca gcgggggcgg cggcggcggc 6780
ggcagcgggg cagcggcggg ggtgggggca gcggcggcgg cggggccccc agtggcggca 6840
gcggccacag tggcggcccc agcagctgcg gcggcgcccc cagcacgagc aggagccggc 6900
cctcccggat cccccagcct gtccgacacc acccccccgt gctggtctcc tctgcagcct 6960
cgagccaggc agaggcagac aagatgtcag agtgaaagca gcagcagtag caacatctcc 7020
accatgttgg tgacacacga ttacacggca gtgaaggagg atgagatcaa cgtctaccaa 7080
ggagaggtcg ttcaaattct ggccagcaac cagcagaaca tgtttctggt gttccgagcc 7140
gccactgacc agtgccccgc agctgagggc tggattccag gctttgtcct gggccacacc 7200
agtgcagtca tcgtggagaa cccggacggg actctcaaga agtcaacatc ttggcacaca 7260
gcactccgtt taaggaaaaa atctgagaaa aaagataaag acggcaaaag ggaaggcaag 7320
ttagagaacg gttatcggaa gtcacgggaa ggactcagca acaaggtatc tgtgaagctt 7380
ctcaatccca actacattta tgacgttccc ccagaattcg tcattccatt gagtgaggtc 7440
acgtgtgaga caggggagac cgttgttctt agatgtcgag tctgtggccg ccccaaagcc 7500
tcaattacct ggaagggccc tgaacacaac accttgaaca acgatggtca ctacagcatc 7560
tcctacagtg acctgggaga ggccacgctg aagattgtgg gcgtgaccac ggaagatgac 7620
ggcatctaca cgtgcatcgc tgtcaatgac atgggttcag cctcatcatc ggccagcctg 7680
agggtcctag gtccagggat ggatgggatc atggtgacct ggaaagacaa ctttgactcc 7740
ttctacagtg aagtggctga gcttggcagg ggcagattct ctgtcgttaa gaaatgtgat 7800

cagaaaggaa ccaagcgagc agtggccact aagtttgtga acaagaagtt gatgaagcgc 7860
gaccaggtca cccatgagct tggcatcctg cagagcctcc agcacccccc gcttgtcggc 7920
ctcctcgaca cctttgagac ccccaccagc tacatcctgg tcttagaaat ggctgaccag 7980
ggtcgcctcc tggactgcgt ggtgcgatgg ggaagcctca ctgaagggaa gatcagggcg 8040
cacctggggg aggttctgga agctgtccgg tacctgcaca actgcaggat agcacacctg 8100
gacctaaagc ctgagaatat cctggtggat gagagtttag ccaagccaac catcaaactg 8160
gctgactttg gagatgctgt tcagctcaac acgacctact acatccacca gttactgggg 8220
aaccctgaat tcgcagcccc tgaaatcatc ctcgggaacc ctgtctccct gacctcggat 8280
acgtggagtg ttggagtgct cacatacgta cttcttagtg gcgtgtcccc cttcctggat 8340
gacagtgtgg aagagacctg cctgaacatt tgccgcttag actttagctt cccagatgac 8400
tactttaaag gagtgagcca gaaggccaag gagttcgtgt gcttcctcct gcaggaggac 8460
cccgccaagc gtccctcggc tgcgctggcc ctccaggagc agtggctgca ggccggcaac 8520
ggcagaagca cgggcgtcct cgacacgtcc agactgactt ccttcattga gcggcgcaaa 8580
caccagaatg atgttcgacc tatccgtagc attaaaaact ttctgcagag caggcttctg 8640
cctagagttt gacctatcca gaagttcttt ctcattctct ttcacctgcc aatcagctgt 8700
taatctgaat tttcaagaga aaacaagcaa acataactga tcagctgccg gtatgttcat 8760
cgtgtgaaat tgcattccaa gtgagctgtg ctcagcagtg cttggacaca gagctgcaag 8820
ctgcgctggg gtggaggacc gtcacttaca ctctgccaag gacggaggtc gcattgctgt 8880
atcacagtat tttttacgga tttctg 8906

<210> 86
<211> 1204
<212> DNA
<213> Homo sapiens

<400> 86
tcggcggcgg tggtatcggc ggcagctgtg agggggttcc gggaagatgg tgctgatcaa 60
ggaattccgt gtggttttgc catgttctgt tcaggagtat caggttgggc agctttactc 120
tgttgcagaa gctagtaaga atgagactgg tggtggagaa ggaattgaag tcttaaagaa 180
tgaaccttat gagaaggatg gagaaaaggg acagtatacg cacaaaattt atcacctaaa 240
gagcaaagtg cctgcattcg tgaggatgat tgctcccgag ggctccttgg tgtttcatga 300
gaaagcctgg aatgcgtacc cctactgtag aacaattgta acgaatgaat atatgaaaga 360
tgatttcttc attaaaatcg aaacatggca caaaccagac ttgggaacat tagaaaatgt 420
acatggttta gatccaaaca catggaaaac tgttgaaatt gtccatatag atattgcaga 480
tagaagtcaa gttgaaccag cagactacaa agctgatgaa gacccagcat tattccagtc 540
agtcaagacc aagagaggcc ctttgggacc caactggaag aaggagctgg caaacagccc 600
tgactgtccc cagatgtgtg cctataagct ggtgaccatc aaattcaagt ggtggggact 660
gcaaagcaaa gtagaaaact tcattcaaaa gcaagaaaaa cggatattta caaacttcca 720
tcgccagctt ttttgttgga ttgacaagtg gatcgatctc acgatggaag acattaggag 780
aatggaagac gagactcaga aagaactaga aacaatgcgt aagaggggtt ccgttcgagg 840
cacgtcggct gctgatgtct agatgagtcc cctgtagggt cagagacaat gtcaaactgt 900
ttacgtaatc aaggtcaagt gaggggaaca agcgcagcca gtgatgagtg aacaacaatc 960
tgaccagtat cttgcagtgt tgacgtttcc cagatgtgtg cttgtgatga tacacacaca 1020
tgcacaggtt ctcaaccacg tgtgtatata tgtatgtgtg catatgtctg tagctgtata 1080
taaagcgcat gtagagctac agatccagat acacacactt gtgtatatat gtacatacag 1140
acatactgaa gggattagta caatttctcc aaagtactgt acctatcttc agcaagaatg 1200
caaa 1204

<210> 87
<211> 892
<212> PRT
<213> Homo sapiens

<400> 87

```
Met Asp His Tyr Asp Ser Gln Gln Thr Asn Asp Tyr Met Gln Pro Glu
 1               5                  10                  15
Glu Asp Trp Asp Arg Asp Leu Leu Leu Asp Pro Ala Trp Glu Lys Gln
            20                  25                  30
Gln Arg Lys Thr Phe Thr Ala Trp Cys Asn Ser His Leu Arg Lys Ala
        35                  40                  45
Gly Thr Gln Ile Glu Asn Ile Glu Glu Asp Phe Arg Asp Gly Leu Lys
    50                  55                  60
Leu Met Leu Leu Leu Glu Val Ile Ser Gly Glu Arg Leu Ala Lys Pro
65                  70                  75                  80
Glu Arg Gly Lys Met Arg Val His Lys Ile Ser Asn Val Asn Lys Ala
                85                  90                  95
Leu Asp Phe Ile Ala Ser Lys Gly Val Lys Leu Val Ser Ile Gly Ala
            100                 105                 110
Glu Glu Ile Val Asp Gly Asn Val Lys Met Thr Leu Gly Met Ile Trp
        115                 120                 125
Thr Ile Ile Leu Arg Phe Ala Ile Gln Asp Ile Ser Val Glu Glu Thr
    130                 135                 140
Ser Ala Lys Glu Gly Leu Leu Leu Trp Cys Gln Arg Lys Thr Ala Pro
145                 150                 155                 160
Tyr Lys Asn Val Asn Ile Gln Asn Phe His Ile Ser Trp Lys Asp Gly
                165                 170                 175
Leu Gly Phe Cys Ala Leu Ile His Arg His Arg Pro Glu Leu Ile Asp
            180                 185                 190
Tyr Gly Lys Leu Arg Lys Asp Asp Pro Leu Thr Asn Leu Asn Thr Ala
        195                 200                 205
Phe Asp Val Ala Glu Lys Tyr Leu Asp Ile Pro Lys Met Leu Asp Ala
    210                 215                 220
Glu Asp Ile Val Gly Thr Ala Arg Pro Asp Glu Lys Ala Ile Met Thr
225                 230                 235                 240
Tyr Val Ser Ser Phe Tyr His Ala Phe Ser Gly Ala Gln Lys Ala Glu
                245                 250                 255
Thr Ala Ala Asn Arg Ile Cys Lys Val Leu Ala Val Asn Gln Glu Asn
            260                 265                 270
Glu Gln Leu Met Glu Asp Tyr Glu Lys Leu Ala Ser Asp Leu Leu Glu
        275                 280                 285
Trp Ile Arg Arg Thr Ile Pro Trp Leu Glu Asn Arg Val Pro Glu Asn
    290                 295                 300
Thr Met His Ala Met Gln Gln Lys Leu Glu Asp Phe Arg Asp Tyr Arg
305                 310                 315                 320
Arg Leu His Lys Pro Pro Lys Val Gln Glu Lys Cys Gln Leu Glu Ile
                325                 330                 335
Asn Phe Asn Thr Leu Gln Thr Lys Leu Arg Leu Ser Asn Arg Pro Ala
            340                 345                 350
Phe Met Pro Ser Glu Gly Arg Met Val Ser Asp Ile Asn Asn Ala Trp
        355                 360                 365
Gly Cys Leu Glu Gln Val Glu Lys Gly Tyr Glu Glu Trp Leu Leu Asn
    370                 375                 380
Glu Ile Arg Arg Leu Glu Arg Leu Asp His Leu Ala Glu Lys Phe Arg
385                 390                 395                 400
Gln Lys Ala Ser Ile His Glu Ala Trp Thr Asp Gly Lys Glu Ala Met
                405                 410                 415
```

Leu Arg Gln Lys Asp Tyr Glu Thr Ala Thr Leu Ser Glu Ile Lys Ala
420 425 430
Leu Leu Lys Lys His Glu Ala Phe Glu Ser Asp Leu Ala Ala His Gln
435 440 445
Asp Arg Val Glu Gln Ile Ala Ala Ile Ala Gln Glu Leu Asn Glu Leu
450 455 460
Asp Tyr Tyr Asp Ser Pro Ser Val Asn Ala Arg Cys Gln Lys Ile Cys
465 470 475 480
Asp Gln Trp Asp Asn Leu Gly Ala Leu Thr Gln Lys Arg Arg Glu Ala
485 490 495
Leu Glu Arg Thr Glu Lys Leu Leu Glu Thr Ile Asp Gln Leu Tyr Leu
500 505 510
Glu Tyr Ala Lys Arg Ala Ala Pro Phe Asn Asn Trp Met Glu Gly Ala
515 520 525
Met Glu Asp Leu Gln Asp Thr Phe Ile Val His Thr Ile Glu Glu Ile
530 535 540
Gln Gly Leu Thr Thr Ala His Glu Gln Phe Lys Ala Thr Leu Pro Asp
545 550 555 560
Ala Asp Lys Glu Arg Leu Ala Ile Leu Gly Ile His Asn Glu Val Ser
565 570 575
Lys Ile Val Gln Thr Tyr His Val Asn Met Ala Gly Thr Asn Pro Tyr
580 585 590
Thr Thr Ile Thr Pro Gln Glu Ile Asn Gly Lys Trp Asp His Val Arg
595 600 605
Gln Leu Val Pro Arg Arg Asp Gln Ala Leu Thr Glu Glu His Ala Arg
610 615 620
Gln Gln His Asn Glu Arg Leu Arg Lys Gln Phe Gly Ala Gln Ala Asn
625 630 635 640
Val Ile Gly Pro Trp Ile Gln Thr Lys Met Glu Glu Ile Gly Arg Ile
645 650 655
Ser Ile Glu Met His Gly Thr Leu Glu Asp Gln Leu Ser His Leu Arg
660 665 670
Gln Tyr Glu Lys Ser Ile Val Asn Tyr Lys Pro Lys Ile Asp Gln Leu
675 680 685
Glu Gly Asp His Gln Leu Ile Gln Glu Ala Leu Ile Phe Asp Asn Lys
690 695 700
His Thr Asn Tyr Thr Met Glu His Ile Arg Val Gly Trp Glu Gln Leu
705 710 715 720
Leu Thr Thr Ile Ala Arg Thr Ile Asn Glu Val Glu Asn Gln Ile Leu
725 730 735
Thr Arg Asp Ala Lys Gly Ile Ser Gln Glu Gln Met Asn Glu Phe Arg
740 745 750
Ala Ser Phe Asn His Phe Asp Arg Asp His Ser Gly Thr Leu Gly Pro
755 760 765
Glu Glu Phe Lys Ala Cys Leu Ile Ser Leu Gly Tyr Asp Ile Gly Asn
770 775 780
Asp Pro Gln Gly Glu Ala Glu Phe Ala Arg Ile Met Ser Ile Val Asp
785 790 795 800
Pro Asn Arg Leu Gly Val Val Thr Phe Gln Ala Phe Ile Asp Phe Met
805 810 815
Ser Arg Glu Thr Ala Asp Thr Asp Thr Ala Asp Gln Val Met Ala Ser
820 825 830
Phe Lys Ile Leu Ala Gly Asp Lys Asn Tyr Ile Thr Met Asp Glu Leu

```
        835                 840                 845
Arg Arg Glu Leu Pro Pro Asp Gln Ala Glu Tyr Cys Ile Ala Arg Met
    850                 855                 860
Ala Pro Tyr Thr Gly Pro Asp Ser Val Pro Gly Ala Leu Asp Tyr Met
865                 870                 875                 880
Ser Phe Ser Thr Ala Leu Tyr Gly Glu Ser Asp Leu
                885                 890
```

<210> 88
<211> 197
<212> PRT
<213> Homo sapiens

<400> 88

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

<210> 89
<211> 739
<212> PRT
<213> Homo sapiens

<400> 89

```
Gly Asp Lys Glu Pro Thr Glu Thr Ile Gly Asp Leu Ser Ile Cys Leu
 1               5                  10                  15
Asp Gly Leu Gln Leu Glu Ser Glu Val Val Thr Asn Gly Glu Thr Thr
            20                  25                  30
Cys Ser Glu Ser Ala Ser Gln Asn Asp Asp Gly Ser Arg Ser Lys Asp
        35                  40                  45
```

Glu Thr Arg Val Ser Thr Asn Gly Ser Asp Asp Pro Glu Asp Ala Gly
50 55 60
Ala Gly Glu Asn Arg Arg Val Ser Gly Asn Asn Ser Pro Ser Leu Ser
65 70 75 80
Asn Gly Gly Phe Lys Pro Ser Arg Pro Pro Arg Pro Ser Arg Pro Pro
85 90 95
Pro Pro Thr Pro Arg Arg Pro Ala Ser Val Asn Gly Ser Pro Ser Ala
100 105 110
Thr Ser Glu Ser Asp Gly Ser Ser Thr Gly Ser Leu Pro Pro Thr Asn
115 120 125
Thr Asn Thr Asn Thr Ser Glu Gly Ala Thr Ser Gly Leu Ile Ile Pro
130 135 140
Leu Thr Ile Ser Gly Gly Ser Gly Pro Arg Pro Leu Asn Pro Val Thr
145 150 155 160
Gln Ala Pro Leu Pro Pro Gly Trp Glu Gln Arg Val Asp Gln His Gly
165 170 175
Arg Val Tyr Tyr Val Asp His Val Glu Lys Arg Thr Thr Trp Asp Arg
180 185 190
Pro Glu Pro Leu Pro Pro Gly Trp Glu Arg Arg Val Asp Asn Met Gly
195 200 205
Arg Ile Tyr Tyr Val Asp His Phe Thr Arg Thr Thr Thr Trp Gln Arg
210 215 220
Pro Thr Leu Glu Ser Val Arg Asn Tyr Glu Gln Trp Gln Leu Gln Arg
225 230 235 240
Ser Gln Leu Gln Gly Ala Met Gln Gln Phe Asn Gln Arg Phe Ile Tyr
245 250 255
Gly Asn Gln Asp Leu Phe Ala Thr Ser Gln Ser Lys Glu Phe Asp Pro
260 265 270
Leu Gly Pro Leu Pro Pro Gly Trp Glu Lys Arg Thr Asp Ser Asn Gly
275 280 285
Arg Val Tyr Phe Val Asn His Asn Thr Arg Ile Thr Gln Trp Glu Asp
290 295 300
Pro Arg Ser Gln Gly Gln Leu Asn Glu Lys Pro Leu Pro Glu Gly Trp
305 310 315 320
Glu Met Arg Phe Thr Val Asp Gly Ile Pro Tyr Phe Val Asp His Asn
325 330 335
Arg Arg Thr Thr Thr Tyr Ile Asp Pro Arg Thr Gly Lys Ser Ala Leu
340 345 350
Asp Asn Gly Pro Gln Ile Ala Tyr Val Arg Asp Phe Lys Ala Lys Val
355 360 365
Gln Tyr Phe Arg Phe Trp Cys Gln Gln Leu Ala Met Pro Gln His Ile
370 375 380
Lys Ile Thr Val Thr Arg Lys Thr Leu Phe Glu Asp Ser Phe Gln Gln
385 390 395 400
Ile Met Ser Phe Ser Pro Gln Asp Leu Arg Arg Arg Leu Trp Val Ile
405 410 415
Phe Pro Gly Glu Glu Gly Leu Asp Tyr Gly Gly Val Ala Arg Glu Trp
420 425 430
Phe Phe Leu Leu Ser His Glu Val Leu Asn Pro Met Tyr Cys Leu Phe
435 440 445
Glu Tyr Ala Gly Lys Asp Asn Tyr Cys Leu Gln Ile Asn Pro Ala Ser
450 455 460
Tyr Ile Asn Pro Asp His Leu Lys Tyr Phe Arg Phe Ile Gly Arg Phe

465 470 475 480
Ile Ala Met Ala Leu Phe His Gly Lys Phe Ile Asp Thr Gly Phe Ser
485 490 495
Leu Pro Phe Tyr Lys Arg Ile Leu Asn Lys Pro Val Gly Leu Lys Asp
500 505 510
Leu Glu Ser Ile Asp Pro Glu Phe Tyr Asn Ser Leu Ile Trp Val Lys
515 520 525
Glu Asn Asn Ile Glu Glu Cys Asp Leu Glu Met Tyr Phe Ser Val Asp
530 535 540
Lys Glu Ile Leu Gly Glu Ile Lys Ser His Asp Leu Lys Pro Asn Gly
545 550 555 560
Gly Asn Ile Leu Val Thr Glu Glu Asn Lys Glu Glu Tyr Ile Arg Met
565 570 575
Val Ala Glu Trp Arg Leu Ser Arg Gly Val Glu Glu Gln Thr Gln Ala
580 585 590
Phe Phe Glu Gly Phe Asn Glu Ile Leu Pro Gln Gln Tyr Leu Gln Tyr
595 600 605
Phe Asp Ala Lys Glu Leu Glu Val Leu Leu Cys Gly Met Gln Glu Ile
610 615 620
Asp Leu Asn Asp Trp Gln Arg His Ala Ile Tyr Arg His Tyr Ala Arg
625 630 635 640
Thr Ser Lys Gln Ile Met Trp Phe Trp Gln Phe Val Lys Glu Ile Asp
645 650 655
Asn Glu Lys Arg Met Arg Leu Leu Gln Phe Val Thr Gly Thr Cys Arg
660 665 670
Leu Pro Val Gly Gly Phe Ala Asp Leu Met Gly Ser Asn Gly Pro Gln
675 680 685
Lys Phe Cys Ile Glu Lys Val Gly Lys Glu Asn Trp Leu Pro Arg Ser
690 695 700
His Thr Cys Phe Asn Arg Leu Asp Leu Pro Pro Tyr Lys Ser Tyr Glu
705 710 715 720
Gln Leu Lys Glu Lys Leu Leu Phe Ala Ile Glu Glu Thr Glu Gly Phe
725 730 735
Gly Gln Glu

<210> 90
<211> 431
<212> PRT
<213> Homo sapiens

<400> 90
Gly Pro Pro Pro Thr Arg Ala Leu Pro Leu Pro Gln Ser Leu Pro Pro
1 5 10 15
Asp Phe Arg Leu Glu Pro Thr Ala Pro Ala Leu Ser Pro Arg Ser Ser
20 25 30
Phe Ala Ser Ser Ser Ala Ser Asp Ala Ser Lys Pro Ser Ser Pro Arg
35 40 45
Gly Ser Leu Leu Leu Asp Gly Ala Gly Ala Gly Gly Ala Gly Gly Ser
50 55 60
Arg Pro Cys Ser Asn Arg Thr Ser Gly Ile Ser Met Gly Tyr Asp Gln
65 70 75 80
Arg His Gly Ser Pro Leu Pro Ala Gly Pro Cys Leu Phe Gly Pro Pro

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

<210> 91
<211> 900
<212> PRT
<213> Homo sapiens

<400> 91
Gly Pro Gly Ser Arg His His Arg Ala Arg Asp Arg Leu Ile His Phe
 1               5                  10                  15
Gly Ala Val Ser Thr Asp Val Leu Gly Cys Ser Ala His Cys Ser Leu
```

```
            20                  25                  30
Thr Gln Ser Pro Lys Met Asn Ile Gln Glu Gln Gly Phe Pro Leu Asp
        35                  40                  45
Leu Gly Ala Ser Phe Thr Glu Asp Ala Pro Arg Pro Pro Val Pro Gly
    50                  55                  60
Glu Glu Gly Glu Leu Val Ser Thr Asp Pro Arg Pro Ala Ser Tyr Ser
65                  70                  75                  80
Phe Cys Ser Gly Lys Gly Val Gly Ile Lys Gly Glu Thr Ser Thr Ala
                85                  90                  95
Thr Pro Arg Arg Ser Asp Leu Asp Leu Gly Tyr Glu Pro Glu Gly Ser
            100                 105                 110
Ala Ser Pro Thr Pro Pro Tyr Leu Lys Trp Ala Glu Ser Leu His Ser
        115                 120                 125
Leu Leu Asp Asp Gln Asp Gly Ile Ser Leu Phe Arg Thr Phe Leu Lys
    130                 135                 140
Gln Glu Gly Cys Ala Asp Leu Leu Asp Phe Trp Phe Ala Cys Thr Gly
145                 150                 155                 160
Phe Arg Lys Leu Glu Pro Cys Asp Ser Asn Glu Glu Lys Arg Leu Lys
                165                 170                 175
Leu Ala Arg Ala Ile Tyr Arg Lys Tyr Ile Leu Asp Asn Asn Gly Ile
            180                 185                 190
Val Ser Arg Gln Thr Lys Pro Ala Thr Lys Ser Phe Ile Lys Gly Cys
        195                 200                 205
Ile Met Lys Gln Leu Ile Asp Pro Ala Met Phe Asp Gln Ala Gln Thr
    210                 215                 220
Glu Ile Gln Ala Thr Met Glu Glu Asn Thr Tyr Pro Ser Phe Leu Lys
225                 230                 235                 240
Ser Asp Ile Tyr Leu Glu Tyr Thr Arg Thr Gly Ser Glu Ser Pro Lys
                245                 250                 255
Val Cys Ser Asp Gln Ser Ser Gly Ser Gly Thr Gly Lys Gly Ile Ser
            260                 265                 270
Gly Tyr Leu Pro Thr Leu Asn Glu Asp Glu Glu Trp Lys Cys Asp Gln
        275                 280                 285
Asp Met Asp Glu Asp Asp Gly Arg Asp Ala Ala Pro Pro Gly Arg Leu
    290                 295                 300
Pro Gln Lys Leu Leu Leu Glu Thr Ala Ala Pro Arg Val Ser Ser Ser
305                 310                 315                 320
Arg Arg Tyr Ser Glu Gly Arg Glu Phe Arg Tyr Gly Ser Trp Arg Glu
                325                 330                 335
Pro Val Asn Pro Tyr Tyr Val Asn Ala Gly Tyr Ala Leu Ala Pro Ala
            340                 345                 350
Thr Ser Ala Asn Asp Ser Glu Gln Gln Ser Leu Ser Ser Asp Ala Asp
        355                 360                 365
Thr Leu Ser Leu Thr Asp Ser Ser Val Asp Gly Ile Pro Pro Tyr Arg
    370                 375                 380
Ile Arg Lys Gln His Arg Arg Glu Met Gln Glu Ser Ala Gln Val Asn
385                 390                 395                 400
Gly Arg Val Pro Leu Pro His Ile Pro Arg Thr Tyr Arg Val Pro Lys
                405                 410                 415
Glu Val Arg Val Glu Pro Gln Lys Phe Ala Glu Glu Leu Ile His Arg
            420                 425                 430
Leu Glu Ala Val Gln Arg Thr Arg Glu Ala Glu Glu Lys Leu Glu Glu
        435                 440                 445
```

```
Arg Leu Lys Arg Val Arg Met Glu Glu Glu Gly Glu Asp Gly Asp Pro
    450                 455                 460
Ser Ser Gly Pro Pro Gly Pro Cys His Lys Leu Pro Pro Ala Pro Ala
465                 470                 475                 480
Trp His His Phe Pro Pro Arg Leu Cys Trp Thr Trp Ala Cys Ala Gly
                485                 490                 495
Leu Arg Asp Ala His Glu Glu Asn Pro Glu Ser Ile Leu Asp Glu His
            500                 505                 510
Val Gln Arg Val Leu Arg Thr Thr Gly Arg Gln Ser Pro Gly Pro Gly
        515                 520                 525
His Arg Ser Pro Asp Ser Gly His Val Ala Lys Met Pro Val Ala Leu
    530                 535                 540
Gly Gly Ala Ala Ser Gly His Gly Lys His Val Pro Lys Ser Gly Ala
545                 550                 555                 560
Lys Leu Asp Ala Ala Gly Leu His His His Arg His Val His His His
                565                 570                 575
Val His His Ser Thr Ala Arg Pro Lys Glu Gln Val Glu Ala Glu Ala
            580                 585                 590
Thr Arg Arg Ala Gln Ser Ser Phe Ala Trp Gly Leu Glu Pro His Ser
        595                 600                 605
His Gly Ala Arg Ser Arg Gly Tyr Ser Glu Ser Val Gly Ala Ala Pro
    610                 615                 620
Asn Ala Ser Asp Gly Leu Ala His Ser Gly Lys Val Gly Val Ala Cys
625                 630                 635                 640
Lys Arg Asn Ala Lys Lys Ala Glu Ser Gly Lys Ser Ala Ser Thr Glu
                645                 650                 655
Val Pro Gly Ala Ser Glu Asp Ala Glu Lys Asn Gln Lys Ile Met Gln
            660                 665                 670
Trp Ile Ile Glu Gly Glu Lys Glu Ile Ser Arg His Arg Arg Thr Gly
        675                 680                 685
His Gly Ser Ser Gly Thr Arg Lys Pro Gln Pro His Glu Asn Ser Arg
    690                 695                 700
Pro Leu Ser Leu Glu His Pro Trp Ala Gly Pro Gln Leu Arg Thr Ser
705                 710                 715                 720
Val Gln Pro Ser His Leu Phe Ile Gln Asp Pro Thr Met Pro Pro His
                725                 730                 735
Pro Ala Pro Asn Pro Leu Thr Gln Leu Glu Glu Ala Arg Arg Arg Leu
            740                 745                 750
Glu Glu Glu Glu Lys Arg Ala Ser Arg Ala Pro Ser Lys Gln Arg Tyr
        755                 760                 765
Val Gln Glu Val Met Arg Arg Gly Arg Ala Cys Val Arg Pro Ala Cys
    770                 775                 780
Ala Pro Val Leu His Val Val Pro Ala Val Ser Asp Met Glu Leu Ser
785                 790                 795                 800
Glu Thr Glu Thr Arg Ser Gln Arg Lys Val Gly Gly Gly Ser Ala Gln
                805                 810                 815
Pro Cys Asp Ser Ile Val Val Ala Tyr Tyr Phe Cys Gly Glu Pro Ile
            820                 825                 830
Pro Tyr Arg Thr Leu Val Arg Gly Arg Ala Val Thr Leu Gly Gln Phe
        835                 840                 845
Lys Glu Leu Leu Thr Lys Lys Gly Ser Tyr Arg Tyr Tyr Phe Lys Lys
    850                 855                 860
Val Ser Asp Glu Phe Asp Cys Gly Val Val Phe Glu Glu Val Arg Glu
```

865 870 875 880
Asp Glu Ala Val Leu Pro Val Phe Glu Glu Lys Ile Ile Gly Lys Val
885 890 895
Glu Lys Val Asp
900

<210> 92
<211> 591
<212> PRT
<213> Homo sapiens

<400> 92
Met Val Pro Val Ala Val Thr Ala Ala Val Ala Pro Val Leu Ser Ile
1 5 10 15
Asn Ser Asp Phe Ser Asp Leu Arg Glu Ile Lys Lys Gln Leu Leu Leu
20 25 30
Ile Ala Gly Leu Thr Arg Glu Arg Gly Leu Leu His Ser Ser Lys Trp
35 40 45
Ser Ala Glu Leu Ala Phe Ser Leu Pro Ala Leu Pro Leu Ala Glu Leu
50 55 60
Gln Pro Pro Pro Pro Ile Thr Glu Glu Asp Ala Gln Asp Met Asp Ala
65 70 75 80
Tyr Thr Leu Ala Lys Ala Tyr Phe Asp Val Lys Glu Tyr Asp Arg Ala
85 90 95
Ala His Phe Leu His Gly Cys Asn Ser Lys Lys Ala Tyr Phe Leu Tyr
100 105 110
Met Tyr Ser Arg Tyr Leu Ser Gly Glu Lys Lys Lys Asp Asp Glu Thr
115 120 125
Val Asp Ser Leu Gly Pro Leu Glu Lys Gly Gln Val Lys Asn Glu Ala
130 135 140
Leu Arg Glu Leu Arg Val Glu Leu Ser Lys Lys His Gln Ala Arg Glu
145 150 155 160
Leu Asp Gly Phe Gly Leu Tyr Leu Tyr Gly Val Val Leu Arg Lys Leu
165 170 175
Asp Leu Val Lys Glu Ala Ile Asp Val Phe Val Glu Ala Thr His Val
180 185 190
Leu Pro Leu His Trp Gly Ala Trp Leu Glu Leu Cys Asn Leu Ile Thr
195 200 205
Asp Lys Glu Met Leu Lys Phe Leu Ser Leu Pro Asp Thr Trp Met Lys
210 215 220
Glu Phe Phe Leu Ala His Ile Tyr Thr Glu Leu Gln Leu Ile Glu Glu
225 230 235 240
Ala Leu Gln Lys Tyr Gln Asn Leu Ile Asp Val Gly Phe Ser Lys Ser
245 250 255
Ser Tyr Ile Val Ser Gln Ile Ala Val Ala Tyr His Asn Ile Arg Asp
260 265 270
Ile Asp Lys Ala Leu Ser Ile Phe Asn Glu Leu Arg Lys Gln Asp Pro
275 280 285
Tyr Arg Ile Glu Asn Met Asp Thr Phe Ser Asn Leu Leu Tyr Val Arg
290 295 300
Ser Met Lys Ser Glu Leu Ser Tyr Leu Ala His Asn Leu Cys Glu Ile
305 310 315 320
Asp Lys Tyr Arg Val Glu Thr Cys Cys Val Ile Gly Asn Tyr Tyr Ser

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

<210> 93
<211> 914
<212> PRT
<213> Homo sapiens

<400> 93
Val Tyr Gln Val Leu Leu Val Gly Ser Thr Leu Leu Lys Glu Val Pro
 1                5                  10                  15
Ser Gly Leu Gln Leu Glu Gln Leu Pro Ser Gln Ser Leu Leu Thr His
            20                  25                  30
Ile Pro Thr Ala Gly Leu Pro Thr Ser Leu Gly Gly Gly Leu Pro Tyr
        35                  40                  45
Cys His Gln Ala Trp Leu Asp Phe Arg Arg Arg Leu Glu Ala Leu Leu
    50                  55                  60
Gln Asn Cys Gln Ala Ala Cys Ala Leu Leu Gln Gly Ala Ile Glu Ser
65                  70                  75                  80
Val Lys Ala Val Pro Gln Pro Met Glu Pro Gly Glu Val Gly Gln Leu
                85                  90                  95
Leu Gln Gln Thr Glu Val Leu Met Gln Gln Val Leu Asp Ser Pro Trp
```

```
                100                 105                 110
Leu Ala Trp Leu Gln Cys Gln Gly Gly Arg Glu Leu Thr Trp Leu Lys
        115                 120                 125
Gln Glu Val Pro Glu Val Thr Leu Ser Pro Asp Tyr Arg Thr Ala Met
    130                 135                 140
Asp Lys Ala Asp Glu Leu Tyr Asp Arg Val Asp Gly Leu Leu His Gln
145                 150                 155                 160
Leu Thr Leu Gln Ser Asn Gln Arg Ile Gln Ala Leu Glu Leu Val Gln
                165                 170                 175
Thr Leu Glu Ala Arg Glu Ser Gly Leu His Gln Ile Glu Val Trp Leu
            180                 185                 190
Gln Gln Val Gly Trp Pro Ala Leu Glu Glu Ala Gly Glu Pro Ser Leu
        195                 200                 205
Asp Met Leu Leu Gln Ala Gln Gly Ser Phe Gln Glu Leu Tyr Gln Val
    210                 215                 220
Ala Gln Glu Gln Val Arg Gln Gly Glu Lys Phe Leu Gln Pro Leu Thr
225                 230                 235                 240
Gly Trp Glu Ala Ala Glu Leu Asp Pro Pro Gly Ala Arg Phe Leu Ala
                245                 250                 255
Leu Arg Ala Gln Leu Thr Glu Phe Ser Arg Ala Leu Ala Gln Arg Cys
            260                 265                 270
Gln Arg Leu Ala Asp Ala Glu Arg Leu Phe Gln Leu Phe Arg Glu Ala
        275                 280                 285
Leu Thr Trp Ala Glu Glu Gly Gln Arg Val Leu Ala Glu Leu Glu Gln
    290                 295                 300
Glu Arg Pro Gly Val Val Leu Gln Gln Leu Gln Leu His Trp Thr Arg
305                 310                 315                 320
His Pro Asp Leu Pro Pro Ala His Phe Arg Lys Met Trp Ala Leu Ala
                325                 330                 335
Thr Gly Leu Gly Ser Glu Ala Ile Arg Gln Glu Cys Arg Trp Ala Trp
            340                 345                 350
Ala Arg Cys Gln Asp Thr Trp Leu Ala Leu Asp Gln Lys Leu Glu Ala
        355                 360                 365
Ser Leu Lys Leu Pro Pro Val Gly Ser Thr Ala Ser Leu Cys Val Ser
    370                 375                 380
Gln Val Pro Ala Ala Pro Ala His Pro Pro Leu Arg Lys Ala Tyr Ser
385                 390                 395                 400
Phe Asp Arg Asn Leu Gly Gln Ser Leu Ser Glu Pro Ala Cys His Cys
                405                 410                 415
His His Ala Ala Thr Ile Ala Ala Cys Arg Arg Pro Glu Ala Gly Gly
            420                 425                 430
Gly Ala Leu Pro Gln Ala Ser Pro Thr Val Pro Pro Pro Gly Ser Ser
        435                 440                 445
Asp Pro Arg Ser Leu Asn Arg Leu Gln Leu Val Leu Ala Glu Met Val
    450                 455                 460
Ala Thr Glu Arg Glu Tyr Val Arg Ala Leu Glu Tyr Thr Met Glu Asn
465                 470                 475                 480
Tyr Phe Pro Glu Leu Asp Arg Pro Asp Val Pro Gln Gly Leu Arg Gly
                485                 490                 495
Gln Arg Ala His Leu Phe Gly Asn Leu Glu Lys Leu Arg Asp Phe His
            500                 505                 510
Cys His Phe Phe Leu Arg Glu Leu Glu Ala Cys Thr Arg His Pro Pro
        515                 520                 525
```

Arg Val Ala Tyr Ala Phe Leu Arg His Arg Val Gln Phe Gly Met Tyr
530 535 540
Ala Leu Tyr Ser Lys Asn Lys Pro Arg Ser Asp Ala Leu Met Ser Ser
545 550 555 560
Tyr Gly His Thr Phe Phe Lys Asp Lys Gln Gln Ala Leu Gly Asp His
565 570 575
Leu Asp Leu Ala Ser Tyr Leu Leu Lys Pro Ile Gln Arg Met Gly Lys
580 585 590
Tyr Ala Leu Leu Leu Gln Glu Leu Ala Arg Ala Cys Gly Gly Pro Thr
595 600 605
Gln Glu Leu Ser Ala Leu Arg Glu Ala Gln Ser Leu Val His Phe Gln
610 615 620
Leu Arg His Gly Asn Asp Leu Leu Ala Met Asp Ala Ile Gln Gly Cys
625 630 635 640
Asp Val Asn Leu Lys Glu Gln Gly Gln Leu Val Arg Gln Asp Glu Phe
645 650 655
Val Val Arg Thr Gly Arg His Lys Ser Val Arg Arg Ile Phe Leu Phe
660 665 670
Glu Glu Leu Leu Leu Phe Ser Lys Pro Arg His Gly Pro Thr Gly Val
675 680 685
Asp Thr Phe Ala Tyr Lys Arg Ser Phe Lys Met Ala Asp Leu Gly Leu
690 695 700
Thr Glu Cys Cys Gly Asn Ser Asn Leu Arg Phe Glu Ile Trp Phe Arg
705 710 715 720
Arg Arg Lys Ala Arg Asp Thr Phe Val Leu Gln Ala Ser Ser Leu Ala
725 730 735
Ile Lys Gln Ala Trp Thr Ala Asp Ile Ser His Leu Leu Trp Arg Gln
740 745 750
Ala Val His Asn Lys Glu Val Arg Met Ala Glu Met Val Ser Met Gly
755 760 765
Val Gly Asn Lys Ala Phe Arg Asp Ile Ala Pro Ser Glu Glu Ala Ile
770 775 780
Asn Asp Arg Thr Val Asn Tyr Val Leu Lys Cys Arg Glu Val Arg Ser
785 790 795 800
Arg Ala Ser Ile Ala Val Ala Pro Phe Asp His Asp Ser Leu Tyr Leu
805 810 815
Gly Ala Ser Asn Ser Leu Pro Gly Asp Pro Ala Ser Cys Ser Val Leu
820 825 830
Gly Ser Leu Asn Leu His Leu Tyr Arg Asp Pro Ala Leu Leu Gly Leu
835 840 845
Arg Cys Pro Leu Tyr Pro Ser Phe Leu Glu Glu Ala Ala Leu Glu Ala
850 855 860
Glu Ala Glu Leu Gly Gly Gln Pro Ser Leu Thr Ala Glu Asp Ser Glu
865 870 875 880
Ile Ser Ser Gln Cys Pro Ser Ala Ser Gly Ser Ser Gly Ser Asp Ser
885 890 895
Ser Cys Val Ser Gly Gln Ala Leu Gly Arg Gly Leu Glu Asp Leu Pro
900 905 910
Cys Val

<210> 94
<211> 277

<212> PRT
<213> Homo sapiens

<400> 94
Leu Asn Tyr Leu Leu Glu Ser Arg Leu Glu Ala Ala Ala His Cys Ala
1 5 10 15
Leu Lys Gln Gly Ile Ala Thr Ala Ser Leu Leu Pro Ala Gln Leu Gln
20 25 30
Pro Ala Val Leu Thr Val Val Thr Cys His Val Val Val Ser Val His
35 40 45
Gly His His Thr Asp Gly Cys Leu Ala Ala Leu Cys Arg Glu Asp Arg
50 55 60
Thr Gly Thr Gly Gly Ala Phe Trp Cys Lys Asn Arg Val Ile Val Ser
65 70 75 80
His Ala Val Asp Val Val Leu His Val His Gly Glu Gly Asn Pro Val
85 90 95
Gln Ala Leu Ile Ala His Gly Ala Pro Glu Ala Ala Trp Val Val Gly
100 105 110
Leu Ala Gln Gly Leu Gln Asp His Phe His Asp Glu Met Ser Thr His
115 120 125
Ala Ala Phe Val Gly Arg Leu Leu Glu Pro Gly Val Gln Glu Val Leu
130 135 140
Leu Ala Val His Phe Leu Thr His Val Val Glu Arg Leu Pro Thr Glu
145 150 155 160
Ser Ser Pro Thr Arg Val Ala Gly Glu Ala Val Ser Val Ile Lys Thr
165 170 175
Pro His Cys Leu Ala Arg Leu Leu Gly Ser Val Asp Ala Lys Pro Thr
180 185 190
Leu Asp Ala Asn Ala Glu Val Val Pro Arg Arg Ala Arg Leu Glu Arg
195 200 205
Pro Leu Gln Leu Pro Gly Glu Arg Leu Gln Pro Pro Leu Gly Arg Ala
210 215 220
Trp Ala Ala Leu Pro Ala Arg Gly Gln Arg Glu Cys Arg Gln Arg Glu
225 230 235 240
Gly Gly Arg Pro Arg Arg Leu Arg Gly Ala Ser Gly Arg Gly Ala Gly
245 250 255
Ala Gly Arg Glu Glu Val Ser Val Gly Phe Ser Ala Gln Trp Glu Phe
260 265 270
Gly Ser Gly Arg His
275

<210> 95
<211> 1120
<212> PRT
<213> Homo sapiens

<400> 95
Met Trp Arg Val Lys Lys Leu Ser Leu Ser Leu Ser Pro Ser Pro Gln
1 5 10 15
Thr Gly Lys Pro Ser Met Arg Thr Pro Leu Arg Glu Leu Thr Leu Gln
20 25 30
Pro Gly Ala Leu Thr Thr Ser Gly Lys Arg Ser Pro Ala Cys Ser Ser
35 40 45

```
Leu Thr Pro Ser Leu Cys Lys Leu Gly Leu Gln Glu Gly Ser Asn Asn
    50                  55                  60
Ser Ser Pro Val Asp Phe Val Asn Asn Lys Arg Thr Asp Leu Ser Ser
65                  70                  75                  80
Glu His Phe Ser His Ser Ser Lys Trp Leu Glu Thr Cys Gln His Glu
                85                  90                  95
Ser Asp Glu Gln Pro Leu Asp Pro Ile Pro Gln Ile Ser Ser Thr Pro
            100                 105                 110
Lys Thr Ser Glu Glu Ala Val Asp Pro Leu Gly Asn Tyr Met Val Lys
        115                 120                 125
Thr Ile Val Leu Val Pro Ser Pro Leu Gly Gln Gln Gln Asp Met Ile
    130                 135                 140
Phe Glu Ala Arg Leu Asp Thr Met Ala Glu Thr Asn Ser Ile Ser Leu
145                 150                 155                 160
Asn Gly Pro Leu Arg Thr Asp Asp Leu Val Arg Glu Glu Val Ala Pro
                165                 170                 175
Cys Met Gly Asp Arg Phe Ser Glu Val Ala Ala Val Ser Glu Lys Pro
            180                 185                 190
Ile Phe Gln Glu Ser Pro Ser His Leu Leu Glu Glu Ser Pro Pro Asn
        195                 200                 205
Pro Cys Ser Glu Gln Leu His Cys Ser Lys Glu Ser Leu Ser Ser Arg
    210                 215                 220
Thr Glu Ala Val Arg Glu Asp Leu Val Pro Ser Glu Ser Asn Ala Phe
225                 230                 235                 240
Leu Pro Ser Ser Val Leu Trp Leu Ser Pro Ser Thr Ala Leu Ala Ala
                245                 250                 255
Asp Phe Arg Val Asn His Val Asp Pro Glu Glu Glu Ile Val Glu His
            260                 265                 270
Gly Ala Met Glu Glu Arg Glu Met Arg Phe Pro Thr His Pro Lys Glu
        275                 280                 285
Ser Glu Thr Glu Asp Gln Ala Leu Val Ser Ser Val Glu Asp Ile Leu
    290                 295                 300
Ser Thr Cys Leu Thr Pro Asn Leu Val Glu Met Glu Ser Gln Glu Ala
305                 310                 315                 320
Pro Gly Pro Ala Val Glu Asp Val Gly Arg Ile Leu Gly Ser Asp Thr
                325                 330                 335
Glu Ser Trp Met Ser Pro Leu Ala Trp Leu Glu Lys Gly Val Asn Thr
            340                 345                 350
Ser Val Met Leu Glu Asn Leu Arg Gln Ser Leu Ser Leu Pro Ser Met
        355                 360                 365
Leu Arg Asp Ala Ala Ile Gly Thr Thr Pro Phe Ser Thr Cys Ser Val
    370                 375                 380
Gly Thr Trp Phe Thr Pro Ser Ala Pro Gln Glu Lys Ser Thr Asn Thr
385                 390                 395                 400
Ser Gln Thr Gly Leu Val Gly Thr Lys His Ser Thr Ser Glu Thr Glu
                405                 410                 415
Gln Leu Leu Cys Gly Arg Pro Pro Asp Leu Thr Ala Leu Ser Arg His
            420                 425                 430
Asp Leu Glu Asp Asn Leu Leu Ser Ser Leu Val Ile Val Glu Phe Leu
        435                 440                 445
Ser Arg Gln Leu Arg Asp Trp Lys Ser Gln Leu Ala Val Pro His Pro
    450                 455                 460
Glu Thr Gln Asp Ser Ser Thr Gln Thr Asp Thr Ser His Ser Gly Ile
```

```
465                 470                 475                 480
Thr Asn Lys Leu Gln His Leu Lys Glu Ser His Glu Met Gly Gln Ala
                485                 490                 495
Leu Gln Gln Ala Arg Asn Val Met Gln Ser Trp Val Leu Ile Ser Lys
            500                 505                 510
Glu Leu Ile Ser Leu Leu His Leu Ser Leu Leu His Leu Glu Glu Asp
        515                 520                 525
Lys Thr Thr Val Asn Gln Glu Ser Arg Arg Ala Glu Thr Leu Val Cys
    530                 535                 540
Cys Cys Phe Asp Leu Leu Lys Lys Leu Arg Ala Lys Leu Gln Ser Leu
545                 550                 555                 560
Lys Ala Glu Arg Glu Glu Ala Arg His Arg Glu Glu Met Ala Leu Arg
                565                 570                 575
Gly Lys Asp Ala Ala Glu Ile Val Leu Glu Ala Phe Cys Ala His Ala
            580                 585                 590
Ser Gln Arg Ile Ser Gln Leu Glu Gln Asp Leu Ala Ser Met Arg Glu
        595                 600                 605
Phe Arg Gly Leu Leu Lys Asp Ala Gln Thr Gln Leu Val Gly Leu His
    610                 615                 620
Ala Lys Gln Glu Glu Leu Val Gln Gln Thr Val Ser Leu Thr Ser Thr
625                 630                 635                 640
Leu Gln Gln Asp Trp Arg Ser Met Gln Leu Asp Tyr Thr Thr Trp Thr
                645                 650                 655
Ala Leu Leu Ser Arg Ser Arg Gln Leu Thr Glu Lys Leu Thr Val Lys
            660                 665                 670
Ser Gln Gln Ala Leu Gln Glu Arg Asp Val Ala Ile Glu Glu Lys Gln
        675                 680                 685
Glu Val Ser Arg Val Leu Glu Gln Val Ser Ala Gln Leu Glu Glu Cys
    690                 695                 700
Lys Gly Gln Thr Glu Gln Leu Glu Leu Glu Asn Ile Arg Leu Ala Thr
705                 710                 715                 720
Asp Leu Arg Ala Gln Leu Gln Ile Leu Ala Asn Met Asp Ser Gln Leu
                725                 730                 735
Lys Glu Leu Gln Ser Gln His Thr His Cys Ala Gln Asp Leu Ala Met
            740                 745                 750
Lys Asp Glu Leu Leu Cys Gln Leu Thr Gln Ser Asn Glu Glu Gln Ala
        755                 760                 765
Ala Gln Cys Val Lys Glu Glu Met Ala Leu Lys His Met Gln Ala Glu
    770                 775                 780
Leu Gln Gln Gln Gln Ala Val Leu Ala Lys Glu Val Arg Asp Leu Lys
785                 790                 795                 800
Glu Thr Leu Glu Phe Ala Asp Gln Glu Asn Gln Val Ala His Leu Glu
                805                 810                 815
Leu Gly Gln Val Glu Cys Gln Leu Lys Thr Thr Leu Glu Val Leu Arg
            820                 825                 830
Glu Arg Ser Leu Gln Cys Glu Asn Leu Lys Asp Thr Val Glu Asn Leu
        835                 840                 845
Thr Ala Lys Leu Ala Ser Thr Ile Ala Asp Asn Gln Glu Gln Asp Leu
    850                 855                 860
Glu Lys Thr Arg Gln Tyr Ser Gln Lys Leu Gly Leu Leu Thr Glu Gln
865                 870                 875                 880
Leu Gln Ser Leu Thr Leu Phe Leu Gln Thr Lys Leu Lys Glu Lys Thr
                885                 890                 895
```

Glu Gln Glu Thr Leu Leu Leu Ser Thr Ala Cys Pro Pro Thr Gln Glu
900 905 910
His Pro Leu Pro Asn Asp Arg Thr Phe Leu Gly Ser Ile Leu Thr Ala
915 920 925
Val Ala Asp Glu Glu Pro Glu Ser Thr Pro Val Pro Leu Leu Gly Ser
930 935 940
Asp Lys Ser Ala Phe Thr Arg Val Ala Ser Met Val Ser Leu Gln Pro
945 950 955 960
Ala Glu Thr Pro Gly Met Glu Glu Ser Leu Ala Glu Met Ser Ile Met
965 970 975
Thr Thr Glu Leu Gln Ser Leu Cys Ser Leu Leu Gln Glu Ser Lys Glu
980 985 990
Glu Ala Ile Arg Thr Leu Gln Arg Lys Ile Cys Glu Leu Gln Ala Arg
995 1000 1005
Leu Gln Ala Gln Glu Glu Gln His Gln Glu Val Gln Lys Ala Lys Glu
1010 1015 1020
Ala Asp Ile Glu Lys Leu Asn Gln Ala Leu Cys Leu Arg Tyr Lys Asn
1025 1030 1035 1040
Glu Lys Glu Leu Gln Glu Val Ile Gln Gln Asn Glu Lys Ile Leu Glu
1045 1050 1055
Gln Ile Asp Lys Ser Gly Glu Leu Ile Ser Leu Arg Glu Glu Val Thr
1060 1065 1070
His Leu Thr Arg Ser Leu Arg Arg Ala Glu Thr Glu Thr Lys Val Leu
1075 1080 1085
Gln Glu Ala Trp Gln Ala Ser Trp Thr Pro Thr Ala Ser Leu Trp Pro
1090 1095 1100
Pro Ile Gly Ser Arg Arg Lys Cys Gly Ser Leu Arg Arg Trp Thr Asn
1105 1110 1115 1120

<210> 96
<211> 540
<212> PRT
<213> Homo sapiens

<400> 96
Met Gly Thr Thr Ala Arg Ala Ala Leu Val Leu Thr Tyr Leu Ala Val
1 5 10 15
Ala Ser Ala Ala Ser Glu Gly Gly Phe Thr Ala Thr Gly Gln Arg Gln
20 25 30
Leu Arg Pro Glu His Phe Gln Glu Val Gly Tyr Ala Ala Pro Pro Ser
35 40 45
Pro Pro Leu Ser Arg Ser Leu Pro Met Asp His Pro Asp Ser Ser Gln
50 55 60
His Gly Pro Pro Phe Glu Gly Gln Ser Gln Val Gln Pro Pro Pro Ser
65 70 75 80
Gln Glu Ala Thr Pro Leu Gln Gln Glu Lys Leu Leu Pro Ala Gln Leu
85 90 95
Pro Ala Glu Lys Glu Val Gly Pro Pro Leu Pro Gln Glu Ala Val Pro
100 105 110
Leu Gln Lys Glu Leu Pro Ser Leu Gln His Pro Asn Glu Gln Lys Glu
115 120 125
Gly Thr Pro Ala Pro Phe Gly Asp Gln Ser His Pro Glu Pro Glu Ser
130 135 140

```
Trp Asn Ala Ala Gln His Cys Gln Gln Asp Arg Ser Gln Gly Gly Trp
145                 150                 155                 160
Gly His Arg Leu Asp Gly Phe Pro Pro Gly Arg Pro Ser Pro Asp Asn
                165                 170                 175
Leu Asn Gln Ile Cys Leu Pro Asn Arg Gln His Val Val Tyr Gly Pro
            180                 185                 190
Trp Asn Leu Pro Gln Ser Ser Tyr Ser His Leu Thr Arg Gln Gly Glu
        195                 200                 205
Thr Leu Asn Phe Leu Glu Ile Gly Tyr Ser Arg Cys Cys His Cys Arg
    210                 215                 220
Ser His Thr Asn Arg Leu Glu Cys Ala Lys Leu Val Trp Glu Glu Ala
225                 230                 235                 240
Met Ser Arg Phe Cys Glu Ala Glu Phe Ser Val Lys Thr Arg Pro His
                245                 250                 255
Trp Cys Cys Thr Arg Gln Gly Glu Ala Arg Phe Ser Cys Phe Gln Glu
            260                 265                 270
Glu Ala Pro Gln Pro His Tyr Gln Leu Arg Ala Cys Pro Ser His Gln
        275                 280                 285
Pro Asp Ile Ser Ser Gly Leu Glu Leu Pro Phe Pro Pro Gly Val Pro
    290                 295                 300
Thr Leu Asp Asn Ile Lys Asn Ile Cys His Leu Arg Arg Phe Arg Ser
305                 310                 315                 320
Val Pro Arg Asn Leu Pro Ala Thr Asp Pro Leu Gln Arg Glu Leu Leu
                325                 330                 335
Ala Leu Ile Gln Leu Glu Arg Glu Phe Gln Arg Cys Cys Arg Gln Gly
            340                 345                 350
Asn Asn His Thr Cys Thr Trp Lys Ala Trp Glu Asp Thr Leu Asp Lys
        355                 360                 365
Tyr Cys Asp Arg Glu Tyr Ala Val Lys Thr His His His Leu Cys Cys
    370                 375                 380
Arg His Pro Pro Ser Pro Thr Arg Asp Glu Cys Phe Ala Arg Arg Ala
385                 390                 395                 400
Pro Tyr Pro Asn Tyr Asp Arg Asp Ile Leu Thr Ile Asp Ile Ser Arg
                405                 410                 415
Val Thr Pro Asn Leu Met Gly His Leu Cys Gly Asn Gln Arg Val Leu
            420                 425                 430
Thr Lys His Lys His Ile Pro Gly Leu Ile His Asn Met Thr Ala Arg
        435                 440                 445
Cys Cys Asp Leu Pro Phe Pro Glu Gln Ala Cys Cys Ala Glu Glu Glu
    450                 455                 460
Lys Leu Thr Phe Ile Asn Asp Leu Cys Gly Pro Arg Arg Asn Ile Trp
465                 470                 475                 480
Arg Asp Pro Ala Leu Cys Cys Tyr Leu Ser Pro Gly Asp Glu Gln Val
                485                 490                 495
Asn Cys Phe Asn Ile Asn Tyr Leu Arg Asn Val Ala Leu Val Ser Gly
            500                 505                 510
Asp Thr Glu Asn Ala Lys Gly Gln Gly Glu Gln Gly Ser Thr Gly Gly
        515                 520                 525
Thr Asn Ile Ser Ser Thr Ser Glu Pro Lys Glu Glu
    530                 535                 540
```

<210> 97
<211> 462

<212> PRT
<213> Homo sapiens

<400> 97

```
Met Gly Lys Glu Lys Thr His Ile Asn Ile Val Val Ile Gly His Val
 1               5                  10                  15
Asp Ser Gly Lys Ser Thr Thr Thr Gly His Leu Ile Tyr Lys Cys Gly
            20                  25                  30
Gly Ile Asp Lys Arg Thr Ile Glu Lys Phe Glu Lys Glu Ala Ala Glu
        35                  40                  45
Met Gly Lys Gly Ser Phe Lys Tyr Ala Trp Val Leu Asp Lys Leu Lys
    50                  55                  60
Ala Glu Arg Glu Arg Gly Ile Thr Ile Asp Ile Ser Leu Trp Lys Phe
65                  70                  75                  80
Glu Thr Ser Lys Tyr Tyr Val Thr Ile Ile Asp Ala Pro Gly His Arg
                85                  90                  95
Asp Phe Ile Lys Asn Met Ile Thr Gly Thr Ser Gln Ala Asp Cys Ala
            100                 105                 110
Val Leu Ile Val Ala Ala Gly Val Gly Glu Phe Glu Ala Gly Ile Ser
        115                 120                 125
Lys Asn Gly Gln Thr Arg Glu His Ala Leu Leu Ala Tyr Thr Leu Gly
    130                 135                 140
Val Lys Gln Leu Ile Val Gly Val Asn Lys Met Asp Ser Thr Glu Pro
145                 150                 155                 160
Pro Tyr Ser Gln Lys Arg Tyr Glu Glu Ile Val Lys Glu Val Ser Thr
                165                 170                 175
Tyr Ile Lys Lys Ile Gly Tyr Asn Pro Asp Thr Val Ala Phe Val Pro
            180                 185                 190
Ile Ser Gly Trp Asn Gly Asp Asn Met Leu Glu Pro Ser Ala Asn Met
        195                 200                 205
Pro Trp Phe Lys Gly Trp Lys Val Thr Arg Lys Asp Gly Asn Ala Ser
    210                 215                 220
Gly Thr Thr Leu Leu Glu Ala Val Asp Cys Ile Leu Pro Pro Thr Arg
225                 230                 235                 240
Pro Thr Asp Lys Pro Leu Arg Leu Pro Leu Gln Asp Val Tyr Lys Ile
                245                 250                 255
Gly Gly Ile Gly Thr Val Pro Val Gly Arg Val Glu Thr Gly Val Leu
            260                 265                 270
Lys Pro Gly Met Val Val Thr Phe Ala Pro Val Asn Val Thr Thr Glu
        275                 280                 285
Val Lys Ser Val Glu Met His His Glu Ala Leu Ser Glu Ala Leu Pro
    290                 295                 300
Gly Asp Asn Val Gly Phe Asn Val Lys Asn Val Ser Val Lys Asp Val
305                 310                 315                 320
Arg Arg Gly Asn Val Ala Gly Asp Ser Lys Asn Asp Pro Pro Met Glu
                325                 330                 335
Ala Ala Gly Phe Thr Ala Gln Val Ile Ile Leu Asn His Pro Gly Gln
            340                 345                 350
Ile Ser Ala Gly Tyr Ala Pro Val Leu Asp Cys His Thr Ala His Ile
        355                 360                 365
Ala Cys Lys Phe Ala Glu Leu Lys Glu Lys Ile Asp Arg Arg Ser Gly
    370                 375                 380
Lys Lys Leu Glu Asp Gly Pro Lys Phe Leu Lys Ser Gly Asp Ala Ala
```

385 390 395 400
Ile Val Asp Met Val Pro Gly Lys Pro Met Cys Val Glu Ser Phe Ser
405 410 415
Asp Tyr Pro Pro Leu Gly Arg Phe Ala Val Arg Asp Met Arg Gln Thr
420 425 430
Val Ala Val Gly Val Ile Lys Ala Val Asp Lys Lys Ala Ala Gly Ala
435 440 445
Gly Lys Val Thr Lys Ser Ala Gln Lys Ala Gln Lys Ala Lys
450 455 460

<210> 98
<211> 2328
<212> PRT
<213> Homo sapiens

<400> 98
Lys Ser Lys Arg Gln Ala Gln Gln Met Val Gln Pro Gln Ser Pro Val
1 5 10 15
Ala Val Ser Gln Ser Lys Pro Gly Cys Tyr Asp Asn Gly Lys His Tyr
20 25 30
Gln Ile Asn Gln Gln Trp Glu Arg Thr Tyr Leu Gly Asn Val Leu Val
35 40 45
Cys Thr Cys Tyr Gly Gly Ser Arg Gly Phe Asn Cys Glu Ser Lys Pro
50 55 60
Glu Ala Glu Glu Thr Cys Phe Asp Lys Tyr Thr Gly Asn Thr Tyr Arg
65 70 75 80
Val Gly Asp Thr Tyr Glu Arg Pro Lys Asp Ser Met Ile Trp Asp Cys
85 90 95
Thr Cys Ile Gly Ala Gly Arg Gly Arg Ile Ser Cys Thr Ile Ala Asn
100 105 110
Arg Cys His Glu Gly Gly Gln Ser Tyr Lys Ile Gly Asp Thr Trp Arg
115 120 125
Arg Pro His Glu Thr Gly Gly Tyr Met Leu Glu Cys Val Cys Leu Gly
130 135 140
Asn Gly Lys Gly Glu Trp Thr Cys Lys Pro Ile Ala Glu Lys Cys Phe
145 150 155 160
Asp His Ala Ala Gly Thr Ser Tyr Val Val Gly Glu Thr Trp Glu Lys
165 170 175
Pro Tyr Gln Gly Trp Met Met Val Asp Cys Thr Cys Leu Gly Glu Gly
180 185 190
Ser Gly Arg Ile Thr Cys Thr Ser Arg Asn Arg Cys Asn Asp Gln Asp
195 200 205
Thr Arg Thr Ser Tyr Arg Ile Gly Asp Thr Trp Ser Lys Lys Asp Asn
210 215 220
Arg Gly Asn Leu Leu Gln Cys Ile Cys Thr Gly Asn Gly Arg Gly Glu
225 230 235 240
Trp Lys Cys Glu Arg His Thr Ser Val Gln Thr Thr Ser Ser Gly Ser
245 250 255
Gly Pro Phe Thr Asp Val Arg Ala Ala Val Tyr Gln Pro Gln Pro His
260 265 270
Pro Gln Pro Pro Pro Tyr Gly His Cys Val Thr Asp Ser Gly Val Val
275 280 285
Tyr Ser Val Gly Met Gln Trp Leu Lys Thr Gln Gly Asn Lys Gln Met

290 295 300
Leu Cys Thr Cys Leu Gly Asn Gly Val Ser Cys Gln Glu Thr Ala Val
305 310 315 320
Thr Gln Thr Tyr Gly Gly Asn Leu Asn Gly Glu Pro Cys Val Leu Pro
325 330 335
Phe Thr Tyr Asn Gly Arg Thr Phe Tyr Ser Cys Thr Thr Glu Gly Arg
340 345 350
Gln Asp Gly His Leu Trp Cys Ser Thr Thr Ser Asn Tyr Glu Gln Asp
355 360 365
Gln Lys Tyr Ser Phe Cys Thr Asp His Thr Val Leu Val Gln Thr Gln
370 375 380
Gly Gly Asn Ser Asn Gly Ala Leu Cys His Phe Pro Phe Leu Tyr Asn
385 390 395 400
Asn His Asn Tyr Thr Asp Cys Thr Ser Glu Gly Arg Arg Asp Asn Met
405 410 415
Lys Trp Cys Gly Thr Thr Gln Asn Tyr Asp Ala Asp Gln Lys Phe Gly
420 425 430
Phe Cys Pro Met Ala Ala His Glu Glu Ile Cys Thr Thr Asn Glu Gly
435 440 445
Val Met Tyr Arg Ile Gly Asp Gln Trp Asp Lys Gln His Asp Met Gly
450 455 460
His Met Met Arg Cys Thr Cys Val Gly Asn Gly Arg Gly Glu Trp Thr
465 470 475 480
Cys Ile Ala Tyr Ser Gln Leu Arg Asp Gln Cys Ile Val Asp Asp Ile
485 490 495
Thr Tyr Asn Val Asn Asp Thr Phe His Lys Arg His Glu Glu Gly His
500 505 510
Met Leu Asn Cys Thr Cys Phe Gly Gln Gly Arg Gly Arg Trp Lys Cys
515 520 525
Asp Pro Val Asp Gln Cys Gln Asp Ser Glu Thr Gly Thr Phe Tyr Gln
530 535 540
Ile Gly Asp Ser Trp Glu Lys Tyr Val His Gly Val Arg Tyr Gln Cys
545 550 555 560
Tyr Cys Tyr Gly Arg Gly Ile Gly Glu Trp His Cys Gln Pro Leu Gln
565 570 575
Thr Tyr Pro Ser Ser Ser Gly Pro Val Glu Val Phe Ile Thr Glu Thr
580 585 590
Pro Ser Gln Pro Asn Ser His Pro Ile Gln Trp Asn Ala Pro Gln Pro
595 600 605
Ser His Ile Ser Lys Tyr Ile Leu Arg Trp Arg Pro Lys Asn Ser Val
610 615 620
Gly Arg Trp Lys Glu Ala Thr Ile Pro Gly His Leu Asn Ser Tyr Thr
625 630 635 640
Ile Lys Gly Leu Lys Pro Gly Val Val Tyr Glu Gly Gln Leu Ile Ser
645 650 655
Ile Gln Gln Tyr Gly His Gln Glu Val Thr Arg Phe Asp Phe Thr Thr
660 665 670
Thr Ser Thr Ser Thr Pro Val Thr Ser Asn Thr Val Thr Gly Glu Thr
675 680 685
Thr Pro Phe Ser Pro Leu Val Ala Thr Ser Glu Ser Val Thr Glu Ile
690 695 700
Thr Ala Ser Ser Phe Val Val Ser Trp Val Ser Ala Ser Asp Thr Val
705 710 715 720

Ser Gly Phe Arg Val Glu Tyr Glu Leu Ser Glu Glu Gly Asp Glu Pro
725 730 735
Gln Tyr Leu Asp Leu Pro Ser Thr Ala Thr Ser Val Asn Ile Pro Asp
740 745 750
Leu Leu Pro Gly Arg Lys Tyr Ile Val Asn Val Tyr Gln Ile Ser Glu
755 760 765
Asp Gly Glu Gln Ser Leu Ile Leu Ser Thr Ser Gln Thr Thr Ala Pro
770 775 780
Asp Ala Pro Pro Asp Pro Thr Val Asp Gln Val Asp Asp Thr Ser Ile
785 790 795 800
Val Val Arg Trp Ser Arg Pro Gln Ala Pro Ile Thr Gly Tyr Arg Ile
805 810 815
Val Tyr Ser Pro Ser Val Glu Gly Ser Ser Thr Glu Leu Asn Leu Pro
820 825 830
Glu Thr Ala Asn Ser Val Thr Leu Ser Asp Leu Gln Pro Gly Val Gln
835 840 845
Tyr Asn Ile Thr Ile Tyr Ala Val Glu Glu Asn Gln Glu Ser Thr Pro
850 855 860
Val Val Ile Gln Gln Glu Thr Thr Gly Thr Pro Arg Ser Asp Thr Val
865 870 875 880
Pro Ser Pro Arg Asp Leu Gln Phe Val Glu Val Thr Asp Val Lys Val
885 890 895
Thr Ile Met Trp Thr Pro Pro Glu Ser Ala Val Thr Gly Tyr Arg Val
900 905 910
Asp Val Ile Pro Val Asn Leu Pro Gly Glu His Gly Gln Arg Leu Pro
915 920 925
Ile Ser Arg Asn Thr Phe Ala Glu Val Thr Gly Leu Ser Pro Gly Val
930 935 940
Thr Tyr Tyr Phe Lys Val Phe Ala Val Ser His Gly Arg Glu Ser Lys
945 950 955 960
Pro Leu Thr Ala Gln Gln Thr Thr Lys Leu Asp Ala Pro Thr Asn Leu
965 970 975
Gln Phe Val Asn Glu Thr Asp Ser Thr Val Leu Val Arg Trp Thr Pro
980 985 990
Pro Arg Ala Gln Ile Thr Gly Tyr Arg Leu Thr Val Gly Leu Thr Arg
995 1000 1005
Arg Gly Gln Pro Arg Gln Tyr Asn Val Gly Pro Ser Val Ser Lys Tyr
1010 1015 1020
Pro Leu Arg Asn Leu Gln Pro Ala Ser Glu Tyr Thr Val Ser Leu Val
1025 1030 1035 1040
Ala Ile Lys Gly Asn Gln Glu Ser Pro Lys Ala Thr Gly Val Phe Thr
1045 1050 1055
Thr Leu Gln Pro Gly Ser Ser Ile Pro Pro Tyr Asn Thr Glu Val Thr
1060 1065 1070
Glu Thr Thr Ile Val Ile Thr Trp Thr Pro Ala Pro Arg Ile Gly Phe
1075 1080 1085
Lys Leu Gly Val Arg Pro Ser Gln Gly Gly Glu Ala Pro Arg Glu Val
1090 1095 1100
Thr Ser Asp Ser Gly Ser Ile Val Val Ser Gly Leu Thr Pro Gly Val
1105 1110 1115 1120
Glu Tyr Val Tyr Thr Ile Gln Val Leu Arg Asp Gly Gln Glu Arg Asp
1125 1130 1135
Ala Pro Ile Val Asn Lys Val Val Thr Pro Leu Ser Pro Pro Thr Asn

```
            1140                1145                1150
Leu His Leu Glu Ala Asn Pro Asp Thr Gly Val Leu Thr Val Ser Trp
        1155                1160                1165
Glu Arg Ser Thr Thr Pro Asp Ile Thr Gly Tyr Arg Ile Thr Thr Thr
    1170                1175                1180
Pro Thr Asn Gly Gln Gln Gly Asn Ser Leu Glu Glu Val Val His Ala
1185                1190                1195                1200
Asp Gln Ser Ser Cys Thr Phe Asp Asn Leu Ser Pro Gly Leu Glu Tyr
                1205                1210                1215
Asn Val Ser Val Tyr Thr Val Lys Asp Asp Lys Glu Ser Val Pro Ile
            1220                1225                1230
Ser Asp Thr Ile Ile Pro Ala Val Pro Pro Pro Thr Asp Leu Arg Phe
        1235                1240                1245
Thr Asn Ile Gly Pro Asp Thr Met Arg Val Thr Trp Ala Pro Pro Pro
    1250                1255                1260
Ser Ile Asp Leu Thr Asn Phe Leu Val Arg Tyr Ser Pro Val Lys Asn
1265                1270                1275                1280
Glu Glu Asp Val Ala Glu Leu Ser Ile Ser Pro Ser Asp Asn Ala Val
                1285                1290                1295
Val Leu Thr Asn Leu Leu Pro Gly Thr Glu Tyr Val Val Ser Val Ser
            1300                1305                1310
Ser Val Tyr Glu Gln His Glu Ser Thr Pro Leu Arg Gly Arg Gln Lys
        1315                1320                1325
Thr Gly Leu Asp Ser Pro Thr Gly Ile Asp Phe Ser Asp Ile Thr Ala
    1330                1335                1340
Asn Ser Phe Thr Val His Trp Ile Ala Pro Arg Ala Thr Ile Thr Gly
1345                1350                1355                1360
Tyr Arg Ile Arg His His Pro Glu His Phe Ser Gly Arg Pro Arg Glu
                1365                1370                1375
Asp Arg Val Pro His Ser Arg Asn Ser Ile Thr Leu Thr Asn Leu Thr
            1380                1385                1390
Pro Gly Thr Glu Tyr Val Val Ser Ile Val Ala Leu Asn Gly Arg Glu
        1395                1400                1405
Glu Ser Pro Leu Leu Ile Gly Gln Gln Ser Thr Val Ser Asp Val Pro
    1410                1415                1420
Arg Asp Leu Glu Val Val Ala Ala Thr Pro Thr Ser Leu Leu Ile Ser
1425                1430                1435                1440
Trp Asp Ala Pro Ala Val Thr Val Arg Tyr Tyr Arg Ile Thr Tyr Gly
                1445                1450                1455
Glu Thr Gly Gly Asn Ser Pro Val Gln Glu Phe Thr Val Pro Gly Ser
            1460                1465                1470
Lys Ser Thr Ala Thr Ile Ser Gly Leu Lys Pro Gly Val Asp Tyr Thr
        1475                1480                1485
Ile Thr Val Tyr Ala Val Thr Gly Arg Gly Asp Ser Pro Ala Ser Ser
    1490                1495                1500
Lys Pro Ile Ser Ile Asn Tyr Arg Thr Glu Ile Asp Lys Pro Ser Gln
1505                1510                1515                1520
Met Gln Val Thr Asp Val Gln Asp Asn Ser Ile Ser Val Lys Trp Leu
                1525                1530                1535
Pro Ser Ser Ser Pro Val Thr Gly Tyr Arg Val Thr Thr Thr Pro Lys
            1540                1545                1550
Asn Gly Pro Gly Pro Thr Lys Thr Lys Thr Ala Gly Pro Asp Gln Thr
        1555                1560                1565
```

Glu Met Thr Ile Glu Gly Leu Gln Pro Thr Val Glu Tyr Val Val Ser
1570 1575 1580
Val Tyr Ala Gln Asn Pro Ser Gly Glu Ser Gln Pro Leu Val Gln Thr
1585 1590 1595 1600
Ala Val Thr Asn Ile Asp Arg Pro Lys Gly Leu Ala Phe Thr Asp Val
1605 1610 1615
Asp Val Asp Ser Ile Lys Ile Ala Trp Glu Ser Pro Gln Gly Gln Val
1620 1625 1630
Ser Arg Tyr Arg Val Thr Tyr Ser Ser Pro Glu Asp Gly Ile His Glu
1635 1640 1645
Leu Phe Pro Ala Pro Asp Gly Glu Glu Asp Thr Ala Glu Leu Gln Gly
1650 1655 1660
Leu Arg Pro Gly Ser Glu Tyr Thr Val Ser Val Val Ala Leu His Asp
1665 1670 1675 1680
Asp Met Glu Ser Gln Pro Leu Ile Gly Thr Gln Ser Thr Ala Ile Pro
1685 1690 1695
Ala Pro Thr Asp Leu Lys Phe Thr Gln Val Thr Pro Thr Ser Leu Ser
1700 1705 1710
Ala Gln Trp Thr Pro Pro Asn Val Gln Leu Thr Gly Tyr Arg Val Arg
1715 1720 1725
Val Thr Pro Lys Glu Lys Thr Gly Pro Met Lys Glu Ile Asn Leu Ala
1730 1735 1740
Pro Asp Ser Ser Ser Val Val Val Ser Gly Leu Met Val Ala Thr Lys
1745 1750 1755 1760
Tyr Glu Val Ser Val Tyr Ala Leu Lys Asp Thr Leu Thr Ser Arg Pro
1765 1770 1775
Ala Gln Gly Val Val Thr Thr Leu Glu Asn Val Ser Pro Pro Arg Arg
1780 1785 1790
Ala Arg Val Thr Asp Ala Thr Glu Thr Thr Ile Thr Ile Ser Trp Arg
1795 1800 1805
Thr Lys Thr Glu Thr Ile Thr Gly Phe Gln Val Asp Ala Val Pro Ala
1810 1815 1820
Asn Gly Gln Thr Pro Ile Gln Arg Thr Ile Lys Pro Asp Val Arg Ser
1825 1830 1835 1840
Tyr Thr Ile Thr Gly Leu Gln Pro Gly Thr Asp Tyr Lys Ile Tyr Leu
1845 1850 1855
Tyr Thr Leu Asn Asp Asn Ala Arg Ser Ser Pro Val Val Ile Asp Ala
1860 1865 1870
Ser Thr Ala Ile Asp Ala Pro Ser Asn Leu Arg Phe Leu Ala Thr Thr
1875 1880 1885
Pro Asn Ser Leu Leu Val Ser Trp Gln Pro Pro Arg Ala Arg Ile Thr
1890 1895 1900
Gly Tyr Ile Ile Lys Tyr Glu Lys Pro Gly Ser Pro Pro Arg Glu Val
1905 1910 1915 1920
Val Pro Arg Pro Arg Pro Gly Val Thr Glu Ala Thr Ile Thr Gly Leu
1925 1930 1935
Glu Pro Gly Thr Glu Tyr Thr Ile Tyr Val Ile Ala Leu Lys Asn Asn
1940 1945 1950
Gln Lys Ser Glu Pro Leu Ile Gly Arg Lys Lys Thr Asp Glu Leu Pro
1955 1960 1965
Gln Leu Val Thr Leu Pro His Pro Asn Leu His Gly Pro Glu Ile Leu
1970 1975 1980
Asp Val Pro Ser Thr Val Gln Lys Thr Pro Phe Val Thr His Pro Gly

1985 1990 1995 2000
Tyr Asp Thr Gly Asn Gly Ile Gln Leu Pro Gly Thr Ser Gly Gln Gln
2005 2010 2015
Pro Ser Val Gly Gln Gln Met Ile Phe Glu Glu His Gly Phe Arg Arg
2020 2025 2030
Thr Thr Pro Pro Thr Thr Ala Thr Pro Ile Arg His Arg Pro Arg Pro
2035 2040 2045
Tyr Pro Pro Asn Val Gly Gln Glu Ala Leu Ser Gln Thr Thr Ile Ser
2050 2055 2060
Trp Ala Pro Phe Gln Asp Thr Ser Glu Tyr Ile Ile Ser Cys His Pro
2065 2070 2075 2080
Val Gly Thr Asp Glu Glu Pro Leu Gln Phe Arg Val Pro Gly Thr Ser
2085 2090 2095
Thr Ser Ala Thr Leu Thr Gly Leu Thr Arg Gly Ala Thr Tyr Asn Ile
2100 2105 2110
Ile Val Glu Ala Leu Lys Asp Gln Gln Arg His Lys Val Arg Glu Glu
2115 2120 2125
Val Val Thr Val Gly Asn Ser Val Asn Glu Gly Leu Asn Gln Pro Thr
2130 2135 2140
Asp Asp Ser Cys Phe Asp Pro Tyr Thr Val Ser His Tyr Ala Val Gly
2145 2150 2155 2160
Asp Glu Trp Glu Arg Met Ser Glu Ser Gly Phe Lys Leu Leu Cys Gln
2165 2170 2175
Cys Leu Gly Phe Gly Ser Gly His Phe Arg Cys Asp Ser Ser Arg Trp
2180 2185 2190
Cys His Asp Asn Gly Val Asn Tyr Lys Ile Gly Glu Lys Trp Asp Arg
2195 2200 2205
Gln Gly Glu Asn Gly Gln Met Met Ser Cys Thr Cys Leu Gly Asn Gly
2210 2215 2220
Lys Gly Glu Phe Lys Cys Asp Pro His Glu Ala Thr Cys Tyr Asp Asp
2225 2230 2235 2240
Gly Lys Thr Tyr His Val Gly Glu Gln Trp Gln Lys Glu Tyr Leu Gly
2245 2250 2255
Ala Ile Cys Ser Cys Thr Cys Phe Gly Gly Gln Arg Gly Trp Arg Cys
2260 2265 2270
Asp Asn Cys Arg Arg Pro Gly Gly Glu Pro Ser Pro Glu Gly Thr Thr
2275 2280 2285
Gly Gln Ser Tyr Asn Gln Tyr Ser Gln Arg Tyr His Gln Arg Thr Asn
2290 2295 2300
Thr Asn Val Asn Cys Pro Ile Glu Cys Phe Met Pro Leu Asp Val Gln
2305 2310 2315 2320
Ala Asp Arg Glu Asp Ser Arg Glu
2325

<210> 99
<211> 188
<212> PRT
<213> Homo sapiens

<400> 99
His Gln Thr His Lys Glu Gly Gly Ser Thr His Ala Ser Ala Asp Ala
1 5 10 15
Trp Glu Ile Ile Glu Leu Glu Thr Glu Ile Glu Lys Phe Lys Ala Glu

```
            20                  25                  30
Asn Ala Ser Leu Ala Lys Leu Arg Ile Glu Arg Glu Ser Ala Leu Glu
        35                  40                  45
Lys Leu Arg Lys Glu Ile Ala Asp Phe Glu Gln Gln Lys Ala Lys Glu
    50                  55                  60
Leu Ala Arg Ile Glu Glu Phe Lys Lys Glu Glu Met Arg Lys Leu Gln
65                  70                  75                  80
Lys Glu Arg Lys Val Phe Glu Lys Tyr Thr Thr Ala Ala Arg Thr Phe
                85                  90                  95
Pro Asp Lys Lys Glu Arg Glu Glu Ile Gln Thr Leu Lys Gln Gln Ile
            100                 105                 110
Ala Asp Leu Arg Glu Asp Leu Lys Arg Lys Glu Thr Lys Trp Ser Ser
        115                 120                 125
Thr His Ser Arg Leu Arg Ser Gln Ile Gln Met Leu Val Arg Glu Asn
    130                 135                 140
Thr Asp Leu Arg Glu Glu Ile Lys Val Met Glu Arg Phe Arg Leu Asp
145                 150                 155                 160
Ala Trp Lys Arg Ala Glu Ala Ile Glu Ser Ser Leu Glu Val Glu Lys
                165                 170                 175
Lys Asp Lys Leu Ala Asn Thr Ser Val Arg Phe Gln
            180                 185

<210> 100
<211> 284
<212> PRT
<213> Homo sapiens

<400> 100
Met Glu Pro Gly Asn Tyr Ala Thr Leu Asp Gly Ala Lys Asp Ile Glu
 1               5                  10                  15
Gly Leu Leu Gly Ala Gly Gly Gly Arg Asn Leu Val Ala His Ser Pro
            20                  25                  30
Leu Thr Ser His Pro Ala Ala Pro Thr Leu Met Pro Ala Val Asn Tyr
        35                  40                  45
Ala Pro Leu Asp Leu Pro Gly Ser Ala Glu Pro Pro Lys Gln Cys His
    50                  55                  60
Pro Cys Pro Gly Val Pro Gln Gly Thr Ser Pro Ala Pro Val Pro Tyr
65                  70                  75                  80
Gly Tyr Phe Gly Gly Gly Tyr Tyr Ser Cys Arg Val Ser Arg Ser Ser
                85                  90                  95
Leu Lys Pro Cys Ala Gln Ala Ala Thr Leu Ala Ala Tyr Pro Ala Glu
            100                 105                 110
Thr Pro Thr Ala Gly Glu Glu Tyr Pro Ser Arg Pro Thr Glu Phe Ala
        115                 120                 125
Phe Tyr Pro Gly Tyr Pro Gly Thr Tyr His Ala Met Ala Ser Tyr Leu
    130                 135                 140
Asp Val Ser Val Val Gln Thr Leu Gly Ala Pro Gly Glu Pro Arg His
145                 150                 155                 160
Asp Ser Leu Leu Pro Val Asp Ser Tyr Gln Ser Trp Ala Leu Ala Gly
                165                 170                 175
Gly Trp Asn Ser Gln Met Cys Cys Gln Gly Glu Gln Asn Pro Pro Gly
            180                 185                 190
Pro Phe Trp Lys Ala Ala Phe Ala Asp Ser Ser Gly Gln His Pro Pro
```

```
        195                 200                 205
Asp Ala Cys Ala Phe Arg Arg Gly Arg Lys Lys Arg Ile Pro Tyr Ser
    210                 215                 220
Lys Gly Gln Leu Arg Glu Leu Glu Arg Glu Tyr Ala Ala Asn Lys Phe
225                 230                 235                 240
Ile Thr Lys Asp Lys Arg Arg Lys Ile Ser Ala Ala Thr Ser Leu Ser
                245                 250                 255
Glu Arg Gln Ile Thr Ile Trp Phe Gln Asn Arg Arg Val Lys Glu Lys
            260                 265                 270
Lys Val Leu Ala Lys Val Lys Asn Ser Ala Thr Pro
        275                 280
```

<210> 101
<211> 676
<212> PRT
<213> Homo sapiens

<400> 101

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

```
        275                 280                 285
Pro Val Gln Pro Arg Thr Pro Ser Val Ser Ala Pro Leu Ala Leu Ser
    290                 295                 300
Cys Pro Arg Gln Gly Gly Leu Pro Arg Ser Asn Ser Gly Leu Gly Gly
305                 310                 315                 320
Glu Val Ser Gly Val Met Ser Lys Pro Asn Val Asp Pro Gln Pro Trp
                325                 330                 335
Phe Gln Asp Gly Pro Lys Ser Tyr Leu Ser Ser Ser Ala Pro Ser Ser
            340                 345                 350
Ser Pro Ala Gly Leu Asp Gly Ser Gln Gln Gly Ala Val Pro Gly Leu
        355                 360                 365
Gly Pro Lys Pro Gly Cys Thr Asp Leu Gly Thr Gly Pro Lys Leu Ser
    370                 375                 380
Pro Thr Ser Leu Val His Pro Val Met Ser Thr Leu Pro Glu Leu Ser
385                 390                 395                 400
Cys Lys Glu Gly Pro Leu Gly Trp Ser Ser Asp Gly Ser Leu Gly Ser
                405                 410                 415
Val Leu Leu Asp Ser Pro Ser Ser Pro Arg Val Arg Leu Pro Cys Gln
            420                 425                 430
Pro Leu Val Pro Gly Pro Glu Leu Arg Pro Ser Ala Ala Glu Leu Lys
        435                 440                 445
Leu Glu Ala Leu Thr Gln Arg Leu Glu Arg Glu Met Asp Ala His Pro
    450                 455                 460
Lys Ala Asp Tyr Phe Gly Ala Cys Val Lys Cys Ser Lys Gly Val Phe
465                 470                 475                 480
Gly Ala Gly Gln Ala Cys Gln Ala Met Gly Asn Leu Tyr His Asp Thr
                485                 490                 495
Cys Phe Thr Cys Ala Ala Cys Ser Arg Lys Leu Arg Gly Lys Ala Phe
            500                 505                 510
Tyr Phe Val Asn Gly Lys Val Phe Cys Glu Glu Asp Phe Leu Tyr Ser
        515                 520                 525
Gly Phe Gln Gln Ser Ala Asp Arg Cys Phe Leu Cys Gly His Leu Ile
    530                 535                 540
Met Asp Met Ile Leu Gln Ala Leu Gly Lys Ser Tyr His Pro Gly Cys
545                 550                 555                 560
Phe Arg Cys Val Ile Cys Asn Glu Cys Leu Asp Gly Val Pro Phe Thr
                565                 570                 575
Val Asp Ser Glu Asn Lys Ile Tyr Cys Val Arg Asp Tyr His Lys Val
            580                 585                 590
Leu Ala Pro Lys Cys Ala Ala Cys Gly Leu Pro Ile Leu Pro Pro Glu
        595                 600                 605
Gly Ser Asp Glu Thr Ile Arg Val Val Ser Met Asp Arg Asp Tyr His
    610                 615                 620
Val Glu Cys Tyr His Cys Glu Asp Cys Gly Leu Glu Leu Asn Asp Glu
625                 630                 635                 640
Asp Gly His Arg Cys Tyr Pro Leu Glu Asp His Leu Phe Cys His Ser
                645                 650                 655
Cys His Val Lys Arg Leu Glu Lys Arg Pro Ser Ser Thr Ala Leu His
            660                 665                 670
Gln His His Phe
        675
```

<210> 102

<211> 296
<212> PRT
<213> Homo sapiens

<400> 102
Ser Thr Gly Ser Glu Phe Pro Leu Cys Thr Lys Ala Ser Pro Cys Ser
1 5 10 15
Ala Ala Arg Ala Gly Gly Arg Ala Leu Gly Trp Arg Leu Gln Gln Gln
20 25 30
Arg Glu Thr Arg Gly Asn Pro Gly Asn Pro Gly Leu Gly Val Ala Ala
35 40 45
Thr Met Thr Gly Ser Asn Met Ser Asp Ala Leu Ala Asn Ala Val Cys
50 55 60
Gln Arg Cys Gln Ala Arg Phe Ser Pro Ala Glu Arg Ile Val Asn Ser
65 70 75 80
Asn Gly Glu Leu Tyr His Glu His Cys Phe Val Cys Ala Gln Cys Phe
85 90 95
Arg Pro Phe Pro Glu Gly Leu Phe Tyr Glu Phe Glu Gly Arg Lys Tyr
100 105 110
Cys Glu His Asp Phe Gln Met Leu Phe Ala Pro Cys Cys Gly Ser Cys
115 120 125
Gly Glu Phe Ile Ile Gly Arg Val Ile Lys Ala Met Asn Asn Asn Trp
130 135 140
His Pro Gly Cys Phe Arg Cys Glu Leu Cys Asp Val Glu Leu Ala Asp
145 150 155 160
Leu Gly Phe Val Lys Asn Ala Gly Arg His Leu Cys Arg Pro Cys His
165 170 175
Asn Arg Glu Lys Ala Lys Gly Leu Gly Lys Tyr Ile Cys Gln Arg Cys
180 185 190
His Leu Val Ile Asp Glu Gln Pro Leu Met Phe Arg Ser Asp Ala Tyr
195 200 205
His Pro Asp His Phe Asn Cys Thr His Cys Gly Lys Glu Leu Thr Ala
210 215 220
Glu Ala Arg Glu Leu Lys Gly Glu Leu Tyr Cys Leu Pro Cys His Asp
225 230 235 240
Lys Met Gly Val Pro Ile Cys Gly Ala Cys Arg Arg Pro Ile Glu Gly
245 250 255
Arg Val Val Asn Ala Leu Gly Lys Gln Trp His Val Glu His Phe Val
260 265 270
Cys Ala Lys Cys Glu Lys Pro Phe Leu Gly His Arg His Tyr Glu Lys
275 280 285
Lys Gly Leu Ala Tyr Cys Glu Leu
290 295

<210> 103
<211> 500
<212> PRT
<213> Homo sapiens

<400> 103
Met Gly Ile Gly Leu Ser Ala Gln Gly Val Asn Met Asn Arg Leu Pro
1 5 10 15
Gly Trp Asp Lys His Ser Tyr Gly Tyr His Gly Asp Asp Gly His Ser

```
                20                  25                  30
Phe Cys Ser Ser Gly Thr Gly Gln Pro Tyr Gly Pro Thr Phe Thr Thr
            35                  40                  45
Gly Asp Val Ile Gly Cys Cys Val Asn Leu Ile Asn Asn Thr Cys Phe
        50                  55                  60
Tyr Thr Lys Asn Gly His Ser Leu Gly Ile Ala Phe Thr Asp Leu Pro
65                  70                  75                  80
Pro Asn Leu Tyr Pro Thr Val Gly Leu Gln Thr Pro Gly Glu Val Val
                85                  90                  95
Asp Ala Asn Phe Gly Gln His Pro Phe Val Phe Asp Ile Glu Asp Tyr
            100                 105                 110
Met Arg Glu Trp Arg Thr Lys Ile Gln Ala Gln Ile Asp Arg Phe Pro
        115                 120                 125
Ile Gly Asp Arg Glu Gly Glu Trp Gln Thr Met Ile Gln Lys Met Val
    130                 135                 140
Ser Ser Tyr Leu Val His His Gly Tyr Cys Ala Thr Ala Glu Ala Phe
145                 150                 155                 160
Ala Arg Ser Thr Asp Gln Thr Val Leu Glu Glu Leu Ala Ser Ile Lys
                165                 170                 175
Asn Arg Gln Arg Ile Gln Lys Leu Val Leu Ala Gly Arg Met Gly Glu
            180                 185                 190
Ala Ile Glu Thr Thr Gln Gln Leu Tyr Pro Ser Leu Leu Glu Arg Asn
        195                 200                 205
Pro Asn Leu Leu Phe Thr Leu Lys Val Arg Gln Phe Ile Glu Met Val
    210                 215                 220
Asn Gly Thr Asp Ser Glu Val Arg Cys Leu Gly Gly Arg Ser Pro Lys
225                 230                 235                 240
Ser Gln Asp Ser Tyr Pro Val Ser Pro Arg Pro Phe Ser Ser Pro Ser
                245                 250                 255
Met Ser Pro Ser His Gly Met Asn Ile His Asn Leu Ala Ser Gly Lys
            260                 265                 270
Gly Ser Thr Ala His Phe Ser Gly Phe Glu Ser Cys Ser Asn Gly Val
        275                 280                 285
Ile Ser Asn Lys Ala His Gln Ser Tyr Cys His Ser Asn Lys His Gln
    290                 295                 300
Ser Ser Asn Leu Asn Val Pro Glu Leu Asn Ser Ile Asn Met Ser Arg
305                 310                 315                 320
Ser Gln Gln Val Asn Asn Phe Thr Ser Asn Asp Val Asp Met Glu Thr
                325                 330                 335
Asp His Tyr Ser Asn Gly Val Gly Glu Thr Ser Ser Asn Gly Phe Leu
            340                 345                 350
Asn Gly Ser Ser Lys His Asp His Glu Met Glu Asp Cys Asp Thr Glu
        355                 360                 365
Met Glu Val Asp Ser Ser Gln Leu Arg Arg Gln Leu Cys Gly Gly Ser
    370                 375                 380
Gln Ala Ala Ile Glu Arg Met Ile His Phe Gly Arg Glu Leu Gln Ala
385                 390                 395                 400
Met Ser Glu Gln Leu Arg Arg Asp Cys Gly Lys Asn Thr Ala Asn Lys
                405                 410                 415
Lys Met Leu Lys Asp Ala Phe Ser Leu Leu Ala Tyr Ser Asp Pro Trp
            420                 425                 430
Asn Ser Pro Val Gly Asn Gln Leu Asp Pro Ile Gln Arg Glu Pro Val
        435                 440                 445
```

```
Cys Ser Ala Leu Asn Ser Ala Ile Leu Glu Thr His Asn Leu Pro Lys
    450                 455                 460
Gln Pro Pro Leu Ala Leu Ala Met Gly Gln Ala Thr Gln Cys Leu Gly
465                 470                 475                 480
Leu Met Ala Arg Ser Gly Ile Gly Ser Cys Ala Phe Ala Thr Val Glu
                485                 490                 495
Asp Tyr Leu His
            500

<210> 104
<211> 387
<212> PRT
<213> Homo sapiens

<400> 104
Met Ala Thr Ser Gly Val Leu Pro Gly Gly Gly Phe Val Ala Ser Ala
 1               5                  10                  15
Ala Ala Val Ala Gly Pro Glu Met Gln Thr Gly Arg Asn Asn Phe Val
            20                  25                  30
Ile Arg Arg Asn Pro Ala Asp Pro Gln Arg Ile Pro Ser Asn Pro Ser
        35                  40                  45
His Arg Ile Gln Cys Ala Ala Gly Tyr Glu Gln Ser Glu His Asn Val
    50                  55                  60
Cys Gln Asp Ile Asp Glu Cys Thr Ala Gly Thr His Asn Cys Arg Ala
65                  70                  75                  80
Asp Gln Val Cys Ile Asn Leu Arg Gly Ser Phe Ala Cys Gln Cys Pro
                85                  90                  95
Pro Gly Tyr Gln Lys Arg Gly Glu Gln Cys Val Asp Ile Asp Glu Cys
            100                 105                 110
Thr Ile Pro Pro Tyr Cys His Gln Arg Cys Val Asn Thr Pro Gly Ser
        115                 120                 125
Phe Tyr Cys Gln Cys Ser Pro Gly Phe Gln Leu Ala Ala Asn Asn Tyr
    130                 135                 140
Thr Cys Val Asp Ile Asn Glu Cys Asp Ala Ser Asn Gln Cys Ala Gln
145                 150                 155                 160
Gln Cys Tyr Asn Ile Leu Gly Ser Phe Ile Cys Gln Cys Asn Gln Gly
                165                 170                 175
Tyr Glu Leu Ser Ser Asp Arg Leu Asn Cys Glu Asp Ile Asp Glu Cys
            180                 185                 190
Arg Thr Ser Ser Tyr Leu Cys Gln Tyr Gln Cys Val Asn Glu Pro Gly
        195                 200                 205
Lys Phe Ser Cys Met Cys Pro Gln Gly Tyr Gln Val Val Arg Ser Arg
    210                 215                 220
Thr Cys Gln Asp Ile Asn Glu Cys Glu Thr Thr Asn Glu Cys Arg Glu
225                 230                 235                 240
Asp Glu Met Cys Trp Asn Tyr His Gly Gly Phe Arg Cys Tyr Pro Arg
                245                 250                 255
Asn Pro Cys Gln Asp Pro Tyr Ile Leu Thr Pro Glu Asn Arg Cys Val
            260                 265                 270
Cys Pro Val Ser Asn Ala Met Cys Arg Glu Leu Pro Gln Ser Ile Val
        275                 280                 285
Tyr Lys Tyr Met Ser Ile Arg Ser Asp Arg Ser Val Pro Ser Asp Ile
    290                 295                 300
```

```
Phe Gln Ile Gln Ala Thr Thr Ile Tyr Ala Asn Thr Ile Asn Thr Phe
305                 310                 315                 320
Arg Ile Lys Ser Gly Asn Glu Asn Gly Glu Phe Tyr Leu Arg Gln Thr
                325                 330                 335
Ser Pro Val Ser Ala Met Leu Val Leu Val Lys Ser Leu Ser Gly Pro
            340                 345                 350
Arg Glu His Ile Val Asp Leu Glu Met Leu Thr Val Ser Ser Ile Gly
        355                 360                 365
Thr Phe Arg Thr Ser Ser Val Leu Arg Leu Thr Ile Ile Val Gly Pro
    370                 375                 380
Phe Ser Phe
385
```

<210> 105
<211> 531
<212> PRT
<213> Homo sapiens

<400> 105

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

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

<210> 106
<211> 480
<212> PRT
<213> Homo sapiens

<400> 106
Met Ala Ala Arg Cys Ser Thr Arg Trp Leu Leu Val Val Val Gly Thr
1 5 10 15
Pro Arg Leu Pro Ala Ile Ser Gly Arg Gly Ala Arg Pro Pro Arg Glu
20 25 30
Gly Val Val Gly Ala Trp Leu Ser Arg Lys Leu Ser Val Pro Ala Phe
35 40 45
Ala Ser Ser Leu Thr Ser Cys Gly Pro Arg Ala Leu Leu Thr Leu Arg
50 55 60
Pro Gly Val Ser Leu Thr Gly Thr Lys His Asn Pro Phe Ile Cys Thr
65 70 75 80
Ala Ser Phe His Thr Ser Ala Pro Leu Ala Lys Glu Asp Tyr Tyr Gln
85 90 95

```
Ile Leu Gly Val Pro Arg Asn Ala Ser Gln Lys Glu Ile Lys Lys Ala
            100                 105                 110
Tyr Tyr Gln Leu Ala Lys Lys Tyr His Pro Asp Thr Asn Lys Asp Asp
        115                 120                 125
Pro Lys Ala Lys Glu Lys Phe Ser Gln Leu Ala Glu Ala Tyr Glu Val
    130                 135                 140
Leu Ser Asp Glu Val Lys Arg Lys Gln Tyr Asp Ala Tyr Gly Ser Ala
145                 150                 155                 160
Gly Phe Asp Pro Gly Ala Ser Gly Ser Gln His Ser Tyr Trp Lys Gly
                165                 170                 175
Gly Pro Thr Val Asp Pro Glu Glu Leu Phe Arg Lys Ile Phe Gly Glu
            180                 185                 190
Phe Ser Ser Ser Ser Phe Gly Asp Phe Gln Thr Val Phe Asp Gln Pro
        195                 200                 205
Gln Glu Tyr Phe Met Glu Leu Thr Phe Asn Gln Ala Ala Lys Gly Val
    210                 215                 220
Asn Lys Glu Phe Thr Val Asn Ile Met Asp Thr Cys Glu Arg Cys Asn
225                 230                 235                 240
Gly Lys Gly Asn Glu Pro Gly Thr Lys Val Gln His Cys His Tyr Cys
                245                 250                 255
Gly Gly Ser Gly Met Glu Thr Ile Asn Thr Gly Pro Phe Val Met Arg
            260                 265                 270
Ser Thr Cys Arg Arg Cys Gly Gly Arg Gly Ser Ile Ile Ile Ser Pro
        275                 280                 285
Cys Val Val Cys Arg Gly Ala Gly Gln Ala Lys Gln Lys Lys Arg Val
    290                 295                 300
Met Ile Pro Val Pro Ala Gly Val Glu Asp Gly Gln Thr Val Arg Met
305                 310                 315                 320
Pro Val Gly Lys Arg Glu Ile Phe Ile Thr Phe Arg Val Gln Lys Ser
                325                 330                 335
Pro Val Phe Arg Arg Asp Gly Ala Asp Ile His Ser Asp Leu Phe Ile
            340                 345                 350
Ser Ile Ala Gln Ala Leu Leu Gly Gly Thr Ala Arg Ala Gln Gly Leu
        355                 360                 365
Tyr Glu Thr Ile Asn Val Thr Ile Pro Pro Gly Thr Gln Thr Asp Gln
    370                 375                 380
Lys Ile Arg Met Gly Gly Lys Gly Ile Pro Arg Ile Asn Ser Tyr Gly
385                 390                 395                 400
Tyr Gly Asp His Tyr Ile His Ile Lys Ile Arg Val Pro Lys Arg Leu
                405                 410                 415
Thr Ser Arg Gln Gln Ser Leu Ile Leu Ser Tyr Ala Glu Asp Glu Thr
            420                 425                 430
Asp Val Glu Gly Thr Val Asn Gly Val Thr Leu Thr Ser Ser Gly Gly
        435                 440                 445
Ser Thr Met Asp Ser Ser Ala Gly Ser Lys Ala Arg Arg Glu Ala Gly
    450                 455                 460
Glu Asp Glu Glu Gly Phe Leu Ser Lys Leu Lys Lys Met Phe Thr Ser
465                 470                 475                 480
```

<210> 107
<211> 572
<212> PRT
<213> Homo sapiens

<400> 107

```
Met Ala Ala Pro Arg Pro Ser Pro Ala Ile Ser Val Ser Val Ser Ala
 1               5                  10                  15
Pro Ala Phe Tyr Ala Pro Gln Lys Lys Phe Gly Pro Val Val Ala Pro
            20                  25                  30
Lys Pro Lys Val Asn Pro Phe Arg Pro Gly Asp Ser Glu Pro Pro Pro
        35                  40                  45
Ala Pro Gly Ala Gln Arg Ala Gln Met Gly Arg Val Gly Glu Ile Pro
    50                  55                  60
Pro Pro Pro Pro Glu Asp Phe Pro Leu Pro Pro Pro Pro Leu Ala Gly
65                  70                  75                  80
Asp Gly Asp Asp Ala Glu Gly Ala Leu Gly Gly Ala Phe Pro Pro Pro
                85                  90                  95
Pro Pro Pro Ile Glu Glu Ser Phe Pro Pro Ala Pro Leu Glu Glu Glu
            100                 105                 110
Ile Phe Pro Ser Pro Pro Pro Pro Pro Glu Glu Glu Gly Gly Pro Glu
        115                 120                 125
Ala Pro Ile Pro Pro Pro Pro Gln Pro Arg Glu Lys Val Ser Ser Ile
    130                 135                 140
Asp Leu Glu Ile Asp Ser Leu Ser Ser Leu Leu Asp Asp Met Thr Lys
145                 150                 155                 160
Asn Asp Pro Phe Lys Ala Arg Val Ser Ser Gly Tyr Val Pro Pro Pro
                165                 170                 175
Val Ala Thr Pro Phe Ser Ser Lys Ser Ser Thr Lys Pro Ala Ala Gly
            180                 185                 190
Gly Thr Ala Pro Leu Pro Pro Trp Lys Ser Pro Ser Ser Ser Gln Pro
        195                 200                 205
Leu Pro Gln Val Pro Ala Pro Ala Gln Ser Gln Thr Gln Phe His Val
    210                 215                 220
Gln Pro Gln Pro Gln Pro Lys Pro Gln Val Gln Leu His Val Gln Ser
225                 230                 235                 240
Gln Thr Gln Pro Val Ser Leu Ala Asn Thr Gln Pro Arg Gly Pro Pro
                245                 250                 255
Ala Ser Ser Pro Ala Pro Ala Pro Lys Phe Ser Pro Val Thr Pro Lys
            260                 265                 270
Phe Thr Pro Val Ala Ser Lys Phe Ser Pro Gly Ala Pro Gly Gly Ser
        275                 280                 285
Gly Ser Gln Pro Asn Gln Lys Leu Gly His Pro Glu Ala Leu Ser Ala
    290                 295                 300
Gly Thr Gly Ser Pro Gln Pro Pro Ser Phe Thr Tyr Ala Gln Gln Arg
305                 310                 315                 320
Glu Lys Pro Arg Val Gln Glu Lys Gln His Pro Val Pro Pro Pro Ala
                325                 330                 335
Gln Asn Gln Asn Gln Val Arg Ser Pro Gly Ala Pro Gly Pro Leu Thr
            340                 345                 350
Leu Lys Glu Val Glu Glu Leu Glu Gln Leu Thr Gln Gln Leu Met Gln
        355                 360                 365
Asp Met Glu His Pro Gln Arg Gln Asn Val Ala Val Asn Glu Leu Cys
    370                 375                 380
Gly Arg Cys His Gln Pro Leu Ala Arg Ala Gln Pro Ala Val Arg Ala
385                 390                 395                 400
Leu Gly Gln Leu Phe His Ile Ala Cys Phe Thr Cys His Gln Cys Ala
                405                 410                 415
```

```
Gln Gln Leu Gln Gly Gln Gln Phe Tyr Ser Leu Glu Gly Ala Pro Tyr
            420                 425                 430
Cys Glu Gly Cys Tyr Thr Asp Thr Leu Glu Lys Cys Asn Thr Cys Gly
        435                 440                 445
Glu Pro Ile Thr Asp Arg Met Leu Arg Ala Thr Gly Lys Ala Tyr His
    450                 455                 460
Pro His Cys Phe Thr Cys Val Val Cys Ala Arg Pro Leu Glu Gly Thr
465                 470                 475                 480
Ser Phe Ile Val Asp Gln Ala Asn Arg Pro His Cys Val Pro Asp Tyr
                485                 490                 495
His Lys Gln Tyr Ala Pro Arg Cys Ser Val Cys Ser Glu Pro Ile Met
            500                 505                 510
Pro Glu Pro Gly Arg Asp Glu Thr Val Arg Val Val Ala Leu Asp Lys
        515                 520                 525
Asn Phe His Met Lys Cys Tyr Lys Cys Glu Asp Cys Gly Lys Pro Leu
    530                 535                 540
Ser Ile Glu Ala Asp Asp Asn Gly Cys Phe Pro Leu Asp Gly His Val
545                 550                 555                 560
Leu Cys Arg Lys Cys His Thr Ala Arg Ala Gln Thr
                565                 570
```

<210> 108
<211> 2861
<212> PRT
<213> Homo sapiens

<400> 108

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

Ile Lys Ala Pro Ile Glu Asp Leu Asp Leu Glu Gly Gln Lys Leu Leu
210 215 220
Gln Arg Ile Gln Ser Ser Glu Ser Phe Pro Lys Lys Asn Ser Gly Ser
225 230 235 240
Gly Asn Ala Asp Leu Gln Asn Leu Leu Pro Lys Val Ser Thr Met Leu
245 250 255
Asp Arg Leu His Ser Thr Arg Gln His Leu His Gln Met Trp His Val
260 265 270
Arg Lys Leu Lys Leu Asp Gln Cys Phe Gln Leu Arg Leu Phe Glu Gln
275 280 285
Asp Ala Glu Lys Met Phe Asp Trp Ile Thr His Asn Lys Gly Leu Phe
290 295 300
Leu Asn Ser Tyr Thr Glu Ile Gly Thr Ser His Pro His Ala Met Glu
305 310 315 320
Leu Gln Thr Gln His Asn His Phe Ala Met Asn Cys Met Asn Val Tyr
325 330 335
Val Asn Ile Asn Arg Ile Met Ser Val Ala Asn Arg Leu Val Glu Ser
340 345 350
Gly His Tyr Ala Ser Gln Gln Ile Arg Gln Ile Ala Ser Gln Leu Glu
355 360 365
Gln Glu Trp Lys Ala Phe Ala Ala Ala Leu Asp Glu Arg Ser Thr Leu
370 375 380
Leu Asp Met Ser Ser Ile Phe His Gln Lys Ala Glu Lys Tyr Met Ser
385 390 395 400
Asn Val Asp Ser Trp Cys Lys Ala Cys Gly Glu Val Asp Leu Pro Ser
405 410 415
Glu Leu Gln Asp Leu Glu Asp Ala Ile His His His Gln Gly Ile Tyr
420 425 430
Glu His Ile Thr Leu Ala Tyr Ser Glu Val Ser Gln Asp Gly Lys Ser
435 440 445
Leu Leu Asp Lys Leu Gln Arg Pro Leu Thr Pro Gly Ser Ser Asp Ser
450 455 460
Leu Thr Ala Ser Ala Asn Tyr Ser Lys Ala Val His His Val Leu Asp
465 470 475 480
Val Ile His Glu Val Leu His His Gln Arg His Val Arg Thr Ile Trp
485 490 495
Gln His Arg Lys Val Arg Leu His Gln Arg Leu Gln Leu Cys Val Phe
500 505 510
Gln Gln Glu Val Gln Gln Val Leu Asp Trp Ile Glu Asn His Gly Glu
515 520 525
Ala Phe Leu Ser Lys His Thr Gly Val Gly Lys Ser Leu His Arg Ala
530 535 540
Arg Ala Leu Gln Lys Arg His Glu Asp Phe Glu Glu Val Ala Gln Asn
545 550 555 560
Thr Tyr Thr Asn Ala Asp Lys Leu Leu Glu Ala Ala Glu Gln Leu Ala
565 570 575
Gln Thr Gly Glu Cys Asp Pro Glu Glu Ile Tyr Gln Ala Ala His Gln
580 585 590
Leu Glu Asp Arg Ile Gln Asp Phe Val Arg Arg Val Glu Gln Arg Lys
595 600 605
Ile Leu Leu Asp Met Ser Val Ser Phe His Thr His Val Lys Glu Leu
610 615 620
Trp Thr Trp Leu Glu Glu Leu Gln Lys Glu Leu Leu Asp Asp Val Tyr

625 630 635 640
Ala Glu Ser Val Glu Ala Val Gln Asp Leu Ile Lys Arg Phe Gly Gln
645 650 655
Gln Gln Gln Thr Thr Leu Gln Val Thr Val Asn Val Ile Lys Glu Gly
660 665 670
Glu Asp Leu Ile Gln Gln Leu Arg Asp Ser Ala Ile Ser Ser Asn Lys
675 680 685
Thr Pro His Asn Ser Ser Ile Asn His Ile Glu Thr Val Leu Gln Gln
690 695 700
Leu Asp Glu Ala Gln Ser Gln Met Glu Glu Leu Phe Gln Glu Arg Lys
705 710 715 720
Ile Lys Leu Glu Leu Phe Leu His Val Arg Ile Phe Glu Arg Asp Ala
725 730 735
Ile Asp Ile Ile Ser Asp Leu Glu Ser Trp Asn Asp Glu Leu Ser Gln
740 745 750
Gln Met Asn Asp Phe Asp Thr Glu Asp Leu Thr Ile Ala Glu Gln Arg
755 760 765
Leu Gln His His Ala Asp Lys Ala Leu Thr Met Asn Asn Leu Thr Phe
770 775 780
Asp Val Ile His Gln Gly Gln Asp Leu Leu Gln Tyr Val Asn Glu Val
785 790 795 800
Gln Ala Ser Gly Val Glu Leu Leu Cys Asp Arg Asp Val Asp Met Ala
805 810 815
Thr Arg Val Gln Asp Leu Leu Glu Phe Leu His Glu Lys Gln Gln Glu
820 825 830
Leu Asp Leu Ala Ala Glu Gln His Arg Lys His Leu Glu Gln Cys Val
835 840 845
Gln Leu Arg His Leu Gln Ala Glu Val Lys Gln Val Leu Gly Trp Ile
850 855 860
Arg Asn Gly Glu Ser Met Leu Asn Ala Gly Leu Ile Thr Ala Ser Ser
865 870 875 880
Leu Gln Glu Ala Glu Gln Leu Gln Arg Glu His Glu Gln Phe Gln His
885 890 895
Ala Ile Glu Lys Thr His Gln Ser Ala Leu Gln Val Gln Gln Lys Ala
900 905 910
Glu Ala Met Leu Gln Ala Asn His Tyr Asp Met Asp Met Ile Arg Asp
915 920 925
Cys Ala Glu Lys Val Ala Ser His Trp Gln Gln Leu Met Leu Lys Met
930 935 940
Glu Asp Arg Leu Lys Leu Val Asn Ala Ser Val Ala Phe Tyr Lys Thr
945 950 955 960
Ser Glu Gln Val Cys Ser Val Leu Glu Ser Leu Glu Gln Glu Tyr Lys
965 970 975
Arg Glu Glu Asp Trp Cys Gly Gly Ala Asp Lys Leu Gly Pro Asn Ser
980 985 990
Glu Thr Asp His Val Thr Pro Met Ile Ser Lys His Leu Glu Gln Lys
995 1000 1005
Glu Ala Phe Leu Lys Ala Cys Thr Leu Ala Arg Arg Asn Ala Asp Val
1010 1015 1020
Phe Leu Lys Tyr Leu His Arg Asn Ser Val Asn Met Pro Gly Met Val
1025 1030 1035 1040
Thr His Ile Lys Ala Pro Glu Gln Gln Val Lys Asn Ile Leu Asn Glu
1045 1050 1055

Leu Phe Gln Arg Glu Asn Arg Val Leu His Tyr Trp Thr Met Arg Lys
1060 1065 1070
Arg Arg Leu Asp Gln Cys Gln Gln Tyr Val Val Phe Glu Arg Ser Ala
1075 1080 1085
Lys Gln Ala Leu Glu Trp Ile His Asp Asn Gly Glu Phe Tyr Leu Ser
1090 1095 1100
Thr His Thr Ser Thr Gly Ser Ser Ile Gln His Thr Gln Glu Leu Leu
1105 1110 1115 1120
Lys Glu His Glu Glu Phe Gln Ile Thr Ala Lys Gln Thr Lys Glu Arg
1125 1130 1135
Val Lys Leu Leu Ile Gln Leu Ala Asp Gly Phe Cys Glu Lys Gly His
1140 1145 1150
Ala His Ala Ala Glu Ile Lys Lys Cys Val Thr Ala Val Asp Lys Arg
1155 1160 1165
Tyr Arg Asp Phe Ser Leu Arg Met Glu Lys Tyr Arg Thr Ser Leu Glu
1170 1175 1180
Lys Ala Leu Gly Ile Ser Ser Asp Ser Asn Lys Ser Ser Lys Ser Leu
1185 1190 1195 1200
Gln Leu Asp Ile Ile Pro Ala Ser Ile Pro Gly Ser Glu Val Lys Leu
1205 1210 1215
Arg Asp Ala Ala His Glu Leu Asn Glu Glu Lys Arg Lys Ser Ala Arg
1220 1225 1230
Arg Lys Glu Phe Ile Met Ala Glu Leu Ile Gln Thr Glu Lys Ala Tyr
1235 1240 1245
Val Arg Asp Leu Arg Glu Cys Met Asp Thr Tyr Leu Trp Glu Met Thr
1250 1255 1260
Ser Gly Val Glu Glu Ile Pro Pro Gly Ile Val Asn Lys Glu Leu Ile
1265 1270 1275 1280
Ile Phe Gly Asn Met Gln Glu Ile Tyr Glu Phe His Asn Asn Ile Phe
1285 1290 1295
Leu Lys Glu Leu Glu Lys Tyr Glu Gln Leu Pro Glu Asp Val Gly His
1300 1305 1310
Cys Phe Val Thr Trp Ala Asp Lys Phe Gln Met Tyr Val Thr Tyr Cys
1315 1320 1325
Lys Asn Lys Pro Asp Ser Thr Gln Leu Ile Leu Glu His Ala Gly Ser
1330 1335 1340
Tyr Phe Asp Glu Ile Gln Gln Arg His Gly Leu Ala Asn Ser Ile Ser
1345 1350 1355 1360
Ser Tyr Leu Ile Lys Pro Val Gln Arg Ile Thr Lys Tyr Gln Leu Leu
1365 1370 1375
Leu Lys Glu Leu Leu Thr Cys Cys Glu Glu Gly Lys Gly Glu Ile Lys
1380 1385 1390
Asp Gly Leu Glu Val Met Leu Ser Val Pro Lys Arg Ala Asn Asp Ala
1395 1400 1405
Met His Leu Ser Met Leu Glu Gly Phe Asp Glu Asn Ile Glu Ser Gln
1410 1415 1420
Gly Glu Leu Ile Leu Gln Glu Ser Phe Gln Val Trp Asp Pro Lys Thr
1425 1430 1435 1440
Leu Ile Arg Lys Gly Arg Glu Arg His Leu Phe Leu Phe Glu Met Ser
1445 1450 1455
Leu Val Phe Ser Lys Glu Val Lys Asp Ser Ser Gly Arg Ser Lys Tyr
1460 1465 1470
Leu Tyr Lys Ser Lys Leu Phe Thr Ser Glu Leu Gly Val Thr Glu His

1475 1480 1485
Val Glu Gly Asp Pro Cys Lys Phe Ala Leu Trp Val Gly Arg Thr Pro
1490 1495 1500
Thr Ser Asp Asn Lys Ile Val Leu Lys Ala Ser Ser Ile Glu Asn Lys
1505 1510 1515 1520
Gln Asp Trp Ile Lys His Ile Arg Glu Val Ile Gln Glu Arg Thr Ile
1525 1530 1535
His Leu Lys Gly Ala Leu Lys Glu Pro Ile His Ile Pro Lys Thr Ala
1540 1545 1550
Pro Ala Thr Arg Gln Lys Gly Arg Arg Asp Gly Glu Asp Leu Asp Ser
1555 1560 1565
Gln Gly Asp Gly Ser Ser Gln Pro Asp Thr Ile Ser Ile Ala Ser Arg
1570 1575 1580
Thr Ser Gln Asn Thr Leu Asp Ser Asp Lys Leu Ser Gly Gly Cys Glu
1585 1590 1595 1600
Leu Thr Val Val Ile His Asp Phe Thr Ala Cys Asn Ser Asn Glu Leu
1605 1610 1615
Thr Ile Arg Arg Gly Gln Thr Val Glu Val Leu Glu Arg Pro His Asp
1620 1625 1630
Lys Pro Asp Trp Cys Leu Val Arg Thr Thr Asp Arg Ser Pro Ala Ala
1635 1640 1645
Glu Gly Leu Val Pro Cys Gly Ser Leu Cys Ile Ala His Ser Arg Ser
1650 1655 1660
Ser Met Glu Met Glu Gly Ile Phe Asn His Lys Asp Ser Leu Ser Val
1665 1670 1675 1680
Ser Ser Asn Asp Ala Ser Pro Pro Ala Ser Val Ala Ser Leu Gln Pro
1685 1690 1695
His Met Ile Gly Ala Gln Ser Ser Pro Gly Pro Lys Arg Pro Gly Asn
1700 1705 1710
Thr Leu Arg Lys Trp Leu Thr Ser Pro Val Arg Arg Leu Ser Ser Gly
1715 1720 1725
Lys Ala Asp Gly His Val Lys Lys Leu Ala His Lys His Lys Lys Ser
1730 1735 1740
Arg Glu Val Arg Lys Ser Ala Asp Ala Gly Ser Gln Lys Asp Ser Asp
1745 1750 1755 1760
Asp Ser Ala Ala Thr Pro Gln Asp Glu Thr Val Glu Glu Arg Gly Arg
1765 1770 1775
Asn Glu Gly Leu Ser Ser Gly Thr Leu Ser Lys Ser Ser Ser Ser Gly
1780 1785 1790
Met Gln Ser Cys Gly Glu Glu Glu Gly Glu Glu Gly Ala Asp Ala Val
1795 1800 1805
Pro Leu Pro Pro Pro Met Ala Ile Gln Gln His Ser Leu Leu Gln Pro
1810 1815 1820
Asp Ser Gln Asp Asp Lys Ala Ser Ser Arg Leu Leu Val Arg Pro Thr
1825 1830 1835 1840
Ser Ser Glu Thr Pro Ser Ala Ala Glu Leu Val Ser Ala Ile Glu Glu
1845 1850 1855
Leu Val Lys Ser Lys Met Ala Leu Glu Asp Arg Pro Ser Ser Leu Leu
1860 1865 1870
Val Asp Gln Gly Asp Ser Ser Ser Pro Ser Phe Asn Pro Ser Asp Asn
1875 1880 1885
Ser Leu Leu Ser Ser Ser Ser Pro Ile Asp Glu Met Glu Glu Arg Lys
1890 1895 1900

Ser Ser Ser Leu Lys Arg Arg His Tyr Val Leu Gln Glu Leu Val Glu
1905 1910 1915 1920
Thr Glu Arg Asp Tyr Val Arg Asp Leu Gly Tyr Val Val Glu Gly Tyr
1925 1930 1935
Met Ala Leu Met Lys Glu Asp Gly Val Pro Asp Asp Met Lys Gly Lys
1940 1945 1950
Asp Lys Ile Val Phe Gly Asn Ile His Gln Ile Tyr Asp Trp His Arg
1955 1960 1965
Asp Phe Phe Leu Gly Glu Leu Glu Lys Cys Leu Glu Asp Pro Glu Lys
1970 1975 1980
Leu Gly Ser Leu Phe Val Lys His Glu Arg Arg Leu His Met Tyr Ile
1985 1990 1995 2000
Ala Tyr Cys Gln Asn Lys Pro Lys Ser Glu His Ile Val Ser Glu Tyr
2005 2010 2015
Ile Asp Thr Phe Phe Glu Asp Leu Lys Gln Arg Leu Gly His Arg Leu
2020 2025 2030
Gln Leu Thr Asp Leu Leu Ile Lys Pro Val Gln Arg Ile Met Lys Tyr
2035 2040 2045
Gln Leu Leu Leu Lys Asp Phe Leu Lys Tyr Ser Lys Lys Ala Ser Leu
2050 2055 2060
Asp Thr Ser Glu Leu Glu Arg Ala Val Glu Val Met Cys Ile Val Pro
2065 2070 2075 2080
Arg Arg Cys Asn Asp Met Met Asn Val Gly Arg Leu Gln Gly Phe Asp
2085 2090 2095
Gly Lys Ile Val Ala Gln Gly Lys Leu Leu Leu Gln Asp Thr Phe Leu
2100 2105 2110
Val Thr Asp Gln Asp Ala Gly Leu Leu Pro Arg Cys Arg Glu Arg Arg
2115 2120 2125
Ile Phe Leu Phe Glu Gln Ile Val Ile Phe Ser Glu Pro Leu Asp Lys
2130 2135 2140
Lys Lys Gly Phe Ser Met Pro Gly Phe Leu Phe Lys Asn Ser Ile Lys
2145 2150 2155 2160
Val Ser Cys Leu Cys Leu Glu Glu Asn Val Glu Asn Asp Pro Cys Lys
2165 2170 2175
Phe Ala Leu Thr Ser Arg Thr Gly Asp Val Val Glu Thr Phe Ile Leu
2180 2185 2190
His Ser Ser Ser Pro Ser Val Arg Gln Thr Trp Ile His Glu Ile Asn
2195 2200 2205
Gln Ile Leu Glu Asn Gln Arg Asn Phe Leu Asn Ala Leu Thr Ser Pro
2210 2215 2220
Ile Glu Tyr Gln Arg Asn His Ser Gly Gly Gly Gly Gly Gly Gly Ser
2225 2230 2235 2240
Gly Ala Ala Ala Gly Val Gly Ala Ala Ala Ala Ala Gly Pro Pro Val
2245 2250 2255
Ala Ala Ala Ala Thr Val Ala Ala Pro Ala Ala Ala Ala Ala Pro Pro
2260 2265 2270
Ala Arg Ala Gly Ala Gly Pro Pro Gly Ser Pro Ser Leu Ser Asp Thr
2275 2280 2285
Thr Pro Pro Cys Trp Ser Pro Leu Gln Pro Arg Ala Arg Gln Arg Gln
2290 2295 2300
Thr Arg Cys Gln Ser Glu Ser Ser Ser Ser Ser Asn Ile Ser Thr Met
2305 2310 2315 2320
Leu Val Thr His Asp Tyr Thr Ala Val Lys Glu Asp Glu Ile Asn Val

2325 2330 2335
Tyr Gln Gly Glu Val Val Gln Ile Leu Ala Ser Asn Gln Gln Asn Met
2340 2345 2350
Phe Leu Val Phe Arg Ala Ala Thr Asp Gln Cys Pro Ala Ala Glu Gly
2355 2360 2365
Trp Ile Pro Gly Phe Val Leu Gly His Thr Ser Ala Val Ile Val Glu
2370 2375 2380
Asn Pro Asp Gly Thr Leu Lys Lys Ser Thr Ser Trp His Thr Ala Leu
2385 2390 2395 2400
Arg Leu Arg Lys Lys Ser Glu Lys Lys Asp Lys Asp Gly Lys Arg Glu
2405 2410 2415
Gly Lys Leu Glu Asn Gly Tyr Arg Lys Ser Arg Glu Gly Leu Ser Asn
2420 2425 2430
Lys Val Ser Val Lys Leu Leu Asn Pro Asn Tyr Ile Tyr Asp Val Pro
2435 2440 2445
Pro Glu Phe Val Ile Pro Leu Ser Glu Val Thr Cys Glu Thr Gly Glu
2450 2455 2460
Thr Val Val Leu Arg Cys Arg Val Cys Gly Arg Pro Lys Ala Ser Ile
2465 2470 2475 2480
Thr Trp Lys Gly Pro Glu His Asn Thr Leu Asn Asn Asp Gly His Tyr
2485 2490 2495
Ser Ile Ser Tyr Ser Asp Leu Gly Glu Ala Thr Leu Lys Ile Val Gly
2500 2505 2510
Val Thr Thr Glu Asp Asp Gly Ile Tyr Thr Cys Ile Ala Val Asn Asp
2515 2520 2525
Met Gly Ser Ala Ser Ser Ser Ala Ser Leu Arg Val Leu Gly Pro Gly
2530 2535 2540
Met Asp Gly Ile Met Val Thr Trp Lys Asp Asn Phe Asp Ser Phe Tyr
2545 2550 2555 2560
Ser Glu Val Ala Glu Leu Gly Arg Gly Arg Phe Ser Val Val Lys Lys
2565 2570 2575
Cys Asp Gln Lys Gly Thr Lys Arg Ala Val Ala Thr Lys Phe Val Asn
2580 2585 2590
Lys Lys Leu Met Lys Arg Asp Gln Val Thr His Glu Leu Gly Ile Leu
2595 2600 2605
Gln Ser Leu Gln His Pro Leu Leu Val Gly Leu Leu Asp Thr Phe Glu
2610 2615 2620
Thr Pro Thr Ser Tyr Ile Leu Val Leu Glu Met Ala Asp Gln Gly Arg
2625 2630 2635 2640
Leu Leu Asp Cys Val Val Arg Trp Gly Ser Leu Thr Glu Gly Lys Ile
2645 2650 2655
Arg Ala His Leu Gly Glu Val Leu Glu Ala Val Arg Tyr Leu His Asn
2660 2665 2670
Cys Arg Ile Ala His Leu Asp Leu Lys Pro Glu Asn Ile Leu Val Asp
2675 2680 2685
Glu Ser Leu Ala Lys Pro Thr Ile Lys Leu Ala Asp Phe Gly Asp Ala
2690 2695 2700
Val Gln Leu Asn Thr Thr Tyr Tyr Ile His Gln Leu Leu Gly Asn Pro
2705 2710 2715 2720
Glu Phe Ala Ala Pro Glu Ile Ile Leu Gly Asn Pro Val Ser Leu Thr
2725 2730 2735
Ser Asp Thr Trp Ser Val Gly Val Leu Thr Tyr Val Leu Leu Ser Gly
2740 2745 2750

Val Ser Pro Phe Leu Asp Asp Ser Val Glu Glu Thr Cys Leu Asn Ile
2755 2760 2765
Cys Arg Leu Asp Phe Ser Phe Pro Asp Asp Tyr Phe Lys Gly Val Ser
2770 2775 2780
Gln Lys Ala Lys Glu Phe Val Cys Phe Leu Leu Gln Glu Asp Pro Ala
2785 2790 2795 2800
Lys Arg Pro Ser Ala Ala Leu Ala Leu Gln Glu Gln Trp Leu Gln Ala
2805 2810 2815
Gly Asn Gly Arg Ser Thr Gly Val Leu Asp Thr Ser Arg Leu Thr Ser
2820 2825 2830
Phe Ile Glu Arg Arg Lys His Gln Asn Asp Val Arg Pro Ile Arg Ser
2835 2840 2845
Ile Lys Asn Phe Leu Gln Ser Arg Leu Leu Pro Arg Val
2850 2855 2860

<210> 109
<211> 271
<212> PRT
<213> Homo sapiens

<400> 109
Met Val Leu Ile Lys Glu Phe Arg Val Val Leu Pro Cys Ser Val Gln
1 5 10 15
Glu Tyr Gln Val Gly Gln Leu Tyr Ser Val Ala Glu Ala Ser Lys Asn
20 25 30
Glu Thr Gly Gly Gly Glu Gly Ile Glu Val Leu Lys Asn Glu Pro Tyr
35 40 45
Glu Lys Asp Gly Glu Lys Gly Gln Tyr Thr His Lys Ile Tyr His Leu
50 55 60
Lys Ser Lys Val Pro Ala Phe Val Arg Met Ile Ala Pro Glu Gly Ser
65 70 75 80
Leu Val Phe His Glu Lys Ala Trp Asn Ala Tyr Pro Tyr Cys Arg Thr
85 90 95
Ile Val Thr Asn Glu Tyr Met Lys Asp Asp Phe Phe Ile Lys Ile Glu
100 105 110
Thr Trp His Lys Pro Asp Leu Gly Thr Leu Glu Asn Val His Gly Leu
115 120 125
Asp Pro Asn Thr Trp Lys Thr Val Glu Ile Val His Ile Asp Ile Ala
130 135 140
Asp Arg Ser Gln Val Glu Pro Ala Asp Tyr Lys Ala Asp Glu Asp Pro
145 150 155 160
Ala Leu Phe Gln Ser Val Lys Thr Lys Arg Gly Pro Leu Gly Pro Asn
165 170 175
Trp Lys Lys Glu Leu Ala Asn Ser Pro Asp Cys Pro Gln Met Cys Ala
180 185 190
Tyr Lys Leu Val Thr Ile Lys Phe Lys Trp Trp Gly Leu Gln Ser Lys
195 200 205
Val Glu Asn Phe Ile Gln Lys Gln Glu Lys Arg Ile Phe Thr Asn Phe
210 215 220
His Arg Gln Leu Phe Cys Trp Ile Asp Lys Trp Ile Asp Leu Thr Met
225 230 235 240
Glu Asp Ile Arg Arg Met Glu Asp Glu Thr Gln Lys Glu Leu Glu Thr
245 250 255

Met Arg Lys Arg Gly Ser Val Arg Gly Thr Ser Ala Ala Asp Val
260 265 270